Synthetic studies on fused $[\pi]$-arene complexes and on tetralindione: development of a new asymmetric acylation catalyst

ENRÍQUEZ GARCÍA, Álvaro

Abstract

Les complexes à chiralité planaire $[\text{Cr}([\eta]6-\text{arène})(\text{CO})3]$ montrent une chimie riche et unique, et trouvent de plus en plus d'applications dans les domaines de la catalyse et de la synthèse de produits naturels. Dans le cadre de cette thèse, une nouvelle synthèse concise et fiable du complexe $[\text{Cr}([\eta]6-5,8-\text{naphthoquinone})(\text{CO})3]$ (1) a été développée. Sa réactivité a été investiguée avec une attention particulière aux réactions asymétriques. Ces études incluent notamment le développement de nouveaux catalyseurs d'acylation asymétriques, des désymétrisations de meso-diols et de complexes dérivés de 1. L' observation du complexe tetralindione a mené à des recherches sur le couple de tautomères dihydroxynaphtalène/tetralindione, ainsi qu'à l' exploration des transformations dudit dione simple. La tetralindione est connue dans la littérature mais n'a jamais été utilisée en synthèse.

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Synthetic Studies on

Fused $\pi$-Arene Complexes and on Tetralindione.

Development of a New Asymmetric Acylation Catalyst

THÈSE

Présentée à la Faculté des sciences de l’Université de Genève
Pour obtenir le grade de Docteur ès sciences, mention chimique

Par

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de Madrid (Espagne)

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La Faculté des sciences, sur le préavis de Messieurs E. P. KUNDIG, professeur ordinaire et directeur de thèse (Département de chimie organique), A. ALEXAKIS, professeur ordinaire (Département de chimie organique), T. IMAMOTO, professeur (Chiba University, Graduate School of Science, Department of chemistry, Chiba, Japan) et A. C. SPIVEY, docteur (Imperial College, Department of chemistry, London, United Kingdom), autorise l'impression de la présente thèse, sans exprimer d'opinion sur les propositions qui y sont énoncées.

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Álvaro Enríquez García
Abbreviations

Ac acetyl
anh. anhydrous
Ar aryl
BINOL 1,1'-Bi-2-naphthol
Boc tert-butoxycarbonyl
bp boiling point
BuLi butyl lithium
BzCl benzoyl chloride
cal calorie
calcld. calculated
CBS Corey, Bashki, Shibata
d doublet
DME 1,2-dimethoxyethane
DMSO dimethylsulfoxide
ee enantiomeric excess
eq equivalent
de diastereomeric excess
DDQ 2,3-dichloro-5,6-dicyanobenzoquinone
DMAP \(N,N'\)-4-dimethylaminopyridine
et al. and others
g gram
h hours
Hz Hertz
IR infra red
HPLC high pressure liquid chromatography
HRMS high resolution mass spectroscopy
LDA lithium diisopropylamide
m multiplet
MeLi methyl lithium
MeO methoxy
mg milligram
min minutes
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<tr>
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<td>N-chlorosuccinimide</td>
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<tr>
<td>MP</td>
<td>melting point</td>
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<tr>
<td>Ms</td>
<td>mesyl</td>
</tr>
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<td>mass spectroscopy</td>
</tr>
<tr>
<td>MS 4Å</td>
<td>molecular sieves 4 angstroms</td>
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<tr>
<td>oop</td>
<td>flexion out of plane</td>
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<td>ORTEP</td>
<td>Oak Ridge thermal ellipsoid plot</td>
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<tr>
<td>Ph</td>
<td>phenyl</td>
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<td>ppm</td>
<td>parts per million</td>
</tr>
<tr>
<td>q</td>
<td>quartet</td>
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<tr>
<td>Red-Al</td>
<td>bis(2-methoxyethoxy)aluminium hydride</td>
</tr>
<tr>
<td>RMN</td>
<td>nuclear magnetic resonance</td>
</tr>
<tr>
<td>rac</td>
<td>racemic</td>
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<td>r.t.</td>
<td>room temperature</td>
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<td>saturated</td>
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<td>t</td>
<td>triplet</td>
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<tr>
<td>T</td>
<td>temperature</td>
</tr>
<tr>
<td>TBAF</td>
<td>tetrabutylammonium fluoride</td>
</tr>
<tr>
<td>TBS</td>
<td>tert-butyldimethylsilyl</td>
</tr>
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<td>THF</td>
<td>tetrahydrofurane</td>
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<td>thin layer chromatography</td>
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<td>TMS</td>
<td>trimethylsilyl</td>
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<tr>
<td>TMSCN</td>
<td>trimethylsilyl cyanide</td>
</tr>
<tr>
<td>λ</td>
<td>wavelength</td>
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<tr>
<td>ν</td>
<td>tension frequency</td>
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1.- Introduction.

Les modifications de réactivité qui surviennent lors de la complexation d'un arène au fragment chrome tricarbonyl donne accès à une variété de transformations inaccessibles par ailleurs. Cette polyvalence a été largement reconnue et, par conséquent, ces complexes ont été utilisés comme synthons dans la synthèse de plusieurs produits naturels ou comme ligands en catalyse asymétrique. [1] Le fragment Cr(CO)$_3$ donne une réactivité sans précédent à l'arène complexé et la chimie de ces complexes est riche et vaste (Figure 1). L’arène η$^6$-coordiné au cycle est sujet à un certain nombre de transformations synthétiques dûs à l’effet électro-attracteur du fragment Cr(CO)$_3$. Le pK$_a$ des acides benzyliques, des anilines et des phénols sont également connus pour être abaissé de plusieurs unités grâce à la complexation. [2, 3]

![Figure 1](image)

Les carbocations benzyliques des arènes complexés au Cr(CO)$_3$ sont stabilisés par la délocalisation de la charge positive sur le chrome. [4] Par conséquent, les groupes partants benzyliques qui peuvent adopter une conformation antiperiplanaire par rapport à l’arène conduisent ainsi à des réactions de type S$_{N}1$ avec rétention de la configuration. Le cation Cr(CO)$_3$ benzylique est de 5 unités de pK$_a$ plus stable que le cation libre benzylique. [5, 6] On attribue ces grandes différences de pK$_a$ à l’effet électro-attracteur du fragment Cr(CO)$_3$. D’autre part, le groupement Cr(CO)$_3$ a été largement utilisé comme groupe stéréodirecteur lors de réactions réalisées sur des chaînes latérales liées à l’arène. [7, 8] De plus, l’arène Cr(CO)$_3$ est susceptible d’être attaqué par des nucléophiles. Cette réaction est de grande importance. L’effet électro-attracteur du fragment Cr(CO)$_3$ permet l’attaque directe de nucléophiles (générés à partir des C - H acides de pKa> 22) sur le cycle en exo par rapport au...
fragment Cr(CO)₃.¹⁰ La gamme de réactifs pouvant être utilisés est limitée par la faible électrophilicité impartie par le métal (LiCH₂CO₂R, LiCH₂CN, KCH₂COC(CH₃)₃, LiCH₂SPh, LiCH=CH₂, PhLi, LiC=CR, LiCH₂C=CH₂). Les additions nucléophiles sur (Cr(η⁶-arène)(CO)₃) sont souvent très régiospécifiques et les η⁵-complexes anioniques générés offrent un large éventail de possibilités de synthèse. Ces faits, ainsi que les conditions douces de réaction sont les principaux avantages de cette méthode.

Les complexes à chiralité planaire [Cr(η⁶-arène)(CO)₃] montrent une chimie riche et unique, et trouvent de plus en plus d’applications dans les domaines de la catalyse et de la synthèse de produits naturels. Dans le cadre des études menées sur les complexes de naphtalène dans notre laboratoire, une voie de synthèse pour l’obtention de [Cr(CO)₃(η⁶-5,8-naphtoquinone)] (57) a été mise au point (Schéma 1). Dès lors nous avons étudié le potentiel de réaction offert par ce substrat. La première tâche a consisté à trouver une synthèse concise et fiable permettant de donner accès à des quantités de l’ordre de grandeurs du gramme de ce complexe. Dès le début, nous avons réalisé le potentiel offert par le fragment Cr(CO)₃ pour la désymétrisation de 57 et de ses dérivés. Les chapitres suivants décrivent les résultats de nos études, un voyage riche en découvertes inattendues qui incluent le développement de nouveaux catalyseurs d’acylation et des études sur la stabilité d’un tautomère oublié depuis longtemps.

Schéma 1

2.- Synthèse de [Cr(CO)₃(η⁶-5,8-naphtoquinone)] (57).

Aucune synthèse efficace de [Cr(CO)₃(η⁶-5,8-naphtoquinone)] (57) n’a été signalée avant les travaux menés dans notre laboratoire. Ma contribution à ce projet a commencé avec une nouvelle idée d’approche pour l’obtention de [Cr(CO)₃(η⁶-5,8-naphtoquinone)] (57), en ayant en tête les limitations connues des précédentes synthèses.¹⁰,¹¹ La complexation du 1,4-dihydroxynaphtalène avec [Cr(NH₃)₃(CO)₃] a donné un mélange brut de couleur orange enrichi en complexe de l’hydroquinone Cr(CO)₃ 63. Le traitement de ce mélange avec Ag₂O a
provoqué un changement de couleur d'orange à pourpre, dû à la formation du complexe 57 souhaité. Nous avons été heureux de constater que, dans ces conditions, 2,5 g [Cr(CO)₃(η⁶-5,8-naphtoquinone)] cristallisé (57) ont été obtenu avec un excellent rendement de 76 % (Schéma 2).

![](image)

Schéma 2

3.- Influence du fragment de chrome sur le comportement tautomérique des énols complexés aromatiques.

Dans la littérature, est décrit en détails la réduction de quinones via un transfert d'électrons en présence de Na₂S₂O₄. Ceci est également applicable à notre système. En agitant vigoureusement le complexe 57 avec 1,2 équivalents de Na₂S₂O₄ en solution aqueuse on abouti à un changement de couleur allant du bleu foncé à l'orange. Le complexe [Cr(CO)₃(η⁶-5,8-dihydroxynaphtalène)] (63) a été obtenu avec un rendement quantitatif (Schéma 3). En chauffant une solution du complexe 63, un changement de couleur de l'orange au rouge a eu lieu; cette couleur étant caractéristique de la dicétone [Cr(CO)₃(η⁶-5,8-tetralindione)] (64). L'équilibre est déplacé entièrement du côté de la forme dicétonique. Dans les mêmes conditions, l’1,4-dihydroxynaphtalène est un énol stable, et aucun changement n’est observé. En effet, un chauffage à 120 °C dans C₆D₆ est nécessaire pour initier la transformation en 1,4-tetralindione (134) correspondante. Un suivi RMN montre qu’un équilibre 1 : 1 est atteint après plus de 20 jours à cette température. En revanche, le complexe du chrome 63 analogue atteint une conversion de 90 % à des températures inférieures (50 °C en seulement 20 heures). Par conséquent, le fragment de chrome a une forte influence sur le comportement tautomérique des ligands 61 et 134. Le taux de tautomérisation est accéléré avec l’addition de CF₃COOH permettant un accès au complexe 64 avec un bon rendement.
4.- Réduction diastéréospécifique de [Cr(CO)₃(η⁶-5,8-naphtoquinone)] (57) et de [Cr(CO)₃(η⁶-5,8-tetralindione)] (64).

Le complexe [Cr(CO)₃(η⁶-5,8-naphtoquinone)] (57) et le complexe [Cr(CO)₃(η⁶-5,8-tetralindione)] (64) sont des composés méso carbonylés qui offrent un large éventail de possibilité de désymétrisation. D'autre part, en l'absence d'une source chirale externe, la réduction d'une fonction carbonyle en position α à un fragment [Cr(arène)(CO)₃] devrait se faire en anti par rapport au fragment métallique. Par conséquent, la bis-réduction des complexes 57 ou 64 devrait aboutir aux complexes méso-diol correspondants. Complexes, qui pourraient eux-mêmes être intéressants en vue d'une future désymétrisation par acylation asymétrique ou par d'autres moyens (Schéma 4).

Schéma 3

Schéma 4
5.- Désymétrisation de \([\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindione})]\) (64) par réduction CBS.

La désymétrisation du complexe \([\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindione})]\) (64) par réduction énantiosélective CBS conduit, sous l’effet du catalyseur, le complexe \((-)-(5R,8R)-[\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindiol})]\) (68) avec une rendement de 80 % et 99 % ee. D’autre part, la monoréduction du complexe (64) a été réalisée en utilisant une procédure modifiée. Cette réduction produit \((-)-(8R)-[\text{Cr(CO)}_3(\eta^6-8\text{-hydroxy-5-tetralone})]\) (69) avec un rendement de 98 % et 97 % ee.

6.- Nouvelles diamines chirales dérivée d’alcaloïdes Cinchona.

Les amines chirales sont de plus en plus utilisées en tant que catalyseurs et en tant que ligands pour les réactions catalysées par les métaux de transition donnant aux chimistes de nouveaux outils efficaces pour la synthèse de molécules complexes.\(^{[17]}\) Nous avons porté notre attention sur le motif structural des alcaloïdes Cinchona (Schéma 6), une importante source de chiralité, qui a inspiré la conception de nombreux catalyseurs et de ligands pour les réactions catalysées par les métaux de transition.\(^{[17,18]}\) Les propriétés électroniques et stérique caractéristiques de ces bases, nous ont permis de trouver une synthèse très pratique pour accéder aux diamines pseudo-énantiomériques \((2S,4S,5R)-N,N\text{-dimethyl-2-aminomethyl-5-}\)
ethylquinuclidine (93) et (2R,4S,5R)-N,N-dimethyl-2-aminomethyl-5-ethene-quinuclidine (94). Les diamines 95 et 96 sont commerciales et permettent un accès très simple à plusieurs grammes de catalyseurs énantiopures 93 et 94 avec un très bon rendement par formylation réductrice et hydrogénation.

Schéma 6

7.- Acylation asymétrique de diols méso.

La réaction du complexe méso-[Cr(CO)₃(η⁶-5,8-dihydro-5,8-dixydoxynaphtalene)] (66) avec BzCl en présence du catalyseur diamine 93 se déroule sans heurt, en fournissant le monobenzoate (-)-(S5,8R)-[Cr(CO)₃(η⁶-5,8-dihydro-8-hydroxy-5-benzoyloxynaphtalene)] (98) avec de bons rendements et de bons à excellents excès énantiomériques. Les diamines pseudo-énantiomériques 93 et 94 donnent accès aux complexes (-)-98 et (+)-98 respectivement.
Schéma 7

Cette méthode a été élargie à la désymétrisation de *méso*-1,2-diols (Schéma 8). L'influence de la concentration, de la température, des différentes bases, des différents réactifs d’acylation substitués et de solvant a été largement étudiée pour l’acylation asymétrique du *méso*-cyclohexane-1,2-diol catalysée par la diamine 93. Un processus extrêmement efficace utilisant le THF ou l’AcOEt comme solvant à très basse température a été mis au point, donnant le monobenzoate (+)-76 énantiomériquement enrichi avec un excellent rendement. Ces conditions ont été appliquées avec succès dans la désymétrisation d'une gamme de *méso*-1,2-diols cycliques et acycliques avec de bons rendements et de bonnes stéréosélectivités à faible taux (2 % mol) catalyseur. Pour contre, une baisse de sélectivité et de conversion ont été obtenus pour les substrats portant une fonctionnalité phénylique.

![Diagramme de Schéma 7](image)

Schéma 8
8.- **Le redécouverte de 1,4-tetralindione (134).**

L’isomérisation facile du complexe \([\text{Cr(CO)}_3(\eta^6-5,8\text{-dihydroxynaphtalène})] (63)\) en son tautomère \([\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindione})] (64)\) nous a conduit à étudier l’isomérisation d’un composé apparenté. Une recherche bibliographique a révélé que cette isomérie n’est pas spécifiques aux complexes du \(\text{Cr(CO)}_3\). La 1,4-tetralindione (134) a été documentée dans la littérature il y a longtemps. En 1933 Madinaveitia et Olay ont signalé l’isolement de la première 1,4-tetralindione (134) en chauffant la 1,4-dihydroxynaphtalène (61) sous vide au-dessus de son point de fusion (210 °C) pendant 10 minutes (Schéma 9).

A cette température, les deux isomères s’interconvertissent et, étonnamment, la dione 134 est un composé cinétiquement stable en refroidissant. La conversion de 61 à 134 peut également être effectuée en présence de CF₃COOH. Laatsch a signalé que l’équilibre tautomérique est fortement influencé par le solvant.[21] Nous avons mis au point une procédure simple et fiable qui donne accès à plusieurs grammes de 134 le défi d'explorer sa réactivité à été relevé (Schéma 2).

![Schéma 9](image.png)

Des études préliminaires ont démontré la forte tendance de la dione 134 à s’isomériser en forme énolique 61 en milieu acide ou basique dans une grande gamme de solvants. En outre, des calculs poussent à dire que la dione 134 est plus stable que son énol 61 en phase gazeuse. Toutefois, en ajoutant l’effet de solvatation, les calculs ont montré que l’énol 134 est thermodynamiquement favorisé dans tous le cas et plus particulièrement dans des solvants polaires. Cette observation a été démontrée expérimentalement. Lorsqu’on ajoute un fragment de \(\text{Cr(CO)}_3\) à l’énol 61, les calculs montrent que l’équilibre tautomérique est déplacé en faveur du complexe 64. Toutefois, l’ajout de solvant favorise la forme énolique \(\text{Cr(CO)}_3\) en désaccord avec les observations expérimentales. Des calculs plus précis sont en cours pour optimiser les résultats.
Grâce à sa simplicité, à sa haute possibilité de fonctionnalisation et à sa symétrie, la 1,4-tetralindione (134) devient un précurseur prometteur pour la synthèse organique. En outre, plusieurs composés naturels biologiquement actifs contiennent le noyau de la tetraline 1,4-disubstitué, rendant la dicétone 134 propice en tant que synthon.[22-26] Curieusement, aucune chimie faisant usage de la dicétone 134 n'a jamais été signalée depuis son isolement en 1933. (Schéma 10). En partant de la dicétone 134 les transformations suivantes ont été possibles:

1) Protection sélective pour donner la TMS cyanohydrine 139.
2) Réduction diastéréosélective au cis-141 ou trans-145 1,4-tetralindiols
3) Bisreduction CBS et monoreduction CBS efficace.
4) Bisallylation énantiosélective.
5) Synthèse énantiosélective d’un précurseurs de la Sertraline.
6) Construction de naphtalènes 1,4-disubstitués.

En dépit de tous les problèmes liés à sa réactivité, la dicétone 134 a fait preuve d'une chimie vaste et riche.

Schéma 10
9.- Références.


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I. General introduction to \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes

The reactivity changes that arise upon complexation of an arene to chromium tricarbonyl fragment allow a variety of transformations otherwise inaccessible. This versatility has been widely recognised and, as a result, these complexes have been used as key building blocks in the synthesis of several natural products or as ligands in asymmetric catalysis. The unique bonding characteristics of aromatics, the stability of the benzene ring system, and the varied and often complex chemistry of arenes and heteroarenes have fascinated chemists for close to two centuries. Benzene rings are omnipresent in organic chemistry and they find important applications in the pharma, agrochemical and polymer fields. New applications of aromatics include sectors such as functional materials and molecular machines. Following the discovery of ferrocene and the determination of its sandwich structure, it did not take long before a large number of sandwich and half sandwich complexes saw the light of the day and became the subject of intense study. These events and the parallel development of the transition metal catalysed reactions were decisive in the vast interest that arose in the study and chemistry of compounds containing metal carbon bonds. In order to address these goals, the present introduction focuses on the reactivity and synthetic possibilities of planar chiral \(\text{Cr(CO)}_3\) complexes showing a rich and varied chemistry.

I.1 Metal arene complexes.

Metal arene complexes are known as stable solids for wide range transition metals. These complexes are generally classified as \(\eta^2\) or \(\eta^6\) according to the number of arene carbons coordinated to the metal (Figure 1). The metal fragment in \(\eta^2\) complexes been prepared by coordination to OsL\(_n\), ReL\(_n\), MoL\(_n\), WL\(_n\) fragments\,[1-4]\). Monosubstituted arenes bind to the metal preferentially at C(5)-C(6) because this allows linear conjugation of the substituent and unbound portion of the aromatic ring. The uncomplexed portion of the \(\pi\) system in \(\eta^2\)-arene complexes tends to behave as a 1,3-diene allowing cycloaddition reactions. In \(\eta^6\)-arene complexes the metal binds to every carbon of the arene which are considered to be pseudotetrahedral. Their preparation involves coordination to \(\text{Cr(CO)}_3\),\,[5] \(\text{Mo(CO)}_3\),\,[6] \(\text{W(CO)}_3\),\,[7] \(\text{Mn(CO)}_3\),\,[8, 9] \(\text{Fe(Cp)}^{+}\)[10] and \(\text{Ru(Cp)}^{+}\)[11, 12] fragments among others. Metal arene compounds interact with aromatic hydrocarbons and often from stable complexes through overlap of the ring \(\pi\) and \(\pi^*\) orbitals with appropriate orbitals of the metal atom. As with
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\(\eta^2\)-coordination, the metal adds a third dimension to the planar aromatic ring and the two faces of the arene with ortho or meta substituents are enantiotopic (Figure 1). Therefore, coordination of the metal to an arene not only alters the reactivity of the ring-carbons and substituents as well as groups in benzylic positions but, in addition, also allow reactions with high stereoselectivities to be carried out.

Hein and co-workers isolated the first molecular arene-metal complex in 1919,\(^{[13]}\) but definitive compositional and structural characterisation of theses complexes was not achieved until the mid-fifties. \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) are widely used in metal-mediated organic synthesis. Numerous reviews have already addressed the advantages of this family of complexes.\(^{[14-20]}\)

![Figure 1](image)

**I.2 Properties of \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes.**

\([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes are yellow to red and exceptionally blue, crystalline and therefore easy to purify. They are stable to air in the solid state and can be stored away from light for long periods of time. In solution, they are weakly air-sensitive and reactions are best performed under \(\text{N}_2\) with degassed solvents. Standard aqueous workup can be employed and purification can be carried by crystallisation, sublimation, flash chromatography or HPLC. \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes are diamagnetic and can be characterised by NMR spectroscopy. NMR chemical shifts for C-H resonances are commonly found in the range of 4-6 ppm, remarkably low values when compared to in free arenes (7-8 ppm). Other factors contribute to such unusual behaviour such as magnetic anisotropy of the Cr-arene bond and partial orbital rehybridisation.

\([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes deliver unprecedented reactivity to the complexed arene system. Activation of arenes by complexation with metals through the \(\pi\)-system is
important in several processes, such as arene hydrogenation, functionalisation and various coupling reactions. In particular functionalisation of arenes using \([\text{Cr(\(\eta^6\)-arene)(CO)}_3]\) complexes is an important process, which has been extensively studied (Figure 2).\[16, 21-23\] The \(\eta^6\)-coordinated arene ring is susceptible to a number of synthetic manipulations due to the electron-withdrawing properties of the \(\text{Cr(CO)}_3\) unit. The ring hydrogens have increased acidity and are therefore prone to deprotonation with lithium amides or organolithium reagents. The pK\(_a\) of benzylic acids, anilines and phenols are also known to be lowered by several pK\(_a\) units upon complexation.\[24, 25\]

![Figure 2](image)

Benzylic carbocations complexed to \(\text{Cr(CO)}_3\) are stabilised by delocalisation of the positive charge onto the chromium.\[26\] Consequently, benzylic leaving groups that can adopt a conformation antiperiplanar to the arene undergo facile cleavage S\(N1\) type reactions with retention of the configuration. The \(\text{Cr(CO)}_3\) benzyl cation is 5 pK\(_a\) units more stable than free benzyl cation.\[27, 28\] These large pK\(_a\) differences have been attributed to the net electron-withdrawing ability of the \(\text{Cr(CO)}_3\) moiety. The ability of the \(\text{Cr(CO)}_3\) moiety to stabilise conjugated ions plays an important role in the formation of new bonds.\[26\] The detailed nature of the interactions between the \(\text{Cr(CO)}_3\) moiety and complexed benzyl reactive intermediates remains firmly established. The key issues are how the free and Chromium complexed species differ in structure and whether the \(\text{Cr(CO)}_3\) group interacts directly with the benzylic position of each reactive intermediate (Figure 3). Computed studies of various benzylic species demonstrates that direct interaction between chromium and the benzylic position is present in cationic complexes but not in the corresponding complexes of anions and radicals.\[29\]
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In addition to this, the \(\text{Cr}(\text{CO})_3\) moiety has found widespread use as stereodirecting group in reactions of side chains attached to the arene ring.\[^{30-33}\]

However, in the context of this introduction, it is the susceptibility of the arene ring to undergo nucleophilic addition reactions which is of most importance. The \(\text{Cr}(\text{CO})_3\) fragment coordinated to the \(\pi\) system of the arene function as strong electron-withdrawal group and enable direct attack by nucleophiles (generated from C-H acids of \(pK_a > 22\)) on the arene ring in \textit{exo} to the \(\text{Cr}(\text{CO})_3\) moiety to give \(\eta^5\)-cycloheadienyl-metal complexes.\[^{20}\] The regioselectivity of the addition is influenced in subtle and indirect ways, compared to the powerful effect of both reactivity and regioselectivity of the electron-withdrawing groups attached to the \(\sigma\) bond system of the arene. The range of nucleophiles that can be used is limited by the moderate electrophilicity imparted by the metal (\(\text{LiCH}_2\text{CO}_2\text{R}, \text{LiCH}_2\text{CN}, \text{KCH}_2\text{COC(CH}_3)_3, \text{LiCH}_2\text{SPh}, \text{LiCH} = \text{CH}_2, \text{PhLi}, \text{LiC} = \text{CR}, \text{LiCH}_2\text{C}=\text{CH}_2\)). Nucleophilic additions to substituted \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) are often highly regioselective and the resulting \(\eta^5\) anionic complex offers a wide range of synthetic possibilities, some of which are presented in the following section. This and the mild reaction conditions are the major advantages of this methodology.

### 1.3 Synthesis of \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes.

The most common and economical method for the synthesis of \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes is thermolysis of \(\text{Cr}(\text{CO})_6\) typically at 140 °C in \(\text{^8Bu}_2\text{O} / \text{THF}\) in the presence of the arene. The polar ether additive (or solvent) promote carbonyl dissociation, stabilise intermediates, and vigorous reflux of lower boiling additives wash sublimed \(\text{Cr}(\text{CO})_6\) back into the reaction mixture. Prior to mixing and heating, solvents are degassed by several freeze / pump / thaw cycles or by bubbling inert gas through the solvent for 5-10 minutes. This allows the preparation of a wide range of complexes with useful functionalities.\[^{20, 23}\]
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(Scheme 1). However, aryl bromides, aryl iodides, benzaldehyde and benzyl halides cannot be directly complexed to \([\text{Cr}(\text{CO})_6]\) due to competing insertion of the zero-valent \([\text{Cr}(\text{CO})_n]\) metal into the aryl-halide bond or other side reactions that come about when refluxing at high temperature.

Alternatively, \([\text{Cr}(\text{CO})_6]\) can be transformed into other \(\text{Cr(CO)}_3\) sources such as \([\text{Cr}(\text{CO})_3(\eta^6\text{-naphthalene})]\) (1),\(^{[34]}\) \([\text{Cr}(\text{CO})_3(\text{NH})_3]\) or \([\text{Cr}(\text{CO})_3(\text{py})_3]\) that permit complexation under milder conditions more compatible with the aforementioned functionalities. \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes can be obtained by refluxing the pyridine and NH\(_3\) precursors in the presence of the arene in dioxane. This allows milder complexation conditions typically in the range of 80-100 °C. Room temperature complexation is also possible by reaction of \([\text{Cr}(\text{CO})_3(\text{NH})_3]\)^{[35]} with BF\(_3\)-Et\(_2\)O in the presence of the arene. The advantages of lower temperatures for arene complexation are higher functional group compatibility and potentially higher chemo- and diastereoselectivities.\(^{[36]}\) While these methods require an additional synthetic step to prepare the corresponding \([\text{Cr}(\text{CO})_3\text{L}_3]\) complex, the ease of the procedures and the high overall yield make them often the method of choice.

One of the main features of \([\text{Cr}(\text{CO})_3(\eta^6\text{-naphthalene})]\) complexes is the ease with which they undergo thermal arene displacement and exchange reactions. In 1966 Bassolo \textit{et al.} proposed ring-slippage species as possible intermediates for arene exchange reactions.\(^{[37]}\)
For more than 30 years, this area has been extensively studied because of fundamental interest in these novel intermediates and their relevance to arene exchange and activation reactions.\textsuperscript{[38]} Theoretical analysis for the degenerate rearrangement of 1 favours a reaction pathway via an exocyclic intermediate (Figure 4).\textsuperscript{[39]} This pathway has also been suggested in a recent theoretical investigation of the haptotropic rearrangement of Cr(CO)\textsubscript{3} complexed sidewalls in carbon nanotubes.\textsuperscript{[40]}

The lability of such complexes is attributed to the slippage of the \(\eta^6\) arene to a \(\eta^4\) - or \(\eta^2\)-coordination (Figure 5). This slippage is easier in naphthalene complexes than in benzene complexes because it is associated with an increase in aromaticity in the non-complexed ring, leading to a lower energy pathway to arene displacement.\textsuperscript{[41]} The value of energy of dissociation for the naphthalene-Cr bond in 1 is 6 Kcal / mol lower that the benzene-chromium bond \([\text{Cr}(\eta^6\text{-benzene})(\text{CO})_3]\) (53 kcal / mol).\textsuperscript{[42, 43]} Thus, when \([\text{Cr}(\eta^6\text{-naphthalene})]\) is heated at 70 °C in Et\textsubscript{2}O / THF in the presence of an arene, equilibration by thermal arene displacement takes place and the corresponding \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) is obtained in high yield.\textsuperscript{[44]} A large excess of the arene may be required to drive the reaction to the product.
These characteristics are complemented by the ease by which the Cr(CO)\textsubscript{3} fragment can be easily removed from the arene at the end of a synthetic sequence. While inert to a large number of reaction conditions, the metal-arene bond can be cleaved upon oxidation of the metal (Ce\textsuperscript{4+}, Fe\textsuperscript{3+}, I\textsubscript{2}, hv/O\textsubscript{2}).\textsuperscript{[45]} The mildest and most economical procedure consists in the exposure of the complex in acetonitrile to sunlight and air for a few hours. Refluxing a [Cr(\eta\textsubscript{6}-arene)(CO)\textsubscript{3}] complex in pyridine cleaves the metal arene bond and allows recycling of chromium in the form of [Cr(CO)\textsubscript{3}(py)\textsubscript{3}].\textsuperscript{[46-48]} In [Cr(CO)\textsubscript{3}(\eta\textsubscript{6}-naphthalene)] complexes the metal arene bond is readily cleaved under one atmosphere of CO or by applying a few bars of pressure.\textsuperscript{[49]}

\textbf{I.4 Asymmetric synthesis of planar chiral [Cr(\eta\textsubscript{6}-arene)(CO)\textsubscript{3}] complexes.}

Most of the approaches to planar chiral [Cr(\eta\textsubscript{6}-arene)(CO)\textsubscript{3}] complexes involves the use of stoichiometric amounts of chiral information. Well established diastereoselective reactions are complemented by a growing number of enantioselective methods, in which planar chirality is generated by an external agent. Frequently used routes to chiral nonracemic complexes include:

\textbf{I.4.1 Resolution of racemates.}

Racemic [Cr(\eta\textsubscript{6}-arene)(CO)\textsubscript{3}] complexes including amine or carboxylic acid functionalities can be resolved by crystallisation of their diastereomeric salts with (+)-camphorsulfonic acid or brucine respectively.\textsuperscript{[50, 51]} \textit{Ortho}-substituted benzaldehyde complexes are usually resolved through the formation of diastereomeric semioxamazones,\textsuperscript{[52]} imines,\textsuperscript{[53]} or aminals\textsuperscript{[54]} that allow flash chromatography separation. After acid hydrolysis, each enantiomer is recovered separately. Enzymatic kinetic resolution has also been used, mostly in enantioselective reductions of chiral aldehydes.\textsuperscript{[55, 56]} Other examples include enzymatic ester hydrolysis and esterification of benzylic alcohols.\textsuperscript{[57, 58]} Resolution of [Cr(\eta\textsubscript{6}-arene)(CO)\textsubscript{3}] complexes by chiral HPLC columns has also been described.\textsuperscript{[59, 60]}
I.4.2 Diastereoselective complexation.

Chiral benzylic functions as alcohols or amines are known to direct the complexation of a Cr(CO)\textsubscript{3} fragment by precoordination to the metal, leading to the formation of the syn complex.\cite{61-63} The π-facial diastereoselectivity is generally higher when using milder complexation conditions, as reported by Schmalz et al. in the preparation of enantiopure tetralol Cr(CO)\textsubscript{3} derivatives. (Scheme 2).\cite{64} The substantially more accessible Cr(CO)\textsubscript{6} gave less satisfactory results. However, the complexation with this chromium source could be optimised by addition of catalytic quantities of THF. Complementarily, bulky alkyl groups tend to direct the metal to the anti face.\cite{65}

\begin{align*}
\text{OH} & \quad \text{a), b) or c)} \\
\text{Cr(CO)\textsubscript{3}} & \quad \text{syn} \\
\text{Cr(CO)\textsubscript{3}} & \quad \text{anti} \\
\text{H} & \quad \text{H}
\end{align*}

\begin{itemize}
  \item a) Cr(CO)\textsubscript{6}, THF / Bu\textsubscript{2}O (1:10), reflux \quad 90 \quad 10
  \item b) [Cr(CO)\textsubscript{3}(η\textsubscript{6}-naphthalene)], THF, Et\textsubscript{2}O, 70 °C \quad 99 \quad 1
  \item c) Cr(CO)\textsubscript{6}, cat THF, Bu\textsubscript{2}O / heptane (1:1), reflux \quad 98 \quad 2
\end{itemize}

\textbf{Scheme 2}

Alexakis et al. used chiral auxiliaries incorporated into the arene to induce diastereoselectivity during complexation, offering an elegant solution to the asymmetric synthesis of ortho substituted benzaldehyde complexes. While, good diastereoselectivities were previously reported for the complexation of acetal \textbf{2},\cite{66} low yields of the corresponding Cr(CO)\textsubscript{3} aldehyde were obtained after hydrolysis. The authors envisaged more sterically demanding chiral aminals \textbf{3a} and \textbf{3b} as more discriminative chiral auxiliaries and these are more easily to cleaved (Scheme 3).\cite{54} Thermal complexation of \textbf{3a} with Cr(CO)\textsubscript{3} gave the corresponding diastereomeric pairs (2S)-\textbf{4a} and (2R)-\textbf{4a} in an 88 / 12 ratio (76 % de, 60 % yield) which could be resolved by flash chromatography.
Better diastereoselectivities were achieved by r.t. complexation with [Cr(CO)₃(η₆-naphthalene)] at room temperature. Surprisingly, under these conditions the opposite diastereoisomer (2R)-4a is the major with a 3 / 97 ratio (94 % de, 80 % yield). This inversion of selectivity might be due either to nitrogen chelation or to steric requirements of the aminal group itself.

I.4.3 Enantioselective lithiation.

For monosubstituted [Cr(η₆-arene)(CO)₃] complexes, a kinetically controlled discrimination between the two enantiotopic ortho hydrogens is possible by metalation with a chiral non-racemic chiral lithium amide base. This strategy was applied to the desymmetrisation of dimethoxybenzene chromium tricarbonyl complex 6 with a stoichiometric amount of lithium amide base 7 and TMSCl (Scheme 4).[67] The metalation must be carried out in the presence of TMSCl at low temperature in order to ensure rapid quench of the lithium anion, which is susceptible of other side reactions. Under room temperature, external quench conditions, the kinetic ortho-lithiated species equilibrates to the thermodynamically preferred meta-isomer.
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The stabilisation of anionic charge in benzylic position by the \(\text{Cr}(\text{CO})_3\) unit allows desymmetrisation of \(\text{meso-}[\text{Cr}(\text{CO})_3(\eta^6-\text{N-methyl-N-pivaloyl-2,6-dimethylaniline})]\) complex (9) by stoichiometric deprotonation with lithium amide base 10 followed by electrophilic quench (Scheme 5). The amide carbonyl oxygen in 9 is found to be syn oriented with respect to the metal fragment while complex 11 presents an anti orientation due to a stereoelectronic effect.

A wide range of electrophiles can be used without much loss in yield or enantioselection contributing to the first asymmetric approach to chiral axial \(\text{N-methylanilidines}\) after photochemical decomplexation of the metal (Et\(_2\)O, 0 °C) with no loss of optical purity.

I.4.4 Diastereoselective lithiation.

Diastereoselective ortho lithiation of \([\text{Cr}(\eta^6-\text{arene})(\text{CO})_3]\) complexes incorporating a chiral auxiliary represents a viable alternative for the synthesis of highly enantioenriched planar chiral chromium complexes. Chung and co-workers explored the use of modified
sugars as stereodirecting groups (Scheme 6). Complex 13 was prepared by following a thermal protocol with Cr(CO)₆ and the readily available benzylic acetal. Deprotonation is then assisted by chelation of "BuLi to the nearby methyl ether followed by selective delivery of the base to the arene. The resulting anion is quenched with Me₃SiCl to give the corresponding ortho-substituted benzaldehyde complex in excellent ee after acetal cleavage under acidic conditions.

In addition, upon changing the sugar moiety from galactose to glucose, the relative position of the directing methyl ether is inverted. Consequently, the same reaction sequence gives benzaldehyde complex 14 with reverse configuration.

Alexakis et al. envisioned aminals bearing a more basic, piperidine-type nitrogen atom would be more efficient coordinating heteroatoms to performed directed ortho-metallation (Scheme 7). Benzaldehyde complex 15 is protected as aminal 16 in high yield. The stair like conformation of these aminals causes a strong bias in the steric environment of the aminal.

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**Scheme 6**

**Scheme 7**
Chapter I: General introduction to [Cr(η^6-arene)(CO)_3] complexes

Lithiation occurs with high diastereoselectivity to give *ortho*-substituted benzaldehyde complex 17 after electrophilic quench with (Ph)_2PCl and aminal hydrolysis. Other electrophiles as MeI, Me_3SnCl, Me_3SiCl or (PhS)_2 can be used with high performance (95-77 % yield, 95-91 % ee).

I.4.5 Nucleophilic addition / Hydride abstraction.

Kündig *et al.* developed an elegant strategy based on a three step / one-pot sequence where an *external* chiral ligand 18 controlled the enantioselective nucleophilic addition of an organolithium reagent (MeLi, BuLi or PhLi) to the arene complex 19 leading to the formation of η^5-cyclohexadienyl complex 20 (Scheme 8).[71] After hydride abstraction and hydrolysis under mild conditions, the corresponding *ortho*-substituted benzaldehyde complex (-)-21 were obtained in high yields and enantioselectivities.

![Scheme 8](image)

The mechanism for the hydride abstraction step in this process is a query that remains unanswered. Trityl cation has been widely used in hydride abstraction from η^5-cyclohexadienyl complexes, but *endo*-hydride abstraction pathways are rarely observed due to the steric requirements of the of the chromium fragment. However, no *exo*-hydride is available in η^5-cyclohexadienyl complex 20 and the *endo*-hydride is not very accessible to the bulky trityl cation. A possible alternative mechanism is an imine assisted *endo*-hydride removal by precoordination of the cation to the nitrogen lone pair.[72]
I.4.6  Palladium catalysed desymmetrisation of prochiral complexes.

As shown all along this section, the great majority of strategies that give access to enantioenriched planar chiral Cr(CO)₃ complexes involve the use of stoichiometric amounts of chiral information. More recent approaches employ catalytic quantities of a palladium source and a chiral ligand in the desymmetrisation of meso-[Cr(CO)₃(η⁶-dihaloarene)] complexes. So far, enantioselective methoxycarboxylation[73] and cross coupling reactions[74, 75] have been shown to be not very efficient in the desymmetrisation of meso-[Cr(CO)₃(η⁶-dihaloarene)] complexes. However, a new synthetic strategy based on enantioselective hydrogenolysis of meso-[Cr(CO)₃(η⁶-5,8-dibromonaphthalene)] complex (22) was developed in our laboratories giving excellent results (Scheme 9).[76] Phosphoramidite ligand 23 afforded monobromonaphthalene complex 24 in moderate yield and high enantioselectivity. The origin of the enantioselection resides in the oxidative addition of palladium in the halide-aryl bond under the influence of the chiral phosphoramidite ligand 23. The final catalytic step in this reaction is likely to involve a reductive elimination of a cis-[Pd(aryl)(H)] moiety. Additionally, kinetic resolution of complex 22 can be conveniently used to increase its enantiopurity.

![Scheme 9](image)

I.4.7  Dötz benzannulation.

[Cr(η⁶-arene)(CO)₃] complexes can also be built from a chromium carbene. Bond formation of carbenes and carbon monoxide with alkynes can be carried out at a chromium centre to yield a [Cr(η⁶-arene)(CO)₃] complex in a process known as Dötz benzannulation.[46, 47] High diastereoselectivities have been observed when either the alkyne or the carbene incorporates chirality. Optically active phenyl(alkoxy)carbene chromium complex 25 gives
diastereomERICALLY enriched complex 26a after benzoannulation with tert-butyl acetylene (Scheme 10). The diastereoisomers were separated by flash chromatography and the Cr(CO)\(_3\) fragments were displaced to the less hindered ring by thermal haptotropic migration at 90 °C in Bu\(_2\)O. Treatment with TBAF cleaved the silyl protecting group and \textit{in situ} oxidation of the hydroquinone with air gave the enantiopure substituted naphthoquinone complex 27 in low yield.

\[ \text{Cr(CO)\(_3\)} \quad \text{O} \quad \text{OR*} \quad \text{Cr(CO)\(_3\)} \quad \text{O} \quad \text{OR*} \]

Scheme 10

I.5 Relevance of \([\text{Cr(}\eta^6\text{-arene})(\text{CO})_3]\) complexes in organic synthesis.

\([\text{Cr(}\eta^6\text{-arene})(\text{CO})_3]\) complexes are valuable materials for organic synthesis. When displaced from the arene, the Cr(CO)\(_3\) unit acts as a catalyst in a variety of transformations. On the other hand, the unique steric features of planar chiral Cr(CO)\(_3\) complexes promotes their use as ligands for transition metal catalysed reactions. Moreover, the changes in reactivity that arise in the arene upon complexation to the Cr(CO)\(_3\) fragment has inspired the synthesis of many natural products and biologically active. The uses of the Cr(CO)\(_3\) moiety in organic synthesis has been widely explored and this section cites only a few the most interesting applications.

I.5.1 \([\text{Cr(}\eta^6\text{-arene})(\text{CO})_3]\) complexes as catalysts.

The arene-Cr bond in \([\text{Cr(CO)}_3(\eta^6\text{-naphthalene})]\) (1) can be easily cleaved upon heating in THF, releasing a coordinatively unsaturated 12 electron Cr(CO)\(_3\) fragment. These
vacant sites are occupied in the presence of a diene and molecular hydrogen leading to the formation of intermediate 28 (Scheme 11). 1,4-hydrogenation takes place to give exclusively the cis-olefin, releasing the chromium fragment allowing its use in catalytic quantities.\textsuperscript{77} This process has been used in the regioselective 1,4-hydrogenation of methyl 2,4-hexanediene giving cis-methyl 3-hexenate which is a useful starting material in the fragrance industry.\textsuperscript{78}

\textbf{Scheme 11}

The efficiency of [Cr(CO)\textsubscript{3}(\eta\textsubscript{6}-naphthalene)] as a hydrogenation catalyst has been extended to the regioselective reduction of \(\alpha,\beta\)-unsaturated ketones. The diene must be able to adopt an \(s\)-cis conformation as in complex 28 to undergo hydrogenation. Consequently, the cyclohexenone fragment in 29 remains unreactive under these conditions due to its fixed \(s\)-trans conformation (Figure 6).

Alkynes also behave as 4 electron donors and are reduced to the corresponding cis-olefins with 100 % selectivity outperforming Lindlar catalysts, cationic rhodium complexes and others.\textsuperscript{79} The mono-olefins, resulting from these reductions, show very poor affinity for Cr(CO)\textsubscript{3} and dissociate rather than undergoing further reduction.
Chapter I: General introduction to [Cr(η⁶-arene)(CO)₃] complexes

Figure 6

In a related process, in the absence of H₂, the Cr(CO)₃ fragment has the ability to isomerise 1,3-dienes by 1,5-hydrogen migration under very mild conditions. In the example shown, the mechanism involves arene-metal cleavage of [Cr(CO)₃(η⁶-naphthalene)] (1) in acetone at r.t. followed by coordination of the diene to give η⁴-diene complex 31 (Scheme 12). Oxidative addition of the metal generates η⁵-pentadienyl hydride complex 32 which delivers back the hydride to the terminal position by reductive elimination with retention of configuration. Thereafter, ligand exchange regenerates complex 31, allowing catalytic use of the metal. The overall process is 1,5-isomerisation to the thermodynamically more stable regioisomer.

Scheme 12
1.5.2 Planar chiral \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes as ligands for asymmetric catalysis.

Planar chiral complexes have been successfully used as ligands for asymmetric catalysis. The use of ferrocenyl catalysts in asymmetric synthesis is now a maturing field and this has prompted the search for additional chiral templates including analogous \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes. Salzer, Stürmer and co-workers reported the highly enantioselective hydrogenation of methyl acetoamidoacrylate 34 into the corresponding amidoester 35 in quantitative yield (Scheme 13).[81] This process was carried out by an *in situ* preformed catalyst by combination of bidentated planar chiral ligand 36, analogous to Josiphos,[82] and \([\text{Rh(cod)Cl}_2]\). Planar chiral complex 36 is easily accessible by metalation of cheap (R)-phenylethanamine. Following complexation, electrophilic introduction of the PPh2 into the *ortho* position, replacement of the amino group by a chloro substituent and dehalogenation in the presence of the secondary phosphine gives 36 in high yield.

![Scheme 13](image)

The bidentate aminophosphine ligand 37 was developed by Hayashi and co-workers based on the planar chiral Cr(CO)3 complex geometry. *In situ* combination with a palladium source gave a complex capable of promoting catalytic asymmetric allylic alkylation of 1,3-diphenyl-1-acetoxypropene (38) in the presence of sodium dimethylmalonate (Scheme 14).[83] The substitution product 39 is obtained in high yield and enantioselectivity at low reaction temperatures. The parent arene ligand lacking the Cr(CO)3 fragment also promoted the transformation but in only 14 % ee, clearly demonstration the steric effect of the metal fragment.
Chapter I: General introduction to \([\text{Cr(\eta}^6\text{-arene})(\text{CO})_3]\) complexes

Based on a similar ligand template, the use of planar chiral chromium complexes was extended into the field of alkene hydrosilylation. The changes in reactivity that arise in the arene under the influence of the \(\text{Cr(CO)}_3\) fragment offer new opportunities for ligand tuning. Jones et al. used ligand 40 in combination with a palladium source to catalyse the addition of trichlorosilane to styrene giving highly enantioenriched \((S)-\)phenylethanol (41) after oxidative cleavage (Scheme 15). \(^{84}\) Bidentate ligand 40 is easily accessible in three steps from \((S)-\)phenethylamine without the need of resolution. Hydrosilylation was performed on a range of substituted styrenes with 85-90 % yield and moderate to high enantioselectivities.

Jones and co-workers envisaged the use of planar chiral chromium complexes with Lewis basic centres as ligands in this field. Having tested a range of Lewis acids and ligands, the pairing of \(\text{Et}_2\text{AlCl}\) and complex 42 was shown to perform best the cycloaddition between 2-methacrolein and cyclopentadiene giving the \(\text{exo}\)-aduct \((S)-44\) \((\text{exo} / \text{endo} \text{ in } 98 : 2 \text{ ratio})\), 81 % yield, 95 % ee (Scheme 16). Ligand and Lewis acid were equilibrated for 1 h prior to the addition of substrates in order to avoid free aluminium species able to catalyse racemic
pathways. Ligand 42 can be prepared in one step from commercially available (1R,2S)-1,2,3,4-tetrahydro-1,2-naphthalenediol.

```
\[
\text{HOC} + \text{MeOH} \xrightarrow{\text{(CO)}_3\text{Cr}} \text{HOC} + \text{(CO)}_3\text{Cr} + 20 \text{ mol \% Et}_2\text{AlCl} \xrightarrow{\text{CH}_2\text{Cl}_2, -95 \degree C} \text{MeH}
\]
```

(S)-44, 95 % ee

**Scheme 16**

### I.5.3 Planar chiral [Cr(η⁶-arene)(CO)₃] complexes in natural product synthesis.

Planar chiral [Cr(η⁶-arene)(CO)₃] complexes represent highly valuable building blocks for the diastereo- and enantio-selective synthesis of natural products and biologically active compounds. The chromium facilitates new transformations in the arene with additional improvement in selectivities (see Section I.2). Different synthetic strategies allow the complexation of the Cr(CO)₃ to the arene. In addition, the metal tolerates a wide range of reaction conditions and is easily cleaved under mild conditions when no longer needed.

Schmalz *et al.* designed an elegant route to natural occurring (1S,4S)-7,8-dihydroxycalamenene by using the Cr(CO)₃ fragment as stereodirecting group, introducing planar chirality when complexed to a tetralin core (Scheme 17). Readily available tetralone 45 was efficiently desymmetrised by CBS reduction and complexed to chromium to give syn-46 as a single diastereoisomer (see Section I.3.2). Removal of hydroxyl function and ortho protection was effected in order to prepare further benzylic alkylations. Thus, tetralol 46 was reduced by ionic hydrogenation and silylated in ortho to the methoxy group. Sequential methylation followed by acetylation in the benzylic positions took place exclusively exo to the chromium fragment. Further construction of the alkenyl chain and silyl group removal gave cis-tetralin 49 in high yield. After methylation, oxidative decomplexation and ether cleavage the target molecule 50 was obtained without loss in enantiomeric purity.
Chapter I: General introduction to [Cr(η^6-arene)(CO)_3] complexes

Scheme 17

The synthesis of (-)-lasubine developed by Kündig et al. exemplifies other aspects of the Cr(CO)_3 fragment as stereodirecting group (Scheme 18). Enantiomerically pure imine complex 51 was obtained by resolution of its aldehyde via imine formation with L-valinol, hydrolysis and recovery of the imine function by condensation with 4-aminobutan-1-ol. The aza-Diels-Alder reaction with Danishefsky’s diene afforded pyridinone substituted complex 52 as a single diastereoisomer. Only π-facial approach from the upper face is allowed since the chromium moiety blocks the lower. Mesylate formation and substitution by bromide prepared the stage for radical cyclisation in which the diastereoselectivity is enhanced by the presence of the chromium fragment. The synthesis of (-)-lasubine was concluded with diastereoselective reduction of ketone 53 with L-selectride and oxidative removal of the metal.
Chapter I: General introduction to \([\text{Cr} \eta^6\text{-arene})(\text{CO})_3]\) complexes

The electron withdrawing effect of the chromium fragment in the arene allows nucleophilic attack to the carbons of the ring in \textit{exo} to the \(\text{Cr(CO)}_3\) unit leading to a \(\eta^5\)-cyclohexadienyl intermediate that offers a wide range of synthetic possibilities (Section I.2). The synthesis of (+)-acetoxytubipofuran was carried in our laboratories based on this synthetic strategy.\(^{\text{[86]}}\) Enantioselective nucleophilic \textit{ortho}-addition of \textit{cis}-ethoxyvinyllithium assisted by chiral ligand \(\text{18}\) (Section I.3.5) is presumed to occur through less hindered transition state \(\text{I}\) leading to the formation of an \(\eta^5\)-cyclohexadienyl intermediate (Scheme 19). At this point, the anionic charge resides on the metal and alkylation, CO insertion and acyl transfer to the arene takes place in the presence of MeI under CO atmosphere. Alkylation followed by imine hydrolysis gave heavily functionalised \textit{trans}-cyclohexadiene \(\text{55}\) in 76 % ee as a single diastereoisomer showing the enormous potential of this one-pot reaction sequence. The synthesis of natural occurring \(\text{56}\) was further achieved in 8 further steps and at some stage, recrystallisation afforded highly enantioenriched product \((> 99 \% \text{ ee})\). The enantiomer, (+)-acetoxytubipofuran was also synthesised by following a similar chromium mediated strategy.
Chapter I: General introduction to \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes

As shown above, planar chiral \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes show a unique and rich chemistry and are increasingly finding applications in the fields of catalysis and natural product synthesis. In the course of studies on naphthalene complexes in this laboratory, a route to \([\text{Cr}(\text{CO})_3(\eta^6\text{-5,8-naphthoquinone})]\) (57) was developed (Scheme 20). We therefore set out to investigate its reactivity and synthetic potential. The first task consisted in finding a concise and reliable procedure that would provide access to multigram quantities of this complex. From the start, we realised the potential offered by \(\text{Cr} \left(\text{CO}\right)_3\) complexation for desymmetrisation of 57 and its derivatives. Catalytic procedures were to be given preference. The following chapters describe the results of our studies, a journey rich of unexpected discoveries that includes the development of new acylation catalysts and studies on long forgotten stable tautomers.
Chapter I: General introduction to \([\text{Cr(\eta^6-arene)(CO)}_3]\) complexes

I.7 References.

Chapter I: General introduction to [Cr(η⁶-arene)(CO)₃] complexes


Chapter I: General introduction to $\text{[Cr(}\eta^6\text{-arene})(\text{CO})_3\text{]}$ complexes


Chapter I: General introduction to \([\text{Cr}(\eta^6\text{-arene})(\text{CO})_3]\) complexes
II. Synthesis and reactivity of $\text{[Cr(CO)}_3(\eta^6\text{-5,8-naphthoquinone})\text{]}$ (57)

In this chapter, we describe a straightforward access to the complex $\text{[Cr(CO)}_3(\eta^6\text{-5,8-naphthoquinone})\text{]}$ (57) and explore its reactivity.

II. 1 Precedents for the synthesis of $\text{[Cr(CO)}_3(\eta^6\text{-5,8-naphthoquinone})\text{]}$ (53).

As reported in Section I.4.7, Dötz and co-workers described the synthesis of the naphthoquinone Cr(CO)$_3$ complex 27 by benzannulation of tert-butylacetylene and a carbene chromium complex, followed by thermal haptotropic rearrangement, deprotection and oxidation.$[^1]$ Complex 27 was obtained in low overall yield (11%) as oxidation led to the recovery of the free quinone.

No efficient synthesis of $\text{[Cr(CO)}_3(\eta^6\text{-5,8-naphthoquinone})\text{]}$ (57) has been reported prior to the work carried out in this laboratory. Unfortunately, electron deficient 1,4-naphthoquinone (58) proved to be an unsuitable ligand for a process that involves electron donation from the ligand to the metal (Section I.3). A comparison of the reduction potential of 1,4-naphthoquinone (58) and the oxidation potential of Cr(CO)$_3$ shows that the Cr(0) $\pi$ complex cannot be formed by direct reaction. Actually, the naphthoquinone complex was found by chance. Parallel to the synthesis of the dihalonaphthalene complexes, we investigated the synthesis of the diacetate naphthalene complex and – finding access to be difficult – the trifluoroacetate derivatives. Ester hydrolysis yielded the corresponding dihydroxy complexes under basic conditions, the red orange solutions of this complex immediately turned blue with even traces of air. The blue complex was subsequently identified as the naphthoquinone complex 57.

After some experimentation, Cyril Poulard$[^2]$ synthesised $\text{[Cr(CO)}_3(\eta^6\text{-5,8-bis(trifluoroacetoxy)naphthalene})\text{]}$ (59) via a non thermal protocol previously used in the synthesis $\text{[Cr(CO)}_3(\eta^6\text{-5,8-dibromonaphthalene})\text{]}$ (22).$[^3]$ All attempts of purification by flash chromatography with silica gel (deactivated with Et$_3$N) led to a deep blue chromium complex presenting $^1$H NMR $\delta$ 6.09 (s, 2H), 5.54-5.51 (m, 2H), 4.41-4.37 (m, 2H) signals consistent with the structure of $\text{[Cr(CO)}_3(\eta^6\text{-5,8-naphthoquinone})\text{]}$ (57). Based on this result, Ryan Bragg$[^4]$ treated $\text{[Cr(CO)}_3(\eta^6\text{-5,8-bis(trifluoroacetoxy)naphthalene})\text{]}$ (59) with two equivalents of Et$_3$N and the orange suspension turned to red immediately due to the formation of
dianionic intermediate 60 (Scheme 1). A gentle stream of air was carefully bubbled into this red solution which became deep violet due to oxidation of dianion 56 to [Cr(CO)₃(η⁶-5,8-naphthoquinone)] (57), then obtained in 30 % yield after purification. Competitive oxidation of the metal caused a considerable amount of decomplexation.

Scheme 1

Subsequently this route was optimised as outlined in Scheme 2.[⁵] Crystalline 1,4-naphthoquinone (58) was reduced with SnCl₂·2H₂O in acidic media to give 1,4-dihydroxynaphthalene (61) in 95 % yield (20 g scale).[⁶] Subsequent bis-acylation proceeded in good yield, although the reaction required 4.7 equivalents of (CF₃CO)₂O in Et₂O. Attempted formation of 62 using 2.2 equivalents of (CF₃CO)₂O and Et₃N returned only starting material. In this case, the ester functions are especially unstable towards base, a property that was exploited later in the synthesis of naphthoquinone complex 57.

Scheme 2
Chapter II: Synthesis and reactivity of \([\text{Cr(CO)}_3(\eta^6-5,8\text{-naphthoquinone})]\)

Complexation using \([\text{Cr(CO)}_3(\text{NH}_3)_3]\) and BF\(_3\).Et\(_2\)O gave, after 6 days stirring at r.t., complex 59 in 80 % yield (6 mmol scale). This reaction could be scaled up to 24 mmol in slightly lower yield (72 %) and the crude material was crystallised from hot toluene. Alternatively, 59 can also be purified by washing with hot hexane since 1,4-bis(trifluoroacetoxy)naphthalene (62) is 40 times more soluble in boiling hexane than its arene complex 59.

An improved synthesis of \([\text{Cr(CO)}_3(\eta^6-5,8\text{-naphthoquinone})]\) (57) avoiding purification by flash chromatography was necessary in order to provide sufficient material to allow its use in further reactions. Complex 59 was treated sequentially with two equivalents of Et\(_3\)N, an stoichiometric amount of 2,3-dicyano-5,6-dichlorobenzoquinone (DDQ) to give naphthoquinone complex 57 in good yield (80 %). Complex 57 was subsequently also synthesised by Dötz \textit{et al.} based on a similar route, but using other protecting groups.[7]

II. 2 A more direct route to \([\text{Cr(CO)}_3(\eta^6-5,8\text{-naphthoquinone})]\) (57).

My contribution to this project began with a new approach to \([\text{Cr(CO)}_3(\eta^6-5,8\text{-naphthoquinone})]\) (57), in view of the limitations implied in the previous synthesis. Experimentation showed that \([\text{Cr(CO)}_3(\eta^6-5,8\text{-dihydroxynaphthalene})]\) (63) could be synthesised directly from the arene when using mild complexation conditions. This made use of the complex \([\text{Cr(CO)}_3(\text{NH}_3)_3]\) and BF\(_3\).Et\(_2\)O,[8] a method that was successfully used previously by us for the synthesis of \([\text{Cr(CO)}_3(\eta^6-5,8\text{-dibromonaphthalene})]\) (22).[9] The separation of the initially formed orange dihydroxynaphthalene complex from excess ligand proved difficult. Manipulation and repeated crystallisation reduced yields drastically.

Its high reactivity might be attributed to the lability of the naphthalene fragment (Section I.3) or oxidation of the Cr(CO)\(_3\) facilitated by donation from the electron-releasing dihydroxynaphthalene moiety. Therefore, purification was abandoned and the orange crude complex was directly treated with 1 eq of DDQ to give a deep blue solution of \([\text{Cr(CO)}_3(\eta^6-5,8\text{-naphthoquinone})]\) (57) (Scheme 3). The much enhanced stability of 57 towards oxidation rendered its isolation straightforward. Aqueous workup and crystallisation from boiling degassed hexane, afforded complex 57 in 61 % yield starting from 1,4-dihydroxynaphthalene (61) in this two step, one pot sequence. (Section II.1).
Chapter II: Synthesis and reactivity of [Cr(CO)₃(η⁶-5,8-naphthoquinone)]

\[
\begin{align*}
\text{[Cr(CO)₃(NH₃)₃]} & \quad 1 \text{ eq} \\
\begin{array}{c}
\text{BF₃·Et₂O} 6 \text{ eq} \\
\text{Et₂O, r.t.} \\ 5 \text{ days}
\end{array}
\rightarrow
\begin{array}{c}
\text{[Cr(CO)₃(NH₃)₃]} \\
\text{DDQ 1 eq} \\
\text{THF / Et₂O}
\end{array}
\rightarrow
\begin{array}{c}
\text{[Cr(CO)₃(NH₃)₃]} \\
\text{Ag₂O 2.5 eq} \\
\text{MgSO₄ 22 eq} \\
\text{Et₂O, 1h}
\end{array}
\rightarrow
\begin{array}{c}
\text{57, 61 % yield}
\end{array}
\end{align*}
\]

Scheme 3

Attempts of improve yield by varying solvent, concentration or the number of equivalents of BF₃·Et₂O during complexation did not meet with success. Taking a cue from a publication by Dötz’s group we changed the oxidant from DDQ to Ag₂O and found that its use improved the synthesis. The optimised procedure used a slight excess (1.4 eq) of ligand 61. We were pleased to find that under these conditions 2.5 g of crystalline [Cr(CO)₃(η⁶-5,8-naphthoquinone)] (57) was obtained in an excellent 76 % overall yield (12 mmol scale) from 1,4-dihydroynaphthalene (61) (Scheme 4).

\[
\begin{align*}
\text{[Cr(NH₃)₃(CO)₃]} & \quad 1 \text{ eq} \\
\begin{array}{c}
\text{BF₃·Et₂O} 6 \text{ eq} \\
\text{Et₂O, r.t.} \\ 5 \text{ days}
\end{array}
\rightarrow
\begin{array}{c}
\text{[Cr(NH₃)₃(CO)₃]} \\
\text{Ag₂O 2.5 eq} \\
\text{MgSO₄ 22 eq} \\
\text{Et₂O, 1h}
\end{array}
\rightarrow
\begin{array}{c}
\text{57, 76 % yield}
\end{array}
\end{align*}
\]

Scheme 4

The structure of complex 57 was determined by X-ray diffraction analysis (Figure 1). The Cr-C arene distances are shorter for the carbons of the ring junction C(1)-C(6). Consequently, the vertical projection of the chromium fragment does not coincide with the geometric centre of the arene but is displaced (Δ 0.04 Å)[5, 10] towards the ring junction (Appendix VI). This shift is opposite to that usually found in complexes of condensed arene ligands with group VI metals and this observation will be discussed later on (Section II.7). Although the carbonyl groups in complex 57 are nearly coplanar with the adjacent ring
(C2-C1-C10-O2 = 2.9°), they are slightly bent towards the Cr(CO)3 moiety as commonly found in complexes with π acceptor substituents. The Cr(CO)3 tripod adopts a staggered conformation with respect to the arene carbons.

Figure 1: ORTEP view of the crystal structure of 57. Ellipsoids are represented at 40% probability.

[Cr(CO)3(η6-5,8-naphthoquinone)] (57) shows different properties when compared to its free ligand 1,4-naphthoquinone (58). The non-metal complexed 58 is yellow since absorbs radiation corresponding to the blue region of the visible spectra. Complexation to an electron withdrawing group such as Cr(CO)3 fragment depresses the energy of the molecular orbitals. This lowers as well the energy of the electronic transitions of the ligand, absorbing now light from the red region of the visible spectra. In this manner [Cr(CO)3(η6-5,8-naphthoquinone)] (57) exhibits a deep blue colour.

II. 3 Synthesis of [Cr(CO)3(η6-5,8-dihyroxynaphthalene)] (63).

Given the purification problems of 63 upon direct complexation, an alternative route was explored. The literature details quinone reduction to the hydroquinone to occur readily upon single electron transfer reduction using aqueous Na2S2O4 reducing 1,4-naphthoquinone to the corresponding 1,4-dihyroxynaphthalene (61) in near quantitative yield. This is also applicable to 57: vigorous stirring with 1.2 eq of aqueous Na2S2O4...
resulted in a colour change of the mentioned mixture from deep blue to orange. Conversion to [Cr(CO)₃(η⁶-5,8-naphthoquinone)] (63) was nearly quantitative (Scheme 5).[15]

![Scheme 5](image)

The structure of complex 63 was determined by X-ray diffraction analysis (Figure 2). In accord with other naphthalene complexes, the projection of the metal atom onto the arene plane shows a displacement (Δ = 0.05 Å) away from the C(1)-C(6) ring junction and the Cr(CO)₃ tripod adopts a staggered conformation with respect to the arene carbons (Appendix VI).[12] The two rings are coplanar and Cr arene distance is 1.7572 Å. Remarkably, both hydroxyl protons are disposed away from the chromium fragment which might orientate this group by electrostatic interaction between the metal and the oxygen lone pairs.

![Figure 2](image)

**Figure 2:** ORTEP view of the crystal structure of 63. Ellipsoids are represented at 40 % probability.
II.4 Influence of the chromium fragment on the tautomeric behaviour of complexed aromatic enols.

[Cr(CO)₃(η⁶-5,8-dihydroxynaphthalene)] (63) has low solubility in toluene and benzene and experiments carried out by Cyril Poulard showed that this posed problems on filtration through celite as 63 tended to precipitate. He found that that slight warming of the filtration unit with a heat gun caused a change of colour from orange to red; this colour is characteristic of the diketone tautomer [Cr(CO)₃(η⁶-5,8-tetralindione)] (64) (Scheme 6).[2] The equilibrium lies entirely on the side of the diketo form. Under the same conditions, 1,4-dihydroxynaphthalene (61) is a stable enol and no tautomerisation is observed. Indeed, heating 61 at 120 °C in C₆D₆ (closed system) is necessary to start the tautomerisation to the corresponding 1,4-tetralindione. A 1 : 1 equilibrium is reached after more than 20 days of NMR monitoring at this temperature. In contrast, the analogous chromium complex 63 reaches 90 % tautomerisation at lower temperature (50 °C) in only 20 h (Figure 3).[16] Therefore, the chromium fragment has a strong influence on the tautomeric behaviour of ligand 61; this issue will be fully discussed in Section V.3.

![Scheme 6](image)

The tautomerisation of complex 63 was further monitored at different temperatures showing reversible first order kinetics. The data was processed according to Equation 1 where the slope gave the rate constant k at each temperature. Low quantities (2-3 %) of free ligand 61 were detected and this is due to arene exchange with the solvent at higher temperatures. Every glassware component involved in this experiment was silylated with N,O-bis-trimethylsilylacetamide (5 % in Et₂O) since the acidic nature of glass caused acceleration of tautomerisation. However, despite this precautions, no coherent trend of
values of $k$ were obtained when monitoring the tautomisation at different temperatures and therefore no activation parameters could be obtained via a Eyring plot.\textsuperscript{[17]}

This lack of reproducibility has its origin in the poor solubility of 63 in C$_6$D$_6$ (1 mg / mL), resulting in exceedingly small scale and dilute reactions. However, we could observe that the reaction is faster at higher temperatures, as expected for an endothermic process.

II.5 Synthesis of [Cr(CO)$_3$(η$^6$-5,8-tetralindione)] (64).

Spontaneous tautomisation of complex 63 was only observed in aromatic solvents. The main problem encountered was the poor solubility of starting material 63 in aromatic solvents. Good conversions (72-75 %, $^1$H-NMR) were achieved when stirring a suspension of enol complex 63 (20 mg / mL) in benzene, toluene or fluorobenzene at 50-60 °C for three days. Nevertheless, arene exchange with the solvent becomes a side reaction (12-17 %, $^1$H-NMR) at these temperatures and extended reaction times. Fortunately, the keto-enol equilibrium could be accelerated by using additives such as silica or CF$_3$COOH. In both cases, a conversion of 92 % to diketo complex 64. Reaction time was then reduced to 3 h at 70 °C in the presence of CF$_3$COOH (1 eq) with the same conversion (Scheme 7). After removing all volatiles under high vacuum, two successive recrystallisations of the red residue from $^3$Pr$_2$O gave [Cr(CO)$_3$(η$^6$-5,8-tetralindione)] (64) in 85 % yield (2.5 mmol scale). When this reaction was carried out at r.t. in neat CF$_3$COOH large amounts of decomplexation were observed.
Chapter II: Synthesis and reactivity of [Cr(CO)₃(η⁶-5,8-naphthoquinone)]

Scheme 7

The structure of complex 64 was unambiguously determined by X-ray diffraction analysis (Figure 4). Like that of 57, this shows a displacement (Δ = 0.04 Å) of the vertical projection of the metal onto the arene plane towards the ring junction (Section II.7 and Appendix VI). As commonly found in ortho disubstituted meso complexes, the Cr(CO)₃ tripod adopts a staggered conformation with respect to the arene carbons.[12]

Figure 4: ORTEP view of the crystal structure of 64.
Ellipsoids are represented at 40% probability.

II. 6 New concise synthesis of [Cr(CO)₃(η⁶-5,8-tetralindione)] (64).

A new shorter route to [Cr(CO)₃(η⁶-5,8-tetralindione)] (64) can be effected following direct complexation of 1,4-dihydroxynaphthalene (Section II.2). Without further purification, the orange crude [Cr(CO)₃(η⁶-5,8-dihydroxynaphthalene)] (63) was treated with 1 eq CF₃COOH for 3 h in benzene at 70 °C. Under these conditions the tautomerisation of enol complex 63 took place smoothly while free ligand 61 remained intact. Complex 60 was then
isolated by recrystallisation from $^1$Pr$_2$O in a modest 48% yield. Presumably, complex 63 is somewhat labile when heated in the presence of free ligand 61 during tautomerisation since this reaction has been proved to be more efficient when starting from pure complex 63 (Section II.3). This observation could be attributed to metal displacement by coordination to the basic centres of 61. Treatment of crude 63 with 2 eq of CF$_3$COOH in toluene during 16 h at r.t. gave higher conversions and [Cr(CO)$_3$(η$^6$-5,8-tetralindione)] (64) was obtained in 65% overall yield (2.8 mmol scale) after recrystallisation (Scheme 8). This procedure represents more efficient route to diketone complex 64.

![Scheme 8](image_url)

### II.7 Diastereospecific reduction of [Cr(CO)$_3$(η$^6$-5,8-naphthoquinone)] (57) and [Cr(CO)$_3$(η$^6$-5,8-tetralindione)] (64).

[Cr(CO)$_3$(η$^6$-5,8-naphthoquinone)] (57) and [Cr(CO)$_3$(η$^6$-5,8-tetralindione)] (64) are both carbonyl-containing meso-compounds that offer a wide variety of desymmetrisation possibilities. In the absence of an external chiral source the reduction of a carbonyl functionality in the position α to a [Cr(arene)(CO)$_3$] fragment is expected to occur in a fashion anti to the bulky metal fragment.$^{[18]}$ Therefore, bis-reduction of complex 57 or 64 should lead to the corresponding meso-diol complexes, which themselves could be interesting substrates for desymmetrisation by asymmetric acylation or other means.$^{[19-21]}$

[Cr(CO)$_3$(η$^6$-5,8-tetralindione)] (64) was reduced with an excess of NaBH$_4$ to give meso-[Cr(CO)$_3$(η$^6$-5,8-dihydroxytetralin)] (65) in good yield.$^{[22]}$ This is accompanied by a change in colour from red to yellow and is thus easily monitored. The reduction is stereospecific under the influence of the chromium fragment and no other diastereoisomer is detected.
Chapter II: Synthesis and reactivity of $[\text{Cr}(\text{CO})_3(\eta^6-5,8\text{-naphthoquinone})]$ (65) was unambiguously determined by X-ray diffraction analysis (Figure 5). The projection of the metal atom onto the arene plane shows a displacement ($\Delta = 0.04$ Å) away from the C(1)-C(6) ring junction (Appendix VI). As commonly found in ortho disubstituted meso complexes, the Cr(CO)$_3$ tripod adopts a staggered conformation with respect to the arene carbon atoms.[12] As regularly observed in tetralol Cr(CO)$_3$ complexes, both hydroxyl protons are disposed away from the chromium fragment.[23]

**Figure 5:** ORTEP view of the crystal structure of 65. Ellipsoids are represented at 40 % probability.

Reduction of $[\text{Cr}(\text{CO})_3(\eta^6-5,8\text{-dihydroxytetralin})]$ (57) was carried out by Thierry Lomberget[24] under Luche’s[25] conditions with NaBH$_4$/CeCl$_3$$\cdot$7H$_2$O in MeOH giving crystalline *meso*-[$\text{Cr}(\text{CO})_3(\eta^6-5,8\text{-dihydro}-5,8\text{-dixhydroxynaphthalene})$] (66) as a single diastereoisomer in excellent yield.[26] Attesting to the activation of the two keto groups by the Cr(CO)$_3$ fragment, free naphthoquinone is not reduced under these conditions.[27]
Chapter II: Synthesis and reactivity of \([\text{Cr(CO)}_3(\eta^6-5,8\text{-naphthoquinone})]\)

**Scheme 10**

The structure and relative configuration of \(\text{meso-}[\text{Cr(CO)}_3(\eta^6-5,8\text{-dihydro-5,8-dihydroxynaphthalene})]\) (66) was unambiguously determined by X-ray diffraction analysis (Figure 6). In accord with other tetralol complexes, the projection of the metal atom onto the arene plane shows a displacement (\(\Delta = 0.05\) Å) away from the C(1)-C(6) ring junction (Appendix VI). As commonly found in \textit{ortho} disubstituted \textit{meso} complexes, the \text{Cr(CO)}_3 tripod adopts a staggered conformation with respect to the arene carbons.\(^{[12]}\) The non complexed ring adopts a pseudo-boat conformation typically found in 1,4-cyclohexadienes.\(^{[28, 29]}\)

**Figure 6:** ORTEP view of the crystal structure of 66.
Ellipsoids are represented at 40 % probability.

II. 8 Desymmetrisation of \([\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindione})]\) (60) by CBS reduction.

The efficiency of \((S)-3,3\text{-diphenyl-1-methyltetrahydro-3H-pyrrolo[1,2-c]-[1,2,3]\-oxazaborole} (67) as catalyst for the enantioselective reduction of carbonyl compounds is well
established. The catalyst, developed by Corey, Bakshi and Shibata\textsuperscript{[30, 31]} and known as the ‘CBS reagent’, is commercially available.

By following a standard CBS reduction protocol,\textsuperscript{[12]} a solution of [Cr(CO)\textsubscript{3}(\eta\textsubscript{6}-5,8-tetralinedione)] (64) in THF was added slowly over a period of 1 h to a solution of BH\textsubscript{3} THF complex (1.2 eq) and catalyst 67 in THF at -10 °C. The red colour of 64 immediately faded to yellow due to the formation of tetralindiol Cr(CO)\textsubscript{3} derivatives. Mild hydrolysis of this mixture with MeOH and flash chromatography afforded (-)-(5R,8R)-[Cr(CO)\textsubscript{3}(\eta\textsubscript{6}-5,8-tetralindiol)] (68) in 80 % yield, 99 % ee (Chapter IV.6).

Complex (-)-68 undergoes oxidative cleavage of the metal when exposed to light and atmospheric oxygen in MeCN solution to give free ligand (-)-(1R,4R)-tetralindiol, whose configuration is already known.\textsuperscript{[32]} The absolute configuration of complex (-)-68 agrees with the reliable stereochemical model for the CBS reduction (catalyst control, CC). However, carbonyl functionalities in a position \(\alpha\) to a Cr(CO)\textsubscript{3} fragment are generally reduced in \emph{anti} to this bulky group (Substrate control, SC). Schmaltz \textit{et al.} proposed four possible transition states for the kinetic resolution of closely related (±)-[Cr(CO)\textsubscript{3}(\eta\textsubscript{6}-5-tetralone)] by CBS reduction (Scheme 10):\textsuperscript{[33]} In our case this model is applied for the reduction of each carbonyl function of complex 64:

- I: Matched case: SC and CC point in the same direction.
- II: Mismatched case: Unfavourable steric interactions involved during \emph{syn} reduction to the Cr(CO)\textsubscript{3} fragment but also in agreement with the CBS stereochemical model.
Chapter II: Synthesis and reactivity of [Cr(CO)$_3$(η$^6$-5,8-naphthoquinone)]

- III: Unfavourable case: Both the Cr(CO)$_3$ fragment and the catalysts are disposed in a very unfavourable rearrangement.

- IV: Mismatched case: Favourable reduction in anti to the Cr(CO)$_3$ fragment but severe steric repulsions with the catalysts.

As shown by the high yield of (-)-68, bisreduction of complex 64 might proceed mostly via a very favourable transition states I followed by II or vice versa. Remarkably, catalyst 67 efficiently differentiates the π-faces of prochiral carbonyl compounds thought one
of the carbonyl groups would be expected to be inert under substrate control. Thus, both anti (I) and syn (II) reduction to the metal unit take place in a predominant catalyst controlled pathway. The high enantiopurity of (-)-68 is explained by the extremely disfavoured transition state III involved in the synthesis of (+)-68 with catalyst (S)-67. In addition, if catalyst (S)-63 is not able to coordinate the more sterically accessible lone pair of the ketone (as in transition state IV), rapid resolution may take place through very favoured transition state I to give the diastereoisomer meso-[Cr(CO)₃(η⁶-5,8-tetralindiol)] (65) obtained in 18 % yield. Complex 65 could be also formed by non catalysed background reaction under a substrate controlled pathway.

Once we had found an efficient protocol for the desymmetrisation of diketone complex 64, research then focused upon the more challenging enantioselective mono-reduction. The reduction of complex 64 from the most hindered syn face proceeds much slower enhancing the regioselectivity. In addition, in dione 64, both carbonyl functionalities are activated by mutual conjugation through the arene behaving as better electrophiles when compared with ketol complex 69. We turned our attention to a variety of CBS reduction protocols, in particular those involving addition of the reducing agent to the substrate. Thus a solution of catecholborane (1.5 eq) in toluene was added over a period of 20 min to a solution of diketone complex 64 and (S)-3,3-diphenyl-1-butyltetrahydro-3H-pyrrolo[1,2-c][1,2,3]oxazaborole (70) in toluene at -78 °C. At this temperature, further stirring for 18 h was required for completion. After aqueous work-up and flash chromatography, (-)-(8R)-[Cr(CO)₃(η⁶-8-hydroxy-5-tetralone)] (69) was obtained in 98 % yield, 96.6 % ee (Scheme 11). The absolute configuration of ketol complex 69 was confirmed by oxidative cleavage of the metal and recovery of known (-)-(4R)-4-hydroxy-1-tetralone⁴, confirming that this reduction is also in agreement with the stereochemical model for the CBS reduction.
Chapter II: Synthesis and reactivity of \([\text{Cr(CO)}_3(\eta^6-5,8\text{-naphthoquinone})]\)

Remarkably, over-reduction under these low-temperature conditions does not take place even in the presence of an excess of catecholborane (1.5 eq), confirming our hypothesis that the steric limitations imposed by the \(\text{Cr(CO)}_3\) fragment (Scheme 10) cause the reduction anti to this fragment to be much less favourable (Section IV.6).

The structure and absolute configuration of \((-)-(8S)-[\text{Cr(CO)}_3(\eta^6-8\text{-hydroxy-5-tetralone})]\) \((69)\) was confirmed by X-ray diffraction analysis (Figure 5). The projection of the metal atom onto the arene plane shows a displacement \((\Delta = 0.02 \, \text{Å})\) towards \(C(1)\) of the ring junction. In general, the projection of chromium fragment onto the arene in \([\text{Cr(\eta}^6\text{-naphthalene)}(\text{CO)}_3]\) type complexes is displaced away from the \(C(1)-C(6)\) ring junction. The ring junction carbon atoms are quaternary and therefore they cannot \(\pi\) interact with the chromium as efficiently as the other four ring carbons. The haptotropic migration of the chromium fragment in \([\text{Cr(\eta}^6\text{-naphthalene)}(\text{CO)}_3]\) complexes has been predicted to proceed via an exocyclic \(\eta^3\) intermediate. This study reveals very high energy values for the thermotropic migration of the chromium through the \(C(1)-C(6)\) ring junction.

All of these findings contribute to the chromium fragment being displaced from the centre of gravity, away from the ring junction and this is already apparent in the ground state structure. All X-ray structures of a \([\text{Cr(\eta}^6\text{-naphthalene)}(\text{CO)}_3]\) complex shown in this manuscript follows this tendency. In \([\text{Cr(CO)}_3(\eta^6-5,8\text{-naphthoquinone})]\) \((57)\), \([\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindione})]\) \((64)\) and \([\text{Cr(CO)}_3(\eta^6-8\text{-hydroxy-5-tetralone})]\) \((69)\) complexes the opposite is observed. The \(\text{Cr-C}\) bonds to the ring junction are shorter than the others. In the case of complex \(69\) only one electron withdrawing group is bonded to the arene and the measurement of bond distances shows that the \(\text{Cr(CO)}_3\) fragment is shifted 0.02 \(\text{Å}\) towards \(C(1)\) and this carbonyl group (Appendix VI). This displacement is typical for electron-withdrawing groups in complexed aromatic rings.

The structure of \(69\) presented two molecules per asymmetric unit which were linked by hydrogen bonding. The \(\text{Cr(CO)}_3\) tripod adopts a staggered conformation with respect to the arene carbons (Figure 7). Both motives present \(C(9)\) methylene in exo conformation with respect to the metal fragment. The hydroxyl proton is disposed away from the chromium fragment which might orientate this group by electrostatic interaction with the oxygen lone pairs.
II.9 Conclusions and perspectives.

We have developed a new efficient synthesis of \([\text{Cr(CO)}_3(\eta^6-5,8\text{-naphthoquinone})] (57)\) and \([\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindione})] (64)\) from 1,4-dihydroxynaphthalene, both in two step sequence from 1,4-dihydroxynaphthalene (57). These complexes represent an attractive starting material for the synthesis of planar chiral chromium complexes using catalytic amounts of chiral information.

Electron transfer reduction of \([\text{Cr(CO)}_3(\eta^6-5,8\text{-naphthoquinone})] (57)\) with \(\text{Na}_2\text{S}_2\text{O}_4\) gives \([\text{Cr(CO)}_3(\eta^6-5,8\text{-dihydroxynaphthalene})] (63)\) in quantitative yield. Surprisingly, enol complex 63 slowly tautomerises into diketone complex 64 at r.t. in aromatic solvents. The equilibrium is completely displaced to the diketone form 64 and their interconversion shows a first order kinetic pattern. This process could be accelerated in the presence of \(\text{CF}_3\text{COOH}\) allowing a more convenient synthetic protocol. Under these conditions 1,4-dihydroxynaphthalene 61 does not tautomerise to the corresponding dione. Therefore, the \(\text{Cr(CO)}_3\) fragment has an strong influence in the tautomeric behaviour of these ligands.

Desymmetrisation of \([\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindione})] (64)\) by enantioselective CBS bis-reduction in THF at -10 °C gave \((-)(5R,8R)-[\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindiol})] (68)\) in 80 % yield, 99 % ee. This reaction proceeded under catalyst control and one carbonyl function is reduced from the same face of the \(\text{Cr(CO)}_3\). On the other hand, mono-reduction of (64) was successfully performed by using a modified procedure in toluene at -78 °C and proceeded...
both under catalyst and substrate control to give (-)-(8R)-[Cr(CO)₃(η⁶-8-hydroxy-5-tetralone)] (69) in 98% yield, 96.6% ee.

To conclude, the Cr(CO)₃ fragment controls the diastereospecific reduction of carbonyl complexes 57 and 64. These meso-diol complexes 65 and 66 offer new opportunities for desymmetrisation via asymmetric acylation (Section III.3).

The research should now be focused on the monoprotection of [Cr(CO)₃(η⁶-5,8-tetralindione)] (64) with TMSCN assisted by a Lewis acid. This would give access to racemic cyanohydrin complex 71 (Scheme 14). Each enantiomer of (±)-71 could be resolved into highly enantioenriched ketol complexes endo 69 and exo 72 by CBS reduction / deprotection sequence.

Under the steric influence of the Cr(CO)₃ fragment, epimerisation of the hydroxyl stereocenter of complex endo 69 under acidic conditions would afford the exo isomer 72 after aqueous treatment (Scheme 15). The inversion of this chiral centre could also be achieved by Mitsunobu reaction if the phosphine reagents involved in the process are compatible with the chromium fragment.

In addition, the stereochemistry cis-diol complex 65 could be inverted in both benzylic positions by treatment with HBF₄ followed by the addition of water or Mitsunobu.
reaction (Scheme 16). This would give exo-diol complex 73 which both hydroxyl functionalities are in exo to the chromium fragment. This complex is suitable of desymmetrisation by our acyl transfer reaction, already performed on its endo diastereoisomer 65\textsuperscript{[22]} The experiment would allow a comparison of the effect of the chromium fragment in each side of the arene in asymmetric acylation.

\[ \text{Scheme 16} \]
II.10 References.

Chapter II: Synthesis and reactivity of [Cr(CO)$_3$(η$^6$-5,8-naphthoquinone)]

Chapter II: Synthesis and reactivity of $\text{[Cr(CO)}_3(\eta^6-5,8\text{-naphthoquinone})]$
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III. New asymmetric acylation catalysts for the desymmetrisation of 
meso-(Cr(CO)$_3$(η$^6$-5,8-tetralindiol)) type complexes and meso-1,2-diols

With an efficient synthesis of meso-[Cr(CO)$_3$(η$^6$-5,8-dihydro-8-hydroxy-5-
benzoyloxytetralin)] (66) and meso-[Cr(CO)$_3$(η$^6$-5,8-dihydroxytetralin)] (65) in hand 
(Section I.8), we were intrigued by the potential of these complexes as substrates for 
desymmetrisation reactions. While there are many systems already known for the 
desymmetrisation of meso-diols (some of which are described below), compounds 65 and 66 
represent a new class of substrate for this type of reaction. Additionally, we wished to use 
these substrates to explore a novel class of acyl transfer catalyst based upon a truncated 
Cinchona alkaloid scaffold. We here report the successful realisation of this goal, affording an 
access to chiral planar complexes by asymmetric acyl transfer reaction mediated by new 
chiral diamines. Before describing this work, a survey of recent literature on the topic is 
included below. This does not include enzymatic methods whose use is outside the scope of 
this brief review.

III.1 Current methods for the desymmetrisation of meso-diols by acyl transfer 
reaction.

Chiral amines are increasingly finding applications as catalysts or ligands in metal 
catalysed reactions, providing chemists with new tools for the efficient synthesis of complex 
molecules.[1] Consequently, the non-enzymatic kinetic resolution of secondary alcohols has 
emerged as a powerful method for obtaining enantioenriched materials.[2-12] Several authors 
have found suitable catalyst architectures that efficiently discriminate one of the two 
enantiomeric forms with high selectivities. However, kinetic resolution is obviously restricted 
to 50 % conversion and, as usually only one enantiomeric form is needed, this approach 
involves discarding or chemically recycling half of the material. Thus a lot of recent research 
has focused upon alternative routes that overcome this limitation with novel dynamic kinetic 
resolution approaches.[13-19] In the last 12 years, a related strategy has been explored by using 
chiral nucleophilic catalysts in the asymmetric desymmetrisation of meso-diols by acyl 
transfer reaction. In such a diol, the two alcohol functions are enantiotopic rather than 
diastereotopic and so full conversion to a single enantiomer is, at least in theory, possible. In
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of \(\text{meso-}^{(\eta^6-5,8\text{-tetralindiol})}\) type complexes and \(\text{meso}\)-1,2-diols

Figure 1 are depicted the catalysts that efficiently desymmetrise a variety of \(\text{meso}\)-diols by acyl transfer reaction.\[^{20-29}\] In general these methods involve the use of an acyl chloride or anhydride. The acyl group is delivered by the chiral nucleophilic catalyst to one of the two enantiotopic alcohol functions of the \(\text{meso}\)-dil. Stoichiometric amounts of base are generally required to trap the acids generated during the process. The following pages describes some of the most efficient methods for such asymmetric acylations of \(\text{meso}\)-1,2-diols catalysed by chiral nucleophilic catalysts.

Oriyama et al. were pioneers in this field, employing chiral diamine catalyst 74,\[^{25, 30}\] which is easily accessible in 2 steps from \(N\)-Boc-(S)-proline in 82\% yield.\[^{31}\] To date, this report still represents one the most efficient protocols for the desymmetrisation of \(\text{meso}\)-cyclohexane-1,2-diol (75). Even at low loadings (0.5 mol \%), this catalyst efficiently promotes the desymmetrisation of 75, affording highly enantioenriched (+)-(1\(S\),2\(R\))-2-hydroxy-1-cyclohexyl-benzoate (76) in 87\% yield, 97\% ee (Scheme 1). Although a number of bases and acylating agents were screened, the simple combination of \(\text{Et}_3\text{N}\) and \(\text{BzCl}\) gave the best results. Reactions worked best at -78 °C in \(\text{CH}_2\text{Cl}_2\) and in the presence of MS 4Å proceeded somewhat faster. The addition of base was limited to 1 eq in order to avoid over-acylation. Low quantities (0-3 \%) of the undesired dibenzoate were isolated in all cases. This method was applied to a range of \(\text{meso}\)-1,2-diols with excellent conversions and good to
moderate enantioselectivities. Diamine 74 turned out to be less efficient in the desymmetrisation of substrates containing phenyl groups, giving lower enantioselectivities (82-66 % ee). As an additional limitation (R)-proline, the starting material for the enantiomer of 74, is much more costly than (S)-proline.

At the same time, Fu et al. submitted a report including the desymmetrisation of meso-1,4-diol 77 catalysed by 1 mol % of planar-chiral DMAP-type catalyst 78, giving the corresponding monobenzoate 79 in excellent yield and enantioselectivity (Scheme 2).[32, 33] Unfortunately, this is the only example reported for the desymmetrisation of a meso-diol catalysed by (-)-78, despite its impressive performance in kinetic resolution of secondary alcohols.[32, 34] Both rate and enantioselectivity highly depend on the solvent and tert-amyl alcohol at 0 °C proved to give the best results. Tert-amyl alcohol itself is not acylated to any significant extent under these conditions. Being strongly nucleophilic, DMAP-type catalyst (-)-78 is able to transfer the acetyl group from an anhydride source, while other diamine catalysts typically require the use of more reactive acyl chlorides. This feature minimises the likelihood of the competing, and undesired, uncatalysed background acylation. In addition, catalyst (-)-78 does not acylate monobenzoate (+)-79 in the presence of an excess of base and anhydride. The main drawback of this method is the difficult access to enantiopure catalyst 78. First, the aminopyridine ligand requires a low yielding multi-step sequence from commercially available materials.[35] Racemic DMAP catalyst 78 is then obtained by
complexation with FeCl₂ in 48 % yield as a racemate and further preparative chiral HPLC resolution is required.[32]

Yamamoto et al. reported a bifunctional catalyst containing a Lewis basic trivalent phosphorous centre and a Brønsted-basic tertiary amino group. This structure is designed both to activate an acylating reagent and to trap a proton during the acylation reaction. The catalyst 80 is generated in situ from the reaction of chlorodiphenylphosphine and cinchonine in the presence of Hüning’s base in CH₂Cl₂. After much experimentation, use of EtCN as solvent was found necessary for high enantioselectivities in acylation. Using the pseudoeantiomeric cinchonidine as catalyst precursor, the monobenzoate of opposite configuration (-)-80 was obtained in quantitative yield and moderate enantioselectivity (86 % ee). Catalyst 80 did not transfer efficiently acyl fragments from o-MeC₆H₄COCl, (PhCO)₂CO or 'BuCOCl; the corresponding monobenzoates were obtained in low yield (36-0 %) when using these reagents. The main drawback of this method is the high catalyst loadings (30 mol %) required for good performance. The weight of the catalyst added in the reaction exceeds the weight of the substrate, which is clearly not desirable. However, the relatively low cost commercial availability of cinchona alkaloids makes this method a reasonably practical way to desymmetrise a meso-diol.
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of \( \text{meso}-(\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindiol})) \) type complexes and \( \text{meso}-1,2\)-diols

The methods described above deal with the desymmetrisation of vicinal \( \text{meso}-1,2\)-diols. Very few reports cover the desymmetrisation of more remote derivatives as \( \text{meso}-1,4\)-diols.\(^{[36]}\) However, some systems have proved suited to such diols. Trost et al. developed an asymmetric dinuclear zinc catalyst\(^{[27]}\) that was successfully applied in the desymmetrisation of a range of 2-substituted-1,3-propanediols where enzymatic methods have shown poor performance. The mechanism involves coordination of both substrate and acylating agent (vinyl acetate). Acyl delivery to the less sterically hindered enantiotopic alcohol function takes place to yield the highly enantioenriched monobenzoate and acetaldehyde. In addition, chiral ligand \( 83 \) is readily synthesised in 4 steps from \( p \)-cresol. This method was extended to the desymmetrisation of \( \text{meso}\)-cyclohexane-1,2-dimethanol \( 84 \) with excellent results (Scheme 4). The product of this reaction (\( 85 \)) had previously proved useful in the synthesis of antiviral agents.\(^{[37]}\) This method has also been applied to the desymmetrisation a variety of \( \text{meso}\)-propane-1,3-diols to give the corresponding monobenzoates in high yield and high to moderate enantiopurity.
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of
meso-(Cr(CO)$_3$(η$^6$-5,8-tetralindiol)) type complexes and meso-1,2-diols

Scheme 4

A very different contribution to this field was made by Vedejs et al., with the development of chiral phosphines as nucleophilic catalysts. The asymmetric acylation of meso-hydrobenzoin 81 catalysed by phosphine 86 in the presence of 2.5 eq of (PhCO)$_2$O was achieved in good 93.7 % ee and moderate 70 % conversion (Scheme 5). This application has not yet been fully developed, but is an extension of the use of these catalysts in the field of kinetic resolution of secondary alcohols. Large amounts of undesired dibenzoate were obtained as a byproduct under all the conditions tested, and high catalyst loadings were needed for high conversions. Catalyst 86 is also not easy to access, being obtained in 5 steps from (S)-Roche’s ester. Unfortunately, this is the only example reported for the desymmetrisation of a meso-diol catalysed by phosphine 86,
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of \textit{meso-}(Cr(CO)\textsubscript{3}(\eta\textsubscript{6}-5,8-tetralindiol)) type complexes and \textit{meso}-1,2-diols

There are also a number of examples of diol desymmetrisation involving metal catalysts with chiral ligands. Pfaltz \textit{et al.} synthesised novel chiral boron-bridged bisoxazolines by assembly of a metalated oxazoline with a diaryl haloborane (Scheme 6).\textsuperscript{[23]} The resulting lithium salts were converted into the protonated ligands during chromatographic work-up on silica gel. This strategy, which differs from synthetic approaches to bisoxazoline ligands, is attractive because the ligand is assembled in a single step from simple oxazolines. Following the work of Matsumura \textit{et al.} in the kinetic resolution of secondary alcohols,\textsuperscript{[9, 40]} the catalyst was then generated \textit{in situ} by complexation of bisoxazoline 87 with CuCl\textsubscript{2}. A catalytic amount of this copper complex (1 mol %) effectively promoted the desymmetrisation of some \textit{meso}-diols in the presence of a stoichiometric amount of Hünig’s base and BzCl at 0 °C to give the corresponding monobenzoates in moderate yields and enantioselectivities [83 yield, 90 % ee for \textit{meso}-cyclohexane-1,2-diol (75)]. This preliminary result gives an example of the great potential of boron-bridged bisoxazolines in enantioselective acyl transfer reactions. Very few \textit{meso}-1,2-diols were desymmetrised under these conditions to give the corresponding monobenzoates in good to moderate yields and enantioselectivities.
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of \( \textit{meso}-(\text{Cr}(\text{CO})_3(\eta^6-5,8\text{-tetralindiol})) \) type complexes and \( \textit{meso}-1,2\)-diols

Recently, Yamada \textit{et al.} introduced a new class of DMAP catalyst having an interesting conformational switch system in which interconversion between self-complexation (88) and decomplexation is induced by acylation and deacylation steps (Scheme 7).\textsuperscript{[36]} The \( \pi \)-interaction between the pyridinium ring and the thiocarbonyl group fixes the conformation of the acylated catalyst, leaving nucleophiles to attack from the less-hindered side. At low loadings, catalyst 89 efficiently desymmetrised \( \textit{meso}-1,4\)-diol 90 in the presence of a slight excess of \((\text{iPr}_2\text{CO})_2\text{O}\) and \(\text{Et}_3\text{N}\). Significantly, catalyst 89 performed best in the desymmetrisation of 1,4 to 1,6 \( \textit{meso} \)-diols. These \( \textit{meso} \)-diols have received little attention by other authors. Catalyst 89 is easily accessible in 2 steps from commercially available 4-chloronicotinic acid by introduction of the dimethylamino group in 4-position and condensation with the chiral oxazolidin-2-thione fragment.
Shirai et al. described a new class of $C_2$-symmetric alicyclic diamine 92 derived from (S)-proline (Scheme 8).\textsuperscript{[21]} Also drawing upon the work of Matsumura et al.,\textsuperscript{[9, 40]} the catalyst was preformed generated in situ by complexation of diamine 92 with CuCl$_2$. The desymmetrisation of a variety of meso-diols proceeded smoothly in the presence of an excess of Hünig’s base and BzCl at low temperature to give the corresponding monobenzoates in high yield and enantiomeric purity. The mechanism of acylation was proposed to involve the bidentate coordination of the starting material with the catalyst conferring a chiral environment to the substrate. Then, enantioselective deprotonation of the less hindered coordinated alcohol function takes place under the influence of ligand. The resulting coordinated alkoxide is then acylated. According to this mechanism, the formation of dibenzoate is severely restricted. Catalyst (−)-92 can be synthesised in 4 steps from (S)-proline in moderate 28 % yield; as with the work of Oriyama, and the low availability of the $R$ enantiomer severely limits the general utility of this method. However, replacing (−)-92 with a
CuCl$_2$-(-)-sparteine complex gave monobenzoate (+)-76 of opposite configuration in 80 % yield and 94 % ee, thus this complexes serves as the pseudoenantiomer of CuCl$_2$-(-)-92.

This section has listed the most efficient methods for the asymmetric desymmetrisation of meso-diols. The methods are generally based on acyl delivery from a chiral nucleophilic catalyst. The number of reports on kinetic resolution of secondary alcohols by similar means is much larger. While this is outside the limited scope of this review, we should mention the enormous contribution of Spivey,[3, 22] Birman,[4, 41] Kawabata,[42, 43] Miller[44-46] and Matsumura[9, 40] to this field.

### III.2 New chiral diamines derived from Cinchona alkaloids.

As discussed above, some of these catalysts require multiple step synthesis, preparative HPLC resolution, or the need of high catalyst loadings for good performance. Therefore, there remains a need for new nucleophilic catalysts of straightforward access as well as new protocols that complement the existing methods.

We turned our attention to the structural motif of the Cinchona alkaloids (Scheme 9), an important chiral pool source that has inspired the design of many organocatalysts and
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meso-(Cr(CO)_3(η^6-5,8-tetralindiol)) type complexes and meso-1,2-diols

ligands for metal catalysed reactions.[1, 47] These alkaloids contain a highly nucleophilic quinuclidine structure which we hoped would behave as an asymmetric acyl transfer catalyst.

Although many applications of Cinchona alkaloids use derivatives of the whole molecule, we sought to simplify our catalysts by using only the quincorine or quinuclidine portions, available by degradation of the natural alkaloids (Scheme 9).[47] In choosing to strip the alkaloids to the core function of chiral nucleophilic quinuclidine with a second tertiary amine we reduce the molecular weight by 40%. It remained to be seen if this would still have the essentials for chiral induction in the reaction under investigation. Taking advantage of the electronic and steric features of this core, we have found a very practical route to access the pseudoenantiomeric diamine catalysts (2S,4S,5R)-N,N-dimethyl-2-aminomethyl-5-ethylquinuclidine (93) and (2R,4S,5R)-N,N-dimethyl-2-aminomethyl-5-ethene-quinuclidine (94).[47-49] Diamines 95 and 96 are commercially available materials that allow an extremely straightforward access to gram quantities of enantiopure catalysts 93 and 94 in high yield by reductive Eshweiler-Clark reaction[50] and hydrogenation. Flash chromatography is avoided as purification can be effected via extraction of the corresponding ammonium salts in acidic aqueous media.

Diamines 95 and 96 react on contact with CO₂ (from the air) to form the primary ammonium carbonate salt as a white solid and thus they should not stand in air for extended periods of time.[51]
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)$_3$(η$^6$-5,8-tetralindiol)) type complexes and meso-1,2-diols

Tertiary diamines 93 and 94 react spontaneously with CH$_2$Cl$_2$ at r.t. to give the corresponding chloromethylammonium chloride salt (the Menshutkin reaction),[52] a consequence of the high nucleophilicity of the quinuclidine core. Identifying this reaction and avoiding this solvent during catalyst synthesis and manipulation therefore improved our initial synthesis greatly. However, diamines 93 and 94 could be used as catalysts using CH$_2$Cl$_2$ as solvent if the diamine solution was prepared and rapidly cooled at the reaction temperature (ca. -40°C). These diamines remained unchanged during 24 h in CDCl$_3$ solution at room temperature.

With an efficient access to diamines 93 and 94 in hand, we proceeded next to test their activity as catalyst for the asymmetric acylation of the ready available meso-1,4-diol complexes described in Section II.7.

III.3 Asymmetric acylation of meso-[Cr(CO)$_3$(η$^6$-5,8-tetraline)] type complexes.

Impressed by the literature results, Thierry Lomberget[53] in our group first tested the (S)-proline derived catalyst 74 developed by Oriyama[25] for the asymmetric acylation of meso-1,2-diols (Scheme 10). Although being a 1,4-diol rather than a 1,2-diol, the reaction of meso-[Cr(CO)$_3$(η$^6$-5,8-dihydro-5,8-dioxynaphthalene)] (66) with BzCl in the presence of Et$_2$N and diamine catalyst 74 proceeded smoothly, providing monobenzoate (-)-(5S,8R)-[Cr(CO)$_3$(η$^6$-5,8-dihydro-5-hydroxy-8-benzoyloxynaphthalene)] (97) in good isolated yields and good to excellent enantiomeric excess (Table 1, Entries 1-2).[54] Small amounts of unstable dibenzoate 98 were also formed as a side product.

(R)-proline, the starting material for the enantiomer of 74 is less accessible and we therefore looked for easily accessible diamines 93 and 94 available in both pseudoenantiomeric forms that might provide an access to either (+)-97 or (-)-97. Indeed, both 93 and 94 outperformed catalyst 74 in the enantioselective monobenzoylation of 66, and as shown in Entry 5, the amount of catalyst can be reduced to 2 mol % without loss of asymmetric induction. Being pseudoenantiomers, diamine 93 and 94 gave access to (-)-97 and (+)-97 respectively. However, we have found diamine 93 promotes a more rapid reaction when compared to 94 under the same conditions (Entries 3 and 4). Best results were obtained when both BzCl and Et$_3$N were stirred under N$_2$ over CaH$_2$ in an H-tube for no more than 1 h and then freshly distilled prior to use.
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of *meso-(Cr(CO)₃(η⁶-5,8-tetralindiol))* type complexes and *meso-1,2-diols*

![Chiral diamine 74, 93 or 94](image)

**Scheme 5**

**Table 1**

<table>
<thead>
<tr>
<th>Entry</th>
<th>T (ºC)</th>
<th>Diamine</th>
<th>Yield (97)a</th>
<th>ee⁰ (enantiomer)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-40</td>
<td>74 (10 mol %)</td>
<td>71 %</td>
<td>96 % (-)</td>
</tr>
<tr>
<td>2</td>
<td>-60</td>
<td>74 (10 mol %)</td>
<td>74 %</td>
<td>98 % (-)</td>
</tr>
<tr>
<td>3</td>
<td>-40</td>
<td>94 (10 mol %)</td>
<td>80 %</td>
<td>97 % (+)</td>
</tr>
<tr>
<td>4</td>
<td>-40</td>
<td>93 (10 mol %)</td>
<td>89 %</td>
<td>99 % (-)</td>
</tr>
<tr>
<td>5</td>
<td>-40</td>
<td>93 (2mol %)</td>
<td>83 %</td>
<td>99 % (-)</td>
</tr>
</tbody>
</table>

a) Isolated yield. b) Determined by HPLC.

The 5S,8R configuration of (-)-97 was unambiguously determined by X-ray diffraction analysis (Figure 2). The projection of the metal atom onto the arene plane shows a displacement (Δ = 0.01 Å) away from the C(1)-C(6) ring junction and the non complexed ring adopts a pseudo-boat conformation typically found in 1,4-cyclohexadienes.⁵⁵, ⁵⁶ The conformation adopted by the Cr(CO)₃ tripod leaves the projection of a carbonyl distorted staggered with respect to C(1) or C(6). Most of the (Cr(η⁶-arene)(CO)₃) that have been studied to date do not present this conformation⁵⁷ and this can be attributed to additional steric repulsions between the Cr(CO)₃ tripod and the benzoyl moiety. The benzoyl fragment presents an intermolecular π stacking interaction (d = 3.4 Å) with the metal coordinated arene.
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)_3(η^6-5,8-tetralindiol)) type complexes and meso-1,2-diols

Figure 2: ORTEP view of the crystal structure of 97. Ellipsoids are represented at 40% probability.

My contribution to this project consisted in the development of an efficient route to these chiral diamine catalysts and the extension of this method to the desymmetrisation of meso-[Cr(CO)_3(η^6-5,8-dihydroxytetralin)] (65) (below) and metal-free meso-1,2-diols (Section III.4 to III.6). As hoped, both 93 and 94 performed well in the acyl transfer reaction, efficiently desymmetrising the analogous meso-diol (65) (Scheme 11). As found in the desymmetrisation of complex 66, quincorine derived diamine 93 perform better than quinidine derived diamine 94 under the same conditions (Table 2, Entries 2-3). Dibenzoate 100 was also isolated in less than 10% yield in all cases.
Chapter III : New asymmetric acylation catalysts for the desymmetrisation of
meso-(Cr(CO)₃(η⁶-5,8-tetralindiol)) type complexes and meso-1,2-diols

Table 2

<table>
<thead>
<tr>
<th>Entry</th>
<th>T (ºC)</th>
<th>Diamine</th>
<th>Yield (99)a</th>
<th>ee⁰ (enantiomer)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-60</td>
<td>74 (10 mol %)</td>
<td>78 %</td>
<td>95 % (-)</td>
</tr>
<tr>
<td>2</td>
<td>-60</td>
<td>94 (10 mol %)</td>
<td>80 %</td>
<td>94 % (+)</td>
</tr>
<tr>
<td>3</td>
<td>-60</td>
<td>93 (10 mol %)</td>
<td>76 %</td>
<td>99 % (-)</td>
</tr>
</tbody>
</table>

a) Isolated yield. b) Determined by HPLC.

The 5S,8R configuration of (-)-99 was assigned based on comparison of its CD spectrum with that of (-)-(5S,8R)-[Cr(CO)₃(η⁶-5,8-dihydro-8-hydroxy-5-benzoyloxytetralin)] (97) (Figure 3).

![Figure 3](image)

III.4 Mechanistic considerations.

Concerning the mechanism for the asymmetric acylation of meso-diols with chiral diamines, we expected the reaction of nucleophilic catalyst 93 with BzCl to form a chiral intermediate responsible for the enantioselective acyl delivery, as previously suggested by Oriyama.[25] In order to support this argument, diamine 93 was dissolved in Et₂O at r. t. and the addition of 1 eq of BzCl resulted in the quantitative formation of a white precipitate as a sole product (Scheme 4).
Chapter III : New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)₃(η₆-5,8-tetralindiol)) type complexes and meso-1,2-diols

The resulting acylammonium chloride complex has been characterised by NMR, IR and LRMS. However, the connectivity of the N-acyl bond is a query that remained unanswered. Long range correlation NMR spectra (HMBC) did not show $J^3 \text{H}^1-\text{C}^{13}$ carbonyl coupling with any proton in CH (2), CH₂ (6) and CH₂ (8) for complex 101 or CH₂ (9) and 2*CH₃ (11) for complex 102. We were unable to elucidate the true N-benzoyl bond connection by using this technique even after further data accumulation (128 NMR scans); this is probably due to the low intensity of the carbonyl $\text{C}^{13}$ signal. On the other hand, the bridgehead nitrogen in diamine 93 should be substantially more nucleophilic that the dimethylamino moiety and one would expect exclusive formation of complex 101. However, the observed spectroscopic data and the literature reported values for similar acylammonium cations do not fully agree with this assumption. All the $^1\text{H}$ and $^{13}\text{C}$ NMR signals of diamine 93 and its benzoyl complex have been assigned and compared, and are discussed below. As shown in Figure 4 and Table 3, a noticeable change in the chemical shift values ($\delta$) for diamine 93 is observed upon incorporation of BzCl in the structure.
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of *meso-(Cr(CO)₃(η⁶-5,8-tetralindiol))* type complexes and *meso*-1,2-diols

![Diagram of complexes](image)

**Figure 4**

**Table 3:** a) $\Delta \delta = \delta (93 + \text{BzCl}) - \delta (93)$.

<table>
<thead>
<tr>
<th>Signal</th>
<th>$\delta$ (93)</th>
<th>$\delta$ (93 + BzCl)</th>
<th>$\Delta \delta^a$</th>
<th>$\delta$ (93)</th>
<th>$\delta$ (93 + BzCl)</th>
<th>$\Delta \delta^a$</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH (2)</td>
<td>2.86</td>
<td>3.35</td>
<td>0.49</td>
<td>53.5</td>
<td>54.9</td>
<td>1.4</td>
</tr>
<tr>
<td>CH₂ (3)</td>
<td>1.81, 0.90</td>
<td>2.15, 1.35</td>
<td>0.45</td>
<td>27.0</td>
<td>25.1</td>
<td>-1.9</td>
</tr>
<tr>
<td>CH (4)</td>
<td>1.69</td>
<td>2.00</td>
<td>0.31</td>
<td>25.5</td>
<td>24.8</td>
<td>-0.7</td>
</tr>
<tr>
<td>CH (5)</td>
<td>1.40</td>
<td>1.83</td>
<td>0.43</td>
<td>37.3</td>
<td>35.5</td>
<td>-1.8</td>
</tr>
<tr>
<td>CH₂ (6)</td>
<td>3.14, 2.38</td>
<td>3.57, 2.72</td>
<td>0.39</td>
<td>57.6</td>
<td>56.0</td>
<td>-1.6</td>
</tr>
<tr>
<td>CH₂ (7)</td>
<td>1.50</td>
<td>1.83</td>
<td>0.33</td>
<td>28.4</td>
<td>23.5</td>
<td>-4.9</td>
</tr>
<tr>
<td>CH₂ (8)</td>
<td>2.95, 2.65</td>
<td>3.25, 3.10</td>
<td>0.37</td>
<td>40.9</td>
<td>41.0</td>
<td>0.1</td>
</tr>
<tr>
<td>CH₂ (9)</td>
<td>2.44, 2.12</td>
<td>2.85, 2.43</td>
<td>0.36</td>
<td>64.0</td>
<td>61.2</td>
<td>-2.8</td>
</tr>
<tr>
<td>CH₃ (11)</td>
<td>2.22</td>
<td>2.33</td>
<td>0.11</td>
<td>45.9</td>
<td>46.0</td>
<td>0.1</td>
</tr>
<tr>
<td>CH₂ (12)</td>
<td>1.35</td>
<td>1.45</td>
<td>0.10</td>
<td>27.5</td>
<td>26.8</td>
<td>-0.7</td>
</tr>
<tr>
<td>CH₂ (13)</td>
<td>0.85</td>
<td>0.90</td>
<td>0.05</td>
<td>12.1</td>
<td>11.8</td>
<td>-0.3</td>
</tr>
</tbody>
</table>
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)$_3$(η$^6$-5,8-tetralindiol)) type complexes and meso-1,2-diols

The $^1$H NMR signals of the groups $\alpha$ to a cationic $N$-acyl group should show a downfield displacement of about 1 ppm upon the formation of benzoylammonium complex 101 or 102, as previously reported for $N$-benzoyltriethylammonium tetraphenylborate and $N$-benzoyltriethylammonium tetrafluoroborate complexes.$^{[58]}$ The highest down-field $\delta$ displacements (0.37-0.49 ppm) were observed for CH (2), CH$_2$ (6) and CH$_2$ (8), consistent with structure 101, but these values did not reach the typical 1 ppm downfield displacement previously reported for benzoylamonium derivatives. In contrast, structure 102 can probably be disregarded as only a small (0.11 ppm) down-field $\delta$ displacement for the dimethylamino fragment is observed when compared to the starting material 93. Remarkably, groups $\beta$ to the bridgehead nitrogen show the expected down-field $\delta$ displacement for CH$_2$ (3), CH (5) and CH$_2$ (7) (0.33-0.45 ppm). Regarding the aromatic region of the $^1$H NMR spectra, insignificant changes are noted in BzCl when compared to its benzoylammonium complex (Table 4). Surprisingly, the $^{13}$C NMR signals of diamine 93 show a general decrease of the $\delta$ values upon complex formation in both the aromatic and aliphatic regions. The carbonyl shows 162.6 ppm $^{13}$C signal, a rather low value when compared to 172.2 ppm reported for $N$-benzoyltriethylammonium tetraphenylborate.

<table>
<thead>
<tr>
<th>Signal</th>
<th>$\delta$ BzCl</th>
<th>$\delta$ (93 + BzCl)</th>
<th>$\delta$ dif</th>
<th>$\delta$ BzCl</th>
<th>$\delta$ (93 + BzCl)</th>
<th>$\delta$ dif</th>
</tr>
</thead>
<tbody>
<tr>
<td>CO</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>168.4</td>
<td>162.3</td>
<td>-6.1</td>
</tr>
<tr>
<td>C</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>133.2</td>
<td>128.7</td>
<td>-4.5</td>
</tr>
<tr>
<td>o-CH$_2$</td>
<td>8.13</td>
<td>8.14</td>
<td>-0.01</td>
<td>131.4</td>
<td>130.5</td>
<td>-0.9</td>
</tr>
<tr>
<td>m-CH$_2$</td>
<td>7.52</td>
<td>7.51</td>
<td>-0.01</td>
<td>128.9</td>
<td>128.8</td>
<td>-0.1</td>
</tr>
<tr>
<td>p-CH</td>
<td>7.69</td>
<td>7.66</td>
<td>-0.03</td>
<td>135.3</td>
<td>134.5</td>
<td>-0.8</td>
</tr>
</tbody>
</table>

The following experiment was carried out in order to shed some light on the true $N$-benzoyl bond connectivity of the benzoylammonium complex of diamine 93. Quinuclidine (103) was stirred in Et$_2$O at r.t. and the addition of 1 eq of BzCl caused the quantitative formation of benzoylquinuclidinium chloride (104) (Scheme 13).
Chapter III : New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)$_3$(η$^6$-5,8-tetralindiol)) type complexes and meso-1,2-diols

![Scheme 8](image)

The spectroscopic analysis of 104 shows several similarities to the spectroscopic data of the benzoylammonium chloride complex of diamine 93:

- $^{13}$C NMR of complex 104: δ (ppm) 162.5, 134.6, 130.7, 129.0, 128.8, 46.4, 23.2, 19.5. The aromatic region presents roughly the same chemical shifts as those found in the benzoylammonium chloride complex of diamine 93. In addition all δ of complex 104 are displaced up-field when compared to quinuclidine (102) itself, as previously observed for diamine 93 and its benzoylammonium chloride complex.

- $^1$H NMR of complex (104): δ (ppm) 8.41 (d, $J = 8.4$ Hz, 2H), 7.67 (t, $J = 7.5$ Hz, 2H), 7.52 (t, $J = 7.5$ Hz, 2H), 3.35-3.25 (m, 6H), 2.21-2.15 (m, 1H), 1.97-1.85 (m, 6H). The aromatic region presents roughly the same chemical shifts than those found in the benzoylammonium chloride complex of diamine 93. Upon addition of BzCl to quinuclidine (103), all $^1$H NMR signals in the aliphatic region are down-field displaced (0.45 ppm). This displacement was also observed for the quinuclidine core signals in diamine 93 upon BzCl addition (Table 3).

This experiment implies that the addition of BzCl to diamine 93 involves nucleophilic attack by the more nucleophilic bridge-head nitrogen of the quinuclidine core, leading to the exclusive formation of complex 101 which we presume be the chiral acyl transfer intermediate responsible for the enantioselective acylation of meso-diols.
Chapter III : New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)₃(η⁶-5,8-tetralindiol)) type complexes and meso-1,2-diols

Infrared spectroscopy is also consistent with the formation of benzyol ammonium complex 101, showing (cm⁻¹) 2967 ν(C-H), 2878 ν(C-H), 2782 ν(C-H), 1789 ν(C=O), 1461 ν(aryl C-C), 1109 ν(C-N) and 909 δ_oosp (aryl C-H).

Unfortunately, labile benzoyl ammonium complex 101 decomposed during low resolution mass spectrometry and the molecular benzyol ammonium cation could not be detected. However, electronic impact mass spectroscopy gave a fragmentation pattern in agreement with the structure of 101 (Section V.3.2).

Fu and co-workers were able to obtain an X-Ray structure of the acetyl ammonium PF₆ salt of their ferrocenyl DMAP catalyst 78 (Section III.1). However, all attempts to crystallise chloride complex 101 or its tetraphenylborate salt failed and structural information is not available. Although the detailed mechanism has not been explained, a reasonable catalytic cycle for the asymmetric acylation process is outlined in Scheme 14. The final enantiopurity of monobenzoate 99 is a combination of the enantioselectivity during the acylation of diol 65 and possible further kinetic resolution during formation of the dibenzoate 100 (very minor product). The catalyst is then regenerated with Et₃N from its ammonium.

![Scheme 9](image-url)
III.5 Asymmetric acylation of *meso*-cyclohexene-1,2-diol (75).

To explore further the potential of quinuclidine organocatalyst 93 in the desymmetrisation of *meso*-1,2-diols, we have studied the enantioselective monobenzylation of *meso*-cyclohexane-1,2-diol (75) as model substrate. As a starting point, we choose the conditions employed for the desymmetrisation of *meso*-*(Cr(arene)(CO)₃)* diol complexes but with lower catalyst loadings.[59, 60] The asymmetric acylation of 75 was carried out in CH₂Cl₂ at -60°C with 5 mol % of catalyst 93, 1.5 eq of BzCl and 1 eq of Et₃N in the presence of molecular sieves (Scheme 15 and Table 5). It was very encouraging to find that this first experiment gave monobenzoate 76 in very high enantiopurity and good conversion (Entry 1). However, a large amount of undesired dibenzoate 105 was also detected together with some unreacted material. This might be due to the low solubility of the starting material 75 in CH₂Cl₂ at low temperature, thus being not entirely available for acylation. At advanced reactions times the mixture is highly enriched with monobenzoate 76 which competes as benzoyl acceptor to give undesired dibenzoate 105. Upon temperature screening, enantiopure monobenzoate 76 was obtained at -30°C in good conversion (Entry 2). However, dibenzoate 105 is still formed as a side product, lowering the efficiency of the process. At 0°C the enantioselectivity drops considerably and therefore -30°C was fixed as the optimal temperature for further optimisation. As shown in Entry 4, doubling the concentration gave the same 76 / 105 ratio with an erosion of the enantioselectivity. The proportion of dibenzoate 105 was effectively reduced under more dilute conditions but a larger amount of starting material remained unreacted and consequently the conversion of monobenzoate 76 did not improve (Entry 5). Remarkably, the enantiomeric excess of 76 is high in this case and this indicates that the second acylation does not improve the ee as a result of kinetic resolution. In conclusion, higher dilution does not improve the process, so the optimal concentration was fixed at 0.11 M. Except for high dilution conditions, the number of equivalents of acyl transferred to *meso*-diol 75 is always close to 1.10 which relies on 1 eq of Et₃N and 0.05 eq of diamine 93 converted to the corresponding ammonium salts during the process. To summarise, the conditions chosen for ongoing use were 0.11 M in CH₂Cl₂, at -30°C with 5 mol % of catalyst, 1.5 eq of BzCl and 1 eq of Et₃N in the presence of molecular sieves.
Chapter III : New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)₃(η⁶-5,8-tetralindiol)) type complexes and meso-1,2-diols

![Scheme 10](image)

**Table 5**

<table>
<thead>
<tr>
<th>Entry</th>
<th>T (ºC)</th>
<th>[75]₀ (M)</th>
<th>% 75ᵃ</th>
<th>% 76ᵃ</th>
<th>% 105ᵃ</th>
<th>eq acylᵇ</th>
<th>% eeᶜ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-60</td>
<td>0.11</td>
<td>13</td>
<td>62</td>
<td>25</td>
<td>1.12</td>
<td>96.2 (+)</td>
</tr>
<tr>
<td>2</td>
<td>-30</td>
<td>0.11</td>
<td>7</td>
<td>74</td>
<td>19</td>
<td>1.12</td>
<td>99.9 (+)</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>0.11</td>
<td>9</td>
<td>77</td>
<td>14</td>
<td>1.05</td>
<td>92.3 (+)</td>
</tr>
<tr>
<td>4</td>
<td>-30</td>
<td>0.22</td>
<td>12</td>
<td>70</td>
<td>18</td>
<td>1.06</td>
<td>93.9 (+)</td>
</tr>
<tr>
<td>5</td>
<td>-30</td>
<td>0.055</td>
<td>16</td>
<td>75</td>
<td>9</td>
<td>0.93</td>
<td>97.3 (+)</td>
</tr>
</tbody>
</table>

ᵃ) NMR ratios. b) Equivalents of benzoyl transferred to 75. c) Monobenzoate 76 HPLC.

The influence of the number of equivalents of benzoyl chloride and Et₃N was also explored. Conversions and enantioselectivities did not vary much when either one of the two reagents was added in excess and the other in stoichiometric amount. It was noticed that a lower or higher number of equivalents of base had a linear influence on the total number of equivalents of benzoyl transferred to 75 when BzCl is in excess. Furthermore, slow addition of either BzCl and/or Et₃N did not result in any significant change to crude ratios or enantiopurity. This indicates that these reagents are both highly reactive in this catalytic cycle since no variation is observed even when reacting at low concentration imposed by its slow addition.

For comparison purposes, the desymmetrisation of meso-cyclohexen-1,2-diol (75) was effected under these conditions using 5 mol % of (2S,4S,5R)-N,N-dimethyl-2-aminomethyl-5-vinylquinuclidine 95, which is the unsaturated analogue of diamine 93 (Scheme 16). After aqueous work up, we observed 75, 76, 105 in 17 : 75 : 8 ratio (¹H NMR) in the crude mixture and 90.7 % ee for monobenzoate (+)-76. In catalyst 93, the ethyl side chain is far away from
Chapter III : New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)₃(η⁶-5,8-tetralindiol)) type complexes and meso-1,2-diols

the nucleophilic centres. However, even this remote structural modification had a dramatic effect upon enantioselectivity.

![Scheme 11](image)

Electronic effects were also investigated by using different para substituted benzoyl chlorides (Scheme 17 and Table 6). The formation of dibenzoate is disfavoured upon addition of a softer electrophile, while more electron deficient p-fluorobenzoyl chloride had the opposite effect (Entries 2 and 3). The asymmetric acylation of meso-cyclohexane-1,2-diol (75) with p-toluoyl chloride did not bring any improvements (Entry 4) and surprisingly, more hindered o-toluoyl derivative brought about a substantial decrease in selectivity (Entry 5). This effect has also been observed by Oriyama in the kinetic resolution of secondary alcohols.[7] The para dimethylamino analogue also performed the acylation of 75 but acted as well as a ‘proton sink’ and high conversion was accompanied by overacylation (Entry 6).[22] Furoyl chloride is an attractive acyl source due to its ready availability from the aldehyde (6 % w in corn) but did not outperform benzoyl chloride (Entry 7). In addition, chiral catalyst 93 did not transfer acyl fragments efficiently from benzoic or acetic anhydrides in CH₂Cl₂ at -30°C or in a more polar medium such as tert-amyl alcohol at 0°C.[33] Similarly, Yamamoto’s catalyst 80 (Section III.1), which includes the quinuclidine core, gave very poor conversions (17-36 %) when using anhydrides as acylating agents.

A small set of bases were also screened. The more hindered Hünig’s base simply gave lower conversion than Et₃N (Entry 8). Quinuclidine, being a better nucleophile, only brought lower selectivities and gave a larger amount of undesired dibenzoate 105 (Entry 9). Remarkably, diamine 93 was not efficiently regenerated through the catalytic cycle with an inorganic base (Cs₂CO₃), with low conversions and enantioselectivities achieved (Entry 10).
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)$_3$(η$^6$-5,8-tetralindiol)) type complexes and meso-1,2-diols

When using proton sponge as base, monobenzoate 76 was obtained in good conversion and enantiopurity but the cheaper Et$_3$N was not outperformed, and so this remained the best base for this process (Entries 1 and 11). In summary, the enantioselectivity and conversion ratio strongly depend on the nature of the base. This suggests either an active participation of the base in the enantioselective transition state or large changes in the background reaction rates (either the non-catalytic benzylation or catalyst regeneration reactions).

\[
\begin{align*}
\text{Scheme 12}
\end{align*}
\]

Table 6

<table>
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<tr>
<th>Entry</th>
<th>R</th>
<th>Base</th>
<th>% 75$^a$</th>
<th>% Mo$^a$</th>
<th>% Di$^a$</th>
<th>eq Acyl$^b$</th>
<th>% ee$^c$</th>
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<td>Et$_3$N</td>
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<td>74</td>
<td>19</td>
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<tr>
<td>2</td>
<td>p-MeOC$_6$H$_5$</td>
<td>Et$_3$N</td>
<td>16</td>
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<td>12</td>
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<td>97.4 (+)</td>
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<td>Et$_3$N</td>
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<td>71</td>
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<td>iPr$_2$EtN</td>
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</tr>
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<td>Quinuclidine</td>
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<td>C$_6$H$_5$</td>
<td>Cs$_2$CO$_3$</td>
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<td>75</td>
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<td>95.9 (+)</td>
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</table>

a) NMR ratios  b) equivalents of acyl transferred to 75  c) HPLC.
Chapter III : New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)$_3$(η$_6$-5,8-tetralindiol)) type complexes and meso-1,2-diols

When the acylation of meso-cyclohexane-1,2-diol (75) was carried out in the absence of catalyst, racemic monobenzoate 76 was detected in low (20 %) yield after 22 h reaction in CH$_2$Cl$_2$ at -30°C, showing that the background reaction can have only a small effect under these conditions. The effect of moisture on the catalytic system was also tested. Non-dried CH$_2$Cl$_2$ (137 ppm H$_2$O) was used as solvent in the absence of molecular sieves and the 75, 76, 105 ratio was determined by NMR as 15 : 52 : 33, revealing very poor performance under undried conditions. However, monobenzoate 76 was still obtained in high enantiopurity (98.3 % ee).

Interesting results were obtained when using diamine catalyst 93 as a preformed CuCl$_2$ complex, as recently described by Shirai et al. for the asymmetric acylation of meso-1,2-diols using an alternative diamine.$^{[21]}$ Monobenzoate 76 was obtained in 98 % conversion but unfortunately very poor (4 %) ee. Dibenzoate 105 was not detected, its formation being restricted under the proposed mechanism for the case of the CuCl$_2$ complex (Section III.1). Lower reaction temperatures (e.g. -78 °C) did not bring any change in ratios or enantioselectivity. Unfortunately, while an excellent organocatalyst it seems that diamine 93 does not induce much enantioselectivity as ligand in this complex.

Returning to the organocatalytic reactions, we wished to simplify our reactions by studying the second benzylation, a process of kinetic resolution, independently. Kinetic resolution could be conveniently used for the synthesis of enantiopure monobenzoates by treatment of meso-diols with a measured excess of both base and acyl transfer reagent in the presence of catalytic amounts of diamine 93. This was done by reaction of (±)-benzoic acid 2-hydroxycyclohexyl ester (76) under the conditions described in Scheme 18. The crude NMR ratios showed a 76 / 105 in a 56 / 46 ratio. Monobenzoate 76 was obtained in and with 76 % ee, which gives a selectivity factor of $S = 10.4.$$^{[61]}$ Once more the reaction is quantitative, limited by the number of equivalents of both Et$_3$N and BzCl. To compare our result, the most efficient kinetic resolution of rac-76 reported to date was using 1 mol % of Spivey’s catalyst, with $S = 19.7.$$^{[22]}$
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of \( \text{meso-}(\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindiol})) \) type complexes and \( \text{meso-1,2-diols} \)

Enantioenriched monobenzoate 76 (50 % ee) was resolved under the same conditions, raising the enantiopurity of 76 to 99.6 % ee, 61 % NMR ratio. The reaction was far from quantitative, \( C = 39 \% \). Therefore, the second acylation of (+)-76 catalysed by diamine 93 is much slower when compared with acylation of its enantiomer (-)-76.

As described above, diamine 93 catalysed the asymmetric acylation of \( \text{meso-cyclohexane-1,2-diol} (75) \) with acceptable values of conversion and enantiopurity is at a very early stage of the research. However, the amount of undesirable dibenzoate 105 obtained as a side product reduces the efficiency of the process while changes of concentration, base or acyl transfer reagent did not bring about any improvement. The poor solubility of the starting material 75 in \( \text{CH}_2\text{Cl}_2 \) at low temperature could be the cause of this drawback, resulting in greater overacylation of alcohol 75 than would be expected. Different solvents were screened in the hope of overcoming this problem and results are listed in Scheme 19 and Table 7. \( \text{CCl}_4 \) gave similar results that those achieved in \( \text{CH}_2\text{Cl}_2 \) (Entries 1 and 2). Dibenzoate 105 was detected as the major product in 1,2-dichloroethane (Entry 3), while \( \text{CHCl}_3 \) (Entry 4) gave very poor conversion, denoting a strong influence of the solvent upon the course of the reaction. Catalyst 93 performs poorly in highly polar solvents as \( \text{MeCN}, \text{acetone or tert-amyl alcohol} \) (Entry 5 to 7). Ethereal solvents generally dissolved the starting material at low temperature and catalyst 93 in THF proved to be highly selective giving monobenzoate 76 in conversions close to 90 % together with undesired dibenzoate 105 in less than 10 % (Entries 8 to 16). However, the enantioselectivity dropped to some extent probably due to the lesser degree of overacylation (Entry 9). This could be improved by lowering the temperature to \(-60^\circ\text{C}\) in THF where a slightly better enantioselectivity was achieved (Entry 10). Colder
temperatures (-78°C) in THF gave lower conversions (Entry 11). Finally, though, we were very pleased to find that AcOEt at -60°C outperformed THF and monobenzoate 76 was obtained in 96 % conversion and 96.6 % ee (Entries 14 to 16).

Scheme 14

Table 7

<table>
<thead>
<tr>
<th>Entry</th>
<th>Solvent</th>
<th>T (°C)</th>
<th>% 75a</th>
<th>% 76a</th>
<th>% 105a</th>
<th>Eq acylb</th>
<th>% ee²</th>
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<tbody>
<tr>
<td>1</td>
<td>CH₂Cl₂</td>
<td>-30</td>
<td>7</td>
<td>74</td>
<td>19</td>
<td>1.12</td>
<td>99.9 (+)</td>
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<td>CCl₄</td>
<td>-30</td>
<td>7</td>
<td>72</td>
<td>22</td>
<td>1.16</td>
<td>97.5 (+)</td>
</tr>
<tr>
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<td>CH₂ClCH₂Cl</td>
<td>-30</td>
<td>18</td>
<td>8</td>
<td>67</td>
<td>1.42</td>
<td>nd</td>
</tr>
<tr>
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<td>CHCl₃</td>
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<td>1.11</td>
<td>86.6 (+)</td>
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<td>tert-Amyl alcohol</td>
<td>-30</td>
<td>20</td>
<td>53</td>
<td>27</td>
<td>1.07</td>
<td>nd</td>
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<td>9</td>
<td>1.07</td>
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<td>9</td>
<td>THF -30°C</td>
<td>-30</td>
<td>5</td>
<td>89</td>
<td>6</td>
<td>1.01</td>
<td>90.5 (+)</td>
</tr>
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<td>10</td>
<td>THF -60°C</td>
<td>-60</td>
<td>4</td>
<td>93</td>
<td>3</td>
<td>1.00</td>
<td>92.7 (+)</td>
</tr>
<tr>
<td>11</td>
<td>THF -78°C</td>
<td>-78</td>
<td>11</td>
<td>87</td>
<td>2</td>
<td>0.91</td>
<td>94.1 (+)</td>
</tr>
<tr>
<td>12</td>
<td>DME -30°C</td>
<td>-30</td>
<td>4</td>
<td>90</td>
<td>6</td>
<td>0.94</td>
<td>92.7 (+)</td>
</tr>
<tr>
<td>13</td>
<td>Dioxane rt</td>
<td>rt</td>
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<td>81</td>
<td>12</td>
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<td>79.9 (+)</td>
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<td>AcOEt -30°C</td>
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<td>3</td>
<td>1.00</td>
<td>92.1 (+)</td>
</tr>
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<td>4</td>
<td>1.04</td>
<td>96.6 (+)</td>
</tr>
<tr>
<td>16</td>
<td>AcOEt -78°C</td>
<td>-78</td>
<td>22</td>
<td>77</td>
<td>2</td>
<td>0.81</td>
<td>96.9 (+)</td>
</tr>
</tbody>
</table>

a) NMR ratios  b) equivalents of benzoyl transferred to 75  c) monobenzoate 76 HPLC.
In summary, the following conditions gave the best results: molecular sieves, 1.5 eq BzCl, 1 eq Et₃N and $[75]_0 = 0.11$ M in two solvent systems (THF and AcOEt) at -60°C. With these conditions there is not much room for improvement in the performance of diamine 73 with this substrate. In addition, the catalyst was found to perform well down to 2 mol % in both solvent systems with no substantial loss of conversion or enantioselectivity and this amount of catalyst was fixed for the following experiments (Table 8).

### Table 8

<table>
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<tr>
<th>Entry</th>
<th>Solvent</th>
<th>Diamine 73</th>
<th>% 75</th>
<th>% 76</th>
<th>% 105</th>
<th>eq acyl</th>
<th>% ee</th>
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<tbody>
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<td>THF</td>
<td>5 mol %</td>
<td>11</td>
<td>87</td>
<td>2</td>
<td>0.91</td>
<td>94.1 (+)</td>
</tr>
<tr>
<td>2</td>
<td>THF</td>
<td>2 mol %</td>
<td>4</td>
<td>93</td>
<td>3</td>
<td>1.00</td>
<td>92.7 (+)</td>
</tr>
<tr>
<td>3</td>
<td>THF</td>
<td>1 mol %</td>
<td>32</td>
<td>68</td>
<td>0</td>
<td>0.68</td>
<td>85.3 (+)</td>
</tr>
<tr>
<td>4</td>
<td>AcOEt</td>
<td>5 mol %</td>
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<td>96</td>
<td>4</td>
<td>1.04</td>
<td>96.6 (+)</td>
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<tr>
<td>5</td>
<td>AcOEt</td>
<td>2 mol %</td>
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<td>94</td>
<td>4</td>
<td>1.02</td>
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<tr>
<td>6</td>
<td>AcOEt</td>
<td>1 mol %</td>
<td>22</td>
<td>74</td>
<td>3</td>
<td>0.81</td>
<td>94.9 (+)</td>
</tr>
</tbody>
</table>

a) NMR ratios  
b) equivalents of benzoyl transferred to 75  
c) monobenzoate 76 HPLC

We note that 2-hydroxycyclohexyl benzoate (76) is configurationally unstable in protic solvents at r.t. In ¹PrOH a 91.5 % ee sample partly racemised over a period of 4 days (86.6 % ee). This suggests an intramolecular mechanism of racemisation, activated by hydrogen bonding between the ester and the acidic proton of the solvent. Pure monobenzoate 76 is configurationally stable neat or in aprotic solvents at r.t., but slow racemisation also occurred in the crude at r.t. or at -20°C and therefore this compound should be purified right after work-up. In addition, Trost et al. have observed complete racemisation of the monobenzoates when using dinuclear zinc catalyst 83 (Section III.1) in the desymmetrisation of meso-1,2-diols, remarking upon the low configurational stability of these derivatives.[27]

Under the new conditions, diamine 94 performed well in the asymmetric acylation of meso-cyclohexane-1,2-diol (75) to give highly enantioenriched (-)-76 with opposite configuration (Scheme 20). However, diamine 94 again showed lower activity that its pseudoenantiomeric partner 93, and a slight decrease in yield and enantioselectivity were
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)₃(η⁶-5,8-tetralindiol)) type complexes and meso-1,2-diols

observed, as previously noted by Yamamoto in a related Cinchona alkaloid-derived catalyst.[24]

Scheme 15

III.6 Asymmetric acylation of other meso-1,2-diols.

Following optimisation, the conditions for the asymmetric acylation of meso-cyclohexane-1,2-diol were applied to other substrates (Scheme 21 and Table 9). Cyclic and acyclic diols were efficiently desymmetrised with good to excellent yields and moderate to excellent enantioselectivities (Entries 1 to 12), while dibenzoates were usually formed in less than 10 % yield. Lower conversions or enantioselectivities were achieved in the desymmetrisation of substrates incorporating phenyl groups (Entries 13 to 18). These compounds are less soluble at low temperatures and this favours the formation of the corresponding dibenzoate. Despite their utility in the desymmetrisation of chromium-containing 1,4-diols 65 and 66, it was also found that chiral diamine 93 could not efficiently desymmetrise purely organic 1,3 or 1,4 meso-diols under these conditions. Meso-4-cyclopentene-1,3-diol, meso-tetralin-1,4-diol and meso-cyclohexane-1,2-dimethanol gave the corresponding monobenzoates in 50-60 % yield and 30-50 % ee.
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)$_3$(η$^6$-5,8-tetralindiol)) type complexes and meso-1,2-diols

![Scheme 16](image)

Table 9

<table>
<thead>
<tr>
<th>Entry</th>
<th>Substrate</th>
<th>Solvent</th>
<th>% Sm$^a$</th>
<th>% Mo$^b$</th>
<th>% Di$^a$</th>
<th>Yield$^b$</th>
<th>% ee$^c$</th>
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<td>1</td>
<td>R$^1$OH</td>
<td>THF</td>
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<td>2</td>
<td>R$^2$OH</td>
<td>AcOEt</td>
<td>3</td>
<td>95</td>
<td>2</td>
<td>82</td>
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<td>THF</td>
<td>3</td>
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<td>82 (+)</td>
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<td>78 (+)</td>
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<td>R$^5$OH</td>
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<td>R$^8$OH</td>
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<td>20</td>
<td>64</td>
<td>89 (+)</td>
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<td>51</td>
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<td>83 (+)</td>
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<td>69</td>
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<td>85</td>
<td>7</td>
<td>85</td>
<td>13 (-)</td>
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</table>

a) NMR ratios  b) isolated yield of monobenzoate  c) HPLC
Chapter III : New asymmetric acylation catalysts for the desymmetrisation of \( \text{meso}-(\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindiol})) \) type complexes and \( \text{meso}-1,2\text{-diols} \)

### III.7 Conclusions and perspectives.

In conclusion, a new efficient route to highly enantioenriched planar chiral complexes has been achieved by asymmetric acylation of the corresponding \( \text{meso}-\text{dil} \) \( \text{Cr(CO)}_3 \) complexes catalysed by new chiral diamines derived from Cinchona alkaloids. This method has been extended to the desymmetrisation of metal free \( \text{meso}-1,2\text{-diols} \). The influence of concentration, temperature, base, different substituted benzoyl chlorides and solvent has been extensively studied for the asymmetric acylation of \( \text{meso}\)-cyclohexane-1,2-diol catalysed by diamine 93. We have found an extremely efficient process in THF or AcOEt at low temperature giving highly enantioenriched monobenzoate (+)-76 in excellent yield. Theses conditions were successfully applied in the desymmetrisation of a range of cyclic and acyclic \( \text{meso}-1,2\text{-diols} \) achieving good yields and good enantioselectivities with low (2 mol%) catalyst loadings. As a limitation, lower selectivities and conversions were achieved for those substrates bearing phenyl functionalities. This method has been tested in the desymmetrisation of 1,3 and 1,4 \( \text{meso}\)-diols but catalyst 93 gave monobenzoates with moderate conversions and poor enantioselectivities. New chiral nucleophilic catalysts 93 and 94 are easily accessible from inexpensive commercially available materials.

Tertiary chiral diamines play a central role in this expanding area of asymmetric catalysis such as acyl transfer desymmetrisation of \( \text{meso}\)-diols. This is just one of the uncountable applications of tertiary diamines as chiral nucleophilic catalysts or as ligands in metal catalysed reactions. We here detail a few transformations were diamines 93 and 94 could be used catalytically in the hope of achieving highly enantioenriched materials.[1]

Optically active \( \alpha\)-hydroxyacids are structural motifs present in numerous natural products and biologically active compounds. Condensations to \( \alpha\)-hydroxy acids with phosgene or one of its equivalents represent a direct route for the preparation of dioxolanediones. Dinamic kinetic resolution of 5-alkyl-1,3-dioxolane-2,4-diones leading to enantioen-riched \( \alpha\)-hydroxyacids could be successfull when carried out in the presence of catalyst 93 (Scheme 22).[62] In the same maner, more valuable \( \alpha\)-aminoacids migh also be obtained from 5-alkyl-3-aza-1-oxolane-2,4-diones.
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)$_3$(η$^6$-5,8-tetralindiol)) type complexes and meso-1,2-diols

Cooper catalysed asymmetric conjugate reductions of α,β-unsaturated ketones could also be performed in the presence of diamine 93. This would possibly give access to enantioenriched 2,4-dialkyl-cyclopentanones via dynamic kinetic resolution of the corresponding 2,4-dialkyl-cyclo-2-pentenones (Scheme 23). This method represents an example of dynamic kinetic resolution with simultaneous creation of two nonadjacent chiral centres.

![Scheme 22](image)

The desymmetrisation of meso-epoxides via the enantioselective addition of nucleophiles is an efficient strategy for asymmetric synthesis since it simultaneously establishes two contiguous stereocenters. Commercial 1,2-aminoalcohol 93 should be tested as ligand in this transformation (Scheme 24). The desymmetrisation strategy requires that epoxide opening occur by exclusive backside attack; however, this also imposes a limitation, namely that the products will necessarily be trans substituted. This limitation can be circumvented by the introduction of a reactive nucleophile such as a halide which could be displaced in subsequent step, thus inverting the stereochemistry at this carbon atom.

![Scheme 23](image)
Chapter III: New asymmetric acylation catalysts for the desymmetrisation of meso-(Cr(CO)$_3$(η$^6$-5,8-tetralindiol)) type complexes and meso-1,2-diols

Optically active aryl propionic acid derivatives can be synthesised through the stereoselective addition of an alcohol to an arylmethylketene. The desymmetrisation of ketenes by nucleophilic addition of alcohols is a very effective method for the enantioselective synthesis of esters bearing a stereogenic centre in α.$^{[65]}$ Diamine 93 is a very promising catalyst for this process (Scheme 25).

**Scheme 24**

**Scheme 25**
Chapter III : New asymmetric acylation catalysts for the desymmetrisation of \( \textit{meso-(Cr(CO)_3(\eta^6-5,8-tetralindiol))} \) type complexes and \( \textit{meso-1,2-diols} \)

### III.8 References.


Chapter III: New asymmetric acylation catalysts for the desymmetrisation of
\( \text{meso-}(\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindiol})) \) type complexes and \( \text{meso-1,2-diols} \)


Chapter III: New asymmetric acylation catalysts for the desymmetrisation of 
meso-(Cr(CO)₃(η⁶-5,8-tetralindiol)) type complexes and meso-1,2-diols
IV. The rediscovery, isolation and synthetic potential of 1,4-tetralindione.

The facile isomerisation of \([\text{Cr(CO)}_3(\eta^6\text{-5,8-dihydroxynaphthalene})] (63)\) into its tautomer \([\text{Cr(CO)}_3(\eta^6\text{-5,8-tetralindione})] (64)\) led us to investigate the tautomer situation in a parent compound (Section II.4). A literature search revealed that this phenomenon is not an exclusivity of the Cr(CO)_3 complex and that the existence of 1,4-tetralindione (134) has been documented in the literature for many years. Surprisingly no literature data is extent on transformation of 134.

IV.1 Rediscovery of 1,4-tetralindione (134).

In 1933 Madinaveitia and Olay reported the first isolation of 1,4-tetralindione (134) by heating 1,4-dihydroxynaphthalene\(^1\) (61) in the vacuum above its melting point (210 °C) for 10 min (Scheme 1).\(^2\) At this temperature both isomers interconvert and, surprisingly, dione 134 is a kinetically stable tautomer upon cooling this melt. Being less polar than 61, dione 134 was then extracted from the crude with boiling petroleum ether and recrystallised on cooling as white needles (MP = 99 °C) in 10 % yield.

\[
\begin{array}{ccc}
\text{61} & \xrightarrow{T > 200 \, ^\circ\text{C}} & \text{134} \\
\end{array}
\]

Scheme 1

Due to the limited spectroscopic resources at that time, the real structure of 1,4-tetralindione (134) was incorrectly assigned as naphthoquinol 135. Two decades later, Thomson repeated this experiment and analysed this material by infrared spectroscopy, observing a band at 1673 cm\(^{-1}\) \(\nu(\text{CO})\) very similar to that found in naphthoquinone (1660 cm\(^{-1}\) \(\nu(\text{CO})\)) and there is no hydroxyl band in the spectrum near 3400 cm\(^{-1}\). This eliminates the previously suggested naphthoquinol 135.\(^3\) This material could be converted to the
corresponding dinitrophenylhydrazone 136 and therefore the 1,4-tetralinedone (134) structure was assigned.

Pearson et al. showed that melting 1,4-dihydroxynaphthalene (61) under vacuum (1 h, 200 °C) generates a 2 : 1 equilibrium with its tautomer 134. The activation parameters of this process were determined by analysing the equilibrium constants at different temperatures and \( \Delta G^\circ = -0.56 \text{ kcal/mol} \), \( \Delta H^\circ = -2.3 \text{ kcal/mol} \) and \( \Delta S^\circ = -3.4 \text{ kcal/mol} \) were calculated using an Eyring plot. Thus, the enol form 61 is thermodynamically favoured. Further substitution with hydroxyl groups in the 5 and 8 positions of 1,4-dihydroxynaphthalene was found to favour the 1,4-diketo compound over the enolic tautomer, and the preferential stabilisation of the carbonyl compound was attributed to intramolecular hydrogen bonding.

The conversion of 61 into 134 can also be effected in neat CF\(_3\)COOH. Laatsch reported that the tautomeric equilibrium is strongly influenced by the solvent (Scheme 2). In CF\(_3\)COOH, the enol form is not detected and 1,4-tetralindone (134) is the only tautomer in solution, while in an acetone / CF\(_3\)COOH mixture a 1 : 1 ratio is observed. However, Laatsch did never isolate dione 134.

In an earlier very short paper, Birch et al. studied the hydrogenation of 1,4-naphthoquinone in benzene with Wilkinson’s catalyst to give the diketone 134 in 70 % yield. No experimental procedure was provided. In our hands, attempts to reproduce this reaction afforded a mixture of 134 (max 59 %) and 1,4-dihydroxynaphthalene (61).

We saw in 1,4-tetralindione (134) a very promising starting material for organic synthesis due to its simplicity, symmetry and high level of functionalisation. In addition, several natural products and biologically active compounds present the 1,4-disubstituted tetralin core, making diketone 134 in a suitable synthon (Figure 1). Surprisingly, no chemistry using 134 has ever been reported since the first isolation in 1933. All these facts
encouraged us to explore the reactivity of diketone 134 and find efficient protocols for its desymmetrisation.

![Chemical structures of compounds](image)

**Figure 1**

**IV.2 Synthesis of 1,4-tetralindione (134).**

The approach of Laatsch seemed like the most viable route to 1,4-tetralindione (129). In agreement with the earlier observation we found complete displacement of the tautomeric equilibrium in favour of diketone 134 by $^1$H NMR when 1,4-dihydroxynaphthalene (61) was dissolved in CF$_3$COOD. For synthetic purposes, 250 mg of 1,4-dihydroxynaphthalene (61) was stirred in CF$_3$COOH for 30 min until complete dissolution. At this point the solvent was rapidly removed under high vacuum and the residue was shown to consist of a mixture of dione 134 and enol 61 in a 3 : 7 $^1$H-NMR ratio. The equilibrium shifted to the enol 61 upon evaporation (no oxidation to 1,4-naphthoquinone was observed). Surprisingly, 1,4-tetralindione (134) proved stable on silica gel and could be purified by flash chromatography in 72 % yield from this crude.

Repeating this reaction on a 2 g scale unfortunately gave 134 in low yield due to precipitation of 61 during evaporation. Subsequently, following tautomerisation in CF$_3$COOH an excess of toluene was added. Faster evaporation of the lower boiling CF$_3$COOH (72 °C)
reduced solvent polarity and also tautomeric equilibration. This afforded a mixture of enol \(61\) / dione \(134\) in a \(1:9\) \(^1\)H NMR ratio. The same result was obtained on a 10 g scale and 1,4-tetralindione was isolated in 74 % yield by simple recrystallisation from \(^i\)Pr\(_2\)O (Scheme 3).\(^{[12]}\)

During the course of our investigations, Doyle \textit{et al.} reported the isolation of 1,4-tetralindione in low (27 %) yield by benzylic oxidation of \(\alpha\)-tetralone catalysed by a dirhodium (II, III) caprolactam complex.\(^{[13]}\)

The structure of \(134\) was determined by X-ray diffraction analysis (Figure 2). A superposition of the structures of \(134\) and its Cr(CO)$_3$ complex \(64\) (Section II.5) gave very high agreement of the conformational preference of the saturated ring. The C-O bond lengths \((d = 1.22 \text{ Å})\) confirm the presence of both keto groups.

![Figure 2: ORTEP view of the crystal structure of 134. Ellipsoids are represented at 40 % probability.](image)
IV.3 Stability and reactivity of 1,4-tetralindione (134).

It is well established that enols are thermodynamically less stable than their carbonyl isomers. However, in the case of 1,4-dihydroxynaphthalene (61) the enol form is slightly favoured over its keto tautomer 134 due to its aromatic character. The relatively low energy difference between tautomers allows for their facile interconversion. We find that the isomerisation of enol 61 into dione 134 can be effected in C₆D₆. Heating in a close system at 120 °C leads to a 1 : 1 equilibrium (¹H NMR ratio) after 25 days (Scheme 4 and Figure 3). In contrast, we recall that [Cr(CO)₃(η⁶-5,8-dihydroxynaphthalene)] (63) reaches 90 % conversion at much lower temperature (50°C) in only 20 h (Section II.4). The metal complexation thus does favour the diketone form.

![Scheme 4](image)

![Figure 3](image)

This influence could have its origin in the electron withdrawing properties of the Cr(CO)₃ unit. On the other hand, tautomerisation from enol 61 to dione 134 is accompanied by a loss of aromaticity and the metal may compensate this energetic cost. However, this is a
very simplistic statement and further investigations will be necessary to resolve this question. We note that the tautomeric equilibrium of phenylpyruvate derivatives is shifted to the ketone form when complexed to Cr(CO)$_3$. In this case, this is due to an alteration of the conjugation with an enolic double bond.$^{[16]}$

It is of interest to summarise the result of the computational analysis that has been carried out at this stage.$^{[17]}$ Calculations have been restricted to the ground state. A first analysis of the gas phase structures indicated that complexation reduced the energy difference between tautomers.

Moreover, in other reports dione 134 has been computed to be 10.2 kcal/mol more stable that its tautomer 61 at the B3LYP/6-31G* level.$^{[18]}$ This value drops to 1 kcal/mol in more recent calculations where dione 134 is slightly favoured in the gas phase.$^{[17]}$ In solution, for both the complexed and the free tautomer, it is found that the tautomeric equilibrium is strongly influenced by the polarity of the solvent. Polar solvents strongly favour the dihydroxy compound 61 (ca. 10 kcal/mol), this value drops to 3 kcal/mol in apolar solvents. In agreement with this observation, additional stabilisation of 1,4-dihydroxynaphthalene (61) is expected in those solvents capable of solvating an enol group more effectively. It is apparent that more accurate studies with implicit solvent models are required in order to emulate the experimental observations.

The stability of 1,4-tetralindione (134) at r.t. in solvents of different nature and polarity was demonstrated by dissolving samples of 134 in CDCl$_3$, DMSO-$d_6$, C$_6$D$_6$, acetone-$d_6$, or MeOH-$d_4$. $^1$H NMR analysis showed no change over a period of 24h. Dione 134 is thus a kinetically stable tautomer in these solvents at r.t. The effect of addition of an acid or a base was proved next (Scheme 5).
When 2 eq of CF₃COOH were added to these solutions:

- C₆D₆ (μ = 0 D, ε = 2.28): Slow formation and precipitation of 61 took place; therefore the true ratio between tautomers cannot be given. Some dione 134 is still present after six days together with other unknown decomposition products.

- CDCl₃ (μ = 1.9 D, ε = 4.7): Slow formation and precipitation of enol 61 took place; again the true ratio between tautomers cannot be given. However, dione 134 appears largely unchanged after six days.

- Acetone-d₆ (μ = 2.9 D, ε = 20.7): Enol 61 was not detected until 6 days in 10 % together with naphthoquinone (10 %); diketone 134 was still present in as 80 % of the mixture.

- MeOH-d₄ (μ = 1.7 D, ε = 32.6): Within one hour the corresponding methanol monoacetal is formed (50 %). After 27 h dione 134 has been largely converted to the diacetal (80 %) and no further change is observed after 6 days. This experiment may indicate a route to monoprotected equivalent of dione 134.

- DMSO-d₆ (μ = 3.9 D, ε = 47.0): The 134 / 61 ratio after 1 h is 90 : 10, after 27 h it is 27 : 73 and after 6 days enol 61 is the only tautomer in solution.

In general, dione 134 largely or completely reverts to enol 61 in the presence of 2 eq of CF₃COOH. The formation of enol 61 is faster in polar solvents. As exception to this rule, in acetone, dione 134 oxidises very slowly to naphthoquinone and enol 61 is only detected after 6 days in low proportion.

The same experiment was carried out by adding 2 eq of Et₃N to freshly prepared sample solutions.

- C₆D₆ (μ = 0 D, ε = 2.28): Fast formation and precipitation of enol 61 took place; therefore the true ratio between tautomers cannot be given. Dione 134 disappeared after one day. No other secondary products were detected.

- CDCl₃ (μ = 1.9 D, ε = 4.7): Slow formation and precipitation of enol 61 took place; the true ratio between tautomers cannot be given. Dione 134 is
barely detectable after six days, and is accompanied by several unknown decomposition products.

- Acetone-$d^6$ ($\mu = 2.9$ D, $\varepsilon = 20.7$): The tautomers reached the equilibrium before 1 h (134/61, 70:30).

- MeOH-$d^4$ ($\mu = 1.7$ D, $\varepsilon = 32.6$): Dione 134 disappears within 1 h, the clear solution gave a clean spectrum of enol 61.

- DMSO-$d^6$ ($\mu = 3.9$ D, $\varepsilon = 47.0$): Dione 134 disappears in 1 h, the clear solution gave a clean spectrum of enol 61.

In general, dione 134 largely or completely tautomerises to enol 61 in the presence of Et$_3$N in these solvents. The more polar the solvent, the faster the formation of 61. Acetone is an exception and the equilibrium favours dione 134.

We conclude that dione 134 is a kinetically stable tautomer in solution at r.t. However, the addition of an acid or base catalyst facilitates its isomerisation to enol 61. In high polarity solvents, the isomerisation is fast and quantitative while in less polar solvents the equilibrium is always shifted favouring the enol 61. These observations show a certain relation with the computed solution values, where enol 61 always predominates and increases in stability in more polar solvents. Notably, the isomerisation of 134 occurred more readily in the presence of Et$_3$N than in CF$_3$COOH. Even though Et$_3$N is not basic enough to appreciably deprotonate a ketone, base catalysed tautomerisation implies the direct aromatisation to the enol of 61.

In order to explore the reactivity of 1,4-tetralindione (134), we fixed our attention upon those processes already performed with success on 1-tetralone and found a rich and varied chemistry for this compound. However, we expected to find more problems using 134 due to the fast isomerisation to the aromatic form 61 in the presence of an acid or a base.

Despite this, we tested a number of procedures known for 1-tetralone. However, the greater sensitivity of 134 turned out to be a major handicap since a great part of the reactions in organic synthesis involve the use of acidic or basic reagents (Scheme 6). In addition, selectivity problems arise due to the presence of two identical functionalities in 134. In summary: a) Attempts to form a single hydrazone function with dimethylhydrazine led to complete tautomerisation to enol 61 in polar or apolar solvents in less than 30 min.$^{[19]}$ b) Reductive amination under mild conditions also caused complete aromatisation.$^{[20]}$ c) During $\alpha$-chlorination, diketone 134 oxidised completely to 1,4-naphthoquinone, presumably by elimination of the halogen in the product assisted by the keto-enol equilibrium.$^{[21]}$ d)
Attempted thioacetal formation gave also decomposition.[22] e) Wittig reaction with 134 at least gave \textit{exo}-4-methylene-1-tetraline (137) in very low yield.[23] Unfortunately the basic character of the reagents partially decomposed the starting material before 1,2-addition of the phosphine ylide. An improved synthesis of 137 will be further discussed in Section IV.4. f) Bisolefination with an excess of phosphine ylide gave \textit{exo}-1,4-dimethylenetetraline 138 also in unsatisfactory 30 \% yield. g-h) All attempts at enolate formation failed due to aromatisation when \(\alpha\) alkylation and aldol reaction were attempted.[24, 25] The low stability of 1,4-tetralindione towards acid or base might explain why no synthetic reactions have been described in the literature since 134 was first isolated in 1933.[2]

\textbf{Scheme 6:} Reagents and conditions: a) \(\text{Me}_2\text{N}_2\text{H}_2\) 1.5 eq, r.t., toluene or MeOH. b) i)\(\text{TiCl}_4\) 2 eq, \(\text{BnNH}_2\) 2.2 eq, \(\text{Et}_3\text{N}\) 6 eq, \(\text{CH}_2\text{Cl}_2\), -78 °C. ii) \(\text{NaBH}_4\) 9 eq, MeOH, -20 °C. c) amberlist 15, NCS 1 eq, AcOEt, r.t. d) 1,3-propanedithiol 1 eq, \(I_2\) 5 mol \%, THF, r.t. e) \(\text{MePPh}_3\text{Br}\) 1.1 eq, \(\text{BuLi}\) 1.1 eq, THF, r.t. f) \(\text{MePPh}_3\text{Br}\) 3.5 eq, THF, \(\text{BuLi}\) 3.5 eq, r.t. g) benzaldehyde 1.2 eq, LDA 1 eq, THF, -78 °C. h) \(\text{NaH}\) 3.5 eq, MeI 3.5 eq, toluene, reflux.
Fortunately, we were able to find other reactions where dione 134 was transformed into the desired product in high yield before isomerisation to the enol 61 giving a wide range of interesting compounds for further use in organic synthesis. These reactions and other ways to overcome this problem will be discussed in the following chapters showing that 1,4-tetralindione (134) is a promising starting material for organic synthesis.

IV.4 Monoprotection of 1,4-tetralindione (134).

Single carbonyl protection of 134 would overcome part of the reactivity problems associated with its conversion to enol 61 and ensure more regioselective reactions. Monoprotection of 134 was attempted to give its acetal,[26] hydrazone[19] or thioacetal[22] with total decomposition of the starting material into the enol 61. Therefore, we turned our attention to other protocols that allow the protection of dione 134 under mild neutral conditions. Cyanosilylation of dione 134 catalysed by 5 mol % of I$_2$ at r.t. in the presence of 1.2 eq of TMSCN gave a crude product composed of starting material 134, monoprotected 139 and bisprotected material in 7 : 80 : 13 $^1$H NMR ratio.[27] Encouraged by this result, the reaction was performed at lower temperatures and at -78 °C we were pleased to find the exclusive formation of the desired cyanohydrin 139 (Scheme 7). The crude product was purified by flash chromatography and 4-carbonitrile-4-trimethylsilanoxy-1-tetralone (139) was obtained in 76 % yield (3 mmol scale). Unfortunately, partial decomposition to 1,4-naphthoquinone (58) took place during purification lowering the yield of the process. The product is very sensitive to acidic cleavage and purification by flash chromatography using silica must be quick. Other stationary phases as alumina deactivated with 10 %v H$_2$O or treatment of silica with Et$_3$N caused the decomposition of the product into 1,4-naphthoquinone. Attempts of purification by distillation under N$_2$ in a Kugelrohr apparatus also failed.

![Scheme 7](image-url)
Furthermore, acidic treatment of 139 gave quantitative cleavage of the silyl group to give cyanohydrin 134 which underwent transformation to dione 134 on attempted purification over silica gel. This problem was circumvented by crystallisation of the crude from iPr₂O giving 4-hydroxy-4-cyano-1-tetralone (140) in 83% yield.

With a protected analogue of dione 134 in hand, we were ready to face the problems of stability in basic media associated with dione 134. In this manner, Wittig reaction between (±)-4-carbonitile-4-trimethylsilanoxy-1-tetralone (139) with 1.1 eq of methyltriphenylphosphine ylide proceeded smoothly to give exo-4-methylene-1-tetralone (137) after TBAF cleavage of the cyanohydrine.[23] Exocyclic olefin 137 slowly decomposes during chromatography to 4-methy-1-naphthol but this still afforded a reasonable 73% yield (Scheme 8).

![Scheme 8](image)

**IV.5 Diastereoselective reduction of 1,4-tetralindione (134).**

Reduction of 1,4-tetralindione (134) with an excess of different hydride sources never caused the formation of the enol 61 and in general, both carbonyls were reduced quantitatively. After hydrolysis and aq. workup, the crude product was filtered through a plug of silica to give a mixture of cis and trans diastereoisomers (Scheme 9). Different reagents and conditions were essayed in order to favour the formation of either the cis or the trans diastereoisomers.
Table 1

<table>
<thead>
<tr>
<th>Entry</th>
<th>Reducing agent</th>
<th>cis-141[a]</th>
<th>trans-142[a]</th>
<th>Yield[a]</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>BH₃·THF</td>
<td>61 %</td>
<td>39 %</td>
<td>93 %</td>
</tr>
<tr>
<td>2</td>
<td>NaBH₄</td>
<td>58 %</td>
<td>48 %</td>
<td>98 %</td>
</tr>
<tr>
<td>3</td>
<td>LiAlH₄</td>
<td>32 %</td>
<td>68 %</td>
<td>94 %</td>
</tr>
<tr>
<td>4</td>
<td>L-selectride</td>
<td>84 %</td>
<td>16 %</td>
<td>98 %</td>
</tr>
<tr>
<td>5</td>
<td>Red-Al</td>
<td>13 %</td>
<td>87 %</td>
<td>76 %</td>
</tr>
</tbody>
</table>

[a] NMR ratios in DMSO-<d₆>. b) Isolated mixture of cis and trans diastereoisomers.

In general, low selectivities were observed when using BH₃·THF, NaBH₄ or LiAlH₄ (Entries 1-3). Reduction with lithium tri-sec-butyl borohydride (L-selectride) afforded a product enriched with cis-1,2-tetralindiol (141) (Entry 4). The high stereoselectivity is a consequence of the bulky reducing agent. Following the formation of the 4-boronate-1-tetralone addition of a second equivalent of L-selectride would be expected to come from the less hindered face. Hydrolysis then yields preferentially the cis diastereoisomer. This mixture could not be efficiently resolved by flash chromatography but recrystallisation from iPr₂O gave cis-1,4-dihydroxytetraline (141) in 66 % yield (Scheme 10).
Conversely, aluminium hydrides gave preferentially the *trans* isomer 142 (Table 1, Entries 3 and 5). Particularly, [Al(H₂)(OCH₂CH₂OMe)₂][Na] (Red-Al) proved promising isomer (Entry 3). Unfortunately bis-reduction is not complete under these conditions and the diastereomeric mixture was recovered in low 76 % yield after hydrolysis with Rochelle’s salt and filtration through a plug of silica. This reaction still requires optimisation. Recrystallisation of the residue from CHCl₃ gave *trans*-1,4-dihydroxytetralin (142) in 55 % yield (Scheme 11). The reason for the observed diastereoselectivity may have its origin in the delivery of the second hydride from the same aluminium moiety.

![Scheme 11](image)

Those reducing agents incorporating several hydride groups are likely to favour the formation of the *trans* isomer 142. On the other hand, reduction with BH₃-THF requires pre-coordination of this Lewis acid to the carbonyl group before hydride transfer and this excludes an intramolecular hydride delivery (Entry 1). Moreover, NaBH₄ might be not nucleophile enough to react intramolecularly since both diastereoisomers are obtained in very similar ratio (Entry 2).

*Cis* 141 and *trans* 142 were previously reported. They are obtained by treatment of tetralin with NBS to give a 1 : 1 mixture of the corresponding *cis* and *trans*-dibromides, which were converted into diacetates with AcOAg in 81 % yield. Hydrolysis with 2 N NaOH and fractional recrystallisation from MeOH / Et₂O then afforded pure *cis* 141 and *trans* 142 though isolated yields were not reported.[28] *Cis* 141 has been used as substrate in the field of enantioselective oxidation[29] and asymmetric acylation.[28, 30]

### IV.6 Desymmetrisation of 1,4-tetralindione (134) by CBS reduction.

Asymmetric of reduction of dione 134 would lead to useful starting materials for natural product synthesis (Section IV.1). Based on the excellent results obtained by CBS
Chapter IV: The rediscovery, isolation and synthetic potential of 1,4-tetralindione

reduction of the complex \([\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindione})]\) (64) (Section II.4),\(^{31-33}\) the same protocol was applied to the diketone 134 to give \((-)-(1R,4R)\)-1,4-tetralindiol (142) in 72 % yield (2.5 g scale), 99 % ee after two successive recrystallisation in \(\text{iPr}_2\text{O}\) (Scheme 12). Starting from dione 134, we have found much easier the synthesis of trans diol 142 in enantiopure form that as a racemate (Section IV.5).

\[
\text{O} \quad \text{OH}
\]

\[
\text{NB} \quad \text{O} \quad \text{Ph}
\]

(-)-trans-142

72 % yield
99 % ee

To our knowledge there is no viable alternative synthetic access to this \(C_2\) symmetric chiral diol. Compound \((-)-(1R,4R)-142\) was previously obtained by HPLC separation of a 1 : 1 mixture of the cis and trans diols obtained in 55 % yield from a four step sequence from \((R)\)-1-tetralol.\(^{34}\) The absolute configuration of complex \((-)-(1R,4R)\) agrees with the reliable stereochemical model for the CBS reduction. Only small amounts (ca. 7 %) of the cis stereoisomer 141 are detected by \(^1\text{H}\) NMR of the mixture after hydrolysis (In contrast, CBS reduction of complexed \([\text{Cr(CO)}_3(\eta^6-5,8\text{-tetralindione})]\) (64) gave slightly higher quantities of undesired cis diastereoisomer 65 (ca. 18 %). This is probably due to the directing effect of the \(\text{Cr(CO)}_3\) fragment which favours the reduction in \(\text{anti}\) to this group (Section II.4).

With an efficient protocol for the desymmetrisation of dione 134 in hand, research then focused on the more challenging task of enantioselective mono-reduction. When the CBS reduction was performed by slow (1 h) addition of dione 134 to a solution of \(\text{BH}_3\text{-THF}\) (0.45 eq) and catalyst 67 background reduction by \(\text{BH}_3\text{-THF}\) was competitive under these conditions and \((-)-(4R)-4\text{-hydroxy-1-tetralone (144)}\) could be isolated in 93 % yield but modest 53 % ee. In dione 134, the two carbonyl functions are mutually activated by conjugation through the arene and thus more reactive when compared with ketol 144. This explains the good yield in mono-reduction.
One way to achieve high ee in mono-reduction was via 4-carbonitrile-4-trimethylsilanoxy-1-tetralone (139) as protected equivalent of dione 134. Slow 2 h addition of a solution of ketone 139 in THF to a solution of BH₃·THF (0.6 eq) and catalyst 67 in THF at -30 °C gave (-)-ketol 144 in 85 % yield, 95 % ee, after MeOH quench and TBAF deprotection (Scheme 13).

The repetition of this experiment at -10 °C gave (-)-ketol 144 in lower enantiopurity (85 % ee). Being chiral, racemnic trimethylsilyl cyanohydrin 139 affords diastereomers in the CBS reduction. This could be the reason of the lower enantioselectivity at -10 °C to the cyanohydrin 139 does not have to be isolated and, the two step procedure affords (-)-ketol 139 in 81 % overall yield, 95 % ee. This strategy avoids the loss of cyanohydrin 139 during purification by flash chromatography and opens the door to larger scale reactions.

The chiral 1,4-disubstituted tetralin unit is central to the commercial antidepressant Sertraline. Several natural products like Preussomerin A, Catalponol, Junglanoside A and Isoshinanolone contain the 4-hydroxy-1-tetralone unit (see Figure 1). In addition, 4-hydroxy-1-tetralone (144) is a naturally occurring compound isolated from Ampelocera edentula with activity against cutaneous Leishmaniasis. Therefore, a more straightforward access to enantioenriched 144 would be useful. As detailed in Section II.4, the CBS monoreduction of [Cr(CO)₃(η⁶-5,8-tetralindione)] (64) proceeded in very high yield and enantioselectivity by using a modified protocol. We have found that slow addition of catecholborane onto a stirred, cooled (-78 °C) solution of dione 134 and catalyst 70 in toluene afforded the desired ketol (-)-144 in 73 % yield and 95.5 % ee (500 mg scale). This bodes
well for a future scale up synthesis. Remarkably, an slight excess of catecholborane (1.2 eq) results in over-reduction while in the case of the Cr(CO)₃ analogue no-over reduction occurred under these conditions due to the steric requirements of the chromium fragment (see Section II.8).[31]

A literature search unveiled two efficient procedures for the synthesis of enantioenriched ketol 144. The first report involves kinetic resolution by enzymatic hydrolysis of the corresponding acetate with *Porcine pancreatic lipase* giving (-)-144 in 47 % yield and 95 % ee.[7] A more recent synthesis uses a palladium catalysed asymmetric oxidation of *meso*-1,4-tetralindiol (141) with (-)-sparteine (20 mol %) to give (+)-144 in 72 % yield and 95 % ee.[29] However, this last approach requires the use of large amounts of chiral information and the availability of the enantiomer, (+)-sparteine is severely restricted.[39]

### IV.7 Enantioselective synthesis of the Sertraline precursor 145.

The CBS mono-reduction of 1,4-tetralindione (134) provides synthetically useful quantities of highly enantioenriched (-)-(R)-4-hydroxy-1-tetralone (144). This could be a key step in a short route to Sertraline (Zoloft®),[35, 40] a major commercial pharmaceutical agent for the treatment of depression, acting in the central nervous system as a serotonin uptake inhibitor.[41, 42] The synthesis of Sertraline has been previously reported in 6 steps (56 % yield) from precursor 1,2-dihydronaphthalene (+)-145 which could also be accessible from ketol 144 (Scheme 15).[43] Our synthetic approach to (+)-145 requires protection of 144 as a silyl ether which was carried out by
following a modified literature procedure.\textsuperscript{[44]} In our case, an excess of TBSCl and \textsuperscript{3}Pr\textsubscript{2}NEt were needed together with longer reaction times in order to achieve complete conversion. Under these conditions ketol (-)-144 was protected in high yield (88\%) to give (+)-(4\textit{R})-4-(\textit{tert}-butyldimethylsiloxy)-1-tetralone (146). Addition of 3,4-dichloro-phenyl magnesium bromide\textsuperscript{[45]} gave after aq. work-up a mixture of diastereomeric tertiary alcohols. Treatment of this mixture with MsCl and Et\textsubscript{3}N gave access to the 1,2-dihydronaphthalene core and further TBAF deprotection in THF afforded (+)-(1\textit{R})-4-(2,3-dichlorophenyl)-1,2-dihydronaphthen-1-ol (145) in 79\% yield from (+)-146 with no loss of enantiopurity.

\begin{center}
\includegraphics[width=\textwidth]{scheme15.png}
\end{center}

\textbf{Scheme 15}

Compound (+)-145 was previously reported in low yield (40\%) from (\textit{R})-1,2-dihydro-1-hydroxynaphthalene in a four step sequence involving the use of toxic organotin and triphenylarsine.\textsuperscript{[43],[46]} Our approach thus represents the most efficient access to precursor (+)-145. The number of efficient routes to Sertraline has increased in the last decade because of its relevance in the pharmaceutical industry.\textsuperscript{[8],[47],[48]} Starting from (+)-145 the synthesis of sertraline has been previously achieved by diastereoselective hydrogenation, Mitsunobu reaction with HN\textsubscript{3} as protic nucleophile, hydrogenation, carbamate formation and reduction to Sertraline (Scheme 16).
Chapter IV: The rediscovery, isolation and synthetic potential of 1,4-tetralindione

IV.8 Enantioselective alkylation of 1,4-tetralinedione (134).

Catalytic asymmetric additions of allyl nucleophiles to carbonyls constitute an important class of C-C bond forming reactions.\[^{49}\] Homoallylic alcohols are versatile materials in organic synthesis. They give a direct access to a wide range of functional groups. Many catalysts will efficiently promote such additions to aldehydes\[^{50}\] Development of catalytic allylations of ketones, has been the subject of relatively few reports.\[^{51, 52}\] Walsh et al. described a very practical enantioselective catalyst for the asymmetric alkylation of ketones based on binol and Ti(iPrO)\(_4\).\[^{53}\] Tetralone gave the corresponding allylic alcohol in 96% yield, 95% ee. It was therefore decided to test this reaction with 1,4-tetralindione (134) (Scheme 17). The catalyst was preformed by mixing (-)-binol and Ti(iPrO)\(_4\) in CH\(_2\)Cl\(_2\) at r.t. Diketone (134) was then added followed by an excess of Sn(allyl)\(_4\) to give C\(_2\) symmetric diol (-)-(5S,8S)-1,4-dihydroxy-1,4-diallyltetraline (148) in excellent 93% yield, 97% ee.
Diol (-)-148 is not a crystalline solid, however its absolute 1S,4S configuration could be determined by X-ray analysis of the corresponding Cr(CO)₃ complex (-)-149 (Figure 4). The complex was obtained by arene exchange in [Cr(CO)₃(η⁶-naphthalene)] with (-)-148 in 93 % yield (Section I.3). The projection of the metal atom onto the arene plane shows a displacement (Δ = 0.04 Å) away from the C(1)-C(6) ring junction. As commonly found in ortho disubstituted meso complexes, the Cr(CO)₃ tripod adopts a staggered conformation with respect to the arene carbons.\textsuperscript{[55]}

**Figure 4:** ORTEP view of the crystal structure of (-)-149. Ellipsoids are represented at 40 % probability.

**IV.9 Easy access to 1,4-disubstituted naphthalenes.**

We envisaged dione 134 also as a precursor of 1,4-disubstituted naphthalenes by nucleophilic addition / dehydration sequence (Scheme 18). A concern was, the basic character these reagents (Section IV.3). Indeed, treatment of dione 134 with an excess of BuLi at low temperature gave low conversion to corresponding diastereomeric tertiary diols together with large amounts of aromatic 61. The mixture was then treated with HCl giving the desired 1,4-dibutyl-naphthalene (144) in a low yield (33 %) (Entry 1). The same reaction sequence was repeated with MeLi to afford 1,4-dimethylnaphthalene (151) in unsatisfactory yield (55 %). This problem was solved by using MeLi / CeCl₃ known to be a less basic and more nucleophilic reagent.\textsuperscript{[56, 57]} This provided 151 in 79 % yield after dehydration. To the best of
our knowledge, this approach represents the most efficient access to $^{151}$ However, using BuLi / CeCl$_3$ with dione 134 gave the corresponding naphthalene 150 in low yield.$^{[55]}$

![Scheme 18](image)

Scheme 18

Table 2

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Reagent</th>
<th>Solvent</th>
<th>T (°C)</th>
<th>Yield</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>butyl</td>
<td>BuLi</td>
<td>THF</td>
<td>-78</td>
<td>33 %</td>
</tr>
<tr>
<td>2</td>
<td>methyl</td>
<td>MeLi, CeCl$_3$</td>
<td>THF</td>
<td>-78</td>
<td>79 %</td>
</tr>
<tr>
<td>3</td>
<td>phenyl</td>
<td>PhLi</td>
<td>DME</td>
<td>-50</td>
<td>75 %</td>
</tr>
<tr>
<td>4</td>
<td>1-naphthyl</td>
<td>1-NapLi</td>
<td>THF</td>
<td>-78</td>
<td>75 %</td>
</tr>
</tbody>
</table>

Moreover, the addition of an excess of either PhLi or 1-naphthyllithium gave 152 or 143 in high 75 % yield after dehydration. This approach to 1,4-diphenyl naphthalene (152) represents an alternative route that complements the existing methods.$^{[60, 61]}$ However, no efficient synthesis of [1,1'-4,1'']ternaphthalene (153) has been previously reported.$^{[62]}$ Interestingly, trinaphthalene 153 was found to consist of a ca. 1 : 1 mixture of cis and trans rotamers in DMSO-d$_6$ at r.t. Rapid interconversion on the NMR time scale was found at 100 °C. At this temperature the $^{13}$C NMR spectra consisted of the expected 15 signals.

Encouraged by the results obtained with the addition of rather basic $sp^2$ organolithium reagents, we tested the performance of analogous vinyl and allylithium. They were generated by transmetalation with BuLi from the corresponding tin derivatives (Scheme 19). However, acidic treatment of the resulting mixture of diastereomeric tertiary alcohols caused polymerisation of the crude mixture. This protocol was repeated in each case and the resulting mixture of diastereoisomers could be resolved by flash chromatography giving moderate yields of the cis and trans 1,2-addition products (Table 3). A milder protocol for the dehydration step was investigated. Each diastereomeric mixture was treated with TsCl and
Et$_3$N at 0 °C in CH$_2$Cl$_2$ to give the corresponding 1,4-disubstituted naphthalenes in low overall yield after flash chromatography. While no synthetic route to 1,4-diallylnaphthalene (158) has been reported, more efficient protocols were found for the construction of naphthalene 157.$^{[63]}$

\[ \text{BuLi, SnR}_4 \quad \text{THF -78°C} \]

\[ \text{OH} \quad \text{OH} \]

\[ \text{OH} \quad \text{OH} \]

\[ \text{trans-} 155, \text{R} = \text{vinyl} \]

\[ \text{trans-} 148, \text{R} = \text{allyl} \]

\[ \text{Et}_3\text{N, MsCl} \quad \text{CH}_2\text{Cl}_2, 0 \degree \text{C} \]

\[ \text{cis-} 154, \text{R} = \text{vinyl} \]

\[ \text{cis-} 156, \text{R} = \text{allyl} \]

\[ 157, \text{R} = \text{vinyl} \]

\[ 158, \text{R} = \text{allyl} \]

Scheme 19

Table 3

<table>
<thead>
<tr>
<th>Entry</th>
<th>R</th>
<th>Yield cis</th>
<th>Yield trans</th>
<th>Yield 1,4-naphthalene</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>vinyl</td>
<td>12 %</td>
<td>61 %</td>
<td>36 %</td>
</tr>
<tr>
<td>2</td>
<td>allyl</td>
<td>10 %</td>
<td>40 %</td>
<td>36 %</td>
</tr>
</tbody>
</table>

Cis and trans stereochemistry of the divinyl diastereoisomers was determined by forming their respective Cr(CO)$_3$ complexes (Scheme 20).

\[ \text{[Cr(CO)$_3$(naphthalene)]} \quad \text{THF, Et}_2\text{O, 70°C} \]

\[ 154 \]

\[ \text{HO} \quad \text{HO} \]

\[ \text{HO} \quad \text{HO} \]

\[ \text{HO} \quad \text{HO} \]

\[ \text{cis-} 154 \]

\[ \text{trans-} 155 \]

\[ \text{meso-} 159 \]

\[ 159 \]

\[ 160 \]

Scheme 20
Complexation of cis-154 with [Cr(CO)_3(η^6-naphthalene)] gave a product with 8 different ^1^H-NMR signals, in agreement with the meso-configuration of complex 159. By contrast, C₂ symmetry in trans-155 is lost upon complexation and 15 different ^1^H-NMR signals are observed for complex 160. The relative configuration of trans-1,4-allyl-1,4-dihydroxynaphthalene (148) has been determined previously (Section IV.6).

IV.10 Tautomerism of substituted 1,4-dihydroxynaphthalenes.

As shown in this chapter, 1,4-tetralindione (134) can be readily obtained by stirring enol 61 in CF₃COOH and it has been proved to be a useful starting material for organic synthesis. Moreover, we have found this reaction to be general for substituted 1,4-naphthalene derivatives as previously remarked by Laatsch. In particular, isomerisation of 5-hydroxy-1,4-dihydroxynaphthalene (161) would give access to dione 162. The 5-hydroxy-1,4-disubstituted core is common in the family of Palmarumicyns with antifungal activity. Hydroxyl groups in the 5 or 8 positions of 1,4-dihydroxynaphthalene was found to favour the 1,4-diketo compound over the enolic tautomer, and the preferential stabilisation of the carbonyl compound was attributed to intramolecular hydrogen bonding.

The different naphthalene diols were prepared by Na₂S₂O₄ reduction of the corresponding commercial naphthoquinones (Scheme 21) and their isomerisation in CF₃COOH was attempted. By following this procedure, 1,4,5-trihydroxynaphthalene (161) tautomerised quantitatively to hydroxyldione 162 and no back isomerisation occurred upon evaporation of the solvent. The addition of toluene was not required in this preparation (Section IV.2). However, partial oxidation to 5-hydroxynaphthoquinone (Juglone) took place during purification by flash chromatography and dione 162 could only be obtained in 70% yield and it would be advisable to carry this operation in the future under N₂ (Scheme 20). The more electronenriched is the substituted tautomer the higher is the tendency to oxidise to the corresponding naphthoquinone. Despite the importance of this compound in natural product synthesis, nowadays, no efficient synthesis of dione 162 has ever been described.

Addition of a methyl group to 1,4-dihydroxynaphthalene in position 2 has been reported to slightly shift the tautomeric equilibrium to the enol form. However, we could observe that substitution on the hydroquinonic ring is also compatible with tautomerisation. Stirring 2-methyl-1,4-dihydroxynaphthalene (163) in CF₃COOH gave a 163 / 164 mixture 5 : 1 ratio after evaporation of the solvent. All attempts to isolate 164 by flash
chromatography resulted into decomposition to 2-methyl-1,4-naphthoquinone but this problem was solved by recrystallisation of the residue from iPr₂O giving 2-methyl dione 164 in 56 % yield. In the case of 1,2,4-trihydroxynaphthalene (165), complete oxidation to 2-hydroxy-1,4-naphthoquinone took place when stirred in CF₃COOH and no hydroxydiketone 166 could be isolated.

![Scheme 21](image)

Concerning other naphthalene diol isomers, we observed no diketone species from 1,3 or 2,3-dihydroxynaphthalene when stirred in CF₃COOH. This is probably due to the lower stability of the corresponding non-conjugated 1,3 or 2,3 diketones. In addition, the interconversion of 161 into 163 in the melt is known but melting 2,3-dihydroxynaphthalene did not cause any reaction. Surprisingly, when 1,3-dihydroxynaphthalene (167) (MP = 153 °C) was heated under N₂ at 200°C in a Kugelrohr apparatus, binaphthyl 168 was obtained in nearly quantitative yield (Scheme 22).

![Scheme 22](image)
We believe that 1,3-dihydroxynaphthalene (167) isomerises to ketone 169 at this temperature and is then attacked by the enol 167. The aldol intermediate 170 is then dehydrated in situ to give binaphthyl 168. None of the three other possible diastereoisomers were detected. To the best of our knowledge, there is no precedent for the self-aldol condensation of an aromatic enol.

IV.11 Conclusions and perspectives.

Despite the fact that 1,4-tetralindione (134) is a kinetically inert tautomer in solution, no chemistry has been ever reported since its first isolation in 1933. We have found dione 134 to be a useful starting material for the synthesis of natural products of interesting biological activities. We developed an easy and reliable procedure that gives access to multigram quantities of 134 and took up the challenge of exploring its reactivity. Starting from diketone 134 we succeeded with the following transformations:

1) Selective protection into TMS cyanohydrine 139.
2) Diastereoselective reduction to cis 141 or trans 142 1,4-tetralindiols.
3) Efficient CBS bisreduction and monoreduction.
4) Enantioselective bisallylation.
5) Enantioselective synthesis of Sertraline precursor 145.
6) Construction of 1,4-disubstituted naphthalenes.

Despite all the difficulties associated with its reactivity, dione 134 has shown a wide and rich chemistry.

Preliminary studies had shown the high tendency of dione 134 to isomerise to the enolic form in acid or basic media in a range of solvents. Moreover, dione 134 has been computed to be slightly more stable that its enol 61 in the gas phase. However, adding solvent interactions has shown that enol 134 is thermodynamically favoured in all cases and especially in more polar solvents as observed experimentally. When adding a Cr(CO)\(_3\) fragment to enol 61 the tautomeric equilibrium has been computed to be displaced to the dione complex 64. However, adding solvent interactions also favour the enol complex in disagreement with experimental observations. To date, these calculations are at low computational level and more accurate studies with implicit solvent models are ongoing.
Chapter IV: The rediscovery, isolation and synthetic potential of 1,4-tetralindione

As shown in Section IV.4, we have found high selective conditions for the monoprotection of dione 134. This achievement could allow those transformations that were not possible starting from 1,4-tetralindione 164 due to its high tendency to tautomerise to the aromatic enol 61 (Scheme 23). With this aim, α-alkylation[67-69], α-halogenation, [70, 71], Baeyern-Villiger[72, 73], asymmetric vinylation[53] and aldol condensation[74, 75] should be attempted with monoprotected 139.

![Scheme 23]

Readily available ketol 144 could also give access to new simple starting materials for organic synthesis or useful ligands for catalysis (Scheme 24). Performing a Mitsunobu reaction with HN₃[81-84] followed by hydrogenation[76-78] and CBS reduction would give 4-amino-1-tetralone 171. We have either found no described preparative procedures for enantioenriched aminoalcohols cis-172 and trans-73. Asymmetric reductive amination[79, 80] of ketol 171 should give access to these compounds.
We have also described an efficient synthesis of $C_2$ symmetric diol 142 by CBS reduction of 1,4-tetralindione by a using an easy procedure that provides multigram quantities of enantiopure diol 142 after crystallisation. The reactivity of this compound must be explored in the future. Double Mitsunobu reaction\[^{81-84}\] with HN$_3$ as protic nucleophile followed by reduction\[^{76-78}\] could give enantiopure $C_2$ symmetric diamine 174 (Scheme 25). Alternatively, cis-hydroxylamine 172 might be accessible by using stoiquiometric amounts of reagents.

It has been isolated a family of bioactive natural products containing a 1,8-dihydroxynaphthalene derived spiroacetal unit linked to more elaborated oxidised naphthalene moiety.\[^{85}\] This compounds are shown to possess antibacterial, antifungal and herbicidal activity\[^{86, 87}\] and some of these molecules could be synthesised in few steps from 1,4-tetralinedione derivatives. The synthesis of Palmarumicyns CP$_1$ and CP$_2$ has already been described in the literature.\[^{64, 85, 88-91}\] We are very interested in the development of an scaled up synthesis of 5-hydroxy-1,4-tetralindione (162) since it could provide access to

---

**Scheme 24**

**Scheme 25**
Palmarumycin CP₁ by acetal formation with 1,8-dihydroxynaphthalene. Protection of the hydroxyl group might be necessary to achieve higher selectivity during spiroacetal formation (Scheme 26).

![Scheme 26](image)

Some approaches to CJ-12,371 have been described in the literature but none of them are asymmetric. \(^{85, 90, 91}\) CBS reduction\(^{32, 33}\) of Palmarumycin CP₁ seems a viable path to this natural occurring compound with antifungal activity (Scheme 27).

![Scheme 27](image)

Juglanoside A was isolated from the fresh rejuvenated fruit of *J. mandshurica*\(^{92}\) and exhibits moderate hepatoprotective effects on drug induced citotoxicity. It has never been prepared and it could be synthesised by condensation of D-glucose and enantioenriched (4S)-4-hydroxy-1-tetralone \(^{144}\) (Scheme 28).\(^{93-97}\)
Catalponol presents is a natural occurring termite repellent\textsuperscript{[98]} is a natural occurring compound that presents antifungal and cytotoxic activity and it has not been synthesised before. It could be accessed from enantioenriched hydroxytetralone 144 by $\alpha$-alkylation\textsuperscript{[67-69]} of its protected available derivative 146. We expect to obtain the desired *anti* isomer Catalponol after TBAF deprotection. The selectivity of the akylation could be tuned by the nature of the silyl ether group (Scheme 29). If the process occurs with low diastereoselectivity, asymmetric $\alpha$-alkylation *via* enamine formation can be attempted as alternative.\textsuperscript{[75]}
IV.12 References.

Chapter IV: The rediscovery, isolation and synthetic potential of 1,4-tetralindione

[40] G. J. Quallich, *Chirality* 2005, 17, S120.
Chapter IV: The rediscovery, isolation and synthetic potential of 1,4-tetralindione


V. Experimental part

V.1 General.

Solvents were purified by filtration on drying columns using Solvtek system or by distillation in the presence of Na / benzophenone ketyl or CaH₂. Chemicals were purchased from Aldrich, Fluka, Acros, Lancaster, TCI organics or Buchler GmbH and used without further purification unless noted. Reactions and manipulations involving organometallic or moisture sensitive compounds were carried out under N₂ atmosphere and glassware was previously dried by heating under high vacuum as necessary. All chromium complexes were kept away from light by covering with aluminium foil during reaction, work-up, purification and storage. These complexes must be handled under N₂ atmosphere with N₂ saturated solvents or degassed by three freeze-pump-thaw cycles unless noted. Plates were visualised using UV light 254-366 nm and chemical staining with a solution of 3,4-dinitrophenylhydrazine¹, phosphomolybdic acid² or cerium ammonium molybdate³. Celite 545 was used as filtering material. Yields refer to homogeneous material purified by crystallisation or Flash column chromatography using Brunschwick silica gel 60 Å (32-63 mesh) or Acros neutral Alumina (50-200 micron). Proton and carbon NMR spectra were recorded on Bruker AMX-500, AMX-400 or AMX-300 Fourier transform spectrometers using an internal deuterium lock. Chemical shifts are quoted in parts per million (ppm) downfield of tetramethylsilane. Coupling constants $J$ are quoted in Hz. Carbon NMR and DEPT-135 spectra were recorded with broad band proton decoupling. Infrared spectra were recorded on a Perkin-Elmer Spectrum One spectrophotometer. Analytical HPLC was performed using an Aligent 1100 series. Electron impact (EI) mass spectra were obtained using Varian CH-4 or SM-1 instruments operating at 40-70eV and for Electrospray ionization (ESI) HRMS analyses were measured on a VG analytical 7070E instrument. Optical rotations were measured at 20°C on a Perkin Elmer 241 polarimeter using a quartz cell ($l = 10$ cm) with a Na high pressure lamp ($\lambda = 589$ nm). Melting points were determined on a Büchi 510 and are uncorrected.

¹ Dissolve 12 g of 2,4-dinitrophenylhydrazine, 60mL of conc. sulfuric acid, and 80mL of water in 200mL of 95% ethanol.
² Dissolve 8.6 g of H₂Mo₁₂O₄₀P aq. in 180 mL EtOH
³ To 235 mL of distilled water was added 12 g of ammonium molybdate, 0.5 g of ceric ammonium molybdate, and 15 mL of H₂SO₄.
Experimental part related to Chapter II.

1,4-dihydroxynaphthalene (61).

Tin chloride dihydrate (34.0 g, 150.7 mmol), crystalline 1,4-naphthoquinone (20.0 g, 126.6 mmol), distilled water (300 mL) and 37 % hydrochloric acid (110 mL) were added to a 2 L round bottomed flask. After stirring for 6 h at r.t. the mixture had turned creamy white in colour. Water (900 mL) was added to the mixture followed by heating to reflux until clear (5 min). Crystallisation was carried out overnight at 5 °C. Filtration, three washings with cold water and drying under high vacuum afforded compound 61 (19.0 g, 94 %) as pale white needles. Experimental data agreed with the reported literature values. MW = 160.18 g / mol; R_F = 0.36 (AcOEt / pentane 1 : 2); MP = 195 °C (under N_2, H_2O); IR (neat, cm^{-1}): 3286, 1642, 1597, 1480, 1336, 1266, 1236, 1061; \textbf{^1}H NMR (400 MHz, d_6-DMSO): δ 9.31 (s, 2H), 8.05-8.00 (m, 2H), 7.43-7.38 (m, 2H), 6.65 (s, 2H); \textbf{^13}C NMR (100 MHz, d_6-DMSO): δ 145.86, 125.77, 125.17, 122.37, 108.32.

1,4-bis(trifluoroacetoxy)naphthalene (62).

Trifluoroacetic anhydride (38 mL, 273 mmol) was added at r.t. to a stirred solution of 1,4-dihydroxynaphthalene (61) (9.30 g, 58 mmol) in Et_2O (184 mL) under N_2. After stirring for 65 h the volatiles were removed under reduced pressure. The crude product was dissolved in boiling hexane, filtered through paper and stored at -20 °C overnight. Separation of the solid formed and three washes with cold hexane afforded 62 (17.71 g, 86 %) as white needles. The solubility of 62 in boiling hexane is 0.05 g / mL; MW = 352.19 g / mol; MP = 119-120 °C (hexane); R_F = 0.52 (Et_2O / pentane 1 : 4); IR (neat, cm^{-1}): 1800, 1602, 1467, 1390, 1350, 1221, 1160, 1122; \textbf{^1}H NMR (400 MHz, CDCl_3): δ 7.94-7.89 (m, 2H), 7.71-7.64 (m, 2H), 7.46 (s, 2H); \textbf{^13}C NMR (125 MHz, CDCl_3): δ 155.9 (q, J 44.1), 143.9, 128.8, 127.0, 121.2, 117.4, 115.0 (q, J 285.4); MS m/z (El): 352 (84, M), 255 (58), 227 (19), 199 (34), 130 (9), 102 (12), 97 (10), 76 (14), 69 (100), 50 (10); HRMS (El) calcd. for C_14H_6O_4F_6 [M^+]: 352.0170, found 352.0137.
A Schlenk tube was charged under N₂ with 1,4-bis(trifluoroacetoxy)naphthalene (62) (2.30 g, 6.53 mmol) and [Cr(CO)₃(NH₃)₃]₃ (1.12 g, 5.98 mmol). Diethyl ether (40 mL) was added followed by BF₃·Et₂O (3.0 cm³, 24.0 mmol). The yellow suspension was degassed three times by freeze-pump-thaw cycles, sealed to N₂ and stirred at r.t. during 6 days, turning from yellow to orange suspension. The reaction mixture was filtered under N₂ through a pad of celite and washed with portions of boiling toluene (20 mL) until all of the orange material had been collected (stirring the surface of the celite with a glass rod is necessary to dissolve this material). The solvent was reduced to 180 mL under high vacuum. The mixture was heated until all had dissolved and then stored at -20 °C overnight. The supernatant was filtered through a canula, the solid precipitate washed with cold hexane (2 x 20 mL) and dried under high vacuum to give complex 59 (2.34 g, 80 %) as a deep orange solid.

**MW** = 488.21 g / mol; **MP** = 162-163 °C (dec., under N₂, toluene); **IR** (methylcyclohexane, cm⁻¹): 1990, 1934, 1922, 1811, 1238, 1114; **¹H NMR** (400 MHz, C₆D₆): δ 6.39 (s, 2H), 5.43-5.39 (m, 2H), 4.39-4.35 (m, 2H). **¹³C NMR** (100 MHz, C₆D₆): δ 229.7, 142.2, 128.0, 116.8, 97.5, 90.9, 81.7; **¹⁹F NMR** (376 MHz, C₆D₆): δ 87.6; **MS m/z** (EI): 488 (4, M⁺), 404 (50), 352 (11), 310 (44), 255 (10), 126 (15), 69 (17), 52 (100); **HRMS** (EI) calcd. for C₁₇H₆O₇CrF₆ [M⁺]: 487.9419, found 487.9422.

**[Cr(CO)₃(η⁶-5,8-naphthoquinone)] (57).**

**Method A:** A Carius tube was charged with 1,4-dihydroxynaphthalene¹ (61) (2.57 g, 16.0 mmol), [Cr(CO)₃(NH₃)₃]₃ (2.14 g, 11.4 mmol), dry Et₂O (120 mL) and BF₃·Et₂O (8.7 mL, 64.9 mmol). The yellow suspension was degassed three times by freeze-pump-thaw cycles, closed to N₂ and stirred at r.t. during 5 days. The contents were cooled with an ice / NaCl bath and Et₂O (40 mL) was added followed by sat. aq. NaHCO₃ (160 mL). The organic layer was transferred at r.t. via canula to a Schlenk tube with MgSO₄ together with several extractions using Et₂O. The combined organic layers were filtered via canula into another Schlenk tube and the volatiles were reduced under high vacuum. To this orange crude material, Ag₂O (6.47 g, 27.9 mmol) was added followed by MgSO₄ (31.4 g, 0.26 mol) and Et₂O (154 mL). The suspension was stirred at r.t. and turned deep violet after 1 h. Reaction was followed by TLC (1 : 1,
Et₂O / pentane). Then the reaction mixture was filtered through a plug of celite in air, rinsed with non-degassed CH₂Cl₂ and all volatiles were evaporated using a rotary evaporator. Toluene (100 mL) and hexane (600 mL) were saturated with N₂ and used to recrystallise the crude product under N₂. This dissolved entirely when boiled and no filtration was needed. After cooling, at -20 °C overnight, the supernatant was filtered through a canula, the solid precipitate was washed with cold hexane (2 x 20 mL) and dried under vacuum to give [Cr(CO)₃(η⁶-5,8-naphthoquinone)] (57) (2.54 g, 76 %) as a dark violet solid.

**Method B:** A Schlenk tube was charged with bistrifluoroacetate complex 59 (2.92 g, 6.00 mmol), silica (9.06 g) and Et₂O (150 mL). The contents were cooled to 0 °C and Et₃N (1.86 mL, 13.20 mmol) was added slowly. The orange colour of the suspension changed to dark red. After stirring for 1 minute, a solution of 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) (1.50 g, 6.60 mmol) in Et₂O / THF (40.5 mL / 19.5 mL) was added slowly via canula; the solution turned deep violet immediately and stirring was continued for 10 min at r.t. The mixture was filtered through celite and washed with CH₂Cl₂ (in air). All volatiles were removed under reduced pressure using a rotary evaporator and the dark violet residue was dissolved in non degassed CH₂Cl₂ (450 mL) and washed sat. aq. NaHCO₃ (3 x). After extraction with CH₂Cl₂ (3 x), the combined organic phases were dried with MgSO₄ and the solvent removed using a rotary evaporator. The residue was recrystallised under N₂ from degassed boiling hexane (600 mL) to give [Cr(CO)₃(η⁶-1,4-naphthoquinone)] (57) (1.41 g, 80 %) as a dark violet solid.

**MW** = 294.18 g / mol; **RF** = 0.44 (Et₂O / cyclohexane 2 : 1); **MP** = decomposition before 300 °C (under N₂, toluene / hexane); **IR** (CH₂Cl₂, cm⁻¹): 1996, 1937, 1668, 1307, 1265; **¹H NMR** (400 MHz, C₆D₆): δ 6.09 (s, 2H), 5.54-5.51 (m, 2H), 4.41-4.37 (m, 2H); **¹³C NMR** (100 MHz, C₆D₆): δ 230.0, 183.7, 137.4, 92.2, 91.8, 89.3; **MS m/z** (EI): 294 (10, M), 238 (5), 210 (34), 158 (46), 104 (8), 101 (112), 86 (58), 57 (23), 52 (100); **HRMS (EI)** calcd. for C₁₃H₆O₅Cr [M⁺]: 293.9620 found 293.9627; **Elemental analysis:** calcd. for C₁₃H₆O₅Cr: 53.08 % C, 2.06 % H found 52.98 % C, 2.18 % H.

[Cr(CO)₃(η⁶-5,8-dihydroxynaphthalene)] (63).

A Schlenk tube was charged with [Cr(CO)₃(η⁶-5,8-naphthoquinone)] (57) (700 mg, 2.38 mmol), Et₂O (25 mL) and a solution of Na₂S₂O₄ (447 mg, 2.85 mmol) in H₂O (25 mL) at r.t. After 10 min stirring, a colour change from deep violet to orange was observed. The organic layer was
transferred via canula to a Schlenk tube with MgSO$_4$ and the aqueous layer was extracted (3x) with small portions of Et$_2$O. The combined organic layers were filtered via canula to another Schlenk tube and all volatiles were removed under high vacuum. The orange solid was then scratched from the walls of the Schlenk, washed with non-degassed pentane and dried under vacuum to give pure complex 63 (651 mg, 93 %) as an orange solid.$^{[4]}$

**MW** = 296.19 g / mol; $R_F$ = 0.68 (dec., Et$_2$O); **MP** = 137-138 °C (under N$_2$, benzene); **IR** (toluene, cm$^{-1}$): 3527, 2927, 2866, 1966, 1897, 1887, 1628, 1460, 1278, 1059; **$^1$H NMR** (500 MHz, C$_6$D$_6$): $\delta$ 6.10-6.07 (m, 2H), 5.64 (s, 2H), 4.59-4.57 (m, 2H), 4.44 (broad s, 2H); **$^{13}$C NMR** (125 MHz, C$_6$D$_6$): $\delta$ 233.0, 145.4, 108.1, 98.4, 91.9, 86.0; **MS** $m/z$ (EI): 296 (11, M$^+$), 240 (7), 212 (42), 160 (26), 131 (9), 104 (9), 77 (6), 52 (100); **HRMS** (EI) calcd. for C$_{13}$H$_8$O$_5$Cr [M+]: 295.9776 found 295.9759.

**[Cr(CO)$_3$(η$^6$-5,8-tetralindione)] (64).**

**Method 1:** A Carius tube was charged with 1,4-dihydroxynaphthalene$^{[1]}$ (61) (687 mg, 4.29 mmol), [Cr(CO)$_3$(NH)$_3$]$^{[3]}$ (536 g, 2.86 mmol), Et$_2$O (30 mL) and BF$_3$.Et$_2$O (2.17 mL, 17.16 mmol). The yellow suspension was degassed three times by freeze-pump-thaw cycles, closed to N$_2$ and stirred at r.t. during 5 days. All organic and aqueous solvents used during the workup were saturated with N$_2$. The contents were cooled with an ice / NaCl bath, Et$_2$O (40 mL) was added followed by sat. aq. NaHCO$_3$ (160 mL), the organic layer was transferred via canula to a Schlenk tube with MgSO$_4$ and the aqueous layer was extracted (3x) with small portions of Et$_2$O. The combined organic layers were filtered via canula to another Schlenk tube and all volatiles were removed under vacuum. The orange residue was mixed with toluene (42 mL) and CF$_3$COOH (440 µL, 5.72 mmol). The suspension was degassed three times by freeze-pump-thaw cycles and the Schlenk tube was closed to N$_2$. After stirring at r.t. for 14 h a deep change of colour from orange to red was observed. The reaction mixture was then cooled at 0 °C, filtered via canula to a Schlenk tube and all volatiles were removed under high vacuum. The residue was recrystallised, under N$_2$, from boiling $^i$Pr$_2$O (30 mL, degassed three times by freeze-pump-thaw cycles) to give [Cr(CO)$_3$(η$^6$-5,8-tetralindione)] (64) (554 mg, 65 %) as a red solid.$^{[4]}$

**Method 2:** Chromium tricarbonyl complex 63 (735 mg, 2.48 mmol) was placed in a Carius tube under N$_2$ with dry benzene (37 mL) and CF$_3$COOH (190 µL, 2.48 mmol). This mixture was then degassed by three freeze-thaw-pump cycles and the Carius tube closed to N$_2$. After stirring at 65° for 3 h a change of colour from orange to red was observed. The reaction
mixture was cooled to r.t. and all volatiles removed under high vacuum. Two successive recrystallisations, under N₂, from boiling iPr₂O (degassed three times by freeze-pump-thaw cycles) gave [Cr(CO)₃(η⁶-5,8-tetralindione)] (64) (624 mg, 85 %) as a red solid.

**MW** = 296.20 g / mol; **Rᶠ** = 0.20 (Et₂O / pentane 1 : 1) decomposition; **MP** = 100-101 °C (under N₂, iPr₂O); **IR** (benzene, cm⁻¹): 3095, 3041, 2926, 1992, 1931, 1701, 1483; **¹H NMR** (400 MHz, C₆D₆): δ 5.44-5.40 (m, 2H), 4.36-4.32 (m, 2H), 2.32-2.22 (m, 2H), 2.01-1.91 (m, 2H); **¹³C NMR** (100 MHz, C₆D₆): δ 229.8, 193.8, 95.8, 92.5, 89.0, 35.6; **MS** m/z (ESI): 297 (8 (M⁺+1)), 296 (24), 295 (100), 173 (88), 113 (68), 63 (8); **HRMS** (EI) calcd. for C₁₃H₈O₅Cr [M⁺]: 295.9776 found 295.9776; **Elemental analysis**: calcd. for C₁₃H₈O₅Cr: 52.71 % C, 2.72 % H found 52.97 % C, 2.96 % H.

**(-)[Cr(CO)₃(η⁶-(5R,8R)-5,8-dihydroxytetraline)] (68).**

**Method 1:** A solution of [Cr(CO)₃(η⁶-5,8-tetralindione)] (64) (100 mg, 0.34 mmol) in dry THF (3.4 mL) was added over a period of 1 h to a stirring, cooled (-10 °C) solution of BH₃·THF (0.41 mL, 1 M THF, 0.41 mmol) and (S)-3,3-diphenyl-1-methyltetrahydro-3H-pyrrolo[1,2-c][1,2,3]oxaza-borole (67) (34 μL, 1 M toluene, 0.034 mmol) in dry THF (2.6 mL). The red colour of 64 rapidly faded to yellow upon addition. Stirring was continued for 30 min. The reaction mixture was then quenched with MeOH (3 mL), warmed to r.t. and all volatiles were removed under reduced pressure. Flash chromatography (CH₂Cl₂ / MeOH 20 : 1) yields (-)[Cr(CO)₃(η⁶-(5R,8R)-5,8-dihydroxytetraline)] (68) (81 mg, 80 % yield, 99 % ee) as a yellow solid, [α]D₂₀ = -124 (c = 0.53, MeOH).

**Method 2:** A 10 mL Carius tube was charged under N₂ with enantiopure (-)-(1R,4R)-1,4-tetralindiol (142) (107 mg, 0.66 mmol), [Cr(CO)₃(η⁶-naphthalene)] (87 mg 0.33 mmol), dry THF (80 μL, 0.66 mmol) and dry Et₂O (330 μL). The mixture was degassed by three freeze-pump-thaw cycles, closed and heated at 70 °C under N₂ for 6 h. A complete change from red to yellow was observed. Evaporation of the solvent under vacuum and purification by flash chromatography (CH₂Cl₂ / MeOH, 20 : 1) gave (-)[Cr(CO)₃(η⁶-(5R,8R)-5,8-dihydroxytetraline)] (68) (99 mg, 99 % yield, 99 % ee) as a yellow solid, [α]D₂₀ = -112 (c = 0.54, MeOH).

**MW** = 300.22 g / mol; **Rᶠ** = 0.17 (AcOEt / pentane 1 : 2); **MP** = 116-115 °C (under N₂, CH₂Cl₂ / hexane); **IR** (CH₂Cl₂, cm⁻¹): 3599, 2955, 1967, 1890, 1451, 1384, 1181, 1107; **¹H NMR** (400 MHz, CDCl₃): δ 5.21 (d, J 7.0, 1H), 5.00 (d, J 6.5, 1H), 4.60 (t, J 6.4, 1H), 4.28-
4.25 (m, 1H), 4.24-4.21 (m, 1H), 3.94-3.92 (m, 1H), 1.61-1.54 (m, 2H), 1.34-1.32 (m, 1H), 1.25-1.22 (m, 1H), 1.08 (m, 1H), 0.93-0.90 (m, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ 233.1, 113.4, 112.3, 94.2, 91.4, 91.1, 90.9, 67.7, 67.2, 30.8, 30.5; HRMS (EI) calcd. for C$_{13}$H$_{12}$O$_5$Cr [M$^+$]: 300.0089 found 300.0090; HPLC Chiralcel OJ, F = 1 mL/min, Hexane / $^t$PrOH 90 : 10, $T_R$ = 113.6 min ((5S,8S)-enantiomer) and 129.1 min ((5R,8R)-enantiomer), $\lambda$ = 254 nm.

(-)-(8$R$)-[Cr(CO)$_3$(η$^6$-8-hydroxy-5-tetralone)] (69).

A solution of catecholborane (1.5 mL, 1 M toluene, 1.52 mmol) was added during 20 min to a stirred on, cooled (-78 °C) solution of [Cr(CO)$_3$(η$^6$-5,8-tetralindione)] (64) (300 mg, 1.01 mmol) and (S)-3,3-diphenyl-1-butyltetrahydro-3H-pyrrolo[1,2-c][1,2,3]oxazaborole$^5$ (65) (1.0 mL, 0.1 M toluene, 0.10 mmol) in dry toluene (5 mL). After stirring for 18 h at -78 °C the reaction faded from red to orange. The mixture was then quenched with sat. aq. NaHCO$_3$ and washed with sat. aq. NaHCO$_3$ (3 x). After extraction with Et$_2$O (3 x), the combined organic layers were dried with Na$_2$CO$_3$ and all volatiles removed under reduced pressure. This residue was purified by flash chromatography (AcOEt / pentane 1 : 2) to give (-)-(5S)-[Cr(CO)$_3$(η$^6$-8-hydroxy-5-tetralone)] (69) (297 mg, 98 % yield, 96.6 % ee) as an orange solid, $[\alpha]_D^{20} = -715$ (c = 0.29, CH$_2$Cl$_2$).

**MW** = 298.21 g / mol; **RF** = 0.22 (AcOEt / pentane 1 : 2); **MP** = decomposition before 184 °C (under N$_2$, $^t$Pr$_2$O / hexane); **IR** (CH$_2$Cl$_2$, cm$^{-1}$): 3602, 3063, 2929, 1981, 1914, 1688, 1523, 1454, 1421, 1326; **$^1$H NMR** (400 MHz, CD$_6$D$_6$): $\delta$ 5.70 (d, $J_{6.8}$, 1H), 5.00 (d, $J_{6.6}$, 1H), 4.56 (t, $J_{6.8}$, 1H), 4.28 (t, $J_{6.8}$, 1H), 3.90-3.78 (m, 1H), 2.27-1.13 (m, 1H), 1.70-1.48 (m, 3H); **$^{13}$C NMR** (75 MHz, CD$_2$Cl$_2$): $\delta$ 231.8, 195.5, 119.8, 94.8, 93.3, 91.2, 91.1, 87.9, 66.7, 36.7, 32.5; **MS** m/z (EI): 297 (100 [M$^+$]), 243 (7), 195 (10), 171 (8), 131 (7), 59 (30); **HRMS** (EI) calcd. for C$_{13}$H$_{11}$O$_5$Cr [M+H$^+$]: 299.0006 found 299.0009; HPLC Chiralcel OJ, F = 0.5 mL/min, Hexane / $^t$PrOH 90 : 10 gradient to 85 / 5 over 60 min, $T_R$ = 48.4 min ((8S)-enantiomer) and 63.0 min ((8R)-enantiomer), $\lambda$ = 254 nm.

**meso-[Cr(CO)$_3$(η$^6$-5,8-dihydro-5,8-dihydroxynaphthalene)] (66).**

A Schlenk tube was charged under N$_2$ with [Cr(CO)$_3$(η$^6$-5,8-naphthoquinone)] complex (57) (1.00 g, 3.40 mmol), CeCl$_3$·7H$_2$O (1.27 g, 3.40 mmol) and MeOH (85 mL, degassed by three freeze-pump thaw cycles). The mixture was cooled to 0°C and NaBH$_4$ (270 mg, 7.10 mmol)
was added in small portions under stirring. Vigorous gas evolution was observed and the deep violet colour turned to pale yellow immediately. The reaction mixture was stirred for 20 min at r.t. before addition of water (42 mL) and brine (42 mL). The mixture was extracted in air with Et₂O (3 x) and the combined organic phases dried over MgSO₄. After filtration the solvent was removed under reduced pressure. Three successive recrystallisations from degassed ¹Pr₂O / hexane gave 66 (845 mg, 83 %) as bright yellow needles. Flash chromatography can also be used for purification (Et₂O / pentane 2 : 1). \( MW = 298.22 \text{ g/mol; } R_F = 0.19 \) (ether / cyclohexane, 2 : 1); \( MP = 139-141^\circ C \) (under N₂, ¹Pr₂O / pentane); \( \text{IR (CH}_2\text{Cl}_2, \text{ cm}^{-1}) \): 3586, 2855, 1969, 1895, 1265, 1260; \( ^1\text{H NMR (400 MHz, C}_6\text{D}_6) \): \( \delta \) 5.52 (s, 2H), 5.24-5.19 (m, 2H), 4.54-4.49 (m, 2H), 4.24 (d, \( J \) 9.8, 2H) 1.59 (d, \( J \) 10.1, 2H); \( ^{13}\text{C NMR (100 MHz, C}_6\text{D}_6) \): \( \delta \) 233.1, 129.2, 111.4, 91.5, 88.9, 62.8; \( \text{MS} \ m/z \) (EI): 298 (2, M⁺), 264 (4), 196 (6), 180 (16), 144 (15), 128 (100), 115 (10), 52 (61); \( \text{HRMS} \) calcd. for C₁₃H₁₀O₅Cr \([\text{M}^+]: \) 297.9933 found 297.9957. \textbf{Elemental analysis:} calcd. for C₁₃H₁₀O₅Cr: 52.36 % C, 3.38 % H found 52.32 % C, 3.44 % H.

\textit{meso-[Cr(CO)₃(\( \eta^6\)-5,8-tetralindiol)] Cr(CO)₃ (65).}

\[ \text{[Cr(CO)₃(\( \eta^6\)-5,8-tetralindione)] (64) (269 mg, 1 mmol) and MeOH (25 mL) were placed under N₂ in a Carius tube. The mixture was stirred at r.t. while NaBH₄ (113 mg, 3 mmol) was added slowly. Vigorous gas evolution was observed and the deep violet colour turned to pale yellow immediately. Stirring was continued for 10 min before addition of water (12 mL) and brine (12 mL). The mixture was extracted with Et₂O (3 x) and the combined organics dried with MgSO₄. After filtration the solvent was removed under reduced pressure to give a dark yellow residue. Purification by flash chromatography (Et₂O / CH₂Cl₂ / pentane, 3:3:2) gave 65 (269 mg, 90 %) as a bright yellow solid.\[^{[4]}\] \( MW = 300.22 \text{ g/mol; } R_F = 0.20 \) (AcOEt / pentane); \( MP = 134-136^\circ C \) (under N₂, CH₂Cl₂ / hexane); \( \text{IR (CH}_2\text{Cl}_2, \text{ cm}^{-1}) \): 1968, 1892, 1270, 1260, 1047; \( ^1\text{H NMR (400 MHz, C}_6\text{D}_6) \): \( \delta \) 4.43-4.90 (m, 2H), 4.40-4.37 (m, 2H), 3.71-3.67 (m, 2H), 1.57-1.48 (m, 2H), 1.33 (d, \( J \) 8.3, 2H), 1.25-1.16 (m, 2H); \( ^{13}\text{C NMR (100 MHz, CD}_2\text{Cl}_2) \): \( \delta \) 233.6, 117.2, 93.0, 91.6, 66.12, 29.0; \( \text{MS} \ m/z \) (ESI): 200 (11, \([\text{M}]^+\)), 244 (25), 216 (30), 196 (52), 180 (37), 146 (38), 130 (100), 129 (88), 105 (20), 69 (23); \( \text{HRMS} \) (ESI) calcd. for C₁₃H₁₃O₅Cr \([\text{M}^+H]^+: \) 301.0162, found 301.0130.
Preparation of samples for NMR monitoring: \( \text{C}_6\text{D}_6 \) four times degassed by freeze-pump-thaw cycles was distilled over CaH\(_2\). NMR tubes were flame-dried under vacuum and silylated under N\(_2\) by treating with a solution of \( N,O\)-bis(trimethylsilyl)acetamide in Et\(_2\)O (5 \%) for 30 min, then rinsed six times with dry Et\(_2\)O and dried in an oven at 60 °C overnight and flame dried again under vacuum. Then, either 1,4-dihydroxynaphthalene (61) (1.4 mg), or 1,4-tetralinedione (134) (1.4 mg) was introduced under N\(_2\) to this silylated and dry NMR tube followed by 1 mL of C\(_6\)D\(_6\). The tube was frozen in liquid N\(_2\) and sealed under high vacuum using an acetylene flame. The relative proportions of tautomers were measured by integration of the deconvoluted \(^1\text{H}-\text{NMR} \) signals at 7.98 ppm and 8.23 ppm for 134 and 61 respectively. In case of monitoring \([\text{Cr(CO)}_3(\eta^6\text{-5,8-dihydroxynaphthalene})]\) (63) and \([\text{Cr(CO)}_3(\eta^6\text{-5,8-tetralinedione})]\) (64), saturated solutions in C\(_6\)D\(_6\) were prepared in a glove box and placed into a screw-threaded teflon capped NMR tube (Young’s tube). The relative proportions of tautomers were found by integration of the deconvoluted signals at 6.08 ppm and 5.42 ppm for 63 and 64 respectively. The \(^1\text{H}-\text{NMR} \) experiments were recorded using a Bruker AMX-300 (for 134 and 61) or AMX-500 (for 63 and 64) Fourier transform spectrometers, NS = 32, d1 = 60 sec.

V.2.1 References:

V.2 Experimental part related to Chapter II
V.3 – Experimental part related to Chapter III.

V.3.1 General.

Solid bases and acyl transfer reagents were purified by sublimation. If liquid, they were distilled under N₂ from CaH₂ in an H-tube and used right away. Molecular sieves (4Å) were activated prior to use by heating at 160 °C under high vacuum for 12 hours. NOTE: Diamines 93 to 94 slowly reacted when dissolved in CH₂Cl₂ to the corresponding chloromethylene chloride salt.

V.3.2 Synthesis of chiral nucleophilic catalysts 93 and 94.

(2S,4S,5R)-N,N-dimethyl-2-aminomethyl-5-ethenyl-quinuclidine (95).

A Schlenk tube equipped with a reflux condenser was rapidly charged with (2S,4S,5R)-2-aminomethyl-5-ethenyl-quinuclidine[1] (1.41 g, 8.51 mmol), evacuated for 30 seconds, filled with N₂, and cooled to 0 °C. Then 98 % formic acid (2.04 mL, 54.1 mmol) and 36.5 % formaldehyde (1.74 mL, 24.5 mmol) were added sequentially and the mixture was refluxed for 3 h. The reaction was then cooled at r.t. and dissolved in a solution (1M) of HCl (30 mL) and extracted with Et₂O (3 x). The aqueous layer was then brought up to pH ≈ 12 with K₂CO₃ and extracted with Et₂O (3 x). The combined organic layers were dried with anh. Na₂SO₄ and volatiles removed under low pressure to give the title compound 95 (1.56 g, 94 % yield) as a colourless oil.

MW = 194.34 g / mol; RF = 0.58 (CHCl₃ 84%; MeOH 14%; NH₃ₐq 2%); [α]D²⁰: +46 (c = 1.64 CHCl₃); IR (neat, cm⁻¹): 3340, 3075, 2934, 2860, 2818, 2764, 1636, 1454, 1320, 1263, 1163, 1123, 1027, 990, 908; ¹H NMR (400 MHz, CDCl₃): δ 5.84 (ddd, J = 17.2, 10.3 and 7.6 Hz, 1H), 5.02-4.94 (m, 2H), 3.13 (dd, J = 13.8 and 10.1, 1H), 2.94-2.79 (m, 2H), 2.65-2.57 (m, 2H), 2.42 (dd, J = 12.5 and 8.3, 1H), 2.26-2.20 (m, 1H), 2.19 (s, 6H), 2.07 (dd, J = 12.5 and 6.5, 1H), 1.86-1.79 (m, 1H), 1.70-1.65 (m, 1H), 1.48-1.41 (m, 2H), 0.89 (dddd, J = 13.3, 6.7, 2.5 and 1.7, 1H); ¹³C NMR (125 MHz, CDCl₃): δ 142.2, 114.1, 64.1, 56.2, 53.6, 45.9, 40.8, 39.9, 28.9, 27.8, 27.4; HRMS (ESI) calcd. for C₁₂H₂₃N₂ [M+H]⁺: 195.1855, found: 195.1861.
**V.3 – Experimental part related to Chapter III**

(2S,4S,5R)-N,N-dimethyl-2-aminomethyl-5-ethylquinuclidine (93).

A two neck round bottom flask equipped charged with (2S,4S,5R)-N,N-dimethyl-2-aminomethyl-5-ethene-quinuclidine (95) (1.12 g, 5.80 mmol) and 10 % palladium on charcoal (123 mg, 0.12 mmol). The flask was evacuated and refilled with H$_2$ from a balloon. Then MeOH (27 mL) was added and the suspension was stirred at r.t. for 16 h. The reaction mixture was filtered and the solvent evaporated under reduced pressure. The residue was dissolved aq. HCl (1M, 45 mL) and extracted with Et$_2$O (3 x). The aqueous layer was then brought to pH ≈ 12 with K$_2$CO$_3$ and extracted with Et$_2$O (3 x). The combined organic layers were dried with anh. Na$_2$SO$_4$ and volatiles removed under low pressure to give the title compound 93 (1.13 g, 95 % yield) as a colourless oil.

**MW** =196.34 g / mol; **R$_f$** = 0.64 (CHCl$_3$ 84%; MeOH 14%; NH$_3$(aq) 2%); **[α]$_{D}^{20}$**: +12 (c = 0.70 CHCl$_3$); **IR** (CHCl$_3$, cm$^{-1}$): 3137, 2934, 2864, 2775, 2822, 1457, 1379, 1264, 1093, 1027;

**1H NMR** (400 MHz, CDCl$_3$): δ 3.17 (dd, $J$ = 13.5 and 9.4, 1H), 2.98-2.81 (m, 2H), 2.71-2.60 (m, 1H), 2.42 (dd, $J$ = 12.3 and 8.0, 1H), 2.46-2.36 (m, 1H), 2.22 (s, 6H), 2.14 (dd, $J$ = 12.3 and 6.8, 1H), 1.85-1.76 (m, 1H), 1.70-1.64 (m, 1H), 1.57-1.30 (m, 5H), 0.87-0.96 (m, 1H), 0.86 (t, $J$ = 7.2, 3H);

**13C NMR** (100 MHz, CDCl$_3$): δ 64.2, 57.8, 53.6, 46.1, 41.0, 37.4, 28.6, 27.6, 27.2, 25.6, 12.2; **HRMS** (ESI) calcd. for C$_{12}$H$_{25}$N$_2$ [M+H]$^+$: 197.2012, found: 197.2013.

(2R,4S,5R)-N,N-dimethyl-2-aminomethyl-5-ethenyl-quinuclidine (96).

A Schlenk tube equipped with a reflux condenser was rapidly charged with (2R,4S,5R)-2-aminomethyl-5-ethenyl-quinuclidine$^2$ (1.00 g, 6.03 mmol), evacuated for 30 seconds, filled with N$_2$, and cooled at 0 °C. Then 98 % formic acid (1.39 mL, 36.0 mmol) and 36.5 % formaldehyde (1.22 mL, 16.4 mmol) were added and the mixture was refluxed for 3 h. Then cooled at r.t., dissolved in a solution (1M) of HCl (30 mL) and extracted with Et$_2$O (3 x). The aqueous layer was brought to pH =12 with K$_2$CO$_3$ and extracted with Et$_2$O (3 x). The combined organic layers were dried with anh. Na$_2$SO$_4$ and volatiles removed under low pressure to give the title compound 96 (1.10 g, 94 % yield) as colourless oil.

**MW** =194.34 g / mol; **R$_f$** = 0.58 (CHCl$_3$ 84%; MeOH 14%; NH$_3$(aq) 2%); **[α]$_{D}^{20}$**: +181 (c = 1.64 CHCl$_3$); **IR** (neat, cm$^{-1}$): 3076, 2934, 2862, 2818, 2763, 1682, 1636, 1455, 1321, 1263, 1202, 1029; **1H NMR** (400 MHz, CDCl$_3$): δ 5.86 (ddd, $J$ = 17.4, 9.9 and 7.3, 1H), 5.02-4.99 (m, 1H), 4.98-4.96 (m, 1H), 2.96-2.78 (m, 4H), 2.67-2.61 (m, 1H), 2.42 (dd, $J$ = 12.5 and 8.2,
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1H), 2.23-2.16 (m, 1H), 2.11 (dd, J = 12.5 and 6.4, 1H), 1.70-1.66 (m, 1H), 1.61-1.46 (m, 3H), 1.26 (ddd, J = 21.6, 8.2, 2.0 and 1.8, 1H); \(^{13}C\) NMR (125 MHz, CDCl\(_3\)): \(\delta\) 141.7, 114.5, 63.1, 53.7, 49.6, 47.7, 46.2, 40.6, 28.0, 27.2, 27.1; HRMS (ESI) calcd. for C\(_{12}\)H\(_{23}\)N\(_2\) [M+H]\(^+\): 195.1855, found: 195.1848.

**N,N-dimethyl-2-aminomethyl-5-ethylquinuclidine (94).**

A two neck round bottom flask was charged with (2\(R\),4\(S\),5\(R\))-N,N-dimethyl-2-aminomethyl-5-ethylquinuclidine (96) (1.11 g, 5.66 mmol) and 10 % palladium on charcoal (120 mg, 0.11 mmol). The flask was evacuated and refilled with H\(_2\) from a balloon. Then MeOH (26 mL) was added and the suspension was stirred at r.t. for 18 h. The reaction mixture was then filtered and the solvent evaporated under reduced pressure. The residue was dissolved in aq. HCl (1 M, 45 mL) and extracted with Et\(_2\)O (3 x). The aqueous layer was brought to pH \(\approx\)12 with K\(_2\)CO\(_3\) and extracted with Et\(_2\)O (3 x). The combined organic layers were dried with anh. Na\(_2\)SO\(_4\) and volatiles removed under low pressure to give the title compound 94 (933 mg, 84 %) as colourless oil.

**Benzoyl ammonium complex 101:**

Reaction under N\(_2\). Benzoyl chloride (27 \(\mu\)L, 0.23 mmol) was added dropwise to a stirring solution of diamine 93 (46 mg, 0.23 mmol) in Et\(_2\)O (3 mL). Stirring was continued for 30 min leading to the formation of a white precipitate. The solvent was evaporated under high vacuum benzoylamonium complex 101 (79 mg, 99 %) was obtained as a white solid.

\(\text{IR (CHCl}_3, \ cm^{-1})\): 3370, 2967, 2878, 2782, 2454, 1289, 1725, 1600, 1461, 1384, 1243, 1173, 1109; \(^{1}H\) NMR (500 MHz,
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CDCl₃): δ 8.15-8.17 (m, 2H), 7.70-7.65 (m, 1H), 7.55-7.50 (m, 2H), 3.61 (dd, J 13.4 and 10.4, 1H), 3.37-3.29 (m, 1H), 3.28-3.21 (m, 1H), 3.14-3.03 (m, 1H), 2.87-2.79 (m, 1H), 2.72 (dd, J 13.2, 6.3 and 2.5, 1H), 2.49-2.49 (m, 1H), 2.32 (s, 6H), 2.14-2.06 (m, 1H), 1.99-1.95 (m, 1H), 1.88-1.77 (m, 3H), 1.46-1.39 (m, 1H), 1.38-1.34 (m, 1H), 0.89 (t, J 7.4, 3H); ¹³C NMR (100 MHz, CDCl₃): δ 162.6, 134.8, 130.8, 129.1, 61.2, 56.0, 54.9, 46.0, 41.0, 35.5, 26.8, 25.3, 25.1, 24.8, 11.8; MS m/z (EI): 299(1), 196 (12, diamine 87), 181 (8), 138 (6), 110 (12), 105 (45, [PhCO]+), 58 (100, [C₆H₅]+), 51 (8);

V.3.3 Asymmetric acylation of meso-[Cr(CO)₃(η⁶-5,8-tetralindiol)] type complexes. General method A:

Dry CH₂Cl₂ was degassed three times by freeze-pump-thaw cycles. A freshly prepared solution of chiral diamine 93 (5.6 mg, 0.025 mmol, 10 mol %) in CH₂Cl₂ (2 mL) was added under N₂ to a solution of diol complex 65 (75 mg, 0.25 mmol) and dried molecular sieves (4Å, 63 mg) in CH₂Cl₂ (2 mL). Then Et₃N (35 µL, 0.25 mmol), followed by benzoyl chloride (44 µL, 0.38 mmol) were added dropwise to this stirred, cooled (-60 °C) solution and the resulting mixture was stirred at this temperature for 22 h. Half of the solvent was then evaporated under vigorous stirring using the vacuum line and the remaining mixture was directly purified by flash chromatography (Et₂O / pentane 2 : 1) to give (-)-(5S,8R)-[Cr(CO)₃(η⁶-5-benzoyloxy-8-hydroxytetralin)] (99) (79 mg, 78 % and 95 % ee) as a dark yellow gum. Dibenzoate 95 was also isolated in 10 % yield.

(-)-(5S,8R)-[Cr(CO)₃(η⁶-5-benzoyloxy-8-hydroxytetralin)] (99).

Yellow gum; MW = 404.33 g / mol; Rf = 0.12 (Et₂O / pentane, 1 : 1); [α]d²⁰ = -108 (c = 0.375, CH₂Cl₂); IR (CH₂Cl₂, cm⁻¹): 3594, 1970, 1893, 1716; ¹H NMR (400 MHz, C₆D₆): δ 8.46-8.40 (m, 2H), 7.14-7.10 (m, 3H), 5.59-5.56 (m, 1H), 4.94 (d, J= 6.4, 1H), 4.85 (d, J= 6.4, 1H), 4.43 (dt, J 6.0 and J 0.8, 1H), 4.27 (dt, J 6.0 and J 1.3, 1H), 3.82-3.73 (m, 1H), 1.80-1.67 (m, 2H), 1.45-1.27 (m, 2H), 1.32 (d, J 6.0, 1H); ¹³C NMR (100 MHz, C₆D₆): δ 233.1, 166.2, 133.6, 130.3, 130.1, 128.8, 116.7, 109.3, 92.6, 91.9, 90.3, 88.8, 66.8, 65.8, 28.2, 25.8; MS m/z (EI): 404 (10 [M⁻]), 348 (13), 302 (55), 180 (30), 129 (81), 115 (55), 105 (100), 77 (70), 52 (67); HRMS (ESI) calcd. for C₂₀H₁₆O₆CrNa [M+Na]⁺: 427.0249, found 427.0249; HPLC analysis of free ligand (monobenzoate 94 was not resolvable). Monobenzoate 94 was dissolved in
MeCN and exposed to sunlight open to air for 1 h. The dark suspension was then filtered through a plug of celite and all volatiles were removed under reduced pressure. This crude was purified by preparative TLC (Et₂O / pentane, 1 : 1), HPLC conditions: Chiralcel OJ-H, eluent: 90:10 hexane / PrOH, flow rate: 1 mL / min: retention times 116.3 min and 143.9 min.

\[
\text{[Cr(CO)₃(η₆-5,8-dibenzoyloxytetralin)] (100).}
\]

Yellow oil; \( MW = 508.53 \text{ g / mol; } R_F = 0.30 \) (Et₂O / pentane, 1 : 1); \( \text{IR (CH}_2\text{Cl}_2, \text{ cm}^{-1}): 3072, 2903, 1890, 1717, 1601, 1315, 1112; \)
\( ^1\text{H NMR (400 MHz, C}_6\text{D}_6) \delta 8.46-8.41 \text{ (m, 4H), 7.12-7.10 \text{ (m, 6H), 5.66-5.64 \text{ (m, 2H), 4.78-4.76 \text{ (m, 2H)}, 4.34-4.31 \text{ (m, 2H), 1.94-1.86 \text{ (m, 2H), 1.52-1.45 \text{ (m, 2H);}}}} \)
\( ^{13}\text{C NMR (100 MHz, C}_6\text{D}_6): \delta 232.8, 166.1, 133.6, 130.3, 130.1, 128.9, 110.1, 91.1, 90.3, 67.0, 25.3; \text{ MS m/z (EI): 508 (1 [M]⁺), 386 (2), 302 (6), 250 (7), 180 (6), 105 (100), 77 (45);} \)

\( ^{(-)}(5S,8R)-[\text{Cr(CO)}₃(\eta₆-5,8-dihydro-5-benzoyloxy-8-hydroxynaphthalene)] (97). \)

Reaction carried out according to the general method A with complex 66 (75 mg, 0.25 mmol) in CH₂Cl₂ at -40 °C with 10 mol % of diamine 93, to give \((-\cdot)\cdot97, \text{ 89 % yield, 97 % ee; Yellow solid; } MW = 402.33 \text{ g / mol; } R_F = 0.20 \) (Et₂O / pentane, 1 : 1); \( [\alpha]_{D}^{20} = -146 \) (c = 0.88, CH₂Cl₂); \( \text{MP = 125-127 °C (toluene / hexane); } ^{1}\text{H NMR (400 MHz, C}_6\text{D}_6): \delta 8.52 \text{ (m, 2H), 7.22 (m, 3H), 6.17 (d, J 4.8, 1H), 5.62 (s, 2H), 5.29 (d, J 4.6, 1H), 4.78 (d, J 6.3, 1H), 4.52 (m, 2H), 4.31-4.29 (m, 1H), 1.83 (1H, broad s);} \)
\( ^{13}\text{C NMR (100 MHz, C}_6\text{D}_6): \delta 232.9, 165.9, 133.6, 130.4, 130.1, 128.7, 128.4, 125.6, 110.8, 106.0, 91.5, 90.9, 89.2, 87.7, 64.5, 62.9. \text{ MS m/z (EI): 402 (1 [M]⁺), 346 (2), 280 (6), 196 (28), 128 (62), 77 (30), 52 (100); \text{ HRMS (ESI) calcd. for C}_{20}\text{H}_{14}\text{O}_{6}\text{CrNa} [\text{M+Na}^-]: 402.0195, found 402.0224. HPLC Chiralcel OJ-H, eluent: 90:10 hexane / PrOH, flow rate: 1 mL / min: retention times 116.3 min and 143.9 min.} \)

\( \text{Dibenzoate 98 was also isolated in 10 % yield. Yellow oil; } MW = 506.43 \text{ R_F = 0.35 (Et}_2\text{O / pentane, 1 : 1); IR (CHCl}_3, \text{ cm}^{-1}): 1977, 1906, 1720; ^{1}\text{H NMR (400 MHz, C}_6\text{D}_6) \delta 8.50-8.45 \text{ (m, 4H), 7.18-7.13 \text{ (m, 6H), 6.13 (s, 2H), 5.59 (s, 2H), 4.75-4.71 \text{ (m, 2 H), 4.40-} \)
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4.35 (m, 2H); $^{13}$C NMR (100 MHz, C$_6$D$_6$): $\delta$ 232.3, 165.6, 133.5, 130.0, 129.3, 128.5, 126.6, 105.2, 90.5, 87.5, 64.1;

V.3.4 Asymmetric acylation of meso-1,2-diols: General method B:

A solution of chiral diamine 93 (3.4 mg, 0.017 mmol, 2 mol %) in dry AcOEt (2 ml) was added under N$_2$ to a mixture of meso-cyclohexane-1,2-diol (75) (100 mg, 0.86 mmol) and activated molecular sieves (4Å, 113 mg) in dry AcOEt (6 ml). To this stirring, cooled (-60 °C) solution, benzoyl chloride (150 µL, 1.29 mmol) followed by Et$_3$N (121 µL, 0.86 mmol) were added drop-wise. The resulting mixture was stirred at -60 °C during 22 hours, quenched with a solution (10 mL) of phosphate buffer (pH = 7) and extracted with Et$_2$O (3 x). The organic layers were dried with MgSO$_4$ and all volatiles were removed under reduced pressure. The residue was purified by flash chromatography (Et$_2$O / pentane) to give benzoic acid 2-hydroxy-cyclohexyl ester (76) (180 mg, 92 % yield, 97.3 % ee).

(+)-(1$S$,2$R$)-2-hydroxy-1-cyclohexyl benzoate (76):

Spectral data agreed with literature values:$^{[3, 4]}$ colourless oil; 

MW = 220.26 g / mol; $R_F$ = 0.16 (Et$_2$O / pentane, 1 : 3); $[\alpha]_D^{20}$: +16 (c= 0.68 CHCl$_3$); IR (neat, cm$^{-1}$): 3441, 2937, 2862, 1715, 1602, 1450, 1272; 

$^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.03-7.99 (m, 2H), 7.60-7.53 (m, 1H), 7.48-7.40 (m, 2H), 5.24-5.20 (m, 1H), 3.99-3.92 (m, 1H), 2.09-1.92 (m, 1H), 1.95 (broad s, 1H), 1.90-1.80 (m, 1H), 1.78-1.62 (m, 4H), 1.51-1.37 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 166.3, 133.1, 130.4, 129.6, 128.4, 74.6, 70.0, 30.4, 27.4, 21.8, 21.6; MS m/z (EI): 202 (2 [M-H$_2$O]+), 174 (2), 149 (4), 115 (14), 105 (100), 98 (95 [M-BzOH$^+$]), 77 (79), 51 (36); HPLC Chiralcel OJ-H, eluent: 95:5 hexane / iPrOH, flow rate: 1 mL / min: retention times 11.3 min ((1$S$,2$R$)-enantiomer) and 13.5 min ((1$R$,2$S$)-enantiomer).

cis-1,2-dibenzoyloxycyclohexane (105):

Conversion: 5 % ($^1$H-NMR). Spectral data agreed with literature values:$^{[5]}$

White solid; MW = 324.37 g / mol; $R_F$ = 0.48 (Et$_2$O / pentane, 1 : 3); MP = 63-64 °C (Ethanol); IR (neat, cm$^{-1}$): 2942, 1786, 1720, 1600, 1450, 1265, 1210; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 8.01 (d, $J$ 7.1, 4H), 7.54 (t, $J$ 8.8, 2H), 7.41 (t, $J$ 8.8, 4H), 5.40-5.38 (m, 2H), 2.14-2.06 (m, 2H), 1.90-1.75 (m, 4H), 1.62-1.53 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 165.8,
132.9, 130.5, 129.6, 128.3, 71.9, 28.0, 21.9; MS m/z (EI): 202 (12 [M-BzOH]+), 198 (15), 182 (5), 122 (3), 105 (100), 77 (81), 51 (62).

\[+\text{-}(1S,2R)-2\text{-hydroxy-1-cyclohexyl } p\text{-methoxybenzoate (106)}:\]

Reaction carried out according to the general method B with diol 75 (100 mg, 0.86 mmol) in CH\(_2\)Cl\(_2\) (8 mL) at -30 °C with 5 mol % of diamine 93, to give \(+\text{-}106\) in 72 % conversion (\(^1\)H NMR), 97.4 % ee; Spectral data agreed with literature values:\(^{[4]}\) white solid; \textbf{MW} = 250.29 g/mol; \textbf{RF} = 0.10 (Et\(_2\)O / pentane, 1: 2); \([\alpha]_D^{20}\) +12 (c= 0.55 CH\(_2\)Cl\(_2\)); \textbf{MP} = 72-73 °C (Et\(_2\)O / pentane); \textbf{IR} (neat, cm\(^{-1}\)): 3446, 2936, 2861, 1704, 1605, 1511, 1275, 1253, 1167, 1102; \(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)): \(\delta\) 8.03-7.99 (m, 2H), 6.94-6.91 (m, 2H), 5.21-5.16 (m, 1H), 3.99-3.92 (m, 1H), 3.87 (s, 3H), 2.05-1.95 (m, 2H), 1.80-1.79 (m, 1H), 1.77-1.62 (m, 4H), 1.50-1.35 (m, 2H); \(^{13}\text{C NMR}\) (100 MHz, CDCl\(_3\)): \(\delta\) 166.2, 163.1, 131.9, 123.1, 113.9, 70.0, 55.7, 30.7, 27.8, 22.1, 21.9; MS m/z (EI): 250 (3 [M]+), 152 (13), 135 (100), 98 (60), 77 (16), 41 (8); HRMS (ESI) calcd. for C\(_{14}\)H\(_{19}\)O\(_4\) [M+H]+: 251.1277, found: 251.1276; HPLC Chiralcel OJ-H, eluent: 95:5 hexane / \(^1\)PrOH, flow rate: 1 mL / min: retention times 21.9 min ((1S,2R)-enantiomer) and 34.4 min ((1R,2S)-enantiomer).

cis-1,2-bis\((p\text{-methoxybenzoyloxy})\)cyclohexane (107):

Conversion: 12 % (\(^1\)H-NMR): white solid; \textbf{MW} = 384.42 g / mol; \textbf{RF} = 0.25 (Et\(_2\)O / pentane, 1: 3); \textbf{IR} (neat, cm\(^{-1}\)): 2938, 2863, 1708, 1605, 1510, 1251, 1166, 1097, 1026; \(^1\text{H NMR}\) (400 MHz, CDCl\(_3\)): \(\delta\) 8.00-7.90 (m, 4H), 6.91-6.85 (m, 4H), 5.37-5.30 (m, 2H), 3.84 (s, 6H), 2.11-2.02 (m, 2H), 1.89-1.72 (m, 4H), 1.60-1.50 (m, 2H); \(^{13}\text{C NMR}\) (100 MHz, CDCl\(_3\)): \(\delta\) 165.9, 163.6, 132.0, 123.3, 113.9, 71.9, 55.8, 28.4, 22.2; HRMS (ESI) calcd. for C\(_{22}\)H\(_{19}\)O\(_6\) [M+H]+: 385.1645, found: 385.1649.
(+)-2-hydroxy-1-cyclohexyl p-fluorobenzoate (108): Reaction carried out according to the general method B with diol 75 (100 mg, 0.86 mmol) in CH2Cl2 (8 mL) at -30 °C with 5 mol % of diamine 93, to give (+)-108 in 60 % conversion (1H-NMR), 99.0 % ee; white solid; MW = 238.25 g / mol; RF = 0.22 (Et2O / pentane, 1: 3); [α]D20: +11 (c= 0.22 CH2Cl2). MP = 52-54 °C (Et2O / cyclohexane); IR (neat, cm –1): 3448, 2939, 2864, 1714, 1603, 1273, 1153, 1110, 1091; 1H NMR (400 MHz, CDCl3): δ 8.10-8.02 (m, 2H), 7.14-7.06 (m, 2H), 5.20 (dt, J 7.3 and 2.3, 1H), 3.99-3.93 (m, 1H), 2.68 (broad s, 1H), 2.05-1.94 (m, 1H), 1.87-1.78 (m, 1H), 1.77-1.59 (m, 4H), 1.51-1.35 (m, 2H); 13C NMR (100 MHz, CDCl3): δ 166.1 (d, J 254.6), 165.7, 132.7 (d, J 9.2), 126.9 (d, J 3.6), 115.8 (d, J 22.1), 75.1, 70.0, 30.7, 27.7, 22.0, 21.9; MS m/z (EI): 220 (2 [M-H2O]+), 192 (2), 178 (2), 123 (100), 98 (90), 95 (80), 70 (18), 41 (14); HRMS (ESI) calcd. for C13H16O3F [M+H]+: 239.1077, found: 239.1085; HPLC Chiralcel OJ-H, eluent: 95:5 hexane / iPrOH, flow rate: 1 mL / min: retention times 9.7 min ((-) enantiomer) and 14.7 min ((+) enantiomer).

cis-1,2-bis(p-fluorobenzoyloxy)cyclohexane (109): Conversion: 5 % (1H-NMR): colourless oil; MW = 360.35 g / mol; RF = 0.66 (Et2O / pentane, 1: 3); IR (neat, cm –1): 2943, 1721, 1604, 1508, 1282, 1154, 1119, 1104, 1090; 1H NMR (400 MHz, CDCl3): δ 8.03-7.98 (m, 4H), 7.10-7.04 (m, 4H), 5.40-5.35 (m, 2H), 2.11-2.01 (m, 2H), 1.90-1.74 (m, 4H), 1.62-1.53 (m, 2H); 13C NMR (100 MHz, CDCl3): δ 166.1 (d, J 253.7), 165.1, 132.5 (d, J 9.2), 126.9 (d, J 3.7), 115.8 (d, J 22.1), 72.3, 28.3, 22.2; MS m/z (EI): 276 (2), 220 (67 [M+-C7H4O2F]+), 192 (2), 178 (2), 123 (100), 95 (22); HRMS (ESI) calcd. for C20H19O4F2 [M+H]+: 361.1245, found: 361.1248.

(+)-2-hydroxy-1-cyclohexyl p-methylbenzoate (110): Reaction carried out according to the general method B with diol 75 (100 mg, 0.86 mmol) in CH2Cl2 (8 mL) at -30 °C with 5 mol % of diamine 93, to give (+)-110 in 66 % conversion (1H NMR), 94.4 % ee; colourless oil; MW = 234.29 g / mol; RF = 0.24 (Et2O / pentane, 1: 3); [α]D20: +14 (c = 0.55 CH2Cl2); IR (neat, cm –1):
2937, 2863, 1708, 1605, 1315, 1280, 1251, 1166, 1097, 1026; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.97-7.92 (m, 2H), 7.26-7.22 (m, 2H), 5.20 (dt, $J$ 7.6 and 2.8, 1H), 3.98-3.94 (m, 1H), 2.41 (s, 3H), 2.17 (broad s, 1H), 2.06-1.96 (m, 1H), 1.90-1.80 (m, 1H), 1.78-1.61 (m, 4H), 1.50-1.36 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 166.6, 144.1, 130.0, 129.4, 127.9, 74.7, 70.0, 30.7, 27.7, 22.1, 22.0, 21.9; MS m/z (EI): 216 [M-H$_2$O]$^+$, 119 (100), 98 (80), 91 (34), 65 (10), 41 (8); HRMS (ESI) calcd. for C$_{14}$H$_{19}$O$_3$ [M+H]$^+$: 235.1328, found: 235.1333.

HPLC Chiralcel OJ-H, eluent: 95:5 hexane / iPrOH, flow rate: 1 mL / min: retention times 10.6 min ((+) enantiomer) and 12.6 min ((-) enantiomer).

cis-1,2-bis-(p-methylbenzoyloxy)cyclohexane (111). Conversion: 21 % ($^1$H-NMR), spectral data agreed with literature values.$^6$ Colourless oil; MW = 352.43 g / mol; $R_F$ = 0.62 (Et$_2$O / pentane, 1:3); IR (neat, cm$^{-1}$): 2941, 2864, 1714, 1611, 1278, 1266, 1176, 1098, 1020; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.89 (d, $J$ 8.3, 4H), 7.20 (d, $J$ 7.9, 4H), 5.40-5.32 (m, 2H), 2.39 (s, 6H), 2.14-2.02 (m, 2H), 1.91-1.72 (m, 4H), 1.61-1.50 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 166.2, 143.8, 130.0, 129.4, 128.1, 72.0, 28.4, 22.2, 21.9; HRMS (ESI) calcd. for C$_{22}$H$_{25}$O$_4$ [M+H]$^+$: 353.1747, found: 353.1456.

(+)-2-hydroxy-1-cyclohexyl o-methylbenzoate (112): Reaction carried out according to the general method B with diol 75 (100 mg, 0.86 mmol) in CH$_2$Cl$_2$ (8 mL) at -30 °C with 5 mol % of diamine 93, to give (+)-112 in 70 % conversion ($^1$H NMR), 81.5 % ee; colourless oil; MW = 234.29 g / mol; $R_F$ = 0.22 (Et$_2$O / pentane, 1:3); $[\alpha]_D^{20}$: +20 (c = 0.72 CH$_2$Cl$_2$); IR (neat, cm$^{-1}$): 3438, 2938, 1715, 1449, 1324, 1261, 1082, 983; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ 7.92 (dd, $J$ 8.2 and 1.5, 1H), 7.40 (td, $J$ 7.6 and 1.5, 1H), 7.28-7.23 (m, 2H), 5.23-5.18 (m, 1H), 4.00-3.95 (m, 1H), 2.61 (s, 3H), 2.05-1.95 (m, 2H), 1.87-1.78 (m, 1H), 1.79-1.61 (m, 4H), 1.51-1.36 (m, 2H); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 167.7, 140.4, 132.4, 132.0, 130.9, 130.2, 126.1, 74.9, 69.9, 30.7, 27.7, 22.2, 22.1, 21.8; HRMS (ESI) calcd. for C$_{14}$H$_{19}$O$_3$ [M+H]$^+$: 235.1328, found: 235.1337; HPLC Chiralcel OJ-H, eluent: 95:5 hexane / iPrOH, flow rate: 1 mL / min: retention times 11.0 min ((+) enantiomer) and 13.9 min ((-) enantiomer).
**cis-1,2-bis-(o-methylbenzoyloxy)cyclohexane (113):**

Conversion: 24% (1H-NMR): colourless oil; \( \text{MW} = 352.43 \text{ g/mol} \); \( R_F = 0.64 \) (Et<sub>2</sub>O / pentane, 1 : 3); IR (neat, cm<sup>-1</sup>): 2943, 1720, 1603, 1457, 1293, 1262, 1144, 1075; \(^1\text{H NMR} \) (400 MHz, CDCl<sub>3</sub>): \( \delta \) 7.89 (d, \( J = 7.6 \), 2H), 7.37 (td, \( J = 7.8 \) and 1.5, 2H), 7.23-7.17 (m, 4H), 5.42-5.37 (m, 2H), 2.55 (s, 6H), 2.12-2.03 (m, 2H), 1.90-1.71 (m, 4H), 1.81-1.50 (m, 1H), 1.56 (broad s, 1H); \(^{13}\text{C NMR} \) (100 MHz, CDCl<sub>3</sub>): \( \delta \) 167.1, 140.6, 132.3, 131.9, 131.0, 130.2, 126.0, 72.0, 28.4, 22.3, 22.2; HRMS (ESI) calcd. for C<sub>22</sub>H<sub>25</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 353.1747, found: 253.1744.

\((*\text{-}) -2\)-hydroxy-1-cyclohexyl \( p \)-dimethylaminobenzoate (114):

Reaction carried out according to the general method B with diol 75 (100 mg, 0.86 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (8 mL) at -30 °C with 5 mol % of diamine 93, to give \(*\text{-})-114 in 62% conversion (1H NMR), 92.1% ee. Spectral data agreed with literature values:[7] white solid; \( \text{MW} = 263.34 \text{ g/mol} \); \( R_F = 0.20 \) (Et<sub>2</sub>O / pentane, 1 : 2); \([\alpha]_D^{20}\): +7 (c = 0.055 CH<sub>2</sub>Cl<sub>2</sub>); \( \text{MP} = 118-120 \text{ °C} \) (AcOEt / cyclohexane); IR (neat, cm<sup>-1</sup>): 3454, 2936, 2862, 1685, 1606, 1526, 1446, 1368, 1342, 1317, 1278, 1183; \(^1\text{H NMR} \) (400 MHz, CDCl<sub>3</sub>): \( \delta \) 7.92 (d, \( J = 9.2 \), 2H), 6.64 (d, \( J = 9.1 \), 2H), 5.20-5.12 (m, 1H), 3.98-3.90 (m, 1H), 3.04 (m, 6H), 2.18 (broad s, 1H), 2.04-1.93 (m, 1H), 1.88-1.78 (m, 1H), 1.79-1.71 (m, 3H), 1.49-1.34 (m, 2H); \(^{13}\text{C NMR} \) (100 MHz, CDCl<sub>3</sub>): \( \delta \) 167.0, 153.7, 131.7, 117.2, 111.0, 74.0, 70.2, 40.4, 30.9, 27.9, 22.2, 22.0; HRMS (ESI) calcd. for C<sub>15</sub>H<sub>22</sub>O<sub>3</sub>N [M+H]<sup>+</sup>: 264.1599, found: 264.1606; HPLC Chiralcel OJ-H, eluent: 95:5 hexane / iPrOH, flow rate: 1 mL / min: retention times 22.0 min ((1S,2R)-enantiomer) and 29.9 min ((1R,2S)-enantiomer).

**cis-1,2-bis-(p-N,N-dimethylbenzoyloxy)cyclohexane (115):**

Conversion: 34% (1H-NMR): colourless oil; \( \text{MW} = 410.52 \text{ g/mol} \); \( R_F = 0.34 \) (AcOEt / pentane, 1 : 2); IR (neat, cm<sup>-1</sup>): 2938, 2861, 1694, 1602, 1525, 1446, 1367, 1314, 1269, 1232, 1177, 1097; \(^1\text{H NMR} \) (400 MHz, CDCl<sub>3</sub>): \( \delta \) 7.89 (d, \( J = 9.1 \), 4H), 6.61 (d, \( J = 9.1 \), 4H), 5.33-5.26 (m, 2H), 3.00 (s, 12H), 2.12-2.02 (m, 2H), 1.87-1.71 (m, 4H), 1.57-1.48 (m, 2H); \(^{13}\text{C NMR} \) (100 MHz, CDCl<sub>3</sub>): \( \delta \) 166.1, 153.1, 131.2, 117.4, 110.6, 71.2, 40.0, 28.1, 21.8; HRMS (ESI)
calcd. for C_{24}H_{31}O_{4}N_{2} [M+H]^+: 411.2278, found: 411.2274.

(+)-(1S,2R)-2-hydroxy-1-cyclohexyl 2-furoate (116):

Reaction carried out according to the general method B with diol 75 (100 mg, 0.86 mmol) in CH_{2}Cl_{2} (8 mL) at -30 °C with 5 mol % of diamine 93, to give (+)-116 in 71 % conversion (\textsuperscript{1}H NMR), 95.6 % ee. Spectral data agreed with literature values:\cite{8} colourless oil; MW = 210.23 g / mol; R_{F} = 0.09 (Et_{2}O / pentane, 1 : 3); \([\alpha]_{D}^{20}\): +1 (c = 0.15 CH_{2}Cl_{2}); IR (neat, cm\textsuperscript{-1}): 3442, 2940, 2864, 1716, 1580, 1397, 1298, 1231, 1182, 1122, 1077; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta\) 7.54-7.27 (m, 1H), 7.21-7.16 (m, 1H), 6.50-6.46 (m, 1H), 5.16-5.09 (m, 1H), 3.96-3.90 (m, 1H), 2.27 (broad s, 1H), 2.01-1.90 (m, 1H), 1.85-1.75 (m, 1H), 1.72-1.56 (m, 4H), 1.47-1.28 (m, 2H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \(\delta\) 158.6, 146.6, 144.9, 118.4, 112.1, 75.1, 69.4, 30.6, 27.4, 22.2, 21.4; HRMS (ESI) calcd. for C_{11}H_{15}O_{4} [M+H]^+: 211.0964, found: 211.0961; HPLC Chiralcel OJ-H, eluent: 95:5 hexane / iPrOH, flow rate: 1 mL / min: retention times 11.9 min ((1R,2S)-enantiomer) and 13.8 min ((1S,2R)-enantiomer).

cis-1,2-difuroyloxyxycyclohexane (117).

Conversion: 20 % (\textsuperscript{1}H-NMR), spectral data agreed with literature values:\cite{9} colourless oil; MW = 304.30 g / mol; R_{F} = 0.21 (Et_{2}O / pentane, 1 : 3); IR (neat, cm\textsuperscript{-1}): 3141, 2943, 2865, 1723, 1579, 1473, 1396, 1229, 1289, 1231, 1181, 1108; \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta\) 7.56 (dd, \(J\) 1.8 and 0.9, 2H), 7.11 (dd, \(J\) 3.5 and 0.9, 2H), 7.48 (dd, \(J\) 3.5 and 1.8, 2H), 5.34-5.30 (m, 2H), 2.08-1.97 (m, 2H), 1.86-1.71 (m, 4H), 1.58-1.47 (m, 2H); \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}): \(\delta\) 158.2, 146.6, 144.9, 118.2, 112.0, 72.0, 28.1, 21.9. HRMS (ESI) calcd. for C_{16}H_{17}O_{6} [M+H]^+: 305.1019, found: 305.1022.

(+)-(2S,3R)-3-hydroxyl-2-butyl benzoate (118):

The starting material was dried with MS 4Å in CH_{2}Cl_{2} solution. Spectral data agreed with literature values:\cite{10} Reaction carried out by following the general method B with meso-butane-1,2-diol (76 mg, 0.86 mmol) in AcOEt (8 mL) at -60 °C with 2 mol % of diamine 93, to give (+)-118 in 82 % yield, 90 % ee; colourless oil; colourless oil; MW = 194.23 g / mol; R_{F} = 0.26 (Et_{2}O / pentane, 1 : 3); \([\alpha]_{D}^{20}\): +17 (c = 0.70 CH_{2}Cl_{2}); IR (neat, cm\textsuperscript{-1}): 3441, 2981,
cis-1,2-bisbenzoyloxybutane (119):

Conversion: 2 % (¹H-NMR), spectral data agreed with literature values.¹¹¹

Colourless oil; MW = 298.34 g / mol; R_F = 0.65 (Et_2O / pentane, 1 : 3); MP = 73-75 °C (CH_2Cl_2 / cyclohexane); IR (neat, cm⁻¹): 2988, 1787, 1717, 1692, 1601, 1584, 1451, 1316, 1266, 1212, 1113, 1096, 1070, 1038, 1016, 996; ¹H NMR (400 MHz, CDCl_3): δ 8.04 (d, J 8.3, 4H), 7.36 (dt, J 7.5 and 1.5, 1H), 7.41 (dt, J 7.5 and 1.5, 2H), 5.24-5.16 (m, 1H), 4.32-4.25 (m, 1H), 2.64 (broad s, 1H), 2.19-1.99 (m, 1H), 1.98-1.87 (m, 3H), 1.82-1.75 (m, 1H), 1.64-1.57 (m, 1H); ¹³C NMR (100 MHz, CDCl_3): δ 166.0, 133.2, 130.5, 129.8, 128.6, 72.5, 15.7; MS m/z (EI): 254 (6), 226 (6), 210 (27), 198 (12), 176 (14 [M-PhCOOH]^+), 149 (13), 132 (12), 105 (100), 77 (70), 51 (47).

(+)-(1S,2R)- 2-hydroxy-1-cyclopentyl benzoate (120):

The starting material was dried with MS 4Å in CH_2Cl_2 solution. Reaction carried out by following the general method B with meso-cyclopropane-1,2-diol (88 mg, 0.86 mmol) in THF (8 mL) at -60 °C with 2 mol % of diamine 93, to give (+)-120 in 83 % yield, 82 % ee. Spectral data agreed with literature values:³, ¹², ¹³ colourless oil; MW = 206.24 g / mol; R_F = 0.22 (Et_2O / pentane, 1 : 3); [α]²⁰_D: +13 (c = 0.45 CH_2Cl_2); IR (neat, cm⁻¹): 3596, 3064, 2974, 2879, 1717, 1602, 1584, 1451, 1272, 1117; ¹H NMR (300 MHz, CDCl_3): δ 8.03 (dd, J 8.3, and 1.1, 2H), 7.36 (dt, J 7.5 and 1.5, 1H), 7.41 (dt, J 7.5 and 1.5, 2H), 5.24-5.16 (m, 1H), 4.32-4.25 (m, 1H), 2.64 (broad s, 1H), 2.19-1.99 (m, 1H), 1.98-1.87 (m, 3H), 1.82-1.75 (m, 1H), 1.64-1.57 (m, 1H); ¹³C NMR (75 MHz, CDCl_3): δ 166.4, 133.1, 130.1, 129.6, 128.4, 77.4, 73.4, 30.9, 28.2, 19.5; MS m/z (EI): 206 (1 [M]^+), 198 (14), 188 (34 [M-H_2O]^+), 106 (50), 105 (100), 77 (73), 51 (50); HRMS (ESI) calcd. for C_12H_14O_3Na [M+Na]^+: 229.0835, found: 229.0829; HPLC Chiralcel OJ-H, eluent: 95:5 hexane / iPrOH, flow rate: 1 mL / min: retention times 10.6 min ((2S,3R)-enantiomer) and 12.0 min ((2R,3S)-enantiomer).
hexane / iPrOH, flow rate: 0.5 mL / min: retention times 22.3 min ((1S,2R)-enantiomer) and 26.7 min ((1R,2S)-enantiomer).

**cis-1,2-bis-benzoyloxy cyclopentane (121):**

Conversion: 7 % (1H-NMR), spectral data agreed with literature values: \(^{[14]}\) white solid; MW = 310.35 g / mol; \( R_f \) = 0.59 (Et<sub>2</sub>O / pentane, 1 : 3); MP = 45-47 °C (ethanol); IR (neat, cm<sup>-1</sup>): 3065, 2962, 1720, 1602, 1584, 1451, 1315, 1283, 1272, 1258, 1177, 1122; \(^1\)H NMR (300 MHz, CDCl<sub>3</sub>): \( \delta \) 7.97 (dd, \( J \) 8.5, and 1.3, 4H), 7.52 (tt, \( J \) 7.5, and 1.5, 2H), 7.40-7.33 (m, 4H), 5.54-5.48 (m, 2H), 2.27-2.13 (m, 2H), 2.10-1.97 (m, 3H), 1.84-1.72 (m, 1H); \(^{13}\)C NMR (125 MHz, CDCl<sub>3</sub>): \( \delta \) 165.9, 132.8, 130.5, 129.6, 128.2, 75.1, 28.6, 19.7; MS m/z (ESI): 311 (100 [M]+), 205 (24), 189 (99), 106 (8); HRMS (ESI) calcd. for C<sub>19</sub>H<sub>19</sub>O<sub>4</sub> [M+H]+: 311.1277, found: 311.1277.

(+)- 4-anhydro-2-acyloxy erytritol (122):

The starting material was dried with MS 4Å in CH<sub>2</sub>Cl<sub>2</sub> solution. Spectral data agreed with literature values: \(^{[15]}\)

Reaction carried out by following the general method B with 4-anhydro erytritol (90 mg, 0.86 mmol) in AcOEt (8 mL) at -60 °C with 2 mol % of diamine 93, to give (+)-122 in 84 % yield, 56 % ee; colourless oil; white solid; MW = 208.22 g / mol; \( R_f \) = 0.07 (Et<sub>2</sub>O / pentane, 1 : 2); \([ \alpha ]_D^{20} \) +4 (c = 0.86 CH<sub>2</sub>Cl<sub>2</sub>); MP = 80-81 °C (CH<sub>2</sub>Cl<sub>2</sub>, cyclohexane); IR (neat, cm<sup>-1</sup>): 3417, 2926, 2874, 1715, 1601, 1584, 1451, 1269, 1177, 1118, 1068; \(^1\)H NMR (400 MHz, CDCl<sub>3</sub>): \( \delta \) 8.05-8.00 (m, 2H), 7.58-7.52 (m, 1H), 7.37-7.34 (m, 2H), 5.34-5.30 (m, 1H), 4.51 (ddd, \( J \) 11.1, 5.5 and 1.6, 1H), 4.11 (ddd, \( J \) 10.2, 5.8 and 1.7, 1H), 3.98 (ddd, \( J \) 9.3, 5.8 and 9.3, 1H), 3.96 (ddd, \( J \) 12.1, 5.8 and 1.7, 1H), 3.74 (ddd, \( J \) 9.3, 5.5 and 1.8, 1H), 2.83 (broad s, 1H); \(^{13}\)C NMR (125 MHz, CDCl<sub>3</sub>): \( \delta \) 166.6, 133.7, 130.0, 129.6, 128.7, 74.5, 72.6, 71.2, 70.7; HRMS (ESI) calcd. for C<sub>11</sub>H<sub>13</sub>O<sub>4</sub> [M+H]: 209.0808, found: 209.0817; HPLC Chiralcel AS-H, eluent: 95:5 hexane / iPrOH, flow rate: 1 mL / min: retention times 38.1 min ((-) enantiomer) and 45.6 min ((+) enantiomer).
**cis-1,2-bisbenzoyloxy-4-anhydroerytritol (123):**

Conversion: 11 % (1H-NMR), spectral data agreed with literature values:\(^{16}\) colourless oil; \(MW = 312.33 \text{ g / mol; } R_F = 0.40 \) (Et\(_2\)O / pentane, 1 : 2); \(\text{IR (neat, cm}^{-1})\): 2925, 2872, 1721, 1602, 1584, 1491, 1451, 1345, 1315, 1277, 1177, 1126; \(^1\text{H NMR (400 MHz, CDCl}_3\)): \(\delta 7.98-7.93 \) (m, 4H), 7.56-7.50 (m, 2H), 7.39-7.32 (m, 4H), 5.70-5.66 (m, 2H), 5.32-5.26 (m, 2H), 4.08-4.03 (m, 2H); \(^{13}\text{C NMR (100 MHz, CDCl}_3\)): \(\delta 166.1, 133.6, 130.1, 129.7, 128.7, 72.6, 70.9\); \(\text{HRMS (ESI)}\) calcd. for C\(_{18}\)H\(_{17}\)O\(_5\) [M+H]: 313.1070, found: 313.1066.

\((+)-(1\text{S},2\text{R})-2\text{-hydroxy-1-cyclohex-4-enyl benzoate (124):}\)

Reaction carried out by following the general method B with \(\text{meso-4-cyclohexene-1,2-diol}^{17}\) (98 mg, 0.86 mmol) in AcOEt (8 mL) at -60 °C with 2 mol % of diamine 93, to give \((+)-124\) in 89 % yield, 84 % ee; colourless oil; \(MW = 218.25 \text{ g / mol; } R_F = 0.08 \) (Et\(_2\)O / pentane, 1 : 3); \(\lbrack\alpha\rbrack_D^{20} + 44 \) (\(c = 0.92 \) CH\(_2\)Cl\(_2\)); \(\text{IR (neat, cm}^{-1})\): 3597, 3064, 3036, 2929, 2853, 1716, 1602, 1584, 1451, 1315, 1275, 1116; \(^1\text{H NMR (500 MHz, CDCl}_3\)): \(\delta 8.04 \) (d, \(J 7.9, 2\)H), 7.58-7.52 (m, 1H), 7.46-7.40 (m, 2H), 5.70-5.58 (m, 2H), 5.35-5.30 (m, 1H), 4.18-4.14 (m, 1H), 2.64 (broad s, 1H), 2.52-2.43 (m, 3H), 2.39-2.32 (m, 1H); \(^{13}\text{C NMR (125 MHz, CDCl}_3\)): \(\delta 166.6, 133.2, 130.3, 129.7, 128.4, 123.9, 123.4, 72.8, 67.6, 31.5, 28.4; \) \(\text{MS m/z (EI): 218 (2 [M]^+)}, 164 (2), 123 (18), 105 (100), 96 (84), 77 (19), 67 (17), 51 (11); \) \(\text{HRMS (ESI)}\) calcd. for C\(_{13}\)H\(_{15}\)O\(_3\) [M+H]^+: 219.1015, found: 219.1009; \(\text{HPLC Chiralcel OJ-H, eluent: 95:5 hexane / iPrOH, flow rate: 0.5 mL / min: retention times 25.3 min ((1\text{S},2\text{R})-enantiomer) and 31.4 min ((1\text{R},2\text{S})-enantiomer).}\)

**cis-1,2-bis-benzoyloxy cyclo-4-hexene (125):**

Conversion: 8 % (1H-NMR): colourless oil; \(MW = 322.36 \text{ g / mol; } R_F = 0.47 \) (Et\(_2\)O / pentane, 1 : 3); \(\text{IR (neat, cm}^{-1})\): 3065, 3038, 2934, 1718, 1584, 1452, 1315, 1303, 1280, 1266, 1253, 1217; \(^1\text{H NMR (500 MHz, CDCl}_3\)): \(\delta 8.03-8.01 \) (m, 4H), 7.57-7.51 (m, 2H), 7.43-7.40 (m, 4H), 5.73 (t, \(J 1.6, 2\)H), 5.80-5.55 (m, 2H), 2.68-2.56 (m, 4H); \(^{13}\text{C NMR (125 MHz, CDCl}_3\)): \(\delta 165.9, 132.9, 130.2, 129.6, 128.3, 123.6, 69.9, 28.8; \) \(\text{HRMS (ESI)}\) calcd. for C\(_{20}\)H\(_{19}\)O\(_4\) [M+H]^+: 323.1277, found:
(+)-(1S,2R)-2-hydroxyl-1-cyclooctanyl benzoate (126):

Reaction carried out by following the general method B with meso-cyclooctane-1,2-diol (124 mg, 0.86 mmol) in AcOEt (8 mL) at -60 °C with 2 mol % of diamine 93, to give (+)-126 in 92 % yield, 77 % ee. Spectral data agreed with literature values:

- Colourless oil; MW = 248.32 g / mol; \( R_f = 0.40 \) (Et\(_2\)O / pentane, 1:2).
- \( [\alpha]_{D}^{20} = +8 \) (c = 0.90 CH\(_2\)Cl\(_2\)); IR (neat, cm\(^{-1}\)): 3425, 3036, 2922, 2856, 1710, 1601, 1584, 1450, 1315, 1271, 1176, 1110.
- \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \): 8.05-8.01 (m, 2H), 7.56-7.52 (m, 1H), 7.45-7.39 (m, 2H), 5.32-5.27 (m, 1H), 4.07 (ddd, \( J = 6.4, 3.9, 2.4 \), 1H) 2.39 (broad s, 1H), 2.23-2.11 (m, 1H), 1.94-1.47 (m, 11H);
- \(^1\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \): 166.1, 132.9, 130.3, 129.5, 128.3, 77.6, 71.7, 30.5, 27.8, 26.8, 25.6, 24.1, 22.0; HRMS (ESI) calcd. for C\(_{15}\)H\(_{21}\)O\(_3\) \([M+H]^+\): 249.1485, found: 249.1481; HPLC Chiralcel OJ-H, eluent: 95:5 hexane / iPrOH, flow rate: 1 mL / min: retention times 8.9 min ((1S,2R)-enantiomer) and 10.7 min ((1R,2S)-enantiomer).

cis-1,2-bisbenzoyloxy cyclooctane (127):

Conversion: 5 % (\(^1\)H-NMR): colourless oil; MW = 352.43 g / mol; \( R_f = 0.44 \) (Et\(_2\)O / pentane, 1:4); IR (neat, cm\(^{-1}\)): 3422, 2924, 2853, 1717, 1451, 1378, 1314, 1278, 1176, 1109, 1069, 1026; \(^1\)H NMR (400 MHz, CDCl\(_3\)): \( \delta \): 8.03-7.98 (m, 4H), 7.57-7.51 (m, 2H), 7.43-7.38 (m, 4H), 5.54-5.49 (m, 2H), 2.30-1.19 (m, 2H), 1.96-1.64 (m, 10H); \(^1\)C NMR (100 MHz, CDCl\(_3\)): \( \delta \): 166.2, 133.2, 130.8, 130.0, 128.7, 75.0, 29.1, 26.7, 23.8; HRMS (ESI) calcd. for C\(_{22}\)H\(_{25}\)O\(_4\) \([M+H]^+\): 353.1747, found: 353.1745.

(+)-(2S,3R)-1,4-bisbenzyloxy-3-hydroxyl-2-butyl benzoate (128):

Reaction carried out by following the general method B with meso-1,4-bisbenzyloxybutane-2,3-diol\(^{[18]} \) (260 mg, 0.86 mmol) in AcOEt (8 mL) at -60 °C with 2 mol % of diamine 93, to give (+)-128 in 51 % yield, 93.5 % ee; colourless oil; colourless oil; MW = 406.48 g / mol; \( R_f = 0.16 \) (Et\(_2\)O / pentane, 1:2); \( [\alpha]_{D}^{20} = +55 \) (c = 0.23 CH\(_2\)Cl\(_2\)); IR (neat, cm\(^{-1}\)): 3464, 3063, 3031, 2865, 1716, 1452, 1270, 1108, 1070, 1026, 737, 712, 698;
\[ ^1H \text{NMR} \ (400 \text{ MHz, CDCl}_3): \delta \ 8.03 \ (d, \ J = 8.3, 2H), 7.58 \ (t, \ J = 7.4, 1H), 7.43-7.41 \ (m, 2H), 7.31-7.22 \ (m, 10H), 5.33 \ (ddd, \ J = 6.7, 4.7, \text{and} 3.5, 1H), 4.61-4.49 \ (m, 4H), 4.27-4.19 \ (m, 1H), 3.91 \ (dd, \ J = 10.9 \text{ and} 4.8, 1H), 3.84 \ (dd, \ J = 10.9 \text{ and} 3.5, 1H), 3.65 \ (dd, \ J = 9.7 \text{ and} 3.9, 1H), 3.60 \ (dd, \ J = 9.5 \text{ and} 5.9, 1H), 2.87 \ (d, \ J = 5.7, 1H); \]
\[ ^{13}C \text{NMR} \ (125 \text{ MHz, CDCl}_3): \delta \ 165.7, 130.8, 137.7, 133.1, 129.9, 129.7, 128.4, 128.37, 128.33, 127.8, 127.7, 127.6, 127.5, 73.4, 73.3, 73.0, 70.6, 69.8, 68.8; \]
\[ \text{HRMS (ESI) calcd. for C}_{25}\text{H}_{27}\text{O}_5 \ [\text{M+H}]^+: 407.1853, \text{found: 407.1862; HPLC Chiralcel AS-H, Gradient 99:1 to 90:10 during 60 min, eluent: hexane / iPrOH, flow rate: 1 mL / min: retention times 35.8 min (}(2S,3R)-enantiomer) \text{ and} 42.6 \text{ min (}(2R,3S)-enantiomer). \]

\[ \text{cis-2,4-bisbenzoyloxy-1,4-benzyloxibutane (129)} \]

Conversion: 26 % (\text{^1H-NMR}); white solid; MW = 510.59 g / mol; \text{RF} = 0.51 (Et\text{2}O / pentane, 1 : 2); \text{MP} = 114-116 \text{ °C (CH}_2\text{Cl}_2 / \text{cyclohexane)}; \text{IR (neat, cm}^{-1}): 3064, 3032, 2928, 2856, 1788, 1719, 1601, 1585, 1451, 1258, 1096; \ [\text{^1H NMR} \ (400 \text{ MHz, CDCl}_3): \delta \ 8.03-7.99 \ (m, 4H), 7.57 \ (tt, \ J = 7.5 \text{ and} 1.3, 2H), 7.44 \ (t, \ J = 7.8, 4H), 7.27-7.18 \ (m, 10H), 5.76-7.72 \ (m, 2H), 4.56 \ (d, \ J = 12.1, 2H), 4.48 \ (d, \ J = 12.1, 2H), 3.88 \ (dd, \ J = 10.8 \text{ and} 3.8, 2H), 3.82 \ (dd, \ J = 10.8 \text{ and} 3.8, 2H); \ [^{13}C \text{NMR} \ (125 \text{ MHz, CDCl}_3): \delta \ 165.5, 138.0, 133.4, 130.2, 130.1, 128.7, 128.6, 128.0, 127.9, 77.3, 73.8, 68.4; \text{MS m/z (EI)}: 403 \ (2 [\text{M-BnO}]^+), 313 \ (65), 267 \ (2), 191 \ (5), 158 \ (4), 105 \ (100), 91 \ (84); \text{HRMS (EI) calcd. for C}_{25}\text{H}_{23}\text{O}_5 \ [\text{M-BnO}]^+: 403.1545, \text{found: 403.1544.} \]

\[ (+)-(2S,3R)-3-hydroxyl-2-tetralinyl benzoate (130) \]

Reaction carried out by following the general method B with \text{meso-tetralin-2,3-dioi}[19] (141 mg, 0.86 mmol) in AcOEt (8 mL) at -60 °C with 2 mol % of diamine 93, to give (+)-130 in 70 % yield, 83 % ee; colourless oil; MW = 268.32 g / mol; \text{RF} = 0.20 (Et\text{2}O / pentane, 1 : 2); [\alpha]_D^{20}: +20 (c = 0.69 \text{ CH}_2\text{Cl}_2), 81.7 \% \text{ ee}; \text{IR (neat, cm}^{-1}): 3423, 3064, 2931, 1712, 1601, 1583, 1495, 1451, 1315, 1270, 1113, 1068; \ [\text{^1H NMR} \ (400 \text{ MHz, CDCl}_3): \delta \ 8.06-8.01 \ (m, 2H), 7.58-7.52 \ (m, 1H), 7.41 \ (t, \ J = 7.8, 2H), 7.20-7.10 \ (m, 4H), 5.55-5.50 \ (m, 1H), 4.37-4.32 \ (m, 1H), 3.31-3.04 \ (m, 4H), 2.75 \ (\text{ broad } s, 1H); \ [^{13}C \text{NMR} \ (100 \text{ MHz, CDCl}_3): \delta \ 166.9, 133.5, 133.2, 132.7, 130.2, 130.0, 129.5, 129.2, 128.6, 126.6, 126.5, 73.3, 68.1, 34.9, 32.1; \text{MS m/z (EI)}: 146 \ (100 [\text{M-PhCOOH}]^+), 145 \ (56), 128 \ (55), 117}\]
(60), 105 (88), 77 (69). **HRMS** (ESI) calcd. for C_{17}H_{17}O_{3} [M+H]^+: 269.1172, found: 269.1179; **HPLC** Chiralcel AS-H, Gradient 99:1 to 90:10 during 60 min, eluent: hexane / iPrOH, flow rate: 1 mL / min: retention times 35.6 ((2S,3R)-enantiomer) min and 47.7 min((2R,3S)-enantiomer).

**cis-2,4-bisbenzoyloxytetralin (131).**

Conversion: 13 % (^1H-NMR); white solid; MW = 372.42 g / mol; \( R_F = 0.69 \) (Et\(_2\)O / pentane, 1 : 2); **MP** = 91 °C (Ethanol); \( IR \) (neat, cm\(^{-1}\)): 3066, 1787, 1720, 1600, 1584, 1451, 1315, 1278, 1212, 1174, 1109, 1040; \(^1\text{H NMR} \) (400 MHz, CDCl\(_3\)): \( \delta \) 8.02-7.95 (m, 4H), 7.57-7.51 (m, 2H), 7.44-7.34 (m, 4H), 7.23-7.15 (m, 4H), 5.75 (t, \( J \) 5.5, 2H), 3.44-3.30 (m, 4H); \(^{13}\text{C NMR} \) (100 MHz, CDCl\(_3\)): \( \delta \) 166.2, 133.3, 132.6, 130.3, 129.9, 129.4, 128.6, 126.8, 70.5, 32.4; **MS** \( m/z \) (EI): 373 (2 [M]^-), 128 (100 [M-2PhCOOH]^+), 105 (85), 77 (72), 51 (32); **HRMS** (ESI) calcd. for C\(_{24}\)H\(_{21}\)O\(_4\) [M+H]^+: 373.1434, found: 373.1439.

\((-\)-(1\text{S},2\text{R})-1,4-diphenyl-2-hydroxyl-1-butyl benzoate (82).**

Reaction carried out by following the general method B with *meso*-1,2-hydrobenzoin\[^{[20]}\] (185 mg, 0.86 mmol) in AcOEt (8 mL) at -60 °C with 2 mol % of diamine 93, to give **-82** in 71 % yield, 34 % ee. Spectral data agreed with literature values:\[^{[3]}\] white solid; MW = 318.38 g / mol; \( R_F = 0.21 \) (Et\(_2\)O / pentane, 1: 3); \([\alpha]^{20}_{D}\): -8 (c= 0.22 CH\(_2\)Cl\(_2\)); **MP** = 158-159 (CH\(_2\)Cl\(_2\) / cyclohexane); **IR** (neat, cm\(^{-1}\)): 3477, 3028, 1720, 1451, 1316, 1272, 1177, 1113, 1027, 701; \(^1\text{H NMR} \) (400 MHz, CDCl\(_3\)): \( \delta \) 8.03-7.98 (m, 2H), 7.59-7.53 (m, 1H), 7.46-7.40 (m, 2H), 7.34-7.26 (m, 10H), 6.16 (d, \( J \) 5.8, 1H), 5.16 (d, \( J \) 5.8, 1H), 2.26 (broad s, 1H); \(^{13}\text{C NMR} \) (125 MHz, CDCl\(_3\)): \( \delta \) 165.7, 139.8, 136.8, 133.5, 130.3, 130.0, 128.8, 128.7, 128.6, 128.5, 128.4, 127.9, 127.3, 79.8, 76.9; **MS** \( m/z \) (EI): 318 (2 [M^-]), 212 (51), 167 (15), 149 (3), 122 (5), 105 (100), 77 (64), 51 (10); **HPLC** Chiralcel OJ-H, eluent: 95:5 hexane / iPrOH, flow rate: 1 mL / min: retention times 33.8 min ((1R,2S)-enantiomer) and 57.3 min ((1S,2R)-enantiomer).
cis-2,3-bisbenzoyloxy-1,4-diphenylbutane (132):

Conversion: 7 % (1H-NMR), spectral data agreed with literature values:\[14\] white solid; \textbf{MW} = 422.49 g / mol; \textbf{R}_f = 0.39 (Et}_2\text{O / pentane, 1 : 2); \textbf{MP} = 241-239 °C (CH}_2\text{Cl}_2 / cyclohexane); \textbf{IR} (neat, cm}^{-1}): 2924, 2852, 1709, 1451, 1266, 1110, 1069, 710; \textbf{^1H NMR} (400 MHz, CDCl}_3): \delta 8.01 (d, J 8.0, 4H), 7.56 (t, J 7.6, 2H), 7.43 (t, J 7.6, 4H), 7.29 (s, 10H), 6.49 (s, 2H); \textbf{^13C NMR} (100 MHz, CDCl}_3): \delta 165.5, 136.2, 133.4, 130.1, 130.0, 128.78, 128.72, 128.4, 127.8, 77.6; \textbf{HRMS} (ESI) calcd. for C\textsubscript{28}H\textsubscript{22}O\textsubscript{4} [M+H]+: 440.1856, found: 440.1851.

V.3.5 References.

[1] purchased from buchler-gmbh
V.3 – Experimental part related to Chapter III
1,4-tetralindione (134).

A 2L round bottomed flask was charged with 1,4-dihydroxynaphthalene\[^{[1]}\] (61) (10 g, 62.4 mmol) and 200 mL of CF\(_3\)COOH. The initial suspension changed to a clear solution upon stirring for 30 min. at r.t. Toluene was added (800 mL) and the solvent removed under low pressure at 35 °C until dryness. The residue was recrystallised from 400 mL of boiling \(^{i}\)Pr\(_2\)O to afford the title compound 134 (7.38 g, 74 %) as a white solid. Spectral data agreed with literature values.\[^{[2-5]}\]

**MW** = 160.17 g / mol; **R\(_F\)** = 0.39 (Et\(_2\)O / pentane, 1: 6); **MP** = 100-101 °C \((^{i}\)Pr\(_2\)O); **IR** (neat, cm\(^{-1}\))): 3352, 2971, 2910, 1683, 1585, 1425, 1282, 1200; **\(^{1}\)H NMR** (300 MHz, CDCl\(_3\)): \(\delta\) 8.05-8.01 (m, 2H), 7.76-7.71 (m, 2H), 3.08 (s, 4H); **\(^{13}\)C NMR** (75 MHz, CDCl\(_3\)): \(\delta\) 196.2, 135.5, 134.5, 126.9, 37.7; **MS m/z** (EI): 160 (90 \([M]^{+}\)), 132 (12), 104 (100), 76 (52), 50 (28); **HRMS** (ESI) calcd. for C\(_{10}\)H\(_9\)O\(_2\) \([M+H]^{+}\): 161.0597 found 161.0603; **Elemental analysis**: calcd. for C\(_{10}\)H\(_8\)O\(_2\): 74.99 % C, 5.03 % H found 74.78 % C, 5.05 % H.

\((\pm)-4\)-carbonitrile-4-trimethylsilanoxy-1-tetralone (139).

A Schlenk tube was charged under N\(_2\) with 1,4-tetralindione (134) (500 mg, 3.12 mmol), I\(_2\) (40 mg, 0.16 mmol) and 31 mL of dry CH\(_2\)Cl\(_2\). This pink solution was cooled at -78 °C and TMSCN (499 µL, 3.74 mmol) was added gently and stirring was continued 3 h more at this temperature. The reaction was then quenched with Na\(_2\)S\(_2\)O\(_3\) aq (1.5 N) and shaken into an extraction funnel until decolouration occurs. The aqueous phase was extracted with CH\(_2\)Cl\(_2\) (3 x). The combined organic layers dried with Na\(_2\)SO\(_4\) and the solvent removed reduced pressure. Flash chromatography (AcOEt / pentane 1 : 19) of the residue yielded the title compound 139 as a colourless pale green oil, 618 mg, 76 % yield.

**MW** = 259.38 g / mol; **R\(_F\)** = 0.60 (Et\(_2\)O / pentane, 1 : 2); **IR** (neat, cm\(^{-1}\))): 2960, 1691, 1598, 1454, 1412, 1346, 1254, 1105, 1077; **\(^{1}\)H NMR** (300 MHz, CDCl\(_3\)): \(\delta\) 8.07 (dd, \(J\) 7.7 and 1.5, 1H), 7.89 (dd, \(J\) 7.8 and 1.5, 1H), 7.68 (td, \(J\) 7.7 and 1.5, 1H), 7.54 (td, \(J\) 7.7 and 1.5, 1H), 2.97 (ddd, \(J\) 18.0, 8.0 and 5.6, 1H), 2.85 (ddd, \(J\) 18.0, 8.0 and 5.6, 1H), 2.63-2.61 (m, 2H), 0.2 (s, 9H); **\(^{13}\)C NMR** (75 MHz, CDCl\(_3\)): \(\delta\) 195.2, 141.2, 134.7, 130.8, 130.5, 128.1, 127.1, 120.4, 69.4, 37.2, 33.8, 1.4; **MS m/z** (EI): 259 (9 \([M]^{+}\)), 244 (98), 231 (37), 226 (38), 217(61), 189(58), 75 (100); **HRMS** (EI) calcd. for C\(_{14}\)H\(_{17}\)O\(_2\)NSi \([M]^{+}\): 259.1028 found 259.1024.

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134

139
4-hydroxy-4-cyano-1-tetralone (140).

A round bottom flask was charged with trimethylsilylcyanohydrin 139 (450 mg, 1.73 mmol), 1.7 mL of MeCN and 1.7 mL of 1 N HCl. This mixture was stirred for 1 h at r.t. and then extracted with AcOEt (3 x). The combined organic layers were dried with MgSO₄ and evaporated under reduced pressure. After two successive recrystallisations of the residue from iPr₂O / pentane, the title compound 140 was obtained as white crystals, 269 mg, 87 % yield.

**MW** = 187.20 g / mol; **Rf** = decomposition; **MP** = 115-117 °C (iPr₂O / pentane); **IR** (Neat, cm⁻¹): 3384, 1682, 1598, 1455, 1411, 1345, 1288, 1195; **¹H NMR** (300 MHz, CDCl₃): δ 8.07 (d, J 7.5, 1H), 7.85 (d, J 7.5, 1H), 7.72 (td, J 7.2 and 1.5, 1H), 7.58 (td, J 7.5 and 1.3, 1H), 3.36 (broad s, 1H), 3.31-2.97 (m, 1H), 2.89-2.76 (m, 1H), 2.73-2.61 (m, 2H); **¹³C NMR** (75 MHz, CDCl₃); δ 195.1, 139.9, 135.1, 130.9, 128.2, 126.8, 120.3, 68.2, 35.7, 33.6; **MS** m/z (EI): 187 (100 [M⁺]), 160 (63), 132 (12), 104 (100), 76 (51), 50 (32); **HRMS** (ESI) calcd. for C₁₁H₁₀O₂Na [M+Na⁺]: 210.0656, found 210.0652. **Elemental analysis:** calcd. for C₁₁H₁₀O₂N: 70.58 % C, 4.85 % H, 7.48 % N, found 70.58 % C, 4.94 % H, 7.35 % N.

4-methylene-1-tetralone (137).

A Schlenk tube was charged under N₂ with methyltriphenylphosphonium bromide (392 mg, 1.1 mmol), 6.6 mL of THF. Then, a solution of BuLi (1.6 M in hexane, 687µL, 1.1 mmol) was added drop-wise to this white suspension and stirring was continued for 30 min to give a clear yellow solution. A solution of ketone 139 (259 mg, 1.0 mmol) in 2.6 mL of THF was then added gently. After 50 min stirring, the reaction mixture was quenched with H₂O (2 mL) and stirred for 5 min. A solution of TBAF (1 M in THF, 2 mL, 2 mmol) was then added and after stirring for 30 min the mixture was extracted with Et₂O (3 x). The combined organic layers were dried with MgSO₄ and evaporated under reduced pressure. After fast flash chromatography (AcOEt / pentane 1 : 20) 137 was obtained as a colourless oil, (116 mg, 73 % yield).

**MW** = 158.20 g / mol; **Rf** = 0.51 (Et₂O / pentane, 1 : 10); **IR** (Neat, cm⁻¹): 2961, 2918, 2849, 1684, 1600, 1282, 1260; **¹H NMR** (400 MHz, CDCl₃): δ 8.04 (dd, J 7.5 and 1.1, 1H), 7.64 (dd, J 7.5 and 1.5, 1H), 7.54 (td, J 7.9 and 1.5, 1H), 7.39 (td, J 7.9 and 1.5, 1H), 5.59 (s, 1H), 5.27 (s, 1H), 2.90-2.81 (m, 2H), 2.82-2.73 (m, 2H); **¹³C NMR** (100 MHz, CDCl₃); δ 198.2, 142.0, 141.3, 134.0, 131.5, 128.8, 127.5, 125.1, 112.0, 39.6, 32.7; **MS** m/z (EI): 158 (100
V.4 - Experimental part related to Chapter IV.

[183x796]V.4 - Experimental part related to Chapter IV.

[M]+, 129 (46), 115 (34), 102 (23), 51 (14); **HRMS** (EI) calcd. for C_{11}H_{10}O [M]⁺: 158.0731 found 158.0732.

1,4-dimethylenetetralin (138).

A Schlenk tube charged under N₂ with methyltriphenylphosphonium bromide (1.67 g, 4.68 mmol) and 24 mL of dry THF. A solution of BuLi (1.6 M in hexane, 2.92 mL, 4.68 mmol) was added drop-wise to this white suspension and stirring was continued for 30 min to give a clear yellow solution. A solution of diketone 134 (250 mg, 1.56 mmol) in 2 mL of THF was then added gently. After 50 min stirring, the reaction mixture was quenched with H₂O (2 mL) and extracted with Et₂O (3 x). The combined organic layers were dried with MgSO₄ and evaporated under reduced pressure. The residue was purified by flash chromatography (pentane) using neutral alumina deactivated by mixing with 10 % v H₂O. The title compound 138 is obtained as a colourless oil, 71 mg, 29 % yield.

MW = 156.22 g / mol; **R**<sub>F</sub> = 0.79 (pentane); **IR** (neat, cm⁻¹): 2944, 1630, 886; **¹H NMR** (300 MHz, CDCl₃): δ 7.66-7.63 (m, 2H), 7.26-7.23 (m, 2H), 5.49 (s, 2H), 5.02 (s, 2H), 2.63 (s, 4H); **¹³C NMR** (75 MHz, CDCl₃): δ 143.7, 134.5, 128.1, 125.7, 108.8, 33.9; **MS** m/z (EI): 156 (100 [M]+), 141 (63) 128 (17), 115 (17); **HRMS** (EI) calcd. for C_{12}H_{12} [M]+: 156.0939 found 156.0933.

(1R,4R)-1,4-tetralindiol (142).

**Method 1:** (1R,4R)-142: A solution of 1,4-tetralindione (134) (2.48 g, 15.5 mmol) in dry THF (124 mL) was added, under N₂, with a syringe pump over 2 h to a stirred, cooled (-10 °C) solution of BH₃·THF (1 M in THF, 18.6 mL, 18.6 mmol) and (S)-3,3-diphenyl-1-methyltetrahydro-3H-pyrrolo[1,2-c][1,2,3]oxazaborole (67) (1 M toluene, 1.56 mL, 1.56 mmol) in dry THF (95 mL). After stirring for 1 h more, the reaction mixture was quenched with MeOH (50 mL) and warmed to r.t. All volatiles were evaporated under reduced pressure and two successive crystallisations of this crude from iPr₂O gave (1R,4R)-1,4-tetralindiol (142) as colourless crystals, 1.83 g, 72 % yield, 99.7 % ee, [α]_<sub>D</sub>²⁰ = -73 (c = 0.30, MeOH). Spectral data agreed with literature values.[⁶, ⁷]

**Method 2:** rac-142: Racemic synthesis: A solution of [Al(H₂)(OCH₂CH₂OMe)₂][Na] (Red-Al) (3.5 M in toluene, 1.33 mL, 4.68 mmol) was added dropwise under N₂ to a stirred,
cold (-78 °C) solution of 1,4-tetralindione (134) (250 mg, 1.56 mmol) in dry THF (31 mL). After stirring for 2 h, the reaction mixture was warmed to r.t., quenched with sat. aq. KNaC4H4O6 (Rochelle salt) (30 mL) and stirred for 1 h. The mixture was then extracted with Et2O (3 x), the combined organic layers were dried over MgSO4 and then volatiles were removed under reduced pressure. The crude product was taken up in AcOEt / pentane (1 : 1) and filtered through a plug of silica to give 192 mg (76 %) of a product shown by 1H-NMR to consist of a mixture of a 16 : 84 mixture of cis- and trans-1,4-tetralindiol. Recrystallisation from hot CHCl3 (12 mL) yielded (±)-trans-1,4-tetralindiol (142) as brown crystals (140 mg, 55 % yield). MW = 164.20 g / mol; RF = 0.13 (Et2O); MP = 141-142 °C (MeOH / Et2O); IR (neat, cm⁻¹): 3218, 2950, 2865, 1484, 1453, 1325, 1201, 1119, 1047, 1009; 1H NMR (400 MHz, CDCl3): δ 7.45-7.43 (m, 2H), 7.35-7.31 (m, 2H), 4.80-4.84 (m, 2H), 2.33-2.27 (m, 2H), 1.86-1.79 (m, 2H), 1.55 (broad s, 2H); 13C NMR (100 MHz, CDCl3): δ 138.5, 128.4, 128.3, 67.9, 28.3; MS m/z (EI): 164 (1, [M]+), 146 (100, [M-H2O]+), 131 (38), 120 (45), 105 (30), 77 (28); Elemental analysis: calcd. for C10H12O2: 73.15 % C, 7.37 % H, found 72.93 % C, 7.36 % H; SFC: Chiralcel OD-H, F = 2 mL/min, Gradient: CO2 + 2 % MeOH for 2 min and increase 1% MeOH / min until 15 % MeOH. T R = 2.7 min ((1S,4S)-enantiomer)) and 3.2 min ((1R,4R)-enantiomer)), λ = 254 nm.

**Reduction of 134 with borane:** A Schlenk tube is charged with 1,4-tetralinedione (134) (250 mg, 1.56 mmol) and MeOH 22 mL. Then cooled at -10°C and a solution of BH3·THF complex (1M in THF, 1.87 mL, 1.87 mmol) is added drop wise. After 1.5 h stirring, quench with 10 mL of MeOH and evaporate the solvent under reduced pressure. The crude product was taken up in AcOEt / pentane (1 : 1) and filtered through a plug of silica to give 235 mg (93 %) of a product shown by 1H NMR to consist of a 61 : 39 mixture of cis 141 and trans-1,4-tetralindiol (142). This diastereomeric mixture was not further resolved.

**Reduction of 134 with NaBH₄:** A Schlenk tube was charged with 1,4-tetralinedione (134) (250 mg, 1.56 mmol) and MeOH 39 mL. Then, NaBH₄ (129 mg, 3.43 mmol) was added in small portions to this cooled (0° C) solution. After 30 minutes stirring, the reaction was quenched with 10 mL of H₂O and 10 mL NaCl sat. The mixture was extracted with Et₂O (3 x) and the combined organic layers were dried with MgSO₄ and the volatiles were removed under reduced pressure. The crude product was taken up in AcOEt / pentane (1 : 1) and filtered through a plug of silica to give 249 mg (98 %) of a product shown by 1H NMR to consist of a 58 : 48 mixture of cis 141 and trans-1,4-tetralindiol (142). This diastereomeric mixture was not further resolved.
Reduction with of 134 LiAlH₄: A Schlenk tube was charged with 1,4-tetralinedione (134) (250 mg, 1.56 mmol) and THF (15 mL). Then LiAlH₄ (71 mg, 1.87 mmol) was added in small portions to this cooled solution (-78°C). After 3 hours stirring quench dropwise with 10 mL of AcOEt, stir for 5 minutes while warming at room temperature. The reaction was then quenched with a saturated aq. solution of KNaC₄H₄O₆ (Rochelle salt) (30 mL) and stirred for 1h. The reaction mixture was extracted with Et₂O (3 x). The combined organic layers were dried over MgSO₄ and the volatiles were removed under reduced pressure. The crude product was taken up in AcOEt / pentane (1 : 1) and filtered through a plug of silica to give 238 mg (94 %) of a product shown by ¹H NMR to consist of a mixture of a 32 : 68 mixture of cis-141 and trans-1,4-tetralindiol (142). This diastereomeric mixture was not further resolved.

cis-1,4-tetralindiol (141).

A solution of L-Selectride (1 M in THF, 4.7 mL, 4.68 mmol) in DME was added dropwise under N₂ to a stirred, cold (~50 °C) solution of 1,4-tetralindione (134) (250 mg, 1.56 mmol) in dry DME (30 mL). After stirring for 3h, the reaction mixture was warmed to r.t. and stirred for 1.5 h (TLC control). The reaction was then quenched with 10 mL of a 3 N solution of NaOH and 3.9 mL of 30 % aq. H₂O₂. After 30 min stirring, the reaction mixture was extracted with AcOEt (4 x). The combined organic layers were dried over MgSO₄ and the volatiles were removed under reduced pressure. The crude product was taken up in AcOEt / pentane (1 : 1) and filtered through a plug of silica to give 248 mg (98 %) of a product shown by ¹H NMR to consist of a 86 : 14 mixture of cis- and trans-1,4-tetralindiol. Three successive recrystallisation in boiling tPr₂O yielded cis-1,4-tetralindiol (141) as white crystals, 166 mg, 66 % yield. Spectral data agreed with literature values.[⁶, ⁷]

MW = 164.20 g / mol; Rf = 0.29 (ether); MP = 137-138 °C (tPr₂O); IR (neat, cm⁻¹): 3257, 2949, 2920, 1486, 1356, 1281, 1196, 1090, 1038; ¹H NMR (400 MHz, CDCl₃): δ 7.50-7.45 (m, 2H), 7.34-7.30 (m, 2H), 4.76-4.72 (m, 2H), 2.09-1.98 (m, 4H), 1.79 (broad s, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 138.9, 128.3, 128.0, 68.3, 28.5; MS m/z (EI): 164 (18, [M⁺]), 146 (95, [M-H₂O⁺]), 131 (30), 120 (100), 105 (50), 77 (48); HRMS (ESI) calcd. for C₁₀H₁₂O₂Na [M+Na⁺]: 187.0729, found 187.0734. Elemental analysis: calcd. for C₁₀H₁₂O₂: 73.15 % C, 7.37 % H, found 72.96 % C, 7.41 % H.
(-)-(4R)-4-hydroxy-1-tetralone (144).

**Method 1:** A Schlenk tube was charged under N₂ with 1,4-tetralindione (134) (500 mg, 3.12 mmol), dry toluene (15 mL) and a solution of (S)-3,3-diphenyl-1-butyltetrahydro-3H-pyrrolo[1,2-c][1,2,3]oxazaborole (70) (3.16 mL, 0.1 M in toluene, 0.31 mmol). This clear solution was cooled to -78 °C and a solution of catecholborane (1 M in toluene, 3.74 mL, 3.74 mmol) was added with a syringe pump over 20 min. After stirring at this temperature for a further 20 h the reaction was quenched with H₂O (5 mL), warmed to r.t. and washed with sat. aq. NaHCO₃ (3 x). After extraction with CH₂Cl₂ (3 x), the combined organic layers were dried with MgSO₄ and the solvent evaporated under reduced pressure. The crude was purified by flash chromatography (AcOEt / pentane 1 : 2) to give (-)-(R)-4-hydroxy-1-tetralone (137) as a brown oil, 367 mg, 73 % yield, 95.5 % ee, [α]D²⁰:-39 (c = 0.70, CH₂Cl₂). Spectral data agreed with literature values.[9, 10]

**Method 2:** A solution of ketone (139) (200 mg, 0.77 mmol) in dry THF (6 mL) was added under N₂ with a syringe pump over 1 h to a stirred, cooled (-30 °C) solution of BH₃-THF (1 M in THF, 462 µL, 0.46 mmol) and (S)-3,3-diphenyl-1-methyltetrahydro-3H-pyrrolo[1,2-c][1,2,3]oxazaborole (67) (21 mg, 0.077 mmol) in dry THF (4.6 mL). After stirring for 30 min more, the reaction mixture was quenched with MeOH (4 mL) and warmed to r.t. Then, a solution of TBAF (1 M in THF, 925 µL, 0.93 mmol) was added and the mixture stirred for a further 30 min. This mixture was washed sat. aq. NaHCO₃ (3 x) and extracted with Et₂O (3 x). All the combined organic layers were dried with MgSO₄ and evaporated under reduced pressure. After flash chromatography (AcOEt / pentane 1 : 2) the title compound (-)-144 was obtained as a brown oil, 106 mg, 85 % yield, 95.5 % ee, [α]D²⁰:-39 (c = 0.70, CH₂Cl₂).

**Method 3:** Racemic synthesis: A solution of BH₃-THF (1 M in THF, 5.61 mL, 5.61 mmol) was added dropwise under N₂ to a stirred, cooled (-10 °C) solution of 1,4-tralindione (134) (2.00 g, 12.5 mmol) in dry THF (120 mL). This clear solution was stirred for 90 min more, quenched with MeOH (30 mL) and warmed at r.t. All volatiles were evaporated under reduced pressure and the residue was purified by flash chromatography (Et₂O / pentane 1 : 2) to give (±)-4-hydroxy-1-tetralone (144) as brown oil, 1.65 g, 81 % yield.

MW = 162.20 g / mol; Rf = 0.29 (AcOEt / pentane, 1: 2); IR (neat, cm⁻¹): 3404, 2951, 1682, 1601, 1329, 1286; ¹H NMR (300 MHz, CDCl₃): δ 7.95 (d, J 7.8, 1H), 7.60-7.50 (m, 2H), 7.30-7.45 (m, 1H), 4.98-4.90 (m, 1H), 2.96-2.76 (m, 1H), 2.61 (broad singlet, OH, 1H), 2.59-2.49 (m, 1H), 2.42-2.31 (m, 1H), 2.19-2.08 (m, 1H); ¹³C NMR (75 MHz, CDCl₃): δ 198.1,
145.7, 134.3, 131.2, 128.4, 127.3, 127.2, 67.9, 35.3, 32.2; **MS** *m/z* (EI): 162 (24 (M+)), 147 (15), 134 (85), 120 (30), 105 (100), 91 (10), 77 (40); **HRMS** (ESI) calcd. for C₆H₁₁O₂ [M+H]+: 163.0753, found 163.0755. **HPLC**: Chiralcel OJ, *F = 1 mL / min*, Hexane / iPrOH 99 : 1 gradient to 90 / 10 over 60 min, *T_R = 39.5 min* ((4R)-enantiomer)) and 41.6 min ((4S)-enantiomer)), _λ_ = 254 nm.

**(4R)-4-(tert-butyldimethylsiloxy)-1-tetralone (146).**

A two neck round bottomed flask equipped with a condenser was charged under N₂ with 4-hydroxy-1-tetralone (144) (400 mg, 2.49 mmol, 95 % ee), CH₂Cl₂ (18 mL), iPr₂EtN (2.17 mL, 12.45 mmol), DMAP (60 mg, 0.50 mmol) and TBSCl (1495 mg, 9.96 mmol). This clear solution was refluxed for 60 h, quenched with H₂O (20 mL) and stirred at r.t. for 3 h. The reaction mixture was extracted with CH₂Cl₂ (3 x) and the combined organic layers dried with Na₂SO₄. Evaporation of the solvent under reduced pressure and purification of the residue by flash chromatography (Et₂O / pentane 1 : 15) gave 4-(tert-butyldimethylsiloxy)-1-tetralone (146) as a white solid, 605 mg, 88 % yield, 95 % ee, [α]D²⁰ = +2 (c = 1.12 CH₂Cl₂). Spectral data agreed with literature values.[11]

**MW** = 276.45 g / mol; **R_F** = 0.67 (Et₂O / pentane, 1: 3); **MP** = 56-58 °C (pentane); **IR** (neat, cm⁻¹): 2954, 2929, 2857, 1689, 1602, 1472, 1361, 1327, 1284, 1252, 1124, 1091; **¹H NMR** (500 MHz, CDCl₃): δ 8.02-7.99 (m, 1H), 7.60-7.56 (m, 1H), 7.51-7.52 (m, 1H), 7.41-7.37 (m, 1H), 4.96 (dd, J 8.7 and 3.9, 1H), 2.92 (ddd, J 13.0, 6.4 and 4.4, 1H), 2.59 (ddd, J 12.7, 10.6 and 4.7, 1H), 2.33-2.28 (m, 1H), 2.19-2.12 (m, 1H), 0.95 (s, 9H), 0.19 (s, 3H), 0.16 (s, 3H); **¹³C NMR** (125 MHz, CDCl₃): δ 197.6, 146.4, 133.8, 131.1, 127.8, 127.0, 126.7, 68.8, 35.6, 32.8, 25.8, 18.2, -4.4, -4.7; **MS** *m/z* (ESI): 261 (3 [M-CH₃]+), 219 (64 [M⁻Bu]+), 201 (100), 185 (9), 145 (10), 115 (14), 75 (89); **HRMS** (ESI) calcd. for C₁₆H₂₄O₂NaSi: 299.1443 found 299.1440; **HPLC**: Chiralcel AS, *F = 0.5 mL / min*, Hexane / iPrOH 95 : 5 gradient to 90 / 10 over 60 min, *T_R = 11.6 min* ((4R)-enantiomer))and 13.2 min ((4S)-enantiomer)), _λ_ = 254 nm.
(+)-(1R)-4-(2,3-dichlorophenyl)-1,2-dihydronaphthalen-1-ol (145).

A two neck round bottomed flask equipped with condenser was charged under N₂ with Mg (50 mg, 2.06 mmol), a crystal of I₂ and Et₂O (1.6 mL). A solution of 4-bromo-1,2-dichlorobenzene (264 µL, 2.06 mmol) in 2.5 mL of Et₂O was added dropwise under stirring over 5 min while heating gently to maintain ebullition. This suspension was further refluxed during 1 h to give a clear solution. Then, a solution of ketone 146 (285 mg, 1.03 mmol, 95 % ee) in Et₂O (2.5 mL) was added dropwise and the mixture was refluxed for 19 h. The reaction was quenched with sat. aq. NH₄Cl and extracted with Et₂O (3 x). The combined organic layers were dried with Na₂SO₄ and volatiles were evaporated under reduced pressure. This crude was dissolved in CH₂Cl₂ (8.6 mL) under N₂. A solution of Et₃N (724 µL, 5.16 mmol) in CH₂Cl₂ (8.6 mL) and a solution of MsCl (319 µL, 4.12 mmol) in CH₂Cl₂ (8.6 mL) were cooled at 0 °C and added sequentially to this stirred, cooled (0 °C) mixture. After further 2 h stirring at 0 °C and 2 h at r.t., the reaction was quenched with sat. aq. NaHCO₃ and extracted with Et₂O (3 x). The organic phases were combined, dried with Na₂SO₄ and the solvent evaporated under reduced pressure. This residue was dissolved in THF (10 mL) and a solution of TBAF (1 M in THF, 1.55 mL, 1.55 mmol) was added at r.t. The mixture was stirred for 1 h, diluted with Et₂O, washed with sat. aq. NaHCO₃ and extracted with Et₂O (3 x). The organic phases were combined, dried with MgSO₄ and evaporated under reduced pressure. Purification by flash chromatography (AcOEt / pentane 1 : 4) gave the title compound 145 as a white solid, 237 mg, 79 % yield, 95.3 % ee, [α]D²⁰ = +35 (c = 0.47 CH₂Cl₂). Spectral data agreed with literature values.[12]

MW = 291.18 g / mol; Rf = 0.30 (Et₂O / pentane, 1: 4); MP = 107-109 °C (CH₂Cl₂ / cyclohexane).[13] IR (neat, cm⁻¹): 3346, 3060, 2928, 2857, 2824, 1547, 1468, 1380, 1333, 1198, 1131, 1029; ¹H NMR (400 MHz, CDCl₃): δ 7.32-7.28 (m, 3H), 7.12 (td, J 7.3 and 1.3, 1H), 7.07 (td, J 7.5 and 1.4, 1H), 7.01 (dd, J 8.2 and 0.0, 1H), 6.86 (d, J 7.5, 1H), 5.83 (t, J 4.5, 1H), 4.65 (t, J 5.9, 1H), 2.52-2.47 (m, 2H), 1.99 (broad s, 1H); ¹³C NMR (100 MHz, CDCl₃): δ 140.4, 137.8, 137.7, 133.0, 132.7, 131.7, 130.9, 130.6, 128.5, 128.47, 128.43, 127.0, 125.9, 125.6, 68.0, 33.0; HRMS (EI) calcd. for C₁₆H₁₀OCl₂ [M-H₂O]⁺: 272.0159, found 272.0156; HPLC: Chiralcel OJ, F = 1 mL / min, Hexane / iPrOH 99 : 1 gradient to 90 / 10 over 60 min, TR = 30.3 min ((4R)-enantiomer)) and 33.6 min ((4S)-enantiomer)), λ = 254 nm.
V.4 - Experimental part related to Chapter IV.

(-)-(1S,4S)-1,4-dihydroxy-1,4-diallyltetralin (148).

A Schlenk tube was charged under N₂ with (-)-(S)-binol (134 mg, 0.47 mmol), dry CH₂Cl₂ (3.7 mL) and Ti(OiPr)₄ (138 µL, 0.47 mmol) at r.t. This mixture was stirred for 10 min and then dry iPrOH (2.14 mL, 31.2 mmol), 1,4-tetralindione (134) (250 mg, 1.56 mmol) and tetraallylstannane (564 µL, 2.34 mmol) were added sequentially. After stirring for 24 h at r.t., the reaction was quenched with sat. aq. NH₄Cl solution and extracted with CH₂Cl₂ (3 x). The combined organic layers were dried with MgSO₄ and filtered through a plug of celite. The solvent was evaporated under reduced pressure and the residue purified by flash chromatography (CH₂Cl₂) to give (-)-trans (148) as a white gum, 395 mg, 93 % yield, 97 % ee, [α]D²⁰: -86 (c = 0.58 CHCl₃).

MW = 244.34 g / mol; Rᵣ = 0.48 (AcOEt / pentane, 1 : 3); IR (neat, cm⁻¹): 3369, 3072, 2940, 1638, 1482, 1452, 1431, 1379, 1194, 1020, 997, 913; ¹H NMR (400 MHz, CDCl₃): δ 7.60-7.51 (m, 2H), 7.36-7.27 (m, 2H), 5.97-5.80 (m, 2H), 5.22-5.12 (m, 4H), 2.64-2.61 (m, 4H), 2.37 (broad s, 2H), 2.21-2.09 (m, 2H), 1.87-1.75 (m, 2H); ¹³C NMR (100 MHz, CDCl₃): δ 142.0, 133.9, 128.2, 126.5, 119.7, 72.5, 47.5, 33.3; MS m/z (ESI): 208 (14[M-2H₂O]+), 203 (58), 185 (100), 167 (27), 144 (84), 115 (29); HRMS (ESI) calcd. for C₁₆H₂₀O₂Na [M+Na]⁺: 267.1360, found 267.1357; SFC: Chiralcel AD, F = 2 mL/min, Gradient: CO₂ + 10 % MeOH for 2 min and increase 1% MeOH/min until 25 % MeOH. Tᵣ = 5.8 min ((1R,4R)-enantiomer)) and 7.6 min ((1S,4S)-enantiomer)), λ = 254 nm.

(-)-(5S,8S)-[Cr(CO)₃(η⁶-5,8-dihydroxy-5,8-diallyltetralin)] (149).

A 10 mL Carus tube was charged under N₂ with (-)-(1S,4S)-1,4-dihydroxy-1,4-diallyltetralin (148) (137 mg, 0.5 mmol), [Cr(CO)₃(η⁶-naphthalene)] (264 mg 1.0 mmol), dry THF (271 µL, 1.0 mmol) and dry Et₂O (2 mL). The mixture was degassed by three freeze-pomp-thaw cycles. The closed tube was heated at 70 °C for 22 h (protected from light). Evaporation of the solvent under high vacuum and purification by flash chromatography (Et₂O / pentane 1 : 2) gave (-)-(5S,8S)-[Cr(CO)₃(η⁶-5,8-dihydroxy-5,8-diallyltetralin)] (149) as a yellow solid, 176 mg, 93 % yield, [α]D²⁰: -82 (c = 0.43, CH₂Cl₂); MW = 380.36 g / mol; Rᵣ = 0.11 (Et₂O / pentane, 1: 2); MP = 88-90 °C (under N₂, hexane); IR (neat, cm⁻¹): 3564, 3446, 3079, 2954, 1951, 1845, 1638, 1453, 1353, 1183, 1029, 997; ¹H NMR (400 MHz, C₆D₆): δ 5.90-5.78 (m, 1H), 5.77-5.64 (m, 1H), 5.21 (d, J 6.5, 1H), 5.09-
4.98 (m, 3H), 4.96 (d, J 6.6, 1H), 4.92 (d, J 17.9, 1H), 4.66 (t, J 6.3, 1H), 4.36 (t, J 6.1 1H), 2.67-2.57 (dd, J 12.0 and 7.9, 1H), 2.52-2.49 (dd, J 14.5 and 6.8, 1H), 2.27-2.20 (m, 2H), 1.74-1.80 (m, 3H), 1.57 (t, J 13.3, 1H), 1.46 (s 1H), 1.27 (t, J 13.3, 1H); \(^{13}\)C NMR (100 MHz, C\(_6\)D\(_6\)): \(\delta\) 233.9, 133.8, 133.5, 121.6, 120.7, 118.9, 116.4, 95.1, 94.7, 90.1, 86.9, 71.1, 70.7, 48.3, 47.3, 32.4, 32.1; MS m/z (EI): 380 (22 [M]\(^+\)), 296 (73), 250 (51), 236 (31), 210 (45), 52 (100); HRMS (EI) calcd. for C\(_{19}\)H\(_{20}\)O\(_5\)Cr \([M]^+\): 380.0715, found 380.0710.

1,4-dimethylnaphthalene (151).

A Schlenk tube was charged under N\(_2\) with anhydrous CeCl\(_3\) (922 mg, 3.74 mmol) and THF (6.1 mL) at 0 °C. The resulting suspension was stirred overnight at r.t. After cooling at -78 °C a solution of MeLi (1.6 M in Et\(_2\)O, 2.17 mL, 3.74 mmol) was added dropwise and stirring was continued at this temperature for 1 h. Then a solution of 1,4-tetralindione (134) (150 mg, 0.94 mmol) in dry THF (10 mL) was added over 1 h with a syringe pump, stirred for 1 h more, warmed to r.t. and stirred for 14 h. This mixture was quenched with sat. aq. AcOH 5 % in NaCl and extracted with AcOEt (3 x). The combined organic layers were dried with MgSO\(_4\) and the solvent was evaporated under reduced pressure. This crude was then dissolved in CH\(_2\)Cl\(_2\) (20 mL) and 35 % HCl (20 mL) and stirred at r.t. for 18 h. The mixture was extracted with CH\(_2\)Cl\(_2\) (3 x) and washed with sat. aq. NaHCO\(_3\). After extraction with CH\(_2\)Cl\(_2\) (3 x), the organic layers were dried with Na\(_2\)SO\(_4\) and the solvent evaporated under reduced pressure. The residue was further purified by flash chromatography (pentane) to give 1,4-dimethylnaphthalene (151) as a colourless oil, 116 mg, 79 % yield. Spectral data agreed with literature values.\[^{14,15}\]

MW = 156.22 g / mol; \(R_F\) = 0.43 (pentane); IR (CH\(_2\)Cl\(_2\), cm\(^{-1}\)): 3073, 2945, 1597, 1464, 1444, 1390, 1024, 909; \(^1\)H NMR (300 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 8.05-7.99 (m, 2H), 7.56-7.51 (m, 2H), 7.22 (s, 2H), 2.66 (s, 6H); \(^{13}\)C NMR (100 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 133.2, 132.9, 126.7, 125.9, 125.2, 19.7.

1,4-diphenynaphthalene (152).

A Schlenk tube was charged under N\(_2\) with 1,4-tetralindione (134) (250 mg, 1.56 mmol) and dry DME (15 mL). This solution was cooled to -50 °C and phenyllithium (2 M Bu\(_2\)O, 2.34 mL, 4.68 mmol) was added drop-wise. The mixture was stirred for 3h, warmed to 0 °C, stirred for 1.5 h and quenched at
0 °C with HCl 35 % (23 mL). This acidic mixture was stirred for 18 h at r.t., extracted with 
Et₂O (3x) and the combined organic layers washed with sat. aq. NaHCO₃. After extraction 
with Et₂O (3 x), the combined organic layers were dried with MgSO₄ and evaporated under 
reduced pressure. The residue was purified by flash chromatography (pentane) to give 1,4-
diphenylnaphthalene (152) as a white solid, 326 mg, 75 % yield. Spectral data agreed with 
literature values.[16]

MW = 280.37 g / mol; MP = 136-137 °C (hexane); Rₛ = 0.26 (pentane); IR (neat, cm⁻¹): 
3054, 2922, 2851, 1949, 1494, 1445, 1385, 1186, 1157, 1071, 1000, 974; 
¹H NMR (300 MHz, CDCl₃): δ 7.97-7.93 (m, 2H), 7.53-7.36 (m, 14H); 
¹³C NMR (75 MHz, CDCl₃): δ 140.8, 139.8, 131.9, 130.1, 128.3, 127.2, 126.4, 126.3, 125.8; MS m/z (EI): 280 
(100 [M]+), 279 (26), 278 (17), 277 (13), 276 (15), 275 (4) 203 (17), 202 (25), 200 (6), 176 
(2), 138 (3), 126(3), 77 (4), 51 (3).

[1,1'-4,1'']ternaphthalene (153).

A Schlenk tube was charged under N₂ with 1-bromonaphthalene (843 
µL, 6.24 mmol) and dry THF (45 mL). A solution of BuLi (1.6 M in 
hexane, 3.9 mL, 6.24 mmol) was added drop-wise to this stirred, cooled 
(-78 °C) solution. After stirring for 15 min a solution of diketone 134 
(250 mg, 1.56 mmol) in dry THF (5 mL) was added drop-wise. Stirring 
was continued for 3.5 h, warmed at r.t., stirred for 2 h and quenched at 
0 °C with of 35 % HCl (33 mL). This acidic mixture was stirred at r.t. for 
18 h, extracted with Et₂O (3 x) and the combined organic layers were washed with sat. aq. 
NaHCO₃. After extraction with Et₂O (3 x), all organic layers were dried with MgSO₄ and 
adsorbed onto silica for further purification by flash chromatography (pentane) to give the 
title compound 153 as a white solid, 442 mg, 75 % yield.

MW = 380.48 g / mol; MP = 179-180 °C (Et₂O); Rₛ = 0.18 (pentane); IR (Neat, cm⁻¹): 
3043, 1736, 1592, 1573, 1506, 1377, 1239, 1044, 1016, 947; ¹H NMR (500 MHz, C₆D₆): δ 7.79 (d, 
J 8.5, 1H), 7.78-7.72 (m, 4H), 7.65 (d, J 8.2, 1H), 7.63-7.92 (m, 2H), 7.55 (dd, J 6.9 and 1.3, 
1H), 7.46 (dd, J 6.9 and 1.3, 1H), 7.43 (d, J 5.6, 2H), 7.39-7.34 (m, 2H), 7.28-7.22 (m, 2H), 
7.14-7.01 (m, 1H), 7.04-7.08 (m, 1H), 6.99-6.94 (m, 2H); ¹³C NMR (125 MHz, DMSO-d₆, 
100 °C): δ 137.3, 132.8, 131.9, 131.8, 127.6, 127.4, 127.2, 127.1, 126.6, 125.6, 125.5, 125.4, 
125.3, 125.2, 124.9; MS m/z (EI): 380 (100 [M]+), 363 (6), 252 (15), 188 (18), 182 (12);
**1,4-dibutynaphthalene (150).**

A solution of 1,4-tetralindione (134) (250 mg, 1.56 mmol) in dry THF (15 mL) was added under N\(_2\) over 1 h into a stirred, cooled (-78 °C) solution of BuLi (1.6 M in hexane, 3.9 mL, 6.24 mmol) in THF (5 mL) at -78 °C. This mixture was stirred 2 h more, stirred at r.t. for 1.5 h, quenched with 35 % HCl and stirred for 20 h. The reaction mixture was extracted with CH\(_2\)Cl\(_2\) (3 x) and the combined organic layers were washed sat. aq. NaHCO\(_3\). After extraction with CH\(_2\)Cl\(_2\) (3 x), the combined organic layers were dried with Na\(_2\)SO\(_4\) and the solvent evaporated under reduced pressure. Further purification of this residue by flash chromatography (pentane) yielded 1,4-dibutynaphthalene (150) as a colourless oil, 123 mg, 33 % yield. Spectral data agreed with literature values.

**MW** = 240.19 g / mol; **R\(_F\)** = 0.58 (pentane); **IR** (CH\(_2\)Cl\(_2\), cm\(^{-1}\)): 2959, 2933, 2872, 1594, 1467, 1393, 1104; \(^1\)H NMR (300 MHz, CD\(_2\)Cl\(_2\)): \(\delta\) 8.13-8.07 (m, 2H), 7.54-7.41 (m, 2H), 7.27 (s, 2H), 3.07 (t, \(J\ 7.7, 4\)H), 1.80-1.70 (m, 4H), 1.54-1.42 (m, 4H), 0.99 (t, \(J\ 7.3, 6\)H); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 137.2, 132.5, 125.8, 125.3, 124.8, 33.3, 33.1, 23.1, 14.2; **MS** \(m/z\) (EI): 240 (78 [M]+), 197 (100), 141 (68), 128 (10), 115 (10); **HRMS** (EI) calcd. for C\(_{18}\)H\(_{24}\) [M]+: 240.1878, found 240.1880.

**cis-1,4-dihydroxy-1,4-divinyltetralin (154), trans-1,4-dihydroxy-1,4-divinyltetralin (155).**

A Schlenk tube was charged with tetravinylstannane (283 µL, 1.56 mmol) and a solution of BuLi (1.6 M in hexane, 3.9 mL, 6.24 mmol) in hexane was added drop-wise at r.t. Stirring was continued for 1 h and the white suspension was then cooled to -78 °C. A solution of 1,4-tetralindione (134) (250 mg, 1.56 mmol) in dry THF (15 mL) was then added over 1 h. Stirring was continued for 1 h at -78 °C, 1 h at -20 °C and 2 h at r.t.. The reaction mixture was quenched at 0 °C with sat. aq. NH\(_4\)Cl and extracted with AcOEt (3 x). After drying the combined organic layers with MgSO\(_4\), the solvent was evaporated under reduced pressure. Purification of this crude by flash chromatography (AcOEt / Pentane 1 : 3) gave **trans 155** as a white gum, 205 mg, 61 % yield and **cis 154** as a white gum, 41 mg, 12 % yield.

**trans-1,4-dihydroxy-1,4-divinyltetralin (155): MW** = 216.28 g / mol; **R\(_F\)** = 0.46 (AcOEt / pentane, 1: 3); **IR** (neat, cm\(^{-1}\)): 3364, 2932, 1485, 1449, 1329, 1188, 995, 972, 923; \(^1\)H NMR
Experimental part related to Chapter IV.

(400 MHz, CDCl$_3$): $\delta$ 7.43-7.36 (m, 2H), 7.33-7.27 (m, 2H), 6.10 (dd, $J$ 16.9 and 10.7, 2H), 5.31 (d, $J$ 16.9, 2H), 5.26 (d, $J$ 10.5, 2H), 2.25 (d, $J$ 10.5, 2H), 1.83-1.98 (m, 4H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 144.2, 139.1, 128.1, 127.7, 113.4, 68.3, 33.4; MS m/z (EI): 216 (2[M$^+$]), 198 (27 [M+-H$_2$O$^+$]), 180 (17), 171 (100), 143 (90), 129 (60), 115 (39); HRMS (ESI) calcd. for C$_{14}$H$_{18}$O$_2$Na [M+Na$^+$]: 239.1047, found 239.1041.

cis-1,4-dihydroxy-1,4-divinyltetralin (154): MW = 216.28 g / mol; $R_F$ = 0.24 (AcOEt / pentane, 1: 3); IR (neat, cm$^{-1}$): 3377, 3062, 2928, 2857, 1721, 1642, 1485, 1448, 1408, 1158; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.41-7.34 (m, 2H), 7.29-7.22 (m, 2H), 5.97 (dd, $J$ 16.9 and 10.7, 2H), 5.16 (dd, $J$ 8.8 and 1.3, 2H), 5.12 (dd, $J$ 13.2 and 1.3, 2H), 2.10-1.90 (m, 6H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 144.4, 140.1, 128.6, 128.0, 114.3, 73.8, 34.2; MS m/z (EI): 198 (8 [M-H$_2$O$^+$]), 189 (23), 170 (100), 143 (81), 129 (44), 115 (31); HRMS (EI) calcd. for C$_{14}$H$_{14}$O [M-H$_2$O$^+$]: 198.1044, found 198.1044.

1,4-divinyl napthalene (157).

A crude mixture of trans-155 and cis-154 was obtained as described above, then dissolved in MeCN, extracted with pentane (4 x) and extracted with MeCN (3 x). The combined portions of MeCN were evaporated under reduced pressure and this crude was dissolved under N$_2$ in CH$_2$Cl$_2$ (13 mL) together with 4-terc-butyl catechol (25 mg, 0.16 mmol). Then a solution of Et$_3$N (865 µL, 6.24 mmol) in CH$_2$Cl$_2$ (13 mL) and a solution of MsCl (362 µL, 4.68 mmol) in CH$_2$Cl$_2$ (13 mL) were to cooled 0 °C and added sequentially to this cooled (0 °C) and stirred mixture. After stirring for 15 min, the reaction mixture was quenched with sat. aq. NaHCO$_3$ and extracted Et$_2$O (3 x). After drying the combined organic layers with MgSO$_4$, the solvent was evaporated under reduced pressure. Purification by flash chromatography (pentane) gave 1,4-divinyl tetralin (157) as a colourless oil, 102 mg, 36 % yield. Spectral data agreed with literature values.$^{[17]}$

MW = 180.25 g / mol; $R_F$ = 0.46 (pentane); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.19 (dd, $J$ 3.2 and 6.4, 2H), 7.66, (s, 2H), 7.57 (dd, $J$ 3.2 and 6.4, 2H), 7.53 (dd, $J$ 11.0 and 17.2, 2H), 5.84 (dd, $J$ 1.6 and 17.2, 2H), 5.52 (dd, $J$ 1.6 and 11.0, 2H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 135.5, 134.3, 131.1, 125.9, 124.2, 123.5, 117.0.
**trans**-[Cr(CO)$_3$(η$^6$-5,8-dihydroxy-5,8-divinyltetralin)] (160).

A 10 mL Carious tube was charged under N$_2$ with **trans**-1,4-dihydroxy-1,4-divinyltetralin (155) (35 mg, 0.16 mmol), [Cr(CO)$_3$(η$^6$-naphthalene)] (22 mg, 0.081 mmol), dry THF (22 µL, 0.16 mmol) and dry Et$_2$O (300 µL). The mixture was degassed by three freeze-pomp-thaw cycles and heated at 70 °C closed under N$_2$ for 6 h covered with aluminium foil. A complete change from red to yellow was observed. Evaporation of the solvent under high vacuum and purification of the crude by flash chromatography (Et$_2$O / pentane 1 : 2) gave **trans**-[Cr(CO)$_3$(η$^6$-5,8-dihydroxy-5,8-divinyltetralin)] (160) as a yellow solid, 16 mg, 57 % yield.

MW = 352.30 g / mol; $R_F$ = 0.15 (Et$_2$O / pentane, 1 : 2); MP = 121-119 °C (under N$_2$, CH$_2$Cl$_2$ / hexane); IR (neat, cm$^{-1}$): 3415, 3093, 2928, 2855, 1955, 1860, 1640, 1447, 1414, 1323, 1186; $^1$H NMR (300 MHz, C$_6$D$_6$): δ 6.16 (dd, $J$ 10.7 and 15.8, 1H), 5.62 (dd, $J$ 17.0 and 10.7, 1H), 5.22 (dd, $J$ 17.0 and 4.3, 2H), 5.09-4.87 (m, 4H), 4.46-4.32 (m, 2H), 2.13-1.99 (m, 1H), 1.90-1.78 (m, 1H), 1.73 (s, 1H), 1.71-1.60 (m, 1H), 1.45-1.34 (m, 1H), 1.01 (s, 1H); $^{13}$C NMR (75 MHz, C$_6$D$_6$): δ 233.6, 144.1, 143.3, 118.4, 114.8, 113.5, 112.9, 92.9, 92.6, 92.1, 91.8, 72.0, 71.5, 33.9, 33.6; MS m/z (EI): 352 (6 [M$^+$]), 250 (6), 232 (20), 167 (60), 153 (100), 115 (23), 52 (84); HRMS (ESI) calcd. for C$_{17}$H$_{16}$O$_5$CrNa [M+Na$^+$]: 375.0300, found 375.0307.

**cis**-[Cr(CO)$_3$(η$^6$-5,8-dihydroxy-5,8-divinyltetralin)] (159).

A 10 mL Carious tube was charged under N$_2$ with **cis**-1,4-dihydroxy-1,4-divinyltetralin (154) (50 mg, 0.23 mmol), [Cr(CO)$_3$(η$^6$-naphthalene)] (61 mg 0.23 mmol), dry THF (94 µL, 0.693 mmol) and dry Et$_2$O (300 µL). The mixture was degassed by three freeze-pomp-thaw cycles and heated at 70 °C closed under N$_2$ for 20 h. A complete change from red to yellow was observed. Evaporation of the solvent under high vacuum and purification of the crude by flash chromatography (Et$_2$O / pentane 1 : 3) gave **cis**-[Cr(CO)$_3$(η$^6$-5,8-dihydroxy-5,8-divinyltetralin)] (159) as a yellow gum, 32 mg, 40 % yield; MW = 352.30 g / mol; IR (neat, cm$^{-1}$): 3429, 3089, 2952, 2932, 1960, 1889, 1871, 1454, 1419, 1376, 1327, 1250, 1163, 1101; $^1$H NMR (300 MHz, C$_6$D$_6$): δ 5.54 (d, $J$ 10.5, 1H), 5.47 (d, $J$ 10.5, 1H), 5.06-4.99 (m, 4H), 4.87 (d, $J$ 10.5, 2H), 4.39-4.36 (m, 2H), 1.84-1.74 (m, 4H), 1.54-1.44 (m, 2H); $^{13}$C NMR (75 MHz, C$_6$D$_6$): δ 233.6, 151.6, 119.6, 115.0, 92.4, 91.4, 71.7, 34.5; MS m/z
cis-1,4-dihydroxy-1,4-diallyltetralin (156) and trans-1,4-dihydroxy-1,4-diallyltetralin (148).

A Schlenk tube was charged with tetrallylstannane (283 µL, 1.56 mmol) and a solution of BuLi (1.6 M in hexane, 3.9 mL, 6.24 mmol) in hexane was added drop-wise at r.t. Stirring was continued for 1 h and the white suspension was cooled at -78° C. A solution of 1,4-tetralindione (134) (250 mg, 1.56 mmol) in dry THF (15 mL) was then added during 40 min. Stirring was continued for 2 h at -78° C and 2 h at r.t. The reaction mixture was quenched at 0° C with sat. aq. NH₄Cl and extracted with AcOEt (3 x). After drying all combined organic layers with MgSO₄, the solvent was evaporated under reduced pressure. This crude was dissolved in MeCN, extracted with pentane (4 x) and extracted with MeCN (3 x). All combined portions of MeCN were evaporated under reduced pressure. Purification of this crude by flash chromatography (AcOEt / Pentane 1 : 5) gave cis 156 as a white gum, 47 mg, 11% yield and trans 148 as a white gum, 171 mg, 40% yield.

cis-1,4-dihydroxy-1,4-diallyltetralin (156): Spectroscopic data in page 173.

trans-1,4-dihydroxy-1,4-diallyltetralin (148): A crude mixture of trans-148 and cis-156 was obtained as described above, dissolved in CH₂Cl₂ (6 mL) and a solution of Et₃N (865 µL, 6.24 mmol) in CH₂Cl₂ (8 mL) and MsCl (362 µL, 4.68 mmol) in CH₂Cl₂ (8 mL) were added sequentially at r.t. Stirring was continued for 8 h, then Et₃N (865 µL, 6.24 mmol) and MsCl (362 µL, 4.68 mmol) were added
sequentially and the mixture was stirred for 2 h more. The reaction mixture was quenched with sat. aq. NaHCO$_3$ and extracted with Et$_2$O (3 x). All combined organic layers were dried with MgSO$_4$ and the volatiles were evaporated under reduced pressure. Purification of this crude by flash chromatography (pentane) gave 1,4-diallylnaphthalene (158) as a colourless oil, 115 mg, 36 % yield.

MW = 208.30 g / mol; $R_F$ = 0.41 (pentane); IR (neat, cm$^{-1}$): 3076, 3004, 2915, 1828, 1637, 1595, 1515, 1442, 1390, 989, 908; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 8.09-8.01 (m, 2H), 7.54-7.45 (m, 2H), 7.28 (s, 2H), 6.16-6.06 (m, 2H), 5.13-5.05 (m, 4H), 3.86-3.80 (m, 4H).

$^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ 137.4, 135.1, 132.6, 126.4, 125.7, 125.0, 116.4, 37.6; HRMS (EI) calcd. for C$_{16}$H$_{16}$ [M$^+$]: 208.1252, found 208.1259.

1,4,5-trihydroxynaphthalene (161).

Juglone (5-hydroxy-1,4-naphthoquinone, 100 mg, 0.57 mmol) was placed in an Schlenk tube with Na$_2$S$_2$O$_4$ (120 mg, 0.69 mmol), Et$_2$O (5 mL) and H$_2$O (5 mL). The reaction mixture was stirred at r.t. during 2 h and Na$_2$S$_2$O$_4$ (120 mg, 0.69 mmol) was added. Stirring was continued for 1 h. Then the mixture was extracted with Et$_2$O (3 x). The combined organic layers were dried with MgSO$_4$ and volatiles were removed under reduced pressure. This crude was purified by flash chromatography (Et$_2$O / pentane 1 : 1) to give naphthotriol 161 as a white solid, 58 mg, 57 % yield. Spectral data agreed with literature values.[18, 19]

MW = 176.17 g / mol; $R_F$ = 0.26 (Et$_2$O / pentane, 1: 1); $^1$H NMR (300 MHz, DMSO-$d_6$): $\delta$ 10.71 (s, 1H), 10.34 (s, 1H), 9.35 (s, 1H), 7.51 (d, J 8.6, 1H), 7.22 (t, J 8.2, 1H), 6.73-6.65 (m, 2H), 6.55 (d, J 8.2, 1H); $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ 154.1, 145.9, 145.7, 127.2, 125.7, 115.2, 113.3, 108.9, 108.5, 108.1.

5-hydroxy-1,4-teralindione (162).

1,4,5-Trihydroxynaphthalene (161) (57 mg, 0.32 mmol) was placed in a round-bottomed flask together with CF$_3$COOH (0.77 mL). The resulting suspension was completely dissolved after stirring for 30 min at r.t. The solvent was removed at 35 °C under reduced pressure until dryness. This crude was purified by flash chromatography (Et$_2$O / pentane 1 : 2) to give diketone 162 as a white solid, 40 mg, 70 % yield. Spectral data agreed with literature values.[18, 19]
V.4 - Experimental part related to Chapter IV.

MW = 176.17 g / mol; RF = 0.38 (Et₂O / pentane, 1 : 2); MP = 96-97 °C (hexane); IR (neat, cm⁻¹): 2962, 1690, 1694, 1604, 1576, 1451, 1348, 1317, 1296, 1223, 1205, 1163, 1122; ¹H NMR (300 MHz, CDCl₃): δ 12.11 (s, 1H), 7.61-7.68 (m, 1H), 7.54 (d, J 7.2, 1H), 7.30-7.22 (m, 1H), 3.16-3.01 (m, 4H); ¹³C NMR (75 MHz, CDCl₃): δ 202.9, 195.5, 161.8, 137.2, 135.5, 124.0, 118.2, 118.0, 37.3, 37.0; MS m/z (El): 176 (100 [M⁺]), 148 (16), 120 (78), 92 (41), 63 (23), 39 (12); HRMS (El) calcd. for C₁₀H₈O₃ [M⁺]: 176.0473, found 176.0475.

1,4-dihydroxy-2-methylnaphthalene (163).

2-methyl-1,4-naphthoquinone (1.00 g, 5.81 mmol) was placed in an Schlenk tube with Na₂S₂O₄ (2.02 g, 11.63 mmol), Et₂O (17 mL) and H₂O (17 mL). The reaction mixture was stirred at r.t. during 2 h and extracted AcOEt (3 x). The combined organic layers were dried with MgSO₄ and all volatiles removed under reduced pressure to give pure 1,4-dihydroxy-2-methylnaphthalene (163) as a white solid, 1.01 g, 99 % yield. Spectral data agreed with literature values.[19, 20]

MW = 174.20 g / mol; MP = 174-175 °C (toluene);[21] RF = 0.62 (AcOEt / pentane, 1: 1); IR (neat, cm⁻¹): 3253, 2921, 1602, 1390, 1360, 1311, 1269, 1202, 1172, 1153, 1068; ¹H NMR (300 MHz, DMSO-d⁶): δ 9.33 (s, 1H), 8.23 (s, 1H), 8.05 (d, J 7.9, 1H), 7.99 (d, J 8.3, 1H), 7.40 (td, J 6.8 and 1.1, 1H), 7.33 (td, J 6.8 and 1.1, 1H), 6.61 (s, 1H), 2.26 (s, 3H); ¹³C NMR (75 MHz, DMSO-d⁶): δ 145.8, 141.7, 126.5, 124.9, 123.8, 123.5, 121.8, 121.7, 118.7, 111.1, 16.6; MS m/z (El): 174 (100 [M⁺]), 145 (8), 131 (25), 105 (18), 77 (10), 39 (8); HRMS (ESI) calcd. for C₁₁H₁₁O₂ [M+H⁺]: 175.0753, found 175.0752.

2-methyl-1,4-teralinedione (164).

1,4-dihydroxy-2-methylnaphthalene (163) (1.01 g, 6.06 mmol) was placed in a round-bottomed flask together with CF₃COOH (29 mL). The resulting suspension was completely dissolved after stirring for 30 min at r.t. All volatiles were removed under reduced pressure and the residue recrystallised in 34 mL of boiling iPr₂O / pentane (1 : 1) to give methyldiketone 164 as a white solid, 575 mg, 56 % yield. Spectral data agreed with literature values.[19, 22]
V.4 - Experimental part related to Chapter IV.

1.35 (d, J 6.6, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): $\delta$ 199.1, 196.2, 135.9, 135.4, 134.6, 134.2, 127.1, 126.7, 45.8, 42.7, 16.7; MS m/z (EI): 174 [M$^+$], 159 (100), 146 (20), 131 (17), 104 (90), 76 (53), 50 (22); HRMS (EI) calcd. for C$_{11}$H$_{10}$O$_2$ [M$^+$]: 174.0680, found 174.0681.

[2,2’]-binaphthalenyl-1,3,4’-triol (168).

1,3-dihydroxynaphthalene (167) (500 mg, 3.12 mmol) was heated at 250 °C under N$_2$ in a Kugelrohr apparatus during 1 h. The melt was cooled with an external bath of water and purified by flash chromatography (AcOEt / pentane 1 : 4); the title compound 168 was obtained as white gum, 430 mg, 92 % yield.

MW = 302.33 g / mol; $R_F$ = 0.54 (AcOEt / pentane, 1: 2); IR (Neat, cm$^{-1}$): 3506, 3053, 2975, 2875, 1633, 1595, 1573, 1505, 1449, 1392, 1354, 1285, 1258, 1237, 1179, 1145, 1118, 1085, 1067; $^1$H NMR (500 MHz, DMSO-$d_6$): $\delta$ 10.02 (s, 1H), 9.53 (s, 1H), 8.75 (s, 1H), 8.19-8.12 (m, 1H), 8.07 (d, J 8.6, 1H), 7.86-7.80 (m, 1H), 7.62 (d, J 7.9, 1H), 7.50-7.40 (m, 2H), 7.37 (td, J 8.3 and 1.1, 1H), 7.32 (s, 1H), 7.23 (td, J 8.3 and 1.1, 1H), 6.88 (d, J 9.1, 1H), 6.83 (s, 1H); $^{13}$C NMR (125 MHz, DMSO-$d_6$): $\delta$ 155.0, 153.3, 151.3, 135.3, 135.0, 133.6, 128.5, 127.3, 126.8, 126.5, 125.3, 124.7, 123.4, 122.8, 122.6, 121.7, 121.2, 117.2, 112.9, 101.9; MS m/z (EI): 302 (100 [M$^+$]), 255 (12), 226 (10), 215 (12); HRMS (ESI) calcd. for C$_{14}$H$_{14}$O$_3$Na [M+Na$^+$]: 325.0840 found 325.0850.

V.4.1 References.


V.4 - Experimental part related to Chapter IV.


V.4 - Experimental part related to Chapter IV.
Appendix 1: List of synthesised compounds

186
Appendix 1: List of synthesised compounds

100

MW = 508.53
C$_{27}$H$_{20}$O$_7$Cr
Page 80

97

MW = 402.33
C$_{20}$H$_{14}$O$_6$Cr
Page 79

98

MW = 506.42
C$_{27}$H$_{18}$O$_7$Cr
Page 79

(+)-76

MW = 220.26
C$_{13}$H$_{16}$O$_3$
Page 88

105

MW = 324.37
C$_{20}$H$_{20}$O$_4$
Page 88

106

MW = 250.29
C$_{14}$H$_{18}$O$_4$
Page 90

107

MW = 384.42
C$_{22}$H$_{18}$O$_6$
Page 90

(+)-108

MW = 238.25
C$_{13}$H$_{16}$O$_3$F
Page 90

109

MW = 360.35
C$_{20}$H$_{18}$O$_4$F$_2$
Page 90

(+)-110

Unknown absolute configuration

111

MW = 352.42
C$_{22}$H$_{24}$O$_4$
Page 90

(+)-112

Unknown absolute configuration
Appendix 1: List of synthesised compounds

113
MW = 352.42
C_{22}H_{24}O_4
Page 90

(+)-114
MW = 263.34
C_{15}H_{20}O_3N
Page 90

115
MW = 410.52
C_{24}H_{30}O_4N_2
Page 90

(+)-116
MW = 210.23
C_{11}H_{14}O_4
Page 90

117
MW = 304.30
C_{16}H_{18}O_6
Page 90

(+)-118
MW = 194.24
C_{11}H_{14}O_3
Page 96

119
MW = 298.34
C_{19}H_{18}O_4
Page 96

(+)-120
MW = 206.24
C_{11}H_{12}O_3
Page 96

121
MW = 310.35
C_{19}H_{16}O_4
Page 96

Unknown absolute configuration

(+)-122

123
MW = 208.22
C_{11}H_{12}O_4
Page 96

124
MW = 218.25
C_{13}H_{14}O_5
Page 96
Appendix 1: List of synthesised compounds

125
MW = 322.36
C_{20}H_{18}O_{4}
Page 96

(+)-126
MW = 248.32
C_{15}H_{20}O_{3}
Page 96

127
MW = 352.43
C_{22}H_{24}O_{4}
Page 96

(+)-128
MW = 406.48
C_{23}H_{26}O_{5}
Page 96

129
MW = 510.59
C_{30}H_{30}O_{6}
Page 96

(+)-130
MW = 268.32
C_{17}H_{16}O_{3}
Page 96

131
MW = 372.42
C_{23}H_{20}O_{4}
Page 96

(-)-82
MW = 318.38
C_{21}H_{18}O_{3}
Page 96

132
MW = 422.49
C_{23}H_{22}O_{4}
Page 96

134
MW = 160.17
C_{10}H_{10}O_{2}
Page 103

139
MW = 259.39
C_{14}H_{17}O_{3}NSi
Page 112

140
MW = 187.20
C_{11}H_{16}O_{2}N
Page 112

137
MW = 158.20
C_{11}H_{10}O
Page 113

138
MW = 156.22
C_{12}H_{22}
Page 111

(-)-142
MW = 164.20
C_{10}H_{10}O_{2}
Page 115

141
MW = 164.20
C_{10}H_{12}O_{2}
Page 114
Appendix 1: List of synthesised compounds

(-)-144
MW = 322.36
C_{10}H_{10}O_2
Page 117

(+)-146
MW = 276.45
C_{16}H_{24}O_2Si
Page 119

145
MW = 291.18
C_{16}H_{12}OCl_2
Page 119

(-)-148
MW = 244.34
C_{16}H_{20}O_2
Page 120

149
MW = 380.36
C_{15}H_{24}O_2Cr
Page 120

151
MW = 156.22
C_{12}H_{12}
Page 122

152
MW = 280.37
C_{22}H_{16}
Page 122

153
MW = 380.48
C_{30}H_{20}
Page 122

154
MW = 240.19
C_{18}H_{24}
Page 122
cis - 154

155
MW = 216.28
C_{14}H_{16}O_2
Page 123
trans - 155

156
MW = 352.30
C_{17}H_{16}O_2Cr
Page 123
cis - 156

157
MW = 180.25
C_{14}H_{12}
Page 123

158
MW = 208.30
C_{16}H_{16}
Page 123
Appendix 1: List of synthesised compounds

162
MW = 176.17
C_{10}H_{8}O_{3}
Page 125

164
MW = 176.17
C_{10}H_{8}O_{3}
Page 125

163
MW = 174.20
C_{11}H_{10}O_{2}
Page 125

164
MW = 174.20
C_{11}H_{10}O_{2}
Page 125

168
MW = 302.33
C_{14}H_{14}O_{3}
Page 125
VI.1 Crystallographic structure of [Cr(CO)$_3$(η$_6$-5,8-naphthoquinone)] (53).

Formule brute: (C$_{10}$H$_6$O$_2$)Cr(CO)$_3$

Poids moléculaire: 294.2

Coefficient d’absorption linéaire: $\mu = 1.01$ mm$^{-1}$ (Mo (K$\alpha$))

Solvant de recristallisation: Et$_2$O

Densité: Do = ?, Dx = 1.708 (gr.cm$^{-3}$)

Diffractomètre: STOE IPDS

Géométrie de la maille

Système cristallin: Triclinique

Groupe d’espace: $P \overline{1}$

a = 7.1180 (8) (Å)  $\alpha = 87.055$ (15)$^\circ$

b = 7.6777 (9)(Å)  $\beta = 73.479$ (14)$^\circ$

c = 10.9461 (14)(Å)  $\gamma = 86.175$ (14)$^\circ$

V = 571.9 (1)(Å$^3$)  Z = 2

Nombre de réflexions pour l’affinement des paramètres: 5241 (6.1$^\circ$ < 2$\theta$ < 56.2$^\circ$)

Forme et dimensions du cristal

Forme: prisme; Couleur: violet/noir

Dimensions: 0.06 x 0.14 x 0.24 mm

Mode de fixation: tige de quartz

Conditions expérimentales pour la collection des intensités

Température: 200 K

Longueur d’onde: 0.7107(Å)

Mode de balayage: $\varphi$-scan

$\Delta \varphi$ / image: 1.8 ($^\circ$)

T Irradiation / image: 2 (min)

$\varphi$ min, max = 0 - 270 ($^\circ$)

Distance cristal / IP: 60 (mm)

Nombre d’images: 150

EMS: 0.006

Moyenne (I/$\sigma$(I)): 14.0

Limites angulaires: 6.1$^\circ$ < 2$\theta$ < 56.2$^\circ$

Limites d’indices: -9 < h < 9; -9 < k < 9; -14 < l < 14

Nombre de réflexions mesurées: 7602
Réduction des données

Corrections : LP  Disp. anomale  Absorption  T min. , max. =  0.8447  ,  0.9436

Nombre de réflexions observables 1788  |Fo|> 4σ(Fo)
Nombre de réflexions non-observables 799
Nombre de réflexions uniques 2587  R int pour 5015 réfl. équivalentes = 0.041

Résolution et affinement de la structure

Résolution: Méthodes directes (SIR97)
Fonction minimisée :  \( \Sigma (\omega (Fo-Fc)^2) \)
Fonction de poids :  \( \omega = 1/([\sigma^2(Fo) + 0.00015 (Fo^2)]) \)
Nombre d'atomes affinés "iso" : 19
Nombre d'atomes affinés "aniso" : 6 (H)
Coordonnées des atomes d'hydrogène: observées et affinées
Programme XTAL 3.2

Valeurs obtenues en fin d'affinement

Nombre de variables: 190
Nombre de réflexions : 1809
Nbe reflexions / Nbe de variables 9.5
Affinement par moindres carrés: Full matrix
"shift/error": moyen : 0.10 \(10^{-4}\) , Maximum : 0.15 \(10^{-3}\)
Résidus (delta F) (eÅ\(^{-3}\)): -1.64 , 0.57
"Goodness of fit": S = 1.55(2)

Facteur résiduel final  \( R = 0.043 \)
Facteur résiduel pondéré  \( \omega R = 0.041 \)

Remarques:

Les hydrogènes ont été observés et affinés (sans restrictions) avec des Uiso fixes (0.05 Å\(^2\)).
### Appendix 2: Crystallographic data

**Bond Distances** (Angstroms)

<table>
<thead>
<tr>
<th>Bond</th>
<th>Distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr-C1</td>
<td>2.188(3)</td>
</tr>
<tr>
<td>Cr-C3</td>
<td>2.224(4)</td>
</tr>
<tr>
<td>Cr-C5</td>
<td>2.208(3)</td>
</tr>
<tr>
<td>Cr-C11</td>
<td>1.860(3)</td>
</tr>
<tr>
<td>Cr-C13</td>
<td>1.851(4)</td>
</tr>
<tr>
<td>C1-C7</td>
<td>1.223(5)</td>
</tr>
<tr>
<td>O1-C7</td>
<td>1.223(5)</td>
</tr>
<tr>
<td>O3-C11</td>
<td>1.154(5)</td>
</tr>
<tr>
<td>C1-C6</td>
<td>1.416(5)</td>
</tr>
<tr>
<td>C2-C3</td>
<td>1.394(4)</td>
</tr>
<tr>
<td>C3-C4</td>
<td>1.420(6)</td>
</tr>
<tr>
<td>C4-C5</td>
<td>1.389(5)</td>
</tr>
<tr>
<td>C5-C6</td>
<td>1.423(4)</td>
</tr>
<tr>
<td>C6-C7</td>
<td>1.483(5)</td>
</tr>
<tr>
<td>C8-C9</td>
<td>1.330(5)</td>
</tr>
<tr>
<td>C9-C10</td>
<td>1.473(5)</td>
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### Bond Angles (degrees)

<table>
<thead>
<tr>
<th>Bond</th>
<th>Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>C11-Cr-C12</td>
<td>88.8(1)</td>
</tr>
<tr>
<td>C12-Cr-C13</td>
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<td>C2-C1-C10</td>
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<tr>
<td>C1-C2-C3</td>
<td>119.7(3)</td>
</tr>
<tr>
<td>C3-C2-H2</td>
<td>125(2)</td>
</tr>
<tr>
<td>C2-C3-H3</td>
<td>115(2)</td>
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<tr>
<td>C3-C4-C5</td>
<td>120.2(3)</td>
</tr>
<tr>
<td>C5-C4-H4</td>
<td>122(3)</td>
</tr>
<tr>
<td>C4-C5-H5</td>
<td>124(3)</td>
</tr>
<tr>
<td>C1-C6-C5</td>
<td>119.7(3)</td>
</tr>
<tr>
<td>C5-C6-C7</td>
<td>119.9(3)</td>
</tr>
<tr>
<td>O1-C7-C8</td>
<td>121.8(3)</td>
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<tr>
<td>C7-C8-C9</td>
<td>122.4(3)</td>
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<td>C9-C8-H8</td>
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<td>C8-C9-H9</td>
<td>122(3)</td>
</tr>
<tr>
<td>O2-C10-C1</td>
<td>121.4(3)</td>
</tr>
<tr>
<td>C1-C10-C9</td>
<td>117.2(3)</td>
</tr>
<tr>
<td>Cr-C12-O4</td>
<td>179.2(3)</td>
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</tbody>
</table>

---

<table>
<thead>
<tr>
<th>Bond</th>
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</thead>
<tbody>
<tr>
<td>Cr-C4</td>
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<tr>
<td>Cr-C6</td>
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<tr>
<td>Cr-C10</td>
<td>1.491(4)</td>
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<td>C1-C2</td>
<td>1.422(5)</td>
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<tr>
<td>C6-C10</td>
<td>1.491(4)</td>
</tr>
<tr>
<td>C1-C2-H2</td>
<td>115(2)</td>
</tr>
<tr>
<td>C2-C3-C4</td>
<td>120.5(3)</td>
</tr>
<tr>
<td>C3-C4-H4</td>
<td>118(3)</td>
</tr>
<tr>
<td>C4-C5-C6</td>
<td>120.1(3)</td>
</tr>
<tr>
<td>C6-C5-H5</td>
<td>116(3)</td>
</tr>
<tr>
<td>C1-C6-C7</td>
<td>120.3(3)</td>
</tr>
<tr>
<td>O1-C7-C6</td>
<td>120.6(3)</td>
</tr>
<tr>
<td>C6-C7-C8</td>
<td>117.5(3)</td>
</tr>
<tr>
<td>C7-C8-H8</td>
<td>114(2)</td>
</tr>
<tr>
<td>C8-C9-C10</td>
<td>122.6(3)</td>
</tr>
<tr>
<td>C10-C9-H9</td>
<td>115(3)</td>
</tr>
<tr>
<td>O2-C10-C9</td>
<td>121.4(3)</td>
</tr>
<tr>
<td>Cr-C11-O3</td>
<td>179.1(3)</td>
</tr>
<tr>
<td>Cr-C13-O5</td>
<td>178.3(3)</td>
</tr>
</tbody>
</table>
### Dihedral Angles (degrees)

<table>
<thead>
<tr>
<th>Dihedral Angle</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>C6-C1-C2-C3</td>
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</tr>
<tr>
<td>C2-C1-C6-C5</td>
<td>-.7(4)</td>
</tr>
<tr>
<td>C10-C1-C6-C5</td>
<td>178.7(3)</td>
</tr>
<tr>
<td>C2-C1-C10-02</td>
<td>2.9(5)</td>
</tr>
<tr>
<td>C6-C1-C10-02</td>
<td>179.1(3)</td>
</tr>
<tr>
<td>C1-C2-C3-C4</td>
<td>1.0(5)</td>
</tr>
<tr>
<td>C3-C4-C5-C6</td>
<td>-.8(5)</td>
</tr>
<tr>
<td>C4-C5-C6-C7</td>
<td>175.1(3)</td>
</tr>
<tr>
<td>C1-C6-C7-C8</td>
<td>4.1(4)</td>
</tr>
<tr>
<td>C5-C6-C7-C8</td>
<td>178.8(3)</td>
</tr>
<tr>
<td>C6-C7-C8-C9</td>
<td>3.8(5)</td>
</tr>
<tr>
<td>C8-C9-C10-02</td>
<td>179.5(3)</td>
</tr>
<tr>
<td>C10-C1-C2-C3</td>
<td>177.2(3)</td>
</tr>
<tr>
<td>C2-C1-C6-C7</td>
<td>176.4(3)</td>
</tr>
<tr>
<td>C10-C1-C6-C7</td>
<td>1.6(4)</td>
</tr>
<tr>
<td>C2-C1-C10-C9</td>
<td>179.2(3)</td>
</tr>
<tr>
<td>C6-C1-C10-C9</td>
<td>1.2(4)</td>
</tr>
<tr>
<td>C2-C3-C4-C5</td>
<td>.3(5)</td>
</tr>
<tr>
<td>C4-C5-C6-C1</td>
<td>2.0(5)</td>
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<tr>
<td>C1-C6-C7-O1</td>
<td>2.5(5)</td>
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<tr>
<td>C5-C6-C7-O1</td>
<td>1.3(5)</td>
</tr>
<tr>
<td>C7-C8-C9-C10</td>
<td>.9(5)</td>
</tr>
</tbody>
</table>

### VI.2 Crystallographic structure of [Cr(CO)₃(η⁶-5,8-dihydroxynaphthalene)] (53).

**Formule brute:** 
\[ [(\text{C}_{10}\text{H}_8\text{O}_2) \text{Cr (CO)}_3] (\text{C}_6\text{H}_6)_{0.5} \]

**Poids moléculaire:** 335.3

**Coefficient d’absorption linéaire** \( \mu = 0.83 \text{ mm}^{-1} (\text{Mo (Kα)}) \)

**Solvant de recristallisation** \( \text{C}_6\text{H}_6 \)

**Densité** \( \text{Do} = ? \)

**Dx = 1.579 (gr.cm}^{-3}\)

**Diffactomètre** STOE IPDS

#### Géométrie de la maille

- **Système cristallin:** Monoclinique
- **a = 14.2611 (9) (Å)**
- **b = 7.2120 (4)(Å)**
- **c = 14.5831 (9)(Å)**
- **V = 1410.5 (2)(Å³)**
- **Z = 4**
- **α = 90°**
- **β = 109.885 (7)°**
- **γ = 90°**
- **Groupe d'espace:** \(P 2_1/c\)
- **Nombre de réflexions pour l'affinement des paramètres:** 8000 \( (9.1° < 2θ < 56.1°) \)

#### Forme et dimensions du cristal

- **Forme:** prisme
- **Couleur:** jaune
- **Dimensions:** 0.054 x 0.21 x 0.29 mm
- **Mode de fixation:** RS3000

#### Conditions expérimentales pour la collection des intensités

<table>
<thead>
<tr>
<th>Paramètre</th>
<th>Valeur</th>
</tr>
</thead>
<tbody>
<tr>
<td>Température</td>
<td>200 K</td>
</tr>
<tr>
<td>Longueur d’onde</td>
<td>0.7107(Å)</td>
</tr>
<tr>
<td>Mode de balayage</td>
<td>φ-scan</td>
</tr>
<tr>
<td>Δφ / image</td>
<td>1.5 (°)</td>
</tr>
<tr>
<td>T Irradiation / image</td>
<td>3 (min)</td>
</tr>
<tr>
<td>φ min, max</td>
<td>0 - 270 (°)</td>
</tr>
<tr>
<td>Distance cristal / IP</td>
<td>60 (mm)</td>
</tr>
<tr>
<td>Nombre d’images</td>
<td>180</td>
</tr>
<tr>
<td>EMS</td>
<td>0.009</td>
</tr>
<tr>
<td>Moyenne (I/σ(I))</td>
<td>12.5</td>
</tr>
<tr>
<td>Limites angulaires</td>
<td>6.0° &lt; 2θ &lt; 56.1°</td>
</tr>
</tbody>
</table>
Appendix 2: Crystallographic data

Limites d'indices

\[-18 < h < 18 ; \quad -9 < k < 9 ; \quad -18 < \iota < 18\]

Nombre de réflexions mesurées: 18'682

Réduction des données

Corrections:
- LP
- Disp. anomalie
- Absorption

\[T \text{ min. , max. } = 0.8274 , 0.9556\]

Nombre de réflexions observables: 2170
Nombre de réflexions non-observables: 1158
Nombre de réflexions uniques: 3328

Statistique des réflexions

Facteur de température global: 2.4 (Å²)
Distribution des \(<E^2>\) : centrique \(<E^2-1> = 0.957\)

Résolution et affinement de la structure

Méthodes directes (SIR97)
Fonction minimisée:
\[\Sigma (\omega (Fo-Fc)^2)\]
Fonction de poids:
\[\omega = 1/\left[\sigma^2(Fo) + 0.00015 (Fo^2)\right]\]
Nombre d'atomes affinés "iso": 11 (H)
Nombre d'atomes affinés "aniso": 22
Coordonnées des atomes d'hydrogène:

Programme: XTAL 3.2

Valeurs obtenues en fin d'affinement

Nombre de variables: 232
Nombre de réflexions: 2245
Nbe reflexions / Nbe de variables: 9.7
Affinement par moindres carrés: Full matrix
"shift/error": moyen : 0.57 \times 10^{-4} , Maximum : 0.70 \times 10^{-3}
Résidus (delta F) (eÅ⁻³): -1.14 , 0.38
"Goodness of fit": \[S = 1.45(2)\]

Facteur résiduel final: \[R = 0.032\]
Facteur résiduel pondéré: \[\omega R = 0.032\]

Remarques:

Les atomes d'hydrogène ont été observés et affinés avec des Uiso fixes.
La molécule de benzène est localisée autour d’un centre d’inversion en $\frac{1}{2}, \frac{1}{2}, \frac{1}{2}$. On a donc $\frac{1}{2}$ molécule de $C_6H_6$ par molécule de complexe.

**Bond Distances (Angstroms)**

<table>
<thead>
<tr>
<th>Bond</th>
<th>Distance (Å)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr-C1</td>
<td>2.290(2)</td>
</tr>
<tr>
<td>Cr-C3</td>
<td>2.239(2)</td>
</tr>
<tr>
<td>Cr-C5</td>
<td>2.242(2)</td>
</tr>
<tr>
<td>Cr-C11</td>
<td>1.854(3)</td>
</tr>
<tr>
<td>Cr-C13</td>
<td>1.825(2)</td>
</tr>
<tr>
<td>O1-H01</td>
<td>0.73(3)</td>
</tr>
<tr>
<td>O2-H02</td>
<td>0.70(3)</td>
</tr>
<tr>
<td>O4-C12</td>
<td>1.154(3)</td>
</tr>
<tr>
<td>C1-C2</td>
<td>1.436(3)</td>
</tr>
<tr>
<td>C1-C10</td>
<td>1.432(4)</td>
</tr>
<tr>
<td>C2-H2</td>
<td>1.02(3)</td>
</tr>
<tr>
<td>C3-H3</td>
<td>0.94(2)</td>
</tr>
<tr>
<td>C4-H4</td>
<td>0.93(3)</td>
</tr>
<tr>
<td>C5-H5</td>
<td>0.95(3)</td>
</tr>
<tr>
<td>C7-C8</td>
<td>1.359(3)</td>
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<tr>
<td>C8-H8</td>
<td>0.95(2)</td>
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<tr>
<td>C9-H9</td>
<td>0.86(3)</td>
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<td>C1a-H1a</td>
<td>0.92(3)</td>
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<tr>
<td>C2a-C3a</td>
<td>1.363(6)</td>
</tr>
<tr>
<td>C3a-H3a</td>
<td>0.98(3)</td>
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</tbody>
</table>

**Note:** la molécule de benzène est localisée autour d’un centre d’inversion en $\frac{1}{2}, \frac{1}{2}, \frac{1}{2}$. Position équivalente pour les atomes (') = 1-x , 1-y , 1-z
Appendix 2: Crystallographic data

### Bond Angles (degrees)

<table>
<thead>
<tr>
<th>Bond 1</th>
<th>Bond 2</th>
<th>Bond 3</th>
<th>Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>C11-Cr-C12</td>
<td>85.9(1)</td>
<td>C11-Cr-C13</td>
<td>90.8(1)</td>
</tr>
<tr>
<td>C12-Cr-C13</td>
<td>88.7(1)</td>
<td>C7-O1-H01</td>
<td>107.3(3)</td>
</tr>
<tr>
<td>C10-O2-H02</td>
<td>108.2(2)</td>
<td>C2-C1-C6</td>
<td>119.0(2)</td>
</tr>
<tr>
<td>C2-C1-C10</td>
<td>121.4(2)</td>
<td>C6-C1-C10</td>
<td>119.6(2)</td>
</tr>
<tr>
<td>C1-C2-C3</td>
<td>120.9(2)</td>
<td>C1-C2-H2</td>
<td>119.2(2)</td>
</tr>
<tr>
<td>C3-C2-C4</td>
<td>120.2(2)</td>
<td>C2-C3-C4</td>
<td>120.1(2)</td>
</tr>
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<td>C2-C3-H3</td>
<td>120.2(2)</td>
<td>C4-C3-H3</td>
<td>120.2(2)</td>
</tr>
<tr>
<td>C3-C4-C5</td>
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<td>C3-C4-H4</td>
<td>122.2(2)</td>
</tr>
<tr>
<td>C5-C4-H4</td>
<td>118.2(2)</td>
<td>C4-C5-C6</td>
<td>120.7(2)</td>
</tr>
<tr>
<td>C4-C5-H5</td>
<td>119.2(2)</td>
<td>C6-C5-H5</td>
<td>120.2(2)</td>
</tr>
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<td>C1-C6-C5</td>
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<td>C1-C6-C7</td>
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<td>C6-C1-C2-C3</td>
<td>-1.6(3)</td>
<td>C6-C1-C2-C4</td>
<td>3.3(3)</td>
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<td>C1-C6-C5-C6</td>
<td>-2.4(3)</td>
<td>C5-C6-C7-C8</td>
<td>-175.7(2)</td>
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<tr>
<td>C1-C6-C7-C8</td>
<td>-2.9(3)</td>
<td>C5-C6-C7-C8</td>
<td>177.6(2)</td>
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<tr>
<td>C6-C1-C2-C3</td>
<td>3.3(3)</td>
<td>C2-C1-C2-C3</td>
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<td>C1-C6-C5-C6</td>
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<td>C4-C5-C6-C7</td>
<td>175.7(2)</td>
</tr>
<tr>
<td>C1-C6-C7-C8</td>
<td>-2.9(3)</td>
<td>C5-C6-C7-C8</td>
<td>-175.7(2)</td>
</tr>
<tr>
<td>C6-C7-C8-C9</td>
<td>5.2(4)</td>
<td>C7-C8-C9-C10</td>
<td>177.3(2)</td>
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<td>C8-C9-C10-C1</td>
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<td>C8-C9-C10-C1</td>
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<td>C1a-C2a-C3a-C1a'</td>
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</tbody>
</table>

### Dihedral Angles (degrees)

<table>
<thead>
<tr>
<th>Dihedral 1</th>
<th>Dihedral 2</th>
<th>Dihedral 3</th>
<th>Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>C6-C1-C2-C3</td>
<td>-1.6(3)</td>
<td>C10-C1-C2-C3</td>
<td>179.6(2)</td>
</tr>
<tr>
<td>C2-C1-C6-C5</td>
<td>-2.4(3)</td>
<td>C2-C1-C6-C7</td>
<td>178.1(2)</td>
</tr>
<tr>
<td>C1-C6-C5-C6</td>
<td>176.4(2)</td>
<td>C1-C6-C5-C6</td>
<td>-3.0(3)</td>
</tr>
<tr>
<td>C2-C1-C10-02</td>
<td>3.8(3)</td>
<td>C2-C1-C10-C9</td>
<td>-174.3(2)</td>
</tr>
<tr>
<td>C6-C1-C10-02</td>
<td>-175.0(2)</td>
<td>C6-C1-C10-C9</td>
<td>6.9(3)</td>
</tr>
<tr>
<td>C1-C2-C3-C4</td>
<td>3.3(3)</td>
<td>C2-C3-C4-C5</td>
<td>-9.3(3)</td>
</tr>
<tr>
<td>C3-C4-C5-C6</td>
<td>-3.2(3)</td>
<td>C4-C5-C6-C7</td>
<td>4.9(3)</td>
</tr>
<tr>
<td>C4-C5-C6-C7</td>
<td>-175.7(2)</td>
<td>C1-C6-C7-C8</td>
<td>178.3(2)</td>
</tr>
<tr>
<td>C1-C6-C7-C8</td>
<td>-2.9(3)</td>
<td>C5-C6-C7-C8</td>
<td>-1.1(3)</td>
</tr>
<tr>
<td>C5-C6-C7-C8</td>
<td>177.6(2)</td>
<td>C1-C7-C8-C9</td>
<td>-176.1(2)</td>
</tr>
<tr>
<td>C6-C7-C8-C9</td>
<td>5.2(4)</td>
<td>C7-C8-C9-C10</td>
<td>-1.3(4)</td>
</tr>
<tr>
<td>C8-C9-C10-C1</td>
<td>177.3(2)</td>
<td>C8-C9-C10-C1</td>
<td>-4.7(3)</td>
</tr>
<tr>
<td>C3a'-C1a-C2a-C3a</td>
<td>-0.0(4)</td>
<td>C1a-C2a-C3a-C1a'</td>
<td>0.0(4)</td>
</tr>
<tr>
<td>H01-O1-C7-C6</td>
<td>180.2(2)</td>
<td>H01-O1-C7-C8</td>
<td>1(2)</td>
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<tr>
<td>H02-O2-C10-C1</td>
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<td>H02-O2-C10-C9</td>
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</tr>
<tr>
<td>C1-C2-C3-H3</td>
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<td>C2-C3-C4-H4</td>
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<tr>
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<td>C2-C3-C4-H4</td>
<td>177.2(2)</td>
</tr>
<tr>
<td>H3-C3-C4-C5</td>
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<td>C3-C4-C5-H5</td>
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</tr>
<tr>
<td>C3-C4-C5-H5</td>
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<td>C4-C5-C6-H5</td>
<td>178.2(2)</td>
</tr>
<tr>
<td>H4-C4-C5-H5</td>
<td>0.3(3)</td>
<td>H5-C5-C6-C1</td>
<td>-177.2(2)</td>
</tr>
<tr>
<td>H5-C5-C6-C7</td>
<td>2.2(2)</td>
<td>O1-C7-C8-H8</td>
<td>3.2(2)</td>
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<tr>
<td>C6-C7-C8-C9</td>
<td>-176.2(2)</td>
<td>C7-C8-C9-H9</td>
<td>176.2(2)</td>
</tr>
<tr>
<td>H8-C8-C9-C10</td>
<td>-180.2(2)</td>
<td>H8-C8-C9-H9</td>
<td>-3.3(3)</td>
</tr>
<tr>
<td>H9-C9-C10-C2</td>
<td>0.2(2)</td>
<td>H9-C9-C10-C2</td>
<td>178.2(2)</td>
</tr>
<tr>
<td>H1a-C1a-C2a-C3a</td>
<td>-176.2(2)</td>
<td>H1a-C1a-C2a-H2a</td>
<td>5(3)</td>
</tr>
<tr>
<td>C3a'-C1a-C2a-C3a</td>
<td>-179.2(2)</td>
<td>C1a-C2a-C3a-C1a'</td>
<td>178.2(2)</td>
</tr>
<tr>
<td>H2a-C2a-C3a-H3a</td>
<td>-3.3(3)</td>
<td>H2a-C2a-C3a-C1a'</td>
<td>179.2(2)</td>
</tr>
</tbody>
</table>
VI.3 Crystallographic structure of [Cr(CO)$_3$(η$^6$-5,8-tetralindione)] (60).

Formule brute: 
(C$_{10}$H$_8$O$_2$)Cr(Co)$_3$

Poids moléculaire: 296.2

Coefficient d'absorption linéaire: $\mu = 0.96$ mm$^{-1}$ (Mo (K$\alpha$))

Solvant de recristallisation: 

Densité: $D_o = ?$

Dx = 1.637 (gr.cm$^{-3}$)

Diffractomètre: STOE IPDS

Géométrie de la maille

Système cristallin: Orthorhombique

Groupe d'espace: $Pna2_1$

$a = 11.2836$ (9) (Å)

$b = 10.3052$ (10) (Å)

$c = 10.3366$ (7) (Å)

$V = 1201.9$ (2) (Å$^3$)

$Z = 4$

Nombre de réflexions pour l'affinement des paramètres: 8000 (9.3$^\circ$ < 2$\theta$ < 55.8$^\circ$)

Forme et dimensions du cristal

Forme: prisme;

Couleur: rouge

Dimensions: 0.08 x 0.20 x 0.25 mm

Mode de fixation: RS3000

Conditions expérimentales pour la collection des intensités

Température: 200 K

Longueur d'onde: 0.7107(Å)

Mode de balayage: $\phi$-scan

$\Delta \phi$ / image: 2.0 (°)

T Irradiation / image: 2.5 (min)

$\phi$ min, max = 0 - 316 (°)

Distance cristal / IP: 60 (mm)

Nombre d'images: 158

EMS: 0.011

Moyenne (I/$\sigma$(I)): 7.42

Limites angulaires: 5.3$^\circ$ < 2$\theta$ < 55.8$^\circ$

Limites d'indices: -14 < h < 14 ; -13 < k < 13 ; -13 < l < 13

Nombre de réflexions mesurées: 18'486

Réduction des données

Corrections:

LP

Disp. anomale

Absorption

T min. , max. = 0.7938 , 0.9263

Nombre de réflexions observables: 1578

|Fo| > 4$\sigma$(Fo)

Nombre de réflexions non-observables: 1356

Nombre de réflexions uniques: 2934

$R_{int}$ pour 14'565 réfl. équivalentes = 0.068
Appendix 2: Crystallographic data

Résolution et affinement de la structure

Résolution: Méthodes directes (SIR97)
Fonction minimisée :
\[ \sum (\omega (Fo-Fc)^2) \]
Fonction de poids :
\[ \omega = 1/\left[\sigma^2(Fo) + 0.0002 (Fo^2)\right] \]
Nombre d'atomes affinés "iso" :
-
Nombre d'atomes affinés "aniso": 19
Coordonnées des atomes d'hydrogène: calculées
Programme XTAL 3.2

Valeurs obtenues en fin d'affinement

Nombre de variables: 172
Nombre de réflexions : 1578
Nbe reflexions / Nbe de variables 9.2
Affinement par moindres carrés: Full matrix
"shift/error": moyen : 0.15 \times 10^{-4} , Maximum : 0.25 \times 10^{-3}
Résidus (delta F) (eÅ^{-3}): -0.65 , 0.34
Configuration absolue: \[ x = -0.02(4) \]
"Goodness of fit": \[ S = 1.24(2) \]

Facteur résiduel final \[ R = 0.027 \]
Facteur résiduel pondéré \[ \omega R = 0.027 \]

Remarques:

La structure est bien non-centrosymétrique.

Voir annexes pour les plans moyens et paramètres de ring slippage.
**Appendix 2: Crystallographic data**

### Bond Distances (Angstroms)

<table>
<thead>
<tr>
<th>Bond</th>
<th>Distance (Angstroms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr-C1</td>
<td>2.183 (6)</td>
</tr>
<tr>
<td>Cr-C3</td>
<td>2.231 (7)</td>
</tr>
<tr>
<td>Cr-C5</td>
<td>2.234 (6)</td>
</tr>
<tr>
<td>Cr-C11</td>
<td>1.862 (5)</td>
</tr>
<tr>
<td>Cr-C13</td>
<td>1.870 (7)</td>
</tr>
<tr>
<td>O2-C10</td>
<td>1.214 (8)</td>
</tr>
<tr>
<td>O4-C12</td>
<td>1.147 (8)</td>
</tr>
<tr>
<td>C1-C2</td>
<td>1.412 (9)</td>
</tr>
<tr>
<td>C1-C10</td>
<td>1.510 (9)</td>
</tr>
<tr>
<td>C3-C4</td>
<td>1.420 (9)</td>
</tr>
<tr>
<td>C5-C6</td>
<td>1.429 (9)</td>
</tr>
<tr>
<td>C7-C8</td>
<td>1.501 (1)</td>
</tr>
<tr>
<td>C9-C10</td>
<td>1.501 (1)</td>
</tr>
</tbody>
</table>

### Bond Angles (degrees)

<table>
<thead>
<tr>
<th>Bond Angles</th>
<th>Angle (degrees)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C11-Cr-C12</td>
<td>86.4 (3)</td>
</tr>
<tr>
<td>C12-Cr-C13</td>
<td>86.8 (3)</td>
</tr>
<tr>
<td>C2-C1-C10</td>
<td>119.7 (5)</td>
</tr>
<tr>
<td>C1-C2-C3</td>
<td>120.2 (6)</td>
</tr>
<tr>
<td>C3-C4-C5</td>
<td>120.9 (6)</td>
</tr>
<tr>
<td>C1-C6-C5</td>
<td>119.2 (6)</td>
</tr>
<tr>
<td>C5-C6-C7</td>
<td>119.6 (5)</td>
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<tr>
<td>O1-C7-C8</td>
<td>122.4 (6)</td>
</tr>
<tr>
<td>C7-C8-C9</td>
<td>114.7 (6)</td>
</tr>
<tr>
<td>O2-C10-C1</td>
<td>121.1 (6)</td>
</tr>
<tr>
<td>C1-C10-C9</td>
<td>117.0 (6)</td>
</tr>
<tr>
<td>Cr-C12-O4</td>
<td>177.1 (6)</td>
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</table>

### Dihedral Angles (degrees)

<table>
<thead>
<tr>
<th>Dihedral Angles</th>
<th>Angle (degrees)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C6-C1-C2-C3</td>
<td>1.1 (9)</td>
</tr>
<tr>
<td>C2-C1-C6-C5</td>
<td>1.5 (9)</td>
</tr>
<tr>
<td>C10-C1-C6-C5</td>
<td>177.5 (5)</td>
</tr>
<tr>
<td>C2-C1-C10-02</td>
<td>8.3 (9)</td>
</tr>
<tr>
<td>C6-C1-C10-02</td>
<td>-167.8 (6)</td>
</tr>
<tr>
<td>C1-C2-C3-C4</td>
<td>1.1 (9)</td>
</tr>
<tr>
<td>C3-C4-C5-C6</td>
<td>3.3 (9)</td>
</tr>
<tr>
<td>C4-C5-C6-C7</td>
<td>174.4 (5)</td>
</tr>
<tr>
<td>C1-C6-C7-C8</td>
<td>10.7 (8)</td>
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<tr>
<td>C5-C6-C7-C8</td>
<td>-166.7 (6)</td>
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<tr>
<td>C6-C7-C8-C9</td>
<td>-34.5 (9)</td>
</tr>
<tr>
<td>C8-C9-C10-02</td>
<td>144.1 (6)</td>
</tr>
</tbody>
</table>
VI.3 Crystallographic structure of meso-[Cr(CO)₃(η⁶-5,8-dihydroxytetralin)] (61).

Formule brute: \((C_{10}H_{12}O_2)Cr(CO)_3\)

Poids moléculaire: 300.3

Coefficient d’absorption linéaire \(\mu = 0.93 \text{ mm}^{-1} \) (Mo (Kα))

Solvant de recristallisation benzene

Densité \(D_o = ?\) \(D_x = 1.607 \text{ (gr.cm}^{-3}\)

Diffraclomètre STOE IPDS

**Géométrie de la maille**

Système cristallin: Triclinique

Groupe d’espace: \(P \bar{I}\)

\(a = 7.3157 \text{ (7) } (Å)\)
\(\alpha = 101.996 \text{ (9)}°\)

\(b = 13.3798 \text{ (11)(Å)\)}
\(\beta = 105.332 \text{ (9)}°\)

\(c = 13.6957 \text{ (11)(Å)}\)
\(\gamma = 97.332 \text{ (10)}°\)

\(V = 1240.7 \text{ (2)(Å}^3)\)
\(Z = 4 \text{ (deux molécules par unité asymétrique)}\)

Nombre de réflexions pour l’affinement des paramètres: 7626 \((6.5° < 2θ < 56.0°)\)

**Forme et dimensions du cristal**

Forme: prisme; Couleur: jaune

Dimensions: \(0.09 \times 0.13 \times 0.16 \text{ mm}\)

Mode de fixation: RS3000

**Conditions expérimentales pour la collection des intensités**

Température: 200 K

Longueur d’onde \(0.7107(Å)\)

Mode de balayage \(\phi\)-scan

\(\Delta \phi / \text{image} = 1.5 (°)\)

T Irradiation / image 3 (min)

\(\phi \text{ min, max} = 0 - 270 (°)\)

Distance cristal / IP 60 (mm)

Nombre d’images 180

EMS 0.008

Moyenne \((I/\sigma(I)) = 8.1\)

Limites angulaires \(5.0° < 2θ < 56.0°\)

Limites d’indices \(-9 < h < 9 \; ; \; -17 < k < 17 \; ; \; -17 < l < 17\)

Nombre de réflexions mesurées: 16'319

**Réduction des données**

Corrections:

LP \(\square\)

Disp. anomale \(\square\)

Absorption \(\square\)

\(T \text{ min., max.} = 0.8589 \; , \; 0.9427\)

Nombre de réflexions observables 2718 \(|F_o| > 4\sigma(F_o)\)

Nombre de réflexions non-observables 2831

Nombre de réflexions uniques 5549 \(R_{int} \text{ pour } 10'770 \text{ réfl. équivalentes} = 0.057\)

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Appendix 2: Crystallographic data

**Statistique des réflexions**

Facteur de température global $1.87 \, (\AA^2)$
Distribution des $<E^2>$ : acentrique $<E^2-1> = 0.742$

**Résolution et affinement de la structure**

Résolution: Méthodes directes (SIR97)
Fonction minimisée : $\Sigma (\omega (Fo-Fc)^2)$
Fonction de poids : $\omega = 1/\left[\sigma^2(Fo) + 0.0002 \, (Fo^2)\right]$
Nombre d'atomes affinés "iso" : 4 (H de -OH)
Nombre d'atomes affinés "aniso" : 38
Coordonnées des atomes d'hydrogène: calculées (H de -OH affinés)
Programme XTAL 3.2

Valeurs obtenues en fin d’affinement

Nombre de variables: 355
Nombre de réflexions : 2899
Nbre reflexions / Nbe de variables 8.2
Affinement par moindres carrés: Full matrix
"shift/error": moyen $0.73 \times 10^{-4}$, Maximum $0.16 \times 10^{-2}$
Résidus (delta F) (eÅ$^{-3}$): -0.64, 0.62
"Goodness of fit": $S = 1.03(1)$

---

**Facteur résiduel final** $R = 0.030$
**Facteur résiduel pondéré** $\omega R = 0.030$

Les hydrogènes des groupes -OH ont été affinés avec restrictions sur les longueurs de liaisons et des Uiso fixes (0.04 Å$^2$). Voir annexes pour les liaisons hydrogènes, la superposition des deux molécules de l’unité asymétrique et les paramètres de *ring slippage*. 
<table>
<thead>
<tr>
<th>Bond Distances (Angstroms)</th>
<th>b</th>
</tr>
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<tbody>
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<td>Cr1a-C1a</td>
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<tr>
<td>Cr1a-C2a</td>
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<tr>
<td>Cr1a-C3a</td>
<td>2.213(4)</td>
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<tr>
<td>Cr1a-C4a</td>
<td>2.206(5)</td>
</tr>
<tr>
<td>Cr1a-C5a</td>
<td>2.219(4)</td>
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<tr>
<td>Cr1a-C6a</td>
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</tr>
<tr>
<td>Cr1a-C11a</td>
<td>1.842(5)</td>
</tr>
<tr>
<td>Cr1a-C12a</td>
<td>1.830(4)</td>
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<tr>
<td>Cr1a-C13a</td>
<td>1.845(4)</td>
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<tr>
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<td>1.421(5)</td>
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<tr>
<td>O3a-C11a</td>
<td>1.151(6)</td>
</tr>
<tr>
<td>O4a-C12a</td>
<td>1.163(5)</td>
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<td>O5a-C13a</td>
<td>1.160(5)</td>
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<td>C1a-C2a</td>
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<td>C1a-C10a</td>
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<tr>
<td>C2a-C3a</td>
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<td>C3a-C4a</td>
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<td>C4a-C5a</td>
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<tr>
<td>C5a-C6a</td>
<td>1.432(6)</td>
</tr>
<tr>
<td>C6a-C7a</td>
<td>1.505(4)</td>
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<tr>
<td>C7a-C8a</td>
<td>1.516(6)</td>
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<tr>
<td>C8a-C9a</td>
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<tr>
<td>C9a-C10a</td>
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<table>
<thead>
<tr>
<th>Bond Angles (degrees)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C11a-Cr1a-C12a</td>
</tr>
<tr>
<td>C11a-Cr1a-C13a</td>
</tr>
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<td>C2a-C1a-C10a</td>
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<td>C6a-C1a-C10a</td>
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<td>C1a-C2a-C3a</td>
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<td>C2a-C3a-C4a</td>
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<td>C3a-C4a-C5a</td>
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<td>C4a-C5a-C6a</td>
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<tr>
<td>C1a-C6a-C5a</td>
</tr>
<tr>
<td>C1a-C6a-C7a</td>
</tr>
<tr>
<td>C5a-C6a-C7a</td>
</tr>
<tr>
<td>O1a-C7a-C6a</td>
</tr>
<tr>
<td>O1a-C7a-C8a</td>
</tr>
<tr>
<td>C6a-C7a-C8a</td>
</tr>
<tr>
<td>C7a-C8a-C9a</td>
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<td>C8a-C9a-C10a</td>
</tr>
<tr>
<td>O2a-C10a-C1a</td>
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<tr>
<td>O2a-C10a-C9a</td>
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<tr>
<td>C1a-C10a-C9a</td>
</tr>
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<td>Cr1a-C11a-O3a</td>
</tr>
<tr>
<td>Cr1a-C12a-O4a</td>
</tr>
<tr>
<td>Cr1a-C13a-O5a</td>
</tr>
</tbody>
</table>
## Appendix 2: Crystallographic data

### Dihedral Angles (degrees)

<table>
<thead>
<tr>
<th>Dihedral Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>C6a-C1a-C2a-C3a</td>
</tr>
<tr>
<td>C10a-C1a-C2a-C3a</td>
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<td>C2a-C1a-C6a-C5a</td>
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<tr>
<td>C2a-C1a-C6a-C7a</td>
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</tr>
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### Hydrogen bonds

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<td>O2a-H02a</td>
<td>0.82(4)</td>
</tr>
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<td>H02a...O1a'</td>
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</tr>
<tr>
<td>O2a...O1a'</td>
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</tr>
<tr>
<td>O2a-H02a...O1a'</td>
<td>160(3)°</td>
</tr>
<tr>
<td>O1b-H01b</td>
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</tr>
<tr>
<td>H01b...O2b'</td>
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</tr>
<tr>
<td>O1b...O2b'</td>
<td>2.729(4)</td>
</tr>
<tr>
<td>O1b-H01b...O2b'</td>
<td>172(3)°</td>
</tr>
</tbody>
</table>

' = x-1, y, z
'' = x+1, y, z+1
VI.4 Crystallographic structure of meso-[Cr(CO)₃(η⁶-5,8-dihydro-5,8-dihydroxynaphthalene)] (62).

Formule brute: (C₁₀H₁₀O₂) Cr (CO)₃
Poids moléculaire: 310.2
Coefficient d’absorption linéaire: μ = 0.96 mm⁻¹ (Mo (Kα))
Solvant de recristallisation: CH₂Cl₂
Densité: Do = ?
Diffractomètre: STOE IPDS

Géométrie de la maille

Système cristallin: Orthorhombique
Groupe d’espace: Pna2₁
a = 14.8724 (8) (Å)  α = 90°
b = 22.0188 (10)(Å)  β = 90°
c = 7.3574 (3)(Å)  γ = 90°
V = 2409.3 (2)(Å³)  Z = 8 (2 molécules par unité asymétrique)
Nombre de réflexions pour l’affinement des paramètres: 8000 (7.5° < 2θ < 53.9°)

Forme et dimensions du cristal

Forme: prisme; Couleur: jaune
Dimensions: 0.08 x 0.13 x 0.35 mm
Mode de fixation: RS3000

Conditions expérimentales pour la collection des intensités

Température: 200 K  Longueur d’onde 0.7107(Å)
Mode de balayage: φ-scan  Δφ / image 1.0 (°)
T Irradiation / image: 3 (min)  φ min, max = 0 - 258 (°)
Distance cristal / IP: 65 (mm)  Nombre d’images 259
EMS: 0.008  Moyenne (I/σ(I)) 8.3
Limites angulaires: 4.6° < 2θ < 53.9°
Limites d’indices: -18 < h < 18 ; -28 < k < 28 ; -9 < l < 9
Nombre de réflexions mesurées: 27'610

Réduction des données

Corrections : LP  
Disp. anomale  
Absorption  T min. , max. = 0.8422 , 0.9356
Nombre de réflexions observables: 3272  |Fo| > 4σ(Fo)
Nombre de réflexions non-observables: 1956
Nombre de réflexions uniques: 5228  R_{int} pour 21'426 réfl. équivalentes = 0.049
Appendix 2: Crystallographic data

Résolution et affinement de la structure

Résolution: Méthodes directes (SIR97)
Fonction minimisée : \( \sum (\omega (F_o - F_c)^2) \)
Fonction de poids : \( \omega = 1/\sigma^2(F_o) + 0.0002 (F_o^2) \)
Nombre d'atomes affinés "iso" : 4 (H de OH)
Nombre d'atomes affinés "aniso" : 38
Coordonnées des atomes d'hydrogène: mixtes (voir remarques)
Programme XTAL 3.2

Valeurs obtenues en fin d'affinement

Nombre de variables: 355
Nombre de réflexions : 3272
Nbe reflexions / Nbe de variables 9.2
Affinement par moindres carrés: Full matrix
"shift/error": moyen : 0.11 \(10^{-3}\), Maximum : 0.28 \(10^{-2}\)
Résidus (delta F) (eÅ\(^{-3}\)): -0.45, 0.41
Structure absolue (Flack parameter): x = -0.02(3)
"Goodness of fit": S = 1.35(2)

Facteur résiduel final \( R = 0.027 \)
Facteur résiduel pondéré \( \omega R = 0.027 \)

Remarques:

Les hydrogènes des groupes -OH ont été affinés avec restrictions sur les longueurs de liaisons et angles de valences. Les autres ont été calculés.
Les deux molécules de l'unité asymétrique sont semblables (voir superposition).
Aucune interaction de stacking n'est observée dans l'empilement cristallin.
### Bond Distances (Angstroms)

<table>
<thead>
<tr>
<th>Bond</th>
<th>Distance</th>
<th>b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr1a-C1a</td>
<td>2.250(6)</td>
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<td>Cr1a-C2a</td>
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<td>Cr1a-C3a</td>
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<td>.96(3)</td>
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<tr>
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<td>.95(3)</td>
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### Bond Angles (degrees)

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### Appendix 2: Crystallographic data

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**Dihedral Angles (degrees)**

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<tr>
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<tr>
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<td>153.0(6)</td>
</tr>
<tr>
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<td>C5a-C6a-C7a-C8a</td>
<td>31.1(8)</td>
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<tr>
<td>C6a-C7a-C8a-C9a</td>
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<td>C6a-C7a-C8a-C9a</td>
<td>152.9(6)</td>
</tr>
<tr>
<td>C6a-C7a-C8a-C9a</td>
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<td>C6a-C7a-C8a-C9a</td>
<td>27.2(9)</td>
</tr>
<tr>
<td>C7a-C8a-C9a-C10a</td>
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<td>C8a-C9a-C10a-C1a</td>
<td>-26.4(8)</td>
</tr>
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</table>

**VI.6 Crystallographic structure of [Cr(CO)₃(CH₃COO)(η⁶-8-hydroxy-5-tetralone)] (68).**

- **Formule brute:** \((C_{10}H_{10}O_{2})\ Cr (CO)_3\)
- **Poids moléculaire:** 298.2
- **Coefficient d’absorption linéaire** \(\mu = 0.94 \text{ mm}^{-1} \ (\text{Mo (K}\alpha))\)
- **Solvant de recristallisation** ?
- **Densité** \(D_\Omega = ? \text{ gr.cm}^{-3}\)
- **Diffractomètre** STOE IPDS

**Géométrie de la maille**

- **Système cristallin:** Monoclinique
- **Groupe d’espace:** \(P 2_1/n\)
- **a = 9.9737 (8) Å**
- **b = 12.1513 (10) Å**
- **c = 10.9492 (9) Å**
- **\(\alpha = 90^\circ\)**
- **\(\beta = 111.947(9)^\circ\)**
- **\(\gamma = 90^\circ\)**
Appendix 2: Crystallographic data

V = 1230.8 (2)(Å³) Z = 4
Nombre de réflexions pour l'affinement des paramètres: 8000 (9.3° < 2θ < 55.9°)

**Forme et dimensions du cristal**

Forme: prisme; Couleur: rouge
Dimensions: 0.10 x 0.22 x 0.30 mm
Mode de fixation: RS3000

**Conditions expérimentales pour la collection des intensités**

| Température: | 200 K | Longueur d'onde | 0.7107(Å) |
| Mode de balayage | φ-scan | Δφ / image | 1.6 (*) |
| T Irradiation / image | 2.5 (min) | φ min, max = 0 - 315.2 (°) |
| Distance cristal / IP | 60 (mm) | Nombre d'images | 197 |
| EMS | 0.009 | Moyenne (I/σ(I)) | 17.6 |
| limites angulaires | 5.2° < 2θ < 55.9° |
| limites d'indices | -13 < h < 13 ; -16 < k < 16 ; -14 < l < 14 |
Nombre de réflexions mesurées: 18'864

**Rédaction des données**

Corrections : LP
Disp. anomale
Absorption T min., max. = 0.8005, 0.9220

Nombre de réflexions observables 1927 |Fo|> 4σ(Fo)
Nombre de réflexions non-observables 907
Nombre de réflexions uniques 2834 R_{int} pour 15'592 réfl. équivalentes = 0.055

**Statistique des réflexions**

Facteur de température global 2.48 (Å²)
Distribution des <E²> : centrique <E²-1> = 0.944

**Résolution et affinement de la structure**

Résolution: Méthodes directes (SIR97)
Fonction minimisée : Σ (ω (Fo-Fc)²)
Fonction de poids : ω = 1/[σ²(Fo) + 0.0002 (Fo²)]
Nombre d'atomes affinés "iso": 10 (H)
Nombre d'atomes affinés "aniso": 19
Coordonnées des atomes d'hydrogène: affinées (xyz)
Programme XTAL 3.2

Valeurs obtenues en fin d'affinement

Nombre de variables: 202
Appendix 2: Crystallographic data

Nombre de réflexions : 1985
Nbe reflexions / Nbe de variables : 9.8
Affinement par moindres carrés: Full matrix
"shift/error": moyen : 0.22 $10^{-4}$ , Maximum : 0.25 $10^{-3}$
Résidus (delta F) (eÅ$^{-3}$): -1.06 , 0.53
"Goodness of fit": S = 1.37(2)

Facteur résiduel final : $R = 0.032$
Facteur résiduel pondéré : \( \omega R = 0.032 \)

Remarques:
Les hydrogènes ont été observés et affinés avec des Uiso fixes (0.04 Å$^2$).

VI.7 Crystallographic structure of \((-\)-(5S,8R)-[Cr(CO)$_3$(η$^6$-5,8-dihydro-8-hydroxy-5-benzoyloxytetralin)] (70b).

Formule brute: \((C_{17}H_{14}O_3)\text{Cr}(CO)_3\)
Poids moléculaire: 402.3
Coefficient d’absorption linéaire: \(\mu = 0.68 \text{ mm}^{-1} \text{(Mo (Kα))}\)
Solvant de recristallisation: toluene
Densité \(D_0 = ?\)
Diffractomètre: STOE IPDS
Appendix 2: Crystallographic data

Géométrie de la maille

Système cristallin: Orthorhombique  
Groupe d'espace: $P\ 2\bar{1}\ 2\bar{1}\ 2\bar{1}$

<table>
<thead>
<tr>
<th>Paramètre</th>
<th>Valeur (erreur)</th>
</tr>
</thead>
<tbody>
<tr>
<td>a</td>
<td>9.1712 (4) Å</td>
</tr>
<tr>
<td>b</td>
<td>9.3088 (5) Å</td>
</tr>
<tr>
<td>c</td>
<td>20.7748 (9) Å</td>
</tr>
<tr>
<td>V</td>
<td>1763.6 (2) Å³</td>
</tr>
</tbody>
</table>

$\alpha = 90^\circ$
$\beta = 90^\circ$
$\gamma = 90^\circ$
$Z = 4$

Nombre de réflexions pour l'affinement des paramètres: 8000 ($9^\circ < 2\theta < 53.9^\circ$)

Forme et dimensions du cristal

Forme: prisme; Couleur: jaune
Dimensions: .15 x .15 x .25 mm
Mode de fixation: RS3000

Conditions expérimentales pour la collection des intensités

<table>
<thead>
<tr>
<th>Paramètre</th>
<th>Valeur</th>
</tr>
</thead>
<tbody>
<tr>
<td>Température</td>
<td>200 K</td>
</tr>
<tr>
<td>Longueur d'onde</td>
<td>0.7107 Å</td>
</tr>
<tr>
<td>Mode de balayage</td>
<td>$\varphi$-scan</td>
</tr>
<tr>
<td>$\Delta \varphi$ / image</td>
<td>1.0 (°)</td>
</tr>
<tr>
<td>T Irradiation / image</td>
<td>3 (min)</td>
</tr>
<tr>
<td>$\varphi$ min, max</td>
<td>0 - 315 (°)</td>
</tr>
<tr>
<td>Distance cristal / IP</td>
<td>65 (mm)</td>
</tr>
<tr>
<td>Nombre d'images</td>
<td>315</td>
</tr>
<tr>
<td>EMS</td>
<td>0.008</td>
</tr>
<tr>
<td>Moyenne (I/$\sigma$(I))</td>
<td>13.2</td>
</tr>
</tbody>
</table>

Limites angulaires | 4.8° < 2$\theta$ < 53.9°
Limites d'indices | -11 < h < 11 ; -11 < k < 11 ; -26 < l < 26

Nombre de réflexions mesurées: 24'754

Réduction des données

<table>
<thead>
<tr>
<th>Corrections</th>
<th>LP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disp. anomale</td>
<td>$\times$</td>
</tr>
<tr>
<td>Absorption</td>
<td>$\times$</td>
</tr>
</tbody>
</table>

T min. , max. = 0.8753 , 0.9251

Nombre de réflexions observables | 2845 | $|F_o| > 4\sigma(F_o)$
Nombre de réflexions non-observables | 998 |
Nombre de réflexions uniques | 3848 | $R_{int}$ pour 20'824 réfl. équivalentes = 0.037
Appendix 2: Crystallographic data

**Statistique des réflexions**

- Facteur de température global: 2.05 (Å²)
- Distribution des \(<E^2>\) : acentrique \(<E^2\cdot1> = 0.735\)

**Résolution et affinément de la structure**

- Résolution: Méthodes directes (SIR97)
- Fonction minimisée: \(\Sigma (\omega (Fo-Fc)^2)\)
- Fonction de poids: \(\omega = 1/\{\sigma^2(Fo) + 0.00015 (Fo^2)\}\)
- Nombre d'atomes affinés "iso": 1 (H03)
- Nombre d'atomes affinés "aniso": 27
- Coordonnées des atomes d'hydrogène: calculées (observée et affinées pour H (-OH))
- Programme: XTAL 3.2

**Valeurs obtenues en fin d'affinement**

- Nombre de variables: 248
- Nombre de réflexions: 2845
- Nbre reflexions / Nbre de variables: 11.5
- Affinément par moindres carrés: Full matrix
- "shift/error": moyen: 0.47 \(10^{-4}\), Maximum: 0.49 \(10^{-3}\)
- Résidus (delta F) (eÅ⁻³): -0.38, 0.27
- Configuration absolue: \(x = -0.01(2)\)
- "Goodness of fit": \(S = 1.70(3)\)

**Facteur résiduel final** 

- R = 0.026
- \(\omega R = 0.026\)

**Remarques:**

L'atome d'hydrogène du –OH a été observé et affiné avec un Uiso fixe (0.04 Å²). Les coordonnées des autres atomes d'hydrogène ont été calculées. Voir annexes pour les interactions de stacking, liaisonhydrogène et « ring slippage parameters ». 

![Diagramme de structure cristalline](image)
## Appendix 2: Crystallographic data

### Bond Distances (Angstroms)

<table>
<thead>
<tr>
<th>Bond</th>
<th>Distance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr-C1</td>
<td>2.227(3)</td>
</tr>
<tr>
<td>Cr-C3</td>
<td>2.222(3)</td>
</tr>
<tr>
<td>Cr-C5</td>
<td>2.203(3)</td>
</tr>
<tr>
<td>Cr-C18</td>
<td>1.828(4)</td>
</tr>
<tr>
<td>Cr-C20</td>
<td>1.837(4)</td>
</tr>
<tr>
<td>O1-C7</td>
<td>1.462(4)</td>
</tr>
<tr>
<td>O2-C11</td>
<td>1.202(4)</td>
</tr>
<tr>
<td>O3-H03</td>
<td>1.81(3)</td>
</tr>
<tr>
<td>O5-C19</td>
<td>1.152(5)</td>
</tr>
<tr>
<td>C1-C2</td>
<td>1.397(4)</td>
</tr>
<tr>
<td>C1-C10</td>
<td>1.531(4)</td>
</tr>
<tr>
<td>C3-C4</td>
<td>1.394(5)</td>
</tr>
<tr>
<td>C5-C6</td>
<td>1.408(5)</td>
</tr>
<tr>
<td>C7-C8</td>
<td>1.495(5)</td>
</tr>
<tr>
<td>O1-C7</td>
<td>1.462(4)</td>
</tr>
<tr>
<td>O2-C11</td>
<td>1.202(4)</td>
</tr>
<tr>
<td>O3-C10</td>
<td>1.149(4)</td>
</tr>
<tr>
<td>O4-C18</td>
<td>1.148(5)</td>
</tr>
<tr>
<td>C1-C6</td>
<td>1.149(4)</td>
</tr>
<tr>
<td>C2-C3</td>
<td>1.409(5)</td>
</tr>
<tr>
<td>C3-C4</td>
<td>1.410(5)</td>
</tr>
<tr>
<td>C4-C5</td>
<td></td>
</tr>
<tr>
<td>C5-C6</td>
<td>1.510(4)</td>
</tr>
<tr>
<td>C6-C7</td>
<td>1.324(5)</td>
</tr>
<tr>
<td>C7-C8</td>
<td>1.510(4)</td>
</tr>
<tr>
<td>C8-C9</td>
<td></td>
</tr>
<tr>
<td>C9-C10</td>
<td>1.148(5)</td>
</tr>
<tr>
<td>C10-C11</td>
<td>1.481(5)</td>
</tr>
<tr>
<td>C11-C12</td>
<td>1.487(5)</td>
</tr>
<tr>
<td>C12-C13</td>
<td>1.387(5)</td>
</tr>
<tr>
<td>C13-C14</td>
<td>1.385(6)</td>
</tr>
<tr>
<td>C15-C16</td>
<td>1.398(6)</td>
</tr>
</tbody>
</table>

### Bond Angles (degrees)

<table>
<thead>
<tr>
<th>Bond Angle</th>
<th>Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>C18-Cr-C19</td>
<td>87.2(2)</td>
</tr>
<tr>
<td>C19-Cr-C20</td>
<td>90.0(2)</td>
</tr>
<tr>
<td>C10-03-H03</td>
<td>105(3)</td>
</tr>
<tr>
<td>C2-C1-C10</td>
<td>119.6(3)</td>
</tr>
<tr>
<td>C1-C2-C3</td>
<td>120.5(3)</td>
</tr>
<tr>
<td>C3-C4-C5</td>
<td>119.0(3)</td>
</tr>
<tr>
<td>C1-C6-C5</td>
<td>119.0(3)</td>
</tr>
<tr>
<td>C5-C6-C7</td>
<td>119.9(3)</td>
</tr>
<tr>
<td>O1-C7-C6</td>
<td>107.2(2)</td>
</tr>
<tr>
<td>O1-C7-C8</td>
<td>109.3(3)</td>
</tr>
<tr>
<td>C7-C8-C9</td>
<td>123.3(3)</td>
</tr>
<tr>
<td>O3-C10-C1</td>
<td>110.8(2)</td>
</tr>
<tr>
<td>C1-C10-C9</td>
<td>112.6(3)</td>
</tr>
<tr>
<td>O1-C11-C12</td>
<td>111.9(3)</td>
</tr>
<tr>
<td>C11-C12-C13</td>
<td>122.6(3)</td>
</tr>
<tr>
<td>C13-C12-C17</td>
<td>119.8(3)</td>
</tr>
<tr>
<td>C13-C14-C15</td>
<td>119.9(4)</td>
</tr>
<tr>
<td>C15-C16-C17</td>
<td>120.2(4)</td>
</tr>
<tr>
<td>Cr-C18-O4</td>
<td>177.7(4)</td>
</tr>
<tr>
<td>Cr-C20-O6</td>
<td>178.5(3)</td>
</tr>
</tbody>
</table>

### Dihedral Angles (degrees)

<table>
<thead>
<tr>
<th>Dihedral Angle</th>
<th>Angle</th>
</tr>
</thead>
<tbody>
<tr>
<td>C11-O1-C7-C6</td>
<td>-157.7(3)</td>
</tr>
<tr>
<td>C7-O1-C11-C12</td>
<td>-178.5(3)</td>
</tr>
<tr>
<td>H03-O3-C10-C1</td>
<td>98(2)</td>
</tr>
<tr>
<td>C6-C1-C2-C3</td>
<td>.2(5)</td>
</tr>
<tr>
<td>C2-C1-C6-C5</td>
<td>.5(4)</td>
</tr>
<tr>
<td>C10-C1-C6-C5</td>
<td>178.5(3)</td>
</tr>
<tr>
<td>C2-C1-C10-C9</td>
<td>-41.3(4)</td>
</tr>
<tr>
<td>C6-C1-C10-C9</td>
<td>140.7(3)</td>
</tr>
<tr>
<td>C1-C2-C3-C4</td>
<td>-.2(5)</td>
</tr>
</tbody>
</table>
Appendix 2: Crystallographic data

<table>
<thead>
<tr>
<th>Bond Configuration</th>
<th>Dihedral Angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C3-C4-C5-C6</td>
<td>1.3 (5)</td>
</tr>
<tr>
<td>C4-C5-C6-C7</td>
<td>177.8 (3)</td>
</tr>
<tr>
<td>C1-C6-C7-C8</td>
<td>165.0 (3)</td>
</tr>
<tr>
<td>C6-C7-C8-C9</td>
<td>15.5 (5)</td>
</tr>
<tr>
<td>C8-C9-C10-O3</td>
<td>-143.1 (3)</td>
</tr>
<tr>
<td>O1-C11-C12-C13</td>
<td>-179.1 (3)</td>
</tr>
<tr>
<td>C11-C12-C13-C14</td>
<td>179.4 (3)</td>
</tr>
<tr>
<td>C12-C13-C14-C15</td>
<td>-0.7 (6)</td>
</tr>
<tr>
<td>C13-C14-C15-C16</td>
<td>1.5 (6)</td>
</tr>
</tbody>
</table>

Hydrogen bond

- O3-H03: 0.81 (3) Å
- H03...O4': 2.11 (3) Å
- O3...O4': 2.919 (4) Å
- O3-H03...O4': 175 (4) °

(') = x-1/2 , 3/2-y ; 1-z

VI.8 Crystallographic structure of 1,4-tetralindione (87).

Formule brute: \( \text{C}_{10}\text{H}_8\text{O}_2 \)
Poids moléculaire: 160.2
Coefficient d’absorption linéaire: \( \mu = 0.09 \text{ mm}^{-1} \) (Mo (Kα))
Solvant de recristallisation: ?
Densité : \( \text{Do} = ? \)
Difféactomètre: STOE IPDS

Géométrie de la maille

Système cristallin: Monoclinique
Groupe d’espace: \( P 2_12_12_1 \)
a = 4.7167 (8) (Å)
b = 7.4607 (10) (Å)
c = 11.285 (2) (Å)
V = 394.2 (1) (Å³)
Nombre de réflexions pour l’affinement des paramètres: 3141 (6.7° < 2θ < 53.7°)

Forme et dimensions du cristal

Forme: prisme; Couleur: jaune clair
Dimensions: 0.10 x 0.27 x 0.29 mm
Mode de fixation: RS3000
**Appendix 2: Crystallographic data**

**Conditions expérimentales pour la collection des intensités**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Température</td>
<td>200 K</td>
</tr>
<tr>
<td>Longueur d'onde</td>
<td>0.7107 Å</td>
</tr>
<tr>
<td>Mode de balayage</td>
<td>ϕ-scan</td>
</tr>
<tr>
<td>Longueur d'onde</td>
<td>2.0 (°)</td>
</tr>
<tr>
<td>T Irradiation / image</td>
<td>4 (min)</td>
</tr>
<tr>
<td>T min, max</td>
<td>0 - 284 (°)</td>
</tr>
<tr>
<td>Distance cristal / IP</td>
<td>65 (mm)</td>
</tr>
<tr>
<td>Nombre d'images</td>
<td>142</td>
</tr>
<tr>
<td>EMS</td>
<td>0.013</td>
</tr>
<tr>
<td>Moyenne (I/σ(I))</td>
<td>13.4</td>
</tr>
<tr>
<td>Limites angulaires</td>
<td>6.7° &lt; 2θ &lt; 53.7°</td>
</tr>
<tr>
<td>Limites d'indices</td>
<td>-5 &lt; h &lt; 5 ; -9 &lt; k &lt; 9 ; -14 &lt; l &lt; 14</td>
</tr>
<tr>
<td>Nombre de réflexions mesurées</td>
<td>4831</td>
</tr>
</tbody>
</table>

**Réduction des données**

- Corrections : LP
- Correction de dispersion anormale
- Absorption

<table>
<thead>
<tr>
<th>Correction</th>
<th>T min., max.</th>
<th>0.9753</th>
<th>0.9922</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nombre de réflexions observables</td>
<td>1123</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nombre de réflexions non-observables</td>
<td>556</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nombre de réflexions uniques</td>
<td>1679</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rint pour 3137 réfl. équivalentes</td>
<td>0.046</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Statistique des réflexions**

- Facteur de température global : 3.34 (Å²)
- Distribution des <E²> : acentrique <E²-1> = 0.736

**Résolution et affinement de la structure**

- Résolution: Méthodes directes (SIR97)
- Fonction minimisée : \( \Sigma (\omega (F_o-F_c)^2) \)
- Fonction de poids : \( \omega = 1/[(\sigma^2(Fo) + 0.0002 (Fo^2)] \)
- Nombre d'atomes affinés "iso" : 
- Nombre d'atomes affinés "aniso" : 12
- Coordonnées des atomes d'hydrogène : calculées
- Programme : XTAL 3.2

**Valeurs obtenues en fin d'affinement**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nombre de variables</td>
<td>108</td>
</tr>
<tr>
<td>Nombre de réflexions</td>
<td>1123</td>
</tr>
<tr>
<td>Nbe reflexions / Nbe de variables</td>
<td>10.4</td>
</tr>
<tr>
<td>Affinement par moindres carrés</td>
<td>Full matrix</td>
</tr>
<tr>
<td>&quot;shift/error&quot;:</td>
<td>moyen : 0.10 (10^{-4}), Maximum : 0.12 (10^{-3})</td>
</tr>
<tr>
<td>Résidus (delta F) (eÅ⁻³):</td>
<td>-0.42 , 0.38</td>
</tr>
<tr>
<td>Configuration absolue</td>
<td>( x = \text{fixé à 0.0} )</td>
</tr>
<tr>
<td>&quot;Goodness of fit&quot;: S</td>
<td>1.52(5)</td>
</tr>
</tbody>
</table>

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Appendix 2: Crystallographic data

Facteur résiduel final  \( R = 0.033 \)
Facteur résiduel pondéré  \( \omega R = 0.031 \)

Remarques:

\( y(O1) \) a été fixé pour définir l’origine polaire.

<table>
<thead>
<tr>
<th>Bond Distances (Angstroms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>O1-C7 1.221(5)</td>
</tr>
<tr>
<td>C1-C2 1.395(7)</td>
</tr>
<tr>
<td>C1-C10 1.499(6)</td>
</tr>
<tr>
<td>C3-C4 1.377(6)</td>
</tr>
<tr>
<td>C5-C6 1.390(6)</td>
</tr>
<tr>
<td>C7-C8 1.494(7)</td>
</tr>
<tr>
<td>C9-C10 1.486(7)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bond Angles (degrees)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C2-C1-C6 119.5(4)</td>
</tr>
<tr>
<td>C6-C1-C10 120.7(4)</td>
</tr>
<tr>
<td>C2-C3-C4 120.4(5)</td>
</tr>
<tr>
<td>C4-C5-C6 120.8(4)</td>
</tr>
<tr>
<td>C1-C6-C7 120.6(4)</td>
</tr>
<tr>
<td>O1-C7-C6 120.9(4)</td>
</tr>
<tr>
<td>C6-C7-C8 117.1(4)</td>
</tr>
<tr>
<td>C8-C9-C10 112.9(4)</td>
</tr>
<tr>
<td>O2-C10-C9 122.3(4)</td>
</tr>
</tbody>
</table>
Appendix 2: Crystallographic data

Dihedral Angles (degrees)

<table>
<thead>
<tr>
<th></th>
<th>1.3 (7)</th>
<th>-179.6 (4)</th>
<th>-177.1 (4)</th>
<th>3.8 (7)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C6-C1-C2-C3</td>
<td>C10-C1-C2-C3</td>
<td>C2-C1-C6-C5</td>
<td>C10-C1-C6-C7</td>
<td>C2-C1-C10-02</td>
</tr>
<tr>
<td>C2-C1-C6-C5</td>
<td>C6-C1-C6-C7</td>
<td>C2-C1-C10-C9</td>
<td>C2-C1-C6-C7</td>
<td>C6-C1-C10-C9</td>
</tr>
<tr>
<td>C10-C1-C6-C5</td>
<td>C6-C1-C10-C9</td>
<td>C2-C1-C10-C9</td>
<td>C2-C1-C6-C7</td>
<td>C6-C1-C10-C9</td>
</tr>
<tr>
<td>C2-C1-C10-02</td>
<td>C2-C1-C6-C7</td>
<td>C2-C1-C6-C7</td>
<td>C2-C1-C6-C7</td>
<td>C6-C1-C10-C9</td>
</tr>
<tr>
<td>C6-C1-C10-02</td>
<td>C2-C1-C6-C7</td>
<td>C2-C1-C6-C7</td>
<td>C2-C1-C6-C7</td>
<td>C6-C1-C10-C9</td>
</tr>
<tr>
<td>C1-C2-C3-C4</td>
<td>C2-C3-C4-C5</td>
<td>C4-C5-C6-C7</td>
<td>C1-C6-C7-C8</td>
<td>C5-C6-C7-C8</td>
</tr>
<tr>
<td>C3-C4-C5-C6</td>
<td>C1-C6-C7-C8</td>
<td>C5-C6-C7-C8</td>
<td>C1-C6-C7-C8</td>
<td>C5-C6-C7-C8</td>
</tr>
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<td>C4-C5-C6-C7</td>
<td>C4-C5-C6-C7</td>
<td>C1-C6-C7-C8</td>
<td>C5-C6-C7-C8</td>
<td>C1-C6-C7-C8</td>
</tr>
<tr>
<td>C6-C7-C8-C9</td>
<td>C8-C9-C10-C1</td>
<td>C8-C9-C10-C1</td>
<td>C8-C9-C10-C1</td>
<td>C8-C9-C10-C1</td>
</tr>
</tbody>
</table>

VI.9 Crystallographic structure of (-)-(5S,8S)-[Cr(CO)₃(η⁶-5,8-dihydroxy-5,8-diallyltetralin)] (14).

Formule brute: (C₁₉H₂₀O₂) Cr (CO)₃
Poids moléculaire: 380.4
Coefficient d’absorption linéaire μ = 0.68 mm⁻¹ (Mo (Kα))
Solvant de recristallisation hexane
Densité Do = ? Dx = 1.438 (gr.cm⁻³)
Diffraactomètre STOE IPDS

Géométrie de la maille

Système cristallin: Orthorhombique
Groupe d'espace: P 2₁2₁2₁
a = 10.7731 (8) (Å)
α = 90°
b = 11.3538 (6)(Å)
β = 90°
c = 14.3597 (9)(Å)
γ = 90°
V = 1756.4 (2)(Å³)
Z = 4
Nombre de réflexions pour l'affinement des paramètres: 8000 (7.4° < 2θ < 55.8°)

Forme et dimensions du cristal

Forme: prisme; Couleur: jaune
Dimensions: 0.14 x 0.14 x 0.27 mm
Mode de fixation: RS3000

Conditions expérimentales pour la collection des intensités

Température: 220 K
Longueur d'onde 0.7107(Å)
Mode de balayage φ-scan
Δφ / image 1.5 (°)
T Irradiation / image 2.5 (min)
ϕ min, max = 0 - 315 (°)
Distance cristal / IP 60 (mm)
Nombre d’images 210
EMS 0.008
Moyenne (I/σ(I)) 10.0
Appendix 2: Crystallographic data

Limites angulaires \[5.2° < 2\theta < 55.8°\]
Limites d'indices \[-14 < h < 14 ; -14 < k < 14 ; -19 < l < 19\]

Nombre de réflexions mesurées: 26'923

Réduction des données

Corrections : LP ☒
Disp. anomale ☒
Absorption ☒
\[T \text{ min. , max. } = 0.8775 , 0.9437\]

Nombre de réflexions observables 2721 \(|Fo| > 4\sigma(Fo)\)
Nombre de réflexions non-observables 1525
Nombre de réflexions uniques 4246 \(R_{int} \) pour 22'608 réfl. équivalentes = 0.052

Statistique des réflexions

Facteur de température global 2.39 (Å²)
Distribution des \(<E^2>\) : acentrique \(<E^2-1> = 0.767\)

Résolution et affinement de la structure

Résolution: Méthodes directes (SIR97)
Fonction minimisée : \(\Sigma (\omega (Fo-Fc)^2)\)
Fonction de poids : \(\omega = 1/[(\sigma^2(Fo) + 0.0002 (Fo^2))]\)
Nombre d'atomes affinés "iso" : 2 (H01, H02)
Nombre d'atomes affinés "aniso" : 25
Coordonnées des atomes d'hydrogène: mixtes
Programme XTAL 3.2

Valeurs obtenues en fin d'affinement

Nombre de variables: 251
Nombre de réflexions : 2721
Nbe reflexions / Nbe de variables 10.8
Affinement par moindres carrés: Full matrix
"shift/error": moyen : 0.11 \(10^{-2}\) , Maximum : 0.71 \(10^{-2}\)
Résidus (delta F) (eÅ⁻³): -0.37 , 0.36
Configuration absolue: \(x = -0.02(3)\)
"Goodness of fit": \(S = 1.64(2)\)

Facteur résiduel final \(R = 0.029\)
Facteur résiduel pondéré \(\omega R = 0.029\)
Remarques:

Un des groupements vinyle (-C12-C13) est désordonné et a été affiné sur deux sites avec des taux d’occupation de 0.5.
Les hydrogènes des groupes -OH ont été affinés avec restrictions sur les longueurs de liaisons et angles de valences. Les autres ont été calculés.
Voir annexes pour les paramètres de « ring slippage » ($\Delta = 0.039$ Å en direction de C4).

<table>
<thead>
<tr>
<th>Bond Distances (Angstroms)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cr-C1</td>
<td>2.274(4)</td>
</tr>
<tr>
<td>Cr-C3</td>
<td>2.222(4)</td>
</tr>
<tr>
<td>Cr-C5</td>
<td>2.216(4)</td>
</tr>
<tr>
<td>Cr-C17</td>
<td>1.838(4)</td>
</tr>
<tr>
<td>Cr-C19</td>
<td>1.858(5)</td>
</tr>
<tr>
<td>O1-C7</td>
<td>1.440(5)</td>
</tr>
<tr>
<td>O2-C10</td>
<td>1.447(5)</td>
</tr>
<tr>
<td>O3-C17</td>
<td>1.158(5)</td>
</tr>
<tr>
<td>O5-C19</td>
<td>1.148(6)</td>
</tr>
<tr>
<td>C1-C6</td>
<td>1.405(6)</td>
</tr>
<tr>
<td>C2-C3</td>
<td>1.396(5)</td>
</tr>
<tr>
<td>C4-C5</td>
<td>1.388(6)</td>
</tr>
<tr>
<td>C6-C7</td>
<td>1.523(6)</td>
</tr>
<tr>
<td>C7-C11</td>
<td>1.553(6)</td>
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<tr>
<td>C9-C10</td>
<td>1.538(6)</td>
</tr>
<tr>
<td>C11-C12</td>
<td>1.54(1)</td>
</tr>
<tr>
<td>C14-C15</td>
<td>1.505(6)</td>
</tr>
<tr>
<td>C11-C12'</td>
<td>1.50(1)</td>
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</tbody>
</table>
### Appendix 2: Crystallographic data

#### Bond Angles (degrees)

<table>
<thead>
<tr>
<th>Bond Pair</th>
<th>Angle (degrees)</th>
<th>Bond Pair</th>
<th>Angle (degrees)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C17-Cr-C18</td>
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<tr>
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<td>C10-O2-H02</td>
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<tr>
<td>Cr-C1-C6</td>
<td>71.4(2)</td>
<td>Cr-C1-C10</td>
<td>134.6(3)</td>
</tr>
<tr>
<td>C2-C1-C6</td>
<td>119.1(3)</td>
<td>C2-C1-C10</td>
<td>118.3(4)</td>
</tr>
<tr>
<td>C6-C1-C10</td>
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<td>Cr-C2-C1</td>
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<td>C1-C2-C3</td>
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<td>O1-C7-C6</td>
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<td>107.1(3)</td>
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<tr>
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<td>O2-C10-C1</td>
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<td>Cr-C18-O4</td>
<td>178.1(4)</td>
<td>Cr-C19-O5</td>
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#### Dihedral Angles (degrees)

<table>
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<tr>
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<th>Angle (degrees)</th>
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</thead>
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<td>C10-C1-C2-C3</td>
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<td>C2-C1-C6-C7</td>
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<td>C10-C1-C6-C7</td>
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<td>C2-C1-C10-O2</td>
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<td>C4-C5-C6-C1</td>
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<td>H02-O2-C10-C1</td>
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