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Ruthenium-catalyzed reduction of racemic tricarbonyl(η^6-aryl ketone)chromium complexes using transfer hydrogenation: A simple alternative to the resolution of planar chiral organometallics

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Abstract

Racemic planar chiral (η^6-aryl ketone)$Cr(CO)_3$ complexes (aryl ketone = 1-indanone, 1-tetralone, 4-chromanone and thiochroman-4-one) were prepared by refluxing the aryl ketone with $Cr(CO)_6$ in a 10:1 mixture of dibutyl ether and THF. The reductions of the organometallic ketones by transfer hydrogenation in 2-propanol containing KOH and the catalyst precursor, generated from $[RuCl_2(\eta^6\text{-benzene})]_2$ and (−)-ephedrine, resulted in optically active *syn*-(*R*,*S*)-(η^6-aryl alcohol)$Cr(CO)_3$ and (*R*)-(η^6-aryl ketone)$Cr(CO)_3$ compounds in 31–97% ee. Reduction of racemic (η^6-thiochroman-4-one)$Cr(CO)_3$ with the catalyst precursor generated from (+)-norephedrine, instead of (−)-ephedrine, inverted the configuration of the products obtained. *Syn*-(*S*,*R*)-(η^6-thiochroman-4-ol)$Cr(CO)_3$ and (*S*)-(η^6-thiochroman-4-one)-$Cr(CO)_3$ were isolated in 49% and >95% ee, respectively. The free aryl ketones were reduced using the same conditions as their respective chromium complexes, giving aryl alcohols in high ee (>95%). Reactions of non-rigid acetophenone, propriophenone and their tricarbonylchromium complexes resulted in moderate to low ee.

Keywords: Arene complexes; Chromium; Transfer hydrogenation; Resolution; Planar chirality; Ruthenium

1. Introduction

Transfer hydrogenation of ketones by ruthenium(II) catalysts has recently emerged as a good alternative to the widely used catalytic hydrogenation for the production of achiral and chiral alcohols. Its operational simplicity, the easy availability of reductants and the possibility in obtaining products in high yields under mild conditions, avoiding the use of hydrogen gas and reactive metal hydrides, are responsible for the increasing interest in catalytic transfer hydrogenation [1]. The solvents 2-propanol and a formic acid–triethylamine mixture have been used almost exclusively as hydrogen donor in conjunction with Ru(II), amino alcohols and diamines as chiral ligands in asymmetric reductions [2]. Chiral diamine-based Ru^{II} complexes are particularly efficient catalysts for the enantioselective reduction of prochiral ketones under mild conditions using 2-propanol and formic acid as hydrogen source [1g]. This kind of ligand is expensive and employs several steps in its synthesis, in contrast to the large variety and ready availability of chiral amino alcohols which allow optimization of the performance of [Ru(η^6-arene)(2-amino alcohol)] systems in terms of activity and enantioselectivity by varying the structure [1c,3] and the functional groups [4].

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A flaw of transfer hydrogenation using 2-propanol is the reversibility of the reaction and its efficiency is highly dependent on the redox properties of the alcohols formed [1g,5]. However, this tendency can be utilized for kinetic resolution of racemic alcohols using acetone as a hydrogen acceptor [6].

Because of the increasing interest in transfer hydrogenation and its reversibility, preventing complete conversion, we decided to verify the possibility to resolve racemic planar chiral tricarbonyl(η^6-aryl ketone)chromium complexes and the effect caused by the organometallic fragment on the stereochemistry of the products using this method.

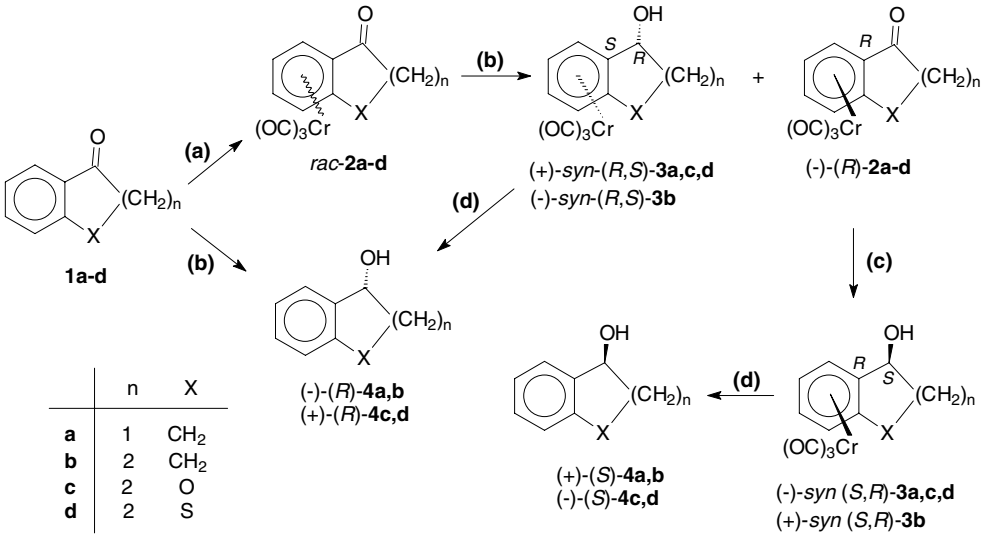
Planar chiral transition-metal complexes, such as ferrocenyl derivatives and tricarbonyl(η^6-arene)chromium compounds, have applications as chiral building blocks for the synthesis of complex organic molecules [7] and as ligands in catalytic reactions [8], including transfer hydrogenation [9]. In the specific case of the tricarbonylchromium fragment on complexation to arenes, modification of steric and eletronic factors and of the symmetry of the substrate ligand can thus be explored in the synthesis of benzene derivatives and dearomatization reactions difficult or impossible to obtain by other methods [7e,7f,10]. Among the various procedures for the preparation of enantiopure planar chiral tricarbonyl(η^6-arene)chromium complexes [11], organometallic aryl alcohols are obtained usually by complexation of racemic alcohols followed by fractionalization of their derivatives [12] or enzymatic resolution [8f,12b]. An efficient method to prepare such complexes of 1-tetralol derivatives consists of the direct diastereoselective coordination of the respective optically active alcohols to the tricarbonylchromium via Kündig's reagent, tricarbonyl(η^6-naphthalene)chromium [13]. The oxidation of enantiomerically enriched (η^6-aryl alcohol)$Cr(CO)_3$ organometallics is normally employed to generate chiral (η^6-aryl ketone)$Cr(CO)_3$ compounds [12,13].

In this work, we investigated a practical system for the direct resolution of racemic mixtures of tricarbonyl(η^6-aryl ketone)chromium. Our strategy consisted in the synthesis of racemic tricarbonylchromium complexes of the bicyclic aryl ketones 1-indanone (**1a**), 1-tetralone (**1b**), 4-chromanone (**1c**) and thiochroman-4-one (**1d**), using the accessible reagent $Cr(CO)_6$ and later reduction of preferentially one enantiomer to the respective alcohol by transfer hydrogenation in 2-propanol catalyzed with chiral 2-amino alcohol-Ru^{II}-(η^6-benzene).

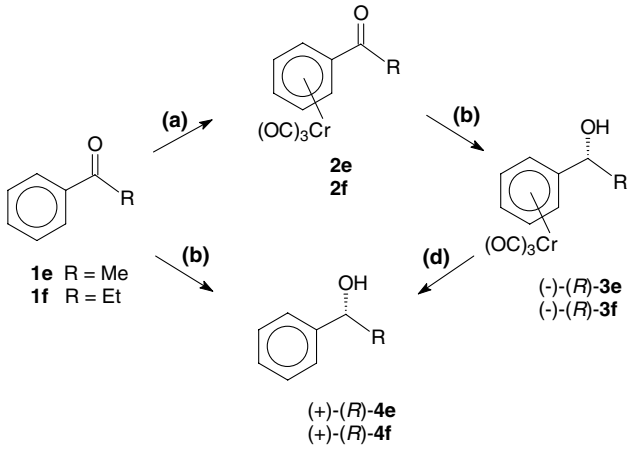
2. Results and discussion

The arene-chromium complexes *rac*-**2a–d** and **2e–f** were synthesized using the standard procedure of refluxing $Cr(CO)_6$ in dibutyl ether:THF (10:1) [14] in the presence of the respective arenes **1a–f** (Schemes 1 and 2). The two faces of the employed cyclic aryl ketones: 1-indanone (**1a**), 1-tetralone (**1b**), 4-chromanone (**1c**) and thiochroman-4-one (**1d**) are enantiotopic and enantiomeric complexes arise from the coordination of the $Cr(CO)_3$ fragment to one of these two faces.

We carried out the catalytic transfer hydrogenation of *rac*-**2a–d**, **2e–f** and of their respective free arenes, **1a–f**, in parallel, for comparison (Schemes 1 and 2). The combinations [$RuCl_2$(η^6-benzene)] and (−)(1*R*,2*S*)-ephedrine (or (+)-(1*S*,2*R*)-norephedrine) were used as catalyst precursor in 2-propanol containing KOH. The reactions were conducted at room temperature (except for the reduction of *rac*-**2c**, carried out at 50 °C, Table 1, entry 4) either overnight or until conversion stabilization.



Scheme 1. (a) $Cr(CO)_6$, Bu_2O:THF (10:1), reflux 24–48 h; (b) 2-PrOH, (−)-ephedrine, [$RuCl_2$(benzene)]$_2$, KOH; (c) $NaBH_4$, EtOH; (d) sunlight, air.



Scheme 2. (a) $Cr(CO)_6$, Bu_2O:THF (10:1), reflux 24–48 h; (b) 2-PrOH, (−)-ephedrine, $[RuCl_2(benzene)]_2$, KOH; (c) $NaBH_4$, EtOH; (d) sunlight, air.

The results of the experiments are summarized in Table 1 (for organochromium complexes) and Table 2 (for free aryl ketones), including conversions, yields, enantiomeric excesses of the alcohols produced and of the remaining organometallic ketones, with optical rotations.

Reduction of the racemic mixture of (η^6-1-indanone)$Cr(CO)_3$ (*rac*-**2a**) showed a conversion of 84% to (+)-*syn*-(1*R*,7a*S*)-(η^6-1-indanol)$Cr(CO)_3$, (*R*,*S*)-**3a** (Table 1, entry 1). This product and the optically active unchanged (−)-(7a*R*)-(η^6-1-indanone)$Cr(CO)_3$, (*R*)-**2a**, were separated by silica gel column chromatography to give yellow and orange solids, respectively (Scheme 1). The ^1H NMR of (*R*,*S*)-**3a** confirmed the *syn* configuration and the positive signal of optical rotation identified the predominant enantiomer [8f,12]. The enantiomeric excess of 31% was determined by GC on

Table 1
Transfer hydrogenation of tricarbonyl(η^6-aryl ketone)chromium compounds in 2-propanol:KOH catalyzed by ruthenium^{II}(η^6 benzene)-(−)-ephedrine complex

Entry	Substrate	Conversion (%)[a]	Alcohol produced				Ketone recovered			
				ee (%)[a]	$[\alpha]_D$[b]	Yield (%)		ee (%)[c]	$[\alpha]_D$[b]	Yield (%)
1	*Rac*-**2a**	84	(*R*,*S*)-**3a**	31[d]	+10(0.42)	56	(*R*)-**2a**	82[d]	−262(0.29)	13
2	*Rac*-**2b**	45	(*R*,*S*)-**3b**	77[d]	−17 (0.36)	20	(*R*)-**2b**	48[d]	−507(1.45)	26
3	*Rac*-**2c**	7	(*R*,*S*)-**3c**	96[e]	–	–	–	–	–	–
4[f]	*Rac*-**2c**	15	(*R*,*S*)-**3c**	97[e]	+243 (0.66)	11	(*R*)-**2c**	25[e]	−241(1.45)	40
5[g]	*Rac*-**2c**	Not observed	–	–	–	–	–	–	–	–
6	*Rac*-**2d**	50	(*R*,*S*)-**3d**	85[e] (95)[e,h]	+295[h] (0.27)	37	(*R*)-**2d**	95[e]	−1320(1.63)	20
7	*Rac*-**2d**	63	(*R*,*S*)-**3d**	70[e] (83)[e,h]	+290[h] (0.95)	40	(*R*)-**2d**	>95[e]	−1388(1.43)	19
8[g]	*Rac*-**2d**	69	(*S*,*R*)-**3d**	49	−162(0.29)	61	(*S*)-**2d**	>95[e]	+1298(1.00)	20
9	**2e**	95	(*R*)-**3e**	33	−6.1(2.3)	44	–	–	–	–
10	**2f**	96	(*R*)-**3f**	4	−3(0.80)	75	-	–	–	–

[a] Determined by GC analysis of the free arene ligands after decomplexation under sunlight/air.
[b] Concentrations of solutions in $CHCl_3$ (g/100 mL) in parenthesis.
[c] Determined after reduction of the ketone complex with borohydride to the respective *syn*-(η^6-aryl alcohol)tricarbonylchromium and GC analysis on chiral phase of the free aryl alcohol obtained after decomplexation under sunlight/air.
[d] Macherey Hydrodex-β 3P capillary column.
[e] Supelco β-dextrin-120 capillary column.
[f] Carried out at 50 °C.
[g] (+)-Norephedrine was used instead of (−)-ephedrine to generate the catalyst.
[h] After recrystallization.

Table 2
Transfer hydrogenation of free aryl ketones in 2-propanol:KOH catalyzed by ruthenium^{II}(η^6benzene)-(−)-ephedrine complex

Entry	Substrate	Conversion (%)[a]	Alcohol	ee (%)[a]	$[\alpha]_D$[b]	Yield (%)
1	**1a**	18	(*R*)-**4a**	96[c]	−29 (0.41)	11
2	**1b**	54	(*R*)-**4b**	96[c]	−37.0 (2.12)	37
3	**1c**	91	(*R*)-**4c**	97[c]	+66.0 (3.03)	76
4[d]	**1c**	54	(*S*)-**4c**	>97[c]	−61 (0.50)	39
5	**1d**	92	(*R*)-**4d**	>97[c]	+141 (2.11)	75
6[d]	**1d**	>99	(*S*)-**4d**	97[c]	−136 (1.00)	80
7	**1e**	97	(*R*)-**4e**	62[e]	–	74
8	**1f**	93	(*R*)-**4f**	41[e]	+10 (2.02)	73

[a] Determined by GC analysis.
[b] Concentrations of solutions in $CHCl_3$ (g/100 mL) in parenthesis.
[c] Supelco β-dextrin-120 capillary column.
[d] (+)-Norephedrine was used instead of (−)-ephedrine to generate the catalyst.
[e] Macherey dydrodex-β 3P capillary column.

a chiral column after photochemical oxidation in air to release the ligand (*R*)-**4a**. The recovered and resolved ketone (*R*)-**2a** showed 82% ee, determined after reduction with sodium borohydride to (−)-*syn*-(*S*,*R*)-**3a** [13,15] followed by decomplexation and GC analysis on a chiral phase of the resultant (*S*)-**4a** (Scheme 1).

A lower conversion (18%) was observed for the reduction of free 1-indanone (**1a**) to 1-indanol (*R*)-**4a**, with 96% ee (Table 2, entry 1). Higher conversions and similar ee were reported with a diamine (*S*,*S*)-TsDPEN and $[RuCl_2(\eta^6\text{-mesitylene})]_2$ combination in 2-propanol (conversion of 45% with 91% ee) [16] or formic acid–triethylamine (conversion >99% and 99% ee) [17].

Hydrogen-transfer reactions of the free 1-tetralone (**1b**) and of the *rac*-$(\eta^6\text{-1-tetralone})Cr(CO)_3$ (*rac*-**2b**) in 2-PrOH, using a (−)-ephedrine and $[RuCl_2(\eta^6\text{-benzene})]_2$ combination, were accompanied by GC on a chiral phase. After 30 min of reaction, the organometallic *rac*-**2b** was reduced to *syn*-(1*R*,8a*S*)-$(\eta^6\text{-1-tetralol})Cr(CO)_3$, (*R*,*S*)-**3b**, with 41% conversion and 84% ee. After 210 min, the conversion was 45% with 78% ee. No gain in conversion was observed after this period. The ^1H and ^{13}C NMR of the crude product displayed signals of *syn*-**3b** and unreacted $(\eta^6\text{-tetralone})Cr(CO)_3$ (**2b**). Separation by silica gel column chromatography gave (−)-(*R*,*S*)-**3b** (20%) and (−)-(*R*)-**2b** (26%) with 77% and 48% ee [18], respectively (Scheme 1, Table 1). The reaction of the free ligand **1b** to give (−)-(*R*)-1-tetralol, (*R*)-**4b**, showed conversion of 60% after 150 min, with excellent enantiomeric excess (98% ee). Additional reaction time was prejudicial. After 24 h of reaction, GC analysis showed 54% of conversion and (*R*)-**4b** was isolated in 37% yield with 96% ee (Table 2, entry 2). Similar results were reported on the reduction of 1-tetralone to 1-tetralol using the more expensive catalytic combinations of $[Ru(\eta^6\text{-cymene})Cl_2]_2$ and *cis*-(1*R*,2*S*)-1-aminoindan-2-ol (40% yield of (*S*)-1-tetralol in 98% ee) [2a] or $[Ru(\eta^6\text{-cymene})Cl_2]_2$ and NH-benzyl (1*R*,2*S*)-norephedrine (68% conversion to (*R*)-1-tetralol in 96% ee) [19].

Reductions of the free 4-chromanone (**1c**) and of the respective racemic tricarbonyl chromium complex (*rac*-**2c**) at room temperature, showed drastically different conversions. To our surprise, only 7% of the organometallic *rac*-**2c** was converted to (+)-(*R*,*S*)-**3c** in 96% ee (Table 1, entry 3), while 91% of the free ligand **1c** was converted to (*R*)-4-chromanol, (*R*)-**4c**, in 76% yield with 97% ee (Table 2, entry 3). At 50 °C, the conversion of *rac*-**2c** to (+)-(*R*,*S*)-**3c** rose to 15% after 6 h of reaction. Extending the reaction time was not effective in increasing the conversion. The product (+)-(*R*,*S*)-**3c** was isolated in 11% yield with high enantioselectivity (97% ee). The unchanged ketone (−)-(*R*)-**2c** was recovered in 40% yield with 25% ee, determined after reduction with borohydride to give (−)-(*S*,*R*)-**3c** [20].

The changing of the heteroatom on the aryl ketone ligand of the organochromium compound, from oxygen (*rac*-**2c**) to sulfur (*rac*-**2d**), resulted in a significant gain of conversion at room temperature: from 7% for *rac*-**2c** (Table 1, entry 3) to 50–63% for *rac*-**2d** (Table 1, entries 6 and 7). The parallel transfer hydrogenation of free thiochroman-4-one (**1d**) gave (*R*)-thiochroman-4-ol, (*R*)-**4d**, in 75% yield (92% conversion) and >97% ee (Table 2, entry 5). This result was similar to that achieved for the reduction of 4-chromanone (**1c**) (Table 2, entry 3), in contrast to the different behaviors observed for the respective organometallic *rac*-**2c** and *rac*-**2d** (Table 1, entries 3, 4, 6 and 7).

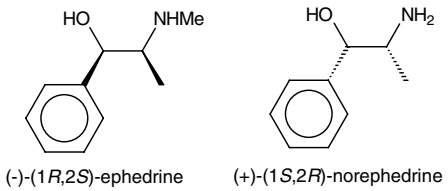
Two experiments were carried out with *rac*-**2d** at room temperature (Table 1, entries 6 and 7). In the first, the enantiomeric excess remained practically unchanged during the reaction (85% ee). The product (+)-tricarbonyl-$(\eta^6\text{-thiochroman-4-ol})$chromium, (+)-**3d**, and the optically active unchanged (−)-**2d** were separated by silica gel column chromatography and crystallized with CH_2Cl_2:hexane to give yellow and red crystals of (+)-**3d** (37% yield) and (−)-**2d** (20% yield), respectively. The ^1H and ^{13}C NMR spectra of (+)-**3d** displayed only the *syn* diastereoisomer resonances, confirmed after comparison with the respective spectra of (−)-*syn*-**3d** (see below). Decomplexation of (+)-**3d** furnished (+)-(*R*)-thiochroman-4-ol, (*R*)-**4d**, with 95% ee (Scheme 1). Consequently, the ee of (+)-*syn*-**3d** was the same (95% ee) and its configuration was attributed as (4*R*,4a*S*)-**3d**, simplified here to (*R*,*S*)-**3d** (Table 1, entry 6).

The reduction of the isolated (−)-**2d** with sodium borohydride gave exclusively the *syn* product (−)-(4*S*,4a*R*)-**3d** [20] in 95% ee, determined for the decomplexed ligand (*S*)-**4** (Scheme 1). This result allowed to determine the *R* configuration for the stereogenic centers on carbons *4a* of (−)-**2d** and (−)-**3d**.

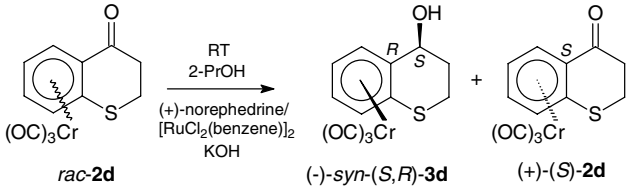
A second experiment carried out with *rac*-**2d** showed an increase in the conversion, 63%, (Table 1, entry 7), but with loss of ee for the alcohol obtained (*R*,*S*)-**3d** (70% ee for the crude product and 83% ee after recrystallization) in comparison to the previous experiment, which gave (+)-(*R*,*S*)-**3d** in 95% ee. We believe that small variations of the temperature and concentrations of the substrate and catalyst components of medium, affected the conversion and the stereoselectivity of the reaction.

Reductions of the non-rigid aryl ketones acetophenone (**1e**) and propiophenone (**1f**) and their respective achiral complexes **2e** and **2f**, with the catalytic system Ru^{II}(benzene)-(−)-ephedrine, resulted in high conversions (93–97%) to their respective alcohols **4e**–**f** and **3e**–**f** (Scheme 2). The reasonable enantiomeric excesses of (*R*)-**4e** (62% ee) and (*R*)-**4f** (41% ee) obtained on the reduction of the free ligands **1e** and **1f** were not surprising with this simple catalytic system (Table 2, entries 7 and 8) [2a]. High ee for the alcohols **4e** and **4f** may be obtained from the free ketones **1e** and **1f** with appropriate catalytic combinations of arene ligand and chiral amino alcohol or diamine auxiliaries on ruthenium

[1g]. The fragment $Cr(CO)_3$ coordinated to the acetophenone and to the propiophenone (complexes **2e** and **2f**) caused a loss in the ee of the aryl alcohols produced: 33% ee for **3e** and 4% ee for **3f** (Table 1, entries 9 and 10).



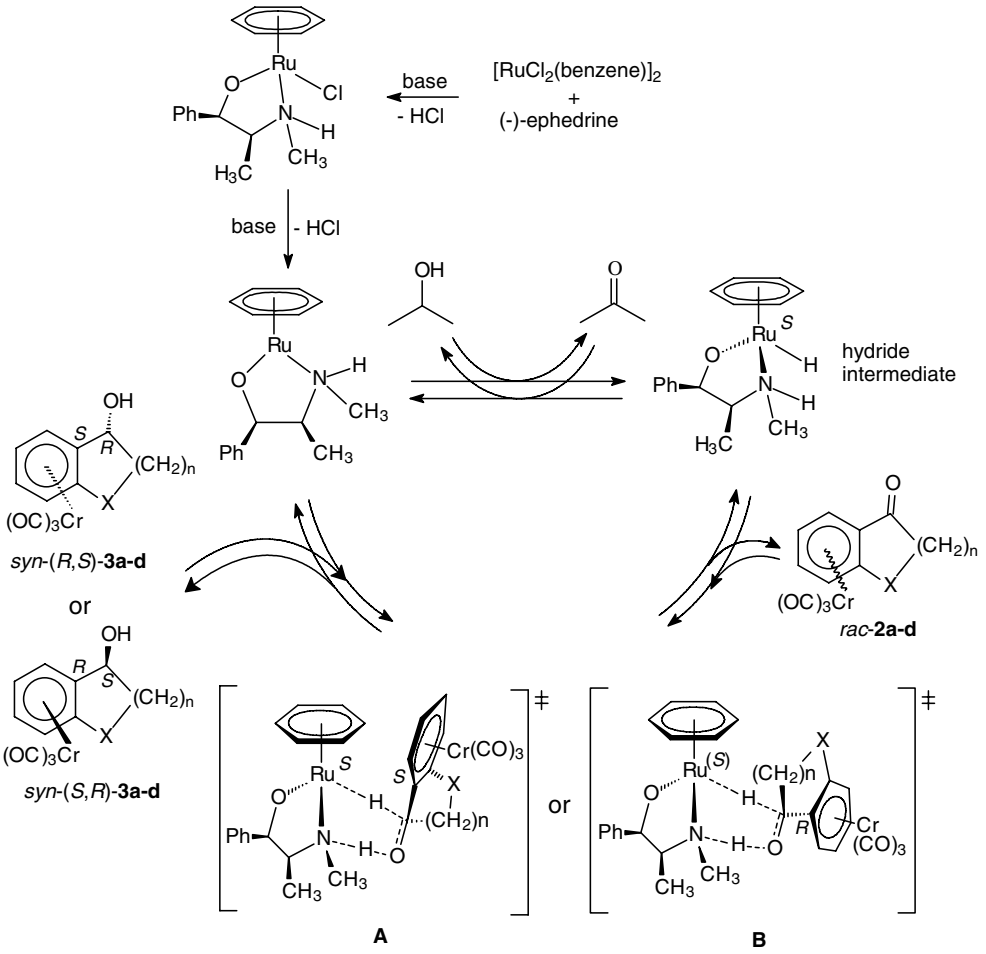
Scheme 3.



Scheme 4.

To verify the influence of the catalyst stereochemistry on the stereoselectivity of the transfer hydrogenation reductions of the racemic tricarbonyl(η^6-aryl ketone)chromium complexes, we carried out the representative reductions of *rac*-**2d** and of the free ligand **1d** with the combination (+)-(1*S*,2*R*)-norephedrine/[$RuCl_2$(η^6-benzene)]$_2$ in 2-propanol. (+)-(1*S*,2*R*)-Norephedrine and (−)-(1*R*,2*S*)-ephedrine are similar molecules with opposite configurations at the stereogenic centers (Scheme 3).

The reduction of *rac*-**2d** by transfer hydrogenation with the combination (+)-(1*S*,2*R*)-norephedrine/[$RuCl_2$(η^6-benzene)]$_2$ in 2-propanol (Scheme 4) showed a conversion of 69% to (*S*,*R*)-**3d** (Table 1, entry 8). The starting material was recovered (20%) as (+)-(*S*)-**2d** (>95% ee) and the alcohol produced, (−)-(*S*,*R*)-**3d**, was isolated in 61% yield (49% ee) after separation by column chromatography. With the same conditions, total conversion was observed for the reduction of the free ligand **1d** to give (−)-(*S*)-**4d** in 80% yield with 97% ee (Table 2, entry 6). These results demonstrated that similar chiral auxiliaries (−)-(1*R*,2*S*)-ephedrine and (+)-(1*S*,2*R*)-norephedrine with ruthenium^{II} catalysts



Scheme 5.

exhibited opposite effects on the stereoselectivity of the hydrogen-transfer reduction of *rac*-**2d** and **1d**.

Rac-**2c** was tentatively reduced with the (+)-(1*S*,2*R*)-norephedrine/[$RuCl_2(\eta^6$-benzene)]$_2$ system, but no conversion was observed. In parallel, the free ligand **1c** was reduced to (*S*)-**4c** (54% conversion) in >97% ee (Table 2, entry 4).

According to Noyori's mechanism for hydrogen transfer reactions catalyzed by Ru^{II}-arene complexes containing 1,2-diamines or 2-amino alcohols as chiral modifiers [2b], the configuration at the Ru stereogenic center is defined by the chiral auxiliary and experimental data and theoretical calculations show that Ru hydride intermediates exist as a single diastereoisomer [21]. In our specific case, the (−)-(1*R*,2*S*)-ephedrine ligand probably leads to the hydride intermediate with *S* configuration at the Ru atom and the (+)-(1*S*,2*R*)-norephedrine leads to the respective intermediate with *R* configuration, since (1*S*,2*R*)-norephedrine derivatives are invoked to generate (*R*)-Ru hydrides, based on NMR and X-ray diffraction studies [22]. According to this proposal, the chiral organometallic ketones (*S*)-**2a**–**d** interact with the Ru hydride catalytic intermediate via the transition state **A** (TS **A**) and the complexes (*R*)-**2a**–**d** interact via TS **B** (Scheme 5). The possibility of TS with the fragment $Cr(CO)_3$ in an internal position was discarded because only *syn*-(η^6-aryl alcohol)$Cr(CO)_3$ diastereoisomers were produced. The ee of the alcohols (*R*,*S*)-**3a**–**d** produced by the reductions of *rac*-**2a**–**d** with the (−)-ephedrine-Ru^{II} catalytic system suggest a preference for TS **A** over TS **B**. The more favorable TS **A** is explained by the CH/π attraction between the η^6-arene-Ru and the aryl substituents in the ketone [23], however, the electron-withdrawing effect of the fragment $Cr(CO)_3$ [7e] probably reduces this attraction, resulting in the lower ee obtained for the complexes (*R*,*S*)-**3a**–**d** and (*R*)-**3e**–**f** (Table 1), in comparison to those observed for the free aryl alcohols (*R*)-**4a**–**f** (Table 2).

3. Conclusions

Our studies using a simple combination of [$RuCl_2(\eta^6$-benzene)]$_2$ and (−)-(1*R*,2*S*)-ephedrine demonstrated that Ru-catalyzed hydrogen transfer in 2-propanol is a practical method for the direct resolution of racemic chiral planar (η^6-arene)$Cr(CO)_3$ with rigid aryl ketones as arene ligands, such as 1-indanone, 1-tetralone, 4-chromanone and thiochroman-4-one. In all cases, the *syn*-(*R*,*S*)-(η^6-aryl alcohol)$Cr(CO)_3$ and (*R*)-(η^6-aryl ketone)$Cr(CO)_3$ complexes were obtained in enantiomeric excess. The use of the chiral auxiliary (+)-(1*S*,2*R*)-norephedrine instead of (−)-(1*R*,2*S*)-ephedrine for the reduction of *rac*-**2d** led to the opposite enantiomers (*S*,*R*)-**3d** and (*S*)-**2d**, demonstrating that the nature of the chiral auxiliary is crucial to define the stereochemistry of the resulting organometallic products. The ee of the recovered organometallic ketones and the organometallic alcohols produced depended of the reaction conversion. Low conversions (<50%) gave alcohols in high to reasonable ee and recovered ketones with low ee (Table 1, entries 2, 3 and 4). High conversions (>50%) showed the contrary effect: alcohols in low to moderate ees and ketones with high and reasonable ee (Table 1, entries 1, 7 and 8). Reduction with 50% of conversion gave more efficient resolutions as observed for the reaction of *rac*-**2d** (Table 1, entry 6). In that experiment, we observed 50% conversion (Table 1, entry 6) to the alcohol (*R*,*S*)-**3d**, crystallized in good ee (95%). The recovered ketone (*R*)-**2d** was also isolated in 95% ee after crystallization. These results open new perspectives in the search for a suitable molecular architecture for chiral metal complexes, coupled with appropriate selection of reaction conditions, which allows an efficient and practical resolution of racemic (η^6-aryl ketone)$Cr(CO)_3$. To our knowledge, this is the first report on the use of hydrogen transfer on the ruthenium-catalyzed reduction of racemic tricarbonyl(η^6-aryl ketone)chromium complexes.

4. Experimental

All reagents and solvents were obtained from commercial sources. Ethyl acetate, hexane and chloroform were distilled under argon before use. The solvents dichloromethane and methanol were distilled under argon from suspensions over calcium hydride and calcium oxide, respectively. Hexane, THF and dibutyl ether were distilled under argon from a mixture containing sodium. Thin layer chromatography (TLC) analyses was performed with precoated aluminium sheets (silica gel 60 Merck) and flash column chromatography was carried out on silica (200–400 mesh, Merck). IR spectra were recorded on a FT-IR BOMEM MB-100 from Hartmann & Braun. ^{1}H NMR spectra were determined at 300 (Varian Gemini 300) or 500 MHz (INOVA-500), and ^{13}C NMR spectra were determined at 75.5 MHz (Varian Gemini 300) or 125.7 MHz (INOVA 500). Chemical shifts are reported in ppm relative to tetramethylsilane (TMS) in $CDCl_3$. Gas chromatographic analyses and mass spectra were obtained on a QP 5000-SHIMADZU or an AGILENT CG 6890/HEWLETT PACKARD 5973 equipped with J. & W. Scientific HP-5 (5% phenylmethylpolysiloxane, 30.0 m × 250 μm × 0.25 μm), Supelco 10710-01B β-dextrin-120 (25.0 m × 250 μm × 0.25 μm) or Macherey 212117/91 Hydrodex-β 3P (25.0 m × 250 μm × 0.25 μm) capillary columns. For tricarbonyl(η^6-arene)chromium compounds, decomplexation under sunlight/air and filtration through a short column of silica and celite was necessary before GC analyses. Gas chromatographic analyses of reaction

mixture samples were made after evaporation, dilution with ethyl acetate, decomplexation under sunlight/air (for chromium complexes) and filtration through a short column of silica and celite. Elemental analyses were performed on a Perkin–Elmer 2400 CHN microanalyser. High-resolution mass spectrum was determined on a VG AUTO SPEC Micromass. Optical rotations were measured with a Perkin–Elmer Polarimeter 341. Melting points were measured on a Microquimica MQ APF-301.

4.1. Synthesis of tricarbonyl(η^6-aryl ketone)chromium complexes rac-**2a–d**, **2e–f**

The complexes were prepared according to the method of Pauson and co-workers [14].

4.1.1. Rac-tricarbonyl(η^6-1-indanone)chromium (rac-**2a**)

Yield: 25% of an orange solid; m.p. 122.5–123.5 °C. IR (Nujol, cm^{-1}): 1969 (vs), 1900 (sh), 1889 (vs), 1713 (s). ^1H NMR ($CDCl_3$, 500 MHz): δ 6.02 (d, J = 6.4 Hz, 1H, Ph), 5.71 (t, J = 6.1 Hz, 1H, Ph), 5.42 (d, J = 6.1 Hz, 1H, Ph), 5.19 (t, J = 6.1 Hz, 1H, Ph), 3.13 [ddd, 1H, J = 16.8 Hz, J = 8.9 Hz, J = 5.5 Hz, C*H*HC(O)], 3.02 [ddd, 1H, J = 16.5 Hz, J = 8.2 Hz, J = 2.1 Hz, CH*H*C(O)], 2.73 (ddd, 1H, J = 19.2 Hz, J = 8.2 Hz, J = 5.2 Hz, C*H*HCH$_2$), 2.63 (ddd, 1H, J = 18.9 Hz, J = 8.9 Hz, J = 2.1 Hz, CH*H*CH$_2$CH$_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 125.7 MHz): δ 230.03 (*C*≡O), 202.40 (*C*=O), 123.15 (Ph), 96.00 (Ph), 95.44 (Ph), 89.76 (Ph), 88.25 (Ph), 86.89 (Ph), 34.53 [C(O)*C*H$_2$], 24.95 (*C*H$_2$). Anal. Calc. for $C_{12}H_8CrO_4$ (268.18 g mol^{-1}): C, 53.74; H, 3.01. Found: C, 53.80; H, 2.82%.

4.1.2. Rac-tricarbonyl(η^6-1-tetralone)chromium (rac-**2b**)

Yield: 30% of an orange solid; m.p. 125–126 °C; lit. [24]: 125–127 °C. IR (Nujol, cm^{-1}): 1970 (vs), 1878 (vs), 1671 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 6.17 (d, J = 6.7 Hz, 1H, Ph), 5.63 (t, J = 6.1 Hz, 1H, Ph), 5.29 (t, J = 6.4 Hz, 1H, Ph), 5.15 (d, J = 6.2 Hz, 1H, Ph), 2.97 [m, 1H, CH$_2$], 2.77 [br s, 1H, CH$_2$], 2.72 [br t, 1H, CH$_2$], 2.45 [m, 1H, CH$_2$], 2.25–2.08 [m, 2H, CH$_2$]. $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75.5 MHz): δ 230.18 (*C*≡O), 195.54 (*C*=O), 115.13 (Ph), 94.63 (Ph), 92.62 (Ph), 91.18 (Ph), 89.70 (Ph), 89.10 (Ph), 37.87 [C(O)*C*H$_2$], 28.51 (*C*H$_2$), 21.84 (*C*H$_2$). Anal. Calc. for $C_{13}H_{10}CrO_4$ (282.22 g mol^{-1}): C, 55.33; H, 3.57. Found: C, 55.34; H, 3.53%.

4.1.3. Rac-tricarbonyl(η^6-4-chromanone)chromium (rac-**2c**)

Yield: 40% of an orange solid; m.p. 121–122 °C. IR (Nujol, cm^{-1}): 1972 (vs), 1913 (vs), 1880 (vs), 1852 (m), 1692 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 6.19 (d, J = 6.2 Hz, 1H, Ph), 5.76 (t, J = 6.2 Hz, 1H, Ph), 5.22 (d, J = 6.0 Hz, 1H, Ph), 5.03 (t, J = 6.2 Hz, 1H, Ph), 4.59–4.41 (m, 2H, OC*H*$_2$CH$_2$C(O)], 2.88 [ddd, J = 17.2 Hz, J = 6.2 Hz, J = 4.7 Hz, 1H, OCH$_2$C*H*HC(O)], 2.77 [ddd, 1H, J = 17.2 Hz, J = 9.1 Hz, J = 5.1 Hz, OCH$_2$CH*H*C(O)]. $^{13}C^1H$ NMR ($CDCl_3$, 75.5 MHz): δ 230.19 (*C*≡O), 189.29 (*C*=O), 144.13 (Ph), 95.23 (Ph), 90.04 (Ph), 85.12 (Ph), 82.03 (Ph), 79.28 (Ph), 66.99 (O*C*H$_2$), 36.79 [C(O)*C*H$_2$]. Anal. Calc. for $C_{12}H_8CrO_5$ (284.19 g mol^{-1}): C, 50.72; H, 2.84. Found: C, 50.59; H, 2.71%.

4.1.4. Rac-tricarbonyl(η^6-thiochroman-4-one)chromium (rac-**2d**)

Yield: 38% of a red solid; m.p. 137.5–138.5 °C. IR (Nujol, cm^{-1}): 1975 (vs), 1898 (vs), 1876 (vs), 1679 (sh), 1660 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 6.32 (dd, J = 6.6 Hz, J = 1.1 Hz, 1H, Ph), 5.73 (td, J = 6.2 Hz, J = 1.1 Hz, 1H, Ph), 5.29 (dd, J = 6.6 Hz, J = 0.7 Hz, 1H, Ph), 5.15 (td, J = 6.4 Hz, J = 1.1 Hz, 1H, Ph), 3.50–3.34 (m, 1H, CH$_2$), 3.15–3.04 (m, 2H, CH$_2$), 2.92–2.78 (m, 1H, CH$_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75.5 MHz): δ 230.32 (*C*≡O), 192.22 (*C*=O), 118.86 (Ph), 94.66 (Ph), 91.67 (Ph), 88.81 (Ph), 88.36 (Ph), 86.90 (Ph), 38.79 [C(O)*C*H$_2$], 26.20 (S*C*H$_2$). Anal. Calc. for $C_{12}H_8CrO_4S$ (300.24 g mol^{-1}): C, 48.00; H, 2.69. Found: C, 48.16; H, 2.66%.

4.1.5. Tricarbonyl(η^6-acetophenone)chromium (**2e**)

Yield: 19% of an orange solid (via its dioxolane derivative); m.p. 85–86 °C; lit. [25]: 84–85 °C. IR (Nujol, cm^{-1}): 1964 (vs), 1904 (vs), 1887 (vs),1687 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 6.06 (br d, J = 6.2 Hz, 2H, Ph), 5.65 (br t, J = 6.2 Hz, 1H, Ph), 5.29 (br t, J = 6.2 Hz, 2H, Ph), 2.46 (s, 3H, C*H*$_3$). Anal. Calc. for $C_{11}H_8CrO_4$ (256.17 g mol^{-1}): C, 51.57; H, 3.15. Found: C, 51.70; H, 2.86%.

4.1.6. Tricarbonyl(η^6-propiophenone)chromium (**2f**)

Yield: 20% of an orange solid; m.p. 96–97 °C. IR (Nujol, cm^{-1}): 1979 (vs), 1965 (vs), 1904 (vs), 1880 (vs), 1681 (s). ^1H NMR ($CDCl_3$, 300 MHz): δ 6.08 (dd, J = 6.8 Hz, J = 0.9 Hz, 2H, Ph), 5.64 (br t, J = 6.6 Hz, 1H, Ph), 5.30 (t, J = 6.6 Hz, 2H, Ph), 2.80 (q, J = 7.3 Hz, 2H, C*H*$_2$) 1.23 (t, J = 7.3 Hz, 3H, C*H*$_3$). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75.5 MHz): δ 230.65 (*C*≡O), 197.82 (*C*=O), 144.13 (Ph), 95.57 (Ph), 95.01 (Ph), 93.83 (Ph), 89.38 (Ph), 30.51 (*C*H$_2$), 8.07 (*C*H$_3$). Anal. Calc. for $C_{12}H_{10}CrO_4$ (270.20 g mol^{-1}): C, 53.34; H, 3.73. Found: C, 53.25; H, 3.51%.

4.2. General procedure for the hydrogen-transfer reduction of the ketones **1a–f**, rac-**2a–d**, **2e–f**

A solution of [RuCl$_2$(η^6-benzene)]$_2$ (6 μmol) and (−)-(1*R*,*S*)-ephedrine hemi-sulfate (24 μmol) in dry 2-propanol (3 mL) was heated at 80 °C for 30 min under argon. It was cooled to room temperature and transferred to a flask containing a solution of the ketone (0.6 mmol) and

KOH (60 μmol) in 2-propanol (3 mL). The resulting mixture was then stirred at room temperature under argon. After evaporation of volatiles under vacuum the products were purified by flash column chromatography on silica gel.

4.2.1. Hydrogen-transfer reduction of 1-indanone (**1a**) (Table 2, entry 1)

(*R*)-1-indanol [(*R*)-**4a**] was isolated as a white solid in 11% yield after flash chromatography on silica gel (ethyl acetate:hexane: 1:9); m.p. 66.5–68.0 °C, $[\alpha]_D^{23} = -29°$ (*c* 0.41, $CHCl_3$), 96% ee. Lit. [12]; m.p. 72 °C, $[\alpha]_D^{22} = +34°$ (*c* 1.895, $CHCl_3$) for *S* enantiomer. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.46–7.42 (m, 1H, Ph), 7.24–7.20 (m, 2H, Ph), 7.14–7.10 (m, 1H, Ph), 5.27 (br t, *J* = 5.9 Hz, 1H, C*H*OH), 3.07 [ddd, *J* = 16.2 Hz, *J* = 8.4 Hz, *J* = 4.8 Hz, 1H, C*H*HCH$_2$CH(OH)], 2.84 (br dd, *J* = 16.2 Hz, *J* = 7.0 Hz, 1H, CH*H*CH$_2$C(OH)H), 2.51 (m, 1H, C*H*HC(OH)H), 1.97 (m, 1H, CH*H*C(OH)H), 1.75 (br s, 1H, O*H*). MS (EI): *m*/*z* (rel intensity) 134 (M^+, 51), 133 (100), 117 (12), 116 (14), 115 (28), 105 (30), 103 (12), 91 (32), 89 (9), 79 (25), 78 (15), 77 (45), 74 (2), 66 (16), 65 (22), 63 (25), 57 (25), 55 (32), 53 (9), 52 (13), 51 (57), 50 (29).

Recovered **1a**: 45%.

4.2.2. Hydrogen-transfer reduction of 1-tetralone (**1b**) (Table 2, entry 2)

(*R*)-1-tetralol [(*R*)-**4b**] was isolated as a colorless oil in 37% yield after flash chromatography on silica gel (ethyl acetate:hexane: 1:9). $[\alpha]_D^{22} = -37.0°$ (*c* 2.12, $CHCl_3$), 96% ee. Lit. [2a]: $[\alpha]_D$ =+34.4° (*c* 1.01, $CHCl_3$) for *S* enantiomer. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.46–7.42 (m, 1H, Ph), 7.24–7.20 (m, 2H, Ph), 7.14–7.10 (m, 1H, Ph), 4.79 (apparent t, *J* = 4.4 Hz, 1H, C*H*OH), 2.85–2.65 (m, 2H, CH_2), 2.05–1.75 (m, 5H, CH_2, CH_2, O*H*). MS (EI): *m*/*z* (rel intensity) 148 (M^+, 18), 147 (25), 131 (18), 129 (43), 128 (20), 127 (13), 121 (8), 120 (80), 119 (67), 115 (28), 105 (47), 104 (15), 92 (20), 91 (100), 90 (15), 89 (15), 79 (10), 78 (30), 77 (34), 66 (10), 65 (47), 64 (30), 63 (41), 62 (10), 60 (10), 57 (11), 55 (10), 53 (14), 52 (16), 51 (69), 50 (28), 43 (23), 41 (31), 40 (12).

Recovered **1b**: 39%.

4.2.3. Hydrogen-transfer reduction of 4-chromanone (**1c**) (Table 2, entry 3)

(*R*)-4-chromanol [(*R*)-**4c**] was isolated as a white solid in 76% yield after flash chromatography on silica gel (ethyl acetate:hexane: 1:9); m.p. 73–74 °C. $[\alpha]_D^{22}$ = +66.0° (*c* 3.03, $CHCl_3$), 97% ee. Lit. [26]: m.p. 77–78 °C, $[\alpha]_D$ = + 68.7° (*c* 0.49, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.33 (dd, *J* = 7.3 Hz, *J* = 1.2 Hz, 1H, Ph), 7.22 (m, 1H, *J* = 7.9 Hz, *J* = 1.5 Hz, 1H, Ph), 6.93 (br t, *J* = 7.3 Hz, 1H, Ph), 6.86 (br d, *J* = 8.4 Hz, 1H, Ph), 4.81 (bt, 1H, C*H*OH), 4.31–4.26 (m, 2H, OCH_2), 2.20–2.00 (m, 2H, CH(OH)CH_2), 1.86 (br s, 1H, O*H*). MS (EI): *m*/*z* (rel intensity) 151 (9), 150 (M^+, 82), 133 (18), 132 (15), 131 (41), 122 (59), 121 (100), 120 (8), 107 (22), 105 (27), 104 (19), 103 (15), 94 (13), 93 (13), 92 (8), 91 (11), 79 (15), 78 (10), 77 (45), 76 (20), 75 (8), 74 (9), 66 (20), 65 (47), 64 (12), 63 (23), 55 (19), 53 (15), 52 (13), 51 (62), 50 (32), 43 (14), 40 (17).

4.2.4. Hydrogen-transfer reduction of thiochroman-4-one (**1d**) (Table 2, entry 5)

(*R*)-thiochroman-4-ol [(*R*)-**4d**] was isolated as a white solid in 75% yield after flash chromatography on silica gel (ethyl acetate:hexane: 1:9); m.p. 79.5–80.5 °C. $[\alpha]_D^{22} = +141°$ (*c* 2.11, $CHCl_3$), >97% ee. Lit. [27]: m.p. 77–79 °C, $[\alpha]_D$ = + 129° (*c* 1.3, MeOH). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.33 (br d, *J* = 7.0 Hz, 1H, Ph), 7.20–7.13 (m, 2H, Ph), 7.11–7.05 (m, 1H, Ph), 4.83 (dd, *J* = 4.4 Hz, *J* = 2.9 Hz, 1H, C*H*OH), 3.34 (dt, *J* = 12.4 Hz, *J* = 2.9 Hz, 1H, SC*H*H), 2.88 (ddd, *J* = 12.8 Hz, *J* = 5.7 Hz, *J* = 3.7 Hz, 1H, SCH*H*), 2.37 (m, 1H, CH(OH)C*H*H), 2.07 (m, 1H, CH(OH)CH*H*), 1.82 (br d, *J* = 4.4 Hz, 1H, O*H*). MS (EI): *m*/*z* (rel intensity) 168 (3), 167 (6), 166 (M^+, 56), 165 (4), 150 (5), 149 (13), 148 (57), 147 (100), 138 (47), 137 (67), 136 (6), 135 (5), 134 (9), 133 (8), 132 (5), 123 (5), 121 (5), 116 (8), 115 (13), 110 (20), 109 (32), 108 (9), 105 (33), 104 (68), 91 (12), 77 (40), 76 (27), 74 (13), 73 (13), 69 (31), 66 (25), 65 (35), 63 (18), 55 (27), 51 (49), 50 (30), 45 (55).

4.2.5. Hydrogen-transfer reduction of acetophenone (**1e**) (Table 2, entry 7)

(*R*)-1-phenylethanol [(*R*)-**4e**] was isolated as colorless oil in 74% yield after flash chromatography on silica gel (ethyl acetate:hexane: 1:9) in 62% ee. MS (EI): *m*/*z* (rel intensity) 122 (M^+, 22), 108 (8), 105 (13), 103 (5), 91 (4), 80 (8), 79 (100), 78 (28), 77 (70), 76(4), 74 (5), 63 (8), 53 (30), 52 (15), 51 (54), 50 (23), 45 (14), 44 (13), 43 (98).

4.2.6. Hydrogen-transfer reduction of propiophenone (**1f**) (Table 2, entry 8)

(*R*)-1-phenylpropanol [(*R*)-**4f**] was isolated as a colorless oil in 73% yield after flash chromatography on silica gel (ethyl acetate:hexane: 1:9). $[\alpha]_D^{22} = +10°$ (*c* 2.02, $CHCl_3$), 41% ee. Lit. [17]: $[\alpha]_D$ − 34.0° (*c* 5.03, EtOH), for *S* enantiomer in 97% ee. MS (EI): *m*/*z* (rel intensity) 136 (M^+, 8), 117 (3), 108 (7), 107 (100), 105 (9), 91 (4), 80 (6), 79 (97), 78 (12), 77 (58), 74 (2), 63 (5), 57 (8), 53 (6), 52 (8), 51 (35), 50 (13), 43 (8), 41 (4).

4.2.7. Hydrogen-transfer reduction of rac-**2a** (Table 1, entry 1)

(*R*)-**2a** and (*R*,*S*)-**3a** were isolated as orange and yellow solids in 13% and 56% yields, respectively, after flash chromatography on silica gel (ethyl acetate:dichloromethane:hexane: 1:10:10) and crystallization from dichloromethane:hexane.

*4.2.7.1. (−)-(7aR)-tricarbonyl(η⁶-1-indanone)chromium [(R)-**2a**].* M.p. 138.5–140.0 °C; $[\alpha]_D^{23} = -262°$ (*c* 0.29, $CHCl_3$), 82% ee. Lit. [12]: m.p. 143 °C; $[\alpha]_D^{22} = -334°$ (*c* 1.165, $CHCl_3$). ^1H NMR analysis was in good agreement with *rac*-**2a** (Section 4.1.1).

*4.2.7.2. (+)-(1R,7aS)-tricarbonyl(η⁶-1-indanol)chromium [(R,S)-**3a**].* $[\alpha]_D^{22} = +10°$ (*c* 0.42, $CHCl_3$), 31% ee. Lit.: $[\alpha]_D^{22} = +61°$ (*c* 1.0, $CHCl_3$) [8f], $[\alpha]_D^{22} = +60.9°$ (*c* 2.07, $CHCl_3$) [12]. ^1H NMR ($CDCl_3$, 500 MHz): δ 5.69 (d, *J* = 6.4 Hz, 1H, Ph), 5.45 (t, *J* = 6.4 Hz, 1H, Ph), 5.27 (d, *J* = 6.4 Hz, 1H, Ph), 5.16 (t, *J* = 6.1 Hz, 1H, Ph), 5.05 (ddd, $J_{1,-OH}$ = 10.7 Hz, $J_{1,2}$ = 8.9 Hz, $J_{1,2'}$ = 7.6 Hz, 1H, C*H*OH), 2.75–2.71 (m, 2H), 2.54 (m, 1H, CH(OH)C*H*H], 1.79 (dq, *J* = 12.5 Hz, *J* = 9.5 Hz, 1H), 1.68 (d, $J_{1,-OH}$ = 10.7 Hz, O*H*). The ^1H NMR analysis was in good agreement with the literature [8f].

*4.2.8. Hydrogen-transfer reduction of rac-**2b** (Table 1, entry 2)*

(*R*)-**2b** and (*R*,*S*)-**3b** were isolated as orange and yellow solids in 26% and 20% yields, respectively, after flash chromatography on silica gel (ethyl acetate:dichloromethane:hexane: 1:10:10) and crystallization from dichloromethane:hexane.

*4.2.8.1. (−)-(8aR)-tricarbonyl(η⁶-1-tetralone)chromium [(R)-**2b**].* M.p. 113.5–116 °C; $[\alpha]_D^{23} = -507°$ (*c* 1.45, $CHCl_3$), 48% ee. Lit.: m.p. 119 °C, $[\alpha]_D = -864°$ (*c* 1.55, $CHCl_3$) [12]; $[\alpha]_D^{20} = -802°$ ($CHCl_3$), 92% ee [13]. ^1H NMR analysis is in good agreement with *rac*-**2b** (Section 4.1.2).

*4.2.8.2. (−)-(1R,8aS)-tricarbonyl(η⁶-1-tetralol)chromium [(R,S)-**3b**].* M.p. 130–133 °C (dec.); $[\alpha]_D^{23} = -17°$ (*c* 0.36, $CHCl_3$), 77% ee. Lit. [8f]: m.p. 140 °C; $[\alpha]_D = -20°$ (*c* 1.45, $CHCl_3$). ^1H NMR ($CDCl_3$, 500 MHz): δ 5.84 (d, *J* = 6.4 Hz, 1H, Ph), 5.52 (t, *J* = 6.4 Hz, 1H, Ph), 5.15 (t, *J* = 6.4 Hz, 1H, Ph), 5.10 (d, *J* = 6.4 Hz, 1H, Ph), 4.55–4.49 (m, 1H, C*H*(OH)], 2.79–2.72 (m, 1H), 2.61 (apparent dt, *J* = 16.8 Hz, *J* = 4.8 Hz, 1H), 2.14–2.09 (m, 1H), 2.02–1.94 (m, 1H), 1.75–1.68 (m, 2H), 1.62 (d, $J_{1,-OH}$ = 10.1 Hz, O*H*). ^1H NMR analysis was in good agreement with the literature [28].

*4.2.9. Hydrogen-transfer reduction of rac-**2c** at 50 °C (Table 1, entry 4)*

(*R*)-**2c** and (*R*,*S*)-**3c** were isolated as orange and yellow solids in 40% and 11% yields, respectively, after flash chromatography on silica gel (ethyl acetate:hexane: 4:6) and crystallization from dichloromethane:hexane.

*4.2.9.1. (−)-(4aR)-tricarbonyl(η⁶-4-chromanone)chromium [(R)-**2c**].* M.p. 120–122 °C. $[\alpha]_D^{20} = -241°$ (*c* 1.45, $CHCl_3$), 25% ee. ^1H and $^{13}C\{^1H\}$ NMR analyses were in good agreement with *rac*-**2c** (Section 4.1.3).

*4.2.9.2. (+)-(4R,4aS)-tricarbonyl(η⁶-4-chromanol)chromium [(R,S)-**3c**].* $[\alpha]_D^{22} = +243°$ (*c* 0.66, $CHCl_3$), 97% ee. IR (Nujol, cm^{-1}): 3581 (m), 3557 (m), 1953 (vs), 1932 (s), 1880 (sh), 1859 (vs), 1826 (sh). ^1H NMR ($CDCl_3$, 300 MHz): δ 5.83 (dd, *J* = 6.2 Hz, *J* = 1.1 Hz, 1H, Ph), 5.63 (dt, *J* = 6.4 Hz, *J* = 1.1 Hz, 1H, Ph), 5.02 (br d, *J* = 6.9 Hz, 1H, Ph), 4.82 (dt, *J* = 6.3 Hz, *J* = 0.7 Hz, 1H, Ph), 4.59 (ddd, $J_{4,-OH}$ = 9.1 Hz, *J* = 6.6 Hz, *J* = 5.1 Hz, 1H, C*H*OH), 4.31 (ddd, *J* = 11.7 Hz, *J* = 6.9 Hz, *J* = 3.3 Hz, 1H, OC*H*H), 4.16 (ddd, *J* = 11.7 Hz, *J* = 6.9 Hz, *J* = 3.3 Hz, 1H, OCH*H*), 2.24–2.04 (m, 2H, CH(OH)CH_2], 1.64 (d, $J_{4,-OH}$ = 9.1 Hz, O*H*). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75.5 MHz): δ 232.66 (*C*≡O), 99.02 (Ph), 96.50 (Ph), 94.49 (Ph), 83.39 (Ph), 77.89 (Ph), 64.25 (*C*HOH), 61.53 (O*C*H_2), 31.31 (CH(OH)*C*H_2). EIHRMS Found: 285.99265. Calc. for $C_{12}H_{10}CrO_5$: 285.99333.

*4.2.10. Hydrogen-transfer reduction of rac-**2d** (Table 1, entry 6)*

(*R*)-**2d** and (*R*,*S*)-**3d** were isolated as red and yellow solids in 20% and 37% yields, respectively, after flash chromatography on silica gel (ethyl acetate:hexane: 4:6) and recrystallization from dichloromethane/hexane.

*4.2.10.1. (−)-(4aR)-tricarbonyl(η⁶-thiochroman-4-one)chromium [(R)-**2d**].* M.p. 151.5–153 °C. $[\alpha]_D^{20} = -1320°$ (*c* 1.63, $CHCl_3$), 95% ee. IR, ^1H and $^{13}C\{^1H\}$ NMR analyses were in good agreement with *rac*-**2d** (Section 4.1.4).

*4.2.10.2. (+)-(4R,4aS)-tricarbonyl(η⁶-thiochroman-4-ol)chromium [(R,S)-**3d**].* $[\alpha]_D^{20} = +295°$ (*c* 0.27, $CHCl_3$), 95% ee. IR (Nujol, cm^{-1}): 3371 (br m), 1943 (vs), 1881 (vs), 1868 (vs), 1859 (vs), 1831 (m). ^1H NMR ($CDCl_3$, 300 MHz): δ 5.93 (br d, *J* = 6.6 Hz, 1H, Ph), 5.58 (br t, *J* = 6.6 Hz, 1H, Ph), 5.14 (br d, *J* = 6.6 Hz, 1H, Ph), 4.97 (br t, *J* = 6.6 Hz, 1H, Ph), 4.58 (dt, $J_{4,-OH}$ = 8.8 Hz, *J* = 8.4 Hz, *J* = 4.4 Hz, 1H, C*H*OH), 3.15–3.01 (m, 2H, SCH_2), 2.43–2.33 (m, 1H, CH(OH)C*H*H], 2.30–2.17 (m, 1H, CH(OH)CH*H*), 1.74 (d, $J_{4,-OH}$ = 8.8 Hz, O*H*). $^{13}C\{^1H\}$ NMR ($CDCl_3$, 75.5 MHz): δ 232.80 (*C*≡O), 107.93 (Ph), 95.13 (Ph), 94.09 (Ph), 86.01 (Ph), 85.90 (Ph), 65.27 (*C*HOH), 31.93 (CH(OH)*C*H_2), 23.98 (S*C*H_2). Anal. Calc. for $C_{12}H_{10}CrO_4S$ (302.26 g mol^{-1}): C, 47.68; H, 3.33. Found: C, 47.35; H, 3.23%.

*4.2.11. Hydrogen-transfer reduction of **2e** (Table 1, entry 9)*

(−)-(1*R*)-tricarbonyl(η⁶-1-phenylethanol)chromium [(*R*)-**3e**] was isolated as a yellow oil in 44% yield after flash chromatography on silica gel (ethyl acetate:hexane: 4:6). $[\alpha]_D^{24} = -6.1$ °C (*c* 2.3, $CHCl_3$), 33% ee. Lit. [29]: $[\alpha]_D^{22} = +18°$ (*c* 2.1, $CHCl_3$) for *S* enantiomer in 89% ee. IR (Nujol, cm^{-1}): 3412 (br m), 1960 (vs), 1871 (vs).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.58 (br d, J = 6.2 Hz, 1H, Ph), 5.45–5.28 (m, 4H, Ph), 4.58 (m, $J_{1,2}$ = 6.2 Hz, $J_{1,-OH}$ = 4.0 Hz, 1H, C*H*OH), 2.03 (br d, $J_{1,-OH}$ = 4.0 Hz, 1H, O*H*), 1.50 (d, $J_{1,2}$ = 6.6 Hz, 3H, CH_3). ^{13}C{^{1}H} NMR ($CDCl_3$, 75.5 MHz): δ 232.35 (*C*≡O), 117.14 (Ph), 92.77 (Ph), 92.53 (Ph), 92.14 (Ph), 90.80 (Ph), 89.46 (Ph), 68.31 (*C*HOH), 25.33 (*C*H_3).

4.2.12. Hydrogen-transfer reduction of **2f** (Table 1, entry 10)

(−)-(1*R*)-tricarbonyl(η^6-1-phenylpropanol)chromium [(*R*)-**3f**] was isolated as an yellow oil in 75% yield after flash chromatography on silica gel (ethyl acetate:hexane: 4/6). $[\alpha]_D^{24} = -3°$ (*c* 0.80, $CHCl_3$), 4% ee. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.59 (br d, J = 6.6 Hz, 1H, Ph), 5.45–5.23 (m, 4H, Ph), 4.30 (dt, $J_{1,2}$ = 6.2 Hz, $J_{1,-OH}$ = 3.6 Hz, 1H, C*H*OH), 1.99 (br d, $J_{1,-OH}$ = 3.6 Hz, 1H, O*H*), 1.75 (quint., J = 7.2 Hz, 2H, CH_2), 1.03 (t, $J_{2,3}$ = 7.3 Hz, 3H, CH_3). ^{13}C{^{1}H} NMR ($CDCl_3$, 75.5 MHz): δ 232.66 (*C*≡O), 116.49 (Ph), 92.86 (Ph), 92.52 (Ph), 92.14 (Ph), 91.34 (Ph), 89.39 (Ph), 73.41 (*C*HOH), 32.39 (CH_2), 10.10 (*C*H_3).

4.3. Hydrogen-transfer reduction of **1c**, **1d** and rac-**2d** using (+)-(1*S*,2*R*)-norephedrine as chiral ligand

The general procedure for the hydrogen-transfer reduction (Section 4.2) was used with (+)-(1*S*,2*R*)-norephedrine instead of the (−)-(1*R*,2*S*)-ephedrine hemisulfate.

4.3.1. Hydrogen-transfer reduction of **1c** (Table 2, entry 4)

(−)-(*S*)-4-chromanol [(*S*)-**4c**] was isolated as a white solid in 39% yield after flash chromatography on silica gel (ethyl acetate:hexane: 1:9); m.p. 73.5–75.0 °C; $[\alpha]_D^{22} = -61°$ (*c* 0.50, $CHCl_3$), >97% ee. Lit. [26]: m.p. 77–78 °C; $[\alpha]_D$ = +68.7° (*c* 0.49, $CHCl_3$) for *R* enantiomer. ^{1}H NMR analysis was in good agreement with (*R*)-**4c** (Section 4.2.3).

Recovered **1c**: 37%.

4.3.2. Hydrogen-transfer reduction of **1d** (Table 2, entry 6)

(−)-(*S*)-thiochroman-4-ol [(*S*)-**4d**] was isolated as a white solid in 80% yield after flash chromatography on silica gel (ethyl acetate:hexane: 1:9); m.p. 77.5–79.5 °C. $[\alpha]_D^{22} = -136°$ (*c* 1.00, $CHCl_3$), 97 % ee. ^{1}H NMR and MS (EI) analyses were in good agreement with (*R*)-**4d** (Section 4.2.4).

4.3.3. Hydrogen-transfer reduction of rac-**2d** (Table 1, entry 8)

(*S*)-**2d** and (*S*,*R*)-**3d** were isolated as red and yellow solids in 20% and 61% yields, respectively, after flash chromatography on silica gel (ethyl acetate:hexane: 4:6).

4.3.3.1. (+)-(4a*S*)-tricarbonyl(η^6-thiochroman-4-one) chromium [(*S*)-**2d**].

M.p. 150–152.5 °C. $[\alpha]_D^{22} = +1298°$ (*c* 1.00, $CHCl_3$), >95% ee. ^{1}H NMR analysis was in good agreement with rac-**2d** (Section 4.1.4).

4.3.3.2. (−)-(4*S*,4a*R*)-tricarbonyl(η^6-thiochroman-4-ol) chromium [(*S*,*R*)-**3d**].

$[\alpha]_D^{22} = -162°$ (*c* 0.27, $CHCl_3$), 49% ee. ^{1}H NMR analysis was in good agreement with (+)-(*R*,*S*)-**3d** (Section 4.2.10.2).

4.4. General procedure for the reduction of (*R*)-**2a–d** and (*S*)-**2d** with sodium borohydride

To a solution of the (*R*)-**2a–d** or (*S*)-**2d** (0.10 mmol) in EtOH (5 mL) was added sodium borohydride (0.15–0.20 mmol) and the mixture was stirred (1–2 h) under argon. It was then acidified with aqueous HCl (1 mol/L) and evaporated. The crude product was extracted with dichloromethane, washed with water, dried over $MgSO_4$ and filtered through a short column of silica gel. The solution was evaporated under reduced pressure to give the respective yellow solids of *syn*-**3a–d**.

4.4.1. (−)-(1*S*,7a*R*)-tricarbonyl(η^6-1-indanol) chromium [(*S*,*R*)-**3a**]

Obtained from (*R*)-**2a** and isolated as a yellow solid in 62% yield. $[\alpha]_D^{23} = -24°$ (*c* 0.25, $CHCl_3$), 82% ee. ^{1}H NMR analysis is in good agreement with (*R*,*S*)-**3a** isolated from the hydrogen-transfer reduction of rac-**2a**.

4.4.2. (+)-(1*S*,8a*R*)-tricarbonyl(η^6-1-tetralol) chromium [(*S*,*R*)-**3b**]

Obtained from (−)-(*R*)-**2b** and isolated as a yellow solid in 90% yield (48% ee). ^{1}H NMR analysis was in good agreement with (−)-(*R*,*S*)-**3b** isolated from the hydrogen-transfer reduction of rac-**2b**.

4.4.3. (−)-(4*S*,4a*R*)-tricarbonyl(η^6-4-chromanol) chromium[(*S*,*R*)-**3c**]

Obtained from (−)-(*R*)-**2c** and isolated as a yellow solid in 60% yield. $[\alpha]_D^{20} = -54°$ (*c* 0.46, $CHCl_3$), 25% ee. ^{1}H NMR analysis was in good agreement with (*R*,*S*)-**3c** isolated from the hydrogen-transfer reduction of rac-**2c**.

4.4.4. (−)-(4*S*,4a*R*)-tricarbonyl(η^6-thiochroman-4-ol) chromium [(*S*,*R*)-**3d**]

Obtained from (−)-(*R*)-**2d** and isolated as a yellow solid in 70% yield. $[\alpha]_D^{20} = -304°$ (*c* 0.37, $CHCl_3$), >95% ee. IR and ^{1}H NMR analyses were in good agreement with (*R*,*S*)-**3d** isolated from the hydrogen-transfer reduction of rac-**2d**.

4.4.5. (+)-(4*R*,4a*S*)-tricarbonyl(η^6-thiochroman-4-ol) chromium [(*R*,*S*)-**3d**]

Obtained from (+)-(*S*)-**2d** and isolated as a yellow solid in 71% yield. $[\alpha]_D^{23} = +358°$ (*c* 0.28, $CHCl_3$), >95% ee.

^{1}H NMR analysis was in good agreement with (+)-(*R*,*S*)-**3d** isolated from the hydrogen-transfer reduction of *rac*-**2d**.

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