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Synthesis and Structural Characterization of Planar Chiral $Cr(CO)_3$-Complexed Aromatic Nitrones – Valuable Substrates for Asymmetric SmI_2-Induced Coupling Reactions

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The synthesis of $Cr(CO)_3$-complexed aromatic nitrones **2** is reported. These new planar-chiral complexes were fully characterized in solution by ^1H and ^{13}C NMR, IR and cyclic voltammetry. Moreover, structural data were obtained from X-ray structures of nitrones **2b**, **2d**, **2e** and **2f**. These analyses converge to give evidence of a favoured *anti* conformation of *ortho*-substituted nitrones, with an unusual N–O···H_{aryl} intramolecular interaction forming a six-membered ring. The reactivity of these chiral nitrones in SmI_2-induced pinacol-type reactions was investigated. The reductive cross-coupling of nitrones **2a–d** with carbonyl compounds proved to be highly chemo- and diastereoselective and afforded precursors of enantioenriched β-amino alcohols in excellent yields.

Introduction

In the last decade, a great deal of interest has been devoted to the chemistry of nitrones. In comparison with other imine derivatives, nitrones exhibit a broad spectrum of reactivity and have therefore found widespread applications in organic synthesis.[1] The 1,3-dipolar reactivity of nitrones has been exploited in [3+2] cycloadditions with alkenes[2] and more recently in [3+3] cycloadditions with cyclopropane derivatives[3] and (trimethylenemethane)palladium complexes.[4] The electrophilic character of nitrones has also been extensively used for nucleophilic addition of various organometallic derivatives.[5] A few years ago, one of us described the first example of the *umpolung* reactivity of nitrones in the presence of SmI_2.[6] Mild reduction of nitrones and reaction of the resulting α-azanucleophilic species with carbonyl compounds allowed the development of an efficient method for the cross-coupling of C=N and C=O bonds,[7] affording β-amino alcohols in high yields, without formation of homocoupling products. The synthetic utility of this process was subsequently demonstrated by its applications in the synthesis of aminocylitols[8] and asymmetric α,α-disubstituted prolinols as potential organocatalysts.[9] In view of the importance of chiral vicinal amino alcohols in asymmetric synthesis,[10] the development of asymmetric versions of this SmI_2-mediated coupling reaction is highly desirable.[11] It remains a challenging task, however, and, although chiral complexes of Sm^{II} for promoting enantioselective reactions could in principle be designed, there is relatively little published work on chiral modifications of Sm^{II} reagents.[11,12] As one example, in an attempt to develop an asymmetric synthesis of (–)-balanol, Skrydstrup et al. observed weak enantioselectivities (0–5% *ee*) in SmI_2-induced reductive cyclizations of carbonyl hydrazone substrates.[13] The difficulties encountered in the development of enantioselective SmI_2-promoted reactions can be attributed to the notoriously labile coordination spheres in lanthanide complexes, the high coordination numbers (6–9 for Sm^{II}) and a multitude of potential geometries.[14]

Consequently, most developments directed towards asymmetric versions of SmI_2-induced reactions have been based on the use of chiral auxiliaries in the substrates. By this approach, *N-tert*-butylsulfinylimines have been employed successfully by the groups of Lin and Bentley to prepare enantioenriched *anti*-β-amino alcohols in high yields.[15] Nitrones bearing chiral auxiliaries on their nitrogen atom have also been used in SmI_2-mediated reductive couplings with α,β-unsaturated esters to produce enantioenriched γ-amino acid derivatives and γ-lactams.[16] Another elegant possibility would be to use the planar chirality of (arene)metal complexes of *C*-aromatic nitrones. Indeed, planar-chiral (η^6-arene)$Cr(CO)_3$ complexes have found

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widespread applications as chiral auxiliaries in asymmetric synthesis[17] and as ligands in enantioselective catalysis.[18] One of the advantages of the use of (η^6-arene)$Cr(CO)_3$ planar-chiral complexes is the ready access to both enantiomeric series of compounds.[19] Moreover, the stereodirecting effects of the organometallic $Cr(CO)_3$ moiety usually induce high levels of stereocontrol for reactions at side-chain positions.[17,20] In this context, tricarbonylchromium-complexed aldehydes and imines have been extensively used; however, the synthetic utility of other C=N derivatives such as nitrones has been little exploited. To the best of our knowledge, only *N*-methyl derivatives have been used as chiral substrates for diastereoselective 1,3-dipolar cycloadditions[21] or for the NMR determination of the enantiomeric purities of their aldehyde precursors.[22]

In this paper we wish to report the synthesis and full characterization of planar-chiral (η^6-arene)$Cr(CO)_3$-based nitrones, together with a comprehensive study of their reactivities in stereoselective SmI_2-induced coupling reactions. Part of this work has been the subject of a preliminary communication.[23]

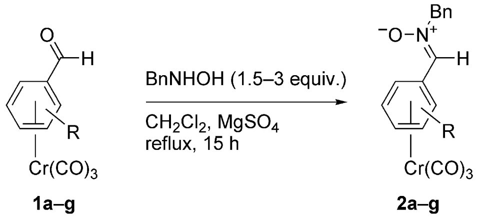
Results and Discussion

Synthesis and Characterization of Nitrones 2

Synthesis of Nitrones 2a–g

Nitrones are readily synthesized by treatment of *N*-substituted hydroxylamines with aldehydes.[24] Because the classical direct complexation of arenes with $Cr(CO)_6$ does not tolerate the presence of electron-withdrawing substituents on the arene ring, the most appropriate approaches for the synthesis of the (η^6-arenecarbaldehyde)$Cr(CO)_3$ complexes **1a**–**c** and **1e**–**g** (Table 1) are based either on complexation of the corresponding acetals[25] or on the oxidation of benzylic alcohol precursors.[26] The silylated aldehyde **1d** was synthesized from the dimethyl acetal of **1a** by *ortho*-lithiation followed by electrophilic quenching with Me_3SiCl.[27] The complexed aldehydes **1a**–**g** were then treated with *N*-benzylhydroxylamine to afford the nitrone derivatives **2a**–**g** (Figure 1) in good to excellent yields, each as a single isomer (Table 1). The choice of the *N*-benzyl substituent in these nitrones was motivated by the possibility of cleaving this group under mild conditions to transform the reductive-coupling products into primary amines.

Table 1. Preparation of $Cr(CO)_3$-complexed nitrones **2a**–**g**.



Entry	Substrate	R	Product	Yield [%]
1	**1a**	H	**2a**	95
2	**1b**	*o*-Me	**2b**	88
3	**1c**	*o*-MeO	**2c**	96
4	**1d**	*o*-Me_3Si	**2d**	88
5	**1e**	*o*-F_3C	**2e**	83
6	**1f**	*m*-Me	**2f**	58[a]
7	**1g**	*m*-MeO	**2g**	78

[a] Not optimized.

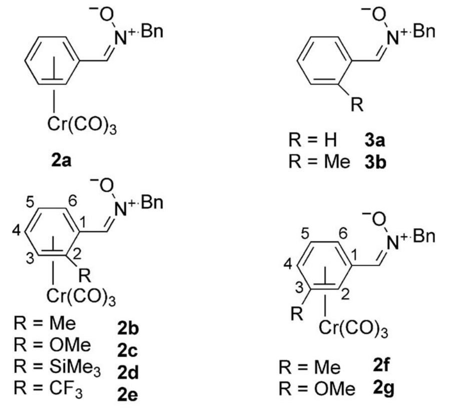


Figure 1. Aromatic nitrones described in this study.

The organic nitrones **3a** and **3b** (Figure 1) were prepared by a similar experimental procedure in 98 % and 78 % yields from benzaldehyde and *ortho*-tolualdehyde, respectively.

^1H and ^{13}C NMR Characterization

As a consequence of the arene complexation to the $Cr(CO)_3$ fragment, the signals of the aromatic protons of the arene chromium moiety are shifted upfield by 1.6–2.1 ppm [Figure 2, spectra (a) and (c), (b) and (d)]. Moreover, their signals are split over a wider area of the spectrum, allowing easier attribution. This phenomenon is attributed to the existence of a preferred conformation of the $Cr(CO)_3$ tripod in solution, with the Cr–CO bonds eclipsing the carbon atoms with the lower electronic density of the aromatic ring.[28] This is particularly evident for nitrone **2c** [Figure 2, spectrum (c)], with a synergic effect of the electron-donating methoxy group situated *ortho* to the electron-withdrawing nitrone strongly favouring an *anti*-eclipsed tripod conformation with respect to the C-1 carbon atom.

Complexes **2a**–**g** are characterized by aromatic proton resonances between δ = 4.91 and 7.82 ppm (Table 2). The benzylic proton 7-H, α to the nitrone function, is less affected by the complexation and resonates between δ = 6.95 and 7.57 ppm, about 0.4 ppm lower than in the corresponding organic nitrone (see Table 2, Entries 1–4 for comparison).

A peculiar observation is the important downfield chemical shift for the signal of the aromatic proton 6-H, *ortho* to the nitrone group, in complexes **2b**–**e** (Table 2, Entries 3 and 5–7), which reaches values between δ = 7.13 and 7.82 ppm. Such a downfield chemical shift is very unusual for the signal of a $Cr(CO)_3$-complexed aromatic proton and is not observed in the corresponding aldehyde precursors **1b**–**e** [5.78 ppm < δ(6-H) < 6.22 ppm]. This phenomenon is also observed in the organic *ortho*-substituted nitrone **3b** [δ(6-H) = 9.13 ppm; Table 2, Entry 4]. In contrast, the unsubsti-

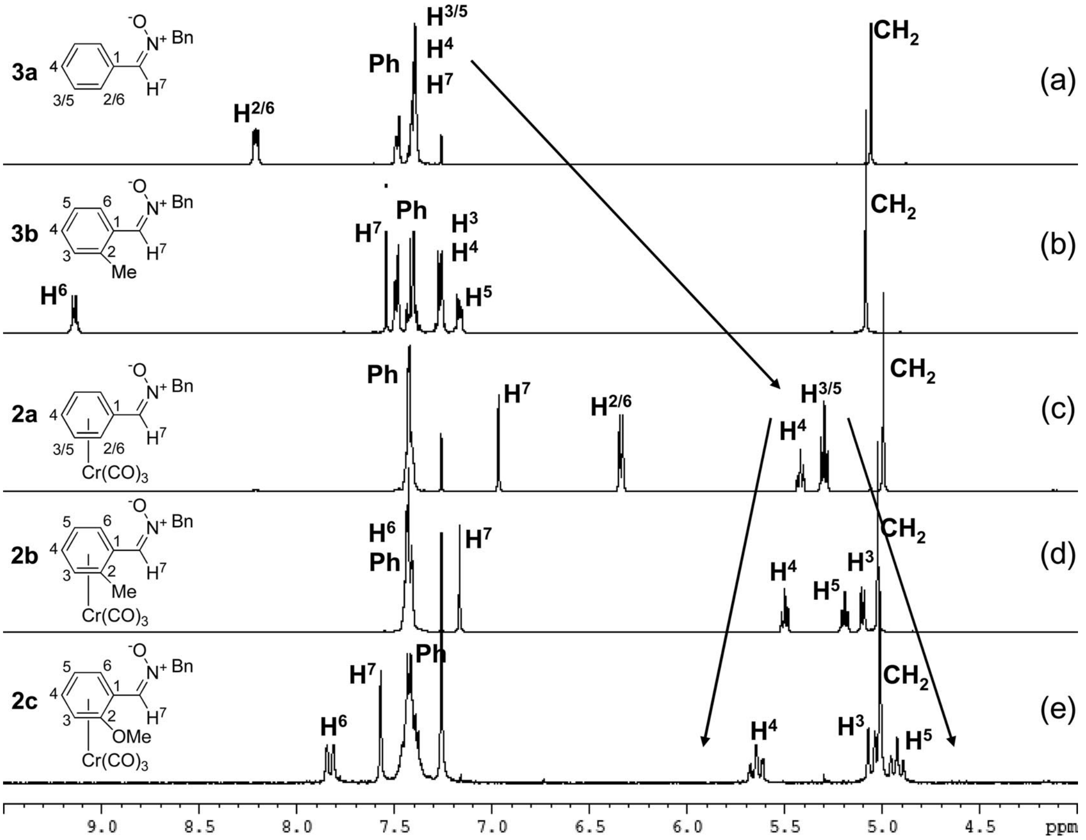


Figure 2. ^1H NMR spectra of organic nitrones **3a**–**b** and complexes **2a**–**c**.

Table 2. Selected ^1H NMR spectroscopic data ($CDCl_3$, δ in ppm) for compounds **2a**–**g**, **3a** and **3b**.[a]

Entry	Nitrone	2-H	3-H	4-H	5-H	6-H	7-H
1	**2a**	6.34	5.30	5.42	5.30	6.34	6.97
2	**3a**	8.20	7.49–7.39	7.49–7.39	7.49–7.39	8.20	7.49–7.39
3	**2b**	–	5.10	5.49	5.18	7.40	7.16
4	**3b**	–	7.26	7.26	7.17	9.14	7.55
5	**2c**	–	5.05	5.63	4.91	7.82	7.57
6	**2d**	–	5.40	5.62	5.18	7.13	6.95
7	**2e**	–	5.67	5.51	5.31	7.30	7.33
8	**2f**	6.22	–	5.24	5.40	6.06	6.98
9	**2g**	5.55	–	5.55	5.17	6.38	7.04

[a] For the proton labelling, see Figure 1.

tuted nitrone **2a**, the organic nitrone **3a** or the *meta*-substituted derivatives **2f** and **2g** do not exhibit such a downfield shift for the signal of 6-H, with chemical shifts only 0.4–0.6 ppm higher than in the corresponding aldehydes (Table 2, Entries 1–2 and 8–9). Moreover, no such variation in chemical shift as a factor of the substitution pattern on the complex is observed for the aldehydes **1a**–**g** [$\Delta\delta$(6-H) < 0.5 ppm, whatever the substitution of the arene ring]. We therefore propose that this downfield shift of the signal for 6-H, only observed in the series of *ortho*-substituted nitrones **2b**–**e**, could be attributed to the existence of an $O\cdots H_{aryl}$ intramolecular interaction,[29] which would originate from a favoured solution conformation in which the nitrone function would be *anti* to the *ortho* substituent (Figure 3), with the $N^+–O^-$ bond pointing toward the 6-H proton. Such conformations have been intensively studied in the case of *ortho*-substituted (η^6-arenecarbaldehyde)$Cr(CO)_3$ complexes[20,30] and were confirmed for nitrones **2b** and **3b** by ^1H NMR NOE examination in $CDCl_3$: in each case an interaction between 7-H and the *o*-Me substituent was clearly present (Figure 3), whereas no interaction was found between 7-H and 6-H. The usual aldonitrone (*Z*) configuration was also confirmed by NOE (interaction between 7-H and the benzylic CH_2 group).

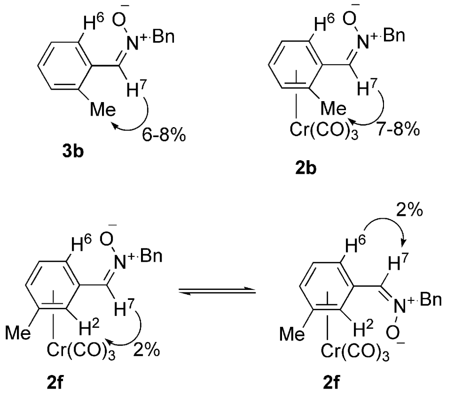


Figure 3. NOEs in nitrones **3b**, **2b** and **2f**.

A corresponding conformational study was carried out with the *meta*-substituted nitrone **2f**; in this case the methyl group is too far away to block the conformation of the nitrone, which freely rotates around the $C^1–C^7$ bond. This is characterized by small interactions between 7-H and both 2-H and 6-H protons.

^{13}C NMR spectroscopic data for compounds **2a**–**g** are in each case characterized by a signal attributable to the carbonyl ligand between δ = 230 and 235 ppm. The upfield shielding of the signals of the aromatic carbon atoms of the complexed arene ring relative to the free arene is, as would be expected, $\Delta\delta(^{13}C) \approx –40$ ppm. The iminyl carbon atom of the nitrone function is not affected by the complexation of the $Cr(CO)_3$ entities and resonate between δ = 127 and 133 ppm.

IR Characterization

In the organometallic chemistry of carbonylmetal complexes it is well known that IR ν_{CO} vibrations reflect π-backbonding into the CO π* orbitals and are therefore very sensitive to changes in electron density at the metal atom.[31] Any increase in the electronic density at the metal atom is delocalized by π-backbonding in the CO ligands and significantly decreases the vibrational frequencies; on the other hand, a decrease in the electronic density at the metal atom results in higher frequencies. The $(\eta^6\text{-arene})Cr(CO)_3$ complexes are characterized by two well-resolved stretching modes, in accordance with their C_{3v} symmetries. In the nitrone complexes **2a**–**f**, the measured frequencies are found in the 1975–1856 cm^{-1} range, very close to those in the parent aldehyde complexes. These values vary according to the electronic characters of the arene substituents. Whereas two ν_{CO} vibrational bands at 1963 and 1885 cm^{-1} are observed for the unsubstituted nitrone **2a**, the *o*-MeO-substituted nitrone **2c** presents bands at lower frequencies (1950 and 1870 cm^{-1}). On the other hand, the *ortho*-trifluoromethyl-substituted **2e** is characterized by two bands at 1975 and 1903 cm^{-1}, in excellent agreement with the electron-withdrawing character of the substituent.

Cyclic Voltammetry

The redox properties of nitrones **2a**–**g** were examined by cyclic voltammetry (Table 3). Although clear reduction waves were obtained for all the compounds, the oxidation waves were not apparent, partly due to the decomposition of the arene complexes in an oxidative environment. A similar observation had previously been made by Uemura et al. in a mechanistic study involving (benzaldehyde)tricarbonylchromium complexes.[32] We have therefore only compared the reduction potentials of **2a**–**g** and of the organic nitrone **3a**.

The nitrones **2a**–**g** are more easily reduced than the uncomplexed nitrone **3a**, as would be expected from the electron-withdrawing character of the $Cr(CO)_3$ organometallic fragment. The substituent effects on the arene ring are less distinct, except in the case of the *ortho*-trifluoromethyl-substituted nitrone **2e**: consistently with the strongly electron-withdrawing character of the CF_3 group, its reduction potential of –1.69 V is about 0.3 V higher than those of the other nitrones. In comparison, the reduction potentials of the unsubstituted nitrone **2a** and the *ortho*- or *meta*-substituted nitrones (**2b**–**d** and **2f**–**g**) are found to be in a narrow range (–1.93 to –2.03 V).

X-ray Studies of Complexes 2b, 2d, 2e and 2f

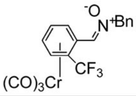
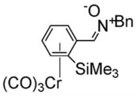
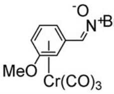
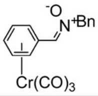
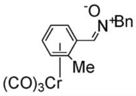
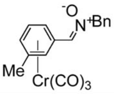
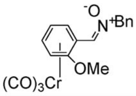
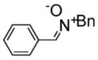
Crystals of nitrones **2b**, **2d**, **2e** and **2f** suitable for X-ray characterization were obtained by slow diffusion of petroleum ether into chloroform solutions. Selected bond lengths and angles for each structure are reported in Table 4.

Table 4. Selected interatomic distances [Å] and angles [°].

	2b	**2d**	**2e**	**2f**
$Cr–C^1$	2.239(4)	2.224(2)	2.204(4)	2.224(8)
$Cr–C^2$	2.243(4)	2.231(2)	2.168(4)	2.223(8)
$Cr–C^3$	2.215(5)	2.206(3)	2.197(5)	2.261(10)
$Cr–C^4$	2.204(6)	2.217(3)	2.208(5)	2.200(11)
$Cr–C^5$	2.195(7)	2.215(3)	2.222(5)	2.199(12)
$Cr–C^6$	2.191(5)	2.213(2)	2.184(5)	2.205(10)
$C^1–C^7$	1.450(5)	1.462(3)	1.455(7)	1.454(12)
$C^7–N$	1.286(5)	1.304(3)	1.296(6)	1.295(10)
$H^6\cdots O^1$	2.227(3)	2.165(2)	2.301(3)	–
$C^6–C^1–C^7–N$	11.1(7)	4.8(4)	26.7(7)	–

The ORTEP views (Figure 4) show classical η^6 coordination of the arene to the $Cr(CO)_3$ tripod, with C–Cr bond lengths between 2.168 and 2.261 Å. The $C^1–C^7$ and $C^7–N$

Table 3. Reduction potentials measured for nitrones **2a**–**g** and **3a** (from the lowest to the highest).

Nitrone:	**2e**	**2d**	**2g**	**2a**
				
$E^{1/2}$:[a]	–1.69	–1.93	–1.97	–1.99
Nitrone:	**2b**	**2f**	**2c**	**3a**
				
$E^{1/2}$:[a]	–2.00	–2.00	–2.03	–2.52

[a] Potentials in V vs. Ag/Ag^+ with a glassy-carbon working electrode, a platinum flag counter electrode, in MeCN with tetrabutylammonium perchlorate (0.1 м) as supporting electrolyte, and a sweep rate of 10 V s^{-1}.

bond lengths vary from 1.450 Å for **2b** to 1.462 Å for **2d** and from 1.286 Å for **2b** to 1.304 Å for **2d**, respectively, comparable with the corresponding bonds in uncomplexed nitrones.[33] In the solid state, the conformation of the $Cr(CO)_3$ entity in each complex is roughly staggered. It is noteworthy that neither the electronic nature of the substituent (for instance, CH_3 vs. CF_3) nor its position on the aromatic ring (*ortho* vs. *meta*) significantly affect this conformation, which is very probably governed by steric effects.

The *anti* conformations of nitrones **2b–e** are also observed in the solid state. Moreover, the corresponding C^6–C^1–C^7–N torsion angles and $H^6\cdots O$ distances (Table 4) are appropriate values for the establishment of $O\cdots H_{aryl}$ intramolecular interactions.[29] The nitrone **2f** also has an *anti* conformation with respect to the *meta*-methyl substituent in the solid state; however, this conformation is not controlled by steric hindrance and is not representative of the conformation in solution, in which the nitrone function can freely rotate around the C^1–C^7 bond as confirmed by NOE experiments (Figure 3).

Applications of $Cr(CO)_3$-Complexed Nitrones 2a–g in SmI_2-Mediated Reductive Couplings

The use of (η^6-arene)$Cr(CO)_3$[32,34] and ferrocenyl[32,35] chiral auxiliaries in SmI_2-promoted cross-couplings of imines and aldehydes has been reported to afford β-amino alcohols in high yields and with excellent diastereo- and enantioselectivities. One of the aims of our study was to evaluate whether the $Cr(CO)_3$-complexed nitrones **2** were suitable reagents for asymmetric reductive coupling reactions induced by the one-electron reductive agent samarium diiodide.[36]

Homocoupling Reactions of Nitrones 2a and Racemic 2b

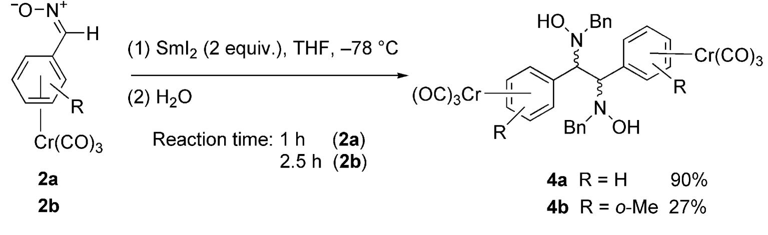
The homocoupling of $Cr(CO)_3$-complexed nitrones could in principle give access to the *N*-hydroxy precursors of vicinal diamines; moreover, the use of planar-chiral enantiopure reagents should theoretically produce enantiopure derivatives. We therefore decided to investigate the reactivities of nitrones **2** in the presence of SmI_2.

Nitrone **2a** was treated with SmI_2 (2 equiv.) in THF; the reaction was complete after 1 h at –78 °C (Scheme 1). The first observation that can be made concerns its high chemoselectivity: ^1H NMR analysis of the crude mixture revealed the presence of a single symmetrical product, characterized by a benzyl CH signal at δ = 4.29 ppm, in good agreement with the structure of a homocoupling product. The crude mixture was washed with pentane, to afford **4a** in 90% yield. The absence of any *N*,*N*-dibenzylhydroxylamine derivative, which could be formed by two-electron reduction of **2a**, should be emphasized; indeed, Uemura et al. were unable to avoid the formation of the dibenzylamine byproduct in their asymmetric synthesis of 1,2-diamines by reductive coupling of (benzaldimine)$Cr(CO)_3$ complexes.[37] However, when the planar-chiral racemic nitrone **2b** was treated under the same conditions, the results were disappointing. The reaction time needed for complete disappearance of the nitrone (TLC) was longer (2.5 h instead of 1 h for **4a**) and, moreover, the coupling was no longer chemoselective, and the presence of many by-products made purification tedious. We succeeded in isolating a pure fraction of **4b** in a poor 27% yield by crystallization from CH_2Cl_2. The steric hindrance created by the methyl group *ortho* to the reactive centre might cause the difference in reactivity between **2a** and **2b**. With regard to the stereochemistry of the homocoupling, the relative configurations of **4a** and **4b** could not be determined from their NMR spectra, both the *meso* and the D,L derivatives having symmetrical structures. Moreover, we failed to obtain crystals suitable for X-ray analysis.

Asymmetric Cross-Coupling with Carbonyl Compounds

We then turned our attention to the development of an asymmetric version of SmI_2-induced cross-coupling between nitrones and carbonyl compounds.[6] The racemic nitrones **2a–g** were treated with acetone, chosen as a typical carbonyl partner. The cross-coupling reactions were each performed with acetone (1 equiv.) and SmI_2 (2 equiv.) in THF at –78 °C.

The reactions are very fast for all the substrates, with total disappearance of the nitrone in less than 0.5 h at –78 °C. However, the cross-coupling reactivity is highly dependent on the substitution pattern of the (arene)chromium moiety. When the achiral nitrone **2a** was employed (Table 5, Entry 1), the expected cross-coupling product **5a** was isolated in 65% yield after purification by silica gel chromatography. No competition between homocoupling and cross-coupling was observed, presumably because the latter is faster. The highest efficiencies were observed when starting with the *ortho*-substituted nitrones **2b** and **2c**; the corresponding β-(hydroxyamino) alcohols **5b** and **5c** were isolated in 95 and 93% yields, respectively (Table 5, Entries 2 and 3). It is noteworthy that only stoichiometric amounts



Scheme 1. SmI_2-induced homocoupling of nitrones **2a** and **2b**.

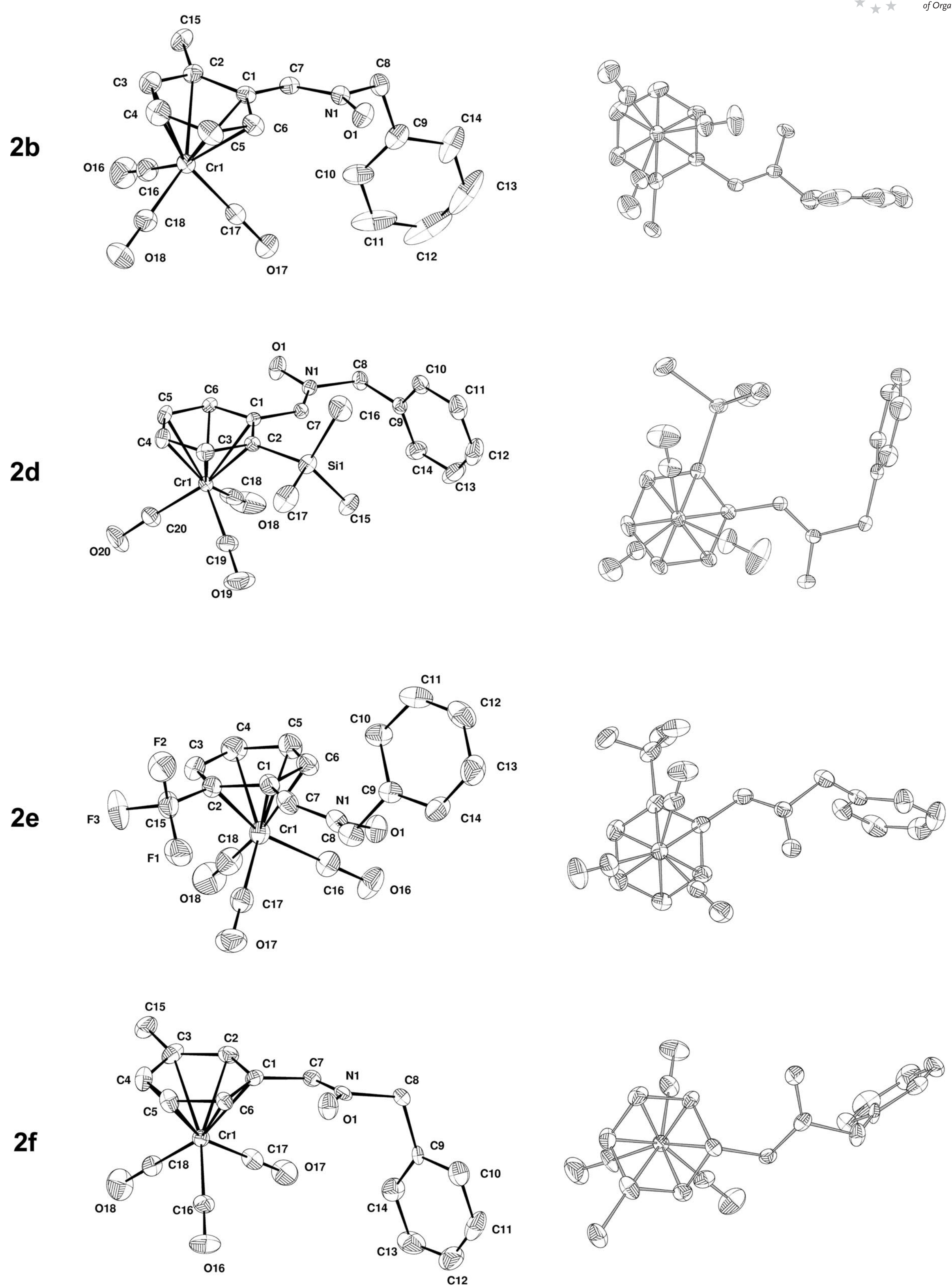
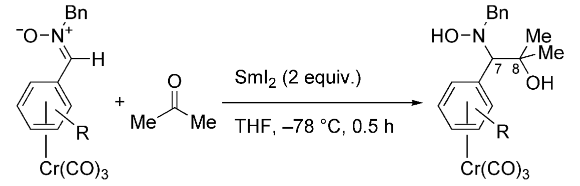


Figure 4. Two views of ORTEP diagrams of each of the complexes **2b**, **2d**, **2e** and **2f** (the thermal ellipsoids are at the 30% probability level and the hydrogen atoms have been omitted for clarity).

of the two partners were employed, and that no additives such as the toxic HMPA or proton sources were necessary for the achievement of high yields.[38] A decrease in the yield was observed with the CF$_3$-substituted nitrone **2e**, the corresponding product **5e** being isolated in only 35% yield (Table 5, Entry 4). The lower efficiency could be correlated with the reduction potential of **2e**: this substrate is indeed the most easily reduced of the series (see Table 3), although no formation of a benzylamine derivative by two-electron reduction of **2e** was observed. A similar loss of efficiency was observed with the *meta*-substituted nitrone **2f** (Table 5, Entry 5), and this was strongly amplified when **2g** (*meta*-methoxy) was employed: with the latter, only traces of the β-(hydroxyamino) alcohol **5g** were formed (Table 5, Entry 6).

Table 5. SmI_2-induced cross-coupling of nitrones **2a**–**g** with acetone.



2a–g **5a–g**

Entry	Substrate	R	Product	Yield [%]	*dr* at C-7
1	**2a**	H	**5a**	65	–
2	**2b**	*o*-Me	**5b**	95	>95:5
3	**2c**	*o*-MeO	**5c**	93	>95:5
4	**2e**	*o*-F_3C	**5e**	35	>95:5
5	**2f**	*m*-Me	**5f**	47	50:50
6	**2g**	*m*-MeO	**5g**	< 5	–

These results highlight the extreme sensitivity of the cross-coupling reactions to the electronic effects induced by the substituents on the coordinated arene rings: on going from the *ortho*-MeO compound **2c** to the *meta*-MeO derivative **2g** the yield of the β-(hydroxyamino) alcohol dramatically decreases from 93% to <5%. To the best of our knowledge, the only other study dealing with the influence of electronic effects of substituted aromatic substrates in SmI_2-induced coupling reactions was that by Hilmersson, Flowers II et al.[39] They also observed a dramatic change in reactivity with *para*-substituted aromatic imines relative to their unsubstituted or *meta*-substituted counterparts. These effects remain difficult to explain, as the exact natures of the reactive α-azanucleophilic species involved in the formation of the cross-coupling products is still unknown.[6] Moreover, after several studies involving $Cr(CO)_3$-complexed benzylic radicals,[37,40] the stabilization of intermediates with radical, anionic or cationic character at the benzylic position by $Cr(CO)_3$ complexation has been demonstrated.[41] This property may also influence the mechanistic course of the cross-coupling.

An important feature of the SmI_2-induced cross couplings between the nitrones **2** and acetone concerns their diastereoselectivity when planar-chiral substrates are employed. Indeed, the reactions were completely diastereoselective with the *ortho*-substituted nitrones **2b**, **2c** and **2e**, with the formation of single diastereoisomers within the limits of ^1H NMR analysis of the crude mixtures. Such high levels of diastereoselectivity could be understood as follows: for steric reasons, the nitrone group in each case adopts an *anti* conformation with respect to the *ortho* group (Figure 4). This conformation was observed in the crystal structure of nitrone **2b** (Figure 4) and confirmed by NOE measurements in solution (Figure 3). Additionally, the $Cr(CO)_3$ tripod efficiently blocks one face of the arene, so that the coupling reaction should preferentially occur *exo* with respect to the metal atom.

When the planar-chiral *meta*-substituted nitrone **2f**, on the other hand, was used as a substrate for reductive cross-coupling with acetone (Table 5, Entry 5), although it was still planar-chiral, no asymmetric induction was observed: as a consequence of the free rotation around the C^1–C^7 bond (Figure 3) the coupling reaction can occur to the same extent on the two diastereotopic faces of the nitrone, to give a 50:50 mixture of the two diastereoisomers.

Fortunately, X-ray analysis of suitable crystals of the racemic β-(hydroxyamino) alcohol **5b** (Figure 5) allowed to establish the relative configuration at C-7 unambiguously as (*R*), coupled with the (*pS*) configuration[42] of the chromium complex, in excellent agreement with the above explanation of the diastereoselectivity.

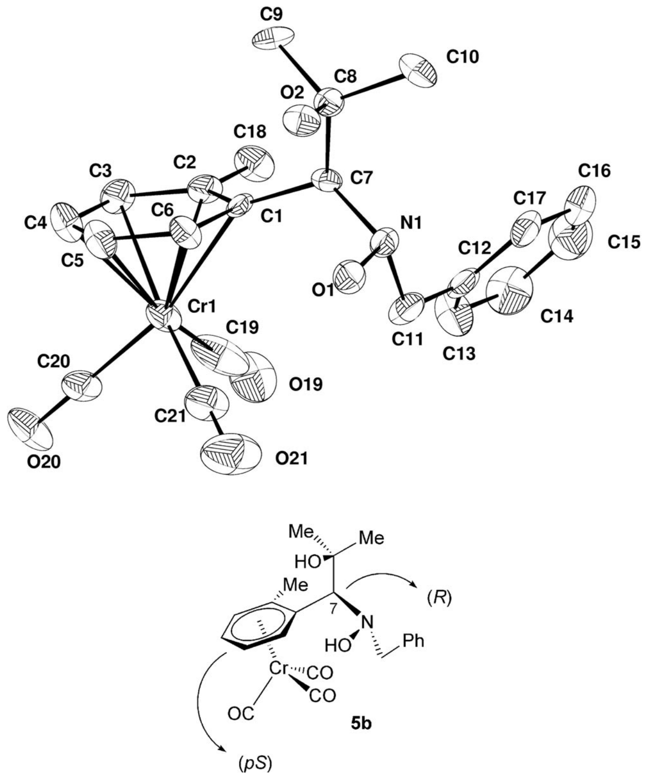
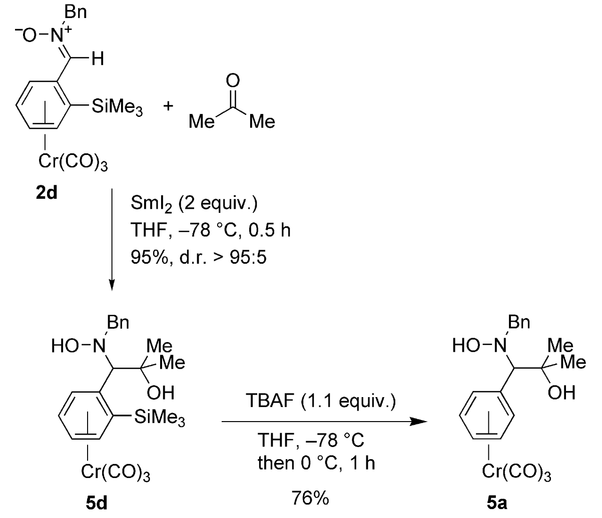


Figure 5. ORTEP view of complex **5b** (the thermal ellipsoids are at the 30% probability level and the hydrogen atoms have been omitted for clarity). Selected bond lengths [Å]: Cr–C^1 2.289(9), Cr–C^2 2.252(9), Cr–C^3 2.225(12), Cr–C^4 2.214(16), Cr–C^5 2.237(12), Cr–C^6 2.214(10), C^1–C^7 1.509(14), C^7–N 1.483(15).

In the (arene)chromium series, the existence of planar chirality and also its efficiency in terms of asymmetric induction strictly rely on the presence of a substituent *ortho* to the reactive centre. However, this requirement could ultimately be a limitation to the synthetic utility of the coupling procedure, such a substituent on an arene ring (Me or MeO for instance) seldom being present in the structures of potentially useful products. We therefore envisaged the use of a nitrone bearing a "cleavable" *ortho* substituent, such as the trimethylsilyl group in **2d**.

Nitrone **2d** was subjected to the cross-coupling procedure with acetone, to give the β-(hydroxyamino) alcohol **5d** in 95% yield and as a single diastereoisomer within the limits of ^1H NMR examination of the crude mixture (Scheme 2). Cleavage of the trimethylsilyl group was subsequently accomplished with TBAF (1 equiv.) in THF at low temperature,[43] to afford the desilylated product **5a** in 76% yield. If this sequence was applied to an enantiopure silylated substrate,[21b] the enantiopure derivative **5a**, unsubstituted on the arene ring, could be obtained, thus broadening the scope of applications.

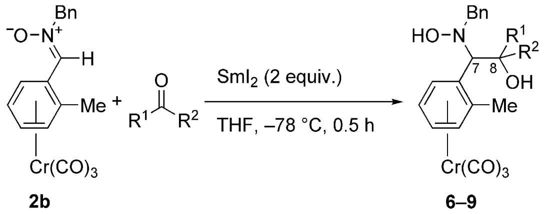


Scheme 2. Cross-coupling with silylated nitrone **2d**, followed by desilylation of β-(hydroxyamino) alcohol **5d**.

The cross-coupling procedure was next extended to various carbonyl compounds, thus demonstrating its versatile character. The nitrone **2b** was treated with cyclohexanone, pivalaldehyde, propionaldehyde and benzaldehyde under conditions identical to those described above.

Use of cyclohexanone (Table 6, Entry 1), pivalaldehyde (Table 6, Entry 2) or propionaldehyde (Table 6, Entry 3) in place of acetone did not erode the efficiency of the cross-couplings. The reactions were still highly chemoselective, and the expected β-(hydroxyamino) alcohols were isolated in excellent yields. With benzaldehyde, on the other hand, control over the chemoselectivity was completely lost (Table 6, Entry 4); only traces of the expected cross-coupling product **9** were detected, together with many by-products. The homocoupling derivatives of the two substrates, compound **4b** and 1,2-diphenylethane-1,2-diol resulting from pinacolization of benzaldehyde, were identified in the mixture. The unsuitability of benzaldehyde, and aromatic aldehydes generally, as coupling partners in SmI_2-induced cross-coupling reactions had already been observed in the organic series.[15a,44]

Table 6. Cross-coupling of nitrone **2b** with various carbonyl compounds.



Entry	R^1	R^2	Product	Yield [%]	*dr* at C-7	*dr* at C-8
1	$–(CH_2)_5–$		6	88	>95:5	–
2	*t*Bu	H	7	96	>95:5	>95:5
3	Et	H	8	83	>95:5	70:30
4	Ph	H	9	≤5	n.d.	n.d.

The remote diastereoselectivity at the carbon atom C-8, bearing the alcohol functionality, seems to be highly dependant on the size of the R^1 group: whereas a single *syn* diastereomer was isolated from the coupling of **2b** with pivalaldehyde (Table 6, Entry 2), a 70:30 diastereomeric mixture was obtained from propionaldehyde (Table 6, Entry 3). The relative configurations at C-7 and C-8 in the racemic complex **7** could be determined by X-ray diffraction analysis. The ORTEP view (Figure 6) shows, as expected, an (*S*) configuration at C-7 coupled with the (*pR*) configuration of the (arene)chromium moiety,[42] together with an (*R*) configuration at C-8.

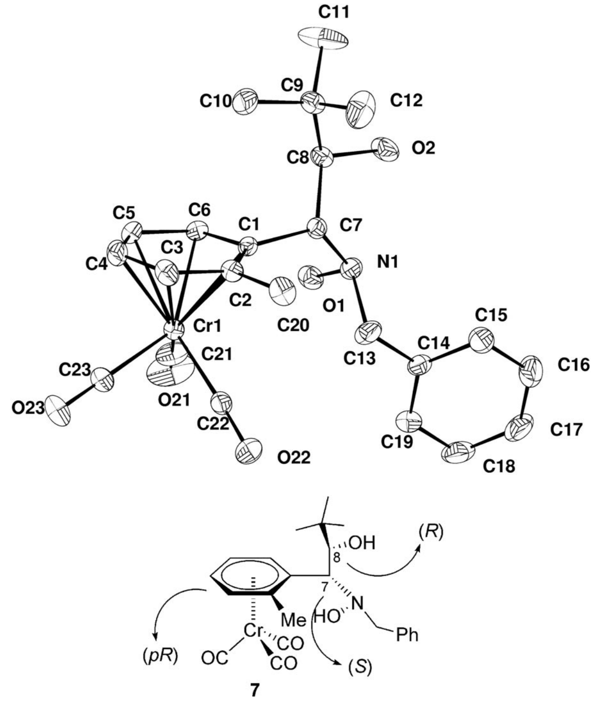
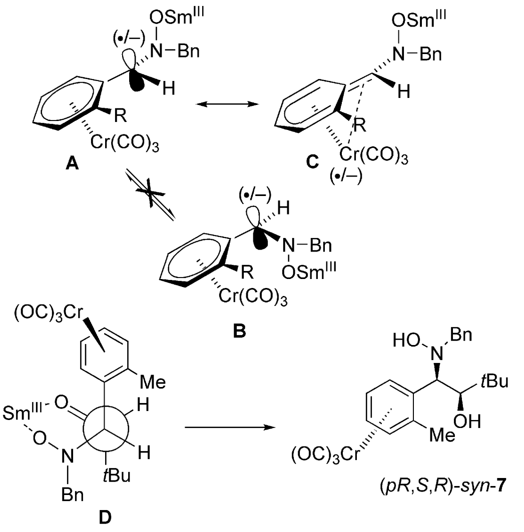


Figure 6. ORTEP view of complex **7** (the thermal ellipsoids are at the 30% probability level and the hydrogen atoms have been omitted for clarity). Selected bond lengths [Å]: Cr–C^1 2.3068(18), Cr–C^2 2.2564(19), Cr–C^3 2.213(2), Cr–C^4 2.210(2), Cr–C^5 2.205(2), Cr–C^6 2.2105(19), C^1–C^7 1.523(2), C^7–N 1.472(3).

Such a stereochemical outcome could be explained as follows (Scheme 3): the $Cr(CO)_3$-complexed nitrone would be reduced by SmI_2 to produce an azanucleophilic species **A** (radical anion or dianion) in a conformation in which the C–N bond would be accommodated in an *anti* orientation relative to the *ortho* substituent. This species would be configurationally stable (no epimerization to **B**), due to an overlap of the p orbital of the α-carbon atom with d orbitals of the chromium atom (species **C**).[37,41] Addition of this negatively charged intermediate to the carbonyl partners (R^1 = *t*Bu or Et; Table 6) would thus occur from the side opposite to the $Cr(CO)_3$ tripod, through a chelated transition state **D** (Scheme 3), so that the steric repulsions would be minimized, to yield products of *syn* configuration.

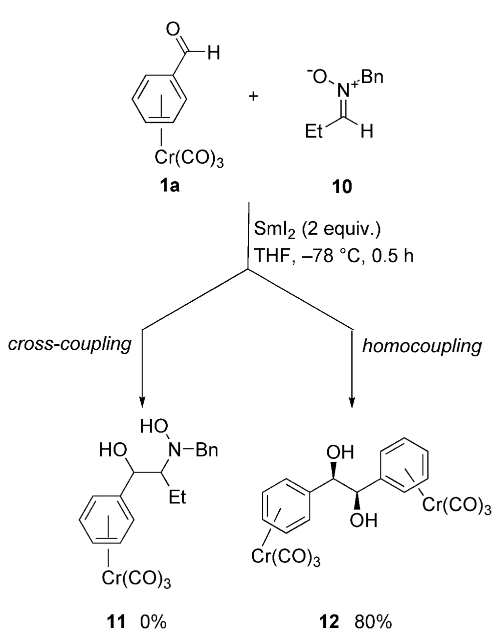


Scheme 3. Explanation for the formation of (*pR*,*S*,*R*)-*syn*-**7**.

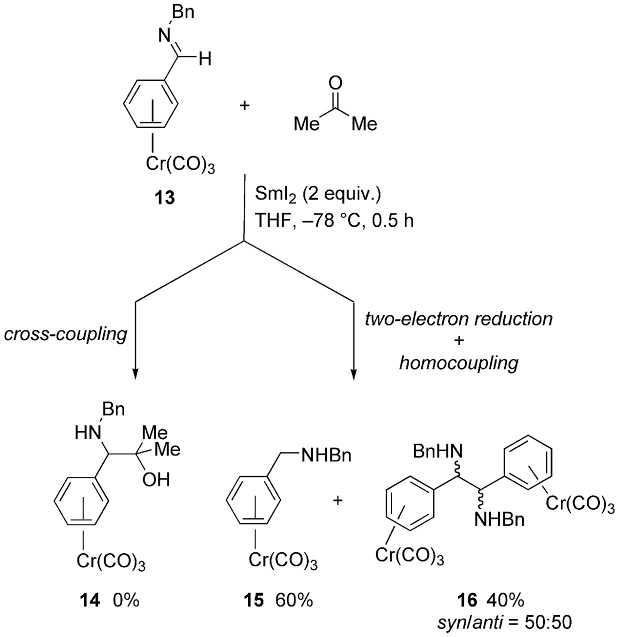
Notably, the nature of the organometallic partner – that is, nitrone rather than carbonyl – proved essential in such reductive coupling reactions; the reaction between, for instance, the (η^6-benzaldehyde)$Cr(CO)_3$ complex **1a** and the organic nitrone **10** (Scheme 4), performed under the experimental conditions described in Tables 5 and 6, did not give the expected cross-coupling product **11** but exclusively afforded the *syn* diol **12** resulting from the pinacol coupling of **1a**,[45] which was isolated in 80% yield.

Moreover, replacement of the $Cr(CO)_3$-complexed nitrone **1a** by the $Cr(CO)_3$-complexed imine **13**[46] did not produce the expected β-amino alcohol **14** at all; two other derivatives, identified as the benzylamine **15** and the diamine **16**,[47] were formed in a 60:40 ratio by two-electron reduction and by homocoupling of the imine, respectively (Scheme 5).[37]

Although the reductive coupling of imines with carbonyl compounds could represent the most straightforward route to β-amino alcohols, it is well known in the literature that satisfactory levels of chemo- and stereoselectivity are difficult to achieve; only a few examples based on this strategy have indeed been successful.[7] When organometallic substrates such as the (arene)chromium or the ferrocenyl systems are employed, Uemura et al. have demonstrated the importance of the *N*-substituent on the imine partner in the modulation of the chemoselectivity.[37]



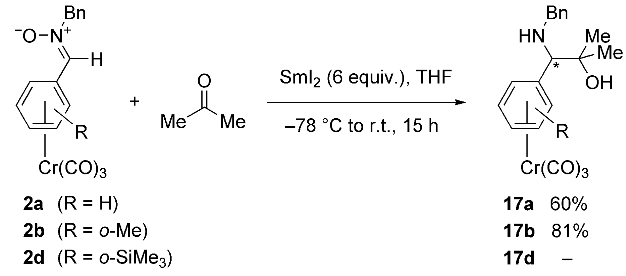
Scheme 4. Reactivity of (η^6-benzaldehyde)$Cr(CO)_3$ complex **1a** with organic nitrone **10**.



Scheme 5. Reactivity of imine **13** with acetone in the presence of SmI_2.

Extension to the One-Pot Synthesis of β-Amino Alcohols

In order to allow direct isolation of chiral β-amino alcohols, a one-pot procedure consisting of cross-coupling followed by the reduction of the hydroxylamine function with SmI_2, as successfully developed in the organic series,[6] was applied to the racemic (arene)chromium substrates (Scheme 6).



Scheme 6. One-pot synthesis of β-amino alcohols.

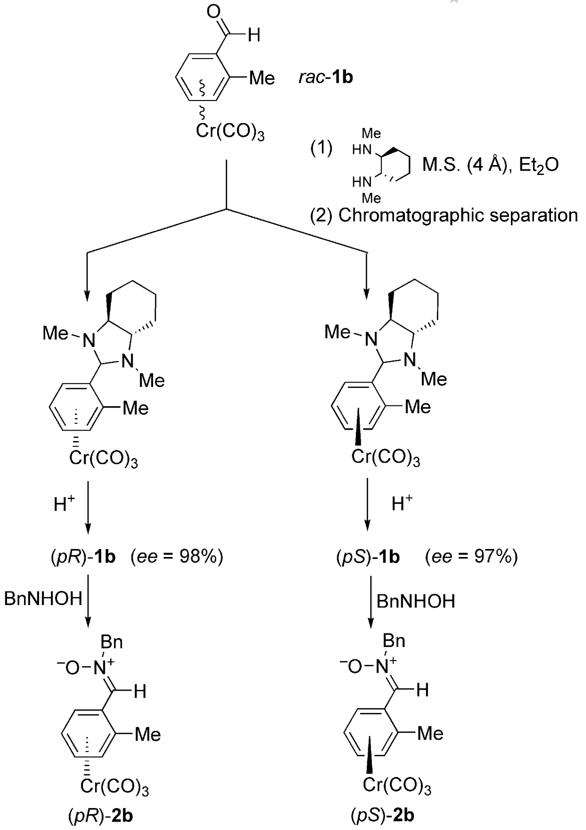
With use of an excess (6 equiv.) of SmI_2, together with a longer reaction time and an increase in the temperature of the reaction mixture (to room temperature), the β-amino alcohols **17** could be isolated in good yields: 60% for **17a** prepared from the achiral nitrone **2a**, and 81% for **17b** from the planar-chiral nitrone **2b** (Scheme 6). As would be expected, the cross-coupling still proceeded with complete diastereoselectivity, and **17b** was isolated as a single diastereoisomer. This therefore represents a valuable alternative for overcoming the lack of chemoselectivity encountered when $Cr(CO)_3$-complexed imines were used.

We also attempted to prepare the *ortho*-silylated β-amino alcohol **17d**, but with a lower chemoselectivity; although the nitrone **2d** was totally converted, the expected product was isolated together with a mixture of silylated by-products, separation of which failed.

Synthesis of Enantioenriched (pR,S)-5b and (pR,S)-17b

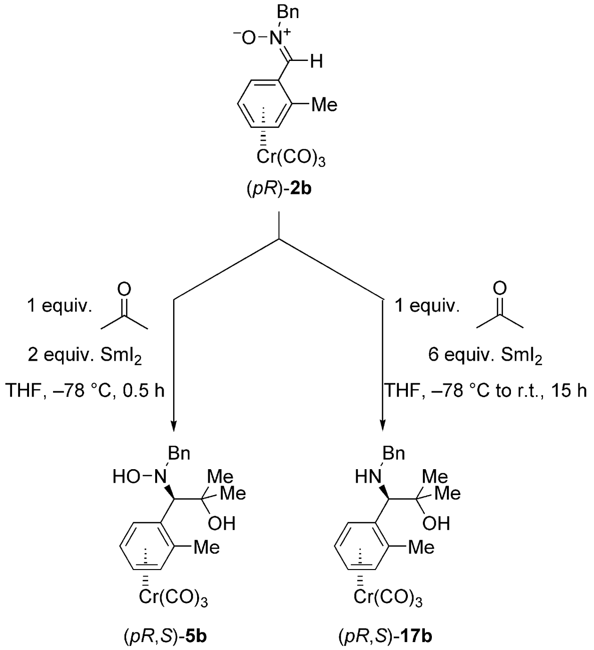
The enantiopure *ortho*-methylbenzaldehyde complexes (*pR*)-**1b** and (*pS*)-**1b** (Scheme 7) were synthesized by the procedure developed in our group a few years ago.[19a] Typically, racemic **1b** was treated with enantiopure (*R*,*R*)-*N*,*N′*-dimethylcyclohexane-1,2-diamine to afford a mixture of two diastereoisomeric aminals. Chromatographic separation on silica gel and subsequent acidic hydrolysis yielded the optically enriched aldehydes[48] (Scheme 7). The enantioenriched nitrones (*pR*)-**2b** and (*pS*)-**2b** were then prepared by treatment of the corresponding aldehydes with *N*-benzylhydroxylamine.

The experimental conditions described above for the synthesis of β-(hydroxyamino) alcohol complexes and the one-pot synthesis of β-amino alcohol complexes were then successfully applied to the enantiopure substrate (*pR*)-**2b**.



Scheme 7. Preparation of enantiopure nitrones (*pR*)-**2b** and (*pS*)-**2b**.

The nitrone (*pR*)-**2b** was first treated with acetone and 2 equiv. of SmI_2 (Scheme 8) to afford the enantiopure β-(hydroxyamino) alcohol (*pR*,*S*)-**5b** in 95% yield. When 6 equiv. of SmI_2 were used in the reaction mixture, the corresponding enantiopure β-amino alcohol complex (*pR*,*S*)-**17b** was also isolated in excellent yield (Scheme 8). The relative stereochemistry at C-7 in these two enantiopure derivatives was attributed on the basis of the X-ray analysis carried out on the racemic β-(hydroxyamino) alcohol **5b** (Figure 5), in which an (*R*) configuration at C-7 was obtained from a (*pS*) planar-chiral moiety. Moreover, the enantiomeric purity of the β-(hydroxyamino) alcohol (*pR*,*S*)-**5b** was confirmed by a practical emerging technique: NMR in ori-



Scheme 8. Enantiopure synthesis of (*pR*,*S*)-**5b** and (*pR*,*S*)-**17b**.

ented solvents. Particularly large enantiodiscrimination was observed by ^{1}H-decoupled ^{13}C NMR spectroscopy in a polypeptidic chiral liquid crystal.[49]

Conclusions

A series of diversely substituted Cr(CO)$_3$-complexed aromatic nitrones has been easily synthesized from the corresponding aldehyde complexes. These nitrones were fully characterized both in solution and in the solid state. The conformations of the nitrone groups, *anti* with respect to *ortho* substituents on the arene rings, have been established and are believed to influence the 6-H proton resonances through intramolecular interactions. These planar-chiral nitrones represent promising substrates that could find wide use in asymmetric synthesis. This has been demonstrated in SmI$_2$-induced asymmetric pinacol-type reactions. The application of planar-chiral nitrones in reductive cross-coupling reactions with carbonyl partners proved to be highly efficient in terms of chemo-, enantio- and diastereoselectivity. The absolute configurations of two cross-coupling products could moreover be unambiguously established by X-ray crystallography. We showed that the efficiencies of the couplings could be correlated with the substitution patterns of the aromatic rings. This procedure allows the enantioselective synthesis of β-(hydroxyamino) alcohol and β-amino alcohol complexes in high yields under mild conditions.

Experimental Section

General Methods: All reactions were routinely performed under dry nitrogen with use of standard Schlenk techniques. THF and Et$_2$O were dried with sodium benzophenone ketyl and distilled. CH$_2$Cl$_2$ was distilled from CaH$_2$. Acetone was distilled from K$_2$CO$_3$. *N*-Benzylhydroxylamine hydrochloride was purchased from Aldrich and was converted into *N*-benzylhydroxylamine by treatment with aq. NaOH prior to use. NMR spectra were recorded with Bruker ARX 200 MHz or Avance 400 MHz spectrometers. ^{1}H and ^{13}C signals of NMR solvents were used as internal standards at δ = 7.26 ppm and δ = 77.36 ppm for CDCl$_3$ and δ = 30.60 ppm for [D$_6$]-acetone. Infrared spectra were measured with a Bruker Tensor 27 spectrometer. Optical rotations were measured with a Perkin–Elmer 343 polarimeter at 589 nm. ES mass spectra were performed by the Groupe de Spectrométrie de Masse (UMR 7613, UPMC). Optical rotations were measured with a Perkin–Elmer 343 polarimeter at 589 nm. Complexes **1a**,[26] **1b**,[26] **1c**,[25] **1d**,[21] **1e**,[50] **1f**,[51] **1g**,[51] (*pR*)-**1b**,[19a] (*pS*)-**1b**,[19a] **3a**,[24] **10**,[24] **12**,[37b] **13**,[46] **15**[37] and **16**[37] and (*R*,*R*)-*N*,*N'*-dimethylcyclohexane-1,2-diamine[52] were synthesized according to previously described literature procedures. The SmI$_2$ solution in THF was prepared from Sm and I$_2$ by a previously reported method.[53] CCDC-737657 (**2b**), -737660 (**2d**), -737655 (**2e**), -737656 (**2f**), -737658 (**5b**) and -737659 (**7**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Typical Procedure for the Synthesis of the Nitrones 2a–g and 3b: A solution of *N*-benzylhydroxylamine (5.0 mmol, 1.5–3 equiv.) was added to a solution of the aldehyde (2.4 mmol, 1 equiv.) in CH$_2$Cl$_2$ (20 mL). Anhydrous MgSO$_4$ (5 g, excess) was added, and the mixture was heated at reflux overnight. After filtration through Celite and evaporation of the solvent, the crude nitrone was purified by silica gel chromatography (ethyl acetate/cyclohexane, 50:50).

Compound 2a: Yield 95%. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.00 (s, 2 H, CH$_2$), 5.30 (t$_{\text{app}}$, ^{3}J = 6.4 Hz, 2 H, 3-H, 5-H), 5.42 (t$_{\text{app}}$, ^{3}J = 6.4 Hz, 1 H, 4-H), 6.34 (d, ^{3}J = 6.4 Hz, 2 H, 2-H, 6-H), 6.97 (s, 1 H, HC=N), 7.39–7.42 (m, 5 H, C$^{\text{Ph}}$) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 91.0 (C-3,5), 93.7 (C-4), 93.8 (C-2,6), 95.5 (C-1), 129.5 (CH$^{\text{Ph}}$), 139.5 (CH$^{\text{Ph}}$), 129.6 (CH$^{\text{Ph}}$), 131.3 (HC=N), 132.8 (C$^{\text{Ph}}$), 232.3 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1963, 1885 [CO (Cr)] cm^{-1}. MS (ESI): *m*/*z* = 370 [M + Na]$^+$, 348 [M + H]$^+$. HRMS (ESI): calcd. for C$_{17}$H$_{13}$CrNO$_4$Na 370.0142; found 370.0140 [M + Na]$^+$.

Compound 2b: Yield 88%. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 2.15 (s, 3 H, CH$_3$), 5.03 (s, 2 H, CH$_2$), 5.10 (d, ^{3}J = 6.3 Hz, 1 H, 3-H), 5.19 (t$_{\text{app}}$, ^{3}J = 6.3 Hz, 1 H, 5-H), 5.50 (t$_{\text{app}}$, ^{3}J = 6.3 Hz, 1 H, 4-H), 7.17 (s, 1 H, HC=N), 7.41–7.45 (m, 6 H, C$^{\text{Ph}}$ + 6-H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 19.5 (CH$_3$), 72.0 (CH$_2$), 88.7 (C-5), 92.7 (C-3), 94.4 (C-1), 94.9 (C-4), 95.0 (C-6), 107.9 (C-2), 128.9 (HC=N), 129.4 (CH$^{\text{Ph}}$), 129.5 (CH$^{\text{Ph}}$), 129.6 (CH$^{\text{Ph}}$), 133.0 (C$^{\text{Ph}}$), 232.7 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1963, 1887 [CO (Cr)] cm^{-1}. MS (ESI): *m*/*z* = 384 [M + Na]$^+$, 362 [M + H]$^+$. HRMS (ESI): calcd. for C$_{18}$H$_{15}$CrNO$_4$Na 384.0299; found 384.0296 [M + Na]$^+$.

Compound (*pR*)-2b: $[\alpha]_{\text{D}}^{20}$ = +2109 (0.22, CHCl$_3$).

Compound (*pS*)-2b: $[\alpha]_{\text{D}}^{20}$ = –2087 (0.23, CHCl$_3$).

Compound 2c: Yield 71%. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 3.77 (s, 3 H, OCH$_3$), 4.91 (t$_{\text{app}}$, ^{3}J = 6.3 Hz, 1 H, 5-H), 5.00 (s, 2 H, CH$_2$), 5.05 (d, ^{3}J = 6.3 Hz, 1 H, 3-H), 5.63 (t$_{\text{app}}$, ^{3}J = 6.3 Hz, 1 H, 4-H), 7.39–7.44 (m, 5 H, C$^{\text{Ph}}$), 7.57 (s, 1 H, HC=N), 7.82 (d, ^{3}J = 6.3 Hz, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 56.3 (OCH$_3$), 71.9 (CH$_2$), 73.1 (C-3), 84.5 (C-5), 86.1 (C-1), 94.2 (C-4), 95.4 (C-6), 127.2 (HC=N), 129.0 (CH$^{\text{Ph}}$), 129.2 (CH$^{\text{Ph}}$), 129.2 (CH$^{\text{Ph}}$), 133.5 (C$^{\text{Ph}}$), 140.7 (C-2), 232.5 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1950, 1870 [CO (Cr)] cm^{-1}. ES-MS: *m*/*z* = 400 [M + Na]$^+$, 378 [M + H]$^+$. HRMS (ESI): calcd. for C$_{18}$H$_{15}$CrNO$_5$Na 400.0248; found 400.0249 [M + Na]$^+$.

Compound 2d: Yield 88%. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.09 (s, 9 H, SiMe$_3$), 5.01 (d, ^{2}J = 14.4 Hz, 1 H, CH$_2$), 5.06 (d, ^{2}J = 14.4 Hz, 1 H, CH$_2$), 5.18 (t$_{\text{app}}$, ^{3}J = 6.3 Hz, 1 H, 4-H), 5.40 (d, ^{3}J = 6.3 Hz, 1 H, 3-H), 5.62 (t$_{\text{app}}$, ^{3}J = 6.3 Hz, 1 H, 5-H), 6.95 (s, 1 H, HC=N), 7.13 (d, ^{3}J = 6.3 Hz, 1 H, 6-H), 7.44–7.45 (m, 5 H, C$^{\text{Ph}}$) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 0.30 (SiMe$_3$), 72.1 (CH$_2$), 90.9 (C-4), 91.9 (C-6), 94.6 (C-5), 99.6 (C-1), 99.7 (C-3), 102.3 (C-2), 129.8 (CH$^{\text{Ph}}$), 130.0 (CH$^{\text{Ph}}$), 130.8 (CH$^{\text{Ph}}$), 131.8 (C$^{\text{Ph}}$), 132.0 (HC=N), 233.1 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1959, 1883 [CO (Cr)] cm^{-1}. HRMS (ESI): calcd. for C$_{20}$H$_{21}$CrNO$_4$SiNa 442.0538; found 442.0534 [M + Na]$^+$.

Compound 2e: Yield 83%. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 5.05 (s, 2 H, CH$_2$), 5.31 (t$_{\text{app}}$, ^{3}J = 6.3 Hz, 1 H, 4-H), 5.51 (t$_{\text{app}}$, ^{3}J = 6.3 Hz, 1 H, 5-H), 5.67 (d, ^{3}J = 6.3 Hz, 1 H, 3-H), 7.30 (d, ^{3}J = 6.3 Hz, 1 H, 6-H), 7.33 (s, 1 H, HC=N), 7.43–7.44 (m, 5 H, C$^{\text{Ph}}$) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 72.9 (CH$_2$), 88.8 (C-4), 89.7 (q, ^{3}J = 4.3 Hz, C-3), 90.5 (C-6), 92.1 (C-5), 93.4 (C-1), 94.1 (q, ^{2}J = 34.5 Hz, C-2), 123.8 (q, ^{1}J = 274.1 Hz, CF$_3$), 127.2 (HC=N), 129.5 (CH$^{\text{Ph}}$), 129.7 (CH$^{\text{Ph}}$), 129.8 (CH$^{\text{Ph}}$), 132.4 (C$^{\text{Ph}}$), 230.2 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1975, 1903 [CO (Cr)] cm^{-1}. HRMS (ESI): calcd. for C$_{18}$H$_{12}$CrF$_3$NO$_4$Na 438.0016; found 438.0013 [M + Na]$^+$.

Compound 2f: Yield 58%. ^{1}H NMR (200 MHz, CDCl$_3$): δ = 2.20 (s, 3 H, OCH$_3$), 5.01 (s, 2 H, CH$_2$), 5.24 (d, *J* = 6.5 Hz, 1 H, 4-H), 5.40 (t$_{\text{app}}$, *J* = 6.5 Hz, 1 H, 5-H), 6.06 (t$_{\text{app}}$, *J* = 6.5 Hz, 1 H, 6-H), 6.22 (s, 1 H, 6-H), 6.98 (s, 1 H, HC=N), 7.43–7.44 (m, 5 H, C^{Ph}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2 (CH_3), 71.8 (CH_2), 91.0 (C-6), 92.7 (C-5), 93.7 (C-4 or C-2), 93.8 (C-2 or C-4), 96.9 (C-1), 108.1 (C-3), 129.5 (CH^{Ph}), 129.6 (CH^{Ph}), 129.7 (CH^{Ph}), 131.8 (C-7), 132.7 (C^{Ph}), 233.0 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1940, 1856 [CO (Cr)] cm^{-1}. HRMS (ESI): calcd. for $C_{18}H_{15}CrNO_4Na$ 384.0298; found 384.0300 $[M + Na]^+$.

Compound 2g: Yield 78%. ^1H NMR (400 MHz, $CDCl_3$): δ = 3.73 (s, 3 H, OCH_3), 5.03 (s, 2 H, CH_2), 5.17 (m, 1 H, 5-H), 5.55 (d, ^3J = 4.0 Hz, 2 H, 4-H, 6-H), 5.63 (s, 1 H, 2-H), 7.04 (s, 1 H, HC=N), 7.42–7.47 (m, 5 H, H^{Ph}) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.2 (OCH_3), 72.1 (CH_2), 77.6 (C-2), 79.7 (C-5), 86.7 (C-6 or C-4), 94.0 (C-4 or C-6), 97.9 (C-1), 129.5 (CH^{Ph}), 129.7 (CH^{Ph}), 129.8 (CH^{Ph}), 132.2 (HC=N), 132.5 (C^{Ph}), 142.3 (C-3), 233.2 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1953, 1866 [CO (Cr)] cm^{-1}. ES-MS: m/z = 400 $[M + Na]^+$, 378 $[M + H]^+$. HRMS (ESI): calcd. for $C_{18}H_{15}CrNO_5Na$ 400.0248; found 400.0249 $[M + Na]^+$.

Compound 3b: Yield 78%. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.28 (s, 3 H, CH_3), 5.08 (s, 2 H, CH_2), 7.17 (m, 1 H, 5-H), 7.26 (m, 2 H, 3-H, 4-H), 7.42 (m, 3 H, H^{Ph}), 7.49 (m, 2 H, H^{Ph}), 7.55 (s, 1 H, HC=N), 9.14 (m, 1 H, 6-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 19.9 (CH_3), 71.9 (CH_2), 126.5 (C-3 or C-4), 128.1 (C-6), 129.0 (C-2), 129.2 ($3\times CH^{Ph}$), 129.4 ($2\times CH^{Ph}$), 130.4 (C-5), 130.5 (C-4 or C-3), 131.6 (HC=N), 133.6 (C^{Ph} or C-1), 136.5 (C-1 or C^{Ph}) ppm. HRMS (ESI): calcd. for $C_{15}H_{15}NONa$ 248.1046; found 248.1046 $[M + Na]^+$.

Synthesis of 1,2-Dihydroxylamines 4: A solution of a nitrone (0.5 mmol) in dry THF (10 mL) was cooled to –78 °C. A solution of SmI_2 (0.1 $mol\,L^{-1}$, 2 equiv.) in THF (10 mL) was then added drop by drop. The mixture was stirred at –78 °C for 1 h (**4a**) or 2.5 h (**4b**) before being quenched by addition of saturated solutions of $Na_2S_2O_3$ (10 mL) and $NaHCO_3$ (10 mL). The yellow mixture was extracted with AcOEt. The combined organic layers were washed with a saturated aqueous NaCl solution, dried with $MgSO_4$ and concentrated under reduced pressure.

Compound 4a: Crude product washed with pentane. Yield 90%. ^1H NMR ($CDCl_3$, 400 MHz): δ = 4.02 (d, J = 12.9 Hz, 2 H, CH_2), 4.08 (d, J = 12.9 Hz, 2 H, CH_2), 4.29 (s, 2 H, 7-H), 5.13 (t_{app}, J = 6.3 Hz, 2 H, 3-H or 5-H), 5.21 (t_{app}, J = 6.3 Hz, 2 H, 5-H or 3-H), 5.46 (t_{app}, J = 6.1 Hz, 2 H, 4-H), 5.69 (d, J = 6.3 Hz, 2 H, 6-H or 2-H), 5.72 (br. s, 2 H, OH), 5.75 (d, J = 6.3 Hz, 2 H, 2-H or 6-H), 7.33–7.39 (m, 10 H, H^{Ph}) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 62.3 (CH_2), 70.7 (C-7), 89.5 (C-5 or C-3), 89.8 (C-3 or C-5), 95.2 (C-4), 96.9 (C-2 or C-6), 97.7 (C-6 or C-2), 106.9 (C-1), 128.4 (CH^{Ph}), 129.1 (CH^{Ph}), 129.9 (CH^{Ph}), 136.8 (C^{Ph}), 233.4 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1957, 1872 [CO (Cr)] cm^{-1}. HRMS (ESI): calcd. for $C_{36}H_{32}Cr_2N_2O_8Na$ 719.0548; found 719.0556 $[M + Na]^+$.

Compound 4b: Crude product crystallized from CH_2Cl_2. Yield 27%. ^1H NMR ($CDCl_3$, 400 MHz): δ = 2.03 (s, 6 H, CH_3), 4.24 (d, J = 12.9 Hz, 2 H, CH_2), 4.44 (s, 2 H, 7-H), 4.77 (m, 6 H, CH_2, 3-H, 5-H), 5.03 (br. s, 2 H, OH), 5.40 (t_{app}, J = 6.1 Hz, 2 H, 4-H), 5.92 (d, J = 6.1 Hz, 2 H, 6-H), 7.34–7.51 (m, 10 H, H^{Ph}) ppm. IR (neat): $\tilde{\nu}$ = 1954, 1850 [CO (Cr)] cm^{-1}. HRMS (ESI): calcd. for $C_{36}H_{32}Cr_2N_2O_8Na$ 747.0861; found 747.0864 $[M + Na]^+$.

Typical Procedure for the Synthesis of β-(Hydroxyamino) Alcohols: A solution of nitrone (0.5 mmol) and the carbonyl compound (1 equiv.) in dry THF (10 mL) was cooled to –78 °C. A solution of SmI_2 (0.1 $mol\,L^{-1}$, 2 equiv.) in THF (10 mL) was then added dropwise. The mixture was stirred at –78 °C for 0.5 h before being quenched by the addition of saturated solutions of $Na_2S_2O_3$ (10 mL) and $NaHCO_3$ (10 mL). The yellow mixture was extracted with AcOEt. The combined organic layers were washed with a saturated aqueous NaCl solution and dried with $MgSO_4$. After concentration under reduced pressure, the crude mixture was purified either by washing with pentane (**5b**, **5c**, **5d** and **8**) or by chromatography on silica gel to afford the pure β-(hydroxyamino) alcohols.

Compound 5a: Yield 65%. ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.29 (s, 3 H, CH_3), 1.38 (s, 3 H, CH_3), 3.30 (s, 1 H, 7-H), 3.49 (br. s, 1 H, OH), 3.98 (d, J = 13.0 Hz, 1 H, CH_2), 4.63 (d, J = 13.0 Hz, 1 H, CH_2), 4.76 (br. s, 1 H, OH), 5.23–5.11 (m, 2 H, 3-H, 5-H), 5.53 (d, J = 6.5 Hz, 1 H, 6-H or 2-H), 5.60 (t_{app}, J = 6.2 Hz, 1 H, 4-H), 6.16 (d, J = 6.5 Hz, 1 H, 2-H or 6-H), 7.30–7.45 (m, 5 H, H^{Ph}) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 27.7 (CH_3), 29.6 (CH_3), 63.3 (CH_2), 74.7 (C-8), 75.3 (C-7), 88.5 (C-5 or C-3), 89.1 (C-3 or C-5), 96.5 (C-4), 98.6 (C-2 or C-6), 98.9 (C-6 or C-2), 105.0 (C-1), 128.1 (CH^{Ph}), 128.9 (CH^{Ph}), 129.9 (CH^{Ph}), 137.9 (C^{Ph}), 233.5 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1957, 1862 [CO (Cr)] cm^{-1}. MS (ESI): m/z 430 $[M + Na]^+$, 408 $[M + H]^+$. HRMS (ESI): calcd. for $C_{20}H_{22}CrNO_5$ 408.0898; found 408.0895 $[M + H]^+$.

Compound 5b: Yield 95%. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.15 (s, 3 H, CH_3), 1.32 (s, 3 H, CH_3), 2.17 (s, 3 H, CH_3), 3.53 (s, 1 H, 7-H), 3.63 (br. s, 1 H, OH), 3.98 (d, J = 12.9 Hz, 1 H, CH_2), 4.80 (br. d, J = 13.1 Hz, 2 H, CH_2, OH), 4.96 (d, J = 6.6 Hz, 1 H, 3-H), 5.06 (t_{app}, J = 6.1 Hz, 1 H, 5-H), 5.65 (t_{app}, J = 6.2 Hz, 1 H, 4-H), 6.39 (d, J = 6.6 Hz, 1 H, 6-H), 7.30–7.49 (m, 5 H, H^{Ph}) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.5 (CH_3), 26.9 (CH_3), 29.0 (CH_3), 63.2 (CH_2), 69.0 (C-7), 75.5 (C-8), 86.8 (C-5), 90.9 (C-3), 97.8 (C-4), 100.5 (C-6), 104.6 (C-1), 111.6 (C-2), 127.8 (CH^{Ph}), 128.6 (CH^{Ph}), 130.0 (CH^{Ph}), 137.6 (C^{Ph}), 233.9 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1955, 1863 [CO (Cr)] cm^{-1}. MS (ESI): m/z = 444 $[M + Na]^+$, 422 $[M + H]^+$. HRMS (ESI): calcd. for $C_{21}H_{23}CrNO_5Na$ 444.0874; found 444.0867 $[M + Na]^+$.

Compound (*pR*,*S*)-5b: $[\alpha]_D^{20}$ = +150 (0.26, $CHCl_3$).

Compound 5c: Yield 93%. ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.13 (s, 3 H, CH_3), 1.31 (s, 3 H, CH_3), 3.61 (br. s, 1 H, OH), 3.76 (s, 3 H, OCH_3), 3.97 (d, J = 13.1 Hz, 1 H, CH_2), 4.07 (s, 1 H, 7-H), 4.86 (t_{app}, J = 6.8 Hz, 1 H, 5-H), 4.88 (d, J = 13.1 Hz, 2 H, CH_2), 5.01 (d, J = 6.8 Hz, 1 H, 3-H), 5.71 (t_{app}, J = 6.8 Hz, 1 H, 4-H), 6.50 (d, J = 6.8 Hz, 1 H, 6-H), 7.30–7.50 (m, 5 H, H^{Ph}) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.7 (CH_3), 28.7 (CH_3), 55.9 (OCH_3), 63.1 (CH_2), 65.8 (C-7), 72.7 (C-3), 75.2 (C-8), 83.7 (C-5), 95.3 (C-1), 95.8 (C-4), 101.1 (C-6), 128.0 (CH^{Ph}), 128.8 (CH^{Ph}), 130.1 (CH^{Ph}), 138.1 (C^{Ph}), 142.5 (C-2), 233.9 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1954, 1864 [CO (Cr)] cm^{-1}. MS (ESI): m/z = 460 $[M + Na]^+$, 438 $[M + H]^+$. HRMS (ESI): calcd. for $C_{21}H_{24}CrNO_6$ 438.1003; found 438.1002 $[M + H]^+$.

Compound 5d: Yield 95%. ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.45 (s, 9 H, $SiMe_3$), 1.23 (s, 3 H, CH_3), 1.41 (s, 3 H, CH_3), 3.34 (br. s, 1 H, OH), 3.75 (s, 1 H, 7-H), 4.09 (d, J = 13.1 Hz, 1 H, CH_2), 4.72 (d, J = 13.1 Hz, 1 H, CH_2), 5.12 (d, J = 6.3 Hz, 1 H, 3-H), 5.37 (t_{app}, J = 6.3 Hz, 1 H, 5-H), 5.56 (t_{app}, J = 6.3 Hz, 1 H, 4-H), 6.19 (d, J = 6.3 Hz, 1 H, 6-H), 7,48–7.29 (m, 5 H, H^{Ph}) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 2.4 ($SiMe_3$), 28.8 (CH_3), 30.2 (CH_3), 64.3 (CH_2), 72.7 (C-7), 75.6 (C-8), 90.6 (C-5), 96.1 (C-3), 97.0 (C-4), 98.0 (C-6), 104.4 (C-1), 115.9 (C-2), 128.0 (CH^{Ph}), 128.9 (CH^{Ph}), 129.7 (CH^{Ph}), 138.1 (C^{Ph}), 233.9 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1956, 1865 [CO (Cr)] cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{30}CrNO_5Si$ 480.1293; found 480.1293 $[M + H]^+$.

Compound 5e: Yield 35%. ^1H NMR ($CDCl_3$, 200 MHz): δ = 1.04 (s, 3 H, CH_3), 1.48 (s, 3 H, CH_3), 3.25 (br. s, 1 H, OH), 3.64 (s, 1 H, 7-H), 3.90 (d, J = 13.2 Hz, 1 H, CH_2), 4.64 (br. s, 1 H, OH), 4.66 (d, J = 13.2 Hz, 1 H, CH_2), 5.22 (t_{app}, J = 1.1, 6.5 Hz, 1 H, 5-H), 5.34 (d, J = 1.1, 6.5 Hz, 1 H, 3-H), 5.70 (t$_{\text{app}}$, J = 6.5 Hz, 1 H, 4-H), 6.46 (d, J = 6.6 Hz, 1 H, 6-H), 7.29–7.47 (m, 5 H, H$^{\text{Ph}}$) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 27.6 (CH$_3$), 29.9 (CH$_3$), 63.0 (CH$_2$), 68.8 (C-7), 76.2 (C-8), 84.7 (q, ^3J = 5.0 Hz, C-3), 87.3 (C-5), 95.4 (C-4), 99.6 (C-6), 101.0 (q, ^2J = 30.2 Hz, C-2), 102.3 (C-1), 128.1 (CH$^{\text{Ph}}$), 128.9 ($2\times$CH$^{\text{Ph}}$), 130.0 ($2\times$CH$^{\text{Ph}}$), 137.6 (C$^{\text{Ph}}$), 231.7 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1970, 1891 [CO (Cr)] cm^{-1}. HRMS (ESI): calcd. for C$_{21}$H$_{20}$CrF$_3$NO$_5$Na 498.0591; found 498.0581 [M + Na]$^+$.

Compound 5f: Mixture of two diastereoisomers in a 50:50 ratio. Yield 47%. ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 1.30 (br. s, 6 H, $2\times$CH$_3$), 1.40 (s, 3 H, CH$_3$), 1.41 (s, 3 H, CH$_3$), 2.18 (s, 3 H, CH$_3$), 2.21 (s, 3 H, CH$_3$), 3.38 (s, 1 H, 7-H), 3.40 (s, 1 H, 7-H), 3.50 (br. s, 1 H, OH), 3.52 (br. s, 1 H, OH), 4.04 (d, J = 13.1 Hz, 2 H, $2\times$CH$_2$), 4.58 (d, J = 13.1 Hz, 2 H, CH$_2$), 4.61 (d, J = 13.1 Hz, 2 H, CH$_2$), 4.88 (br. s, 1 H, OH), 4.91 (br. s, 1 H, OH), 5.18 (t$_{\text{app}}$, J = 6.8 Hz, 1 H, 5-H), 5.25 (t$_{\text{app}}$, J = 6.8 Hz, 1 H, 5-H), 5.39 (d, J = 6.8 Hz, 1 H, 6-H), 5.47 (m, 3 H, 2-H, 4-H, 6-H), 5.99 (d, J = 6.8 Hz, 1 H, 4-H), 6.05 (s, 1 H, 2-H), 7.30–7.45 (m, 10 H, H$^{\text{Ph}}$) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 21.1 (CH$_3$), 21.4 (CH$_3$), 28.0 (CH$_3$), 28.1 (CH$_3$), 29.9 ($2\times$CH$_3$), 63.5 (CH$_2$), 63.6 (CH$_2$), 74.9 (C-7), 75.0 (C-7), 75.1 ($2\times$C-8), 89.4 (C-5), 90.1 (C-5), 96.1 (C-4), 96.6 (C-4), 96.8 (C-6), 97.3 (C-6), 99.0 (C-2), 99.6 (C-2), 104.8 (C-1 or C-3), 105.7 (C-1 or C-3), 106.5 (C-3 or C-1), 106.8 (C-3 or C-1), 128.1 ($2\times$CH$^{\text{Ph}}$), 128.9 ($4\times$CH$^{\text{Ph}}$), 129.7 ($2\times$CH$^{\text{Ph}}$), 129.8 ($2\times$CH$^{\text{Ph}}$), 137.9 ($2\times$C$^{\text{Ph}}$), 233.8 (CO), 233.9 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1953, 1861 [CO (Cr)] cm^{-1}. HRMS (ESI): calcd. for C$_{21}$H$_{24}$CrNO$_5$ 422.1054; found 422.1051 [M + H]$^+$.

Compound 6: Yield 88%. ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 1.02–2.07 [m, 10 H, (CH$_2$)$_n$], 2.16 (s, 3 H, CH$_3$), 3.24 (br. s, 1 H, OH), 3.47 (s, 1 H, 7-H), 4.02 (d, J = 13.0 Hz, 1 H, CH$_2$), 4.64 (br. s, 1 H, OH), 4.78 (d, J = 13.0 Hz, 1 H, CH$_2$), 4.96 (d, J = 6.2 Hz, 1 H, 3-H), 5.07 (t$_{\text{app}}$, J = 6.2 Hz, 1 H, 5-H), 5.65 (t$_{\text{app}}$, J = 6.2 Hz, 1 H, 4-H), 6.43 (d, J = 6.2 Hz, 1 H, 6-H), 7.30–7.49 (m, 5 H, H$^{\text{Ph}}$) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 21.6 (CH$_3$), 21.7 (CH$_2$), 22.2 (CH$_2$), 26.0 (CH$_2$), 34.6 (CH$_2$), 36.8 (CH$_2$), 63.1 (CH$_2$), 69.3 (C-7), 76.4 (C-8), 86.8 (C-5), 90.9 (C-3), 97.9 (C-4), 101.1 (C-6), 104.4 (C-1), 111.8 (C-2), 128.1 (CH$^{\text{Ph}}$), 129.0 (CH$^{\text{Ph}}$), 130.0 (CH$^{\text{Ph}}$), 137.7 (C$^{\text{Ph}}$), 233.8 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1949, 1863 [CO (Cr)] cm^{-1}. HRMS (ESI): calcd. for C$_{24}$H$_{27}$CrNO$_5$Na 484.1187; found 484.1177 [M + Na]$^+$.

Compound 7: Yield 96%. ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 0.84 [s, 9 H, (CH$_3$)$_3$], 2.17 (s, 3 H, CH$_3$), 3.57 (d, J = 6.6 Hz, 1 H, 7-H or 8-H), 3.72 (d, J = 6.6 Hz, 1 H, 8-H or 7-H), 4.00 (d, J = 13.1 Hz, 1 H, CH$_2$), 4.53 (br. s, 1 H, OH), 4.78 (br. d, J = 13.1 Hz, 1 H, CH$_2$), 4.97 (d, J = 6.1 Hz, 1 H, 3-H), 5.13 (t$_{\text{app}}$, J = 6.1 Hz, 1 H, 5-H), 5.61 (t$_{\text{app}}$, J = 6.1 Hz, 1 H, 4-H), 6.19 (d, J = 6.1 Hz, 1 H, 6-H), 7.30–7.46 (m, 5 H, H$^{\text{Ph}}$) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 20.5 (CH$_3$), 27.4 [(CH$_3$)$_3$], 35.6 [C(CH$_3$)$_3$], 61.7 (CH$_2$), 63.0 (C-8 or C-7), 81.5 (C-7 or C-8), 87.4 (C-3), 91.5 (C-5), 97.3 (C-4), 100.2 (C-6), 107.5 (C-2 or C-1), 110.1 (C-1 or C-2), 128.1 (CH$^{\text{Ph}}$), 129.0 (CH$^{\text{Ph}}$), 129.8 (CH$^{\text{Ph}}$), 137.3 (C$^{\text{Ph}}$), 233.8 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1955, 1854 [CO (Cr)] cm^{-1}. HRMS (ESI): calcd. for C$_{23}$H$_{27}$CrNO$_5$Na 470.1242; found 470.1028 [M + Na]$^+$.

Compound 8: Mixture of two diastereoisomers in a 70:30 ratio. Yield 83%. Major diastereoisomer (51%): ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 0.96 (t, J = 7.4 Hz, 3 H, CH$_3$), 1.26 (m, 2 H, CH$_2$), 2.16 (s, 3 H, CH$_3$), 3.47 (d, J = 8.8 Hz, 1 H, 7-H), 3.85 (m, 2 H, 8-H, OH), 3.97 (d, J = 13.0 Hz, 1 H, CH$_2$), 4.64 (br. s, 1 H, OH), 4.77 (d, J = 13.0 Hz, 1 H, CH$_2$), 4.95 (dd, J = 1.0, 6.5 Hz, 1 H, 3-H), 5.06 (t$_{\text{app}}$, J = 1.0, 6.5 Hz, 1 H, 5-H), 5.62 (t$_{\text{app}}$, J = 1.0, 6.5 Hz, 1 H, 4-H), 6.09 (d, J = 1.0, 6.5 Hz, 1 H, 6-H), 7.31–7.48 (m, 5 H, H$^{\text{Ph}}$) ppm. ^{13}C NMR [(CD$_3$)$_2$CO, 100 MHz]: δ = 12.2 (CH$_3$), 21.8 (CH$_3$), 27.8 (CH$_2$), 63.4 (CH$_2$), 69.7 (C-7), 76.6 (C-8), 90.3 (C-5), 94.0 (C-3), 99.8 (C-4), 101.8 (C-6), 109.6 (C-2 or C-1), 114.2 (C-1 or C-2), 129.0 (CH$^{\text{Ph}}$), 130.0 (CH$^{\text{Ph}}$), 131.4 (CH$^{\text{Ph}}$), 140.7 (C$^{\text{Ph}}$), 236.2 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1955, 1858 [CO (Cr)] cm^{-1}. HRMS (ESI): calcd. for C$_{21}$H$_{24}$CrNO$_5$ 422.1054; found 422.1051 [M + H]$^+$.

Desilylation Procedure: A solution of the β-(hydroxyamino) alcohol **5d** (70 mg, 0.15 mmol) in dry THF (2 mL) was cooled to –78 °C for the addition of TBAF (1 M solution in THF, 165 µL, 1.1 equiv.). The reaction mixture was allowed to warm to 0 °C and was stirred at this temperature for 1 h before being quenched by addition of H$_2$O. The mixture was extracted twice with Et$_2$O. The combined organic layers were washed with a saturated NaCl solution and dried with MgSO$_4$. After concentration under reduced pressure, the crude mixture was purified by chromatography on silica gel to afford **5a** (46 mg) in 76% yield.

Typical Procedure for the One-Pot Synthesis of β-Amino Alcohols: A solution of a nitrone (0.5 mmol) and acetone (1 equiv.) in dry THF (10 mL) was cooled to –78 °C. A solution of SmI$_2$ (0.1 mol L^{-1}, 6 equiv.) in THF (30 mL) was then added dropwise. The mixture was stirred at –78 °C for 0.5 h and then at room temperature for 15 h before being quenched by addition of saturated solutions of Na$_2$S$_2$O$_3$ (10 mL) and NaHCO$_3$ (10 mL). The yellow mixture was extracted with AcOEt. The combined organic layers were washed with a saturated aqueous NaCl solution and dried with MgSO$_4$. After concentration in vacuo, the crude mixture was purified by chromatography on silica gel to afford the pure β-amino alcohol.

Compound 17a: Yield 60%. ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 1.05 (s, 3 H, CH$_3$), 1.26 (s, 3 H, CH$_3$), 2.88 (br. s, 1 H, OH or NH), 3.25 (d, J = 5.1 Hz, 1 H, 7-H), 3.85 (dd, J = 8.1, 12.3 Hz, 1 H, CH$_2$), 4.32 (dd, J = 5.1, 12.3 Hz, 1 H, CH$_2$), 5.18 (t$_{\text{app}}$, J = 6.3 Hz, 1 H, 3-H or 5-H), 5.24 (t$_{\text{app}}$, J = 6.3 Hz, 1 H, 5-H or 3-H), 5.51–5.45 (m, 2 H, 6-H or 2-H, 4-H), 5.70 (d, J = 6.3 Hz, 1 H, 2-H or 6-H), 7.45–7.27 (m, 5 H, H$^{\text{Ph}}$) ppm. ^{13}C NMR (CDCl$_3$, 100 MHz): δ = 25.5 (CH$_3$), 28.3 (CH$_3$), 54.4 (CH$_2$), 69.8 (C-7), 73.2 (C-8), 89.3 (C-5 or C-3), 89.9 (C-3 or C-5), 92.8 (C-2 or C-6), 95.5 (C-4), 97.1 (C-6 or C-2), 110.0 (C-1), 127.7 (CH$^{\text{Ph}}$), 128.9 ($2\times$CH$^{\text{Ph}}$), 140.2 (C$^{\text{Ph}}$), 233.4 (CO) ppm. IR (neat): $\tilde{\nu}$ = 1957, 1866 [CO (Cr)] cm^{-1}. HRMS (ESI): calcd. for C$_{20}$H$_{22}$CrNO$_4$ 392.0949; found 392.0951 [M + H]$^+$.

Compound 17b: Yield 81%. ^{1}H NMR (CDCl$_3$, 400 MHz): δ = 1.03 (s, 3 H, CH$_3$), 1.24 (s, 3 H, CH$_3$), 2.27 (s, 3 H, CH$_3$), 3.02 (s, 1 H, 7-H), 3.41 (br. s, 1 H, OH), 3.88 (br. d, J = 12.4 Hz, 1 H, CH$_2$), 4.27 (d, J = 12.4 Hz, 1 H, CH$_2$), 5.03 (dd, J = 1.0, 6.3 Hz, 1 H, H^3), 5.11 (td, J = 1.0, 6.3 Hz, 1 H, 5-H), 5.55 (td, J = 1.0, 6.3 Hz, 1 H, 4-H), 5.74 (dd, J = 1.0, 6.3 Hz, 1 H, 6-H), 7.29–7.45 (m, 5 H, H$^{\text{Ph}}$) ppm. HRMS (ESI): calcd. for C$_{20}$H$_{22}$CrNO$_4$ 406.1101; found 406.1105 [M + H]$^+$.

Compound (*pR,S*)-17b: $[\alpha]_{\text{D}}^{20}$ = +17 (0.24, CHCl$_3$).

Supporting Information (see footnote on the first page of this article): Selected ^{1}H NMR spectroscopic data for aldehyde substrates **1a**–**g**. ^{1}H and ^{13}C NMR spectra for all new compounds. Crystal data for **2b**, **2d**, **2e**, **2f**, **5b** and **7**.

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