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Two-step synthesis of homochiral monoaminals of tricarbonylphthalaldehydechromium complex

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Tricarbonylphthalaldehydechromium complex can be prepared using a 'one pot' procedure starting from tricarbonylbenzenechromium: the protection of one aldehyde function by chiral diamines leads to the formation of two diastereoisomers of the monoaminal of the phthlaldehyde complexes, efficient precursors of enantiopure *ortho*-substituted alkenyl arene complexes.

Tricarbonyl(η^6-arene)chromium complexes have been considered as important intermediates in organic synthesis.[1] Since unsymmetrically 1,2- or 1,3-substituted complexes have planar chirality, recent research in this field has been focused on the development of efficient routes to optically active complexes.[2–6]

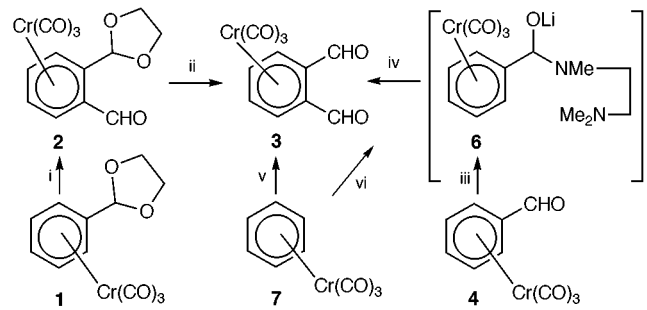
We have shown that chiral diamines having a C_2 axis of symmetry can be considered as an efficient tool for the asymmetric formation of aminals of *o*-substituted tricarbonyl(benzaldehyde)chromium complexes.[3a,7] The ease of handling such aminal complexes prompted us to use them in the preparation of enantiopure monoaminals of tricarbonylphthaldehydechromium complexes, which could be used as precursors of homochiral *o*-substituted styrene complexes for example.[4,8,9]

We now present results which demonstrate that chiral diamines may be used for the preparation of homochiral *o*-substituted styrene complexes from tricarbonylphthaldehydechromium complex **3**. This new synthon has several attractive features, among which the most interesting is the possibility of differentiating the two aldehyde functionalties, thus breaking the plane of symmetry and introducing asymmetry. Compound **3** is easily and efficiently synthesised in a 'one-pot' procedure, by a new methodology, starting from a simple complex: tricarbonylbenzenechromium **7**.

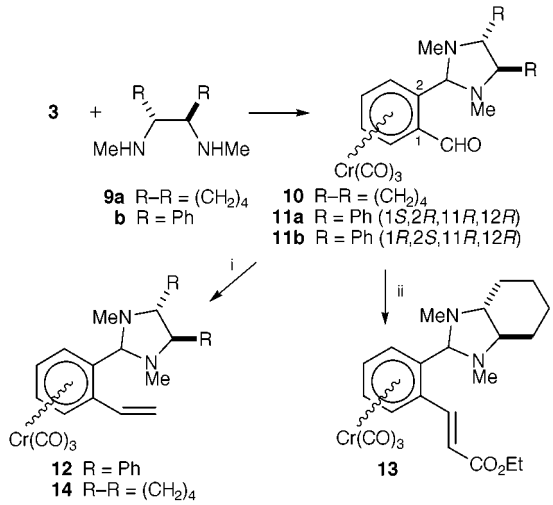
Our first attempts to prepare synthon **3** were as follows: benzaldehyde ethane-1,2-diyl acetal **1** treated with BuLi (4 equiv.) at −78 °C and then with DMF was converted into the monoacetal of phthlaldehyde **2** in 49% yield. Hydrolysis of the acetal did not occur in good yield, as decomplexation of the tricarbonylchromium function became the dominant mode of reaction.[10b] Indeed complex **3** was obtained only in 22 and 19% using either H_2SO_4[3b,c,10] or HCO_2H[11] (Scheme 1). It was also possible to obtain complex **3** by treating tricarbonylbenzaldehydechromium complex **4** with the diamine $MeNHCH_2CH_2NMe_2$ **5** and BuLi.[12] Indeed the amino alcoholate intermediate **6** can be *ortho*-lithiated in order to react with DMF, giving complex **3** in 35% yield only (Scheme 1). Thus, we examined the possibility of obtaining complex **3** directly from tricarbonylbenzenechromium complex **7**, in a one-pot procedure, using the amide $Me_2NCH_2CH_2NMeCHO$ **8**. Complex **7** at −78 °C was treated with BuLi (1.2 equiv.). The formamide **8** (1 equiv.) was added and stirred for 30 min at −30 °C. BuLi (3 equiv.) and DMF (3 equiv.) were then added sequentially. Hydrolysis of the reaction mixture with 0.1 M HCl gave a red solution, which was chromatographed on a silica gel column. Benzaldehyde complex **4** was the first product eluted with a 3:2 mixture of Et_2O–light petroleum (15% after recrystallisation). The second product, the phthaldaldehydechromium complex **3**, eluted with a 7:3 mixture of Et_2O–light petroleum and was obtained in 41% yield after recrystallisation as red crystals (Scheme 1).

Among the various ways to desymmetrise **3**, we focussed on the selective formation of the chiral monoaminal. Condensation of (*R*,*R*)-1,2-bis(*N*-methylamino)cyclohexanediamine **9a**[2] with complex **3** gave two diastereoisomers **10**† in 76% yield which were easily separated by silica gel chromatography (44 and 32% yield) (Scheme 2). After separation, the diastereomeric composition of each stereoisomer was checked by ^{1}H NMR[3a] which showed one singlet for the aminalic proton H7 at δ 4.81 and 4.23. Alternatively, condensation of (*R*,*R*)-1,2-bis(*N*-methylamino)-1,2-diphenylethane[7,8] **9b** with phthalaldehyde **3** at room temperature for 30 min gave two diastereoisomers **11**, inseparable by silica gel chromatography, in the ratio 56:44 in 78% yield. Fortunately, their separation could be achieved by precipitation of one diastereomer **11a** (whose aminalic proton resonated at low field: δ 5.53), which gave suitable crystals for an X-ray analysis, and thus allowed assignment of the aminalic proton chemical shift of this diastereomer by ^{1}H NMR. The ORTEP view, shown in Fig.1, indicated a (1*S*,2*R*) configuration.‡ It is worth noting that the conformation of the $Cr(CO)_3$ tripod is almost staggered with respect to the carbons of the arene ring and that unexpectedly the aldehyde function is not in the plane of the arene ring. Indeed we observed a 12° angle between the carbon–oxygen double bond and the plane of the ring in the direction opposite to the organometallic moiety.

Once synthon **3** was desymmetrised, the free aldehyde functionality of monoaminals **10** and **11** may be reacted with various reagents. As an illustration of this concept, we describe



Scheme 1 *Reagents and conditions:* i, BuLi, DMF, THF, 49%; ii, H_2SO_4, 22% or HCO_2H, 19%; iii, BuLi, $NMe_2CH_2CH_2NHMe$ **5**, THF; iv, BuLi, DMF, THF, 35% from **4**; v, BuLi, $Me_2NCH_2CH_2NMeCHO$ **8**, THF, then BuLi, DMF, then 0.1 M HCl, 41% (and **4**, 15%); vi, BuLi, $Me_2NCH_2CH_2N$-MeCHO **8**, THF.



Scheme 2 *Reagents and conditions:* i, separation of the diastereoisomers, then $MePPh_3Br$, $NaNH_2$, Et_2O, 16% for **12a**, 28% for **12b**; ii, separation of the diastereoisomers, then $[P(O)(OEt)_2]NaCHCO_2Et$, room temp., 87% for **13a**, 85% for **13b**.

here the olefination of the free aldehyde, to obtain optically pure *o*-substituted styrene complexes. Treating the diastereoisomers **10a** or **10b** with $MePPh_3Br$ and $NaNH_2$ in dry Et_2O gave the styrene derivatives **12a** in 16% yield or **12b** in 28% yield. Complexes **11a** and **11b** also reacted with $MePPh_3Br$ and $NaNH_2$ to afford the optically pure styrene derivatives **14a** and **14b** (in 23 and 18% yield) which can be separated by column chromatography. More interestingly, reaction of complex **10a** with the carbanion of the phosphonate $[P(O)(OEt)_2]NaCHCO_2Et$ occured smoothly giving complex **13a**† as orange crystals in 87% yield. The same reaction with diastereoisomer **10b** gave complex **13b**† in 85% yield.

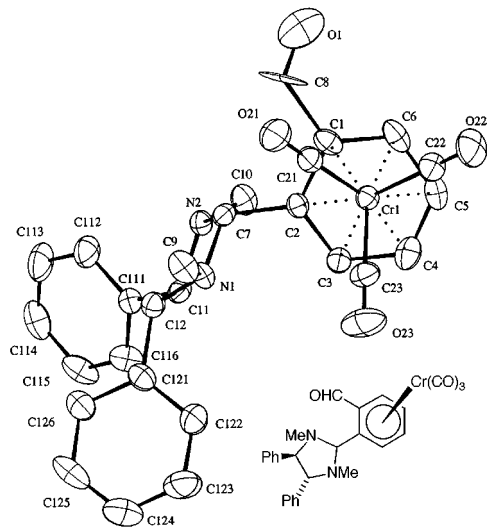


Fig. 1 ORTEP view of the molecular structure of complex **11a**. Selected interatomic distances (Å): Cr(1)–C(1) 2.180(7); Cr(1)–C(2)2.220(6); Cr(1)–C(3) 2.196(6); Cr(1)–C(4) 2.199(7); Cr(1)–C(5) 2.199(7); Cr(1)–C(6) 2.191(7).

In conclusion, these preliminary results open up, *via* a 'one-pot' procedure from benzenechromium complex, a ready access to phthalaldehydechromium complex. It is worth noting that this represents a *facile bifunctionnalisation of benzene* which can lead to chiral *ortho*-disubstituted arenechromium complexes. It can be used for the synthesis of enantiomerically pure styrenechromium complexes substituted at the *ortho* position by potentially versatile aminal groups. The scope of the applications of these new homochiral complexes is currently being investigated in our laboratory.

Notes and references

† *Typical procedure* for **10**: A mixture of complex **3** (0.1 g, 0.37 mmol), diamine **9a** (63 mg, 0.45 mmol) and molecular sieves in dry Et_2O (25 ml) was stirred for 25 min at room temperature under N_2. The solution turned orange. After silica gel chromatography, the first diastereoisomer was eluted with Et_2O–NEt_3–cyclohexane (70 : 0.01 : 30) and obtained in 44% yield (64 mg). The second diastereoisomer was eluted with Et_2O–0.01% NEt_3 and obtained in 32% yield (46 mg). *Selected data* for **10b**: δ_H(400 MHz, $CDCl_3$) 1.13–1.37 (m, 4H), 1.84–2.1 (m, 4H), 2.37 (s, 3H), 2.49 (s, 3H), 2.58 (m, 2H), 4.23 (s, 1H, H7), 5.49 (m, 2H, H4, H5), 5.58 (m, 1H, H6), 5.62 (m, 1H, H3), 10.3 (s, 1H); $[\alpha]_D^{20}$ −98 ($CHCl_3$, *c* 0.08). For **13b**: δ_H 1.23–1.19 (m, 4H), 131 (t, *J* 7, 3H), 1.78–1.82 (m, 4H), 2.27 (s, 3H), 2.28 (m, 2H), 2.56 (s, 3H), 4.30 (q, *J* 7, 2H), 5.21 (d, *J* 6, 1H, H6), 4.39 (s, 1H, H7), 5.30 (d, *J* 6, 1H, H6), 5.36 (m, 1H, H5), 5.47 (m, 1H, H4), 6.03 (d, *J* 6, 1H, H3), 6.22 (d, *J* 15, 1H), 7.87 (d, *J* 15, 1H); $[\alpha]_D^{20}$ +340 ($CHCl_3$, *c* 0.01). All novel complexes (**10**–**14**) were characterised by microanalyses, NMR and IR spectra and low resolution MS.

‡ *Crystal data* for **11a**: $C_{27}H_{24}N_2O_4Cr$, M = 492.5, orthorhombic, space group $P2_12_12_1$, a = 7.333(2), b = 14.455(3), c = 22.976(4) Å, D_C = 1.34 g cm^{-3} , Z = 4, 0.20 × 0.20 × 0.64 mm, μ = 4.91 cm^{-1}, 1466 data collected at room temperature on a Nonius CAD4 diffractometer. Absorption correction using DIFABS was applied (T_{min} = 0.92, T_{max} = 1). Anomalous dispersion terms and correction of secondary extinction were applied. The structure was solved by standard Patterson–Fourier techniques and refined by least-squares analysis using anisotropic thermal parameters for all non-hydrogen atoms. H atoms were located on a difference Fourier map and introduced in the refinement as fixed contributors with an overall isotropic thermal parameter. 1771 reflections, with $I > 3\sigma(I)$, were used to solve and refine the structure to R = 0.042 and R_w = 0.048 (unit weights), 309 least-squares parameters. The programs used were CRYSTALS and CAMERON. The shape of the anisotropic displacement ellipsoid for C8 suggests some disorder. Unfortunately, attempts to deal with this disorder failed. CCDC 182/1409. See http://www.rsc.org/suppdata/cc/1999/2061 for crystallographic data in .cif format.

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