Generation of and Cycloaddition to an Enantiomerically Pure α-Oxy-*ortho*-quinodimethane–Tricarbonylchromium Complex Intermediate

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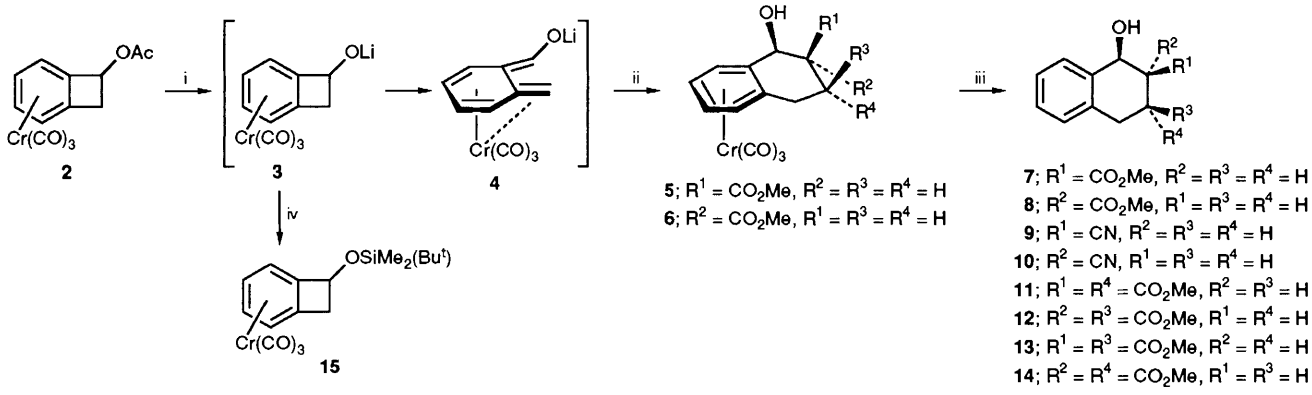
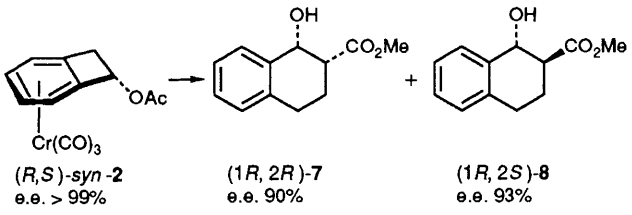
The reaction of Bu^{n}Li with either *syn*- or *anti*-η^6-(1-acetoxycyclobutabenzene)Cr(CO)$_3$ generates under mild conditions the planar chiral *ortho*-quinodimethane complex intermediate **4** which reacts with dienophiles (methyl acrylate, acrylonitrile, dimethyl fumarate) highly stereoselectively from the face opposite the metal to give the *anti*-1-hydroxytetrahydronaphthalene–Cr(CO)$_3$ complexes (X-ray structures of **5** and **6**) and, after decomplexation, the 1-hydroxytetrahydronaphthalenes **7–14** (asymmetric synthesis of **7** and **8**).

ortho-Quinodimethanes can be generated in a number of ways, foremost among these is by electrocyclic ring opening of cyclobutabenzenes.[1] Extensive application in synthesis is based on the high reactivity of these intermediates in Diels–Alder reactions.[2] Asymmetric variants include chiral auxiliaries attached to a terminal carbon of the diene[3] or to the dienophile.[4] We here show a different method centred on the blocking of one enantioface of an achiral *o*-quinodimethane coordinated to a transition metal group which results in high asymmetric induction in a cycloaddition reaction. The procedure is based on our previous finding that η^6-(1-ethoxycyclobutabenzene)Cr(CO)$_3$ undergoes ring opening and a stereoselective cycloaddition reaction without loss of metal coordination to yield a tetrahydronaphthalene complex.[5] A severe limitation of this reaction is the requirement of very bulky dienophiles in order to prevent addition to the metal



Scheme 1 *Reagents and conditions*: Bu^{n}Li (2.1 equiv.), THF, −78 °C, 30 min; ii, dienophile (10 equiv.), −78 to 0 °C, 3 + 1 h, sat. aq. NH_4Cl; iii, air, *hν*, Et_2O, 20 °C; iv, $TfOSiMe_2(Bu^t)$ (Tf = CF_3SO_2)



Scheme 2 *Reagents and conditions*: see Scheme 1

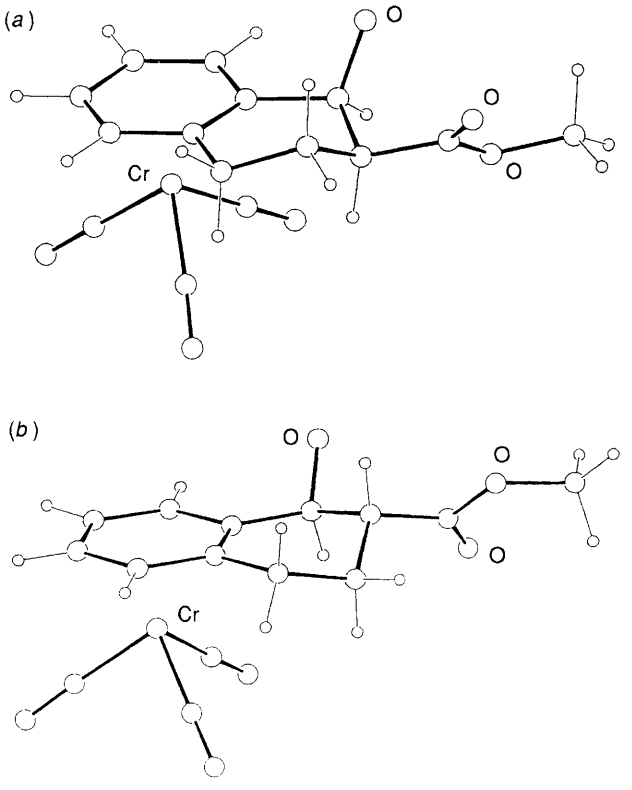


Fig. 1 Molecular structures of complexes (*a*) **5** and (*b*) **6**

(CO exchange) and ensuing complex decomposition at the high temperature (160 °C) required for the generation of the *o*-quinodimethane complex intermediate. The electrocyclic ring opening can be accelerated by resonance donor substitutents,[2c] and, most efficiently, as shown recently by Choy *et al.*, by the generation of an anionic centre α to the four-membered ring.[6] This methodology can be successfully applied to the transition metal complex **2**.

Bu^{n}Li (2 mol dm^{-3} in hexane, 2.1 mmol) was added dropwise to a solution of (1-acetoxycyclobutabenzene)-Cr(CO)$_3$† **2** (1 mmol) in tetrahydrofuran (THF) at −78 °C (bath temperature). After 30 min, methyl acrylate (10 mmol) was introduced and the homogeneous solution was warmed to 0 °C over a 3 h period. The reaction with the dienophile was accompanied by a colour change, beginning at −20 °C from yellow-brown to orange.‡ The mixture was stirred at 0 °C for 1 h, recooled to −78 °C, and then treated with saturated aqueous ammonium chloride. Extraction with diethyl ether followed by evaporation yielded a yellow oil shown by ^{1}H NMR spectroscopy to consist of a 3:1 mixture of the complexes **5** and **6**. Decomplexation by exposing the ethereal solution to air and sunlight gave the tetrahydronaphthalenes **7** and **8** in 70% isolated yield (ratio 3:1, Scheme 1).§ Identical results were obtained separately with *syn*- and with *anti*-**2** and this shows that the common intermediate is most likely the chiral complex **4**. Confirmation of the molecular structure of **5** and **6** comes from single crystal X-ray diffraction studies (see Fig. 1) which show that both complexes have the 1-OH group *anti* to the Cr(CO)$_3$ group.¶ The cycloaddition reaction, as in the previous example,[5] thus takes place with high regio- and diastereo-selectivity with respect to the diene face of the putative *o*-quinodimethane complex intermediate **4**. The absence of a product having the 1-OH group *syn* to the metal shows that the cycloaddition does not proceed *via* an intermediate in which the dienophile is coordinated to the metal. The low diastereoselectivity at C(2) may be ascribed to completion between *endo* (favoured) and *exo* transition states in the cycloaddition reaction. Another possibility is that complex **5** is formed exclusively in the cycloaddition reaction, but that it equilibrates under the basic conditions.

Analogous reactions with acrylonitrile gave **9** and **10** (3:1, 57%) and with dimethyl fumarate **11** and **12** (2.8:1, 73%). Dimethyl maleate gave a 78% yield of a mixture of **11**–**14** in the ratio of 11:5:1:2. The *cis*–*trans*-isomerisation may be caused by the presence of alkoxides in the reaction mixture[8] or by a polar, stepwise mechanism for the cycloaddition reaction.

The highly selective dienophile addition of methyl acrylate to the face *anti* to the Cr(CO)$_3$ fragment was confirmed by carrying out the reaction with enantiomerically pure (*R,S*)-*syn*-**2** prepared by the above route from (*S*)-1-acetoxycyclobutabenzene **1**.‖ The cycloaddition reaction, followed by decomplexation gave (1*R*,2*R*)-**7** (90% enantiomeric excess,

† This complex was prepared in 70% yield *via* arene exchange in (naphthalene)Cr(CO)$_3$ (THF, 70 °C, 9 h).[7] Diastereoisomers *syn*-**2** and *anti*-**2** (1:1 mixture) were readily separated by column chromatography (eluent diethyl ether–hexane, 1:4).

‡ We take this as the temperature of formation of the *o*-quinodimethane intermediate **4** which reacts rapidly with the dienophile, the colour being that of the deprotonated cycloaddition products. In the absence of the dienophile, the colour change at the same temperature is to burgundy red. The generation of **3** was demonstrated by trapping reactions with TfOSiMe$_2$(Bu^t) at −78 and −23 °C to give the cyclobutabenzene complex **15** in 74 and 70% yield, respectively.

§ The reaction with uncomplexed 1-acetoxycyclobutabenzene **1** and methyl acrylate gave **6** and **7** in an 18:1 ratio (78% yield).

¶ *^{1}H NMR data* for **5** and **6** (400 MHz; C_6D_6): **5**: δ 5.04 (d, 1H, *J* 6 Hz, H_{arom}), 4.63 (br.s, 1H, 1-H), 4.47 (t, 1H, *J* 6 Hz, H_{arom}), 4.30 (t, 1H, *J* 6 Hz, H_{arom}), 4.25 (d, 1H, *J* 6 Hz, H_{arom}), 3.25 (s, CO_2Me), 3.15 (s, OH), 2.68–2.63 (dt, 1H, *J* 4, 12 Hz, 2-H), 2.35–2.26 (ddd, 1H, *J* 4, 8, 11 Hz, 4-H), 2.0–1.94 (m, 1H, 4-H), 1.91–1.8 (m, 1H, 3-H) and 1.75–1.65 (m, 1H, 3-H).

6: δ 5.52 (d, 1H, *J* 6 Hz, H_{arom}), 4.90 (d, 1H, *J* 10 Hz, 1-H), 4.50 (t, 1H, *J* 6 Hz, H_{arom}), 4.45 (t, 1H, *J* 6 Hz, H_{arom}), 4.23 (d, 1H, *J* 6 Hz, H_{arom}), 3.28 (S, CO_2ME), 2.90 (s, OH), 2.20–2.14 (ddd, 1H, *J* 4, 10, 12 HZ, 2-H), 2.10–1.96 (m, 2H, 4-H) and 1.78–1.60 (m, 2H, 3-H).

Crystal data for **5**: yellow crystal, $C_{15}H_{14}CrO_6$, M = 342.3, monoclinic, space group $P2_1/c$, a = 7.1955(10), b = 24.903(5), c = 8.6860(12) Å, β = 107.71(1)°, U = 1482.7(4) Å^3, D_c = 1.53 g cm^{-3}, Z = 4, Mo-Kα radiation, λ = 0.71069 Å, μ = 7.76 cm^{-1}, $F(000)$ = 704. Final R and R_w [$w = 1/\sigma^2(F_o)$] values 0.071 and 0.034 for 1519 observed reflections [$|F_o| > 4\sigma(F_o)$].

For **6**: yellow crystal, $C_{15}H_{14}CrO_6$, M = 342.3, triclinic, space group $P\bar{1}$, a = 7.3633(11), b = 8.0332(12), c = 13.355(2) Å, α = 96.23(1), β = 102.16(1), γ = 97.41(1)°, U = 758.3(2) Å^3, D_c = 1.50 g cm^{-3}, Z = 2, Mo-Kα radiation, λ = 0.71069 Å, μ = 7.59 cm^{-1}, $F(000)$ = 352. Final R and R_w [$w = 1/\sigma^2(F_o)$] values 0.062 and 0.043 for 1449 observed reflections [$|F_o| > 4\sigma(F_o)$]. Both compounds: Philips PW1100 diffractometer, structure solved by direct methods. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

‖ This compound was obtained by enzymatic asymmetric hydrolysis of racemic **1** using literature methodology[9] [lipase from *Pseudomonas fluorescens*, SAMII (Fluka), phosphate buffer, pH = 7, 10 °C, 4.5 days, giving enantiomerically enriched (*S*)-**1** (95% e.e) in 43% yield]. Enantiomerically pure (*R,S*)-*syn*-**2** {>99% e.e., $[\alpha]_D^{20}$ −288.3° (*c* = 1.1, $CHCl_3$)} was obtained following complexation, chromatographic separation of *syn*- and *anti*-products, and recrystallisation.

e.e.) and (1*R*,2*S*)-**8** (93% e.e.) in the same ratio and yield as found in the reaction with racemic **2**.[10]**

This work demonstrates the generation of a chiral *o*-quinodimethane–$Cr(CO)_3$ complex intermediate under very mild conditions and the efficient blocking of one enantioface in cycloaddition reactions.

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** *Note added in proof*: since completion of this work a communication describing the generation of racemic **4** and its cycloaddition with dimethyl fumarate has been published. See, H. G. Wey and H. Butenschön, *Angew. Chem., Int. Ed. Engl.*, 1991, **30**, 880.