Unexpected Proximal Ring Opening Reactions of Benzocyclobutene Complexes

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An unexpected opening of a *proximal* bond in the anellated four-membered ring of benzocyclobutene tricarbonylchromium(0) complexes occurs when the 1-hydroxy-1-hex-5-enyl complex **2** is treated with base: in general, rupture of the *distal* bond is observed. The reaction of tricarbonyl-η⁶-(1-oxobenzocyclobutene)chromium(0) **1** with primary amines also causes a proximal ring-opening reaction.

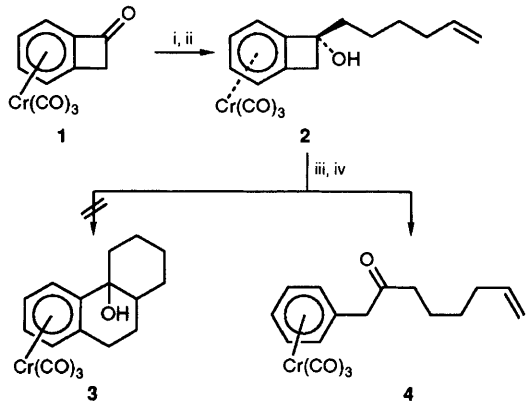
We recently reported the ring opening of the alcoholate of tricarbonyl-η⁶-(1-hydroxybenzocyclobutene)chromium(0) under very mild reaction conditions and the trapping of the intermediate *ortho*-quinodimethane complex with dimethyl fumarate.[1] The educt complex is available, in almost quantitative yield and diastereoselectivity, from tricarbonyl-η⁶-(1-oxobenzocyclobutene)chromium(0) **1** by reduction with lithium aluminium hydride. We have now found that Grignard reagents add to the keto group in **1** also with high yield and diastereoselectivity. Use of a Grignard reagent containing a dienophile functionality could open the way for an intramolecular cycloaddition.

We therefore treated ketone complex **1** with hex-5-en-1-yl magnesium bromide and obtained the corresponding adduct **2**† in 93% yield [diastereoisomeric excess (d.e.) > 90%, NMR]. As the attack of the Grignard reagent should occur from the sterically less hindered side, we suggest an *endo*-hydroxy-*exo*-hexenyl configuration at C-1, which would be in accord with earlier findings concerning the reduction product.[1] The availability of the hexenyl adduct **2** induced us to study its behaviour in intramolecular cycloaddition which was expected to yield a tricyclic complex **3**. However, **3** was not formed, instead, the proximal ring opened product **4**† was obtained in 83% yield.

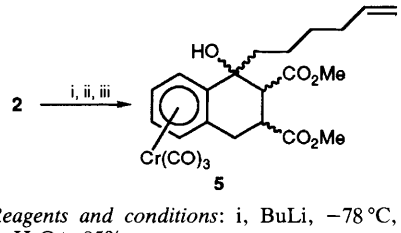
Apparently a competing reaction to the usual distal ring opening was kinetically preferred, because the hexenyl dienophile incorporated in the side chain is not sufficiently reactive in the desired cycloaddition. A control experiment in which the more electron deficient dimethyl fumarate was added to the reaction mixture under otherwise identical reaction conditions indeed gave cycloadduct **5** as a mixture of diastereoisomers in 95% yield. This confirms the formation of an *ortho*-quinodimethane complex, probably in equilibrium[2] with the alcoholate of **2** and a proximal ring opened intermediate, on the one hand and shows on the other, that the reactivity of the hexenyl side chain is reduced in comparison with dimethyl fumarate, although the reaction would be intramolecular in the first case.

A base-induced proximal ring opening of a benzocyclobuten-1-ol derivative is unusual; normally the distal bond is broken.[3,4] For comparison the uncomplexed ligand **6** was prepared by Grignard addition to 1-oxobenzocyclobutene in 86% yield. Treatment of **6** with butyllithium under the same reaction conditions that were applied to complex **1** caused exclusively distal ring opening with formation of **7**† in 75% yield, this observation is in complete accord with the findings of Choy *et al.*[3] and Cava *et al.*[4]

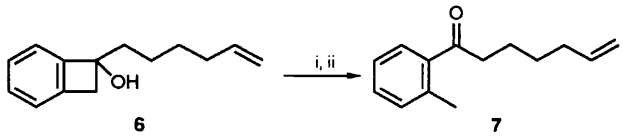
1-Oxobenzocyclobutene complex **1** is chiral and in connection with the ring opening–cycloaddition chemistry performed in our laboratory we saw the chance to generate enantiomerically pure *ortho*-quinodimethane intermediates if the enantiomers of **1** could be separated. Such intermediates would be important for enantioselective syntheses involving *ortho*-quinodimethane intermediates, *e.g.* steroid syntheses. Therefore, **1** was treated with chiral primary amines with the



Scheme 1 *Reagents and conditions*: i, $BrMg(CH_2)_4CH{=}CH_2$, −78 °C, ii, H_3O^+, 93%, d.e. > 90%; iii, BuLi, −78 °C, iv, H_3O^+, 83%



Scheme 2 *Reagents and conditions*: i, BuLi, −78 °C, ii, dimethyl fumarate, iii, H_3O^+, 95%



Scheme 3 *Reagents and conditions*: i, BuLi, −78–25 °C, ii, H_3O^+, 75%

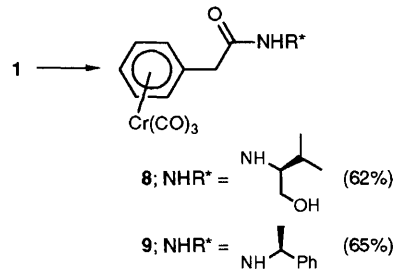
† All new compounds were fully characterised. Selected analytical data: **2**: IR (THF): ν 1964 cm^{-1} (s, CO), 1888 (s, CO). ^1H NMR (200 MHz, [$^2H_8$] THF): δ 1.34–1.65 (m, 4H, 7-H, 8-H), 1.78–1.89 (m, 2H, 9-H), 2.07 (m, 2H, 10-H), 3.00 (AB line system, 1H, *exo*-2-H or *endo*-2-H), 3.10 (Ab line system, 1H, *exo*-2-H or *endo*-2-H), 4.32 (s, 1H, OH), 4.96 (m, 2H, 12-H), 5.05 (dd, 1H, 4-H), 5.40 (dd, 1H, 5-H), 5.46 (d, 1H, 6-H or 3-H), 5.73 (d, 1H, 3-H or 6-H), 5.80 (m, 1H, 11-H).

4: IR (THF): ν 1965 cm^{-1} (s, CO), 1888 (s, CO), 1719 (w, keto-CO). ^1H NMR (200 MHz, [$^2H_8$]THF): δ 1.29–1.65 (m, 4H, 8-H, 9-H), 2.04 (m, 2H, 10-H), 2.47 (t, 2H, 7-H), 2.88 (s, 2H, 5-H), 4.90 (dd, 1H, *cis*-12-H), 4.97 (dd, 1H, *trans*-12-H), 5.36 (dd, 2H, 2-H o 3-H), 5.53 (dd, 2H, 2-H o 3-H), 5.74–5.83 (m, 1H, 4-H), 5.79 (dd, 1H, 11-H).

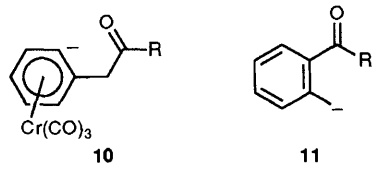
7: B.p. 135 °C/10^{-2} mbar. IR (film): ν 1687 cm^{-1} (s, keto-CO). ^1H NMR (200 MHz, $CDDl_3$): δ 1.47 (m, 2H, 8-H or 9-H), 1.72 (m, 2H, 8-H or 9-H), 2.08 (ttd, 2H, 10-H), 2.47 (s, 3H, 1-H), 2.87 (t, 2H, 7-H), 4.94 (tdd, 1H, *cis*-12-H), 5.00 (tdd, 1H, *trans*-12-H), 5.79 (tdd, 1H, 11-H), 7.17–7.37 (m, 3H, 2-H, 3-H, 4-H), 7.59 (m, 1H, 5-H).

8: M.p. 134 °C, $[\alpha]_D^{20}$ −27° (*c* 1.75, THF). IR (THF): ν 1963 cm^{-1} (s, CO) 1887 (s, CO), 1682 (m, amide-CO). ^1H NMR (200 MHz, [$^2H_8$]THF): δ 0.88 (d, 3H, 12-H), 0.92 (d, 3H, 13-H), 1.89 (m, 1H, 11-H), 3.22 (s, 2H, 7-H), 3.51 (m, 2H, 10-H), 3.65 (m, 1H, 9-H), 3.45–3.8 (br, 2H, OH, NH), 5.35 (dd, 1H, 3-H or 4-H or 5-H), 5.4–5.75 (m, 4H, 2-H or 3-H or 4-H or 5-H or 6-H).

9: M.p. 137 °C, $[\alpha]_D^{20}$ −5.3° (*c* 1.65, THF). IR (THF): ν 1970 cm^{-1} (s, CO) 1895 (s, CO), 1683 (m, amide-CO). ^1H NMR (200 MHz, [$^2H_8$]THF): δ 1.29 (d, 3H, 10-H), 3.06 (s, 2H, 7-H), 4.92 (dd, 1H, 3-H or 4-H or 5-H), 5.24 (d, 1H, 2-H or 6-H), 5.33 (m, 4H, 3-H or 4-H or 5-H, 9-H), 7.0–7.3 (m, 5H, 12,13,14,15,16-H).



Scheme 4 *Reagents and conditions*: H_2NR^*



objective of generating separable diastereoisomers of the corresponding imines.[5] However, instead of the desired imines a proximal ring opening occurred with formation of amides **8**† (62%) and **9** (65%). No starting material was recovered.

In the reaction of uncomplexed 1-oxobenzocyclobutene **6** with *S*-2-amino-3-methylbutan-1-ol under identical reaction conditions the uncomplexed amide is also formed, however, with lower conversion (45%) beside 34% of unreacted **6**. This shows a remarkable propensity of the complexed derivative to react with the proximal bond.

The results reported here can be rationalised by the enhanced stability of aryl anions when complexed to a $Cr(CO)_3$ fragment. When the proximal ring opening occurs, one has to consider **10** as an intermediate, when the distal bond opens, benzylic anion **11** should be an intermediate.

The electron-withdrawing effect of the tricarbonylchromium group allows not only a fission of a C–H bond in the course of metallation reactions at the arene ligand[6] but also a fission of a C–C bond resulting in the formation of a stabilized aryl anion.

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