

# Syntheses of Benzocyclooctenedione Derivatives, Cyclopenta[*a*]indanones and a Benzo-annelated Tetraquinane *via* Sequential Transformations of Tricarbonyl( $\eta^6$ -1,2-dioxobenzocyclobutene)chromium(0)

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Tricarbonyl( $\eta^6$ -1,2-dioxobenzocyclobutene)chromium(0) **1** can be converted into benzocyclooctenedione derivatives **3**, **7** and **8** as well as fused five-membered ring systems **2**, **4** and **6** by addition of vinyl lithium derivatives and following double anionic oxy-Cope rearrangement under very mild reaction conditions ( $-78^\circ\text{C}$ ); product ratios depend on the method of hydrolysis.

Arene tricarbonyl chromium complexes serve as useful intermediates in organic synthesis.<sup>1-4</sup> Recently, we reported the synthesis and structure of tricarbonyl( $\eta^6$ -1,2-dioxobenzocyclobutene)chromium(0)<sup>5</sup> **1**. This complex, which contains a highly strained four-membered ring, undergoes a sequential transformation<sup>6</sup> consisting of the double addition of vinyl lithium to the keto groups and subsequent double anionic oxy-Cope rearrangement under very mild reaction conditions. Although the oxy-Cope rearrangement is a well established method in organic synthesis,<sup>7,8</sup> only a few examples of the double anionic type are known.<sup>9-11</sup> Here we report further investigations of the reaction of **1** with various vinyl lithium derivatives to get a more mechanistic view of the double anionic oxy-Cope rearrangement and to explore its value in stereoselective syntheses of highly substituted benzocyclooctenediones and cyclopenta[*a*]indanones.


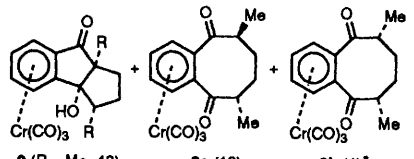

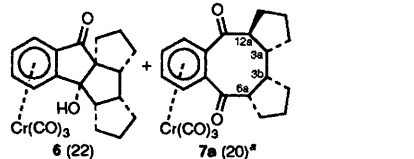
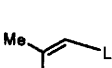
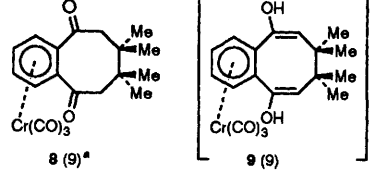
Compound **1** was treated with an excess of prop-2-enyllithium (6 equiv.) at  $-78^\circ\text{C}$  (Scheme 1). After hydrolysis with HCl (aq), the crude product mixture consisted of three components **2**, **3a** and **b** (6:2:1, Table 1,‡) which were separated by crystallisation and column chromatography. The constitution of the three products and the relative configurations of the benzocyclooctenediones **3a** and **b** were assigned by NMR spectroscopy. For cyclopenta[*a*]indanone complex **2**, the relative configuration could not be assigned by spectroscopic methods. An X-ray structure analysis<sup>12</sup> revealed that both methyl groups and the alcohol function are placed at the coordinated face of the tricyclic ligand.

The stereochemical course of the described reaction, which leads to a certain product ratio, can be explained by the assumption of an initial double attack of prop-2-enyllithium from the *exo* face of the 1,2-dioxobenzocyclobutene ligand yielding a *cis* divinyl species.§ The following double anionic oxy-Cope rearrangement leads to bis-enolate **5** as common precursor for **2** and **3** [**5** can be converted into the corresponding bis(trimethylsilyl) dienol ether in 60% yield].<sup>5</sup> It can be assumed from molecular models that the predominant conformations<sup>13</sup> of **5** are the boat form **5a** and the twisted conformer **5b**. Double protonation of **5b** gives the diastereoisomeric complexes **3a** and **b**, whereas single protonation of **5a** leads to a transannular aldol reaction forming **2** stereoselectively *via* an attack of the remaining enolate on the carbonyl group from the *exo* face. Hydrolysis at  $-78^\circ\text{C}$  with HCl (aq) can be regarded as slow because the main quantity of the aqueous reagent is frozen under these conditions and hydrolysis becomes a heterogeneous reaction. Consequently, the thermodynamically less stable conformer **5a** is transformed into the main product **2**. As expected, repetition of the reaction of **1** with prop-2-enyllithium and hydrolysis using the strong

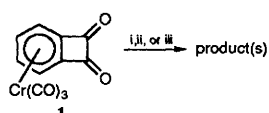
soluble trifluoromethane sulfonic acid leads to a change of the product ratio with the main product being the *trans* diastereoisomer **3a** (**2**:**3a**:**3b** = 3:11:4, yield 48%). Transformation of **1** into cyclopenta[*a*]indanone derivative **4** can be carried out using 1-lithiostyrene<sup>14</sup> (30%, Scheme 1).

To increase the degree of substitution of the oxy-Cope products, a cyclic vinyl lithium derivative was employed. Treatment of diketone complex **1** with cyclopentenyllithium at  $-78^\circ\text{C}$  and subsequent hydrolysis with HCl (aq) yielded an approximately 1:1 mixture (NMR) of the benzo-annelated tetraquinane complex **6** and the double cyclopentano-anel-

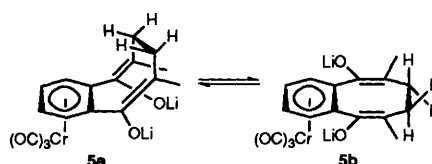
Table 1 Double anionic oxy-Cope rearrangements

Vinyl lithium derivative	Products (yield,%)
	 <b>2</b> (R = Me, 48) <b>4</b> (R = Ph, 30) <b>2</b> (R = Me, 8) + <b>3a</b> (29) + <b>3b</b> (11) <sup>b</sup>
	 <b>6</b> (22) + <b>7a</b> (20) <sup>a</sup> <b>6</b> (9) + <b>7a</b> (27) + <b>7b</b> (10) <sup>b</sup>
	 <b>8</b> (9) <sup>a</sup> + <b>9</b> (9)

<sup>a</sup> Step ii from Scheme 1. <sup>b</sup> Step iii from Scheme 1.



Scheme 1 Reagents and conditions: i, vinyl lithium derivative (6 equiv.),  $-78^\circ\text{C}$ ; ii, aq. HCl (exc.); iii,  $\text{F}_3\text{CSO}_3\text{H}$  (6 equiv.)



Scheme 2

lated benzocyclooctenedione complex **7a** (Table 1). Both compounds can be separated by column chromatography (ethyl acetate-pentane 1:4, 42% yield) and were obtained as single diastereoisomers.

The relative configuration of the tetraquinane derivative **6** was confirmed by X-ray structure analysis (Fig. 1) which shows the all *syn* configuration of the alcohol group and the anellated five-membered rings as expected by comparison with **2**.<sup>†</sup> In the <sup>1</sup>H NMR spectrum of **7a** the same pattern for the aromatic protons as for **3a** is observed indicating a similar relative configuration. Because of the large difference of the chemical shifts observed for the protons attached to C-6a and C-12a ( $\delta$  2.87/3.44) it is assumed that these protons are on opposite faces of the organic ligand. Following the stereochemical pathway of the oxy-Cope rearrangement, hydrolysis of a dienolate conformer comparable with **5b** should lead to a *syn* substitution at C-3a and C-3b.

Using CF<sub>3</sub>SO<sub>3</sub>H instead of HCl as reagent for the hydrolysis, again a change in the product ratio is observed and furthermore a new complex **7b** is obtained as a minor product. Under these altered conditions, **7a** becomes the main product (**6**:**7a**:**7b** 1:3:1, yield 45%). When the reaction sequence consisting of double addition and oxy-Cope rearrangement is carried out using a  $\beta$ -disubstituted vinyl lithium derivative, the yield decreases. This was demonstrated by treatment of diketone complex **1** with 2-methylprop-2-enyllithium. The tetramethylated benzocyclooctenedione complex **8** was obtained in only 9% yield. Surprisingly, product **8** is in equilibrium with its dienol **9** as shown by NMR spectroscopy. In acetone or methylene chloride as solvent **9** is the major tautomer. A possible reason for **9** being favoured over **8** could be the reduced torsional strain of the four neighbouring methyl groups and the  $\alpha$ -methylene groups in **9**.

The carbon skeletons in **6** and **7** are of high synthetic interest. Natural compounds containing tetraquinane<sup>15</sup> or triquinane<sup>16,17</sup> fragments (**6** can be considered as angular or as linear triquinane) are widely known. Also, the interest in the synthesis of eight-membered rings has increased significantly<sup>18,19</sup> in the last decade, especially in the context with the development of antitumour agents. The described reactions of complexed 1,2-dioxobenzocyclobutene offer a simple and general access to highly substituted eight-membered ring compounds as well as polyquinanes.<sup>||</sup>

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## Footnotes

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<sup>‡</sup> All new compounds were fully characterised.

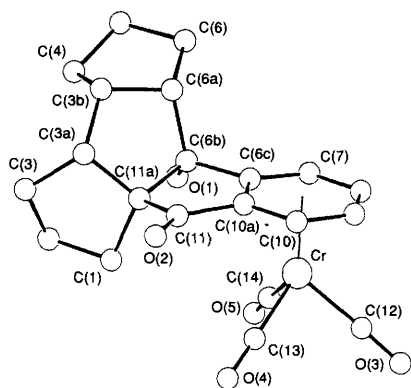
<sup>§</sup> Reaction of **1** with an excess of ethyl magnesium iodide yields a double *cis* adduct in 60% yield (M. Brands and H. Butenschön, unpublished results). In the monoanionic case only *cis* divinyl cyclobutanes undergo an oxy-Cope rearrangement whereas the *trans* isomer reacts in a retro-ene reaction.<sup>20</sup>

<sup>¶</sup> Crystal data for **6**: C<sub>21</sub>H<sub>20</sub>O<sub>5</sub>Cr, *M<sub>r</sub>* 404.4 g mol<sup>-1</sup>, crystal colour red, crystal size 0.18 × 0.25 × 0.53 mm, crystal system monoclinic, space group P2<sub>1</sub>/n, *a* = 9.972(1), *b* = 13.203(1), *c* = 14.669(1) Å,  $\beta$  = 109.61(1)°, *V* = 1819.4 Å<sup>3</sup>, *D<sub>c</sub>* = 1.48 g cm<sup>-3</sup>,  $\mu$  = 6.41 cm<sup>-1</sup>, Mo-K $\alpha$  radiation,  $\lambda$  = 0.71069 Å, *F*(000) = 840 e, *Z* = 4, Enraf-Nonius CAD4 diffractometer, scan mode  $\omega$ -2 $\theta$ , [(sin $\theta$ )/ $\lambda$ ] = 0.65 Å<sup>-1</sup>, 7657 measured reflections ( $\pm h$ ,  $\pm k$ ,  $\pm l$ ), 4140 independent reflections, 3195 observed reflections [*I* > 2 $\sigma$ (*I*)] for 324 refined parameters, structure solved by heavy atom method, H atom positions found and refined isotropically, *R* = 0.037, *R<sub>w</sub>* = 0.042, residual electron density 0.42 e Å<sup>-3</sup>. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

<sup>||</sup> After submission of this paper a relevant publication concerning double anionic oxy-Cope rearrangements starting from squaric acid derivatives has appeared.<sup>21</sup>

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**Fig. 1** Molecular structure of complex **6**. Selected distances (Å): C(11)–O(2) 1.223(3), C(10a)–C(11) 1.475(3), C(11)–C(11a) 1.519(3), C(11a)–C(6b) 1.552(3), C(6b)–C(6a) 1.560(3), C(6b)–O(1) 1.414(2), C(6c)–C(6b) 1.517(3); selected angles (°): C(6c)–C(6b)–C(6a) 110.4(2), C(11a)–C(6b)–C(6a) 103.1(2), C(6a)–C(6b)–O(1) 113.7(2), C(11a)–C(6b)–O(1) 109.9(2), C(6c)–C(6b)–O(1) 114.2(2), C(11a)–C(6b)–C(6c) 104.7(2), C(11a)–C(11)–O(2) 124.9(2), C(10a)–C(11)–O(2) 125.9(2), C(11a)–C(11)–C(10a) 109.1(2).