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Arene chromium complexes with functionalized anellated rings. Selective formation of highly substituted polycycles*

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Abstract: Tricarbonylchromium complexes of benzocyclobutenone, benzocyclobutenedione, and 1,3-indandione are readily prepared by hydrolysis of the complexes of the corresponding acetals. Reduction of the benzocyclobutenone complex gives rise to an oxy-anion-driven ring opening to the corresponding *ortho*-quinodimethane intermediate, which can be trapped with dienophiles. Addition of 1-ethoxy-1-lithioethene allows a stereoselective ring expansion followed by an anionic ketol rearrangement with complete diastereoselectivity. Addition of 1-lithio-1-methoxyallene gives rise to a rare anionic 1-vinylcyclobutenol-cyclohexadienol rearrangement. Diaddition of alkenylmetal reagents at both keto groups in benzoyclobutenedione complexes causes dianionic oxy-Cope rearrangements to occur at –78 °C, which are followed by diastereoselective intramolecular aldol additions. In some cases, a completely regioselective mono hydrolysis of di(enolates) was observed. Dianionic oxy-Cope rearrangements can also be realized with unstrained benzil derivatives giving 1,6-hexanediones and the corresponding aldol adducts. The 1,2,3-indantrione complex is obtained by oxidation of the 1,3-indandione complex with dimethyldioxirane in good yield and reacts with its central ketone group in hetero Diels–Alder cycloadditions.

INTRODUCTION

Arene tricarbonylchromium complexes with functionalized anellated rings have been investigated for some time. Our investigations in this field have focused on systems showing a higher preparative potential than that of just one carbonyl function. In particular, our chemistry involves complexes **1–5** derived from the strained benzocyclobutenone and benzocyclobutenedione, as well as 1,3-, 1,2-indandione, and 1,2,3-indantrione [1].

The chemistry of benzocyclobutenone complexes **1** (R = H, OMe, CF_3) is dominated by nucleophilic addition reactions at the ketone function, giving access to benzocyclobutenolates that readily open the anellated 4-membered ring with formation of an *ortho*-quinodimethane intermediate. Subsequent [4+2] cycloadditions lead to highly substituted tetralin complexes. In addition to this oxy-anion-driven ring opening reaction we found other oxy-anion-driven ring expansion reactions in this context. The synthesis, structures, and reactions of benzocyclobutenedione complexes **2** (R = H, OMe) form the main body of this contribution. In contrast to the uncoordinated benzocyclobutenedione, complexes **2** allow a double nucleophilic addition at both ketone groups. This sets the stage for a dianionic oxy-Cope rearrangement, which after an intramolecular aldol addition provides polycyclic systems under mild reaction conditions in high yield and diastereoselectivity. In the context of our interest in

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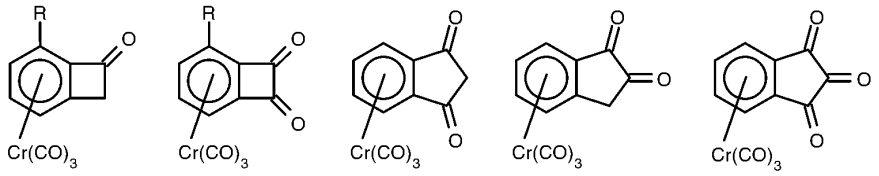
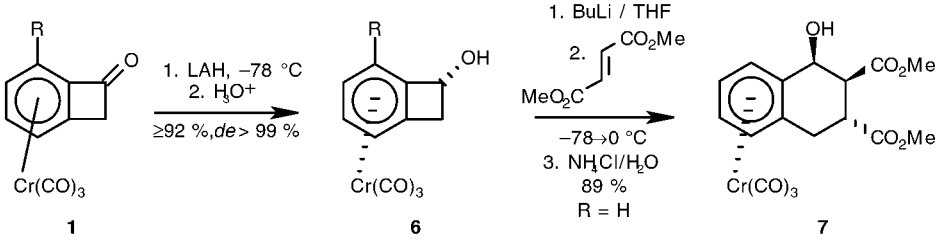
similar systems with a 5-membered anellated ring, the investigation of some indantrione acetals led to a short synthesis of benzocyclobutenedione. With respect to the indandione and indantrione complexes, the syntheses of **3** and **5** and some reactions are presented.



1 **2** **3** **4** **5**

BENZOCYCLOBUTENONE TRICARBONYLCHROMIUM COMPLEXES: OXY-ANION-DRIVEN RING EXPANSION REACTIONS

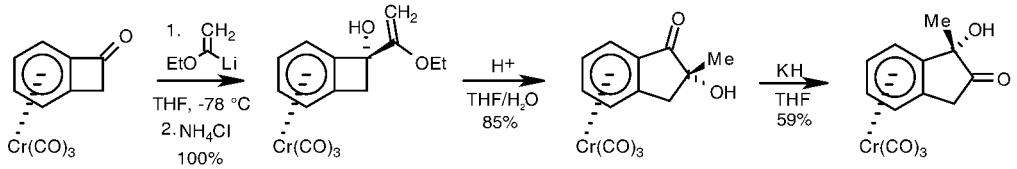
Benzocyclobutenone tricarbonylchromium complexes **1** (R = H, OMe) are conveniently prepared by complexation of the ligand acetals with a suitable complexation reagent, e.g., $Cr(CO)_3(NH_3)_3$, followed by hydrolysis of the acetal in high yield. Reduction of the keto function of **1** gives the alcohol **6** in excellent yield.



1 **6** **7**

After deprotonation of **6**, a ring opening to an *ortho*-quinodimethane intermediate occurs at about –30 °C, which can be trapped by reaction with a dienophile [2–4]. The ring opening temperature can be tuned by choice of the counter cation [5]. With most dienophiles the expected *endo* cycloadducts like **7** are obtained. However, vinyl sulphones give the *exo* cycloadducts, presumably because of steric interactions disfavoring an *endo* transition state [3,6]. **1** (R = H) can be obtained in enantiomerically pure form by several procedures, and Kündig *et al*. have shown that the chiral information is efficiently transferred to the cycloadduct formed [3,7].

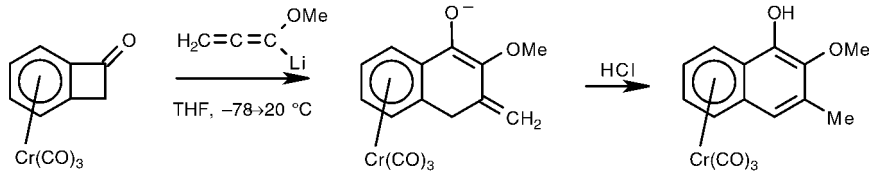
According to the work of Liebeskind *et al*., addition of acyl anion equivalents to benzocyclobutenedione causes a ring expansion to an indanone derivative [8]. However, the stereoselectivity of this reaction had not been studied. Diastereoselective addition of 1-ethoxy-1-lithioethene at the corresponding *enantiomerically pure* chromium complex **1** (R = H) from the face opposite to the tricarbonylchromium group gave **8** quantitatively, whose hydrolysis under acidic reaction conditions resulted in a complete transfer of chirality to ring expansion product **9**, and the subsequent oxy-anion-driven α-ketol rearrangement to **10** proceeded completely diastereoselectively as well [9].



1 (R = H) **8** **9** **10**

Oxy-anion-driven vinylcyclobutenol–cyclohexadienol rearrangements are known. However, in most of the reported cases, the vinyl and the hydroxy substituents are not bound at the same carbon

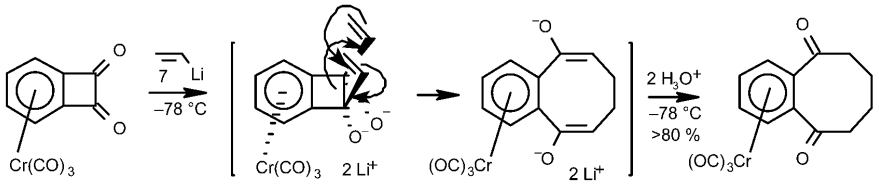
atom. Upon treatment of **2** with lithiated methoxyallene, a rare case of an anionic 1-oxy-1-vinylcyclobutene–cyclohexdienol rearrangement was observed giving naphthol complex **12** via **11** [9].



1 (R = H) **11** **12** (65%)

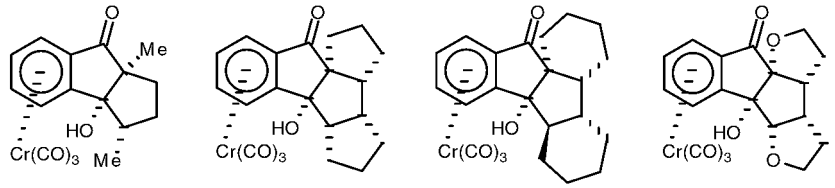
BENZOCYCLOBUTENEDIONE TRICARBONYLCHROMIUM COMPLEXES: DIANIONIC OXY-COPE REARRANGEMENTS

Benzocyclobutenedione tricarbonylchromium complexes **2** are prepared just in the same way as the monoketone complexes. The diacetals can be hydrolyzed in conc. HCl within 2–3 h in 83–95% yield. The benzocyclobutenedione complexes **2** show an interesting structural anomaly in that the ligand, although it contains only sp^2 hybridized carbon atoms, is not planar. The anellated 4-membered ring is bent toward the tricarbonylchromium group by 9.4° (R = H) and by 8.2° (R = OMe) [4,10–12]. Recently, his effect was also found in DFT calculations of complexes **2** and is presumably due to an electrostatic attractive interaction between the highly electropositive ketone carbon atoms and the more electronegative tricarbonylchromium moiety.



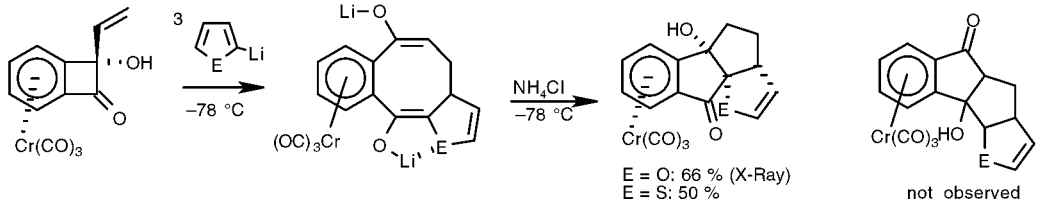
2 (R = H) **13** **14** **15**

With respect to the reactivity of complexes **2**, it is important to note that nucleophilic 1,2-diadditions are well possible—this is not the case with the uncoordinated ligand system. Such 1,2-diadditions strictly take place from the face opposite to the tricarbonylchromium group and yield the respective *endo*-1,2-diols after hydrolytic workup. In the addition of an excess of vinyllithium, thereby, a *cis*-1,2-divinyldiolate **13** is formed, which meets the stereochemical requirements of a dianionic oxy-Cope rearrangement [13] This rare reaction takes place at –78 °C, an exceptionally low temperature for such a process, and yields the ring expanded benzocyclooctene dienolate **14**, which can be trapped as the bis(trimethylsilylenol) ether or hydrolyzed to the benzocyclooctenedione complex **15** in high yield. The reaction temperature of –78 °C is by far the lowest one reported for a dianionic oxy-Cope rearrangement [11,14]. It is possible to sequentially use two different alkenylmetal reagents resulting in asymmetrically substituted benzocyclooctenedione complexes. In many cases, the dianionic oxy-Cope rearrangement is followed by an intramolecular aldol addition as a result of the first hydrolysis step, creating a ketone and an enolate moiety in the 8-membered ring. In all the numerous cases investigated so far, this intramolecular aldol addition takes place with complete diastereoselectivity by attack of the enolate moiety at the ketone function from the face opposite to the tricarbonylchromium fragment. Representative reaction products of these reactions using 2-propenyllithium, 1-cyclopentenyllithium, 1-cyclohexenyllithium, and 3,4-dihydro-2-lithiofuran as alkenylmetal reagents are **16–19**. The last example demonstrates the possibility to selectively construct heteropolycycles by this process [11,14–17].



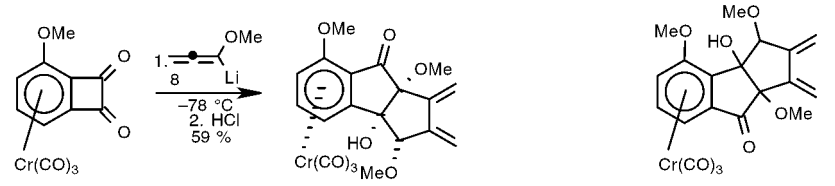
16 **17** **18** **19**

In the context of the dianionic oxy-Cope rearrangement, the question was raised in how far it might be possible to use aromatic heterocyclic systems like 2-lithiofuran or 2-lithiothiophene, as these would require an elimination of the aromaticity of *both* of the added aromatic units. The experiment revealed that in addition to some mono adduct to **2** only ring-opened products were formed. However, a sequential reaction involving first the monoaddition of vinyllithium giving **20** and then the addition of 2-lithiofuran or 2-lithiothiophene showed that the reaction works with the elimination of the aromaticity of *one* aromatic heterocycle. More interesting, the reaction came out to be completely regioselective: Due to the asymmetry of **20** the enloate **21** formed by the anionic oxy-Cope rearrangement is asymmetric, so that there are two reaction paths principally available. If the enolate moiety next to the anellated heterocycle is hydrolyzed first, formation of the aldol adduct **23** would occur. However, no **23** was formed; instead good yields of **22** (E = O, S) were obtained clearly indicating a selective hydrolysis of the enolate moiety opposite to the anellated heterocycle. As a rationale for this regioselective hydrolysis of a di(enolate), we envisage a chelation of the lithium ion of the enolate moiety next to the heterocycle by the heterocycle oxygen or sulfur atom [17].



20 **21** **22** **23**

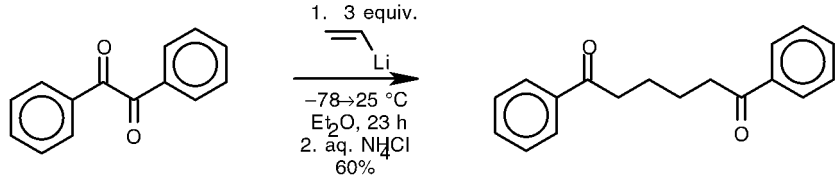
The dianionic oxy-Cope rearrangement initiated by alkenylmetal addition to benzocyclobutenedione tricarbonylchromium complexes allows to create a remarkable amount of molecular complexity with full diastereoselectivity and in an atom-economic way [18]. An impressing example for this is the addition of 1-lithio-1-methoxy allene to **2** resulting in the first head-to-head coupling of two methoxyallene units. When the dianionic oxy-Cope rearrangement was done starting from the methoxy-substituted benzocyclobutenedione complex **2** (R = OMe), the corresponding product **24** was obtained in 59% yield. The alternative complex **25** was not formed—again, the intermediate di(enolate) had been regioselectively hydrolyzed. Presumably, the enolate moiety next to the methoxy substituent was stabilized by chelation, and therefore the other one was first hydrolyzed. A similar regioselective hydrolysis of such di(enolates) was observed in a number of other cases [12].



2 (R = OMe) **24** **25**

The dianionic oxy-Cope rearrangements explored in our group start from benzocyclobutenedione tricarbonylchromium complexes; similar, albeit mechanistically different reactions found by Paquette *et al*. start from squaric acid esters [19, 20]. One reason for dianionic oxy-Cope rearrangements being possible with the benzocyclobutenedione complexes is the stereodirecting effect of the metal fragment causing a *syn* diaddition of the alkenylmetal from the face opposite to the $Cr(CO)_3$ group, thereby fulfilling the stereochemical requirement for a Cope rearrangement of a cyclobutene derivative [13]. In addition, the electron-withdrawing effect of the tricrbonylchromium group facilitates the nucleophilic addition. In this context, the question was raised if it is really neccessary to start from strained cyclobutenediones. Would it be possible to induce a dianionic oxy-Cope rearrangement by addition of vinyllithium to unstrained 1,2-diones?

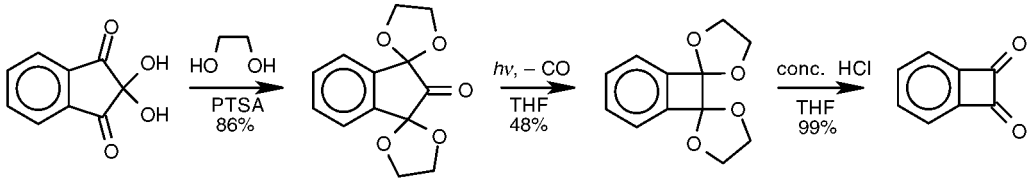
An investigation along these lines led to the remarkable result that such a process is indeed possible by addition of vinyllithium to a number of unstrained benzil derivatives. The reaction of unsubstituted benzil (**26**) with 3 equiv of vinyllithium at –78 → 0 °C afforded 1,6-diphenylhexane-1,2-dione (**27**) in 60% yield.[21]



26 **27**

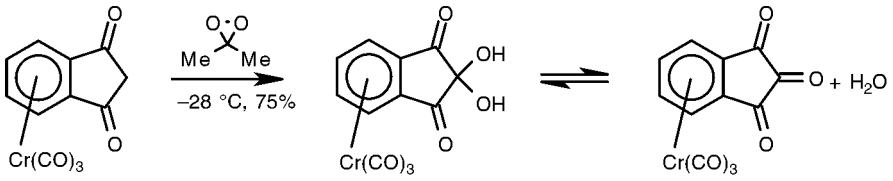
Having explored the chemistry of arene omplexes with an anellated 4-membered ring and the dianionic oxy-Cope rearrangement to some extent, we became interested in the question in how far multifunctionalized indane complexes would show a comparatively interesting behavior. As it was not possible to obtain such complexes by direct complexation of the respective ligands, the acetal route was envisaged, which had been succesful in the benzocyclobutene complex chemistry.

A first remarkable result was achieved when ninhydrin (**28**) was treated with ethane-1,2-diol in the presence of *para* toluenesulfonic acid-yielded diacetal **29** in 86%. Photolysis of this ketone resulted in a photodecarbonylation, giving diacetal **30** in 48% yield. **30** is the ligand necessary for the formation of benzocyclobutenedione complex **2** (R = H) and can be quantitatively hydrolyzed to give benzocyclobutenedione (**31**). This 3-step route to benzocyclobutenedione (**31**) with an overall yield of 41% represents the shortest synthesis of **31**, which is a key element in a number of syntheses of natural and biologically active naphthoquinone derivatives. Remarkably, in some cases, the photolysis in the presence of a dienophile directly gives the respective naphthoquinone derivative.



28 **29** **30** **31**

While efforts to prepare tricarbonyl(1,2-indandione)tricarbonylchromium (**4**) also in enantiomerically pure form are under way, the complex **3** of 1,3-indandione is easily made via the acetal route. Direct oxidation of **3** with dimethyl dioxirane at –28 °C affords a 1:1 mixture of ninhydrin complex **32** and 1,2,3-indantrione complex **5** in 75% yield. Remarkably, the equilibrium mixture of **32** and **5** preferentially reacts with the central keto group in **5**, which is by far the most reactive site, e.g., in hetero Diels–Alder cycloadditions [22]. Efforts to further explore the preparative potential of arene tricar-



3 32 5

bonylchromium complexes with functionalized anellated rings for selective syntheses of polycyclic products under mild reaction conditions are in progress in our laboratories.

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