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From Maleic Anhydrides to Substituted Resorcinols

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Abstract. Symmetrically substituted maleic anhydrides react at $-78\text{ }^{\circ}\text{C}$ with lithiummethyl phenyl sulfone to give the corresponding 4-hydroxy-4-(phenylsulfonylmethyl)-buteno-4-lactones, which, on treatment with MeI/ K_2CO_3 in acetone, are transformed into 5-methyl-5-phenylsulfonylcyclopent-2-ene-1,4-diones. These compounds rearrange in the presence of an excess of lithiummethyl phenyl sulfone at $-78\text{ }^{\circ}\text{C}$ and then butyllithium at $-5\text{ }^{\circ}\text{C}$ to ambient temperature into 4,5-disubstituted 6-methyl-2-phenylsulfonyl-resorcinols.

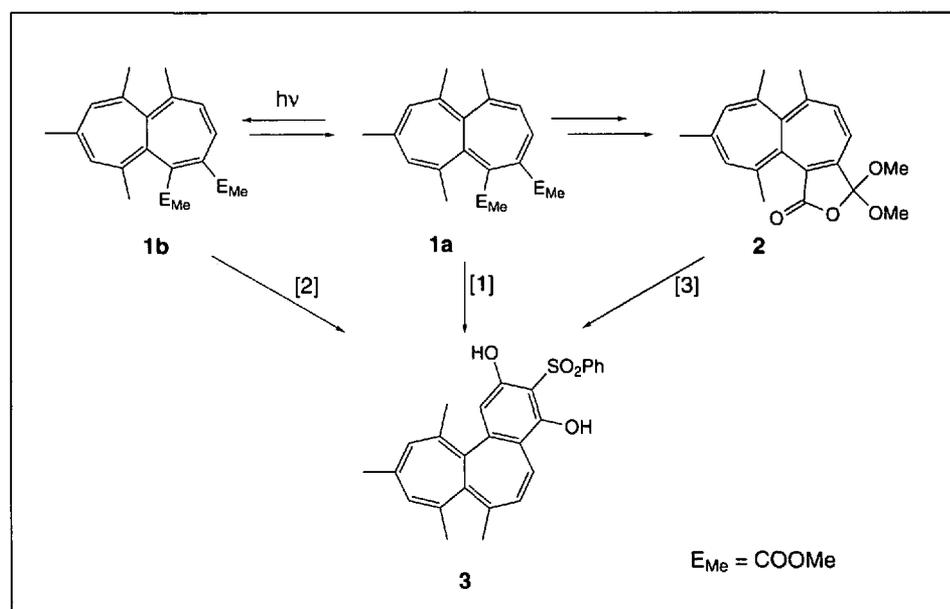
Keywords: Cyclopent-2-ene-1,4-diones · Five to six membered ring enlargement · Oxidoenolate-bisenolate rearrangement · Resorcinols

It has been shown in recent publications that heptalene-4,5- or better -1,2-dicarboxylates such as **1a** [1] and **1b** [2] or corresponding pseudo-ester forms of it such as **2** [3] (Scheme 1), on treatment with an excess of lithiummethyl phenyl sulfone at $-78\text{ }^{\circ}\text{C}$, followed by addition of BuLi at $-5\text{ }^{\circ}\text{C}$ and warming to ambient temperature, are transformed in a 'one-pot' reaction into 3-sulfonyl-substituted benzo[*a*]heptalene-2,4-diols such as **3**. The question is whether these transformations are linked to heptalene-dicarboxylates or represent a general principle for the construction of resorcinols starting with analogues of the aforementioned dicarboxylates. In order to give an answer to this question, the following reactions and transformations were undertaken.

The symmetrically substituted maleic anhydrides **4** were reacted with lithiumme-

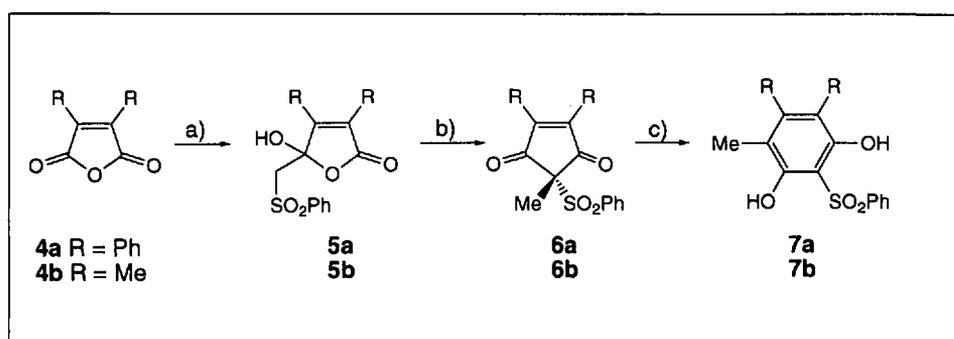
thyl phenyl sulfone (formed from the sulfone and BuLi) at $-78\text{ }^{\circ}\text{C}$ in THF, which gave the crystalline 4-hydroxybuteno-4-lactones **5** in good yields (Scheme 2). Treatment of the latter with MeI/ K_2CO_3 in acetone at r.t. led by a ring-opening

and ring-closure sequence to the thermodynamically favored 5-methyl-5-phenylsulfonylcyclopent-2-ene-1,4-diones **6**, which again were crystalline. Characteristic for the diones **6** is the sharp *s* for Me-C(5) in their NMR spectra (CDCl_3),

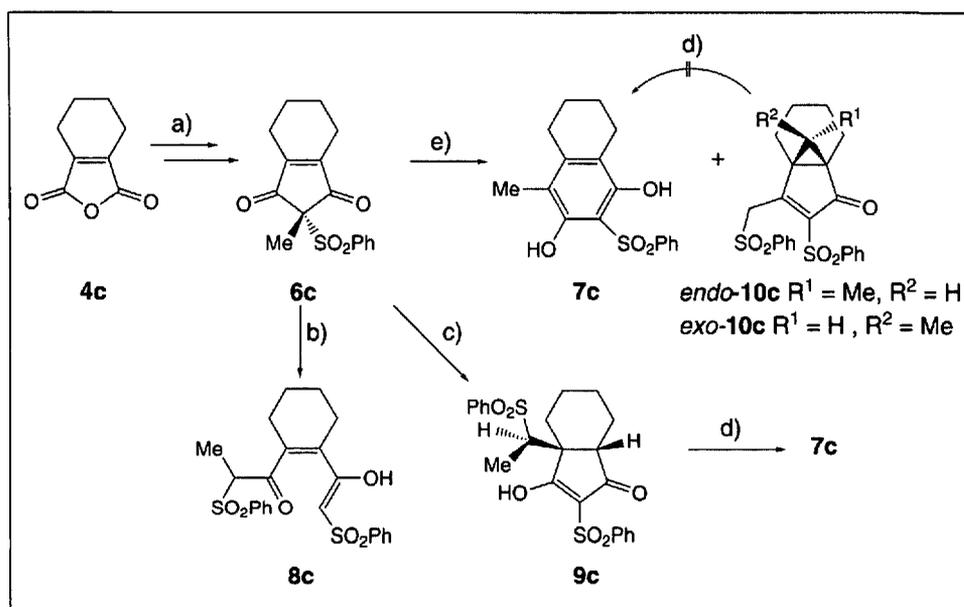


Scheme 1.

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Scheme 2. a) 2 Mol-equiv. $\text{LiCH}_2\text{SO}_2\text{Ph}/\text{THF}$, Ar, $-78^\circ\text{C}/1\text{ h}$, 77% **5a**, 77% **5b**. b) $\text{MeI}/\text{K}_2\text{CO}_3$, acetone, r.t./8 h, 80% **6a**, 65% **6b**. c) 1. 4 Mol-equiv. $\text{LiCH}_2\text{SO}_2\text{Ph}/\text{THF}$, Ar, $-78^\circ\text{C} \rightarrow -5^\circ\text{C}/3\text{ h}$; 2. 4 mol-equiv. BuLi , $-5^\circ\text{C} \rightarrow \text{r.t.}/0.5\text{ h}$, r.t./15 h, 70% **7a**, 5–6% **7b**.



Scheme 3. a) According to Scheme 2; 67% over both steps. b) 3 Mol-equiv. $\text{LiCH}_2\text{SO}_2\text{Ph}/\text{THF}$, Ar, $-78^\circ\text{C} \rightarrow 0^\circ\text{C}/2\text{ h}$, 41%. c) 1. 3 Mol-equiv. $\text{LiCH}_2\text{SO}_2\text{Ph}/\text{THF}$, Ar, $-78^\circ\text{C} \rightarrow -5^\circ\text{C}/2\text{ h}$; 2. 3 mol-equiv. BuLi , $-5^\circ\text{C} \rightarrow \text{r.t.}/2\text{ h}$, 86%. d) 4 Mol-equiv. BuLi/THF , Ar, $-5^\circ\text{C} \rightarrow \text{r.t.}/0.5\text{ h}$, r.t. 15 h, 21%. e) 1. 5 Mol-equiv. $\text{LiCH}_2\text{SO}_2\text{Ph}/\text{THF}$, Ar, $-78^\circ\text{C} \rightarrow -5^\circ\text{C}/3\text{ h}$; 2. 4 Mol-equiv. BuLi/THF , $-5^\circ\text{C} \rightarrow \text{r.t.}/0.5\text{ h}$, r.t./15 h, 12% **7c** and 25% *endo*-**10c**/*exo*-**10c** (5:1).

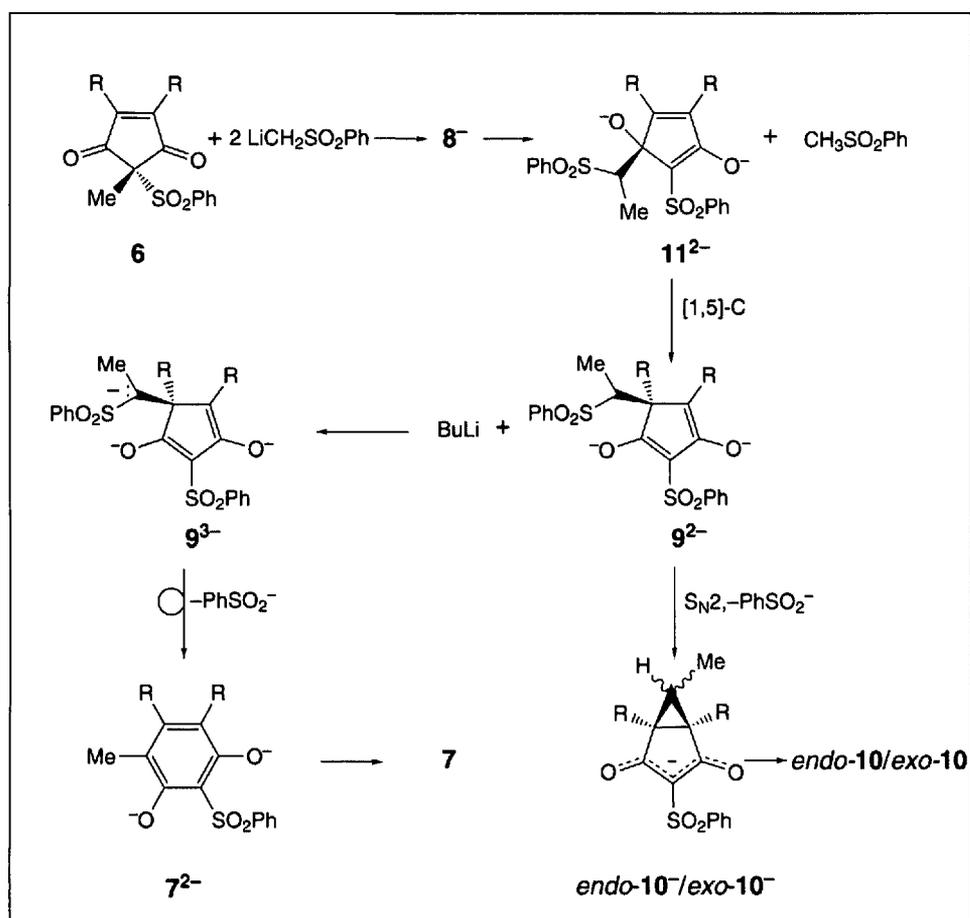
which appears in the range of 1.5–1.75 ppm. When the diones **6** were reacted first with 4 mol-equiv. of lithiomethyl phenyl sulfone at -78 to -5°C in THF and then with 4 mol-equiv. of BuLi at -5 to 20°C , followed by stirring at r.t. during 15 h, the resorcinols **7** could be isolated in yields of 70 and 5%, respectively. The low yield of **7b** can be attributed to the two Me groups, which both are in β -position at a conjugated enone system.

The structures of **7a** and **7b** could easily be deduced from their NMR spectra: an aromatic Me group in the range of 1.9 to 2.1 ppm and a sharp *s* for two phenolic OH groups, forming H-bridges with the sulfonyl group. In the case of the unsymmetrically substituted resorcinol **7a** two sharp *s* at 9.74 and 7.69 ppm for two OH groups were observed, whereas the symmetrically substituted resorcinol **7b** showed only one sharp *s* at 8.58 ppm for two OH groups. The symmetry of **7b** was

also documented by the Me signals, which appeared as two sharp *s* in a ratio of 2:1. Finally, both structures were unequivocally established by X-ray crystal structure analysis.

In order to gain more insight into the pathways, **6** \rightarrow **7**, further experiments were performed with the ene-dione **6c**, formed in good overall yield from 3,4,5,6-tetrahydrophthalic anhydride (**4c**) in the manner described for **7a** and **7b**. When **6c** was reacted with 3 mol-equiv. $\text{LiCH}_2\text{SO}_2\text{Ph}$ at -78°C and warming to 0°C within 2 h, no resorcinol **7c** was observed (Scheme 3, b). However, **8c** was found in the reaction mixture. Its structure assignment is based on MS (M^+ at $m/z = 460$) and ^1H and ^{13}C NMR (CDCl_3), which revealed the presence of a $\text{PhSO}_2(\text{CH}_3)\text{CH}$ fragment linked to a $\text{C}=\text{O}$ group (CH_3 : *d* at 1.45 ppm; H: *q* at 3.65 ppm) and a $\text{PhSO}_2\text{CH}=\text{C}(\text{OH})$ partial structure according to two *s* at 4.56

ppm (OH) and 4.75 ppm ($-\text{CH}=\text{}$). When **6c** was reacted with 3 mol-equiv. $\text{LiCH}_2\text{SO}_2\text{Ph}$ at -78 to -5°C followed by addition of 3 mol-equiv. of BuLi at -5°C and stirring for 2 h at r.t. (Scheme 3, c), **9c** was isolated in 86% yield. Its structure was solved by an X-ray crystal structure determination, whereby the position of the H-atom of the OH group could not be localized, presumably due to the presence of two tautomeric forms in the crystals. All other spectral data were in full agreement with the X-ray structure. When **9c** was treated with 4 mol-equiv. of BuLi in THF at -5°C , warmed to r.t. and stirred for 15 h (Scheme 3, d), the expected resorcinol **7c** (OH signals at 8.88 and 8.71 ppm and Me signal at 2.01 ppm) was obtained in 21% yield, showing that deprotonated **9c** must be a crucial intermediate in the formation of **7c**. Indeed, **7c** was also formed in 12% yield in the 'one-pot' procedure, whereby **6c**



Scheme 4

was first reacted with 5 mol-equiv. $\text{LiCH}_2\text{SO}_2\text{Ph}$ at -78 to -5 °C, followed by addition of 4 mol-equiv. of BuLi and stirring for 15 h at r.t. (Scheme 3, e). A 5:1 mixture of the two stereoisomers *endo-10c* and *exo-10c* could be isolated. The main stereoisomer could be purified by crystallization from $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$. The chemical shifts of the H-atom (1.72 ppm; q , $J_{\text{vic}} = 6.6$ Hz) and the Me group (1.19 ppm; d , $J_{\text{vic}} = 6.6$ Hz) as well as the comparably small J_{vic} value suggested a $>\text{CH}-\text{CH}_3$ substructure as part of a 3-membered ring. A X-ray crystal-structure analysis confirmed the presence of a 3-membered ring with the Me group above the cyclohexane ring (*endo-10c*). Thus, the minor stereoisomer has to carry the Me group above the 5-membered ring (*exo-10c*). Both stereoisomers seem to be side products and 'dead ends' of the benzene-ring forming reaction, because they could not be converted to **7c** on prolonged treatment with BuLi in THF at r.t.

The described results of resorcinol (**7**) formation from ene-diones of type **6** are in agreement with a reaction sequence, whose essential steps are a sigmatropic [1,5]-C shift (**11²⁻** \rightarrow **9²⁻**), driven by the transformation of an oxidoenolate (**11²⁻**) into a better resonance-stabilized bisenolate (**9²⁻**), followed by ring enlargement

to (**7²⁻**) in a type of Bamford-Stevens rearrangement of a carbenoid intermediate, formed by α -elimination of PhSO_2^- from a trisanion (**9³⁻**; Scheme 4).

In future experiments the carbene-forming step has to be improved by better leaving groups than PhSO_2^- .

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- [1] K. Abou-Hadeed, H.-J. Hansen, *Helv. Chim. Acta* **1997**, *80*, 2535.
- [2] M. Lutz, A. Linden, K. Abou-Hadeed, H.-J. Hansen, *Helv. Chim. Acta* **1999**, *82*, 372.
- [3] M. Meyer, K. Abou-Hadeed, H.-J. Hansen *Helv. Chim. Acta* **2000**, *83*, 2383.