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Synthesis of bicyclic quinones via 1,4-diacetoxyanthracene

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Abstract—1,4-Diacetoxyanthracene is introduced as a convenient intermediate for the syntheses of bicyclic quinones and diquinones.

1. Introduction

Bicyclic quinones and diquinones are attracting chemists' attention as building blocks for organic synthesis,[1] particularly for molecules, mimicking intramolecular photoelectron transfer.[2] Recently a series of triptoquinones and triptodiquinones have shown a wide spectrum of biological activity such as anti-inflammatory,[3] antimalaria[4] activity, and cytotoxicity against daunorubicin resistant leukemia cell lines.[4] Triptodiquinones have been available through the Diels–Alder addition of an appropriately substituted benzoquinone to 1,4-dimethoxyanthracene, followed by a sequence of chemical transformations of the adduct.[1–4] However, the preparation of 1,4-dimethoxyanthracene involves the use of dangerous sodium hydride,[4] and according to our experiments, the final step of oxidative dimethylation with cerium ammonium nitrate (CAN)[4] is difficult to reproduce. Although electrochemical[5] and biological[6] properties of the unsubstituted triptodiquinone **1** are described in the literature, the compound itself and its precursor **5** have never been properly characterized. Neither NMR-spectra nor other supplementary data for these compounds are available.

We describe a convenient synthesis of **1**, starting from 1,4-diacetoxyanthracene **2**, synthesized by a known procedure.[7] Refluxing of **2** with 2 equiv of 1,4-benzoquinone in chlorobenzene readily produces adduct **3** (with no impurities of **4**), which partially isomerizes to hydroquinone **4** during purification on silica gel. Interestingly, if the cycloaddition is performed with only 1 equiv of benzoquinone, adduct **3** enolizes to **4** in the reaction mixture, and after extended refluxing (31 h) yields only the isomerized product **4**. This observation has allowed us to develop a one-pot synthesis of quinone **6** from **2**. Interestingly, the influence of the diene–dienophile ratio on the synthetic outcome of this reaction is well reproducible, but its reason remains unclear. Refluxing of adduct **3** in chlorobenzene alone does not cause the isomerization, which is probably catalyzed by a side product of addition to benzoquinone. This control experiment does not rule out the possibility that the interaction of the second equivalent of benzoquinone with **3** retards its enolization. However, such an interaction cannot be considered as the only reason of the suppressing effect of benzoquinone on the enolization of **3**. Deacetylation and subsequent isomerization of adduct **3** in refluxing methanol with a catalytic amount of HCl led to known 1,4,5,8-tetrahydroxytriptycene **5** (Scheme 1). Along with the NMR-data, this reaction has provided an additional structural proof for the diastereomeric mixture **3**. Silver oxide in acetone oxidizes phenolic compound **5** to triptodiquinone **1** as described.[5]

The oxidation of **4** with silver oxide yielded another bicyclic quinone **6**, whose structure was confirmed by NMR and elemental analysis.

In a separate experiment, the conversion of 1,4-diacetoxyanthracene **2** to quinone **6** was performed in an overall yield of 86% without the separation of the intermediate hydroquinone **4**, which gave us a practically efficient procedure for the synthesis of **6**.

A similar approach was applied to synthesize another bicyclic quinone **8**, bearing two carbomethoxy-functionalities (Scheme 2). The first step of Diels–Alder addition

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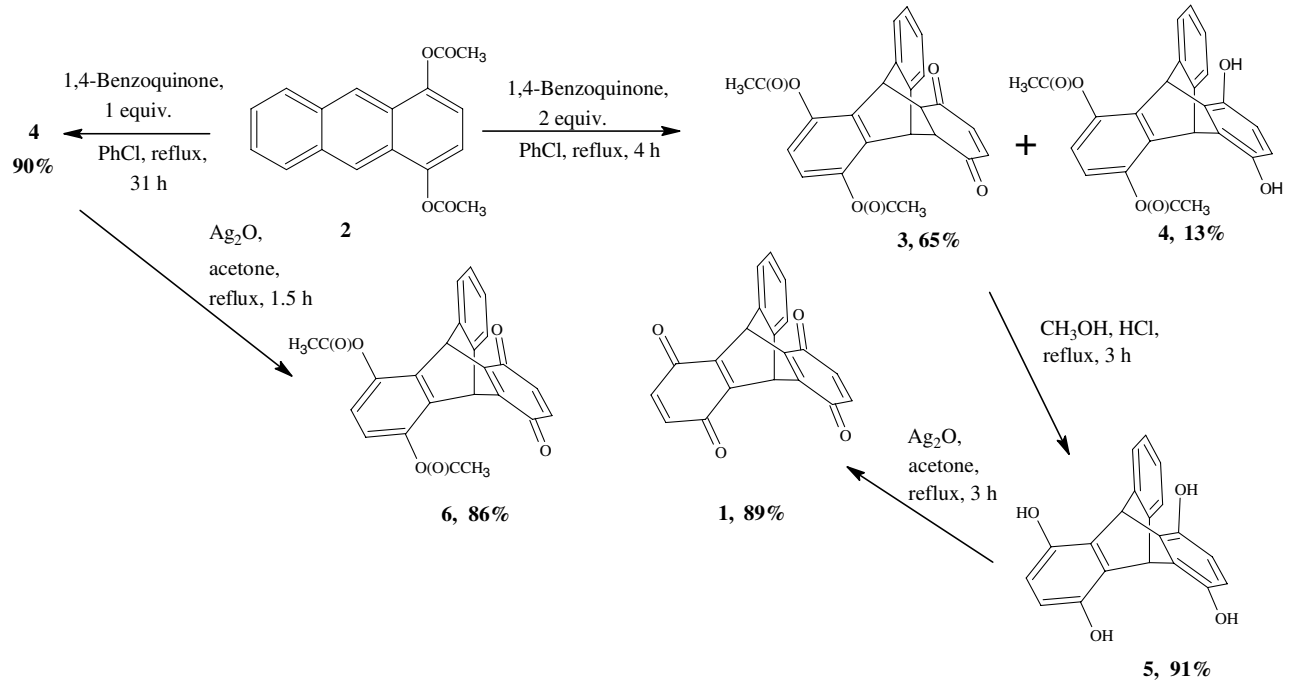
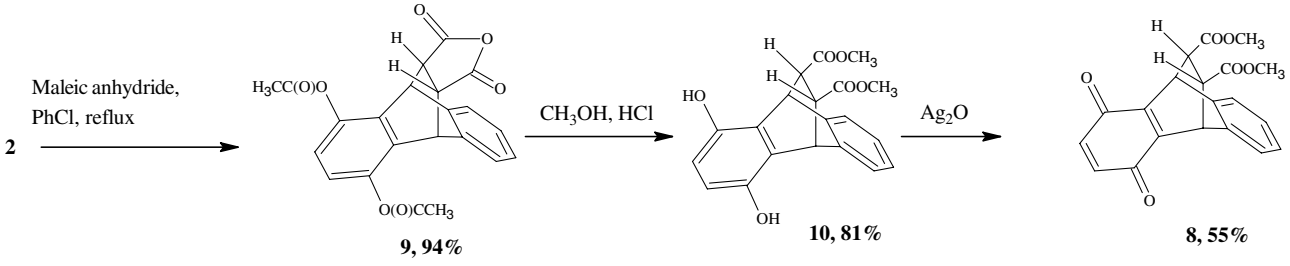


Scheme 1.



Scheme 2.

selectively proceeded in the anti-fashion. The structure of adduct **9** was confirmed by the X-ray analysis of the final quinone **8**.

The observed stereochemistry of addition of maleic anhydride to **2** formally contradicts the rule of 'accumulation of multiple bonds' and can be explained by the opposite orientations of the dipole moments of 1,4-diacetoxyanthracene and maleic anhydride at the moment of Diels–Alder addition.

In summary, we introduced a simple addition–deprotection–oxidation sequence of chemical transformations that provides an easy access to a variety of practically useful bicyclic quinones and diquinones.

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Supplementary data

Experimental procedures and ^{1}H NMR spectra for all synthesized compounds, elemental analysis for compound **3**, and the X-ray data for compound **8**. Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.10.048.

References and notes

1. Ryan, D. E. *Tetrahedron Lett.* **1996**, *37*, 6089–6092.
2. Wiehe, A.; Senge, M. O.; Kurreck, H. *Liebigs Ann.* **1997**, 1951–1963.

3. Xanthopoulou, N. J.; Kourounakis, A. P.; Spyroudis, S.; Kourounakis, P. N. *Eur. J. Med. Chem.* **2003**, *38*, 621–626.
4. Hua, D. H.; Tamura, M.; Huang, X.; Stephany, H. A.; Helfrich, B. A.; Perchellet, E. M.; Sperfslage, B. J.; Perchellet, J. P.; Jiang, S.; Kyle, D. E.; Chiang, P. K. *J. Org. Chem.* **2002**, *67*, 2907–2912.
5. Iwamura, H.; Makino, K. *J. Chem. Soc., Chem. Commun.* **1978**, *57*, 720–721.
6. Perchellet, E. M.; Magill, M. J.; Huang, X.; Brantis, E. C.; Hua, D. H.; Perchellet, J. P. *Anti-Cancer Drugs* **1999**, *10*, 749–766.
7. Kosman, D.; Stock, L. M. *J. Am. Chem. Soc.* **1969**, *91*, 2011–2021.