

## Synthesis of 2-Methylene-1,3-dioxygenated Cyclopentanes and Cyclopentenest

Nuanphun Chantarasiri, Pranee Dinprasert, Chachanat Thebtaranonth, Yodhathai Thebtaranonth,\* and Chavi Yenjai

*Department of Chemistry, Faculty of Science, Mahidol University, Rama 6 Road, Bangkok 10400, Thailand*

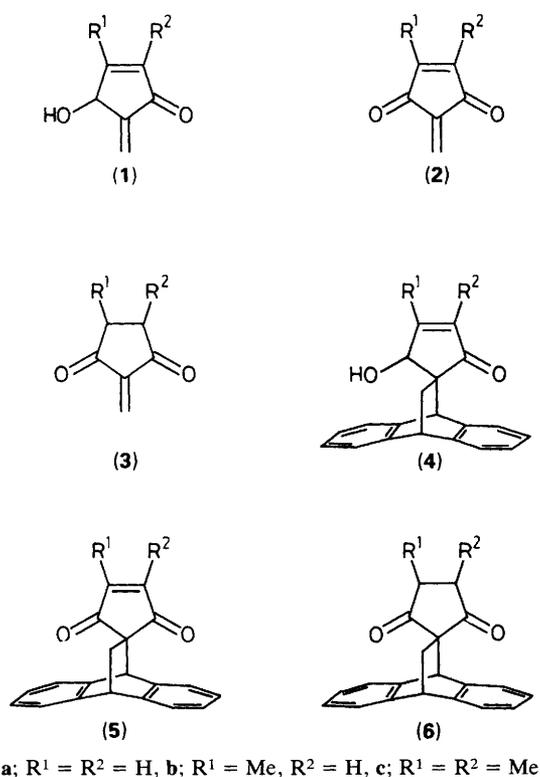
Anthracene adducts (4)–(6) are synthesized *via* a convenient general synthesis and subjected to a retro Diels–Alder reaction to furnish the corresponding 2-methylene-1,3-dioxygenated cyclopentenenes and cyclopentanes (1)–(3) *via* either flash vacuum pyrolysis or room temperature silica gel-catalysed decomposition.

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3-Hydroxy-2-methylene-4-cyclopentenones [*e.g.*, (1)] constitute the core structure in various eicosanoid-derived marine

natural products such as the clavulones,<sup>1</sup> hence considerable effort has lately been directed towards their synthesis.<sup>2</sup> Likewise, 2-methylenecyclopentene- and cyclopentane-diones (2) and (3) are of interest, with regard to both their synthetic potential and their physical and chemical proper-

† Part of this work was presented at the 22nd Sheffield Stereochemistry Symposium, 14th December 1988.



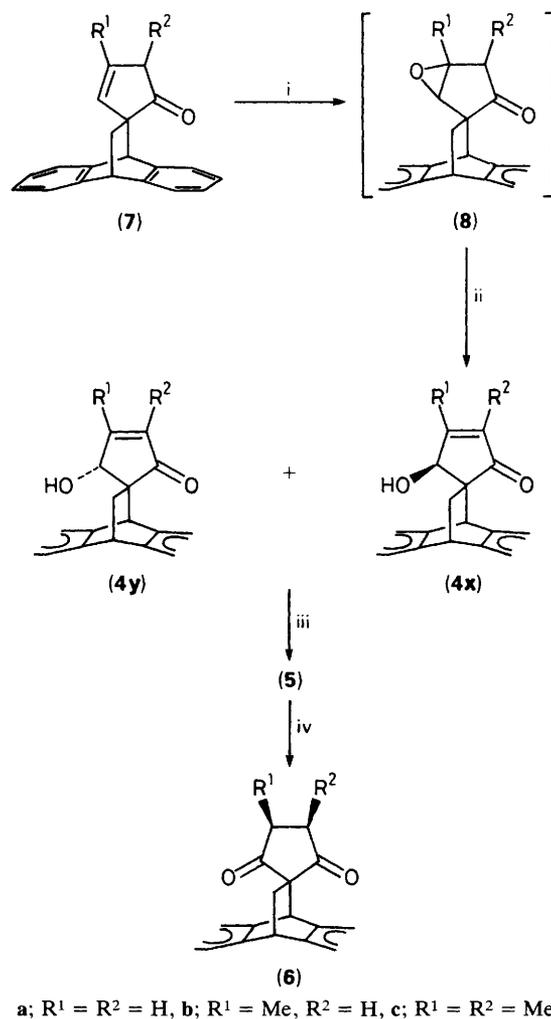
ties.<sup>3</sup> In view of the importance of these molecules we have developed a short and convenient general synthesis of anthracene adducts (4)—(6) which undergo retro Diels–Alder reactions leading to 2-methylene-1,3-dioxycyclopentanes and cyclopentanes (1)—(3).

The requisite key intermediate in the synthesis of compounds (4)—(6), spirocyclopentenone adduct (7), is easily prepared by the three-carbon annelation method reported previously.<sup>4</sup> *m*-Chloroperbenzoic acid (MCPBA) oxidation followed by treatment of crude epoxide (8) with a small amount of triethylamine effects a clean conversion to spiroketol (4), separable by PLC (silica gel, dichloromethane) into (4X) and (4Y).<sup>‡</sup> Spiro-enediones (5a—c) are then obtained by pyridinium dichromate (PDC) oxidation of ketols (4) (single or mixed stereoisomers) in dimethylformamide (DMF) solutions (83—85% yields). Catalytic hydrogenation (10% palladium on charcoal, ethyl acetate) of (5a) and (5b) yields, respectively, (6a) and a single isomer (6b) (94 and 60%) with the tentative stereochemistry shown in Scheme 1.<sup>‡</sup>

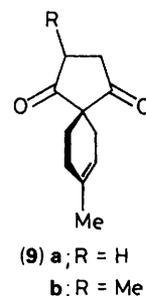
Surprisingly, hydrogenation of (5c) does not give rise to the expected (6c), but alternatively yields ketol (4Xc) (64%) which is also obtained upon treatment of (5c) with sodium borohydride at 0°C. Other methods of reduction also fail, *e.g.*, treatment of (5c) with zinc in acetic acid gives a complex mixture. The synthesis of (6c) has not been pursued.

Flash vacuum pyrolysis of (4a—c) (either singly or as isomeric mixtures) and (5a—c) give, respectively, (1a—c) and

<sup>‡</sup> (4Xa) 33%, (4Ya) 59%; (4Xb) 26%, (4Yb) 65%; (4Xc) 52%, (4Yc) 43%, calculated from (7). While two isomers of (4) were obtained, reactions leading to (6b), (10), and (12) each gave only one product. Apart from (2), all compounds described have been fully characterized (elemental analyses were performed by the Scientific and Technological Research Equipment Center, Chulalongkorn University, Bangkok). Compounds (2a—c) are rather unstable, hence only IR, NMR, and mass spectra were obtained. (2a) was additionally characterized by formation of its isoprene adduct.

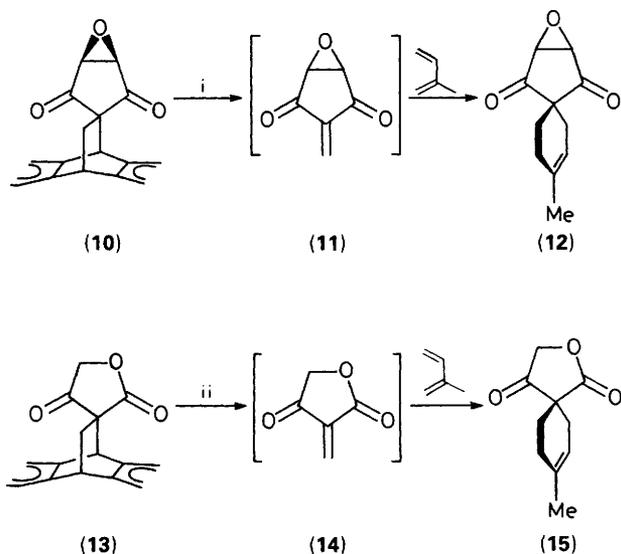


Scheme 1. Reagents: i, MCPBA, CH<sub>2</sub>Cl<sub>2</sub>; ii, Et<sub>3</sub>N, tetrahydrofuran; iii, PDC, DMF; iv, H<sub>2</sub>, Pd on C, EtOAc.



(2a—c) in near quantitative yields, the hydroxycyclopentenones (1a—c) being notably stable while the cyclopentenediones (2) [especially (2b) and (c)] spontaneously polymerize in solution to give gums. Adducts (6a) and (b), on the other hand, fail to deliver the corresponding methylenecyclopentenediones (3a) and (b), and at various high temperatures only anthracene and polymerized materials are detected.

In fact, it is most probable that products (3a) and (b) are formed but cannot survive the pyrolytic conditions. [In its first preparation *via* elimination of sulphoxide from the corresponding 2-methyl-2-phenylthio-1,3-cyclopentanedione, (3a) could not be isolated but was trapped *in situ* with isoprene.<sup>3c</sup>]



**Scheme 2.** Reagents and conditions: i and ii, silica gel, toluene, room temperature.

Recently, anthracene adduct (**6a**), synthesized by a different route, was reported to undergo rapid trifluoroacetic acid-catalysed retro Diels–Alder reaction at room temperature to give anthracene and (**3a**), which readily underwent further reaction.<sup>3a</sup> We have earlier observed that a toluene solution of (**6a**) is decomposed in the presence of a trace amount of silica gel at room temperature, releasing anthracene and (**3a**), which we could trap and isolate as the corresponding isoprene adduct (**9a**) (60%).<sup>5</sup> Applying this treatment now to adduct (**6b**) we obtain (**9b**) (62%) as a diastereoisomeric mixture. However, no reaction occurs with adducts (**4a–c**) and (**5a–c**) under the said reaction conditions and starting materials are recovered unchanged.

In connection with this study we have also found that other nonconjugated keto adducts closely related to (**6**) such as epoxydione (**10**)<sup>‡</sup> and ketolactone (**13**) [respectively obtained from alkaline hydrogen peroxide oxidation of (**5a**), and PDC oxidation of the corresponding hydroxylactone<sup>6</sup>] also undergo

a silica gel-catalysed retro Diels–Alder reaction at room temperature. Thus (**10**) and (**13**) decompose upon treatment of their toluene solutions with silica gel in the presence of excess isoprene to give, respectively, (**11**) and (**14**), isolated as the corresponding isoprene adducts (**12**)<sup>‡</sup> and (**15**) (Scheme 2).

Although reasonably well precedented,<sup>7</sup> the low temperature retro Diels–Alder reaction has barely been explored compared to the forward addition process. Besides an extremely convenient general synthesis of 2-methylene-1,3-dioxygenated cyclopentanes and cyclopentenones, therefore, this study also provides an interesting example of the use of the low temperature retro Diels–Alder reaction in synthesis.

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## References

- H. Kikuchi, Y. Tsukitani, K. Iguchi, and Y. Yamada, *Tetrahedron Lett.*, 1982, **23**, 5171.
- L. S. Liebeskind, D. Mitchell, and B. S. Foster, *J. Am. Chem. Soc.*, 1987, **109**, 7908.
- (a) W. H. Bunnelle and W. R. Shangraw, *Tetrahedron*, 1987, **43**, 2005; (b) L. S. Liebeskind and R. Chidambaran, *J. Am. Chem. Soc.*, 1987, **109**, 5025; (c) P. E. Eaton and W. H. Bunnelle, *Tetrahedron Lett.*, 1984, **25**, 23; (d) D. R. Gedge and G. Pattenden, *J. Chem. Soc., Chem. Commun.*, 1978, 880.
- T. Siwapinyoyos and Y. Thebtaranonth, *J. Org. Chem.*, 1982, **47**, 598. Employing the cyclisation procedure described in this reference followed by saturated ammonium chloride work-up at 0 °C we obtained (**7a**) (87%) as the sole product; (**7b**) (44%) together with its  $\alpha,\beta$ -unsaturated isomer (44%); and (**7c**) (97%) from subsequent methylation of (**7b**).
- N. Chantarasiri, M.Sc. Thesis, Mahidol University, 1985.
- P. Dinprasert, C. Mahidol, C. Thebtaranonth, and Y. Thebtaranonth, *Tetrahedron Lett.*, 1989, **30**, 1149.
- Y. Chung, B. F. Duerr, T. A. McKelvey, P. Nanjappan, and A. W. Czarnik, *J. Org. Chem.*, 1989, **54**, 1018; A. P. Marchand and V. Vidyasagar, *J. Org. Chem.*, 1988, **53**, 4412; M. J. Hassinger and F. E. Lytle, *J. Am. Chem. Soc.*, 1983, **105**, 5495; reviews: J. Sauer and R. Sustmann, *Angew. Chem., Int. Ed. Engl.*, 1980, **19**, 779; J. L. Ripoll, A. Rouessac, and F. Rouessac, *Tetrahedron*, 1978, **34**, 19.