Synthesis of 2-Methylene-1,3-dioxygenated Cyclopentanes and Cyclopentenes†

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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 cyclopentenes and cyclopentanes (**1**)—(**3**) *via* either flash vacuum pyrolysis or room temperature silica gel-catalysed decomposition.

3-Hydroxy-2-methylene-4-cyclopentenones [*e.g.*, (**1**)] constitute the core structure in various eicosanoid-derived marine natural products such as the clavulones,[1] hence considerable effort has lately been directed towards their synthesis.[2] Likewise, 2-methylenecyclopentene- and cyclopentanediones (**2**) and (**3**) are of interest, with regard to both their synthetic potential and their physical and chemical proper-

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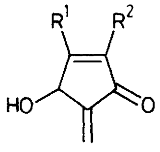
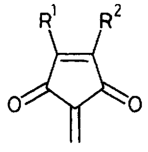
† Part of this work was presented at the 22nd Sheffield Stereochemistry Symposium, 14th December 1988.



(1)



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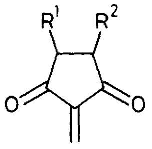

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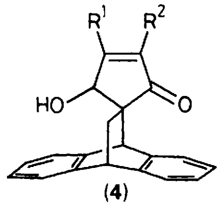

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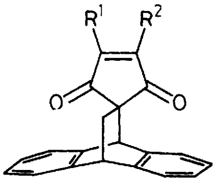

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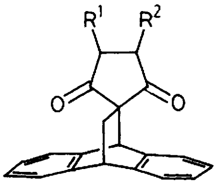


(6)

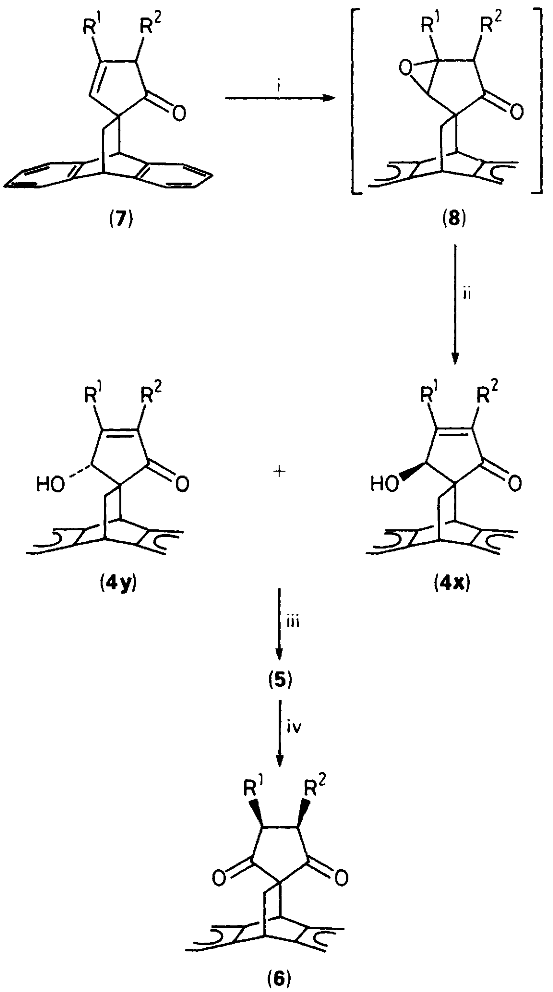
a; $R^1 = R^2 = H$, b; $R^1 = Me$, $R^2 = H$, c; $R^1 = R^2 = Me$

ties.[3] 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-dioxygenated cyclopentenes 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.[4] *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**).‡ 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.‡

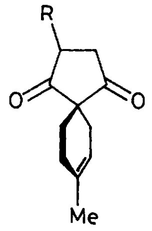
Surprisingly, hydrogenation of (**5c**) does not give rise to the expected (**6c**), but alternatively yields ketol (**4Xc**) (64%) which is also obtained upon treatment of (**5c**) with sodium borohydride at 0 °C. Other methods of reduction also fail, *e.g.*, treatment of (**5c**) with zinc in acetic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



a; $R^1 = R^2 = H$, b; $R^1 = Me$, $R^2 = H$, c; $R^1 = R^2 = Me$

Scheme 1. *Reagents:* i, MCPBA, CH_2Cl_2; ii, Et_3N, tetrahydrofuran; iii, PDC, DMF; iv, H_2, Pd on C, EtOAc.



(**9**) **a**; R = H
b; R = Me

(**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 methylenecyclopentanediones (**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.[3c]]

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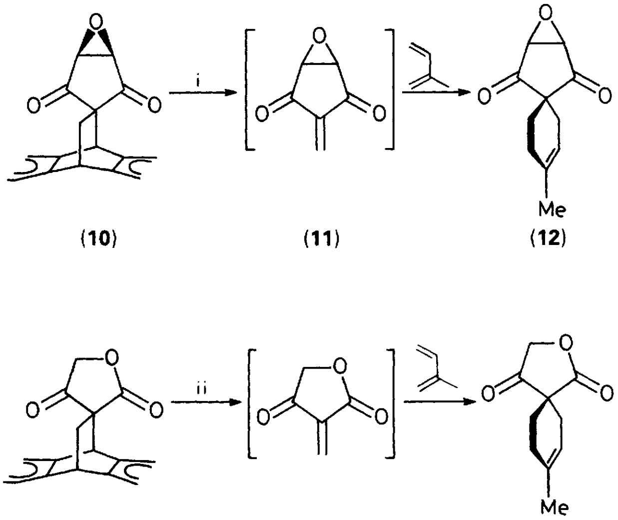
‡ (**4Xa**) 33%, (**4Ya**) 59%; (**4Xb**) 26%, (**4Yb**) 65%; (**4Xc**) 52%, (**4Yc**) 43%, calculated from (**7**). While two isomers of (**4**) were obtained, reactions leading to (**6b**), (**10**), and (**12**) each gave only one product. Apart from (**2**), all compounds described have been fully 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.



(10) (11) (12)

(13) (14) (15)

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.[3a] 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%).[5] 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**)‡ and ketolactone (**13**) [respectively obtained from alkaline hydrogen peroxide oxidation of (**5a**), and PDC oxidation of the corresponding hydroxylactone[6]] 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**)‡ and (**15**) (Scheme 2).

Although reasonably well precedented,[7] 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 cyclopentenes, 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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