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A FACILE SYNTHESIS OF FUNCTIONALIZED CYCLOPENTADIENONE EPOXIDES BY FLASH THERMOLYTIC CYCLOREVERSION OF TRICYCLODECENONES

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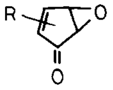
Abstract. A practical synthesis of cyclopentadienone epoxides 10 and their dimethyl acetals 12 by thermal cycloreversion of appropriate tricyclo|5.2.1.$0^{2,6}$|decenone epoxides is described.

Cyclopentadienone epoxides are elusive structures which have mainly been postulated as transient intermediates in the photochemical transformation of 4-pyrones to 2-pyrones[1]. Although aryl substituted derivatives are known since 1937[2], the parent compound 1 (R=H) has been synthesized only very recently whereas no practical synthesis to aliphatically substituted and functionalized cyclopentadienone epoxides 1 are known yet. Chapman and Hess[3] obtained the parent cyclopentadienone epoxide by thermal fragmentation of the tetracyclic structure 2 which formally can be considered as a Diels Alder adduct, and trapping this labile species in a hydrocarbon matrix at 77°K. For synthetic purposes this approach suffers serious drawbacks as the precursor 2 can only be obtained indirectly via a many step synthesis from the dimer of cyclopentadienone and functionalization is hardly conceivable. Attempts to generate 1 (R=H) by flash vacuum pyrolysis of 3, which from a synthetic point of view is an attractive precursor, were unsuccessful as it led exclusively to 2-pyrone instead. Although it is assumed that cyclopentadienone epoxide is the primary thermolysis product, it apparently undergoes a facile rearrangement into 2-pyrone at the severe conditions needed for the thermal cleavage of 3. As a consequence of its limited availability, the chemistry of cyclopentadienone epoxides has scarcely been studied and factors governing their thermal rearrangement into α-pyrones are unknown. Appropriate functionalization of 1 may considerably alter its thermal stability, reasons for us to study the thermal fragmentation of functionalized tricyclo|5.2.1.$0^{2,6}$|decenone epoxides 3 which are conceivably the most adequate precursors for these structures.



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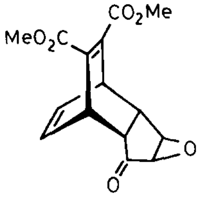

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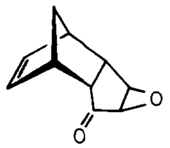

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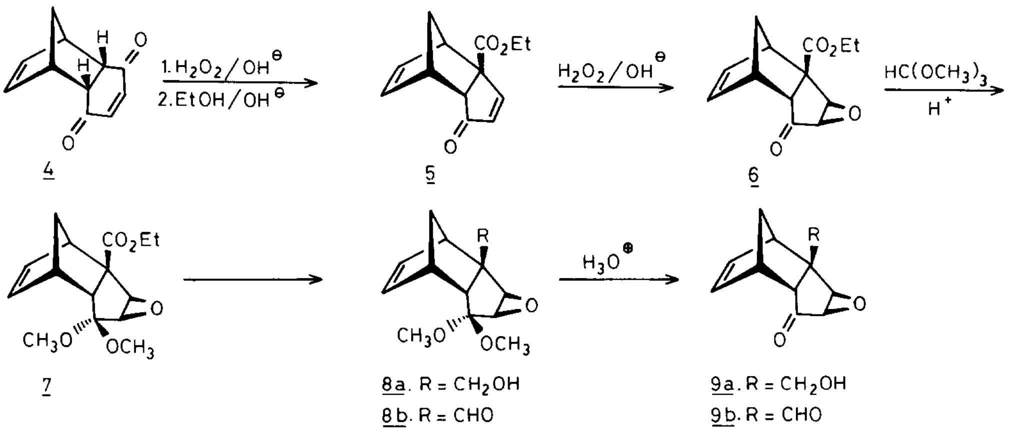
In this paper we report on a practical synthesis of functionalized cyclopentadienone epoxides and their dimethyl acetals starting from the benzoquinone-cyclopentadiene adduct 4 (Scheme 1).

scheme 1



4

5

6

7

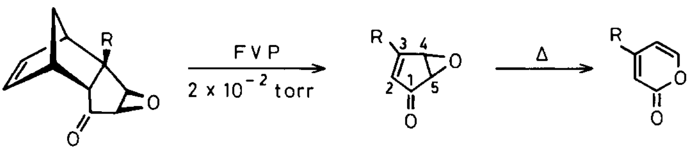
8a. R = CH_2OH
8b. R = CHO

9a. R = CH_2OH
9b. R = CHO

Ester 5 was readily synthesized from this adduct 4[4]. Alkaline epoxidation of 5 with H_2O_2 gave epoxide 6 in almost quantitative yield[5]. The stereochemistry of 6 is based on the assumption that the attack of the hydroperoxide ion occurs at the less hindered convex side of the molecule. In order to achieve a selective conversion of the ester function, the cyclopentanone carbonyl group was protected as a dimethyl acetal. Treatment of 6 with trimethyl orthoformate smoothly produced 7 in 95% yield. Reduction of 7 with $LiAlH_4$ in ether gave alcohol 8a (yield 88%). Under these reductive conditions the epoxide ring is not affected due to steric blocking of its rear side by the bulky olefin bridge. When $i\text{-}Bu_2AlH$ was used as the reducing agent a 1:1.5 mixture of the desired aldehyde 8b and alcohol 8a was formed. More efficently, the aldehyde 8b was obtained by oxidation of alcohol 8a with pyridinium chlorochromate (PCC). In this manner aldehyde 8b was isolated as a single product in a yield of 80%. Deprotection of the ketone function in 8 was accomplished in quantitative yield with HCl aq.

The ketones 6 and 9 as well as their dimethyl acetals were subjected to flash vacuum pyrolysis[6]. The results of these experiments are depicted in the Schemes 2 and 3. Thermolysis of

scheme 2



6 R = CO_2Et
9a R = CH_2OH
9b R = CHO

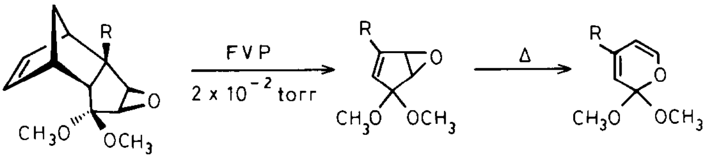
10a 55% (430°)
10b –
10c 95% (420°)

11a 90-95% (510°)
11b 80% (540°)
11c 95% (550°)

both the ester 6 and aldehyde 9b at 460° produced mixtures of cyclopentadienone epoxide 10 and α-pyrone 11. By carefully varying the oven temperature, the yield of each product could be optimized (both optimum yields and temperatures are shown in the Schemes). Only in case of the aldehyde 9b the pyrolysis could be controlled in such a way that epoxide 10c was formed as the exclusive product. However, epoxide 10a could readily be isolated from the pyrolysis mixture containing besides 10a mainly α-pyrone 11a and some starting material, by preparative TLC. Thermal reaction of tetracyclic alcohol 9a did not lead to any epoxide 10b. At 400-450° only starting alcohol and α-pyrone 11b were obtained. Raising the thermolysis temperature to 540° led to the exclusive formation of α-pyrone alcohol 11b. Apparently, the thermal conditions which are required for the cycloreversion of precursor 9a also bring about an efficient rearrangement of 10b into α-pyrone 11b and accordingly no epoxide 10b can be isolated.

The dimethyl acetals 7 and 8 were found to be thermally more stable than their corresponding ketones (Scheme 3). Notwithstanding the somewhat higher temperatures needed to achieve an efficient cycloreversion reaction, both the ester 7 and aldehyde 8b afforded the cyclopentadienone acetal epoxides 12a and 12c in good to excellent yields upon flash vacuum pyrolysis at 460° and 475°, respectively. Again, at these temperatures the thermal cleavage of the alcohol derivative 8a did not yield any epoxide 12b. When the oven temperature was raised to 500-600° mixtures of products were formed from which the α-pyrone dimethyl acetals 13 could readily be isolated. No epoxides 12 could be detected.

scheme 3



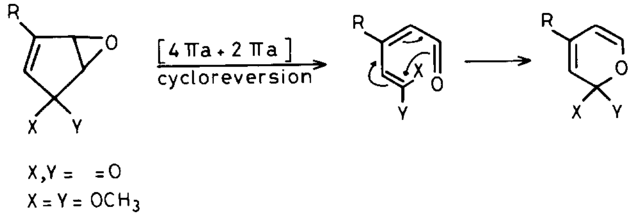
7 R = CO_2Et	12a 65% (460°)	13a 60% (520°)
8a R = CH_2OH	12b –	13b 65% (600°)
8b R = CHO	12c 90% (475°)	13c 55% (580°)

The identity of both the cyclopentadienone epoxides and α-pyrones were unequivocally established by their spectroscopic properties. The IR spectra of epoxides 10a and 10c show a characteristic cyclopentenone carbonyl absorption at 1730 cm ^{1}. Their 'H NMR spectra are particularly decisive as they feature a characteristic three proton resonance pattern for the ring protons. Typically, the 'H NMR (CCl_4) spectrum of 10a displays a doublet of doublets (J_{H_2,H_5}=2.1; J_{H_2,H_4}=1.9 Hz) at δ6.42 for the olefinic proton H_2, a doublet of doublets (J_{H_5,H_4}=2.3; J_{H_5,H_2}=2.1 Hz) at δ3.68 for H_5 and a broad triplet (J~2 Hz) at δ4.33 for H_4. A similar NMR pattern is observed for the dimethoxy derivatives 12a and 12c. The α-pyrones 11 are characterized in the IR by a carbonyl absorption at 1720 cm^{-1} and two olefinic absorptions at 1635 and 1550 cm^{-1}. The 'H NMR spectra of both 11 and 13 exhibit a typical three proton resonance pattern for the olefinic ring protons, which unambiguously prove the structures shown.

From the results it may be concluded that the thermal stability of cyclopentadienone epoxides is considerably enhanced *by extending the conjugation of the cyclo-enone system*. As a consequence cyclopentadienone epoxides such as 10a and 10c, and their corresponding acetals 12a and 12c can efficiently be generated by thermal cycloreversion of appropriate tricyclodecenones. When such an extended Π-electron system is lacking, the cyclopentadienone epoxides rapidly rearrange to the corresponding α-pyrones under the conditions of the thermal fragmentation.

The thermal rearrangement of cyclopentadienone epoxides and their acetals into the corresponding α-pyrone derivatives is suggested to proceed through a thermally allowed two step synchronous process[7] (Scheme 4).

scheme 4



For preparative purposes this cycloreversion of tricyclo|5.2.1.$0^{2,6}$|decenones constitutes a useful route to cyclopentadienone epoxides and their acetals. An application employing this approach for the stereospecific synthesis of (±) terrein, a mould metabolite, is reported in the accompanying paper[8].

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