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A GENERAL SYNTHESIS OF 5-ALKYLIDENE-4-HYDROXY-2-CYCLOPENTENONES

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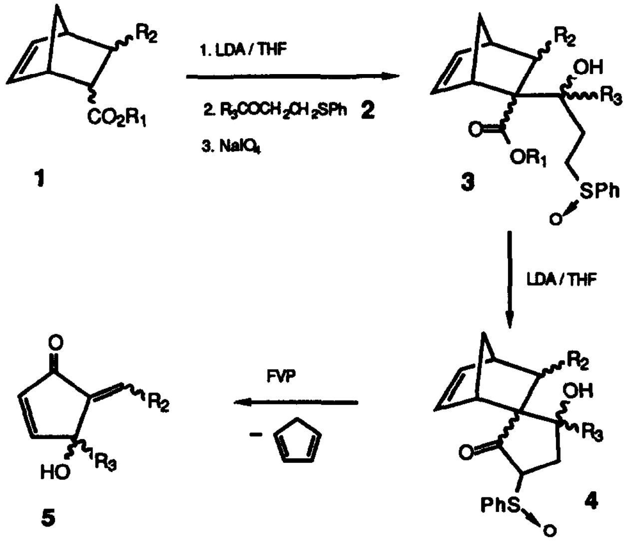
Summary: A new general method for the preparation of 5-alkylidene-4-hydroxy-2-cyclopentenones, involving the intramolecular acylation of α- sulfinyl carbanion followed by flash vacuum pyrolysis, is described.

Highly functionalised cyclopentanoids are of increasing interest because of their occurence in a wide range of natural products, many of which are of biological significance e.g. clavulones, chlorovulones, bromovulones and plunaglandins.[1] These compounds contain 5- alkylidene-4-oxygenated 2-cyclopentenone moiety. Few methods for the preparation of such important nucleus have been reported in the literature.[1,2] In connection with our recent report concerning the synthesis of 4-oxygenated spiro-alkenones[3] prompted us to report a new general synthesis of the title compounds, starting from simple bicyclic esters (cyclopentadiene - α,β-unsaturated ester Diels-Alder adducts). The synthetic sequence was shown in Scheme 1. The key reaction of this route involves the intramolecular acylation of α-sulfinyl carbanion followed by flash vacuum pyrolysis.



Scheme 1

Table 1 Preparation of compounds 3, 4 and 5.

R_1	R_2	R_3	3 (%)^{a,b,c}	4 (%)^{b,c}	5 (%)^{c}
Et	H	H	34	72	57
Et	H	Me	53	85	88
Et	H	Et	54	35	73
Et	Me	H	75	88	60^{b}
Me	Ph	H	58	66	80^{b}

a. Isolated yield based on the starting ester.

b. Obtained as a mixture of stereoisomers.

c. All products have been characterised by spectral data (IR, ^{1}H - NMR and MS) and elemental analysis for 3 and 4 (compound 5 polymerised gradually on standing).

The reaction of lithium enolate anion (1 equiv.) derived from the ester 1[4] (1 equiv., LDA 1.1 equiv./ THF, 0°) with the ketosulfide 2 (1.1 equiv.) at -78° for 2 hr followed by oxidation of the resulting crude adduct with $NaIO_4$ in aqueous methanol afforded a mixture of diastereomers of the sulfoxide 3 in moderate yield. Cyclisation of 3 to the ketosulfoxide 4 *via* the intramolecular acylation of α–sulfinyl carbanion was effected by employing LDA (3.2 equiv.) in THF at -78° for 1hr and at 0° for 1-2 hr.The ketosulfoxides 4 were obtained in 35 - 78 % as mixtures of diastereomers after preparative thin-layer chromatography (silica gel). Having the ketosulfoxide 4 in hand, it was subjected to flash vacuum pyrolysis (350° - 400° , 0.03 - 0.05 torr), furnishing the desired 5-alkylidene-4-hydroxy 2-cyclopentenones 5 in good yields after purification by preparative thin-layer chromatography (silica gel). The results are summarized in table1.

The method described here appeared to offer a conveneient and general entry to the synthesis of a wide range of prostanoids natural products containing the basic skeleton as in the compound of the type 5. Application of this synthetic method for preparing prostanoid-type natural products is now being investigated.

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4. A mixture of exo- and endo- isomers of 1 was used.

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