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A PHOTOCHEMICAL SYNTHESIS OF βγ-EPOXYCYCLOHEXANONES

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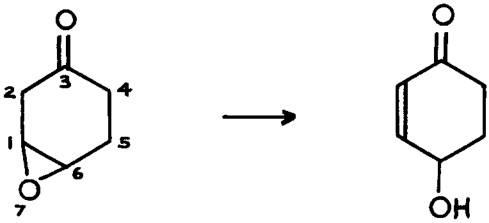
Summary: The βγ-epoxycyclohexanones (1), (9) and (10) have been prepared by photolysis of the pyruvate esters derived from the corresponding epoxyalcohols.

Whilst αβ-epoxycyclohexanones are well-known, and form useful synthetic intermediates,[1] the corresponding βγ-isomers (7-oxabicyclo[4.1.0]heptan-3-ones) have not been characterised. It appears that enolisable βγ-epoxycyclohexanones are readily isomerised by acids, bases or silica gel[2-4] to give γ-hydroxy-αβ-enones [*e.g.* (1)→(2)].



(1) (2)

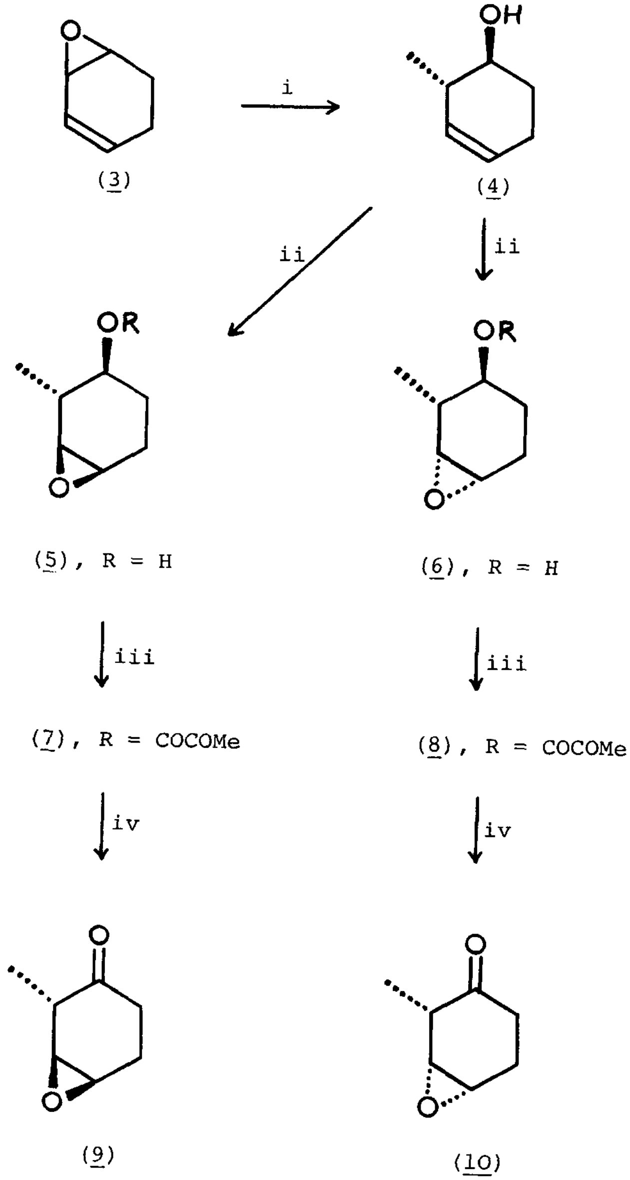
We now report the synthesis of some βγ-epoxycyclohexanones under neutral conditions using photochemical oxidation of the corresponding βγ-epoxyalcohols.[5]

Our route to the two isomeric α-methyl-βγ-epoxycyclohexanones (9) and (10) is outlined in Scheme 1. The reaction of methyl-lithium with 3,4-epoxycyclohexene (3) gave *trans*-2-methylcyclohex-3-enol (4) in low yield (20%).[6] Non-selective epoxidation with buffered *m*-chloroperoxybenzoic acid[7] gave the two stereoisomeric epoxyalcohols (5) and (6), which were separated by column chromatography on silica gel (32% and 27% yields, respectively). A mild synthetic method, avoiding chromatography at the last step, is required for their oxidation, and this is provided by Binkley's method[5] which involves photolysis of the pyruvate esters derived from alcohols. Conversion of each of the epoxyalcohols to their pyruvate esters (7) and (8) (86% and 89%, respectively) was easily achieved using pyruvoyl chloride and pyridine.[8] U.v. photolysis[9] of the pyruvates proceeded cleanly to give, after evaporation, the crude epoxyketones (9) and (10) in an estimated >80% purity by ^{1}H and ^{13}C nmr. The ketones were purified by extraction into pentane and distillation, to give 69% and 57% overall isolated yields respectively from the pyruvates.[10]

A similar synthesis, starting from cyclohex-3-enol (derived by dehydration of cyclohexane-1,4-diol) gave the parent βγ-epoxycyclohexanone (1) (51% overall yield) as a colourless oil showing ^{13}C nmr signals at 207.4 (C=O), 51.2, 50.8 (C-1, C-6), 38.9 (C-2), 34.9 (C-4) and 22.3 (C-5) p.p.m.[11] These values are close (±3.7 p.p.m.) to those calculated for (1) using the literature shifts of cyclohexanone and epoxycyclohexane.[12] Compound (1) showed reasonable thermal stability (largely unchanged after heating under reflux in toluene, 110°C, 10 mins.) and it could be detected by analytical g.l.c. at 125°C. Nmr spectroscopy showed that treatment of (1) (0.35 *M* in $CDCl_3$ solution) at 30°C with triethylamine (0.015 *M*) led steadily and cleanly to hydroxyenone (2) formation in *ca.* 50% conversion after 20 mins. The rearrangement of (1) to (2) was very rapid on contact with silica gel.

With these compounds in hand, we can now assess the importance of βγ-epoxyketone formation in the photolysis and thermolysis of endoperoxides.[3,13]

We thank the University of London Intercollegiate Research Service at Queen Mary College for 400 MHz proton spectra.



SCHEME 1. <u>Reagents</u>:
i, MeLi, Et_2O, 0°C;
ii, m-$ClC_6H_4CO_3H$, solid Na_2CO_3, CH_2Cl_2;
iii, MeCOCOCl, pyridine;
iv, $h\nu$, Pyrex, C_6H_6.

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7. cf. K.B. Sharpless and R.C. Michaelson, J.Am.Chem.Soc., 1973, 95, 6136.

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9. 450 W. Medium-pressure mercury arc, Pyrex apparatus, 0.3% v/v solution of the pyruvate in benzene, 1.25-3 h. irradiation, 20°C.

10. Compound (9), a colourless oil, showed $\nu_{max.}$ (film) 1720 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 3.40 (1H, dd, *J* 4 and 3 Hz, H-6), 3.17 (1H, dd, *J* 4 and 1.5 Hz, H-1), 2.83 (1H, bq, *J* 7.5 and 1.5 Hz, H-2), 2.6-2.4 (2H, m, H-4 and H-5), 2.3-2.1 (2H, m, H-4 and H-5), and 1.22 (3H, d, *J* 7.5 Hz, CH_3); δ_C 210.2 (C=O), 55.8 (C-1), 51.4 (C-6), 42.6 (C-2), 33.8 (C-4), 22.6 (C-5), and 13.7 (CH_3) p.p.m. Compound (10), a colourless oil, showed $\nu_{max.}$ (film) 1720 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 3.42 (1H, m, H-6), 3.25 (1H, ddd, *J* 4, 2 and 1 Hz, H-1), 2.67 (1H, qdd, *J* 7.3, 2 and 1 Hz, H-2), 2.45-2.35 (2H, m, H-4 and H-5), 2.3-2.2 (2H, m, H-4 and H-5) and 1.32 (3H, d, *J* 7.3 Hz, CH_3); δ_C 210.9 (C=O), 56.6 (C-1), 52.4 (C-6), 42.5 (C-2), 34.2 (C-4), 22.8 (C-5) and 13.8 (CH_3) p.p.m.

11. Compound (1) also showed $\nu_{max.}$ (film) 1715 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 3.41 (1H, dd, *J* 4.5 and 2 Hz, H-6), 3.35 (1H, ddd, *J* 4.5, 2.2 and 1.8 Hz, H-1), 2.92 (1H, dd, *J* 19.5 and 1.8 Hz, H-2), 2.68 (1H, ddd, *J* 19.5, 2.2 and 1.2 Hz, H-2), 2.50-2.38 (2H, m, H-4 and H-5) and 2.24-2.20 (2H, m, H-4 and H-5).

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