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FORMATION OF DIASTEREOISOMERIC CYCLOBUTANOLS AND 3-OXETANOLS BY PHOTOCYCLIZATION OF PHENYL KETONES

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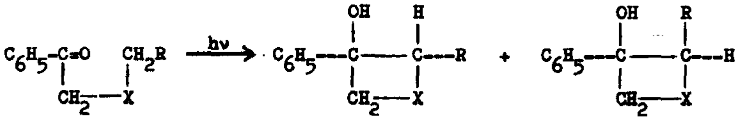
The formation of cyclobutanols by the irradiation of ketones possessing a γ-CH grouping has been demonstrated by Yang[1] and Jeger[2] and coworkers; Yates and Szabo[3] recently showed that the reaction can be extended to the formation of 3-oxetanols by irradiation of α-alkoxy ketones. Although the synthetic applicability of this reaction has been demonstrated convincingly,[4] only limited information regarding the stereochemistry of the products is available. The formation of diastereoisomeric mixtures of products has been demonstrated in certain photocyclizations leading to simple cyclobutanols, though no stereochemical preference was demonstrated.[5,6] In studies of the more rigid steroidal ketones, the formation of cyclasteroids proceeds stereoselectively in some instances.[4,5] Yates and Szabo[3] suggested that photocyclization of α-ethoxyacetophenone gave largely or entirely a single diastereoisomeric 3-oxetanol.

We have recently investigated the photocyclization of three simple ketones (Ia, Ib, Id) which yield separable mixtures of cis- (II) and trans- (III) products for which stereochemical assignments can be made readily. In each case, formation of the trans-isomer is preferred.

Irradiation of a 5% solution of valerophenone (Ia) in acetone under nitrogen with a 450 watt Hanovia Hg lamp (Pyrex filter) for four hours gave a mixture of acetophenone (85%) and cis- and trans-2-methyl-1-phenyl-



(I) (II) (III)

(a) $R = CH_3$, $X = CH_2$
(b) $R = C_6H_5$, $X = CH_2$
(c) $R = H$, $X = CH_2$
(d) $R = C_6H_5$, $X = O$
(e) $R = H$, $X = O$
(f) $R = C_6H_5$, $X = S$

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cyclobutanols (IIa, IIIa, 15%). The mixture of isomers was separated by silicic acid chromatography to give the pure cis- (IIa, 5.4%) and trans- (IIIa, 9.6%) isomers as oils. The n.m.r. spectrum of each of the isomers was in accord with the postulated structure. IIa showed a methyl doublet at $\tau = 9.33$, a methine complex at $\tau = 8.85$, a complex due to methylene and hydroxyl at $\tau = 7.73$-8.17 and a broad aromatic singlet at $\tau = 2.82$ p.p.m. IIIa showed a methyl doublet at $\tau = 8.94$, a complex due to methylene and methine at $\tau = 7.20$-8.42, a hydroxyl singlet at $\tau = 7.83$ and an aromatic complex at $\tau = 2.85$ p.p.m. The stereochemical assignment is based upon the chemical shift of the methyl group in each isomer; the cis-relationship of phenyl and methyl should result in shielding of the methyl protons and an upfield shift as observed in IIa.

Similar irradiation of γ-phenylbutyrophenone (Ib) led to the isolation of acetophenone (69%), styrene (73%) and cis- and trans-1,2-diphenylcyclobutanols (IIb, IIIb). The isomeric cyclobutanols were separated by silicic acid chromatography to give IIb (7.0%) and IIIb (8.8%). IIb was obtained as a crystalline material, m.p. 89-90° (from hexane); IIIb failed to crystallize. The n.m.r. spectra of IIb and IIIb were in complete accord with the postulated structures; for these compounds, the shielding effect of a cis-phenyl on the hydroxyl chemical shift was clearly observed, i.e. $\tau_{OH} = 6.48$ for IIb and 8.25 p.p.m. for IIIb. Irradiation of butyrophenone

(Ic) gave a 7.7% yield of 1-phenylcyclobutanol.[7]

Irradiation of a 2.5% solution of α-benzyloxyacetophenone (Id) in acetone for two hours gave acetophenone (48.4%) and benzaldehyde (51.4%). Silicic acid chromatography of the residues gave ca. 5% each of dibenzoylmethane and dibenzoylethane, cis- (IId, 5.3%) and trans- (IIId, 18.8%) 2,3-diphenyl-3-oxetanols. IIId was obtained as an oil, while IId crystallized on standing, m.p. 109-110° (from cyclohexane-hexane). Assignment of stereochemistry to IId and IIId was based on hydroxyl shielding by cis-phenyl, i.e., $\tau_{OH} = 6.54$ for IId and 7.58 p.p.m. for IIId. For both IId and IIId, the methylene protons gave a typical AB spectrum ($J_{AB} = 7.1$ c/s) with further stereospecific long-range couplings to the methine proton. Irradiation of α-methoxyacetophenone (Ie) gave 3-phenyl-3-oxetanol (10.4%) in agreement with the results of Yates.[3]

The observed trans:cis ratios for each of the three cases studied (Ia, 1.8:1; Ib, 1.25:1; Id, 3.6:1) indicate a definite stereoselectivity in this cyclization reaction. The changes in ratios probably reflect a combination of structural effects on diradical stability[1,4] and minimization of transition state non-bonding interactions. The relative total yields of cyclized products in the series Ia-e indicate diradical stability to be an important factor.

In an attempted extension of the cyclization procedure to the formation of thietanols, If was irradiated; no evidence for the formation of a 3-thietanol was obtained. Irradiation of the sulfone $C_6H_5COCH(C_6H_5)SO_2CH_2C_6H_5$ led to extensive cleavage and the isolation of bidesyl (32%), bibenzyl (3%) and a wide melting amorphous solid. Attempted photocyclization of benzoylacetone led to a 93.5% recovery of starting material.

All of the compounds reported in this study gave satisfactory elemental analyses and the infrared and n.m.r. spectra (δ, J, and integrated intensities) were in complete accord with the postulated structures. The stereochemical assignments were also supported by the elution characteristics of the isomers.

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