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# RING-CONTRACTION REACTIONS OF METHYL BENZ[d]-3,1-OXAZEPINE 5-CARBOXYLATES[1]

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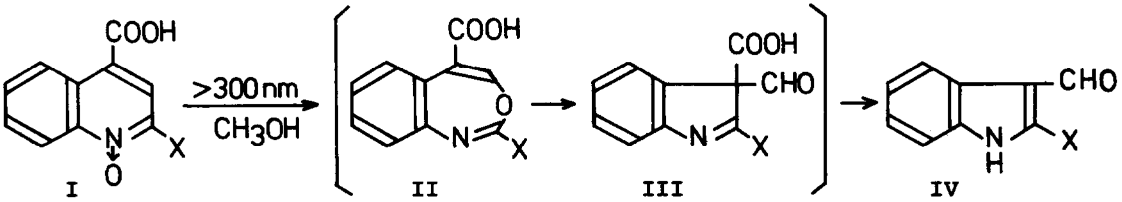
In the previous paper of this series,[2] we have reported that irradiation of quinoline 1-oxides having a carboxylic acid function at the 4-position (I) resulted in the formation of indole 3-carboxaldehydes (IV) in appreciable amounts and proposed the mechanism including initial formation of benz[d]-3,1-oxazepines (II), subsequent ring-contraction to III and decarbonylation. However, since an actual isolation of II or III was not accomplished in these experiments, its detailed mechanism has remained to be clarified.

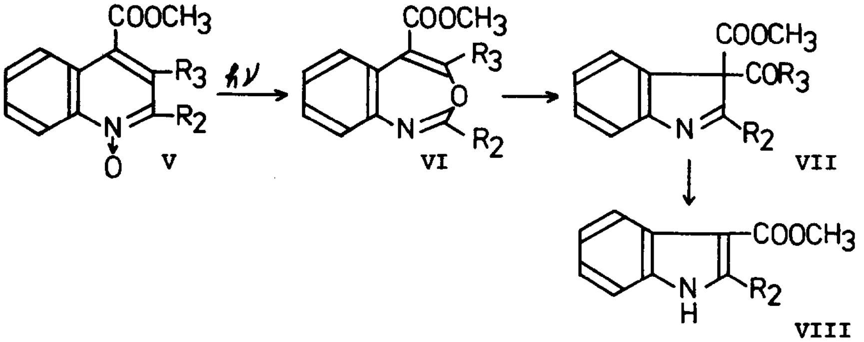


In order to verify the mechanism of these transformations (I→IV) and also to enlarge the scope of this ring-contraction reaction, we have irradiated three 1-oxides of methyl quinoline 4-carboxylates (Va-Vc) in an aprotic solvent.

In a typical experiment, 2 g of Va was irradiated by 400W-high pressure mercury lamp (Toshiba 400P) with a Pyrex filter in 1 l of acetone.[3] After irradiation for 5 hr, the reaction mixture was evaporated under a reduced pressure and the residue was chromatographed over a silica gel affording methyl 2-phenylindole 3-carboxylate[4] (VIIIa) [mp 150-151°] and methyl 2-phenylquinoline 4-carboxylate (IXa) in the respective yields of 82 and 9%. The structure of the former was identified by the acceptable spectroscopic data[5] [ $\delta$: 3.75 (3H, s), 8.16 (1H, m)] as well as its conversion to 2-phenylindole[6] by acid hydrolysis.

If in the above experiment, the irradiation was terminated by 20 min, an appreciable amount (ca. 80% based on the consumed Va) of the oxazepine (VIa) [oil, $\delta$: 3.82 (3H, s), 7.44 (1H, s); $\lambda_{max}$ nm: 255 (4.43), 313.5 (3.82); $\nu_{max}^{CHCl_3}$ cm$^{-1}$: 1720] was obtained, together with small amounts of VIIIa and IXa and the recovered 1-oxide (ca. 40%). While VIa was stable in acetone or acetonitrile in a dark (refluxing for 24 hr in these solvents caused no change of VIa), irradiation of VIa under an identical condition resulted in an almost quantitative formation of VIIIa. It should be noted that the conversion of VIa to VIIIa could also be effected in refluxed methanol in a dark (10 hr).

In a similar manner,[7] we also obtained methyl 2-methylindole 3-carboxylate[8] (VIIIb) [mp 160-162°, $\delta$: 2.73 (3H, s), 3.95 (3H, s), 8.10 (1H, m)] in 68% yield as the major product by irradiation of Vb using acetone or acetonitrile as a solvent. Though as yet, we could not succeed in the isolation of the 3H-indole species (VIIa or VIIb) in these experiments, the mechanism shown below is proposed as the most reasonable.



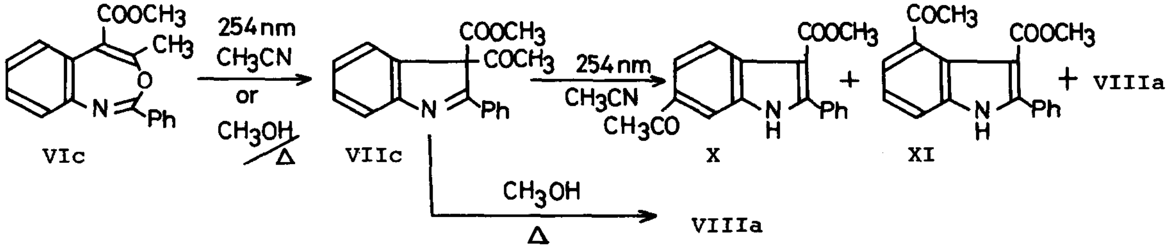
|   | $R_2$ | $R_3$ |
|---|---|---|
| a | phenyl | H |
| b | $CH_3$ | H |
| c | phenyl | $CH_3$ |

The failure in the isolation of the 3H-indole species (VII) in the above irradiation experiments seems to be reasonably explained by analogy from the fact that conformationally rigid 'out-of plane' analogs of $\alpha$-aryl aldehyde[9] (e.g., 3-formyl-3-methylindoline) or the related $\beta,\gamma$-unsaturated aldehydes[10] suffer photodecarbonylation with high efficiency ($\phi$ =ca. 0.5). Also, a facile decarbonylation of 3H-indole species in a protic medium has ample precedent[11] and this accounts for the failure in isolation of VIIa in the thermal conversion of VIa to VIIIa performed in hot methanol.

Intermediacy of such 3H-indole species in these ring-contraction reactions was finally demonstrated by an actual isolation of methyl 3-acetyl-2-phenyl-3H-indole 3-carboxylate[12] (VIIc) [mp 88-90°, δ: 1.72 (3H, s), 3.68 (3H, s); $\lambda_{max}$ nm: 251 (4.16), 318 (4.20), $\nu_{max}$ $cm^{-1}$: 1735, 1705, 1650 (sh.)] from VIc [mp 81-82°, δ: 2.33 (3H, s), 3.80 (3H, s), $\lambda_{max}$ nm: 251 (4.52), 258, sh. (4.50), 308 (3.94), $\nu_{max}$ $cm^{-1}$: 1715, 1645]. As expected from a β-diketone-like structure of VIIc, this indolenine afforded VIIIa by heating in methanol (100° in a sealed tube, 4 hr) or in methanol at room temperature in presence of HCl or KOH.

This oxazepine (VIc) was quite stable for irradiation by >300 nm rays and thus obtained in 89% yield from Vc by irradiation in an aprotic solvent. Heating of VIc in methanol in a sealed tube for 2 hr at 100° afforded, after silica gel chromatography, two ring contraction products (VIIIa and VIIc) in the respective yields of 21 and 23%, together with the recovered material (43%). The longer heating under these conditions resulted in an almost quantitative formation of VIIIa with the consumption of both VIc and VIIc. This experiment indicates clearly that the thermal conversion of VIc to VIIIa occurs through VIIc.

Irradiation of VIc in acetonitrile by the same light source without filter afforded, added to VIIIa (39%), two acetyl derivatives (X and XI) in the respective yields of 14 and 12%. The shorter irradiation gave rise to the indolenine (VIIc) and the starting oxazepine (VIc), together with the above three indoles. Under an identical irradiation condition, these three indoles (VIIIa, X and XI) were also obtained from VIIc in an almost same ratio as above (41, 15 and 14%), it is clear that the conversion of VIc to VIIc has also been effected photochemically by 254 nm rays.[13] The structures of these two acetyl derivatives (X and XI) were assigned tentatively as 6-acetyl- and 4-acetyl-2-phenyl-3-carbomethoxyindoles based on the nmr spectra: X [mp 194.5-195.5°; δ: 2.64 (3H, s), 3.84 (3H, s), 7.82 ($H_5$, dd, J=8.6 and 1.6 Hz), 8.06 ($H_7$, dd, J=1.6 and 0.8), 8.18 ($H_4$, dd, J=8.6 and 0.8), 9.22 (N<u>H</u>, b.s)] and XI [mp 195.5-196.5°; δ: 2.62 (3H, s), 3.77



(3H, s), 7.15-7.70 (8H, m), 8.84 (NH, b.s)]. The nmr spectrum of XI lacks signals at around $\delta$ 8.1 characteristic of H-4 in an alkyl indole 3-carboxylate.[14]

Further work on the syntheses of such 3H-indole derivatives (e.g., VIIc) from 2,3,4-trisubstituted quinoline 1-oxides is currently being persued.

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