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THE PHOTOCHEMICAL REACTION OF 3,5-DISUBSTITUTED ISOXAZOLES

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3,5-Dimethyl-, 3-methyl-5-phenyl-, and 5-methyl-3-phenylisoxazole suffered a photo-induced solvent attack, as well as the usual photo-transposition isomerization, to give open-chain compounds as the main product. No solvent participation was, however, observed with 3,5-diphenylisoxazole.

The photo-induced rearrangement of five-membered heterocyclic aromatic compounds has been described for a variety of systems. A general rearrangement process involving the interchange of ring atoms has been accounted for by (1) ring contraction-expansion,1) (2) valence isomerization,2) (3) Wynberg mechanism,3) and (4) a mechanism which includes these within a single framework.4) The solvent employed in most of these studies is ether, although other solvent systems including alcohol are also reported. It is notable that alcoholic solvent has not been trapped in products in the photo-reaction of isoxazoles where highly reactive azirine intermediate is involved.1a) Recently some methanol adducts were isolated as transients in the photo-isomerization involving transfer of a substituent from 2-position to 3-position in the 2-cyanofuran and 2-cyanopyrrole systems.5)

We observed an anomalous phenomenon that a heterocyclic aromatic ring system was irreversibly cleaved by methanol on irradiation in cases of 1a, 1b, and 1c.

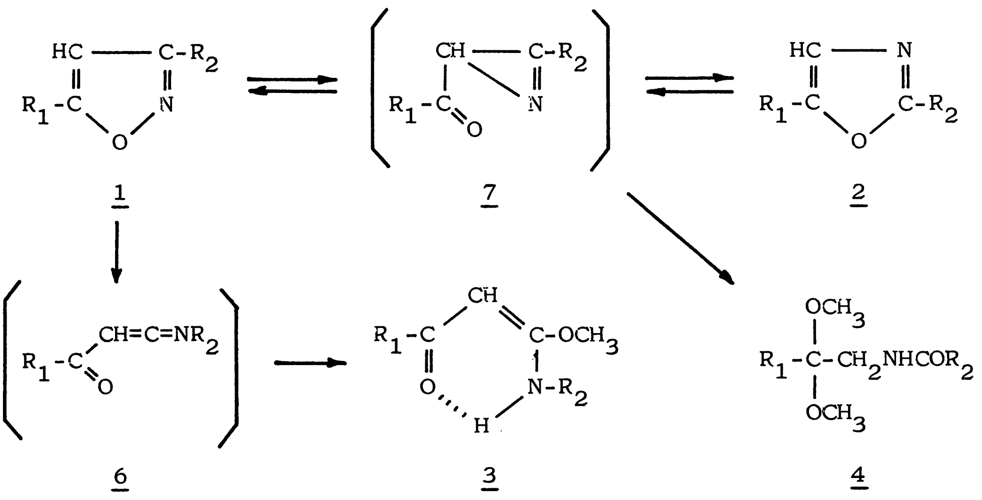
A methanol solution of 1a (1.3 g/150 ml) was irradiated with 100W high pressure mercury lamp in quartz vessel while monitoring the reaction by gas chromatographic analysis. The result is represented in Fig. 1. The identification of two new compounds (3a and 4a) was effected by referring to the spectroscopic and elemental analyses data obtained with pure samples collected by preparative gas chromatography.

3a: MS: m/e 129 (M^+), and 114 ($M^+ - CH_3$); IR (CCl_4): 3400-3200 1633, and 1125 cm^{-1}; NMR (CCl_4): δ 1.95 (3H, s, CH_3-CO), 2.90 (3H, d, J = 5 Hz, CH_3-N), 3.82 (3H, s, CH_3-O), 4.70 (1H, s, =CH-), and 10.4 (1H, bs, NH); UV (CH_3OH): λ_{max} 286 nm (ε 20300).6)

4a: MS: m/e 129 ($M^+ - CH_3OH$), 87 ($M^+ - OCH_3 - COCH_3$), and 72 ($M^+ - OCH_3 - NHCOCH_3$); IR (CCl_4): 3300, 1665, 1180, and 1050 cm^{-1}; NMR (CCl_4): δ 1.18 (3H, s, CH_3-C), 2.00 (3H, s, CH_3-CO), 3.18 (6H, s, CH_3-O), 3.30 (2H, d, J = 6 Hz, CH_3-N), and 7.50 (1H, t, J = 6 Hz, NH); UV (CH_3OH): end absorption at $>$ 210 nm.

It was found that both 3a and 4a were photolabile: when methanol solution of each compound was irradiated for 22 hr, 3a was destructed completely and 4a reduced to one-half its original amount. The product, however, was not identified in either case.

The absence of induction period for the formation of 3a would imply that 1a cleaves to ketoketenimine (6a) which immediately adds methanol to afford 3a.$^{6)}$ The intervention of 6a is inferred from the observation in triphenylisoxazole photochemistry.$^{1d)}$ In search of the possibility of oxazole 2a being an intermediate for the formation of 4a, the photo-reaction of 2a was carried out. 3a and 4a were actually obtained, but the rates of formation were much slower than those expected from the result shown in Fig. 1. This observation induced us to assume that 2a converted slowly to an intermediate from which 3a and 4a were derived. An azirine (7a) would be the most probable candidate for this intermediate, in view of the results reported so far with these systems, and reaction paths as shown in Scheme 1 are proposed for the photochemistry of 1a. The presence of induction periods for the formations of 2a and 4a is also consistent with the scheme.



a: $R_1 = R_2 = CH_3$; b: $R_1 = Ph$, $R_2 = CH_3$

c: $R_1 = CH_3$, $R_2 = Ph$; d: $R_1 = R_2 = Ph$

Scheme 1

The irradiation of 1a in ethanol afforded an ethoxy derivative corresponding to 3a, although diethoxy amide corresponding to 4a could not be isolated in this case.

When ether was used as solvent, the photo-reaction of 1a was extremely slow and accompanied by the polymer formation. Gas chromatographic analysis of the volatile material indicated that only few per cent of a photo-product was present in the mixture, the rest being the starting material. The identifi-

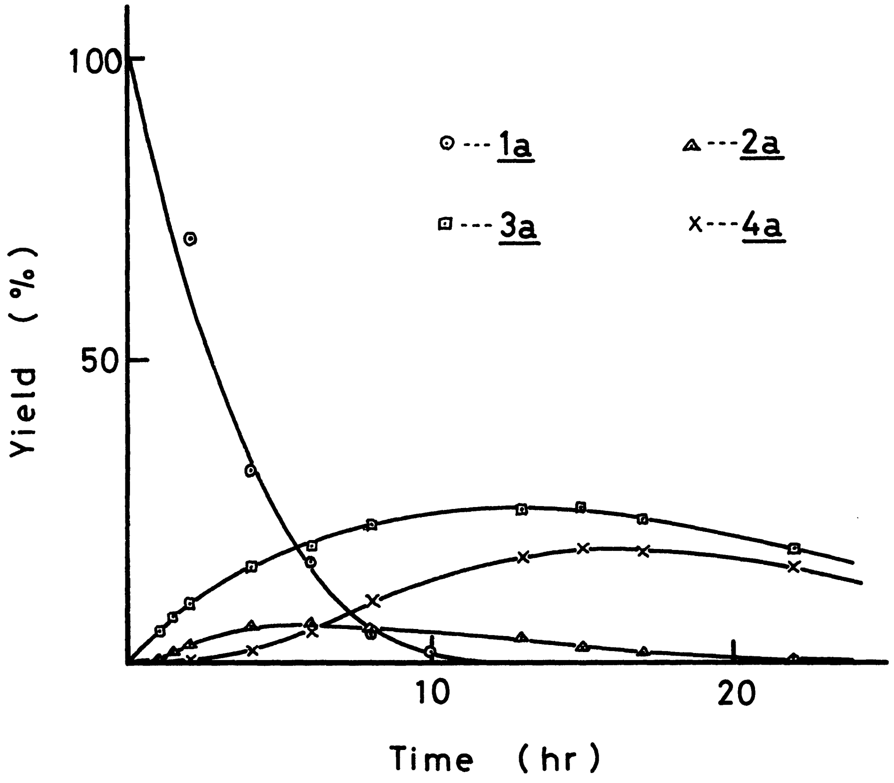


Fig. 1. Yields of products as a function of time in the photolysis of 3,5-dimethylisoxazole

cation of the product has not been established as yet. The recovery of the starting material after 15 hr irradiation amounted to about 50%.

Similar solvent-participated products (3b, 3c, and 4c) were obtained as well as the usual transpositional products (2b and 2c) in the photo-reaction of 1b and 1c, although the final assignment of products from 1c has not definitely been accomplished.7)

The solvent participation as described above was not observed with 3,5-diphenylisoxazole (1d). The tracing of the reaction by UV spectroscopic and TLC analyses indicated that 1d behaved in a similar way both in methanol and in ether, although the rate was greater in methanol. No signal assignable to methoxyl group was observed in the NMR spectrum of the crude photo-reaction mixture of 1d in methanol. In accord with the result by Singh and Ullman,1a) 2,5-diphenyloxazole was the product.

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7) From 1b: Two compounds (2b and 3b) were isolated on an alumina-column chromatography. Oxazole 2b was identical with the authentic sample[8] (mp, mixed mp, NMR and IR spectra). IR and UV spectra, elemental analysis, and mp of 3b were identical with the reported data.[6] NMR spectrum was also consistent with the structure 3b: δ 2.83 (3H, d, J = 5 Hz, CH_3-N), 3.83 (3H, s, CH_3-O), 5.18 (1H, s, =CH-), 7.1-7.7 (5H, m, Ph), and 10.7 (1H, bs, NH). From 1c: The starting material 1c (mp 42°C) was found to contain 30% of the isomeric 1b.[1b] The material could not be readily freed from the isomeric impurity and was used as such. Four fractions (2c, 3c, 4c, and benzamidoacetone) were obtained as photo-reaction products in not completely pure state on a column-chromatographic separation of the crude reaction mixture and the structures were speculated from NMR and IR spectroscopic data.

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