The Photochemistry of 2-Pyridylacetate Methides and their Pyrimidine Analogues

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Photolysis of 1-benzyl-2-imino-1,2-dihydropyrimidine (IIIa) was found to afford 2-benzylaminopyrimidine (IVa), a Dimroth rearrangement product, but the 1-methyl analogue (IIIb) does not give 2-methylaminopyrimidine (IVb). A similar photochemical 1,3-alkyl migration was observed for 1-alkyl-2-ethoxycarbonylmethylene-1,2-dihydropyridines (VI) giving ethyl α-alkyl-2-pyridylacetates (VII). For example, the 1-benzyl compound (VIa) gives (VIIa) readily, but the 1-methyl counterpart (VIc) yields (VIIc) inefficiently. A mechanism involving homolytic cleavage and recombination is postulated for the rearrangement.

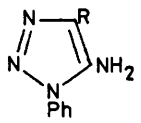
DIMROTH discovered the rearrangement of 5-amino-1-phenyl-1,2,3-triazoles (I) to 5-anilino-1,2,3-triazoles (II) in boiling pyridine or sodium ethoxide.[1] The rearrangement was extended to 1-alkyl-2-(or 4-)imino-1,2-dihydropyrimidines,[2-4] which react by pyrimidine ring opening followed by recyclisation through the equilibrium (Va) ⇌ (Vb).

In our work,[5] photolysis of the triazole (I; R = H) in ethanol was found to give reversibly the isomer (II; R = H). We have extended this by attempting the photorearrangement of 2-iminopyrimidines (III) and (IV) [equation (2)] and 1-alkyl-2-ethoxycarbonylmethylene-1,2-dihydropyridines (VI) and (VII) [equation (3)].

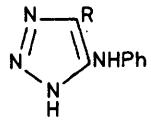
Photolysis of 1-*Alkyl*-2-*imino*-1,2-*dihydropyrimidine.*

[1] O. Dimroth, *Annalen*, 1909, **364**, 183.
[2] (*a*) D. J. Brown and J. S. Harper, *J. Chem. Soc.*, 1963, 1276; (*b*) D. D. Perrin, *ibid.*, p. 1284.
[3] A. Albert (*a*) *J. Chem. Soc.* (*C*), 1970, 230; (*b*) *J.C.S. Perkin I*, 1973, 2659.
[4] (*a*) D. J. Brown and B. T. England, *J. Chem. Soc.* (*C*), 1971, 2507; (*b*) D. J. Brown and K. Ienaga, *J.C.S. Perkin I*, 1974, 372.
[5] Y. Ogata, K. Takagi, and E. Hayashi, to be published.

—Irradiation of 1-benzyl-2-imino-1,2-dihydropyrimidine (IIIa) in diethyl ether with a high pressure mercury lamp gave 2-benzylaminopyrimidine (IVa) (10%),

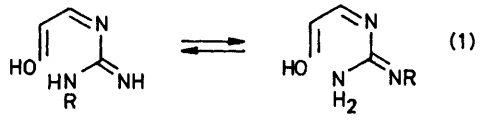


(I)



(II)

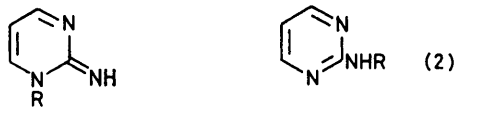
bibenzyl (3%), and an unknown product (decomp. 195—197°) (30 wt%). Photolysis of 2-imino-1-methyl-1,2-dihydropyrimidine (IIIb) gave no 2-methylaminopyrimidine (IVb), but a yellow unidentified solid (m.p. >280°).



(1)

(Va) (Vb)

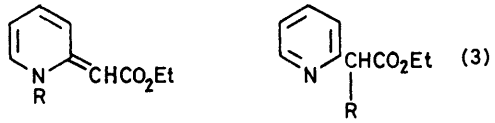
Photolysis of 1-*Alkyl*-2-*ethoxycarbonylmethylene*-1,2-*dihydropyridine*.—Irradiation of 1-benzyl-2-ethoxycarbonylmethylene-1,2-dihydropyridine (VIa) in ethyl



(2)

(III) (IV)

a; R = CH_2Ph
b; R = Me



(3)

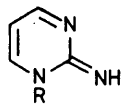
(VI) (VII)

a; R = CH_2Ph
b; R = $CH_2C_6H_4Me$-*p*
c; R = Me
d; R = H

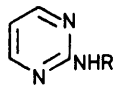
ether with Pyrex-filtered light gave ethyl 1-(2-pyridyl)-2-phenylpropionate (VIIa) (29%), ethyl 2-pyridylacetate (11%), and bibenzyl (7%). The propionate (VIIa) was hydrolysed and then decarboxylated to 1-(2-pyridyl)-2-phenylethane (VIIIa) by refluxing in 1N-HCl.[6]

Photolysis of the 1-*p*-methylbenzyl compound (VIb) gave ethyl 1-(2-pyridyl)-2-(*p*-tolyl)propionate (VIIb) (15%), but photolysis of the 1-methyl derivative (VIc) afforded only a trace of the corresponding propionate (VIIc).[7]

Although apparent 1,3-alkyl migration occurred in both the photochemical and the thermal (Dimroth) reaction, the mechanism of the former may be different from that of the latter in regard to the effect of a migrating *N*-alkyl substituent on the photoreactivity.



(III)



(IV)

Thus, the *N*-methyl compounds (IIIb) and (VIc) disfavour alkyl migration in photolysis, whereas in the thermal Dimroth reaction there is smooth migration to give the *N*-benzyl derivatives (IIIa) and (VIa and b).

It was noted that *N*-alkylanthranilates (IXa—c) were not formed from photolysis of (VIa—c), although it is known that irradiation of ethyl 2-pyridylacetate (Xd) gave ethyl anthranilate (IXd),[8] and also that a tautomer of (X), 2-ethoxycarbonylmethylene-1,2-dihydropyridine (VId) exists in equilibrium with (X) in the dark.[9]

(4)

(Xd) (IXd)

Hence, the intermediacy of (VId) in the photoisomerisation (Xd) ⟶ (IXd) is less probable in view of the low concentration of (VId) in the equilibrium (VId) ⇌ (Xd).

Generally, 2-methylene-1,2-dihydropyridines (VI) possess absorption maxima at 310 (ε *ca.* 20 000) and 390 nm (ε *ca.* 7 000). The quantum yields (ϕ) for disappearance of the methides were measured by two light sources, one with a maximum at *ca.* 360 nm close to the charge transfer band of (VI) (*ca.* 390 nm), and the other at *ca.* 310 nm. The ϕ values were 0.001 2 at 360, and 0.008 9 at 310 for (VIa) and 0.011 at 310 nm for (VIb).

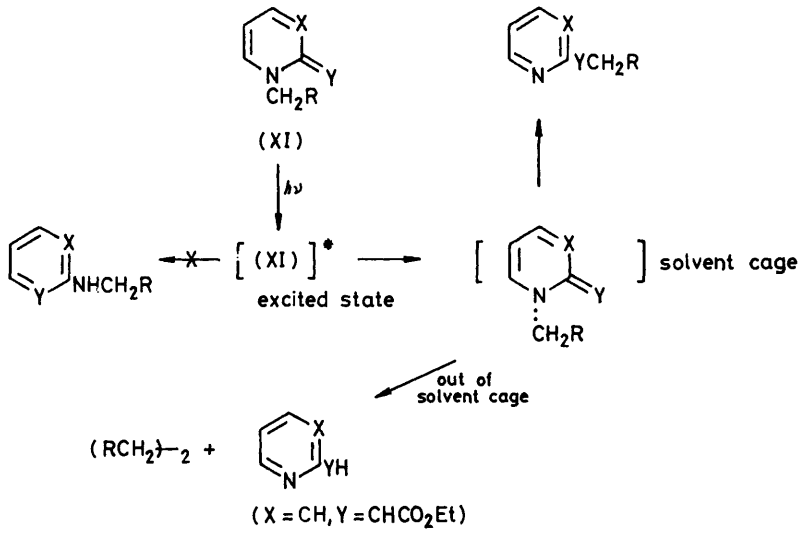
The 1,3-alkyl migration (VI) ⟶ (VII) with ϕ 10^{-2}—10^{-3} is much less efficient than the photoisomerisation (Xd) ⟶ (IXd) with ϕ 0.1—0.2.[8] Therefore, it is unlikely that photoisomerisation of (VI) to (IX) is suppressed by the process (VI) ⟶ (VII).

That the 1,3-alkyl migrations (III) ⟶ (IV) and (VI) ⟶ (VII) may proceed by *N*-alkyl bond homolysis followed by recombination of the resulting alkyl radicals is indicated by the formation of bibenzyl, a coupling product of the radicals. Photolysis of a *p*-xylene solution of (VIa) gave no (VIIb) (g.l.c.), implying that the reaction proceeds intramolecularly or that the resulting free radical cannot abstract a hydrogen atom from the solvent, *p*-xylene, to form *p*-methylbenzyl radical. Intramolecularity was confirmed by the addition of thiophenol, a radical scavenger, to an ethereal solution of (VIa), where no influence was observed on the yield of (VIIa), while bibenzyl was not detectable.

[6] F. W. Bergstrom, T. R. Norton, and R. A. Seibert, *J. Org. Chem.*, 1945, **10**, 452.
[7] J. Izdebski, *Roczniki Chem.*, 1965, **39**, 1625 (*Chem. Abs.*, 1966, **64**, 17,536b).
[8] (*a*) Y. Ogata and K. Takagi, *J. Amer. Chem. Soc.*, 1974, **96**, 5933; (*b*) K. Takagi and Y. Ogata, *J.C.S. Perkin II*, in the press.
[9] S.-O. Chua, M. J. Cook, and A. R. Katritzky, *J.C.S. Perkin II*, 1973, 2111.

Hence, the 1,3-alkyl shift proceeds either intramolecularly or in a solvent cage as shown in the Scheme. We reported previously the analogous 1,3-shift of *N*-benzylaniline to give *o*- and *p*-benzylanilines on photolysis;[10] in this case there is no formation of mixed products from two *N*-alkylanilines suggesting an intramolecular scheme.

Finally, the photoreaction (VIa) ⟶ (VIIa) was not quenched by piperylene of concentrations up to 0.007 5M in the photolysis of (VIa) (4.0×10^{-4}M), which implies the reaction goes through an excited singlet state. The



SCHEME

absence of an oxygen effect also indicates that the singlet state is responsible for the reaction. Additional evidence was provided by an experiment using a reagent containing a heavy atom, Bu^nBr (two moles per mole of substate); addition of the bromide does not increase the yield of product. Nevertheless there remains the possibility that the reaction proceeds through a short-lived triplet state.

EXPERIMENTAL

U.v. spectra were recorded on a Hitachi spectrophotometer (model 124). G.l.c. analysis was carried out with a Yanagimoto gas chromatograph (model GCG-550F) with flame ionisation detector employing either a 1.7 m × 2.5 mm column packed with PEG 20M on Chamelite CS or a 1.0 m × 2.5 mm column with SE-30 on Chromosorb W. Products were identified on g.l.c. by these two columns. N.m.r. spectra were obtained with a JEOL C60 HL instrument. Irradiation were carried out using a Halos 300 W high pressure mercury lamp.

Materials.—1-Alkyl-2-imino-1,2-dihydropyrimidine (III) was prepared by the reaction of 2-aminopyrimidine with the corresponding alkyl halide followed by addition of KOH and recrystallised from ethanol; (IIIa) had m.p. 110—111°, picrate m.p. 164—165° (lit.,[11] 165°), (IIIb) m.p. 99—101° (lit.,[12] 102—104°). The corresponding 2-alkylaminopyrimidines were synthesised by the literature procedure; [12] (IVa) had m.p. 84—84.5°, (IVb) m.p. 59—60°.

1-Alkyl-2-ethoxycarbonylmethylene-1,2-dihydropyridines (VI) were prepared by heating ethyl 2-pyridylacetate with an equimolar quantity of alkyl halide followed by treatment with aqueous NaOH giving pale yellow needles; (VIa) had m.p. 95—96° (lit.,[13] 94—95°), $\lambda_{max.}$ (EtOH) 308 (ε *ca.* 17 200), 316 (*ca.* 19 700), and 390 nm (*ca.* 7 030); (VIb) m.p. 87—88°, $\lambda_{max.}$ (EtOH) 306s (ε *ca.* 16 700), 316 (*ca.* 19 000), and 390 nm (*ca.* 6 430); (VIc) m.p. 50—52° (lit.,[14] 52—54°), $\lambda_{max.}$ (EtOH) 306s (ε *ca.* 16 590), 313 (*ca.* 19 150), and 384 nm (*ca.* 6 570).

Photolysis of 1-*Benzyl*-2-*imino*-1,2-*dihydropyrimidine* (IIIa).—The dihydropyrimidine (IIIa) (301 mg) in diethyl ether (200 ml) was irradiated for 16 h until the original yellow colour had almost disappeared. The mixture, after being condensed *in vacuo*, was chromatographed on silica with benzene as eluant to give crystals (10%), m.p. 80°, shown to be (IVa) by comparison of g.l.c. retention times with those of an authentic specimen; $\lambda_{max.}$ (MeOH) 238 and 307 nm, δ (CCl_4) 7.90 (2 H, d), 7.18 (5 H, s), 6.70 (1 H, m), 6.30 (1 H, t, NH), and 4.54 (2 H, d). Bibenzyl was also detected (3% by g.l.c.).

Photolysis of 1-*Benzyl*-2-*ethoxycarbonylmethylene*-1,2-*dihydropyridine* (VIa).—A solution of (VIa) (0.52 g) in diethyl ether (500 ml) was irradiated under nitrogen using Pyrex-filtered light. After 16 h, the yellow colour disappeared. Separation of the products was carried out on silica using benzene as eluant. First eluted was bibenzyl (13 mg, 7%), m.p. 51—52°. Second was a pale yellow oil, shown to be ethyl 2-pyridylacetate (37 mg, 11%) by comparison of its g.l.c. retention time with that of an authentic sample. Third was a pale yellow oil (148 mg, 28.6%), ethyl 1-(2-pyridyl)-2-phenylpropionate (VIIa), δ (CCl_4) 8.35 (1 H, d), 7.35 (1 H, dd), 7.0 (2 H, m), 6.98 (5 H, s), 4.05 (1 H, dd), 3.95 (2 H, q, *J* 7 Hz), 3.15 (2 H, dd), and 1.08 (3 H, t, *J* 7 Hz); $\lambda_{max.}$ (MeOH) 255, 260, and 266 nm; $\nu_{max.}$ 1 730,

[10] Y. Ogata and K. Takagi (*a*) *J. Org. Chem.*, 1970, **35**, 1642; (*b*) *Bull. Chem. Soc. Japan*, 1971, **44**, 2186.
[11] J. Goerdeler and W. Roth, *Chem. Ber.*, 1963, **96**, 534.
[12] D. J. Brown, E. Hoerger, and S. F. Mason, *J. Chem. Soc.*, 1955, 4035.
[13] T. Melton and D. G. Wibberly, *J. Chem. Soc.* (*C*), 1967, 983.
[14] R. A. Jones and A. R. Katritzky, *Austral. J. Chem.*, 1964, **17**, 455 (*Chem. Abs.*, 1964, **60**, 15,824e).

749, and 695 cm^{-1}. Structure (VIIa) was further confirmed as follows: (VIIa) was hydrolysed and then decarboxylated by refluxing in 1N-HCl for 3 h to yield 1-(2-pyridyl)-2-phenylethane (VIIIa) quantitatively; picrate, m.p. 125—126° (lit.,[6] 125.5—126°).

Photolysis of 2-*Ethoxycarbonylmethylene*-1-(p-*methylbenzyl*)-1,2-*dihydropyridine* (VIb).—A solution of (VIb) (170 mg) in diethyl ether (200 ml) was irradiated for 15 h. A photoproduct, ethyl 1-(2-pyridyl)-2-(*p*-tolyl)propionate (VIIb), was isolated by g.l.c. as a yellow oil (25.1 mg, 15%), δ (CCl_4) 8.62 (1 H, d), 7.65 (1 H, m), 7.20 (1 H, m), 7.05 (4 H, s), 4.07 (2 H, q), 3.15 (2 H, dd), 2.35 (3 H, s), and 1.12 (3 H, t); $\nu_{max.}$ 1 725, 805, and 780 cm^{-1}; $\lambda_{max.}$ (MeOH) 267s, 261, and 255 nm.

Photolysis of (VIa) *in the Presence of Thiophenol.*—A solution of (VIa) (1.8×10^{-4} mol) in diethyl ether (150 ml) in the presence of thiophenol (4.2×10^{-3} mol) was irradiated for 2 h. G.l.c. analysis shows formation of (VIIa) and inhibition of formation of bibenzyl.

Quantum Yields.—A solution (*ca.* 10^{-5}M) of the methide (VI) (5 ml) was degassed by several freeze–thaw cycles and sealed *in vacuo* in a quartz cubic cell. The cell was irradiated through either a Pyrex and Corning colour filter (7-54) (300—400 nm) or a Corning colour filter (7-51) which is transparent at *ca.* 360 ± 40 nm using a 300 W high pressure mercury lamp. The disappearance of the starting methides was monitored at their absorption maximum of *ca.* 310 nm. Actinometries were measured using a ferrioxalate actinometer.[15]

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[15] C. H. Hatchard and C. A. Parker, *Proc. Roy. Soc.*, 1956, *A*, **235**, 518.