

Photochemical Behaviour of Some Furo- and Pyrrolo-[3,2-*b*]pyridin-2-ones

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When 4-acetyl- or 4-methyl-5,6-dihydrofuro[3,2-*b*]pyridin-2(4*H*)-one or 4-acetyl-7-bromo-1,4,5,6-tetrahydro-pyrrolo[3,2-*b*]pyridin-2-one † is irradiated, dimeric products are obtained. Irradiation of 5,6-dihydrofuro[3,2-*b*]pyridin-2(4*H*)-one in benzene gives a dimer, whereas irradiation in methanol causes electrocyclic ring opening, giving 3-methoxymethylamino-hexa-2,4- and -2,5-dien-4-olides [(15)—(17)].

WE have reported^{1,2} that tetrahydro-4-oxoisoxazolo-[2,3-*a*]pyridinium bromide (1) and its oxime (2) can be converted by acetic anhydride into the *N*-acetylfuro- and -pyrrolo-pyridinones (3) and (4), hydrolysis of which yields the deacetylated derivatives (5) and (6). The preparation of the *N*-methyl derivative (7) from the amide (5) proved more difficult than initially expected; use of sodium hydride with methyl iodide or dimethyl sulphate gave the product (7) in very poor yield, possibly owing to the ability of the reactive anion (8) to yield polymeric products. A better yield was obtained when lithium bis(trimethylsilyl)amide was used as the base and dimethyl sulphate as the methylating agent, possibly because of the covalent nature of the metal-nitrogen bond which helped to stabilise the lithium derivative (9).

The two *N*-acetyl derivatives (3) and (4) have only one u.v. absorption band, whereas compounds (5)—(7),

† Named as the 5,6-dihydro-4*H*-pyrrolo[3,2-*b*]pyridin-2(1*H*)-one in ref. 1.

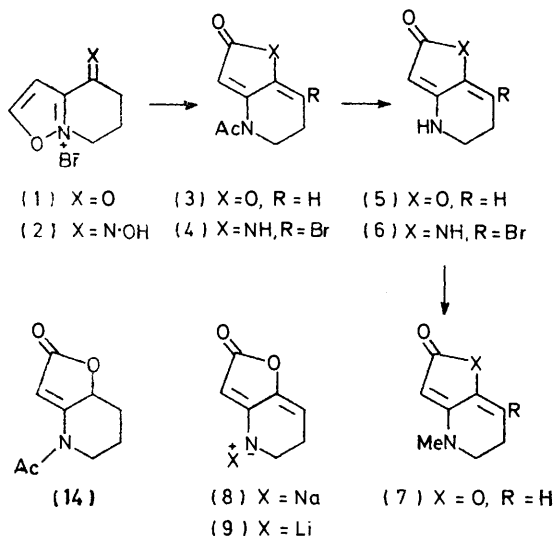
in which the nitrogen atom is not involved in an amide bond, show two bands, one of which has a maximum at *ca.* 300 nm. The use of a Pyrex filter removes all the radiation at wavelengths below 285 nm and 94% of that below 300 nm. Thus in photodimerisation reactions of the *N*-acetyl compounds only the tail of the absorption was utilised.

Irradiation of the derivatives (3), (4), and (7) (in methanol) and (5) (in benzene) resulted in [2 + 2] cycloadditions to give the dimers (10)—(13), respectively. Four possible isomers could be generated in each case by this dimerisation. Only two of these are shown; the other two, where the R² groups are *cis* to each other, do not appear to be likely because of considerable steric interference between the two halves of the molecule in one of the two possible conformations of the six-membered ring. The 100 MHz spectrum of the *N*-

¹ G. Jones and J. R. Phipps, *J.C.S. Perkin I*, 1974, 158.

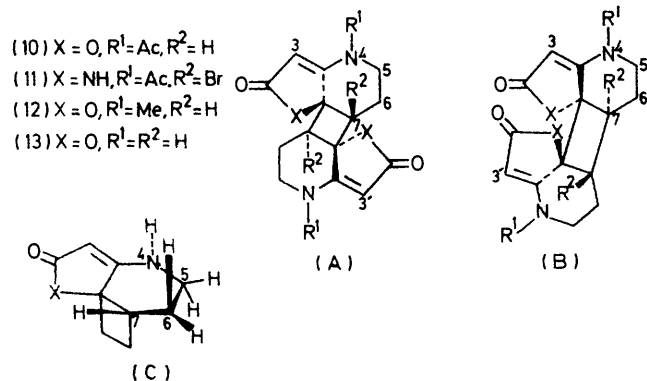
² R. H. Good, G. Jones, and J. R. Phipps, *J.C.S. Perkin I*, 1972, 2241.

methyl derivative (12) shows that there is sufficient symmetry in the molecule to ensure that the signal due to the alkene protons H-3 and H-3' and that due to the *N*-methyl groups both appear as singlets. In this case



the signal due to H-7 (H-7') is a triplet with a very small coupling constant; hence the C(7)-H bond bisects the angle made by the two C(6)-H bonds. Similarly the equatorial C(5)-H bond also bisects this angle. These observations exclude the second possible conformation of the *cis*-fused system; in this (relatively) unhindered conformation H-7 (H-7') is quasi-axial, and the C(7)-H bond cannot bisect the angle mentioned. Models do not enable us to distinguish between formulae (A) (head-to-tail) and (B) (head-to-head), although it is clear that the six-membered rings must have a skew boat conformation, as shown in partial formula (C).

The dimer (10) reverts to the starting material (3) on heating; as this is thermally forbidden by a concerted mechanism it is possible that it occurs by either an ionic or a free-radical process. Alkaline hydrolysis of dimer (10) gave the dimer (13) produced by irradiation of compound (5) in benzene.



There is a close resemblance between the u.v. spectra of these dimeric products and that of the hydrogenated

N-acetylfuro-pyridin-2-one (14). Also there is only one absorption maximum even when R¹=H. It seems likely that the longer wavelength absorption involves the double bond in the six-membered ring as well as the nitrogen lone pair and is responsible for the different photoreaction shown by the pyridin-2-one (5) now described.

Irradiation of the furo-pyridin-2-one (5) in methanol gave five products, one of which was the dimer (13). The amount of dimer produced could be reduced to such an extent that it could not be seen on thin-layer plates, by the use of very dilute solutions. The four major products (15)–(18) were those derived from opening of the six-membered ring. The *cis*- and *trans*-isomers (15) and (16) could be distinguished and the structures assigned by a study of the n.m.r. spectra in the alkene region. Compound (15) showed a doublet (*J* 1 Hz) at δ 5.06, due to the proton at C-2, showing long-range coupling to the alkene C-5 proton at δ 5.63, which in turn gave rise to a pair of quartets (*J* 8 and 1 Hz). In compound (16) and also in the amine (18) the equivalent protons at δ 4.98 and 4.87, respectively, gave sharp singlets. Accordingly these two latter compounds are assigned the *cis,trans*-arrangement of double bonds.

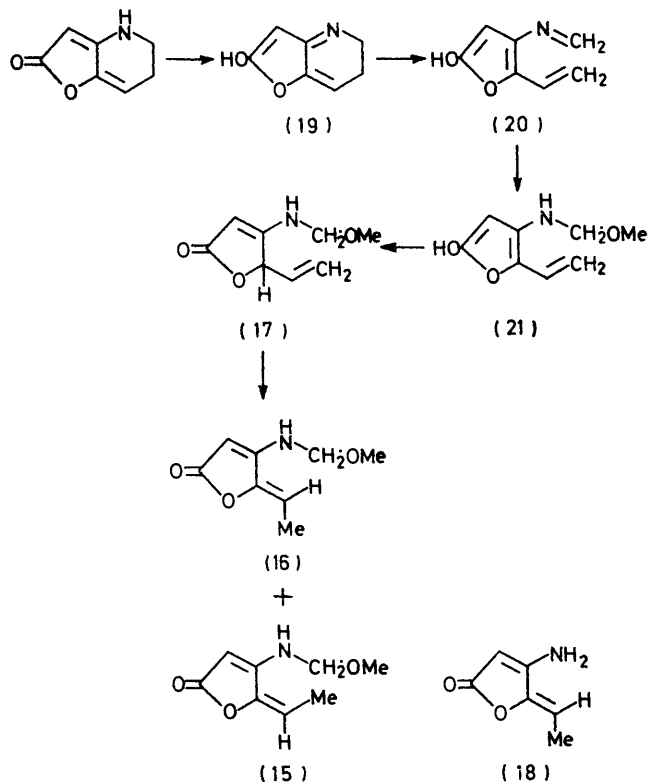
The yield of the furanone (17) was very variable, depending on the method of work-up. When a grade IV alumina column was used none of this product was isolated; the furanone (17) could only be obtained by using preparative layer chromatography with carefully purified solvents. The furanone (17) appears to be an intermediate in the production of the more stable products (15) and (16). Changes which were observed in the u.v. spectrum and on thin-layer chromatograms after addition of base to a solution of compound (17) indicated that the non-conjugated double bond very easily isomerises to the conjugated form as in (15) or (16).

Compound (17) is probably not a photochemical intermediate since it absorbs at 254 nm; irradiation of a solution of the *trans*-isomer (16) in methanol was performed to see whether compound (17) could be generated. T.l.c. after irradiation for 6 h showed the presence of the *cis*- (15) and *trans*- (16) isomers but nothing corresponding to the isomer (17).

These monocyclic products may be considered as arising from the azacyclohexadiene system (19), which could open to give the azahexatriene system (20). This reactive species would react with methanol to give the amino-ether (21), which could rearrange to the isolated intermediate (17), which in turn could rearrange to the two isomeric products (15) and (16). The minor compound (18) may be produced by hydrolysis; a similar hydrolysis product has been obtained on photolysis of some 2,3-dihydropyrazines.³ The hydrogen shift from nitrogen must be important in the mechanism since photolysis of the *N*-methyl derivative (7) does not lead to monocyclic products.

³ P. Beak and J. S. Miesel, *J. Amer. Chem. Soc.*, 1967, **89**, 2375.

Electrocyclic reactions of nitrogen-containing systems are not as well documented as those of the isoelectronic



hydrocarbon counterparts, although it has been reported that 2,3-disubstituted dihydropyridazines undergo ready photoisomerisation to substituted imidazoles *via* an intermediate enedi-imine.³⁻⁵

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. Thick-layer chromatography was carried out on 40 cm plates with Merck silica gel PF₂₅₄; alumina chromatography was performed on Woelm alumina (activity as indicated).

Photolytic work was carried out initially under nitrogen with a Hanovia photochemical reactor with a Pyrex filter. The work done on larger volumes (*i.e.* 300 cm³) was performed in a Rayonet RS preparative photochemical reactor with lamps which transmit radiation mainly at 300 nm.

4-Methyl-5,6-dihydrofuro[3,2-*b*]pyridin-2(4H)-one (7).—To a stirred solution of 5,6-dihydrofuro[3,2-*b*]pyridin-2(4H)-one (5) (0.5 g) in dry benzene (30 cm³) was added lithium bis(trimethylsilyl)amide (0.5 g). The solution was then heated under reflux until t.l.c. indicated complete salt formation. An excess of dimethyl sulphate was then added, and boiling was maintained (0.5 g), generation of the methylated product being followed by t.l.c. The solution was allowed to cool to room temperature, water (10 cm³) was added, and the organic layer was separated. The aqueous layer was extracted thoroughly with chloroform and the organic layers were combined, dried (MgSO₄), and evaporated. The product was the *N*-methyl derivative

⁴ A. Padwa and E. Glazer, *J. Amer. Chem. Soc.*, 1972, **94**, 7788.

(7) (0.4 g, 73%), m.p. 42–45° (from benzene) (Found: C, 63.2; H, 6.35; N, 9.1. C₈H₈N₂O requires C, 63.55; H, 6.05; N, 9.25%); λ_{max.} (95% EtOH) 261 and 316 nm (log ε 4.11 and 3.92); ν_{max.} (CHCl₃) 1758 and 1620 cm⁻¹; δ (CDCl₃) 2.75–2.30 (2H, m), 2.9 (3H, s), 3.25 (2H, t), 4.62 (1H, d, *J* 1 Hz), and 5.6 (1H, d, *J* 4 and 1 Hz); *m/e* 151 (*M*⁺).

Irradiation of 4-Acetyl-5,6-dihydrofuro[3,2-*b*]pyridin-2(4H)-one (3).—Compound (3) (0.5 g) dissolved in dry methanol (35 cm³) was irradiated through a Pyrex filter (3 h). The experiment was followed by t.l.c. with chloroform as eluant. The product crystallised out on the sides of the reaction vessel; filtration and recrystallisation from methanol gave the dimer (10), m.p. 200–201° (0.38 g, 75%) (Found: C, 60.3; H, 5.3; N, 7.8. Calc. for C₁₈H₁₈N₂O₆: C, 60.4; H, 5.05; N, 7.8%); λ_{max.} (95% EtOH) 276 nm (log ε 4.37); ν_{max.} (Nujol) 1765, 1685, and 1618 cm⁻¹; δ (CF₃·CO₂H) 2.3 (4H, m), 2.6 (6H, s), 3.12 (2H, m), 4.35 (4H, m), and 6.5 (2H, s); *m/e* 358 (*M*⁺).

On heating the dimer (10) under vacuum to 250 °C the monomer (3) sublimed out quantitatively.

Irradiation of 5,6-Dihydrofuro[3,2-*b*]pyridin-2(4H)-one (5).—Irradiation of compound (5) (0.5 g) in benzene (40 cm³) (4 h) and evaporation gave the dimer (13), m.p. >300° (0.1 g, 20%) (Found: C, 60.9; H, 5.65; N, 9.9. Calc. for C₁₄H₁₄N₂O₄: C, 61.3; H, 5.15; N, 10.2%); λ_{max.} (95% EtOH) 276 nm (log ε 4.45); ν_{max.} (Nujol) 3320, 1740, and 1620 cm⁻¹; δ (CF₃·CO₂H) 2.1 (4H, m), 3.30br (2H, s), 3.85 (4H, m), and 5.0 (2H, m), *m/e* 274 (*M*⁺).

Hydrolysis of the Dimer (10).—The dimer (10) (0.51 g) was dissolved in ethanol (95%; 100 cm³) and sodium hydroxide solution (2*N*) was added slowly. When the hydrolysis was complete, as shown by t.l.c., the solution was neutralised with hydrochloric acid (2*N*) and evaporated, and the hydrolysis product (13) was recrystallised from methanol; m.p. >300°; yield 0.38 g (40%). It was identical with that prepared from compound (5).

Irradiation of 4-Methyl-5,6-dihydrofuro[3,2-*b*]pyridin-2(4H)-one (7).—The irradiation and work-up were as described for the preparation of compound (10) and gave the dimer (12), m.p. 216° (decomp.) (35%) (Found: C, 63.4; H, 6.05; N, 9.1. Calc. for C₁₆H₁₈N₂O₄: C, 63.55; H, 6.05; N, 9.25%); λ_{max.} (95% EtOH) 237 and 277 nm (log ε 3.99 and 4.46); ν_{max.} (CHCl₃) 1730 and 1630 cm⁻¹; δ (CDCl₃) 1.80 (4H, m), 2.55 (2H, m), 3.0 (6H, s), 3.1 (2H, t), 3.24 (2H, t), 3.70–4.04 (2H, m), and 4.42 (2H, s); *m/e* 302 (*M*⁺).

Irradiation of 4-Acetyl-7-bromo-1,4,5,6-tetrahydropyrrolo-[3,2-*b*]pyridin-2-one (4).—The irradiation and work-up were carried out as described for the preparation of compound (10) and gave the dimer (11), m.p. >300° (44%); λ_{max.} (95% EtOH) 242sh nm (log ε 4.09); ν_{max.} (Nujol) 1720, 1690, and 1640 cm⁻¹; δ (CF₃·CO₂H) 2.31 (6H, s), 3.0 (4H, m), 3.9 (4H, m), and 5.5 (2H, s); *m/e* 511.9699 (Calc. for C₁₈H₁₈Br₂N₄O₄: *M*, 511.9695).

Irradiation of Compound (5) in Methanol.—Irradiation of compound (5) (0.5 g) in dry methanol (40 cm³) (4 h) gave five products (t.l.c.), one of which was the dimer (11). Irradiation of a dilute solution (5) (0.5 g in 300 cm³) gave four major products, which were separated by preparative layer chromatography with chloroform-methanol (9:1) as eluant. The products in order of decreasing *R_F* value were: (a) a crystalline solid, 3-methoxymethylamino-hexakis,cis-2,4-dien-4-olide (15), m.p. 107–108° (0–9%) (Found:

⁵ A. Padwa, J. Smolanoff, and S. I. Wetmore, jun., *J. Org. Chem.*, 1973, **38**, 1333.

C, 57.0; H, 6.35; N, 8.3. $C_8H_{11}NO_3$ requires C, 56.8; H, 6.55; N, 8.3%; λ_{\max} (95% EtOH) 299 and 260 nm ($\log \epsilon$ 3.68 and 3.88); ν_{\max} ($CHCl_3$) 3480, 1740, and 1610 cm^{-1} ; δ ($CDCl_3$) 1.92 (3H, d, J 8 Hz), 3.25 (3H, s), 4.54 (2H, d, J 6 Hz), 5.06 (1H, d, J 6 Hz), 5.63 (1H, split q, J 8 and 1 Hz), and 6.03br (1H, exchangeable, t) (on addition of D_2O the doublet at δ 4.54 collapsed to a singlet); (b) a crystalline solid, 3-methoxymethylaminohexa-cis,trans-2,4-dien-4-olide (16), m.p. 146–148° (10–30%) (Found: C, 57.0; H, 6.5; N, 8.4. $C_8H_{11}NO_3$ requires C, 56.8; H, 6.55; N, 8.3%); λ_{\max} (95% EtOH) 298 and 257.5 nm ($\log \epsilon$ 3.62 and 3.90); ν_{\max} ($CHCl_3$) 3445, 1755, and 1610 cm^{-1} ; δ ($CDCl_3$) 1.86 (3H, d, J 7 Hz), 3.28 (3H, s), 4.55 (2H, d, J 6 Hz), 4.98 (1H, s), 5.48 (1H, q, J 7 Hz), and 6.7br (1H, exchangeable, t) (on addition of D_2O the doublet

at δ 4.55 collapsed to a singlet); (c) an oil, shown by its spectral characteristics to be 3-(methoxymethylamino)-hexa-cis-2,5-dien-4-olide (17) (yield variable); λ_{\max} (95% EtOH) 254.5 nm ($\log \epsilon$ 4.17); ν_{\max} ($CHCl_3$) 3420, 1735, and 1630 cm^{-1} ; δ ($CDCl_3$) 3.28 (3H, s), 4.55 (2H, d, J 6 Hz), 4.88 (1H, s), 5.05–5.7 (3H, m), and 6.1br (1H, exchangeable, t) (on addition of D_2O the doublet at δ 4.55 collapsed to a singlet); and (d) a very small amount of a crystalline material shown by spectral evidence to be 3-aminohexa-cis,trans-2,4-dien-4-olide (18) (<5%); m.p. 120–124°; λ_{\max} (95% EtOH) 303 and 255 nm ($\log \epsilon$ 3.64 and 3.82); ν_{\max} ($CHCl_3$) 3420, 3340, 1710, and 1640 cm^{-1} ; δ ($CDCl_3$) 1.82 (3H, d, J 7 Hz), 4.87 (1H, s), 5.1br (2H, exchangeable, s), and 5.26 (1H, q, J 7 Hz).

[4/1577 Received, 29th July, 1974]