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PHOTOLYSIS OF 4-OXO-4H-BENZISOXAZOLO[2,3-*a*]PYRIDINES

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Photolysis of 4-oxo-4H-benzisoxazolo[2,3-*a*]pyridines (**1a-d**) and their C_1-monobromides (**4a-d**) afforded benzofuro[3,2-*b*]pyridines (**2a-d**) *via* initial N_5-O_6 bond fission. However, similar photolysis of 9-methoxy-4-oxo-4H-benzisoxazolo[2,3-*a*]pyridine analog (**4f**) gave a pyridine derivative (**5**).

KEYWORDS —— photolysis; photo-isomerization; 4-oxo-4H-benzisoxazolo[2,3-*a*]pyridines; benzofuro[3,2-*b*]pyridines; Friedlaender reaction; ring transformation

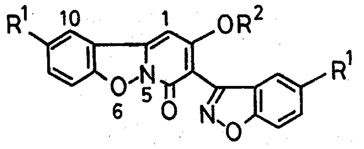
In the preceding communication,1) we described the synthesis of benzisoxazolo[2,3-*a*]pyridine derivatives (**1**). In these studies, it was noted that **1** gradually underwent a photo-induced isomerization even in the course of repeated recrystallization from $CHCl_3$. Although it has been reported that only thermolysis of 9-nitrobenzisoxazolo[2,3-*a*]pyridinium tetrafluroborate gave 8-nitrobenzofuro[3,2-*b*]pyridine in 20% yield,2) any rearrangements of benzisoxazolo[2,3-*a*]pyridine (**1**) were unknown. We now report the photochemical ring transformation of **1**.

Photolysis [low-pressure Hg-lamp (0.5 h) or sun light (12-24 h), $CHCl_3$3)] of **1a** afforded benzofuro[3,2-*b*]pyridine derivative (**2a**).4) Other benzofuro[3,2-*b*]-pyridine derivatives (**2**) obtained by similar photolyses are shown in Table I. Photolysis of 9-methoxy-analogs (**1e-f**), however, gave a dirty reaction mixture from which crystalline products could not be isolated.

The ^{1}H-NMR (PMR) spectrum (DMSO-d_6) of **2a** lacked a characteristic singlet signal attributed to C_1-H of **1a**,1) and showed one proton signal at δ 12.8–13.4 which was exchangable with D_2O. The IR spectrum (KBr) of **2a** exhibited the bands (ν_{NH} 2750, $\nu_{C=O}$ 1640 cm^{-1}) attributable to the 2-pyridone moiety. Treatment of **2a** with Ac_2O-pyridine gave an O-acetate (**3**) [mp 189-191°C, $\nu^{KBr}_{C=O}$ 1760 cm^{-1}, PMR ($CDCl_3$) δ 2.06 (3H, s, $OCOCH_3$)].

The structure of **2** was unequivocally confirmed by an alternative synthesis of **2d** from ethyl 3-aminobenzofuran-2-carboxylate (**6**).5) Treatment of **6** with 2-(1,2-benzisoxazol-3-yl)acetyl chloride1) afforded an amide (**7**) (mp 193-195°C (dec)) which was considered to be an intermediate of the Friedlaender reaction.6) Cyclization of **7** was accomplished in the presence of NaH in DMF at 50°C to give **2d** in 20% yield.

On the other hand, bromination of **1** in acetic acid at 60-80°C gave monobromide (**4**) as shown in Table I. With such bromination, O-acetates, **1b** and **1f**,



1a R^1=H, R^2=Ts

1b R^1=H, R^2=Ac

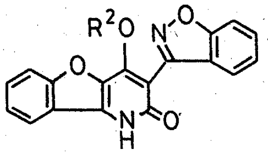
1c R^1=H, R^2=Bz

1d R^1=R^2=H

1e R^1=OCH_3, R^2=Ts

1f R^1=OCH_3, R^2=Ac

1g R^1=OCH_3, R^2=H

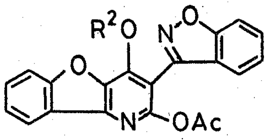


2a R^2=Ts

2b R^2=Ac

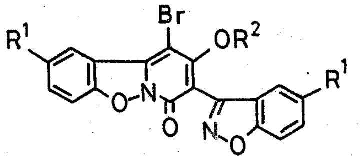
2c R^2=Bz

2d R^2=H



3 R^2=Ts

($Ts=p-CH_3C_6H_4SO_2$
$Ac=CH_3CO$
$Bz=C_6H_5CO$)



4a R^1=H, R^2=Ts

4b R^1=H, R^2=Ac

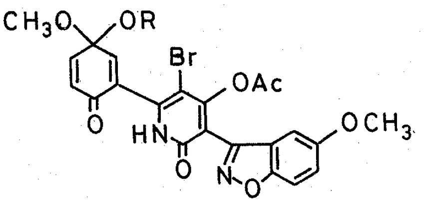
4c R^1=H, R^2=Bz

4d R^1=R^2=H

4e R^1=OCH_3, R^2=Ts

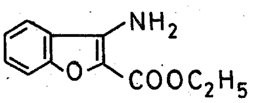
4f R^1=OCH_3, R^2=Ac

4g R^1=OCH_3, R^2=H



5a R=C_2H_5

5b R=CH_3



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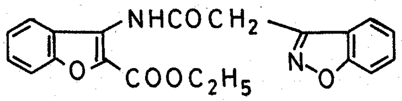

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Table I Photolysis and Bromination of 4-Oxo-4H-benzisoxazolo[2,3-a]pyridines

Compound No.	Yield(%) 1→2	1→4	4→2	mp °C	IR(KBr) $\nu_{C=O}$ cm^{-1}	MS (m/z) M^+
2a	62		43	266-269	1640	472
2b	90		80[a)]	>300	1650, 1780	360
2c	47		65	254-256	1650, 1760	422
2d	98		74	>290	1650	318
4a		93		248-252	1660	550, 552
4b		91[a)]		235-236	1670, 1770	438, 440
4c		93		242-245	1650, 1750	500, 502
4d		99		244-246	1660	396, 398
4e		91		248-252(dec)	1660	610, 612
4f		88[a)]		235-236	1660, 1760	498, 500

a) Over-all yield of photolysis followed by acetylation with Ac_2O-pyridine.

gave deacetylbromides, 4d and 4g,[7] respectively. These deacetylbromides were converted to the corresponding O-acetates, 4b and 4f, by acetylation. The substituted position of the bromine atom at C_1 was deduced from the PMR spectra of 4 which lacked C_1-H signal of the starting materials (1).

Photolysis (sun light, 12-24 h, $CHCl_3$[3a]) of the bromides, 4a, 4b, 4c and 4d, afforded 2a, 2d (accompanied by deacetylation), 2c and 2d, respectively (Table I). However, similar photolysis of 9-methoxy-analog (4f) in $CHCl_3$[3a] gave a pyridine derivative (5a)[8] (mp 190-194°C) in 28% yield. The structure of 5a was deduced from its elemental analysis, IR spectrum, mass spectrum (MS), and PMR data.[8] It was assumed that the ethoxyl group of 5a originated from EtOH in commercial chloroform. This assumption was confirmed by the following experiments. Photolysis of 4f in 5% EtOH-$CHCl_3$ and in EtOH gave 5a in 60% and 40% yields, respectively. Furthermore, photolysis (sun light, 4 h) of 4f in MeOH gave a methoxy-analog (5b)[8] (mp 202-204°C) in 40% yield.

In the dark condition, no isomerization of 1 and 4 was observed and the starting materials (1 and 4) were recovered unchanged. Thus, it may be considered that the ring transformation of 4-oxo-4H-benzisoxazolo[2,3-a]pyridines proceeded by initial homolytic N_5-O_6 bond fission as in the case of the well-known photolysis of isoxazole rings.

REFERENCES AND NOTES

1) S. Naruto, N. Nagamoto, H. Mizuta, T. Yoshida, and H. Uno, Chem. Pharm. Bull., preceding paper in this issue.
2) R. A. Abramovitch and M. N. Inbasekaran, J. Chem. Soc. Chem. Commun., 1978, 149. They reported that photolysis of benzisoxazolo[2,3-a]pyridinium tetrafluroborate did not give any benzofuro[3,2-b]pyridines.
3) a) $CHCl_3$: commercial chloroform containing 0.5-1.0% of EtOH as stabilizer.
   b) It was noted that 1a-d were sparingly insoluble in MeOH, EtOH and dioxane at room temperature and that photolysis (sun light, 4 h) of 1a in MeOH (concentration of 0.08 mM) afforded several products in which 2a, 2d and methyl tosylate were detected. Of these products of the above photolysis, 2d was isolated in 10% yield.
4) All new compounds except 4g in this paper gave satisfactory spectral (PMR, IR, and MS) and analytical data.
5) S. S. Sangapure and Y. S. Agasimundin, Indian J. Chem., 14B, 688 (1976).
6) V. P. Vaidya, S. B. Mahajan, and Y. S. Agasimundin, Indian J. Chem., 20B, 391 (1981).
7) This compound (4g) was used for acetylation without further purification.
8) 5a: IR (KBr) 3200-2400, 1770, 1640 cm^{-1}. PMR (δ in $CDCl_3$) quinone moiety; OCH_3 2.95 (3H, s), OCH_2CH_3 0.99 (3H, t), OCH_2CH_3 3.3 (2H, m), vinyl protons 6.88 (1H, d, J=3.0 Hz), 6.38 (1H, dd, J=10.5, 3.0 Hz), 6.02 (1H, d, J=10.5 Hz). Pyridine moiety; OH 14.0 (1H, bs, exchangable with D_2O), $COCH_3$ 2.19 (3H, s). Benzisoxazole moiety; OCH_3 3.95 (3H, s), aromatic protons 7.01 (1H, dd, J=2.5, 0.5 Hz), 7.18 (1H, dd, J=9.0, 2.5 Hz), 7.48 (1H, dd, J=9.0, 0.5 Hz).
   5b: PMR (δ in $CDCl_3$) $COCH_3$ 2.20 (3H, s), OCH_3 2.94 (6H, s), aromatic OCH_3 3.91 (3H, s).

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