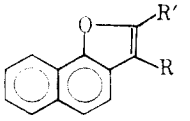
TABLE I

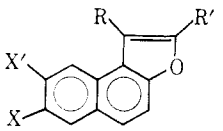
2,3-BIS(ALKOXYPHENYL)NAPHTHO[1,2-*b*]FURANS

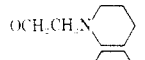
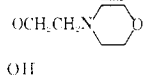
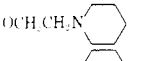
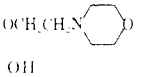
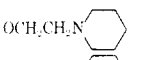
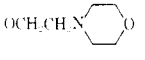
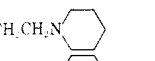
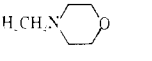
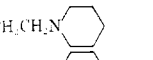
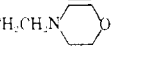


No.	R	R′	Yield, %	Mp, °C	Formula	Calcd, % C	Calcd, % H	Found, % C	Found, % H
2	*o*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	20.5	113–115	$C_{26}H_{20}O_3$	82.12	5.26	81.34	5.60
3	*o*-$OCH_3C_6H_4$	*o*-$OCH_3C_6H_4$	26	125	$C_{26}H_{20}O_3$	82.12	5.26	81.42	5.36
4	3,4-$CH_2O_2C_6H_3$	3,4-$CH_2O_2C_6H_3$	25	125	$C_{26}H_{16}O_5$	76.49	3.91	76.28	4.5

TABLE II

7- AND 8-HYDROXY- AND DIALKYLAMINOALKOXY-1,2-BIS(ALKOXYPHENYL)NAPHTHO[2,1-*b*]FURANS



No.	X	X′	R	R′	Yield, %	Mp, °C	Formula	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
6	$OCH_2CH_2N(C_2H_5)_2$	H	*p*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	90	101–102	$C_{32}H_{33}NO_4$			2.82			2.75
7		H	*p*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	92	99	$C_{33}H_{33}NO_4$			2.75			2.71
8		H	*p*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	92	87–88	$C_{33}H_{33}NO_5$			2.74			2.81
9	OH	H	*o*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	65	178	$C_{28}H_{20}O_4$	78.80	5.04		79.11	5.12	
10	$OCH_2CH_2N(C_2H_5)_2$	H	*o*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	88	96	$C_{32}H_{33}NO_4$			2.82			2.73
11		H	*o*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	90	88–89	$C_{33}H_{33}NO_4$			2.75			2.78
12		H	*o*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	84	96–97	$C_{33}H_{31}NO_5$			2.74			2.79
13	OH	H	*o*-$OCH_3C_6H_4$	*o*-$OCH_3C_6H_4$	70	183–184 dec	$C_{28}H_{20}O_4$	78.80	5.04		78.34	5.21	
14	$OCH_2CH_2N(C_2H_5)_2$	H	*o*-$OCH_3C_6H_4$	*o*-$OCH_3C_6H_4$	86	91–92	$C_{32}H_{33}NO_4$			2.82			2.78
15		H	*o*-$OCH_3C_6H_4$	*o*-$OCH_3C_6H_4$	90	88–89	$C_{33}H_{33}NO_4$			2.75			2.79
16		H	*o*-$OCH_3C_6H_4$	*o*-$OCH_3C_6H_4$	92	90	$C_{33}H_{31}NO_5$			2.74			2.65
17	H	OH	*p*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	67	142–144	$C_{28}H_{20}O_4$	78.80	5.04		78.41	5.1	2.79
18	H	$OCH_2CH_2N(C_2H_5)_2$	*p*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	84	92	$C_{32}H_{33}NO_4$			2.82			
19	H		*p*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	89	94–95	$C_{33}H_{33}NO_4$			2.75			2.79
20	H		*p*-$OCH_3C_6H_4$	*p*-$OCH_3C_6H_4$	91	87–88	$C_{33}H_{31}NO_5$			2.74			2.81
21	H	OH	*o*-$OCH_3C_6H_4$	*o*-$OCH_3C_6H_4$	63	173–175	$C_{28}H_{20}O_4$	78.80	5.04		78.71	5.01	
22	H	$OCH_2CH_2N(C_2H_5)_2$	*o*-$OCH_3C_6H_4$	*o*-$OCH_3C_6H_4$	90	100–101	$C_{32}H_{33}NO_4$			2.82			2.80
23	H		*o*-$OCH_3C_6H_4$	*o*-$OCH_3C_6H_4$	85	110–111	$C_{33}H_{33}NO_4$			2.75			2.78
24	H		*o*-$OCH_3C_6H_4$	*o*-$OCH_3C_6H_4$	82	96	$C_{33}H_{31}NO_5$			2.74			2.82

Some 2-Aryl-5-nitrobenzimidazole 3-Oxides

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Received April 10, 1967

Derivatives of benzimidazole are of interest as potential antimetabolites. The synthesis of some 2-aryl-5-nitrobenzimidazole 3-oxides is reported here.[2] The starting material, 4-nitro-2-nitrosoaniline,[3] was prepared by an improved procedure.

Experimental Section[4]

4-Nitro-2-nitrosoaniline.[3]—DL-Alanine (8.9 g) and Na_2CO_3 (20.0 g) in water (400 ml) were stirred at 40° with fluoro-2,4-dinitrobenzene (12.0 ml) for 2 hr, and the clear solution of N-(2,4-dinitrophenyl)alanine was diluted to 8 l. with 5% (w/v) aqueous $NaHCO_3$. The diluted solution[5] was photolyzed in 1-l. portions in a standard Hanovia 1-l. photochemical reactor[6] at room temperature for 16 hr while being stirred vigorously both with a magnetic stirrer and with a brisk flow of air to remove the acetaldehyde formed. The product [12.7 g, λ_{max} 284, 348 mμ (ε 15,100, 11,200)] was filtered off, washed well with water, and dried at 110°. It was obtained as a green crystalline powder, mp 183–186°, sufficiently pure for further use.

2-Aryl-5-nitrobenzimidazole 3-Oxides.—A solution of 4-nitro-2-nitrosoaniline (2 mmoles) and the appropriate aldehyde (2.2

(1) Biochemistry Department, Dalhousie University, Halifax, Nova Scotia, Canada.

(2) For a preliminary report see D. W. Russell, *Chem. Commun.*, 198 (1965).

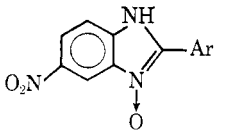
(3) D. W. Russell, *J. Chem. Soc.*, 894 (1963).

(4) Melting points were determined on a hot stage and are corrected. Microanalyses were by Dr. F. Pascher, Bonn, West Germany.

(5) To each 1 l. of solution, 0.3 g of finely powdered, recrystallized 4-nitro-2-nitrosoaniline[3] was added before photolysis. This acted as a seed and prevented deposition of the reaction product upon the glass surfaces of the reaction vessel. The amount added was subtracted in calculating the yield.

(6) Engelhard Hanovia Lamps, Bath Road, Slough, Bucks, England.

TABLE I
2-ARYL-5-NITROBENZIMIDAZOLE 3-OXIDES FROM ALDEHYDES (ArCHO)

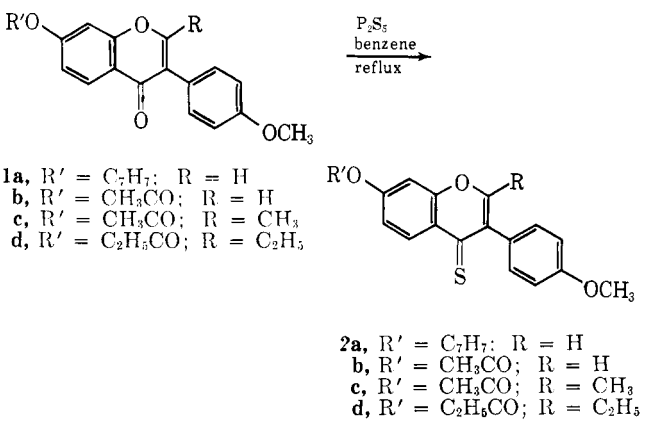


Ar	Yield, %[a]	Mp, °C[b]	Vol. of recrystn solvent, ml/g	Color	Formula	N, % Calcd	N, % Found
C_6H_5	56	272–273	25	Cream	$C_{13}H_9N_3O_3$[c]	16.47	16.20[d]
4-ClC_6H_4	64	249–250[e]	20	Yellow	$C_{13}H_8N_3O_3Cl$	14.50	14.39[f]
2-$MeOC_6H_4$	64	255–257	30	Yellow	$C_{14}H_{11}N_3O_4$	14.74	14.58
3-$MeOC_6H_4$	62	267–269	20	Cream	$C_{14}H_{11}N_3O_4$	14.74	14.52
4-$MeOC_6H_4$	64	273–274	35	Pale yellow	$C_{14}H_{11}N_3O_4$	14.74	14.39
3,4-$(MeO)_2C_6H_3$	62	268–270	30	Pale yellow	$C_{15}H_{13}N_3O_5$	13.33	12.89
2-Naphthyl	62	258–259	20	Pale yellow	$C_{17}H_{11}N_3O_3$	13.75	13.56
4-Pyridyl[g]	59	279–280	25	Pale yellow	$C_{12}H_8N_4O_3$	21.87	21.82

[a] Of recrystallized product. Crude yields were generally in excess of 70%. [b] All compounds melted with decomposition. [c] This compound was identical (melting point, mixture melting point, infrared spectrum) with a sample prepared by photolysis of N-(2,4-dinitrophenyl)-C-phenylglycine at pH 3 as described by R. J. Pollitt, *Chem. Commun.*, 262 (1965). [d] *Anal.* Calcd: C, 61.18; H, 3.55. Found: C, 61.39; H, 3.72. [e] This compound resolidified on further heating and melted again at 296–298° dec. [f] *Anal.* Calcd: Cl, 12.24. Found: Cl, 12.03. [g] The reaction mixture contained an additional 2.2 mmoles of *p*-toluenesulfonic acid, and water (20 ml) instead of ethanol was used to precipitate the product.

mmoles) in glacial acetic acid (2.5 ml) containing *p*-toluenesulfonic acid (33 mg)[7] was boiled under reflux for 30 min, during which time part of the product generally crystallized. The hot reaction mixture was cautiously diluted with ethanol (7 ml) and set aside overnight at room temperature to complete the precipitation. The product after being washed with ethanol was crystallized from 1-butanol–pyridine (3:2) with addition of a little decolorizing charcoal. Compounds prepared by this procedure are given in Table I.

(7) Reaction was faster in glacial than in the 50% AcOH originally used[2] and was still more rapid in the presence of catalytic amounts of the sulfonic acid.



1a, R′ = C_7H_7; R = H
b, R′ = CH_3CO; R = H
c, R′ = CH_3CO; R = CH_3
d, R′ = C_2H_5CO; R = C_2H_5

2a, R′ = C_7H_7; R = H
b, R′ = CH_3CO; R = H
c, R′ = CH_3CO; R = CH_3
d, R′ = C_2H_5CO; R = C_2H_5

Flavonoids. V. Thiation of Isoflavones[1,2]

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Received March 3, 1967

A biological significance of isoflavonoids is well documented in the example of genistein, an isoflavone which occurs in clover and has been responsible for the failure of ewes to lamb.[3] In this connection we have prepared for biological evaluation a few isoflavthiones (**2**): the synthetic method employed here has precedent in Baker's thiation of flavone.[4]

The general procedure described herein (Experimental Section) was inadequate for the thiation of 3-(*p*-methoxyphenyl)-7-methoxycoumarin.[5]

Experimental Section[6]

General Procedure for the Thiation of Isoflavones 1a–d.—A suspension of equal weights of isoflavone and P_2S_5[7] in benzene (20 ml/g of isoflavone) was stirred and heated under reflux (bath temperature, 80–85°), protected from atmospheric moisture. The reaction progress was followed by tlc; chromatograms were eluted in 10% ethyl acetate–benzene (the isoflavones fluoresce blue light under an ultraviolet light source; the isoflavthiones move as yellow zones, are nonfluorescent, and are further developed by 5% phosphomolybdic acid in ethanol reagent). The remainder of the total quantity of P_2S_5 was added during the course of the reaction. At the end of the refluxing period (2–4 hr), as judged by tlc, the hot reaction solution was decanted through a fluted filter and the residual solids were washed with two small portions of hot benzene. The crude isoflavthione was precipitated (or crystallized) by adding a 4–5-fold volume of petroleum ether (bp 30–60°), keeping the solution at ~−10°. In the case of **2d** (the slowest to crystallize), the precipitation of yellow solid preceded the crystallization of product; this being the case, the supernatant was decanted into a clean flask, and cooling was continued until separation of product was complete. The yields and melting points of the isoflavthiones reported in Table I (on the following page) were obtained after one recrystallization from ethyl acetate.

(1) This research was carried out under Contract SA-43-ph-4351 of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health.

(2) Paper IV in this series: K. H. Dudley, H. W. Miller, R. C. Corley, and M. E. Wall, *J. Org. Chem.*, **32**, 2317 (1967).

(3) R. B. Bradbury and D. E. White, *J. Chem. Soc.*, 3447 (1951).

(4) W. Baker, J. B. Harborne, and W. D. Ollis, *ibid.*, 1303 (1952).

(5) N. Campbell in "Chemistry of Carbon Compounds," Vol. IVB, E. H. Rodd, Ed., Elsevier Publishing Co., Amsterdam, 1959, p 877.

(6) Melting points were determined on a Kofler hot stage microscope using a calibrated thermometer. Ultraviolet spectra were measured with a Cary Model 14 spectrophotometer, infrared spectra with a Perkin-Elmer 221 spectrophotometer (KBr disks). Microanalyses were carried out by Triangle Chemical Laboratories, Carrboro, N. C., and Micro-Tech Laboratories, Skokie, Ill.

(7) P_2S_5 (Matheson Coleman and Bell) was employed without further purification.