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Received August 8, 19806-Alkylthio- and 6-phenylthio-5*H*-benzo[*a*]phenoxazin-5-ones have been synthesized by the photochemical reaction of 5*H*-benzo[*a*]phenoxazin-5-one with alkylthiols and thiophenol.*J. Heterocyclic Chem.*, **18**, 259 (1981).

Although benzophenoxazinones are known to possess pharmacological activities (1-3), few synthetic methods are available for their preparation (4-7). Reactions of benzo-phenoxazinone with some nucleophiles (8-12) have been studied and 9-arylthio-5*H*-benzo[*a*]phenoxazin-5-ones were prepared in 26-36% yields by the reaction of 5*H*-benzo[*a*]phenoxazin-5-one (**1**) with substituted thiophenols in refluxing acidic ethanol solution according to the procedure of Afanas'eva, *et al.* (11). However, photochemical reaction of benzophenoxazinones have not yet received attention. It seemed that it would be interesting to investigate what type of reaction occurs between 5*H*-benzo[*a*]phenoxazin-5-one and thiophenol on irradiation. We report here the photochemical reactions of 5*H*-benzo[*a*]phenoxazin-5-one (**1**) with alkylthiols (**2a-e**) and thiophenol (**2f**).

Upon irradiation of a benzene solution of 5*H*-benzo[*a*]-

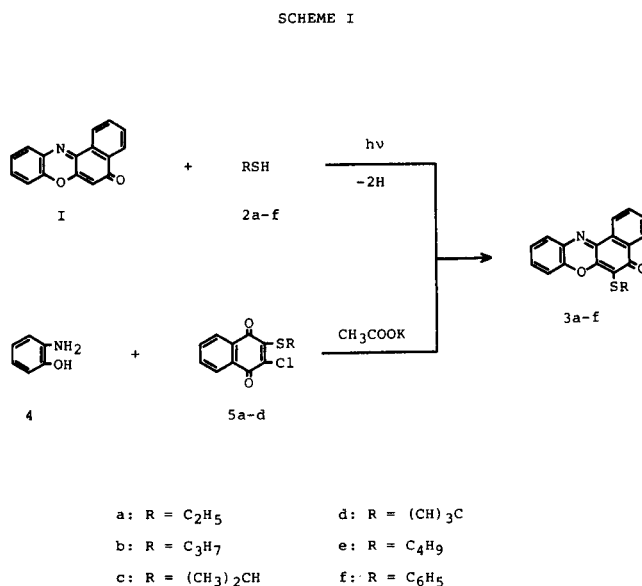
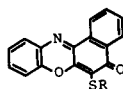


Table 1

6-Alkylthio- and 6-Phenylthio-5*H*-benzo[*a*]phenoxazin-5-one (**3a-f**)

Compound No.	R	Procedure Yield, %	M.p., °C	Molecular Formula	Elemental Analysis		
					Analysis C	Calcd. H	(Found) N
3a	C ₂ H ₅	A, 44 (a)	150-151	C ₁₈ H ₁₃ NO ₂ S (307.4)	70.36	4.23	4.56
		B, 33 (b)			(70.59)	(4.27)	(4.34)
3b	C ₃ H ₇	A, 31 (a)	138-139	C ₁₉ H ₁₅ NO ₂ S (321.4)	71.03	4.67	4.36
		B, 25 (b)			(70.69)	(4.78)	(4.19)
3c	(CH ₃) ₂ CH	A, 24 (a)	165-166	C ₁₉ H ₁₅ NO ₂ S (321.4)	71.03	4.67	4.36
		B, 30 (b)			(70.98)	(4.69)	(4.21)
3d	C ₆ H ₅	A, 35 (a)	84-85	C ₂₀ H ₁₇ NO ₂ S (335.4)	71.64	5.07	4.18
		B, 24 (b)			(71.85)	(5.06)	(4.00)
3e	(CH ₃) ₃ C	A, 32 (a)	181-182	C ₂₀ H ₁₇ NO ₂ S (335.4)	71.64	5.07	4.18
					(71.82)	(4.99)	(3.94)
3f	C ₆ H ₅	A, 40 (a)	161-162	C ₂₂ H ₁₃ NO ₂ S (335.4)	74.36	3.66	3.94
					(74.51)	(3.53)	(3.64)

(a) Yield of product based on 5*H*-benzo[*a*]phenoxazin-5-one consumed. (b) Yield of isolated product.

Table 2

Spectroscopic Data of 6-Alkylthio- and 6-Phenylthio-5*H*-benzo[*a*]phenoxazin-5-one (**3a-f**)

Compound	Mass	Infrared Spectrum cm ⁻¹	¹ H Nmr Spectrum (deuteriochloroform) ppm
3a	307 (M ⁺)	2990, 2870, 1632 (C=O), 1595, 1540, 1292, 765	1.10-1.44 (t, 3H), 3.00-3.32 (q, 2H), 7.23-7.88 (m, 6H, arom), 8.14-8.35 (m, 1H, arom), 8.49-8.73 (m, 1H, arom)
3b	321 (M ⁺)	2980, 2880, 1636 (C=O), 1600, 1555, 1300, 790	0.80-1.20 (t, 3H), 1.27-1.86 (m, 2H), 2.91-3.23 (t, 2H), 7.22-7.87 (m, 6H, arom), 8.12-8.33 (m, 1H, arom), 8.49-8.70 (m, 1H, arom)
3c	321 (M ⁺)	2980, 2870, 1635 (C=O), 1598, 1550, 1298, 774	1.18-1.42 (d, 6H), 3.62-4.32 (m, 1H), 7.23-7.91 (m, 6H, arom), 8.12-8.39 (m, 1H, arom), 8.53-8.76 (m, 1H, arom),
3d	335 (M ⁺)	2970, 2875, 1637 (C=O), 1600, 1555, 1299, 774	0.70-1.02 (t, 3H), 1.06-1.83 (m, 4H), 2.90-3.22 (t, 2H), 7.20-7.84 (m, 6H, arom), 8.04-8.33 (m, 1H, arom), 8.47-8.69 (m, 1H, arom)
3e	335 (M ⁺)	2975, 2870, 1645 (C=O), 1602, 1545, 1302, 782	1.38 (s, 9H), 7.25-7.90 (m, 6H, arom), 8.19-8.39 (m, 1H, arom), 8.53-8.73 (m, 1H, arom)
3f	335 (M ⁺)	1630 (C=O), 1598, 1542, 1298, 750	6.85-7.78 (m, 11H, arom), 8.09-8.35 (m, 1H, arom), 8.42-8.68 (m, 1H, arom)

phenoxazin-5-one (**1**) and alkylthiols (**2a-e**) in a Pyrex vessel using 100 Watt high pressure mercury lamp, 6-alkylthio-5*H*-benzo[*a*]phenoxazin-5-ones (**3a-e**) were obtained in 24-44% yields. When thiophenol (**2f**) was used in place of alkylthiols (**2a-e**), 6-phenylthio-5*H*-benzo[*a*]phenoxazin-5-one (**3f**) was obtained under the same conditions in 40% yield.

The structures of the photoproducts (**3a-f**) were fully supported by microanalytical results and spectral data. In particular, the nmr spectrum (deuteriochloroform) of **1** exhibited a characteristic singlet at 6.30 ppm due to the olefinic proton, but those of the photoproducts (**3a-f**) of **1** with **2a-e** and **2f** did not show a characteristic singlet at 6.30 ppm. Furthermore, the photoproducts (**3a-d**) were identified by direct comparison with a sample prepared by an alternate route. This route involves the condensation of 2-aminophenol (**4**) with an appropriate 2-alkylthio-3-chloro-1,4-naphthoquinones (**5a-d**) to furnish the corresponding 6-substituted-5*H*-benzo[*a*]phenoxazin-5-ones (**3a-d**) in an alcoholic medium in the presence of anhydrous potassium acetate.

The present report offers a facile method for the photochemical synthesis of 6-alkylthio- and 6-arylthio-5*H*-benzo[*a*]phenoxazin-5-ones from readily available starting material. The detailed mechanism is not clear at present and further studies are now in progress.

apparatus and are uncorrected. The infrared spectra were recorded on a Jasco DS 701G spectrometer. Absorption frequencies are quoted in reciprocal centimeters. Nuclear magnetic resonance spectra were determined on a Hitachi R-20B spectrometer using tetramethylsilane as an internal reference. Chemical shifts are quoted in parts per million (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet). Mass spectra were determined on a Hitachi M-52 spectrometer.

General Procedure A for the Preparation of 6-Alkylthio- and 6-Arylthio-5*H*-benzo[*a*]phenoxazin-5-ones (**3a-f**).

5*H*-Benzo[*a*]phenoxazin-5-one (**1**) (0.15 g., 0.6 mmole) and an alkylthiol (or a thiophenol) (3 mmole) were dissolved in benzene (100 ml.). The solution was irradiated in a Pyrex glass tube for 20 hours from outside by means of 100 Watt high-pressure mercury arc lamp in a nitrogen atmosphere through a 7 cm-thick layer of cold water (0-5°) and then bubbled with air for several minutes. After the removal of the solvent under reduced pressure, the residue was chromatographed on a silica gel column (benzene as eluent). The photoproducts (**3**) thus obtained were further purified by recrystallization from ethanol.

General Procedure B for the Preparation of 6-Alkylthio-5*H*-benzo[*a*]phenoxazin-5-ones (**3a-d**).

6-Alkylthio-5*H*-benzo[*a*]phenoxazin-5-ones (**3a-d**) were synthesized using a slight modification of the procedure described by Agarwal, *et al.* (13). In a three-neck flask fitted with stirrer, condenser, and dropping funnel, a solution of 2-aminophenol (**4**) (0.22 g., 2 mmoles) in ethanol (20 ml.) was gradually added with stirring to a refluxing suspension of 2-alkylthio-3-chloro-1,4-naphthoquinone (**14**) (**5a-d**) (2 mmoles) and anhydride potassium acetate (0.40 g., 4 mmoles) in ethanol (10 ml.). Stirring and refluxing was continued for additional 3 hours, and then the reaction mixture was evaporated to dryness under vacuum. The residual solid was collected, washed well with cold water, and recrystallized from ethanol.

EXPERIMENTAL

Melting points were determined on a Yanagimoto micromelting

REFERENCES AND NOTES

(1) R. L. Margaret, P. G. Philip and A. S. Henry, *Cancer Res.*, **9**, 736

- (1949).
- (2) Y. Funasaki, Japan, *J. Tuberc.*, **6**, 51 (1958).
- (3) T. K. Pashkevich, G. B. Afanas'eva, I. Y. Postovskii, K. I. Pashkevich, T. S. Viktorova and N. N. Froblova *Khim-Farm. Zh.*, **10**, 77 (1976).
- (4) F. Kehrmann, J. Markusfeld and B. Mascioni, *Chem. Ber.*, **28**, 353 (1895).
- (5) J. A. VanAllan and G. A. Reynolds, *J. Org. Chem.*, **28**, 527 (1963).
- (6) O. F. Hepp, *Chem. Ber.*, **36**, 1807 (1903).
- (7) G. B. Afanas'eva, K. I. Pashkevich and I. Ya. Postovskii, *Khim. Geterotsikl. Soedin.*, 742 (1971).
- (8) I. Ya. Postovskii and G. B. Afanas'eva, *Dokl. Akad. Nauk SSSR*, **153**, 612 (1963).
- (9) G. B. Afanas'eva and I. Ya. Postovskii, *Zh. Obshch. Khim.*, **34**, 1741 (1964).
- (10) G. B. Afanas'eva and I. Ya. Postovskii, *ibid.*, **36**, 1938 (1966).
- (11) G. B. Afanas'eva, K. I. Pashkevich, I. Y. Postovskii, V. G. Vykhristyuk, N. P. Shimanskaya and V. D. Bezuglyi, *Khim. Geterotsikl. Soedin.*, 1345 (1972).
- (12) I. A. Postovskii, K. I. Pashkevich and G. B. Afanas'eva, *ibid.*, 464 (1974).
- (13) N. L. Agarwal and R. L. Mital, *Indian J. Chem.*, **B14**, 382 (1976).
- (14) L. F. Fieser and R. H. Brown, *J. Am. Chem. Soc.*, **71**, 3609 (1949).