INVESTIGATIONS IN THE FIELD OF THE CHEMISTRY OF PHENOXAZINES

VI.* RADICAL SUBSTITUTION REACTIONS FOR PHENOXAZINONES AND THEIR ARYLTHIO DERIVATIVES

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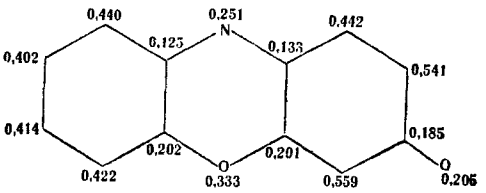
In the radical bromination of phenoxazin-3-one, its benzo derivatives, and arylthiophenoxazinones, the hydrogen atom in the ortho position to the two oxygen atoms is replaced. The results obtained agree satisfactorily with those of quantum-chemical calculations.

The information available at the present time on the chemistry of the phenoxazinones is devoted mainly to the study of reactions with nucleophilic agents [1-3]. With the exception of one paper [4], there is no information in the literature on radical and electronic reactions for phenoxazinones, although these reactions offer definite interest from the point of view of obtaining new phenoxazinone derivatives.

Calculation of the free-valence indices for phenoxazin-3-one and its benzo and dibenzo derivatives shows the basic possibility of the occurrence of radical substitution reactions at the quinoid ring in the ortho position with respect to the exocyclic oxygen atom. As an example, the values of the free-valence indices are given for phenoxanin-3-one.



For the benzo- and dibenzophenoxazinones these values are very close to those given. (The π-electronic charges, the bond orders, and the parameters taken in the calculation have been given previously [5].)

To investigate the possibility of the radical substitution of phenoxazinones, in the present work we performed the bromination of phenoxazin-3-one (I), benzo[*a*]phenoxazin-9-one (II), benzo[c]phenoxazin-3-one (III), 1-methylbenzo[c]phenoxazin-3-one (IV), benzo[*a*]phenoxazin-5-one (V), and dibenzo[*a*,j]phenoxazin-5-one (VI) with bromosuccinimide in carbon tetrachloride in the presence of benzoyl peroxide as initiator. It was found that boiling the reaction mixture for 2-5 h formed the monobromo derivatives of the phenoxazinones (VII-XII, Table 1).

The possibility of the radical bromination both of phenoxazin-3-one without fused-on rings (I) and its benzo derivatives (II-VI) in which, in turn, positions 1 and 2, 6 and 7, and 8 and 9 of the phenoxazin-3-one molecule are covered permits the conclusion that the radical attack of a bromine atom takes place in the quinoid ring, in position 4.†

*For Communication V, see [1].

† Numbering given for phenoxazin-3-one.

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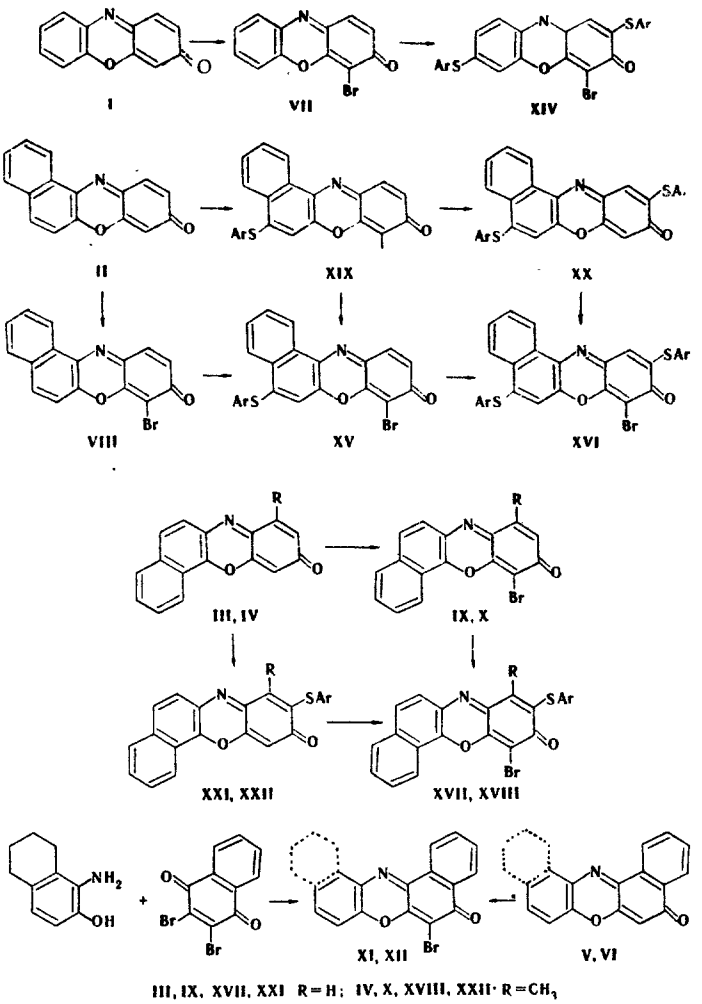

III, IX, XVII, XXI R = H; IV, X, XVIII, XXII R = CH_3

The position of entry of the bromine was confirmed by the independent synthesis of 6-bromobenzo-[*a*]phenoxazin-5-one (XI) and 6-bromodibenzo[*a*,j]phenoxazin-5-one (XII) by the condensation of dibromonaphthoquinone with o-aminophenol and with α-amino-β-naphthol, respectively. This reaction was performed in methanol in the presence of KOH. A similar procedure has been used [6] to obtain unsubstituted benzo[a]phenoxazin-5-one from o-aminophenol and 2,3-dichloronaphthoquinone. However, in contrast to this [6], in the case of 2,3-dibromonaphthoquinone no formation of benzo[a]phenoxazin-5-one (V) or dibenzo[*a*,j]phenoxazin-5-one (VI) was observed and in both cases only the respective monobromo derivative (XI) or (XII) was isolated. To confirm the published results [6], the condensation was repeated for dichloronaphthoquinone and o-aminophenol, but in this case only 6-chlorobenzo[*a*]phenoxazin-5-one was isolated, and not benzo[*a*]phenoxazin-5-one (V), as stated by Van-Allen and Reynolds [6].

In the preparation of 1,2,4-trichlorophenoxazin-3-one [7] by the condensation of chloranil with o-aminophenol, again the retention of the halogen atoms in the ortho positions to the condensed benzene nucleus was observed. Thus, the results given in [6] are not reproducible.

Low mobility of a halogen atom is also observed in the reaction of the bromophenoxazinones obtained with thiophenols. Here, again, replacement of the bromine does not take place but only the formation of arylthio bromo derivatives of the phenoxazinones (XIV-XVIII, Table 1). As in the case of the unbrominated phenoxazinones, it proved to be possible to add two molecules of thiophenol to 4-bromophenoxazin-3-one (VII) and to 8-bromobenzo[*a*]phenoxazin-9-one (VIII) and only one molecule to 4-bromobenzo[c]phenoxazin-3-one (IX) and 4-bromo-1-methylbenzo[c]phenoxazin-3-one (X).

The bromine derivatives (X) and (XI) do not react with nucleophiles because of the passivating action of the benzene nucleus fused to the quinoid moiety [5]. The reaction of thiophenols with bromophenoxazinones, like the reaction with unsubstituted phenoxazinones, takes place through a stage of the production of a leuco form passing into the oxo form on oxidation.

TABLE 1. Bromine Derivatives of the Phenoxazinones and Arylthiophenoxaxinones

Compound	Reaction time, h	mp, °C	Empirical formula	Found, %				Calc., %				R_f[a]	λ_{max}, nm	log ε	Yield, %
				C	H	Br	S	C	H	Br	S				
VII	1.5	200—202[b]	$C_{12}H_6BrNO_2$	52,0	2,3	29,3	—	52,2	2,2	29,0	—	0,44	470	4,08	28
VIII	5	217—218[c]	$C_{16}H_8BrNO_2$ [e]	58,7	2,6	24,9	—	58,9	2,5	24,5	—	0,36	510	3,90	36
IX	4	222—223[d]	$C_{16}H_8BrNO_2$ [e]	59,0	2,6	24,5	—	58,9	2,5	24,5	—	0,36	522	4,08	30
X	3,5	232—234[f]	$C_{17}H_{10}BrNO_2$	60,4	3,1	23,8	—	60,0	3,0	23,5	—	0,39	512	3,86	24
XI	5	188—189[d]	$C_{16}H_8BrNO_2$	59,3	2,5	24,7	—	58,9	2,5	24,5	—	0,63	448	4,13	40
XII	6	254—256[d]	$C_{20}H_{10}BrNO_2$[g]	—	—	21,3	—	—	—	21,6	—	0,65	495	4,28	45
XIV	2	230—232[f]	$C_{28}H_{18}BrNO_2S_2$	59,4	3,2	15,2	—	59,4	3,5	15,6	—	0,59	—	—	32
XV	5	242—243[h]	$C_{23}H_{14}BrNO_2S$	61,7	3,2	18,1	7,0	61,6	3,2	17,8	7,2	0,29	517	4,18	25
XVI	7	279—281[i]	$C_{30}H_{20}BrNO_2S_2$	63,8	3,8	13,9	11,0	63,6	3,5	14,0	11,1	0,65	544	4,17	50
XVII	4	259—261[f]	$C_{23}H_{14}BrNO_2S$	62,1	3,4	17,7	7,2	61,6	3,2	17,8	7,1	0,58	564	4,20	28
XVIII	4	216—218[f]	$C_{24}H_{16}BrNO_2S$	62,6	3,7	17,9	7,1	62,4	3,5	17,3	6,9	0,65	549	4,11	34

[a]On Al_2O_3 of activity grade II in the anhydrous chloroform system. [b]From a mixture of isoamyl alcohol and pyridine, 3:1. [c]From a mixture of pyridine and water, 9:1. [d]From isoamyl alcohol. [e]Found, %: N 4.4. Calculated, %: N 4.3. [f]From butanol. [g]Found, %: N 3.7. Calculated, %: N 3.7. [h]From pyridine. [i]From a mixture of pyridine and ethanol, 9:1.

In the radical bromination of arylthio derivatives of phenoxazinones (XIX-XXII) under conditions similar to those described above, arylthio bromo derivatives of phenoxazinones (XIV-XVIII) are formed, these being identical with the corresponding compounds obtained by the reaction of thiophenols with bromophenoxazinones.

EXPERIMENTAL

The electronic spectra of compounds (VII-XXII) in the visible region were taken on an SF-10 spectrophotometer in chloroform at a concentration of $5 \cdot 10^{-4}$ M.

The initial compounds were obtained by literature methods, as indicated: phenoxazin-3-one (I) [8]; benzo[*a*]phenoxazin-9-one (II) [2]; benzo[c]phenoxazin-3-one (III) [9]; 1-methylbenzo[c]-phenoxazin-3-one (IV) [1]; benzo[*a*]phenoxazin-5-one (V) [10]; dibenzo[*a*,j]phenoxazin-5-one (VI) [11], and 5-p-tolylthiobenzo[*a*]-phenoxazin-9-one (XIX), 5,10-di(p-tolylthio)benzo[*a*]phenoxazin-9-one (XX), 2-p-tolylthiobenzo[c]phenoxazin-3-one (XXI), and 1-methyl-2-p-tolylthiobenzo[c]phenoxazin-3-one (XXII) [1].

4-Bromophenoxazin-3-one (VII). To 1 g (5 mmoles) of phenoxazin-3-one in 25 ml of carbon tetrachloride was added 2 g (11 mmoles) of bromosuccinimide, followed by a solution of 0.2 g of benzoyl peroxide in 3 ml of chloroform, and the mixture was heated on the boiling water bath for 1 h 30 min, after which it was cooled, and the precipitate that had deposited was filtered off. The precipitate was covered with hot water, triturated, and filtered off. This operation was repeated twice, and the reaction product was dried, dissolved in chloroform, and chromatographed on a column of Al_2O_3 (eluent—anhydrous chloroform). The second, orange, fraction was collected and evaporated, giving, after recrystallization of the residue, 0.4 g of (VII).

8-Bromobenzo[*a*]phenoxazin-9-one (VIII), 4-bromobenzo[c]-phenoxazin-3-one (IX), 4-bromo-1-methylbenzo[c]phenoxazin-3-one (X), 6-bromobenzo[*a*]phenoxazin-5-one (IX), and 6-bromodibenzo[*a*,j]phenoxazin-5-one (XII) were obtained and isolated similarly.

6-Bromobenzo[*a*]phenoxazin-5-one (XI). To a solution of 1.2 g of KOH in 15 ml of absolute methanol were added 1.2 g (0.10 mole) of o-aminophenol and 3.2 g (0.12 mole) of dibromonaphthoquinone, and the mixture was boiled on the water bath for 3 h. After cooling, the precipitate that had deposited was filtered off, dried, and chromatographed on a column of Al_2O_3 (eluent—anhydrous chloroform). The first, bright yellow fraction was collected and evaporated, and recrystallization of the residue gave 0.8-1 g of (XI) identical in its melting point, R_f value, and electronic spectrum in the visible region with the product obtained by the direct bromination of benzo[*a*]phenoxazin-5-one.

6-Bromodibenzo[*a*,j]phenoxazin-5-one (XII) was obtained similarly from dibromonaphthoquinone and α-amino-β-naphthol.

6-Chlorobenzo[*a*]phenoxazin-5-one (XIII) was obtained in a similar manner to (XI), except that dichloronaphthoquinone was used in place of dibromonaphthoquinone. mp 194-195°C (from benzene) [11]. Found, %: C 68.5; H 2.3; Cl 12.9. $C_{16}H_8ClNO_2$. Calculated, %: C 68.6; H 2.8; Cl 12.7.

4-Bromo-2,7-di(p-tolylthio)phenoxazin-3-one (XIV). Onto 0.3 g (1.5 mmole) of 4-bromophenoxazin-3-one (VII) was poured 10 ml of ethanol, and then 0.3 g (2.5 mmoles) of p-thiocresol and one drop of hydrochloric acid were added and the mixture was stirred until the initial bromophenoxazinone had dissolved completely. Oxidation was carried out by the addition of 5 ml of a 10% ethanolic solution of ferric chloride. The precipitate that deposited was filtered off, washed with ethanol, dried, and chromatographed on a column of alumina (eluent – anhydrous chloroform). The first, red-brown fraction was collected and evaporated to give 0.1-0.15 g of (XIV).

8-Bromo-5-(p-tolylthio)benzo[*a*]phenoxazin-9-one (XV). A. To 0.5 g (1.5 mmoles) of 8-bromobenzo[*a*]phenoxazin-9-one (VIII) in 25 ml of ethanol was added 0.2 g (1.8 mmole) of p-thiocresol and two drops of hydrochloric acid, and the mixture was kept at room temperature for two days with occasional stirring. The light-yellow solution of the leuco compound was oxidized with 10 ml of a 10% ethanolic solution of ferric chloride, and the precipitate that deposited was filtered off, washed with ethanol, dried, dissolved in chloroform, and chromatographed on a column of Al_2O_3 (eluent–anhydrous chloroform). The second, violet fraction was also collected and evaporated, and after crystallization of the residue 0.25 g of (XV) was obtained.

B. A suspension of 0.5 g of 5-(p-tolylthio)benzo[*a*]phenoxazin-9-one (XIX) in 15 ml of carbon tetrachloride was treated with 0.4 g of bromosuccinimide and 0.1 g of benzoyl peroxide in 3 ml of chloroform. The mixture was boiled on the water bath for 4 h, another 0.2 g of bromosuccinimide and 0.1 g of benzoyl peroxide were added, and the mixture was boiled again for 4 h. Then it was cooled, and the precipitate was filtered off, washed with hot water, dried, dissolved in chloroform, and chromatographed on a column of Al_2O_3. The violet fraction was collected and evaporated to give 0.1 g of (XV), identical, according to its melting point and R_f value, with the compound obtained by the addition of p-thiocresol to (VIII).

8-Bromo-5,10-di(p-tolylthio)benzo[*a*]phenoxazin-9-one (XVI). A. A mixture of 0.6 g (1.8 mmole) of 8-bromobenzo[*a*]phenoxazin-9-one (VIII), 0.5 g of p-thiocresol (5 mmoles), and five drops of hydrochloric acid in 25 ml of ethanol was boiled on the water bath for 6 h, and then another 0.2 g of p-thiocresol was added and boiling was continued for 2 h. To complete the oxidation, 5 ml of a 10% ethanolic solution of ferric chloride was added, and then the precipitate that had deposited was filtered off, washed with ethanol, and dried. The dry residue was chromatographed on a column of Al_2O_3 (eluent–anhydrous chloroform). The first, violet fraction was collected and evaporated to give 0.25-0.30 g of (XVI).

B. A suspension of 1 g of 5,10-di(p-tolylthio)benzo[*a*]phenoxazin-9-one in 25 ml of carbon tetrachloride was treated with 1 g of bromosuccinimide and 0.2 g of benzoyl peroxide in 25 ml of chloroform, and the mixture was boiled for 10 h. Then another 0.5 g of bromosuccinimide and 0.1 g of benzoyl peroxide in 3 ml of chloroform were added and the mixture was boiled again for 8 h. After cooling, the precipitate was filtered off, washed with hot water until the filtrate was colorless, and dried. After recrystallization, 0.4 g of (XVI) was obtained; it was identical with respect to melting point and R_f value with the compound obtained by the addition of p-thiocresol to (VIII).

4-Bromo-2,7-di(p-tolylthio)phenoxazin-3-one (XIV), 4-bromo-2-(p-tolylthio)benzo[c]phenoxazin-3-one (XVII), and 4-bromo-1-methyl-2-(p-tolylthio)benzo[c]phenoxazin-3-one (XVIII) were obtained similarly.

LITERATURE CITED

1. G. B. Afanas'eva, K. I. Pashkevich, I. Ya. Postovskii, V. G. Bykhristyuk, N. P. Shimanskaya, and V. D. Bezuglyi, Khim. Geterotsikl. Soedin., 1345 (1972).
2. O. Fischer and E. Hepp, Ber., 36, 1803 (1903).
3. F. Kehrmann and H. Gottrau, Ber., 38, 2574 (1905).
4. E. Huber, US Patent No. 2,069,475 (1936); Chem. Abstr., 31, 2018 (1937).
5. K. I. Pashkevich, G. B. Afanas'eva, E. G. Kovalev, and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., 1316 (1970).
6. I. Van-Allan and G. Reynolds, J. Org. Chem., 28, 1019 (1963).
7. R. S. Chlenova, Ts. M. Gel'fer, and S. F. Petrov, Zh. Obshch. Khim., 28, 2977 (1958).
8. S. Granick, L. Michaelis, and M. Schubert, J. Amer. Chem. Soc., 62, 1802 (1940).
9. G. B. Afanas'eva, K. I. Pashkevich, and I. Ya. Postovskii, Khim. Geterotsikl. Soedin., 742 (1971).
10. F. Kehrmann, Ber., 28, 354 (1895).
11. H. Goldstein and H. Radovanovitch, Helv. Chim. Acta, 9, 776 (1926).