CHEMISTRY OF PHENOXAZINES

IV.* ADDITION OF THIOPHENOLS TO PHENOXAZIN-3-ONE

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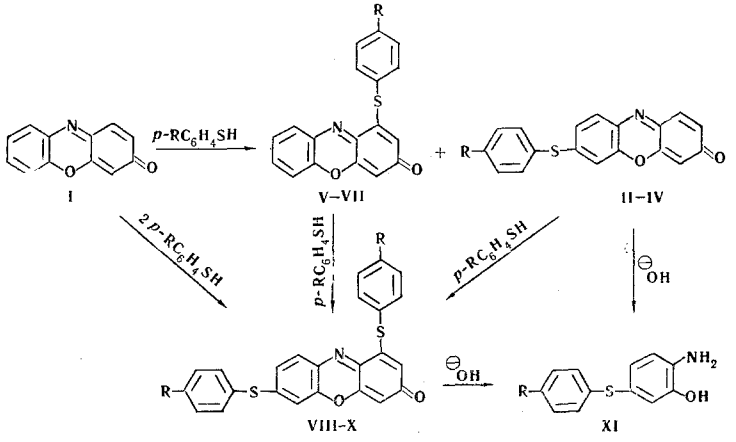
UDC 547.867.6:543.5

In agreement with the previously performed Huckel MO calculation of its electronic structure, phenoxazin-3-one adds one or two molecules of nucleophile (thiophenol, p-thiocresol, p-nitrothiophenol). The structures of the arylthiophenoxazinones were confirmed by alkaline decomposition.

The ready addition of one molecule of nucleophile (amide [2] or thiophenol [3]) at the para position relative to the heterocyclic nitrogen atom has been noted for benzophenoxazinones. A previous [4] Huckel MO calculation of the electronic structure of phenoxazin-3-one and its benzo derivatives demonstrated that phenoxazinones that do not have a benzene ring annelated to the quinoid portion of the phenoxazin-3-one molecule contain a second electrophilic center – the ortho position relative to the heterocyclic nitrogen atom in the quinoid ring – at which one might expect the addition of a second molecule of nucleophile. The conclusions drawn from the calculations are confirmed in our research in which we studied the reaction of phenoxazin-3-one with several nucleophiles (p-thiocresol, thiophenol, and p-nitrothiophenol).

The addition of thiophenols to phenoxazin-3-one proceeds through a step involving the formation of a leuco compound which is readily converted to the oxo form on standing in air or under the influence of mild oxidizing agents. Identical products were isolated when the reaction



II, V, VIII, XI R=CH_3; III, VI, IX R=H; IV, VII, X R=NO_2

was carried out in alcohol (with and without the addition of catalytic amounts of hydrochloric acid) and in anhydrous benzene (without the addition of hydrochloric acid), although acid accelerates the reaction considerably.

*See [1] for communication III.

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TABLE 1. Thio Derivatives of Phenoxazin-3-one

Comp.	R	mp °C (crystallization solvent)	R_f*	λ_{max}, nm (lg ε)
II	*p*-CH_3	161—162 (butanol)	0,29	482 (4,40)
III	H	162—163 (dimethylformamide + water)	0,32	475 (4,42)
IV	*p*-NO_2	250—251 (dimethylformamide + alcohol)	0,28	460 (4,36)
V	*p*-CH_3	225—226 (butanol)	0,52	433 (4,51)
VI	H	247—248 (butanol)	0,55	432 (4,45)
VII	*p*-NO_2	304—305 (dimethylformamide)	0,49	428 (4,44)
VIII	*p*-CH_3	232—233 (butanol)	0,53	486 (4,59)
IX	H	223—224 (butanol)	0,59	480 (4,55)
X	*p*-NO_2	258—259 (dimethylformamide + alcohol)	0,41	458 (4,59)

Comp.	Empirical formula	Found %				Calc. %				Yield, %
		C	H	N	S	C	H	N	S	
II	$C_{19}H_{13}NO_2S$	—	—	4,4	9,4	—	—	4,4	10,0	16
III	$C_{18}H_{11}NO_2S$	—	—	4,8	10,6	—	—	4,6	10,5	10
IV	$C_{18}H_{10}N_2O_4S$	61,9	3,1	—	9,0	61,7	2,9	—	9,2	22
V	$C_{19}H_{13}NO_2S$	—	—	4,0	10,2	—	—	4,4	10,0	12
VI	$C_{18}H_{11}NO_2S$	—	—	5,0	10,8	—	—	4,6	10,5	18
VII	$C_{18}H_{10}N_2O_4S$	61,7	3,1	8,4	9,2	61,7	2,9	8,0	9,2	15
VIII	$C_{26}H_{19}NO_2S_2$	70,9	4,4	3,2	14,5	70,6	4,3	3,2	14,5	32
IX	$C_{24}H_{15}NO_2S_2$	70,0	3,8	3,2	15,2	69,7	3,6	3,4	14,8	26
X	$C_{24}H_{13}N_3O_6S_2$	57,4	2,8	—	12,7	57,3	2,6	—	12,7	20

*On activity II Al_2O_3 with an anhydrous chloroform system.

†In chloroform, λ_{max} for phenoxazin-3-one is 447 nm.

A mixture of three products – II, V, and VIII in the addition of thiocresol, III, VI, and IX in the addition of thiophenol, and IV, VII, and X in the addition of p-nitrophenol (see scheme) – is formed as a result of the addition of thiophenols to phenoxazin-3-one. These products have different colors and R_f values (Table 1). They were separated by column chromatography on aluminum oxide.

Analysis established that II and V, III and VI, and IV and VII are isomeric products of the addition of one molecule of thiophenol to I, while VIII-X are the products of the addition of two molecules of thiophenols to I. Isomeric products II-IV and V-VII can add yet another molecule of thiophenol to form VIII-X.

Two monosubstituted II and disubstituted VIII were subjected to alkaline decomposition in order to establish the positions of the arylthio residues in isomeric compounds II-IV and V-VII as well as in VIII-X. It is known [5] that the benzoid portion of the molecule gives o-hydroxyaminophenol derivatives in the alkaline decomposition of phenoxazinone compounds. Identical hydroxyamines containing one tolylthio residue were obtained in the alkaline cleavage of II and VIII. This result makes it possible to conclude that the second arylthio residue in VIII-X is situated in the quinoid ring. This confirms the calculated data, according to which phenoxazin-3-one has two electrophilic positions – one in the benzoid ring and the other in the quinoid ring. The alkaline cleavage of II makes it possible to assume that II-IV ($R_f \approx 0.3$) have an arylthio residue in the benzoid ring, while the isomeric V-VII ($R_f \approx 0.5$) have an arylthio residue in the quinoid ring.

From the calculated data [4] and the results of alkaline cleavage, the most probable sites of addition of nucleophiles to I are the 1- and 7-positions.

In an investigation of the light absorption of II-X in the visible region (Table 1), it turned out that the addition of an arylthio residue to the quinoid ring leads to a hypsochromic shift of the first absorption band, while the addition of an arylthio residue to the benzoid ring results in a bathochromic shift of this band as compared with the absorption of I. The addition of two arylthio residues also results in a bathochromic shift of the first absorption band, but the shift is somewhat larger than in the case of II-IV. Similar shifts of the first absorption band also occur on annelation of the benzoid and quinoid halves of the phenoxazin-3-one molecule; the annelated benzene ring acts as an electron donor with respect to the fundamental phenoxazinone skeleton. Arylthio residues are also apparently electron donors with respect to phenoxazin-3-one.

EXPERIMENTAL

Addition of Thiocresol to Phenoxazin-3-one: 7-Tolylthiophenoxazin-3-one (II), 1-Tolylthiophenoxazin-3-one (V), and 1,7-Ditolylthiophenoxazin-3-one (VIII). Five to six drops of concentrated hydrochloric acid and 1.4 g (0.011 mole) of p-thiocresol were added to 1 g (0.005 mole) of phenoxazin-3-one in 20 ml of alcohol, and the mixture was allowed to stand at room temperature for 2.5-3 h after stirring for 10-15 min until the phenoxazin-3-one had dissolved completely to give a light-green solution of the leuco compound. To oxidize the leuco compound, two 5-6 ml portions of freshly prepared 10% alcoholic ferric chloride were added carefully with stirring at room temperature to a solution of the leuco compounds, allowing the mixture to stand for 10 min after each addition. Another 12-15 ml of the ferric chloride solution was added, and the mixture was heated at 50° for 15-20 min. The mixture was cooled, and the precipitate was filtered, washed with water and alcohol, and chromatographed in anhydrous chloroform on three 25 by 500 columns filled with activity II aluminum oxide. The first (red-orange) fraction was collected and evaporated to give 0.95 g of a mixture of V and VIII. The mixture was dissolved in boiling butanol, and the solution was filtered and cooled to 40°. The resulting crystals were filtered to give 0.45 g of VIII. The mother liquor was cooled to 0°, and the crystalline precipitate was filtered to give 0.15 g of V. The second (red) fraction was collected and evaporated to give 0.4 g of II (Table 1). Each compound was recrystallized.

Addition of Thiophenol and p-Nitrothiophenol to Phenoxazin-3-one. The reaction of phenoxazin-3-one with thiophenol proceeds in similar fashion in 24 h. Compounds VI and IX were fractionally crystallized from alcohol–chloroform (2:3).

The reaction of phenoxazin-3-one with p-nitrothiophenol was carried out by heating them at 50-60° for 4-5 h in alcohol–chloroform (1:1). The first (yellow) fraction from column chromatography contained VII, the second (red) fraction contained X, and the third (red) fraction contained IV.

1,7-Ditolylthiophenoxazin-3-one (VIII). One to two drops of concentrated HCl and 0.1 g (0.008 mole) of p-thiocresol were added to 0.2 g (0.0063 mole) of II or V in 5 ml of alcohol, and the mixture was heated on a water bath at 60-70° for 3-4 h until II or V had completely dissolved to give a light-green solution. The mixture was then oxidized as described above. The product was identical to VIII obtained from I according to the visible spectrum, melting point, and elementary analysis.

3-Hydroxy-4-amino-4-methyldiphenyl Sulfide (XI). 7-Tolylthiophenoxazin-3-one (II) [0.3 g (0.00094 mole)] or 0.4 g (0.0009 mole) of 1,7-ditolylthiophenoxazin-3-one (VIII) were moistened with 3-4 drops of alcohol, 8 ml of 4 N KOH was added, and the mixture was heated under argon on a boiling-water bath (for 1 h for II and for 3 h for VIII) until it no longer gave a spot for the starting compound (II or VIII) for thin-layer chromatography with aluminum oxide (in anhydrous chloroform). It was then cooled, filtered, and acidified to pH 3-4 with dilute hydrochloric acid. The resulting precipitate was filtered and dissolved in 0.05 N alkali. The solution was acidified to pH 3-4, and the precipitate was filtered. This operation was repeated two to three times, after which all of the mother liquors were combined, boiled with charcoal, filtered, cooled, and neutralized with ammonium bicarbonate. The precipitated amine was filtered and reprecipitated from weakly acid aqueous solution to give 0.03 g (14%) of XI with mp 109-110°. Found %: C 67.6; H 5.6; N 6.0; S 13.7. $C_{13}H_{13}NOS$. Calculated %: C 67.7; H 5.6; N 6.0; S 13.8.

Phenoxazin-3-one was obtained by the method in [6].

The visible spectra of 10^{-4} mole/liter solutions of I-X in chloroform were recorded with an SF-10 spectrophotometer.

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