OXIDATION OF ETHERS OF DERIVATIVES OF o-AMINOPHENOL BY LEAD DIOXIDE

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In developing the work described earlier [1] on the elucidation of the mechanism of the oxidation of o-aminophenol derivatives, we investigated the interaction of lead dioxide on a series of new ethers of o-amino-p-tert-butylphenol and their chloro derivatives.

The amines subjected to oxidation were produced through stepwise nitration of p-tert-butylphenol, alkylation of the nitroproduct with dimethyl sulfate or the corresponding alkyl halide, and catalytic reduction [2]. The step of chlorination of o-nitrophenols with gaseous chlorine was additionally conducted under various conditions for the production of chloro derivatives, depending on the desired end product [3].

Tables 1 and 2 present the characteristics of the ethers of derivatives of o-nitrophenol obtained and the amines corresponding to them.

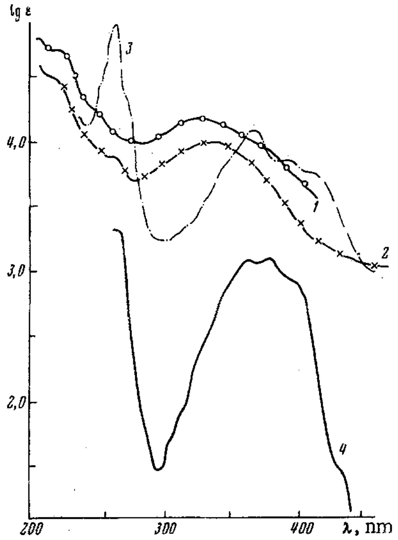
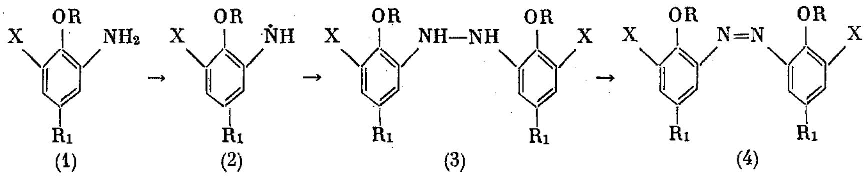


Fig. 1. UV spectra: 1) 3,3',5,5'-tetrachloro-2,2'-dimethoxyazobenzene (XX) with mp 204-205° (in ethanol); 2) 3,3'-dichloro-2,2'-dimethoxy-5,5'-di-tert-butylazobenzene (XVIII) with mp 160-161° (in ethanol); 3) 4,8-dichloro-2,6-di-tert-butylphenazine (XXIII) with mp 336° (subl.) (in CCl_4); 4) 2,6-dichlorophenazine (XXIV) with mp 260° (in CCl_4).

As a result of the oxidation of the amines obtained, in all cases, with the only exception the methyl ether of 4,6-dichloro-2-aminophenol (XIV), the formation of azo and phenazine compounds and a substantial amount of resinous products was observed, and the initial ether was also partially recovered.

The formation of the same 2,6-di-tert-butylphenazine (XXII) in the oxidation of various ethers of o-amino-p-tert-butylphenol [propyl (VIII), isopropyl (IX), and butyl (X)] is additional evidence that one of the reaction pathways is elimination of the alkoxyl group and cyclization of the molecule. Dehydrogenation at the amino group with the formation of the corresponding amines of azo compounds also proceeds simultaneously. Unfortunately, in view of the laboriousness of the separation of phenazine and azo derivatives and the multiplicity of operations on their purification, we were unable to establish the dependence of the predominant reaction pathway on the structure of the initial ether.

By analogy with the scheme of electrolytic oxidation of pentafluoroaniline proposed in [6], the possibility of simultaneous formation of the azo and phenazine derivatives in our case can be represented as follows



R = CH_3, i-C_3H_7, n-C_3H_7, C_4H_9; $R_1 = X$, t-C_4H_9; X = H, Cl

The free radical (2) initially obtained from the original amine (1) can dimerize to give the hydrazo compound (3), which is

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TABLE 1. Characteristics of the Ethers of o-Nitrophenol Derivatives Obtained

Compound No.	Ether	Bp, °C (p, mm Hg). Mp, °C	n_D^{20}	Found, %				Calculated, %				Yield, % of the theoretical (on the basis of reacted (XXVI))
				C	H	N	Cl	C	H	N	Cl	
I	Butyl ether of o-nitro-p-tert-butylphenol	158—159 (2,5)	1,5175	67,23 67,19	8,61 8,46	5,28 5,20	—	66,90	8,42	5,57	—	43,22 (92,38)
II	Isopropyl ether of o-nitro-p-tert-butylphenol	146—147 (2)	1,5180	65,77 65,89	7,78 8,06	5,75 5,41	—	65,80	8,07	5,90	—	40,44
III	Propyl ether of o-nitro-p-tert-butylphenol	136—137 (2,5)	1,5213	65,94 65,95	8,00 7,86	5,76 5,48	—	65,80	8,07	5,90	—	32,31
IV	Methyl ether of 4-chloro-2-nitrophenol	96,5—97,5 *	—	44,98 44,74	2,98 3,02	7,50 7,56	18,80 19,00	44,80	3,20	7,46	18,93	72,80
V	Methyl ether of 4,6-dichloro-2-nitrophenol	42,5—43†	—	—	—	6,59 6,31	32,15	—	—	6,30	31,96	44,90
VI	Methyl ether of 6-chloro-2-nitro-4-tert-butylphenol	49,5—50	—	54,67 54,55	5,88 5,86	5,73 5,80	15,04 15,23	54,54	5,80	5,80	14,54	84,90
VII	Ethyl ether of 6-chloro-2-nitro-4-tert-butylphenol	157—158 (2,5)	1,5265	55,50 55,76	5,95 5,92	5,72 6,15	13,77 14,29	55,92	6,25	6,25	13,70	61,60 (85,79)

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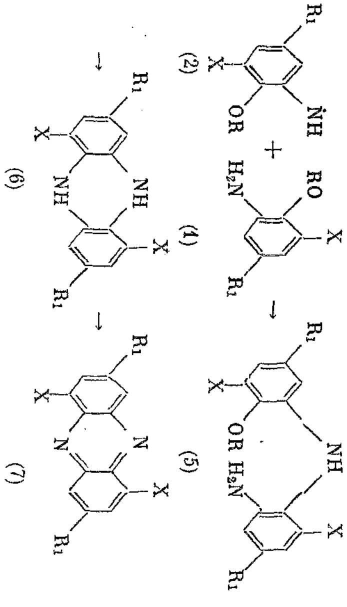
* According to the data of [4]: mp 97°.

†According to the data of [5]: mp 44°.

subsequently oxidized to the azo derivative (4). Phenazines can be obtained in the interaction of radical (2) with the amine (1) with the formation of 2-amino-2'-alkoxy-4,5'-di-tert-butyldiphenylamine (5), when $R_1 = C(CH_3)_3$, X = H. The latter, undergoing intramolecular cyclization upon further oxidation, is converted to a 9,10-dihydrophenazine compound (6), and, finally, to the phenazine derivative (7)



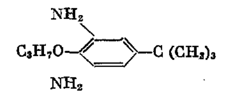
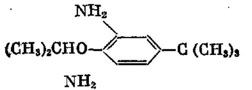
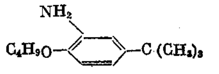
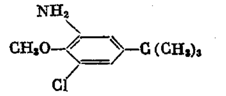
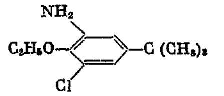
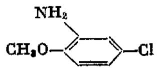
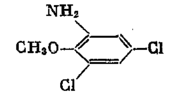
Attempts to detect free radicals by the EPR method were unsuccessful. Evidently the lifetime of the radicals formed under these conditions is too short, and they immediately enter into secondary reactions. The phenazine and azo compounds formed were obtained in pure form from the mixture by growing crystals, by mechanical selection, and subsequent repeated recrystallization. Their characteristics are cited in Table 3. The phenazines isolated are light-yellow crystals with a high melting point, sparingly soluble in organic solvents, and most readily soluble in chloroform. The azo compounds are relatively readily soluble in many solvents; in comparison with the phenazines they have a lower melting point; they were obtained in the form of bright red prisms or needles, while the chloro derivatives had a yellow or brown color. The structure of the isolated oxidation products was confirmed by the UV spectra (Fig. 1), which were compared with those obtained earlier [1].

EXPERIMENTAL

6-Chloro-2-nitro-4-tert-butylphenol (XXV). Synthesized by the chlorination of o-nitro-p-tert-butylphenol (XXVI) with n_D^{20} 1.5528 with gaseous Cl_2 in the presence of 2 g $AlCl_3$ for 2 h at 60°C. After washing with water, dilution of the reaction mass with ethanol, and evaporation of the solvent, a mixture of yellow crystals with liquid was obtained. The liquid, representing the starting material (XXVI), in an amount of 27.93 g was removed by filtration from the crystals with mp 58-80°C (18.55 g, 84.50% of the reacted starting material). After several recrystallizations from ethanol and petroleum ether, we isolated (XXV), in the form of lemon yellow crystals with mp 74-74.5°C. In addition, we obtained a small quantity (XXIX) with mp 120-120.5°C.

Synthesis of 4-Chloro-2-nitrophenol (XXVII). The synthesis was conducted with 13.6 g (XXVI) in 7 ml CCl_4

TABLE 2. Characteristics of the Amines Obtained

Number	Compound	Bp, °C (p, mm Hg), Mp, °C	n_D^{20}	Found, %		Calculated, %		Yield, %
				N	Cl	N	Cl	
VIII		36—37	—	6,57 6,70	—	6,75	—	93,53
IX		117,5 (3)	1,5208	6,43 6,29	—	6,75	—	94,36
X		143,5—144 (2,5)	1,5188	6,02 5,97	—	6,32	—	93,61
XI		117,5—118 (2)	1,5476	6,31 6,52	16,95 16,75	6,55	16,62	87,10
XII		144 (2)	1,5389	5,58 5,77	15,53	6,15	15,52	71,89
XIII		81,5—82 *	—	8,79 8,98	23,18 23,34	8,88	22,50	65,20
XIV		111—113 (2,5)	1,5848	6,75 7,02	36,96	7,29	37,26	97,59

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* According to the data of [4]: mp 82°.

in the presence of 0.02 g I_2. When Cl_2 was passed through, the temperature of the reaction mixture rose spontaneously to 40°. The time of chlorination was 2 h 10 min, resulting in the isolation of 11.70 g (96.6%) of a crystalline mass with an extended mp 49-85°. After several recrystallizations from petroleum ether, we isolated 2.5 g (20.6%) (XXVII) with mp 86-87°. The remaining, lower-melting portion was a mixture of unknown composition.

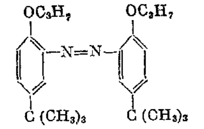
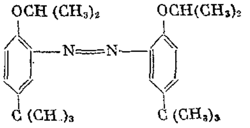
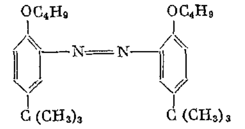
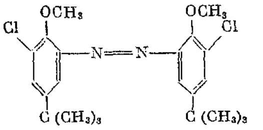
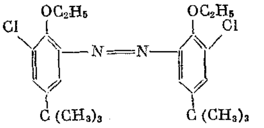
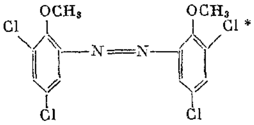
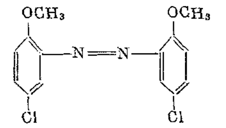
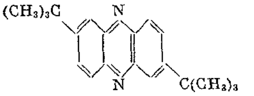
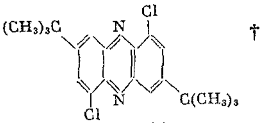
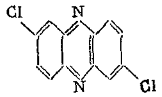
4,6-Dichloro-2-nitrophenol (XXVIII). Produced by chlorination of the phenolate of o-nitrophenol (50 g in 50 ml of 40% KOH) in the presence of 2 g $AlCl_3$ and a small crystal of I_2. When Cl_2 was passed through, the temperature rose spontaneously to 80°. After 2 h 40 min elapsed, the entire mass was diluted with water (to 1000 ml); filtration of the precipitated crystals and recrystallization from petroleum ether isolated (XXIX) with mp 121°; 12.6 g (16.25%).

Synthesis of the Butyl Ether of o-Nitro-p-tert-butylphenol (I). The synthesis was conducted in a four-necked flask equipped with a mixer, reflux condenser, dropping funnel and thermometer. To the phenolate, produced from 39 g (XXVI) and 8.0 g NaOH (10% excess) in 200 ml of ethanol, 110.4 C_4H_9I was added dropwise over a period of 3.5 h at the boiling point of the alcohol. Then mixing was continued for another 4.5 h under the same conditions. The alcohol was distilled off under a slight vacuum; a NaI precipitate appeared in the flask. The product, diluted with ether, was washed repeatedly with 2% NaOH to remove the initial nitrophenol (XXVI), until coloration of the alkaline solution ceased, then washed with water. The unreacted product (XXVI) was isolated from the wash waters by decomposing the phenolate with a concentrated solution of HCl, extracted with ether, and washed with water. After the ether was evaporated, 20.73 g of the starting material with n_D^{20} 1.5528 was isolated from the solution, dried over Na_2SO_4.

The ether solution after the alkaline washings was dried over Na_2SO_4, and after the solvent was distilled off by vacuum distillation (I) was isolated with bp 158-159° (2.5 mm) and n_D^{20} 1.5175; 21.70 g [43.2% of the theoretical and 92.38% of the reacted (XXV)].

Methyl Ether of 6-Chloro-2-nitro-4-tert-butylphenol (VI). Synthesized by the dropwise addition of 11 ml dimethyl sulfate over a period of 25 min at 70° to the phenolate obtained from 25.16 g 6-chloro-2-nitro-4-tert-butylphenol and 6.76 g KOH in 200 ml of water. The end of the reaction was judged according

TABLE 3. Characteristics of the Isolated Oxidation Products

Number	Compound	Mp, °C	Found, %		Calculated, %	
			N	Cl	N	Cl
XV		141—141,5	6,51 6,80	—	6,82	—
XVI		131—132	6,84 7,14	—	6,82	—
XVII		105	6,40 6,45	—	6,38	—
XVIII		160—161	6,84 7,03	16,46 16,50	6,62	16,77
XIX		124,5—125	6,29 6,21	16,03 15,86	6,20	15,50
XX	 *	204—205	7,63	37,26 37,45	7,36	37,34
XXI		199,5—200	9,19 9,07	22,89	8,99	22,81
XXII		215,5—216	—	—	—	—
XXIII	 †	336 (subl)	8,11 8,03	19,27 19,32	7,74	19,64
XXIV	 ‡	260	11,13 11,27	28,51	11,24	28,49

* Found: C 44.27; 44.36; H 2.71; 2.80%. Calculated: C 44.22; H 2.65%.

†Found: C 67.19; 67.13; H 6.20; 6.39%. Calculated: C 66.60; H 6.15%.

‡According to the data of [7]: mp 265°.

to clarification of the solution. After treatment analogous to that described above, the alkaline solutions were used for six repeated reactions without isolation of the starting material. When the solvent was evaporated from the ether solution, crystals were isolated in the form of needles with mp 47-49°; 22.7 g (84.90% of the theoretical). Recrystallization from ethanol yielded (VI) with mp 49.5-50°.

Methyl ethers of 4, 6-dichloro-2-nitrophenol (V) and 4-chloro-2-nitrophenol (IV) were synthesized analogously to (VI). The isopropyl ether of o-nitro-p-tert-butylphenol (II), the propyl ether of

TABLE 4. Yields of Oxidation Products

Starting material (g)	Oxidation products, color, and form of crystals	Yield		Method of isolation and purification of individual substances
		reaction mixture after oxidation, g(mixture of crystalline products, g)	pure individual substances, g/% of theoretical (% of reacted starting material)	
VIII (10)	XV, bright red rods	10 (2,69)	XV $\frac{1,30}{6,56\,(7,31)}$	Grown from alcohol
	XXII, light-yellow plates		XXII $\frac{1,1}{7,80\,(8,68)}$	Recrystallized from benzene
			VIII $\frac{1,02}{10,2}$	Vacuum distillation of resinous substance
IX (10)	XVI, dark red rods	10 (0,55)	XVI $\frac{0,03}{0,15}$	The same as the corresponding (XV), (XXII), and (VIII)
	XXII		XXII $\frac{0,54}{3,83}$	
			IX, several drops	
X (10)	XVII, bright red rods	9,58 (2,75)	XVII $\frac{1,88}{9,49\,(12,72)}$	The same
	XXII		XXII $\frac{0,57}{4,32\,(5,78)}$	
			X $\frac{2,54}{25,4}$	
XI (7,22)	XVIII, terra cotta rods	(0,99)	XVIII $\frac{0,65}{4,68\,(4,90)}$	Recrystallized from petroleum ether
	XXIII, yellow plates		XXIII $\frac{0,22}{1,70\,(1,72)}$	Purification by sublimation under vacuum at 3 mm
			XI $\frac{0,12}{16,6}$	At beginning of sublimation
XII (8,15)	XIX, terra cotta rods	8,15	XIX $\frac{1,28}{7,92\,(10,87)}$	Growth of crystals from petroleum ether, crystallization from acetic acid
	XXIII		XXIII $\frac{0,16}{1,24\,(1,85)}$	Crystallization from petroleum ether
			XII $\frac{2,71}{33,1}$	Vacuum sublimation
XIII (2,92)	XXI, brown needles	2,52	XXI $\frac{0,56}{9,80}$	Successive crystallization from petroleum ether, alcohol, and CCl_4
	XXIV, pale yellow needles		XXIV $\frac{0,05}{1,08}$	Crystallization from acetic acid
XIV (5,92)	XX, orange needles	5,06	XX $\frac{0,28}{2,5\,(4,00)}$	From benzene
			$\frac{2,4}{40,5}$	Vacuum distillation

o-nitro-p-tert-butylphenol (III), and the ethyl ether of 6-chloro-2-nitro-4-tert-butylphenol (VII) were produced similarly to (I) by the interaction of the phenolate of the nitro product with the corresponding alkyl iodide.

Oxidation of the Propyl Ether of o-Amino-p-tert-butylphenol (VIII). To 10.0 g (VIII) in 70 ml dry benzene we added 57.70 g PbO_2 (5 moles per mole of the ether) and boiled the reaction mixture with a reflux condenser for 1 h. In this case the appearance of drops of water on the walls of the flask and a change in the color first to yellow, then to brownish red, were observed. After cooling, the solution was filtered twice through a double filter. The precipitate was washed repeatedly with benzene with heating, followed by decantation and filtration until an uncolored solution was obtained (~200 ml of benzene consumed). After the benzene was distilled off from the filtrate, a crystalline product remained with a dark-colored resin in an amount of 10 g. Washing with petroleum ether (70 ml) isolated 2.69 g of the product, representing a mixture of two types of crystals. Crystallization from benzene isolated 1.1 g [7.8% of the theoretical, 8.68% of the reacted (VIII)] of 2,6-di-tert-butylphenazine (XXII) with mp 215.5-216° in the form of yellow plates. A mixed sample with the previously isolated (XXII) [1] gave no depression of the melting point. The second oxidation product could not be isolated by crystallization on account of a constant impurity of (XXII). To obtain it in pure form, large crystals were grown from an alcohol solution, followed by their mechanical selection under a magnifier. Thus, we isolated 1.3 g [6.56% of the theoretical and 7.31% of the reacted (VIII)] of 2,2'-dipropoxy-5,5'-di-tert-butylazobenzene (XV) in the form of red needles with mp 141-141.5°. From the resin remaining 1.02 g of the starting material (VIII) was isolated by vacuum distillation. All the synthesized amines were oxidized with lead dioxide and treated analogously to that described above. Table 4 indicates the isolated oxidation products in each case, their yields, and the differences in the conditions of isolation or purification.

CONCLUSIONS

1. In the oxidation of the ethers of derivatives of o-aminophenol studied with lead dioxide, the reaction proceeds simultaneously in two directions: with the formation of phenazine derivatives and azo compounds.

2. Twenty previously undescribed substances were produced and characterized.

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