

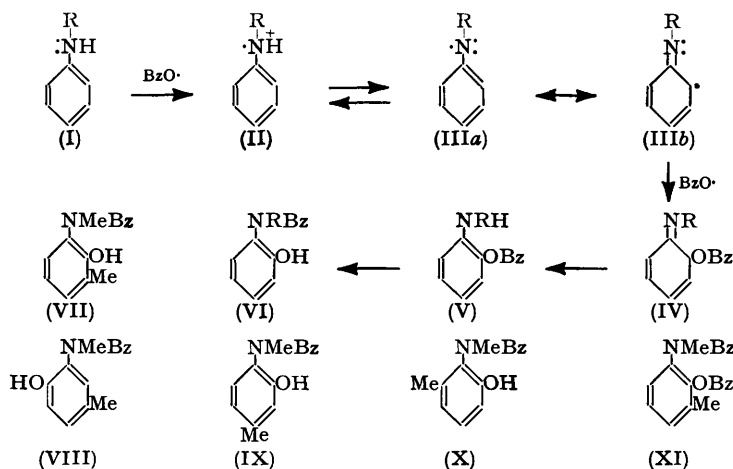
The Oxidation of N-Alkylanilines and Related Compounds with Benzoyl Peroxide.

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Monoalkylamino-aromatic compounds are oxidized by benzoyl peroxide to *o*-benzamidophenols.

BECAUSE of the widespread occurrence in Nature of *o*-aminophenolic compounds (*e.g.*, 3-hydroxyanthranilic acid, damascanene, vomicine), methods for their preparation by the direct oxidation of aromatic amines are of some interest. Gambarjan (*Ber.*, 1909, **42**, 4003) found that diphenylamine (I; R = Ph) was oxidized by benzoyl peroxide to *o*-*N*-phenylbenzamidophenol (VI; R = Ph) in 38% yield. The reaction is generally applicable to secondary aromatic amines, as shown by the results in Table I. Yields are low, but the simplicity of the reaction and the ease of isolating the phenol will commend the method



in some instances. With most amines the reaction is complete in 10–15 minutes. However, *p*-chloro-*N*-methylaniline is oxidized more slowly, and *N*-methylanthranilic acid resists attack (cf. Horner and Scherf, *Annalen*, 1951, **573**, 35).

Except for *o*-*N*-methylbenzamidophenol (VI; R = Me) (Clark, *J.*, 1926, 232) and its ethyl analogue (VI; R = Et) (Anderson and Bell, *J.*, 1949, 2668), the phenols in Table 1 are new compounds. The structures (VI; R = Me, Et, and CH₂Ph) for the phenols from *N*-methyl-, *N*-ethyl-, and *N*-benzyl-aniline were proved by preparing these phenols also by the alkylation of 2-phenylbenzoxazole and hydrolysis of the benzoxazolium salts (cf. Clark, *loc. cit.*). The phenols (VI; R = Prⁿ and Buⁿ) were obtained in small yield by the alkylation and subsequent benzylation of *o*-aminophenol; the *o*-benzamidophenol also formed was converted into 2-phenylbenzoxazole by heating the product to 170°, the unchanged *o*-*N*-alkylbenzamidophenols being extracted from the cooled melt with alkali. They were identical with the phenols obtained by oxidizing (I; R = Prⁿ and Buⁿ). 1-Benzoyl-1 : 2 : 3 : 4-tetrahydro-8-hydroxyquinoline was prepared by benzylation of 1 : 2 : 3 : 4-tetrahydro-8-hydroxyquinoline in sodium carbonate solution, and identified (m. p. and mixed m. p.) with the oxidation product of 1 : 2 : 3 : 4-tetrahydroquinoline.

The assumption that the other phenols are also *o*-benzamidophenols results in unambiguous structures for all of them except that obtained from *N*-methyl-*m*-toluidine, which could be (VII) or (VIII). The infra-red absorption spectrum of this compound (A)

TABLE 1. Phenols from the oxidation of amines with benzoyl peroxide.

Amine oxidized	Phenol	Yield, %	M. p.	Formula	C, H, %	
					Found	Reqd.
<i>N</i> -Methylaniline	<i>o</i> - <i>N</i> -Methylbenzamidophenol	30	158—159° ^a	C ₁₄ H ₁₃ O ₂ N	74.4	5.8
<i>N</i> -Ethylaniline	<i>o</i> - <i>N</i> -Ethylbenzamidophenol	37	160—162 ^b	C ₁₅ H ₁₅ O ₂ N	74.6	6.2
<i>N</i> -Propylaniline	<i>o</i> - <i>N</i> -Propylbenzamidophenol	20	131—134	C ₁₆ H ₁₇ O ₂ N	75.0	6.4
<i>N</i> -Butylaniline	<i>o</i> - <i>N</i> -Butylbenzamidophenol	35	120—122	C ₁₇ H ₁₉ O ₂ N	75.7	6.8
<i>N</i> - <i>iso</i> Pentylaniline	<i>o</i> - <i>N</i> - <i>iso</i> Pentylbenzamidophenol	20	77—81	C ₁₈ H ₂₁ O ₂ N	76.5	7.4
<i>N</i> -Benzylaniline	<i>o</i> - <i>N</i> -Benzylbenzamidophenol	8	159—160	C ₂₀ H ₁₇ O ₂ N ^c	79.2	5.6
<i>N</i> -Methyl- <i>o</i> -toluidine	3-Methyl-2- <i>N</i> -methylbenzamidophenol	8	152—155	C ₁₅ H ₁₅ O ₂ N	74.3	6.1
<i>N</i> -Methyl- <i>m</i> -toluidine	4-Methyl-2- <i>N</i> -methylbenzamidophenol	10	213—215	C ₁₅ H ₁₅ O ₂ N	74.0	6.5
<i>N</i> -Methyl- <i>p</i> -toluidine	5-Methyl-2- <i>N</i> -methylbenzamidophenol	31	189—193	C ₁₅ H ₁₅ O ₂ N	74.3	6.2
<i>p</i> -Chloro- <i>N</i> -methylaniline	5-Chloro-2- <i>N</i> -methylbenzamidophenol	19	210—211	C ₁₄ H ₁₂ O ₂ NCl	64.5	4.4
<i>N</i> -Ethyl- α -naphthylamine	1- <i>N</i> -Ethylbenzamido-2-naphthol	40	228—230	C ₁₉ H ₁₇ O ₂ N	77.4	5.7
1 : 2 : 3 : 4-Tetrahydroquinoline	1-Benzoyl-1 : 2 : 3 : 4-tetrahydro-8-hydroxyquinoline	16	174—175	C ₁₈ H ₁₅ O ₂ N ^d	75.7	5.9

^a Clark (*loc. cit.*) reports m. p. 164°. ^b Anderson and Bell (*loc. cit.*) report m. p. 164°. ^c Found : N, 4.6. Required : N, 4.7%. ^d Found : N, 5.6. Required : N, 5.5%.

TABLE 2. Infra-red absorption of some benzamidophenols.

	1 : 2 : 4-Compounds			1 : 2 : 3-Compounds	
	Normal *	(IX)	A	Normal *	(X)
C-H out-of-plane deformation	810	807	806	770	(774, 778) †
"Ring-breathing" frequency	1000w	—	1003w	1010s	1008s
C-H in-plane deformation	1125	1128	1121	1095	1104

w = weak, s = strong.

* Whiffen and Thompson, *J.*, 1945, 268; Whiffen, personal communication.

† The second band is probably due to the vibration (unknown) giving rise to a band at 785 cm.⁻¹ in (IX) and 781 cm.⁻¹ in A.

in a Nujol mull over the range 1300—670 cm.⁻¹ (Table 2) indicates that it is most probably a 1 : 2 : 4-trisubstituted benzene, and so favours (VIII); the spectra of the phenols (IX) from *N*-methyl-*p*-toluidine and (X) from *N*-methyl-*o*-toluidine are included for comparison. (For these measurements and their interpretation I am greatly indebted to Dr. D. H.

Whiffen.) The formula (VII) for the phenol from *N*-methyl-*m*-toluidine would, on the mechanism advanced below, require (XI) as an intermediate; and space-filling models show that the formation of this compound is extremely difficult because of steric hindrance.

The neutral products of the oxidations were usually intractable tars. Very small quantities of crystalline products could be separated by chromatography on alumina; the structure of these compounds is uncertain, and is being investigated further.

The work of Horner and his co-workers (*loc. cit.*; Horner and Schwenk, *Annalen*, 1950, 566, 69; Horner and Betzel, *ibid.*, 1953, 579, 175; Horner and Hubenett, *Ber.*, 1952, 85, 804) indicates strongly that the first stage in the attack of benzoyl peroxide on an aromatic amine is the abstraction of one electron and the formation of an aminium ion-radical. In the case of secondary amines (I) the aminium ion (II) may lose a proton to the benzoate ion and form the conjugate base (III) which, like (II), exists as a resonance hybrid of which two canonical forms are shown. The subsequent steps (IIIb \rightarrow IV \rightarrow V \rightarrow VI) all find ample analogy in the literature, the last stage being the ready *ortho*-O \rightarrow N migration of an acyl group (Taylor and Baker, "Sidgwick's Organic Chemistry of Nitrogen," Clarendon Press, Oxford, 1945, p. 75). This mechanism is similar to that of Cosgrove and Waters (*J.*, 1949, 3189) for the oxidation of phenols by benzoyl peroxide.

EXPERIMENTAL

Formation of Phenols by Oxidation with Benzoyl Peroxide.—Benzoyl peroxide was crystallized by addition of methanol to a concentrated solution in chloroform, and dried thoroughly *in vacuo* at room temperature. It was added to an equimolar quantity of the amine dissolved in about 20 volumes of benzene and cooled in ice. After 20 min. (or overnight for *p*-chloro-*N*-methylaniline) the solution was extracted with dilute aqueous sodium hydroxide. The gummy solid obtained on acidification was washed with sodium hydrogen carbonate to remove benzoic acid, and then digested with a small quantity of aqueous methanol. The yield of crude phenol is recorded in Table 1; one or two recrystallizations from aqueous methanol (charcoal) afforded the pure phenol as colourless needles or rhombs.

The phenol from *N*-ethyl- α -naphthylamine crystallized directly from the reaction mixture in almost pure condition; extraction of the benzene solution with alkali removed only a very small additional quantity of impure product.

Equally good yields of phenols were obtained by conducting the oxidations in formamide or chloroform solution, but use of ethyl ether gave lower yields. The yield decreased when the molar ratio of amine to peroxide was greater or less than 1 : 1. Alteration of the temperature of the reaction had little effect.

The phenols, like *o*-benzamidophenol, gave no colour with aqueous ferric chloride or with anhydrous ferric chloride in chloroform-pyridine (cf. Soloway and Wilson, *Analyt. Chem.*, 1952, 34, 979). They gave a feeble Millon reaction. In concentrated sulphuric acid, on addition of a drop of 40% aqueous formaldehyde, 1-*N*-ethylbenzamido-2-naphthol gave a blue colour fading to green, *o*-*N*-benzylbenzamido-phenol gave a red, and 4-methyl-2-*N*-methylbenzamido-phenol a pink colour. It was necessary to heat the mixture containing 3-methyl-2-*N*-methylbenzamido-phenol (orange red) and the *o*-*N*-alkylbenzamido-phenols (gold or sherry colours); even under these conditions 5-chloro-2-*N*-methylbenzamido-phenol gave no colour.

Formation of Phenols from 2-Phenylbenzoxazole.—The benzoxazolium compounds were prepared by refluxing a solution of 2-phenylbenzoxazole with an alkylating agent (methyl sulphate in benzene for 7 hr.; ethyl sulphate in xylene for 3 hr.; benzyl bromide in dimethylformamide for 5 hr.). The cooled solution was treated with aqueous alkali, the aqueous solution was extracted with benzene to remove neutral materials, and the *o*-benzamido-phenols (VI; R = Me, Et, and CH₂Ph) were precipitated by acidification. These were identical (m. p. and mixed m. p.) with those from the oxidation of (I; R = Me, Et, and CH₂Ph). The m. p.s of R = Me and Et) are lower than those reported in the literature, but are very greatly affected by the rate of heating.

Formation of Phenols from o-Aminophenol.—*n*-Propyl bromide (2 c.c.) and *o*-aminophenol (2 g.) were heated in ethanol (15 c.c.) under reflux for 4 hr. The residue after removal of the ethanol was benzoylated in aqueous sodium carbonate and the phenols were extracted with benzene. They were then transferred to aqueous alkali, and the mixed benzamidophenols (m. p. ca. 100°) precipitated by making the solution strongly acidic. This material was heated to 170° for 10 min.; unchanged *o*-*N*-propylbenzamido-phenol was extracted from the cooled

melt with alkali, and crystallized from aqueous methanol as clear cubes. It was identical (m. p. and mixed m. p.) with the phenol from the oxidation of (I; R = Prⁿ). In the same way (VI; R = Buⁿ) was prepared and proved identical with the oxidation product of (I; R = Buⁿ).

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