

Oxidation of *N*-Hydroxy-amines by Sulphuryl Chloride

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Reactions of *N*-hydroxy-amines with sulphuryl chloride in ether gave *N*-chloro-*N*-hydroxyammonium salts. Work-up of these salts with aqueous potassium hydroxide afforded nitrones or nitrosobenzenes, depending on the starting materials. Reactions in acetonitrile, in which the intermediate salts are soluble, yielded products of further reaction of the nitrones.

THE preparation of nitrones or *C*-nitroso-compounds from the corresponding hydroxylamines has been achieved by a variety of oxidizing agents, such as molecular oxygen,¹ cerium(IV),² hexacyanoferrate(III),² and evidence suggesting that the reaction proceeds by a one-electron oxidation to give an intermediate nitroxide radical has

RESULTS AND DISCUSSION

Reaction of NN-Dibenzylhydroxylamine.—When *NN*-dibenzylhydroxylamine (1) in ether was added slowly to a mixture of sulphuryl chloride and ether at room temperature, a white solid precipitated out quantitatively. This solid, which was unstable in solution, was

TABLE I

Physical data of *NN*-dibenzylhydroxylamine hydrochloride and its analogues

	M.p. (°C)	$\nu_{\max.}/\text{cm}^{-1}$	δ^a	<i>m/e</i>
[PhCH ₂ ·NCl(OH)·CH ₂ Ph] ⁺ Cl ⁻ (2)	157—161	2 750, 2 700, 2 600	4.47 (2 H, d, <i>J</i> 14 Hz), 4.69 (2 H, d, <i>J</i> 14 Hz)	211
[PhCH ₂ ·NBr(OH)·CH ₂ Ph] ⁺ Br ⁻	136—139	2 749, 2 685, 2 640, 2 590	4.47 (2 H, d, <i>J</i> 14 Hz), 4.69 (2 H, d, <i>J</i> 14 Hz)	211
[PhCH ₂ ·NH(OH)·CH ₂ Ph] ⁺ Cl ⁻ (3)	173—175	2 760, 2 700, 2 629	4.42 (2 H, d, <i>J</i> 12 Hz), ^b 4.68 (2 H, d, <i>J</i> 12 Hz) ^b	213
[PhCH·N(OH)·CH ₂ Ph] ⁺ Cl ⁻ (4)	104—108	2 470, 2 150	5.70 (2 H, s), 8.84 (1 H, s)	211

* Methan[²H]ol used as solvent. ^b Data at -30 °C; at room temperature a broad doublet [δ 4.42 (4 H, *J* 8 Hz)] was observed.

been obtained. Recently it was reported that iodine and *N*-bromosuccinimide can oxidize *NN*-dibenzylhydroxylamine, and it was proposed that this reaction proceeds through a similar intermediate.³ However we now report that *N*-hydroxy-amines are oxidized by sulphuryl chloride *via* formation of an *N*-chloro-*N*-hydroxyammonium salt followed by elimination of two molecules of hydrogen chloride.

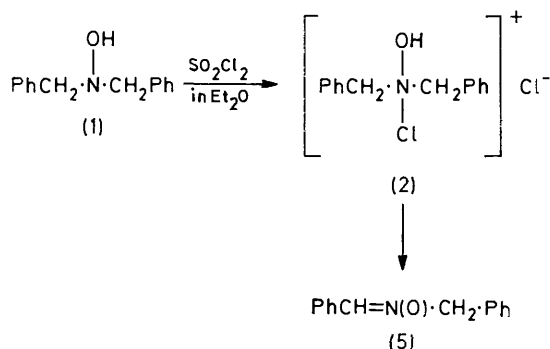
identified as *N*-chloro-*N*-hydroxydibenzylammonium chloride (2) as follows. Its physical properties were similar to those of *NN*-dibenzylhydroxylamine hydrochloride (3) (Table I). Its i.r. spectrum suggested that it was a hydroxyammonium salt, and no sulphonyl absorption was detected. The n.m.r. spectrum of the salt (2) was almost identical with that of (3), when it was measured just after dissolution in methan[²H]ol. The

¹ D. J. Cowley and W. A. Waters, *J. Chem. Soc. (B)*, 1970, 96.

² C. J. W. Gutch and W. A. Waters, *J. Chem. Soc.*, 1965, 751.

³ P. A. S. Smith and S. E. Gloyer, *J. Org. Chem.*, 1975, 40, 2508.

spectrum then changed gradually to that of the mixture of (2) and *N*-benzyl-*N*-hydroxybenzylideneammonium chloride (4). The mass spectrum of (2), which loses hydrogen chloride easily upon heating, was identical with that of (4). Treatment of the salt (2) with aqueous potassium hydroxide gave the nitrone (5) quantitatively. When the salt (2) was treated with hydrochloric acid, *NN*-dibenzylhydroxylamine (1) was recovered quantitatively. The reaction of the hydroxylamine (1) with bromine similarly afforded an intermediate salt (Table 1), and after conventional work-up the nitrone (5) was again obtained in quantitative yield.



The products from the corresponding reaction in acetonitrile, in which the intermediate (2) is soluble,

unstable in methan[²H]ol, giving an n.m.r. spectrum identical with that of the nitrone (8) hydrochloride (Table 2). The mass spectrum consisted of peaks due to a mixture of hydrochlorides of the nitrones (8) and (9). The products depend markedly on the conditions of work-up. When the salt (7) was added to methanolic potassium hydroxide at -70°C , the nitrone (9) was obtained in 75% yield, however treatment with aqueous potassium hydroxide at 0°C afforded only the nitrone (8) (73%). Although no conclusive evidence was obtained we consider that the salt (7) is *N*-chloro-*N*-hydroxybenzyl(phenyl)ammonium chloride from the above results. The mode of formation of the nitrone (8) is not clear; it is not obtained by treatment of the nitrone (9) with hydrogen chloride or sulphuryl chloride. The reaction of (6) with sulphuryl chloride in acetonitrile afforded only benzaldehyde.

Reaction of N-Phenylhydroxylamine.—The salt (11) obtained from the reaction of *N*-phenylhydroxylamine (10) with sulphuryl chloride was very unstable at room temperature, and was not isolated. The derived products depend on the reaction temperature. When the reaction was performed at -30°C and the mixture was immediately poured into ice-cold potassium hydroxide, nitrosobenzene (12) was obtained in 55% yield. On the other hand, reaction at 0°C afforded only 4,4'-dichloroazoxybenzene (13). In reactions with bromine,

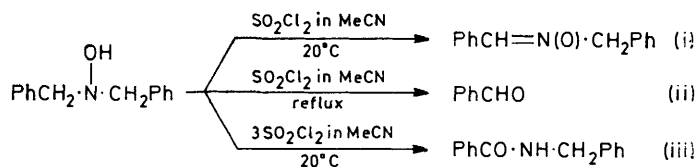
TABLE 2

Physical data of *N*-benzyl-*N*-phenylhydroxylamine hydrochloride and its analogues

	M.p. ($^\circ\text{C}$)	$\nu_{\text{max.}}$ /cm ⁻¹	δ^a	m/e
[PhCH ₂ ·NCl(OH)Ph] ⁺ Cl ⁻ (7)	<i>b</i>	2 550—2 400	<i>c</i>	233, 231, 197
[PhCH ₂ ·NH(OH)Ph] ⁺ Cl ⁻	94.0—95.5	2 520—2 370	4.75 (2 H, s)	199
[PhCH ₂ ·N(OH)·C ₆ H ₄ Cl- <i>p</i>] ⁺ Cl ⁻	154—158	2 150—2 000	8.70 (1 H, s)	233, 231

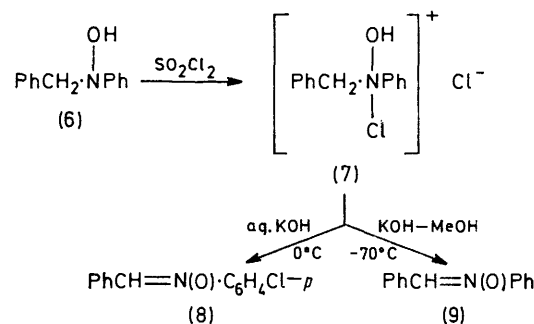
^a In methan[²H]ol. ^b No sharp m.p. ^c N.m.r. spectrum in methan[²H]ol identical with that of (8) hydrochloride.

depend on the reaction conditions. When the hydroxylamine (1) reacted with 1 mol. equiv. of sulphuryl chloride at room temperature, the salt (2) was formed, and treatment with aqueous potassium hydroxide gave the nitrone (5) in 59% yield [reaction (i)]. A similar reaction at reflux temperature afforded benzaldehyde (90% yield) [reaction (ii)]. It is well known that the salt (3) is hydrolysed easily in the presence of hydrochloric acid to give benzaldehyde and *N*-benzylhydroxylamine.⁴ Use of 3 mol. equiv. of sulphuryl chloride at room temperature gave *N*-benzylbenzamide (95%) [reaction (iii)], presumably by the sulphuryl chloride-catalysed isomerization of the nitrone (5).⁵



Reaction of N-Benzyl-N-phenylhydroxylamine.—The reaction of *N*-benzyl-*N*-phenylhydroxylamine (6) with sulphuryl chloride also afforded a salt (7). This salt is

even at low temperature, 4,4'-dibromoazoxybenzene only was obtained (72% yield). The initial production of

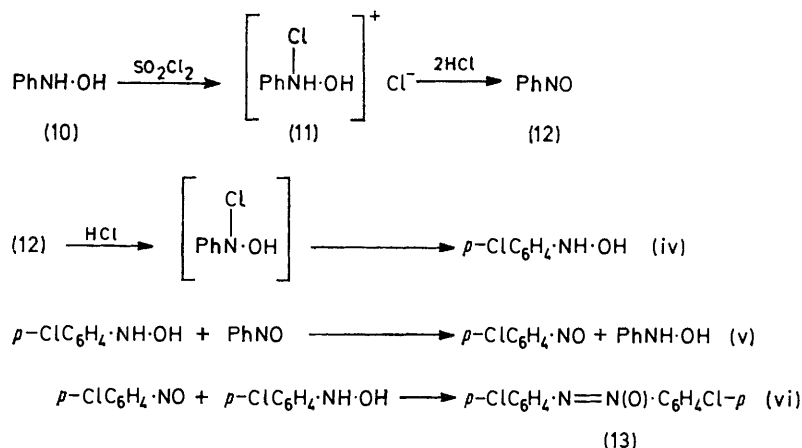


N-chloro-*N*-hydroxyanilinium chloride (11) reasonably explains the formation of nitrosobenzene. Treatment of nitrosobenzene (12) with hydrogen chloride in ether at 0°C gave 4,4'-dichloroazoxybenzene (13) in 88% yield. Thus (12) is apparently the precursor of (13) in this

⁴ F. Kroehnke, *Angew. Chem.*, 1953, **65**, 612.

⁵ J. Tananescu and J. Nanu, *Ber.*, 1942, **75**, 1287.

reaction. It has been suggested the reaction of nitrosobenzene (12) with hydrochloric acid affords *N*-(*p*-chlorophenyl)hydroxylamine *via* *N*-chloro-*N*-phenylhydroxylamine [reaction (iv)],⁶ and it is reported that the reaction of *p*-chloronitrosobenzene with *N*-phenylhydroxylamine yields (13) as the major product, by a route involving rapid preliminary equilibration between the reactants [reaction (v)].⁷ However the formation of (13) from nitrosobenzene and hydrogen chloride in such a high yield as 88% cannot be explained in terms only



of reactions (iv)–(vi). Some other process, such as oxidation by air, appears to be operating.

EXPERIMENTAL

¹H N.m.r. spectra were obtained with a JEOL JNM-PS-100 spectrometer, i.r. spectra with a Hitachi 215 spectrometer, and mass spectra with a Hitachi RMV-6E spectrometer.

NN-Dibenzylhydroxylamine (1),⁸ *N*-benzyl-*N*-phenylhydroxylamine (6),⁹ and *N*-phenylhydroxylamine (10)⁹ were prepared according to the reported methods.

Isolation of the Salts (2) and (7).—To a stirred solution of sulphuryl chloride (10 mmol) in ether (20 ml) kept at -30°C was added a mixture of the *N*-hydroxyamine (10 mmol) and ether (20 ml) during 30 min, and stirring was continued for 1 h. The precipitate was collected and dried over silica gel under reduced pressure for 30 min. Physical data of the salts are given in Tables 1 and 2.

Reactions of the Salts (2) and (7).—The salt (2) (10 mmol) was poured into ice-cold aqueous potassium hydroxide, and the product was extracted with ether. The combined extracts were dried (Na_2SO_4) and evaporated to leave a white solid. Recrystallization from ethanol gave *N*-benzylidenebenzylamine *N*-oxide (5) (210 mg, 95%), m.p. $81.5\text{--}83.0^\circ$ (lit.,¹⁰ $81.5\text{--}83.5^\circ$), δ 5.02 (2 H, s), 7.28–7.56 (9 H, m), and 8.12–8.30 (2 H, m).

⁶ E. Bamberger, H. Busdorf, and B. Szolayski, *Ber.*, 1899, **32**, 210.

⁷ Y. Ogata, M. Tsuchida, and Y. Takagi, *J. Amer. Chem. Soc.*, 1957, **79**, 3397.

⁸ L. W. Jones and C. N. Sneed, *J. Amer. Chem. Soc.*, 1917, **39**, 674.

⁹ G. E. Utzinger, *Annalen*, 1944, **556**, 50.

¹⁰ A. C. Cope and A. C. Haven, jun., *J. Amer. Chem. Soc.*, 1950, **72**, 4896.

When the salt (7) was added to a solution of potassium hydroxide in methanol kept at -70°C , *N*-benzylideneaniline *N*-oxide (9) was obtained in 75% yield; m.p. $111.5\text{--}112.0^\circ$ (lit.,¹¹ 113°), δ 7.36–7.80 (6 H, m), 7.66–7.80 (2 H, m), 7.87 (1 H, s), and 8.28–8.42 (2 H, m).

Treatment of the salt (7) with aqueous potassium hydroxide at 0°C afforded *N*-benzylidene-*p*-chloroaniline *N*-oxide (8) in 73% yield; m.p. $177\text{--}178^\circ$ (lit.,¹² 181°), δ 7.36–7.56 (5 H, m), 7.71 (2 H, d, J 8 Hz), 7.86 (1 H, s), and 8.28–8.44 (2 H, m).

Reaction of N-Phenylhydroxylamine (10) with Sulphuryl

Chloride in Ether.—When a solution of the hydroxylamine (10) (30 mmol) in ether (20 ml) was added to a mixture of sulphuryl chloride (30 mmol) and ether (20 ml) at -30°C during 30 min, a white solid (11) was precipitated. An ethereal solution of (11) kept at -30°C was poured into ice-cold aqueous potassium hydroxide and the product extracted with ether to give nitrosobenzene (12) (580 mg, 55%), m.p. $64\text{--}65^\circ$ (from ethanol) (lit.,¹³ $64\text{--}67^\circ$).

On treatment of the hydroxylamine (10) (20 mmol) with 1 mol. equiv. of sulphuryl chloride in ether at 0°C , a viscous black liquid separated. Conventional work-up gave 4,4'-dichloroazoxybenzene (13) (46%), m.p. $150\text{--}153^\circ$ (lit.,¹⁴ $155\text{--}156^\circ$), δ 7.32–7.52 (4 H, q) and 8.04–8.20 (4 H, t).

Reaction of NN-Dibenzylhydroxylamine (1) with Sulphuryl Chloride in Acetonitrile.—To a solution of sulphuryl chloride (4.7 mmol) in acetonitrile (50 ml) was added the hydroxylamine (1) (4.7 mmol), and the mixture was stirred at room temperature for 1 h. The nitrone (5) was isolated in 57% yield. When the reaction of (1) (4.7 mmol) with sulphuryl chloride was performed under reflux for 1 h, benzaldehyde (90%) was obtained. From the reaction of (1) with 3 mol. equiv. of sulphuryl chloride, *N*-benzylbenzamide (95%) was isolated; m.p. $101\text{--}103^\circ$ (lit.,¹⁵ $102\text{--}104^\circ$).

Preparation of Hydrochlorides of Compounds (1), (5), (6), and (8).—Hydrochloride salts of compounds (1), (5), (6), and (8) were prepared by bubbling hydrogen chloride into an ethereal solution at 0°C for 1 h, and purified by recrystallization from ethanol.

¹¹ G. E. Utzinger and F. A. Regenass, *Helv. Chim. Acta*, 1954, **37**, 1892.

¹² O. A. Wheeler and P. H. Gore, *J. Amer. Chem. Soc.*, 1956, **78**, 3363.

¹³ G. H. Coleman, *Org. Synth.*, Coll. Vol. III, 1955, p. 668.

¹⁴ P. H. Gore and O. H. Wheeler, *J. Amer. Chem. Soc.*, 1956, **78**, 2160.

¹⁵ A. H. Feuselau, E. H. Hamamura, and J. G. Moffatt, *J. Org. Chem.*, 1970, **35**, 3546.

Reactions of N-Hydroxy-amines with Bromine.—To a solution of bromine (10 mmol) in ether (20 ml), was added a mixture of the hydroxylamine (1) (10 mmol) and ether (20 ml) at 0 °C during 30 min. After stirring for a further 30 min, the solid was filtered off and added to ice-cold potassium hydroxide. Recrystallization of the product from ethanol gave the nitrone (V) in 90% yield.

The reaction of the hydroxylamine (6) with bromine was performed at -25 °C. Conventional work-up afforded *N-benzylidene-p-bromoaniline N-oxide* (68%), m.p. 179.5–180.0° (Found: C, 56.55; H, 3.6; Br, 28.95; N, 5.05.

¹⁶ P. H. Gore and O. H. Wheeler, *J. Amer. Chem. Soc.*, **1956**, **78**, 2160.

$C_{13}H_{10}BrNO$ requires C, 56.55, H, 3.65; Br, 28.95; N, 5.05%, δ 7.40–7.54 (3 H, m), 7.61 (4 H, s), 7.87 (1 H, s), and 8.28–8.46 (2 H, m); *m/e* 277 and 275.

The reaction of *N*-phenylhydroxylamine with 1 mol. equiv. of bromine at -30 °C gave 4,4'-dibromoazoxybenzene (72%), m.p. 157–160° (lit.,¹⁶ 168.5–169.5°), δ 7.53–7.68 (4 H, q) and 8.00–8.20 (4 H, t).

Reaction of Nitrosobenzene with Hydrogen Chloride.—Into a solution of nitrosobenzene (20 mmol) in ether (50 ml), hydrogen chloride was bubbled at 0 °C for 1 h. Recrystallization of the product from ethanol gave 4,4'-dichloroazoxybenzene (88%).

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