SULFONATE ESTERS OF α-CHLOROALDOXIMES, ALDOXIMES, AND AMIDOXIMES VIA "SULFENE" ADDITION

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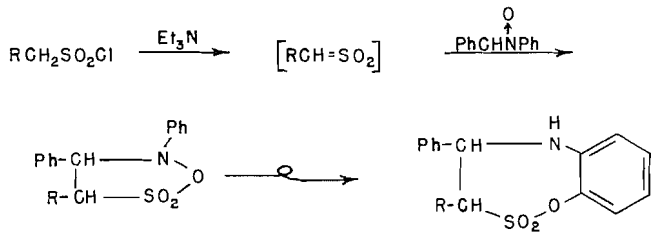
ABSTRACT

Reaction of aromatic nitrile oxides with methanesulfonyl and benzylsulfonyl chlorides in the presence of triethylamine yielded sulfonate esters of α-chloroaldoximes ($R-\overset{Cl}{\overset{|}{C}}=NO_3SCH_2R'$). Under the same reaction conditions, aldoximes yielded sulfonate esters, which decomposed to nitriles, and amidoximes yielded amidoxime O-sulfonates, which were also prepared by the action of ammonium hydroxide on $R-\overset{Cl}{\overset{|}{C}}=NO_3SCH_2Ph$. Chemical as well as nuclear magnetic resonance spectroscopic evidence confirms the formula $R-\overset{NH_2}{\overset{|}{C}}=NOH$ for amidoximes.

Inasmuch as cycloadditions of "sulfenes" to certain nucleophilic olefinic compounds to give products with four-membered rings have been realized (1), it became of interest to determine whether "sulfenes" would also cyclize with 1,3-dipolar systems. In fact, Truce *et al.* (2) have found that methanesulfonyl chloride reacts with C,N-diphenylnitrone in the presence of triethylamine to give a seven-ring aza-sultone, presumably via the sequence of steps shown in Reaction Scheme 1.



REACTION SCHEME 1.

The present report concerns the behavior of another 1,3-dipolar system, nitrile N-oxides (3, 4), under "sulfene"-producing conditions. When an ethereal solution of benzonitrile oxide containing triethylamine was treated with benzylsulfonyl chloride, a crystalline product was obtained. Analysis of that product suggested the empirical formula $C_{14}H_{12}NO_3Cl$, indicating the presence of 1 mole of hydrogen chloride over that expected of a cycloadduct. The infrared spectrum showed bands at 1 180 cm^{-1} and 1 380 cm^{-1} ($\rangle SO_2$). The nuclear magnetic resonance spectrum showed a singlet at 4.7 p.p.m. (relative area 1) and aromatic protons at 7.4–8.2 p.p.m. (relative area 5). The singlet is nearly in the same position as the singlet for the benzylic protons (4.78 p.p.m.) in benzylsulfonic anhydride (5). From these limited data the product was assigned the structure α-chlorobenzaldoxime benzylsulfonate.

$$Ph-C\equiv N\rightarrow O + PhCH_2SO_2Cl \xrightarrow[Et_2O]{Et_3N} Ph-\overset{Cl}{\overset{|}{C}}=NO_3SCH_2Ph$$

Similar compounds were obtained by like reactions of benzylsulfonyl chloride (Et_3N) and methanesulfonyl chloride (Et_3N) with *p*-chlorobenzonitrile N-oxide and *m*-nitrobenzonitrile N-oxide. However, the structurally hindered 2,4,6-trimethylbenzonitrile N-oxide yielded only 2,4,6-trimethylphenylisocyanate.

Nitrile oxides are prepared by dehydrohalogenation of α-chloroaldoximes ($R-\overset{Cl}{\overset{|}{C}}=NOH$, hydroxamic acid chlorides) with triethylamine (3). However, the reverse can be effected, i.e. nitrile oxides add hydrogen chloride (6) and thiols (7). This suggests the occurrence of the following equilibrium under the above reaction conditions.

$$R-\overset{Cl}{\overset{|}{C}}=NOH + Et_3N \rightleftharpoons R-C\equiv N\rightarrow O + Et_3NHCl$$

Thus, there may be present a small but significant amount of α-chloroaldoxime in the medium, and this α-chloroaldoxime may be adding to "sulfene" to give the ester, with the equilibrium shifting to the left as the reaction proceeds.

$$R-CH_2SO_2Cl \xrightarrow{Et_3N} [R-CH=SO_2] \xrightarrow{R'-\overset{Cl}{\overset{|}{C}}=NOH} RCH_2SO_3N=\overset{Cl}{\overset{|}{C}}-R'$$

I–VI

I	R = C_6H_5, R′ = C_6H_5	(m.p. 105–107°)
II	R = C_6H_5, R′ = *p*-ClC_6H_4	(m.p. 102–103°)
III	R = C_6H_5, R′ = *m*-$NO_2C_6H_4$	(m.p. 144–146°)
IV	R = H, R′ = C_6H_5	(m.p. 110–111°)
V	R = H, R′ = *p*-ClC_6H_4	(m.p. 80°)
VI	R = H, R′ = *m*-$NO_2C_6H_4$	(m.p. 98–100°)

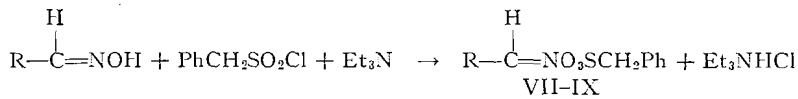
In fact, benzylsulfonyl chloride reacts with nitrile oxides in ether in the presence of triethylammonium chloride to give the corresponding esters. But, it adds to neither benzonitrile oxide nor *p*-chlorobenzonitrile oxide in the absence of triethylammonium chloride (the highly reactive *m*-nitrobenzonitrile oxide did give a small quantity of ester under the latter conditions). The maximum yield of ester was obtained when triethylamine was added to a mixture of α-chloroaldoxime and sulfonyl chloride in benzene or ether (Table I) at room temperature or ice-bath temperature.

TABLE I

Yield of $R-\overset{Cl}{\overset{|}{C}}=NO_3SCH_2Ph$ in the reaction of $R-C\equiv N\rightarrow O$ with $PhCH_2SO_2Cl$

	R = C_6H_5 (I)	R = *p*-ClC_6H_4 (II)	R = *m*-$O_2NC_6H_4$ (III)
Ether + Et_3N	36%	37%	63%
Benzene + Et_3N	50%	43.6%	76%
Chloroform + Et_3N	24%	33.4%	
Ether	0%	0%	24%
Ether + $Et_3N\cdot HCl$	22%	39%	
Addition of Et_3N to a mixture of $RC(Cl)=NOH$ and $PhCH_2SO_2Cl$	57%	75%	81%

Also, *syn*-benzaldoxime, *syn*-*p*-chlorobenzaldoxime, and *anti*-*m*-nitrobenzaldoxime gave the corresponding sulfonic acid esters when treated under phenylsulfene-generating conditions.



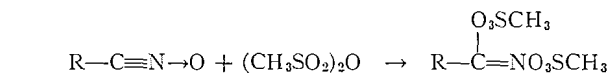
VII–IX

VII R = C_6H_5 (m.p. 77–79°)
VIII R = *p*-ClC_6H_4 (m.p. 103°)
IX R = *m*-$O_2NC_6H_4$ (m.p. 90–92°)

Under identical reaction conditions benzaldoxime did not react with *p*-toluenesulfonyl chloride.

Not many sulfonate esters of aldoximes are known (8, 9), because they are very unstable. *syn*-Aldoxime sulfonates decompose to nitriles spontaneously or when they are passed through an alumina column (8*a*). Such facile dehydrosulfonation was substantiated in this work and provided a simple and clean method for the overall dehydration of aldoximes to nitriles. The strained mesitaldoxime ester was too unstable to isolate, and decomposed to nitrile immediately.

It has been observed that methanesulfonic and benzylsulfonic anhydrides do generate "sulfenes" on reaction with triethylamine (5). Therefore, it was hoped that methanesulfonic anhydride might react with nitrile oxides as follows.



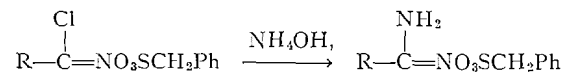
However, treatment of *p*-chlorobenzonitrile oxide and *m*-nitrobenzonitrile oxide with methanesulfonic anhydride in ether or chloroform in the presence of triethylamine yielded only starting nitrile oxide or its dimer.

In conclusion, the above facts do not clearly preclude a reaction sequence involving initial addition of "sulfene" to the nitrile oxide ($R'C\overset{+}{N}O_3\overset{-}{S}CHR$) followed by addition of hydrogen chloride, as against initial addition of hydrogen chloride to the nitrile oxide followed by addition of "sulfene".

Attempts were made, without success, to replace the "carbonyl" hydrogen of benzaldoxime benzylsulfonate and *p*-chlorobenzaldoxime benzylsulfonate with chlorine.

The esters I and II, on treatment with alcoholic KOH, gave benzonitrile and *p*-chlorobenzonitrile and, under more vigorous conditions, benzamide and *p*-chlorobenzamide, respectively. The ester III, on reaction with triethylamine, gave only *m*-nitrobenzonitrile. Presumably these reactions involve initial attack by the base on chlorine, with expulsion of the sulfonate anion to give the nitrile, which may be hydrolyzed further to the amide.

A cursory look at the structures of the esters indicates that there is a reactive chlorine atom, which should be replaced easily. The esters did not react with gaseous ammonia at room temperature. However, reaction with ammonium hydroxide in acetone at room temperature or higher yielded the corresponding amidoxime esters.



X–XII

X R = C_6H_5 (m.p. 102° (decomp.))
XI R = *p*-ClC_6H_4 (m.p. 89–90° (decomp.))
XII R = *m*-$NO_2C_6H_4$ (m.p. 127° (decomp.))

The amidoxime esters were also prepared by the reaction of amidoximes with benzylsulfonyl chloride in the presence of triethylamine. The required amidoximes were prepared by the reaction of nitriles with hydroxylamine or by the action of gaseous ammonia on α-chloroaldoximes.

$$R{-}C{\equiv}N + NH_2OH \rightarrow R{-}\overset{NH_2}{\overset{|}{C}}{=}NOH$$

$$R{-}\overset{Cl}{\overset{|}{C}}{=}NOH + NH_3 \rightarrow R{-}\overset{NH_2}{\overset{|}{C}}{=}NOH$$

$$R{-}\overset{NH_2}{\overset{|}{C}}{=}NOH + [PhCH{=}SO_2] \rightarrow R{-}\overset{NH_2}{\overset{|}{C}}{-}NO_3SCH_2Ph$$

Amidoximes theoretically could exist in two tautomeric forms *a* and *b*.

$$R{-}\overset{NH_2}{\overset{|}{C}}{=}NOH \qquad (a) \qquad\qquad R{-}\overset{NH}{\overset{\|}{C}}{-}NHOH \qquad (b)$$

Although structure *a* has been accepted as the correct structure of amidoximes, this preference was based on infrared spectroscopy (10 and references therein). However, more definitive support for structure *a* was provided by nuclear magnetic resonance spectroscopy (10, 11). Our synthesis of these compounds not only provides a proof for the structures of the sulfonate esters of α-chloroaldoximes but also provides chemical evidence for the structure of amidoximes.

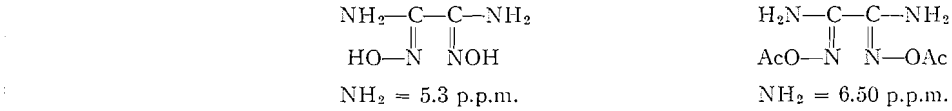
Infrared spectra of the amidoximes that were studied showed asymmetric and symmetric NH_2 stretching modes as two weak but sharp bands at 3 400 – 3 500 and 3 300 – 3 400 cm^{-1} and a broad band at 3 200 cm^{-1} caused by an associated OH function (11). On esterification only the band caused by OH disappeared. The amidoximes as well as their sulfonate esters exhibited strong bands at 1 630 – 1 675 cm^{-1} caused by C=N (11).

TABLE II

Chemical shifts (δ) in dimethyl sulfoxide

	Assignments:			
	OH	C_6H_5	NH_2	CH_2
Ph—$\overset{NH_2}{\overset{\|}{C}}$=NOH	9.64	7.2–7.8	5.74	
Ph—$\overset{NH_2}{\overset{\|}{C}}$=$NO_3SCH_2Ph$		7.0–8.0		4.74
p-ClPh—$\overset{NH_2}{\overset{\|}{C}}$=NOH	9.64	7.2–7.8	5.8	
p-ClPh—$\overset{NH_2}{\overset{\|}{C}}$=$NO_3SCH_2Ph$		7.0–8.0		4.8
m-NO_2Ph—$\overset{NH_2}{\overset{\|}{C}}$=NOH	9.96	7.4–8.6	6.1	
m-NO_2Ph—$\overset{NH_2}{\overset{\|}{C}}$=$NO_3SCH_2Ph$		6.8–8.6		4.8

The nuclear magnetic resonance spectra of the amidoximes and amidoxime sulfonates have been studied (Table II). The singlets at 9.6–10.0 p.p.m. are caused by N—OH (10, 11). The aromatic proton bands appear as a complex at 7.00 to 8.6 p.p.m., depending on the substitution on the aromatic ring. The NH_2 band appears as a singlet at 5.7 to 6.1 p.p.m. in amidoximes, a little higher than the literature values (10, 11). In the amidoxime sulfonate esters the singlet caused by OH disappears, and the singlet caused by NH_2 now shifts to the aromatic region and is not readily distinguished from the aromatic protons. However, the integration values support this conclusion. In the ester there is another band caused by benzylic protons at 4.78–4.80 p.p.m. as expected. The type of band shift observed for NH_2 has been reported (10) for oxamidoxime and its diacetate.



Variations in the chemical shifts observed and reported in the literature may be due to different solvents employed, e.g. it was observed that singlets caused by N—OH and NH_2 of benzamidoxime appear at 9.64 p.p.m. and 5.74 p.p.m. in dimethyl sulfoxide, but in deuterated chloroform they appear at 9.57 p.p.m. and 4.9 p.p.m., respectively.

EXPERIMENTAL*

Materials

The oximes were prepared according to the standard procedure. The α-chloroaldoximes were prepared by the action of chlorine on oximes in chloroform (12) or in 8 *N* HCl (4, 13) at ice-bath temperature. The solution first turns deep blue and finally slight orange. α-Chlorobenzaldoxime, m.p. 45–47° (lit. (4) m.p. 45°), is unstable and appears to be hydrolyzed to aldehyde when it is allowed to stand. *p*-Chloro(α-chloro)-benzaldoxime, m.p. 88–89° (lit. (4) m.p. 82–86°); *m*-nitro(α-chloro)benzaldoxime, m.p. 96–98° (lit. (4) m.p. 96°). Nitrile N-oxides were prepared *in situ* in most cases by the action of triethylamine on α-chloro-aldoximes in ether. However, *p*-chlorobenzonitrile oxide, m.p. 68–70° (lit. (14) m.p. 82–83°), was isolated for characterization. Triethylamine (Matheson, Coleman and Bell) was dried over KOH. Mallinckrodt anhydrous diethyl ether was used as obtained. Benzene was Baker spectrophotometric grade.

α-Chlorobenzaldoxime Benzylsulfonate (I)

To a continuously stirred solution of 1.55 g (0.01 mole) of α-chlorobenzaldoxime in about 100 ml of ether, maintained in an ice bath, was rapidly added 2 g (0.02 mole) of triethylamine. After 5 min, 2 g (slightly over 0.01 mole) of benzylsulfonyl chloride dissolved in about 15 ml of ether was added, dropwise, during a period of ½ h. After the solution was stirred for an additional hour, it was filtered and evaporated to dryness, and the residue was dissolved in benzene. Dilution with hexane and cooling yielded 0.5 g of 3,4-diphenylfuroxan, which, on further crystallization, had m.p. 112–114° (lit. (14) m.p. 114°). The mother liquor was evaporated to dryness and the residue was crystallized from alcohol to yield 1.1 g (36%) of the benzylsulfonate of α-chlorobenzaldoxime (I), m.p. 103–105° (raised to 105–107° after several crystallizations).

Anal. Calcd. for $C_{14}H_{12}ClNO_3S$: C, 54.28; H, 3.88; Cl, 11.45; N, 4.51; S, 10.32; mol. wt. 309.5. Found: C, 54.21; H, 4.13; Cl, 11.18; N, 4.71; S, 10.63; mol. wt. 313.

Infrared spectrum: 1 180 cm^{-1} (vs), 1 380 cm^{-1} (vs). Nuclear magnetic resonance spectrum: multiplets at 7.4–8.2 p.p.m. (relative area 5), singlet at 4.7 p.p.m. (relative area 1).

p-Chloro(α-chloro)benzaldoxime Benzylsulfonate (II)

To an ethereal solution containing 1 g of *p*-chlorobenzonitrile oxide and 1 g of triethylamine was added an ether solution of 1.5 g of benzylsulfonyl chloride as above. The residue remaining after the ether had been evaporated was dissolved in benzene, and the solution was filtered, diluted with hexane, and cooled. The precipitate was filtered off to give 0.6 g (37%) of the ester, m.p. 92–97°; after crystallization from benzene–hexane, m.p. 102–103°.

Anal. Calcd. for $C_{14}H_{11}Cl_2NO_3S$: C, 48.84; H, 3.20; Cl, 20.64; S, 9.30; mol. wt. 344. Found: C, 49.15; H, 3.56; Cl, 20.33; S, 9.71; mol. wt. 341.

The infrared spectrum was practically identical with that of I.

**All melting points are uncorrected. Microanalyses were performed by Dr. C. S. Yey and staff of the Microanalytical Laboratory, Purdue University. Nuclear magnetic resonance spectra were recorded on a Varian A-60 high-resolution spectrometer.*

Mesitonitrile N-Oxide

An aqueous basic solution of 12.7 g of the sodium salt of mesitaldoxime was added, while it was being filtered, to a stirred solution of sodium hypobromite (at 0 to 10°) prepared by adding 7 ml of bromine to 100 ml of 20% aqueous NaOH at 0 to 10°. The precipitate was filtered off, and the residue was washed with water and crystallized from hexane (first crop, m.p. 107–110°, yield 9.2 g; second crop, m.p. 104–106°, yield 2.1 g (lit. (6) m.p. 114°)).

Reaction of Mesitonitrile N-Oxide with Benzylsulfonyl Chloride in the Presence of Triethylamine

To an ether solution of 1.6 g (0.01 mole) of mesitonitrile oxide (m.p. 107–110°, lit. m.p. 114°) and 1 g of triethylamine was added an ethereal solution of 2 g of benzylsulfonyl chloride, as above. Evaporation of ether left a liquid residue, which was crystallized from hexane to give 1.1 g of 2,4,6-trimethylphenylisocyanate, m.p. 44–46°.

Anal. Calcd. for $C_{10}H_{11}NO$: C, 74.53; H, 6.83; N, 8.70. Found: C, 74.64; H, 6.93; N, 8.55.

In the infrared spectrum there was a very strong band at 2 260 cm^{-1}. In the literature (15) the isocyanate has been reported as a liquid. The urea derivative was prepared by treating the isocyanate with aniline, and had m.p. 240–242° (lit. (6) m.p. 245°).

m-Nitro(α-chloro)benzaldoxime Benzylsulfonate (III)

To an ice-cooled ethereal solution of 2 g (0.01 mole) of *m*-nitro(α-chloro)benzaldoxime was slowly added 1 g of triethylamine. After 5 min, 2 g of benzylsulfonyl chloride was added followed by the addition, over a ½ h period, of 1 g of triethylamine dissolved in ether. The residue obtained when the reaction mixture was filtered contained jelly-like material besides triethylammonium chloride. The residue was extracted with boiling benzene and the benzene solution evaporated to yield 1.65 g of the ester, m.p. 132–138°. The original ether mother liquor was evaporated to yield 550 mg of the ester, m.p. 135–140°; total yield 2.2 g (63%). After the product was crystallized from ether, it had m.p. 145–146°.

Anal. Calcd. for $C_{14}H_{11}ClN_2O_5S$: C, 47.46; H, 3.10; Cl, 10.00; N, 7.91; S, 9.00. Found: C, 47.73; H, 3.29; Cl, 10.28; N, 7.93; S, 8.72.

Although it is reported in the literature (14) that *m*-nitrobenzonitrile oxide is fairly stable, we could not isolate it in a pure form. On concentration it invariably turned to jelly-like material, possibly a dimer or trimer of the nitrile oxide. Therefore, the required nitrile oxide was always prepared *in situ* in dilute solution.

Reaction of Nitrile N-Oxides with Benzylsulfonyl Chloride in the Presence of Triethylamine in Benzene

The reactions in benzene were carried out the same as those in ether at a temperature of 10 to 15°. The yields of esters were: I, 50%; II, 43.6%; III, 76%.

Reaction of Nitrile N-Oxides with Benzylsulfonyl Chloride in the Presence of Triethylamine in Chloroform

The reactions in chloroform were carried out the same as those in ether at room temperature. The products could not be purified by crystallization and therefore were separated on acid-washed alumina columns. From the columns a 33.4% yield of compound II and a 24% yield of compound I were isolated.

Reaction of Nitrile N-Oxides and Benzylsulfonyl Chloride in Ether

Reaction of *p*-chlorobenzonitrile N-oxide with benzylsulfonyl chloride in ether yielded a white solid (after the solution had been stirred for 2 h at ice-bath temperature and the ether evaporated), which, when it was crystallized from benzene–hexane, yielded 1.55 g (75%) of benzylsulfonyl chloride and 0.9 g of crude nitrile oxide dimer.

Benzonitrile oxide which had similarly been treated with benzylsulfonyl chloride in ether yielded a white solid, which on work-up offered 1.9 g (95%) of benzylsulfonyl chloride.

After *m*-nitrobenzonitrile N-oxide had been treated with benzylsulfonyl chloride in ether as above, a small quantity (24%) of ester III (m.p. 140–143°) separated from the ether solution on concentration and cooling.

Reaction of Nitrile N-Oxides with Benzylsulfonyl Chloride in Ether in the Presence of 1 Equivalent of Triethylammonium Chloride

Without filtering off the triethylammonium chloride from the reaction of the α-chloroaldoxime and triethylamine (1 mole each) in ether, we treated the reaction mixture with 1 equivalent of benzylsulfonyl chloride, stirred it for 2 h at ice-bath temperature, and worked it up as before. When the ether was evaporated off, a liquid residue remained, in contrast to the preceding experiments. *p*-Chlorobenzonitrile oxide yielded 39% of ester II, and benzonitrile oxide yielded 22% of ester I.

Addition of 1 Equivalent of Triethylamine to a Mixture of 1 Mole of α-Chloroaldoxime and 1 Mole of Benzylsulfonyl Chloride

To an ether solution of a mixture of α-chloroaldoxime and benzylsulfonyl chloride (1 equivalent each) was added an ether solution of 1 equivalent of triethylamine at ice-bath temperature as before to yield: I, 57%; II, 75%; III, 81%.

α-Chlorobenzaldoxime Methanesulfonate (IV)

To an ether solution of 1.6 g of α-chlorobenzaldoxime was added 2 g of triethylamine at once at ice-bath

temperature followed by the addition of an ethereal solution of 1.2 g of methanesulfonyl chloride as before. From the residue, obtained after the ether had been evaporated, was isolated 0.8 g (33%) of ester IV (m.p. 106–109°), which, on further crystallization from benzene–hexane, had m.p. 110–111°.

Anal. Calcd. for $C_8H_8ClNO_3S$: C, 41.20; H, 3.43; Cl, 15.23; N, 6.01; S, 13.73. Found: C, 41.53; H, 3.46; Cl, 15.33; N, 5.94; S, 13.59.

p-Chloro(α-chloro)benzaldoxime Methanesulfonate (V)

Prepared as above, m.p. 80°.

Anal. Calcd. for $C_8H_7Cl_2NO_3S$: C, 35.82; H, 2.61; Cl, 26.50; N, 5.22; S, 11.94. Found: C, 35.76; H, 2.72; Cl, 26.35; N, 5.25; S, 12.21.

m-Nitro(α-chloro)benzaldoxime Methanesulfonate (VI)

Prepared as above with benzene as solvent (10 to 15° bath temperature); 1.4 g (50%) of crude ester VI was obtained (m.p. 91–95°), which, on further crystallization from benzene, had m.p. 98–100°.

Anal. Calcd. for $C_8H_7ClN_2O_5S$: C, 34.40; H, 2.51; Cl, 12.70; N, 10.03; S, 11.50. Found: C, 34.67; H, 2.51; Cl, 22.82; N, 9.96; S, 11.26.

syn-Benzaldoxime Benzylsulfonate (VII)

By using the method described for I, compound VII was prepared. The crude product, when it was dissolved in benzene and diluted with hexane, had m.p. 67–73°, and on further crystallization had m.p. 77–79°. The ester is unstable and decomposes to nitrile at room temperature in a couple of days. The infrared spectrum showed typical $\rangle SO_2$ stretching bands at 1 175 cm^{-1} and 1 370 cm^{-1}.

The α-hydrogen of the aldoxime in the ester was not successfully replaced by chlorine as follows. (*a*) Dry chlorine was passed through a solution of 0.5 g of the ester at ice temperature for 20 min. When the solvent was evaporated, unchanged ester was recovered. (*b*) The same reaction was conducted at room temperature without success. (*c*) The ester was suspended in 8 *N* HCl and chlorine was passed through at room temperature, but only the unchanged ester was recovered.

syn-p-Chlorobenzaldoxime Benzylsulfonate (VIII)

The ester was prepared as above, m.p. 103°. The ester could not be chlorinated further.

Anal. Calcd. for $C_{14}H_{12}ClNO_3S$: C, 54.20; H, 3.87; N, 4.51; Cl, 11.42; S, 10.32; mol. wt. 310. Found: C, 54.29; H, 4.01; N, 4.42; Cl, 11.49; S, 10.19; mol. wt. 311.

The ester, when it was passed through an alumina column, decomposed to nitrile, m.p. 92° (lit. (16) m.p. 93–94°).

anti-m-Nitrobenzaldoxime Benzylsulfonate (IX)

The ester was prepared as above. The yield was quantitative (m.p. 90–92°).

Anal. Calcd. for $C_{14}H_{12}N_2O_5S$: C, 52.50; H, 3.75; N, 8.75; S, 10.00. Found: C, 52.48; H, 3.79; N, 8.55; S, 10.19.

Attempted Preparation of syn-2,4,6-Trimethylbenzaldoxime Benzylsulfonate

The same method was employed as described above, 3.26 g of oxime being used. The ester was a white solid at ice temperature. When it was dissolved in benzene at room temperature it decomposed spontaneously. Next day the solution was chromatographed on acid-washed alumina and the following compounds were isolated: 2,4,6-trimethylbenzonitrile (2 g), m.p. 49–51° (lit. m.p. 54°); *syn*-2,4,6-trimethylbenzaldoxime (100 mg), m.p. 125°; 2,4,6-trimethylformanilide (100 mg), m.p. 177–178° (lit. (17) m.p. 177°).

Hydrolysis of I and II

The esters (500 mg each) were hydrolyzed with 1 g of KOH dissolved in 50 ml of ethanol at room temperature (1 h) or at reflux temperature (½ h). The solution was diluted with water and the ethanol was removed under vacuum. The remaining solution was extracted with chloroform, dried over sodium sulfate, and evaporated to dryness. II at reflux temperature yielded 110 mg of *p*-chlorobenzamide, m.p. 172–174°, which, on further crystallization, had m.p. 176–177°; mixed melting point with an authentic sample, 175–176°. The same ester, on hydrolysis at room temperature, yielded a few milligrams of amide and 110 mg of crude *p*-chlorobenzonitrile, m.p. 80–87°. Hydrolysis of I at reflux temperature yielded 30 mg of benzamide, m.p. 125–126°, and at room temperature about 100 mg of crude benzonitrile.

Reaction of III with Triethylamine in Benzene

To a solution of 1.6 g of ester III in 50 ml of dry benzene was added 10 ml of triethylamine, and the solution was heated under reflux for 1 h. The solution was concentrated and added to an acid-washed alumina column prepared in hexane. Elution with benzene gave 340 mg of *m*-nitrobenzonitrile, m.p. 115–116° (lit. (18) m.p. 117–118°).

Reaction of m-Nitrobenzonitrile N-Oxide with Methanesulfonic Anhydride in Ether in the Presence of Triethylamine

To an ether (50 ml) solution of 1.75 g of methanesulfonic anhydride was added at ice-bath temperature

an ether solution of 1.65 g of *m*-nitrobenzonitrile oxide. To the stirred solution was added, dropwise, an ether solution of 1 g of triethylamine (20 min). The solution was evaporated and the residue was treated with benzene, from which 0.4 g of the dimer of *m*-nitrobenzonitrile oxide was isolated. The residue was an orange liquid, which could not be identified further. However, the liquid did not show any characteristic $\rangle SO_2$ stretching bands in the infrared spectrum.

Reaction of p-Chlorobenzonitrile N-Oxide with Methanesulfonic Anhydride in the Presence of Triethylamine

The reaction was conducted as above, 1.9 g of *p*-chloro(α-chloro)benzaldoxime being used. The residue (after the ether had been evaporated) was treated with water and filtered to yield only *p*-chlorobenzonitrile oxide, as determined from its infrared spectrum (band at 2 300 cm^{-1} (vs)). The product was dissolved in benzene and worked up the next day to yield 1.1 g of the dimer of the nitrile oxide (m.p. 139–142°).

In a similar reaction in chloroform at room temperature 0.9 g of the dimer of the nitrile oxide (m.p. 139–142°) was obtained; the remaining residue was also a solid which showed a weak band at 2 300 cm^{-1} in its infrared spectrum caused by nitrile oxide but no bands caused by $\rangle SO_2$ stretching.

m-Nitrobenzamidoxime

Gaseous ammonia was passed through a benzene (50 ml) solution of 2.5 g of *m*-nitro(α-chloro)benzaldoxime for 15 min. The benzene solution was evaporated to dryness, and the residue was treated with water to remove ammonium chloride and crystallized from aqueous ethanol. The first crop was orange, m.p. 164–167°. The infrared spectrum showed two sharp bands at 3 500 – 3 400 cm^{-1} (vw) and 3 400 – 3 300 cm^{-1} (vw), a broad band at 3 200 cm^{-1}, and a sharp peak at 1 675 cm^{-1}. The second crop was greyish white, m.p. 167–170°, and there was a depression in the mixed melting point of the two. The first crop, on further crystallization, had m.p. 169–170°, yield 0.9 g (lit. (19) m.p. 174°).

When a similar experiment was done in ethanol at room temperature, a large amount of solid precipitated from the ethanol solution, m.p. 179–181°, which was not the dimer of the nitrile oxide. The yield of *m*-nitrobenzamidoxime was about the same as above. When ammonia was passed through the alcoholic solution at *ice-bath* temperature, the yield of *m*-nitrobenzamidoxime was doubled.

m-Nitrobenzamidoxime was also prepared by the reaction of *m*-nitrobenzonitrile and hydroxylamine, and the product was crystallized from water.

Nuclear magnetic resonance spectrum: singlet at 9.96 p.p.m. (relative area 1), multiplets at 7.4–8.6 p.p.m. (relative area 4), singlet at 6.1 p.p.m. (relative area 2).

p-Chlorobenzamidoxime

Gaseous ammonia was passed through an ethanol solution of 1 g of *p*-chloro(α-chloro)benzaldoxime at ice-bath temperature for 5 min. The solution was diluted with water and filtered. The clear solution was concentrated and cooled to give 740 mg of *p*-chlorobenzamidoxime, m.p. 127–130°. On further crystallization from water it melted at 132–133° (lit. (20) m.p. 134°). The infrared spectrum showed two sharp bands at 3 400 – 3 500 cm^{-1} (vw) and 3 300 – 3 400 cm^{-1} (vw), a broad band at 3 200 cm^{-1}, and a strong band at 1 650 cm^{-1}. Nuclear magnetic resonance spectrum: singlet at 9.64 p.p.m. (relative area 1), multiplets at 7.2–7.8 p.p.m. (relative area 4), singlet at 5.8 p.p.m. (relative area 2).

p-Chlorobenzamidoxime was also prepared by heating under reflux overnight a clear aqueous alcoholic solution of *p*-chlorobenzonitrile and hydroxylamine.

Benzamidoxime

A clear aqueous alcoholic solution of 0.1 mole of hydroxylamine and 0.1 mole of benzonitrile was gently heated under reflux overnight, concentrated, and cooled. The oil which separated out was poured on a porous plate, where it solidified. The solid was dissolved in benzene and crystallized, m.p. 76–78° (lit. (21) m.p. 78°). Infrared spectrum: two sharp bands at 3 400 – 3 500 cm^{-1} (vw) and 3 300 – 3 400 cm^{-1} (vw), a broad band at 3 200 cm^{-1}, and a band at 1 640 cm^{-1} (vs). Nuclear magnetic resonance spectrum: singlet at 9.64 p.p.m. (relative area 1), multiplets at 7.2 to 7.8 p.p.m. (relative area 5), singlet at 5.74 p.p.m. (relative area 2).

m-Nitrobenzamidoxime O-Benzylsulfonate (XII)

To an acetone (30 ml) solution of 1.75 g (0.005 mole) of the ester III was added 5 ml of ammonium hydroxide, and the mixture was stirred for ½ h at room temperature. Most of the acetone was removed under vacuum and diluted with water. A brown oil separated which soon solidified. The solid was dissolved in chloroform and diluted with hexane to give 1.1 g of crude XII (m.p. 117–120°). The mother liquor, on further concentration, gave a second fraction (m.p. 135–141°) which was mainly III. The first fraction, on further crystallization from benzene, had m.p. 127° (decomp.).

Anal. Calcd. for $C_{14}H_{13}N_3O_5S$: C, 50.15; H, 3.91; N, 12.53; S, 9.55. Found: C, 50.40; H, 3.95; N, 12.36; S, 9.72.

Infrared spectrum: two sharp bands at 3 400 – 3 500 cm^{-1} (vw) and 3 300 – 3 600 cm^{-1} (vw), a band at 1 640 cm^{-1} (s). Nuclear magnetic resonance spectrum: multiplets at 6.8–8.6 p.p.m. (relative area 11), singlet at 4.8 p.p.m. (relative area 2).

When ammonia was passed through the solution of the ester III in benzene at room temperature, only the starting material was recovered quantitatively.

m-Nitrobenzamidoxime O-benzylsulfonate was also prepared by the reaction of *m*-nitrobenzamidoxime with benzylsulfonyl chloride in the presence of triethylamine in tetrahydrofuran at ice-bath temperature. The solution was evaporated to dryness under reduced pressure and water was added to remove *m*-nitrobenzamidoxime. The ester was crystallized from benzene. The yield was quantitative, m.p. 126–127° (decomp.). The mixed melting point with the above ester was 125–126° (decomp.) and the infrared spectra of the two were identical.

p-Chlorobenzamidoxime O-Benzylsulfonate (XI)

The reaction was done as above with 1 g of II, except that the solution was gently heated under reflux for ½ h. The crude product (510 mg) was crystallized from benzene–hexane, m.p. 89–90° (decomp.).

Infrared spectrum: two sharp bands at 3 400 – 3 500 cm^{-1} and 3 300 – 3 400 cm^{-1}, a band at 1 640 cm^{-1}.

Compound XI was also prepared from *p*-chlorobenzamidoxime in ether as above. The white residue obtained after the ether had been evaporated was shaken with water to remove unreacted *p*-chlorobenzamidoxime, and the residue (90%) was crystallized. The first fraction (1 g) was pure XI, m.p. 87–89° (decomp.). The infrared spectrum was identical with that of the above material and there was no depression in the mixed melting point. The second fraction melted at 87–89°, but left a residue. The third fraction, m.p. 139–140°, had an infrared spectrum which indicated that it was a quaternary ammonium salt; also present were characteristic $\rangle SO_2$ stretching vibrations, indicating that the ester might be unstable and might decompose in the process of purification.

Anal. Calcd. for $C_{14}H_{13}ClN_2O_3S$ (m.p. 87–89°): C, 51.45; H, 4.01; Cl, 10.8; N, 8.6; S, 10.00. Found: C, 51.61; H, 3.97; Cl, 10.97; N, 8.40; S, 9.60.

Benzamidoxime O-Benzylsulfonate (X)

The reaction was done as above with 1 g of ester I, except that the reaction mixture was kept (well corked) for 2½ h at room temperature; 440 mg of crude X was obtained, m.p. 94° (decomp.). The compound is slightly soluble in benzene and ether. On crystallization from ether it had m.p. 98° (decomp.).

Infrared spectrum: two sharp bands at 3 400 – 3 500 cm^{-1} and 3 300 – 3 400 cm^{-1}, a strong band at 1 629 cm^{-1}.

Compound X was also prepared from benzamidoxime in ether as above. When the crude product was crystallized from ether, the ester had m.p. 102° (decomp.). The infrared spectrum was identical with that of the above material and a mixed melting point of the two was 98° (decomp.).

Anal. Calcd. for $C_{14}H_{14}N_2O_3S$: C, 57.93; H, 4.82; N, 9.6; S, 11.03. Found: C, 57.82; H, 5.00; N, 9.39; S, 10.84.

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