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DIPOLAR ADDITION REACTIONS OF NITRILEOXIDES. III*
THE REACTION OF BENZONITRILEOXIDES WITH SULPHONIC AND CARBOXYLIC ACID CHLORIDES

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The capacity of the transient 'methylenesulphene' (II) to undergo various interesting cycloaddition reactions has clearly been demonstrated over the past four years (1). Sometime ago we initiated a project directed towards the cycloaddition of nitrileoxides to 'methylenesulphene' (II), both generated in situ. The first experiment, in which a solution of equimolar quantities of 4-chlorobenzhydroxamoyl chloride (III) and methanesulphonyl chloride (I) in absolute ether was treated with two molar equivalents of triethylamine, gave surprising results. Instead of the expected cycloadduct (V), a substance having the molecular formula $C_8H_7Cl_2NO_3$ and subsequently identified as O-methanesulphonyl-4-chlorobenzhydroxamoyl chloride (VI) was isolated in good yield. The possible alternate structure (VII) for the compound was ruled out immediately on

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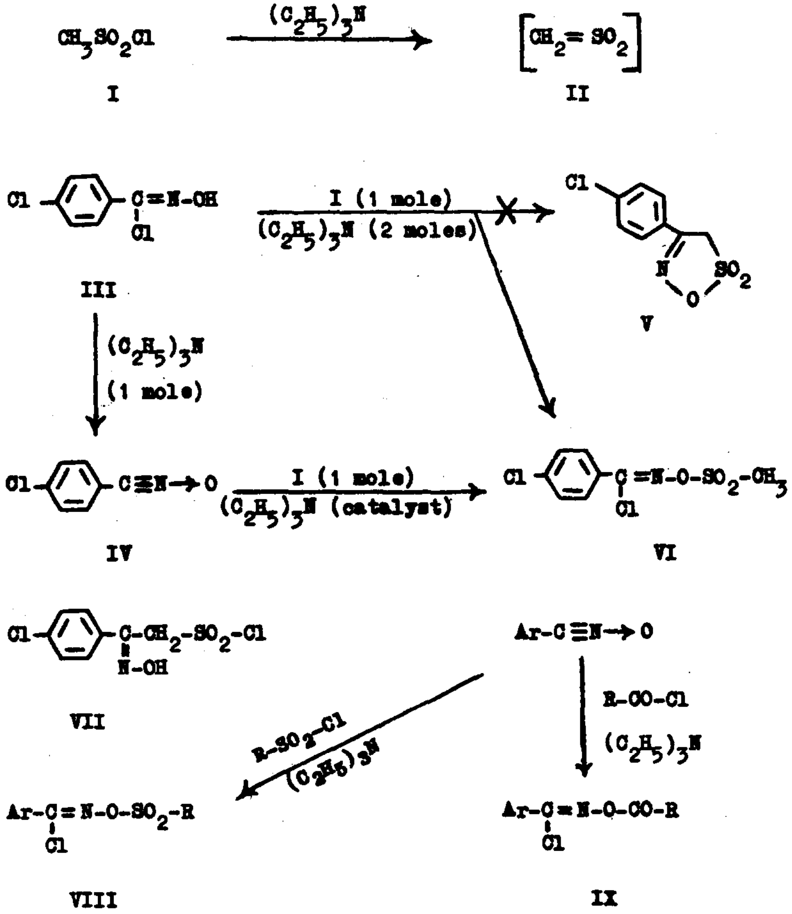
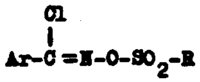
the basis of its NMR spectrum (determined in a Varian A60 instrument) which carries (besides signals corresponding to the four aromatic protons) a methyl signal (singlet) at 6.82 τ. This would not be the case if structure VII were correct.



In order to preclude the possibility of the direct mesylation of 4-chlorobenzhydroxamoyl chloride (III) taking precedence over the formation of 4-chlorobenzonitrileoxide (IV) and methylenesulphene (II), the experiment was repeated with equimolar quantities of the freshly liberated nitrileoxide (IV), methanesulphonyl chloride (I) and triethylamine, but the result was still the same. This led us to examine, in detail, the reaction of a number of sulphonic and carboxylic acid chlorides with typical benzonitrileoxides and we would now like to report that it is indeed general leading to arylhydroxamoyl chloride esters of the types VIII and IX (Tables 1 and 2) respectively. The structure of one such compound (IXa, Table 2) was confirmed by an independent synthesis. 3,4-Dichlorobenzhydroxamoyl chloride was acetylated with acetic anhydride according to the procedure of Hackmann and Harthoorn (2). The product was identical, in all respects, with IXa.

It is important to note that the reaction does not proceed to any appreciable extent in the absence of triethylamine as catalyst, dimerisation of the nitrileoxides being predominant. It is reasonable, then, to assume that triethylamine binds the positive centre of the dipolar nitrileoxide to assist the negatively charged oxygen in smoothly displacing the chloride ion from the sulphonyl or carboxyl chloride in a nucleophilic reaction. The chloride ion thus displaced attacks, in turn, to expel the triethylamine molecule in a second nucleophilic reaction. The alternate mechanism involving the nucleophilic

TABLE 1

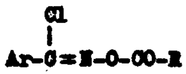


$$Ar-\overset{Cl}{\overset{|}{C}}=N-O-SO_2-R$$

VIII

	Ar	R	M.P.		Analysis C	Analysis H	Analysis N
a.	4-Chlorophenyl	Methyl	81-83°	Calcd.	35.87	2.63	5.22
				Found	36.24	2.44	5.53
b.	3-Nitrophenyl	Benzyl	142-145°	Calcd.	47.40	3.13	7.89
				Found	47.72	3.27	8.38
c.	3,4-Dichlorophenyl	Phenyl	122-124°	Calcd.	42.83	2.21	3.84
				Found	42.95	2.22	3.94
d.	Phenyl	Methyl	110-113°	Calcd.	41.13	3.45	5.99
				Found	41.45	3.49	6.18
e.	4-Chlorophenyl	Benzyl	101-103°	Calcd.	48.86	3.22	4.07
				Found	48.74	3.28	4.44
f.	4-Chlorophenyl	4-Nitrophenyl	124-126°	Calcd.	41.62	2.15	7.47
				Found	41.91	2.24	7.72
g.	3-Nitrophenyl	Methyl	95-99°	Calcd.	34.48	2.53	10.06
				Found	34.75	2.93	10.04

Table 2



$$Ar\text{-}\overset{Cl}{\overset{|}{C}}{=}N\text{-}O\text{-}CO\text{-}R$$

IX

					Analysis		
	Ar	R	M.P.		C	H	N
a.	3,4-Dichlorophenyl	Methyl	75-78°	Calcd.	40.56	2.27	5.26
				Found	40.93	2.74	5.28
b.	4-Chlorophenyl	Benzyl	62-65°	Calcd.	58.46	3.59	4.55
				Found	58.72	3.77	5.05
c.	4-Chloro-3-nitrophenyl	Phenyl	168-170°	Calcd.	49.58	2.38	8.26
				Found	49.37	2.47	7.91
d.	3-Nitrophenyl	2-Thienyl	167-170°	Calcd.	46.39	2.27	9.02
				Found	46.72	2.44	8.85
e.	4-Chlorophenyl	2-Furyl	114-116°	Calcd.	50.73	2.49	4.93
				Found	50.79	2.09	5.28
f.	3-Nitrophenyl	4-Pyridyl	150-152°	Calcd.	51.09	2.64	13.75
				Found	51.10	2.80	13.52

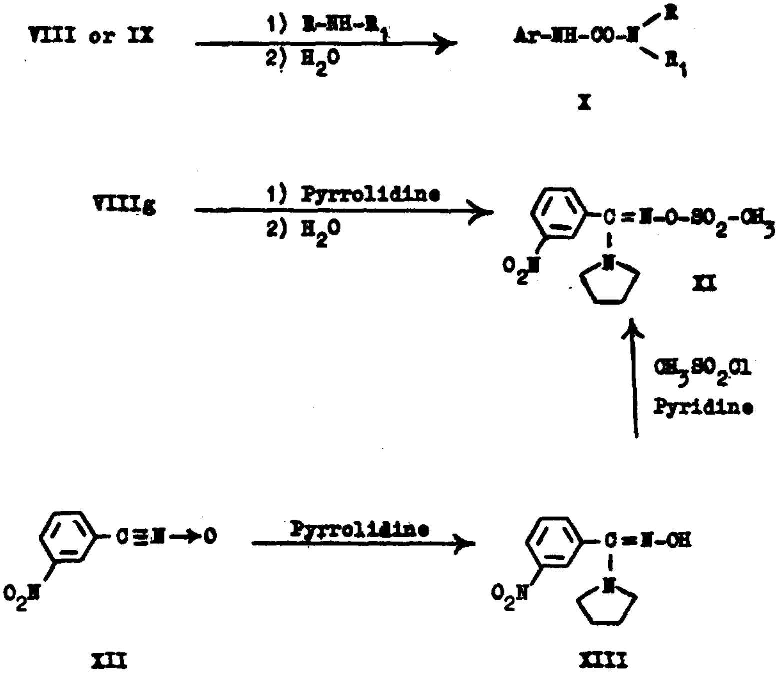
attack of the nitrileoxide on the acid chloride-triethylamine complex is equally possible.

The general procedure for the preparation of compounds of the types VIII and IX is as follows: A solution of the arylhydroxamoyl chloride (0.05 mole) in absolute benzene is cooled to 10°, stirred and treated with anhydrous triethylamine (0.05 mole) added in one lot. After two to three minutes of stirring, the mixture is filtered rapidly and the residue washed with a small quantity of absolute benzene. The combined filtrates are stirred and treated, immediately and in quick succession, with the acid chloride (0.05 mole) and anhydrous triethylamine (0.013 mole). The mixture is then refluxed, with stirring, for two hours, cooled and stripped of benzene under reduced pressure. The residue is triturated with cold hexane, filtered and recrystallised from a suitable solvent.

On the basis of our results it could safely be assumed that the method which Wieland and Kitasato (3) employed for the benzoylation of benzhydroxamoyl chloride also proceeds through the nitrileoxide formed in situ.

Most of the arylhydroxamoyl chloride esters (VIII and IX) listed in Tables 1 and 2 react vigorously with secondary bases as pyrrolidine, piperidine and morpholine, yielding, after treatment with water, ureas of the type X, whose identity was established by comparison with authentic samples. A notable exception is O-methanesulphonyl-3-nitrobenzhydroxamoyl chloride (VIIIg, Table 1) which when treated with excess of pyrrolidine furnished the amidoxime mesylate, XI, instead.

It is clear, then, that the formation of the ureas (X) proceeds through a Tiemann type of rearrangement (4) of the intermediate amidoxime esters as, for example, XI.



The structure of XI was confirmed by an alternate synthesis. Freshly liberated 3-nitrobenzonitrileoxide (XII), on treatment with a molar equivalent of pyrrolidine, furnished the amidoxime (XIII) which was mesylated with methanesulphonyl chloride in the presence of anhydrous pyridine. The product was identical with XI.

This new reaction of benzonitrileoxides is now being extended to carbamyl, sulphamyl and other active halides.

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