Heterocycles from Nitrile Oxides. I. 5-Imino-Δ^2-1,4,2-Oxathiazolines

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The reaction of some arylnitrile oxides with potassium thiocyanate in acetone at ambient temperature, has been investigated. Those having *para*- or *meta*-halo (or nitro) substituents give 3-aryl-5-imino-Δ^2-1,4,2-oxathiazolines as stable cycloadducts. *ortho*-Substitution, on the other hand, led directly to the corresponding 5-(carbamido)imino analogues. The structures of these new heterocycles are supported by elemental analyses and spectral data.

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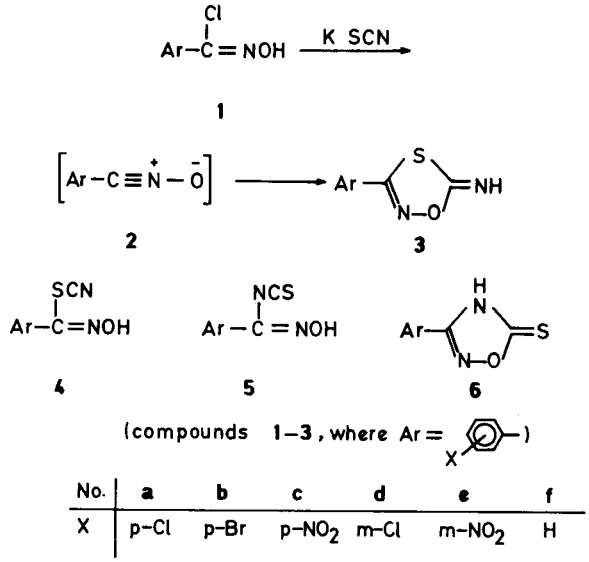
While 1,3-dipolar addition reactions of nitrile oxides with a variety of nucleophilic species have been extensively studied (1-3), the reaction with the thiocyanate anion has received limited attention in the literature. The expected cycloadduct **3** (Scheme I) has so far been described as unstable (Ar = C_6H_5) (4), or hypothesized as intermediate (5). On the other hand, Hackmann (6) claimed the isolation of the acyclic adduct **4** from the reaction of **1** (Ar = 2,6-$Cl_2C_6H_3$) and potassium thiocyanate.

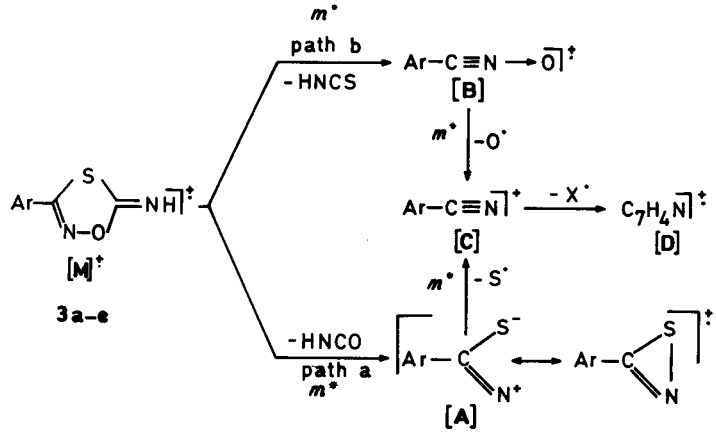


Scheme I

In the present work we have reinvestigated the reaction between **1** and potassium thiocyanate. The reaction proceeds readily in acetone at room temperature to give the expected cycloadducts **3** in good yields. To the best of our knowledge, these compounds **3** represent the first examples of stable 3-aryl-5-imino-Δ^2-1,4,2-oxathiazolines (Scheme I, Table I). The ir spectra of these oxathiazolines exhibit absorption bands in the range 3200-3100, and 1650-1630 cm^{-1}, attributed to the imino N-H and C=N stretching modes, respectively. No absorption bands are observed in the range 2250-2100 cm^{-1}, indicative of the absence of a free thiocyanato or isothiocyanato groups (7). Consequently, acyclic structures analogous to **4** (or its isomeric isothiocyanate **5**) are thus excluded.

The pmr spectra of compounds **3a-f** show, in addition to the aromatic protons' signals (4H), a broad signal centered around 6.0 ppm (-NH; 1H).

The mass spectra of compounds **3a-e** show the correct molecular ions, $[M]^{+\cdot}$, expected for the molecular formulae. Fragmentation of the molecular ion (Scheme II) proceeds by expulsion of either HNCO (path a) or HNCS, in a



Scheme II

retro-1,3-dipolar addition manner (path b). The latter process predominates as indicated by the relative peak intensities of the corresponding fragment ions [A] and [B] (Table II). The one-step expulsion of HNCO from the molecular ion lends further support to structure **3** and excludes **6** as a possible alteranative structure for the cycloadduct. The primary fragment ions [A] and [B] then lose sulfur or oxygen atoms, respectively, to give ion [C].

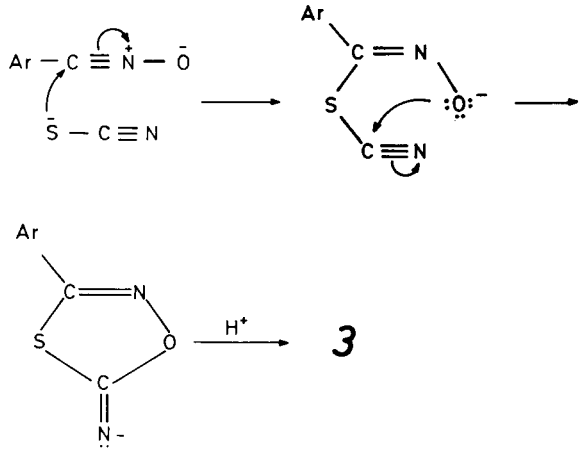
The formation of **3** from **1** and KSCN apparently involves the intermediacy of nitrile oxide **2**. The latter then adds thiocyanate in a normal 1,3-dipolar addition manner, followed by cyclization (two-step mechanism) as depicted in Scheme III. In agreement with this view, the oxygen-

Table I

Physical Data for Compounds **3a-e** and **8g, h**

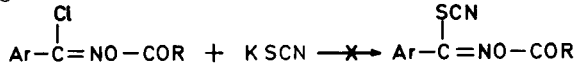
No.	Yield (%)	Mp (°C)	Formula	(Mol Wt)	Analyses (%) Calcd. C	H	N	Found C	H	N
3a	72	159-160 (a)	$C_8H_5ClN_2OS$	(212.7)	45.18	2.37	13.17	45.01	2.41	13.28
3b	76	155-156 (a)	$C_8H_5BrN_2OS$	(257.1)	37.37	1.96	10.90	36.96	2.01	10.95
3c	83	121-122 (a)	$C_8H_5N_3O_3S$	(223.2)	43.05	2.26	18.83	42.94	2.29	18.80
3d	68	119-120 (b)	$C_8H_5ClN_2OS$	(212.7)	45.18	2.37	13.17	45.18	2.46	13.23
3e	86	105-106 (a)	$C_8H_5N_3O_3S$	(223.2)	43.05	2.26	18.83	42.60	2.30	18.70
8g	35	144-145 (b)	$C_9H_6ClN_3O_2S$	(255.7)	42.28	2.37	16.43	42.22	2.42	16.38
8h	37	136-137 (a)	$C_9H_6BrN_3O_2S$	(300.1)	36.02	2.02	14.00	36.07	2.06	14.09

(a) Crystallized from chloroform. (b) Crystallized from chloroform + petroleum ether (bp 40-60°).



Scheme III

substituted hydroxamoyl chlorides **7** (Scheme IV) were found to be unreactive towards KSCN. This is because the formation of nitrile oxides from these compounds, lacking an oximino-hydrogen, is blocked. Thus, when compounds **7** were refluxed with excess KSCN in acetone for 24 hours no reaction could be detected. The failure of *O*-phenylbenzhydroxamoyl chloride to undergo unimolecular solvolysis in aqueous dioxane, as experimented by Hegarty and coworkers (2), could also be explained by similar reasoning.



7

a : Ar = R = C_6H_5

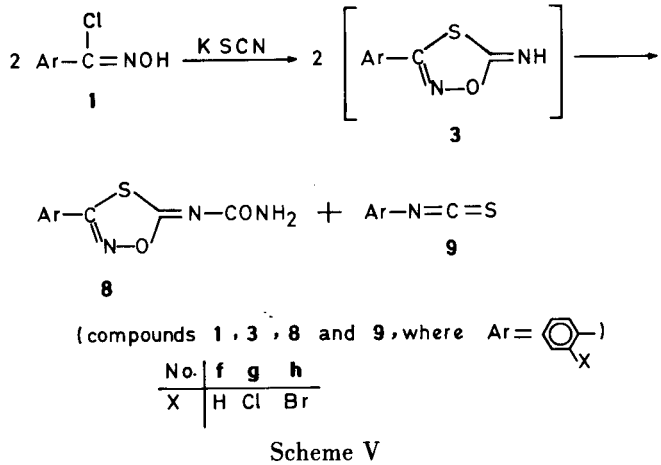
b : Ar = R = p-$NO_2C_6H_4$

c : Ar = R = m-$NO_2C_6H_4$

d : Ar = m-$NO_2C_6H_4$; R = $COCH_3$

Scheme IV

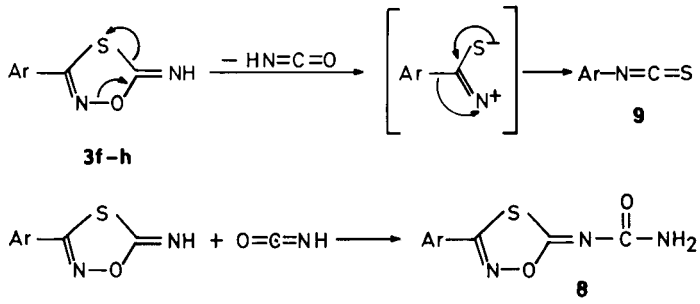
Whereas *para-* and *meta*-substituted benzhydroxamoyl chlorides **1a-e** yield stable adducts with KSCN, the parent heterocycle **3f** is rather unstable. As previously noted by Musante (4), the latter compound is found to be transformed readily, during attempted crystallization, to the corresponding (carbamido)imino derivative **8f**. Moreover, the *ortho*-substituted benzhydroxamoyl chlorides **1g,h** give directly **8g,h** (Scheme V) upon treatment with KSCN under the conditions specified for the preparation of **3a-e**. Besides **8f-h**, the coresponding arylisothiocyanates **9f-h** are also isolated from the reaction mixtures and identified.



Scheme V

It appears that *ortho*-substituents sterically destabilize the heteroring of the initially formed cycloadducts **3g,h**. These thermally labile heterocycles decompose readily to the corresponding isothiocyanates **9g,h** and 3-aryl-5(carbamido)imino-Δ^2-1,4,2-oxathiazolines **8g,h** presumably formed as postulated in Scheme VI. In these compounds **8**, the heteroring gains stabilization through extended conjugation with the exocyclic -(carbamido)imino moiety.

The ir spectra of **8f-h** exhibit two absorption bands in the region 3300-3150 cm^{-1} (primary amide- NH_2 group), and a strong absorption band around 1670 cm^{-1} (conjugated amide-carbonyl group). The pmr spectra show two

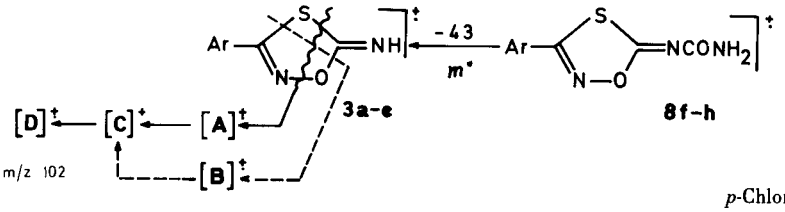


Scheme VI

broad signals centered at 6.9 (1H) and 7.1 (1H) ppm, in addition to the aromatic protons' signals. The mass spectra give the correct molecular ions $[M]^{+\cdot}$. The latter ion suffers elimination of HNCO from the (carbamido)imino side-chain to produce the corresponding $[M-43]^{+}$. This ion then undergoes further fragmentation analogous to that of the parent adduct **3** (see Scheme II and Table II).

Table II

m/z Values (relative abundance in parentheses) (a) of the Principal Fragments for Compounds **3a-e** and **8f-h**



No.	$[M]^{+\cdot}$		$[A]^{+\cdot}$	$[B]^{+\cdot}$	$[C]^{+}$
3a	212/214 (28)		169/171 (5)	153/155 (100)	137/139 (31)
3b	256/258 (21)		213/215 (6)	179/199 (100)	181/183 (16)
3c	223 (27)		180 (24)	164 (82)	148 (56)
3d	212/214 (28)		169/171 (3)	153/155 (100)	137/139 (24)
3e	223 (2)		180 (37)	164 (40)	148 (59)
		$[M-43]^{+\cdot}$			
8f	221 (13)	178 (3)	135 (33)	119 (68)	103 (33)
8g	255/257 (19)	212/214 (3)	169/171 (35)	153/155 (100)	137/139 (77)
8h	299/301 (19)	256/258 (3)	213/215 (36)	197/199 (85)	181/183 (73)

(a) Fragment $[D]^{+\cdot}$ is the base peak for compounds **3c**, **3e** and **8h**. (%) Ion abundance belongs to the light halogen isotope.

EXPERIMENTAL

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. The ir spectra were recorded on a Perkin Elmer Model 577 spectrophotometer; unless otherwise stated, the spectra were obtained as potassium bromide pellets. A Varian T-60A spectrometer was used for obtaining pmr spectra in deuteriochloroform, with tetramethylsilane as internal reference. Mass spectra were determined on a Varian CH-5 spectrometer using the direct inlet technique (70 eV; 100 μA; temperature of ion source, 200°). Microanalyses were performed at the Microanalytisches Labor Pascher (Bonn).

General Procedure for the Preparation of Hydroxamoyl Chlorides **1**.

A slow stream of dry chlorine was bubbled through a solution of the appropriate aldoxime (0.02 mole) in chloroform (30 ml) at -15° for 30 minutes (8). The solution first turned deep blue and finally light orange. After standing in the ice-bath for 2 hours, excess chlorine was removed by flushing with nitrogen. The solvent was then removed under reduced pressure, and the residue crystallized from chloroform-petroleum ether (40-60°). The hydroxamoyl chlorides listed below were obtained following this procedure. Being unstable they were used immediately, or stored in a refrigerator for only few days before use.

p-Chlorobenzhydroxamoyl Chloride (**1a**).

This compound was obtained in a yield of 70%, mp 88-90° [lit (9) 88.5-89.5°].

m-Chlorobenzhydroxamoyl Chloride (**1d**).

This compound was obtained in a yield of 62%, mp 73-74° [lit (9) 72-73°].

o-Chlorobenzhydroxamoyl Chloride (**1g**).

This compound was obtained in a yield of 32%, mp 57-58° [lit (9) 57-58°].

p-Nitrobenzhydroxamoyl Chloride (**1c**).

This compound was obtained in a yield of 68%, mp 123-124° [lit (9) 124-125°].

m-Nitrobenzhydroxamoyl Chloride (**1e**).

This compound was obtained in a yield of 75%, mp 99-100° [lit (9) 100-102°].

p-Bromobenzhydroxamoyl Chloride (**1b**).

This compound was obtained in a yield of 70%, mp 76-78° [lit (10) 72-74°].

o-Bromobenzhydroxamoyl Chloride (**1h**).

This compound was obtained in a yield of 30%, mp 68-69° [lit (9) 67-68°].

Benzhydroxamoyl Chloride (**1f**).

This compound was obtained in a yield of 50%, mp 48-50° [lit (9) 51-52°].

Benzhydroxamoyl chloride was crystallized from pentane (cooling to -70°). This compound was prepared according to the directions of Piloty and Steinbock (11) by passing chlorine gas through a solution of benzaldoxime (0.1 mole) in 8*N* hydrochloric acid (60 ml) at 0° for 15-30 minutes. The precipitated product was filtered, washed with ice-cold water and used as such.

General Procedure for the Preparation of 3-Aryl-5-imino-Δ^2-1,4,2-oxathiazolines (**3a-e**).

Potassium thiocyanate (0.012 mole) and the particular hydroxamoyl chloride **1** (0.01 mole) were stirred in dry acetone until the precipitation of sodium chloride was completed (2-3 hours). Water (150 ml) was then added to the reaction mixture, and the precipitated product was collected and crystallized from the appropriate solvent.

3-(*o*-Chlorophenyl)-5-(carbamido)imino-Δ^2-1,4,2-oxathiazoline (**8g**).

o-Chlorobenzhydroxamoyl chloride (**1g**) was treated with potassium thiocyanate as specified for **3** above. Extraction of the filtrate, left after removal of the product, with diethyl ether gave *o*-chlorophenylisothiocyanate (**9g**), yield 40%, mp (phenylthiourea derivative) 163-164° [lit (12) 163-165°]; ir (carbon tetrachloride): 2165-2150 cm^{-1}.

3-(*o*-Bromophenyl)-5-(carbamido)imino-Δ^2-1,4,2-oxathiazoline (**8h**).

This compound was prepared from *o*-bromobenzhydroxamoyl chloride (**1h**) and potassiuam thiocyanate as described above for **3** and **8g**. The corresponding *o*-bromophenylisothiocyanate (**9h**) was also isolated, yield 45%, mp (phenylthiourea derivative) 160-161° [lit (12) 161°]; ir (carbon tetrachloride): 2165-2155 cm^{-1}.

3-Phenyl-5-(carbamido)imino-Δ^2-1,4,2-oxathiazoline (**8f**).

A solution of 3-phenyl-5-imino-Δ^2-1,4,2-oxathiazoline (**3f**, 0.01 mole) in chloroform (30 ml) was refluxed for 10 minutes. Upon cooling, the title compound crystallized out, yield 40%, mp 161-162° [lit (4) 165-166°].

O-(Aroyl)arylhydroxamoyl Chlorides (**7a-c**).

These compounds were prepared by direct aroylation of the particular hydroxamoyl chloride with the appropriate aroyl chloride in ether/pyridine at 0°, following literature procedure (13).

O-Benzoylbenzhydroxamoyl Chloride (**7a**).

This compound had mp 110-111° [lit (13) 108-109°].

O-(*p*-Nitrobenzoyl)-*p*-nitrobenzhydroxamoyl Chloride (**7b**).

This compound had mp 203-204° [lit (13) 203-204°].

O-(*m*-Nitrobenzoyl)-*m*-nitrobenzhydroxamoyl Chloride (**7c**).

This compound had mp 192-193° [lit (13) 191-192°].

O-Acetyl-*m*-nitrobenzhydroxamoyl Chloride (**7d**).

m-Nitrobenzhydroxamoyl chloride (0.01 mole) and acetic anhydride (10 ml) were refluxed for 1 hour (6). The resulting mixture was cooled, the precipitate collected and crystallized from ethanol, yield 30%, mp 62-64°; ir: 1760 cm^{-1}.

Anal. Calcd. for $C_9H_7ClN_2O_4$: C, 44.55; H, 2.91; N, 11.55. Found: C, 44.31; H, 2.94; N, 11.46.

Attempted Synthesis of *O*-Substituted Arylhydroxamoyl Thiocyanates.

The appropriate *O*-Substituted arylhydroxamoyl chloride **7** (0.01 mole) was stirred with potassium thiocyanate (0.02 mole) in acetone (80 ml) at room temperature for 24 hours. Work-up of the reaction mixture gave the unchanged starting material (80-90% recovery). The same result was also obtained when the reaction was conducted in acetone or ethanol at reflux temperatures for 24 hours.

Acknowledgements.

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