Ring-Opening Reactions of 1,3,4-Oxadiazol-2-ones and Thiones[1]

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Certain 1,3,4-oxadiazol-2-ones have been found to react with water to form 1,5-diacylcarbohydrazides. The pathway of this reaction appears to be hydrolytic ring opening to form a hydrazide which, in turn, attacks remaining oxadiazolone to form the observed product. The reaction of hydrazides with oxadiazolones generally produces 1,5-diacylcarbohydrazides, whereas arylhydrazines form 1-acyl-5-arylcarbohydrazides. 5-(5-Nitro-2-furyl)-1,3,4-oxadiazol-2-thione has been found to react with amines and hydrazines but not with water, to give products analogous to those obtained with the oxadiazolone.

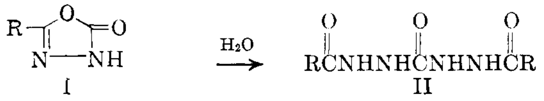
Previous workers have reported ring opening reactions of 1,3,4-oxadiazol-2-ones with such reagents as hydrazine,[2] ammonia,[3] and amines.[3] When hydrazine is the base employed, 1-acylcarbohydrazides are formed. When amines are used, 1-acylsemicarbazides are produced.

We have found that many 1,3,4-oxadiazol-2-ones react with water to form 1,5-diacylcarbohydrazides as the exclusive products. For example, when 5-(2-furyl)-1,3,4-oxadiazol-2-one (Ia) is heated under reflux in water for two hours, 1,5-bis(-2-furoyl)carbohydrazide (IIa) is formed in 98% yield. As shown in Table I, this reaction has also been carried out on 5-nitro-2-furyl-(Ib), phenyl-(Ic), 2-chlorophenyl-(Id), and 4-pyridyl (Ie)-oxadiazolone.

In general, the reactions result in good yields of the carbohydrazides; however, they proceed with increasing difficulty in the order a, b, c, d, e (see Table I). When a solution of 5-(*p*-nitrophenyl)-1,3,4-oxadiazol-2-one (If) in water is heated under reflux for sixty-four hours, only starting material can be recovered. At 150° in water, decomposition occurs to give unknown products.

It would not be surprising if the ease of ring opening could be correlated with the electron-withdrawing power of the groups in the 5-position of the oxadiazolone. However, attempts to find such a relationship have been unsuccessful. For example, it might be expected that the pK_α' values of these compounds would be related to the electron-withdrawing properties of the substituent in the 5-position and that this might be related to the reactivity in the ring opening reaction. It can be seen in Table I that although the pK_α' of the *p*-nitrophenyloxadiazolone (If) is lower than those of Ia, Ic, and Id, it is less reactive than the latter compounds. Also, Ia and Id have similar pK_α' values but different reactivities. The reason for this variation in reactivity in the ring opening reaction thus remains unclear.

TABLE I

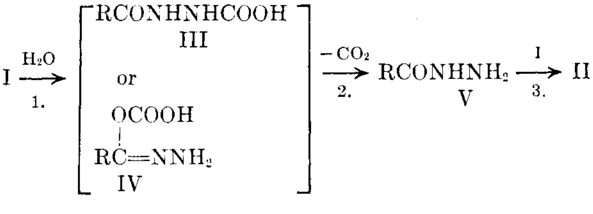


$$\text{I} \xrightarrow{H_2O} R\overset{O}{\overset{\|}{C}}NHNH\overset{O}{\overset{\|}{C}}NHNH\overset{O}{\overset{\|}{C}}R \quad \text{II}$$

R	Time, hr.	Temperature, °C.	Yield, %	p$K_\alpha'^a$
(a) 2-Furyl	2	100	98	7.7
(b) 5-Nitro-2-furyl-	2	100	75	6.6
(c) Phenyl-	64	100	95	8.1
(d) 2-Chlorophenyl	64	100	43	7.8
(e) 4-Pyridyl-	10	150	22	6.8
(f) *p*-Nitrophenyl-	64	100	0	7.3

[a] The pK_α' determinations were carried out by R. U. Robinson and staff of Abbott Laboratories. The measurements were made in 66% dimethylformamide-water solution.

We propose that this reaction takes place in the following manner: (1) a hydrolytic ring opening of the oxadiazolone (I) to produce either an acylhydrazinoformic acid (III) or the acyl hydrazono carbonic anhydride (IV), followed by (2) loss of carbon dioxide from either III or IV to produce a hydrazide (V) which (3) reacts with remaining oxadiazolone (I) to give the carbohydrazide (II).



$$\text{I} \xrightarrow[1.]{H_2O} \left[\begin{array}{c} RCONHNHCOOH \\ \text{III} \\ \text{or} \\ OCOOH \\ | \\ RC{=}NNH_2 \\ \text{IV} \end{array}\right] \xrightarrow[2.]{-CO_2} \underset{\text{V}}{RCONHNH_2} \xrightarrow[3.]{\text{I}} \text{II}$$

This proposal is supported by evidence obtained in reactions of 5-(5-nitro-2-furyl)-1,3,4-oxadiazole-2-one (Ib).

When Ib is heated under reflux with ethanol for ninety-six hours, a compound is formed which appears to be 1-(5-nitro-2-furoyl)-2-carbethoxyhydrazine (VI). Elemental analysis and the infrared spectrum[4] (3.09 μ [s], 5.70 μ [s], 5.90 μ [s], 6.27 μ [w] in 5% dioxane solution) support the structure assigned. A structure analogous to IV would be expected to show —NH_2 bending in the 6.1–6.3-μ region. The only absorption in this portion of the spectrum is at 6.27 μ. This weak

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(1) Presented before the Division of Medicinal Chemistry, 138th Meeting, American Chemical Society, New York City, September 11–16, 1960.

(2) O. Diels and H. Okada, *Ber.*, **45**, 2437 (1912).

(3) A. Stempel, J. Zelauskas, and J. A. Aeschlimann, *J. Org. Chem.*, **20**, 412 (1955).

(4) Infrared spectra were determined by W. Washburn and staff of Abbott Laboratories, whose aid in the interpretation of this data is acknowledged. Spectra were measured on a Perkin-Elmer Model 21 spectrophotometer.

TABLE II

REACTION BETWEEN 5-(5-NITRO-2-FURYL)-1,3,4-OXADIAZOL-2-ONE (Ib) AND 5-NITRO-2-FUROYLHYDRAZINE (Vb)

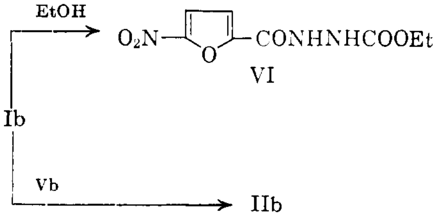
Solvent	Temperature, °C.	Time, hr.	Yield, %	Dielectric constant
Water	100	0.25	64	55.33[a]
1:1 ethanol–water	82	1	33	36.51[b,c]
1:1 dioxane–water	90	0.5	32	25.05[b,d]
Ethanol	79	1	8	18.31[c,e]
Dioxane	101	0.25	0	2.09[b,d]
Ethanol	79	17	64	
Dioxane	101	24	59	

[a] 100°. [b] 80°. [c] See G. Akerlof [*J. Am. Chem. Soc.*, **54**, 4125 (1932)]. [d] See G. Akerlof and O. A. Short [*ibid.*, **58**, 1241 (1936)]. [e] 70°.

band is characteristically present in many furans. The absence of a doublet in the 3-μ region also supports the absence of —NH_2.

The formation of the carbethoxy derivative (VI) supports step 1 in the reaction sequence and also points to III as the unstable intermediate which is formed, rather than IV.

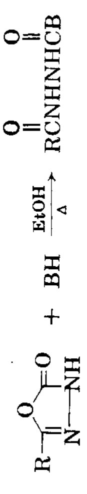
It is known that hydrazine[2] reacts with 1,3,4-oxadiazolones to form carbohydrazides. We have shown in this work that hydrazides and substituted hydrazines react in a similar way. For example, 5-nitro-2-furoylhydrazine (Vb) reacts with 5-(5-nitro-2-furyl)-1,3,4-oxadiazolone (Ib) in dioxane, ethanol and in other solvents to form 1,5-bis(5-nitro-2-furoyl)carbohydrazide (IIb). Therefore, it is reasonable to suppose that hydrazide formed by loss of carbon dioxide from III would react with remaining oxadiazolone to produce the product observed in the water reaction.



An independent preparation of the bisnitrofuroylcarbohydrazide (IIb) from carbohydrazide and 5-nitro-2-furoyl chloride has established the identity of this compound.

In Table II it can be seen that the reaction, in water at 100°, between the nitrofuryloxadiazolone (Ib) and the nitrofuroylhydrazine (Vb) takes place within fifteen minutes to give a 64% yield of the diacylcarbohydrazide (IIb). However, if Ib is heated alone in water at 100°, no IIb can be isolated after fifteen minutes, but after two hours the yield is 75%. Measurements[5] taken during these reactions show that the pH of the reaction mixture remains at 3.65 ± 0.25. It thus seems that the two reactions take place under comparable

TABLE III



R	BH	Reaction time, hr.	Yield, %	Crystallization solvent	M.p.,[a] °C.	Empirical formula	Calculated C	Calculated H	Calculated N	Found C	Found H	Found N
5-Nitro-2-furyl-	Benzhydrazide	1	53	DMF–H_2O	231.5–232.5 (dec.)	$C_{13}H_{11}N_5O_6$	46.85	3.33	21.02	46.95	3.28	21.21
5-Nitro-2-furyl-	Phenylhydrazine	24	43	Ethanol	201.5–202 (dec.)	$C_{12}H_{11}N_5O_5$	47.21	3.63	22.95	47.19	3.78	23.00
5-Nitro-2-furyl-	Benzylamine	2	62	Methanol	187–188.5 (dec.)	$C_{13}H_{12}N_4O_5$	51.31	3.98	18.42	51.14	3.92	18.46
5-Nitro-2-furyl-	*p*-Toluidine	8	47	Methanol	221–223 (dec.)	$C_{13}H_{12}N_4O_5$	51.31	3.98	18.42	51.60	4.19	18.55
5-Nitro-2-furyl-	*p*-Chloroaniline	16	40	Methanol	228–230 (dec.)	$C_{12}H_9ClN_4O_5$	44.39	2.79	17.25	44.65	2.60	17.22
5-Nitro-2-furyl-	Isobutylamine	1	34	Ethanol	192–193 (dec.)	$C_{10}H_{14}N_4O_5$	44.44	5.22	20.73	44.74	5.47	20.88
5-Nitro-2-furyl-	*p*-Nitrophenylhydrazine	6	57	DMF–H_2O	252–254 (dec.)	$C_{12}H_{10}N_6O_7$	41.15	2.88	24.00	41.16	2.87	23.92
2-Furyl-	*p*-Nitrophenylhydrazine	20	66	Methanol–H_2O	238–240 (dec.)	$C_{12}H_{11}N_5O_5$	47.21	3.63	22.95	47.34	3.57	23.08
2-Chlorophenyl-	*p*-Nitrophenylhydrazine	96	37	Methanol	240–241 (dec.)	$C_{14}H_{12}ClN_5O_4$	48.07	3.49	20.01	48.03	3.62	19.87
Phenyl-	*p*-Nitrophenylhydrazine	240	16	Methanol	248–249 (dec.)	$C_{14}H_{13}N_5O_4$	53.33	4.16	22.22	53.41	4.25	22.07
4-Pyridyl-	*p*-Nitrophenylhydrazine	168	46	Ethanol	239–240 (dec.)	$C_{13}H_{12}N_6O_4$	49.37	3.82	26.57	49.56	3.72	26.31
4-Nitrophenyl-[b]	*p*-Nitrophenylhydrazine	168	25	Methanol	263–265 (dec.)	$C_{14}H_{12}N_6O_6$	46.67	3.36	23.33	46.68	3.38	23.21

[a] See ref. 6. [b] See O. Diels and H. Okada [*Ber.*, **46**, 1872 (1913)].

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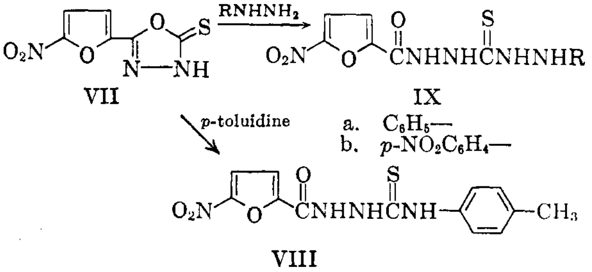
(5) Measurements were made using a Beckman 8970-2 reference electrode, 4990-75 glass electrode, and Model 9600 pH meter, set to pH 7.0 at the boiling point of Beckman 3501 buffer solution.

conditions and that the reaction of water with the oxadiazolone is the slower process. It follows that the ring-opening by water is the rate-determining step in the proposed sequence.

Another interesting aspect of this reaction can be seen in Table II. The first five entries in the table are roughly comparable in reaction time, assuming a rate doubling for a 10° increase in temperature. In pure dioxane or ethanol the process is much slower than in pure water. In 1:1 ethanol–water or dioxane–water, the rate is increased. It is interesting that the higher yields of product are obtained in the solvents with the higher dielectric constants. This may be the result of increased polarization of the oxadiazolone carbonyl in the more polar solvents.

The ring-opening of oxadiazolones with hydrazine and with amines is known to produce carbohydrazides and semicarbazides. This reaction has now been found to be quite general, occurring with hydrazides and substituted hydrazines as well as with amines (see Table III). In one case, the reaction of 5-(5-nitro-2-furyl)-1,3,4-oxadiazol-2-one (Ib) with benzylamine, a salt is formed between the two compounds initially. This salt can be converted to the semicarbazide by heating in ethanol under reflux.

In attempts to carry out conversions of 5-(5-nitro-2-furyl)-1,3,4-oxadiazol-2-thione (VII) analogous to those described above, it soon became clear that this thione is less reactive than the oxadiazolone Ib. For example, VII does not react with water to form a bisacylthiocarbohydrazide, nor does ethanol produce the carbethoxythiohydrazide analogous to VI. Although *p*-toluidine reacts with thione (VII) to form 1-(5-nitro-2-furyl)-4-(*p*-tolyl)-thiosemicarbazide (VIII), benzylamine and isobutylamine form such stable salts that ring-opening cannot be induced. Phenylhydrazine also forms a salt with VII, but this can be converted to the thiocarbohydrazide (IXa) by heating in ethanol solution. *p*-Nitrophenylhydrazine reacts with VII to give the thiocarbohydrazide (IXb) directly.



Experimental[6]

1,5-Bis(2-furoyl)carbohydrazide (IIa).—A suspension of 4.0 g. (0.026 mole) of 5-(2-furyl)-1,3,4-oxadiazole-2-one[7] (Ia) in 100 ml. of water was heated under reflux for 2 hr. The resulting solution was cooled and the crystalline product collected; yield, 3.6 g. (98%); m.p. 220–223° (dec.). Recrystallization from water raised the melting point to 224–225° (dec.).

Anal. Calcd. for $C_{11}H_{10}N_4O_5$: C, 47.48; H, 3.62; N, 20.14. Found: C, 47.25; H, 3.70; N, 20.00.

1,5-Bis(5-nitro-2-furoyl)carbohydrazide (IIb). Procedure A.—A suspension of 5.0 g. (0.025 mole) of 5-(5-nitro-2-furyl)-1,3,4-oxadiazol-2-one[8] (Ib) in 100 ml. of water was heated under reflux for 2 hr. During this time carbon dioxide was evolved by the reaction mixture and the product separated from the boiling solution. Cooling completed the precipitation of the product which was isolated as tan-colored platelets, m.p. 232° (dec.), 3.5 g. (75%). Crystallization from dimethylformamide gave 3.09 g. of IIb, m.p. 234.5–235° (dec.). For analysis a sample was dried for 3 hr. at 80°, *in vacuo*.

Anal. Calcd. for $C_{11}H_8N_6O_9$: C, 35.88; H, 2.19; N, 22.83. Found: C, 35.70; H, 2.19; N, 22.67.

To establish with certainty that the oxodiazolone (Ib) was not thermally decomposing to carbohydrazide (IIb), a sample of Ib was refluxed in dioxane for 48 hr. Only starting material (Ib) was recovered.

For comparative purposes, a solution of 1.97 g. (0.01 mole) of Ib in 160 ml. of water was heated under reflux for 15 min. Only starting material (Ib) was recovered.

Procedure B.—A solution of 1.97 g. (0.01 mole) of Ib and 1.71 g. (0.01 mole) of 5-nitro-2-furoylhydrazine[9] (Vb) in 50 ml. of dioxane was heated under reflux for 24 hr. The solution was then diluted with water to precipitate 2.16 g. (59%) of tan platelets. By mixed melting point and infrared spectrum[4] (in dimethylformamide solution) this material proved to be identical with IIb obtained by procedure A. Work-up of the mother liquor gave 0.71 g. of Ib (36% recovery). Based on this, the yield of IIb is 92%.

For purposes of comparison, the reaction between Ib and Vb was run in several solvents. The results may be seen in Table II. Typically, a solution of 1.97 g. (0.01 mole) of Ib and 1.71 g. (0.01 mole) of Vb in 50 ml. of ethanol was heated under reflux for 1 hr. Carbohydrazide (IIb), 0.30 g. (8%); hydrazide (Vb), 0.77 g. (45%); and oxadiazolone (Ib), 1.16 g. (59%) were obtained from the reaction mixture.

Procedure C.—A solution of 0.90 g. (0.01 mole) of carbohydrazide in 200 ml. of pure dioxane was added slowly to a stirred solution of 3.5 g. (0.02 mole) of 5-nitro-2-furoyl chloride in 20 ml. of dioxane. The mixture was heated on a steam bath for 30 min., filtered, and 250 ml. of water added. After cooling, the crystalline product was collected; m.p. 230–237° (dec.); weight 2.2 g. (60%). Crystallization from dimethylformamide–water gave IIb identical with that obtained by the above procedures.

1,5-Dibenzoylcarbohydrazide (IIc).—A solution of 4.0 g. (0.025 mole) of 5-phenyl-1,3,4-oxadiazol-2-one[10] (Ic) in 100 ml. of water was heated under reflux for 64 hr. Cooling precipitated 3.5 g. (95%) of product melting at 209–213°. Crystallization from water raised the m.p. to 217–218° (lit.[11] m.p. 205°). For analysis, a sample was dried overnight at 100° *in vacuo*.

Anal. Calcd. for $C_{15}H_{14}N_4O_3$: C, 60.39; H, 4.73; N, 18.78. Found: C, 60.63; H, 4.58; N, 18.83.

5-(2-Chlorophenyl)-1,3,4-oxadiazol-2-one (Id).—Phosgene gas was introduced into a solution of 8.5 g. (0.05 mole) of

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[6] All melting points are uncorrected and were determined on a Fisher–Johns melting point apparatus.

[7] H. L. Yale, K. A. Losee, F. M. Perry, and J. Bernstein, *J. Am. Chem. Soc.*, **76**, 2208 (1954).

[8] W. R. Sherman, *J. Org. Chem.*, **26**, 88 (1961).

[9] H. L. Yale, K. Losee, J. Martins, M. Holsing, F. Perry, and J. Bernstein, *J. Am. Chem. Soc.*, **75**, 1933 (1953).

[10] A. Dornow and K. Bruncken, *Ber.*, **82**, 121 (1949).

[11] R. Stolle and K. Krauch, *ibid.*, **47**, 727 (1914).

2-chlorobenzhydrazide[12] in 200 ml. of 10% hydrochloric acid cooled to 0°. After 45 min., the precipitate which had formed was collected, and the mother liquor was treated with phosgene for an additional 30 min. The combined crops were crystallized from methanol to give 5.5 g. (56%) of Id, m.p. 168–169°. An additional 3 g. of product, m.p. 163–166°, was obtained from the methanol mother liquor.

Anal. Calcd. for $C_8H_5ClN_2O_2$: C, 48.88; H, 2.57; N, 14.25. Found: C, 48.67; H, 2.87; N, 14.32.

1,5-Bis(2-chlorobenzoyl)carbohydrazide (IId).—Two grams (0.01 mole) of 5-(2-chlorophenyl)-1,3,4-oxadiazol-2-one (Id) was heated under reflux in 200 ml. of water. After 12 hr., the reaction had not gone to completion, but after 64 hr., 0.8 g. (43%) of the carbohydrazide (IId) was obtained. Crystallization from water gave product melting at 230–232°.

Anal. Calcd. for $C_{15}H_{12}Cl_2N_4O_3$: C, 49.06; H, 3.30; N, 15.26. Found: C, 49.30; H, 3.13; N, 15.27.

1,5-Bis(isonicotinyl)carbohydrazide (IIe). **Procedure A.**—One gram (0.0061 mole) of 5-(4-pyridyl)-1,3,4-oxadiazol-2-one[3] (Ie) was heated with 20 ml. of water in a steel bomb at 150° for 10 hr. After cooling, 0.4 g. (22%) of product was obtained, which, after crystallization from dimethylformamide–water, melted at 261–261.5° (dec.). Another crystallization gave white needles, m.p. 267.5° (dec.).

Anal. Calcd. for $C_{13}H_{12}N_6O_3$: C, 52.00; H, 4.03; N, 27.99. Found: C, 51.82; H, 3.92; N, 27.91.

Procedure B.—While the carbohydrazide (IIe) could not be obtained by simply heating the oxadiazolone (Ie) in boiling water, use of a pH 3 McIlvaine buffer facilitated the reaction. Thus, 2.0 g. (0.012 mole) of Ie was converted to 0.6 g. (32%) of IIe by refluxing for 24 hr. in pH 3 buffer. The product obtained in this way was identical with that obtained above.

1-(5-Nitro-2-furoyl)-2-carbethoxyhydrazine (VI).—A solution of 12.0 g. (0.061 mole) of nitrofuryloxadiazolone (Ib) in 200 ml. of ethanol was heated under reflux for 96 hr. On cooling, 6.6 g. of white crystals separated, m.p. 183–185° (dec.). Concentration of the mother liquor provided an additional 2.2 g. of product, m.p. 177–181° (dec.). Total crude yield was 60%. Crystallization from acetone–water gave analytically pure material, m.p. 183.5–184.5° (dec.).

Anal. Calcd. for $C_8H_9N_3O_6$: C, 39.51; H, 3.73; N, 17.28. Found: C, 39.80; H, 3.84; N, 17.52.

Carbohydrazides and Semicarbazides from Oxadiazolones.—The compounds described in Table III were prepared by heating the required oxadiazolone and base together, in ethanol solution, under reflux. In general, the products were obtained on cooling and concentrating the reaction mixture. In one case, described below, a salt was obtained, which gave the required product on further heating in solution.

Salt of Benzylamine and 5-(5-Nitro-2-furyl)-1,3,4-oxadiazol-2-one (Ib).—When Ib (5.9 g., 0.03 mole) was added to a solution of benzylamine (3.9 g., 0.03 mole) in 75 ml. of ethanol, a precipitate formed which did not entirely dissolve at the boiling point. Cooling provided 8.6 g. (93%) of a water-soluble material, m.p. 143–145° (dec.). This bright yellow-colored compound was crystallized from methanol (charcoal) to give material melting at 146–147° (dec.).

Anal. Calcd. for $C_{13}H_{12}N_4O_5$: C, 51.31; H, 3.98; N, 18.42. Found: C, 51.42; H, 3.96; N, 18.56.

1-(5-Nitro-2-furoyl)-4-(4-tolyl)thiosemicarbazide (VIII).—A mixture of 2.1 g. (0.01 mole) of 5-(5-nitro-2-furyl)-1,3,4-oxadiazol-2-thione (VII)[8] and 1.1 g. (0.01 mole) of *p*-toluidine was refluxed in 100 ml. of ethanol for 16 hr. The ethanol was then evaporated and the residual oil taken up in chloroform and chilled. In this way was obtained 1.3 g. (40%) of product, m.p. 177–180° (dec.). Crystallization from methanol (charcoal) gave product, m.p. 185–186° (dec.).

Anal. Calcd. for $C_{13}H_{12}N_4O_4S$: C, 48.74; H, 3.77; N, 17.49. Found: C, 48.75; H, 3.73; N, 17.36.

Salt of Benzylamine with VII.—When 1.1 g. (0.005 mole) of VII and 0.54 g. (0.005 mole) of benzylamine were dissolved in 150 ml. of ethanol, a water-soluble precipitate formed (1.3 g., 80%) which melted at 185–189° (dec.). Crystallization from ethanol gave yellow crystals, m.p. 185–186° (dec.).

Anal. Calcd. for $C_{13}H_{12}N_4O_4S$: C, 48.75; H, 3.77; N, 17.49. Found: C, 48.66; H, 3.52; N, 17.60.

Salt of Isobutylamine with VII.—A solution of 2.1 g. (0.01 mole) of VII and 0.73 g. (0.01 mole) of isobutylamine in 50 ml. of ethanol was taken to dryness and the resulting oil crystallized from chloroform. This gave 2.8 g. (98%) of water soluble yellow crystals, m.p. 164–167° (dec.). Crystallization from ethanol gave product, m.p. 166–168° (dec.).

Anal. Calcd. for $C_{10}H_{14}N_4O_4S$: C, 41.95; H, 4.92; N, 19.57. Found: C, 41.95; H, 5.19; N, 19.77.

1-(5-Nitro-2-furoyl)-5-phenyl-3-thiocarbohydrazide (IXa).—A solution of 10.6 g. (0.05 mole) of VII and 5.4 g. (0.05 mole) of phenylhydrazine in 400 ml. of ethanol was refluxed for 18 hr. After this time, the solvent was removed and the residual oil taken up in chloroform. On cooling, 4.2 g. (26%) of yellow crystals separated. This material, melting at 176–181° (dec.), was crystallized from boiling ethanol (charcoal), to give pure IXa melting at 192.5–193° (dec.).

Anal. Calcd. for $C_{12}H_{11}N_5O_4S$: C, 44.88; H, 3.45; N, 21.79. Found: C, 44.79; H, 3.75; N, 21.56.

If this reaction is carried out in 60 ml. of ethanol, a canary-yellow product separates in 81% yield, m.p. 132—133° (dec.). This is water-soluble and may be converted to IXa by heating, as above, in ethanol. This is the salt formed by VII and phenylhydrazine.

Anal. Calcd. for $C_{12}H_{11}N_5O_4S$: C, 44.88; H, 3.45; N, 21.79. Found: C, 44.95; H, 3.39; N, 21.77.

1-(5-Nitro-2-furoyl)-5-(*p*-nitrophenyl)-3-thiocarbohydrazide (IXb).—A solution of 4.3 g. (0.02 mole) of VII and 3.1 g. (0.02 mole) of *p*-nitrophenylhydrazine in 100 ml. of ethanol was refluxed for 24 hr. The mixture was then taken to dryness and the resulting oil extracted with chloroform. Cooling gave 3.8 g. (51%) of yellow product, m.p. 200–203° (dec.). Crystallization from methanol-water gave product, m.p. 203–205° (dec.).

Anal. Calcd. for $C_{12}H_{10}N_6O_6S$: C, 39.32; H, 2.75; N, 22.96. Found: C, 39.05; H, 2.91; N, 22.76.

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