mum was at 240 mμ (ε 25,400), the infrared spectrum was consistent, and the titration gave a $pK_a = 4.75$ (apparent mol. wt., 535; calcd., 529).

Sodium O-2-Thenoyl-7-(2-thiopheneacetamido)cephalosporadesate.—As described above, 1.0 g. (0.00255 mole) of potassium 7-(2-thiopheneacetamido)cephalosporadesate was treated with 2.93 g. (0.02 mole) of 2-thenoyl chloride. After evaporation of the acetone and extraction with ethyl acetate, a yellow precipitate of the sodium salt separated from the water solution. Additional salt was obtained by the addition of saturated NaCl solution. The combined precipitates when dried weighed 800 mg. Recrystallization of this solid from methanol–2-propanol gave 400 mg. of the product (32%), m.p. 137–142° dec.

Anal. Calcd. for $C_{19}H_{15}N_2NaO_6S_3$: C, 46.90; H, 3.10; N, 5.76. Found: C, 47.11; H, 3.28; N, 5.55.

The ultraviolet maximum was at 240 mμ (ε 18,400), the infrared was consistent, and the titration indicated a $pK_a = 4.7$ (apparent mol. wt., 482; calcd., 486).

Sodium O-Benzoyl-7-(2-thiopheneacetamido)cephalosporadesate.—In the usual fashion, 3.3 g. (0.00842 mole) of potassium desacetyl acid salt was treated with 8.0 g. (0.057 mole) of benzoyl chloride and NaOH. The sodium salt was precipitated from the water solution after acetone evaporation by the addition of saturated NaCl solution. The crude, dried solid weighed 2.54 g. and an infrared spectrum indicated it was of fair quality. Purification, however, was quite difficult. The solid was dissolved by suspension in water and addition of acetone until solution was effected except for a trace which was filtered off. Some acetone was then evaporated until the product just started to precipitate. The mixture was chilled and a gelatinous precipitate separated which was filtered and dried (1 g.). It had darkened in color. It was then dissolved in hot methanol, a dark fraction was filtered off, and the solution was concentrated and then diluted with 2-propanol to cloudiness. The solution deposited a light cream solid on chilling which was centrifuged and vacuum dried, m.p. 148–150° dec., 220-mg. yield. The product, chromatographed on paper (70% 2-propanol–water), gave one spot by bioautography. The ultraviolet spectrum gave a maximum absorption at 233 mμ (ε 22,100) and the titration showed a pK_a of 4.85 (apparent mol. wt., 526; calcd., 480).

Anal. Calcd. for $C_{21}H_{17}N_2NaO_6S_2$: C, 52.49; H, 3.56; N, 5.83. Found: C, 52.36; H, 3.66; N, 5.84.

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Syntheses with 5-Nitro-2-furonitrile

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5-Nitro-2-furonitrile has been prepared by the dehydration of 5-nitro-2-furamide with phosphorus oxychloride. Reaction of the nitrile with thioacetamide in dimethylformamide saturated with HCl has provided 5-nitro-2-thiofuramide. The thiofuramide with α-bromo ketones has given 2-(5-nitro-2-furyl)-4-methyl-, -phenyl-, and -(5-nitro-2-furyl)thiazoles. Oxidation with iodine has provided 3,5-bis(5-nitro-2-furyl)-1,2,4-thiadiazole. 5-Nitro-2-furamidoxime is obtained by the addition of hydroxylamine to the nitrile. This amidoxime is O-acylated by acetyl, benzoyl, and chloroacetyl chloride as well as phosgene and ethyl chloroformate. O- as opposed to N-acylation is established by the infrared spectra of typical members of this group. Heating the acetyl, benzoyl, and chloroacetyl esters at their melting points has provided the corresponding 5-substituted 3-(5-nitro-2-furyl)-1,2,4-oxadiazoles. Reaction of the amidoxime with acetaldehyde and benzaldehyde has given the corresponding 5-substituted 3-(5-nitro-2-furyl)-Δ^2-1,2,4-oxadiazolines. 5-Nitro-2-furamidine is obtained from the nitrile *via* the ethyl imidate ester by reacting the imidate with methanolic ammonium chloride. The amidine has been condensed with the appropriate β-diketones to give 2-(5-nitro-2-furyl)-4,6-dimethyl-, -4,6-di(trifluoromethyl)-, -4-methyl-6-trifluoromethyl-, -4-trifluoromethyl-6-(2-furyl)-, and -4-trifluoromethyl-6-(2-thienyl)-pyrimidines. The antibacterial properties of the most active members of this series of compounds are presented.

As a means of extending our previous studies of 5-nitrofuran antibacterials[2] we looked on 5-nitro-2-furonitrile (I) as a potentially versatile starting material. This simple compound presented the opportunity of developing a variety of heteroaliphatic and heterocyclic systems at the 2-position of 5-nitrofuran.

At the outset of this work two methods for the preparation of nitrile I had been described: the nitration of 2-furonitrile[3] and the dehydration of 5-nitro-2-furaldoxime by means of acetic anhydride.[4] A more accessible starting material for us was methyl 5-nitro-2-furoate. This remarkably reactive ester is converted in 87% yield to 5-nitro-2-furamide by dissolving it in liquid ammonia at −33°. The amide may then be converted to the nitrile in 63% yield by the action of phosphorus oxychloride.

We have found that I undergoes many of the usual reactions of nitriles, its possibilities as a starting material being limited mainly by the base instability of the 5-nitrofuran system. The three principal intermediates (III–V) which are used in this work are prepared from I. Thus, when I is treated with ethanolic HCl in the manner of Pinner,[5] ethyl 5-nitro-2-furimidate hydrochloride (II) is formed in 92% yield. After conversion to the free base by liquid ammonia at −33°, with which it does not react further, the imido ester is heated with methanolic ammonium chloride, after Barber and Slack,[6] to form 5-nitro-2-furamidine hydrochloride (V) in 73% yield. Another useful intermediate, 5-nitro-2-thiofuramide (III), is formed in 52% yield by

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(2) W. R. Sherman, *J. Org. Chem.*, **26**, 88 (1961); W. R. Sherman and D. E. Dickson, *ibid.*, **27**, 1351 (1962); W. R. Sherman and A. A. Alter, *ibid.*, **27**, 2237 (1962); W. R. Sherman and A. Von Esch, *ibid.*, **27**, 3472 (1962).

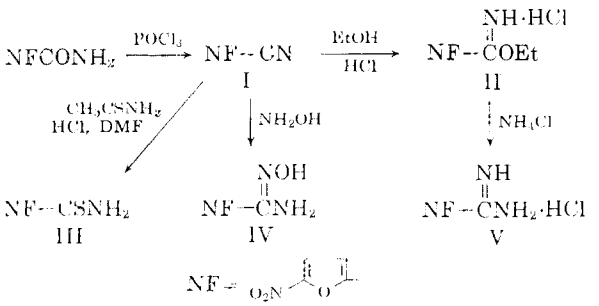
(3) J. M. Straley, *Iowa State J. Sci.*, **11**, 115 (1936).

(4) C. D. Nenitzescu and C. Bucur, *Rev. chim., Acad. rep. populaire Roumaine*, **1**, 155 (1956).

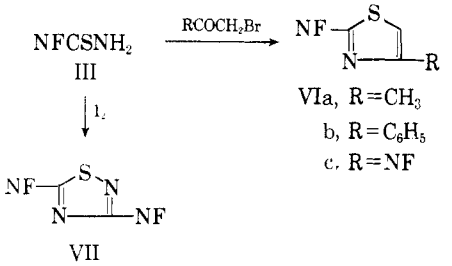
(5) A. Pinner, *Ber.*, **25**, 1414 (1892).

(6) H. J. Barber and R. Slack, *J. Am. Chem. Soc.*, **66**, 1607 (1944).

means of the reaction first described by Taylor and Zoltewicz[7] of treating a nitrile with thioacetamide in dimethylformamide saturated with HCl. The third intermediate obtained from I is 5-nitro-2-furamidoxime (IV), which is formed in 70% yield by the addition of hydroxylamine. Attempts to add hydrazine to I to form 5-nitro-2-furyliminohydrazide were unsuccessful, always resulting in tars.

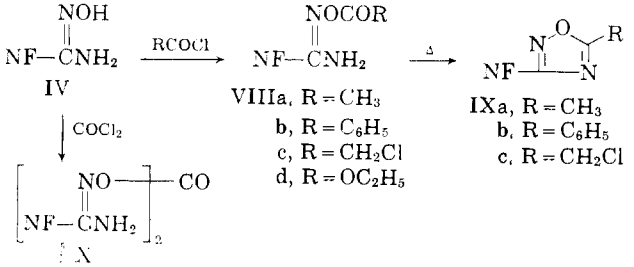


Reaction of thioamide III with several α-bromo ketones in the manner of Hantzsch[8] gave the 5-nitro-2-furylthiazoles (VIa–c). Oxidation by iodine converted the thioamide to 3,5-bis(5-nitro-2-furyl)-1,2,4-thiadiazole (VII) in a reaction typical of that first observed by Hofmann.[9]



While amidoximes are known to be converted to 1,2,4-oxadiazoles by the direct action of carboxylic acid chlorides,[10] this led only to amidoxime O-esters VIIIa–c in the case of 5-nitro-2-furamidoxime (IV). However, when esters VIIIa–c were heated at their melting points, they were converted, in the manner described by Tiemann and Kruger,[11] to the 1,2,4-oxadiazoles (IXa–c).

Attempts to prepare 3-(5-nitro-2-furyl)-1,2,4-oxadiazol-5-one by pyrolysis of VIIId, by heating VIIId in ethanol, water, or acetic acid, or by the action of phosgene on amidoxime IV were uniformly unsuccessful. Further, the reaction of phosgene with amidoxime IV gave a 22% yield of bis(5-nitro-2-furamidoxime)carbonate ester (X), instead of the hoped for oxadiazolone.



(7) E. C. Taylor and J. A. Zoltewicz, *J. Am. Chem. Soc.*, **82**, 2656 (1960).
(8) A. Hantzsch, L. Arapides, and V. Traetmann, *Ann.*, **249**, 1 (1888).
(9) A. W. Hofmann, *Ber.*, **2**, 645 (1869); see also M. W. Crooyn and T. W. Nakagawa, *J. Am. Chem. Soc.*, **74**, 3023 (1952).
(10) E. G. Bergmann, H. Berglas, and V. d'Avilla, *J. Org. Chem.*, **18**, 61 (1953).
(11) F. Tiemann and P. Krager, *Ber.*, **17**, 1685 (1884).

This behavior has been reported by Falck,[12] in the case of benzamidoxime.

The assignment of the O-acyl structure to the amidoxime esters is based on their infrared spectra (see Table I). As in the case of O-acetylformamidoxime,[13] these compounds show two sharp absorptions in the 3400-cm.$^{-1}$ region, presumably due to the NH stretching of the free amino group. In the case of the N-acetylamidoxime, only one sharp band is observed, the other absorption in this region, due to OH, being broad. Carbonyl absorption is near 1750 cm.$^{-1}$ while what is probably C=N is at about 1650 cm.$^{-1}$.

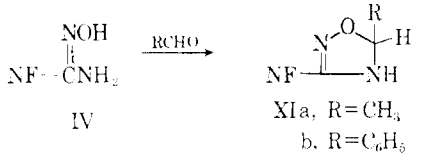
TABLE I

INFRARED SPECTRA OF ACYLAMIDOXIMES[a]

Cmpd.	X-H	C=Y
O-Acetylformamidoxime[4]	3420, 3295	1735, 1655
N-Acetylformamidoxime[6]	3335, (3300–2900)[c]	1730, 1675
VIIIa	3440, 3310	1765, 1650
VIIIb	3470, 3375	1735, 1630
VIIIc	3460, 3350	1770, 1637

[a] All X-H absorptions are medium intensity; all C=Y absorptions are strong. Spectra of VIIIa–c were determined in Nujol mull, frequencies are cm.$^{-1}$. [b] See ref. 13. [c] Broad.

When amidoximes are heated with aldehydes, they are converted to Δ^2-1,2,4-oxadiazolines.[14] Thus, IV reacted with acetaldehyde and benzaldehyde to give XIa and b.



In general, 5-nitro-2-furamidine hydrochloride (V) was decomposed under conditions strenuous enough for reaction of the amidine function. For example, attempts to prepare 2-(5-nitro-2-furyl)imidazoles by condensing V with α-bromo ketones were unsuccessful because of the necessity of using excess base with resulting degradation of the 5-nitrofuran system. However, one series of reactions was carried out, following the method of Pinner[15] for the condensation of β-diketones with amidines. Thus the 2-(5-nitro-2-furyl)pyrimidines XIIa–e were prepared from V and the appropriate diketones.

In general, while most of the compounds described had antimicrobial activity[16] *in vitro*, they were largely ineffective in controlling experimental infections in animals. Table II describes the antibacterial properties

(12) E. Falck, *Ber.*, **18**, 2470 (1885).
(13) F. Eloy, R. Lenaers, and C. Moussebois, *Helv. chim. Acta*, **45**, 437 (1962).
(14) F. Tiemann, *Ber.*, **22**, 2112 (1889).
(15) A. Pinner, *ibid.*, **26**, 2124 (1893).
(16) Antimicrobial activity was determined by W. Grundy, R. H. Goss, J. Bolper, D. Kenney, and staff of Abbott Laboratories.

TABLE II

ANTIBACTERIAL ACTIVITIES[a,b]

Compd.	*Staphylococcus aureus* Smith	*Pseudomonas aeruginosa* BMH 10	*Proteus vulgaris*, Abbott J.J.	*Proteus mirabilis* Finland 9	*Escherichia coli* Juhl	*Salmonella typhimurium* Abbott
5-Nitro-2-furaldehyde semicarbazone[c]	12.5	>400	50	50	25	12.5
I	3.1	50	25	25	6.2	12.5
III	6.2	100	25	12.5	6.2	6.2
V	12.5	50	50	50	25	25
VIa	25	>200	>200	100	6.2	6.2
VIIIa	12.5	>200	200	100	6.2	<6.2
VIIIc	50	>200	>200	100	12.5	12.5
VIIId	100	>200	>200	200	25	25
IXa	100	>200	200	100	12.5	12.5
IXc	12.5	>200	>200	100	12.5	12.5
XIa	≤3.1	>200	200	100	6.2	6.2
XIIa	12.5	100	200	200	50	50

[a] Values represent parts per million required to completely inhibit growth in a broth dilution test at 24 hr. Appropriate amounts of the compound in diluent (dissolved in dimethylformamide and water) are added at 2-fold dilution levels to 5 ml. of BHI broth (Difco). Twenty-four hour cultures in BHI broth are diluted 1:100 in sterile water, and 0.1 ml. of the diluted culture is used as the inoculum for each tube. The tubes are incubated at 37°, and the presence or absence of growth in the tubes is recorded at 24 hr. [b] See ref. 16. [c] Furacin®.

of the most active of the nitrofurans in the *in vitro* test. Compounds not present in the table which are described in this paper were found to be less active.

In addition to the antibacterial activity shown, the thioamide III and the chloromethyloxadiazole VIIIc were also inhibitory to *Chaetomium globosum*, *Myrothecium verrucaria*, and an *Alternaria* at concentrations of 10 p.p.m.

Experimental[17]

5-Nitro-2-furamide.—This amide, which was first prepared by the action of ammonia on nitrofuroyl chloride,[18] may be prepared more conveniently by the following method. One part of dry powdered methyl 5-nitro-2-furoate was added portionwise with mechanical stirring to three parts of liquid ammonia in an open vessel. The rate of addition was such that the evaporation of ammonia was kept under control. After the addition, the solution was stirred until all the ammonia had evaporated, then crystallized from ethanol to give product, m.p. 162–164°. Total yield including second and third crops from crystallization mother liquor was 87%.

5-Nitro-2-furonitrile (I).—5-Nitro-2-furamide (100 g., 0.64 mole) and phosphorus oxychloride (100 g., 0.65 mole) were heated together at 100° until HCl no longer was liberated (about 1.5 hr.). The reaction mixture was poured onto 750 g. of ice with stirring and the crude product was collected by filtration. After crystallization from carbon tetrachloride (charcoal) the pure nitrile weighed 56.0 g. (63% yield) and melted at 63–64°.

Anal. Calcd. for $C_5H_2N_2O_3$: C, 43.49; H, 1.46; N, 20.29. Found: C, 43.56; H, 1.41; N, 20.23.

Ethyl 5-Nitro-2-furimidate (II).—Anhydrous HCl was bubbled through a solution of 5-nitro-2-furonitrile (6.9 g., 0.05 mole) and absolute ethanol (3.2 ml., 0.055 mole) in 50 ml. of anhydrous ether. After 2 hr. the imido ether hydrochloride was collected by filtration and washed on the filter with ether. The yield of hydrochloride was 10.2 g. (93%). This salt was unstable and discolored rapidly on standing. Heating the salt above 100° converted it to 5-nitro-2-furamide, presumably with loss of ethyl chloride. Upon warming the salt in aqueous solution, the ethyl ester was formed. For analysis and for storage, the salt was best converted to the free base. This was done by suspending the hydrochloride in liquid ammonia (about 1 g./3 ml.) and allowing the ammonia to evaporate. The free furimidate was extracted with boiling carbon tetrachloride, from which it crystallized on cooling. The over-all yield of II was 7.6 g. (82%), m.p. 73–74°.

Anal. Calcd. for $C_7H_8N_2O_4$: C, 45.65; H, 4.38; N, 15.21. Found: C, 45.90; H, 4.17; N, 15.00.

(17) All melting points are uncorrected and were determined on a Fisher-Johns melting point apparatus.

(18) R. Marquis, *Compt. rend.*, **137**, 520 (1903).

5-Nitro-2-furamidine Hydrochloride (V).—A solution of ethyl 5-nitro-2-furimidate (9.2 g., 0.05 mole) and ammonium chloride (2.7 g., 0.05 mole) in 225 ml. of methanol was heated under reflux for 4 hr. The solution was concentrated to 25 ml. and diluted with 100 ml. of ether. The crude amidine hydrochloride separated as a white solid, m.p. 245–250° dec., weighing 7.0 g. (73%). For analysis the product was crystallized from pyridine to give material melting at 247–249° dec.

Anal. Calcd. for $C_5H_5N_3O_3 \cdot HCl$: C, 31.35; H, 3.15; N, 21.93. Found: C, 31.42; H, 3.19; N, 21.82.

5-Nitro-2-furamidoxime (IV).—To a solution of hydroxylamine hydrochloride (6.9 g., 0.01 mole) and KOH (5.6 g., 0.01 mole) in 500 ml. of ethanol was added 5-nitro-2-furonitrile (13.8 g., 0.01 mole). The mixture was heated under reflux for 10 min., treated with charcoal, filtered, and concentrated to 300 ml. Upon cooling, the product separated as yellow needles, m.p. 175–177° dec., weighing 12 g. (70%). Material melting from 177–178° dec. was obtained by crystallization from ethanol.

Anal. Calcd. for $C_5H_5N_3O_4$: C, 35.09; H, 2.95; N, 24.56. Found: C, 35.01; H, 3.06; N, 24.68.

5-Nitro-2-thiofuramide (III).—Thioacetamide (15.0 g., 0.2 mole) and 5-nitro-2-furonitrile (13.8 g., 0.1 mole) were dissolved in 250 ml. of N,N-dimethylformamide saturated with anhydrous HCl. The solution was heated for 0.5 hr. on a steam bath, concentrated to 125 ml., and poured onto 500 g. of ice. The solid product was collected by filtration and crystallized from ethanol (charcoal) to give 9.0 g. (52%), m.p. 178–182° dec. A second crystallization from ethanol gave analytically pure material, m.p. 185–187° dec.

Anal. Calcd. for $C_5H_4N_2O_3S$: C, 34.88; H, 2.34; N, 16.28. Found: C, 35.14; H, 2.40; N, 16.15.

2-(5-Nitro-2-furyl)-4-methylthiazole (VIa).—A solution of 5-nitro-2-furylthioamide (3.4 g., 0.02 mole) and chloroacetone (1.85 g., 0.02 mole) was heated under reflux in 100 ml. of ethanol for 24 hr. and cooled; the product which separated (2.5 g., m.p. 140–144°) was recrystallized from ethanol (charcoal); yield 2.0 g. (48%), m.p. 142–143°.

Anal. Calcd. for $C_8H_6N_2O_3S$: C, 45.71; H, 2.87; N, 13.33. Found: C, 45.41; H, 3.13; N, 13.16.

2-(5-Nitro-2-furyl)-4-phenylthiazole (VIb).—A solution of 5-nitro-2-furylthioamide (3.4 g., 0.02 mole) and chloroacetophenone (3.1 g., 0.02 mole) in 100 ml. of ethanol was heated for 5 min. The product which formed was collected by filtration and washed with ethanol, and the combined ethanol wash and filtrate was heated under reflux for 12 hr. The product obtained on cooling was combined with the first crop (m.p. 172–175°, 5.4 g., 100%) and recrystallized for analysis from ethanol (charcoal) to give 3.8 g. (70%) of yellow needles, m.p. 172–173°.

Anal. Calcd. for $C_{13}H_8N_2O_3S$: C, 57.34; H, 2.96; N, 10.29. Found: C, 57.46; H, 3.03; N, 10.44.

2,4-Bis(5-nitro-2-furyl)thiazole (VIc).—A solution of 5-nitro-2-furylthioamide (3.4 g., 0.02 mole) and 2-bromoacetyl-5-

nitrofuran[19] (4.5 g., 0.02 mole) in 100 ml. of ethanol was heated under reflux for 4 hr. and cooled, and the product was collected by filtration. The crude product weighing 6.0 g. (98%), m.p. 250–253° dec., was crystallized for analysis from ethanol (charcoal) to give 4.2 g. (68%) of bright yellow crystals, m.p. 252–254° dec.

Anal. Calcd. for $C_{11}H_5N_3O_6S$: C, 43.00; H, 1.64; N, 13.67. Found: C, 43.12; H, 1.81; N, 13.52.

3,5-Bis(5-nitro-2-furyl)-1,2,4-thiadiazole (VII).—Iodine (5.1 g., 0.04 g.-atom) and 5-nitro-2-furylthioamide (1.7 g., 0.01 mole) were heated together under reflux in 60 ml. of ethanol for 10 min. The cooled solution provided 1 g. (65%) of crude product, m.p. 220–235° dec., which after crystallization from ethanol melted at 239–242° dec.

Anal. Calcd. for $C_6H_4N_4O_6S$: C, 38.97; H, 1.31; N, 18.15. Found: C, 39.12; H, 1.56; N, 18.20.

5-Nitro-2-furamidoxime Acetate Ester (VIIIa).—Acetyl chloride (7.8 g., 0.1 mole) and 5-nitro-2-furamidoxime (17.2 g., 0.1 mole) were heated under reflux in 900 ml. of benzene for 12 hr. The mixture was concentrated to about 400 ml. and cooled, and the product was collected by filtration and crystallized from ethanol. In this way, 13.8 g. (65%) of yellow crystals, m.p. 158–161°, was obtained.

Anal. Calcd. for $C_7H_7N_3O_5$: C, 39.44; H, 3.31; N, 19.72. Found: C, 39.58; H, 3.32; N, 19.81.

5-Nitro-2-furamidoxime Benzoate Ester (VIIIb).—To a solution of 5-nitro-2-furamidoxime (5.1 g., 0.03 mole) in 500 ml. of benzene containing 4 ml. of pyridine (3.9 g., 0.05 mole) was added benzoyl chloride (4.2 g., 0.03 mole), and the mixture then was heated under reflux for 3 hr. The reaction mixture was cooled and the product was collected and crystallized from ethanol to give 4.7 g. (57%) of cream-colored plates, m.p. 209–210° dec.

Anal. Calcd. for $C_{12}H_9N_3O_5$: C, 52.37; H, 3.30; N, 15.27. Found: C, 52.67; H, 3.03; N, 15.17.

5-Nitro-2-furamidoxime Chloroacetate Ester (VIIIc).—A solution of chloroacetyl chloride (4.6 g., 0.04 mole) and 5-nitro-2-furamidoxime (6.8 g., 0.04 mole) in 900 ml. of benzene was heated under reflux for 48 hr. The mixture was then cooled and the product, which separated, was collected and crystallized from ethyl acetate; yield 5.2 g. (53%), m.p. 178–181° dec. A second crystallization gave material melting at 182–183° dec.

Anal. Calcd. for $C_7H_6ClN_3O_5$: C, 33.95; H, 2.44; N, 16.97. Found: C, 34.22; H, 2.62; N, 17.26.

5-Nitro-2-furamidoxime Ethyl Carbonate Ester (VIIId).—A solution of 5-nitro-2-furamidoxime (6.8 g., 0.04 mole) and pyridine (6.3 g., 0.08 mole) in 500 ml. of ethanol was heated to boiling and ethyl chloroformate (4.9 g., 0.045 mole) in 50 ml. of benzene was added dropwise. The mixture was heated under reflux for 3 hr. and then concentrated to dryness. After crystallization from ethanol (charcoal), pale yellow plates were obtained, m.p. 147–149°, weighing 6.2 g. (64%). For analysis the material was crystallized a second time from ethanol to give product, m.p. 151–152°.

Anal. Calcd. for $C_8H_9N_3O_6$: C, 39.51; H, 3.73; N, 17.28. Found: C, 39.75; H, 3.78; N, 17.20.

Bis(5-nitro-2-furamidoxime) Carbonate Ester (X).—A solution of 5-nitro-2-furamidoxime (1.7 g., 0.01 mole) in 100 ml. of 10% HCl was cooled to 0° and phosgene gas was passed through the solution until no further precipitation occurred. The product was collected by filtration and crystallized from dimethylformamide–water to give 0.4 g. (22%) of product, m.p. 189–191° dec.

Anal. Calcd. for $C_{11}H_8N_8O_9$: C, 35.88; H, 2.19; N, 22.83. Found: C, 36.02; H, 1.92; N, 22.71.

3-(5-Nitro-2-furyl)-5-methyl-1,2,4-oxadiazole (IXa).—5-Nitro-2-furamidoxime acetate ester (5.3 g., 0.025 mole) was heated at 170° for 15 min. and the resulting oil crystallized from ethanol (charcoal) to give 3.2 g. (66%), m.p. 100–103°. A second crystallization raised the melting point to 105°.

Anal. Calcd. for $C_7H_5N_3O_4$: C, 43.08; H, 2.58; N, 21.54. Found: C, 43.30; H, 2.67; N, 21.66.

3-(5-Nitro-2-furyl)-5-phenyl-1,2,4-oxadiazole (IXb).—5-Nitro-2-furamidoxime benzoate ester was heated in an oil bath at 215° until water ceased to be evolved. The cooled, black residue was then ground to a powder and crystallized from ethanol (charcoal). In this way was obtained 2.75 g. (36.6%) of cream-colored crystals, m.p. 196–197°. For analysis this was crystallized again from ethanol, with 80% recovery, to give product, m.p. 200–201°.

Anal. Calcd. for $C_{12}H_7N_3O_4$: C, 56.03; H, 2.74; N, 16.34. Found: C, 55.93; H, 2.65; N, 16.13.

3-(5-Nitro-2-furyl)-5-chloromethyl-1,2,4-oxadiazole (IXc).—5-Nitro-2-furamidoxime chloroacetate ester was heated at its melting point (183°) for 5 min. and the resulting product was crystallized from ethanol (charcoal). In this way the product was obtained analytically pure in a yield of 0.5 g. (54%), m.p. 109–110°.

Anal. Calcd. for $C_7H_4ClN_3O_3$: C, 36.62; H, 1.75; N, 18.31. Found: C, 36.91; H, 1.79; N, 18.25.

3-(5-Nitro-2-furyl)-5-methyl-Δ^2-1,2,4-oxadiazoline (XIa).—A solution of 5-nitro-2-furamidoxime (5.1 g., 0.03 mole) and 50 ml. of acetaldehyde in 100 ml. of ethanol was heated under reflux for 5 hr. Concentrating and cooling gave 3.6 g. (61%) of bright yellow product, m.p. 154–156°. For analysis this was crystallized several times from ethanol to give material, m.p. 157–158°.

Anal. Calcd. for $C_7H_7N_3O_4$: C, 42.64; H, 3.58; N, 21.32. Found: C, 42.77; H, 3.61; N, 21.33.

3-(5-Nitro-2-furyl)-5-phenyl-Δ^2-1,2,4-oxadiazoline (XIb).—A solution of 5-nitro-2-furamidoxime (6.0 g., 0.035 mole) in 50 ml. of benzaldehyde was heated at 100° for 4 hr. The benzaldehyde was removed at 10 mm. pressure, with care taken to keep the bath temperature below 100°. The residue was washed with ether and crystallized from ethanol (charcoal) to give pale yellow crystals, m.p. 155–157°, 3.5 g. (39%).

Anal. Calcd. for $C_{12}H_9N_3O_4$: C, 55.60; H, 3.50; N, 16.21. Found: C, 55.35; H, 3.55; N, 16.37.

2-(5-Nitro-2-furyl)-4,6-dimethylpyrimidine (XIIa).—A solution of 5-nitro-2-furamidine hydrochloride (9.6 g., 0.05 mole), 2,4-pentanedione (5.2 g., 0.052 mole), and anhydrous sodium acetate (8.2 g., 0.1 mole) in 100 ml. of glacial acetic acid was heated under reflux for 2 hr. The acetic acid was then removed at reduced pressure and water was added to the resulting residue. The insoluble precipitate was crystallized from ethanol (charcoal) to give 3.2 g. (29%) of cream-colored product, m.p. 141–142°. For analysis this was crystallized again from ethanol to give material, m.p. 145–146°.

Anal. Calcd. for $C_{10}H_9N_3O_3$: C, 54.79; H, 4.14; N, 19.17. Found: C, 54.66; H, 4.16; N, 18.98.

2-(5-Nitro-2-furyl)-4,6-bis(trifluoromethyl)pyrimidine (XIIb).—This was prepared in the same manner as XIIa only using 1,1,1,5,5,5-hexafluoro-2,4-pentanedione. The product was obtained in 9.0% yield, melting at 107–108°.

Anal. Calcd. for $C_{10}H_3F_6N_3O_3$: C, 36.71; H, 0.92; N, 12.84. Found: C, 36.77; H, 1.11; N, 12.72.

2-(5-Nitro-2-furyl)-4-trifluoromethyl-6-methylpyrimidine (XIIc).—This was prepared in the same manner as XIIa only using 1,1,1-trifluoro-2,4-pentanedione to give 70% of product, m.p. 99–100°.

Anal. Calcd. for $C_{10}H_6F_3N_3O_3$: C, 43.96; H, 2.22; N, 15.38. Found: C, 44.15; H, 2.32; N, 15.65.

2-(5-Nitro-2-furyl)-4-trifluoromethyl-6-(2-furyl)pyrimidine (XIId).—This was prepared in the same manner as XIIa only using 1,1,1-trifluoro-4-(2-furyl)-2,4-butanedione, in 9% yield, m.p. 153° dec.

Anal. Calcd. for $C_{13}H_6F_3N_3O_4$: C, 48.01; H, 1.86; N, 12.92. Found: C, 48.06; H, 2.00; N, 12.95.

2-(5-Nitro-2-furyl)-4-trifluoromethyl-6-(2-thienyl)pyrimidine (XIIe).—This was prepared in the same manner as XIIa only using 1,1,1-trifluoro-4-(2-thienyl)-2,4-butanedione in 10% yield, m.p. 187–189°.

Anal. Calcd. for $C_{13}H_6F_3N_3O_3S$: C, 45.76; H, 1.77; N, 12.31. Found: C, 45.97; H, 1.56; N, 12.39.

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