dium on charcoal (15 g.), and this mixture hydrogenated at 70° for 2 hr. at 35 kg./cm.^{2} A slightly greater than theoretical uptake of hydrogen was obtained. The catalyst was filtered off and the solution concentrated to an oil *in vacuo*. The residual oil was distilled through a 15 cm. Vigreux column at atmospheric pressure. The fraction distilling at 85–95° was collected, cooled, and an excess of sulfuric acid was added. A white solid crystallized; yield, 90 g., m.p. 133–140° (dec.). Two recrystallizations from 80% ethanol–water gave the pure compound, m.p. 143–144°.

Anal. Calcd. for $CH_6N_2 \cdot H_2SO_4$: C, 8.3; H, 5.6; N, 19.4; S, 22.2. Found: C, 8.4; H, 5.4; N, 19.6; S, 21.9.

Reduction of Nitrofurans. I. Aminofurans

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A number of 2-substituted 5-nitrofurans have been reduced catalytically to the corresponding aminofurans. The aminofurans are relatively stable solids which can be acetylated with acetic anhydride, or condensed with 5-nitro-2-furaldehyde. Several new 2-substituted 5-aminothiophene compounds have been prepared.

The reduction of a number of nitrofurans by various body tissues and bacteria has been studied by several workers.[1] In this paper we present some studies on the chemical reduction of selected nitrofurans.

Prior to this work only three 5-nitrofuran derivatives have been reduced unequivocally to the corresponding aminofurans by chemical means. Reduction of ethyl and of β-diethylamino 5-nitro-2-furoates has been effected with aluminum amalgam[2] and with hydrogen over platinum.[3] Reduction of 5-nitro-2-furaldehyde semicarbazone (I) with Raney nickel[4] in water gave a solid which was identified as 4-cyano-2-oxobutyraldehyde semicarbazone (III), with 5-amino-2-furaldehyde semicarbazone (II) being postulated as the intermediate. However, reduction of I in absolute alcohol with palladium on charcoal

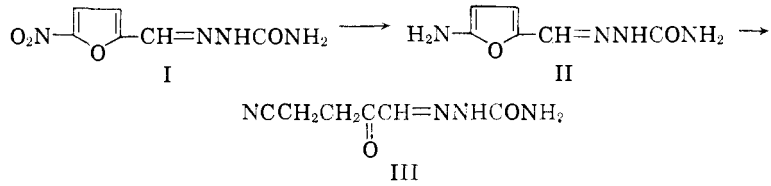
(1) (a) D. L. Cramer, *J. Bact.*, **54**, 119 (1947); (b) R. C. Bender and H. E. Paul, *J. Biol. Chem.*, **191**, 217 (1951); (c) A. Beckett and A. Robinson, *J. Med. Pharm. Chem.*, **1**, 135 (1959); (d) A. Beckett and A. Robinson, *ibid.*, **1**, 155 (1959); (e) J. D. Taylor, H. E. Paul and M. F. Paul, *J. Biol. Chem.*, **191**, 223 (1951); (f) R. E. Asnis and J. S. Gots, *Arch. Biochem.*, **30**, 35 (1951); (g) R. E. Asnis, *Arch. Biochem. Biophys.*, **66**, 208 (1957); (h) H. E. Paul, V. R. Ells, F. Kopko and R. C. Bender, *J. Med. Pharm. Chem.*, **2**, 563 (1960).

(2) (a) R. Marquis, *Compt. rend.*, **136**, 1454 (1903); (b) O. Dann, *Ber.*, **76**, 419 (1943).

(3) H. Gilman and G. Wright, *Iowa State Coll. J. Sci.*, **5**, 85 (1931).

(4) F. L. Austin, *Chem. and Ind.* (London), 523 (1957).

was reported[10,5] to give a dark red scaly solid, identified as II by infrared analysis.



I II III

The reduction of 5-nitro-2-furaldehyde dimethylacetal with hydrazine followed by acetic anhydride acetylation and condensation with thiosemicarbazide to yield 5-acetamido-2-furaldehyde thiosemicarbazone has been reported.[6] Reduction of 5-nitro-2-furaldehyde diacetate with hydrazine and then acetylation was reported[7] to yield 5-acetamido-2-furaldehyde diacetate. In our hands the latter reaction gave the hydrazone of 5-nitro-2-furaldehyde. However, we were able to obtain 5-acetamido-2-furaldehyde thiosemicarbazone by the hydrogenation of 5-nitro-2-furaldehyde thiosemicarbazone followed by acetylation.

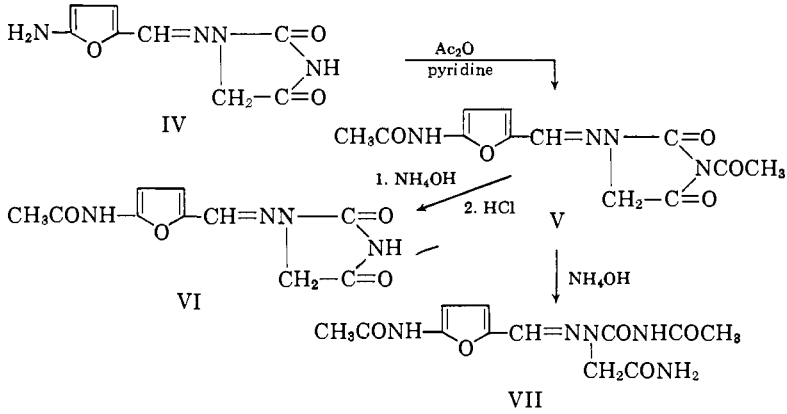
We have found that a wide variety of 5-nitro-2-furaldehyde derivatives can be reduced catalytically to the corresponding amino derivatives. These aminofurans are stable in the solid state, in most cases can be recrystallized from organic solvents, decompose slowly in aqueous solution and can be acetylated. As expected, the acetylated derivatives are more stable in aqueous solution. Table I lists the amino- and acetamido-furans characterized and their physical properties.

Most of the reductions were carried out in methanol with 5% palladium on charcoal catalyst at 2–3 atmospheres pressure. With the exception of the thione compounds the reductions proceed rapidly to completion within one hour using 4–5 g. of catalyst per 0.1 mole of compound. In the case of the thione compounds, it was necessary to use a large excess of catalyst (30 g./0.1 mole) to overcome the poisoning effect of the sulfur and to complete the reduction within 15 hours. When the appropriate amount of hydrogen had been absorbed, the mixture was filtered. If the product was insoluble in methanol, it was isolated by recrystallization, the catalyst being removed by filtration of the hot solution; or the mixture of catalyst and product was extracted with dimethyl sulfoxide, filtered and the

(5) A. H. Beckett and A. Robinson, *Chem. and Ind.*, 523 (1957).
(6) G. Carvajal and J. Erdos, *Arzneimitt. Forsch.*, **4**, 580 (1954).
(7) G. Fenech and A. Tommasini, *Atti. soc. peloritani. sci. fis. mat. e nat.*, **3**, 412 (1956–7).

filtrate diluted with water. The crude product obtained by the latter procedure was purified either by recrystallization or by solution in acid and reprecipitation with base. The methanol soluble products were isolated by removal of the methanol and recrystallization or reprecipitation of the crude residue.

The acetamido compounds were obtained by reaction of the aminofurans with acetic anhydride. Acetic anhydride acetylation of 1-(5-aminofurfurylideneamino)-hydantoin (IV) in the presence of pyridine at room temperature yielded 1-(5-acetamidofurfurylideneamino)-3-acetylhydantoin (V). This compound on treatment with concentrated ammonium hydroxide gave the monoacetylated aminofuran (VI), and a minor amount of an ammonia insoluble product tentatively assigned structure VII.



IV V VI VII

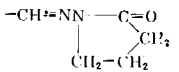
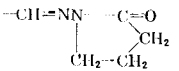
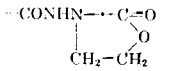
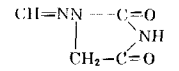
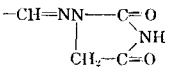
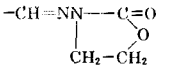
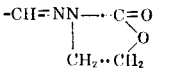
The aminofurans were characterized by elemental analysis and showed infrared absorption consistent with such structures, *i.e.*, bands at approximately 8.1 and 9.8 μ characteristic of the furan ring,[8] absence of nitro bands, bands in the NH region and retention of bands characteristic of the side chain. The ultraviolet data also are consistent with these structures and are shown with data for the corresponding nitro compounds in Table II.

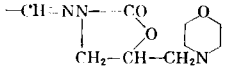
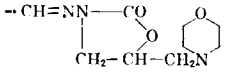
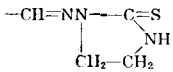
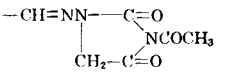
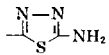
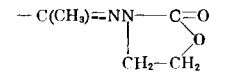
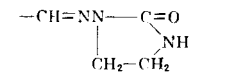
Additional palladium on carbon reductions of I in absolute ethanol or methanol verified the original reports[1c,4,5] on the instability of the corresponding aminofuran (II) in these solvents. The instability of II in contrast to the other aminofurans in this series may be explained by the following hydrogen bonded form which might be more susceptible to furan ring cleavage. In most of the other compounds in Table II such hydrogen bonding is impossible.

(8) A. H. J. Cross, S. G. E. Stevens, and T. H. E. Watts, *J. Appl. Chem.* (London), **7**, 562 1957).

TABLE I

5-AMINOFURANS R'NH—  —R

No.	R	R'	Method	Yield, %	M.p., °C.	Solvent[a]	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
1	—CH=NNHCSNH$_2$	H	C	33	169.5	A	$C_6H_8N_4OS$	39.13	39.17	4.38	4.38	17.40[c]	17.28[c]
2	—CH=NNHCSNH$_2$	$COCH_3$	D	63	235[b]	B	$C_8H_{10}N_4O_2S$	42.48	42.42	4.46	4.70	14.15[c]	14.11[c]
3	—CH=NN(CH_2CH_2OH)CSNH$_2$	H	C	26	126–127	C	$C_8H_{12}N_4O_2S$	42.10	42.23	5.30	5.66	14.05[c]	13.90[c]
4	—CH=NN(CH_3)$COCH_3$	H	C	13	148.5-151.5	D	$C_8H_{11}N_3O_2$	53.03	53.10	6.12	5.98	23.19	23.47
5		H	A	30	222–223	E	$C_9H_{11}N_3O_2$	55.95	55.83	5.74	5.81	21.75	22.00
6		$COCH_3$	E	65	231–232	C	$C_{11}H_{13}N_3O_3$	56.16	56.24	5.57	5.62	17.86	17.87
7		$COCH_3$	F	43	249–250	F	$C_{10}H_{11}N_3O_5 \cdot H_2O$	44.40	44.63	4.80	4.65	15.50	15.54
8		H	B	75	249–250	G	$C_8H_8N_4O_3$	46.15	46.02	3.87	4.20	26.92	26.63
9		$COCH_3$	G	37	300	H	$C_{10}H_{10}N_4O_4$	48.00	47.86	4.02	4.17	22.39	22.60
10		H	B	57	202–203	F	$C_8H_9N_3O_2$	49.23	49.11	4.65	4.68	21.53	21.60
	Compound 10, Picrate				153–154		$C_{14}H_{12}N_6O_{10}$	39.63	39.65	2.85	2.72	19.81	19.57
11		$COCH_3$	E	68	231–232	F	$C_{10}H_{11}N_3O_4$	50.63	50.53	4.67	4.68	17.72	17.63

No.	R	R′	Method	Yield, %	M.p., °C.	Sol. vent[a]	Formula	Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
12		H	A	50	209	E	$C_{12}H_{16}N_4O_4$	53.05	53.19	6.16	6.52	19.04	18.74
13		$COCH_3$	D	53	248–249	E	$C_{16}H_{20}N_4O_5$	53.56	53.48	5.99	5.87	16.66	17.07
14		H	C	69	194–195	G	$C_8H_{10}N_4OS$	45.71	45.48	4.80	4.94	15.25[c]	15.09[c]
15		$COCH_3$	G	57	217–220	I	$C_{12}H_{12}N_4O_5$	49.31	49.19	4.14	4.44		
16	—CH=NN(CH_2CONH_2)CONHAc	$COCH_3$	G	14	210–215	J	$C_{12}H_{16}N_5O_5$	46.60	46.40	4.89	4.73	22.65	22.70
17		H	I	62	137–138.5	K	$C_6H_6N_4OS$	39.56	39.57	3.32	3.61	17.60[c]	17.47[c]
18	—CH=NNHCONH$_2$	H	H	—	—	—	$C_6H_8N_4O_2$	42.85	42.79	4.80	5.23		
19	—CH=NNHCONH$_2$·HCl	H	I	67	165–175	—	$C_6H_8N_4O_2$·HCl	35.25	35.52	4.43	4.64	17.33[d]	17.38
20		H	I	29	144–148	C	$C_9H_{11}N_3O_3$	51.67	51.90	5.30	5.39	20.09	20.00
21		H	B	31	210–212	—	$C_8H_{10}N_4O_2$	49.48	49.70	5.19	5.34		
22	—CHO	H	I	14	150–175	C	$C_5H_5NO_2$	54.05	53.92	4.54	4.87	12.61	12.51
23	—CH=NNHCOCH$_3$	H	I	58	158–161	C	$C_7H_9N_3O_2$	50.29	50.10	5.43	5.44	25.14	25.00

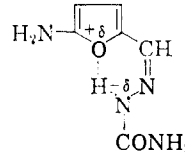
[a] Solvents used in recrystallization: A, 95% ethanol; B, nitromethane–dimethylformamide; C, acetonitrile; D, benzene; E, nitromethane; F, methanol; G, acid-base precipitation; H, water–dimethylformamide; I, acetic anhydride; J, water; K, dioxane. [b] Reference 6, m.p. 276–278°. [c] Calcd. and found values for sulfur. [d] Calcd. and found values for chlorine.

TABLE II

ULTRAVIOLET ABSORPTION SPECTRA OF AMINOFURANS AND CORRESPONDING NITROFURANS

	Aminofuran		Nitrofuran		
No.[a]	λ max.[b] mμ	ε	λ max.[b] mμ	ε	Ref.
1	360	28,300	383	19,200	9
2	340	33,900	383	19,200	9
3	363	28,000	388	20,000	10
4	345	21,450	375	18,050	11
5	350	23,700	370	18,200	12
6	333	26,800	370	18,200	12
7	295	18,950	305	12,650	10
8	348	23,800	368	17,920	13
9	328	27,700	368	17,920	13
10	340	22,250	367	16,800	14
11	323	27,650	367	16,800	14
12	340	23,900	366	17,600	15
13	324	28,300	366	17,600	15
14	360	23,900	393	18,900	16
15	326	27,500	365	18,300	10
16	323	24,700	368	16,850	10
17	340	8,300	379	14,500	17
18	335	14,900	375	15,650	18
19	340	16,500	375	15,650	18
20	365	18,450	350	10,550	14
21	335	21,500	387	17,600	12
22	350	29,600	310	11,420	19
23	349	19,700	363	16,300	18

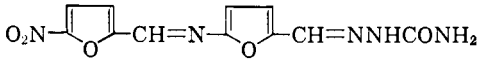
[a] Numbers correspond to compounds described in Table I. [b] In water.



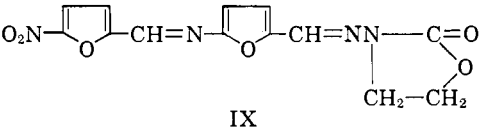
In an effort to obtain more conclusive evidence for the existence of II in the reduction solutions, an attempt was made to isolate a derivative of II. When a freshly reduced methanol solution of I reacted with 5-nitro-2-furaldehyde in the presence of dilute hydrochloric acid, a dark red Schiff base (VIII) was obtained which was unmelted at 300° and unstable in water.

By an analogous condensation 3-(5-aminofurfurylideneamino)-2-oxazolidinone gave a Schiff base (IX).

Compounds VIII and IX exhibited maxima in the ultraviolet at approximately 335 mμ in water (2% DMF) indicating regeneration of the aminofurans. Elemental analyses and infrared absorption



VIII



IX

data are in agreement with the structures assigned to VIII and IX.

Since aminofurans are susceptible to ring opening in aqueous or alcoholic solution,[1c,d,4] the use of a non-hydroxylic solvent, such as ethyl acetate, for the preparation of II and other aminofurans that could not be obtained in methanol or absolute ethanol was investigated.

Hydrogenation of a suspension of I in ethyl acetate in the presence of 5% palladium on charcoal and anhydrous magnesium sulfate gave, after filtration and dilution with ethanol, a clear pale yellow solution having a single absorption maximum at 340 mμ. Evaporation of the ethyl acetate solution under reduced pressure gave an amorphous solid which showed one peak at 335 mμ in water with the appearance of a second peak at 275 mμ and a concomitant decrease of the 335 mμ absorption after 6 hr. These spectrophotometric results are in agreement with the findings of Beckett and Robinson.[5] Elemental analysis of the solid gave the expected results for II (Table I).

Addition of the amorphous solid to a minimum of absolute ethanol caused the formation of a yellow crystalline material melting at 97–104°. Its infrared spectrum (2.9, 2.03, 6.0, 6.1, 9.8 μ) supported structure II and ultraviolet absorption properties were identical with those of the amorphous material. However, carbon and hydrogen analyses (*Anal.* Calcd. for $C_6H_9N_4O_2$: C, 42.85; H, 4.80. Found: C, 42.72; H, 5.56) were unsatisfactory. The lability of the compound made further purification impossible.

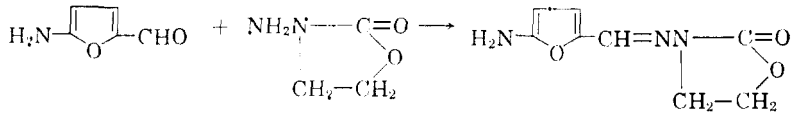
The hydrochloride of II was isolated readily by precipitation from an ethanol dilution of the ethyl acetate reduction solution with 10%

(9) W. B. Stillman and A. B. Scott, U. S. Patent 2,416,239, Feb. 18, 1947.
(10) Unpublished work at Eaton Laboratories, Div. Norwich Pharmacal Co., Norwich, N.Y.
(11) M. P. Natt, U. S. Patent 2,943,019, June 28, 1960.
(12) J. G. Michels and G. Gever, *J. Am. Chem. Soc.*, **78**, 5349 (1956).
(13) K. J. Hayes, U. S. Patent 2,610,181, Sept. 9, 1952.
(14) G. Gever, C. O'Keefe, G. Drake, F. Ebetino, J. Michels, and K. Hayes, *J. Am. Chem. Soc.*, **77**, 2277 (1955).
(15) G. Gever, U. S. Patent 2,802,002, Aug. 6, 1957.
(16) J. G. Michels, U. S. Patent 2,920,074, Jan. 5, 1960.
(17) K. Skagius, *Acta Chem. Scand.*, **14**, 1054 (1960).
(18) W. B. Stillman and A. B. Scott, U. S. Patent 2,416,234, Feb. 18, 1947.
(19) H. Gilman and G. Wright, *J. Am. Chem. Soc.*, **52**, 2552 (1930).

hydrochloric acid and analytically pure material was obtained without subsequent purification. Condensation of this hydrochloride with 5-nitro-2-furaldehyde gave VIII. It was found that the use of magnesium sulfate was unnecessary, and that a mixture of ethyl acetate and absolute ethanol for the reduction of I resulted in high yields (66.5%) of II·HCl.

Other aminofurans that previously could not be obtained in alcoholic reductions but were obtainable in ethyl acetate–ethanol are compounds 20, 22 and 23 in Table I.

The structure of 5-amino-2-furaldehyde (compound 22) was substantiated by infrared and ultraviolet analyses and by condensation with 3-amino-2-oxazolidinone in the presence of acid to give compound 10 previously prepared by reduction of the nitro compound.

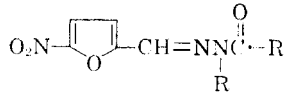


5-Amino-2-furaldehyde acetylhydrazone (compound 23) on acetylation with acetic anhydride in the presence of pyridine produced a solid that could not be purified by recrystallization. Infrared and ultraviolet spectra and R_f value of the product were identical to that of 5-acetamido-2-furaldehyde acetylhydrazone, a metabolite of 5-nitro-2-furaldehyde acetylhydrazone. The isolation of this metabolite and spectral and chromatographic analyses of these compounds were reported by Olivard, Valenti and Buzard.[20]

For comparative purposes, the 5-nitrothiophene analogs of I and 3-(5-nitrofurfurylideneamino)-2-oxazolidinone were reduced catalytically in methanol over 5% palladium on carbon. Acetic anhydride acetylation of the amines readily produced the acetamidothiophenes.

The aminothiophene derivatives are very stable in aqueous solution. The infrared and ultraviolet absorption data for these compounds are reported in the experimental section.

In view of the above results we are unable to agree with the conclusion reached by Beckett and Robinson[1d] that the aminofurans derived from "type B" nitrofurans are ". . . so unstable that furan



(20) J. Olivard, S. Valenti, and J. A. Buzard, *J. Med. Pharm. Chem.*, **5**, 524 (1962).

ring cleavage immediately occurs . . . ." (Type B nitrofurans are defined as shown in the preceding formula, where R = alkyl or hydroxyalkyl or is part of a ring involving R'.)

For example, an aqueous solution of 1-(5-aminofurfurylideneamino)-hydantoin even after 18 hr. standing at 25° exhibited no peak shift although the $E^{1\%}_{1cm}$ value dropped from 1075 to 600 (Fig. 1).

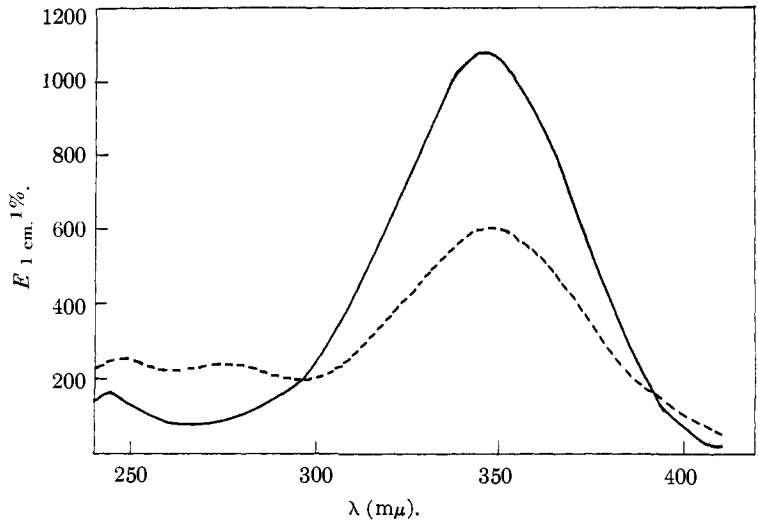


Fig. 1.—Ultraviolet absorption spectra of 1-(5-aminofurfurylideneamino)-hydantoin in water: ———; and after 18 hr. in water, - - - - - - - -.

Similarly, a solution of 3-(5-aminofurfurylideneamino)-5-morpholinomethyl-2-oxazolidinone after standing at 25° for 6 hr. showed no change in the shape of the curve and only 15% decomposition.

From the reduction of some of the nitrofurans we have isolated the corresponding 4-cyano-2-oxobutyraldehyde derivatives. These compounds will be reported in a subsequent paper.

The aminofurans were screened, using a serial tube dilution method employing brain-heart infusion broth or a disc agar plate method employing brain-heart agar and a 24 hour incubation period at 37°, against the following bacterial species: *Micrococcus pyogenes* var. *aureus*, *Escherichia coli*, *Salmonella typhosa*, *Pasturella multocida*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Streptococcus pyogenes*, *Ersipelothrix rhusiopathiae* and *Streptococcus agalactiae*. None of the compounds exhibited significant *in vitro* activity against these organisms.

Experimental[21]

Materials.—Literature references for the preparations of the nitrofurans used in this work are given in Table II.

Preparations of 5-aminofurans in Table I, Method A: A mixture of 0.1 mole of the appropriate nitrofuran and 4–5 g. of 5% palladium on carbon catalyst in 200 ml. of methanol was hydrogenated in a Parr low pressure apparatus. After the theoretical amount of hydrogen was taken up, the insoluble solid was filtered and recrystallized.

Method B: This method is the same as A except that the organic compound was separated from the catalyst by stirring the mixture with dimethyl sulfoxide, filtering the catalyst, and diluting the filtrate with water or a mixture of 2-propanol and ether to precipitate the amine.

Method C: A mixture of 0.1 mole of the appropriate nitrofuran and 4–5 g. of 5% palladium on charcoal or 30 g. of catalyst for the thione compounds, in 150 ml. of methanol, was hydrogenated until the theoretical amount of hydrogen was taken up. The catalyst was filtered and the filtrate cooled to give the product, or concentrated and the resulting solid recrystallized.

Method D: The appropriate aminofuran in acetic anhydride (*e.g.*, 0.2 mole/150 ml.) was heated on the steam bath for 15 min. After cooling, the solid was filtered and recrystallized.

Method E: The appropriate aminofuran (0.055 mole) was mixed with 100 ml. of acetic anhydride and 20 ml. of pyridine and stirred at room temperature for 4 hr. After standing overnight the solid was filtered and recrystallized.

Method F: 3-(5-Nitro-2-furamido)-2-oxazolidinone (0.1 mole) and 3 g. 5% palladium on carbon in 200 ml. of acetic anhydride were hydrogenated. After the theoretical amount of hydrogen was taken up, the solid was filtered and recrystallized.

Method G: 1-(5-Aminofurfurylideneamino)-hydantoin (IV) (0.264 mole) was added to 500 ml. of acetic anhydride and 100 ml. of pyridine, and stirred at room temperature for 24 hr. The diacetylated product (V) was filtered and washed with 2-propanol.

The diacetylated compound (V) (0.0068 mole) was suspended in 50 ml. of water and treated with 10 ml. of concentrated ammonium hydroxide solution to dissolve the solid. On cooling, a solid (VII) precipitated and was recrystallized. The reaction filtrate was neutralized with hydrochloric acid, and the precipitated solid (VI) was filtered and recrystallized.

Method H: A suspension of 0.05 mole of nitrofuran, 10 g. of 5% palladium on charcoal and 2 g. of anhydrous magnesium sulfate in 150 ml. of ethyl acetate was hydrogenated. The hydrogenation was stopped after 0.15 mole of hydrogen was introduced (10 min.) and the mixture filtered. The pale yellow filtrate was concentrated under vacuum to a yellow scaly solid which crystallized when treated with a minimum amount of absolute ethanol. The solid could not be purified further.

Method I: A mixture of 0.05 mole of nitrofuran and 1.5–3.5 g. of 5% palladium on charcoal in a mixture of 150 ml. of ethyl acetate and 50 ml. of absolute alcohol was hydrogenated. After complete hydrogenation (24–45 min.) the catalyst

(21) All melting points were taken on a Fisher–Johns melting point apparatus and are uncorrected. Nitrogen analyses were done by Schwartzkopf Microanalytical Laboratory, New York.

was filtered and the filtrate concentrated under vacuum. The residual solid was washed with 2-propanol and recrystallized.

In the preparation of compound 19, 6 g. of catalyst was used and the reaction filtrate was cooled and acidified with 10% hydrochloric acid to precipitate the hydrochloride salt.

5-(5-Nitrofurfurylideneamino)-2-furaldehyde Semicarbazone (VIII).—Method A: A suspension of 10 g. (0.05 mole) of 5-nitro-2-furaldehyde semicarbazone[18] in 150 ml. of absolute ethanol was hydrogenated in the presence of 5 g. of 5% Pd/C. The theoretical amount of hydrogen for the reduction of the nitro group was taken up in 17 min. To half of the filtered solution was added a solution of 3.5 g. (0.025 mole) of 5-nitro-2-furaldehyde in 50 ml. of absolute ethanol. On acidification with 10% hydrochloric acid, 2.8 g. of a dark red solid separated. Purification was accomplished by dissolving the solid in dimethylformamide, clarifying with charcoal and precipitating the solid by pouring the solution into 2-propanol. The solid did not melt to 300°; $\lambda_{max.}$ 2% DMF 330 mμ (ϵ 11,900). The infrared spectrum (mull) had broad bands at 3.0, 6.0, 7.4, 8.05 and 9.85 μ.

Anal. Calcd. for $C_{11}H_9N_5O_5$: C, 45.36; H, 3.12. Found: C, 45.38; H, 3.67.

Method B: To a solution of 20.5 g. (0.1 mole) of 5-amino-2-furaldehyde semicarbazone hydrochloride in 400 ml. of water was added a solution of 14.1 g. (0.1 mole) of 5-nitro-2-furaldehyde in 360 ml. of ethanol. The red precipitate was filtered, rinsed with 50% ethanol and air dried; yield, 21 g. (72%), m.p. >300°. The infrared and ultraviolet spectra were identical with spectra of the compound prepared by Method A.

3-[5-(5-Nitrofurfurylideneamino)furfurylideneamino]-2-oxazolidinone (IX).—A dimethylformamide (80 ml.) solution of 5.0 g. (0.0256 mole) of 3-(5-aminofurfurylideneamino)-2-oxazolidinone was treated with a solution of 3.6 g. (0.0256 mole) of 5-nitro-2-furaldehyde in 50 ml. of absolute ethanol and acidified with 10% hydrochloric acid. The resulting red solution was diluted with 200 ml. of absolute ethanol and then poured into 750 ml. of ether to give a maroon solid, 8.1 g. (100%), m.p. >300°; $\lambda_{max.}$ 2% DMF 335 mμ (ϵ 13,250). The infrared spectrum (mull) had bands at 5.7, 7.4 and 9.82 μ.

Anal. Calcd. for $C_{13}H_{10}N_4O_6 \cdot 0.5H_2O$: C, 47.75; H, 3.39; N, 17.12. Found: C, 47.99; H, 3.66; N, 16.60.

5-Amino-2-thiophenecarboxaldehyde Semicarbazone.—5-Nitro-2-thiophenecarboxaldehyde semicarbazone[22] (10.7 g. 0.05 mole) in 150 ml. methanol was reduced in a low pressure hydrogenator in the presence of 10 g. of 5% Pd/C over 40 min. The catalyst was filtered and the filtrate concentrated *in vacuo* to a light tan solid, 6 g. (65%), m.p. 173–175°. An analytical sample was prepared by recrystallization from 2-propanol to a constant melting point, 176–177°; $\lambda_{max.}$ H_2O 345 mμ (ϵ 19,450). The infrared spectrum (mull) had bands at 2.92, 5.95, 6.1 and 6.25 μ.

Anal. Calcd. for $C_6H_8N_4OS$: C, 39.13; H, 4.38; S, 17.41. Found: C, 39.07; H, 4.47; S, 17.50.

The acetyl derivative was prepared by heating the amine in acetic anhydride at steam bath temperature; m.p. 257° dec. (lit.,[23] m.p. 260.5–261°). The infrared spectrum (mull) had bands at 2.93, 5.95, 6.02, 6.3 and 6.4 μ.

3-(5-Amino-2-thenylideneamino)-2-oxazolidinone.—A mixture of 24 g. (0.1 mole) of 3-(5-nitro-2-thenylideneamino)-2-oxazolidinone[10] and 10 g. of 5% Pd/C in

(22) T. Patrick and W. Emerson, *J. Am. Chem. Soc.*, **74**, 1356 (1952)

(23) J. Cymerman-Craig and D. Willis, *J. Chem. Soc.*, 1071 (1955).

200 ml. of methanol was reduced in a low pressure hydrogenator over 24 hr. The insoluble solid and catalyst were filtered and recrystallized from 550 ml. of nitromethane to give 13.4 g. (63.5%). An analytical sample decomposed at 224–225°, $\lambda_{max.}$ 5% EtOH 348 mμ (ϵ 20,750). The infrared spectrum (mull) had bands at 3.0, 3.05, 5.8 and 6.3 μ.

Anal. Calcd. for $C_8H_9N_3O_2S$: C, 45.50; H, 4.30; S, 15.15. Found: C, 45.55; H, 4.48; S, 15.15.

The acetyl derivative was prepared in 98% yield by heating the amine in acetic anhydride at steam bath temperature. After several recrystallizations from a 2:1 mixture of nitromethane and dimethylformamide, the compound decomposed at 269–271°, $\lambda_{max.}$ 2% DMF 338 mμ (ϵ 21,000). The infrared spectrum (mull) had bands at 3.1, 5.78, 5.95, 6.0 and 6.42 μ.

Anal. Calcd. for $C_{11}H_{10}N_3O_3S$: C, 47.41; H, 4.38; S, 12.67. Found: C, 47.05; H, 4.77; S, 12.69.

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The Metabolism of 5-Nitro-2-furaldehyde Acetylhydrazone

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The identification of 5-acetamido-2-furaldehyde acetylhydrazone in the urine of rabbits fed 5-nitro-2-furaldehyde acetylhydrazone is reported. Identification of 1,2-diacetylhydrazine and evidence for 5-amino-2-furaldehyde acetylhydrazone, 5-diacetylamino-2-furaldehyde acetylhydrazone and 5-nitro-2-furoic acid also are given. A yellow material, found in the urine of animals fed 5-nitro-2-furaldehyde acetylhydrazone, can be synthesized from a photochemical product of 5-nitro-2-furaldehyde diacetate.

A reductive metabolic pathway for nitrofuraldehyde hydrazone derivatives analogous to that demonstrated for certain aromatic