formed which crystallized upon standing. The crystals were filtered and washed with cold dry ether. The salt weighed 3.95 g. (67.1%). Recrystallization from absolute ethanol raised the melting point to 199–200° (with dec.) with darkening at 185°.

Anal. Calcd. for $C_{14}H_{18}N_2S_2Cl_2$ (349.4): C, 48.13; H, 5.19; N, 8.02. Found: C, 48.24; H, 5.34; N, 8.11.

The *picrate* crystallized from 80% ethanol, m.p. 166° (with dec.).

Anal. Calcd. for $C_{26}H_{22}N_8O_{14}S_2$ (734.6): N, 15.25. Found: N, 15.44.

2-(4-Pyridyl)ethanesulfonic acid. Oxidation of 2-(4-pyridium)ethanethiol chloride in a manner similar to that described above for 2-(2-pyridinium)ethanethiol chloride afforded the acid (91%) which was identical with that in the literature.[5a]

Thiourea p-toluenesulfonate. A mixture of thiourea (1.52 g.; 0.02 mole) and *p*-toluenesulfonic acid monohydrate (3.8 g.; 0.02 mole) was boiled in ethanol (25 ml.) until a solution was obtained. On cooling, the crystals which formed were filtered and washed with cold ethanol. The crystals weighed 4.76 g. (96%), m.p. 173–174°. Recrystallization from ethanol did not raise the melting point. Mixedm elting point with thiourea (m.p. 180–181°) was depressed to 137–152° (with dec.).

Anal. Calcd. for $C_8H_{12}N_2O_3S_2$ (248.3): N, 11.23. Found: N, 11.22.

CHICAGO 12, ILL.

[CONTRIBUTION FROM THE ORGANIC CHEMISTRY LABORATORY, PIONEERING RESEARCH DIVISION, QUARTERMASTER RESEARCH AND ENGINEERING CENTER, U. S. ARMY]

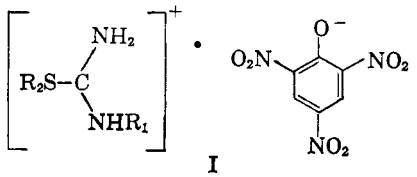
Isothiuronium, Alkylthioöxazolinium, and Alkylthiothiazolinium Picrates[1]

LOUIS LONG, JR., RICHARD C. CLAPP, FRANK H. BISSETT, AND TORSTEN HASSELSTROM

Received February 22, 1960

N-Substituted *S*-alkylisothiuronium picrates are shown to be useful derivatives in the identification of *N*-substituted thioureas derived from naturally occurring isothiocyanates, and a series of twenty-four picrates has been prepared. The procedure has been adapted to micro techniques. Conditions for the alkylation of 2-thioöxazolidones and for the preparation of a similar picrate derivative from (−)-5-vinyl-2-thioöxazolidone (goitrin) are described. The infrared spectra of the compounds are reported, and certain features are discussed.

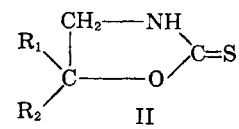
During an investigation of the naturally occurring isothiocyanates in certain plants, an attempt was made to find a derivative that would be useful in the separation and identification of substituted thioureas obtained from the isothiocyanates. The use of *S*-alkylisothiuronium picrates to identify alkyl halides has been described.[2] It is reported in the present paper that *N*-substituted *S*-alkylisothiuronium picrates (I) also constitute satisfactory



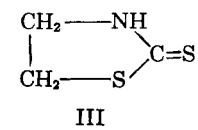
I

derivatives for *N*-substituted thioureas. The yield of picrates obtained (85–90%), their high molecular weight, their low solubility, and their crystallinity, as demonstrated in several instances by well-defined x-ray diffraction patterns,[3] favored the use of these derivatives in the isolation and identification of micro quantities.[4]

Since a derivative to assist in the identification of (—)-5-vinyl-2-thioöxazolidone (IIc), a goitrogenic compound isolated from *Brassica* seeds[5] and found to be present in micro quantities in cabbage,[6] was also desired, the preparation of a similar derivative from this compound was investigated. Hopkins[7] has reported that 5,5-dimethyl-2-thioöxazolidone (IIb) "does not combine with methyl iodide under ordinary conditions, nor does it form a picrate." However, the alkylation of 2-thiothiazolidone (III) with methyl iodide under alkaline[8] and neutral[9] conditions and the formation of a picrate from the resulting 2-methylthio-2-thiazoline have been described. Model experiments with 2-thiothiazolidone and 2-thioöxazolidone (IIa) dem-



II



III

a. $R_1 = R_2 = H$
b. $R_1 = R_2 = CH_3$
c. $R_1 = CH_2{=}CH$, $R_2 = H$

(1) Presented at the 136th National Meeting of the American Chemical Society, Atlantic City, N. J., September 1959.

(2) (a) E. L. Brown and N. Campbell, *J. Chem. Soc.*, 1699 (1937); (b) W. J. Levy and N. Campbell, *J. Chem. Soc.*, 1442 (1939); (c) L. Schotte, *Arkiv Kemi*, 5, 11 (1952).

(3) We are indebted to Dr. G. Susich and Mr. A. King of this Laboratory for the x-ray diffraction patterns.

(4) R. C. Clapp, L. Long, Jr., G. P. Dateo, F. H. Bissett, and T. Hasselstrom, *J. Am. Chem. Soc.*, 81, 6278 (1959).

(5) E. B. Astwood, M. A. Greer, and M. G. Ettlinger, *J. Biol. Chem.*, 181, 121 (1949).

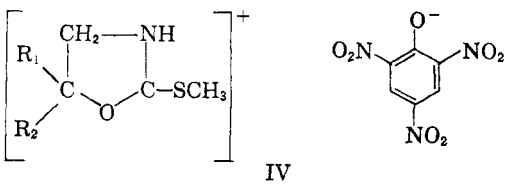
(6) (a) M. R. Altamura, L. Long, Jr., and T. Hasselstrom, *J. Biol. Chem.*, 234, 1847 (1959); (b) A. I. Virtanen, M. Kreula, and M. Kiesvaara, *Acta Chem. Scand.*, 12, 580 (1958).

(7) C. Y. Hopkins, *Can. J. Research*, 16B, 341 (1938).

(8) S. Gabriel, *Ber.*, 22, 1139 (1889).

(9) A. F. McKay, D. J. Whittingham, and M.-E. Kreling, *J. Am. Chem. Soc.*, 80, 3339 (1958).

onstrated that the alkylation could be effected most satisfactorily in absolute alcohol in the presence of sodium ethylate. 2-Methylthio-2-oxazolinium picrates (IV) could then be obtained from the 2-methylthio-2-oxazolines prepared under these conditions.



IV

a. $R_1 = R_2 = H$
b. $R_1 = R_2 = CH_3$
c. $R_1 = CH_2{=}CH$, $R_2 = H$

Infrared spectra. In the accompanying tables are shown the maxima between 3 μ and 15 μ for the *N*-substituted isothiuronium picrates. In Table I are presented those peaks which are constant for the entire group, and in Table II are listed those which vary.

TABLE I

MAJOR ABSORPTION BANDS (μ) COMMON TO *N*-SUBSTITUTED *S*-ETHYL ISOTHIURONIUM PICRATES[a]

2.91–2.94 s[b]	6.04–6.08 vs	7.88–7.91 vs
3.02 w	6.13–6.16 vs	8.61–8.65 s
3.08 w	6.28–6.30 s	9.27–9.30 s
3.18–3.19 s	6.68–6.75 s	10.99–11.02 s
3.24 m	6.99–7.02 s	12.62–12.65 s
3.34 w–m	7.30 s	13.40–13.44 s
3.40 w–m	7.50–7.52 vs	14.06–14.15 s
3.47 w–m	7.63–7.65 vs	

[a] It was not possible to distinguish between the spectra of the *S*-methyl and *S*-ethyl isothiuronium picrates. [b] vs = very strong; s = strong; m = medium; w = weak.

The spectra of all the isothiuronium picrates have strong, characteristic maxima at 6.13–6.16 μ and at 6.28–6.30 μ. Interference from picrate ion bands in this region has been eliminated by comparison with the spectrum of the corresponding iodide salt, as shown in Fig. 1 for the *N*-ethyl-*S*-methylisothiuronium salts. The maximum at 6.13–6.16 μ is probably due to an NH_2 deformation mode; in thiourea the NH_2 deformation was found to be at 6.18 μ.[10]

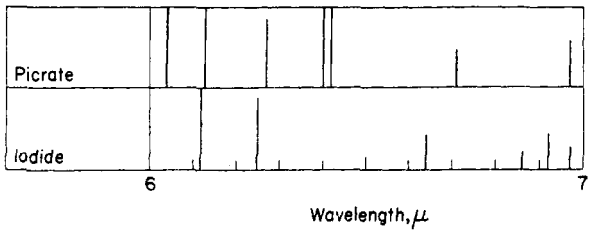


Fig. 1. Comparison of the infrared absorption bands between 6 and 7 μ of *N*-ethyl-*S*-methylisothiuronium picrate and its iodide

(10) J. E. Stewart, *J. Chem. Phys.*, **26**, 248 (1957).

The strong maximum at 6.28–6.30 μ in the isothiuronium picrates can be assigned to an N—C—N system and is analogous to the strong "thioureide"[11] band which was found to be at 6.39–6.49 μ in the corresponding substituted thioureas. The lower wave length of this band in the spectra of the isothiuronium compounds compared to that in the thioureas is the result of the alkylation of the sulfur atom, and it is indicative of the increased double bond character of the C—N bonds in the N—C—N system.

In the cyclic compounds, the effect of *S*-alkylation can be similarly observed by a quantitative shift of the "thioureide" peak at 6.60 μ in 2-thiothiazolidone[12] and in 2-thioöxazolidone,[13] which are true thiones, to a shorter wave length at 6.44 μ, due to an increase in the order of the carbon-nitrogen bond.

EXPERIMENTAL[14]

N-Substituted S-alkylisothiuronium picrates. The thioureas were obtained from isothiocyanates by treatment with ammonia in methanol. Unavailable isothiocyanates were prepared from amines by the method of Hodgkins and Ettlinger.[15]

In a typical preparation, a solution of 0.01 mole of the substituted thiourea and 0.011 mole of alkyl iodide in 10 ml. of 95% ethanol was refluxed for 10 min. A solution of 0.01 mole of picric acid in 15–20 ml. of hot 95% ethanol was added. Water was then added slowly until the crystalline picrate began to separate, and the precipitate was collected after cooling. In some instances the picrates separated without the addition of water. The compounds were purified by crystallization from ethanol, water, or aqueous ethanol.

The picrates prepared are listed in Table III. Several of the picrates have been reported in the literature but with incomplete characterization.

2-Methylthio-2-oxazolinium picrate (IVa). To a solution of 0.26 g. (0.0113 g.-atom) of sodium in 15 ml. of absolute ethanol was added 1.17 g. (0.0113 mole) of 2-thioöxazolidone.[16] A solution of 1.64 g. (0.0115 mole) of methyl iodide in 7 ml. of absolute ethanol was added in portions. After the mixture had been allowed to stand at room temperature for 1 hr., it was refluxed for 45 min. It was then concentrated under reduced pressure, and the residue was extracted with ether. Concentration of the ether afforded a liquid that was dissolved in 20 ml. of ethanol. When the solution was treated with 2.6 g. (0.011 mole) of picric acid in 50 ml. of ethanol, a precipitate (1.75 g.; 44% yield) of fine yellow crystals, m.p. 122–123.5°, resulted. Two crystallizations from acetone gave glistening yellow plates, m.p. 124.5–125.5°.

Anal. Calcd. for $C_{10}H_{10}N_4O_8S$: C, 34.68; H, 2.91; S, 9.26. Found: C, 34.78; H, 3.00; S, 9.20.

The infrared spectrum showed the following bands and intensities: 2.84(m), 3.30(m), 3.41(w), 6.06(vs), 6.16(s),

(11) *Cf.* H. M. Randall, R. G. Fowler, N. Fuson, and J. R. Dangl, *Infrared Determination of Organic Structures*, D. Van Nostrand Co., Inc., New York, 1949, p. 5.

(12) Ref. 11, p. 189.

(13) M. G. Ettlinger, *J. Am. Chem. Soc.*, **72**, 4699 (1950).

(14) We are indebted to Mr. C. DiPietro and Mr. W. Sassaman of this Laboratory for the microanalyses. Melting points were determined in capillary tubes in a Hershberg apparatus; final melting points are corrected.

(15) J. E. Hodgkins and M. G. Ettlinger, *J. Org. Chem.*, **21**, 404 (1956).

(16) M. G. Ettlinger, *J. Am. Chem. Soc.*, **72**, 4792 (1950).

TABLE II

CHARACTERISTIC ABSORPTION BANDS (μ) IN *N*-SUBSTITUTED *S*-ETHYL ISOTHIURONIUM PICRATES[a]

Methyl	Ethyl	*n*-Propyl	Iso-propyl	Allyl	*n* Butyl	*sec*-Butyl	Isobutyl	3-Butenyl	3-Methylthio-propyl
6.42 vs[b]	6.39 vs	6.39 vs	6.33 vs	6.39 vs	6.33 vs	6.33 vs	6.33 vs	6.39 vs	6.33 vs
6.62 m	6.43 vs	6.43 vs	6.45 vs	6.43 vs	6.45 vs	6.45 vs	6.45 vs	6.43 vs	6.45 vs
6.81 vw	6.62 w	6.62 m	6.89 w	6.81 m	6.62 m	6.64 m	6.62 m	6.65 m	6.92 s
6.90 m	6.89 w	6.81 m	7.16 m	6.88 m	6.89 s	6.85 m	6.89 m	6.88 s	7.24 w
7.09 m	7.20 w	6.89 w	8.53 m	7.22 m	7.23 w	10.65 w	7.18 w	7.25 w	8.80 w
8.85 m	7.25 m	7.21 m	8.80 vw	8.05 vs	10.70 w	10.88 w	10.62 w	10.05 w	12.15 w
10.65 vw	8.83 m	8.80 w	10.64 w	10.11 m	12.30 w			10.65 s	12.45 w
10.75 m	10.67 vw	10.67 vw	12.50 vw	10.72 s				10.72 s	13.00 m
12.52 vw	10.80 w	10.80 m		10.79 s				12.25 m	
	12.52 w	12.50 m		12.50 w					

[a] Table I, footnote a. [b] vs = very strong; s = strong; m = medium; w = weak.

TABLE III

N-SUBSTITUTED ISOTHIURONIUM PICRATES[a] (I)

R_1	R_2	Formula	M.P.	Carbon, %		Hydrogen, %	
				Calcd.	Found	Calcd.	Found
Methyl	Methyl	$C_9H_{11}N_5O_7S$[b]	183–184.5	32.43	32.37	3.33	3.59
Methyl	Ethyl	$C_{10}H_{13}N_5O_7S$	161–162.5[c]	34.58	34.49	3.77	3.88
Ethyl	Methyl	$C_{10}H_{13}N_5O_7S$	163–164	34.58	34.37	3.77	3.65
Ethyl	Ethyl	$C_{11}H_{15}N_5O_7S$	126–127	36.56	36.49	4.18	4.19
n-Propyl	Methyl	$C_{11}H_{15}N_5O_7S$	153–154	36.56	36.49	4.18	4.15
n-Propyl	Ethyl	$C_{12}H_{17}N_5O_7S$	119–120	38.39	38.15	4.57	4.42
Isopropyl	Methyl	$C_{11}H_{15}N_5O_7S$	167–168	36.56	36.66	4.18	4.14
Isopropyl	Ethyl	$C_{12}H_{17}N_5O_7S$	154–155	38.39	38.44	4.57	4.41
Allyl	Methyl	$C_{11}H_{13}N_5O_7S$	148–149[d]	—	—	—	—
Allyl	Ethyl	$C_{12}H_{15}N_5O_7S$	124.5–125[e]	38.60	38.49	4.05	3.96
n-Butyl	Methyl	$C_{12}H_{17}N_5O_7S$	154–155	38.39	38.35	4.57	4.71
n-Butyl	Ethyl	$C_{13}H_{19}N_5O_7S$	122–123	40.10	40.11	4.92	5.07
sec-Butyl	Methyl	$C_{12}H_{17}N_5O_7S$	143–144	38.39	38.21	4.57	4.46
sec-Butyl	Ethyl	$C_{13}H_{19}N_5O_7S$	112.5–114	40.10	39.94	4.92	4.83
Isobutyl	Methyl	$C_{12}H_{17}N_5O_7S$	163.5–164.5	38.39	38.77	4.57	4.72
Isobutyl	Ethyl	$C_{13}H_{19}N_5O_7S$	151–152	40.10	39.86	4.92	4.87
3-Butenyl	Methyl	$C_{12}H_{15}N_5O_7S$	135.5–136.5	38.60	38.53	4.05	4.26
3-Butenyl	Ethyl	$C_{13}H_{17}N_5O_7S$	129–130	40.31	40.32	4.42	4.51
3-Methylthio-propyl	Methyl	$C_{12}H_{17}N_5O_7S_2$	112.5–113.5	35.37	35.16	4.21	4.28
3-Methylthio-propyl	Ethyl	$C_{13}H_{19}N_5O_7S_2$	103–104	37.05	37.25	4.54	4.56
Phenyl	Methyl	$C_{14}H_{13}N_5O_7S$	176–177.5[f]	42.53	42.18	3.31	3.25
Phenyl	Ethyl	$C_{15}H_{15}N_5O_7S$	198.5–199.5[g]	—	—	—	—
Benzyl	Methyl	$C_{15}H_{15}N_5O_7S$	173–174	44.01	44.10	3.69	3.76
Benzyl	Ethyl	$C_{16}H_{17}N_5O_7S$	143.5–144.5	45.39	45.25	4.05	4.12

[a] These compounds are indexed in *Chem. Abstr.* as picrates of, for example, 2,3-dimethyl-2-thiopseudourea. [b] J. Goerdeler, A. Huppertz, and K. Wember, *Ber.*, **87**, 68 (1954). Used in purification without characterization. [c] H. L. Wheeler and G. S. Jamieson, *J. Biol. Chem.*, **4**, 111 (1908), reported 157°. No analysis given. [d] A. E. Dixon, *J. Chem. Soc.*, 550 (1903), reported 149–150°. [e] Melted partially at 112.5–113.5° and formed complete melt at 124.5–125°. R. Douris, *Bull. sci. pharmacol.*, 15, 629 (1908), reported sintering at 114° and melting at 123°. No analysi given. [f] Lit. (ref. *d*) 176–177°. No analysis given. [g] J. D. Brooks, P. T. Charlton, P. E. Macey, D. A. Peak, and W. F. Short, *J. Chem. Soc.*, 452 (1950), reported 199.5°.

6.44(vs), 6.71(s), 6.97(m), 7.31(m), 7.52(vs), 7.86(vs), 8.17(m), 8.61(w), 9.25(w), 10.95(m), 12.61(w), 13.40(w), 14.10(w), 14.26(w), and 15.70(w) μ.

When the alkylation was carried out in aqueous ethanol in the presence of sodium hydroxide,[17] a 24% yield of picrate was obtained. When an attempt was made to alkylate 2-thioöxazolidone or 5,5-dimethyl-2-thioöxazolidone with methyl iodide in refluxing ethanol without alkali, no picrate was obtained, nor could the thioöxazolidone be recovered. Decomposition may result from the acid formed in the reaction. When solutions of the oxazolinium picrates were heated, evidence of decomposition could be observed.

2-Methylthio-5-vinyl-2-oxazolinium picrate (IVc). Alkylation of 0.5 g. of *dl*-5-vinyl-2-thioöxazolidone[16] with methyl iodide and sodium ethylate in absolute ethanol followed by treatment with picric acid yielded 0.48 g. (33%) of the picrate of the *dl*-isomer, m.p. 101–103.5°. It crystallized from chloroform-heptane (10:7) as yellow needles, m.p. 104.5–105.5°.

Anal. Calcd. for $C_{12}H_{12}N_4O_8S$: C, 38.71; H, 3.25; S, 8.61. Found: C, 38.79; H, 3.47; S, 8.65.

When 150 mg. of (−)-5-vinyl-2-thioöxazolidone, isolated from rutabaga seeds,[5] was methylated in a similar manner, 142 mg. (33% yield) of the picrate of the 1-isomer, m.p.

(17) H. W. Barrett, I. Goodman, and K. Dittmer, *J. Am. Chem. Soc.*, **70**, 1753 (1948), preferred these conditions for the methylation of 2-thiouracil.

103–104°, was obtained. Recrystallization from chloroform-heptane afforded yellow needles, m.p. 104.5–105.5°, $[\alpha]_D^{25}$ −32.8° (*c*, 0.2 in methanol).

Anal. Calcd. for $C_{12}H_{12}N_4O_8S$: C, 38.71; H, 3.25. Found: C, 38.58; H, 3.36.

5,5-Dimethyl-2-methylthio-2-oxazolinium picrate (IVb). Methylation of 0.5 g. of 5,5-dimethyl-2-thioöxazolidone[18] in absolute ethanol, as described above, gave 0.82 g. (57% yield) of picrate, m.p. 132–134°. Yellow prismatic crystals, m.p. 133–134.5°, were obtained on recrystallization from chloroform-heptane.

Anal. Calcd. for $C_{12}H_{14}N_4O_8S$: C, 38.50; H, 3.77; S, 8.56. Found: C, 38.64; H, 3.87; S, 8.54.

Thiazolinium picrates. When 2-thiothiazolidone was refluxed in ethanol with a slight excess of methyl iodide for 45 min., 2-methylthio-2-thiazoline was isolated as the picrate in 51% yield.[19] When the reactants were refluxed for 45 min. in the presence of sodium ethylate, the picrate was obtained in 84% yield.

The preparation of 2-methylthio-2-thiazoline by the cyclization of methyl 2-hydroxyethyldithiocarbamate has been reported by Crawhall and Elliott[20] and the melting point of the picrate given as 123°. The picrate obtained in this Laboratory, however, melted at 150–151°. Since the structures of the cyclization products involved are of considerable interest,[16,21] the preparation by the method of Crawhall and Elliott was repeated. The resulting picrate melted at 150–151°, and the products from the two methods were found to be identical.

The infrared spectrum of 2-methylthio-2-thiazolinium picrate showed the following bands and intensities: 2.84(w), 6.14(s), 6.21(vs), 6.39(vs), 6.45(vs), 6.58(s), 6.74(m), 6.97(m), 7.32(s), 7.51(s), 7.61(s), 7.95(vs), 8.65(s), 9.30(m), 9.52(m), 10.88(m), 11.00(m), 12.65(m), 13.46(m), 14.25(s), and 15.12(m) μ.

2-Ethylthio-2-thiazolinium picrate, prepared by ethylation under alkaline conditions, formed prismatic crystals, m.p. 112.5–114°, from aqueous acetone.

Anal. Calcd. for $C_{11}H_{12}N_4O_7S_2$: C, 35.10; H, 3.22. Found: C, 35.24; H, 3.30.

Infrared spectra. The spectra in the 2–8 μ region were obtained employing a Perkin-Elmer model 112, single beam, double pass infrared spectrophotometer equipped with calcium fluoride optics. In the 8 μ to 16 μ region spectra were obtained from a Baird model A, double beam infrared spectrophotometer using sodium chloride optics. All samples were run as potassium bromide disks with approximately equal weights of samples.

Acknowledgments. We wish to thank Dr. M. G. Ettlinger of The Rice Institute for his valuable suggestions and advice. We thank also Dr. J. D. Margerum and his associates of the Spectroscopy Section for assistance in determining the infrared spectra.

NATICK, MASS.

(18) H. A. Bruson and J. N. Eastes, *J. Am. Chem. Soc.*, 59, 2011 (1937).

(19) The preparation of 2-methylthio-2-thiazolinium iodide from 2-thiothiazolidone and methyl iodide in 87% yield by refluxing for 2 hr. in methanol has recently been reported by McKay, *et al.*[9]

(20) J. C. Crawhall and D. F. Elliott, *J. Chem. Soc.*, 3094 (1952).

(21) A. A. Rosen, *J. Am. Chem. Soc.*, 74, 2994 (1952).

[CONTRIBUTION FROM THE ORGANIC CHEMISTRY DEPARTMENT, RESEARCH DIVISION, ABBOTT LABORATORIES]

5-Nitro-2-furyl-substituted 1,3,4-Oxadiazoles, 1,3,4-Thiadiazoles, and 1,3,5-Triazines[1]

WILLIAM R. SHERMAN

Received April 18, 1960

The preparation of two new types of antibacterial nitrofurans is described. In these compounds antibacterial activity is shown for the first time to be present in 5-nitrofurans which are joined at the 2-position directly to a carbon atom in another heterocycle. Two systems of this type have been prepared. The first is one in which the atomic configuration C=N—N—C= is contained in a cyclic arrangement. This is found in the 1,3,4-oxadiazoles and 1,3,4-thiadiazoles. In the second type of system there is no C=N—N—C= arrangement in the heterocycle, but antibacterial activity is retained. This is represented by the 1,3,5-triazines described.

In 1944 Dodd and Stillman[1a] published their finding that furans with a nitro group in the 5-position possessed antibacterial activity. In a later paper[2] the generalization was made, that, in order to be effective *in vivo*, the 2-position of the 5-nitrofuran must be substituted by a group of the general type C=N—N—C=. An example is the semicarbazone of 5-nitro-2-furaldehyde. In subsequent years, the great bulk of work carried out in this area has followed along these lines, *e.g.* nitrofurfurylidene derivatives and their vinylogs.[3]

It has now been found that the C=N—N—C= system described by Dodd *et al.*,[2] may be incorporated in a heterocycle and still retain *in vivo* activity.[3a] Such a compound is described in general terms by structure I. Two groups of such com-

(1) Presented before the Division of Medical Chemistry, 136th Meeting, American Chemical Society, Atlantic City, N. J., September 13–18, 1959.

(1a) M. C. Dodd and W. B. Stillman, *J. Pharmacol. Exptl. Therap.*, 82, 11 (1944).

(2) M. C. Dodd, D. L. Cramer, and W. C. Ward, *J. Am. Pharm. Assoc.*, 39, 313 (1950).

(3) See, for example: K. Hayes, *J. Am. Chem. Soc.*, 77, 2333 (1955) and previous papers; H. Saikachi and H. Ogawa, *J. Am. Chem. Soc.*, 80, 3642 (1958).

(3a) Detailed information regarding the *in vitro* and *in vivo* antibacterial activity of these compounds will be published elsewhere.