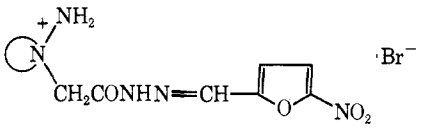
TABLE III

5-NITRO-2-FURALDEHYDE HYDRAZONIUMACETHYDRAZONES



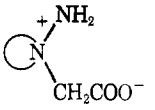
| No. | N | Method | Yield, % | Crystn solvent | Mp, °C | Formula[a] |
|---|---|---|---|---|---|---|
| 1 | $NMe_2$ | B | 95 | EtOH–$H_2O$ | 217 | $C_9H_{14}BrN_5O_4$ |
| 2 | $NEt_2$ | B | 30[b] | 95% EtOH | 184–186 | $C_{11}H_{18}BrN_5O_4$[c] |
| 3 | Pyrrolidino | B | 86 | MeOH | 217 | $C_{11}H_{16}BrN_5O_4$ |
| 4 | Piperidino | B | 87 | EtOH | 199 dec | $C_{12}H_{18}BrN_5O_4$ |
| 5 | Morpholino | B | 69 | EtOH–$H_2O$ | 228 dec | $C_{11}H_{16}BrN_5O_5$ |

[a] All compds were analyzed for C, H, N, Br. [b] The corresponding ester **2b** and hydrazide **3b** were not isolated because of their hygroscopicity. [c] *Anal.* C, H, N, O.

*vacuo*. The distn also removed the *N*-aminomorpholine. The residue was crystd (Table IV).

TABLE IV

BETAINES



| N | Method | Yield, % | Crystn solvent | Mp, °C | Formula[a] |
|---|---|---|---|---|---|
| Pyrrolidino | C | 75 | EtOH–$Et_2O$ | 159–161 | $C_6H_{11}N_2O_2$ |
| Piperidino | C | 50 | EtOH–$Et_2O$ | 200–202 | $C_7H_{14}N_2O_2$ |
| Morpholino | C | 37 | | | |
| | D | 87 | 95% EtOH–$Et_2O$ | 236–238 | $C_6H_{12}N_2O_3$ |

[a] All compds were analyzed for C, H, N.

***N*-Pyrrolidinoacetic Acid (7c).**[10]—A soln of 1.44 g (0.01 mole) of **6c** in 20 ml of MeOH was hydrogenated in presence of 0.3 g of 10% Pd/C at atmospheric pressure and at room temp. When the absorption of $H_2$ ceased, the catalyst was filtered and the soln was evapd. The residue was crystd from *i*-PrOH–$Et_2O$; yield 1 g (78%), mp 138–140°. *Anal.* ($C_6H_{11}NO_2$) C, H, N.

This compd was obtd also by hydrolysis of ethyl *N*-pyrrolidinoacetate with 1 *N* HCl. After hydrolysis the soln was passed through a strong cationic exchanger Relite CFS and **7c** was eluted with 1 *N* $NH_4OH$. The soln was evapd to dryness *in vacuo* and the residue was crystd; yield 88%.

(10) By this procedure were obtained **7b**, **7d**, and **7e** [R. E. Bowman, *J. Chem. Soc.*, 1346 (1950); C. A. Bischoff, *Chem. Ber.*, **31**, 2839 (1898); A. L. Remizon, *Zh. Obshch. Khim.*, **34**, 3187 (1964); *Chem. Abstr.*, **62**, 4106 (1965)].

## Some New Antibacterial Quinoxaline *N*,*N*-Dioxide Derivatives

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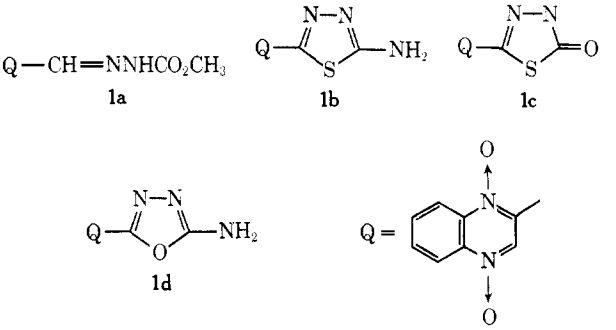
Several relatively simple derivatives of quinoxaline-2-carboxaldehyde 1,4-dioxide, notably the carbomethoxyhydrazone derivative[1] (**1a**), exhibit interesting antibacterial activity.[1,2]

We have now prepared the aminothiadiazole **1b** and the thiadiazolone **1c** from the corresponding thiosemicarbazone. The oxadiazole **1d** could be obtained from brominative oxidation of the corresponding semicarbazone, but resisted purification efforts.

The compounds were generally poorly soluble and difficult to purify. The thiadiazolone was not obtained analytically pure, but the structure was confirmed by the exact mass of the parent ion and a reasonable fragmentation pattern in the mass spectrum.



**1a** **1b** **1c**



**1d**

**Biological Results.**—Two of the derivatives, **1c** and **1d**, were active against a *Salmonella gallinarum* infection in chicks when fed in the diet at the 0.1% level, and the latter was partially effective at 0.025%; **1a** was highly active at the 0.025% level. Similarly **1b** was highly active against *Escherichia coli* infections in chicks at 40 mg/kg single oral dose, but this was only *ca.* 0.25 the activity of **1a**, and the other derivatives were inactive. **1b** was inactive *vs. E. coli* and *Staphylococcus Smith* infections in mice at levels at which **1a** was efficacious.

### Experimental Section[3]

**2-(5-Amino-1,3,4-thiadiazol-2-yl)quinoxaline 1,4-Dioxide (1b).**—A mixt of 13.7 g (0.052 mole) of quinoxaline-2-carboxaldehyde 1,4-dioxide thiosemicarbazone and 42.0 g (0.156 mole) of $FeCl_3 \cdot 6H_2O$ in 1250 ml of $H_2O$ was refluxed 4 hr, then filtered hot to give 13.3 g (97% yield) of yellow powder, mp 278–82° dec. Recrystn from a large amt of EtOH gave anal. pure material, mp 291–293° dec. *Anal.* ($C_{10}H_7N_5O_2S$) C, H, N, S.

**2-(2-Quinoxalinyl)-$\Delta^2$-1,3,4-thiadiazolin-5-one, Quinoxaline 1,4-Dioxide (1c).**—Compd **1b** (11.0 g, 0.042 mole) in 45 ml of $H_2O$ and 230 ml of concd $H_2SO_4$ was diazotized at 10° with 10.3 g (0.15 mole) of $NaNO_2$ in 45 ml of $H_2O$ and stirred overnight at room temp. The reaction mixt was cooled below 0° as a total of 430 ml of 10 *N* NaOH soln was added dropwise with the addn of crushed ice to facilitate cooling. The resulting product was filtered and washed thoroughly with $H_2O$ to give 9.7 g (88% yield) of brown powder, mp 270–273° dec. Another run gave an 89% yield of crude product as a yellow powder, mp 277–280° dec. Recrystn from 95% EtOH, glac HOAc, $Me_2CO_3$, or DMF was possible but in each case the mp was lower or the same and microanal. was worse than for the crude product. *Anal.* Calcd for $C_{10}H_6N_4O_3S$: C, 45.80; H, 2.31; N, 21.36; S, 12.23. Found: C, 43.46; H, 2.24; N, 20.45; S, 11.29. The mass spectrum exhibited a weak but correct molecular ion ($C_{10}H_6N_4O_3S$ Calcd: 260.0161. Found: 262.0152).

**Acknowledgment.**—The antibacterial testing was conducted under the direction of Dr. G. Kemp, Princeton, N. J., and Mr. G. Redin of Lederle Laboratories. The mass spectrum was run by T. L. Chang, American Cyanamid Company, Stamford Laboratories.

(1) Chas. Pfizer & Co., U. S. Patents 3,371,090, 3,433,871 (1968).

(2) Research Corporation, U. S. Patent 3,398,141 (1968).

(3) Melting points were determined on a Thomas-Hoover apparatus and are uncorrected. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Where analyses are indicated only by symbols of the elements, anal. results obtained for these elements were within ±0.4% of the theor values.