## Pyridazines I

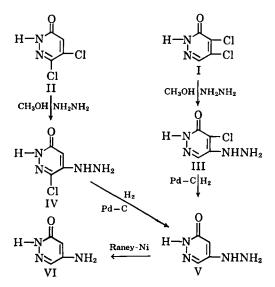
4-Halo-5-hydrazino-3-pyridazone and Its Derivatives

By WINNIFRED M. OSNER, RAYMOND N. CASTLE, and DUANE L. ALDOUS

When 4,5-dichloro-3-pyridazone, 4,5-dibromo-3-pyridazone, or 4,5-dichloro-2-phenyl-3-pyridazone in methanol was allowed to react with 95% hydrazine, a mono-halo mono-hydrazino-3-pyridazone was obtained. An unequivocal proof of struc-ture for 4-chloro-5-hydrazino-3-pyridazone is reported. Twenty-five hydrazones of 4-bromo-5-hydrazine-3-pyridazone and twenty-seven hydrazones of 4-chloro-5-hydrazino-3-pyridazone were prepared. One cyclized derivative of 4-chloro-5-hydrazino-2-phenyl-3-pyridazone is also reported.

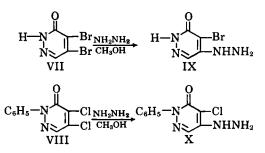
DURING investigations in this laboratory of the relative reactivity of the chlorine atoms of 4,5-dicbloro-3-pyridazone (I), the very facile reaction of this compound with hydrazine to yield a mono-halo mono-hydrazino-3-pyridazone was noted. The structure of 4-chloro-5-hydrazino-3-pyridazone (III) was determined by catalytic dechlorination followed by Raney-Ni cleavage of the hydrazino group to give the known 5-amino-3-pyridazone (VI) first prepared by Kuraishi (1).

Further confirmation was obtained by allowing 5,6-dichloro-3-pyridazone (II) to react with hydrazine. The product, compound IV, was catalytically dechlorinated to produce a compound (V) identical in all respects to that obtained from 4,5-dichloro-3-pyridazone under the same conditions.



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4,5-Dibromo-3-pyridazone (VII) was also treated with hydrazine as was 4,5-dichloro-2phenyl-3-pyridazone (VIII) and structures for the products-compounds IX and X, respectively -were assigned by analogy. The properties of compounds III through VI, IX, and X are listed in Table I.



The pyridazines have long been the subject of pharmacological studies, and the activities attributed to compounds of this ring system vary greatly (2-5). Similarly, the hydrazino group has frequently been found to confer activity upon a given structure. A complete review of hydrazine derivatives used as medicinals was published by Jucker in 1959 (6). With these facts in mind, it was deemed appropriate to prepare several carbonyl derivatives of both the bromo and chloro hydrazino compounds.

The properties of the derivatives are listed in Table II. Where a 1,3- or 1,4-dicarbonyl compound was employed, a cyclized derivative was obtained. Structures and properties for these products are given in Table III.

Infrared and ultraviolet absorption spectra of all the compounds prepared were recorded and contribute confirmatory evidence for the structure assigned.1

Data have been received concerning 23 of the compounds submitted to Cancer Chemotherapy National Service Center, National Cancer Insti-

analytical data reported.

<sup>&</sup>lt;sup>1</sup> The spectra appear in the doctoral dissertation by Winni-fred M. Osner. Copies are available through University Microfilm, Inc., 313 N. First St., Ann Arbor, Mich.

			<i>_</i>	————Anal	ysis————	
Compound	М.р., °С.	Formula	Calcd.	Found	Calcd.	Found
III	195 dec.	C <sub>4</sub> H <sub>5</sub> N <sub>4</sub> OCl	29.92	30.27	3.14	3.22
IV	268 dec.	C <sub>4</sub> H <sub>5</sub> N <sub>4</sub> OCl	29.92	30.29	3.14	3.19
v	259 dec.	C <sub>4</sub> H <sub>6</sub> N <sub>4</sub> O	38.09	38.16	4.79	4.59
VI	289 dec.	C <sub>4</sub> H <sub>5</sub> N <sub>3</sub> O	43.24	42.94	4.54	4.10
IX	180 dec.	C <sub>4</sub> H <sub>5</sub> N <sub>4</sub> OBr <sup>a</sup>	23.43	23.78	2.46	2.14
X	164 dec.	C <sub>10</sub> H <sub>9</sub> N <sub>4</sub> OCl <sup>a</sup>	50.75	50.47	3.83	3.51

TABLE I.--HYDRAZINO AND AMINO-3-PYRIDAZONES

<sup>a</sup> Inactive in first stage of screening.

tute, for tissue culture screening. Though it is in no way complete or conclusive, this information as indicated in the tables is included here for consideration.

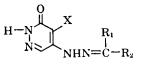
## EXPERIMENTAL

All melting points were determined with a Vanderkamp Melt-Pointer and are uncorrected.

**4 - Chloro - 5 - hydrazino - 3 - pyridazone** (III).— Thirty-three Gm. (0.2 mole) of 4,5-dichloro-3pyridazone (I) prepared by the method of Mowry (7) were dissolved in 560 ml. of boiling methanol. To this solution 19 Gm. (0.6 mole) of 95% hydrazine was added portionwise, and a yellow precipitate appeared after 10 minutes. The mixture was allowed to reflux a total of 1.5 hours; then it was cooled and filtered. Recrystallization from water afforded 20 Gm. (62%) of pale yellow needles, m.p. 195° dec.

**4 - Bromo - 5 - hydrazino - 3 - pyridazone (IX).** 4,5-Dibromo-3-pyridazone prepared by the method

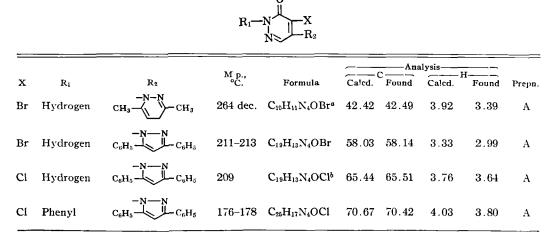
TABLE II.—DERIVATIVES OF 4-HALO-5-HYDRAZINO-3-PYRIDAZONE



$ \begin{array}{c c c c c c c c c c c c c c c c c c c $						Analysis				
Br         Hydrogen         Phenyl         241 dec.         Cu HINOCI*         53.11         53.33         3.65         3.57           CI         Hydrogen         m-Hydroxyphenyl         267 dec.         Cu HINOCI*         53.11         53.30         8.65         3.57           Dr         Hydrogen         m-Hydroxyphenyl         267 dec.         Cu HINOCI*         53.11         53.30         8.65         3.57           Dr         Hydrogen         3.4 Dimethoxyphenyl         267 dec.         Cu HINOCI*         50.75         50.57         50.57         50.57         4.24         4.11           Dr         Methyl         Phenyl         220 dec.         Cu HINNOCI*         54.88         54.66         4.22         3.99           Dr         Methyl         P-Methylphenyl         220 dec.         Cu HINNOCI *         50.16         50.29         4.51         4.64           Br         Methyl         3.4 Dimethylphenyl         220 dec.         Cu HINNOCI *         3.83         3.83         3.83         3.83         3.84         4.64           Br         Methyl         3.4 Dichlorophenyl         230 dec.         Cu HINNOCI *         3.82         3.87         3.87         3.87         3.87         3.87 <th>x</th> <th>R</th> <th>R,</th> <th>М.р., °С.</th> <th>Formula</th> <th>Caled.</th> <th>Found</th> <th></th> <th></th> <th>Prepn.</th>	x	R	R,	М.р., °С.	Formula	Caled.	Found			Prepn.
Ci         Hydrogen         Phenyi         304 dec.         CuHsNOCl <sup>b</sup> 53.11         53.30         3.65         3.57           Br         Hydrogen         m-Hydroxyphenyi         207 dec.         CuHsNOCl <sup>b</sup> 42.74         42.49         2.93         2.86           Cl         Hydrogen         3.4 Dimethoxyphenyi         207 dec.         CuHsNOCl <sup>b</sup> 49.91         49.73         3.42         3.21           Br         Hydrogen         3.4 Dimethoxyphenyi         276 dec.         CuHuNOCl <sup>c</sup> 50.57         50.55         4.24         4.11           Br         Methyl         Phenyi         220 dec.         CuHuNOCl <sup>c</sup> 50.57         50.55         4.73         4.64           Cl         Methyl         Phenyi         220 dec.         CuHuNOCl <sup>c</sup> 51.86         0.99         4.73         4.64           Cl         Methyl         -Hydroxyphenyi         223 dec.         CuHuNOCl <sup>c</sup> 57.81         57.81         5.20         4.78           Br         Methyl         -Hydroxyphenyi         234 dec.         CuHuNOCl <sup>c</sup> 58.23         87.2         2.41         2.41           Cl         Methyl         -Hydroxyphenyi         234 dec.         CuHuNOCl			Phenyl	241 dec	CuHoNiOBrb	45 07	44 93	3 09	3 01	A
Br       Hýdrozyphenyl       267 dec.       Cn.HsN.OxBr       42.74       42.49       2.93       2.86         Br       Hydrozen       3.4-Dimethoxyphenyl       248 dec.       Cn.HsN.OxBr       44.20       44.19       3.71       3.29         Br       Hydrozen       3.4-Dimethoxyphenyl       248 dec.       Cn.HsN.OxBr       44.20       44.19       3.71       3.29         CH       Methyl       Phenyl       225 dec.       Cn.HsN.OxBr       46.92       46.96       3.61       3.40         CH       Methyl       Phenyl       225 dec.       Cn.HuN.OBr       46.92       46.92       4.68       8.66       4.22       3.99         GL       Methyl       P-Methylphenyl       220 dec.       Cn.HuN.OBr       48.61       48.70       4.08       3.92         GL       Methyl       3.4-Dimethylphenyl       220 dec.       Cn.HuN.OBr       44.60       4.79       3.43       3.50         CL       Methyl       9-Hydroxyphenyl       231 dec.       Cn.HuN.OBr       48.61       48.67       4.03       8.83         Br       Methyl       9-Hydroxyphenyl       131 dec.       CnHuN.OBr       56.43       56.38       47.4       42       48       41.03<										Â
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CL       Hydrogen       3.4.Dimethoxyphenyl       276 dec.       CiHINAOBr       50.57       50.55       4.24       4.11         Br       Methyl       Phenyl       220 dec.       CiHINAOBr       46.96       3.61       3.40         Cl       Methyl       Phenyl       223 dec.       CiHINAOBr       48.61       48.70       40.98       3.99         Cl       Methyl       Phenyl       223 dec.       CiHINAOBr       48.61       48.70       40.83       3.99         Cl       Methyl       S.4.Dimethylphenyl       220 dec.       CiHINAOBr       50.16       50.29       4.73       4.64         Br       Methyl       O.Hydroxyphenyl       233 dec.       CiHINAOBr       50.16       50.29       4.73       4.64         Cl       Methyl       O.Hydroxyphenyl       234 dec.       CiHINAOBr       50.16       50.29       4.73       4.83       3.50         Cl       Methyl       J.4.Dichlorophenyl       240 dec.       CiHINAOBr       48.61       46.70       2.74       2.68         Br       Methyl       J.4.Dichlorophenyl       117-218       CiHINAOBr       50.16       50.16       50.14       45.17       5.20       4.90       3.84										Ă
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Br $n \cdot Propyl$ Phenyl $175 \cdot 176$ $C_{1}H_{11}N_{10}OBr$ $50.16$ $50.14$ $4.51$ $4.21$ CI $n \cdot Propyl$ Phenyl $217 - 218$ $C_{11}H_{11}N_{10}OBr^4$ $50.16$ $49.75$ $4.51$ $4.21$ CIIsopropylPhenyl $221$ dec. $C_{11}H_{11}N_{10}OBr^4$ $50.16$ $49.75$ $4.51$ $4.25$ CIIsopropylPhenyl $251$ $C_{11}H_{11}N_{10}OBr^4$ $50.16$ $49.75$ $4.51$ $4.25$ CI $n \cdot Butyl$ Phenyl $151$ $C_{11}H_{11}N_{10}OBr^4$ $50.90$ $52.72$ $5.20$ $4.97$ CI $n \cdot Butyl$ Phenyl $233$ dec. $C_{11}H_{11}N_{10}OBr^4$ $60.04$ $60.63$ $30.52$ $2.78$ CI $2 \cdot Carboxyvinyl$ Phenyl $255$ dec. $C_{11}H_{11}N_{10}OBr^4$ $60.30$ $46.36$ $3.05$ $2.78$ CI $2 \cdot Carboxyvinyl$ Phenyl $207$ dec. $C_{11}H_{11}N_{10}OBr^4$ $50.46$ $51.02$ $3.93$ $3.85$ CIMethylStyryl $214$ dec. $C_{11}H_{12}N_{10}OBr^4$ $55.46$ $3.54$ $4.32$ BrPhenylPhenyl $299$ dec. $C_{11}H_{12}N_{10}OBr^4$ $55.46$ $3.54$ $4.22$ CIPhenylPhenyl $232$ $C_{11}H_{12}N_{10}OBr^4$ $57.25$ $4.31$ $4.02$ BrBenzylPhenyl $232$ $C_{11}H_{12}N_{10}OBr^4$ $57.45$ $51.46$ $3.74$ $4.26$ BrBenzyl <td< td=""><td>CI</td><td>Ethyl</td><td>Phenyl</td><td>209 - 210</td><td>C13H13N4OClb</td><td>56.43</td><td>56.38</td><td>4.74</td><td>4.49</td><td>A</td></td<>	CI	Ethyl	Phenyl	209 - 210	C13H13N4OClb	56.43	56.38	4.74	4.49	A
			Phenyl	175 - 176	C14H15N4OBr	50.16	50.14	4.51	4.21	A
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Br         Methyl         Styryl         207 dec.         Cu HusNiOBr         50.46         51.02         3.93         3.85           Ci         Methyl         Styryl         214 dec.         Cu HusNiOBr         50.46         51.02         3.93         3.85           Ci         Methyl         Styryl         214 dec.         Cu HusNiOBr         55.34         58.96         4.54         4.47           Br         Phenyl         Phenyl         2199 dec.         Cu HusNiOBr         55.30         55.46         3.54         3.82           Cl         Phenyl         Phenyl         304 dec.         Cu HusNiOBr         55.30         55.46         3.54         3.32           Cl         Phenyl         Phenyl         304 dec.         Cu HusNiOBr         54.15         54.23         3.79         3.52           Cl         Phenyl         P-Methoxyphenyl         232         Cu HusNiOrBr         54.15         54.23         3.79         3.53           Br         Benzyl         P-Methylphenyl         236         dec.         Cu HusNiOrBr         54.14         4.86         4.73           Br         Benzyl         Benzyl         192 dec.         Cu HusNiOrBr         54.15         53.69										A A
Ci       Methyl       Styryl       214 dec.       CuHusNOCI       58.34       58.96       4.54       4.47         Br       Phenyl       Phenyl       299 dec.       CuHusNOCI       58.34       58.96       4.54       4.47         Br       Phenyl       Phenyl       299 dec.       CuHusNOEr       55.30       55.46       3.54       3.32         Cl       Phenyl       Phenyl       304 dec.       CuHusNOEr       55.30       55.46       3.54       3.32         Br       Phenyl       Phenyl       304 dec.       CuHusNOEI       62.87       4.03       4.02         Br       Phenyl       Phenyl       232       CuBHusNOEI       61.16       61.11       61.11       4.11       4.74       4.93       4.09         Br       Benzyl       Phenylphenyl       276 dec.       CuBHusNOEI       64.68       64.41       4.86       4.73         Br       Benzyl       Benzyl       192 dec.       CuBHusNOEI       64.68       64.53       4.86       4.41         Br       Phenyl       Phenylhydroxymethyl       240 dec.       CuBHusNOEI       64.18       66.8       64.53       4.86       4.31       3.06         Cl										Â
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $										Â
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $										A B
Br         Phenyl         Phethoxyphenyl         232         CisHusNiOrBr         54.15         54.23         3.79         3.52           Cl         Phenyl         P-Methoxyphenyl         252         CisHusNiOrBr         54.15         54.23         3.79         3.52           Cl         Phenyl         P-Methoxyphenyl         252         CisHusNiOrBr         54.15         54.23         3.79         3.52           Br         Benzyl         P-Methylphenyl         236         dec.         CisHusNiOrBr         54.14         57.25         4.31         4.09           Cl         Benzyl         P-Methylphenyl         236         dec.         CisHusNiOrBr         54.44         57.25         4.31         4.09           Br         Benzyl         Benzyl         192         dec.         CisHusNiOrBr         54.45         57.45         3.33         4.31         4.30           Cl         Benzyl         Benzyl         207         CisHusNiOrBr         54.15         53.69         3.79         3.31           Cl         Phenyl         Benzyl         240         dec.         CisHusNiOrBr         54.12         54.11         3.30         3.06           Cl         Phenyl         Ben										H H
Ci         Phenyl         p-Methoxyphenyl         252         CaHabNAOcCl         61.11         61.11         4.27         4.29           Br         Benzyl         p-Methylphenyl         236         dec.         CaHabNAOcCl         61.11         61.11         4.27         4.29           Br         Benzyl         p-Methylphenyl         236         dec.         CaHabNAOcCl         61.11         61.11         4.27         4.29           Br         Benzyl         p-Methylphenyl         236         dec.         CaHabNAOcCl         64.8         64.41         4.86         4.31         4.09           Br         Benzyl         Benzyl         192         dec.         CaHabNAOcCl         64.86         64.53         4.31         4.30           Cl         Benzyl         Phenylhydroxymethyl         240         dec.         CaHabNAOcBr         54.15         53.69         3.79         3.31           Cl         Phenyl         Phenylhydroxymethyl         250         dec.         CaHabNAOcBr         54.42         54.11         3.30         3.06           Cl         Phenyl         Benzoyl         225         CaHabNAOcCl         64.98         53.63         3.71         3.55										B A
Br         Benzyl         P-Methylphenyl         236 dec.         CirHirNiOBra         57.44         57.25         4.31         4.09           Cl         Benzyl         P-Methylphenyl         276 dec.         CirHirNiOBra         57.44         57.25         4.31         4.09           Br         Benzyl         P-Methylphenyl         276 dec.         CirHirNiOCI         64.68         64.41         4.86         4.73           Br         Benzyl         192 dec.         CirHirNiOCI         64.68         64.41         4.86         4.73           Br         Benzyl         Benzyl         207         CirHirNiOCI         64.68         64.53         4.86         4.41           Br         Phenyl         Phenylhydroxymethyl         240         62.         CirHirNiOEr         54.15         53.69         3.79         3.31           Cl         Phenyl         Benzoyl         220         62.         CirHirNiOFrd         51.42         54.11         3.30         3.06           Cl         Phenyl         Benzoyl         220         62.         CirHirNiOFrd         61.43         3.71         3.55           Cl         Hydrogen         2-Furyl         259         667         66.										Â
Ci         Benzyl         p-Methylphenyl         276 dec.         Ci+H1:NOCl         64.68         64.41         4.86         4.73           Br         Benzyl         Benzyl         192 dec.         Ci+H1:NOCl         64.68         64.41         4.86         4.73           Br         Benzyl         Benzyl         192 dec.         Ci+H1:NOCl         64.68         64.41         4.86         4.30           Cl         Benzyl         Benzyl         192 dec.         Ci+H1:NOCl         64.68         64.53         4.86         4.31           Br         Phenyl         Phenylhydroxymethyl         240 dec.         Ci+H1:NO2Br         54.15         53.69         3.79         3.31           Cl         Phenyl         Benzoyl         225         Ci+H1:NO2Br         54.12         54.11         3.03         3.06           Cl         Phenyl         Benzoyl         225         Ci+H1:NO2Br         54.12         54.11         3.03         3.06           Cl         Phenyl         Benzoyl         225         Ci+H1:NO2Br         54.12         54.11         3.06         2.62         78           Br         Methyl         3-Pyridyl         2259         dec.         Ci+H1:NO2Br <t< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>Â</td></t<>										Â
Br         Benzyl         192 dec.         CisHuNAOBra         57.44         57.33         4.31         4.30           Cl         Benzyl         Benzyl         207         CisHuNAOBra         57.44         57.33         4.31         4.30           Cl         Benzyl         Benzyl         207         CisHuNAOEI         64.68         64.53         4.86         4.41           Br         Phenyl         Phenylhydroxymethyl         240 dec.         CusHuNAOEBr         54.15         53.69         3.79         3.31           Cl         Phenyl         Phenylhydroxymethyl         250 dec.         CusHuNAOEBr         54.42         54.11         3.30         3.06           Cl         Phenyl         Benzoyl         250 dec.         CusHuNAOEBr         54.42         54.11         3.30         3.06           Cl         Phenyl         Benzoyl         220 dec.         CusHuNAOEBr         54.42         54.11         3.30         3.06           Cl         Phenyl         Benzoyl         259 dec.         CusHuNAOEBr         54.25         3.27         3.19           Br         Methyl         3-Pyridyl         267 dec.         CuHuNAOCH         45.05         3.27         3.19 <tr< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr<>										
Cl         Benzyl         Benzyl         207         CieHu:NAOCI         64.68         64.53         4.86         4.41           Br         Phenyl         Phenylhydroxymethyl         240         dec.         CieHu:NAOCI         60.81         4.26         3.93           Br         Phenyl         Phenylhydroxymethyl         259         dec.         CieHu:NAOCI         60.93         60.81         4.26         3.93           Br         Phenyl         Benzoyl         225         Cu/Hu:NAOCI         60.93         60.81         4.26         3.93           Cl         Phenyl         Benzoyl         220         Cu/Hu:NAOCI         61.03         60.81         4.26         3.93           Cl         Hydrogen         2-Furyl         250         dec.         Cu/Hu:NAOCI         61.03         60.81         4.26         3.93           Br         Methyl         Benzoyl         220         dec.         Cu/Hu:NAOCI         61.03         60.81         3.77         3.06           Cl         Hydrogen         2-Furyl         250         dec.         Cu/Hu:NAOCI         61.03         8.27         3.18           Cl         Methyl         3-Pyridyl         280         Cu/Hu:NAO										A
Br         Phenyl         Phenylhydroxymethyl         240 dec.         Cia Hia NiOaBr         54.15         53.69         3.79         3.31           Cl         Phenyl         Phenylhydroxymethyl         259 dec.         Cia Hia NiOaBr         54.15         53.69         3.79         3.31           Cl         Phenyl         Phenylhydroxymethyl         259 dec.         Cia Hia NiOaBr         54.15         53.69         3.79         3.31           Br         Phenyl         Benzoyl         259 dec.         Cia Hia NiOaBr         54.42         54.11         3.00         3.06           Cl         Phenyl         Benzoyl         220         Cu Hia NiOaBr         54.42         54.11         3.30         3.06           Cl         Phenyl         Benzoyl         220         Cu Hia NiOaBr         54.42         54.11         3.30         3.06           Cl         Phenyl         Benzoyl         220         225         Cu Hia NiOaBr         54.20         54.13         3.71         3.55           Cl         Hydrogen         3-Pyridyl         259 dec.         Cu Hia NiOaBra         42.87         43.05         3.27         3.19           Cl         Methyl         3-Pyridyl         280 dec.										A
Cl         Phenyl         Phenylbydroxymethyl         259 dec.         CuHusNAOrCl         60.93         60.81         4.26         3.93           Br         Phenyl         Benzoyl         225         CuHusNAOrCl         60.93         60.81         4.26         3.93           Cl         Phenyl         Benzoyl         225         CuHusNAOrCl         61.28         61.43         3.71         3.55           Cl         Hydrogen         2-Furyl         250 dec.         CuHusNAOrCl         61.28         61.43         3.71         3.55           Cl         Hydrogen         2-Furyl         250 dec.         CuHusNAOrCl         45.30         45.05         2.96         2.78           Br         Methyl         3-Pyridyl         267 dec.         CuHusNAOR         42.81         3.27         3.19           Cl         Methyl         3-Pyridyl         280 dec.         CuHusNAOR         42.81         3.27         3.18           Cl         Hydrogen         3-Pyridyl         280 dec.         CuHusNAOR         48.11         47.63         3.23         3.11           Br         Methyl         2-Pyridyl         213 dec.         CuHusNAOR         48.11         47.63         3.23         3.11<										A
Br         Phenyl         Benzoyl         225         CuHubNiO2Br         54.42         54.11         3.30         3.06           Cl         Phenyl         Benzoyl         220 dec.         CuHubNiO2Cl <sup>d</sup> 61.28         61.43         3.71         3.55           Cl         Hydrogen         2-Furyl         259 dec.         CuHubNiO2Cl <sup>d</sup> 61.28         61.43         3.71         3.55           Br         Methyl         3-Pyridyl         267 dec.         CuHubNiOBra         42.87         43.05         3.27         3.19           Cl         Methyl         3-Pyridyl         280 dec.         CuHubNiOBra         42.87         43.05         3.27         3.19           Cl         Methyl         3-Pyridyl         280 dec.         CuHubNiOBra         42.87         43.05         3.27         3.19           Br         Methyl         2-Pyridyl         251 dec.         CuHubNiOBra         42.87         42.81         3.27         3.18           Cl         Hydrogen         3-Pyridyl         251 dec.         CuHubNiOBra         42.87         42.81         3.23         3.11           Br         Phenyl         p-Dimethylaminophenyl         213 dec.         CuHubNiOBr         55.35 </td <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td>A</td>										A
Cl         Phenýl         Benzoýl         220 dec.         Cu Huði NorCl <sup>d</sup> 61.28         61.43         3.71         3.55           Cl         Hydrogen         2-Furyl         259 dec.         Cu Huði NorCl <sup>d</sup> 45.30         45.05         2.96         2.78           Br         Methyl         3-Pyridyl         267 dec.         Cu Huði NorCl <sup>d</sup> 45.30         45.05         2.96         2.78           Br         Methyl         3-Pyridyl         267 dec.         Cu Huði NorCl         50.10         49.80         3.82         3.69           Br         Methyl         3-Pyridyl         280 dec.         Cu Huði NOBra         42.87         43.05         3.27         3.18           Cl         Hydrogen         3-Pyridyl         280 dec.         Cu Huði NOBra         42.87         43.05         3.23         3.11           Br         Phenyl         2-Pyridyl         287 dec.         Cu Huði NOBra         42.81         47.63         3.23         3.11           Br         Phenyl         p-Dimethylaminophenyl         213 dec.         Cu Huði NoBra         55.35         55.34         4.40         4.66           Cl         Phenyl         p-Dimethylaminophenyl         258 dec.         <										A
Cl         Hydrogen         2-Furyl         259 dec.         CH <sub>1</sub> N <sub>1</sub> O <sub>2</sub> Cl <sup>b</sup> 45.30         45.05         2.96         2.78           Br         Methyl         3-Pyridyl         267 dec.         C <sub>1</sub> H <sub>10</sub> N <sub>10</sub> Bra         42.87         43.05         3.27         3.19           Cl         Methyl         3-Pyridyl         280 dec.         C <sub>11</sub> H <sub>10</sub> N <sub>2</sub> OR <sup>a</sup> 42.87         42.81         3.27         3.19           Br         Methyl         2-Pyridyl         251 dec.         C <sub>11</sub> H <sub>10</sub> N <sub>2</sub> OBr <sup>a</sup> 42.87         42.81         3.27         3.18           Cl         Hydrogen         3-Pyridyl         287 dec.         C <sub>11</sub> H <sub>10</sub> N <sub>2</sub> OBr <sup>a</sup> 42.87         42.81         3.27         3.18           Cl         Hydrogen         3-Pyridyl         287 dec.         C <sub>11</sub> H <sub>10</sub> N <sub>2</sub> OBr <sup>a</sup> 42.87         42.81         3.27         3.18           Cl         Phenyl         p-Dimethylaminophenyl         213 dec.         C <sub>12</sub> H <sub>10</sub> N <sub>2</sub> OCl         65.35         55.34         4.40         4.66           Cl         Phenyl         p-Dimethylaminophenyl         258 dec.         C <sub>12</sub> H <sub>10</sub> N <sub>3</sub> OCl         62.04         61.53         4.93         4.68									3.06	A
Br         Methyl         3-Pyridyl         267 dec.         Cli HubNoBra         42.87         43.05         3.27         3.19           Cl         Methyl         3-Pyridyl         280 dec.         CuHubNoBra         42.87         43.05         3.27         3.19           Br         Methyl         3-Pyridyl         280 dec.         CuHubNoBra         42.87         43.05         3.27         3.18           Br         Methyl         2-Pyridyl         251 dec.         CuHubNoBra         42.87         42.81         3.27         3.18           Cl         Hydrogen         3-Pyridyl         251 dec.         CuHubNoCl         50.10         49.80         3.23         3.11           Br         Phenyl         287 dec.         CuHubNoCl         55.35         55.34         4.40         4.66           Cl         Phenyl         258 dec.         CuHuBNoCl         62.04         61.53         4.93         4.68									3.55	A
Cl         Methyl         3-Pyridyl         280 dec.         CnHn0NOCI         50.10         49.80         3.82         3.69           Br         Methyl         2-Pyridyl         251 dec.         CnHn0NOBra         42.87         42.81         3.27         3.18           Cl         Hydrogen         3-Pyridyl         287 dec.         CnHn0NOBra         42.87         42.81         3.23         3.11           Br         Phenyl         p-Dimethylaminophenyl         213 dec.         CnHn0NOBra         55.35         55.34         4.40         4.66           Cl         Phenyl         p-Dimethylaminophenyl         258 dec.         Cl         Phenyl         6.64         4.68         4.68         4.68										A
Br         Methyl         2-Pyridyl         251 dec.         Cli H <sub>10</sub> N <sub>5</sub> OBr <sup>4</sup> 42.87         42.81         3.27         3.18           Cl         Hydrogen         3-Pyridyl         287 dec.         CuH10N50Cl         48.11         47.63         3.23         3.11           Br         Phenyl         p-Dimethylaminophenyl         213 dec.         C12H10N50Cl         55.35         55.34         4.40         4.66           Cl         Phenyl         258 dec.         C12H16N50Cl         62.04         61.53         4.93         4.68										B
Cl         Hydrógen         3-Pýridýl         287 dec.         CuHaNiOCI         48.11         47.63         3.23         3.11           Br         Phenyl         p-Dimethylaminophenyl         213 dec.         CuHaNiOBr         55.35         55.34         4.40         4.66           Cl         Phenyl         258 dec.         CuHaNiOCI         62.04         61.53         4.93         4.68										A
Br         Phenyl         p-Dimethylaminophenyl         213         dec.         C1.9HigNsOBr         55.35         55.34         4.40         4.66           Cl         Phenyl         p-Dimethylaminophenyl         258         dec.         C1.9HigNsOCl         62.04         61.53         4.93         4.68										B
Cl Phenyl p-Dimethylaminophenyl 258 dec. C19H18NsOCl 62.04 61.53 4.93 4.68										Α
										Α
Cl. A Dimethylaminophenyl A Dimethylaminophenyl 953 dec. C. H. N.OCK 61 99 61 10 5 64 5 19										A
	CI					61.38			5.18	A
Cl Hydrogen p-Dimethylaminophenyl 252 dec. C11H14N6OCl 53.52 53.54 4.84 4.64	Cl	Hydrogen	p-Dimethylaminophenyl	252 dec.	C11H14N6OCl	53.52	53.54	4.84	4.64	A

a Inactive in first stage of screening. <sup>b</sup> Active in first stage; inactive in second stage. <sup>c</sup> Active in first stage; no data on second stage. <sup>d</sup> Active through first and second stages.

TABLE III.—Cyclic Derivatives of 4-Halo-5-hydrazino-3-pyridazone



<sup>a</sup> Active in first stage; inactive in second stage. <sup>b</sup> Active in first stage; no data on second stage.

of Bistrzycki (9) was treated with hydrazine as described above for compound III. Recrystallization from water produced dark yellow needles, m.p. 180° dec.

4- Chloro -5- hydrazino - 2 - phenyl - 3 - pyridazone (X)-4,5- Dichloro - 2- phenyl -3- pyridazone (VIII) prepared by the method of Mowry (7), when allowed to react with hydrazine as described above, gave a 75% yield of fine yellow needles, m.p.  $164^{\circ}$ dec.

6 - Chloro - 5 - hydrazino - 3 - pyridazone (IV).-5,6-Dichloro-3-pyridazone (II), prepared by the method of Kuraishi (8), was similarly treated with hydrazine. The product (94%) was recrystallized from water to yield white crystals, m.p. 268° dec.

5-Hydrazino-3-pyridazone (V).-4-Chloro-5-hydrazino-3-pyridazone (III) (4.8 Gm., 0.05 mole) dissolved in 200 ml. of 1% sodium hydroxide was treated with hydrogen in the presence of 1.2 Gm. of 5% Pd-C catalyst at atmospheric pressure and room temperature. Following absorption of the theoretical amount of hydrogen, the catalyst was separated and washed with 50 ml. of 1% sodium hydroxide followed by methanol until washings were no longer basic. The filtrate and washings were neutralized with glacial acetic acid and the solution concentrated on a steam bath under reduced pressure. After cooling 48 hours, 2.8 Gm. (74%) of a dark orange solid was collected. Recrystallization from 95% ethanol (norite) afforded pale yellow needles, m.p. 267° dec.

5-Amino-3-pyridazone (VI) .-- A mixture of 1.75 Gm. (0.014 mole) of 5-hydrazino-3-pyridazone (V) dissolved in 85% ethanol and Raney-Ni W-2 (prepared from 15 Gm. of Raney-Ni alloy) was allowed to reflux 2 hours. The catalyst was removed and the filtrate evaporated on a steam bath under reduced pressure to approximately one-half volume. After cooling overnight, 0.9 Gm. (60%) of gray plates was collected and recrystallized from water (Norite) to yield white crystals, m.p. 288° dec.

General Procedure A .--- One-tenth mole of the appropriate halo-hydrazino-pyridazone was treated with 8 ml. concentrated sulfuric acid followed by 70 ml. water and the mixture heated gently just until the solid dissolved, at which time the hot solution was poured into a second flask containing 1 ml. of carbonyl compound dissolved in 40-80 ml. 95% ethanol. After standing 12 to 48 hours, the solid was filtered and recrystallized usually from 95% ethanol.

General Procedure B.- To one-tenth mole of the halo-hydrazino-pyridazone were added 10 ml. concentrated hydrochloric acid in 10 ml. water and 15 ml. 95% ethanol. The mixture was heated then added to 1 Gin. of the carbonyl compound dissolved in 10 ml. of ethanol. After cooling 24 hours, the precipitate was filtered and recrystallized from an appropriate solvent.

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