246–250°; yield 50%. *Anal.* Calcd. for $C_6H_7N_5S$: C, 39.8; H, 3.9; N, 35.2. Found: C, 39.7; H, 3.4; N, 35.2.

5,7-Dithiol-2-methylthiazolo[5,4-d]pyrimidine was prepared at 150° from 5-acetamido-2,4,6-trihydroxypyrimidine,[13] giving long orange needles melting at 298°; yield 8%. *Anal.* Calcd. for $C_6H_5N_3S_3$: C, 33.5; H, 2.3; N, 19.5. Found: C, 33.7; H, 2.4; N, 19.4.

2-*p*-Chlorophenyl-5,7-diaminothiazolo[5,4-d]pyrimidine was prepared from 5-*p*-chlorobenzamido-2,4-diamino-6-hydroxypyrimidine at 180°. The yield of yellow needles, m. p. 297–299°, was 76%. *Anal.* Calcd. for $C_{11}H_8ClN_5S$: N, 25.3. Found: N, 25.4.

Deamination of 5,7-Diamino-2-methylthiazolo[5,4-d]-pyrimidine.—One gram of 5,7-diamino-2-methylthiazolo-[5,4-d]pyrimidine was dissolved in 65 ml. of 0.5 *N* hydrochloric acid and a solution of 0.5 g. of sodium nitrite in 10 ml. of water was added in small portions over thirty minutes. The solution was warmed on the steam-bath for one hour and then neutralized with ammonium hydroxide. The precipitate was collected, and recrystallized by solution in dilute alkali and precipitation with dilute acetic acid. A white powder is formed which decomposes at about 320°. One amino group was replaced by an hydroxyl by this procedure. *Anal.* Calcd. for $C_6H_6N_4OS$: N, 30.8. Found: N, 30.6.

Dibenzoyl Derivative of 5,7-Dihydroxy-2-phenylthiazolo[5,4-d]pyrimidine.—One gram of the ammonium salt of thiouramil[9,10] was refluxed with 50 ml. of benzoyl chloride for two hours. The benzoyl chloride was removed *in vacuo*, and the residue was leached with 25 ml. of 50% ethanol, washed several times with ether and then recrystallized from ethyl acetate. The compound was obtained as colorless needles, m. p. 240°. The yield was 1.25 g. (50%). *Anal.* Calcd. for $C_{25}H_{17}N_3O_4S$: C, 66.0; H, 3.7; N, 9.3. Found: C, 66.4; H, 3.8; N, 9.7.

5,7-Dihydroxy-2-phenylthiazolo[5,4-d]pyrimidine. A. From the Dibenzoyl Derivative.—One-half gram of the above dibenzoyl derivative was boiled with 50 ml. of 1 *N* sodium hydroxide solution until it had dissolved completely. The solution was neutralized with acetic acid; the precipitate was collected, washed with ethanol and ether and recrystallized by solution in aqueous alkali and precipitation with acetic acid. The compound is a white powder which does not melt at 340°. Benzoic acid was recovered from the filtrate. *Anal.* Calcd. for $C_{11}H_7N_3O_2S$: N, 17.2. Found: N, 17.2.

(13) Piloty and Finckl, *Ann.*, **333**, 85 (1904).

B. By Deamination of 5,7-Diamino-2-phenylthiazolo-[5,4-d]pyrimidine.—To 0.6 g. of 5,7-diamino-2-phenylthiazolo[5,4-d]pyrimidine were added 5 ml. of 10 *N* sulfuric acid and 1 g. of sodium nitrite dissolved in 5 ml. of water. The mixture was warmed on the steam-bath for one hour and then neutralized with ammonium hydroxide. The precipitate was recrystallized from ethanol and formed yellow plates which do not melt at 330°. The above compound (0.18 g.) was heated with 50 ml. of 6 *N* hydrochloric acid in a bomb at 140° for sixteen hours. The solution was evaporated to dryness on the steam-bath and the residue was taken up in dilute alkali and precipitated with dilute acetic acid. The resulting compound does not melt at 340°. It has an ultraviolet absorption spectrum identical with that of the compound obtained by saponification of the dibenzoyl derivative. *Anal.* Calcd. for $C_{11}H_7N_3O_2S$: C, 53.8; H, 2.9; N, 17.2. Found: C, 53.6; H, 2.8; N, 17.3.

5,7-Dihydroxy-2-methylthiazolo[5,4-d]pyrimidine.—This compound was prepared by refluxing 1.0 g. of the ammonium salt of thiouramil with 30 ml. of acetic anhydride.[9,10] After recrystallization from water, the compound was dried at 140°. It did not melt at 340°.[14] *Anal.* Calcd. for $C_6H_5N_3O_2S$: C, 39.4; H, 2.7; N, 22.9. Found: C, 39.7; H, 2.6; N, 22.9.

Ultraviolet Absorption Spectra.—The spectra were measured with a Beckman spectrophotometer. For solutions of *p*H 1, 0.1 *N* hydrochloric acid was used and for *p*H 11, a glycine–sodium hydroxide buffer.

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Summary

Several 5-amino-, 5,7-diamino- and 5,7-dithiolthiazolo[5,4-d]pyrimidines, substituted in the 2-position by methyl or phenyl, have been synthesized by the reaction of 5-acetamido(and benzamido)-4-hydroxy(or amino)-pyrimidines with phosphorus pentasulfide.

(14) Fischer and Ach[9] give a melting point of 220–221° while Weidel and Niemilowicz[11] state that the compound does not melt above 300°. The method of preparation employed by the two authors and the other properties of the products are essentially identical and in agreement with the present observations.

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The Reaction of Amines with 2-Nitramino-1,3-diaza-2-cycloalkenes

BY A. F. MCKAY,[1] J. R. COLEMAN AND GORDON A. GRANT

Primary amines have been shown[2] to combine with 2-nitramino-1,3-diaza-2-cycloalkenes I to give 2-alkylamino- or 2-aralkylamino-1,3-diaza-2-cycloalkenes II. The picrates of several of these 1,3-diaza-2-cycloalkenes are described in Table I.

It was previously[2] noted that water liberated during this reaction was responsible for the formation of cyclic ureas as side products. The cyclic ureas were thought to form almost exclusively from the action of water on the 2-substituted amino-1,3-diaza-2-cycloalkenes. Further work on this reaction has shown that 2-nitramino-1,3-diaza-2-cycloalkenes are hydrolyzed almost quantitatively to the corresponding cyclic ureas by refluxing with excess water containing a low concentration of an amine, *e. g.*, benzylamine. The following cyclic ureas were prepared in this manner, the yields are given in parentheses: 4-hydroxy-2,6-diaza-1-cyclohexanone (98), *m. p.* 210–211°[3]; 2,6-diaza-1-cyclohexanone (98), *m. p.* 265–266°[2,4,5]; 3-methyl-2,6-diaza-1-cyclohexanone

(1) Defense Research Chemical Laboratories, Ottawa, Ontario.

(2) A. F. McKay, M. N. Buchanan and Gordon A. Grant, THIS JOURNAL, **71**, 766 (1949).

(3) J. Tafel and L. Reindl, *Ber.*, **34**, 3289 (1901), reported a melting point of 185–195°.

(4) E. Fischer and H. Koch, *Ann.*, **232**, 224 (1886).

(5) A. P. N. Franchimont and H. Friedmann, *Rec. trav. chim.*, **26**, 218 (1907).

TABLE I

2-SUBSTITUTED AMINO-1,3-DIAZA-2-CYCLOALKENES

Compound	Yield, %	B. p. °C.	Mm.	Picrate[e] m. p., °C.	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
2-(3-Methylbutylamino)-1,3-diaza-2-cyclopentene	89.0	170–173	1.0	178–179	$C_{14}H_{20}N_6O_7$	43.7	44.0	5.25	5.67	21.9	21.9
2-(3-Diethylaminopropylamino)-1,3-diaza-2-cyclopentene	96.0	166–170	1.5	133–134	$C_{22}H_{28}N_{10}O_{14}$[f]	40.2	40.3	4.30	4.09	21.3	21.5
2-Cyclohexylamino-1,3-diaza-2-cyclopentene	73.0	.....	...	227–228	$C_{15}H_{20}N_6O_7$	45.4	45.4	5.09	5.35	21.2	21.6
2-Cyclohexylamino-4(or 5)-methyl-1,3-diaza-2-cyclopentene	86.5	.....	...	197–198	$C_{16}H_{22}N_6O_7$	46.8	46.7	5.40	5.22	20.5	20.3
N-2-(1,3-Diaza-2-cyclopentene)-ethylenediamine[a]	45.9[b]	200–208	2.0	205–206.5	$C_{17}H_{18}N_{10}O_{14}$[f]	34.8	34.7	3.10	3.05	23.9	23.9
N,N'-2-(1,3-Diaza-2-cyclopentene)-ethylenediamine	54.0[b]	.....	...	268–269 (dec.)	$C_{20}H_{22}N_{12}O_{14}$[f]	36.7	36.4	3.39	3.35	25.6	25.4
N-2-(1,3-Diaza-2-cyclohexene)-ethylenediamine	28.8[c]	170–176	1.5	195–196	$C_{18}H_{20}N_{10}O_{14}$[f]	36.0	35.8	3.36	3.34	23.3	23.4
N,N'-2-(1,3-Diaza-2-cyclohexene)-ethylenediamine	68.0[c]	.....	...	283–286	$C_{22}H_{26}N_{12}O_{14}$[f]	38.7	38.5	3.84	3.40	24.6	24.5
N-2-(4(or 6)-Methyl-1,3-diaza-2-cyclohexene)-ethylenediamine	49.1[d]	169–173	1.5	216.5–217.5	$C_{19}H_{22}N_{10}O_{14}$[f]	37.1	37.3	3.61	3.70	22.8	22.8
N,N'-2-(4(or 6)-Methyl-1,3-diaza-2-cyclohexene)-ethylenediamine	47.4[d]	.....	...	288–289 (dec.)	$C_{24}H_{30}N_{12}O_{14}$[f]	40.5	40.3	4.26	4.15	23.6	23.7

[a] Previously reported[2] m. p. 199–200°. [b,c,d] Both compounds in each pair obtained from one run. [e] All melting points uncorrected. [f] Dipicrates. Note: Cyclic areas present were crystallized out during purification of picrates.

(98.4), m. p. 204–205°[2,6]; 2,5-diaza-1-cyclopentanone (87), m. p. 131–132.5°[4] and 3-methyl-2,5-diaza-1-cyclopentanone (98), m. p. 121–122°.[7]

When 2-nitramino-1,3-diaza-2-cyclopentene in 0.3% sodium hydroxide solution was refluxed for twenty-eight hours, it was converted in large part to ethylenediamine.

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Experimental

4-Hydroxy-2,6-diaza-1-cyclohexanone.—2-Nitriamino-5-hydroxy-1,3-diaza-2-cyclohexene (19.71 g., 0.137 mole) was refluxed for fourteen hours in 150 cc. of water containing 2.0 cc. of benzylamine. The white residue left on removal of the water *in vacuo* was washed with ether and air dried. This crude product (m. p. 207.4–210.5°) was crystallized from 95% ethanol (3 times) to give crystals melting at 210–211°.

Anal. Calcd. for $C_4H_8N_2O_2$: C, 41.3; H, 6.94; N, 24.1. Found: C, 41.2; H, 7.12; N, 24.8.

A sample of 4-hydroxy-2,6-diaza-1-cyclohexanone on nitration in an acetic anhydride–nitric acid medium gave 2,6-dinitro-4-nitroxy-2,6-diaza-1-cyclohexanone[8] (m. p. 113–114.2°) which was identified by a mixed melting point determination with an authentic sample.

The other cyclic ureas described were prepared in a similar manner.

2-Substituted Amino-1,3-diaza-2-cycloalkenes.—The compounds reported in Table I were prepared by heating 2-nitramino-1,3-diaza-2-cycloalkenes in the presence of anhydrous amines as described[2] earlier.

Summary

A series of 2-substituted amino-1,3-diaza-2-cycloalkenes have been prepared by the reaction of anhydrous amines with 2-nitramino-1,3-diaza-2-cycloalkenes. The quantitative hydrolyses of 2-nitramino-1,3-diaza-2-cycloalkenes to cyclic ureas is described.

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