Reaction of Some 4-Chloro-5-nitropyrimidines with Sodium Azide. Oxadiazolo[3,4-*d*]pyrimidine 1-Oxides[1]

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The reaction of some 4-chloro-5-nitropyrimidines with sodium azide gave products which apparently were formed from both the intermediate 4-azido-5-nitropyrimidines and tetrazolo[1,5-*c*]pyrimidines. From 4-amino-6-chloro-5-nitropyrimidine (**1**), 7-amino[1.2.5]oxadiazolo[3,4-*d*]pyrimidine 1-oxide (**3**) and α-nitro-5-tetrazoleacetamidine (**15**) were obtained. Reaction of 4-chloro-2,6-diamino-5-nitropyrimidine (**2**) with sodium azide gave 5,7-diamino-8-nitrotetrazolo[1,5-*c*]pyrimidine hydrate (**13**), which was converted on heating, presumably *via* a 4-azidopyrimidine, into 5,7-diamino[1.2.5]oxadiazolo[3,4-*d*]pyrimidine 1-oxide (**4**). Other 4-chloro-5-nitropyrimidines also gave representatives of this new ring system.

Previous reports on the tetrazole–azidoazomethine equilibrium in pyrimidines showed that the presence of electron-withdrawing groups in a system tend to favor the azido tautomer.[2] The preparation and study of some representatives of the 8-nitrotetrazolo[1,5-*c*]-pyrimidine–4-azido-5-nitropyrimidine system was attempted by reaction of a series of 4-chloro-5-nitropyrimidines with NaN_3. In only one reaction was an azido or tetrazolo isomer observed. However, the involvement of both isomers as intermediates was indicated by the identification of the reaction products, which is the subject of this paper. (See Scheme I.)

Reaction of 4-amino-6-chloro-5-nitropyrimidine (**1**)[3] with NaN_3 in hot THF gave a product, which was homogeneous by thin layer chromatography and analyzed for $C_4H_3N_5O_2$ rather than for the azidopyrimidine **8** ($C_4H_3N_7O_2$) or its tetrazolo[1,5-*c*]pyrimidine isomer (**10**). The assigned empirical formula was confirmed by molecular weight determination. Hydrogenation of this product with a palladium catalyst gave 4,5,6-triaminopyrimidine, identified by comparison of the ultraviolet and infrared spectra of the reduction product with those of an authentic sample. Apparently the loss of nitrogen from the intermediate 4-azido-5-nitropyrimidine **8** gave a monovalent nitrogen derivative, which underwent intramolecular cyclization with the adjacent nitro group to give 7-amino[1.2.5]oxadiazolo-[3,4-*d*]pyrimidine 1-oxide (**3**). A similar type of reaction occurs both in the pyridine series to give pyrido[2.3]furazan oxides[4] and in the benzene series to give benzofurazan oxides.[5] The equilibration of the latter in solution between the 1- and 3-oxide structures presumably *via* a dinitrosobenzene intermediate has been demonstrated.[6] This type of equilibrium might also occur in the pyrimidine system to give a mixture of **3**, **5**, and **6**, the relative amounts of each isomer depending upon its thermodynamic stability. Evidence that the product was mainly one isomer was provided by the proton magnetic resonance (pmr) spectrum in deuterated DMSO over the temperature range 40–100° in which only one CH peak was observed. Since a dinitrosobenzene is thought to be only a transient intermediate in the benzofurazan oxide equilibrium, the existence of **5** as a major isomer seems unlikely. The assignment of structure **3** rather than **6** to this product is based on the following observations. The pmr spectrum showed the NH_2 protons as two broad peaks (τ 0.75, 1.55), which coalesced to give a single broad peak (τ 1.37) at about 100°, but again gave two peaks when the medium was cooled. These nonequivalent protons are attributed to hindered rotation of the amino group resulting from hydrogen bonding between the oxide oxygen and amino group protons as shown in **7**.[7] Although a resonance form (**11**) of **6** might result in nonequivalent NH_2 protons,[8] the extensive contribution of this *o*-quinone form with maximum separation of charge is remote. The imine **12** is another possible structure, but no spin–spin coupling between the 5-CH and 6-NH of **12** was observed in the pmr spectrum.[9] The removal of the oxide oxygen of **3** was attempted with triphenylphosphine,[10] but only an unidentified product of empirical formula $C_4H_4N_4O$ was obtained. Although it is recognized that other isomers are possible, the 1-oxide structure is also assigned to the [1.2.5]-oxadiazolo[3,4-*d*]pyrimidines described below.

Although the reaction of **1** with sodium azide in THF gave **3**, the same reactants in 2 *N* HCl gave a different product in 88% yield. This solid, analysis of which showed $C_4H_5N_7O_3$, might be assigned structure **8** or **10** hydrate. However, both compounds were eliminated from consideration, **8** by the absence of an azido absorption band in the infrared spectrum, and **10** by the stability of the product at 140°. At this temperature **10** probably would lose H_2O and N_2 to give **3** (see below). Thus, this product is assigned structure **14**, which apparently results from opening of the pyrimidine ring of the intermediate tetrazolo[1,5-*c*]pyrimidine **10**. Support for structure **14** was provided by the infrared spectrum, which showed a carbonyl band at 1700 cm^{-1}. A ring-opened product in which the formyl group is located on the tetrazole ring is also possible, but this product would be expected to deformylate readily under the conditions of the reaction.[11] The recy-

(1) This investigation was supported by the C. F. Kettering Foundation and by the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Contract No. PH43-64-51.

(2) C. Temple, Jr., W. C. Coburn, Jr., M. C. Thorpe, and J. A. Montgomery, *J. Org. Chem.*, **30**, 2395 (1965), and references therein.

(3) W. R. Boone, W. G. M. Jones, and G. R. Ramage, *J. Chem. Soc.*, 99 (1951).

(4) J. H. Boyer and W. Schoen, *J. Amer. Chem. Soc.*, **78**, 423 (1956); **75**, 5298 (1953).

(5) (a) F. B. Mallory, S. L. Manatt, and C. S. Wood, *ibid.*, **87**, 5433 (1965), and references therein; (b) A. J. Boulton, A. C. G. Gray, and A. R. Katritzky, *J. Chem. Soc.*, 5958 (1965), and references therein.

(6) A. J. Boulton, A. R. Katritzky, M. J. Sewell, and B. Wallis, *ibid.*, 914 (1967).

(7) Steric inhibition of rotation in **3** is unlikely since 7-benzyladenine shows only one NH_2 peak at τ 3.12 in DMSO.

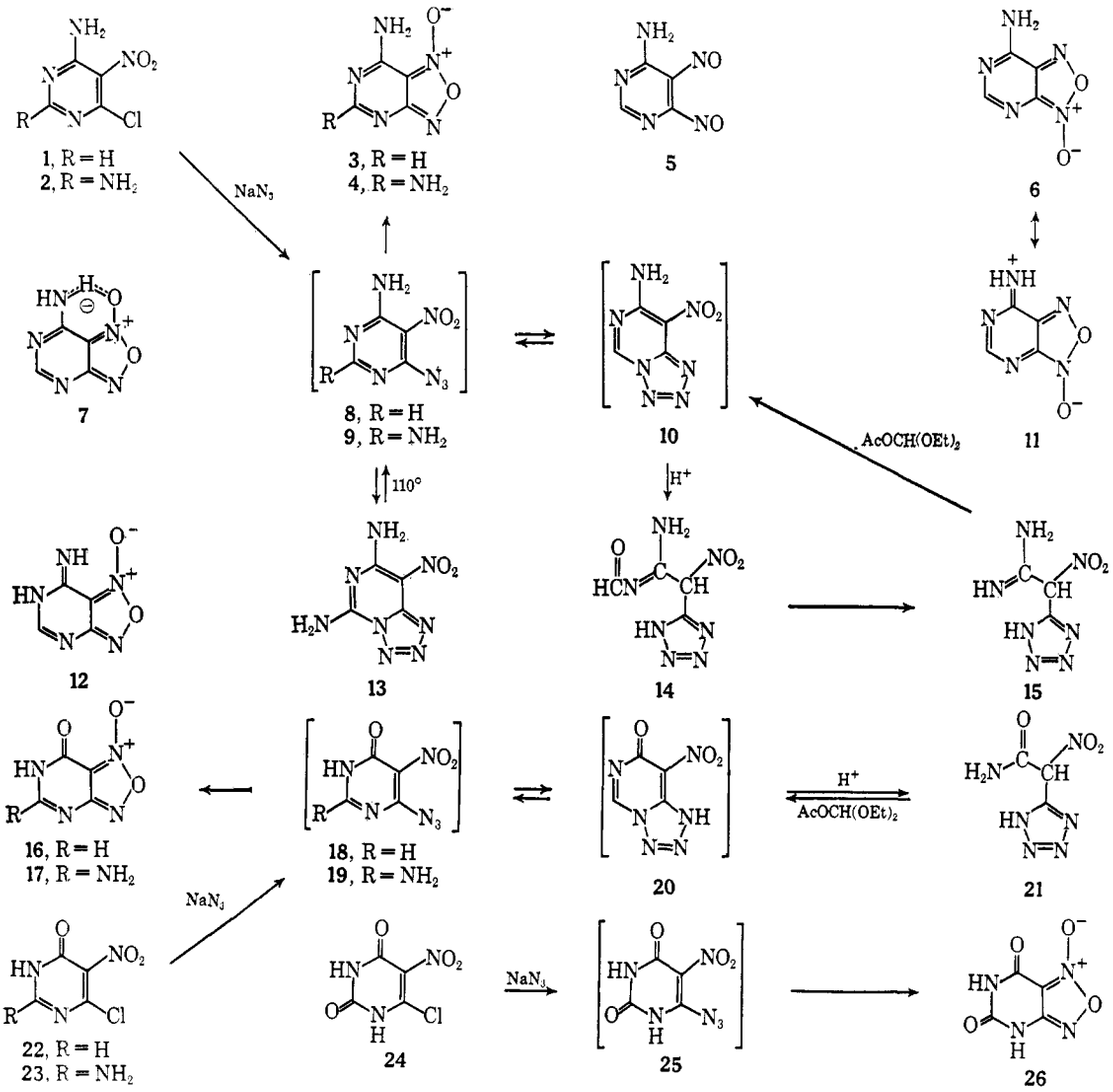
(8) (a) H. T. Miles, R. B. Bradley, and E. D. Becker, *Science*, **142**, 1569 (1963); (b) A. R. Katritzky and A. J. Waring, *J. Chem. Soc.*, 3046 (1963).

(9) Only one broad NH_2 peak at τ 1.92 is observed in the pmr spectrum of the related 7-aminotriazolo[4,5-*d*]pyrimidine in deuterated DMSO.

(10) F. B. Mallory and S. P. Varimbi, *J. Org. Chem.*, **28**, 1656 (1963).

(11) F. R. Benson in "Heterocyclic Compounds," Vol. 8, R. C. Elderfield, Ed., John Wiley and Sons, Inc., New York, N. Y., 1967, p 78 ff.

SCHEME I



clization of **14** to **10** was attempted in DMF at 145°, but these conditions resulted in deformylation of **14** to give α-nitro-5-tetrazoleacetamidine (**15**). The removal of the formyl group of **14** to give **15** was also effected with 11% methanolic HCl. Recently the reaction of 4-chloropyrimidines, not containing a 5-nitro group, with NaN_3 under acidic conditions was also reported to result in opening of the pyrimidine ring to give tetrazole derivatives similar to **15**.[12] Treatment of either **14** or **15** with diethoxymethyl acetate, a potent cyclization reagent,[13] at 100° gave **3** presumably *via* **10** and **8**, respectively. In the pmr spectra of **14** and **15** the proton of the $>CHNO_2$ moiety was not detected, apparently because of rapid exchange with the NH protons.

In contrast to the products obtained in the reactions described above, treatment of 4-chloro-2,6-diamino-5-nitropyrimidine[14] with NaN_3 gave the hydrate of the tetrazolo[1,5-*c*]pyrimidine **13**. The structure of **13** was confirmed by elemental analyses, the absence of an azido absorption band in its infrared spectrum, and the presence of an H_2O band in its pmr spectrum in deuterated DMSO. In this spectrum the NH_2 protons of one amino group are nonequivalent presumably because of hydrogen bonding with the nitro group. When the removal of the water of crystallization of **13** was attempted at 110°, this sample was quantitatively converted into 5,7-diamino[1.2.5]oxadiazolo[3,4-*d*]pyrimidine 1-oxide (**4**), presumably *via* the intermediate 4-azidopyrimidine **9**.

Both the nitrosation of 5-amino-4-hydrazinopyrimidine-6(1H)-one[15] and the reaction of **22**[15] with NaN_3 in THF gave good yields of [1.2.5]oxadiazolo-[3,4-*d*]pyrimidine-7(6H)-one 1-oxide (**16**). The pmr spectrum of either a deuterated DMSO or CF_3CO_2H solution of **16** showed only one CH peak. Gases were evolved when a solution of **16** in 1 *N* NaOH was acidified or when a solution of **16** in 1 *N* HCl was heated. In the latter medium the absence of absorption in the ultraviolet spectrum indicated that degradation of the ring system had occurred. Although **16** was the major product in the reaction of **22** with NaN_3 in 1 *N* HCl, an 8% yield of pure α-nitro-5-tetrazoleacetamide (**21**) was also obtained. Reaction of **21** with diethoxymethyl acetate gave a complex mixture, which was shown to

(12) I. Y. Postovskii and N. B. Smirnova, *Dokl. Akad. Nauk, SSSR*, **170**, 604 (1966).

(13) C. Temple, Jr., C. L. Kussner, and J. A. Montgomery, *J. Org. Chem.*, **30**, 3601 (1965).

(14) D. E. O'Brien, C. C. Cheng, and W. Pfleiderer, *J. Med. Chem.*, **9**, 573 (1966).

(15) C. Temple, Jr., R. L. McKee, and J. A Montgomery, *J. Org. Chem.*, **30**, 829 (1965).

contain **16** by thin layer chromatography. Finally the reaction of the 4-chloro-5-nitropyrimidines **23**[16] and **24**,[17] respectively, with NaN_3 gave products that gave the correct analyses for the [1.2.5]oxadiazolo[3,4-*d*]-pyrimidine 1-oxides **17** and **26** apparently formed *via* the corresponding azidopyrimidine intermediates **19** and **25**.

Experimental Section

The ultraviolet spectra were determined with a Cary Model 14 recording spectrophotometer. The infrared spectra were determined in pressed potassium bromide disks with a Perkin-Elmer Model 521 spectrophotometer. The pmr spectra were determined with a Varian A-60 or A-60A spectrometer at a probe temperature of about 40° using tetramethylsilane as an internal reference. The relative peak areas are given to the nearest whole number. The melting points were determined on a Kofler Heizbank apparatus and are corrected.

7-Amino[1.2.5]oxadiazolo[3,4-*d*]pyrimidine 1-Oxide (3). A.—A solution of **1**[3] (1.0 g) in the THF (50 ml) containing NaN_3 (0.5 g) was refluxed for 8 hr. The residue was removed by filtration and washed with hot THF (90 ml). The combined filtrate and wash was diluted with petroleum ether (bp 85–105°) (350 ml) to give the product in two crops to yield 0.71 g (81%). A portion of this solid was recrystallized from a mixture of THF–petroleum ether (bp 85–105°) to give the analytical sample, which exploded at 200–220°: λ_{max} in mμ ($\epsilon \times 10^{-3}$),[18a] pH 7, 270 (sh) (2.82), 290 (3.80), 297 (sh) (3.69), 365 (5.10); $\bar{\nu}_{max}$ in cm^{-1}, 3430, 3200, 1680 (NH) and 1615, 1550, 1510 (C=C, C=N); pmr (10% DMSO-d_6 w/v), τ 1.82 (1, CH), 1.55, 0.75 (1, 1, NH), and (10% CF_3COOH w/v), 1.37 (CH).

Anal. Calcd for $C_4H_3N_5O_2$: C, 31.38; H, 1.96; N, 45.75; O, 20.90; mol wt, 153. Found: C, 31.28; H, 1.95; N, 45.58; O, 20.71; mol wt, 156.

B.—A mixture of **15** (100 mg) and diethoxymethyl acetate (5 ml) was heated at 100° for 5 hr. The resulting solution was evaporated to dryness *in vacuo*, and the residue was treated as described above to give 82 mg (92%) of **3**. Also, treatment of **14** (500 mg) with diethoxymethyl acetate (10 ml) at 100° for 5 hr gave a quantitative yield of crude **3**.

5,7-Diamino[1.2.5]oxadiazolo[3,4-*d*]pyrimidine 1-Oxide (4).—The hydrate of **13** (200 mg) was dried *in vacuo* over P_2O_5 at 110° for 18 hr to yield 157 mg (100%): mp >264°; λ_{max} in mμ ($\epsilon \times 10^{-3}$),[18b] pH 7, 289 (12.0), 365 (2.64); $\bar{\nu}_{max}$ in cm^{-1}, 3425, 3320, 3115, 1645 (NH) and 1600, 1580, 1560, 1520 (C=C, C=N); pmr (2.5% DMSO-d_6 w/v), τ 1.87 (broad), 2.97 (1, 1, NH_2).

Anal. Calcd for $C_4H_4N_6O_2$: C, 28.58; H, 2.40; N, 49.99. Found: C, 28.80; H, 2.60; N, 49.80.

5,7-Diamino-8-nitrotetrazolo[1,5-*c*]pyrimidine Hydrate (13).—A mixture of **2**[14] (1.0 g) and NaN_3 (0.50 g) in 1:10 water–THF (110 ml) was stirred at room temperature for 18 hr. The gummy solid was collected by filtration, washed with water (20 ml), and then stirred in 1 *N* HCl (20 ml) for 2 hr. The resulting solid was collected by filtration, washed with water, and dried *in vacuo* over P_2O_5 to give the hydrate of **13** in a yield of 0.65 g (58%). This material exploded at about 199°: λ_{max} in mμ ($\epsilon \times 10^{-3}$),[18c] pH 7, 235 (16.6), 278 (6.10), 354 (18.4); $\bar{\nu}_{max}$ in cm^{-1}, 3505, 3435, 3370, 3140, 1680, 1630 (NH), 1605, 1565 (C=C, C=N), and 1080, 1010 (tetrazole ring);[19] pmr (10% DMSO-d_6 w/v), 6.63 (1, H_2O) and 1.10, 1.00, 0.85 (2, NH).[20]

Anal. Calcd for $C_4H_4N_8O_2 \cdot H_2O$: C, 22.43; H, 2.81; N, 52.32. Found: C, 22.70; H, 3.24; N, 52.39.

N-Formyl-α-nitro-5-tetrazoleamidine (14).—Solid **1**[3] (1.0 g) was added to a cold solution of sodium azide (1.0 g) in 2 *N* HCl (24 ml). After stirring at room temperature for 1.5 hr the mixture was diluted with water (25 ml), and the residue was collected by filtration. The solid was dissolved in warm N,N-dimethylformamide (150 ml), and the solution was diluted with warm (60°) water (450 ml). After cooling the solid was collected by filtration and dried *in vacuo* over P_2O_5 at 140° for 8 hr to yield 980 mg (86%): mp >264°; λ_{max} in mμ ($\epsilon \times 10^{-3}$),[18c] pH 7, 346 (18.0); $\bar{\nu}_{max}$ in cm^{-1}, 3320, 3215 (NH), 1700 (CO), 1645 (NH), 1545 (C=N), and 1100, 1055, 1030, 1000 (tetrazole ring);[19] pmr (10% DMSO-d_6 w/v), τ 1.18 (1, CHO) and −0.38, −2.00 (4, CH, NH).

Anal. Calcd for $C_4H_5N_7O_3$: C, 24.14; H, 2.51; N, 49.25. Found: C, 24.48; H, 2.52; N, 49.18.

α-Nitro-5-tetrazoleacetamidine (15). A.—A mixture of **1**[3] (1.0 g) and sodium azide (0.44 g) in dioxane (60 ml) and water (10 ml) was refluxed for 4 hr and evaporated to dryness *in vacuo*. The resulting residue was suspended in DMF (34 ml) and heated at 145° for 2 hr. After removing the residue by filtration, the filtrate was evaporated to dryness *in vacuo*. The resulting solid was recrystallized from H_2O and dried *in vacuo* over P_2O_5 at 110° to yield 0.77 g (79%): mp >264°; λ_{max} in mμ ($\epsilon \times 10^{-3}$),[18c] pH 7, 320 (14.5); $\bar{\nu}_{max}$ in cm^{-1}, 3425, 3340, 3200, 3160, 1640 (NH), 1560, 1495 (C=N), 1525, 1330 (NO_2), and 1095, 1080, 1040, 1020 (tetrazole ring);[19] pmr (10% DMSO-d_6 w/v), τ 1.30 (4, CH, NH), −5.87 (1, NH).

Anal. Calcd for $C_3H_5N_7O_2$: C, 21.05; H. 2.94; N, 57.29. Found: C, 20.68; H, 2.76; N, 57.45.

B.—A solution of **14** (115 mg) in DMF (5 ml) was heated at 145° for 2 hr and treated as described above to give 28 mg of **15**. Also treatment of **14** (500 mg) with 11% methanolic hydrogen chloride for 18 hr at room temperature gave 448 mg of crude **15**.

[1.2.5]Oxadiazolo[3,4-*d*]pyrimidin-7(6H)-one 1-Oxide (16). A.—To a suspension of 4-hydrazino-5-nitropyrimidin-6(1H)-one[15] (1.0 g) in 0.5 *N* hydrochloric acid (20 ml), cooled in an ice bath, was added with stirring a solution of sodium nitrite (0.70 g) in water (5 ml). Ethanol (5 ml) was added to decrease the foaming, which subsided within 30 min. Then the mixture was stirred at room temperature for 1.5 hr and evaporated to dryness *in vacuo*. The resulting residue was recrystallized from a mixture of THF–petroleum ether (bp 85–105°) to yield 0.67 g (74%): mp 206° dec with premelting from 199°; λ_{max} in mμ ($\epsilon \times 10^{-3}$),[18a] pH 7, 255 (sh) (3.16), 282 (4.35), 359 (4.18); $\bar{\nu}_{max}$ in cm^{-1}, 3200 (broad), 3130 (NH), 1730 (CO), and 1645, 1600, 1520, 1495 (C=C, C=N); pmr (10% DMSO-d_6 w/v), τ 1.92 (1, CH), −2.43 (1, NH), and (<10% CF_3COOH w/v), τ 1.45 (CH).

Anal. Calcd for $C_4H_2N_4O_3$: C, 31.18; H, 1.30; N, 36.35; O, 31.15; mol wt, 154. Found: C, 31.03; H, 1.61; N, 36.66; O, 30.90; mol wt, 160.

B.—A mixture of **22**[15] (2.0 g) and NaN_3 (1.0 g) in THF was refluxed for 8 hr, and the residue was removed by filtration. The filtrate was evaporated to dryness, and the resulting solid was recrystallized as described in A to yield 1.2 g (69%), mp 205–206° dec.

C.—Treatment of **15** (50 mg) with diethoxymethyl acetate (5 ml) at 100° for 5 hr gave a complex mixture, which was shown to contain **16** by thin layer chromatography [$CHCl_3$:MeOH (9:1)].

5-Amino[1.2.5]oxadiazolo[3,4-*d*]pyrimidin-7(6H)-one 1-Oxide (17).—A mixture of **23**[16] (3.4 g) and NaN_3 (1.5 g) in 20% aqueous dioxane (160 ml) was refluxed for 4 hr and evaporated to dryness *in vacuo*. The resulting residue was washed with water (30 ml), and then stirred in 2 *N* HCl (25 ml) for 1 hr. The solid was collected by filtration and dried *in vacuo* over P_2O_5 for 4 hr at 78° to yield 1.3 g (43%): mp >264°; $\bar{\nu}_{max}$ in cm^{-1}, 3350, 3285, 3170 (NH), 1725 (CO), 1700 (NH_2), and 1630, 1590, 1550 (C=C, C=N).

Anal. Calcd for $C_4H_3N_5O_3$: C, 28.41; H, 1.79; N, 41.42. Found: C, 28.30; H, 2.05; N, 41.41.

α-Nitro-5-tetrazoleacetamide (21).—Solid **22**[15] (2.0 g) was added slowly with stirring to a solution of NaN_3 (2.0 g) in 1 *N* HCl at 10°. After stirring the mixture for 1.5 hr at room temperature, 0.35 g of **22** wa recovered by filtration. When the filtrate was refrigerated for 18 hr, a precipitate (0.34 g) was obtained, which was shown to be a mixture of **16** and **21** by thin layer chromatography [BuOH:AcOH:H_2O (5:2:3)]. On standing the filtrate then deposited pure **21** in a yield of 0.15 g (8%). This material melted and exploded at 192–195°: λ_{max} in mμ ($\epsilon \times 10^{-3}$),[18d] pH 7, 295 (11.1); $\bar{\nu}_{max}$ in cm^{-1}, 3410, 3300, 3250 (NH), 1620 (CO), 1580 (C=N), 1530, 1340 (NO_2), and 1100, 1060, 1020, 1000 (tetrazole ring).[19]

Anal. Calcd for $C_3H_4N_6O_3$: C, 20.94; H, 2.34; N, 48.84. Found: C, 20.69; H, 2.73; N, 48.59.

(16) A. Stuart, D. W. West, and H. C. S. Wood, *J. Chem. Soc.*, 4769 (1964).

(17) R. M. Cresswell and H. C. S. Wood, *ibid.*, 4768 (1960).

(18) Each solution contains 10% of the dissolving solvent and 90% of the appropriate aqueous solvent: (a) CH_3OH; (b) DMF; (c) 8% methanolic DMSO; (d) H_2O.

(19) E. Lieber, D. Levering, and L. Patterson, *Anal. Chem.*, **23**, 1594 (1951).

(20) Three peaks are observed apparently because the protons of one NH_2 group are nonequivalent.

From the filtrate 0.63 g of crude **16** was obtained.

[1.2.5]Oxadiazolo[3,4-*d*]pyrimidine-5(4H),7(6H)-dione 1-Oxide (26).—A solution of **24**[17] (2.0 g) in THF (100 ml) containing NaN_3 (1.0 g) was stirred at room temperature for 3 hr. The residue was collected by filtration, washed with water (10 ml), and dissolved in 2 *N* HCl (25 ml). After 3 hr this solution was evaporated to dryness, and the solid was recrystallized from a mixture of THF–petroleum ether (bp 85–105°) and dried *in vacuo* over P_2O_5 at 78° to yield 510 mg (29%). This sample melted with decomposition at about 260°: λ_{max} in mμ ($\epsilon \times 10^{-3}$),[18d] pH 7, 272 (9.15), 346 (3.65); $\bar{\nu}_{max}$ in cm^{-1}, 3300, 3190, 3105 (NH), 1740, 1715 (CO), and 1640, 1600, 1530 (C=C, C=N).

Anal. Calcd for $C_4H_2N_4O_4$: C, 28.24; H, 1.18; N, 32.94. Found: C, 28.11; H, 1.37; N, 32.92.

Registry No.—Sodium azide, 12136-89-9; **3**, 16206-18-1; **4**, 16206-19-2; **13**, 16206-20-5; **14**, 16206-21-6; **15**, 16214-85-0; **16**, 16206-22-7; **17**, 16206-23-8; **21**, 16206-24-9; **26**, 16206-25-0.

Acknowledgments.—The authors are indebted to Dr. W. J. Barrett and the members of the Analytical and Physical Chemistry Division of Southern Research Institute for the spectral and microanalytical determinations. Some of the analyses reported were performed by the Galbraith Microanalytical Laboratories, Knoxville, Tenn.

Oxidations with Lead Tetraacetate. II. Δ^3-1,3,4-Oxadiazolines from Ketocarbohydrazones and a Δ^3-1,3,4-Thiadiazoline from Acetone Thiocarbohydrazone[1]

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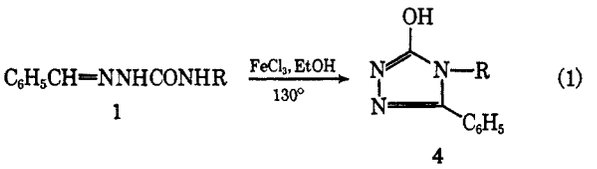
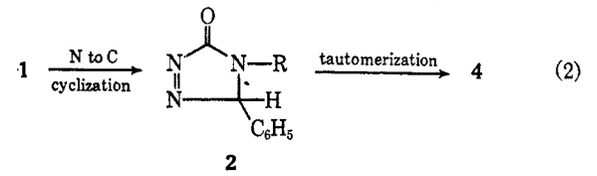
Acetone thiocarbohydrazone is cyclized by lead tetraacetate (LTA), in low yield, to 2-isopropylidenehydrazono-5,5-dimethyl-Δ^3-1,3,4-thiadiazoline (**10**). Spectra of **10** led to reassignment of the structures of the products obtained from oxidation of ketocarbohydrazones with LTA. Those products, which were earlier thought to be 4-ketimino-Δ^1-1,2,4-triazolin-3-ones (**7**), are shown to be 2-alkylidene-hydrazono-Δ^3-1,3,4-oxadiazolines (**8**). Spectra and some reactions of **8** are reported. Carbohydrazones of dialkyl ketones are shown to be much more reactive toward LTA than those of diaryl ketones. As a consequence the mixed carbohydrazone from acetone and benzophenone is cyclized primarily to the isopropylidene carbon rather than to the benzhydrylidene carbon. Diphenylmethylene diacetate is a by-product of oxidation of benzophenone carbohydrazone with LTA.

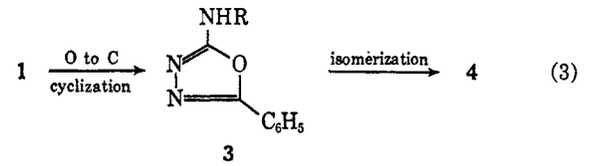
Oxidation of benzaldehyde semicarbazones with alcoholic $FeCl_3$ leads to cyclized products, *i.e.*, the 1,2,4-triazoles of eq 1.[3–6] Two ways in which the process can be formulated are shown in eq 2 and 3. Although



(1)

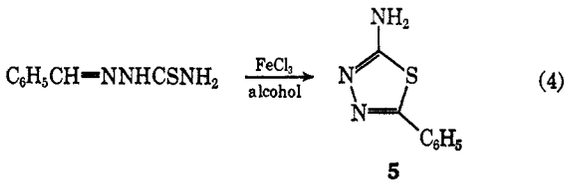


(2)



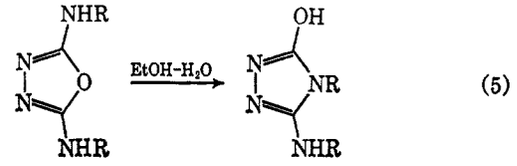
(3)

triazolinones (**2**) have not been isolated we do not know of any evidence which rules out the intermediacy of such compounds in the reaction. On the other hand, there is precedent for formation of products like **3**. A 1,3,4-thiadiazole (**5**) has been isolated from the reaction of benzaldehyde thiosemicarbazone with $FeCl_3$[7] (eq 4). Moreover, some oxadiazoles[8,9] are known to



(4)

isomerize to triazoles (eq 5) under conditions like those used in oxidation with $FeCl_3$.[9] It is possible then, that, where a five-membered ring can be formed



(5)

to either nitrogen or oxygen (eq 2 and 3), cyclization to oxygen is kinetically favored.

Oxidative cyclization of symmetrical ketocarbohydrazones (**6**) could, by analogy, occur in either sense

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(8) The oxadiazoles were not prepared by oxidative cyclization but by a dehydration process.[9]

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