terial was removed by filtration and the filtrate was distilled, leaving a glass.

9-(2′,3′-O-Isopropylidene-D-mannofuranosyl)adenine (III).—The glass (II) was dissolved in 150 ml. of 70% acetic acid at 50° and permitted to stand at this temperature for 2.5 hr., after which the solution was evaporated to a syrup and absolute ethanol was added and removed three times. Addition and removal of toluene gave a glass which was treated with 20 ml. of 1 *N* methanolic sodium methoxide in 100 ml. of absolute methanol, refluxed 50 min., and neutralized with glacial acetic acid. The solution was filtered and the solvent was removed *in vacuo* (45°). The residue was partitioned between 130 ml. each of water and chloroform, and the chloroform layer was further extracted five times with 50-ml. portions of water. The aqueous extracts were combined and the water was removed under reduced pressure (45°). During this process crystallization took place. The product was removed by filtration and recrystallized from water: yield 1.96 g. (29%). Two additional crops brought the total yield to 2.56 g. (38%). The product softened between 240 and 246°, m.p. 249–250°, $[\alpha]^{21}D$ +32.5° (*c* 1.26, 0.1 *N* HCl) after 3 min. No change was observed after 1 hr. Paper chromatography with 5% aqueous disodium hydrogen phosphate[14] (without the organic phase) on Whatman No. 1 paper gave one spot, R_{Ad} 1.41 and 1.53 in *n*-butyl alcohol–acetic acid–water (4:1:5 v./v.).

Ultraviolet and infrared spectra showed the following: $\lambda_{max}^{H_2O}$ 260 mμ (ε 14,200); λ_{max}^{KBr} 2.9, 3.0 (OH, NH), 6.0, 6.12, 6.3, 6.4 (NH and purine ring), 7.28 (CH_3), 8.95, 9.2, 9.4, 9.5 (C–O–C, C–O–H), 11.65 (isopropylidene) μ.

Anal. Calcd. for $C_{14}H_{19}N_5O_5$: C, 49.85; H, 5.68; N, 20.76. Found: C, 49.91; H, 5.63; N, 20.88.

The nucleoside was treated with excess periodate and formaldehyde was determined by the dimedone test[15] (0.81 mole HCHO/mole of nucleoside).

9-D-Mannofuranosyladenine (IV).—To 118 ml. of 25% acetic acid solution was added 2.36 g. (7 mmoles) of III. The mixture was stirred at 100° for 3.5 hr., cooled quickly to room temperature, and allowed to stand an additional 0.5 hr. The solvent was removed *in vacuo* (45°) to leave a white residue. This material was recrystallized from ethanol–water to give beautiful tiny rods: 1.09 g. (52%); m.p. 237–237.5°; $[\alpha]^{21}D$ +74.8° (*c* 3.05, 1 *N* HCl); R_{Ad} 1.53 in 5% aqueous disodium hydrogen phosphate,[14] 0.15 in water-saturated butanol, and 0.49 in *n*-butyl alcohol–acetic acid–water (4:1:5 v./v.).

Ultraviolet and infrared spectra showed the following: $\lambda_{max}^{H_2O}$ 259 mμ (ε 14,800); λ_{max}^{KBr} 2.95 (OH, NH), 6.2, 6.3, 6.7 (NH and purine ring), 9.1, 9.2, 9.35, 9.6 (C–O–C, C–O–H) μ.

Anal. Calcd. for $C_{11}H_{15}N_5O_5$: C, 44.45; H, 5.09; N, 23.56. Found: C, 44.36; H, 5.12; N, 23.33.

A formaldehyde determination with the dimedone reagent,[15] after treatment with excess periodate, yielded 0.98 mole of HCHO/mole of nucleoside.

(14) C. E. Carter, *J. Am. Chem. Soc.*, **72**, 1466 (1950).
(15) J. R. Dyer, *Methods Biochem. Anal.*, **3**, 111 (1956).

Free-Radical Chemistry of Peptide Bonds. II. Conversion of Lactams to Imides

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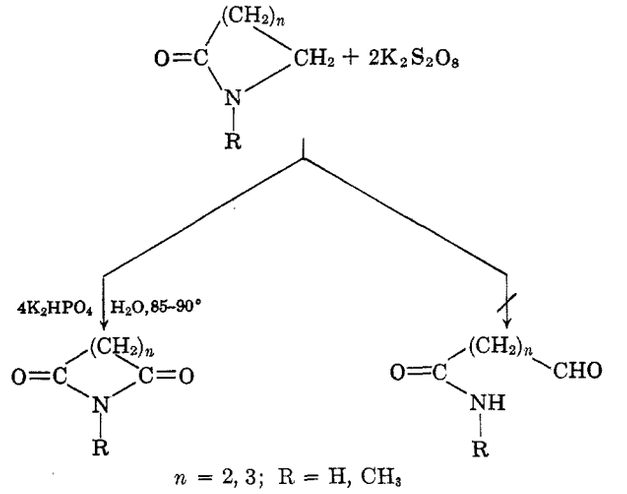
Received July 13, 1965

Recently, N-dealkylation of N-alkyl- and N,N-dialkylamides by persulfate was reported.[2,3] These dealkylations were believed to proceed *via* free-radical attack of the methylene adjacent to the amide nitrogen. It appeared that this dealkylation might provide a novel method for opening lactam rings to produce the corresponding ω-aldehydoamides; however, reactions of five- and six-membered lactams with persulfate yielded imides as the primary product (23–61%).



n = 2, 3; R = H, CH_3

In contrast, caprolactam with aqueous persulfate gave a low molecular weight polymer in 76% yield as the only isolable product. The 2,5-diketopiperazines, 2,5-piperazinedione and 1,4-dimethyl-2,5-piperazinedione (which contain two amide groups in the ring), were fairly stable to persulfate attack and were recovered from the reaction mixture in 89 and 82% yield, respectively. Low yields of carbon dioxide and ammonia were also found, and some formaldehyde (8%) was liberated from 1,4-dimethyl-2,5-piperazinedione. Products and yields from these reactions are listed in Table I.

TABLE I
PERSULFATE OXIDATION PRODUCTS

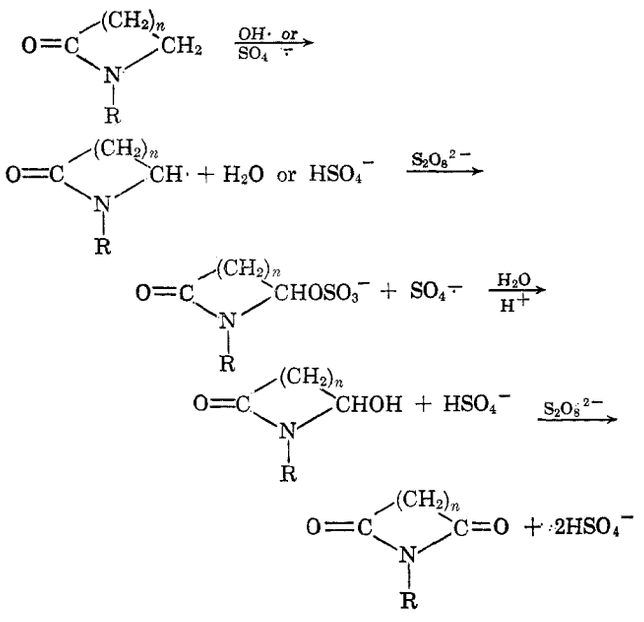
Reactant	Products	% yield
2-Pyrrolidinone	Succinimide	61
	Carbon dioxide	2
1-Methyl-2-pyrrolidinone	N-Methylsuccinimide	35
2-Piperidone	Glutarimide	23
1-Methyl-3-piperidone	N-Methylglutarimide	47
Caprolactam	Polymer	76
	Carbon dioxide	3
2,5-Piperazinedione[a]	Carbon dioxide	15
	Ammonia	11
1,4-Dimethyl-2,5-piperazinedione[b]	Carbon dioxide	3
	Ammonia	3
	Formaldehyde	8

[a] 89% recovery of starting material. [b] 82% recovery of starting material.

In the absence of persulfate, recoveries of known amounts of imide from the reaction mixture were 70% or better. Control experiments with imides in the presence of persulfate showed that attack by persulfate on imide lowered recoveries of imide from solution to some extent and formed water-soluble tars that could not be purified. Gas–liquid partition chromatography of crude oils from the action of persulfate on the five- and six-membered lactams showed imides to be greater than 95% of the volatile reaction products present.

(1) A laboratory of the Western Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.
(2) H. L. Needles and R. E. Whitfield, Abstracts, 147th National Meeting of the American Chemical Society, Philadelphia, Pa., April 1964, p. 50N.
(3) H. L. Needles and R. E. Whitfield, *J. Org. Chem.*, **29**, 3632 (1964).

Free-radical attack of the methylene adjacent to the amide nitrogen has been observed before.[2-6] The exothermicity, high reaction rate, oxygen inhibition, and reaction products of these oxidations are consistent with a chain process similar to that proposed[3] for the dealkylation of amides. In the five- and six-membered lactams oxidation to the imide is apparently favored over ring opening.



It is of interest to note that N-methyl was not attacked in the N-methyl lactams studied and that only attack of methylene α to the amide nitrogen was observed. Limited demethylation of 1,4-dimethyl-2,5-piperazinedione was observed, however.

Carbon dioxide and ammonia from oxidation of the 2,5-piperazinediones probably results from initial cleavage of the ring followed by further oxidation of the ring scission products. Methylene groups in the diketopiperazines are apparently less susceptible to attack owing to the presence of a carbonyl adjacent to the methylene.

Experimental Section[7]

Infrared spectra were determined on a Perkin-Elmer Infracord 137 spectrophotometer. Gas–liquid partition chromatograms were obtained on an Aerograph Hy-Fl chromatograph, Model A-600-B, using a 6-ft. column packed with 10% neopentyl glycol succinate on firebrick at 200°. Analyses for ammonia nitrogen were performed by H. M. Wright of this laboratory.

Reactions with Potassium Persulfate.—The procedure was similar to that for the dealkylation of amides[3] with the following modifications. Since 2 moles of persulfate/mole of lactam was necessary for complete reaction, 0.05 mole of lactam was used rather than 0.10 mole. In the oxidation of 2-piperidone, 400 ml. of water was used. Each imide was characterized by comparing its boiling point or melting point and infrared spectrum with those of an authentic sample.[8] Glutarimide was purified by recrystallization from water.

Each reaction was performed two or more times, and the results were reproducible within a few per cent. In control experiments recoveries of known quantities of imides were 70% or greater by the methods of isolation used. To determine the effect of persulfate on imide, 0.05 mole of imide was treated under the above conditions. In each case the reaction formed water-soluble, intractable tars and yielded less imide than did control mixtures without persulfate. The product yields based on starting material are listed in Table I.

(4) W. Walter, M. Steffen, and K. Heyns, *Chem. Ber.*, **94**, 2462 (1961).

(5) C. H. Bamford and E. F. T. White, *J. Chem. Soc.*, 1860 (1959); 4490 (1960).

(6) K. Schwetlick, *Angew. Chem.*, **72**, 208 (1960).

(7) Reference to a company or product name does not imply approval or recommendation of the product by the U. S. Department of Agriculture to the exclusion of others that may be suitable.

(8) Imides were prepared by the method of S. S. G. Sircar, *J. Chem. Soc.*, 600 (1927).

3-Cyano-4-aminopyrazolo[3,4-*d*]pyrimidine. An Azalog of the Aglycone of Toyocamycin[1]

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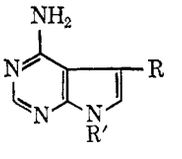
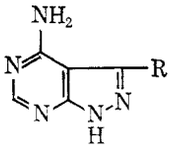
Received May 10, 1965

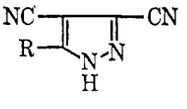
We recently described[2] the synthesis of 3-cyano-4-aminopyrrolo[2,3-*d*]pyrimidine (**1**) and 4-aminopyrrolo-[2,3-*d*]pyrimidine (**2**), the aglycones of the antibiotics Toyocamycin (**3**) and Tubercidin (**4**), starting from tetracyanoethylene as the aliphatic precursor. In view of the observation[3] that the unusual toxicity of **4** (and thus presumably of **3** also) is related to its action as a nucleic acid antagonist, the preparation of a Toyocamycin analog derived from 4-aminopyrazolo-[3,4-*d*]pyrimidine[4] appeared particularly worthwhile. We wish to describe in this Note the preparation of 3-cyano-4-aminopyrazolo[3,4-*d*]pyrimidine (**5**), the desired "azalog" of the aglycone **1**.



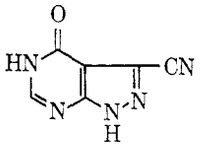
1, R = CN; R′ = H
2, R = R′ = H
3, R = CN; R′ = *d*-ribose
4, R = H; R′ = β-*d*-ribose



5, R = CN
6, R = COOH
7, R = H



8, R = NH_2
9, R = N=$CHOC_2H_5$
10, R = NHCHO



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Condensation of tetracyanoethylene with semicarbazide hydrochloride, followed by hydrolysis, has been shown to give 5-aminopyrazole-3,4-dicarbonitrile (**8**) in good yield.[5] Since this intermediate contains the *o*-aminonitrile grouping requisite for conversion to a condensed 4-aminopyrimidine system,[6] it appeared to

(1) This work was supported by a grant (CA-02551) to Princeton University from the National Cancer Institute, National Institutes of Health, U. S. Public Health Service.

(2) E. C. Taylor and R. W. Hendess, *J. Am. Chem. Soc.*, **87**, 1995 (1965).

(3) G. Acs, E. Reich, and M. Mori, *Proc. Natl. Acad. Sci. U. S.*, **52**, 493 (1964).

(4) For a discussion of the biological activity of this purine antagonist, see E. Y. Sutcliffe, K. Y. Zee-Cheng, C. C. Cheng, and R. K. Robins, *J. Med. Pharm. Chem.*, **5**, 588 (1962).

(5) C. L. Dickinson, J. K. Williams, and B. C. McCusick, *J. Org. Chem.*, **29**, 1915 (1964).

(6) For a discussion and leading references, see ref. 2.