favorable results were obtained during catalytic desulfuration of the *S*-benzyl derivative (IIIb).

EXPERIMENTAL[10]

6,8-Dihydroxypurine (II). A solution of 2-thiouric acid (I) (4 g.) in 2.5% sodium hydroxide (80 ml.) was refluxed with Raney nickel (4 g.) [prepared according to *Org. Syntheses*, **Coll. Vol. III**, 176 (1955)] during 1.5 hr. The catalyst was removed by filtration and the filtrate acidified with dilute sulfuric acid. Overnight, 2.1 g. (64%) of colorless. needles precipitated. The purity of this material was tested by its absorption spectrum and R_F value (see Table I).

TABLE I

PHYSICAL PROPERTIES OF PURINES

Compound	λ_{max} at *p*H 8, mμ	R_F	Fluorescence
6,8-Dihydroxypurine (II)	263	0.28	Violet
8-Hydroxypurine-6-thione (III)	309–310	0.42	Blue
8-Hydroxy-6-methylmercaptopurine(IIIa)	301–302	0.73	Whitish
8-Hydroxy-6-benzylmercaptopurine(IIIb)	301–302	0.81	Blue
8-Hydroxypurine (IV)	280	0.55	Dark blue

8-Hydroxypurine-6-thione (III). A mixture of 6,8-dihydroxypurine (3 g.) and phosphorus pentasulfide (10 g.) in dry pyridine (100 ml.) was refluxed for 6 hr. under vigorous stirring. The solvent was removed under reduced pressure and the residue decomposed with water (30 ml.) at 80° during 30 min. The solution was freed from a small amount of sulfur by filtration and kept overnight in a refrigerator. Recrystallization from water and decolorization with charcoal gave 2 g. (74%) of white needles, which decompose above 300°. The properties of this material were in agreement with those of an authentic sample.[11]

Desulfuration of 8-hydroxypurine-6-thione (III). A solution of III (2 g.) in concd. ammonia (30 ml.) was refluxed with Raney nickel (2 g.) for 2.5 hr. under vigorous stirring. The catalyst was filtered off and washed with boiling water. The collected filtrates were concentrated *in vacuo* to a small volume. Overnight, 0.5 g. of white crystals precipitated (= 30%). 8-Hydroxypurine crystallizes from water in short rods of m.p. 305–307°. The material showed properties identical with those of an authentic sample[5] (see Table I).

8-Hydroxy-6-methylmercaptopurine (IIIa). A solution of II (1 g.) and methyl iodide (0.5 ml.) in pyridine (25 ml.) was kept at room temperature for 2 hr. and then overnight in a refrigerator. The pyridine hydriodide, which had crystallized, was filtered off, the solvent removed *in vacuo*, and the residue recrystallized from water: short needles, 450 mg. (42%), dec. p. > 300°.

Anal. Calcd. for $C_6H_6N_4OS.H_2O$: N, 28.0. Found: N, 27.7.

6-Benzylmercapto-8-hydroxypurine (IIIb). To a solution of 8-hydroxypurine-6-thione (III) (1 g.) in 10% sodium hydroxide (2.5 ml.), kept at room temperature, was added dropwise and under vigorous stirring benzyl chloride (0.8 ml.). During 15 min. a white precipitate had formed, which crystallized from dioxane in long, colorless rods of m.p. 295°; yield 1.2 g. (78%). IIIb is much less alkali-sensitive than its methyl analog (IIIa).

Anal. Calcd. for $C_{12}H_{10}N_4OS$: C, 55.8; H, 3.9. Found: C, 55.8; H, 3.9.

Absorption spectra were measured in 0.01*M* phosphate buffer of *p*H 8.0. R_F values were determined on Whatman paper No. 1 by the descending method, using the following solvent: 95% ethanol, 85 ml.; glacial acetic acid, 5 ml.; water, 10 ml. Spots were detected by their fluorescence under a Mineralight ultraviolet lamp, emitting light of about 255 mμ.

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(10) All melting points are uncorrected.

(11) G. B. Elion, I. Goodman, W. Lange, and G. H. Hitchings, *J. Am. Chem. Soc.*, **81**, 1898 (1959).

The Sulfonation of 1,3-Dinitronaphthalene

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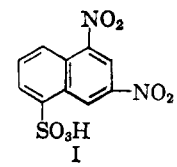
The sulfonation of 1,3-dinitronaphthalene was studied as part of a program on the chemistry of 2-nitronaphthalene derivatives. Graebe[1] briefly mentions the reaction of the 1,3-dinitro isomer with dilute oleum but the product was not characterized.

In the present work, it was found that an excess of 100% sulfuric acid at room temperature will sulfonate the dinitronaphthalene to the 5-monosulfonic acid (I). This orientation was proved by reaction of the sulfonic acid with phosphorus pentachloride to form the known 1,3,5-trichloronaphthalene. Identity was shown by comparison of the infrared spectra of the phosphorus pentachloride reaction product with a known sample of the trichloronaphthalene.



I

The sulfonyl chloride and sulfonamide were prepared as derivatives. The dinitro acid was also reduced to the corresponding diaminosulfonic acid.

The sulfonic acid group therefore goes into the 5-position in 1,3-dinitronaphthalene, in distinction to the 8-position which is entered on nitration. This orientation is consistent with the usual rules of substitution in naphthalene chemistry, and with the Armstrong-Wynne rules.[2]

Dannerth has claimed the synthesis of I by the action of fuming nitric acid on naphthsultam or its iso derivative.[3] When the reaction was repeated,

(1) C. Graebe, *Ann.*, **335**, 139 (1904).

(2) H. E. Armstrong and W. P. Wynne, *Ber.*, **24R**, 718 (1891).

(3) F. Dannerth, *J. Am. Chem. Soc.*, **29**, 1319 (1907).

only unidentified products and dinitronaphthsultam were obtained. The compound described in the present work could not be isolated from the mixture.

In other work,[4] it was shown that 1,3-dinitronaphthalene-5-sulfonic acid was formed as a minor product in the nitration of 2-nitronaphthalene-8-sulfonic acid. Evidence has also been obtained of the further sulfonation of 1,3-dinitronaphthalene-5-sulfonic acid to a disulfonic acid by heating with oleum.

EXPERIMENTAL

1,3-Dinitronaphthalene-5-sulfonic acid, sodium salt. 1,3-Dinitronaphthalene (4 g.) was added gradually to 40 ml. of 100% sulfuric acid at room temperature, and the red-black solution left 24 hr. It was then poured slowly with stirring onto an excess of ice. The mixture was heated to 60° and filtered from a little starting material, and the filtrate cooled and saturated with sodium chloride. The sodium salt was filtered and washed with brine. It was redissolved in warm water containing a little hydrochloric acid and resalted to eliminate sulfate. The air dried product weighed 10.4 g. and contained some sodium chloride. It formed a light yellow crystalline powder.

Incomplete sulfonation can be avoided by use of a larger excess of sulfuric acid or by the inclusion of a little oleum. Ordinary concentrated sulfuric acid does not sulfonate 1,3-dinitronaphthalene during 4 days' standing in the cold. The aqueous sulfonic acid solution can be salted out also by potassium chloride, giving a more granular and dense precipitate than is formed with sodium chloride.

The aqueous solution of the sodium salt becomes red with sodium or ammonium hydroxide. The latter, when mixed with a strong ammoniacal cupric sulfate solution, soon yields a crystalline powder of the sparingly soluble complex cupric-ammine salt of the sulfonic acid. The ammino-zinc salt is precipitated more slowly as crystalline grains.

The free sulfonic acid will precipitate from a solution containing a high concentration of sulfuric acid, but is dissolved by warming or on dilution with water. It was not obtained pure for analysis.

1,3-Dinitronaphthalene-5-sulfonyl chloride. A mixture of 3.9 g. of the salted sodium salt and 12 g. of phosphorus pentachloride was ground in a mortar and then placed in a lightly closed flask in an oil bath at 135°. After 1 hr., the product was cooled and stirred vigorously with ice and water until hydrolysis of the phosphorus oxychloride was complete. The solid was filtered, washed with water, and dried. The acetone solution of the material was filtered from inorganic salts and the sulfonyl chloride crystallized by gradual addition of ice water. After washing and drying, the yield was 1.3 g. Recrystallized from benzene-hexane, the sulfonyl chloride had m.p. 123–124°.

Anal. Calcd. for $C_{10}H_5N_2O_6SCl$: Cl 11.2. Found: Cl 11.4.

The percentage yields of the sodium salt of the sulfonic acid and the sulfonyl chloride were not calculated as the salt is unavoidably contaminated with sodium chloride in either case.

1,3-Dinitronaphthalene-5-sulfonamide. A solution of 1.3 g. of the sulfonyl chloride in 15 ml. of dioxane was treated at 5–10° with 5 ml. of ammonium hydroxide solution, added in portions. At first, a dark red color was produced and a precipitate rapidly formed, but after all of the ammonium hydroxide had been added the precipitate dissolved. The mixture was left in the cold bath for 15 min. and then 7 ml. of acetic acid was added during 5 min. The light red solution was treated slowly with an excess of ice water yielding a crystalline deposit of the amide. After 0.5 hr., this was filtered, washed with water, and dried. The yield of the light yellow crude product was 1.2 g. or 98%. The compound was recrystallized three times from aqueous methanol and then had m.p. 258–259°.

Anal. N as NO_2 was determined by $TiCl_3$ titration. Calcd. for $C_{10}H_7N_3O_6S$: N as NO_2, 9.43; S, 10.77. Found: $NaSNO_2$, 9.62; S, 10.30.

Conversion of the sulfonyl chloride to 1,3,5-trichloronaphthalene. A sample of the sulfonyl chloride was ground with five times its weight of phosphorus pentachloride and the mixture kept in an oil bath at 170° for 4.5 hr. The sublimed pentachloride was scraped back periodically during the heating. When cold, the product was added cautiously to ice. After complete hydrolysis, the solid was filtered, washed with water, and dried. Without further purification, the infrared spectrum was identical to that of authentic 1,3,5-trichloronaphthalene.

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(4) D. C. Morrison, unpublished work, Hyman Laboratories, Inc.

Preparation of Some Additional Sulfonylureas[1]

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Two sulfonylureas, 1-*n*-butyl-3-(4-tolylsulfonyl)-urea (tolbutamide) and 1-(4-chlorobenzenesulfonyl)-3-*n*-propylurea (chlorpropamide), are clinically effective as hypoglycemic agents.[2,3] Research in our laboratory, as well as in others,[4–8] has been underway for some time to prepare antidiabetic agents of even superior therapeutic usefulness. This note reports some further compounds prepared in this program.

(1) For preceding papers see W. M. McLamore, G. M. Fanelli, S. Y. P'an, and G. D. Laubach, *Ann. N. Y. Acad. Sci.*, **74**(3), 443 (1959); G. F. Holland, D. A. Jaeger, R. L. Wagner, G. D. Laubach, W. M. McLamore, and S. Y. P'an, *J. Med. Phar. Chem.*, **3**(1) 99 (1961).

(2) R. Levine, "The Effects of the Sulfonylureas and Related Compounds in Experimental and Clinical Diabetes," *Ann. N. Y. Acad. Sci.*, **71**(1), 1–292 (1957).

(3) M. G. Goldner, "Chlorpropamide and Diabetes Mellitus," *Ann. N. Y. Acad. Sci.*, **74**(3), 413–1028 (1959).

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(5) F. J. Marshall and M. V. Sigal, Jr., *J. Org. Chem.*, **23**, 927 (1958).

(6) E. Haack, *Arzneimittel-Forsch.*, **8**(7a), 444 (1958).

(7) H. Ruschig, C. Korger, W. Aumueller, H. Wagner, and R. Weyer, *Arzneimittel-Forsch.*, **8**(7a), 448 (1958).

(8) S. Onisi, *J. Phar. Soc. Japan*, **79**, 559, 628, 632, (1959).