After removal of the solvent a noncrystalline material resulted at first. Upon drying *in vacuo* over magnesium perchlorate 69.5 mg. (66%) of phosphorylcholine was obtained as a white solid,[9] m.p. 235–240° with decomposition.

Anal. Calcd. for $C_5H_{16}NO_5P$: N, 6.96; P, 15.40. Found: N, 7.10; P, 15.56.

The solution of the unchanged choline, above, was acidified with hydrochloric acid, the solvent evaporated *in vacuo*, and choline hydrochloride extracted from the residue with absolute ethanol. After dilution with unlabeled choline chloride, addition of phosphoric acid and removal of the solvent, another reaction cycle was performed. This gave a 57% yield and a total recovery of 75% of the radioactivity.

Addition of hydrochloric acid to a solution of phosphorylcholine in water, followed by removal of the solvent gave a white powder of *phosphorylcholine chloride*, m.p. 108–111° dec., soluble in water and ethanol. The compound readily lost hydrogen chloride upon drying at temperatures of 60–100°.

Anal. Calcd. for $C_5H_{15}ClNO_5P$: Cl, 14.86. Found: Cl, 15.15.

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(9) This compound showed an infrared spectrum identical to that of a product obtained by passing a solution of commercial calcium phosphorylcholine hydrochloride (California Foundation for Biochemical Research, Los Angeles 63) successively through Dowex 50 in the hydrogen form (elution with a hydrochloric acid gradient), and through Dowex 1 formate, as described above.

On the Reaction of Dihydroxypurines with Phosphorus Pentasulfide

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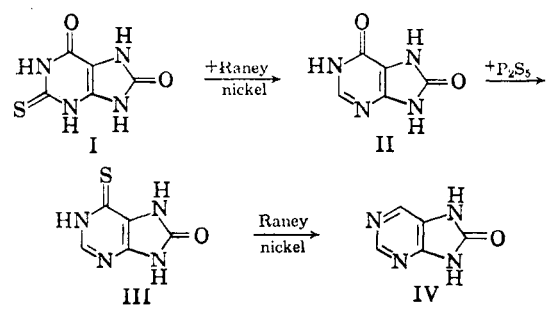
It is known that in xanthine and 4,5-diaminouracil reaction with phosphorus pentasulfide exchanges selectively the oxygen atom at C-6.[1,2] On the other hand, in the reaction with uric acid, one obtains—in addition to the main product, 6-thiouric acid—products thiated at position 8.[3] In order to determine the directive influence of oxygen in various positions of the purine ring on the thiation process, we have studied the behavior of the isomeric dihydroxypurines.

2,8-Dihydroxypurine was not attacked by phosphorus pentasulfide under a variety of conditions, using either pyridine or tetraline as solvent. However, 6,8-dihydroxypurine (II) reacted smoothly to give a 75% yield of pure 8-hydroxypurine-6-thione (III). No other purine derivative was found in the reaction mixture. As II is accessible from 2-thiouric acid (I), the thio derivative III has now become easily available.

For the synthesis of II, it has been found preferable to desulfurate 2-thiouric acid instead of 2-mercapto-6-hydroxy-4,5-diaminopyrimidine.[4] Although the latter procedure gives an 89% yield of the 6-hydroxy derivative, subsequent cyclization with urea[5] or phosgene[6] leaves much to be desired. On the other hand, direct cyclization of the above mercaptopyrimidine gives 2-thiouric acid in almost quantitative yield[7,8] and subsequent catalytic desulfuration results in a 64% yield of 6,8-dihydroxypurine (I).

8-Hydroxypurine-6-thione (III) in its turn may serve as a source of 8-hydroxypurine (IV). Desulfuration of III was tried under a variety of conditions. Even the best yields, obtained by carrying out the reaction in concentrated ammonia, were only 30%. Therefore, this route to IV has no advantage over the conventional method of cyclization of 4,5-diaminopyrimidine.[5]

In view of the low yields of IV, and taking into account previous experience with 3,7-dimethyl-2-hydroxypurine-6-thione,[9] desulfuration of the *S*-methyl ether (IIIa) of III was also tried. IIIa can not be prepared by methylation in the presence of sodium hydroxide because of the great sensitivity of the ether to alkali. By using pyridine instead, a 41% yield of IIIa was secured. Conversion of IIIa into IV proved even less satisfactory than the desulfuration of III. With IIIa, the reaction cannot be carried out in the presence of sodium hydroxide or ammonia. When working in aqueous suspension at a temperature of 70–80°, a large portion of the starting material was recovered. At higher temperatures, a considerable part of IV was apparently converted into a dihydro derivative as judged by the fact that the optical density of the solution at 280 mμ, the λ_{max} of IV, first increased, but then diminished again. Similar un-



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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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The Sulfonation of 1,3-Dinitronaphthalene

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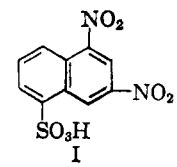
The sulfonation of 1,3-dinitronaphthalene was studied as part of a program on the chemistry of 2-nitronaphthalene derivatives. Graebe[1] briefly mentions the reaction of the 1,3-dinitro isomer with dilute oleum but the product was not characterized.

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,

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