methylamine[5] (20 ml.). The flask was heated until the temperature of the contents reached about 210°. The residue (viscous brown oil) was cooled, dissolved in hot 95% ethanol, decolorized with Norit A, and filtered. On cooling, 5.5 g. (56%) of white woolly crystals, m.p. 147–150°, was obtained. Two recrystallizations from the same solvent raised the melting point to 154–155° (short woolly needles).

Anal. Calcd. for $C_{14}H_{17}NO_5$: C, 60.21; H, 6.10; N, 5.01. Found: C, 60.32; H, 6.30; N, 5.21.

N-Methyl-2-(3,5-dimethoxy-4-hydroxyphenyl)succinimide (IV).—The reaction was carried out as for III. From I (10 g., 0.037 mole), IV (6.4 g., 66%) was obtained as yellowish white crystals, m.p. 183–186°. Two recrystallizations, using Norit A once for decolorization, raised the melting point to 186–187°, white crystals.

Anal. Calcd. for $C_{13}H_{15}NO_5$: C, 58.87; H, 5.66; N, 5.28. Found: C, 58.67; H, 5.76; N, 5.15.

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Synthesis of Some Hydroxylamine Derivatives of Pyrimidines and Purines[1]

PAULINE K. CHANG

Department of Pharmacology, Yale University School of Medicine, New Haven, Connecticut

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Because of interest in orotic acid analogs in this laboratory,[2] 6-N-hydroxylaminouracil (I) and uracil-6-hydroxamic acid (II) have been synthesized. 6-N-Hydroxylaminopurine ribonucleoside (III) was regarded as an analog of adenosine, because 6-N-hydroxylaminopurine[3] is active as an analog of both adenine and hypoxanthine.[4]

2,4-Dimethoxy-6-chloropyrimidine[5,6] failed to react with hydroxylamine; however, the demethylated derivative, 6-chlorouracil,[7] reacted smoothly with hydroxylamine to give I. Compound II was prepared from methyl orotate,[8] whereas III was prepared from 6-chloropurine ribonucleoside[9] and hydroxylamine.

Experimental Section[10]

6-N-Hydroxylaminouracil (I).—A solution of KOH (11.2 g., 0.2 mole) in ethanol (40 ml.) was added to a solution of hydroxylamine hydrochloride (12 g., 0.17 mole) in boiling ethanol (200 ml.). The precipitated KCl was filtered. 6-Chlorouracil[7] (1 g., 0.007 mole) was added to the solution of hydroxylamine. The mixture was refluxed for 1 hr. and allowed to cool to room temperature with stirring (1 hr.). The product, which separated as a solid, was washed with water and ethanol to give analytically pure I (0.73 g., 74%), m.p. 280° dec., $\lambda_{\max}^{\mathrm{pH}\,2}$ 264 mμ (ϵ 6250).

Anal. Calcd. for $C_4H_5N_3O_2$: C, 33.57, H, 3.52; N, 29.36. Found: C, 33.56; H, 3.77; N, 29.25.

Uracil-6-hydroxamic Acid (II).—A mixture of methyl orotate[8] (1.25 g., 0.0074 mole), $NH_2OH \cdot HCl$ (1.4 g., 0.02 mole), and water (10 ml.) was cooled to 0°. With stirring, NaOH (12.5 *N*, 3.6 ml.) was added to the mixture dropwise at 3°. The now clear solution was adjusted to pH 5 with concentrated HCl. Crude II, which separated out as a yellow solid, was recrystallized from water to yield the monohydrate (1.2 g., 86%), m.p. 250° dec., $\lambda_{\max}^{\mathrm{pH}\,2}$ 274 mμ (ϵ 7420). It was recrystallized twice from water to give the analytical sample.

Anal. Calcd. for $C_5H_5N_3O_4 \cdot H_2O$ [sample dried at 60° (0.1 mm.)]: C, 31.75; H, 3.73; N, 22.22. Found: C, 31.72; H, 3.99; N, 22.29. Calcd. for $C_5H_5N_3O_4$ [sample dried at 120° (0.1 mm.)]: C, 35.10; H, 2.95; N, 24.56. Found: C, 35.22; H, 3.15; N, 24.37.

6-N-Hydroxylamino-9-β-D-ribofuranosylpurine (III).—To a solution of hydroxylamine hydrochloride (0.7 g., 0.01 mole) in boiling ethanol (10 ml.) was added a solution of KOH (0.56 g., 0.01 mole) in ethanol (3 ml.). The precipitated KCl was filtered. 6-Chloro-9-β-D-ribofuranosylpurine[9,11] (0.286 g., 0.002 mole), dissolved in ethanol (20 ml.), was added to the solution of NH_2OH. The mixture was refluxed for 1 hr. and then concentrated *in vacuo* at 40°. The residue (412 mg.) was recrystallized from hot ethanol to yield the pure product (200 mg., 70%), m.p. 195° dec., $\lambda_{\max}^{\mathrm{pH}\,2}$ 262.5 mμ (ϵ 16,700). The analytical sample was recrystallized once more from ethanol.

Anal. Calcd. for $C_{10}H_{13}N_5O_5$: C, 42.40; H, 4.63; N, 24.72. Found: C, 42.42; H, 4.77; N, 24.94.

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Quinoxaline Sulfonamides

S. H. DANDEGAONKER AND C. K. MESTA

Department of Chemistry, Karnatak University, Dharwar, India

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The development of the field of chemotherapy has more recently led to a renewed interest in the quinoxalines in connection with their potential values as pharmaceuticals.[1–5] We have synthesized some halogenated quinoxaline sulfonamides in view of the reported effect of chlorine atoms on the activity of quinoxalines.[6]

Sulfonamides on condensation with 2,3-dichloroquinoxaline using the procedure of Wolf, *et al.*,[7] gave disulfonamide derivatives when 2 moles of sulfonamide was used, and a mixture of predominantly mono- and small amounts of disulfonamides when 1 mole of sulfonamide was employed. The reaction of sulfanilamide and 2,3-dichloroquinoxaline confirmed the findings of Wolf and co-workers[7] and Platt and Sharp[8] that the free amino group does not take part in condensation.

2,3-Dichloroquinoxaline on reaction with benzamide in different ratios gave only 2,3-dibenzamidoquinoxaline under similar conditions. Acetamide, on heating with dichloroquinoxaline at 130° or refluxing in ethanol, afforded a mixture of products, with or without chlorine. Interaction of sodamide with dichloroquinoxaline in boiling toluene either in a stoichiometric ratio or with an excess gave a mixture of unidentifiable products.

Experimental Section

2,3-Dihydroxyquinoxaline[9] (91%), white needles, m.p. 320°; 2,3-dichloroquinoxaline[10] (75%), colorless shining long needles,

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