The resulting solution was neutralized with NaOH pellets and extracted with Et_2O. After drying (Na_2SO_4), the mixture was purified by column chromatography over 10 g of alumina. The pure product (0.12 g, 55%), a light yellow liquid, was eluted with Et_2O. Tlc indicated a single component with an R_f of 0.78 (Al_2O_3–Et_2O). *Anal.* ($C_{10}H_8ClN$) C, H, Cl.

"Complex" from the Hydrolysis of 3-Phenyl-4-methoxypyridine.—3-Phenyl-4-methoxypyridine, 30 g (0.162 mole), was refluxed for 3 hr with 200 ml of 58% HI, and the mixture was cooled and diluted with 100 ml of ice slush. Na_2SO_3 was added until the solution changed from dark red to light orange. NaOH pellets were added (with cooling) until a buffered pH of *ca.* 5 was reached. The semisolid that came out of solution was filtered off and triturated repeatedly with Et_2O to remove 6.3 g of starting methoxy compound. The residue (39 g) was a stable, colorless solid, mp 50–90°. The precise composition of this complex was not elucidated. *Anal.* Found: C, 44.3; H, 3.53; N, 4.59; I, 35.5. Upon treatment with aqueous NaOH, however, it was converted to a mixture of 4-methoxy-3-phenylpyridine and 4-hydroxy-3-phenylpyridine. Recrystallization from H_2O (low recovery) gave a solid containing 19.3% iodine.

When treated with ω-dialkylaminoalkylamines, the complex was converted to 4-dialkylaminoalkylamino-3-phenylpyridines nearly as efficiently as was 4-chloro-3-phenylpyridine. The formation of the complex, rather than the mixture of 4-methoxy- and 4-hydroxypyridines that was obtained previously, was apparently a function of the lower pH of the solution from which the complex was isolated.

4-Dialkylaminoalkylamino-3-phenylpyridines. General Procedure.—A mixture of 1 part of the 3-phenylpyridine substrate (4-chloro-3-phenylpyridine or "complex") and 2.5–5 parts of the appropriate ω-dialkylaminoalkylamine was heated in a steel bomb at 185–215° for 15–16 hr. The reaction mixture was cooled and poured into H_2O, and the crude product was isolated by Et_2O extraction. Column chromatography over alumina, using Et_2O or 5% MeOH in Et_2O as eluent, provided pure products as nearly colorless oils. Yields were best when a large excess of diamine was employed. In general, 5.0 g of complex provided between 1.3 and 4.3 g of pure free base. In the one instance where it was used (n = 3, Table I), 4-chloro-3-phenylpyridine provided an 83% yield of product.

Although not used as a preparative method, it was found in later small-scale experiments that 4-methoxy-3-phenylpyridine would serve as well as 4-chloro-3-phenylpyridine in the displacement reaction.

Oxalate salts were prepared in a pure state by adding acetone solutions (*ca.* 10%) of 2 molar equiv of oxalic acid to acetone solutions of the amines. Recrystallization was not usually necessary.

4-Amino-1-(β-D-ribofuranosyl)benzimidazole

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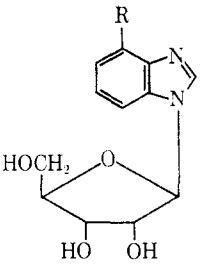
We recently described the synthesis of 4-amino-1-(β-D-ribofuranosyl)indole[2] as an example of a trideazaadenosine. A logical extension of this work would be the synthesis of a dideazaadenosine. From among the three possibilities, 4-amino-1-(β-D-ribofuranosyl)benzimidazole (I) was chosen because of the interesting biological properties of several benzimidazoles. 4-Nitro-1-(β-D-ribofuranosyl)benzimidazole (II) had been reported[3] earlier but its conversion to the related 4-amino-1-(β-D-ribofuranosyl)benzimidazole (I) was not described. This conversion was accomplished by the hydrogenation of II in the presence of a palladium-on-carbon catalyst.



I, R = NH_2
II, R = NO_2

The previous[3] assignment of a β-anomeric configuration to II was confirmed through the observation that I shows a negative Cotton effect in its ORD curve. For use in comparison with I in biological testing, a sample of 4-aminobenzimidazole (III)[4] was similarly synthesized by catalytic hydrogenation of 4-nitrobenzimidazole.[5]

In cytotoxicity tests against KB cells III showed an ED_{50} at 5 μg/ml, whereas I had an ED_{50} at >100 μg/ml.[5]

Experimental Section

4-Amino-1-(β-D-ribofuranosyl)benzimidazole.—A suspension of 510 mg (1.73 mmoles) of 4-nitro-1-(β-D-ribofuranosyl)benzimidazole and 510 mg of 5% Pd-C in 125 ml of MeOH was shaken with H_2 at 3.5 kg/cm² at 25° for 30 min. The catalyst was removed and the filtrate was concentrated to about 10 ml and kept at 5° for 16 hr. A crop of crystals (314 mg, mp 86°) was removed and the filtrate was concentrated to 4 ml. A second crop of crystals (100 mg, mp 86°) was obtained. The combined crops were recrystallized from 2 ml of H_2O and the product was dried over P_2O_5 at 80° and reduced pressure for 2 hr. The yield was 320 mg (70%), mp 137–138°;[6] $[\alpha]_D$ −49°, $[\alpha]_{578}$ −52° (*c* 1, H_2O); $[\phi]_{350}$ −660°, $[\phi]_{300}$ −1640° (tr), $[\phi]_{275}$ −490° (pk), $[\phi]_{265}$ −920° (tr), $[\phi]_{255}$ 0°, $[\phi]_{254}$ +270° (pk); $\lambda_{max}^{H_2O}$ [mμ (ε × 10⁻³)] pH 1—222 (14.2), 255 (3.8), 267 (4.5), 274 (4.6), 287 (2.5); pH 7—218 (25.6), 263 (7.6), 287 (4.4); pH 13—263 (7.5), 287 (4.4); R_f 0.59, tlc on cellulose in H_2O (visualized by uv absorption and $KMnO_4$ spray); τ^{D_2O} 3.46 ppm (d, C-1′ proton, $J_{1',2'}$ = 4.8 cps).

Anal. Calcd for $C_{12}H_{15}N_3O_4$: C, 54.33; H, 5.70; N, 15.84. Found: C, 54.33; H, 5.70; N, 15.68.

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(5) Personal communication from Dr. C. O. Gitlerman of the Merck Sharp & Dohme Research Laboratories.

(6) The melting point of 86° obtained above was probably that of a solvate of undetermined composition.

Terpene Compounds as Drugs. V. Terpenyl Derivatives of Salicylic Acid

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Continuing our studies in the field of terpene chemistry, we esterified salicyclic acid with terpenyl acids in order to seek possible differences from acetylsalicylic acid in analgetic and antiinflammatory activity and in a decrease of undesirable side effects. The new substances, which are listed in Table I, displayed on a whole better gastric tolerance than acetylsalicylic acid, however, at markedly decreased activity.