Nucleotides. I. The Reaction of Cyclouridines with Benzyl Hydrogen Phosphoric Benzoic Anhydride[1]

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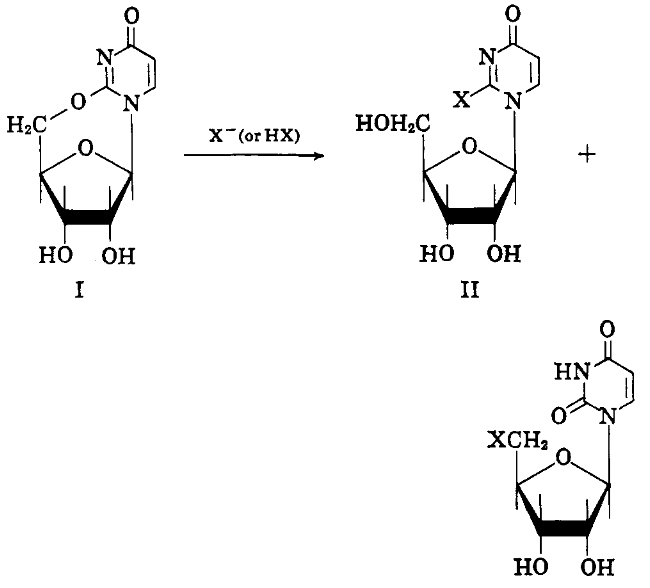
Pyrimidine cyclonucleosides are versatile intermediates for the transformation of preformed nucleosides into other nucleosides. The synthesis of uridine-5′-phosphate (X) and related compounds by reaction of 2′,3′-O-isopropylidene-2,5′-cyclouridine (IV) with mixed phosphoric carboxylic anhydrides is discussed.

It has been demonstrated that the pyrimidine cyclonucleosides, *e.g.*, I, are versatile intermediates for the transformation of preformed nucleosides into a considerable number of other nucleosides.[2-4] The key step in this transformation involves nucleophilic displacement at C-2 or at the carbon participating in the ether bond formation.



I

II

III

The facile displacement reaction presented above suggests that it may be possible to convert pyrimidine cyclonucleosides into nucleotides (including oligonucleotides) by the use of phosphates (or the nucleotides) as the nucleophile. In this phosphorylation an essential feature may be the formation of phosphate esters by activation of the substrate (the alcohol). One of the advantages of this type of phosphorylation over the usual phosphorylation method, *e.g.*, use of a phosphate monoester in combination with dicyclohexylcarbodiimide,[5] is that there is no need to activate the phosphoric acid. Another advantage may be that, at least theoretically, this type of phosphorylation might permit the hydroxyl group(s) other than that involved directly in the reaction to remain unblocked. This feature may be of particular value for the synthesis of the oligonucleotides.

With these considerations in mind, the reaction of the pyrimidine cyclonucleosides with the phosphates was examined. This paper deals with the successful synthesis of uridine-5′-phosphate (X) and related compounds by reaction of 2′,3′-O-isopropylidene-2,5′-cyclouridine (IV) with a mixed phosphoric carboxylic anhydride.[6]

2′,3′-O-Isopropylidene-2,5′-cyclouridine (IV)[7] was chosen as a substrate because of its relative accessibility and its superior reactive nature[8] among the three types of cyclouridines (2,2′-, 2,3′-, and 2,5′-cyclouridines). As a nucleophile, di(tri-*n*-butylammonium) benzyl phosphate (XI)[9] was first tried.

A dioxane solution of IV was treated with a threefold molar excess of XI at 37°. The progress of the reaction was readily followed by paper chromatography in combination with ultraviolet spectroscopy. On the paper chromatogram, a spot corresponding to the cyclouridine IV (R_f 0.73, λ_{max} 238 mμ[10]) diminished as the reaction proceeded with concurrent appearance of a new spot (R_f 0.68, λ_{max} 261 mμ[10]) due to the 1-substituted uracil. This reaction proceeded sluggishly and even after 48 hr. of reaction time roughly 70% of IV remained unreacted. On the other hand, under the same conditions, the reaction of IV and benzyl hydrogen phosphoric benzoic anhydride (tri-*n*-butylammonium salt, VI) took place quite smoothly and was virtually completed within 15 hr. From this reaction, a nucleotidic product (VIII) was isolated in 50% yield by ion-exchange chromatography. Catalytic debenzylation of VIII to IX, followed by removal of the isopropylidene group afforded crystalline uridine-5′-phosphate in 37% yield (based on IV). The structure confirmation of the product (X) rests upon the elementary analysis and paper chromatographic properties. The absorption spectrum was also compatible with the structure assigned. (See Chart I.)

We have no explanation for the superiority of VI as an attacking group over the benzyl phosphate XI, except the suggestion that the benzoyl group in VI plays a role as a readily replaceable blocking group

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[1] A preliminary report of part of this work was read at the 19th National Meeting of the Pharmaceutical Society of Japan, Tokyo, April 1964: Abstract, p. 254.

[2] (a) A. M. Michelson and A. R. Todd, *J. Chem. Soc.*, 816 (1955); (b) D. M. Brown, D. B. Parihar, A. R. Todd, and S. Varadarajan, *ibid.*, 3028 (1958); (c) D. M. Brown, D. B. Parihar, and A. R. Todd, *ibid.*, 3035 (1958).

[3] (a) R. Fecher, J. F. Codington, and J. J. Fox, *J. Am. Chem. Soc.*, **83**, 1889 (1961); (b) J. J. Fox and N. C. Miller, *J. Org. Chem.*, **28**, 936 (1963); (c) J. F. Codington, I. L. Doerr, and J. J. Fox, *ibid.*, **29**, 558 (1964).

[4] See also A. M. Michelson, "The Chemistry of Nucleosides and Nucleotides," Academic Press Inc., New York, N. Y., 1963, pp. 15–23.

[5] G. M. Tener, *J. Am. Chem. Soc.*, **83**, 159 (1961).

[6] After the present work was concluded (June 1964), J. Zemlicka and J. Smrt [*Tetrahedron Letters*, **No. 31**, 2081 (1964)] reported, in preliminary form, the results of their work along these lines. Our present study differs in that the mixed phosphoric carboxylic anhydride was employed as a nucleophile.

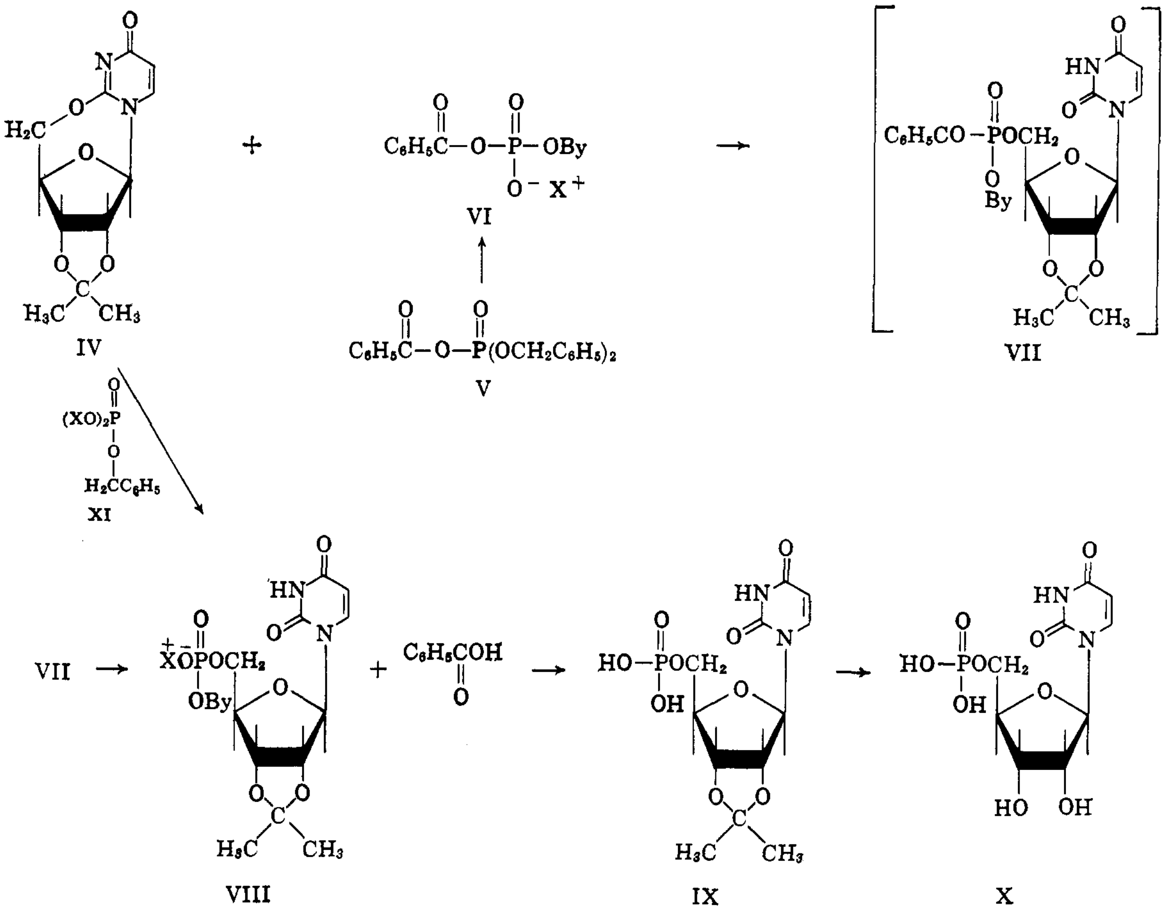
[7] D. M. Brown, A. R. Todd, and S. Varadarajan, *J. Chem. Soc.*, 868 (1957).

[8] See ref. 4, pp. 18 and 20.

[9] J. Baddiley, V. M. Clark, J. J. Michelski, and A. R. Todd, *J. Chem. Soc.*, 815 (1949).

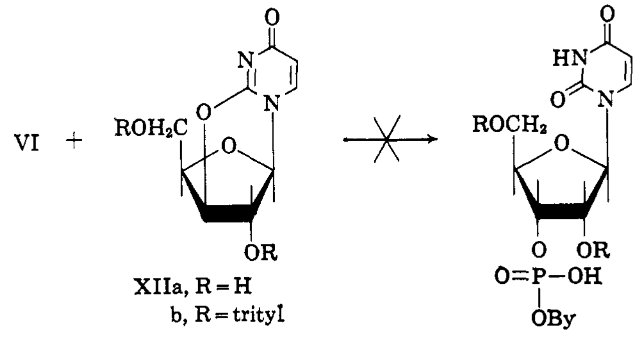
[10] R_f values were measured in the solvent system: isopropyl alcohol–ammonia–water (7:1:2); the absorption spectrum of an extract of the spot was measured as described in the Experimental.

CHART I



of phosphoric acid and that the benzoic acid detached from the mixed anhydride might serve as an acidic catalyst by analogy with the accepted mode of the nucleophilic displacement involving other nucleophiles.[11]

In a similar reaction involving VI and 2,3′-cyclouridines XIIa and XIIb,[12] numerous attempts[13] to phosphorylate XIIa and XIIb to XIII were unsuccessful. This decrease in reactivity of these 2,3′-cyclouridines (XIIa and XIIb) toward VI presumably reflects the relative stability, due to their somewhat relieved bond strain as compared with the bond strain in 2,5′-cyclouridine.[8]



XIIa, R = H
b, R = trityl

By = benzyl
XIIIa, R = H
b, R = trityl

Experimental

General.—Melting points are corrected. Infrared spectra were measured on a Koken Model DS-301 infrared recording spectrophotometer. Ultraviolet spectra were determined on a Beckman DK-2 spectrophotometer. Except where noted removal of the solvent was performed under reduced pressure with the help of a water aspirator (15–18 mm.). Paper chromatography was performed by the use of the ascending technique; the filter paper used in this work was Toyo Roshi 51A; the solvent systems employed were system A, isopropyl alcohol–ammonia–water, 7:1:2, system B, *n*-butyl alcohol–water, 84:16, and system C, isopropyl alcohol–1% ammonium sulfate, 2:1. Unless otherwise stated, spots were detected by the ultraviolet lamp. Ultraviolet spectra of spots on the paper chromatograms were measured as follows. The spots were pencil marked, cut out separately, and extracted with 5 ml. of a solvent (unless otherwise stated, water); the spectrum of each extract was determined using a blank extract (an extract of the same area of paper with 5 ml. of the same solvent) as a control. Quantitative data were obtained by comparing the ultraviolet absorption of each of these extracts at appropriate wave lengths. Microanalyses were performed by Mrs. T. Tohma and her staff of our laboratories.

Dibenzyl Phosphoric Benzoic Anhydride (V).[14]—The mixed anhydride V was prepared by an extension of Ogle's method.[15] To a magnetically stirred suspension of silver dibenzyl phosphate (2.88 g., 6.05 mmoles) in 40 ml. of dried ether was added an ether solution (10 ml.) of benzoyl chloride (0.85 g., 6.05 mmoles) over a period of 30 min. at 0° shutting out the light; stirring was

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[11] See ref. 3b.

[12] N. C. Yung and J. J. Fox, *J. Am. Chem. Soc.*, **83**, 3065 (1961).

[13] Numerous attempts were made by varying the solvent, temperature, ratio of reactants, and substrates.

[14] The formation of compound V by the reaction of 1-ethoxyvinyl dibenzyl phosphate and benzoic acid has been reported by H. H. Wasserman and D. Cohn [*J. Org. Chem.*, **29**, 1817 (1964)]. However, V was not isolated in pure state, nor were its physical properties described, except for the P=O frequency (1790 cm.⁻¹) in the infrared spectrum.

[15] (a) D. M. Brown, *Advan. Org. Chem.*, **3**, 142 (1963). (b) The authors are most grateful to Dr. J. R. Ogle of the Radiochemical Center, Amersham, Buckinghamshire, England, for his personal letter concerning the details of the synthesis of phenylacetic dibenzyl phosphoric anhydride from silver dibenzyl phosphate and phenylacetyl chloride.

continued in the dark for 4 hr. at room temperature and then an additional 0.58 g. of silver dibenzyl phosphate (1.5 mmoles) was added. After being stirred for an additional 4 hr. at room temperature, the silver chloride formed was filtered off on Celite and washed with two 5-ml. portions of ether. The combined filtrate and washings were concentrated to dryness. The residue was recrystallized from ether to afford prism-shaped crystals, 1.46 g. (54.9%), m.p. 62–65°. The infrared spectrum of this sample (1790, 1270, and 1110 cm.$^{-1}$) was compatible with the structure assigned.[16]

Anal. Calcd. for $C_{21}H_{19}O_5P$: C, 65.96; H, 4.97; P, 8.11. Found: C, 65.98; H, 4.98; P, 7.58.

Further Structure Confirmation of the Product (V).—To a magnetically stirred solution of V (121 mg.) was added an ether solution of 0.2 ml. of aniline to afford crystals immediately. Stirring was continued for 30 min. at room temperature; crystals (277 mg.) were collected and recrystallized from ethanol to afford a pure product, m.p. 161–162°. A mixture melting point with authentic sample of benzanilide did not show depression.

The purity (97%) of the above-mentioned sample of V was determined by a reported procedure using succinic anhydride as a standard sample.[17]

Tri-*n*-butylammonium Salt of Benzyl Hydrogen Phosphoric Benzoic Anhydride (VI).—The following procedure was essentially that reported by Clark, Kirby, and Todd.[18] To a solution of V (778 mg., 2 mmoles) in 20 ml. of dioxane was added 200 mg. of 5% palladium on carbon, and the suspension was hydrogenated in the presence of tri-*n*-butylamine (378 mg.) at room temperature in hydrogen atmosphere until 45 ml. of hydrogen was absorbed. The catalyst was filtered off and washed with two 5-ml. portions of dioxane. The combined filtrate and washings were concentrated at 20° to thin sirup,[19] 1.02 g. (109%). The sirup was dissolved in a small amount of acetone. Ether was added to the solution until the solution was just turbid and the solution was kept in a refrigerator overnight to afford a solid. The solid was collected, washed with ether, and dried *in vacuo*, 930 mg. (99%); the purity, determined by the colorimetric assay,[17] of this sample was 96%. The infrared absorption spectrum, whose maxima appeared at 3400, 2500, 1730 (benzoyl C=O), 1630, 1310, and 1260 (broad, P=O) cm.$^{-1}$, differed definitely from that of an equimolar mixture of benzoic anhydride and the di(tri-*n*-butylammonium) salt of P^1,P^2-dibenzyl pyrophosphate,[20] a mixture anticipated to be formed by disproportionation.

Anal. Calcd. for $C_{26}H_{40}NO_5P$: N, 2.94; P, 6.50. Found: N, 2.85; P, 6.10.

2′,3′-O-Isopropylidene-2,5′-cyclouridine (IV).—IV was prepared from 5′-*p*-tolylsulfonyloxy-2′,3′-O-isopropylideneuridine[7] in 72% yield using the procedure for the preparation of 2′,3′-O-isopropylidene-4,5′-cyclopseudouridine from pseudouridine[21]: m.p. 190° dec.; R_f 0.73 (system A), R_f 0.68 (system B), and R_f 0.73 (system C); λ_{max} 238 mμ.

Anal. Calcd. for $C_{12}H_{14}N_2O_5$: C, 54.13; H, 5.30; N, 10.52. Found: C, 53.95; H, 5.60; N, 10.50.

Reaction of IV with Phosphates. Method A. With Tri-*n*-butylammonium Salt of Benzyl Hydrogen Phosphoric Benzoic Anhydride (VI).—To a magnetically stirred solution of IV (27 mg., 0.10 mmole) in 2 ml. of dried dioxane was added VI (148 mg., 0.29 mmole). Stirring was continued at 37° in a stoppered bottle. The progress of the reaction was followed by paper chromatography, using system A, until the spot (R_f 0.73) corresponding to IV almost disappeared. It required about 15 hr. The paper chromatogram (system A) of the reaction mixture at this stage showed the presence of three ultraviolet-absorbing (R_f 0.42, 0.68, and 0.80)[22] in addition to a faint spot (R_f 0.73, IV). The spot with R_f 0.68 was also detected with the Hanes and Isherwood reagent for phosphorus.[23] The spot (R_f 0.68) was excised and extracted with water. The ultraviolet absorption of the extract was λ_{max} 262 mμ. The ratio of optical density at 262 mμ of the extract (R_f 0.68) to that at 238 mμ of the spot (R_f 0.73) was 25:2.

Method B. With Di(tri-*n*-butylammonium) Benzyl Phosphate (XI).—Compound IV (27 mg., 0.11 mmole) in 2 ml. of dried dioxane was treated with di(tri-*n*-butylammonium) benzyl phosphate (XI, 162 mg., 0.29 mmole) as described above. Even after the solution had been stirred for 24 hr., paper chromatography in system A showed the presence of a spot with R_f 0.73 as well as a spot with R_f 0.68.[22] At this stage of the reaction, the ratio of optical density at 262 mμ of an extract of the spot with R_f 0.68 to that at 238 mμ of the spot with R_f 0.73 was 9:17, indicating *ca.* 70% of the starting material (IV) remained unreacted. After the solution had been stirred for another 24 hr., this ratio (9:17) did not change.

Preparation of Uridine-5′-phosphate (X).—The reaction of method A was repeated on a larger scale. To a solution of VI (1.86 g., 3.9 mmoles) in 20 ml. of dioxane was added IV (103.6 mg., 0.389 mmole). After the mixture had been magnetically stirred in a stoppered bottle at 37° for 24 hr., paper chromatography in system A showed the absence of IV (R_f 0.73) and the presence of a product with R_f 0.68. The solvent was removed under reduced pressure to afford a sirup (1.79 g.). The sirup was dissolved in 10 ml. of water. The solution was treated with three 10-ml. portions of ether. The ether solution was discarded. The aqueous solution was concentrated to dryness (1.25 g.). The residue was dissolved in 50 ml. of water and the solution was adjusted to pH 9 with ammonia; the optical density unit[24] of this solution was 1630 (*ca.* 50% yield, based on IV). This solution was applied to ion-exchange column (Dowex 1, formate form, 200–400 mesh, 2 × 40 cm.). The column was washed with water (1 l.) to elute benzoic acid, and then the eluting system was switched to a mixture of 0.05 *N* ammonium formate and 0.01 *N* formic acid (1:1, 100 ml.). Eight milliliters of eluate was collected as one fraction and an elution pattern drawn by plotting the optical density at 260 mμ of each eluate against the tube number consisted of only a single peak. Eluates corresponding to the peak whose optical density unit was 1350 (86% recovery) were combined and concentrated under reduced pressure to 10 ml. Paper chromatography of this solution indicated the presence of a single substance (R_f 0.68, system A), λ_{max} 262 mμ, λ_{min} 234 mμ. The above solution was adjusted to pH 2 with 5% hydrochloric acid. This solution was subjected to catalytic debenzylation on 5% palladium on carbon (100 mg.) to afford 2′3′-O-isopropylideneuridine-5′-phosphate with R_f 0.16 in 2-propanol–ammonia–water (7:2:1).[25] The mixture was then allowed to stand at 37° until the removal of the isopropylidene group was completed.[26] The catalyst was filtered off and washed with 5 ml. of a mixture of 3% ammonium hydroxide and 50% aqueous ethanol (1:1). The combined filtrate and washing were concentrated to a sirup: R_f 0.14 (system A), R_f 0.01 (system B), and R_f 0.60 (system C)[27]; $\lambda_{max}^{ph\ 7}$ 261 mμ. The above sirup was dissolved in 1 *N* barium hydroxide solution (10 ml.). After neutralization with 1 *N* sulfuric acid, the barium sulfate formed was removed by centrifugation. The supernatant layer was concentrated to *ca.* 1 ml. To the solution was added 3 vol. of anhydrous ethanol and the precipitated

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[16] (a) The C=O and P=O frequencies are primarily dependent upon the electronegativity of the substituent groups, so that with strongly electronegative substituents the frequencies rise.[16b] Thus, the C=O frequency of diethyl phosphoric benzoic anhydride appears at 1800 and 1760 cm.$^{-1}$ [16c]; the P=O frequency of phosphoenol pyruvic acid anhydride appears at 1290 cm.$^{-1}$,[16d] (b) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1958, pp. 167, 313; (c) F. Cramer and K. G. Gaertner, *Chem. Ber.*, **91**, 709 (1958); (d) V. M. Clark and A. J. Kirby, *J. Am. Chem. Soc.*, **85**, 3705 (1963).

[17] F. Lipmann and L. C. Tutle, *J. Biol. Chem.*, **159**, 21 (1945).

[18] (a) V. M. Clark, G. W. Kirby, and A. Todd, *J. Chem. Soc.*, 3039 (1958); (b) also see R. W. Chambers and H. G. Khorana, *J. Am. Chem. Soc.*, **80**, 3749 (1958).

[19] Purity of this sample was *ca.* 90% as determined by the colorimetric assay.[17]

[20] N. Anand, V. M. Clark, R. H. Hall, and A. R. Todd, *J. Chem. Soc.*, 3668 (1952).

[21] A. M. Michelson and W. F. Cohn, *Biochemistry*, **1**, 490 (1962).

[22] R_f values in system A of 2′,3′-O-isopropylidene-5′-benzyl hydrogen phosphate (VIII), VI, and benzoic acid were 0.68, 0.42, and 0.80, respectively.

[23] C. S. Hanes and F. A. Isherwood, *Nature*, **164**, 1107 (1948).

[24] One optical density is defined as that amount of material per milliliter which, in a 1-cm. light path at 260 mμ, gives a spectrophotometric reading of 1.

[25] The R_f value of 2′,3′-O-isopropylideneuridine-5′-phosphate in this solvent system was 0.16: T. Ukita, N. Imoto, K. Nagasawa, and N. Aimi, *Chem. Pharm. Bull.* (Tokyo), **10**, 1113 (1962).

[26] The progress of deacetonization was followed by paper chromatography using metaperiodate–benzidine as a spray reagent.

[27] R_f values of an authentic sample of uridine-5′-phosphate were 0.14 (in system A), 0.01 (in system B), and 0.60 (in system C).

barium salt was collected and purified by reprecipitation from its aqueous solution with ethanol. The sample was dried over phosphorus pentoxide *in vacuo:* 72 mg. (36%).

Anal. Calcd. for $C_9H_{11}BaN_2O_9P \cdot 3H_2O$: C, 21.05; H, 3.34; N, 5.46; P, 6.03. Found: C, 20.13; H, 3.41; N, 5.27; P, 5.89.

Attempted Synthesis of Uridine-3′-phosphate by Reaction of X with VI.—To a solution of VI (34 mg.) in 3 ml. of dioxane was added 2′,5′-di-O-trityl-2,3′-cyclouridine (Xb, 10 mg.). The solution was stirred at 37°. The process of the reaction was followed as described above. After the solution had been stirred at the same temperature for 3 days, paper chromatography showed the presence of only the starting materials (Xb and VI) indicating that no reaction had taken place. The same reaction was repeated at 60°, but even after 12 hr. reaction did not occur. 2,3′-Cyclouridine (Xa) in place of Xb was tried as a substrate, the other conditions being kept constant. However, on paper chromatography no indication of the presence of any nucleotidic products in the reaction mixture could be obtained. In each experiment, replacement of the dioxane by dimethylformamide or dimethyl sulfoxide was found to be ineffective in phosphorylation of Xa and Xb.

Azabicyclic Alcohols. III. Stereochemistry of the 7- and 8-Hydroxyindolizidines[1]

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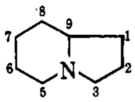
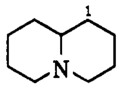
Each of the 7- and 8-hydroxyindolizidine racemates has been synthesized and characterized. Configurational and conformational assignments have been made on the basis of infrared, n.m.r., g.l.c., pK_a, and chemical evidence. In all cases, the *trans* ring fusion prevails, and no significant fraction (>2%) of the *cis* ring fusion could be detected by infrared methods. In the 8-hydroxy series, intramolecular hydrogen bonding exists between the nitrogen and an axial β-hydroxyl group. The Bohlmann correlation, originally deduced for conformational assignment of the quinolizidine ring fusion, has been shown to be valid for application to the indolizidine system.

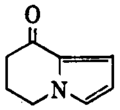
We have investigated the hydroxyindolizidines (*cf.* I) as part of a broader stereochemical study of simple azabicyclic ring systems. In a preceding paper in this series,[2] it was shown that the 1-, 2-, and 3-hydroxyquinolizidines (*cf.* II) exist in a *trans* ring fusion, and the presence of the *cis* fusion could not be detected by infrared methods. The present study constitutes a similar investigation of the 7- and 8-hydroxyindolizidines. In each of these, two epimeric racemates are possible, depending upon the configuration of the hydroxyl group relative to that of the bridgehead (C-9) hydrogen.



indolizidine
I



quinolizidine
II



III

Neither of the 7-hydroxyindolizidines has been reported; a picrate of one of the 8-hydroxy racemates has been described.[3] Alkaloids containing a substituted 8-hydroxyindolizidine ring system recently have been reported.[4] The chemistry of the indolizidine ring system has been reviewed.[5] Its stereochemistry is analogous to that of the better known hydrindane system,[6] except that the ring fusion is not necessarily fixed owing to the possible inversion of the bridgehead nitrogen.

Results

The 7- and 8-ketoindolizidines were reduced by both chemical and catalytic methods to give mixtures (see Tables I and II) of the corresponding hydroxyindolizidine racemates. These epimeric racemates were con-

TABLE I

EPIMERIC RATIOS OF 7-HYDROXYINDOLIZIDINES RESULTING FROM REDUCTIONS OF THE CORRESPONDING KETONE

Catalyst or reducing agent	Medium	Epimer A–B,[a] %
PtO_2	EtOH	24–76
5% Rh-carbon	EtOH	20–80
5% Ru-carbon	EtOH	45–55
10% Pd-carbon	EtOH	16–84
PtO_2	Aq. HCl	23–77
5% Rh-carbon	Aq. HCl	23–77
5% Ru-carbon	Aq. HCl	38–62
10% Pd-carbon	Aq. HCl	28–72[b]
Na-EtOH	Benzene	4–96
K-EtOH	Benzene	2–98
$NaBH_4$	H_2O	6–94
$LiAlH_4$	Ether	8–92

[a] Determined by g.l.c. analysis. [b] Results reproducible only within ±5%.

TABLE II

EPIMERIC RATIOS OF 8-HYDROXYINDOLIZIDINES RESULTING FROM REDUCTIONS OF THE CORRESPONDING KETONE

Catalyst or reducing agent	Medium	Epimer A–B, %
PtO_2	EtOH	60–40
5% Rh-carbon	EtOH	80–20
5% Ru-carbon	EtOH	82–18
10% Pd-carbon	EtOH	8–92
PtO_2	Aq. HCl	49–51
5% Rh-carbon	Aq. HCl	79–21
5% Ru-carbon	Aq. HCl	82–18
10% Pd-carbon	Aq. HCl	31–69
Na-EtOH	Benzene	27–73
Na-*n*-BuOH	Benzene	22–78
K-EtOH	Benzene	20–80
$NaBH_4$	H_2O	23–77
$LiAlH_4$	Ether	23–77

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[1] Presented in part at the 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964.

[2] H. S. Aaron, G. E. Wicks, Jr., and C. P. Rader, *J. Org. Chem.*, **29**, 2248 (1964).

[3] N. J. Leonard, S. Swann, Jr., and J. Figueras, Jr., *J. Am. Chem. Soc.*, **74**, 4620 (1952).

[4] R. Kuhn and I. Loew, *Chem. Ber.*, **95**, 1748 (1962); T. R. Govindachari, B. R. Pai, I. S. Ragade, S. Rajappa, and N. Viswanathan, *Chem. Ind.* (London), 966 (1960).

[5] W. L. Mosby, "Heterocyclic Compounds with Bridgehead Nitrogen," part I, Interscience Publishers, Inc., New York, N. Y., 1961, p. 302.

[6] E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p. 276.