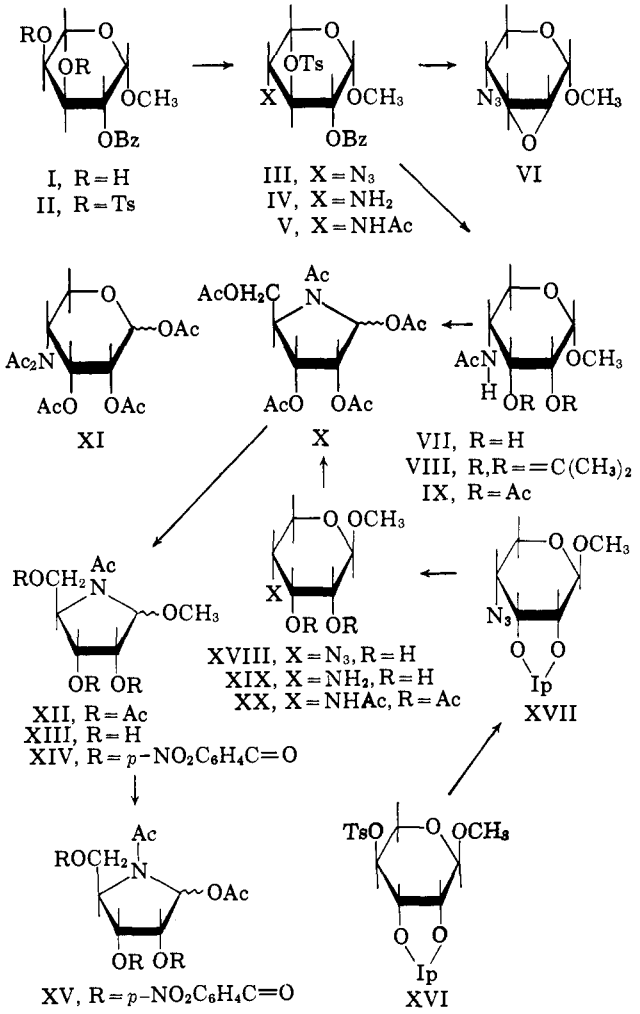
of the 1-O-acetate (XV) from which one anomer could be removed by crystallization from 2-propanol–ethyl acetate, m.p. 164.5–165.5°.

The second synthetic sequence to 4-acetamido-4-deoxy-D-ribofuranose derivatives started with the displacement of methyl 2,3-O-isopropylidene-4-O-(*p*-tolylsulfonyl)-α-L-lyxopyranoside[4] (XVI) by sodium azide in DMF to give methyl 4-azido-4-deoxy-2,3-O-isopropylidene-β-D-ribopyranoside (XVII) as an analytically pure oil, b.p. 76–78° (0.3 mm.), in 30% yield. Deacetonation of XVII with acetic acid gave a quantitative yield of the azide XVIII which was hydrogenated directly over 5% palladium-on-carbon to afford the crystalline methyl 4-amino-4-deoxy-β-D-ribopyranoside (XIX), m.p. 109.5–111.0° (from ethyl acetate) in 30% yield. Acetylation of XIX gave the sirupy triacetate (XX). Acetolysis of XX gave the pentaacetate (X) which was identical in all respects with the pentaacetate (X) obtained by route I starting with the ditosylate (II). Identity was further confirmed by conversion of the pentaacetate (X) from route II to the same crystalline trinitrobenzoate (XIV) obtained from route I.



The contraction of the 4-acetamido-4-deoxyribopyranosides to the furanose ring under acid conditions is noteworthy. This is in direct contrast to the behavior of methyl 4-acetamido-2,3,6-tri-O-acetyl-4-deoxy-α-D-glucopyranoside which maintained the pyranose ring under these same conditions.[11] It is interesting to note that 5-acetamido-5-deoxy-D-ribose showed a greater tendency toward furanose formation than did the analogous xylose and arabinose derivatives.[12]

(11) E. J. Reist, D. F. Calkins, R. R. Spencer, and L. Goodman, unpublished results.

(12) S. Hanessian and T. H. Haskell, *J. Org. Chem.*, **28**, 2604 (1963).

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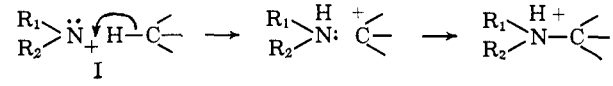
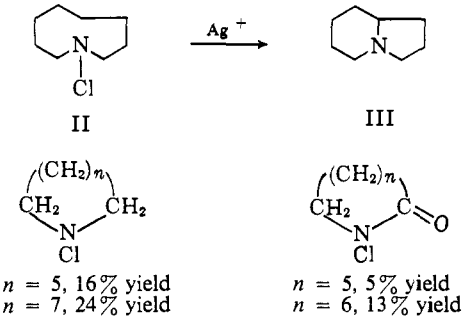
Transannular Reactions of Nitrenium Ions[1]

Sir:

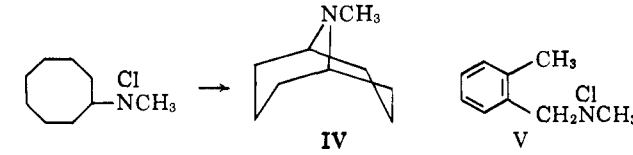
Interest in substitution of nitrogen at saturated unactivated carbon[2] led us to examine the reactions of nitrenium ions (I). The anticipated process was



Initially, medium-ring secondary amines and amides were chosen for study in view of the well-known transannular hydride abstraction by carbonium ions in the carbocyclic analogs.[3] The corresponding N-chloro derivatives were prepared using dichloramine T in pentane or pentane–ether mixture or N-chlorosuccinimide in methylene chloride. These were freed from solvent and dissolved in aqueous dioxane, and the nitrenium ion was generated by the action of silver ions. The reaction proceeded fairly rapidly at room temperature in the case of the chloramines but slowly at 80° with the chloramides. The maximum yield of transannular insertion product was obtained with N-chloroazacyclononane (II). Indolizidine (III) was formed in 68% yield and identified by comparison of he picrate with an authentic sample.[4]



The use of the reaction in a geometrically less ideal case is illustrated in a synthesis of N-methylgranatanine (IV) in 5% yield from N-chloro-N-methylcyclooctylamine. Chloramine V under the above conditions



gave *o*-tolualdehyde (35%) and the parent secondary

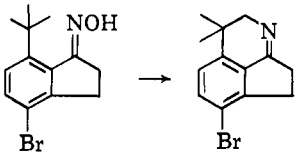
(1) Presented in part at the Symposium on Reactive Intermediates in Organic Chemistry, Laval University, Aug. 27–29, 1964.
(2) R. A. Abramovitch and B. A. Davis, *Chem. Rev.*, **64**, 149 (1964).
(3) V. Prelog and G. J. Traynham in "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., pp. 593–615.
(4) M. G. Reinecke and L. R. Kray, *J. Org. Chem.*, **29**, 1736 (1964). We thank Dr. Reinecke for reference samples.

amine. No appreciable attack on the *o*-methyl group was observed. Apparently the β-elimination of a benzylic hydrogen to give the aldimine provides a lower energy reaction path.

Two observations support the suggestion that abstraction of hydride ion from dioxane is the major competing reaction: (a) the formation of parent secondary amine as the main basic by-product; (b) treatment of N-chloropiperidine in aqueous tetrahydrofuran with silver fluoroborate gave a 52% yield of γ-hydroxybutyraldehyde (as its dinitrophenylhydrazone, calculated on the basis of chloramine used).

The scope of the reactions and use of less reactive solvents is being investigated. A concerted dehalogenation–hydride abstraction mechanism is not excluded by our observations.

A closely related reaction is the cyclization of oxime VI to VII by hot polyphosphoric acid.[5]



VI VII

Adam and Schreiber have just reported a base-catalyzed counterpart to the above reactions in the cyclization of a chloramino steroid.[6]

Acknowledgments. The authors wish to thank the Abbott Laboratories for financial support (for J. W. A.).

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(7) Guest worker of the National Research Council of Canada, summer 1964.

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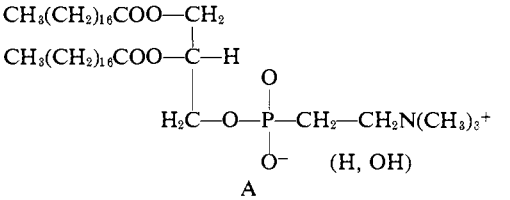
Phosphonolipids. III. Synthesis of a Phosphonic Acid Analog of L-α-(Distearoyl)lecithin

Sir:

The isolation of 2-aminoethylphosphonic acid from the hydrolysates of proteolipid-like fractions of ciliate protozoa of sheep rumen,[1] of ethanolic extracts of the sea anemone *Anthopleura elegantissima*,[2,3] and of the insoluble proteinaceous material of *Metridium dianthus*[4] has been reported. A more extensive distribution of phosphonic acid in natural materials is indicated by the recent isolation of α-amino-β-phosphonopropionic acid from extracts of the Zoanthid, *Zoanthus sociatus*,[5] as well as the isolation of eight other substituted phosphonic acids from *Coelenterata*.[5] Five of these new phosphonic acids were ninhydrin positive. In fact, there is sufficient evidence to suggest that in the lower forms of the plant and animal kingdoms a variety of phosphonic acid containing lipids may exist that are structural analogs of the well-known phospholipids. Thus, Rouser, *et al.*,[3] succeeded in isolating a phosphonic acid containing lipid which proved to be a ceramide aminoethylphosphonate. There is also reasonable evidence for the occurrence in sea anemones of phosphonic acid analogs of lecithins or sphingomyelins.[6]

The synthesis of phosphonic acid analogs of estercephalins[7] and ether-cephalins[8] has been reported recently from this laboratory. The possibility of a natural existence of phosphonic acid analogs of lecithins prompted us to undertake their synthesis. The first of this type, the phosphonic acid analog of L-α-(distearoyl)lecithin (compound A), was obtained *via*



A

the following series of intermediates: (I) diethyl 2-bromoethylphosphonate[9] → (II) 2-bromoethylphosphonic acid monoanilinium salt (m.p. 150–151.5° dec., sintering at 132°. *Anal.* Calcd. for $C_8H_{13}O_3NPBr$ (282.1): C, 34.06; H, 4.64; N, 4.96; P, 10.98; Br, 28.33. Found: C, 33.97; H, 4.67; N, 4.88; P, 10.80; Br, 28.20) → (III) 2-bromoethylphosphonic acid (m.p. 93–95°. *Anal.* Calcd. for $C_2H_6O_3PBr$ (189.0): C, 12.72; H, 3.20; P, 16.39; Br, 42.29. Found: C, 12.80; H, 3.21; P, 16.36; Br, 42.60) → (IV) 2-bromoethylphosphonic acid monochloride (not isolated) → (V) distearoyl L-α-glyceryl-(2-bromoethyl)phosphonate. The analytical data indicated that it was not a pure compound. It was difficult to purify, but after two crystallizations from chloroform–methanol (1:10), treatment of compound V with trimethylamine in dimethylformamide gave in fairly good yield compound VI which was readily obtained in pure state → (VI) distearoyl L-α-glyceryl-(2-trimethylammoniumethyl)-phosphonate (m.p. 198–202°, sintering at 195°; $[\alpha]^{25}D$ +6.9° (*c* 9.4, ethanol-free chloroform–methanol, 3:2, v./v.). *Anal.* Calcd. for $C_{44}H_{90}O_8NP$ (792.2): C, 66.71; H, 11.45; N, 1.77; P, 3.91. Found: C, 66.74; H, 11.11; N (Kjeldahl), 1.68, N (Dumas), 1.79; P, 3.96. The purity of the phosphonolecithin was confirmed by chromatography on silicic acid-impregnated paper[10] with diisobutyl ketone–acetic acid–water (40:25:5), by one-dimensional thin layer chromatography on silica gel H with chloroform–methanol–water (65:25:4), and by two-dimensional thin layer chromatography on silica gel H (1) with chloroform–methanol–water (65:25:4) and (2) with chloroform–methanol–7 *M* ammonium hydroxide (230:90:15). In each case a single spot was obtained. The synthesis of the phosphonic acid analogs of dipalmitoyl and dimyristoyl-L-α-lecithin, and a study of the enzymatic

(1) M. Horiguchi and M. Kandatsu, *Nature*, **184**, 901 (1959).
(2) J. S. Kittredge, E. Roberts, and D. G. Simonsen, *Biochemistry*, 1, 624 (1962).
(3) G. Rouser, G. Kritchevsky, D. Heller, and E. Lieber, *J. Am. Oil Chemists' Soc.*, **40**, 425 (1963).
(4) L. D. Quin, *Science*, **144**, 1133 (1964).
(5) J. S. Kittredge and R. R. Hughes, *Biochemistry*, **3**, 991 (1964).
(6) Private communication from A. A. Benson.
(7) E. Baer and N. Z. Stanacev, *J. Biol. Chem.*, **239**, 3209 (1964).
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