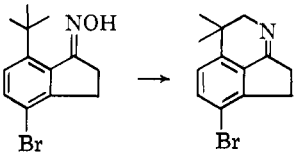
amine. No appreciable attack on the *o*-methyl group was observed. Apparently the β-elimination of a benzylic hydrogen to give the aldimine provides a lower energy reaction path.

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]

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O. E. Edwards, D. Vocelle
Pure Chemistry Division
National Research Council of Canada
Ottawa, Canada

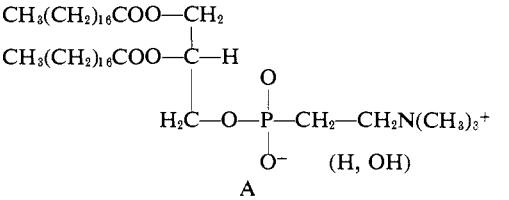
J. W. ApSimon,[7] F. Haque
Department of Chemistry
Carleton University, Ottawa, Canada
Received December 17, 1964

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

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hydrolysis of phosphonolecithins by lecithinase C (from *Cl. welchii*), are in progress in this laboratory.

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Erich Baer, Nikola Z. Stanacev
Subdepartment of Synthetic Chemistry in Relation to Medical Research
Banting and Best Department of Medical Research
University of Toronto, Toronto, Canada
Received December 16, 1964

Convenient Deuterium Labeling for Mass Spectrometry *via* Exchange of Enolizable Hydrogen on a Gas–Liquid Chromatography Column

Sir:

The elucidation of electron-impact-induced fragmentation mechanisms and hydrogen rearrangement processes in organic molecules usually requires substitution of deuterium for hydrogen at certain positions. Direct exchange at activated sites in the molecule is carried out whenever desirable, and a wide variety of "wet" chemical procedures is available for this purpose.[1] A novel procedure is the application of column chromatography which is performed on alumina pretreated with deuterium oxide.[2]

We wish to report the quantitative exchange (96% average total incorporation) of enolizable hydrogen atoms in ketones which is effected during a single pass through a g.l.c. column pretreated with deuterium.[3] In order to ascertain the scope of such an effective exchange procedure, over 50 compounds of various structural types containing exchangeable hydrogen were examined. The compounds listed in Table I were chromatographed at the physical parameters indicated, in each case (but one) a single passage of the sample through the column was performed, and the collected sample was analyzed mass spectrometrically[4] for its deuterium content. The compounds examined were mainly ketones and showed a deuterium uptake on the average of about 96% (see Table I). Under these conditions tetrahydrodicyclopentadiene-8-one[5] failed to incorporate deuterium, as expected, since its enolization would require double bond formation at a bridgehead position. In addition a nitrile, a lactam (cotinine), and an amide were investigated; however, the latter proved to be less susceptible to efficient exchange. Employing this procedure, the results for aldehydes, esters, and lactones were less satisfactory and are currently the subject of further studies.

It is interesting to note that two successive passes of β-naphthyl methyl ketone over neutral, predeuter-

Table I

Deuterated compound[a]	Total deuterium exchange, %	G.l.c. conditions: column temp. (°C.)/retention time (min.)/flow rate (cc./min.)	Remarks
Methyl *n*-nonyl ketone-d_5	97	200/6/80	
2,11-Dodecanedione-d_{10}	93	200/50/80	
Cyclohexanone-d_4	91	160/3 × 4/60	3 passes, 5-ft. column
4-Isopropylcyclohexanone-d_4	96	180/12/40	
Carvomenthone-d_4	94	180/6/60	5-ft. column
Carvone-d_4	96	180/20/40	
Camphor-d_2	94	210/4/120	
Tetrahydrodicyclopentadiene-8-one	0	180/20/40	
cis-10-Methyl-2-decalone-d_4	96	180/35/40	
trans-10-Methyl-2-decalone-d_4	96	180/37/40	
$\Delta^{9(1)}$-10-Methyl-2-octalone-d_5	95	200/32/80	
cis-4,4,10-Trimethyl-5,6-methylene-7-decalone-d_2	90	210/37/120	Rapid loss of deuterium in inlet system
Phenylacetone-d_5	97	180/19/40	
Isovalerophenone-d_2	93	180/21/80	
β-Naphthyl methyl ketone-d_3	95	200/122/80	Ref. 2
Phenylacetonitrile-d_2	96	183/30/80	Measured at 10 e v. ionizing voltage to suppress M − 1 peaks; 96% represents a minimum va ue.
N,N-Diethylacetamide-d_3	42	200/4/80	
Cotinine-d_2 (5′-oxonicotine)	94	210/152/120	Measured at 10 e.v. ionizing voltage to suppress M − 1 peak; 96% represents a minimum value

[a] All compounds listed were, unless stated otherwise, chromatographed on a 10-ft. g.l.c. column.

(1) For a comprehensive review of deuteration procedures, see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. 1., Holden-Day Inc., San Francisco, Calif., 1964, Chapter 2.

(2) K. Mislow, M. A. Glass, H. B. Hopps, E. Simon, and G. H. Wahl, Jr., *J. Am. Chem. Soc.*, **86**, 1710 (1964).

(3) The column packing consisted of Gaschrom Z (100-120 mesh) coated with 10% Carbowax 6000, and 10% KOD (prepared from KOH and D_2O (99.7%)). A 10-ft. column was ready for use after an initial injection of 300 μl. of D_2O and a stabilization period of a few hours. Regeneration of the column was not necessary during the entire course of the current investigation.

(4) All mass spectra were determined on a modified C.E.C. 21-103C mass spectrometer (for details of modifications and performance, see F. C. Walls and A. L. Burlingame, *Anal. Chem.*, in preparation) equipped with a heated glass inlet system operated at 200°. Most spectra were recorded at ionizing voltage 70 e.v., ionizing current 10–50 μa., and 160–180 v. per stage on the multiplier. Representative samples were determined employing a direct inlet system (see A. L. Burlingame, *Advan. Mass Spectrometry*, 3, in press) and scanning the entire mass spectrum in 30 sec.

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