

Fig. 1.—Visible absorption spectra of saturated solution of Na in NaI at 675°.

The spectra were obtained by means of a Beckman DK, double-beam, recording spectrophotometer. Each metal-salt mixture was compared to air in the reference compartment. In order to balance the instrument, the reference beam was attenuated. The results as shown are therefore reported as relative per cent transmission.

Removal of water from reagent grade NaI was done by repeated washings with dry liquid ammonia. Additions of sodium metal were made by carrying the sodium metal over in a diffusion stream of ammonia into the salt. The residual ammonia was removed from the metal-salt mixture by pumping. This method of preparing a mixture of sodium and sodium iodide is identical with the previously described procedure for preparing a mixture of lithium metal with the eutectic LiCl-KCl.¹ This procedure has the advantage of introducing an excess of metal into the salt in order that a concentrated solution be formed upon melting of the salt. In this work the most stringent vacuum conditions were maintained analogous to the work of Dewald and Lepoutre.²

The visible absorption spectra of a saturated solution of Na in NaI at 675° are shown in Fig. 1. The fact that the solution was saturated was indicated by the presence of excess sodium at the bottom of the cuvette upon freezing and by the fact that, as the temperature was raised above 700°, the solution became completely absorbing and no peak structure was observed. Prior to the melting of the salt, the appearance of liquid sodium at the bottom of the cuvette was observed. As the heating was continued, the solid NaI melted at approximately 650° yielding a more transparent region resembling a dark blue solution of sodium in liquid ammonia. In the cell, the monochromatic beam passed through this more transparent region. We arbitrarily chose to make our measurements of this system at 675°. As the temperature was raised above 700°, the system became completely absorbing. When the temperature was lowered to 675°, the band initially observed was reproduced. Upon lowering the temperature still further to 650°, where the NaI began to freeze, the system became opaque.

No discoloration of the glass was observed at the glass-liquid interface. However, in the space above the liquid, the glass was discolored to a dark brown, presumably owing to sodium metal attack.

The location of the F center band in crystalline NaI

- (1) J. Greenberg and I. Warshawsky, *J. Am. Chem. Soc.*, **86**, 3572 (1964).
 (2) J. F. Dewald and G. Lepoutre, *ibid.*, **76**, 3369 (1954).

has been reported to be at both 6090 and 5880 Å.³ Since increasing temperatures cause the peak of the band to shift to lower energies,⁴ the theoretical position of an F band in molten NaI would be at longer wave lengths. The presence of a band with a peak approximately at 570 mμ for a saturated solution of Na in NaI at 675° does not, therefore, appear to be a function of F center formation. Sodium atoms and molecules, however, do absorb in the region of the observed band. Since the position of the peak is close to that of the observed transition for sodium atoms, it is likely that the primary absorbing species are sodium atoms. The absorption at shorter wave lengths may be due to sodium molecules.⁵ The presence of dimers (molecules) in solutions of alkali metals in their molten halides has already been suggested to explain a minimum in the electrical conductances of these systems.⁶

It appears that the alkali metal can be present in three forms in the melt. In the case of dilute solutions (10⁻³ mole % metal) there is a possible interaction of the alkali metal with the melt to form an F center. This has been suggested by Bredig⁷ and can be inferred from the fact that the spectra of such dilute solutions are independent of the metal that has been added. As the concentration of the metal is increased, the spectra can be interpreted in terms of atomic and molecular species of the metal as has been done here for the saturated solution at 675°. Upon further increasing the metal concentration, the solution becomes optically opaque in the visible and typical of the metallic state above the consolute temperature.⁶

(3) H. F. Ivey, *Phys. Rev.*, **72**, 341 (1947).

(4) N. F. Mott and R. W. Gurney, "Electronic Processes in Ionic Crystals," Clarendon Press, London, 1948, p. 116.

(5) G. H. Herzberg, "Spectra of Diatomic Molecules," D. Van Nostrand Co., Inc., Princeton, N. J., 1950.

(6) H. R. Bronstein and M. A. Bredig, *J. Am. Chem. Soc.*, **80**, 2077 (1958).

(7) M. Blander, "Molten Salt Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1964, p. 382.

NATIONAL AERONAUTICS AND SPACE ADMINISTRATION
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Synthesis of L-Ribofuranose and L-Adenosine¹

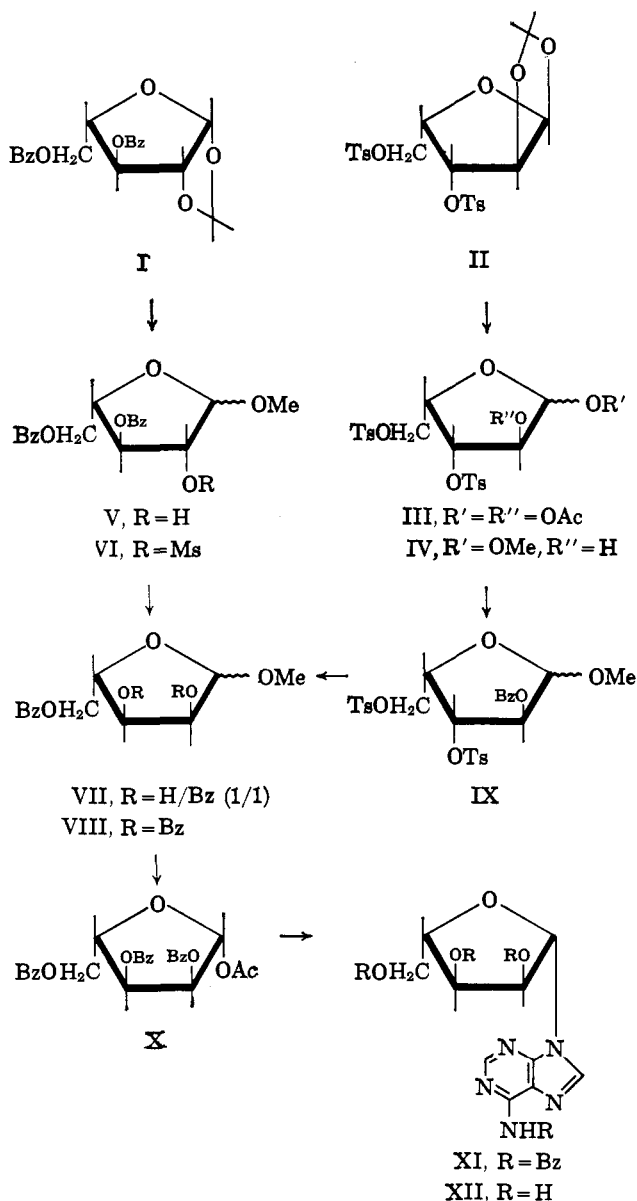
Sir:

Nucleosides of L-ribose would be enantiomorphous with the natural RNA components, and consequently are of great interest for studying physical and biological properties of nucleic acids. Furthermore, L-ribosides of fraudulent heterocyclic bases, *e.g.*, 6-mercaptapurine or 6-thioguanine, might be free of some of the biological properties, *e.g.*, enzymatic cleavage, which lessen the therapeutic value of the widely studied D-ribonucleosides² of these bases. An efficient preparation of L-ribose in the furanose form is essential for the synthesis of L-nucleosides. We now report two new and convenient syntheses of the L-ribofuranose derivative X by application of the sodium benzoate-dimethylformamide (DMF) inversion^{3,4} of sugar sulfonates, and the use of

(1) This work was carried out under the auspices of the Cancer Chemotherapy National Service Center, National Cancer Institute, National Institutes of Health, Public Health Service, Contract No. Ph 43-64-500. The opinions expressed in this paper are those of the authors and not necessarily those of the Cancer Chemotherapy National Service Center.

(2) G. A. LePage and I. G. Junga, *Cancer Res.*, **23**, 739 (1963), and leading references cited therein.

(3) E. J. Reist, L. Goodman, and B. R. Baker, *J. Am. Chem. Soc.*, **80**, 5775 (1958).



X to form the enantiomer XII of adenosine. This is apparently the first enantiomer of a natural D-ribo-nucleoside to be reported.

To start with, the common sugar L-arabinose was converted, as described⁵ for the D-form, to 3,5-di-O-benzoyl-1,2-O-isopropylidene-L-arabinofuranose⁶ (I), m.p. 83–84°, $[\alpha]^{25}_D -20.2^\circ$,⁷ in 22.5% over-all yield. Refluxing methanolic 1% hydrogen chloride⁸ afforded the methyl α,β -furanoside V, which was converted to the 2-O-mesylate VI (19.8% based on L-arabinose). Seventy-two hours was required for nearly complete reaction of VI with sodium benzoate in refluxing DMF; the n.m.r. spectrum of the product showed that 3–5% of unchanged VI remained. The infrared spectrum suggested that the product was largely a monohydroxy-

dibenzoate, as would result⁴ from participation of the neighboring 3-O-benzoyl group in VI. The product, presumably VII, was hydrolyzed with base and then acid to the free sugar, which consisted (60–70%) of L-ribose contaminated with L-arabinose (10%) and L-xylose (20–30%), as determined by paper chromatography and by gas-liquid partition chromatography of the tetrakis-O-(trimethylsilyl) derivatives.⁹ Since the L-arabinose and L-xylose were well over the amounts (3–5% combined) expected to be formed from the unreacted VI (by opening of a 2,3-epoxide), it was concluded that the L-arabino and L-xylo derivatives were actually formed in the inversion step. This is unlike results obtained recently⁴ in the inversion of furanosides in which the sulfonyl and benzoyl groups at C-2 and C-3 were transposed, relative to VI. Further studies of the inversion of VI and attempts to improve the yield of VII will be reported. The inversion product containing VII was benzoylated and acetolyzed to form a mixture of 1-O-acetyl-2,3,5-tri-O-benzoylfuranoses, from which the L-ribo compound X, not previously reported, could be crystallized in 17% yield (2% based on L-arabinose). The infrared and n.m.r. spectra of X, m.p. 130–131°, $[\alpha]^{25}_D -43.6^\circ$,⁷ were identical with those of the D-enantiomer (m.p. 131–132° for a commercial sample, lit.¹⁰ m.p. 130–131°, $[\alpha]_D +44.2$).

A much improved yield of X was obtained (12% over-all¹¹ yield) when the relatively expensive sugar L-xylose was used as starting material. 1,2-O-Isopropylidene-3,5-di-O-tosyl-L-xylofuranose¹⁴ (II, 66% from L-xylose) was converted to the methyl α,β -furanoside IV in 88% yield by acetolysis and mild methanolysis of the intermediate III; direct acidic methanolysis of II to IV was avoided since this apparently entailed side reaction of the tosyl groups and resulted in impure IV. Benzoylation of IV afforded the 2-O-benzoate IX as a semisolid. Methanol crystallization of crude IX afforded 67% of α,β -IX, m.p. 96–110°. Fractional recrystallization resolved the anomers; the less soluble was assumed to be β -IX, m.p. 121–122°, $[\alpha]^{25}_D -23.6^\circ$.⁷ The more soluble α -IX, m.p. 87–89°, $[\alpha]^{25}_D -150.3^\circ$ ⁷ was identified by comparison with its D-enantiomer, m.p. 87–89°, $[\alpha]^{25}_D +156.6^\circ$ ⁷ (obtained from methyl 2-O-benzoyl- α -D-xylofuranoside¹⁵). In inverting crystallized α,β -IX with sodium benzoate-dimethylformamide, 6 hr. at reflux was just sufficient to completely eject the tosyl group. The shorter reaction period, compared to that with VI, may reflect the shift of the sulfonate from C-2 in VI to C-3 in IX, since 6 hr. was sufficient to invert other 2-benzoyl-3-sulfonates recently studied.⁴ The inversion product was again the monohydroxydibenzoate VII, and upon benzoylation and acetolysis, as before, afforded crystalline X. The yield from VIII, 48%, compares well with the 56%

(9) C. C. Sweeley, R. Bentley, M. Makita, and W. W. Wells, *J. Am. Chem. Soc.*, **85**, 2497 (1963).

(10) R. K. Ness, H. W. Diehl, and H. G. Fletcher, Jr., *ibid.*, **76**, 763 (1954).

(11) Methods available in the literature, but not so far applied to the synthesis of X, would entail partial conversion of L-arabinose to L-ribose by oxidation of the arabinol,¹² and formation of X from L-ribose as for the D-form,¹⁴ with an over-all yield of 5.6%.

(12) F. L. Humoller, *Methods Carbohydrate Chem.*, **1**, 83 (1962).

(13) E. F. Recondo and H. Rinderknecht, *Helv. Chim. Acta.*, **42**, 1171 (1959).

(14) L. Vargha, *Chem. Ber.*, **87**, 1351 (1954).

(15) R. E. Schaub and M. J. Weiss, *J. Am. Chem. Soc.*, **80**, 4683 (1958).

(4) K. J. Ryan, H. Arzoumanian, E. M. Acton, and L. Goodman, *J. Am. Chem. Soc.*, **86**, 2497, 2503 (1964).

(5) E. J. Reist, P. A. Hart, L. Goodman, and B. R. Baker, *ibid.*, **81**, 5176 (1959).

(6) Satisfactory elemental analyses were obtained for the new compounds described herein.

(7) Optical rotations were determined in 1% chloroform solutions, except for those of L- and D-adenosine which were done in 0.5% aqueous solutions.

(8) Prepared with concentrated hydrochloric acid instead of anhydrous hydrogen chloride to avoid dimerization⁴ of the sugar. We are indebted to Dr. E. J. Reist of these laboratories for the suggestion.

reported¹⁶ for acetylation of the β -D-ribofuranose tetra-benzoate.

9-(β -L-Ribofuranosyl)adenine (L-adenosine, XII) was prepared from X by coupling of the resultant chloro sugar with chloromercuri-6-benzamidopurine, according to the procedure for D-adenosine¹⁷; after deblocking of XI and regeneration of XII picrate, the yield of L-adenosine from X was 43%, m.p. 232–235°, $[\alpha]^{25D} +61.4^\circ$, $\lambda_{\max}^{\text{pH}11}$ 257 m μ (ϵ 14,600), $\lambda_{\max}^{\text{pH}13}$ 260 m μ (ϵ 15,200). Values for natural D-adenosine, lit.¹⁷ m.p. 233–235°, determined simultaneously were $[\alpha]^{25D} -60.2^\circ$, $\lambda_{\max}^{\text{pH}11}$ 257 m μ (ϵ 14,600), $\lambda_{\max}^{\text{pH}13}$ 260 (15,100).

The preparation of other L-nucleosides, for example, those derived from 6-mercaptapurine, guanine, and thioguanine, is in progress.

(16) R. K. Ness and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **76**, 1663 (1954).

(17) J. Davoll and B. A. Lowy, *ibid.*, **73**, 1650 (1951), wherein the chloro sugar was the triacetate.

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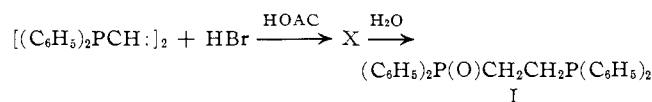
EDWARD M. ACTON
KENNETH J. RYAN
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RECEIVED SEPTEMBER 30, 1964

Reduction and Isomerization of *cis*- and *trans*-1,2-Vinylenebis(diphenylphosphines) and Disulfides

Sir:

cis-1,2-Vinylenebis(diphenylphosphine) has been reported to be resistive to catalytic hydrogenation.¹ We have found that vinylenebis(diphenylphosphines) react with hydrogen bromide in hot glacial acetic acid, leading to the isolation of 1,2-ethylenebis(diphenylphosphine) monoxide, by aqueous work-up.

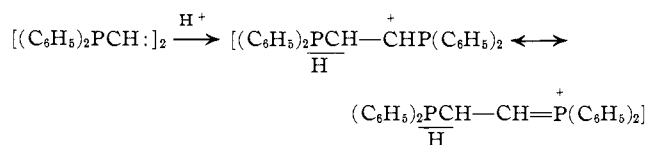


Crystals of I precipitated from the reaction mixture upon standing at room temperature. After air drying, I melted at 190.5–193°. *Anal.* Calcd. for $\text{C}_{26}\text{H}_{24}\text{O-P}_2$: C, 75.40; H, 5.80; P, 14.99. Found: C, 74.94; H, 5.77; P, 14.87. The infrared spectrum of I indicates the presence of a phosphoryl group. The p.m.r. spectrum of a deuteriochloroform solution of I shows a phenyl hydrogen complex centered at $\delta = 7.4$ p.p.m. and a doublet centered at $\delta = 2.37$ p.p.m., $J_{\text{P-CH}} = 2.0$ c.p.s., integrating in the ratio of 5:1, respectively. Whereas the methylenes of 1,2-ethylenebis(diphenylphosphine) showed up as a triplet, those of the corresponding dioxide, di(N-phenylimine), and disulfide appear as doublets in the p.m.r. spectra.² The methylenes of 1,2-ethylenebis(triphenylphosphonium) dibromide also give rise to a doublet.³ The surprising lack of differentiation between the two sets of methylene protons in the monoxide by p.m.r. is not fully understood at present.

Assignment of the ethylenebis(diphenylphosphine) monoxide structure to I is supported by its ready conversion to 1,2-ethylenebis(diphenylphosphine) dioxide and its reaction with benzyl bromide to yield a phosphonium salt. Further support for the structure assignment comes from comparison of the retention

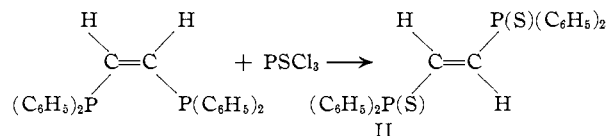
times of the two peaks obtained from I on a 3 ft. \times 1/8 in. silicone DC-200 column at 310° with those of the last two peaks of the three progressively smaller peaks obtained upon introduction of 1,2-ethylenebis(diphenylphosphine) into the column.⁴ The last of these peaks has been shown to be identical in retention time with that of 1,2-ethylenebis(diphenylphosphine) dioxide. The larger, shorter retention-time peak from I is identical with the second, medium-size peak of the diphosphine.

Protonation of the 1,2-vinylenebis(diphenylphosphines) at either the carbon or phosphorus would be expected to lead to a carbonium ion α and β to trivalent phosphorus atoms.



Similar treatment of α -hydroxy- and alkoxyalkyl-diphenylphosphines has been shown by Trippett to lead to alkyldiphenylphosphine oxides, indicating that α -phosphinylcarbonium ions may behave as phosphonium ions.⁵ Formation of cyclic polyphosphonium ions followed by hydrolysis cannot be excluded as a possible explanation. β -Phosphinylcarbonium ions would be expected to form cyclic phosphonium salts by either an intermolecular or intramolecular process.

Attempts at pyrolytic or photochemical isomerization of 1,2-vinylenebis(diphenylphosphines) have failed. Phosphorus trichloride is also ineffective. We have found that thiophosphoryl chloride in refluxing tetrahydrofuran converts *cis*- or *trans*-1,2-vinylenebis(diphenylphosphine) to *trans*-1,2-vinylenebis(diphenylphosphine) disulfide (II).



Treatment of *trans*-1,2-vinylenebis(diphenylphosphine) with sulfur in benzene also produced II, m.p. 196–197°. *Anal.* Calcd. for $\text{C}_{26}\text{H}_{22}\text{P}_2\text{S}_2$: C, 67.82; H, 5.78; P, 13.47; S, 13.91; mol. wt., 460. Found: C, 67.78; H, 4.77; P, 13.48; S, 13.89; mol. wt., 434 (Rast) after recrystallization from ethanol-water. The infrared spectrum of II showed bands at 8.9 (m) and 10.18 (m) μ which are not present in the *cis* isomer or saturated analog, indicative of the *trans* structure. The p.m.r. spectrum of a tetrahydrofuran solution of II showed a triplet centered at δ 8.2 p.p.m., $J_{\text{P-CH}} = 24$ c.p.s. overlapping with the phenyl protons centered at about $\delta = 7.6$ and 7.92 p.p.m. Integration showed the ratio to be essentially 1:10. Treatment of II with 30% hydrogen peroxide in glacial acetic acid produced *trans*-1,2-vinylenebis(diphenylphosphine) dioxide.⁶

Sulfur treatment of a benzene solution of *cis*-1,2-vinylenebis(diphenylphosphine) led to *cis*-1,2-vinylenebis(diphenylphosphine) disulfide (III), which had a

(1) A. M. Aguiar and D. Daigle, *J. Am. Chem. Soc.*, **86**, 2299 (1964).

(2) A. M. Aguiar and J. Beisler, *J. Org. Chem.*, **29**, 1660 (1964).

(3) C. E. Griffin, private communication.

(4) A. M. Aguiar, H. J. Greenberg, and K. E. Rubenstein, *J. Org. Chem.*, **28**, 2091 (1963).

(5) S. Trippett, *J. Chem. Soc.*, 2813 (1961).

(6) A. M. Aguiar, J. Beisler, and A. Mills, *J. Org. Chem.*, **27**, 1001 (1962).