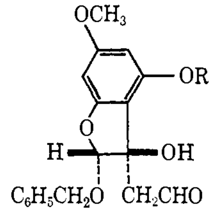
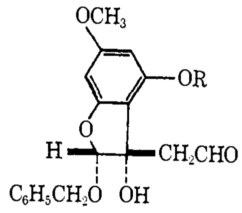
The bromoketone **6**, mp 170–172° (86%), prepared from the ketone **5** and phenyltrimethylammonium perbromide[11] in tetrahydrofuran on treatment with hot benzyl alcohol in the presence of calcium carbonate, gave the dibenzyl ether **7**, mp 45–47° (70%). Addition of allylmagnesium bromide in ether to a solution of the ketone **7** in tetrahydrofuran produced a mixture of epimeric allyl carbinols. When the latter was submitted to the action of sodium periodate–osmium tetroxide[12] in aqueous dioxane, a mixture of epimeric aldehydes (60% from **7**) containing 12 parts of the oily *trans* epimer **10** and one part of the *cis* isomer **8**, mp 90–91°, was formed.

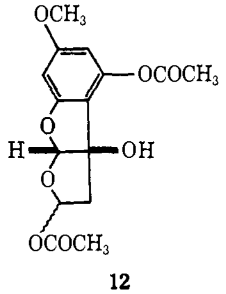


8, R = $CH_2C_6H_5$
9, R = CH_3CO

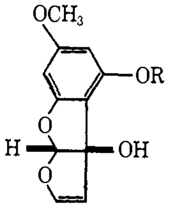


10, R = $CH_2C_6H_5$
11, R = CH_3CO

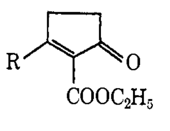
Catalytic hydrogenolysis of **8** or **10** over a 10% Pd–C catalyst in benzene–acetic anhydride containing sodium acetate eliminated one of the two benzyl groups and produced the diastereomeric acetates **9** or **11**. A second reduction of either **9** or **11** over the same catalyst, but in ethyl acetate solution followed by acetylation of the crude product with acetic anhydride in pyridine at −30°, furnished the tricyclic diacetate **12**, mp 129–131° (35% from either **8** or **10**). Pyrolysis of a toluene solution of the diacetate **12**, in a short-contact continuous-flow system at 450°, afforded the vinyl ether **13**, mp 118–120° (75%). The corresponding oily phenol **14** (94%) prepared by hydrolysis of the acetate **13** with sodium bicarbonate in methanol–water could not be condensed with 2-carbethoxycyclopentane-1,3-dione (**15**)[13] although a variety of catalysts were explored. The more electrophilic chloride **16** (80%), prepared from the enol **15** and oxalyl chloride in benzene solution at 0°, however, condensed rapidly with the phenol **14** in methylene chloride in the presence of zinc carbonate to give the coumarin **1** (20%). Identity with natural, optically active aflatoxin-M$_1$ was established by comparison of infrared, ultraviolet, and mass spectra as well as by thin layer chromatographic behavior.[14]



12



13, R = $COCH_3$
14, R = H



15, R = OH
16, R = Cl

The biological properties of racemic aflatoxin-M$_1$ will be discussed in forthcoming papers by Professor G. N. Wogan, Department of Food Science and Nutrition, Massachusetts Institute of Technology.

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[14] We are much indebted to Drs. A. C. Keyl and A. C. Waiss, Western Regional Research Laboratory, Agricultural Research Service, U. S. Department of Agriculture, Albany, Calif., for a sample of natural aflotoxin-M$_1$.

[15] National Institutes of Health Postdoctoral Fellow, 1967–1968.

G. Büchi, Steven M. Weinreb[15]
Department of Chemistry
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Received July 9, 1969

Arabinonucleotides. II. The Synthesis of O^2,2′-Anhydrocytidine 3′-Phosphate, a Precursor of 1-β-D-Arabinosylcytosine

Sir:

We have recently described a thermal rearrangement of polynucleotidic 2′,3′,5′-cyclic triesters obtained from oligouridylic acid, which provides a convenient route to the synthesis of oligoarabinouridylic acid.[1] A related idea proved to be useful for the synthesis of O^2,2′-anhydrocytidine 3′-phosphate, which is a precursor[2] of 1-β-D-arabinosylcytosine,[3] an antiviral[4] and carcinostatic[5] agent. The cyclic trimethylsilyl ester moiety in fully trimethylsilylated cytidine 2′,3′-cyclic phosphate (**1**) was expected and found to be a good intramolecular leaving group in a sense as outlined in Scheme I. The structure of the intermediates **1** and **2** has not yet been firmly established.

The preparation can be very simply performed at any scale ranging from 0.1 to 20 mmol. Dry tri-*n*-butylammonium cytidine 2′,3′-cyclic phosphate[6] was suspended in a mixture of 50 equiv of anhydrous pyridine and 2 equiv of tri-*n*-butylamine to which 6–10 equiv of trimethylsilyl chloride was added dropwise at room temperature. The reaction mixture was kept for 1 hr at 80° and then concentrated *in vacuo* to a gum, which was shaken with ice and chloroform. The pH of the aqueous phase should be around 4.5. Colorless needles of pure O^2,2′-anhydrocytidine 3′-phosphate (**3**) were obtained directly from the aqueous solution or upon the addition of 10–20% acetone (yield over 50%). Further addition of acetone precipitated a slightly contaminated material, which could be purified by passing through a small column of Dowex 1-X2 (formate) resin in water. Total isolated yield of O^2,2′-anhydrocytidine 3′-phosphate was consistently between 70 and 80%.

The analytical sample was obtained on recrystallization from water–acetone and after drying 12 hr at 0.02 mm over P_2O_5.

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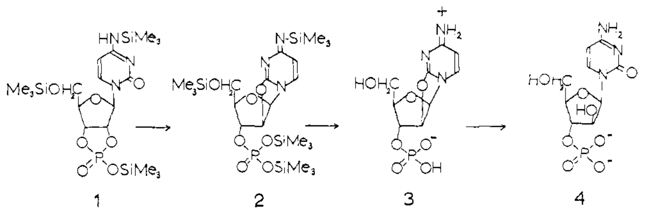
Anal. Calcd for $C_9H_{12}N_3O_7P \cdot H_2O$ (323.20): C, 33.45; H, 4.35; N, 13.01; P, 9.60. Found: C, 33.47; H, 4.44; N, 12.90; P, 9.8 (titration). The uv spectrum exhibited the characteristic features of this system:[3] λ_{max} 231 (ϵ 9550), 262.5 mμ (ϵ 10,640); λ_{min} 243 mμ (ϵ 6480) in water, pH 1–7. Characteristic ir frequencies were 1665, 1376, 1358, 1252, 1212, 1060, and 932 cm^{-1}. The nmr spectrum taken at 100 MHz in D_2O at pD 7 featured the following resonances [δ ppm (J Hz) relative to TMS]: a doublet of H-6 at 8.61 (7.5); two unresolved doublets of H-5 and H-1′ centered at 7.09 (7.5) and 7.15 (5.5), respectively; a doublet of H-2′ at 6.24 (5.5). The clear separation of the H-2′ signal is remarkable when compared with other nucleotide spectra,[7] and it must be due to the combined deshielding effect of the isourea and phosphate groups. The ORD characteristics in water ([M] at c 10^{-4} M) were: peak at 282 mμ, +6200°, trough at 239 mμ, −20,800°; crossover at 268 mμ.

Several interesting reactions of **3** are currently under study. Its hydrolysis is pH dependent and general base catalyzed above its pK_2 (5.7).[2] At pH 1 to 7 a partial conversion to cytidine 2′,3′-cyclic phosphate can take place, which can be followed by electrophoresis at pH 6. Treatment with alkali or bicarbonate gave aracytidine 3′-phosphate[8] (**4**) as the only product.

Scheme I



The identification of **4** was carried out by comparison with all published data. Its 100-MHz nmr spectrum in D_2O exhibited the following signals relative to acetone as internal standard: at pD 7: H-6, δ 5.65 (8); H-5, 3.83 (8); H-1′, 4.03 (3); at pD 4: H-6, 5.87 (8); H-5, 4.02 (8); H-1′, 3.99 (3). The nmr and uv spectra were in good agreement with those of Wechter.[9] The ORD characteristics in 0.1 M Na_2HPO_4, pH 7.8 ([M] at c 9.3 × 10^{-5} M) were: peak at 288 mμ, +15,900°; broad trough centered at 240 mμ, −18,800°; crossover at 272 mμ. We also obtained good elementary analysis from the crystalline free acid. Furthermore, alkaline phosphatase hydrolysis liberated 1-β-D-arabinosylcytosine which was identical with the commercial sample (Sigma) by all usual criteria.

The concept of a cyclic phosphate derivative as an intramolecular leaving group has already been proposed[10] as the mechanism of anhydronucleotide formation in polyphosphoric acid.[3] Our work on the alkyl[1] and silyl esters of cytidine 2′,3′-cyclic phosphate represents a direct experimental proof and a further development of the same general concept. This novel reaction provides an extremely simple and economical way to the most suitable intermediate for a direct polymerization of aracytidylic acid. The possibility of similar rearrangements should also be considered in connection with mass-spectrometric work on oligonucleotides. It is noteworthy that the trimethylsilylated uridine 2′,3′-cyclic phosphate and adenosine 3′,5′-cyclic phosphate did not show any change under the same conditions.

Acknowledgment. The author gratefully acknowledges the contribution of Dr. D. H. O'Brien in taking the nmr spectra and Mr. B. J. Henrici in performing some of the experiments. This work was supported by grants from the National Institutes of Health (GM-16213) and the Texas A&M Research Council.

Joseph Nagyvary
Department of Biochemistry & Biophysics
Texas A & M University
College Station, Texas 77843
Received May 15, 1969

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(10) See Ph.D. theses of E. R. Walwick and W. K. Roberts, University of California, Berkeley, 1958 and 1960, respectively; also T. Ueda and J. J. Fox, *Advan. Carbohyd. Chem.*, **22**, 369 (1967).

A New Class of Tripty cene-Like Binuclear Ions Containing Three 1,2- *Dihapto*pyrazolide Bridges

Sir:

We wish to report a new class of binuclear ions of triptycene-like structure which contain an array of three 1,2-*dihapto*pyrazolide[1] units acting as one trinegative bistridentate ligand of D_{3h} symmetry.

Instances of three identical ligands bridging two like nuclei have been scarce. They include the old example of $Fe_2(CO)_9$ containing three carbonyl bridges, the trihalo-bridged molybdenum carbonyl species [π-$C_3H_5(CO)_2Mo(X)_3Mo(CO)_2$-$\pi$-$C_3H_5$]$^-$ reported by Murdoch,[2] the alkoxy and alkylthio analogs derived therefrom,[3] as well as the more recent examples of tri-μ-hydrido- and tri-μ-alkoxy-dirhenate(I) ions.[4] In each of these cases the two metals are bridged by the same atom. It was thought that pyrazolide ion (of C_{2v} symmetry) should be capable of acting similarly as a tris-bridging 1,2-*dihapto* ligand, especially since bridging of two unlike nuclei by what may be formally regarded as pyrazolide ions has been demonstrated in the special case of transition metal tris(1-pyrazolyl)borates.[5]

This expectation has been realized and the new class of complexes is illustrated by the following two examples of a cationic, tetrahedral species I and an anionic, octahedral species, II.

I was synthesized in 22% yield by the reaction of pyrazolide ion with ethylborylene bis-p-toluenesulfonate[6] and was isolated as the hexafluorophosphate, mp 299–301°.

The structure of this salt was established by analysis (*Anal.* Calcd for $C_{13}H_{19}B_2F_6N_6P$: C, 36.7; H, 4.47; F, 26.8; N, 19.7; P, 7.28. Found: C, 36.9; H, 4.54; F, 26.9; N, 20.1; P, 7.31) and particularly by the nmr spectrum which had a doublet (J = 2.5 cps)

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(1) For the *hapto* nomenclature see F. A. Cotton, *J. Am. Chem. Soc.*, **90**, 6230 (1968).

(2) H. D. Murdoch, *J. Organometal. Chem.*, 4, 119 (1965).

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(6) Ethylborylene bis-p-toluenesulfonate was prepared *in situ* in a manner analogous to that used for making dialkylboryl sulfonates,[7] except that the triethylborane:p-toluenesulfonic acid ratio was 1:2 and longer heating was required to complete the evolution of 2 equiv of ethane.

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