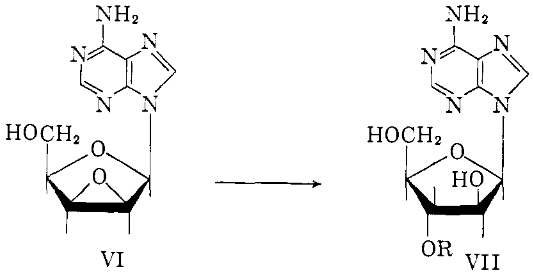
fluorodeoxyuridine,[3] which is *cleaved in vivo* with resultant decrease in biological activity.[4,5] Since nucleosides derived from β-D-arabinofuranose (I) have many of the substrate properties of 2′-deoxynucleosides, except cleavage of the base, nucleosides such as I with a fraudulent base could have useful anticancer properties.

Chemical formation of a nucleoside from 2,3,5-tri-O-acetyl-D-arabinofuranosyl bromide with the properly substituted adenine gave the *alpha*-anomer of 9-(D-arabinofuranosyl)-adenine[6] with the now predictable[7] C_1C_2-*trans* configuration. By a presumably general method that should have considerable utility for synthesis of the desired fraudulent-base nucleosides of Type I, this Communication reports the first synthesis of a 9-(D-arabinofuranosyl)-purine with the *beta*-configuration.

9-(3′,5′-O-Isopropylidene-β-D-xylofuranosyl)-adenine (III)[8] with methanesulfonyl chloride in pyridine gave 9-(3′,5′-O-isopropylidene-2′-O-methanesulfonyl-β-D-xylofuranosyl)-adenine (IV), m.p. 212°, in 63% yield (Found for $C_{14}H_{19}N_5O_6S$: C, 43.4; H, 4.95; N, 18.1). Deacetonation of IV with 90% aqueous acetic acid at 100° for 6 hours gave a 60% yield of 9-(2′-O-methanesulfonyl-β-D-xylofuranosyl)-adenine (V), m.p. 171–172° (Found for $C_{11}H_{15}N_5O_6S$: C, 38.4; H, 4.43; N, 20.2; S, 9.01). Treatment of V in refluxing methanolic sodium methoxide for 12 minutes resulted in an 87% yield, after purification via the picrate of VI, of the very water-soluble anhydronucleoside VI, m.p. 205–206° (Found for $C_{10}H_{11}N_5O_3$: C, 48.2· H, 4.50· N, 27.9).

When VI was heated at reflux with sodium benzoate in N,N-dimethylformamide (DMF) containing 5% water for 6 hours, a 54% crude yield of crystalline 9-(β-D-arabinofuranosyl)-adenine (VII, R = H),[9] m.p. 257° after recrystallization, $[\alpha]^{27}_D$ −5° (0.25% in water),[10] could be isolated as a hemihydrate (Calcd. for $C_{10}H_{13}N_5O_4 \cdot 0.5H_2O$: C, 43.5; H, 5.11; N, 25.4. Found: C, 43.9; H, 4.81; N, 25.5). The arabinoside (VII, R = H) was readily separable from the isomeric 9-(β-D-xylofuranosyl)-adenine[8] on paper chromatography in three solvent systems, and the crude product showed only a trace of this isomeric xyloside. The very predominant opening of VI at C_3 follows the usual pattern.[11]



VI VII

The conversion of VI to VII (R = H) could also be effected in comparable yield with sodium acetate in 95% DMF but could only be obtained in trace amounts (as shown by paper chromatography) by the reaction of sodium benzoate in diethylene glycol dimethyl ether containing 5% water, under the same conditions of time and temperature as in the DMF reactions. One of the usual reagents for opening sugar epoxides, namely, potassium hydroxide,[12] caused cleavage of VI to adenine and no VII (R = H) was formed. With sodium acetate in boiling acetic acid containing acetic anhydride, VI was recovered unchanged after deacetylation.

These results suggest that a complex between DMF and the carboxylate salts is formed which enhances the nucleophilicity of the latter; this Communication, then, adds another important example of the utility of the DMF–sodium benzoate reagent.[13]

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[3] R. Duschinsky, E. Pleven, J. Malbica and C. Heidelberger, Abstr. 132nd Meeting, Am. Chem. Soc., 1957, p. 19-C; M. Hoffer, R. Duschinsky, J. J. Fox and N. Yung, THIS JOURNAL, **81**, 4112 (1959), and references therein.

[4] S. S. Cohen, J. G. Flaks, H. D. Barner, M. R. Loeb and J. Lichtenstein, *Proc. Natl. Acad. Sci.*, **44**, 1004 (1958).

[5] N. K. Chaudhuri, K. L. Mukherjee and C. Heidelberger, *Biochemical Pharmacology*, **1**, 328 (1959).

[6] N. W. Bristow and B. Lythgoe, *J. Chem. Soc.*, 2306 (1959).

[7] B. R. Baker in G. E. W. Wolstenholm and C. M. O'Conner, "The Chemistry and Biology of Purines," J. and A. Churchill Ltd., London, 1957, p. 120.

[8] B. R. Baker and K. Hewson, *J. Org. Chem.*, **22**, 966 (1957).

[9] In the original conversion of VI to VII, a sodium methoxide treatment was included in the processing to convert any VII (R = Bz) that may have been formed to VII (R = H). In later experiments which omitted the sodium methoxide treatment, paper chromatography of the crude product showed that only traces, if any, of the 3′-O-benzoate of VII could have been present. Evidently the first-formed benzoate VII (R = Bz) is hydrolyzed to VII (R = H) in the slightly alkaline medium.

[10] Compound VII (R = H) is only slightly soluble in water and the $[\alpha]_D$ value reported in this Communication is subject to a large uncertainty. The value is being redetermined in a better solvent but the present value affords a comparison with the α-anomer which had m.p. 208° and $[\alpha]^{17}_D$ +69° (1.1% in water) as the anhydrous compound.[1]

[11] For further discussion of this point, see (a) C. D. Anderson, L. Goodman and B. R. Baker, THIS JOURNAL, **81**, 898 (1959), and (b) R. E. Schaub and M. J. Weiss, *ibid.*, **80**, 4683 (1958).

[12] G. J. Robertson and W. Whitehead, *J. Chem. Soc.*, 319 (1940).

[13] (a) E. J. Reist, R. R. Spencer and B. R. Baker, *J. Org. Chem.*, **24**, 1618 (1959); (b) E. J. Reist, L. Goodman and B. R. Baker, THIS JOURNAL, **80**, 5775 (1958).

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RECEIVED APRIL 2, 1960

HIGHLY STRAINED BICYCLIC SYSTEMS. III. THE STEREOCHEMISTRY AND REARRANGEMENT OF THE 1,5,5-TRIMETHYLBICYCLO[2,1,1]HEXANE-6-CARBOXYLIC ACIDS[1]

Sir:

The demonstration by Horner and Spietschka that photolysis of diazocamphor (I) leads to a 1,5,5-trimethylbicyclo[2,1,1]hexane-6-carboxylic acid (II)[2] (equation 1), has opened the way to the synthesis of a variety of interesting bicyclic systems.[3] One important feature of this work which remained to be clarified was the stereochemistry of the product. In studying a related

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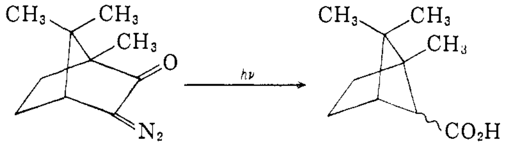
[1] The support of this work by the National Science Foundation and the Alfred P. Sloan Foundation is gratefully acknowledged.

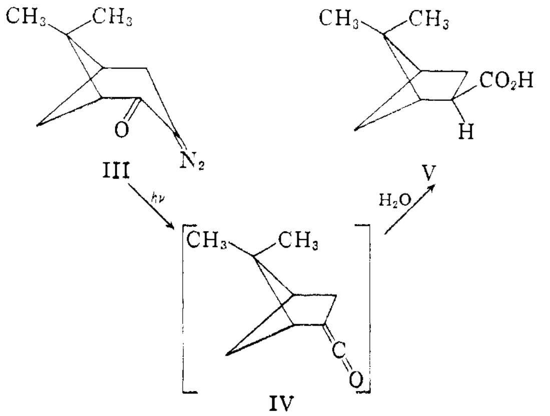
[2] L. Horner and E. Spietschka, *Chem. Ber.*, **88**, 934 (1955).

[3] See, for example, J. Meinwald and P. G. Gassman, Abstracts of Papers presented at the April 1959 meeting of the American Chemical Society in Boston, p. 14-O. A fuller account of this work will soon appear in THIS JOURNAL.



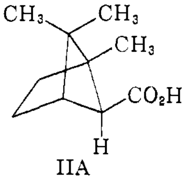
I II (1)

reaction sequence applied to the diazoketone III,[4,5] we have come to the general conclusion that hindered ketenes generated by the technique of irradiation at moderate temperatures hydrate from the less hindered side of the molecule, to give the less stable of the two possible epimeric acids (equation 2).

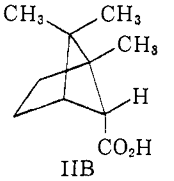


(2)

That the acid II (m.p. 100-101°, $[\alpha]_D$ +13.8° ($CHCl_3$)) is in fact the less stable of the two possible epimers (IIA and IIB) has now been demonstrated by its quantitative isomerization, brought



IIA

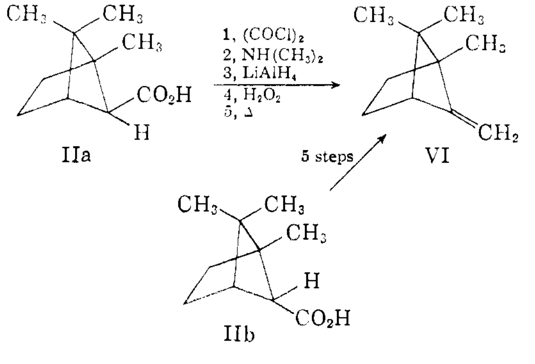


IIB

about by esterification with diazomethane (giving the expected methyl ester, b.p. 100° (18 mm.), n^{28}_D 1.4570, $[\alpha]_D$ +29° (EtOH)), then simultaneous epimerization and saponification in aqueous-alcoholic base. The new isomer[5] (m.p. 43.0-43.5°, $[\alpha]_D$ +68.7° ($CHCl_3$)) gave a methyl ester (b.p. 98° (19 mm.), n^{28}_D 1.4545, $[\alpha]_D$ +64.4° (EtOH)) easily distinguishable from that of the original acid in the fingerprint region of its infrared spectrum; the two isomers were readily separable by gas chromatography.

The epimeric relationship between these two isomeric acids was demonstrated rigorously by the conversion of each to the common olefin, VI (m.p. 60-61°, $\lambda\lambda_{max}$ 3.29, 5.96, 11.56 μ) as outlined in Chart 1. Using the elegant tables recently set up by Wilcox,[6] it is possible to assign the *exo*-configuration (IIA) to the photolysis product, and the *endo*-configuration (IIB) to the more stable, lower-melting epimer. Thus, it can be estimated that the distance from the *center* of the carboxyl carbon of IIA to the *edge* of the *syn*-C_5 methyl group hydrogen is only 0.80 Å., while the distance from the center of the carboxyl carbon of IIB to the edge of the transannular hydrogen atoms is 1.12 A.[7] (see Fig. 1.)

CHART I



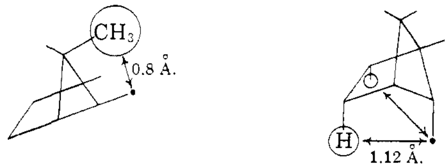


Fig. 1.

These results take on additional interest for the reason that an "epimer" of II had been described by Horner as having quite different properties from those of our product. We have prepared some of this "epimer," essentially by Horner's procedure involving treatment of II with concentrated sulfuric acid, in order to clarify the rather confusing picture. The acidic product obtained in *ca.* 20% yield had properties in agreement with those reported[2] (m.p. 81-82°, $[\alpha]_D$ −26.9° ($CHCl_3$)), and appears therefore to be a third isomeric form of II. Although we have not yet determined the structure of this material, it is clear that *its formation must have involved a hitherto unsuspected rearrangement.*

The *chief product* formed in the reaction of sulfuric acid with IIA or IIB was found to be a rearranged γ-lactone, $C_{10}H_{16}O_2$ (b.p. 75-77° (0.7 mm.), m.p. 36-37°, $[\alpha]_D$ +3.9° (EtOH), λ_{max} 5.64 μ). Consideration of the reactions that II might undergo in strong acid, and of the properties of the known γ-lactones with the formula $C_{10}H_{16}O_2$, led to the conclusion that this product might be *dihydro-β-campholenolactone*, VII. This conclusion has been confirmed by a direct comparison of our product with an authentic sample of VII[8] (superimposable infrared spectra) and of its lithium aluminum hydride reduction product with an authentic sample of the diol VIII[8] (mixture m.p. undepressed, superimposable infrared spectra).

---

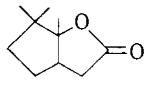
[4] J. Meinwald and P. G. Gassman, THIS JOURNAL, **82**, in press (1960).

[5] Satisfactory analytical data were obtained for all new compounds encountered in this work.

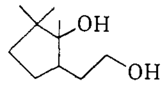
[6] C. F. Wilcox, Jr., THIS JOURNAL, **82**, 414 (1960).

[7] The values for van der Waals radii of hydrogen and methyl used in this calculation were those given by L. Pauling, "The Nature of the Chemical Bond," 3rd Ed., Cornell University Press, Ithaca, N. Y., 1960, p. 260.

[8] J. D. Connolly and K. H. Overton, *Proc. Chem. Soc.*, 188 (1959). We are most grateful to Dr. Overton for supplying samples of VII and VIII.



VII



VIII

These results (1) establish the configurations of photolytically generated II and its previously unknown epimer and (2) uncover a novel rearrangement of IIA and B to give VII and an isomeric acid of unknown structure.

[9] Fellow of the Alfred P. Sloan Foundation.

[10] National Science Foundation Cooperative Fellow, 1959–1960.

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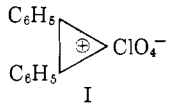
RECEIVED MARCH 24, 1960

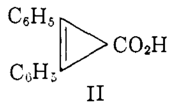
THE DIPHENYLCYCLOPROPENIUM ION: PYROLYSIS OF 3,3-BIS-(1,2-DIPHENYLCYCLOPROPENYL) ETHER

Sir:

We wish to report a convenient synthesis of diphenylcyclopropenium perchlorate (I).[1] Reaction of 1,2-diphenylcyclopropene-3-carboxylic acid (II)[2] with 10% perchloric acid in acetic anhydride[3] at 0–10° resulted in the evolution of carbon monoxide[4] with concomitant formation of colorless needles of the explosive I, isolated in 70% yield, m.p. 149.5–150.5° (dec.) (from acetonitrile–benzene). Found: C, 61.81; H, 4.25; Cl, 12.23. The presence of perchlorate ion in the product was indicated by a positive test with methylene blue[5] and the presence of strong absorption at 9.1μ characteristic of perchlorate ion in its infrared spectrum. The substance is insoluble in benzene and dichloromethane, but soluble in acetonitrile, dimethylformamide and aqueous sulfuric acid. The spectral properties of I provide interesting confirmation of its ionic nature in that the infrared spectrum exhibits a sharp band at 3.18μ absent from the spectra of the covalent diphenylcyclopropenes encountered in this work, while the ultraviolet spectrum in acetonitrile–10% ethanol exhibits a transition from that characteristic of the covalent diphenylcyclopropenes[6] (λ_m 318, 303, 288, 231, 223 mμ; log ϵ 4.38, 4.50, 4.37, 4.22, 4.31) below *ca.* 0.05 *N* perchloric acid to one very similar (λ_m 305, 292, 246; log ϵ 4.52, 4.50, 4.03) to that of the triphenylcyclopropenium ion[6] in 0.05 to 0.1 *N* perchloric acid. Chemical evidence for the assigned structure was provided by hydrolysis of I in aqueous potassium hydroxide to give α-phenylcinnamaldehyde identical with an authentic sample.[7] The general utility of the preparative method for I is suggested by the similar preparation of dipropylcyclopropenium perchlorate by Breslow and Höver.[8]



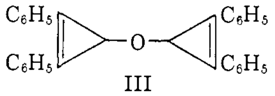
I



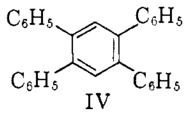
II

Hydrolysis of I in aqueous sodium bicarbonate resulted in the formation of 3,3-bis-(1,2-diphenylcyclopropenyl) ether (III), m.p. 163–165° (dec.). Found: C, 90.37; H, 5.58. The structural assignment follows from the spectroscopic properties of the product; λ_m (CH_3CN) 319, 303, 290, 231, 224; log ϵ 4.63, 4.74, 4.63, 4.54, 4.61; λ_m (0.1 *N* $HClO_4$, CH_3CN) 305, 292, 246; log ϵ 4.82, 4.80, 4.28. Pyrolysis of III at 180° for a short time yielded a mixture of products containing, as the major component, 1,2,4,5-tetraphenylbenzene (IV), m.p. 264.5–267°, identical with an authentic sample.[9] In addition, *2,3,4,6-tetraphenylphenol* (V) m.p. 247–248°, identical with an authentic specimen,[10] was isolated as the only phenolic component detectable by infrared spectroscopy.

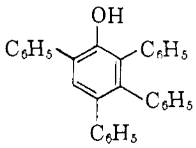
The photolysis of III, and the mechanistic implications of its pyrolysis are currently under investigation.



III



IV



V

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[1] Salts of this cation have been prepared independently by R. Breslow and J. Lockhart, unpublished work, by reaction of phenylchlorocarbene with phenylacetylene. We wish to thank Professor Breslow for a pre-publication account of his results.

[2] R. Breslow, R. Winter and M. Battiste, *J. Org. Chem.*, **24**, 415 (1959).

[3] *Cf.* M. J. S. Dewar and C. Ganellin, *J. Chem. Soc.*, 2438 (1959).

[4] F. Feigl, "Spot Tests in Organic Analysis," Elsevier, New York, N. Y., 1956, p. 327.

[5] G. Charlot, "Quantitative Inorganic Analysis," John Wiley and Sons, New York, N. Y., (1954) p. 271 (Translation).

[6] R. Breslow and C. Yuan, THIS JOURNAL, **80**, 5991 (1958).

[7] K. Alder, J. Hayden, K. Heimbach, K. Neufang, G. Hansen and W. Gerhard, *Ann.*, **586**, 110 (1954).

[8] R. Breslow and H. Höver, THIS JOURNAL, **82**, 2644 (1960).

[9] W. Dilthey, I. Thewalt and O. Trosken, *Ber.*, **67B**, 2004 (1934).

[10] P. Yates and J. Hyre, unpublished work. The authors affirm their indebtedness to Professor Yates for supplying spectroscopic data and comparison samples of the three isomeric tetraphenylphenols.

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RECEIVED APRIL 7, 1960

A CARBON-SKELETON REARRANGEMENT DURING THE OXIDATIVE DEPHOSPHORYLATION OF A NEW TYPE OF PHOSPHORUS COMPOUND. REACTION OF MOLECULAR OXYGEN WITH THE CRYSTALLINE 1:1 ADDUCTS DERIVED FROM TERTIARY PHOSPHITE ESTERS AND *alpha*-DIKETONES[1]

Sir:

During our investigations[2] of the reactions of phosphite esters with quinones and with other carbonyl compounds, we have encountered a carbon-skeleton rearrangement which we believe to be new and significant. This rearrangement

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[1] Acknowledgment is made to the Donors of the Petroleum Research Fund Administered by the American Chemical Society for partial support of this Research (Grant 286-A), and to the National Cancer Institute of the National Institutes of Health (Grant CY-4769).

[2] (a) F. Ramirez and N. B. Desai, THIS JOURNAL, **82**, 2652 (1960); (b) F. Ramirez, E. H. Chen and S. Dershowitz, *ibid.*, **81**, 4338 (1959), and reference therein.