The solid that remained was crystallized from acetonitrile with treatment with charcoal to give 6.4 g. (85%) of III, m.p. 214–216°. A sample was prepared for analysis by an additional crystallization from acetonitrile to give white crystals, m.p. 222–223°.

Anal. Calcd. for $C_{18}H_{16}N_4$: C, 75.0; H, 5.59; N, 19.4; mol. wt., 288. Found: C, 74.9; H, 5.62; N, 19.5; mol. wt., 294.

3,3,4,4-Tetracyano-8,11-dibromo-8,11-bis-(bromomethyl)-tricyclo[4.3.3.0]dodecane.—To a solution of 1.44 g. of the adduct III in 75 ml. of warm chloroform was added 1.6 g. of bromine. Solid began to separate after 10 minutes. After 30 minutes the bromine color had faded and 1.9 g. of solid was collected by filtration. Crystallization of 1.6 g. of the crude product from acetonitrile gave 0.9 g. of 3,3,4,4-tetracyano-8,11-dibromo-8,11-bis-(bromomethyl)-tricyclo-[4.3.3.0]-dodecane, m.p. 217.5–219°. An additional crystallization from the same solvent gave a sample for analysis melting at 218.5–220°.

Anal. Calcd. for $C_{18}H_{16}N_4Br_4$: C, 35.6; H, 2.65; N, 9.22; Br, 52.6. Found: C, 35.7; H, 2.68; N, 9.53; Br, 53.1.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY, ITHACA, N. Y.]

The Mechanism of Reductive Furan Formation

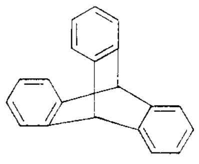
BY CHARLES F. WILCOX, JR., AND MALCOLM P. STEVENS[1]

RECEIVED SEPTEMBER 29, 1961

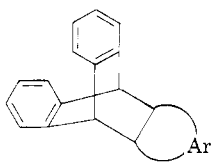
During the attempted preparation of heteroatom analogs of triptycene, reductive furan formation from 2-ene-1,4-diones has been observed. The mechanism of this type of reaction is re-examined and a modified formulation in terms of a Lewis acid and a reducing agent is proposed. From this study two new syntheses of furans are suggested.

Introduction

Previous work from this Laboratory[2-4] has been concerned with the preparation and interpretation of the ultraviolet spectra of triptycene (I) and its derivatives. These compounds are of interest because they permit the study of chromophore interaction through space with molecules of relatively fixed and certain geometry. One extension of this study to be developed was the preparation of triptycene analogs (II) in which one of the benzene rings has been replaced by another aromatic nucleus.



I

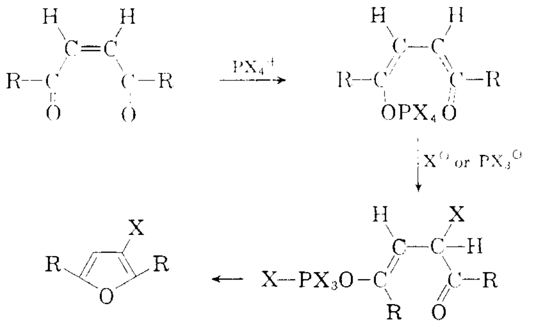


II

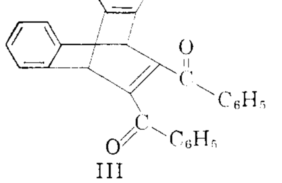
During the attempted preparation of such compounds, several interesting reactions have been observed which shed new light on the recently proposed mechanism of Newman[5] for the abnormal reaction of PBr_5 with certain ketones to give furans. This paper will be concerned solely with these reactions, the modification they require in the mechanism for abnormal furan formation and their potential extrapolation to a new furan synthesis. A subsequent paper will discuss the interpretation of the ultraviolet spectra of the various compounds described here.

Discussion

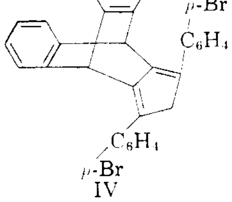
When α,β-unsaturated 1,4-diketones like 1,4-diphenylbutene-1,4-dione are treated with PCl_5 or PBr_5 a chlorinated or brominated furan results. These cyclizations have been tentatively interpreted by Newman and Wood[5] in their general PX_5–ketone reaction mechanism as involving first the equilibrium formation of PX_4^+ and PX_6^- followed by attack of the PX_4^+ on the ketone to yield the furan in the manner



A dominating feature of this mechanism is the addition of a halide ion to the initially formed Lewis salt so that a halogenated furan inevitably results. With this in mind, it is interesting to observe that when III, an unsaturated 1,4-diketone incapable of such halogenation, was treated with PBr_5 at 200°, the furan IV was formed in 67% yield (after purification).



III



IV

The identity of this product was established by: (1) a comparison of its physical properties with those previously reported for the compound prepared by a different route,[6] (2) its nitric acid oxida-

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[1] Taken from a dissertation submitted by M. Stevens to Cornell University in partial fulfillment of the requirements for the Ph.D. degree, June, 1961.

[2] A. C. Craig and C. F. Wilcox, Jr., *J. Org. Chem.*, **24**, 1619 (1959).

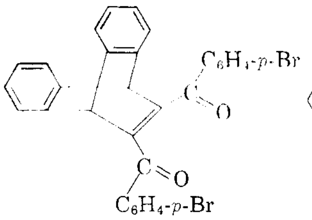
[3] C. F. Wilcox, Jr., *J. Chem. Phys.*, **33**, 1874 (1960).

[4] C. F. Wilcox, Jr., and A. C. Craig, *J. Org. Chem.*, **26**, 2491 (1961).

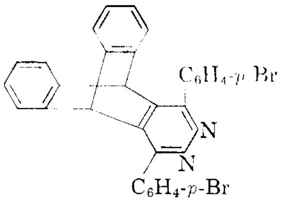
[5] M. S. Newman and L. L. Wood, Jr., *J. Am. Chem. Soc.*, **81**, 4300 (1959), and references therein.

[6] P. Baumgarten and G. Hugel, *Bull. soc. chim. France*, **21**, 1105 (1954).

tion to the known[6] diketone V followed by conversion of this diketone to the known[6] pyridazine VI and finally (3) the consistency of its infrared and ultraviolet spectra with the assigned structure.



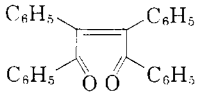
V



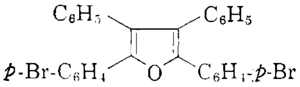
VI

That a furan possessing halogens on the appended phenyl rings is formed with PBr_5 suggests that the sequence of this reaction involves initial furan formation with subsequent halogenation of the phenyl rings.[7]

Still another example of furan formation with compounds outside the scope of the Newman mechanism is the reaction of *cis*-dibenzoylstilbene (VII) with PBr_5. In spite of the absence of α-hydrogens a 58% yield of the dibromotetraphenylfuran



VII

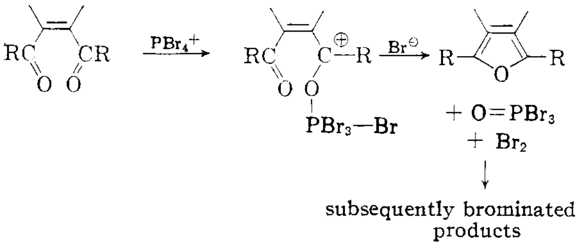


VIII

(VIII) was formed at room temperature. The structure of VIII was assigned on the basis of: (1) the coincidence of its melting point with the "dibromolepidene" prepared by Zinin[8] from "lepidene" (tetraphenylfuran) and bromine, (2) its ready nitric acid oxidation to a diketone apparently identical to the diketone prepared from "dibromolepidene," and (3) its ultraviolet showed essentially the same red shift ($\Delta = 12$ mμ) and enhancement of intensity ($\Delta \log \epsilon = 0.18$) relative to tetraphenylfuran that 2,5-bis-(p-bromophenyl)-furan does relative to 2,5-diphenylfuran ($\Delta = 11$ mμ, $\Delta \log \epsilon = 0.15$).

These two examples require a modified mechanism for furan formation since neither has the "essential" unsubstituted α-position in the starting material. One possible modification[9] which accounts for the examples cited by Newman as well as those presented here is

$$PBr_5 \rightleftarrows PBr_4^+ + Br^- \text{ (or } PBr_6^-\text{)}$$

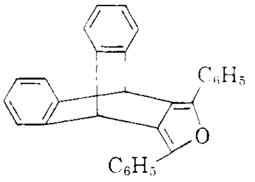


Further support for the idea that introduction of halogen occurs *in general* after formation of the furan rather than before comes from the data of Lutz and Wilder[10] that the appropriate non-halogenated furans react with PCl_5 or PBr_5 to give halogenated furans which are identical with those resulting from the phosphorus pentahalide reactions. A possible halogenating agent in these PX_5 reactions is the molecular halogen arising from the equilibrium

$$PX_5 \rightleftarrows PX_3 + X_2$$

This source of X_2 could be especially important with phosphorus pentabromide since the available data indicate that dissociation occurs to a considerable extent even at room temperature.[11]

Consideration of this equilibrium, which probably has a constant much greater than that for formation of PX_4^+, suggested that PX_3 might be an active agent for furan formation. When III was heated with phosphorus tribromide, a vigorous reaction set in at 140° to give eventually a 63% yield of the unhalogenated furan IX identical with a sample prepared by a known[6] and unambiguous route. Since this furan formation occurred at a



IX

temperature some 60° below that required for the PBr_5 reaction, it suggests that PBr_3 was *the* active agent there as well. A possible mechanism might be initial complexing of the PBr_3 with the diketone followed by cyclization and ejection of $POBr_3$. This mechanism involves an expansion of the phosphorus octet at the complex stage. An intriguing alternate possibility based on an analogy to the Conant mechanism[12] for reaction of PCl_3

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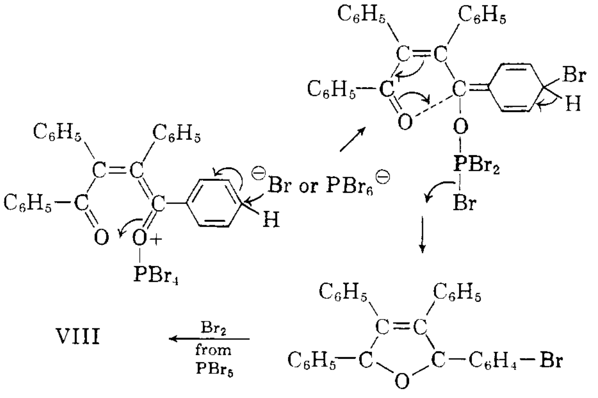
[7] When III was heated with PCl_5 a non-halogenated amorphous material was obtained. An apparently identical product as judged by melting point and infrared spectrum was obtained from the furan IX and PCl_5 under the same conditions.

[8] N. Zinin, *J. prakt. Chem.*, **101**, 160 (1867); *Bull. soc. chim. France*, [2] **8**, 271 (1867).

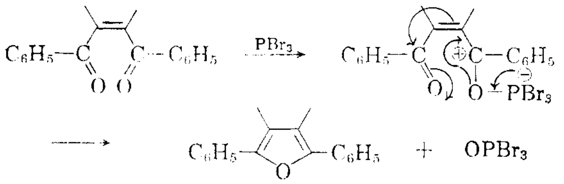
[9] A referee has emphasized that the evidence presented thus far does not exclude an alternative mechanism for the introduction of the *first* bromine atom which is simply a vinylog of the Newman proposal



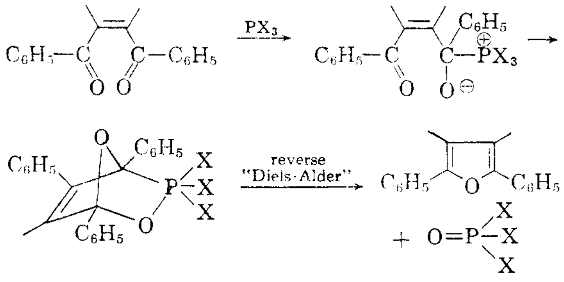
We feel that this alternative is made less probable by the evidence presented in the following paragraph, namely that PBr_3 (which is known to be present in equilibrium with the PBr_5) brings about furan formation at a much lower temperature than does PBr_5.

[10] R. E. Lutz and F. N. Wilder, *J. Am. Chem. Soc.*, **56**, 2145 (1934).

[11] See J. R. Van Wazer, "Phosphorus and its Compounds," Vol. I, Interscience Publishers, Inc., New York, N. Y., 1958, p. 239, and references therein.

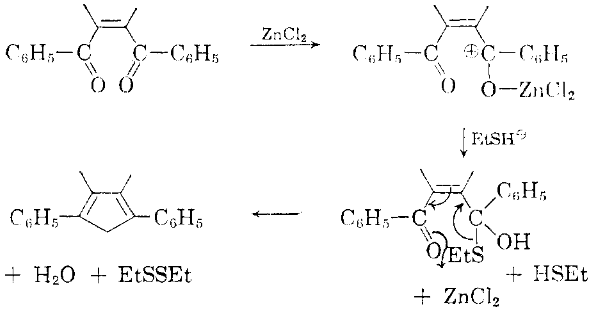


with α,β-unsaturated ketones can be formulated.[13] This mechanism assigns PX_3 the role of a nucleophile to give the sequence



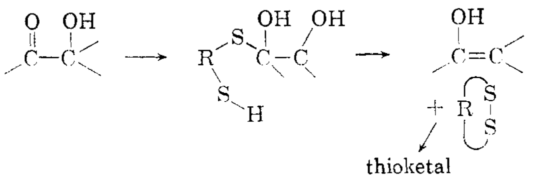
Whatever the details of the PX_3 reaction, the previously established point still stands out clearly—halogenation occurs subsequent to furan formation.

In the foregoing examples it was possible to formulate the various furan formations in terms of an initial electrophilic attack (oxidation) followed by a formal reduction of the intermediate to yield the furan.[14] This generalization suggested that other Lewis acid-reducing agent combinations might be effective. Interestingly, when the diketone III was treated with zinc chloride and ethyl mercaptan at 0° overnight, a 76% yield of furan was obtained. The same result was obtained when 1,2-ethanedithiol was substituted for ethyl mercaptan and when boron trifluoride etherate was substituted for zinc chloride, but no reaction occurred unless both thiol and Lewis acid were present together. Similarly, no reaction occurred when ethanol, ether or acetonitrile was substituted for the mercaptan as solvent. When the reaction was conducted on a larger scale using equivalent amounts of reactants and a methylene chloride-ether mixed solvent to dissolve both the diketone III and the zinc chloride, a 43% yield of the expected diethyl disulfide was isolated along with an 86% yield of furan IX. Precautions were taken to ensure that the disulfide did not result from air oxidation of ethyl mercaptan. The yield of disulfide is reasonable considering the large volume of solvent that had to be removed and the fact that the disulfide was distilled directly from the residual furan. The following schematic oxidation-reduction mechanism, analogous to the previous phosphorus halide furanization, can be formulated.[15]



This mechanism is intended to show only the proposed gross oxidation-reduction steps and not details such as the timing of proton transfers, the actual leaving group or the possible incursion of a thioketal intermediate.

Some possible further details of this reductive furan formation are suggested by a related thiol reduction reported by Cram and Cordon.[16] These workers removed the hydroxyl group of acyloins with 1,3-propanedithiol in the presence of zinc chloride and hydrochloric acid. Their reaction mechanism can be effectively reformulated in the same general terms used above where, as before, the complicating details are passed over.



Pertinent here is their observation that the reduction failed with ethyl mercaptan. While this might only reflect a more difficultly reduced substrate which requires the favorable entropy factor of a cyclic disulfide for noticeable reaction, it also suggests that the active reducing agent might be the mercaptide anion present in significant concentrations in the present neutral reductions but absent under the highly acidic Cram and Cordon conditions.

Two points are brought out by the foregoing results. First, "abnormal" formation of halofurans by the action of phosphorus pentahalides on α,β-unsaturated-1,4-diones most likely proceeds by initial furan formation followed by subsequent halogenation. Second, the essential requirements for this furan formation are a Lewis acid and a reducing agent. This double requirement may be satisfied by a mixture of reagents such as the zinc chloride-ethyl mercaptan combination or by a single reagent possessing both features such as PBr_3.

The present results open two new potential routes to unhalogenated furans. If a low temperature is desired the Lewis acid-mercaptan combination is a possibility where the enedione would not give other reactions with the mercaptan. For car-

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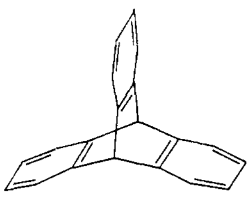
[12] J. B. Conant and A. A. Cooke, *J. Am. Chem. Soc.*, **42**, 830 (1920).

[13] This possibility was suggested to us by Professor J. R. Johnson of this department.

[14] In the case of the PBr_3 reaction this formal reduction of the complex is intramolecular.

[15] The alternate possibility of initial reduction followed by normal furanization can be excluded. First, such a possibility is made less likely by the observation that only starting material was isolated when the Lewis acid was left out. Moreover, Lutz has noted (*J. Am. Chem. Soc.*, **57**, 1953 (1935)) that whereas dibenzoylfuran is formed by the action of Zn-$ZnBr_2$-HOAc on dibenzoylethylene the furan is not formed from the reduction product, dibenzoylethane, under the same conditions. In connection with the phosphorus pentahalide furanizations Lutz has made the generalized observation (*J. Am. Chem. Soc.*, **56**, 2145 (1934)) that the unsaturated systems are furanized with "distinctly greater ease" than the saturated analogs.

[16] D. J. Cram and M. Cordon, *J. Am. Chem. Soc.*, **77**, 1810 (1955).



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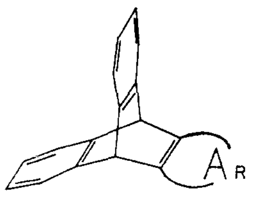

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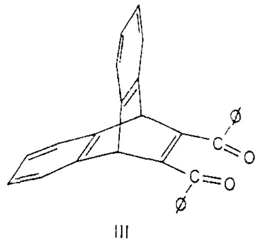

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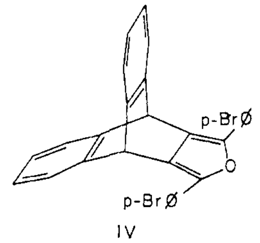
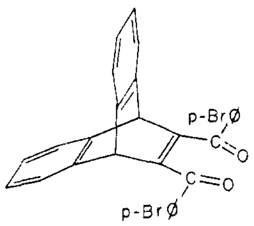


IV



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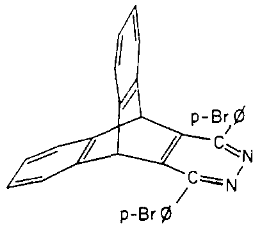
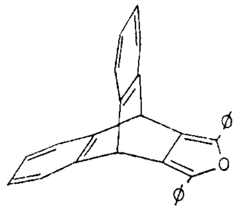


VI



IX

bonyl compounds more prone to undergo side reactions such as thioketal formation or Michael addition the higher temperature phosphorus tribromide reaction is a possibility. These suggestions are necessarily tentative because the examples so far studied are rather special with atypical steric environments. It is hoped that this study can be continued to outline the scope and limitations of these reagents.

Experimental[17]

9,10-Dihydro-9,10-(1,2-dibenzoyletheno)-anthracene-(III).—1,4-Diphenyl-2-butyne-1,4-diol was prepared by the method of Dupont[18] and oxidized to dibenzoylacetylene by the method of Bowden, *et al.*[19] The desired adduct III when prepared by the method of Baumgarten and Hugel[6] required many recrystallizations to be obtained in pure form and the resulting yields were unsatisfactory. The procedure was improved as follows using aluminum chloride catalysis.[20] In 0.1 l. of methylene chloride was dissolved 23.4 g. (0.1 mole) of dibenzoylacetylene, 17.8 g. (0.1 mole) of anthracene and 13.3 g. (0.1 mole) of anhydrous aluminum chloride. After 30 min. at room temperature, the resulting deep red solution was poured onto ice and the methylene chloride layer separated and dried over magnesium sulfate. Evaporation of the solvent yielded 40.6 g. of a solid which after one recrystallization from acetic acid melted at 212–212.5° (lit.[6] 211–212.5°) and appeared to be identical in all respects with the adduct III prepared by the literature procedure. The analysis was 0.46% low in carbon.

9,10-Dihydro-9,10-(2,5-di-*p*-bromophenylfurano)-anthracene (IV).—One gram of diketone III and 2 g. of phosphorus pentabromide were fused together at 200° (below this temperature no significant reaction occurred). After cooling, the residue was crystallized from an acetonitrile–N,N-dimethylformamide mixture to yield 0.9 g. of a white, crystalline compound, m.p. 350–351° (lit.[6] 342–343°). Its infrared spectrum contained no carbonyl band, but did have a strong peak at 9.3 μ, characteristic of 5-membered ring cyclic ethers.[21] An isoöctane solution showed maxima in mμ (log ε) in the ultraviolet at: 330 (4.80), 275 (4.58), 272 (4.62), 256 (4.47), and 232 (4.49).

The oxidation of 0.4 g. of IV in 40 ml. of acetic acid with 2 ml. of fuming nitric acid gave 0.21 g. of diketone V, m.p. 237–238° (lit.[6] m.p. 235°). Its infrared spectrum showed a strong carbonyl band at 6.10 μ.

The pyridazine of diketone V was prepared by refluxing 0.1 g. of the diketone with 1 ml. of 85% hydrazine hydrate in 5 ml. of acetic acid for 1 hr. After recrystallization of the product from ethanol it melted at 258° (lit.[6] m.p. 258°).

***cis*-Dibenzoylstilbene (VII).**[22]—A solution of 2.0 g. of tetracyclone (tetraphenylcyclopentadienone, L. Light and Co. Ltd., Colnbrook, Eng.) in 400 ml. of benzene was mixed with a solution of 0.1 g. of methylene blue in methylene chloride. The mixture was surrounded by an optical filter bath of saturated sodium nitrite solution and allowed to stand in sunlight until the reaction was complete as judged by the change of color from deep purple-black to the paler blue of the methylene blue. In intense sunlight, the reaction required 3 days. After the solvent was removed the remaining solid was recrystallized from ethanol with use of charcoal to reduce the methylene blue content. A 65% yield of *cis*-dibenzoylstilbene, m.p. 215–216° (lit.[23] m.p. 213), with an infrared spectrum identical to that previously reported,[23] was obtained.

When the filter bath was not used, the *trans* isomer, m.p. 232–233°, was obtained (lit.[23] m.p. 230–232°).

***p,p'*-Dibromotetraphenylfuran (VIII).**—A mixture of 0.1 g. of *cis*-dibenzoylstilbene with 0.2 g. of phosphorus pentabromide reacted vigorously at room temperature to yield 0.092 g. of a white solid, m.p. 192° after recrystallization from N,N-dimethylformamide (lit.[8] for "dibromolepidene" is 192°). The infrared showed no carbonyl absorption and strong absorption at 9.3 μ.[21] An isoöctane solution showed maxima in mμ (log ε) in the ultraviolet at: 338 (4.43), 267 (4.31) and 237 (4.43).

Anal. Calcd. for $C_{28}H_{18}Br_2O$: C, 63.39; H, 3.39; Br, 30.18. Found: C, 63.96; H, 3.71; Br, 27.64.

Oxidation of VIII with nitric acid in acetic acid afforded an excellent yield of dibromidibenzoylstilbene, m.p. 225° (lit.[8] for "dibromoöxylepidene" is 222°).

Tetraphenylfuran, prepared by the method of Zinin[8] from VIII *via* reduction with zinc in acetic acid, showed maxima in mμ (log ε) in the ultraviolet in isoöctane solution at: 326 (4.25), 255 (4.24) and 233 (4.37).

9,10-Dihydro-9,10-(2',5'-diphenylfurano)-anthracene-(IX) by Phosphorus Tribromide Furanization.—When 2.06 g. of diketone III was heated with 8 ml. of phosphorus tribromide, a vigorous reaction set in at 140°. After the heat evolution had ceased, the mixture was cooled and water added dropwise. The resulting precipitate was collected by filtration and recrystallized from acetonitrile to yield 1.24 g. of IX, the infrared spectrum, melting point and mixed melting point of which were identical with an authentic sample prepared by the method of Baumgarten and Hugel.[6]

9,10-Dihydro-9,10-(2',5'-diphenylfurano)-anthracene (IX) by Ethyl Mercaptan Furanization.—A mixture of 0.25

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[17] Analyses were performed by the Schwarzkopf Microanalytical Laboratory, Woodside 77, N. Y., and the Scandinavian Microanalytical Laboratory, Box 1257, Copenhagen S, Denmark. Unless indicated otherwise all of the previously known compounds gave analyses within ±0.3% in carbon and hydrogen.

(18) G. Dupont, *Ann. chim. phys.*, [8] **30**, 490 (1913).

(19) K. Bowden, *et al.*, *J. Chem. Soc.*, 39 (1946).

(20) P. Yates and P. Eaton, *J. Am. Chem. Soc.*, **82**, 4436 (1960).

(21) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," 2nd Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, p. 119.

(22) The potential success of this procedure was suggested by some unpublished preliminary results of Dr. D. G. Farnum of this department.

(23) N. M. Bikales and E. I. Becker, *J. Org. Chem.*, **21**, 1405 (1956).

g. of diketone III, 1.0 g. of anhydrous sodium sulfate, 0.5 g. of freshly fused zinc chloride and 20 ml. of ethyl mercaptan was stored overnight in a 0° refrigerator. After the excess mercaptan was removed under vacuum, 10 ml. of water and 10 ml. of ether were added. The aqueous layer was separated and extracted three times with 10-ml. portions of ether. The combined ether extracts were dried over sodium sulfate. After the solvent was removed the residual solid was recrystallized from acetonitrile to give 0.164 g. of furan IX, m.p. 220–221°, identical in all respects with an authentic sample.

Isolation of Diethyl Disulfide.—A mixture of 20.6 g. (0.05 mole) of diketone III, 6.8 g. (0.05 mole) of freshly fused zinc chloride and 6.2 g. (0.10 mole) of ethyl mercaptan was dissolved in a mixture of 150 ml. of deaerated methylene chloride and 150 ml. of deaerated ether. After the solution was stored for 24 hr. at room temperature, it was washed twice with water and dried over magnesium sulfate. The solvents were removed by slow careful distillation through a 1-foot glass helices-packed column. The column was replaced with a small Vigreux column and the solid residue vacuum distilled. The fraction collected from 45–47° at 11 mm. was redistilled to give 2.62 g. (43%) of diethyl disulfide, n^{25}D 1.5044 (lit.[24] 1.5046, 1.5047), the infrared spectrum of which was identical with that recorded.[25]

Recrystallization of the solid residues from acetonitrile gave 17.0 g. (86%) of the furan IX.

Other Furanization Conditions.—The furan IX was obtained in similar high yield from 0.1 g. of the diketone III, 2 ml. of 1,2-ethanedithiol and 5 drops of boron trifluoride etherate.[26]

No reaction occurred when ether, ethanol or acetonitrile were substituted for ethyl mercaptan in the presence of zinc chloride or boron trifluoride etherate. Similarly, no reaction occurred in ethyl mercaptan when the zinc chloride was not present.

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[24] E. Emmet Reid, "Organic Chemistry of Bivalent Sulfur," Vol. III, Chemical Publishing Co., Inc., New York, N. Y., 1958, p. 396, and references therein.

[25] American Petroleum Institute Catalog of Infrared Spectral Data, Serial No. 1113.

[26] E. E. van Tamelen and C. I. Judd, *J. Am. Chem. Soc.*, **80**, 6305 (1958).

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2-Deoxy-D-ribose. VIII.[1] Synthesis of the Anomeric 2-Deoxy-D-ribofuranose 1-Phosphates[2]

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Condensation of 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribosyl chloride with disilver phosphate affords a mixture of the anomeric 2-deoxy-α-D-ribofuranose 1-phosphates which is comparatively rich in the α-anomer. The latter was obtained in a purity approaching that of the natural phosphate. Condensation of the same chloride with tri-*n*-pentylamine phosphate gives a mixture of anomers in which the β-isomer predominates; this was purified. Comparison of the properties of the two 2-deoxy-D-ribofuranose phosphates supports the assumption that the natural anomer has the α-D-configuration.

Chemical synthesis of the two anomeric D-ribofuranose 1-phosphates[3] has established the structure of the ribose phosphate, originally obtained through the cleavage of a ribonucleoside by a nucleoside phosphorylase,[4] as α-D-ribofuranose 1-phosphate. Analogy suggests that the extremely acid-labile 2-deoxy-D-ribose 1-phosphate which is formed through the action of the appropriate nucleoside phosphorylases on deoxynucleosides[5–7] may also be an α-furanose isomer. The optical rotation of the cyclohexylammonium salt of the substance, $[\alpha]^{20}$D +38.8°,[7] tends to support this assumption. Synthesis of the β-anomer, hitherto unknown, and comparison of its rotation with that of the natural phosphate, should provide further evidence[8] bearing on the anomeric configuration in question. The present paper describes the chemical synthesis of both the natural 2-deoxy-D-ribose 1-phosphate and its anomer.

Although various 3,5-di-*O*-acyl-2-deoxy-D-ribosyl chlorides have been obtained in crystalline form[9,10] (and, therefore, presumably, represent essentially pure anomeric forms) condensation of these with various salts is not, normally, stereospecific, both anomeric 2-deoxy-D-ribofuranose derivatives being obtained.[1,9] Variations in the nature of the salt have, however, a marked effect upon the proportions of anomers formed. This phenomenon was used to advantage in the present research.

Condensation of 2-deoxy-3,5-di-*O*-*p*-toluoyl-D-ribosyl chloride[9,10] in benzene solution with disilver phosphate occurred rapidly at room temperature; after removal of the toluoyl groups with alkali the product was converted to a cyclohexylammonium salt which was isolated in about 40% yield. After removal of inorganic phosphate as magnesium ammonium phosphate, the product (26%) showed a specific rotation of $[\alpha]^{20}$D *ca.* 24° in water. Chromatography on paper revealed that it was still contaminated with a phosphorus-containing material.[11] Preparative paper chromatography

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[1] 2-Deoxy-D-ribose. VII: R. K. Ness, D. L. MacDonald and H. G. Fletcher, Jr., *J. Org. Chem.*, **26**, 2895 (1961).

[2] Preliminary communication: D. L. MacDonald and H. G. Fletcher, Jr., *J. Am. Chem. Soc.*, **82**, 1832 (1960).

[3] R. S. Wright and H. G. Khorana, *ibid.*, **78**, 811 (1956); G. M. Tener, R. S. Wright and H. G. Khorana, *ibid.*, **79**, 441 (1957).

[4] H. M. Kalckar, *J. Biol. Chem.*, **167**, 477 (1947).

[5] M. Friedkin and H. M. Kalckar, *ibid.*, **184**, 437 (1950).

[6] M. Friedkin, *ibid.*, **184**, 449 (1950); M. Friedkin and D. Roberts, *ibid.*, **207**, 257 (1954).

[7] H. L. A. Tarr, *Can. J. Biochem. Physiol.*, **36**, 517 (1958).

[8] R. U. Lemieux and M. Hoffer [*Can. J. Chem.*, **39**, 110 (1961)] have recently discovered that two pyrimidine 2-deoxy-D-ribonucleosides and some of their derivatives constitute exceptions to Hudson's rule [C. S. Hudson, *J. Am. Chem. Soc.*, **31**, 66 (1909)]. While there is consistency among the rotations of a wide variety of 2-deoxy-D-ribofuranose esters and glycosides and no evidence currently available to indicate that Hudson's rule is not applicable to such substances. It is obvious that some dubiety regarding the anomeric configuration of all 2-deoxy-D-ribofuranose derivatives must remain in the absence of absolute physical or chemical proof.

[9] M. Hoffer, R. Duschinsky, J. J. Fox and N. Yung, *J. Am. Chem. Soc.*, **81**, 4112 (1959).

[10] M. Hoffer, *Chem. Ber.*, **93**, 2777 (1960).

[11] This impurity did not migrate in the isopropyl alcohol–ammonia–water system. It appears to contain no organic moiety and