1,4-Bis-(4-ethylphenyl)-butane (XIII).—The diketone (VI), 3.7 g., was converted to the hydrocarbon by a modified Wolff–Kishner reduction.[16] The reaction mixture was diluted with water and the product was extracted with ether. Filtration of the ether phase gave 0.65 g. of a yellow solid which was not investigated. The filtrates were washed and dried, and the ether was evaporated in vacuum. The residual oil was taken up in pentane and chromatographed on 100 g. of neutral alumina of activity II.[18] The white solid obtained from the first 100 ml. of eluate was crystallized from acetone–methanol at −80° to yield white plates, 1.45 g. (43%), m.p. 26.2–26.8°.

Anal. Calcd. for $C_{20}H_{26}$: C, 90.16; H, 9.84. Found: C, 89.92; H, 9.55.

LOS ANGELES, CALIFORNIA

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NORTHWESTERN UNIVERSITY]

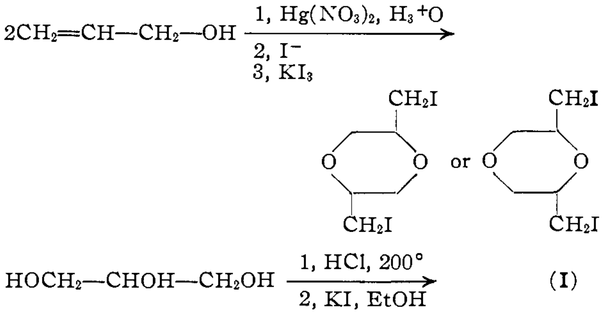
The Configurations of 2,6-Bis-(iodomethyl)-*p*-dioxanes and 2,6-*p*-Dioxanedicarboxylic Acids. The Structure of Diepiiodohydrin

BY R. K. SUMMERBELL AND JAMES R. STEPHENS

RECEIVED AUGUST 24, 1953

The known and a new form of 2,6-bis-(iodomethyl)-*p*-dioxane have been prepared. Their structure has been shown by oxidizing them to the corresponding 2,6-*p*-dioxanedicarboxylic acids, and the interconversion of these acids. The configurations of the compounds are indicated by the conversion of only one of the iodides to morpholine derivatives, and the hydrolysis of a monomeric acid anhydride to form one of these acids. This work constitutes the first proof of the configuration of a polysubstituted dioxane. Diepiiodohydrin has long been assigned the ambiguous structure of 2,5- or 2,6-bis-(iodomethyl)-*p*-dioxane, but since only *cis*- and *trans*-2,6-bis-(iodomethyl)-*p*-dioxanes can exist, the isomeric diepiiodohydrin must be 2,5-bis-(iodomethyl)-*p*-dioxane. The polar-equatorial substitution concept which has previously been used to explain physical properties of the *cis* and *trans* forms of disubstituted cyclohexanes seems to be applicable to the 2,6-disubstituted-*p*-dioxanes.

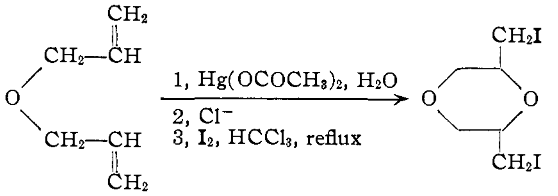
Previous investigators[1] who have prepared diepiiodohydrin (I) have postulated its structure as a bis-(iodomethyl)-*p*-dioxane. This has been shown to be correct by Burlingame[2] who obtained the same di-*n*-butyl-*p*-dioxane from the appropriate alkylation of either diepiiodohydrin or a dichloro-*p*-dioxane. The methods employed for the production of diepiiodohydrin (see below) eliminate the 2,3-bis-(iodomethyl)-*p*-dioxane structure from consideration but do not permit a choice between the 2,5- or the 2,6-bis-(iodomethyl)-*p*-dioxane structure for I.



(I)

Additional but inconclusive evidence concerning diepiiodohydrin's structure was provided in 1943 by Nesmeyanov and Lutsenko[3] who cyclized allyl ether by the action of aqueous mercuric acetate to produce a dimercury derivative which could be precipitated as the chloride and then iodinated to a cyclic ether II, an isomer of I, to which they assigned the structure of 2,6-bis-(iodomethyl)-*p*-dioxane. II was not shown to be a *p*-dioxane derivative but postulated to have this structure from the method of synthesis. Even if II is proved to be 2,6-bis-(iodomethyl)-*p*-dioxane, diepiiodohydrin may have the same structure since the 2,6-derivative can exist as either the *cis* or the *trans* isomer.

We have repeated the work of Nesmeyanov and Lutsenko, and in addition to obtaining their product we have succeeded in isolating a new isomer III. If II and III are *p*-dioxanes the iodomethyl groups must be substituted in the 2,6-positions since the starting material of the synthesis was allyl ether. Diepiiodohydrin would then be assigned the 2,5-bis-(iodomethyl)-*p*-dioxane structure.



II and III

Infrared absorption curves of II and III in chloroform solution indicated them to be different chemical entities rather than dimorphic forms of the same compound.

The *p*-dioxane structures of II and III were shown by converting them to the acids IV and V, respectively, by the action of hot concentrated nitric acid. In addition IV and V were converted to the dimethyl esters VI and VII, respectively, by reaction with diazomethane. Formation of the diesters, neutral equivalents, analysis and molecular weights indicated dicarboxylic acid structures for IV and V. The formation of these dicarboxylic acids was significant as it eliminated the possibility that either II or III could be the seven-membered ring compound 2-iodomethyl-6-iodo-1,4-dioxocycloheptane, since such a compound would be expected to lose a carbon atom on oxidation to a dicarboxylic acid. Stability of IV and

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(1) (a) C. Stoehr, *J. prakt. Chem.*, [2] **55**, 78 (1897), see also M. Fauconnier and J. Sanson, *Bull. soc. chim.*, [2] **48**, 237 (1887); (b) E. Biilman, *Ber.*, **33**, 1644 (1900), and J. Sand, *ibid.*, **34**, 1394 (1901).

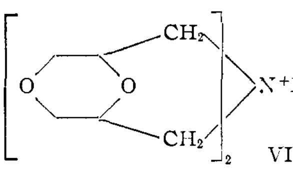
(2) A. L. Burlingame, Ph.D. Dissertation, Northwestern University, 1950.

(3) A. N. Nesmeyanov and I. F. Lutsenko, *Bull. acad. sci. U.R.S.S., Classe sci. chim.*, 296–304 (1943).

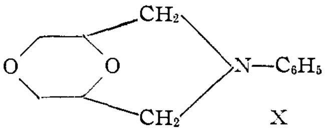
V to concentrated acid solution would seem to eliminate the possibility of a five-membered dioxolane ring. IV and V must therefore contain the six-membered dioxane ring. Finally the interconversion of V to IV by the action of hot aqueous potassium hydroxide[4] showed conclusively that the acids are geometric isomers of the same structure, which from previous considerations must be a 2,6-disubstituted-*p*-dioxane. Their precursors III and II must have the same fundamental structure. Since only *cis*- and *trans*-2,6-bis-(iodomethyl)-*p*-dioxanes are possible, the isomeric diepiiodohydrin I must be a 2,5-bis-(iodomethyl)-*p*-dioxane.

Of late there has been much interest in the configurations of disubstituted cyclohexanes and a number of erroneous assignments based on older empirical rules have been corrected by direct chemical evidence.[5] The *cis* isomers of 1,3-diosubstituted cyclohexanes appear to be uniformly more stable than the corresponding *trans* derivatives. The polar-equatorial concept of Beckett, Pitzer and Spitzer[6] seems to offer an adequate explanation of this phenomenon.[5b,5d] It might be expected that this same concept would apply to dioxanes, but no test of this assumption has been possible since no configurations of disubstituted dioxanes are known with certainty. We therefore decided to determine the configurations of our compounds by chemical means.

An examination of molecular models indicates that *cis*-2,6-bis-(iodomethyl)-*p*-dioxane should condense with ammonia and primary and secondary amines to give morpholine derivatives, whereas the *trans* isomer could not. The treatment of II with aqueous ammonia at high temperatures gave rise to a compound VIII whose properties and analysis are best explained by a quaternary ammonium iodide structure. The action of the same reagent on III was not as well defined. An amine was produced which was not stable outside of solution, but benzoylation of the reaction mixture *in situ* did produce a small quantity of a dibenzamide IX of a diamine. The action of aniline in refluxing xylene on II and III was more conclusive since II gave a derivative that was indicated by analysis and molecular weight to be 3-phenyl-7,9-dioxa-3-azabicyclo[3.3.1]nonane (X); no identifiable reaction product was formed from III. The molecular weight of X was particularly significant since only the *cis* form of 2,6-bis-(iodomethyl) - *p* - dioxane could form the simple derivative. II then must be the *cis* isomer, which leaves the *trans* configuration to be assigned to III.

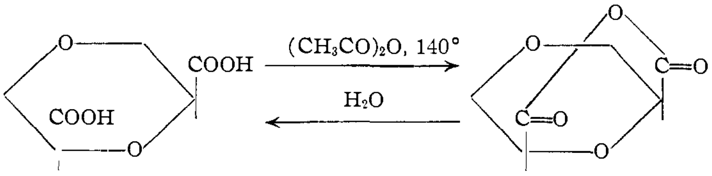


VIII



X

From other work concerning similar 2,5-derivatives, we have found that the concentrations and temperatures of nitric acid used to convert II and III to the acid IV and V do not change the configuration of the carboxyl groups on the dioxane ring. Also, we have found that IV, when reacting with boiling acetic anhydride, is converted smoothly to an anhydride XI which was shown to be monomeric by a molecular weight determination. XI, upon hydrolysis, regenerates IV.



IV XI

By referring to molecular models, it is seen that this behavior is possible only with the *cis* form of the acid. From this and previous considerations, the 2,6-*p*-dioxanedicarboxylic acids and their methyl esters may now be assigned configurations. Thus, IV and VI are *cis*-, and V and VII are *trans*-2,6-disubstituted-*p*-dioxanes.

In all the cases described in this paper the *cis*-2,6-disubstituted-*p*-dioxanes have higher melting points than the corresponding *trans* isomers. An examination of a molecular model of *p*-dioxane shows that the geometry of the ring is analogous to that of cyclohexane. With the chair, or staggered, conformation of *p*-dioxane the substituents can take up the more symmetrical diequatorial, (e-e), or dipolar, (p-p), orientation in the *cis* derivative, while the *trans* configuration is capable only of the less symmetrical polar-equatorial, (p-e), orientation. Insofar as the higher melting point is indicative of a more symmetrical molecular configuration of an isomeride of a *cis–trans* pair of isomers the theory of Beckett, Pitzer and Spitzer is applicable to the 2,6-disubstituted dioxanes encountered in this work. It should be pointed out, however, that all melting points of *trans*-2,6-disubstituted-*p*-dioxanes encountered here are those of racemic mixtures. No information is available at the present time on the melting point of an optical antimer of this form.

In a later paper we shall present the stereochemistry of some 2,5-disubstituted-*p*-dioxanes and show an extension of the above theory.

Experimental

2,6-Bis-(chloromercurimethyl)-*p*-dioxane.—This material was prepared by the procedure of Nesmeyanov and Lutsenko.[3] (These authors assigned the correct structure to it, but did not observe that it is actually a mixture of *cis* and *trans* isomers and assumed that it was a pure chemical compound.)

The Isomers of 2,6-Bis-(iodomethyl)-*p*-dioxane II and III.—The mixture of these isomers was prepared using the procedure of Nesmeyanov and Lutsenko for the preparation of II. They were also prepared by a modification of their procedure. This modified synthesis did not increase the yield but shortened the time of refluxing and permitted an easier work-up of the reaction mixture. Our synthesis follows.

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[4] The acid rather than the ester was chosen for epimerization on the basis of work with the related 2,5-derivatives which will be described and discussed in a future paper.

[5] (a) H. L. Goering and C. Serres, Jr., THIS JOURNAL, **74**, 5908 (1952); (b) D. S. Noyce and D. B. Denny, *ibid.*, **74**, 5912 (1952); (c) D. S. Noyce and R. J. Nagel, *ibid.*, **75**, 127 (1953); (d) S. Siegel, *ibid.*, **75**, 1317 (1953).

[6] C. W. Beckett, K. S. Pitzer and R. Spitzer, *ibid.*, **69**, 2488 (1947). See also M. Kilpatrick and J. G. Morse, *ibid.*, **75**, 1850 (1953).

A mixture of 761 g. (3.0 moles) of iodine, 996.7 g. (1.70 moles) of powdered 2,6-bis-(chloromercurimethyl)-*p*-dioxane and 3 l. of methanol was placed in a large flask and refluxed 24 hours. The clear yellow reaction solution was decanted off and evaporated down to a solid residue by heating under reduced pressure. The residue was then extracted by 2 l. of hot chloroform and the chloroform extract evaporated down with gentle heating and a stream of air to a solid residue. Concentrated aqueous potassium iodide was then added and the mixture heated with stirring until the organic iodides liquefied and the red mercuric salts were dissolved. The liquid organic phase was washed again with warm potassium iodide solution, then with warm water. It solidified on cooling after which it was recrystallized from methanol. The product melted at 57-82°[7] and weighed 218 g. (35%).

The Separation of the Isomers of 2,6-Bis-(iodomethyl)-*p*-dioxane. The *cis* Isomer II.—A satisfactory separation of II from the mixture of isomers provided by the above synthesis was effected by the exhaustive recrystallization from methanol. The higher melting crops eventually yield material of melting point 92° (Nesmeyanov and Lutsenko report the melting point as 94°.)

Anal. Calcd. for $C_6H_{10}O_2I_2$: C, 19.53; H, 2.74; I, 68.98; mol. wt., 368. Found: C, 19.45; H, 2.66; I, 69.16; mol. wt. cryoscopic in benzene, 380.

The *trans* Isomer III.—The waste liquors from the above recrystallization, upon rapid evaporation or cooling, deposit material melting at 56°. This material, apparently a eutectic mixture of isomers, could not be fractionated by conventional means. These lower crops were dissolved in methanol and the solution allowed to evaporate slowly (*ca.* one month) in erlenmeyer flasks. Two types of large crystals that weighed up to one gram were slowly deposited. The crystals melted at either 92 or 70°, and when mixed melted at 56°. Large crystals melting at 70° were separated out by hand and recrystallized. If the melting point remained unchanged after this operation the material was considered to be a pure isomeride.

Anal. of the m.p. 70° isomer III. Calcd. same as for II. Found: C, 19.74; H, 2.83; I, 69.3; mol. wt. cryoscopic in benzene, 384.

Infrared Spectra of I, II and III.—Three chloroform solutions of these isomers were made up by dissolving 247.7 mg. of each in separate 5.00-ml. portions of chloroform. Absorption curves of all three differed, especially in the region between 10.3 and 11.6 μ.

***cis*-2,6-*p*-Dioxanedicarboxylic Acid (IV).**—To 7 g. (0.0190 mole) of II in a large beaker was added 110 ml. of concd. (sp. gr. 1.42) nitric acid. The mixture was heated on a steam-bath and after a few minutes a vigorous reaction took place, evolving iodine and nitrogen dioxide. Heating was continued until the solution was evaporated down to a sirup. To this residue was added water with continued heating and concentration. This operation was repeated until the odor of nitric acid was no longer apparent. With complete evaporation to dryness a white solid was obtained. A hot 3:1 dioxane-benzene solution was added to this solid until most of it was dissolved. The extract was then filtered (from some iodic acid) into three times its volume of pentane. Colorless crystals precipitated and additional pentane was added until precipitation was complete. The crystals were filtered and heated for 1.5 hours at 100° and 5 mm. of pressure. The product then weighed 2.30 g. (69%) and melted at 177-178°.

Anal. Calcd. for $C_6H_8O_6$: C, 40.91; H, 4.58; neut. equiv., 88. Found: C, 41.24; H, 4.56; neut. equiv., 90.

***cis*-Dimethyl-2,6-*p*-dioxanedicarboxylate (VI).**—An ethereal solution of diazomethane was prepared[8] and slowly added to a solution of 84.7 mg. (0.481 mmole) of IV in 20 ml. of ethyl ether until the yellow color of diazomethane persisted. The solution was then evaporated to dryness with heating and a stream of nitrogen. The crystalline residue melted at 101°. It was recrystallized from ligroin to 65.4 mg. (67%) of crystals that melted at 103°.

Anal. Calcd. for $C_8H_{12}O_6$: C, 47.06; H, 5.93. Found: C, 47.19; H, 5.97.

***trans*-2,6-Dioxanedicarboxylic Acid (V).**—This acid was prepared by the same procedure used in the synthesis of IV from II. From 1.73 g. (0.0472 mole) of III was obtained 0.570 g. (69%) of V. This acid melted at 162° and when mixed with IV melted at 140-155°.

Anal. Calcd. same as (IV). Found: neut. equiv., 90.

***trans*-Dimethyl-2,6-*p*-dioxanedicarboxylate (VII).**—This compound was prepared by the same procedure used in the synthesis of VI from IV. From 19.8 mg. (0.112 mmole) of V was obtained 17.4 mg. (76%) of VII. This ester melted at 89° and when mixed with VI melted at 70°.

Anal. Calcd. same as (VI). Found: C, 47.57; H, 5.97.

The Isomerization of *trans*-2,6-*p*-Dioxanedicarboxylic Acid (V) to *cis*-2,6-*p*-Dioxanedicarboxylic Acid (IV).—In a solution of 2 g. of potassium hydroxide in 7.5 ml. of water was dissolved 288 mg. (1.63 mmoles) of V. The solution was heated for 12 hours at a temperature of 90° then cooled and acidified with concd. hydrochloric acid. The acidic solution was evaporated to dryness and then heated 15 minutes at 115°. To the solid residue was added 50 ml. of ethyl ether, then an ethereal solution of diazomethane[8] until the yellow color was no longer discharged. The solution containing excess diazomethane was then decanted from the residue of potassium chloride and evaporated down to a solid. This solid was recrystallized from hexane yielding crystals of m.p. 101°. Recrystallization again from hexane raised the m.p. to 103°. A mixed melting point with VI was not depressed. 98.3 mg. of the ester melting at 103° was obtained, which indicated at least 30% isomerization of V.

The Action of Ammonium Hydroxide on II and III.—Parallel reactions were run on the isomers in the following manner: Mixtures of 2 g. (0.00544 mole) of II and 1 g. (0.00272 mole) of III, with 30 ml. and 15 ml. of concd. ammonium hydroxide, respectively, were sealed in Pyrex tubes and heated in a Carius oven. The temperature was raised to 140° and held there for a period of 1.5 hours. The oven was then allowed to cool overnight and the tubes were opened and inspected.

With II. The Preparation of Bis-(2,6-*p*-dioxanedimethylene)-ammonium Iodide (VIII).—A clear colorless solution was obtained which was evaporated down on the steam-bath to a white solid. This was dried at 105° and then extracted with 100 ml. of boiling absolute ethanol. The ethanol extract was concentrated to a volume of 50 ml. and then cooled to 0° whereupon 0.723 g. (72%) of colorless needles precipitated. The needles were dissolved in a minimum amount of water and reprecipitated by the addition of concd. aqueous sodium hydroxide. This basic mixture was heated at 90° for two hours to destroy traces of ammonium iodide. It was then filtered and the solid dried. Upon recrystallization from ethanol, needles were obtained that melted with decomposition at 263-267°, and contained ionic iodide.

Anal. Calcd. for $C_{12}H_{20}O_4NI$: C, 39.04; H, 5.46; N, 3.79; I, 34.4. Found: C, 38.36; H, 5.45; N, 3.98; ionic I, 34.2.

With III. The Isolation of *trans*-2,6-Bis-(benzamidomethyl)-*p*-dioxane (IX).—A yellow colored solution was obtained along with 16 mg. of a tan brittle solid that could not be identified. The filtered solution was made basic by the slow addition of 3 g. of solid sodium hydroxide. Nitrogen was passed through the solution until the odor of ammonia disappeared, 1 ml. of benzoyl chloride was added and the mixture shaken vigorously for five minutes. A brown solid was formed which was decolorized and recrystallized by heating with a mixture of methanol, water and norite. The product then melted at 170-174° and weighed 0.15 g. (16%). It was recrystallized from a ligroin-ethanol mixture which raised the m.p. to 175°.

Anal. Calcd. for $C_{20}H_{22}O_4N_2$: N, 7.91. Found: N, 7.71.

With III.—The experiment was repeated and the reaction solution worked up in the same manner as with II. Evaporation of the solution to dryness produced a tar. The tar was water soluble and could be precipitated from aqueous solution by the addition of sodium hydroxide, but could not be purified.

The Reaction of II and III with Aniline.—Parallel reactions were run on the two isomers in the following manner: Two solutions were prepared containing 1 g. (0.00272 mole) of either II or III, 1.24 ml. (0.0136 mole) of aniline, and 10 ml. of b.p. 140° "xylene." Each solution was refluxed 5 hours and then worked up as follows.

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[7] All melting points were taken on a Fisher-Johns block.

[8] F. Arndt, *Org. Syntheses*, **15**, 4 (1935).

The Reaction Mixture from II. The Preparation of 3-Phenyl-7,9-dioxa-3-azabicyclo[3.3.1]nonane (X).—The reaction mixture was filtered from aniline hydroiodide (0.48 g.) and steam distilled until all xylene and excess aniline was removed and only unreacted II and water distilled. The contents of the distilling flask were then made 6 *N* with sulfuric acid and heated with agitation on the steam-bath for 15 minutes. The acidic mixture was cooled and filtered. The filtrate was made basic by the addition of solid sodium hydroxide. The solid that separated was filtered and dried. It was extracted by hot ligroin and the extract evaporated and cooled to yield 0.12 g. (22%) of light yellow plates of m.p. 132–134°. The product was recrystallized again from ligroin to yield colorless plates, m.p. 134°.

Anal. Calcd. for $C_{12}H_{15}NO_2$: C, 70.22; H, 7.37; N, 6.82; mol. wt., 205.3. Found: C, 69.92; H, 7.36; N, 6.68; mol. wt. cryoscopic in benzene, 211.

The Reaction Mixture from III.—The reaction mixture was filtered from 0.08 g. of aniline hydroiodide (indicating some reaction) and then worked up in the same manner as the reaction mixture from II. When the aqueous acidic solution was made basic a tar (*ca.* 30 mg.) precipitated. It was extracted into hot ligroin, but could not be recrystallized from ligroin or ethanol. The tar could not be solidified at −70°.

The Preparation and Hydrolysis of 2,6-*p*-Dioxanedicarboxylic Anhydride (XI).—One and sixty-eight hundredths grams (0.00954 mole) of *cis*-2,6-*p*-dioxanedicarboxylic acid (IV) was dissolved in 50 ml. of hot acetic anhydride and the solution boiled down at atmospheric pressure to a volume of 5 ml. It was then heated at 80° under reduced pressure to remove excess acetic anhydride. Fifty ml. of hexane was added to the cooled reaction product and the resulting immiscible liquids were agitated while 15 ml. of benzene was slowly added to the mixture. The reaction product formed large crystals during this operation. The crystals were filtered off and dissolved in 25 ml. of hot benzene. The benzene solution was poured into 40 ml. of hexane and 1.14 g. (76%) of colorless crystals was precipitated. They were dried for 2 hours at 5 mm., m.p. 106°.

Anal. Calcd. for $C_6H_6O_5$: neut. equiv., 79.1; mol. wt., 158.1. Found: neut. equiv., 79; mol. wt. cryoscopic in benzene, 169.

Thirty-three hundredths gram of this anhydride was dissolved in 5 ml. of water and the solution evaporated to dryness at 105°. The acidic residue weighed 0.34 g. and melted at 179°. The mixed melting point with IV was 177–178°.

Acknowledgment.—We wish to express our thanks to the Abbott Foundation of Northwestern University for the grant of financial aid that made this work possible.

EVANSTON, ILLINOIS

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF DUKE UNIVERSITY]

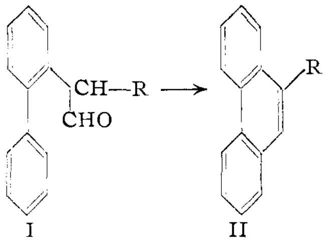
Aromatic Cyclodehydration. XXVII.[1] Cyclization of Aldehydes, Ketones and Ketonitriles

BY CHARLES K. BRADSHER AND WINSTON J. JACKSON, JR.[2]

RECEIVED OCTOBER 5, 1953

It has been shown that (2-biphenylyl)-acetaldehyde, some of its homologs and (2-biphenylyl)-acetone may be cyclized rapidly and in good yield to phenanthrene and 9-alkylphenanthrenes. Cyclization of acyl-(2-biphenylyl)-acetonitriles with hydrobromic and acetic acids affords a new route to 9-alkyl-10-phenanthronitriles and -phenanthramides.

Several years ago it was predicted that 2-biphenylyl-acetaldehyde (I, R = H) "as well as any compound converted to it under conditions of the cyclization, can be made to yield phenanthrene."[3]



I II

(R = H, CH_3, C_2H_5)

An earlier attempt to test the first part of this prediction was thwarted when the general synthesis of Darzens and Meyer[4] failed to yield the desired aldehyde.[5]

It has now been found possible to prepare the aldehyde in 46% yield by the Rosenmund reduction of 2-biphenylylacetyl chloride. In a similar manner, we have made α-(2-biphenylyl)-propionaldehyde (I, R = CH_3) and α-(2-biphenylyl)-butyraldehyde. The required α-(2-biphenylyl)-propionic acid was synthesized in a manner analogous to that described[6] for the α-(2-biphenylyl)-butyric acid. Since the acid chlorides could undergo an intramolecular Friedel and Crafts reaction, they were not purified by distillation. It appeared that little cyclization occurred under the conditions of the reduction, since only traces of phenolic material could be recovered from the reaction mixture. The chief loss in the reduction appeared to come from the further reduction of some of the aldehyde.

In boiling hydrobromic–acetic acid, the aldehydes were rapidly cyclized to the expected phenanthrene derivatives (II). The hydrocarbons crystallized in almost pure condition (melting point not more than one degree below that of a pure sample) from the cooled cyclization mixture. As an indication of the rapidity of the reaction, the biphenylylpropionaldehyde gave a 93% yield of 9-methylphenanthrene after a refluxing time of only *two minutes.*

In order to prepare 3-hydroxy-10-methylphenanthrene, α-(5-methoxy-2-biphenylyl)-propionitrile (III) was prepared from (5-methoxy-2-biphenylyl)-acetonitrile[1] by alkylation. Hydrolysis of the alkylated nitrile III with alcoholic potassium hydroxide solution yielded the acid IV. The acid was con-

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[1] For the preceding communication of this series, see THIS JOURNAL, **74**, 4880 (1952).

[2] Public Health Service Fellow of the National Cancer Institute (1950–1952).

[3] C. K. Bradsher and R. W. Wert, THIS JOURNAL, **62**, 2806 (1940).

[4] G. Darzens and M. Meyer, *Compt. rend.*, **196**, 489 (1933); M. Meyer, *ibid.*, **204**, 508 (1937).

[5] S. Thomas Amore, Thesis presented in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of Arts and Sciences of Duke University, 1944.

[6] C. K. Bradsher and W. J. Jackson, Jr., THIS JOURNAL, **73**, 3235 (1951).