and benzaldehyde. It was purified by distillation; b. p. 160–167° at 3 mm.

Anal. Calcd. for $C_{15}H_{16}O$: C, 84.9; H, 7.6. Found: C, 85.0; H, 7.8.

The diarylmethyl bromide (yield 70%; b. p., 154–155° at 1 mm.) was converted into the hydrocarbon by the regular procedure; white crystals from benzene-methanol; yield 30%; m. p. 160–174° dec. in air.

Anal. Calcd. for $C_{34}H_{30}$: C, 93.09; H, 6.91. Found: C, 93.00; H, 7.00.

Rate Measurements.—The rates of dissociation of the hydrocarbons in *o*-dichlorobenzene at 80° were determined by the procedure of Bachmann and Osborn.[7b] For hydrocarbons of relatively short half-life period, titrations were carried out at one minute and fractional parts of one-minute intervals for a total period of not over five to six minutes. For hydrocarbons with longer half-life periods, readings were usually taken at one minute intervals up to a total of ten minutes. In agreement with the previous work of Bachmann and co-workers, the rate-controlling step proved to be a reaction of the first order. The equation for the first order reaction may be written

$$k = \frac{-2.3}{t}\log\left(1-\frac{x}{a}\right)$$

where $\frac{x}{a}$ is the fraction of the pentaarylethane reacting and is calculated as the actual absorption of iodine to the theoretical absorption. Straight lines were obtained when $-\log(1-(x/a))$ was plotted against t. To obtain the velocity constants k, the slopes of the lines were multiplied by 2.3. In Table II are shown typical data obtained in a representative experiment.

TABLE II

TYPICAL DATA OBTAINED IN REPRESENTATIVE EXPERIMENT

1,1,1,2-Tetraphenyl-2-(3-*o*-xylyl)-ethane, 0.1025 g. Solvent mixture: *o*-dichlorobenzene, 89.3%; pyridine, 4.7%; ethanol, 6.0%. Theoretical absorption of 0.1061 *N* iodine, 4.41 cc. Temp., 80°.

Time, min.	0.1061 *N* iodine absorbed, cc.	$-\log(1-(x/a))$	x/a Found	x/a Calcd.[a]	Diff.
1.25	0.27	0.0274	0.061	0.062	−0.001
2.0	.45	.0468	.102	.099	+ .003
2.75	.56	.0590	.127	.132	− .005
3.5	.73	.0785	.166	.165	+ .001
4.25	.88	.0966	.200	.197	+ .003
5.0	1.01	.1130	.229	.227	+ .002

[a] x/a Calcd. is from the rate constant 0.0515.

Acknowledgment.—The authors are very grateful to Mrs. J. H. Woods of Calgary, Alberta, for financial aid which has helped to make this work possible.

Summary

Five tetraphenylxylylethanes have been prepared and their rates of dissociation have been measured.

EDMONTON, ALBERTA, CANADA RECEIVED APRIL 28, 1947

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ALBERTA]

Some Tetramethylanthracenes

BY J. CHARLES NICHOL[1] AND REUBEN B. SANDIN

The work reported in this paper is a continuation of a study of model compounds structurally related to the more potent carcinogens. 1,2,9,10-Tetramethylanthracene, which has been considered as a model of the highly active carcinogen, 9,10-dimethyl-1,2-benzanthracene has been synthesized[2] and has been found to be sensitive to air. The authors of the present paper considered it worth while to synthesize 1,2,5,6-tetramethylanthracene as a model of the carcinogen, 1,2,5,6-dibenzanthracene.

The preparation of 1,2,5,6-tetramethylanthracene involves a typical phthalic anhydride synthesis.[3] The required 3,4-dimethylphthalic anhydride (I) was obtained in 36% yield by the bromine dehydrogenation of 3,4-dimethyl-1,2,3,6-tetrahydrophthalic acid (II). The latter was obtained in satisfactory yield from maleic anhydride and 3-methylpentadiene-1,3. The keto acid mixture produced from I and the Grignard reagent of 3-bromo-*o*-xylene was separated without difficulty and afforded a low yield of III, and a moderately good yield of the lower melting isomer IV. The structure of IV follows from the results of decarboxylation in the presence of copper and cleavage of the resulting ketone. The combined reactions afforded 3,4-dimethylbenzoic acid. That none of the isomeric 2,3-dimethylbenzoic acid was isolated is in agreement with the observations of Bachmann.[4] Due to the lack of material it was impossible to carry out a similar experiment with III. However, the structure assigned to III is consistent from the standpoint of yield and melting point with the structures of other compounds obtained by the action of Grignard reagents on unsymmetrical phthalic anhydride derivatives.[5]

Reduction of the keto carboxylic acids III and IV with zinc and sodium hydroxide presented no difficulty and afforded good yields of 2-(2′,3′-dimethylbenzyl)-3,4-dimethylbenzoic acid (V) and 2-(2′3′-dimethylbenzyl)-5,6-dimethylbenzoic

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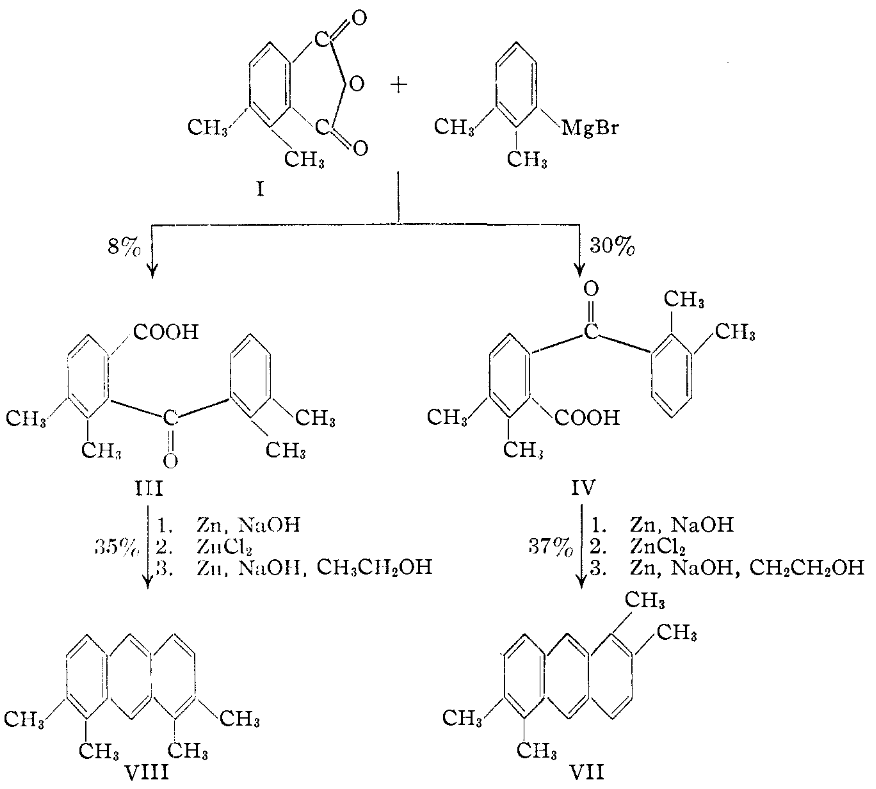
[1] Present address: Department of Chemistry, University of Wisconsin, Madison, Wisconsin.

[2] Sandin, Kitchen and Fieser, THIS JOURNAL, **65**, 2018 (1943).

[3] Fieser, "The Chemistry of Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1936, pp. 93–96.

[4] Bachmann, THIS JOURNAL, **57**, 737 (1935). In the cleavage of unsymmetrical ketones by potassium hydroxide, Bachmann found that the *o*-tolyl group (hindered) is easily separated from the carbonyl while the *m*- and *p*-tolyl radicals (unhindered) are not.

[5] (a) Fieser and Newman, THIS JOURNAL, **58**, 2376 (1936); (b) Sandin and Fieser, *ibid.*, **62**, 3098 (1940).



acid (VI), respectively. Subsequent cyclization and reduction of V and VI gave in satisfactory yields the hydrocarbons 1,2,7,8-tetramethylanthracene (VII) and 1,2,5,6-tetramethylanthracene (VIII) which were found to be relatively stable in air.

Cyclization of the keto acid IV with sulfuric acid gave a mixture of 1,2,5,6-tetramethylanthraquinone and what is believed to be 1,2,7,8-tetramethylanthraquinone. The formation of the latter compound evidently involves a rearrangement of the type encountered by Hayashi[6] and elucidated by Cook.[7]

Experimental[8]

Tiglaldehyde was prepared by the method described by Bernhauer and Skudrzyk.[9] 3-Methylpentadiene-1,3[10] was prepared by the iodine catalyzed dehydration[11] of methylpentenol[12] obtained from tiglaldehyde and ethylmagnesium iodide.

3,4-Dimethyl-1,2,3,6-tetrahydrophthalic Acid (II).—The method of Brunner, Hofer and Stein[13] was used for this preparation, yield 80%, m. p. 64–65°.

3,4-Dimethylphthalic Anhydride (I).—The dehydrogenation method described by Newman and McLeary[14] for the preparation of 3-methylphthalic anhydride was followed for the dehydrogenation of II. To a boiling solution of 48 g. of 3,4-dimethyl-1,2,3,6-tetrahydrophthalic acid (II) in glacial acetic acid (100 ml.) there was added 120 g. of bromine in glacial acetic acid (230 ml.) over a period of two hours. The solution was refluxed until the bromine color disappeared. The acetic acid was removed by vacuum distillation and the residue was heated at 210–220° for fifteen hours. Vacuum distillation and recrystallization from benzene–hexane afforded 17.5 g. of 3,4-dimethylphthalic anhydride melting at 119–122°.[15]

Reaction of 3,4-Dimethylphthalic Anhydride with the Grignard Reagent of 3-Bromo-*o*-xylene.—Following the procedure of Fieser and Newman[16] the Grignard reagent from 20 g. of 3-bromo-*o*-xylene in ether was added rapidly to a well-stirred solution of 20 g. of 3,4-dimethylphthalic anhydride in 300 ml. of warm thiophene-free benzene. The mixture was refluxed for two hours, cooled, treated with dilute hydrochloric acid, and the benzene–ether layer was separated and extracted thoroughly with sodium carbonate solution. Acidification of the soda extracts afforded a crude keto acid mixture which on crystallization from acetic acid gave 2.4 g. (8%) of almost pure 2-(2′,3′-dimethylbenzoyl)-3,4-dimethylbenzoic acid (III). For analysis it was crystallized from benzene. It formed white crystals, m. p. 246–248°.

Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.6; H, 6.4. Found: C, 76.5; H, 6.5.

After the removal of III, the above acetic acid solution was evaporated to dryness and the residue taken up in benzene. The addition of ligroin caused the precipitation of tarry material, from which the clear solution was separated. The latter was evaporated to dryness and the residue was dissolved in a hot saturated solution of sodium carbonate. This was allowed to cool slowly and the salt of 2-(2′,3′-dimethylbenzoyl)-5,6-dimethylbenzoic acid (IV) separated in a crystalline condition. The acid liberated from the crystalline salt was almost pure. The yield was 9 g. (30%). For analysis it was crystallized from a mixture of benzene and ligroin from which it separated as white crystals, m. p. 161°.

Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.6; H, 6.4. Found: C, 76.3; H, 6.6.

One gram of IV was decarboxylated in the presence of copper and without isolating the resulting ketone, the reaction mixture was heated with potassium hydroxide according to the directions of Bachmann.[4] The reaction mixture afforded 3,4-dimethylbenzoic acid m. p. 166°. A mixed melting point with an authentic sample of 3,4-dimethylbenzoic acid m. p. 166° was not depressed. None of the expected 2,3-dimethylbenzoic acid was isolated.

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[6] Hayashi, *J. Chem. Soc.*, 2516 (1927); 1513, 1520, 1524 (1930). See also Barnett and Marrison, *Ber.*, **64**, 535 (1931).

[7] Cook, *J. Chem. Soc.*, 1472 (1932).

[8] All melting points are corrected.

[9] Bernhauer and Skudrzyk, *J. prakt. Chem.*, **155**, 310 (1940).

[10] Farmer and Warren, *J. Chem. Soc.*, 3221 (1931).

[11] Kenyon and Young, *ibid.*, 1547 (1940).

[12] Abelmann, *Ber.*, **43**, 1574 (1910).

[13] Brunner, Hofer and Stein, *Monatsh.*, **63**, 79 (1933).

[14] Newman and McLeary, THIS JOURNAL, **63**, 1543 (1941).

[15] Brunner, Hofer and Stein have reported a m. p. of 124–125° for the anhydride. They have also reported a m. p. of 149–150° for the 3,4-dimethylphthalic acid (with rapid heating). The present authors have found that the acid melts at 154–156° with decomposition when the bath temperature is raised at a rate of one degree per minute.

[16] Fieser and Newman, THIS JOURNAL, **58**, 2376 (1936).

2-(2′,3′-Dimethylbenzyl)-5,6-dimethylbenzoic Acid (VI).—A solution of 2-(2′,3′-dimethylbenzoyl)-5,6-dimethylbenzoic acid (1 g.) in 1 *N* potassium hydroxide (100 ml.) was refluxed for forty-eight hours with zinc dust (5 g.) activated with copper sulfate. After the removal of excess zinc, the solution was acidified and afforded 0.9 g. of VI, m. p. 146–150°. After crystallization from acetic acid it melted at 152–153°.

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.6; H, 7.5. Found: C, 80.0; H, 7.5.

2-(2′,3′-Dimethylbenzyl)-3,4-dimethylbenzoic acid (V) was obtained in 75% yield from III by the same procedure. After crystallization from acetic acid it melted at 187–189°.

Anal. Calcd. for $C_{18}H_{20}O_2$: C, 80.6; H, 7.5. Found: C, 80.7; H, 7.7.

1,2,5,6-Tetramethylanthracene (VII).—2-(2′,3′-Dimethylbenzyl)-5,6-dimethylbenzoic acid (0.9 g.) was mixed with anhydrous zinc chloride (2 g.) and heated at 180–185° for thirty minutes. After cooling, the melt was powdered, extracted with water and warmed with 0.1 *N* sodium carbonate to remove a trace of unaltered acid. A solution of the crude anthrone in 1 *N* sodium hydroxide (100 ml.) and ethyl alcohol (50 ml.) was refluxed for sixty hours with zinc dust (5 g.). The resulting solid was collected and extracted with benzene–alcohol. Addition of picric acid to the extract afforded almost black crystals of the picrate of 1,2,5,6-tetramethylanthracene. The picrate was recrystallized from benzene–alcohol, m. p. 187–189°.

Anal. Calcd. for $C_{18}H_{18}\cdot C_6H_3O_7N_3$: C, 62.2; H, 4.6. Found: C, 62.4; H, 4.6.

The regenerated hydrocarbon (ammonia) was crystallized from acetic acid and formed pale yellow needles, m. p. 204°. The over-all yield of 1,2,5,6-tetramethylanthracene from 1 g. of IV was 0.3 g. (37%).

Anal. Calcd. for $C_{18}H_{18}$: C, 92.3; H, 7.7. Found: C, 92.0; H, 8.0.

1,2,7,8-Tetramethylanthracene (VIII).—The picrate of the hydrocarbon was obtained from V by the above procedure. It formed red needles, m. p. 183–185°, from benzene–alcohol.

Anal. Calcd. for $C_{18}H_{18}\cdot C_6H_3O_7N_3$: C, 62.2; H, 4.6. Found: C, 62.3; H, 4.8.

The regenerated hydrocarbon (ammonia) formed pale yellow crystals, m. p. 140–141°. The over-all yield of hydrocarbon from the keto acid was about 35%.

Anal. Calcd. for $C_{18}H_{18}$: C, 92.3; H, 7.7. Found: C, 92.5; H, 8.1.

1,2,5,6-Tetramethylanthraquinone.—One gram of the keto acid IV was cyclized by treatment with concentrated sulfuric acid at 90–100° for three hours. This afforded a mixture of 1,2,5,6-tetramethylanthraquinone (IX) and a compound which is believed to be 1,2,7,8-tetramethylanthraquinone (X). Quinone IX (0.3 g.) crystallized from glacial acetic acid as yellow-brown needles, m. p. 201–202°.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.8; H, 6.1. Found: C, 81.5; H, 6.5.

A small amount of 1,2,5,6-tetramethylanthracene dissolved in glacial acetic acid was treated with chromic acid. The reaction product was crystallized from acetic acid and when mixed with some of the above 1,2,5,6-tetramethylanthraquinone showed no depression of the melting point.

Quinone X (0.3 g.) crystallized from dilute acetic acid as yellow-brown needles, m. p. 160–161°.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.8; H, 6.1. Found: C, 81.4; H, 6.3.

Because of the lack of material the authors were unable to supply a rigid proof for the structure of this compound.

Acknowledgment.—The authors wish to express their appreciation to Mrs. J. H. Woods of Calgary, Alberta, for financial aid in the pursuance of this research. The authors are also grateful to a Friend of the University for financial aid which has helped to make this work possible.

Summary

1,2,5,6-Tetramethylanthracene, of interest as a model of the carcinogen 1,2,5,6-dibenzanthracene, has been synthesized. 1,2,7,8-Tetramethylanthracene has also been synthesized and characterized in the form of the picrate.

EDMONTON, ALBERTA, CANADA RECEIVED APRIL 28, 1947

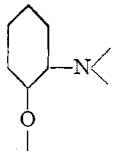
[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF PARKE, DAVIS AND CO.]

Derivatives of 3-Amino-4-hydroxybenzenearsonic Acid

BY L. A. SWEET, JOHN CONTROULIS, E. W. TILLOTSON[1] AND C. K. BANKS

A large portion of the compounds used as treponemicidal agents have the basic structure I.

I.



One of the most active of the pentavalent arsenicals derived from this nucleus is 3-amino-4-β-hydroxyethoxybenzenearsonic acid.[2,3] In a systematic investigation of further derivatives having the 4-β-hydroxyethoxyl group, a number of substituted 3-amino compounds were prepared. These were analogous to derivatives of *p*-arsanilic acid previously examined, principally tryparsamide,[4] arsonophenylglycine[5] and *p*-biguanidobenzenearsonic acid.[6]

3-Amino-4-β-hydroxyethoxybenzenearsonic acid reacted with chloroacetic acid and chloroacetamide to yield the glycine and glycineamide derivatives respectively. In common with many other arsenicals of structure I, the products isolated from solution and dried of superficial moisture had one or more molecules of water associated with

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(2) Sweet and Hamilton, THIS JOURNAL, **56**, 2409 (1934).

(3) Tatum, *et al.*, *J. Pharmacol.*, **59**, 241 (1937).

(4) Jacobs and Heidelberger, THIS JOURNAL, **41**, 1587 (1919).

(5) Jacobs and Heidelberger, *ibid.*, **41**, 1440 (1919).

(6) Banks, *et al.*, *ibid.*, **68**, 2102 (1946).