hours. Evaporation of the ether left 0.775 g. (83.5% yield) of white material m. p. 131–133°. The compound crystallized from hot water in the form of needles, m. p. *ca.* 90°. This appeared to be a hydrated form since when dried in a pistol at 80° the needles disappeared and an amorphous product, m. p. 139–140°, was obtained.

Anal. Calcd. for $C_8H_{10}O_2N_2S$: C, 48.46; H, 5.08; N, 14.13; S, 16.17. Found: C, 48.56; H, 4.97; N, 13.93; S, 15.83.

Acknowledgments.—The authors wish to thank Mr. A. W. Spang and Margaret McCarthy Ledyard for the microanalyses and Dr. O. D. Bird for the microbiological assays.

Summary

2′-Keto-3,4-imidazolido-2-γ-phenoxypropylthiophene (VIa) and 2′-keto-3,4-imidazolido-2-γ-benzyloxypropylthiophene (VIb) have been synthesized from Ia and Ib, respectively, by means of the Curtius degradation.

2′-Keto-3,4-imidazolido-2-γ-hydroxypropylthiophene (VIc) has been prepared from VIb by cleavage of the benzyl ether with sodium in liquid ammonia.

DETROIT, MICHIGAN RECEIVED OCTOBER 1, 1945

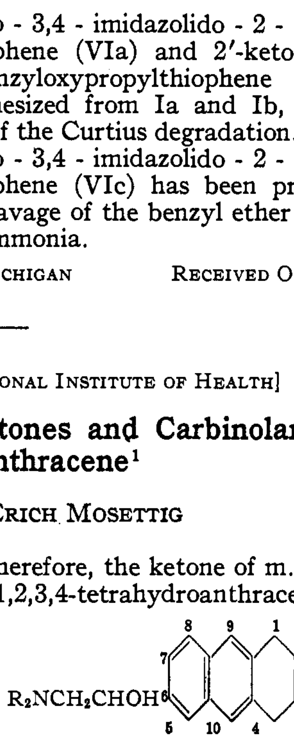
[CONTRIBUTION FROM THE DIVISION OF PHYSIOLOGY, NATIONAL INSTITUTE OF HEALTH]

Studies in the Anthracene Series. I. Methyl Ketones and Carbinolamines Derived from 1,2,3,4-Tetrahydroanthracene[1]

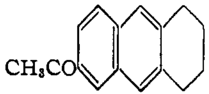
BY EDWARD A. GARLOCK, JR., AND ERICH MOSETTIG

In the course of an extended chemotherapeutic research program, the preparation of tetrahydroanthryl carbinolamines of formula I was warranted. The most convenient starting materials for these compounds are apparently the methyl ketones of which three aromatically substituted isomers are possible.

When, under mild conditions, 1,2,3,4-tetrahydroanthracene was allowed to react with acetyl chloride in the presence of aluminum chloride, a mixture of methyl ketones was obtained in a yield of about sixty to seventy per cent. One of the isomers could be separated readily by triturating the mixture with petroleum ether. It melts at 101–102°. By chromic acid oxidation it was converted to a quinone to which, by reasons of analogy,[2] the formula of an acetyltetrahydro-9,10-anthraquinone was assigned. On dehydrogenation with sulfur it yielded the known 2-acetylanthracene of m. p. 188–189.5°.[3] Moreover, it is oxidized with sodium hypochlorite to a tetrahydroanthracenecarboxylic acid whose ester is dehydrogenated to the corresponding 2-anthracene derivative. A migration of the acetyl or carbethoxyl group from position 1 to position 2 cannot be entirely excluded[4] but the moderate conditions of the dehydrogenation, together with the relatively high melting point of the tetrahydroacetyl compound support very strongly the assumption that no migration has taken place, and that, therefore, the ketone of m. p. 101–102° is 6-acetyl-1,2,3,4-tetrahydroanthracene (II).



I



II

The oil remaining after separation of the crystalline ketone was purified repeatedly through the semicarbazone and picrate until a nearly colorless mobile oil of constant refractive index resulted. It gave on chromic acid oxidation a quinone to which, again by reasons of analogy,[2] the structure of an acetyltetrahydro-9,10-anthraquinone was assigned, and on dehydrogenation the known 1-acetylanthracene of m. p. 108°.[4a,5] In both operations the yields of pure end-product were rather low. Sodium hypochlorite oxidation of the carefully purified oily ketone, followed by esterification, gave an acid and its ester, respectively, which gave correct analytical results but had rather unsharp melting points in spite of repeated recrystallization. No explanation can be offered at present for this behavior. Moreover, the possibility that in the Friedel–Crafts reaction the hydrogenated ring was attacked cannot be overlooked entirely. Although other evidence indicates the probable structure of 5-acetyl-1,2,3,4-tetrahydroanthracene for the oily ketone, we suggest this as a tentative structure only. We expect to offer, within reasonable time, for this compound as well as for the solid ketone, an unambiguous structural proof. In the Friedel–Crafts reaction described above, nitrobenzene

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(1) The work described in this paper was done in part under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the National Institute of Health.

(2) 1,2,3,4-Tetrahydroanthracene is readily oxidized by chromic acid to 1,2,3,4-tetrahydro-9,10-anthracene quinone, ref. 6a. Meerwein and Migge, *Ber.*, **62**, 1046 (1929).

(3) (a) I. G. Farbenindustrie, A.-G., German Patents 492,247 and 493,688, *C. A.*, **24**, 2472, 2757 (1930); (b) Buu-Hoï and Cagniant, *Rec. trav. chim.*, **62**, 713 (1943).

(4) (a) Waldmann and Marmorstein, *Ber.*, **70**, 106 (1937); (b) I. G. Farbenindustrie, A.-G., German Patent 499,051; *C. A.*, **24**, 4065 (1930).

(5) King, THIS JOURNAL, **66**, 894 (1944). Reference 7.

was used as solvent. When instead, tetrachloroethane was employed, the formation of the 6-acetyl derivative was almost entirely suppressed, while the oily ketone was formed in approximately the same yield as in the nitrobenzene experiment.

Of amino alcohols of type I, carrying the side chain in position 6, we prepared the diamylamino-, diheptylamino- and dinonylamino derivatives in the usual manner, *via* the ω-bromo ketone and the amino ketones. The latter were reduced with aluminum isopropoxide in isopropanol solution.

In the catalytic hydrogenation of anthracene[6] to tetrahydroanthracene, copper chromite catalyst is more convenient than Raney nickel catalyst. With the former the reduction can be more easily controlled. Under the conditions employed by us (Cu-Cr catalyst), 9,10-dihydroanthracene appears to be the intermediate reduction product. Incidentally, by lowering the temperature, the high-pressure reduction of anthracene with copper-chromite catalyst becomes a very convenient preparative method for 9,10-dihydroanthracene.

We wish to express our thanks to Dr. Robert C. Elderfield for supplying us generously with diheptyl- and dinonyl-amine.

Experimental[7]

Hydrogenation of Anthracene. 1,2,3,4-Tetrahydroanthracene.—(a) A mixture of 89 g. of purified anthracene,[8] 5 g. of copper chromite catalyst[9] and 300 cc. of decalin[10] was placed in a high-pressure hydrogenation bomb (1-liter content). Hydrogen was admitted (1400 lb. at room temperature) and shaking was commenced at a pressure of 2300 lb. and a temperature of 250°. The pressure dropped 450 lb. within three minutes (corresponding to the formation of 9,10-dihydroanthracene). At this point the rate of hydrogen absorption changed abruptly. A further drop in pressure of 450 lb. took twenty-four minutes, when the reaction was interrupted. During the whole reduction period the temperature was maintained between 240–260°. The catalyst was filtered through Filter-Cel from the decalin solution of the reduction products, and the decalin was distilled off in an oil-pump vacuum (at approximately 80°). The residue, a white crystalline solid, was dissolved in 200 cc. of alcohol and to this hot solution was added a hot solution of 115 g. of picric acid (containing 10% water) in 300 cc. of alcohol. The picrate began to form immediately and was collected when the solution had cooled to room temperature.[11] It formed long yellow-red needles, melting at 109–113°; yield 88 g. The hydrocarbon was liberated by heating the picrate in *ca.* one and one-half liters of 1% sodium hydroxide solution on the steam-bath. Tetrahydroanthracene was filtered and well washed with hot water. It melted at 96–98° and weighed 39 g. (43% yield). One crystallization from alcohol gave 35.6 g. of colorless plates melting at 98–100°.

The mother liquor of the first picrate crystallizate yielded on further standing two fractions of picrate weighing *ca.* 30 g. Both fractions contained a considerable amount of white crystals (needles and plates), consisting chiefly of dihydro- and octahydro-anthracene. Various attempts to isolate from these fractions pure tetrahydroanthracene picrate, failed.

In some twenty reduction experiments, according to these directions, the yields of tetrahydroanthracene varied approximately ±5%.

(b) When anthracene (89 g.) in decalin (300 cc.) was reduced at a pressure of about 1500 lb., at 130°, using Raney nickel catalyst (10–15 g.), tetrahydroanthracene was obtained in a considerably lower yield (20–25 g., *ca.* 25% yield, the average of five experiments).

(c) From **Dihydroanthracene.**—Dihydroanthracene (m. p. 110.5–112°) absorbed under the conditions of experiment (a) one mole of hydrogen in *ca.* 40 minutes. The reaction mixture yielded *ca.* 26% of pure tetrahydroanthracene and 7% nearly pure dihydroanthracene.

9,10-Dihydroanthracene.—When anthracene was reduced under the conditions of experiment (a) but at a temperature of 150°, one mole of hydrogen was absorbed within five minutes and the reduction came to a standstill. The yield of pure dihydroanthracene was 95%.

The Friedel–Crafts Reaction with 1,2,3,4-Tetrahydroanthracene.—To a solution of 20.5 cc. of redistilled acetyl chloride and 60 g. of resublimed aluminum chloride in 190 cc. of dry nitrobenzene was added slowly, with mechanical stirring, a solution of 45.5 g. of tetrahydroanthracene in 145 cc. of dry nitrobenzene while the reaction mixture was kept between −3 and −7°. When all was added the solution was allowed to warm up slowly to 5°, and was kept at this temperature for twenty hours. The dark red solution was poured onto ice and hydrochloric acid. The grayish nitrobenzene layer was separated and washed with water. After removal of nitrobenzene with steam, the reaction product was extracted with ether, and the dried ethereal extract evaporated to dryness. The residual oil gave on distillation (160–170° at *ca.* 0.1 mm.) 48 g. of a light yellow oil, which crystallized partially on cooling. It was treated with about 200 cc. of ligroin (b. p. 90–100°), allowed to stand at room temperature for several hours, and finally kept over night at 5° in order to complete as nearly as possible the separation of the solid ketone.

6-Acetyl-1,2,3,4-tetrahydroanthracene (II).—The crystalline ketone was collected and washed with an ether–ligroin mixture. It weighed 17.6 g. and melted at 99–101°. It crystallized from benzene–ligroin in long white needles. After sublimation *in vacuo* it melted at 101–102°.

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.67; H, 7.19. Found: C, 85.43; H, 7.10.

5-Acetyl-1,2,3,4-tetrahydroanthracene.—The ligroin mother liquor of the solid ketone (II) was concentrated to dryness and the oily residue dissolved in 250 cc. of hot alcohol. A concd. aqueous solution of the calculated amounts of semicarbazide hydrochloride and sodium acetate was added, the mixture was heated to boiling for several minutes and filtered while still hot. A small amount of a sparingly soluble semicarbazone was collected and washed with hot water (2 g., m. p. 246–250° dec.). The alcoholic filtrate was allowed to stand overnight and finally cooled in ice. The voluminous precipitate was collected, washed with alcohol and dried. It weighed 21.5 g. and melted at 200–202°. The semicarbazone was decomposed by refluxing with 3 *N* hydrochloric acid, the ketone extracted with ether and finally distilled evaporatively in an oil pump vacuum (*ca.* 170°, 0.1 mm.) yielding 13.5 g. of a nearly colorless, mobile oil, $n^{25}D$ 1.6338. The ketone was converted into the picrate, which in turn gave on decomposition a ketone with the refractive index $n^{25}D$ 1.6333.

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(6) (a) Schroeter, *Ber.*, **57**, 2003 (1924); (b) Fries and Schilling, *ibid.*, **65**, 1494 (1932); (c) Burger and Mosettig, THIS JOURNAL, **58**, 1857 (1936); (d) Orchin, *ibid.*, **66**, 535 (1944).

(7) All melting points given are corrected.

(8) Anthracene (a 98% pure, Reilly product) was refluxed (in 2-kg. lots) with 1.5% sodium and distilled. It melted after recrystallization from thiophene-free benzene at 215.5–217°; yield 60–70%.

(9) Connor, Folkers and Adkins, THIS JOURNAL, **54**, 1138 (1932); Adkins, "Reactions of Hydrogen," The University of Wisconsin Press, 1937, p. 13.

(10) Decalin (commercial) was shaken with small quantities of fuming sulfuric acid until a nearly colorless and clear acid layer resulted. It was washed with dilute soda solution, dried over calcium chloride, distilled and kept over sodium.

(11) This is the most critical point of the preparation. Sometimes it is advisable to filter the picrate before the mixture has cooled to room temperature, namely, if one observes the formation of colorless plates or needles.

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.67; H, 7.19. Found: C, 85.36; H, 7.52.

Derivatives of 6-Acetyl-1,2,3,4-tetrahydroanthracene (II). Semicarbazone.—The ketone was heated for a short time in an ethanol solution of semicarbazide hydrochloride and sodium acetate. The sparingly soluble semicarbazone was recrystallized from Cellosolve. White irregular plates formed, m. p. 251.5–252.5°.

Anal. Calcd. for $C_{17}H_{19}N_3O$: N, 14.94. Found: N, 14.73.

Oxime.—A warm concentrated aqueous solution of 0.19 g. of hydroxylamine hydrochloride and 0.37 g. of sodium acetate trihydrate was added to a warm solution of 0.55 g. of ketone in 4 cc. of alcohol, and the mixture was refluxed for five minutes. The oxime crystallized from alcohol in white plates of m. p. 165.5–167°, yield 0.5 g.

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16. Found: C, 80.63; H, 7.59.

Picrate.—Equimolecular amounts of ketone and picric acid were warmed in ethanol solution. The picrate crystallized from ethanol in light yellow needles, m. p. 118–120°.

Anal. Calcd. for $C_{22}H_{19}N_3O_8$: C, 58.28; H, 4.22. Found: C, 58.47; H, 4.05.

6-Acetyl-1,2,3,4-tetrahydro-9,10-anthraquinone.—To a solution of 4.4 g. of ketone in 25 cc. of glacial acetic acid was added gradually a warm solution of 5 g. chromic anhydride in 3 cc. of water and 22 cc. of glacial acetic acid. The temperature was not allowed to rise above 50°. Finally the solution was warmed to 60° for ten minutes and allowed to stand at room temperature for one hour. By pouring the green solution into 100 cc. of water the quinone was precipitated. It was collected, washed with water and recrystallized from alcohol (Norite). The yield was 2.2 g., m. p. 157.5–161°. Two crystallizations from absolute alcohol gave yellow needles melting at 169–170°.

Anal. Calcd. for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.18; H, 5.83.

6-(ω-Bromoacetyl)-1,2,3,4-tetrahydroanthracene.—To a stirred cooled solution (5°) of 8.96 g. of the ketone in 360 cc. of absolute ether was added dropwise 2.1 cc. of bromine (one drop of bromine had been added at room temperature, to initate the reaction). A heavy red-orange precipitate appeared while the reaction mixture became warm. The precipitate disappeared after several minutes leaving a colorless solution, from which very shortly the bromo ketone precipitated in nearly white needles. After cooling (−5°) the precipitate was filtered and washed with cold ether. After recrystallization from acetone light-yellow tinged needles of m. p. 113.5–115° were obtained, yield 8 g.

Anal. Calcd. for $C_{16}H_{15}BrO$: C, 63.38; H, 4.99. Found: C, 62.94; H, 5.34.

The ethereal mother liquors of the first crop gave 2.2 g. of bromo ketone melting at 108.5–111°.

6-(1-Hydroxyethyl)-1,2,3,4-tetrahydroanthracene.—One and one-tenth grams of the ketone was reduced with 6.5 cc. of 3 *N* isopropoxide isopropanol solution according to Lund's[12] modification of the Meerwein–Ponndorf–Verley reduction method.[13] The reduction was completed in fifteen minutes. The solvent was removed *in vacuo*, the residue treated with dilute sodium hydroxide and extracted with ether. The ethereal residue yielded 0.9 g. of white needles which, after sublimation, melted at 87.5–88.5°.

Anal. Calcd. for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 84.80; H, 8.14.

6-Ethyl-1,2,3,4-tetrahydroanthracene.—A mixture of 2.2 g. of ketone, 10 g. of amalgamated zinc, 20 cc. of glacial acetic acid, 20 cc. of concd. hydrochloric acid and 8 cc. of toluene was refluxed for twenty-four hours. Three 6-cc. portions of concd. hydrochloric acid were added during this period. The reaction mixture was extracted with ether. The ethereal extract was washed with carbonate, dried and evaporated. The residue was evaporatively distilled in an oil-pump vacuum. A colorless oil was obtained which crystallized soon, and melted at 35–36.5°; yield 1.9 g. It crystallized from alcohol in colorless irregular plates which melted at 38–39.5°.

Anal. Calcd. for $C_{16}H_{18}$: C, 91.37; H, 8.63. Found: C, 91.06; H, 8.76.

The picrate prepared in the usual manner consisted of bright red plates melting at 96–97°. After one recrystallization from ethanol, it melted at 100–101°. Because of its instability, no consistent analytical values could be obtained.

1,2,3,4-Tetrahydroanthracene-6-carboxylic Acid.—To a sodium hypochlorite solution (prepared from 7.5 g. of H. T. H., 90 cc. of water, 4.1 g. of sodium carbonate and 1.2 g. of sodium hydroxide in 45 cc. of water) was added 3.3 g. of ketone, and the mixture was refluxed with stirring for two hours. Warm water was added to bring all the sodium salt in solution and a small amount of unchanged ketone was filtered off. The acid was precipitated by the addition of sodium bisulfite and concd. hydrochloric acid, and weighed after drying 2.8 g. The acid crystallized from glacial acetic acid in white plates and was finally sublimed *in vacuo*, m. p. 264–266°.

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.69; H, 6.65.

Ethyl Ester.—A mixture of 1 g. of acid, 20 cc. of absolute alcohol and 1.8 g. of concd. sulfuric acid was refluxed for three hours. The ester precipitated on cooling as white plates. The alcohol was removed *in vacuo*, the residue treated with ether, and the ethereal extract washed with dilute alkali. The ethereal residue gave on sublimation *in vacuo* 1.2 g. of white needles melting at 113°.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.29; H, 7.13. Found: C, 80.57; H, 7.46.

Dehydrogenations.—(a) A mixture of 0.5 g. of ketone and 0.17 g. of sulfur was heated in an evacuated sealed bulb-tube at 220° for one hour. (Bubbles of hydrogen sulfide were given off rapidly during the first fifteen minutes.) The temperature was then raised to 250° over a thirty minute period. The tube was opened, a small amount of zinc dust[14] added, and the mixture heated to 220° for five minutes. The solid reaction mass was transferred to a sublimation bulb and the organic material sublimed in an oil-pump vacuum. The main sublimate (0.3 g.) melted at 180–189°. By recrystallization from benzene yellow plates melting at 188–189.5° were obtained. The mixture melting point with an authentic sample of 2-acetylanthracene of m. p. 189–189.5° was 188.5–190°.

(b) A mixture of 0.25 g. of the ethyl ester of tetrahydroanthracene-6-carboxylic acid and 0.1 g. of sulfur was heated as above at 210–225° for one hour. The mixture with copper-bronze powder was heated for ten minutes at 200–210°. The reaction mixture was subjected to sublimation in an oil-pump vacuum. The sublimate was treated with Norite in hot benzene, the benzene solution evaporated and the residue recrystallized from methanol. One-tenth of a gram of light yellow plates was obtained, which melted after sublimation at 138–139°.

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.58; H, 5.64. Found: C, 81.49; H, 6.17.

The mixture with an authentic sample of the ethyl ester of 2-anthroic acid of m. p. 137.5–139° melted at 137.5–139°.

6-(2-Diamylamino-1-hydroxyethyl)-1,2,3,4-tetrahydroanthracene Hydrochloride.—To a suspension of 6.06 g. (0.02 mole) of 6-ω-bromoacetyltetrahydroanthracene in 50 cc. of absolute ether was added 6.38 g. (0.04 mole) of diamylamine. The mixture was shaken for three hours and

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[12] Lund, *Ber.*, **70**, 1520 (1937).

[13] Adams, "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1944, p. 178.

[14] Fieser, "Experiments in Organic Chemistry," 2nd ed., D. C. Heath and Company, Boston, Mass., 1941, p. 456.

then placed in the refrigerator for one hour. The soapy precipitate of the aliphatic amine hydrobromide (3.9 g.) was filtered off and washed with cold ether. The ethereal filtrate was evaporated to dryness, and the remaining oily amino ketone was reduced with 30 cc. of 3 *N* aluminum isopropoxide isopropanol solution.[13] The reduction proceeded rapidly and refluxing was continued for one-half hour after the test for acetone had become negative. Isopropanol was removed *in vacuo*, the residue treated with dilute sodium hydroxide solution, and extracted with ether. The dried ethereal solution left on evaporation an oily amino alcohol which was evaporatively distilled in an oil pump vacuum (*ca.* 0.1 mm.). A small amount of diamylamine was collected below 150° while the amino alcohol distilled slowly as a yellowish viscous oil at 210–220°. The base (4.6 g.) was dissolved in absolute ether and acidified carefully with gaseous hydrochloric acid. First a small amount of diamylamine hydrochloride precipitated and was removed by filtration. Then the amino alcohol precipitated as greyish-white crystals which melted at 107–112° (4.5 g.). After two crystallizations from an ethanol–ether mixture, the hydrochloride was obtained as white leaflets melting at 111.5–114° (3.5 g.). The analytical sample (m. p. 114.5–116°) was dried *in vacuo* at 80° for one-half hour.

Anal. Calcd. for $C_{26}H_{40}ClNO$: C, 74.70; H, 9.65. Found: C, 74.80; H, 9.38.

6-(2-Diheptylamino-1-hydroxyethyl)-1,2,3,4-tetrahydroanthracene Hydrochloride.—A suspension of 5.7 g. of bromo ketone in 35 cc. of absolute ether was shaken with 8.7 g. of diheptylamine for two hours and the reaction mixture allowed to stand in the refrigerator overnight. The aliphatic amine hydrobromide (5.2 g.) was filtered, the ethereal filtrate evaporated and the residue treated with 25 cc. of a 3 *N* aluminum isopropoxide isopropanol solution. The amino alcohol was isolated as described for the lower homolog. The hydrochloride precipitated from an ether-petroleum ether solution as white leaflets (4.2 g.), m. p. 113–116°. After two recrystallizations from ether-petroleum ether, it melted at 114.5–116.5°.

Anal. Calcd. for $C_{30}H_{48}ClNO$: C, 75.99; H, 10.20. Found: C, 76.07; H, 10.30.

6-(2-Dinonylamino-1-hydroxyethyl)-1,2,3,4-tetrahydroanthracene Hydrochloride.—A suspension of 6.06 g. of bromo ketone in 50 cc. of absolute ether was shaken with 11.8 g. of dinonylamine for three hours and the reaction mixture allowed to stand in the refrigerator for one and one-half hours. The isolation of amino ketone and its reduction to the amino alcohol were carried out as above. In this instance vacuum distillation proved to be unnecessary. The crude hydrochloride of the base weighed 4.1 g. and melted at 107–115°. After recrystallization from a mixture of absolute ethanol, ether and petroleum ether, it melted at 112–116°. The compound may also be recrystallized from ethyl acetate (colorless leaflets).

Anal. Calcd. for $C_{34}H_{56}ClNO$: C, 77.01; H, 10.65. Found: C, 76.84; H, 10.81.

Derivatives of 5-Acetyl-1,2,3,4-tetrahydroanthracene.[15]

Semicarbazone.—It crystallized from ethanol in white fine needles and melted at 209–211°.

Anal. Calcd. for $C_{17}H_{19}N_3O$: C, 72.57; H, 6.81. Found: C, 72.48; H, 7.13.

Oxime.—A mixture of 0.22 g. of ketone in 1 cc. of absolute alcohol, and a concd. aqueous solution of 0.08 g. hydroxylamine hydrochloride and 0.16 g. of sodium acetate trihydrate was heated for four hours. The oxime precipitated on standing as white needles melting at 124.5–127°. By crystallization from ethanol it was obtained as colorless plates melting at 120.5–122.5°.

Anal. Calcd. for $C_{16}H_{17}NO$: C, 80.30; H, 7.16. Found: C, 80.30; H, 7.22.

Picrate.—It was obtained by warming the components in ethanol solution. It crystallized in light yellow needles of m. p. 115–116°.

Anal. Calcd. for $C_{22}H_{19}N_3O_8$: C, 58.28; H, 4.22. Found: C, 58.19; H, 4.33.

5-Acetyl-1,2,3,4-tetrahydro-9,10-anthraquinone.—A solution of 1.3 g. of chromic anhydride in 1 cc. of water and 5 cc. of glacial acetic acid was added in small portions to a solution of 1.1 g. of ketone in 4 cc. of glacial acetic acid. The temperature was kept at approximately 60°. After one hour of standing at room temperature, the solution was poured into water, whereby a yellow sticky product precipitated. The solution was decanted, the precipitate dissolved in hot methanol and allowed to crystallize. Two-tenths gram of light yellow needles was obtained. After vacuum sublimation the product melted at 122–124°.

Anal. Calcd. for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.85; H, 5.56.

5-(1-Hydroxyethyl)-1,2,3,4-tetrahydroanthracene.—Two and two-tenths grams of the ketone was reduced in 30 cc. of 3 *N* aluminum isopropoxide–isopropanol solution. The reduction was completed in thirty minutes, and the carbinol (1.9 g.) isolated as described for the 6-isomer. After crystallization from petroleum ether (b. p. 90–100°) the product melted at 73.5–76.5°, yield 1.6 g.

Anal. Calcd. for $C_{16}H_{18}O$: C, 84.91; H, 8.02. Found: C, 84.75; H, 8.20.

The carbinol (1 g.) was reoxidized with chromic anhydride in glacial acetic acid[16] yielding eventually 0.3 g. of a picrate melting at 112.5–113.5°. On decomposition it gave an oil which after vacuum distillation showed the refractive index $n^{19}D$ 1.6342.

1,2,3,4-Tetrahydroanthracene-5-carboxylic Acid.—Three and three-tenths grams of ketone was oxidized with sodium hypochlorite in the manner described for the 6-isomer. The acid obtained melted at 188–194° and weighed 2.3 g. After crystallization from glacial acetic acid it melted at 190–196°.

Anal. Calcd. for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.43; H, 6.42.

In two other experiments acids of m. p. 187–195° and m. p. 189–199°, respectively, were obtained.

Ethyl Ester.—This was prepared by refluxing the acid in ethanol and sulfuric acid, and melted after recrystallization from methanol at 64–70°. The melting points of neither the acid nor the ester could be narrowed to a smaller range by repeated recrystallization.

Anal. Calcd. for $C_{17}H_{18}O_2$: C, 80.29; H, 7.13. Found: C, 80.52; H, 6.71.

Dehydrogenation.—A mixture of 1.0 g. of highly purified ketone and 0.3 g. of sulfur was heated at 205–220° for one hour. The temperature was then raised to 230° for twenty minutes. The bulb was opened, zinc dust was added, and the mixture heated at 210–230° for ten minutes. The reaction mass was extracted with hot benzene, and the residue distilled *in vacuo*. Two-tenths gram of an oil was obtained which solidified to a red-yellow crystalline mass. It crystallized from alcohol in bright yellow plates of m. p. 102.5–107.5°. The mixture with an authentic sample of 1-acetylanthracene of m. p. 106–109° melted at 104–106°.

Preparation of Anthracene-2-carboxylic Acid from 2-Acetylanthracene.—One and one-tenth grams of 2-acetylanthracene (m. p. 186–187.5°) was heated in a mixture of 90 cc. of alkaline sodium hypochlorite solution (from 5 g. of H. T. H.) and 90 cc. of dioxane for one hour under reflux. The reaction mixture was filtered and the acid precipitated by addition of sodium bisulfite and hydrochloric acid. Seven-tenths gram of acid melting at 279.5–281° was obtained. It crystallized from glacial acetic acid in yellow prisms melting at 284.5–286°.

The ethyl ester prepared with ethanol and sulfuric acid melted after recrystallization from ethanol at 137.5–139°.

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(15) The derivatives listed below were prepared from an oily ketone that had been purified at least once through the semicarbazone and the picrate.

(16) The directions of Bachmann and Boatner [THIS JOURNAL, 58, 2097 (1936)] for an analogous oxidation were followed closely.

These two melting points are in fair agreement with the melting points given in the literature.(17)

Summary

1. The preparation of 9,10-dihydroanthracene and 1,2,3,4-tetrahydroanthracene by high-pressure hydrogenation of anthracene is described.

2. The Friedel–Crafts reaction of tetrahydroanthracene with acetyl chloride yields two methyl ketones. To the solid ketone of m. p. 101–102° the structure of a 6-acetyl derivative is assigned. For the oily ketone the structure of a 5-acetyl derivative is tentatively assumed.

3. Three amino alcohols of the type —CH-OHCH$_2$NR$_2$ were prepared from 6-acetyl-1,2,3,4-tetrahydroanthracene.

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(17) (a) Börnstein, *Ber.*, **16**, 2609 (1883); (b) Limpricht, *Ann.*, **309**, 96 (1899); (c) Weigert and Kummerer, *Ber.*, **47**, 898 (1914); (d) Lauer, *ibid.*, **70**, 1288 (1937).

[CONTRIBUTION FROM THE CENTRAL RESEARCH DIVISION OF THE MONSANTO CHEMICAL COMPANY]

Isomerization of Alkyl Phosphites. IV. The Synthesis of Some Alkaryl Phosphonic Acids and Esters

BY GENNADY M. KOSOLAPOFF

The difficulties encountered in the synthesis of aromatic phosphonic acids present a rather effective barrier against a thorough study of the chemistry of these substances. The specific difficulties which occur in the classical Friedel–Crafts type synthesis are usually very poor yields and conversions and a degree of uncertainty as to the site of substitution (except in the relatively few cases of primarily simple hydrocarbons). The synthesis through the aryl mercurials is not a satisfactory one chiefly because of the tendency for by-product formation and because of the hazards connected with the toxicity of the intermediates.

A certain progress may be reported now in an indirect solution of the above difficulties, a solution based on the view that the greater part of the chemical characteristics of the true aromatic phosphonic acids are carried over into the class of alkaryl phosphonic acids, *i. e.*, aromatically chain-substituted alkanephosphonic acids. The method previously reported for the synthesis of aliphatic phosphonic acids[1] was successfully applied to the synthesis of compounds of this type in satisfactory yields in standard laboratory apparatus. The present paper deals with the synthesis of a number of the simpler members of the series, covering most of the principal aromatic nuclei and is limited to the compounds in which the bridge between the phosphono group and the aromatic nucleus is the shortest possible, *i. e.*, one methylene group.

The compounds of this type may be readily prepared by chloromethylation of the desired hydrocarbon, reaction of the chloromethyl derivative with an alkyl phosphite (either a trialkyl phosphite or a sodium dialkyl phosphite may be used) to form the corresponding dialkyl phosphonate and hydrolysis of the ester to the free phosphonic acid. Although bromo- and iodomethyl derivatives may be used in this scheme, the obvious economy of the chloromethyl compounds and the relative ease of their preparation need not be stressed. The choice of tri-alkyl or di-alkyl phosphites is resolved in favor of the latter by the reason of their considerably lower cost; the reactivity of the chloromethyl aromatics is generally sufficiently high to enable them to react with tri-alkyl phosphites satisfactorily, in contrast with the alkyl halides.[1] In the present paper the sodium dibutyl phosphite was again selected as the phosphonating agent for reasons which were cited earlier,[1] with one example of the use of a tri-alkyl phosphite being cited. Examples of the extension of this reaction to the preparation of di-phosphonic acids of this type are also presented for hydrocarbons which readily yield bis-chloromethyl derivatives. The general reaction scheme may be represented as

$$\mathrm{RH} \longrightarrow \mathrm{RCH_2Cl} \longrightarrow \mathrm{RCH_2P(O)(OR')_2} \longrightarrow \mathrm{RCH_2P(O)(OH)_2}.$$

Experimental

The preparation of sodium dibutyl phosphite and the procedure of its use were described previously.[1]

Phenylmethanephosphonic Acid (Benzylphosphonic Acid).—Benzyl chloride (63.3 g., 0.5 mole) was treated with sodium dibutyl phosphite prepared from 97 g. (0.5 mole) of dibutyl phosphite, the reaction being run in 300 cc. of xylene. After three hours of refluxing, the mixture was cooled, washed thoroughly with water to remove sodium chloride and distilled under reduced pressure to yield 121 g. (85%) of dibutyl benzylphosphonate as a colorless liquid, b. p. 140–143° (4 mm.); $n^{25}\mathrm{D}$ 1.4820; calcd. P, 10.9; found: P, 10.8.

When the above ester was refluxed overnight with 250 cc. of concentrated hydrochloric acid, it was essentially quantitatively hydrolyzed to benzylphosphonic acid, which was recovered by the distillation of the hydrolyzate to approximately a half of its original volume, followed by the evaporation of the residue under an infra-red ray lamp to dryness. The acid, which readily crystallized on cooling, was recrystallized from water and had the melting point of 166°, in accord with the literature data.

***p*-Methylphenylmethanephosphonic Acid.**—*p*-Methylbenzyl chloride (30 g., 0.213 mole) was treated as above with 0.213 mole of sodium dibutyl phosphite in 200 cc. of toluene. There was obtained 54 g. (85%) of dibutyl *p*-

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(1) G. M. Kosolapoff, THIS JOURNAL, **67**, 1180 (1945).