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Studies in the Hydroxyanthracene Series. Part I. Some Reactions of 1-Anthrol

S. S. LELE, N. H. SHAH, AND SURESH SETHNA

Received April 9, 1956

1-Anthrol takes part in the Gattermann reaction to give the 4-formyl derivative in good yield. Oxidation of the methyl ether of the 4-formyl derivative with alkaline permanganate gave 1-hydroxyanthraquinone-4-carboxylic acid. On Friedel-Crafts acetylation of 1-anthrol, both at room temperature and on the steam-bath, 2-acetyl-1-anthrol was formed. This latter product also resulted from the Nencki acetylation of 1-anthrol, as well as from the Fries rearrangement of 1-anthrolacetate at 140°. When carried out at room temperature, however, the Fries rearrangement gave a mixture of the 2-acetyl and 4-acetyl isomers.

1-Anthrol-2-carboxylic acid has been synthesized in good yield by a modified method. When 1-anthrol was condensed with ethyl acetoacetate and ethyl benzoylacetate in the presence of 80% sulfuric acid the corresponding anthra-α-pyrones were formed.

Among the hydroxyanthracene derivatives there has been very little work with 1-anthrol. It was therefore thought of interest to study the various reactions of 1-anthrol.

The Gattermann reaction on 1-anthrol gave a product in good yield which formed a 2,4-phenylhydrazone but which did not give any color with alcoholic ferric chloride. The structure of 4-formyl-1-anthrol has therefore been assigned to this product. Upon methylation and subsequent oxidation with alkaline potassium permanganate this product gave an acid which in turn gave a blood-red color with alkali and on decarboxylation with quinoline and copper powder yielded 1-hydroxyanthraquinone. The structure of 1-hydroxyanthraquinone-4-carboxylic acid has therefore been assigned to this acid. This acid had previously been synthesized by Birukoff[1] by the condensation of *p*-cresol with phthalic anhydride and subsequent oxidation of the 4-methyl-1-hydroxyanthraquinone formed to the acid. In addition 4-formyl-1-anthrol has been reduced by Clemmensen's method to 4-methyl-1-anthrol.

Upon Friedel and Crafts acetylation, both at room temperature as well as on the steam-bath, 1-anthrol yielded a ketone (A) which gave a bluish-violet coloration with alcoholic ferric chloride. This ketone was methylated and the methyl ether was oxidized with sodium hypochloride solution whereupon another ketone (B) was obtained. Ketone (B) gave a blood-red color with zinc and alkali and upon further oxidation with the same reagent it yielded the known 1-methoxyanthraquinone-2-carboxylic acid. This latter acid was identified by direct comparison with an authentic specimen which had been prepared by the nitration of 2-methylanthraquinone following the method of Roemer and Link[2] to yield 1-nitro-2-methylanthraquinone which then was oxidized with a mixture of chromic anhydride and concentrated nitric acid to 1-nitroanthraquinone-2-carboxylic acid.[3] This latter product was converted to 1-methoxyanthraquinone-2-carboxylic acid by boiling with potassium hydroxide in methyl alcohol.[4] From this it follows that the ketone (B) is 2-acetyl-1-methoxyanthraquinone and consequently product (A) is 2-acetyl-1-anthrol.

The Nencki acetylation of 1-anthrol also provided the same ketone (A) in good yield; in addition, the Fries rearrangement of 1-anthrolacetate at 140° gave ketone (A). At room temperature, however, the Fries rearrangement of 1-anthrolacetate gave 2-acetyl-1-anthrol and a second ketone in low yield. Since this latter ketone did not give a color with alcoholic ferric chloride it has been assigned the structure of 4-acetyl-1-anthrol.

Laska and Haller[5] prepared an acid of melting point 200° by heating the alkali salt of 1-anthrol at about 220° with carbon dioxide under pressure. They assigned the structure of 1-anthrol-2-carboxylic acid to this substance. Kranzlein and Corell[6] claim to have prepared the same acid by fusing a compound they believed to be 2-carboxy-1-anthracenesulfonic acid with alkali. For the 1-anthrol-2-carboxylic acid they reported a melting point of 268°.

Consequently it was thought of interest to prepare 1-anthrol-2-carboxylic acid and to establish its structure. When 1-anthrol was heated with potassium bicarbonate at 120° in glycerine for four hours an acid of melting point 200° was obtained. Upon methylation of this product with dimethyl sulfate in acetone in the presence of potassium carbonate a methoxy ester (X) was obtained which upon hydrolysis with 10% sodium hydroxide yielded a methoxy acid (Y). This acid upon oxidation with sodium hypochlorite solution gave the known 1-methoxyanthraquinone-2-carboxylic acid which had been prepared as described above. Therefore, (Y) is 1-methoxyanthracene-2-carboxylic

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[1] Birukoff, *Ber.*, **20**, 2438 (1887).

[2] Roemer and Link, *Ber.*, **16**, 695 (1883).

[3] Terres, *Ber.*, **46**, 1634 (1913).

[4] Eckert and Endler, *British Abstracts*, **120**, i 871 (1921).

[5] Laska and Haller, German Patent 559,333, [*Chem. Abstr.*, **27**, 735 (1933)].

[6] Kranzlein and Corell, German Patent 564,129, [*Chem. Abstr.*, **27**, 1000 (1933)].

acid and (X) is methyl 1-methoxyanthracene-2-carboxylate. These results confirm the structure of 1-hydroxyanthracene-2-carboxylic acid as assigned by Laska and Haller[5] to their product; in consequence the acid of Kranzlein and Corell[6] must have some other structure.

On the Pechmann condensation with ethyl acetoacetate and ethyl benzoylacetate in the presence of 80% sulfuric acid, 1-anthrol yielded products to which the structures of 4′-methyl-1,2-anthra-α-pyrone and 4′-phenyl-1,2-anthra-α-pyrone respectively have been assigned. These assignments were made since upon treatment with alkali and dimethyl sulfate the two products yielded acrylic acids; this is a characteristic test for coumarin derivatives.[7]

EXPERIMENTAL

All melting points are uncorrected.

4-Formyl-1-anthrol. 1-Anthrol (prepared according to Dienel)[8] (5 g.) in sodium-dried ether (200 ml.) and zinc cyanide (10 g.) were mixed in a three-necked flask provided with a mercury-sealed stirrer. A stream of hydrogen chloride gas then was passed into the mixture for two hours and it was left to stand overnight. The following day the ether was decanted and the product was refluxed with 50% alcohol for 30 minutes. The product which was obtained upon cooling was crystallized from benzene in yellow needles (5 g.), m.p. 206°. It did not give any color with an alcoholic ferric chloride solution.

Anal. Calc'd for $C_{15}H_{10}O_2$: C, 81.1; H, 4.5. Found: C, 81.0; H, 4.7.

The *2,4-dinitrophenylhydrazone* was prepared in the usual manner and had melting point 286°.

Anal. Calc'd for $C_{21}H_{14}N_4O_5$: N, 13.9. Found: N, 13.8.

The methyl ether of 4-formyl-1-anthrol was prepared by dissolving the 4-formyl-1-anthrol (1 g.) in 50 ml. of dry acetone and refluxing with 0.62 g. of dimethyl sulfate and 2 g. of anhydrous potassium carbonate for 20 hours. Upon removal of the acetone a product was obtained which, when recrystallized from dilute alcohol, formed yellow needles of m.p. 112°; yield 0.8 g.

Anal. Calc'd for $C_{16}H_{12}O_2$: C, 81.3; H, 5.1. Found: C, 81.1; H, 5.0.

1-Hydroxyanthraquinone-4-carboxylic acid. 4-Formyl-1-methoxyanthracene (0.5 g.) was suspended in 20 ml. of 20% sodium hydroxide solution and 0.5 g. of potassium permanganate was added. The flask was heated gently on a wire gauze for four hours; then the reaction mixture was filtered free of manganese dioxide and the filtrate was acidified. The product so obtained was purified through a sodium bicarbonate solution and then was recrystallized from dilute alcohol to form yellow needles, of m.p. 232–234°. (Birukoff[1] gives m.p. 236°).

Anal. Calc'd for $C_{15}H_8O_5$: C, 67.2; H, 3.0. Found: C, 67.0; H, 3.6.

This acid on decarboxylation in quinoline solution with copper powder gave a product of m.p. 190°. A mixture m.p. with 1-hydroxyanthraquinone prepared according to Ullmann[9] was not depressed.

4-Methyl-1-anthrol. A solution of 4-formyl-1-anthrol (0.5 g.) in acetic acid (20 ml.) was added drop by drop during 30 minutes to zinc amalgam (prepared from zinc dust, 5 g.) suspended in dilute hydrochloric acid (1:1, 8 ml.). Concentrated hydrochloric acid (1 ml.) then was added and the heating was continued one hour longer. The solution then was filtered hot and the filtrate was diluted with water. The product obtained was crystallized from dilute alcohol in needles (0.2 g.), m.p. 134–136°.

Anal. Calc'd for $C_{15}H_{12}O$: C, 86.5; H, 5.8. Found: C, 86.9; H, 5.9.

2-Acetyl-1-anthrol. A solution of 1-anthrol (1.9 g.) and acetic anhydride (1.3 g.; 1.2 moles) in nitrobenzene (10 ml.) was mixed with a solution of anhydrous aluminum chloride (2.7 g.; 2 moles) in nitrobenzene (20 ml.) and the reaction mixture, protected from moisture, was left for 72 hours at room temperature. It was then treated with ice and hydrochloric acid and the nitrobenzene was steam-distilled. The black product obtained was repeatedly extracted with alkali. The product obtained on acidification of the alkaline extracts crystallized from dilute acetic acid in brownish needles, m.p. 182°. It gave a bluish-violet coloration with alcoholic ferric chloride.

Anal. Calc'd for $C_{16}H_{12}O_2$: C, 81.4; H, 5.1. Found: C, 80.9; H, 4.6.

The same product was obtained (i) on heating the above reaction mixture on a steam-bath for 2 hours, (ii) in the Fries rearrangement of 1-anthrolacetate (2.4 g.) by heating in an oil-bath at 140° for 3 hours with anhydrous aluminum chloride (2.7 g.), and (iii) by heating 1-anthrol (1 g.) for 2 minutes with acetic acid (1 ml.) and acetic anhydride (0.25 ml.) in the presence of zinc chloride (0.65 g.).

The *2,4-dinitrophenylhydrazone* prepared as usual gave m.p. 292°.

Anal. Calc'd for $C_{22}H_{16}N_4O_5$: N, 13.5. Found: N, 13.6.

The methyl ether. 2-Acetyl-1-anthrol (1 g.) was dissolved in dry acetone (50 ml.) and refluxed with dimethyl sulfate (0.6 g.) and anhydrous potassium carbonate (2 g.) for 20 hours. The product thus obtained was crystallized from dilute acetone in yellow needles, m.p. 126°.

Anal. Calc'd for $C_{17}H_{14}O_2$: C, 81.6; H, 5.6. Found: C, 81.9; H, 5.9.

2-Acetyl-1-methoxyanthraquinone. Sodium hydroxide (5.5 g.) in water (5.0 ml.) was added to crushed ice (50 g.) and chlorine was passed through the solution until the solution was neutral to litmus. Additional sodium hydroxide (2.5 g.) in water (10 ml.) was then added. To the resulting solution at 65°, 2-acetyl-1-methoxyanthracene (1 g.) was added portion-wise during half an hour. The temperature rose to 85° and was kept there for 3 hours. The separated product was filtered after cooling and was crystallized from dilute acetic acid in orange needles, m.p. 214°. It gave a red color with zinc and alkali.

Anal. Calc'd for $C_{17}H_{12}O_4$: C, 72.8; H, 4.3. Found: C, 72.7; H, 4.6.

1-Methoxyanthraquinone-2-carboxylic acid. 2-Acetyl-1-methoxyanthraquinone (1 g.) was suspended in sodium hypochlorite solution (prepared from 5 g. of sodium hydroxide as described above) and the mixture was refluxed in a water-bath at 85–90° for about 3 hours. After cooling an excess of sodium bisulphite was added to destroy the excess sodium hypochlorite and the solution was acidified with dilute hydrochloric acid. The product thus obtained was crystallized from glacial acetic acid in clusters of yellow needles, m.p. 254°. A mixture m.p. with an authentic sample, prepared as mentioned in the theoretical portion, was not depressed.

4-Acetyl-1-anthrol. A solution of 1-anthrolacetate (2.4 g.) in nitrobenzene (40 ml.) was mixed with a solution of anhydrous aluminum chloride (2.7 g.; 2 moles) in nitrobenzene (20 ml.) and the reaction mixture was left for 48 hours at room temperature. It then was treated with ice and hydrochloric acid and the nitrobenzene was steam-distilled. The black product thus obtained was repeatedly extracted with cold dilute alkali. On acidification of the combined alkaline extracts, a product was obtained which was dissolved in hot alcohol. On cooling, a small crop of crystals separated; these were found to be 2-acetyl-1-anthrol. The mother liquor on

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(7) Canter and Robertson, *J. Chem. Soc.*, 1875 (1931).

(8) Dienel, *Ber.*, 2863 (1905).

(9) Ullmann, *Ber.*, **53**, 829 (1920).

dilution with water gave 4-acetyl-1-anthrol which was crystallized from alcohol in yellow shining plates, m.p. 260°.

Anal. Calc'd for $C_{16}H_{12}O_2$: C, 81.4; H, 5.1. Found: C, 81.6; H, 5.5.

The *2,4-dinitrophenylhydrazone* prepared as usual gave m.p. 274°.

Anal. Calc'd for $C_{22}H_{16}N_4O_5$: N, 13.5. Found: N, 13.1.

1-Anthrol-2-carboxylic acid. A mixture of 1-anthrol (1 g.), potassium bicarbonate (1.8 g.), and glycerine (5 ml.) was heated at 120° in an oil-bath for 4 hours. Carbon dioxide was bubbled through the solution during heating. The reaction mixture then was treated with water and the solution was filtered. The product obtained on acidifying the filtrate crystallized from dilute alcohol, m.p. 200° (decom.). Laska and Haller[5] give the same m.p.

Anal. Calc'd for $C_{15}H_{10}O_3$: C, 75.6; H, 4.2. Found: C, 75.4; H, 4.5.

Methyl-1-methoxyanthracene-2-carboxylate. 1-Anthrol-2-carboxylic acid (1 g.) was dissolved in dry acetone (50 ml.) and refluxed with dimethyl sulfate (1.1 g., 2.2 moles) and anhydrous potassium carbonate (2 g.) for 15 hours. The product thus obtained was crystallized from dilute alcohol in needles, m.p. 107°.

Anal. Calc'd for $C_{17}H_{14}O_3$: C, 76.7; H, 5.3. Found: C, 77.0; H, 5.5.

1-Methoxyanthracene-2-carboxylic acid. The above ester (0.5 g.) was heated on a steam-bath with 10% sodium hydroxide for 4 hours. The product obtained on acidification with dilute hydrochloric acid crystallized from benzene in shining plates, m.p. 207°.

Anal. Calc'd for $C_{16}H_{12}O_3$: C, 76.2; H, 4.8. Found: C, 76.7; H, 5.2.

1-Methoxyanthraquinone-2-carboxylic acid. The above acid (1 g.) was suspended in sodium hypochlorite solution (prepared from 5 g. of sodium hydroxide as described before) and the mixture was heated in a water-bath at 85–90° for about 3 hours. After cooling an excess of sodium bisulphite was added to destroy unreacted sodium hypochlorite and the solution was acidified with dilute hydrochloric acid. The product was crystallized from glacial acetic acid in clusters of yellow needles, m.p. 254°. A mixture melting point with an authentic sample, prepared as described before, was not depressed.

4′-Methyl-1,2-anthra-α-pyrone. A mixture of 1-anthrol (1.94 g.), ethyl acetoacetate (1.3 g.), and sulfuric acid (80%; 20 ml.) was kept at room temperature for 24 hours. The reaction mixture then was poured into ice-cold water. The separated solid on repeated crystallization from alcohol gave yellow shining needles (1 g.), m.p. 230°.

Anal. Calc'd for $C_{18}H_{12}O_2$: C, 83.1; H, 4.6. Found: C, 83.0; H, 4.7.

β-Methyl-β,2-(1-methoxyanthryl)-acrylic acid. 4′-Methyl-1,2-anthra-α-pyrone (1 g.) was dissolved in a boiling mixture of acetone (100 ml.) and sodium hydroxide (4%; 20 ml.) and to this solution dimethyl sulfate (2 ml.) was added with continuous vigorous shaking. More of the alkali and dimethyl sulfate were added with shaking and the mixture was heated on a steam-bath for a few minutes after making it distinctly alkaline. The product obtained on acidification with dilute hydrochloric acid, was crystallized from dilute alcohol in tiny yellow needles, m.p. 185°. It decolorized a dilute potassium permanganate solution.

Anal. Calc'd for $C_{19}H_{16}O_3$: C, 78.1; H, 5.5. Found: C, 78.1; H, 5.5.

4′-Phenyl-1,2-anthra-α-pyrone. A mixture of 1-anthrol (1.94 g.), ethyl benzoylacetate (1.92 g.), and sulfuric acid (80%; 20 ml.) was kept at room temperature for 24 hours. The product obtained on working up the reaction mixture as before crystallized from ethyl acetate in needles (1 g.), m.p. 203°.

Anal. Calc'd for $C_{23}H_{14}O_2$: C, 85.7; H, 4.4. Found: C, 85.9; H, 4.8.

β-Phenyl-β,2-(1-methoxyanthryl)acrylic acid. 4′-Phenyl-1,2-anthra-α-pyrone (1 g.) in warm sodium hydroxide solution (10%; 20 ml.) was treated with dimethyl sulfate (2 ml.) as described above. The product obtained upon acidification, was crystallized from dilute alcohol as a yellow amorphous powder, m.p. 190°. It decolorized a dilute potassium permanganate solution.

Anal. Calc'd for $C_{24}H_{18}O_3$: C, 81.3; H, 5.1. Found: C, 81.2; H, 4.8.

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