refluxed for 4 hr. The products were isolated by distillation at reduced pressure and allowed to crystallize.

Acknowledgment. The authors are grateful to the Research Corporation for a Frederick Gardner Cottrell grant in support of this work.

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Studies in the Hydroxyanthracene Series, II.[1] Synthesis of Some Heterocyclic Compounds from 2-Anthrol

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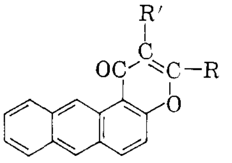
Received April 22, 1959

The present work deals with the synthesis of pyrone and furan derivatives from 2-anthrol.

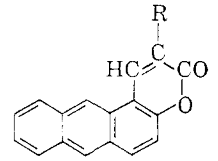
In the Pechmann condensation of 2-anthrol with ethyl acetoacetate in presence of either concentrated or 80% sulfuric acid, a pure condensation product could not be obtained. However, in the presence of phosphorus pentoxide (Simonis reaction) 2′-methyl-2,1-anthra-γ-pyrone (Ia) was obtained. This gave a styryl derivative with benzaldehyde and on hydrolysis gave 1-acetyl-2-anthrol. A similar reaction with ethyl benzoylacetate gave 2′-phenyl-2,1-anthra-γ-pyrone(Ib). On condensation with malic acid in presence of concentrated sulfuric acid, 2-anthrol gave an unworkable mass, but the desired 2,1-anthra-α-pyrone(IIa) was synthesised by the Perkin acetylation of 1-formyl-2-anthrol, as well as by the Knoevanagel condensation of malonic ester with 1-formyl-2-anthrol and subsequent hydrolysis and decarboxylation of ethyl-2,1-anthra-α-pyrone-3′-carboxylate (IIb) formed.

1-Acetyl-2-anthrol on Kostanecki-Robinson acetylation gave 2′-methyl-3′-acetyl-2,1-anthra-γ-pyrone (Ic), which on heating with dilute alcoholic sodium carbonate solution gave 2′-methyl-2,1-anthra-γ-pyrone (Ia) described above. The same ketone on Kostanecki-Robinson benzoylation gave 2′ - phenyl - 3′ - benzoyl - 2, 1 - anthra - γ - pyrone (Id) which on heating with dilute alcoholic sodium hydroxide on a steam bath gave 2′-phenyl-2,1-anthra-γ-pyrone (Ib) described before. 1-Acetyl-2-anthrol required for this work was prepared by the Friedel-Crafts acetylation of 2-anthrol, and also by the Fries rearrangement of 2-anthrolacetate at room temperature in nitrobenzene solution. Its structure was proved by oxidation of its methyl ether with sodium hypochlorite solution to 2-methoxyanthraquinone - 1 - carboxylic acid, previously prepared by Ch. Marschalk[2] by the nuclear methylation of 2-hydroxyanthraquinone to 1-methyl-2-hydroxyanthraquinone and subsequent oxidation of its methyl ether.

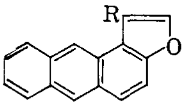
1-Formyl-2-anthrol condensed with ethyl bromoacetate to give ethyl-1-formyl-2-anthroxyacetate which on hydrolysis and ring closure gave anthra [2,1-b] furan (IIIa). Through the same series of reactions, 1-acetyl-2-anthrol furnished 1-methyl-anthra [2,1-b] furan (IIIb).



I



II



III

a. R = CH_3, R′ = H
b. R = C_6H_5, R′ = H
c. R = CH_3, R′ = $COCH_3$
d. R = C_6H_5, R′ = COC_6H_5

a. R = H
b. R = $COOC_2H_5$
c. R = COOH

a. R = H
b. R = CH_3

EXPERIMENTAL

All melting points are uncorrected.

2′-Methyl-2,1-anthra-γ-pyrone (Ia). To a mixture of 2-anthrol (1.94 g.) (prepared according to Perkin and Hall[3]) and ethyl acetoacetate (1.3 g.), phosphorus pentoxide (2.5 g.) was gradually added with stirring. The reaction mixture was heated on a steam bath for 1 hr. Crushed ice was then added and the residue taken up in ether. The ethereal layer was repeatedly washed with alkali (2%, 200 ml. in all) and then with water. The residue obtained on evaporating the ether, crystallized from dilute acetic acid (charcoal) in light brown needles, m.p. 173°. It gave a bluish green fluorescence with concentrated sulfuric acid.

Anal. Calcd. for $C_{18}H_{12}O_2$: C, 83.1; H, 4.6. Found: C, 82.9; H, 4.5.

This compound (0.5 g.) on heating with alcoholic potassium hydroxide (30%, 20 ml.) on a steam bath for 10 hr. gave 1-acetyl-2-anthrol described below.

2′-Styryl-2,1-anthra-γ-pyrone, prepared from the above pyrone, crystallized from absolute alcohol in long yellow needles, m.p. 237–238°.

Anal. Calcd. for $C_{25}H_{16}O_2$: C, 86.2; H, 4.6. Found: C, 86.1; H, 4.6.

2′-Phenyl-2,1-anthra-γ-pyrone (Ib). Obtained from 2-anthrol (1 g.), and ethyl benzoylacetate (0.65 g.) in dry ether (10 ml.) and phosphorus pentoxide (2 g.), crystallized from dilute acetic acid in pale yellow needles, m.p. 219°.

Anal. Calcd. for $C_{23}H_{14}O_2$: C, 85.7; H, 4.3. Found: C, 85.7; H, 4.8.

2,1-Anthra-α-pyrone (IIa). A mixture of 1-formyl-2-anthrol (prepared according to Jain and Seshadri[4]) (2.22 g.), acetic anhydride (2 g.) and fused sodium acetate (0.82 g.) to which a crystal of iodine was added, was refluxed in an

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(1) Part I, S. S. Lele, N. H. Shah, and Suresh Sethna, *J. Org. Chem.*, **21**, 1293 (1956).

(2) Ch. Marschalk, *Bull. soc. chim.*, **6**, 655 (1939); [*Chem. Abstr.*, **33**, 5388 (1939)].

(3) J. Hall and A. G. Perkin, *J. Chem. Soc.*, 2031 (1923).

(4) A. C. Jain and T. R. Seshadri, *J. Sci. Industr. Res.*, **15B**, 61 (1956).

oil bath at 180° for 8 hr. The product obtained crystallized from dilute alcohol (charcoal) in needles, m.p. 192°.

Anal. Calcd. for $C_{17}H_{10}O_2$: C, 82.9; H, 4.1. Found: C, 83.1; H, 4.6.

Ethyl-2,1-anthra-α-pyrone-3'-carboxylate (IIb). A mixture of 1-formyl-2-anthrol (2.22 g.), diethyl malonate (1.92 g.) and a few drops of piperidine was kept at room temperature for 4 days. The product, which separated on treating the reaction mixture with dilute hydrochloric acid, crystallized from alcohol (charcoal) in yellow needles, m.p. 194°.

Anal. Calcd. for $C_{20}H_{14}O_4$: C, 75.5; H, 4.4. Found: C, 75.3; H, 4.6.

2,1-Anthra-α-pyrone-3'-carboxylic acid (IIc). Obtained on alkaline hydrolysis of the above ester was first crystallized from dilute alcohol and then from benzene in fine red needles, m.p. 305–306° (dec.).

Anal. Calcd. for $C_{18}H_{10}O_4$: C, 74.5; H, 3.5. Found: C, 74.7; H, 3.7.

The acid on decarboxylation in quinoline solution with copper powder gave 2,1-anthra-α-pyrone described above.

1-Acetyl-2-anthrol. 2-Anthrol (1.9 g.) and acetic anhydride (1.3 g.) in nitrobenzene (30 ml.) was mixed with a solution of anhydrous aluminium chloride (2.7 g.) in nitrobenzene (20 ml.), and the reaction mixture, protected from moisture, was kept for 72 hr. at room temperature. It was then treated with ice and hydrochloric acid, and the nitrobenzene steam-distilled. The product obtained was extracted with alkali, and the alkaline extract acidified with hydrochloric acid. The precipitated solid crystallized from dilute alcohol (charcoal) in yellow needles, m.p. 112–113°. (Jain and Seshadri[4] who prepared it by the Fries migration of 2-anthrolacetate at higher temperature give m.p. 219°). It gave a bluish coloration with alcoholic ferric chloride, which turned green on keeping.

Anal. Calcd. for $C_{16}H_{12}O_2$: C, 81.4; H, 5.1. Found: C, 81.3; H, 5.2.

The same product was obtained in inferior yield (i) on heating the above reaction mixture on a steam bath for 2 hr. and (ii) in the Fries rearrangement of 2-anthrolacetate in nitrobenzene by keeping for 24 hr. at room temperature.

The *2,4-dinitrophenylhydrazone* prepared as usual crystallized from acetic acid, m.p. 235°.

Anal. Calcd. for $C_{22}H_{16}O_5N_4$: N, 13.5. Found: N, 14.1.

The *methyl ether* crystallized from dilute alcohol in small yellowish plates, m.p. 99°.

Anal. Calcd. for $C_{17}H_{14}O_2$: C, 81.6; H, 5.6. Found: C, 82.0; H, 5.7.

On sodium hypochlorite oxidation at 85° it gave a product which crystallized from acetic acid in small yellow needles, m.p. and mixed m.p. with 2-methoxyanthraquinone-1-carboxylic acid, prepared according to Ch. Marschalk[2] was 276–277°.

2'-Methyl-3'-acetyl-2,1-anthra-γ-pyrone (Ic). 1-Acetyl-2-anthrol (1 g.) was heated with freshly fused sodium acetate (3 g.) and acetic anhydride (6 ml.) in an oil bath at 180° for 8 hr. The product obtained on working up the reaction mixture crystallized from acetic acid (charcoal) in yellow needles m.p. 252–253°.

Anal. Calcd. for $C_{20}H_{14}O_3$: C, 79.5; H, 4.6. Found: C, 79.6; H, 4.9.

The above γ-pyrone (0.5 g.) in alcohol (50%, 50 ml.) when refluxed with sodium carbonate (2 g.) for 2 hr. gave the deacetylated product, which crystallized from dilute acetic acid in needles, m.p. and mixed m.p. with 2'-methyl-2,1-anthra-γ-pyrone, described above, was 173°.

2'-Phenyl-3'-benzoyl-2,1-anthra-γ-pyrone (Id). 1-Acetyl-2-anthrol (1 g.) was heated with freshly fused sodium benzoate (1.5 g.) and benzoic anhydride (5 g.) in an oil bath at 180° for 8 hr. The reaction mixture was then treated repeatedly with hot water and sodium bicarbonate solution. The residue crystallized from acetic acid in small yellow needles, m.p. 270°.

Anal. Calcd. for $C_{30}H_{18}O_3$: C, 84.5; H, 4.2. Found: C, 84.1; H, 4.2.

The above γ-pyrone (0.2 g.) was refluxed with alcoholic sodium hydroxide (5%, 20 ml.) on a steam bath for 1 hr. and the product obtained crystallized from dilute acetic acid in pale yellow needles. M.p. and mixed m.p. with 2'-phenyl-2,1-anthra-γ-pyrone described above was 219°.

Ethyl-1-formyl-2-anthroxyacetate. 1-Formyl-2-anthrol (0.5 g.) was dissolved in dry acetone (50 ml.) and refluxed on a steam bath with ethyl bromoacetate (0.5 ml.) and anhydrous potassium carbonate (3 g.) for 3 hr. The product obtained on working up the reaction mixture crystallized from alcohol (charcoal) in yellow needles, m.p. 140°.

Anal. Calcd. for $C_{19}H_{16}O_4$: C, 74.0; H, 5.2. Found: C, 73.9; H, 5.1.

1-Formyl-2-anthroxyacetic acid obtained on alkaline hydrolysis of the above ester, crystallized from dilute acetone (charcoal) in reddish yellow needles, m.p. 222–223°.

Anal. Calcd. for $C_{17}H_{12}O_4$: C, 72.8; H, 4.3. Found: C, 72.4; H, 4.2.

Anthra[2,1-b]furan (IIIa). The above acid (0.1 g.), acetic anhydride (2 ml.) and freshly fused sodium acetate (0.3 g.) was boiled for 30 min. The product, which separated on addition of water, crystallized from dilute acetic acid (charcoal) in greenish yellow plates, m.p. 177–178°.

Anal. Calcd. for $C_{16}H_{10}O$: C, 88.1; H, 4.6. Found: C, 88.1; H, 4.7.

Ethyl-1-acetyl-2-anthroxyacetate was obtained from 1-acetyl-2-anthrol and ethyl bromoacetate. It crystallized from alcohol (charcoal) in greenish yellow needles, m.p. 127–128°.

Anal. Calcd. for $C_{20}H_{18}O_4$: C, 74.5; H, 5.6. Found: C, 74.7; H, 5.7.

1-Acetyl-2-anthroxyacetic acid was obtained on alkaline hydrolysis of the above ester. It crystallized from dilute acetic acid in greenish yellow needles, m.p. 190°.

Anal. Calcd. for $C_{18}H_{14}O_4$: C, 73.5; H, 4.8. Found: C, 73.5; H, 4.4.

1-Methylanthra[2,1-b]furan (IIIb) was obtained on cyclization of the above acid with acetic anhydride and fused sodium acetate. It crystallized first from dilute acetic acid (charcoal) and then from alcohol in needles, m.p. 139–140°.

Anal. Calcd. for $C_{17}H_{12}O$: C, 87.9; H, 5.2. Found: C, 87.5; H, 5.4.

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Alkylidene- and Arylideneaminomorpholines

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Received April 27, 1959

A study of the dimethylhydrazones described recently[1] as of interest as isosteres of 3,3-dimethyl-1-phenyltriazene in tumor growth retardation studies disclosed a border line activity in some derivatives and prompted the study of additional related hydrazones. This report describes the preparation, infrared absorption characteristics, and preliminary evaluation of the 4-aminomorpholine derivatives (III) of some of the alkyl and aromatic aldehydes which, as dimethylhydrazones, showed such activity. The only previously known compounds of this

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(1) Richard H. Wiley, S. C. Slaymaker, and H. Kraus, *J. Org. Chem.*, 204 (1957).