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THE ACTION OF DIBORANE AND OF SODIUM BOROHYDRIDE-BORON TRIFLUORIDE-ETHERATE ON ANTHRAQUINONES : A NEW SYNTHESIS OF ALOE-EMODIN AND CITREOROSEIN AND A GENERAL METHOD FOR THE REDUCTION OF ANTHRAQUINONES TO ANTHRACENE DERIVATIVES

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IN the course of a programme of work on the synthesis of naturally occurring anthraquinone colouring matters[1] the possibility of preparing anthraquinone-2-carbinols, such as aloe-emodin (I) and citreorosein (II), by the reduction of the appropriate derivatives of anthraquinone-2-carboxylic acid was investigated. Reduction of methyl anthraquinone-2-carboxylate in ether by lithium aluminium hydride, followed by air oxidation, gave anthraquinone-2-carbinol in 70% yield,[1] but the method presented difficulties when applied to methyl 4,5-dimethoxyanthraquinone-2-carboxylate for the preparation of (I). Anthraquinone itself, according to two reports, yields anthrahydroquinone (9,10-dihydroxyanthracene)[2] or 9,10-dihydro-9,10-dihydroxyanthracene[3]

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[1] K. Venkataraman, Festschrift Arthur Stoll p. 360. Birkhauser, Basel (1957).

[2] R.F. Nystrom and W.G. Brown, J. Amer. Chem. Soc. 70, 3738 (1948).

[3] E. Boyland and D. Manson, J. Chem. Soc. 1837 (1951).

by reduction with lithium aluminium hydride under apparently similar conditions.

Chaikin and Brown[4] were unable to isolate boron-free compounds when anthraquinone suspended in dioxane or diethyl carbitol (diethylene glycol diethyl ether) was treated with sodium borohydride. Panson and Weill[5] reported that sodium borohydride in pure diglyme (diethylene glycol dimethyl ether) in an argon atmosphere did not reduce anthraquinone to anthrahydroquinone, but that the reduction took place when diglyme exposed to air for several weeks was used. However, we found that anthraquinone was readily reduced by sodium borohydride in pure diglyme at room temperature to anthrahydroquinone, from which on air oxidation anthraquinone was recovered in nearly quantitative yield; acetylation of the reduction product gave 9,10-diacetoxyanthracene.

Brown and Subba Rao have described the reduction of carboxylic acids to the corresponding primary alcohols by sodium borohydride - aluminium chloride in diglyme or by diborane in any ether medium.[6] Preliminary experiments showed that the former procedure was not suitable for our purpose, and attention was directed to diborane reduction. Diborane, generated by adding a diglyme solution of sodium borohydride to boron trifluoride - etherate in diglyme, was led into a solution of an acetoxyanthraquinone-2-carboxylic acid in diglyme or monoglyme (ethylene glycol

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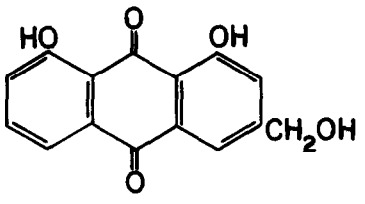
[4] S.J. Chaikin and W.G. Brown, J. Amer. Chem. Soc. 71, 122 (1949).

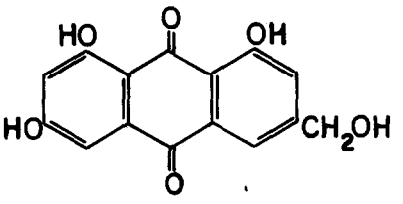
[5] G.S. Panson and C.E. Weill, J. Org. Chem. 22, 120 (1957).

[6] H.C. Brown and B.C. Subba Rao, J. Amer. Chem. Soc. 77, 3164 (1955); 78, 2582 (1956); J. Org. Chem. 22, 1135 (1957).

dimethyl ether) at room temperature, until an intense orange to red colour developed; further passage of the gas resulted in the appearance of a bluish green fluorescence and precipitation of a white flocculent boron complex indicating reaction with the quinone group. After 15 minutes ethanol was added and the solvents were removed under reduced pressure. The product, which was the acetoxyanthraquinone-2-carbinol, was dissolved in cold dilute sodium hydroxide solution and acidified. Thus 1-hydroxyanthraquinone-3-carbinol was prepared from 1-acetoxyanthraquinone-3-carboxylic acid, aloe-emodin (I) from rhein diacetate (III), and citreorosein (II) from emodic acid triacetate (IV) in about 60% yield. We are indebted to Professor M. L. Khorana and Professor T. Posternak for samples of natural aloe-emodin and citreorosein. Rhein, emodic acid, chrysophanol and emodin, intermediates for these syntheses, were prepared by the new methods outlined earlier[1] and described in detail in a paper under publication. Aloe-emodin and citreorosein



I



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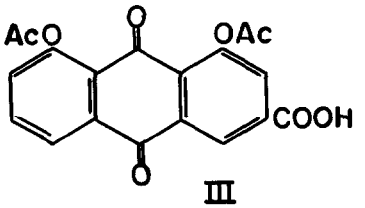
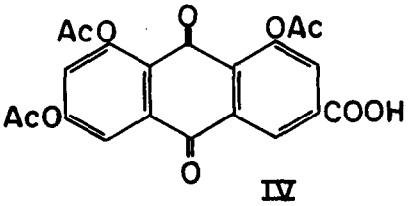


III



IV

have been synthesised earlier by other workers,[7] but the methods were not free from ambiguity.

An important feature of the action of diborane on anthraquinone-2-carboxylic acids was the preferential reduction of the carboxyl group, the quinone group being attacked only at a later stage. In this connection it seemed desirable to examine the action of a mixture of sodium borohydride and boron trifluoride-etherate, as distinct from diborane, on anthraquinone derivatives, and a new general method for their reduction to anthracene derivatives thus became available. A typical reduction of anthraquinone to anthracene was carried out as follows: To a stirred suspension of anthraquinone (2 g) in diglyme (10 ml) a solution of sodium borohydride in diglyme (10 ml of M solution) was added. The quinone dissolved to a deep red solution with a slight rise in temperature. The flask was externally cooled to 25° and a solution of boron trifluoride-etherate in diglyme (5 ml of 2 M solution) was slowly added during 5 min. The red colour changed to yellow, and a precipitate appeared. The flask was stoppered and magnetically stirred for 2 hr at 25 - 30°. The reaction proceeded with a colour change from yellow to pale cream and the development of fluorescence in ultra-violet light. At the end of the reaction the mixture was acidified to destroy the excess of hydride and the solvent was removed under reduced pressure. The residue was extracted with hexane, and the solution run through a short column of alumina. The colourless fluorescent percolate yielded anthracene (1.25 g). A modification of the procedure was to add a solution of boron trifluoride-etherate and sodium borohydride in diglyme to a solution or suspension of the quinone in diglyme. The time of reaction had to be increased in some

[7] For references see R.H. Thomson, Naturally Occurring Quinones. Butterworths, London (1957).

cases to 3 or 4 hr and the temperature to 50 - 60°. The following reductions have been carried out in yields of 60 - 70%: 1-chloroanthraquinone ⟶ 1-chloroanthracene; 2-chloroanthraquinone → 2-chloroanthracene; 2-aminoanthraquinone → 2-aminoanthracene; 2-hydroxyanthraquinone → 2-hydroxyanthracene; 2-methoxyanthraquinone → 2-methoxyanthracene; anthraquinone-2-carboxylic acid → anthracene-2-carbinol; 3,4,9,10-dibenzopyrene-5,8-quinone → 3,4,9,10-dibenzopyrene;[8] 2-methyl-1,4-naphthoquinone → 2-methylnaphthalene.

2-Methyl-1-nitroanthraquinone gave 2-methyl-1-nitroanthracene in a yield of about 50%, but byeproducts were formed which are under examination. The sodium borohydride-boron trifluoride etherate reagent also provides a convenient method for the reduction of the carbonyl group in chromones and chromanones to the methylene group.

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[8] Cf. B. D. Tilak, M. K. Unni and K. Venkataraman, Tetrahedron 3, 62 (1958).