THE IDENTIFICATION AND CONFIGURATION OF A *trans-cisoid-trans*-PERHYDROANTHRACEN-2-OL

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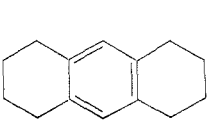
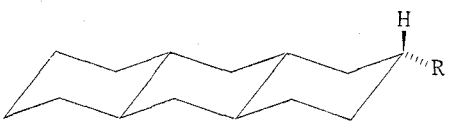
Treibs and Runge[1] prepared four *trans-cisoid-trans*-perhydroanthracenols via their nitrate esters. Two of these alcohols (Ia and IV of ref.[1]) were identified as isomers of *trans-cisoid-trans*-anthracen-9-ol since each could be oxidized to *trans-cisoid-trans*-anthracen-9-one. This paper describes the preparation and identification of *trans-cisoid-trans*-perhydroanthracen-2-ol, which was found to correspond to "Alkohol VII" of the above authors and was shown to have an equatorial hydroxyl group.

The alcohol was prepared by oral administration of *trans-cisoid-trans*-perhydroanthracene to rabbits. Previous investigations[2,3] had indicated that such a hydrocarbon would be hydroxylated *in vivo* at a carbon atom β to the ring junction, and this indeed occurred.



(1)



(2a) R = H (2b) R = OH

Experimental

Melting points are uncorrected. Where a specific reference is not given, the melting points were taken from ref.[4]

1,2,3,4,5,6,7,8-Octahydroanthracene (1)

This compound was prepared by hydrogenation of anthracene at 100 atm and 180° with W-7 Raney nickel in ethanol. After isolation and purification, the product had m.p. 72–75° (lit. 78°). The n.m.r. spectrum showed a singlet at δ 6·71, a broad singlet at δ 2·66, and a multiplet at δ 1·72.

trans-cisoid-trans-*Perhydroanthracene (2a)*

Compound (1) (10 g) was suspended in diaminoethane (150 ml) under nitrogen. Lithium (10 g) was added in small pieces over 2 hr After gentle refluxing for 2 hr, the reaction mixture was left overnight. Ice-water was carefully added, and then dilute HCl, with stirring. The product was extracted with ether; g.l.c. showed complete absence of starting material. Removal of the ether

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[1] Treibs, W., and Runge, J., *J. prakt. Chem.*, 1962, **15**, 147.
[2] Elliott, T. S., Robertson, J. S., and Williams, R. T., *Biochem. J.*, 1966, **100**, 403.
[3] Robertson, J. S., and Champion, D. I., *Biochem. J.*, 1970, **119**, 299.
[4] Heilbron, I., Cook, A. H., Bunbury, H. M., and Hey, D. H., "Dictionary of Organic Compounds." (Eyre & Spottiswoode: London 1965.)

yielded an oil (9 g), shown by n.m.r. to contain two tetrasubstituted double bonds. The oil was further hydrogenated in acetic acid for 3 days, at atmospheric pressure and 80°, with 10% w/w palladium-on-charcoal (Koch–Light, Colnbrook, Bucks., England). Removal of catalyst, extraction, and recrystallization from methanol gave *trans-cisoid-trans*-perhydroanthracene (2a) (3 g), m.p. 88–89° (lit. 92°). The i.r. and n.m.r. spectra were identical to those of Clarke[5] for the *trans-cisoid-trans* isomer.

trans-cisoid-trans-*Perhydroanthracen-2-ol* (*2b*)

The perhydroanthracene (2a) was administered orally to rabbits. The urine collected up to 72 hr after administration showed a marked increase in content of conjugated glucuronic acid, as estimated by the method of Kamil, Smith, and Williams.[6] The pooled urine, after adjusting to approximately pH 1 with 6N HCl, was hydrolysed by refluxing for 2 hr. Steam distillation of the hydrolysate yielded a white solid which, after recrystallization from hexane, had m.p. 159–160°, $[\alpha]_D^{20}$ 0·0 (*c*, 1% in ethanol). The i.r. spectrum showed absorption at 3220 nm.

The parent ion of the compound in the mass spectrum occurred at *m/e* 208, and was shown to be $C_{14}H_{24}O^+$ by mass matching. The n.m.r. spectrum showed a multiplet at δ 3·65 and a broad multiplet (δ 0·7–2·0), the latter corresponding to 22 alicyclic protons plus the alcoholic proton (confirmed by D_2O exchange). At this stage, the compound could be formulated as $C_{14}H_{23}OH$. The location and configuration of the hydroxyl group was determined from the 100-MHz n.m.r. spectrum. The multiplet at δ 3·65 was shown to be a septet with splitting of 5 Hz, centred at 359 Hz from tetramethylsilane.

It has been established[7] that such an n.m.r. spectrum is indicative of a proton located axially on a carbon atom bearing a substituent such as hydroxyl or acetate, with a methylene group on either side forming part of a cyclohexane ring in the chair conformation. The compound must therefore be *trans-cisoid-trans*-perhydroanthracen-2-ol, having an equatorial hydroxyl group (2b).

Acetylation of (*2b*)

trans-cisoid-trans-Perhydroanthracen-2-ol (150 mg), acetic anhydride (15 g), and pyridine (0·3 ml) were stirred for 3 days at 20°. The initial suspension finally changed to a clear solution, which was poured on crushed ice and set aside. The white solid (120 mg) which precipitated was collected and recrystallized from methanol, m.p. 90°. After vacuum distillation, the product, *trans-cisoid-trans*-2-acetoxyperhydroanthracene, had m.p. 94–95° (Found: C, 76·6; H, 10·6. Calc. for $C_{16}H_{26}O_2$: C, 76·75; H, 10·5%). The acetate showed i.r. absorption at 1742 nm with a corresponding loss of alcoholic absorption.

Oxidation of (2b) with Jones reagent[8] yielded a compound which, after purification, had m.p. 81°, and which formed a dinitrophenylhydrazone, m.p. 227°. The "Alkohol VII" of Treibs and Runge had m.p. 161°, and formed a ketone, m.p. 81°, whose dinitrophenylhydrazone had m.p. 227°. Thus, "Alkohol VII" was in fact *trans-cisoid-trans*-perhydroanthracen-2-ol, possessing an equatorial hydroxyl group. Three of the alcohols obtained by Treibs and Runge, "Alkohols Ia, V, and VII", were each oxidizable to different ketones, which in turn were reduced to the same rigidly fused hydrocarbon, *trans-cisoid-trans*-perhydroanthracene. This means that no hydroxyl group was located at a bridgehead and that these alcohols were not equatorial–axial isomers. Thus the hydroxyl groups could only be located at C 1, C 2, and C 9. From the foregoing, "Alkohol V" must be *trans-cisoid-trans*-perhydroanthracen-1-ol. The fourth alcohol, "Alkohol IV", was oxidizable to *trans-cisoid-trans*-perhydroanthracen-9-one; this indicates that it was an isomer of *trans-cisoid-trans*-perhydroanthracen-9-ol.

[5] Clarke, R. L., *J. Am. chem. Soc.*, 1961, **83**, 965.
[6] Kamil, I. A., Smith, J. N., and Williams, R. T., *Biochem. J.*, 1952, **50**, 235.
[7] Bhacca, N. S., and Williams, D. H., "Applications of NMR Spectroscopy in Organic Chemistry." p. 78. (Holden–Day: San Francisco 1964.)
[8] Bowers, A., Halsall, T. G., Jones, E. R. H., and Lemin, A. J., *J. chem. Soc.*, 1953, 2548.