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OXIDATION OF 7, 8, 12-TRIMETHYLBENZ(a)ANTHRACENE WITH LEAD TETRAACETATE

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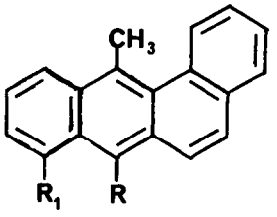
The potent carcinogen, 7, 12-dimethylbenz(a)anthracene (7, 12-DMBA, 1), causes destruction of two zones of the rat's adrenal[1]. Its higher homolog, 7, 8, 12-trimethylbenz(a)anthracene (7, 8, 12-TMBA, 2), a powerful carcinogen in itself, is devoid of this adrenocorticolytic property. The adrenocorticolytic activity of 7, 12-DMBA is due to its metabolite 7-hydroxymethyl-12-methylbenz(a)anthracene (3)[2]. The inactivity of 7, 8, 12-TMBA might be explained by steric hidrance of the methyl group at C-7 opposing the enzymatic hydroxylation in the organism. To test this hypothesis, we intended to prepare 7-hydroxymethyl-8, 12-dimethylbenz(a)anthracene (4) by oxidation of 2 with lead tetraacetate. Boyland and Sims[3] successfully applied this method to introduce

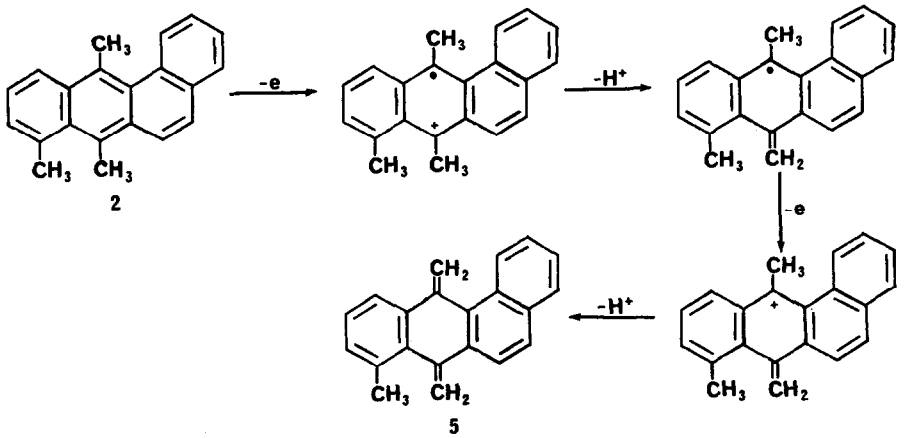


1 $R=CH_3$; $R_1=H$
2 $R=R_1=CH_3$
3 $R=CH_2OH$; $R_1=H$
4 $R=CH_2OH$; $R_1=CH_3$

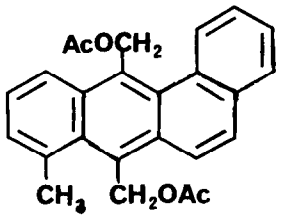
the oxygen function in 7, 12-DMBA. They obtained as reaction products 7-acetoxymethyl-12-methyl-, 12-acetoxymethyl-7-methyl-, and 7, 12-diacetoxymethyl-benz(a)anthracene. In connection with an earlier work[4], we had occasion to repeat the lead tetracetate oxidation of 7, 12-DMBA and we could confirm the results of Boyland and Sims.

In the reaction of 2 with one molecular equivalent of lead tetraacetate in glacial acetic acid at 93-95° a compound was formed, isolated in 37% yield after chromatography, which contained no oxygen. The product is rather heat sensitive, turning into an amorphous material on attempted recrystallization. Purification was effected by repeated filtration of a methylene chloride solution through silica gel. The new hydrocarbon, m. p. 136-140°, analyzed for $C_{21}H_{16}$ and showed in the nmr spectrum a methyl signal at 1. 6 ppm and vinyl proton signals between 5. 6-6 ppm corresponding to four hydrogens. We assign to it the structure of 7, 12-dimethylene-8-methyl-7, 12-dihydrobenz(a)anthracene (5). The mechanism of the dehydrogenation is represented by Scheme 1 in a stepwise fashion.

Scheme 1



Subsequently, we investigated the oxidation with two equivalents of $Pb(oAc)_4$. In this reaction no 5 was formed. Instead, we obtained the normal oxidation product, 7,12-di(acetoxymethyl-8-methylbenz(a)anthracene (6), $C_{25}H_{22}O_4$, m.p. 180-181°, in 50% yield. The nmr spectrum showed a singlet at 2.93 ppm for the C-8 methyl. The methyls of the acetoxy groups resonated at 2.2 and 2.3 ppm, while the 7- and 12-methylene groups appeared at 5.9 and 5.95 ppm, respectively.



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