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Improved Synthesis of Benzo[a]pyren-1-ol and Isolation of a Covalent Benzo[a]pyrene-Lead Compound

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Summary A two-step synthesis of benzo[a]pyren-1-ol from 6-bromobenzo[a]pyrene via consecutive reactions with lead tetra-acetate and n-butyl-lithium is described.

BENZO[a]pyrene (BaP) is a potent carcinogen¹ and an ubiquitous environmental contaminant.² Search for the metabolically activated form of this carcinogen has been handicapped by the non-availability of potential BaP metabolites. One of the latter, BaP-1-ol (3), has been

found as a major metabolite in some studies,³ while in others⁴ it has not been detected. The recent synthesis of (3) from phenanthrene-9-carbaldehyde *via* a complex multistep synthesis⁵ prompts us to report a simple two-step synthesis of (3) from 6-Br-BaP (1).

In this sequence, (1), which is readily obtained from BaP through bromination with N-bromosuccinimide,⁶ is treated with lead tetra-acetate in refluxing benzene-acetic acid (9:1) to afford principally the 1-acetoxy-compound (2).

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Reaction of the latter with n-butyllithium removes both the acetate group and the halogen atom to furnish (3). The overall yield of pure (3), m.p. 225-227° (decomp.; sealed capillary), following chromatography and recrystallization at each stage was 32%, which compares favourably with the 0.5-2% from the previous syntheses.^{5,7}



The products of acetoxylation were separated by chromatography on Florisil into crude (2) contaminated with the 3-acetoxy-isomer (< 5% by n.m.r.) and the unusual leadcontaining compound (4). Recrystallization of the former thrice from benzene afforded pure (2), m.p. 232-233° (40%), while recrystallization of the latter gave pure (4), m.p. $231-232^{\circ}$ (23%). The covalent nature of (4) was shown by formation of a mixture of dimethyl-BaP isomers on treatment of (4) with n-butyl-lithium followed by methyl bromide. Presumably (4) is a mixture of the 1- and 3isomers, although the position of attachment remains to be established. Products of plumbation have previously been detected from reactions of lead tetra-acetate,⁸ but (4) is the first example having a polycyclic ring system. Further characterization of (3) was provided by methylation with sodium hydroxide in hexamethylphosphoramide and methyl iodide⁹ to afford an essentially quantitative yield of 1methoxy-BaP which after chromatography on Florisil and recrystallization from benzene-ethanol had m.p. 146-147° (lit.,⁷ 143-144°).

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