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

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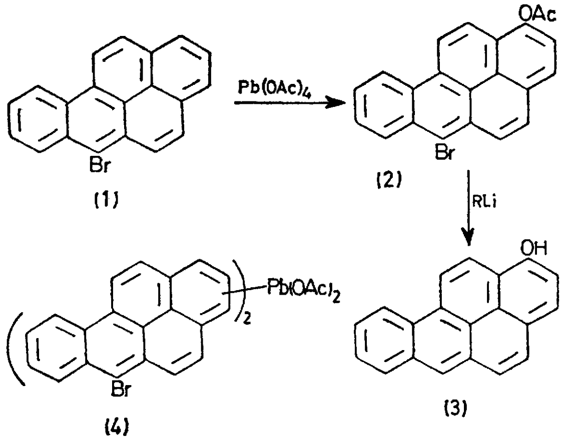
Summary A two-step synthesis of benzo[*a*]pyren-1-ol from 6-bromobenzo[*a*]pyrene *via* consecutive reactions with lead tetra-acetate and n-butyl-lithium is described.

BENZO[*a*]pyrene (BaP) is a potent carcinogen[1] 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 others[4] it has not been detected. The recent synthesis of (**3**) from phenanthrene-9-carbaldehyde *via* a complex multi-step synthesis[5] 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**).

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 lead-containing 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° (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 3-isomers, 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 iodide[9] to afford an essentially quantitative yield of 1-methoxy-BaP which after chromatography on Florisil and recrystallization from benzene–ethanol had m.p. 146—147° (lit.,[7] 143—144°).

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