

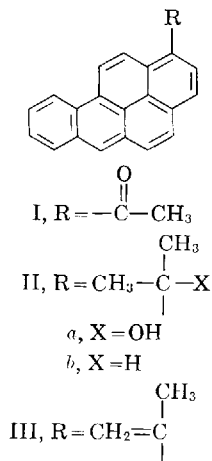
Unusual Grignard Reaction of 1-Acetylbenzo[*a*]pyrene

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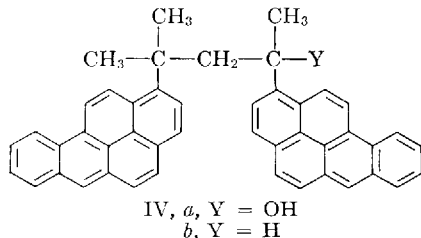
A unique dimeric alcohol, 2,4-bis(1-benzo[*a*]pyrenyl)-4-methyl-2-pentanol (IV*a*), was formed in excellent yield by the Grignard reaction of 1-acetylbenzo[*a*]pyrene (I) and methyl magnesium iodide. This unusual product was isolated when a hydrochloric acid solution was used in the work-up. Use of an ammonium chloride work-up did not give the dimeric alcohol. The preparation and some properties of other 1-substituted benzo[*a*]pyrenes are described.

IN THE course of the authors' program dealing with the carcinogenesis of polynuclear aromatic hydrocarbons, it became of paramount importance to prepare some 1-substituted benzo[*a*]pyrene derivatives.

Whereas methyl aryl ketones (1, 2) undergo Grignard reactions with methylmagnesium iodide to give excellent yields of carbinol or olefin, we find that 1-acetylbenzo[*a*]pyrene (3) (I) reacts with methylmagnesium iodide in an unexpected manner. The reaction of 1-acetylbenzo[*a*]pyrene (I) with methylmagnesium iodide, on subsequent acidification with hydrochloric acid, did not yield the expected product, either dimethyl-1-benzo[*a*]pyrenylcarbinol (II*a*) or 1-isopropenylbenzo[*a*]pyrene (III).



Rather, the reaction gave a dimeric alcohol, 2,4-bis(1-benzo[*a*]pyrenyl)-4-methyl-2-pentanol (IV*a*), in 84% yield.



The nuclear magnetic resonance spectrum of the product is in complete agreement with the proposed

structure. Integration of the NMR spectrum in aromatic and aliphatic regions showed a ratio of 22:11 of aromatic to aliphatic hydrogens. An ebulliometric molecular weight measurement in benzene gave a value of 590, in excellent agreement with the calculated value of 602. The infrared spectrum showed a small, rather broad band, centered around 3400 cm^{-1} , characteristic of a hydroxyl group (4). Finally, elemental analyses supported the structure.

The structure of 2,4-bis(1-benzo[*a*]pyrenyl)-4-methyl-2-pentanol (IV*a*) was further supported by chemical evidence. Reaction of 2,4-bis(1-benzo[*a*]pyrenyl)-4-methyl-2-pentanol (IV*a*) with red phosphorus and iodine in refluxing acetic acid (5) gave the corresponding hydrocarbon, 2,4-bis(1-benzo[*a*]pyrenyl)-2-methylpentane (IV*b*), in 77% yield. The structure of IV*b* was supported by elemental analyses and infrared spectrum. The infrared spectrum of the compound did not show a peak for hydroxyl.

Mechanistically speaking, the formation of the dimeric compound can be rationalized by assuming that dimethyl-1-benzo[*a*]pyrenylcarbinol (II*a*) in acid medium forms an oxonium ion which undergoes facile cleavage to the corresponding carbonium ion and 1-isopropenylbenzo[*a*]pyrene (III). The 1-isopropenylbenzo[*a*]pyrene (III), in turn, combines with the carbonium ion in such a way as to give rise to a new stable tertiary carbonium ion (V) which is attacked in the aqueous medium by a nucleophilic water molecule with subsequent loss of a proton to afford 2,4-bis(1-benzo[*a*]pyrenyl)-4-methyl-2-pentanol (Scheme I).

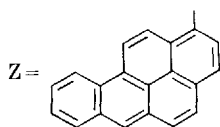
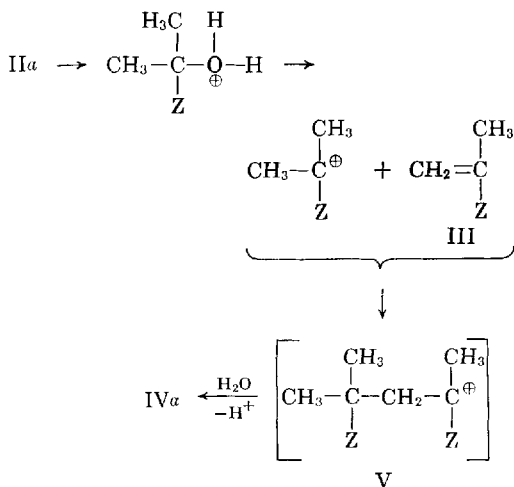
A study of molecular models clearly shows the dimeric carbonium ion (V) to be sterically crowded so that reaction with another isopropenyl moiety appears all but impossible, thus explaining why further polymerization does not occur.

When the Grignard reaction of 1-acetylbenzo[*a*]pyrene (I) with methylmagnesium iodide was carried out with subsequent acidification with ammonium chloride solution, the dimeric alcohol (IV*a*) did not form. The substance isolated, on the basis of the nuclear magnetic resonance spectrum, was a 60:40 mixture of dimethyl-(1-benzo[*a*]pyrenyl)carbinol (II*a*) and 1-isopropenylbenzo[*a*]pyrene (III). The mixture was dissolved in glacial acetic acid and heated in a water bath to 50°. Almost instantly, bright-yellow needles of 1-isopropenylbenzo[*a*]pyrene (III) began to precipitate. The infrared spectrum of the collected crystalline material was different from that of the mixture. Furthermore, the nuclear magnetic resonance spectrum indicated an 11:5 ratio of aromatic to aliphatic hydrogens and displayed peaks at $\delta = 5.2$ and 5.6 p.p.m., indicative of an α -methylstyrene moiety (6). Elemental analyses supported the structure, and the

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Scheme I

compound gave a m. p. 110–112° in agreement with the literature.¹

The isopropenyl compound (III) was converted to 1-isopropylbenzo[a]pyrene (IIb) in 75% yield by room temperature hydrogenation for 2 hr. using a 2:1 ratio of substrate to palladium black catalyst at 52 p.s.i. The nuclear magnetic resonance spectrum of the compound showed a characteristic 7-line pattern for the methine proton, and was void of peaks at $\delta = 5.2$ and 5.6 p.p.m., indicating that the double bond of the α -methylstyrene moiety had been reduced to give the isopropyl derivative (IIb).

EXPERIMENTAL²

2,4 - Bis(1 - benzo[a]pyrenyl) - 4 - methyl - 2 - pentanol (IV).—A Grignard reagent was prepared from 2.3 Gm. (83 mmoles) of magnesium, 6.4 ml. (100 mmoles) of methyl iodide, and 44 ml. of dry ether. When the reaction was complete, a slurry

of 4.4 Gm. (15 mmoles) of 1-acetylbenzo[a]pyrene (I) in 420 ml. of dry benzene was added. The mixture was stirred and heated under reflux for 4 hr., cooled, and decomposed with 300 ml. of ice-cold 10% hydrochloric acid solution and worked up in the usual way. The product crystallized when triturated with cold ethanol and was purified by passing its benzene solution through an alumina column. In this way was obtained 3.6 Gm. (84%), m.p. 200–205° (gradual decomposition).

Anal.—Calcd. for $\text{C}_{46}\text{H}_{34}\text{O}$: C, 91.66; H, 5.69; mol. wt., 602. Found: C, 91.68; H, 5.64; mol. wt., 592.

1-Isopropenylbenzo[a]pyrene (III).—A Grignard reaction was carried out using the same procedure and quantities of magnesium, methyl iodide, and 1-acetylbenzo[a]pyrene, as above, except that the reaction was decomposed with 300 ml. of ice-cold saturated ammonium chloride solution. The oily product obtained was dissolved in 25 ml. of glacial acetic acid and heated to 50°, at which time bright-yellow needles precipitated. After chilling, the solid was collected by suction filtration and recrystallized from absolute ethanol, yielding 2.2 Gm. (50%) of bright yellow needles, m.p. 110–112° [Lit. (3) m.p. 114.°]

Anal.—Calcd. for $\text{C}_{23}\text{H}_{16}$: C, 94.48; H, 5.52. Found: C, 94.37; H, 5.46.

1-Isopropylbenzo[a]pyrene (IIb).—A solution of 2.0 Gm. (4.3 mmoles) of III in 100 ml. of benzene was hydrogenated at a pressure of 52 p.s.i. and at room temperature using 1.0 Gm. of palladium black as the catalyst. After 2 hr., the catalyst and solvent were removed. The crude yield was quantitative. Recrystallization from absolute alcohol yielded 1.5 Gm. (75%), m.p. 128–130°.

Anal.—Calcd. for $\text{C}_{23}\text{H}_{18}$: C, 93.84; H, 6.16. Found: C, 93.76; H, 6.21.

2,4 - Bis - (1 - benzo[a]pyrenyl) - 2 - methyl - pentane (IVb).—In 125 ml. of glacial acetic acid and 10 ml. of water was suspended 1.0 Gm. (1.6 mmoles) of IVa, 200 mg. of iodine, and 200 mg. of red phosphorus. The mixture was stirred and heated under reflux for 29 hr., cooled, then extracted with three 80-ml. portions of benzene. The combined organic layers were washed with water and then dried over anhydrous sodium sulfate. Filtration and concentration yielded a crystalline solid which after recrystallization from benzene-ligroin afforded 603 mg. (77%), m.p. 210–215° dec.

Anal.—Calcd. for $\text{C}_{46}\text{H}_{34}$: C, 94.16; H, 5.86. Found: C, 93.87; H, 6.01.

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¹ See Reference 3, p. 162. Windaus reported the synthesis of 1-isopropenylbenzo[a]pyrene by heating the product from the reaction of methylmagnesium iodide with 1-acetylbenzo[a]pyrene after an ammonium chloride workup at 230–280° under high vacuum in the presence of powdered zinc.

² All melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. All analyses and molecular weight determinations were carried out by Galbraith Laboratories, Inc., Knoxville, Tenn. Infrared absorption spectra were taken as Nujol mulls and determined on a Perkin-Elmer model 137 spectrophotometer. The NMR spectra were determined on a Varian A-60 spectrometer with tetramethylsilane as the internal reference. Deuteriochloroform solutions were used for all spectra.