Acyl Migration in Anions Derived from Nonenolizable Esters of Polycyclic Aromatic Hydrocarbons

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The strategy involving regioselective lithiation through the use of a metalation director, followed by trapping of the metalated species by an external electrophile, is an elegant method to achieve selective functionalization of aromatic systems. As part of our research program in chemical carcinogenesis we have been interested in the *peri*-functionalization of the terminal tetrahydrobenzo rings of polycyclic aromatic hydrocarbons for subsequent elaboration of these compounds to their metabolically activated forms.[1] For this purpose we envisioned introduction of the requisite *peri*-functionalities through the directed metalation approach. Hydroxyl groups themselves are known to direct lithiation; for example, benzyl alcohol and 1,2,3,4-tetrahydronaphthalen-1-ol undergo *ortho*- and *peri*-lithiation, respectively.[2] However, in our case solubility constraints imposed by the tetrahydro alcohols of polycyclic aromatic hydrocarbons precluded the use of solvents where the extent of *peri*-lithiation is maximal. Additionally, the yields in these hydroxyl-directed reactions are known to be dependent upon the fine dispersion of the initially formed lithium alkoxides.[3] On the other hand, there is relatively sparce information on *peri*-functionalization through the use of other metalation directors and in the reported cases *peri*-functionalized compounds are minor components of the product mixtures.[4] Although carbamates are excellent metalation directors[5] the harsh conditions required for their hydrolysis prompted us to consider other functionalities that could be cleaved under relatively mild conditions. Thus, we decided to evaluate the utility of sterically bulky, nonenolizable esters as lithiation-directing groups. During the course of our investigation we have encountered an unprecedented O → C acyl migration resulting in an isomerization of the ester to an α-hydroxy ketone. Intramolecular displacements of metalation directing groups subsequent to lithiation are well-documented in the literature. For instance, formation of hydroxy amides by migration of carbamoyl moieties after aromatic[5,6] or benzylic[7] lithiations of carbamates have been well studied. Analogous acyl migrations in esters containing *enolizable* protons are also known, such as acyl transfers α to carbonyl and sulfonyl moieties.[8,9] However, acyl migration upon benzylic deprotonation of a *nonenolizable* ester, to our knowledge, is presently unknown. Further, as described here, this type of acyl transfer seems general to the benzylic esters of tetrahydrobenzo[*a*]pyrene, phenanthrene, and benzo[*a*]anthracene as well as that of fluorene.

Results and Discussion

For our study the pivaloyl ester was selected as the potential directing group primarily for two reasons: (a) the ester unit itself was not expected to undergo any unwanted lithiations and (b) the steric bulk of the *tert*-butyl group was expected to diminish addition of the lithiating agent to the carbonyl moiety. Lithium diisopropylamide (LDA) was the base of choice due to its non-nucleophilic character compared to other lithiating agents. The required 7-(7,8,9,10-tetrahydrobenzo[*a*]pyrenyl) pivalate (**1**) was readily prepared by acylation of commercially available 7-hydroxy-7,8,9,10-tetrahydrobenzo-[*a*]pyrene (BaP 7-ol) with pivaloyl chloride in pyridine in the presence of a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine (DMAP) at 80–85 °C (83% yield). At the onset of our work, in order to assess the course of the lithiation reaction we decided to quench the reaction mixture with trimethylsilyl chloride (TMSCl). This was primarily because the expected differences in mobilities between starting material and product on thin-layer chromatography would allow for facile evaluation of the reaction course. Therefore, ester **1** (Scheme 1) was subjected to lithiation in THF with 2–3 equiv of LDA at −50 °C and allowed to warm to 0 °C.[10] Addition of TMSCl, after the lithiation was allowed to proceed at 0 °C for 1 h, resulted in the formation of a product that was slightly less polar compared to **1** on thin-layer chromatography (silica gel, eluted with 5% EtOAc in hexane). Inspection of the ^{1}H NMR spectrum of this compound (**2a**) surprisingly indicated the presence of not only the expected *tert*-butyl and trimethylsilyl proton resonances but the *peri*-H-6 resonance as well, indicating that no lithiation had occurred at C-6. An additional feature in the spectrum of the product was the presence of only six aliphatic protons and the absence of an H-7 resonance. At this stage although deprotonation at C-7 seemed likely it was unclear whether such a deprotonation had resulted in the attachment of the TMS unit directly at this site or whether some other process was in operation prior to the addition of TMSCl. In order to explore these possibilities **1** was subjected to the lithiation conditions described above, but the reaction was

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(10) Either a 2M LDA solution in heptane–THF–ethylbenzene or a 1.5 M solution of a 1:1 LDA–THF complex in cyclohexane can be used.

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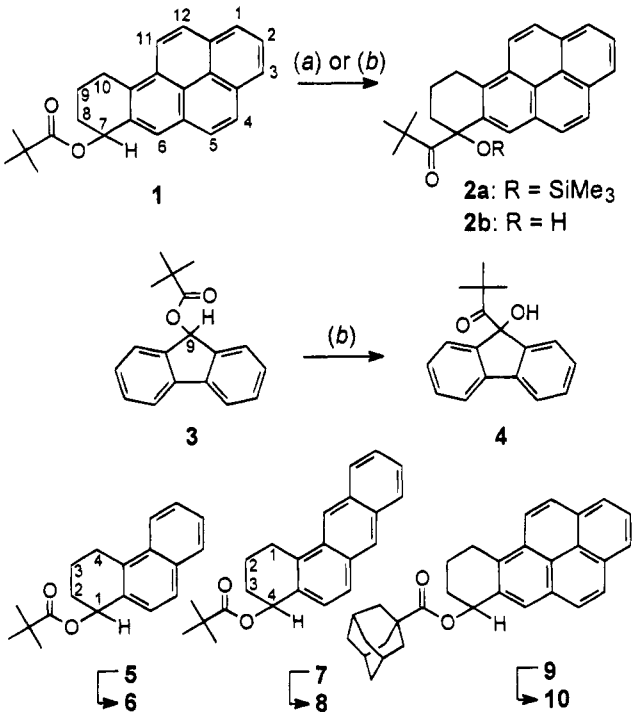
Scheme 1



Conditions: (*a*) LDA, THF, -50° to 0 °C, Me_3SiCl
(*b*) LDA, THF, -50° to 0 °C, aq. NH_4Cl

quenched with aqueous NH_4Cl (Scheme 1). This time a product was obtained (in ca. 70% yield) that was marginally more polar than the ester (silica chromatography, 20% EtOAc in hexane as eluant).[11] The proton NMR spectrum of this product indicated the disappearance of the H-7 resonance as before and the appearance of a new signal, a singlet, at 5.33 ppm which is exchangeable with MeOH-d_4. Additionally, the H-6 resonance was shifted upfield from 8.06 ppm in **1** to 7.64 ppm in the product. On the basis of these observations we reasoned that lithiation at C-7 was followed by migration of the acyl moiety from the oxygen to the carbon resulting in the α-hydroxy ketone **2b**. Such a product would account for the NMR results: the exchangeable singlet for the hydroxyl proton, the disappearance of the H-7 resonance, as well as the upfield shift of H-6 due to the anisotropy effect of the proximal carbonyl group. With this information in hand the relationship between **2b** and the product **2a** initially obtained by quenching the reaction with TMSCl had to be established. Therefore, **2b** was subjected to silylation with TMS triflate (CH_2Cl_2, Et_3N, 0 °C, 15 min, 77% yield). This product was identical to **2a** indicating that **2a** was produced by reaction of TMSCl with the alkoxide generated by the acyl migration. In order to unambiguously ascertain the structures of the products obtained in these reactions we have prepared **2a** and **2b** through independent synthesis (*vide infra*).

At this stage we were interested in determining the generality of this rearrangement with respect to both the hydrocarbon and the acyl functionality. The facile formation of a stable 6π-electron system upon deprotonation of cyclopentadienes prompted an investigation on 9-fluorenyl pivalate (**3**). Compound **3** upon lithiation as described earlier resulted in the exclusive formation of the rearranged product **4** in 80% yield.[12] This product, as in the case of benzo[*a*]pyrene, displayed an exchangeable proton at 5.61 ppm and showed an upfield shift of the neighboring *peri*-protons in the ^1H NMR spectrum. The acyl migration also proceeds reasonably well in 1-(1,2,3,4-tetrahydrophenanthryl) pivalate (**5**), which bears a smaller aromatic residue compared to **1** (55% yield of the product **6**).[13] Finally, in the case of the tetrahydrobenzo[*a*]anthryl pivalate (**7**) the yield of the rearranged product **8** was 62%.[13] It should be pointed out that minor variations in the experimental conditions were needed for optimal product formation in individual cases (see the Experimental Section for details). The overall trend in these reactions seems to indicate that generation of a stable anion by benzylic deprotonation results predominantly in acyl migration (as in the benzo[*a*]pyrene and fluorene cases). In order to evaluate whether other nonenolizable esters would undergo this rearrangement, the adamantane carboxylic acid ester of BaP 7-ol **9** was subjected to the rearrangement conditions, with two variations: (a) the LDA–THF complex was added in two aliquots and (b) the temperature was maintained at −15 to −20 °C instead of 0 °C. Under these conditions the rearranged product **10** was obtained in 80% yield. When conditions for the preparation of **2b** were applied to **9**, the yield was lower with the appearance of hydrolyzed BaP 7-ol. Thus, in every case it is possible that hydrolysis is a competing reaction and can be diminished by slight changes in the experimental conditions such as portionwise addition of LDA and/or lowering of temperatures. A single attempt on 7,8,9,10-tetrahydrobenzo[*a*]pyren-7-yl benzoate under the reaction conditions described for **2b** produced hydrolyzed BaP 7-ol almost exclusively. At this time it is not clear whether the carbonyl of the ester directs lithiation to the aromatic ring of the benzoate moiety, thereby eliminating the deprotonation at C-7. However, it is conceivable that the aryl ring is not sufficiently large to inhibit the addition of LDA to the carbonyl.

Finally, in order to unequivocally establish the structures of the rearrangement products in the benzo[*a*]pyrene series, we have derived **2a** and **2b** through the route shown in Scheme 2. In principle, addition of the anion derived from the 1,3-dithiane derivative of pivalaldehyde to 9,10-dihydrobenzo[*a*]pyren-7(8*H*)-one (**11**), followed by cleavage of the dithiane should provide the target compound **2b**. However, several attempts at addition of the dithiane proved unsuccessful with only recovery of the starting ketone. On the other hand, the anion generated from the cyanohydrin TMS ether[14] of pivalaldehyde (**12**) underwent addition to ketone **11** in low yield.[15] The product of this addition was identical to the TMS derivative **2a**. This indicates that addition of the anion to the ketone was followed by a migration of the TMS unit from the cyanohydrin moiety to the newly formed alkoxide, with a concomittant expulsion of cya-

(11) In some cases a trace amount of 7-hydroxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene was formed, and no attempt was made to quantitate it.

(12) In the case of 9-fluorenyl pivalate the reaction can also be performed in Et_2O (88% yield of the rearranged product). When THF was used as the solvent the yield of the product was 80%.

(13) The major side products in the reactions of **5** and **7** are the corresponding alcohols. It should also be noted that in these cases as well a dramatic upfield shift in the resonance of the *peri*-proton is noticed in the NMR spectra (6.93 ppm in **6** and 6.90 ppm in **8**).

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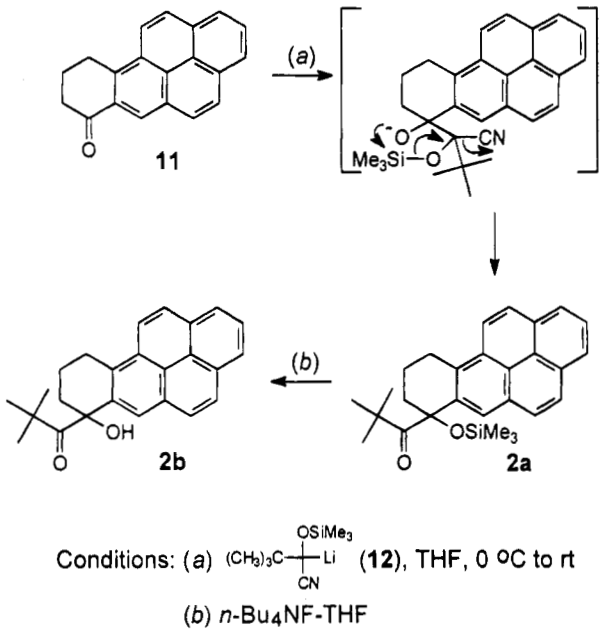
(15) The overall yield for the conversion of 9,10-dihydrobenzo[*a*]pyren-7(8*H*)-one (**11**) to the product **2b** was 12%. The initial addition of the anion **12** to the ketone is the low-yielding step in the synthesis.

Scheme 2



nide (Scheme 2). As a final step in structure determination, treatment of the silyl ether with n-Bu_4NF produced a compound that was identical to **2b**.

Conclusion

In this paper we have delineated a mode for acyl transfer in anions produced by deprotonation of nonenolizable esters through the use of a sterically bulky ester unit and a hindered base. With the availability of a variety of sterically demanding lithium amides it should be possible to reduce the cleavage reaction of the ester, thereby enhancing the yield of the rearranged products. Additionally, an evaluation of the types of esters that permit such a rearrangement is also needed. Since good yields of the hydroxy ketone are obtained by this rearrangement, this method could provide facile access to specifically acylated aromatic systems.

Experimental Section

Pyridine and methylene chloride were distilled from calcium hydride, THF from $LiAlH_4$, and diethyl ether from sodium benzophenone. Melting points were obtained on a Kofler apparatus and are uncorrected. Proton NMR spectra were recorded on a Varian VXR-300 spectrometer in $CDCl_3$. Chemical shifts (δ) are reported in ppm, and coupling constants (J) are in Hz. Nominal mass spectra (EI) and high-resolution mass measurements were obtained on a VG Analytical Autospec Q spectrometer. IR spectra were obtained in Nujol on a Perkin-Elmer 1720X FT-IR spectrometer. Elemental analysis was performed using a Perkin-Elmer Elemental Analyzer 2400 CHN.

7-(7,8,9,10-Tetrahydrobenzo[*a*]pyrenyl) Pivalate (1). 7-Hydroxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene (0.2 g, 0.73 mmol) was dissolved in dry pyridine (2 mL). A catalytic amount of DMAP was added followed by the addition of pivaloyl chloride (0.27 mL, 2.2 mmol). The mixture was heated at 80–85 °C for 1 h, cooled to room temperature, and diluted with EtOAc. The reaction mixture was sequentially washed with 10% aqueous HCl (2 × 25 mL), saturated aqueous $NaHCO_3$, and water. The organic layer was dried over Na_2SO_4 and evaporated under reduced pressure. Chromatography of the crude product on a silica gel column using CH_2Cl_2 provided **1** (0.217 g, 83%), mp 132–133.5 °C (pale yellow powder, crystallization from methanol/methylene chloride). ^1H NMR: 8.29–7.96 (m, 8H, aromatic), 6.40 (t, 1H, J = 4.5), 3.61 (dt, 1H, J = 17.4; 5.2), 3.36 (m, 1H), 2.15 (m, 4H), 1.23 (s, 9H, *tert*-butyl). IR: 1728, 1158 cm^{-1}. MS (rel int): 357 (M^+ + 1, 5), 356 (M^+, 18), 256 (15), 255 (50), 254 (100), 253 (41), 252 (30), 250 (9), 241 (5), 240 (22), 239 (36), 226 (8), 215 (9), 213 (5), 127 (6), 126 (14), 125 (6), 119 (12), 113 (8), 69 (8), 57 (21), 55 (6). HRMS: calcd for $C_{25}H_{24}O_2$ 356.1776, found 356.1779. Anal. Calcd for $C_{25}H_{24}O_2$: C, 84.24; H, 6.79. Found: C, 84.15; H, 6.80.

9-Fluorenyl pivalate (3). The acylation of 9-hydroxyfluorene (1 g, 5.5 mmol) as described for the preparation of **1** afforded **3** (1.22 g, 84%), mp 64–65.5 °C (colorless crystals, crystallization from methanol). ^1H NMR: 7.70–7.26 (m, 8H, aromatic), 6.79 (s, 1H), 1.27 (s, 9H, *tert*-butyl). IR: 1728, 1144 cm^{-1}. MS (rel int): 267 (M^+ + 1, 11), 266 (M^+, 49), 183 (10), 182 (61), 181 (44), 180 (9), 166 (28), 165 (100), 164 (15), 163 (18), 153 (9), 152 (15), 139 (7), 115 (5), 85 (16), 58 (6), 57 (88). HRMS: calcd for $C_{18}H_{18}O_2$ 266.1306, found 266.1309. Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.34; H, 6.85.

1-(1,2,3,4-Tetrahydrophenanthryl) Pivalate (5). The acylation of 1-hydroxy-1,2,3,4-tetrahydrophenanthrene[16] (200 mg, 1.01 mmol) as described for the preparation of **1** afforded **5** (283 mg, 99%). ^1H NMR: 8.04–7.28 (m, 6H, aromatic), 6.09 (t, 1H, J = 3.4), 3.29 (dm, 1H, J_{app} = 17.1), 3.04 (m, 1H), 2.04 (m, 2H), 1.22 (s, 9H, *tert*-butyl). MS (rel int): 283 (M^+ + 1, 4), 282 (M^+, 15), 197 (5), 182 (17), 181 (63), 180 (100), 179 (24), 178 (13), 167 (5), 166 (20), 165 (26), 153 (6), 152 (8), 141 (10), 139 (5), 115 (6), 57 (21). HRMS: calcd for $C_{19}H_{22}O_2$ 282.1620, found 282.1630.

4-(1,2,3,4-Tetrahydrobenzo[*a*]anthryl) Pivalate (7). The acylation of 4-hydroxy-1,2,3,4-tetrahydrobenzo[*a*]anthracene[16] (218 mg, 1 mmol) as described for the preparation of **1** proceeded slower and after 7 h of heating followed by workup afforded **7** (182 mg, 73% based on 55 mg of recovered alcohol). ^1H NMR: 8.56–7.24 (m, 8H, aromatic), 6.10 (m, 1H), 3.40 (dm, 1H, J_{app} = 17.3), 3.15 (m, 1H), 2.09 (m, 4H), 1.24 (s, 9H, *tert*-butyl). MS (rel int): 333 (M^+ + 1, 5), 332 (M^+, 19), 232 (11), 231 (55), 230 (100), 229 (18), 228 (9), 216 (16), 215 (18), 202 (5), 170 (8), 149 (13), 141 (8), 113 (5), 97 (6), 85 (7), 83 (7), 77 (8), 71 (10), 69 (8), 57 (29), 55 (11). HRMS: calcd for $C_{23}H_{24}O_2$ 332.1776, found 332.1779.

7-[[(1-Adamantyl)carbonyl]oxy]-7,8,9,10-tetrahydrobenzo[*a*]pyrene (9). 7-Hydroxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene (0.544 g, 2 mmol) was dissolved in THF (5 mL), 1-adamantanecarboxylic acid (1.08 g, 6 mmol) and DMAP (0.195 g, 1.6 mmol) were added, and the mixture was cooled to 0 °C. Subsequently, dicyclohexylcarbodiimide (1.236 g, 6 mmol) was added, and the mixture was heated at 45–50 °C for 3 days. After being cooled to room temperature the mixture was diluted with $CHCl_3$, and the precipitated material was filtered. The filtrate was sequentially extracted with 0.5 N HCl (2 × 20 mL) and saturated aqueous $NaHCO_3$ (2 × 20 mL). The organic layer upon drying over Na_2SO_4 and evaporation gave a solid which was stirred with 30% EtOAc in hexane, filtered, and rewashed with 30% EtOAc in hexane. The filtrate was evaporated, and chromatography of the resulting crude product on a silica column using 20% hexane in CH_2Cl_2 gave **9** (0.777 g, 86%) mp 166.5–168.5 °C (colorless crystals from acetone). ^1H NMR: 8.26–7.93 (m, 8H aromatic), 6.41 (t, 1H, J = 4.1), 3.59 (dm, 1H, J_{app} = 17.5), 3.33 (m, 1H), 2.32–2.06 (m, 4H), 2.03–1.93 (m, 9H), 1.69 (m, 6H). IR: 1723, 1225 cm^{-1}. MS (rel int): 435 (M^+ + 1, 10), 434 (M^+, 21), 256 (15), 255 (46), 254 (100), 253 (24), 252 (17), 241 (6), 240 (19), 239 (26), 226 (6), 215 (7), 180 (7), 136 (5), 135 (22), 107 (5), 93 (12), 91 (9), 81 (5), 79 (14), 77 (6), 67 (7), 55 (6). HRMS: calcd for $C_{31}H_{30}O_2$ 434.2246, found 434.2256. Anal. Calcd for $C_{31}H_{30}O_2$: C, 85.68; H, 6.96. Found: C, 85.37; H, 7.19.

7-(2,2-Dimethyl-1-oxopropyl)-7,8,9,10-tetrahydrobenzo-[*a*]pyren-7-ol (2b) via Deprotonation. To a stirred solution of **1** (30 mg, 84.3 μmol) in anhydrous THF (0.5 mL) at −50 °C (dry ice/acetone) under argon was added a 2 M solution of LDA in heptane–THF–ethylbenzene (84 μL, 0.17 mmol, 2 equiv). The color of the reaction mixture changed from clear to black. The dry ice/acetone mixture was replaced with an ice bath, and the mixture was stirred for 1 h. The reaction mixture was quenched by the addition of a mixture of EtOAc and saturated aqueous NH_4Cl. The organic layer was separated, dried over Na_2SO_4 and evaporated under reduced pressure. Chromatography of the product on a preparative silica plate (2 mm, 20 × 20 cm) using 20% EtOAc in hexane yielded **2b** (20.8 mg, 69%), mp 218–219.5 °C (pale yellow needles, crystallization from methanol/acetone).

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^{1}H NMR: 8.33–7.88 (m, 7H, aromatic), 7.64 (s, 1H, aromatic), 5.33 (br s, 1H$_{OH}$), 3.80 (br d, 1H, J_{app} = 17.5), 3.22 (apparent quintet, 1H, J_{app} = 8.8), 2.48 (m, 1H), 2.30 (m, 2H), 2.00 (br d, 1H, J_{app} = 15), 0.95 (s, 9H, *tert*-butyl). IR: 3429, 1672 cm^{-1}. MS (rel int): 356 (M$^+$, 4), 338 (5), 281 (9), 272 (44), 271 (100), 270 (16), 255 (20), 254 (42), 253 (45), 252 (26), 240 (10), 239 (24), 229 (11), 227 (10), 226 (11), 216 (10), 215 (42), 214 (13), 213 (12), 202 (12), 126 (12), 84 (12), 81 (11), 69 (22), 57 (20), 55 (11). HRMS: calcd for $C_{25}H_{24}O_2$ 356.1776, found 356.1780. Anal. Calcd for $C_{25}H_{24}O_2$: C, 84.24; H, 6.79. Found: C, 84.11; H, 6.79.

9-(2,2-Dimethyl-1-oxopropyl)-fluoren-9-ol (4). To a stirred solution of **3** (50 mg, 0.19 mmol) in anhydrous Et_2O (1 mL) at −50 °C (dry ice/acetone) under argon was added a 1.5 M solution of 1:1 LDA–THF complex in cyclohexane (0.38 mL, 0.57 mmol, 3 equiv). The dry ice/acetone mixture was replaced by an ice bath, and the mixture was stirred for 2 h, at which time the color of the mixture was black. The reaction mixture was diluted by the addition of a mixture of EtOAc and saturated aqueous NH_4Cl. The organic layer was separated, dried over Na_2SO_4 and evaporated. Chromatography of the crude product on a preparative silica plate (2 mm, 20 × 20 cm) using 10% EtOAc in hexane provided **4** (44 mg, 88%), mp 107–108.5 °C (colorless crystals, crystallization from pentane). ^{1}H NMR: 7.72–7.25 (m, 8H, aromatic), 5.61 (br s, 1H$_{OH}$), 0.79 (s, 9H, *tert*-butyl). IR: 3415, 1676 cm^{-1}. MS (rel int): 266 (M$^+$, 1.3), 221 (8), 210 (5), 182 (25), 181 (100), 180 (11), 165 (5), 163 (6), 153 (21), 152 (33), 151 (14), 150 (6), 127 (6), 126 (6), 85 (8), 76 (5), 57 (30). HRMS: calcd for $C_{18}H_{18}O_2$ 266.1306, found 266.1310. Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 81.05; H, 6.85.

1-(2,2-Dimethyl-1-oxopropyl)-1,2,3,4-tetrahydrophenanthren-1-ol (6). To a stirred solution of the phenanthryl pivalate ester **5** (44 mg, 0.156 mmol) in anhydrous THF (0.39 mL) at −50 °C under argon was added a 1.5 M solution of 1:1 LDA–THF complex in cyclohexane (208 μL, 0.312 mmol, 2 equiv). The mixture was transferred to an ice bath and stirred for 2 h. The mixture was recooled to −50 °C, another aliquot of the LDA solution was added (156 μL, 0.234 mmol, 1.5 equiv), and the stirring was continued at 0 °C for 2 h. A mixture of EtOAc and saturated aqueous NH_4Cl was added to the reaction mixture, and the organic layer was separated, dried over Na_2SO_4 and evaporated. Chromatography of the crude product on a preparative silica plate (2 mm, 20 × 20 cm) using 30% EtOAc in hexane provided **6** (24 mg, 55%). ^{1}H NMR: 8.10–7.46 (m, 5H, aromatic), 6.93 (d, 1H, aromatic, J = 8.7), 5.14 (br s, 1H$_{OH}$), 3.48 (br d, 1H, J_{app} = 17.1), 2.93 (m, 1H), 2.36 (m, 1H), 2.18 (m, 2H), 1.86 (dm, 1H, J_{app} = 13.5), 1.01 (s, 9H, *tert*-butyl). MS (rel int): 282 (M$^+$, 0.7), 266 (2), 265 (8), 237 (2), 198 (31), 197 (100), 196 (13), 179 (20), 178 (14), 165 (15), 155 (13), 153 (13), 152 (15), 142 (11), 141 (42), 140 (14), 139 (14), 128 (12), 115 (14), 57 (27). HRMS: calcd for $C_{19}H_{22}O_2$ 282.1620, found 282.1628.

4-(2,2-Dimethyl-1-oxopropyl)-1,2,3,4-tetrahydrobenzo[*a*]anthracen-4-ol (8). To a stirred solution of the benzanthryl pivalate ester **7** (45 mg, 0.136 mmol) in anhydrous THF (0.4 mL) at −50 °C under argon was added a 1.5 M solution of 1:1 LDA–THF complex in cyclohexane (181 μL, 0.272 mmol, 2 equiv). The color of the mixture turned from clear to dark brown. The mixture was transferred to an ice bath and stirred for 2 h. The mixture was recooled to −50 °C, another aliquot of the LDA solution was added (136 μL, 0.204 mmol, 1.5 equiv), and the stirring was continued at 0 °C for 2 h. A mixture of EtOAc and saturated aqueous NH_4Cl was added to the reaction mixture, and the organic layer was separated, dried over Na_2SO_4 and evaporated. Chromatography of the crude product on a preparative silica plate (2 mm, 20 × 20 cm) using 20% EtOAc in hexane yielded **8** (28 mg, 62%). ^{1}H NMR: 8.64–7.44 (m, 7H, aromatic), 6.90 (d, 1H, aromatic, J = 8.8), 5.17 (br s, 1H$_{OH}$), 3.62 (br d, 1H, J_{app} = 18), 3.05 (m, 1H), 2.37 (m, 1H), 2.24 (m, 2H), 1.89 (dm, 1H, J_{app} = 12.7), 1.03 (s, 9H, *tert*-butyl). MS (rel int): 333 (M$^+$ + H, 4), 332 (M$^+$, 2), 291 (3), 290 (10), 248 (36), 247 (100), 246 (11), 231 (18), 230 (32), 229 (19), 228 (12), 216 (10), 215 (16), 203 (10), 202 (11), 191 (25), 189 (12), 178 (11), 149 (19), 85 (11), 71 (14), 69 (15), 57 (29), 55 (12). HRMS: calcd for $C_{23}H_{24}O_2$ 332.1776, found 332.1786.

7-[(1-Adamantyl)oxomethyl]-7,8,9,10-tetrahydrobenzo[*a*]pyren-7-ol (10). To a stirred solution of **9** (0.1 g, 0.23 mmol), in anhydrous THF (1.37 mL) at −50 °C under argon, was added a 1.5 M solution of 1:1 LDA–THF complex in cyclohexane (307 μL, 0.46 mmol, 2 equiv). The color of the reaction mixture changed from clear to dark brown. The reaction mixture was stirred at −15 to −20 °C for 2 h and recooled to −50 °C, and another aliquot of the LDA solution was added (230 μL, 0.345 mmol, 1.5 equiv). The mixture was again stirred at −15 to −20 °C for 1 h. The reaction mixture was quenched by the addition of a mixture of EtOAc and saturated aqueous NH_4Cl. The organic layer was separated, dried over Na_2SO_4, and evaporated under reduced pressure. Chromatography of the product on a preparative silica plate (2 mm, 20 × 20 cm) using 30% EtOAc in hexane yielded **10** (0.08 g, 80%), mp 241–245 °C (colorless crystals from benzene). ^{1}H NMR: 8.36–7.88 (m, 7H, aromatic), 7.62 (s, 1H, aromatic), 5.43 (br s, 1H$_{OH}$), 3.81 (br d, 1H, J_{app} = 17.1), 3.27 (apparent quintet, 1H, J_{app} = 8.8), 2.56 (m, 1H), 2.31 (m, 2H), 1.99 (br d, 1H, J_{app} = 13), 1.76 (m, 6H), 1.61–1.37 (m, 9H). IR: 3416, 1667 cm^{-1}. MS (rel int): 435 (M$^+$ + 1, 1.5), 434 (M$^+$, 4), 273 (6), 272 (36), 271 (100), 270 (22), 254 (6), 253 (17), 252 (7), 243 (5), 239 (7), 229 (8), 228 (5), 227 (6), 226 (5), 216 (8) 215 (30), 214 (9), 213 (6), 202 (8), 135 (14), 93 (6), 91 (9), 79 (8). HRMS: calcd for $C_{31}H_{30}O_2$ 434.2246, found 434.2235. Anal. Calcd for $C_{31}H_{30}O_2$: C, 85.68; H, 6.96. Found: C, 85.13; H, 6.97.

7-(2,2-Dimethyl-1-oxopropyl)-7-[(trimethylsilyl)oxy]-7,8,9,10-tetrahydrobenzo[*a*]pyrene (2a) via Silylation of 2b. The hydroxy ketone **2b** obtained by the rearrangement of **1** (2.8 mg, 7.9 μmol) was dissolved in dry CH_2Cl_2 and cooled to 0 °C. Triethylamine (6.6 μL, 47.4 μmol) and TMS triflate (7.6 μL, 39.3 μmol) were added, and the mixture was allowed to stir at 0 °C for 15 min. The mixture was diluted with CH_2Cl_2 and washed with water. Separation of the organic phase, drying over Na_2SO_4, and evaporation gave the crude silyl ether which was chromatographed on a silica plate (250 μm, 10 × 20 cm) using 10% EtOAc in hexane. The silyl ether **2a** was obtained as a colorless solid (2.6 mg, 77%).

Preparation of Pivalaldehyde Cyanohydrin-*O*-trimethylsilyl Ether. To a stirred solution of pivalaldehyde (0.444 g, 5.2 mmol) and trimethylsilyl cyanide (0.82 mL, 6.2 mmol) in CH_2Cl_2 (4 mL) was added ZnI_2 (11 mg, 34.5 μmol). The mixture was stirred at room temperature for 3 h and the volatiles were evaporated. The crude reddish oil (0.945 g, 99%) was used for the next step without any purification. ^{1}H NMR: 3.97 (s, 1H), 1.00 (s, 9H), 0.19 (s, 3H).

Synthesis of 2a and 2b from 9,10-dihydrobenzo[*a*]pyren-7(8*H*)-one (11). To a stirred solution of the cyanohydrin TMS ether of pivalaldehyde (42.5 mg, 0.23 mmol) in 0.2 mL of anhydrous THF at 0 °C was added a 2 M solution of LDA in heptane–THF–ethylbenzene (0.126 mL, 0.25 mmol, 1.1 equiv). After the mixture was stirred at 0 °C for 15 min, a solution of **11** in 0.5 mL of anhydrous THF was added, and the stirring was continued for 1 h. Since very little product was observed after 1 h, an additional aliquot of the cyanohydrin was subjected to deprotonation (using 81.4 mg (0.44 mmol) of cyanohydrin in 0.2 mL of THF and 0.24 mL (0.48 mmol, 1.1 equiv) of the 2 M LDA solution) and added to the initial reaction mixture. The ice bath was removed, and the mixture was stirred overnight and then quenched by adding EtOAc-saturated aqueous NH_4Cl. The organic layer was separated, dried over Na_2SO_4, and evaporated. The product was purified on a preparative silica plate (1 mm, 20 × 20 cm) using CH_2Cl_2 as the eluant. This product was identical to **2a** produced by the rearrangement of **1**. The unreacted ketone in this reaction was not recovered.

The product obtained above was dissolved in THF (0.1 mL), and a 1 M solution of *n*-Bu_4NF in THF (0.1 mL) was added. The mixture was stirred at room temperature for 20 min, diluted with EtOAc, and washed with water. The organic layer was dried over Na_2SO_4 and evaporated. The crude product was purified using a preparative silica plate (1 mm, 20 × 20 cm), eluted with 20% EtOAc in hexane. The product obtained (4 mg, 12% for the above two steps) was identical to **2b** obtained by the rearrangement of **1**.

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