δ 1.13 (t, 3 H), 3.89 (s, 3 H), 3.91 (q, 2 H), 3.92 (s, 3 H), 5.85 (d, 1 H, J = 13 Hz), 6.83 (m, 3 H), 6.91 (d, 1 H, J = 13 Hz); mass spectrum, m/e 208 (M^+); high-resolution mass spectrum calcd for $C_{12}H_{16}O_3$ 208.1100, found 208.1116.

2-(4-Chlorophenyl)-1-ethoxyethene: bp 130 °C (13 mm); n^{20}_D = 1.5638; IR (neat) 3070, 3040, 1660, 1640 cm^{-1}; ^{1}H NMR δ 1.26 (t, 3 H), 3.86 (q, 2 H), 5.77 (d, 1 H, J = 13 Hz), 6.93 (d, 1 H, J = 13 Hz), 6.9–7.2 (m, 4 H); mass spectrum, m/e 182.184 (M^+); high-resolution mass spectrum calcd for $C_{10}H_{11}ClO$ 182.0499, 182.0470, found 182.0525, 184.0496.

2-(4-Acetylphenyl)-1-ethoxyethene: bp 180 °C (13 mm); mp 58 °C; IR (neat) 1675, 1635, 1595, 945 cm^{-1}; ^{1}H NMR δ 1.33 (t, 3 H), 2.57 (s, 3 H), 3.97 (q, 2 H), 5.89 (d, 1 H, J =13 Hz), 7.16 (d, 1 H, J = 13 Hz), 7.31 (d, 2 H), 7.88 (d, 2 H), mass spectrum, m/e 190 (M^+); high-resolution mass spectrum calcd for $C_{12}H_{14}O_2$ 190.0991, found 190.0988.

2-[2-(Carboethoxy)phenyl]-1-ethoxyethene: bp 105 °C (0.3 mm); n^{20}_D = 1.5444; IR (neat) 3060, 1715, 1635, 1600 cm^{-1}; ^{1}H NMR δ 1.38 (t, 3 H), 1.41 (t, 3 H), 3.99 (q, 2 H), 4.41 (q, 2 H), 6.78 (d, 1 H, J = 13 Hz), 7.03 (d, 1 H, J = 13 Hz), 7.1–7.55 (m, 3 H), 7.96 (d, 1 H); mass spectrum, m/e 220 (M^+); high-resolution mass spectrum calcd for $C_{13}H_{16}O_3$ 220.1100, found 220.1101.

2-Naphthyl-1-ethoxyethene: bp 80 °C (0.07 mm); n^{20}_D = 1.6248; IR (neat) 3060, 1655, 1640, 1595 cm^{-1}; ^{1}H NMR δ 1.30 (t, 3 H), 3.96 (q, 2 H), 6.48 (d, 1 H, J = 12 Hz), 6.92 (d, 1 H, J = 12 Hz), 7.2–8.2 (m, 7 H); mass spectrum, m/e 198 (M^+); high-resolution mass spectrum calcd for $C_{14}H_{14}O$ 198.1044, found 198.1084.

3-Phenyl-1-ethoxypropene: bp 100 °C (13 mm); n^{20}_D = 1.5109; IR (neat) 3060, 3030, 1675, 1655, 1605 cm^{-1}; ^{1}H NMR δ 1.21 (t, 3 H), 3.19 (d, 2 H, J = 7 Hz), 3.70 (q, 2 H), 4.89 (dt, 1 H, J = 13, 7 Hz), 6.31 (d, 1 H, J = 13 Hz), 7.22 (s, 5 H); mass spectrum; m/e 162 (M^+); high-resolution mass spectrum calcd for $C_{11}H_{14}O$ 162.1042, found m/e 162.1015.

3-(2-Bromophenyl)-1-ethoxypropene: n^{20}_D = 1.5422; IR (neat) 3060, 1670, 1650 cm^{-1}; ^{1}H NMR δ 1.27 (t, 3 H), 3.40 (d, 2 H, J = 7 Hz), 3.78 (q, 2 H), 4.97 (dt, 1 H, J = 7, 13 Hz), 6.41 (d, 1 H, J = 13 Hz), 7.0–7.4 (m, 3 H), 7.59 (d, 1 H); mass spectrum, m/e 240.242 (M^+); high-resolution mass spectrum calcd for $C_{11}H_{13}OBr$ 240.0150, 242.0131, found 240.0154, 242.0146.

3-[2-(Carboethoxy)phenyl]-1-ethoxyethene: bp 98 °C (0.07 mm); n^{20}_D = 1.5142; IR (neat) 3060, 1720, 1675, 1655 cm^{-1}; ^{1}H NMR δ 1.21 (t, 3 H), 1.36 (t, 3 H), 3.61 (d, 2 H, J = 7 Hz), 4.38 (q, 2 H), 4.48 (dt, 1 H, J = 7, 14 Hz), 6.37 d, 1 H, J = 14 Hz), 7.2–7.55 (m, 3 H), 7.90 (d, 1 H); mass spectrum, m/e 234 (M^+); high-resolution mass spectrum calcd for $C_{14}H_{18}O_3$ 234.1254, found 234.1237.

Registry No. 1, 32763-41-0; 2, 81206-43-1; 3 (Ar = Ph), 20565-86-0; 3 (Ar = 4-MeC_6H_4), 31026-84-3; 3 (Ar = 4-$MeOC_6H_4$), 31026-83-2; 3 (Ar = 2-$MeOC_6H_4$), 81206-44-2; 3 [Ar = 3,4-$(MeO)_2C_6H_3$], 81206-45-3; 3 (Ar = 4-ClC_6H_4), 31026-90-1; 3 (Ar = 4-AcC_6H_4), 81206-46-4; 3 (Ar = 2-$EtO_2CC_6H_4$), 81206-47-5; 3 (Ar = naphthyl), 81206-48-6; 4 (Ar = Ph), 16630-96-9; 4 (Ar = 2-BrC_6H_4), 81206-49-7; 4 (Ar = 2-$EtO_2CC_6H_4$), 81218-98-6; EtOC≡CH, 927-80-0; BH_3, 13283-31-3; 1,3,2-benzodioxaborole, 274-07-7; 3,4-$(MeO)_2C_6H_3I$, 5460-32-2; PhBr, 108-86-1; PhI, 591-50-4; 4-MeC_6H_4I, 591-50-4; 4-$MeOC_6H_4I$, 624-31-7; 2-$MeOC_6H_4I$, 529-28-2; 4-ClC_6H_4I, 637-87-6; 4-BrC_6H_4Ac, 99-90-1; 2-$EtO_2CC_6H_4I$, 1829-28-3; $C_{10}H_7I$, 90-14-2; $PhCH_2I$, 620-05-3; 2-$BrC_6H_4CH_2I$, 81206-50-0; 2-$EtO_2CC_6H_4Cl$, 7335-25-3.

Synthesis of Polycyclic Aromatic Hydrocarbons via a Novel Annelation Method

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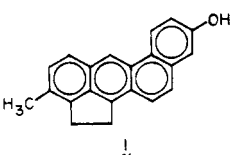
A new general synthetic approach to polycyclic aromatic hydrocarbons is described. The method is based on the convenient availability of *o*-lithioarylamides from regiospecific metalation of *N,N*-diethylarylamides with alkyllithium–amine reagents. Addition of the *o*-lithioarylamide to an aryl ketone or aldehyde affords a lactone. Reduction of the latter with zinc and alkali or HI generates the free acid which undergoes cyclization with $ZnCl_2$ and Ac_2O and reduction with zinc and alkali or HI to furnish the fully aromatic polyarene. Compounds synthesized via this route include 3-methylcholanthrene, benz[*a*]anthracene, dibenz[*a,h*]anthracene, dibenz[*a,j*]anthracene, benzo[*a*]pyrene, and their methyl derivatives. Overall yields are generally good. Competitive enolate anion formation depresses the yield in the initial step in the reactions of enolizable ketones. However, this pathway can be suppressed with substantial improvement in yield through deuterium exchange of the hydrogens α to the carbonyl. The last three steps of the general method can be condensed to only one step through reductive cyclization of the lactone intermediates with hydriodic acid in acetic acid. While tertiary lactones are resistant to HI under these conditions, the corresponding free acids undergo reductive cyclization under similar conditions.

Chemical and biological studies of polycyclic hydrocarbons are currently hampered by the relative complexity of existing synthetic methods, most of which were developed many years earlier.[1] We recently reported a novel synthesis of polycyclic arenes from *o*-quinones having one fewer ring.[2]

We now report a convenient new synthesis of polycyclic aromatic molecules utilizing a novel annelation method. This research was stimulated by the need for 9-hydroxy-3-methylcholanthrene (**1**), a potential synthetic precursor[3]



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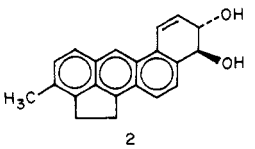

2

of the 9,10-dihydrodiol of 3-methylcholanthrene (**2**), tentatively identified as the principal active carcinogenic metabolite of 3-methylcholanthrene (3-MC).[4,5] The es-

(1) Clar, E. "Polycyclic Hydrocarbons"; Academic Press: New York, 1964; Vol. I, II.

(2) Sukumaran, K. B.; Harvey, R. G. *J. Org. Chem.* **1981**, *46*, 2740.

(3) Sukumaran, K. B.; Harvey, R. G. *J. Org. Chem.* **1980**, *45*, 4407.

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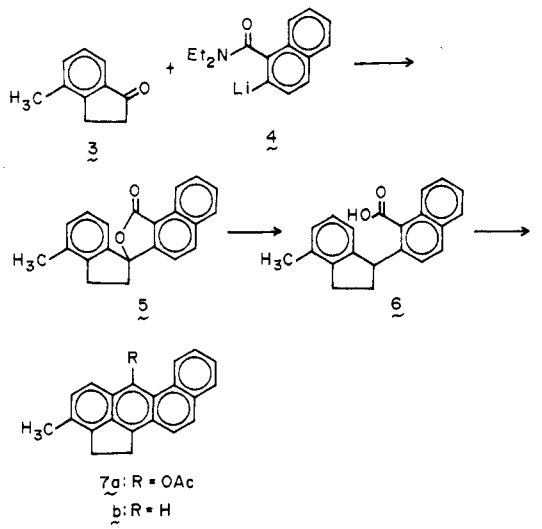
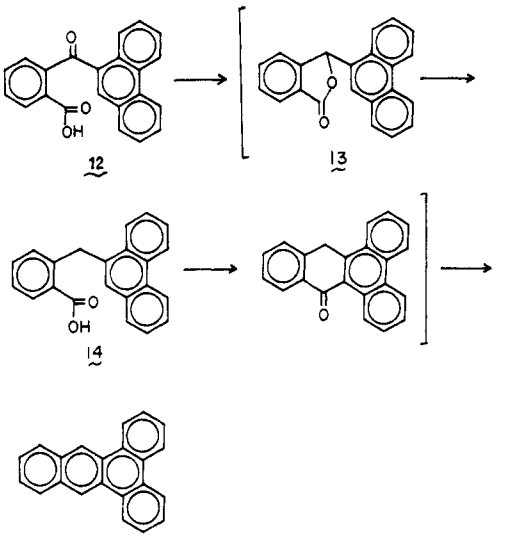
Scheme I



Scheme II

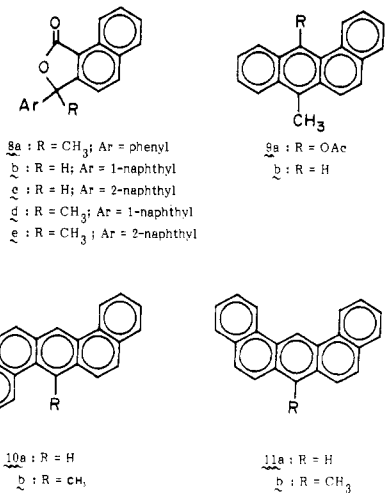


tablished synthesis of 3-MC was unpromising, entailing two sealed-tube pyrolysis steps and reportedly affording low or zero yields with methoxy substituents in the angular ring.[6,7] The alternative synthesis of 3-MC developed in our laboratory was reported in a preliminary communication.[8] We now report full details of this method and its application to the synthesis of a wider range of polycyclic hydrocarbons and their substituted derivatives.

Results

Synthesis of 3-MC (**7b**) was achieved via the sequence in Scheme I. This synthetic approach is based on the availability of ortho-lithiated arylamides (e.g., **4**) through directed metalation of *N,N*-dialkylarylamides with alkyllithium–amine reagents by the method of Beak.[9] Condensation of 4-methylindanone (**3**) with 2-lithio-*N,N*-diethyl-1-naphthamide (**4**) in ether at −60 °C afforded smoothly the carbonyl addition product which on treatment with methanesulfonic acid in refluxing CH_2Cl_2 underwent conversion to the lactone. Reductive cleavage of **5** with zinc and alkali gave the reduced acid **6** which on brief treatment with $ZnCl_2$ in acetic acid–acetic anhydride furnished 6-acetoxy-3-methylcholanthrene (**7a**). Deacetoxylation of **7a** was accomplished by reduction with either zinc and alkali or hydriodic acid in refluxing propionic acid[10] to provide 3-MC (**7b**). Yields exceeded 90% in all steps except the first which was 30%. Presumably, the lower yield in the initial step is due to competitive enolate anion formation by proton abstraction from **3**.

Extension of this synthetic approach to a wider range of polycyclic aromatic compounds was next investigated. Analogous reaction of acetophenone with **4** furnished smoothly the corresponding lactone **8a** in 71% yield.



Evidently, enolate anion formation is less serious in this case. The lactone underwent conversion via an analogous sequence of transformations to afford 7-methylbenz[*a*]anthracene (**9b**). Analogous reactions of 1- and 2-naphthaldehyde with **4** took place similarly to afford the corresponding lactones (**8b,c**), which in turn underwent transformation via the same sequence of steps to dibenz[*a,h*]anthracene (**10a**) and dibenz[*a,j*]anthracene (**11a**). Overall yields were in excess of 50%.

Similar reactions of 1- and 2-acetylnaphthalene with **4** provided the corresponding methyl-substituted lactones (**8d,e**) in somewhat lower yields (~50%) than those for the analogous reactions of the related aldehydes (~70%). Presumably, this difference is also a consequence of competition with enolate anion formation in the case of the ketones. Conversion of the lactones **8d** and **8e** via the same reaction sequence furnished the 7-methyl derivatives of dibenz[*a,h*]anthracene (**10b**) and dibenz[*a,j*]anthracene (**11b**), respectively.

The possibility of telescoping the last three steps of the synthetic sequence, from lactone to fully aromatic hydrocarbon, into a single step was suggested by the earlier observation that the keto acid **12** underwent reductive cyclization with HI in acetic acid directly to dibenz[*a,c*]anthracene (Scheme II).[11] Additional examples of this

(4) King, H. W. S.; Osborne, M. R.; Brookes, P. *Int. J. Cancer* **1977**, *20*, 564. Thakker, D. R.; Levin, W.; Wood, A. W.; Conney, A. H.; Storming, T. A.; Jerina, D. M. *J. Am. Chem. Soc.* **1978**, *100*, 645. Malaveille, C.; Bartsch, H.; Marquardt, H.; Baker, S.; Tierney, B.; Hewer, A.; Grover, P. L.; Sims, P. *Biochem. Biophys. Res. Commun.* **1978**, *85*, 1568.

(5) Harvey, R. G. *Acc. Chem. Res.* **1981**, *14*, 218.

(6) Prior to these studies, 3-MC derivatives were synthetically accessible only through the Elbs reaction in a sealed tube at ~400 °C: Feiser, L. F.; Seligman, A. M. *J. Am. Chem. Soc.* **1936**, *58*, 2482; **1935**, *57*, 228, 942.

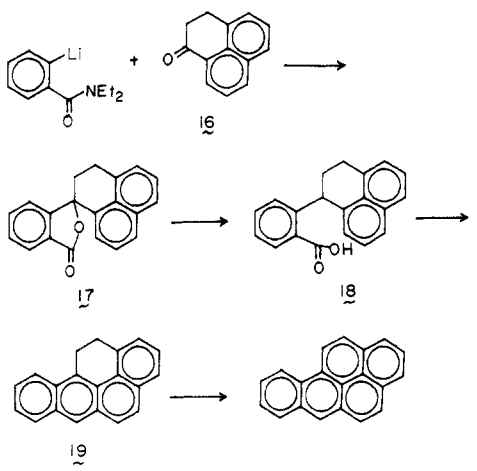
(7) Failure of the Elbs synthesis of 10- and 11-MeO-3-MC and 11- and 12-F-3-MC is reported by: Newman, M. S.; Khanna, V. K. *J. Org. Chem.* **1980**, *45*, 4507. These authors point out the need for an alternative synthetic approach to 3-MC derivatives.

(8) Jacobs, S.; Harvey, R. G. *Tetrahedron Lett.* **1981**, *22*, 1093.

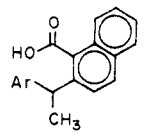
(9) Beak, P.; Brown, R. A. *J. Org. Chem.* **1977**, *42*, 1823; **1979**, *44*, 4463.

(10) Reduction of phenols and quinones with HI in acetic acid was recentlydescribed by: Konieczny, M., Harvey, R. G. *J. Org. Chem.* **1979**, *44*, 4813. The present method differs in the use of hypophosphorus acid which serves to inhibit formation of iodinated side products through reduction of the iodine formed.

Scheme III



transformation have recently been reported by Platt and Oesch.[12] Evidence was presented[11] in support of a mechanism involving initial reduction of the keto group, presumably via a lactone intermediate **13**, followed by cyclization of the reduced acid **14** to the ketone and reduction to the fully aromatic hydrocarbon. This mechanism parallels the final three steps of our synthetic sequence, suggesting the potential utility of HI as a reagent for the reductive cyclization of lactones directly to hydrocarbons. As a test of this possibility, the lactone **8b**, obtained from condensation of 1-naphthaldehyde with **4**, was heated with HI and H_3PO_2 (or red P) in refluxing acetic acid. There was obtained dibenz[*a*,*h*]anthracene (**10a**) directly in one step. While there was no attempt to optimize the yield (55%), it was comparable to that obtained by the three-step route. In contrast, attempted reductive cyclization of the homologous lactone **8d** with HI failed to take place, furnishing only recovered **8d**. However, the corresponding reduced acid **15a** on treatment



15a: Ar = 1-naphthyl
b: Ar = 2-naphthyl

with HI and H_3PO_2 in acetic acid underwent conversion to 7-methyldibenz[*a*,*j*]anthracene (**10b**). Evidently, methyl substitution on the benzylic carbon of the lactone markedly inhibits reduction of the lactone function by hydriodic acid. The 2-naphthyl analogues **8c** and **8e** exhibited similar behavior. Thus, the lactone **8c** underwent reductive cyclization with HI to dibenz[*a*,*j*]anthracene (**11a**), while its methyl-substituted homologue **8e** failed to react, and the reduced acid **15b** underwent conversion to 7-methyldibenz[*a*,*j*]anthracene (**11b**). The lactone **5** also failed to enter into reaction with HI. In general, it appears that tertiary lactones (i.e., lactones with oxygen covalently attached to a tertiary benzylic carbon atom) are resistant to HI reduction, while related secondary lactones undergo relatively facile reduction with this reagent.

In view of the importance of benzo[*a*]pyrene and its derivatives in carcinogenesis research,[5] it was of interest to determine the applicability of this method to the synthesis of the derivatives of benzo[*a*]pyrene (Scheme III). Reaction of 2-lithio-*N*,*N*-diethylbenzamide with phenalanone (**16**) furnished the expected lactone **17** which in turn underwent reduction with zinc and alkali to the carboxylic acid **18**. Reductive cyclization of **18** with hydriodic acid in refluxing acetic acid furnished directly 11,12-dihydrobenzo[*a*]pyrene **19** accompanied by benzo[*a*]pyrene and tetrahydrobenzo[*a*]pyrene (detected by NMR and TLC analysis). Apparently disproportion of **19** takes place in the acidic medium. From a purely synthetic viewpoint disproportionation is unimportant, since the total product mixture on treatment with DDQ underwent facile dehydrogenation to benzo[*a*]pyrene.

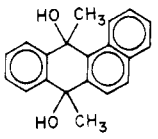
In order to determine whether the enolate anion pathway could be partially suppressed through deuterium exchange of the hydrogens α to the carbonyl, we prepared 2,2-dideuterio-4-methylindanone from **3** by K_2CO_3-catalyzed exchange with deuteriomethanol. Reaction of this deuterated ketone with **4** gave the expected dideuterated lactone analogue of **5** in substantially improved yield (52%). Analogous reaction of **4** with the α,α-dideuterated analogue of phenalanone (**16**) also furnished the expected product in markedly improved yield (50%) in comparison with similar reaction of undeuterated phenalanone (22%). These results indicate that the deuterium isotope effect can be utilized synthetically to substantially enhance the yield of alkylation of enolizable ketones. These findings were reported in a preliminary communication.[13] Following completion of these studies, Reitz et al. reported a similar effect in the reaction of α-lithio-*N*,*N*-dialkyl-2,2-diethylbutyramide with acetone.[13] Insofar as we are aware, these are the first examples of this relatively dramatic effect.

Discussion

The synthetic approach developed for 3-MC (Scheme I) and extended to benz[*a*]anthracene, dibenz[*a*,*h*]anthracene, dibenz[*a*,*j*]anthracene, benzo[*a*]pyrene, and their methyl derivatives provides a new general synthesis of polycyclic aromatic hydrocarbons. In other studies, to be reported separately, 9-methoxy-3-methylcholanthrene and 9-*tert*-butylbenzo[*a*]pyrene[14] have also been synthesized in good overall yield via this same synthetic approach. In principle, the method appears adaptable to the preparation of a wide range of substituted and unsubstituted polycyclic aromatic compounds, including oxidized metabolites required in carcinogenesis research.

While the four-step synthetic sequence can in some cases be telescoped to only two steps through reductive cyclization of the lactone intermediates with HI in acetic acid, this abbreviated procedure is less general in scope. As already shown, the two-step method is inapplicable to tertiary lactones such as **5**, **8d**, and **8e**, demonstrated to be resistant to HI under the conditions employed. More vigorous conditions were not investigated due to the likelihood of reduction of the polycyclic aromatic ring systems.[10,11,15] Failure of reduction of tertiary lactones is somewhat surprising in view of the fact that tertiary benzylic alcohols such as **20** undergo facile reduction with

(11) Harvey, R. G.; Leyba, C.; Konieczny, M.; Fu, P. P.; Sukumaran, K. B. *J. Org. Chem.* **1978**, *43*, 3423.
(12) Platt, K. L.; Oesch, F. *J. Org. Chem.* **1981**, *46*, 2601. We find that H_3PO_2 allows a more convenient workup and provides cleaner products than red phosphorus as employed by these authors.
(13) Jacobs, S.; Cortez, C.; Harvey, R. G. *J. Chem. Soc., Chem. Commun.* **1981**, 1215. A similar effect was reported essentially simultaneously by: Reitz, D. B.; Beak, P.; Tse, A. *J. Org. Chem.* **1981**, *46*, 4316. The deuterium isotope effect also has been utilized recently to direct dehydration of steroidal alcohols regioselectively to endo olefins: Miyano, M. *J. Org. Chem.* **1981**, *46*, 1854.
(14) Pataki, J.; Konieczny, M.; Harvey, R. G. *J. Org. Chem.* **1982**, *47*, 1133.
(15) Konieczny, M.; Harvey, R. G. J. Org. *Chem.* **1980**, *45*, 1308.



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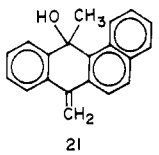

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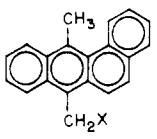

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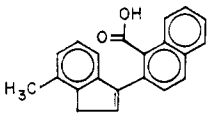

23

this reagent.[15] This difference apparently reflects underlying differences in mechanism. Thus, there is substantial evidence that the mechanism of reduction of **20** involves initial dehydration to **21** followed by nucleophilic attack of a halide anion on methylene, loss of hydroxyl, rearrangement to the fully aromatic **22**, and reduction.[15,16] However, the olefin **23** could not be detected as a product of treatment of **5** with HI in acetic acid, and **23** (obtained as a minor product of reaction of **3** with **4**) failed to undergo reduction with HI. Thus, a mechanism involving initial ring opening to an olefinic acid such as **23** does not appear to be available to these tertiary lactones. In cases where HI reductive cyclization is feasible, relatively prolonged reaction periods (1–10 days) are required for optimum yield. Apparently this is because HI is a less efficient catalyst than $ZnCl_2$ or HF for cyclization of the acid intermediates. For these reasons, the HI method must be considered a useful alternative rather than the method of exclusive choice.

Utilization of the deuterium isotope effect to suppress competitive enolate anion formation during alkylation appears to be of potentially broad synthetic applicability. Careful search of the literature revealed, surprisingly, no precedent, except for a report by Reitz et al. which appeared subsequent to these studies.[13] The deuterium isotope can be retained in the final product (e.g., 3-MC) through reduction of the phenol acetate with HI and H_3PO_2 under mild conditions and short reaction times or completely removed by exchange with more prolonged treatment with acid.

Precedent exists for the preparation of polyarenes through reaction of metalated compounds with aryl aldehydes. Directed metalation has previously been employed by Newman to prepare certain benz[*a*]anthracene derivatives from ortho-lithiated isoxazolines via a formally related synthetic sequence.[17] While studies by Beak indicate the dialkylamide function to be superior to the isoxazoline function in metalation–alkylation reactions,[9] the latter may be a useful alternative in some applications. Also Snieckus has reported reactions of several ortho-lithiated arylamides with aryl aldehydes in the presence of excess *sec*-BuLi to furnish quinone as well as lactone products.[18] In cases where cyclization could occur in two directions, both isomeric quinones were produced. Under the conditions employed in the present study (i.e., no excess *sec*-BuLi reagent), quinones were not detected as significant secondary products; moreover, cyclization appeared to take place regiospecifically in one direction. Reduction of the quinones provides an alternative route to polycyclic aromatic hydrocarbons. However, this method offers no significant advantage, except in the preparation of isomeric polycyclic aromatic compounds not available via the more general method presented herein. A disadvantage of the quinone route is the incompatibility of excess alkylithium reagent with functional groups (e.g., methoxy) susceptible to competitive metalation.

Studies in progress of the carcinogenic activities of the meso-region methyl derivatives of dibenz[*a*,*h*]anthracene and dibenz[*a*,*j*]anthracene indicate these compounds to be more potent carcinogens than the unsubstituted parent hydrocarbons. Results of these studies will be reported separately.

Experimental Section

General Methods. The NMR spectra were recorded on Varian EM-360 and/or Bruker HX-270 spectrometers with tetramethylsilane as an internal standard in $CDCl_3$ unless otherwise specified. Melting points are uncorrected. All new compounds gave satisfactory analyses for C and H within ±0.3% and/or mass spectra consistent with the assigned structures. THF was distilled from $LiAlH_4$ immediately before use, and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) was distilled from KOH. *sec*-Butyllithium solution in cyclohexane, Adogen 464, and α-bromo-*o*-xylene were purchased from the Aldrich Chemical Co. Perinaphthanone (**16**) was synthesized by the method of Fieser.[19]

4-Methyl-1-indanone (3). To a solution of α-bromo-*o*-xylene (24.8 g, 134 mmol), diethyl malonate (27.2 g, 170 mmol), and Adogen 464 (0.5 g) in CH_2Cl_2 (100 mL) was added slowly with stirring a solution of NaOH (27.6 g) in 50 mL of water. After 30 min, when the exothermic reaction had moderated, 50 mL more water as added, and stirring was continued overnight. The usual workup[20] gave the crude (*o*-methylbenzyl)malonic acid (24.5 g) which was decarboxylated by heating gradually to 200 °C. Recrystallization of the product from ethanol–water gave 3-(*o*-methylphenyl)propionic acid (18 g) which was dissolved in liquid HF and left at room temperature overnight.[21] The HF was evaporated and the residue worked up conventionally to provide crude **3**. Recrystallization from ethanol gave pure **3**: 15.0 g; mp 99 °C (lit.[22] mp 98–101 °C); NMR δ 2.35 (s, 3, CH_3), 2.67 (m, 2, H_3), 2.99 (m, 2, H_2), 7.28–7.58 (m, 3, aromatic).

2,2-Dideuterio-4-methyl-1-indanone. A mixture of K_2CO_3 (0.5 g) and **3** (5 g) in 50 mL of benzene was heated to reflux, the heat source was removed, CH_3OD (5 mL) was added, and the mixture was stirred for 1 h. The benzene–methanol azeotrope was then distilled out until the vapor temperature reached 78 °C. The heat source was again removed, a fresh 5-mL portion of methanol-*d* was added, and the procedure was repeated twice more. A conventional workup gave 2,2-dideuterio-4-methyl-1-indanone, the proton NMR spectrum of which matched that of **3** except for the absence of the multiplets at δ 2.5–3.2, assigned to the methylene protons, which were replaced by a broad singlet at δ 3.0, assigned to the unexchanged benzylic protons.

***N*,*N*-Diethyl-1-naphthamide.** To 1-naphthoic acid (20 g) and $SOCl_2$ (15 g) in benzene (25 mL) was added 4 mL of dimethylformamide with stirring. Vigorous gas evolution ensued with gradual dissolution of the solid. After 2 h the bottom phase was washed with benzene, and the washings combined with the upper phase were evaporated under reduced pressure. If there was no phase separation, the entire solution was evaporated in vacuo.

A solution of the crude acid chloride in ethyl ether (50 mL) was cooled in an ice bath while a solution of Et_2NH (18 g) in 50 mL of ether was added slowly with stirring. After addition of the amine was complete, stirring was continued for 1 h. Conventional workup gave an oil which was distilled in vacuo to give *N*,*N*-diethyl-1-naphthamide: 18.5 g; NMR δ 3.25–3.88 (dual t,

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6, CH_3), 2.7–3.3 (apparent q, 4, CH_2), 7.0–8.0 (m, 7, aromatic).

Synthesis of 3-Methylcholanthrene (7b). A solution of *sec*-butyllithium (22.4 mmol) was added to a solution of *N,N*-diethylnaphthamide (4.5 g, 20 mmol) and TMEDA (2.5 g, 21.5 mmol) in diethyl ether (150 mL) under argon at −60 °C. After 1 h, to this solution was added dropwise a solution of **3** (2.6 g, 22 mmol) in THF (30 mL). Then the cooling was removed, and the mixture was stirred overnight. A conventional workup furnished the crude product which was dissolved in CH_2Cl_2. Methanesulfonic acid (1 mL) was added, and the solution was refluxed briefly and worked up to afford the lactone **5**; 1.7 g (30%); mp 217 °C (toluene); NMR δ 2.4 (s, 3, CH_3), 2.5–3.4 (m, 4, CH_2), 6.5–9.2 (m, 9, aromatic); mass spectrum, *m/e* 300 (M^+), 256 ($M^+ - CO_2$), 227 ($M^+ - C_3H_5O_2$), 212 (227 − CH_3), 155, 146, 92. Acid catalysis was not essential for lactone formation which took place spontaneously at a somewhat slower rate on heating in the absence of acid.

A solution of the lactone **5** (3.5 g, 12 mmol) in pyridine (50 mL) was added to 20 g of zinc dust (activated by consecutive treatment with 10% HCl, H_2O, 5% cuprammonium sulfate, and H_2O) suspended in a solution of KOH (5 g) in 20 mL of H_2O and 50 mL of CH_3OH. The mixture was stirred at reflux for 2.5 h and worked up to afford the reduced acid **6**: 3.2 g (91%); mp 218–219 °C; NMR δ 2.35 (s, 3, CH_3), 2.5–3.3 (m, 4, CH_2), 5.76 (t, 1, CH), 6.6–8.0 (m, 9, aromatic).

To a solution of **6** (1.0 g, 3.3 mmol) in glacial acetic acid (20 mL) was added $ZnCl_2$ (60 mg), and the mixture was stirred at reflux for 20 min. Recrystallization of the product from dimethylformamide gave **7a**: 1.0 g (90%); mp >210 °C dec; NMR δ 9.8 (dd, 1, H_7), 7.4–7.8 (m, 7, aromatic), 3.7 (m, 2, H_2), 3.4 (m, 2, H_1), 2.6 (s, 3, CH_3CO), 2.4 (s, 3, CH_3).

A solution of **7a** (100 mg), HI (2 mL of 56% solution), and hypophosphorus acid (0.5 mL of 50% solution) in 50 mL of propionic acid was heated at reflux for 10 min. The usual workup followed by chromatography on basic alumina afforded 7b: 76 mg (93%); mp 179–180 °C (cyclohexane) (lit.[6] mp 178.5–179.5 °C); a mixture melting point with authentic 3-MC was not depressed.

Reaction of 4 with 2,2-D_2-3. Reaction of **4** with the deuterated analogue of **3** (3.0 g, 20 mmol) was conducted essentially by the procedure employed with **3**. A similar conventional workup gave a residual gum which was taken up in cyclohexane and a small amount of CH_2Cl_2 and warmed on a steam bath for 24 h. The crude lactone which precipitated was recrystallized from ethanol to give 3.1 g (52%) of **5**-d_2, mp 215–216 °C; the NMR spectrum was identical with that of **5** except for replacement of the multiplets at δ 2.7 and 3.2 (2 H each) by a broad singlet at δ 3.2.

General Method. Synthesis of 7-Methylbenz[*a*]anthracene (9b). A solution of *N,N*-diethyl-1-naphthamide (1.13 g, 5 mmol), TMEDA (0.5 g, 5 mmol), and a few crystals of triphenylmethyl chloride in ether (50 mL) under N_2 was cooled to −78 °C. Then a solution of *sec*-butyllithium (1.4 M in cyclohexane) was added dropwise until the light yellow color of the trityl carbanion appeared (indicative of consumption of moisture). Addition of *sec*-butyllithium (5.5 mmol from a 1.4 M solution) imparted a dark orange color to the solution which was stirred at −78 °C for 1 h.

To the solution of **4** prepared above was added acetophenone (1.2 g, 10 mmol), and stirring was continued at −78 °C for 1 h. The solution was allowed to warm to room temperature for 3 h additional and then was worked up conventionally to afford the crude lactone **8a** which was dissolved in benzene and passed through a column of silica gel. Recrystallization from benzene–hexane gave pure **8a**: 0.97 g (71%); mp 173–174 °C (lit.[23] mp 173.8–174.2 °C); NMR δ 2.10 (s, 3, CH_3), 7.20–7.90 (m, 10, aryl), 9.13 (m, 1, aryl).

A mixture of activated zinc (14 g), **8a** (0.97 g, 3.54 mmol), 10% KOH (100 mL), and pyridine (10 mL) was heated at reflux overnight. The product was cooled and filtered, and the filtrate was acidified with dilute HCl. A conventional workup followed by recrystallization from benzene–hexane afforded pure 2-(1-phenylethyl)-1-naphthoic acid: 0.91 g (93%); mp 115–117 °C (lit.[23] mp 128–129 °C); NMR δ 1.76 (d, 3, CH_3, J = 6.6 Hz), 4.73 (q, 1, CH, J = 6.6 Hz), 7.16–8.30 (m, 11, aryl), 10.0 (br s, 1, OH).

A mixture of 2-(1-phenylethyl)-1-naphthoic acid (980 mg, 3.6 mmol), $ZnCl_2$ (100 mg), acetic acid (25 mL), and acetic anhydride (12.5 mL) was heated at reflux for 2 h. The solution was cooled and water added to precipitate the crude product (990 mg). The latter was dissolved in benzene and purified by passage through a short column of Florisil and recrystallization from benzene–hexane to furnish 12-acetoxy-7-methylbenz[*a*]anthracene (**9a**): 960 mg (89%); mp 155–157 °C; NMR δ 2.61 (s, 3, CH_3), 3.06 (s, 3, CH_3CO), 7.50–8.50 (m, 10, aryl), 9.30 (m, 1, aryl).

A mixture of **9a** (0.96 g, 3.2 mmol), zinc dust (40 g, activated with $CuSO_4$), and aqueous NaOH (35 g in 225 mL of H_2O) in dioxane (50 mL) was stirred at reflux overnight. The usual workup gave crude **9b** (0.83 g) which was purified by chromatography on a short column of silica gel and recrystallization from benzene–hexane to afford pure **9b**: 650 mg (85%); mp 139–140 °C (lit.[23] mp 140 °C); NMR δ 5.16 (s, 3, CH_3), 7.45–8.65 (m, 9, aryl), 8.58 (m, 1, H_1), 9.13 (br s, 1, H_{12}).

Dibenz[*a*,*h*]anthracene (10a). Reaction of **4** with 1-naphthaldehyde (1.56 g, 10 mmol) and subsequent reactions were carried out by essentially the same procedures as those employed in the preceding synthetic sequence. The crude product (2.54 g) and *p*-toluenesulfonic acid (250 mg) were heated in refluxing benzene for 6 h and then worked up conventionally to afford the lactone **8b** (1.4 g) which was recrystallized from benzene–hexane to furnish **8b**: 1.04 g (67%); mp 164–166 °C (lit.[18] mp 166 °C).

Reduction of **8b** (1.02 g) with zinc and alkali gave 2-(1-naphthylmethyl)-1-naphthoic acid: 860 mg (83%); mp 195–196 °C (benzene–hexane); NMR δ 4.76 (s, 2, CH_2), 7.00–8.50 (m, 13, aryl). Cyclization of this acid (860 mg) with $ZnCl_2$, acetic anhydride, and acetic acid furnished 7-acetoxydibenz[*a*,*h*]anthracene: 900 mg (97%); mp 241-241.5 °C; NMR δ 2.70 (s, 3, CH_3), 7.56–8.16 (m, 10, aryl), 8.78 (s, 1, H_{14}), 8.66–9.33 (m, 2, $H_{1,8}$).

Reduction of the phenol acetate with zinc and alkali afforded dibenz[*a*,*h*]anthracene: 690 mg (93%); mp 265–266 °C (lit.[24] mp 262–263 °C). The NMR spectrum was identical with that of an authentic sample: δ 7.50–9.33 (m, 10, aryl), 8.91 (m, 2, $H_{1,8}$), 9.16 (s, 2, $H_{7,14}$).

Dibenz[*a*,*j*]anthracene (11a). Procedures were based on the general method. Reaction of **4** with 2-naphthaldehyde (1.56 g, 10 mmol) furnished the lactone **8c**: 1.09 g (70%); mp 154–155 °C (lit.[18] mp 148 °C); NMR δ 6.56 (s, 1, CH), 7.00–8.16 (m, 11, aryl), 9.26 (m, 1, aryl). Reduction of **8c** with zinc and alkali gave 2-(2-naphthylmethyl)naphthoic acid: 900 mg (83%); mp 155–156 °C; NMR δ 4.41 (s, 2, CH_2), 7.10–8.13 (m, 13, aryl). $ZnCl_2$-catalyzed cyclization of this acid furnished 14-acetoxydibenz[*a*,*j*]anthracene: 958 mg (99%); mp 204–206 °C; NMR δ 2.53 (s, 3, CH_3), 7.50–8.16 (m, 10, aryl), 8.30 (s, 1, H_7), 9.50 (m, 2, $H_{1,13}$).

Reduction of the phenol acetate with zinc and alkali gave dibenz[*a*,*j*]anthracene: 90%; mp 197–198 °C (lit.[24] mp 195–197 °C). The NMR spectrum was identical with that of an authentic sample: δ 7.46–8.10 (m, 10, aryl), 8.38 (s, 1, H_7), 9.05 (m, 2, $H_{1,13}$), 10.08 (s, 1, H_{14}).

7-Methyldibenz[*a*,*h*]anthracene (10b). Procedures were based on the general method. Reaction of **4** with 1-acetylnaphthalene (3.40 g, 20 mmol) provided the lactone **8d**: 1.68 g (52%); mp 176–177 °C (lit.[25] mp 194.5–195 °C); NMR δ 2.31 (s, 3, CH_3), 7.30–9.33 (m, 13, aryl). Reduction of **8d** (1.08 g) in the usual manner afforded the corresponding reduced acid: 950 mg (87%); mp 220–221 °C (lit.[25] mp 221–222 °C); NMR δ 1.88 (d, 3, CH_3, J = 7 Hz), 5.40 (q, 1, CH, J = 7 Hz), 7.03–8.50 (m, 13, aryl). $ZnCl_2$-catalyzed cyclization of the free acid (850 mg) gave 14-acetoxy-7-methyldibenz[*a*,*h*]anthracene: 790 mg (85%); mp 190–192 °C (lit.[25] mp 192–192.5 °C); NMR δ 2.62 (s, 3, CH_3), 3.36 (s, 3, CH_3CO), 7.33–10.0 (m, 12, aryl). Reduction of the phenol acetate (790 mg) by the usual procedure afforded **10b**: 60 mg (91%); mp 193–194 °C (lit.[25] mp 192–194.5 °C); NMR δ 3.38 (s, 3, CH_3), 7.33–9.08 (m, 13, aryl).

7-Methyldibenz[*a*,*j*]anthracene (11b). Reaction of **4** with 2-acetylnaphthalene (3.40 g, 20 mmol) by the general procedure afforded the crude lactone **8e** (4.8 g) which failed to crystallize after purification by chromatography on silica gel. The lactone was employed directly in the next step. Reduction of **8e** with zinc and alkali furnished the corresponding free acid: 1.89 g (58%

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overall from 2-acetylnaphthalene); mp 175–176 °C; NMR δ 1.83 (d, 3, CH_3, J = 7 Hz), 4.86 (d, 1, CH, J = 7 Hz), 6.75–8.65 (m, 13, aryl). Cyclization of the acid (0.89 g) with $ZnCl_2$ in the usual manner gave 14-acetoxy-7-methyldibenz[a,j]anthracene: 940 mg (99%); 249–250 °C; NMR δ 2.50 (s, 3, CH_3), 3.11 (s, 3, CH_3CO), 7.33–8.40 (m, 10, aryl), 9.50 (m, 2, $H_{1,13}$). Reduction of the phenol acetate (400 mg, 1.14 mmol) by the usual procedure afforded **11b**: 330 mg (96%); mp 243–244 °C; NMR δ 3.10 (s, 3, CH_3), 7.33–8.40 (m, 10, aryl), 9.06 (m, 2, $H_{1,13}$), 10.05 (s, 1, H_{14}).

Benzo[*a*]pyrene. Reaction of *N,N*-diethyl-2-lithiobenzamide with **16** (910 mg, 5 mmol was conducted by the general procedure employed in preceding syntheses. The crude lactone **17** (1.5 g) was utilized directly in the next step. Reduction of **17** with zinc and alkali afforded the acid **18**: 310 mg (22%); mp 149–150 °C; NMR δ 2.36 (br t, 2, CH_2), 3.10 (br t, 2, benzylic), 5.60 (t, 1, CH), 6.66–8.33 (m, 10, aryl).

A solution of **18** (300 mg), HI (1.6 mL of 56% solution), and H_3PO_2 (0.4 mL of 50% solution) in glacial acetic acid (50 mL) was heated at reflux for 24 h. The reaction mixture was poured into ice–water and the precipitate collected by filtration. The crude 11,12-dihydrobenzo[*a*]pyrene (250 mg) was shown by NMR analysis and TLC on 2,4,7-trinitrofluorenone[26] to contain benzo[*a*]pyrene and tetrahydrobenzo[*a*]pyrene. The crude **19** was taken up in benzene with excess DDQ and heated at reflux for 2 h. The reaction mixture was poured onto a column of silica gel. Elution with hexane gave benzo[*a*]pyrene: 180 mg (70%); mp 177–178 °C (lit.[1] mp 176.5–177.5 °C); a mixture melting point with authentic benzo[*a*]pyrene was not depressed.

Reductive Cyclization of 8b and 8c with HI. A solution of **8b** (200 mg, 0.67 mmol), HI (1.3 mL of 56% solution), and red P (240 mg) in glacial acetic acid (50 mL) was heated at reflux for 56 h and then poured into a 1% aqueous sodium bisulfite solution. The precipitate was collected by filtration, washed with water, and dried. Chromatography on silica gel gave dibenz[a,h]anthracene: 100 mg (54%); mp 264–265 °C (lit.[24] mp 262–263 °C); the NMR spectrum matched that of an authentic sample. A similar reaction conducted with hypophosphorus acid in place of red P gave a slightly lower yield (49%) of **10a**.

Analogous reaction of **8c** (with H_3PO_2) for 10 days afforded dibenz[a,j]anthracene (80%); a lower yield was obtained with shorter reaction times.

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Registry No. **3**, 24644-78-8; **3**-d_2, 81194-73-2; **4**, 81194-74-3; **5**, 78606-93-6; **5**-d_2, 81194-75-4; **6**, 78606-94-7; **7a**, 78606-95-8; **7b**, 56-49-5; **8a**, 81194-76-5; **8b**, 73540-67-7; **8c**, 73540-68-8; **8d**, 81194-77-6; **8e**, 81194-78-7; **9a**, 17526-28-2; **9b**, 2541-69-7; **10a**, 53-70-3; **10b**, 15595-02-5; **11a**, 224-41-9; **11b**, 78606-97-0; **15a**, 81194-79-8; **15b**, 81194-80-1; **16**, 518-85-4; **16**-d_2, 81194-81-2; **17**, 81194-82-3; **18**, 81205-70-1; **19**, 81194-83-4; **23**, 81194-84-5; acetophenone, 98-86-2; 2-(1-phenylethyl)-1-naphthoic acid, 81194-85-6; 1-naphthaldehyde, 66-77-3; 2-(1-naphthylmethyl)-1-naphthoic acid, 77321-47-2; 7-acetoxydibenz[a,h]anthracene, 63077-06-5; 2-naphthaldehyde, 66-99-9; 2-(2-naphthylmethyl)-1-napthoic acid, 81194-86-7; 14-acetoxydibenz[a,j]anthracene, 81205-71-2; 1-acetylnaphthalene, 941-98-0; 14-acetoxy-7-methyldibenz[a,h]anthracene, 81194-87-8; 2-acetylnaphthalene, 93-08-3; 14-acetoxy-7-methyldibenz[a,j]anthracene, 81194-88-9; benzo[*a*]pyrene, 50-32-8; *N,N*-diethyl-1-naphthamide, 5454-10-4.

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Reductive Alkylation/Arylation of Arylcarbinols and Ketones with Organosilicon Compounds

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Arylcarbinols react with certain organosilanes in the presence of boron trifluoride to yield hydrocarbons resulting from transfer of an R group from silicon to carbon. The transfer works well with aryl- and allylsilanes and fails with alkylsilanes. Allylation of ionizable carbinols is sometimes accompanied by cation-mediated oligomerization. This can be offset by converting the carbinols in question to their respective allyldimethylsilyl ethers followed by rearrangement of the ethers with BF_3. While diaryl ketones are sluggishly bisallylated, the corresponding ketals undergo smooth bisallylation at 0 °C with allytrimethylsilane/BF_3/CH_2Cl_2.

The reductive alkylation of carbinols and ketones is a synthetically useful transformation for which few direct methods are available.

Sequential methods such as the tandem alkylation–reduction of aromatic carbonyl compounds[1] and α,β,γ,δ-unsaturated ketones[2] or the phenylation–reduction of aldehydes and ketones[3] are limited in that only one alkyl group is introduced at the site of reduction. Geminal reductive alkylation of tosyl hydrazones via a sequence of nucleophilic followed by electrophilic attack has been described;[4,5] however, no direct reductive alkylation of carbinols or geminal reductive alkylation of ketones of general utility is known.[6] (Reductive alkylation of carbinols effectively constitutes a geminal reductive alkylation of ketones since the carbinols can be obtained by reaction of the ketone with a suitable organometallic reagent.)

The known reduction of carbinols in acidic media via hydride transfer from silicon[7] and the well-established[8]

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