a protected form, thus permitting further elaboration of the carboxylic acid residue.

Experimental Section

General Procedure for Formation of *N*-*t*-Boc Derivatives. To a 0.50 M solution of *N*-benzylbenzamide (2.0 g, 9.47 mmol) in methylene chloride were added triethylamine (1.32 mL, 9.47 mmol), di-*tert*-butyl dicarbonate (4.13 g, 18.94 mmol), and 4-(dimethylamino)pyridine (1.16 g, 9.47 mmol). The solution was stirred for 7 h at 25 °C under an argon atmosphere. The volatiles were removed, and the residue was purified by rapid chromatography on silica gel. Elution with hexane/ether (6:1) afforded 2.63 g (90%) of the desired *N*-*tert*-butoxycarbonyl-*N*-benzylbenzamide: IR ($CHCl_3$) 1725, 1670 cm^{-1}; NMR ($CDCl_3$) δ 1.08 (s, 9 H), 4.96 (s, 2 H), 7.24–7.64 (m, 10 H).

General Procedure for Hydrolysis of *N*-*t*-Boc Derivatives. To a 0.20 M solution of *N*-*tert*-butoxycarbonyl-*N*-benzylbenzamide (1.09 g, 3.51 mmol) in tetrahydrofuran was added 10.54 mL (10.54 mmol) of a 1.0 N solution of lithium hydroxide. The solution was stirred for 6 h at 25 °C. After removal of tetrahydrofuran in vacuo, the basic aqueous residue was acidified by the addition of 10% acetic acid and extracted with ether. Drying ($MgSO_4$) and concentration afforded 883 mg of crude material. The acid was characterized by esterification: the crude acid was dissolved in 10.0 mL of ether and treated with excess ethereal diazomethane. After 10 min the excess diazomethane was quenched with glacial acetic acid, and the volatiles were removed in vacuo. Chromatography (silica gel, pentane/ether, 20:1) afforded 396 mg (83%) of methyl benzoate.

General Procedure for Methanolysis of *N*-*t*-Boc Derivatives. A solution of *N*-*tert*-butoxycarbonyl-*N*-benzylbenzamide (981 mg, 3.15 mmol) in 1.40 mL of methanol, under an argon atmosphere, was cooled to 0 °C. To this solution was added 1.75 mL (3.47 mmol) of a 2.0 M solution of sodium methoxide in methanol. After 10 min the solution was poured into brine and extracted with ether. After drying ($MgSO_4$) and concentration, the residue was chromatographed on silica gel. Elution with pentane/ether, 20:1, afforded 402 mg (94%) of methyl benzoate.

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Registry No. 1, 675-20-7; 2, 85908-96-9; 3 (R = H), 27219-07-4; 3 (R = Me), 85908-97-0; 4, 85908-98-1; 5, 85908-99-2; $PhCH_2CONHCH_2Ph$, 7500-45-0; $PhCONHCH_2Ph$, 1485-70-7; *t*-$C_6H_{13}CH{=}CHCONHC_4H_9$, 85909-00-8; $PhCH_2CON(CH_2Ph)$-*t*-Boc, 85909-01-9; $PhCON(CH_2Ph)$-*t*-Boc, 85909-02-0; *t*-$C_6H_{13}CH{=}CHCON(C_4N_9)$-*t*-Boc, 85909-03-1; $HOOC(CH_2)_3NH$-*t*-Boc, 57294-38-9; $MeOOC(CH_2)_3NH$-*t*-Boc, 85909-04-2; $HOOC(CH_2)_3CH[CH_2CH_2OSi(Ph)_2$-*t*-Bu$]NH$-*t*-Boc, 85909-05-3; $MeOOC(CH_2)_3CH[CH_2CH_2OSi(Ph)_2$-*t*-Bu$]NH$-*t*-Boc, 85909-06-4; $PhCH_2COOH$, 103-82-2; $PhCH_2COOMe$, 101-41-7; PhCOOH, 65-85-0; PhCOOMe, 93-58-3; *t*-$C_6H_{13}CH{=}CHCOOH$, 14812-03-4; *t*-$C_6H_{13}CH{=}CHCOOMe$, 14952-06-8; γ-butyrolactam, 616-45-5; 5-[2-[(*tert*-butyldiphenylsilyl)oxy]ethyl]-δ-valerolactam, 85909-07-5; *N*-(*tert*-butoxycarbonyl)-γ-butyrolactam, 85909-08-6; *N*-(*tert*-butoxycarbonyl)-5-[2-[(*tert*-butyldiphenylsilyl)oxy]-ethyl]-δ-valerolactam, 85909-09-7.

Synthesis of 3,6-Dimethylcholanthrene[1]

Melvin S. Newman* and P. K. Sujeeth[2]

Chemistry Department, The Ohio State University, Columbus, Ohio 43210

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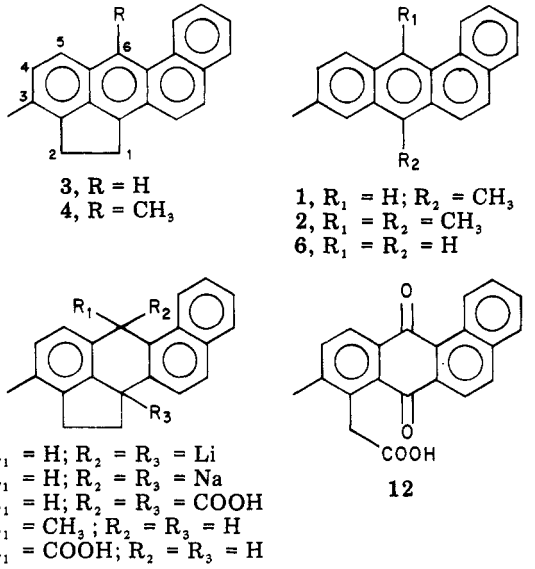
7-Methylbenz[*a*]anthracene (7-MBA, **1**; Chart I) is the most potent carcinogenic monomethylbenz[*a*]anthracene[3] and is undoubtedly a planar hydrocarbon.[4] The addition of a methyl group at position 12 to afford 7,12-dimethylbenz[*a*]anthracene (7,12-DMBA, **2**) not only increases the carcinogenic potency[5] but renders the molecule nonplanar[6] because of the steric effect of the 12-methyl group. We were interested to see whether the introduction of a methyl group at position 6 of 3-methylcholanthrene (3-MC, **3**) would increase the carcinogenic activity of 3-MC and cause 3,6-dimethylcholanthrene (3,6-DMC, **4**) to be nonplanar.[7]

Chart I



Alkali metals are known[8,9] to add across the meso positions in anthracene[10] (**5**), benz[*a*]anthracene[8] (BA, **6**), and 3-MC,[8] giving rise to intensely colored anionic intermediates. Alcoholysis of these intermediates was shown[8] to be an excellent route to the corresponding dihydrohydrocarbons. But the scope of alkylation (reductive alkylation) has been limited by low yields, complexity of products, and over alkylation.[11]

Subtle differences in color and reactivity were noticed between the disodio and the dilithio derivatives.[12] Thus

(1) Research supported by Grant CA07934 from the National Cancer Institute.

(2) Postdoctoral Research Associate.

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(6) For the latest X-ray structure and discussion of DMBA, see D. W. Jones and J. M. Sowden, *Cancer Biochem. Biophys.*, 281 (1976).

(7) Recent preliminary reports by Drs. J. A. and E. C. Miller, McArdle Laboratory for Cancer Research, Dr. W. Levin et al., Hoffmann-La Roche, M. S. Newman, Ohio State University, and D. Jerina et al., National Institute of Arthritis, NIH, indicate that **4** is considerably more tumorigenic than 3-MC.

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dilithio-3-MC (7) yielded[12] 42% of 6,12b-dicarboxy-6,12b-dihydro-3-methylcholanthrene (9) on carbonation, while disodio-3-MC (8) gave 59% of a monocarboxylic acid of unknown[13] structure.

On the basis of these data we hoped monomethylation of 8 would yield the desired 6,12-dihydro-3,6-dimethylcholanthrene (10). We now report the formation of 10 from 3 in 61% yield[14] and dehydrogenation of 10 with sulfur to pure 3,6-DMC (4) in 71.5% yield. The assigned structures 4 and 10 were confirmed by oxidation of 4 to 5-(6-methyl-1,2-benz[a]anthraquinoyl)acetic acid[8] (12).

Experimental Section[15]

6,12b-Dihydro-3,6-dimethylcholanthrene (10). To the stirred solution at room temperature of 8 prepared[8] from 2.5 g (9.3 mmol) of 3[16] in 400 mL of ether (dried by distillation from BuMgBr): benzene (1:1) was added 2 g (14.1 mmol) of methyl iodide. After 5 min the reaction mixture was quenched with a milliliter of methanol and filtered through a pad of silica gel. After evaporation of the solvent the residue was triturated twice with 10 mL each of hot acetone and the remainder was crystallized from 1-propanol to yield 0.89 g of 10 as long white needles, mp 167.5–168.5 °C. The purest 10 melted at 172–173 °C after several recrystallizations. Lower melting fractions[17] gave NMR spectra that were indistinguishable from that of pure 10. The total yield of stereoisomeric forms of 10 was 61%. Data for 10: mp 168 °C; UV (hexane) λ_{max} at 227, 231, 256 (sh), 264, 274, 283, 292, 306, 313, 321 nm; NMR ($CDCl_3$) δ 1.46 (d, 3, 6-CH_3), 2.26 (s, 3, 3-CH_3), 2.0–3.2 (m, 4, 1- and 2-CH_2), 4.0–5.0 (m, 2-, 6-, and 12b-CH), 6.8–8.3 (m, 8, aromatic); mass spectrum, m/e 284 (M^+).

3,6-Dimethylcholanthrene (4). A mixture of 1.422 g of 10 (mp 165–167.5 °C) and 0.175 g sulfur was initially melted at 170 °C and maintained at 160–165 °C for 1 h. The crude product in a small amount of benzene mixed with 5 g of picric acid in hot alcohol (100 mL) gave 2.42 g of 3,6-dimethylcholanthrene picrate, as dark reddish-black needles, mp 147.5–149 °C. One recrystallization from 90 mL of alcohol gave 2.13 g of pure picrate, mp 148.5–149.5 °C. On chromatography over basic alumina (benzene) 1.01 g (71%) of pure 3,6-DMC (4) was obtained as light-yellow needles (mp 135–136 °C[18]) after crystallization from 1-propanol. Data for 4: UV (hexane λ_{max} 267, 277, 288, 299, 336, 350, 367, 386 nm; NMR ($CDCl_3$) δ 2.3 (s, 3, 3-CH_3), 3.13 (s, 3, 6-CH_3), 2.8–3.5 (br m, 4, 1- and 2-CH_2), 7.0–8.8 (m, 8, aromatic); mass spectrum, m/e 282 (M^+). Anal. Calcd for $C_{22}H_{18}$: C, 93.57; H, 6.43. Found: C, 93.38; H, 6.51.

5-(6-Methyl-1,2-benz[a]anthraquinoyl)acetic Acid[8] (12). A mixture of 40 mg of 4 and 200 mg of sodium dichromate in 4 mL of acetic acid was held at reflux for 0.5 h and then diluted with dilute H_2SO_4. The IR spectrum of the precipitated yellow solid (32 mg, mp 250–260 dec) was superimposable with that of 5-(6-methyl-1,2-benz[a]anthraquinoyl)acetic acid (12) obtained[8] by oxidation of 3: IR (KBr) 1700, 1665, 1590, 1462, 1430, 1300, 1063, 848, 785, 762 cm^{-1}.

Registry No. 3, 56-49-5; 4, 85923-37-1; 4 picrate, 85923-38-2; 10 (isomer 1), 85923-39-3; 10 (isomer 2), 85923-40-6; 12, 85923-41-7.

(13) We believe this acid has the structure 11, since monomethylation of 8 gives the 6-methyl derivative.

(14) The yield of 10 and the number of coproducts formed varied with the amount of methyl iodide used. A slight excess of methyl iodide (1.5 equiv) enhanced the isolated yield of 10 by depressing the amount of 6,12b-dihydro-3-methylcholanthrene (seen by NMR of mother liquor) formed, while a large excess (>2 equiv) resulted in the formation of small quantities of two different isomers of trimethylcholanthrene (M^+ at m/e 296) of unknown structure.

(15) All melting points are uncorrected. Analysis was done by the Galbraith Laboratories, Inc., Knoxville, TN.

(16) A commercial sample from Baker. 3-MC was also synthesized from 7-(4-methylhydrindyl) 1-naphthyl ketone as per L. F. Fieser and A. M. Seligman, *J. Am. Chem. Soc.*, **58**, 2482 (1936).

(17) Stereoisomeric with crystals, mp 172–173 °C; for a discussion on formation of stereoisomers in similar reductive methylations, see ref 9.

(18) On slow heating 3,6-DMC melts in a range of 133–136 °C primarily due to air oxidation as determined by the TLC of the dark-colored melt. When the melting point was taken in an evacuated tube, the melting point was 135–136 °C and no dark spot was obtained in the TLC.

1,4- and 1,5-Diketones via Palladium-Catalyzed Allylation of Potassium Enoxyborates[1]

Ei-ichi Negishi* and Fen-Tair Luo

Department of Chemistry, Purdue University, West Lafayette, Indiana 47907

Anthony J. Pecora and Augustine Silveira, Jr.

Department of Chemistry, State University of New York at Oswego, Oswego, New York 13126

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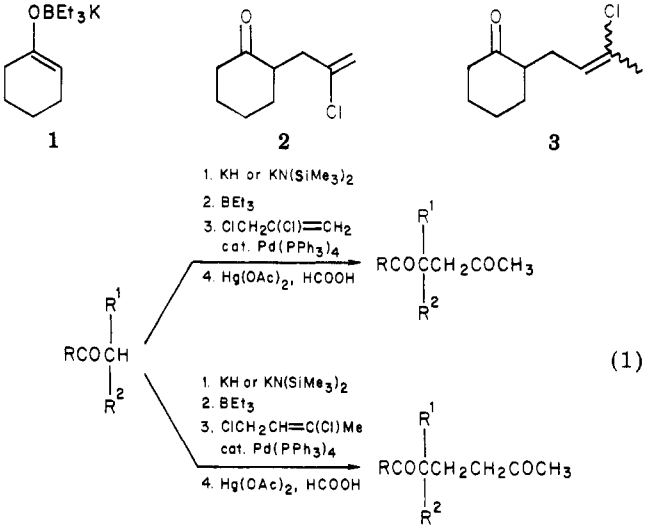
We have recently reported a Pd-catalyzed, highly regio- and stereoselective allylation of enoxyborates derived from ketones.[2] One particularly attractive feature of potential significance is that Pd catalysts significantly enhance the reactivity of otherwise relatively unreactive allylic electrophiles containing electron-withdrawing substituents. This presumably is because the oxidative addition reaction between allylic electrophiles and Pd complexes is accelerated by electron-withdrawing groups. Thus, for example, 2,3-dichloropropene and 1,3-dichloro-2-butene, both of which react only sluggishly with enolates, undergo a rapid and selective allylation with potassium cyclohexenoxytriethylborate (1) in the presence of 5 mol % of $Pd(PPh_3)_4$ to give 2 and 3 in 92% and 86% yields, respectively.

In view of the significance of γ- and δ-chloro-γ,δ-unsaturated ketones as precursors to 1,4- and 1,5-diketones, respectively, we investigated the generality and regiospecificity of the Pd-catalyzed reaction of potassium enoxyborates with 2,3-dichloropropene and 1,3-dichloro-2-butene. As the results summarized in Table I indicate, the reaction indeed appears to be not only general with respect to the structure of ketones but also highly regiospecific. Coupled with a recently developed procedure for converting alkenyl chlorides into ketones,[3] the herein-described method offers a satisfactory, potentially general, and regiospecific route to 1,4- and 1,5-diketones (eq 1).



(1)

R = alkyl; R^1,R^2 = H or alkyl

The following observations are noteworthy. First, all five cyclic and acyclic potassium enoxytriethylborates tested

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