reaction mixture was worked up as described above.

(*E*,*E*)-3,6-Dimethyl-3,5-octadiene (2):[16] H^1 NMR (CCl_4) δ 1.8 (t, 6 H, J = 8 Hz), 1.77 (s, 6 H), 2.2 (q, 4 H, J = 8 Hz), 5.5 (m, 2 H); t_R = 29.6 min. Anal. Calcd for $C_{10}H_{18}$: C, 86.88; H, 13.12. Found: C, 86.76; H, 13.19.

(*Z*,*Z*)-3,6-Dimethyl-3,5-octadiene (3):[16] H^1 NMR (CCl_4) δ 1.8 (t, 6 H, J = 8 Hz), 1.75 (s, 6 H), 2.2 (q, 4 H, J = 8 Hz), 5.9 (m, 2 H); t_R = 33.1 min. Anal. Calcd for $C_{10}H_{18}$: C, 86.88; H, 13.12. Found: C, 86.76; H, 13.19.

3,5-Dimethyl-2-ethyl-1,4-hexadiene (4): H^1 NMR (CCl_4) δ 1.05 (superimposed t and d, 6 H, J = 8 Hz), 1.65 (s, 3 H), 1.70 (s, 3 H), 2.0 (q, 2 H, J = 8 Hz), 3.05 (dd, 1 H, J = 8, 10 Hz), 4.8 (m, 2 H), 4.9 (d, 1 H, J = 10 Hz); t_R = 15.2 min. Anal. Calcd for $C_{10}H_{18}$: C, 86.88; H, 13.12. Found: C, 86.76; H, 13.19.

5-Ethyl-2-methyl-2,4-heptadiene (5):[17] H^1 NMR (CCl_4) δ 1.10 (t, 3 H, J = 8 Hz), 1.14 (t, 3 H, J = 8 Hz), 1.80 (s, 3 H, 1.75 (s, 3 H), 2.20 (q, 2 H, J = 8 Hz), 2.24 (q, 2 H, J = 8 Hz), 5.7 (m, 2 H); t_R = 33.3 min. Anal. Calcd for $C_{10}H_{18}$: C, 86.88; H, 13.12. Found: C, 86.76; H, 13.19.

Ozonolysis of 5-Ethyl-2-methyl-2,4-heptadiene (5). Ozone was added to 50 mL of 8 dissolved in 3 mL of methylene chloride at −70 °C until the solution turned a clear light blue. A mixture of 0.5 g of sodium iodide, 1 mL of methanol, and 0.25 mL of acetic acid was added to this solution and the mixture allowed to stir overnight. The solution was decolorized to a pale yellow with sodium bisulfite, neutralized with sodium carbonate, and gravity filtered to remove any remaining solid. The 2,4-dinitrophenylhydrazones were prepared by classical methods. Because they were soluble in the methylene chloride solution, after vacuum filtration the solution was used directly for TLC analysis on silica gel with toluene as the developing solvent. The mixture gave three spots, R_f 0.01, 0.34, and 0.51. The retention times for the 2,4-dinitrophenylhydrazones of acetone, 3-pentanone, and 2-butanone are 0.34, 0.51, and 0.46, respectively.

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Preparation of a Tetrahydrobenzocycloheptene and Its Intramolecular Cyclization

James D. McChesney* and Richard A. Swanson†

Department of Medicinal Chemistry, School of Pharmacy, The University of Kansas, Lawrence, Kansas 66045

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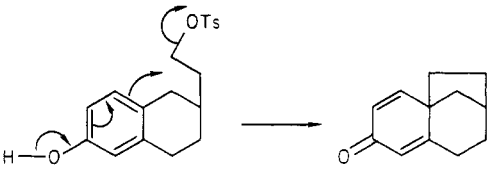
In connection with our interest in preparation of tetracyclic diterpenes of the kuarene group,[1] we sought to determine the feasibility of formation of the BCD rings through an intramolecular cyclization of a tetrahydrobenzocycloheptene precursor. Masamune[2] had shown that a tetrahydronaphthalene precursor could be successfully closed intramolecularly to the BCD ring skeleton. However, no one has explored the utilization of the conformationally less flexible[3] tetrahydrobenzocycloheptene. In order to examine the possible utilization of a tetrahydrobenzocycloheptene, we needed a convenient method of preparation of that ring system. We report herein such a method and an exploration of the practicality of its intramolecular cyclization.

Scheme I



I

The synthesis of 6,7,8,9-tetrahydro-4a,7-methano-4a*H*-benzocyclohepten-2(5*H*)-one (I) has been reported.[2] Masamune, utilizing the so-called Ar_15 participation, has prepared I from a tetrahydronaphthalene tosylate by treatment with strong base (Scheme I).

The dienone I can in principle be prepared by similar intramolecular cyclization of the tetrahydrobenzocycloheptene derivative II. Toward this goal the synthesis of II from the readily available 6-methoxy-2-tetralone was undertaken (Scheme II).

The synthesis of ethyl 2-hydroxy-6-methoxy-1,2,3,4-tetrahydronaphthalene-2-acetate (III) and its subsequent dehydration have been reported.[2] Dehydration of the hydroxy ester III produced a mixture of isomeric olefins IV and V. These isomers were partially separable by distillation and could be readily distinguished spectrally. In the IR spectrum, the carbonyl absorption of IV occurred at 1738 cm^{-1}, and in the ^1H NMR spectrum, the vinyl hydrogen resonance of IV appeared as a singlet at 6.30 ppm while that of V appeared as a broad singlet at 5.70 ppm.

The dehydration could be effected with any of several agents, but none was wholly satisfactory. The preferred method of dehydration involved refluxing a benzene solution of III in the presence of a catalytic amount of concentrated sulfuric acid. This procedure afforded, in 91% yield, a 76:24 mixture of olefins IV and V, respectively.

The mixture of isomers IV and V, which was not readily separable, was ozonolized, and the resulting ozonide was reduced with zinc in acetic acid to afford a mixture of 6-methoxy-2-tetralone and keto aldehyde VI. The oxidation could also be effected with osmium tetraoxide and sodium periodate by using the procedure of Lemieux and Johnson,[4] but lower yields were obtained than with ozonolysis.

The aldehyde VI was not stable, and on silica gel chromatography or, more efficiently, on treatment with fused potassium bisulfate in benzene, it underwent a facile intramolecular aldol condensation with concomitant loss of water to yield the dihydrobenzocycloheptene VII. This substance was characterized by elemental analysis and spectroscopic techniques, but owing to its instability, it was normally hydrogenated over palladium on carbon to the tetrahydrobenzocycloheptene VIII without purification.

* Present address: The Department of Pharmacognosy, School of Pharmacy, The University of Mississippi, University, MS 38677.
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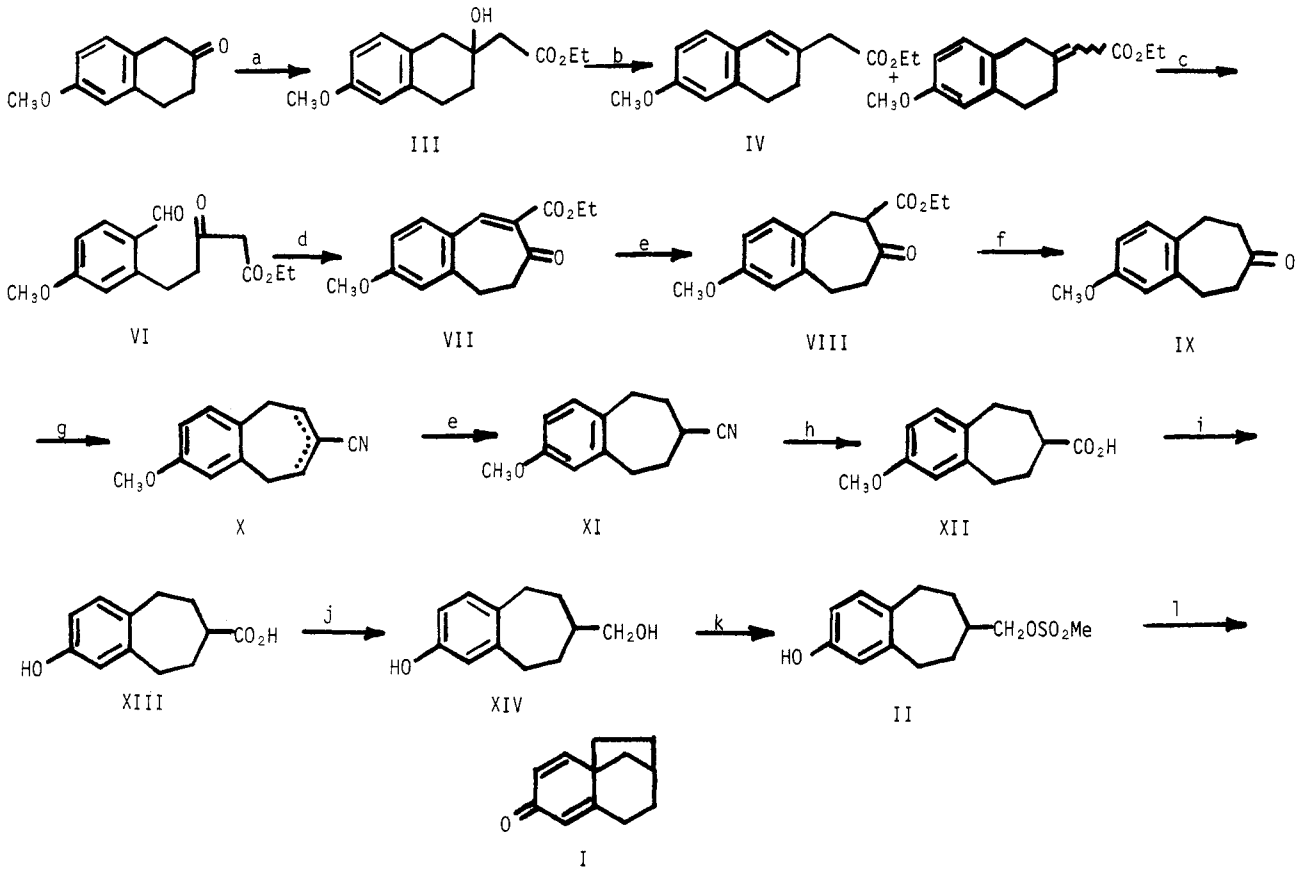
Scheme II[a]



[a] Reagents: a, $BrCH_2CO_2Et/Zn$; b, H_2SO_4/C_6H_6; c, (1) O_3/EtOAc, (2) Zn/HOAc; d, $KHSO_4/C_6H_6$; e, H_2/Pd/C; f, 10% H_2SO_4; g, (1) KH_2PO_4/NaCN/EtOH/H_2O, (2) $POCl_3/C_5H_5N$; h, NaOH/H_2O/$HOCH_2CH_2OH$; i, BBr_3/CH_2Cl_2; j, NaAl-$(CH_3OCH_2CH_2O)_2H_2/C_6H_6$; k, CH_3OSO_2Cl/C_5H_5N; l, *t*-BuOK/*t*-BuOH.

The overall conversion of the dihydronaphthalene IV to the tetrahydrobenzocycloheptene VIII proceeded in yields which varied from 65% to 70%. Recovery of 6-methoxy-2-tetralone was not feasible because of its instability. Transformation of VIII to the desired derivative II involved hydrolysis and decarboxylation with 10% sulfuric acid to afford the decarbethoxy ketone IX. Phenolic nitrile X was prepared from the ketone IX by using the buffered system of sodium cyanide, potassium dihydrogen phosphate, ethanol, and water. These reaction conditions afforded, in good yield, the cyanohydrin. The cyanohydrin was subsequently dehydrated without purification by the action of phosphoryl chloride in pyridine to a mixture of isomeric olefins X. The unresolved olefin mixture X was hydrogenated in the presence of palladium on carbon to afford the cyano ester derivative XI. Basic hydrolysis of the methoxy nitrile XI, with ethylene glycol as a cosolvent, afforded the methoxy acid XII. Cleavage of the methyl ether by the action of boron tribromide in dichloromethane produced the phenolic acid XIII. The phenolic acid XIII was reduced to the corresponding alcohol XIV with sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al) in benzene. When the phenolic alcohol XIV was allowed to react with an equimolar amount of methanesulfonyl chloride in pyridine solution at 0 °C for 1.5 h, selective esterification of the primary alcohol occurred. The mesylate II was isolated in nearly quantitative yield as indicated by the ^1H NMR spectrum of the crude reaction product. The chemical shift of the methylene protons α to the oxygen atom changed from 3.35 ppm in the alcohol XIV to 4.05 ppm in the mesylate. Since this ester was expected to be unstable, it was utilized without purification.

Treatment of the phenolic mesylate with potassium *tert*-butoxide in a dilute *tert*-butyl alcohol solution afforded the tricyclic dienone I in 57% purified yield. The successful preparation of the 6,7,8,9-tetrahydro-4a,7-methano-4a*H*-benzocyclohepten-2(5*H*)-one system (I) from the tetrahydrobenzocycloheptene system XIV demonstrates the feasibility of the basic approach being pursued. It is thus established that a tetrahydrobenzocycloheptene can assume a conformation from which intramolecular reaction can occur. The effect of substituents in the cycloheptene ring on the course of cyclization is being investigated.

Experimental Section

All melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were taken on Beckman IR-33 and Perkin-Elmer 727 spectrophotometers. Ultraviolet spectra were obtained by using a Cary 14 recording spectrophotometer. Proton magnetic resonance spectra were obtained with Varian Associates A-60A, EM-360, and T-60 spectrometers with tetramethylsilane as an internal standard. The T-60 spectrometer was equipped with a Nicolet Technology Corp. TT-7 pulsed RF Fourier transform system. In ^1H NMR descriptions, s = singlet, d = doublet, t = triplet, m = multiplet, and brs = broad singlet. Mass spectra were recorded by using a Varian Associates CH-5 spectrometer; ionization was by electron impact. Microanalyses were performed on an F&M 185 A CHN analyzer and on a Hewlett-Packard 185 B CHN analyzer at the University of Kansas. Chromatography reported for silica gel employed Brinkmann silica gel 60 (70–325 mesh) and Florisil chromatography employed Fisher F-101 (100–200 mesh). Dry column chromatography was performed by using nylon tubing and adsorbent to which 0.5% Du Pont Luminescent Chemical No. 609 had been added. Thin-layer chromatography was performed by utilizing Brinkmann precoated plates. All chroma-

tography solvents were either AR grade or distilled immediately before use. Skelly B refers to petroleum ether, boiling point range 60–68 °C.

Ethyl 6-Methoxy-3,4-dihydronaphthalene-2-acetate (IV). To a stirred solution of the hydroxy ester III (74 g, 0.28 mol) in 250 mL dry benzene under argon were added 12 drops of concentrated H_2SO_4. The reaction mixture was refluxed for 2 h, during which time water was removed in a Dean–Stark trap. After cooling, the reaction mixture was washed with saturated $NaHCO_3$ and brine, and dried (Na_2SO_4), and the solvent was removed in vacuo. Distillation afforded 62.88 g (91%) of olefin mixture which contained 76% of the desired isomer by ^1H NMR: bp 125 °C (0.05 mm) [lit.[3] bp 135–137 °C (0.09 mm)]; ^1H NMR ($CDCl_3$) δ 1.26 (3 H, t, J = 7 Hz, OCH_2CH_3), 2.36 (2 H, m, C_4H), 2.80 (2 H, m, C_2H), 3.18 (2 H, s, CH_2CO_2), 3.77 (3 H, s, OCH_3), 4.16 (2 H, q, J = 7 Hz, OCH_2CH_3), 6.30 (1 H, brs, C_1H), 6.5–7.1 (3 H, m, Ar); IR (neat) 1738, 1620 (sh), 1610 cm^{-1}. Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.36. Found: C, 72.97; H, 7.43.

2-Methoxy-6-carbethoxy-8,9-dihydro-7*H*-benzocycloheptene-7-one (VII). An adaptation of the procedures of Pryde and co-workers[5] and Symes and Dawson[6] was employed. A solution of ethyl 6-methoxy-3,4-dihydronaphthalene-2-acetate (IV; 10 g, 0.041 mol, 76% isomeric purity) and 250 mL of ethyl acetate was cooled in an ozonolysis flask to −78 °C. Ozone (2% in oxygen) was passed at a rate of 1.08 L/min through the cooled solution and then through a 10% aqueous KI solution. When iodine was produced in the KI solution (40 min), ozonolysis was stopped, and the reaction mixture was transferred to a flask containing 200 mL of glacial acetic acid. To the vigorously stirred solution was added zinc (40 g); the resulting mixture was stirred at −5 to −15 °C for 8 h and filtered, and 500 mL of dichloromethane was added. The solution was washed with water (each wash was back-washed with a small amount of dichloromethane) until free of acid, dried (Na_2SO_4), and concentrated in vacuo. Dry benzene (200 mL) and freshly fused potassium bisulfate (10 g) were added, and the stirred mixture was refluxed under argon for 6 h during which time water was removed in a Dean–Stark trap. The mixture was cooled, filtered, washed with water and brine, dried (Na_2SO_4), and concentrated in vacuo. Although the product was pure enough for reduction, a small amount was removed, and an analytical sample was prepared by preparative TLC (2 mm × 20 cm × 20 cm, silica gel, $CHCl_3$). The product fraction (R_f 0.18) was isolated and recrystallized (ethyl acetate/Skelly B) to yield analytically pure VII: mp 132–133 °C; ^1H NMR ($CDCl_3$) δ 1.36 (3 H, t, J = 7.5 Hz, OCH_2CH_3), 2.95 (4 H, m, $ArCH_2CH_2C{=}O$), 3.87 (3 H, s, OCH_3), 4.33 (2 H, q, J = 7.5 Hz, OCH_2CH_3), 6.83 (2 H, m, C_1 and C_3H), 7.4 (1 H, d, J = 9.8 Hz, C_4H), 7.77 (1 H, s, C_5H); IR (KBr) 1720, 1652, 1606 cm^{-1}. Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.22; H, 6.20. Found: C, 68.93; H, 6.19.

2-Methoxy-6-carbethoxy-5,6,8,9-tetrahydro-7*H*-benzocyclohepten-7-one (VIII). The procedure of Mukharji and co-workers was used.[7] The olefin VII (from previous reaction) was shaken for 10 h with hydrogen in a Paar apparatus in ethyl acetate (30 mL) as the solvent and 10% palladium on carbon (0.2 g) as a catalyst. Filtration, removal of the solvent, and chromatography on a 500-g silica gel dry column (5 × 50 cm) developed with 33% ethyl acetate in Skelly B yielded 4.5 g of VIII. An analytical sample was recrystallized from Skelly B: mp 58–59 °C; ^1H NMR ($CDCl_3$) 1.21 (3 H, t, J = 7.5 Hz, OCH_2CH_3), 2.7–2.9 (4 H, m, C_5 and C_8H), 3–3.2 (2 H, m, C_9H), 3.53 (1 H, m, C_6H), 3.82 (3 H, s, OCH_3), 4.15 (2 H, q, J = 7.5 Hz, OCH_2CH_3), 6.72 (1 H, m, C_3H), 6.79 (1 H, s, C_1H), 7.15 (1 H, m, C_4H); IR (KBr) 1740, 1705, 1615 cm^{-1}; MS, m/e 262 (M^+), 233 ($M - C_2H_5$), 217 ($M - OC_2H_5$), 189 (base peak, $M - CO_2C_2H_5$). Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.41; H, 6.99.

2-Methoxy-5,6,8,9-tetrahydro-7*H*-benzocycloheptene-7-one (IX). A solution of the β-keto ester VIII (10.1 g, 0.039 mol) in 10% sulfuric acid (100 mL) was degassed with argon and refluxed under argon for 10 h. The cooled solution was diluted with water, saturated with NaCl, and extracted with ethyl acetate (6 × 25 mL). The combined extracts were washed with saturated $NaHCO_3$ and brine, dried (Na_2SO_4), and concentrated in vacuo. The crude reaction product was chromatographed on a 500-g silica gel dry column (5 × 50 cm) which was developed with 33% ethyl acetate in Skelly B to afford 6.8 g (92%) of IX as a pale yellow oil: ^1H NMR ($CDCl_3$) δ 2.35–2.68 (4 H, m, Ar CH_2CH_2CO), 2.68–3.01 (4 H, m, Ar CH_2CH_2CO), 3.80 (3 H, s, OCH_3), 6.63–6.88 (1 H, m, C_3H), 6.81 (1 H, s, C_1H), 7.03–7.28 (1 H, m, C_4H): IR (neat) 1708, 1610 cm^{-1}; MS, m/e 190 (base peak, M^+), 162 ($M - CO$), 148 ($M - CO - CH_2$). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.72; H, 7.31.

2-Methoxy-7-cyanodihydro-5*H*-benzocycloheptene (X). The procedure employed for the preparation of the cyanohydrin was a modification of that used by Colonge, Watteau, and Cumet.[8] Solutions of sodium cyanide (1.56 g, 0.032 mol) in 8 mL of water and potassium dihydrogen phosphate (3.6 g, 0.027 mol) in 14 mL water were simultaneously added to a stirred solution, cooled to 10 °C, of the ketone IX (1.0 g, 0.0053 mol) in 35 mL of 95% ethanol. The reaction mixture was maintained at 10–15 °C for 2 h. To the reaction mixture were added concentrated sulfuric acid (5 mL) and enough water to dissolve the precipitated salts. The reaction mixture was saturated with sodium chloride and extracted with ethyl acetate (5 × 30 mL). The combined extracts were dried (Na_2SO_4), and the solvent was removed in vacuo to yield 1.0 g of the unpurified cyanohydrin.

The dehydration was effected by using the procedure of Sarett.[9] The crude cyanohydrin was dissolved in pyridine (30 mL), phosphoryl chloride (7 mL) was added, and the resulting solution was stirred under nitrogen for 12 h. Small pieces of ice were added to the stirred reaction mixture at a rate such that vigorous but controlled reflux was maintained. When cool, the reaction mixture was acidified with 6 N hydrochloric acid and extracted, with benzene (5 × 20 mL). The combined extracts were washed once with 5% HCl, dried (Na_2SO_4), and concentrated in vacuo. The crude olefin mixture was chromatographed on a 100-g silica gel dry column (2.5 × 30 cm) which was developed with 33% ethyl acetate in Skelly B to yield 0.7 g (66%) of the isomeric olefin mixture X: IR (neat) 2222, 1610 cm^{-1}; MS, m/e 199 (base peak, M^+) 184 ($M - CH_3$). Anal. Calcd for $C_{13}H_{13}NO$: C, 78.36; H, 6.58; N, 7.03. Found: C, 78.58; H, 6.64; N, 6.70.

2-Methoxy-7-cyano-6,7,8,9-tetrahydro-5*H*-benzocycloheptene (XI). The olefinic mixture X (0.7 g, 0.0035 mol) was shaken for 24 h under 50 psi of hydrogen in a Paar apparatus with ethyl acetate (10 mL) as the solvent and 10% palladium on carbon (0.1 g) as a catalyst. Filtration, removal of solvent, and chromatography on a 100-g silica gel dry column (2.5 × 30 cm) developed with 33% ethyl acetate in Skelly B afforded 0.6 g of XI: mp 69–75 °C; ^1H NMR ($CDCl_3$) δ 1.72–2.1 (4 H, m, C_6 and C_8H), 2.58–3.13 (5 H, m, C_5, C_7, and C_9H), 3.77 (3 H, s, OCH_3), 6.5–6.77 (1 H, m, C_3H), 6.69 (1 H, s, C_1H), 6.88–7.13 (1 H, m, C_4H); IR ($CHCl_3$) 2245, 1610 cm^{-1}; MS, m/e 201 (base peak, M^+), 186 ($M - CH_3$), 174 ($M - HCN$), 159 ($M - HCN - CH_3$). Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96. Found: C, 77.36; H, 7.57; N, 6.68.

2-Methoxy-6,7,8,9-tetrahydro-5*H*-benzocycloheptene-7-carboxylic Acid (XII). A solution consisting of methoxy nitrile XI (1.4 g, 0.007 mol), sodium hydroxide (0.56 g, 0.014 mol), water (4.5 mL), and ethylene glycol (4.5 mL) was refluxed under argon for 8 h. When cool, the reaction mixture was extracted with dichloromethane (2 × 25 mL, discarded), neutralized with 6 N HCl, saturated with sodium chloride, and extracted with dichloromethane (4 × 25 mL). The extracts of the neutralized reaction mixture were dried (Na_2SO_4) and concentrated in vacuo. The crude reaction product was chromatographed on a 100-g silica gel dry column (2.5 × 30 cm) which was developed with ethyl acetate/Skelly B/acetic acid (33:66:0.7). The product band (R_f 0.33) was recrystallized from ether to afford 1.05 g (68.5%) of XII: mp 136.5–138 °C; ^1H NMR ($CDCl_3$) δ 1.2–2.5 (4 H, m, C_6 and C_8H), 2.5–2.8 (1 H, m, C_7H), 2.78–3.0 (4 H, m, C_5 and C_9H), 3.78 (3 H, s, OCH_3), 6.5–6.8 (1 H, m, C_3H), 6.70 (1 H, s, C_1H), 6.9–7.2 (1 H, m, C_4H), 7.75 (1 H, brs, CO_2H); IR (KBr) 3460, 3020, 2950, 2870, 1690, 1615 cm^{-1}; MS, m/e 220 (base peak, M^+), 205 (M –

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CH_3), 175 (M - CO_2H), 174 (M - CO_2H - H^+). Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.67; H, 7.23.

2-Hydroxy-6,7,8,9-tetrahydro-5*H*-benzocycloheptene-7-carboxylic Acid (XIII). The procedure used was adapted from that of McOmie, Watts, and West.[10] To a stirred solution of methoxy acid XII (1.0 g, 0.0045 mol) in dichloromethane (200 mL) was added a 1.02 M solution of boron tribromide in dichloromethane (10.6 mL, 0.011 mol). The reaction mixture was stirred at 23 °C for 0.5 h in an argon atmosphere and water was added, and when the vigorous reaction had subsided, enough ethyl acetate was added so that the organic phase was less dense than water. The organic phase was separated, washed with water (3 × 20 mL) and once with brine, and dried (Na_2SO_4), and the solvent was removed in vacuo. The crude product was chromatographed on a 100-g silica gel dry column (2.5 × 30 cm) which was developed with ethyl acetate/Skelly B/methanol (33:66:0.7) to yield 0.55 g of XIII: mp 174–175 °C; ^1H NMR (acetone-d_6) δ 1.2–2.0 (4 H, m, C_6 and C_8H), 2.5 (1 H, m, C_7H), 2.6–3.0 (4 H, m, C_5 and C_9H), 6.4–6.7 (1 H, m, C_3H), 6.59 (2 H, brs, OH and CO_2H), 6.64 (1 H, s, C_1H), 6.85–7.05 (1 H, m, C_4H); IR (KBr) 3365, 3100, 2955, 2860, 1715, 1610 cm^{-1}; MS, *m/e* 206 (base peak, M^+), 161 (M - CO_2H), 160 (M - CO_2H - H^+). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.75; H, 6.89.

2-Hydroxy-7-(hydroxymethyl)-6,7,8,9-tetrahydro-5*H*-benzocycloheptene (XIV). A modification of the procedure of Cerny and Malek was used.[11] To a stirred, refluxing solution of phenolic acid XIII (0.24 g, 0.0012 mol) in dry benzene (10 mL) under argon was added dropwise over 1 h a 0.36 M solution of sodium bis(2-methoxyethoxy)aluminum hydride in benzene (Red-Al; 1.34 mL, 0.0036 mol). When the addition was complete, reflux was continued for 2 h, and after the mixture cooled, 9 N sulfuric acid was added until all salts dissolved. The reaction mixture was saturated with sodium chloride and extracted with ethyl acetate (4 × 10 mL). The combined organic phases were washed with sodium bicarbonate and with brine and dried (Na_2SO_4), and the solvent was removed to yield a semisolid which was chromatographed on a silica gel preparative thin-layer plate (2 mm × 20 cm × 20 cm) with 50% ethyl acetate in Skelly B as the eluent to yield 0.12 g (54%) of XIV: mp 138 °C; ^1H NMR (acetone-d_6) 0.7–2.2 (5 H, m, C_6, C_7, and C_8H), 2.6–2.88 (4 H, m, C_5 and C_9H), 3.35 (2 H, d, J = 5.5 Hz, CH_2OH), 3.4 (2 H, brs, OH), 6.38–6.7 (1 H, m, C_3H), 6.6 (1 H, s, C_1H), 6.75–7.05 (1 H, m, C_4H); IR (KBr) 3440, 3040, 2940, 2865, 1612 cm^{-1}; MS, *m/e* 192 (base peak, M^+), 174 (M - H_2O), 160 (M - H_2O - CH_2), 159 (M - H_2O - CH_2 - H^+). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.77; H, 8.30.

Preparation of Potassium *tert*-Butoxide. A 0.011 M solution of potassium *tert*-butoxide in *tert*-butyl alcohol was prepared by heating at reflux under argon a mixture of potassium (0.215 g, 0.0055 mol) and dry *tert*-butyl alcohol (0.5 L) until all the potassium dissolved. The solution was stored in a sealed flask under argon.

6,7,8,9-Tetrahydro-4a,7-methano-4a*H*-benzocyclohepten-2(5*H*)-one (I). The mesylate II was prepared by the procedure of Pazdernik.[12] A solution of the phenolic alcohol XIV (0.1 g, 0.00052 mol) in dry pyridine (2 mL) was cooled in an ice bath under argon; methanesulfonyl chloride was added, and the solution was stirred at 0 °C for 1.5 h. The reaction mixture was poured onto ice, and the aqueous phase was acidified with 6 N HCl, saturated with sodium chloride, and extracted with ethyl acetate (3 × 20 mL). The combined extracts were washed with 5% HCl and brine, dried (Na_2SO_4), and concentrated in vacuo.

The crude mesylate II was cyclized to the tricyclic dienone I as described by Masamune.[2] A solution of the mesylate II in 0.011 M potassium *tert*-butoxide in *tert*-butyl alcohol (52 mL, 0.000 55 mol) was refluxed under argon for 7 h, and the solvent was removed on a rotary evaporator to yield a dark solid. The crude reaction product was triturated with ethyl acetate (4 × 20 mL), and the combined extracts were dried (Na_2SO_4) and concentrated in vacuo to yield a viscous oil which was chromatographed on a preparative silica gel thin-layer plate (0.5 mm × 20 cm × 20 cm) with 33% ethyl acetate in Skelly B as the eluent to yield 0.052 g (57%) of I: ^1H NMR ($CDCl_3$) δ 1.35–2.0 (4 H, m, C_5 and C_8H), 1.75–2.0 (2 H, m, C_8 and methano H), 1.95–2.4 (1 H, m, C_7H), 2.35–2.75 (2 H, m, C_9H), 6.0 (1 H, brs, C_1 H), 6.25 (1 H, dd, J = 9.5, 2 Hz, C_3H), 6.7 (1 H, d, J = 9.5 Hz, C_4H); IR (neat) 1660, 1628, 1605 cm^{-1}; MS, *m/e* 174 (M^+), 146 (M - CH_2=CH_2), 145 (M - CH_2=CH_2 - H^+). Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.72; H, 8.17.

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Reactions of 2,6-Dimethylphenol and 2,6-Dimethylanisole with Electrophilic Allylating Agents[1]

Bernard Miller* and Michael P. McLaughlin

Department of Chemistry, University of Massachusetts, Amherst, Massachusetts 01003

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Electrophilic substitution reactions of phenols and phenyl ethers normally take place exclusively at positions ortho or para to the activating oxygen functions, providing such positions are available for attack. Even in reactions of 2,6-dialkylphenols and 2,6-dialkylphenyl ethers, in which the alkyl groups direct attack to meta positions, most electrophilic substitution reaction,[2] including Friedel–Crafts reactions with *tert*-butyl and isopropyl chloride,[3] have been shown to proceed solely at the para positions.

Friedel–Crafts benzylations are exceptions to this rule.[4] Benzylation of 2,6-dimethylphenol (2,6-DMP) with a variety of benzylating agents, solvents, and catalysts yields ca. 38% of meta-benzylation products, while benzylation of 2,6-dimethylanisole (2,6-DMA) and other 2,6-dialkylphenyl alkyl ethers yields predominately (ca. 70%) meta-substitution products.[4]

Allylation reactions would be expected to closely resemble benzylation reactions, but difficulties can arise due to the reactivity of the double bonds of allylic halides and alcohols. Thus, our attempts to react either 2,6-DMP or 2,6-DMA with allyl alcohol, catalyzed by sulfuric acid, resulted in formation of higher molecular weight products from the allyl alcohol but no reaction with the phenol or anisole. Similar results were obtained by employing either allyl chloride or allyl bromide with anhydrous zinc chloride as the catalyst.

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