8.7 Hz, 2 H), 7.43 (d, J = 8.7 Hz, 2 H), 6.71 (dd, J = 17.5, 10.5 Hz, 1 H), 5.83 (d, J = 17.5 Hz, 1 H), 5.34 (d, J = 10.5 Hz, 1 H), 2.93 (q, J = 7.9 Hz, 2 H), 1.20 (t, J = 7.9 Hz, 3 H). Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.49; H, 7.48.

Pyrolysis of Polyvinylbenzophenone. Polyvinylbenzophenone was prepared from polystyrene and benzoyl chloride by the procedure adopted for polyvinylpropiophenone: yield 97%; IR (KBr) 1658 cm^{-1}. Anal. Calcd for $C_{15}H_{12}O$: C, 86.51; H, 5.81. Found: C, 86.42; H, 5.78.

Polyvinylbenzophenone (5 g) was pyrolyzed in a distillation flask over an open flame for 20 min at 0.1 mm. The viscous yellow liquid obtained (3.8 g) was purified by column chromatography on silica with benzene as eluent, to give a viscous colorless oil (2.8 g), which solidified on standing: mp 50–52 °C; IR (KBr) 1655 cm^{-1} (C=O); ^1H NMR (270 MHz) δ 7.78 (d, J = 8.3 Hz, 4 H), 7.60–7.40 (m, 5 H), 6.76 (dd, J = 17.6, 10.5 Hz, 1 H), 5.88 (d, J = 17.6 Hz, 1 H), 5.39 (d, J = 10.5 Hz, 1 H). Anal. Calcd for $C_{15}H_{12}O$: C, 86.51; H, 5.81. Found: C, 86.58; H, 5.73.

A Simple and Highly Stereoselective Route to (±)-Podocarpic Acid

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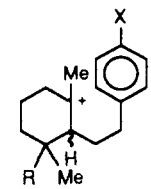
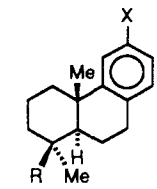
The ring C aromatic resin acids form an important group of naturally occurring diterpenoids, which are broadly classified into two types, viz., abietane and podocarpane differing in the configuration of 4-CO_2H (α in the former and β in the latter in the natural 5α series). Quite a number of syntheses of both the stereoisomeric forms have been reported over the last few decades.[1] Of the various methods, the acid-catalyzed intramolecular cycloalkylation route presents a simple and convergent synthesis of these aromatic resin acids, particularly those related to a podocarpic acid ring system.[2]

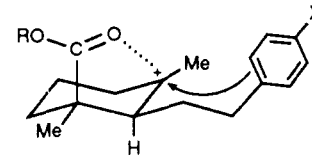
Recent reports[5,6] have shown that by using milder conditions (P_2O_5–$MeSO_3H$), the cycloalkylation reaction of 2-(2-arylethyl)-1,3,3-trimethylcyclohexyl cation **1a** (or its precursors) proceeds with high stereoselectivity, leading almost exclusively to the A/B *trans*-podocarpatriene derivatives **2a**. We have extended this method to the cycloalkylation of cations such as **1b**, leading to a simple and totally stereoselective synthesis of (±)-deoxypodocarpic acid (**2c**)[7] and (±)-*O*-methylpodocarpic acid (**2f**). It may be pointed out that these two compounds, which contain 17 of the 20 carbon atoms of the diterpenes, serve as intermediates for the synthesis of a number of naturally occurring diterpenoids.



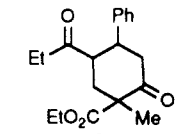
1a: R = Me; X = H or OMe
1b: R = CO_2Et or CO_2Me; X = H or OMe



2a: R = Me; X = H or OMe
2b: R = CO_2Me; X = H
2c: R = CO_2H; X = H
2d: R = CO_2Et; X = H
2e: R = CO_2Me; X = OMe
2f: R = CO_2H; X = OMe
2g: R = CO_2H; X = OH



1c: R = Et or Me; X = H or OMe



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Results and Discussion

The syntheses of both the acids **2c** and **2f** were successfully accomplished according to the sequence depicted in Scheme I. The cyclohexanonecarboxylates **7a** and **7b**, precursors of the cycloalkylation substrates **8a** and **8b**, were prepared in good yields starting with ethyl (or methyl) 2-methyl-3-oxobutyrate, which was condensed with an appropriate aromatic aldehyde in pyrrolidine–acetic acid to the corresponding styryl keto ester **3a** or **3b** in addition to some high boiling products, which were not investigated further. Robinson annulation reaction of **3a** and **3b** afforded[8] the styrylcyclohexenone carboxylates **5a** and **5b**, which on catalytic hydrogenation yielded the cyclohexanones **7a** and **7b**, respectively, in quantitative yield. Sodium borohydride reduction of **7a** and **7b** gave a mixture of the respective cyclohexanols and δ-lactones (**8a** and **9a** in the case of **7a**, **8b** and **9b** with **7b**). Subsequent cyclization of the individual mixture with P_2O_5–$MeSO_3H$ (1:10) yielded ethyl (±)-deoxypodocarpate (**2d**) and methyl (±)-*O*-methylpodocarpate (**2e**), as appropriate, in 40–42% overall yield, apart from the recovered δ-lactones **9a** and **9b** (54–55%). The esters **2d** and **2e** on alkaline hydrolysis generated the corresponding acids (±)-deoxypodocarpic acid (**2c**) and (±)-*O*-methylpodocarpic acid (**2f**). Although the δ-lactones **9a** and **9b** were inert to P_2O_5–$MeSO_3H$ treatment, they underwent smooth cyclization with Haworth's reagent [H_2SO_4/AcOH (1:9)] to furnish the acids **2c** and **2f** in 28% and 33% yields, respectively. The acid **2c** on treatment with ethereal diazomethane gave methyl (±)-deoxypodocarpate (**2b**).

The high stereoselectivity observed in the cyclization of **8a** and **8b** with P_2O_5–$MeSO_3H$, leading only to the respective trans esters **2d** and **2e** with the axial carboalkoxy function, clearly reveals that the reaction proceeds exclusively through the carbonyl-participating carbocation **1c** as suggested by Ghatak et al.[4c]

As the conversion of (±)-*O*-methylpodocarpic acid (**2f**) to (±)-podocarpic acid (**2g**) has already been reported,[3b] the present work constitutes a formal total synthesis of (±)-podocarpic acid (**2g**).

(1) Ghatak, U. R. *J. Indian Chem. Soc.* **1988**, *65*, 9 and references cited therein.

(2) Acid-catalyzed cyclization using H_2SO_4–AcOH is reported[3] to give poor yield in this system, whereas use of polyphosphoric acid affords a stereoisomeric mixture of A/B *trans*- and A/B *cis*-podocarpic acids.[4]

(3) (a) Haworth, R. D.; Barker, R. L. *J. Chem. Soc.* **1939**, 1299. (b) Haworth, R. D.; Moore, B. P. *Ibid.* **1946**, 633. (c) Bhattacharyya, B. K. *J. Indian Chem. Soc.* **1945**, *22*, 165. (d) Fringuelli, F.; Manicini, V.; Taticchi, A. *Tetrahedron* **1969**, *25*, 4249.

(4) (a) King, F. E.; King, T. J.; Topliss, J. G. *Chem. Ind.* **1956**, 113. (b) Nasipuri, D.; De Dalal, I. *J. Chem. Soc., Perkin Trans. I* **1975**, 2052. (c) Ghatak, U. R.; Chatterjee, N. R.; Sanyal, B. *J. Org. Chem.* **1979**, *44*, 1992 and references cited therein.

(5) Axon, B. W.; Davis, B. R.; Woodgate, P. D. *J. Chem. Soc., Perkin Trans. I* **1981**, 2956.

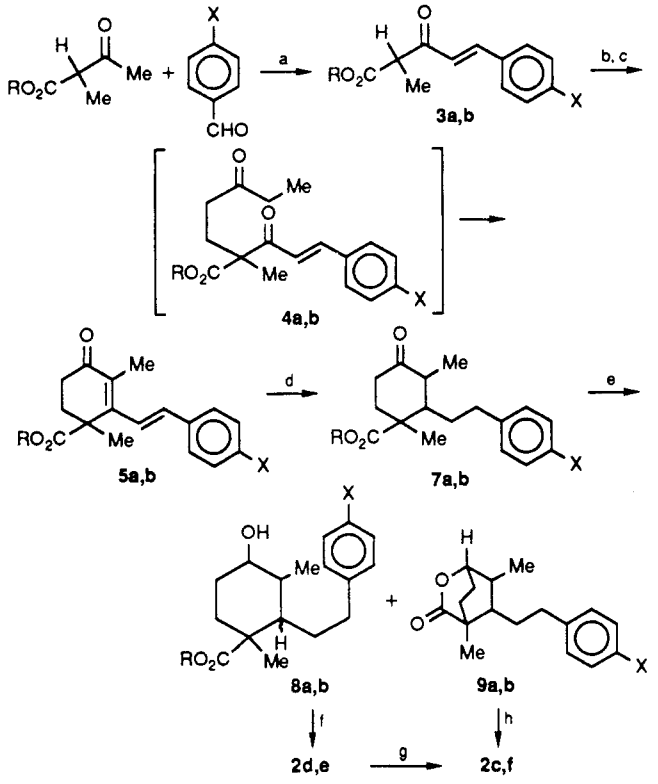
(6) Banik, B. K.; Ghosh, S.; Ghatak, U. R. *Tetrahedron* **1988**, *44*, 6947.

(7) For a preliminary account see: Nasipuri, D.; Banerjee, A. K.; Pakrashi, S. C. *Indian J. Chem.* **1988**, *27B*, 875.

(8) In the case of styryl keto ester **3a** minor side product **6** was also obtained, presumably through a second intramolecular Michael reaction of the intermediate **4a**. No such product was, however, isolated in the reaction with *p*-methoxystyryl keto ester **3b**, presumably due to the relatively poor Michael acceptor character of the styryl double bond in **4b**.

0022-3263/90/1955-3952$02.50/0

Scheme I[a]



[a] R = Et, X = H for **a**; R = Me, X = OMe for **b**. Reagents and conditions: (a) pyrrolidine–acetic acid, Δ; (b) $EtCOCH_2CH_2N^+(Et)_2MeI^-$; (c) NaOEt or NaOMe; (d) H_2–Pd/C; (e) $NaBH_4$; (f) P_2O_5–$MeSO_3H$ (1:10); (g) KOH/diethylene glycol, Δ; (h) H_2SO_4–AcOH (1:9), Δ.

Experimental Section

All melting points, determined in a sulfuric acid bath using open capillaries, and boiling points are uncorrected. IR spectra were recorded on a Perkin-Elmer 177 instrument. ^1H NMR spectra were taken in a JEOL FX-100 instrument using TMS as internal standard and the mass spectra (EI) obtained on a Hitachi RMU-6L instrument. Light petroleum ether refers to the fraction of bp 60–80 °C. Anhydrous sodium sulfate was used as drying agent. The homogeneity of the final products were routinely checked by TLC in different solvent systems.

The acids **2c** and **2f** and the esters **2b** and **2e** have been characterized by comparison (mixture mps, IR and ^1H NMR spectra) with authentic samples.

Ethyl 2-Methyl-3-oxo-5-phenylpent-4-enoate (3a). A solution of ethyl 2-methyl-3-oxobutyrate (20.0 g, 0.14 mol) and benzaldehyde (20.0 g, 0.19 mol) in a mixture of ethanol (90 mL), water (10 mL), pyrrolidine (8.7 mL), and glacial acetic acid (7.9 mL) was refluxed under nitrogen for 20 h. The solvents were removed under reduced pressure and the residue was taken up in ether. The ethereal solution was washed successively with sodium bicarbonate solution (5%), hydrochloric acid (5%), and water and dried. Distillation afforded the unsaturated keto ester **3a** (20.5 g, 64%) as a light yellow oil: bp 150–152 °C/0.05 mm; IR (neat) 1735, 1690 cm^{-1}; ^1H NMR δ 7.68 (d, 1 H, J = 16 Hz, 5-H), 6.86 (d, 1 H, J = 16 Hz, 4-H), 7.24–7.74 (m, 5 H, Ar-H), 4.22 (q, 2 H, J = 7 Hz, OCH_2), 3.85 (q, 1 H, J = 7 Hz, 2-H), 1.45 (d, 3 H, J = 7 Hz, 2-CH_3), 1.26 (t, 3 H, J = 7 Hz, OCH_2CH_3). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.48; H, 7.15.

Methyl 5-(4-Methoxyphenyl)-2-methyl-3-oxopent-4-enoate (3b). It was prepared under the same reaction conditions described above for **3a**, taking methyl 2-methyl-3-oxobutyrate (10 g, 0.077 mol) and 4-methoxybenzaldehyde (15 g, 0.11 mol) in a mixture of methanol (45 mL), water (5 mL), pyrrolidine (4.5 mL), and glacial acetic acid (4 mL) as solvent. Reaction time was 24 h. Yield: 11.5 g (61%). **3b**: bp 190–195 °C/0.01 mm; IR (neat) 1735, 1685 cm^{-1}; ^1H NMR δ 7.65 (d, 1 H, J = 16 Hz, 5-H), 7.33 and 6.91 (m, 4 H, AA'BB', Ar-H), 6.73 (d, 1 H, J = 16 Hz, 4-H), 3.80–3.96 (m, 1 H, 2-H), 3.84 (s, 3 H, Ar-OCH_3), 3.73 (s, 3 H, CO_2CH_3), 1.44 (d, 3 H, J = 7 Hz, 2-CH_3). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.83; H, 6.38.

2,4-Dimethyl-4-(ethoxycarbonyl)-3-(2-phenylethenyl)-cyclohex-2-en-1-one (5a) and 2-(Ethoxycarbonyl)-2-methyl-5-phenyl-4-propionylcyclohexan-1-one (6). To an ice-cold solution of sodium (0.5 g, 0.022 g atom) in dry ethanol (30 mL), was added the styryl keto ester **3a** (5.0 g, 0.02 mol) in ethanol (20 mL) under nitrogen. The reaction mixture was stirred at room temperature for 30 min and then again cooled in an ice-bath. A solution of the methiodide prepared from 1-(diethylamino)pentan-3-one (3.4 g, 0.02 mol) and methyl iodide (3.1 g, 0.02 mol) in dry ethanol (15 mL) was then added during 15 min and stirring continued for another 2 h in the cold. A yellow semisolid mass was formed to which a fresh solution of sodium ethoxide prepared from sodium (0.5 g) and ethanol (30 mL) was added, and the mixture was refluxed for 2 h under nitrogen. The reaction mixture was treated with sulfuric acid (0.1 N) and crushed ice and extracted with ether (400 mL). The ethereal extract was washed with brine and dried and the solvent was distilled off. The residue, a reddish yellow oil, was chromatographed over silica gel (100–200 mesh). Elution with light petroleum ether–ethyl acetate (17:3) afforded **5a** (3.43 g, 54%) as a pale yellow liquid: bp 175–178 °C/0.005 mm; IR (neat) 1730, 1670 cm^{-1}; ^1H NMR δ 7.20–7.60 (m, 5 H, Ar-H), 6.96 and 6.67 (dd, 2 H, J = 16 Hz, vinylic H), 4.19 (q, 2 H, J = 7 Hz, OCH_2-), 2.00 (s, 3 H, 2-CH_3), 1.54 (s, 3 H, 4-CH_3), 1.18 (t, 3 H, J = 7 Hz, OCH_2CH_3). Anal. Calcd for $C_{19}H_{22}O_3$: C, 76.48; H, 7.43. Found: C, 76.59; H, 7.56.

Further elution with the same solvent mixture (17:3 to 4:1) gave the side product **6** (0.5 g, 7%) as a colorless crystalline solid: mp 143–144 °C; IR (Nujol) 1730, 1710 cm^{-1}; ^1H NMR δ 7.08–7.60 (m, 5 H, Ar-H), 4.22 (q, 2 H, J = 7 Hz, OCH_2-), 1.52 (s, 3 H, 2-CH_3), 1.28 (t, 3 H, J = 7 Hz, OCH_2CH_3), 0.80 (t, 3 H, J = 7 Hz, $COCH_2CH_3$); MS, m/z (relative intensity) 316 (M^+, 2), 145 (83), 131 (98), 117 (97), 91 (100). Anal. Calcd for $C_{19}H_{24}O_4$: C, 72.12; H, 7.65. Found: C, 72.28; H, 7.85.

2,4-Dimethyl-4-(methoxycarbonyl)-3-[2-(4-methoxyphenyl)ethenyl]cyclohex-2-en-1-one (5b). This was obtained from **3b** in 54% yield under the same reaction conditions as above but using sodium methoxide and methanol: bp 195–200 °C/0.005 mm; IR (neat) 1725, 1660 cm^{-1}; ^1H NMR δ 7.39 and 6.90 (m, 4 H, AA'BB', Ar-H), 6.86 and 6.62 (dd, 2 H, J = 16 Hz, vinylic H), 3.81 (s, 3 H, Ar-OCH_3), 3.68 (s, 3 H, CO_2CH_3), 2.00 (s, 3 H, 2-CH_3), 1.58 (s, 3 H, 4-CH_3). Anal. Calcd for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.69; H, 7.23.

2,4-Dimethyl-4-(ethoxycarbonyl)-3-(2-phenylethyl)cyclohexan-1-one (7a). The unsaturated keto ester **5a** (1 g, 3.3 mmol) was mixed with palladium–charcoal (10%; 150 mg) in dry ethanol (100 mL) and hydrogenated by being stirred in a hydrogen atmosphere when 1.73 mol of hydrogen was consumed within 4 h. The catalyst was filtered off and the product after usual workup furnished **7a** (0.99 g, 97%) as an oil: bp 130–140 °C/0.01 mm; IR (neat) 1730, 1710 cm^{-1}; ^1H NMR δ 1.00–1.46 (m, 9 H), 1.52–3.12 (m, 10 H), 4.00–4.20 (m, 2 H), 7.00–7.48 (m, 5 H). Anal. Calcd for $C_{19}H_{26}O_3$ C, 75.46; H, 8.67. Found: C, 75.59; H, 8.52.

2,4-Dimethyl-4-(methoxycarbonyl)-3-[2-(4-methoxyphenyl)ethyl]cyclohexan-1-one (7b). Compound **7b** was prepared by the above procedure from **5b** as an oil in 98% yield: bp 205–210 °C/0.04 mm; IR (neat) 1725, 1710 cm^{-1}; ^1H NMR δ 6.72–7.24 (m, 4 H, Ar-H), 3.77 (s, 3 H, Ar-OCH_3), 3.69 (s, 3 H, CO_2CH_3), 1.22 (s, 3 H, 4-CH_3), 1.04–3.08 (m, 13 H). Anal. Calcd for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.80; H, 8.14.

Ethyl (±)-Deoxypodocarpate (2d) and δ-Lactone 9a. A solution of the saturated keto ester **7a** (0.3 g, 1 mmol) in dry ethanol (15 mL) was added dropwise to a stirred ice-cold solution of sodium borohydride (75 mg, 2 mmol) in dry ethanol (10 mL) during 20 min. The reaction mixture was stirred for 2 h in the cold and 10 h at room temperature. The product was decomposed with crushed ice and extracted with dichloromethane. On removal of the solvent, a colorless oil (0.29 g) was obtained, which proved to be a mixture of **8a** and **9a**: IR (neat) 3490 (OH), 1750 (lactone), and 1720 (ester) cm^{-1}. The mixture (0.26 g) was treated without separation with a solution of phosphorus pentoxide in methanesulfonic acid (1:10, 5 g) in the cold (5–10 °C) with stirring. A red color developed immediately. The stirring was continued

for a further 30 min in the cold and 1 h at room temperature. Usual workup gave a light yellow oil, which was chromatographed over silica gel (100–200 mesh). Elution with light petroleum ether–ethyl acetate (97:3) afforded **2d** (110 mg; 42%) as a colorless oil: IR (neat) 1720, 760, 730 cm^{-1}; ^1H NMR δ 7.00–7.40 (m, 4 H, Ar-H), 4.14 (q, 2 H, J = 7 Hz, $CO_2CH_2CH_3$), 1.28 (t, 3 H, J = 7 Hz, $CO_2CH_2CH_3$), 1.28 (s, 3 H, 4-CH_3), 1.06 (s, 3 H, 10-CH_3). Anal. Calcd for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.75, H, 8.92.

Further elution with the same solvent mixture (9:1) furnished unreacted lactone **9a** (130 mg, 54%) as a colorless oil: IR (neat) 1750 cm^{-1}; ^1H NMR δ 7.02–7.48 (m, 5 H, Ar-H), 4.36–4.60 (m, 1 H, OCH-), 1.16 (s, 3 H, CH_3), 1.11 (d, 3 H, J = 6.5 Hz, CH_3). Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 78.82; H, 8.69.

Methyl (±)-*O*-Methylpodocarpate (2e) and δ-Lactone 9b. Similarly, the saturated keto ester **7b** (0.5 g) on sodium borohydride reduction in methanol yielded the mixture of cyclohexanol carboxylate **8b** and δ-lactone **9b** as a colorless oil (0.495 g): IR (neat) 3490, 1750, and 1720 cm^{-1}. The mixture (0.49 g) was treated with P_2O_5–$MeSO_3H$ (1:10, 7 g) under the same reaction conditions as above. After usual workup, the product was chromatographed over silica gel (100–200 mesh). Elution with light petroleum ether–ethyl acetate (9:1) yielded **2e** (0.192 g, 40%) as a white solid: mp 138–139 °C (lit.[9] mp 136–138 °C); IR (Nujol) 1720 and 1615 cm^{-1}; ^1H NMR δ 6.98 (dd, 1 H, J = 8 and 1 Hz, 14-H), 6.82 (d, 1 H, J = 7 Hz, 11-H), 6.67 (dd, 1 H, J = 8 and 2 Hz, 13-H), 3.76 (s, 3 H, Ar-OCH_3), 3.65 (s, 3 H, CO_2CH_3), 1.32–2.48 (m, 9 H), 1.26 (s, 3 H, 4-CH_3), and 1.03 (s, 3 H, 10-CH_3); MS, m/z (relative intensity) 302 (M^+, 93), 287 (6), 229 (32), 228 (100), 173 (29), 147 (34), 121 (36), 91 (20). Anal. Calcd for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.57; H, 8.51.

Further elution of the column with the same solvent mixture (3:1) furnished the lactone **9b** (0.25 g, 55%) as a colorless oil, which solidified on scratching: mp 80–82 °C; IR (Nujol) 1745, 1615 cm^{-1}; ^1H NMR δ 7.09 and 6.79 (m, AA'BB', 4 H, Ar-H), 4.42 (m, 1 H, OCH-), 3.76 (s, 3 H, Ar-OCH_3), 1.14 (s, 3 H, CCH_3) and 1.09 (d, 3 H, J = 7 Hz, $CHCH_3$). Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.91; H, 8.48.

(±)-Deoxypodocarpic Acid (2c) and Methyl (±)-Deoxypodocarpate (2b). (±)-Ethyl deoxypodocarpate (**2d**) (0.5 g, 1.7 mmol) and potassium hydroxide (1.0 g) in diethylene glycol (90%; 25 mL) was refluxed for 20 h under nitrogen. The reaction mixture was diluted with water and extracted with ether (4 × 50 mL). The ether layer was washed with brine and dried. After removal of the solvent a light yellow oil (0.415 g) was obtained, which was characterized as the starting material **2d**.

The basic aqueous solution was acidified with sulfuric acid (2 N) and extracted with ether (4 × 50 mL). The ethereal solution treated as above furnished a light yellow solid, which on crystallization from methanol–water afforded white crystals of **2c** (70 mg, 91% on the basis of recovered starting material): mp 234–235 °C (lit.[3a] mp 232–233 °C); IR (KBr) 1705 cm^{-1}. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 78.88; H, 8.62.

The above acid **2c** (50 mg) was esterified with an excess of ethereal diazomethane to afford **2b** (47 mg) as white crystals: mp 134–135 °C (lit.[10] mp 131–132 °C); IR (KBr) 1720, 770, 735 cm^{-1}; ^1H NMR δ 7.00–7.40 (m, 5 H, Ar-H), 3.64 (s, 3 H, CO_2CH_3), 1.26 (s, 3 H, 4-CH_3), and 1.03 (s, 3 H, 10-CH_3); MS, m/z (relative intensity) 272 (M^+, 36), 257 (67), 197 (100), 141 (38), 91 (12). Anal. Calcd for $C_{18}H_{24}O_2$: C, 79.37; H, 8.88. Found: C, 79.33; H, 8.95.

(±)-*O*-Methylpodocarpic Acid (2f). Methyl (±)-*O*-methylpodocarpate (**2e**) (0.1 g, 0.33 mmol) on hydrolysis furnished **2f** (52 mg, 91% on the basis of recovered starting material) as white crystals: mp 193–194 °C (lit.[9] mp 194–195 °C); IR (KBr) 1705, 1610 cm^{-1}. Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.92; H, 8.44.

Cyclization of δ-Lactone 9a to (±)-Deoxypodocarpic Acid (2c). The δ-lactone (0.5 g, 2 mmol) was mixed with glacial acetic acid (9 mL) and concentrated sulfuric acid (1 mL), and the solution was gently refluxed for 10 h under nitrogen. The dark brown solution obtained was poured into crushed ice and extracted with ethyl acetate (4 × 50 mL). The combined ethyl acetate extract was washed thoroughly with potassium hydroxide solution (2%, 100 mL). The aqueous alkaline solution was acidified with dilute hydrochloric acid and extracted with ethyl acetate (400 mL). Usual workup gave a light brown solid, which on treatment with Norite in methanol furnished white microcrystals of **2c** (142 mg, 28%).

Cyclization of δ-Lactone 9b to (±)-*O*-Methylpodocarpic Acid (2f). The δ-lactone (0.24 g, 0.83 mmol) on similar cyclization as above furnished **2f** (80 mg, 33%) as white crystals.

Acknowledgment. We are indebted to Prof. U. R. Ghatak, Indian Association for the Cultivation of Science, Calcutta-700032, for providing authentic specimens of compounds **2b**, **2c**, **2e**, and **2f** and for stimulating discussion.

Registry No. (±)-**2b**, 16957-27-0; (±)-**2c**, 5708-75-8; (±)-**2d**, 122571-56-6; (±)-**2e**, 41437-72-3; (±)-**2f**, 80408-73-7; (±)-**3a**, 122571-50-0; (±)-**3b**, 126753-78-4; (±)-**5a**, 122571-53-3; (±)-**5b**, 126753-79-5; **6**, 122571-52-2; **7a**, 122571-57-7; **7b**, 126753-80-8; **8a**, 122571-55-5; **8b**, 126753-81-9; **9a**, 122571-54-4; **9b**, 126753-82-0; (±)-$EtO_2CCHMeCOMe$, 64854-05-3; (±)-$MeO_2CCHMeCOMe$, 59057-05-5; PhCHO, 100-52-7; 4-$MeOC_6H_4CHO$, 123-11-5; $EtCO(CH_2)_2N^+Et_2MeI^-$, 52103-30-7.

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A Stereoselective Synthesis of *d,l*-16-Oxa-15α-methyl-19-nortestosterone

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Recently we reported that stereoselective copper-catalyzed vinylation[1] of **1** followed by trapping the regiospecifically generated enolate with formaldehyde gas afforded an excellent yield of alcohol **2**, which contains the prerequisite functionality for further elaboration of the transfused C,D ring system[2] in steroids. Of particular interest to us was the utilization of **2** in the construction of various 16-substituted testosterone derivatives[3] for biological evaluation. We report herein a facile synthesis of the 16-oxa analogue **13** as delinated below.

Reaction of alcohol **2**[4] (Scheme I) with methanesulfonyl chloride in the presence of triethylamine gave a 97% yield of mesylate **3**. Subsequent treatment of **3** with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in benzene afforded the exocyclic methylene **4** (90%). The resonance signals at δ 6.04 and 5.19 are consistent with an intact exocyclic methylene.

Construction of the potential A and B ring systems in **13** was in turn realized by Michael addition of ethyl 7,7-(ethylenedioxy)-3-oxooctanoate (**5**)[5] to **4** (Scheme II). Thus reaction of **5** with **4** in the presence of 0.1 N sodium methoxide in methanol at 0 °C and subsequent acidifica-

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