Accessible Route to 4-Substituted "Bird-Cage" Hydrocarbon Derivatives

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Advances in the chemistry of the pentacycloundecane series of hydrocarbons ($C_{11}H_{14}$)[1,2] are partially due to the facile synthesis of starting materials such as pentacyclo-[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione[3] (**1c**) with two conveniently oriented functional groups. The carbonyl groups are suitable for the introduction of substituents into the molecular framework and for rearrangement of the carbon skeleton itself.[4,5] We have investigated the Knoevenagel reaction of pentacycloundecane ketones with isopropylidenemalonate (Meldrum's acid) as a means of preparing new derivatives of the pentacycloundecanes and their skeletal isomers. The preparation of derivatives with Meldrum's acid and their subsequent chemical rearrangements have been reported previously;[6–8] however, their use in expanding the synthetic possibilities in the chemistry of polyhedral molecules has not been exploited.

Discussion

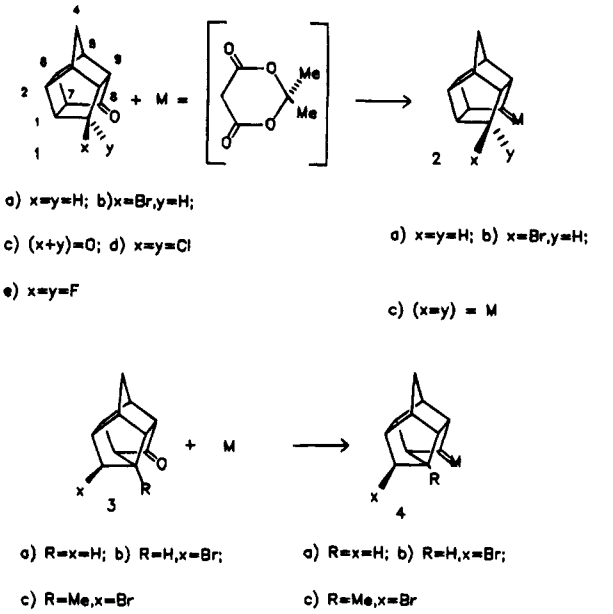
The keto derivatives of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]-undecane (**1a–c**) and of pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]-undecane (**3a–c**) readily form condensation products with Meldrum's acid in pyridine solution (see Scheme 1). The formation of **2a–c** and **4a–c** can be followed by the appearance of the C=C band (1610–1645 cm^{-1}) and the C=O bands (Meldrum's acid moiety, 1725–1750 cm^{-1}) in the IR spectra. In the ^{1}H NMR spectra of **1a–e** no cage proton appears downfield from 3.5 ppm, but in **2a** the two newly formed allylic protons appear at 3.97 and 4.16 ppm and at 3.97 and 4.12 ppm in **2b**. In the more-symmetric compound **2c** the allylic protons are shifted to lower field appearing at 4.57 and 4.69 ppm. In compound **4a** the two allylic protons are chemically equivalent and the protons absorb at 3.56 ppm while in **4b** they occur at 3.72 ppm and at 3.53 and 3.73 ppm in **4c**. The dichloro and difluoro compounds **1d** and **1e** do not react with Meldrum's acid.

The formation of compound **2b** is unexpected since the reaction of **1b** with the sodium salt of malonic ester leads to transannular cyclization and the formation of 12-oxahexacyclo[7.2.1.0^{2,8}.0^{3,7}.0^{4,11}.0^{6,10}]dodecane.[9] The reaction of Meldrum's acid with **1a–c** was run in pyridine for 5 days at room temperature (see Experimental Section), and monitoring during this period indicated only starting material and **2b** with the ratio changing as a function of time. Malonic ester under the same conditions did not react. This excludes the possibility of the formation of a 12-oxahexacyclododecane type intermediate. The pathway involving the formation of the alkoxyanion after attack on the C=O group and the subsequent displacement of the bromine atom does not occur in this system. The acidity of the Meldrum's acid may be sufficient to neutralize the alkoxyanion.

The products from the reaction of **2a–c** and **4a–c** with sodium borohydride depends upon the nature of the starting product. For compounds **2a–c** the hydride ion first attacks the β-carbon of the double bond (relative to the alkoxycarbonyl fragment) from the exo direction. This is confirmed by the multiplicity of the NMR signal of this proton in compound **5** which occurs at 1.92 ppm (dt). The observed 3-Hz coupling constant is consistent with the 3-5 Hz constant observed for exo protons in these systems compared to less than 1-Hz constant for endo proton couplings.[9] Only the simple reduction product is recovered from the reaction of **2a**. Compound **5** is also obtained when **2a** is reduced with $LiAlH_4$ in THF. The reduction of **4a** gives the only possible product **6** (monosubstituted D_3-trishomocubane) while reduction of **4b** gives **7a** and **7b** in equal amounts implying no stereospecificity for hydride attack on the double bond. The stereochemistry of the bromine atom at carbon 4 is fixed and the two epimers were separated by column chromatography with the stereochemistry 4*S*,7*R* assigned to **7a** and 4*S*,7*S* to **7b**.[10–12]

The anion formed from the hydride addition to **2b** immediately displaces the bromide ion giving compound

Scheme 1



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(1) Marchand, A. P. *Chem. Rev.* **1989**, *89*, 1011–1033.
(2) Marchand, A. P. In *Advances in Theoretically Interesting Molecules*; Thummel, R. P., Ed.; JAI: Greenwich, CT, 1989; Vol. 1, pp 357–399.
(3) Cookson, R. C.; Crundwell, E.; Hill, R. R.; Hudec, J. *J. Chem. Soc.* **1964**, 3062–3075.
(4) Mehta, G.; Srikrishna, A.; Reddy, A. V.; Nair, M. S. *Tetrahedron* **1981**, *37*, 4543–4559.
(5) Chapman, N. B.; Key, J. M.; Toyne, K. J. *J. Org. Chem.* **1970**, *35*, 3860–3867.
(6) Scharp, J.; Wiersum, U. E. *J. Chem. Soc. Chem. Commun.* **1983**, 629–630.
(7) Brown, R. F. C.; Browne, N. R.; Coulston, K. J.; Danen, L. B.; Eastwood, F. W.; Irvine, M. J.; Pullin, D. E. *Tetrahedron Lett.* **1986**, *27*, 1075–1078.
(8) Aleksandrov, A. M.; Sorochinskii, A. E.; Krasnoshchek, A. P. *Zh. Org. Khim.* **1979**, *15*, 336–342 (*Chem. Abstr.* **1979**, *91*, 56443t).
(9) Aleksandrov, A. M.; Kashyap, R. P.; Pehk, R. J.; Petrenko, A. E.; Watson, W. H. *J. Org. Chem.* **1993**, *58*, 1831–1834.
(10) Dekker, T. G.; Oliver, D. W.; Pachler, K. G. R.; Wessels, P. L.; Woundenberg, M. *Org. Mag. Reson.* **1981**, *15*, 188–192.
(11) Oliver, D. W.; Dekker, T. G.; *South Afr. J. Sci.* **1988**, *84*, 407–409.
(12) Nakazaki, M.; Naemura, K.; Arashiba, N. *J. Org. Chem.* **1978**, *43*, 689–692.

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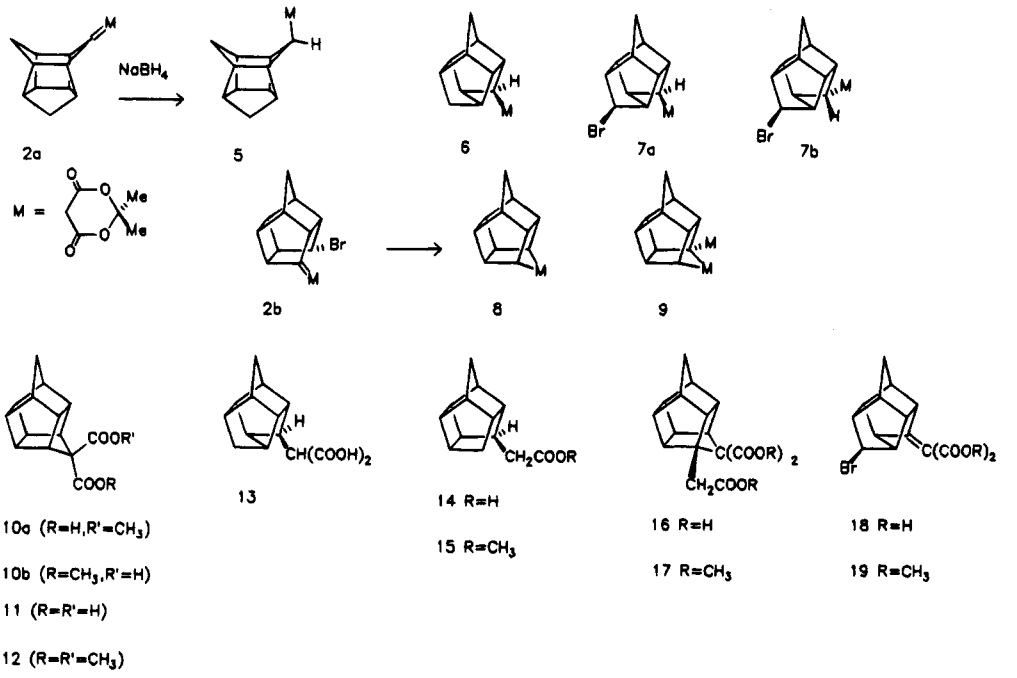
Scheme 2



8 while the anion from **2c** attacks the double bond of the adjacent Meldrum's acid adduct to form **9**. Both compounds are derivatives of the "bird-cage" hydrocarbon hexacyclo[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]dodecane.[13,14]

Although "bird-cage" compound **8** was synthesized easily from **1b**, to be synthetically more useful the 1,3-dioxane ring must be cleaved. When **8** was treated with alkaline methanol, only compounds **10a** and **10b** were recovered. The saponification of **5** with KOH in methanol was unsatisfactory. When compound **8** was boiled in a mixture of HCl and acetic acid for 2.5 h, the diacid **11** was produced. Reaction of **11** with diazomethane in ether yielded the diester **12**. The same diester is produced by the reaction of diazomethane with compounds **10a** and **10b**. The analogous acid hydrolysis with **6** and **5** produced the substituted malonic acid **13** and the decarboxylated monoacid **14**. Treatment of **14** with diazomethane gave ester **15**. Acid hydrolysis of **9** gave the triacid **16** which was converted to the triester **17** for easier purification and characterization. Acid hydrolysis of **4b** yielded the diacid **18** which gave the ester **19** upon reaction with diazomethane. The diacid, monoacid and ester derivatives of the "bird-cage" hydrocarbon hexacyclo-[5.4.1.$0^{2,6}$.$0^{3,10}$.$0^{5,9}$.$0^{8,11}$]dodecane are suitable precursors for the further elaboration of this cage system. We anticipate the use of **14** in the preparation of compounds with stereospecific substitution at C(8), and the preparation of heterocyclic compound from **11** and **12**.

Experimental Section

All ^{1}H and ^{13}C NMR spectra were recorded on 200-MHz or 500-MHz instruments using TMS as reference in $CDCl_3$. IR spectra were recorded in methylene chloride, and all chromatography was performed on silica gel columns. Melting points are uncorrected.

General Procedure for the Reaction of Compound 1a–c and 3a–c with Isopropylidene Malonate (Meldrum's acid). To 0.020 mol of the carbonyl compound in 20 mL of pyridine was added 0.024 mol of isopropylidene malonate. In the case of the diketone **1c** to 0.020 mol of the diketone in 40 mL pyridine was added 0.04 mol of Meldrum's acid. Several times during the first hour the mixture was agitated to dissolve the acid, and then the mixture was left standing for 5 days (**1a–c**) or 10 days (**3a–c**). Then the reaction mixture was poured into water (200 mL) and the precipitated compounds were recovered by filtration.

2a: **1a** (3.20 g, 20 mmol) was treated with 3.46 g (24 mmol) of isopropylidene malonate, yield 4.64 g (81%), mp 157–158 °C (from aqueous acetone); ^{1}H NMR δ 1.17 and 1.26 (AB dd, J_{AB} = 10.5 Hz), 1.46 and 1.85 (AB dd, J_{AB} = 11.0 Hz), 1.65 (s), 1.66 (s), 2.45 (m, 2H), 2.61 (m, 1H), 2.74 (m, 1H), 2.90 (m, 1H), 3.11 (m, 1H), 3.97 (m, 1H), 4.16 (m, 1H); ^{13}C NMR δ 26.7, 27.3, 30.5, 36.5, 39.4, 42.5, 42.6, 43.8, 47.1, 47.5, 50.2, 50.4, 103.5, 111.2, 160.6, 160.8, 194.1; IR (cm^{-1}) 1610, 1730. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.24; H, 6.34.

2b: **1b** (4.78 g, 20 mmol) was treated with 3.46 g (24 mmol) of isopropylidene malonate, yield 6.13 g (84%), mp 178–179 °C (from acetone); ^{1}H NMR δ 1.63 and 1.95 (AB dd, J_{AB} = 11.6 Hz), 1.71 (s), 1.74 (s), 2.69 (m, 2H), 2.99–3.13 (m, 2H), 3.20–3.35 (m, 2H), 3.97 (s, 1H), 4.12 (m, 1H), 4.30 (m, 1H); IR 1612, 1730. Anal. Calcd for $C_{17}H_{17}BrO_4$: C, 55.90; H, 4.69; Br, 21.88. Found: C, 56.03; H, 4.72; Br, 21.98.

2c: **1c** (3.48 g, 20 mmol) was treated with 5.76 g (40 mmol) of isopropylidene malonate, yield 7.76 g (91%), decomposition and darkening without melting at 225 °C; ^{1}H NMR δ 1.63 (s, 6H), 1.68 (s, 6H), 1.83 and 2.15 (AB dd, J_{AB} = 11.4 Hz), 2.84 (br s, 2H), 2.97 (br s, 2H), 4.57 (br s, 2H), 4.69 (br s, 2H); IR (cm^{-1}) 1635, 1750. Anal. Calcd for $C_{23}H_{22}O_8$: C, 64.78; H, 5.20. Found: C, 64.52; H, 51.7.

4a: **3a** (3.20 g, 20 mmol) was treated with 3.46 g (24 mmol) of isopropylidene malonate, yield 4.47 g (78%), mp 175.5–176.5 °C (from aqueous acetone); ^{1}H NMR δ 1.52 and 1.63 (AB dd, J_{AB} = 10.8 Hz), 1.74 (s, 6H), 2.36 (br.s, 6H), 3.56 (br.s, 2H); IR (cm^{-1}) 1625, 1640, 1730, 1770. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.28; H, 6.35.

4b: **3b** (4.78 g, 20 mmol) was reacted with 3.46 g (24 mmol) of isopropylidene malonate, yield 4.97 g (68%), mp 159–160 °C (from methanol); ^{1}H NMR δ 1.65 (br s, 2H), 1.74 (s, 6H), 2.46 (m, 1H), 2.53 (m, 2H), 2.60 (m, 2H), 3.15 (m, 1H), 3.72 (m, 2H), 4.16 (br s, 1H); IR (cm^{-1}): 1635, 1725. Anal. Calcd for $C_{17}H_{17}BrO_4$: C, 55.90; H, 4.69; Br, 21.88. Found: C, 55.92; H, 4.71; Br, 21.75.

4c: **3c** (5.06 g, 20 mmol) was treated with 3.46 g (24 mmol) of isopropylidene malonate, yield 5.54 g (73%), mp 186–187 °C (from methanol); ^{1}H NMR δ 1.06 (s), 1.64 (br s, 2 H), 1.74 (s), 1.77 (s), 2.12 (t, J = 5.9 Hz, 1H), 2.52 (m, 3H), 3.17 (m, 1H), 3.53 (m, 1H), 3.73 (m, 1H), 4.05 (s, 1H); IR (cm^{-1}) 1643, 1735. Anal.

(13) Marchand, A. P.; Rajapaksa, D. *Tetrahedron Lett.* **1993**, *34*, 1463–1466.
(14) Marchand, A. P.; Wu, A.-H. *J. Org. Chem.* **1986**, *51*, 1897–1900.

Calcd for $C_{18}H_{19}BrO_4$: C, 57.00; H, 5.05; Br, 21.07. Found: C, 57.07; H, 5.12; Br, 21.12.

General Procedure for the Reduction of Compounds 2a–2c, 4a, and 4b with $NaBH_4$. To a suspension of 0.01 mol of unsaturated compound **2a–c, 4a, or 4b** in 200 mL of absolute ethanol was added 0.011 mol of $NaBH_4$ in small portions keeping the reaction mixture below 30 °C. After adding all of the $NaBH_4$ the reaction mixture was stirred for 1 h and then filtered. The filtrate was reduced to half the volume on a rotary evaporator and poured into a mixture of water (200 mL) and acetic acid (3 mL). After 2 h the solid was filtered, washed with water (200 mL), dried, and recrystallized.

5: **2a** (2.86 g, 10 mmol) was treated with 0.42 g (11 mmol) of $NaBH_4$, yield 2.39 g (83%), mp 136–137 °C (from aqueous acetone); ^{1}H NMR δ 1.14 and 1.24 (AB dd, J_{AB} = 10.5 Hz), 1.72 and 1.82 (AB dd, J_{AB} = 13.2 Hz), 1.73 (s), 1.75 (s), 1.92 (dt, J = 9.9 Hz, J = 3 Hz, 1H), 2.25 (m, 2H), 2.48 (m, 1H), 2.60 (m, 3H), 2.85 (m, 2H), 3.92 (d, J = 9.9 Hz, 1H); IR (cm^{-1}) 1748. Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 7.00. Found: C, 71.06; H, 7.15.

6: **4a** (2.86 g, 10 mmol) was treated with 0.42 g (11 mmol) of $NaBH_4$, yield 2.36 g (82%), mp 128–129 °C (from aqueous methanol); ^{1}H NMR δ 1.32 (br.s, 2H), 1.33 and 1.37 (AB dd, J_{AB} = 10.9 Hz), 1.72 (s), 1.74 (s), 1.94 (m, 1H), 1.99 (m, 1H), 2.05 (m, 1H), 2.07 (m, 1H), 2.08 (m, 1H), 2.19 (d, J = 10.7 Hz, 1H), 2.34 (m, 1H), 2.35 (m, 1H), 2.40 (m, 1H), 3.25 (d, J = 10.7 Hz, 1H); ^{13}C NMR δ 27.6, 28.9, 32.6, 33.0, 39.9, 41.6, 44.4, 46.0, 46.3, 47.2, 47.2, 47.6, 50.4, 52.2, 105.0, 165.1, 165.7; IR (cm^{-1}) 1755, 1790. Anal. Calcd for $C_{17}H_{20}O_4$: C, 70.81; H, 7.00. Found: C, 70.79; H, 6.94.

7a and 7b: **4b** (0.36 g, 1 mmol) was treated with 0.42 g (1.1 mmol) of $NaBH_4$, yield of **7a**, 0.1 g (27%), mp 177–178 °C (from ethyl acetate–hexane 1:1); ^{1}H NMR δ 1.42 (br s, 1H), 1.49 (br s, 1H), 1.76 (s), 1.78 (s), 2.14 (q, J = 6 Hz, 1H), 2.29 (m, 1H), 2.30 (m, 1H), 2.31 (m, 1H), 2.39 (m, 1H), 2.59 (m, 1H), 2.62 (m, 1H), 2.64 (m, 1H), 2.92 (m, 1H), 3.20 (d, J = 10.6 Hz, 1H), 4.16 (s, 1H); ^{13}C NMR δ 27.4, 29.0, 32.3, 39.8, 41.8, 46.0, 47.0, 47.4, 48.0, 51.4, 53.2, 53.4, 54.9, 105.2, 164.8, 165.3; IR (cm^{-1}) 1755, 1790. Anal. Calcd for $C_{17}H_{19}BrO_4$: C, 55.60; H, 5.22; Br, 21.76. Found: C, 55.56; H, 5.24; Br, 21.89. Yield of **7b**, 0.1 g (27%), mp 173–174 °C (from ethyl acetate–hexane 1:1); ^{1}H NMR δ 1.49 (br s, 2H), 1.76 (s), 1.77 (s), 2.16 (q, J = 6 Hz, 1H), 2.26 (m, 1H), 2.27 (m, 1H), 2.30 (m, 1H), 2.39 (m, 1H), 2.55 (m, 1H), 2.58 (m, 1H), 2.65 (m, 1H), 2.89 (m, 1 H), 3.24 (d, J = 10.6 Hz, 1H), 4.09 (s, 1H); ^{13}C NMR δ 27.6, 29.0, 31.9, 40.3, 41.3, 45.5, 45.9, 46.5, 46.8, 48.7, 50.5, 53.7, 54.4, 105.3, 164.7, 165.5; IR (cm^{-1}) 1755, 1790. Anal. Calcd for $C_{17}H_{19}BrO_4$: C, 55.60; H, 5.22; Br, 21.76. Found: C, 55.65; H, 5.20; Br, 21.69.

8: **2b** (3.65 g, 10 mmol) was treated with 0.42 g (11 mmol) of $NaBH_4$, yield 1.57 g (55%), mp 148–149 °C (from ethanol); ^{1}H NMR δ 1.53 and 1.93 (AB dd, J_{AB} = 10.6 Hz), 1.76 (s, 6H), 2.43 (br s, 2H), 2.64 (br s, 2H), 2.82 (m, 2H), 3.08 (m, 4H); IR (cm^{-1}) 1747, 1770. Anal. Calcd for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.36; H, 6.37.

9: **2c** (2.13 g, 5 mmol) was treated with 0.23 g (6 mmol) of $NaBH_4$, yield 1.65 g (77%), mp 200–210 °C (from acetone); ^{1}H NMR δ 1.53 and 1.83 (AB dd, J_{AB} = 10.8 Hz), 1.70 (s), 1.80 (s, 6H), 1.88 (s), 2.47 (m, 1H), 2.61 (m, 2H), 2.78 (m, 3H), 2.95 (m, 1H), 3.37 (m, 1H), 3.50 (m, 1H), 3.92 (s, 1H); IR (cm^{-1}) 1730, 1770. Anal. Calcd for $C_{23}H_{24}O_8$: C, 64.48; H, 5.65. Found: C, 64.24; H, 5.80.

General Procedure for Acidic Cleavage of Compounds 4b, 5, 6, 8, and 9. A mixture of one of the above (0.01 mol), acetic acid (20 mL), and hydrochloric acid (35%, 4 mL) was heated at reflux for 2.5 h. After cooling, the reaction mixture was poured into 150 mL of water (except for compound **9**). Compound **11** occurred as a microcrystalline solid which was filtered. Compounds **13**, **14**, and **18** were extracted with ether (3 × 75 mL), the organic layer was dried, and the ether was removed by distillation. The residue was recrystallized. Compound **16** was recovered by rotary evaporation of the reaction mixture and was not purified further. The residue was treated with an ether solution of diazomethane and converted into the methyl ester **17** for characterization. Compound **18** was recovered by treatment of the residue with a mixture of hexane–ether 5:1. Methyl esters **12**, **15**, **17**, and **19** were prepared by treatment of the corresponding acid with ethereal diazomethane solution.[15]

11: **8** (2.87 g, 10 mmol) was heated at reflux with a mixture of 20 mL of acetic acid and 4 mL of HCl, yield 1.64 g (62%), mp 221–222 °C (from aqueous methanol); ^{1}H NMR ($CDCl_3$ + CD_3OD) δ 1.46 and 1.82 (AB dd, J_{AB} = 10.5 Hz), 2.40 (br s, 2H), 2.61 (br s, 2H), 2.78 (br s, 4H), 2.85 (br s, 2H); IR (cm^{-1}): 1720, 1745. Anal. Calcd for $C_{14}H_{14}O_4 \cdot H_2O$: C, 63.62; H, 6.00. Found: C, 63.65; H, 6.11.

12: **11** (0.26 g, 1 mmol) was treated with an ether solution of diazomethane, yield 0.26 g (93%), mp 115–116 °C (from hexane–ethyl acetate); ^{1}H NMR δ 1.45 and 1.82 (AB dd, J_{AB} = 10.5 Hz), 2.40 (br s, 2H), 2.60 (br s, 2H), 2.73 (br s, 2H), 2.80 (br s, 4H), 3.66 (s), 3.72 (s); IR (cm^{-1}) 1730. Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.05; H, 6.61. Found: C, 70.04; H, 6.68.

13: **6** (2.9 g, 10 mmol) was heated at reflux with a mixture of 20 mL of acetic acid and 4 mL of HCl, yield 1.44 g (58%), mp 168–169 °C (from ethyl acetate–hexane); ^{1}H NMR ($CDCl_3$ + CD_3OD) δ 1.32 and 1.44 (AB dd, J = 10.9 Hz), 1.33 (br s, 2H), 1.98 (m, 1H), 2.02 (m, 1H), 2.05 (m, 1H), 2.07 (m, 2H), 2.12 (m, 1H), 2.19 (m, 1H), 2.38 (m, 1H), 2.43 (d, J = 11.5 Hz, 1H), 3.30 (d, J = 11.5 Hz, 1H); ^{13}C NMR δ 32.9, 33.2, 40.2, 42.4, 44.4, 45.6, 47.1, 47.7, 50.0, 50.9, 52.7, 174.5, 174.9. Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.50. Found: C, 67.69; H, 6.51.

14: **5** (2.9 g, 10 mmol) was heated at reflux with a mixture of 20 mL of acetic acid and 4 mL of HCl, yield 1.28 g (63%), mp 76–77 °C (from hexane); ^{1}H NMR δ 1.02 and 1.67 (AB, dtd, J_{AB} = 12.8 Hz, J = 3.6 Hz), 1.16 and 1.67 (AB, dd, J_{AB} = 10.5 Hz), 1.91 (m, 1H), 2.17 (m, 1H), 2.21 (m, 1H), 2.23 (m, 1H), 2.30 (m, 1H), 2.54 (m, 2H), 2.58 (m, 1H), 2.56 and 2.65 (dd, J = 7.2 Hz, J = 15.7 Hz), 2.66 (m, 1H); ^{13}C NMR δ 28.4, 34.0, 34.7, 36.0, 37.7, 38.8, 41.2, 41.6, 42.3, 44.8, 46.8, 47.2, 180.6; IR (cm^{-1}) 1715. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.43; H, 7.87.

15: **14** (3.1 g, 15 mmol) was treated with an ether solution of diazomethane, yield 3.1 g (95%), bp 85 °C (0.25 mm); ^{1}H NMR δ 1.00 and 1.66 (AB, dmd, J_{AB} = 12.7 Hz), 1.14 and 1.65 (AB, dmdt, J_{AB} = 10.5 Hz, J = 1.6 Hz), 1.90 (m, 1H), 2.16 (m, 1H), 2.19 (m, 1H), 2.20 (m, 1H), 2.28 (d, J = 9 Hz, 1H), 2.51 (dd, J = 7.3 Hz, J = 15.6 Hz, 1H), 2.52 (m, 1H), 2.53 (m, 1H), 2.55 (m, 1H), 2.60 (dd, J = 7.3 Hz, J = 15.6 Hz, 1H), 2.65 (m, 1H), 3.63 (s); ^{13}C NMR δ 28.5, 34.0, 34.7, 36.0, 38.1, 38.9, 41.2, 41.6, 42.3, 44.9, 46.8, 47.2, 51.3, 174.2. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.02; H, 8.33.

17: **9** (2.14 g, 5 mmol) was heated at reflux with a mixture of 15 mL of acetic acid and 4 mL of hydrochloric acid. The reaction mixture was evaporated and treated with an ether solution of diazomethane yielding the triester which was purified by column chromatography, yield 0.72 g (42%), bp 175–176 °C (0.2 mm); ^{1}H NMR δ 1.37 and 1.71 (AB, dtdt, J_{AB} = 10.5 Hz, J = 1.4 Hz, J = 1.6 Hz, 2H), 2.25 (m, 1H), 2.33 (m, 1H), 2.48 (m, 1H), 2.52 (m, 1H), 2.62 (m, 1H), 2.68 (m, 1H), 2.72 (m, 1H), 2.75 (d, J = 13.7 Hz, 2H), 2.77 (m, 1H), 2.81 (m, 1H), 3.54 (s), 3.57 (s), 3.62 (s); ^{13}C NMR δ 35.6, 40.1, 42.1, 42.3, 42.8, 45.0, 46.1, 47.4, 51.1, 51.2, 51.8, 51.9, 53.0, 56.3, 60.1, 74.4, 169.5, 170.2, 172.5; IR (cm^{-1}) 1740. Anal. Calcd for $C_{19}H_{22}O_6$: C, 65.88; H, 6.40. Found: C, 65.73; H, 6.44.

18: **4b** (3.6 g, 10 mmol) was heated at reflux with a mixture of 20 mL of acetic acid and 4 mL of HCl, yield 1.66 g (51%), mp 215–216 °C (from ethyl acetate–hexane); ^{1}H NMR ($CDCl_3$ + CD_3OD) δ 1.60 (br s, 2H), 2.37 (m, 1H), 2.45 (m, 1H), 2.50–2.60 (m, 3H), 3.06 (br s, 1H), 3.37 (m, 2H), 4.16 (br s, 1H). Anal. Calcd for $C_{14}H_{13}BrO_4$: C, 51.71; H, 4.03; Br, 24.58. Found: C, 51.89; H, 4.08; Br, 24.52.

19: **14** (1.62 g, 5 mmol) was treated with an ether solution of diazomethane, yield 1.62 g (92%), bp 132–133 °C (0.3 mm), mp 58–59 °C; ^{1}H NMR δ 1.57 (br s, 2H), 2.33 (t, J = 5.9 Hz, 1H), 2.42 (m, 1H), 2.50 (m, 3H), 3.02 (m, 3H), 3.75 (s), 3.78 (s, 6H), 4.12 (br s, 1H); IR (cm^{-1}) 1650, 1680, 1730. Anal. Calcd for $C_{16}H_{17}BrO_4$: C, 54.40; H, 4.85; Br, 22.62. Found: C, 54.54; H, 4.90; Br, 22.87.

Supplementary Material Available: ^{1}H and ^{13}C NMR and IR assignments (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(15) Eistert, B.; Arndt, F.; Loewe, L.; Ayca, A. *Chem. Ber.* **1951**, *84*, 156–169.