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Synthesis of Polycycles by Single or Double Domino Nucleophilic Substitution/Diels–Alder Reaction

Pelayo Camps,*[a] David Lozano,[a] and Mercè Font-Bardia[b,c]

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New hexacyclo and octacyclo compounds have been synthesized by a short route whose key step consists of a single or double domino nucleophilic substitution of neopentyl-type iodides with potassium cyclopentadienide, followed by intramolecular Diels–Alder cycloaddition.

Introduction

Polycyclic and cage compounds are of current interest in medicinal chemistry.[1–4] In connection with this potential application, we recently described the synthesis of a 2,8-ethanonoradamantane derivative.[5] Diamondoid derivatives[6] are of interest in connection with host-guest molecular recognition, materials chemistry, molecular machines and rotors, etc. Polytwistanes[7,8] are being studied as chiral hydrocarbon nanotubes, and polynorbornane derivatives[9] have been used to prepare coordination cages (Figure 1). In this paper, a short route to functionalized bridged di- and tri-norbornane derivatives is described. These compounds might be used, among other applications, as new scaffolds for the preparation of biologically active compounds, or as building blocks for the synthesis of new polynorbornane-based ligands.

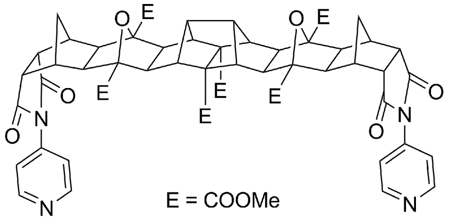
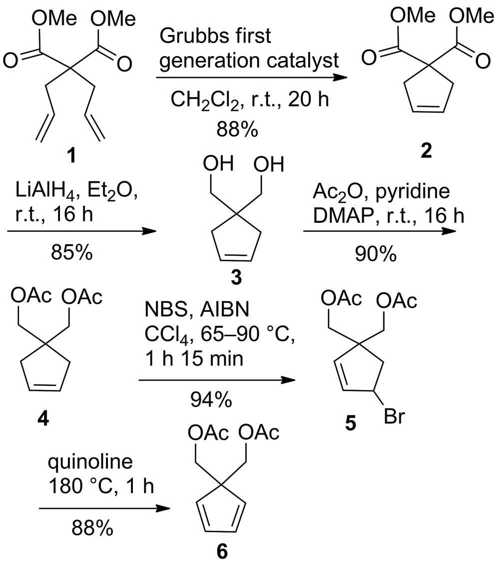


Figure 1. A polynorbornane-based ligand.

Results and Discussion

An important feature of these syntheses was the preparation of cyclopenta-2,4-diene-1,1-diylbis(methylene) diacetate (**6**) according to Scheme 1. Dimethyl bisallylmalonate (**1**)[10,11] was transformed into dimethyl cyclopent-3-ene-1,1-dicarboxylate (**2**) by reaction with Grubbs first generation catalyst. Compound **2** was alternatively prepared by reaction of dimethyl malonate with *cis*-1,4-dichloro-2-butene.[12] Reduction of diester **2** followed by acetylation gave known diacetate **4**. Reaction of **4** with *N*-bromosuccinimide (NBS) in the presence of 2,2′-azo-bis(isobutyronitrile) (AIBN) as described in a related case,[13] gave allylic bromide **5**, which, on reaction with quinoline at high temperature,[14] gave the desired diacetate (i.e., **6**).



Scheme 1. Preparation of cyclopentadiene **6**; DMAP = 4-(dimethylamino)pyridine.

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[a] Laboratori de Química Farmacèutica (Unitat Associada al CSIC), Facultat de Farmàcia, Universitat de Barcelona, and Institut de Biomedicina (IBUB), Universitat de Barcelona,
Av. Joan XXIII 27–31, 08028 Barcelona, Spain
E-mail: camps@ub.edu
http://www.ub.edu/farmaco/
[b] Departament de Cristallografia, Mineralogia i Dipòsits Minerals, Universitat de Barcelona,
Martí Franquès s/n, 08028 Barcelona, Spain
[c] Unitat de Difracció de RX, Centres Científics i Tecnològics de la Universitat de Barcelona (CCiTUB), Universitat de Barcelona,
Solé i Sabarís 1–3, 08028 Barcelona, Spain

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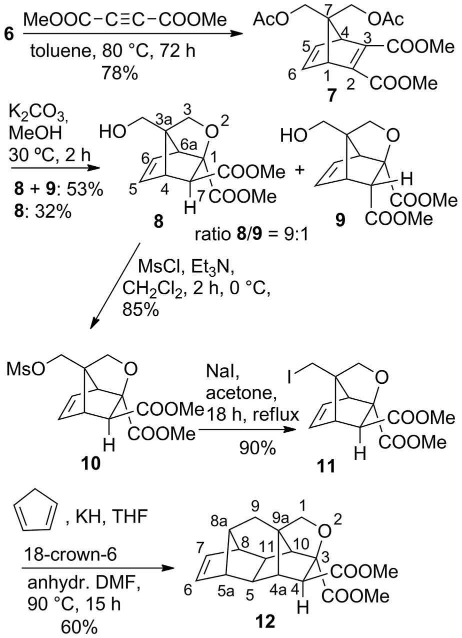
Reaction of cyclopentadiene **6** with dimethyl acetylenedicarboxylate (1.5 equiv.) gave the corresponding Diels–Alder adduct **7** in good yield (Scheme 2). Methanolysis of the acetate groups of this compound with K_2CO_3 in MeOH gave a stereoisomeric mixture of alcohols **8** and **9** in a ratio **8/9** of about 9:1 [on the basis of integration of the singlet signals of one of the COOMe groups of **8** (δ = 3.70 ppm) and **9** (δ = 3.57 ppm) in the ^{1}H NMR spectrum of the mixture]. These compounds are reasonably formed by Michael addition of the *syn* alcohol functionality of the intermediate diol onto the butenedioate substructure. Compound **8** was isolated as a racemate from its mixture with **9** by crystallization from EtOAc, and was fully characterized spectroscopically. The *exo* stereochemistry of the ester functionality at C-7 was clearly assigned on the basis of its ^{1}H NMR spectrum, in which the 7-H proton appears as a singlet as the value of its coupling constant with 4-H is close to zero (dihedral angle H–C-7–C-4–H close to 90°). The stereochemistry of **8** was also secured by X-ray diffraction analysis. Figure 2 shows the ORTEP representation of one of the enantiomers. The synthetic sequence was continued with racemic alcohol **8**. Mesylation of **8** by a standard procedure gave mesylate **10**, which was transformed into iodide **11** by reaction with NaI in acetone. Both transformations took place in good yield.



Scheme 2. Synthesis of hexacyclo derivative **12**.

Treatment of this iodide with potassium cyclopentadienide in DMF in the presence of 18-crown-6 (5 mol-%)[15,16] gave polycycle **12**, as a result of nucleophilic substitution of the neopentyl-type iodide by the cyclopentadienide anion, followed by intramolecular Diels–Alder reaction, in good yield. Although polycycle **12** was fully characterized spectroscopically, and by elemental analysis and accurate mass measurement, its structure was secured by X-ray diffraction analysis. Figure 3 shows the ORTEP representation of one of the enantiomers of **12**.

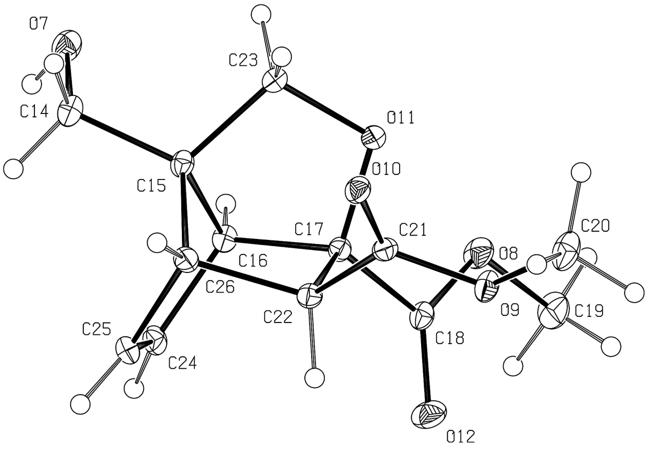


Figure 2. ORTEP representation of one of the enantiomers of alcohol **8**.

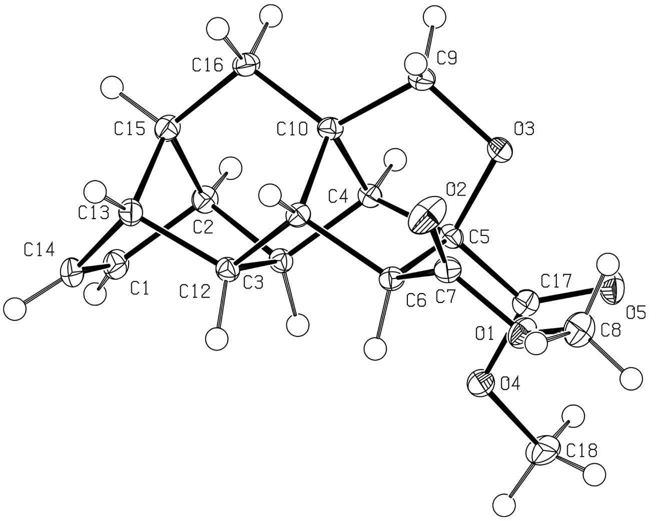
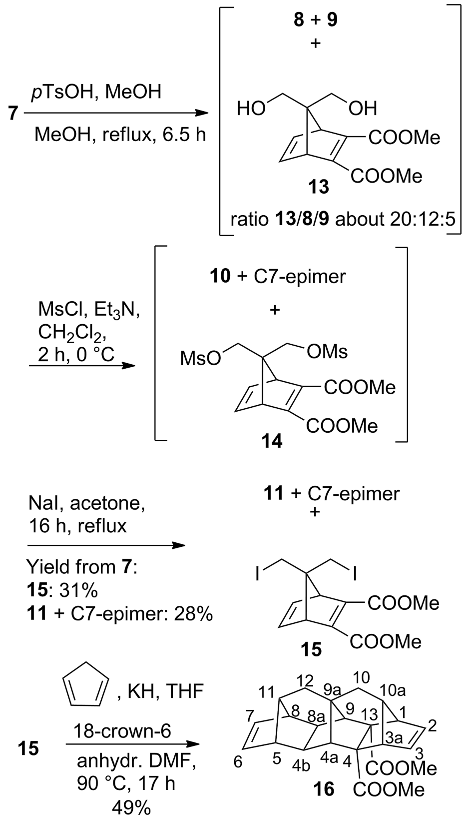


Figure 3. ORTEP representation of one of the enantiomers of polycycle **12**.

Acid-catalyzed methanolysis of diacetate **7** gave a mixture of diol **13** plus alcohols **8** and **9** in a ratio about 20:12:5 (by ^{1}H NMR spectroscopy; Scheme 3). From this mixture, diol **13** could not be isolated in pure form since partial conversion into alcohols **8** and **9** took place during attempted purification by silica gel column chromatography. Consequently, the above mixture was transformed into a mixture of dimesylate **14** and monomesylate **10** and its C-7 epimer. Upon treatment with NaI in acetone, this mixture gave a mixture of diiodide **15** and monoiodide **11** and its C-7 epimer. This mixture was separated by silica gel column chromatography into two fractions: diiodide **15** (31 % overall yield from diacetate **7**), and a mixture of monoiodide **11** and its C-7 epimer (28 % overall yield from **7**).

Reaction of diiodide **15** with potassium cyclopentadienide as before gave polycycle **26** in 49 % yield. The formation of this compound implies a double nucleophilic substitution of the neopentyl-type iodides by the cyclopentadienide anion, followed by a double intramolecular Diels–Alder re-



Scheme 3. Synthesis of polycyclo derivative **16**.

action. Compound **16** was fully characterized analytically and spectroscopically, including X-ray diffraction analysis. Figure 4 shows the ORTEP representation of polycycle **16**.

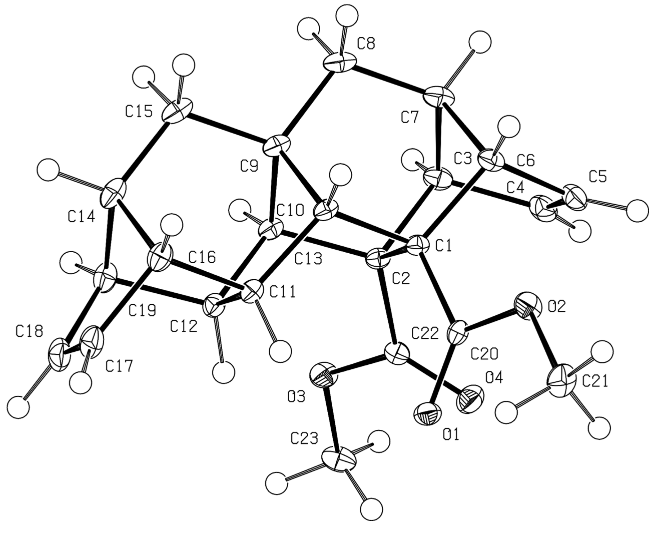


Figure 4. ORTEP representation of octacyclo **16**.

To the best of our knowledge, although these domino processes appear conventional, the only related transformation described to date[17] is the reaction of a stereoisomeric mixture of dimethyl 7-(dimethoxymethyl)norborna-2,5-diene-2,3-dicarboxylate with trimethylsilylcyclopentadiene catalyzed by $TiCl_4$. This gave a mixture, which was not separated, of products of condensation and Diels–Alder addition.

Conclusions

In conclusion, a short route to complex functionalized polycycles that could be of interest as new scaffolds for the preparation of biologically active compounds and coordination cages has been developed. The key points of the synthesis are: (i) a convenient preparation of 1,1-disubstituted cyclopentadiene **6**, and (ii) a single or double domino nucleophilic substitution of neopentyl-type iodides by cyclopentadienide anion/Diels–Alder reaction that introduces three or six new rings into the corresponding products, i.e., **11** or **15** respectively, in a one-pot transformation.

Experimental Section

General Methods: Melting points were determined in open capillary tubes with an MFB 595010M Gallenkamp melting-point apparatus. ^1H and ^{13}C NMR spectra were recorded with a Varian Mercury 400 (400 MHz for ^1H; 100.6 MHz for ^{13}C) spectrometer in $CDCl_3$. Chemical shifts (δ) are reported in parts per million relative to tetramethylsilane, and spectra were calibrated using internal tetramethylsilane or residual $CHCl_3/CDCl_3$. Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad, or their combinations. Assignments given for the NMR spectra are based on DEPT, COSY, NOESY, $^1H/^{13}C$ single quantum correlation (gHSQC sequence), and $^1H/^{13}C$ multiple bond correlation (gHMBC sequence) spectra. IR spectra were recorded with an FTIR Perkin–Elmer Spectrum RX1 spectrometer using the attenuated total reflectance (ATR) technique. Absorption values are given as wavenumbers (cm^{-1}), and the intensity of the absorptions are given as strong (s), medium (m), or weak (w). High-resolution mass spectra (HRMS) were carried out at the mass spectrometry unit of the Centres Científics i Tecnològics de la Universitat de Barcelona (CCiTUB) with an LC/MSD-TOF spectrometer with electrospray ionization (ESI-TOF-MS) from Agilent Technologies. Elemental analyses were carried out at the IIQAB (CSIC) of Barcelona, Spain, with elemental microanalyzers (A5) model Flash 1112 series and (A7) model Flash 2000 series from Thermofinnigan for (C, H, N) and (C, H, N, S) determinations, respectively. Silica gel 60 AC (35–70 mm, SDS, ref. 2000027) was used for flash column chromatography. The eluents used are reported as volume/volume percentages. Thin-layer chromatography (TLC) was carried out on aluminum-backed sheets with silica gel 60, 254 nm indicator (Fluka–Sigma–Aldrich), and spots were visualized with UV light or a solution of $KMnO_4$ (1% aq.). X-ray diffraction analysis was carried out with a D8 Venture diffractometer at the CCiTUB of the University of Barcelona. Allyl bromide, NBS, 18-crown-6, 4-(dimethylamino)pyridine, dimethyl acetylenedicarboxylate, dimethyl malonate, Grubbs first generation catalyst, KH (30%), $LiAlH_4$, and *p*-toluenesulfonic acid were obtained from Sigma–Aldrich; AIBN, dicyclopentadiene, and quinoline were obtained from Fluka; all of these reagents were used without further purification.

(4-Bromocyclopent-2-ene-1,1-diyl)bis(methylene) Diacetate (5): NBS (856 mg, 4.81 mmol) and AIBN (79 mg, 0.48 mmol, 10 mol-%) were added to a magnetically stirred solution of diacetate **4** (1.02 g, 4.81 mmol) in CCl_4 (14.6 mL) under an Ar atmosphere. The resulting orange-colored stirred suspension was heated at 65 °C for 15 min, and then at 90 °C for 1 h. The grey suspension was then cooled with an ice/water bath; the solid precipitate was removed by filtration, and washed with cold CH_2Cl_2 (3× 5 mL). The combined filtrate and washings were washed with saturated aqueous $NaHCO_3$ (3× 10 mL) and brine (10 mL), dried (anhydrous Na_2SO_4), and concentrated in vacuo to give crude bromide **5** (1.31 g, 94%) as a yellow oil, which was used as such in the next step. R_f (hexane/EtOAc, 1:1): 0.42. IR (ATR): $\tilde{\nu}$ = 3067 (w), 2952 (m), 2893 (w), 1736 (s), 1466 (m), 1437 (m), 1379 (s), 1364 (s), 1232 (s), 1183 (m), 1043 (s), 981 (m), 906 (m), 809 (m), 786 (m), 765 (m) cm^{-1}. HRMS: calcd. for $[C_{11}H_{15}{}^{79}BrO_4 + H]^+$ 291.0226; found 292.0219. ^1H NMR: δ = 2.05 (s, 3 H) and 2.09 (s, 3 H) (2 CH_3COO), 2.35 (dd, J = 15.6, J' = 2.4 Hz, 1 H, 5-H_a), 2.47 (dd, J = 15.6, J' = 7.6 Hz, 1 H, 5-H_b), 3.95 (d, J = 11.0 Hz, 1 H) and 4.10 (d, J = 11.0 Hz, 1 H) (CH_2OAc), 4.20 (s, 2 H, CH_2OAc), 5.05–5.08 (ddt, J = 7.6, J' = 2.4, J'' = 0.8 Hz, 1 H, 4-H), 5.80 (d, J = 5.6 Hz, 1 H, 2-H), 6.08 (dd, J = 5.4, J' = 2.2 Hz, 1 H, 3-H) ppm. ^{13}C NMR: δ = 20.75 (CH_3) and 20.85 (CH_3) (2 $OCOCH_3$), 41.0 (CH_2, C-5), 52.7 (CH, C-4), 53.5 (C, C-1), 65.6 (CH_2) and 66.7 (CH_2, 2 CH_2OAc), 135.7 (CH) and 136.0 (CH, C-2 and C-3), 170.7 (C) and 170.8 (C, 2 CH_3COO) ppm.

Cyclopenta-2,4-diene-1,1-diylbis(methylene) Diacetate (6): A magnetically stirred solution of bromo diacetate **5** (3.79 g, 13.0 mmol) in anhydrous quinoline (6.9 mL, 58.6 mmol) under an Ar atmosphere was heated at 180 °C for 1 h. The dark mixture was cooled with an ice/water bath, then Et_2O (15 mL) was added. The mixture was stirred for 5 min, and then it was washed with HCl (2 N aq.; 4× 10 mL) and water (20 mL). The brown organic phase was dried (anhydrous Na_2SO_4), and concentrated in vacuo to give diene **6** (2.38 g, 88%) as a brown oil, which was used as such in the next step. An analytical sample of **6** was obtained by column chromatography of a sample of the above product (205 mg) [35–70 µm silica gel (6.1 g), pentane/EtOAc mixtures]. On elution with pentane/EtOAc, 96:4, diene **6** (165 mg) was isolated as a pale yellow oil that solidified on standing. m.p. 42–43 °C. R_f (silica gel, 10 cm, hexane/EtOAc, 1:1): 0.56. IR (ATR): $\tilde{\nu}$ = 3076 (w), 2978 (m), 2959 (m), 2897 (m), 2850 (w), 1736 (s), 1466 (m), 1430 (m), 1376 (s), 1227 (s), 1078 (m), 1032 (s), 978 (s), 922 (m), 896 (m), 753 (s) cm^{-1}. $C_{11}H_{14}O_4$ (210.23): calcd. C 62.85, H 6.71; found C 62.97, H 6.90. HRMS: calcd. for $[C_{11}H_{14}O_4 + NH_4]^+$ 228.1230; found 228.1233; calcd. for $[C_{11}H_{14}O_4 + H]^+$ 211.0965; found 211.0965. ^1H NMR: δ = 2.08 (s, 6 H, 2 CH_3COO), 4.07 (s, 4 H, 2 CH_2OAc), 6.33–6.35 [m, 2 H, 2(5)-H], 6.47–6.48 [m, 2 H, 3(4)-H] ppm. ^{13}C NMR: δ = 20.9 (CH_3, 2 $OCOCH_3$), 59.5 (C, C-1), 63.6 (CH_2, 2 CH_2OAc), 133.6 [CH, C-2(5)], 137.4 [CH, C-3(4)], 170.7 (C, 2 CH_3COO) ppm.

Dimethyl 7,7-Bis(acetoxymethyl)bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (7): A solution of crude diene **6** (624 mg, 2.97 mmol) and dimethyl acetylenedicarboxylate (0.55 mL, 633 mg, 4.45 mmol) in toluene (5 mL) was heated at 80 °C for 72 h. The solution was then cooled to room temperature, and the solvent was removed in vacuo. The brown oily residue was subjected to column chromatography [35–70 µm silica gel (25 g), hexane/EtOAc mixtures]. On elution with hexane/EtOAc, 3:1, adduct **7** (820 mg, 78%) was isolated as a pale yellow oil. R_f (silica gel, 10 cm, hexane/EtOAc, 3:7): 0.47. IR (ATR): $\tilde{\nu}$ = 3000 (w), 2955 (w), 1731 (s), 1713 (s), 1630 (m), 1435 (m), 1376 (m), 1366 (m), 1317 (m), 1218 (s), 1099 (m), 1031 (s), 734 (m) cm^{-1}. $C_{17}H_{20}O_8$ (352.34): C 57.95, H 5.72%; found C 57.98, H 5.89%. HRMS: calcd. for $[C_{17}H_{20}O_8 + H]^+$ 353.1231; found 353.1239. ^1H NMR: δ = 2.028 (s, 3 H) and 2.031 (s, 3 H, 2 CH_3COO), 3.74 [pseudo t, J = 2.0 Hz, 2 H, 1(4)-H], 3.79 [s, 6 H, C-2(3)-COOMe], 4.25 (s, 2 H, *syn*-CH_2OAc) and 4.29 (s, 2 H, *anti*-CH_2OAc), 6.87 [pseudo t, J = 2.2 Hz, 2 H, 5(6)-H] ppm. NOESY: irradiation at δ = 6.87 ppm shows an NOE with the protons appearing at δ = 3.74 [1(4)-H] and 4.25 (*syn*-CH_2OAc) ppm. ^{13}C NMR: δ = 20.7 (CH_3, CH_3COO), 20.8 (CH_3, CH_3COO), 52.2 (CH_3, 2 $COOCH_3$), 56.7 [CH, C-1(4)], 63.7 (CH_2, CH_2OAc), 63.8 (CH_2, CH_2OAc), 85.7 (C, C-7), 140.9 [CH, C-5(6)], 150.2 [C, C-2(3)], 164.7 [C, C-2(3)-COOMe], 170.50 (C, *anti*-CH_3COO), 170.54 (C, *syn*-CH_3COO) ppm.

Dimethyl (1*RS*,3a*RS*,4*SR*,6a*SR*,7*SR*)-3a-(Hydroxymethyl)-3,3a,4,6a-tetrahydro-1*H*-1,4-methanocyclopenta[*c*]furan-1,7-dicarboxylate (8): Anhydrous K_2CO_3 (40 mg, 0.29 mmol) was added to a solution of diacetate **7** (413 mg, 1.17 mmol) in anhydrous MeOH (2.5 mL), and the mixture was stirred at 30 °C for 2 h. The mixture was cooled to 0 °C (ice/water bath), and filtered. The solid was washed with MeOH (4× 5 mL). The combined filtrate and washings were concentrated in vacuo to give a brown solid (369 mg), containing a stereoisomeric mixture of **8** and its C-7 epimer **9**, in a ratio **8**/**9** = 9:1 (by ^1H NMR spectroscopy). This mixture was subjected to column chromatography [35–70 µm silica gel (11 g), hexane/EtOAc mixtures]. On elution with hexane/EtOAc, 3:2 to 1:1, a stereoisomeric mixture of **8** and **9** (168 mg), in a ratio **8**/**9** = 9:1, was obtained. By heating this solid in refluxing EtOAc (0.5 mL), an analytical sample of **8** (101 mg, 32%) was obtained as a white solid. m.p. 118–120 °C (EtOAc). R_f (silica gel, 10 cm, hexane/EtOAc, 3:7): 0.28. IR (ATR): $\tilde{\nu}$ = 3488 (m), 3426 (m), 2954 (w), 2903 (w), 2871 (w), 1721 (s), 1439 (m), 1325 (s), 1217 (s), 1196 (s), 1170 (s), 1156 (s), 1064 (s), 1037 (s), 1016 (s), 1000 (m), 926 (m), 888 (m), 730 (s), 658 (m) cm^{-1}. $C_{13}H_{16}O_6$ (268.26): C 58.20, H 6.01; found C 58.20, H 6.14. HRMS: calcd. for $[C_{13}H_{16}O_6 + Na]^+$ 291.0839; found 291.0841. ^1H NMR: δ = 1.59 (s, 1 H, OH), 2.74 (s, 1 H, 7-H), 3.07–3.09 (m, 1 H, 6a-H), 3.19–3.21 (m, 1 H, 4-H), 3.62 (br. d, J = 9.0 Hz, 1 H) and 3.68 (br. d, J = 9.0 Hz, 1 H, CH_2OH), 3.70 (s, 3 H, C-1-$COOCH_3$), 3.81 (s, 3 H, C-7-$COOCH_3$), 3.96 (d, J = 8.8 Hz, 1 H) and 4.00 (d, J = 8.8 Hz, 1 H, 3-H_a and 3-H_b), 5.93–5.95 (ddd, J = 5.8, J' = 3.0, J'' = 1.0 Hz, 1 H, 6-H), 6.39–6.42 (dd, J = 5.8, J' = 3.0 Hz, 1 H, 5-H) ppm. ^{13}C NMR: δ = 48.0 (CH, C-4), 52.2 (CH_3, C-1-$COOCH_3$), 52.6 (CH_3, C-7-$COOCH_3$), 56.9 (CH, C-7), 59.1 (CH, C-6a), 59.6 (CH_2, CH_2OH), 68.6 (CH_2, C-3), 75.4 (C, C-3a), 85.7 (C, C-1), 128.0 (CH, C-6), 139.8 (CH, C-5), 170.9 (C, C-7-COOMe), 171.1 (C, C-1-COOMe) ppm.

NMR spectroscopic data of **9**: A mixture of **8** and **9** (120 mg) in a ratio of ca. 1.5:10 was obtained by silica gel column chromatography as part of an operation to prepare diol **13** (see below). The NMR spectroscopic data for **9** are given based on this mixture. ^1H NMR: δ = 1.53 (br. s, 1 H, OH), 3.02–3.04 (m, 1 H, 6a-H), 3.12–3.15 (m, 1 H, 4-H), 3.34 (d, J = 4.4 Hz, 1 H, 7-H), 3.57 (s, 3 H, C-1-COOMe), 3.61 (br. d, J = 11.2 Hz, 1 H) and 3.69 (br. d, J = 11.2 Hz, 1 H, CH_2OH), 3.77 (s, 3 H, C-7-COOMe), 3.82 (d, J = 9.0 Hz, 1 H) and 3.98 (d, J = 9.0 Hz, 1 H, 3-H_a and 3-H_b), 6.10 (ddd, J = 5.6, J' = 3.2, J'' = 0.8 Hz, 1 H, 6-H), 6.16 (dd, J = 5.6, J' = 2.8 Hz, 1 H, 5-H) ppm. ^{13}C NMR: δ = 49.0 (CH, C-4), 51.7 (CH_3, C-1-$COOCH_3$), 52.3 (CH_3, C-7-$COOCH_3$), 55.8 (CH, C-6a), 55.9 (CH, C-7), 59.4 (CH_2, CH_2OH), 68.2 (CH_2, C-3), 73.1 (C, C-3a), 88.8 (C, C-1), 129.6 (CH, C-6), 135.7 (CH, C-5), 169.3 (C, C-7-COOMe), 169.7 (C, C-1-COOMe) ppm.

Dimethyl (1*RS*,3a*RS*,4*SR*,6a*SR*,7*SR*)-3a-{[(Methylsulfonyl)-oxy]methyl}-3,3a,4,6a-tetrahydro-1*H*-1,4-methanocyclopenta[*c*]-furan-1,7-dicarboxylate (10): Methanesulfonyl chloride (0.03 mL, 0.36 mmol) was added dropwise to a cold (0 °C, ice/water bath) and magnetically stirred solution of alcohol **8** (80 mg, 0.3 mmol) and anhydrous Et_3N (0.1 mL, 0.69 mmol) in CH_2Cl_2 (3.3 mL) under an Ar atmosphere. The mixture was stirred at this temperature for 2 h. Saturated aqueous $NaHCO_3$ (1 mL) was then added. The organic phase was separated, and was washed with saturated aqueous $NaHCO_3$ (3 × 3 mL). The combined aqueous phases were extracted with CH_2Cl_2 (3 × 5 mL). The combined organic phase and extracts were washed with water (3 mL) and brine (3 mL), dried (anhydrous Na_2SO_4), and concentrated in vacuo to give a solid residue (101 mg) that was subjected to column chromatography [35–70 µm silica gel (1.0 g), hexane/EtOAc]. On elution with hexane/EtOAc, 7:3, mesylate **10** (87 mg, 85%) was obtained as a white solid. m.p. 144–145 °C (hexane/EtOAc). R_f (silica gel, 10 cm, hexane/EtOAc, 1:4): 0.45. IR (ATR): $\tilde{\nu}$ = 2960 (w), 2923 (w), 2901 (w), 2850 (w), 1731 (s), 1462 (w), 1439 (m), 1346 (s), 1338 (s), 1329 (s), 1224 (s), 1084 (s), 1172 (s), 1161 (s), 1066 (s), 956 (s), 938 (s), 854 (s), 836 (s), 742 (s), 729 (s) cm^{-1}. $C_{14}H_{18}O_8S$ (346.35): C 48.55, H 5.24, S 9.26%; found C 48.64, H 5.42, S 9.07%. HRMS: calcd. for $[C_{14}H_{18}NO_8S + H]^+$ 347.0795; found 347.0793; calcd. for $[C_{14}H_{18}NO_8S + NH_4]^+$ 364.1061; found 364.1060. ^1H NMR: δ = 2.79 (s, 1 H, 7-H), 2.99 (s, 3 H, CH_3SO_3), 3.14–3.16 (m, 1 H, 6a-H), 3.29–3.31 (m, 1 H, 4-H), 3.72 (s, 3 H, C-1-$COOCH_3$), 3.83 (s, 3 H, C-7-$COOCH_3$), 3.94 (d, *J* = 8.8 Hz, 1 H) and 4.01 (d, *J* = 8.8 Hz, 1 H, 3-H_a and 3-H_b), 4.23 (d, *J* = 10.4 Hz, 1 H) and 4.30 (d, *J* = 10.4 Hz, 1 H, CH_2OMs), 5.99–6.02 (ddd, *J* = 5.8, *J'* = 3.0, *J''* = 0.8 Hz, 1 H, 6-H), 6.44–6.46 (dd, *J* = 5.8, *J'* = 3.0 Hz, 1 H, 5-H) ppm. ^{13}C NMR: δ = 37.5 (CH_3, CH_3SO_3), 48.3 (CH, C-4), 52.4 (CH_3, C-1-$COOCH_3$), 52.8 (CH_3, C-7-$COOCH_3$), 56.6 (CH, C-7), 59.3 (CH, C-6a), 66.2 (CH_2, CH_2OMs), 67.9 (CH_2, C-3), 72.7 (C, C-3a), 85.4 (C, C-1), 128.4 (CH, C-6), 139.5 (CH, C-5), 170.1 (C, C-7-*C*$OOCH_3$), 170.6 (C, C-1-*C*$OOCH_3$) ppm.

Dimethyl (1*RS*,3a*RS*,4*SR*,6a*SR*,7*SR*)-3a-(Iodomethyl)-3,3a,4,6a-tetrahydro-1*H*-1,4-methanocyclopenta[*c*]furan-1,7-dicarboxylate (11): Powdered NaI (347 mg, 2.3 mmol) was added to a solution of mesylate **10** (80 mg, 0.23 mmol) in anhydrous acetone (2.9 mL), and the mixture was heated at reflux under Ar for 18 h. The mixture was cooled to room temperature, and concentrated in vacuo. The solid residue was subjected to column chromatography [35–70 µm silica gel (1.0 g), hexane/EtOAc mixtures]. On elution with hexane/EtOAc, 96:4, iodide **11** (78 mg, 90%) was isolated as a pale yellow oil. R_f (silica gel, 10 cm, hexane/EtOAc, 3:7): 0.54. IR (ATR): $\tilde{\nu}$ = 2949 (w), 2889 (w), 2843 (w), 1731 (s), 1435 (m), 1326 (m), 1257 (m), 1217 (s), 1189 (s), 1164 (s), 1102 (m), 1069 (s), 1000 (m), 728 (s) cm^{-1}. $C_{13}H_{15}IO_5$ (378.16): C 41.29, H 4.00; I 33.56%; found C 41.43, H 4.14; I 33.30%. HRMS: calcd. for $[C_{13}H_{15}IO_5 + H]^+$ 379.0037; found 379.0033; calcd. for $[C_{13}H_{15}IO_5 + Na]^+$ 400.9856; found 400.9856. ^1H NMR: δ = 2.73 (s, 1 H, 7-H), 3.06–3.09 (br. s, 1 H, 6a-H), 3.23 (d, *J* = 10.4 Hz, 1 H) and 3.27 (d, *J* = 10.4 Hz, 1 H, CH_aI and CH_bI), 3.32–3.35 (br. s, 1 H, 4-H), 3.71 (s, 3 H, C-1-$COOCH_3$), 3.81 (s, 3 H, C-7-$COOCH_3$), 3.89 (d, *J* = 8.8 Hz, 1 H) and 3.98 (d, *J* = 8.8 Hz, 1 H, 3-H_a and 3-H_b), 5.98–6.01 (ddd, *J* = 5.6, *J'* = 2.8, *J''* = 1.2 Hz, 1 H, 6-H), 6.45–6.47 (ddm, *J* = 5.6, *J'* = 3.0 Hz, 1 H, 5-H) ppm. ^{13}C NMR: δ = 3.4 (CH_2, CH_2I), 50.1 (CH, C-4), 52.3 (CH_3, C-1-$COOCH_3$), 52.7 (CH_3, C-7-$COOCH_3$), 57.2 (CH, C-7), 62.6 (CH, C-6a), 70.9 (CH_2, C-3), 73.8 (C, C-3a), 85.5 (C, C-1), 127.9 (CH, C-6), 139.6 (CH, C-5), 170.5 (C, C-7-*C*$OOCH_3$), 170.6 (C, C-1-*C*$OOCH_3$) ppm.

Dimethyl (3*RS*,4*SR*,4a*SR*,5*SR*,5a*RS*,8*SR*,8a*RS*,9a*RS*,10*SR*,11*RS*)-4a,5,5a,8,8a,9-Hexahydro-1*H*-3,9a,5,8-(epiethane[1,1,-2,2]tetrayl)cyclopenta[*g*]isochromene-3,4(4*H*)-dicarboxylate (12): In a 10 mL flask, KH (30% in mineral oil; 67 mg, 0.50 mmol) was washed with anhydrous THF (5 × 1 mL) under an Ar atmosphere. Anhydrous THF (1 mL) was added to the washed KH, and the resulting suspension was cooled to 0 °C in an ice/water bath. Freshly distilled cyclopentadiene (50 µL, 36 mg, 0.54 mmol) was added, and the mixture was stirred at this temperature for 10 min. 18-Crown-6 (7 mg, 26 µmol, ca. 5% relative to KH) was added, and the mixture was stirred at 0 °C for 10 min, and at room temperature for 15 min to give a pinkish-colored suspension. In a 25 mL flask equipped with a magnetic stirrer bar and reflux condenser, under an Ar atmosphere, a solution of iodide **11** (50 mg, 0.13 mmol) in anhydrous DMF (0.8 mL) was prepared. The solution was cooled to 0 °C in an ice/water bath and then, part of the above solution of potassium cyclopentadienide (0.5 M; 0.27 mL, 0.13 mmol) was added dropwise. The mixture was stirred at 0 °C for 5 min, and at room temperature for 10 min, and then it was heated to 90 °C for 17 h. The mixture was cooled to room temperature, MeOH (10 µL) was added, and the mixture was stirred for 10 min. Then, EtOAc (5 mL) and water (5 mL) were added, and the organic phase was separated. The aqueous phase was extracted with EtOAc (4 × 5 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ (3 × 5 mL), water (2 × 5 mL), and brine (5 mL), dried (anhydrous Na_2SO_4), and concentrated in vacuo to give crude diester **12** (45 mg) as a brown oil. This crude product was subjected to column chromatography [35–70 µm silica gel (1.3 g), hexane/EtOAc mixtures] to give, on elution with hexane/EtOAc, 94:6, diester **12** (25 mg, 60%) as a white solid. Crystallization of the above product from CH_2Cl_2/pentane gave an analytical sample of **12** as a white solid. m.p. 160–161 °C. R_f (silica gel, 10 cm, hexane/EtOAc, 3:7): 0.72. IR (ATR): $\tilde{\nu}$ = 2971 (w), 2954 (m), 2928 (m), 2892 (w), 2852 (w), 1755 (s), 1728 (s), 1426 (m), 1349 (m), 1207 (s), 1188 (s), 1164 (s), 1072 (s), 1042 (s), 973 (m), 932 (m), 739 (s), 698 (m) cm^{-1}. $C_{18}H_{20}O_5 \cdot 1/3H_2O$ (322.36): C 67.07, H 6.46%; found C 66.79, H 6.23%. HRMS: calcd. for $[C_{18}H_{20}O_5 + Na]^+$ 339.1203; found 339.1205. ^1H NMR: δ = 1.62 (dd, *J* = 13.8, *J'* = 3.0 Hz, 1 H, 9-H_a), 1.68 (br. d, *J* = 6.0 Hz, 1 H, 5-H), 1.76 (dd, *J* = 14.0, *J'* = 2.8 Hz, 1 H, 9-H_b), 1.92–1.95 (m, 1 H, 8a-H), 2.03 (br. d, *J* = 5.6 Hz, 1 H, 11-H), 2.06 (d, *J* = 1.6 Hz, 1 H, 10-H), 2.42–2.44 (br. s, 2 H, 4a-H and 8-H), 2.49–2.51 (br. s, 1 H, 5a-H), 2.79 (s, 1 H, 4-H), 3.66 (s, 3 H, C-3-$COOCH_3$), 3.70 (d, *J* = 7.6 Hz, 1 H, 1-H_a), 3.81 (s, 3 H, C-4-$COOCH_3$), 3.92 (dd, *J* = 7.6, *J'* = 0.8 Hz, 1 H, 1-H_b), 6.07 (pseudo t, *J* = 1.8 Hz, 2 H, 6-H and 7-H) ppm. ^{13}C NMR: δ = 28.5 (CH_2, C-9), 38.5 (CH, C-11), 46.3 (CH, C-4a), 47.9 (CH, C-5), 49.0 (CH, C-5a), 49.4 (CH, C-8), 52.0 (CH_3, C-3-COO*C*H_3), 52.3 (CH_3, C-4-COO*C*H_3), 52.4 (CH, C-8a), 53.3 (C, C-9a), 56.6 (CH, C-4), 59.5 (CH, C-10), 71.9 (CH_2, C-1), 88.0 (C, C-3), 136.3 (CH, C-7), 136.8 (CH, C-6), 170.4 (C, C-3-*C*$OOCH_3$), 171.5 (C, C-4-*C*$OOCH_3$) ppm.

Dimethyl (1*R*,4*S*)-7,7-Bis(iodomethyl)bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (15)

(a) Mixture of Alcohol 8, its C-7 Epimer, and Dimethyl (1*R*,4*S*)-7,7-Bis(hydroxymethyl)bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (13): *p*TsOH·H_2O (144 mg, 0.76 mmol) was added to a solution of diacetate **7** (1.34 g, 3.80 mmol) in anhydrous MeOH (13.5 mL), and the resulting solution was heated under reflux for 6.5 h. The solution was cooled to room temperature, and the solvent was removed under vacuum. The residue was dissolved in CH_2Cl_2 (30 mL). This solution was washed with saturated aqueous $NaHCO_3$ solution (2 × 8 mL) and brine (10 mL), dried (anhydrous Na_2SO_4), and concentrated in vacuo to give a mixture of diol **13** and tricyclic alcohols **8** and **9**, approximate ratio **13**/**8**/**9** 20:12:5 by ^1H NMR spectroscopy (by integration of the olefinic signals) (837 mg) as a yellow oil, which was used as such in the next step. The combined aqueous washings were extracted with CH_2Cl_2 (3 × 20 mL). These combined organic extracts were washed with brine (10 mL), dried (anhydrous Na_2SO_4), and concentrated in vacuo to give an orange oily residue (120 mg). This was a mixture of diol **13** and a stereoisomeric mixture of tricyclic alcohols **8** and **9**, approximate ratio **13**/**8**/**9** 10:1.3:1 by ^{1}H NMR spectroscopy.

(b) Mixture of Mesylate 10, its C-7 Epimer, and Dimethyl (1*R*,4*S*)-7,7-Bis(methylsulfonyloxymethyl)bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (14): Methanesulfonyl chloride (0.6 mL, 7.5 mmol) was added dropwise to a cold (0 °C, ice/water bath) and magnetically stirred solution of a mixture of diol **13** and alcohols **8** and **9** (837 mg, approximate ratio **13**/**8**/**9** 20:12:5, 1.69 mmol **13**, 1.43 mmol **8** + **9**) and anhydrous Et_3N (1.7 mL, 12.5 mmol) in anhydrous CH_2Cl_2 (34 mL) under an Ar atmosphere. The mixture was stirred at this temperature for 1.5 h. Saturated aqueous $NaHCO_3$ (2.5 mL) was added, and the organic phase was separated, and washed with saturated aqueous $NaHCO_3$ (3× 10 mL). The combined aqueous phases were extracted with CH_2Cl_2 (3× 20 mL). The combined organic phase and extracts were washed with water (15 mL) and brine (15 mL), dried (anhydrous Na_2SO_4), and concentrated in vacuo to give a mixture of dimesylate **14** and the tricyclic mesylates **10** and its C-7 epimer (1.15 g) as an orange oil.

(c) Dimethyl (1*R*,4*S*)-7,7-Bis(iodomethyl)bicyclo[2.2.1]hepta-2,5-diene-2,3-dicarboxylate (15): Powdered NaI (4.86 g, 32.4 mmol) was added to a solution of dimesylate **14** and monomesylates **10** and its C-7 epimer (1.15 g, 1.60 mmol **14** and 1.36 mmol **10** + C-7 epimer) in anhydrous acetone (36 mL). The mixture was heated under reflux for 16 h. The mixture was then cooled to room temperature, and the solvent was removed under reduced pressure. The resulting yellow solid residue (6.1 g) was subjected to column chromatography [silica gel 35–70 µm (20 g), hexane/EtOAc mixtures] to give, on elution with hexane/EtOAc, 97.5:2.5, diiodide **15** (574 mg, 31% from diacetate **7**) as a yellow oil, and on elution with hexane/EtOAc, 85:15, a stereoisomeric mixture of iodides **11** and its C-7 epimer (404 mg, 28% from diacetate **7**) as a pale yellow oil.

Analytical and spectroscopic data for **15**: R_f (silica gel, 10 cm, hexane/EtOAc, 3:7): 0.62. IR (ATR): $\tilde{\nu}$ = 2998 (m), 2950 (m), 2849 (w), 1731 (s), 1713 (s), 1629 (m), 1434 (s), 1324 (s), 1281 (s), 1255 (s), 1222 (s), 1202 (s), 1165 (m), 1100 (s), 1053 (m), 821 (m), 778 (m), 762 (m), 732 (m), 643 (m) cm^{-1}. HRMS: calcd. for $[C_{13}H_{14}I_2O_4 + H]^+$ 488.9054; found 488.9051; calcd. for $[C_{13}H_{14}I_2O_4 + Na]^+$ 510.8874; found 510.8864. ^{1}H NMR: δ = 3.716 (br. s, 2 H, *syn*-CH_2I), 3.720 (br. s, 2 H, *anti*-CH_2I), 3.81 [s, 6 H, C-2(3)-$COOCH_3$], 3.84 [t, J = 2.0 Hz, 2 H, 1(4)-H], 6.92 [pseudo t, J = 2.0 Hz, 2 H, 5(6)-H] ppm. NOESY: irradiation at δ = 6.92 [5(6)-H] ppm shows an NOE with the protons at δ = 3.84 [1(4)-H] and 3.716 (*syn*-C*H*$_2$I) ppm. ^{13}C NMR: δ = 11.5 (CH_2I), 12.3 (CH_2I), 52.3 (*C*H$_3$, 2 CO-O*C*H$_3$), 60.7 [CH, C-1(4)], 87.2 (C, C-7), 141.1 [CH, C-5(6)], 150.0 [C, C-2(3)], 164.6 [C, C-2(3)-*C*OOCH$_3$] ppm.

Dimethyl (1*R*,3a*S*,4*R*,4a*R*,4b*S*,5*R*,8*S*,8a*R*,9*S*,9a*s*,10a*s*,11*s*,13*S*)-1,3a,4,4a,4b,5,8,8a,9,10,10a-Decahydro-4*H*-5,8,9a-(epiethane[1,1,2]-triyl)-1,4,9-(epimethanetriyl)cyclopenta[*b*]fluorene-4,13-dicarboxylate (16): In a 10 mL flask, KH (30% in mineral oil; 134 mg, 1.0 mmol) was washed with anhydrous THF (5× 2 mL) under an Ar atmosphere. Anhydrous THF (2 mL) was added to the washed KH, and the suspension was cooled to 0 °C in an ice/water bath. Freshly distilled cyclopentadiene (0.1 mL, 73 mg, 1.1 mmol) was added, and the mixture was stirred at this temperature for 10 min. 18-Crown-6 (13 mg, 50 µmol, 5 mol-% relative to KH) was added, and the mixture was stirred at 0 °C for 10 min, and then at room temperature for 15 min. A solution of diiodide **15** (83 mg, 0.17 mmol) in anhydrous DMF (1 mL) was prepared in a 10 mL flask equipped with a magnetic stirrer bar and a reflux condenser, under an Ar atmosphere. The solution was cooled to 0 °C in an ice/water bath, and then part of the above solution of potassium cyclopentadienide (0.5 M; 0.75 mL, 0.37 mmol) was added dropwise. The mixture was stirred at 0 °C for 5 min, and at room temperature for 10 min, and then it was heated to 90 °C for 17 h. The mixture was cooled to room temperature, then MeOH (20 µL) was added, and the mixture was stirred for 10 min. Then, EtOAc (5 mL) and water (5 mL) were added and the organic phase was separated. The aqueous phase was extracted with EtOAc (4× 15 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ (3× 5 mL), water (2× 8 mL) and brine (8 mL), dried (anhydrous Na_2SO_4), and concentrated in vacuo to give crude diester **16** (73 mg) as a brown paste. This material was subjected to column chromatography [35–70 µm silica gel (1.5 g), hexane/EtOAc mixtures] to give, on elution with hexane/EtOAc, 99:1 to 95:5, diester **16** (30 mg, 49%) as a pale yellow oil. By treating this oil with Et_2O, and washing the solid thus formed with pentane, an analytical sample of **16** was obtained as a pale grey solid. m.p. 92.5–94 °C. R_f (silica gel, 10 cm, hexane/EtOAc, 3:7): 0.50. IR (ATR): $\tilde{\nu}$ = 3055 (w), 2944 (m), 2912 (m), 2842 (m), 1745 (s), 1727 (s), 1432 (m), 1315 (m), 1256 (s), 1241 (s), 1224 (s), 1152 (s), 1141 (s), 1106 (s), 1070 (s), 1038 (s), 1028 (s), 1010 (s), 741 (m), 709 (s), 665 (m) cm^{-1}. $C_{23}H_{24}O_4\cdot 1/3H_2O$ (370.45): C 74.57, H 6.71%; found C 74.63, H 7.00%. HRMS: calcd. for $[C_{23}H_{24}O_4 + H]^+$ 365.1747; found 365.1754. ^{1}H NMR: δ = 1.49 (d, J = 2.8 Hz, 2 H, 12-H$_2$), 1.54 (d, J = 2.8 Hz, 2 H, 10-H$_2$), 1.78–1.82 (m, 1 H, 11-H), 1.83 [s, 2 H, 4a(9)-H], 1.92–1.95 (m, 1 H, 10a-H), 1.98 [s, 2 H, 4b(8a)-H], 2.38–2.40 [m, 2 H, 5(8)-H], 2.69–2.71 [m, 2 H, 1(3a)-H], 3.59 [s, 6 H, C-4(13)-$COOCH_3$], 6.03 [t, J = 1.8 Hz, 2 H, 6(7)-H], 6.15 [t, J = 1.8 Hz, 2 H, 2(3)-H] ppm. ^{13}C NMR: δ = 34.3 (CH$_2$, C-10), 35.2 (CH$_2$, C-12), 42.27 [CH$_2$, C-4a(9)], 42.34 (C, C-9a), 49.3 [CH, C-5(8)], 51.2 [CH$_3$, C-4(13)-COO*C*H$_3$], 51.9 (CH, C-11), 53.5 (CH, C-10a), 54.7 [CH, C-4a(9)], 54.8 [CH, C-1(3a)], 64.6 [C, C-4(13)], 137.2 [CH, C-6(7)], 137.4 [CH, C-2(3)], 172.4 [C, C-4(13)-*C*O-OCH$_3$] ppm.

X-ray Crystal-Structure Determination of Compound 8: A colorless prism-like specimen of $C_{13}H_{16}O_6$, approximate dimensions 0.228 mm × 0.427 mm × 0.578 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured with a D8 Venture system equipped with a Multilayer monochromator and a Mo microfocus (λ = 1.54178 Å). A total of 4683 frames were collected. The total exposure time was 26.02 h. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 13259 reflections to a maximum θ angle of 72.20° (0.81 Å resolution), of which 4742 were independent (average redundancy 2.796, completeness: 98.7%, R_{int} = 3.42%, R_{sig} = 3.56%), and 4718 (99.49%) were greater than $2\sigma(F^2)$. The final cell constants of a = 5.8773(8) Å, b = 30.253(4) Å, c = 7.0235(9) Å, β = 100.153(3)°, V = 1229.3(3) Å^3, are based on the refinement of the *XYZ*-centroids of 120 reflections above $20\sigma(I)$ with $21.75° < 2\theta < 116.5°$. Data were corrected for absorption effects using the multi-scan method (SADABS). The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6325 and 0.7536. The structure was solved using the Bruker SHELXTL software package, and refined using SHELXL[18] and the space group $P2_1$, with Z = 4 for the formula unit, $C_{13}H_{16}O_6$. The final anisotropic full-matrix least-squares refinement on F^2 with 353 variables converged at $R1$ = 3.18%, for the observed data and $wR2$ = 8.72% for all data. The goodness-of-fit was 1.051. The largest peak in the final difference electron density synthesis was 0.278 eÅ^{-3} and the largest hole was –0.218 eÅ^{-3} with an RMS deviation of 0.044 eÅ^{-3}. On the basis of the final model, the calculated density was 1.449 g cm^{-3} and $F(000)$, 568 e (Table 1).

X-ray Crystal-Structure Determination of Compound 12: A colorless prism-like specimen of $C_{18}H_{20}O_5$, approximate dimensions 0.222 mm × 0.308 mm × 0.554 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured with a D8 Venture system equipped with a multilayer monochromator and a Mo microfocus (λ = 0.71073 Å). The frames were integrated with the Bruker SAINT software package using a Narror-frame algorithm. The integration of the data using a triclinic unit cell yielded a total of 15320 reflections to a maximum θ angle of 26.45° (0.80 Å resolution), of which 3007 were independent (average redundancy 5.095, completeness: 99.6%, R_{int} = 2.06%, R_{sig} = 1.39%), and 2847 (94.68%) were greater than $2\sigma(F^2)$. The final cell constants of a = 9.1711(3) Å, b = 9.8643(4) Å, c = 10.2303(4) Å, α = 66.5310(10)°, β = 64.5980(10)°, γ = 65.2720(10)°, V = 731.86(5) Å^3, are based on the refinement of the XYZ-centroids of reflections above $20\,\sigma(I)$. Data were corrected for absorption effects using the multi-scan method (SADABS). The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.6847 and 0.7454. The structure was solved using the Bruker SHELXTL software package, and refined using SHELXL[18] and the space group $P\bar{1}$, with Z = 2 for the formula unit, $C_{18}H_{20}O_5$. The final anisotropic full-matrix least-squares refinement on F^2 with 210 variables converged at $R1$ = 3.85%, for the observed data and wR_2 = 10.47% for all data. The goodness-of-fit was 1.081. The largest peak in the final difference electron density synthesis was 0.323 e Å^{-3} and the largest hole was –0.292 e Å^{-3} with an RMS deviation of 0.064 e Å^{-3}. On the basis of the final model, the calculated density was 1.435 g cm^{-3} and $F(000)$, 336 e (Table 1).

X-ray Crystal-Structure Determination of Compound 16: A colorless plate-like specimen of $C_{23}H_{24}O_4$, approximate dimensions 0.096 mm × 0.216 mm × 0.285 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured with a D8 Venture system equipped with a multilayer monochromator and a Mo microfocus (λ = 0.71073 Å). The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 46427 reflections to a maximum θ angle of 28.34° (0.75 Å resolution), of which 4298 were independent (average redundancy 10.802, completeness: 99.8%, R_{int} = 4.10%, R_{sig} = 1.82%), and 3654 (85.02%) were greater than $2\sigma(F^2)$. The final cell constants of a = 9.6672(4) Å, b = 10.5955(5) Å, c = 17.0896(7) Å, β = 99.698(2)°, V = 1725.45(13) Å^3, are based on the refinement of the XYZ-centroids of reflections above $20\,\sigma(I)$. Data were corrected for absorption effects using the multiscan method (SADABS). The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.7050 and 0.7457. The structure was solved using the Bruker SHELXTL Software Package, and refined using SHELXL[18] and the space group $P2_1/c$, with Z = 4 for the formula unit, $C_{23}H_{24}O_4$. The final anisotropic full-matrix least-squares refinement on F^2 with 258 variables converged at $R1$ = 3.95%, for the observed data and wR_2 = 10.72% for all data. The goodness-of-fit was 1.047. The largest peak in the final difference electron density synthesis was 0.364 e Å^{-3} and the largest hole was –0.265 e Å^{-3} with an RMS deviation of 0.058 e Å^{-3}. On the basis of the final model, the calculated density was 1.403 g cm^{-3} and $F(000)$, 776 e (Table 1).

Table 1. Experimental data[a] of the X-ray crystal-structure determination of compounds **8**, **12** and **16**.

	8[b]	**12**	**16**
Molecular formula	$C_{13}H_{16}O_6$	$C_{18}H_{20}O_5$	$C_{23}H_{24}O_4$
Molecular mass	268.26	316.34	364.42
Wavelength	1.54178 Å	0.71073 Å	0.71073 Å
Crystal system	monoclinic	triclinic	monoclinic
Space group	$P2_1$	$P\bar{1}$	$P2_1/c$
Unit cell dimensions			
a	5.8773(8) Å	9.1711(3) Å	9.6672(4) Å
b	30.253(4) Å	9.8643(4) Å	10.5955(5) Å
c	7.0235(9) Å	10.2303(4) Å	17.0896(7) Å
α	90°	66.5310(10)°	90°
β	100.153(3)°	64.5980(10)°	99.698(2)°
γ	90°	65.2720(10)°	90°
V	1229.3(3) Å^3	731.86(5) Å^3	1725.45(13) Å^3
Z	4	2	4
Density	1.449 Mg m^{-3}	1.435 Mg m^{-3}	1.403 Mg m^{-3}
Absorption coefficient	0.977 mm^{-1}	0.104 mm^{-1}	0.095 mm^{-1}
$F(000)$	568	336	776
Crystal size	0.578 × 0.427 × 0.228 mm^3	0.554 × 0.308 × 0.222 mm^3	0.285 × 0.216 × 0.092 mm^3
Theta range for data collection	2.921 to 72.200°	2.287 to 26.446°	2.271 to 28.339°
Index ranges	$-7 \leq h \leq 7$; $-37 \leq k \leq 37$; $-8 \leq l \leq 8$	$-11 \leq h \leq 11$; $-12 \leq k \leq 12$; $-12 \leq l \leq 12$	$-12 \leq h \leq 12$; $-14 \leq k \leq 14$; $-22 \leq l \leq 22$
Reflections collected	13259	15320	46427
Independent reflections	4742 [R_{int} = 0.0342]	3007 [R_{int} = 0.0206]	4298 [R_{int} = 0.0410]
Completeness to theta	67.679° (98.6%)	25.242° (99.9%)	25.242° (99.9%)
Max. and min. transmission	0.7536 and 0.6325	0.7454 and 0.6847	0.7457 and 0.7050
Data/restraints/parameters	4742/1/354	3007/0/210	4298/0/258
Goodness-of-fit on F^2	1.051	1.081	1.047
Final R indices [$I > 2\sigma(I)$]	R_1 = 0.0318, $wR2$ = 0.0870	R_1 = 0.0385, $wR2$ = 0.1033	R_1 = 0.0395, $wR2$ = 0.1017
R indices (all data)	R_1 = 0.0319, $wR2$ = 0.0872	R_1 = 0.0399, $wR2$ = 0.1047	R_1 = 0.0486, $wR2$ = 0.1072
Largest diff. peak and hole	0.278 and –0.218 e Å^{-3}	0.323 and –0.292 e Å^{-3}	0.364 and –0.265 e Å^{-3}

[a] Temperature: 100(2) K; absorption correction: semi-empirical from equivalents; refinement method: full-matrix least-squares on F^2; extinction coefficient: n/a. [b] Absolute structure parameter: 0.44(15).

CCDC-1063995 (for **8**), -1063996 (for **12**), and 1063997 (for **16**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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