Syntheses of Pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-4,8,11-trione, Pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-4,7,11-trione (D_3-Trishomocubanetrione), and 4,4,7,7,11,11-Hexanitro[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (D_3-Hexanitrotrishomocubane)

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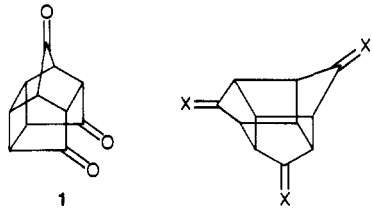
Recent interest in polycyclic cage systems that possess unusual symmetry properties[1] prompts us to report our syntheses of the title compounds (**1**, **2a**, and **2b**, respectively). Compounds **2a** and **2b** are members of a rare class of rigid, polycyclic organic molecules that belongs to the chiral D_3 point group.[1c-f,2]



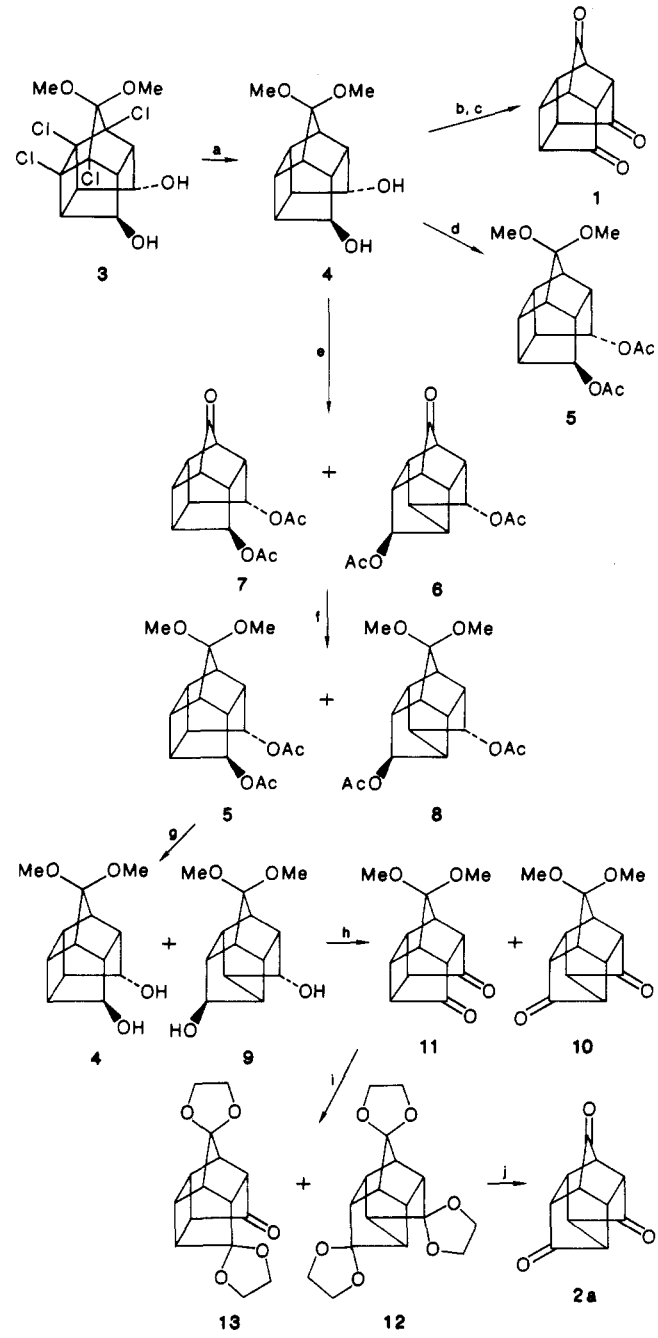
1 **2a** (X = O) **2b** [X = $(NO_2)_2$]

Our synthetic approach to **1** and **2a** is outlined in Scheme I. Readily available compound **3**[3] was employed as starting material. Hydrogenolysis of the carbon–chlorine bonds in **3** with lithium in *tert*-butyl alcohol[4] afforded diol **4**; hydrolysis of **4** followed by oxidation with pyridinium chlorochromate[5] afforded **1** in excellent yield.

Acid-promoted rearrangement of **4** to the D_3-trishomocubyl ring system was performed by using the method described by Smith and Barborak.[6] This rearrangement proceeded with concomitant hydrolysis of the ketal functionality to afford an intractable mixture of keto diacetates, presumably **6** and **7**,[6] which was characterized spectrally. Attempted hydrolysis of the mixture of **6** and **7** with hot aqueous potassium hydroxide solution afforded a water-soluble product that could not be recovered via liquid–liquid extraction with water-insoluble organic solvents. Alternatively, the ketone carbonyl groups in **6** and **7** were converted into the corresponding dimethyl ketals, thereby affording a mixture of products, **5** and **8**. Characterization of this product mixture was aided materially via comparison with authentic **5** (synthesized via esterification of **4** with acetic anhydride–pyridine reagent). The mixture of **5** and **8** was then reduced with lithium aluminum hydride in tetrahydrofuran, thereby affording an intractable mixture of (water insoluble) diols (**4** and **9**).

Oxidation of the mixture of **4** and **9** with pyridinium dichromate[5] afforded an intractable mixture of diketones (**10** and **11**) which was characterized spectrally. Separation of this mixture could be effected via its reaction with excess ethylene glycol in the presence of *p*-toluenesulfonic acid (catalytic amount). Whereas **10** could be converted

Scheme I[a,b]



[a] (a) Li, *t*-BuOH, THF, liquid NH_3, −33 °C (92%); (b) excess 10% aqueous HCl, reflux 4 h (100%); (c) PCC, CH_2Cl_2 (100%); (d) Ac_2O, pyridine, room temperature, 10 h (87%); (e) glacial HOAc, concentrated H_2SO_4, 150 °C (sealed tube), 42 h (55%); (f) HC(OMe)$_3$, TsOH (catalytic amount), overnight at room temperature (91%); (g) $LiAlH_4$, THF–Et_2O, room temperature, 6 h (95%); (h) PDC, CH_2Cl_2, room temperature, 4 days (90%); (i) $HOCH_2CH_2OH$, TsOH (catalytic amount), benzene, reflux 48 h [**12** (29%) + **13** (27%)]; (j) concentrated H_2SO_4, CH_2Cl_2, room temperature, 2 days (69%). [b] Stereochemical assignments for, e.g., **6**, **8**, and **9** were made on the basis of (i) simple mechanistic considerations and (ii) analysis of the ^1H and ^{13}C NMR spectra of these compounds.

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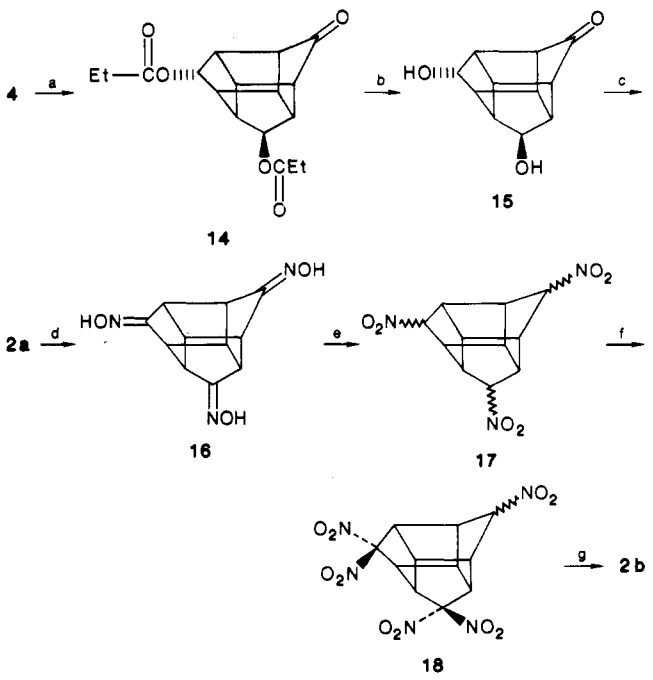
Scheme II[a,b]



[a] (a) $EtCO_2H$, concentrated H_2SO_4, 150 °C, 72 h, N_2 (51%); (b) Na, dry MeOH, room temperature, 1 h (100%); (c) PCC, CH_2Cl_2, room temperature, 2 h (46%); (d) NH_2OH·HCl, NaOAc, aqueous MeOH, 0 °C → room temperature, overnight (70%); (e) $(CF_3CO)_2O$, 90% H_2O_2, $NaHCO_3$, urea, CH_3CN, 70–75 °C, overnight (35%); (f) NaOH, aqueous MeOH, 3 h; then $K_3Fe(CN)_6$, aqueous $NaNO_2$, Et_2O, 1 h (65%); (g) NaOH, aqueous MeOH, 24 h; then $K_3Fe(CN)_6$, aqueous $NaNO_2$, Et_2O, 12 h (62%). [b] Stereochemical assignments for **14** and **15** were made on the basis of (i) simple mechanistic considerations and (ii) analysis of the ^1H and ^{13}C NMR spectra of these compounds.

smoothly into the corresponding tris(ethylene ketal) (i.e., **12**), compound **11** instead afforded bis(ketal) **13**, (Scheme I). Compound **13** was characterized via comparison with an authentic sample that was prepared via oxidation of the corresponding diol **4**. The behavior noted for **11** was expected by analogy with the known[7] propensity of pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-8,11-dione to afford the corresponding mono- (rather than the more sterically hindered bis-)ethylene ketal under similar conditions.

Upon dilution of the mixture of **12** and **13** thereby produced with methanol, compound **12** precipitated and could be isolated via suction filtration. Once isolated, this material proved to be insoluble in common organic solvents and could not be further purified by recrystallization. Characterization of **12** was accomplished via high-resolution mass spectral analysis. The synthesis of **2a** was then completed via hydrolysis of tris(ethylene ketal) **12** by using the method described by Scherer.[8]

Subsequently, it was found that by increasing the reaction time to 72 h, the acetic acid promoted rearrangement of **4** could be optimized to afford exclusively the rearranged keto diacetate **6**. More recently, we have found that the simple expedient of substituting propionic acid for acetic acid in this step leads similarly to exclusive formation of the corresponding rearranged diester (i.e., **14**, Scheme II) in 51% yield. The latter procedure possesses the advantage that the rearrangement can be carried out at atmospheric pressure, whereas the corresponding rearrangement in acetic acid solvent must be performed in a sealed ampule (see Experimental Section). Ester interchange, promoted via reaction of **14** with sodium in dry methanol, afforded the corresponding keto diol, **15**, in quantitative yield. Subsequent oxidation of **15** with pyridinium chlorochromate then afforded triketone **2a** in 46% yield.

There is considerable current interest in the synthesis and chemistry of energetic polynitropolycyclic "cage" compounds.[9] It was therefore of interest to utilize triketone **2a** as starting material for the synthesis of the corresponding D_3-hexanitrotrishomocubane (**2b**). Conversion of cage triketone **2a** to the corresponding D_3-hexanitro derivative (**2b**) was performed by using a sequence of reactions that follows directly from our previously published syntheses of polynitro-substituted 1,3-bishomocubanes (Scheme II).[9c,d] The results of a study of the thermal behavior and detonation properties of **2b** will be published elsewhere.[10]

Experimental Section

Melting points and boiling points are uncorrected. NMR chemical shifts are reported in parts per million (δ) downfield from internal tetramethylsilane. High-resolution mass spectra were obtained by the Midwest Center for Mass Spectrometry at the University of Nebraska—Lincoln. Low-resolution mass spectra were obtained by using a Hewlett-Packard Model 5970A GC/MS system.

4,4-Dimethoxypentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-*exo*,*exo*-8,11-diol (4). Into a three-necked round-bottom flask (500 mL) fitted with a dry ice condenser, a dropping funnel, and a drying tube were added dry tetrahydrofuran (THF, 100 mL) and lithium metal (3.60 g, 0.514 mol). Liquid ammonia (150 mL) was then added to the reaction mixture under a nitrogen atmosphere. A solution of diol **3**[3] (6.0 g, 16 mmol) and *tert*-butyl alcohol (14 g, 0.19 mol) in dry THF (100 mL) was then added dropwise to the reaction mixture during 30 min. The reaction temperature was maintained at −33 °C during the addition via application of an external cooling bath. After the addition had been completed, the cooling bath was removed and the reaction mixture was stirred overnight at ambient temperature. The reaction mixture was then cooled and quenched via addition of saturated aqueous ammonium chloride solution (100 mL). The aqueous layer was separated and extracted with THF. The combined organic layers were then filtered through a silica gel pad, and the filtrate was concentrated in vacuo. Diol **4** (3.6 g, 92%) was thereby obtained as a colorless solid. Recrystallization of this material from ethanol afforded pure **4** (3.0 g, 77%) as colorless fluffy needles, mp 198–199 °C: IR (KBr) 3500–3000 (s, br), 2980 (s), 2948 (s), 1466 (m), 1438 (m), 1337 (s), 1309 (s), 1166 (s), 1140 (s), 1114 (s), 1095 (s), 1068 (vs, br), 995 (s), 968 (s), 925 (m), 882 (m), 834 cm^{-1} (m); ^1H NMR (DMSO-d_6) δ 2.35–2.62 (m, 8 H), 3.15 (s, 3 H), 3.21 (s, 3 H), 4.13 (br s, 4 H; the intensity of this peak dropped to 2 H after the sample had been shaken with D_2O); ^{13}C NMR (DMSO-d_6) δ 39.44 (d), 41.71 (d), 46.59 (q), 47.18 (q), 50.11 (d), 50.22 (d), 69.67 (d), 114.42 (s); mass spectrum (70 eV), m/e (relative intensity) 238.1 (molecular ion, 10.9), 208.1 (16.5), 207.1 (100.0).

Anal. Calcd for $C_{13}H_{18}O_4$: C, 65.51; H, 7.62. Found: C, 65.39; H, 7.67.

Pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-4,8,11-trione (1). Dimethyl ketal **4** (500 mg, 2.1 mmol) was hydrolyzed by being

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refluxed in excess 10% aqueous hydrochloric acid solution for 4 h. Workup of the reaction mixture afforded a colorless microcrystalline solid in essentially quantitative yield. This material was dissolved in dry methylene chloride and oxidized with excess pyridinium chlorochromate (2.3 g, 10.7 mmol)[5]. Workup afforded trione **1** (ca. 390 mg, 100%) as a colorless microcrystalline solid, mp 265–270 °C: IR (CH_2Cl_2) 1765 (s), 1740 (br, vs), 1730 cm^{-1} (sh, s); ^1H NMR ($CDCl_3$) δ 2.7 (br m, 2 H), 3.1 (br m, 4 H), 3.6 (br m, 2 H); ^{13}C NMR ($CDCl_3$) δ 32.52 (d), 43.25 (d), 44.93 (d), 46.87 (d), 206.86 (s), 208.31 (s); mass spectrum (70 eV) *m/e* (relative intensity) 188.0473 (molecular ion, 100.0), 160.0518 ($C_{10}H_8O_2$, 23.8), 131.0495 (C_9H_7O, 92.7), 104.0623 (C_8H_8, 88.6), 103.0546 (C_8H_7, 59.7); exact mass calcd for $C_{11}H_8O_3$ M_r 188.0473, found (high-resolution mass spectrometry) M_r 188.0473.

4,4-Dimethoxy-*exo*,*exo*-8,11-diacetoxypentacyclo-[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (5). To a cooled (0 °C), stirred solution of **4** (0.476 g, 2.0 mmol) in pyridine (10 mL) was added acetic anhydride (0.612 g, 6.0 mmol). The cooling bath was then removed, and the reaction mixture was stirred at ambient temperature for 10 h. The reaction was then quenched via addition of crushed ice, and the resulting mixture was extracted with chloroform. The organic layer was washed successively with 5% aqueous hydrochloric acid, 5% aqueous sodium bicarbonate, and then brine. The organic layer was dried (anhydrous sodium sulfate) and filtered, and the filtrate was concentrated in vacuo. The resulting solid residue was recrystallized from acetone, thereby affording pure diacetate **5** (0.560 g, 87%) as a colorless microcrystalline solid, mp 165–166 °C: IR (KBr) 2988 (m), 2974 (sh, m), 2941 (sh, m), 2838 (m), 1732 (br, vs), 1381 (s), 1326 (s), 1274 (s), 1246 (br, vs), 1172 (m), 1148 (s), 1120 (s), 1104 (s), 1076 (s), 1061 (s), 1046 (vs), 974 (s), 916 (m), 884 (w), 823 cm^{-1} (w); ^1H NMR (7:1 $CDCl_3$–C_6D_6) δ 1.82 (s, 6 H), 2.37–2.91 (m, 8 H), 3.21 (s, 3 H), 3.25 (s, 3 H), 5.20 (br s, 2 H); ^{13}C NMR (7:1 $CDCl_3$–C_6D_6) δ 20.82 (q), 39.62 (d), 39.71 (d), 44.60 (d), 47.62 (d), 50.56 (q), 50.62 (q), 75.27 (d), 114.49 (s), 169.91 (s); mass spectrum (70 eV), *m/e* (relative intensity) 322.1 (molecular ion, 1.1), 138.9 (100.0).

Anal. Calcd for $C_{17}H_{22}O_6$: C, 63.34; H, 6.87. Found: C, 63.58; H, 7.00.

Acid-Promoted Rearrangement of 4.[6] A mixture of **4** (2.0 g, 8.4 mmol), glacial acetic acid (27.7 mL, 483 mmol), and concentrated sulfuric acid (0.228 g, 2.33 mmol) was sealed in a glass ampule and heated to 150 °C for 42 h. The reaction mixture was then cooled, and the ampule was opened. The reaction mixture was then treated with anhydrous sodium acetate (1.50 g, 18.3 mmol) and subsequently with activated charcoal. The resulting mixture was stirred for 1 h at ambient temperature and filtered, and the filtrate was concentrated in vacuo. The residue thereby obtained was dissolved in acetone and filtered, and the filtrate was concentrated in vacuo. The brown oil thereby obtained was further purified via elution chromatography (silica gel stationary phase, 1:1 acetone–hexane eluent). An inseparable mixture of keto diacetates (presumably[6] **6** and **7**, 1.5 g, 55%) was obtained as a yellow oil. This material was further purified via elution chromatography (silica gel stationary phase, 1:1 ethyl acetate–hexane eluent). A colorless microcrystalline solid was thereby obtained, mp 118–124 °C: IR (neat) 1725 (s), 1360 (m), 1235 (s), 1058 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 2.03 (s, 6 H), 2.18–2.34 (m, 2 H), 2.50–2.77 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 19.90 (q), 20.00 (q), 37.67 (d), 40.92 (d), 41.51 (d), 41.78 (d), 45.09 (d), 45.20 (d), 45.52 (d), 74.07 (d), 78.40 (d), 168.87 (s), 169.31 (s), 210.75 (s), 211.78 (s); mass spectrum (70 eV), *m/e* (relative intensity) 276.0 (molecular ion, 5.2), 43.0 (100.0); exact mass calcd for $C_{15}H_{16}O_5$ M_r 276.0997, found (high-resolution mass spectroscopy) M_r 276.0998. This material was used without further purification.

The acid-promoted rearrangement of **4** (2.0 g, 8.4 mmol) was repeated by using the same conditions described above with the exception that the sealed reaction mixture was heated to 150 °C for a longer time (i.e., 72 h). Workup of the reaction mixture as described above afforded a brown oil which was further purified via elution chromatography (silica gel stationary phase, 1:9 ethyl acetate–hexane eluent). Pure **6** (1.2 g, 52%) was thereby obtained as a colorless microcrystalline solid: mp 236 °C; IR (KBr) 1725 (s), 1365 (m), 1058 cm^{-1} (s); ^1H NMR ($CDCl_3$) δ 1.96 (s, 6 H), 2.29–2.30 (m, 2 H), 3.08–3.10 (m, 6 H), 5.06 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 22.95 (q), 38.39 (d), 43.81 (d), 44.40 (d), 48.16 (d), 76.60 (d), 171.93 (s), 215.12 (s); mass spectrum (70 eV), *m/e* (relative intensity) 276.0 (molecular ion, 5.2), 43.0 (100.0).

Conversion of a Mixture of 6 and 7 to a Mixture of the Corresponding Dimethyl Ketals (5 and 8). A mixture of **6** and **7** (1.50 g, 5.43 mmol) was dissolved in trimethyl orthoformate (5 mL, excess). A catalytic amount of *p*-toluenesulfonic acid (50 mg) was added, and the resulting mixture was stirred overnight at room temperature. The reaction mixture was then diluted with chloroform and quenched via addition of excess 5% aqueous sodium carbonate solution. The layers were separated, and the organic layer was washed successively with 5% aqueous sodium carbonate solution and brine and then dried (anhydrous sodium sulfate). The chloroform solution was then filtered, and the filtrate was concentrated in vacuo to afford a mixture of isomeric dimethyl ketals (crude **5** and **8**, 1.6 g, 91%) as a viscous oil. The oil was triturated with hexane and then allowed to stand overnight at room temperature, whereupon a microcrystalline solid was formed. The solid was recrystallized from acetone, thereby affording an inseparable mixture of isomeric dimethyl ketals **5** and **8** as a colorless microcrystalline solid, mp 154–155 °C: IR (neat) 1744 (vs), 1449 (br, m), 1367 (s), 1325 (s), 1240 (br, vs), 1067 (sh, vs), 1037 (vs), 939 (m), 915 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.74, 1.80 (two singlets, total 6 H), 2.02–2.39, 2.45–2.71 (two multiplets, total 8 H), 3.05, 3.06, 3.11 (three singlets, total 6 H), 4.67 (br s, 2 H), 5.01 (br s, 2 H); ^{13}C NMR ($CDCl_3$) **5** δ 20.62 (q), 39.35 (2C, d), 44.29 (d), 47.35 (d), 50.40 (2C, q), 74.98 (d), 114.20 (s), 169.60 (s); **8**: δ 20.49 (q), 39.74 (d), 44.81 (d), 44.94 (d), 46.83 (d), 49.82 (q), 78.24 (d), 112.38 (s), 170.06 (s); mass spectrum (70 eV), *m/e* (relative intensity) 322.1 (molecular ion, 0.6), 43.0 (100.0); exact mass calcd for $C_{17}H_{22}O_6$ M_r 322.1447, found (high-resolution mass spectroscopy) M_r 322.1402. This material was used without further purification.

Reduction of a Mixture of 5 and 8. A suspension of lithium aluminum hydride (0.454 g, 12 mmol) in dry ether (10 mL) was cooled to 0 °C via external application of an ice–salt bath. To the stirred suspension of lithium aluminum hydride in ether was added a solution of **5** and **8** (1.61 g, 5.0 mmol) in dry THF (10 mL), and the resulting mixture was stirred for 6 h at room temperature. The reaction mixture was then cooled and quenched via sequential addition of water (0.5 mL), 15% aqueous sodium hydroxide (0.5 mL), and water (1.5 mL). The reaction mixture was then filtered through a Fluorisil pad, and the residue was washed thoroughly with tetrahydrofuran. The filtrate was then dried (anhydrous sodium sulfate) and filtered, and the filtrate was concentrated in vacuo to afford a mixture of the corresponding diols (crude **4** and **9**, 1.1 g, 95%). Recrystallization of the crude product from acetone afforded an inseparable mixture of isomeric diols as a colorless microcrystalline solid, mp 162–166 °C: IR (KBr) 3500–3000 (s, br), 1443 (m, br), 1315 (s), 1165 (s), 1116 (s), 1061 cm^{-1} (vs); ^{13}C NMR (DMSO-d_6) δ 40.1 (d), 41.9 (d), 46.8 (d), 47.0 (d), 47.4 (d), 47.7 (d), 48.0 (d), 49.6 (q), 50.4 (q), 69.9 (d), 75.2 (d), 113.1 (s), 114.6 (s); mass spectrum (70 eV), *m/e* (relative intensity) 238.0 (molecular ion, 9.3), 207.0 (100.0). This material was used without further purification.

Oxidation of a Mixture of Diols 4 and 9. To a stirred, cooled (0 °C) solution of **4** and **9** (0.426 g, 2.0 mmol) in methylene chloride (10 mL) was added pyridinium dichromate (3.76 g, 10.0 mmol). The reaction mixture was allowed to warm slowly to ambient temperature and stirred for 4 days. The reaction mixture then was diluted with ether and filtered through a Fluorisil pad. The filtrate was concentrated in vacuo, affording a mixture of diones **10** and **11** (0.420 g, 90%) as a gummy semisolid. The product showed a single spot upon TLC analysis. Upon trituration with hexane, a colorless solid formed; recrystallization of this solid from ether afforded pure **10**, mp 119–120 °C: IR (KBr) 1761 (br, vs), 1319 (s), 1112 (s), 1066 cm^{-1} (s); ^{13}C NMR ($CDCl_3$) δ 35.38 (d), 41.75 (d), 43.84 (d), 44.55 (t), 50.34 (d), 114.07 (s), 209.47 (s); mass spectrum (70 eV), *m/e* (relative intensity) 234.1 (molecular ion, 44.1), 131.0 (100.0).

Anal. Calcd for $C_{13}H_{14}O_4$: C, 66.66; H, 5.98. Found: C, 66.40; H, 6.17.

Reaction of a Mixture of Diketones 10 and 11 with Excess Ethylene Glycol. A mixture of **10** and **11** (1.00 g, 4.27 mmol), ethylene glycol (1.324 g, 21.0 mmol), and *p*-toluenesulfonic acid (100 mg, catalytic amount) in benzene (20 mL) was refluxed for 48 h; water was removed azeotropically during the distillation via a Dean–Stark apparatus. At the conclusion of the reflux period,

chloroform was added to the reaction mixture, and the resulting mixture was washed with saturated aqueous sodium bicarbonate solution. The organic layer was dried (anhydrous sodium sulfate) and filtered, and the filtrate was concentrated in vacuo. A gummy semisolid (1.03 g) was thereby obtained. Upon trituration of the crude product with methanol, a solid precipitated which was subsequently collected by suction filtration and washed with several portions of methanol. Compound **12** was thereby obtained as a colorless microcrystalline solid (0.426 g, 29%): mp >330 °C; IR (KBr) 2982 (s), 2944 (m), 2874 (s), 1476 (w), 1338 (vs), 1279 (m), 1222 (s), 1179 (m), 1120 (vs), 1077 (vs), 1044 (s), 1014 (s), 974 (s), 953 (s), 932 (s), 884 (m), 869 (m), 804 (m), 762 cm^{-1} (m); mass spectrum (70 eV), *m/e* (relative intensity) 320.1 (molecular ion, 93.9), 183.1 (100.0); exact mass calcd for $C_{17}H_{20}O_6$ M_r 320.1268, found (high-resolution mass spectroscopy) M_r 320.1256.

The filtrate was combined with the methanol soluble material that remained after **12** had been isolated and then concentrated in vacuo. The residue (0.590 g) was further purified via preparative thick layer chromatography by using a Chromatotron (silica gel stationary phase, 1:1 ethyl acetate–hexane eluent), thereby affording **13** (0.400 g, 27%) as a viscous syrup which solidified after standing for several days at ambient temperature. The resulting solid was recrystallized from dichloromethane–hexane mixed solvent. Pure **13** was thereby obtained: mp 139 °C; IR (KBr) 1730 (s), 1485 (m), 1350 (m), 1325 (m); ^1H NMR ($CDCl_3$) δ 2.15–2.19 (m, 1 H), 2.35–2.37 (m, 1 H), 2.58–2.68 (m, 4 H), 3.00–3.02 (m, 1 H), 3.14–3.18 (m, 1 H), 3.78–3.95 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 33.84 (d), 39.42 (d), 41.01 (d), 42.99 (d), 44.69 (d), 47.87 (d), 48.12 (d), 49.70 (d), 64.48 (t), 65.06 (t), 65.13 (t), 65.72 (t), 113.81 (s), 121.77 (s), 213.48 (s); mass spectrum (70 eV), *m/e* (relative intensity) 276.1 (molecular ion, 46.0), 149.1 (100.0); exact mass calcd for $C_{15}H_{16}O_5$ M_r 276.0998, found (high-resolution mass spectroscopy) M_r 276.1003.

4,4:11,11-Bis(ethylenedioxy)pentacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-8-one (13). A mixture of **11** (200 mg, 0.86 mmol), ethylene glycol (266 mg, 4.19 mmol), and *p*-toluenesulfonic acid (10 mg, catalytic amount) in dry benzene (20 mL) was refluxed for 24 h; water was removed azeotropically during the distillation via a Dean–Stark apparatus. Workup of the reaction mixture by using the procedure described above for the corresponding reaction of a mixture of **10** and **11** with excess ethylene glycol afforded pure **13** (150 mg, 65%): mp 139 °C. The IR and NMR spectra of this material are identical with the corresponding spectral data given above for **13**.

Pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-4,7,11-trione (D_3-Trishomocubanetrione, 2a). Hydrolysis of **12** was carried out by using the method described by Scherer.[8] A solution of **12** (0.100 g, 0.312 mmol) in methylene chloride (10 mL) was poured slowly into concentrated sulfuric acid (0.5 mL), and the resulting mixture was stirred at ambient temperature for 2 days. The organic layer was separated and then shaken with excess solid sodium bicarbonate. The resulting mixture was then filtered, and the residue was washed with methylene chloride. The combined filtrates were concentrated in vacuo, thereby affording **2a** as a colorless microcrystalline solid (40 mg, 69%): mp 308–310 °C (sealed tube), [lit.[1f] mp 290–291 °C (sealed tube)]; IR (KBr) 1754 (s, br), 1279 (w), 1253 (w), 1224 (w), 1207 (w), 1147 (m), 906 (w), 882 (m), 812 (w, br), 752 cm^{-1} (w); ^1H NMR ($CDCl_3$) δ 2.46–2.54 (m, 6 H), 2.82–3.18 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 29.64 (d), 40.91 (d), 207.33 (s); mass spectrum (70 eV), *m/e* (relative intensity) 189.0 (M + 1, 8.1), 188.0 (molecular ion, 65.0), 131.0 (100.0); exact mass calcd for $C_{11}H_8O_3$ M_r 188.0497, found (high-resolution mass spectroscopy) M_r 188.0468.

***exo*,*exo*-7,11-Bis(propionyloxy)pentacyclo-[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecan-4-one (14).** A mixture of **4** (10 g, 42 mmol), propionic acid (180 mL, excess), and concentrated sulfuric acid (7 mL) was refluxed (150 °C) under nitrogen for 72 h. The reaction mixture was then cooled to room temperature, sodium acetate (21 g, excess) was added, and the resulting mixture was stirred at room temperature for 1 h. The reaction mixture was then filtered, and the filtrate was concentrated in vacuo to remove excess propionic acid. Methylene chloride was added to the residue, and the resulting solution was washed with saturated sodium bicarbonate solution (2 × 50 mL). The organic layer was dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography (silica gel stationary phase, 20% ethyl acetate–ligroin mixed solvent as eluent), thereby affording pure **14** (6.5 g, 51%). Analytically pure **14** was obtained via careful fractional recrystallization of this material from ether as a colorless microcrystalline solid: mp 93 °C; IR (KBr) 1760 (s), 1725 (s), 1460 (w), 1425 (w), 1340 (m), 1185 (s), 1085 cm^{-1} (m); ^1H NMR ($CDCl_3$) δ 1.13 (t, 6 H), 2.10–2.45 (overlapping q, 4 H and s, 2 H), 2.54 (m, 6 H), 5.10 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 8.59 (q), 27.12 (t), 38.24 (d), 42.14 (d), 45.72 (d), 46.18 (d), 78.82 (d), 173.3 (s), 212.7 (s); mass spectrum (70 eV), *m/e* (relative intensity) 304.1 (molecular ion, 1.1), 146.1 (29.7), 57.0 (100.0).

Anal. Calcd for $C_{17}H_{20}O_5$: C, 67.10; H, 6.58. Found: C, 67.20; H, 6.87.

4-Oxopentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-*exo*,*exo*-7,11-diol (15). To a solution of **14** (3.04 g, 10 mmol) in dry methanol (50 mL) was added sodium (ca. 20 mg). The resulting mixture was stirred at room temperature for 1 h. The reaction mixture was then neutralized via addition of oxalic acid, and the resulting mixture was filtered through a solid sodium bicarbonate pad. The filtrate was then concentrated in vacuo, thereby affording crude **15** (1.92 g, 100%) as a hygroscopic, gummy solid. Pure **15** was obtained via sublimation in vacuo (5 mm) at 120 °C; a colorless, gummy solid was thereby obtained: mp 100–102 °C; IR (KBr) 3500–3000 (s, br), 1715 (s, br), 1335 (m), 1265 (m), 1060 cm^{-1} (s, br); ^1H NMR (DMSO-d_6) δ 2.47 (m, 6 H), 3.25 (m, 4 H), 3.41 (br s, 2 H); ^{13}C NMR (DMSO-d_6) δ 38.26 (d), 44.57 (d), 46.52 (d), 48.54 (d), 76.31 (d), 215.9 (s); mass spectrum (70 eV), *m/e* (relative intensity) 192.0787 (molecular ion, 38.7), 146.0728 ($C_{10}H_{10}O$, 77.3), 117.0683 (C_9H_9, 100.0) 91.0546 (C_7H_7, 52.8), 82.0423 (C_5H_6O, 81.9); exact mass calcd for $C_{11}H_{12}O_3$ M_r 192.0783, found (high-resolution mass spectroscopy) M_r 192.0787.

Oxidation of 15. To a suspension of pyridinium chlorochromate (PCC, 17.8 g 83 mmol) and powdered 3-A molecular sieves (17.8 g) in methylene chloride (80 mL) was added **15** (3.20 g, 16.6 mmol). The mixture was stirred at room temperature and monitored by thin layer chromatography; oxidation of **15** was complete in ca. 2 h. Diethyl ether was then added, and the resulting mixture was filtered through a Florisil pad. The filtrate was then concentrated in vacuo, thereby affording **2a** (1.5 g, 46%). The material thereby obtained was purified via sublimation in vacuo (1 mm) at 180–190 °C. The sublimate was recrystallized from ethyl acetate to afford pure **2a** as a colorless microcrystalline solid: mp 308–310 °C (sealed tube). The IR, ^1H NMR, and ^{13}C NMR spectra of this material were identical in all respects with the corresponding spectra obtained for the material that was synthesized via hydrolysis of **12**, (vide supra).

4,4,7,7,11,11-Hexanitropentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (2b). Pentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane-4,7,11-trione tris(oxime) (**16**) was synthesized in 70% yield via reaction of **2a** (400 mg, 2.12 mmol) with hydroxylamine hydrochloride; the method described by Corey et al. was employed for this purpose.[11] To a vigorously stirred, heated (75–90 °C) mixture of **16** (116 mg, 0.50 mmol), sodium bicarbonate (0.945 g, 11.3 mmol), and urea (0.150 g, 2.50 mmol) in acetonitrile (13.5 mL) was added dropwise during 10 min a solution of 90% hydrogen peroxide (0.1 mL, 4 mmol) and trifluoroacetic anhydride (0.6 mL, 4 mmol) in acetonitrile (1.5 mL). After the addition of the oxidizing agent had been completed, the mixture was heated (75–90 °C) with stirring overnight. The reaction mixture was then concentrated in vacuo, and the residue was diluted with cold water (25 mL). The resulting mixture was chilled and filtered, and the filtrate was concentrated in vacuo, thereby affording crude **17** (mixture of epimers, 45 mg, 35%). The crude product was purified via column chromatography (silica gel stationary phase, 20% ethyl acetate–ligroin mixed solvent as eluent), thereby affording pure **17** (mixture of isomers, 20 mg, 16%) as a colorless microcrystalline solid: mp 195–200 °C; IR (KBr) 1535 (s), 1385 (m), 765 cm^{-1} (w); ^1H NMR (DMSO-d_6) δ 2.89 (m, 2 H), 3.41 (m, 6 H), 5.26 (m, 3 H); mass spectrum (70 eV), *m/e* (relative intensity) (no molecular ion) 235.2 (7.1), 159.1 (48.5), 141.2 (100.0), 129.2 (50.7), 128.2 (54.1), 115.2 (72.3), 91.1 (69.6); exact mass calcd for $C_{11}H_{12}N_3O_6$ (M_r + H)

(11) Corey, E. J.; Melvin, L. S.; Haslanger, M. F. *Tetrahedron Lett.* **1975**, *3117*.

282.0726, found (high-resolution mass spectrometry) (M_r + H) 282.0725. This material was used without further purification to complete the synthesis of **2b**.

Compound 17 was further nitrated by using the procedure reported by Kornblum and co-workers.[12] Thus, **17** (35.0 mg, 0.125 mmol) was added under nitrogen to a rapidly stirred solution which contained sodium hydroxide (19 mg, 0.48 mmol), methanol (0.8 mL), and water (1.0 mL). The resulting mixture was allowed to stir under nitrogen at room temperature for 3 h, at which time a clear yellow solution was obtained. This solution was then added dropwise under nitrogen to a vigorously stirred solution of potassium ferricyanide (670 mg, 2.04 mmol) and sodium nitrite (280 mg, 4.05 mmol) in water (4.1 mL). Diethyl ether (8.2 mL) was then added, and the resulting mixture was stirred for 1 h. The ether layer was separated, and the aqueous layer was extracted twice with ether. The combined organic extracts were dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo to afford 4,7,7,11,11-pentanitropentacyclo[6.3.0.0^{2,6}.0^{3,10}.0^{5,9}]undecane (**18**, 30 mg, 65%) as a colorless microcrystalline solid: mp 237-239 °C; IR (KBr) 1565 (s, br), 1375 (m), 1335 (m), 1205 (w), 800 cm^{-1} (s); ^{1}H NMR (DMSO-d_6) δ 3.09-3.81 (m, 8 H), 5.39 (s, 1 H); ^{13}C NMR (DMSO-d_6) δ 42.95 (d), 43.35 (d), 44.20 (d), 44.66 (d), 45.87 (d), 45.95 (d), 46.00 (d), 48.05 (d), 90.92 (d), 129.07 (s), 129.43 (s); exact mass calcd for $C_{11}H_{10}N_5O_{10}$ (M_r + H) 372.0428, found (high-resolution mass spectrometry) (M_r + H) 372.0428. This material was used without further purification to complete the synthesis of **2b**.

Further nitration of **18** was carried out again by using the Kornblum[12] procedure with a somewhat longer reaction time than was employed above. Thus, **18** (15 mg, 10 mmol) was added under nitrogen to a rapidly stirred solution which contained sodium hydroxide (5.0 mg, 0.13 mmol), methanol (0.2 mL), and water (0.2 mL). The resulting mixture was allowed to stir under nitrogen at room temperature for 24 h. The resulting yellow solution was added dropwise under nitrogen to a vigorously stirred solution of potassium ferricyanide (90 mg, 0.27 mmol) and sodium nitrite (40 mg, 0.58 mmol) in water (1.4 mL). Diethyl ether (2.8 mL) was then added, and the resulting mixture was stirred overnight at room temperature. The ether layer was separated, and the aqueous layer was extracted with ethyl acetate. The combined organic extracts were dried (anhydrous magnesium sulfate) and filtered, and the filtrate was concentrated in vacuo. The residue was purified via column chromatography by using silica gel as stationary phase (5% ethyl acetate-ligroin mixed solvent as eluent), thereby affording pure **2b** (10 mg, 62%) as a colorless microcrystalline solid: mp 197-200 °C dec; IR (KBr) 1565 (s), 1365 (w), 1335 (w), 1315 (w) 800 cm^{-1} (m); ^{1}H NMR (DMSO-d_6) δ 3.30-3.38 (bs, 6 H), 3.80 (s, 2 H); ^{13}C NMR (DMSO-d_6) δ 47.55 (d), 47.95 (d), 123.17 (s); mass spectrum (70 eV), m/e (relative intensity) (no molecular ion) 278.0442 ($C_{11}H_8N_3O_6$, 3.2), 139.0539 ($C_{11}H_7$, 25.5), 128.0586 ($C_5H_8N_2O_2$, 83.5), 115.0538 (C_9H_7, 100.0); exact mass calcd for $C_{11}H_8N_6O_{12}$ M_r 417.0278, found (high-resolution chemical ionization mass spectroscopy) M_r 417.0259.

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Registry No. 1, 110243-21-5; **2a**, 108635-94-5; **2b**, 110270-87-6; **3**, 101312-34-9; **4**, 110311-61-0; **5**, 110243-22-6; **6**, 110243-23-7; **7**, 110243-24-8; **8**, 110243-25-9; **9**, 110243-26-0; **10**, 110243-27-1; **11**, 110243-28-2; **12**, 110243-29-3; **13**, 110243-30-6; **14**, 110243-31-7; **15**, 110243-32-8; **16**, 110243-33-9; **17**, 110243-34-0; **18**, 110243-35-1; propionic acid, 79-09-4.

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A Direct Route for the Synthesis of (*E*)-3-Alkyl-4-oxo-2-butenoic Acid Esters

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Esters of (*E*)-3-alkyl-4-oxo-2-butenoic acid (1) are useful intermediates in organic synthesis. Thus, compound **1a** is an important synthon in many retinoic acids syntheses;[1] moreover this ester has recently been used as a dienophile.[2] We required ester **1b** as a diene precursor in order to synthesize aklavinone.[3] Although several syntheses of compound **1a** have already been published[4] none are general methods that can easily be used to prepare ester **1b**. In this paper we report a direct route to *E* esters 1 based on the condensation of aliphatic aldehyde enamines **2** with glyoxylic acid esters.

It has previously been shown that aldol condensation of glyoxylic acid with aliphatic or cyclic ketones led, either in basic or acid medium, to α-hydroxy-γ-oxo carboxylic acids and/or γ-oxo-α,β-unsaturated carboxylic acids in low to moderate yields.[5] However, this process suffers from severe drawbacks (mainly self-aldolization) when aliphatic aldehydes are used instead of ketones, and it is not therefore surprising that so few successful examples of such a condensation have been described in the literature. In 1972, H. H. Inhoffen[6] reported that the aldol condensation of substituted cyclohexylacetaldehydes with glyoxylic acid in acid medium yielded butenolides **3** (Y = OH). Similarly, L. Weiler[7] described in 1979 the condensation of cyclopentylacetaldehyde with glyoxylic acid in basic medium; the crude product yielded 73% of butenolide **3** (R^2 = cyclopentyl, Y = OH) after acid treatment. More recently, C. G. Wermuth[8] reported that condensation of aliphatic aldehydes with glyoxylic acid in the presence of morpholine led, depending on the experimental conditions, to α,γ-dimorpholinobutanolides and/or butenolides **3** (Y = OH).

Somewhat surprisingly, none of the three previous papers mentioned the isolation of 3-formyl 2-enoic acids although the formation of these compounds is highly probable in such condensations. We therefore decided to reinvestigate this reaction in order to obtain the useful target esters 1. For this purpose, we first examined the aldol condensation of butyraldehyde with glyoxylic acid in basic medium (1.15 equiv of KOH in MeOH). After acid treatment, we observed the formation of the desired *E* acid 1 (R^1 = H, R^2 = Et) and butenolide **3b** (Y = OH) isolated with 40% and 10% yields, respectively. Although this acid could be efficiently transformed into *E* ester **1b**, the whole process could not be generally applied, being hampered by the self-condensation of starting aldehydes and/or the formation of large amounts of undesired butenolides **3**.

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