JOC The Journal of Organic Chemistry

J. Org. Chem., 1998, 63(4), 1098-1101, DOI:10.1021/jo971515k

Supporting Information: Experimental Section

1,2-Bis(trimethylsiloxy)cyclohexene (4, n=3). A solution of 10 g (57 mmol) of dimethyl adipate (Aldrich, 98%) and 5 mL (4.3 g, 40 mmol) of TMSCl in 150 mL dried toluene was added to a stirred suspension of 6.9 g (0.3 mol) Na sand and 35 mL (30 g, 0.28 mol) of TMSCl in 400 mL dried toluene at 45-50 °C over 3 h. The reaction mixture was refluxed for 16 h. The precipitate from the cooled and filtered reaction was rinsed with 100 mL dried toluene, and the rinse was combined with the filtrate. The toluene was removed at atmospheric pressure, and the residue was distilled (10 mmHg) using a short path distillation column. A slightly yellow liquid (12.6 g, 87%) was collected at about 100 °C: GC purity 92%. The procedure was repeated twice, yielding 12.4 g (85%) and 13.0 g (90%) with GC purity of 96% and 95%, respectively. The combined material was fractionally distilled at 10 mmHg and 30.6 g (70%) of **4** (n=3) was collected between 99-101 °C as a pale yellow liquid; GC purity 94%; lit. bp 110 °C (10 mm Hg),[7j] 66-70 °C (2 mm Hg, Kugelrohr),[15] 102-105 °C (10-12 mm Hg);[16] IR (neat) 1700, 1255, 1220, 1130, 960, 910, 850 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.06 (m, 4H), 1.59 (m, 4H), 0.16 (s, 18H)(lit.[15]); GC-MS m/z 262 (M + 4), 261, 260, 259, 258 (M^+, base), 215, 148, 147, 142, 75, 73, 45. This compound was unstable to column chromatography and to the presence of nucleophilic solvents. On standing, it was slowly converted to 2-hydroxycyclohexanone (identical to a sample intentionally prepared by hydrolysis[16]), which becomes a crystalline dimer on standing.[1] Methanolysis is also rapid to produce the methylated dimer.[1]

1,2-Bis(trimethylsiloxy)cycloheptene (4, n = 4). A solution of 10.7 g (57 mmol) of dimethyl pimelate (Aldrich, 97%) and 5 mL (4.3 g, 40 mmol) of TMSCl in 200 mL dried toluene was added over 5 h to a stirred suspension of 7.2 g (0.31 mol) Na sand and 40 mL (34.2 g, 0.32 mol) of TMSCl in 400 mL of dried toluene at 50 °C. The reaction was refluxed with stirring for 16 h. After cooling, the reaction was filtered and the precipitate rinsed with 100 mL dried toluene. The combined toluene solutions were

distilled to remove solvent. The procedure was repeated with addition over 3 h at 80 °C. The two residues were combined and distilled at 15 mmHg using a short path distillation column. The product was a pale yellow liquid (21.2 g, 73%), bp 120-125 °C (lit. 97 °C (3 mm Hg),[7j] 104-106 °C (4 mm Hg),[6] 117 °C (13 mm Hg)[13]); GC purity 87 %; IR (neat) 1682, 1447, 1250, 1204, 1073, 891, 841 cm^{-1} (lit.[6] 1670, 1440, 1250, 1240, 1200 cm^{-1}); ^1H NMR ($CDCl_3$) δ 2.20 (m, 4H), 1.62 (m, 6H), 0.16 (s, 18H) (lit.[6] δ 2.29-2.08 (m, 4H), 1.69-1.44 (m, 6H), 0.20 (s, 18H)); GC-MS m/z 276, 275, 274, 273, 272 (M^+, base), 243, 157, 155, 148, 147, 75, 74, 73, 45.

1,2-Bis(trimethylsiloxy)cyclooctene (4, n = 5). A solution of 11.7 g (58 mmol) of dimethyl suberate (Aldrich, 99%) and 20 mL (17.1 g, 0.16 mol) TMSCl in 190 mL dried toluene was added over 28 h to a stirred suspension of 7.3 g (0.32 mol) of Na sand and 25 mL (21.4 g, 0.20 mol) of TMSCl at reflux. The reaction was refluxed an additional 18 h. The cooled reaction mixture was filtered and the precipitate washed with 200 mL dried toluene. The combined toluene solutions were concentrated under reduced pressure and the residue distilled using a short path distillation column. Product was a pale yellow liquid (12.1 g, 74 %), GC purity 94 %; bp 130-139 °C (15 mm Hg) (lit.[7j] 80 °C (0.5 mm Hg)); IR (neat) 1676, 1455, 1245, 1212, 830 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.20 (m, 4H), 1.62 and 1.54 (2m, 8H), 0.18 (s, 18H).

1,2-Bis(trimethylsiloxy)cyclononene (4, n =6). Dimethyl azelate (Pfaltz & Bauer, 90 %) was purified by fractional distillation at 20 mm Hg. A solution of 13.8 g (64 mole) of dimethyl azelate (GC purity 94.5%) and 20 mL (17.1 g, 0.16 mol) of TMSCl in 200 mL dried toluene was added dropwise over 25 h to a stirred suspension of 7.2 g (0.31 mol) Na sand and 25 mL (21.4 g, 0.20 mol) of TMSCl in 300 mL dried toluene at reflux. The reaction was refluxed an additional 23 h and worked up as previously described. The residue was distilled by a short path distillation apparatus with a 16 cm Vigreux column. Product was a pale yellow liquid (7.2 g, 40%), GC purity 85 %, bp 140-150 °C (15 mm Hg) (lit.[13] 140-142 °C (14 mm Hg)); IR (neat) 1709, 1678, 1468, 1445, 1250, 1220, 1072,

844 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.21 (m, 4H), 1.56 (br m, 10H), 0.19 (s, 18H); GC-MS m/z 303, 302, 301, 300 (M^+), 182, 169, 155, 147, 142, 129, 75, 73 (base), 45. Pot residue indicated the presence of a dimer from intermolecular condensation.[13]

1,6-Bis(trimethylsiloxy)bicyclo[4.1.0]heptane (5, n =3). As described above, 100 mL (0.11 mol) of diethylzinc (15 wt% (1.1 M) in toluene) was added to a solution of 10.4 g (40 mmol) of cyclohexene **4** (n =3) (GC purity 97%) and 8.2 mL (27.3 g, 0.10 mol) diiodomethane in 50 mL toluene over 1 h at 0 °C. The reaction was stirred for 2 h at rt and worked up as described earlier. The residue obtained after removal of solvents was distilled using a short path distillation column. Product distilling at 118-123 °C (15 mm Hg) (lit.[13] 63 °C (0.2 mm Hg)) was 9.1 g (86%) of the desired colorless liquid **5** (n = 3), GC purity 97 %; IR (neat) 3085, 1466, 1249, 1212, 840 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.95 (m, 4H), 1.44 (m, 2H), 1.13 (m, 2H), 0.79 (d, J = 6, 1H), 0.57 (d, J = 6, 1H), 0.10 (s, 18H); ^{13}C NMR ($CDCl_3$) δ 58.7, 33.7, 24.1, 22.0, 1.4, 1.3; GC-MS m/z 275, 274, 273, 272 (M^+), 271, 244, 243 (base), 215, 183, 182, 169, 167, 155, 149, 148, 147, 143, 133, 81, 75, 74, 73, 45.

1,7-Bis(trimethylsiloxy)bicyclo[5.1.0]octane (5, n =4). As in the general procedure, 64 mL of a solution of diethylzinc (1.1 M, 0.10 mol) in toluene was added to a stirred solution of 10.1 g (37 mmol) of cycloheptene **4** (n = 4) (GC purity 87 %) and 8.1 mL (26.9 g, 0.10 mol) of diiodomethane in 50 mL dried toluene at 0 °C over 1 h. The reaction was stirred for 2 h at rt, then worked-up as described. A second batch was prepared in a similar manner using 9.8 g (36 mmol) of **4** (n = 4) (GC purity 87 %). The combined residues were distilled using a short path column to yield 15.1 g (83 %) of the desired product as a colorless liquid; GC purity 89 %; bp 132-134 °C (15 mm Hg) (lit.[6] 104-106 °C (4 mm Hg)); IR (neat) 3078, 1455, 1251, 841 cm^{-1} (lit.[6] 3080, 2920, 2850, 1450, 1240, 830 cm^{-1}); ^1H NMR ($CDCl_3$) δ 2.25 (m, 2H), 1.78 (m, 3H), 1.52 (m, 2H), 1.21 (m, 3H), 0.89 (d, J = 7, 1H), 0.74 (d, J = 7, 1H), 0.18 (s, 18H) (lit.[6] ($CDCl_3$) δ 2.40-2.00 (m, 4H), 1.80-1.20 (m, 6H), 0.90 (d, J = 7, 1H), 0.75 (d, J = 7, 1H), 0.20 (s, 18H));

GC-MS m/z 289, 288, 287, 286 (M^+), 285, 244, 243, 215, 196, 155, 147, 75, 73 (base), 45.

1,8-Bis(trimethylsiloxy)bicyclo[6.1.0]nonane (5, n =5). Following the general procedure, 96 mL (0.11 mol) of a 1.1 M solution of 15 wt% diethylzinc in toluene was added over 1.5 h to a stirred solution of 11.4 g (40 mmol) of cyclooctene **4** (n = 5) (GC purity 93 %) and 7.8 mL (25.9 g, 97 mmol) of diiodomethane in 50 mL dried toluene at 0 °C. The reaction was stirred for 2.8 h at rt. The distillate was 9.6 g (86 %) of product; bp 134-144 °C (15 mm Hg); GC purity 90 %; IR (neat) 3076, 1463, 1250, 839 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.13 (d of d of d, J = 16, 8, and 4, 2H), 1.74 (m, 2H), 1.61 (m, 2H), 1.31 (m, 4H), 1.09 (m, 2H), 0.75 (d, J = 6, 1H), 0.38 (d, J = 6, 1H), 0.17 (s, 18H).

1,9-Bis(trimethylsiloxy)bicyclo[7.1.0]decane (5, n =6). Using the general procedure, 75 mL (82 mmol) of a solution of diethylzinc in toluene (15 wt%, 1.1 M) was added over 1 h to a stirred solution of 12.5 g (42 mmol) of cyclononene **4** (n = 6) (GC purity 80 %) and 8.4 mL (27.9 g, 104 mmol) of diiodomethane in 50 mL of dried toluene at 0 °C. The reaction was stirred overnight at rt. The distillate yielded 4.1 g (39 %) of product (GC purity 76%), bp 152-157 °C (15 mm Hg); IR (neat) 3075, 1475, 1249, 839 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.11 (d of d of d, 2H), 1.90 (m, 2H), 1.67-1.10 (3m, 12H), 0.74 (d, J = 6.6, 1H) 0.29 (d, J = 6.3, 1H), 0.17 (s, 18H).

Cycloheptan-1,3-dione (3, n = 3). A sample of bicycloheptane **5** (n = 3) (9.0 g, 33 mmol, GC purity 94 %) was added to a stirred solution of 22 g (0.14 mol) of anhyd $FeCl_3$ in 30 mL DMF. The reaction mixture was stirred for 16 h at 60 °C. The reaction was then poured into 200 mL of 10 % aq. HCl and extracted with 4 x 150 mL $CHCl_3$. The combined organic layers were washed with 10 % aq. HCl (2 x 100 mL) followed by 100 mL brine. The $CHCl_3$ and residual DMF were removed under reduced pressure. The crude dione was distilled at 112 °C (10 mm Hg) to collect 2.9 g (74%, GC purity 98%) of distillate (lit. 119-120 °C (15 mm Hg)[7c], 119-122 °C (15 mm Hg)[7a], 114-120 °C (9-10 mm Hg)[7b], 122 °C (10 mm Hg)[7e]). A 1 g portion of the dione was purified by column

chromatography using Whatman Partisil prep 40 (53 micron) silica gel and a 90/5/5 mixture of n-hexane, THF, and 2-propanol. Purified dione was obtained as a colorless liquid (0.5 g, GC purity 100 %): TLC (silica gel GF, 90/5/5 n-hexane/ THF/ 2-propanol, short wave UV) three trace spots and one minor spot; IR (neat) 3400, 1720, 1700, 1460, 1210 cm^{-1} (lit. (CCl_4)[7a] 3415 (very weak), 1728 and 1704 (strong), 929 cm^{-1}, (film)[7b] 1724, 1709 cm^{-1}); ^1H NMR ($CDCl_3$) δ 3.61 (s, 2H), 2.58 (m, 4H), 1.96 (m, 4H), (lit. ($CDCl_3$)[7c] δ 3.53 (s, 2H), 2.46 (m, 4H), 2.1-1.33 (m, 4H), (CCl_4)[7a] δ 3.47 (s, 2H), 2.52 (m, 4H), 2.00 (m, 4H)); GC-MS m/z 127, 126 (M^+), 98, 97, 84, 83, 70, 69, 68, 56, 55 (base), 43, 42, 41, 39. Anal. Calcd for $C_7H_{10}O_2$: C, 66.65; H, 7.99. Found: C, 66.56; H, 7.96.

Cyclooctan-1,3-dione (3, n = 4). As described in the general procedure, a solution of 12.6 g (44 mmol, GC purity 89 %) of bicyclooctane **5** (n = 4) in 20 mL DMF was added to a stirred solution of 23 g (0.14 mol) anhyd $FeCl_3$ in 50 mL DMF. The reaction was stirred for 1.5 h at 60-65 °C. The crude dione (4.8 g, 87 %, GC purity 98 %) was obtained after work-up. Flash chromatography (85:15 n-hexane:acetone) yielded product as a colorless amorphous solid (GC purity 99.9 %); lit. bp 88 °C (3 mm Hg)[6], 95 °C (3 mm Hg)[7e], 110-112 °C (8 mm Hg)[7f], lit.mp 46-48 °C [7f]; IR (neat) 3390, 1712 (sh), 1687 cm^{-1} (lit.[6] 2920, 2850, 1650, 1380, 1250, 1090, 730, 650 cm^{-1}); ^1H NMR ($CDCl_3$) δ 3.50 (s, 2H), 2.48 (m, 4H), 1.80 (m, 4H), 1.63 (m, 2H) (lit.[6] δ 3.5 (s, 2H), 2.6-2.3 (m, 4H), 1.9-1.5 (m, 6H)); ^{13}C NMR ($CDCl_3$) δ 206.1, 58.8, 43.9, 27.2, 24.0; GC-MS m/z 141, 140 (M^+), 112, 98, 97, 84, 83, 70, 69, 58, 56, 55 (base), 43, 42, 41, 39.

Cyclononan-1,3-dione (3, n = 5). As described above, a solution of 10.2 g (34 mmol, GC purity 89 %) of bicyclononane **5** (n = 5) in 20 mL DMF was added to a stirred solution of 22 g (0.14 mol) anhyd $FeCl_3$ in 50 mL DMF. The reaction was stirred for 3 h at 60-70 °C. The reaction was extracted and reextracted as described prior to bulb-to-bulb distillation (80-90 °C, 3 mm Hg). This dione (4.6 g, 100 %, GC purity 90 %) was combined with dione prepared in the same manner from a second reaction (4.6 g, 100 %, GC purity 88 %) and redistilled bulb-to-bulb. Flash chromatography (90:10 n-hexane:

acetone) produced pure product as a colorless amorphous solid: GC purity 100 %; lit. bp 99 °C (3 mm Hg)[7e], 121-123 °C (10 mm Hg)[7f]; IR (neat) 3391, 1718, 1691 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.66 (s, 2H), 2.52 (m, 4H), 1.78 (m, 4H), 1.42 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 205.3, 61.7, 42.5, 25.2, 23.7; GC-MS m/z 155, 154 (M^+), 126, 112, 111, 108, 98, 97, 94, 84, 83, 79, 71, 70, 69, 68, 67, 58, 56, 55 (base), 53, 43, 42, 41, 40, 39; UV (n-hexane) λ_{max} 206 nm (ε 886), broad band between 240-350 nm with max at 282 nm (ε 59), 300 (ε 82), 311 (ε 100), 333 (ε 59) (lit.[7h] (CH_2Cl_2, n-hexane) transparent).

Cyclodecan-1,3-dione (3, n = 6). As described, a solution of 9.9 g (31 mmol, GC purity 72 %) of bicyclodecane **5** (n = 6) in 20 mL DMF was added to a stirred solution of 21 g (0.13 mol) of anhyd $FeCl_3$ in 50 mL DMF. The solution was stirred at 60-70 °C for 3.5 h. After work-up, the crude dione was distilled (bulb-to-bulb, 3 mm Hg) at 80-100 °C. The product (4.9 g, 129 %, GC purity 74 %) was redistilled bulb-to-bulb and purified by flash chromatography (85:10:5 hexanes: THF: 2-propanol) to give a slightly yellow liquid (GC purity 98 %); lit. bp 80 °C (0.1 mm Hg)[12], 118-123 °C (10 mm Hg)[7f]; IR (neat) 3390, 1723 (sh), 1691 cm^{-1} (lit.[7f] (CH_2Cl_2) 1712 (sh), 1695 cm^{-1}); ^1H NMR ($CDCl_3$) δ 3.65 (s, 2H), 2.55 (m, 4H), 1.80 (m, 4H), 1.38 and 1.28 (m, m, 6H); ^{13}C NMR ($CDCl_3$) δ 205.8, 62.0, 40.6, 26.0, 24.1, 23.2; GC-MS m/z 169, 168 (M^+), 150, 125, 112, 111, 110, 108, 98 (base), 97, 93, 84, 83, 82, 81, 71, 70, 69, 68, 67, 58, 56, 55, 53, 43, 42, 41, 39.

3-Ethoxy-2-cycloocten-1-one (1, n = 4, R = Et). As described in the general procedure, 7.4 mL of a 1.0 M solution of potassium *tert*-butoxide in THF (7.4 mmol) was added to a solution of 0.86 g (6.1 mmol) of cyclooctan-1,3-dione (**3**, n = 4) in dried HMPA. After 15 min stirring at rt, 3.0 g (15 mmol) of ethyl tosylate was added to the reaction mixture. The stirring was continued for 2.5 h and the reaction worked-up as described in the general procedure. Flash chromatography was performed sequentially using 85 n-hexane/ 15 acetone and 80 n-hexane/ 20 ethyl acetate. The desired product (0.79 g, 77 %, GC purity 99%) was a colorless liquid containing 0.4 % ethyl tosylate and 0.4 % unreacted starting material **3**. Flash chromatography was repeated using 75 CH_2Cl_2/

20 n-hexane/ 5 ether until the product was obtained 100 % GC pure: TLC slight decomposition on plate; IR (neat) 3492, 3247, 3062, 2981, 2934, 2859, 1637, 1601, 1229 cm^{-1} (lit.[6] 2980, 2920, 1630, 1600, 1380, 1230 cm^{-1}); ^1H NMR ($CDCl_3$) δ 5.54 (s, 1H), 3.78 (q, J = 7, 2H), 2.73 (m, 4H), 1.67 and 1.55 (2m, 6H), 1.30 (t, J = 7, 3H) (lit.[6] ($CDCl_3$) δ 5.56 (s, 1H), 3.80 (q, J = 7, 2H), 2.80 (m, 4H), 1.90-1.40 (m, 6H), 1.32 (t, J = 7, 3H)); ^{13}C NMR ($CDCl_3$) δ 201.1, 172.1, 108.4, 63.8, 41.4, 33.0, 23.6, 23.2, 23.0, 14.1; GC-MS m/z 170, 169, 168 (M^+), 140, 125, 112, 98, 97 (base), 84, 83, 69, 55, 43, 42, 41, 39 (lit.[6] HRMS m/z 168.1150); UV (n-hexane) λ_{max} 245 nm (ε 15400), 319 nm (ε 66) (lit.[6] (cyclohexane) λ_{max} 245 nm (ε 12600) tail to 340 (ε 106 at 320 nm)).

The GC-MS of the above impure reaction product provided evidence for 1,3-diethoxy-1,3-cyclooctadiene (**9**, n = 4, R = Et) : m/z 198, 197, 196 (M^+), 168, 167 (base), 154, 151, 140, 139, 126, 125, 124, 123, 112, 111, 98, 97, 96, 95, 93, 84, 83, 82, 81, 79, 77, 69, 67, 55, 53, 43, 41, 39. The same GC-MS also provided evidence for 2-ethylcyclooctan-1,3-dione (**6**, n = 4, R = Et) and 2,2-diethylcyclooctan-1,3-dione (**7**, n = 4, R = Et), both prepared in greater quantities by other procedures (see below).

2-Ethylcyclooctan-1,3-dione (6, n = 4, R = Et). A solution (0.43 mL, 0.43 mmol) of potassium *tert*-butoxide (1.0 M in THF) was added to a stirred solution of 50 mg (0.36 mmol) of cyclooctan-1,3-dione (**3**, n = 4) in 10 mL DME at rt. After 15 min stirring, 144 μL of ethyl iodide (281 mg, 1.8 mmol) was added to the mixture. The reaction was stirred for 4 h, then diluted with 75 mL n-hexane and washed with 25 mL of water. The hexane layer was dried (anhyd Na_2SO_4) and filtered, and the hexane then removed under reduced pressure. The residue was purified by flash chromatography (80 n-hexane/ 20 ethyl acetate) to give **6** (n = 4, R = Et) in 94 % GC purity: ^1H NMR ($CDCl_3$) δ 3.36 (t, J = 7, 1H), 2.46 (m, 4H), 1.9-1.5 (3 overlapping m, m centered at 1.85 (J = 7), 8H), 0.89 (t, J = 7, 3H); GC-MS m/z 170, 169, 168 (M^+), 140, 112, 111 (base), 98, 97, 83, 81, 71, 70, 69, 55, 43, 42, 41, 39; IR of similarly prepared material with 78 % GC purity (neat) 3389, 1715, 1692, 1462 cm^{-1}.

2,2-Diethylcyclooctan-1,3-dione (7, n = 4, R = Et). A solution (0.46 mL, 0.46 mmol) of potassium *tert*-butoxide (1.0 M in THF) was added to a stirred solution of 54 mg (0.39 mmole) of cyclooctan-1,3-dione (**3**, n = 4) in 10 mL HMPA at rt. After 15 min stirring, 154 μL of ethyl iodide (300 mg, 1.9 mmol) was added. The reaction was stirred for 3 h, then diluted with 75 mL of n-hexane and washed with 3 x 25 mL water. The hexane was removed under reduced pressure after it was dried (anhyd Na_2SO_4) and filtered. The residue was purified by flash chromatography (80 hexane/ 20 ethyl acetate) and combined with a similarly prepared fraction from the purification of 2-ethylcyclooctan-1,3-dione (above). The combined fractions were a white crystalline solid (GC purity 94 % with 5 % of **6** (n = 4, R = Et)) : IR (neat) 1684 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.41 (m, 4H), 1.89 (q, J = 7, 4H), 1.72 (m, 4H), 1.58 (m, 2H), 0.67 (t, 6H); GC-MS m/z 198, 197, 196 (M^+), 181, 167, 153, 139, 125, 121, 99, 98 (base), 97, 83, 81, 71, 69, 55, 42, 41, 39.

3-Ethoxy-2-cyclononen-1-one (1, n = 5, R = Et). Following the general procedure, 7.6 mL (7.6 mmol) of potassium *tert*-butoxide solution (1.0 M in THF) was added to a solution of 0.97 g (6.3 mmol) of cyclononan-1,3-dione (**3**, n = 5) in 10 mL dried HMPA. As described, 2.95 g (14.7 mmol) of ethyl tosylate was added. The desired product (1.0 g, 87 %, GC purity 99.5 %) was obtained after extraction and flash chromatography (48 n-hexane/ 48 CH_2Cl_2/ 4 acetone) as a colorless liquid containing 0.3 % ethyl tosylate and 0.2 % starting dione. Flash chromatography was performed twice more (as above, then 90 n-hexane/10 acetone) to obtain GC and TLC 100% pure product: IR (neat) 3491, 3241, 3059, 1630, 1609, 1229, 1158 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.43 (s, 1H), 3.77 (q, J = 7, 2H), 2.70 (m, 4H), 1.77 (m, 2H), 1.59 (m, 4H), 1.46 (m, 2H), 1.30 (t, J = 7, 3H); ^{13}C NMR ($CDCl_3$) δ 203.8, 172.2, 107.7, 63.6, 40.6, 31.3, 29.0, 28.7, 26.6, 24.9, 14.2; GC-MS m/z 184, 183, 182 (M^+), 153, 140, 139, 126, 125, 111, 99, 98, 97 (base), 86, 84, 83, 69, 68, 67, 55, 53, 43, 42, 41, 39; UV (n-hexane) λ_{max} 247 nm (ε 15300), 316 nm (ε 123).

2-Ethylcyclononan-1,3-dione (6, n = 5, R = Et). A solution (0.84 mL, 0.84 mmol) of potassium *tert*-butoxide (1.0 M in THF) was added to a stirred solution of 100 mg (0.65 mmol) of cyclononan-1,3-dione (**3**, n = 5) in 10 mL HMPA at rt. After 15 min stirring, 2 mL of ethyl iodide (3.9 g, 25 mmol) was added. The reaction was stirred for 3 h, then diluted with 75 mL of hexanes and washed with 3 x 50 mL of water. After extracting the combined aqueous extracts with 75 mL hexanes, this hexane layer was washed (3 x 50 mL water) and added to the hexane layer from the previous step. The hexane was dried (anhyd Na_2SO_4), filtered, and solvent removed under reduced pressure. This residue was combined with that from a similar reaction in DME (107 mg cyclononan-1,3-dione (0.69 mmol), 0.76 ml of 1.0 M potassium *tert*-butoxide (0.76 mmol), 275 μL ethyl iodide (0.54 g, 3.4 mmol), 23 h at rt). The combined residues were purified by flash chromatography (90 n-pentane/ 10 acetone) to give the desired product **6**: GC purity 95 %; ^{1}H NMR ($CDCl_3$) δ 3.71 (t, J = 7, 1H), 2.48 (m, 4H), 1.85 (m, J = 7, 2H), 1.75 (m, 4H), 1.4 (m, 4H), 0.84 (t, J = 7, 3H); GC-MS m/z 184, 183, 182 (M^+), 154, 139, 125, 112, 111, 97, 84, 83, 71, 70, 69, 68, 67, 56, 55 (base), 43, 42, 41, 39.

2,2-Diethylcyclononan-1,3-dione (7, n = 5, R = Et). Partially purified 7 (n = 5) was obtained from the above procedure. Further flash chromatography (93 n-hexane/ 7 ether) afforded a white crystalline solid: GC purity 98 %; IR (Nujol) 1698 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.38 (m, 4H), 1.96 (q, J = 7, 4H), 1.66 (m, 4H), 1.34 (m, 4H), 0.66 (t, J = 7, 6H); ^{13}C NMR ($CDCl_3$) δ 210.7, 35.2, 25.3, 23.4, 21.1, 20.0, 7.7; GC-MS m/z 211, 210 (M^+), 167, 153, 139, 125, 113, 112, 111, 110, 99, 98, 97, 95, 84, 83 (base), 81, 71, 69, 68, 67, 57, 56, 55, 53, 43, 42, 41, 39.

1,3-Diethoxy-1,3-cyclononadiene (9, n = 5, R = Et). A solution (0.43 mL, 0.43 mmol) of potassium *tert*-butoxide (1.0 M in THF) was added to a stirred solution of 66 mg (0.43 mmol) of cyclononan-1,3-dione (**3**, n = 5) in 10 mL HMPA at rt. After stirring 15 min, 256 mg of ethyl tosylate (1.3 mmol) was added. The mixture was stirred for 1.5 h; a second aliquot (0.43 mL, 0.43 mmol) of the potassium *tert*-butoxide solution was

added. After an additional 9 h, a third aliquot (0.1 mL, 0.1 mmol) of the potassium *tert*-butoxide solution was added. Seven days later, the reaction was diluted with 150 mL of n-hexane and washed with 75 mL of water. The hexane layer was dried (anhyd Na_2SO_4), filtered, and solvents removed under reduced pressure. The residue was combined with two partially purified fractions of **9** obtained from similar reactions performed in HMPA. The combined residue was purified by flash chromatography (97 n-pentane/ 3 ether) to afford a pale yellow liquid (GC purity 97 %): IR (neat) 3051, 1652, 1637, 1451, 1379, 1189, 1142, 1118 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.83 (s, 1H), 4.69 (t, 1H), 3.81 (q, 2H), 3.73 (q, 2H), 2.28 (m, 2H), 2.09 (m, 2H), 1.7-1.4 (2m, 6H), 1.30 (q: 2 overlapping triplets, 6H); ^{13}C NMR ($CDCl_3$) δ 162.9, 153.9, 101.8, 92.8, 62.5, 62.4, 32.9, 29.7, 28.6, 28.2, 24.8, 14.9, 14.5; GC-MS m/z 212, 211, 210 (M^+), 168, 167 (base), 165, 154, 139, 137, 126, 125, 111, 98, 97, 95, 91, 79, 69, 67, 55, 43, 41.

(E)-3-Ethoxy-2-cyclodecen-1-one (1, n = 6, R = Et). Using the general procedure, 2.3 mL (2.3 mmol) of potassium *tert*-butoxide (1.0 M in THF) was added to a solution of 0.32 g (1.9 mmol) of cyclodecan-1,3-dione (**3**, n = 6) in 15 mL of dried HMPA at rt. After 15 min stirring, 0.94 g (4.7 mmol) of ethyl tosylate was added. Stirring continued for 2 h at rt. The reaction was diluted with 150 mL of n-hexane and worked-up as described. Flash chromatography (85 n-hexane/ 15 acetone) was followed by a second flash chromatography (95 n-hexane/ 5 acetone) to give 0.2 g (54 %, GC purity 99%) of **1** as a white crystalline solid. This solid was combined with 0.23 g of **1** obtained similarly, and the combination was subjected to an additional flash chromatography (95 n-hexane/ 5 acetone). The resulting white solid was pure by TLC and GC; IR (KBr) 3072, 1669, 1608, 1469, 1378, 1268, 1159 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.47 (s, 1H), 3.79 (q, J = 7, 2H), 2.55 (t, 2H), 2.38 (m, 2H), 1.89 (m, 2H), 1.49 (m, 4H), 1.34 (t, J = 7, 3H), 1.23 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 208.2, 166.2, 103.6, 63.1, 45.4, 28.4, 26.6, 23.8, 23.0, 21.8, 21.6, 14.3; GC-MS m/z 198, 197, 196 (M^+), 167, 153, 152, 150, 140, 139, 138, 126, 125, 113, 112,

111, 110, 99, 98, 97, 95, 93, 86, 84, 83, 81, 79, 71, 69 (base), 68, 67, 58, 55, 53, 43, 42, 41, 39; UV (n-hexane) λ_{max} 249 nm (ε 8300), 311 nm (ε 101).

2-Ethylcyclodecan-1,3-dione (6, n = 6, R = Et). Typically, a solution (0.20 mL, 0.20 mmol) of potassium *tert*-butoxide (1.0 M in THF) was added to a stirred solution of 20 mg (0.12 mmol) of cyclodecan-1,3-dione (**3**, n = 6) in 10 mL DME at rt. After 15 min of stirring, 48 μL of ethyl iodide (94 mg, 0.6 mmol) was added. The reaction was stirred for 3 h; then it was diluted with n-hexane and washed with water. The hexane layer was removed under reduced pressure after it had been dried (anhyd Na_2SO_4) and filtered.

A number of similar reactions were combined. Repeated flash chromatography using mixtures of n-hexane and acetone (90:10 and 95:5) followed by flash chromatography using 90 n-hexane/ 10 ether produced a slightly yellow liquid: GC purity 98 %; IR (neat) 3392, 1726 (sh), 1693, 1468, 1444, 1133, 1040 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.63 (t, J = 7, 1H), 2.46 (m, 4H), 1.86 and 1.78 (2m, J(δ 1.86) = 7, 6H), 1.33 and 1.23 (2m, 6H), 0.86 (t, J = 7, 3H); ^{13}C NMR ($CDCl_3$) δ 208.4, 73.4, 39.1, 26.2, 24.1, 23.0, 21.5, 11.7; GC-MS m/z 197, 196 (M^+), 168, 153, 139, 126, 125, 111, 110, 99, 98, 97, 84, 83, 82, 81, 79, 71, 70, 69, 67, 58, 55 (base), 43, 42, 41, 39.

2,2-Diethylcyclodecan-1,3-dione (7, n = 6, R = Et). A solution (2.5 mL, 2.5 mmol) of potassium *tert*-butoxide (1.0 M in THF) was added to a stirred solution of 213 mg (1.26 mmol) of cyclodecan-1,3-dione (**3**, n = 6) in 10 mL DME at rt. After 30 min of stirring, 0.5 mL of ethyl iodide (0.98 g, 6.3 mmol) was added. The reaction was stirred for 3 h; a second aliquot (1 mL, 1.0 mmol) of the potassium *tert*-butoxide solution was then added. After 1 additional h of stirring, the reaction was diluted with diethyl ether and washed with water. The ether layer was dried (anhyd Na_2SO_4), filtered, and the solvent removed under reduced pressure. The residue was subjected to flash chromatography twice (90 n-hexane/ 10 ether) to give the product 7 as a white crystalline solid : GC purity 93 %; IR (KBr) 3377, 1686, 1473 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.43 (m, 4H), 1.95 (q, J = 7.6, 4H), 1.77 (m, 4H), 1.38 (m, 6H), 0.67 (t, J = 7.6, 6H); ^{13}C NMR ($CDCl_3$) δ 209.8,

73.5, 37.5, 26.1, 26.0, 23.4, 20.4, 7.5; GC-MS m/z 225, 224 (M^+), 195, 181, 167, 153, 126, 125, 123, 112, 111, 110, 109, 99, 98, 97, 96, 95, 86, 84, 83, 82, 81, 71, 69, 67, 57, 56, 55 (base), 53, 43, 42, 41, 39.

2,2,4-Triethylcyclodecan-1,3-dione (10, n = 6, R = Et). The above separation also produced material corresponding to **10**. Additional flash chromatography (90 n-hexane/ 10 ether) provided **10** in 92 % GC purity: IR (neat) 1690, 1462 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.75 (m, 2H), 2.14 (m, 2H), 1.98 (m, 4H), 1.7-1.0 (m, 12H), 0.88 (t, 3H), 0.69 (m (2 overlapping triplets), 6H); GC-MS m/z 254, 253, 252 (M^+), 223, 209, 195, 153, 135, 125, 111, 110, 109, 99, 98, 97, 95, 86, 83, 81, 71, 69, 67, 57, 56, 55 (base), 53, 43, 42, 41, 39.

2-Ethyl-3-ethoxy-2-cyclodecen-1-one (8, n = 6, R = Et). A solution (0.79 mL, 0.79 mmol) of potassium *tert*-butoxide (1.0 M in THF) was added to a stirred solution of 133 mg (0.79 mmol) of cyclodecan-1,3-dione (**3**, n = 6) in 10 mL of HMPA at rt. After stirring for 15 min, 64 μL of ethyl iodide (124 mg, 0.79 mmol) was added. The reaction mixture was stirred for 3 h. A second aliquot (0.79 mL, 0.79 mmol) of the potassium *tert*-butoxide was then added. Following stirring for 15 min, 320 mg of ethyl tosylate (1.6 mmol) was added. Stirring was continued for 2.5 h, and the reaction was then diluted with n-hexane and washed with water. The hexane was dried (anhyd Na_2SO_4), filtered, and removed under reduced pressure. The residue was combined with partially purified **8** obtained during the purification of **7** (above). Further purification by flash chromatography (90 hexanes/ 10 ether) produced **8** as a white crystalline solid with GC purity of 96 %: IR (Nujol) 1663, 1614, 1252, 1051 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.86 (q, J = 7, 2H), 2.60-2.35 (m, q (J = 7.5), 6H), 1.85 (m, 2H), 1.55-1.35 (m, 4H), 1.35-1.09 (m,t (J = 7), 7H), 0.95 (t, J = 7.5, 3H); ^{13}C NMR ($CDCl_3$) δ 212.2, 154.3, 128.4, 63.3, 43.3, 28.6, 23.7, 22.7, 22.1, 21.6, 21.4, 19.8, 15.4, 13.7; GC-MS m/z 225, 224 (M^+), 195, 181, 179, 167, 153, 149, 141, 140, 139 (base), 138, 135, 127, 126, 125, 123, 114, 112, 111, 110,

109, 108, 107, 99, 98, 97, 95, 93, 91, 86, 84, 83, 81, 79, 77, 71, 69, 68, 67, 65, 55, 53, 43, 42, 41, 39.

1,3-Diethoxy-1,3-cyclodecadiene (9, n = 6, R = Et). A solution (0.29 mL, 0.29 mmol) of potassium *tert*-butoxide (1.0 M in THF) was added to a stirred solution of 52 mg (0.31 mmol) of cyclodecan-1,3-dione (**3**, n = 6) in 10 mL dried HMPA at rt. After stirring for 15 min, 130 mg (0.65 mmol) of ethyl tosylate was added. The reaction was stirred for 4 h. A second aliquot (0.29 mL, 0.29 mmol) of the potassium *tert*-butoxide solution was then added. After 15 min of stirring, a second portion of ethyl tosylate (130 mg, 0.65 mmol) was added. The mixture was stirred for an additional 3 h. GC analysis after work-up showed 46 % of a diethoxycyclodecadiene assigned structure **9** and 23% of 3-ethoxy-2-cyclodecen-1-one (**1**, n = 6, R = Et). The GC-MS of this mixture indicated the following m/z for **9** : 225, 224 (M^+), 209, 195, 181, 180, 179, 168, 167 (base), 154, 153, 151, 139, 126, 125, 112, 111, 109, 107, 97, 95, 93, 91, 83, 81, 79, 69, 67, 55, 43, 41. The same material was observed by GC-MS as a minor component in the alkylation of **3** (n = 6) using TEO in THF.

3-Methoxy-2-cyclodecen-1-one (1, n = 6, R = Me). A solution (0.31 mL, 0.31 mmol) of potassium *tert*-butoxide (1.0 M in THF) was added to a stirred solution of 44 mg (0.26 mmol) of cyclodecan-1,3-dione (**3**, n = 6) in 10 mL dried DMSO at rt. After stirring for 30 min, 61 μL of dimethyl sulfate (Eastman, practical) (81 mg, 0.64 mmol) was added. The reaction was stirred for 2 h and then extracted with water and chloroform. The chloroform layer was dried over anhyd Na_2SO_4, filtered, and solvent removed under reduced pressure. The ^1H NMR of the crude residue (40% **1** by GC) showed a singlet at δ 5.53 from the vinyl proton and a singlet at δ 3.63 from the methoxy protons.

2-Methylcyclodecan-1,3-dione (6, n = 6, R = Me). A solution (0.42 mL, 0.42 mmol) of potassium *tert*-butoxide (1.0 M in THF) was added to a stirred solution of 65 mg (0.39 mmol) of cyclodecan-1,3-dione (**3**, n = 6) in 10 mL dried DME at rt. After 30 min stirring, 91 μL of dimethyl sulfate (121 mg, 0.96 mmol) was added. The reaction was

stirred for 2 h and then diluted with diethyl ether. The ^{1}H NMR of the residue after removal of solvent under reduced pressure (78 % **6** by GC) showed δ 3.56 (q, 1H), 2.41 (m, 4H), 1.68 (m, 4H), 1.33-1.14 (m), 1.21 (d which overlaps m); GC-MS m/z 183, 182 (M^+), 154, 153, 135, 126, 125, 112, 111, 110, 107, 98, 97, 95, 93, 85, 84, 83, 82, 81, 79, 72, 70, 69, 68, 67, 57, 56, 55 (base), 53, 43, 42, 41, 39.

2,2-Dimethylcyclodecan-1,3-dione (7, n = 6, R = Me). A solution (0.73 mL, 0.73 mmol) of potassium *tert*-butoxide (1.0 M in THF) was added to a stirred solution of 82 mg (0.49 mmol) of cyclodecan-1,3-dione (**3**, n = 6) in 10 mL dried DMSO at rt. After stirring 30 min, 0.16 mL of methyl iodide (MCB) (0.36 g, 2.5 mmol) was added. The reaction was stirred for 1 h, and then extracted with water and chloroform. The chloroform layer was dried (anhyd Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was 59 % of **7** and 39 % of **6** (n = 6, R = Me). GC-MS m/z 197, 196 (M^+), 181, 153, 126, 125, 111, 107, 98, 97, 86, 85, 84, 83, 82, 81, 79, 71, 70, 69, 67, 55, 53, 43, 42, 41 (base), 40, 39; ^{1}H NMR δ 1.32 (s, gem-dimethyl).

Supporting Information: Table 5. Alkylation of Cyclodecan-1,3-dione (3, n = 6) in DME

System (equivalents)[a]	Temp	**3**[b]	**1**	**6**	**7**	**8**	O/C Ratio[9]
EtI (5X)[c]	rt	2	6	48	20	2	0.1
EtI (5X)[d,e]	rt	<1	<1	70	23	4	< 0.1
Me_2SO_4 (2.5X)	rt	4	4	78	9	--	< 0.1
EtTos (5X)	rt	1	6	82	<1	<1	0.1
EtTos (2.5X)[f]	rt	4	5	89	--	--	0.1
Et_3OBF_4 (1.2X)	- 41°	64	13	18	--	--	0.7
Et_3OBF_4 (1.3X)	0°	37	24	14	3	3	1.2
Et_3OBF_4 (1.2X)	rt	31	34	14	4	3	1.6
Et_3OBF_4 (1.1X)[g]	rt	44	29	14	2	1	1.7
Et_3OBF_4 (1.7X)[h]	rt	46	23	6	--	2	2.9
Et_3OBF_4 (2.5X)	rt	39	23	8	--	3	2.1
Solvent: THF:							
Et_3OBF_4 (1.7X)	0°	56	17	6	3	3	1.4
Et_3OBF_4 (1.3X)	0°	43	20	12	1	1	1.4

[a] A solution of potassium *t*-butoxide (1.1-1.2 equivalents) was added to a stirred solution of cyclodecan-1,3-dione (0.1 - 0.7 mmol) in 10 mL solvent under N_2. After 0.5 h stirring, the alkylating agent was added and the reaction monitored by GC.

[b] Percent cyclodecan-1,3-dione remaining.

[c] Added 1.7 equivalents of base.

[d] Used 1.3 mmol of dione with 2 equivalents of base.

[e] Also produced 2,2,4-triethylcyclodecan-1,3-dione (**10**).

[f] Used KHMDS as the base.

[g] Reaction was stirred for 5 min before addition of Et_3OBF_4.

[h] Added additional 2.5 equivalents of base.

Supporting Information: Table 6. Alkylation of Cyclodecan-1,3-dione (3, n = 6) in 80% DME/ 20 % HMPA

System (equivalents)[a]	**3**[b]	**1**	**6**	**7**	**8**	O/C Ratio[9]
Me_2SO_4 (3.4X)	12	27	49	6	--	0.5
EtTos (2.5X)	1	38	47	2	7	0.7
Et_3OBF_4 (2X)	37	35	21	3	2	1.3

[a] A solution of potassium *t*-butoxide (1.1-1.2 equivalents) was added to a stirred solution of cyclodecan-1,3-dione (0.2 - 0.5 mmol) in 80% DME/ 20% HMPA (10 mL) under N_2 at rt. After stirring for 0.5 h, the alkylating agent was added and the reaction monitored by GC.

[b] Percent cyclodecan-1,3-dione remaining.

Supporting Information: Table 7. Alkylation of Cyclodecan-1,3-dione (3, n = 6) in DMSO

System (equivalents)[a]	**3**[b]	**1**	**6**	**7**	**8**	O/C Ratio[9]
MeI (5X)[c]	0	1	39	59	--	< 0.1
Me_2SO_4 (2.5X)[d]	< 1	40	4	44	--	0.8
Me_2SO_4 (14X)[e]	19	36	40	4	--	0.8
EtTos (2.5X)	3	61	29	1	3	1.8
Et_3OBF_4 (1.2X)	32	33	27	2	2	1.1

[a] A solution of potassium *t*-butoxide (1.1-1.2 equivalents) was added to a stirred solution of cyclodecan-1,3-dione (0.2 - 0.5 mmol) in 10 mL DMSO under N_2 at rt. After stirring for 0.5 h, the alkylating agent was added and the reaction monitored by GC.

[b] Percent cyclodecan-1,3-dione remaining.

[c] Added 1.5 equivalents of base.

[d] Product mixture contained 9% of an unknown material.

[e] Added 0.9 equivalents of base.

Supporting Information: Table 8. Alkylation of Cyclodecan-1,3-dione (3, n = 6) in HMPA

System (equivalents)[a]	Temp	**3**[b]	**1**	**6**	**7**	**8**	O/C Ratio[9]
EtI (1X)	rt	4	8	78	8	2	0.1
Me_2SO_4 (17X)[c]	rt	13	31	15	1	--	1.9
EtTos (2.5X)	rt	<1	72	20	1	4	2.9
EtTos (2.5X)[d]	rt	<1	70	18	1	6	2.8
EtTos (1.2X)	rt	1	70	16	1	4	3.3
EtTos (2.5X)[d]	35°	<1	71	19	1	3	3.1
EtTos (2.5X)[e]	rt	1	69	15	1	4	3.4
Et_3OBF_4 (1.7X)	rt	35	30	32	--	--	0.9

[a] A solution of potassium *t*-butoxide (0.9-1.1 equivalents) was added to a stirred solution of cyclodecan-1,3-dione (0.1- 0.8 mmol) in 10 mL HMPA under N_2. After stirring for 0.5 h, the alkylating agent was added and the reaction monitored by GC.

[b] Percent cyclodecan-1,3-dione remaining.

[c] Product mixture contained 38% of an unknown material.

[d] Reaction in 6 mL HMPA.

[e] Used KHMDS as the base. Product mixture contained 5% of an unknown material.