

Hydrogenolysis of Unstrained Carbon-Carbon sigma-Bonds: Stereoselective Entry Into Benzylic Tertiary Centers

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Supporting Information 1

General Procedures and Specific Compound Information

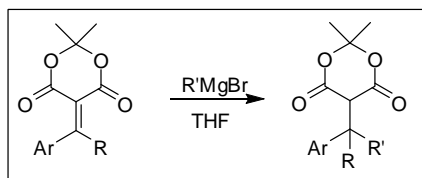
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General Methods

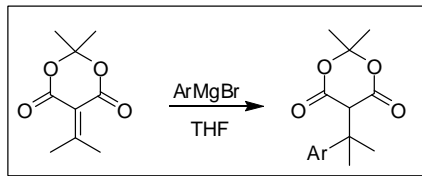
1,2-Dimethoxyethane was distilled from sodium-benzophenone ketyl under nitrogen and degassed via freeze-pump-thaw method. THF was dried and purified from a solvent system based on the published procedure.¹ MeOH (ACS grade), MeMgBr (3.0 M in Et₂O), EtMgBr (3.0 M in Et₂O), Et₂Zn (1.0 M in hexanes), *i*-Pr₂Zn (1.0 M in toluene) were obtained from commercial sources and used without further purification. ¹H NMR and ¹³C NMR were obtained in CDCl₃ at 300 MHz and 75 MHz. Proton spectra was referenced to residual ¹H shift in CDCl₃ (7.24 ppm), carbon spectra was referenced to CDCl₃ (77.0 ppm). Melting points are uncorrected. Flash chromatography was performed using 230-400 mesh silica gel. Chiral HPLC was performed using a Chiralcel AD-H or OD-H 250 × 4.6 mm column. 2,2-Dimethyl-5-(1-methyl-phenylethyl)-1,3-dioxane-4,6-dione (**1c**)² and (*R*)-2,2-dimethyl-5-[1-methyl-1-(4-phenylphenyl)propyl]-1,3-dioxane-4,6-dione (*R*-**1m**)³ were prepared according to literature procedures.

Preparation of Benzyl Meldrum's Acids – General Procedure A.



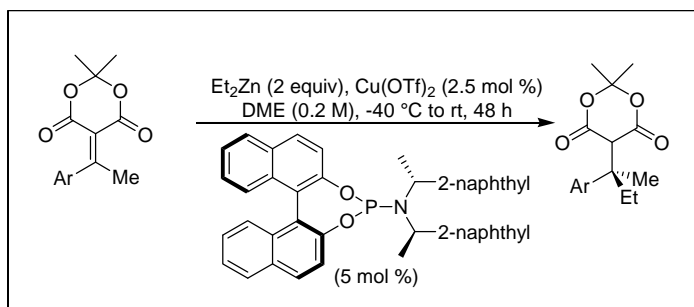
Benzyl Meldrum's acids were prepared by the addition of Grignard reagents to alkylidene Meldrum's acids. In a typical reaction, a Grignard reagent solution (2-3 equiv) was added under nitrogen to a solution of alkylidene Meldrum's acid in dry THF (0.5 M) at 0 °C. The reaction was slowly warmed up to room temperature and stirred for 24 h. The reaction was quenched with 5% HCl and was extracted with EtOAc (3X). The combined organic layers were washed with brine (1X), dried over MgSO₄, filtered, and concentrated. The crude product was purified by either recrystallization or flash chromatography on silica gel.

Preparation of Benzyl Meldrum's Acids – General Procedure B.



Benzyl Meldrum's acids were prepared by the addition of aryl Grignard reagents (2-3 equiv) to a solution of 2,2-dimethyl-5-(propan-2-ylidene)-1,3-dioxane-4,6-dione in dry THF (0.5 M) under nitrogen at 0 °C. The reaction was stirred at room temperature until completion of reaction or for 24 h. The reaction was quenched with 5% HCl and was extracted with EtOAc (3X). The combined organic layers were washed with brine (1X), dried over MgSO₄, filtered and concentrated. The crude product was purified by either flash chromatography or recrystallization.

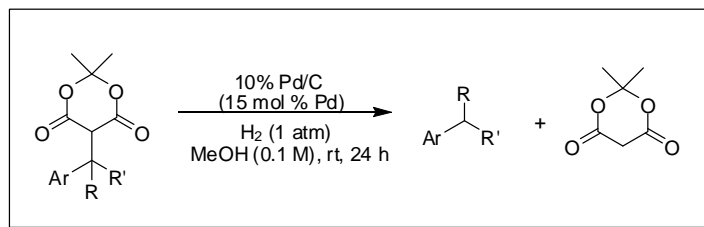
Preparation of Enantioenriched Benzyl Meldrum's Acids – General Procedure C.



Enantioenriched benzyl Meldrum's acids were prepared by the conjugate addition of Et₂Zn to alkylidene Meldrum's acids.³ In a glove box, Cu(OTf)₂ (2.5 mol %) and the phosphoramidite ligand (5 mol %) were charged in a flame-dried round bottom flask. DME was then added to the round bottom flask to wash down any residual solids to the bottom. The reaction mixture was allowed to stir at ambient temperature for 15 minutes, outside the glove box, and then cooled to -40 °C. In the dry box, a Et₂Zn solution (2.0 equiv) was transferred to a round-bottom flask equipped with a septum. This solution was added to the round bottom flask containing the copper/ligand mixture dropwise and the

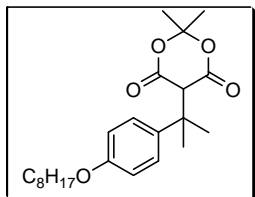
resulting solution stirred for 5 min. A solution of freshly crystallized alkylidene Meldrum's acid (1.0 equiv) in DME was then added dropwise. Finally, DME was added to wash down the remaining solid on the sides of the round bottom flask. The reaction mixture was allowed to warm up slowly to room temperature. After 48 h of stirring, saturated NH_4Cl (aq) and ether were added to the reaction mixture. The layers were partitioned and the aqueous layer was extracted with diethyl ether (3X). The combined organic layers were washed with brine (1X), dried over anhydrous MgSO_4 , filtered and concentrated. The crude residue was purified by flash column chromatography on silica gel using hexanes in EtOAc to yield the desired product. HPLC using a chiral column OD-H or AD-H was used to measure the enantiomeric ratio of the products. This reaction was performed up to 5 mmol of alkylidene Meldrum's acid. The racemates were prepared using EtMgBr (2.5 equiv) in THF according to general procedure A.

Hydrogenolysis of Benzyl Meldrum's Acids – General Procedure D.



The reactions were carried out using 0.2-0.4 mmol of substrates. MeOH (ACS grade) was degassed/purged with vacuum/nitrogen three times. To a 20 mL vial was added benzyl Meldrum's acid and 10% Pd/C (15 mol %). MeOH was added to the vial through a septum via a syringe under nitrogen. The vial was degassed/purged with vacuum/H₂ (balloon) three times. The reaction was stirred under an atmosphere of hydrogen (balloon) for 24 h then filtered through a pad of celite and washed with Et₂O. The solvent was removed under reduced pressure at 0 °C due to the low boiling points of the products. The crude product was purified by flash chromatography. The product was dried under reduced pressure at 0 °C.

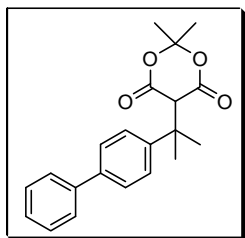
Substrate Specific Information



2,2-Dimethyl-5-(2-(4-(octyloxy)phenyl)propan-2-yl)-1,3-dioxane-4,6-dione

(1a): Prepared according to general procedure A. Purification by flash column chromatography eluting with 8:1 hexanes:EtOAc afforded a white solid in 31% yield. M.p. 54-55 °C; ¹H NMR (CDCl₃, 300 MHz) δ 7.22 (d, *J* = 9.0 Hz, 2H),

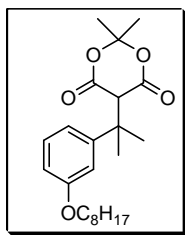
6.82 (d, *J* = 8.8 Hz, 2H), 3.90 (t, *J* = 6.6 Hz, 2H), 3.48 (s, 1H), 1.74 (quintet, *J* = 7.7 Hz, 2H), 1.63 (s, 6H), 1.59 (s, 3H), 1.41 (quintet, *J* = 7.7 Hz, 2H), 1.28-1.26 (m, 8H), 1.22 (s, 3H), 0.86 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 164.3 (C), 157.9 (C), 135.9 (C), 127.3 (CH), 114.1 (CH), 105.1 (C), 67.8 (CH₂), 57.7 (CH), 42.2 (C), 31.7 (CH₂), 29.3 (CH₃), 29.2 (CH₂), 29.1 (2×CH₂), 28.0 (CH₃), 27.2 (CH₃), 25.9 (CH₂), 22.5(CH₂), 14.0 (CH₃). HRMS(EI) *m/z* calcd for C₂₃H₃₄O₅ (M⁺): 390.2406. Found: 390.2417.



2,2-Dimethyl-5-(2-(4-(phenyl)phenyl)propan-2-yl)-1,3-dioxane-4,6-dione

(1b): Prepared according to general procedure A. Purification by flash column chromatography eluting with 8:1 hexanes:EtOAc afforded a white solid in 34% yield. M.p. 140-141 °C; ¹H NMR (CDCl₃, 300 MHz) δ 7.56 (d, *J* = 6.9 Hz, 4H),

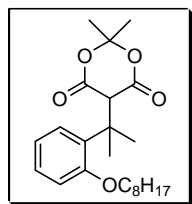
7.44-7.3 (m, 5H), 3.63 (s, 1H), 1.71 (s, 6H), 1.63 (s, 3H), 1.28 (s, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 164.0 (C), 143.6 (C), 140.4 (C) 139.7 (C), 128.7 (CH), 127.3 (CH), 127.0 (CH), 126.6 (CH), 105.2 (C), 57.5 (CH), 42.4 (C), 29.2 (CH₃), 27.7 (CH₃), 27.3 (CH₃); HRMS(EI) *m/z* calcd for C₂₁H₂₂O₄ (M⁺): 338.1518. Found: 338.1521.



2,2-Dimethyl-5-(2-(3-(octyloxy)phenyl)propan-2-yl)-1,3-dioxane-4,6-dione (1d):

Prepared according to general procedure A. Purification by flash column chromatography eluting with 5:1 hexanes:EtOAc afforded a white solid in 45% yield. M.p. 92-93 °C; ¹H NMR (CDCl₃, 300 MHz) δ 7.20 (t, *J* = 8.1 Hz, 1H), 6.98-6.85 (m,

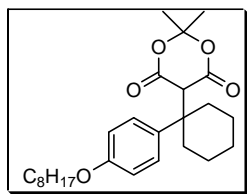
2H), 6.74 (dd, $J = 8.1, 2.1$ Hz, 1H), 3.91 (t, $J = 6.6$ Hz, 2H), 3.60 (s, 1H), 1.75 (quintet, $J = 6.6$ Hz, 2H), 1.63 (s, 6H), 1.62 (s, 3H), 1.43 (quintet, $J = 6.6$ Hz, 2H), 1.29-1.27 (m, 11H), 0.87 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 164.0 (C), 159.0 (C), 146.4 (C), 129.1 (CH), 118.1 (CH), 113.1 (CH), 112.1 (CH), 104.9 (C), 67.8 (CH_2), 57.2 (CH), 42.3 (C), 31.7 (CH_2), 29.3 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 28.9 (CH_3), 27.6 (CH_3), 27.4 (CH_3), 26.0 (CH_2), 22.5 (CH_2), 14.0 (CH_3). HRMS(EI) m/z calcd for $\text{C}_{23}\text{H}_{34}\text{O}_5$ (M^+): 390.2406. Found: 390.2417.



2,2-Dimethyl-5-(2-(2-(octyloxy)phenyl)propan-2-yl)-1,3-dioxane-4,6-dione (1e):

Prepared according to general procedure B. Purification by flash column chromatography eluting with 19:1 hexanes:EtOAc, followed by 9:1 hexanes:EtOAc afforded a white solid in 72% yield. M.p. 50-51 °C; ^1H NMR (CDCl_3 , 300 MHz) δ

7.35 (d, $J = 7.8$ Hz, 1H), 7.20 (t, $J = 7.6$ Hz, 1H), 6.96 (t, $J = 7.5$ Hz, 1H), 6.88 (s, $J = 8.2$ Hz, 1H), 5.31 (s, 1H), 4.02 (t, $J = 6.7$ Hz, 2H), 1.82 (quintet, $J = 7.0$ Hz, 2H), 1.76 (s, 3H), 1.69 (s, 3H), 1.66 (s, 6H), 1.47 (quintet, $J = 6.8$ Hz, 2H), 1.29 (broad s, 8H), 0.89 (t, $J = 5.8$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 164.0 (C), 156.0 (C), 134.9 (C), 127.5 (CH), 127.1 (CH), 120.8 (CH), 112.0 (CH), 103.6 (C), 68.1 (CH_2), 52.7 (CH), 40.3 (C), 31.6 (CH_2), 29.4 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 28.4 (CH_3), 26.7 (CH_3), 26.1 (CH_2), 25.0 (CH_3), 22.5 (CH_2), 14.0 (CH_3). HRMS(EI) m/z calcd for $\text{C}_{23}\text{H}_{34}\text{O}_5$ (M^+): 390.2406. Found: 390.2407.

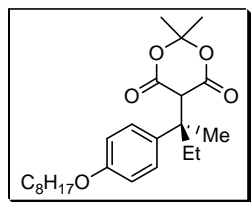


2,2-Dimethyl-5(1-(4-(octyloxy)phenyl)cyclohexyl)-1,3-dioxane-4,6-dione (1f):

Prepared according to general procedure B. However, 5-cyclohexylidene-2,2-dimethyl-1,3-dioxane-4,6-dione was used instead of 2,2-dimethyl-5-(propan-2-

ylidene)-1,3-dioxane-4,6-dione. Purification by flash column chromatography eluting with 12:1 hexanes:EtOAc afforded a pale yellow solid in 57% yield. M.p. 36-37 °C; ^1H NMR (CDCl_3 , 300 MHz) δ 7.15 (d, $J = 8.4$ Hz, 2H), 6.82 (d, $J = 8.3$ Hz, 2H), 3.89 (t, $J = 6.5$ Hz, 2H), 3.39 (s, 1H), 2.44 (dd, $J = 13, 3.8$ Hz, 2H), 1.97 (t, $J = 8.6$ Hz, 2H), 1.72 (quintet, $J = 6.9$ Hz, 2H), 1.65-1.50 (m, 2H), 1.45-1.25

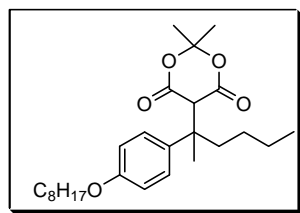
(m, 17H), 0.85 (t, $J = 6.4$ Hz, 3H), 0.79 (s, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 164.6 (C), 158.2 (C), 131.3 (C), 128.8 (CH), 114.5 (CH), 105.6 (C), 67.9 (CH_2), 57.3 (CH), 46.8 (C), 35.7 (CH_2), 31.7 (CH_2), 30.5 (CH_3), 29.3 (CH_2), 29.2 (CH_2), 29.1 (CH_2), 26.4 (CH_3), 25.9 (CH_2), 25.7 (CH_2), 22.6 (CH_2), 22.2 (CH_2), 14.0 (CH_3). HRMS(EI) m/z calcd for $\text{C}_{26}\text{H}_{38}\text{O}_5$ (M^+): 430.2719. Found: 430.2733.



2,2-Dimethyl-5-((*R*)-2-(4-(octyloxy)phenyl)butan-2-yl)-1,3-dioxane-4,6-dione

(*R*-1g): Prepared according to general procedure C. Purification by flash column chromatography eluting with 9:1 hexanes/EtOAc afforded a beige solid in 86% yield. M.p. 53-54 °C ; ^1H NMR (CDCl_3 , 300 MHz) δ 7.16 (d, $J = 8.8$ Hz, 2H),

6.82 (d, $J = 8.8$ Hz, 2H), 3.90 (t, $J = 6.6$ Hz, 2H), 3.49 (s, 1H), 2.17-2.03 (m, 2H), 1.73 (quintet, $J = 6.9$ Hz, 2H), 1.57 (s, 3H), 1.56 (s, 3H), 1.38 (quintet, $J = 7.6$ Hz, 2H), 1.35-1.26 (m, 8H), 1.15 (s, 3H), 0.86 (t, $J = 6.2$ Hz, 3H), 0.76 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 164.7 (C), 164.2 (C), 158.0 (C), 133.6 (C), 128.0 (CH), 114.2 (CH), 105.2 (C), 67.9 (CH_2), 57.3 (CH), 46.0 (C), 32.7 (CH_2), 31.7 (CH_2), 29.7 (CH_3), 29.3 (CH_2), 29.2 ($2 \times \text{CH}_2$), 27.0 (CH_3), 26.0 (CH_2), 22.6 (CH_2), 22.3 (CH_3), 14.0 (CH_3), 8.7 (CH_3). HRMS(EI) m/z calcd for $\text{C}_{24}\text{H}_{36}\text{O}_5$ (M^+): 404.2563. Found: 404.2569. An enantiomeric ratio of 98.5:1.5 (*R*:*S*) was measured by chiral HPLC OD-H, 10% *i*-PrOH/hexanes, 0.5 mL/min, $t_{\text{R}1} = 12.1$ min (*S*), $t_{\text{R}2} = 13.8$ min (*R*). The absolute stereochemistry was assigned by analogy to known (*R*)-2,2-dimethyl-5-(2-phenylbutan-2-yl)-1,3-dioxane-4,6-dione.³

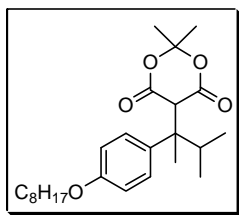


2,2-Dimethyl-5-(2-(4-(octyloxy)phenyl)hexan-2-yl)-1,3-dioxane-4,6-dione

(1h): Prepared according to general procedure A. Recrystallization from MeOH afforded a white solid in 28% yield. M.p. 66-67 °C; ^1H NMR (CDCl_3 , 300 MHz) δ 7.16 (d, $J = 8.7$ Hz, 2H), 6.81 (d, $J = 8.7$ Hz, 2H), 3.90 (t, $J = 6.5$

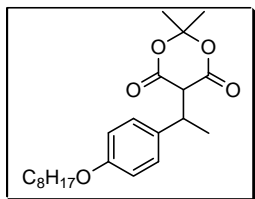
Hz, 2H), 3.49 (s, 1H), 2.14-1.92 (m, 2H), 1.73 (quintet, $J = 7.2$ Hz, 2H), 1.59 (s, 3H), 1.56 (s, 3H), 1.41 (t, $J = 7.3$ Hz, 2H), 1.26 (broad s, 12H), 1.16 (s, 3H), 0.86-0.81 (m, 6H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 164.7 (C), 164.2 (C), 157.9 (C), 133.9 (C), 127.9 (CH), 114.1 (CH), 105.2 (C), 67.9 (CH_2), 57.6 (CH),

45.7 (C), 39.9 (CH₂), 31.7 (CH₂), 29.7 (CH₃), 29.3 (CH₂), 29.2 (2×CH₂), 27.1 (CH₃), 26.5 (CH₂), 26.0 (CH₂), 23.1 (CH₃), 23.0 (CH₂), 22.6 (CH₂), 14.0 (CH₃), 13.9 (CH₃). HRMS(EI) *m/z* calcd for C₂₆H₄₀O₅ (M⁺): 432.2876. Found: 432.2884.



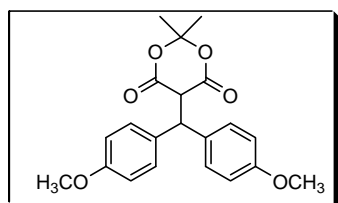
2,2-Dimethyl-5-(3-methyl-2-(4-(octyloxy)phenyl)butan-2-yl)-1,3-dioxane-4,6-dione (1i): Prepared according to general procedure C. However, the racemic ligand 2,2'-*O,O*-(1,1'-binaphthyl)-*O,O'*-dioxo-*N,N*-dimethylphospholidine⁴ was used. The reaction was quenched with saturated NH₄Cl (aq) instead of 5 % HCl.

Purification by flash column chromatography eluting with 5:1 hexanes:EtOAc afforded a yellow oil in 43% yield. ¹H NMR (CDCl₃, 300 MHz) δ 7.17 (d, *J* = 8.8 Hz, 2H), 6.80 (d, *J* = 8.8 Hz, 2H), 3.89 (t, *J* = 6.5 Hz, 2H), 3.67 (s, 1H), 2.89 (septet, *J* = 6.6 Hz, 1H), 1.72 (quintet, *J* = 6.6 Hz, 2H), 1.51 (s, 3H), 1.50 (s, 3H), 1.40 (quintet, *J* = 7.4 Hz, 2H), 1.26-1.25 (m, 8H), 1.09 (d, *J* = 6.5 Hz, 3H), 0.92 (s, 3H), 0.85 (t, *J* = 6.9 Hz, 3H), 0.67 (d, *J* = 6.7 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 165.1 (C), 164.4 (C), 158.0 (C), 133.2 (C), 128.3 (CH), 114.1 (CH), 105.2 (C), 67.9 (CH₂), 54.5 (CH), 49.4 (C), 32.5 (CH), 31.7 (CH₂), 29.9 (CH₃), 29.3 (CH₂), 29.2 (2×CH₂), 26.7 (CH₃), 26.0 (CH₂), 22.6 (CH₂), 18.0 (CH₃), 17.8 (CH₃), 17.0 (CH₃), 14.0 (CH₃). HRMS(EI) *m/z* calcd for C₂₅H₃₈O₅ (M⁺): 418.2719. Found: 418.2719.



2,2-Dimethyl-5-(1-(4-(octyloxy)phenyl)ethyl)-1,3-dioxane-4,6-dione (1j): To a flask containing 2,2-dimethyl-5-(1-(4-(octyloxy)phenyl)ethylidene)-1,3-dioxane-4,6-dione [prepared by condensation⁵ of Meldrum's acid and 1-(4-(octyloxy)phenyl)ethanone] in EtOH (0.2 M) was added NaBH₄ (2 equiv) at 0 °C. The reaction was stirred at room temperature for 2 h and then cooled to 0 °C. After 5% HCl was added to quench the reaction, the mixture was concentrated on the rotovap. The crude mixture was diluted with 10% HCl and extracted with EtOAc (3X). The organic layers were combined, dried over MgSO₄, filtered and concentrated. Purification of the crude product afforded a solid in 77% yield. M.p. 76-78 °C; ¹H NMR (CDCl₃, 300 MHz) δ 7.22 (d, *J* = 9 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 3.97-3.87 (m, 3H), 3.62 (d, *J* =

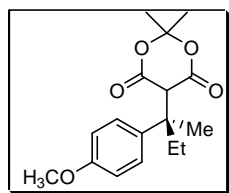
3Hz, 1H), 1.73 (quintet, $J = 7.2$ Hz, 2H), 1.64 (s, 4H), 1.61 (s, 2H), 1.41 (quintet, $J = 7.8$ Hz, 2H), 1.30-1.26 (m, 11H), 0.86 (t, $J = 7.2$ Hz, 3H). ^{13}C NMR (CDCl_3 , 75 MHz) δ 165.3 (C), 164.8 (C), 158.4 (C), 132.7 (C), 129.4 (CH), 114.4 (CH), 105.2 (C), 68.0 (CH_2), 52.7 (CH), 39.2 (CH), 31.8 (CH_2), 29.3 (CH_2), 29.2 ($2\times\text{CH}_2$), 28.1 (CH_2), 26.0 (CH_3), 22.6 (CH_2), 18.3 (CH_3), 14.1 (CH_3). HRMS(EI) m/z calcd for $\text{C}_{22}\text{H}_{32}\text{O}_5$ (M^+): 376.2250. Found: 376.2260.



5-(Bis(4-methoxyphenyl)methyl)-2,2-dimethyl-1,3-dioxane-4,6-dione

(1k): Prepared according to general procedure A. Purification by flash column chromatography eluting with 3:1 hexanes:EtOAc afforded a solid

in 83% yield. M.p. 114-116 °C. ^1H NMR (CDCl_3 , 300 MHz) δ 7.21 (d, $J = 8.6$ Hz, 4H), 6.81 (d, $J = 8.6$ Hz, 4H), 5.27 (d, $J = 2.1$ Hz, 1H), 4.23 (d, $J = 2.6$ Hz, 1H), 3.77 (s, 6H), 1.72 (s, 3H), 1.50 (s, 3H). ^{13}C NMR (CDCl_3 , 75 MHz) δ 164.8 (C), 158.4 (C), 132.3 (C), 130.1 (CH), 113.6 (CH), 105.0 (C), 55.1 (CH_3), 51.3 (CH), 47.8 (CH), 28.1 (CH_3), 27.5 (CH_3). HRMS(EI) m/z calcd for $\text{C}_{21}\text{H}_{22}\text{O}_6$ (M^+): 370.1416. Found: 370.1426.

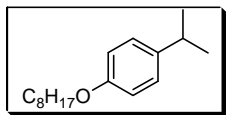


5-((R)-2-(4-Methoxyphenyl)butan-2-yl)-2,2-dimethyl-1,3-dioxane-4,6-dione (R-1l)

(1l): Prepared according to general procedure C. Purification by flash column chromatography eluting with 5:1 hexanes:EtOAc, followed by 3:1 and 1:1 hexanes,

EtOAc afforded white solid in 87% yield. M.p. 61-63 °C; ^1H NMR (CDCl_3 , 300 MHz) δ 7.18 (d, $J = 8.8$ Hz, 2H), 6.83 (d, $J = 8.7$ Hz, 2H), 3.76 (s, 3H), 3.50 (s, 1H), 2.19-2.01 (m, 2H), 1.57 (s, 3H), 1.56 (s, 3H), 1.16 (s, 3H), 0.76 (t, $J = 7.3$ Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 164.7 (C), 164.2 (C), 158.4 (C), 133.9 (C), 128.1 (CH), 113.6 (CH), 105.2 (C), 57.3 (CH), 55.1 (CH_3), 46.0 (C), 32.7 (CH_2), 29.6 (CH_3), 27.1 (CH_3), 22.2 (CH_3), 8.7 (CH_3). HRMS(EI) m/z calcd for $\text{C}_{17}\text{H}_{22}\text{O}_5$ (M^+): 306.3536. Found: 306.1465. An enantiomeric ratio of 98.5:1.5 ($R:S$) was measured by chiral HPLC AD-H, 10% *i*-PrOH/hexanes, 1.0 mL/min, $t_{\text{R}1} = 8.1$ min (S), $t_{\text{R}2} = 8.8$ min (R). The absolute stereochemistry was assigned by analogy to known (R)-2,2-dimethyl-5-(2-phenylbutan-2-yl)-1,3-dioxane-4,6-dione.³

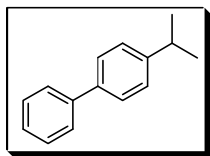
Product Specific Information



1-Isopropyl-4-(octyloxy)benzene (2a): Prepared according to general procedure D.

Purification by flash column chromatography eluting with 5:1 hexanes:CH₂Cl₂

afforded a clear liquid in 76% yield. ¹H NMR (CDCl₃, 300 MHz) δ 7.13 (d, *J* = 8.6 Hz, 2H), 6.83 (d, *J* = 8.6 Hz, 2H), 3.93 (t, *J* = 6.6 Hz, 2H), 2.86 (septet, *J* = 6.9 Hz, 1H), 1.77 (quintet, *J* = 7.8, 2H), 1.47 (quintet, *J* = 7.3 Hz, 2H), 1.32-1.29 (m, 8H), 1.23 (d, *J* = 7.0 Hz, 6H), 0.90 (m, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 157.2 (C), 140.8 (C), 127.16 (CH), 114.3 (CH), 68.0 (CH₂), 33.3 (CH), 31.8 (CH₂), 29.4 (2×CH₂), 29.3 (CH₂), 26.1 (CH₂), 24.2 (CH₃), 22.7 (CH₂), 14.1 (CH₃). GC/MS calcd for C₁₇H₂₈O (M⁺): 248. Found: 248.

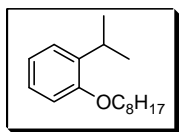


4-Isopropylbiphenyl (2b):⁶ Prepared according to general procedure D. Purification

by flash column chromatography eluting with 100% hexanes afforded a clear liquid

in 71% yield. ¹H NMR (CDCl₃, 300 MHz) δ 7.58 (d, *J* = 7.2 Hz, 2H), 7.54 (d, *J* = 8.1

Hz, 2H), 7.42 (t, *J* = 7.2 Hz, 2H), 7.29 (t, *J* = 7.8 Hz, 3H), 2.95 (septet, *J* = 6.9 Hz, 1H), 1.29 (d, *J* = 6.9 Hz, 6H); ¹³C NMR (CDCl₃, 75 MHz) δ 147.9 (C), 141.2 (C), 138.7 (C), 128.7 (CH), 127.1 (CH), 127.0 (CH), 126.9 (CH), 126.8 (CH), 33.8 (CH), 24.0 (CH₃).

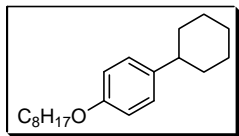


1-Isopropyl-2-(octyloxy)benzene (2e): Prepared according to general procedure D.

Purification by flash column chromatography eluting with 5:1 hexanes:CH₂Cl₂ afforded

a clear liquid in 65% yield. ¹H NMR (CDCl₃, 300 MHz) δ 7.22 (dd, *J* = 7.5, 1.6 Hz, 1H), 7.16 (dt, *J* = 7.7, 1.6 Hz, 1H), 6.92 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 8.1 Hz, 1H), 3.97 (t, *J* = 6.4 Hz, 2H), 3.36 (septet, *J* = 6.9 Hz, 1H), 1.82 (quintet, *J* = 6.6 Hz, 2H), 1.51 (quintet, *J* = 5.7 Hz, 2H), 1.45-1.30 (m, 8H), 1.24 (d, *J* = 6.9 Hz, 6H), 0.91 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 156.3 (C), 137.0 (C), 126.4 (CH), 126.0 (CH), 120.3 (CH), 111.1 (CH), 67.8 (CH₂), 31.8 (CH₂), 29.4 (CH₂), 29.3 (CH₂), 29.2

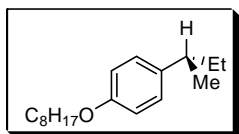
(CH₂), 26.9 (CH), 26.2 (CH₂), 22.6 (CH₂), 22.6 (CH₃), 14.1 (CH₃). GC/MS calcd for C₁₇H₂₈O (M⁺): 248. Found: 248.



1-Cyclohexyl-4-(octyloxy)benzene (2f): Prepared according to general procedure

D. Purification by flash column chromatography eluting with 5:1 hexanes:CH₂Cl₂

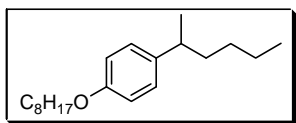
afforded a white solid in 81% yield. M.p. 41-42 °C; ¹H NMR (CDCl₃, 300 MHz) δ 7.10 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.5 Hz, 2H), 3.92 (t, *J* = 8.5 Hz, 2H), 2.43 (broad s, 1H), 1.85-1.71 (m, 6H), 1.44-1.28 (m, 16 H), 0.88 (t, *J* = 6.9 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 157.2 (C), 140.1 (C), 127.5 (CH), 114.2 (CH), 67.9 (CH₂), 43.7 (CH), 34.7 (CH₂), 31.8 (CH₂), 29.4 (2×CH₂), 29.3 (CH₂), 27.0 (CH₂), 26.2 (CH₂), 26.1 (CH₂), 22.7 (CH₂), 14.1 (CH₃). GC/MS calcd for C₂₀H₃₂O (M⁺): 288. Found: 288



(S)-1-sec-Butyl-4-(octyloxy)benzene (S-2g): Prepared according to general

procedure D. Purification by flash column chromatography eluting with 5:1

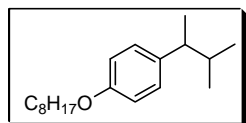
hexanes:CH₂Cl₂ afforded a clear liquid in 93% yield. ¹H NMR (CDCl₃, 300 MHz) δ 7.07 (d, *J* = 8.6 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 3.92 (t, *J* = 6.6 Hz, 2H), 2.53 (sextet, *J* = 7.0 Hz, 1H), 1.78 (quintet, *J* = 6.8 Hz, 2H), 1.52 (quintet, *J* = 7.3 Hz, 2H), 1.44 (quintet, *J* = 7.4 Hz, 2H), 1.30-1.28 (m, 8H), 1.20 (d, *J* = 6.9 Hz, 3H), 0.88 (t, *J* = 6.9 Hz, 3H), 0.80 (t, *J* = 7.4 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 157.2 (C), 139.5 (C), 127.8 (CH), 114.2 (CH), 67.9 (CH₂), 40.8 (CH), 31.8 (CH₂), 31.3 (CH₂), 29.4 (2×CH₂), 29.3 (CH₂), 26.1 (CH₂), 22.7 (CH₂), 22.0 (CH₃), 14.1 (CH₃), 12.2 (CH₃). GC/MS calcd for C₁₈H₃₀O (M⁺): 262. Found: 262. An enantiomeric ratio of 96:4 (*S*:*R*) was measured by chiral HPLC OD-H, 100% *n*-heptane, 0.5 mL/min, *t*_{R1} = 9.2 min (*S*), *t*_{R2} = 10.7 min (*R*). Absolute stereochemistry was assigned by analogy to known compound *S*-**2i** (see below).



1-(Hexan-2-yl)-4-(octyloxy)benzene (2h): Prepared according to general

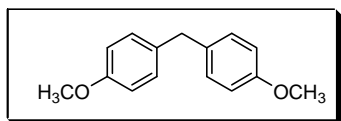
procedure D. Purification by flash column chromatography eluting with 5:1

hexanes:CH₂Cl₂ afforded a clear liquid in 90% yield. ¹H NMR (CDCl₃, 300 MHz) δ 7.07 (d, *J* = 8.1 Hz, 2H), 6.85 (d, *J* = 8.1 Hz, 2H), 3.92 (t, *J* = 6.5 Hz, 2H), 2.61 (sextet, *J* = 7.0 Hz, 1H), 1.76 (quintet, *J* = 7.1 Hz, 2H), 1.55-1.39 (m, 4H), 1.30-1.18 (m, 15H), 0.90-0.82 (m, 6H); ¹³C NMR (CDCl₃, 75 MHz) δ 157.2 (C), 139.9 (C), 127.7 (CH), 114.2 (CH), 67.9 (CH₂), 39.0 (CH₃), 38.3 (CH₂), 31.8 (CH₂), 29.9 (CH₂), 29.4 (2×CH₂), 29.3 (CH₂), 26.1 (CH₂), 22.8 (CH₂), 22.7 (CH₂), 22.5 (CH₃), 14.1 (CH₃), 14.0 (CH₃). GC/MS calcd for C₂₀H₃₄O (M⁺): 290. Found: 290.



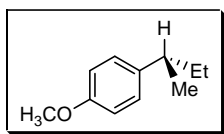
1-(3-Methylbutan-2-yl)-4-(octyloxy)benzene (2i): Prepared according to general

procedure D. However, 10% Pd/C (1 equiv) was used. Purification by flash column chromatography eluting with 9:1 hexanes:EtOAc afforded a clear liquid in 70% yield. ¹H NMR (CDCl₃, 300 MHz) δ 7.04 (d, *J* = 8.4 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 2H), 3.91 (t, *J* = 6.6 Hz, 2H), 2.36 (quintet, *J* = 7.2 Hz, 1H), 1.80-1.71 (m, 3H), 1.44 (quintet, *J* = 5.7 Hz, 2H), 1.30-1.27 (m, 8H), 1.19 (d, *J* = 7.2 Hz, 3H), 0.91-0.85 (m, 6H), 0.73 (d, *J* = 6.6 Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 157.2 (C), 138.9 (C), 128.4 (CH), 113.9 (CH), 67.9 (CH₂), 45.9 (CH), 34.5 (CH), 31.8 (CH₂), 29.4 (2×CH₂), 29.3 (CH₂), 26.1 (CH₂), 22.7 (CH₂), 21.0 (CH₃), 20.2 (CH₃), 18.9 (CH₃), 14.1 (CH₃). GC/MS calcd for C₁₉H₃₂O (M⁺): 276. Found: 276.



Bis(4-methoxyphenyl)methane (2k): Prepared according to general

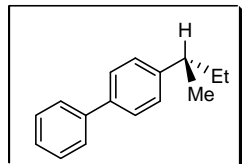
procedure D. Purification by flash column chromatography eluting with 9:1 hexanes:EtOAc afforded a white solid in 96% yield. M.p. 44-45 °C. ¹H NMR (CDCl₃, 300 MHz) δ 7.10 (d, *J* = 8.4 Hz, 4H), 6.82 (d, *J* = 8.4 Hz, 4H), 3.87 (s, 2H), 3.77 (s, 6H); ¹³C NMR (CDCl₃, 75 MHz) δ 157.9 (C), 133.7 (C), 129.7 (CH), 113.8 (CH), 55.2 (CH₃), 40.1 (CH₂). GC/MS calcd for C₁₅H₁₆O₂ (M⁺): 228. Found: 228.



(S)-2-(4-Methoxy-phenyl)butane (S-2l):⁷ Prepared according to general

procedure D. Purification by flash column chromatography eluting with 5:1 hexanes:CH₂Cl₂ afforded a clear liquid in 72% yield. ¹H NMR (CDCl₃, 300 MHz)

δ 7.09 (d, J = 8.4 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 3.78 (s, 3H), 2.54 (sextet, J = 6.9 Hz, 1H), 1.56 (quintet, J = 7.5 Hz, 2H), 1.21 (d, J = 6.9 Hz, 3H), 0.81 (t, J = 7.5 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 157.6 (C), 139.8 (C), 127.8 (CH), 113.6 (CH), 55.2 (CH_3), 40.8 (CH), 31.3 (CH_2), 22.0 (CH_3), 12.2 (CH_3). An enantiomeric ratio of 93.5:4.5 (S : R) was measured by chiral HPLC OD-H, 100% n -heptane, 0.5 mL/min, $t_{\text{R}1}$ = 14.4 min (S), $t_{\text{R}2}$ = 16.0 min (R).



(S)-1-sec-Butyl-4-phenylbenzene (S -2m) [16236-40-1]: Prepared according to general procedure D. Purification by flash column chromatography eluting with 100% hexanes afforded a clear liquid in 51% yield. ^1H NMR (CDCl_3 , 300 MHz) δ

7.61 (d, J = 7.3 Hz, 2H), 7.55 (d, J = 8.1 Hz, 2H), 7.45 (t, J = 7.4 Hz, 2H), 7.35 (d, J = 7.1 Hz, 1H), 7.28 (d, J = 8.1 Hz, 2H), 2.67 (sextet, J = 7.0 Hz, 1H), 1.66 (quintet, J = 7.4 Hz, 2H), 1.30 (d, J = 7.0 Hz, 3H), 0.89 (t, J = 8.0 Hz, 3H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 146.8 (C), 141.2 (C), 138.7 (C), 128.7 (CH), 127.4 (CH), 127.0 (CH), 126.9 (CH), 41.3 (CH), 31.2 (CH_2), 21.8 (CH_3), 12.3 (CH_3). An enantiomeric ratio of 90.5:9.5 (S : R) was measured by chiral HPLC OD-H, 100% n -heptane, 1 mL/min, $t_{\text{R}1}$ = 12.2 min (S), $t_{\text{R}2}$ = 20.6 min (R). Absolute stereochemistry was assigned by analogy to known compound ***S*-21** (see above).

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