Synthesis of All-Carbon, Quaternary Center-Containing Cyclohexenones through an Organocatalyzed, Multi-Component Coupling

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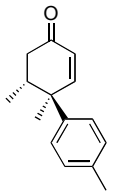
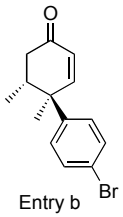
Electronic Supplementary Information: Structures Appendix

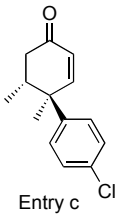
Appendix to Table 2. Initial Exploration of Reaction Scope: Structures of Products with Yield, Enantioselectivity and Diastereoselectivity.



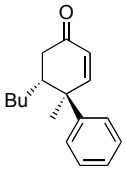
Entry a
35a
56% yield
94.4:5.6 (>20:1)



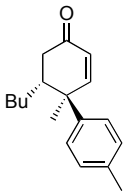
Entry b
35b
54% yield
93.6:6.4 (>20:1)



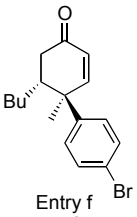
Entry c
35c
52% yield
93.6:6.4 (>20:1)



Entry d
35d
84% yield
95.7:4.3 (>20:1)

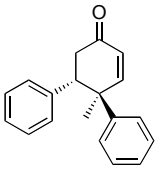


Entry e
35e
76% yield
91.5:8.5 (>20:1)

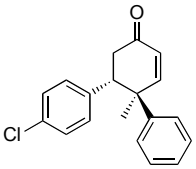


Entry f
35f
68% yield
95.9:4.1 (>20:1)

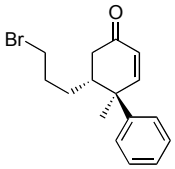
Appendix to Scheme 3. Further Exploration of Reaction Scope: Structures of Products with Yield, Enantioselectivity and Diastereoselectivity.



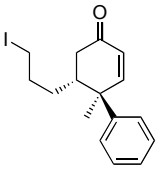
38
47% yield
97.5:2.5 er, >20:1 dr



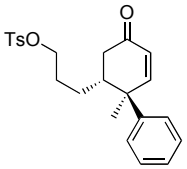
39
43% yield
87.8:11.8 er, >20:1 dr



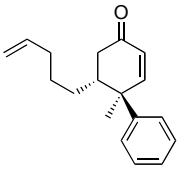
44
55% yield
63.8:36.2 er, >20:1 dr



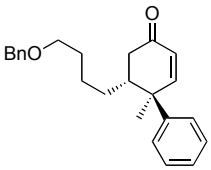
45
65% yield
56.6:43.4 er, >20:1 dr



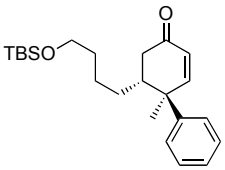
46
32% yield
88.3:11.7 er, 16:1 dr



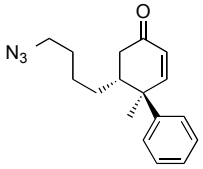
47
79% yield
92.6:7.4 er, >20:1 dr



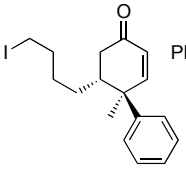
53
68% yield
92.7:7.3 er, >20:1 dr



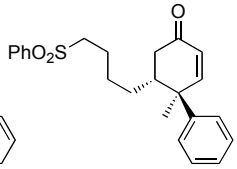
54
68% yield
89.7:10.3 er, >20:1 dr



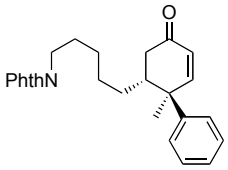
55
54% yield
91.4:8.6 er, >20:1 dr



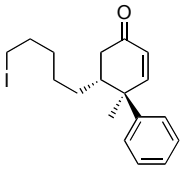
56
62% yield
81.6:18.4 er, >20:1 dr



57
39% yield
39%, 98.8:1.2 er, >20:1 dr



60
61% yield
96.9:3.1 er, 8:1 dr



61
55% yield
9 92.8:7.2 er, 15:1

Synthesis of All-Carbon, Quaternary Center-Containing Cyclohexenones through an Organocatalyzed, Multi-Component Coupling

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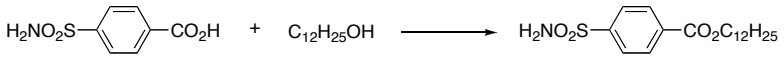
Electronic Supplementary Information: Experimental

General. Infrared spectra were recorded neat unless otherwise indicated and are reported in cm^{-1}. ^1H NMR spectra were recorded in deuterated solvents and are reported in ppm relative to tetramethylsilane and referenced internally to the residually protonated solvent. ^{13}C NMR spectra were recorded in deuterated solvents and are reported in ppm relative to tetramethylsilane and referenced internally to the residually protonated solvent. Chiral HPLC was performed with chiral columns (chirapak AD, OD, OJ, AS-H columns, (Daicel Chemical Ind., Ltd.)).

Routine monitoring of reactions was performed using EM Science DC-Alufolien silica gel, aluminum-backed TLC plates. Flash chromatography was performed with the indicated eluents on EM Science Gedurian 230-400 mesh silica gel.

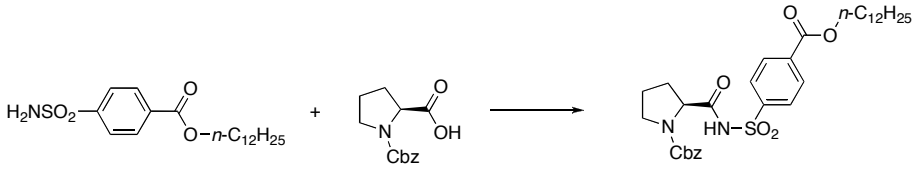
Air and/or moisture sensitive reactions were performed under usual inert atmosphere conditions. Reactions requiring anhydrous conditions were performed under a blanket of argon, in glassware dried in an oven at 120°C or by flame, then cooled under argon. Dry THF and DCM were obtained via a solvent purification system. All other solvents and commercially available reagents were either purified via literature procedures or used without further purification. 4Å Molecular Sieves was grounded and heated in the oven at 120ºC for 13 h before use.

2-(4-Methylphenl)-propanal **32**[1], 2-(4-bromophenl)-propanal **33**[2], 2-(4-chlorophenl)-propanal **34**[2]**,** 7-iodo-3-hepten-2-one **40**[3], 3-octen-8-[[(4-methylphenyl)sulfonyl]oxy]-2-one **42**[4], 8-[[(1,1-dimethylethyl)-dimethylsilyl]oxy]-3-octen-2-one **49**[5], [(5-hexen-1-yloxy)methyl]-benzene **63**[6]**,** 6-azido-1-hexene **64**[7], and 8-bromo-3-octen-2-one **65**[3] were prepared according to the reported procedure.



26 **27**

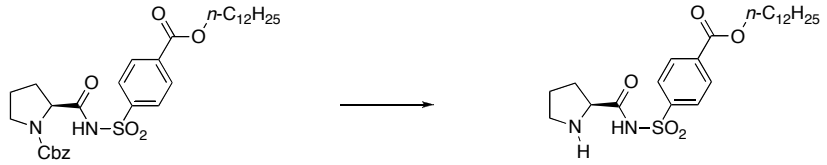
Sulfonamide 27: To a solution of 1-dodecanol (9.30 g, 50 mmol) in DMF (100 mL) was added sulfonamide **26** (5.03 g, 25 mmol), DMAP (1.53 g, 12.5 mmol) and EDCI (4.80 g, 25 mmol) respectively. The reaction mixture was stirred at room temperature for 48 h before being partitioned between EtOAc (150 mL) and aq. HCl (50 mL, 1 N). The organic layer was washed with brine (3 x 100 mL). The dried (Na_2SO_4) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 5-25% EtOAc/CH_2Cl_2, to give sulfonamide **27** (7.26 g, 19.7 mmol, 79%) as a white solid. Mp: 105-106ºC; IR (neat) 3330, 2916, 2845, 1713, 1282, 1157, 1124, 765, 738, 694 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, J = 8.4 Hz, 2H), 8.02 (d, J = 8.4 Hz, 2H), 4.99 (br s, 2H), 4.38 (t, J = 6.8 Hz, 2H), 1.79-1.83 (m, 2H), 1.29-1.46 (m, 18H), 0.90 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.2, 145.6, 134.4, 130.4, 126.5, 66.0, 31.9, 29.64, 29.58, 29.53, 29.4, 29.3, 28.6, 26.0, 22.7, 14.1; HRMS (EI+) calcd. for $C_{19}H_{31}NO_4S$ (M+), 369.1974 found 369.1971.



27 **28** **29**

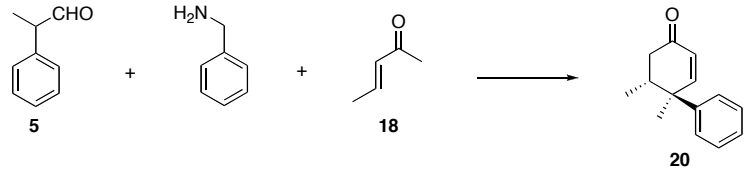
Z-L-sulfonamide 29: To a solution of *Z*-L-proline **28** (2.88 g, 11.6 mmol) in CH_2Cl_2 (58 mL) was added sulfonamide **27** (4.27 g, 11.6 mmol), DMAP (1.41 g, 11.6 mmol) and EDCI (2.22 g, 11.6 mmol) respectively. The reaction mixture was stirred at room temperature for 4 d before being partitioned between DCM (50 mL) and aq. HCl (50 mL, 1 N). The organic layer was washed with half-saturated brine (3 x 80 mL). The dried (Na_2SO_4) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 10-60% EtOAc/CH_2Cl_2, to give Z-L-sulfonamide **29** (5.06 g, 8.42 mmol, 73%) as a colorless oil. $[\alpha]_D^{23}$ = -94.0° (c=3.1, $CHCl_3$); IR (neat) 3477, 2922, 2851, 1718, 1691, 1615, 1435, 1266, 1092, 863, 770, 700, 6 18 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.0 Hz, 2H), 7.94 (d, J = 7.6 Hz, 2H), 7.19-

7.29 (m, 5H), 5.06 (d, J = 12.4 Hz, 1H), 4.91 (d, J = 12.4 Hz, 1H), 4.23-4.31 (m, 3H), 3.35-3.39 (m, 2H), 1.69-2.01 (m, 6H), 1.29-1.43 (m, 19H), 0.90 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 156.2, 146.1, 136.3, 133.2, 129.6, 128.4, 127.9, 127.7, 127.0, 67.3, 65.5, 62.8, 46.9, 31.9, 29.7, 29.6, 29.4, 28.7, 26.0, 24.3, 22.7, 14.1; HRMS (CI+) calcd. for $C_{32}H_{45}N_2O_7S$ (M+1), 601.2947 found 601.2921.

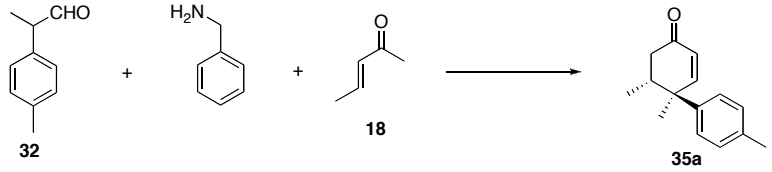


Sulfonamide 25: To a solution of Z-L-sulfonamide **29** (3.72 g, 6.20 mmol) in MeOH (100 mL) was added Pd/C (0.37 g, 10 %). The mixture was stirred at rt for under an atmosphere of hydrogen. After 20 h, the reaction was filtered through celite and silica gel pad, and the filtrate was concentrated *in vacuo* to give white solid. The crude product was purified by chromatography over silica gel, eluting with 1-20% MeOH / CH_2Cl_2, to give sulfonamide **25** (2.37 g, 5.08 mmol, 82%) as a white solid. Mp: 166-168 ºC; $[\alpha]_D^{23}$ = -88.1° (c=0.7, $CHCl_3$); IR (neat) 3129, 3074, 2922, 1729, 1620, 1560, 1391, 1266, 857, 732, 618 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (br s, 1H), 8.12 (d, J = 8.4 Hz, 2H), 8.00 (d, J = 8.4 Hz, 2H), 4.33-4.38 (m, 3H), 3.37-3.51 (m, 2H), 2.35-2.38 (m, 1H), 1.75-2.05 (m, 5H), 1.29-1.45 (m, 19H), 0.90 (t, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 165.6, 146.9, 133.3, 129.8, 126.5, 65.7, 63.0, 46.8, 31.9, 29.9, 29.63, 29.55, 29.4, 29.3, 28.7, 26.0, 24.6, 22.7, 14.1; HRMS (CI+) calcd. for $C_{24}H_{39}N_2O_5S$ (M+1), 467.2580 found 467.2566.

General procedure for three-component reaction (20 mol% catalyst): The aldehyde (0.25 mmol), benzyl amine (0.25 mmol) and 4Å MS (0.1 g) were added to dichloroethane solution (0.25 mL) in a vial. After stirring at room temperature for 30 min, the corresponding enone (0.75 mmol, 3 equiv.) and sulfonamide **25** (23.3 mg, 0.05 mmol) were added to it at room temperature. After stirring at same temperature, reaction was loaded directly onto silica gel and was purified by chromatography, eluting with EtOAc / hexanes, to give the corresponding product.

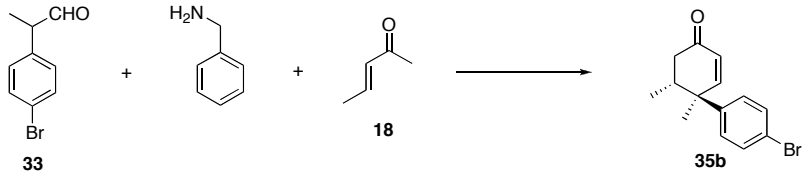


4,5-Dimethyl-4-phenyl-2-cyclohexen-1-one 20: Reaction time 60 h. Purified by chromatography over silica gel, eluting with 1-4% EtOAc / hexanes, to give enone **20** (37.3 mg, 75%, 94.6:5.4 er, >20:1 dr, colorless crystal). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OD column, 99:1 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 13.3 min (major) and 16.1 min (minor)] to be 94.6:5.4 er: Mp: 48-50ºC; $[\alpha]_D^{23}$ = -63.4° (c=1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27-7.40 (m, 5H), 6.84 (d, J = 10.0 Hz, 1H), 6.10 (d, J = 10.0 Hz, 1H), 2.36-2.45 (m, 3H), 1.47 (s, 3H), 0.84-0.86 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 159.1, 146.2, 128.4, 127.4, 126.8, 126.7, 44.2, 42.6, 40.6, 16.9, 15.8; HRMS (CI+) calcd. for $C_{14}H_{17}O$ (M+1), 201.1279 found 201.1269.

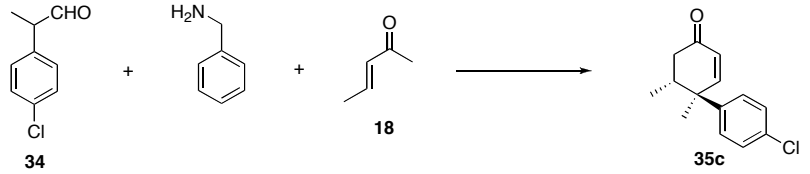


4,5-Dimethyl-4-(4-methylphenyl)-2-cyclohexen-1-one 35a: Reaction time 60 h. Purified by

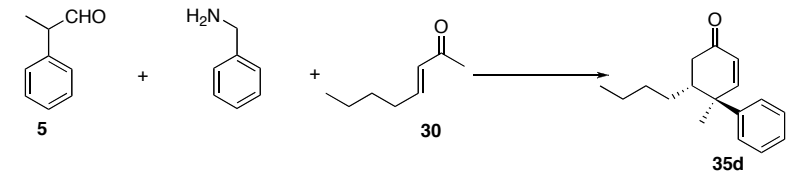
chromatography over silica gel, eluting with 1-4% EtOAc / hexanes, to give enone **35a** (30.1 mg, 56%, 94.4:5.6 er, >20:1 dr, colorless crystal). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OJ column, 95:5 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 9.89 min (major) and 18.5 min (minor)] to be 94.4:5.6 er: Mp: 64-66ºC; $[\alpha]_D^{23}$ = -90.4° (c=1.2, $CHCl_3$); IR (neat) 2961, 1680, 1455, 1385, 1276, 1116, 816, 778 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.18-7.22 (m, 4H), 6.83 (d, *J* = 10.0 Hz, 1H), 6.09 (d, *J* = 10.0 Hz, 1H), 2.36-2.46 (m, 6H), 1.45 (s, 3H), 0.86-0.87 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.0, 159.4, 143.3, 136.4, 129.1, 127.3, 126.7, 43.9, 42.6, 40.6, 20.9, 16.9, 15.8; HRMS (CI+) calcd. for $C_{15}H_{19}O$ (M+1), 215.1436 found 215.1435.



4-(4-Bromophenyl)-4,5-dimethyl-2-cyclohexen-1-one 35b: Reaction time 60 h. Purified by chromatography over silica gel, eluting with 1-5% EtOAc / hexanes, to give enone **35b** (37.4 mg, 54%, 93.6:6.4 er, >20:1 dr, colorless crystal). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OJ column, 98:2 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 16.6 min (major) and 20.3 min (minor)] to be 93.6:6.4 er: Mp: 144-146ºC; $[\alpha]_D^{23}$ = -101.6° (c=1.3, $CHCl_3$); IR (neat) 2976, 1685, 1457, 1081, 808, 792, 716 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.47-7.51 (m, 1H), 7.17-7.20 (m, 1H), 6.78 (d, *J* = 10.0 Hz, 1H), 6.10 (d, *J* = 10.4 Hz, 1H), 2.34-2.44 (m, 3H), 1.44 (s, 3H), 0.84 (d, *J* = 6.0 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 158.1, 145.4, 131.5, 128.7, 127.8, 120.8, 44.0, 42.4, 40.6, 16.9, 15.7; HRMS (CI+) calcd. for $C_{14}H_{16}OBr$ (M+1), 279.0385 found 279.0382.

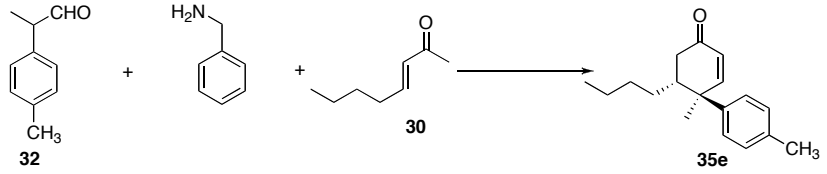


4-(4-Chlorophenyl)-4,5-dimethyl-2-cyclohexen-1-one 35c: Reaction time 60 h. Purified by chromatography over silica gel, eluting with 1-5% EtOAc / hexanes, to give enone **35c** (30.6 mg, 52%, 93.6:6.4 er, >20:1 dr, light yellow crystal). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OJ column, 95:5 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 11.6 min (major) and 14.2 min (minor)] to be 93.6:6.4 er: Mp: 133-135ºC; $[\alpha]_D^{23}$ = -97.6° (c=1.3, $CHCl_3$); IR (neat) 2965, 2927, 1685, 1484, 1457, 1271, 1005, 814, 732, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34-7.36 (m, 2H), 7.23-7.28 (m, 2H), 6.79 (d, *J* = 10.4 Hz, 1H), 6.10 (d, *J* = 10.0 Hz, 1H), 2.33-2.47 (m, 3H), 1.44 (s, 3H), 0.84 (d, *J* = 6.0 Hz, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 158.3, 144.8, 132.7, 128.5, 128.3, 127.7, 44.0, 42.5, 40.6, 16.9, 15.7; HRMS (CI+) calcd. for $C_{14}H_{16}OCl$ (M+1), 235.0890 found 235.0883.

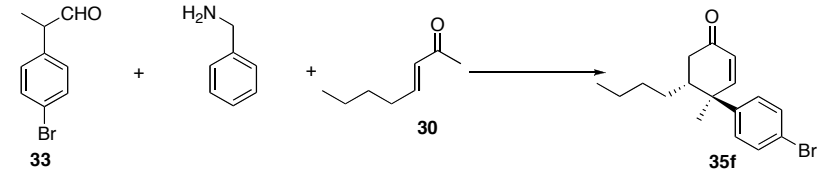


5-Butyl-4-methyl-4-phenyl-2-cyclohexen-1-one 35d: Reaction time 4 d. Purified by chromatography over silica gel, eluting with 1-3% EtOAc / hexanes, to give enone **35d** (50.9 mg, 84%, 95.7:4.3 er, >20:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OD column, 99.5:0.5 Hexanes / *i*-PrOH, 0.8 mL min^{-1}, retention times 17.0 min (major) and 12.6 min (minor)] to be 95.7:4.3 er: $[\alpha]_D^{23}$ = -100.9° (c=2.0, $CHCl_3$); IR (neat) 2253, 2930, 1680, 1498, 1373, 1272, 1023, 762, 704

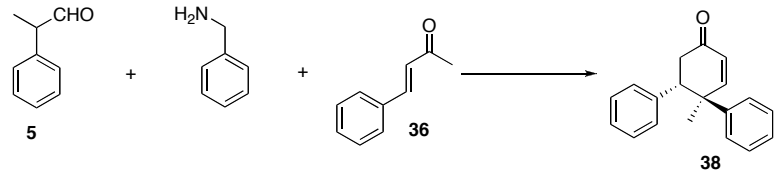
cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26-7.39 (m, 4H), 6.80 (d, *J* = 10.0 Hz, 1H), 6.07 (d, *J* = 10.0 Hz, 1H), 2.61 (dd, *J* = 16.0, 3.2 Hz, 1H), 2.18-2.34 (m, 2H), 1.46 (s, 3H), 0.92-1.30 (m, 7H), 0.73 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.0, 159.5, 146.3, 128.4, 127.2, 127.0, 126.7, 45.4, 44.4, 39.6, 29.2, 29.1, 22.4, 16.9, 13.8; HRMS (CI+) calcd. for $C_{17}H_{23}O$ (M+1), 243.1749 found 243.1748.



5-Butyl-4-methyl-4-(4-methylphenyl)-2-cyclohexen-1-one 35e: Reaction time 3 d. Purified by chromatography over silica gel, eluting with 1-4% EtOAc / hexanes, to give enone **35e** (48.9 mg, 76%, 91.5:8.5 er, >20:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel AS-H column, 98:2 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 33.9 min (major) and 38.1 min (minor)] to be 91.5:8.5 er: $[\alpha]_D^{23}$ = -97.4° (c=2.0, $CHCl_3$); IR (neat) 2954, 2927, 1685, 1457, 1266, 1124, 1021, 814, 776, 721 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17-7.22 (m, 4H), 6.78 (d, *J* = 10.0 Hz, 1H), 6.06 (d, *J* = 10.0 Hz, 1H), 2.61 (dd, *J* = 16.4, 3.6 Hz, 1H), 2.38 (s, 3H), 2.17-2.34 (m, 2H), 1.45 (s, 3H), 0.94-1.29 (m, 6H), 0.77 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.1, 159.8, 143.3, 136.3, 129.1, 127.0, 126.8, 45.3, 44.1, 39.6, 29.3, 29.1, 22.5, 20.9, 17.0, 13.8; HRMS (CI+) calcd. for $C_{18}H_{25}O$ (M+1), 257.1905 found 257.1910.

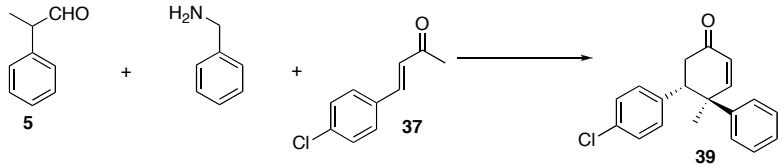


4-(4-Bromophenyl)-5-butyl-4-methyl-2-cyclohexen-1-one 35f: Reaction time 3 d. Purified by chromatography over silica gel, eluting with 1-5% EtOAc / hexanes, to give enone **35f** (54.5 mg, 68%, 95.9:4.1 er, >20:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel AS-H column, 90:10 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 36.8 min (major) and 28.2 min (minor)] to be 95.9:4.1 er: $[\alpha]_D^{23}$ = -125° (c=1.5, $CHCl_3$); IR (neat) 2953, 2930, 1680, 1490, 1077, 1003, 816, 723 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49-7.52 (m, 2H), 7.18-7.21 (m, 2H), 6.74 (d, *J* = 10.0 Hz, 1H), 6.08 (d, *J* = 10.0 Hz, 1H), 2.62 (dd, *J* = 16.8, 4.0 Hz, 1H), 2.14-2.33 (m, 2H), 1.45 (s, 3H), 0.89-1.31 (m, 6H), 0.77 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 158.6, 145.4, 131.5, 128.8, 127.5, 120.8, 45.4, 44.3, 39.5, 29.3, 29.1, 22.4, 16.9, 13.8; HRMS (CI+) calcd. for $C_{17}H_{22}OBr$ (M+1), 321.0854 found 321.0860.

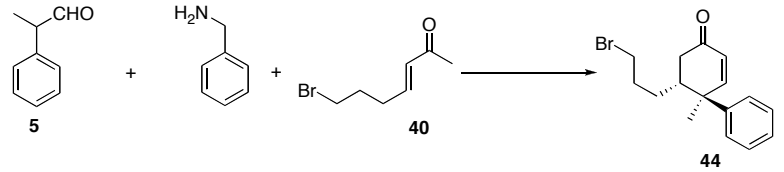


4,5-Diphenyl-4-methyl-2-cyclohexen-1-one 38: Reaction time 4 d. Purified by chromatography over silica gel, eluting with 1-4% EtOAc / hexanes, to give enone **38** (31.1 mg, 47%, 97.5:2.5 er, >20:1 dr, white solid). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OD column, 99:1 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 29.1 min (major) and 23.8 min (minor)] to be 97.5:2.5 er: Mp: 104-106ºC; $[\alpha]_D^{23}$ = -102.9° (c=1.4, $CHCl_3$); IR (neat) 3020, 2971, 1669, 1495, 1446, 1266, 798, 770, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.32 (m, 4H), 7.12-7.21 (m, 3H), 7.05 (dd, *J* = 8.0, 2.4 Hz, 1H), 6.97 (d, *J* = 10.0 Hz, 1H), 6.64 (d, *J* = 7.2 Hz, 2H), 6.22 (d, *J* = 10.0 Hz, 1H), 3.57 (dd, *J* = 14.0, 3.6 Hz, 1H), 3.11

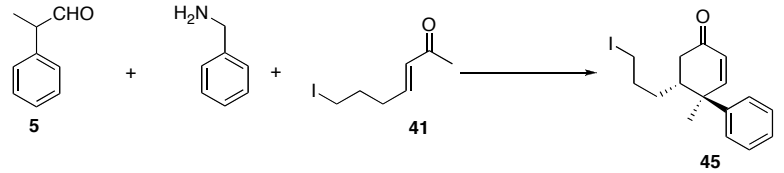
(dd, *J* = 16.8, 14.2 Hz, 1H), 2.63 (dd, *J* = 16.8, 4.0 Hz, 1H), 1.40 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9, 158.8, 145.5, 138.9, 129.0, 128.2, 127.6, 127.19, 127.17, 127.0, 126.9, 52.2, 45.4, 40.1, 17.3; HRMS (CI+) calcd. for $C_{19}H_{19}O$ (M+1), 263.1436 found 263.1437.



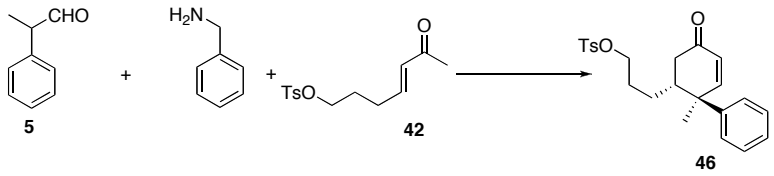
5-(4-Chlorophenyl)-4-phenyl-4-methyl-2-cyclohexen-1-one 39: Reaction time 4 d. Purified by chromatography over silica gel, eluting with 1-5% EtOAc / hexanes, to give enone **39** (32.2 mg, 43%, 87.8:12.2 er, >20:1 dr, light yellow crystal). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel AS-H column, 90:10 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 44.5 min (major) and 37.6 min (minor)] to be 87.8:12.2 er: Mp: 106-108ºC; $[\alpha]_D^{23}$ = -150.2° (c=1.1, $CHCl_3$); IR (neat) 3031, 2976, 1685, 1495, 1255, 1097, 1015, 830, 759, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) 7.28-7.34 (m, 3H), 7.11 (d, *J* = 8.4 Hz, 2H), 7.04 (dd, *J* = 8.0, 2.0 Hz, 2H), 6.96 (d, *J* = 10.4 Hz, 1H), 6.54 (d, *J* = 8.4 Hz, 2H), 6.22 (d, *J* = 10.4 Hz, 1H), 3.54 (dd, *J* = 14.4, 3.6 Hz, 1H), 3.06 (dd, *J* = 16.8, 14.8 Hz, 1H), 2.60 (dd, *J* = 16.4, 3.6 Hz, 1H), 1.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 158.6, 145.1, 137.4, 132.9, 130.2, 128.3, 127.8, 127.2, 127.1, 51.6, 45.2, 39.9, 17.1; HRMS (CI+) calcd. for $C_{19}H_{18}OCl$ (M+1), 297.1046 found 297.1044.



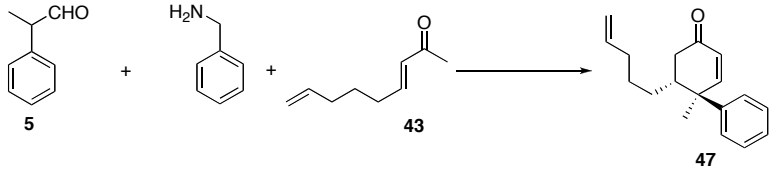
5-(3-Bromopropyl)-4-methyl-4-phenyl-2-cyclohexen-1-one 44: Reaction time 4 d. Purified by chromatography over silica gel, eluting with 1-5% EtOAc / hexanes, to give enone **44** (42.2 mg, 55%, 63.8:36.2 er, >20:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OD column, 98:2 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 20.0 min (major) and 24.0 min (minor)] to be 63.8:36.2 er: $[\alpha]_D^{23}$ = -26.7° (c=1.1, $CHCl_3$); IR (neat) 2926, 1684, 1660, 1501, 770, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.41 (m, 5H), 6.81 (d, *J* = 10.4 Hz, 1H), 6.09 (d, *J* = 10.0 Hz, 1H), 3.13-3.29 (m, 2H), 2.58 (dd, *J* = 16.4, 3.6 Hz, 1H), 2.21-2.39 (m, 2H), 1.77-1.89 (m, 1H), 1.24-1.57 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 159.2, 145.8, 128.6, 127.2, 127.0, 126.9, 45.1, 44.4, 39.7, 33.2, 30.3, 28.5, 16.9; HRMS (EI+) calcd. for $C_{16}H_{19}OBr$ (M+), 306.0619 found 306.0618.



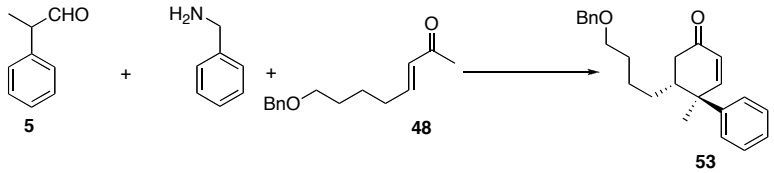
5-(3-Iodopropyl)-4-methyl-4-phenyl-2-cyclohexen-1-one 45: Reaction time 4 d. Purified by chromatography over silica gel, eluting with 1-3% EtOAc / hexanes, to give enone **45** (57.6 mg, 65%, 56.6:43.4 er, >20:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OD column, 99:1 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 23.9 min (major) and 19.8 min (minor)] to be 56.6:43.4 er: IR (neat) 2957, 2918, 2848, 1680, 1455, 1369, 1276, 1023, 781, 766, 704 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.41 (m, 5H), 6.81 (d, *J* = 10.0 Hz, 1H), 6.09 (d, *J* = 10.0 Hz, 1H), 2.91-3.07 (m, 2H), 2.57 (dd, *J* = 16.4, 3.6 Hz, 1H), 2.24-2.38 (m, 2H), 1.71-1.89 (m, 1H), 1.24-1.57 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 159.2, 145.8, 128.6, 127.2, 127.0, 126.9, 44.8, 44.3, 39.7, 31.0, 30.8, 16.9, 6.0; HRMS (CI+) calcd. for $C_{16}H_{19}OI$ (M+), 354.0481 found 354.0478.



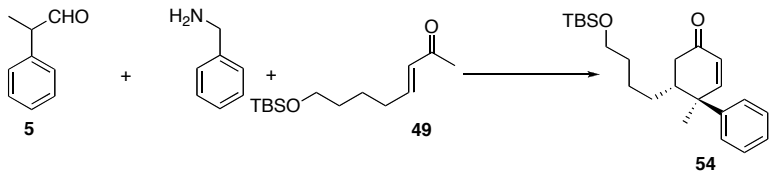
4-Methyl-4-phenyl-5-(3-tosyloxylbutyl)-2-cyclohexen-1-one 46: Reaction time 4 d. Purified by chromatography over silica gel, eluting with 2-20% EtOAc / hexanes, to give enone **46** (31.8 mg, 32%, 88.3:11.7 er, 16:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel AD column, 90:10 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 36.7 min (major) and 30.2 min (minor)] to be 88.3:11.7 er: $[\alpha]_D^{23}$ = -24.6° (c=1.1, $CHCl_3$); IR (neat) 2957, 2926, 1677, 1357, 1178, 953, 918, 816, 762, 704, 661 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.0 Hz, 2H), 7.26-7.40 (m, 7H), 6.78 (d, *J* = 10.0 Hz, 1H), 6.07 (d, *J* = 10.0 Hz, 1H), 3.82-3.88 (m, 2H), 2.47-2.52 (m, 4H), 2.14-2.31 (m, 2H), 1.61-1.62 (m, 1H), 1.44(s, 3H), 1.23-1.29 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.1, 159.1, 145.8, 144.8, 133.1, 129.8, 128.6, 127.9, 127.1, 127.0, 126.8, 70.1, 45.2, 44.3, 39.4, 26.5, 25.9, 21.7, 17.0; HRMS (CI+) calcd. for $C_{23}H_{26}O_4S$ (M+), 398.1552 found 398.1543.



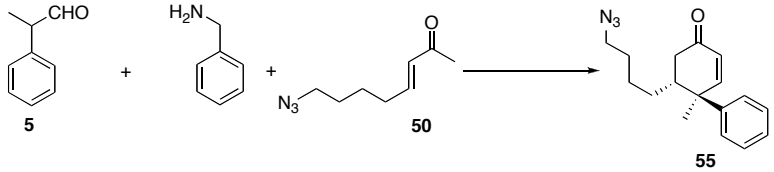
4-Methyl-5-(4-pentenyl)-4-phenyl-2-cyclohexen-1-one 47: Reaction time 4 d. Purified by chromatography over silica gel, eluting with 1-3% EtOAc / hexanes, to give enone **47** (50.2 mg, 79%, 92.6:7.4 er, >20:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OD column, 99.5:0.5 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 13.5 min (major) and 17.6 min (minor)] to be 92.6:7.4 er: $[\alpha]_D^{23}$ = -78.5° (c=1.2, $CHCl_3$); IR (neat) 3058, 3023, 2926, 2852, 1684, 1498, 1459, 1264, 1023, 992, 914, 789, 762, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.27-7.40 (m, 5H), 6.80 (d, *J* = 10.0 Hz, 1H), 6.08 (d, *J* = 10.0 Hz, 1H), 5.58-5.66 (m, 1H), 4.81-4.86 (m, 2H), 2.61 (dd, *J* = 16.4, 2.8 Hz, 1H), 2.19-2.35 (m, 2H), 1.76-1.95 (m, 2H), 1.46 (s, 3H), 1.05-1.46 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.8, 159.4, 146.2, 138.2, 128.4, 127.2, 127.0, 126.8, 114.6, 45.3, 44.4, 39.6, 33.3, 29.0, 26.1, 16.9; HRMS (CI+) calcd. for $C_{18}H_{22}O$ (M+), 254.1671 found 254.1663.



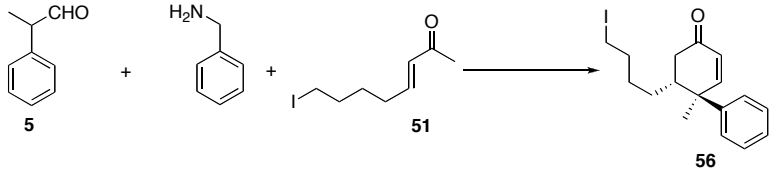
4-Methyl-4-phenyl-5-(4-phenylmethoxybutyl)-2-cyclohexen-1-one 53: Reaction time 4 d. Purified by chromatography over silica gel, eluting with 1-5% EtOAc / hexanes, to give enone **53** (59.2 mg, 68%, 92.7:7.3 er, >20:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OJ column, 85:15 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 20.9 min (major) and 29.2 min (minor)] to be 92.7:7.3 er: $[\alpha]_D^{23}$ = -51.3° (c=1.6, $CHCl_3$); IR (neat) 2926, 2852, 1680, 1451, 1097, 758, 735, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.39 (m, 10H), 6.80 (d, *J* = 10.0 Hz, 1H), 6.08 (d, *J* = 10.0 Hz, 1H), 4.41 (s, 2H), 3.28-3.31 (m, 2H), 2.62 (dd, *J* = 16.0, 2.8 Hz, 1H), 2.19-2.34 (m, 2H), 1.02-1.46 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.8, 159.4, 146.2, 138.5, 128.43, 128.35, 127.6, 127.5, 127.2, 127.0, 126.8, 72.9, 69.9, 45.4, 44.4, 39.6, 29.5, 29.4, 23.6, 16.9; HRMS (EI+) calcd. for $C_{24}H_{28}O_2$ (M+), 348.2089 found 348.2085.



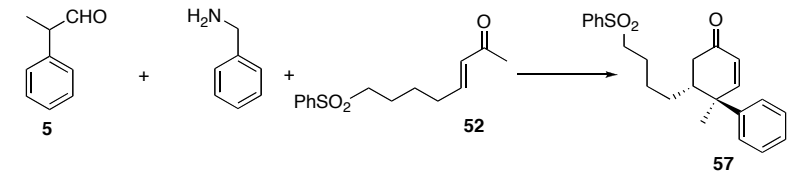
5-[4-[(1,1-Dimethylethyl)dimethylsilyl]oxybutyl]-4-methyl-4-phenyl-2-cyclohexen-1-one 54: Reaction time 5 d. Purified by chromatography over silica gel, eluting with 1-5% EtOAc / hexanes, to give enone **54** (62.9 mg, 68%, 89.7:10.3 er, >20:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OJ column, 85:15 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 11.8 min (major) and 14.7 min (minor)] to be 89.7:10.3 er: $[\alpha]_D^{23}$ = -59.0° (c=2.0, $CHCl_3$); IR (neat) 2949, 2930, 2852, 1684, 1470, 1385,1252, 1101, 1027, 836, 774, 704, 665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.26-7.39 (m, 5H), 6.80 (d, *J* = 10.4 Hz, 1H), 6.07 (d, *J* = 10.0 Hz, 1H), 3.44 (t, *J* = 6.4 Hz, 2H), 2.61 (dd, *J* = 16.0, 3.2 Hz, 1H), 2.23-2.34 (m, 2H), 1.46 (s, 3H), 1.37 (m, 7H), 0.86 (s, 9H), -0.005 (s, 3H), -0.008 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.8, 159.5, 146.2, 128.4, 127.2, 126.9, 126.8, 62.7, 45.5, 44.4, 39.6, 32.5, 29.4, 26.0, 23.2, 18.3, 16.9, -5.32; HRMS (CI+) calcd. for $C_{23}H_{37}O_2Si$ (M+1), 373.2563 found 373.2549.



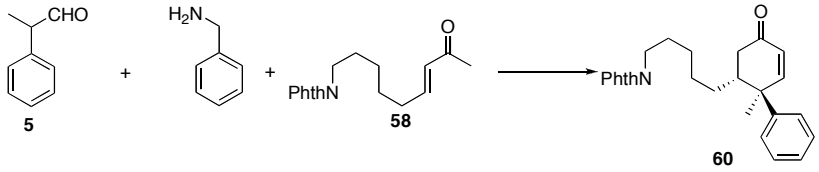
5-(4-Azidobutyl)-4-methyl-4-phenyl-2-cyclohexen-1-one 55: Reaction time 4 d (no light). Purified by chromatography over silica gel, eluting with 1-5% EtOAc / hexanes, to give enone **55** (38.2 mg, 54%, 91.4:8.6 er, >20:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OD column, 98:2 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 20.0 min (major) and 25.8 min (minor)] to be 91.4:8.6 er: $[\alpha]_D^{23}$ = -67.9° (c=1.2, $CHCl_3$); IR (neat) 2934, 2860, 2093, 1684, 1260, 766, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.28-7.41 (m, 5H), 6.81 (d, *J* = 10.0 Hz, 1H), 6.08 (d, *J* = 10.0 Hz, 1H), 3.07 (t, *J* = 6.4 Hz, 2H), 2.60 (dd, *J* = 16.4, 3.2 Hz, 1H), 2.18-2.36 (m, 2H), 1.46 (s, 3H), 1.05-1.45 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 159.3, 146.0, 128.5, 127.2, 126.9, 51.0, 45.3, 44.4, 39.6, 29.0, 28.5, 24.0, 16.8; HRMS (EI+) calcd. for $C_{17}H_{21}N_3O$ (M+), 283.1685 found 283.1677.



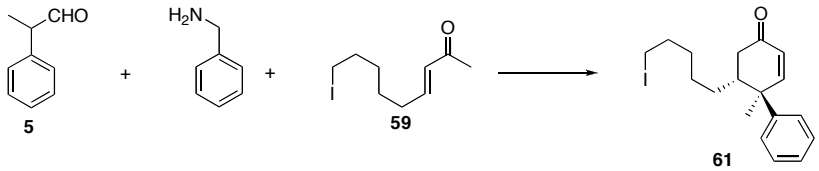
5-(4-Iodobutyl)-4-methyl-4-phenyl-2-cyclohexen-1-one 56: Reaction time 4 d. Purified by chromatography over silica gel, eluting with 1-5% EtOAc / hexanes, to give enone **56** (57.1 mg, 62%, 81.6:18.4 er, >20:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OD column, 99:1 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 18.1 min (major) and 23.5 min (minor)] to be 81.6:18.4 er: $[\alpha]_D^{23}$ = -27.3° (c=1.6, $CHCl_3$); IR (neat) 2926, 2856, 1680, 1498, 1459, 1369, 1101, 1027, 766, 707 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.42 (m, 5H), 6.82 (d, *J* = 10.4 Hz, 1H), 6.09 (d, *J* = 10.0 Hz, 1H), 2.96-3.02 (m, 2H), 2.63 (dd, *J* = 16.4, 3.6 Hz, 1H), 2.23-2.37 (m, 2H), 1.09-1.65 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 159.3, 146.0, 128.5, 127.2, 126.9, 45.2, 44.4, 39.6, 32.9, 28.4, 27.8, 16.8, 6.23; HRMS (EI+) calcd. for $C_{17}H_{21}OI$ (M+), 368.0638 found 368.0625.



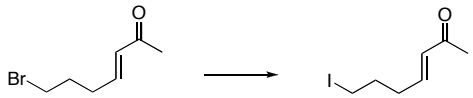
4-Methyl-4-phenyl-5-(4-phenylsulfonyl)-2-cyclohexen-1-one 57: Reaction time 5 d. Purified by chromatography over silica gel, eluting with 5-20% EtOAc / hexanes, to give enone **57** (37.2 mg, 39%, 98.8:1.2 er, 15:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OD column, 90:10 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 37.2 min (major) and 28.2 min (minor)] to be 98.8:1.2 er: $[\alpha]_D^{23}$ = -55.9° (c=1.8, $CHCl_3$); IR (neat) 2922, 2867, 1677, 1447, 1307, 1143, 1085, 766, 707, 684, 598 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83-7.85 (m, 2H), 7.54-7.68 (m, 4H), 7.26-7.39 (m, 4H), 6.77 (d, *J* = 10.0 Hz, 1H), 6.06 (d, *J* = 10.4 Hz, 1H), 2.85 (t, *J* = 8.0 Hz, 2H), 2.51 (dd, *J* = 16.4, 3.6 Hz, 1H), 2.14-2.30 (m, 2H), 1.02-1.60 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.3, 159.2, 145.9, 139.1, 133.7, 129.3, 128.6, 128.0, 127.2, 127.0, 126.9, 55.8, 45.1, 44.3, 39.5, 29.0, 25.6, 22.3, 16.8; HRMS (EI+) calcd. for $C_{23}H_{26}O_3S$ (M+), 382.1603 found 382.1584.



4-Methyl-4-phenyl-5-(6-phthalimidohexyl)-2-cyclohexen-1-one 60: Reaction time 5 d. Purified by chromatography over silica gel, eluting with 1-6% EtOAc / hexanes, to give enone **60** (61.3 mg, 61%, 96.9:3.1 er, 8:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OD column, 90:10 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 26.4 min (major) and 24.5 min (minor)] to be 96.9:3.1 er: $[\alpha]_D^{23}$= -38.3° (c=1.0, $CHCl_3$); IR (neat) 2933, 2851, 1767, 1718, 1680, 1467, 1391, 1369, 1064, 765, 721, 705 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70-7.86 (m, 4H), 7.22-7.37 (m, 5H), 6.78 (d, *J* = 10.0 Hz, 1H), 6.06 (d, *J* = 10.0 Hz, 1H), 3.58 (t, *J* = 7.2 Hz, 2H), 2.59 (dd, *J* = 16.4, 3.2 Hz, 1H), 2.00-2.33 (m, 3H), 1.10-1.64 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.8, 168.4, 159.4, 146.2, 133.9, 132.2, 128.4, 128.3, 127.9, 127.1, 126.9, 126.8, 123.2, 45.4, 44.4, 39.6, 37.8, 29.5, 28.3, 26.63, 26.56, 16.9; HRMS (EI+) calcd. for $C_{26}H_{27}NO_3$ (M+), 401.1991 found 401.183.



5-(5-Iodopentyl)-4-methyl-4-phenyl-2-cyclohexen-1-one 61: Reaction time 5 d. Purified by chromatography over silica gel, eluting with 1-5% EtOAc / hexanes, to give enone **61** (52.6 mg, 55%, 92.8:7.2 er, 16:1 dr, colorless oil). Enantiomeric excess was determined by chiral HPLC [4.6 x 250 mm Daicel OD column, 99:1 Hexanes / *i*-PrOH, 1.0 mL min^{-1}, retention times 16.9 min (major) and 21.9 min (minor)] to be 92.8:7.2 er: $[\alpha]_D^{23}$ = -64.2° (c=2.1, $CHCl_3$); IR (neat) 2922, 2851, 1685, 1451, 1364, 1260, 1168, 1026, 787, 765, 700 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.40 (m, 5H), 6.80 (d, *J* = 10.0 Hz, 1H), 6.08 (dd, *J* = 10.4, 0.8 Hz, 1H), 3.06 (t, *J* = 7.2 Hz, 2H), 2.59 (dd, *J* = 16.8, 2.8 Hz, 1H), 1.59-1.66 (m, 2H), 1.46 (s, 3H), 1.12-1.33 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.7, 159.4, 146.1, 128.5, 127.2, 126.94, 126.86, 45.3, 44.4, 39.6, 33.0, 30.1, 20.3, 25.8, 16.9, 6.84; HRMS (EI+) calcd. for $C_{18}H_{23}OI$ (M+), 382.0794 found 382.0809.

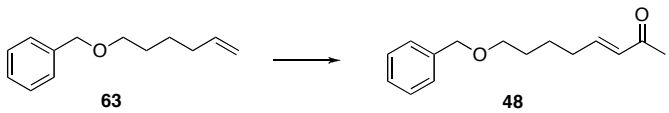


40 **41**

7-Iodo-3-hepten-2-one 41[8]**:** To a solution of bromide **40** (0.397 g, 2.08 mmol) in acetone (6.0 mL) was added NaI (0.934 g, 6.23 mmol). The reaction mixture was heated to reflux. After 36 h, the reaction was cooled to rt and the solvent was removed *in vacuo*. The reaction mixture was loaded directly onto silica gel and was purified by chromatography, eluting with 2-10% Ether / hexanes, to give the iodide **41** (0.423 g, 1.78 mmol, 85%) as colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (dt, *J* = 16.0, 6.8 Hz, 1H), 6.16 (dd, *J* = 16.0, 1.2 Hz, 1H), 3.22 (t, *J* = 6.8 Hz, 2H), 2.36-2.42 (m, 2H), 2.27 (s, 3H), 2.02 (p, *J* = 6.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.2, 145.4, 132.1, 33.0, 31.5, 27.1, 5.26.

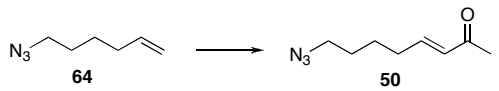
62 **44**

3, 8-Nonadien-2-one 44[9]**:** To a solution of 5-hexen-1-ol **62** (0.5 g, 5.0 mmol) and 4 Å MS (1.0 g) in CH_2Cl_2 (10 mL) was added *N*-methylmorpholine-*N*-oxide (1.17 g, 10 mmol) and TPAP (87.8 mg, 0.25 mmol). After 6 h, the suspension was diluted with hexanes (5 mL), filtered through silica gel pad, washed with 20% EtOAc in hexanes, and then concentrated *in vacuo* to give crude aldehyde. The crude aldehyde was immediately redissovled in THF (25 mL), and 1-(triphenylphosphoranylidene)-2-propanone (1.91 g, 6.0 mmol) was added to the solution. The resulting mixture was heated to reflux. After 16 h, the reaction was concentrated *in vacuo* and loaded directly onto silica gel. It was purified by chromatography, eluting with 2-15% Ether / hexanes, to give (0.491 g, 3.55 mmol, 71%) as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (dt, *J* = 16.0, 6.8 Hz, 1H), 6.06 (dt, *J* = 15.6, 1.6 Hz, 1H), 5.74-5.81 (m, 1H), 4.96 (m, 2H), 2.20-2.26 (m, 5H), 2.05-2.11 (m, 2H), 1.57 (p, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.6, 148.0, 137.9, 131.5, 115.2, 33.1, 31.7, 27.2, 26.8.



63 **48**

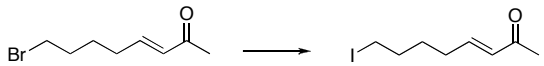
8-(Phenylmethoxy)-3-octen-2-one 48: To a solution of alkene **63** (0.760 g, 4.0 mmol) in CH_2Cl_2 (4.0 mL) was added 2nd Gen. Grubbs catalyst (84.9 mg, 0.1 mmol) and 3-penten-2-one (1.01 g, 1.8 mL, 12.0 mmol, 65% pure). After stirring at 40ºC for 24 h, the reaction was concentrated *in vacuo* and loaded directly onto silica gel. It was purified by chromatography, eluting with 1-20% EtOAc / hexanes, to give **48** (0.824 g, 3.54 mmol, 89%) as colorless oil: IR (neat) 2938, 2856, 1696, 1673, 1621, 1455, 1361, 1252, 1101, 984, 739, 696, 610 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.38 (m, 5H), 6.81 (dt, *J* = 16.0, 6.8 Hz, 1H), 6.09 (dt, *J* = 16.0, 1.2 Hz, 1H), 4.52 (s, 2H), 3.50 (t, *J* = 6.0 Hz, 2H), 2.24-2.30 (m, 5H), 1.58-1.69 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.8, 148.1, 138.5, 131.5, 128.4, 127.63, 127.58, 73.0, 69.9, 32.2, 29.3, 26.9, 24.8; HRMS (EI+) calcd. for $C_{15}H_{20}O_2$ (M+), 232.1463 found 232.1467.



64 **50**

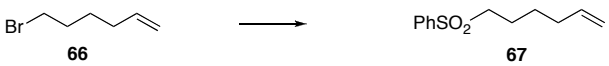
8-Azido-3-octen-2-one 50: To a solution of alkene **64** (0.292 g, 2.33 mmol) in CH_2Cl_2 (2.3 mL) was added 2nd Gen. Hoveyda-Grubbs catalyst (36.5 mg, 0.058 mmol) and 3-penten-2-one (0.587 g, 1.05 mL, 6.99 mmol, 65% pure). After stirring in the dark at rt for 6 h, the reaction was concentrated *in vacuo* and loaded directly onto silica gel. It was purified by chromatography, eluting with 2-10% Ether / hexanes, to give **50** (0.167 g, 1.0 mmol, 43%) as colorless oil: IR (neat) 2941, 2864, 2093, 1673, 1622, 1365, 1252, 976 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (dt, *J* = 16.0, 6.8 Hz, 1H), 6.10 (dt, *J* = 16.0, 1.6 Hz, 1H), 3.31 (t, *J* = 6.4

Hz, 2H), 2.26-2.31 (m, 5H), 1.58-1.67 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 147.1, 131.7, 51.1, 31.8, 28.4, 26.9, 25.2.



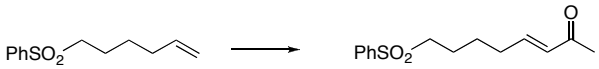
65 51

8-Iodo-3-octen-2-one 51[10]**:** To a solution of bromide **65** (0.282 g, 1.38 mmol) in acetone (4.2 mL) was added NaI (0.620 g, 4.13 mmol). The reaction mixture was heated to reflux. After 36 h, the reaction was cooled to rt and the solvent was removed *in vacuo*. The reaction mixture was loaded directly onto silica gel and was purified by chromatography, eluting with 2-6% Ether / hexanes, to give the iodide **51** (0.318 g, 1.26 mmol, 91%) as colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.79 (dt, *J* = 16.0, 6.8 Hz, 1H), 6.10 (dd, *J* = 16.0, 1.2 Hz, 1H), 3.21 (t, *J* = 6.8 Hz, 2H), 1.86 (p, *J* = 7.2 Hz, 2H), 1.61 (p, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3, 147.2, 131.7, 32.8, 31.3, 28.9, 27.0, 6.15.



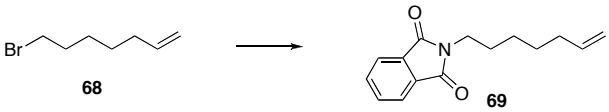
66 67

(5-Hexen-1-ylsulfonyl)-benzene[11]**:** To a solution of 6-bromo-hexene **66** (1.63 g, 10.0 mmol) in DMF (10 mL) was added $NaSO_2Ph$ (1.97 g, 12.0 mmol). After 6 h, diethyl ether (30 mL) was added to the reaction mixture. The resulting solution was washed with brine (3 x 30 mL). The dried (Na_2SO_4) extract was concentrated *in vacuo* and purified by chromatography over silica gel, eluting with 2-10% EtOAc / hexanes, to give sulphone **67** (1.51 g, 6.73 mmol, 67%) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.2 Hz, 2H), 7.65 (t, *J* = 7.2 Hz, 1H), 7.56 (t, *J* = 7.2 Hz, 2H), 5.65-5.74 (m, 1H), 4.91-4.98 (m, 2H), 3.07-3.11 (m, 2H), 2.02 (q, *J* = 7.2 Hz, 2H), 1.68-1.76 (m, 2H), 1.45 (p, *J* = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.2, 137.5, 133.7, 129.3, 128.0, 115.3, 56.1, 33.0, 27.4, 22.1.



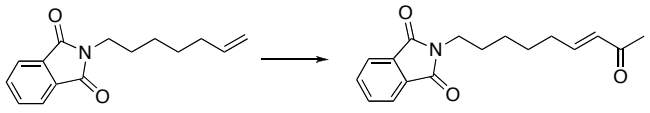
67 52

8-(Phenylsulfonyl)-3-octen-2-one 52: To a solution of alkene **67** (0.448 g, 2.0 mmol) in CH_2Cl_2 (2.0 mL) was added 2nd Gen. Grubbs catalyst (42.5 mg, 0.05 mmol) and 3-penten-2-one (0.504 g, 0.899 mL, 6.0 mmol, 65% pure). After stirring at rt for 13 h, the reaction was concentrated *in vacuo* and loaded directly onto silica gel. It was purified by chromatography, eluting with 10-30% EtOAc / hexanes, to give enone **52** (0.498 g, 1.87 mmol, 93%) as colorless oil: IR (neat) 2941, 2871, 1696, 1673, 1626, 1447, 1365, 1303, 1147, 1089, 980, 750, 692, 563 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91-7.93 (m, 1H), 7.68 (tt, *J* = 7.6, 1.2 Hz, 1H), 7.29-7.61 (m, 2H), 6.72 (dt, *J* = 16.0, 1.2 Hz, 1H), 6.05 (dt, *J* = 16.0, 1.2 Hz, 1H), 3.09-3.03 (m, 2H), 2.20-2.26 (m, 5H), 1.57-1.82 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.3, 146.4, 139.1, 133.8, 131.8, 129.4, 128.0, 55.9, 31.8, 27.0, 26.7, 22.3; HRMS (EI+) calcd. for $C_{14}H_{18}O_3S$ (M+), 266.0977 found 266.0972.



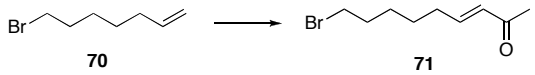
68 69

2-(6-Hepten-1-yl)-1H-isoindole-1,3(2H)-dione 69: To a solution of TBAI (36.9 mg, 0.1 mmol) and potassium phthalimide (1.85 g, 10 mmol) in benzene (40 mL) was added 7-bromo-1-heptene **68** (0.886 g, 5.0 mmol) dropwise. The resulting mixture was heated at 95ºC for 24 h. The suspension was cooled to rt, diluted with ether (50 mL), filtered through celite, then concentrated *in vacuo*. It was purified by chromatography, eluting with 5-15% Ether / hexanes, to give **69** (1.18 g, 4.85 mmol, 97%) as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72-7.87 (m, 4H), 5.76-5.86 (m, 1H), 4.93-5.03 (m, 2H), 3.70 (t, *J* = 7.2 Hz, 2H), 2.04-2.10 (m, 2H), 1.71 (p, *J* = 7.6 Hz, 2H), 1.34-1.50 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 138.7, 133.8, 132.2, 123.1, 114.5, 38.0, 33.5, 28.4, 26.3.



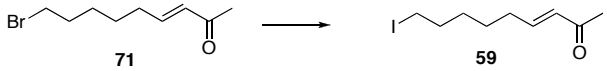
69 58

2-(8-Oxo-6-nonen-1-yl)-1H-isoindole-1,3(2H)-dione 58: To a solution of alkene **69** (0.365 g, 1.5 mmol) in CH_2Cl_2 (1.5 mL) was added 2nd Gen. Grubbs catalyst (31.8 mg, 0.0375 mmol) and 3-penten-2-one (0.375 g, 0.675 mL, 4.5 mmol, 65% pure). After stirring at 45ºC for 36 h, the reaction was concentrated *in vacuo* and loaded directly onto silica gel. It was purified by chromatography, eluting with 5-30% Ether / hexanes, to give enone **58** (0.293 g, 1.03 mmol, 68%) as colorless oil: IR (neat) 2938, 2860, 1770, 1712, 1669, 1618, 1439, 1361, 1252, 1047, 980, 875, 797, 723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71-7.86 (m, 4H), 6.78 (dt, *J* = 16.0, 6.8 Hz, 1H), 6.06 (t, *J* = 16.0 Hz, 1H), 3.69 (t, *J* = 7.2 Hz, 2H), 2.21-2.26 (m, 5H), 1.71 (p, *J* = 7.6 Hz, 2H), 1.54 (p, *J* = 8.0 Hz, 2H), 1.35-1.43 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.6, 168.4, 148.0, 133.9, 132.1, 131.5, 123.2, 37.7, 32.2, 28.3, 27.6, 26.9, 26.3; HRMS (EI+) calcd. for $C_{17}H_{19}NO_3$ (M+), 285.1365 found 285.1376.



70 71

9-Bromo-3-nonen-2-one 71: To a solution of alkene **70** (1.24 g, 7.0 mmol) in CH_2Cl_2 (35 mL) was added 2nd Gen. Grubbs catalyst (297 mg, 0.35 mmol) and 3-penten-2-one (0.588 g, 1.05 mL, 7.0 mmol, 65% pure). After 48 h, the reaction was concentrated *in vacuo* and loaded directly onto silica gel. It was purified by chromatography, eluting with 1-20% Ether / hexanes, to give enone **71** (792 mg, 3.6 mmol, 52%) as colorless oil: IR (neat) 2938, 2856, 1677, 1626, 1431, 1361, 1256, 980, 731, 645 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.80 (dt, *J* = 16.0, 6.8 Hz, 1H), 6.09 (dt, *J* = 16.0, 1.2 Hz, 1H), 3.42 (t, *J* = 6.8 Hz, 2H), 2.21-2.26 (m, 5H), 1.85-1.94 (m, 2H), 1.47-1.55 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.6, 147.8, 131.5, 33.6, 32.5, 32.2, 27.7, 27.2, 27.0; HRMS (EI+) calcd. for $C_9H_{15}OBr$ (M+), 218.0306 found 218.0302.



71 59

9-Iodo-3-nonen-2-one 59: To a solution of bromide **71** (0.371 g, 1.69 mmol) in acetone (5.1 mL) was added NaI (0.760 g, 5.07 mmol). The reaction mixture was heated to reflux. After 36 h, the reaction was cooled to rt and the solvent was removed *in vacuo*. The reaction mixture was loaded directly onto silica gel and was purified by chromatography, eluting with 2-10% Ether / hexanes, to give iodide **59** (0.413 g, 1.55 mmol, 92%) as colorless liquid: IR (neat) 2933, 2856, 1677, 1626, 1427, 1361, 1256, 1198, 980, 731 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 6.81 (dt, *J* = 16.0, 6.8 Hz, 1H), 6.10 (dt, *J* = 16.0, 1.6 Hz, 1H), 3.21 (t, *J* = 6.8 Hz, 2H), 2.24-2.30 (m, 5H), 1.86 (p, *J* = 6.8 Hz, 2H), 1.45-1.57 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 147.7, 131.5, 33.1, 32.2, 30.0, 27.0, 26.9, 6.53; HRMS (EI+) calcd. for $C_9H_{15}OI$ (M+), 266.0168 found 266.0176.

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