A Modular Approach to the Synthesis of 2,3,4-Trisubstituted Tetrahydrofurans.

Christopher G. Nasveschuk, Nathan T. Jui and Tomislav Rovis*

Department of Chemistry Colorado State University, Fort Collins, CO, 80523

E-mail: rovis@lamar.colostate.edu

General Methods: All reactions were performed under an inert atmosphere of argon in flame-dried glassware with magnetic stirring. Acetonitrile (ACS grade) was purchased from Fisher Scientific and distilled from CaH_2 before use. Column chromatography was performed on EM Science silica gel 60 (230-400 mesh). Thin layer chromatography was performed on EM Science 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light, $KMnO_4$, or aqueous ceric ammonium molybdate followed by heating.

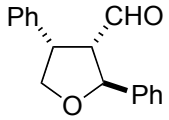
TMSOTf was purchased from Aldrich Chemical Co. and was used as a 0.2M stock solution in acetonitrile and used within five days. $Pd(OAc)_2$ was purchased from Fluka. All other chemicals were purchased from Aldrich Chemical Co. and used without further purification.

^1H NMR spectra are reported as follows: chemical shift in parts per million (δ, ppm) from an internal standard [deuterated chloroform ($CDCl_3$)], multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), integration, and coupling constant (Hz). ^{13}C NMR chemical shifts are reported in ppm from ($CDCl_3$) taken as 77.23 ppm. Mass spectra were obtained on Fisons VG Autospec. Gas chromatography was performed on a Varian Cp 3800 gas chromatograph equipped with a flame ionization detector using a Chromopack Cp-Sil 8 CB (15 M X 0.25 mm) capillary column.

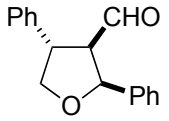
General Procedure for the Heck Reaction of 1,3-dioxepins. A round bottom flask was charged with $Pd(OAc)_2$ (0.05 equiv), PPh_3 (0.10 equiv), K_2CO_3 (1.78 equiv), and *n*-$Bu_4NCl{\cdot}H_2O$ (1 equiv). The flask was purged with argon and a 9:1 mixture of acetonitrile and deionized water were added (0.5M with respect to 1,3-dioxepin). After mixing for 0.25h at 50 °C 1,3-dioxepin (1 equiv) and sp^2-iodide (1.05 equiv) were added. The reaction was allowed to stir for 12-36 h. Standard work-up proceeded with the addition of $MgSO_4$ (1 g/0.5 mL H_2O) and dilution with Et_2O (6 mL/1 mL of reaction mixture) and mixed for 15 min. This solution was flushed through a small pad of celite on top of a small pad of silica gel and eluted with Et_2O. To this solution was added $MgSO_4$ and activated charcoal, allowed to stir at ambient temperature for 1h and then filtered through a pad of celite. The solvents were removed in *vacuo* and the residue was purified by column chromatography (9:1-6:1, Hex : EtOAc).

General Procedure for the [1,3] Ring Contraction of 1,3-Dioxepins. A flame-dried round-bottomed flask was charged with 1,3-dioxepin (1 equiv) and freshly distilled MeCN (0.05M with respect to 1,3-dioxepin) and cooled to -40 °C. TMSOTf (0.1 equiv, 0.2M solution in MeCN) was added dropwise and the reaction was monitored by TLC. Upon disappearance of 1,3-dioxepin (typically 1h) the reaction was quenched with 0.5 mL of sat. aq. NH_4Cl and then diluted with ether. $MgSO_4$ was added and the reaction

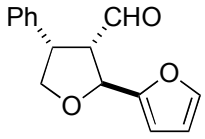
was mixed for 0.25 h, then filtered through a pad of celite and the solvent was removed in *vacuo*. The product was purified by column chromatography (9:1-3:1, Hex : EtOAc).



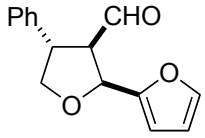
2,4-Diphenyl-tetrahydro-furan-3-carbaldehyde (9). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.39 (1H, d, J = 1.9), 7.40-7.22 (10H, m), 5.56 (1H, d, J = 7.0), 4.51 (1H, dd, J = 8.8, 6.5), 4.24 (1H, dd, J = 8.8, 5.9), 3.99 (1H, m), 3.33 (1H, ddd, J = 8.9, 6.8, 1.9); ^{13}C NMR (100 MHz $CDCl_3$) δ 200.7, 141.9, 137.8, 129.3, 129.0, 128.3, 127.9, 126.3, 125.7, 79.5, 74.3, 64.3, 48.0; IR (NaCl dep from CH_2Cl_2) 3030, 2863, 1720, 1494, 1068, 700 cm^{-1}; HRMS (FAB+) calcd for $C_{17}H_{16}O_2$, 253.1229. Found 253.1227.



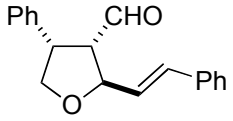
2,4-Diphenyl-tetrahydro-furan-3-carbaldehyde (9a). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.01 (1H, d, J = 3.0), 7.31-7.14 (10H, m), 5.47 (1H, d, J = 8.5), 4.65-4.58 (1H, m), 3.95-3.87 (1H, m), 3.32 (1H, dddd, J = 11.5, 8.6, 5.8, 3.1); ^{13}C NMR (100 MHz $CDCl_3$) δ 200.7, 139.7, 137.5, 129.2, 129.0, 128.4, 127.9, 127.5, 126.3, 82.6, 75.1, 63.6, 45.4; IR (NaCl dep from CH_2Cl_2) 3030, 2857, 1720, 1495, 1067, 700 cm^{-1}; HRMS (FAB+) calcd for $C_{17}H_{16}O_2$, 253.1229. Found 253.1227.



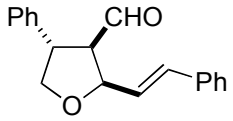
4-Phenyl-2,3,4,5-tetrahydro-[2,2']bifuranyl-3-carbaldehyde (11). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.32 (1H, d, J = 1.5), 7.41-7.21 (6H, m), 6.37-6.30 (2H, m), 5.55 (1H, d, J = 6.4), 4.41 (1H, dd, 8.7, 6.4), 4.18-4.02 (2H, m), 3.68 (1H, ddd, J = 8.5, 6.4, 1.5); ^{13}C NMR (100 MHz $CDCl_3$) δ 200.0, 143.1, 137.7, 129.3, 129.2, 128.3, 127.8, 110.6, 108.4, 73.9, 73.0, 59.9, 48.0; IR (NaCl dep from CH_2Cl_2) 2868, 1721, 1495, 1068, 703 cm^{-1}; HRMS (FAB+) calcd for $C_{15}H_{14}O_2$, 242.0943. Found 242.0939.



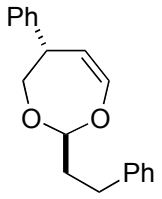
4-Phenyl-2,3,4,5-tetrahydro-[2,2']bifuranyl-3-carbaldehyde (11a). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.35 (1H, d, J = 2.8), 7.42-7.22 (6H, m), 6.38-6.32 (2H, m), 5.46 (1H, d, J = 8.7), 4.54 (1H, dd, 8.2, 8.2), 4.12 (1H, dd, J = 16.6, 8.2), 3.94 (1H, dd, J = 8.6, 8.6), 3.41 (1H, dt, J = 8.7, 3.0); ^{13}C NMR (100 MHz $CDCl_3$) δ 199.2, 151.2, 143.3, 139.4, 129.2, 127.8, 127.5, 110.7, 109.4, 75.7, 75.1, 62.9, 45.5; IR (NaCl dep from CH_2Cl_2) 2865, 1721, 1496, 1149, 1066, 700 cm^{-1}; HRMS (FAB+) calcd for $C_{15}H_{14}O_2$, 242.0943. Found 242.0939.



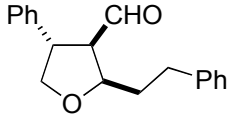
4-Phenyl-2-styryl-tetrahydro-furan-3-carbaldehyde (13). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.34 (1H, d, J = 2.1), 7.42-7.20 (10H, m), 6.71 (1H, d, J = 15.8), 6.22 (1H, dd, J = 15.8, 6.2), 5.12 (1H, dd, J = 6.6, 6.6), 4.40 (1H, dd, J = 9.0, 6.6), 4.16 (1H, dd, J = 9.0, 5.8), 3.99-3.90 (1H, m); 3.22 (1H, ddd, J = 9.0, 7.0, 2.1); ^{13}C NMR (100 MHz $CDCl_3$) δ 200.7, 137.8, 136.5, 131.7, 129.3, 129.1, 128.7, 128.1, 127.7, 127.6, 126.8, 78.8, 73.8, 61.9, 47.8; IR (NaCl dep from CH_2Cl_2) 3028, 2862, 1721, 1494, 1072, 696 cm^{-1}; HRMS (FAB+) calcd for $C_{19}H_{18}O_2$, 279.1385. Found 279.1398.



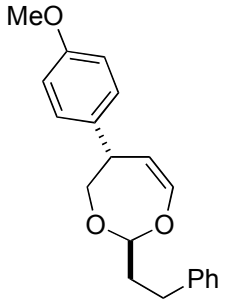
4-Phenyl-2-styryl-tetrahydro-furan-3-carbaldehyde (13a). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.70 (1H, d, J = 2.8), 7.38-7.22 (10H, m), 6.76 (1H, d, J = 16.0), 6.21 (1H, dd, J = 15.8, 7.0), 5.07 (1H, dd, J = 7.3, 7.3), 4.49 (1H, dd, J = 7.5, 7.5), 4.02-3.88 (2H, m), 3.36 (1H, ddd, J = 15.4, 8.3, 3.0); ^{13}C NMR (100 MHz $CDCl_3$) δ 200.6, 139.8, 136.1, 133.3, 129.2, 128.9, 128.4, 127.8, 127.5, 127.0, 125.0, 81.5, 74.8, 63.5, 45.5; IR (NaCl dep from CH_2Cl_2) 3028, 2854, 1720, 1494, 1044, 695 cm^{-1}; HRMS (FAB+) calcd for $C_{19}H_{18}O_2$, 279.1385. Found 279.1398; Gas chromatography analysis- gas flow 3 mL/min with constant 150 °C oven temperature. Major diastereomer: 46.9 min, minor diastereomer: 61.5 min.



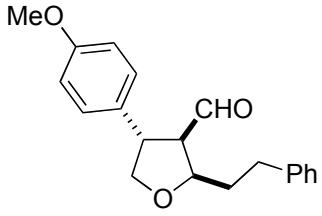
2-Phenethyl-5-phenyl-4,5-dihydro-[1,3]dioxepine (14). ^{1}H NMR (400 MHz $CDCl_3$) δ 7.37-7.18 (10H, m), 6.43 (1H, dd, J = 7.5, 3.0), 4.89 (1H, d, J = 7.5), 4.59 (1H, dd, J = 5.3, 5.3), 4.09 (1H, dd, J = 11.5, 5.1), 3.89 (1H, dddd, J = 10.7, 7.7, 5.1, 2.6), 3.20 (1H, dd, J = 11.4, 11.4), 2.81 (2H, t, J = 2.8), 2.18-2.06 (2H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ 145.3, 141.7, 140.9, 128.9, 128.7, 128.7, 128.1, 127.2, 126.1, 112.5, 106.9, 76.2, 48.4, 37.3, 30.8; IR (NaCl dep from CH_2Cl_2) 3027, 2867, 1647, 1453, 1145, 700 cm^{-1}; HRMS (FAB+) calcd for $C_{19}H_{20}O_2$, 280.1463. Found 280.1471.



2-Phenethyl-4-phenyl-tetrahydro-furan-3-carbaldehyde (15). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.76 (1H, d, J = 3.2), 7.34-7.18 (10H, m), 4.44 (1H, dd, J = 8.1, 8.1), 4.34 (1H, ddd, J = 8.1, 4.3, 4.1), 3.88 (1H, dd, J = 7.7, 7.7), 3.80 (1H, dd, J = 8.6, 8.6), 3.15 (1H, ddd, J = 7.9, 6.6, 3.4), 2.94-2.76 (2H, m), 2.05-1.84 (2H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ 201.3, 141.3, 140.3, 129.0, 128.7, 127.7, 127.3, 126.3, 81.0, 74.6, 62.5, 45.8, 33.6, 32.9; IR (NaCl dep from CH_2Cl_2) 3028, 2859, 1721, 1454, 1066, 700 cm^{-1}; HRMS (FAB+) calcd for $C_{19}H_{20}O_2$, 280.1463. Found 280.1475; Gas chromatography analysis- gas flow 3 mL/min with constant 150 °C oven temperature. Minor diastereomer: 42.7 min, minor diastereomer: 49.1 min, major diastereomer: 53.2 min.

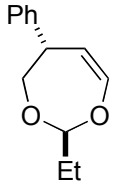


5-(4-Methoxy-phenyl)-2-phenethyl-4,5-dihydro-[1,3]dioxepine (16). ^{1}H NMR (400 MHz $CDCl_3$) δ 7.38-7.18 (7H, m), 6.94-6.88 (2H, m), 6.45 (1H, dd, J = 7.5, 3.0), 4.90 (1H, ddd, J = 7.5, 1.9, 1.3), 4.62 (1H, dd, J = 5.5, 5.5), 4.10 (1H, ddd, J = 11.7, 5.3, 1.3), 3.91-3.82 (4H, m), 3.20 (1H, dd, J = 11.5, 11.5), 2.84 (2H, t, J = 7.5), 2.22-2.08 (2H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ 158.8, 145.1, 141.7, 132.9, 129.4, 128.7, 128.6, 126.1, 114.2, 112.9, 106.9, 76.3, 55.5, 47.6, 37.3, 30.8; IR (NaCl dep from CH_2Cl_2) 2956, 1646, 1512, 1250, 1036, 700 cm^{-1}; HRMS (FAB+) calcd for $C_{20}H_{22}O_3$, 311.1647. Found 311.311.1635.

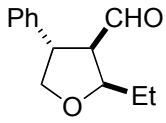


4-(4-Methoxy-phenyl)-2-phenethyl-tetrahydro-furan-3-carbaldehyde (17). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.77 (1H, d, J = 3.6), 7.35-7.14 (7H, m), 6.90-6.84 (2H, m), 4.44 (1H, dd, J = 8.1, 8.1), 4.35 (1H, ddd, J = 9.6, 8.1, 4.3),

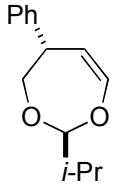
3.94-3.76 (5H, m), 3.12 (1H, ddd, *J* = 8.1, 6.6, 3.6), 2.96-2.68 (2H, m), 2.06-1.84 (2H, m), 2.76 (1H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ 201.5, 141.3, 132.1, 128.8, 128.7, 126.3, 114.4, 80.9, 74.8, 62.6, 55.5, 45.2, 33.6, 32.9; IR (NaCl dep from CH_2Cl_2) 2935, 2837, 1719, 1514, 1034, 701 cm^{-1}; HRMS (FAB+) calcd for $C_{20}H_{22}O_3$, 311.1647. Found 311.1633.



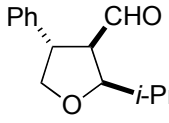
2-Ethyl-5-phenyl-4,5-dihydro-[1,3]dioxepine (18). ^{1}H NMR (400 MHz $CDCl_3$) δ 7.34-7.21 (5H, m), 6.40 (1H, dd, *J* = 7.3, 3.0), 4.85 (1H, ddd, *J* = 7.5, 1.3, 1.3), 4.55 (1H, dd, *J* = 5.3, 5.3), 4.06 (1H, ddd, *J* = 11.7, 5.3, 1.1), 3.85 (1H, dddd, *J* = 11.3, 8.0, 5.3, 2.8), 3.21 (1H, dd, *J* = 11.3, 11.3), 1.85-1.72 (2H, m), 0.99 (3H, t, *J* = 7.5); ^{13}C NMR (100 MHz $CDCl_3$) δ 145.3, 141.0, 128.9, 128.1, 127.2, 112.3, 108.9, 76.2, 48.5, 29.1, 8.9; IR (NaCl dep from CH_2Cl_2) 2879, 1650, 1493, 1279, 1097, 700 cm^{-1}; HRMS (FAB+) calcd for $C_{13}H_{16}O_2$, 204.1150. Found 204.1142.



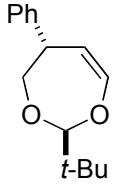
2-Ethyl-4-phenyl-tetrahydro-furan-3-carbaldehyde (19). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.80 (1H, d, *J* = 3.6), 7.36-7.22 (5H, m), 4.43 (1H, dd, *J* = 7.9, 7.9), 4.28 (1H, ddd, *J* = 8.1, 8.1, 5.8), 3.91-3.78 (2H, m), 3.16 (1H, ddd, *J* = 7.8, 6.0, 3.4), 1.77-1.65 (2H, m), 1.06 (3H, t, *J* = 7.5); ^{13}C NMR (100 MHz $CDCl_3$) δ 201.5, 140.5, 129.1, 127.8, 127.3, 83.6, 74.6, 62.5, 45.8, 24.9, 11.2; IR (NaCl dep from CH_2Cl_2) 2967, 2876, 1721, 1455, 1075, 701 cm^{-1}.



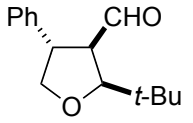
2-Isopropyl-5-phenyl-4,5-dihydro-[1,3]dioxepine (20). ^{1}H NMR (400 MHz $CDCl_3$) δ 7.34-7.19 (5H, m), 6.40 (1H, dd, *J* = 7.5, 2.9), 4.81 (1H, ddd, *J* = 7.5, 1.3, 1.3), 4.35 (1H, d, *J* = 4.7), 4.07 (1H, ddd, *J* = 11.5, 5.3, 0.9), 3.85 (1H, dddd, *J* = 10.9, 8.1, 5.3, 2.8), 3.17 (1H, dd, *J* = 11.4, 11.4), 2.02-1.89 (1H, m), 0.98 (3H, d, *J* = 3.0), 0.97 (3H, d, *J* = 3.0); ^{13}C NMR (100 MHz $CDCl_3$) δ 145.4, 141.0, 128.9, 128.1, 127.2, 111.8, 111.5, 76.4, 48.5, 33.7, 17.5, 17.3; IR (NaCl dep from CH_2Cl_2) 2961, 2872, 1645, 1454, 1104, 701 cm^{-1}.



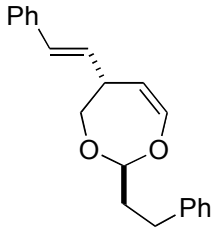
2-Isopropyl-4-phenyl-tetrahydro-furan-3-carbaldehyde (21). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.80 (1H, d, *J* = 4.3), 7.34-7.19 (5H, m), 4.51 (1H, dd, *J* = 8.0, 8.0), 3.87-3.70 (3H, m), 3.05 (1H, ddd, *J* = 8.3, 6.8, 4.3), 1.99-1.88 (1H, m), 1.07 (3H, d, *J* = 6.4), 0.95 (3H, d, *J* = 6.6); ^{13}C NMR (100 MHz $CDCl_3$) δ 201.4, 141.0, 129.1, 127.7, 127.3, 88.8, 74.8, 61.8, 46.4, 29.5, 20.6, 19.3; IR (NaCl dep from CH_2Cl_2) 2961, 2873, 1720, 1470, 1073, 700 cm^{-1}; Gas chromatography analysis- gas flow 3 mL/min with constant 130 °C oven temperature. Minor diastereomer: 3.4 min, minor diastereomer: 7.1 min, major diastereomer: 8.2 min.



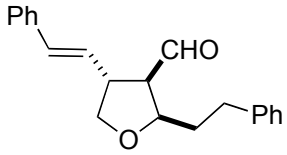
2-*tert*-Butyl-5-phenyl-4,5-dihydro-[1,3]dioxepine (22). ^{1}H NMR (400 MHz $CDCl_3$) δ 7.37-7.24 (5H, m), 6.44 (1H, dd, *J* = 7.7, 3.2), 4.83 (1H, ddd, *J* = 3.4, 2.3, 1.5), 4.23 (1H, s), 4.12 (1H, ddd, *J* = 11.7, 5.5, 1.3), 3.89 (1H, m), 3.18 (1H, dd, *J* = 11.4, 11.4), 1.00 (9H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ 145.5, 141.1, 128.9, 128.2, 127.2, 113.7, 111.4, 76.4, 48.5, 36.1, 25.1; IR (NaCl dep from CH_2Cl_2) 2957, 2869, 1647, 1363, 1142, 700 cm^{-1}.



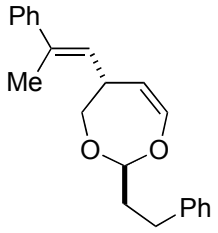
2-*tert*-Butyl-4-phenyl-tetrahydro-furan-3-carbaldehyde (23). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.88 (1H, d, J = 4.7), 7.34-720 (5H, m), 4.48 (1H, dd, J = 8.3, 8.3), 3.92 (1H, d J = 6.8), 3.85 (1H, dd, J = 8.5, 7.9), 3.80-3.70 (1H, m), 1.02 (9H, s); ^{13}C NMR (100 MHz $CDCl_3$) δ 201.3, 140.9, 129.1, 127.8, 127.3, 92.0, 74.4, 63.1, 46.1, 34.3, 27.5; IR (NaCl dep from CH_2Cl_2) 2958, 2871, 1716, 1077, 1055, 700 cm^{-1}; Gas chromatography analysis- gas flow 3 mL/min with constant 130 °C oven temperature. Minor diastereomer: 3.4 min, minor diastereomer: 3.8 min, major diastereomer: 19.2 min.



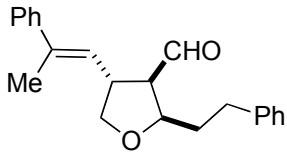
2-Phenethyl-5-styryl-4,5-dihydro-[1,3]dioxepine (24). ^{1}H NMR (400 MHz $CDCl_3$) δ 7.35-7.15 (10H, m), 6.49 (1H, d, J = 16.0), 6.33 (1H, dd, J = 3.8), 6.03 (1H, dd, J = 15.8, 8.1), 4.74 (1H, ddd, J = 7.5, 2.4, 1.1), 4.47 (1H, dd, J = 5.6, 5.6), 4.07 (1H, ddd, J = 11.5, 5.1, 0.9), 3.58-3.38 (1H, m), 3.12 (1H, dd, J = 11.3, 11.3), 2.76 (2H, t, J = 7.7), 2.12-1.98 (2H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ 145.0, 141.6, 137.1, 132.0, 128.8, 128.7, 128.7, 128.2, 127.8, 126.4, 126.1, 111.4, 106.7, 74.0, 44.9, 37.2, 30.8; IR (NaCl dep from CH_2Cl_2) 3026, 2958, 1650, 1455, 1131, 698 cm^{-1}.



2-Phenethly-4-styryl-tetrahydro-furan-3-carbaldehyde (25). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.72 (1H, d, J = 3.6), 7.35-7.13 (10H, m), 6.46 (1H, d, J = 15.8), 6.04 (1H, dd, J = 15.8, 8.5), 4.28 (1H, dd, J = 8.3, 8.3), 4.22-4.14 (1H, m), 3.59 (1H, dd, J = 8.3, 8.3), 3.52-3.41 (1H, m), 2.99-2.74 (2H, m), 2.74-2.62 (1H, m), 2.00-1.80 (2H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ 201.2, 141.3, 136.7, 132.4, 128.8, 128.7, 127.9, 126.4, 126.3, 80.5, 72.8, 60.7, 44.1, 33.5, 32.9; IR (NaCl dep from CH_2Cl_2) 2934, 2857, 1720, 1495, 1049, 696 cm^{-1}; HRMS (FAB+) calcd for $C_{21}H_{22}O_2$, 307.1698. Found 307.1709.

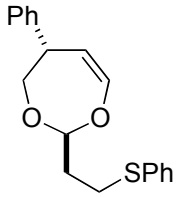


2-Phenethyl-5-(2-phenyl-propenyl)-4,5-dihydro-[1,3]dioxepine (26). ^{1}H NMR (400 MHz $CDCl_3$) δ 7.40-7.16 (10H, m), 6.33 (1H, dd, J = 7.3, 2.8), 5.51 (1H, d, J = 9.6), 4.68 (1H, d, J = 7.2), 4.45 (1H, dd, J = 5.3, 5.3), 3.99 (1H, dd, J = 11.5, 5.1), 3.72-3.62 (1H, m), 3.08 (1H, dd, J = 11.3, 11.3), 2.77 (2H, t, J = 7.9), 2.12-2.00 (5H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ 144.9, 143.3, 141.7, 137.7, 128.7, 128.6, 128.5, 127.4, 126.1, 125.9, 125.8, 113.0, 106.7, 73.1, 41.5, 37.3, 30.9, 16.3; IR (NaCl dep from CH_2Cl_2) 3026, 2863, 1645, 1455, 1145, 698 cm^{-1}; HRMS (FAB+) calcd for $C_{22}H_{24}O_2$, 321.1855. Found 321.1841.

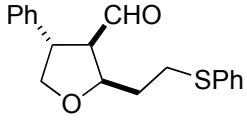


2-Phenethly-4-(2-phenyl-propenyl)-tetrahydro-furan-3-carbaldehyde (27). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.75 (1H, d, J = 3.6), 7.34-7.14 (10H, m), 5.59 (1H, d, J = 9.4), 4.30 (1H, dd, J = 8.2, 8.2), 4.16 (1H, ddd, J = 11.7, 9.4, 4.5), 3.74-3.64 (1H, m), 3.50 (1H, dd, J = 8.4, 8.4), 2.90-2.82 (2H, m), 2.72-2.62 (1H, m), 2.12-1.82 (6H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ 201.6, 143.1, 141.3, 138.2, 128.7, 128.6, 128.5, 127.4, 126.7, 126.3, 125.9, 80.6, 73.2, 61.7, 40.1, 33.5, 33.0, 16.7; IR (NaCl

dep from CH_2Cl_2) 2934, 2858, 1719, 1494, 1060, 698 cm^{-1}; HRMS (FAB+) calcd for $C_{22}H_{24}O_2$, 321.1855. Found 321.1848; Gas chromatography analysis- gas flow 3 mL/min with constant 130 °C oven temperature. Minor diastereomer: 6.3 min, minor diastereomer: 7.1 min, major diastereomer: 7.4 min.



5-Phenyl-2-(2-phenylsulfanyl-ethyl)-4,5-dihydro-[1,3]dioxepine (28). ^{1}H NMR (400 MHz $CDCl_3$) δ 7.39-7.16 (10H, m), 6.40 (1H, dd, *J* = 7.5, 3.0), 4.90 (1H, ddd, *J* = 7.5, 1.9, 1.5), 4.80 (1H, dd, *J* = 5.3, 5.3), 4.05 (1H, ddd, *J* = 11.5, 5.1, 1.1), 3.86 (1H, dddd, *J* = 11.1, 7.9, 5.1, 2.8), 3.21 (1H, dd, *J* = 11.5, 11.5), 3.09 (2H, t, *J* = 7.3), 2.18-2.06 (2H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ 145.2, 140.8, 136.4, 129.5, 129.2, 128.9, 128.1, 127.3, 126.2, 112.8, 106.0, 76.2, 48.4, 35.4, 28.8; IR (NaCl dep from CH_2Cl_2) 3028, 2869, 1646, 1438, 1144, 701cm^{-1}; HRMS (FAB+) calcd for $C_{19}H_{20}O_2S$, 313.1262. Found 313.1270.



4-Phenyl-2-(2-phenylsulfanyl-ethyl)-tetrahydro-furan-3-carbaldehyde (29). ^{1}H NMR (400 MHz $CDCl_3$) δ 9.70 (1H, d, *J* = 3.2), 7.35-7.14 (10H, m), 4.50 (1H, ddd, *J* = 10.2, 8.1, 3.8), 4.34 (1H, dd, *J* = 7.9, 7.9), 3.84 (1H, dd, *J* = 15.3, 8.1), 3.77 (1H, dd, *J* = 8.5, 8.5), 3.21-3.12 (1H, m), 3.04-2.95 (1H, m), 2.04-1.82 (2H, m); ^{13}C NMR (100 MHz $CDCl_3$) δ 201.0, 140.2, 136.1, 129.4, 129.2, 129.1, 127.7, 127.4, 126.3, 80.0, 74.6, 62.4, 45.7, 31.5, 30.7; IR (NaCl dep from CH_2Cl_2) 2937, 2856, 1720, 1439, 1071, 700 cm^{-1}; HRMS (FAB+) calcd for $C_{19}H_{20}O_2S$, 313.1262. Found 313.1252.

Stereochemical Assignment (nOe experiments):