# Regioselective Nucleophilic Addition to Carbonyl Ylide Intermediates: A Novel Diastereoselective Synthesis of Cycloalkyl Fused Furan-3-ones

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## Contents

**Experimental details, characterization data for all new compounds**

**General:** All reactions were carried out in oven-dried glassware under an atmosphere of argon. All solvents were freshly purified by distillation. Precaution has been taken for the preparation of diazo carbonyl compounds. All the materials used are purchased from Aldrich. IR spectra were recorded using KBr pellets or $CH_2Cl_2$ on a Perkin-Elmer Spectrum GX FT-IR spectrophotometer. $^1H$ NMR and $^{13}C$ NMR spectra were recorded (200 and 50.3 MHz, respectively) on a Bruker Avance DPX 200 using $CDCl_3$ or Acetone-$d_6$. Chemical shifts for proton and carbon resonances are reported in ppm (δ) relative to tetramethylsilane (δ 0.00) and chloroform (δ 77), respectively. Multiplicities are indicated by singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m). Coupling constants (*J*) were reported in Hertz (Hz). Carbon types were determined from $^{13}C$ NMR and DEPT experiments. High resolution mass analyses were performed using electrospray ionization (ESI) technique on a Waters QTof-micro mass spectrometer. Elemental analyses were performed on a Perkin-Elmer model 2400 analyzer. Single-crystal X-ray crystallographic analyses were carried out in a Bruker Smart Apex CCD diffractometer. Melting points were determined on a capillary melting point apparatus and are uncorrected. Analytical thin layer chromatography (TLC) was performed on silica and components were visualized by observation under iodine, UV-light or sulfuric acid charring. Column chromatography was performed on a silica gel (100-200 mesh) column.

**Experiments:**

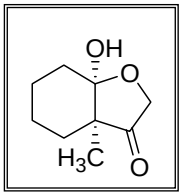
**General Procedure, Method A**: A mixture of α-diazo ketone **1a** or **1b** (1.0 mmol) and the appropriate alcohol or amine or thiol (1.1 mmol) was taken in dry DCM (25 mL) under an argon atmosphere. To the above solution, 1 mol% of rhodium(II) acetate dimer catalyst

was added and stirred at room temperature for 30 minutes. The progress of the reaction was monitored by TLC. The solvent was removed under reduced pressure and the resulting residue purified using 100-200 mesh silica gel column chromatography (hexane/EtOAc) to afford the respective substituted 3a-methylhexahydro-1-benzofuran-3(2*H*)-one or 3a-methyltetrahydro-2*H*-cyclopenta[*b*]furan-3(3a*H*)-one derivative. The requisite starting materials such as α-diazo ketones[1] were prepared according to the literature work.

**Method B**: A mixture of ethyl 2-diazo-3-(1-methyl-2-oxocyclohexyl)-3-oxopropanoate or ethyl 2-diazo-3-(1-methyl-2-oxocyclopentyl)-3-oxopropanoate (1.0 mmol) and the appropriate alcohol or amine or thiol (1.1 mmol) was taken in dry benzene (25 mL) under an argon atmosphere. To the above solution, 1 mol% of rhodium(II) acetate dimer catalyst was added and stirred for 30 minutes at reflux conditions. The progress of the reaction was monitored by TLC and purified as above to afford the respective substituted 3a-methylhexahydro-1-benzofuran-3(2*H*)-one or 3a-methyltetrahydro-2*H*-cyclopenta[*b*] furan-3(3a*H*)-one derivative.

**Method C**: A mixture of α-diazo ketone **1a** or **1b** (2.2 mmol) and the appropriate alcohol (1.0 mmol) was taken in dry DCM (50 mL) under an argon atmosphere. To the above solution, 1 mol% of rhodium(II) acetate dimer catalyst was added and stirred for 30 minutes at room temperature. The progress of the reaction was monitored by TLC and purified as above to afford the respective bis-3a-methylhexahydro-1-benzofuran-3(2*H*)-one or 3a-methyltetrahydro-2*H*-cyclopenta[*b*]furan-3(3a*H*)-one derivative.

**7a-Hydroxy-3a-methylhexahydro-1-benzofuran-3(2H)-one (2a):** α-Diazo ketone **1b** (180 mg, 1.0 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in moist dichloromethane (25 mL) according to method A to afford **2a** (153 mg, 90%) as a colorless solid; mp 120-122 °C (EtOAc/hexane); $R_f$ 0.68 (30:70 EtOAc:hexane).




$^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 4.17 (d, 1H, OC*H*$_2$, $J$ = 16 Hz), 4.02 (d, 1H, OC*H*$_2$, $J$ = 16 Hz), 2.34 (broad s, 1H, OH), 1.92-1.88 (m, 1H, C*H*$_2$), 1.66-1.26 (m, 7H, C*H*$_2$), 1.06 (s, 3H, C*H*$_3$).

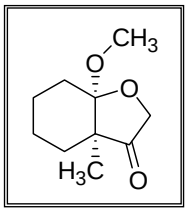
$^{13}$C NMR ($CDCl_3$, 50.3 MHz) $\delta$ 217.6 (*C*=O), 106.0 (*quat-C*), 67.9 (O*C*H$_2$), 51.3 (*quat-C*), 34.0 (*C*H$_2$), 33.1 (*C*H$_2$), 23.5 (*C*H$_2$), 21.0 (*C*H$_2$), 13.7 (*C*H$_3$).

$\nu_{max}$(KBr)/cm$^{-1}$ 3380, 2944, 2911, 1760, 1457, 1413, 1232, 1097, 1076, 1020, 938.

MS (EI, 70 eV): m/z (%) 170 (M$^+$, 24), 153 (20), 142 (6), 124 (8), 112 (63), 97 (48), 83 (48), 69 (69), 55 (96), 41 (100).

Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.46; H, 8.28.

**7a-Methoxy-3a-methylhexahydro-1-benzofuran-3(2*H*)-one** (**2b):** A mixture of α-diazo ketone **1b** (180 mg, 1.0 mmol) and dry methanol (2ml) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2b** (158 mg, 86%) as a colorless oil; $R_f$ 0.83 (20:80 EtOAc:hexane).



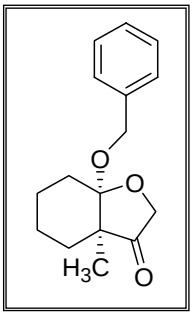
$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 4.12 (d, 1H, OC$H_2$, $J$ = 16.0 Hz), 3.78 (d, 1H, OC$H_2$, $J$=16.0 Hz), 3.16 (s, 3H, OC$H_3$), 2.21-2.15 (m, 1H, C$H_2$), 1.70-1.19 (m, 7H, C$H_2$), 1.01 (s, 3H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) $\delta$ 216.7 (*C*=O), 107.3 (*quat-C*), 67.0 (O*C*$H_2$), 51.1 (*quat-C*), 47.8 (O*C*$H_3$), 32.6 (*C*$H_2$), 27.3 (*C*$H_2$), 22.5 (*C*$H_2$), 20.6 (*C*$H_2$), 12.8 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 2944, 2911, 1760, 1457, 1413, 1232, 1097, 1076, 1020, 938.

HRMS (ESI+) calcd for $C_{10}H_{16}O_3Na$ $(M+Na)^+$: 207.0997, found 207.1011.

**7a-(Benzyloxy)-3a-methylhexahydro-1-benzofuran-3(2*H*)-one (2c):** A mixture of α-diazo ketone **1b** (180 mg, 1.0 mmol) and benzyl alcohol (118 mg, 1.10 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2c** (187 mg, 72%) as a colorless oil; $R_f$ 0.88 (20:80 EtOAc:hexane).



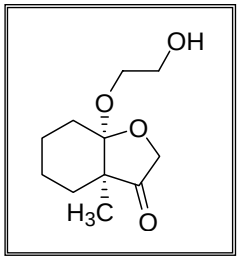

$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.27-7.21 (m, 5H, Arom-*H*), 4.52 (s, 2H, OC$H_2$), 4.24 (d, 1H, OC$H_2$, $J$ = 16 Hz), 4.11 (d, 1H, OC$H_2$, $J$ = 16 Hz), 2.42-1.22 (m, 8H, C$H_2$), 1.09 (s, 3H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 214.9 (*C*=O), 155.4 (*quat-C*), 129.0 (=*C*H), 127.9 (=*C*H), 127.5 (=*C*H), 104.2 (*quat-C*), 68.0 (O*C*$H_2$), 63.0 (O*C*$H_2$), 52.4 (*quat-C*), 33.3 (*C*$H_2$), 29.2 (*C*$H_2$), 22.3 (*C*$H_2$), 21.4 (*C*$H_2$), 13.7 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$3057, 2942, 2867, 1760, 1706, 1451, 1378, 1265, 1093, 1020, 740.

HRMS (ESI+) calcd for $C_{16}H_{20}O_3Na$ $(M+Na)^+$: 283.1310, found 283.1301.

**7a-(2-Hydroxy-ethoxy)-3a-methylhexahydro-1-benzofuran-3(2*H*)-one (2d):** A mixture of α-diazo ketone **1b** (180 mg, 1.0 mmol) and 1,2-ethanediol (68 mg, 1.10 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2d** (188 mg, 88%) as a colorless thick oil; $R_f$ 0.55 (30:70 EtOAc:hexane).



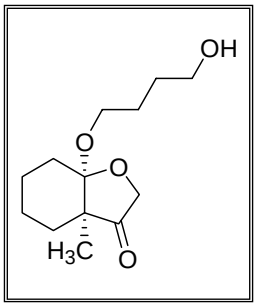

$^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 4.21 (d, 1H, OC*H*$_2$, $J$ = 16 Hz), 3.93 (d, 1H, OC*H*$_2$, $J$ = 16 Hz), 3.66-3.57 (m, 4H, OC*H*$_2$), 2.43 (broad s, 1H, OH), 2.27-2.21 (m, 1H, C*H*$_2$), 1.72-1.34 (m, 7H, C*H*$_2$), 1.11 (s, 3H, C*H*$_3$);

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 216.8 (*C*=O), 107.4 (*qua*t-*C*), 67.0 (O*C*H$_2$), 61.8 (O*C*H$_2$), 51.2 (*qua*t-*C*), 32.5 (*C*H$_2$), 28.1 (*C*H$_2$), 22.4 (*C*H$_2$), 20.4 (*C*H$_2$), 12.8 (*C*H$_3$).

$\nu_{max}$ (neat)/cm$^{-1}$ 3496, 2938, 2866, 1762, 1704, 1450, 1274, 1234, 1176, 1092.

HRMS (ESI+) calcd for $C_{11}H_{18}O_4Na$ $(M+Na)^+$: 237.1103, found 237.1116.

**7a-(4-Hydroxybutoxy)-3a-methylhexahydro-1-benzofuran-3(2*H*)-one (2e):** A mixture of α-diazo ketone **1b** (180 mg, 1.0 mmol) and 1,4-butanediol (99 mg, 1.10 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2e** (193 mg, 80%) as a colorless thick oil; $R_f$ 0.56 (30:70 EtOAc:hexane).



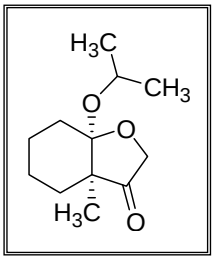

$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 4.20 (d, 1H, OC$H_2$, $J$ = 16 Hz), 3.86 (d, 1H, OC$H_2$, $J$ = 16 Hz), 3.63-3.51 (m, 4H, OC$H_2$), 2.36 (s, 1H, OH), 2.26-2.20 (m, 1H, C$H_2$), 1.73-1.32 (m, 11H, C$H_2$), 1.09 (s, 3H, C$H_3$);

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 217.0 (*C*=O), 107.2 (*qua*t-*C*), 67.0 (O*C*H$_2$), 62.3 (O*C*H$_2$), 59.9 (O*C*H$_2$), 51.2 (*qua*t-*C*), 32.4 (*C*H$_2$), 29.6 (*C*H$_2$), 28.1 (*C*H$_2$), 26.1 (*C*H$_2$), 22.4 (*C*H$_2$), 20.4 (*C*H$_2$), 12.8 (*C*H$_3$).

$\nu_{max}$ (neat)/cm$^{-1}$ 3497, 2939, 2867, 1762, 1704, 1450, 1275, 1235, 1178, 1093.

HRMS (ESI+) calcd for $C_{13}H_{22}O_4Na$ (M+Na)$^+$: 265.1416, found 265.1408.

**7a-Isopropoxy-3a-methylhexahydro-1-benzofuran-3(2*H*)-one (2f):** A mixture of α-diazo ketone **1b** (180 mg, 1.0 mmol) and 2-propanol (66 mg, 1.10 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2f** (165 mg, 78%) as a colorless thick oil; $R_f$ 0.82 (10:90 EtOAc:hexane).



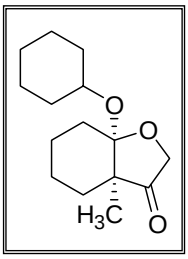

$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 4.23-4.15 (m, 2H, OC$H_2$ and OC*H*), 3.92 (d, 1H, OC$H_2$, $J$ = 16 Hz), 2.26-2.21 (m, 1H, C$H_2$), 1.71-1.29 (m, 7H, C$H_2$), 1.11-1.06 (m, 9H, C$H_3$)

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 216.9 (*C*=O), 107.6 (*qua*t-*C*), 67.1 (O*C*$H_2$), 63.1 (O*C*H), 51.7 (*qua*t-*C*), 32.4 (*C*$H_2$), 29.2(*C*$H_2$), 24.3(*C*$H_3$), 23.7 (*C*$H_3$), 22.7 (*C*$H_2$), 20.5 (*C*$H_2$), 12.9 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3056, 2974, 2940, 2866, 1761, 1716, 1447, 1376, 1268, 1176, 1093, 740.

HRMS (ESI+) calcd for $C_{12}H_{20}O_3Na$ $(M+Na)^+$: 235.1310, found 235.1301.

**7a-(Cyclohexyloxy)-3a-methylhexahydro-1-benzofuran-3(2*H*)-one (2g):** A mixture of α-diazo ketone **1b** (180 mg, 1.0 mmol) and cyclohexanol (110 mg, 1.10 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2g** (141 mg, 56%) as a colorless oil; $R_f$ 0.80 (10:90 EtOAc:hexane).




$^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 4.19 (d, 1H, OC$H_2$, $J$ = 16 Hz), 3.94 (d, 1H, OC$H_2$, $J$ = 16 Hz), 3.85-3.82 (m, 1H, OC*H*), 2.27-1.25 (m, 18H, C$H_2$), 1.09 (s, 3H, C$H_3$).

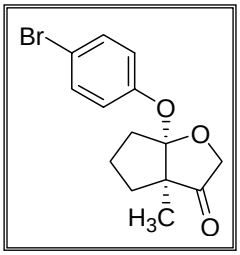
$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 216.9 (*C*=O), 107.1 (*qua*t-*C*), 69.4 (O*C*$H_2$), 68.0 (O*C*H), 51.0 (*qua*t-*C*), 35.1 (*C*$H_2$), 34.5 (*C*$H_2$), 33.1 (*C*$H_2$), 26.3 (*C*$H_2$), 24.7 (*C*$H_2$), 23.5 (*C*$H_2$), 21.3(*C*$H_2$), 13.7 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3057, 2937, 2860, 1763, 1726, 1449, 1376, 1272, 1173, 1093, 1047, 738.

HRMS (ESI+) calcd for $C_{15}H_{24}O_3Na$ $(M+Na)^+$: 275.1623, found 275.1645.

**6a-(4-Bromophenoxy)-3a-methyltetrahydro-2*H*-cyclopenta[*b*]furan-3(3a*H*)-one (2h):** A mixture of α-diazo ketone **1a** (166 mg, 1.0 mmol) and 4-bromophenol (190 mg, 1.10

mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2h** (287 mg, 92%) as a colorless liquid; $R_f$ 0.85 (10:90 EtOAc:hexane).



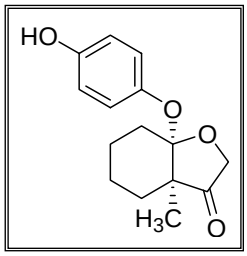

$^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.38 (d, 2H, Arom-*H*, *J* = 8 Hz), 7.05 (d, 2H, Arom-*H*, *J* = 8 Hz), 4.30 (d, 1H, OC$H_2$, *J* = 16 Hz), 4.20 (d, 1H, OC$H_2$, *J* = 16 Hz), 2.34-1.63 (m, 6H, C$H_2$), 1.27 (s, 3H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 216.5 (*C*=O), 154.5 (*qua*t-*C*), 132.1 (=*C*H), 121.9 (=*C*H), 120.0 (*qua*t-*C*), 115.7 (*qua*t-*C*), 70.0 (O*C*$H_2$), 57.3 (*qua*t-*C*), 36.0 (*C*$H_2$), 34.7 (*C*$H_2$), 22.2 (*C*$H_2$), 16.7 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3055, 2974, 2875, 1759, 1584, 1485, 1452, 1266, 1226, 1160, 1041, 741.

HRMS (ESI+) calcd for $C_{14}H_{15}BrO_3Na$ $(M+Na)^+$: 333.0102, found 333.0128.

**7a-(4-Hydroxyphenoxy)-3a-methylhexahydro-1-benzofuran-3(2*H*)-one (2i):** A mixture of α-diazo ketone **1b** (180 mg, 1.0 mmol) and hydroquinone (121 mg, 1.10 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2i** (230 mg, 88%) as a pale yellow thick oil; $R_f$ 0.52 (30:70 EtOAc:hexane).



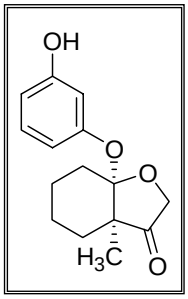

$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.08 (broad s, 1H, OH), 6.91 (d, 2H, Arom-*H*, *J* = 10 Hz), 6.74 (d, 2H, Arom-*H*, *J* = 10 Hz), 4.36 (d, 1H, OC$H_2$, *J* = 16 Hz), 4.21 (d, 1H, OC$H_2$, *J* = 16 Hz), 2.60-1.34 (m, 8H, C$H_2$), 1.26 (s, 3H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 216.3 (*C*=O), 152.1 (*qua*t-*C*), 146.8 (*qua*t-*C*), 123.0 (=*C*H), 115.6 (=*C*H), 110.4 (*qua*t-*C*), 67.4 (O*C*H$_2$), 51.8 (*qua*t-*C*), 32.6 (*C*H$_2$), 29.0 (*C*H$_2$), 22.6 (*C*H$_2$), 20.5 (*C*H$_2$), 13.2 (*C*H$_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3407, 3055, 2943, 2867, 1760, 1507, 1266, 739.

HRMS (ESI-) calcd for $C_{15}H_{18}O_4$: 262.1205, found 262.1192.

**7a-(3-Hydroxyphenoxy)-3a-methylhexahydro-1-benzofuran-3(2*H*)-one (2j):** A mixture of α-diazo ketone **1b** (180 mg, 1.0 mmol) and resorcinol (121 mg, 1.10 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2j** (225 mg, 86%) as a pale yellow thick oil; $R_f$ 0.55 (30:70 EtOAc:hexane).




$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.09 (t, 1H, Arom-*H*, *J* = 10 Hz), 6.89-6.55 (m, 3H, Arom-*H*), 6.07 (broad s, 1H, OH), 4.35 (d, 1H, OC$H_2$, *J* = 16 Hz), 4.18 (d, 4H, OC$H_2$, *J* = 16

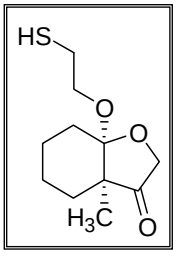
Hz), 2.70-1.36 (m, 8H, C$H_2$), 1.26 (s, 3H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 216.1 (*C*=O), 156.6(*qua*t-*C*), 154.9 (*qua*t-*C*), 129.6 (=*C*H), 113.6 (=*C*H), 110.6(=*C*H), 108.9 (=*C*H), 107.6 (*qua*t-*C*), 67.3 (O*C*$H_2$), 51.9 (*qua*t-*C*), 32.6 (*C*$H_2$), 28.7 (*C*$H_2$), 22.5 (*C*$H_2$), 20.4 (*C*$H_2$), 13.2 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3409, 2943, 2866, 1757, 1707, 1595, 1483, 1266, 740.

HRMS (ESI-) calcd for $C_{15}H_{18}O_4$: 262.1205, found 262.1191.

**3a-Methyl-7a-(2-sulfanylethoxy)hexahydro-1-benzofuran-3(2*H*)-one (2k):** A mixture of α-diazo ketone **1b** (180 mg, 1.0 mmol) and 2-mercaptoethanol (85 mg, 1.1 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2k** (174 mg, 76%) as a colorless thick oil; $R_f$ 0.70 (20:80 EtOAc:hexane).



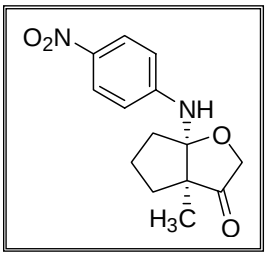

$^1$H NMR (Acetone-$d_6$, 200 MHz) $\delta$ 4.23 (d, 1H, OC$H_2$, $J$ = 16 Hz), 3.93 (d, 1H, OC$H_2$, $J$ = 16 Hz), 3.63 (t, 2H, OC$H_2$, $J$ = 6 Hz), 2.83 (s, 1H, SH), 2.64 (q, 2H, SC$H_2$, $J$ = 6 Hz), 2.24-2.19 (m, 1H, C$H_2$), 1.77-1.21 (m, 7H, C$H_2$), 1.06 (s, 3H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 216.4 (*C*=O), 107.3 (*qua*t-*C*), 67.1 (O*C*$H_2$), 62.0 (O*C*$H_2$), 51.1 (*qua*t-*C*), 32.4 (*C*$H_2$), 28.2 (*C*$H_2$), 24.7 (*C*$H_2$), 22.5 (*C*$H_2$), 20.4 (*C*$H_2$), 12.8 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3495, 3056, 2941, 2865, 1760, 1714, 1447, 1269, 1177, 1093, 1020, 739.

HRMS (ESI+) calcd for $C_{11}H_{18}O_3SNa$ $(M+Na)^+$: 253.0874, found 253.0885.

**6a-[(4-Nitrophenyl)amino]-3a-methyltetrahydro-2*H*-cyclopenta[*b*]furan-3(3a*H*)-one (2l):** A mixture of α-diazo ketone **1a** (166 mg, 1.0 mmol) and 4-nitro aniline (151 mg, 1.1 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2l** (248 mg, 90%) as a yellow solid; mp 109-110° C (EtOAc/hexane); $R_f$ 0.52 (30:70 EtOAc:hexane).



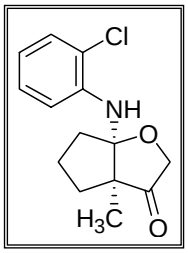

$^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 8.07 (d, 2H, Arom-*H*, *J* = 8 Hz), 6.98 (d, 2H, Arom-*H*, *J* = 8 Hz), 5.04 (s, 1H, NH), 4.26 (d, 1H, OC$H_2$, *J* = 18 Hz), 4.06 (d, 1H, OC$H_2$, *J* = 18 Hz), 2.88-2.81 (m, 1H, C$H_2$), 2.18-1.65 (m, 5H, C$H_2$), 1.28 (s, 3H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 216.9 (*C*=O), 150.9 (*qua*t-*C*), 139.7 (*qua*t-*C*), 125.6 (=*C*H), 114.9 (=*C*H), 103.6 (*qua*t-*C*), 69.2 (O*C*$H_2$), 58.1 (*qua*t-*C*), 37.6 (*C*$H_2$), 36.6 (*C*$H_2$), 22.8 (*C*$H_2$), 16.1 (*C*$H_3$).

$\nu_{max}$ (KBr)/cm$^{-1}$ 3403, 2969, 2940, 1755, 1597, 1522, 1502, 1480, 1327, 1174, 1051, 839.

HRMS (ESI+) calcd for $C_{14}H_{16}N_2O_4Na$ $(M+Na)^+$: 299.1008, found 299.1014.

**6a-[(2-Chlorophenyl)amino]-3a-methyltetrahydro-2*H*-cyclopenta[*b*]furan-3(3a*H*)-one (2m):** A mixture of α-diazo ketone **1a** (166 mg, 1.0 mmol) and 2-chloroaniline (139 mg, 1.1 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2m** (251 mg, 95%) as a colorless thick oil; $R_f$ 0.80 (30:70 EtOAc:hexane).



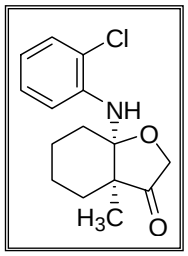

$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.41-7.00 (m, 3H, Arom-*H*), 6.77-6.65 (m, 1H, Arom-*H*), 4.87 (s, 1H, NH), 4.20 (d, 1H, OC*H*$_2$, *J* = 16 Hz), 4.07 (d, 1H, OC*H*$_2$, *J* = 16 Hz), 2.79-2.72 (m, 1H, C*H*$_2$), 2.14-1.39 (m, 5H, C*H*$_2$), 1.28 (s, 3H, C*H*$_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 217.4 (*C*=O), 141.0 (*qua*t-*C*), 128.9 (=*C*H), 127.4 (=*C*H), 121.1 (*qua*t-C), 119.6 (=*C*H), 116.6 (=*C*H), 103.9 (*qua*t-*C*), 68.8 (O*C*H$_2$), 58.0 (*qua*t-*C*), 37.1 (*C*H$_2$), 36.8 (*C*H$_2$), 23.0 (*C*H$_2$), 16.5 (*C*H$_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3379, 3057, 2971, 2877, 1728, 1699, 1594, 1517, 1440, 1300, 1057, 742.

HRMS (ESI+) calcd for $C_{14}H_{17}ClNO_2$ $(M+H)^+$: 266.0948, found 266.0932.

**7a-[(2-Chlorophenyl) amino]-3a-methylhexahydro-1-benzofuran-3(2*H*)-one (2n):** A mixture of α-diazo ketone **1b** (180 mg, 1.0 mmol) and 2-chloro aniline (139 mg, 1.10 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2n** (256 mg, 92%) as a colorless thick oil; $R_f$ 0.85 (30:70 EtOAc:hexane).




$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.58-6.72 (m, 4H, Arom-*H*), 4.56 (s, 1H, NH), 4.27 (d, 1H, OC*H*$_2$, *J* = 16 Hz), 4.06 (d, 1H, OC*H*$_2$, *J* = 16 Hz), 2.62-2.55 (m, 1H, C*H*$_2$), 1.69-1.37 (m,

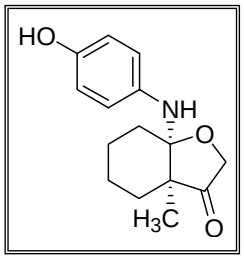
7H, C$H_2$), 1.29 (s, 3H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 215.9 (*C*=O), 140.5 (*qua*t-*C*), 129.0 (=*C*H), 127.4 (=*C*H), 122.0 (*qua*t-*C*), 120.0 (=*C*H), 117.6 (=*C*H), 94.5 (*qua*t-*C*), 66.6 (O*C*$H_2$), 51.6 (*qua*t-*C*), 32.3 (*C*$H_2$), 29.7 (*C*$H_2$), 22.0 (*C*$H_2$), 20.7 (*C*$H_2$), 13.6 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3381, 3056, 2941, 2864, 1758, 1713, 1594, 1447, 1301, 1171, 1096, 740.

HRMS (ESI+) calcd for $C_{15}H_{19}ClNO_2$ $(M+H)^+$: 280.1104, found 280.1121.

**7a-(4-Aminophenoxy)-3a-methylhexahydro-1-benzofuran-3(2*H*)-one (2o):** A mixture of α-diazo ketone **1b** (180 mg, 1.0 mmol) and 4-aminophenol **1b** (119 mg, 1.10 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2o** (229 mg, 88%) as a colorless thick oil; $R_f$ 0.52 (30:70 EtOAc:hexane).



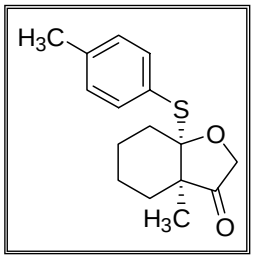

$^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.82 (broad s, 1H, OH), 6.87 (d, 2H, Arom-*H*, *J* = 8 Hz), 6.68 (d, 2H, Arom-*H*, *J* = 8 Hz), 4.28-4.20 (d, 1H, OC$H_2$, *J* = 16 Hz), 4.17-4.09 (d, 1H, OC$H_2$, *J* = 16 Hz), 2.94, (broad s, 1H, NH), 2.27-2.21 (m, 1H, C$H_2$), 1.67-1.25 (m, 7H, C$H_2$), 1.18 (s, 3H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 217.6 (*C*=O), 150.7 (*qua*t-*C*), 136.6 (*qua*t-*C*), 121.4 (=CH), 115.6 (=CH), 95.0 (*qua*t-*C*), 66.5 (O*C*$H_2$), 51.5 (*qua*t-*C*), 32.1 (*C*$H_2$), 30.0 ($CH_2$), 22.1 ($CH_2$), 20.8 ($CH_2$), 14.0 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3396, 2942, 2864, 1753, 1512, 1266, 741.

HRMS (ESI+) calcd for $C_{15}H_{19}NO_3Na$ $(M+Na)^+$: 284.1263, found 284.1250.

**3a-Methyl-7a-[(4-methylphenyl)sulfanyl]hexahydro-1-benzofuran-3(2*H*)-one (2p):** A mixture of α-diazo ketone **1b** (180 mg, 1.0 mmol) and 4-thiocresol (135 mg, 1.1 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2p** (215 mg, 78%) as a colorless solid; mp: 68-70°C $R_f$ 0.85 (10:90 EtOAc:hexane).



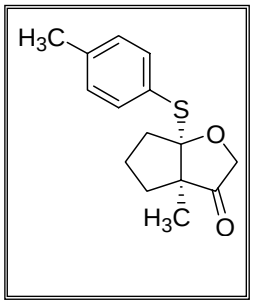

$^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.33 (d, 2H, Arom-*H*, *J* = 8 Hz), 7.13 (d, 2H, Arom-*H*, *J* = 8 Hz), 4.35 (d, 1H, OC$H_2$, *J* = 16 Hz), 4.25 (d, 1H, OC$H_2$, *J* = 16 Hz), 2.33 (s, 3H, C$H_3$), 2.11-1.30 (m, 8H, C$H_2$), 1.25 (s, 3H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 214.8 (*C*=O), 138.7 (*qua*t-*C*), 136.3 (=*C*H), 129.3 (=*C*H), 126.4 (*qua*t-*C*), 109.2 (*qua*t-*C*), 67.5 (O*C*H$_2$), 51.9 (*qua*t-*C*), 33.4 (*C*H$_2$), 32.4 (*C*H$_2$), 22.1 (CH$_2$), 21.1 (*C*H$_3$), 20.4 (*C*H$_2$), 14.0 (*C*H$_3$).

$\nu_{max}$(KBr)/cm$^{-1}$ 2941, 2862, 1759, 1491, 1458, 1440, 1240, 1087, 1044, 1027, 809, 748.

HRMS (ESI+) calcd for $C_{16}H_{20}O_2SNa$ $(M+Na)^+$: 299.1082, found 299.1088.

**3a-Methyl-6a-[(4-methylphenyl)sulfanyl]tetrahydro-2*H*-cyclopenta[*b*]furan-3(3a*H*)-one (2q):** A mixture of α-diazo ketone **1a** (166 mg, 1.0 mmol) and 4-thiocresol (135 mg, 1.1 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (25 mL) according to method A to afford **2q** (209 mg, 80%) as a colorless thick oil; $R_f$ 0.85 (10:90 EtOAc:hexane).



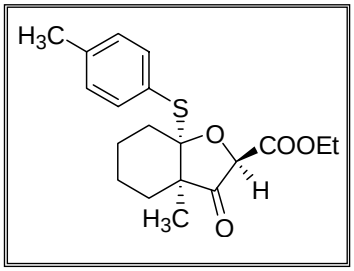

$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.44 (d, 2H, Arom-*H*, *J*= 8 Hz), 7.13 (d, 2H, Arom-*H*, *J* = 8 Hz), 4.24 (d, 1H, OC*H*$_2$, *J* = 16 Hz), 4.13 (d, 1H, OC*H*$_2$, *J* = 16 Hz), 2.34 (s, 3H, C*H*$_3$), 2.16-2.03 (m, 3H, C*H*$_2$), 1.74-1.66 (m, 3H, C*H*$_2$), 1.24 (s, 3H, C*H*$_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 216.8 (*C*=O), 138.6 (*qua*t-*C*), 135.6(=*C*H), 129.4 (=*C*H), 127.7 (*qua*t-*C*), 105.8 (*qua*t-*C*), 68.8 (O*C*H$_2$), 58.6 (*qua*t-*C*), 41.5 (*C*H$_2$), 38.7 (*C*H$_2$), 23.1 (*C*H$_2$), 21.1 (*C*H$_3$), 18.1 (*C*H$_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3055, 2971, 2873, 1756, 1491, 1450, 1377, 1313, 1266, 1050, 901, 739.

HRMS (ESI+) calcd for $C_{15}H_{18}O_2S$: 262.1027, found 262.1020.

**Ethyl 3a-methyl-7a-[(4-methylphenyl)sulfanyl]-3-oxooctahydro-1-benzofuran-2-carboxylate (5a):** A mixture of ethyl 2-diazo-3-(1-methyl-2-oxocyclohexyl)-3-oxopropanoate (252 mg, 1.0 mmol) and 4-thiocresol (136 mg, 1.1 mmol) in dry benzene (25 mL) was allowed to reflux in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) according to method B to afford **5a** as a diastereomeric mixture (285 mg, 82%, 98:2 based on crude NMR); colorless thick oil; $R_f$ 0.72 (30:70 EtOAc:hexane).




Selected signal for the above major isomer:

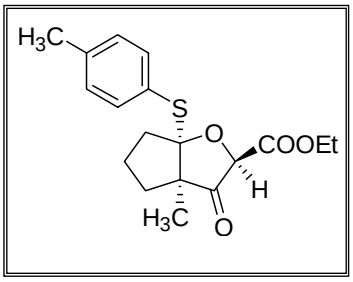
$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.32 (d, 2H, Arom-*H*, *J* = 8 Hz), 7.13 (d, 2H, Arom-*H*, *J* = 8 Hz), 4.94 (s, 1H, OC*H*), 4.35-4.23 (m, 2H, OC$H_2$), 2.34 (s, 3H, C$H_3$), 2.15-1.52 (m, 8H, C$H_2$), 1.36-1.29 (m, 6H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 207.3 (*C*=O), 165.4 (C=O), 139.0 (*qua*t-C), 136.2 (=*C*H), 129.5 (=*C*H), 125.8 (*qua*t-C), 97.3 (*qua*t-C), 77.5 (O*C*H), 62.0 (O*C*$H_2$), 52.4 (*qua*t-C), 33.3 (*C*$H_2$), 31.3 (*C*$H_2$), 21.9 ($CH_2$), 21.1 (*C*$H_3$), 20.4 (*C*$H_2$), 14.7 (*C*$H_3$), 14.0 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 2986, 2942, 2867, 1773, 1746, 1264, 747.

HRMS (ESI+) calcd for $C_{19}H_{24}O_4SNa$ $(M+Na)^+$: 371.1293, found 371.1280.

**Ethyl 3a-methyl-6a-[(4-methylphenyl)sulfanyl]-3-oxohexahydro-2*H*-cyclopenta[*b*] furan-2-carboxylate (5b):** A mixture of ethyl 2-diazo-3-(1-methyl-2-oxocyclopentyl)-3-oxopropanoate (238 mg, 1.0 mmol) and 4-thiocresol (136 mg, 1.1 mmol) in dry benzene (25 mL) was allowed to reflux in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) according to method B to afford **5b** as a diastereomeric mixture (280 mg, 84%, 85:15 based on crude NMR); colorless thick oil; $R_f$ 0.72 (30:70 EtOAc:hexane).




Selected signal for the above major isomer:

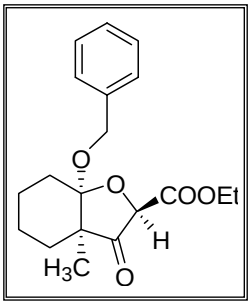
$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.44 (d, 2H, Arom-*H*, *J* = 8 Hz), 7.12 (d, 2H, Arom-*H*, *J* =8 Hz), 4.76 (s, 1H, OC*H*), 4.32-4.18 (m, 2H, OC$H_2$), 2.34 (s, 3H, C$H_3$), 2.20-1.64 (m, 6H, C$H_2$), 1.33-1.26 (m, 6H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 210.2 (*C*=O), 165.4 (*C*=O), 138.8 (*qua*t-C), 135.6 (=*C*H), 129.5 (=*C*H), 127.1 (*qua*t-C), 105.1 (*qua*t-C), 78.6 (O*C*H), 61.9 (O*C*$H_2$), 58.9 (*qua*t-C), 41.4 (*C*$H_2$), 39.0 (*C*$H_2$), 23.1 (*C*$H_2$), 21.1 (*C*$H_3$), 18.5 (*C*$H_3$), 13.9 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 2975, 2872, 1770, 1746, 1492, 1448, 1325, 1193, 1067.

HRMS (ESI+) calcd for $C_{18}H_{22}O_4SNa$ $(M+Na)^+$: 357.1136, found 357.1141

**Ethyl 7a-(benzyloxy)-3a-methyl-3-oxooctahydro-1-benzofuran-2-carboxylate (5c):** A mixture of ethyl 2-diazo-3-(1-methyl-2-oxocyclohexyl)-3-oxopropanoate (252 mg, 1.0 mmol) and benzylalcohol (129 mg, 1.10 mmol) in dry benzene (25 mL) was allowed to reflux in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) according to method B to afford **5c** as a diastereomeric mixture (298 mg, 90%, 75:25 based on crude NMR); colorless thick oil; $R_f$ 0.71 (30:70 EtOAc:hexane).




Selected signal for the above major isomer:

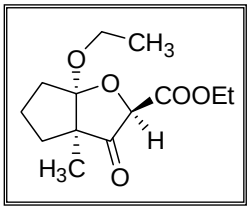
$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.27-7.23 (m, 5H, Arom-*H*), 4.62 (s, 2H, OC$H_2$), 4.46 (s, 1H, OC*H*), 4.36-4.23 (m, 2H, OC$H_2$), 2.47-2.39 (s, 1H, C$H_2$), 1.69-1.34 (m, 7H, C$H_2$), 1.30-1.11 (m, 6H, C$H_3$);

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 208.4 (*C*=O), 165.7 (*C*=O), 138.1 (*qua*t-*C*), 128.2 (=*C*H), 127.2 (=*C*H), 126.7 (=*C*H), 106.9 (*qua*t-*C*), 76.9 (O*C*H), 62.5 (O*C*$H_2$), 61.9 (O*C*$H_2$), 51.6 (*qua*t-*C*), 31.2 (*C*$H_2$), 28.3 (*C*$H_2$), 22.3 (*C*$H_2$), 20.4 (*C*$H_2$), 13.8 (*C*$H_3$), 13.5 (*C*$H_3$).

$\nu_{max}$ (neat)/cm$^{-1}$ 2978, 2942, 2868, 1773, 1746, 1453, 1371, 1268, 1193, 1088, 963, 738.

HRMS (ESI+) calcd for $C_{19}H_{24}O_5Na$ $(M+Na)^+$: 355.1521, found 355.1511

**Ethyl 6a-ethoxy-3a-methyl-3-oxohexahydro-2*H*-cyclopenta[*b*]furan-2-carboxylate (5d):** A mixture of ethyl 2-diazo-3-(1-methyl-2-oxocyclopentyl)-3-oxopropanoate (238 mg, 1.0 mmol) and dry ethanol (2 mL) in dry benzene (25 mL) was allowed to reflux in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) according to method B to afford **5d** as a diastereomeric mixture (209 mg, 82%, 75:25 based on crude NMR); colorless thick oil; $R_f$ 0.76 (30:70 EtOAc:hexane).




Selected signal for the above major isomer:

$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 4.59 (s, 1H, OC*H*), 4.32-4.21 (m, 2H, OC$H_2$), 3.83-3.45 (m,

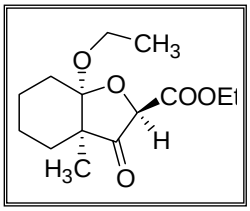
2H, OC$H_2$), 2.39 (m, 1H, C$H_2$), 1.98-1.82 (m, 5H, C$H_2$), 1.35-1.21 (m, 3H, C$H_3$), 1.17-1.11 (m, 6H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 210.9 (*C*=O), 166.0 (*C*=O), 118.0 (*qua*t-*C*), 78.8 (O*C*H), 61.9 (O*C*$H_2$), 59.7 (O*C*$H_2$), 56.6 (*qua*t-*C*), 35.9 (*C*$H_2$), 33.5 (*C*$H_2$), 21.8 (*C*$H_2$), 16.8 (*C*$H_3$), 15.4 (*C*$H_3$), 14.0 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 2979, 2879, 1769, 1746, 1449, 1265, 1191, 1130, 1070.

HRMS (ESI+) calcd for $C_{13}H_{20}O_5Na$ $(M+Na)^+$: 279.1208, found 279.1214.

**Ethyl 7a-ethoxy-3a-methyl-3-oxooctahydro-1-benzofuran-2-carboxylate (5e):** A mixture of ethyl 2-diazo-3-(1-methyl-2-oxocyclohexyl)-3-oxopropanoate (252 mg, 1.0 mmol) and dry ethanol (2 mL) in dry benzene (25 mL) was allowed to reflux in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) according to method B to afford **5e** as a diastereomeric mixture (234 mg, 87%, 77:23 based on crude NMR); colorless thick oil; $R_f$ 0.79 (30:70 EtOAc:hexane).




Selected signal for the above major isomer:

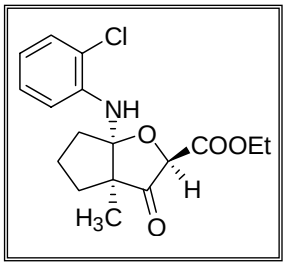
$^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 4.45 (s, 1H, OC*H*), 4.35-4.20 (m, 2H, OC$H_2$), 3.64-3.52 (m, 2H, OC$H_2$), 2.39-2.33 (m, 1H, C$H_2$), 1.72-1.39 (m, 7H, C$H_2$), 1.33 (t, 3H, C$H_3$, $J$ = 8Hz), 1.14-1.08 (m, 6H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 208.8 (*C*=O), 165.8 (*C*=O), 106.4 (*qua*t-*C*), 76.7 (O*C*H), 61.7 (O*C*$H_2$), 55.8 (O*C*$H_2$), 51.4 (*qua*t-*C*), 31.0 (*C*$H_2$), 28.0 (*C*$H_2$), 22.1 (*C*$H_2$), 20.4 (*C*$H_2$), 15.1 (*C*$H_3$), 13.9 (*C*$H_3$), 13.3 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 2985, 2882, 1773, 1746, 1452, 1268, 1193, 1132, 1072.

HRMS (ESI+) calcd for $C_{14}H_{22}O_5Na$ $(M+Na)^+$: 293.1365, found 293.1362.

**Ethyl 6a-[(2-chlorophenyl)amino]-3a-methyl-3-oxohexahydro-2*H*-cyclopenta[*b*] furan-2-carboxylate (5f):** A mixture of ethyl 2-diazo-3-(1-methyl-2-oxocyclopentyl)-3-oxopropanoate (238 mg, 1.0 mmol) and 2-chloro aniline (139 mg, 1.1 mmol) in dry benzene (25 mL) was allowed to reflux in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) according to method B to afford **5f** as a diastereomeric mixture (306 mg, 91%, 75:25 based on crude NMR); colorless thick oil; $R_f$ 0.65 (30:70 EtOAc:hexane).




Selected signal for the above major isomer:

$^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.47 (d, 1H, Arom-*H*, *J* = 8 Hz), 7.24 (d, 1H, Arom-*H*, *J* = 8 Hz), 7.12 (t, 1H, Arom-*H*, *J* = 8 Hz), 6.75 (t, 1H, Arom-*H*, *J* = 8 Hz), 4.79 (s, 1H, NH), 4.66 (s, 1H, OC*H*), 4.32-4.20 (m, 2H, OC$H_2$), 2.20-1.65 (m, 6H, C$H_2$), 1.34-1.25 (m, 6H, C$H_3$).

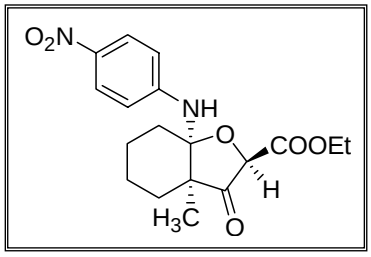
$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 210.4 (*C*=O), 165.8 (*C*=O), 140.6 (*qua*t-*C*), 128.9 (=*C*H), 127.4 (=*C*H), 121.9 (*qua*t-*C*), 120.0 (=*C*H), 117.0 (=*C*H), 103.7 (*qua*t-*C*), 78.4 (O*C*H), 61.9 (O*C*$H_2$), 58.4 (*qua*t-*C*), 36.8 (*C*$H_2$), 36.7 (*C*$H_2$), 22.7 (*C*$H_2$), 16.8 (*C*$H_3$), 13.9 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3372, 2979, 2876, 1767, 1744, 1594, 1518, 1442, 1372, 1297, 1035, 752.

HRMS (ESI+) calcd for $C_{17}H_{20}ClNO_4Na$ $(M+Na)^+$: 360.0979, found 360.0971.

**Ethyl 7a-[(4-nitrophenyl)amino]-3a-methyl-3-oxooctahydro-1-benzofuran-2-carboxylate (5g):** A mixture of ethyl 2-diazo-3-(1-methyl-2-oxocyclohexyl)-3-oxopropanoate

(252 mg, 1.0 mmol) and 4-nitroaniline (151 mg, 1.1 mmol) in dry benzene (25 mL) was allowed to reflux in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) according to method B to afford **5g** as a diastereomeric mixture (322 mg, 89%, 70:30 based on crude NMR). This mixture was successfully separated by crystallization technique (ethyl acetate/hexane) to furnish the pure major isomer (150 mg) as a pale yellow solid; mp 188-190°C; $R_f$ 0.60 (30:70 EtOAc:hexane).




$^1$H NMR (Acetone-$d_6$, 200 MHz) $\delta$ 8.05 (d, 2H, Arom-*H*, *J* = 8 Hz), 7.14 (d, 2H, Arom-*H*, *J* = 8 Hz), 5.85 (s, 1H, NH), 4.54 (s, 1H, OC*H*), 4.25 (q, 2H, OC$H_2$ $J_1$ = 14 Hz, $J_2$ = 8 Hz), 2.09-1.51 (m, 8H, C$H_2$), 1.35 (s, 3H, C$H_3$), 1.27 (t, 3H, C$H_3$, *J* = 8 Hz).

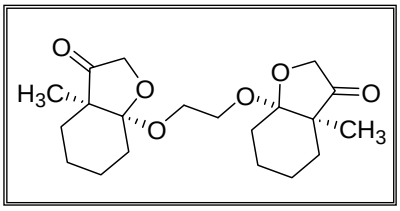
$^{13}$C NMR (Acetone-$d_6$, 50.3 MHz) δ 207.4 (*C*=O), 165.3 (*C*=O), 150.9 (*qua*t-*C*), 124.9 (=*C*H), 124.3 (*qua*t-*C*), 115.6 (=*C*H), 93.5 (*qua*t-*C*), 76.5 (O*C*H), 61.4 (O*C*$H_2$), 51.6 (*qua*t-*C*), 31.0 (*C*$H_2$), 29.2 (*C*$H_2$), 21.5 (*C*$H_2$), 20.1 (O*C*$H_2$), 13.4 (*C*$H_3$), 13.2 (*C*$H_3$).

$\nu_{max}$(KBr)/cm$^{-1}$ 3384, 2995, 2944, 2599, 1776, 1731, 1597, 1483, 1332, 1301, 1087, 1026.

HRMS (ESI+) calcd for $C_{18}H_{24}N_2O_6$ $(M+2H)^+$: 364.1634, found 364.1614.

**7a,7a'-[Ethane-1,2-diylbis(oxy)]bis(3a-methylhexahydro-1-benzofuran-3(2*H*)-one)**

**6a:** A mixture of α-diazo ketone **1b** (396 mg, 2.2 mmol) and 1,2-ethanediol (62 mg, 1.0 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (50 mL) according to method C to afford **6a** (175 mg, 48% based on 1,2-ethanediol) as a colorless thick oil; $R_f$ 0.65 (30:70 EtOAc:hexane).



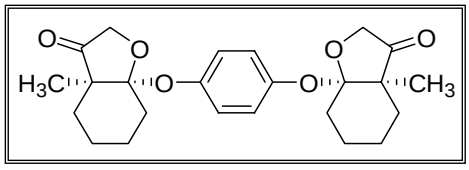
$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 4.21 (d, 2H, OC$H_2$, $J$ = 16 Hz), 3.93 (d, 2H, OC$H_2$, $J$ = 16 Hz), 3.63 (s, 4H, OC$H_2$), 2.27-2.14 (m, 2H, C$H_2$), 1.72-1.26 (m, 14H, C$H_2$), 1.07 (s, 6H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 216.6 (*C*=O), 107.4 (*quat*-*C*), 67.0 (O*C*$H_2$), 61.8 (O*C*$H_2$), 51.2 (*quat*-*C*), 32.5 (*C*$H_2$), 28.1 (*C*$H_2$), 22.4 (*C*$H_2$), 20.4 (*C*$H_2$), 12.8 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3006, 2957, 2910, 1729, 1440, 1325, 1216, 1134.

HRMS (ESI+) calcd for $C_{20}H_{30}O_6Na$ $(M+Na)^+$: 389.1940, found 389.1948.

**7a,7a'-[1,4-phenylenebis(oxy)]bis(3a-methylhexahydro-1-benzofuran-3(2*H*)-one) (6b):** A mixture of α-diazo ketone **1b** (396 mg, 2.2 mmol) and hydroquinone (110 mg, 1.0 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (50 mL) according to method C to afford **6b** (298 mg, 72% based on hydroquinone) as a colorless thick oil; $R_f$ 0.60 (30:70 EtOAc:hexane).



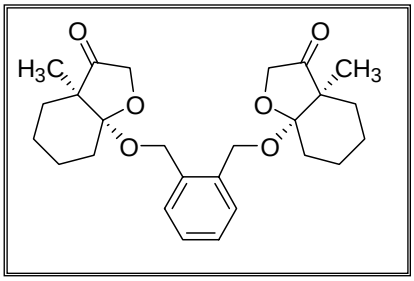
$^{1}$H NMR ($CDCl_3$, 200 MHz) $\delta$ 6.96 (s, 4H, Arom-*H*), 4.36 (d, 2H, OC$H_2$, $J$ = 16 Hz), 4.19 (d, 2H, OC$H_2$, $J$ = 16 Hz), 2.50-1.36 (m, 16H, C$H_2$), 1.21 (s, 6H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 215.5 (*C*=O), 149.4 (*quat*-*C*), 122.4 (=*C*H), 122.1 (=*C*H), 110.4 (*quat*-*C*), 67.4 (O*C*$H_2$), 51.6 (*quat*-*C*), 32.5 (*C*$H_2$), 28.8 (*C*$H_2$), 22.4 (*C*$H_2$), 20.6 (*C*$H_2$), 13.1 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 3056, 2943, 2867, 1762, 1728, 1502, 1451, 1266, 1214, 741.

HRMS (ESI+) calcd for $C_{24}H_{30}O_6Na$ $(M+Na)^+$: 437.1940, found 437.1949.

**7a,7a'-[1,2-Phenylenebis(methyleneoxy)]bis(3a-methylhexahydro-1-benzofuran-3(2*H*)-one) (6c):** A mixture of α-diazo ketone **1b** (396 mg, 2.2 mmol) and 1,2-benzenedimethanol (138 mg, 1.0 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (50 mL) according to method C to afford **6c** (309 mg, 70% based on 1,2-benzenedimethanol) as a colorless solid; mp 149-150°C; $R_f$ 0.60 (30:70 EtOAc:hexane).




$^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.31-7.19 (m, 4H, Arom-*H*), 4.66-4.52 (m, 4H, OC$H_2$), 4.26-4.17 (m, 2H, OC$H_2$), 3.86-3.73 (m, 2H, OC$H_2$), 2.47-1.25 (m, 16H, C$H_2$), 1.16 (s, 6H, C$H_3$).

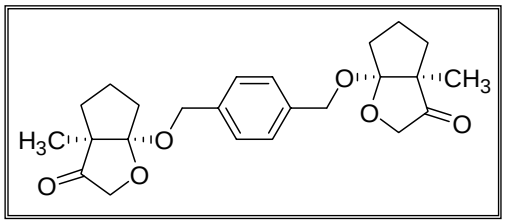
$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 216.3 (*C*=O), 136.1 (*qua*t-*C*), 127.3 (=*C*H), 107.9 (*qua*t-*C*), 67.2 (O*C*$H_2$), 60.0 (O*C*$H_2$), 51.4 (*qua*t-*C*), 32.6 (*C*$H_2$), 28.4 (*C*$H_2$), 22.6 (*C*$H_2$), 20.5 (*C*$H_2$), 13.0 (*C*$H_3$).

$\nu_{max}$(KBr)/cm$^{-1}$ 2944, 2863, 1755, 1461, 1447, 1180, 1106, 1093, 1075, 1016, 951.

HRMS (ESI+) calcd for $C_{26}H_{34}O_6Na$ $(M+Na)^+$: 465.2253, found 465.2243.

**6a,6a'-[1,4-Phenylenebis(methyleneoxy)]bis(3a-methyltetrahydro-2*H*-cyclopenta[*b*]furan-3(3a*H*)-one) (6d):** A mixture of α-diazo ketone **1a** (365 mg, 2.2 mmol) and 1,4-benzenedimethanol (138 mg, 1.0 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (50 mL) according to method C to afford **6d**

(277 mg, 67% based on 1,4-benzenedimethanol) as a colorless solid; mp 100-101°C; $R_f$ 0.58 (30:70 EtOAc:hexane).



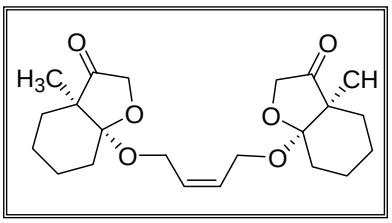
$^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 7.28 (s, 4H, Arom-*H*), 4.77 (d, 2H, OC$H_2$, $J$ = 12 Hz), 4.57 (d, 2H, OC$H_2$, $J$ = 12 Hz), 4.23-4.15 (d, 2H, OC$H_2$, $J$ = 16 Hz), 4.07-3.99 (d, 2H, OC$H_2$, $J$ = 16 Hz), 2.31-2.30 (m, 2H, C$H_2$), 2.00-1.58 (m, 10H, C$H_2$), 1.15 (s, 6H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 217.8 (*C*=O), 137.8 (*qua*t-*C*), 127.0 (=*C*H), 118.7 (*qua*t-*C*), 69.6 (O*C*$H_2$), 65.5 (O*C*$H_2$), 56.5 (*qua*t-*C*), 36.0 (*C*$H_2$), 34.0 (*C*$H_2$), 22.0 (*C*$H_2$), 16.6 (*C*$H_3$).

$\nu_{max}$(KBr)/cm$^{-1}$ 2959, 2936, 2871, 1759, 1708, 1453, 1322, 1273, 1171, 1054, 1017, 915.

HRMS (ESI+) calcd for $C_{24}H_{30}O_6Na$ $(M+Na)^+$: 437.1940, found 437.1948.

**7a,7a'-[(2*Z*)-But-2-ene-1,4-diylbis(oxy)]bis(3a-methylhexahydro-1-benzofuran-3(2*H*)-one) (6e):** A mixture of α-diazo ketone **1b** (396 mg, 2.0 mmol) and cis-2-butene-1,4-diol (88 mg, 1.0 mmol) was allowed to react in the presence of $Rh_2(OAc)_4$ (4.4 mg, 1 mol%) in dry DCM (50 mL) according to method C to afford **6e** (254 mg, 65% based on *cis*-2-butene-1,4-diol) as a colorless thick oil; $R_f$ 0.60 (30:70 EtOAc:hexane).



$^1$H NMR ($CDCl_3$, 200 MHz) $\delta$ 5.52-5.49 (m, 2H, =C*H*), 4.21 (d, 2H, OC$H_2$, $J$ = 16 Hz),

4.09-4.07 (m, 4H, OC$H_2$), 3.86 (d, 2H, O$CH_2$, $J$ = 16 Hz), 2.23-1.40 (m, 16H, C$H_2$), 1.10 (s, 3H, C$H_3$).

$^{13}$C NMR ($CDCl_3$, 50.3 MHz) δ 216.6 (*C*=O), 128.5 (*C*H), 107.6 *(qua*t-*C*), 67.1 (O*C*$H_2$), 56.7 (O*C*$H_2$), 51.3 (*qua*t-*C*), 32.5 (*C*$H_2$), 28.3 (*C*$H_2$), 22.6 (*C*$H_2$), 20.5 (*C*$H_2$), 12.9 (*C*$H_3$).

$\nu_{max}$(neat)/cm$^{-1}$ 2980, 2878, 2242, 1742, 1450, 1368, 1297, 1193, 1025.

HRMS (ESI+) calcd for $C_{22}H_{32}O_6Na$ $(M+Na)^+$: 415.2097, found 415.2104.

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**ORTEP view of compounds 2a,5g and their details**

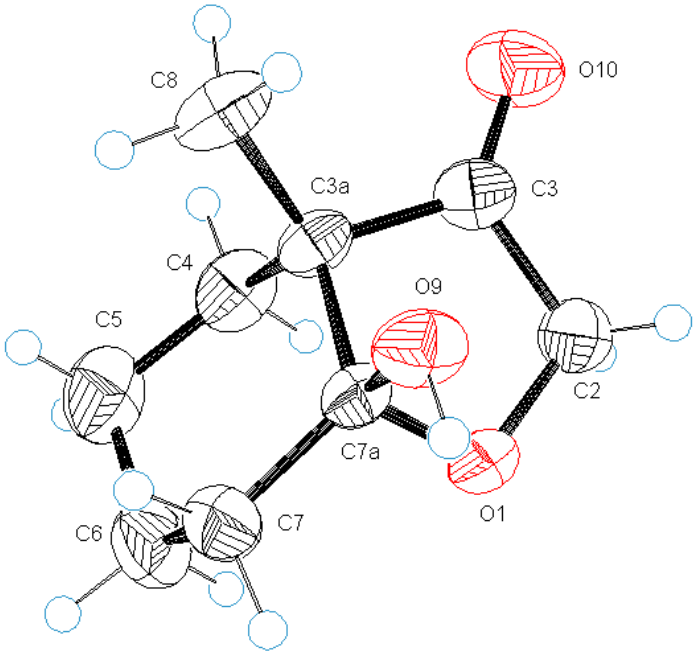


**Fig. S1** ORTEP view of compound **2a**.

Crystal data for the compound **2a**: $C_9H_{14}O_3$, $M$ = 170.20, 0.36 x 0.28 x 0.22 $mm^3$, Orthorhombic, space group Pbca with $a$ = 5.9697(5) Å, $b$ = 13.3048(12) Å, $c$ = 22.401(2) Å, $\alpha = 90°$, $\beta = 90°$, $\gamma = 90°$, $V$ = 1779.2(3) $Å^3$, $T$ = 273(2) K, $R_1$ = 0.0522, $wR_2$ = 0.1358 on observed data, z = 8, $D_{calcd}$ = 1.271 g $cm^{-3}$, $F(000)$ = 736, Absorption coefficient = 0.094 $mm^{-1}$, $\lambda$ = 0.71073 Å, 9533 reflections were collected on a smart apex CCD single crystal diffractometer, 2087 observed reflections ($I \geq 2\sigma(I)$). The largest difference peak and hole = 0.314 and -0.166 e $Å^{-3}$, respectively. The structure was solved by direct methods and refined by full-matrix least squares on $F^2$ using SHELXL–97 software.

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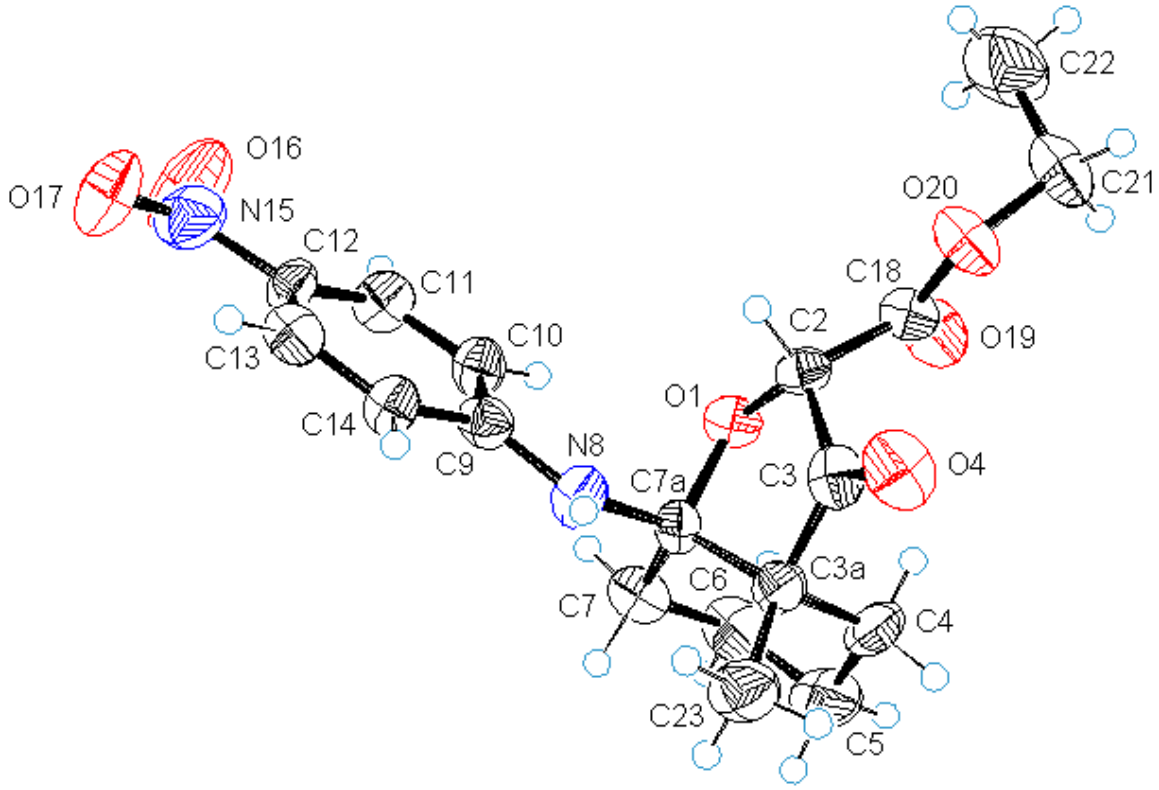


**Fig. S2** ORTEP view of compound **5g**.

Crystal data for the compound **5g**: $C_{18}H_{22}N_2O_6$, $M$ = 362.38, 0.12 x 0.08 x 0.04 $mm^3$, Triclinic, space group P-1 with $a$ = 6.6119(9) Å, $b$ = 10.4176(14) Å, $c$ = 13.0721(17) Å, $\alpha$ = 91.049(3)°, $\beta$ = 95.024(3)°, $\gamma$ = 95.584(3)°, $V$ = 892.4(2) $Å^3$, $T$ = 273(2) K, $R_1$ = 0.0778, $wR_2$ = 0.1642 on observed data, z = 2, $D_{calcd}$ = 1.349 g $cm^{-3}$, $F(000)$ = 384, Absorption coefficient = 0.102 $mm^{-1}$, $\lambda$ = 0.71073 Å, 4345 reflections were collected on a smart apex CCD single crystal diffractometer, 2995 Independent reflections ($I \geq 2\sigma(I)$). The largest difference peak and hole = 0.261 and -0.313 e $Å^{-3}$, respectively. The structure was solved by direct methods and refined by full-matrix least squares on $F^2$ using SHELXL–97 software.

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## Energy minimized structures of carbonyl ylides 4

The energy minimized structures (Figures S4-S7) of cycloalkyl fused five- as well as six-membered-ring carbonyl ylide dipoles **4a,b** and their ester substituted derivatives are shown below. The calculated results showed that the reactive center of dipoles is completely planar. The fused cyclopentane or cyclohexane ring adopts envelope or chair like conformation, respectively. All AM1 level semiemprical calculations have been performed using Mopac version 6.0.[2]

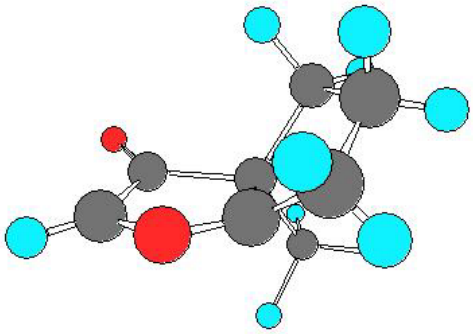

**Figure S3**. Energy minimized five-membered-ring carbonyl ylide **4a**.

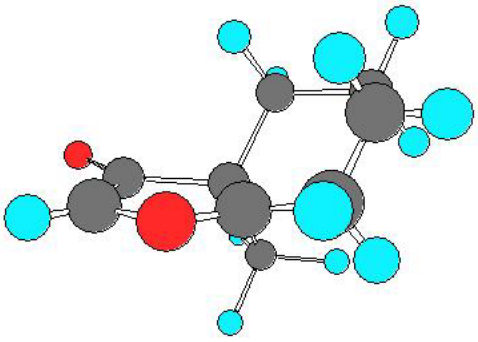

**Figure S4**. Energy minimized six-membered-ring carbonyl ylide **4b**.[2]

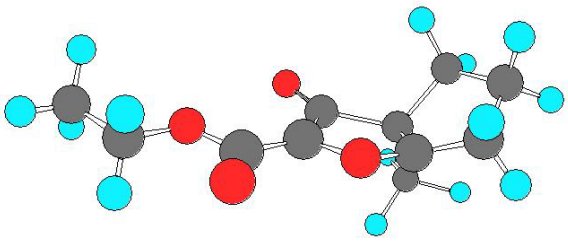

**Figure S5**. Energy minimized five-membered-ring carbonyl ylide **4a** having an ester substituent.

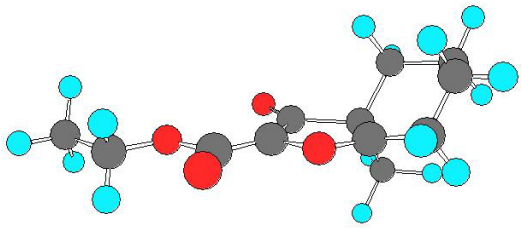

**Figure S6**. Energy minimized six-membered-ring carbonyl ylide **4b** having an ester substituent.

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**Proposed mechanism for the nucleophilic addition to carbonyl ylide 4**

A nucleophile approach can be either syn or anti to the bridgehead methyl group of these facially dissymmetric carbonyl ylide dipoles. In line with our previous study[3] with the dipolarophiles, the nucleophiles also prefer syn to methyl group (Figure S8). The 1,3-diaxial hydrogens present in the cycloalkane ring system sterically hinder the one of the reactive centers ($C=O^{+}-C^{-}$) in the anti face and hence the nucleophile prefers to approach from the syn face of the dipole. The oxygen, nitrogen, sulfur or di-nucleophile approaches syn to methyl group to furnish compounds **2** with cis-stereochemistry. Similar observations were made in the case of ester substituted carbonyl ylide dipoles to afford products **5**. As a second step, the proton shift from the nucleophile preferably takes place syn to methyl group affording the major diastereomer in products **5**.

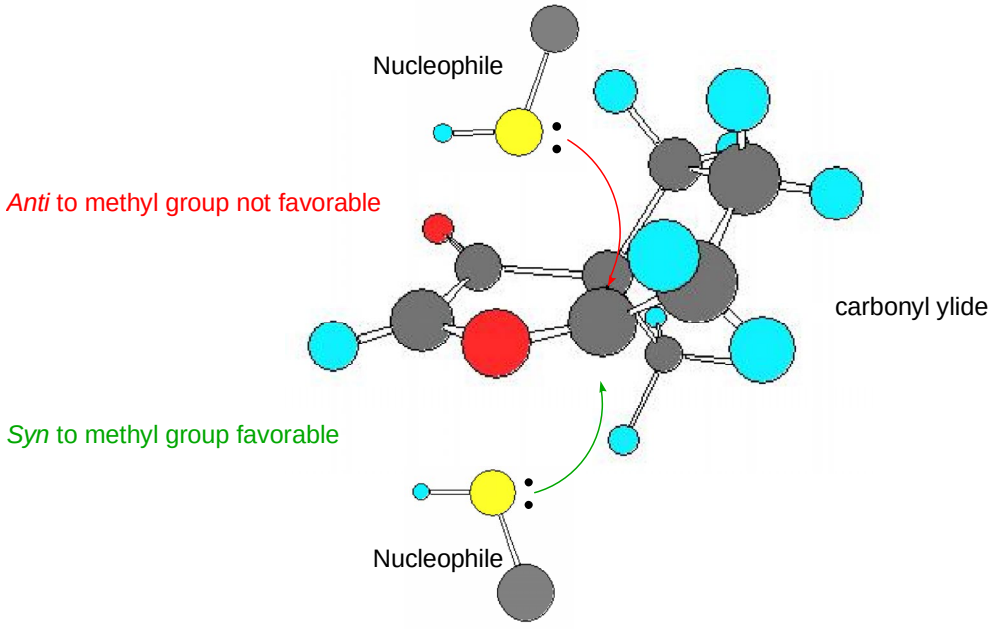


**Figure S7**

## References


1. S. Muthusamy, S. A. Babu, C. Gunanathan, E. Suresh, P. Dastidar, and R. V. Jasra, *Tetrahedron*, 2000, **56**, 6307.
2. Dewar, M. J. S.; Zoebish, E. G.; Healy, E. F.; Stewart, J. J. P.; *J. Am. Chem. Soc*. **1985**, *107*, 3902.
3. Muthusamy, S.; Babu, S. A.; Gunanathan, C.; Ganguly, B.; Suresh, E.; Dastidar, P. *J. Org. Chem.* **2002**, *67*, 8019.


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