Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Rapid Synthesis of Substituted Pyrrolines and Pyrrolidines by Nucleophilic Ring Closure at Activated Oximes

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General Procedures

(A) Michael addition (methyl vinyl ketone) [1-7]

Methyl vinyl ketone (1.2 eq.) was added dropwise to a well-stirred mixture of malonate (1.0 eq.) and anhydrous K_2CO_3 (1.5 eq.) in dry CH_2Cl_2 and the mixture stirred for 15 hr at rt or till completion of the reaction by TLC. Water and EtOAc was added sequentially and the organic layer was separated, washed with 1 M HCl, water, brine and dried over Na_2SO_4. Concentration of the organic layer gave the crude product, which was purified by flash column chromatography (eluting with EtOAc : petrol) to afford the Michael adduct.

(B) Michael addition (chalcone) [1-7]

Chalcone (1.1 eq.) in dry CH_2Cl_2 was added dropwise to a well-stirred mixture of malonate (1.0 eq.) and anhydrous K_2CO_3 (1.5 eq.) in dry CH_2Cl_2 and the mixture was heated to reflux for 15 hr or till completion of the reaction by TLC. H_2O and EtOAc were added sequentially; the organic layer was separated, washed with 1 M HCl, water, brine and dried over Na_2SO_4. Concentration of the organic layer gave the crude product, which was purified by flash column chromatography (eluting with EtOAc : petrol) to afford the Michael adduct.

(C) Oxime from Michael adduct[8, 9]

To a solution of the Michael adduct from procedure **A** or **B** (1.0 eq.) in EtOH, was added $NH_2OH{\cdot}HCl$ (2.0 eq.) and Et_3N (2.5 eq.) and the reaction mixture was heated to reflux for 2 hr (7 hr in case of chalcone adduct). The progress of the reaction was monitored by TLC, and on

completion, the reaction mixture was allowed to cool to rt. EtOH was removed under reduced pressure and the residue was dissolved in EtOAc and H_2O added. The organic layer was separated, washed with brine and dried over Na_2SO_4. Concentration of the organic layer gave the crude product, which was purified by flash column chromatography (eluting with EtOAc : petrol) to afford the oxime product.

(D) Oxime ether (2,4-dinitrofluorobenzene) from oxime[8, 9]

The oxime (1.0 eq.) from procedure **C** was dissolved in EtOH and sodium metal (1.1 eq.) was added. The mixture was stirred for 30 min at rt to ensure complete reaction. The reaction mixture was cooled to 0 °C before 2,4-dinitrofluorobenzene (1.5 eq.) was added slowly, during which the reaction colour suddenly changes to deep yellow-orange. The reaction was stirred till completion by TLC. After completion of the reaction, EtOH was removed under reduced pressure and the residue was dissolved in dilute HCl. The oxime ether was extracted by EtOAc, washed with saturated $NaHCO_3$, water and brine, dried over Na_2SO_4 and on concentration gave the product, which was purified by flash column chromatography (eluting with EtOAc : petrol).

(E) Tosyl or mesyl oxime from oxime [10]

To a stirred solution of oxime (1.0 eq.) from procedure **C** in dry CH_2Cl_2 at 0 °C was treated with Et_3N or pyridine (2.0 eq.) followed by slow addition of *p*-toluenesulphonyl chloride or methanesulfonyl chloride (1.2 eq.). The reaction was further stirred for 2 hr while progress was monitored by TLC, and after completion of reaction, HCl (1 M) was added, the product was extracted by CH_2Cl_2, and the extracts were washed with saturated $NaHCO_3$ and dried over Na_2SO_4. Concentration of CH_2Cl_2 gave crude product which was purified by flash column chromatography (eluting with EtOAc : petrol).

(F) Ring closure reaction[8, 9]

To a solution of oxime ether or tosyl oxime (1.0 eq.) from procedure **D** or **E** in dry THF at rt, a dispersion of NaH (3.0 eq. 60% dispersion in mineral oil) was added and heated to reflux for 30 min to 1 hr and the progress of the reaction was monitored by TLC. After completion of the

reaction, saturated NH_4Cl was added and the pyrroline product was extracted with EtOAc. The extracts were dried over Na_2SO_4, and concentration of reaction mixture gave the crude product which was purified by flash column chromatography (eluting with EtOAc : petrol).

(G) Reduction of the cyclised product (H-Cube Hydrogenation)

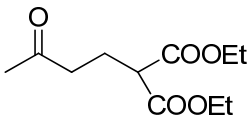
The solution of the cyclised product pyrroline (1.0 eq.) in EtOH was passed through the capillary of a H-Cube hydrogenation plant (0.5 mL per min) at 50 °C, using 10% Pd/C as catalyst. EtOH was removed under reduced pressure and the crude product was purified by flash column chromatography (eluting with EtOAc : petrol).

H) Reduction of the cyclised product ($NaBH_3CN$)[11]

To a solution of pyrroline product (1.0 eq.) in MeOH was added 2 M HCl in MeOH, followed by $NaBH_3CN$ (3.0 eq.) and additional 2 M HCl in MeOH was added periodically to maintain the acidic pH of the reaction mixture. The progress of the reaction was monitored by TLC, and after 30-60 min, MeOH was removed and the residue extacted with dilute $NaHCO_3$ and EtOAc, washed with water, brine, dried over Na_2SO_4 and the organic layer concentrated and purified by flash column chromatography (eluting with EtOAc : petrol).

Experimental Procedures

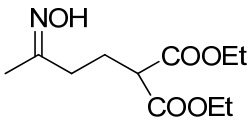
Diethyl 2-(3-ox butyl)malonate, 3a



Following general procedure **A**, methyl vinyl ketone (2.84 g, 40.6 mmol) was added to a solution of diethyl malonate (5.01 g, 31.3 mmol) and anhydrous K_2CO_3 (6.28 g, 46.9 mmol) in dry CH_2Cl_2 (30 mL) stirred at rt, to give the crude product which was purified by flash column chromatography to afford adduct **3a** (6.40 g, 90%) as a colourless oil; R_f = 0.51 (EtOAc : petrol, 1:2); υ_{max}(film)/cm^{-1} 2983,1730, 1447, 1367, 1157, 1097, 860; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.25 (6H, t, *J* 7.1 Hz, 2 × OCH_2CH_3), 2.12 (3H, s, $COCH_3$), 2.13 (2H, m, CH_2CH_2CH), 2.56 (2H, t, *J* 7.3 Hz, CH_2CH_2CH),

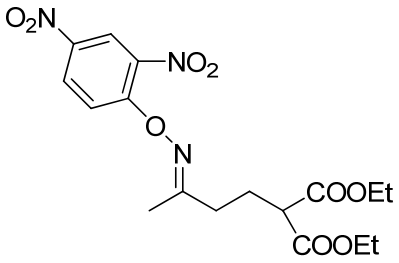
3.36 (1H, t, *J* 7.3 Hz, CH_2CH_2CH), 4.17 (4H, q, *J* 7.1 Hz, 2 × OCH_2CH_3); δ_C (100 MHz; $CDCl_3$; Me_4Si) 14.1 (2 × OCH_2CH_3), 22.4 (CH_2CH_2CH), 29.9 ($COCH_3$), 40.4 (CH_2CH_2CH), 50.7 (CH_2CH_2CH), 61.4 (2 × OCH_2CH_3), 169.1 (2 × *C*OO), 207.2 (*C*O); m/z (ESI^+) 289 ($[M+CH_3CN+NH_4]^+$, 50%), 229 ($[M-H]^-$, 100%), HRMS (ESI^+) $C_{11}H_{18}O_5^+$ ($[M^+]$) requires 230.1154; found 230.1149.

Diethyl 2-(3-(hydroxyimino)butyl)malonate, 4a



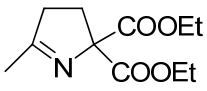
Following general procedure **C**, to a solution of adduct **3a** (6.20 g, 27.0 mmol) in EtOH (40 mL), was added $NH_2OH.HCl$ (3.72 g, 53.9 mmol) and Et_3N (6.80 g, 67.4 mmol) which was heated to reflux for 2 hr, to give the crude product which was purified by flash column chromatography to afford oxime **4a** (5.70 g, 86%) as a colourless oil; R_f = 0.47 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3440, 3260, 2983, 1732, 1447, 1370, 1153, 1096, 861; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.26 (6H, t, *J* 7.1 Hz, 2 × OCH_2CH_3), 1.88 (3H, s, $COCH_3$), 2.10 (2H, m, CH_2CH_2CH), 2.24, 2.41 (2H, t, *J* 7.7 Hz, CH_2CH_2CH), 3.36 (1H, t, *J* 7.2 Hz, CH_2CH_2CH), 4.19 (4H, q, *J* 7.1 Hz, 2 × OCH_2CH_3), 8.73 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.5 ($CNOHCH_3$), 14.0 (2 × OCH_2CH_3), 25.2 (CH_2CH_2CH), 33.4 (CH_2CH_2CH), 51.1, 51.6 (CH_2CH_2CH), 61.5 (2 × OCH_2CH_3), 156.9 (*C*=NOH), 169.1 (2 × *C*OO); m/z (ESI^+) 304 ($[M+CH_3CN+NH_4]^+$, 100%), 268 ($[M+Na]^+$, 35%), 244 ($[M-H]^-$, 100%), HRMS (ESI^+) $C_{11}H_{19}NO_5^+$ ($[M-H]^-$) requires 244.1190; found 244.1180.

Diethyl 2-(3-(2,4-dinitrophenoxyimino)butyl)malonate, 5a



Following general procedure **D**, to a solution of oxime **4a** (501 mg, 2.04 mmol) in EtOH (20 mL), was added sodium metal (52 mg, 2.24 mmol) followed by 2,4-dinitrofluorobenzene after 30 min at 0 °C. EtOH was removed to give the crude product which was purified by flash column chromatography to afford ether **5a** (569 mg, 68%) as a yellow oil; R_f = 0.61 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 3040, 2984, 1730, 1606, 1533, 1473, 1343, 1289, 1147, 1066, 925, 831, 743, 719; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.28 (6H, t, *J* 7.1 Hz, 2 × OCH_2CH_3), 2.19 (3H, s, $COCH_3$), 2.26 (2H, m, CH_2CH_2CH), 2.49 and 2.67 (2H, t, *J* 7.7 Hz, CH_2CH_2CH), 3.44 (1H, t, *J* 7.1 Hz, CH_2CH_2CH), 4.20-4.30 (4H, m, 2 × OCH_2CH_3), 7.94 (1H, d, *J* 7.4 Hz, Ar*H*), 8.41 (1H, dd, *J* 7.4, 2.7 Hz, Ar*H*), 8.87 (1H, d, *J* 2.7 Hz, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (2 × OCH_2CH_3), 16.4 ($CNOHCH_3$), 24.6 (CH_2CH_2CH), 33.4 (CH_2CH_2CH), 50.1 (CH_2CH_2CH), 61.7 (2 × OCH_2CH_3), 117.2, 122.1, 129.4, 135.8, 140.6 (Ar*C*), 157.3 (*C*=NOAr), 165.8 and 166.5 (quaternary Ar*C*), 168.7 and 168.9 (2 × *C*OO); m/z (ESI$^+$) 470 ([M+CH_3CN+NH_4]$^+$, 100%), HRMS (ESI$^+$) $C_{17}H_{21}N_3O_9^+$ ([M+Na]$^+$) requires 434.1170; found 434.1160.

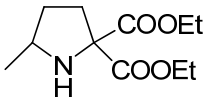
Diethyl 5-methyl-3,4-dihydro-2H-pyrrole-2,2-dicarboxylate, 7a



Following general procedure **F**, to ether **5a** (402 mg, 0.97 mmol) in dry THF (15 mL) was added NaH (70 mg, 2.91 mol, 60%) and the mixture heated to reflux for 30 min, to give crude product which was purified by flash column chromatography to afford pyrroline **7a** (119 mg, 54%) as a colourless oil; R_f = 0.15 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2984, 1735, 1644, 1446, 1380, 1267, 1158, 1022; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.27 (6H, t, *J* 7.1 Hz, 2 × OCH_2CH_3), 2.14 (3H, s,

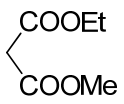
C*H*$_3$C=N), 2.45 (2H, t, *J* 7.5 Hz, C(4)*HH*), 2.67 (2H, t, *J* 7.7 Hz, C(3)*HH*), 4.23 (4H, q, *J* 7.1 Hz, 2 × OC*H*$_2$CH$_3$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (2 × OCH$_2$*C*H$_3$), 19.9 (*C*H$_3$C=N), 30.4 (*C*4), 39.5 (*C*3), 61.9 (2 × O*C*H$_2$CH$_3$), 86.6 (*C*2), 169.9 (2 × *C*OO), 180.9 (*C*5); m/z (ESI$^+$) 513 ([2M+CH$_3$CN+NH$_4$]$^+$, 100%), 455 ([2M+H]$^+$, 75%), 286 ([M+CH$_3$CN+ NH$_4$]$^+$, 60%), 228 ([M+H]$^+$, 72%), HRMS (ESI$^+$) $C_{11}H_{17}NO_4^+$ ([M+H]$^+$) requires 228.1236; found 228.1230.

(±)Diethyl 5-methylpyrrolidine-2,2-dicarboxylate, 9a [11]



Following general procedure **H**, to a solution of pyrroline **7a** (51 mg, 0.22 mmol) in MeOH (3 mL) was added $NaBH_3CN$ (21 mg, 0.33 mmol) and 2 M HCl in MeOH (2 mL), which after work-up gave crude product which was purified by column chromatography to afford pyrrolidine **9a** (47 mg, 93%) as a colourless oil; R_f = 0.63 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3353, 2966, 1734, 1448, 1367, 1272, 1190, 1145, 1026, 863; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.11 (3H, d, *J* 6.2 Hz, C*H*$_3$CHNH), 1.20 (6H, t, *J* 7.1 Hz, 2 × OCH$_2$C*H*$_3$), 1.33 (1H, m, C(4)*H*H), 1.86 (1H, m, C(4)H*H*), 2.20 (1H, m, C(3)*H*H), 2.41 (1H, m, C(3)H*H*), 3.27 (1H, m, (C5)*H*), 4.10-4.20 (4H, m, 2 × OC*H*$_2$CH$_3$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (2 × OCH$_2$*C*H$_3$), 21.0 (*C*H$_3$CHNH), 32.9 (*C*4), 33.4 (*C*3), 54.9 (*C*5), 61.9 (2 × O*C*H$_2$CH$_3$), 72.3 (*C*2), 171.6, 172.3 (2 × *C*OO); m/z (ESI$^+$) 230 ([M+H]$^+$, 100%), HRMS (ESI$^+$) $C_{11}H_{19}NO_4^+$ ([M+H]$^+$) requires 230.1387; found 230.1384.

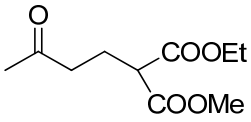
Ethyl methyl malonate



To a solution of ethyl 3-chloro-3-oxopropanoate (519 mg, 3.46 mmol) in MeOH (20 mL) was added Et_3N (698 mg, 6.92 mmol) and the mixture stirred at rt to afford ethyl methyl malonate (486 mg, 96%) as a colourless oil; υ_{max}(film)/cm^{-1} 2986, 1736, 1438, 1370, 1336, 1152, 1034; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.28 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 3.38 (2H, s, C*H*$_2$), 3.75 (3H, s, COOC*H*$_3$),

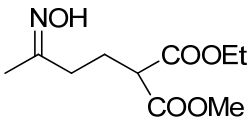
4.20 (2H, q, *J* 7.1 Hz, OC*H*$_2$CH$_3$), δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (OCH$_2$*C*H$_3$), 41.4 (*C*H$_2$), 52.5 (COO*C*H$_3$), 61.6 (O*C*H$_2$CH$_3$), 166.5, 167.1 (2 × *C*OO); m/z (ESI$^+$), 169 ([M+Na]$^+$, 100%), 145 ([M-H]$^-$, 30%), HRMS (ESI$^+$) $C_6H_{10}NaO_4^+$ ([M+Na]$^+$]) requires 169.0471; found 169.0470.

(±)1-Ethyl 3-methyl 2-(3-oxobutyl)malonate, 3b



Following general procedure **A**, methyl vinyl ketone (259 mg, 3.70 mmol) was added to a solution of methyl ethyl malonate (451 mg, 3.08 mmol) and anhydrous K_2CO_3 (620 mg, 4.63 mmol) in dry CH_2Cl_2 (20 mL) and the mixture stirred at rt, to give crude product which was purified by flash column chromatography to afford adduct **3b** (608 mg, 91%) as a colourless oil; R_f = 0.48 (EtOAc : petrol, 1:2); υ_{max}(film)/cm^{-1} 2956, 1732, 1438, 1370, 1158, 1097, 858; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.24 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 2.12 (3H, s, COC*H*$_3$), 2.23 (2H, m, CH$_2$C*H*$_2$CH), 2.52 (2H, t, *J* 7.3 Hz, C*H*$_2$CH$_2$CH), 3.38 (1H, dd, *J* 7.3, 7.0 Hz, CH$_2$CH$_2$C*H*), 3.72 (3H, s, COOC*H*$_3$), 4.18 (2H, q, *J* 7.1 Hz, OC*H*$_2$CH$_3$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (OCH$_2$*C*H$_3$), 22.4 (CH$_2$*C*H$_2$CH), 29.9 (CO*C*H$_3$), 40.4 (*C*H$_2$CH$_2$CH), 50.5 (CH$_2$CH$_2$*C*H), 52.5 (COO*C*H$_3$), 61.4 (O*C*H$_2$CH$_3$), 169.0, 169.6 (2 × *C*OO), 207.2 (*C*O); m/z (ESI$^+$) 239 ([M+Na]$^+$, 75%), 455 ([2M+Na]$^+$, 20%), HRMS (ESI$^+$) $C_{10}H_{16}NaO_5^+$ ([M+Na]$^+$) requires 239.0890; found 239.0890**.**

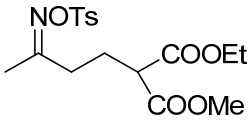
(±)1-Ethyl 3-methyl 2-(3-(hydroxyimino)butyl)malonate, 4b



Following general procedure **B**, to a solution of adduct **3b** (586 mg, 2.71 mmol) in EtOH (20 mL) was added $NH_2OH.HCl$ (374 mg, 5.42 mmol) and Et_3N (685 mg, 6.78 mmol) and heated to reflux for 2 hr, to give crude product which was purified by flash column chromatography to afford oxime **4b** (583 mg, 93%) as a colourless oil; R_f = 0.43 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3263, 2955,

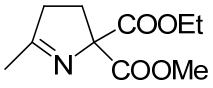
1733, 1438, 1370, 1154, 1025; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.27 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.89 (3H, s, $CNOHCH_3$), 2.13 (2H, m, CH_2CH_2CH), 2.25 (2H, m, CH_2CH_2CH), 3.40 (1H, dd, *J* 7.3, 7.0 Hz, CH_2CH_2CH), 3.75 (3H, s, $COOCH_3$), 4.20 (2H, m, OCH_2CH_3), 8.36 (1H, bs, OH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.5 ($CNOHCH_3$), 14.0 (OCH_2CH_3), 25.2 (CH_2CH_2CH), 33.4 (CH_2CH_2CH), 50.9 ($COOCH_3$), 52.5 (CH_2CH_2CH), 61.6 (OCH_2CH_3), 157.0, 157.3 (*C*NOH), 168.9, 169.6 (2 × *C*OO); m/z (ESI^+) 230 ($[M-H]^-$, 100%), 254 ($[M+Na]^+$, 65%), 290 ($[M+CH_3CN+NH_4]^+$, 5%), 485 ($[2M+Na]^+$, 60%), HRMS (ESI^+) $C_{10}H_{17}NaO_5^+$ ($[M+Na]^+$) requires 254.0999; found 254.0994.

(±)1-Ethyl 3-methyl 2-(3-(tosyloxyimino)butyl)malonate, 6b



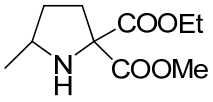
Following general procedure **E**, to a solution of oxime **4b** (100 mg, 0.86 mmol) in dry CH_2Cl_2 (10 mL) was added Et_3N (175 mg, 1.73 mmol) at 0 °C, followed by *p*-toluenesulphonyl choride (197 mg, 1.03 mmol), and the mixture stirred at rt for 2 hr, to give crude product which was purified by flash column chromatography to afford tosyl oxime **6b** (305 mg, 92%) as a colourless oil; R_f = 0.53 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3069, 2982, 1713, 1656, 1494, 1258, 1187, 995, 838, 766; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.12, 1.26 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.92, 1.95 (3H, s, $CNOTsCH_3$), 2.06 (2H, m, CH_2CH_2CH), 2.29 (2H, t, *J* 7.3 Hz, CH_2CH_2CH), 2.44, 2.49 (3H, s, $ArCH_3$), 3.31 (1H, t, *J* 7.3 Hz, CH_2CH_2CH), 3.72, 3.75 (3H, s, $COOCH_3$), 4.18, 3.22 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 7.34, 7.41 (2H, d, *J* 8.5 Hz, ArH), 7.85, 7.92 (2H, d, *J* 8.5 Hz, ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 ($CNOTsCH_3$), 15.8 (OCH_2CH_3), 21.4, 21.6, ($ArCH_3$), 24.3 (CH_2CH_2CH), 33.2, (CH_2CH_2CH), 50.5 ($COOCH_3$), 52.6 (CH_2CH_2CH), 61.6 (OCH_2CH_3), 127.0, 128.8, 129.5, 129.6, 130.7, 137.4, 141.6, 142.9 (ArC), 144.9, 146.8 (quarternary ArC) 165.9, 157.3 (*C*NOTs), 168.7, 169.3 (2 × *C*OO); m/z (ESI^+) 793 ($[2M+Na]^+$, 100%), 444 ($[M+CH_3CN+NH_4]^+$, 25%), 408 ($[M+Na]^+$, 100%), HRMS (ESI^+) $C_{17}H_{23}NNaO_6S^+$ ($[M+Na]^+$) requires 408.1087; found 408.1086.

(±)2-Ethyl 2-methyl 5-methyl-3,4-dihydro-2H-pyrrole-2,2-dicarboxylate, 7b



Following general procedure **F**, to tosyl oxime **6b** (210 mg, 0.54 mmol) in dry THF (10 mL) was added NaH (39 mg, 1.63 mmol, 60%) and heated to reflux for 30 min, to give crude product which was purified by flash column chromatography to afford pyrroline **7b** (76 mg, 65%) as a colourless oil; R_f = 0.14 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 2983, 1713, 1657, 1596, 1462, 1211, 1187, 995; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.28 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.15 (3H, s, $NCCH_3$), 2.46 (2H, m, C(4)*HH*), 2.68 (2H, t, *J* 7.2 Hz, C(3)*HH*), 3.78 (3H, s, $COOCH_3$), 4.20-4.30 (2H, m, OCH_2CH_3); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (OCH_2CH_3), 19.9 (CH_3C=N), 30.4 (*C*4), 39.5 (*C*3), 52.9 ($COOCH_3$), 61.8 (OCH_2CH_3), 86.6 (*C*2), 169.8 and 170.4 (2 × *C*OO), 180.9 (*C*5); m/z (ESI$^+$) 214 ([M+H]$^+$, 40%), 236 ([M+Na]$^+$, 100%), 449 ([2M+Na]$^+$, 65%), HRMS (ESI$^+$) $C_{10}H_{15}NNaO_4^+$ ([M+Na]$^+$) requires 236.0893; found 236.0899.

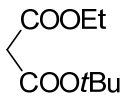
(±)2-Ethyl 2-methyl 5-methylpyrrolidine-2,2-dicarboxylate, 9b



Following general procedure **H**, to a solution of pyrroline **7b** (52 mg, 0.24 mmol) in MeOH (3 mL) was added $NaBH_3CN$ (21 mg, 0.33 mmol) and 2 M HCl in MeOH at rt, to give crude product which was purified by flash column chromatography to afford pyrrolidine **9b** (48 mg, 91%) as a colourless oil; R_f = 0.57 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3255, 2955, 1729, 1438, 1369, 1222, 1151, 1095, 937; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.16 (3H, d, *J* 6.1Hz, CH_3CH), 1.25 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.38 (1H, m, C(4)*H*H), 1.91 (1H, m, C(4)H*H*), 2.26 (1H, m, C(3)*H*H), 2.47 (1H, C(3)H*H*), 2.78 (1H, bs, N*H*), 3.32 (1H, m, C(5)*H*), 3.75 (3H, s, $COOCH_3$), 4.22 (2H, q, *J* 7.1 Hz, OCH_2CH_3); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 and 14.0 (OCH_2CH_3), 20.9 and 21.0 (CH_3CH), 32.9 and 33.0 (*C*4), 33.1 and 33.3 (*C*3), 52.82 and 52.84 (*C*5), 54.8 and 54.9 ($COOCH_3$), 61.7 and 61.8

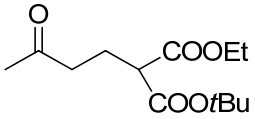
(OCH_2CH_3), 72.2 and 72.3 (*C*2), 171.6 and 171.63, 172.0 and 172.3 (2 × COO); m/z (ESI^+) 216 ($[M+H]^+$, 30%), 238 ($[M+Na]^+$, 65%), HRMS (ESI^+) $C_{10}H_{17}NNaO_4^+$ ($[M+Na]^+$) requires 238.1050; found 238.1050.

tert-Butyl ethyl malonate



To a solution of ethyl 3-chloro-3-oxopropanoate (712 mg, 4.74 mmol) in dry CH_2Cl_2 (20 mL) was added *tert*-butyl alcohol (385 mg, 5.21 mmol) and Et_3N (718 mg, 7.11 mmol) and the mixture stirred at rt, to afford *tert*-butyl ethyl malonate (809 mg, 94%) as a colourless oil; υ_{max}(film)/cm^{-1} 2982, 1731, 1369, 1333, 1144, 1034, 967, 839; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.27 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.48 (9H, s, $(CH_3)_3C$), 3.27 (2H, s, CH_2), 4.18 (2H, q, *J* 7.1 Hz, OCH_2CH_3); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH_2CH_3), 27.9 ($CH_3)_3C$), 42.9 (CH_2), 61.3 (OCH_2CH_3), 81.9 ($(CH_3)_3C$), 165.8, 167.1 (2 × *C*OO); m/z (ESI^+) 211 ($[M+Na]^+$, 35%), 399 ($[2M+Na]^+$, 100%), HRMS (ESI^+) $C_9H_{16}NaO_4^+$ ($[M+Na]^+$) requires 211.0941; found 211.0942.

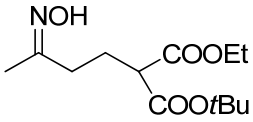
(±)1-*tert*-Butyl 3-ethyl 2-(3-oxobutyl)malonate, 3c



Following general procedure **A**, methyl vinyl ketone (340 mg, 4.87 mmol) was added to a solution of *tert*-butyl ethyl malonate (763 mg, 4.05 mmol) and anhydrous K_2CO_3 (814 mg, 6.07 mmol) in dry CH_2Cl_2 (20 mL) and the mixture stirred at rt, to give crude product which was purified by flash column chromatography to afford adduct **3c** (947 mg, 90%) as a colourless oil; R_f = 0.53 (EtOAc : petrol, 1:2); υ_{max}(film)/cm^{-1} 2983, 1734, 1256, 1368, 1334, 1145, 967, 838; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.25 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.44 (9H, s, $(CH_3)_3C$), 2.10 (2H, m, CH_2CH_2CH), 2.13 (3H, s, $COCH_3$), 2.52 (2H, t, *J* 7.3 Hz, CH_2CH_2CH), 3.26 (1H, t, *J* 7.3 Hz, CH_2CH_2CH), 4.10-4.20

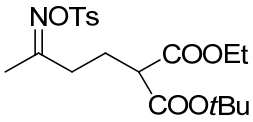
(2H, m, OC*H*$_2$CH$_3$), δ_C(100 MHz; CDCl$_3$; Me$_4$Si) 14.1 (OCH$_2$*C*H$_3$), 22.4 (CH$_2$*C*H$_2$CH), 27.8 (*C*H$_3$)$_3$C), 29.9 (CO*C*H$_3$), 40.5 (*C*H$_2$CH$_2$CH), 51.7 (CH$_2$CH$_2$*C*H), 61.2 (O*C*H$_2$CH$_3$), 81.9 (CH$_3$)$_3$*C*), 168.2, 169.4 (2 × *C*OO), 207.4 (*C*OCH$_3$); m/z (ESI$^+$) 257 ([M-H]$^-$, 100%), 281 ([M+Na]$^+$, 65%), 317 [M+CH$_3$CN+NH$_4$]$^+$, 100%), 539 ([2M+Na]$^+$, 20%), HRMS (ESI$^+$) $C_{13}H_{22}NaO_5^+$ ([M+Na]$^+$) requires 281.1359; found 281.1359.

(±)1-*tert*-Butyl 3-ethyl 2-(3-(hydroxyimino)butyl)malonate, 4c



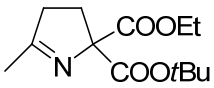
Following general procedure **C**, to a solution of adduct **3c** (906 mg, 3.51 mmol) in EtOH (20 mL) was added NH$_2$OH.HCl (485 mg, 7.02 mmol) and Et$_3$N (886 mg, 8.77 mmol) and the mixture heated to reflux for 2 hr, to give crude product which was purified by flash column chromatography to afford oxime **4c** (892 mg, 93%) as a colourless oil; R_f = 0.57 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3287, 2980, 1729, 1449, 1369, 1254, 1149, 1026, 848; (major isomer) δ_H(400 MHz; CDCl$_3$; Me$_4$Si) 1.26 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.45 (9H, s, (C*H*$_3$)$_3$C), 1.88 and 1.89 (3H, s, CNOHC*H*$_3$), 2.08 (2H, m, CH$_2$C*H*$_2$CH), 2.23 (2H, t, *J* 7.2 Hz, C*H*$_2$CH$_2$CH), 3.25 (1H, t, *J* 7.2 Hz, CH$_2$CH$_2$C*H*), 4.10-4.20 (2H, m, OC*H*$_2$CH$_3$), 7.75 (1H, bs, O*H*); δ_C(100 MHz; CDCl$_3$; Me$_4$Si) 13.6 (CNOH*C*H$_3$), 14.0 (OCH$_2$*C*H$_3$), 24.4 (CH$_2$*C*H$_2$CH), 27.8, 27.9 (*C*H$_3$)$_3$C), 33.2, 33.4 (*C*H$_2$CH$_2$CH), 51.2 (CH$_2$CH$_2$*C*H), 61.3 (O*C*H$_2$CH$_3$), 82.0 (CH$_3$)$_3$*C*), 157.3, 157.6 (*C*NOHCH$_3$), 168.2, 169.2 (2 × *C*OO); m/z (ESI$^+$) 272 ([M-H]$^-$, 85%), 296 ([M+Na]$^+$, 65%), HRMS (ESI$^+$) $C_{13}H_{23}NNaO_5^+$ ([M+Na]$^+$) requires 296.1468; found 296.1470.

(±)1-*tert*-butyl 3-Ethyl 2-(3-(tosyloxyimino)butyl)malonate, 6c



Following general procedure **E**, to a solution of oxime **4c** (651 mg, 2.38 mmol) in dry CH_2Cl_2 (25 mL) was added Et_3N (482 mg, 4.77 mmol) at 0 °C followed by *p*-toluenesulphonyl choride (542 mg, 2.85 mmol) and the mixture stirred for 2 hr, to give crude product which was purified by column chromatography to afford tosyl oxime **6c** (996 mg, 97%) as a colourless oil; R_f = 0.54 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2981, 1732, 1450, 1254, 1149, 1023, 847; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.26, 1.28 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.45 and 146 (9H, s, $(CH_3)_3C$), 1.58, 1.57 (3H, s, $CNOTsCH_3$), 2.11 (2H, m, CH_2CH_2CH), 2.14 (3H, s, $ArCH_3$), 2.53 (2H, t, *J* 7.3 Hz, CH_2CH_2CH), 3.28 (1H, t, *J* 7.3 Hz, CH_2CH_2CH), 4.19 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 7.33 (2H, d, *J* 8.2 Hz, Ar*H*), 7.86 (2H, d, *J* 8.2 Hz, ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH_2CH_3), 15.7 ($CNOHCH_3$), 22.4 ($ArCH_3$), 27.8 ($(CH_3)_3C$), 29.9 (CH_2CH_2CH), 40.6 (CH_2CH_2CH), 51.7 (CH_2CH_2CH), 61.3 (OCH_2CH_3), 82.1 ($(CH_3)_3C$), 128.8, 128.8, 129.5, 129.6 (Ar*C*), 132.8, 144.8 (quaternary *C*), 166.2 ($CNOTsCH_3$) and 168.2, 169.9 (2 × *C*OO); m/z (ESI$^+$) 450 ([M+Na]$^+$, 100%), 877 ([2M+Na]$^+$, 100%), HRMS (ESI$^+$) $C_{20}H_{29}NNaO_7S^+$ ([M+Na]$^+$) requires 450.1557; found 450.1559.

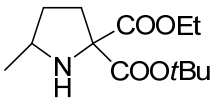
(±)2-*tert*-Butyl 2-ethyl 5-methyl-3,4-dihydro-2H-pyrrole-2,2-dicarboxylate, 7c



Following general procedure **F**, to tosyl oxime **6c** (176 mg, 0.41 mmol) in dry THF (10 mL) was added NaH (32 mg, 1.23 mol, 60%) and heated to reflux for 30 min, to give crude product which was purified by flash column chromatography to afford pyrroline **7c** (73 mg, 69%) as a colourless oil; R_f = 0.16 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2979, 1730, 1367, 1278, 1154, 1034; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.29 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.46 (9H, s, $(CH_3)_3C$), 2.13 (3H, s, $NCCH_3$), 2.35 (1H, m, C(4)H*H*), 2.44 (1H, m, C(4)*H*H), 2.47 (1H, m, C(3)H*H*), 2.65 (1H, m, C(3)*H*H), 4.20 and 4.29 (2H, q, *J* 7.1 Hz, OCH_2CH_3); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH_2CH_3), 19.7, 19.8 ($NCCH_3$), 27.9 ($(CH_3)_3C$), 30.3 (*C*4), 39.4 (*C*3), 61.6 (OCH_2CH_3), 82.4

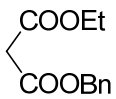
($CH_3)_3C$), 87.2 (*C*2) 168.9, 170.1 (2 × *C*OO), 180.6 (*C*5); m/z (ESI^+) 256 ($[M+H]^+$, 40%), 278 ($[M+Na]^+$, 100%), 533 ($[2M+Na]^+$, 80%), HRMS (ESI^+) $C_{13}H_{21}NNaO_4^+$ ($[M+Na]^+$) requires 278.1363; found 278.1360.

(±)2-*tert*-Butyl 2-ethyl 5-methylpyrrolidine-2,2-dicarboxylate, 9c



Following general procedure **H**, to a solution of pyrroline **7c** (53 mg, 0.21 mmol) in MeOH (3 mL) was added $NaBH_3CN$ (20 mg, 0.31 mmol) and 2 M HCl in MeOH (2 mL), to give the crude product which was purified by flash column chromatography to afford pyrrolidine **9c** (49 mg, 92%) as a colourless oil; R_f = 0.77 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 2976, 1732, 1368, 1282, 1144; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.14 (3H, d, *J* 6.2 Hz, C*H*$_3$CH), 1.24 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.43 (9H, s, ($CH_3)_3$C), 1.91 (2H, m, C(4)*HH*), 2.32 (2H, m, C(3)*HH*), 3.30 (1H, m, C(5)*H*), 4.19 (2H, q, *J* 7.1 Hz, OCH_2CH_3); δ_C (100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH_2CH_3), 20.9 (CH_3CH), 28.0 ($CH_3)_3$C), 32.9 (*C*4), 33.5 (*C*3), 54.9 (*C*5), 61.5 (OCH_2CH_3), 72.9 (*C*2), 82.0 ($(CH_3)_3C$), 171.0, 172.3 (2 × *C*OO); m/z (ESI^+) 258 ($[M+H]^+$, 85%), 537 ($[2M+Na]^+$, 100%), HRMS (ESI^+) $C_{13}H_{24}NO_4^+$ ($[M+H]^+$) requires 258.1700; found 258.1707.

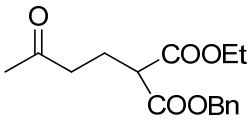
Benzyl ethyl malonate



To a solution of ethyl 3-chloro-3-oxopropanoate (524 mg, 3.49 mmol) in dry CH_2Cl_2 (20 mL) was treated with benzyl alcohol (414 mg, 3.84 mmol) and Et_3N (529 mg, 5.24 mmol) and the mixture stirred at rt, to afford benzyl ethyl malonate (721 mg, 93%) as a colourless oil; υ_{max}(film)/cm^{-1} 3082, 2970, 1733, 1455, 1370, 1272, 1149, 1032, 738; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.26 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.43 (2H, s, CH_2), 4.20 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 5.19 (2H, s, $COOCH_2$), 7.35-7.38

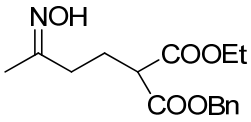
(5H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (OCH_2CH_3), 41.6 (CH_2), 61.6 (OCH_2CH_3), 67.2 ($COOCH_2$), 126-9-129.7 (Ar*C*), 135.3 (quaternary Ar*C*), 166.4, 166.5 (2 × *C*OO); m/z (ESI^+), 221 ($[M-H]^-$, 75%), 245 ($[M+Na]^+$, 20%), HRMS (ESI^+) $C_{12}H_{14}NaO_4^+$ ($[M+Na]^+$) requires 245.0784; found 245.0780.

(±)1-Benzyl 3-ethyl 2-(3-oxobutyl)malonate, 3d



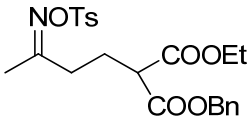
Following general procedure **A**, methyl vinyl ketone (185 mg, 2.65 mmol) was added to a solution of benzyl ethyl malonate (491 mg, 2.21 mmol) and anhydrous K_2CO_3 (444 mg, 3.31 mmol) in dry CH_2Cl_2 (10 mL) and the mixture stirred at rt, to give crude product which was purified by flash column chromatography to afford adduct **3d** (573 mg, 89%) as a colourless oil; R_f = 0.51 (EtOAc : petrol, 1:2); υ_{max}(film)/cm^{-1} 3079, 2981, 1729, 1497, 1454, 1370, 1163, 1096, 740; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.15-1.25 (3H, m, OCH_2CH_3), 2.09 (3H, s, $COCH_3$), 2.18 (1H, m, CH_2CHHCH), 2.38 (1H, m, CH_2CHHCH), 2.50 (2H, t, *J* 7.3 Hz, CH_2CH_2CH), 3.45 (1H, t, *J* 7.3 Hz, CH_2CH_2CH), 4.10-4.20 (2H, m, OCH_2CH_3), 5.19 (2H, s, $COOCH_2$), 7.35-7.37 (5H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (OCH_2CH_3), 22.4 (CH_2CH_2CH), 29.9 ($COCH_3$), 40.3 (CH_2CH_2CH), 50.6 (CH_2CH_2CH), 61.5 (OCH_2CH_3), 67.1 ($COOCH_2$), 126.9, 127.6, 128.2, 128.5, 129.7 (Ar*C*), 135.4 (quaternary Ar*C*), 168.9, 169.0 (2 × *C*OO), 207.1 (*C*O); m/z (ESI^+) 291 ($[M-H]^-$, 100%), 351 ($[M+CH_3CN+NH_4]^+$, 65%), HRMS (ESI^+) $C_{16}H_{20}NaO_5^+$ ($[M+Na]^+$) requires 315.1203; found 315.1197.

(±)1-Benzyl 3-ethyl 2-(3-(hydroxyimino)butyl)malonate, 4d



Following general procedure **C**, to a solution of adduct **3d** (551 mg, 1.88 mmol) in EtOH (25 mL) was added $NH_2OH.HCl$ (260 mg, 3.77 mmol) and Et_3N (475 mg, 4.70 mmol) and the mixture heated to reflux for 2 hr, to give crude product which was purified by flash column chromatography to afford oxime **4d** (520 mg, 90%) as a colourless oil; R_f = 0.71 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3263, 3077, 2981, 1731, 1498, 1454, 1370, 1152, 1025, 751; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.19 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.86 (3H, s, $CNOHCH_3$), 2.13 (2H, m, CH_2CH_2CH), 2.23 (2H, t, *J* 7.3 Hz, CH_2CH_2CH), 3.43 (1H, t, *J* 7.3 Hz, CH_2CH_2CH), 4.15 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 5.14, 5.20 (2H, d, *J* 12.3 Hz, $COOCH_2$), 7.35-7.37 (5H, m, Ar*H*), 8.68 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.5 (OCH_2CH_3), 13.9, 14.0 ($CNOHCH_3$), 25.2 (CH_2CH_2CH), 33.3, 33.4 (CH_2CH_2CH), 51.1 (CH_2CH_2CH), 61.5, 61.6 (OCH_2CH_3), 67.1 ($COOCH_2$), 128.2, 128.3, 128.5, 128.6, (Ar*C*), 135.4 (quaternary Ar*C*), 156.9 (*C*NOH), 168.9, 169.0 (2 × *C*OO); m/z (ESI$^+$) 306 ([M-H]$^-$, 100%), 330 ([M+Na]$^+$, 10%), 366 [M+CH_3CN+NH_4]$^+$, 15%), HRMS (ESI$^+$) $C_{16}H_{21}NNaO_5^+$ ([M+Na]$^+$) requires 330.1312; found 330.1305

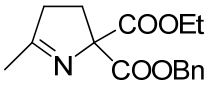
(±)1-Benzyl 3-ethyl 2-(3-(tosyloxyimino)butyl)malonate, 6d



Following general procedure **E**, to a solution of oxime **4d** (561 mg, 1.82 mmol) in dry CH_2Cl_2 (20 mL) was added Et_3N (367 mg, 3.64 mmol) at 0 °C followed by *p*-toluenesulphonyl choride (415 mg, 2.18 mmol) and the mixture stirred at rt for 2 hr, to give crude product which was purified by flash column chromatography to afford tosyl oxime **6d** (721 mg, 86%) as a colourless oil; R_f = 0.56 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3075, 2983, 1731, 1157, 1033, 1009, 817, 751; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.19 and 1.25 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.89 (3H, s, $CNOTsCH_3$), 2.08 (2H, m, CH_2CH_2CH), 2.27 (2H, t, *J* 7.3 Hz, CH_2CH_2CH), 2.41 and 2.43 (3H, s, $ArCH_3$), 3.35 (1H, t, *J* 7.3 Hz, CH_2CH_2CH), 4.16 (2H, m, OCH_2CH_3), 5.14 and 5.19 (2H, 2 x d, *J* 12.2 Hz, $COOCH_2$), 7.28 (2H, d, *J* 8.6 Hz, SO_2ArH), 7.35-7.37 (5H, m, Ar*H*), 7.83 (2H, d, *J* 8.6 Hz, SO_2ArH); δ_C(100 MHz;

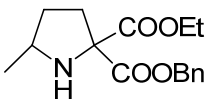
$CDCl_3$; Me_4Si) 13.9 and 14.0 (OCH_2CH_3), 15.8 and 19.7 ($CNOTsCH_3$), 21.6 and 21.7 ($ArCH_3$), 24.3 and 24.4 (CH_2CH_2CH), 33.1 an 33,3 (CH_2CH_2CH), 50.6 and 50.7 (CH_2CH_2CH), 61.6 and 61.7 (OCH_2CH_3), 67.2 and 67.3 ($COOCH_2$), 128.2, 129.3, 128.5, 128.6, 128.8, 129.5, 129.6 (ArC), 132.7, 135.3, 144.9 (quaternary Ar*C*), 165.9 and 166.6 (*C*NOTs), 168.5 and 168.6, 168.7 and 168.8 (2 × *C*OO); m/z (ESI^+) 484 ($[M+Na]^+$, 100%), 945 ($[2M+Na]^+$, 85%), HRMS (ESI^+) $C_{23}H_{27}NNaO_7S^+$ ($[M+Na]^+$) requires 484.1400; found 484.1402.

(±)2-Benzyl 2-ethyl 5-methyl-3,4-dihydro-2H-pyrrole-2,2-dicarboxylate, 7d



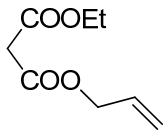
Following general procedure **F**, to tosyl oxime **6d** (206 mg, 0.44 mmol) in dry THF (10 mL) was added NaH (32 mg, 1.34 mol, 60%) and the mixture heated to reflux for 30 min, to give crude product which was purified by flash column chromatography to afford pyrroline **7d** (82 mg, 63%) as a colourless oil; R_f = 0.20 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3161, 2929, 1732, 1618, 1445, 1325, 1229, 1092, 977, 840, 728; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.14 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.14 (3H, s, $NCCH_3$), 2.45 (2H, m, C(4)*HH*), 2.67 (2H, t, *J* 7.6 Hz, C(3)*HH*), 4.10-4.30 (2H, m, OCH_2CH_3), 5.18 and 5.26 (2H, 2 x d, *J* 12.2 Hz, $COOCH_2$), 7.31 (5H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (OCH_2CH_3), 19.9 ($NCCH_3$), 30.5 (*C*4), 39.6 (*C*3), 62.0, (OCH_2CH_3), 67.4 ($COOCH_2$), 86.7 (*C*2), 128.1, 128.2, 128.3, 128.5, (Ar*C*), 135.4 (quaternary Ar*C*), 169.6, 169.7 (2 × *C*OO), 181.2 (*C*5); m/z (ESI^+) 290 ($[M+H]^+$, 63%), 312 ($[M+Na]^+$, 90%), 601 ($[2M+Na]^+$, 100%), HRMS (ESI^+) $C_{16}H_{19}NNaO_4^+$ ($[M+Na]^+$) requires 312.1206; found 312.1206.

(±)2-Benzyl 2-ethyl 5-methylpyrrolidine-2,2-dicarboxylate, 9d



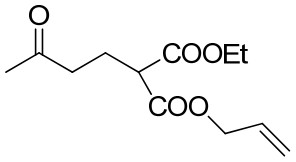
Following general procedure **H**, to a solution of pyrroline **7d** (63 mg, 0.22 mmol) in MeOH (3 mL) was added $NaBH_3CN$ (21 mg, 0.33 mmol) and 2 M HCl in MeOH (2 mL), to give crude product which was purified by flash column chromatography to afford pyrrolidine **9d** (56 mg, 88%) as a colourless oil; R_f = 0.77 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3466, 3092, 2981, 1728, 1664, 1587, 1369, 1216, 1147, 946, 825, 739; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.10 – 1.20 (6H, m, C*H*$_3$CH and OCH$_2$C*H*$_3$), 1.38 (1H, m, C(4)H*H*), 1.90 (1H, m, C(4)*H*H), 2.25 (1H, m, C(3)H*H*), 2.48 (1H, m, C(3)*H*H), 3.32 (1H, m, C(5)*H*), 4.10-4.30 (2H, m, OC*H*$_2$CH$_3$), 5.10 - 5.30 (2H, m, COOC*H*$_2$), 7.31-7.33 (5H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.8 and 14.0 (OCH$_2$*C*H$_3$), 21.0 and 21.04 (CH*C*H$_3$), 32.9 and 33.0 (*C*4), 33.4 (*C*3), 54.9 (*C*5), 61.7 and 61.9, (O*C*H$_2$CH$_3$), 67.2 (COO*C*H$_2$), 72.3 (*C*2), 128.0. 128.1, 128.3, 128.5 (Ar*C*), 135.5 (quaternary Ar*C*), 171.4 and 172.1 (2 × *C*OO); m/z (ESI$^+$) 292 ([M+H]$^+$, 100%), 314 ([M+Na]$^+$, 55%), 605 ([2M+Na]$^+$, 15%), HRMS (ESI$^+$) $C_{16}H_{22}NO_4^+$ ([M+H]$^+$) requires 292.1543; found 292.1543.

Allyl ethyl malonate



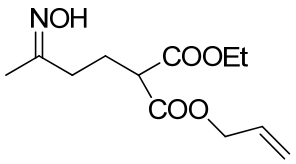
To a solution of ethyl 3-chloro-3-oxopropanoate (1.63 g, 10.9 mmol) in dry CH_2Cl_2 (30 mL) was added allyl alcohol (693 mg, 12.0 mmol) and Et_3N (1.65 g, 16.3 mmol) and the mixture stirred at rt to afford allyl ethyl malonate (1.79 g, 96%) as a colourless oil; υ_{max}(film)/cm^{-1} 2981, 1741, 1690, 1649, 1566, 1440, 1366, 1250, 1080, 799; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.24 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 3.36 (2H, s, C*H*$_2$), 4.17 (2H, q, *J* 7.1 Hz, OC*H*$_2$CH$_3$), 4.61 (2H, d, *J* 5.1 Hz, OC*H*$_2$), 5.26 (2H, dd, *J* 17.2, 10.4 Hz, CH=C*H*$_2$), 5.87 (1H, m, C*H*=CH$_2$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.7 (OCH$_2$*C*H$_3$), 41.3 (*C*H$_2$), 61.3 (O*C*H$_2$CH$_3$), 65.7 (OCH$_2$), 118.4 (CH=*C*H$_2$), 131.2 (*C*H=CH$_2$), 165.9, 166.1 (2 × *C*OO); m/z (ESI$^+$), 195 ([M+Na]$^+$, 100%), 171 ([M-H]$^-$, 50%), HRMS (ESI$^+$) $C_8H_{12}NaO_4^+$ ([M+Na]$^+$]) requires 195.0628; found 195.0628.

(±)1-Allyl 3-ethyl 2-(3-oxobutyl)malonate, 3e



Following general procedure **A**, methyl vinyl ketone (708 mg, 10.1 mmol) was added to solution of allyl ethyl malonate (1.45 g, 8.43 mmol) and anhydrous K_2CO_3 (1.69 g, 12.6 mmol) in dry CH_2Cl_2 (20 mL) and the mixture stirred at rt, to give crude product which was purified by flash column chromatography to afford adduct **3e** (1.72 g, 84%) as a colourless oil; R_f = 0.41 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 2984, 1731, 1649, 1446, 1370, 1154, 1097, 1026, 939, 859; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.16 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.03 (3H, s, CH_3CO), 2.06 (2H, m, CH_2CH_2CH), 2.45 (2H, t, *J* 7.2 Hz, CH_2CH_2CH), 3.33 (1H, t, *J* 7.2 Hz, CH_2CH_2CH), 4.09 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.52 (2H, d, *J* 5.5 Hz, OCH_2), 5.18 (2H, dd, *J* 17.2, 10.4 Hz, $CH=CH_2$), 5.79 (1H, m, $CH=CH_2$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH_2CH_3), 22.5 (CH_2CH_2CH), 29.9 (CH_3CO), 40.4 (CH_2CH_2CH), 50.6 (CH_2CH_2CH), 61.5 (OCH_2CH_3), 65.8 (OCH_2), 118.6 ($CH=CH_2$), 131.6 ($CH=CH_2$), 168.8, 168.9 (2 × *C*OO), 207.1 (*C*O); m/z (ESI$^+$), 265 ([M+Na]$^+$, 100%), 241 ([M-H]$^-$, 50%), HRMS (ESI$^+$) $C_{12}H_{18}NaO_5^+$ ([M+Na]$^+$]) requires 265.1046; found 265.1052.

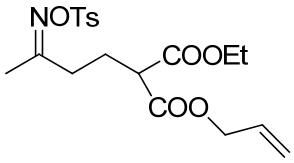
(±)1-Allyl 3-ethyl 2-(3-(hydroxyimino)butyl)malonate, 4e



Following general procedure **C**, to a solution of adduct **3e** (1.46 g, 6.03 mmol) in EtOH (20 mL) was added $NH_2OH.HCl$ (832 mg, 12.06 mmol) and Et_3N (1.52 g, 15.1 mmol) and the mixture heated to reflux for 2 hr, to give crude product which was purified by flash column chromatography to afford oxime **4e** (1.43 mg, 92%) as a colourless oil; R_f = 0.52, 0.37 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3261, 2986, 1732, 1447, 1370, 1152, 1096, 1024 and 936; (major isomer) δ_H(400

MHz; $CDCl_3$; Me_4Si) 1.24 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.86 (3H, s, CH_3CNOH), 2.11 (2H, m, CH_2CH_2CH), 2.23 (2H, m, CH_2CH_2CH), 3.39 (1H, t, *J* 7.1Hz, CH_2CH_2CH), 4.17 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.61 (2H, d, *J* 5.6Hz, OCH_2), 5.26 (2H, dd, J 17.2, 10.4 Hz, $CH=CH_2$) 5.87 (1H, m, $CH=CH_2$) and 8.85 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.3 (CH_3CNOH), 13.7 (OCH_2CH_3), 24.9 (CH_2CH_2CH), 33.1 (CH_2CH_2CH), 50.8 (CH_2CH_2CH), 61.3 (OCH_2CH_3), 65.7 (OCH_2), 118.3 ($CH=CH_2$), 131.3 ($CH=CH_2$), 156.6 (*C*=NOH), 168.5, 168.7 (2 × *C*OO); m/z (ESI^+), 537 ($[2M+Na]^+$, 55%), 280 ($[M+Na]^+$, 80%), 256 ($[M-H]^-$, 100%), HRMS (ESI^+) $C_{12}H_{19}NNaO_5^+$ ($[M+Na]^+$]) requires 280.1155; found 280.1156.

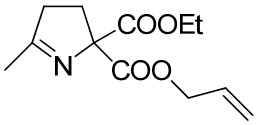
(±)1-Allyl 3-ethyl 2-(3-(tosyloxyimino)butyl)malonate, 6e



Following general procedure **E**, to a solution of oxime **4e** (1.29 g, 5.05 mmol) in dry CH_2Cl_2 (30 mL) was added Et_3N (764 mg, 7.57 mmol) at 0 °C followed by *p*-toluenesulphonyl choride (1.06 g, 5.55 mmol) and the mixture stirred for 2 hr, to give crude product which was purified by flash column chromatography to afford tosyl oxime **6e** (1.62 g, 78%) as a colourless oil; R_f = 0.61 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 2983, 1732, 1371, 1191, 1179, 1096, 1021, 789; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.26 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.91 (3H, s, CH_3CNO), 2.04 (2H, m, CH_2CH_2CH), 2.43 (3H, s, $ArCH_3$), 2.48 (2H, t, *J* 7.3Hz, CH_2CH_2CH), 3.32 (1H, t, *J* 7.3Hz, CH_2CH_2CH), 4.20 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.63 (2H, d, *J* 5.7Hz, OCH_2), 5.29 (2H, dd, *J* 17.9, 10.8 Hz, $CH=CH_2$) 5.89 (1H, m, $CH=CH_2$), 7.32 (2H, d, *J* 8.0Hz, ArH), 7.83 (2H, d, *J* 8.0 Hz, ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.7 (OCH_2CH_3), 19.4 (CH_3CNO), 21.4 ($ArCH_3$), 24.2 (CH_2CH_2CH), 27.7 (CH_2CH_2CH), 50.8 (CH_2CH_2CH), 61.6 (OCH_2CH_3), 65.9 (OCH_2), 118.6 ($CH=CH_2$), 128.5, 128.6, 129.3 (Ar*C*), 131.1 ($CH=CH_2$), 132.4 144.8 (quaternary Ar*C*), 166.3

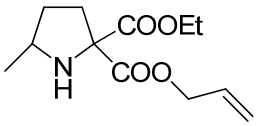
(*C*=NO), 168.0, 168.2 (2 × *C*OO); m/z (ESI$^+$), 845 ([2M+Na]$^+$, 100%), 434 ([M+Na]$^+$, 85%), 412 ([M+H]$^+$, 20%), HRMS (ESI$^+$) $C_{19}H_{25}NNaO_7S^+$ ([M+Na]$^+$) requires 434.1244; found 434.1243.

(±)2-Allyl 2-ethyl 5-methyl-3,4-dihydro-2H-pyrrole-2,2-dicarboxylate, 7e



Following general procedure **F**, to tosyl oxime **6e** (238 mg, 0.57 mmol) in dry THF (10 mL) was added NaH (41 mg, 1.73 mol, 60%) and the mixture heated to reflux for 30 min, to give crude product which was purified by flash column chromatography to afford pyrroline **7e** (78 mg, 56%) as a colourless oil; R_f = 0.39 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 2983, 1735, 1268, 1158, 1089; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.27 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.14 (3H, s, CH_3C=N), 2.40-2.50 (2H, m, C(4)*HH*), 2.60-2.70 (2H, m, C(3)*HH*), 4.10-4.30 (2H, m, OCH_2CH_3), 4.60-4.70 (2H, m, OCH_2), 5.28 (1H, d, *J* 5.0 Hz, CH=C*H*), 5.40 (1H, d, *J* 16.5 Hz, CH=C*H*), 5.85-5.95 (1H, m, C*H*=CH_2); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.6 (OCH_2CH_3), 19.5 (CH_3C=N), 30.2 (*C*4), 39.2 (*C*3), 61.6 (OCH_2CH_3), 65.9 (OCH_2), 86.3 (*C*2), 118.3 (CH=CH_2), 131.1 (*C*H=CH_2), 169.2, 169.4 (2 × *C*OO), 180.8 (*C*5); m/z (ESI$^+$) 501 ([2M+Na]$^+$, 100%), 262 ([M+Na]$^+$, 100%), 240 ([M+H]$^+$, 70%), HRMS (ESI$^+$) $C_{12}H_{17}NNaO_4^+$ ([M+Na]$^+$]) requires 262.1050; found 262.1051.

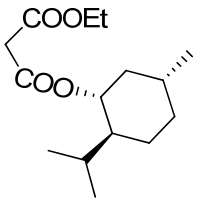
(±)2-Allyl 2-ethyl 5-methylpyrrolidine-2,2-dicarboxylate, 9e



Following general procedure **H**, to a solution of pyrroline **7e** (52 mg, 0.22 mmol) in MeOH (3 mL) was added $NaBH_3CN$ (20 mg, 0.33 mmol) and 2 M HCl in MeOH (2 mL), to give crude product which was purified by flash column chromatography to afford pyrrolidine **9e** (48 mg, 92%) as a colourless oil; R_f = 0.54 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 3352, 2965, 1732, 1649, 1453, 1368,

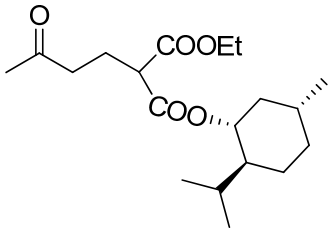
1273, 1190, 1022, 936; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.11 (3H, d, *J* 6.2 Hz, C*H*$_3$CHNH), 1.19 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.35 (1H, m, C(4)H*H*), 186 (1H, m, C(4)*H*H), 2.21 (1H, m, C(3)H*H*), 2.43 (1H, m, C(3)*H*H), 2.83 (1H, bs, N*H*), 3.28 (1H, m, C(5)*H*), 4.15 (2H, m, OC*H*$_2$CH$_3$), 4.59 (2H, m, OC*H*$_2$), 5.17 (1H, d, *J* 10.5 Hz, CH=CH*H*), 5.25 (1H, d, *J* 15.3 Hz, CH=C*H*H), 5.83 (1H, m, C*H*=CH$_2$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.7 (OCH$_2$*C*H$_3$), 20.7 (*C*H$_3$CH), 33.0 (*C*3), 33.1 (*C*4), 54.9 (*C*5), 61.6 (O*C*H$_2$CH$_3$), 66.0 (O*C*H$_2$), 72.3 (*C*2), 118.4 (CH=*C*H$_2$), 131.3 (*C*H=CH$_2$), 171.2 and 171.4, 171.7 and 171.8 (2 × *C*OO); m/z (ESI$^+$) 264 ([M+Na]$^+$, 100%), 242 ([M+H]$^+$, 75%), HRMS (ESI$^+$) $C_{12}H_{20}NO_4^+$ ([M+H]$^+$]) requires 242.1387; found 242.1387.

Ethyl (1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl malonate



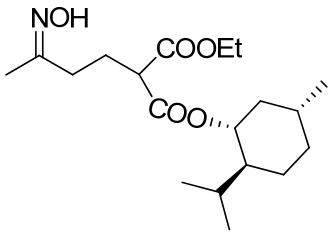
To a solution of ethyl 3-chloro-3-oxopropanoate (100 mg, 1.33 mmol) in CH_2Cl_2 (10 mL) was added (1*R*, 2*S*, 5*R*)-menthol (228 mg, 1.46 mmol) and Et_3N (202 mg, 2.00 mmol) and the mixture stirred at rt, to afford ethyl menthyl malonate (340 mg, 94%) as a colourless oil; υ_{max}(film)/cm^{-1} 2956, 1733, 1459, 1369, 1258, 1147, 1036, 990; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.74 (3H, d, *J* 6.9 Hz, C*H*$_3$CH), 0.84 (1H, m, CH$_3$CHC*H*H), 0.90 (6H, d, J 6.8 Hz, C*H*$_3$CHC*H*$_3$), 0.94 (1H, m, OCHC*H*H), 0.99 (1H, m, CHC*H*H), 1.28 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.39 (1H, m, OCHC*H*), 1.49 (1H, m, CH$_3$C*H*), 1.66 (1H, m, CH$_3$CHCH*H*), 1.70 (1H, m, CHCH*H*), 1.89 (1H, m, CH$_3$C*H*CH$_3$), 2.03 (1H, m, OCHCH*H*), 3.35 (2H, s, C*H*$_2$), 4.20 (2H, q, *J* 7.1 Hz, OC*H*$_2$CH$_3$), 4.73 (1H, m, OC*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH$_2$*C*H$_3$), 16.1 (*C*H$_3$CH), 20.7, 21.9 (*C*H$_3$CH*C*H$_3$), 23.3 (CH*C*H$_2$), 26.0 (CH$_3$*C*HCH$_3$), 31.4 (CH$_3$*C*H), 34.1 (CH$_3$CH*C*H$_2$), 40.6 (OCH*C*H$_2$), 42.1 (*C*H$_2$), 46.9 (OCH*C*H), 61.5 (O*C*H$_2$CH$_3$), 75.6 (O*C*H), 166.1, 166.7 (2 × *C*OO); m/z (ESI$^+$), 329 ([M+CH$_3$CN+NH$_4$]$^+$, 100%), 269 ([M-H]$^-$, 25%), HRMS (ESI$^+$) $C_{15}H_{26}NaO_4^+$ ([M+Na]$^+$]) requires 293.1723; found 293.1719.

(±)1-Ethyl 3-(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 2-(3-oxobutyl)malonate, 3f



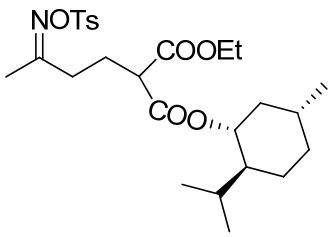
Following general procedure **A**, methyl vinyl ketone **(**124 mg, 1.77 mmol) was added to solution of ethyl menthyl malonate (319 mg, 1.18 mmol) and anhydrous K_2CO_3 (237 mg, 1.77 mmol) in dry CH_2Cl_2 (20 mL) and the mixture stirred at rt, to give crude product which was purified by flash column chromatography to afford adduct **3f** (396 mg, 98%) as a colourless oil; R_f = 0.43 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2956, 2871, 1728, 1454, 1369, 1159, 1097, 1036, 985, 913; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.70 (3H, d, *J* 6.9 Hz, C*H*$_3$CH), 0.84 (6H, d, *J* 6.8 Hz, C*H*$_3$CHC*H*$_3$), 0.92 (1H, m, CHC*H*H), 0.99 (1H, m, OCHC*H*H), 1.20 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.33 (1H, m, OCHC*H*), 1.43 (1H, m, CH$_3$C*H*), 1.60 (1H, m, CHCH*H*), 1.64 (2H, m, CH$_3$CHC*H*$_2$), 1.81 (1H, m, CH$_3$C*H*CH$_3$), 1.94 (2H, m, OCHCH$_2$), 2.08 (3H, s, COC*H*$_3$), 2.11 (2H, m, CHC*H*$_2$CH$_2$), 2.48 (2H, t, *J* 7.0 Hz, CHCH$_2$C*H*$_2$), 3.31 (1H, dd, *J* 7.4, 7.0, C*H*CH$_2$CH$_2$), 4.10-4.20 (2H, m, OC*H*$_2$CH$_3$), 4.65 (1H, m, OC*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.7 (OCH$_2$*C*H$_3$), 15.7 (*C*H$_3$CH), 20.5 (*C*H$_3$CH*C*H$_3$), 22.1 (CH*C*H$_2$), 22.8 (CH*C*H$_2$CH$_2$), 25.7 (CH$_3$*C*HCH$_3$), 29.6 (CH$_3$*C*H), 31.1 (CO*C*H$_3$), 33.8 (CH$_3$CH*C*H$_2$), 40.1 (OCH*C*H$_2$), 40.4 (CHCH$_2$*C*H$_2$), 46.7 (OCH*C*H), 50.9 (*C*HCH$_2$CH$_2$), 61.4 (O*C*H$_2$CH$_3$), 75.2 (O*C*H), 168.6 and 169.0 (2 × *C*OO), 207.1 (*C*O); m/z (ESI$^+$), 399 ([M+CH$_3$CN+NH$_4$]$^+$, 100%), 339 ([M-H]$^-$, 100%), HRMS (ESI$^+$) $C_{19}H_{32}NaO_5^+$ ([M+Na]$^+$]) requires 363.2166; found 363.2151.

(±)1-Ethyl 3-(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 2-(3-(hydroxyimino)-butyl)malonate, 4f



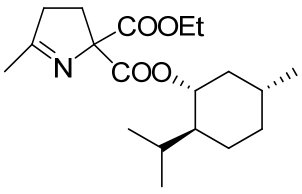
Following general procedure **C**, to a solution of adduct **3f** (382 mg, 1.12 mmol) in EtOH (15 mL) was added $NH_2OH.HCl$ (115 mg, 1.68 mmol) and Et_3N (226 mg, 2.24 mmol) and heated to reflux for 2 hr, to give crude product which was purified by flash column chromatography to afford oxime **4f** (347 mg, 87%) as a colourless oil; R_f = 0.49 (EtOAc : petrol, 6:4); υ_{max}(film)/cm^{-1} 3264, 2956, 2871, 1730, 1430, 1453, 1369, 1149, 1096, 983, 845; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.73 (3H, d, *J* 6.9 Hz, C*H*$_3$CH), 0.87 (6H, d, *J* 6.8 Hz, C*H*$_3$CHC*H*$_3$), 0.88 (1H, m, CHC*H*H), 0.95 (1H, m, OCHC*H*H), 1.04 (1H, m, CH$_3$CHC*H*H), 1.24 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.37 (1H, m, OCHC*H*), 1.46 (1H, m, CH$_3$C*H*), 1.63 (1H, CH$_3$CHCH*H*), 1.67 (1H, m, CHCH*H*), 1.82 (1H, m, CH$_3$C*H*CH$_3$), 1.86 (3H, s, C*H*$_3$C=N), 1.94 (1H, m, OCHCH*H*), 2.09 (2H, m, CHC*H*$_2$CH$_2$), 2.22 (2H, t, *J* 7.5 Hz, CHCH$_2$C*H*$_2$), 3.33 (1H, t, *J* 7.5 Hz, C*H*CH$_2$CH$_2$), 4.10-4.20 (2H, m, OC*H*$_2$CH$_3$), 4.70 (1H, m, OC*H*), 8.75 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.4 (OCH$_2$*C*H$_3$), 15.9 (*C*H$_3$C=N), 20.7 (*C*H$_3$CH), 21.9 (*C*H$_3$CH*C*H$_3$), 23.1 CH*C*H$_2$CH$_2$), 25.1 (CH*C*H$_2$), 25.8 (CH$_3$*C*HCH$_3$), 31.3 (CH$_3$*C*H), 33.4 (CHCH$_2$*C*H$_2$), 34.1 (CH$_3$CH*C*H$_2$), 40.4 (OCH*C*H$_2$), 46.7 (OCH*C*H), 51.4 (*C*HCH$_2$CH$_2$), 61.4 (O*C*H$_2$CH$_3$), 75.3 (O*C*H), 156.8 (CH$_3$*C*=N), 168.5, 168.9 (2 × *C*OO); m/z (ESI^+), 414 ($[M+CH_3CN+NH_4]^+$, 100%), 354 ($[M-H]^-$, 100%), HRMS (ESI^+) $C_{19}H_{33}NNaO_5^+$ ($[M+Na]^+$]) requires 378.2251; found 378.2249.

(±)1-Ethyl 3-(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 2-(3-(tosyloxyimino)-butyl)malonate, 6f



Following general procedure **E**, to a solution of oxime **4f** (308 mg, 5.09 mmol) in dry CH_2Cl_2 (20 mL) was added Et_3N (130 mg, 1.29 mmol) at 0 °C followed by *p*-toluenesulphonyl choride (197 mg, 1.04 mmol) and the mixture stirred at rt for 2 hr, to give crude product which was purified by flash column chromatography to afford tosyl oxime **6f** (373 mg, 84%) as a colourless oil; R_f = 0.63 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2956, 1730, 1179, 1453, 1009, 816, 682; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.72 (3H, d, *J* 6.9 Hz, C*H*$_3$CH), 0.88 (6H, d, *J* 6.8 Hz, C*H*$_3$CHC*H*$_3$), 0.95 (1H, m, CHC*H*H), 1.00 (1H, m, CH$_3$CHC*H*H), 1.10 (1H, m, OCHC*H*H), 1.24 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.36 (1H, m, OCHC*H*), 1.46 (1H, m, CH$_3$C*H*), 1.65 (1H, CH$_3$CHCH*H*), 1.68 (1H, m, CHCH*H*), 1.82 (1H, m, CH$_3$C*H*CH$_3$), 1.92 (1H, m, OCHCH*H*), 1.94 (3H, s, C*H*$_3$C=N), 2.04 (2H, m, CHC*H*$_2$CH$_2$), 2.26 (2H, t, *J* 7.3 Hz, CHCH$_2$C*H*$_2$), 2.42 (3H, s, ArC*H*$_3$), 3.26 (1H, t, *J* 7.5 Hz, C*H*CH$_2$CH$_2$), 4.10-4.30 (2H, m, OC*H*$_2$CH$_3$), 4.69 (1H, m, OC*H*), 7.31 (2H, d, *J* 8.2 Hz, Ar*H*), 7.83 (2H, d, *J* 8.2 Hz, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (OCH$_2$*C*H$_3$), 15.8 (*C*H$_3$C=N), 20.6 (*C*H$_3$CH), 21.6 (*C*H$_3$CH*C*H$_3$), 21.9 (Ar*C*H$_3$), 23.1 CH*C*H$_2$CH$_2$), 24.3 (CH*C*H$_2$), 25.8 (CH$_3$*C*HCH$_3$), 31.2 (CH$_3$*C*H), 33.1 (CHCH$_2$*C*H$_2$), 34.0 (CH$_3$CH*C*H$_2$), 40.6 (OCH*C*H$_2$), 46.8 (OCH*C*H), 50.9 (*C*HCH$_2$CH$_2$), 61.5 (O*C*H$_2$CH$_3$), 75.6 (O*C*H), 128.7, 128.8, 129.4, 129.5 (Ar*C*), 132.6, 144.7 (quaternary ArC), 165.9 (CH$_3$*C*=N), 168.3 and 168.7 (2 × *C*OO); m/z (ESI$^+$), 532 ([M+Na]$^+$, 60%), 509 ([M-H]$^-$, 35%), HRMS (ESI$^+$) $C_{26}H_{39}NNaO_7^+$ ([M+Na]$^+$]) requires 532.2339; found 532.2338.

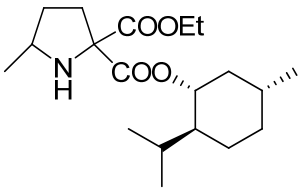
(±)2-Ethyl 2-(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 5-methyl-3,4-dihydro-2H-pyrrole-2,2-dicarboxylate, 7f



Following general procedure **F**, to tosyl oxime **6f** (146 mg, 0.23 mmol) in dry THF (7 mL) was added NaH (21 mg, 0.86 mol, 60%) and the mixture heated to reflux for 30 min, to give crude product which was purified by flash column chromatography to afford pyrroline **7f** (51 mg, 70%) as

a colourless oil; R_f = 0.43 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2956, 2870, 1732, 1645, 1455, 1379, 1269, 1161, 1088, 956, 845, 731; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.73 (3H, d, *J* 6.9 Hz, C*H*$_3$CH), 0.86 (6H, d, *J* 7.0 Hz, C*H*$_3$CHC*H*$_3$), 0.89 (1H, m, CHC*H*H), 0.98 (1H, m, CH$_3$CHC*H*H), 1.04 (1H, m, OCHC*H*H), 1.27 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.44 (1H, m, OCHC*H*), 1.46 (1H, m, C*H*$_3$CH), 1.63 (1H, m, CH$_3$CHCH*H*), 1.67 (1H, m, CHCH*H*), 1.88 (1H, m, CH$_3$C*H*CH$_3$), 1.98 (1H, m, OCHCH*H*) 2.12 (3H, s, C*H*$_3$C=N), 2.29 (1H, m, C(4)*H*H), 2.43 (1H, m, C(4)H*H*), 2.54 (1H, m, C(3)*H*H), 2.65 (1H, m, C(3)H*H*), 4.10-4.40 (2H, m, OC*H*$_2$CH$_3$), 4.7-4.80 (1H, m, OC*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (OCH$_2$*C*H$_3$), 15.9 (*C*H$_3$CH), 19.8 (*C*H$_3$C=N), 20.6 and 21.8 (*C*H$_3$CH*C*H$_3$), 23.0 (*C*4), 25.7 (CH$_3$*C*HCH$_3$), 30.5 (CH*C*H$_2$), 31.3 (CH$_3$*C*H), 34.1 (*C*3), 39.4 (CH$_3$CH*C*H$_2$), 40.2 (OCH*C*H$_2$), 46.7 (OCH*C*H), 61.9 (O*C*H$_2$CH$_3$), 75.7 (O*C*H), 86.7 (*C*2), 169.4, and 169.5 (2 × *C*OO), 180.7 and 180.8 (*C*5); m/z (ESI$^+$), 697 ([2M+Na]$^+$, 100%), 360 ([M+Na]$^+$, 60%), 338 ([M+H]$^+$, 40%), HRMS (ESI$^+$) $C_{19}H_{31}NNaO_4^+$ ([M+Na]$^+$]) requires 360.2145; found 360.2150.

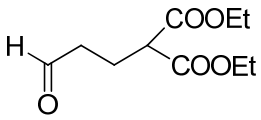
(±)2-Ethyl 2-(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl 5-methylpyrrolidine-2,2-dicarboxylate, 9f



Following general procedure **H**, to a solution of pyrroline **7f** (53 mg, 0.16 mmol) in MeOH (3 mL) was added $NaBH_3CN$ (6 mg, 0.23 mmol) and 2 M HCl in MeOH (2 mL), to give crude product which was purified by flash column chromatography to afford pyrrolidine **9f** (48 mg, 90%) as a colourless oil; R_f = 0.25 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3351, 2955, 2870, 1731, 1524, 1440, 1207, 1123, 910, 860, 776; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.73 (3H, d, *J* 6.9 Hz, C*H*$_3$CH), 0.86 (6H, d, *J* 6.6 Hz, C*H*$_3$CHC*H*$_3$), 0.89 (1H, m, CHC*H*H), 0.98 (1H, m, CH$_3$CHC*H*H), 1.04 (1H, m, OCHC*H*H), 1.13 (3H, d, *J* 6.1 Hz, C*H*$_3$CHNH), 1.23 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.36 (1H, m,

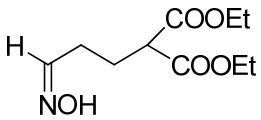
OCHC*H*), 1.63 (1H, m, CH_3CHCH*H*), 1.67 (1H, m, CHCH*H*), 1.88 (1H, m, CH_3CHCH_3), 1.98 (1H, m, OCHCH*H*) 2.12 (3H, s, CH_3C=N), 2.29 (1H, m, C(4)*H*H), 2.40-2.50 (1H, m, C(4)H*H*), 2.50-2.60 (1H, m, C(3)*H*H), 2.60-2.70 (1H, m, C(3)H*H*), 4.00-4.25 (2H, m, OCH_2CH_3), 4.73 (1H, m, OC*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.8 (OCH_2CH_3), 15.7 (CH_3CH), 19.6 (CH_3C=N), 20.9 and 21.3 (CH_3CHCH_3), 22.9 and 23.0 (*C*4), 25.7 (CH_3CHCH_3), 31.3 ($CHCH_2$), 31.2 (*C*5), 33.1 (*C*3), 40.2 (CH_3CHCH_2), 40.3 ($OCHCH_2$), 46.5 (OCHCH), 61.8 (OCH_2CH_3), 75.6 (OCH), 86.5 (*C*2), 171.4 and 171.7 (2 × *C*OO); m/z (ESI^+), 340 ($[M+H]^+$, 40%), HRMS (ESI^+) $C_{19}H_{33}NNaO_4^+$ ($[M+Na]^+$]) requires 340.2482; found 340.2472.

Diethyl 2-(3-isopropyl)malonate, 3g



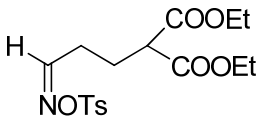
Following general procedure **A**, acrolein (1.14 g, 19.6 mmol) was added to a solution of diethyl malonate (2.09 g, 13.1 mmol) and anhydrous K_2CO_3 (1.98 g, 14.5 mmol) in CH_2Cl_2 (25 mL) and the mixture stirred at rt, to give crude product which was purified by flash column chromatography to afford adduct **3g** (2.41 g, 85%) as a colourless oil; R_f = 0.57 (EtOAc : petrol, 1:3); υ_{max}(film)/cm^{-1} 2957, 1730, 1436, 1234, 1155, 1048; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.15-1.30 (6H, m, 2 × OCH_2CH_3), 2.19 (2H, m, CH_2CH_2CH), 2.57 (2H, t, *J* 7.3 Hz, CH_2CH_2CH), 3.38 (1H, t, *J* 7.3 Hz, CH_2CH_2CH), 4.10-4.30 (4H, m, 2 × OCH_2CH_3), 9.75 (1H, t *J* 1.0 Hz , *H*C=O); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.4 (2 × OCH_2CH_3), 20.9 (CH_2CH_2CH), 40.4 (CH_2CH_2CH), 50.6 (CH_2CH_2CH), 60.9 (2 × OCH_2CH_3), 168.3 (2 × *C*OO), 100.1 (*C*O); m/z (ESI^+) 491 ($[2M+CH_3CN+NH_4]^+$, 100%), 215 ($[M-H]^-$, 70%), HRMS (ESI^-) $C_{10}H_{15}O_5^-$ ($[M-H]^-$) requires 215.0925; found 215.0923.

Diethyl 2-(3-(hydroxyimino)propyl)malonate, 4g



Following general procedure **C**, to a solution of adduct **3g** (2.20 g, 10.2 mmol) in EtOH (50 mL) was added $NH_2OH.HCl$ (1.41 g, 20.4 mmol) and Et_3N (3.08 g, 30.5 mmol) and heated to reflux for 1 hr, to give crude product which was purified by flash column chromatography to afford oxime **4g** (2.13 g, 90%) as a colourless oil; R_f = 0.30, 0.22 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 3454, 2983, 1731, 1447, 1367, 1157, 1096, 932, 861; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.25 (6H, t, *J* 7.1 Hz, 2 × OCH_2CH_3), 2.09 (2H, m, CH_2CH_2CH), 2.26 (1H, m, $CHHCH_2CH$), 2.43 (1H, m, $CHHCH_2CH$), 3.36 (1H, t, *J* 7.3 Hz, CH_2CH_2CH), 4.19 (4H, q, *J* 7.1 Hz, 2 × OCH_2CH_3), 6.71 and 7.39 (1H, t, *J* 5.7 Hz, *H*C=NOH), 8.52, 8.94 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (2 × OCH_2CH_3), 22.8, 27.2 (CH_2CH_2CH), 25.1, 25.4 (CH_2CH_2CH), 51.0 (CH_2CH_2CH), 61.5, 61.6 (2 × OCH_2CH_3), 150.28, 150.7 (*HC*=NOH), 169.0 (2 × *C*OO); m/z (ESI$^+$) 485 ([2M+Na]$^+$, 35%), 254 ([M+Na]$^+$, 55%), 230([M-H]$^-$, 100%) HRMS (ESI$^+$) $C_{10}H_{17}NNaO_5^+$ ([M+Na]$^+$) requires 254.0999; found 254.0998.

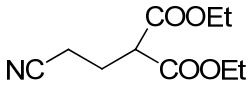
Diethyl 2-(3-(tosyloxyimino)propyl)malonate, 6g



Following general procedure **E**, to a solution of oxime **4g** (262 mg, 1.13 mmol) in dry CH_2Cl_2 (20 mL) was added Et_3N (229 mg, 2.27 mmol) at 0 °C followed by *p*-toluenesulphonyl chloride (322 mg, 1.69 mmol) and the mixture stirred at rt for 2 hr, to give the crude products which were purified by flash column chromatography to afford tosyl oxime **6g** (140 mg, 32%) and diester nitrile **10** (135 mg, 56%) both as colurless oils; **6g** R_f = 0.43 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3068, 2986, 1729, 1656, 1495, 1252, 1187, 995, 838, 769; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.23 (6H, t, *J* 7.1 Hz, 2 × OCH_2CH_3), 1.62 (2H, m, CH_2CH_2CH), 2.02 (3H, s, $ArCH_3$), 2.41 (2H, m, CH_2CH_2CH), 3.38 (1H, m, CH_2CH_2CH), 4.16 (4H, q, *J* 7.1 Hz, 2 × OCH_2CH_3), 7.29 (2H, d, *J* 7.6 Hz, Ar*H*), 7.35 (1H, t, *J* 7.3 Hz, *H*C=NOAr), 7.77 (2H, d, *J* 8.1 Hz, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (2 × OCH_2CH_3), 21.7 ($ArCH_3$), 22.6 (CH_2CH_2CH), 29.2 (CH_2CH_2CH), 51.3 (CH_2CH_2CH), 61.5, 61.7 (2

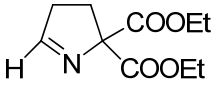
× O*C*H$_2$CH$_3$), 126.3-129.5 (Ar*C*), 130.1, 130.2 (quaternary Ar*C*), 154.0, 150.7 (*C*=NOTs), 169.1, 171.5 (2 × *C*OO); m/z (ESI$^+$) 408 ([M+Na]$^+$, 20%), 384 ([M-H]$^-$, 100%), HRMS (ESI$^+$) $C_{17}H_{23}NNaO_7S^+$ ([M+Na]$^+$) requires 408.1087; found 408.1095.

Diethyl 2-(2-cyanoethyl)malonate, 10



Isolated from the above procedure, R_f = 0.58 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2938, 2360, 1730, 1436, 1234, 1155, 1048; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.26 (6H, t, J 7.1 Hz, 2 × OCH$_2$C*H*$_3$), 2.22 (2H, m, CH$_2$C*H*$_2$CH), 2.49 (2H, m, C*H*$_2$CH$_2$CH), 3.48 (1H, t, *J* 7.3 Hz, CH$_2$CH$_2$C*H*), 4.20 (4H, q, *J* 7.1 Hz, 2 × OC*H*$_2$CH$_3$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (2 × OCH$_2$*C*H$_3$), 15.0 (*C*H$_2$CH$_2$CH), 24.4 (CH$_2$*C*H$_2$CH), 50.1 (CH$_2$CH$_2$*C*H), 61.8 (2 × O*C*H$_2$CH$_3$), 118 (*C*N), 168.0 (2 × *C*OO); m/z (ESI$^+$) 236 ([M+Na]$^+$, 100%), HRMS (ESI$^+$) $C_{10}H_{15}NNaO_4^+$ ([M+Na]$^+$) requires 236.0893; found 236.0892.

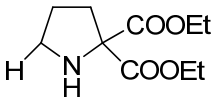
Diethyl 3,4-dihydro-2H-pyrrole-2,2-dicarboxylate, 7g



Following general procedure **D**, to a solution of oxime **4g** (103 mg, 0.44 mmol) in EtOH (5 mL) sodium metal (11 mg, 0.49 mmol) was added and the mixture stirred at rt for 30 min followed by slow addition of 2,4-dinitrofluorobenzene (99 mg, 0.53 mmol) at 0 °C to give product which was purified by flash column chromatography to afford pyrroline **7g** (42 mg, 45%) as a colourless oil; **OR** Following general procedure **F**, tosyl oxime **6g** (73 mg, 0.19 mmol) in dry THF (5 mL) was added NaH (14 mg, 0.57 mol, 60%) and heated to reflux for 30 min, to give ring closure product pyrroline **7g** after flash column chromatography (13 mg, 32%) as a colourless oil; R_f = 0.22 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2987, 1733, 1542, 1495, 1253, 1202, 1121, 861; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.20-1.35 (6H, m, 2 × OCH$_2$C*H*$_3$), 2.20-2.30 (2H, m, C(4)*H*$_2$), 2.50-2.60 (2H, m, C(3)*H*$_2$),

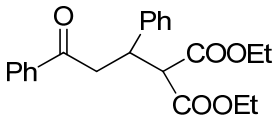
4.15-4.30 (4H, m, 2 × OC*H*$_2$CH$_3$), 7.85 (1H, t, *J* 8.1 Hz, C(5)*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (2 × OCH$_2$*C*H$_3$), 21.0 (*C*4), 27.1 (*C*3), 61.9 (2 × O*C*H$_2$CH$_3$), 75.5 (*C*2), 168.1 (*C*1), 168.9 (2 × *C*OO); m/z (ESI$^+$) 427 ([2M+H]$^+$, 80%), 214 ([M+H]$^+$, 40%), HRMS (ESI$^+$) $C_{10}H_{16}NO_4^+$ ([M+H]$^+$) requires 214.1074; found 214.1080.

Diethyl pyrrolidine-2,2-dicarboxylate, 9g



Following general procedure **H**, to a solution of pyrroline **7g** (30 mg, 0.14 mmol) in MeOH (2 ml) $NaBH_3CN$ (18 mg, 0.28 mmol) and 2 M HCl in MeOH (1 mL) was added at rt, to give crude product which was purified by flash column chromatography to afford pyrrolidine **9g** (22 mg, 74%) as a colourless oil; R_f = 0.16 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3378, 29738 1738, 1512, 1362, 1234, 1213, 1177, 1077, 836; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.15-1.30 (6H, m, 2 × OCH$_2$C*H*$_3$), 2.31 (1H, m, C(4)H*H*), 2.44 (1H, m, C(4)*H*H), 2.60 (1H, m, C(3)H*H*), 2.71 (1H, m, C(3)*H*H), 2.93 (1H, m, C(5)H*H*), 3.04 (1H, m, C(5)*H*H), 4.10-4.40 (4H, m, 2 × OC*H*$_2$CH$_3$), 6.38 (1H, bs, N*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0, 14.2 (2 × OCH$_2$*C*H$_3$), 27.9 (*C*4), 29.2 (*C*3), 51.0 (*C*5), 61.9 and 62.7 (2 × O*C*H$_2$CH$_3$), 67.9 (*C*2), 168.6 (2 × *C*OO); m/z (ESI$^+$) 429 ([2M-H]$^-$, 100%), 216 ([M+H]$^+$, 15%), HRMS (ESI$^+$) $C_{10}H_{18}NO_4^+$ ([M+H]$^+$) requires 216.1230; found 216.1235.

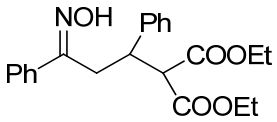
(±)Diethyl 2-(3-oxo-1,3-diphenylpropyl)malonate, 3h



Following general procedure **B**, chalcone (3.15 g, 15.2 mmol) in dry CH_2Cl_2 (10 mL) was added to a solution of diethyl malonate (2.02 g, 12.6 mmol) and anhydrous K_2CO_3 (2.51 g, 18.9 mmol) in dry CH_2Cl_2 (30 ml) and was heated to reflux for 15 hr, to give crude product which was purified by flash column chromatography to afford adduct **3h** (3.99 g, 86%) as a white solid; m.p. = 76-78 °C;

R_f = 0.31 (EtOAc : petrol, 1:9) υ_{max}(film)/cm^{-1} 3029, 2982, 1731, 1686, 1597, 1496, 1449, 1255, 1154, 1096, 861, 750; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.01 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.25 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.46 (1H, dd, *J* 16.7, 6.9 Hz, PhCOC*H*H), 3.55 (1H, dd, *J* 16.7, 9.1 Hz, PhCOCH*H*), 3.83 (1H, d, *J* 9.7 Hz, C*H*CHPh), 3.95 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.18 (1H, m, CHC*H*Ph), 4.20 (2H, m, OCH_2CH_3), 7.15-7.90 (10H, m, 2 × Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.8 and 14.0 (2 × OCH_2CH_3), 40.8 (CH*C*HPh), 42.6 (PhCO*C*H_2), 57.6 (*C*HCHPh), 61.6 (2 × OCH_2CH_3), 127.1, 128.0, 128.2, 128.4, 128.5, 133.0 (Ar*C*), 136.78, 140.0 (quaternary Ar*C*), 167.7, 168.4 (2 × *C*OO), 197.5 (*C*O); m/z (ESI$^+$), 367 ([M-H]$^-$, 75%), 391 ([M+Na]$^+$, 10%), 427 ([M+CH_3CN+NH_4]$^+$, 100%); HRMS (ESI$^+$) $C_{22}H_{24}NaO_5^+$ ([M+Na]$^+$) requires 391.1516; found 391.1520.

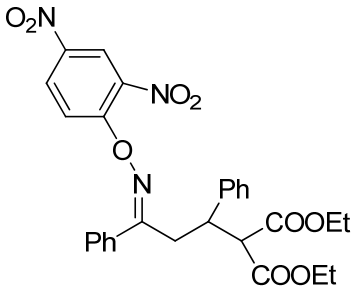
(±)Diethyl 2-(3-(hydroxyimino)-1,3-diphenylpropyl)malonate, 4h



Following general procedure **C**, to a solution of adduct **3h** (3.69 g, 10.0 mmol) in EtOH (50 mL) was added $NH_2OH.HCl$ (1.38 g, 20.1 mmol) and Et_3N (2.53 g, 25.1 mmol) and heated to reflux for 7 hr, to give crude product which was purified by flash column chromatography to afford oxime **4h** (3.72 g, 97%) as a semi-solid; R_f = 0.26 (EtOAc : petrol, 2:8); υ_{max}(film)/cm^{-1} 3441, 3027, 2982, 1731, 1496, 1454, 1369, 1301, 1252, 1156, 1095, 914, 880, 759; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.88 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.28 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.14 (1H, m PhCHC*H*H), 3.44 (1H, m, PhCHCH*H*), 3.78 (1H, d, *J* 9.6 Hz, C*H*CHPh), 3.82 (1H, m, CHC*H*Ph), 3.85 (2H, m, OCH_2CH_3), 4.24 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 7.01-7.30 (10H, m, 2 × Ar*H*), 8.70 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.6 and 14.1 (2 × OCH_2CH_3), 30.2 (CH_2CHPh), 42.4 (CH*C*HPh), 58.2 (*C*HCHPh), 61.2, 61.8 (2 × OCH_2CH_3), 126.6, 127.1, 127.9, 128.1, 128.2, 128.3, 128.6, 129.0, (Ar*C*), 135.2, 139.0 (quaternary Ar*C*), 157.4 (*C*NOH), 167.6 and 168.3 (2 × *C*OO);

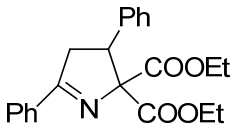
m/z (ESI^+), 442 ($[M+CH_3CN+NH_4]^+$, 100%), 406 ($[M+Na]^+$, 15%), 384 ($[M+H]^+$, 15%), 382 ($[M-H]^-$, 100%), HRMS (ESI^+) $C_{22}H_{25}NNaO_5^+$ ($[M+Na]^+$]) requires 406.1625; found 406.1621.

(±)Diethyl 2-(3-(2,4-dinitrophenoxyimino)-1,3-diphenylpropyl)malonate, 5h



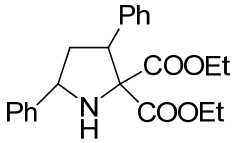
Following general procedure **D**, to a solution of oxime **4h** (2.11 g, 5.51 mmol) in EtOH (30 mL) was added sodium metal (139 mg, 6.06 mmol) and the mixture stirred at rt 30 min followed by 2,4-dinitrofluorobenzene (1.53 g, 8.26 mmol) at 0 °C slowly, to give crude product which was purified by flash column chromatography to afford ether **5h** (2.26 g, 75%) as a yellow semi-solid; R_f = 0.50 (EtOAc : petrol, 2:8); υ_{max}(film)/cm^{-1} 3028, 2985, 1731, 1605, 1532, 1473, 1343, 1259, 1144, 925, 831, 761; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.85 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.33 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.33 (1H, dd, *J* 13.4, 9.7 Hz, PhCHC*H*H), 3.63 (1H, m, PhCHCH*H*), 3.82 (2H, m, OCH_2CH_3), 3.86 (1H, m, CHC*H*Ph), 3.96 (1H, d, *J* 9.3 Hz, C*H*CHPh), 4.31 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 7.23-7.73 (10H, m, 2 × Ar*H*), 7.63 (1H, d, *J* 9.4 Hz, Ar*H*), 8.29 (1H, dd, *J* 9.4, 2.7 Hz, Ar*H*), 8.87 (1H, d, *J* 2.7 Hz, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.6 and 14.1 (2 × OCH_2CH_3), 32.3 (PhCHCH_2), 43.1 (CHCHPh), 57.4 (*C*HCHPh), 61.4, 62.0 (2 × OCH_2CH_3), 127.3, 127.5, 127.9, 128.4, 128.9, 129.2, 131.1, 132.4, 135.76 (Ar*C*), 137.9, 134.6 (quaternary Ar*C*), 156.9 (*C*NOAr), 164.9 (quaternary ArO*C*), 167.3 and 168.3 (2 × *C*OO); m/z (ESI^+), 608 ($[M+CH_3CN+NH_4]^+$, 100%), 572 ($[M+Na]^+$, 20%), 548 ($[M-H]^-$, 100%), HRMS (ESI^+) $C_{28}H_{27}N_3NaO_9^+$ ($[M+Na]^+$]) requires 572.1664; found 572.1650.

(±)Diethyl 3,5-diphenyl-3,4-dihydro-2H-pyrrole-2,2-dicarboxylate, 7h



Following general procedure **F**, to ether **5h** (506 mg, 0.92 mmol) in dry THF (15 mL) was added NaH (66 mg, 2.76 mmol, 60%) and the mixture heated to reflux for 30 min, to give crude product which was purified by flash column chromatography to afford pyrroline **7h** (262 mg, 78%) as a colourless oil; R_f = 0.73 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3023, 2982, 1731, 1611, 1448, 1345, 1266, 1216, 1098, 1044, 760; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.85 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.32 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.42 (1H, dd, *J* 17.4, 9.0 Hz, C(4)*H*H), 3.60 (1H, q, *J* 7.1 Hz, $OCHHCH_3$), 3.67 (1H, dd, *J* 17.4, 6.8 Hz, C(4)H*H*), 3.83 (1H, q, *J* 7.1 Hz, $OCHHCH_3$), 4.22 (1H, m, $OCHHCH_3$), 4.41 (1H, m, $OCHHCH_3$), 4.54 (1H, dd, *J* 9.0, 5.5 Hz, C(3)*H*), 7.20-8.02 (10H, m, 2 × Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.5 and 14.0 (2 × OCH_2CH_3), 43.7 (*C*4), 48.4 (*C*3), 61.3, 62.3 (2 × OCH_2CH_3), 91.6 (*C*2), 127.3, 128.3, 128.3, 128.5, 128.6, 131.6, (Ar*C*), 133.2, 139.6 (quaternary Ar*C*), 167.7 and 169.0 (2 × *C*OO), 177.8 (*C*5); m/z (ESI$^+$), 424 ([M+CH_3CN+NH_4]$^+$, 100%), 366 ([M+H]$^+$, 85%), HRMS (ESI$^+$) $C_{22}H_{23}NO_4^+$ ([M+Na]$^+$]) requires 388.1519; found 388.1523.

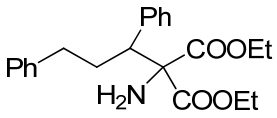
(±)Diethyl 3,5-diphenylpyrrolidine-2,2-dicarboxylate, 9h



Following general procedure **H**, to a solution of pyrroline **7h** (108 mg, 0.29 mmol) in MeOH (5 mL) was added $NaBH_3CN$ (27 mg, 0.43 mmol) and 2 M HCl in MeOH (2 mL), to give crude product which was purified by flash column chromatography to afford pyrrolidine **9h** (104 mg, 96%) as a colourless oil; R_f = 0.65 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3392, 3027, 2981, 1739, 1602, 1494, 1454, 1367, 1197, 1094, 1028, 861, 752; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.65 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.10 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.24 (1H, m, C(4)*H*H), 2.41 (1H, m,

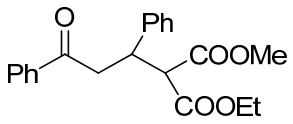
C(4)H*H*), 3.47 and 3.73 (2H, 2 x m, OC*H*$_2$CH$_3$), 4.07 and 4.18 (2H, 2 x m, OC*H*$_2$CH$_3$), 4.24 (1H, t, *J* 7.0 Hz, C(3)*H*), 4.42 (1H, m, C(5)*H*), 7.09-7.58 (10H, m, 2 × Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.2 and 13.7 (2 × OCH$_2$*C*H$_3$), 42.2 (*C*4), 50.4 (*C*3), 60.9 (*C*5), 61.3 and 61.5 (2 × O*C*H$_2$CH$_3$), 77.2 (*C*2), 126.8, 126.9, 127.4, 127.5, 127.6, 127.8, 127.9, 128.5 (Ar*C*), 140.2 and 142.8 (quaternary Ar*C*), 170.6 and 171.3 (2 × *C*OO); m/z (ESI$^+$), 757 ([2M+Na]$^+$, 80%), 426 ([M+CH$_3$CN+NH$_4$]$^+$, 75%), 368 ([M+H]$^+$, 75%), HRMS (ESI$^+$) $C_{22}H_{26}NO_4^+$ ([M+H]$^+$]) requires 368.1856; found 368.1852.

(±)Diethyl 2-amino-2-(1,3-diphenylpropyl)malonate, 11



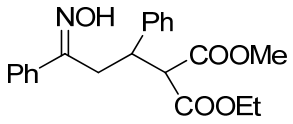
Following general procedure **G**, pyrroline **7h** (59 mg, 0.16 mmol) in EtOH (10 mL) was passed through H-Cube hydrogenation plant (0.5 mL per min) at 50 °C loaded with 10% Pd/C as a catalyst. EtOH was removed on reduced pressure and the crude product amino ester **11** was obtained (57 mg, 96%) as a colourless a oil, R_f = 0.38 (EtOAc : petrol, 2:8); υ_{max}(film)/cm^{-1} 3297, 3005, 2981, 1728, 1604, 1496, 1454, 1367, 1267, 1205, 1112, 1038, 761, 699; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.13 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.27 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.94 (1H, m, PhCH$_2$C*H*H), 1.98 (2H, bs, N*H*$_2$), 2.29 (1H, m, PhCH$_2$CH*H*), 2.41 (2H, m, PhC*H*$_2$CH$_2$), 3.64 (1H, dd, *J* 11.6, 8.8 Hz, PhC*H*CH$_2$), 3.99 (2H, m, OC*H*$_2$CH$_3$), 4.25 (2H, m, OC*H*$_2$CH$_3$), 7.07-7.36 (10H, m, 2 × Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 and 14.0 (2 × OCH$_2$*C*H$_3$), 32.2 (PhCH$_2$*C*H$_2$), 33.7 (Ph*C*H$_2$CH$_2$), 49.6 (Ph*C*HCH$_2$), 61.9 and 62.2 (2 × O*C*H$_2$CH$_3$), 70.4 (quaternary *C*NH$_2$), 125.7, 127.4, 128.2, 128.3, 128.4, 129.6 (Ar*C*), 138.6, 141.9 (quaternary Ar*C*), 170.5, 170.6 (2 × *C*OO); m/z (ESI$^+$), 428 ([M+CH$_3$CN+NH$_4$]$^+$, 100%), 392 ([M+Na]$^+$, 20%), HRMS (ESI$^+$) $C_{22}H_{27}NNaO_4^+$ ([M+Na]$^+$]) requires 392.1832; found 392.1830.

(±)1-Ethyl 3-methyl 2-(3-oxo-1,3-diphenylpropyl)malonate, 3i



Following general procedure **B**, chalcone (3.13 g, 15.1 mmol) in dry CH_2Cl_2 (10 mL) was added to a solution of ethyl methyl malonate (2.00 g, 13.7 mmol) and anhydrous K_2CO_3 (2.75 g, 20.5 mmol) in dry CH_2Cl_2 (30 mL) and the mixture heated to reflux for 15 hr, to give crude product which was purified by flash column chromatography to afford adduct **3i** (3.95 g, 81%) as a white solid; m.p. = 79-82 °C; R_f = 0.46 (EtOAc : petrol, 1:4); υ_{max}(film)/cm^{-1} 3029, 2954, 1733, 1686, 1597, 1449, 1258, 1155, 1027, 750, 700; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.99 and 1.24 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.51 (2H, m, $PhCOCH_2$), 3.73 (3H, s, OCH_3), 3.86 (1H, d, *J* 7.2 Hz, CHCHPh), 3.95 and 4.17 (2H, 2 x m, OCH_2CH_3), 4.22 (1H, m, CHCHPh), 7.18-7.55 (10H, m, 2 × Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.7 and 14.0 (OCH_2CH_3), 40.7 and 40.8 (CHCHPh), 42.3 and 42.6 ($PhCOCH_2$), 52.4 and 52.6 (OCH_3), 57.3 and 57.4 (*C*HCHPh), 61.4 and 61.7 (OCH_2CH_3), 127.2, 128.1, 128.2, 128.4, 128.5, 128.6 (Ar*C*), 133.1, 136.8, 140.4, 140.5 (quaternary Ar*C*), 167.7, 168.1, 168.3, 168.7, 168.8 (2 × *C*OO), 197.5 (*C*O); m/z (ESI$^+$), 731 ([2M+Na]$^+$, 100%), 413 ([M+CH_3CN+NH_4]$^+$, 20%), 377 ([M+Na]$^+$, 95%), 353 ([M-H]$^-$, 75%); HRMS (ESI$^+$) $C_{21}H_{22}NaO_5^+$ ([M+Na]$^+$) requires 377.1359; found 377.1360.

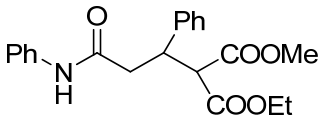
(±)1-Ethyl 3-methyl 2-(3-(hydroxyimino)-1,3-diphenylpropyl)malonate, 4i



Following general procedure **C**, to a solution of adduct **3i** (3.64 g, 10.3 mmol) in EtOH (50 mL) was added $NH_2OH.HCl$ (1.41 g, 20.6 mmol) and Et_3N (2.59 g, 25.7 mmol) and heated to reflux for 7 hr to give crude product, which was purified by flash column chromatography to afford oxime **4i** (3.22 g, 85%) as a semi-solid; R_f = 0.59 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3463, 2954, 1735, 1687, 1598, 1496, 1256, 1026, 756, 699; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.87 and 1.28

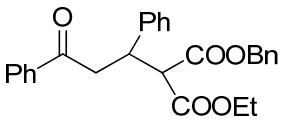
(3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.14 (2H, m, $PhCHCH_2$), 3.38 and 3.76 (3H, 2 x s, OCH_3), 3.43 (1H, m, CHCHPh), 3.81 (1H, d, *J* 4.9, CHCHPh), 3.85 and 4.25 (2H, 2 x m, OCH_2CH_3), 7.02-7.31 (10H, m, 2 × ArH), 8.72 (1H, bs, OH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.5 and 14.0 (OCH_2CH_3), 29.9 and 30.1 ($PhCHCH_2$), 42.4 and 42.5 (CHCHPh), 52.4 and 52.6 (OCH_3), 57.9 and 58.0 (CHCHPh), 61.3 and 61.8 (OCH_2CH_3), 126.5, 127.2, 128.0, 128.2, 128.3, 129.0 (ArC), 135.2 and 139.0 (quaternary ArC), 157.4 (CNOH), 167.5, 167.9, 168.0, 168.6, 168.8 (2 × COO); m/z (ESI^+), 761 ($[2M+Na]^+$, 80%), 392 ($[M+Na]^+$, 95%), 370 ($[M+H]^+$, 50%), 368 ($[M-H]^-$, 100%); HRMS (ESI^+) $C_{21}H_{23}NNaO_5^+$ ($[M+Na]^+$) requires 392.1468; found 392.1468.

(±)1-Ethyl 3-methyl 2-(3-oxo-1-phenyl-3-(phenylamino)propyl)malonate, 8i



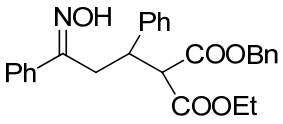
Following general procedure **E**, to a solution of oxime **4i** (124 mg, 0.33 mmol) in dry CH_2Cl_2 (5 mL) was added Et_3N (67 mg, 0.66 mmol) at 0 °C followed by *p*-toluenesulphonyl chloride (94 mg, 0.50 mmol) and the mixture stirred for 3 hr, to give crude product, which was purified by flash column chromatography to afford amide **8** (67 mg, 67%) as a white solid; m.p. = 154-156 °C; R_f = 0.26 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3309, 3076, 2977, 1734, 1661, 1600, 1543, 1310, 1151, 757, 699; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.99 and 1.26 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.76 and 2.92 (2H, m, $PhCHCH_2$), 3.49 and 3.76 (3H, s, OCH_3), 3.87 and 3.90 (1H, m, CHCHPh), 4.00 (1H, m, CHCHPh), 3.94 and 4.23 (2H, m, OCH_2CH_3), 7.07 (1H, bs, NH), 7.29-7.35 (10H, m, 2 × ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.7 and 13.9 (OCH_2CH_3), 41.7 and 42.0 (CHCHPh), 42.2 and 42.3 ($COCH_2$), 52.4 and 52.7 (OCH_3), 56.7 and 56.9 (CHCHPh), 61.6 and 61.9 (OCH_2CH_3), 119.7-128.0 (ArC), 137.6 and 140.0 (quaternary ArC), 167.5, 168.1, 168.4, 168.6, 167.0, 172.4 (2 × COO, CONH); m/z (ESI^+), 761 ($[2M+Na]^+$, 100%), 368 ($[M-H]^-$, 100%); HRMS (ESI^+) $C_{21}H_{23}NNaO_5^+$ ($[M+Na]^+$) requires 392.1468; found 392.1471.

(±)1-Benzyl 3-ethyl 2-(3-oxo-1,3-diphenylpropyl)malonate, 3j



Following general procedure **B**, chalcone (1.77 g, 8.52 mmol) in CH_2Cl_2 (10 mL) was added to a solution of benzyl ethyl malonate (1.72 g, 7.74 mmol) and anhydrous K_2CO_3 (1.55 g, 11.6 mmol) in CH_2Cl_2 (30 mL) and the mixture heated to reflux for 15 hr, to give crude product which was purified by flash column chromatography to afford adduct **3j** (2.93 g, 88%) as a white solid; m.p. = 96-98 °C); R_f = 0.59 (EtOAc : petrol, 1:4); υ_{max}(film)/cm^{-1} 3072, 2954, 1733, 1687, 1598, 1496, 1448, 1256, 1026, 757, 699; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.98 and 1.19 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.47 (2H, d, *J* 7.2 Hz, $PhCHCH_2$), 3.89 (1H, d, *J* 7.2 Hz, *CH*CHPh), 3.90-4.00 and 4.10-4.20 (3H, m, OCH_2CH_3 and CHCHPh), 5.20 and 5.25 (2H, 2 x d, *J* 12.2 Hz, CH_2Ph), 7.17-7.90 (15H, m, 3 × Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.7 and 14.0 (OCH_2CH_3), 40.7 and 40.8 (CH*C*HPh), 42.4 and 42.5 ($PhCOCH_2$), 57.3 and 57.6 (*C*HCHPh), 61.4 and 61.7 (OCH_2CH_3), 67.0 and 67.3 (CH_2Ph), 127.1, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6 (Ar*C*), 133.0, 135.3, 136.7, 140.4 (quaternary Ar*C*), 167.6, 167.7, 168.1 (2 × *C*OO), 197.4 and 197.5 (*C*O); m/z (ESI$^+$), 883 ([2M+Na]$^+$, 100%), 453 ([M+Na]$^+$, 50%), 429 ([M-H]$^-$, 20%); HRMS (ESI$^+$) $C_{27}H_{26}NaO_5^+$ ([M+Na]$^+$) requires 453.1672; found 453.1663.

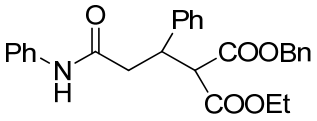
(±)1-Benzyl 3-ethyl 2-(3-(hydroxyimino)-1,3-diphenylpropyl)malonate, 4j



Following general procedure **C**, to a solution of adduct **3j** (2.43 g, 5.65 mmol) in EtOH (30 mL) was added $NH_2OH.HCl$ (780 mg, 11.3 mmol) and Et_3N (1.43 g, 14.1 mmol) and the mixture heated to reflux for 7 hr, to give crude product which was purified by flash column chromatography to afford oxime **4j** (2.17 g, 86%) as a semi-solid; R_f = 0.38 (EtOAc : petrol, 1:4); υ_{max}(film)/cm^{-1} 3445, 3032, 2982, 1732, 1599, 1566, 1496, 1370, 1253, 1154, 755, 697; δ_H(400 MHz; $CDCl_3$; Me_4Si)

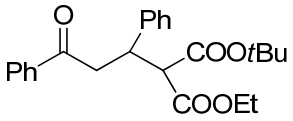
0.86 and 1.24 (3H, 2 x t, *J* 7.1 Hz, OCH_2CH_3), 3.12 (2H, m, $PhCHCH_2$), 3.46 (1H, m, CHCHPh), 3.87 (1H, d, *J* 6.6 Hz, CHCHPh), 3.8 and 4.22 (2H, 2 x m, OCH_2CH_3), 4.83 and 5.20 (2H, 2 x d, *J* 12.3 Hz, CH_2Ph), 7.03-7.37 (15H, m, 3 × ArH), 8.82 (1H, bs, OH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.6 and 14.0 (OCH_2CH_3), 29.9 and 30.1 ($PhCOCH_2$), 42.4 and 42.5 (CHCHPh), 58.1 and 58.2 (CHCHPh), 61.3 and 61.8 (OCH_2CH_3), 66.9 and 67.3 (CH_2Ph), 126.6, 127.2, 127.9, 128.0, 128.1, 128.3, 128.4, 128.5, 128.6, 129.0 (ArC), 135.1, 135.2, 135.3, 139.0 (quaternary ArC), 157.4 (CNOH), 167.4, 167.5, 168.1 (2 × COO); m/z (ESI^+), 913 ($[2M+Na]^+$, 100%), 468 ($[M+Na]^+$, 75%), 446 ($[M+H]^+$, 40%), 444 ($[M-H]^-$, 100%); HRMS (ESI^+) $C_{27}H_{27}NNaO_5^+$ ($[M+Na]^+$) requires 468.1781; found 468.1784.

(±)1-Benzyl 3-ethyl 2-(3-oxo-1-phenyl-3-(phenylamino)propyl)malonate, 8j



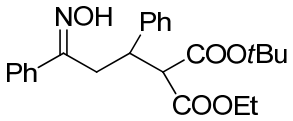
Following general procedure **E**, to a solution of oxime **4j** (1.53 g, 3.43 mmol) in dry CH_2Cl_2 (20 mL) was added Et_3N (694 mg, 6.87 mmol) at 0 °C followed by *p*-toluenesulphonyl chloride (979 mg, 5.15 mmol) and the mixture stirred at rt for 4 hr, to give the crude product which was purified by flash column chromatography to give the product **8** (1.67 mg, 81%) as a white solid; m.p. = 162-164 °C; R_f = 0.39 (EtOAc : petrol, 1:4); υ_{max}(film)/cm^{-1} 3430, 3033, 2970, 1732, 1542, 1443, 1378, 12534, 1148, 697; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.95 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.70-2.90 (2H, m, $PhCHCH_2$), 3.89 (2H, m, OCH_2CH_3), 3.92 (1H, m, CHCHPh), 4.01 (1H, m, CHCHPh), 5.26 (2H, s, CH_2Ph), 7.16 (1H, s, NH), 7.26-7.33 (15H, m, 3 × ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.7 (OCH_2CH_3), 41.8 ($PhCHCH_2$), 42.4 (CHCHPh), 57.0 (CHCHPh), 61.6 (OCH_2CH_3), 67.1 (CH_2Ph), 119.8, 129.2, 127.2, 127.5, 128.0, 128.2, 128.3, 128.4, 128.6, 128.7, 128.8 (ArC), 135.2, 137.6, 140.0 (quaternary ArC), 167.4, 168.3, 168.5 (CONH, 2 × COO); m/z (ESI^+), 913 ($[2M+Na]^+$, 100%), 468 ($[M+Na]^+$, 65%), 444 ($[M-H]^-$, 20%); HRMS (ESI^+) $C_{27}H_{27}NNaO_5^+$ ($[M+Na]^+$) requires 468.1781; found 468.1782.

(±)1-*tert*-Butyl 3-ethyl 2-(3-oxo-1,3-diphenylpropyl)malonate, 3k



Following general procedure **B**, chalcone (1.89 g, 9.13 mmol) in dry CH_2Cl_2 (10 mL) was added to a solution of *tert*-butyl ethyl malonate (1.56 g, 8.29 mmol) and anhydrous K_2CO_3 (1.66 g, 12.4 mmol) in dry CH_2Cl_2 (25 mL) and heated to reflux for 15 hr, to give crude product which was purified by flash column chromatography to afford adduct **3k** (2.72 g, 83%) as a white solid m.p. = 72-74 °C; R_f = 0.53 (EtOAc : petrol, 1:4); υ_{max}(film)/cm^{-1} 3032, 2979, 1729, 1687, 1598, 1496, 1449, 1368, 1257, 1145, 1028, 848, 750, 699; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.18 (9H, s, $(CH_3)_3C$), 1.26 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.35-3.55 (2H, m, $PhCHCH_2$), 3.74 (1H, d, *J* 5.6 Hz, CHCHPh), 4.12 (1H, m, CHCHPh), 4.23 (2H, m, OCH_2CH_3), 7.16-7.90 (10H, m, 2 × ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.8 and 14.1 (OCH_2CH_3), 27.5 and 27.9 ($CH_3)_3C$), 40.8 and 40.9 (CHCHPh), 42.6 and 43.3 ($PhCOCH_2$), 58.4 and 58.5 (CHCHPh), 61.5 (OCH_2CH_3), 81.9 $(CH_3)_3C$), 127.0, 128.1, 128.3, 128.5, 128.51, 132.9 (ArC), 136.8 and 140.6 (quaternary ArC), 166.7, 167.5, 168.7 (2 × COO), 197.7 (CO); m/z (ESI$^+$), 395 ([M-H]$^-$, 20%), 419 ([M+Na]$^+$, 40%), 455 ([M+CH_3CN+NH_4]$^+$, 15%), 815 ([2M+Na]$^+$, 100%), HRMS (ESI$^+$) $C_{24}H_{28}NaO_5^+$ ([M+Na]$^+$) requires 419.1829; found 419.1824.

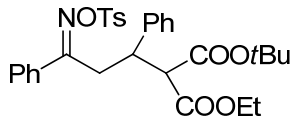
(±)1-*tert*-Butyl 3-ethyl 2-(3-(hydroxyimino)-1,3-diphenylpropyl)malonate, 4k



Following general procedure **C**, to a solution of adduct **3k** (2.45 g, 6.18 mmol) in EtOH (30 mL) was added $NH_2OH.HCl$ (1.06 g, 15.5 mmol) and Et_3N (1.87 g 18.6 mmol) and the mixture heated to reflux for 7 hr, to give crude product which was purified by column chromatography to afford oxime **4k** (2.30 g, 90%) as a semi-solid; R_f = 0.37 (EtOAc : petrol, 1:4); υ_{max}(film)/cm^{-1} 3470, 3031,

2980, 1730, 1598, 1449, 1369, 1256, 1147, 1027, 848, 759, 698; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.93 and 1.30 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.08 (9H, s, $(CH_3)_3C$), 3.13 and 3.44 (2H, m, $PhCHCH_2$), 3.69 (1H, m, CHCHPh), 3.72 (1H, m, CHCHPh), 3.87 and 4.26 (2H, m, OCH_2CH_3), 7.03-7.36 (10H, m, 2 × ArH), 8.20 (1H, bs, OH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.7 and 14.1 (OCH_2CH_3), 27.3 and 27.9 ($(CH_3)_3C$), 30.0 and 30.4 ($PhCHCH_2$), 42.3 and 42.5 (CHCHPh), 58.9 and 59.2 (CHCHPh), 60.9 and 61.4 (OCH_2CH_3), 81.7 and 82.3 ($(CH_3)_3C$), 125.8 - 130.0 (ArC), 135.3, 135.4, 139.2, 139.3 (quaternary ArC), 157.7, 157.8 (C=NOH), 166.6, 167.3, 167.8 (2 × COO); m/z (ESI^+), 845 ($[2M+Na]^+$, 85%), 823 ($[2M+H]^+$, 75%), 513 ($[M+CH_3CN+NH_4]^+$, 100%), 434 ($[M+Na]^+$, 50%), 412 ($[M+H]^+$, 60%), 310 ($[M-H]^-$, 100%); HRMS (ESI^+) $C_{24}H_{29}NNaO_5^+$ ($[M+Na]^+$) requires 434.1938; found 434.1933.

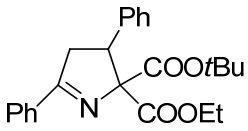
(±)1-*tert*-Butyl 3-ethyl 2-(1,3-diphenyl-3-(tosyloxyimino)propyl)malonate, 6k



Following general procedure **E**, to a solution of oxime **4k** (1.25 g, 3.04 mmol) in dry CH_2Cl_2 (25 mL) was added Et_3N (614 mg, 6.08 mmol) at 0 °C followed by *p*-toluenesulphonyl chloride (866 mg, 4.56 mmol) and the mixture stirred for 5 hr, to give mixture of crude products which were purified by column chromatography to afford tosyl oxime **6k** (692 g, 40%) as a semi-solid and pyrroline **7k** (413 mg 24%) as a colourless oil; tosyl oxime **6k** R_f = 0.42 (EtOAc : petrol, 1:5); υ_{max}(film)/cm^{-1} 3065, 2980, 1729, 1598, 1494, 1454, 1370, 1256, 1192, 1178, 1097, 816, 736, 698; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.93 and 1.26 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.08 and 1.45 (9H, s, $(CH_3)_3C$), 2.48 (3H, s, $ArCH_3$), 2.91 and 3.23 (2H, m, $PhCOCH_2$), 3.37 (1H, m, CHCHPh), 3.49 (1H, m, CHCHPh), 3.85 and 4.25 (2H, 2 x m, OCH_2CH_3), 6.84-7.69 (10H, m, 2 × ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.7 and 14.1 (OCH_2CH_3), 21.7 ($ArCH_3$), 27.3 and 27.6 ($(CH_3)_3C$), 38.5 and 39.1 ($PhCHCH_2$), 42.0 and 42.2 (CHCHPh), 58.7 and 58.9 (CHCHPh), 61.1 and 61.5 (OCH_2CH_3), 81.9 and 82.4 ($(CH_3)_3C$), 126.7-129.8 (ArC), 130.1-144.5 (quaternary ArC), 165.0 and 165.1

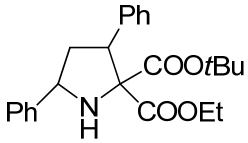
(*C*=NOAr), 166.3, 166.9, 167.6, 168.2 (2 × *C*OO); m/z (ESI$^+$), 588 ([M+Na]$^+$, 100%); HRMS (ESI$^+$) $C_{31}H_{35}NNaO_7S^+$ ([M+Na]$^+$) requires 588.2026; found 588.2026.

(±)2-tert-Butyl 2-ethyl 3,5-diphenyl-3,4-dihydro-2H-pyrrole-2,2-dicarboxylate, 7k



Following general procedure **F**, to a solution of tosyl oxime **6k** (51 mg, 0.09 mmol) in dry THF (5 mL) was added NaH (6 mg, 0.27 mmol, 60%) and the mixture heated to reflux for 30 min, to give crude product which was purified by flash column chromatography to afford pyrroline **7k** (24 mg, 69%) as a colourless oil; R_f = 0.65 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 2987, 1739, 1588, 1549, 1369, 1266, 1147, 1043, 848, 758, 688; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.04 (9H, s, $(CH_3)_3C$), 1.34 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.38 (1H, m, C(4)H*H*), 3.67 (1H, m, C(4)*H*H), 4.20 and 4.40 (2H, 2 x m, OCH_2CH_3), 4.49 (1H, dd, *J* 5.6, 4.6 Hz C(3)*H*), 7.24-8.01 (10H, m, 2 × Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.6 and 14.1 (OCH_2CH_3), 27.3 and 27.9 ($CH_3)_3C$), 44.2 and 44.6 (*C*4), 48.1 and 48.4 (*C*3), 60.9 and 62.1 (OCH_2CH_3), 81.9 and 82.9 ($(CH_3)_3C$), 91.7 and 92.5 (*C*2), 127.1-131.4 (Ar*C*), 133.4, 133.5, 140.3, 140.6 (quaternary Ar*C*), 166.3, 167.3, 167.7, 168.0, 169.3 (2 × *C*OO), 177.6 (Ph*C*N); m/z (ESI$^+$), 809 ([2M+Na]$^+$, 95%), 416 ([M+Na]$^+$, 100%), 394 ([M+H]$^+$, 80%); HRMS (ESI$^+$) $C_{24}H_{28}NaO_4^+$ ([M+H]$^+$) requires 394.2013; found 394.2013.

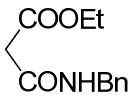
(±)2-*tert*-Butyl 2-ethyl 3,5-diphenylpyrrolidine-2,2-dicarboxylate, 9k



Following general procedure **O**, to a solution of pyrroline **7k** (53 mg, 0.13 mmol) in MeOH (3 mL) was added $NaBH_3CN$ (6 mg, 0.27 mmol) and 2 M HCl in MeOH (2 mL) to give crude product which was purified by flash column chromatography to afford pyrrolidine **9k** (51 mg, 94%) as a

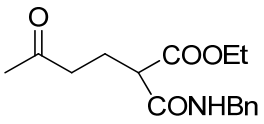
colourless oil; R_f = 0.79 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 3395 2977, 1722, 1588, 1368, 1266, 1155, 689; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.02 (9H, s, $(CH_3)_3C$), 1.30 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.19 (1H, m, C(4)H*H*), 2.58 (1H, m, C(4)*H*H), 3.13 (1H, bs, N*H*), 4.17 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.24 (1H, m, C(3)*H*), 4.37 (1H, m, C(5)*H*), 7.21-7.59 (10H, m, 2 × Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH_2CH_3), 27.2 ($(CH_3)_3C$), 42.4 (*C*4), 49.5 (*C*3), 61.1 (*C*5), 61.7 (OCH_2CH_3), 76.7 (*C*2), 82.0 ($(CH_3)_3C$), 126.9, 127.5, 128.1, 128.5, 129.1 (2 x Ar*C*), 140.4, 142.1 (quaternary Ar*C*), 168.9 and 171.6 (2 × *C*OO); m/z (ESI$^+$), 813 ([2M+Na]$^+$, 100%), 418 ([M+Na]$^+$, 100%), 396 ([M+H]$^+$, 100%); HRMS (ESI$^+$) $C_{24}H_{30}NO_4^+$ ([M+H]$^+$) requires 396.2169; found 396.2169.

Ethyl 3-(benzylamino)-3-oxopropanoate



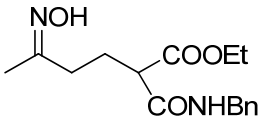
To a solution of ethyl 3-chloro-3-oxopropanoate (1.26 g, 8.40 mmol) in dry CH_2Cl_2 (20 mL) was added benzyl amine (988 mg, 9.24 mmol) and Et_3N (1.27 g, 12.7 mmol) and the mixture stirred at rt for 2 hr then washed with HCl (1 M), followed by water, extracted by CH_2Cl_2 and extracts were dried over Na_2SO_4, and concentrated to afford malonamide (1.80 g, 97%) as a pale yellow oil; R_f = 0.29 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3295, 3066, 2983, 1739, 1653, 1552, 1497, 1369, 1188, 1030, 734; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.28 (3H, *t*, J 7.1 Hz, OCH_2CH_3), 3.35 (2H, s, CH_2), 4.19 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.48 (2H, d, *J* 5.7 Hz, $CONHCH_2$), 7.26-7.35 (5H, m, Ar*H*), 7.47 (1H, bs, N*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (OCH_2CH_3), 41.1 (CH_2), 43.5 ($CONHCH_2$), 61.6 (OCH_2CH_3), 127.5, 127.7, 127.8, 128.4, 128.6 (Ar*C*), 137.8 (quaternary Ar*C*), 164.9 (*C*ONH), 169.8 (*C*OO); m/z (ESI$^+$) 280 ([M+CH_3CN+NH_4]$^+$, 100%), 244 ([M+Na]$^+$, 20%), 220 ([M-H]$^-$, 60%), HRMS (ESI$^+$) $C_{12}H_{15}NNaO_3^+$ ([M+Na]$^+$]) requires 244.0944; found 244.0946.

(±)Ethyl 2-(benzylcarbamoyl)-5-oxohexanoate, 3l



Following general procedure **A**, methyl vinyl ketone (676 mg, 9.66 mmol) was added to a solution of the above malonamide (1.78 g, 8.05 mmol) and anhydrous K_2CO_3 (1.62 mg, 12.07 mmol) in dry CH_2Cl_2 (30 mL) and the mixture stirred at rt, to give crude product which was purified by flash column chromatography to afford adduct **3l** (573 mg, 89%) as a colourless oil; R_f = 0.31 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3372, 3064, 2981, 1717, 1658, 1605, 1538, 1454, 1367, 1262, 1185, 858; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.29 (3H, m, OCH_2CH_3), 2.15 (3H, s, $COCH_3$), 2.20 (2H, m, CH_2CH_2CH), 2.37 (2H, m, CH_2CH_2CH), 3.33 (1H, *t*, *J* 7.2 Hz, CH_2CH_2CH), 4.21 (2H, m, OCH_2CH_3), 4.49 (2H, m, $CONHCH_2$), 7.23 (1H, bs, N*H*), 7.29-7.39 (5H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (OCH_2CH_3), 24.1 (CH_2CH_2CH), 29.9 ($COCH_3$), 30.4 (CH_2CH_2CH), 43.6 ($CONHCH_2$), 51.5 (CH_2CH_2CH), 61.6 (OCH_2CH_3), 127.5, 127.6, 127.7, 127.8, 128.7 (Ar*C*), 137.9 (quaternary Ar*C*), 167.9 (*C*ONH), 169.3 (*C*OO), 207.1 and 207.7 (*C*O); m/z (ESI$^+$) 350 ([M+CH_3CN+NH_4]$^+$, 75%), 290 ([M-H]$^-$, 100%), HRMS (ESI$^+$) $C_{16}H_{21}NNaO_4^+$ ([M+Na]$^+$) requires 314.1363; found 314.1355.

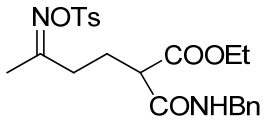
(±)Ethyl 2-(benzylcarbamoyl)-5-(hydroxyimino)hexanoate, 4l



Following general procedure **C**, to a solution of adduct **3l** (1.89 g, 3.51 mmol) in EtOH (30 mL) was added $NH_2OH.HCl$ (672 mg, 9.74 mmol) and Et_3N (1.31 g, 13.0 mmol) and heated to reflux for 2 hr, to give crude product which was purified by flash column chromatography to afford oxime **4l** (1.85 g, 92%) as a colourless oil; R_f = 0.44 (EtOAc : petrol, 6:4); υ_{max}(film)/cm^{-1} 3374, 3279, 3066, 2935, 1736, 1652, 1548, 1453, 1368, 1254, 1027, 914, 854, 732; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.22 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.82 (3H, s, CH_3CNOH), 2.12 (2H, m,

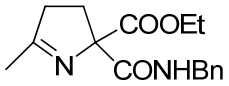
CH_2CH_2CH), 2.19 (2H, m, CH_2CH_2CH), 3.27 (1H, m, CH_2CH_2CH), 4.14 (2H, m, OCH_2CH_3), 4.43 (2H, m, $CONHCH_2$), 7.07 (1H, bs, N*H*), 7.24-7.33 (5H, m, Ar*H*), 8.70 (1H, s, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.6 (OCH_2CH_3), 14.0 (CH_3CNOH), 26.1 (CH_2CH_2CH), 33.2 (CH_2CH_2CH), 43.6 ($CONHCH_2$), 51.9 (CH_2CH_2CH), 61.6 (OCH_2CH_3), 127.4, 127.6, 127.8, 128.2 (Ar*C*), 138.0 (Ar*C*), 157.4 (*C*NOH) 168.2 (*C*ONH), 171.1 (*C*OO); m/z (ESI$^+$) 365 ($[M+CH_3CN+NH_4]^+$, 100%), 305 ($[M-H]^-$, 100%), HRMS (ESI$^+$) $C_{16}H_{22}N_2NaO_4^+$ ($[M+H]^+$) requires 307.1652; found 307.1647.

(±)Ethyl 2-(benzylcarbamoyl)-5-(tosyloxyimino)hexanoate, 6l



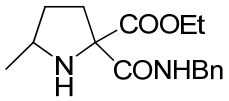
Following general procedure **E**, to a solution of oxime **4l** (1.56 g, 5.09 mmol) in dry CH_2Cl_2 (30 mL) was added Et_3N (771 mg, 7.63 mmol) at 0 °C followed by *p*-toluenesulphonyl choride (1.16 g, 6.11 mmol) and the mixture stirred at rt for 2 hr, to give crude product which was purified by flash column chromatography to afford tosyl oxime **6l** (1.82 g, 77%) as a white semi-solid; R_f = 0.61 (EtOAc : petrol, 6:4); υ_{max}(film)/cm^{-1} 3273, 3065, 2983, 1734, 1668, 1554, 1496, 1372, 1212, 1158, 1008, 815, 725; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.23 (3H, m, OCH_2CH_3), 1.90 (3H, s, CH_3CNOAr), 1.8-2.1 (2H, m, CH_2CH_2CH), 2.26 (2H, m, CH_2CH_2CH), 2.39 and 2.40 (3H, 2 x s, $ArCH_3$), 3.23 (1H, t, *J* 7.2 Hz, CH_2CH_2CH), 4.16 (2H, m, OCH_2CH_3), 4.4-4.50 (2H, m, $CONHCH_2$), 6.78 (1H, bs, N*H*), 7.24-7.81 (10H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 and 14.0 (OCH_2CH_3), 15.59 and 15.62 (CH_3CNOAr), 21.4 and 21.6 ($ArCH_3$), 24.8 and 25.0 (CH_2CH_2CH), 32.2 and 32.4 (CH_2CH_2CH), 43.6 and 43.7 ($CONHCH_2$), 51.2 and 51.8 (CH_2CH_2CH), 61.6 and 61.9 (OCH_2CH_3), 136.0, 127.5, 127.6, 128.5, 128.6, 128.7, 128.8, 129.1, 129.5 (Ar*C*), 132.6, 132.7, 137.9, 138.0, 145.0 (quaternary Ar*C*), 166.1 and 166.2 (*C*NOAr), 166.5, 166.8, 167.1 and 167.4 (*C*ONH), 169.2, 169.6. 170.2 (*C*OO); m/z (ESI$^+$) 943 ($[2M+Na]^+$), 100%), 483 ($[M+Na]^+$), 100%), HRMS (ESI$^+$) $C_{23}H_{28}N_2NaO_6S^+$ ($[M+Na]^+$) requires 483.1560; found 483.1562.

(±)Ethyl 2-(benzylcarbamoyl)-5-methyl-3,4-dihydro-2H-pyrrole-2-carboxylate, 7l



Following general procedure **F**, to tosyl oxime **6l** (91 mg, 0.19 mmol) in dry THF (5 mL) was added NaH (14 mg, 0.59 mol, 60%) and the mixture heated to reflux for 30 min, to give crude product which was purified by flash column chromatography to afford pyrroline **7l** (27 mg, 48%) as a colourless oil; **OR** To a stirring solution of tosyl oxime **6l** (96 mg, 0.21mmol) in dry CH_2Cl_2 (5 mL) was added anhydrous Cs_2CO_3 (136 mg, 0.42 mmol) and the mixture heated to reflux for 30 min to give the crude product, which was purified by flash column chromatography to afford pyrroline **7l** (39 mg 65%) as colourless oil: R_f = 0.15 (EtOAc : petrol, 8:2) υ_{max}(film)/cm^{-1} 3387, 2982, 1737, 1672, 1523, 1454, 1262, 1172, 1090, 1022, 700; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.27 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.11 (3H, s, CH_3C=N), 2.31 (1H, m, C(3)H*H*), 2.64 (1H, m, C(3)*H*H), 2.75 - 2.79 (2H, m, C(4)*H*H), 4.21 (2H, m, OCH_2CH_3), 4.32 (1H, dd, *J* 14.9, 5.2 Hz, NHCH*H*), 4.67 (1H, dd, *J* 14.9, 5.9 Hz, NHC*H*H), 7.13 (1H, bs, N*H*), 7.26-7.31 (5H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (OCH_2CH_3), 19.9 (CH_3C=N), 29.9 (*C*4), 40.1 (*C*3), 43.2 ($NHCH_2$), 62.1 (OCH_2CH_3), 87.3 (C2), 127.3, 127.5, 127.6, 128.5, 128.7 (Ar*C*), 138.1 (quaternary Ar*C*), 169.9 (*C*ONH), 170.4 (*C*OO), 181.3 (*C*5); m/z (ESI$^+$) 347 ([M+CH_3CN+NH_4]$^+$, 100%), 289 ([M+H]$^+$, 32%), HRMS (ESI$^+$) $C_{16}H_{20}N_2NaO_3^+$ ([M+H]$^+$) requires 311.1366; found 311.1369.

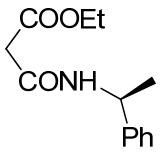
(±)Ethyl 2-(benzylcarbamoyl)-5-methylpyrrolidine-2-carboxylate, 9l



Following general procedure **H**, to a solution of pyrroline **7l** (41 mg, 0.14 mmol) in MeOH (2 mL) was added $NaBH_3CN$ (13 mg, 0.21 mmol) and 2 M HCl in MeOH (1 ml), to give the crude product which was purified by flash column chromatography to afford pyrrolidine **9l** (40 mg, 97%) as a colourless oil; υ_{max}(film)/cm^{-1} 3369, 2958, 1728, 1680, 1243, 1192, 1090, 921; R_f = 0.16 (EtOAc : petrol, 8:2) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.1 and 1.27 (3H, 2 x m, OCH_2CH_3), 1.41 (3H, d, *J* 6.7

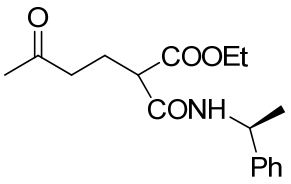
Hz, C*H*$_3$CHNH), 1.61 (1H, m, C(4)H*H*), 2.11 (1H, m, C(4)*H*H), 2.54 (1H, m, C(3)H*H*), 2.60 (1H, m, C(3)*H*H), 3.63 (1H, m, C(5)*H*), 4.0 and 4.27 (2H, 2 x m, OC*H*$_2$CH$_3$), 4.39 (1H, dd, *J* 14.7, 5.7 Hz, NHCH*H*), 4.52 (1H, dd, J 14.7, 5.2 Hz, NHC*H*H), 7.26-7.36 (5H, m, Ar*H*), 8.27 (1H, bs, N*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.8, 13.9, 14.0 (OCH$_2$*C*H$_3$), 19.1 (*C*H$_3$CHNH), 25.2 and 29.6 (*C*4), 32.3, 33.3 and 34.1 (*C*3), 43.9 (NH*C*H$_2$), 56.5 (*C*5), 62.0, 62.3 and 63.3 (O*C*H$_2$CH$_3$), 74.1 (*C*2), 125.7, 127.4, 127.5, 127.7, 128.2, 128.4, 128.6, 128.7 (Ar*C*), 137.8 and 141.8 (quaternary Ar*C*), 169.1 (*C*ONH), 170.3 (*C*OO); m/z (ESI$^+$) 313 ([M+Na]$^+$, 65%), 291 ([M+H]$^+$, 95%), HRMS (ESI$^+$) $C_{16}H_{23}N_2O_3^+$ ([M+H]$^+$) requires 291.1703; found 291.1709.

(*S*)-Ethyl 3-oxo-3-(1-phenylethylamino)propanoate



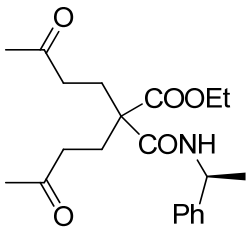
To a solution of ethyl 3-chloro-3-oxopropanoate (1.36 g, 9.06 mmol) in dry CH_2Cl_2 (20 mL) was added (*S*)-methyl benzylamine (1.21 g, 9.96 mmol) and Et_3N (1.37 g, 9.06 mmol) and the mixture stirred at rt for 2 hr, washed with HCl (1 M) followed by water and the product was extracted with CH_2Cl_2, dried over Na_2SO_4 and concentrated to afford malonamide (2.10 g, 98%) as a pale yellow oil; R_f = 0.30 (EtOAc : petrol, 1:1), $[\alpha]_D^{21}$ = -29º (c = 2.0, MeOH), υ_{max}(film)/cm^{-1} 3289, 3064, 2980, 1740, 1649, 1550, 1495, 1369, 1157, 1034, 763; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.28 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.50 (3H, d, *J* 6.9Hz, C*H*$_3$CHNH), 3.30 (2H, s, C*H*$_2$), 4.19 (2H, q, *J* 7.1 Hz, OC*H*$_2$CH$_3$), 5.14 (1H, m, CH$_3$C*H*NH), 7.23-7.36 (5H, m, Ar*H*), 7.52 (1H, d, *J* 6.3 Hz N*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (OCH$_2$*C*H$_3$), 22.0 (*C*H$_3$CHNH), 41.0 (*C*H$_2$), 48.8 (CH$_3$*C*HNH), 61.6 (O*C*H$_2$CH$_3$), 126.0, 127.3, 128.6 (Ar*C*), 142.9 (quaternary Ar*C*), 164.0 (*C*ONH), 169.6 (*C*OO); m/z (ESI$^+$) 294 ([M+CH$_3$CN+NH$_4$]$^+$, 100%), 258 ([M+Na]$^+$, 15%), 234 ([M-H]$^-$, 55%), HRMS (ESI$^+$) $C_{13}H_{17}NNaO_3^+$ ([M+Na]$^+$]) requires 258.1101; found 258.1133.

(±)Ethyl 5-oxo-2-((*S*)-1-phenylethylcarbamoyl)hexanoate, 3m



Following general procedure **A**, methyl vinyl ketone (441 mg, 5.74 mmol) was added to solution of the above malonamide (1.35 g, 6.31 mmol) and anhydrous K_2CO_3 (769 mg, 5.74 mmol) in dry CH_2Cl_2 (20 ml) and the mixture stirred at rt, to give crude products which were purified by flash column chromatography to afford adduct **3m** (1.16 g, 66%) as a colourless oil and double Michael addition product (351 mg, 20%) as a colourless oil; **3m** R_f = 0.27 (EtOAc : petrol, 6:4); υ_{max}(film)/cm^{-1} 3293, 3064, 2977, 1736, 1715, 1645, 1540, 1414, 1259, 1129, 948, 861, 804; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.26 (3H, m, OCH_2CH_3), 1.48 (3H, d, *J* 6.3 Hz, CH_3CHNH), 2.09 (3H, s, CH_3CO), 2.15 (2H, m, CH_2CH_2CH), 2.49 (2H, m, CH_2CH_2CH), 3.24 (1H, m, CH_2CH_2CH), 4.17 (2H, m, OCH_2CH_3), 5.08 (1H, m, CH_3CHNH), 6.83 (1H, m, NH), 7.23-7.34 (5H, m, ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH_2CH_3), 21.9 (CH_3CHN), 23.9 (CH_2CH_2CH), 29.9 (CH_3CO), 40.3 (CH_2CH_2CH), 48.9 (CH_3CHN), 51.4 (CH_2CH_2CH), 61.5 (OCH_2CH_3), 125.9, 126.0, 127.2, 127.3, 128.6 (ArC), 142.9 (quaternary ArC), 166.9 (CONH), 171.3 (COO), 207.8 (CO); m/z (ESI$^+$) 633 ([2M+Na]$^+$, 55%), 328 ([M+Na]$^+$, 100%), 304 ([M-H]$^-$, 65%), HRMS (ESI$^+$) $C_{17}H_{23}NNaO_4^+$ ([M+Na]$^+$]) requires 328.1519; found 328.1520.

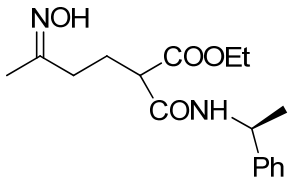
(±)(S)-Ethyl 5-oxo-2-(3-oxobutyl)-2-(1-phenylethylcarbamoyl)hexanoate



This by-product isolated from the above reaction (351 mg, 20%, 0:1 dr) as a colourless oil R_f = 0.26 (EtOAc : petrol, 6:4); υ_{max}(film)/cm^{-1} 3294, 3066, 2979, 1732, 1718, 1645, 1540, 1414, 1258, 1125, 948, 861, 804, 753; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.27 (3H, m, OCH_2CH_3), 1.50 (3H, d, *J* 6.9 Hz, CH_3CHNH), 1.96 and 2.12 (6H, s, 2 x CH_3CO), 2.07-2.34 (4H, m, CH_2CH_2C), 2.37-2.49 (4H, m, CH_2CH_2C), 4.19 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 5.09 (1H, m, CH_3CHNH), 7.23-7.36 (5H, m, ArH),

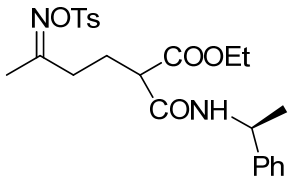
8.11 (1H, d, *J* 7.6 Hz, N*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (OCH_2CH_3), 22.2 (CH_3CHN), 29.8, 29.9 (CH_2CH_2C), 30.2, 30.7 (2 x CH_3CO), 38.9, 39.3 (CH_2CH_2C), 49.3 (CH_3CHN), 55.7 (CH_2CH_2C), 61.9 (OCH_2CH_3), 126.0, 127.3, 128.6 (Ar*C*), 143.5 (quaternary Ar*C*), 168.9 (*C*ONH), 174.5 (*C*OO), 207.1, 207.2 (*C*O); m/z (ESI$^+$) 773 ($[2M+Na]^+$, 100%), 398 ($[M+Na]^+$, 10%), 374 ($[M-H]^-$, 80%), HRMS (ESI$^+$) $C_{21}H_{29}NNaO_5^+$ ($[M+Na]^+$]) requires 398.1938; found 398.1924.

(±)Ethyl 5-(hydroxyimino)-2-((*S*)-1-phenylethylcarbamoyl)hexanoate, 4m



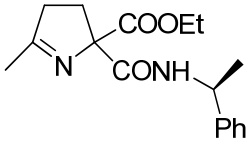
Following general procedure **C**, to a solution of adduct **3m** (969 mg, 3.18 mmol) in EtOH (20 mL) was added $NH_2OH.HCl$ (328 mg, 4.76 mmol) and Et_3N (642 mg, 6.36 mmol) and the mixture heated to reflux for 2 hr, to give crude product which was purified by flash column chromatography to afford oxime **4m** (947 mg, 93%) as a semi-solid; R_f = 0.34 (EtOAc : petrol, 6:4); υ_{max}(film)/cm^{-1} 3381, 3294, 3088, 2980, 1731, 1650, 1606, 1538, 1453, 1254, 1187, 915, 859, 729; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.18 and 1.23 (3H, m, OCH_2CH_3), 1.45 (3H, d, *J* 6.8 Hz, CH_3CHN), 1.80 and 1.82 (3H, 2 x s, CH_3C=N), 2.09 (2H, m, CH_2CH_2CH), 2.16 (2H, m, CH_2CH_2CH), 3.25 (1H, m, CH_2CH_2CH), 4.13 (2H, m, OCH_2CH_3), 5.07 (1H, m, CH_3CHN), 7.02 (1H, m, N*H*), 7.22-7.31 (5H, m, Ar*H*), 9.34 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.6 and 13.7 (CH_3C=N), 13.9 (OCH_2CH_3), 21.7 and 21.8 (CH_3CHN), 25.5 and 25.9 (CH_2CH_2CH), 33.18 and 33.2 (CH_2CH_2CH), 45.8 and 48.9 (CH_3CHN), 51.9 and 52.4 (CH_2CH_2CH), 61.6 (OCH_2CH_3), 125.9, 126.1, 127.2, 127.3, 128.5, 128.6 (Ar*C*), 142.9, 143.0, 143.1 (quaternary Ar*C*), 157.2, 157.3, 157.6 (*C*=NOH), 167.2 and 167.3 (*C*ONH), 170.9, 171.0. 171.1 and 171.2 (*C*OO**);** m/z (ESI$^+$) 663 ($[2M+Na]^+$, 100%), 343 ($[M+Na]^+$, 15%), 321 ($[M+H]^+$, 25%), HRMS (ESI$^+$) $C_{17}H_{24}N_2NaO_4^+$ ($[M+Na]^+$]) requires 343.1628; found 343.1628.

(±)Ethyl 2-((*S*)-1-phenylethylcarbamoyl)-5-(tosyloxyimino)hexanoate, 6m



Following general procedure **E**, to a solution of **4m** (789 mg, 2.46 mmol) in dry CH_2Cl_2 (20 mL) was added Et_3N (372 mg, 3.69 mmol) at 0 °C followed by *p*-toluenesulphonyl choride (562 mg, 2.95 mmol) and the mixture stirred for 2 hr, to give crude product which was purified by flash column chromatography to afford tosyl oxime **6m** (968 mg, 83%) as white semi-solid; R_f = 0.63 (EtOAc : petrol, 6:4); υ_{max}(film)/cm^{-1} 3273, 3061, 2979, 1734, 1649, 1550, 1495, 1375, 1264, 1207, 1121, 913, 815, 733; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.21 and 1.28 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.49 (3H, 2 x d, *J* 6.7 Hz, CH_3CHN), 1.87 and 1.93 (3H, 2 x s, $ArCH_3$), 2.07 (2H, m, CH_2CH_2CH), 2.26 (2H, m, CH_2CH_2CH), 2.40 and 2.42 (3H, s, $CH_3C{=}N$), 3.25 (1H, m, CH_2CH_2CH), 4.17 (2H, m, OCH_2CH_3), 5.10 (1H, m, CH_3CHN), 6.66 (1H, m, NH), 7.26-7.83 (10H, m, 2 x ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 and 14.0 (OCH_2CH_3), 15.8 and 15.9 ($ArCH_3$), 21.6 and 21.7 (CH_3CHN), 21.8 ($CH_3C{=}N$), 24.8 (CH_2CH_2CH), 32.9 and 33.0 (CH_2CH_2CH), 49.0 and 49.1 (CH_3CHN), 51.0 and 51.2 (CH_2CH_2CH), 61.6 and 61.6 (OCH_2CH_3), 126.0, 126.1, 127.3, 127.4, 128.6, 128.7, 128.8, 129.6 (ArC), 132.7, 142.9, 143.1, 144.9 (quaternary ArC), 166.4 and 166.5 ($C{=}NOAr$), 166.8 and 166.9 (CONH), 170.4 and 170.5 (COO); m/z (ESI^+) 497 ($[M+Na]^+$, 100%), 475 ($[M+H]^+$, 25%), 473 ($[M-H]^-$, 75%), HRMS (ESI^+) $C_{24}H_{30}N_2NaO_6S^+$ ($[M+Na]^+$]) requires 497.1717; found 497.1710.

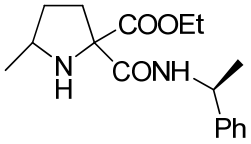
(±)Ethyl 5-methyl-2-((*S*)-1-phenylethylcarbamoyl)-3,4-dihydro-2H-pyrrole-2-carboxylate, 7m



Following general procedure **F**, to tosyl oxime **6m** (109 mg, 0.23 mmol) in dry THF (5 mL) was added NaH (17 mg, 0.68 mol, 60%) and heated to reflux for 30 min, to give crude product which was purified by column chromatography to afford pyrroline **7m** (51 mg, 73%) as a colourless oil; R_f

= 0.32 (EtOAc : petrol, 6:4); υ_{max}(film)/cm^{-1} 3294, 3063, 2977, 1736, 1714, 1645, 1541, 1495, 1369, 1258, 1208, 1129, 1097, 949, 861, 762; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.16 and 1.30 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.48 and 1.55 (3H, d, *J* 6.9 Hz, CH_3CHN), 2.10 and 2.14 (3H, s, CH_3C=N), 2.32 (1H, m, C(4)H*H*), 2.64 (1H, m, C(4)*H*H), 2.67 (1H, m, C(3)H*H*), 2.76 (1H, m, C(3)*H*H), 4.10-4.30 (2H, m, OCH_2CH_3), 5.14 (1H, m, CH_3CHN), 7.07 (1H, d, *J* 7.9 Hz, N*H*), 7.23-7.39 (5H, m, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 and 14.6 (OCH_2CH_3), 19.91 and 19.93 (CH_3C=N), 21.7 and 21.8 (CH_3CHN), 29.7 and 29.8 (*C*4), 40.0 and 40.1 (*C*3), 48.5 and 48.7 (CH_3CHN), 62.0 (OCH_2CH_3), 87.2 and 87.3 (*C*2), 125.9, 126.1, 126.3, 127.1, 127.3, 128.2, 128.4, 128.6, 129.8 (Ar*C*), 142.9 and 143.0 (quaternary Ar*C*), 169.4 (*C*ONH), 170.0 (*C*OO), 180.1 and 181.3(C5); m/z (ESI$^+$) 325 ([M+Na]$^+$, 80%), HRMS (ESI$^+$) $C_{17}H_{22}N_2NaO_3^+$ ([M+Na]$^+$) requires 325.1523; found 325.1522.

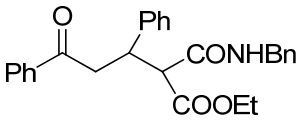
(±)Ethyl 5-methyl-2-((*S*)-1-phenylethylcarbamoyl)pyrrolidine-2-carboxylate, 9m



Following general procedure **H**, to a solution of pyrroline **7m** (43 mg, 0.14 mol) in MeOH (3 ml) was added $NaBH_3CN$ (13 mg, 0.21 mmol) and 2 M HCl in MeOH (1 mL) at rt, to give crude product which was purified by flash column chromatography to afford **9m** (39 mg, 90%) as a colourless oil; R_f = 0.18 (EtOAc : petrol, 8:2); υ_{max}(film)/cm^{-1} 3271, 3060, 2975, 1736, 1535, 1495, 1365, 1281, 1213, 1177, 1077, 836, 762; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.17 (3H, d, *J* 6.2 Hz, CH_3CHCH_2), 1.23 (3H, m, OCH_2CH_3), 1.49 (3H, m, CH_3CHNH), 1.93 (1H, m, C(4)*H*H), 2.26 (1H, m, C(4)H*H*), 2.30 (1H, m, C(3)*H*H), 2.49 (1H, m, C(3)H*H*), 3.10-3.40 (1H, m, C(5)*H*), 4.20 (2H, OCH_2CH_3), 5.06 (1H, m, CH_3CHNH), 7.24 (1H, d, *J* 7.3 Hz, N*H*), 7.26-7.35 (5H, m, Ar*H*), 8.15 (1H, d, *J* 8.1 Hz, CH_3CHNH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.7 (OCH_2CH_3), 21.8 and 21.9 (CH_3CHNH), 29.7 and 30.1 (CH_3CHN), 31.9 and 33.1 (*C*4), 34.2 and 34.2 (*C*3), 48.3 and 48.4 (*C*2), 54.3 and 55.1 (*C*5), 62.0 and 62.2 (OCH_2CH_3), 73.0 and 73.1 (*C*2), 125.8, 125.9, 126.0, 127.1, 127.2, 128.5, 128.6, 129.7 (Ar*C*), 143.1, 143.2, 143.4 (quaternary Ar*C*), 170.3, 170.7, 172.3,

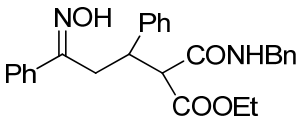
172.5 (*C*ONH), 172.0 (*C*OO); m/z (ESI$^+$) 327 ([M+Na]$^+$, 75%), 305 ([M+H]$^+$, 100%), HRMS (ESI$^+$) $C_{17}H_{25}N_2NaO_3^+$ ([M+Na]$^+$) requires 305.1860; found 305.1858.

(±)Ethyl 2-(benzylcarbamoyl)-5-oxo-3,5-diphenylpentanoate, 3n



Following general procedure **B**, chalcone (1.05 g, 5.07 mmol) in dry CH_2Cl_2 (10 mL) was added to a solution of benzyl ethyl malonamide (1.02 g, 4.62 mmol) and anhydrous K_2CO_3 (637 mg, 4.62 mmol) in dry CH_2Cl_2 (20 mL) and heated to reflux for 15 hr, to give crude product which was purified by flash column chromatography to afford adduct **3n** (911 mg, 92%) as a pale yellow solid; m.p. = 162-164 °C; R_f = 0.50 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 3302, 3063, 2980, 1734, 1651, 1597, 1545, 1496, 1452, 1204, 1156, 1028, 911, 749, 699; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.87 and 1.25 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.48 (1H, m, CH_2CHPh), 3.60 (1H, m, CH*H*CHPh), 3.73 and 3.77 (1H, d, *J* 8.6 Hz, CHPhC*H*), 3.87 and 4.12 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.09 (1H, m, C*H*HCHPh), 4.26 and 4.44 (2H, d, *J* 8.4 Hz, $NHCH_2Ph$), 6.82 (1H, t, *J* 5.5 Hz, N*H*), 7.22-7.92 (15H, m, 3 x Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.6, 14.1 (OCH_2CH_3), 42.3 (CH_2CHPh), 43.3 ($NHCH_2Ph$), 43.7 (*C*HPhCH), 58.0, 59.3 (CHPh*C*H), 61.4, 61.7 (OCH_2CH_3), 127.1-133.0 (3 x Ar*C*), 136.7, 137.6, 139.6 (3 x quaternary Ar*C*), 166.4 (*C*ONH), 170.8 (*C*OO), 197.6 (*C*O); m/z (ESI$^+$) 881 ([2M+Na]$^+$, 40%), 452 ([M+Na]$^+$, 45%), 428 ([M-H]$^-$, 100%), HRMS (ESI$^+$) $C_{27}H_{27}KNO_4^+$ ([M+K]$^+$) requires 468.1572; found 468.1556.

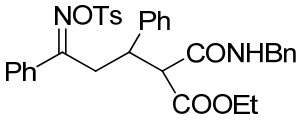
(±)Ethyl 2-(benzylcarbamoyl)-5-(hydroxyimino)-3,5-diphenylpentanoate, 4n



Following general procedure **C**, to a solution of adduct **3n** (1.01 g, 2.35 mmol) in EtOH (40 mL) was added $NH_2OH.HCl$ (324 mg, 4.70 mmol) and Et_3N (712 mg, 7.05 mmol) and the mixture heated to reflux for 7 hr, to give crude product which was purified by flash column chromatography to afford oxime **4n** (918 mg, 88%) as a white solid; m.p. = 136-138 °C; R_f = 0.41, 0.36 (EtOAc :

petrol, 1:1); υ_{max}(film)/cm^{-1} 3302, 3293, 3087, 2980, 1731, 1606, 1539, 1497, 1367, 1254, 1187, 1158, 1096, 935, 859, 731; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.81 and 1.27 (3H, 2 x t, *J* 7.1 Hz, OCH_2CH_3), 3.14, 3.40 (2H, 2 x m, CH_2CHPh), 3.68 (1H, m, CHPhCH), 3.81 and 4.22 (2H, m, OCH_2CH_3), 4.14 (1H, d, *J* 6.3 Hz, CHPhCH), 4.37, 4.60 (2 x 2H, 2 x m, $NHCH_2Ph$), 6.40 and 6.78 (1H, t, *J* 5.7 Hz, NH), 6.99-7.33 (15H, m, 3 x ArH), 9.07 (1H bs, OH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.5, 14.0 (OCH_2CH_3), 30.3, 30.6 (CH_2CHPh), 43.45, 43.5 (CHPhCH), 43.8, 44.7 ($NHCH_2Ph$), 59.5, 59.7 (CHPhCH), 60.0, 61.9 (OCH_2CH_3), 126.4-128.6 (3 x ArC), 135.2, 137.5, 138.9 (3 x quaternary ArC), 157.5, 157.7 (C=NOH), 166.4, 167.2 (CONH), 170.5, 170.9 (COO); m/z (ESI$^+$) 467 ([M+Na]$^+$, 35%), 443 ([M-H]$^-$, 100%), HRMS (ESI$^+$) $C_{27}H_{27}N_2O_4^-$ ([M-H]$^-$) requires 443.1965; found 443.1972.

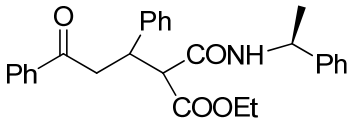
(±)Ethyl 2-(benzylcarbamoyl)-3,5-diphenyl-5-(tosyloxyimino)pentanoate, 6n



Following general procedure **E**, to a solution of oxime **4n** (503 mg, 1.32 mmol) in dry CH_2Cl_2 (20 mL) was added Et_3N (266 mg, 2.64 mol) at 0 °C followed by *p*-toluenesulphonyl chloride (376 mg, 1.98 mmol) and the mixture stirred at rt for 5 hr, to give crude product which was purified by column chromatography to afford tosyl oxime **6n** (289 mg, 42%) as a white semi-solid; R_f = 0.53 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3269, 3060, 2980, 1739, 1649, 1552, 1495, 1307, 1264, 1207, 1152, 1008, 914, 815, 763; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.86 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.48 (3H, s, $ArCH_3$), 2.94 (1H, dd, *J* 15.3, 10.5 Hz, CHHCHPh), 3.09 (1H, dd, *J* 15.3, 4.1 Hz CHHCHPh), 3.35 (1H, m, CHPhCH), 3.55 (1H, d, *J* 10.8 Hz, CHPhCH), 3.83 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.35 (1H, dd, *J* 14.7, 5.6 Hz, NHCHHPh), 4.52 (1H, dd, *J* 14.7, 6.1 Hz, NHCHHPh), 6.96 (1H, t, *J* 5.6 Hz, NH), 6.81-7.71 (15H, m, 3 x ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (OCH_2CH_3), 21.7 ($ArCH_3$), 38.7 (CH_2CHPh), 43.7 (CHPhCH), 44.5 ($NHCH_2Ph$), 58.5 (CHPhCH), 61.1 (OCH_2CH_3), 127.1-129.3 (3 x ArC), 132.4, 137.6, 137.9, 144.4 (4 x quaternary

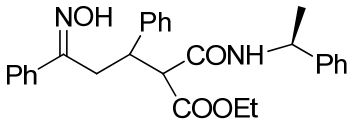
Ar*C*), 166.7 (*C*=NOAr), 170.3 (*C*ONH), 170.5 (*C*OO); m/z (ESI$^+$) 621 ([M+Na]$^+$, 100%), 597 ([M-H]$^-$, 30%), HRMS (ESI$^+$) $C_{34}H_{34}N_2NaO_6S^+$ ([M+Na]$^+$) requires 621.2030; found 621.2029.

(±)Ethyl 5-oxo-3,5-diphenyl-2-((*S*)-1-phenylethylcarbamoyl)pentanoate, 3o



Following general procedure **B**, chalcone (508 mg, 2.44 mmol) in dry CH_2Cl_2 (5 mL) was added to a solution of ethyl (*S*)-methyl benzyl malonamide (522 mg, 2.22 mmol) and anhydrous K_2CO_3 (306 mg, 2.22 mol) in dry CH_2Cl_2 (15 mL) and heated to reflux for 15 hr, to give crude product which was purified by flash column chromatography to afford adduct **3o** (911 mg, 92%) as a pale yellow solid**;** m.p. = 171-174 °C; R_f = 0.49 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 3302, 3063, 2980, 1734, 1651, 1597, 1545, 1496, 1452, 1204, 1156, 1028, 911, 749, 699; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.25 (3H, m, OCH_2CH_3), 1.29 (3H, d, *J* 6.6Hz, CH_3CHNH), 3.50 – 3.80 (4H, m, CH_2CHPh, CHPhC*H*, and $CH(C(O)_2)$, 4.13 (1H, m, CH_2CHPh), 4.20 (2H, m, OCH_2CH_3), 4.94 (1H, m, CH_3CHNH), 6.72 (1H, d, *J* 7.7Hz, NH), 7.05-7.94 (15H, m, 3 x Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (OCH_2CH_3), 21.5 (CH_3CHNH), 42.3 (CH_2CHPh), 42.5 (CH_2CHPh), 48.6 (CH_3CHNH), 57.7 (CHPh*C*H), 61.6 (OCH_2CH_3), 125.8-128.5 (3 x Ar*C*), 133.0, 136.7, 139.7 (3 x quaternary Ar*C*), 165.5 (*C*ONH), 171.1 (*C*OO), 197.7 (*C*O); m/z (ESI$^+$) 502 ([M+CH_3CN+NH_4]$^+$, 100%), 444 ([M+H]$^+$, 10%), 442 ([M-H]$^-$, 100%), HRMS (ESI$^+$) $C_{28}H_{29}NNaO_4^+$ ([M+Na]$^+$) requires 466.1989; found 466.1998.

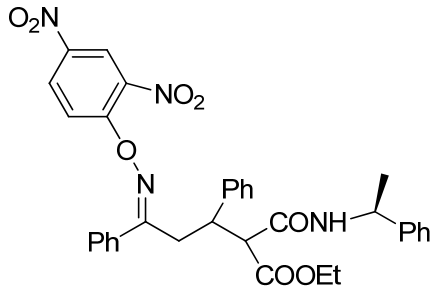
(±)Ethyl 5-(hydroxyimino)-3,5-diphenyl-2-((*S*)-1-phenylethylcarbamoyl pentanoate, 4o



Following general procedure **C**, to a solution of adduct **3o** (816 mg, 1.84 mmol) in EtOH (15 mL) was added $NH_2OH.HCl$ (254 mg, 3.68 mmol) and Et_3N (465mg, 4.60 mol) and the mixture heated to reflux for 7 hr, to give crude product which was purified by flash column chromatography to

afford oxime **4o** (801 mg, 95%) as a pale yellow solid; m.p. = 86-88 °C; R_f = 0.41, 0.36 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 3302, 3283, 3063, 2982, 1730, 1649, 1602, 1543, 1446, 1325, 1215, 1177, 1094, 983, 929, 859, 756; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.80 and 0.87, (3H, m, OCH_2CH_3), 1.04 and 1.19 (3H, d, *J* 6.8Hz, CH_3CHNH), 3.14 (2H, m, CH_2CHPh), 3.39 (1H, m, CHPhC*H*), 3.68 (1H, m, CH_2CHPh), 3.81 and 4.21 (2H, m, OCH_2CH_3), 4.81 (1H, m, CH_3CHNH), 6.37 (1H, d, *J* 8.4 Hz, N*H*), 6.87-7.38 (15H, m, 3 x Ar*H*), 9.44 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.5 and 14.0 (OCH_2CH_3), 21.8 and 22.6 (CH_3CHNH), 30.1 (CH_2CHPh), 43.3 and 44.6 (CH_2CHPh), 49.2, 48.5 (CH_3CHNH), 59.7, 59.6 (CHPhCH), 61.9, 61.8 (OCH_2CH_3), 125.9-128.7 (3 x Ar*C*), 135.3-142.0 (3 x quaternary Ar*C*), 157.5, 157.4 (*C*=NOH), 166.4, 165.6 (*C*ONH), 171.1, 70.5 (*C*OO); m/z (ESI$^+$) 939 ([2M+Na]$^+$, 60%), 517 ([M+CH_3CN+NH_4]$^+$, 75%), 481 ([M+Na]$^+$, 80%), 459 ([M+H]$^+$, 35%), 457 ([M-H]$^-$, 100%), HRMS (ESI$^+$) $C_{28}H_{30}N_2NaO_4^+$ ([M+Na]$^+$) requires 481.2098; found 481.2094.

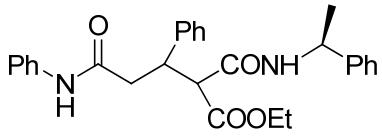
(±)Ethyl 5-(2,4-dinitrophenoxyimino)-3,5-diphenyl-2-((S)-1-phenylethyl- carbamoyl) pentanoate, 5o



Following general procedure **D**, to a solution of oxime **4o** (507 mg, 1.10 mmol) in EtOH (20 mL) sodium metal (30 mg, 1.32 mmol) was added and the mixture stirred at rt for 30 min and followed by 2,4-dinitrofluorobenzene (308 mg, 1.66 mmol) at 0 °C slowly, to give crude product which was purified by flash column chromatography to afford ether **5o** (499 mg, 72%) as a yellow semi-solid; R_f = 0.55 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 3320, 3052, 2982, 1738, 1659, 1605, 1531, 1473, 1343, 1260, 1056, 909, 831, 761, 699; δ_H(400 MHz; $CDCl_3$; Me_4Si) 0.83 and 1.26 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 0.99 and 1.53 (3H, d, *J* 6.9Hz, CH_3CHNH), 3.20 and 3.30 (2H, dd, *J* 13.0, 4.0 Hz, CH_2CHPh), 3.6 – 3.90 (2H, m, CHPhC*H* and C*H*PhCH), 3.83 and 4.25 (2H, q, *J* 7.1 Hz,

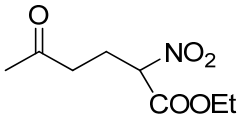
OC*H*$_2$CH$_3$), 4.76 (1H, m, CH$_3$C*H*NH), 5.90 and 6.90 (1H, d, *J* 8.0Hz, N*H*), 6.99-8.88 (18H, m, 4 x Ar*H*); δ_C(100 MHz; CDCl$_3$; Me$_4$Si) 13.4 and 14.0 (OCH$_2$*C*H$_3$), 20.7 and 21.9 (*C*H$_3$CHNH), 32.1 and 32.5 (*C*H$_2$CHPh), 43.5 and 44.5 (CH$_2$*C*HPh), 48.6 and 49.4 (CHPh*C*H), 59.2 and 59.3 (CH$_3$*C*HNH), 61.5 and 61.9 (O*C*H$_2$CH$_3$), 116.9-132.6 (4 x Ar*C*), 135.6-142.6 (5 x quaternary Ar*C*), 157.0 and 157.1 (*C*=NOAr), 165.1 and 165.2 (*C*ONH), 165.8 (quaternary Ar*C*), 169.3 and 169.7 (*C*OO); m/z (ESI$^+$) 683 ([M+CH$_3$CN+NH$_4$]$^+$, 65%), 647 ([M+Na]$^+$, 45%), 623 ([M-H]$^-$, 35%), HRMS (ESI$^+$) $C_{34}H_{32}N_4NaO_8^+$ ([M+Na]$^+$) requires 647.2112; found 647.2114.

(±)Ethyl 5-oxo-3-phenyl-5-(phenylamino)-2-(1-phenylethylcarbamoyl) pentanoate, 8



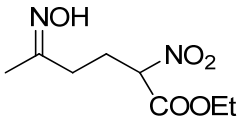
Following general procedure **F**, ether **5o** (139 mg, 0.22 mmol) in dry THF (10 mL) was added NaH (16mg, 0.66 mol, 60%) and the mixture heated to reflux for 30 min, to give crude product which was purified by flash column chromatography as the Beckman rearrangement product **8** (262 mg, 78%) as a yellow crystal m.p. = 236-238 °C; R_f = 0.43 (EtOAc : petrol, 2:1); υ_{max}(film)/cm^{-1} 3311, 3205, 3064, 2980, 1737, 1678, 1654, 1601, 1548, 1364, 1263, 1180, 1082, 990, 860, 753; δ_H(400 MHz; CDCl$_3$; Me$_4$Si) 1.29 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.37 (3H, d, *J* 6.9 Hz, C*H*$_3$CHNH), 2.60 (1H, dd, *J* 13.3, 5.5 Hz CH*H*CHPh), 3.14 (1H, dd, *J* 13.3, 10.1 Hz C*H*HCHPh), 3.75 (1H, d, *J* 6.1 Hz, CHPhC*H*), 3.87 (1H, m, C*H*PhCH), 4.18 (2H, q, *J* 7.1 Hz, OC*H*$_2$CH$_3$), 5.12 (1H, m, CH$_3$C*H*NH), 6.90-7.36 (15H, m, 3 x Ar*H*), 7.56 (1H, d, *J* 7.9 Hz, CH$_3$CHN*H*), 9.04 (1H, s, CON*H*); δ_C(100 MHz; CDCl$_3$; Me$_4$Si) 13.7, 14.1 (OCH$_2$*C*H$_3$), 21.2, 21.4 (*C*H$_3$CHNH), 41.3, 41.7 (*C*H$_2$CHPh), 44.5 (*C*HPhCH), 48.6 (CH$_3$*C*HNH), 53.7 (CHPh*C*H), 61.5 (O*C*H$_2$CH$_3$), 119.4, 123.6, 126.0, 127.1, 127.2, 127.5, 128.1, 128.2, 128.3, 128.5 (3 x Ar*C*), 137.8, 138.6, 142.0 (3 x quaternary Ar*C*), 165.8 (*C*ONH), 169.3 (*C*ONH), 171.1 (*C*OO); m/z (ESI$^+$) 481 ([M+Na]$^+$, 100%), 459 ([M+H]$^+$, 95%), 457 ([M-H]$^-$, 95%), HRMS (ESI$^+$) $C_{28}H_{30}N_2NaO_4^+$ ([M+Na]$^+$) requires 481.2098; found 481.2102.

(±)Ethyl 2-nitro-5-oxohexanoate 3p



Following general procedure **A**, methyl vinyl ketone (400 g, 3.81 mmol) was added to a solution of ethyl nitroacetate (508 mg, 3.81 mmol) and anhydrous K_2CO_3 (789 mg, 5.72 mmol) in CH_2Cl_2 (20 mL) and the mixture stirred at rt, to give crude product which was purified by flash column chromatography to afford adduct **3p** (612 mg, 80%) as a semi-solid; R_f = 0.33 (EtOAc : petrol, 6:4); υ_{max}(film)/cm^{-1} 2981, 1747, 1554, 1445, 1339, 1240, 860; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.28 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.14 (3H, s, $COCH_3$), 2.45 (2H, m, CH_2CH_2CH), 2.58 (2H, m, CH_2CH_2CH), 4.25 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 5.21 (1H, dd, *J* 8.3, 6.1 Hz, CH_2CH_2CH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.8 (OCH_2CH_3), 24.0 (CH_2CH_2CH), 29.9 ($COCH_3$), 38.3 (CH_2CH_2CH), 63.0 (OCH_2CH_3), 86.7 (CH_2CH_2CH), 164.2 (*C*OO), 206.0 (*C*O); m/z (ESI$^+$) 202 ([M-H]$^-$, 75%), HRMS (ESI$^-$) $C_8H_{12}NO_3^-$ ([M-H]$^-$) requires 202.0721; found 202.0722.

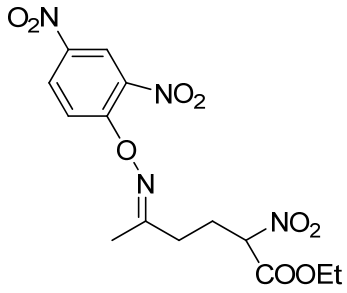
(±)Ethyl 5-(hydroxyimino)-2-nitrohexanoate, 4p



Following general procedure **C**, to a solution of adduct **3p** (572 mg, 2.81 mmol) in EtOH (20 mL) was added $NH_2OH.HCl$ (486 mg, 7.04 mmol) and Et_3N (853 mg, 8.45 mmol) and heated to reflux for 2 hr, to give crude product which was purified by flash column chromatography to afford oxime **4p** (602 mg, 98%) as a pale yellow solid; m.p. = 94 °C; R_f = 0.47 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3319, 2983, 1748, 1555, 1445, 1371, 1243, 858; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.29 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.88 and 1.90 (3H, s, $CNOHCH_3$), 2.30 – 2.42 (4H, m, CH_2CH_2), 4.27 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 5.22 (1H, dd, *J* 8.9, 6.8 Hz, CH_2CH_2CH), 7.98 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (OCH_2CH_3), 19.9 ($CNOHCH_3$), 26.0

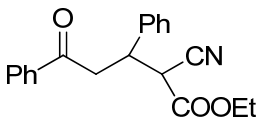
(CH_2CH_2CH), 31.5 (CH_2CH_2CH), 63.1 (OCH_2CH_3), 87.0 (CH_2CH_2CH), 155.9 ($CNOHCH_3$), 164.3 and 164.4 (COO); m/z (ESI^-) 217 ($[M-H]^-$, 100%), 241 ($[M+Na]^+$, 20%), HRMS (ESI^+) $C_8H_{13}N_2O_5^-$ ($[M-H]^-$) requires 217.0830; found 217.0821.

(±)Ethyl 5-(2,4-dinitrophenoxyimino)-2-nitrohexanoate, 5p



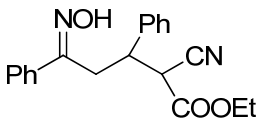
Following general procedure **D**, to a solution of oxime **4p** (201 mg, 0.92 mmol) in EtOH (10 mL) sodium metal (23 mg, 1.02 mmol) was added and the mixture stirred at rt for 30 min and followed by slow addition of 2,4-dinitrofluorobenzene (256 mg, 1.38 mmol) at 0 °C, to give crude product which was purified by flash column chromatography to afford ether **5p** (252 mg, 65%) as a yellow semi-solid; R_f = 0.44 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2983, 1750, 1607, 1562, 1532, 1473, 1343, 1287, 925, 831, 743; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.32 and 153 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.21 (3H, s, $CNOArCH_3$), 2.57 (2H, m, CH_2CH_2CH), 2.64 (2H, m, CH_2CH_2CH), 4.32 (2H, m, OCH_2CH_3), 5.26 (1H, dd, *J* 8.6, 5.9 Hz, CH_2CH_2CH), 7.89 (1H, d, *J* 9.3 Hz, Ar*H*), 8.43 (1H, dd, *J* 9.3, 2.7 Hz, Ar*H*), 8.88 (1H, d, *J* 2.7 Hz, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 and 14.3 (OCH_2CH_3), 16.6 ($CNOArCH_3$), 25.9 (CH_2CH_2CH), 31.8 (CH_2CH_2CH), 63.3 (OCH_2CH_3), 86.7 (CH_2CH_2CH), 117.0, 121.8, 122.1, 129.0, 129.5 (Ar*C*), 157.0 ($CNOArCH_3$), 164.0 (quaternary Ar*C*), 164.5 (COO); m/z (ESI^-) 383 ($[M-H]^-$, 100%), 407 $[M+Na]^+$, 100%), HRMS (ESI^+) $C_{14}H_{16}N_4O_9^+$ ($[M+Na]^+$) requires 407.0809; found 407.0806.

(±)Ethyl 2-cyano-5-oxo-3,5-diphenylpentanoate, 3q



Following general procedure **B**, chalcone (2.26 g, 10.9 mmol) was added to a solution of ethyl cyanoacetate (1.12 g, 9.91 mmol) and anhydrous K_2CO_3 (1.36 g, 10.9 mmol) in CH_2Cl_2 (50 mL) and the mixture heated to reflux for 15 hr, to give crude product which was purified by flash column chromatography to afford adduct **3q** (2.87 g, 93%) as a white solid; m.p. = 147-150 °C ; R_f = 0.53 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 3065, 2984, 2210, 1744, 1685, 1597, 1497, 1449, 1370, 1253, 1210, 853, 754, 702; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.1, 1.20 and 1.32 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.54 and 3.68 (2H, m, CH_2CHPh), 3.83 (1H, d, *J* 6.8 Hz, CHPhC*H*), 4.17, 4.27 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 4.18, 5.53 (1H, m, C*H*PhCH), 7.26-7.61 (10H, m, 2 x Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (OCH_2CH_3), 40.3 (*C*HPhCH), 41.8 (CH_2CHPh), 43.5 (CHPh*C*H), 62.9 (OCH_2CH_3), 115.8 (*C*N), 127.9-133.9 (Ar*C*), 136.4, 138.5 (quaternary Ar*C*), 165.1 (*C*OO), 196.6 and 197.1 (*C*O); m/z (ESI$^+$) 665 ([2M+Na]$^+$, 100%), 344 ([M+Na]$^+$, 90%), 320 ([M-H]$^-$, 100%), HRMS (ESI$^+$) $C_{20}H_{19}NNaO_3^+$ ([M+Na]$^+$) requires 344.1257; found 344.1261.

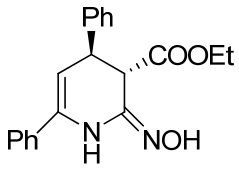
(±)Ethyl 2-cyano-5-(hydroxyimino)-3,5-diphenylpentanoate, 4q



Following general procedure **J**, to a solution of adduct **232** (1.12 g, 3.48 mmol) in EtOH (30 mL) was added $NH_2OH.HCl$ (264 mg, 3.83 mmol) and sodium acetate (342 mg, 1.2 mmol) and heated to reflux for 1 hr, gave a mixture of crude products from which was isolated by column chromatography substituted pyridine **17** (355 mg, 30%) as a crystals, along with oxime **4q** (680 mg, 58%) as a colourless oil, R_f = 0.47 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3417, 3073, 2986, 2208, 1743, 1605, 1476, 1454, 1255, 1026, 953, 853, 762; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.00-1.20 (3H, m, OCH_2CH_3), 3.28 and 3.59 (2H, m, CH_2CHPh), 3.79 (1H, m, C*H*PhCH), 3.88 (1H, d, *J* 6.6 Hz, CHPhC*H*), 4.00-4.20 (2H, m, OCH_2CH_3), 7.18-7.44 (10H, m, 2 x Ar*H*), 9.56 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.8 (OCH_2CH_3), 29.2 and 30.4 (CH_2CHPh), 42.7 (CHPh*C*H), 44.0 and 44.5 (*C*HPhCH), 62.8 and 62.9 (OCH_2CH_3), 115.5 (*C*N), 126.2-129.4 (Ar*C*), 134.6, 137.6 (quaternary

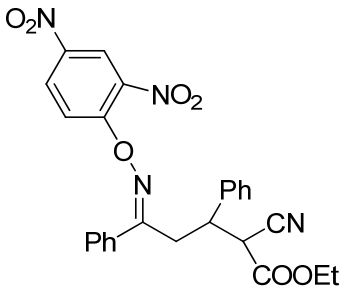
Ar*C*), 156.8 and 156.9 (*C*NOH), 165.0 and 165.2 (*C*OO); m/z (ESI$^+$) 695 ([2M+Na]$^+$, 100%), 359 ([M+Na]$^+$, 65%), HRMS (ESI$^+$) $C_{20}H_{20}N_2NaO_3^+$ ([M+Na]$^+$) requires 359.1366; found 359.1362.

(±) (3*S*,4*R*)-ethyl 2-(hydroxyimino)-4,6-diphenyl-1,2,3,4-tetrahydropyridine-3-carboxylate, 17



Pyridine **17** was isolated as a by-product which after recrystallisation (355 mg, 30%) was obtained as pale yellow crystals; m.p. = 92-94 °C; R_f = 0.30 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3423, 3074, 2985, 1735, 1607, 1476, 1248, 1026, 910, 762, 698; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.16 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.06 (1H, bs, O*H*), 3.57 (1H, d, *J* 7.1 Hz, (C3)*H*), 4.10-4.20 (2H, m, OCH_2CH_3), 4.22 (1H, dd, *J* 7.1, 4.6 Hz, (C4)*H*), 5.29 (1H, d, *J* 4.6 Hz, (C5)*H*), 7.22-7.54 (10H, m, 2 x Ar*H*), 8.06 (1H, bs, N*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 and 14.2 (OCH_2CH_3), 41.8 (*C*4), 49.7 (*C*3), 61.5 (OCH_2CH_3), 102 (*C*5), 125.4-128.9 (Ar*C*), 135.6, 136.5 (quaternary Ar*C*), 141.5 (*C*5), 145.9 (*C*2), 169.7 (*C*OO); m/z (ESI$^+$) 335 ([M-Na]$^-$, 35%), HRMS (ESI$^+$) $C_{20}H_{19}N_2O_3^-$ ([M-Na]$^-$) requires 335.1401; found 335.1401.

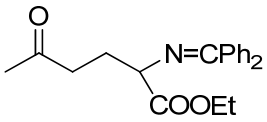
(±)Ethyl 2-cyano-5-(2,4-dinitrophenoxyimino)-3,5-diphenylpentanoate, 5q



Following general procedure **D**, to a solution of oxime **4q** (357 mg, 1.06 mmol) in EtOH (15 mL) sodium metal (29 mg, 1.27 mmol) was added followed by 2,4-dinitrofluorobenzene (296 mg, 1.59 mmol) at 0 °C slowly and the mixture stirred at rt for 30 min, to give crude product which was purified by column chromatography to afford ether **5q** (385 mg, 72%) as a yellow semi-solid; R_f =

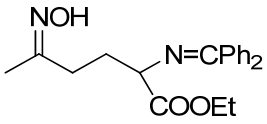
0.36 (EtOAc : petrol, 2:8); υ_{max}(film)/cm^{-1} 3016, 2983, 2203, 1731, 1605, 1532, 1473, 1259, 1144, 925, 761; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.05 and 1.13 and 1.53 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.50-3.70 (2H, m, CH_2CHPh), 3.78-3.80 (1H, m, CHPhCH), 3.93 (1H, d, *J* 6.5 Hz, CHPhCH), 4.04 and 4.13 and 4.32 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 7.10-8.93 (13H, m, 3 x ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.6, 13.8 and 14.2 (OCH_2CH_3), 31.9, 32.9 (CH_2CHPh), 43.0 (CHPhCH), 43.6 (CHPhCH), 63.0, 63.1 and 66.7 (OCH_2CH_3), 114.2 (CN), 117.0-129.4 (ArC), 131.2, 132.4, 135.5, 136.3 (quaternary ArC); m/z (ESI$^+$) 525 ([M+Na]$^+$, 95%), 501 ([M-Na]$^-$, 45%), HRMS (ESI$^+$) $C_{26}H_{22}N_4NaO_7^+$ ([M+Na]$^+$) requires 525.1381; found 525.1379.

(±)Ethyl 2-(diphenylmethyleneamino)-5-oxohexanoate, 3r



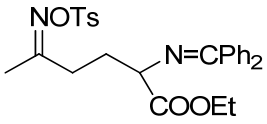
Following general procedure **A**, methyl vinyl ketone (666 mg, 9.52 mmol) was added to solution of ethyl 2-(diphenylmethyleneamino)acetate (2.12 g, 7.94 mmol) and anhydrous Cs_2CO_3 (3.87 g, 11.91 mmol) in dry CH_2Cl_2 (25 mL) and the mixture heated to reflux for 1 hr, to give crude product which was purified by flash column chromatography to afford adduct **3r** (2.39 g, 89%) as a white solid; m.p. = 87-90 °C; R_f = 0.65 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3059, 2981, 1734, 1657, 1598, 1446, 1318, 1276, 1192, 941, 857; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.25 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.11 (3H, s, $COCH_3$), 2.17 (2H, m, CH_2CH_2CH), 2.51 (2H, t, *J* 7.1 Hz, CH_2CH_2CH), 4.08 (1H, t, *J* 6.8 Hz, CH_2CH_2CH), 4.16 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 7.16-7.64 (10H, m, 2 x ArH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.8 (OCH_2CH_3), 27.3 (CH_2CH_2CH), 29.5 ($COCH_3$), 39.4 (CH_2CH_2CH), 60.6 (OCH_2CH_3), 63.8 (CH_2CH_2CH), 127.4, 127.7, 128.2, 128.4, 128.5, 130.1 (ArC), 135.9, 139.0 (quaternary ArC), 170.5 (N=CPh_2), 171.5 (COO), 207.7 (CO); m/z (ESI$^+$) 338 ([M+H]$^+$, 40%), 360 ([M+Na]$^+$, 90%), 697 ([2M+Na]$^+$, 85%), HRMS (ESI$^+$) $C_{21}H_{23}NNaO_3^+$ ([M+Na]$^+$) requires 360.1570; found 360.1569.

(±)Ethyl 2-(diphenylmethyleneamino)-5-(hydroxyimino)hexanoate, 4r



Following general procedure **C**, to a solution of adduct **3r** (2.02 g, 5.99 mmol) in EtOH (30 mL) $NH_2OH.HCl$ (454 mg, 6.59 mmol) and Et_3N (908 mg, 8.99 mmol) was added and stirred at rt for 1 hr, to give crude product which was purified by column chromatography to afford oxime **4r** (1.39 g, 66%) as a colourless oil; R_f = 0.52 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3153, 3080, 3023, 2982,1734, 1649, 1598, 1429, 1274, 1188, 1031, 998, 811, 767; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.24, 1.28 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.84 (3H, s, $CNOHCH_3$), 2.19 (2H, m, CH_2CH_2CH), 2.53 (2H, t, *J* 6.9 Hz, CH_2CH_2CH), 4.07, 4.66 (1H, t, *J* 6.8 Hz, CH_2CH_2CH), 4.17 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 7.16-7.65 (10H, m, 2 x Ar*H*), 8.19, 9.34 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.2, 13.8 (OCH_2CH_3), 19.3 $CNOHCH_3$), 26.2, 29.8 (CH_2CH_2CH), 32.0, 38.9 (CH_2CH_2CH), 60.6, 60.7 (OCH_2CH_3), 64.3, 73.7 (CH_2CH_2CH), 127.3-132.5 (Ar*C*), 136.1, 139.0 (quaternary Ar*C*), 157.1, 157.4 *C*=NOH), 170.6, 171.5 (N=*C*Ph_2), 172.1, 176.4 (*C*OO); m/z (ESI^+) 353 ($[M+H]^+$, 65%), 375 ($[M+Na]^+$, 95%), 727 ($[2M+Na]^+$, 100%), HRMS (ESI^+) $C_{21}H_{24}N_2NaO_3^+$ ($[M+Na]^+$) requires 375.1679; found 375.1680.

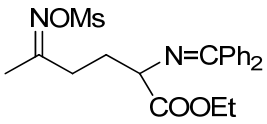
(±)Ethyl 2-(diphenylmethyleneamino)-5-(tosyloxyimino)hexanoate, 5r



Following general procedure **E**, to a solution of oxime **4r** (509 mg, 1.44 mmol) in dry CH_2Cl_2 (20 mL) was added Et_3N (290 mg, 2.88 mmol) at 0 °C followed by *p*-toluenesulphonyl choride (410 mg, 2.16 mmol) and the mixture stirred for 5 hr at rt to give crude product, which was purified by flash column chromatography to afford tosyl oxime **5r** (496 mg, 67%) as a colourless semi-solid; R_f = 0.62 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3032, 2982, 1734, 1649, 1444, 1275, 1190, 997, 910, 767, 727; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.26 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.91 (3H,

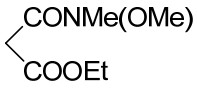
s, CNOArCH_3), 2.10 (2H, m, CH_2CH_2CH), 2.31 (2H, m, CH_2CH_2CH), 2.41 (3H, s, ArCH_3), 4.11 (1H, t, *J* 6.9 Hz, CH_2CH_2CH), 4.18 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 7.09-7.82 (10H, m, 2 x Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9, 15.5 (OCH_2CH_3), 19.5 CNOArCH_3), 21.1, 21.4 (ArCH_3), 26.9 (CH_2CH_2CH), 32.0 (CH_2CH_2CH), 60.7, 61.2 (OCH_2CH_3), 63.7, 64.1 (CH_2CH_2CH), 127.7-129.7 (Ar*C*), 137.4, 139.3, 144.5 (quaternary Ar*C*), 166.6 (*C*=NOAr), 167.0 (N=*C*Ph_2), 170.7 (*C*OO); m/z (ESI^+) 507 ($[M+H]^+$, 100%), HRMS (ESI^+) $C_{28}H_{30}N_2O_5S^+$ ($[M+H]^+$) requires 507.1948; found 507.1947.

(±)Ethyl 2-(diphenylmethyleneamino)-5-(methylsulfonyloxyimino)hexanoate



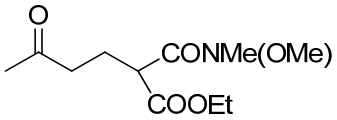
Following general procedure **E**, to a solution of oxime **4r** (241 mg, 0.68 mmol) in dry CH_2Cl_2 (10 mL) was added pyridine (108 mg, 1.37 mmol) at 0 °C followed by methanesulphonyl chloride (93 mg, 0.82 mmol) and the mixture stirred for 2 hr at rt, to give crude product which was purified by flash column chromatography to afford mesyl oxime (213 mg, 73%) as a colourless oil; R_f = 0.42 (EtOAc : petrol, 3:7); υ_{max}(film)/cm^{-1} 2986, 1738, 1623, 1523, 1445, 1367, 1223, 1156, 1097, 860, 782; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.26 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.01 (3H, s, CNOMsCH_3), 2.19 (2H, m, CH_2CH_2CH), 2.37 (2H, t, *J* 6.8 Hz, CH_2CH_2CH), 3.01, 3.03 (3H, s, SO_2CH_3), 4.10 (1H, t, *J* 6.8 Hz, CH_2CH_2CH), 4.16 (2H, q, *J* 7.1 Hz, OCH_2CH_3), 7.15-7.64 (10H, m, 2 x Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH_2CH_3), 15.7 (CNOMsCH_3), 29.3 (CH_2CH_2CH), 32.2 (CH_2CH_2CH), 36.2 (SO_2CH_3), 61.1 (OCH_2CH_3), 64.2 (CH_2CH_2CH), 127.5-130.5 (Ar*C*), 136.0, 138.9 (quaternary Ar*C*), 167.5 *C*=NOMs), 168.1 (N=*C*Ph_2), 171.3 (*C*OO); m/z (ESI^+) 453 ($[M+Na]^+$, 100%), 883 ($[2M+Na]^+$, 90%), HRMS (ESI^+) $C_{22}H_{26}N_2NaO_5S^+$ ($[M+Na]^+$) requires 453.1455; found 453.1441.

Ethyl 3-(methoxy(methyl)amino)-3-oxopropanoate, 13a



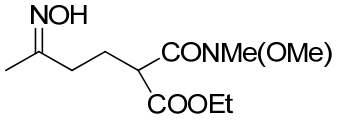
To a solution of ethyl 3-chloro-3-oxopropanoate (2.12 g, 14.1 mmol) in dry CH_2Cl_2 (30 mL) was added *N,O*-dimethylhydroxylamine (1.51 g, 15.5 mmol) and Et_3N (3.56 g, 35.3 mmol) and the mixture stirred at rt to afford malonamide **13a** (2.34 g, 95%) as a pale yellow oil; R_f = 0.24 (EtOAc : petrol, 1:1) υ_{max}(film)/cm^{-1} 2983, 1741, 1671, 1302, 1254, 1181, 936, 810; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.24 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 3.18 (3H, s, NCH_3), 3.45 (2H, s, CH_2), 3.67 (3H, s, $NOCH_3$), 4.16 (2H, q, *J* 7.1 Hz, OCH_2CH_3); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.8 (OCH_2CH_3), 31.9 (NCH_3), 39.9 (CH_2), 61.0 (OCH_2CH_3), 61.1 ($NOCH_3$), 162.1 (*C*ON), 167.1 (*C*OO); m/z (ESI$^+$) 198 ([M+Na]$^+$, 50%), 373 ([2M+Na]$^+$, 20%), HRMS (ESI$^+$) $C_7H_{13}NNaO_4^+$ ([M+Na]$^+$) requires 198.0737; found 198.0739.

(±)Ethyl 2-(methoxy(methyl)carbamoyl)-5-oxohexanoate, 14a



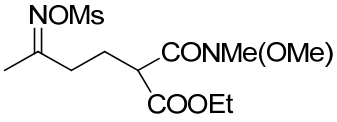
Following general procedure **A**, methyl vinyl ketone (0.94 g, 11.2 mmol) was added to a solution of malonamide **13a** (1.96 g, 13.4 mmol) and anhydrous Cs_2CO_3 (4.00 g, 12.3 mmol) in dry CH_2Cl_2 (30 mL) and the mixture stirred at rt for 3 hr, to give the crude product which was purified by flash column chromatography to afford adduct **14a** (2.23 g, 81%) as a colourless oil; R_f = 0.22 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2981, 1732, 1370, 1163, 1097, 1028, 860; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.20-1.21 (3H, m, OCH_2CH_3), 2.09 (3H, s, $COCH_3$), 2.10-2.10 (2H, m, CH_2CH_2CH), 2.50-2.60 (2H, m, CH_2CH_2CH), 3.17 (3H, s, NCH_3), 3.65 (3H, s, $NOCH_3$), 3.65-3.66 (1H, m, CH_2CH_2CH), 4.10-4.11 (2H, m, OCH_2CH_3); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH_2CH_3), 22.3 (CH_2CH_2CH), 29.9 ($COCH_3$), 32.4 (NCH_3), 40.4 (CH_2CH_2CH), 47.2 (CH_2CH_2CH), 61.3 (OCH_2CH_3), 61.9 ($NOCH_3$), 167.4 (*C*ON), 169.7 (*C*OO), 207.8 (*C*O); m/z (ESI$^+$) 246 ([M+H]$^+$, 40%), 268 ([M+Na]$^+$, 90%), HRMS (ESI$^+$) $C_{11}H_{19}NNaO_5^+$ ([M+Na]$^+$) requires 268.1155; found 268.1158.

(±)Ethyl 5-(hydroxyimino)-2-(methoxy(methyl)carbamoyl)hexanoate, 14b



Following the general procedure **C**, to a solution of adduct **14a** (1.91 g, 7.79 mmol) in EtOH (30 mL) was added $NH_2OH.HCl$ (1.07 g, 15.6 mmol) and Et_3N (1.96 g, 19.5 mmol) and the mixture heated to reflux for 2 hr, to give the crude product which was purified by flash column chromatography to afford oxime **14b** (1.89 g, 93%) as a colourless oil; R_f = 0.26 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3295, 2983, 1731, 1523, 1442, 1218, 1044, 853; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.20-1.30 (3H, m, OCH_2CH_3), 1.86 (3H, s, $CNOHCH_3$), 2.00-2.10 (2H, m, CH_2CH_2CH), 2.20-2.30 (2H, m, CH_2CH_2CH), 3.18 (3H, s, NCH_3), 3.66 (3H, s, $NOCH_3$), 3.60-3.70 (1H, m, CH_2CH_2CH), 4.10-4.20 (2H, m, OCH_2CH_3), 8.83 (1H, bs, OH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.5 ($CNOHCH_3$), 14.0 and 14.1 (OCH_2CH_3), 24.3 and 24.9 (CH_2CH_2CH), 32.5 (NCH_3), 33.3 and 33.5 (CH_2CH_2CH), 47.7 and 48.2 (CH_2CH_2CH), 61.0 (OCH_2CH_3), 61.27 and 61.33 ($NOCH_3$), 157.4 and 157.8 (CONOH), 167.4 (CON), 169.7 (COO); m/z (ESI$^+$) 283 ([M+Na]$^+$, 80%), 543 ([2M+Na]$^+$, 100%), HRMS (ESI$^+$) $C_{11}H_{20}N_2NaO_5^+$ ([M+Na]$^+$) requires 283.1264; found 283.1264.

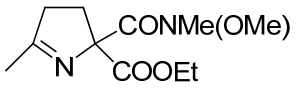
(±)Ethyl 2-(methoxy(methyl)carbamoyl)-5-(methylsulfonyloxyimino)hexanoate, 14c



Following general procedure **E**, to a solution of oxime **14b** (1.73 g, 6.65 mmol) in dry CH_2Cl_2 (30 mL) was added Et_3N (1.01 g, 9.97 mmol) at 0 °C followed by methanesulfonyl chloride (0.91 g, 7.98 mmol) and the mixture stirred at rt for 4 hr, to give the crude product which was purified by column chromatography to afford mesyl oxime **14c** (1.92 g, 85%) as a colourless oil; R_f = 0.48 (EtOAc : petrol, 6:4); υ_{max}(film)/cm^{-1} 2982, 1734, 1667, 1446, 1363, 1181, 1025, 972, 876, 793;

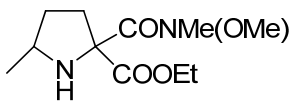
(major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.19 and 1.20 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.97 and 1.99 (3H, s, $CNOMsCH_3$), 2.0-2.2 (2H, m, CH_2CH_2CH), 2.30-2.40 (2H, m, CH_2CH_2CH), 3.07 (3H, s, NCH_3), 3.15 (3H, s, SO_2CH_3), 3.64 (3H, s, $NOCH_3$), 3.69 (1H, t, *J* 6.8 Hz, CH_2CH_2CH), 4.11 (2H, q, *J* 7.1 Hz, OCH_2CH_3); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH_2CH_3), 15.8 ($CNOMsCH_3$), 24.2 (CH_2CH_2CH), 32.4 (SO_2CH_3), 33.4 (CH_2CH_2CH), 36.4 (NCH_3), 47.4 and 47.8 (CH_2CH_2CH), 61.4 and 61.5 (OCH_2CH_3), 61.2 ($NOCH_3$), 167.2 and 166.7 (*C*ONOMs), 169.1 (*C*ON), 169.4 (*C*OO); m/z (ESI^+) 361 ($[M+Na]^+$, 85%), 699 ($[2M+Na]^+$, 100%), HRMS (ESI^+) $C_{12}H_{22}N_2NaO_7S^+$ ($[M+Na]^+$) requires 361.1040; found 361.1035.

(±)Ethyl 2-(methoxy(methyl)carbamoyl)-5-methyl-3,4-dihydro-2H-pyrrole-2-carboxylate, 15



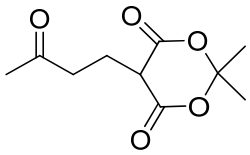
Following general procedure **F**, to a solution of mesyl oxime **14c** (512 mg, 1.52 mmol) in dry acetonitrile (20 mL) was added DBU (345 mg, 2.27 mmol) at 0 °C and the mixture stirred at rt for 1 hr, to give the crude product which was purified by flash column chromatography to afford pyrroline **15** (253 mg, 69%) as a colourless oil; R_f = 0.24 (EtOAc : petrol, 8:2); υ_{max}(film)/cm^{-1} 2952, 1733, 1706, 1667, 1528, 1438, 1258, 1028, 917, 752; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.24 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 2.07 (1H, m, C(3)H*H*), 2.11 (3H, s, CH_3C=N), 2.63 (2H, m, C(4)*HH*), 2.78 (1H, m, C(3)*H*H), 3.20 (3H, s, NCH_3), 3.77 (3H, s, $NOCH_3$), 4.19 (2H, q, *J* 7.1 Hz, OCH_2CH_3); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.9 (OCH_2CH_3), 19.8 (CH_3C=N), 30.6 (*C*3), 32.9 (NCH_3), 39.1 (*C*4), 60.9 (OCH_2CH_3), 61.2 ($NOCH_3$), 85.4 (*C*2), 154.8 (*C*ON), 170.4 (*C*OO), 180.0 (*C*5); m/z (ESI^+) 265 ($[M+Na]^+$, 100%), 507 ($[2M+Na]^+$, 85%), HRMS (ESI^+) $C_{11}H_{18}N_2NaO_4^+$ ($[M+Na]^+$) requires 265.1159; found 265.1162.

(±)Ethyl 2-(methoxy(methyl)carbamoyl)-5-methylpyrrolidine-2-carboxylate, 16



Following general procedure **H**, to a solution of pyrroline **15** (248 mg, 1.02 mmol) in MeOH (10 mL) $NaBH_3CN$ (76 mg, 1.23 mmol) and 2 M HCl in MeOH (5 mL) was added and the mixture stirred at rt, to gave the crude product which was purified by flash column chromatography to afford pyrrolidine **16** (248 mg, 98%) as a colourless oil; R_f = 0.49 (EtOAc : petrol, 8:2); υ_{max}(film)/cm^{-1} 3336, 2965, 1742, 1668, 1454, 1376, 1292, 1258, 1175, 1023, 983, 895; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.10-1.15 (3H, m, CH_3CH), 1.20-1.25 (3H, m, OCH$_2$CH_3), 1.30-1.35 (1H, m, C(4)H*H*), 1.80-2.00 (1H, m, C(4)*H*H), 2.10-2.20 (1H, m, C(3)H*H*), 2.40-2.50 (2H, m, C(3)*H*H), 3.15 (3H, s, NCH_3), 3.260-3.30 (1H, m, CH$_3$C*H*), 3.60 (3H, s, NOCH_3), 4.0.4.2 (2H, m, OCH_2CH$_3$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH$_2$*C*H$_3$), 20.8 and 20.9 (*C*H$_3$CH), 33.4 (*C*4), 33.87 (N*C*H$_3$), 33.89 (*C*3), 55.0, 55.2 (*C*5), 60.5 (O*C*H$_2$CH$_3$), 61.2 (NO*C*H$_3$), 71.3 and 71.35 (*C*2), 171.9 and 172.5 (*C*OO), 173.3, 174.1 (*C*ON); m/z (ESI$^+$) 267 ([M+Na]$^+$, 100%), 511 ([2M+Na]$^+$, 100%), HRMS (ESI$^+$) $C_{11}H_{21}N_2O_4^+$ ([M+H]$^+$) requires 245.1496; found 245.1495.

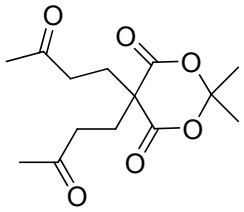
Dimethyl-5-(3-oxobutyl)-1,3-dioxane-4,6-dione, 18a [12]



To a stirring solution of Meldrum's acid (2.21 g, 15.3 mmol) in acetonitrile (40 mL) was added anhydrous K_2CO_3 (2.05 g, 15.34 mmol) and benzyltriethylammonium chloride (3.48 g, 15.34 mmol). The mixture was stirred for 15 min at rt and methyl vinyl ketone (1.07 g, 15.34 mmol) was then added and the resultant mixture was stirred for 8 hr at 50 °C. After monitoring by TLC, the mixture was cooled to rt, the reaction was quenched with water and mixture was washed with diethyl ether and then acidified by 6 N HCl. The adduct was extracted by diethyl ether, dried over Na_2SO_4, to give crude product, which was purified by recrystallization using EtOAc and petroleum ether to afford adduct **18a** (2.67 g, 81%) as pale yellow solid (m.p. = 116-118 °C, lit.[13]119-120 °C) and the double Michael addition product was also isolated in 18% as pale yellow solid m.p. 102-104 °C; R_f = 0.16 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2892, 1785, 1747, 1710, 1382, 1303, 1249,

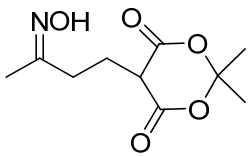
1165, 1010, 986, 730; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.74 and 1.78 (6H, s, C(CH_3)$_2$), 2.13 (3H, s, COCH_3), 2.78 (2H, m, CH_2CH_2CH), 2.75 (2H, t, *J* 7.1 Hz, CH_2CH_2CH), 3.86 (1H, t, *J* 5.4 Hz, CH_2CH_2CH); δ_C(100 MHz; $CDCl_3$; Me_4Si) 20.1 (CH_2CH_2CH), 26.4 and 28.5 C(CH_3)$_2$), 30.1 (COCH_3), 39.2 (CH_2CH_2CH), 44.6 (CH_2CH_2CH), 105.1 (C(CH_3)$_2$), 165.3 (2 x *C*OO), 208.1 (*C*O); m/z (ESI$^-$) 213 ([M-H]$^-$, 100%), HRMS (ESI$^-$) $C_{10}H_{13}O_5^-$ ([M-H]$^-$) requires 213.0768; found 213.0762.

2,2-Dimethyl-5,5-bis(3-oxobutyl)-1,3-dioxane-4,6-dione



The double Michael adduct was isolated in the above reaction R_f = 0.23 (EtOAc : petrol, 8:3); υ_{max}(film)/cm^{-1} 2846, 1771, 1734, 1721, 1420, 1394, 1315, 1270, 1203, 1166, 1119, 1062, 993; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.72 (6H, s, C(CH_3)$_2$), 2.04 (6H, s, 2 x COCH_3), 2.10-2.20 (4H, m, CH_2CH_2C), 2.44 (4H, t, *J* 7.7 Hz, CH_2CH_2C); δ_C(100 MHz; $CDCl_3$; Me_4Si), 29.1 C(CH_3)$_2$), 29.8 (2 x COCH_3), 30.9 (CH_2CH_2C), 38.0 (CH_2CH_2C), 50.9 (CH_2CH_2C), 105.8 (C(CH_3)$_2$), 168.5 (2 x *C*OO), 206.2 (*C*O); m/z (ESI$^-$) 307 ([M+Na]$^+$, 100%), 275 ([M+H]$^+$, 70%); HRMS (ESI$^-$) $C_{14}H_{20}O_6^+$ ([M+Na]$^+$) requires 307.1152; found 307.1148.

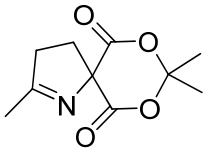
5-(3-(Hydroxyimino)butyl)-2,2-dimethyl-1,3-dioxane-4,6-dione, 18b



Following general procedure **C**, to a solution of adduct **18a** (1.38 g, 6.44 mmol) in EtOH (30 mL) was added $NH_2OH.HCl$ (489 mg, 7.09 mmol) and Et_3N (1.30 g, 12.89 mmol) and the mixture was gently heated (50 °C) for 30 min, to give crude product which was purified by flash column

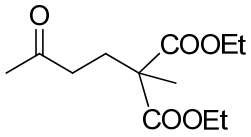
chromatography to afford oxime **18b** (1.14 g, 77%) as pale yellow semi-solid; R_f = 0.23 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3319, 2982, 1786, 1743, 1715, 1372, 1307, 1240, 1176, 1012, 982, 731; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.74 and 1.78 (6H, s, C(C*H*$_3$)$_2$), 1.94 and 1.91 (3H, s, CNOHC*H*$_3$), 2.31 (2H, m, CH$_2$C*H*$_2$CH), 2.44 and 2.63 (2H, m, C*H*$_2$CH$_2$CH), 3.68 (1H, m, CH$_2$CH$_2$C*H*), 9.33 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.2 and 15.3 (CNOH*C*H$_3$), 21.3 and 22.1 (CH$_2$*C*H$_2$CH), 26.4 and 27.6 (C(*C*H$_3$)$_2$), 32.4 and 36.1 (*C*H$_2$CH$_2$CH), 45.0 and 45.7 (CH$_2$CH$_2$*C*H), 105.1 and 106.3 (*C*(CH$_3$)$_2$), 156.1, 157.9, 158.4 (*C*=NOH), 162.9, 165.2 (2 x *C*OO); m/z (ESI$^-$) 228 ([M-H]$^-$, 100%), HRMS (ESI$^-$) $C_{10}H_{14}NO_5^-$ ([M-H]$^-$) requires 228.0877; found 228.0881.

2,8,8-Trimethyl-7,9-dioxa-1-azaspiro[4.5]dec-1-ene-6,10-dione, 19



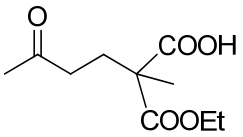
Following general procedure **L**, to a solution of oxime **18b** (412 mg, 1.79 mmol) in dry CH_2Cl_2 (20 mL) was added Et_3N (363 mg, 3.59 mmol) at 0 °C followed by *p*-toluenesulphonyl chloride (410 mg, 2.15 mol) and the mixture stirred for 30 min to give crude product which was purified by flash column chromatography to afford spirobicyclic pyrroline **19** (297 mg, 78%) as a crystalline solid; m.p. = 98 °C; R_f = 0.63 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2933, 1782, 1731, 1452, 1170, 914, 731; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.78 and 2.06 (C(C*H*$_3$)$_2$), 2.12 (3H, s, COC*H*$_3$), 2.58 (2H, t, *J* 7.6 Hz, C(4)*HH*), 2.94 (2H, t, *J* 7.6 Hz, C(3)*HH*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 19.5 (CO*C*H$_3$), 28.6, 28.8 C(*C*H$_3$)$_2$), 31.8 (*C*4), 41.5 (*C*3), 81.0 (*C*2), 106.5 *C*(CH$_3$)$_2$), 167.8 (2 x *C*OO), 183.3 (*C*5); m/z (ESI$^+$) 445 ([2M+Na]$^+$, 100%), 234 ([M+Na]$^+$, 95%), HRMS (ESI$^+$) $C_{10}H_{13}NNaO_5^+$ ([M+Na]$^+$) requires 234.0737; found 234.0737.

Diethyl 2-methyl-2-(3-oxobutyl)malonate, 20a



Following general procedure **A**, methyl vinyl ketone (0.92 g, 11.9 mmol) was added to a solution of diethyl 2-methylmalonate (2.08 g, 13.1 mmol) and anhydrous K_2CO_3 (2.48 g, 17.9 mmol) in dry CH_2Cl_2 (50 mL) heated to reflux for 5 hr, to give crude product which was purified by flash column chromatography to afford adduct **20a** (2.71 g, 96%) as a colourless oil; R_f = 0.48 (EtOAc : petrol, 1:2); υ_{max}(film)/cm^{-1} 2982, 1729, 1447, 1377, 1171, 1097, 940; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.21 (6H, t, *J* 7.1 Hz, 2 × OCH_2CH_3), 1.35 (3H, s, CH_3C), 2.07 (2H, t, *J* 7.3 Hz, CH_2CH_2C), 2.10 (3H, s, $COCH_3$), 2.45 (2H, t, *J* 7.3 Hz, CH_2CH_2C), 4.13 (4H, q, *J* 7.1 Hz, 2 × OCH_2CH_3); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (2 × OCH_2CH_3), 20.3 (CH_3C), 29.3 (CH_2CH_2C), 29.8 ($COCH_3$), 38.8 (CH_2CH_2C), 52.7 (CH_2CH_2C), 61.3 (2 × OCH_2CH_3), 171.9 (2 × *C*OO), 207.4 (*C*O); m/z (ESI$^+$) 267 ([M+Na]$^+$, 45%), 283 ([M+K]$^+$, 100%), HRMS (ESI$^+$) $C_{12}H_{20}NaO_5^+$ ([M+Na]$^+$) requires 267.1203; found 267.1210.

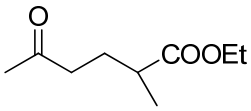
(±)2-(Ethoxycarbonyl)-2-methyl-5-oxohexanoic acid, 20c



A solution of KOH (609 mg, 10.9 mmol) in EtOH was added to a solution of adduct **20a** (2.66 g, 10.9 mmol) in EtOH at 0 °C and reaction mixture was stirred for 2 hr. The reaction mixture was then heated to reflux for 1 hr, cool and quenched with 1 M HCl, washed with water, extracted by EtOAc, and concentrated to give crude product which was purified by flash column chromatography to afford acid **20c** (312 mg, 16%) and ketone **20b** (1.51 g, 79%) as colourless oils; **202a** R_f = 0.21 (EtOAc : petrol, 3:1); υ_{max}(film)/cm^{-1} 2980, 1715, 1594, 1462, 1355, 1255, 1173, 1115, 863; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.24 (3H, t, *J* 7.1 Hz, OCH_2CH_3), 1.41 (3H, s, CH_3C), 2.11 (2H, t, *J* 7.3 Hz, CH_2CH_2C), 2.13 (3H, s, $COCH_3$), 2.50 (2H, t, *J* 7.3 Hz, CH_2CH_2C), 4.17 (2H,

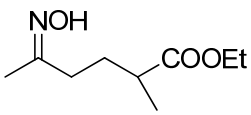
q, *J* 7.1 Hz, OC*H*$_2$CH$_3$), 9.04 (1H, bs, COO*H*); δ_C(100 MHz; CDCl$_3$; Me$_4$Si) 13.8 (OCH$_2$*C*H$_3$), 20.6 (C*H*$_3$C), 29.3 (CH$_2$*C*H$_2$C), 29.8 (CO*C*H$_3$), 38.7 (*C*H$_2$CH$_2$C), 52.6 (CH$_2$CH$_2$*C*), 61.7 (O*C*H$_2$CH$_3$), 171.8 (*C*OO), 177.0 (*C*OOH), 207.5 (*C*O); m/z (ESI$^+$) 239 ([M+Na]$^+$, 100%), 215 ([M-H]$^-$, 40%), HRMS (ESI$^+$) $C_{10}H_{16}NaO_5^+$ ([M+Na]$^+$) requires 239.0895; found 239.0890.

(±)Ethyl 2-methyl-5-oxohexanoate, 20b



A solution of KOH (59 mg, 1.06 mmol) in EtOH was added to a solution of acid **20c** (260 mg, 1.06 mmol) in EtOH at 0 °C and reaction mixture stirred for 2 hr. The reaction mixture was heated to reflux for 15 hr, cooled and quenched with 1 M HCl, washed with water, extracted by EtOAc, and concentrated to give crude product which was purified by column chromatography to afford ketone **20b** (163 mg, 91%) as a colourless oil; R_f = 0.36 (EtOAc : petrol, 1:2); υ_{max}(film)/cm^{-1} 2982, 1729, 1594, 1377, 1256, 1171, 940; δ_H(400 MHz; CDCl$_3$; Me$_4$Si) 1.10 (3H, d, *J* 7.0 Hz, C*H*$_3$CH), 1.20 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.69 (1H, m, CH$_2$CH*H*CH), 1.81 (1H, m, CH$_2$C*H*HCH), 2.08 (3H, s, COC*H*$_3$), 2.37 (1H, m, CH$_3$C*H*), 2.42 (2H, t, *J* 6.9 Hz, C*H*$_2$CH$_2$CH), 4.07 (2H, q, *J* 7.1 Hz, OC*H*$_2$CH$_3$); δ_C(100 MHz; CDCl$_3$; Me$_4$Si) 14.2 (OCH$_2$*C*H$_3$), 17.1 (C*H*$_3$CH), 27.3 (CH$_2$*C*H$_2$CH), 29.9 (CO*C*H$_3$), 38.6 (CH$_3$C*H*), 40.9 (*C*H$_2$CH$_2$CH), 60.2 (O*C*H$_2$CH$_3$), 176.0 (*C*OO), 208.0 (*C*O); m/z (ESI$^+$) 195 ([M+Na]$^+$, 100%), HRMS (ESI$^+$) $C_9H_{16}NaO_3^+$ ([M+Na]$^+$) requires 195.0992; found 195.0992.

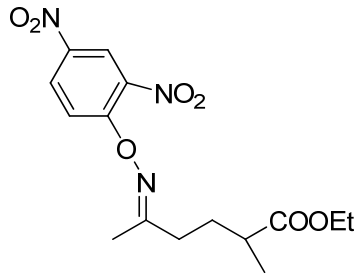
(±)Ethyl 5-(hydroxyimino)-2-methylhexanoate, 21a



Following general procedure **C**, to a solution of ketone **20b** (1.48 g, 8.60 mmol) in EtOH (25 mL) was added NH$_2$OH.HCl (1.18 g, 17.2 mmol) and Et$_3$N (1.73 g, 17.2 mmol) and heated to reflux for

1 hr, to give crude product which was purified by flash column chromatography to afford oxime **21a** (1.46 g, 91%) as a colourless oil; R_f = 0.73, 0.61 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3309, 2981, 1731, 1448, 1379, 1186, 1110, 1030; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.13 (3H, d, *J* 7.0 Hz, C*H*$_3$CH), 1.22 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.58 (1H, m, CH$_2$CH*H*CH), 1.86 (1H, m, CH$_2$C*H*HCH), 1.85 (3H, s, C*H*$_3$CNOH), 2.17 (2H, t, *J* 7.8 Hz, C*H*$_2$CH$_2$CH), 2.41 (1H, m, CH$_3$C*H*), 4.10 (2H, q, *J* 7.1 Hz, OC*H*$_2$CH$_3$), 8.22 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 13.5 (CH$_3$CNOH), 14.2 (OCH$_2$*C*H$_3$), 17.0 (*C*H$_3$CH), 29.9 (CH$_2$*C*H$_2$CH), 33.4 (*C*H$_2$CH$_2$CH), 38.9 (CH$_3$C*H*), 60.3 (O*C*H$_2$CH$_3$), 157.8 (CH$_3$*C*NOH), 176.2 (*C*OO); m/z (ESI$^+$) 210 ([M+Na]$^+$, 85%), 397 ([2M+Na]$^+$, 100%), HRMS (ESI$^+$) $C_9H_{17}NNaO_3^+$ ([M+Na]$^+$) requires 210.1101; found 210.1108.

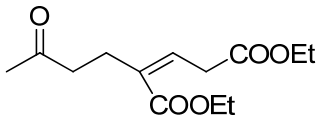
(±)Ethyl 5-(2,4-dinitrophenoxyimino)-2-methylhexanoate, 21b



Following general procedure **D**, to a solution of oxime **20b** (1.09 g, 5.83 mmol) in EtOH (20 mL) sodium metal (134 mg, 5.83 mmol) was added and the mixture stirred for 30 min at rt and followed by the addition of 2,4-dinitrofluorobenzene (1.30 g, 6.99 mmol) at 0 °C slowly, to give crude product which was purified by flash column chromatography to afford ether **21b** (1.67 g, 81%) as a yellow semi-solid; R_f = 0.53 (EtOAc : petrol, 2:8); υ_{max}(film)/cm^{-1} 3117, 2979, 1729, 1606, 1535, 1473, 1343, 1289, 1143, 831, 743, 719; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.19 (3H, d, *J* 7.0 Hz, C*H*$_3$CH), 1.23 (3H, t, *J* 7.1 Hz, OCH$_2$C*H*$_3$), 1.72 (1H, m, CH$_2$CH*H*CH), 2.00 (1H, m, CH$_2$C*H*HCH), 2.14 (3H, s, C*H*$_3$CNOAr), 2.39 (2H, t, *J* 7.8 Hz, C*H*$_2$CH$_2$CH), 2.48 (1H, m, CH$_3$C*H*), 4.11 (2H, q, *J* 7.1 Hz, OC*H*$_2$CH$_3$), 7.89 (1H, d, *J* 9.3 Hz, Ar*H*), 8.37 (1H, dd, *J* 9.3, 2.7 Hz, Ar*H*), 8.83 (1H, d, *J* 2.7 Hz, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.2 (*C*H$_3$CNOAr), 16.1 (OCH$_2$*C*H$_3$),

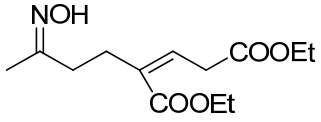
17.1 (C*H*$_3$CH), 29.4 (CH$_2$*C*H$_2$CH), 33.3 (*C*H$_2$CH$_2$CH), 38.8 (CH$_3$C*H*), 60.4 (O*C*H$_2$CH$_3$), 117.1, 122.0, 122.4, 129.3 (Ar*C*), 140.4, 166.5 (quaternary Ar*C*), 157.3 (CH$_3$*C*NOAr), 175.8 (*C*OO); m/z (ESI$^+$) 412 ([M+CH$_3$CN+NH$_3$]$^+$, 45%), 352 ([M-H]$^-$, 55%), HRMS (ESI$^+$) $C_{15}H_{19}N_3NaO_7^+$ ([M+Na]$^+$) requires 376.1115; found 376.1109.

(±) (*Z*)-Diethyl 2-(3-oxobutyl)pent-2-enedioate, 22a



Following general procedure **A**, methyl vinyl ketone (346 mg, 4.95 mmol) was added to a solution of diethyl glutaconate (768 mg, 4.13 mmol) and anhydrous K_2CO_3 (830 mg, 6.19 mmol) in CH_2Cl_2 (20 mL) and the mixture stirred at rt, to give crude product which was purified by flash column chromatography to afford adduct **22a** (799 mg, 76%) as a colourless oil; R_f = 0.32 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 2981, 1721, 1650, 1602, 1493, 1371, 1258, 1177, 1029, 954, 756; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.26 and 1.29 (6H, t, *J* 7.1 Hz, 2 x OCH$_2$C*H*$_3$), 2.12 (3H, s, COC*H*$_3$), 2.54 (2H, t, *J* 6.9 Hz, CH$_2$C*H*$_2$C), 2.60 (2H, t, *J* 6.9 Hz, C*H*$_2$CH$_2$C), 3.29 (2H, d, *J* 7.3, C*H*$_2$COOEt), 4.15 and 4.20 (4H, q, *J* 7.1 Hz, 2 x OC*H*$_2$CH$_3$), 6.93 (1H, t, *J* 7.3 Hz, C*H*CH$_2$COOEt); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (2 x OCH$_2$*C*H$_3$), 21.3 (CH$_2$*C*H$_2$C), 29.9 (CO*C*H$_3$), 34.1(*C*H$_2$COOEt), 42.3 (*C*H$_2$CH$_2$C), 60.7, 61.1 (2 x O*C*H$_2$CH$_3$), 133.7, 134.2 (*C*HCH$_2$COOEt), 144.3 (CH$_2$CH$_2$*C*), 166.8, 170.5 (2 × *C*OO), 207.1 (*C*O); m/z (ESI$^+$) 279 ([M+Na]$^+$, 100%), 255 ([M-Na]$^-$, 100%), HRMS (ESI$^+$) $C_{13}H_{20}NaO_5^+$ ([M+Na]$^+$) requires 279.1203; found 279.1203.

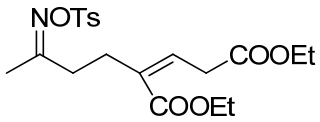
(±)(2*Z*)-Diethyl 2-(3-(hydroxyimino)butyl)pent-2-enedioate, 22b



Following general procedure **C**, to a solution of adduct **22a** (729 mg, 2.85 mmol) in EtOH (20 mL) was added $NH_2OH.HCl$ (392 mg, 5.69 mmol) and Et_3N (719 mg, 7.13 mmol) and heated to reflux

for 2 hr, to give crude product which was purified by flash column chromatography to afford oxime **22b** (568 mg, 74%) as a colourless oil; (major isomer) R_f = 0.38 (EtOAc : petrol, 1:1); υ_{max}(film)/cm^{-1} 3509, 2983, 1732, 1653, 1258, 1178, 1029, 876; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.26 and 1.31 (6H, t, *J* 7.1 Hz, 2 x OCH_2CH_3), 1.35 (3H, s, $CNOHCH_3$), 1.880-1.90 (2H, m, CH_2CH_2C), 2.31 and 2.56 (2H, m, CH_2CH_2C), 3.19 (2H, d, *J* 4.6, CH_2COOEt), 4.12 and 4.22 (4H, 2 x q, *J* 7.1 Hz, 2 x OCH_2CH_3), 6.53 (1H, bs, O*H*), 6.94 (1H, t, *J* 4.9 Hz, $CHCH_2COOEt$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.2 (2 x OCH_2CH_3), 21.0 ($CNOHCH_3$), 21.6 (CH_2CH_2C), 28.8 (CH_2CH_2C), 48.6, 48.7 (CH_2COOEt), 60.4, 61.0 (2 x OCH_2CH_3), 129.6 ($CHCH_2COOEt$), 132.9 (CH_2CH_2C), 165.7 (*C*=NOH), 171.2 and 176.3 (2 × *C*OO); m/z (ESI$^+$) 272 ([M+H]$^+$, 30%), HRMS (ESI$^+$) $C_{13}H_{22}NO_5^+$ ([M+H]$^+$) requires 272.1492; found 272.1494.

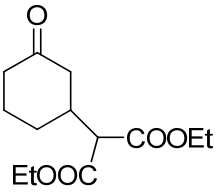
(±)(2Z)-Diethyl 2-(3-(tosyloxyimino)butyl)pent-2-enedioate, 22c



Following general procedure **E**, to a solution of oxime **22b** (432 mg, 1.59 mmol) in dry CH_2Cl_2 (20 mL) was added Et_3N (240 mg, 2.38 mmol) at 0 °C followed by *p*-toluenesulfonyl chloride (362 mg, 1.90 mmol) and the mixture stirred at rt for 2 hr, to give the crude product which was purified by flash column chromatography to afford tosyl oxime **22c** (521 mg, 76%) as a colourless oil; R_f = 0.53 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3032, 2983, 1715, 1605, 1345, 1260, 1168, 1088, 915, 676; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.31 (6H, t, *J* 7.1 Hz, 2 x OCH_2CH_3), 1.80 (3H, s, $CNOArCH_3$), 2.10 (2H, m, CH_2CH_2C), 2.35, 2.62 (2H, m, CH_2CH_2C), 2.46 (3H, s, $ArCH_3$), 3.53 (2H, d, *J* 5.0 Hz, CH_2COOEt), 4.13, 4.22 (4H, q, *J* 7.1 Hz, 2 x OCH_2CH_3), 6.84 (1H, t, *J* 4.8 Hz, $CHCH_2COOEt$), 7.37 (2H, d, *J* 8.1 Hz, Ar*H*), 7.86 (2H, d, *J* 8.3 Hz, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1, 14.2 (2 x OCH_2CH_3), 21.2 ($CNOArCH_3$), 21.3 (CH_2CH_2C), 21.7 ($ArCH_3$), 29.7 (CH_2CH_2C), 48.7 (CH_2COOEt), 61.2 (2 x OCH_2CH_3), 128.2 ($CHCH_2COOEt$), 129.3, 129.8 (Ar*C*),

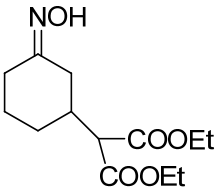
133.3 (quaternary Ar*C*), 133.6 (CH_2CH_2C), 145.9 (quaternary Ar*C*), 165.5 (*C*=NOAr), 171.3 (2 × *C*OO); m/z (ESI^+) 448 ($[M+H]^+$, 70%).

(±)Diethyl 2-(3-oxocyclohexyl)malonate, 23a



Following general procedure **A**, cyclohex-2-enone (2.25 g, 23.4 mol) was added to a solution of diethyl malonate (3.12 g, 19.5 mmol) and anhydrous K_2CO_3 (3.92 g, 29.3 mmol) in dry CH_2Cl_2 (30 mL) and the mixture stirred at rt, to give crude product which was purified by flash column chromatography to afford adduct **23a** (4.10 g, 82%) as a colourless oil; R_f = 0.53 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 2982, 1731, 1448, 1423, 1297, 1229, 1156, 1061, 965; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.23 (6H, m 2 × OCH_2CH_3), 1.47 and 1.65 (2H, m, $COCH_2CH_2CH_2$), 1.90 (2H, m, $COCH_2CH_2CH_2$), 2.23 (2H, m, $COCH_2CH_2CH_2$), 2.39 (2H, m, $COCH_2CH$), 2.49 (1H, m, $COCH_2CH$), 3.26 (1H, d, *J* 7.9 Hz $CH(COOEt)_2$), 4.17 (4H, m, 2 × OCH_2CH_3); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.1 (OCH_2CH_3), 24.5 ($COCH_2CH_2CH_2$), 28.8 ($COCH_2CH_2CH_2$), 38.0 ($COCH_2CH$), 41.0 ($COCH_2CH_2CH_2$), 45.0 ($COCH_2CH$), 56.9 ($CH(COOEt)_2$), 61.5 (OCH_2CH_3), 167.8 and 167.9 (2 x *C*OO), 209.7 (*C*O); m/z (ESI^+) 535 ($[2M+Na]^+$, 85%), 279 ($[M+Na]^+$, 60%), 255 ($[M-H]^-$, 100%), HRMS (ESI^+) $C_{13}H_{20}NaO_5^+$ ($[M+Na]^+$) requires 279.1203; found 279.1199.

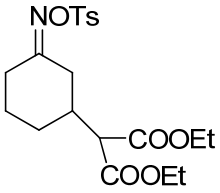
(±)Diethyl 2-(3-(hydroxyimino)cyclohexyl)malonate, 23b



Following general procedure **C**, to a solution of adduct **23a** (3.82 g, 14.9 mmol) in EtOH (40 mL) was added $NH_2OH.HCl$ (1.54 g, 22.4 mmol) and Et_3N (3.01 g, 29.8 mmol) and the mixture heated

to reflux for 1 hr, to give crude product which was purified by flash column chromatography to afford oxime **23b** (3.82 g, 94%) as a colourless oil; R_f = 0.45, 0.37 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 3240, 2938, 1731, 1448, 1369, 1233, 1156, 1096, 966, 862; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.17 (6H, m, 2 × OCH_2CH_3), 1.34 (2H, m, $CCH_2CH_2CH_2$), 1.70 (2H, m, $CCH_2CH_2CH_2$), 1.93 (2H, m, $CCH_2CH_2CH_2$), 2.26 (2H, m, CCH_2CH), 3.11 (1H, m, CCH_2CH), 3.19 (1H, d, *J* 8.3 Hz $CH(COOEt)_2$), 4.11 (4H, m, 2 × OCH_2CH_3), 9.40 (1H, bs, O*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (OCH_2CH_3), 23.7 and 23.8 ($CCH_2CH_2CH_2$), 25.1 and 27.8 ($CCH_2CH_2CH_2$), 29.4 and 29.5 ($CCH_2CH_2CH_2$), 31.6 and 35.5 (CCH_2CH), 36.7 and 37.7 (CCH_2CH), 56.9 and 57.0 ($CH(COOEt)_2$), 61.3 and 61.4 (OCH_2CH_3), 158.4 and 158.7 (*C*=NOH), 168.02, 168.08, 168.1 and 168.2 (2 x *C*OO); m/z (ESI$^+$) 565 ([2M+Na]$^+$, 100%), 294 ([M+Na]$^+$, 50%), 270 ([M-H]$^-$, 100%), HRMS (ESI$^+$) $C_{13}H_{21}NNaO_5^+$ ([M+Na]$^+$) requires 294.1312; found 294.1310.

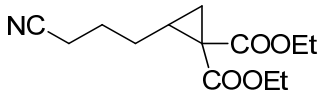
(±)Diethyl 2-(3-(tosyloxyimino)cyclohexyl)malonate, 23c



Following general procedure **E**, to a solution of oxime **23b** (1.38 g, 5.09 mmol) in dry CH_2Cl_2 (25 mL) was added Et_3N (1.02 g, 10.2 mmol) at 0 °C followed by *p*-toluenesulphonyl chloride (1.45 g, 7.63 mmol) and the mixture stirred for 2 hr at rt, to give crude product which was purified by column chromatography to afford tosyl oxime **23c** (1.82 g, 84%) as colourless a oil; R_f = 0.59 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 2938, 1730, 1447, 1369, 1155, 1032, 817, 732; (major isomer) δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.23 (6H, m, 2 × OCH_2CH_3), 1.47 (2H, m, $CCH_2CH_2CH_2$), 1.86 (2H, m, $CCH_2CH_2CH_2$), 2.03 (2H, m, $CCH_2CH_2CH_2$), 2.28 (2H, m, CCH_2CH), 2.39 (3H, s, $ArCH_3$), 2.49 (1H, m, CCH_2CH), 3.26 (1H, d, *J* 7.9 Hz $CH(COOEt)_2$), 4.16 (4H, m, 2 × OCH_2CH_3), 7.29 (2H, d, *J* 8.1 Hz, Ar*H*), 7.79 (2H, d, *J* 8.1 Hz, Ar*H*); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (OCH_2CH_3), 21.7 ($ArCH_3$), 23.8 ($CCH_2CH_2CH_2$), 28.7 ($CCH_2CH_2CH_2$), 37.4 (CCH_2CH), 40.9 ($CCH_2CH_2CH_2$),

45.1 (C*C*H$_2$CH), 56.3 (*C*H(COOEt)$_2$), 61.5 (O*C*H$_2$CH$_3$), 128.7, 129.5, 132.7, 144.8 (Ar*C*), 167.7 (*C*=NOTs), 167.8 and 167.8 (2 x *C*OO); m/z (ESI$^+$) 873 ([2M+Na]$^+$, 100%), 448 ([M+Na]$^+$, 80%), HRMS (ESI$^+$) $C_{20}H_{27}NNaO_7S^+$ ([M+Na]$^+$) requires 448.1400; found 448.1400.

(±)Diethyl 2-(3-cyanopropyl)cyclopropane-1,1-dicarboxylate, 24



Following general procedure **F**, to tosyl oxime **23c** (256 mg, 0.60 mmol) in dry THF (10 mL) was added NaH (43 mg, 1.80 mmol, 60%) and the mixture heated to reflux for 30 min, giving crude product which was purified by flash column chromatography to afford cyclopropane **24** (113 mg, 74%) as a colourless oil; R_f = 0.49 (EtOAc : petrol, 4:6); υ_{max}(film)/cm^{-1} 2938, 2256, 1731, 1431, 1447, 1369, 1156, 1096, 1030, 967, 916, 862; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.24 and 1.27 (6H, m, 2 × OCH$_2$C*H*$_3$), 1.33 (2H, m, NCCH$_2$CH$_2$C*H*$_2$), 1.39 (1H, m, CHCH*H*C), 1.55 (1H, m, C*H*CH$_2$C), 1.74 (1H, m, CHC*H*HC), 1.82 (2H, m, NCCH$_2$C*H*$_2$CH$_2$), 2.33 (2H, t, *J* 7.1 Hz NCC*H*$_2$CH$_2$CH$_2$), 4.10-4.20 (4H, m, 2 × OC*H*$_2$CH$_3$); δ_C(100 MHz; $CDCl_3$; Me_4Si) 14.0 (OCH$_2$*C*H$_3$), 16.7 (NC*C*H$_2$CH$_2$CH$_2$), 20.5 (CH*C*H$_2$C), 24.8 (NCCH$_2$*C*H$_2$CH$_2$), 26.7 (*C*HCH$_2$C), 27.6 (NCCH$_2$CH$_2$*C*H$_2$), 34.0 (*C*(COOEt)$_2$), 61.5 (O*C*H$_2$CH$_3$), 119.2 (*C*N), 167.9 170.1 (2 x *C*OO); m/z (ESI$^+$) 276 ([M+Na]$^+$, 100%), HRMS (ESI$^+$) $C_{13}H_{19}NNaO_4^+$ ([M+Na]$^+$) requires 276.1206; found 276.1207.

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