Supplementary Material (ESI) for Organic & Biomolecular Chemistry

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Cascade condensation, cyclization, intermolecular dipolar cycloaddition by multi-component coupling and application to a synthesis of (±)-crispine A

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1. Procedures and data for the following compounds:

5-Chloro-2,2-dimethylpentanenitrile 2: *n*-BuLi (2.5 M in hexane, 26.0 mL, 65.1 mmol) was added to diisopropylamine (9.8 mL, 69.4 mmol) in THF (30 mL) at –78 ºC. After 15 minutes, isobutyronitrle **1** (3.89 mL, 43.4 mmol) in THF (15 mL) was added. After 30 minutes, 1-bromo-3-chloropropane (6.4 mL, 65.1 mmol) in THF (15 mL) was added. After 1.5 h, saturated aqueous ammonium chloride solution (20 mL) was added and the mixture was extracted with Et_2O (4 × 50 mL). The organic layer was washed with water (2 × 10 mL) and brine (10 mL) and

was dried ($MgSO_4$). The solvent was evaporated and the mixture was purified by column chromatography, eluting with petrol–EtOAc (95:5), to give the nitrile **2** (5.42 g, 86%) as an oil; R_f 0.50 [EtOAc–petrol (5:95)]; ν_{max}/cm^{-1} 2980, 2235, 1470; ^1H NMR ($CDCl_3$, 500 MHz) δ = 3.58 (t, *J* 6.5 Hz, 2H), 2.00–1.94 (m, 2H), 1.71–1.67 (m, 2H), 1.37 (s, 6H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ = 124.4, 44.2, 38.1, 31.7, 28.2, 26.4; HRMS (ES) Found: M^+ (ES), 145.0663. $C_7H_{12}NCl$ requires M^+ 145.0658.

5-Chloro-2,2-dimethylpentanal 3: DIBAL-H (15.46 mL, 15.46 mmol, 1.0 M in hexanes) was added to the nitrile **2** (1.5 g, 10.31 mmol) in CH_2Cl_2 (40 mL) at –78 °C. After 1.5 h, aqueous HCl (15 mL, 1 M) was added. After 30 min, the mixture was allowed to warm to room temp. Aqueous HCl (20 mL, 2 M) was added and the mixture was extracted with Et_2O (6 × 30 mL). The organic layer was washed with water (2 × 10 mL) and brine (10 mL) and was dried ($MgSO_4$). The solvent was evaporated and the mixture was purified by column chromatography, eluting with petrol–EtOAc (9:1), to give the aldehyde **3** (1.35 g, 88%) as an oil; R_f 0.65 [EtOAc–petrol (5:95)]; ν_{max}/cm^{-1} 2925, 2855, 1725, 1460; ^1H NMR ($CDCl_3$, 400 MHz) δ = 9.46 (s, 1H), 3.52 (t, *J* 6 Hz, 2H), 1.74–1.59 (m, 4H), 1.08 (s, 6H); data consistent with the literature.[1]

2,2-Dimethyl-4-(trimethylsilyloxy)butanenitrile 4: In the same way as the nitrile **2**, *n*-BuLi (2.5 M in hexane, 18.84 mL, 47.1 mmol), diisopropylamine (7.54 mL, 54.35 mmol), isobutyronitrle **1** (2.50 g, 36.2 mmol) and 1-bromoethyl trimethylsilyl ether (8.56 g, 43.5 mmol) gave, after purification by column chromatography, eluting with petrol–EtOAc (95:5), the nitrile **4** (6.6 g, 98%) as an oil; R_f 0.50 [EtOAc-petrol (5:95)]; ν_{max}/cm^{-1} 2955, 2230, 1405; ^1H NMR ($CDCl_3$, 400 MHz) δ = 3.76 (t, *J* 7 Hz, 2H), 1.75 (t, *J* 7 Hz, 2H), 1.35 (s, 6H), 0.10 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 124.7, 59.0, 42.7, 32.9, 27.1, 0.7; HRMS (ES) Found: MH^+ (ES), 186.1317. $C_9H_{20}NOSi$ requires MH^+ 186.1314; LRMS *m/z* (ES) 186 (100%, MH^+).

4-Hydroxy-2,2-dimethylbutanenitrile 5: The nitrile **4** (1.0 g, 5.4 mmol) was stirred with aqueous HCl (10 mL, 1 M) at room temperature. After 1 h, the mixture was extracted with EtOAc (4 × 50 mL). The organic layer was washed with water (2 × 10 mL) and brine (10 mL) and was dried ($MgSO_4$). The solvent was evaporated and the mixture was purified by column chromatography, eluting with petrol–EtOAc (4:1), to give the nitrile **5** (520 mg, 86%) as an oil; R_f 0.33 [EtOAc–petrol (1:3)]; ν_{max}/cm^{-1} 3415, 2980, 2235; ^1H NMR ($CDCl_3$, 250 MHz) δ = 3.81 (t, *J* 7 Hz, 2H), 2.71 (br s, 1H), 1.79 (t, *J* 7 Hz, 2H), 1.37 (s, 6H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ = 125.0, 59.1, 42.7, 30.6, 27.0; HRMS (ES) Found: M^+ (ES), 113.0842. $C_6H_{11}NO$ requires M^+ 113.0840.

4-Chloro-2,2-dimethylbutanenitrile 6: PPh_3 (4.63 g, 17.7 mmol) in THF (15 mL) was added to *N*-chlorosuccinimide (2.84 g, 21.2 mmol) in THF (20 mL) at room temperature. After 30 min, the alcohol **5** (2.00 g, 17.7 mmol) in THF (15 mL) was added. After 4 h, the solvent was evaporated and the mixture was purified by column chromatography, eluting with petrol–EtOAc (9:1), to give the chloride **6** (1.86 g, 81%) as an oil; R_f 0.46 [EtOAc–petrol (1:9)]; ν_{max}/cm^{-1} 2980, 2235, 1470, 1450; ^1H NMR ($CDCl_3$, 250 MHz) δ = 3.61 (t, *J* 8 Hz, 2H), 1.99 (t, *J* 8 Hz, 2H), 1.35 (s, 6H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ = 123.6, 43.0, 39.5, 31.4, 26.4; HRMS (ES) Found: M^+ (ES), 131.0502. $C_6H_{10}ClN$ requires M^+ 131.0501; LRMS *m/z* (ES) 131 (55%, M^+).

4-Chloro-2,2-dimethylbutanal 7: In the same way as the aldehyde **3**, DIBAL-H (17.11 mL, 17.11 mmol, 1.0 M in hexanes) and the nitrile **6** (1.5 g, 11.4 mmol) gave, after purification by column chromatography, eluting with petrol–EtOAc (9:1), to give the aldehyde **7** (860 mg, 56%) as an oil; R_f 0.54 [EtOAc-petrol (1:9)]; ^1H NMR ($CDCl_3$, 250 MHz) δ = 9.45 (s, 1H), 3.45 (t, *J* 8 Hz, 2H), 1.98 (t, *J* 8 Hz, 2H), 1.07 (s, 6H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ = 204.5, 45.4, 40.3, 39.8, 21.3.

6-Chloro-2,2-dimethylhexanenitrile 8: In the same way as the nitrile **2**, *n*-BuLi (2.2 M in hexanes, 9.91 mL, 21.8 mmol), diisopropylamine (3.3 mL, 23.3 mmol), isobutyronitrile **1** (1.3 mL, 14.6 mmol) and 1-bromo-4-chlorobutane (2.2 mL, 18.0 mmol) gave, after purification by column chromatography, eluting with petrol–EtOAc (99:1–97:3), the nitrile **8** (2.01 g, 86%) as an oil; R_f 0.50 [petrol–EtOAc (19:1)]; ν_{max}/cm^{-1} 2980, 2235, 1460; ^1H NMR ($CDCl_3$, 250 MHz) δ = 3.58 (t, *J* 6.5 Hz, 2H), 1.91–1.77 (m, 2H), 1.75–1.49 (m, 4H), 1.37 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 124.9, 44.5, 40.3, 32.4, 32.3, 26.6, 22.7; HRMS (ES) Found: MH^+ (ES), 160.0893. $C_8H_{14}NCl$ requires MH^+, 160.0889; LRMS *m/z* (ES) 160 (15%, MH^+).

6-Chloro-2,2-dimethylhexanal 9: In the same way as the aldehyde **3**, DIBAL-H (13.8 mL, 13.8 mmol, 1.0 M in hexanes) and the nitrile **8** (1.7 g, 10.6 mmol) gave, after purification by column chromatography, eluting with petrol–EtOAc (97:3), the aldehyde **9** (1.53 g, 89%) as an oil; R_f 0.50 [petrol–EtOAc (19 :1)]; ν_{max}/cm^{-1} 2960, 1725, 1460; ^1H NMR ($CDCl_3$, 400 MHz) δ = 9.47 (s, 1H), 3.55 (t, *J* 7 Hz, 2H), 1.78 (quin, *J* 7 Hz, 2H) , 1.55–1.48 (m, 2H), 1.48–1.34 (m, 2H) 1.08 (s, 6H); data consistent with the literature.[1,2]

6-Iodo-2,2-dimethylhexanal 10: The aldehyde **9** (1.75 g, 10.7 mmol) and NaI (6.4 g, 42.8 mmol) were heated under reflux in acetone (25 mL). After 12 h, the mixture was diluted with water and extracted with Et_2O (4 × 50

mL). The organic layer was washed with sodium thiosulfate (20 mL), H_2O (3 × 10 mL) and brine (10 mL) and was dried ($MgSO_4$). The solvent was evaporated to give the aldehyde **10** (2.70 g, 99%) as an oil; R_f 0.50 [petrol–EtOAc (19:1)]; ν_{max}/cm^{-1} 2960, 1725, 1460; ^1H NMR ($CDCl_3$, 400 MHz) δ = 9.48 (s, 1H), 3.20 (t, *J* 7 Hz, 2H), 1.83 (quin, *J* 7 Hz, 2H), 1.54–1.46 (m, 2H), 1.40–1.31 (m, 2H) 1.10 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 206.0, 45.7, 35.9, 33.8, 25.3, 21.3, 6.3; HRMS (ES) Found: MH^+ (ES), 255.0241. $C_8H_{16}OI$ requires MH^+, 255.0246; data consistent with the literature.[1]

(3a*RS*,9a*SR*,9b*SR*)-2,9,9-Trimethyloctahydro-1*H*-pyrrolo[3,4-a]indolizine-1,3(2*H*)-dione 15a and (3a*SR*,9a*SR*,9b*RS*)- 2,9,9-Trimethyloctahydro-1*H*-pyrrolo[3,4-a]indolizine-1,3(2*H*)-dione 15b: The aldehyde **3** (100 mg, 0.67 mmol), *N*-methylmaleimide (112 mg, 1.00 mmol) and glycine (202 mg, 2.69 mmol) were heated under reflux in toluene (7 mL). After 24 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the cycloadducts **15** (110 mg, 70%) as two separable diastereoisomers (dr 1:1):

15a: needles; m.p. 85–86 °C; R_f 0.20 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 1695; ^1H NMR ($CDCl_3$, 400 MHz) δ = 3.43 (t, *J* 9 Hz, 1H), 3.26 (q, *J* 9 Hz, 1H), 3.04 (t, *J* 9 Hz, 1H), 2.98 (dt, *J* 11, 2.5 Hz, 1H), 2.93 (s, 3H), 2.11 (t, *J* 9 Hz, 1H), 1.94 (td, *J* 11, 3 Hz, 1H), 1.78 (d, *J* 9 Hz, 1H), 1.70–1.59 (m, 1H), 1.49–1.41 (m, 2H), 1.12 (td, *J* 13.5, 4 Hz, 1H), 1.07 (s, 3H), 0.96 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 177.9, 177.6, 74.6, 56.3, 52.8, 46.9, 43.5, 39.5, 32.9, 29.1, 24.8, 21.8, 19.7; HRMS (ES) Found: MH^+ (ES), 237.1597. $C_{13}H_{21}N_2O_2$ requires MH^+ 237.1603; LRMS *m/z* (ES) 237 (100%, MH^+); Anal. Calc. for $C_{13}H_{20}N_2O_2$: C, 66.07; H, 8.53; N, 11.85. Found: C, 66.16; H, 8.67; N, 11.84%.

15b: needles; m.p. 86–88 °C; R_f 0.33 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2935, 1685; ^1H NMR ($CDCl_3$, 400 MHz) δ = 3.48 (d, *J* 9 Hz, 1H), 3.18 (t, *J* 8.5 Hz, 1H), 3.10–3.02 (m, 2H), 2.95 (s, 3H), 2.16 (dd, *J* 9.5, 7 Hz, 1H), 1.91 (d, *J* 9 Hz, 1H), 1.80–1.74 (m, 1H), 1.70–1.61 (m, 2H), 1.41–1.35 (m, 1H), 1.21 (s, 3H), 1.09–1.01 (m, 1H), 0.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 179.1, 178.6, 76.3, 56.9, 54.1, 46.2, 44.2, 42.5, 33.2, 27.2, 25.0, 21.3, 19.0; HRMS (ES) Found: MH^+ (ES), 237.1601. $C_{13}H_{21}N_2O_2$ requires MH^+ 237.1603; LRMS *m/z* (ES) 237 (100%, MH^+); Anal. Calc. for $C_{13}H_{20}N_2O_2$: C, 66.07; H, 8.53; N, 11.85. Found: C, 66.07; H, 8.63; N, 11.64%.

(3a*RS*,9a*SR*,9b*SR*)-9,9-Dimethyl-2-phenyloctahydro-1*H*-pyrrolo[3,4-a]indolizine-1,3(2*H*)-dione 16a and (3a*SR*,9a*SR*,9b*RS*)-9,9-Dimethyl-2-phenyloctahydro-1*H*-pyrrolo[3,4-a]indolizine-1,3(2*H*)-dione 16b: The aldehyde **3** (100 mg, 0.67 mmol), *N*-phenylmaleimide (174 mg, 1.00 mmol) and glycine (202 mg, 2.69 mmol) were heated under reflux in toluene (7 mL). After 24 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the cycloadducts **16** (125 mg, 63%) as two separable diastereoisomers (dr 1:1):

16a: oil; R_f 0.29 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2930, 1710, 1500; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.49 (t, *J* 7.5 Hz, 2H), 7.41 (t, *J* 7.5 Hz, 1H), 7.29 (d, *J* 7.5 Hz, 2H), 3.59 (t, *J* 9 Hz, 1H), 3.47 (q, *J* 9 Hz, 1H), 3.26 (t, *J* 9 Hz, 1H), 3.08 (dt, *J* 11, 2.5 Hz, 1H), 2.33 (t, *J* 9 Hz, 1H), 2.04 (td, *J* 11, 2.5, Hz, 1H), 1.98 (d, *J* 8 Hz, 1H), 1.78–1.67 (m, 1H), 1.57–1.49 (m, 2H), 1.24–1.17 (m, 1H), 1.14 (s, 3H), 1.05 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 176.6, 131.8, 129.1, 128.6, 126.6, 75.1, 56.7, 52.8, 46.9, 43.6, 39.6, 33.1, 29.1, 21.8, 19.8; HRMS (ES) Found: MH^+ (ES), 299.1751. $C_{18}H_{23}N_2O_2$ requires MH^+ 299.1760; data consistent with the literature.[1]

16b: oil; R_f 0.44 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2930, 1710, 1500; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.49–7.44 (m, 2H), 7.41–7.37 (m, 1H), 7.30–7.27 (m, 2H), 3.59 (d, *J* 9 Hz, 1H), 3.35 (t, *J* 9 Hz, 1H), 3.22 (dd, *J* 9, 7 Hz, 1H), 3.16 (dt, *J* 11, 2 Hz, 1H), 2.25 (dd, *J* 9, 7 Hz, 1H), 2.02 (d, *J* 9 Hz, 1H), 1.86–1.80 (m, 1H), 1.77–1.65 (m, 1H), 1.47–1.40 (m, 2H), 1.25 (s, 3H), 1.15–1.08 (m, 1H), 1.01 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 178.2, 177.6, 132.3, 129.1, 128.5, 126.5, 76.7, 57.2, 54.2, 46.4, 44.3, 42.6, 33.5, 27.2, 21.4, 19.6; HRMS (ES) Found: MH^+ (ES), 299.1760. $C_{18}H_{23}N_2O_2$ requires MH^+ 299.1760; data consistent with the literature.[1]

(1*SR*,2*RS*,8a*SR*)-Dimethyl 8,8-dimethyloctahydroindolizine-1,2-dicarboxylate 17a and (1*RS*,2*SR*,8a*SR*)-Dimethyl 8,8-dimethyloctahydroindolizine-1,2-dicarboxylate 17b: The aldehyde **3** (120 mg, 0.80 mmol), dimethyl maleate (173 mg, 1.20 mmol) and glycine (243 mg, 3.23 mmol) were heated under reflux in toluene (8 mL). After 24 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the cycloadducts **17** (135 mg, 63%) as two separable diastereoisomers (dr 1:1):

17a: oil; R_f 0.43 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2990, 1740, 1730, 1445; ^1H NMR ($CDCl_3$, 400 MHz) δ = 3.59 (s, 3H), 3.58 (s, 3H), 3.14–3.06 (m, 2H), 3.02–2.96 (m, 2H), 2.63–2.55 (m, 1H), 2.10 (d, *J* 9 Hz, 1H), 1.98 (td, *J* 12, 2.5 Hz, 1H), 1.67–1.55 (m, 1H), 1.43–1.34 (m, 2H), 1.08 (td, *J* 13.5, 4 Hz, 1H), 0.76 (s, 3H), 0.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 174.6, 172.1, 76.4, 56.3, 53.1, 51.8, 46.4, 44.8, 39.5, 32.8, 28.1, 21.9, 19.3; HRMS (ES) Found: MH^+ (ES), 270.1713. $C_{14}H_{24}NO_4$ requires MH^+ 270.1705; data consistent with the literature.[1]

17b: oil; R_f 0.29 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2990, 1735, 1440; ^1H NMR ($CDCl_3$, 400 MHz) δ = 3.81 (dd, *J* 10, 6.5 Hz, 1H), 3.65 (s, 3H), 3.64 (s, 3H), 3.33 (dd, *J* 8, 5.5 Hz, 1H), 3.19–3.09 (m, 2H), 2.47 (t, *J* 11 Hz, 1H), 2.15 (d, *J* 5.5 Hz, 1H), 1.94 (td, *J* 11, 3 Hz, 1H), 1.77–1.66 (m, 1H), 1.42–1.32 (m, 2H), 1.07–1.00 (m, 1H), 1.03 (s, 3H), 0.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 173.1, 172.3, 76.6, 55.0, 54.5, 51.9, 51.6, 47.5, 43.9, 41.7, 33.1, 27.9,

21.9, 18.9; HRMS (ES) Found: MH^+ (ES), 270.1704. $C_{14}H_{24}NO_4$ requires MH^+ 270.1705; data consistent with the literature.[1]

(3a*SR*,4*RS*,9a*SR*,9b*RS*)-2,4,9,9-tetramethyloctahydro-1*H*-pyrrolo[3,4-a]indolizine-1,3(2*H*)-dione 18a and (3a*RS*,4*RS*,9a*SR*,9b*SR*)-2,4,9,9-tetramethyloctahydro-1*H*-pyrrolo[3,4-a]indolizine-1,3(2*H*)-dione 18b: The aldehyde **3** (150 mg, 1.01 mmol), *N*-methylmaleimide (168 mg, 1.51 mmol) and alanine (360 mg, 4.04 mmol) were heated under reflux in toluene (10 mL). After 24 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the cycloadducts **18** (130 mg, 52%) as two separable diastereoisomers (dr 1.3:1):
18a (major isomer): oil; R_f 0.52 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2970, 1700, 1420; ^1H NMR ($CDCl_3$, 400 MHz) δ = 3.81 (q, *J* 7 Hz, 1H), 3.23 (dd, *J* 9, 8 Hz, 1H), 2.92 (s, 3H), 2.82–2.78 (m, 1H), 2.77 (d, *J* 8 Hz, 1H), 2.52 (d, *J* 9 Hz, 1H), 2.19(td, *J* 11.5, 3 Hz, 1H), 1.62–1.50 (m, 1H), 1.38–1.37 (m, 2H), 1.17 (s, 3H), 1.03–0.94 (m, 1H), 0.97 (d, *J* 7 Hz, 3H), 0.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 178.9, 178.7, 69.7, 58.9, 52.0, 48.3, 46.0, 42.9, 33.2, 27.2, 24.9, 21.3, 18.7, 11.1; HRMS (ES) Found: MH^+ (ES), 251.1762. $C_{14}H_{23}N_2O_2$ requires MH^+ 251.1760; LRMS *m/z* (ES) 251 (100%, MH^+).
18b (minor isomer): oil; R_f 0.36 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2910, 1700, 1420; ^1H NMR ($CDCl_3$, 400 MHz) δ = 3.70 (m, 1H), 3.36 (t, *J* 9 Hz, 1H), 3.03 (dd, *J* 9, 6.5 Hz, 1H), 2.94 (s, 3H), 2.81–2.77 (m, 1H), 2.51 (d, *J* 6.5 Hz, 1H), 2.34 (td, *J* 12, 3 Hz, 1H), 1.69–1.57 (m, 1H), 1.51–1.40 (m, 2H), 1.13 (td, *J* 13.5, 4 Hz, 1H), 1.05 (s, 3H), 0.93 (s, 3H), 0.83 (d, *J* 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 178.7, 177.3, 68.2, 58.0, 48.6, 47.6, 46.8, 39.5, 32.7, 29.2, 24.6, 21.4, 19.8, 8.6; HRMS (ES) Found: MH^+ (ES), 251.1756. $C_{14}H_{23}N_2O_2$ requires MH^+ 251.1760; LRMS *m/z* (ES) 251 (100%, MH^+).

(1*RS*,2*SR*,3*RS*,8a*SR*)-Dimethyl 3,8,8-trimethyloctahydroindolizine-1,2-dicarboxylate 19a and (1*SR*,2*RS*,3*RS*,8a*SR*)- Dimethyl 3,8,8-trimethyloctahydroindolizine-1,2-dicarboxylate 19b: The aldehyde **3** (150 mg, 1.01 mmol), dimethyl maleate (218 mg, 1.51 mmol) and alanine (360 mg, 4.04 mmol) were heated under reflux in toluene (10 mL). After 24 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the cycloadducts **19** (145 mg, 51%) as two separable diastereoisomers (dr 1:1.2):
19a (minor isomer): oil; R_f 0.61 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2950, 1730, 1435; ^1H NMR ($CDCl_3$, 400 MHz) δ = 3.62 (s, 3H), 3.57 (s, 3H), 3.52 (quintet, *J* 7 Hz, 1H), 3.23 (dd, *J* 11, 7 Hz, 1H), 2.89 (dd, *J* 11, 8 Hz, 1H), 2.76–2.73 (m, 1H), 2.64 (d, *J* 8 Hz, 1H), 2.29 (td, *J* 11, 2 Hz, 1H), 1.61–1.51 (m, 1H), 1.35 (t, *J* 13.5 Hz, 2H), 1.10–0.99 (m, 1H), 1.00 (d, *J* 7 Hz, 3H), 0.84 (s, 3H), 0.73 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 175.2, 172.6, 71.4, 59.9, 51.8, 51.5, 49.7, 48.1, 44.8, 39.5, 32.9, 28.0, 22.0, 19.0, 8.6; HRMS (ES) Found: MH^+ (ES), 284.1851. $C_{15}H_{26}NO_4$ MH^+ requires 284.1862; LRMS *m/z* (ES) 284 (100%, MH^+).
19b (major isomer): oil; R_f 0.30 [EtOAc-petrol (3:7)]; ν_{max}/cm^{-1} 2950, 1730, 1435; ^1H NMR ($CDCl_3$, 400 MHz) δ = 4.01 (quintet, *J* 7 Hz, 1H), 3.63 (s, 3H), 3.61 (s, 3H), 3.26 (dd, *J* 7, 5 Hz, 1H), 2.99–2.97 (m, 1H), 2.57 (t, *J* 7 Hz, 1H), 2.53 (d, *J* 5 Hz, 1H), 2.31 (td, *J* 11.5, 3 Hz, 1H), 1.69–1.58 (m, 1H), 1.42–1.38 (m, 1H), 1.32–1.28 (m, 1H), 1.18 (d, *J* 7 Hz, 3H), 1.00–0.93 (m, 1H), 0.99 (s, 3H), 0.82 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 173.3, 172.1, 73.5, 56.8, 54.4, 51.8, 51.6, 48.1, 47.0, 41.8, 33.2, 28.1, 22.1, 18.9, 17.4; HRMS (ES) Found: MH^+ (ES), 284.1872. $C_{15}H_{26}NO_4$ requires MH^+ 284.1862; LRMS *m/z* (ES) 284 (100%, MH^+).

(3a*SR*,4*SR*,9a*SR*,9b*RS*)-Ethyl 2,9,9-Trimethyl-1,3-dioxodecahydro-1*H*-pyrrolo[3,4-a]indolizine-4-carboxylate 20a: The aldehyde **3** (200 mg, 1.34 mmol), glycine ethyl ester hydrochloride (282 mg, 2.02 mmol), *N*-methylmaleimide (224 mg, 2.02 mmol) and *N*,*N*-diisopropylethylamine (261 mg, 2.02 mmol) were heated under reflux in toluene (13 mL). After 6 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the cycloadducts **20** (400 mg, 94%) as mixture of three isomers in 2.2:2:1 ratio. The major isomer **20a** was separated as needles; m.p. 83–85 °C; R_f 0.58 [Et_2O–petrol (1:1)]; ν_{max}/cm^{-1} 2945, 1690, 1435; ^1H NMR ($CDCl_3$, 400 MHz) δ = 4.12 (s, 1H), 4.12 (q, *J* 7 Hz, 2H), 3.38 (dd, *J* 9, 8 Hz, 1H), 3.13 (d, *J* 8 Hz, 1H), 2.97–2.94 (m, 1H), 2.90 (s, 3H), 2.84 (d, *J* 9 Hz, 1H), 2.05 (td, *J* 11.5, 2.5 Hz, 1H), 1.58–1.46 (m, 1H), 1.33–1.30 (m, 2H), 1.24 (t, *J* 7 Hz, 3H), 1.13 (s, 3H), 1.00 (td, *J* 13.5, 4 Hz, 1H), 0.71 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 178.4, 177.0, 170.4, 70.9, 66.1, 60.6, 49.2, 48.1, 46.6, 42.4, 33.4, 26.9, 25.1, 21.2, 18.3, 14.4; HRMS (ES) Found: MH^+ (ES), 309.1808. $C_{16}H_{25}N_2O_4$ requires MH^+ 309.1814; LRMS *m/z* (ES) 309 (100%, MH^+); Anal. Calc. for $C_{16}H_{24}N_2O_4$: C, 62.32; H, 7.84; N, 9.08. Found: C, 62.09; H, 7.57; N, 9.04%.

3-Ethyl 1,2-Dimethyl-8,8-dimethyloctahydroindolizine-1,2,3-tricarboxylate 21: The aldehyde **3** (50 mg, 0.34 mmol), glycine ethyl ester hydrochloride (71 mg, 0.51 mmol), dimethyl maleate (74 mg, 0.51 mmol) and *N*,*N*-diisopropylethylamine (66 mg, 0.51 mmol) were heated under reflux in toluene (4 mL). After 6 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the cycloadducts **21** (85 mg, 74%) as a mixture of three isomers in 2.5:1:1 ratio. The major isomer was separated as an oil; R_f 0.67 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2950, 1730, 1435; ^1H NMR ($CDCl_3$, 500 MHz) δ = 4.45 (d, *J* 7.5 Hz, 1H, C3-H), 4.25–4.16 (m, 2H), 3.63 (s, 3H), 3.62 (s, 3H), 3.54 (t, *J* 7.5 Hz, 1H), 3.36 (dd, *J* 7.5, 5.5

Hz, 1H), 2.99–2.98 (m, 1H), 2.74 (d, *J* 5.5 Hz, 1H), 2.14 (td, *J* 11.5, 3 Hz, 1H), 1.70–1.62 (m, 1H), 1.39–1.36 (m, 1H), 1.29 (t, *J* 7 Hz, 3H), 1.29–1.23 (m, 1H), 1.05–0.99 (m, 1H), 1.00 (s, 3H), 0.81 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ = 172.9, 172.8, 171.1, 73.6, 65.3, 60.9, 52.0, 51.6, 49.5, 48.3, 46.8, 41.3, 33.2, 27.9, 21.7, 18.6, 14.3; HRMS (ES) Found: MH^+ (ES), 342.1919. $C_{17}H_{28}NO_6$ requires MH^+ 342.1917; LRMS *m/z* (ES) 342 (100%, MH^+).

(3*RS*,8a*SR*)-3-Ethyl 1,2-Dimethyl 8,8-dimethyl-3,5,6,7,8,8a-hexahydroindolizine-1,2,3-tricarboxylate 22: The aldehyde **3** (250 mg, 1.7 mmol), glycine ethyl ester (260 mg, 2.6 mmol) and *N*,*N*-diisopropylethylamine (0.89 mL, 5.1 mmol) were heated under reflux in toluene (20 mL). After 2 h, the mixture was cooled to room temperature and dimethoxy acetylene dicarboxylate (0.31 mL, 2.6 mmol) was added. After 12 h, the solvent was evaporated and the mixture was purified by column chromatography, eluting with petrol–EtOAc (9:1), to give the cycloadduct **22** (256 mg, 45%) as an oil; R_f 0.30 [petrol–EtOAc (9:1)]; ν_{max}/cm^{-1} 2940, 1725, 1650, 1435; ^{1}H NMR ($CDCl_3$, 500 MHz) δ = 4.62 (d, *J* 5.5 Hz, 1H), 4.24–4.09 (m, 2H) 3.85–3.81 (m, 4H), 3.71 (s, 3H), 2.95 (dd, *J* 11, 5 Hz, 1H), 2.43 (td, *J* 11, 3 Hz, 1H), 1.78–1.65 (m, 1H), 1.44–1.34 (m, 2H), 1.26 (t, *J* 7 Hz, 3H), 1.17 (td, *J* 13.5, 4.5 Hz, 1H), 1.01 (s, 3H), 0.87 (s, 3H); ($CDCl_3$, 125 MHz) δ = 169.5, 166.7, 162.1, 148.9, 131.1, 77.6, 69.7, 60.8, 52.4, 50.9, 46.3, 39.4, 33.9, 27.5, 21.9, 19.5, 14.5; HRMS (ES) Found: MH^+ (ES), 340.1761. $C_{17}H_{26}NO_6$ requires MH^+, 340.1760; LRMS *m/z* (ES) 340 (100%, MH^+).

(1*SR*,2*RS*,7a*SR*)-Dimethyl 7,7-dimethylhexahydro-1*H*-pyrrolizine-1,2-dicarboxylate 23a and (1*RS*,2*SR*,7a*SR*)-Dimethyl 7,7-dimethylhexahydro-1*H*-pyrrolizine-1,2-dicarboxylate 23b: The aldehyde **7** (80 mg, 0.59 mmol), dimethyl maleate (94 mg, 0.65 mmol) and glycine (177 mg, 2.36 mmol) were heated under reflux in toluene (6 mL). After 6 h, the mixture was cooled to room temperature and filtered. The solid was washed with CH_2Cl_2 (20 mL) and the solvent was evaporated. The residue was purified by column chromatography, eluting with CH_2Cl_2–MeOH (95:5), to give the cycloadducts **23** (80 mg, 52%) as an inseparable mixture of two isomers (dr 1:1); R_f 0.35 [MeOH–CH_2Cl_2 (5:95)]; ν_{max}/cm^{-1} 2950, 1730, 1435; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 3.80 (dd, *J* 9, 7.5 Hz, 1H), 3.67 (s, 3H), 3.66 (s, 3H), 3.65 (s, 3H), 3.64 (s, 3H), 3.58 (d, *J* 8 Hz, 1H), 3.52–3.34 (m, 6H), 3.22–3.13 (m, 2H), 2.98–2.88 (m, 3H), 2.51 (dt, *J* 10.5, 8 Hz, 1H), 1.93 (dt, *J* 12, 9.5 Hz, 1H), 1.78–1.71 (m, 1H), 1.67–1.61 (m, 1H), 1.59–1.53 (m, 1H), 1.17 (s, 3H, Me), 1.14 (s, 3H, Me), 1.09 (s, 3H, Me), 0.95 (s, 3H, Me); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 173.3, 172.5, 172.4, 169.9, 79.0, 75.2, 57.3, 55.9, 54.7, 53.2, 52.1, 52.0, 51.9, 51.8, 49.8, 48.5, 46.8, 46.7, 41.5, 40.6, 39.9, 38.9, 30.4, 28.2, 23.7, 22.7; HRMS (ES) Found: MH^+ (ES), 256.1538. $C_{13}H_{22}NO_4$ requires MH^+ 256.1549; LRMS *m/z* (ES) 256 (100%, MH^+).

(1*RS*,2*SR*,3*SR*,7a*SR*)-3-Ethyl 1,2-Dimethyl 7,7-dimethylhexahydro-1*H*-pyrrolizine-1,2,3-tricarboxylate 24: The aldehyde **7** (120 mg, 0.89 mmol), glycine ethyl ester hydrochloride (187 mg, 1.34 mmol), dimethyl maleate (193 mg, 1.34 mmol) and *N*,*N*-diisopropylethyl amine (173 mg, 1.34 mmol) were heated under reflux in toluene (9 mL). After 4 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the cycloadducts **24** (180 mg, 62%) as three separable diastereoisomers (dr 15:2:1); data for **24** (major isomer)**:** oil; R_f 0.58 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2950, 1730, 1440; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 4.20–4.12 (m, 2H), 4.03 (d, *J* 10 Hz, 1H), 3.69 (dd, *J* 10, 6 Hz, 1H), 3.60 (s, 3H), 3.57 (s, 3H), 3.38 (d, *J* 6 Hz, 1H), 3.25 (td, *J* 9.5, 7.5 Hz, 1H), 3.11 (t, *J* 6 Hz, 1H), 2.85 (td, *J* 9.5, 3.5 Hz, 1H), 1.69–1.62 (m, 1H), 1.37–1.31 (m, 1H), 1.23 (t, *J* 7 Hz, 3H), 1.03 (s, 3H), 1.02 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 173.8, 173.3, 170.5, 78.9, 69.6, 60.7, 54.8, 52.6, 51.9, 51.4, 48.2, 40.3, 38.5, 30.5, 22.8, 14.0; HRMS (ES) Found: MH^+ (ES), 328.1763. $C_{16}H_{26}NO_6$ requires MH^+ 328.1760; LRMS *m/z* (ES) 328 (100%, MH^+).

(2*SR*,3*RS*,3a*SR*)-Dimethyl 4,4-Dimethylhexahydro-2*H*-isoxazolo[2,3-*a*]pyridine-2,3-dicarboxylate 25a and **(2*RS*,3*SR*,3a*SR*)-Dimethyl 4,4-Dimethylhexahydro-2*H*-isoxazolo[2,3-*a*]pyridine-2,3-dicarboxylate 25b:** The aldehyde **3** (150 mg, 1.01 mmol), hydroxylamine hydrochloride (105 mg, 1.51 mmol), dimethyl maleate (218 mg, 1.51 mmol) and *N*,*N*-diisopropylethylamine (392 mg, 3.03 mmol) were heated under reflux in toluene (10 mL). After 24 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the diesters **25** (210 mg, 77%) as two separable diastereoisomers (dr 1.6:1):
25a (major isomer): oil; R_f 0.41 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 1735; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 4.60 (d, *J* 10 Hz, 1H), 3.72 (s, 3H), 3.66 (s, 3H), 3.52–3.48 (m, 1H), 3.45 (t, *J* 10 Hz, 1H), 2.64–2.58 (m, 1H), 2.47 (d, *J* 10 Hz, 1H), 1.79–1.65 (m, 2H), 1.38 (d, *J* 13 Hz, 1H), 1.15 (td, *J* 13, 5 Hz, 1H), 0.98 (s, 3H), 0.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 172.1, 168.9, 78.5, 76.5, 55.5, 52.4, 52.2, 52.0, 38.6, 34.9, 28.1, 21.5, 19.5; HRMS (ES) Found: MH^+ (ES), 272.1501. $C_{13}H_{22}NO_5$ requires MH^+ 272.1498; LRMS *m/z* (ES) 272 (100%, MH^+); 294 (95%, MNa^+).
25b (minor isomer): oil; R_f 0.63 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2950, 1735, 1440; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 4.56 (d, *J* 5 Hz, 1H), 3.76 (s, 3H), 3.72 (s, 3H), 3.52–3.47 (m, 2H), 2.49–2.44 (m, 1H), 2.38 (d, *J* 9.5 Hz, 1H), 1.79–1.68 (m, 1H), 1.63–1.60 (m, 1H), 1.34 (d, *J* 13.5 Hz, 1H), 1.13 (td, *J* 13.5, 5, Hz, 1H), 0.94 (s, 3H), 0.89 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 172.9, 171.8, 78.5, 77.4, 55.6, 52.7, 52.4, 51.9, 38.7, 35.0, 28.3, 21.5, 19.5; HRMS (ES) Found: MH^+ (ES), 272.1491. $C_{13}H_{22}NO_5$ requires MH^+ 272.1498; LRMS *m/z* (ES) 272 (100%, MH^+); 294 (55%, MNa^+).

(3a*RS*,8a*RS*,8b*SR*)-2,8,8-Trimethylhexahydro-1*H*-dipyrrolo[1,2-*b*;3',4'-*d*]isoxazole-1,3(2*H*)-dione 26: The aldehyde **7** (90 mg, 0.67 mmol), hydroxylamine hydrochloride (70 mg, 1.0 mmol), *N*-methylmaleimide (74 mg, 0.67 mmol) and *N*,*N*-diisopropylethylamine (260 mg, 2.0 mmol) were heated under reflux in toluene (7 mL). After 4 h, the solvent was evaporated and the mixture was purified by column chromatography, eluting with petrol–EtOAc (1:1), to give the imide **26** (50 mg, 34%) as an oil; R_f 0.17 [EtOAc–petrol (2:3)]; ν_{max}/cm^{-1} 2955, 1700, 1435; ^1H NMR ($CDCl_3$, 400 MHz) δ = 4.73 (d, *J* 7 Hz, 1H), 3.56 (d, *J* 7 Hz, 1H), 3.47–3.40 (m, 1H), 3.38 (s, 1H), 3.13–3.05 (m, 1H), 3.02 (s, 3H), 2.12–2.03 (m, 1H), 1.73–1.67 (m, 1H), 1.56 (s, 3H), 1.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 176.3, 175.1, 79.2, 76.3, 53.4, 50.6, 40.7, 30.9, 29.1, 26.9, 25.1; HRMS (ES) Found: MH^+ (ES), 225.1229. $C_{11}H_{17}N_2O_3$ requires MH^+ 225.1239; LRMS *m/z* (ES) 225 (100%, MH^+).

(3a*SR*,3b*RS*,9*SR*,9a*RS*)-Ethyl 4,4-Dimethyl-1,3-dioxo-2-phenyldodecahydro-2,8a-diaza-cyclopenta[*a*]azulene-9-carboxylate 27a: The aldehyde **10** (500 mg, 2.0 mmol), glycine ethyl ester hydrochloride (420 mg, 3.0 mmol), *N*-phenylmaleimide (520 mg, 3.0 mmol) and *N*,*N*-diisopropylethylamine (1.1 mL, 6.0 mmol) were heated under reflux in toluene (20 mL). After 12 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc gradient (9:1 to 4:1), to give the cycloadducts **27** (500 mg, 65%) as a mixture of three isomers (an inseparable mixture of two isomers and a single separable diastereoisomer); data for single diastereomer **27a:** needles; m.p. 115–118 °C; ν_{max}/cm^{-1} 2925, 1735, 1705, 1455; ^1H NMR ($CDCl_3$, 500 MHz) δ = 7.47–7.42 (m, 2H), 7.39–7.35 (m, 1H) 7.30–7.25 (m, 2H), 4.32–4.17 (m, 2H), 3.49 (d, *J* 8 Hz, 1H), 3.38 (d, *J* 8 Hz, 1H), 3.38 (t, *J* 8 Hz, 1H), 3.00–2.95 (m, 1H), 2.54 (d, *J* 8 Hz, 1H), 2.38–2.31 (m, 1H), 1.84–1.46 (m, 6H), 1.33, (s, 3H) 1.30 (t, *J* 7.5 Hz, 3H), 1.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ = 176.5, 174.8, 169.8, 132.0, 129.0, 128.6, 126.6, 79.2, 69.3, 61.1, 51.6, 46.4, 46.1, 43.0, 35.8, 29.6, 24.3, 22.7, 19.2, 14.1; HRMS (ES) Found: MH^+(ES), 385.2127. $C_{22}H_{29}N_2O_4$ requires MH^+, 385.2121; LRMS *m/z* (ES) 385 (100%, MH^+). Anal. Calc. for $C_{22}H_{29}N_2O_4$: C, 68.73; H, 7.34; N, 7.29. Found: C, 68.68; H, 7.20; N, 7.15%.

9,9-Dimethyloctahydropyrrolo[1,2-*a*]azepine-1,2,3-tricarboxylic acid 3-ethyl ester 1,2-dimethyl ester 28: The aldehyde **10** (250 mg, 1.0 mmol), glycine ethyl ester hydrochloride (290 mg, 1.5 mmol), dimethyl maleate (0.19 mL, 1.5 mmol) and *N*,*N*-diisopropylethylamine (0.53 mL, 3.0 mmol) were heated under reflux in toluene (10 mL). After 12 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc gradient (19:1 to 9:1), to give the cycloadducts **28** (167 mg, 46%) as a mixture of three isomers (an inseparable mixture of two isomers and a single separable diastereoisomer); data for single diastereomer **28** as an oil, R_f 0.15 [petrol–EtOAc (19:1)]; ν_{max}/cm^{-1} 2925, 1730, 1435; ^1H NMR ($CDCl_3$, 400 MHz) δ = 4.25–4.1 (m, 2H), 3.77–3.71 (m, 4H) 3.65 (s, 3H), 3.56–3.45 (m, 2H), 3.20–3.12 (m, 1H), 2.97 (d, *J* 8 Hz, 1H), 2.85–2.77 (m, 1H), 1.80–1.69 (m, 1H), 1.63–1.49 (m, 2H), 1.49–1.39 (m, 2H), 1.34–1.21 (m, 4H), 0.86 (s, 3H) 0.81 (t, *J* 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 175.6, 171.5, 170.9, 77.3, 69.8, 60.5, 58.1, 52.2, 52.0, 49.4, 48.4, 44.9, 36.5, 29.7, 27.3, 21.9, 21.4, 14.2; HRMS (ES) Found: MH^+(ES), 356.2083. $C_{18}H_{30}NO_6$ requires MH^+, 356.2073; LRMS *m/z* (ES) 356 (100%, MH^+).

Ethyl 9,9-Dimethyl-1-(phenylsulfonyl)octahydro-1*H*-pyrrolo[1,2-*a*]azepine-3-carboxylate 29a and Ethyl 9,9-Dimethyl-2-(phenylsulfonyl)octahydro-1*H*-pyrrolo[1,2-*a*]azepine-3-carboxylate 29b: The aldehyde **10** (500 mg, 2.0 mmol), glycine ethyl ester hydrochloride salt (420 mg, 3.0 mmol) and *N*,*N*-diisopropylethylamine (1.06 mL, 6.0 mmol) were heated under reflux in toluene (20 mL). After 6 h, phenyl vinyl sulfone (500 mg, 3.0 mmol) was added and heating was continued. After 16 h, the solvent was evaporated. Benzylamine (0.44 mL, 4.5 mmol) in toluene (25 mL) was added and the mixture was heated under reflux for 1 h (to remove excess phenyl vinyl sulfone). The solvent was evaporated and the mixture was purified by column chromatography, eluting with petrol–EtOAc (9:1), to give the ester **29** (286 mg, 45%) as a mixture of four isomers of which two pairs of isomers (possibly the two regioisomers) (ratio 1.3:1) were separable:

29a (major)**:** Mixture of isomers (1:1); R_f 0.21 [petrol–EtOAc (9:1)]; ν_{max}/cm^{-1} 2925, 1725, 1450; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.98–7.89 (m, 5H), 7.70–7.51 (m, 5H), 4.27–4.10 (m, 2H), 4.06–3.94 (m, 2H), 3.91 (d, *J* 7 Hz, 1H), 3.78 (dd, *J* 11, 7 Hz, 1H), 3.51 (d, *J* 7 Hz, 1H), 3.37–3.32 (m, 1H), 3.04–2.96 (m, 1H), 2.89–2.65 (m, 3H), 2.57–2.01 (m, 3H), 2.25–2.15 (m, 1H), 1.70–1.15 (m, 14H), 1.31 (s, 3H), 1.23 (s, 3H), 1.10 (t, *J* 7 Hz, 6H), 0.82 (s, 3H) 0.56 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 173.8, 173.1, 141.0, 137.8, 133.9, 133.3, 129.3, 129.1, 129.0, 128.0, 72.6, 71.4, 66.9, 66.0, 65.3, 63.5, 60.6, 60.5, 54.5, 50.6, 46.5, 43.8, 38.3, 36.9, 32.2, 31.0, 30.4, 29.8, 28.2, 26.6, 23.9, 22.9, 22.1, 21.5, 14.2, 14.1 ; HRMS (ES) Found: MH^+ (ES), 380.1884. $C_{20}H_{30}NO_4S$ requires MH^+, 380.1896; LRMS *m/z* (ES) 380 (100%, MH^+).

29b (minor)**:** Mixture of isomers (1:1); R_f 0.20 [petrol–EtOAc (9:1)]; ν_{max}/cm^{-1} 2925, 1726, 1445; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.97–7.85 (m, 5H), 7.70–7.50 (m, 5H), 4.30–3.92 (m, 6H), 3.87 (dd, *J* 8.5, 2.5 Hz, 1H), 3.76 (td, *J* 9, 4 Hz, 1H), 3.64 (d, *J* 2.5 Hz, 1H), 3.47 (dt, *J* 9, 2.5 Hz, 1H), 3.28–3.19 (m, 1H), 3.07–3.01 (m, 1H), 2.97–2.88 (m, 1H), 2.84–2.76 (m, 1H), 2.69–2.60 (m, 1H), 2.58–2.51 (m, 1H), 2.42–2.29 (m, 1H), 2.18–2.02 (m, 3H), 1.80–1.12 (m, 10H), 1.30 (t, *J* 7.5 Hz, 3H), 1.16 (t, *J* 7.5 Hz, 3H), 0.96–0.73 (m, 12H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 173.0,

171.8, 139.0, 138.0, 133.8, 133.6, 129.2, 129.1, 129.0, 128.9, 128.2, 70.6, 70.5, 67.6, 66.2, 65.5, 64.7, 60.9, 60.7, 49.2, 48.8, 41.8, 41.4, 39.2, 36.0, 34.6, 31.1, 30.4, 29.8, 28.8, 26.5, 23.5, 22.6, 20.7, 18.9, 14.3, 14.2; HRMS (ES) Found: MH^+ (ES), 380.1908. $C_{20}H_{30}NO_4S$ requires MH^+, 380.1896; LRMS *m/z* (ES) 380 (100%, MH^+).

(8*RS*,8a*RS*,11a*SR*,11b*RS*)-Ethyl 10-Methyl-9,11-dioxo-5,8,8a,9,10,11,11a,11b-octahydro-6*H*-pyrrolo[3',4':3,4]pyrrolo[2,1-*a*]isoquinoline-8-carboxylate 30a and (8*RS*,8a*SR*,11a*RS*,11b*RS*)-Methyl 10-Methyl-9,11-dioxo-5,8,8a,9,10,11,11a,11b-octahydro-6*H*-pyrrolo[3',4':3,4]pyrrolo[2,1-*a*]isoquinoline-8-carboxylate 30b: The aldehyde **13** (260 mg, 1.22 mmol), glycine ethyl ester hydrochloride (205 mg, 1.46 mmol), *N*-methylmaleimide (149 mg, 1.34 mmol) and *N*,*N*-diisopropylethylamine (378 mg, 2.93 mmol) were heated under reflux in toluene (12 mL). After 3 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the cycloadducts **30** (310 mg, 78%) as two separable diastereoisomers (dr 1:1):

30a: needles; m.p. 121–123 °C; R_f 0.57 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2930, 2800, 1690, 1440; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.45 (d, *J* 7.5 Hz, 1H), 7.24 (t, *J* 7.5 Hz, 1H), 7.18 (t, *J* 7.5 Hz, 1H), 7.09 (d, *J* 7.5 Hz, 1H), 4.50 (d, *J* 8 Hz, 1H), 4.27–4.19 (m, 2H), 4.21 (s, 1H), 3.73 (t, *J* 8 Hz, 1H), 3.63 (d, *J* 8 Hz, 1H), 3.18–3.14 (m, 1H), 3.01–2.93 (m, 1H), 2.88–2.82 (m, 1H), 2.87 (s, 3H), 2.71 (d, *J* 15.5 Hz, 1H), 1.32 (t, *J* 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 177.8, 175.5, 169.8, 134.2, 131.9, 128.7, 128.2, 126.7, 125.0, 66.5, 62.0, 61.2, 47.4, 46.4, 45.1, 30.0, 25.1, 14.4; HRMS (ES) Found: MH^+ (ES), 329.1488. $C_{18}H_{21}N_2O_4$ requires MH^+, 329.1501; data consistent with the literature.[3]

30b: oil; R_f 0.34 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2930, 1695, 1435; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.44 (d, *J* 8 Hz, 1H), 7.27 (t, *J* 8 Hz, 1H), 7.20 (t, *J* 8 Hz, 1H), 7.09 (d, *J* 8 Hz, 1H), 4.78 (br s, 1H), 4.34–4.20 (m, 2H), 4.03 (d, *J* 8.5 Hz, 1H), 3.55 (t, *J* 8.5 Hz, 1H), 3.47 (dd, *J* 8.5, 3 Hz, 1H), 3.31 (ddd, *J* 13, 6, 2 Hz, 1H), 3.14 (td, *J* 13, 5 Hz, 1H), 3.06–2.96 (m, 1H), 3.04 (s, 3H), 2.60 (br d, *J* 16.5 Hz, 1H), 1.33 (t, *J* 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 177.3, 176.0, 169.3, 135.0, 133.6, 129.1, 127.0, 126.9, 126.7, 63.4, 62.4, 61.4, 50.7, 47.3, 43.1, 25.4, 22.9, 14.1; HRMS (ES) Found: MNa^+ (ES), 351.1320. $C_{18}H_{20}N_2O_4Na$ requires MNa^+, 351.1321; data consistent with the literature.[3]

(8*RS*,8a*RS*,11a*SR*,11b*RS*)-9,11-Dioxo-10-phenyl-5,8,8a,9,10,11,11a,11b-octahydro-6*H*-pyrrolo[3',4':3,4]pyrrolo[2,1-*a*]isoquinoline-8-carboxylic acid ethyl ester 31a and (8*RS*,8a*SR*,11a*RS*,11b*RS*)-9,11-Dioxo-10-phenyl-5,8,8a,9,10,11,11a,11b-octahydro-6*H*-pyrrolo[3',4':3,4]pyrrolo[2,1-*a*]isoquinoline-8-carboxylic acid ethyl ester 31b: The aldehyde **13** (125 mg, 0.58 mmol), glycine ethyl ester hydrochloride (99 mg, 0.70 mmol), *N*-phenylmaleimide (111 mg, 0.64 mmol) and *N*,*N*-diisopropylethylamine (180 mg, 1.39 mmol) were heated under reflux in toluene (6 mL). After 3 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the cycloadducts **31** (190 mg, 83%) as two separable diastereoisomers (dr 1:1):

31a: oil; R_f 0.61 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 1710, 1500, 1375; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.48 (d, *J* 7.5 Hz, 1H), 7.40 (t, *J* 7.5 Hz, 2H), 7.34 (d, *J* 7.5 Hz, 1H), 7.26–7.11 (m, 5H), 4.63 (d, *J* 8 Hz, 1H), 4.38 (s, 1H), 4.32–4.24 (m, 2H), 3.90 (t, *J* 8 Hz, 1H), 3.84 (d, *J* 8 Hz, 1H), 3.27–3.23 (m, 1H), 3.09–2.93 (m, 2H), 2.79 (d, *J* 15 Hz, 1H), 1.36 (t, *J* 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 176.8, 174.4, 169.8, 134.2, 131.7, 128.9, 128.7, 128.4, 128.3, 126.8, 126.2, 125.2, 67.3, 62.5, 61.3, 47.7, 46.7, 45.4, 30.1, 14.4; HRMS (ES) Found: MNa^+ (ES), 413.1464. $C_{23}H_{22}N_2O_4Na$ requires MNa^+, 413.1477; LRMS *m/z* (ES) 413 (100%, MNa^+).

31b: oil; R_f 0.37 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2925, 1710, 1495, 1385; ^1H NMR ($CDCl_3$, 400 MHz) δ = 7.57 (d, *J* 8 Hz, 1H), 7.49 (t, *J* 8 Hz, 2H), 7.42–7.36 (m, 3H), 7.28 (t, *J* 8 Hz, 1H), 7.22 (t, *J* 8 Hz, 1H), 7.12 (d, *J* 8 Hz, 1H), 4.85 (d, *J* 3.5 Hz, 1H), 4.31–4.22 (m, 2H), 4.18 (d, *J* 8.5 Hz, 1H), 3.75 (t, *J* 8.5 Hz, 1H), 3.64 (dd, *J* 8.5, 3.5 Hz, 1H), 3.31–3.27 (m, 1H), 3.14 (dd, *J* 11, 4 Hz, 1H), 3.04 (dd, *J* 11, 6 Hz, 1H), 2.70 (d, *J* 15.5 Hz, 1H), 1.31 (t, *J* 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 176.4, 175.2, 169.5, 135.2, 133.6, 129.1, 129.0, 128.7, 127.0, 126.8, 126.6, 63.9, 63.4, 61.5, 51.0, 47.2, 43.9, 24.4, 14.2; HRMS (ES) Found: MH^+ (ES), 391.1671. $C_{23}H_{23}N_2O_4$ requires MH^+, 391.1658; LRMS *m/z* (ES) 413 (100%, MNa^+); 391 (20%, MH^+).

(1*RS*,2*SR*,3*SR*,10b*SR*)-1,2,3,5,6,10b-Hexahydropyrrolo[2,1-*a*]isoquinoline-1,2,3-tricarboxylic acid 3-ethyl ester 1,2-dimethyl ester 32: The aldehyde **13** (212 mg, 0.99 mmol), glycine ethyl ester hydrochloride (166 mg, 1.18 mmol), dimethyl maleate (157 mg, 1.09 mmol) and *N*,*N*-diisopropylethylamine (307 mg, 2.38 mmol) were heated under reflux in toluene (10 mL). After 3 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the cycloadduct **32** (270 mg, 75%) as needles; mp 71–72 °C; R_f 0.55 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2935, 1710, 1430; ^1H NMR ($CDCl_3$, 500 MHz) δ = 7.15–7.05 (m, 4H), 4.90 (d, *J* 7 Hz, 1H), 4.36 (d, *J* 9 Hz, 1H), 4.27 (q, *J* 7 Hz, 2H), 3.83 (dd, *J* 9, 7 Hz, 1H), 3.77 (t, *J* 7 Hz, 1H), 3.65 (s, 3H), 3.21–3.17 (m, 1H), 3.18 (s, 3H), 3.02–2.97 (m, 1H), 2.85–2.80 (m, 1H), 2.67–2.62 (m, 1H), 1.32 (t, *J* 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ = 173.0, 172.0, 170.7, 136.3, 133.5, 128.3, 127.3, 126.4, 125.5, 66.4, 63.1, 61.2, 52.2, 51.4, 51.2, 48.9, 46.0, 27.6, 14.2; HRMS (ES) Found: MH^+ (ES), 362.1610. $C_{19}H_{24}NO_6$ requires MH^+, 362.1604; LRMS *m/z* (ES) 362 (100%, MH^+). Anal. Calc. for $C_{19}H_{23}NO_6$: C, 63.15; H, 6.41; N, 3.88. Found: C, 62.91; H, 6.36; N, 3.59%.

Ethyl 2-Benzenesulfonyl-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-3-carboxylate 33a and Ethyl 1-Benzenesulfonyl-1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline-3-carboxylate 33b: The aldehyde **13** (200 mg, 0.94 mmol), glycine ethyl ester hydrochloride (157 mg, 1.13 mmol), phenyl vinyl sulfone (174 mg, 1.03 mmol) and *N*,*N*-diisopropylethylamine (292 mg, 2.26 mmol) were heated under reflux in toluene (9 mL). After 3h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (7:3), to give the cycloadducts **33** (260 mg, 72%) as a mixture of four isomers of which the regioisomers (ratio 1:2.7) were separable:

33a (minor regioisomer)**:** Mixture of diastereoisomers (dr 1:1); R_f 0.49 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2985, 1740, 1450; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.05–8.03 (m, 2H), 7.93–7.90 (m, 2H), 7.74–7.54 (m, 6H), 7.44 (d, *J* 8 Hz, 1H), 7.20–7.11 (m, 6H), 7.00–6.98 (m, 1H), 4.38 (dd, *J* 11, 6 Hz, 1H), 4.26–4.09 (m, 6H), 3.92–3.86 (m, 1H), 3.49–3.42 (m, 3H), 3.25–3.14 (m, 2H), 3.01–2.74 (m, 5H), 2.60–2.49 (m, 2H), 2.37–2.30 (m, 2H), 1.26 (t, *J* 7 Hz, 3H), 1.23 (t, *J* 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 171.1, 170.9, 138.2, 135.9, 135.7, 134.7, 134.1, 133.8, 129.6, 129.2, 128.7, 128.6, 128.4, 127.0, 126.5, 126.4, 126.0, 125.8, 125.3, 66.6, 66.4, 65.6, 63.6, 61.5, 61.1, 60.9, 47.8, 46.3, 33.9, 32.3, 28.8, 14.1; HRMS (ES) Found: MH^+ (ES), 386.1422. $C_{21}H_{24}NO_4S$ requires MH^+, 386.1426; LRMS *m/z* (ES) 386 (100%, MH^+); 408 (75%, MNa^+).

33b (major regioisomer)**:** Mixture of diastereoisomers (dr 1:1); R_f 0.40 [EtOAc–petrol (3:7)]; ν_{max}/cm^{-1} 2940, 1735, 1690, 1450; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 8.03–7.50 (m, 6H), 7.32–6.92 (m, 12H), 5.14 (d, *J* 3.5 Hz, 1H), 4.83 (d, *J* 6 Hz, 1H), 4.26–4.10 (m, 4H), 3.91 (dd, *J* 8.5, 3.5 Hz, 1H), 3.79–3.68 (m, 2H), 3.34–3.19 (m, 2H), 3.10–2.96 (m, 3H), 2.83–2.77 (m, 1H), 2.62–2.48 (m, 6H), 2.28–2.21 (m, 1H), 1.31 (t, *J* 7 Hz, 3H), 1.28 (t, *J* 7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 172.7, 171.2, 139.6, 137.8, 136.1, 135.7, 134.4, 133.9, 132.9, 130.7, 129.3, 129.0, 125.1, 69.7, 67.3, 62.5, 61.8, 61.1, 60.8, 60.7, 60.2, 44.7, 43.4, 30.8, 30.3, 28.9, 21.9, 14.2, 14.1; HRMS (ES) Found: MH^+ (ES), 386.1418. $C_{21}H_{24}NO_4S$ requires MH^+, 386.1426; LRMS *m/z* (ES) 386 (100%, MH^+).

(8a*RS*,11a*SR*,11b*RS*)-10-Methyl-5,6,8,8a,11a,11b-hexahydro-pyrrolo[3',4':3,4]pyrrolo[2,1-*a*]isoquinoline-9,11-dione 34a and (8a*SR*,11a*RS*,11b*RS*)-10-Methyl-5,6,8,8a,11a,11b-hexahydro-pyrrolo[3',4':3,4]pyrrolo[2,1-*a*]isoquinoline-9,11-dione 34b: The aldehyde **13** (200 mg, 0.94 mmol), glycine (282 mg, 3.76 mmol) and *N*-methylmaleimide (125 mg, 1.13 mmol) were heated under reflux in toluene (10 mL). After 24 h, the mixture was cooled to room temperature, evaporated and was purified by column chromatography, eluting with petrol–EtOAc (3:2), to give the cycloadducts **34** (120 mg, 50%) as two separable diastereoisomers (dr 1:1):

34a: oil; R_f 0.23 [EtOAc–petrol (4:6)]; ν_{max}/cm^{-1} 2920, 2800, 1695, 1430; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.51 (d, *J* 7 Hz, 1H), 7.24 (t, *J* 7 Hz, 1H), 7.19 (t, *J* 7 Hz, 1H), 7.11 (d, *J* 7 Hz, 1H), 3.65 (t, *J* 7 Hz, 1H), 3.60 (d, *J* 7 Hz, 1H), 3.48 (d, *J* 9 Hz, 1H), 3.28 (t, *J* 7 Hz, 1H), 3.20–3.15 (m, 1H), 3.12–3.04 (m, 1H), 2.88 (s, 3H), 2.72 (dd, *J* 16, 4 Hz, 1H), 2.59 (dd, *J* 9, 7 Hz, 1H), 2.42 (td, *J* 11, 4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 179.2, 175.9, 134.4, 132.2, 128.6, 127.6, 126.8, 124.9, 67.3, 56.4, 48.3, 45.9, 43.6, 29.5, 24.9; HRMS (ES) Found: MH^+ (ES), 257.1287. $C_{15}H_{17}N_2O_2$ requires MH^+, 257.1290; LRMS *m/z* (ES) 257 (100%, MH^+).

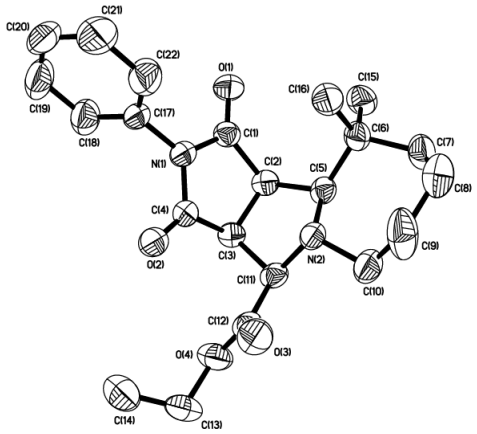
34b: oil; R_f 0.19 [EtOAc–petrol (4:6)]; ν_{max}/cm^{-1} 2925, 1690, 1435; ^{1}H NMR ($CDCl_3$, 400 MHz) δ = 7.51 (d, *J* 7.5 Hz, 1H), 7.26 (t, *J* 7.5 Hz, 1H), 7.19 (t, *J* 7.5 Hz, 1H), 7.10 (d, *J* 7.5 Hz, 1H), 4.29 (d, *J* 3.5 Hz, 1H), 3.44 (dd, *J* 8, 3.5 Hz, 1H), 3.34–3.26 (m, 2H), 3.19–3.14 (m, 1H), 3.09–2.99 (m, 3H), 3.05 (s, 3H), 2.63 (d, *J* 14 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ = 178.8, 178.3, 135.1, 133.7, 129.0, 126.9, 126.8, 126.7, 64.6, 51.9, 51.6, 45.0, 44.7, 25.2, 23.8; HRMS (ES) Found: MH^+ (ES), 257.1281. $C_{15}H_{17}N_2O_2$ requires MH^+, 257.1290; LRMS *m/z* (ES) 257 (100%, MH^+).

2. X-ray data for compounds 27a, 32 and 38a

The X-ray of compound **20a** has been reported,[4] and the data deposited at CCDC-690593.

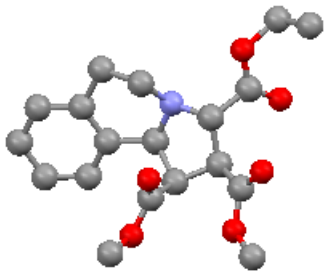
a) Compound **27a**

Identification code	lw1x_0m
Empirical formula	C22 H28 N2 O4
Formula weight	384.46
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1n$
Unit cell dimensions	a = 10.8538(5) Å a= 90°.
	b = 10.2423(4) Å b= 100.106(2)°.
	c = 18.5130(7) Å g = 90°.
Volume	2026.12(14) $Å^3$
Z	4
Density (calculated)	1.260 Mg/m^3
Absorption coefficient	0.087 mm^{-1}
F(000)	824
Crystal size	0.32 x 0.32 x 0.28 mm^3
Theta range for data collection	2.23 to 27.50°.
Index ranges	-14<=h<=13, -8<=k<=13, -24<=l<=22
Reflections collected	16441
Independent reflections	4645 [R(int) = 0.0256]
Completeness to theta = 25.00°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9761 and 0.9728
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4645 / 0 / 256
Goodness-of-fit on F^2	1.026
Final R indices [I>2sigma(I)]	R1 = 0.0474, wR2 = 0.1159
R indices (all data)	R1 = 0.0733, wR2 = 0.1344
Largest diff. peak and hole	0.157 and -0.245 $e.Å^{-3}$



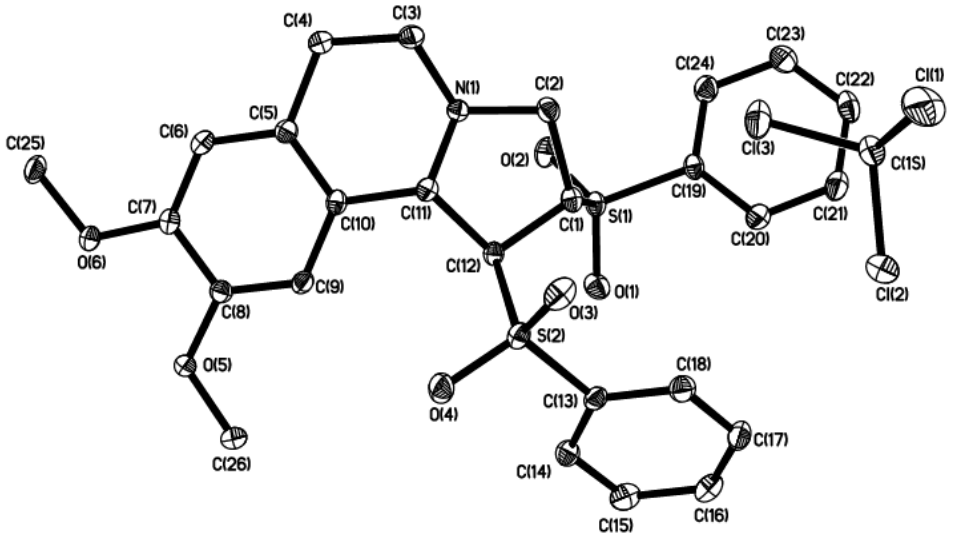
b) Compound **32**

Identification code	oic82p21c
Empirical formula	C19 H23 N O6
Formula weight	361.38
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic
Space group	$P2_1/c$
Unit cell dimensions	a = 11.8340(4) Å a= 90°.
	b = 16.5803(5) Å b= 110.5560(10)°.
	c = 9.4455(3) Å g = 90°.
Volume	1735.31(10) $Å^3$
Z	4
Density (calculated)	1.383 Mg/m^3
Absorption coefficient	0.103 mm^{-1}
F(000)	768
Crystal size	0.38 x 0.28 x 0.12 mm^3
Theta range for data collection	1.84 to 27.50°.
Index ranges	-15<=h<=15, -21<=k<=21, -12<=l<=12
Reflections collected	29528
Independent reflections	3991 [R(int) = 0.0328]
Completeness to theta = 25.00°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9877 and 0.9619
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3991 / 0 / 238
Goodness-of-fit on F^2	1.047
Final R indices [I>2sigma(I)]	R1 = 0.0358, wR2 = 0.0952
R indices (all data)	R1 = 0.0403, wR2 = 0.0988
Largest diff. peak and hole	0.483 and -0.228 $e.Å^{-3}$



c) Compound **38a**

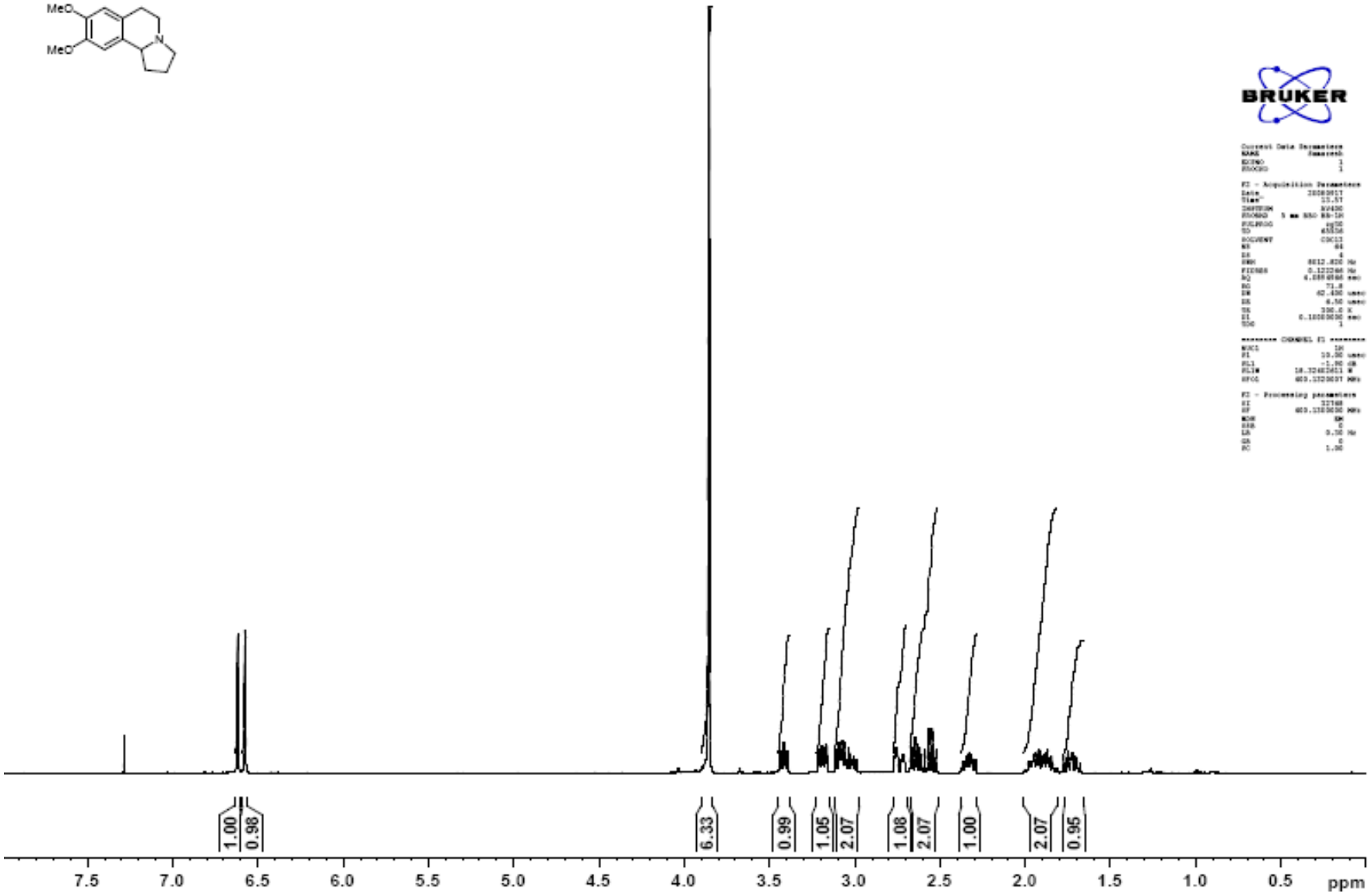
Identification code	sj223_0m
Empirical formula	C27 H28 Cl3 N O6 S2
Formula weight	632.97
Temperature	150(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 9.0677(3) Å a= 88.777(2)°. b = 12.2382(4) Å b= 73.519(2)°. c = 13.3377(4) Å g = 80.784(2)°.
Volume	1400.53(8) $Å^3$
Z	2
Density (calculated)	1.501 Mg/m^3
Absorption coefficient	0.520 mm^{-1}
F(000)	656
Crystal size	0.32 x 0.21 x 0.12 mm^3
Theta range for data collection	1.59 to 27.50°.
Index ranges	-11<=h<=9, -15<=k<=15, -17<=l<=17
Reflections collected	17709
Independent reflections	6433 [R(int) = 0.0179]
Completeness to theta = 25.00°	100.0 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9402 and 0.8513
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6433 / 0 / 354
Goodness-of-fit on F^2	1.040
Final R indices [I>2sigma(I)]	R1 = 0.0292, wR2 = 0.0745
R indices (all data)	R1 = 0.0345, wR2 = 0.0778
Largest diff. peak and hole	0.467 and -0.358 $e.Å^{-3}$

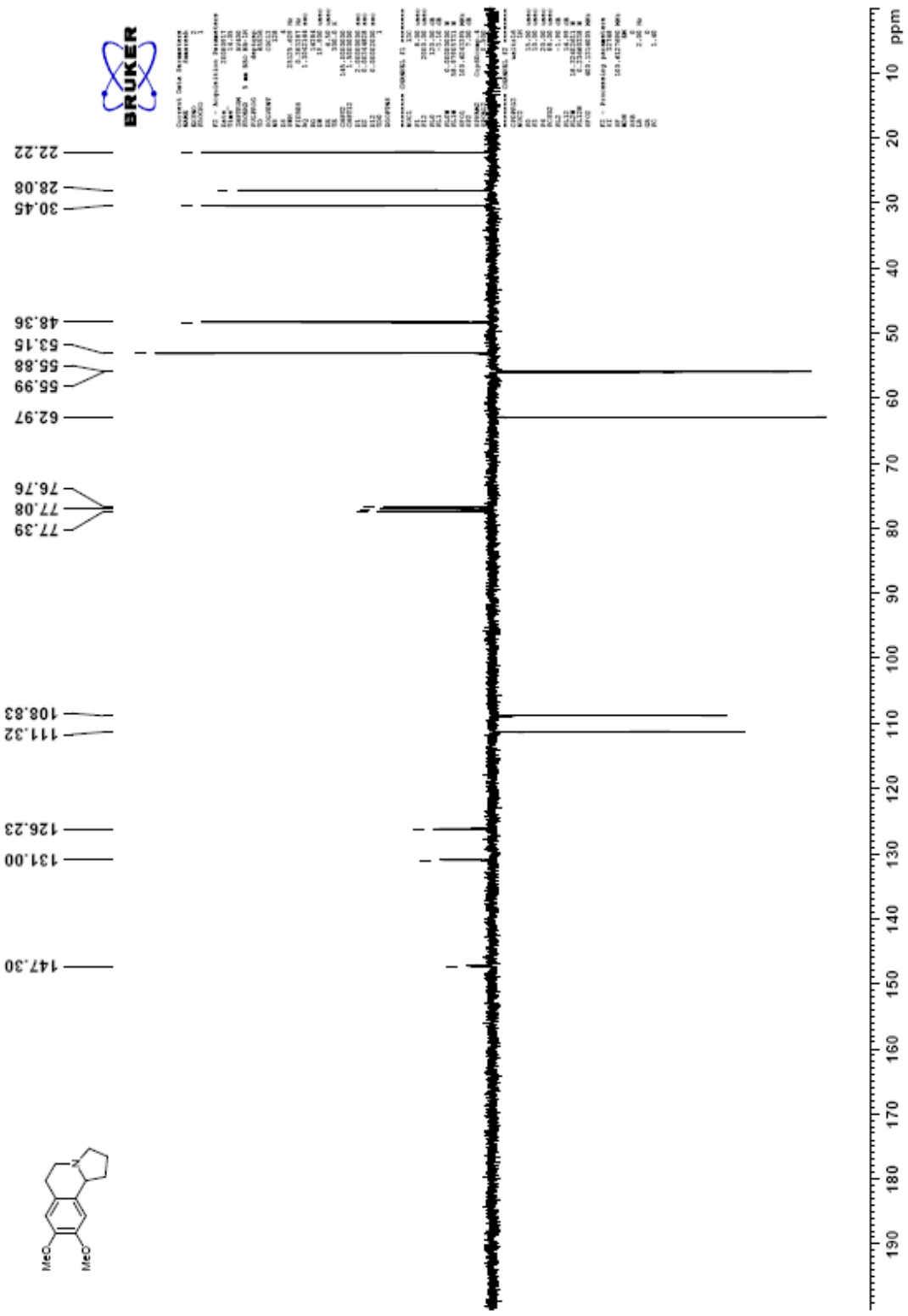


3. References

1. W. H. Pearson, P. Stoy and Y. Mi, *J. Org. Chem*., 2004, **69**, 1919.
2. J.-F. Le Borgne, *J. Organomet. Chem.*, 1976, **122**, 123.
3. H. Ardill, X. L. R. Fontaine, R. Grigg, D. Henderson, J. Montgomery, V. Sridharan and S. Surendrakumar, *Tetrahedron*, 1990, **46**, 6449.
4. I. Coldham, S. Jana, L. Watson and C. D. Pilgram, *Tetrahedron Lett*., 2008, **49**, 5408.

4. Copies of NMR spectra for crispine A




22.22
28.08
30.45
48.36
53.15
55.88
55.99
62.97
76.76
77.08
77.39
108.83
111.32
126.23
131.00
147.30
MeO
MeO
ppm