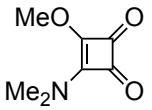
1. General Remarks

Tetrahydrofuran, hexane and pentane were all distilled from sodium benzophenone ketyl under argon. All air sensitive reactions were carried out under argon using flame dried apparatus. Reactions were monitored by TLC on Merck Silica Gel 60 Å F TLC plates and visualised with 254 nm UV followed by aqueous 1% $KMnO_4$ or CAMPH. Flash chromatography was performed under slight positive pressure on Sigma Aldrich 40–63 µm 60 Å 230–400 Å silica. Reaction and chromatography solvents were removed using a rotary evaporator equipped with a diaphragm pump. ^{1}H and ^{13}C NMR spectroscopy was performed on a Bruker AV400 (400/100 MHz) spectrometer at 298 K in $CDCl_3$. Chemical shifts are quoted as δ values in ppm using residual solvent peaks as the reference. Coupling constants *J* are given in Hz and multiplicity is described as follows: s, singlet; d, doublet; t, triplet; q, quartet; quin, quintet; m, multiplet; br, broad. HRMS data were obtained using a Bruker APEX III FT-ICR-MS with samples run in HPLC grade methanol. Electrospray mass spectrometry was performed on a directly injected Waters quadrupole MSD using ESI+ or ESI– ionisation with MeOH as solvent. Infrared spectroscopy was performed on a Nicolet iS5 Laboratory FT-IR spectrometer and spectra were acquired from evaporated $CDCl_3$ or DCM solutions. Absorption maxima (ν_{max}) are quoted in wavenumbers (cm^{-1}) with the following abbreviations used to describe their intensity: s, strong; m, medium; w, weak; br, broad. Cyclobutenones **1a**,[1] **1b**,[2,3] **1c**,[4] **16a**,[5] and **16b**[2,5] were prepared using literature proceduces. All other starting materials and reagents were used as supplied from commercial sources.

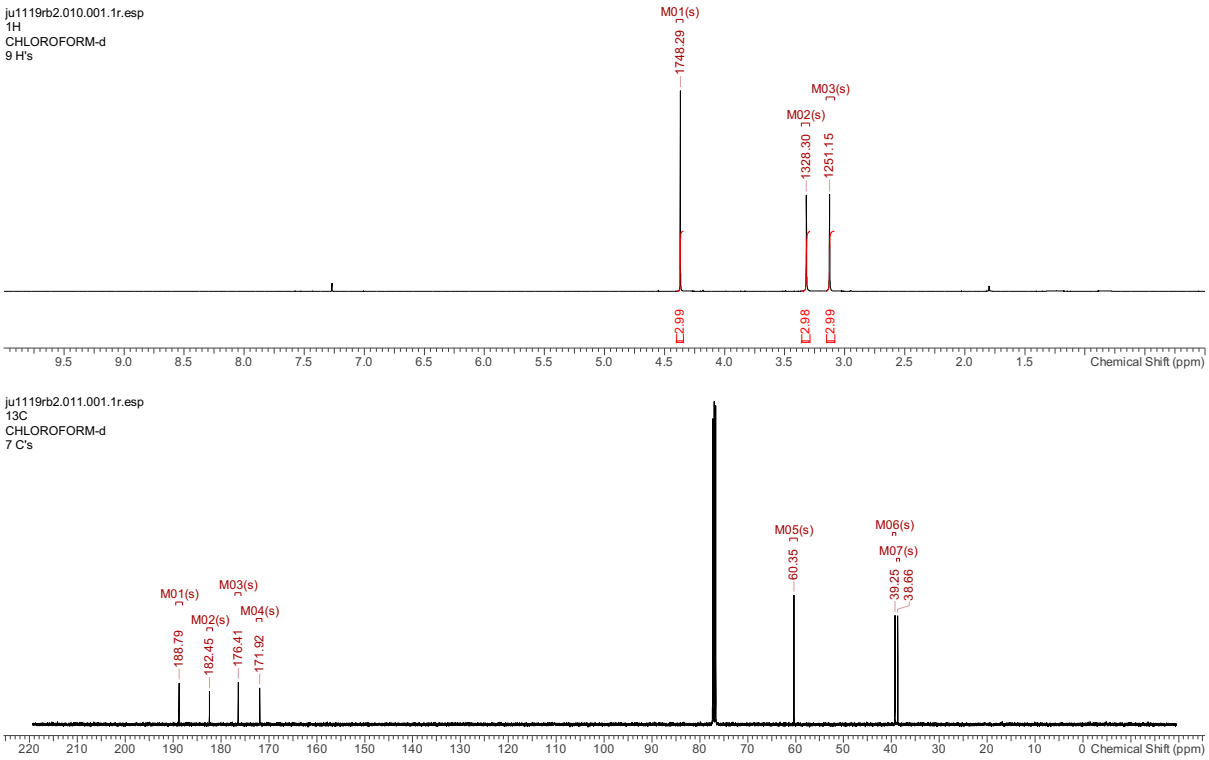
2. Procedures

2.1. Preparation of Cyclobutenediones

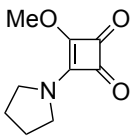
3-(Dimethylamino)-4-methoxycyclobut-3-ene-1,2-dione, 9a[6]



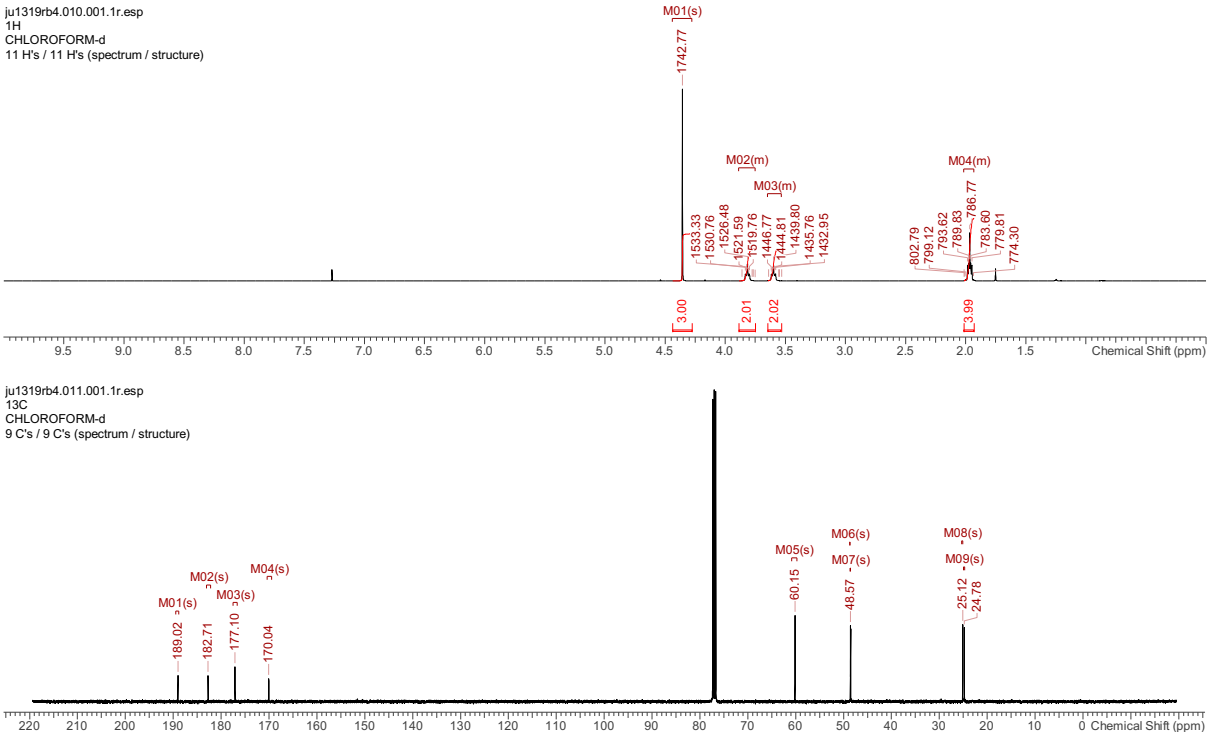
To a solution of dimethyl squarate **1a** (500 mg, 3.51 mmol) in methanol (80 mL) was added $Me_2NH{\bullet}HCl$ (286 mg, 3.51 mmol) followed by triethylamine (0.49 mL, 3.51 mmol). After 2 h the solution was concentrated *in vacuo* to a yellow solid, then purified by column chromatography (60–80 % EtOAc/petrol) gave the title compound **9a** (496 mg, 3.19 mmol, 91 %) as a white solid, m.p. 142–143 °C (EtOAc/hexane); ν_{max} (film) 2941 (br), 2358 (br), 1801 (m), 1700 (s), 1609 (s), 1497 (s), 1417 (m), 1393 (s), 1277 (m), 1187 (m); δ_H (400 MHz, $CDCl_3$) 4.37 (s, 3H, C**H**$_3$), 3.32 (s, 3H, C**H**$_3$), 3.13 (s, 3H, C**H**$_3$); δ_C (100 MHz, $CDCl_3$) 188.8 (**C**), 182.4 (**C**), 176.4 (**C**), 171.9 (**C**), 60.4 (**C**H$_3$), 39.2 (**C**H$_3$), 38.7 (**C**H$_3$); LRMS (ESI^+) 156 (100 %, $[MH]^+$); HRMS (ESI^+) $C_7H_9NNaO_3$ $[M+Na]^+$ calculated 178.0475, observed 178.0478.



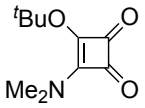
3-Methoxy-4-(pyrrolidin-1-yl)cyclobut-3-ene-1,2-dione, 9b



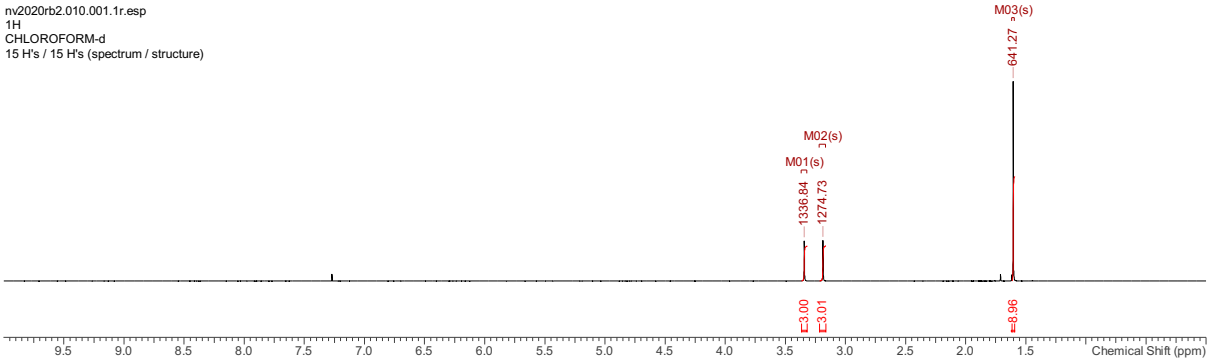
To a solution of dimethyl squarate **1a** (500 mg, 3.51 mmol) in methanol (80 mL) was added pyrrolidine (0.29 mL, 3.51 mmol). After 3 h the solution was concentrated *in vacuo* to a yellow solid, then purified by column chromatography (60 % EtOAc/petrol) to give the title compound **9b** (540 mg, 2.98 mmol, 85 %) as a white solid, m.p. 139–141 °C (Et_2O/petrol); ν_{max} (film) 2981 (br), 2885 (m), 2359 (br), 1792 (m), 1703 (s), 1649 (s), 1593 (w), 1489 (s), 1462 (s), 1405 (s); δ_H (400 MHz, $CDCl_3$) 4.36 (s, 3H, C**H**$_3$), 3.88–3.75 (m, 2H, 2×NC**H**H), 3.65–3.53 (m, 2H, 2×NCH**H**), 2.01–1.93 (m, 4H, 2×C**H**$_2$); δ_C (100 MHz, $CDCl_3$) 189.0 (**C**), 182.7 (**C**), 177.1 (**C**), 170.0 (**C**), 60.1 (**C**H$_3$), 48.6 (**C**H$_2$), 48.5 (**C**H$_2$), 25.1 (**C**H$_2$), 24.8 (**C**H$_2$); LRMS (ESI$^+$) 182 (100 %, [MH]$^+$); HRMS (ESI$^+$) $C_9H_{12}NO_3$ [MH]$^+$ calculated 182.0812, observed 182.0814.

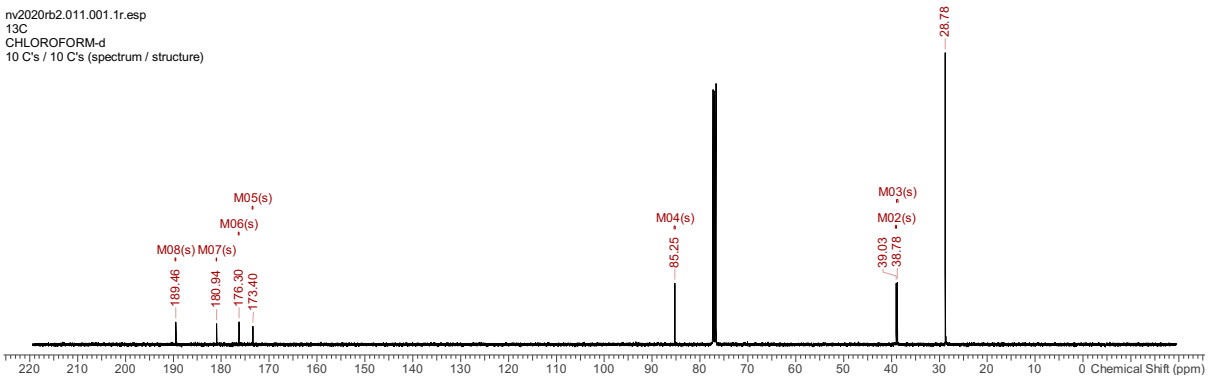


3-(*tert*-Butoxy)-4-(dimethylamino)cyclobut-3-ene-1,2-dione, 9c

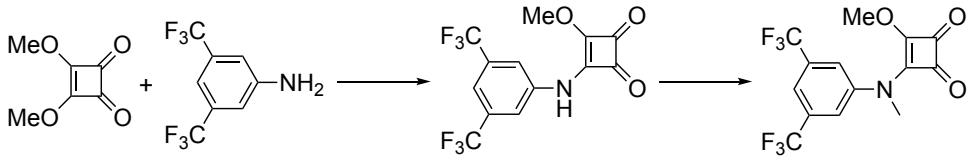


To a solution of di-*tert*-butyl squarate **1c** (679 mg, 3.00 mmol) in methanol (40 mL) was added Me_2NH•HCl (245 mg, 3.00 mmol) followed by triethylamine (0.42 mL, 3.00 mmol). After 24 h the solution was concentrated *in vacuo* to a yellow solid, then purified by column chromatography (20–50 % EtOAc/petrol) to afford the title compound **9c** (496 mg, 3.19 mmol, 91 %) as a white solid, m.p. 129–130 °C (Et_2O/hexane); ν_{max} (film) 2952 (w), 2924 (w), 2852 (w), 1772 (m), 1663 (s), 1557 (s), 1522 (s), 1461 (w), 1445 (m), 1412 (s); δ_H (400 MHz, $CDCl_3$) 3.34 (s, 3H, NC**H**$_3$), 3.19 (s, 3H, NC**H**$_3$), 1.60 (s, 9H, C(C**H**$_3$)$_3$); δ_C (100 MHz, $CDCl_3$) 189.5 (**C**), 180.9 (**C**), 176.3 (**C**), 173.4 (**C**), 85.3 (**C**), 39.0 (**C**H$_3$), 38.8 (N**C**H$_3$), 28.8 (**C**H$_3$); LRMS (ESI$^+$) 220 (100 %, [M+Na]$^+$), 198 (45 %, [MH]$^+$); HRMS (ESI$^+$) $C_{10}H_{15}NNaO_3$ [M+Na]$^+$ calculated 220.0944, observed 220.0942; $C_{10}H_{16}NO_3$ [MH]$^+$ calculated 198.1125, observed 198.1122.

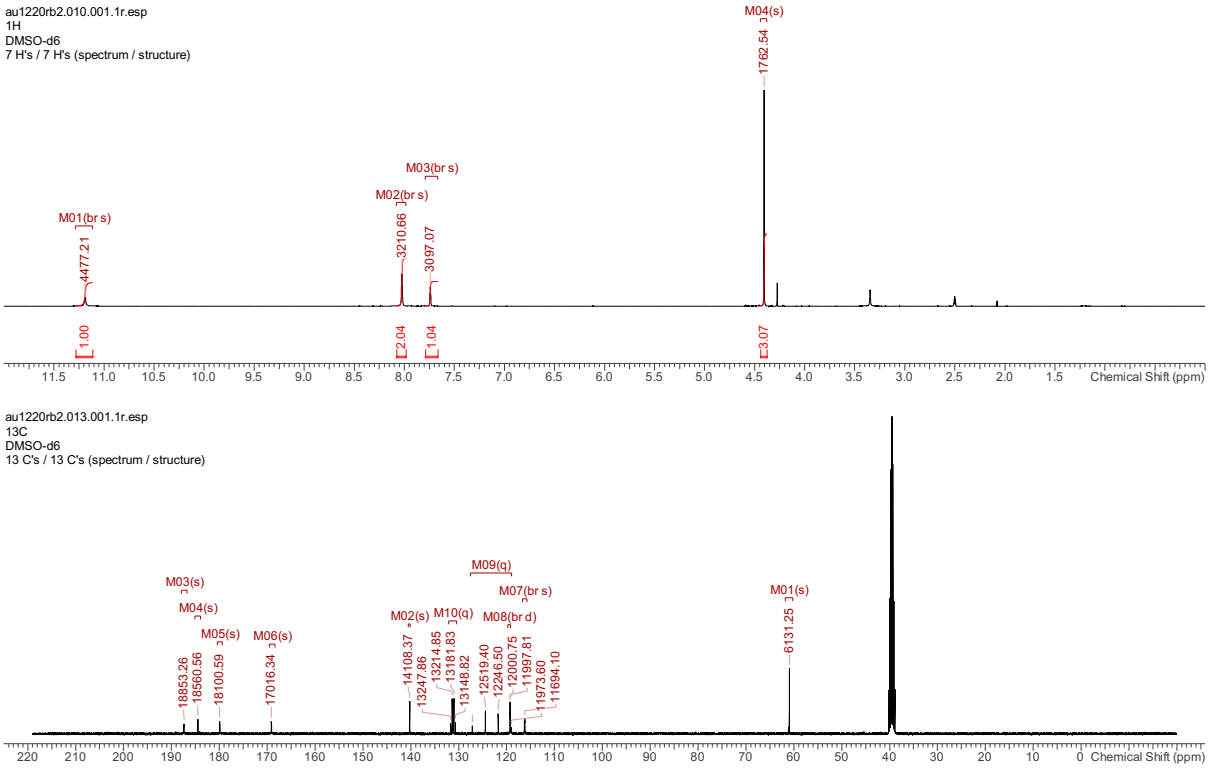


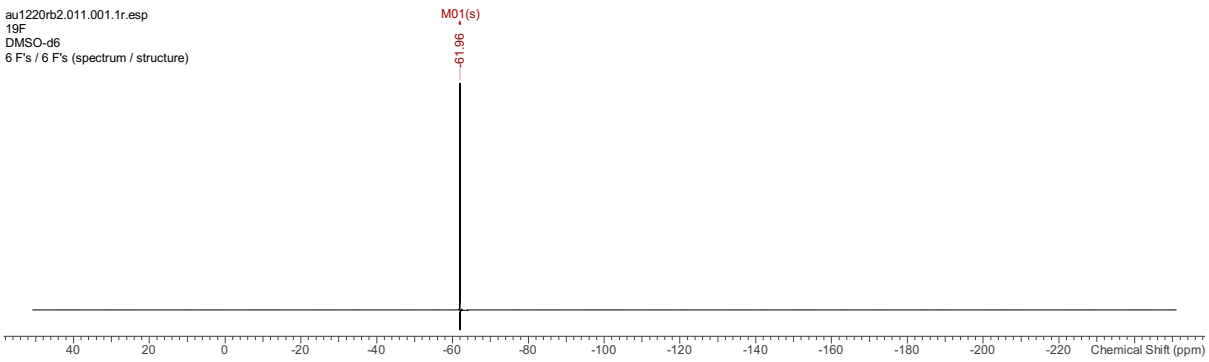


3-((3,5-Bis(trifluoromethyl)phenyl)(methyl)amino)-4-methoxycyclobut-3-ene-1,2-dione, 9d

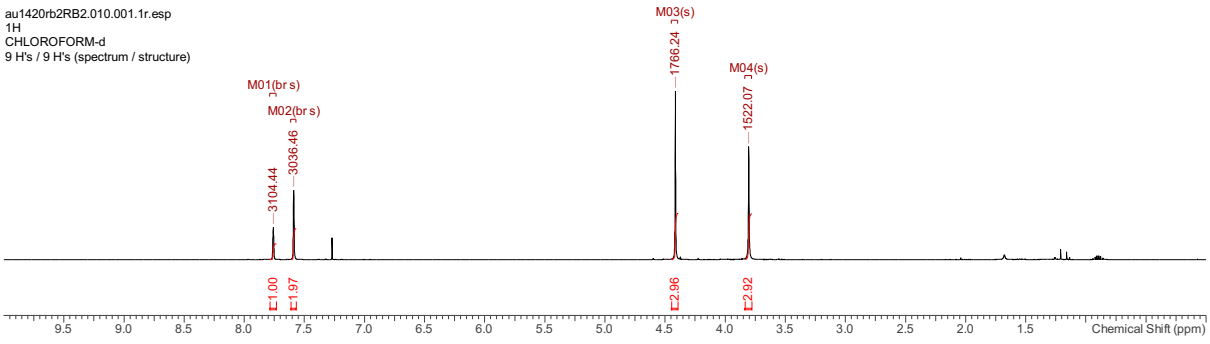


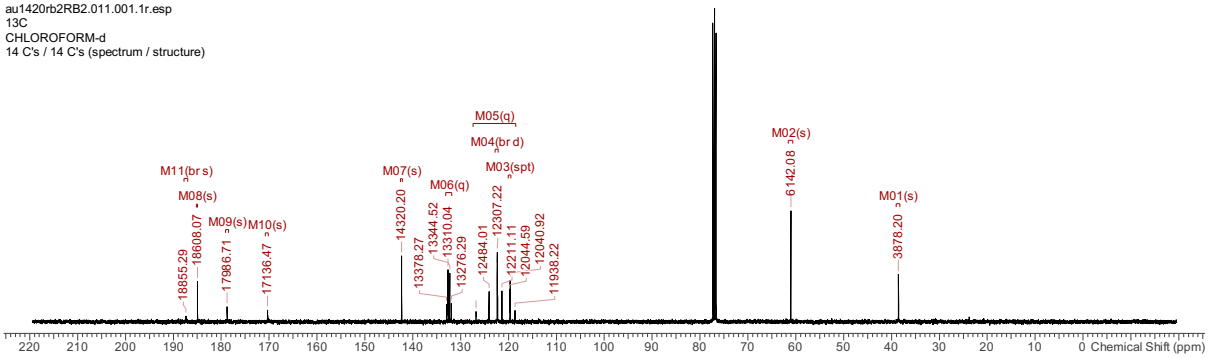
To a solution of dimethyl squarate **1a** (711 mg, 5.00 mmol) in methanol (25 mL) was added 3,5-bis(trifluoromethyl)aniline (0.78 mL, 5.00 mmol). After 48 h the solution was concentrated *in vacuo* and purified by column chromatography (20 % EtOAc/petrol) to give 3-((3,5-bis(trifluoromethyl)phenyl)amino)-4-methoxycyclobut-3-ene-1,2-dione (1.091 g, 3.21 mmol, 64 %) as a pale yellow solid, m.p. dec. 193 °C; ν_{max} (neat) 3101 (w), 2972 (br), 1796 (w), 1735 (w), 1698 (m), 1629 (w), 1586 (s), 1534 (m), 1473 (m), 1373 (s); δ_H (400 MHz, DMSO-d_6) 11.19 (br s, 1H, N**H**), 8.02 (br s, 2H, 2×Ar**H**), 7.74 (br s, 1H, Ar**H**), 4.40 (s, 3H, C**H**$_3$); δ_C (100 MHz, DMSO-d_6) 187.4 (**C**), 184.5 (**C**), 179.9 (**C**), 169.1 (**C**), 140.2 (**C**), 131.2 (q, J = 33.0 Hz, 2×**C**CF$_3$), 123.1 (q, J = 272.9 Hz, 2×**C**F$_3$), 119.2 (br d, J = 2.9 Hz, 2×**C**H), 116.2 (m, **C**H), 60.9 (**C**H$_3$); δ_F (376MHz, DMSO-d_6) δ –61.96 (s, 6F, 2×CF$_3$); LRMS (ESI$^+$) 340 (100 %, [MH]$^+$); HRMS (ESI$^+$) $C_{13}H_7F_6NNaO_3$ [M+Na]$^+$ calculated 362.0222, observed 362.0220, $C_{13}H_8F_6NO_3$ [MH]$^+$ calculated 340.0403, observed 340.0399.

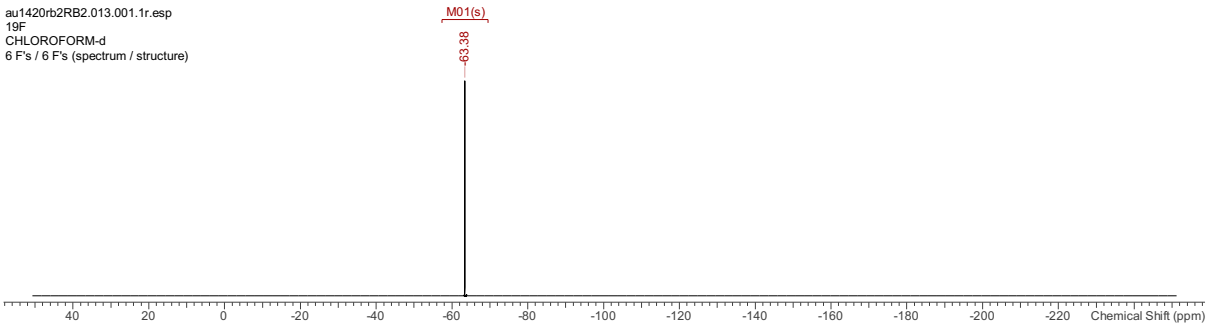




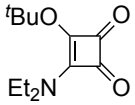
To a solution of bis(trifluoromethyl)phenyl)amino)-4-methoxycyclobut-3-ene-1,2-dione (1.02 g, 3.00 mmol) in DMF (15 mL) was added K_2CO_3 (621 mg, 4.50 mmol) followed after 30 min by MeI (0.37 mL, 6.00 mmol). After 24 h, water (15 mL) was added then the aqueous phase was extracted with EtOAc (3×90 mL). The organic phases were combined, washed with water (3×270 mL), dried over $MgSO_4$ and concentrated *in vacuo* to a yellow solid. Purification by column chromatography (15–20 % EtOAc/petrol) gave the title compound **9d** (880 mg, 2.49 mmol, 83 %) as a pale yellow solid, m.p. 95–96 °C; ν_{max} (neat) 2988 (br), 2901 (br), 1796 (m), 1723 (m), 1572 (s), 1491 (s), 1460 (m), 1422 (w), 1392 (s), 1373 (s); δ_H (400 MHz, DMSO-d_6) 7.76 (br s, 1H, Ar**H**), 7.59 (br s, 2H, 2×Ar**H**), 4.41 (s, 3H, OC**H**$_3$), 3.80 (s, 3H, NC**H**$_3$); δ_C (100 MHz, DMSO-d_6) 187.4 (**C**), 184.9 (**C**), 178.8 (**C**), 170.3 (**C**), 142.3 (**C**), 132.5 (q, J = 33.8 Hz, 2×**C**CF$_3$), 122.7 (q, J = 237.1 Hz, 2×**C**F$_3$), 122.3 (br q, J = 2.9 Hz, 2×**C**H), 119.7 (spt, J = 3.7 Hz, **C**H), 61.0 (**C**H$_3$), 38.5 (**C**H$_3$); LRMS (ESI$^+$) 354 (100 %, [MH]$^+$); HRMS (ESI$^+$) $C_{14}H_9F_6NNaO_3$ [M+Na]$^+$ calculated 376.0379, observed 376.0381; $C_{14}H_{10}F_6NO_3$ [MH]$^+$ calculated 354.0559, observed 354.0560.



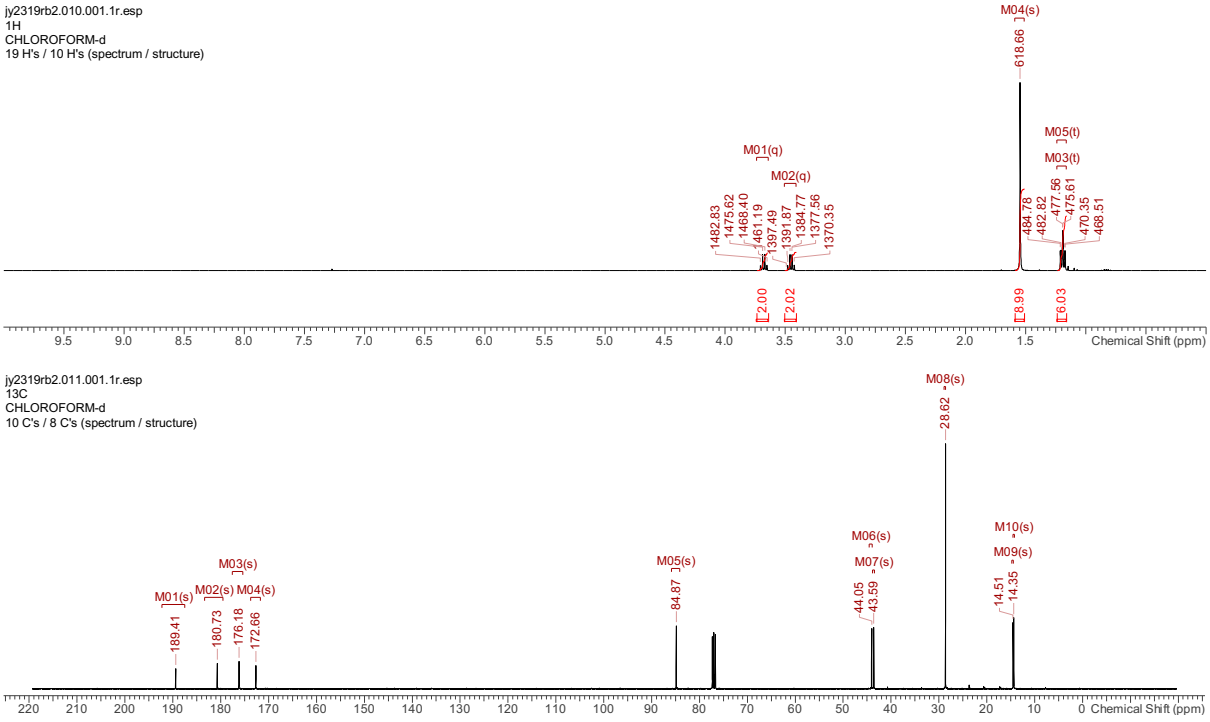




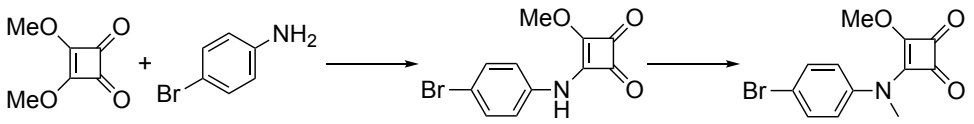
3-(*tert*-Butoxy)-4-(diethylamino)cyclobut-3-ene-1,2-dione, 9e



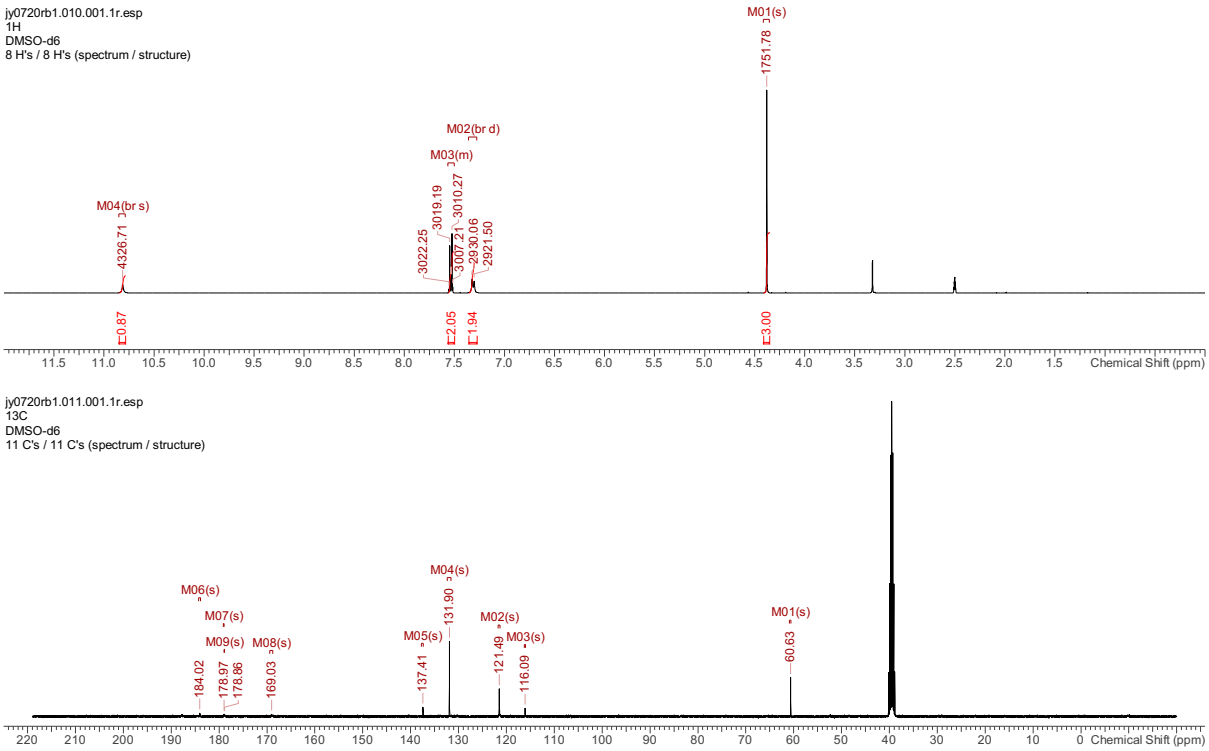
To a solution of di-*tert*-butyl squarate **1c** (905 mg, 4.00 mmol) in methanol (70 mL) was added diethylamine (0.41 mL, 4.00 mmol). After 3 h the solution was concentrated *in vacuo*, then purified by column chromatography (10–20 % EtOAc/petrol) to give the title compound **9e** (799 mg, 3.54 mmol, 89 %) as an off-white solid, m.p. 61–63 °C (Et_2O); ν_{max} (film) 2976 (m), 2360 (w), 1796 (m), 1704 (s), 1592 (s), 1426 (s), 1397 (w), 1371 (m), 1306 (s), 1270 (w); δ_H (400 MHz, $CDCl_3$) 3.68 (q, *J* = 7.2 Hz, 2H, C**H**$_2$), 3.45 (q, *J* = 7.2 Hz, 2H, C**H**$_2$), 1.55 (s, 9H, 3×C**H**$_3$), 1.194 (t, *J* = 7.2 Hz, 3H, C**H**$_3$), 1.189 (t, *J* = 7.2 Hz, 3H, C**H**$_3$); δ_C (100 MHz, $CDCl_3$) 189.4 (**C**), 180.7 (**C**), 176.2 (**C**), 172.7 (**C**), 84.9 (**C**), 44.1 (**C**H$_2$), 43.6 (**C**H$_2$), 28.6 (3×**C**H$_3$), 14.5 (**C**H$_3$), 14.4 (**C**H$_3$); LRMS (ESI$^+$) 248 (73 %, $[M+Na]^+$), 226 (4 %, $[MH]^+$); HRMS (ESI$^+$) $C_{12}H_{19}NNaO_3$ $[M+Na]^+$ calculated 248.1257, observed 248.1259, $C_{12}H_{20}NO_3$ $[MH]^+$ calculated 226.1438, observed 226.1441.



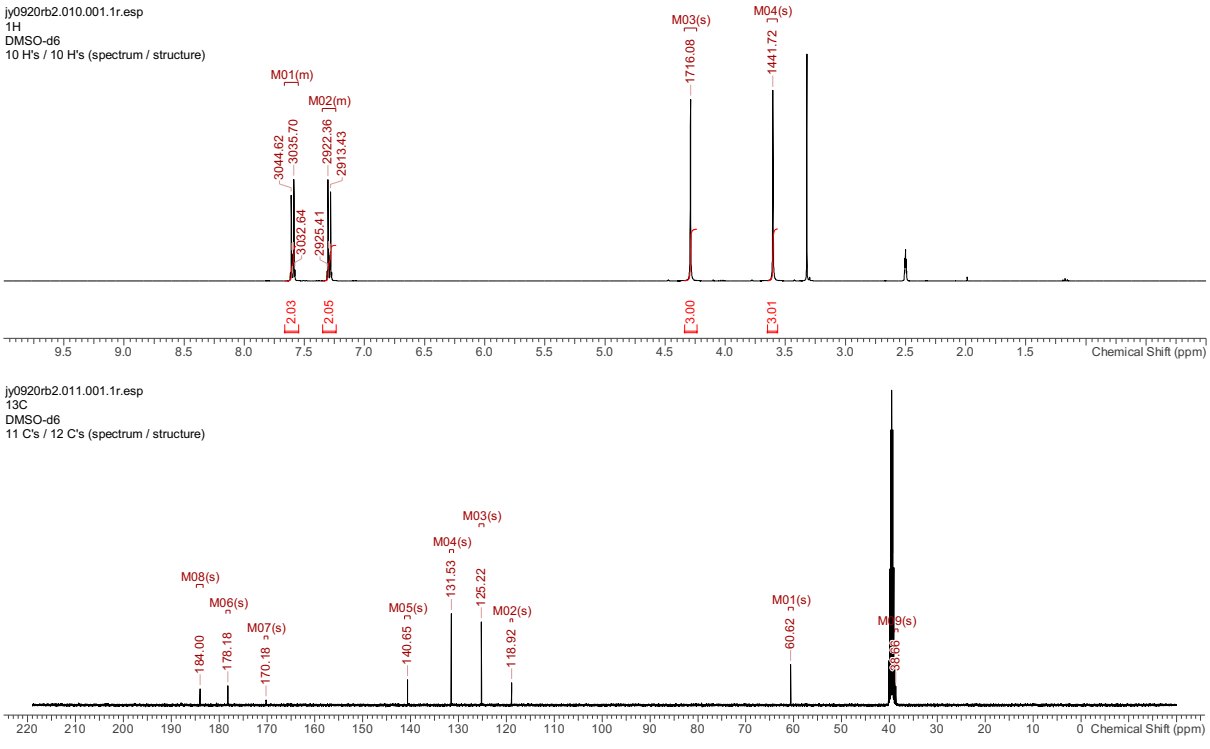
3-((4-Bromophenyl)(methyl)amino)-4-methoxycyclobut-3-ene-1,2-dione, 9f



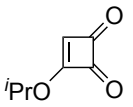
To a solution of dimethyl squarate **1a** (711 mg, 5.00 mmol) in methanol (25 mL) was added 4-bromoaniline (946 mg, 5.50 mmol). After 24 h the solution was concentrated *in vacuo* then purified by column chromatography (40–100 % EtOAc/petrol) to give 3-((4-bromophenyl)amino)-4-methoxycyclobut-3-ene-1,2-dione (1.12 g, 3.97 mmol, 79 %) as an off-white solid, m.p. 233 °C (dec.); ν_{max} (neat) 3243 (w), 3190 (w), 3095 (w), 2988 (br), 1794 (m), 1703 (m), 1609 (s), 1566 (s), 1511 (s), 1494 (m); δ_H (400 MHz, DMSO-d_6) 10.81 (br s, 1H, N**H**), 7.56–7.50 (m, 2H, 2×Ar**H**), 7.31 (br d, *J* = 8.6 Hz, 2H, 2×Ar**H**), 4.38 (s, 3H, C**H**$_3$); δ_C (100 MHz, DMSO-d_6) 184.0 (**C**), 179.0 (**C**), 178.9 (**C**), 169.0 (**C**), 137.4 (**C**), 131.9 (2×**C**H), 121.5 (2×**C**H), 116.1 (**C**), 60.6 (**C**H$_3$); LRMS (ESI$^+$) 284 (54 %, $[M\{^{81}Br\}H]^+$,) 282 (66 %, $[M\{^{79}Br\}H]^+$); HRMS (ESI$^+$) $C_{11}H_9{}^{79}BrNO_3$ $[MH]^+$ calculated 281.9760, observed 281.9755.



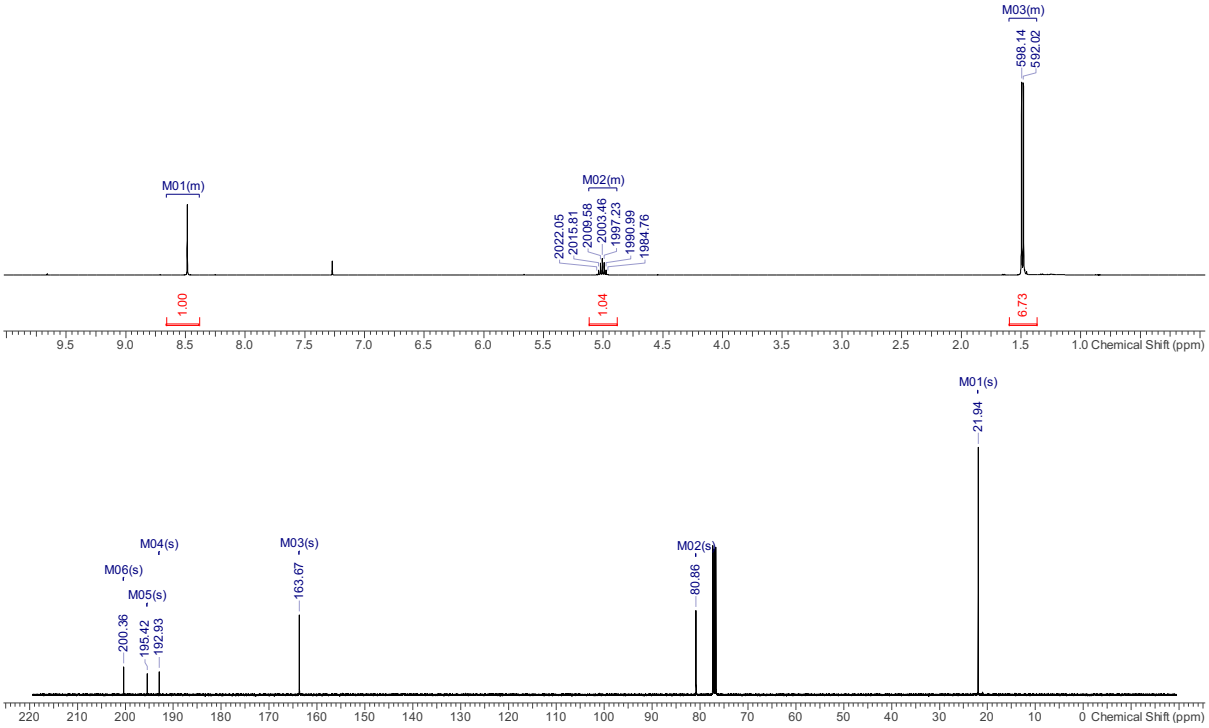
To a solution of 3-((4-bromophenyl)amino)-4-methoxycyclobut-3-ene-1,2-dione (846 mg, 3.00 mmol) in DMF (15 mL) was added K_2CO_3 (621 mg, 4.50 mmol), followed after 30 min by MeI (0.37 mL, 6.00 mmol). After 24 h, water (15 mL) was added then the aqueous phase was separated and extracted with EtOAc (3×90 mL). The organic phases were combined, washed with water (3×270 mL), dried over $MgSO_4$ and concentrated *in vacuo* to an orange solid. Trituration with diethyl ether gave the title compound **9f** (713 mg, 2.41 mmol, 80 %) as a pale yellow powder, m.p. 201–202 °C (DCM/hexane); ν_{max} (neat) 2970 (br), 2360 (w), 1796 (s), 1712 (s), 1591 (s), 1570 (s), 1473 (s), 1427 (m), 1406 (m), 1362 (s); δ_H (400 MHz, DMSO-d_6) 7.66–7.55 (m, 2H, 2×Ar**H**), 7.35–7.24 (m, 2H, 2×Ar**H**), 4.29 (s, 3H, OC**H**$_3$), 3.60 (s, 3H, NC**H**$_3$); δ_C (100 MHz, DMSO-d_6) 184.0 (**C**), 178.2 (**C**), 170.2 (**C**), 140.7 (**C**), 131.5 (2×**C**H), 125.2 (2×**C**H), 118.9 (**C**), 60.6 (O**C**H$_3$), 38.7 (N**C**H$_3$) one **C** coincident or not observed; LRMS (ESI$^+$) 298 (90 %, [M{^{81}Br}H]$^+$) 296 (100 %, [M{^{79}Br}H]$^+$); HRMS (ESI$^+$) $C_{12}H_{10}BrNNaO_3$ [M+Na]$^+$ calculated 317.9736, observed 317.9734, $C_{12}H_{11}BrNO_3$ [MH]$^+$ calculated 295.9917, observed 295.9914.



3-Isopropylcyclobut-3-ene-1,2-dione, 25[7]

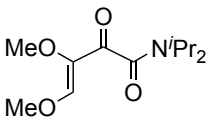


To a solution of diisopropyl squarate **1b** (4.99 g, 25.2 mmol) in THF (300 mL) at –20 °C was added $LiAl(O^tBu)_3H$ (8.01 g, 31.5 mmol). After 1 h the solution was warmed to RT then after a further 165 min sat. rochelle salt (90 mL) was added. After 30 min, the aqueous phase was separated and extracted with $CHCl_3$ (3×100 mL). The organic phases were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo* to a pale yellow oil. DCM (150 mL) was added, then the resulting solution was cooled to 0 °C and TFAA (4.20 mL, 30.2 mmol) added. After a further 30 min the reaction was warmed to RT for 16 h then sat. NH_4Cl (50 mL) was added. The aqueous phase was separated and extracted with DCM (3×30 mL) then the organic phases were combined, dried over $MgSO_4$, filtered and concentrated *in vacuo*. Purification by column chromatography (10-20% EtOAc/cyclohexane) gave the title compound **25** (2.65 g, 18.9 mmol, 75%) as an orange oil, ν_{max} (film) 3102 (w), 2986 (w), 2938 (w), 1793 (s), 1763 (s), 1557 (s), 1466 (w), 1380 (m), 1298 (m), 1280 (s), 1198 (w), 1144 (w), 1063 (s); δ_H (400 MHz, $CDCl_3$) 8.48 (s, 1H, =C**H**), 5.01 (spt, *J* = 6.2 Hz, 1H, C**H**CH_3), 1.49 (d, *J* = 6.1 Hz, 6H, 2×C**H**$_3$); δ_C (100 MHz, $CDCl_3$) 200.4 (**C**), 195.4 (**C**), 192.9 (**C**), 163.7 (**C**H), 80.9 (**C**H), 21.9 (2×**C**H_3); LRMS (ESI^+) 163 (8%, $[M+Na]^+$), 141 (32%, $[MH]^+$). These data are consistent with literature values.[5]

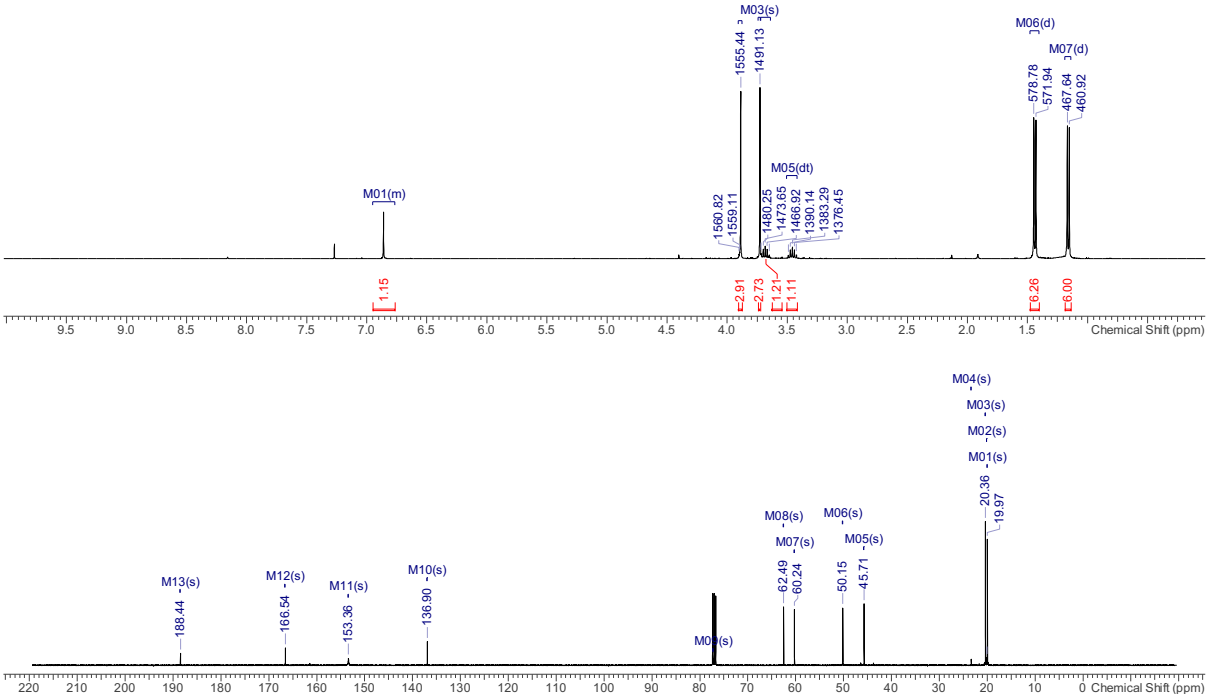


2.2. Reactions of Cyclobutenediones with Lithium Amides

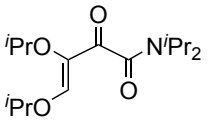
(*Z*)-3,4-Dimethoxy-*N*,*N*-diisopropyl-2-oxobut-3-enamide, 7a



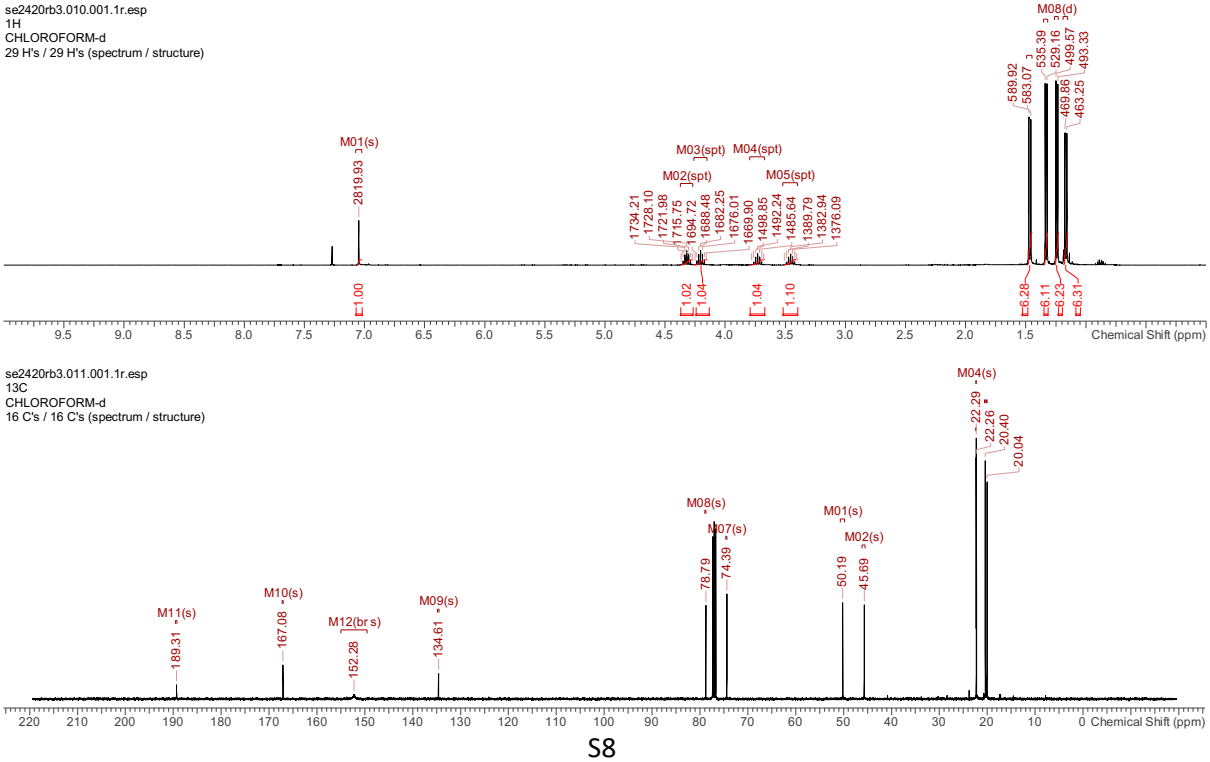
To a solution of DIPA (0.29 mL, 2.10 mmol) in THF (20 mL) at 0 °C was added ^{n}BuLi (2.5 M in hexane, 0.84 mL, 2.10 mmol) dropwise. After 15 min the solution was added *via* cannula to a solution of dimethyl squarate **1a** (284 mg, 2.00 mmol) in THF (50 mL) at –78 °C. After a further 2 h H_2O (20 mL) was added, and the solution was warmed to RT. The aqueous phase was separated and extracted with DCM (2×50 mL) then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (30–80% EtOAc/petrol) gave the title compound **7a** (326 mg, 1.34 mmol, 65%) as a yellow oil, ν_{max} (film) 2974 (br), 1636 (s), 1446 (m), 1371 (m), 1239 (m), 1210 (m), 1139 (m), 1033 (m) ; δ_H (400 MHz, $CDCl_3$) 6.86 (1 H, s, =C**H**), 3.89 (3 H, s, OC**H**$_3$), 3.73 (3 H, s, OC**H**$_3$), 3.68 (1 H, dt, *J* = 13.3, 6.6 Hz, NC**H**$(CH_3)_2$), 3.46 (1 H, dt, *J* = 13.7, 6.9 Hz, NC**H**$(CH_3)_2$), 1.44 (6 H, d, *J* = 6.9 Hz, NCH$(C\mathbf{H}_3)_2$), 1.16 (6 H, d, *J* = 6.7 Hz, NCH$(C\mathbf{H}_3)_2$); δ_C (100 MHz, $CDCl_3$) 188.4 (**C**), 166.5 (**C**), 153.4 (**C**), 136.9 (**C**H), 62.5 (**C**H_3), 60.2 (**C**H_3), 50.1 (**C**H), 45.7 (**C**H), 20.4 (2×**C**H_3), 20.0 (2×**C**H_3); LRMS (ESI^+) 244 ($[MH]^+$, 100%), 266 ($[M+Na]^+$, 30%); HRMS (ESI^+) $C_{12}H_{22}NO_4$ $[MH]^+$ calculated 244.1543, observed 244.1544.



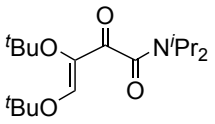
(*Z*)-3,4-Diisopropoxy-*N*,*N*-diisopropyl-2-oxobut-3-enamide, 7b



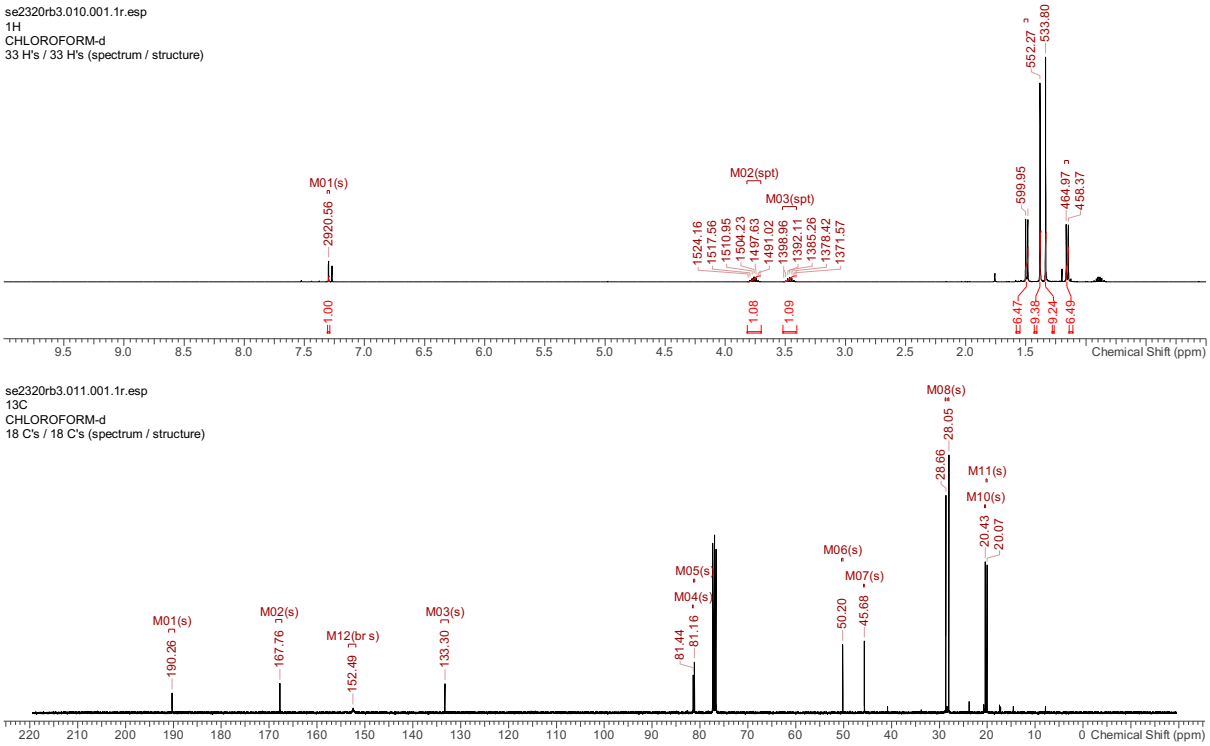
To a solution of cyclobutenedione **1b** (198 mg, 1.00 mmol) in THF (40 mL) at –78 °C was added LDA (1.0 M in THF/hexanes, 1.05 mL, 1.05 mmol). After 8 h, water (20 mL) was added, and the solution was warmed to RT. The aqueous phase was separated and extracted with DCM (3×30 mL) then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (20 % EtOAc/petrol) gave the title compound **7b** (182 mg, 0.61 mmol, 61 %) as a yellow oil, ν_{max} (film) 2975 (s), 2935 (w), 1619 (s), 1448 (m), 1372 (m), 1347 (m), 1212 (s), 1138 (m), 1098 (s), 1056 (w); δ_H (400 MHz, $CDCl_3$) 7.05 (s, 1H, =C**H**), 4.32 (spt, *J* = 6.2 Hz, 1H, OC**H**), 4.20 (spt, *J* = 6.2 Hz, 1H, OC**H**), 3.73 (spt, *J* = 6.8 Hz, 1H, C**H**$(CH_3)_2$), 3.46 (spt, *J* = 6.8 Hz, 1H, C**H**$(CH_3)_2$), 1.47 (d, *J* = 6.8 Hz, 6H, CH(C**H**$_3)_2$), 1.33 (d, *J* = 6.2 Hz, 6H, CH(C**H**$_3)_2$), 1.24 (d, *J* = 6.2 Hz, 6H, CH(C**H**$_3)_2$), 1.17 (d, *J* = 6.8 Hz, 6H, CH(C**H**$_3)_2$); δ_C (100 MHz, $CDCl_3$) 189.3 (**C**), 167.1 (**C**), 152.3 (**C**H), 134.6 (**C**), 78.8 (**C**H), 74.4 (**C**H), 50.2 (**C**H), 45.7 (**C**H), 22.3 (2×**C**H_3), 22.3 (2×**C**H_3), 20.4 (2×**C**H_3), 20.0 (2×**C**H_3); LRMS (ESI^+) 322 (38 %, $[M+Na]^+$), 300 (100 %, $[MH]^+$); HRMS (ESI^+) $C_{16}H_{29}NNaO_4$ $[M+Na]^+$ calculated 322.1989, observed 322.1991; $C_{16}H_{30}NO_4$ $[MH]^+$ calculated 300.2169, observed 300.2165.



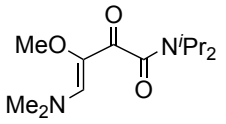
(*Z*)-3,4-Di-*tert*-butoxy-*N*,*N*-diisopropyl-2-oxobut-3-enamide, 7c



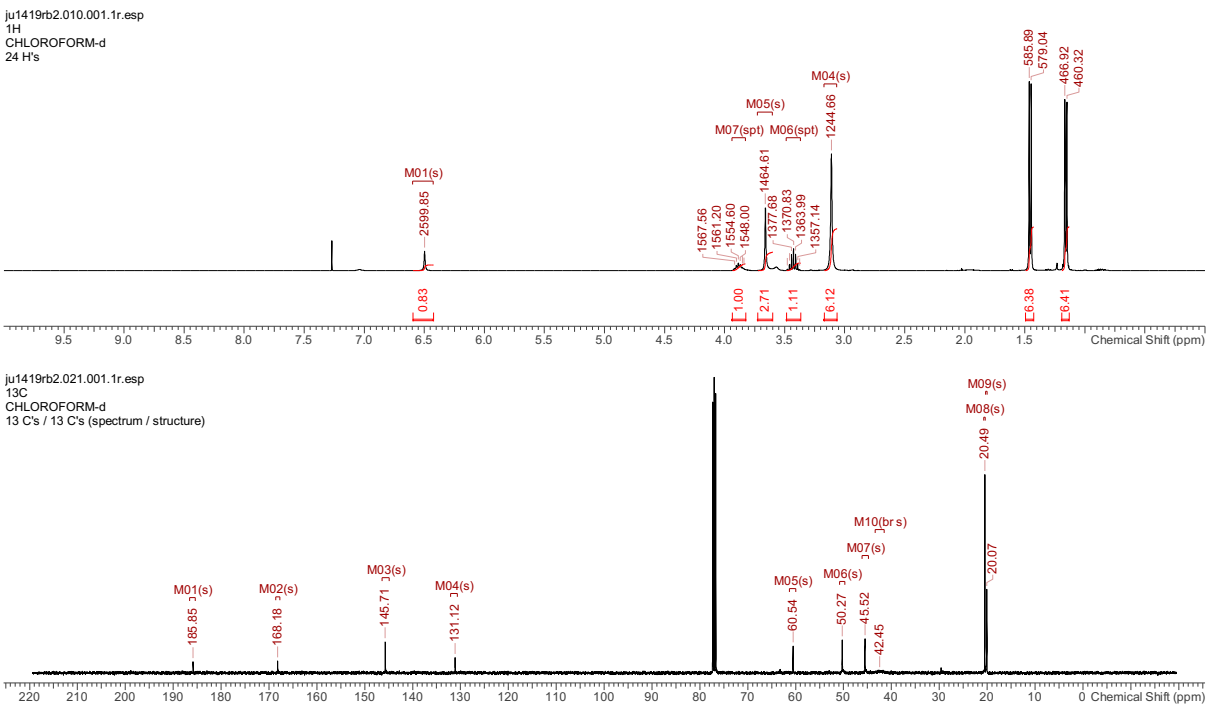
To a solution of cyclobutenedione **1c** (226 mg, 1.00 mmol) in THF (40 mL) at –78 °C was added LDA (1.0 M in THF/hexanes, 1.05 mL, 1.05 mmol). After 8 h, water (20 mL) was added, and the solution was warmed to RT. The aqueous phase was separated and extracted with DCM (3×30 mL) then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (10–20 % EtOAc/petrol) gave the title compound **7c** (184 mg, 0.56 mmol, 56 %) as a yellow oil, ν_{max} (film) 2975 (br), 2936 (w), 1665 (w), 1613 (s), 1448 (m), 1370 (m), 1349 (w), 1269 (w), 1231 (m), 1216 (w); δ_H (400 MHz, $CDCl_3$) 7.30 (s, 1H, =C**H**), 3.76 (spt, *J* = 6.6 Hz, 1H, C**H**$(CH_3)_2$), 3.46 (spt, *J* = 6.8 Hz, 1H, C**H**$(CH_3)_2$), 1.49 (d, *J* = 6.8 Hz, 6H, CH(C**H**$_3)_2$), 1.38 (s, 9H, C(C**H**$_3)_3$), 1.33 (s, 9H, C(C**H**$_3)_3$), 1.15 (d, *J* = 6.6 Hz, 6H, CH(C**H**$_3)_2$); δ_C (100 MHz, $CDCl_3$) 190.3 (**C**), 167.8 (**C**), 152.5 (br, **C**H), 133.3 (**C**), 81.4 (**C**), 81.2 (**C**), 50.2 (**C**H), 45.7 (**C**H), 28.7 (3×**C**H_3), 28.0 (3×**C**H_3), 20.4 (2×**C**H_3), 20.1 (2×**C**H_3); LRMS (ESI$^+$) 350 (32 %, $[M+Na]^+$), 328 (100 %, $[MH]^+$); HRMS (ESI$^+$) $C_{18}H_{33}NNaO_4$ $[M+Na]^+$ calculated 350.2302, observed 350.2311; $C_{18}H_{34}NO_4$ $[MH]^+$ calculated 328.2482, observed 328.2487.



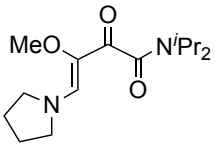
(*Z*)-4-(Dimethylamino)-*N*,*N*-diisopropyl-3-methoxy-2-oxobut-3-enamide, 11a



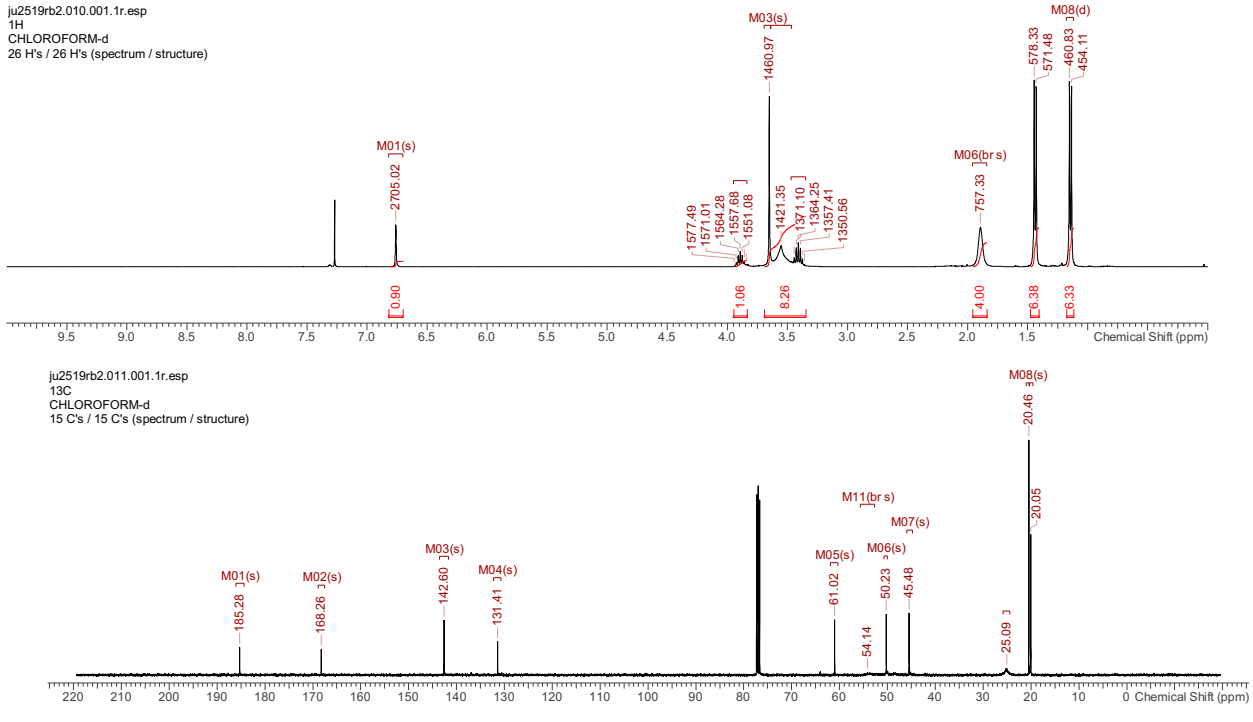
To a solution of cyclobutenedione **9a** (155 mg, 1.00 mmol) in THF (40 mL) at –78 °C was added LDA (2.0 M in THF/ethylbenzene/hexanes, 0.53 mL, 1.05 mmol). After 90 min, water (10 mL) was added and the reaction mixture was warmed to RT. The aqueous phase separated and extracted with DCM (3×30 mL) then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (50–80 % EtOAc/petrol) gave the title compound **11a** (173 mg, 0.67 mmol, 67 %) as a yellow oil, ν_{max} (film) 3482 (br), 2970 (m), 2932 (br), 2359 (br), 1654 (w), 1629 (m), 1560 (s), 1445 (m), 1421 (m), 1404 (m); δ_H (400 MHz, $CDCl_3$) 6.50 (s, 1H, =C**H**), 3.88 (spt, *J* = 6.7 Hz, 1H, C**H**$(CH_3)_2$), 3.66 (s, 3H, OC**H**$_3$), 3.43 (spt, *J* = 6.8 Hz, 1H, C**H**$(CH_3)_2$), 3.11 (s, 6H, N(C**H**$_3)_2$), 1.46 (d, *J* = 6.8 Hz, 6H, CH(C**H**$_3)_2$), 1.16 (d, *J* = 6.6 Hz, 6H, CH(C**H**$_3)_2$); δ_C (100 MHz, $CDCl_3$) 185.9 (**C**), 168.2 (**C**), 145.7 (**C**H), 131.1 (**C**), 60.5 (**C**H_3), 50.3 (**C**H), 45.5 (**C**H), 42.5 (br s, 2×**C**H_3) 20.5 (2×**C**H_3), 20.1 (2×**C**H_3); LRMS (ESI$^+$) 257 (100 %, $[MH]^+$); HRMS (ESI$^+$) $C_{13}H_{24}N_2NaO_3$ $[M+Na]^+$ calculated 279.1679, observed 279.1679; $C_{13}H_{25}N_2O_3$ $[MH]^+$ calculated 257.1860, observed 257.1862.



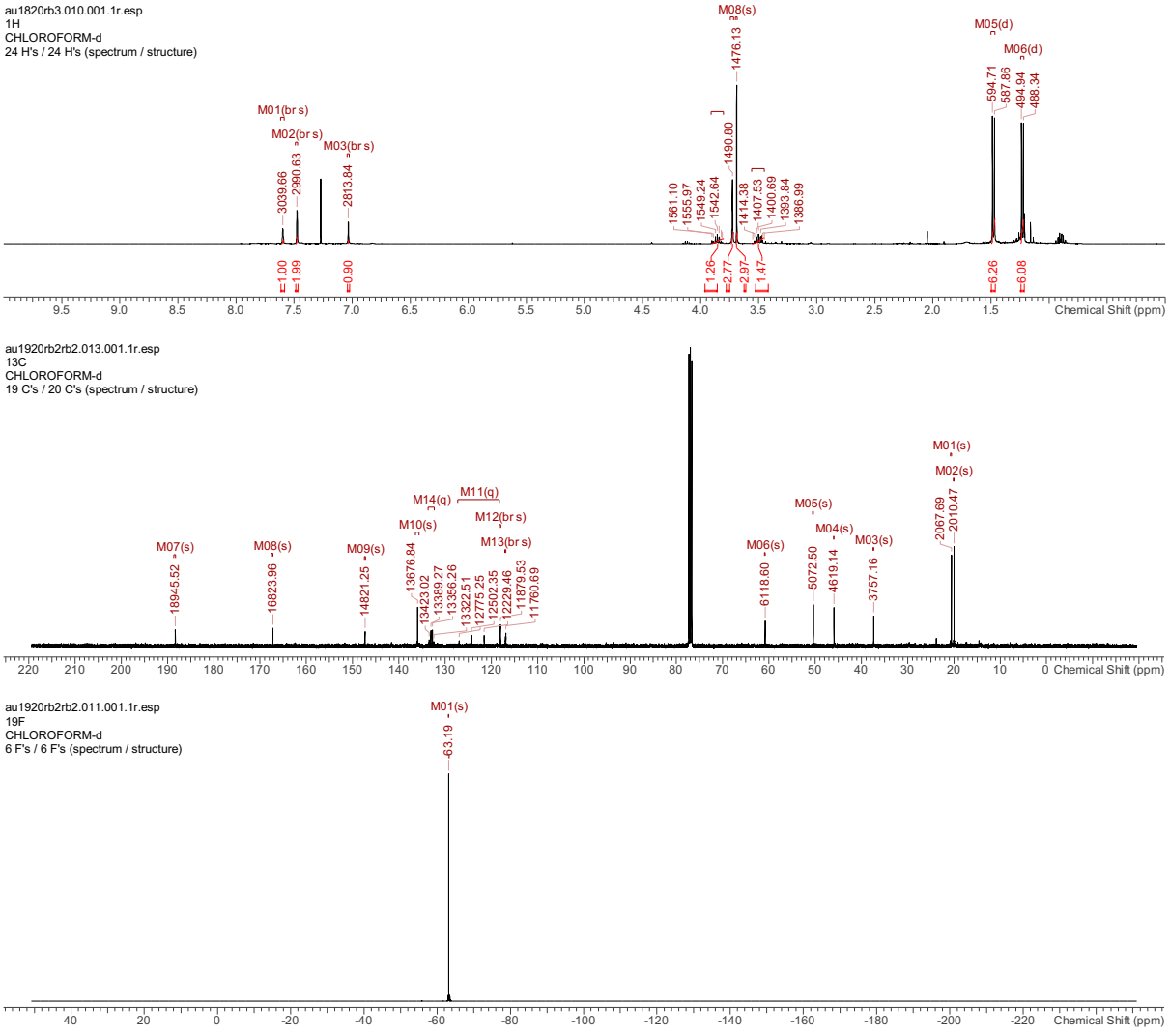
(*Z*)-*N*,*N*-Diisopropyl-3-methoxy-2-oxo-4-(pyrrolidin-1-yl)but-3-enamide, 11b



To a solution of cyclobutenedione **9b** (181 mg, 1.00 mmol) in THF (40 mL) at -78 °C was added LDA (2.0M in THF/ethylbenzene/hexanes, 0.53 mL, 1.05 mmol) followed by water (10 mL) after 90 min. The solution was warmed to RT and the aqueous phase separated and extracted with DCM (3×30 mL). The organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo* to a yellow oil. Purification by column chromatography (50 – 80 % ethyl acetate/petroleum ether) afforded the title compound (183 mg, 0.65 mmol, 65 %) as a yellow oil; ν_{max} (film) 3481 (br), 2970 (m), 2875 (br), 2359 (br), 1629 (s), 1565 (s), 1443 (m), 1410 (m), 1365 (m), 1340 (w); δ_H (400 MHz, $CDCl_3$) 6.76 (s, 1H, =C**H**), 3.89 (spt, *J* = 6.6 Hz, 1H, C**H**$(CH_3)_2$), 3.65 (s, 3H, OC**H**$_3$), 3.55 (br s, 4H, 2×NC**H**$_2$), 3.41 (spt, *J* = 6.8 Hz, 1H, C**H**$(CH_3)_2$), 1.89 (br s, 4H, 2×NCH_2C**H**$_2$), 1.44 (d, *J* = 6.8 Hz, 6H, CH(C**H**$_3)_2$), 1.14 (d, *J* = 6.6 Hz, 6H, CH(C**H**$_3)_2$); δ_C (100 MHz, $CDCl_3$) 185.3 (**C**), 168.3 (**C**), 142.6 (**C**H), 131.4 (**C**), 61.0 (O**C**H_3), 54.1 (br, 2×CH_2), 50.2 (**C**H$(CH_3)_2$), 45.5 (**C**H$(CH_3)_2$), 25.1 (br, 2×CH_2), 20.5 (CH(**C**$H_3)_2$), 20.0 (CH(**C**$H_3)_2$); LRMS (ESI^+) 283 (100 %, $[MH]^+$); HRMS (ESI^+) $C_{15}H_{27}N_2O_3$ $[MH]^+$ calculated 283.2016, observed 283.2020.



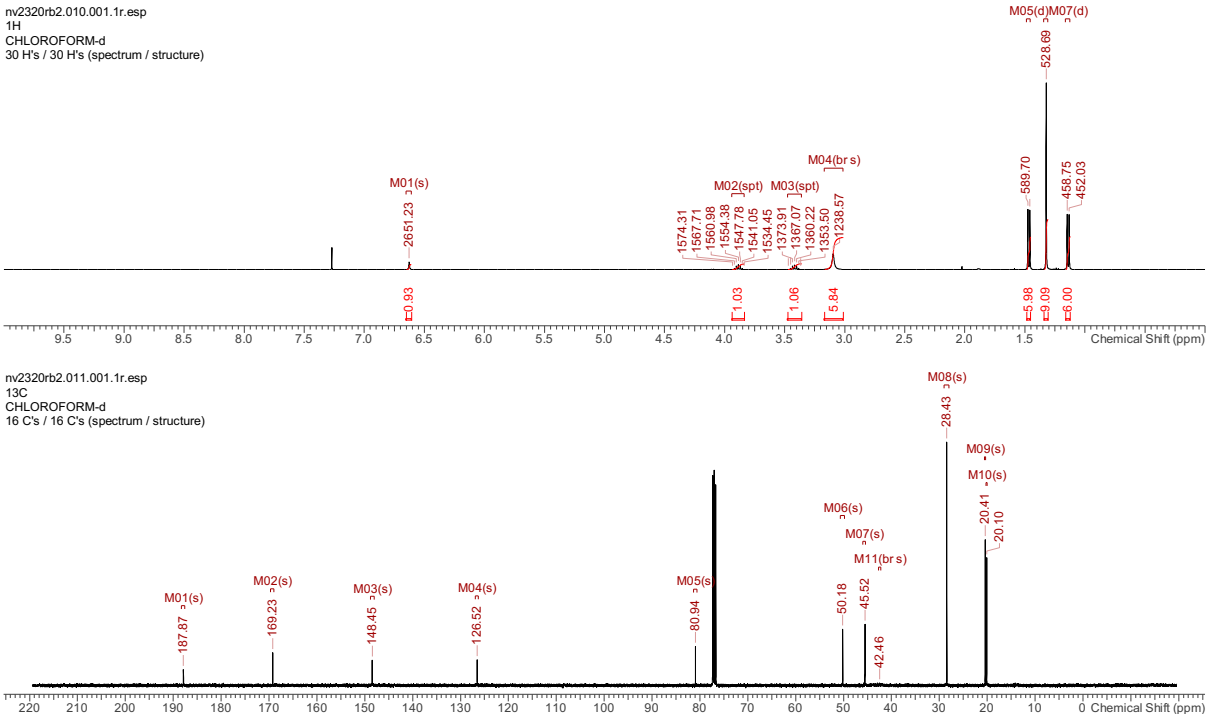
(*Z*)-4-((3,5-Bis(trifluoromethyl)phenyl)(methyl)amino)-*N*,*N*-diisopropyl-3-methoxy-2-oxobut-3-enamide, 11c. To a solution of cyclobutenedione **9c** (353 mg, 1.00 mmol) in THF (40 mL) at –78 °C was added LDA (2.0 M in THF/ethylbenzene/hexanes, 0.60 mL, 1.20 mmol). After 2 h, water (20 mL) was added then the reaction was warmed to RT. The aqueous phase was separated and extracted with DCM (3×30 mL) then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (20 % EtOAc/petrol) gave the title compound **11c** (282 mg, 0.62 mmol, 62 %) as a red oil, ν_{max} (film) 2976 (br), 1629 (s), 1594 (s), 1473 (w), 1384 (s), 1352 (w), 1277 (s), 1263 (m), 1218 (w), 1185 (s); δ_H (400 MHz, $CDCl_3$) 7.60 (br s, 1H, Ar**H**), 7.47 (br s, 2H, 2×Ar**H**), 7.03 (s, 1H, =C**H**), 3.86 (spt, *J* = 6.7 Hz, 1H, C**H**$(CH_3)_2$), 3.72 (br s, 3H, C**H₃**), 3.69 (s, 3H, C**H₃**), 3.50 (spt, *J* = 6.8 Hz, 1H, C**H**$(CH_3)_2$), 1.48 (d, *J* = 6.8 Hz, 6H, CH(C**H**$_3)_2$), 1.23 (d, *J* = 6.7 Hz, 6H, CH(C**H**$_3)_2$); δ_C (100 MHz, $CDCl_3$) 188.3 (**C**), 167.2 (**C**), 147.3 (**C**H), 135.9 (**C**), 132.9 (q, *J* = 33.8 Hz, 2×**C**), 122.9 (q, *J* = 272.9 Hz, 2×**C**F_3), 118.1 (br s, 2×**C**H), 116.9 (br s, **C**H), 60.8 (**C**H_3), 50.4 (**C**H), 45.9 (**C**H), 37.3 (**C**H_3), 20.6 (2×**C**H_3), 20.0 (2×**C**H_3), one **C** not observed; δ_F ($CDCl_3$, 376MHz) –63.19 (s, 6F, 2×C**F**$_3$); LRMS (ESI$^+$) 477 (5 %, $[M+Na]^+$), 455 (100 %, $[MH]^+$); HRMS (ESI$^+$) $C_{20}H_{24}F_6N_2NaO_3$ $[M+Na]^+$ calculated 477.1583, observed 477.1586; $C_{20}H_{25}F_6N_2O_3$ $[MH]^+$ calculated 455.1764, observed 455.1763.



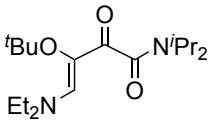
(*Z*)-3-(*tert*-Butoxy)-4-(dimethylamino)-*N*,*N*-diisopropyl-2-oxobut-3-enamide, 11d

To a solution of cyclobutenedione **9d** (100 mg, 0.51 mmol) in THF (20 mL) at –78 °C was added LDA (1.0 M in THF/hexanes, 0.56 mL, 0.56 mmol). After 2 h, water (20 mL) was added then the reaction was warmed to RT. The aqueous phase was separated and extracted with DCM (3×20 mL) then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (50 % EtOAc/petrol) gave the

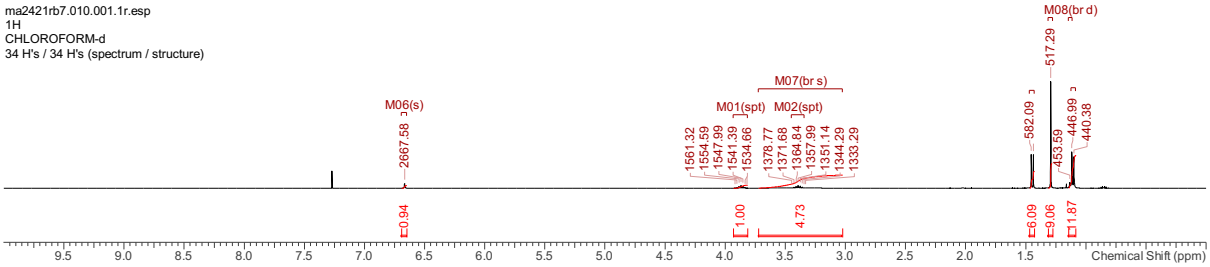
title compound **11d** (126 mg, 0.42 mmol, 83 %) as a yellow oil that solidified on standing, m.p. 112–113 °C; ν_{max} (film) 2972 (m), 2932 (m), 1629 (s), 1572 (s), 1445 (m), 1421 (w), 1365 (s), 1279 (s), 1204 (m), 1166 (w); δ_H (400 MHz, $CDCl_3$) 6.63 (s, 1H, =C**H**), 3.88 (spt, *J* = 6.6 Hz, 1H, C**H**$(CH_3)_2$), 3.42 (spt, *J* = 6.8 Hz, 1H, C**H**$(CH_3)_2$), 3.10 (br s, 6H, N(C**H**$_3)_2$), 1.47 (d, *J* = 6.8 Hz, 6H, CH(C**H**$_3)_2$), 1.32 (s, 9H, C(C**H**$_3)_3$), 1.14 (d, *J* = 6.6 Hz, 6H, NCH(C**H**$_3)_2$); δ_C (100 MHz, $CDCl_3$) 187.9 (**C**), 169.2 (**C**), 148.5 (**C**H), 126.5 (**C**), 80.9 (**C**), 50.2 (**C**H), 45.5 (**C**H), 42.5 (br, 2×**C**H_3), 28.4 (3×**C**H_3), 20.4 (2×**C**H_3), 20.1 (2×**C**H_3); LRMS (ESI$^+$) 321 (14 %, $[M+Na]^+$), 299 (100 %, $[MH]^+$); HRMS (ESI$^+$) $C_{16}H_{30}N_2NaO_3$ $[M+Na]^+$ calculated 321.2149, observed 321.2151; $C_{16}H_{31}N_2O_3$ $[MH]^+$ calculated 299.2329, observed 299.2329.

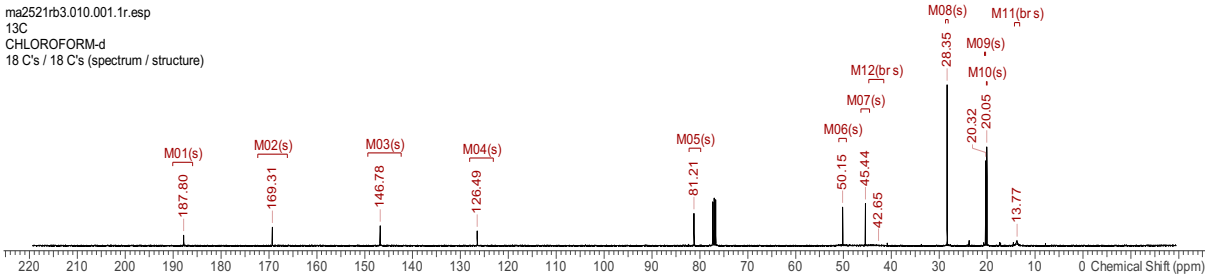


(*Z*)-3-(*tert*-Butoxy)-4-(diethylamino)-*N*,*N*-diisopropyl-2-oxobut-3-enamide, 11e

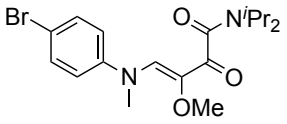


To a solution of DIPA (0.17 mL, 1.2 mmol) in THF (15 mL) at 0 °C was added *n*-butyllithium (2.5 M in hexane, 0.48 mL, 1.20 mmol) dropwise. After 20 min, the solution was added *via* cannula to a solution of cyclobutenedione **9e** (225 mg, 1.00 mmol) in THF (15 mL) at – 78 °C. After a further 90 min, water (10 mL) was added, and the solution warmed to RT. The aqueous phase was separated and extracted with DCM (3×30 mL) then the combined organic phases were dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (20 – 40 % ethyl acetate/petrol) afforded firstly recovered starting material (81 mg, 0.36 mmol, 36 %) as a white solid followed by the title compound **11e** (161 mg, 0.49 mmol, 49 %) as a colourless oil, ν_{max}, (film) 2972 (br), 2934 (w), 2359 (w), 1629 (m), 1569 (s), 1444 (m), 1367 (m), 1307 (w), 1253 (s), 1212 (w); δ_H (400 MHz, $CDCl_3$) 6.67 (s, 1H, =C**H**), 3.87 (spt, *J* = 6.6 Hz, 1H, NC**H**), 3.40 (br s, 4H, N(CH_2C$H_3)_2$), 3.39 (spt, *J* = 6.8 Hz, 1H, NC**H**), 1.45 (d, *J* = 6.8 Hz, 6H, NCH(C**H**$_3)_2$), 1.29 (s, 9H, C(C**H**$_3)_3$), 1.12 (br t, *J* = 6.7 Hz, 6H, N(CH$_2$C**H**$_3)_2$), 1.11 (d, *J* = 6.6 Hz, 6H, NCH(C**H**$_3)_2$); δ_C (100 MHz, $CDCl_3$) 187.8 (**C**), 169.3 (**C**), 146.8 (**C**H), 126.5 (**C**), 81.2 (**C**), 50.2 (**C**H), 45.4 (**C**H), 42.7 (br, 2×**C**H_2), 28.4 (3×**C**H_3), 20.3 (4×**C**H_3), 20.0 (4×**C**H_3), 13.8 (br, 2×**C**H_3); LRMS (ESI$^+$) 327 (100 %, $[MH]^+$); HRMS (ESI$^+$) $C_{18}H_{34}N_2NaO_3$ $[M+Na]^+$ calculated 349.2462, observed 349.2470, $C_{18}H_{35}N_2O_3$ $[MH]^+$ calculated 327.2642, observed 327.2649.

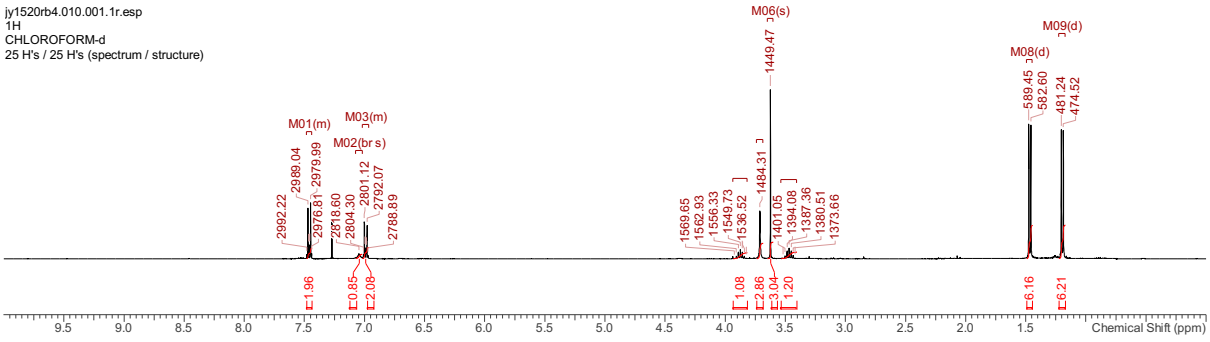


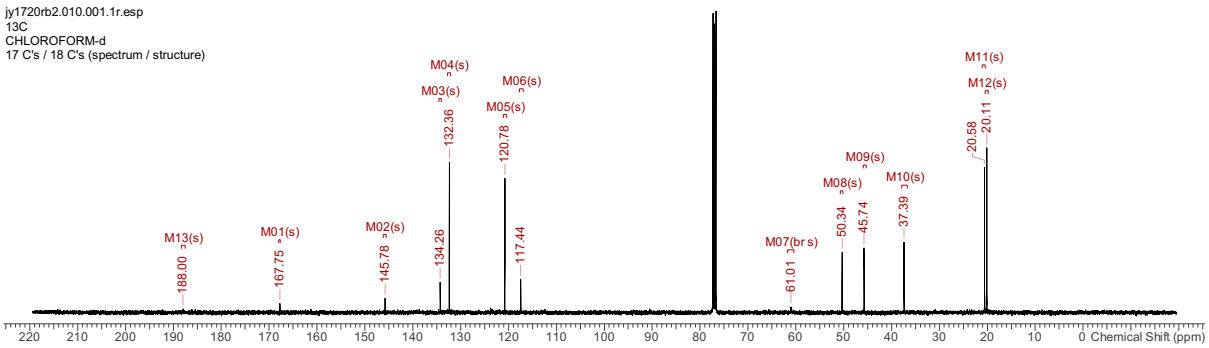


(*Z*)-4-((4-Bromophenyl)(methyl)amino)-*N*,*N*-diisopropyl-3-methoxy-2-oxobut-3-enamide, 11f

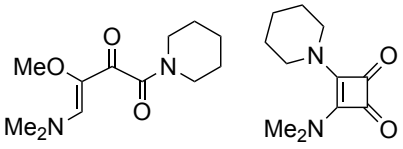


To a solution of cyclobutenedione **9f** (296 mg, 1.00 mmol) in THF (40 mL) at –78 °C was added LDA (2.0M in THF/ethylbenzene/hexanes, 0.60 mL, 1.20 mmol). After 2 h, water (20 mL) was added then the solution was warmed to RT. The aqueous phase was separated and extracted with DCM (3×30 mL) then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (20–30 % EtOAc/petrol) gave the title compound **11f** (257 mg, 0.65 mmol, 65 %) as a red solid, mp 171–173 °C; ν_{max} (film) 2972 (br), 2935 (br), 1630 (s), 1600 (s), 1572 (s), 1491 (s), 1446 (s), 1446 (m), 1415 (w), 1370 (w); δ_H (400 MHz, $CDCl_3$) 7.48–7.44 (m, 2H, 2×Ar**H**), 7.04 (br s, 1H, =C**H**), 7.02–6.96 (m, 2H, 2×Ar**H**), 3.87 (spt, *J* = 6.6 Hz, 1H, NC**H**), 3.71 (br s, 3H, C$\mathbf{H}_3$), 3.62 (s, 3H, C$\mathbf{H}_3$), 3.47 (spt, *J* = 6.8 Hz, 1H, NC**H**), 1.46 (d, *J* = 6.8 Hz, 6H, CH(C$\mathbf{H}_3$)$_2$), 1.19 (d, *J* = 6.6 Hz, 6H, CH(C$\mathbf{H}_3$)$_2$); δ_C (100 MHz, $CDCl_3$) 188.0 (**C**), 167.8 (**C**), 145.8 (**C**H), 134.3 (**C**), 132.4 (2×**C**H), 120.8 (2×**C**H), 117.4 (**C**), 61.0 (**C**H_3), 50.3 (**C**H_3), 45.7 (**C**H), 37.4 (**C**H), 20.6 (2×**C**H_3), 20.1 (2×**C**H_3), one **C** coincident or not observed; LRMS (ESI$^+$) 421 (24 %, [M{^{81}Br}+Na]$^+$, 419 (25 %, [M{^{79}Br}+Na]$^+$), 399 (100 %, [M{^{81}Br}H]$^+$), 397 (90 %, [M{^{79}Br}H]$^+$); HRMS (ESI$^+$) $C_{18}H_{25}{}^{79}BrN_2NaO_3$ [M+Na]$^+$ calculated 419.0941, observed 419.0940; $C_{18}H_{26}{}^{79}BrN_2O_3$ [MH]$^+$ calculated 397.1121, observed 397.1118; X-ray CCDC2042398.





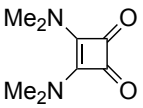
(*Z*)-4-(Dimethylamino)-3-methoxy-1-(piperidin-1-yl)but-3-ene-1,2-dione, 12a and **3-Methoxy-4-(pyrrolidin-1-yl)cyclobut-3-ene-1,2-dione, 13a**[8]



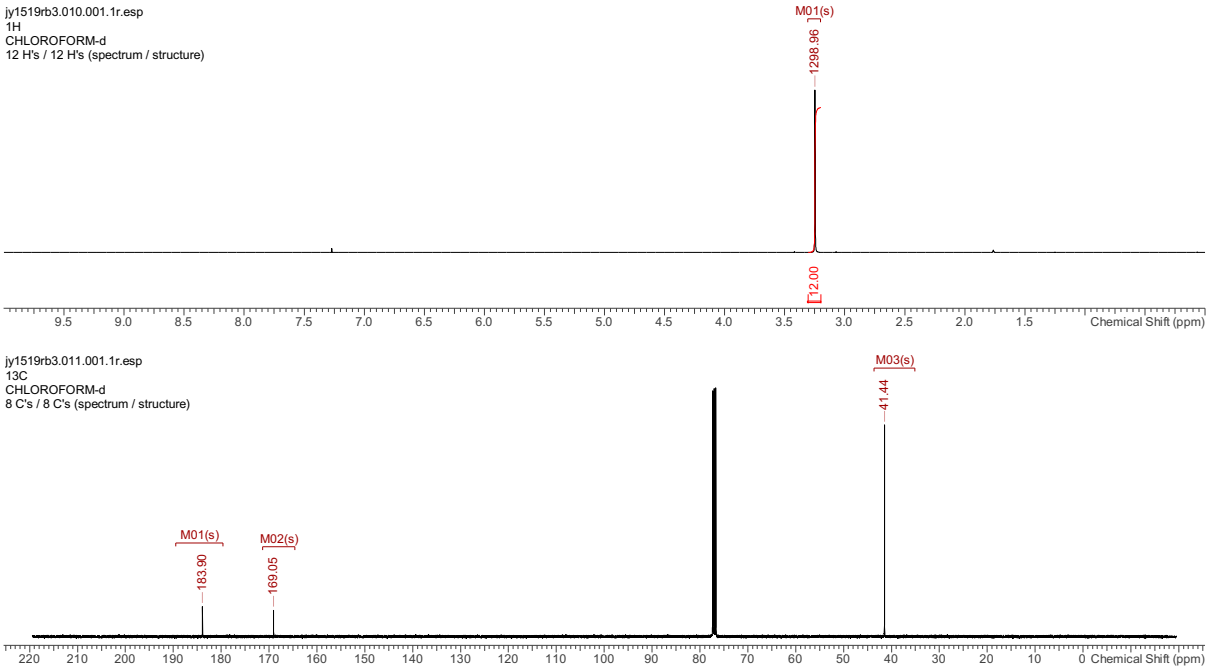
To a solution of piperidine (0.11 mL, 1.11 mmol) in THF (40 mL) at 0 °C was added *n*-butyllithium (2.5 M in hexanes, 0.44 mL, 1.10 mmol) dropwise. After 20 min, the solution was cooled to –78 °C then cyclobutenedione **9a** (155 mg, 1.00 mmol) in THF (10 mL) was added. After a further 2 h, water (20 mL) was added then the solution was warmed to RT. The aqueous phase was separated and extracted with DCM (3×40 mL) then the organic phases were combined, dried over $MgSO_4$

and concentrated *in vacuo*. Purification by column chromatography (90–100 % EtOAc/petrol) afforded firstly cyclobutenedione **13a** (21 mg, 0.10 mmol, 10 %) as a white solid, m.p. 138–140 °C; ν_{max} (film) 3016 (w), 2943 (w), 1786 (w), 1677 (m), 1585 (s), 1522 (s), 1449 (m), 1411 (m), 1304 (w), 1247 (w); δ_H (400 MHz, $CDCl_3$) 3.64–3.58 (m, 4H, 2×NC**H**$_2$), 3.21 (s, 6H, N(C**H**$_3$)$_2$), 1.71–1.67 (m, 6H, 3×C**H**$_2$); δ_C (100 MHz, $CDCl_3$) 184.3 (**C**), 184.3 (**C**), 169.6 (**C**), 168.1 (**C**), 49.9 (2×**C**H$_2$), 41.0 (2×**C**H$_3$), 26.0 (2×**C**H$_2$), 23.6 (**C**H$_2$); LRMS (ESI$^+$) 231 (15 %, [M+Na]$^+$), 209 (100 %, [MH]$^+$); HRMS (ESI$^+$) $C_{11}H_{16}N_2NaO_2$ [M+Na]$^+$ calculated 231.1104, observed 231.1106; $C_{11}H_{17}N_2O_2$ [MH]$^+$ calculated 209.1285, observed 209.1286; then the title compound **12a** (147 mg, 0.61 mmol, 61 %) as a yellow oil, ν_{max} (film) 2936 (br), 2858 (w), 1626 (s), 1563 (s), 1445 (m), 1420 (m), 1404 (m), 1364 (w), 1323 (s), 1282 (w); δ_H (400 MHz, $CDCl_3$) 6.58 (s, 1H, =C**H**), 3.66 (s, 3H, OC**H**$_3$), 3.56–3.52 (m, 2H, 2×NC**H**H), 3.35–3.30 (m, 2H, 2×NCH**H**), 3.12 (s, 6H, N(C**H**$_3$)$_2$), 1.67–1.60 (m, 2H, C**H**$_2$), 1.60–1.52 (m, 4H, 2×C**H**$_2$); δ_C (100 MHz, $CDCl_3$) 185.2 (**C**), 166.8 (**C**), 146.1 (**C**H), 131.6 (**C**), 60.6 (**C**H$_3$), 47.4 (**C**H$_2$), 42.1 (**C**H$_2$), 41.4 (br, 2×**C**H$_3$), 26.3 (**C**H$_2$), 25.5 (**C**H$_2$), 24.4 (**C**H$_2$); LRMS (ESI$^+$) 263 (10 %, [M+Na]$^+$), 241 (100 %, [MH]$^+$); HRMS (ESI$^+$) $C_{12}H_{20}N_2NaO_3$ [M+Na]$^+$ calculated 263.1366, observed 263.1369; $C_{12}H_{21}N_2O_3$ [MH]$^+$ calculated 241.1547, observed 241.1549.

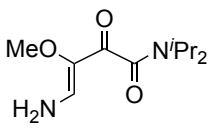
3,4-Bis(dimethylamino)cyclobut-3-ene-1,2-dione, 13b[9]



To a solution of cyclobutenedione **9a** (155 mg, 1.00 mmol) in THF (40 mL) at –78 °C was added $LiNMe_2$ (5 wt% in hexanes, 1.80 mL, 1.20 mmol). After 3 h, water (20 mL) was added then the solution was warmed to RT. The aqueous phase was separated and extracted with DCM (3×40 mL), then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (0–10 % MeOH/EtOAc) afforded firstly recovered starting material **9a** (61 mg, 0.40 mmol, 40 %) as a white solid the the title compound **13b** (81 mg, 0.48 mmol, 48 %) as a white solid, m.p. 219–220 °C (Et_2O) δ_H (400 MHz, $CDCl_3$) 3.25 (s, 4×NC**H**$_3$); δ_C (100 MHz, $CDCl_3$) 183.9, (2×**C**) 169.1 (2×**C**), 41.4 (4×**C**H$_3$); LC-MS (ESI$^+$) 191 (22 %, [M+Na]$^+$), 169 (100 %, [MH]$^+$). Data consistent with literature values.[9]

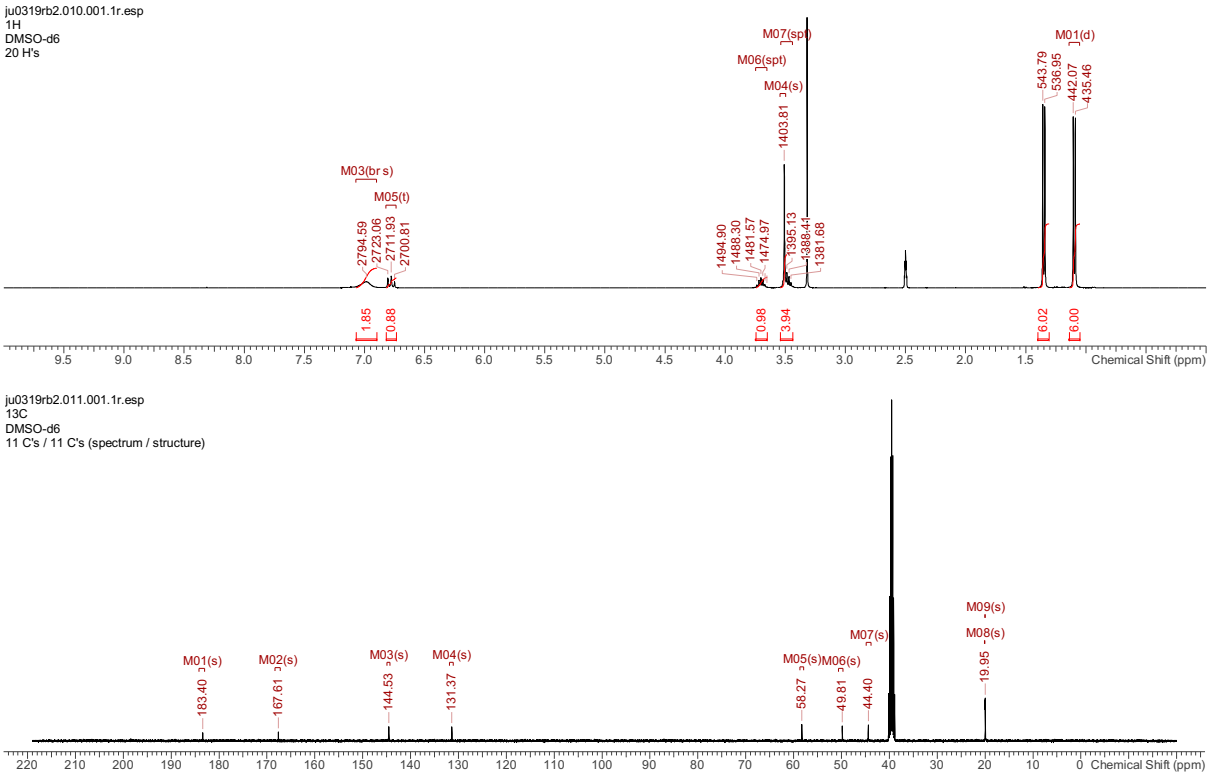


(*Z*)-4-Amino-*N,N*-diisopropyl-3-methoxy-2-oxobut-3-enamide, 14

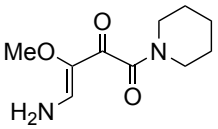


To a solution of DIPA (0.16 mL, 1.11 mmol) in THF (10 mL) at 0 °C was added *n*-butyllithium (2.5 M in hexanes, 0.47 mL, 1.17 mmol) dropwise. After 20 min the solution was added *via* cannula to a solution of cyclobutenedione **1a** (150 mg, 1.06 mmol) in THF (30 mL) at –78 °C. After a further 2 h, ammonia (7 M in methanol, 10 mL) was added then the reaction mixture was warmed to RT over 1 h. The aqueous phase was separated and extracted with DCM (3×30 mL) then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (30–80 % EtOAc/petrol) gave the title compound **14** (171 mg, 0.75

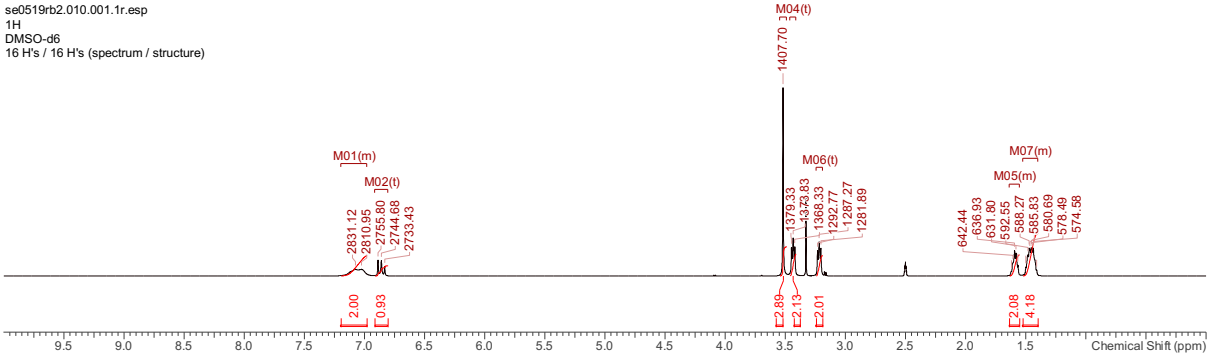
mmol, 71 %) as a white solid, m.p. 216–218 °C (EtOAc/hexane); ν_{max} (neat) 3371 (m), 3198 (br), 2982 (br), 2360 (m), 1665 (m), 1628 (s), 1612 (s), 1535 (s), 1469 (m), 1457 (m); δ_H (400 MHz, DMSO-d_6) 6.98 (br s, 2H, N**H**$_2$), 6.78 (t, *J* = 10.8 Hz, 1H, =C**H**), 3.70 (spt, *J* = 6.5 Hz, 1H, NC**H**), 3.51 (s, 3H, OC**H**$_3$), 3.49 (spt, *J* = 6.7 Hz, 1H, NC**H**), 1.35 (d, *J* = 6.8 Hz, 6H, CH(C**H**$_3$)$_2$), 1.10 (d, *J* = 6.6 Hz, 6H, CH(C**H**$_3$)$_2$); δ_C (100 MHz, DMSO-d_6) 183.4 (**C**), 167.6 (**C**), 144.5 (**C**H), 131.4 (**C**), 58.3 (**C**H$_3$), 49.8 (**C**H), 44.4 (**C**H), 20.0 (2×**C**H$_3$), 19.9 (2×**C**H$_3$); LRMS (ESI$^+$) 229 (100 %, [MH]$^+$); HRMS (ESI$^+$) $C_{11}H_{20}N_2NaO_3$ [M+Na]$^+$ calculated 251.1366, observed 251.1367.

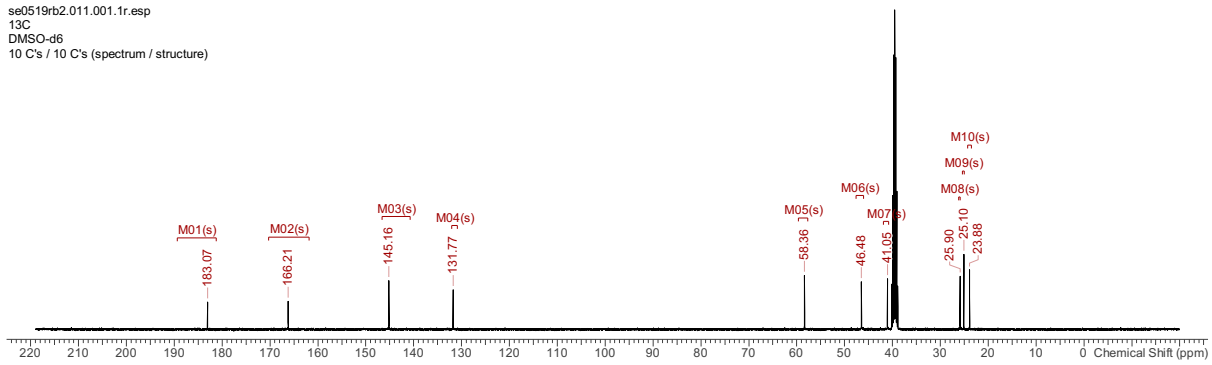


(*Z*)-4-Amino-3-methoxy-1-(piperidin-1-yl)but-3-ene-1,2-dione, 15

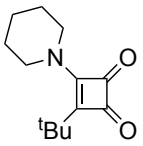


To a solution of piperidine (0.11 mL, 1.11 mmol) in THF (10 mL) at 0 °C was added *n*-butyllithium (2.5 M in hexanes, 0.47 mL, 1.17 mmol) dropwise. After 20 min the solution was added *via* cannula to a solution of cyclobutenedione **1a** (150 mg, 1.06 mmol) in THF (30 mL) at –78 °C. After a further 2 h, ammonia (7 M in methanol, 10 mL) was added then the reaction mixture was warmed to RT over 1 h. The aqueous phase was separated and extracted with DCM (3×30 mL) then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (50–80 % EtOAc/petrol) gave the title compound **15** (157 mg, 0.74 mmol, 70 %) as a white solid, m.p. 204–205 °C (EtOAc/hexane); ν_{max} (neat) 3377 (m), 3288 (w), 3236 (w), 2932 (m), 2859 (w), 2360 (w), 1665 (w), 1628 (s), 1610 (s), 1540 (s); δ_H (400 MHz, DMSO-d_6) 7.19–6.98 (m, 2H, N**H**$_2$), 6.86 (t, *J* = 11.3 Hz, 1H, =C**H**), 3.52 (s, 3H, OC**H**$_3$), 3.45–3.42 (m, 2H, 2×NC**H**H), 3.23–3.20 (m, 2H, 2×NCH**H**), 1.63–1.55 (m, 2H, C**H**$_2$), 1.52–1.40 (m, 4H, 2×C**H**$_2$); δ_C (100 MHz, DMSO-d_6) 183.1 (**C**), 166.2 (**C**), 145.2 (**C**H), 131.8 (**C**), 58.4 (**C**H$_3$), 46.5 (**C**H$_2$), 41.0 (**C**H$_2$), 25.9 (**C**H$_2$), 25.1 (**C**H$_2$), 23.9 (**C**H$_2$); LRMS (ESI$^+$) 213 (100 %, [MH]$^+$); HRMS (ESI$^+$) $C_{10}H_{16}N_2NaO_3$ [M+Na]$^+$ calculated 235.1053, observed 235.1052; $C_{10}H_{17}N_2O_3$ [MH]$^+$ calculated 213.1234, observed 213.1232.

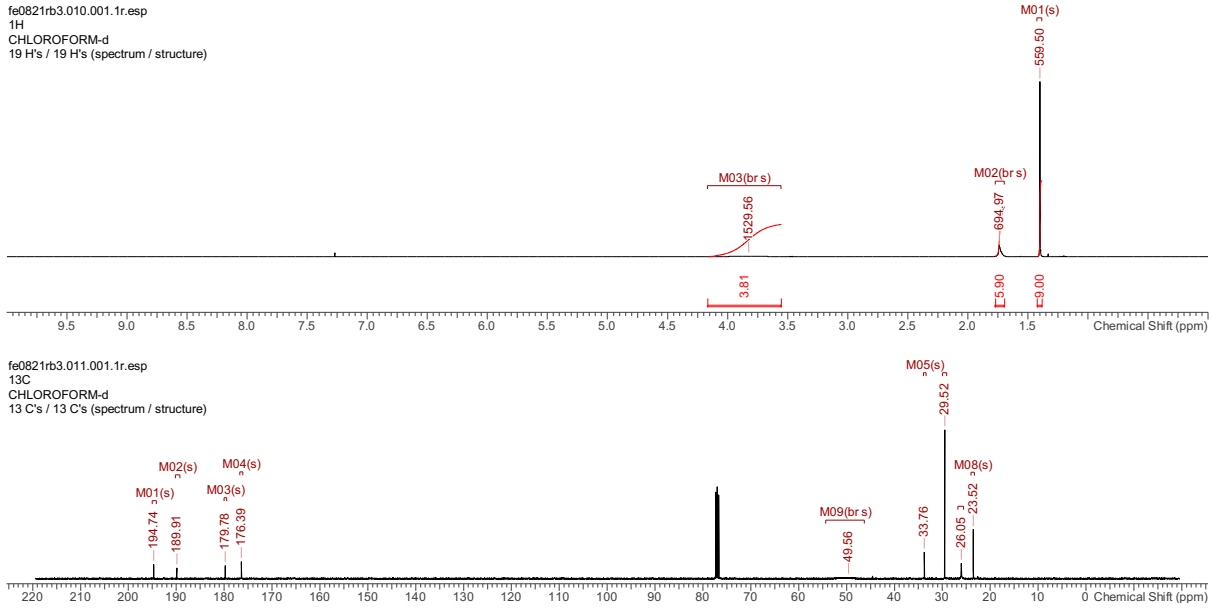




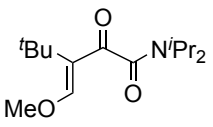
3-(*tert*-Butyl)-4-(piperidin-1-yl)cyclobut-3-ene-1,2-dione (17)



To a solution of piperidine (0.11 mL, 1.05 mmol) in THF (40 mL) at 0 °C was added *n*-butyllithium (2.5 M in hexanes, 0.42 mL, 1.05 mmol). After 20 min, the solution was cooled to –78 °C and cyclobutenedione **16a** (168 mg, 1.00 mmol) was added, followed after 2 h by water (20 mL). After warming to RT, the aqueous phase was separated and extracted with DCM (3×40 mL) then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (30 – 50 % ethyl acetate/petrol) gave the title compound **17** (88 mg, 0.40 mmol, 40 %) as a yellow oil, ν_{max} (film) 2940 (s), 2863 (m), 1772 (s), 1721 (m), 1580 (s), 1452 (m), 1413 (w), 1286 (m), 1259 (w), 1191 (m); δ_H (400 MHz, $CDCl_3$) 3.82 (br s, 4H, 2×C**H**$_2$), 1.74 (br s, 6H, 3×C**H**$_2$), 1.40 (s, 9H, C(C**H**$_3$)$_3$); δ_C (100 MHz, $CDCl_3$) 194.7 (**C**), 189.9 (**C**), 179.8 (**C**), 176.4 (**C**), 49.6 (br, 2×**C**H$_2$), 33.8 (**C**), 29.5 (3×**C**H$_3$), 26.0 (br, 2×**C**H$_2$), 23.5 (**C**H$_2$); LR-MS (ESI$^+$) 244 (58 %, [M + Na]$^+$), 222 (100 %, [M + H]$^+$); HR-MS (ESI$^+$) $C_{13}H_{19}NNaO_2$ [M + Na]$^+$ calculated 244.1308, observed 244.1308, $C_{13}H_{20}NO_2$ [M + H]$^+$ calculated 222.1489, observed 222.1492

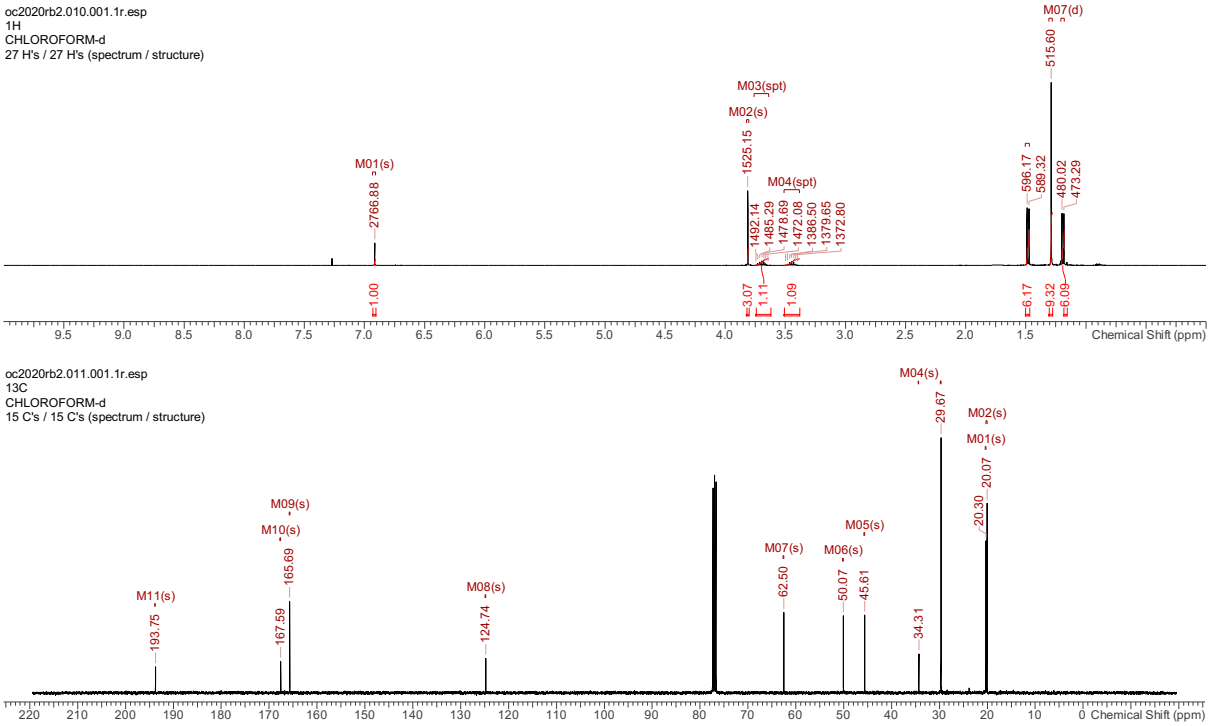


(*E*)-*N*,*N*-Diisopropyl-3-(methoxymethylene)-4,4-dimethyl-2-oxopentanamide (18a)

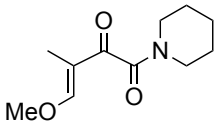


To a solution of cyclobutenedione **16a** (168 mg, 1.00 mmol) in THF (40 mL) at –78 °C was added LDA (1.0 M in THF/hexanes, 1.05 mL, 1.05 mmol). After 2 h, water (20 mL) was added and the solution was warmed to RT. The aqueous phase was separated and extracted with DCM (3×30 mL) the the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (10 – 20 % EtOAc/petrol) gave the title compound **18a** (92 mg, 0.34 mmol, 34 %) as yellow crystals, m.p. 84 – 85 °C; ν_{max} (film): 2971 (br), 1614 (s), 1446 (m), 1371 (m), 1349 (w), 1273 (s), 1243 (w), 1214 (m), 1140 (m), 1114 (w); δ_H (400 MHz, $CDCl_3$) 6.91 (s, 1H, =C**H**), 3.81 (s, 3H, OC**H**$_3$), 3.70 (spt, *J* = 6.6 Hz, 1H, NC**H**), 3.45 (spt, *J* = 6.9 Hz, 1H, NC**H**), 1.48 (d, *J* = 6.9 Hz, 6H, CH(C**H**$_3$)$_2$), 1.29 (s, 9H, C(C**H**$_3$)$_3$), 1.19 (d, *J*=6.6 Hz, 6H, CH(C**H**$_3$)$_2$); δ_C (100 MHz, $CDCl_3$) 193.7 (**C**), 167.6 (**C**),

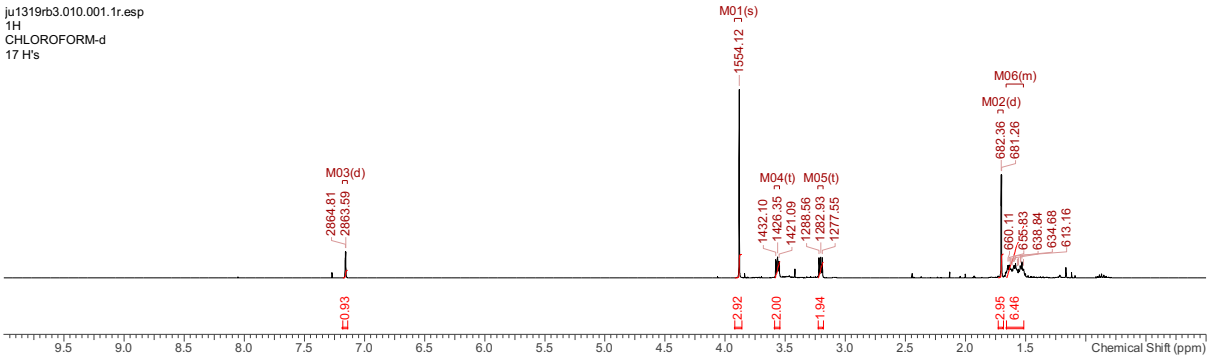
165.7 (**C**H), 124.7 (**C**), 62.5 (**C**H_3), 50.1 (**C**H), 45.6 (**C**H), 34.3 (**C**), 29.7 (C(**C**H_3)$_3$), 20.3 (CH(**C**H_3)$_2$), 20.1 (CH(**C**H_3)$_2$); LR-MS (ESI$^+$) 292 (10 %, [M + Na]$^+$), 270 (100 %, [M + H]$^+$); HR-MS (ESI$^+$): $C_{15}H_{27}NNaO_3$ [M + Na]$^+$ calculated 292.1883, observed 292.1885, $C_{15}H_{28}NO_3$ [M + H]$^+$ calculated 270.2064, observed 270.2063.

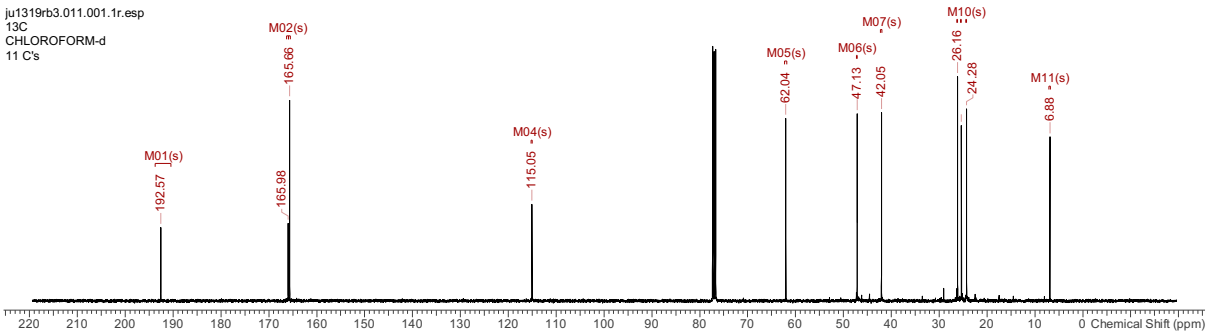


(*E*)-4-Methoxy-3-methyl-1-(piperidin-1-yl)but-3-ene-1,2-dione, 18b

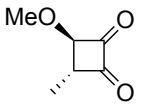


To a solution of piperidine (0.10 mL, 1.05 mmol) in THF (10 mL) at 0 °C was added *n*-butyllithium (2.5M in hexanes, 0.42 mL, 1.05 mmol) dropwise. After 20 min the solution was added *via* cannula to a solution of cyclobutenedione **16b** (126 mg, 1.0 mmol) in THF (30 mL) at –78 °C. After a further 90 min, water (10 mL) was added, and the reaction mixture was warmed to RT. The aqueous phase was separated and extracted with DCM (3×30 mL) then the organic phases were combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (30–80 % EtOAc/petrol) gave the title compound **18b** (167 mg, 0.79 mmol, 79 %) as a yellow oil, ν_{max} (film) 3482 (br), 2939 (br), 2858 (m), 1734 (br), 1612 (s), 1446 (m), 1395 (w), 1365 (w), 1314 (w), 1248 (s); δ_H (400 MHz, $CDCl_3$) 7.16 (q, *J* = 1.2 Hz, 1H, =C**H**), 3.88 (s, 3H, OC**H**$_3$), 3.58–3.55 (m, 2H, NC**H**H), 3.22–3.19 (m, 2H, NCH**H**), 1.70 (d, *J* = 1.1 Hz, 3H, C**H**$_3$), 1.67–1.51 (m, 6H, 3×C**H**$_2$); δ_C (100 MHz, $CDCl_3$) 192.6 (**C**), 166.0 (**C**), 165.7 (**C**H), 115.1 (**C**), 62.0 (**C**H_3), 47.1 (**C**H_2), 42.1 (**C**H_2), 26.2 (**C**H_2), 25.4 (**C**H_2), 24.3 (**C**H_2), 6.9 (**C**H_3); LRMS (ESI$^+$) 212 (100 %, [MH]$^+$); HRMS (ESI$^+$) $C_{11}H_{18}NO_3$ [MH]$^+$ calculated 212.1281, observed 212.1283.

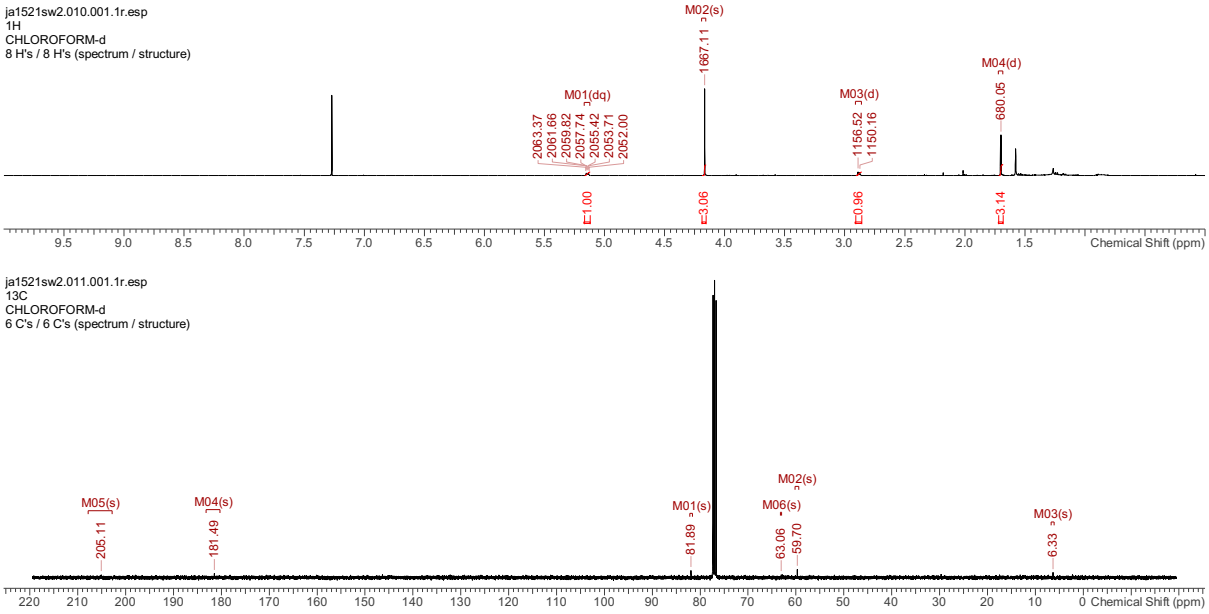




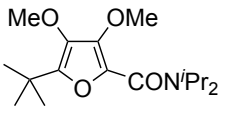
3-Methoxy-4-methylcyclobutane-1,2-dione, 19



To a solution of cyclobutenedione **16b** (187 mg, 1.48 mmol) in THF (50 mL) at –78 °C was added LDA (1 M in THF/hexanes, 1.56 mL, 1.56 mmol) followed after 2 h by water (20 mL). After warming to RT, the aqueous phase was separated and extracted with DCM (3×40 mL). The organic phases were then combined, dried over $MgSO_4$ and concentrated *in vacuo*. Purification by column chromatography (ethyl acetate) yielded the title compound **19** (113 mg, 0.88 mmol, 60 %) as a sensitive yellow oil, ν_{max} (film) 2925 (m), 1751 (m), 1616 (s), 1457 (m), 1385 (m), 1341 (s), 1150 (w), 1046 (w), 974 (w) 814 (w); δ_H (400 MHz, $CDCl_3$) 5.14 (dq, *J*=6.3, 1.8 Hz, 1H, C**H**), 4.17 (s, 3H, OC**H**$_3$), 2.88 (d, *J*=6.3 Hz, 1H, C**H**), 1.70 (d, *J*=1.8 Hz, 3H, C**H**$_3$); δ_C (100 MHz, $CDCl_3$) 205.1 (**C**), 181.5 (**C**), 81.9 (**C**H), 63.1 (**C**H), 59.7 (O**C**H$_3$), 6.3 (**C**H$_3$); LR-MS (ESI$^+$) 151 (3 %, [M + Na]$^+$), 129 (100 %, [M + H]$^+$); HR-MS (ESI$^+$) $C_6H_8NaO_3$ [M + Na]$^+$ calculated 151.0366, observed 151.0361.

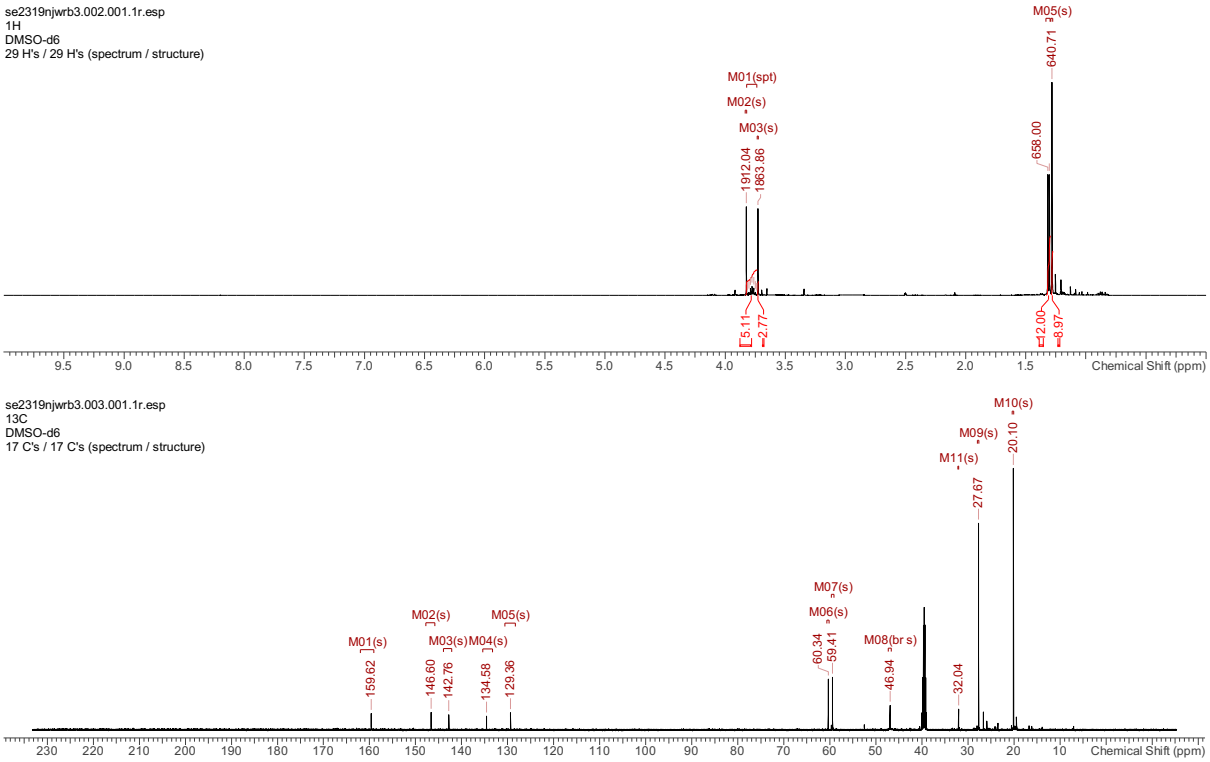


5-(*tert*-Butyl)-*N*,*N*-diisopropyl-3,4-dimethoxyfuran-2-carboxamide, 8a

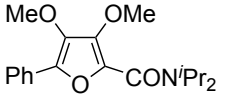


To a solution of cyclobutenedione **1a** (142 mg, 1.0 mmol) in THF (30 mL) at –78 °C was added LDA (2.0 M in THF/ethylbenzene/hexanes, 0.55 mL, 1.10 mmol) dropwise. After 90 min, trimethylacetaldehyde (0.14 mL, 1.3 mmol) was added. After a further 30 min the reaction mixture was warmed to RT for 2 h then returned to –78 °C. TFAA (0.18 mL, 1.2 mmol) was added, followed after 90 min by water (10 mL). On warming to RT, the aqueous phase was separated and extracted with DCM (3×20 mL). The organic phases were then combined, dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5–10 % EtOAc/petrol) to give the title compound **8a** (103 mg, 0.33 mmol, 33 %) as a yellow oil, ν_{max} (film) 2967 (m), 2934 (w), 1622 (s), 1571 (m), 1483 (w), 1462 (w), 1408 (m), 1369 (m), 1340 (s), 1288 (m); δ_H (500 MHz, DMSO-d_6, 373 K) 3.82 (s, 3H, OC**H**$_3$), 3.78 (spt, *J* = 6.7 Hz, 2H, 2×NC**H**), 3.73 (s, 3H, OC**H**$_3$), 1.31 (d, *J* = 6.8 Hz, 12H, N(CH(C**H**$_3$)$_2$)$_2$), 1.28 (s, 9H, C(C**H**$_3$)$_3$); δ_C (126 MHz, DMSO-d_6, 373 K) 159.6 (**C**), 146.6 (**C**), 142.8 (**C**), 134.6 (**C**), 129.4 (**C**), 60.3 (**C**H$_3$), 59.4 (**C**H$_3$), 46.9 (br, 2×**C**H), 32.0 (**C**), 27.7 (3×**C**H$_3$), 20.1 (4×**C**H$_3$); LRMS (ESI$^+$) 312 (100 %, [MH]$^+$); HRMS (ESI$^+$)

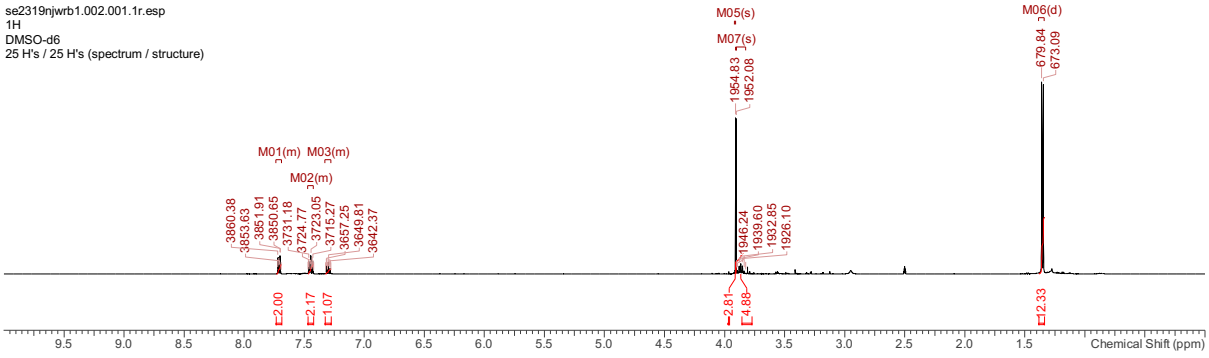
$C_{17}H_{29}NNaO_4$ [M+Na]$^+$ calculated 334.1989, observed 334.1991; $C_{17}H_{30}NO_4$ [MH]$^+$ calculated 312.2169, observed 312.2173.

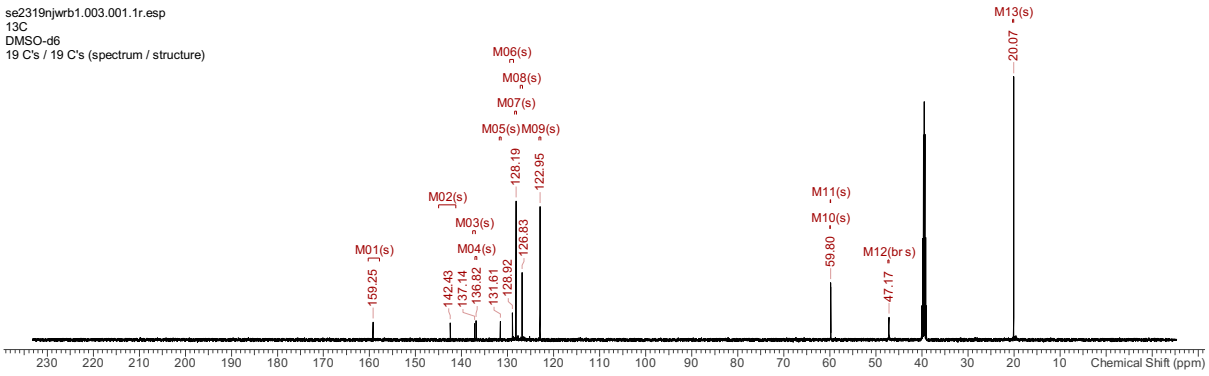


***N*,*N*-Diisopropyl-3,4-dimethoxy-5-phenylfuran-2-carboxamide, 8b**

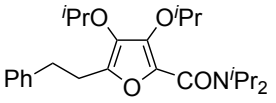


To a solution of cyclobutenedione **1a** (142 mg, 1.0 mmol) in THF (30 mL) at –78 °C was added LDA (2.0 M in THF/ethylbenzene/hexanes, 0.55 mL, 1.10 mmol) dropwise. After 90 min, benzaldehyde (0.12 mL, 1.2 mmol) was added. After a further 30 min the reaction mixture was warmed to RT for 2 h then returned to –78 °C. TFAA (0.18 mL, 1.2 mmol) was added, followed after 90 min by water (10 mL). On warming to RT, the aqueous phase was separated and extracted with DCM (3×20 mL). The organic phases were then combined, dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5–10 % EtOAc/petrol) to give the title compound **8b** (102 mg, 0.31 mmol, 31 %) as a yellow oil, ν_{max} (film) 2971 (m), 2936 (w), 2359 (m), 2343 (w), 1623 (s), 1580 (w), 1559 (w), 1465 (s), 1448 (s), 1410 (m); δ_H (500 MHz, DMSO-d_6, 373 K) 7.73–7.69 (m, 2H, 2×Ar**H**), 7.47–7.42 (m, 2H, 2×Ar**H**), 7.32–7.27 (m, 1H, Ar**H**), 3.91 (s, 3H, OC**H**$_3$), 3.90 (s, 3H, OC**H**$_3$), 3.87 (spt, *J* = 6.7 Hz, 2H, 2×NC**H**), 1.35 (d, *J* = 6.8 Hz, 12H, N(CH(C**H**$_3$)$_2$)$_2$); δ_C (126 MHz, DMSO-d_6, 373 K) 159.3 (**C**), 142.4 (**C**), 137.1 (**C**), 136.8 (**C**), 131.6 (**C**), 128.9 (**C**), 128.2 (2×**C**H), 126.8 (**C**H), 122.9 (2×**C**H), 59.83 (**C**H$_3$), 59.80 (**C**H$_3$), 47.2 (br, 2×**C**H), 20.1 (4×**C**H$_3$); LRMS (ESI$^+$) 332 (100 %, [MH]$^+$); HRMS (ESI$^+$) $C_{19}H_{25}NNaO_4$ [M+Na]$^+$ calculated 354.1676, observed 354.1682; $C_{19}H_{26}NO_4$ [MH]$^+$ calculated 332.1856, observed 332.1863.

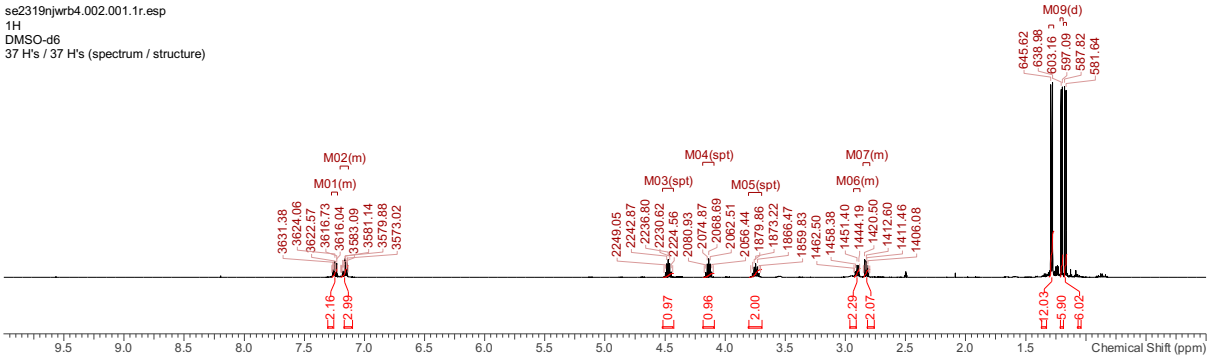


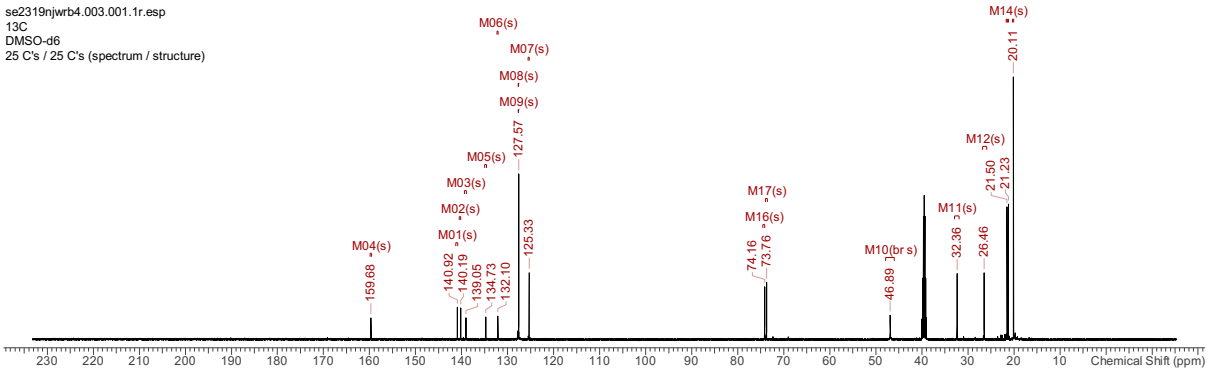


3,4-Diisopropoxy-*N*,*N*-diisopropyl-5-phenethylfuran-2-carboxamide, 8c

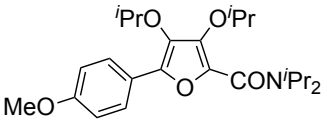


To a solution of cyclobutenedione **1b** (198 mg, 1.0 mmol) in THF (30 mL) at –78 °C was added LDA (2.0 M in THF/ethylbenzene/hexanes, 0.55 mL, 1.10 mmol) dropwise. After 90 min, 3-phenylpropionaldehyde (0.16 mL, 1.2 mmol) was added. After a further 30 min the reaction mixture was warmed to RT for 2 h then returned to –78 °C. TFAA (0.18 mL, 1.2 mmol) was added, followed after 90 min by water (10 mL). On warming to RT, the aqueous phase was separated and extracted with DCM (3×20 mL). The organic phases were then combined, dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5–10 % EtOAc/petrol) to give the title compound **8c** (170 mg, 0.41 mmol, 41 %) as a yellow oil, FT-IR (ν_{max}, $CHCl_3$) 2972 (s), 2931 (m), 2360 (w), 1624 (s), 1570 (w), 1497 (w), 1453 (m), 1421 (w), 1371 (s), 1359 (w) cm^{-1}; δ_H (500 MHz, DMSO-d_6, 373 K) 7.27–7.22 (m, 2H, 2×Ar**H**), 7.20–7.13 (m, 3H, 3×Ar**H**), 4.47 (spt, *J* = 6.1 Hz, 1H, OC**H**), 4.14 (spt, *J* = 6.1 Hz, 1H, OC**H**), 3.75 (spt, *J* = 6.7 Hz, 2H, 2×NC**H**), 2.93–2.87 (m, 2H, C$\mathbf{H}_2$), 2.85–2.79 (m, 2H, C$\mathbf{H}_2$), 1.28 (d, *J* = 6.7 Hz, 12H, N(CH(C$\mathbf{H}_3$)$_2$)$_2$), 1.20 (d, *J* = 6.1 Hz, 6H, OCH(C$\mathbf{H}_3$)$_2$), 1.17 (d, *J* = 6.1 Hz, 6H, OCH(C$\mathbf{H}_3$)$_2$); δ_C (126 MHz, DMSO-d_6, 373 K) 159.7 (**C**), 140.9 (**C**), 140.2 (**C**), 139.1 (**C**), 134.7 (**C**), 132.1 (**C**), 127.58 (2×**C**H), 127.57 (2×**C**H), 125.3 (**C**H), 74.2 (**C**H), 73.8 (**C**H), 46.9 (br, 2×**C**H), 32.4 (**C**H_2), 26.5 (**C**H_2), 21.5 (2×**C**H_3), 21.2 (2×**C**H_3), 20.1 (4×**C**H_3); LRMS (ESI$^+$) 416 (100 %, [MH]$^+$); HRMS (ESI$^+$) $C_{25}H_{37}NNaO_4$ [M+Na]$^+$ calculated 438.2615, observed 438.2621; $C_{25}H_{38}NO_4$ [MH]$^+$ calculated 416.2795, observed 416.2802.

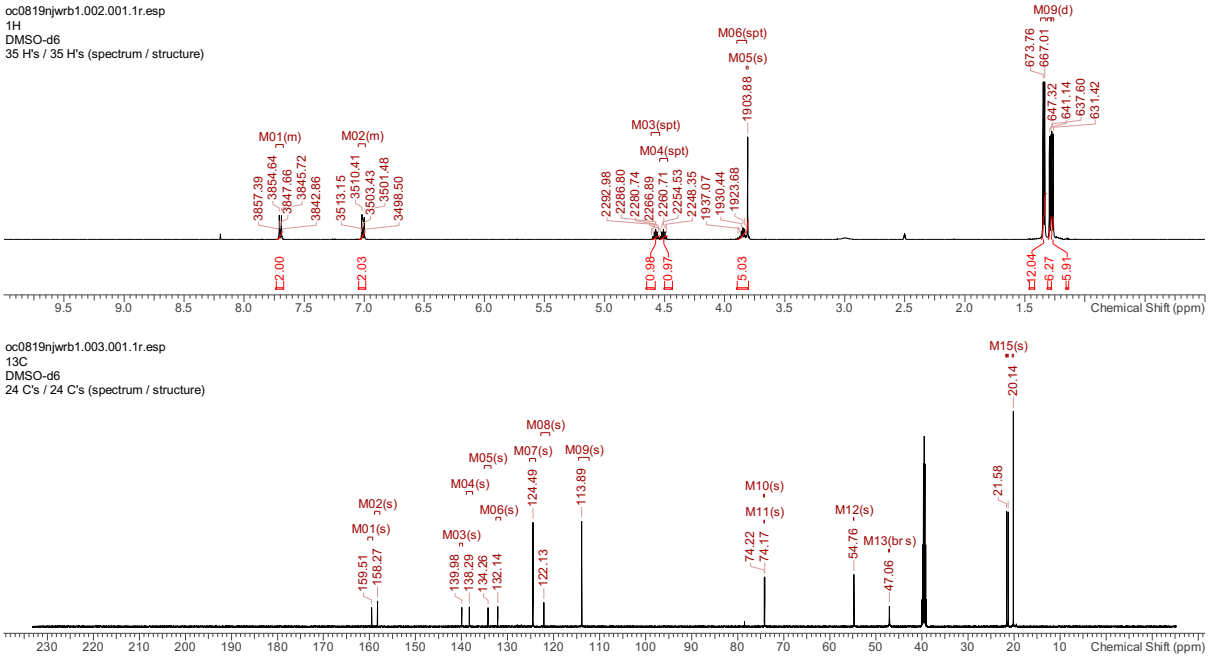




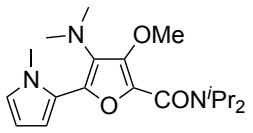
3,4-Diisopropoxy-*N*,*N*-diisopropyl-5-(4-methoxyphenyl)furan-2-carboxamide, 8d



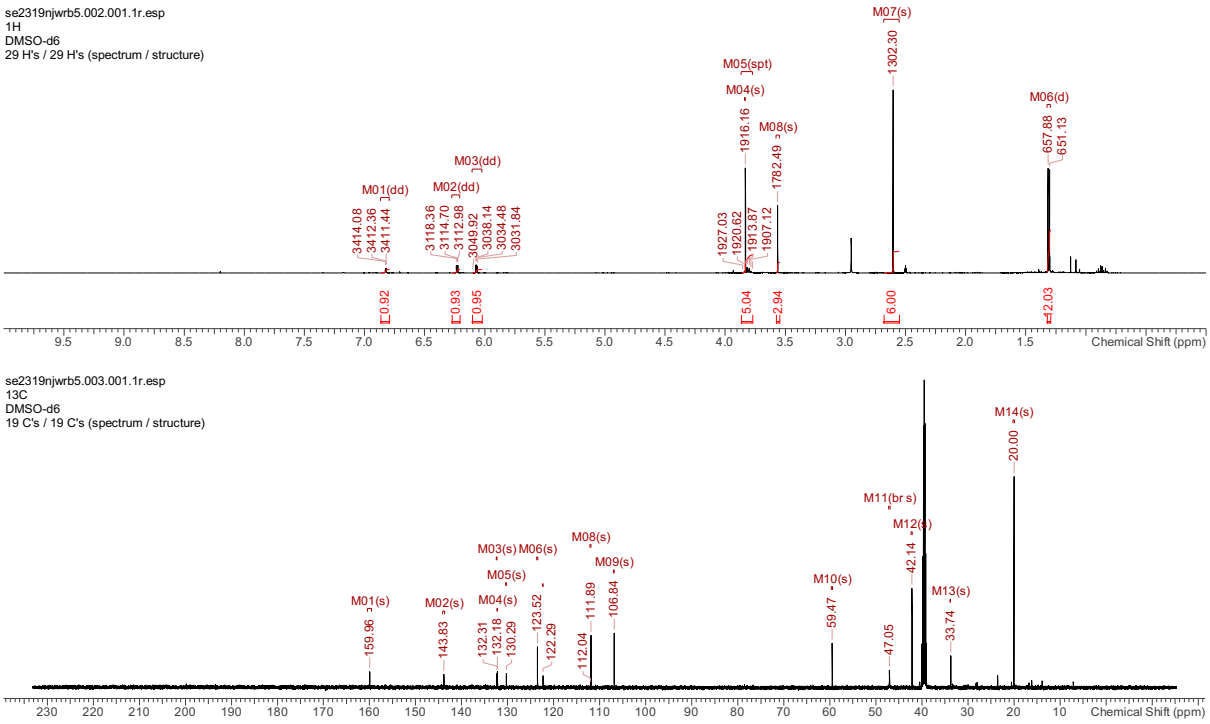
To a solution of cyclobutenedione **1b** (155 mg, 1.0 mmol) in THF (30 mL) at –78 °C was added LDA (2.0 M in THF/ethylbenzene/hexanes, 0.55 mL, 1.10 mmol) dropwise. After 90 min, *p*-anisaldehyde (0.15 mL, 1.2 mmol) was added. After a further 30 min the reaction mixture was warmed to RT for 2 h then returned to –78 °C. TFAA (0.18 mL, 1.2 mmol) was added, followed after 90 min by sat. sodium bisulfite (10 mL). On warming to RT, the aqueous phase was separated and extracted with DCM (3×20 mL). The organic phases were then combined, dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (5–10 % EtOAc/petrol) to give the title compound **8d** (155 mg, 0.37 mmol, 37 %) as a yellow oil, ν_{max} (film) 2975 (m), 2935 (w), 1621 (s), 1562 (w), 1509 (s), 1456 (s), 1426 (m), 1373 (s), 1336 (m), 1300 (m); δ_H (500 MHz, DMSO-d_6, 373 K) 7.73–7.67 (m, 2H, 2×Ar**H**), 7.05–6.99 (m, 2H, 2×Ar**H**), 4.57 (spt, *J* = 6.2 Hz, 1H, OC**H**), 4.51 (spt, *J* = 6.2 Hz, 1H, OC**H**), 3.85 (spt, *J* = 6.7 Hz, 2H, N(C**H**$(CH_3)_2)_2$), 3.81 (s, 3H, OC$\mathbf{H}_3$), 1.34 (d, *J* = 6.7 Hz, 12H, N(CH(C$\mathbf{H}_3)_2)_2$), 1.29 (d, *J* = 6.2 Hz, 6H, OCH(C$\mathbf{H}_3)_2$), 1.27 (d, *J* = 6.2 Hz, 6H, OCH(C$\mathbf{H}_3)_2$); δ_C (126 MHz, DMSO-d_6, 373 K) 159.5 (**C**), 158.3 (**C**), 140.0 (**C**), 138.3 (**C**), 134.3 (**C**), 132.1 (**C**), 124.5 (2×**C**H), 122.1 (**C**), 113.9 (2×**C**H), 74.22 (**C**H), 74.17 (**C**H), 54.8 (**C**H_3), 47.1 (br, 2×**C**H), 21.6 (2×**C**H_3), 21.3 (2×**C**H_3), 20.1 (4×**C**H_3); LRMS (ESI$^+$) 418 (100 %, $[MH]^+$); HRMS (ESI$^+$) $C_{24}H_{35}NNaO_5$ $[M+Na]^+$ calculated 440.2407, observed 440.2409; $C_{24}H_{36}NO_5$ $[MH]^+$ calculated 418.2588, observed 418.2596.



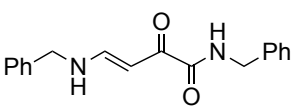
4-(Dimethylamino)-*N*,*N*-diisopropyl-3-methoxy-5-(1-methyl-1*H*-pyrrol-2-yl)furan-2-carboxamide, 8e

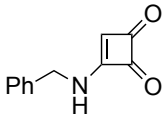


To a solution of cyclobutenedione **9a** (155 mg, 1.0 mmol) in THF (30 mL) at –78 °C was added LDA (2.0 M in THF/ethylbenzene/hexanes, 0.55 mL, 1.10 mmol) dropwise. After 90 min, *N*-methyl-2-pyrrolecarboxaldehyde (0.13 mL, 1.2 mmol) was added. After a further 30 min the reaction mixture was warmed to RT for 2 h then returned to –78 °C. TFAA (0.18 mL, 1.2 mmol) was added, followed after 90 min by sat. sodium bisulfite (10 mL). On warming to RT, the aqueous phase was separated and extracted with DCM (3×20 mL). The organic phases were then combined, dried over $MgSO_4$, concentrated *in vacuo* and purified by column chromatography (10–15 % EtOAc/petrol) to give the title compound **8e** (131 mg, 0.38 mmol, 38 %) as a yellow oil, ν_{max} (film) 2970 (m), 2934 (w), 2791 (w), 2360 (w), 1625 (s), 1527 (w), 1458 (s), 1395 (w), 1370 (m), 1346 (s); δ_H (500 MHz, DMSO-d_6, 373 K) 6.82 (dd, *J* = 2.7, 1.8 Hz, 1H, Ar**H**), 6.23 (dd, *J* = 3.7, 1.7 Hz, 1H, Ar**H**), 6.07 (dd, *J* = 3.6, 2.7 Hz, 1H, Ar**H**), 3.83 (s, 3H, OC$\mathbf{H}_3$), 3.81 (spt, *J* = 6.7 Hz, 2H, N(C**H**$(CH_3)_2)_2$), 3.56 (s, 3H, NC$\mathbf{H}_3$), 2.60 (s, 6H, N(C$\mathbf{H}_3)_2$), 1.31 (d, *J* = 6.8 Hz, 12H, N(CH(C$\mathbf{H}_3)_2)_2$); δ_C (126 MHz, DMSO-d_6, 373 K) 160.0 (**C**), 143.8 (**C**), 132.3 (**C**), 132.2 (**C**), 130.3 (**C**), 123.5 (**C**H), 122.3 (**C**), 111.9 (**C**H), 106.8 (**C**H), 59.5 (**C**H_3), 47.0 (br, 2×**C**H), 42.1 (2×**C**H_3), 33.7 (**C**H_3), 20.0 (4×**C**H_3); LRMS (ESI$^+$) 348 (100 %, $[MH]^+$); HRMS (ESI$^+$) $C_{19}H_{29}N_3NaO_3$ $[M+Na]^+$ calculated 370.2101, observed 370.2102; $C_{19}H_{30}N_3O_3$ $[MH]^+$ calculated 348.2282, observed 348.2290.

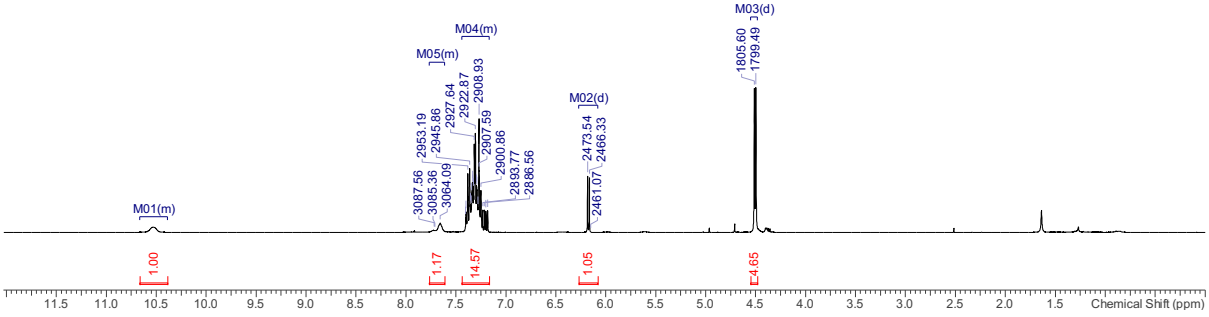


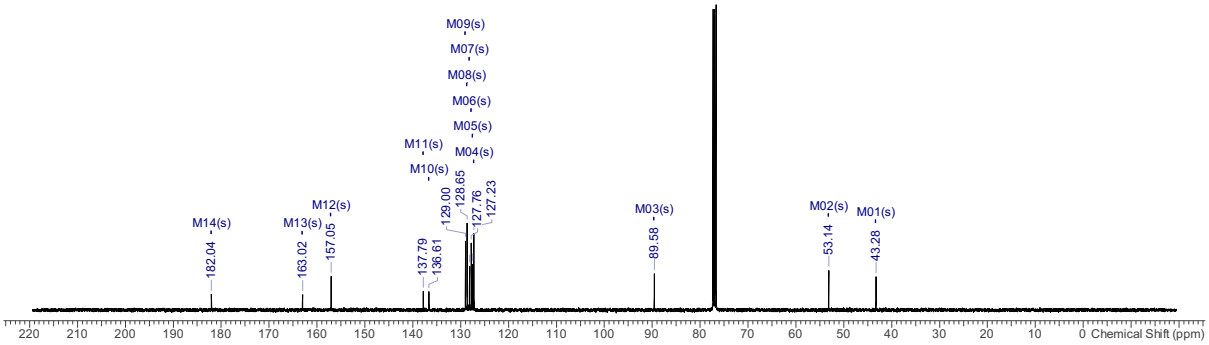
3-(Benzylamino)cyclobut-3-ene-1,2-dione, 26 and **(*E*)-*N*-benzyl-4-(benzylamino)-2-oxobut-3-enamide, 27**

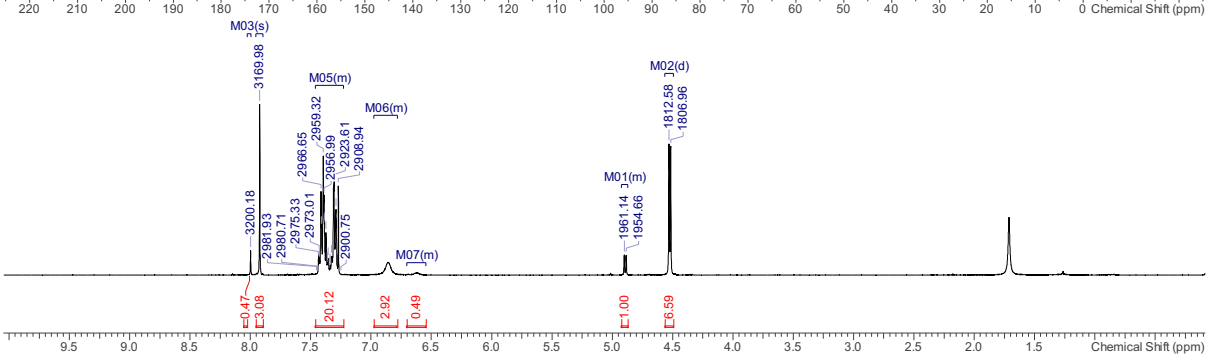


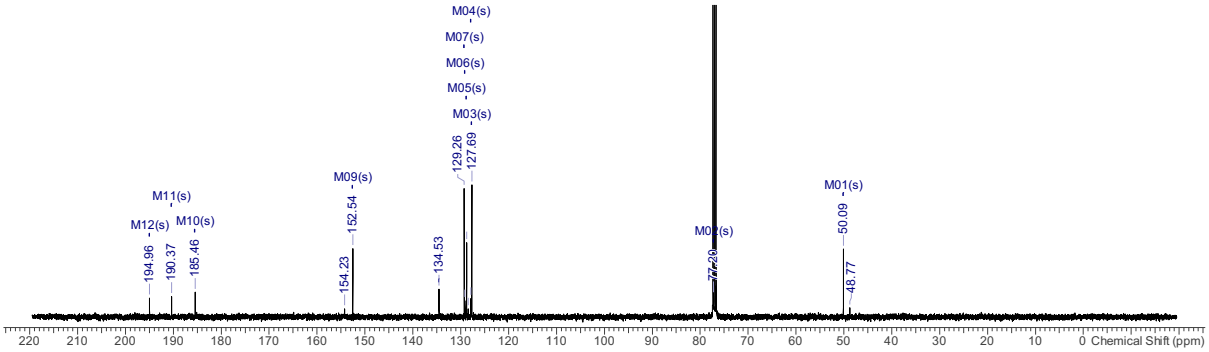


To 3-isopropoxycyclobut-3-ene-1,2-dione **25** (538 mg, 3.84 mmol) in ^{i}PrOH (30 mL) at 0 °C was added benzylamine (0.63 mL, 5.77 mmol) dropwise. After 1 h, the solution was warmed to RT, concentrated *in vacuo* and purified by column chromatography (10-30% EtOAc/petrol) to afforded firstly the title compound **27** (288 mg, 0.98 mmol, 25%) as a cream solid, m.p. 120–122 °C; ν_{max} (neat) 3379 (br m), 3321 (br m), 3089 (w), 3060 (w), 3029 (w), 2924 (w), 2873 (w), 1674 (m), 1628 (s), 1569 (m), 1514 (m), 1482 (s), 1453 (m), 1359 (br w), 1291 (br m), 1236 (br m); δ_H (400 MHz, $CDCl_3$) 10.53 (br s, 1H, N**H**), 7.66 (br s, 1H, N**H**), 7.40–7.25 (m, 10H, 10×Ar**H**), 7.21 (dd, *J* = 13.2, 7.2 Hz, 1H, NHC**H**=CH), 6.17 (d, *J* = 7.2 Hz, 1H, NHCH=C**H**), 4.51 (s, 2H, C$\mathbf{H}_2$), 4.50 (s, 2H, C$\mathbf{H}_2$); δ_C (100 MHz, $CDCl_3$) 182.0 (**C**), 163.0 (**C**), 157.1 (**C**H), 137.8 (**C**), 136.6 (**C**), 129.0 (2×**C**H), 128.7 (2×**C**H), 128.1 (**C**H), 127.8 (2×**C**H), 127.5 (**C**H), 127.2 (2×**C**H), 89.6 (**C**H), 53.1 (C$\mathbf{H}_2$), 43.3 (C$\mathbf{H}_2$); LRMS (ESI$^+$) 317 ([M+Na]$^+$, 37%), 295 ([MH]$^+$, 100%); HRMS (ESI$^+$) $C_{18}H_{18}N_2NaO_2$ [M+Na]$^+$ calculated 317.1260, observed 317.1266; X-ray CCDC CCDC1500038; then cyclobutenedione **26** (291 mg, 1.55 mmol, 40%) as a brown solid, m.p. 89–91 °C; ν_{max} (neat) 3199 (br m), 3091 (br w), 2991 (br w), 1775 (s), 1740 (s), 1595 (s), 1453 (m), 1356 (m), 1107 (m); δ_H (400 MHz, $CDCl_3$) major rotamer: 7.92 (s, 1H, CH), 7.44–7.29 (m, 5H, 5×Ar**H**), 6.86 (br s, 1H, N**H**), 4.53 (d, *J* = 5.6 Hz, 2H, C$\mathbf{H}_2$), minor rotamer: 8.00 (s, 1H, CH), 7.44–7.29 (m, 5H, 5×Ar**H**), 6.62 (br s, 1H, N**H**), 4.90 (d, *J* = 6.5 Hz, 2H, C$\mathbf{H}_2$); δ_C (100 MHz, $CDCl_3$) 195.0 (**C**), 190.4 (**C**), 185.5 (**C**), 152.5 (**C**H), 134.5 (**C**), 129.3 (2×**C**H), 128.8 (**C**H), 127.7 (2×**C**H), 50.1 (C$\mathbf{H}_2$), minor rotamer: 195.0 (**C**), 190.4 (**C**), 185.5 (**C**), 154.2 (**C**H), 134.5 (**C**), 129.1 (2×**C**H), 128.4 (**C**H), 127.9 (2×**C**H), 48.8 (C$\mathbf{H}_2$); LRMS (ESI$^+$) 210 ([M+Na]$^+$, 16%), 188 ([MH]$^+$, 100%); HRMS (ESI$^+$) $C_{11}H_{10}NO_2$ [MH]$^+$ calculated 188.0706, observed 188.0708.



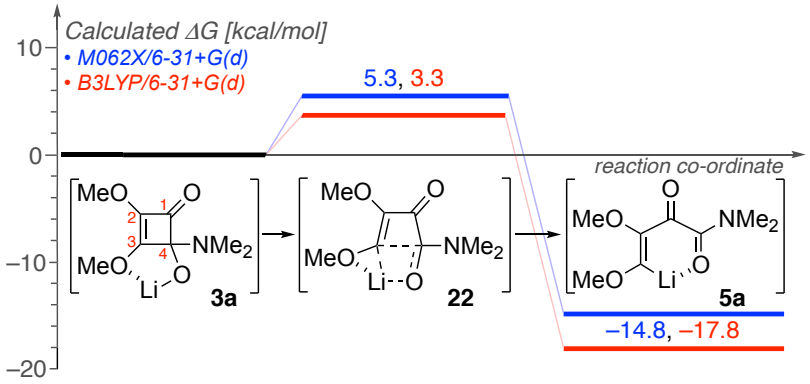

M09(s)
M07(s)
M08(s)
M06(s)
M05(s)
M11(s)
M04(s)
M10(s)
M12(s)
M14(s)
M13(s)
M03(s)
M02(s)
M01(s)
182.04
163.02
157.05
137.79
136.61
129.00
128.65
127.76
127.23
89.58
53.14
43.28
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 Chemical Shift (ppm)


M03(s)
3169.98
M05(m)
M06(m)
M02(d)
1812.58
1806.96
2966.65
2959.32
2956.99
2923.61
2908.94
M01(m)
3200.18
2981.93
2980.71
2975.33
2973.01
2900.75
1961.14
1954.66
M07(m)
0.47
3.08
20.12
2.92
0.49
1.00
6.59
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 Chemical Shift (ppm)

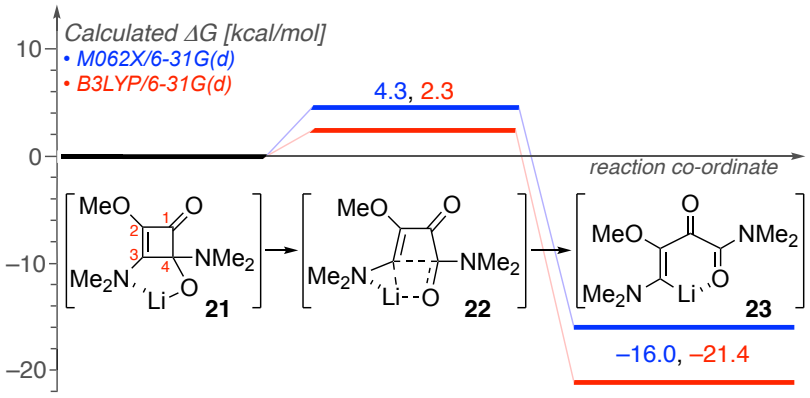

M04(s)
M07(s)
M06(s)
M05(s)
M03(s)
M09(s)
M11(s)
M12(s)
M10(s)
M02(s)
M01(s)
194.96
190.37
185.46
154.23
152.54
134.53
129.26
127.69
77.29
50.09
48.77
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 Chemical Shift (ppm)

3. DFT Calculations

DFT calculations for Figures 1 and 2 were carried out with the Gaussian 09W C.01 program.[10] Gibbs free energies (ΔG) were calculated at the B3LYP/6-31G(d) and M062X/6-31G(d) level of theory. The geometries of all intermediate species were optimized and confirmed by the absence of imaginary frequencies. The transition states were found by relaxed scans of the bond distance between atoms directly involved and checked by the existence of a single imaginary frequency corresponding to their reaction coordinates.



Compound	Calculations	Hartree/particle	
		B3LYP/6-31G(d)	**M062X/6-31G(d)**
3a	Zero-point correction	0.201314	0.203857
	Thermal correction to Energy	0.217258	0.219601
	Thermal correction to Enthalpy	0.218203	0.220545
	Thermal correction to Gibbs Free Energy	0.158308	0.160848
	Sum of electronic and zero-point Energies	–674.992487	–674.730872
	Sum of electronic and thermal Energies	–674.976543	–674.715128
	Sum of electronic and thermal Enthalpies	–674.975598	–674.714184
	Sum of electronic and thermal Free Energies	–675.035493	–674.773881
20	Zero-point correction	0.200543	0.203102
	Thermal correction to Energy	0.216085	0.218379
	Thermal correction to Enthalpy	0.217029	0.219323
	Thermal correction to Gibbs Free Energy	0.157810	0.160502
	Sum of electronic and zero-point Energies	–674.987565	–674.722804
	Sum of electronic and thermal Energies	–674.972023	–674.707527
	Sum of electronic and thermal Enthalpies	–674.971079	–674.706583
	Sum of electronic and thermal Free Energies	–675.030299	–674.765405
5a	Zero-point correction	0.202140	0.204567
	Thermal correction to Energy	0.218159	0.220355
	Thermal correction to Enthalpy	0.219103	0.221299
	Thermal correction to Gibbs Free Energy	0.158699	0.161408
	Sum of electronic and zero-point Energies	–675.020443	–674.754326
	Sum of electronic and thermal Energies	–675.004425	–674.738537
	Sum of electronic and thermal Enthalpies	–675.003481	–674.737593
	Sum of electronic and thermal Free Energies	–675.063885	–674.797485



Compound	Calculations	Hartree/particle	
		B3LYP/6-31G(d)	**M062X/6-31G(d)**
21	Zero-point correction	0.242442	0.246389
	Thermal correction to Energy	0.259720	0.263110
	Thermal correction to Enthalpy	0.260665	0.264054
	Thermal correction to Gibbs Free Energy	0.198278	0.203286
	Sum of electronic and zero-point Energies	–694.404812	–694.106618
	Sum of electronic and thermal Energies	–694.387533	–694.089897
	Sum of electronic and thermal Enthalpies	–694.386589	–694.088953
	Sum of electronic and thermal Free Energies	–694.448976	–694.149721
22	Zero-point correction	0.241687	0.245158
	Thermal correction to Energy	0.258562	0.261709
	Thermal correction to Enthalpy	0.259507	0.262653
	Thermal correction to Gibbs Free Energy	0.198016	0.201720
	Sum of electronic and zero-point Energies	–694.401664	–694.099388
	Sum of electronic and thermal Energies	–694.384788	–694.082837
	Sum of electronic and thermal Enthalpies	–694.383844	–694.081893
	Sum of electronic and thermal Free Energies	–694.445334	–694.142826
23	Zero-point correction	0.242647	0.246285
	Thermal correction to Energy	0.260478	0.263700
	Thermal correction to Enthalpy	0.261422	0.264644
	Thermal correction to Gibbs Free Energy	0.196716	0.201275
	Sum of electronic and zero-point Energies	–694.437143	–694.130139
	Sum of electronic and thermal Energies	–694.419312	–694.112724
	Sum of electronic and thermal Enthalpies	–694.418367	–694.111780
	Sum of electronic and thermal Free Energies	–694.483073	–694.175150

4. References for Supporting Information

1. H. Liu, C. S. Tomooka, S. L. Xu, B. R. Yerxa, R. W. Sullivan, Y. Xiong, H. W. Moore, S. Manabe and K. Koga, *Org. Synth.*, 1999, **76**, 189; M. Mohamed, T. P. Goncalves, R. J. Whitby, H. F. Sneddon and D. C. Harrowven, *Chem. Eur. J.*, 2011, **17**, 13698; D. J. Asby, M. G. Radigois, D. C. Wilson, F. Cuda, C. L. L. Chai, A. Chen, A. S. Bienemann, M. E. Light, D. C. Harrowven and A. Tavassoli, *Org. Biomol. Chem.*, 2016, **4**, 9330.
2. E. Packard, D. D. Pascoe, J. Maddaluno, T. P. Goncalves and D. C. Harrowven, *Angew. Chem. Int. Ed.*, 2013, **52**, 13076.
3. L. S. Liebeskind, R. W. Fengl, K. R. Wirtz and T. T. Shawe, *J. Org. Chem.*, 1988, **53**, 2482.
4. H. Liu, C. S. Tomooka and H. W. Moore, *Synth. Commun.*, 1997, **27**, 2177; T. P. Goncalves, M. Mohamed, R. J. Whitby, H. F. Sneddon and D. C. Harrowven, *Angew. Chem. Int. Ed.*, 2015, **54**, 4531.
5. M. W. Reed, D. J. Pollart, S. T. Perri, L. D. Foland and H. W. Moore, *J. Org. Chem.*, 1988, **53**, 2477; F. Liu and L. S. Liebeskind, *J. Org. Chem.*, 1998, **63**, 2835.
6. K. E. Benenato, E. S. Kumarasinghe and M. Cornebise, *WO Pat.* 2017, 49245; K. E. Benenato, E. S. Kumarasinghe and M. Cornebise, *WO Pat.* 2018, 170306.
7. L. S. Liebeskind, R. W. Fengl, K. R. Wirtz and T. T. Shawe, *J. Org. Chem.*, 1988, **53**, 2482; H. Tsukamoto, S. Hanada, Y. Nomura and T. Doi, *J. Org. Chem.*, 2018, **83**, 9430.
8. K. Koehler, G. Offermann and G. Seitz, *Chem. Ber.*, 1986, **119**, 182.
9. N. Fu, A. D. Allen, S. Kobayashi, T. T. Tidwell, S. Vukovic, S. Arumugam, V. V. Popik and M. Mishima, *J. Org. Chem.*, 2007, **72**, 1951.
10. Gaussian 09, Revision C.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, N. J. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski and D. J. Fox, Gaussian Inc., Wallingford CT, 2009.