

Pyruvate Enolate Arylation and Alkylation: OBO Ester Protected Pyruvates as Useful Reagents in Organic Synthesis

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1. General methods

Solvents were dried over 4 Å molecular sieves or activated alumina columns. Dry ethanol used for OBO deprotection experiments was purified following a literature procedure.¹ All reagents were purchased from Sigma-Aldrich, Alfa Aesar, Acros Organics or Fluorochem and used without further purification. All reactions requiring dry equipment were carried out using glassware flame-dried under vacuum. Flash column chromatography was performed using Merck Kieselgel 60 (0.040 – 0.063 mm) silica gel following the established literature method.² Thin layer chromatography was performed on Merck Kieselgel 60 F₂₅₄ 0.25 mm pre-coated aluminum-backed plates. Product spots were visualized under UV light ($\lambda_{\text{max}} = 254$ nm) and/or by staining with vanillin, phosphomolybdic acid or basic potassium permanganate solutions. Nuclear magnetic resonance (NMR) spectra were recorded using a Bruker AVII400 or AVIII400 instruments at 400 MHz for ¹H NMR, 101 MHz for ¹³C NMR and 376 MHz for ¹⁹F NMR. ¹³C NMR spectra were recorded with broadband proton decoupling and ¹⁹F NMR spectra were recorded without broadband proton decoupling. Chemical shifts, δ , are reported relative to residual solvent peaks and quoted in parts per million (ppm) to the nearest 0.01 ppm for ¹H and to the nearest 0.1 ppm for ¹³C and ¹⁹F. Coupling constants, J , are quoted to the nearest 0.1 Hz. Assignments were made on DEPT, COSY and HSQC experiments. High-resolution mass spectra were acquired using electrospray ionisation (ESI) as ionization source and were recorded on a Thermo Exactive orbitrap spectrometer equipped with a Waters Equity LC system. Infrared spectra (IR) were obtained from evaporated films using a Bruker Tensor 27 spectrometer, equipped with a Pike Miracle Attenuated Total Reflectance (ATR) sampling accessory. Absorption is quoted in wavenumbers (cm⁻¹) for the range 3500 – 600 cm⁻¹. Melting points (m.p.) were obtained by using a Lecia VMTG heated-stage microscope with a Testo 720 thermometer and are uncorrected. Compound names were generated by the software ChemDraw Professional 15.1.

2. General Procedures

General procedure A: α -arylation of methyl-OBO ketones (with excess of aryl halide).

To a flame-dried vial capped with a rubber septum were added methyl-OBO ketone (100 mg, 0.58 mmol, 1.0 eq.), the corresponding aryl halide (0.64 mmol, 1.1 eq.) if the aryl halide is a solid and Pd(dtbpf)Cl₂ (19 mg, 29 μ mol, 5 mol%). The rubber septum was replaced by an aluminium cap which was firmly crimped to the vial and then THF (5.1 mL), the aryl halide (0.64 mmol, 1.1 eq.) if the aryl halide is a liquid, and 2 M NaOtBu in THF (0.72 mL, 1.45 mmol, 2.5 eq.) were added *via* syringe. The vial was flushed with argon for 5 mins and then heated at 50 °C for 24 h. The resulting mixture was filtered through a plug of silica using EtOAc as eluent, concentrated *in vacuo* and purified as indicated.

General procedure B: α -arylation of methyl-OBO ketones (with excess of methyl-OBO-ketone).

To a flame-dried vial capped with a rubber septum were added methyl-OBO ketone (100 mg, 0.58 mmol, 1.5 eq.), the corresponding aryl halide (0.39 mmol, 1.0 eq.) if the aryl halide is a solid and Pd(dtbpf)Cl₂ (13 mg, 19 μ mol, 5 mol%). The rubber septum was replaced by an aluminium cap which was firmly crimped to the vial and then THF (5.3 mL), the aryl halide (0.39 mmol, 1.0 eq.) if the aryl halide is a liquid and 2 M NaOtBu in THF (0.49 mL, 0.98

mmol, 2.5 eq.) were added *via* syringe. The vial was flushed with argon for 5 mins and then heated at 70 °C for 24 h. The resulting mixture was filtered through a plug of silica using EtOAc as eluent, concentrated *in vacuo* and purified as indicated.

General procedure C: α,α -diarylation of methyl-OBO ketones.

To a flame-dried vial capped with a rubber septum were added methyl-OBO ketone (100 mg, 0.58 mmol, 1.0 eq.), the corresponding aryl halide (1.74 mmol, 3.0 eq.) if solid and Pd(dtbpf)Cl₂ (19 mg, 29 μ mol, 5 mol%). The rubber septum was replaced by an aluminium cap which was firmly crimped to the vial and then THF (5.1 mL), the aryl halide (1.74 mmol, 3.0 eq.) if liquid and 2 M NaOtBu in THF (0.72 mL, 1.45 mmol, 2.5 eq.) were added *via* syringe. The vial was flushed with argon for 5 mins and then heated at 80 °C for 24 h. The resulting mixture was filtered through a plug of silica using EtOAc as eluent, concentrated *in vacuo* and purified as indicated.

General procedure D: α,α -heterodiarylation of methyl-OBO ketones.

The indicated aryl halide was subjected to the indicated α -arylation general procedure for 8 h, followed by the addition of the second aryl halide (2.5 eq.). The mixture was heated at 80 °C for 16 h and then cooled to RT, filtered through a plug of silica using EtOAc as eluent, concentrated *in vacuo* and purified as indicated.

General procedure E: one-pot α -arylation of methyl-OBO ketones followed by the addition of electrophiles.

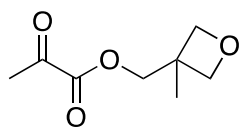
The indicated aryl halide was subjected to the indicated α -arylation general procedure, followed by the addition of the indicated amount of electrophile for the indicated time (the consumption of the arylated methyl-OBO ketone intermediate was closely monitored by TLC). Once the intermediate was completely consumed, the mixture was cooled to RT, filtered through a plug of silica using EtOAc as eluent, concentrated *in vacuo* and purified as indicated.

General procedure F: synthesis of ethyl pyruvates.

To a flame-dried vial were added *p*-toluenesulfonic acid (1.0 eq.), the corresponding OBO-protected pyruvate (1.0 eq.) and dry EtOH (0.1 M to the OBO-protected pyruvate). The vial was sealed, flushed with argon for 5 mins and stirred at the indicated temperature for the indicated time. After cooling down to RT, NaHCO₃ (2.0 eq.) was added and the mixture was concentrated *in vacuo*. The crude product was purified by flash column chromatography as indicated.

3. Characterization data

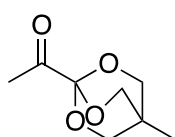
(3-Methyloxetan-3-yl)methyl 2-oxopropanoate (3)



To a flame-dried flask were added pyruvic acid (1.0 mL, 14 mmol, 1.0 eq.), DMF (22 μ L, 0.29 mmol, 2 mol%) and dry DCM (29 mL). Oxalyl chloride (1.3 mL, 16 mmol, 1.1 eq.) was added at RT over 1 h and then the reaction mixture was stirred for another 3 h. After cooling the mixture to -40 $^{\circ}$ C, a solution of 3-methyl-3-oxetanemethanol (1.4 mL, 14 mmol, 1.0 eq.) in pyridine (2.9 mL, 36 mmol, 2.5 eq.) was added over 30 mins and then slowly warmed to RT and stirred for 1 h. The reaction was finally quenched and extracted with 3 M HCl (14 mL, 3 eq.) and the aqueous layer extracted with DCM three times. The organic extracts were combined and concentrated *in vacuo*. The resulting oil was purified by flash column chromatography using pentane/EtOAc (30%) as eluent to afford **3** (1.91 g, 77%) as a colourless oil. Alternatively, when performed at a 288 mmol scale, the crude product can be distilled under reduced pressure (bp = 79 $^{\circ}$ C, 4.0 mbar) to afford pyruvate **3** in 69%.

IR: ν_{\max} (thin film) 2934, 2874, 1730, 1702, 1134, 977, 754 cm^{-1} . **HRMS:** calculated for $\text{C}_8\text{H}_{13}\text{O}_4$, 173.08084 $[\text{M}+\text{H}]^+$, found m/z 173.08086, $\Delta = 0.14$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 4.52 (2H, d, $J = 6.1$ Hz, $\text{CH}_a\text{H}_b\text{OCH}_a\text{H}_b$), 4.43 (2H, d, $J = 6.1$ Hz, $\text{CH}_a\text{H}_b\text{OCH}_a\text{H}_b$), 4.36 (2H, s, $\text{CO}_2\text{CH}_2\text{C}$), 2.48 (3H, s, $\text{CH}_3\text{C}(\text{O})$), 1.37 (3H, s, CCH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 191.1 ($\text{CH}_3\text{C}(\text{O})$), 160.7 ($\text{C}(\text{O})\text{CO}_2$), 79.2 (CH_2OCH_2), 70.4 (OCH_2C), 39.1 (CCH_3), 26.8 ($\text{CH}_3\text{C}(\text{O})$), 20.9 (CCH_3).

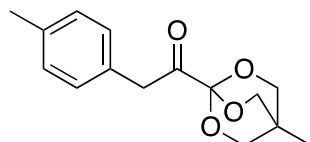
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (4).



To a flame-dried flask were added (3-methyloxetan-3-yl)methyl-2-oxopropanoate (40.0 g, 232 mmol) and dry DCM (500 mL). The mixture was cooled to 0 $^{\circ}$ C and $\text{BF}_3 \cdot \text{OEt}_2$ (8.6 mL, 70 mmol, 0.3 eq.) added over 10 mins and stirred at 0 $^{\circ}$ C for 16 h. The reaction was quenched with Et_3N (9.7 mL, 70 mmol, 0.3 eq.), concentrated *in vacuo* and the resulting crude oil was filtered through a plug of silica using DCM as eluent. The crude solid was then crystallised from methyl *tert*-butyl ether to afford methyl-OBO-ketone **4** as white crystals (25.5 g, 64%).

m.p.: $112 - 113$ $^{\circ}$ C. **IR:** ν_{\max} (thin film) 1734, 979, 638 cm^{-1} . **HRMS:** calculated for $\text{C}_8\text{H}_{13}\text{O}_4$, 173.08084 $[\text{M}+\text{H}]^+$, found m/z 173.08095, $\Delta = 0.65$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 3.76 (6H, s, $3 \times \text{OCH}_2$), 2.00 (3H, s, $\text{CH}_3\text{C}(\text{O})$), 0.63 (3H, s, CH_3C). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 196.0 ($\text{C}(\text{O})$), 102.8 (CO_3), 72.5 (OCH_2), 30.3 (CH_3C), 24.0 ($\text{CH}_3\text{C}(\text{O})$), 13.5 (CH_3C). Analytical data are consistent with those previously reported.³

1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(*p*-tolyl)ethan-1-one (6a).

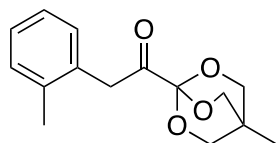


4-Bromotoluene (109 mg, 0.64 mmol, 1.1 eq.) was subjected to general procedure A and purified by flash column chromatography using toluene/MeCN (7%) as eluent, affording OBO-ketone **6a** (130 mg, 85%) as a brown solid.

m.p.: $166 - 168$ $^{\circ}$ C. **IR:** ν_{\max} (thin film) 2881, 1755, 1033, 994 cm^{-1} . **HRMS:** calculated for $\text{C}_{15}\text{H}_{19}\text{O}_4$, 263.12779 $[\text{M}+\text{H}]^+$, found m/z 263.12784, $\Delta = 0.20$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.13 (2H, d, $J = 8.1$ Hz, HC_{Ar}), 7.07 (2H, d, $J = 8.2$ Hz, HC_{Ar}), 4.02 (6H, s, $3 \times \text{OCH}_2$), 3.95 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 2.33 (3H, s, CH_3Ph), 0.85 (3H, s, CCH_3). **^{13}C NMR** (101

MHz, CDCl₃) δ_C : 195.9 (C(O)), 136.4, 130.3 (2 \times C_{Ar}), 129.8, 129.1 (2 \times HC_{Ar}), 103.8 (CO₃), 73.1 (OCH₂), 42.7 (CH₂C(O)), 30.9 (CCH₃), 21.1 (CH₃Ph), 14.2 (CCH₃).

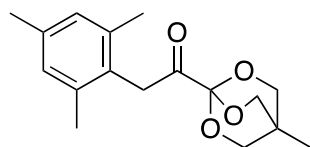
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(*o*-tolyl)ethan-1-one (6b)



2-Bromotoluene (109 mg, 0.64 mmol, 1.1 eq.) was subjected to general procedure A and purified by flash column chromatography using pentane/EtOAc (30%) as eluent, affording OBO-ketone **6b** (122 mg, 80%) as needle-like white crystals.

m.p.: 110 – 112 °C. **IR:** ν_{\max} (thin film) 2925, 2885, 1749, 1462, 1398, 1350, 1278, 1194, 1075, 1049, 1035, 994, 888, 871, 747, 734 cm⁻¹. **HRMS:** calculated for C₁₅H₁₉O₄, 263.1278 [M+H]⁺, found m/z 263.1279, Δ = 0.40 ppm. **¹H NMR** (400 MHz, CDCl₃) δ_H : 7.20 – 7.05 (4H, m, 4 \times HC_{Ar}), 4.04 (6H, s, 3 \times OCH₂), 4.00 (2H, s, CH₂C(O)), 2.19 (3H, s, PhCH₃), 0.87 (3H, s, CCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ_C : 195.5 (C(O)), 137.4, 132.3 (2 \times C_{Ar}), 130.8, 130.2, 127.4, 126.0 (4 \times HC_{Ar}), 103.8 (CO₃), 73.2 (OCH₂), 41.6 (CH₂C(O)), 31.0 (CCH₃), 19.6 (CH₃Ph), 14.3 (CCH₃).

2-Mesityl-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6c).

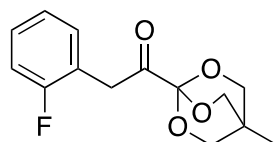


2-Bromomesitylene (98 μ L, 0.64 mmol, 1.1 eq.) was subjected to general procedure A and purified by flash column chromatography using heptane/EtOAc (30%) as eluent, affording OBO-ketone **6c** (167 mg, 99%) as an off-white solid.

Large scale synthesis following general procedure A: To a flame-dried flask capped with a rubber septum were added methyl-OBO ketone (1.00 g, 5.81 mmol, 1.0 eq.), 2-bromomesitylene (0.98 mL, 6.39 mmol, 1.1 eq.) and Pd(dtbpf)Cl₂ (76 mg, 116 μ mol, 2 mol%). THF (51 mL) and 2 M NaOtBu in THF (7.25 mL, 14.5 mmol, 2.5 eq.) were then added *via* syringe. The flask was flushed with argon for 5 mins and then heated at 50 °C for 24 h. The resulting mixture was filtered through a plug of silica using EtOAc as eluent and concentrated *in vacuo*. The crude material was crystallised from EtOH, affording OBO-ketone **6c** (1.45 g, 86%) as an off-white solid.

m.p.: 170 – 174 °C. **IR:** ν_{\max} (thin film) 2971, 2888, 1739, 1623, 1195, 1071, 1049, 974, 946 cm⁻¹. **HRMS:** calculated for C₁₇H₂₃O₄, 291.15909 [M+H]⁺, found m/z 291.15910, Δ = 0.04 ppm. **¹H NMR** (400 MHz, CDCl₃) δ_H : 6.86 (2H, s, 2 \times HC_{Ar}), 4.06 (6H, s, 3 \times OCH₂), 4.03 (2H, s, CH₂C(O)), 2.27 (3H, s, CH₃Ar), 2.16 (6H, s, 2 \times CH₃Ar), 0.88 (3H, s, CCH₃). **¹³C NMR** (101 MHz, CDCl₃) δ_C : 195.5 (C(O)), 137.2, 136.5 (2 \times C_{Ar}), 128.7 (HC_{Ar}), 128.0 (C_{Ar}), 103.9 (CO₃), 73.2 (OCH₂), 37.7 (CH₂C(O)), 30.9 (CH₃C), 21.0 (CH₃Ar), 20.1 (CH₃Ar), 14.3 (CH₃).

2-(2-Fluorophenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6d).

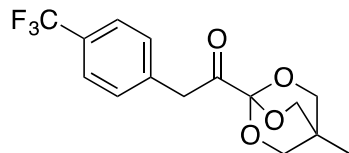


1-Bromo-2-fluorobenzene (42 μ L, 0.39 mmol, 1.0 eq.) was subjected to general procedure B and purified by flash column chromatography using DCM as eluent, affording OBO-ketone **6d** (69 mg, 67%) as a brown solid.

m.p.: 85 – 89 °C. **IR:** ν_{\max} (thin film) 2970, 2889, 1753, 1074, 1045, 1028, 991, 761 cm⁻¹. **HRMS:** calculated for C₁₄H₁₆FO₄, 267.10271 [M+H]⁺, found m/z 267.10275, Δ = 0.15 ppm. **¹H NMR** (400 MHz, CDCl₃) δ_H : 7.28 – 7.20 (1H, m, HC_{Ar}), 7.15 (1H, dd, J = 7.5, 2.0 Hz, HC_{Ar}), 7.10 – 6.99 (2H, m, 2 \times HC_{Ar}), 4.03 (8H, s, CH₂C(O)) + 3 \times OCH₂, 0.86 (3H, s,

CH_3). ^{13}C NMR (101 MHz, CDCl_3) δ_{C} : 194.5 ($\text{C}(\text{O})$), 161.3 (d, $J = 246$ Hz, CF), 132.0 (d, $J = 4.8$ Hz, HC_{Ar}), 129.0 (d, $J = 7.9$ Hz, HC_{Ar}), 124.0 (d, $J = 3.5$ Hz, HC_{Ar}), 120.8 (d, $J = 16.7$ Hz, FCC), 115.3 (d, $J = 21.5$ Hz, FCCH), 103.8 (CO_3), 73.2 (OCH_2), 36.9 ($\text{CH}_2\text{C}(\text{O})$), 31.0 (CH_3C), 14.3 (CH_3). ^{19}F NMR (376 MHz, CDCl_3) δ_{F} : -116.9 – -117.1 (1F, m, CF).

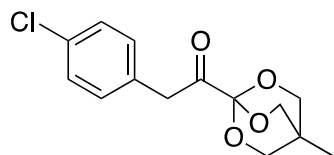
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(4-(trifluoromethyl)-phenyl)-ethan-1-one (6e).



4-Bromobenzotrifluoride (54 μL , 0.39 mmol, 1.0 eq.) was subjected to general procedure B and purified by flash column chromatography using CHCl_3 as eluent, affording OBO-ketone **6e** (111 mg, 91%) as a white solid.

m.p.: 63 – 65 $^{\circ}\text{C}$. **IR:** ν_{max} (thin film) 2967, 2889, 1757, 1325, 1108, 995, 741 cm^{-1} . **HRMS:** calculated for $\text{C}_{15}\text{H}_{16}\text{O}_4\text{F}_3$, 317.09952 $[\text{M}+\text{H}]^+$, found m/z 317.09958, $\Delta = 0.19$ ppm. ^1H NMR (400 MHz, CDCl_3) δ_{H} : 7.55 (2H, d, $J = 8.2$ Hz, $2 \times \text{CF}_3\text{CCH}$), 7.29 (2H, d, $J = 8.2$ Hz, $2 \times \text{CH}_2\text{CCH}$), 4.02 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 4.02 (6H, s, $3 \times \text{OCH}_2$), 0.85 (3H, s, CH_3). ^{13}C NMR (101 MHz, CDCl_3) δ_{C} : 195.0 ($\text{C}(\text{O})$), 137.6 ($\text{CCH}_2\text{C}(\text{O})$), 130.4 (F_3CCCHCH), 129.2 (q, $J = 32.4$ Hz, F_3CC), 125.3 (q, $J = 4.0$ Hz, CF_3CCH), 124.3 (q, $J = 270$ Hz, CF_3), 103.8 (CO_3), 73.2 (OCH_2), 42.9 ($\text{CH}_2\text{C}(\text{O})$), 31.0 (CH_3C), 14.2 (CH_3). ^{19}F NMR (376 MHz, CDCl_3) δ_{F} : -62.45 (3F, s, CF_3).

2-(4-Chlorophenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6f).

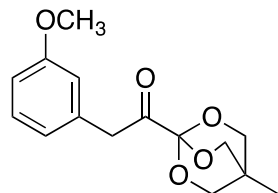


1-Bromo-4-chlorobenzene (122 mg, 0.64 mmol, 1.1 eq.) was subjected to general procedure A and purified by flash column chromatography using toluene/MeCN (7%) as eluent, affording OBO-ketone **6f** (125 mg, 76%) as a white solid.

Alternatively, the crude material could also be crystallized from methyl *tert*-butyl ether to afford the product **6f** (109 mg, 66%).

m.p.: 145 – 149 $^{\circ}\text{C}$. **IR:** ν_{max} (thin film) 2967, 2879, 1726, 1272, 1172, 1092, 1015 cm^{-1} . **HRMS:** calculated for $\text{C}_{14}\text{H}_{16}\text{O}_4\text{Cl}$, 283.07316 $[\text{M}+\text{H}]^+$, found m/z 283.07315, $\Delta = -0.04$ ppm. ^1H NMR (400 MHz, CDCl_3) δ_{H} : 7.27 (2H, d, $J = 8.2$ Hz, HC_{Ar}), 7.11 (2H, d, $J = 8.1$ Hz, HC_{Ar}), 4.01 (6H, s, $3 \times \text{OCH}_2$), 3.94 (2H, $\text{CH}_2\text{C}(\text{O})$), 0.85 (3H, s, CH_3). ^{13}C NMR (101 MHz, CDCl_3) δ_{C} : 195.4 ($\text{C}(\text{O})$), 132.8, 131.9 ($2 \times \text{C}_{\text{Ar}}$), 131.3, 128.5 ($2 \times \text{HC}_{\text{Ar}}$), 103.7 (CO_3), 73.1 (OCH_2), 42.4 ($\text{CH}_2\text{C}(\text{O})$), 30.9 (CCH_3), 14.1 (CH_3).

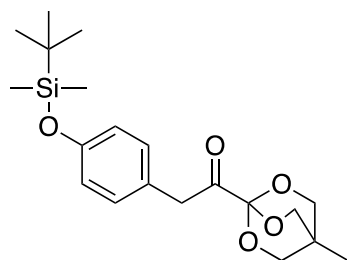
2-(3-Methoxyphenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6g)



1-Bromo-3-methoxybenzene (120 mg, 0.64 mmol, 1.1 eq.) was subjected to general procedure A and purified by flash column chromatography using pentane/EtOAc (30%) as eluent, affording OBO-ketone **6g** (128 mg, 80%) as pale orange flakes.

m.p.: 145 – 149 $^{\circ}\text{C}$. **IR:** ν_{max} (thin film) 2941, 2883, 1752, 1256, 1076, 1050, 1036, 999 cm^{-1} . **HRMS:** calculated for $\text{C}_{15}\text{H}_{18}\text{O}_5\text{Na}$, 301.1046 $[\text{M}+\text{Na}]^+$, found m/z 301.1047, $\Delta = 0.0$ ppm. ^1H NMR (400 MHz, CDCl_3) δ_{H} : 7.21 (1H, t, $J = 7.6$ Hz, HC_{Ar}), 6.81 – 6.71 (3H, m, $3 \times \text{HC}_{\text{Ar}}$), 4.02 (6H, s, $3 \times \text{OCH}_2$), 3.95 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 3.77 (3H, s, OCH_3), 0.87 (3H, s, CCH_3). ^{13}C NMR (101 MHz, CDCl_3) δ_{C} : 195.6 ($\text{C}(\text{O})$), 159.6, 134.9 ($2 \times \text{C}_{\text{Ar}}$), 129.4, 122.4, 115.5, 112.7 ($4 \times \text{HC}_{\text{Ar}}$), 103.8 (CO_3), 73.2 (OCH_2), 55.3 (OCH_3), 43.2 ($\text{CH}_2\text{C}(\text{O})$), 31.0 (CCH_3), 14.3 (CCH_3).

2-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6h)

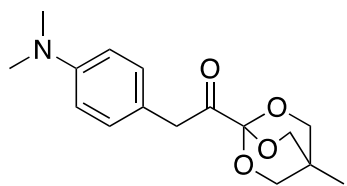


(4-Bromophenoxy)(*tert*-butyl)dimethylsilane (184 mg, 0.64 mmol, 1.1 eq.) was subjected to general procedure A and purified by flash column chromatography using pentane/EtOAc (30%) as eluent, affording OBO-ketone **6h** (132 mg, 60%) as pale orange flakes.

m.p.: 89 – 91 °C. **IR:** ν_{\max} (thin film) 2957, 2931, 2883, 2859, 1754, 1510, 1257, 1076, 1051, 1036, 996, 913, 839, 780 cm^{-1} .

HRMS: calculated for $\text{C}_{20}\text{H}_{30}\text{O}_5\text{NaSi}$, 401.17547 $[\text{M}+\text{Na}]^+$, found m/z 401.17532, $\Delta = -0.37$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.03 (2H, d, $J = 8.2$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 6.76 (2H, d, $J = 8.2$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 4.02 (6H, s, $3 \times \text{OCH}_2$), 3.89 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 0.97 (9H, s, $\text{Si}(\text{CH}_3)_3$), 0.87 (3H, s, CCH_3), 0.18 (6H, s, $\text{Si}(\text{CH}_3)_2$). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 196.1 ($\text{C}(\text{O})$), 154.6 (C_{Ar}), 131.0 (HC_{Ar}), 126.1 (C_{Ar}), 120.0 (HC_{Ar}), 103.9 (CO_3), 73.2 (OCH_2), 42.4 ($\text{CH}_2\text{C}(\text{O})$), 31.1 (CCH_3), 25.8 ($\text{SiC}(\text{CH}_3)_3$), 18.3 ($\text{SiC}(\text{CH}_3)_3$), 14.4 (CCH_3), -4.3 ($\text{Si}(\text{CH}_3)_2$).

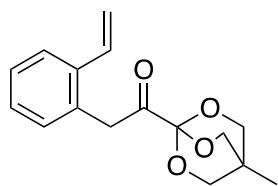
2-(4-(Dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6i).



4-Bromo-*N,N*-dimethylaniline (77 mg, 0.39 mmol, 1.0 eq.) was subjected to general procedure B at 50 °C and purified by flash column chromatography using $\text{CHCl}_3/\text{MeOH}$ (1%) as eluent, affording OBO-ketone **6i** (103 mg, 91%) as an off-white solid.

m.p.: 166 – 169 °C. **IR:** ν_{\max} (thin film) 2959, 2884, 1751, 1524, 1029, 998, 975, 946, 806, 781 cm^{-1} . **HRMS:** calculated for $\text{C}_{16}\text{H}_{22}\text{NO}_4$, 292.15433 $[\text{M}+\text{H}]^+$, found m/z 292.15416, $\Delta = -0.61$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.08 – 7.02 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 6.72 – 6.67 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 4.01 (6H, s, $3 \times \text{OCH}_2$), 3.89 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 2.92 (6H, s, $\text{N}(\text{CH}_3)_2$), 0.85 (3H, s, CCH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 196.4 ($\text{C}(\text{O})$), 149.6 (C_{Ar}), 130.5 (HC_{Ar}), 121.1 (C_{Ar}), 112.8 (HC_{Ar}), 103.8 (CO_3), 73.1 (OCH_2), 42.2 ($\text{CH}_2\text{C}(\text{O})$), 40.7 ($\text{N}(\text{CH}_3)_2$), 30.9 (CCH_3), 14.2 (CCH_3).

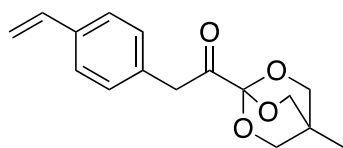
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(2-vinylphenyl)ethan-1-one (6j).



2-Bromostyrene (49 μL , 0.39 mmol, 1.0 eq.) was subjected to general procedure B and purified by flash column chromatography using toluene/MeCN (7%) as eluent, affording OBO-ketone **6j** (89 mg, 84%) as a brown solid.

m.p.: 122 – 123 °C. **IR:** ν_{\max} (thin film) 2938, 2882, 1751, 1074, 1048, 1035, 991, 772, 719 cm^{-1} . **HRMS:** calculated for $\text{C}_{16}\text{H}_{18}\text{O}_4\text{Na}$, 297.10973 $[\text{M}+\text{Na}]^+$, found m/z 297.10965, $\Delta = -0.27$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.52 (1H, dd, $J = 7.5$, 1.9 Hz, HC_{Ar}), 7.29 – 7.18 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 7.09 (1H, dd, $J = 7.3$, 2.0 Hz, HC_{Ar}), 6.75 (1H, dd, $J = 17.3$, 10.9 Hz, CH_2CH), 5.62 (1H, dd, $J = 17.3$, 1.8 Hz, $\text{CH}_a\text{H}_b\text{CH}$), 5.28 (1H, dd, $J = 10.9$, 1.7 Hz, $\text{CH}_a\text{H}_b\text{CH}$), 4.07 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 4.04 (6H, s, $3 \times \text{OCH}_2$), 0.87 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 195.3 ($\text{C}(\text{O})$), 137.7 (C_{Ar}), 134.4 (CH_2CH), 131.2 (HC_{Ar}), 131.2 (C_{Ar}), 127.8, 127.6, 125.9 ($3 \times \text{HC}_{\text{Ar}}$), 116.3 (CH_2CH), 103.8 (CO_3), 73.2 (OCH_2), 41.2 ($\text{CH}_2\text{C}(\text{O})$), 31.0 (CH_3C), 14.3 (CH_3).

1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(4-vinylphenyl)ethan-1-one (6k).

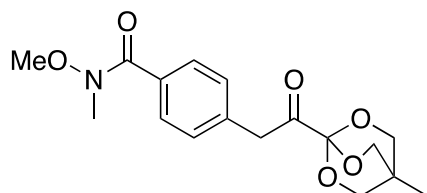


4-Bromostyrene (51 μ L, 0.39 mmol, 1.0 eq.) was subjected to general procedure B and purified by flash column chromatography using toluene/MeCN (7%) as eluent, affording OBO-ketone **6k** (85 mg, 79%) as a brown solid.

Alternatively, 4-bromostyrene (106 mg, 0.58 mmol) was subjected to the same general procedure and the crude material was crystallised from EtOH, affording OBO-ketone **6k** (115 mg, 72%).

m.p.: 135 – 139 °C. **IR:** ν_{\max} (thin film) 2935, 2882, 1751, 1075, 1049, 993, 715 cm^{-1} . **HRMS:** calculated for $\text{C}_{16}\text{H}_{19}\text{O}_4$, 275.12779 $[\text{M}+\text{H}]^+$, found m/z 275.12779, $\Delta = -0.25$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.35 (2H, d, $J = 8.1$ Hz, HC_{Ar}), 7.14 (2H, d, $J = 8.2$ Hz, HC_{Ar}), 6.69 (1H, dd, $J = 17.6, 10.9$ Hz, CH_2CH), 5.72 (1H, d, $J = 17.6$ Hz, $\text{CHCH}_{\text{trans}}\text{H}_{\text{cis}}$), 5.21 (1H, d, $J = 10.9$ Hz, $\text{CHCH}_{\text{trans}}\text{H}_{\text{cis}}$), 4.02 (6H, s, $3 \times \text{OCH}_2$), 3.97 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 0.86 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 195.7 ($\text{C}(\text{O})$), 136.7 (CHCH_2), 136.3, 133.0 ($2 \times \text{C}_{\text{Ar}}$), 130.1, 126.3 ($2 \times \text{HC}_{\text{Ar}}$), 113.7 (CHCH_2), 103.8 (CO_3), 73.2 (OCH_2), 43.0 ($\text{CH}_2\text{C}(\text{O})$), 31.0 (CH_3C), 14.3 (CCH_3).

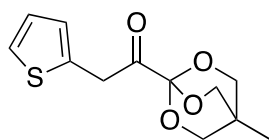
N-Methoxy-N-methyl-4-(2-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-oxoethyl)-benzamide (6l).



4-Bromo-N-methoxy-N-methylbenzamide (94 mg, 0.39 mmol, 1.0 eq.) was subjected to general procedure B and purified by flash column chromatography using Et_2O as eluent, affording OBO-ketone **6l** (100 mg, 77%) as a white solid.

m.p.: 69 – 72 °C. **IR:** ν_{\max} (thin film) 2936, 2884, 1752, 1636, 1076, 1049, 910, 726 cm^{-1} . **HRMS:** calculated for $\text{C}_{17}\text{H}_{22}\text{NO}_6$, 336.14416 $[\text{M}+\text{H}]^+$, found m/z 336.14373, $\Delta = -1.30$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.58 (2H, d, $J = 7.8$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 7.17 (2H, d, $J = 7.8$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 3.97 (6H, s, $3 \times \text{OCH}_2$), 3.96 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 3.51 (3H, s, OCH_3), 3.29 (3H, s, NCH_3), 0.81 (3H, s, CCH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 195.2 ($\text{C}(\text{O})$), 169.6 ($\text{C}(\text{O})\text{N}$), 136.2, 132.5 ($2 \times \text{C}_{\text{Ar}}$), 129.5, 128.3 ($2 \times \text{HC}_{\text{Ar}}$), 103.6 (CO_3), 73.1 (OCH_2), 61.0 (OCH_3), 42.9 ($\text{CH}_2\text{C}(\text{O})$), 33.9 (NCH_3), 30.9 (CCH_3), 14.1 (CCH_3).

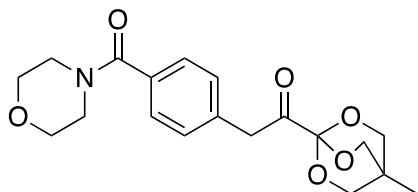
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(thiophen-2-yl)ethan-1-one (6m).



2-Bromothiophene (37 μ L, 0.39 mmol, 1.0 eq.) was subjected to general procedure B and purified by flash column chromatography using DCM as eluent, affording OBO-ketone **6m** (65 mg, 66%) as a light yellow solid.

m.p.: 104 – 107 °C. **IR:** ν_{\max} (thin film) 2966, 2889, 1756, 1044, 1029, 990, 928, 715 cm^{-1} . **HRMS:** calculated for $\text{C}_{12}\text{H}_{14}\text{O}_4\text{SNa}$ 277.05050 $[\text{M}+\text{Na}]^+$, found m/z 277.05051, $\Delta = 0.02$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.21 (1H, dd, $J = 5.1, 1.2$ Hz, SCH), 6.96 (1H, dd, $J = 5.1, 3.5$ Hz, SCHCH), 6.91 – 6.88 (1H, m, SCCH), 4.19 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 4.03 (6H, s, $3 \times \text{OCH}_2$), 0.87 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 194.3 ($\text{C}(\text{O})$), 134.2 (SCCH), 127.3 (SCCH), 126.9 (SCHCH), 125.1 (SCH), 103.8 (CO_3), 73.2 (OCH_2), 37.2 ($\text{CH}_2\text{C}(\text{O})$), 31.0 (CH_3C), 14.3 (CH_3).

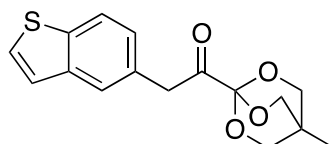
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(4-(morpholine-4-carbonyl)phenyl)ethan-1-one (6n).



(4-Bromophenyl)(morpholino)methanone (105 mg, 0.39 mmol, 1.0 eq.) was subjected to general procedure B and purified by flash column chromatography using EtOAc as eluent, affording OBO-ketone **6n** (113 mg, 81%) as a white solid.

m.p.: 138 – 140 °C. **IR:** ν_{\max} (thin film) 3390, 2962, 2930, 2888, 1748, 1625, 1455, 1027, 991, 972, 938 cm^{-1} . **HRMS:** calculated for $\text{C}_{19}\text{H}_{24}\text{NO}_6$, 362.15981 $[\text{M}+\text{H}]^+$, found m/z 362.15973, $\Delta = -0.23$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.33 (2H, d, $J = 8.2$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 7.21 (2H, d, $J = 8.1$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 4.02 (6H, s, $3 \times \text{OCH}_2$), 3.98 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 3.85 – 3.35 (8H, m, $2 \times \text{OCH}_2\text{CH}_2\text{N}$), 0.86 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 195.2 ($\text{CH}_2\text{C}(\text{O})$), 170.3 ($\text{C}(\text{O})\text{N}$), 135.4, 133.8 ($2 \times \text{C}_{\text{Ar}}$), 130.1, 127.3 ($2 \times \text{HC}_{\text{Ar}}$), 103.7 (CO_3), 73.2 (OCH_2), 66.9 ($2 \times \text{OCH}_2$), 48.3 ($\text{C}_a\text{H}_2\text{NC}_b\text{H}_2$, br.), 42.9 ($\text{CH}_2\text{C}(\text{O})$), 42.6 ($\text{C}_a\text{H}_2\text{NC}_b\text{H}_2$, br.), 31.0 (CH_3C), 14.2 (CH_3).

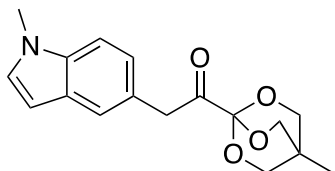
2-(Benzo[b]thiophen-5-yl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6o).



5-Bromo-1-benzothiophene (83 mg, 0.39 mmol, 1.0 eq.) was subjected to general procedure B and purified by flash column chromatography using DCM/MeOH (0.5%) as eluent, affording OBO-ketone **6o** (91 mg, 77%) as a yellow solid.

m.p.: 90 – 92 °C. **IR:** ν_{\max} (thin film) 3484, 2938, 2882, 1746, 1046 cm^{-1} . **HRMS:** calculated for $\text{C}_{16}\text{H}_{17}\text{O}_4^{32}\text{S}$, 305.08421 $[\text{M}+\text{H}]^+$, found m/z 305.08426, $\Delta = 0.17$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.73 (1H, d, $J = 8.3$ Hz, SCH), 7.56 (1H, d, $J = 2.0$ Hz, CCHC), 7.33 (1H, d, $J = 5.4$ Hz, HC_{Ar}), 7.20 (1H, dd, $J = 8.3, 0.6$ Hz, HC_{Ar}), 7.09 (1H, dd, $J = 8.3, 2.0$ Hz, SCHCH), 4.10 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 4.04 (6H, s, $3 \times \text{OCH}_2$), 0.87 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 196.0 ($\text{C}(\text{O})$), 140.0, 138.5, 129.5 ($3 \times \text{C}_{\text{Ar}}$), 126.7 (HC_{Ar}), 126.4 (SCHCH), 124.9 (CH_2CCHC), 123.8 (HC_{Ar}), 122.5 (SCH), 103.9 (CO_3), 73.3 (OCH_2), 43.1 ($\text{CH}_2\text{C}(\text{O})$), 31.1 (CH_3C), 14.3 (CH_3).

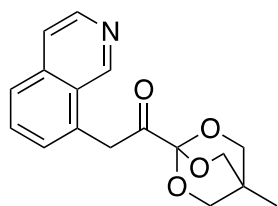
2-(1-Methyl-1H-indol-5-yl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6p).



5-Bromo-1-methylindole (81 mg, 0.39 mmol, 1.0 eq.) was subjected to general procedure B and purified by flash column chromatography using DCM as eluent, affording OBO-ketone **6p** (105 mg, 90%) as a light red solid.

m.p.: 175 – 178 °C. **IR:** ν_{\max} (thin film) 2939, 2881, 1749, 1074, 1047, 1034, 993, 749, 721, 672 cm^{-1} . **HRMS:** calculated for $\text{C}_{17}\text{H}_{20}\text{NO}_4$, 302.13868 $[\text{M}+\text{H}]^+$, found m/z 302.13879, $\Delta = 0.36$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.44 (1H, s, HC_{Ar}), 7.27 (1H, d, $J = 8.4$ Hz, HC_{Ar}), 7.05 (1H, d, $J = 8.4$ Hz, HC_{Ar}), 7.02 (1H, d, $J = 3.2$ Hz, HC_{Ar}), 6.43 (1H, s, $J = 3.4$ Hz, HC_{Ar}), 4.10 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 4.03 (6H, s, $3 \times \text{OCH}_2$), 3.74 (3H, s, NCH_3), 0.85 (3H, s, CCH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 196.6 ($\text{C}(\text{O})$), 135.9 (C_{Ar}), 129.1 (HC_{Ar}), 128.7, 124.0 ($2 \times \text{C}_{\text{Ar}}$), 123.5, 122.0, 109.2 ($3 \times \text{HC}_{\text{Ar}}$), 103.9 (CO_3), 100.7 (HC_{Ar}), 73.1 (OCH_2), 43.3 ($\text{CH}_2\text{C}(\text{O})$), 32.9 (NCH_3), 30.9 (CH_3C), 14.2 (CCH_3).

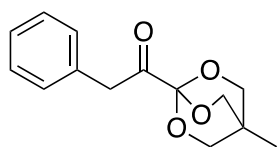
2-(Isoquinolin-8-yl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-ethan-1-one (6q).



8-Bromoisoquinoline (81 mg, 0.39 mmol, 1.0 eq.) was subjected to general procedure B and purified by flash column chromatography using DCM/MeOH (5%) as eluent, affording OBO-ketone **6q** (84 mg, 72%) as a brown solid.

m.p.: 105 – 108 °C. **IR:** ν_{\max} (thin film) 2940, 2883, 1751, 1076, 1048, 1034, 991, 839, 726 cm^{-1} . **HRMS:** calculated for $\text{C}_{17}\text{H}_{18}\text{NO}_4$, 300.12303 $[\text{M}+\text{H}]^+$, found m/z 300.12311, $\Delta = 0.24$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 9.27 (1H, s, NCHC), 8.50 (1H, d, $J = 5.6$ Hz, HC_{Ar}), 7.71 (1H, d, $J = 8.3$ Hz, HC_{Ar}), 7.62 – 7.55 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 7.37 (1H, d, $J = 7.0$ Hz, HC_{Ar}), 4.48 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 4.05 (6H, s, $3 \times \text{OCH}_2$), 0.85 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 195.1 ($\text{C}(\text{O})$), 149.4 (NCHC), 142.9 (HC_{Ar}), 136.3, 131.3 ($2 \times \text{C}_{\text{Ar}}$), 130.0, 130.0 ($2 \times \text{HC}_{\text{Ar}}$), 127.3 (C_{Ar}), 126.5, 120.9 ($2 \times \text{HC}_{\text{Ar}}$), 103.9 (CO_3), 73.3 (OCH_2), 40.2 ($\text{CH}_2\text{C}(\text{O})$), 31.1 (CH_3C), 14.2 (CH_3).

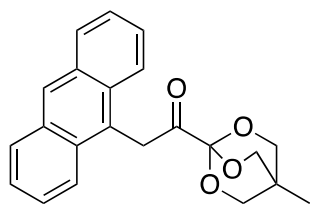
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-phenylethan-1-one (6r).



Chlorobenzene (65 μL , 0.64 mmol, 1.1 eq.) was subjected to general procedure A and purified by flash column chromatography using heptane/EtOAc (30%) as eluent, affording OBO-ketone **6r** (113 mg, 78%) as a white solid.

m.p.: 118 – 120 °C. **IR:** ν_{\max} (thin film) 2890, 1752, 1076, 1046, 1029, 992, 726 cm^{-1} . **HRMS:** calculated for $\text{C}_{14}\text{H}_{17}\text{O}_4$, 249.11214 $[\text{M}+\text{H}]^+$, found m/z 249.11228, $\Delta = 0.58$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.42 – 7.20 (5H, m, $5 \times \text{HC}_{\text{Ar}}$), 4.08 (6H, s, $3 \times \text{OCH}_2$), 4.05 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 0.91 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 195.7 ($\text{C}(\text{O})$), 133.4 (C_{Ar}), 129.9, 128.4, 126.9 ($3 \times \text{HC}_{\text{Ar}}$), 103.7 (CO_3), 73.1 (OCH_2), 43.1 ($\text{CH}_2\text{C}(\text{O})$), 30.9 (CH_3C), 14.2 (CH_3).

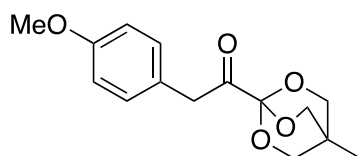
2-(Anthracen-9-yl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6s)



9-Chloroanthracene (82 mg, 0.39 mmol, 1.0 eq.) was subjected to general procedure B and purified by flash column chromatography using toluene/MeCN (7%) as eluent, affording OBO-ketone **6s** (103 mg, 76%) as a yellow solid.

m.p.: 180 – 183 °C. **IR:** ν_{\max} (thin film) 3056, 2938, 2882, 1752, 1058, 1032, 990, 729 cm^{-1} . **HRMS:** calculated for $\text{C}_{22}\text{H}_{21}\text{O}_4$, 349.14344 $[\text{M}+\text{H}]^+$, found m/z 349.14377, $\Delta = 0.95$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 8.44 (1H, s, $\text{C}_{\text{Ar}}\text{HC}_{\text{Ar}}\text{C}_{\text{Ar}}$), 8.08 (2H, d, $J = 8.8$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 8.02 (2H, d, $J = 8.2$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 7.56 – 7.44 (4H, m, $4 \times \text{HC}_{\text{Ar}}$), 5.05 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 4.07 (6H, s, $3 \times \text{OCH}_2$), 0.77 (3H, s, CCH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 195.3 ($\text{C}(\text{O})$), 131.5, 130.9 ($2 \times \text{C}_{\text{Ar}}$), 129.2 (HC_{Ar}), 127.3 ($\text{C}_{\text{Ar}}\text{HC}_{\text{Ar}}\text{C}_{\text{Ar}}$), 126.1 (HC_{Ar}), 125.9 (C_{Ar}), 124.9, 124.3 ($2 \times \text{HC}_{\text{Ar}}$), 104.1 (CO_3), 73.3 (OCH_2), 36.5 ($\text{CH}_2\text{C}(\text{O})$), 30.9 (CCH_3), 14.1 (CCH_3).

2-(4-Methoxyphenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6t)

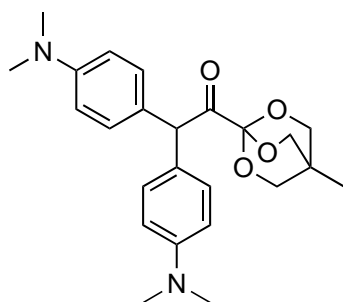


1-Chloromethoxybenzene (55 mg, 0.39 mmol, 1.0 eq.) was subjected to general procedure B and purified by flash column

chromatography using toluene/MeCN (5%) as eluent, affording OBO-ketone **6t** (89 mg, 83%) as a yellow solid.

m.p.: 154 – 156 °C. **IR:** ν_{\max} (thin film) 2969, 2885, 1754, 1515, 1247, 1077, 1047, 1033, 999 cm^{-1} . **HRMS:** calculated for $\text{C}_{15}\text{H}_{18}\text{O}_5\text{Na}$, 301.1046 $[\text{M}+\text{Na}]^+$, found m/z 301.1048, $\Delta = 0.50$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.09 (2H, d, $J = 8.7$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 6.84 (2H, d, $J = 8.7$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 4.02 (6H, s, $3 \times \text{OCH}_2$), 3.91 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 3.78 (3H, s, OCH_3), 0.87 (3H, s, CCH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 196.1 ($\text{C}(\text{O})$), 158.6 (C_{Ar}), 131.0 (HC_{Ar}), 125.4 (C_{Ar}), 114.0 (HC_{Ar}), 103.8 (CO_3), 73.2 (OCH_2), 55.3 (OCH_3), 42.4 ($\text{CH}_2\text{C}(\text{O})$), 31.0 (CCH_3), 14.4 (CCH_3).

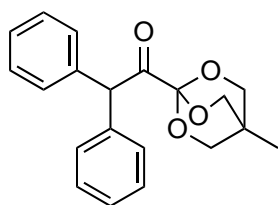
2,2-Bis(4-(dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]-octan-1-yl)-ethan-1-one (7a).



4-Bromo-*N,N*-dimethylaniline (349 mg, 1.74 mmol, 3.0 eq.) was subjected to general procedure C and purified by flash column chromatography using pentane/EtOAc (30% to 45%) as eluent, affording OBO-ketone **7a** (193 mg, 81%) as a white solid.

m.p.: 202 – 205 °C. **IR:** ν_{\max} (thin film) 2980, 2881, 2784, 1745, 1612, 1560, 1071, 1037, 997, 790 cm^{-1} . **HRMS:** calculated for $\text{C}_{24}\text{H}_{31}\text{N}_2\text{O}_4$, 411.22783 $[\text{M}+\text{H}]^+$, found m/z 411.22656, $\Delta = -3.09$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.14 (4H, d, $J = 8.7$ Hz, $4 \times \text{HC}_{\text{Ar}}$), 6.67 (4H, d, $J = 8.7$ Hz, $4 \times \text{HC}_{\text{Ar}}$), 5.61 (1H, s, ArCHAr), 3.98 (6H, s, $3 \times \text{OCH}_2$), 2.91 (12H, s, $2 \times \text{N}(\text{CH}_3)_2$), 0.81 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 197.4 ($\text{C}(\text{O})$), 149.4 (C_{Ar}), 129.6 (HC_{Ar}), 127.3 (C_{Ar}), 112.6 (HC_{Ar}), 104.2 (CO_3), 73.1 (OCH_2), 54.8 (ArCHAr), 40.7 ($\text{N}(\text{CH}_3)_2$), 31.0 (CH_3C), 14.3 (CH_3).

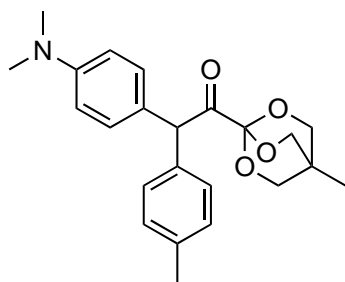
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2,2-diphenylethan-1-one (7b).



Chlorobenzene (176 μL , 1.74 mmol, 3.0 eq.) was subjected to general procedure C and purified by flash column chromatography using pentane/EtOAc (30%) as eluent, affording OBO-ketone **7b** (137 mg, 73%) as a white solid.

m.p.: 112 – 113 °C. **IR:** ν_{\max} (thin film) 2884, 1745, 996, 906, 727, 697 cm^{-1} . **HRMS:** calculated for $\text{C}_{20}\text{H}_{21}\text{O}_4$, 325.14344 $[\text{M}+\text{H}]^+$, found m/z 325.14334, $\Delta = -0.29$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.33 – 7.20 (10H, m, $10 \times \text{HC}_{\text{Ar}}$), 5.81 (1H, s, PhCHPh), 3.98 (6H, s, $3 \times \text{OCH}_2$), 0.81 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 196.5 ($\text{C}(\text{O})$), 138.6 (C_{Ar}), 129.1, 128.5, 127.0 ($3 \times \text{HC}_{\text{Ar}}$), 104.2 (CO_3), 73.2 (OCH_2), 56.7 (PhCHPh), 31.1 (CH_3C), 14.2 (CH_3).

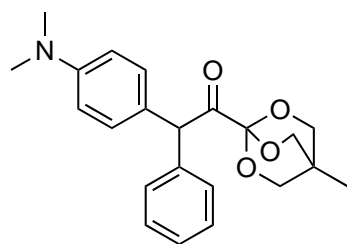
2-(4-(Dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(*p*-tolyl)ethan-1-one (7c).



4-Methyl-bromobenzene (109 mg, 0.64 mmol, 1.1 eq.) was subjected to general procedure A, followed by the addition of 4-bromo-*N,N*-dimethylaniline (290 mg, 1.45 mmol, 2.5 eq.) according to general procedure D. The resulting solid was purified by flash column chromatography using pentane/EtOAc (30%) as eluent, affording OBO-ketone **7c** (149 mg, 67%) as a white solid.

m.p.: 184 – 187 °C. **IR:** ν_{\max} (thin film) 2980, 2971, 2885, 1740, 1614, 1521, 1068, 1049, 1035, 1005, 776, 714 cm^{-1} . **HRMS:** calculated for $\text{C}_{23}\text{H}_{28}\text{NO}_4$, 382.20128 $[\text{M}+\text{H}]^+$, found m/z 382.20091, $\Delta = -0.98$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.16 – 7.06 (6H, m, $6 \times \text{H}_{\text{CAr}}$), 6.69 – 6.64 (2H, m, $2 \times \text{H}_{\text{CAr}}$), 5.65 (1H, s, Ar^1CHAr^2), 3.98 (6H, s, $3 \times \text{OCH}_2$), 2.91 (6H, s, $\text{N}(\text{CH}_3)_2$), 2.30 (3H, s, PhCH_3), 0.82 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 197.1 ($\text{C}(\text{O})$), 149.6, 136.6, 136.3 ($3 \times \text{C}_{\text{Ar}}$), 129.7, 129.1, 128.8 ($3 \times \text{H}_{\text{CAr}}$), 126.5 (C_{Ar}), 112.6 (H_{CAr}), 104.3 (CO_3), 73.2 (OCH_2), 55.4 (Ar^1CHAr^2), 40.7 ($\text{N}(\text{CH}_3)_2$), 31.1 (CCH_3), 21.1 (PhCH_3), 14.4 (CCH_3).

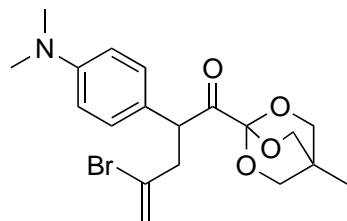
2-(4-(Dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-phenylethan-1-one (7d).



4-Bromo-*N,N*-dimethylaniline (116 mg, 0.58 mmol, 1.0 eq.) was subjected to general procedure B at 50 °C, followed by the addition of chlorobenzene (147 μL , 1.45 mmol, 2.5 eq.) according to general procedure D. The resulting solid was purified by flash column chromatography using pentane/EtOAc (30%) as eluent, affording OBO-ketone **7d** (151 mg, 71%) as a white solid.

m.p.: 136 – 138 °C. **IR:** ν_{\max} (thin film) 2961, 2881, 1746, 1611, 1518, 1070, 1035, 1002, 725, 696 cm^{-1} . **HRMS:** calculated for $\text{C}_{22}\text{H}_{26}\text{NO}_4$, 368.18563 $[\text{M}+\text{H}]^+$, found m/z 368.18564, $\Delta = 0.01$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.31 – 7.17 (5H, m, $5 \times \text{H}_{\text{CAr}}$), 7.16 – 7.11 (2H, m, $2 \times \text{H}_{\text{CAr}}$), 6.69 – 6.64 (2H, m, $2 \times \text{H}_{\text{CAr}}$), 5.69 (1H, s, Ar^1CHAr^2), 3.98 (6H, s, $3 \times \text{OCH}_2$), 2.92 (6H, s, $\text{N}(\text{CH}_3)_2$), 0.82 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 197.0 ($\text{C}(\text{O})$), 149.6, 139.6 ($2 \times \text{C}_{\text{Ar}}$), 129.8, 129.0, 128.3, 126.7 ($4 \times \text{H}_{\text{CAr}}$), 126.1 (C_{Ar}), 112.6 (H_{CAr}), 104.2 (CO_3), 73.2 (OCH_2), 55.8 (Ar^1CHAr^2), 40.6 ($\text{N}(\text{CH}_3)_2$), 31.1 (CCH_3), 14.3 (CCH_3).

4-Bromo-2-(4-(dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo-[2.2.2]octan-1-yl)pent-4-en-1-one (8a).

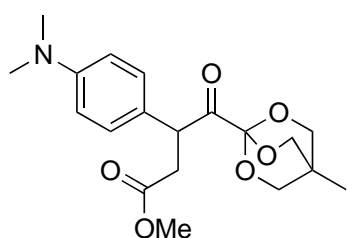


as a light red solid.

4-Bromo-*N,N*-dimethylaniline (116 mg, 0.58 mmol, 1.0 eq.) was subjected to general procedure B at 50 °C, followed by the addition of 2,3-dibromopropene (90 μL , 0.87 mmol, 1.5 eq.), reacted at 50 °C for 3 h following general procedure E and was purified by flash column chromatography using toluene/MeCN (2% to 5%) as eluent, affording OBO-ketone **8a** (165 mg, 69%)

m.p.: 89 – 92 °C. **IR:** ν_{\max} (thin film) 2936, 2882, 1745, 1612, 1520, 1349, 1325, 1125, 1066, 1031, 987, 947 cm^{-1} . **HRMS:** calculated for $\text{C}_{19}\text{H}_{25}\text{NO}_4\text{Br}$, 410.09615 $[\text{M}+\text{H}]^+$, found m/z 410.09586, $\Delta = -0.71$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.11 – 7.06 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 6.66 – 6.60 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 5.46 – 5.43 (1H, m, $\text{CH}_a\text{CH}_b\text{CBr}$), 5.29 (1H, d, $J = 2.0$ Hz, $\text{CH}_a\text{H}_b\text{CBr}$), 4.57 (1H, t, $J = 7.3$ Hz, CHCH_2), 3.93 (6H, s, $3 \times \text{OCH}_2$), 3.09 (1H, ddd, $J = 14.8, 7.0, 1.0$ Hz, $\text{CHCH}_a\text{H}_b\text{CBr}$), 2.91 (6H, s, $\text{N}(\text{CH}_3)_2$), 2.76 (1H, ddd, $J = 14.8, 7.7, 0.8$ Hz, $\text{CHCH}_a\text{H}_b\text{CBr}$), 0.80 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 197.2 ($\text{C}(\text{O})$), 149.7 (C_{Ar}), 131.0 (CBr), 129.5 (HC_{Ar}), 124.1 (C_{Ar}), 119.1 (CH_2CBr), 112.5 (HC_{Ar}), 104.0 (CO_3), 73.1 (OCH_2), 49.5 (CHCH_2), 44.8 (CHCH_2), 40.6 ($\text{N}(\text{CH}_3)_2$), 31.0 (CCH_3), 14.3 (CCH_3).

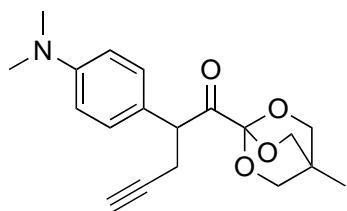
Methyl 3-(4-(dimethylamino)phenyl)-4-(4-methyl-2,6,7-trioxabicyclo-[2.2.2]-octan-1-yl)-4-oxobutanoate (8b).



4-Bromo-*N,N*-dimethylaniline (77 mg, 0.39 mmol, 1.0 eq.) was subjected to general procedure B at 50 °C, followed by the addition of methyl bromoacetate (37 μL , 0.39 mmol, 1.0 eq.), reacted at 50 °C for 3 h following general procedure E and was purified by flash column chromatography using pentane/EtOAc (50%) as eluent, affording OBO-ketone **8b** (104 mg, 74%) as a brown solid.

m.p.: 110 – 112 °C. **IR:** ν_{\max} (thin film) 2950, 2882, 1734, 1612, 1520, 1033, 1002 cm^{-1} . **HRMS:** calculated for $\text{C}_{19}\text{H}_{26}\text{NO}_6$, 364.17546 $[\text{M}+\text{H}]^+$, found m/z 364.17502, $\Delta = -1.22$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.10 – 7.05 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 6.65 – 6.60 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 4.66 (1H, dd, $J = 8.9, 6.4$ Hz, CHCH_2), 3.91 (6H, s, $3 \times \text{OCH}_2$), 3.59 (3H, s, OCH_3), 3.09 (1H, dd, $J = 16.7, 8.9$ Hz, $\text{CH}_a\text{H}_b\text{CO}_2\text{Me}$), 2.91 (6H, s, $\text{N}(\text{CH}_3)_2$), 2.62 (1H, dd, $J = 16.7, 6.4$ Hz, $\text{CH}_a\text{H}_b\text{CO}_2\text{Me}$), 0.79 (3H, s, CCH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 197.5 ($\text{C}(\text{O})$), 172.2 (CO_2), 149.8 (C_{Ar}), 129.3 (HC_{Ar}), 124.1 (C_{Ar}), 112.6 (HC_{Ar}), 104.1 (CO_3), 73.1 (OCH_2), 51.8 (OCH_3), 47.2 (CHCH_2), 40.6 ($\text{N}(\text{CH}_3)_2$), 37.9 (CHCH_2), 30.9 (CCH_3), 14.3 (CCH_3).

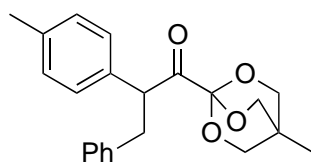
2-(4-(Dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)pent-4-yn-1-one (8c).



4-Bromo-*N,N*-dimethylaniline (116 mg, 0.58 mmol, 1.0 eq.) was subjected to general procedure B at 50 °C, followed by the addition of propargyl bromide 80% in toluene (63 μL , 0.58 mmol, 1.0 eq.), reacted at 50 °C for 3 h following general procedure E and was purified by flash column chromatography using toluene/MeCN (5% to 10%) as eluent, affording OBO-ketone **8c** (146 mg, 76%) as a light red solid.

m.p.: 111 – 113 °C. **IR:** ν_{\max} (thin film) 3282, 2881, 2810, 1729, 1611, 1523, 1072, 1029, 1004, 984, 794, 671, 647 cm^{-1} . **HRMS:** calculated for $\text{C}_{19}\text{H}_{24}\text{NO}_4$, 330.16998 $[\text{M}+\text{H}]^+$, found m/z 330.16989, $\Delta = -0.28$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.13 – 7.08 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 6.67 – 6.62 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 4.38 (1H, dd, $J = 8.2, 7.1$ Hz, CHCH_2), 3.92 (6H, s, $3 \times \text{OCH}_2$), 2.92 (6H, s, $\text{N}(\text{CH}_3)_2$), 2.79 (1H, ddd, $J = 16.8, 7.0, 2.6$ Hz, CHCH_aH_b), 2.57 (1H, ddd, $J = 16.8, 8.3, 2.7$ Hz, CHCH_aH_b), 1.89 (1H, t, $J = 2.6$ Hz, CH_2CCH), 0.80 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 197.0 ($\text{C}(\text{O})$), 149.8 (C_{Ar}), 129.2 (HC_{Ar}), 124.2 (C_{Ar}), 112.5 (HC_{Ar}), 104.0 (CO_3), 82.1 (CHC), 73.1 (OCH_2), 69.5 (CHCCH_2), 50.3 (CHCH_2), 40.5 ($\text{N}(\text{CH}_3)_2$), 31.0 (CCH_3), 23.0 (CHCH_2), 14.3 (CH_3).

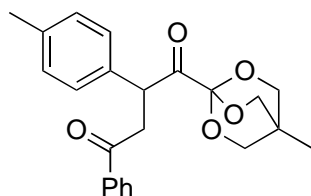
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-3-phenyl-2-(*p*-tolyl)-propan-1-one (8d).



4-Methyl-bromobenzene (109 mg, 0.64 mmol, 1.1 eq.) was subjected to general procedure A, followed by the addition of benzyl bromide (76 μ L, 0.64 mmol, 1.1 eq.), reacted at 50 °C for 3 h following general procedure E and was purified by flash column chromatography using pentane/EtOAc (20%) as eluent, affording OBO-ketone **8d** (136 mg, 66%) as an off-white solid.

m.p.: 136 – 139 °C. **IR:** ν_{\max} (thin film) 2933, 2881, 1742, 1074, 1053, 1031, 1000, 986, 748, 698 cm^{-1} . **HRMS:** calculated for $\text{C}_{22}\text{H}_{25}\text{O}_4$, 353.17474 $[\text{M}+\text{H}]^+$, found m/z 353.17468, $\Delta = -0.15$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.21 – 7.00 (9H, m, $9 \times \text{HC}_{\text{Ar}}$), 4.51 (1H, dd, $J = 8.7, 6.2$ Hz, $\text{CHC}(\text{O})$), 3.90 (6H, s, $3 \times \text{OCH}_2$), 3.34 (1H, dd, $J = 13.8, 6.5$ Hz, CHCH_aH_b), 2.98 (1H, dd, $J = 13.8, 8.6$ Hz, CHCH_aH_b), 2.29 (3H, s, CH_3Ph), 0.79 (3H, s, CCH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 198.0 ($\text{C}(\text{O})$), 139.4, 136.5, 134.6 ($3 \times \text{C}_{\text{Ar}}$), 129.2, 129.1, 128.7, 128.1, 126.0 ($5 \times \text{HC}_{\text{Ar}}$), 104.0 (CO_3), 73.0 (OCH_2), 53.5 (CHCH_2), 39.7 (CHCH_2), 30.9 (CCH_3), 21.2 (CH_3Ph), 14.3 (CCH_3).

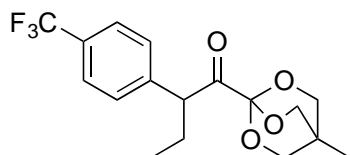
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-4-phenyl-2-(*p*-tolyl)-butane-1,4-dione (8e).



4-Methyl-bromobenzene (109 mg, 0.64 mmol, 1.1 eq.) was subjected to general procedure A at 50 °C, followed by the addition of bromoacetophenone (231 mg, 1.16 mmol, 2.0 eq.), reacted at 80 °C for 8 h following general procedure E and was purified by flash column chromatography using pentane/EtOAc (30%) as eluent, affording OBO-ketone **8e** (165 mg, 75%) as a brown solid.

m.p.: 116 – 118 °C. **IR:** ν_{\max} (thin film) 2936, 2881, 1741, 1686, 1069, 1034, 996, 754, 691 cm^{-1} . **HRMS:** calculated for $\text{C}_{23}\text{H}_{25}\text{O}_5$, 381.16965 $[\text{M}+\text{H}]^+$, found m/z 381.16946, $\Delta = -0.49$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.96 – 7.91 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 7.55 – 7.49 (1H, m, HC_{Ar}), 7.44 – 7.37 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 7.17 (2H, d, $J = 8.1$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 7.10 (2H, d, $J = 8.2$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 4.96 (1H, dd, $J = 9.2, 5.0$ Hz, CHCH_2), 3.95 (6H, s, $3 \times \text{OCH}_2$), 3.87 (1H, dd, $J = 18.1, 9.2$ Hz, CHCH_aH_b), 3.31 (1H, dd, $J = 18.1, 5.0$ Hz, CHCH_aH_b), 2.31 (3H, s, CH_3Ph), 0.80 (3H, s, CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 197.7 ($\text{C}_a(\text{O})$), 197.2 ($\text{C}_b\text{C}(\text{O})$), 136.8, 136.4, 134.3 ($3 \times \text{C}_{\text{Ar}}$), 133.1, 129.3, 128.5, 128.5, 128.2 ($5 \times \text{HC}_{\text{Ar}}$), 104.1 (CO_3), 73.0 (OCH_2), 46.8 (CHCH_2), 43.2 (CHCH_2), 30.9 (CCH_3), 21.1 (CH_3Ph), 14.3 (CCH_3).

1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(4-(trifluoromethyl)-phenyl)butan-1-one (8f).

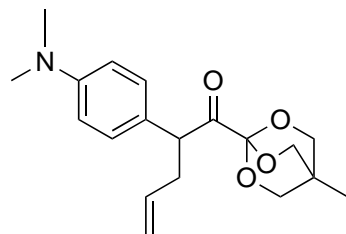


4-Bromobenzotrifluoride (81 μ L, 0.58 mmol, 1.0 eq.) was subjected to general procedure B at 70 °C, followed by the addition of ethyl iodide (93 μ L, 1.16 mmol, 2.0 eq.), reacted at 70 °C for 3 h following general procedure E and was purified by flash column chromatography using toluene/MeCN (3%) as eluent, affording OBO-ketone **8f** (153 mg, 77%) as a white solid.

m.p.: 85 – 86 °C. **IR:** ν_{\max} (thin film) 2968, 2882, 1746, 1323, 1163, 1067, 1048, 1034, 993 cm^{-1} . **HRMS:** calculated for $\text{C}_{17}\text{H}_{20}\text{F}_3\text{O}_4$, 345.13082 $[\text{M}+\text{H}]^+$, found m/z 345.13086, $\Delta = 0.11$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.52 (2H, d, $J = 8.3$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 7.37 (2H, d, J

= 8.3 Hz, 2 × HC_{Ar}), 4.22 (1H, t, J = 7.5 Hz, $CHC(O)$), 3.93 (6H, s, 3 × OCH_2), 2.12 – 1.98 (1H, m, $CH_aH_bCH_3$), 1.79 – 1.66 (1H, m, $CH_aH_bCH_3$), 0.81 (3H, s, CCH_3), 0.81 (3H, t, J = 7.3 Hz, CH_2CH_3). ^{13}C NMR (126 MHz, $CDCl_3$) δ_C : 198.0 ($C(O)$), 142.6 ($CHC(O)$), 129.1 (q, J = 31.7 Hz, F_3CC), 129.0 ($HC_{Ar}C_{Ar}CH$), 125.3 (q, J = 3.8 Hz, F_3CCCH), 124.3 (q, J = 271.9 Hz, CF_3), 104.0 (CO_3), 73.1 (OCH_2), 53.6 ($CHC(O)$), 31.1 (CCH_3), 27.2 (CH_2CH_3), 14.3 (CCH_3), 12.1 (CH_2CH_3). ^{19}F NMR (377 MHz, $CDCl_3$) δ_F : –62.6 (3F, s, CF_3).

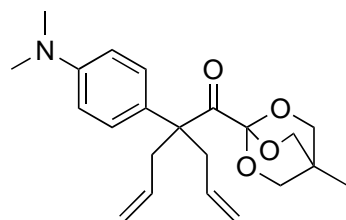
2-(4-(Dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)pent-4-en-1-one (8g).



4-Bromo-*N,N*-dimethylaniline (116 mg, 0.58 mmol, 1.0 eq.) was subjected to general procedure B at 50 °C, followed by the addition of allyl bromide (50 μ L, 0.58 mmol, 1.0 eq.), reacted at 50 °C for 3 h following general procedure E and was purified by flash column chromatography using toluene/MeCN (2% to 5%) as eluent, affording OBO-ketone **8g** (158 mg, 82%) as an off-white solid.

m.p.: 86 – 88 °C. **IR:** ν_{max} (thin film) 2935, 2880, 1740, 1612, 1519, 1347, 1075, 1051, 1033, 990 cm^{-1} . **HRMS:** calculated for $C_{19}H_{26}NO_4$, 332.18563 $[M+H]^+$, found m/z 332.18539, Δ = –0.72 ppm. 1H NMR (400 MHz, $CDCl_3$) δ_H : 7.14 – 7.08 (2H, m, 2 × HC_{Ar}), 6.68 – 6.62 (2H, m, 2 × HC_{Ar}), 5.70 – 5.58 (1H, m, CH_2CHCH_2), 5.02 (1H, dd, J = 17.1, 1.8 Hz, CH_aH_bCH), 4.93 (1H, dd, J = 10.2, 1.8 Hz, CH_aH_bCH), 4.23 (1H, t, J = 7.6 Hz, $CHC(O)$), 3.93 (6H, s, 3 × OCH_2), 2.91 (6H, s, $N(CH_3)_2$), 2.78 – 2.68 (1H, m, $CH_aH_bCHC(O)$), 2.49 – 2.38 (1H, m, $CH_aH_bCHC(O)$), 0.80 (3H, s, CCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ_C : 198.1 ($C(O)$), 149.6 (C_{Ar}), 136.0 (CH_2CHCH_2), 129.3 (HC_{Ar}), 125.4 (C_{Ar}), 116.5 ($CH_2CHCH_2C(O)$), 112.6 (HC_{Ar}), 104.0 (CO_3), 73.0 (OCH_2), 50.8 ($CHC(O)$), 40.6 ($N(CH_3)_2$), 37.9 ($C(O)CH$), 30.9 (CCH_3), 14.3 (CCH_3).

2-Allyl-2-(4-(dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo-[2.2.2]octan-1-yl)pent-4-en-1-one (8h).

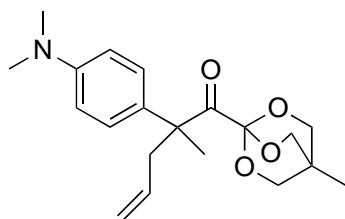


4-Bromo-*N,N*-dimethylaniline (116 mg, 0.58 mmol, 1.0 eq.) was subjected to general procedure B at 50 °C, followed by the addition of allyl bromide (151 μ L, 1.74 mmol, 3.0 eq.) and 2 M NaOtBu in THF (0.58 mL, 2.0 eq.). The mixture was reacted at 80 °C for 3 h following general procedure E and was purified by flash column chromatography using toluene/MeCN (7%) as

eluent, affording OBO-ketone **8h** (183 mg, 85%) as a white solid.

m.p.: 140 – 142 °C. **IR:** ν_{max} (thin film) 2964, 2931, 2881, 1720, 1615, 1521, 1258, 1027, 1001, 654 cm^{-1} . **HRMS:** calculated for $C_{22}H_{30}NO_4$, 372.21693 $[M+H]^+$, found m/z 372.21698, Δ = 0.12 ppm. 1H NMR (400 MHz, $CDCl_3$) δ_H : 7.04 – 6.99 (2H, m, 2 × HC_{Ar}), 6.68 – 6.62 (2H, m, 2 × HC_{Ar}), 5.54 – 5.40 (2H, m, 2 × CH_2CH), 5.05 – 4.96 (4H, m, 2 × CH_2CHCH_2C), 3.78 (6H, s, 3 × OCH_2), 3.01 (2H, dd, J = 14.0, 7.2 Hz, 2 × CCH_aH_b), 2.93 (6H, s, $N(CH_3)_2$), 2.66 (2H, dd, J = 14.0, 7.2 Hz, 2 × CCH_aH_b), 0.72 (3H, s, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ_C : 199.4 ($C(O)$), 149.0 (C_{Ar}), 134.4 ($CHCH_2$), 128.0 (HC_{Ar}), 127.9 (C_{Ar}), 118.1 (CH_2CHCH_2C), 112.2 (HC_{Ar}), 104.9 (CO_3), 72.7 (OCH_2), 56.2 ($CC(O)$), 40.7 ($N(CH_3)_2$), 37.8 (CCH_2), 30.7 (CCH_3), 14.4 (CCH_3).

2-(4-(Dimethylamino)phenyl)-2-methyl-1-(4-methyl-2,6,7-trioxabicyclo-[2.2.2]octan-1-yl)pent-4-en-1-one (8i).

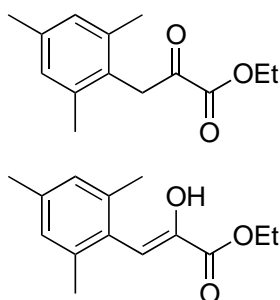


4-Bromo-*N,N*-dimethylaniline (116 mg, 0.58 mmol, 1.0 eq.) was subjected to general procedure B at 50 °C, followed by the addition of methyl iodide (36 μ L, 0.58 mmol, 1.0 eq.) and was reacted at 50 °C for 3 h following general procedure E. Allyl bromide (126 μ L, 1.45 mmol, 2.5 eq.) and 2 M NaOtBu in THF (0.58 mL, 1.16 mmol, 2.0 eq.) were then added and the mixture

was reacted at 80 °C for 3 h. The crude material was purified by flash column chromatography using pentane/EtOAc (20% to 30%) as eluent, affording OBO-ketone **8i** (96 mg, 48%) as a white solid.

m.p.: 134 – 137 °C. **IR:** ν_{max} (thin film) 2928, 2876, 1721, 1639, 1521, 1030, 998, 918, 814, 737 cm^{-1} . **HRMS:** calculated for $\text{C}_{20}\text{H}_{28}\text{NO}_4$, 346.20128 $[\text{M}+\text{H}]^+$, found m/z 346.20081, $\Delta = -1.38$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 7.10 – 7.05 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 6.68 – 6.63 (2H, m, $2 \times \text{HC}_{\text{Ar}}$), 5.57 – 5.44 (1H, m, $\text{CH}_2\text{CHCH}_2\text{CH}$), 5.06 – 4.92 (2H, m, $\text{CH}_2\text{CHCH}_2\text{CH}$), 3.82 (6H, s, $3 \times \text{OCH}_2$), 2.92 (6H, s, $\text{N}(\text{CH}_3)_2$), 2.83 (1H, dd, $J = 13.8, 7.3$ Hz, CCH_aH_b), 2.57 (1H, dd, $J = 13.8, 7.2$ Hz, CCH_aH_b), 1.58 (3H, s, $\text{CH}_3\text{CC}(\text{O})$), 0.75 (3H, s, CCH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 199.3 ($\text{C}(\text{O})$), 149.0 (C_{Ar}), 135.1 ($\text{CH}_2\text{CHCH}_2\text{CH}$), 129.5 (C_{Ar}), 127.5 (HC_{Ar}), 117.7 ($\text{CH}_2\text{CHCH}_2\text{CH}$), 112.3 (HC_{Ar}), 104.7 (CO_3), 72.7 (OCH_2), 52.7 ($\text{CC}(\text{O})$), 44.4 ($\text{CH}_2\text{CC}(\text{O})$), 40.7 ($\text{N}(\text{CH}_3)_2$), 30.8 (CCH_3), 20.8 ($\text{C}(\text{O})\text{CCH}_3$), 14.4 (CCH_3).

Ethyl 3-mesityl-2-oxopropanoate (9a).



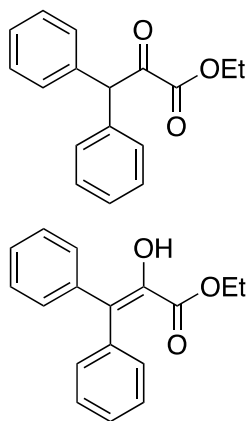
OBO-ketone **6c** (87 mg, 0.30 mmol, 1.0 eq.) was subjected to general procedure F heated for 3 h at 90 °C and purified by flash column chromatography using pentane/EtOAc (5%) as eluent, affording pyruvate **9a** (61 mg, 87%) as a colourless oil. The product exists as a mixture of the ketone and enol isomers (87:13). Alternatively, to a flame-dried vial capped with a rubber septum were added methyl-OBO ketone (103 mg, 0.60 mmol, 1.0 eq.) and Pd(dtbpf) Cl_2 (20 mg, 30 μ mol, 5 mol%). The rubber septum was replaced by an aluminium cap and then THF (5.3 mL), 2-

bromomesitylene (101 μ L, 0.66 mmol, 1.1 eq.), and 2 M NaOtBu in THF (0.75 mL, 1.50 mmol, 2.5 eq.) were added *via* syringe. The vial was flushed with argon for 5 mins and then heated at 50 °C for 24 h. The cap was removed and the solvent evaporated *in vacuo*. EtOH (6.0 mL) and *p*-toluenesulfonic acid (310 mg, 1.80 mmol, 3.0 eq.) were added to the same vial, which was capped again and heated at 90 °C for 3 h. After cooling down to RT, NaHCO_3 (101 mg, 1.20 mmol, 2.0 eq.) was added and the mixture was concentrated *in vacuo*. The crude product was purified by flash column chromatography using pentane/EtOAc (5%) as eluent, affording pyruvate **9a** (118 mg, 84%) as a colourless oil [mixture of the ketone and enol isomers (87:13)].

IR: ν_{max} (thin film) 3390, 2980, 1725, 1262, 1052, 851 cm^{-1} . **HRMS:** calculated for $\text{C}_{14}\text{H}_{19}\text{O}_3$, 235.13287 $[\text{M}+\text{H}]^+$, found m/z 235.13301, $\Delta = 0.59$ ppm. **^1H NMR** (400 MHz, CDCl_3) *keto tautomer* δ_{H} : 6.89 (2H, s, $2 \times \text{HC}_{\text{Ar}}$), 4.33 (2H, q, $J = 7.2$ Hz, OCH_2CH_3), 4.17 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 2.28 (3H, s, ArCH_3), 2.21 (6H, 2 \times ArCH_3), 1.35 (3H, t, $J = 7.2$ Hz, OCH_2CH_3). *enol tautomer* δ_{H} : 6.90 (2H, s, $2 \times \text{HC}_{\text{Ar}}$), 6.61 (1H, s, CHCOH), 5.91 (1H, s, OH), 4.39 (2H, q, $J = 7.1$ Hz, OCH_2CH_3), 2.29 (3H, s, ArCH_3), 2.25 (6H, s, 2 \times ArCH_3), 1.42 (3H, t, $J = 7.1$ Hz, OCH_2CH_3). **^{13}C NMR** (101 MHz, CDCl_3) *keto tautomer* δ_{C} : 192.5

(C(O)), 165.5 (CO₂), 137.2, 137.1 (2 × C_{Ar}), 129.1 (HC_{Ar}), 126.9 (C_{Ar}), 62.6 (OCH₂CH₃), 40.4 (CH₂C(O)), 21.0 (ArCH₃), 20.3 (ArCH₃), 14.1 (OCH₂CH₃). *enol tautomer* δ_C: 165.5 (CO₂), 139.4, 137.3, 136.6, 130.3 (3 × C_{Ar} + COH), 128.3 (HC_{Ar}), 110.2 (CHCOH), 62.2 (OCH₂CH₃), 21.1 (ArC_aH₃), 20.5 (ArC_bH₃), 14.4 (OCH₂CH₃).

Ethyl 2-oxo-3,3-diphenylpropanoate (**9b**).

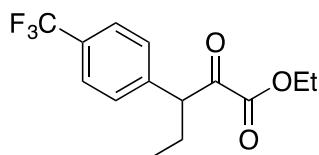


OBO-ketone **7b** (97 mg, 0.3 mmol, 1.0 eq.) was subjected to general procedure F heated for 4 h at 90 °C and purified by flash column chromatography using pentane/EtOAc (7%) as eluent, affording pyruvate **9b** (73 mg, 91%) as a colourless oil. The product exists as a mixture of ketone and enol isomers (85%/15%).

Alternatively, to a flame-dried vial capped with a rubber septum were added methyl-OBO ketone (103 mg, 0.60 mmol, 1.0 eq.) and Pd(dtbpf)Cl₂ (20 mg, 30 μmol, 5 mol%). The rubber septum was replaced by an aluminium cap and then THF (5.3 mL), chlorobenzene (183 μL, 1.80 mmol, 3.0 eq.), and 2 M NaOtBu in THF (0.75 mL, 1.50 mmol, 2.5 eq.) were added *via* syringe. The vial was flushed with argon for 5 mins and then heated at 80 °C for 24 h. The cap was removed and the solvent evaporated *in vacuo*. EtOH (6.0 mL) and *p*-toluenesulfonic acid (206 mg, 1.20 mmol, 2.0 eq.) were added to the same vial, which was capped again and heated at 90 °C for 4 h. After cooling down to RT, NaHCO₃ (101 mg, 1.20 mmol, 2.0 eq.) was added and the mixture was concentrated *in vacuo*. The crude product was purified by flash column chromatography using pentane/EtOAc (5%) as eluent, affording product pyruvate **9b** (98 mg, 61%) as a colourless oil [mixture of ketone and enol isomers (85%/15%)].

IR: ν_{max} (thin film) 3029, 2983, 1727, 1253, 1055, 698 cm⁻¹. **HRMS:** calculated for C₁₇H₁₇O₃, 269.11722 [M+H]⁺, found *m/z* 269.11740, Δ = 0.67 ppm. **¹H NMR** (400 MHz, CDCl₃) *keto tautomer* δ_H: 7.40 – 7.25 (10H, m, 10 × HC_{Ar}) 5.92 (1H, s, Ph₂CH), 4.24 (2H, q, *J* = 7.2 Hz, OCH₂CH₃), 1.24 (3H, t, *J* = 7.1 Hz, OCH₂CH₃). *enol tautomer* δ_H: 7.50 – 7.45 (2H, m, 2 × HC_{Ar}), 7.40 – 7.25 (6H, m, 6 × HC_{Ar}), 7.21 – 7.17 (2H, m, 2 × HC_{Ar}), 6.40 (1H, s, OH), 4.02 (2H, q, *J* = 7.1 Hz, OCH₂CH₃), 0.86 (3H, t, *J* = 7.2 Hz, OCH₂CH₃). **¹³C NMR** (101 MHz, CDCl₃) *keto tautomer* δ_C: 192.0 (C(O)), 161.5 (CO₂), 136.4 (C_{Ar}), 129.3, 128.9, 127.8 (3 × HC_{Ar}), 62.7 (OCH₂CH₃), 59.3 (CHC(O)), 13.9 (OCH₂CH₃). *enol tautomer* δ_C: 166.7 (CO₂), 140.3, 138.8, 137.1 (2 × C_{Ar} + CCOH), 130.1, 130.1, 128.0, 127.8, 127.7, 127.1 (6 × HC_{Ar}), 62.1 (OCH₂CH₃), 13.3 (OCH₂CH₃).

Ethyl 2-oxo-3-(4-(trifluoromethyl)phenyl)pentanoate (**9c**).

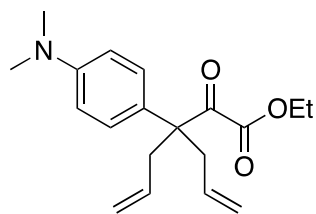


OBO-ketone **8f** (103 mg, 0.3 mmol, 1.0 eq.) was subjected to general procedure F for 8 h at 90 °C and purified by flash column chromatography using pentane/Et₂O (5%) as eluent, affording pyruvate **9c** (55 mg, 64%) as a colourless oil.

IR: ν_{max} (thin film) 2970, 2937, 2879, 2849, 1730, 1325, 1165, 1125, 1068, 1049 cm⁻¹. **HRMS:** calculated for C₁₄H₁₆F₃O₃, 289.10461 [M+H]⁺, found *m/z* 289.10477, Δ = 0.56 ppm. **¹H NMR** (400 MHz, CDCl₃) δ_H: 7.59 (2H, d, *J* = 8.3 Hz, 2 × HC_{Ar}), 7.35 (2H, d, *J* = 8.2 Hz, HC_{Ar}), 4.38 (1H, dd, *J* = 8.3, 6.5 Hz, CHC(O)), 4.26 – 4.14 (2H, m, OCH₂CH₃), 2.18 – 2.06 (1H, m, CH_aH_bCH₃), 1.85 – 1.73 (1H, m, CH_aH_bCH₃), 1.25 (3H, t, *J* = 7.2 Hz, OCH₂CH₃), 0.87 (3H, t, *J* = 7.4 Hz, CH₂CH₃). **¹³C NMR** (126 MHz,

CDCl₃) δ_C : 193.0 (C(O)), 160.9 (CO₂), 140.4 (C_{Ar}), 129.9 (q, J = 32.7 Hz, CCF₃), 129.3 (F₃CCCHCH), 125.8 (q, J = 4.3 Hz, F₃CCCH), 124.0 (q, J = 272.2 Hz, CF₃), 62.6 (OCH₂CH₃), 55.4 (CHC(O)), 24.9 (CH₂CH₃), 13.8 (OCH₂CH₃), 11.7 (CH₂CH₃). ¹⁹F NMR (376 MHz, CDCl₃) δ_F : -62.6 (3F, s, CF₃).

Ethyl 3-allyl-3-(4-(dimethylamino)phenyl)-2-oxohex-5-enoate (**9d**).

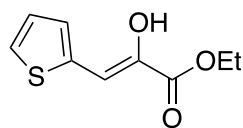


OBO-ketone **8h** (111 mg, 0.3 mmol, 1.0 eq.) was subjected to general procedure F for 4 h at 90 °C and purified by flash column chromatography using toluene as eluent, affording pyruvate **9d** (77 mg, 81%) as a yellow solid.

Alternatively, to a flame-dried vial capped with a rubber septum were added methyl-OBO ketone (155 mg, 0.90 mmol, 1.5 eq.), Pd(dtbpf)Cl₂ (20 mg, 30 μ mol, 5 mol%) and 4-Bromo-*N,N*-dimethylaniline (120 mg, 0.60 mmol, 1.0 eq.). The rubber septum was replaced by an aluminium cap and then THF (5.3 mL) and 2 M NaOtBu in THF (0.75 mL, 1.50 mmol, 2.5 eq.) were added *via* syringe. The vial was flushed with argon for 5 mins and then heated at 50 °C for 24 h. Allyl bromide (156 mL, 1.80 mmol, 3.0 eq.) and 2 M NaOtBu in THF (0.60 mL, 1.20 mmol, 2.0 eq.) were then added sequentially and the mixture was heated at 90 °C for 3 h. The cap was removed and the solvent evaporated *in vacuo*. EtOH (6.0 mL) and *p*-toluenesulfonic acid (310 mg, 1.80 mmol, 3.0 eq.) were added to the same vial, which was capped again and heated at 90 °C for 3 h. After cooling down to RT, NaHCO₃ (101 mg, 1.20 mmol, 2.0 eq.) was added and the mixture was concentrated *in vacuo*. The crude product was purified by flash column chromatography using pentane/EtOAc (5%) as eluent, affording product pyruvate **9d** (124 mg, 65%) as a yellow solid.

m.p.: 53 – 56 °C. **IR**: ν_{\max} (thin film) 3077, 2922, 2804, 1731, 1714, 1611, 1521, 1065, 918, 844 cm⁻¹. **HRMS**: calculated for C₁₉H₂₆NO₃, 316.19072 [M+H]⁺, found m/z 316.19101, Δ = 0.92 ppm. ¹H NMR (400 MHz, CDCl₃) δ_H : 7.05 (2H, d, J = 8.9 Hz, 2 \times HC_{Ar}), 6.69 (2H, d, J = 8.9 Hz, 2 \times HC_{Ar}), 5.57 – 5.44 (2H, m, 2 \times CHCH₂), 5.12 – 5.03 (4H, m, 2 \times CH₂CHCH₂C), 4.06 (2H, q, J = 7.1 Hz, OCH₂CH₃), 3.02 (2H, dd, J = 14.1, 8.2 Hz, CCH_aH_b), 2.94 (6H, s, N(CH₃)₂), 2.71 (2H, dd, J = 14.1, 6.5 Hz, CCH_aH_b), 1.11 (3H, t, J = 7.1 Hz, OCH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ_C : 196.5 (C(O)), 162.1 (CO₂), 149.7 (C_{Ar}), 133.1 (CHCH₂), 127.8 (HC_{Ar}), 125.7 (C_{Ar}), 118.9 (CH₂CHCH₂C), 112.5 (HC_{Ar}), 61.5 (OCH₂CH₃), 56.0 (CC(O)), 40.4 (N(CH₃)₂), 37.2 (CCH₂), 13.8 (OCH₂CH₃).

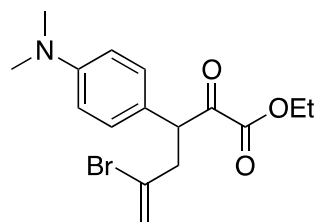
Ethyl 2-hydroxy-3-(thiophen-2-yl)acrylate (**9e**).



OBO-ketone **6m** (76 mg, 0.3 mmol, 1.0 eq.) was subjected to general procedure F for 2 h at 110 °C and purified by flash column chromatography using pentane/EtOAc (10%) as eluent, affording enol **9e** (49 mg, 82%) as an off-white solid.

m.p.: 58 – 60 °C. **IR**: ν_{\max} (thin film) 3385, 2981, 1684, 1247, 1219, 1108, 1016, 855, 763, 668 cm⁻¹. **HRMS**: calculated for C₉H₁₁O₃S 199.04234 [M+H]⁺, found m/z 199.04259, Δ = 1.23 ppm. ¹H NMR (400 MHz, CDCl₃) δ_H : 7.41 (1H, d, J = 5.0 Hz, HC_{Ar}), 7.30 (1H, d, J = 3.7 Hz, HC_{Ar}), 7.07 (1H, dd, J = 5.1, 3.7 Hz, SCHCH), 6.85 (1H, s, CHCOH), 6.48 (1H, d, J = 1.2 Hz, OH), 4.36 (2H, q, J = 7.2 Hz, OCH₂CH₃), 1.38 (3H, t, J = 7.2 Hz, OCH₂CH₃). ¹³C NMR (101 MHz, CDCl₃) δ_C : 165.7 (C(O)), 137.5, 137.0 (C_{Ar} + COH), 129.0, 128.3 (2 \times HC_{Ar}), 127.2 (SCHCH), 105.8 (CHCOH), 62.6 (OCH₂CH₃), 14.4 (OCH₂CH₃). Spectroscopic data are consistent with those previously reported.⁴

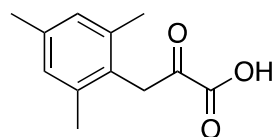
Ethyl 5-bromo-3-(4-(dimethylamino)phenyl)-2-oxohex-5-enoate (**9f**).



OBO-ketone (123 mg, 0.3 mmol, 1.0 eq.) was subjected to general procedure F for 3 h at 110 °C and purified by flash column chromatography using pentane/EtOAc (5%) as eluent, affording pyruvate **9f** (67 mg, 63%) as a colourless oil.

IR: ν_{\max} (thin film) 2984, 2904, 2805, 1923, 1610, 1520, 1354, 1165, 1076, 1028, 812 cm^{-1} . **HRMS:** calculated for $\text{C}_{16}\text{H}_{21}\text{NO}_3^{79}\text{Br}$, 354.06993 $[\text{M}+\text{H}]^+$, found m/z 354.07010, $\Delta = 0.47$ ppm. **^1H NMR** (400 MHz, CDCl_3) δ_{H} : 6.99 (2H, d, $J = 8.9$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 6.58 (2H, d, $J = 8.8$ Hz, $2 \times \text{HC}_{\text{Ar}}$), 5.48 (1H, s, $\text{CH}_a\text{H}_b\text{C}(\text{Br})\text{CH}_2\text{C}$), 5.34 (1H, d, $J = 2.2$ Hz, $\text{CH}_a\text{C}(\text{Br})\text{CH}_2\text{C}$), 4.75 (1H, t, $J = 7.3$ Hz, $\text{CHC}(\text{O})$), 4.25 – 4.12 (2H, m, OCH_2CH_3), 3.17 (1H, dd, $J = 14.8, 6.8$ Hz, CHCH_aH_b), 2.93 (6H, s, $3 \times \text{OCH}_2$), 2.80 (1H, dd, $J = 14.8, 7.8$ Hz, CHCH_aH_b), 1.24 (3H, t, $J = 7.2$ Hz, OCH_2CH_3). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 191.7 ($\text{C}(\text{O})$), 161.1 (CO_2), 150.2, 130.7 ($2 \times \text{C}_{\text{Ar}}$), 130.0 (HC_{Ar}), 121.0 (CBr), 119.5 ($\text{CH}_2\text{C}(\text{Br})\text{CH}_2\text{C}$), 112.8 (HC_{Ar}), 62.5 (OCH_2CH_3), 51.4 ($\text{CHC}(\text{O})$), 43.0 (CHCH_2), 40.5 ($\text{N}(\text{CH}_3)_2$), 14.0 (OCH_2CH_3).

3-Mesityl-2-oxopropanoic acid (**10**).



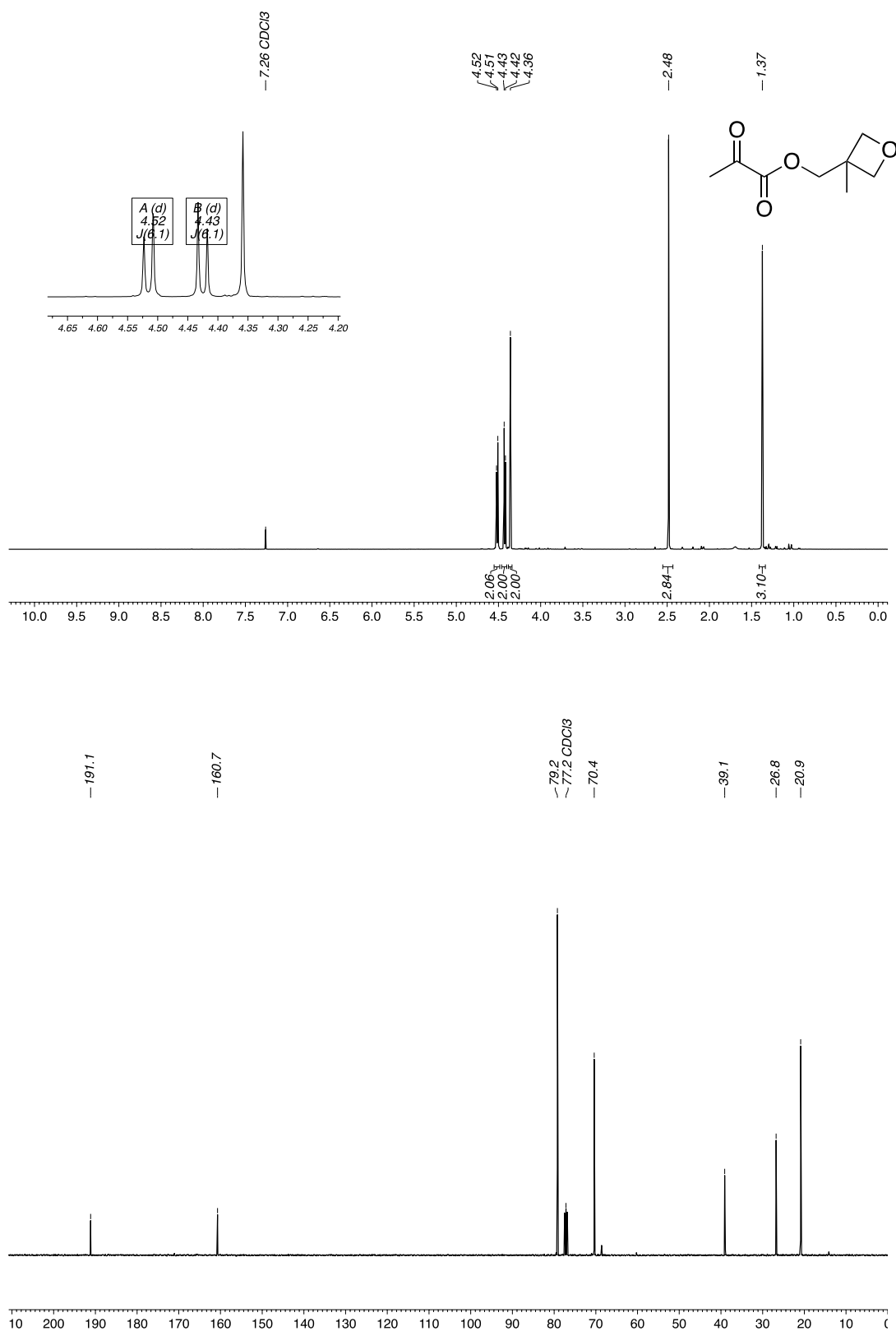
To a flame-dried vial capped with a rubber septum were added methyl-OBO ketone (100 mg, 0.58 mmol, 1.0 eq.) and $\text{Pd}(\text{dtbpf})\text{Cl}_2$ (19 mg, 29 μmol , 5 mol%). The rubber septum was replaced by an aluminium cap and then THF (5.1 mL), 2 M NaOtBu in THF (0.72 mL, 1.45 mmol, 2.5 eq.) and 2-bromomesitylene (98 μL , 0.64 mmol, 1.1 eq.) were added *via* syringe. The vial was flushed with argon for 5 mins and then heated at 50 °C for 24 h. A solution of NaHSO_4 (244 mg, 2.03 mmol, 3.5 eq.) in 1 mL of H_2O was added and the mixture was stirred at RT for 3 h. Solid LiOH (70 mg, 2.9 mmol, 5.0 eq.) was then added and the mixture was stirred at RT for 2 h. The reaction was diluted with DCM and extracted three times with 1 M NaOH (3×10 mL). The aqueous layers were combined, the pH adjusted to 1 using 3 M HCl and the resulting cloudy solution was extracted three times with DCM. The organic layers were combined, dried over MgSO_4 , filtered and concentrated *in vacuo* to afford pyruvic acid **10** (116 mg, 97%) as a white solid.

m.p.: 115 – 117 °C. **IR:** ν_{\max} (thin film) 3463, 2917, 2850, 1723, 1485, 1446, 1309, 1248, 1055, 844, 683 cm^{-1} . **HRMS:** calculated for $\text{C}_{12}\text{H}_{13}\text{O}_3$, 205.08702 $[\text{M}-\text{H}]^-$, found m/z 205.08673, $\Delta = -1.40$ ppm. **^1H NMR** (400 MHz, $\text{DMSO}-d_6$) δ_{H} : 6.78 (2H, s, $2 \times \text{HC}_{\text{Ar}}$), 3.92 (2H, s, $\text{CH}_2\text{C}(\text{O})$), 2.18 (3H, s, ArCH_3), 2.10 (6H, s, $2 \times \text{ArCH}_3$). **^{13}C NMR** (101 MHz, CDCl_3) δ_{C} : 203.2 ($\text{C}(\text{O})$), 168.3 (COOH), 136.6, 134.8, 129.8 ($3 \times \text{C}_{\text{Ar}}$), 128.2 (HC_{Ar}), 40.1 ($\text{CH}_2\text{C}(\text{O})$), 20.6 (ArCH_3), 19.9 (ArCH_3).

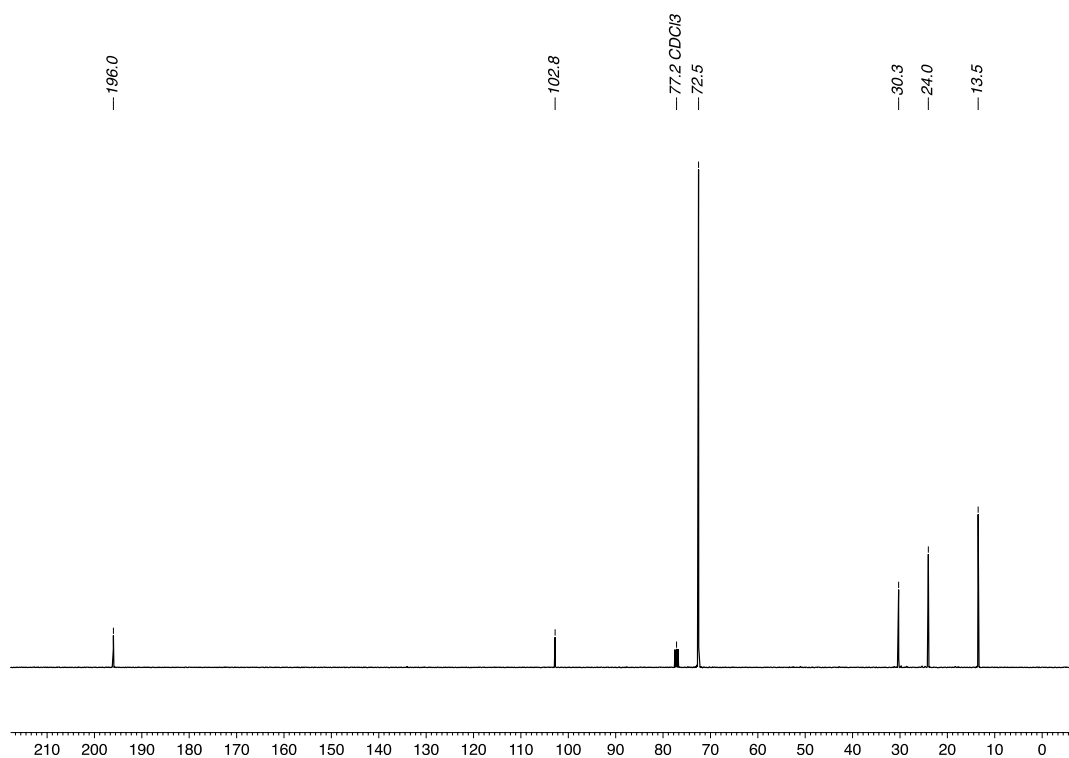
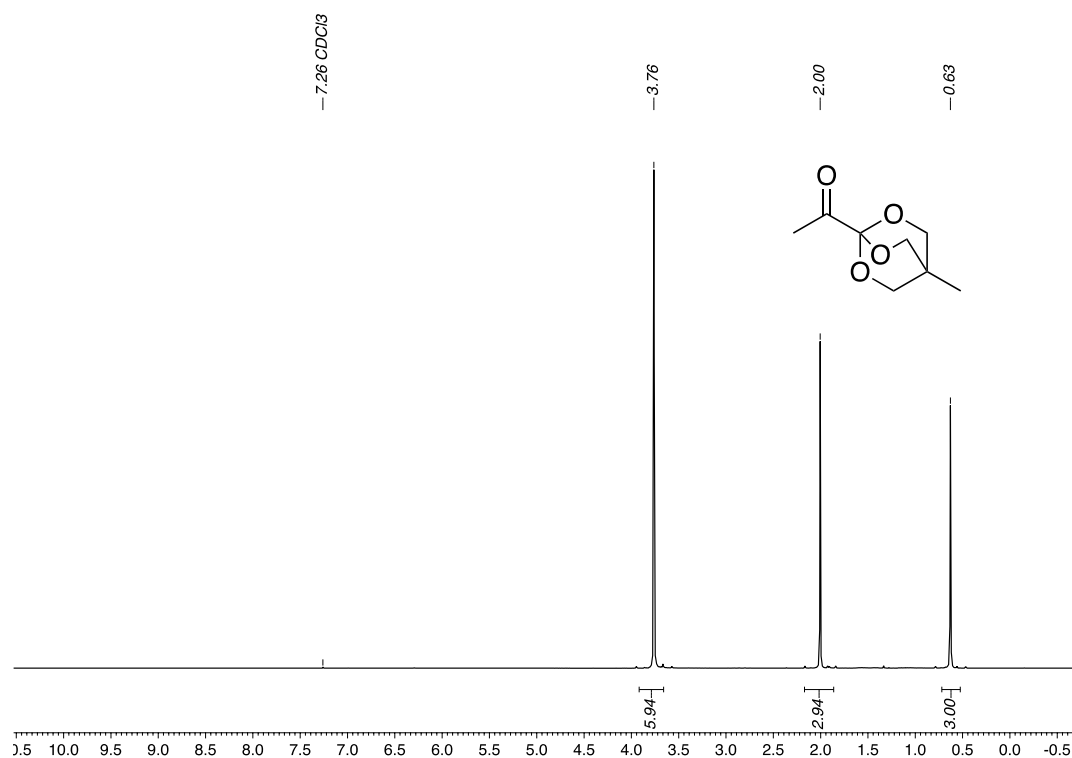
4. ^1H and ^{13}C NMR spectra

(3-Methyloxetan-3-yl)methyl 2-oxopropanoate (3)

Acquired in CDCl_3 – 400 MHz (^1H NMR) and 101 MHz (^{13}C NMR).

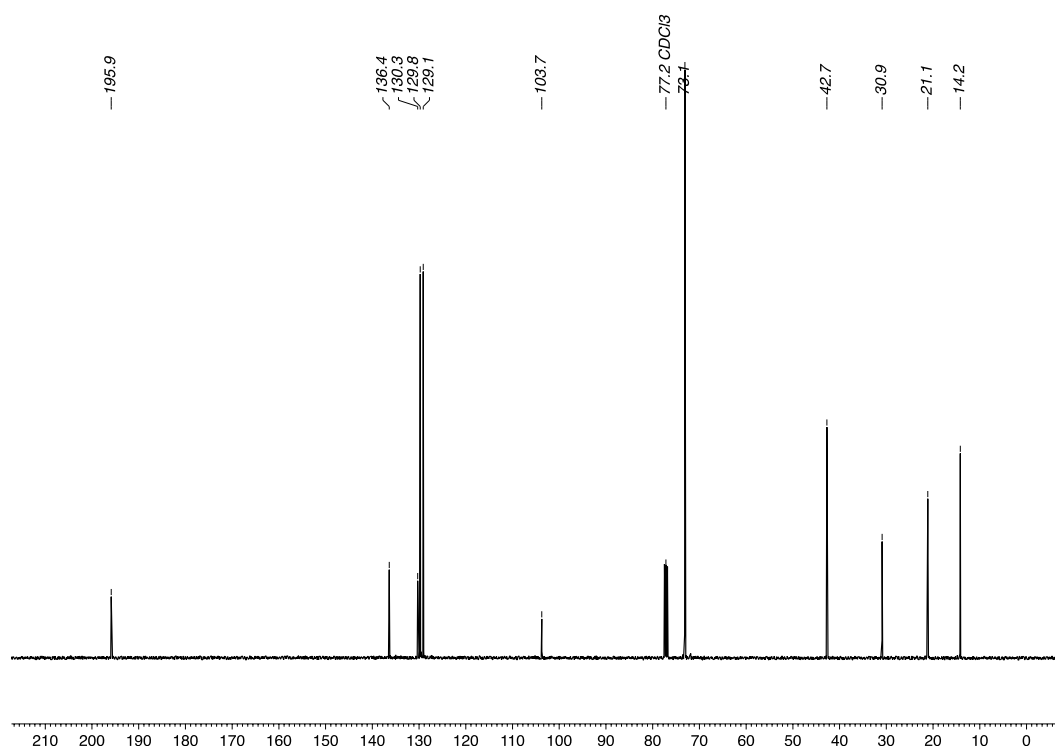
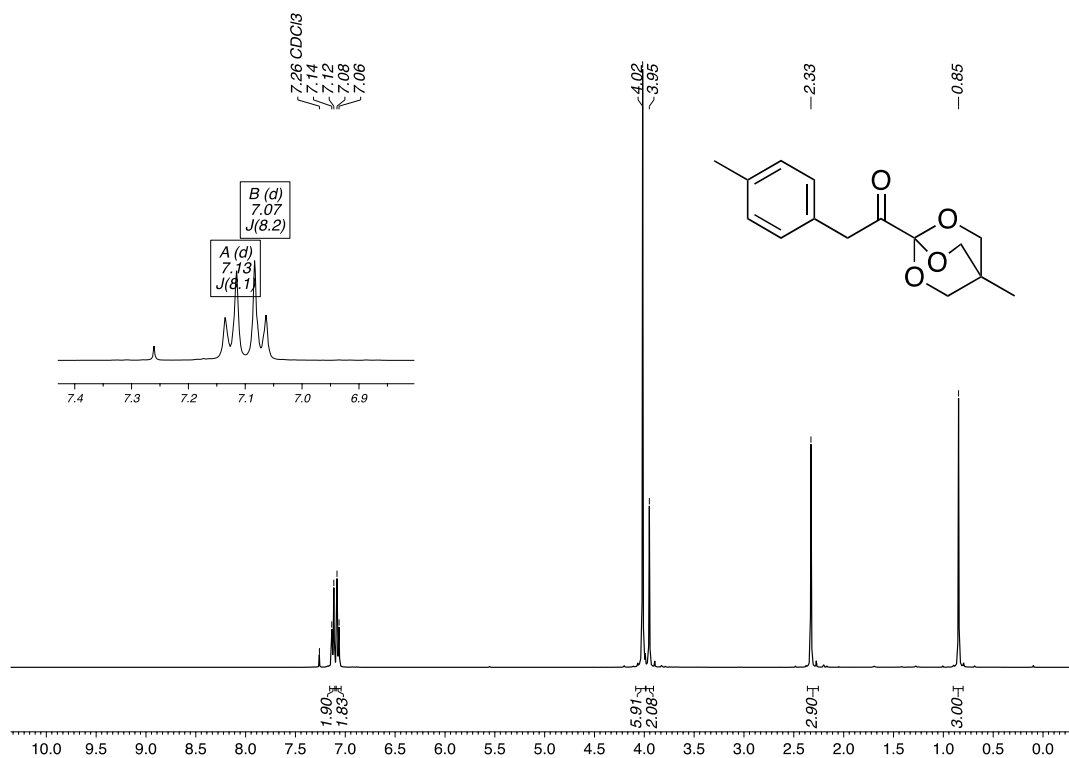


1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (4)
 Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



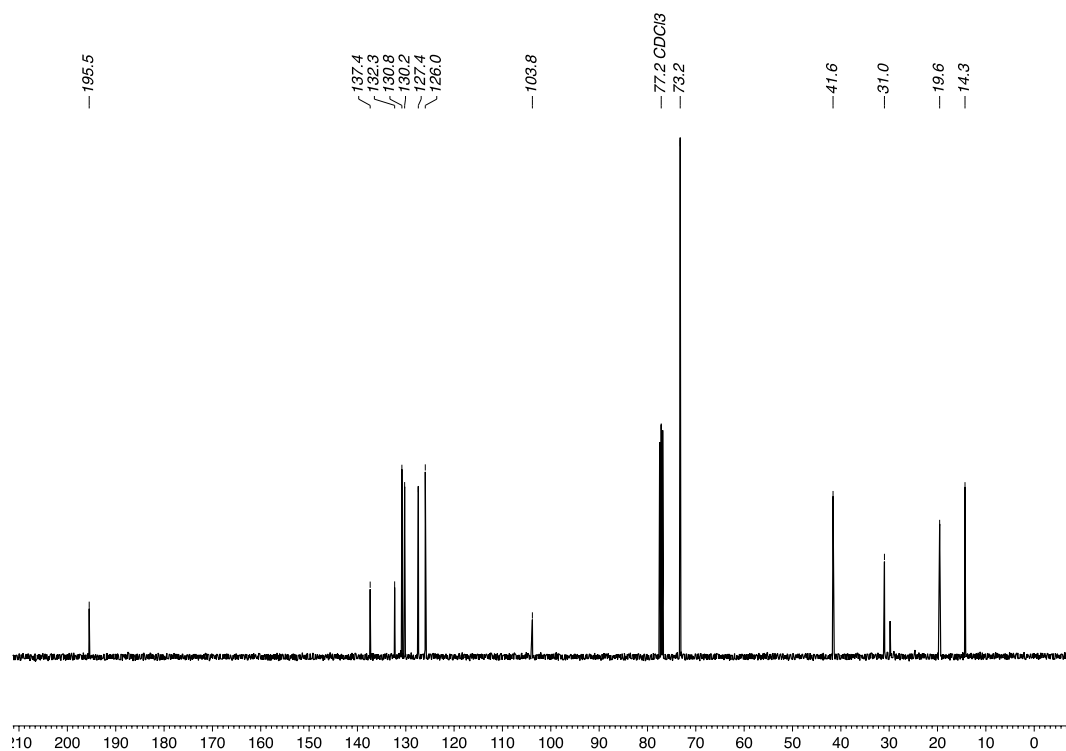
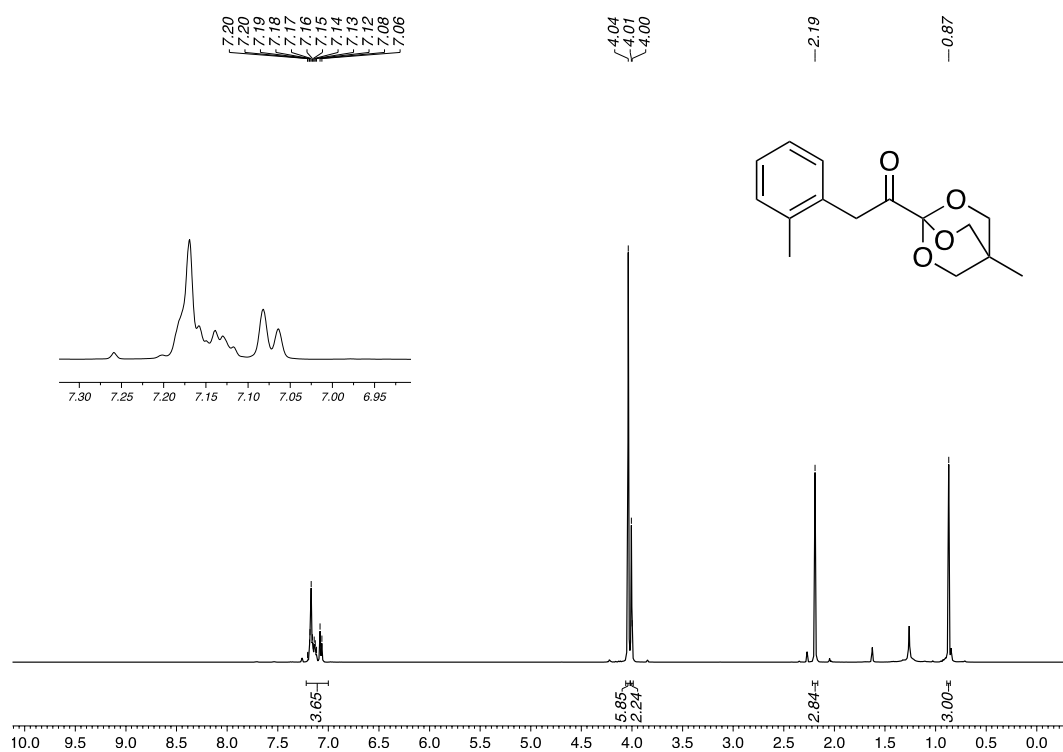
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(*p*-tolyl)ethan-1-one (6a)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



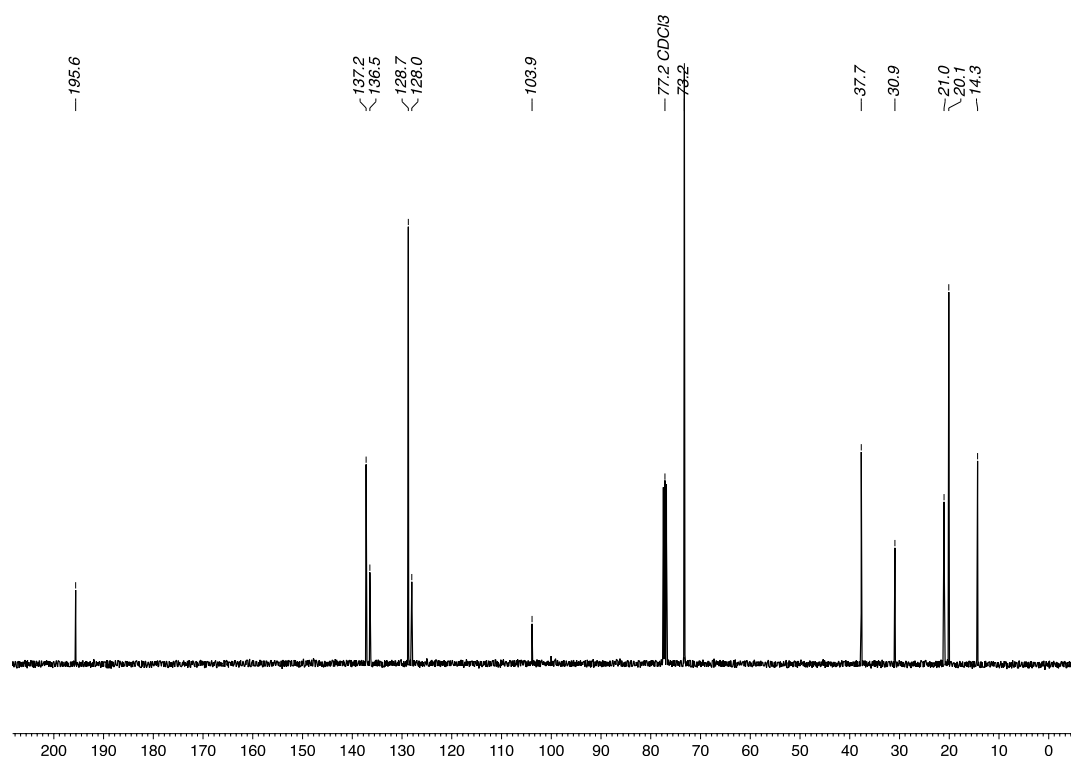
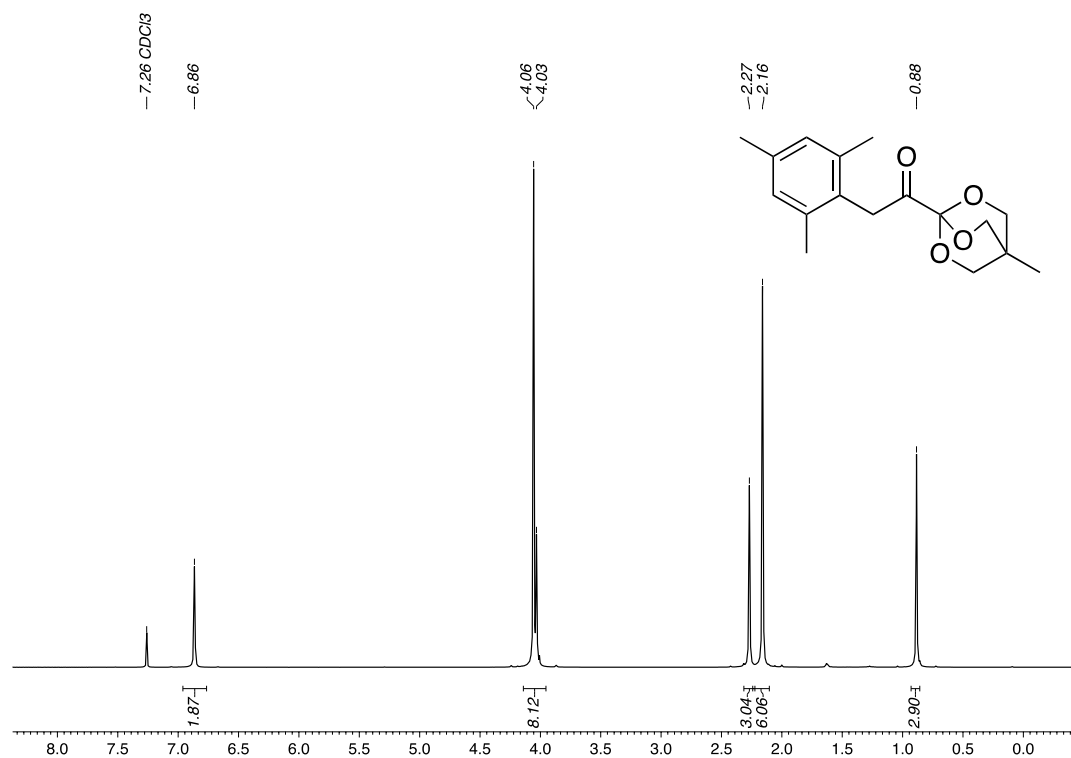
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(*o*-tolyl)ethan-1-one (6b)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

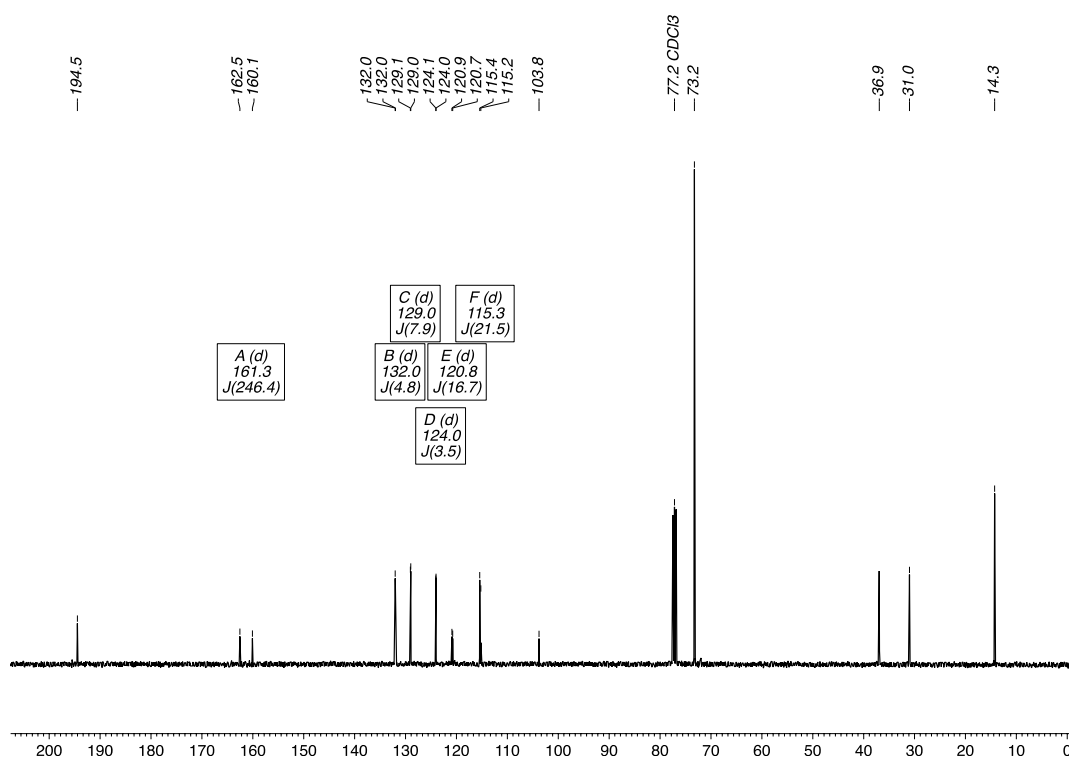
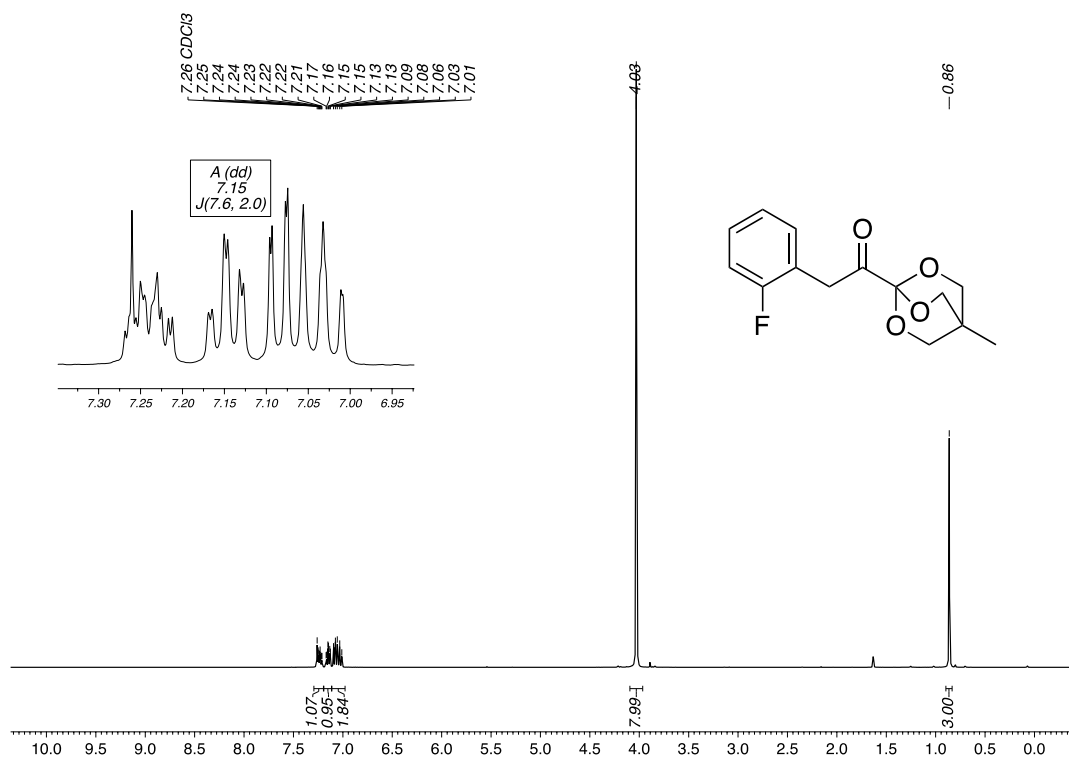


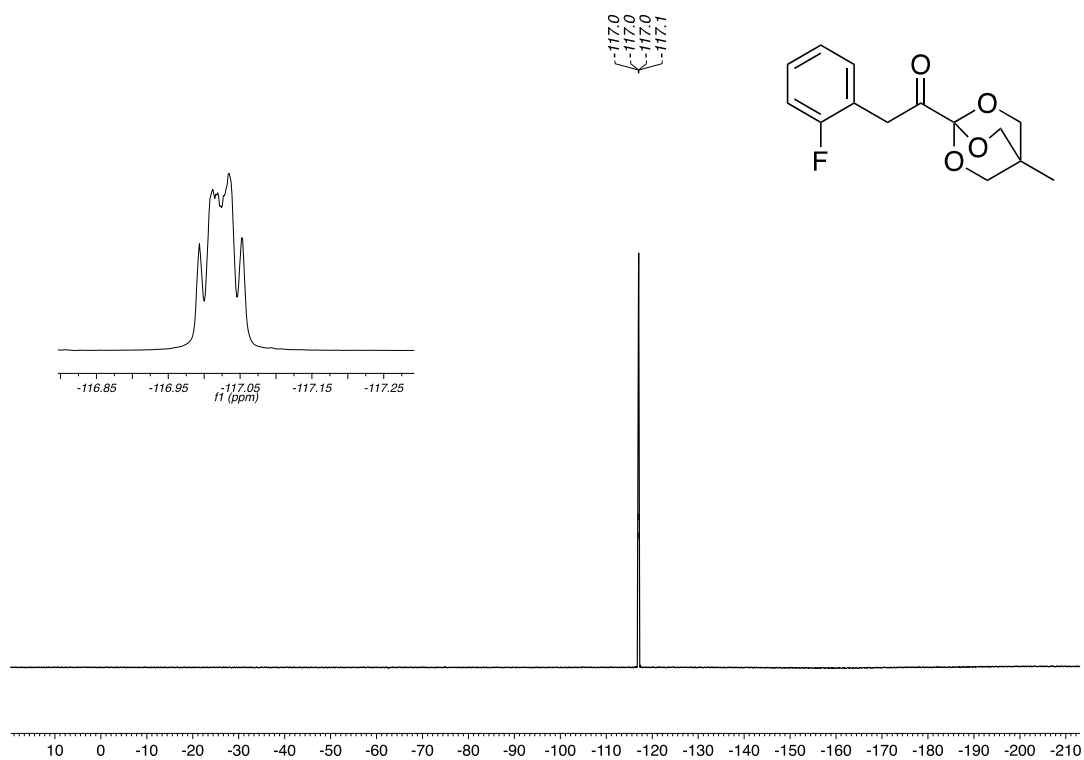
2-Mesityl-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6c)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



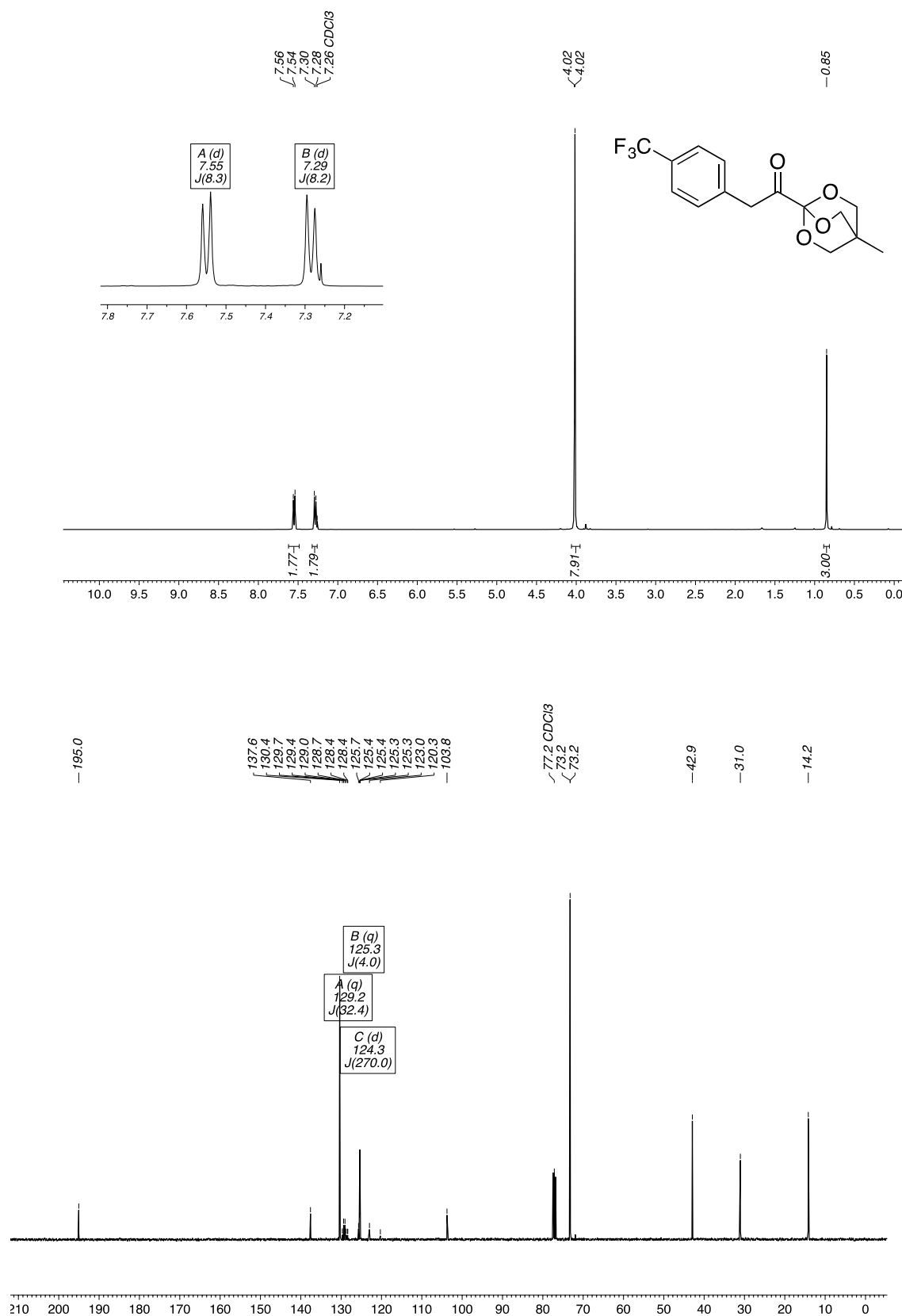
2-(2-Fluorophenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6d)
 Acquired in CDCl₃ – 400 MHz (¹H NMR), 101 MHz (¹³C NMR) and 376 MHz (¹⁹F).

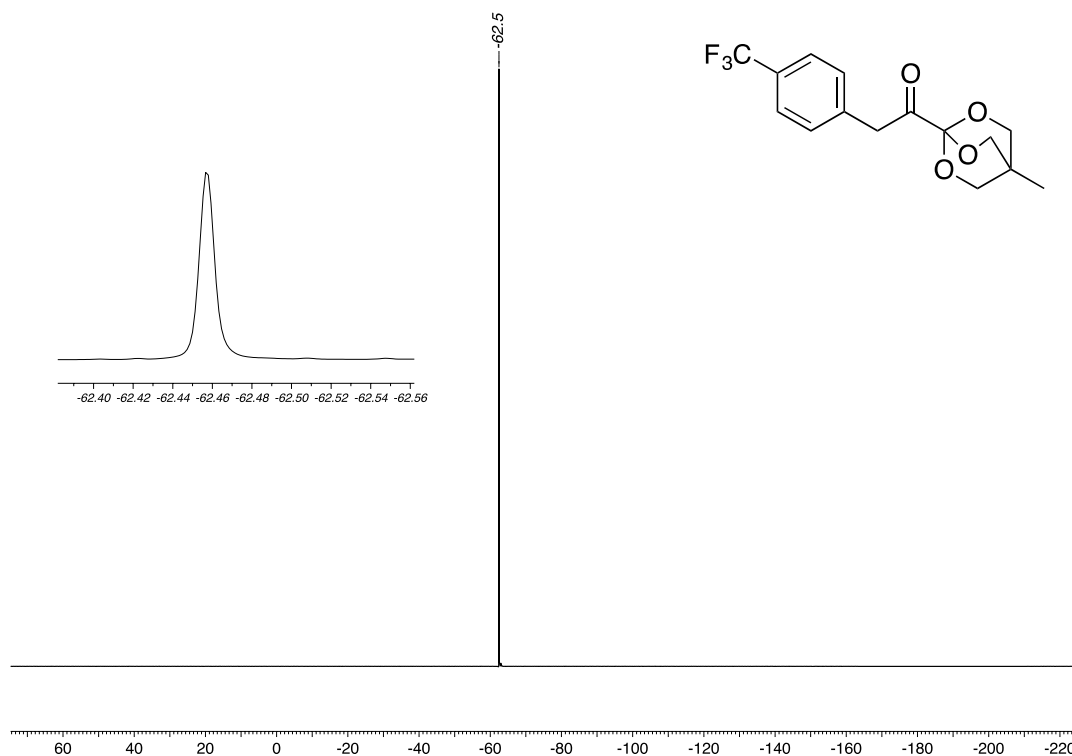




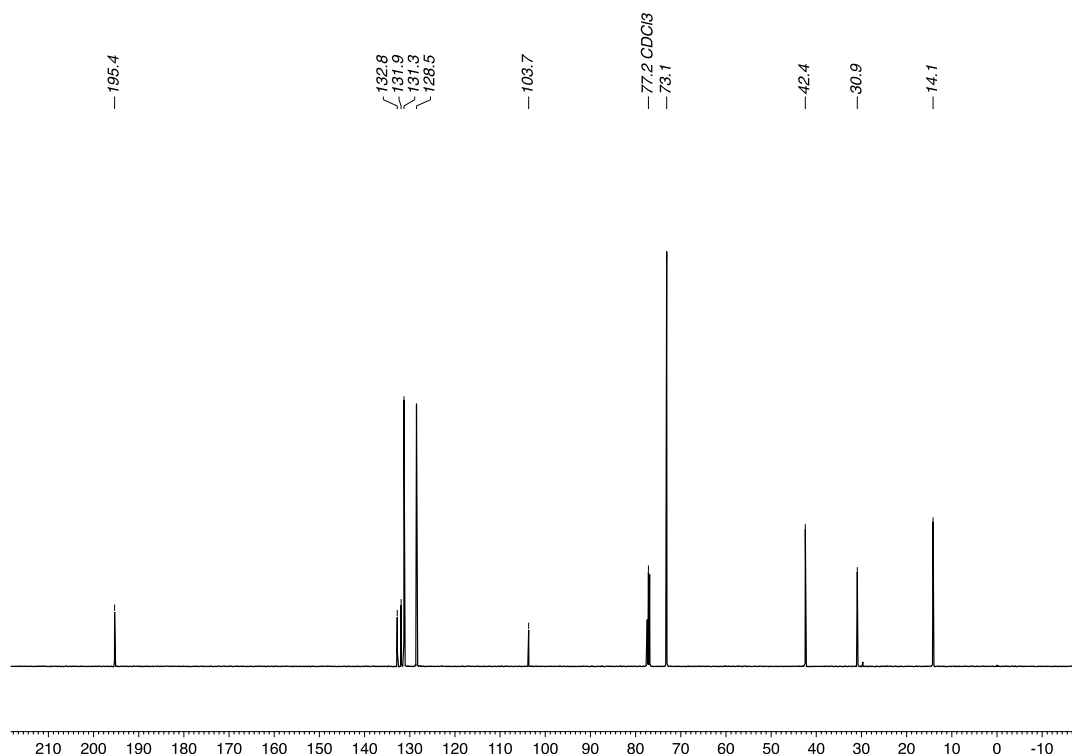
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(4-(trifluoromethyl)phenyl)-ethan-1-one (6e)

Acquired in CDCl₃ – 400 MHz (¹H NMR), 101 MHz (¹³C NMR) and 376 MHz (¹⁹F).

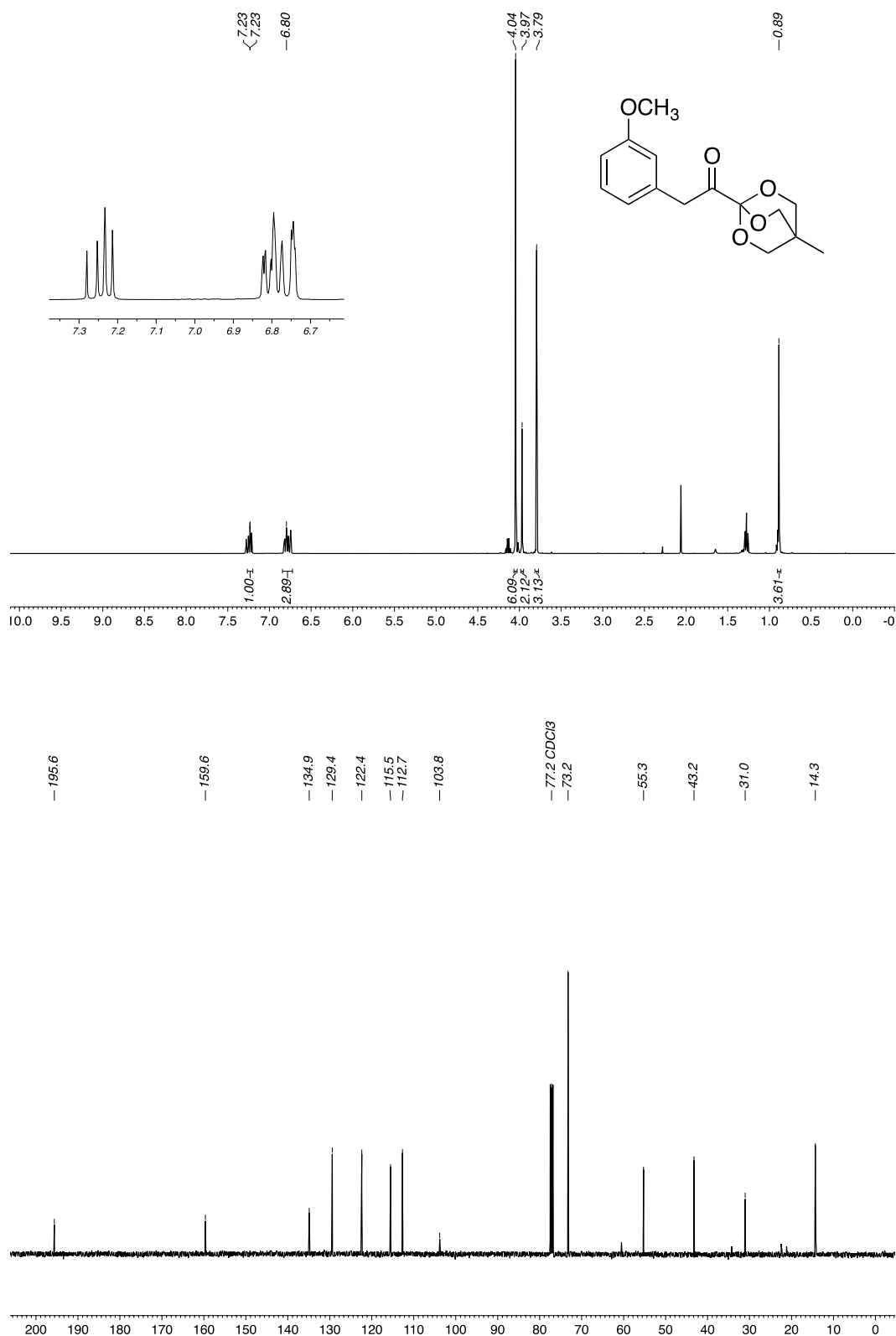




2-(4-Chlorophenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6f)
 Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

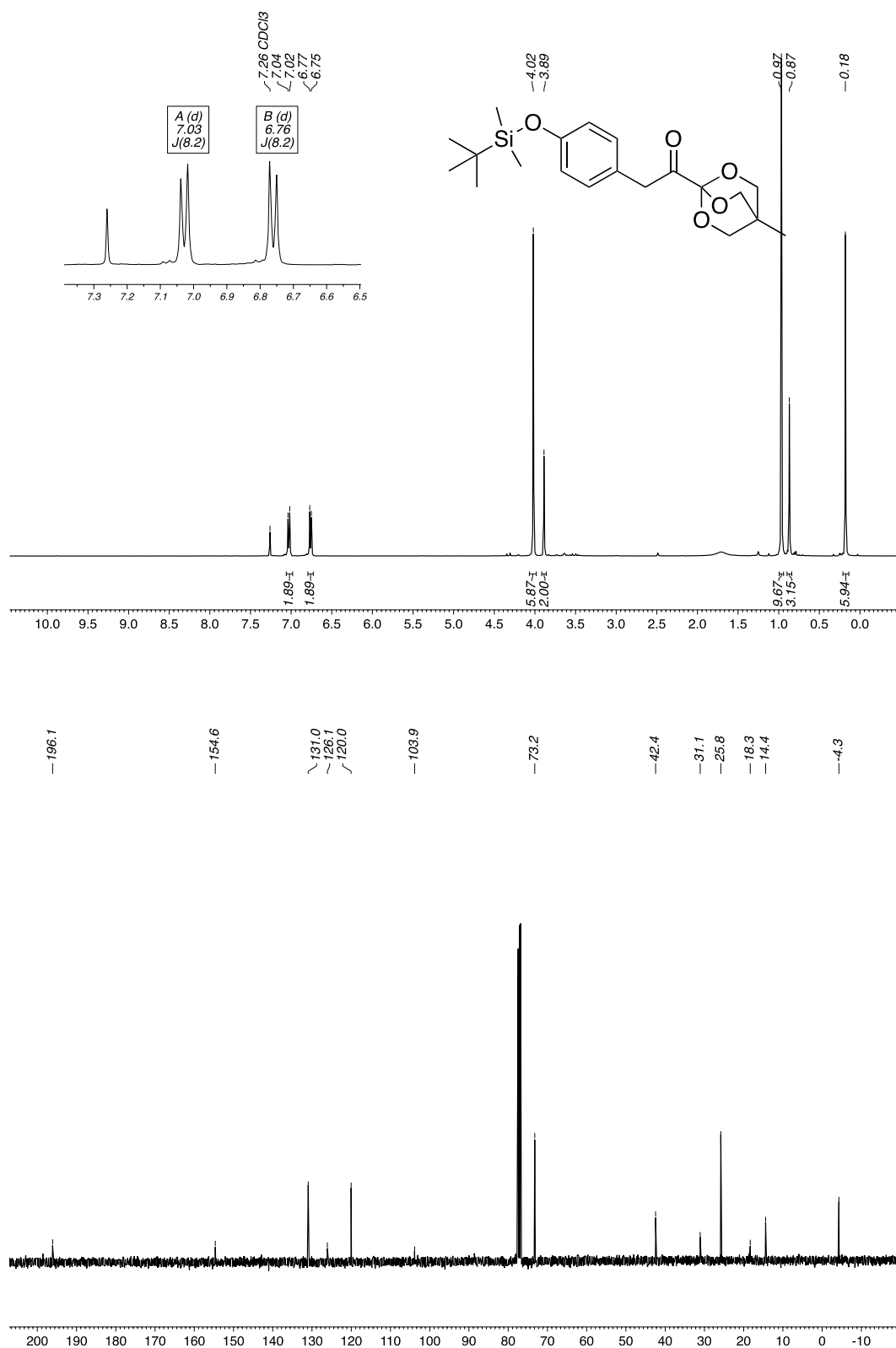


2-(3-Methoxyphenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6g)
 Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



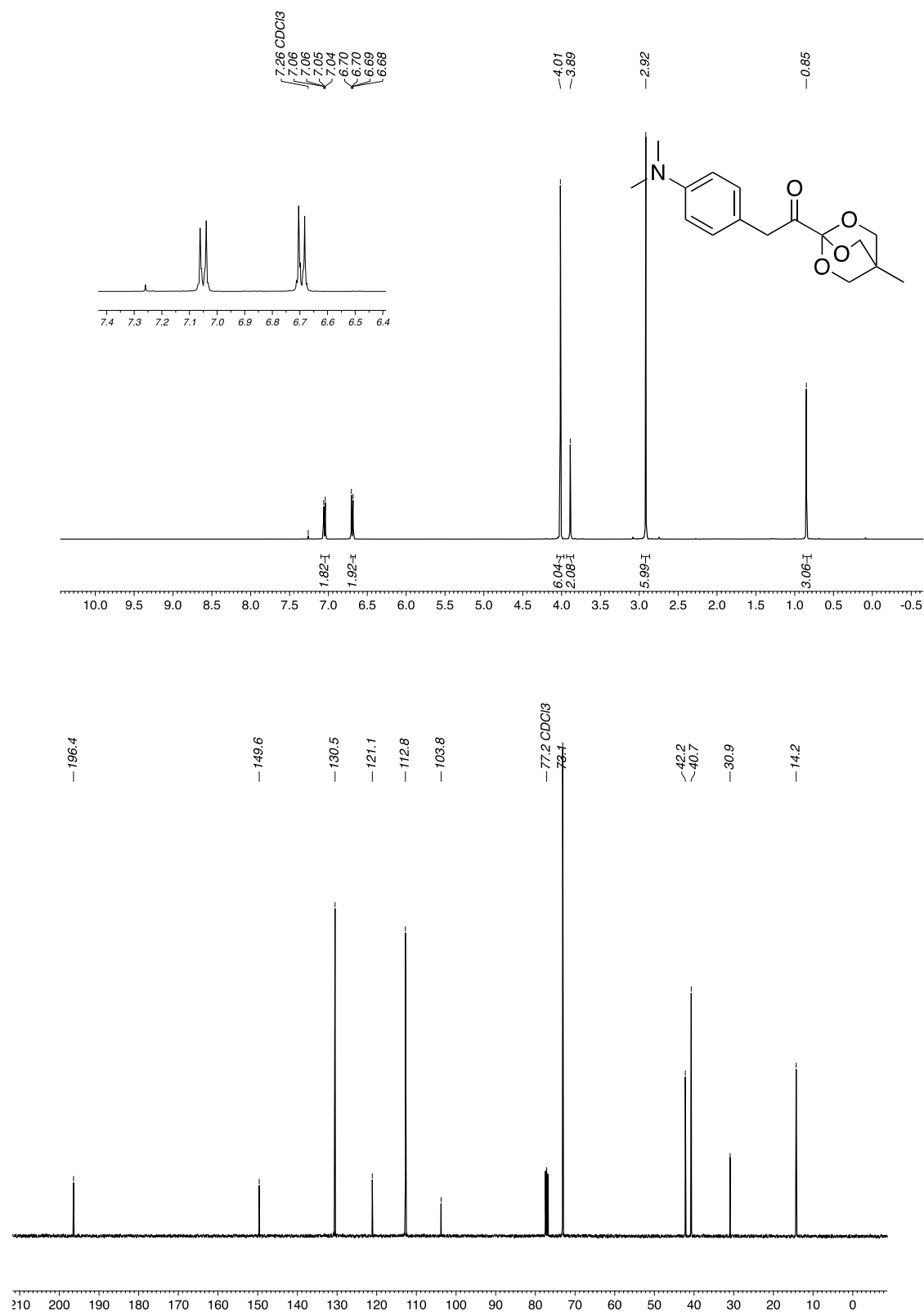
2-(4-((*tert*-Butyldimethylsilyl)oxy)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6h)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

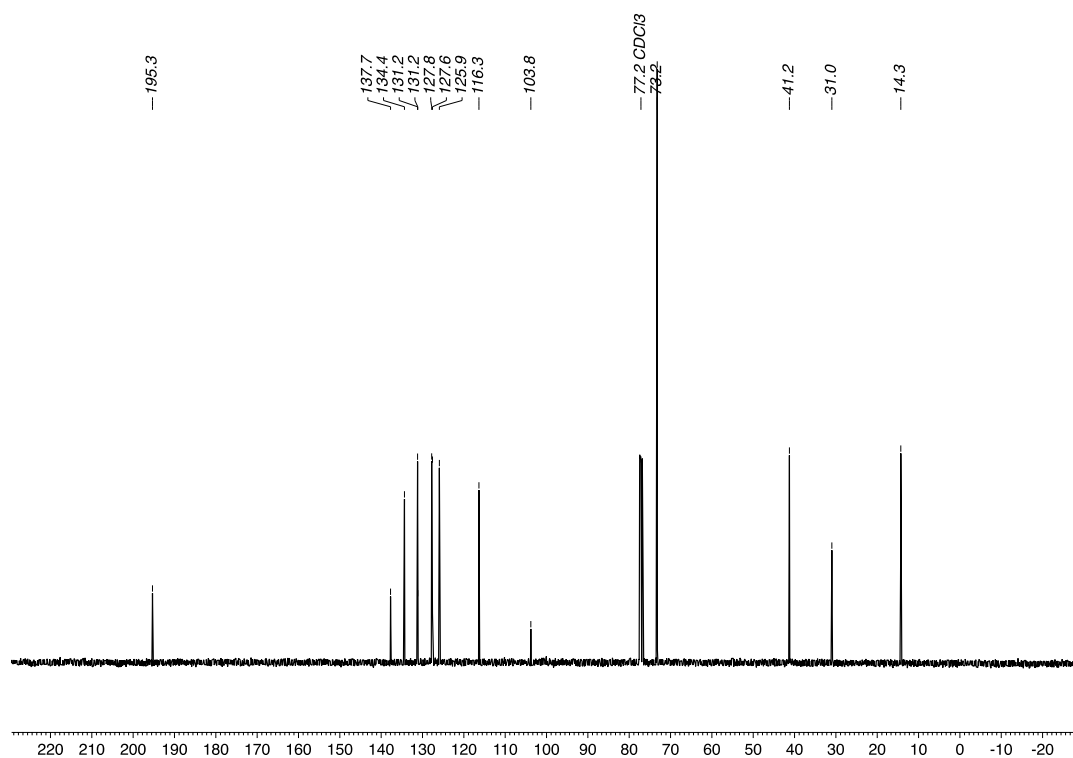


2-(4-(Dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-ethan-1-one (6i)

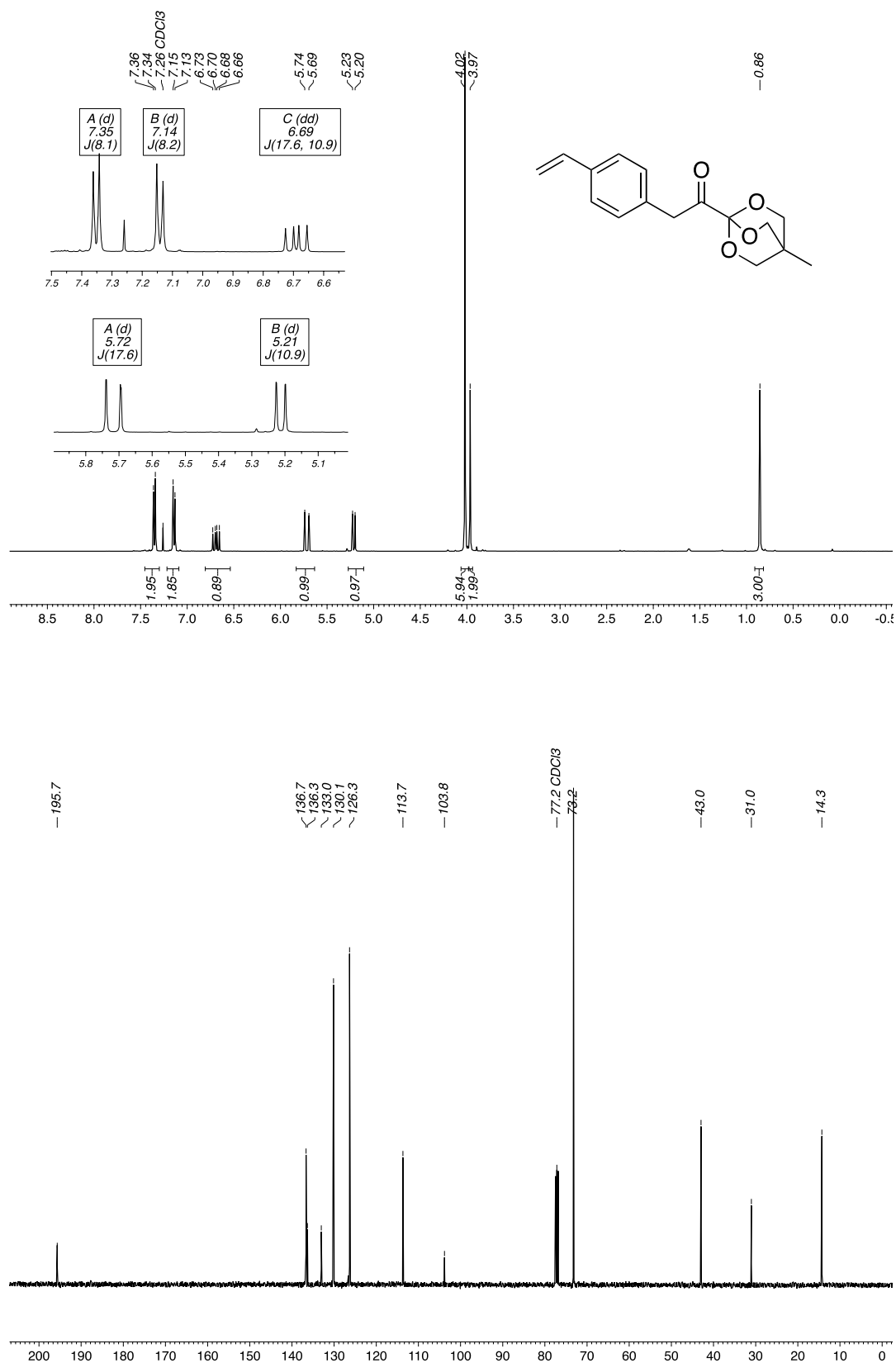
Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(2-vinylphenyl)ethan-1-one (6j)
 Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

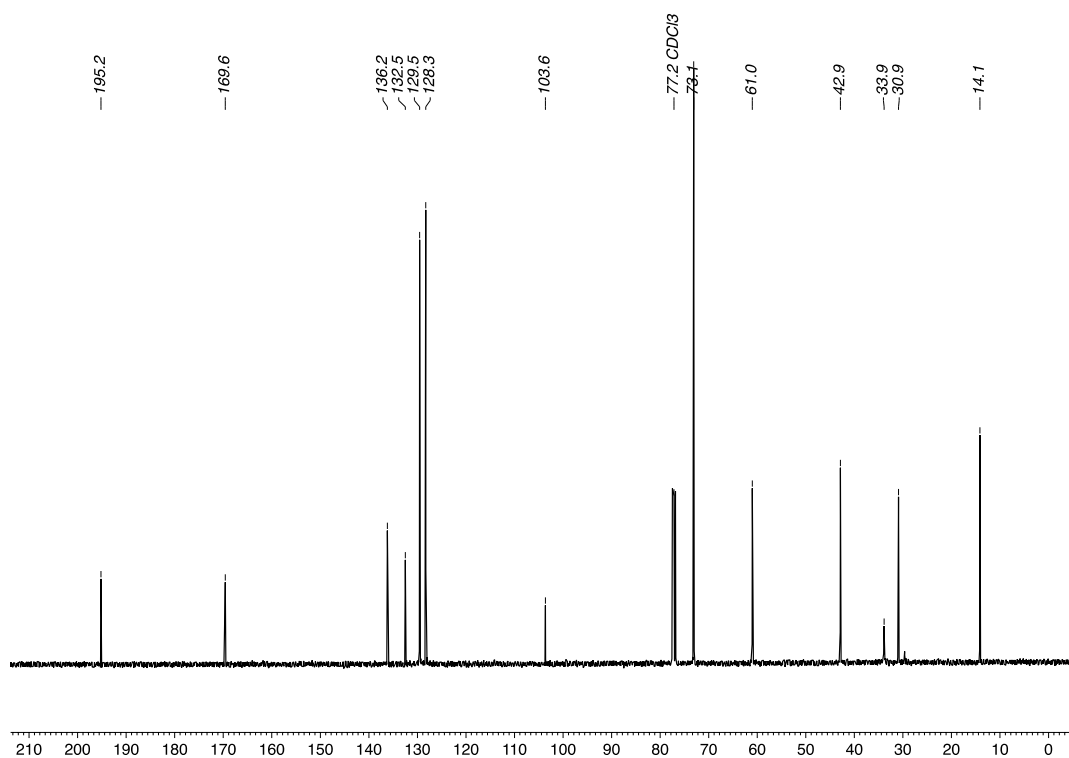
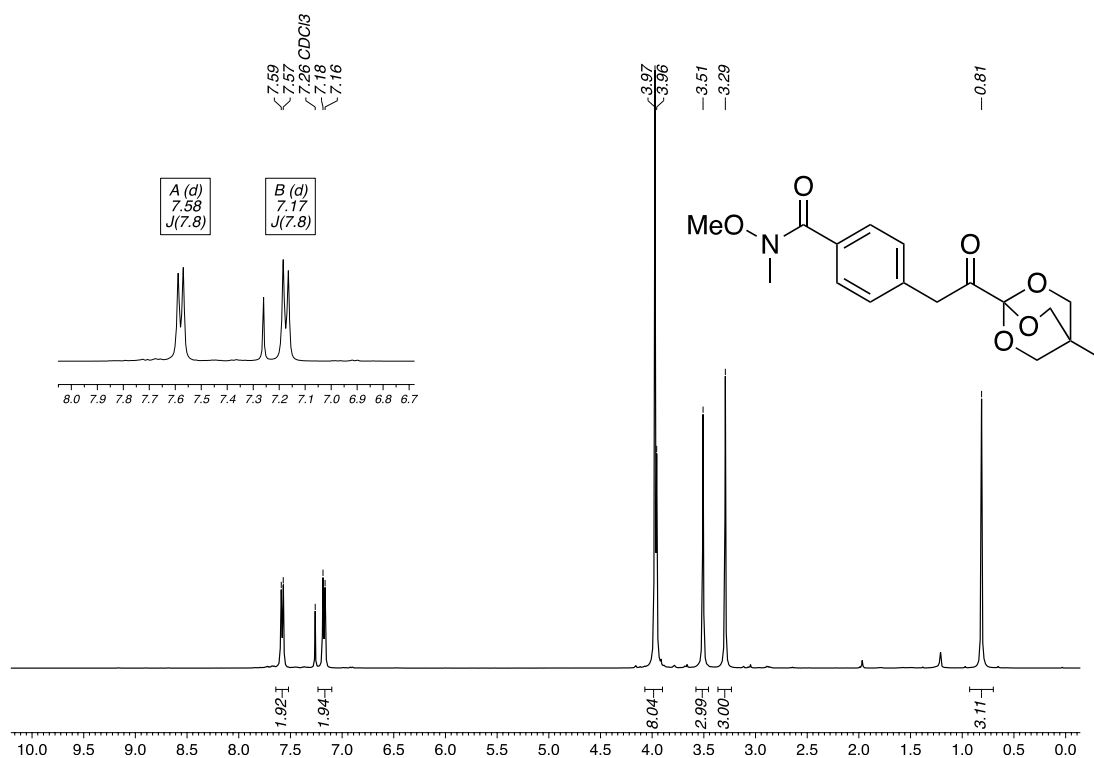


1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(4-vinylphenyl)ethan-1-one (6k)
 Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

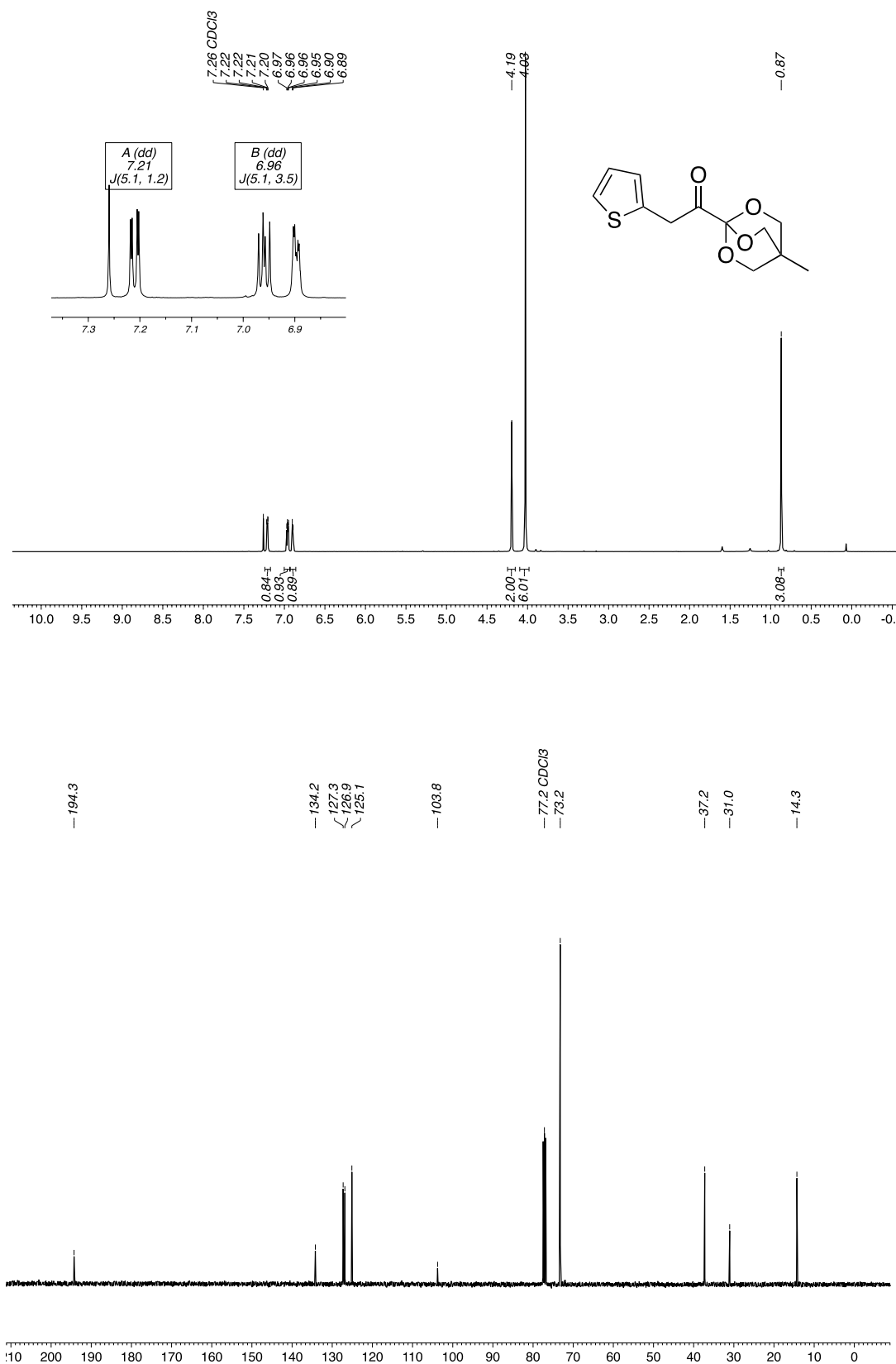


***N*-Methoxy-*N*-methyl-4-(2-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-oxoethyl)benzamide (6l)**

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

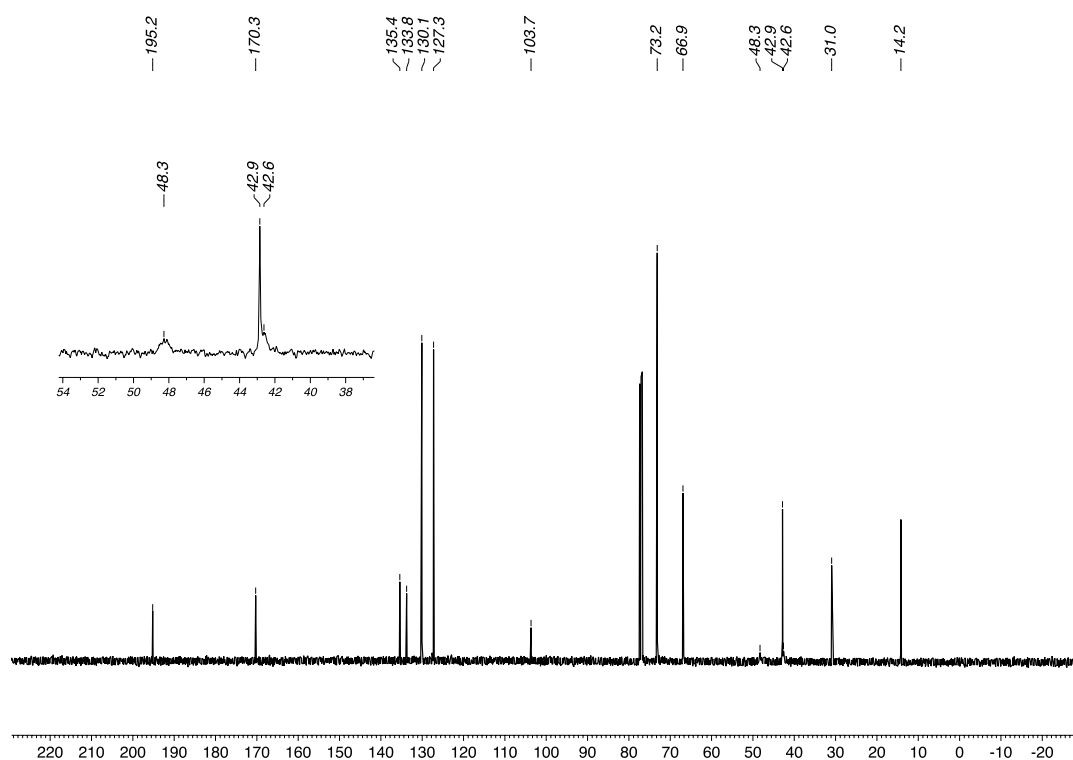
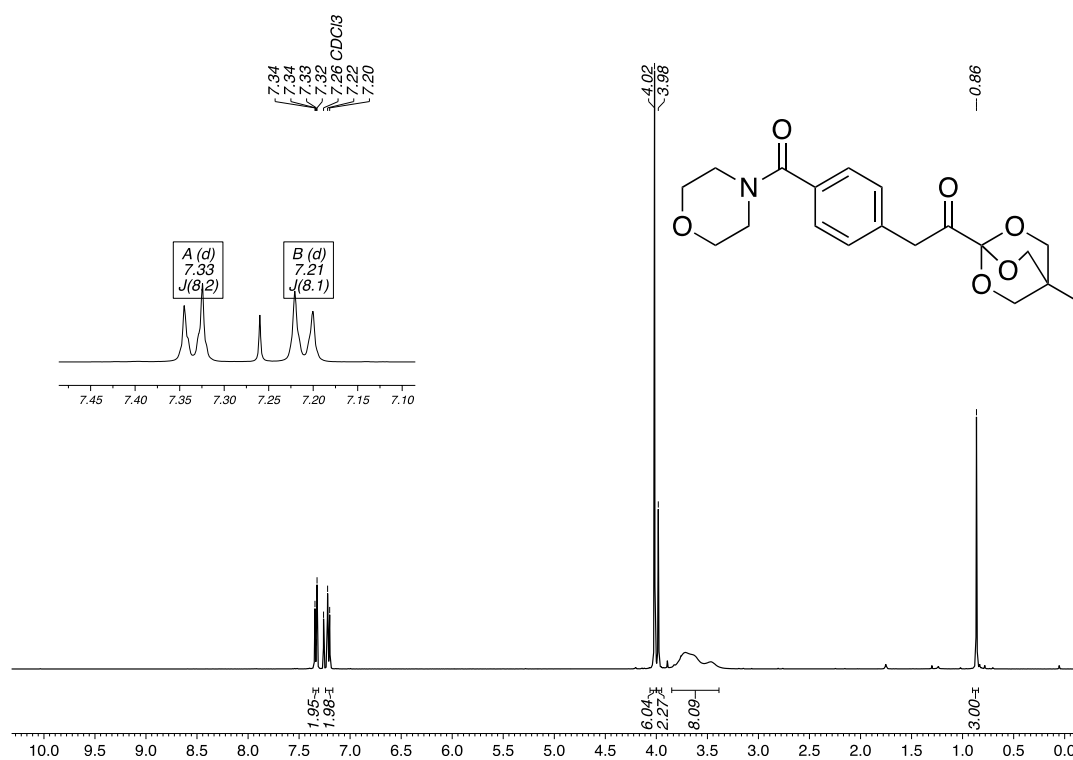


1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(thiophen-2-yl)ethan-1-one (6m)
 Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



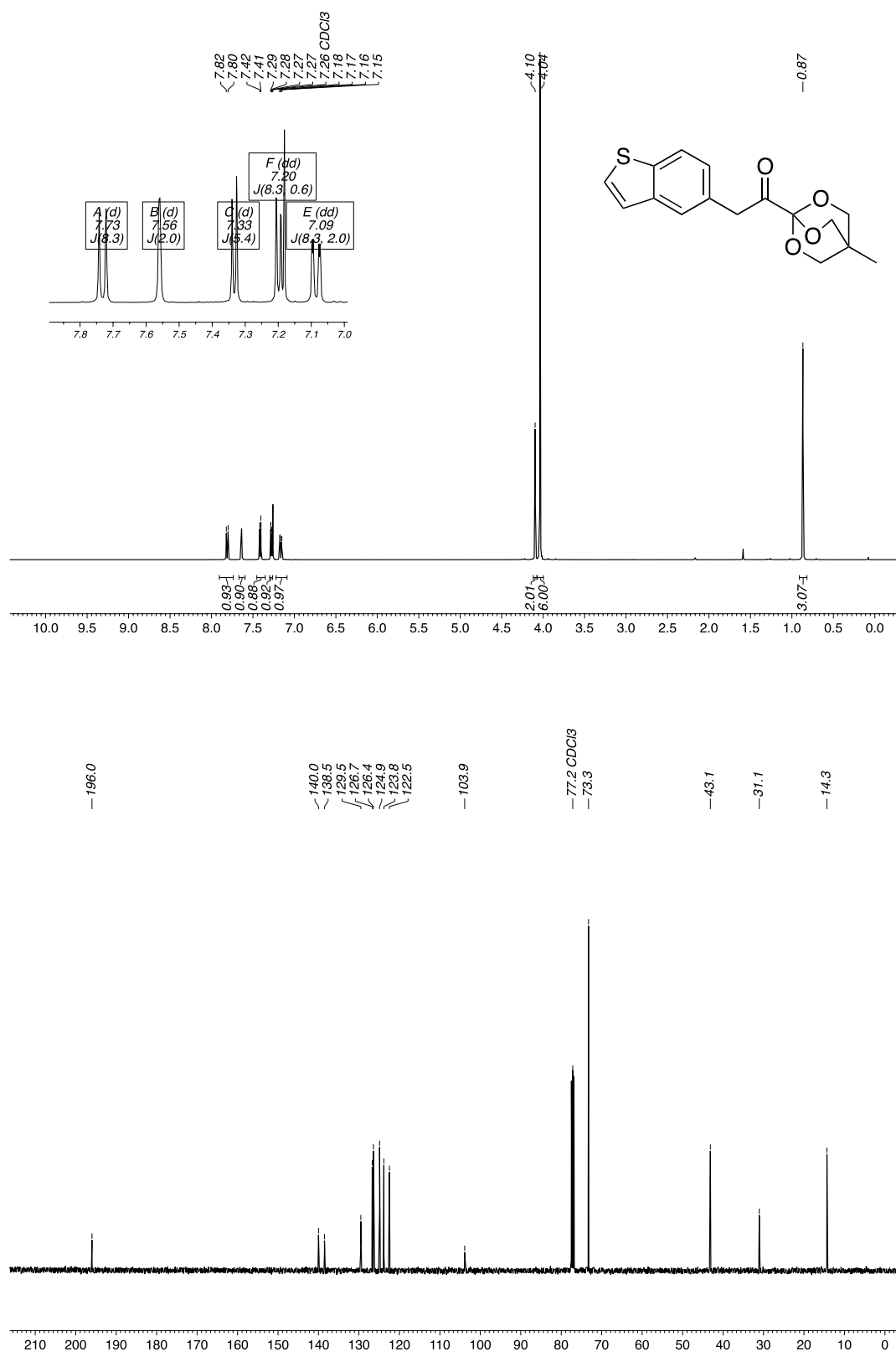
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(4-(morpholine-4-carbonyl)-phenyl)ethan-1-one (6n)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



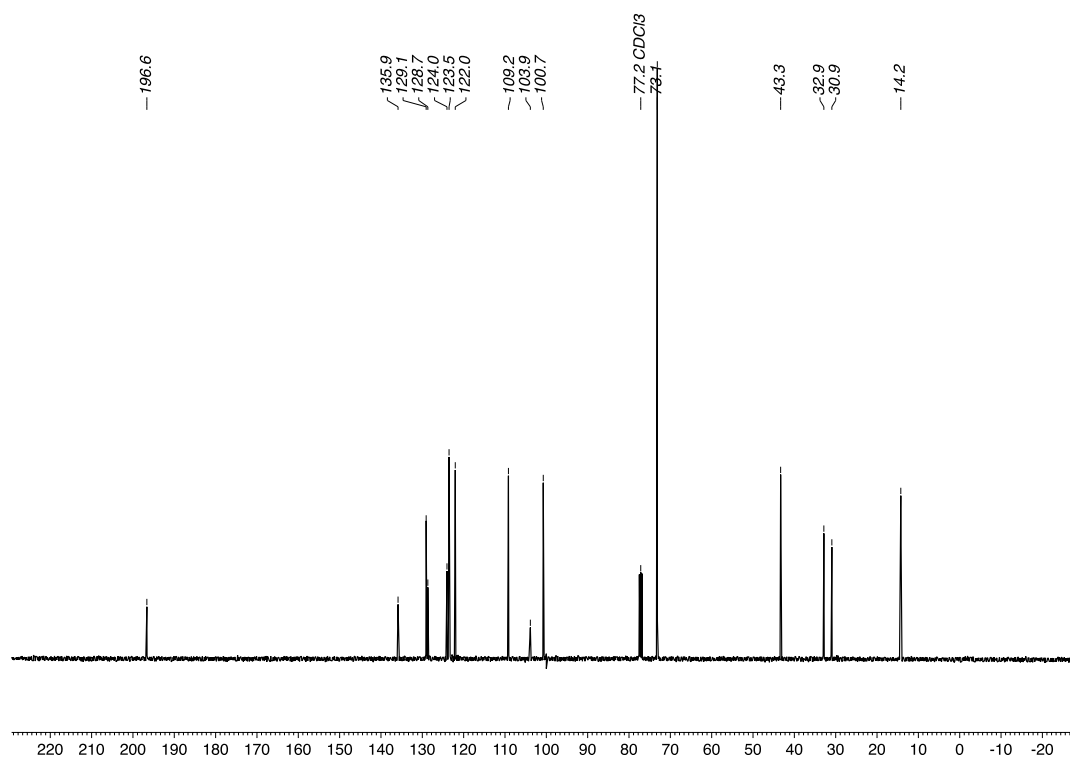
2-(Benzo[*b*]thiophen-5-yl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one
(60)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

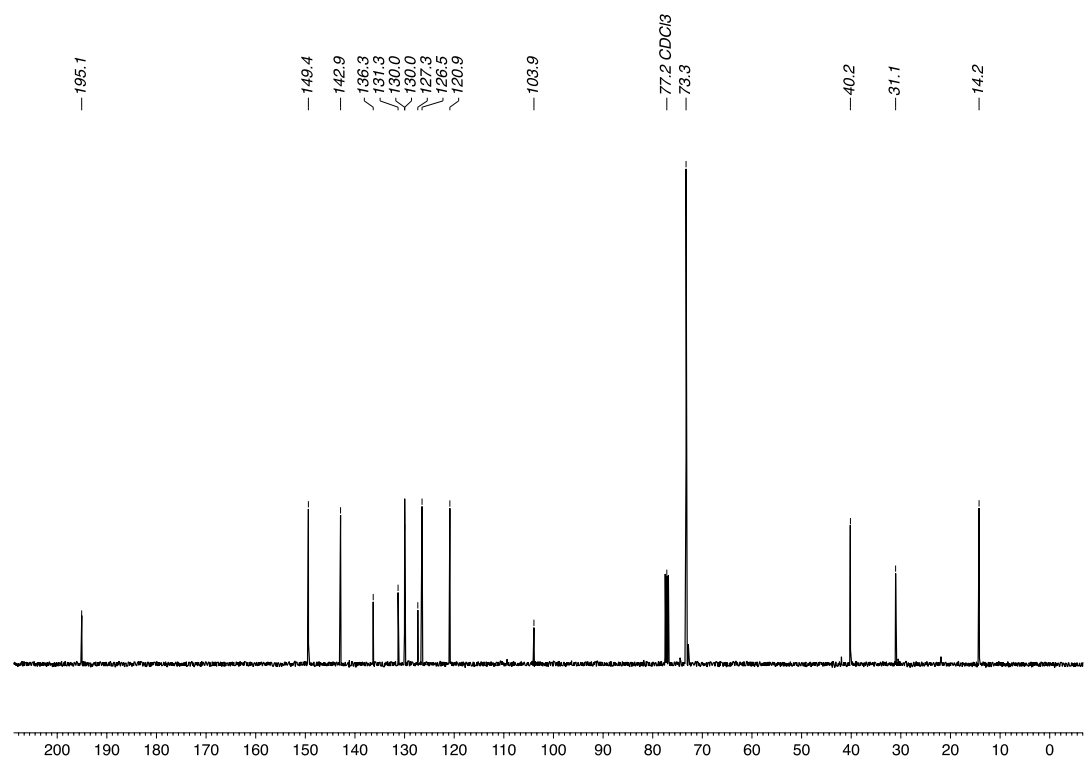
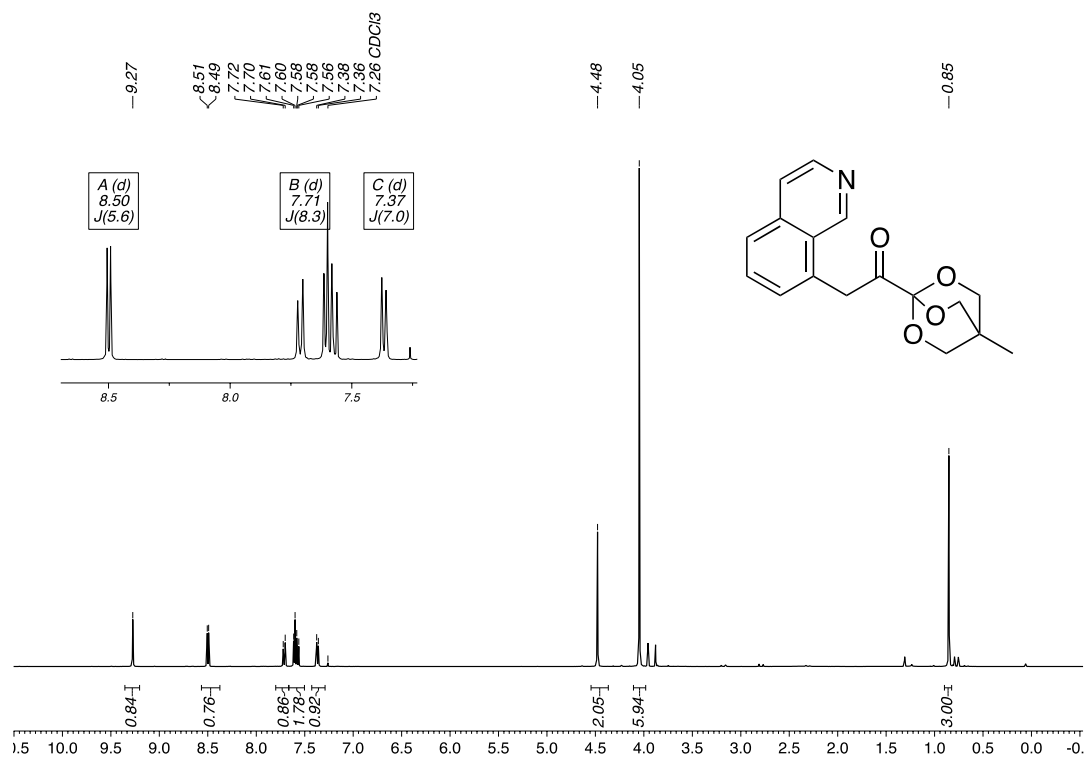


2-(1-Methyl-1*H*-indol-5-yl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-ethan-1-one (6p)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

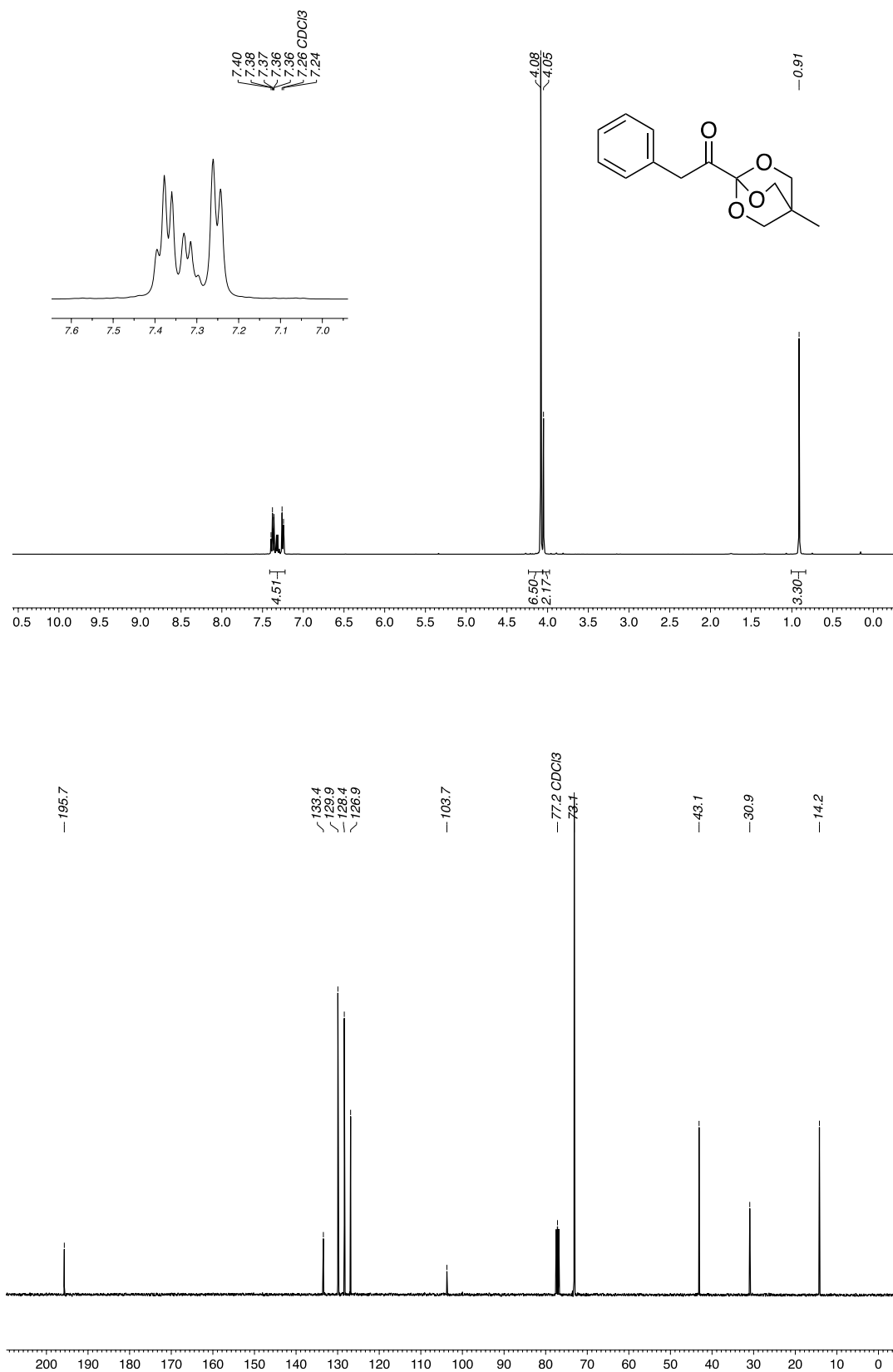


2-(Isoquinolin-8-yl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6q)
 Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

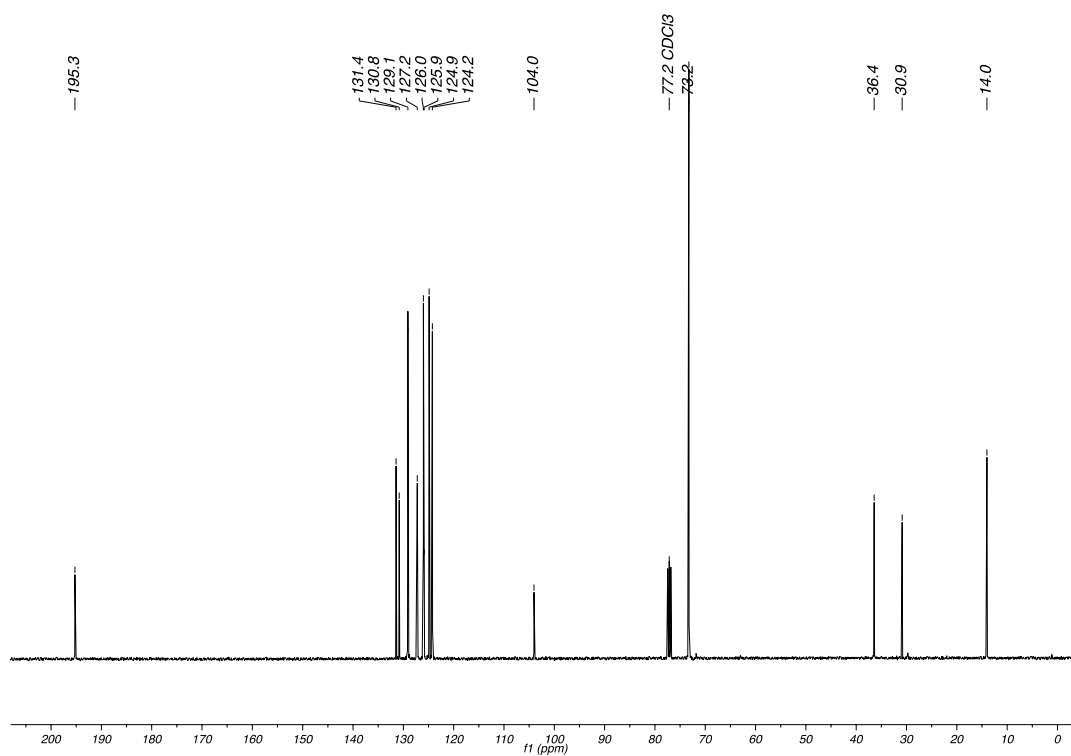


1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-phenylethan-1-one (6r)

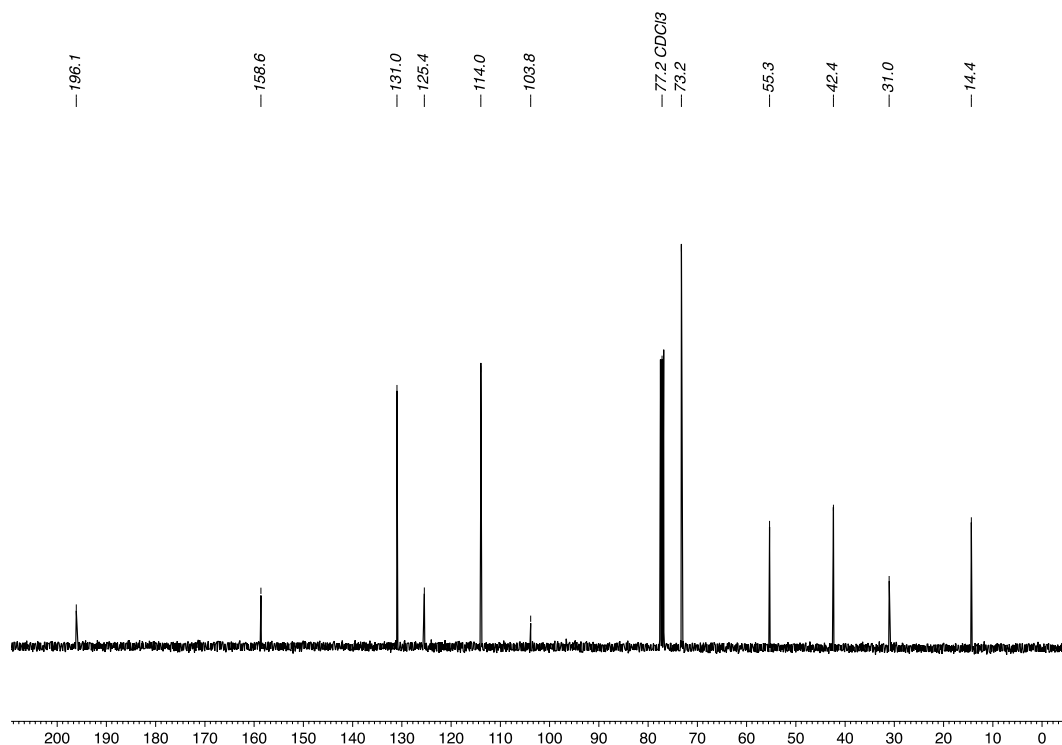
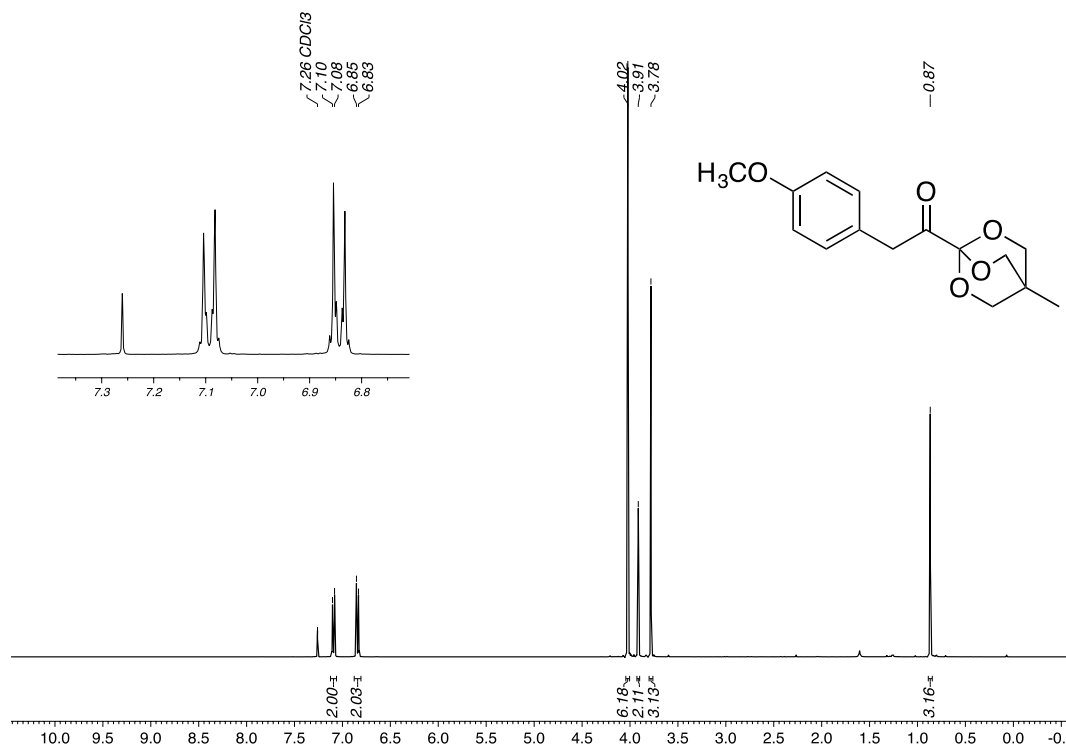
Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



2-(Anthracen-9-yl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6s)
 Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

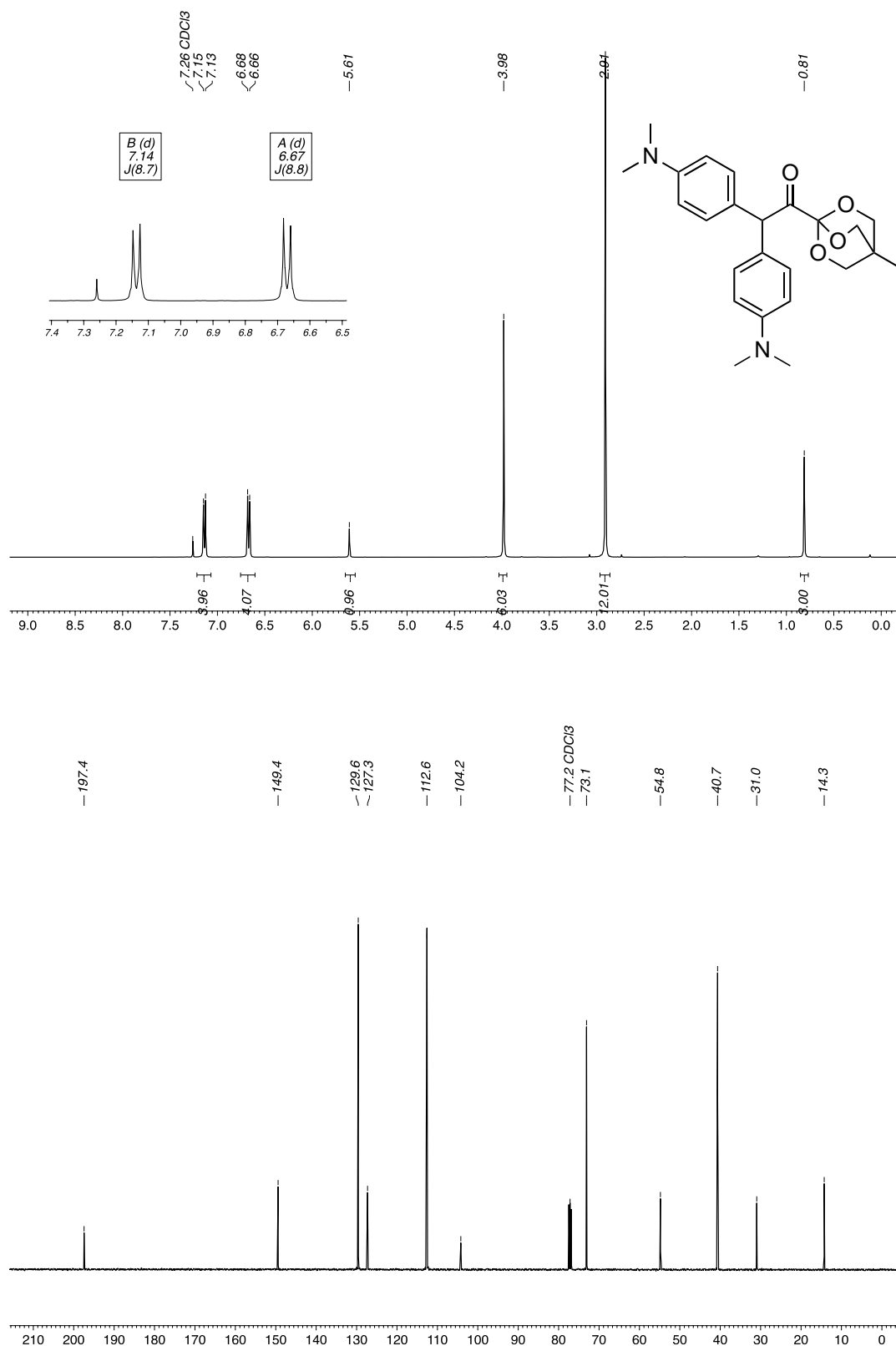


2-(4-Methoxyphenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)ethan-1-one (6t)
 Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



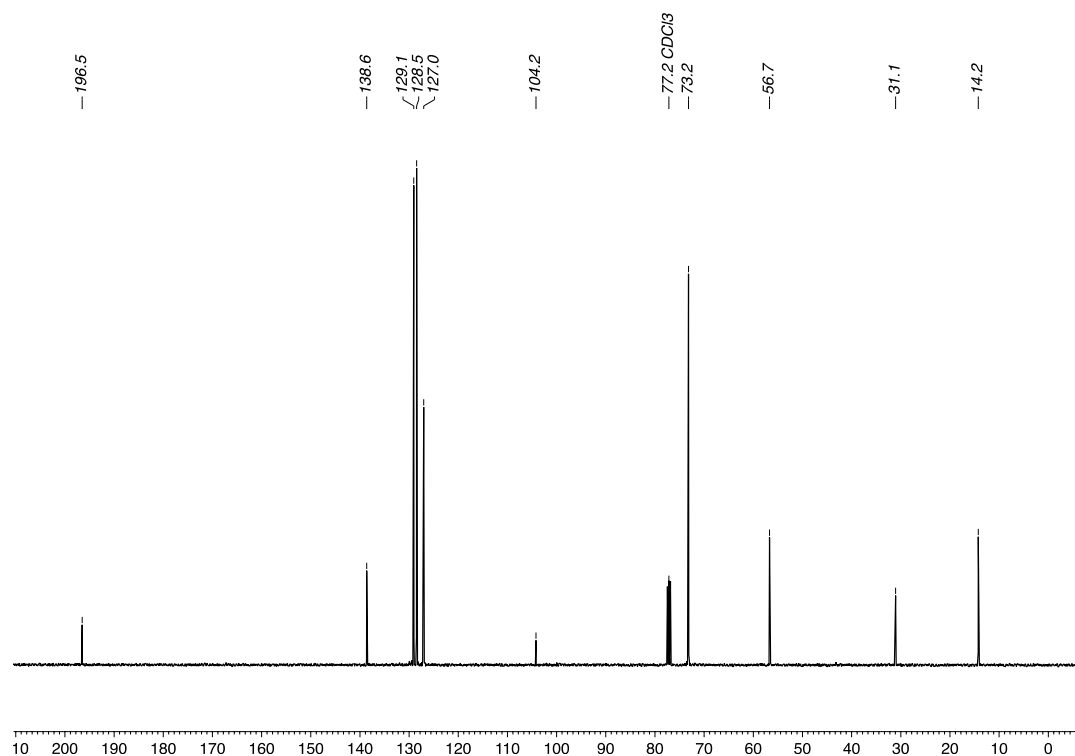
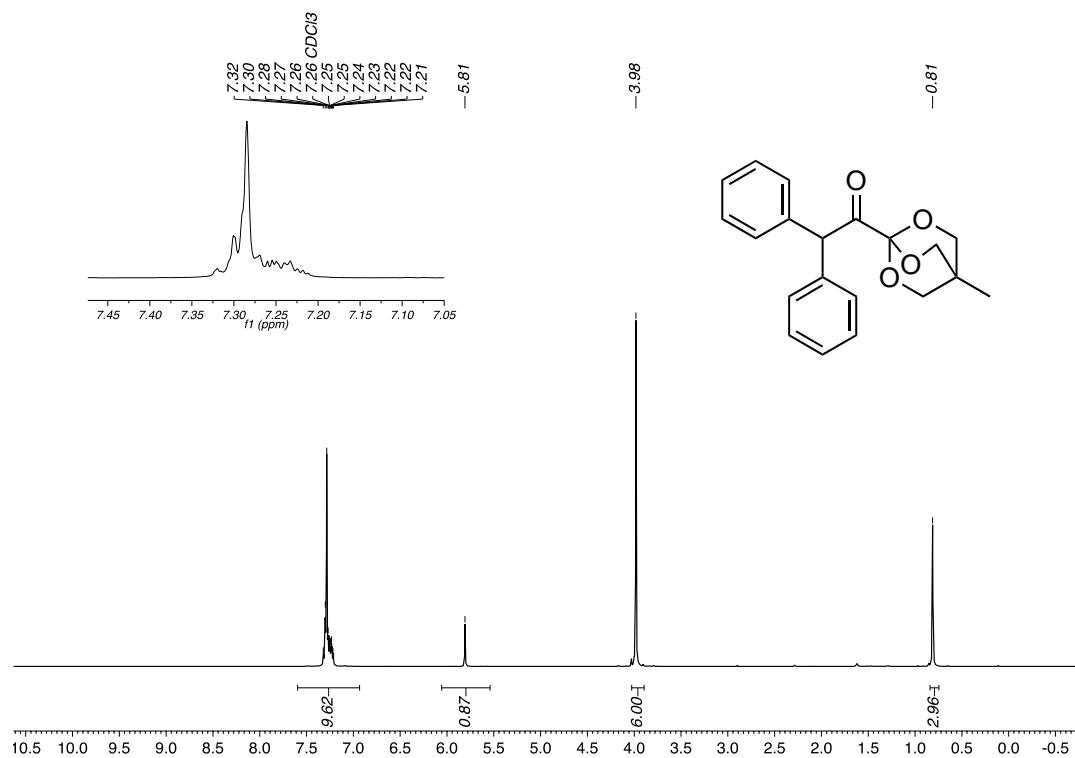
2,2-Bis(4-(dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-ethan-1-one (7a)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



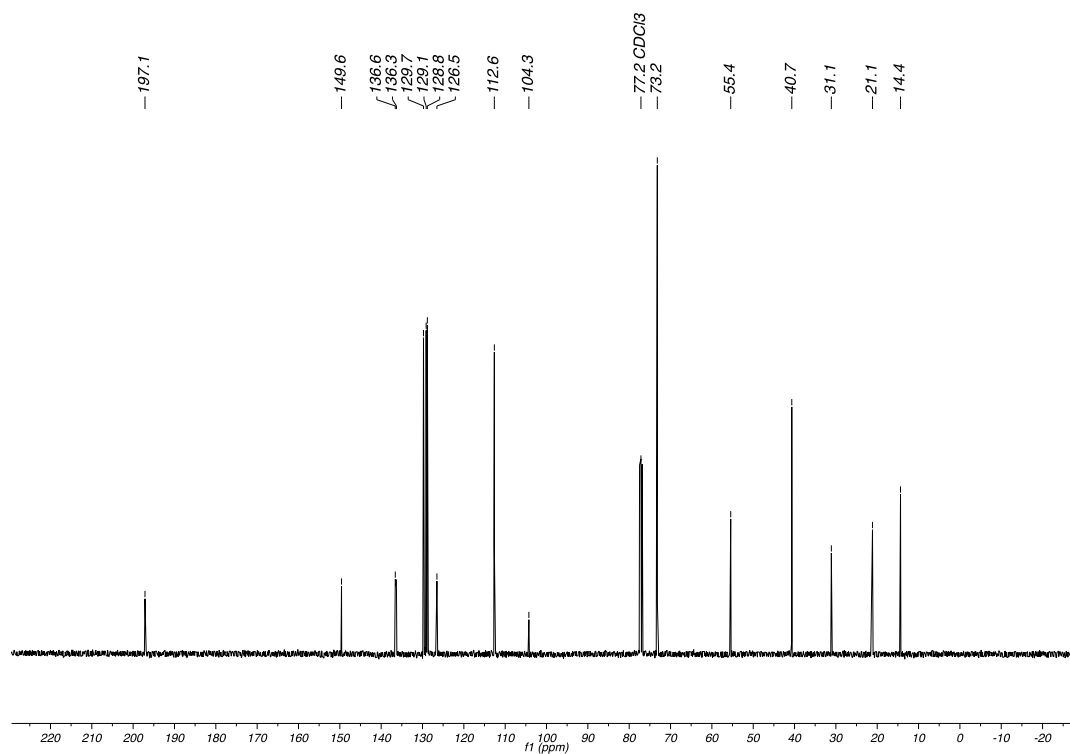
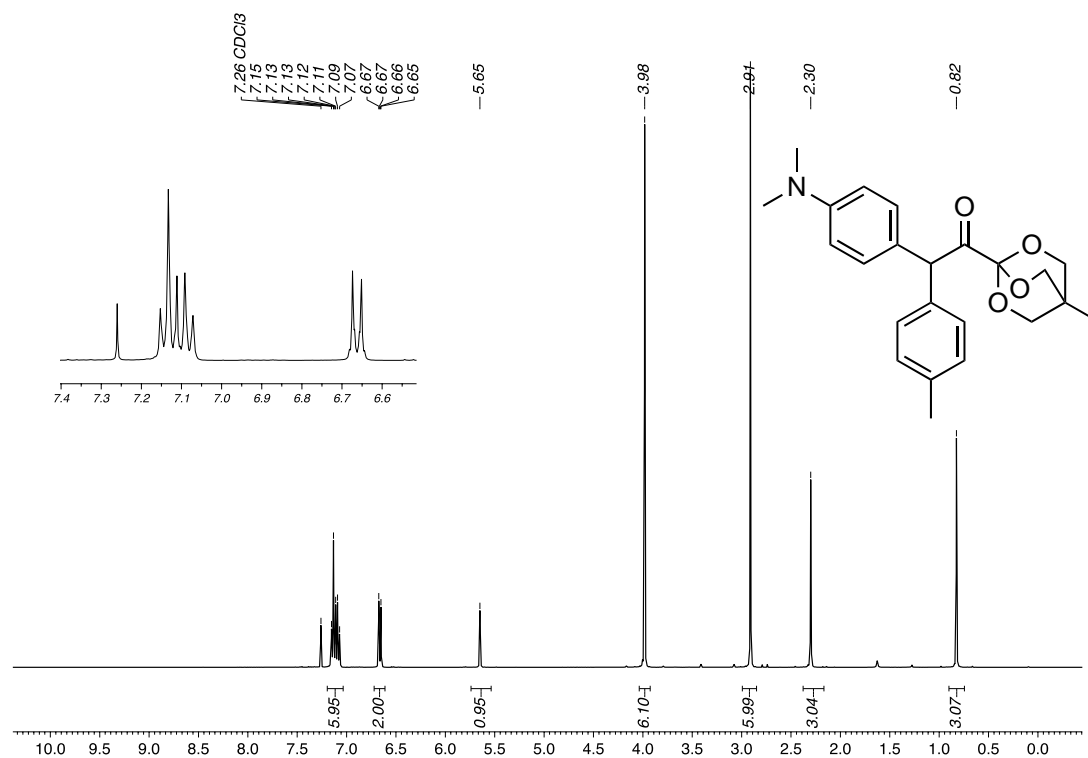
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2,2-diphenylethan-1-one (7b)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



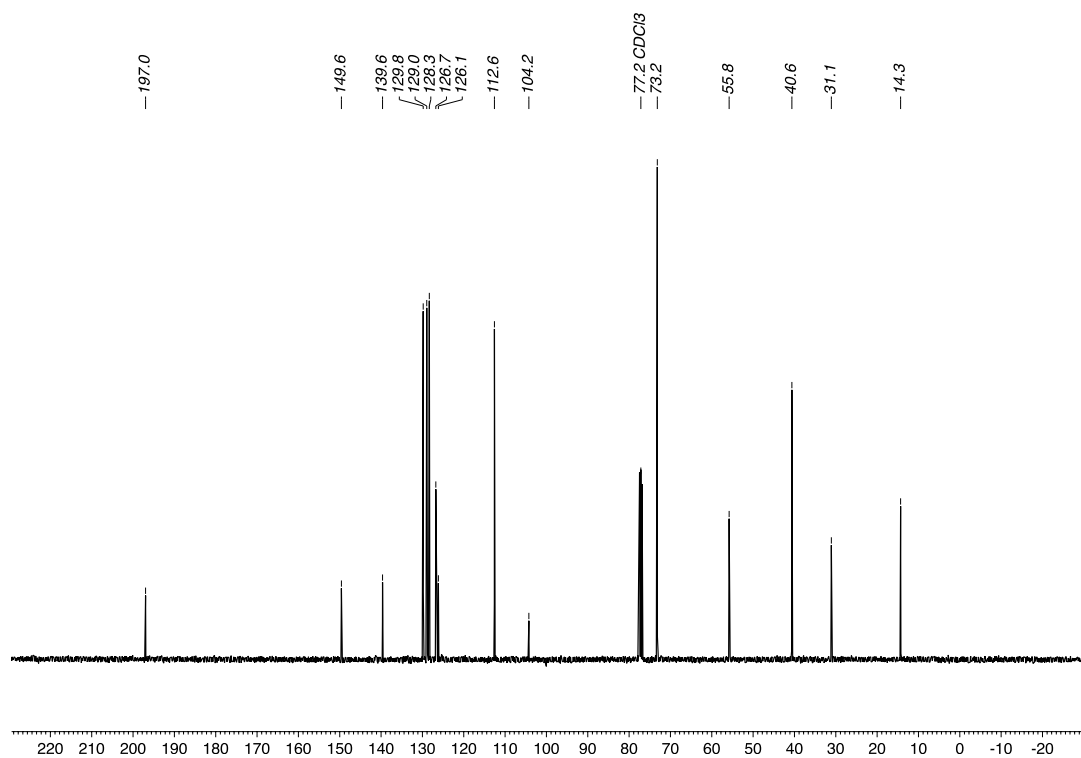
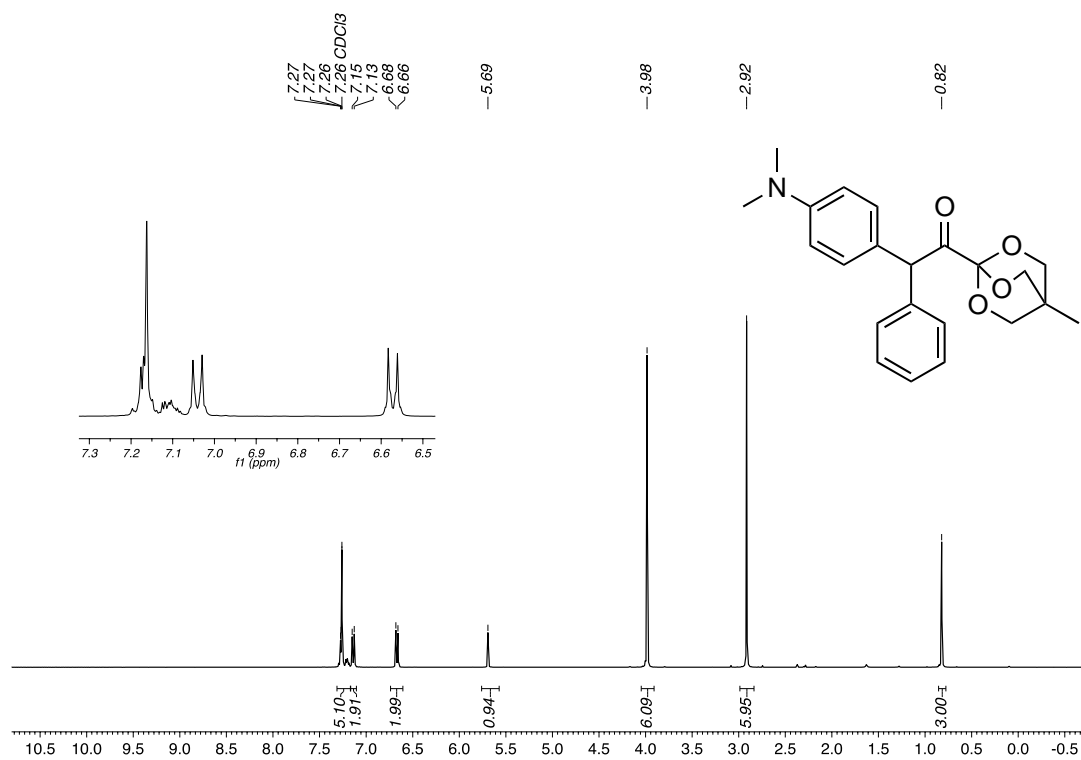
2-(4-(Dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(*p*-tolyl)ethan-1-one (7c)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



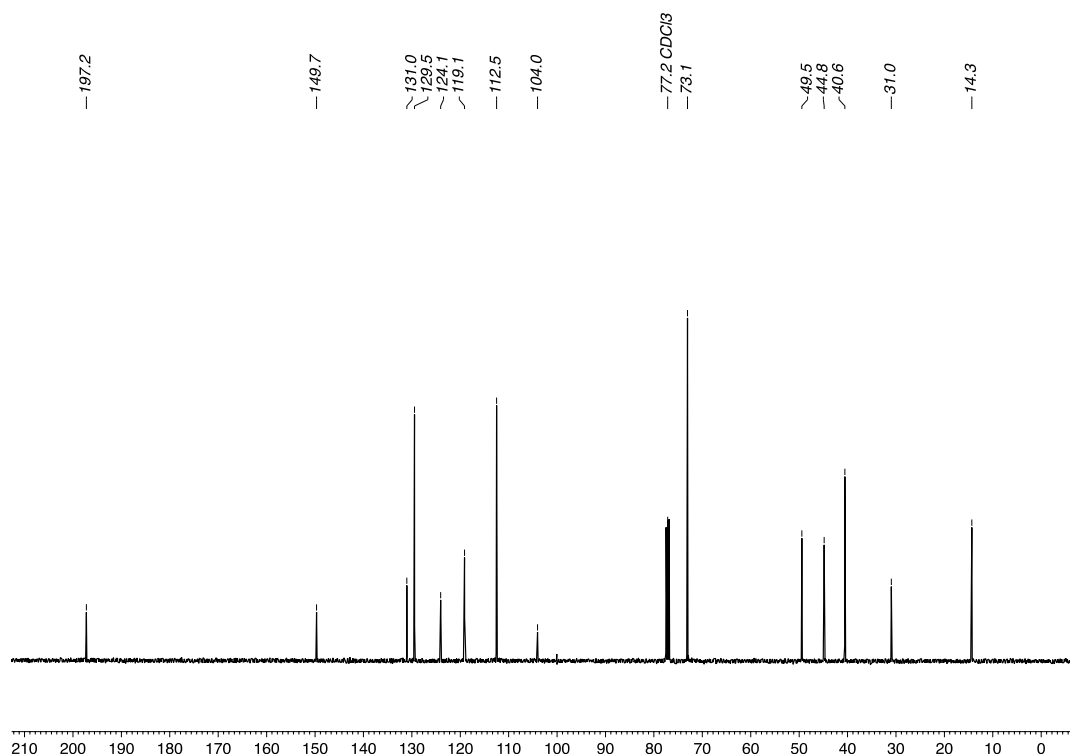
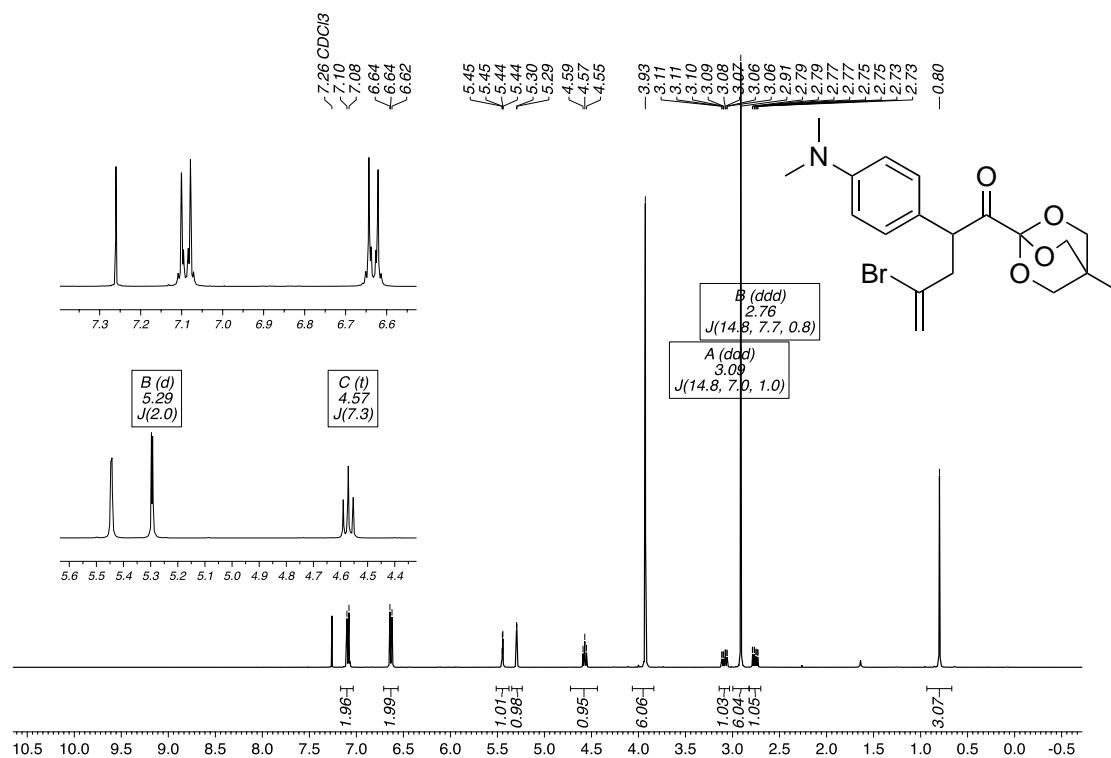
2-(4-(Dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-phenylethan-1-one (7d)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



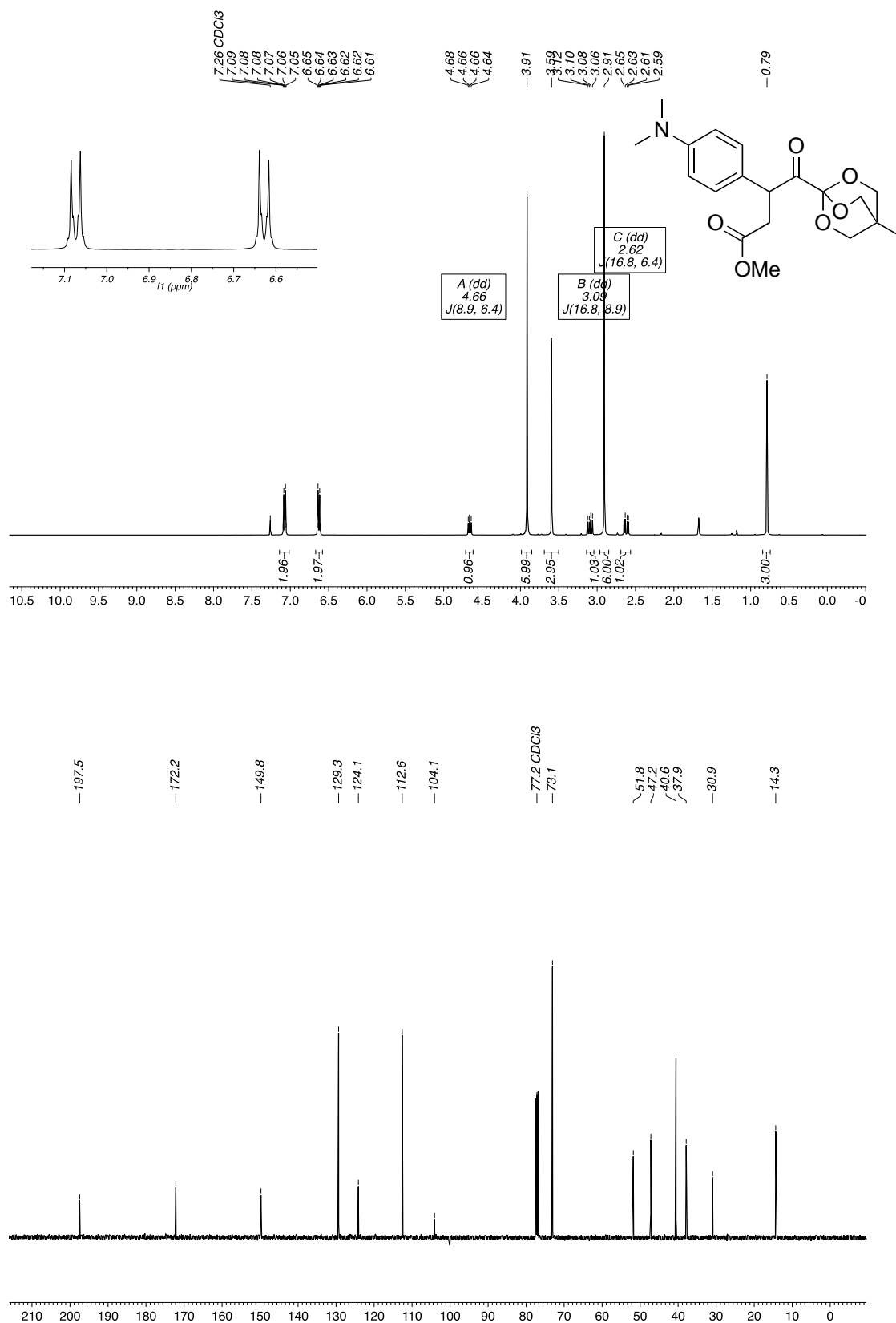
4-Bromo-2-(4-(dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]-octan-1-yl)pent-4-en-1-one (8a)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



Methyl 3-(4-(dimethylamino)phenyl)-4-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-4-oxobutanoate (8b)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

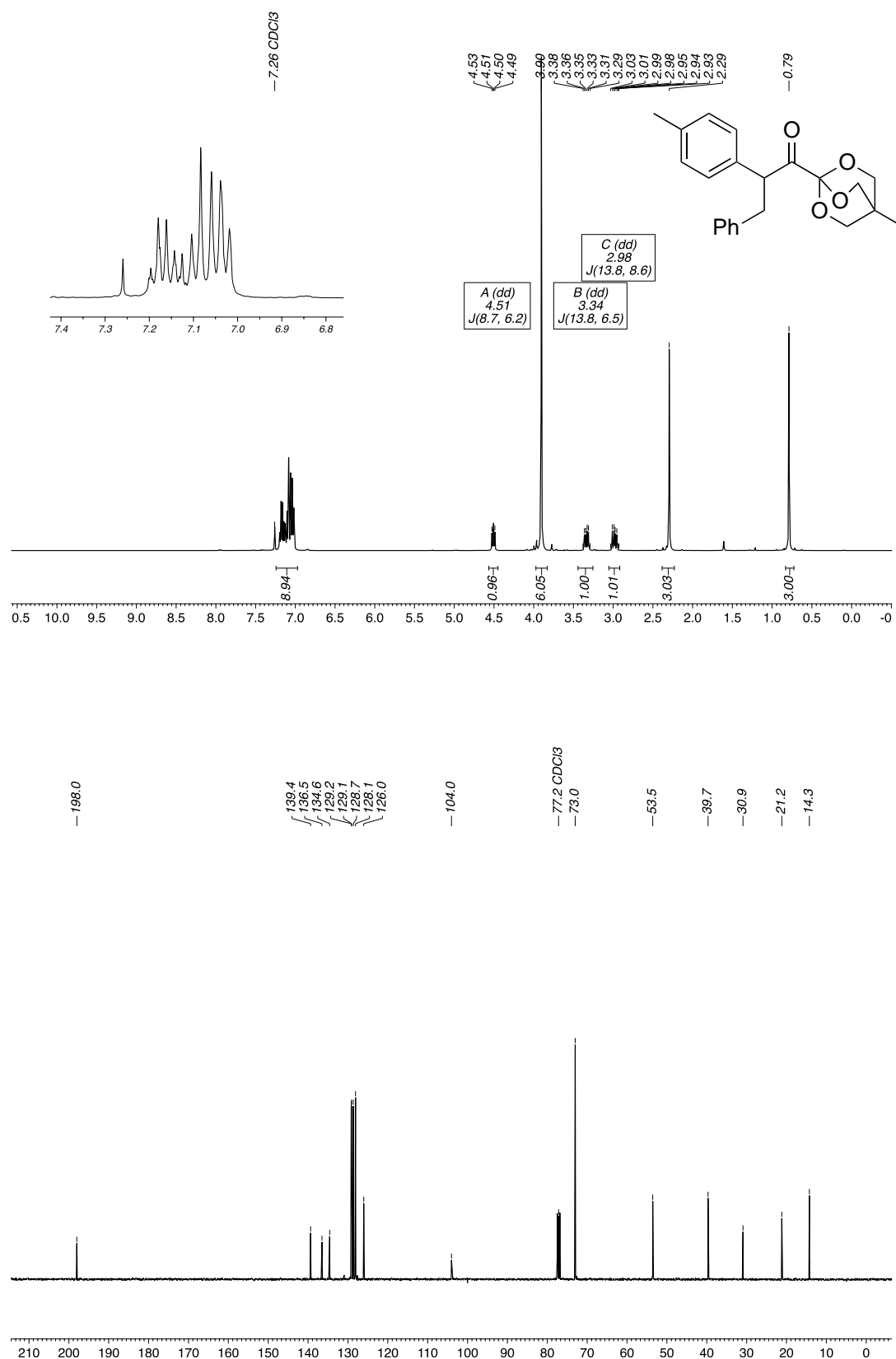


2-(4-(Dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)pent-4-yn-1-one (8c)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

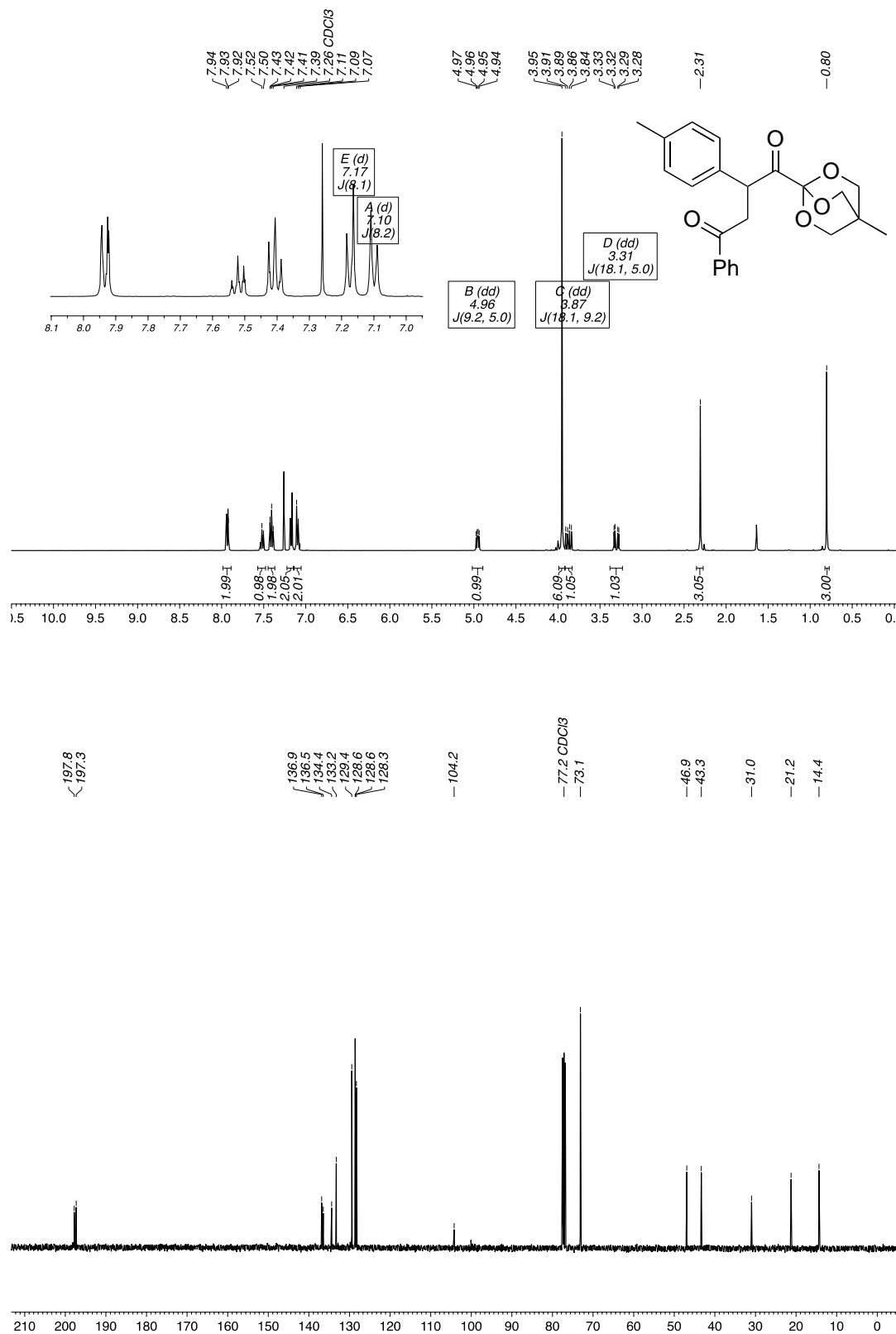


1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-3-phenyl-2-(*p*-tolyl)propan-1-one (8d)
 Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



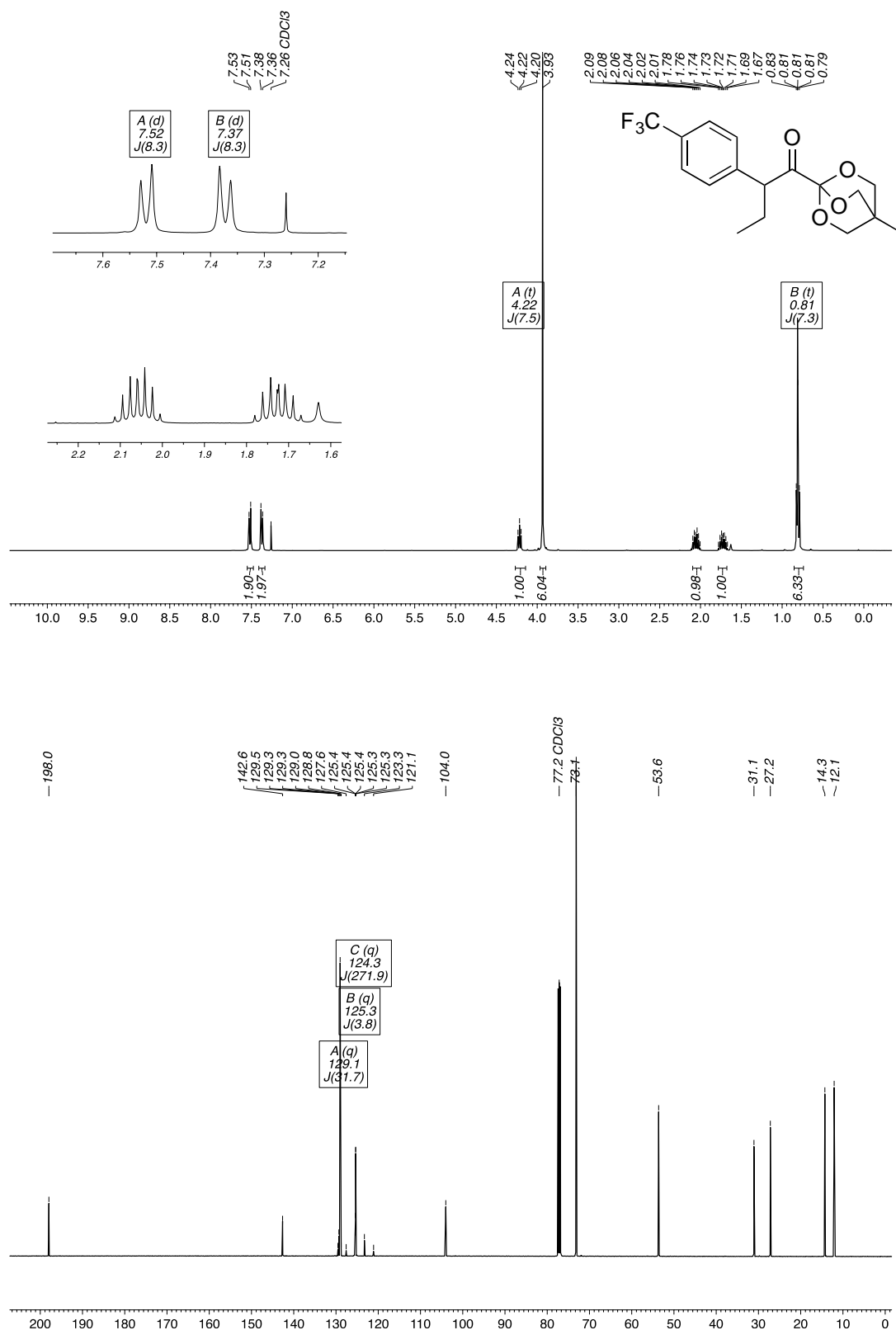
1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-4-phenyl-2-(*p*-tolyl)butane-1,4-dione (8e)

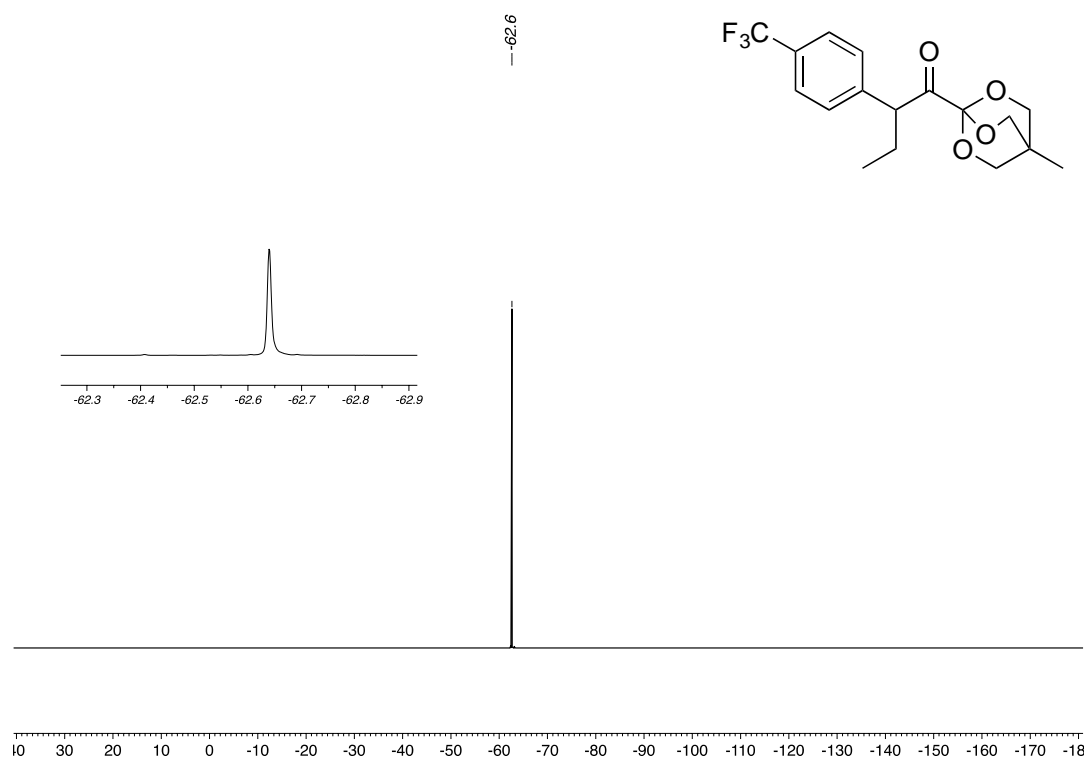
Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



1-(4-Methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)-2-(4-(trifluoromethyl)phenyl)-butan-1-one (8f)

Acquired in CDCl₃ – 400 MHz (¹H NMR), 101 MHz (¹³C NMR) and 376 MHz (¹⁹F).





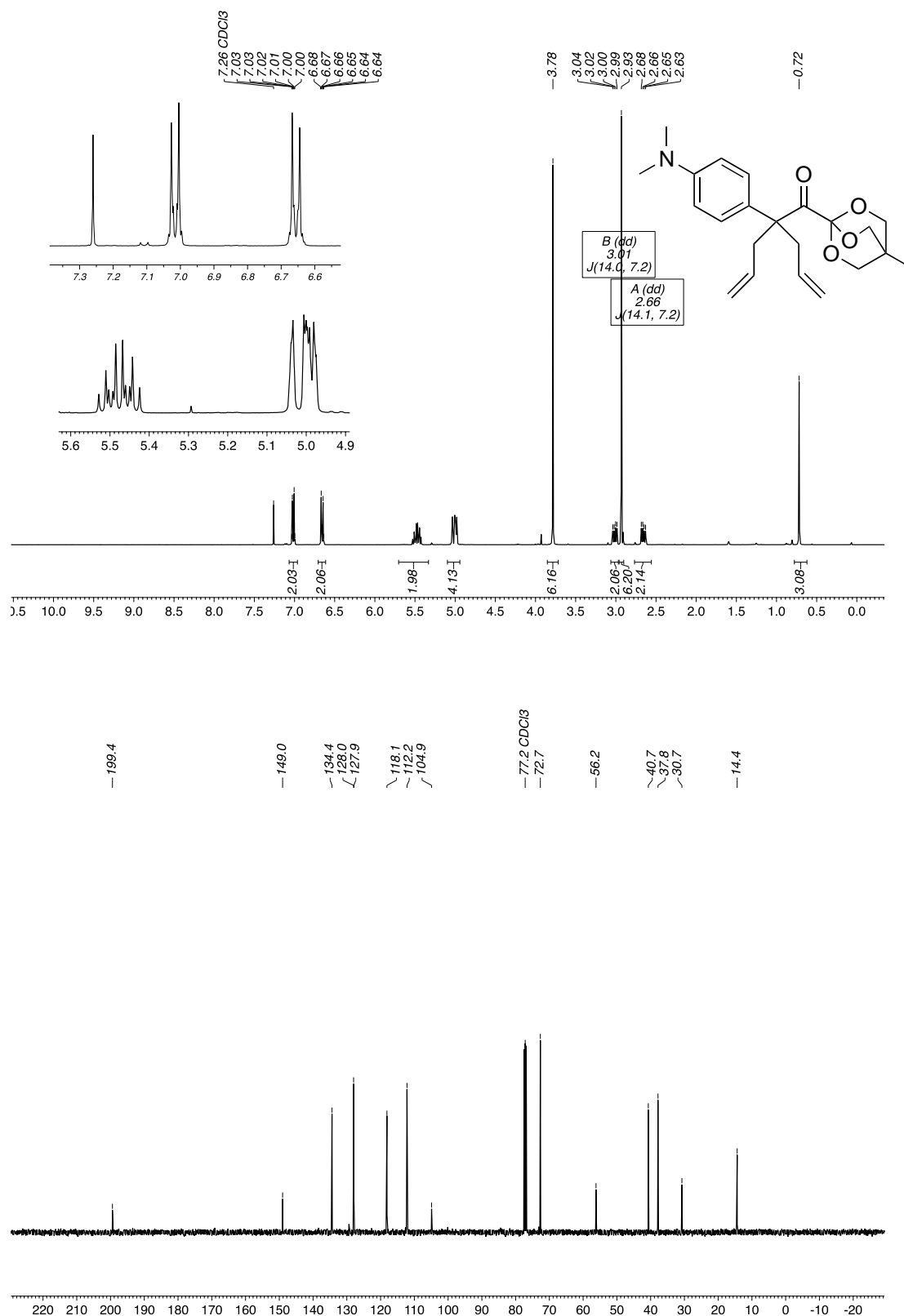
2-(4-(Dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)pent-4-en-1-one (8g)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



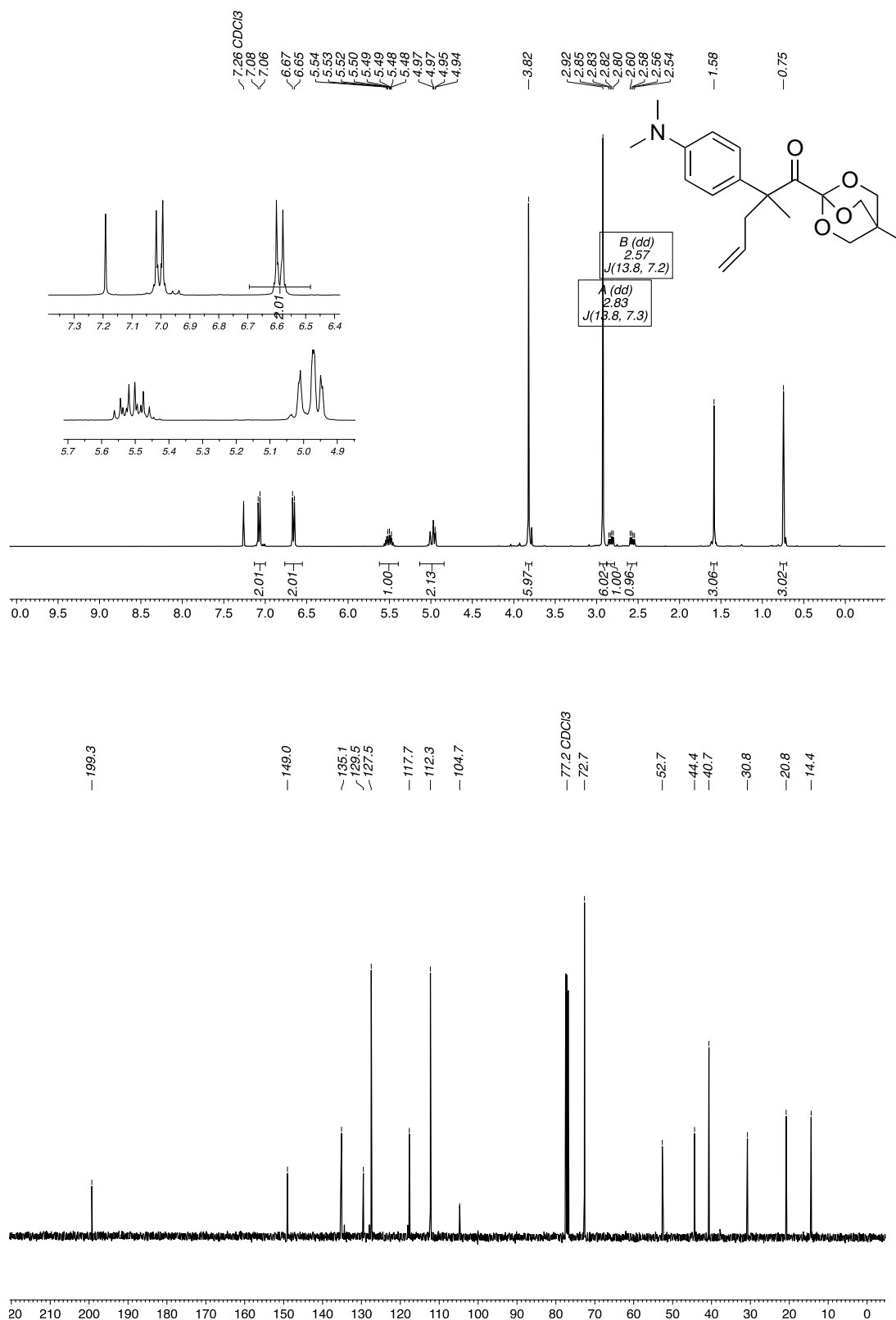
2-Allyl-2-(4-(dimethylamino)phenyl)-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]octan-1-yl)pent-4-en-1-one (8h)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



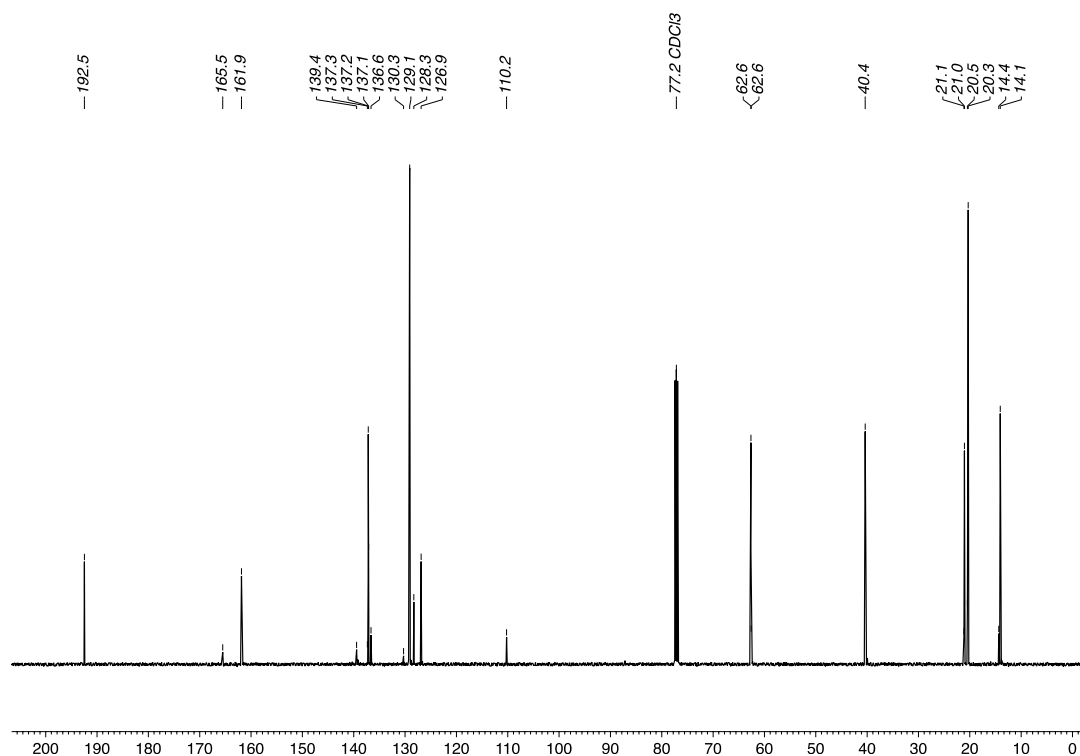
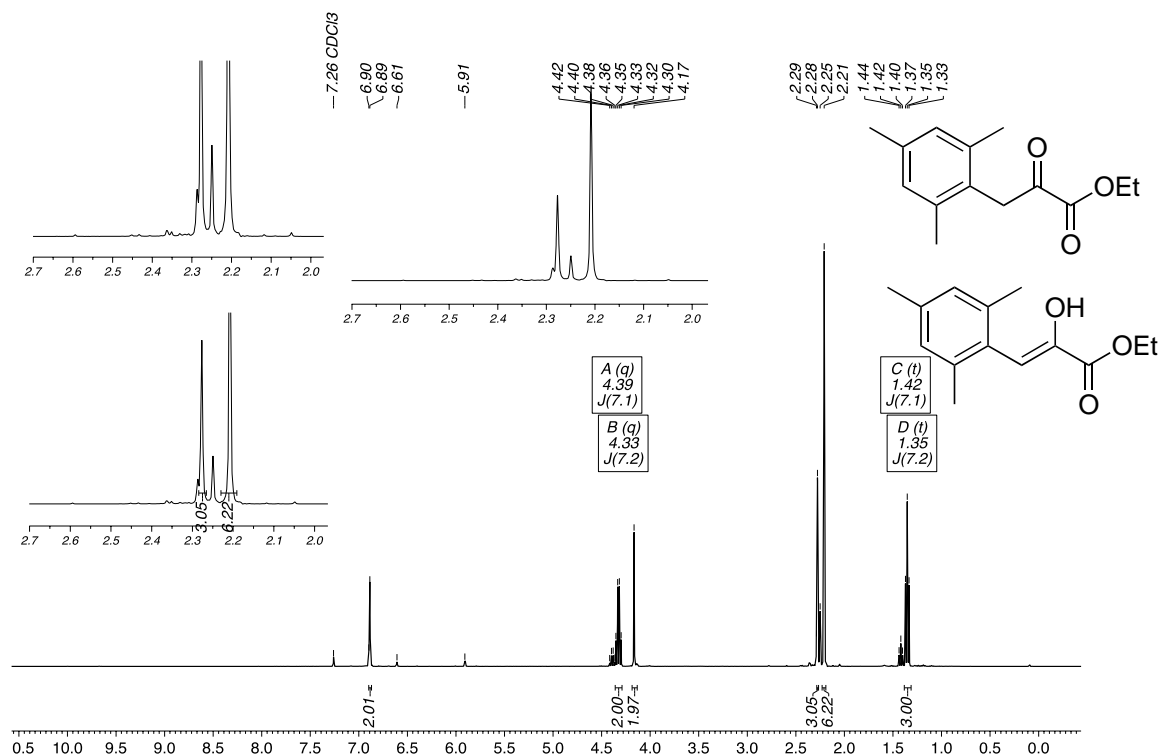
2-(4-(Dimethylamino)phenyl)-2-methyl-1-(4-methyl-2,6,7-trioxabicyclo[2.2.2]-octan-1-yl)pent-4-en-1-one (8i)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



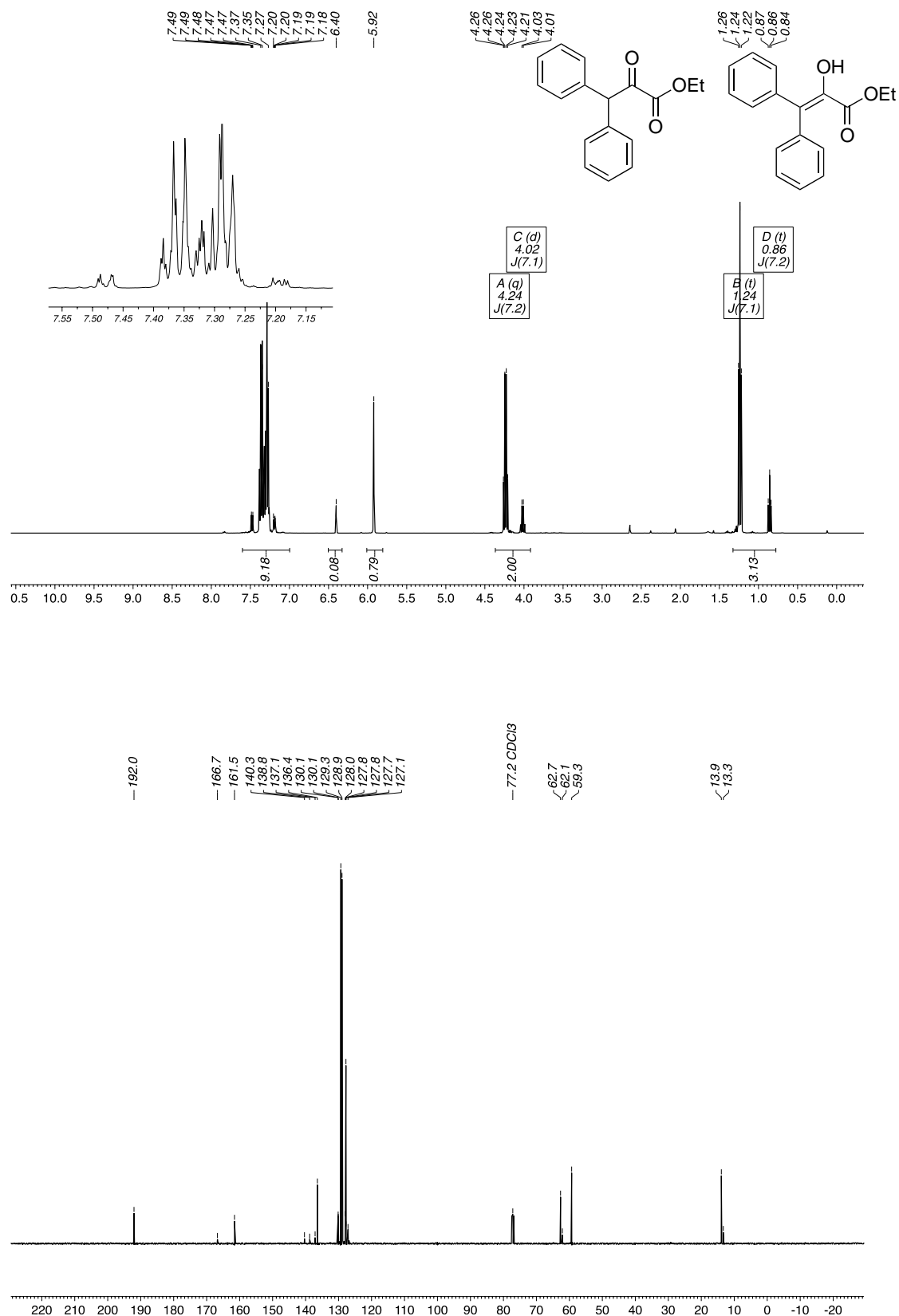
Ethyl 3-mesityl-2-oxopropanoate (9a)

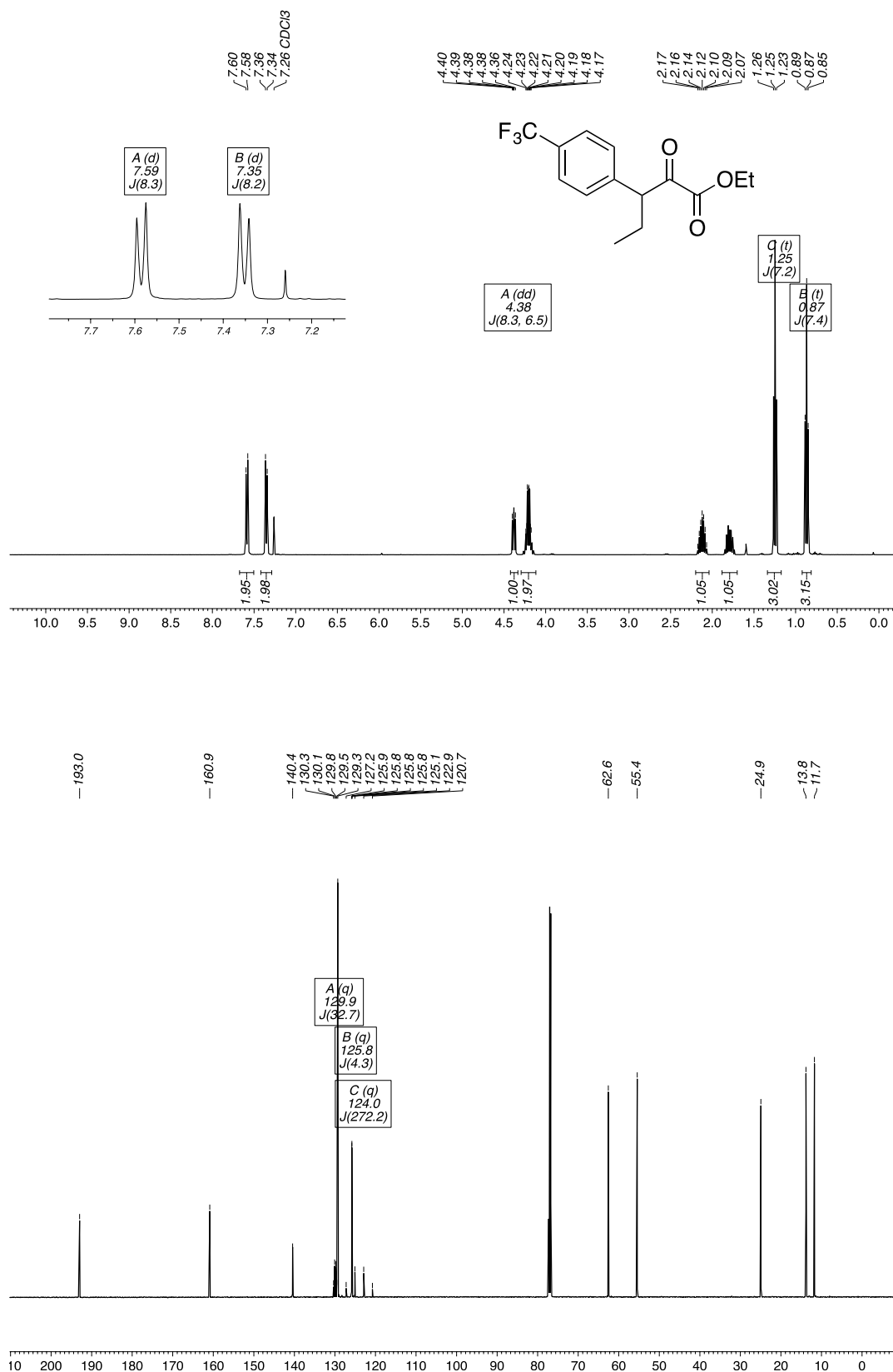
Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

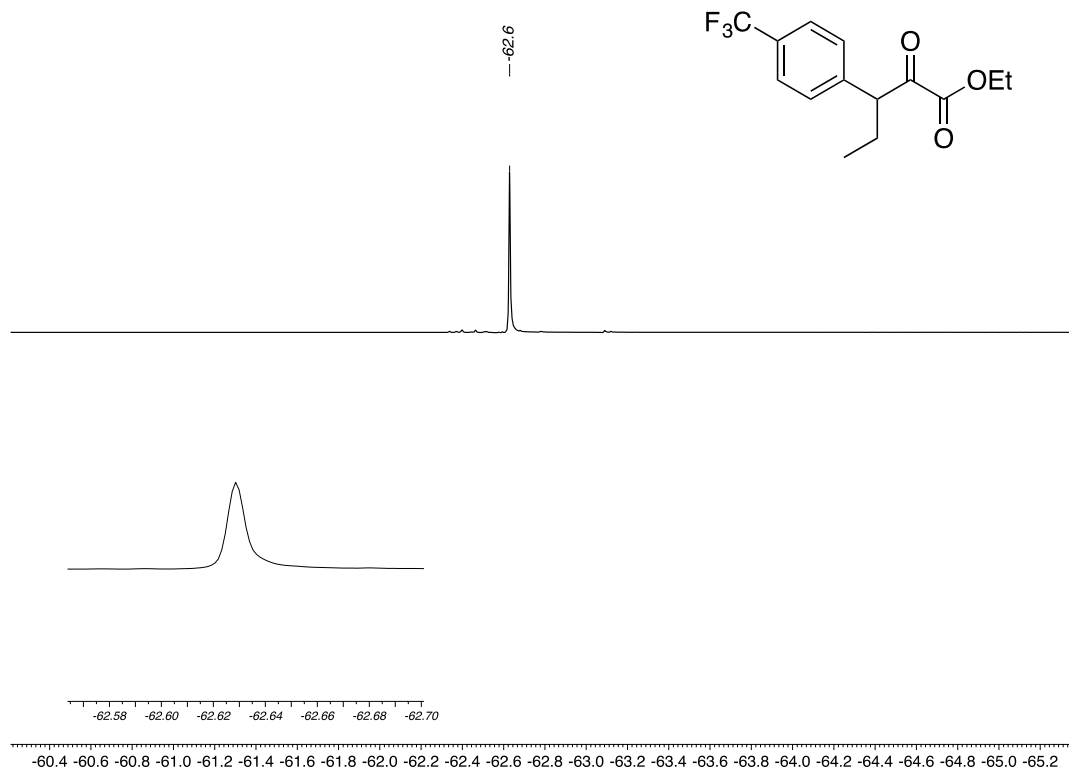


Ethyl 2-oxo-3,3-diphenylpropanoate (9b)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).

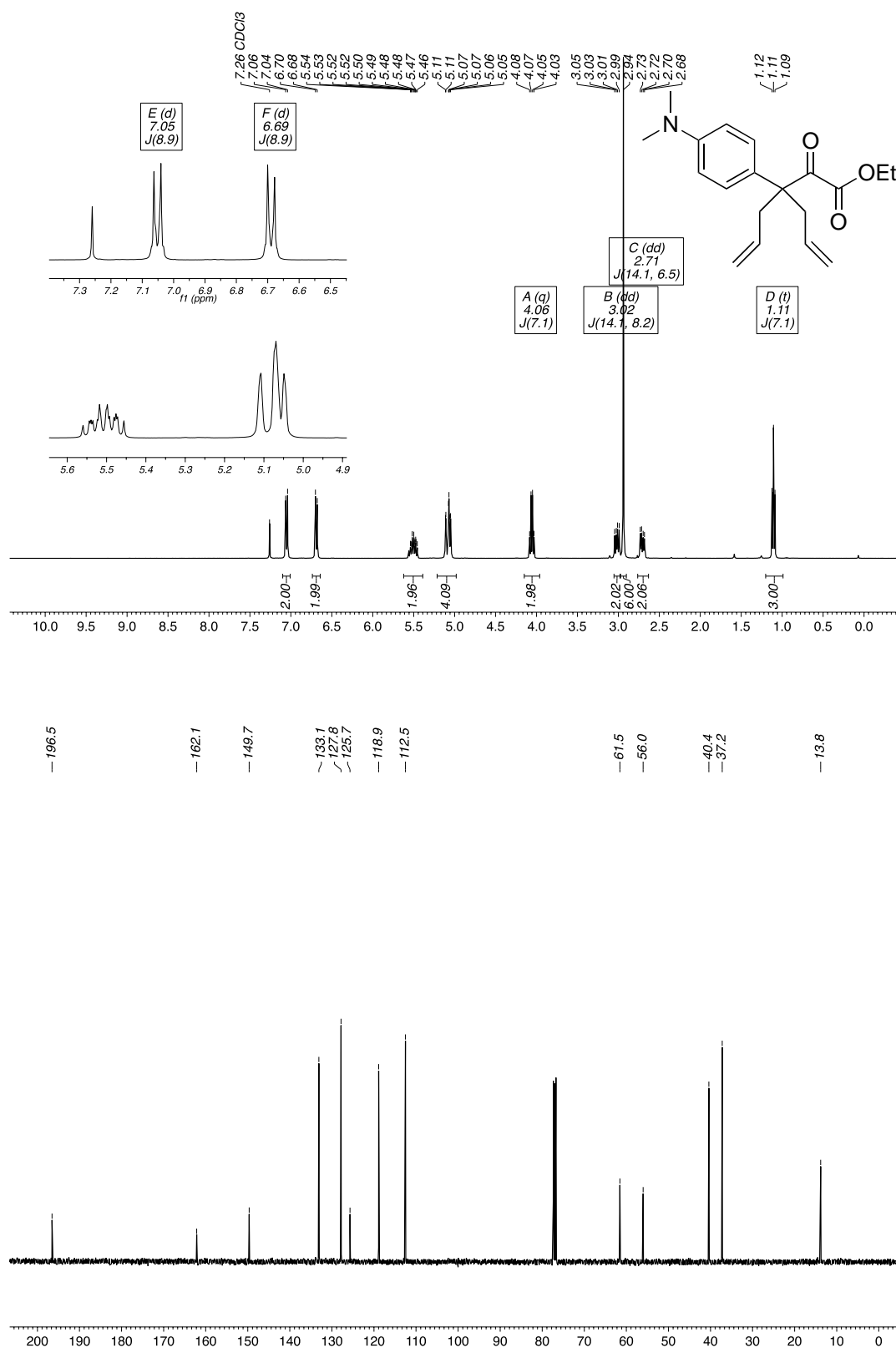


Ethyl 2-oxo-3-(4-(trifluoromethyl)phenyl)pentanoate (9c)Acquired in CDCl₃ – 400 MHz (¹H NMR), 101 MHz (¹³C NMR) and 376 MHz (¹⁹F).



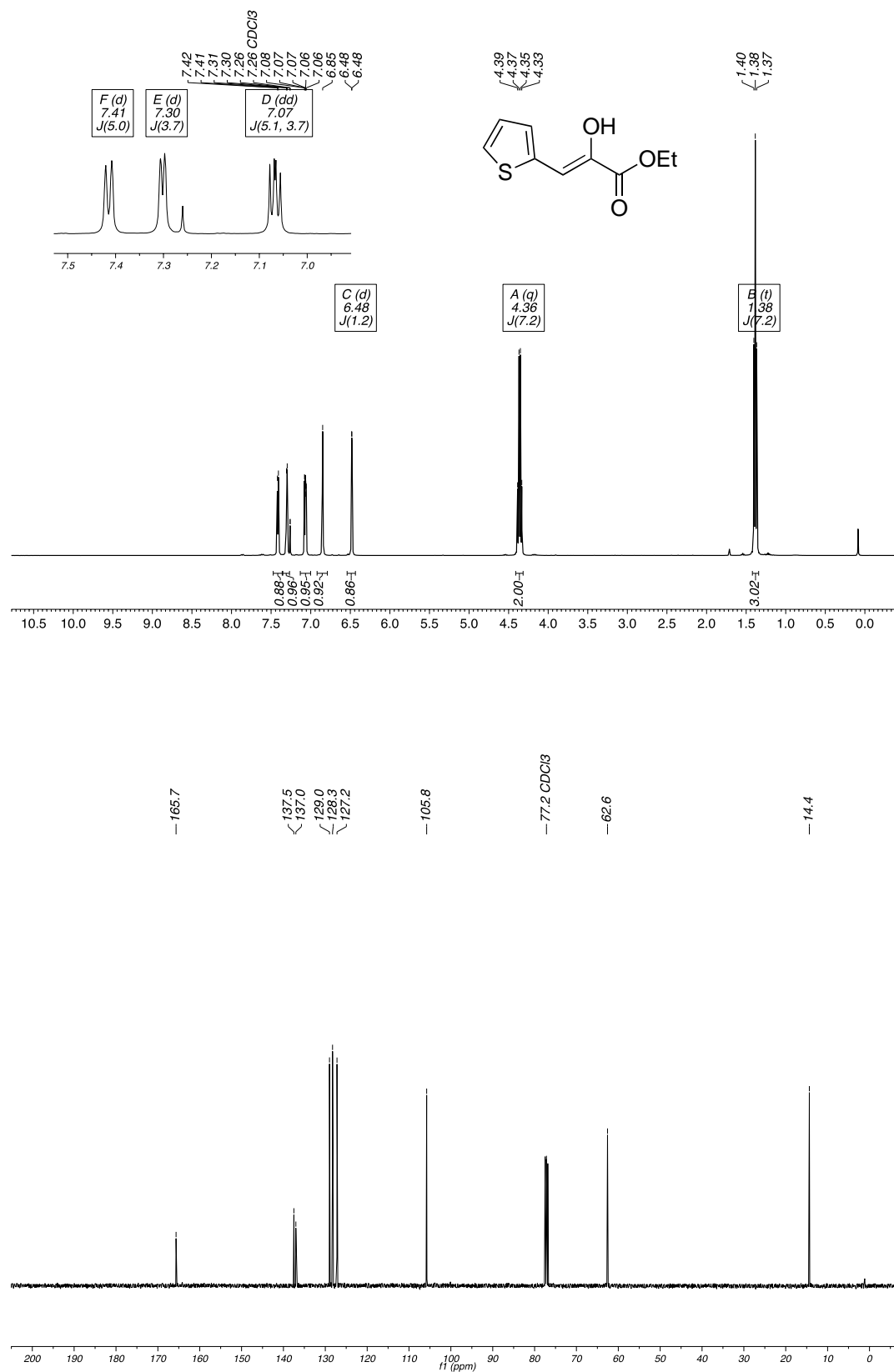
Ethyl 3-allyl-3-(4-(dimethylamino)phenyl)-2-oxohex-5-enoate (9d)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



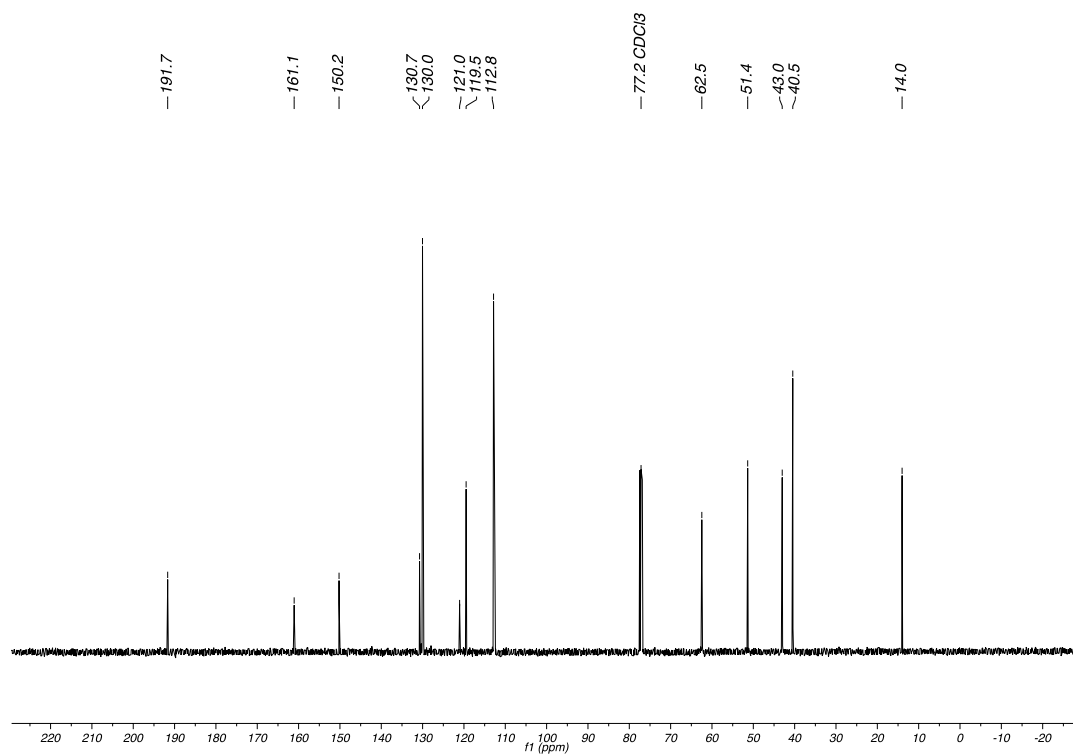
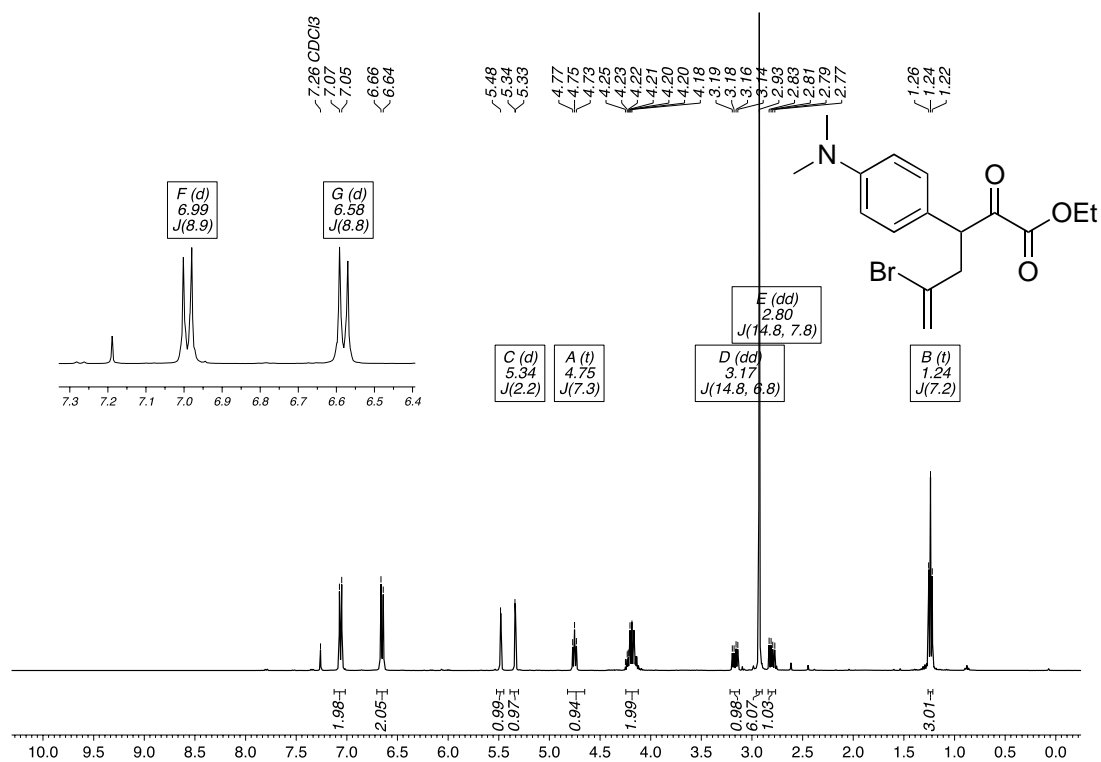
Ethyl (Z)-2-hydroxy-3-(thiophen-2-yl)acrylate (9e)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



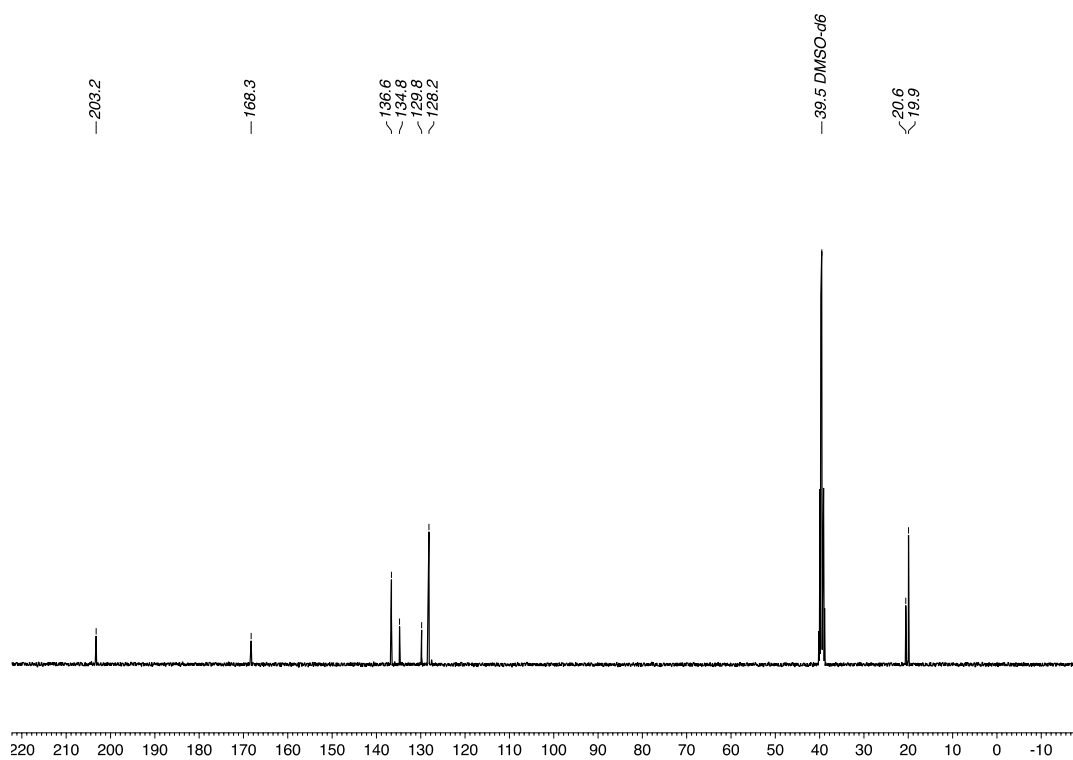
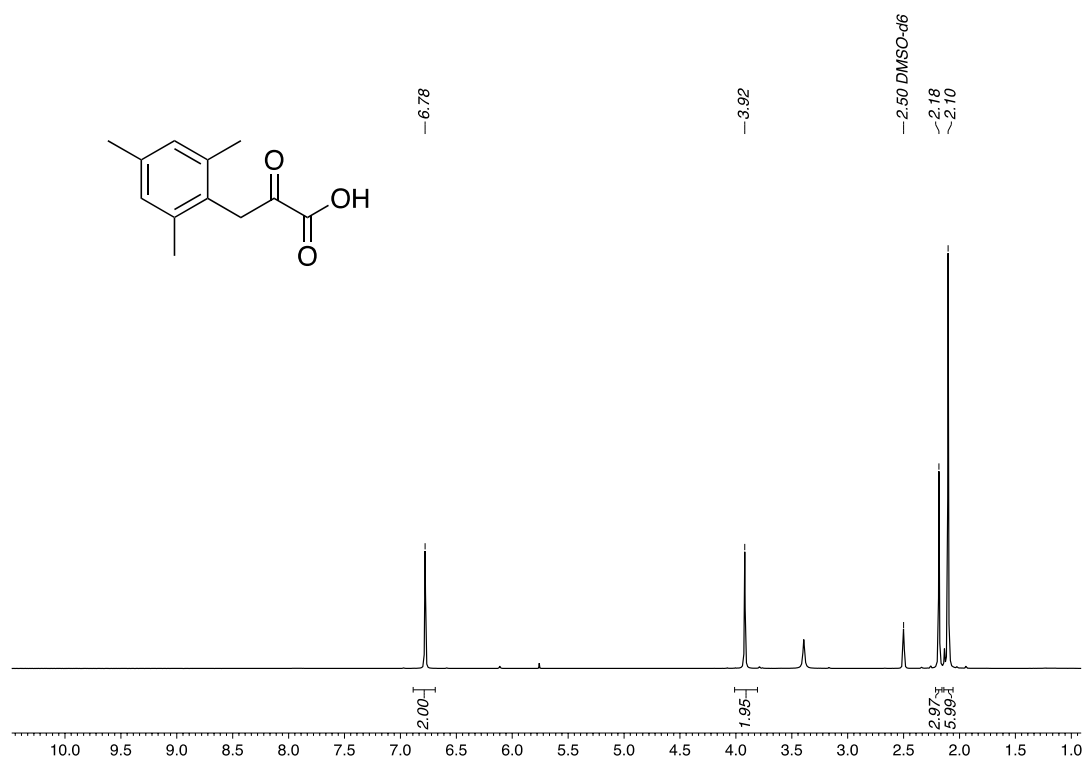
Ethyl 5-bromo-3-(4-(dimethylamino)phenyl)-2-oxohex-5-enoate (9f)

Acquired in CDCl₃ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



3-Mesityl-2-oxopropanoic acid (10)

Acquired in DMSO-d₆ – 400 MHz (¹H NMR) and 101 MHz (¹³C NMR).



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- ³ Norimura, Y.; Yamamoto, D.; Makino, K. *Organic and Biomolecular Chemistry* **2017**, *15*, 640–648.
- ⁴ Solladié-Cavallo, A.; Lupattelli, P.; Bonini, C.; De Bonis, M. *Tetrahedron Letters* **2003**, *44*, 5075–5078.