

High-Load, Hybrid Si-ROMP Reagents

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General Procedures

All air and moisture sensitive reactions were carried out in flame- or oven-dried glassware under argon atmosphere using standard gastight syringes, and septa. CH₂Cl₂ and toluene were purified by passage through a Solv-Tek¹ (www.solvtek.com) purification system employing activated Al₂O₃ and degassed with argon. Flash column chromatography was performed with SiO₂ (Sorbent Technologies 30930M-25, Silica Gel 60 Å, 40-63 µm). Thin layer chromatography was performed on silica gel 60F 254 plates. Visualization of TLC spots was effected using KMnO₄ stain. ¹H and ¹³C NMR spectra were recorded in CDCl₃ (unless otherwise mentioned) on a Bruker DRX-500 spectrometer operating at 500 MHz, and 125 MHz, respectively and calibrated to the solvent peak. High-resolution mass spectrometry (HRMS) was recorded on a LCT Premier Spectrometer (Micromass UK Limited) operating on ESI (MeOH). The nanoparticles were analyzed by scanning electron microscopy (Hitachi S-2700 equipped with a quartz PCI digital capture) and FTIR Perkin Elmer Spectrum 100 FT-IR spectrometer. All other commercially available compounds were used as received. Metathesis catalyst [(IMesH₂)(PCy₃)(Cl)₂Ru=CHPh was provided by Materia Inc. and used without further purification. Deuterated solvents were purchased from Cambridge Isotope laboratories.

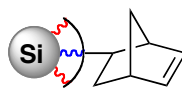
[1] R. H. Grubbs, R. K. Rosen, F. J. Timmers, *Organometallics* **1996**, *15*, 1518.

General procedure A for tagging of silica-particles with 5-(Bicycloheptenyl)-triethoxysilane to yield Nb-tagged silica 2.

Spherical silica (50g) [70Å, 20 μm particle size] was heated under vacuum at 200 °C for 48 h. After such time, the silica was cooled to 0 °C under Ar and suspended in dry CH₂Cl₂ (0.46M, 150 cm³). To this stirring slurry was added 5-(bicycloheptenyl)-triethoxysilane (15.0g, 58.4 mmol) and the reaction was heated at 50 °C for 24 h. Trimethoxymethylsilane (12 cm³, 84.1 mmol) and dimethoxydimethylsilane (8 cm³, 57.4 mmol) was added to the crude reaction mixture, which was heated at 50 °C for an additional 30-40 h. Upon completion the crude reaction was filtered, washed with CH₂Cl₂ (4 x 50 cm³), collected and dried under vacuum to yield Si-Nb **2** (average load = 5x10⁻⁵ mol).

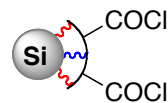
General procedure B for the grafting of norbornenyl monomers via surface-initiated ROMP from Si-Nb 2.

To a stirring suspension of norbornenyl-tagged silica particles Si-Nb **2** (1 eq.) in dry CH₂Cl₂ (0.016M), was added cat-**B** (0.6-0.8 equiv.). The reaction mixture was heated at 45 °C for 30 min, and added to a solution of Nb-monomer (50 equiv. for 50-mer) in dry CH₂Cl₂. The reaction mixture was heated further for 30 min – 2 h, and monitored via TLC for disappearance of Nb-monomer. After such time, the reaction was cooled to RT, whereby the reaction was quenched by addition of ethyl vinyl ether (EVE) (5-10 drops). The crude reaction was filtered, washed with CH₂Cl₂ (4x), dried under vacuum, and ground to a fine powder when required, to yield the desired hybrid material as an off white, free flowing powder.



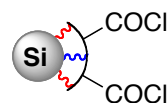
Norbornenyl-tagged Silica particles (Si-Nb) 2

FTIR (ν/cm^{-1}) 1062, 801.



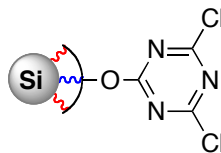
Silica-oligomeric bis-acid chloride hybrid (Si-OBAC₅₀) 4

FTIR (ν/cm^{-1}) 1782, 1042, 796.



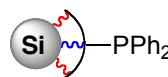
Silica-oligomeric bis-acid chloride hybrid (Si-OBAC₁₀₀) 5

FTIR (ν/cm^{-1}) 1776, 1046, 793.



Silica-oligomeric dichlorotriazine (Si-ODCT₅₀) 7

FTIR (ν/cm^{-1}) 1700, 1542, 1394, 1042, 804.



Silica-oligomeric triphenylphosphine (Si-OTPP₅₀) 9

FTIR (ν/cm^{-1}) 1694, 1541, 1511, 1397, 1302, 1258, 1042, 803.

Example theoretical Load calculation: Si-OBAC₁₀₀ 5

2.37 g hybrid material = 1.37 g OBAC + 1.0 g Silica

divide by 1.37 = 1.0 g OBAC + 0.729 g Silica

OBAC load = 9.1 mmol/g

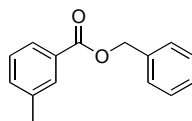
Therefore, Si-OBAC₁₀₀ load = 9.1 mmol/(1.0 g OBAC + 0.729 g Silica)

= 9.1 mmol/1.729 g

= 5.26 mmol/g

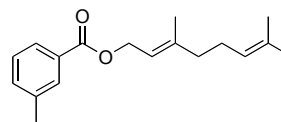
General procedure C for the coupling of benzoyl chlorides and alcohols for the synthesis of benzylesters 6 a – h utilizing Si-OBAC scavenging.

To a 1 dram vial, was added alcohol (1.5 equiv., 0.403 mmol), Et₃N (1 equiv., 0.269 mmol), and dry CH₂Cl₂ (0.1 M). The reaction mixture was stirred for 10 min, followed by the addition of carboxylic acid chloride (1 equiv., 0.269 mmol). The reaction was stirred for 2 h at RT, after which time, Si-OBAC₅₀ **4** or **5** (1 eq. 0.269 mmol) was added and the reaction was stirred for an additional 2 – 4 h (TLC monitoring). Upon completion, the reaction was filtered through a celite SPE and concentrated under *vacuum* to yield the desired ester.



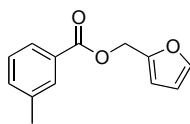
Benzyl 3-methylbenzoate (6a).

According to general procedure C, **6a** (55.9 mg, 0.24 mmol, 92 %) was isolated as a clear oil. ¹H NMR (500 MHz, CDCl₃) δ 7.90 (dd, *J* = 4.9, 4.2 Hz, 2H), 7.46 (dt, *J* = 3.3, 2.2 Hz, 2H), 7.43 – 7.36 (m, 3H), 7.36 – 7.31 (m, 2H), 5.36 (d, *J* = 7.5 Hz, 2H), 2.40 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 166.6, 138.2, 136.1, 133.8, 130.2, 130.0, 128.6, 128.3, 128.2, 126.8, 66.6, 21.3; HRMS (TOF MS ES⁺, *m/z*): [M + Na]⁺ calcd for C₁₅H₁₄O₂Na, 249.0862; found, 249.0868.



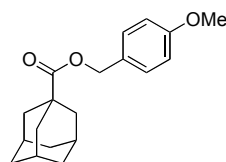
(*E*)-3,7-Dimethylocta-2,6-dien-1-yl 3-methylbenzoate (6b).

According to general procedure C, **6b** (68.8 mg, 0.252 mmol, 94 %) was isolated as a clear oil. ¹H NMR (500 MHz, CDCl₃) δ 7.88 – 7.83 (m, 2H), 7.37 – 7.29 (m, 2H), 5.47 (tdd, *J* = 7.0, 2.5, 1.2 Hz, 1H), 5.10 (tdd, *J* = 4.1, 3.3, 1.3 Hz, 1H), 4.85 – 4.82 (m, 2H), 2.40 (s, 3H), 2.16 – 2.05 (m, 4H), 1.78 – 1.76 (m, 3H), 1.68 (d, *J* = 1.0 Hz, 3H), 1.61 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 166.8, 142.3, 138.1, 133.5, 131.8, 130.4, 130.1, 128.2, 126.7, 123.7, 118.4, 61.8, 39.6, 26.3, 25.7, 21.3, 17.7, 16.5; HRMS (TOF MS ES⁺, *m/z*): [M + Na]⁺ calcd for C₁₈H₂₄O₂Na, 272.1776; found, 272.1769.



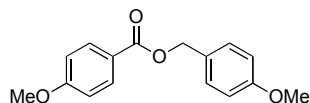
Furan-2-ylmethyl 3-methylbenzoate (6c).

According to general procedure C, **6c** (52.3 mg, 0.24 mmol, 90 %) was isolated as a yellow oil. ^1H NMR (500 MHz, CDCl_3) δ 7.89 – 7.84 (m, 2H), 7.45 (dt, J = 6.0, 3.0 Hz, 1H), 7.36 (dd, J = 6.1, 1.4 Hz, 1H), 7.33 – 7.29 (m, 1H), 6.50 – 6.48 (m, 1H), 6.39 (dd, J = 3.2, 1.9 Hz, 1H), 5.30 (d, J = 7.8 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 166.4, 149.6, 143.3, 138.1, 133.8, 130.3, 129.8, 128.3, 126.9, 110.7, 110.6, 58.4, 21.2; HRMS (TOF MS ES⁺, m/z): $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{12}\text{O}_3\text{Na}$, 239.0684; found, 239.0677.



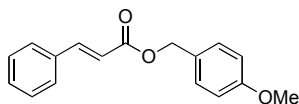
4-Methoxybenzyl adamantane-1-carboxylate (6d).

According to general procedure C, **6d** (71.9 mg, 0.24 mmol, 89 %) was isolated as a yellow oil. ^1H NMR (500 MHz, CDCl_3) δ 7.21 (dt, J = 3.1, 2.0 Hz, 2H), 6.84 – 6.80 (m, 2H), 4.97 (s, 2H), 3.73 (s, 3H), 1.94 (s, 3H), 1.87 – 1.81 (m, 6H), 1.69 – 1.62 (m, 6H); ^{13}C NMR (126 MHz, CDCl_3) δ 177.6, 159.4, 129.5, 113.8, 65.6, 55.3, 38.8, 36.5, 27.9; HRMS (TOF MS ES⁺, m/z): $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{24}\text{O}_3\text{Na}$, 323.1623; found, 323.1627.



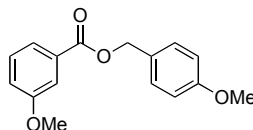
4-Methoxybenzyl 4-methoxybenzoate (6e).

According to general procedure C, **6e** (67.3 mg, 0.24 mmol, 92 %) was isolated as a clear oil. ^1H NMR (500 MHz, CDCl_3) δ 8.04 – 8.00 (m, 2H), 7.41 – 7.38 (m, 2H), 6.93 – 6.88 (m, 4H), 5.27 (s, 2H), 3.85 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 166.3, 163.3, 159.5, 131.7, 130.0, 128.4, 122.7, 113.9, 113.6, 66.2, 55.4, 55.3; HRMS (TOF MS ES⁺, m/z): $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{16}\text{O}_4\text{Na}$, 295.0946; found, 295.0938.



4-Methoxybenzyl cinnamate (6f).

According to general procedure C, **6f** (64.9 mg, 0.24 mmol, 90 %) was isolated as a clear oil. ^1H NMR (500 MHz, CDCl_3) δ 7.72 (d, J = 16.0 Hz, 1H), 7.54 – 7.49 (m, 2H), 7.41 – 7.35 (m, 5H), 6.94 – 6.90 (m, 2H), 6.47 (d, J = 16.0 Hz, 1H), 5.19 (s, 2H), 3.82 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 166.9, 159.7, 145.0, 134.4, 130.2, 128.9, 128.2, 128.1, 118.0, 113.9, 66.2, 55.3; HRMS (TOF MS ES⁺, m/z): $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{17}\text{H}_{16}\text{O}_3\text{Na}$, 291.0997; found, 291.1003.

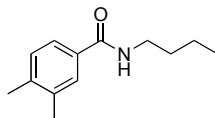


4-Methoxybenzyl 3-methoxybenzoate (**6g**).

According to general procedure C, **6g** (66.6 mg, 0.24 mmol, 91 %) was isolated as a clear oil. ^1H NMR (500 MHz, CDCl_3) δ 7.67 – 7.64 (m, 1H), 7.58 (dd, J = 2.6, 1.5 Hz, 1H), 7.41 – 7.37 (m, 2H), 7.33 (dd, J = 10.3, 5.6 Hz, 1H), 7.09 (ddd, J = 8.2, 2.7, 1.0 Hz, 1H), 6.94 – 6.90 (m, 2H), 5.30 (s, 2H), 3.84 (s, 3H), 3.82 (s, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 166.4, 159.6, 159.5, 131.6, 130.1, 129.4, 128.1, 122.1, 119.4, 114.1, 113.9, 66.6, 55.4, 55.3; HRMS (TOF MS ES⁺, m/z): $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{16}\text{O}_4\text{Na}$, 295.0946; found, 295.0942.

General procedure D for the coupling of acids and amines with Si-ODCT to synthesize amides **11 a – h**.

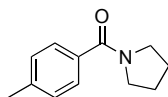
Into a 1-dram vial was added Si-ODCT **7** or **8** (2 equiv., 0.274 mmol), dry CH_2Cl_2 (0.075 M), acid (1 equiv., 0.136 mmol) and NMM (3 equiv., 0.408 mmol). The crude reaction mixture was stirred for 10 min at RT, after such time was added amine (1 equiv., 0.136 mmol) and the reaction was stirred for 2-6 h. After such time, the crude reaction mixture was filtered through a celite/silica SPE and concentrated to yield the desired amide.



N-Butyl-3,4-dimethylbenzamide (**11a**).

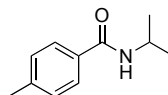
According to general procedure D, **11a** (25.9 mg, 0.12 mmol, 93 %) was isolated as a clear oil. ^1H NMR (500 MHz, CDCl_3) δ 7.55 (d, J = 1.8 Hz, 1H), 7.46 (dd, J = 7.8, 1.9 Hz, 1H), 7.15 (d, J = 7.7 Hz, 1H), 6.19 (s, 1H), 3.43 (td, J = 7.2, 5.8 Hz, 2H), 2.28 (s, 6H), 1.58 (dq, J = 12.6, 7.6 Hz, 2H), 1.44 – 1.35 (m, 2H), 0.93 (q, J = 7.6 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 167.6, 140.3, 136.8, 132.4, 129.6, 128.1, 124.1, 39.7,

31.8, 20.2, 19.8, 19.7, 13.8; HRMS (TOF MS ES⁺, m/z): [M + Na]⁺ calcd for C₁₃H₁₉NONa, 228.1364; found, 228.1361.



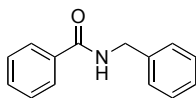
Pyrrolidin-1-yl(p-tolyl)methanone (11b).

According to general procedure **D**, **11b** (24.2 mg, 0.12 mmol, 94 %) was isolated as a clear oil. ¹H NMR (500 MHz, CDCl₃) δ 7.43 – 7.40 (m, 2H), 7.18 (dd, *J* = 8.4, 0.6 Hz, 2H), 3.63 (t, *J* = 7.0 Hz, 2H), 3.43 (t, *J* = 6.6 Hz, 2H), 2.36 (s, 3H), 1.98 – 1.91 (m, 2H), 1.89 – 1.82 (m, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 169.8, 139.8, 134.3, 128.8, 127.2, 49.6, 46.2, 26.4, 24.4, 21.4; HRMS (TOF MS ES⁺, m/z): [M + Na]⁺ calcd for C₁₂H₁₅NONa, 212.1051; found, 212.1047.



N-Isopropyl-4-methylbenzamide (11c).

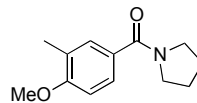
According to general procedure **D**, **11c** (21.2 mg, 0.12 mmol, 88 %) was isolated as a clear oil. ¹H NMR (500 MHz, CDCl₃) δ 7.66 – 7.62 (m, 2H), 7.21 (dd, *J* = 8.4, 0.5 Hz, 2H), 5.94 (s, 1H), 4.31 – 4.23 (m, 1H), 2.38 (s, 3H), 1.25 (s, 3H), 1.24 (s, 3H); ¹³C NMR (126 MHz, CDCl₃) δ 165.4, 140.4, 130.9, 127.9, 125.6, 40.6, 21.7, 20.2; HRMS (TOF MS ES⁺, m/z): [M + Na]⁺ calcd for C₁₁H₁₅NONa, 200.1051; found, 200.1042.



N-Benzylbenzamide (11d).

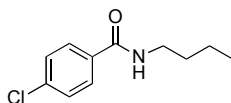
According to general procedure **D**, **11d** (27.4 mg, 0.13 mmol, 96 %) was isolated as a clear oil. ¹H NMR (500 MHz, CDCl₃) δ 7.79 (dt, *J* = 8.5, 1.8 Hz, 2H), 7.54 – 7.47 (m, 1H), 7.46 – 7.40 (m, 2H), 7.36 (dd, *J* = 6.7, 3.1 Hz, 4H), 7.33 – 7.27 (m, 1H), 6.40 (s, 1H), 4.66 (d, *J* = 5.7 Hz, 2H); ¹³C NMR (126 MHz, CDCl₃) δ 167.3, 138.1, 134.4, 131.6, 128.8, 128.6, 127.9, 127.6, 126.9, 44.1; HRMS (TOF MS ES⁺, m/z): [M + Na]⁺ calcd for C₁₄H₁₃NONa, 234.0895; found, 234.0894.

(4-Methoxy-3-methylphenyl)(pyrrolidin-1-yl)methanone (11e).



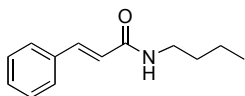
According to general procedure **D**, **11e** (28.3 mg, 0.13 mmol, 95 %) was isolated as a white solid. ^1H NMR (500 MHz, CDCl_3) δ 7.37 – 7.34 (m, 2H), 6.79 (d, J = 8.1 Hz, 1H), 3.83 (s, 3H), 3.61 (t, J = 6.9 Hz, 2H), 3.46 (t, J = 6.5 Hz, 2H), 2.20 (s, 3H), 1.96 – 1.89 (m, 2H), 1.87 – 1.80 (m, 2H); ^{13}C NMR (126 MHz, CDCl_3) δ 169.7, 158.9, 129.9, 128.9, 126.4, 126.3, 109.0, 55.4, 49.8, 46.3, 26.5, 24.4, 16.2; HRMS (TOF MS ES+, m/z): $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{17}\text{NO}_2\text{Na}$, 242.1157; found, 242.1150.

***N*-Butyl-4-chlorobenzamide (11f).**

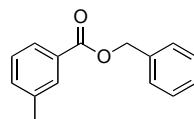


According to general procedure **D**, **11f** (26.1 mg, 0.13 mmol, 91 %) was isolated as a clear oil. ^1H NMR (500 MHz, CDCl_3) δ 7.72 – 7.67 (m, 2H), 7.41 – 7.37 (m, 2H), 6.14 (s, 1H), 3.44 (td, J = 7.2, 5.8 Hz, 2H), 1.59 (dq, J = 12.6, 7.6 Hz, 2H), 1.45 – 1.35 (m, 2H), 0.95 (t, J = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 166.4, 137.5, 133.2, 128.8, 128.3, 39.9, 31.7, 20.1, 13.8; HRMS (TOF MS ES+, m/z): $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{11}\text{H}_{14}\text{ClN}\text{ONa}$, 234.0662; found, 234.0652.

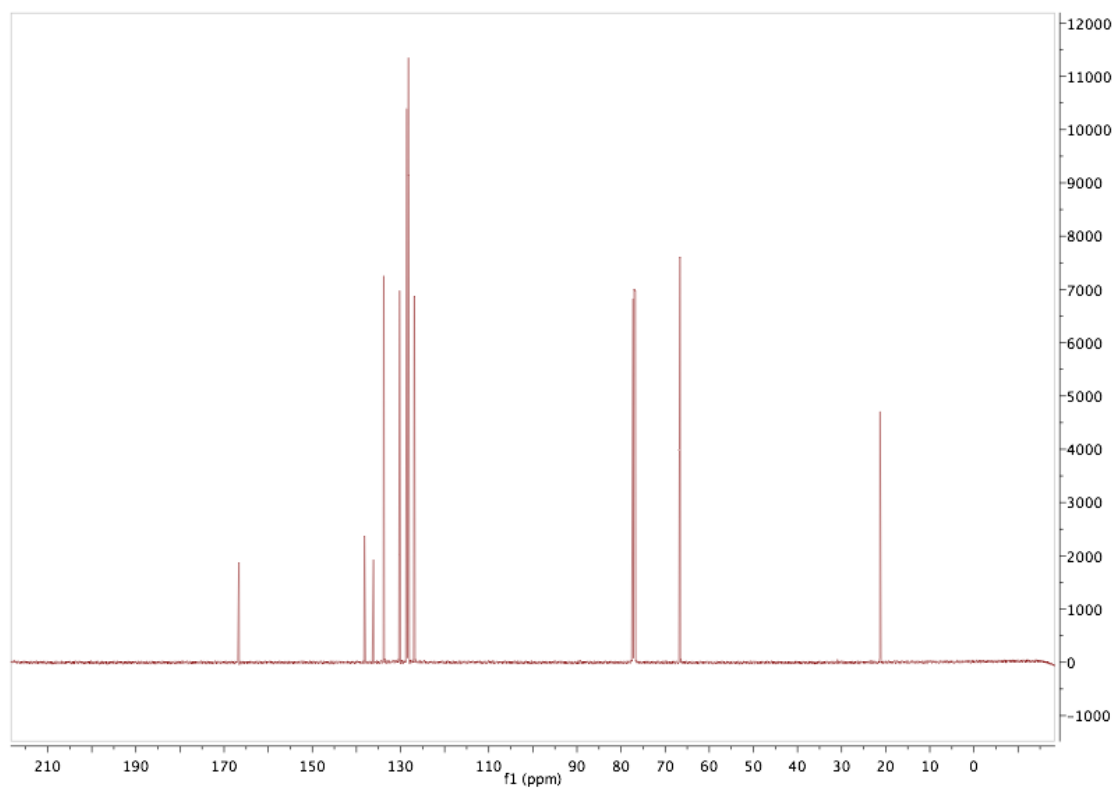
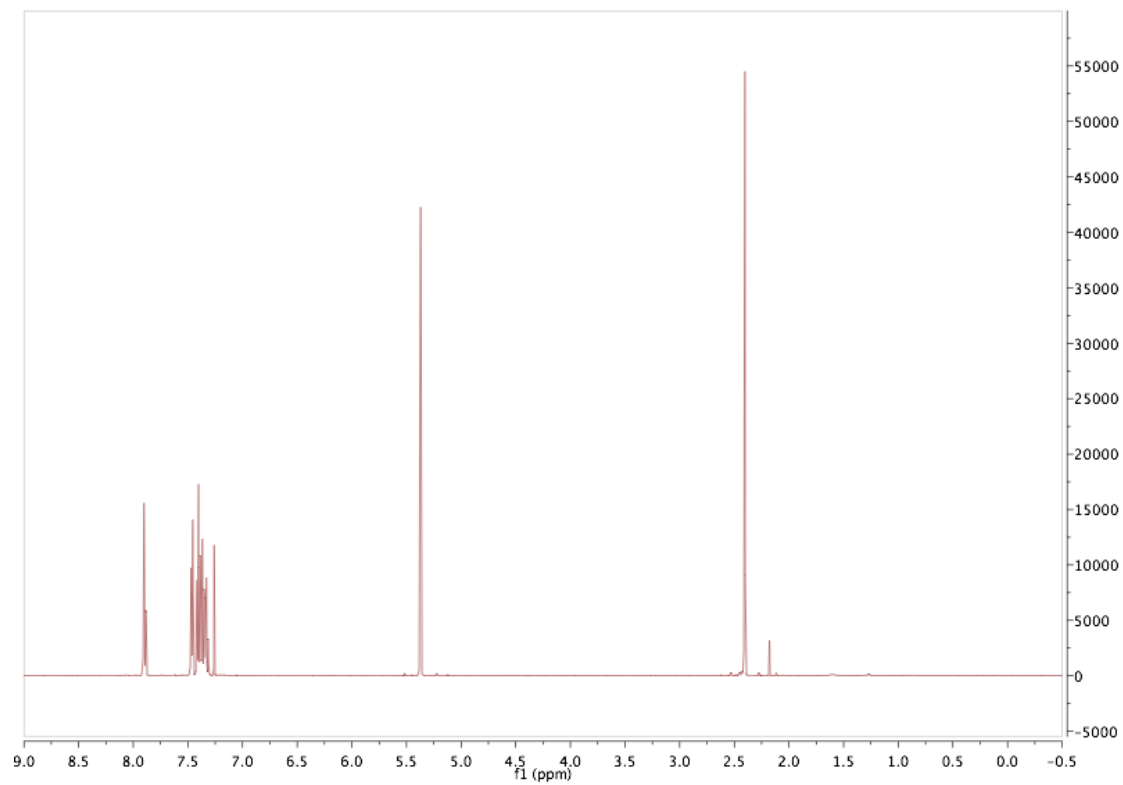
***N*-Butylcinnamamide (11g).**

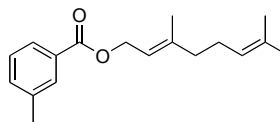


According to general procedure **D**, **11g** (26.5 mg, 0.13 mmol, 96 %) was isolated as a clear oil. ^1H NMR (500 MHz, CDCl_3) δ 7.62 (d, J = 15.6 Hz, 1H), 7.52 – 7.47 (m, 2H), 7.38 – 7.32 (m, 3H), 6.40 (d, J = 15.6 Hz, 1H), 5.74 (s, 1H), 3.39 (td, J = 7.2, 5.9 Hz, 2H), 1.60 – 1.52 (m, 2H), 1.43 – 1.34 (m, 2H), 0.94 (t, J = 7.4 Hz, 3H); ^{13}C NMR (126 MHz, CDCl_3) δ 165.8, 140.8, 134.9, 129.6, 128.8, 127.7, 120.8, 39.5, 31.7, 20.1, 13.7; HRMS (TOF MS ES+, m/z): $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{13}\text{H}_{17}\text{NONa}$, 226.1208; found, 226.1204.

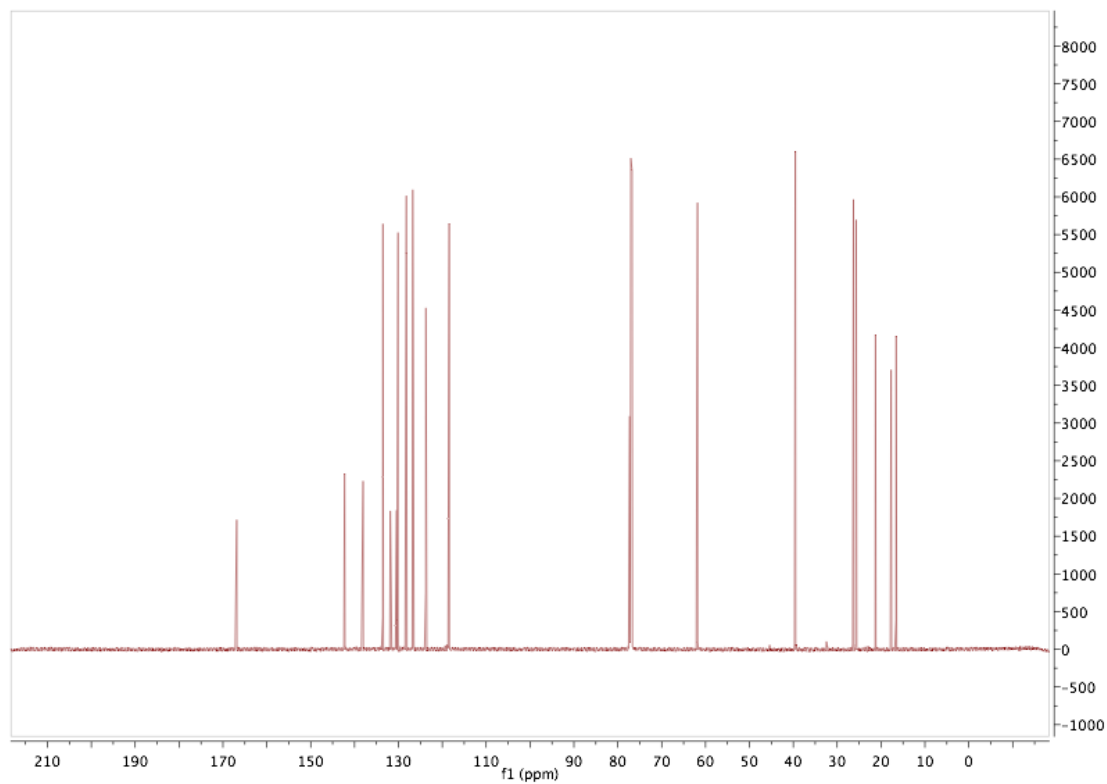
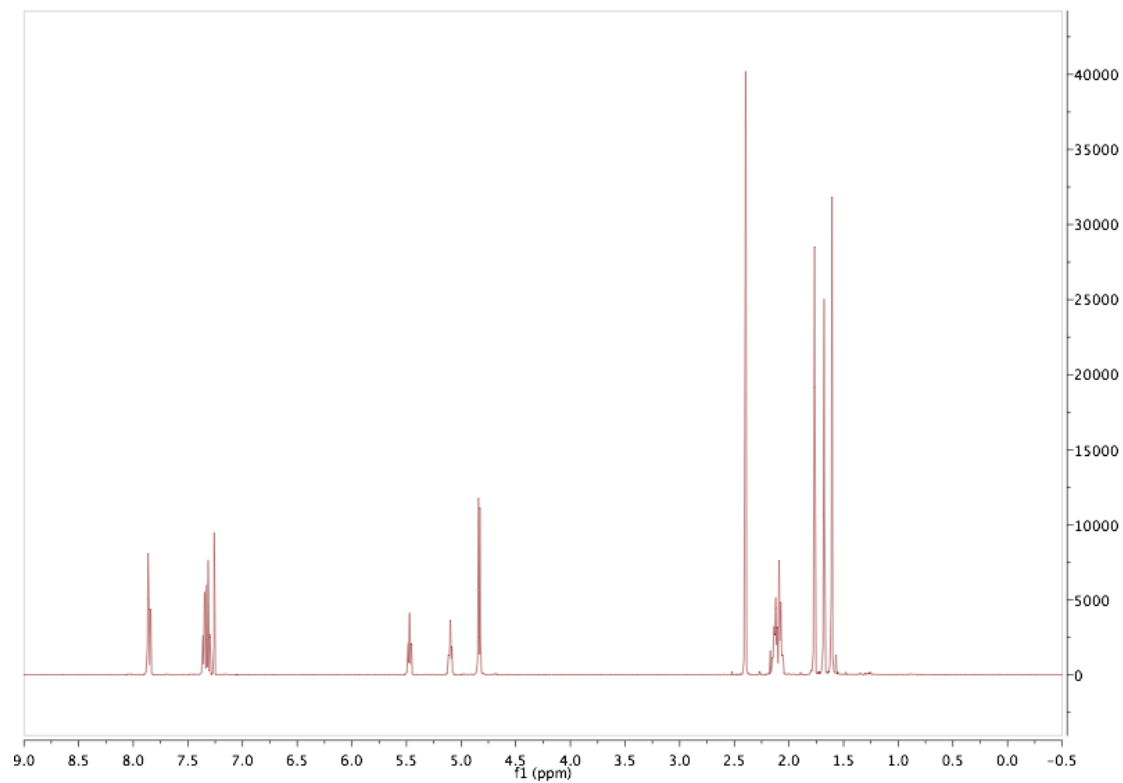


Benzyl 3-methylbenzoate (6a).

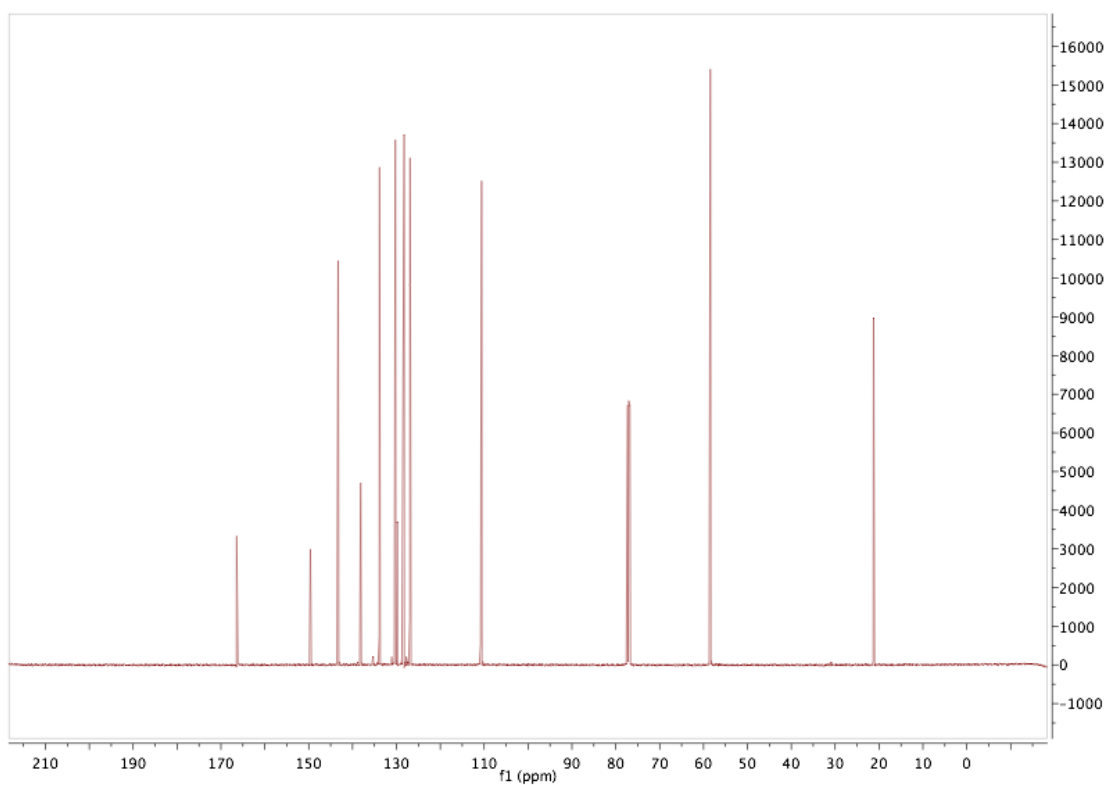
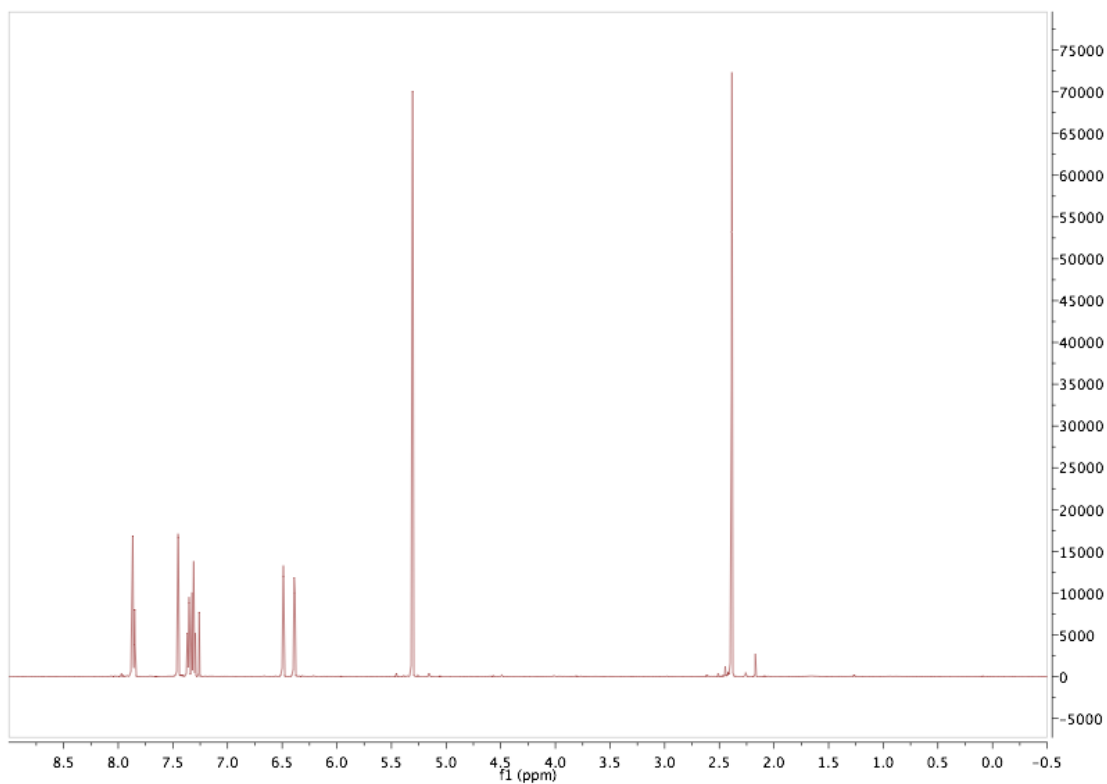
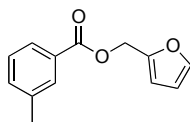


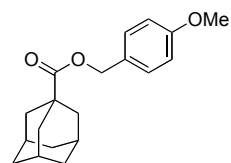


(*E*)-3,7-Dimethylocta-2,6-dien-1-yl 3-methylbenzoate (6b).

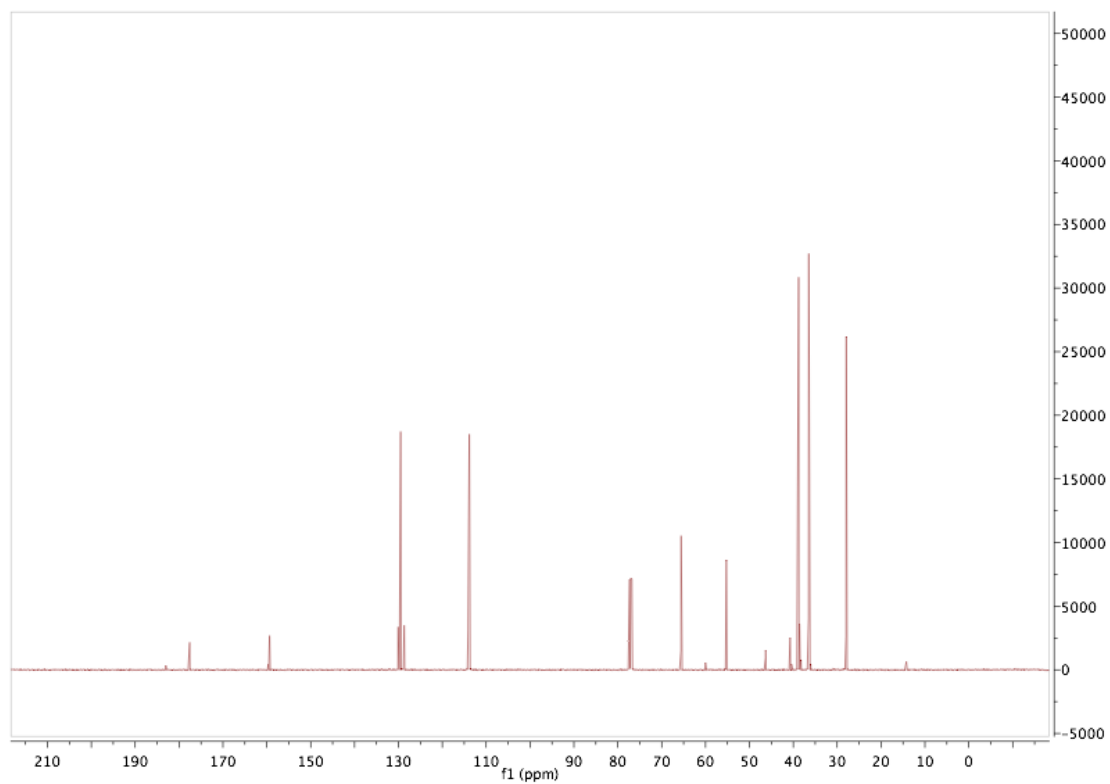
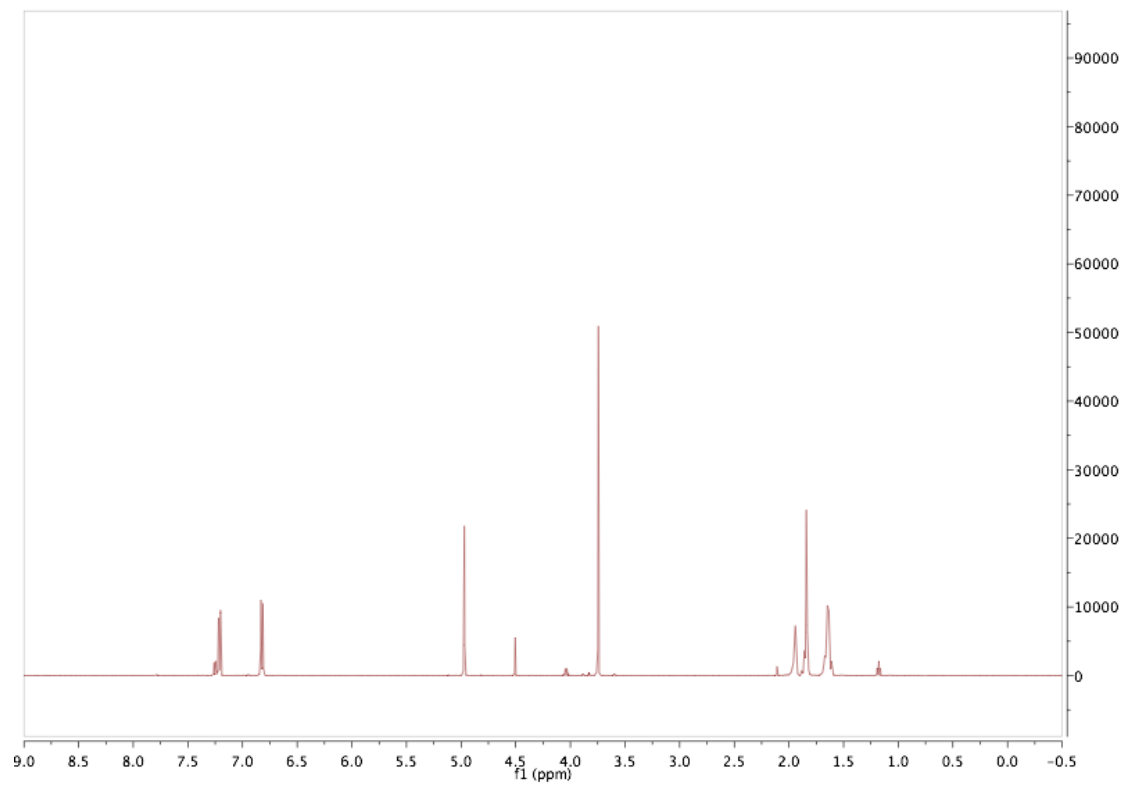


Furan-2-ylmethyl 3-methylbenzoate (6c).

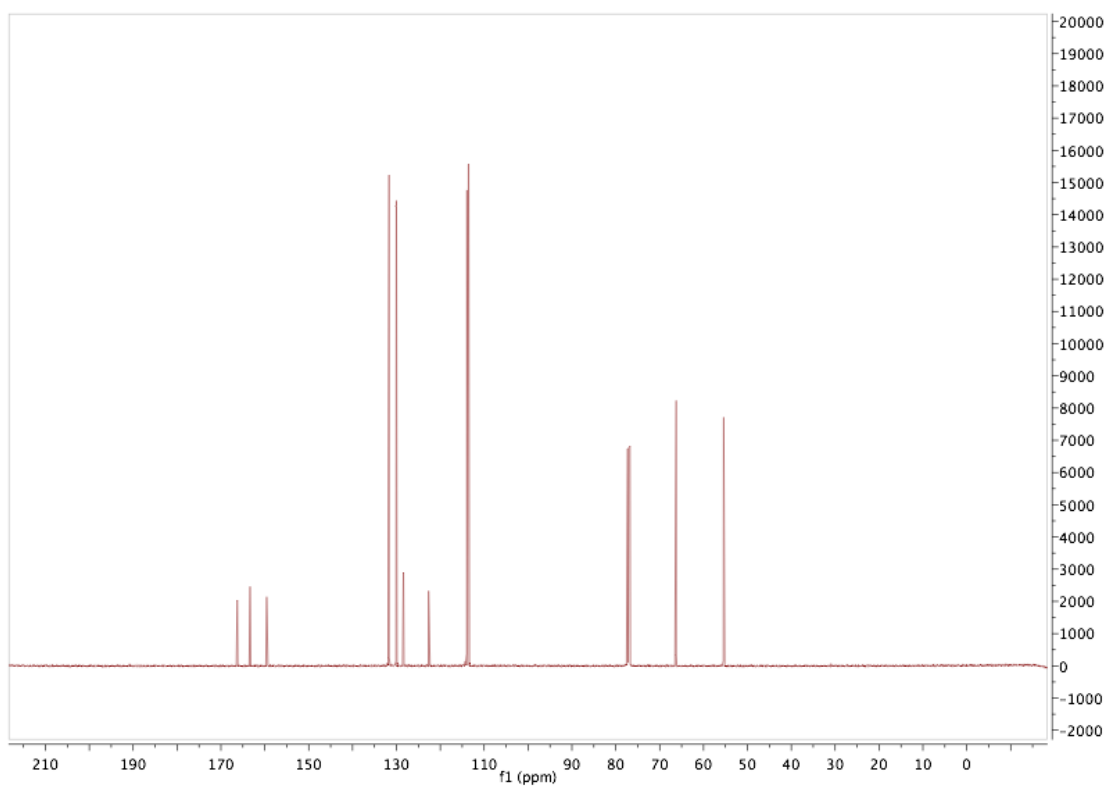
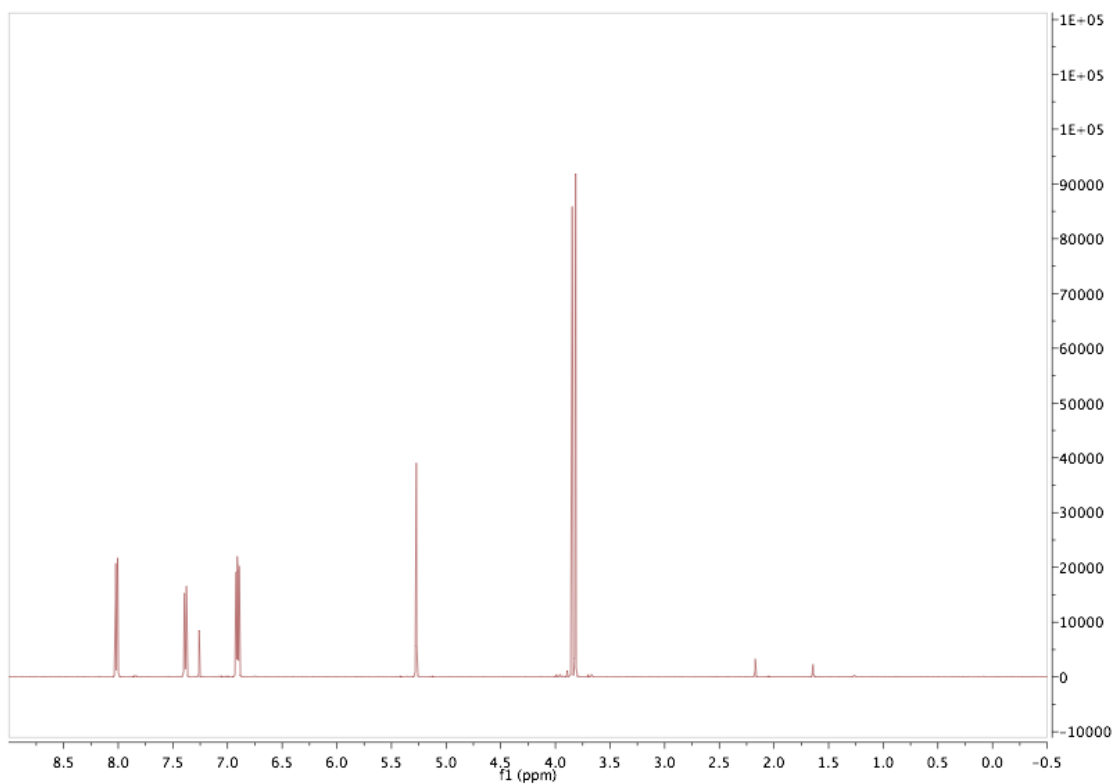
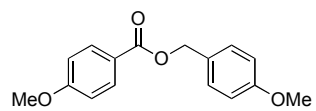




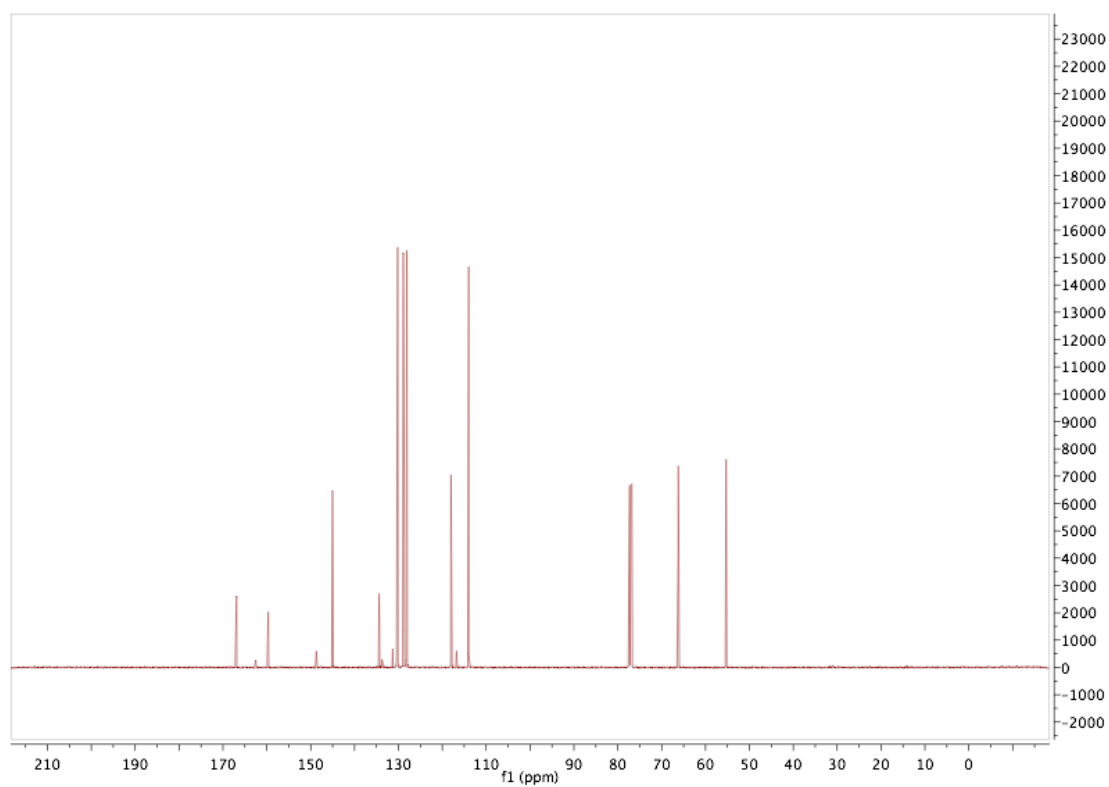
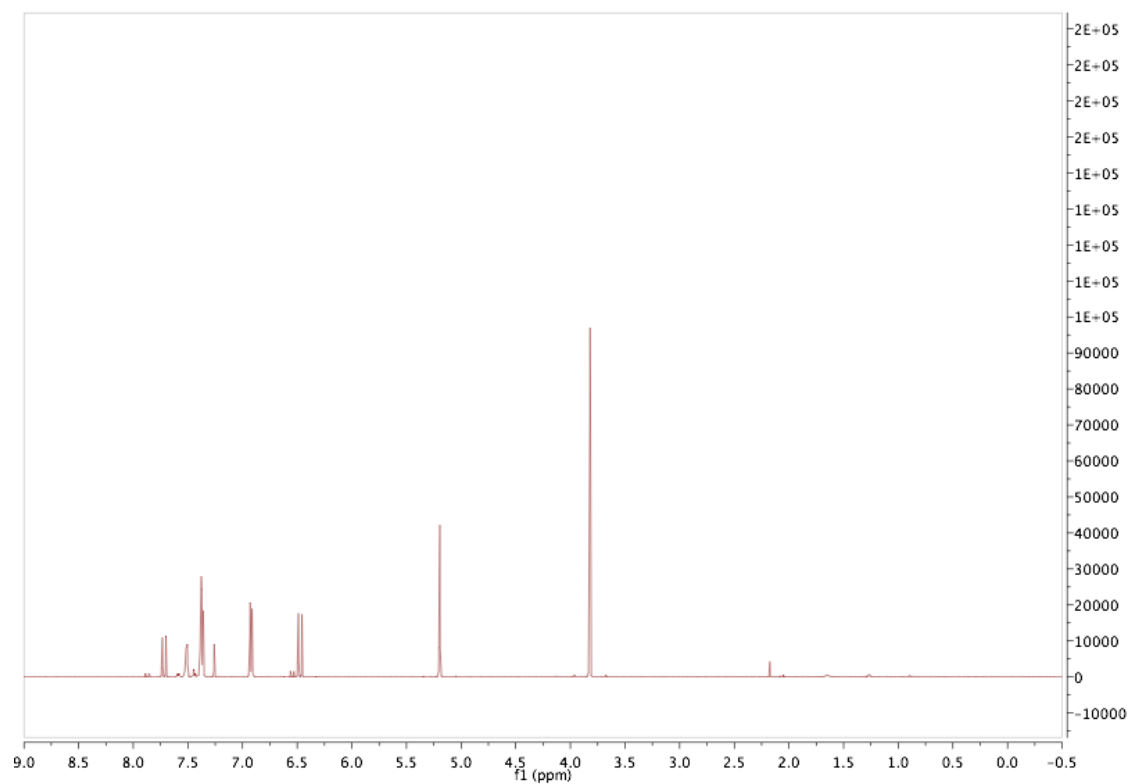
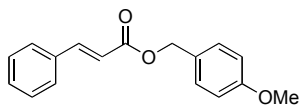
(3*r*,5*r*,7*r*)-4-Methoxybenzyl adamantane-1-carboxylate (6d).



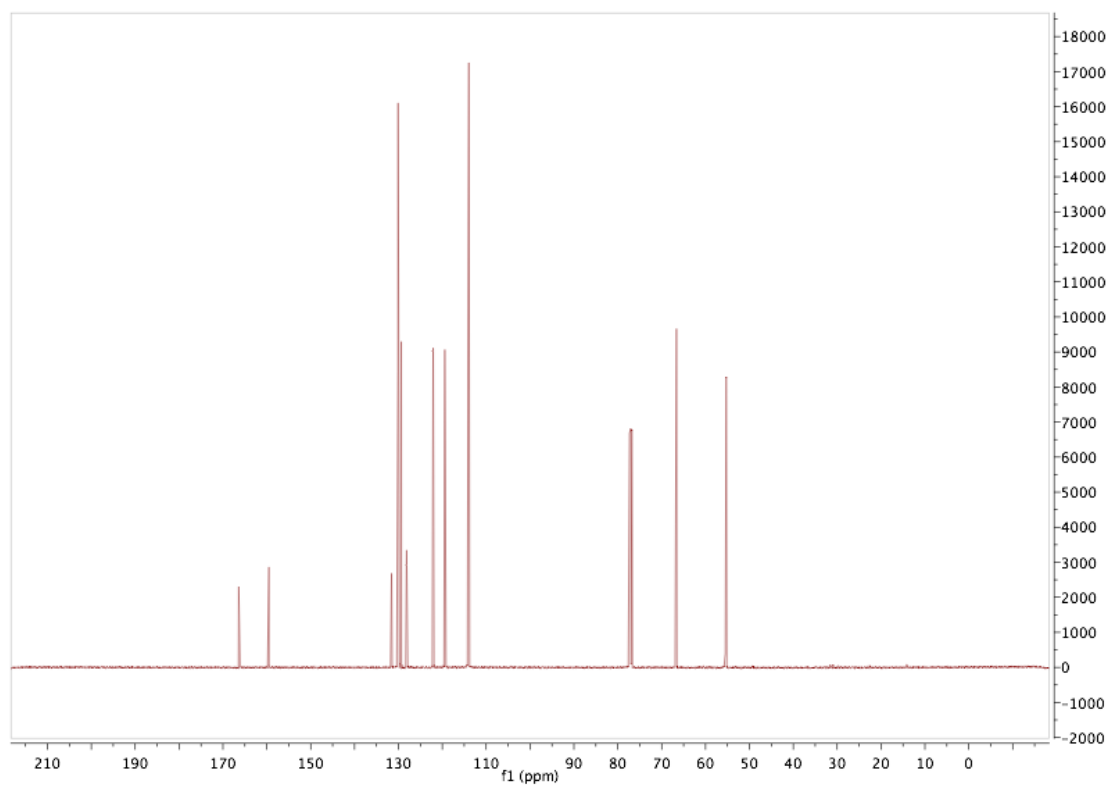
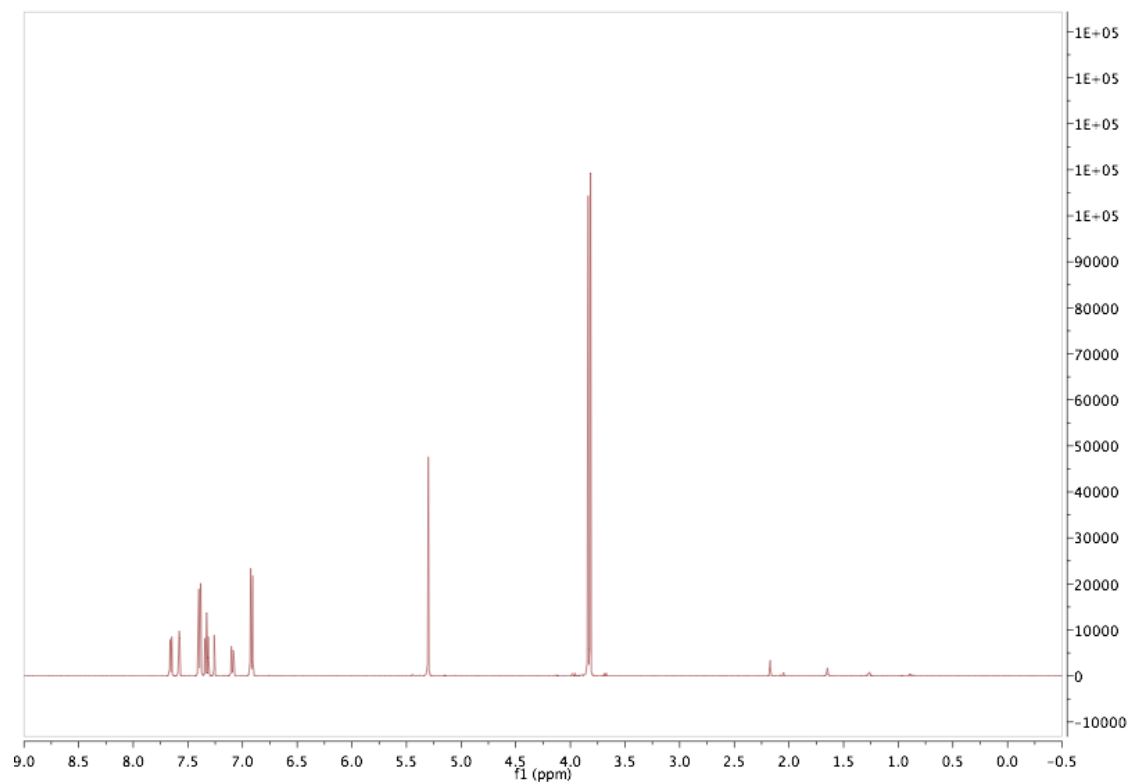
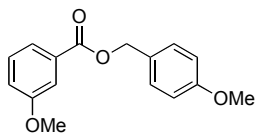
4-Methoxybenzyl 4-methoxybenzoate (6e).



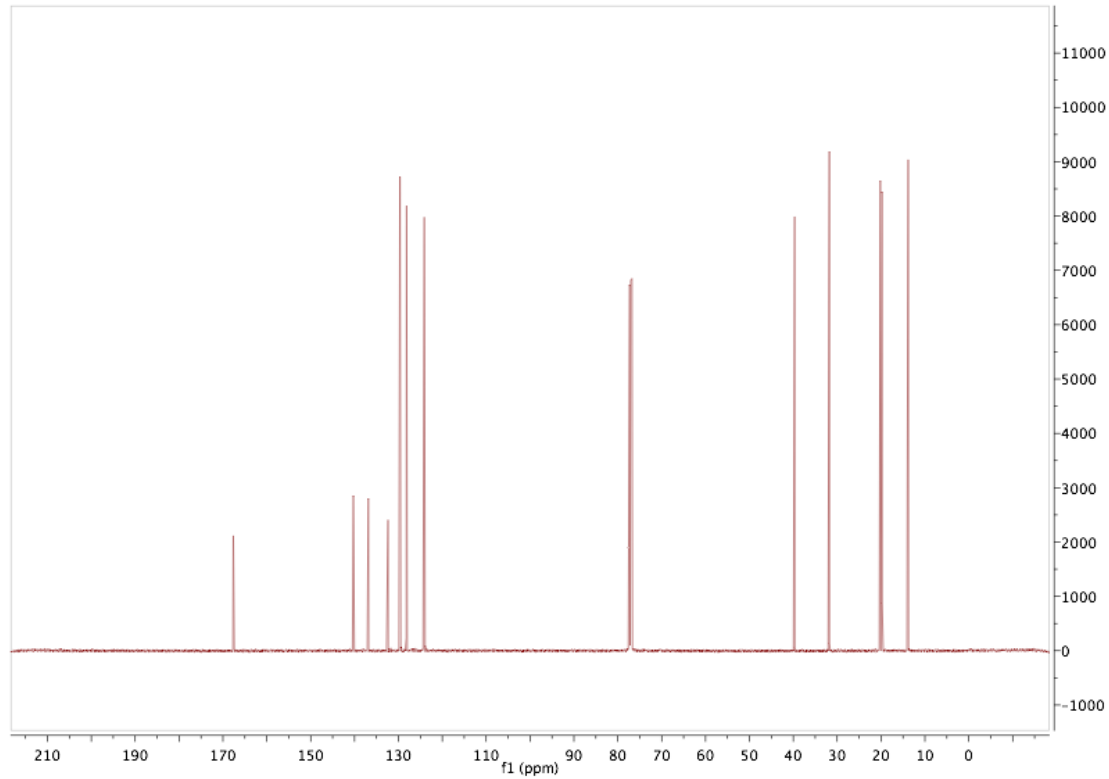
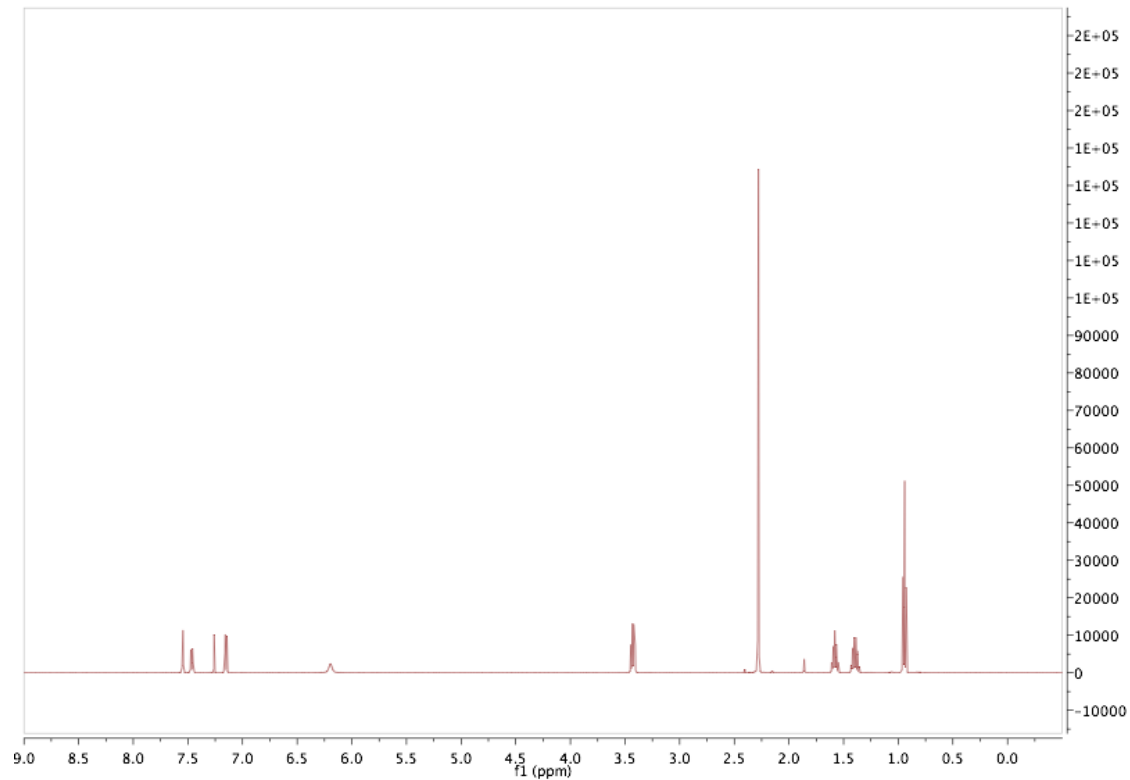
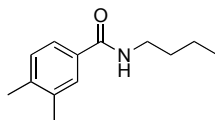
4-methoxybenzyl cinnamate (6f).



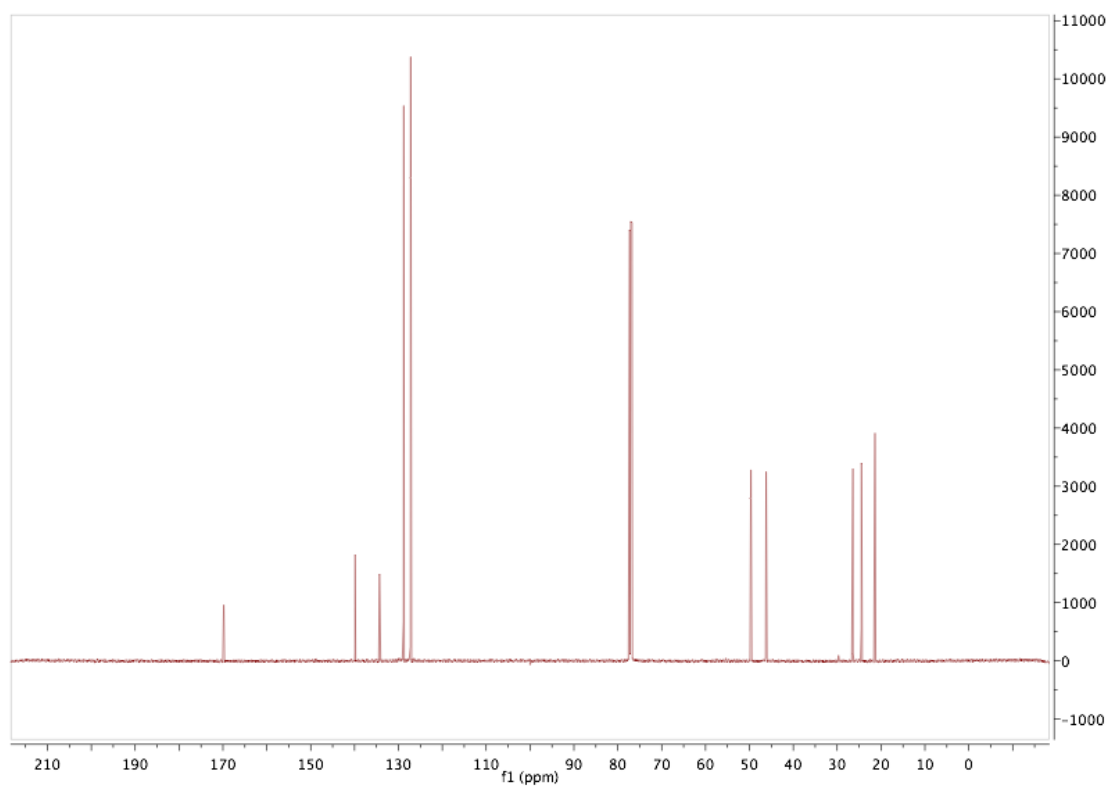
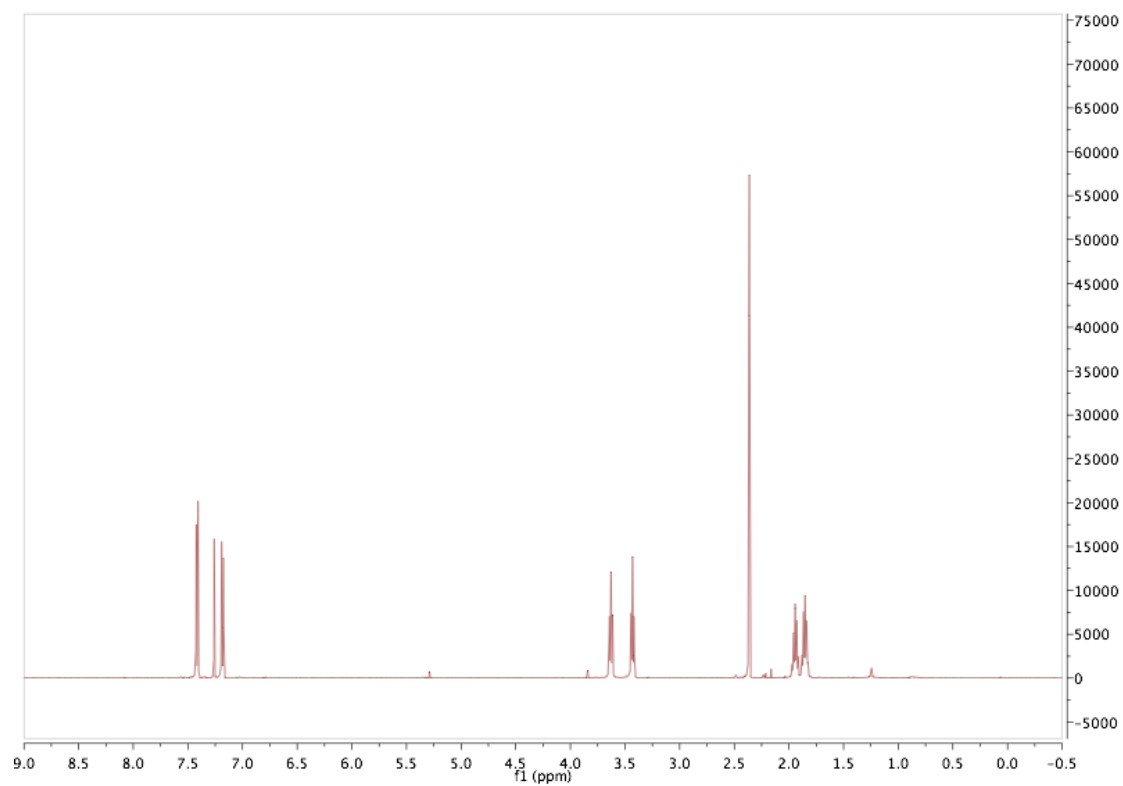
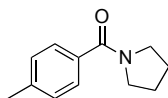
4-methoxybenzyl 3-methoxybenzoate (6g).



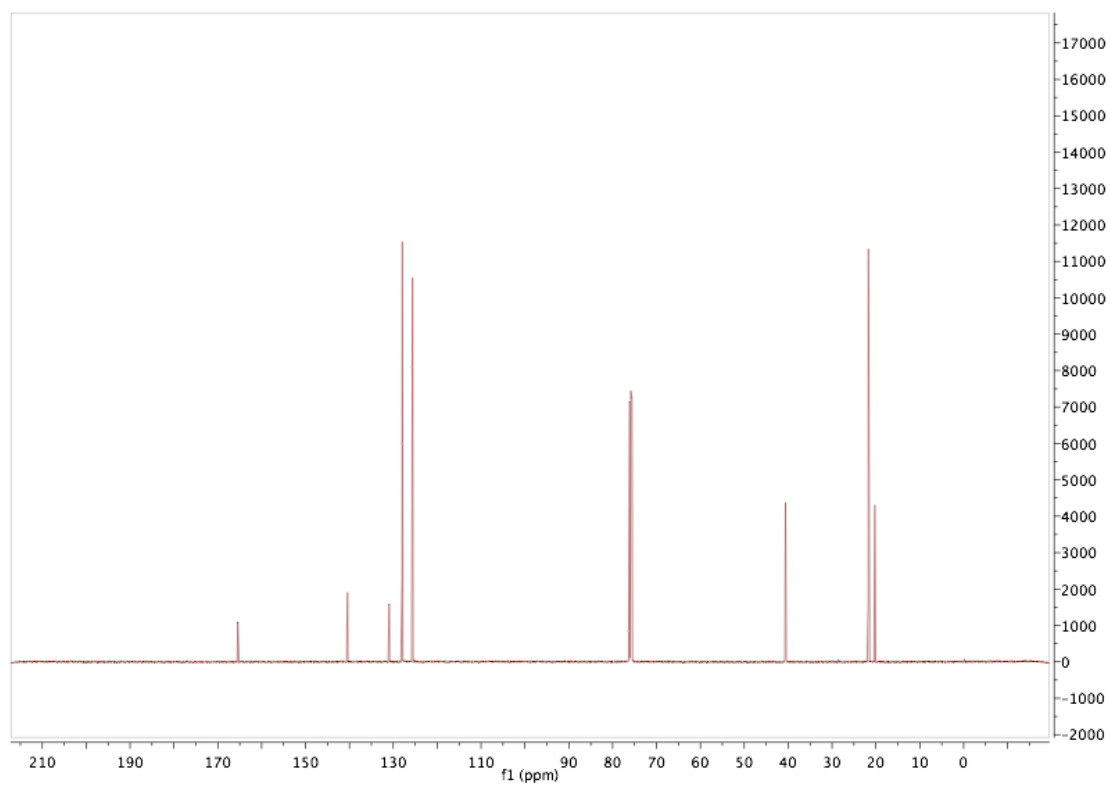
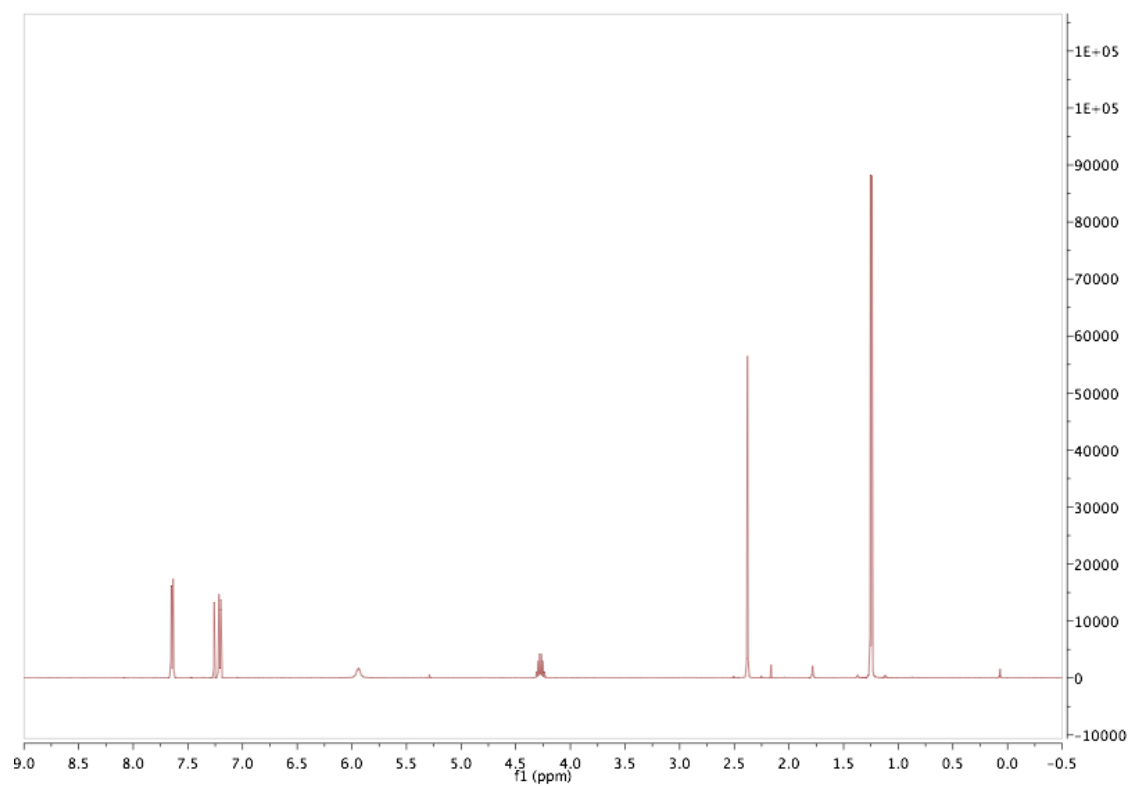
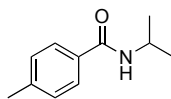
***N*-Butyl-3,4-dimethylbenzamide (11a).**



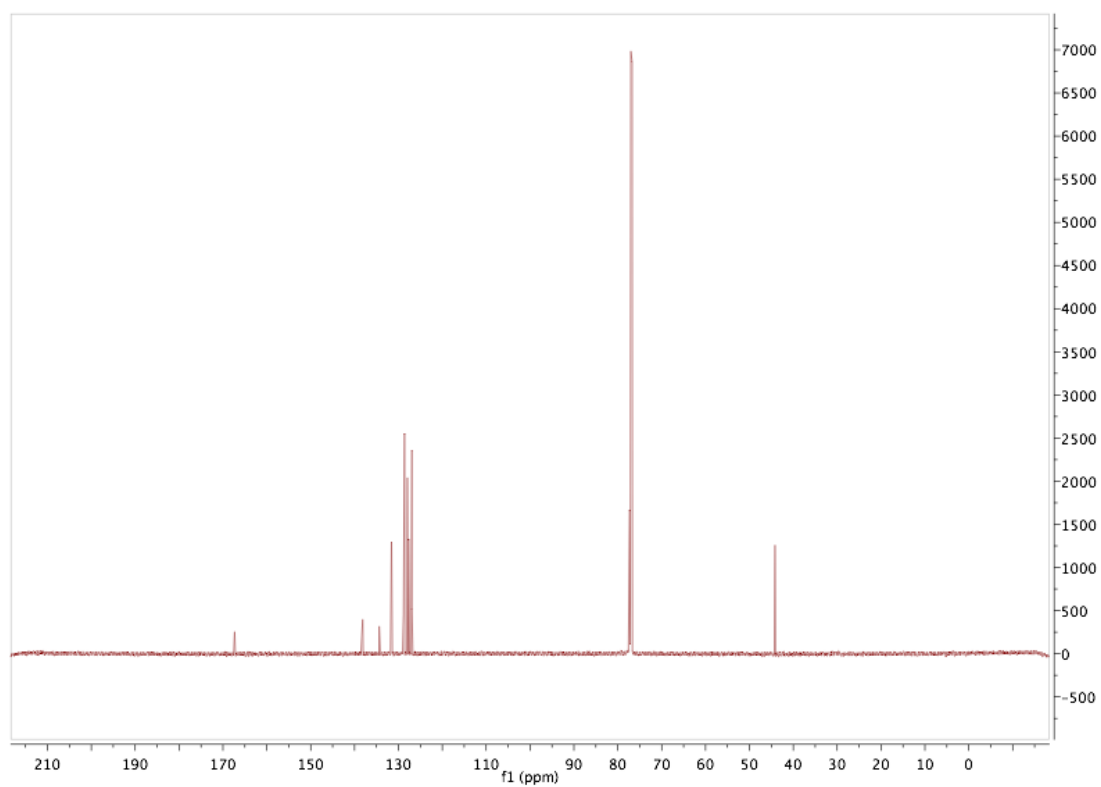
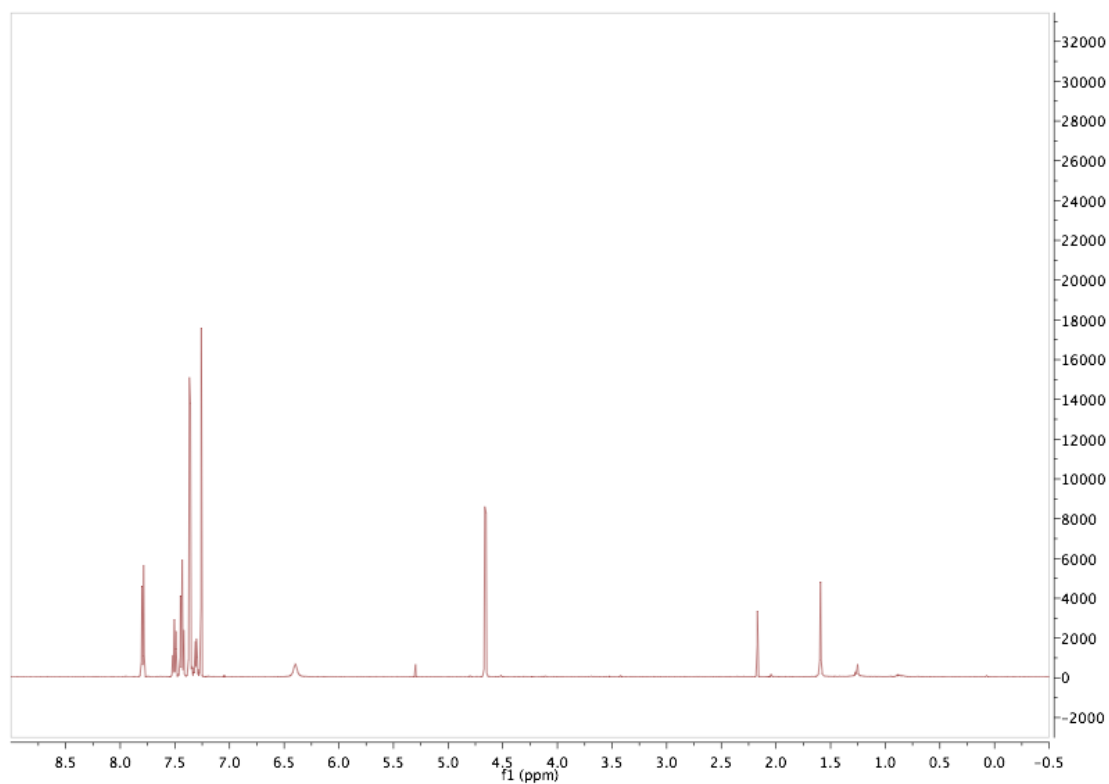
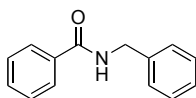
Pyrrolidin-1-yl(*p*-tolyl)methanone (11b).



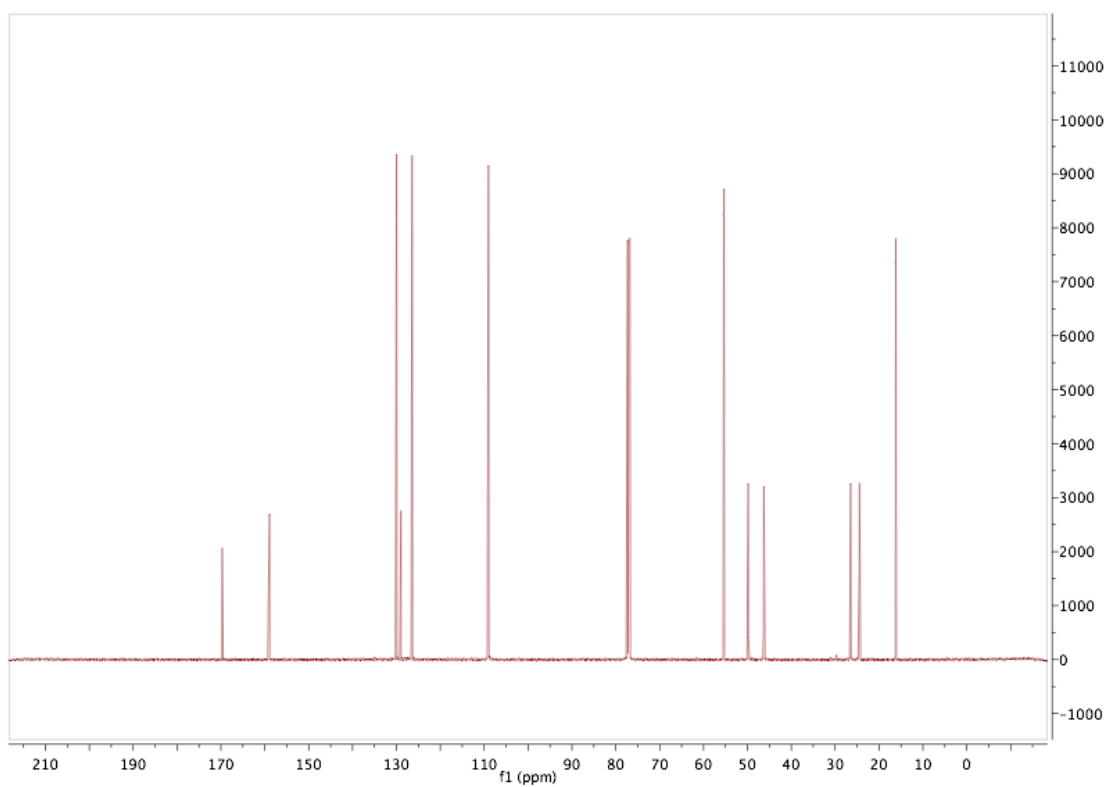
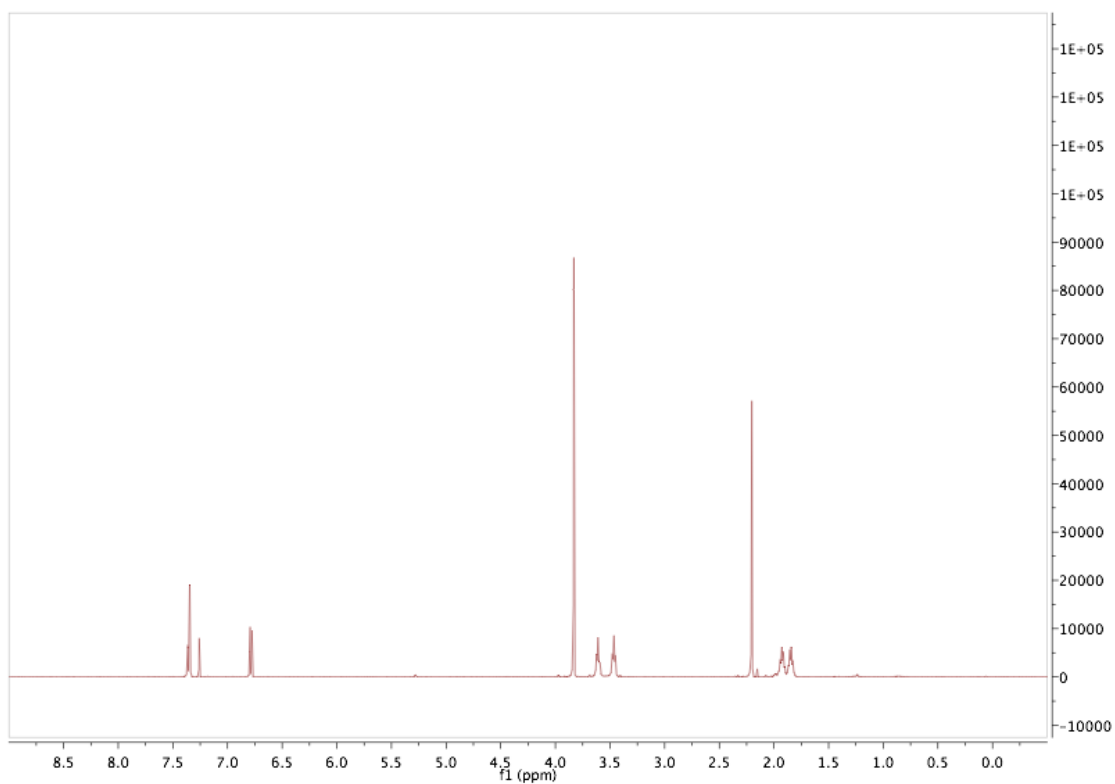
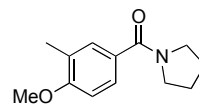
***N*-Isopropyl-4-methylbenzamide (11c).**



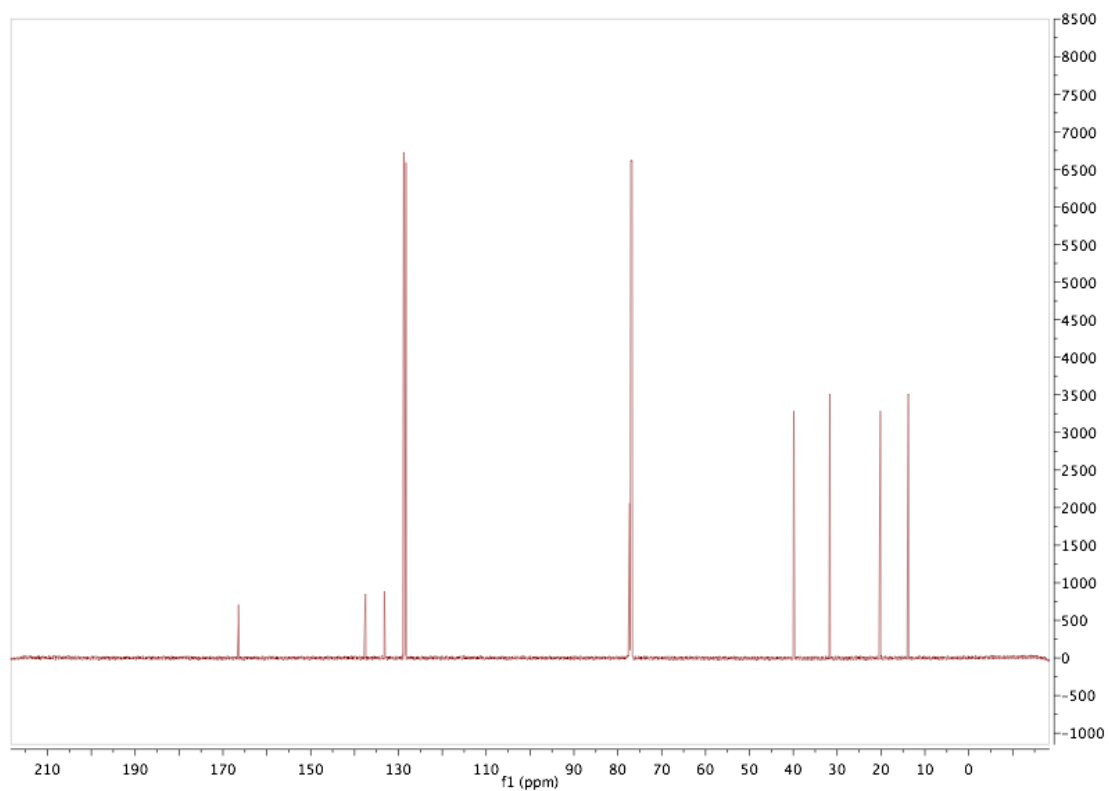
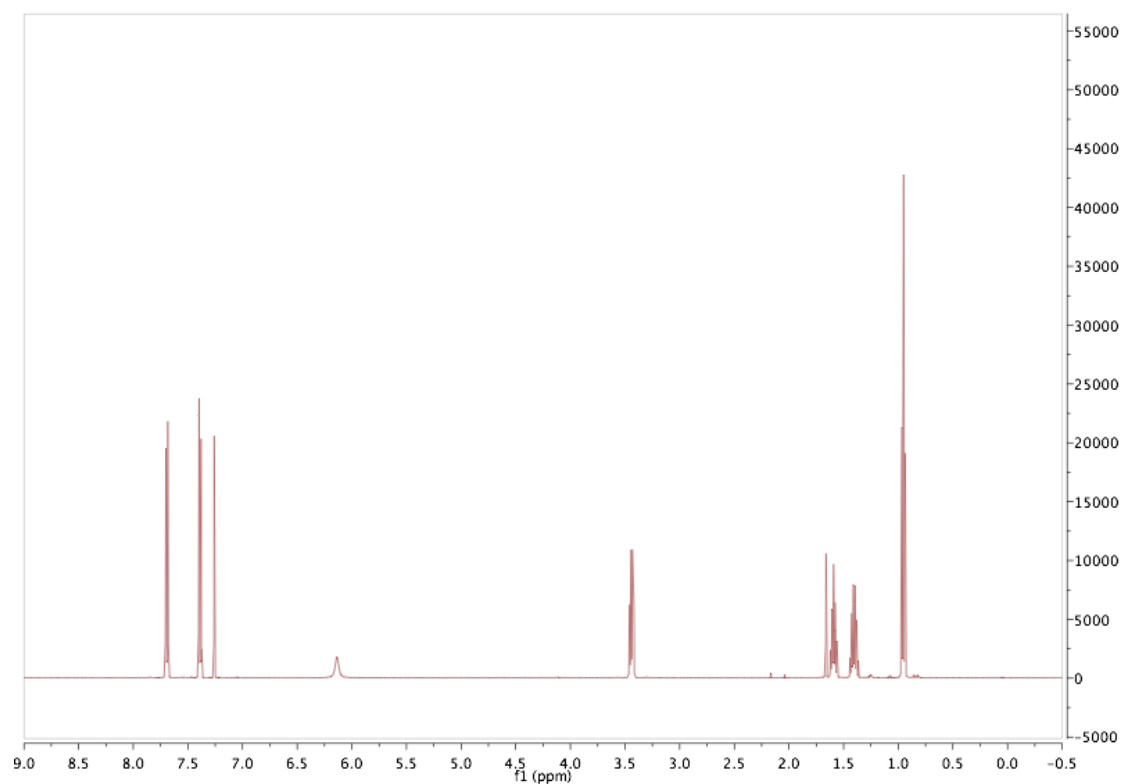
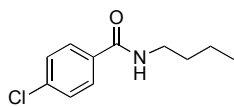
N-benzylbenzamide (11d).



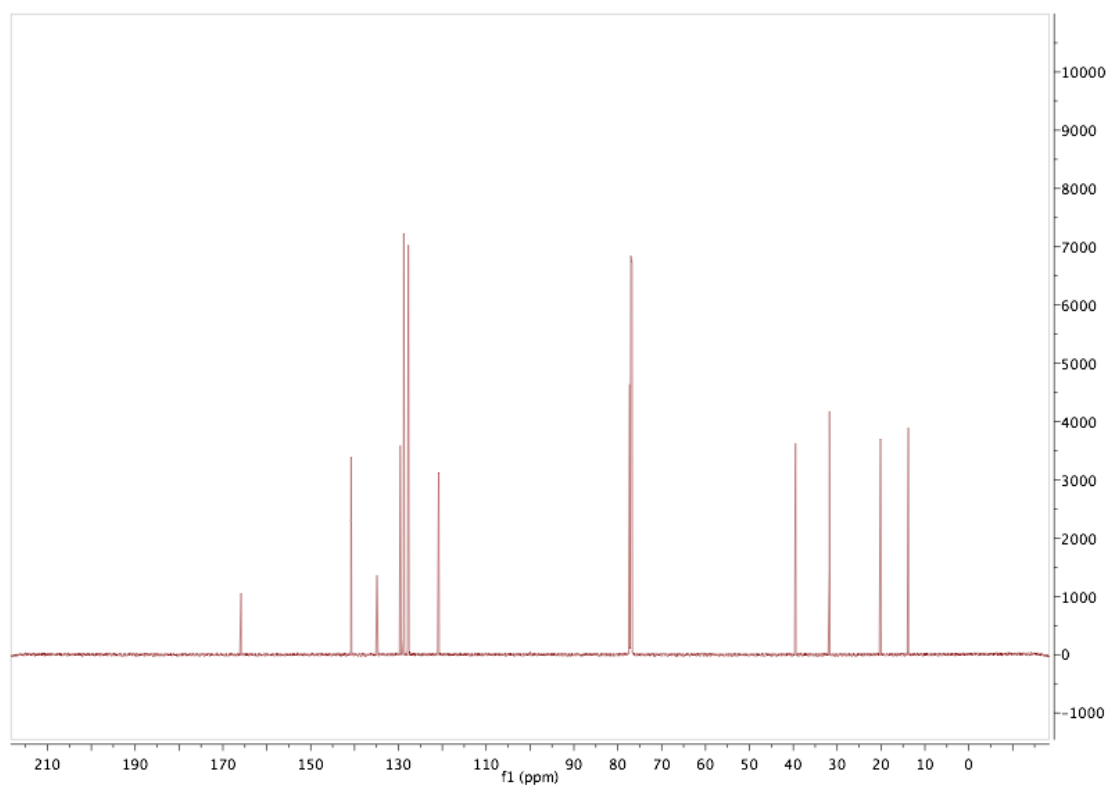
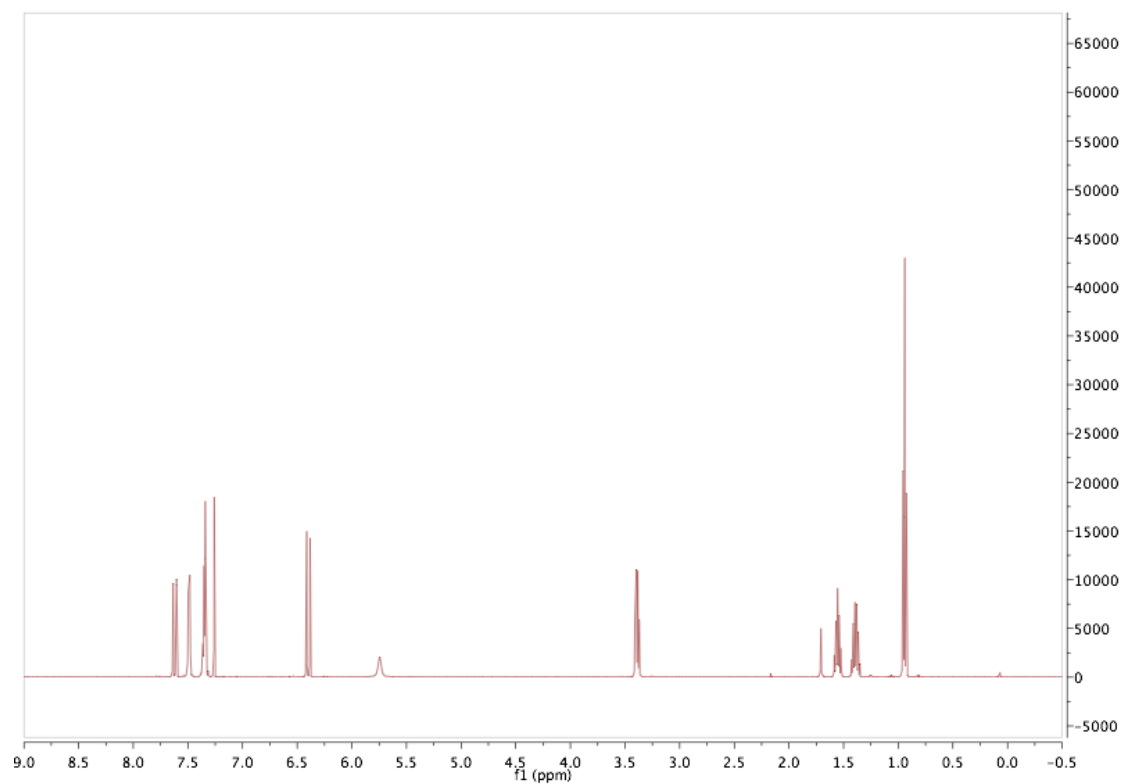
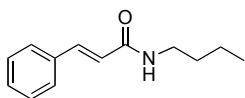
(4-Methoxy-3-methylphenyl)(pyrrolidin-1-yl)methanone (11e).



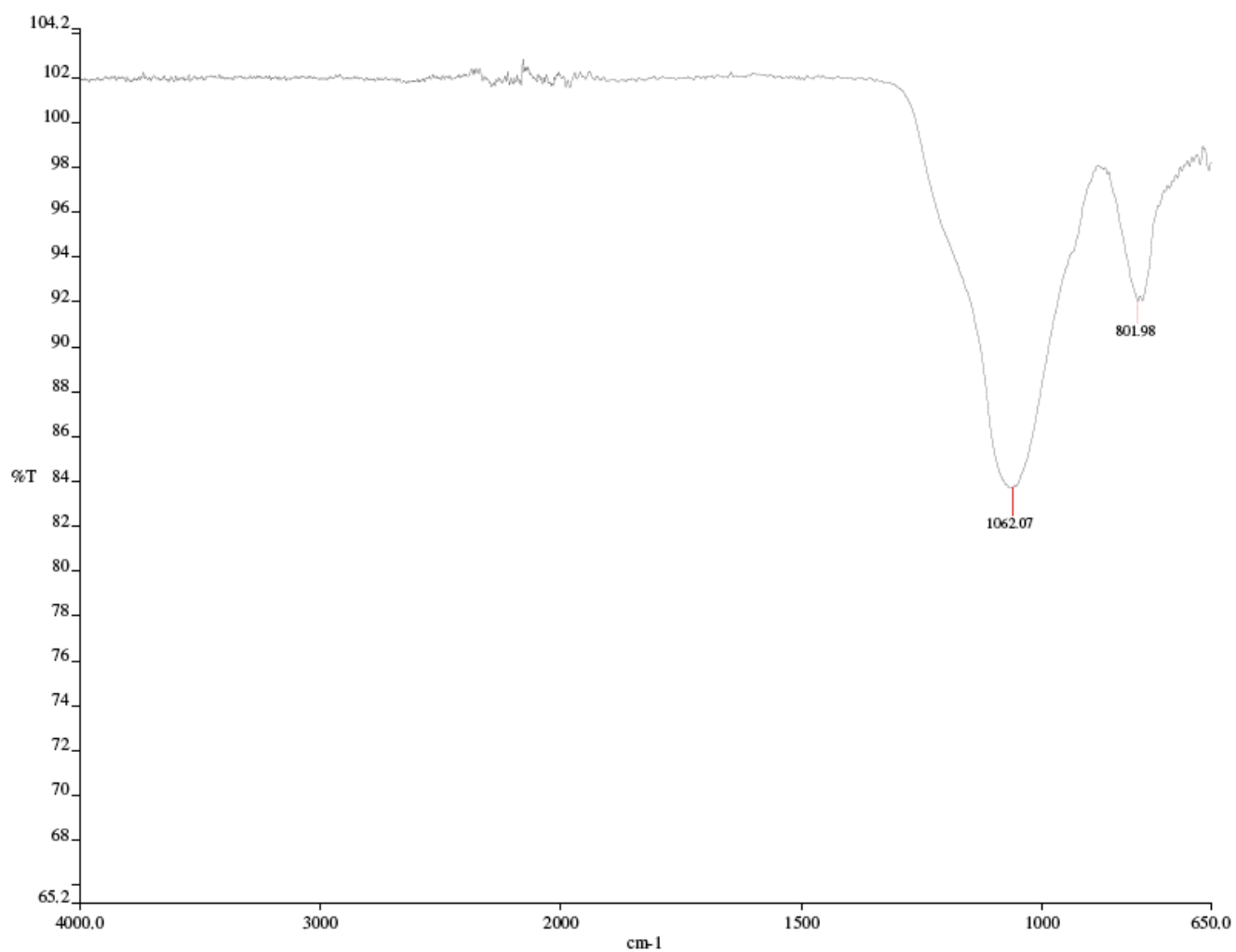
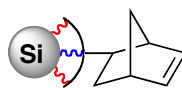
***N*-Butyl-4-chlorobenzamide (11f).**

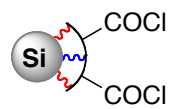


***N*-Butylcinnamamide (11g).**

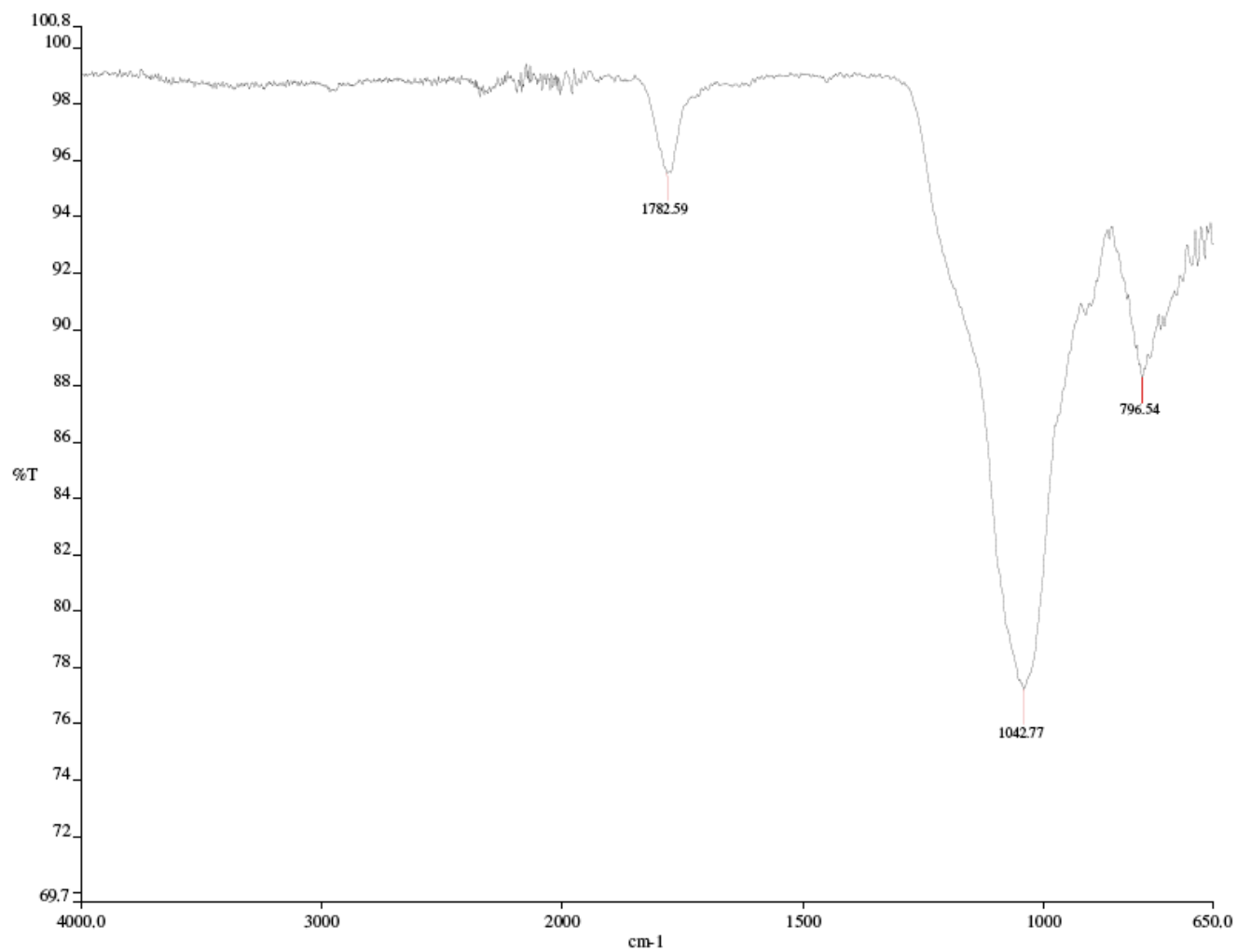


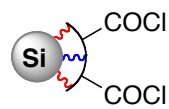
Norbornenyl-tagged silica particles (Si-Nb) 2



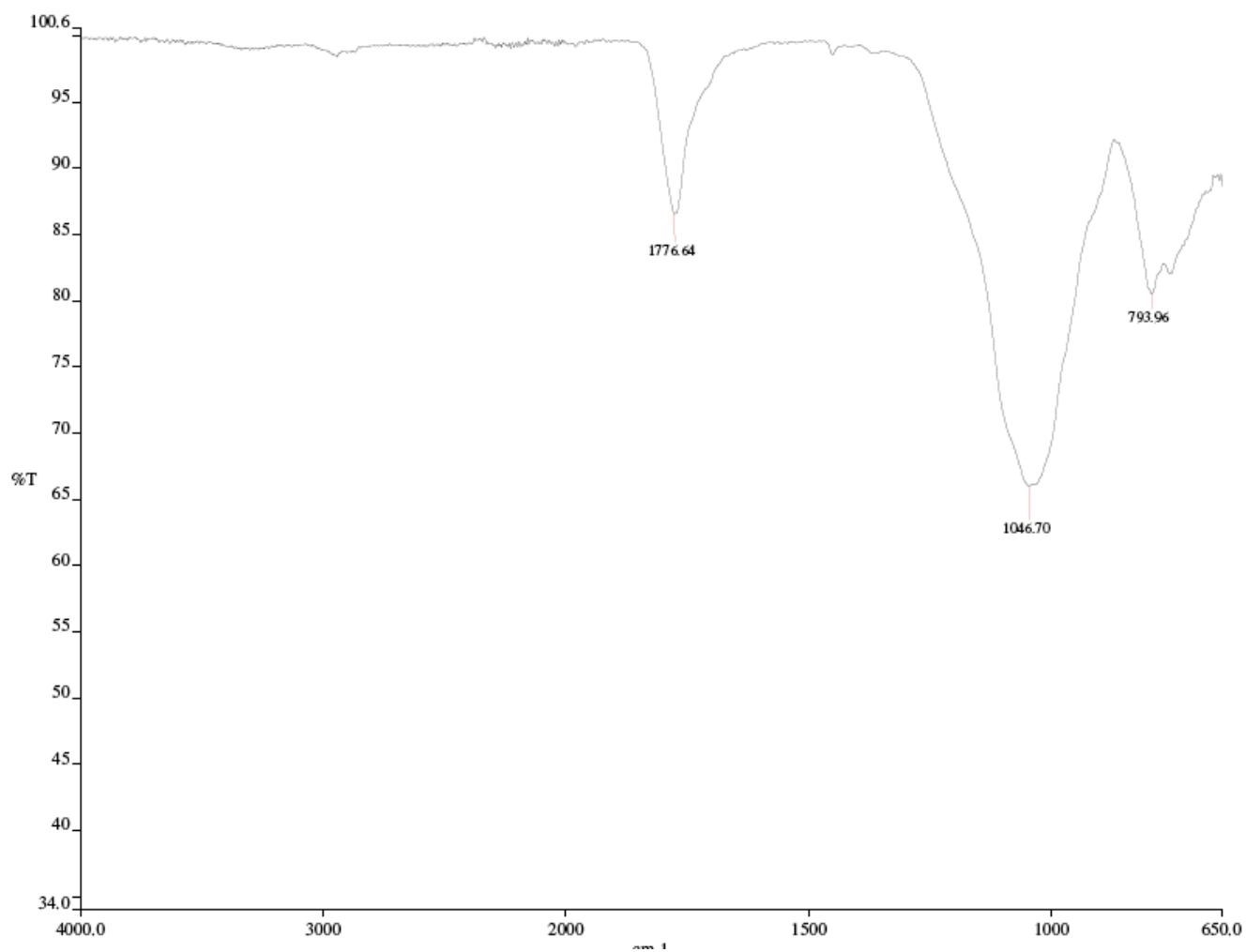


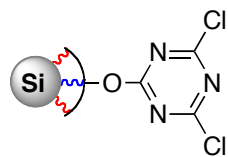
Silica-oligomeric bis-acid chloride hybrid (Si-OBAC₅₀) 4



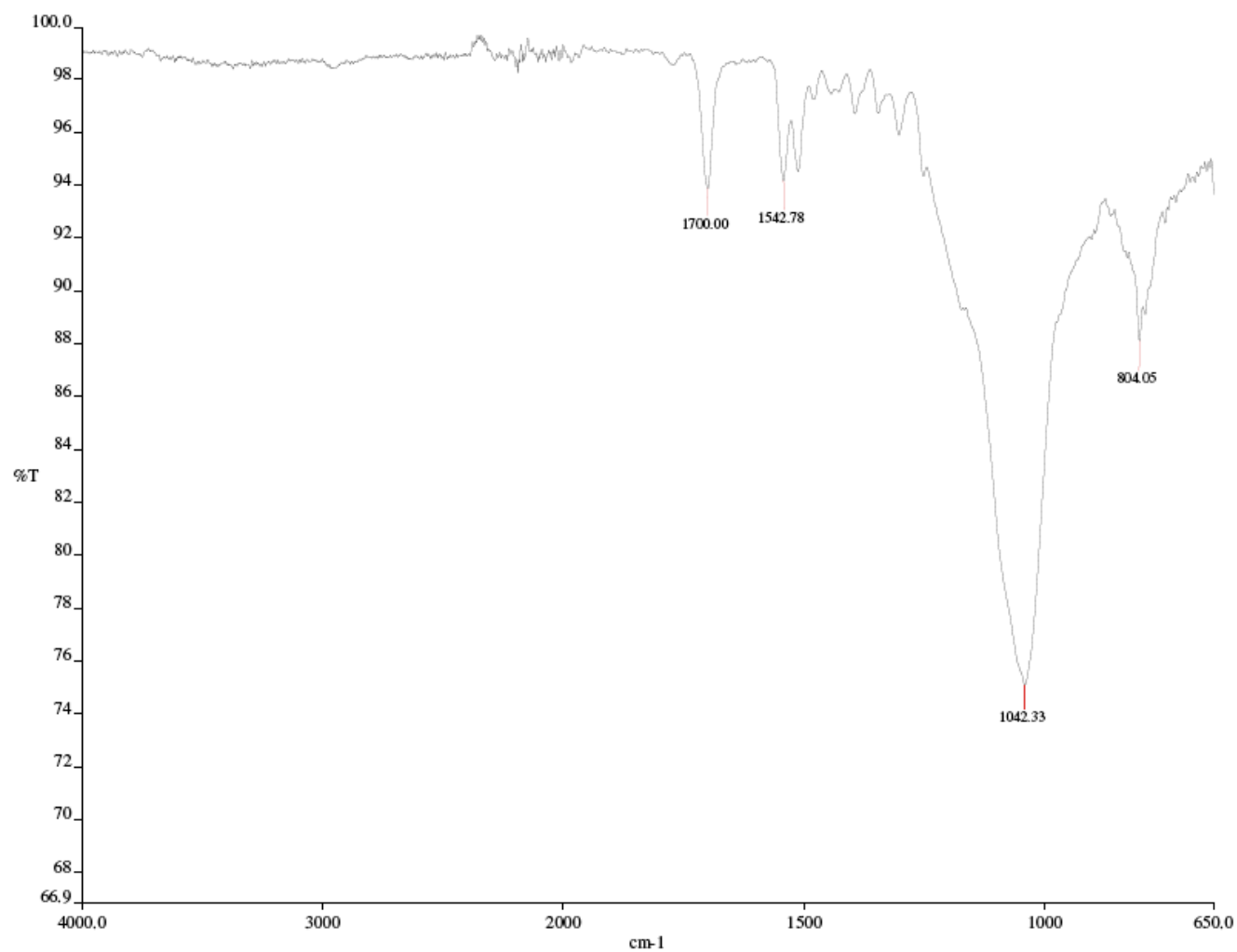


Silica-oligomeric bis-acid chloride hybrid (Si-OBAC₁₀₀) 5





Silica-oligomeric dichlorotriazine (Si-ODCT₅₀) 7



Silica-oligomeric triphenylphosphine (Si-OTPP₅₀) 9

