SUPPORTING INFORMATION

Synthesis of Enantioenriched *α*,*α*-Dichloro- and *α*,*α*-Difluoro-*β*-Hydroxy Esters and Amides by Ruthenium-Catalyzed Asymmetric Transfer Hydrogenation

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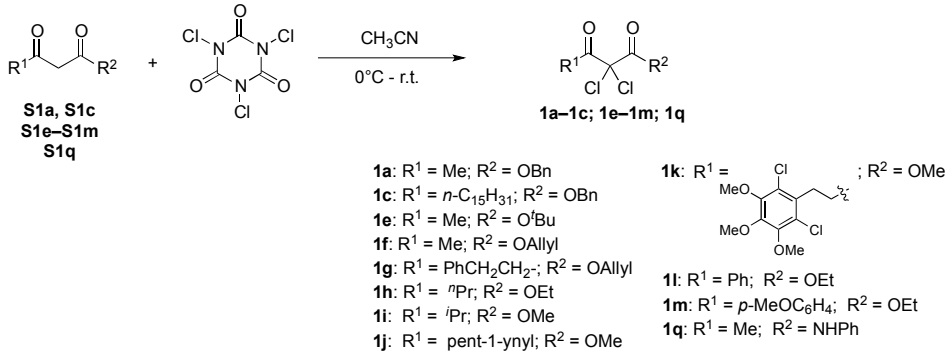
Contents

1. General information

All air and/or water sensitive reactions were carried out under an argon atmosphere. THF, Et_2O, CH_2Cl_2, DMF and toluene were dried over alumina columns in a solvent purification apparatus (Innovative technology). Reactions were monitored by thin layer chromatography carried out on precoated silica gel plates (Merck 60 F254) and revealed with either a ultra-violet lamp (λ = 254 nm) or a potassium permanganate solution. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded using a Bruker AC 300 (300 MHz) or a Bruker AC 400 (400 MHz). The chemical shifts are expressed in parts per million (ppm) referenced to residual chloroform (7.26 ppm). Data are reported as follows: chemical shifts (δ), multiplicity (recorded as s, singlet; d, doublet; t, triplet; q, quadruplet; quint, quintuplet; sext, sextuplet; hept, heptuplet; m, multiplet; and br, broad), coupling constants and integration. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were recorded using a Bruker AC 300 (75 MHz) or a Bruker AC 400 (100 MHz). The chemical shifts are expressed in parts per million (ppm) relative to the centre line of the triplet at 77.16 ppm for $CDCl_3$. Mass spectra (MS) were recorded by the ENSCP Mass Spectroscopy Service on a Hewlett-Packard HP 5989 A spectrometer. Ionization was obtained either by electronic impact (EI, 70eV) or chemical ionization with ammonia (CI, NH_3) and data are reported as *m/z* (relative intensity). Melting points (m.p.) were determined on a Kofler melting point apparatus. Optical rotations were measured on a Perkin-Elmer 241 polarimeter or a Jasco P-1010 polarimeter. High resolution mass spectrometric (HRMS) analyses were measured on LTQ-Orbitrap (Thermo Fisher Scientific) at Pierre et Marie Curie University. β-Dicarbonyl compounds **S1c, S1f, S1g, S1j** and **S1k** were prepared according to reported procedures,[1] while the others were commercially available.

2. General procedures for the synthesis of compounds 1a–1r

Method A:[2]

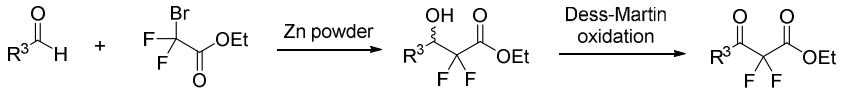


To a stirred solution of the β-dicarbonyl compound (10 mmol, 1.0 eq) in CH_3CN (40 mL) was added trichloroisocyanuric acid (1.58 g, 6.8 mmol, 0.68 eq) at room temperature in small portions. The reaction was monitored by TLC. After completion of the reaction, the suspension was filtered and the filtrate was concentrated under vacuum. The residue was partitioned between CH_2Cl_2 (30 mL) and satd. $NaHSO_3$ (20 mL).

[1] (a) Prévost, S.; Ayad, T.; Phansavath, P.; Ratovelomanana-Vidal, V. *Adv. Synth. Catal.* **2011**, *353*, 3213. (b) Nakamura, H.; Tsukano, C.; Yasui, M.; Yokouchi, S.; Igarashi, M.; Takemoto, Y. *Angew. Chem. In. Ed.* **2015**, *54*, 3136. (c) Palos Pacheco, R.; Eismin, R. J.; Coss, C. S.; Wang, H.; Maier, R. M.; Polt, R.; Pemberton, J. E. *J. Am. Chem. Soc.* **2017**, *139*, 5125.
[2] Mendonça, G. F.; Sindra, H. C.; de Almeida, L. S.; Esteves, P. M.; de Mattos, M. C. S. *Tetrahedron Lett.* **2009**, *50*, 473.

The aqueous phase was extracted with CH_2Cl_2 (2 x 30 mL), the combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification of the residue by flash column chromatography afforded pure **1**.

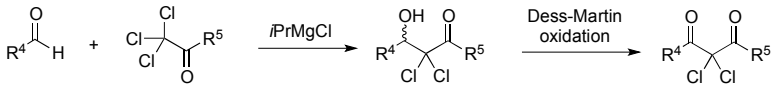
Method B:



1n: R^3 = hexyl,
1o: R^3 =$PhCH_2CH_2$ -

Step1: To a solution of aldehyde (1.0 eq) and ethyl bromodifluoroacetate (1.5 eq) in THF was added zinc powder (1.5 eq) at room temperature in small portions. The reaction was monitored by TLC. After completion, the reaction was quenched with satd. NH_4Cl and filtered through a short pad of celite. The filtrate was concentrated to remove THF. The resulting mixture was extracted with CH_2Cl_2 (3 x 30 mL), the combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification of the residue by flash column chromatography afforded the alcohol. **Step 2**: To the purified alcohol (1.0 eq) in CH_2Cl_2, was added Dess-Martin periodinane (1.2 eq) at 0 ºC. After completion of the reaction monitored by TLC (0.5 ~1 h), the mixture was quenched with satd. $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification of the residue by flash column chromatography afforded the pure keto ester.

Method C:

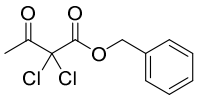


1b: R^4 = *n*-pentyl, R^5 = OBn,
1d: R^4 = *i*-Bu , R^5 = OBn
1r: R^4 = Me, R^5 = NBn(Allyl)

Step 1: To a solution of trichloro ester or amide (4 mmol, 1.0 eq) in THF (20 mL) was added ^{i}PrMgCl (2.0 M in THF, 4.4 mmol, 1.1 eq) at –20 ºC and the mixture was stirred at room temperature for 10 min, then cooled to –20 ºC and the aldehyde (4.4 mmol, 1.1 equiv) was added. The mixture was stirred for 30 min then warmed to room temperature. After completion of the reaction monitored by TLC, the mixture was quenched with satd. NH_4Cl at 0 ºC. After evaporation of THF under reduced pressure, and extraction with CH_2Cl_2, the combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification of the residue by flash column chromatography afforded the pure alcohol.

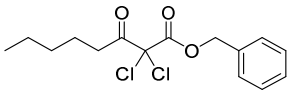
Step 2: To the purified alcohol (2 mmol, 1.0 eq) in CH_2Cl_2 at 0 ºC was added Dess-Martin periodinane (2.4 mmol, 1.2 eq). After completion of the reaction monitored by TLC (1 h), the mixture was quenched with satd. $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated under reduced pressure. Purification of the by flash column chromatography afforded the pure ketone.

3. Analytical data for compounds 1a–1r



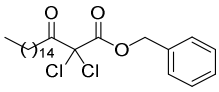
Benzyl 2,2-dichloro-3-oxobutanoate (1a)

Method A: **1a** (4.4 g, 98% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.36 (m, 5H), 5.32 (s, 2H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.3, 163.3, 134.0, 129.1, 128.9 (2C), 128.5 (2C), 82.0, 70.1, 23.5.



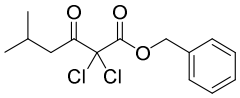
Benzyl 2,2-dichloro-3-oxooctanoate (1b)

Method C: **1b** (340 mg, 45% yield, two steps), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.34 (m, 5H), 5.31 (s, 2H), 2.73 (t, *J* = 7.3 Hz, 2H), 1.62 (quint, *J* = 7.4 Hz, 2H), 1.34 – 1.17 (m, 4H), 0.87 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.1, 163.5, 134.1, 129.1, 128.8 (2C), 128.6 (2C), 82.1, 70.0, 35.9, 31.0, 24.0, 22.4, 14.0.



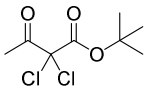
Benzyl 2,2-dichloro-3-oxoheptadecanoate (1c)

Method A: **1c** (1.02 g, 85% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.35 (m, 5H), 5.31 (s, 2H), 2.73 (t, *J* = 7.3 Hz, 2H), 1.63 – 1.60 (m, 2H), 1.26 – 1.24 (m, 24H), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.2, 163.5, 134.1, 129.1, 128.9 (2C), 128.6 (2C), 82.1, 70.0, 36.0, 32.1, 29.8 (5C), 29.7, 29.55, 29.52, 29.4, 28.9, 24.3, 22.8, 14.3.



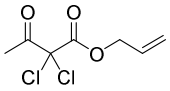
Benzyl 2,2-dichloro-5-methyl-3-oxohexanoate (1d)

Method C: **1d** (496 mg, 51% yield, two steps), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.35 (s, 5H), 5.32 (s, 2H), 2.62 (d, *J* = 6.8 Hz, 2H), 2.19 (hept, *J* = 6.7 Hz, 1H), 0.91 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.3, 163.5, 134.1, 129.1, 128.8 (2C), 128.6 (2C), 82.2, 70.0, 44.4, 24.7, 22.2 (2C).



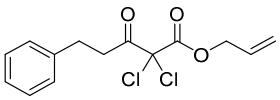
***tert*-Butyl 2,2-dichloro-3-oxobutanoate (1e)**

Method A: **1e** (2.0 g, 88% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.46 (s, 3H), 1.53 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.5, 162.0, 86.5, 82.9, 27.6 (3C), 23.8.



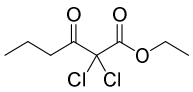
Allyl 2,2-dichloro-3-oxobutanoate (1f)

Method A: **1f** (1.58 g, 75% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 (ddt, *J* = 16.4, 10.6, 5.8 Hz, 1H), 5.45 – 5.39 (m, 1H), 5.36 – 5.32 (m, 1H), 4.79 (d, *J* = 5.8 Hz, 2H), 2.50 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.5, 163.2, 130.2, 120.4, 81.9, 68.8, 23.6.



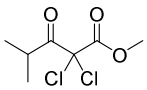
Allyl 2,2-dichloro-3-oxo-5-phenylpentanoate (1g)

Method A: **1g** (0.68 g, 66% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.2 Hz, 2H), 7.24 – 7.19 (m, 3H), 5.95 – 5.83 (m, 1H), 5.40 (dq, *J* = 17.2, 1.4 Hz, 1H), 5.33 (dd, *J* = 10.4, 1.1 Hz, 1H), 4.73 (dt, *J* = 5.9, 1.2 Hz, 2H), 3.18 – 3.14 (m, 2H), 3.00 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.4, 163.2, 139.9, 130.2, 128.8 (2C), 128.5 (2C), 126.7, 120.5, 81.9, 68.8, 37.9, 30.4.



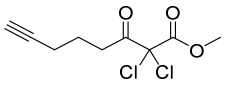
Ethyl 2,2-dichloro-3-oxohexanoate (1h)

Method A: **1h** (1.73 g, 95% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.36 (q, *J* = 7.1 Hz, 2H), 2.80 (t, *J* = 7.2 Hz, 2H), 1.72 (sext, *J* = 7.3 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.2, 163.6, 82.1, 64.7, 37.8, 17.9, 14.0, 13.5.



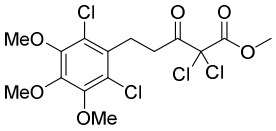
Methyl 2,2-dichloro-4-methyl-3-oxopentanoate (1i)

Method A: **1i** (1.33 g, 78% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.92 (s, 3H), 3.29 (hept, *J* = 6.7 Hz, 1H), 1.26 (d, *J* = 6.7 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 198.5, 164.2, 82.0, 55.0, 35.8, 21.1 (2C).



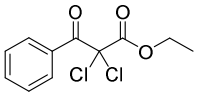
Methyl 2,2-dichloro-3-oxooct-7-ynoate (1j)

Method A: **1i** (1.58 g, 74% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.91 (s, 3H), 2.99 (t, *J* = 7.1 Hz, 2H), 2.27 (t, *J* = 6.8 Hz, 2H), 1.99 (s, 1H), 1.90 (quint, *J* = 6.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.9, 164.0, 83.0, 81.7, 69.7, 55.1, 34.5, 23.0, 17.6.



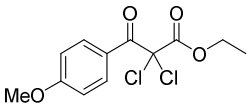
Methyl 2,2-dichloro-3-oxo-5-(3,4,5-trimethoxyphenyl)pentanoate (1k)

Method A: **1k** (0.68 g, 66% yield), white solid, mp 50 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.94 (s, 3H), 3.93 (s, 3H), 3.90 (s, 6H), 3.29 – 3.25 (m, 2H), 3.07 – 3.03 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 193.0, 164.0, 149.4 (2C), 146.9, 131.5, 124.2 (2C), 81.7, 61.5, 61.3 (2C), 55.2, 34.3, 26.8.



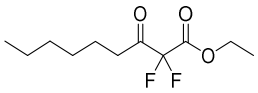
Ethyl 2,2-dichloro-3-oxo-3-phenylpropanoate (1l)

Method A: **1l** (0.9 g, 69% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.02 (m, 2H), 7.64 – 7.60 (m, 1H), 7.50 – 7.46 (m, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 1.18 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 183.3, 164.1, 134.3, 130.9, 130.1 (2C), 128.7 (2C), 82.0, 64.8, 13.7.



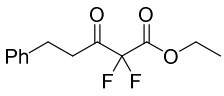
Ethyl 2,2-dichloro-3-(4-methoxyphenyl)-3-oxopropanoate (1m)

Method A: **1m** (0.62 g, 43% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.02 (m, 2H), 6.96 – 6.91 (m, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 3.89 (s, 3H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 182.0, 164.4 (2C), 132.8 (2C), 123.4, 114.0 (2C), 82.3, 64.7, 55.7, 13.8.



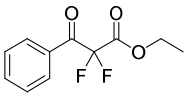
Ethyl 2,2-difluoro-3-oxononanoate (1n)

Method B: **1n** (0.61 g, 63% yield, two steps), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.39 (q, *J* = 7.1 Hz, 2H), 2.75 (t, *J* = 7.2 Hz, 2H), 1.70 – 1.63 (m, 2H), 1.39 – 1.32 (m, 9H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.34 – 1.23 (m, 6H), 0.91 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.6 (t, *J* = 28.0 Hz), 161.6 (t, *J* = 30.6 Hz), 108.3 (t, *J* = 264.0 Hz), 63.8, 36.8, 31.5, 28.6, 22.6 (2C), 14.1, 14.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ –113.9.



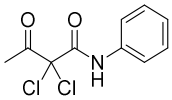
Ethyl 2,2-difluoro-3-oxo-5-phenylpentanoate (1o)

Method B: **1o** (1.31 g, 59% yield, two steps), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.24 – 7.18 (m, 3H), 4.33 (q, *J* = 7.1 Hz, 2H), 3.10 – 3.05 (m, 2H), 2.99 – 2.95 (m, 2H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 196.6 (t, *J* = 28.2 Hz), 161.3 (t, *J* = 30.7 Hz), 139.8, 128.7 (2C), 128.4 (2C), 126.6, 108.3 (t, *J* = 264.0 Hz), 63.9, 38.5, 28.5, 13.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ –113.9.



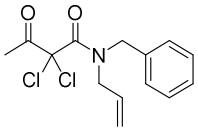
Ethyl 2,2-difluoro-3-oxo-3-phenylpropanoate (1p)

Following a reported procedure,[3] **1p** (0.246 g, 36% yield), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 – 8.07 (m, 2H), 7.70 – 7.66 (m, 1H), 7.55 – 7.51 (m, 2H), 4.39 (q, *J* = 7.1 Hz, 2H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 185.6 (t, *J* = 27.5 Hz), 161.9 (t, *J* = 30.6 Hz), 135.2, 131.1, 130.0 (2C), 129.1 (2C), 109.90 (t, *J* = 264.6 Hz), 63.9, 13.9.



2,2-dichloro-3-oxo-N-phenylbutanamide (1q)

Method A: **1q** (2.3 g, 93% yield), white solid, m.p. < 48 ºC. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 7.55 (d, *J* = 8.0 Hz, 2H), 7.41 – 7.37 (m, 2H), 7.25 – 7.21 (m, 1H), 2.55 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 191.7, 161.0, 136.0, 129.3 (2C), 126.0, 120.5 (2C), 83.2, 24.5.



***N*-allyl-N-benzyl-2,2-dichloro-3-oxobutanamide (1r)**

Method C: **1c** (714 mg, 65% yield, two steps), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$, at this temperature, two rotamers (A: major; B: minor) in 60:40 ratio are visible) δ 7.44 – 7.20 (m, 5H) [A + B], 5.90 [A] (ddt, *J* = 16.3, 11.7, 6.0 Hz, 1 H), 5.74 [B] (ddt, *J* = 16.2, 11.1, 5.8 Hz, 1H), 5.39 [A] (d, *J* = 9.7 Hz, 1H), 5.29 [A] (d, *J* = 17.2 Hz, 1H), 5.24 [B] (d, *J* = 10.3 Hz, 1H), 5.14 [B] (d, *J* = 17.1 Hz, 1H), 4.97 [B] (s, 2H), 4.62 [A] (s, 2H), 4.25 [A] (d, *J* = 5.9 Hz, 2H), 3.89 [B] (d, *J* = 5.6 Hz, 2H), 2.56 [B] (s, 3H), 2.53 [A] (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, major rotamer) δ 190.2, 163.7, 135.8, 132.1, 128.9 (2C), 128.0 (2C), 127.9, 120.1, 83.8, 50.3, 48.3, 25.56; ^{13}C NMR (101 MHz, $CDCl_3$, minor rotamer) δ 190.2, 163.8, 135.1, 130.8, 128.9 (2C), 128.1, 127.5 (2C), 118.5, 83.6, 51.4, 48.2, 25.64.

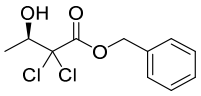
4. General procedure for the synthesis of 2a–2h and 2j–2r by ATH.

A round-bottomed tube equipped with a balloon of argon was charged with the corresponding dihalogeno β-keto ester (or dihalo β-keto amide) **1** (1.0 mmol [or 0.6 mmol]) and the [RuCl(*p*-cymene)(*R,R*)-TsDPEN] complex (0.005 mmol, 0.5 mol% [or 0.006 mmol, 1.0 mol%]). The mixture was subjected to three vacuum/argon cycles before degassed dichloromethane (5 mL [or 3 mL]) was added. The mixture was stirred at room temperature for 3-5 min, then HCO_2H/Et_3N (5:2) azeotropic mixture (168 μL, 2.0 mmol, 2.0 eq [or 101 μL, 1.2 mmol, 2.0 eq]) was added dropwise. and the reaction was heated at 30 ºC. After complete consumption of the starting material (monitored by TLC or ^{1}H NMR), the catalyst was removed through a short pad of silica gel (petroleum ether/ethyl acetate 4:1 to 3:1). The filtrate was concentrated under vacuum to give the crude product. The

[3] Stavber, G.; Stavber, S. *Adv. Synth. Catal.* **2010**, *352*, 2838.

conversion was determined by ^{1}H NMR analysis of the crude product. After purification of the crude product by flash column chromatography, the enantiomeric excess was determined by SFC or HPLC analysis (CHIRALPAK IA, IB, ID, IE).

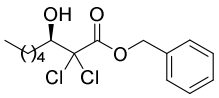
5. Analytical data for compounds 2a–2h and 2j–2r.



Benzyl (*R*)-2,2-dichloro-3-hydroxybutanoate (2a)

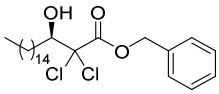
Colorless oil, 152 mg, 96% yield, > 99% ee. $[\alpha]_D^{25}$ = –7.1 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 – 7.33 (m, 5H), 5.32 (s, 2H), 4.53 – 4.43 (m, 1H), 2.61 (d, *J* = 7.2 Hz, 1H), 1.44 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 134.4, 128.9, 128.8 (2C), 128.2 (2C), 87.2, 73.6, 69.4, 17.2.

SFC: Chiralpak IA-H, *sc*CO_2/ ^{i}PrOH 96/4, 3.0 mL/min, P = 150 bar, λ = 215 nm, t_R = 8.86 min (major), t_R = 9.86 min. HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_{11}H_{12}Cl_2O_3Na$ 285.0061, found 285.0057.



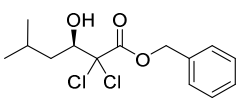
Benzyl (*R*)-2,2-dichloro-3-hydroxyoctanoate (2b)

Colorless oil, 134 mg, 70% yield, >99% ee. $[\alpha]_D^{25}$ = +13.4 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.35 (m, 5H), 5.36, 5.28 (ABq, J_{AB} = 13.5 Hz, 2H), 4.21 (ddd, *J* = 9.3, 7.4, 1.9 Hz, 1H), 2.44 (d, *J* = 7.4 Hz, 1H), 1.84 – 1.74 (m, 1H), 1.59 (m, 2H), 1.43 – 1.23 (m, 5H), 0.89 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 134.4, 128.91, 128.85 (2C), 128.3 (2C), 87.3, 77.5, 69.4, 31.6, 31.2, 25.7, 22.6, 14.1. SFC: Chiralpak IA-H, *sc*CO_2/ ^{i}PrOH 96/4, 3.0 mL/min, P = 150 bar, λ = 215 nm, t_R = 12.44 min, t_R = 14.67 min (major). HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_{15}H_{20}Cl_2O_3Na$ 341.0687, found 341.0682.



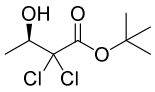
Benzyl (*R*)-2,2-dichloro-3-hydroxyheptadecanoate (2c)

White solid, m.p. < 48 ºC. 204 mg, 90% yield, 98% ee. $[\alpha]_D^{25}$ = +9.8 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.37 (m, 5H), 5.36, 5.28 (ABq, J_{AB} = 13.0 Hz, 2H), 4.23 – 4.19 (m, 1H), 2.44 (d, *J* = 7.4 Hz, 1H), 1.83 – 1.76 (m, 1H), 1.64 – 1.50 (m, 2H), 1.26 (br s, 25H), 0.88 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 134.4, 128.91, 128.85 (2C), 128.3 (2C), 87.3, 77.5, 69.4, 32.1, 31.3, 29.8 (6C), 29.7, 29.6, 29.51, 29.46, 26.0, 22.8, 14.3. HPLC: Chiralpak IB, Hexane/^{i}PrOH 97/3, 1.0 mL/min, λ = 215 nm, t_R = 7.81 min, t_R = 9.48 min (major). MS (ESI): *m/z* = 476 $[M + NH_4]^+$.



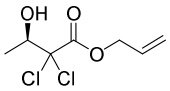
Benzyl (*R*)-2,2-dichloro-3-hydroxy-5-methylhexanoate (2d)

White solid, m.p. 54 ºC, 47.6 mg, 26% yield, >99% ee. $[\alpha]_D^{25}$ = +16.0 (*c* 1.01, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.34 (m, 5H), 5.42, 5.26 (ABq, J_{AB} = 13.7 Hz, 2H), 4.29 (ddd, *J* = 9.6, 7.4, 2.3 Hz, 1H), 2.45 (d, *J* = 7.3 Hz, 1H), 1.92 – 1.82 (m, 1H), 1.60 – 1.48 (m, 2H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.91 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 134.4, 128.93, 128.86 (2C), 128.4 (2C), 87.5, 75.9, 69.4, 40.2, 24.8, 23.8, 21.6. SFC: Chiralpak IA-H, *sc*CO_2/ ^{i}PrOH 96/4, 3.0 mL/min, P = 150 bar, λ = 215 nm, t_R = 7.98 min, t_R = 8.94 min (major). HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_{14}H_{18}Cl_2O_3Na$ 327.0531, found 327.0526.



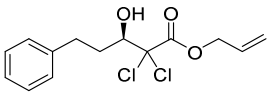
***tert*-Butyl (*R*)-2,2-dichloro-3-hydroxybutanoate (2e)**

White solid, m.p. < 50 ºC, 192 mg, 84% yield, 99% ee. $[\alpha]_D^{25}$ = –7.3 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.41 (quint, *J* = 6.3 Hz, 1H), 2.68 (d, *J* = 7.0 Hz, 1H), 1.54 (s, 9H), 1.43 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.7, 88.1, 85.5, 73.6, 27.7, 17.4 (3C). HPLC: Chiralpak IE, Hexane/^{i}PrOH 98/2, 1.0 mL/min, λ = 215 nm, t_R = 10.05 min, t_R = 13.36 min (major). HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_8H_{14}Cl_2O_3Na$ 251.0218, found 251.0213.



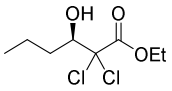
Allyl (*R*)-2,2-dichloro-3-hydroxybutanoate (2f)

Colorless oil, 158 mg, 74% yield, >99% ee. $[\alpha]_D^{25}$ = –7.0 (*c* 1.06, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.95 (ddt, *J* = 17.1, 10.5, 5.7 Hz, 1H), 5.44 (dq, *J* = 17.2, 1.4 Hz, 1H), 5.33 (dq, *J* = 10.5, 1.1 Hz, 1H), 4.78 (dt, *J* = 5.7, 1.3 Hz, 2H), 4.64 – 4.34 (m, 1H), 2.65 (d, *J* = 7.2 Hz, 1H), 1.46 (d, *J* = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.7, 130.5, 119.8, 87.1, 73.6, 68.2, 17.2. HPLC: Chiralpak IB, Hexane/^{i}PrOH 98/2, 1.0 mL/min, λ = 215 nm, t_R = 10.80 min (major), t_R = 14.30 min. HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_7H_{10}Cl_2O_3Na$ 234.9905, found 234.9900.



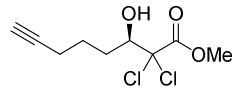
Allyl (*R*)-2,2-dichloro-3-hydroxy-5-phenylpentanoate (2g)

Colorless oil, 147 mg, 78% yield, > 99% ee. $[\alpha]_D^{25}$ = +28.0 (*c* 1.02, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 2H), 7.24 – 7.19 (m, 3H), 5.92 (ddt, *J* = 16.5, 11.0, 5.7 Hz, 1H), 5.42 (d, *J* = 17.2 Hz, 1H), 5.32 (d, *J* = 10.5 Hz, 1H), 4.76 (d, *J* = 5.7 Hz, 2H), 4.23 (ddd, *J* = 9.6, 7.0, 1.7 Hz, 1H), 2.98 (ddd, *J* = 14.1, 9.4, 4.9 Hz, 1H), 2.75 (dt, *J* = 13.9, 8.4 Hz, 1H), 2.64 (d, *J* = 7.0 Hz, 1H), 2.25 – 2.16 (m, 1H), 1.97 (dtd, *J* = 14.2, 9.6, 4.9 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 141.1, 130.4, 128.56 (2C), 128.52 (2C), 126.3, 119.9, 86.7, 76.6, 68.2, 32.7, 31.9. SFC: Chiralpak IA-H, *sc*CO_2/ ^{i}PrOH 96/4, 3.0 mL/min, P = 150 bar, λ = 215 nm, t_R = 12.14 min, t_R = 14.87 min (major). HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_{14}H_{16}Cl_2O_3Na$ 325.0374, found 325.0370.



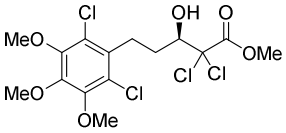
Ethyl (*R*)-2,2-dichloro-3-hydroxyhexanoate (2h)

Colorless oil, 100 mg, 72% yield, >99% ee. $[\alpha]_D^{25}$ = +15.5 (*c* 1.03, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 4.36 (q, *J* = 7.1 Hz, 2H), 4.22 (ddd, *J* = 9.3, 7.4, 1.8 Hz, 1H), 2.50 (d, *J* = 7.3 Hz, 1H), 1.87 – 1.78 (m, 1H), 1.71 – 1.55 (m, 2H), 1.50 – 1.42 (m, 1H), 1.37 (t, *J* = 7.1 Hz, 3H), 0.98 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.0, 87.2, 77.2, 64.1, 33.2, 19.2, 13.9 (2C). HPLC: Chiralpak IB, Hexane/^{i}PrOH 98/2, 1.0 mL/min, λ = 215 nm, t_R = 8.37 min, t_R = 9.11 min (major). HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_8H_{14}Cl_2O_3Na$ 251.0218, found 251.0213.



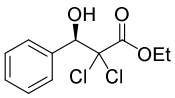
Methyl (*R*)-2,2-dichloro-3-hydroxyoct-7-ynoate (2j)

Colorless oil, 109 mg, 76% yield, > 99% ee. $[\alpha]_D^{25}$ = +18.5 (*c* 1.05, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 4.29 – 4.22 (m, 1H), 3.92 (s, 3H), 2.59 (d, *J* = 7.3 Hz, 1H), 2.29 (td, *J* = 6.7, 2.6 Hz, 2H), 2.10 – 2.01 (m, 1H), 1.98 (t, *J* = 2.6 Hz, 1H), 1.92 – 1.82 (m, 1H), 1.78 – 1.64 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 86.6, 83.8, 77.0, 69.1, 54.7, 30.0, 24.8, 18.2. HPLC: Chiralpak IE, Hexane/^{i}PrOH 95/5, 1.0 mL/min, λ = 215 nm, t_R = 10.25 min, t_R = 12.48 min (major). HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_9H_{12}Cl_2NaO_3$ 261.0061, found 261.0057.



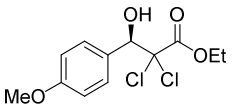
Methyl (*R*)-2,2-dichloro-5-(2,6-dichloro-3,4,5-trimethoxyphenyl)-3-hydroxypentanoate (2k)

Colorless oil, 127 mg, 48% yield, 98% ee. $[\alpha]_D^{25}$ = +12.6 (*c* 1.03, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 4.33 (ddd, *J* = 9.6, 7.7, 1.6 Hz, 1H), 3.92 (s, 3H), 3.91 (s, 3H), 3.90 (s, 6H), 3.27 (ddd, *J* = 13.0, 11.3, 5.0 Hz, 1H), 3.02 (ddd, *J* = 13.2, 11.0, 5.5 Hz, 1H), 2.65 (d, *J* = 7.6 Hz, 1H), 2.19 – 2.11 (m, 1H), 1.84 (ddd, *J* = 13.9, 10.1, 5.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.3, 149.2 (2C), 146.5, 133.1, 124.2 (2C), 86.5, 77.5, 61.5, 61.3 (2C), 54.7, 29.9, 28.4. HPLC: Chiralpak IA, Hexane/^{i}PrOH 95/5, 1.0 mL/min, λ = 215 nm, t_R = 9.93 min, t_R = 11.62 min (major). HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_{15}H_{18}Cl_4O_6Na$ 456.9755, found 456.9750.



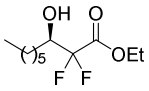
Ethyl (*R*)-2,2-dichloro-3-hydroxy-3-phenylpropanoate (2l)

Colorless oil, 79 mg, 50% yield, 70% ee. $[\alpha]_D^{25}$ = –11.3 (*c* 1.0, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.51 (m, 2H), 7.40 – 7.36 (m, 3H), 5.42 (d, *J* = 5.2 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.31 (d, *J* = 5.1 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 135.6, 129.3, 129.0 (2C), 127.9 (2C), 86.1, 78.8, 64.4, 13.9. HPLC: Chiralpak IE, Hexane/^{i}PrOH 90/10, 1.0 mL/min, λ = 215 nm, t_R = 7.13 min, t_R = 8.34 min (major). HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_{11}H_{12}Cl_2O_3Na$ 285.0061, found 285.0057.



Ethyl (*R*)-2,2-dichloro-3-hydroxy-3-(4-methoxyphenyl)propanoate (2m)

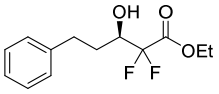
Colorless oil, 59 mg, 33.5% yield, 71% ee. $[\alpha]_D^{25}$ = –9.5 (*c* 1.07, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.44 (m, 2H), 6.92 – 6.88 (m, 2H), 5.38 (d, *J* = 5.1 Hz, 1H), 4.36 (q, *J* = 7.1 Hz, 2H), 3.82 (s, 3H), 3.20 (d, *J* = 5.1 Hz, 1H), 1.36 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.1, 160.2, 130.2 (2C), 127.7, 113.3 (2C), 86.6, 78.5, 64.3, 55.4, 13.9. HPLC: Chiralpak IE, Hexane/^{i}PrOH 94/6, 1.0 mL/min, λ = 254 nm, t_R = 18.37 min, t_R = 19.11 min (major). HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_{12}H_{14}Cl_2O_4Na$ 315.0167, found 315.0163.



Ethyl (*R*)-2,2-difluoro-3-hydroxynonanoate (2n)

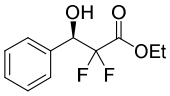
Colorless oil, 143 mg, 99% yield, 98% ee. $[\alpha]_D^{25}$ = +19.7 (*c* 1.11, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.36 (q, *J* = 7.1 Hz, 2H), 4.07 – 3.97 (m, 1H), 1.96 (d, *J* = 6.0 Hz, 1H), 1.71 – 1.49 (m, 4H), 1.37 (t, *J* = 7.1 Hz, 3H), 1.33 – 1.25 (m, 6H), 0.89 (t, *J* = 6.6 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ –115.0 (dd, *J* = 264.5, 7.4 Hz), –122.4 (dd, *J* = 264.5, 14.9 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.9 (t, *J* = 32.0 Hz), 115.4 (t, *J* = 255.4 Hz), 71.8 (t, *J* = 26.1 Hz), 63.2, 31.7, 29.3, 29.1, 25.3, 22.7, 14.1, 14.0.

HPLC: Chiralpak ID, Hexane/^{i}PrOH 98/2, 1.0 mL/min, λ = 215 nm, t_R = 8.90 min, t_R = 10.02 min (major). HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_{11}H_{20}F_2O_3Na$ 261.1278, found 261.1274.



Ethyl (*R*)-2,2-difluoro-3-hydroxy-5-phenylpentanoate (2o)[4]

Colorless oil, 153 mg, 99% yield, 98% ee. $[\alpha]_D^{25}$ = +31.9 (*c* 1.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.28 (m, 2H), 7.23 – 7.20 (m, 3H), 4.34 (q, *J* = 7.1 Hz, 2H), 4.09 – 3.95 (m, 1H), 2.93 (ddd, *J* = 14.1, 9.1, 5.2 Hz, 1H), 2.74 (dt, *J* = 13.9, 8.3 Hz, 1H), 2.07 (d, *J* = 7.1 Hz, 1H), 2.05 – 1.97 (m, 1H), 1.89 (m, 1H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ –114.88 (dd, *J* = 266.0, 7.6 Hz), –121.89 (dd, *J* = 266.0, 14.5 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7 (t, *J* = 31.8 Hz), 140.9, 128.7 (2C), 128.6 (2C), 126.4, 114.7 (t, *J* = 262.0 Hz), 71.1 (t, *J* = 26.2 Hz), 63.3, 31.3, 30.8, 14.0. SFC: Chiralpak IA-H, *sc*CO_2/ ^{i}PrOH 96/4, 3.0 mL/min, P = 150 bar, λ = 215 nm, t_R = 5.06 min, t_R = 5.94 min (major).

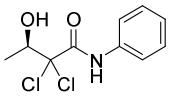


Ethyl (*R*)-2,2-difluoro-3-hydroxy-3-phenylpropanoate (2p)

Colorless oil, 136.7 mg, 99% yield, 56% ee. $[\alpha]_D^{25}$ = –6.8 (c 1.0, $CHCl_3$), [Lit.[5] $[\alpha]_D^{24}$ = –13.4 (c 1.29, $CHCl_3$, 97% ee)]. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.40 (m, 2H), 7.41 – 7.38 (m, 3H), 5.18 (ddd, *J* = 15.3,

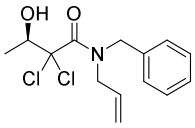
[4] Kuroki, Y.; Asada, D.; Iseki, K. *Tetrahedron Lett.* **2000**, *41*, 9853.

7.9, 5.3 Hz, 1H), 4.31 (q, J = 7.1 Hz, 2H), 2.62 (d, J = 5.3 Hz, 1H), 1.29 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.7 (t, J = 31.7 Hz), 134.6, 129.3 (2C), 128.5, 127.8 (2C), 113.9 (dd, J = 259.2, 254.2 Hz), 73.8 (dd, J = 27.5, 24.6 Hz), 63.3, 13.9. HPLC: Chiralpak IC, Hexane/^{i}PrOH 90/10, 1.0 mL/min, λ = 215 nm, t_R = 5.70 min (major), t_R = 7.09 min.



(*R*)-2,2-dichloro-3-hydroxy-N-phenylbutanamide (2q)

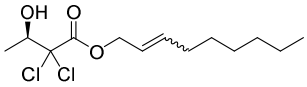
White solid, m.p. 78 ºC, 230 mg, 93% yield, 98.5% ee. $[\alpha]_D^{25}$ = –11.9 (*c* 1.02, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.55 (d, J = 7.7 Hz, 2H), 7.39 (t, J = 7.9 Hz, 2H), 7.21 (t, J = 7.4 Hz, 1H), 4.64 (quint, J = 6.1 Hz, 1H), 3.39 (d, J = 5.0 Hz, 1H), 1.50 (d, J = 6.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.1, 136.3 (2C), 129.3, 125.8, 120.6 (2C), 88.8, 73.2, 17.1. HPLC: Chiralpak IB, Hexane/^{i}PrOH 90/10, 1.0 mL/min, λ = 215 nm, t_R = 7.29 min (major), t_R = 8.06 min. HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_{10}H_{11}Cl_2NO_2Na$ 270.0065, found 270.0061.



(*R*)-N-allyl-N-benzyl-2,2-dichloro-3-hydroxybutanamide (2r)

Colorless oil, 179.5 mg, 99% yield, 98% ee. $[\alpha]_D^{25}$ = +19.7 (*c* 1.11, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$, at this temperature, two rotamers (A: major; B: minor) in 60:40 ratio are visible) δ 7.40 – 7.25[A+B] (m, 4H), 7.23 – 7.16 [A+B] (m, 1H), 5.91 [A] (ddt, J = 16.5, 11.9, 6.0 Hz, 1H), 5.72 [B] (ddt, J = 15.9, 10.6, 5.5 Hz, 1H), 5.34 [A] (d, J = 10.2 Hz, 1H), 5.25 [A] (d, J = 17.2 Hz, 1H), 5.19 [B] (d, J = 10.5 Hz, 1H), 5.15 [B] (d, J = 16.3 Hz, 1H), 5.09 [A] (d, J = 18.0 Hz, 1H), 5.00 [B] (d, J = 16.1 Hz, 1H), 4.69 – 4.55 [A+B] (m, 2H), 4.50 – 4.30 [A+B] (m, 2H), 3.96 – 3.79 [A+B] (m, 1H), 1.50 [A+B] (d, J = 6.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$, at this temperature, two rotamers (A: major; B: minor) are visible) δ 166.7 [A+B]; 136.0 [A], 135.6 [B]; 132.5 [A], 131.1 [B]; 128.9 [A+B] (2C); 128.0 [B], 127.7 [A]; 127.6 [A+B] (2C); 119.9 [A], 117.9 [B]; 85.6 [A], 85.5 [B]; 74.2 [A+B]; 52.1 [B], 51.2 [A]; 48.5 [A+B]; 16.3 [A+B]. HPLC: Chiralpak IE, Hexane/^{i}PrOH 98/2, 1.0 mL/min, λ = 215 nm, t_R = 15.79 min, t_R = 18.88 min (major). HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_{14}H_{17}Cl_2NO_2Na$ 324.0534, found 324.0530.

6. Analytical data for compounds 4–6.



(*Z*/*E*)-non-2-en-1-yl (*R*)-2,2-dichloro-3-hydroxybutanoate (4)

[5] Iseki, K.; Kuroki, Y.; Asada, D.; Takahashi, M.; Kishimoto, S.; Kobayashi, Y. *Tetrahedron* **1997**, *53*, 10271.

In a round-bottom tube, charged with Grubbs II catalyst (17 mg, 0.02 mmol) under an argon atmosphere, was added a solution of allyl (*R*)-2,2-dichloro-3-hydroxybutanoate (**2e**, 43 mg, 0.2 mmol) and 1-octene (63 μL, 0.4 mmol) in degassed DCM (2 mL). The mixture was heated to reflux until the conversion was complete as indicated by TLC (24 h). The solvent was removed under vacuum and the residue was purified by flash column chromatography with silica gel (petroleum ether/EtOAc, 20:1 to 15:1) to give compound **4** (40 mg, 67% yield, *Z*/*E* = 1/5.8) as a colorless oil.

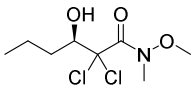
(*Z*)-non-2-en-1-yl (*R*)-2,2-dichloro-3-hydroxybutanoate (4)

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 – 5.72 (m, 2 H), 4.83 (d, *J* = 6.9 Hz, 2H), 4.47 (quint, *J* = 6.4 Hz, 1H), 2.67 – 2.64 (m, 1H), 2.17 – 2.13 (m, 2H), 1.45 (d, *J* = 6.2 Hz, 3H), 1.40 – 1.28 (m, 8H), 0.88 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 137.8, 121.5, 87.2, 73.6, 63.7, 29.4, 29.0, 28.5, 27.8, 22.6, 17.2, 14.2.

(*E*)-non-2-en-1-yl (*R*)-2,2-dichloro-3-hydroxybutanoate (4)

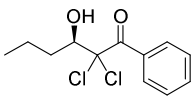
^{1}H NMR (400 MHz, $CDCl_3$) δ 5.88 (dt, *J* = 14.3, 6.6 Hz, 1H), 5.59 (dt, *J* = 13.9, 6.0 Hz, 1H), 4.72 (d, *J* = 6.5 Hz, 2H), 4.47 (quint, *J* = 6.4 Hz, 1H), 2.66 (d, *J* = 6.9 Hz, 1H), 2.07 (q, *J* = 7.4, 6.9 Hz, 2H), 1.45 (d, *J* = 6.2 Hz, 3H), 1.40 – 1.28 (m, 8H), 0.88 (t, *J* = 6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.8, 138.9, 122.1, 87.2, 73.6, 68.7, 32.4, 31.8, 28.9, 28.8, 22.7, 17.2, 14.2.

HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_{13}H_{22}Cl_2O_3Na$ 319.0844, found 319.0839.



(*R*)-2,2-dichloro-3-hydroxy-*N*-methoxy-*N*-methylhexanamide (5)

To a solution of *N,O*-dimethylhydroxylamine hydrochloride (0.87 g, 8.9 mmol) in THF (15 mL) was added ^{i}PrMgCl (2.0 M in THF, 8.9 mL, 17.8 mmol) at –30 ºC. The cooling bath was removed for 10 min, then the mixture was cooled again to –30 ºC, and a solution of ethyl (*R*)-2,2-dichloro-3-hydroxyhexanoate (**2h**, > 99% ee, 204 mg, 0.89 mmol) in THF (3 mL) was added. The reaction mixture was stirred at –30 ºC for 1 h, then warmed to room temperature for 30 min, quenched by satd. NH_4Cl (10 mL), and extracted with $^iPr_2O$ (3 x 20 mL). The combined extracts were dried (Mg_2SO_4), filtered and concentrated. Purification of the residue by flash column chromatography (petroleum ether/EtOAc 12:1 to 8:1) gave **5** (185 mg, 85% yield) as a colorless oil, $[\alpha]_D^{25}$ = – 34.3 (*c* 1.8, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.25 (ddd, *J* = 9.5, 4.1, 1.9 Hz, 1H), 3.82 (s, 3H), 3.78 (s, 1H), 3.36 (s, 3H), 1.92 – 1.84 (m, 1H), 1.75 – 1.62 (m, 2H), 1.51 – 1.40 (m, 1H), 0.98 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.6, 84.6, 77.3, 60.9, 34.9, 32.2, 19.4, 14.0. HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_8H_{15}Cl_2NO_3Na$ 266.0327, found 266.0323.



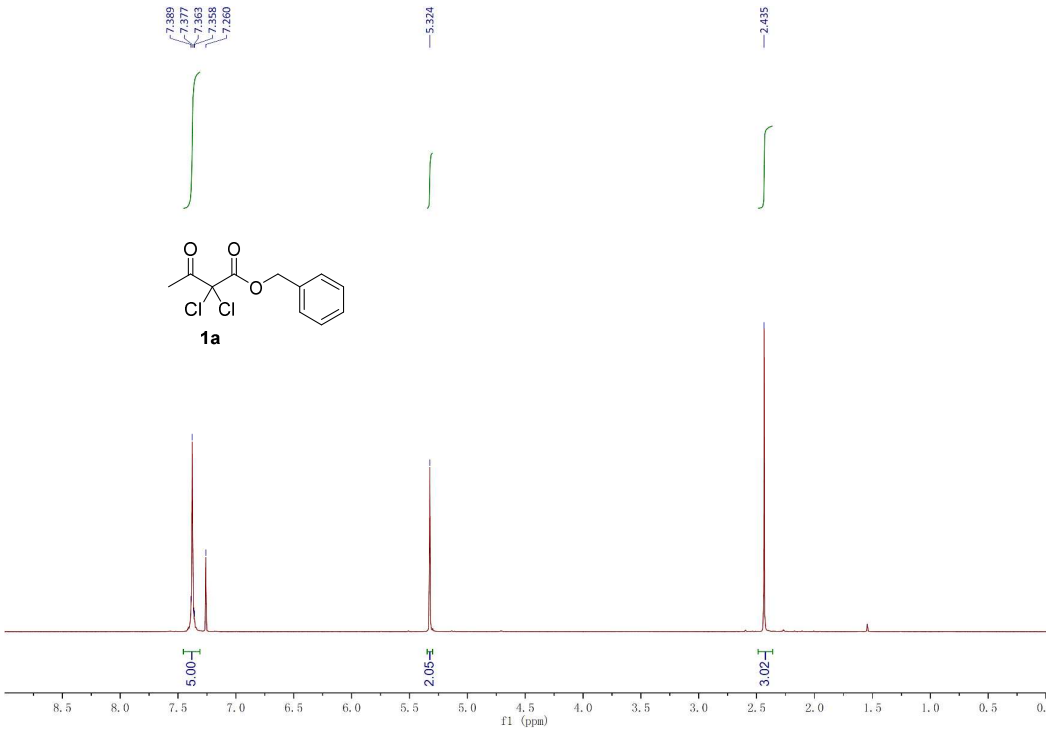
(*R*)-2,2-dichloro-3-hydroxy-1-phenylhexan-1-one (6)

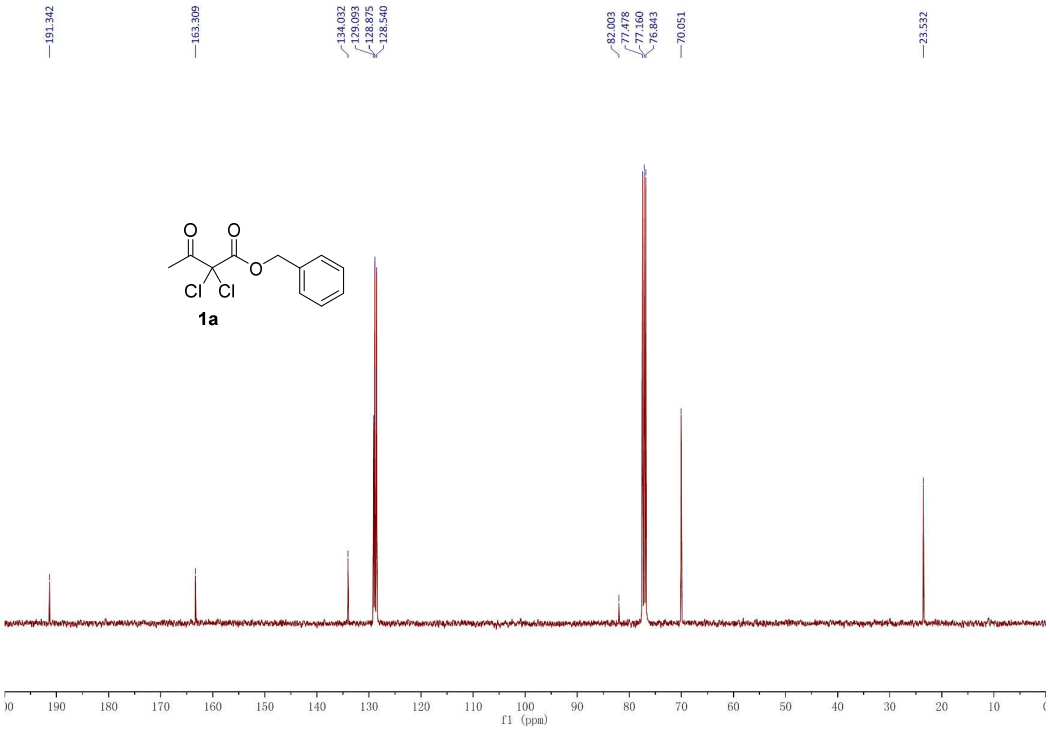
To a solution of **5** (49 mg, 0.2 mmol) in THF (1 mL) was added PhMgCl (2.0 M in THF, 0.5 mL, 1.0 mmol) at 0 ºC. The reaction mixture was stirred at this temperature for 3 h, quenched with satd. NH_4Cl (10 mL) and extracted with $^iPr_2O$ (3 x 20 mL). The combined extracts were washed with brine, dried ($MgSO_4$), filtered and

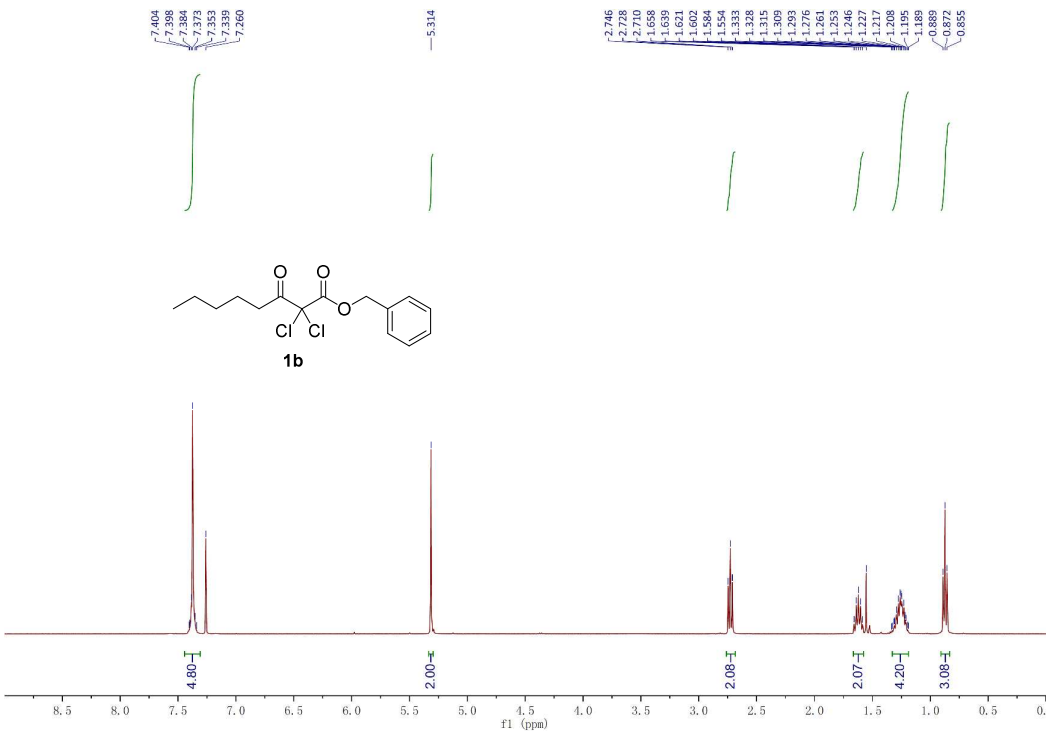
concentrated. Purification of the residue by flash column chromatography (petroleum ether/EtOAc 15:1) afforded **6** (28 mg, 54% yield) as a colorless oil, $[\alpha]_D^{25} = -13.7$ (*c* 0.8, $CHCl_3$).

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29 (dt, *J* = 8.6, 1.6 Hz, 2H), 7.64 – 7.59 (m, 1H), 7.51 – 7.46 (m, 2H), 4.40 (ddd, *J* = 9.7, 5.0, 1.9 Hz, 1H), 3.13 (dd, *J* = 5.1, 1.8 Hz, 1H), 2.00 – 1.92 (m, 1H), 1.80 – 1.68 (m, 2H), 1.53 – 1.47 (m, 1H), 1.01 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.3, 134.1, 132.0, 131.2 (2C), 128.3 (2C), 88.2, 76.7, 32.7, 19.4, 14.1. HRMS (ESI/ion trap): *m/z* $[M+Na]^+$ calcd for $C_{12}H_{14}Cl_2O_2Na$ 283.0269, found 283.0264.

7. NMR spectra of compounds 1a–1r



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1.293
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1.253
1.246
1.227
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1.208
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1.189
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0.872
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Cl
Cl
O
1b
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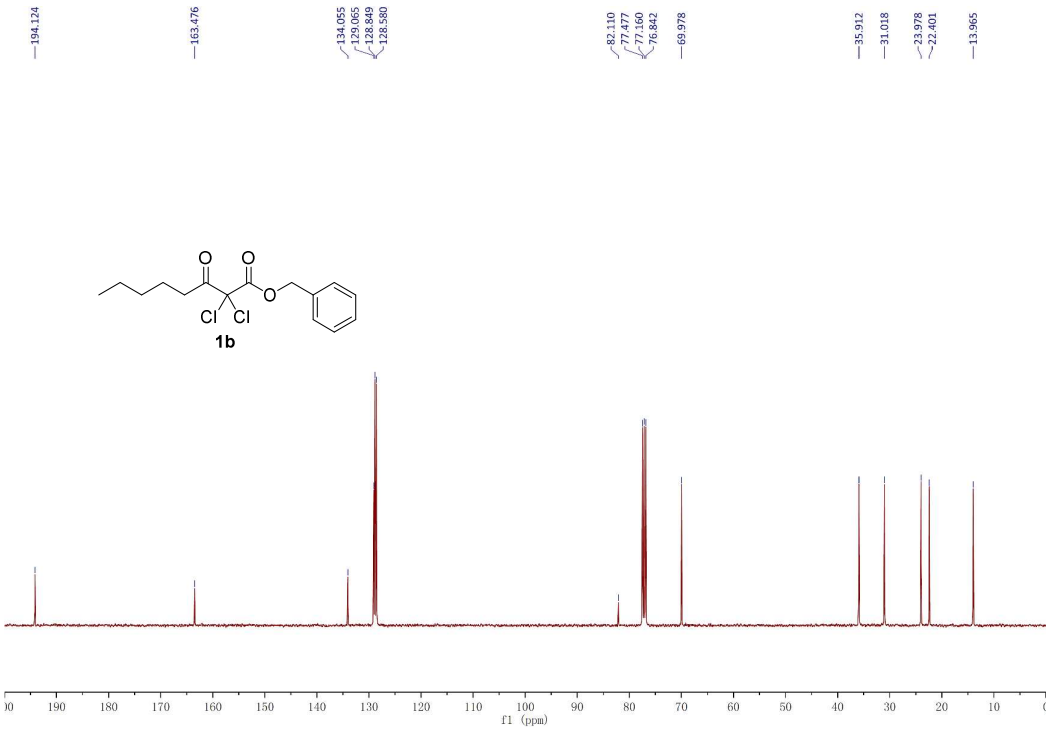
2.08
2.07
4.20
3.08
f1 (ppm)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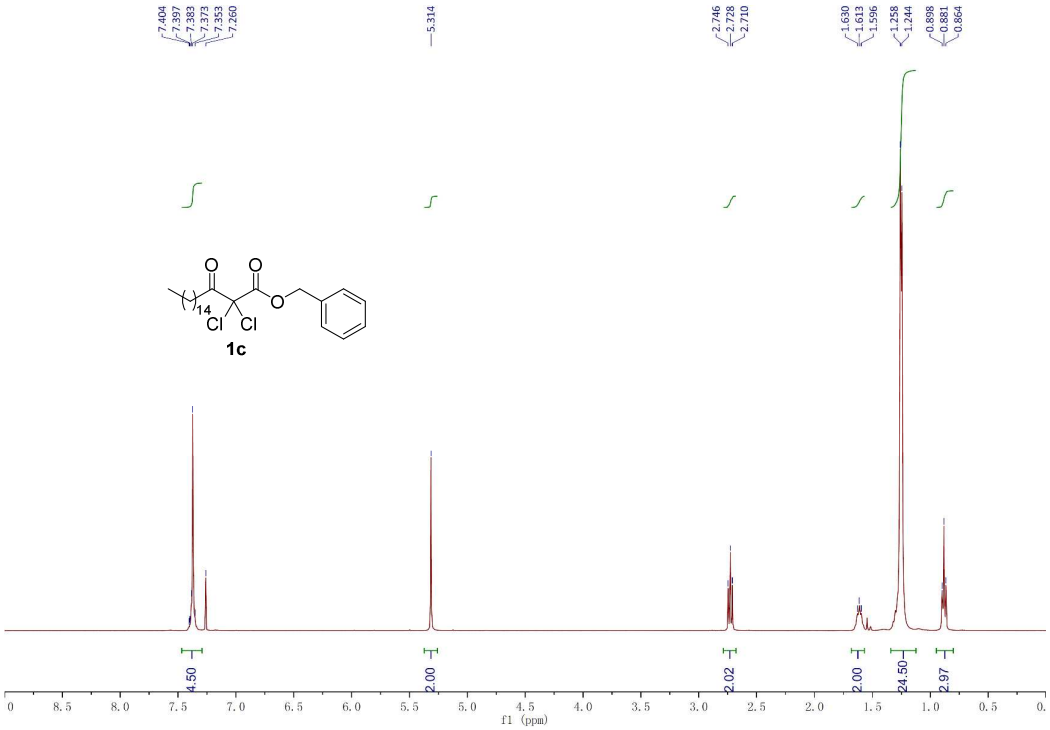
1b
f1 (ppm)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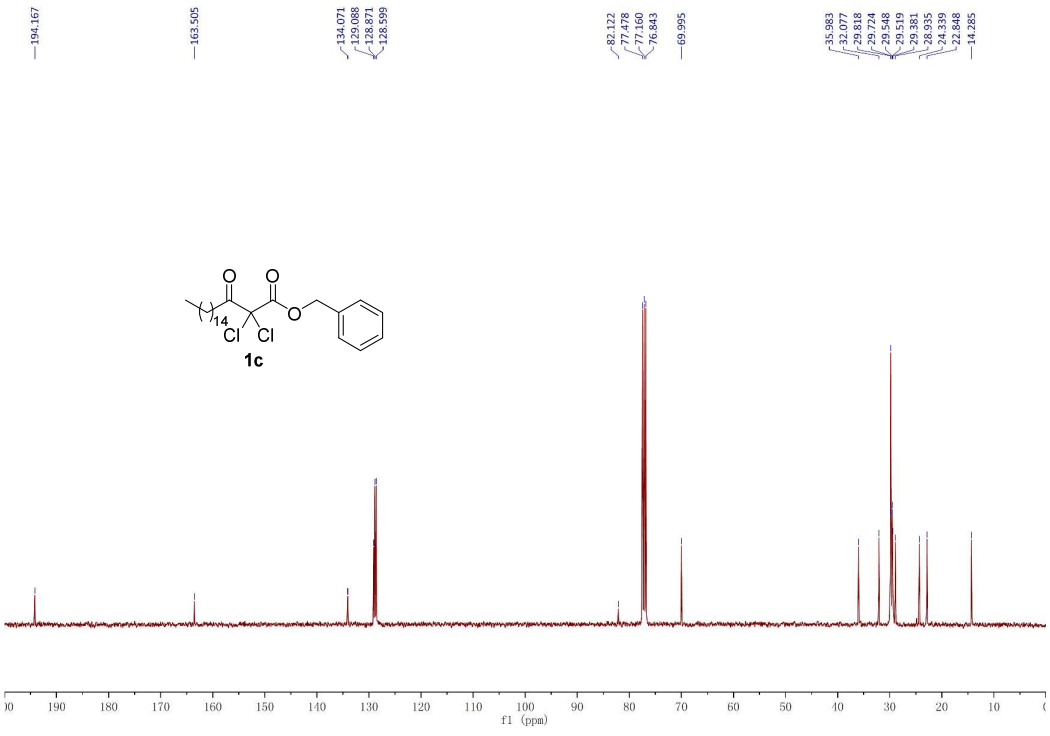
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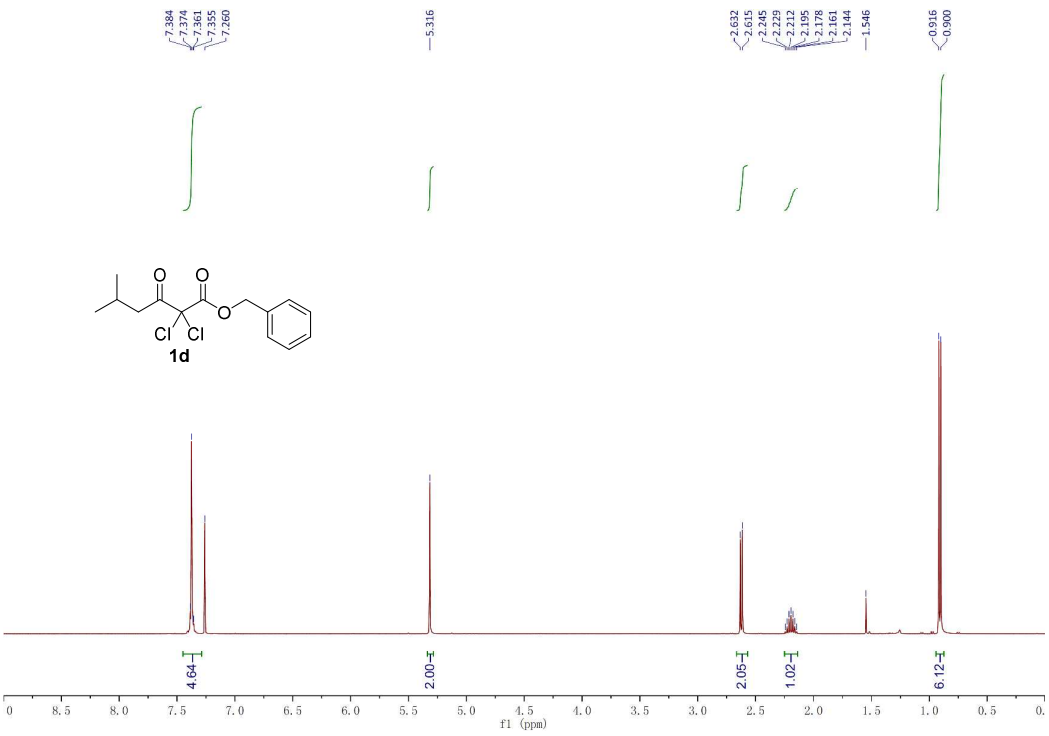
Cl
1c
f1 (ppm)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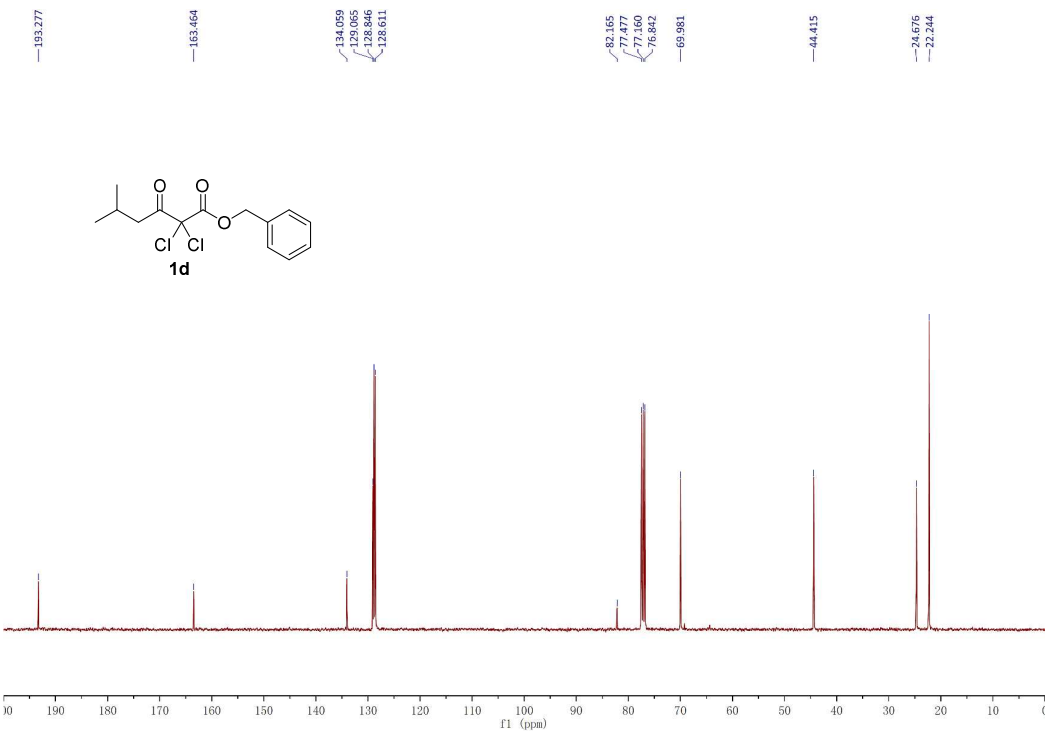
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Cl
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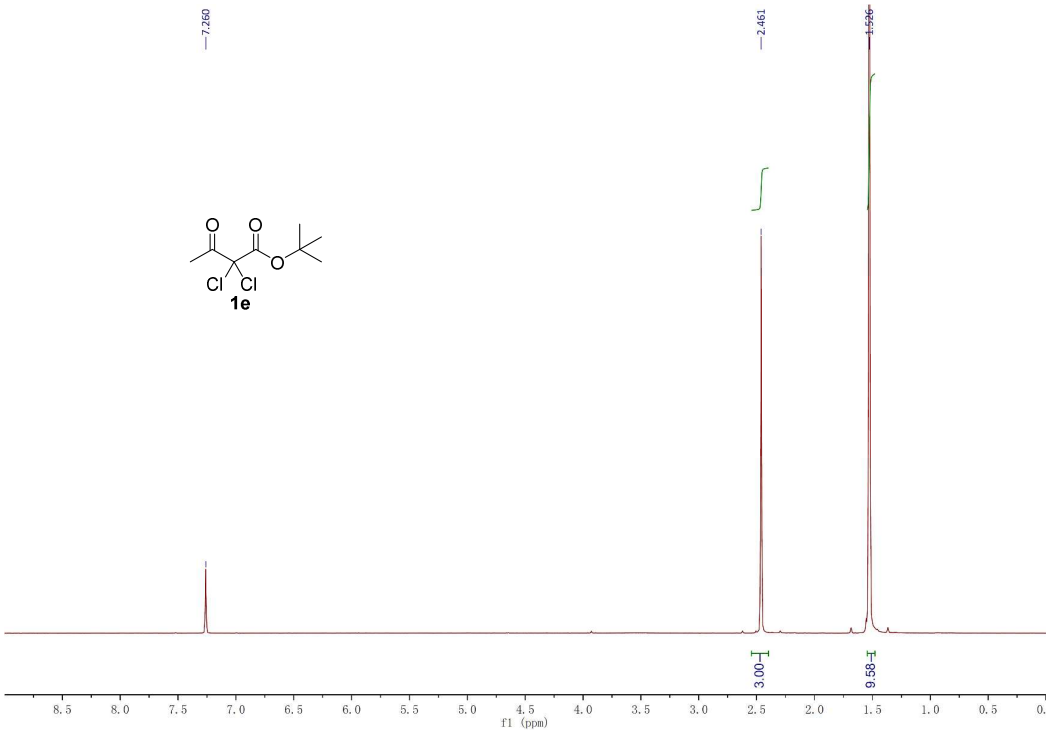
f1 (ppm)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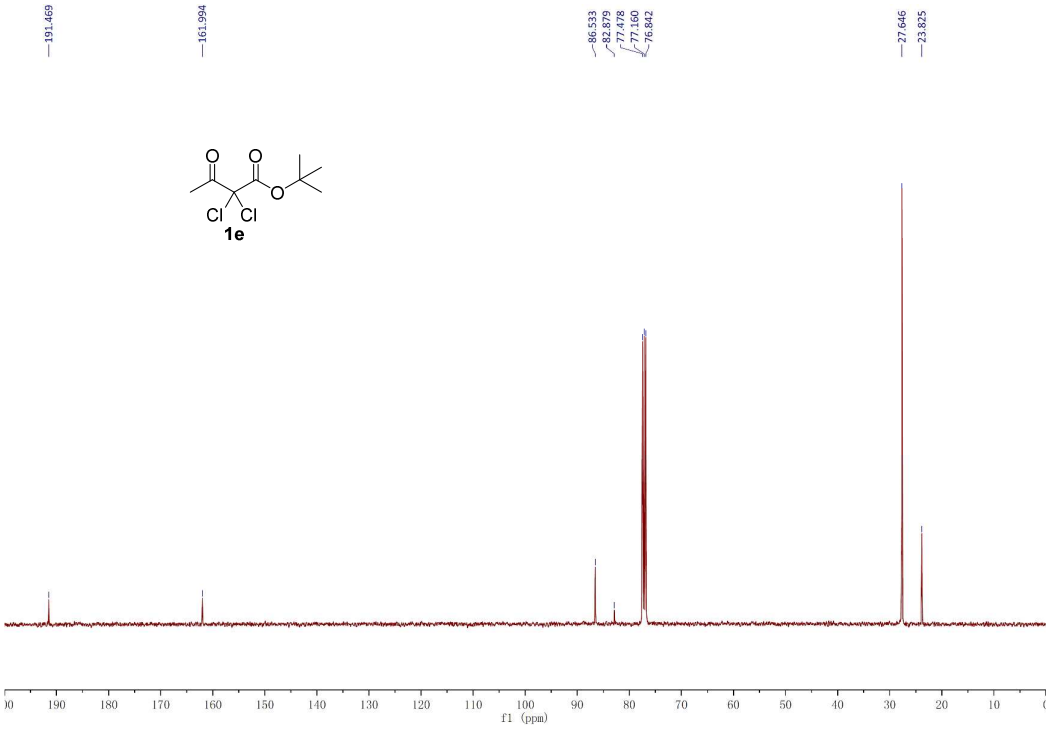
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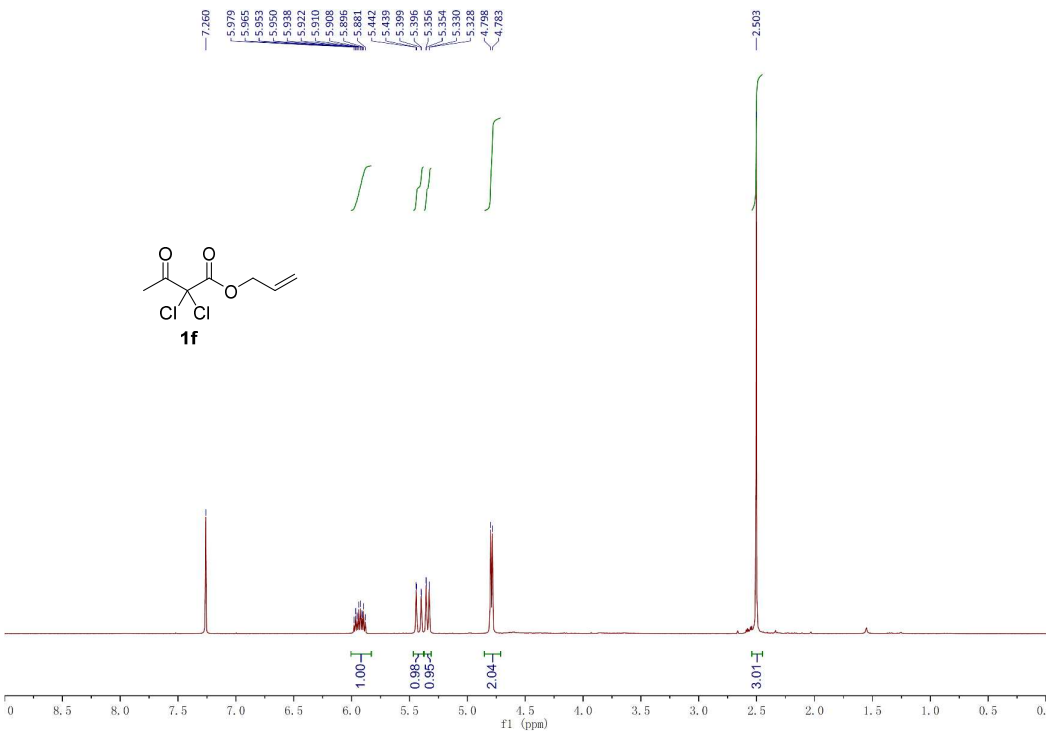
f1 (ppm)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5.399
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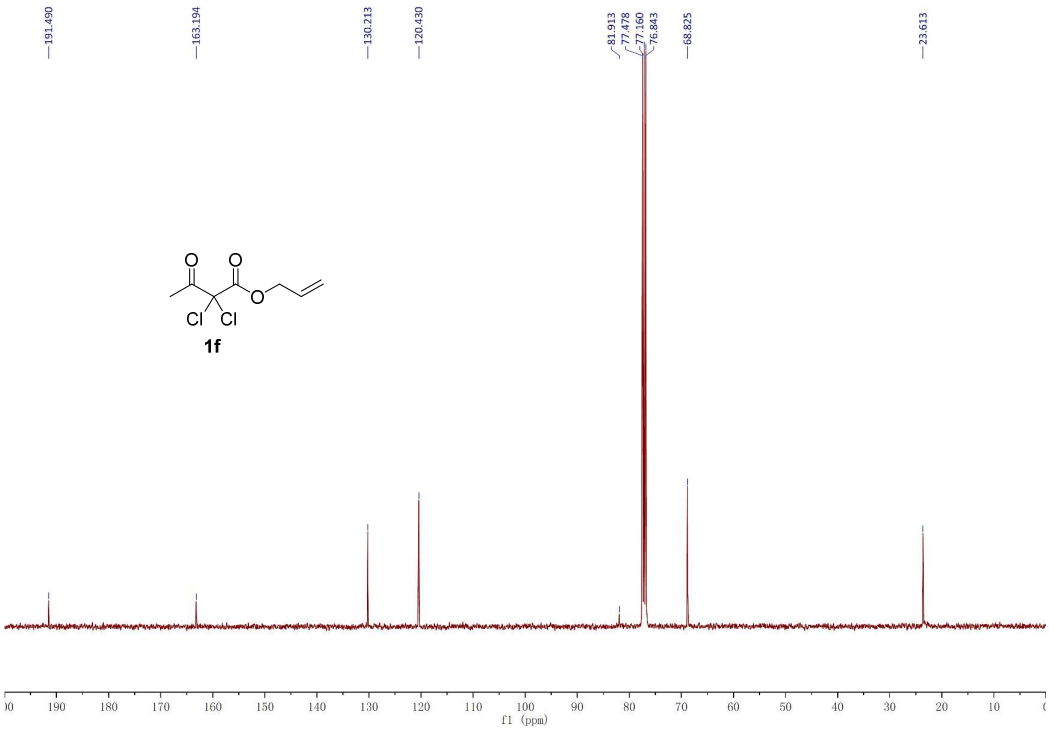
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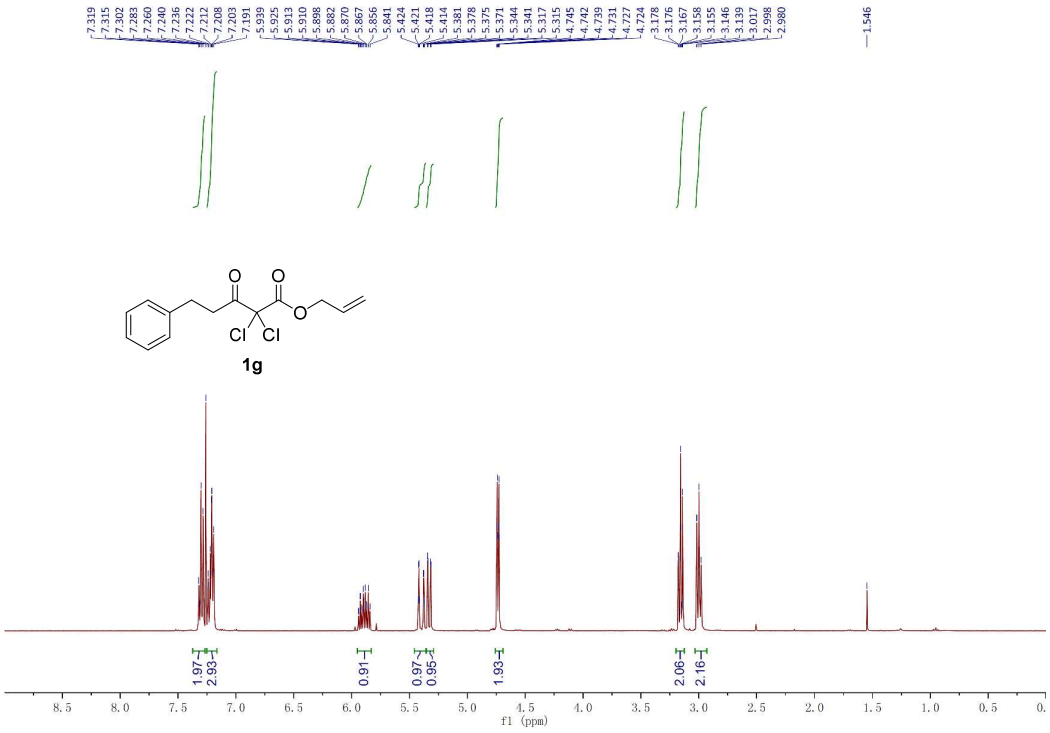
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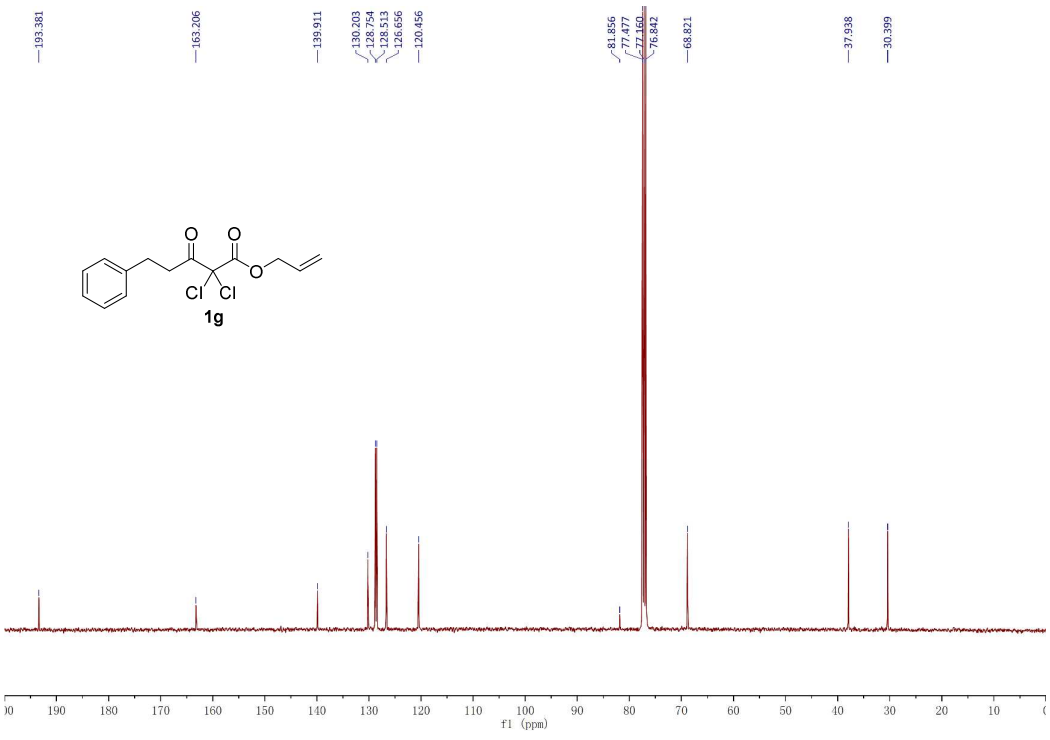
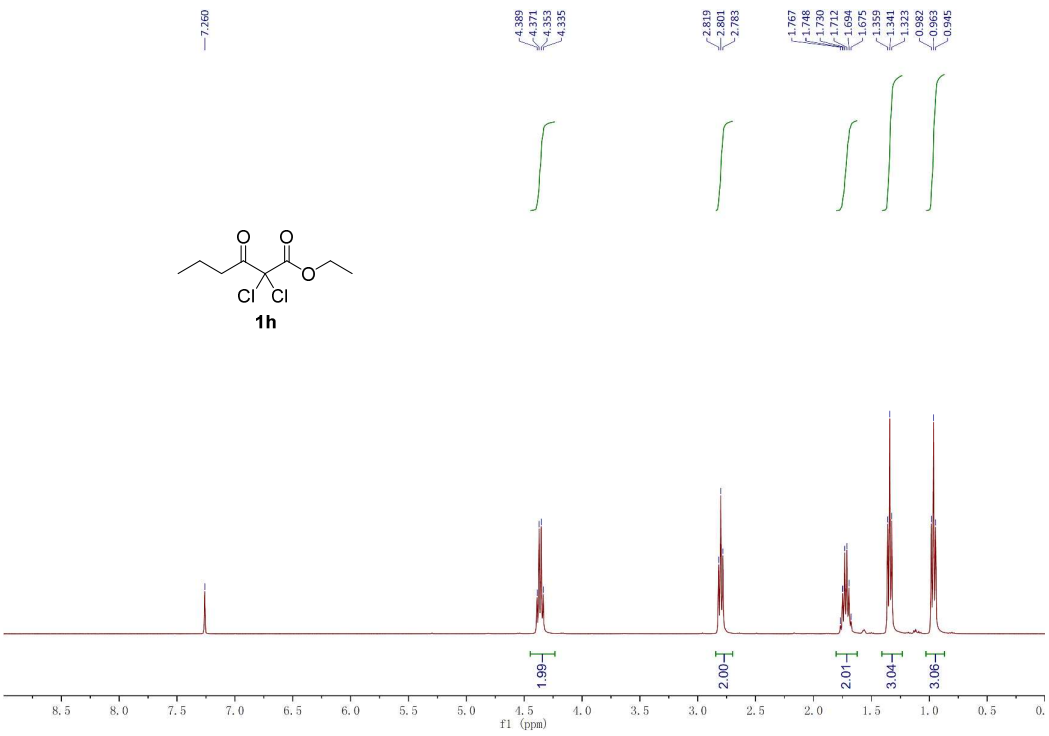
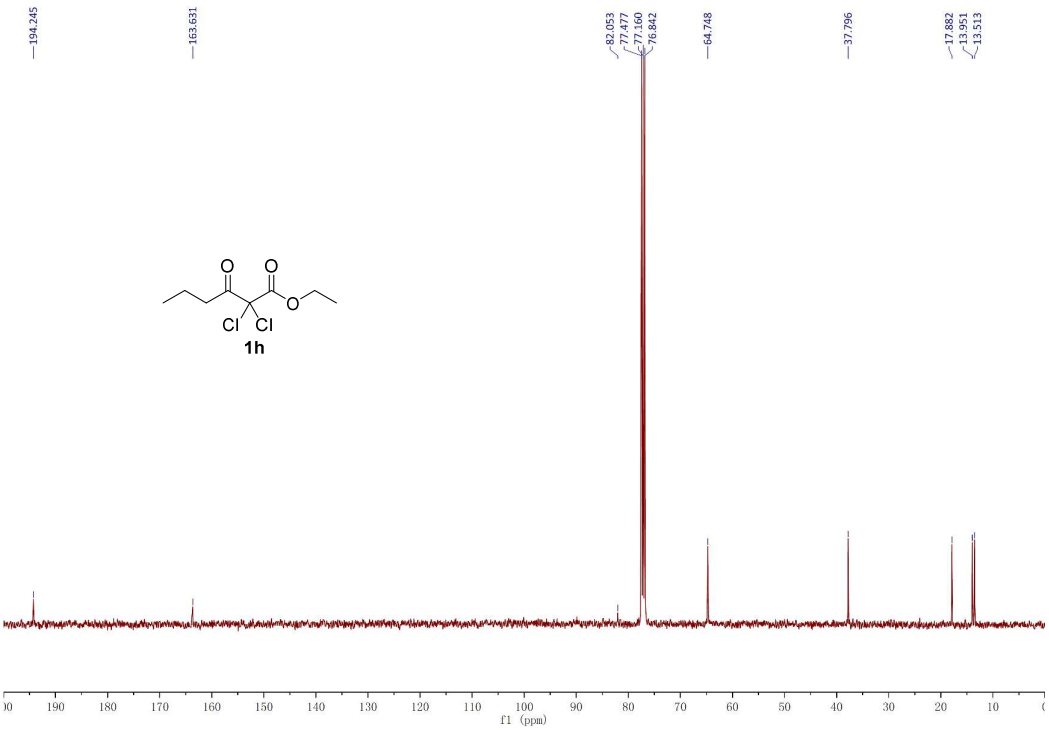
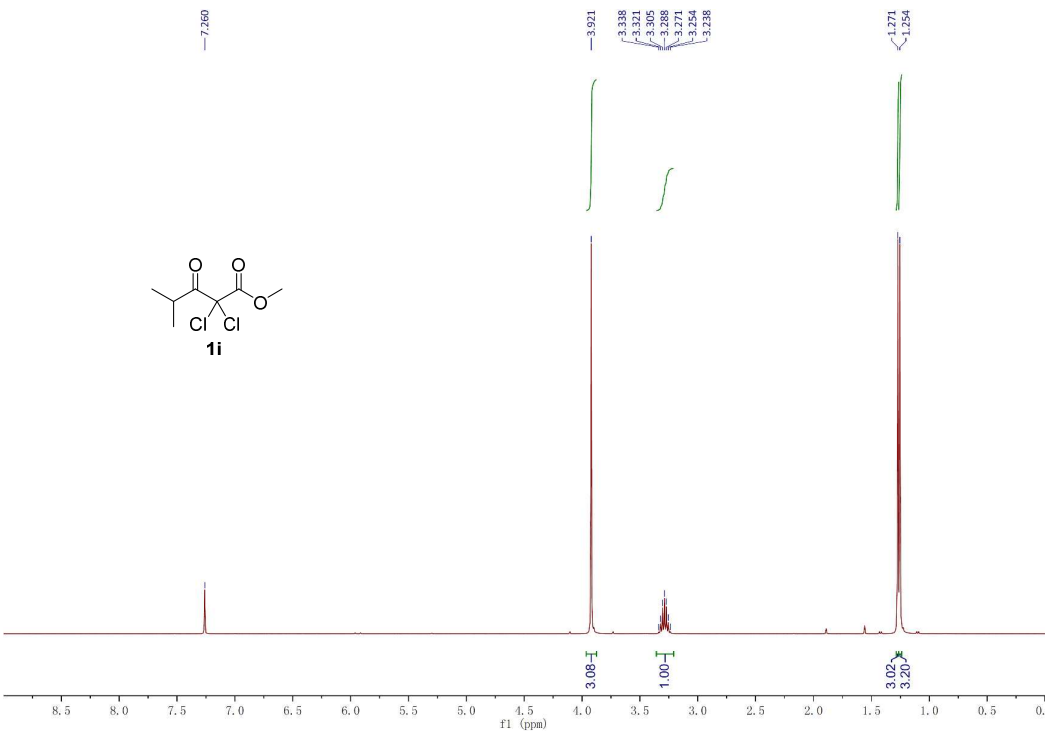
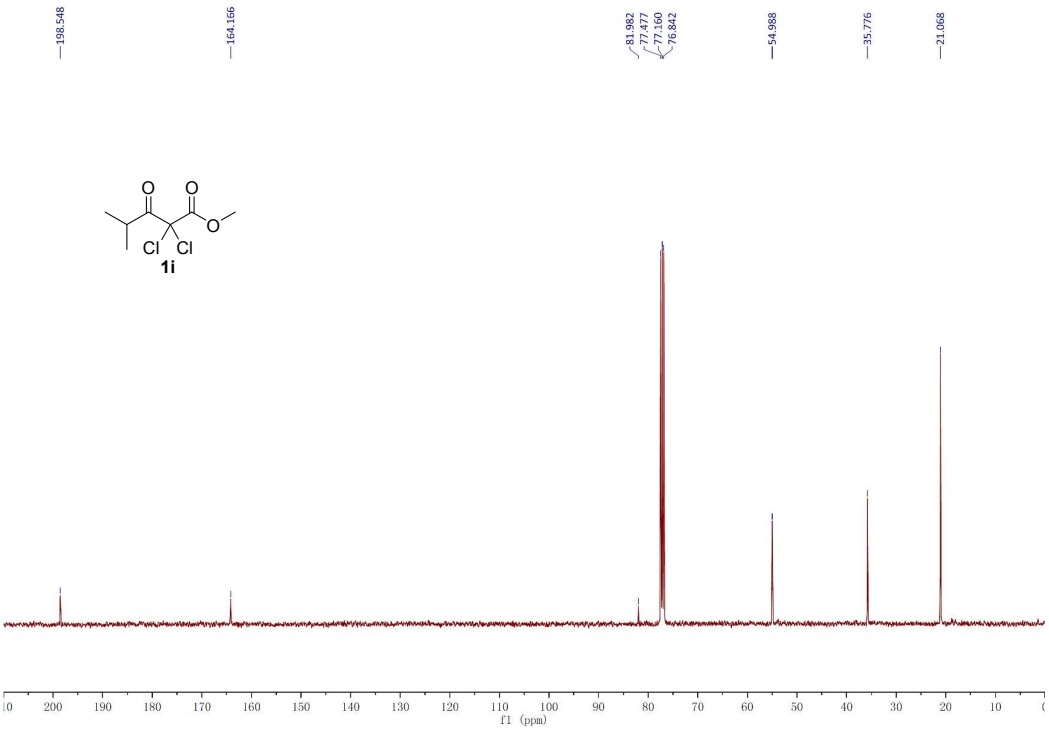
5.882
5.870
5.867
5.856
5.841
5.424
5.421
5.418
5.414
5.381
5.378
5.375
5.371
5.344
5.341
5.317
5.315
4.745
4.742
4.739
4.731
4.727
4.724
3.178
3.176
3.167
3.158
3.155
3.146
3.139
3.017
2.998
2.980
1.546
O
O
O
Cl
Cl
1g
1.97
2.93
0.91
0.97
0.95
1.93
2.06
2.16
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

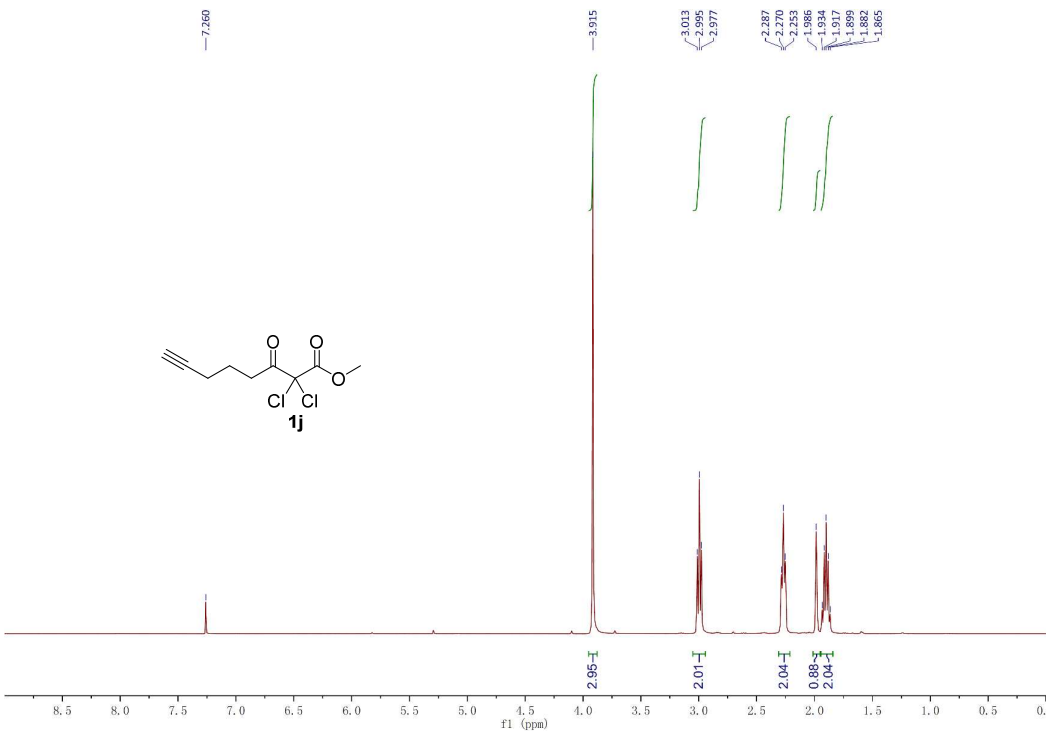

193.381
163.206
139.911
130.203
128.754
128.513
126.656
120.456
81.856
77.477
77.160
76.842
68.821
37.938
30.399
O
O
O
Cl
Cl
1g
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

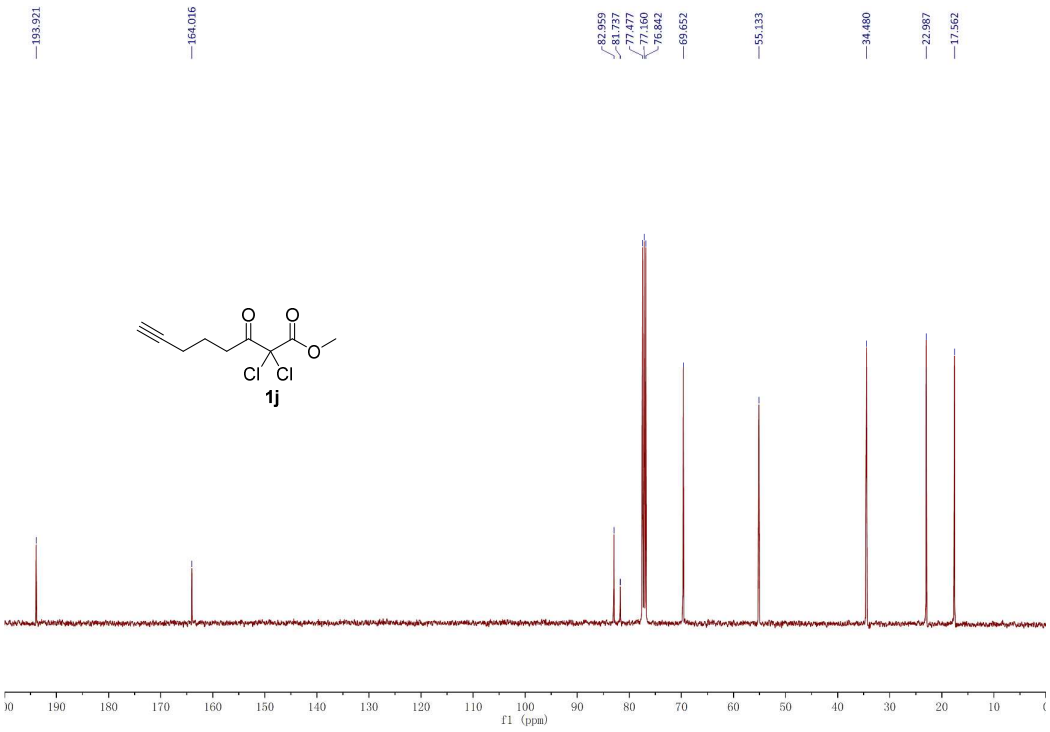

7.260
4.389
4.371
4.353
4.335
2.819
2.801
2.783
1.767
1.748
1.730
1.712
1.694
1.675
1.359
1.341
1.323
0.982
0.963
0.945
Cl Cl
1h
1.99
2.00
2.01
3.04
3.06
f1 (ppm)

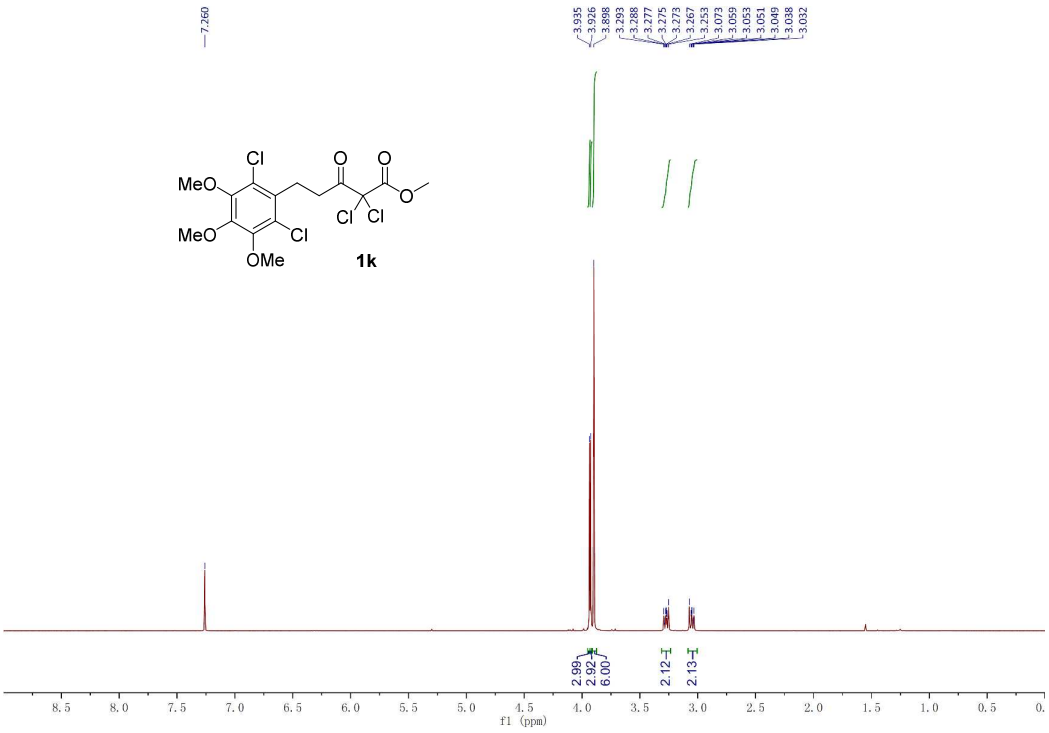

194.245
163.631
82.053
77.477
77.160
76.842
64.748
37.796
17.882
13.951
13.513
Cl Cl
1h
f1 (ppm)

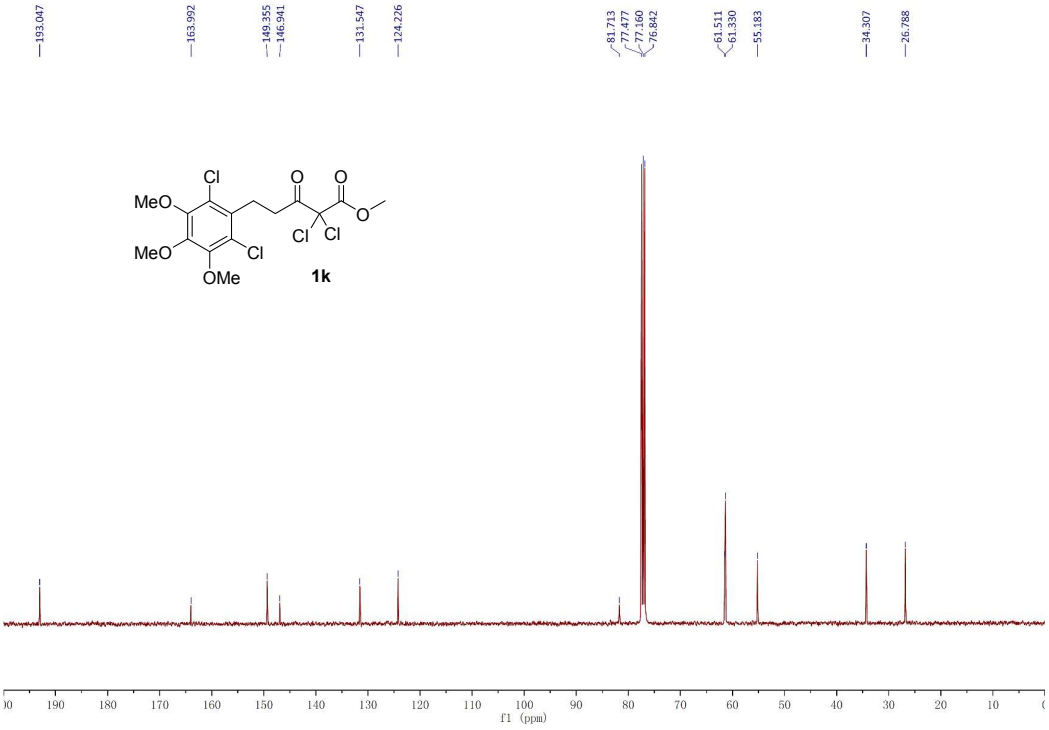

7.260
3.921
3.338
3.321
3.305
3.288
3.271
3.254
3.238
1.271
1.254
O
O
O
Cl
Cl
1i
3.08
1.00
3.02
3.20
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

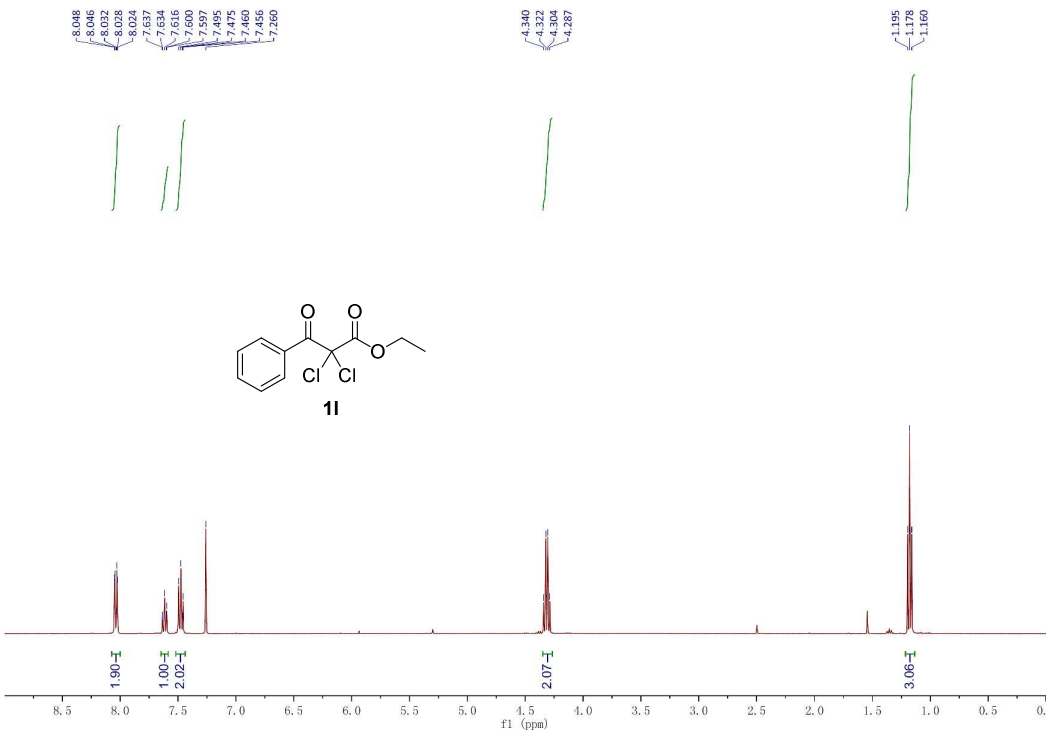

198.548
164.166
81.982
77.477
77.160
76.842
54.988
35.776
21.068
O
O
O
Cl
Cl
1i
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

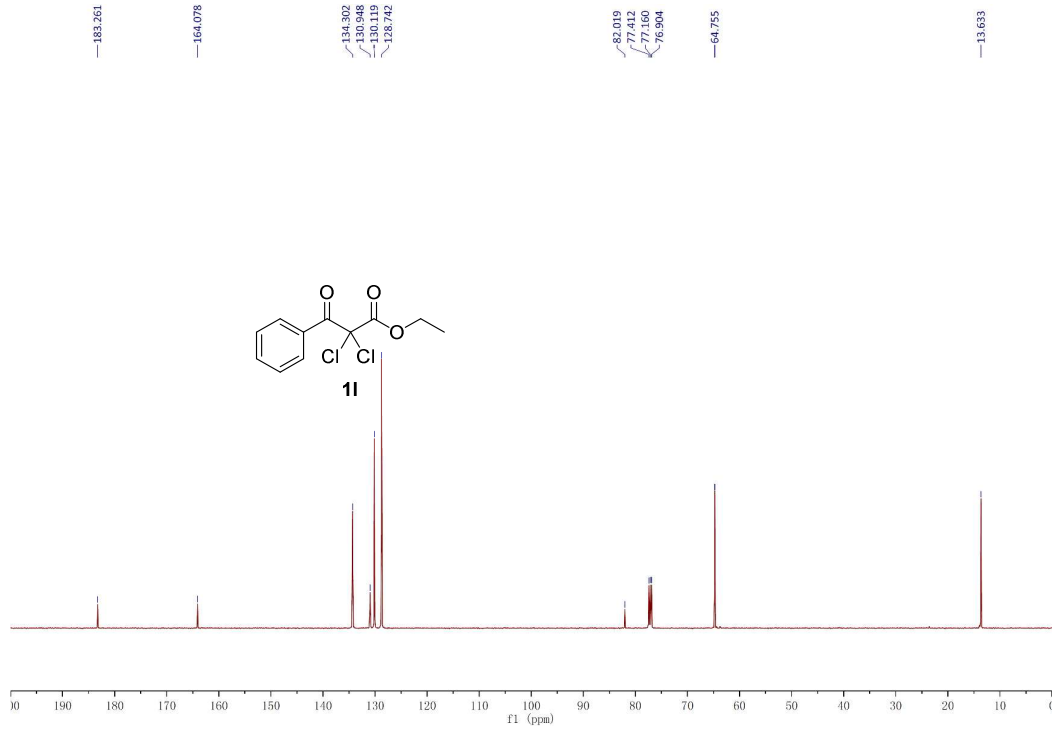

7.260
3.915
3.013
2.995
2.977
2.287
2.270
2.253
1.986
1.934
1.917
1.899
1.882
1.865
O
O
O
Cl
Cl
1j
2.95
2.01
2.04
0.88
2.04
f1 (ppm)

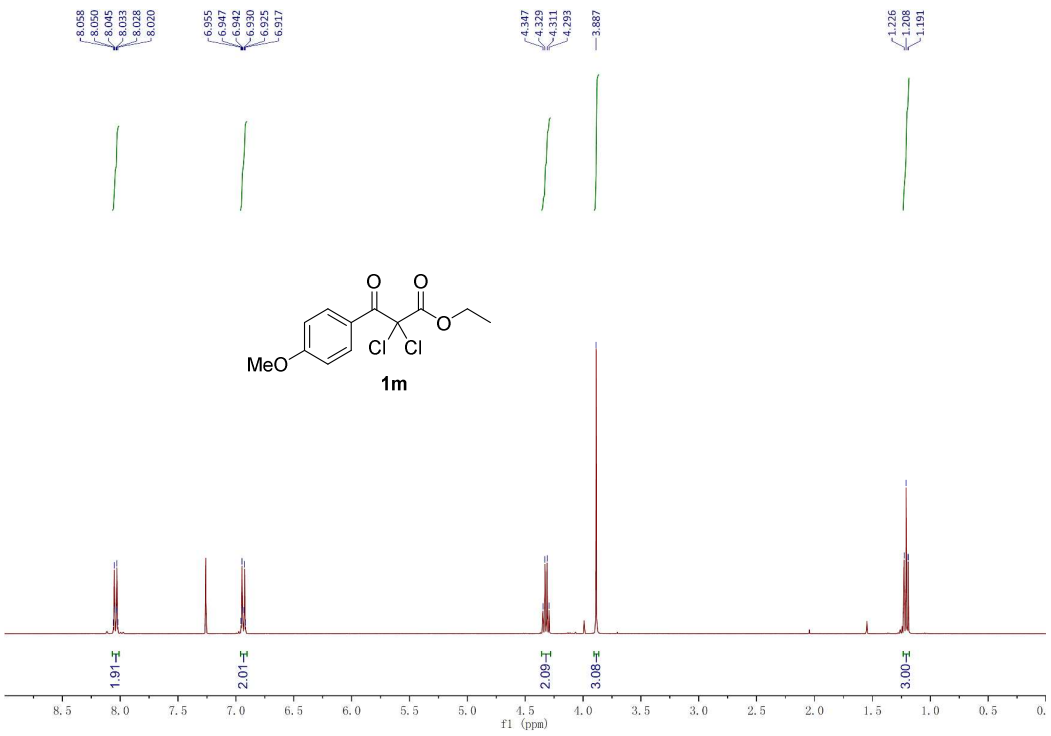

193.921
164.016
82.959
81.737
77.477
77.160
76.842
69.652
55.133
34.480
22.987
17.562
O
O
O
Cl
Cl
1j
f1 (ppm)

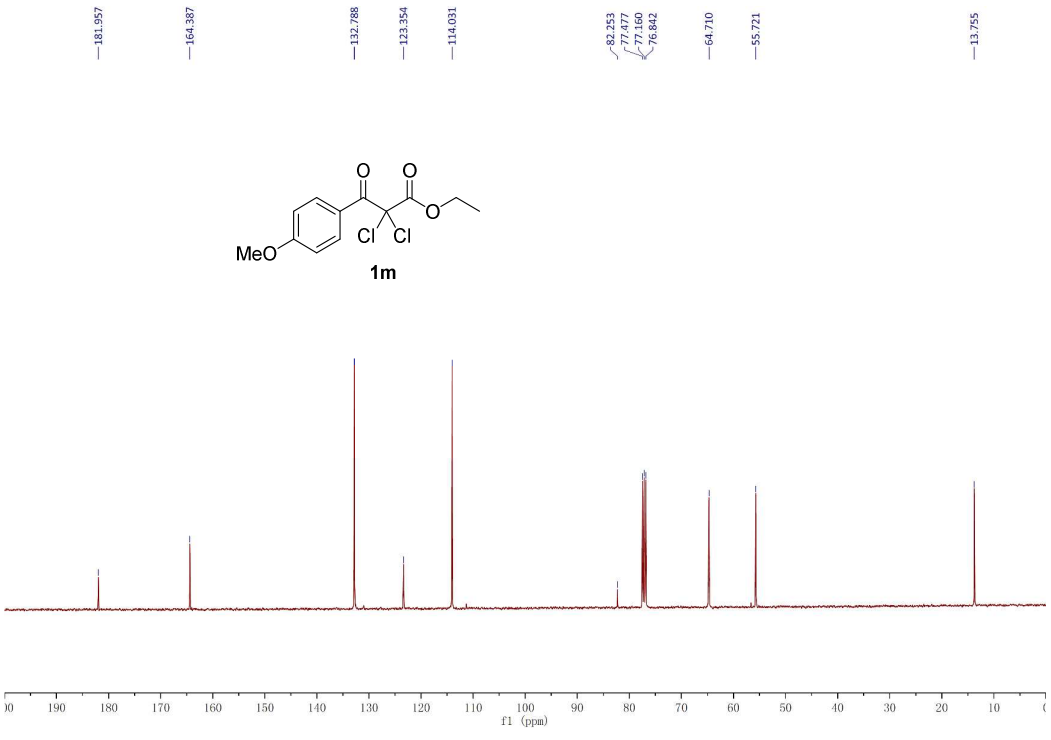

7.260
3.935
3.926
3.898
3.293
3.288
3.277
3.275
3.273
3.267
3.253
3.073
3.059
3.053
3.051
3.049
3.038
3.032
Cl
O
O
MeO
O
Cl
Cl
MeO
Cl
OMe
1k
2.99
2.92
6.00
2.12
2.13
f1 (ppm)

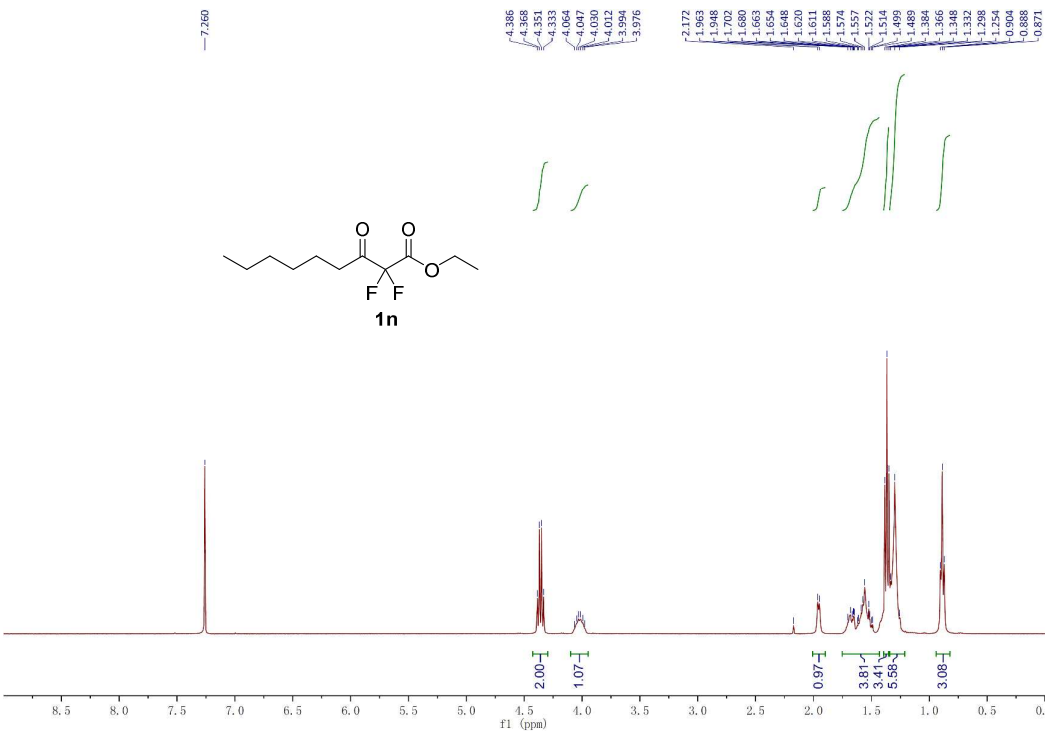

193.047
163.992
149.355
146.941
131.547
124.226
81.713
77.477
77.160
76.842
61.511
61.330
55.183
34.307
26.788
Cl
O
O
MeO
O
Cl
Cl
MeO
Cl
OMe
1k
f1 (ppm)

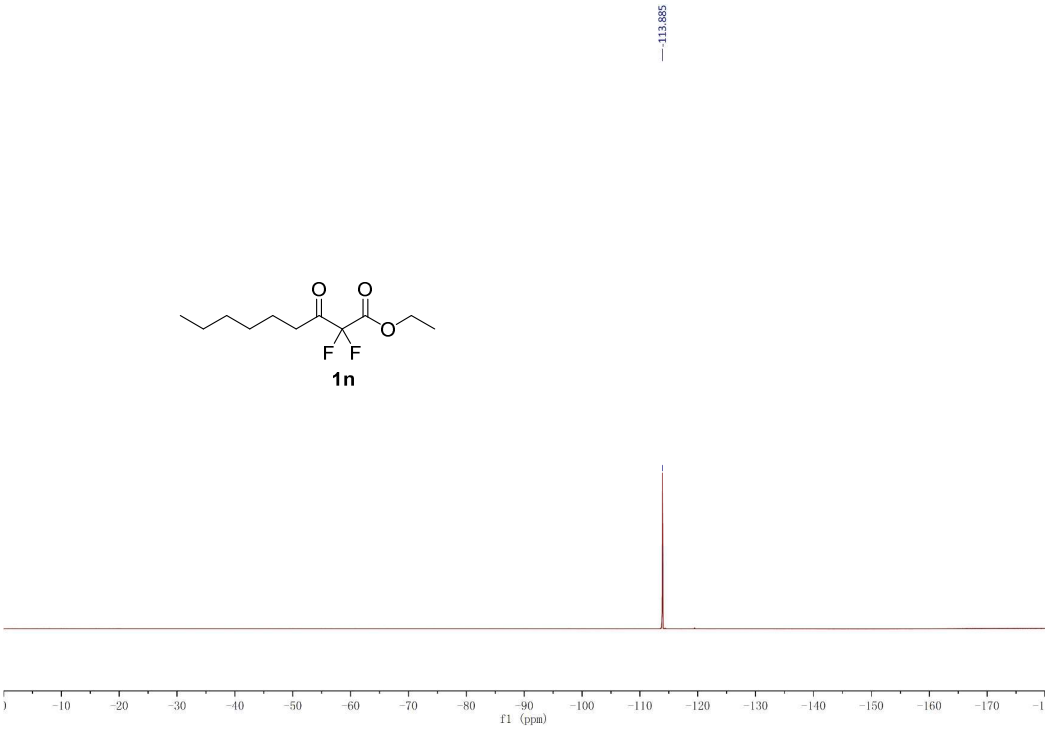

8.048
8.046
8.032
8.028
8.024
7.637
7.634
7.616
7.600
7.597
7.495
7.475
7.460
7.456
7.260
4.340
4.322
4.304
4.287
1.195
1.178
1.160
O
O
O
Cl
Cl
1l
1.90
1.00
2.02
2.07
3.06
f1 (ppm)

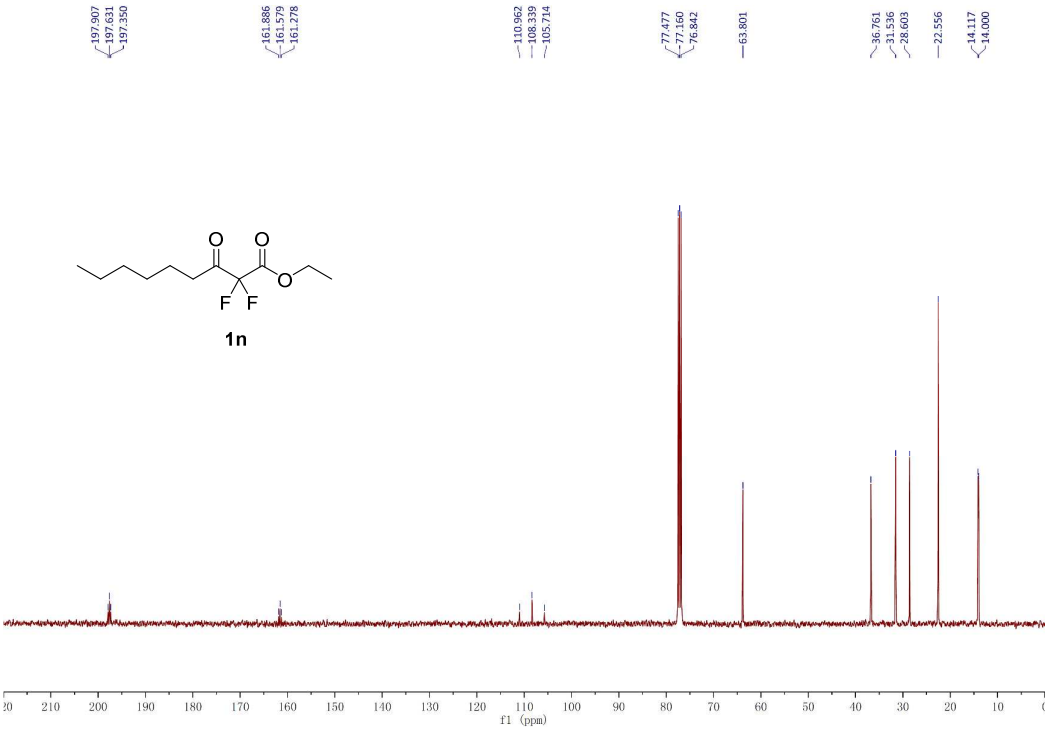

183.261
164.078
134.302
130.948
130.119
128.742
82.019
77.412
77.160
76.904
64.755
13.633
O
O
O
Cl
Cl
1l
f1 (ppm)

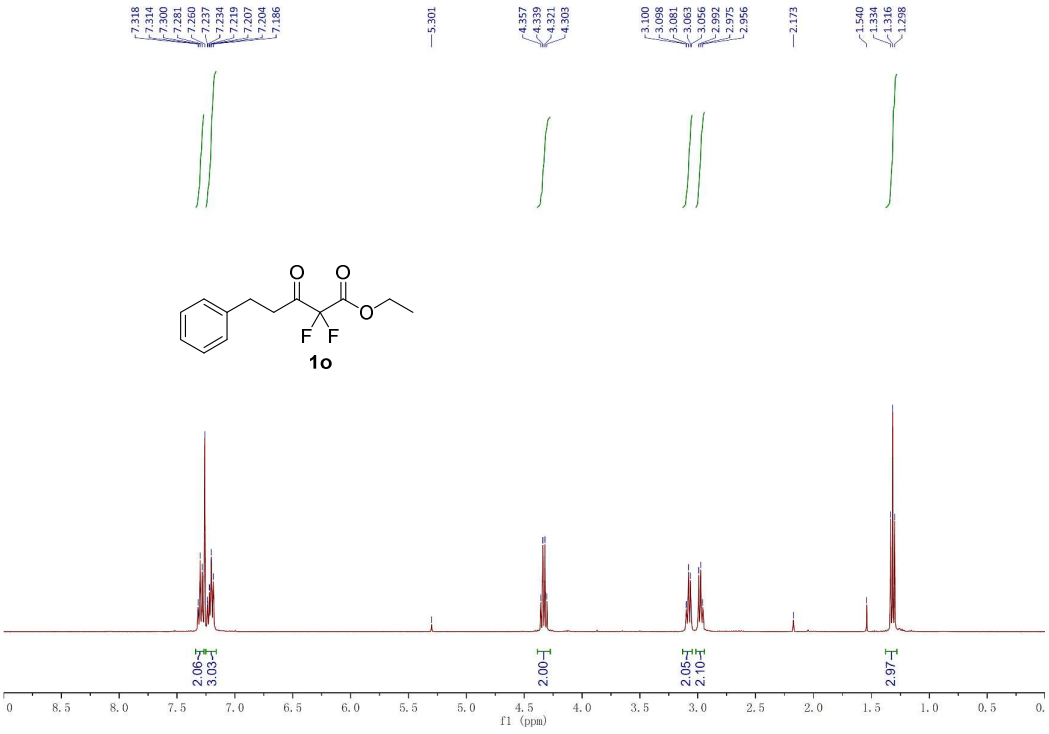

8.058
8.050
8.045
8.033
8.028
8.020
6.955
6.947
6.942
6.930
6.925
6.917
4.347
4.329
4.311
4.293
3.887
1.226
1.208
1.191
O
O
O
Cl
Cl
MeO
1m
1.91
2.01
2.09
3.08
3.00
f1 (ppm)

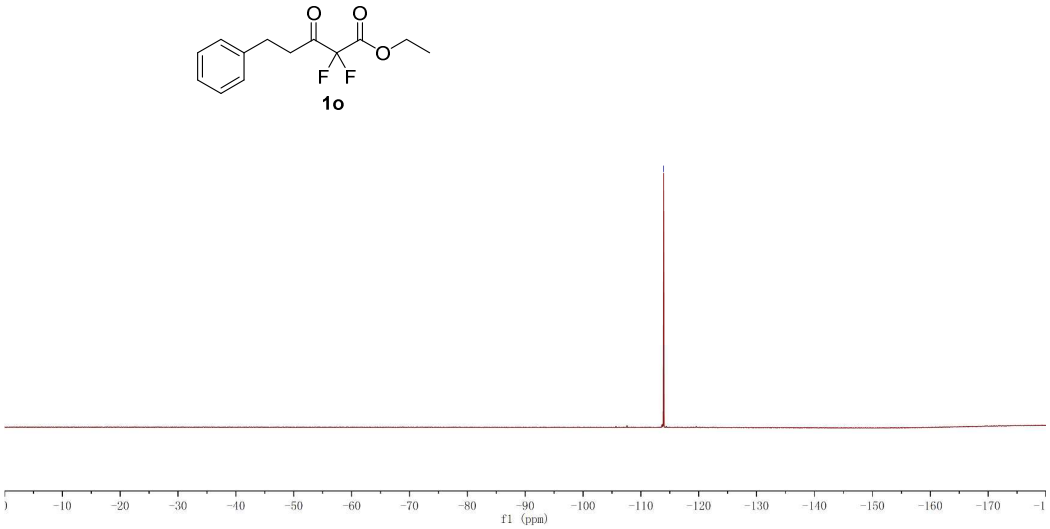

181.957
164.387
132.788
123.354
114.031
82.253
77.477
77.160
76.842
64.710
55.721
13.755
O
O
O
Cl
Cl
MeO
1m
f1 (ppm)

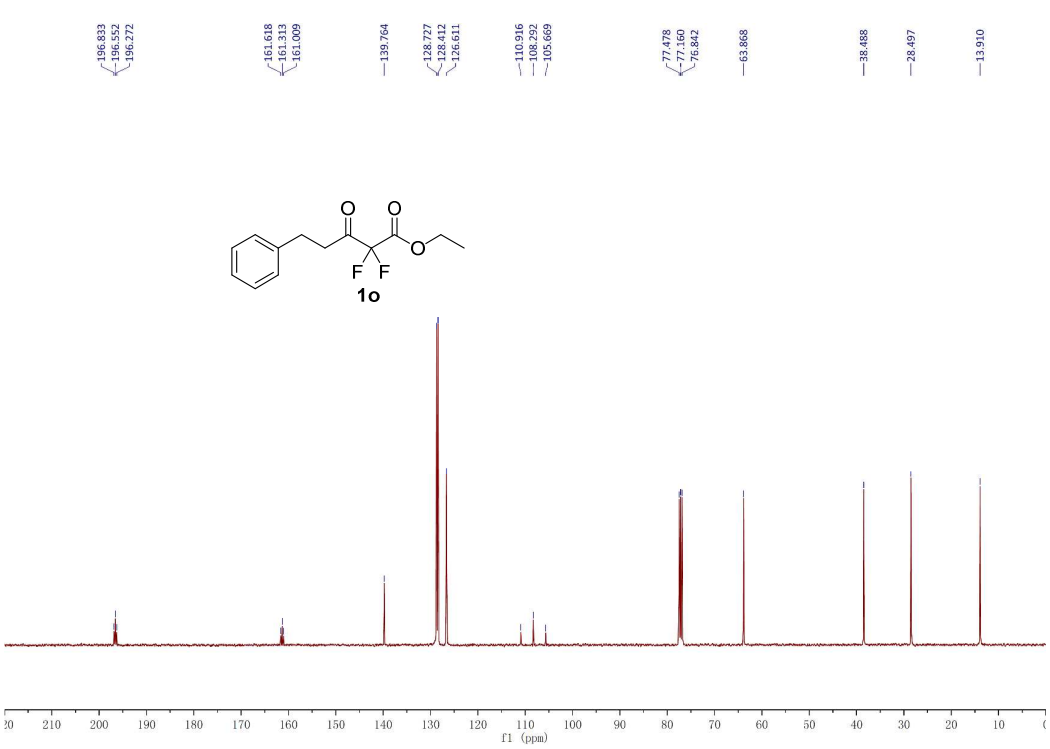

7.260
4.386
4.368
4.351
4.333
4.064
4.047
4.030
4.012
3.994
3.976
2.172
1.963
1.948
1.702
1.680
1.663
1.654
1.648
1.620
1.611
1.588
1.574
1.557
1.522
1.514
1.499
1.489
1.384
1.366
1.348
1.332
1.298
1.254
0.904
0.888
0.871
O
O
O
F F
1n
2.00
1.07
0.97
3.81
3.41
5.58
3.08
f1 (ppm)

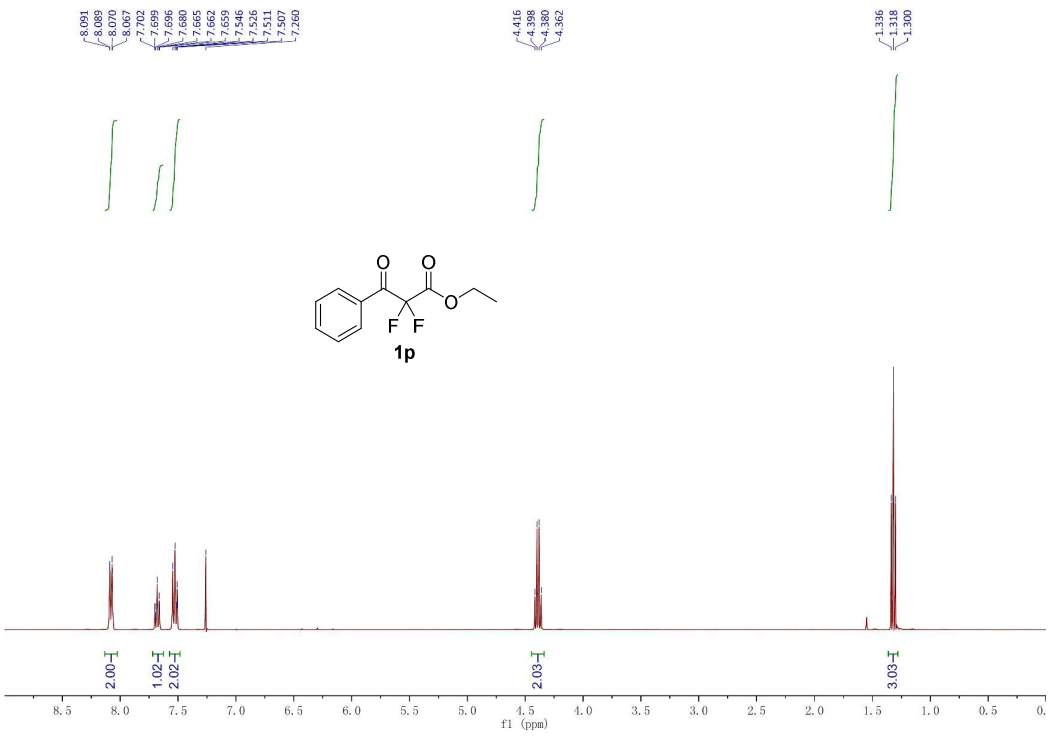

-113.885
O
O
O
F F
1n
f1 (ppm)

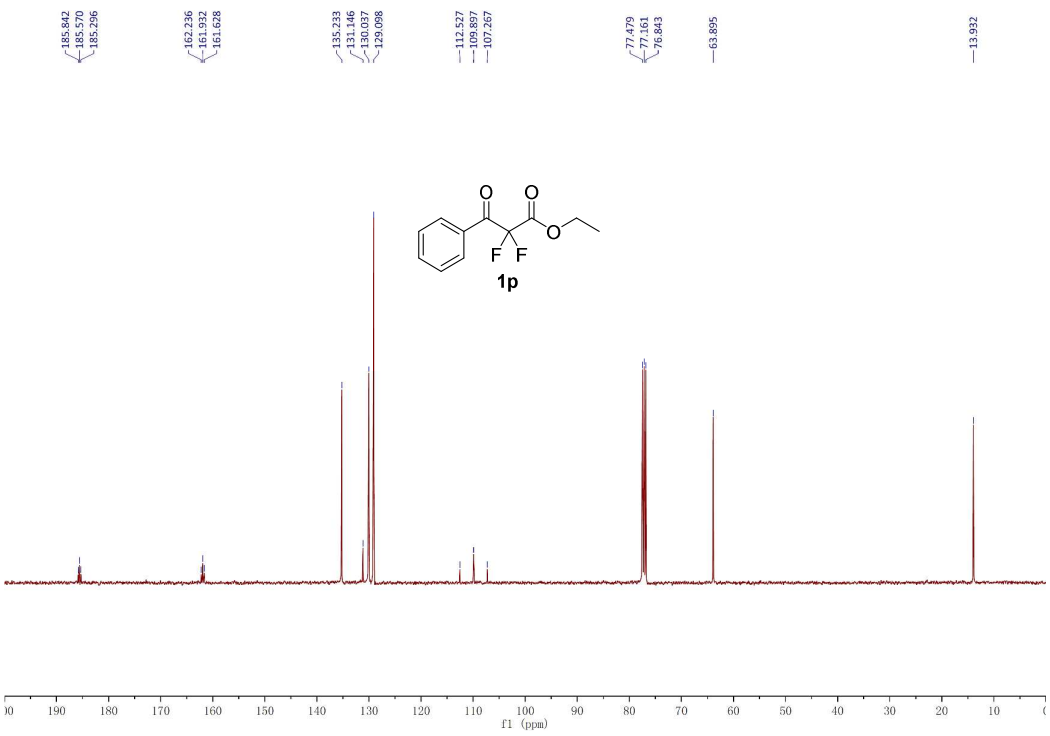

197.907
197.631
197.350
161.886
161.579
161.278
110.962
108.339
105.714
77.477
77.160
76.842
63.801
36.761
31.536
28.603
22.556
14.117
14.000
O
O
O
F F
1n
f1 (ppm)

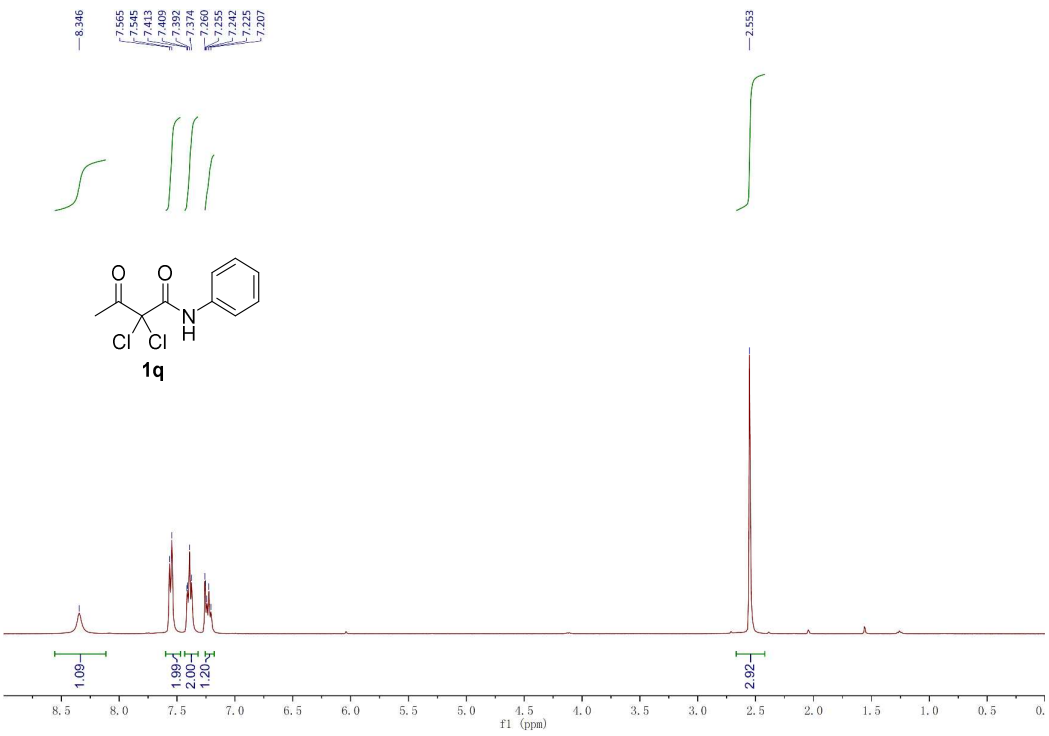

7.318
7.314
7.300
7.281
7.260
7.237
7.234
7.219
7.207
7.204
7.186
5.301
4.357
4.339
4.321
4.303
3.100
3.098
3.081
3.063
3.056
2.992
2.975
2.956
2.173
1.540
1.334
1.316
1.298
O
O
O
F F
1o
2.06
3.03
2.00
2.05
2.10
2.97
f1 (ppm)


-113.914
O
O
O
F
F
1o
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
f1 (ppm)


196.833
196.552
196.272
161.618
161.313
161.009
139.764
128.727
128.412
126.611
110.916
108.292
105.669
77.478
77.160
76.842
63.868
38.488
28.497
13.910
O
O
O
F
F
1o
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

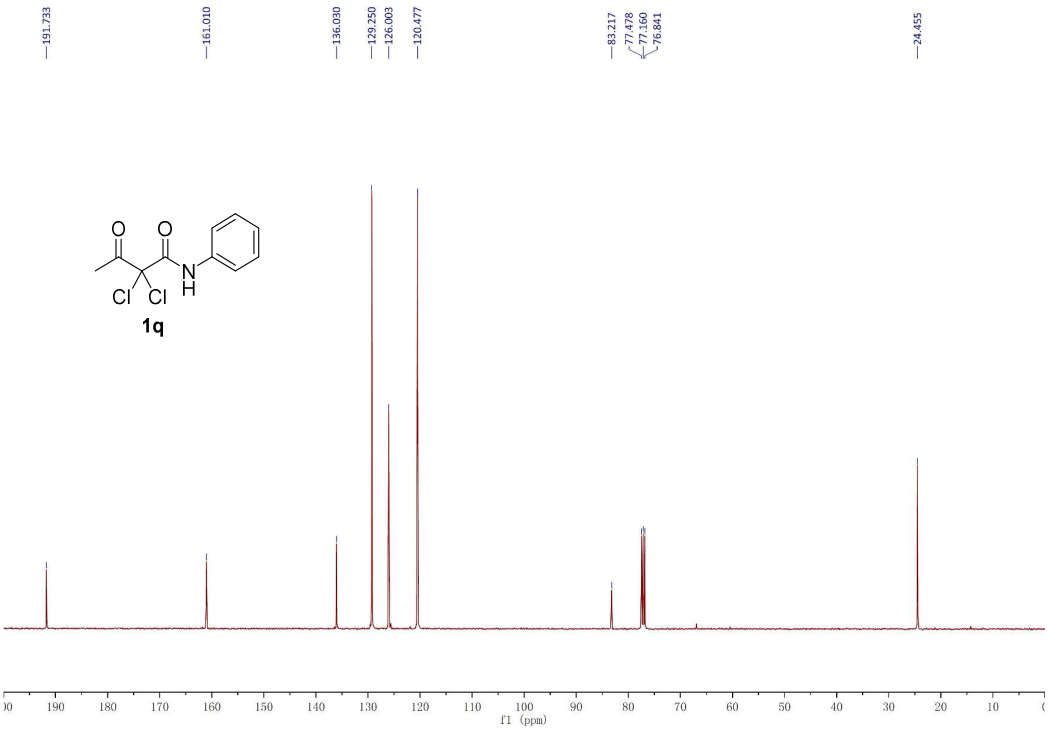

8.091
8.089
8.070
8.067
7.702
7.699
7.696
7.680
7.665
7.662
7.659
7.546
7.526
7.511
7.507
7.260
4.416
4.398
4.380
4.362
1.336
1.318
1.300
O
O
O
F F
1p
2.00
1.02
2.02
2.03
3.03
f1 (ppm)


185.842
185.570
185.296
162.236
161.932
161.628
135.233
131.146
130.037
129.098
112.527
109.897
107.267
77.479
77.161
76.843
63.895
13.932
O
O
O
F F
1p
f1 (ppm)


8.346
7.565
7.545
7.413
7.409
7.392
7.314
7.260
7.255
7.242
7.225
7.207
2.553
1.09
1.90
2.00
1.20
2.92
f1 (ppm)

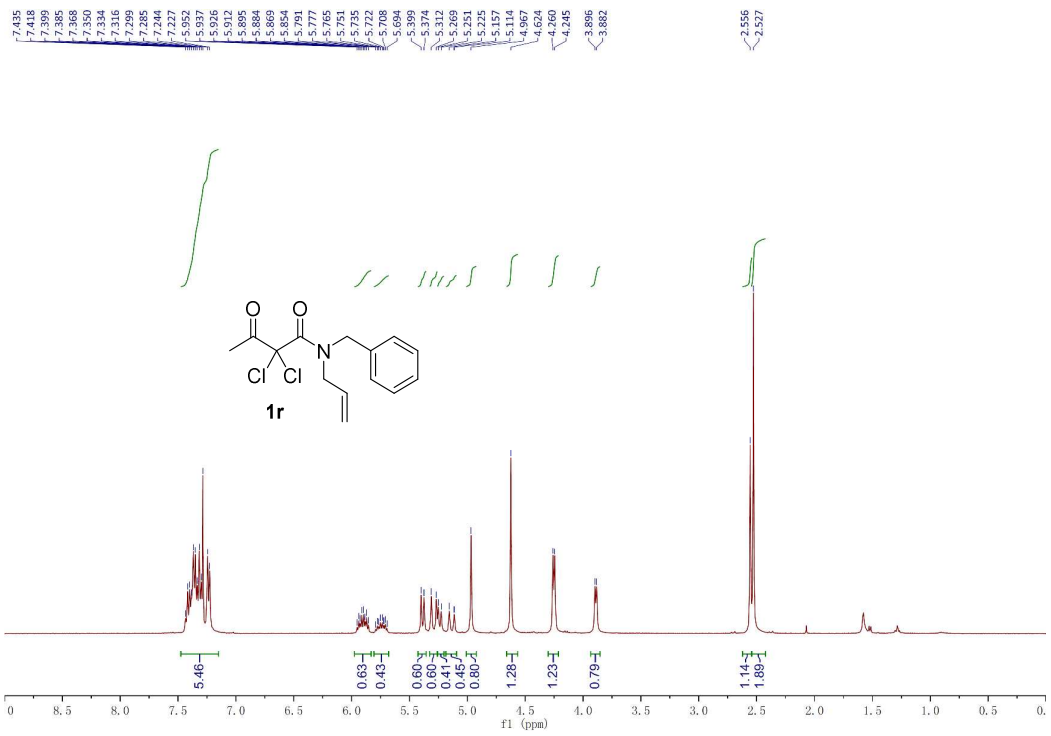
O
O
N
H
Cl
Cl

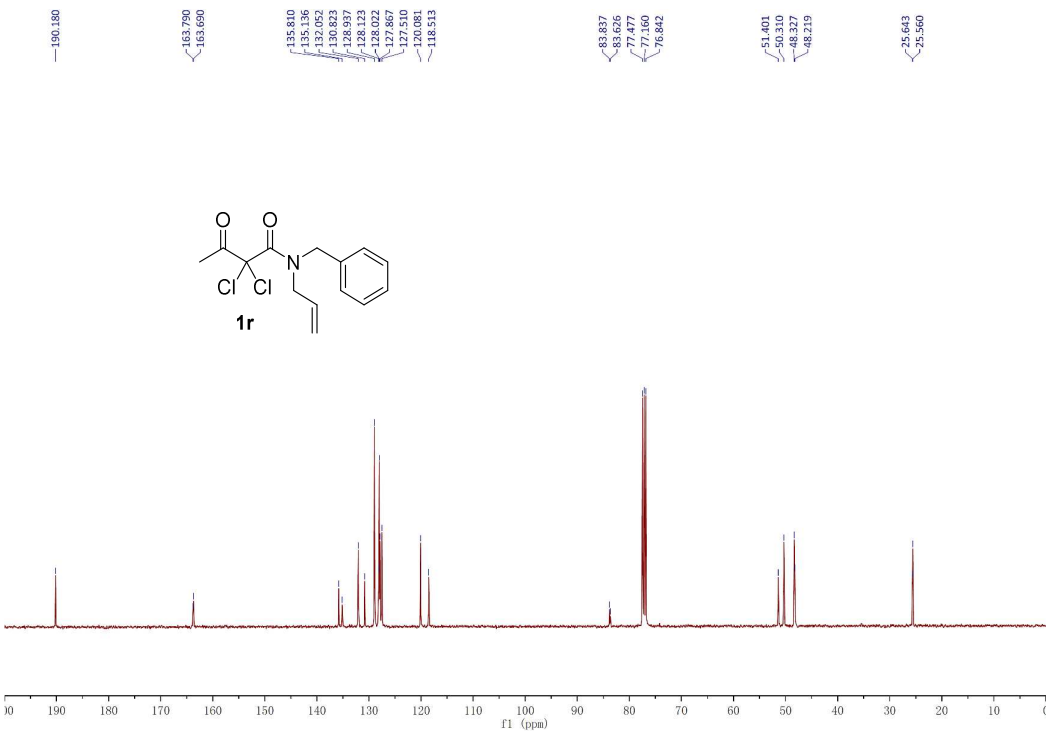
1q


191.733
161.010
136.030
129.250
126.003
120.477
83.217
77.478
77.160
76.841
24.455
f1 (ppm)

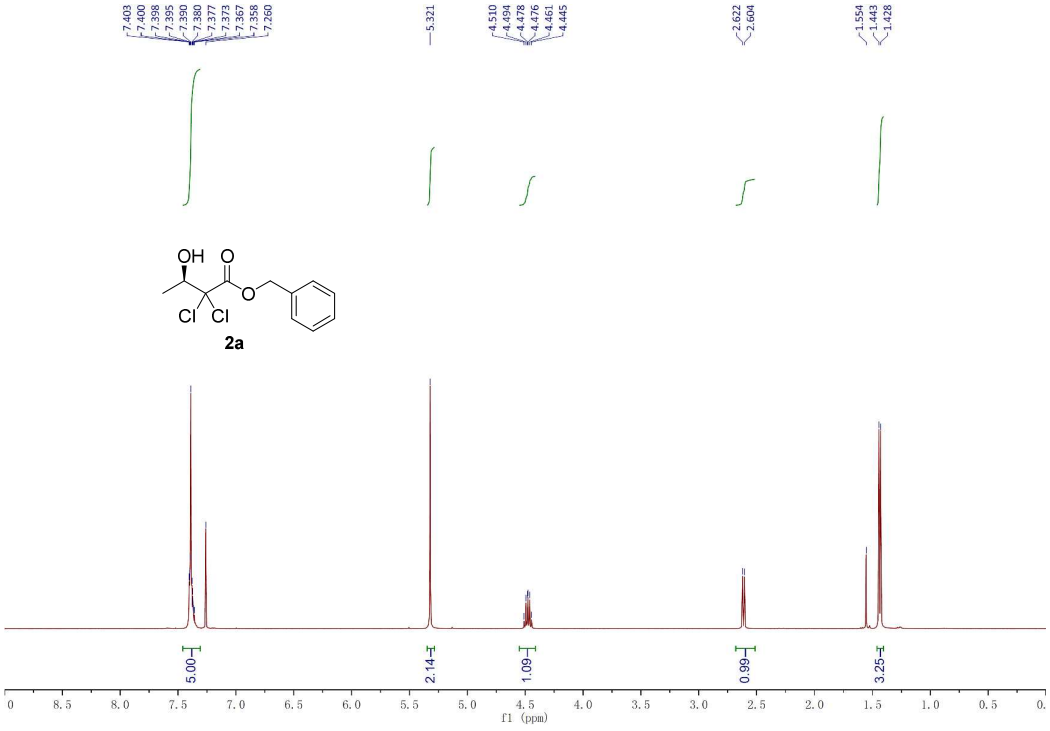
O
O
N
H
Cl
Cl

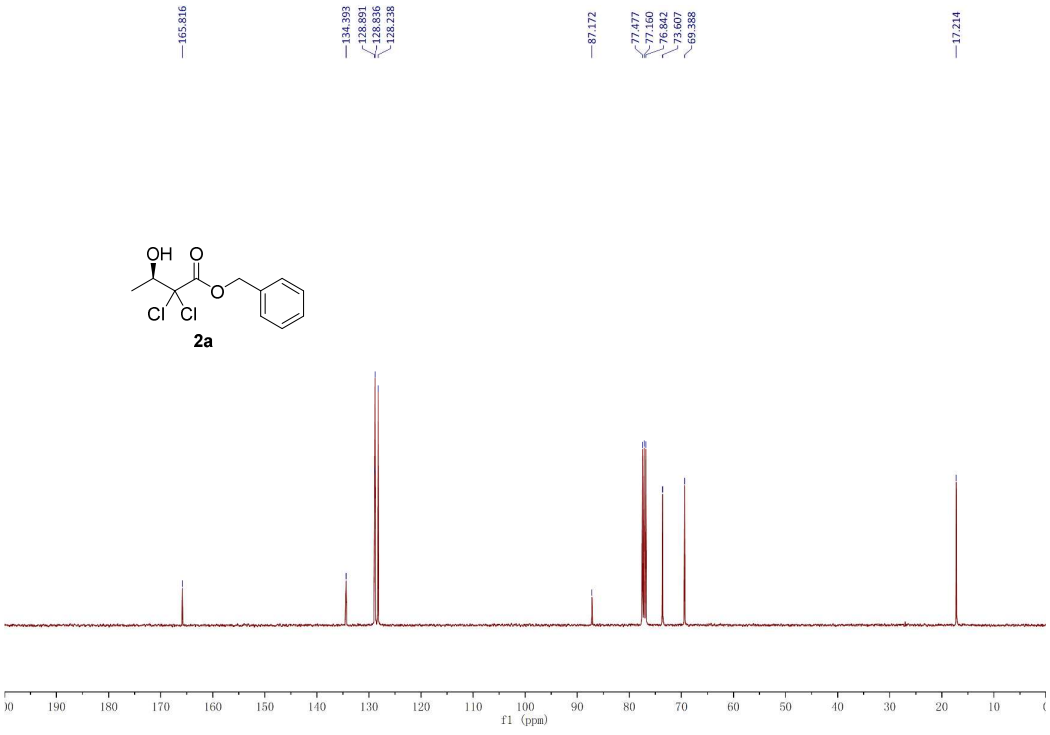
1q

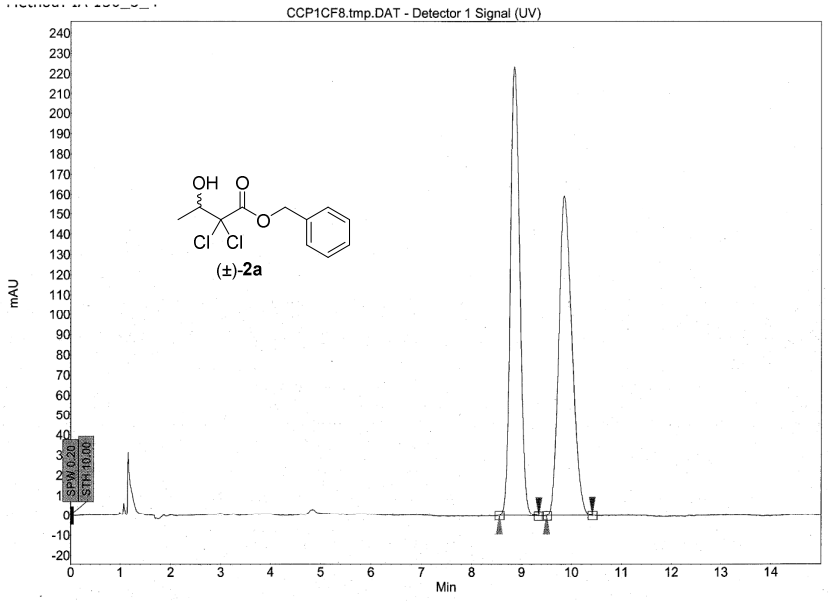

7.435
7.418
7.399
7.385
7.368
7.350
7.334
7.316
7.299
7.285
7.244
7.227
5.952
5.937
5.926
5.912
5.895
5.884
5.869
5.854
5.791
5.777
5.765
5.751
5.735
5.722
5.708
5.694
5.399
5.374
5.312
5.269
5.251
5.225
5.157
5.114
4.967
4.624
4.260
4.245
3.896
3.882
2.556
2.527
O
O
N
Cl
Cl
1r
5.46
0.63
0.43
0.60
0.60
0.41
0.45
0.80
1.28
1.23
0.79
1.14
1.89
f1 (ppm)


190.180
163.790
163.690
135.810
135.136
132.052
130.823
128.937
128.123
128.022
127.867
127.510
120.081
118.513
83.837
83.626
77.477
77.160
76.842
51.401
50.310
48.327
48.219
25.643
25.560
O
O
N
Cl
Cl
1r
f1 (ppm)

8. NMR spectra and HPLC or SFC chromatograms for 2a–2h and 2j–2r

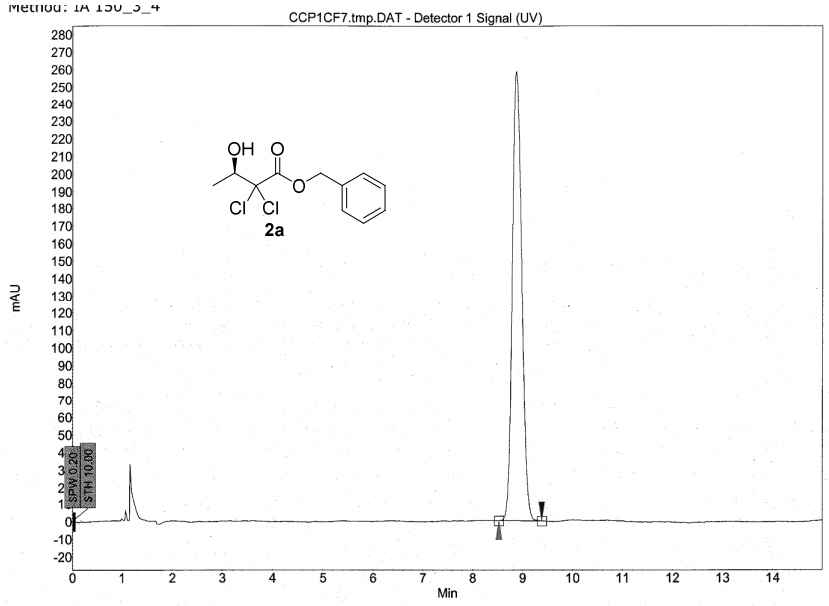






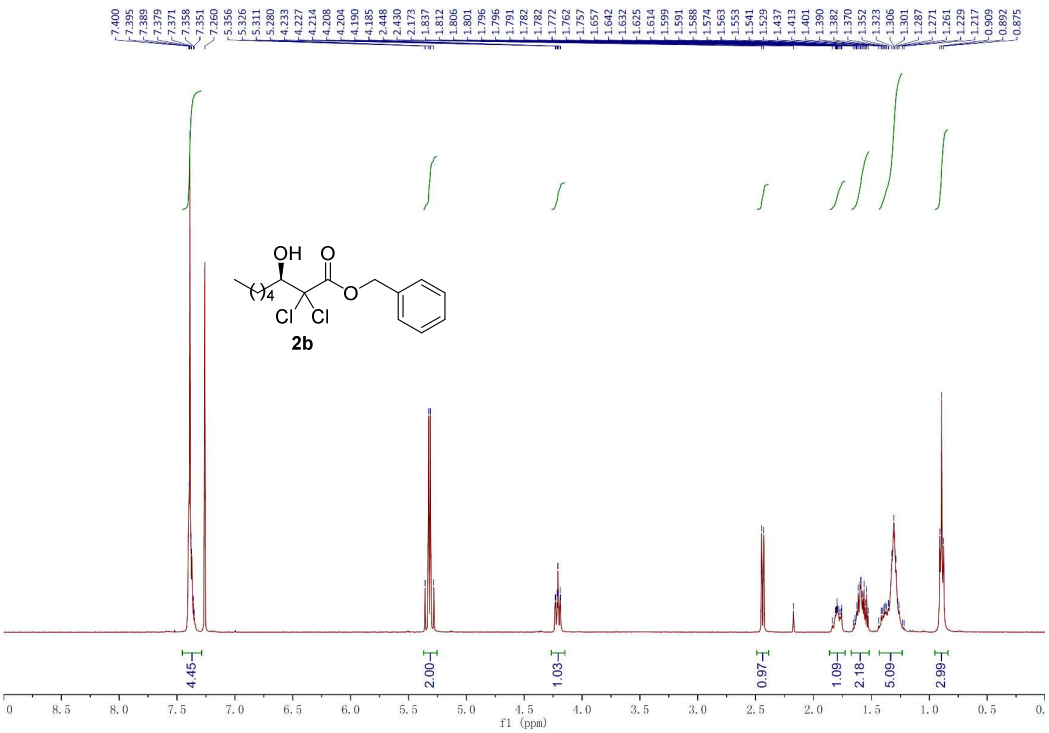
Results Table:

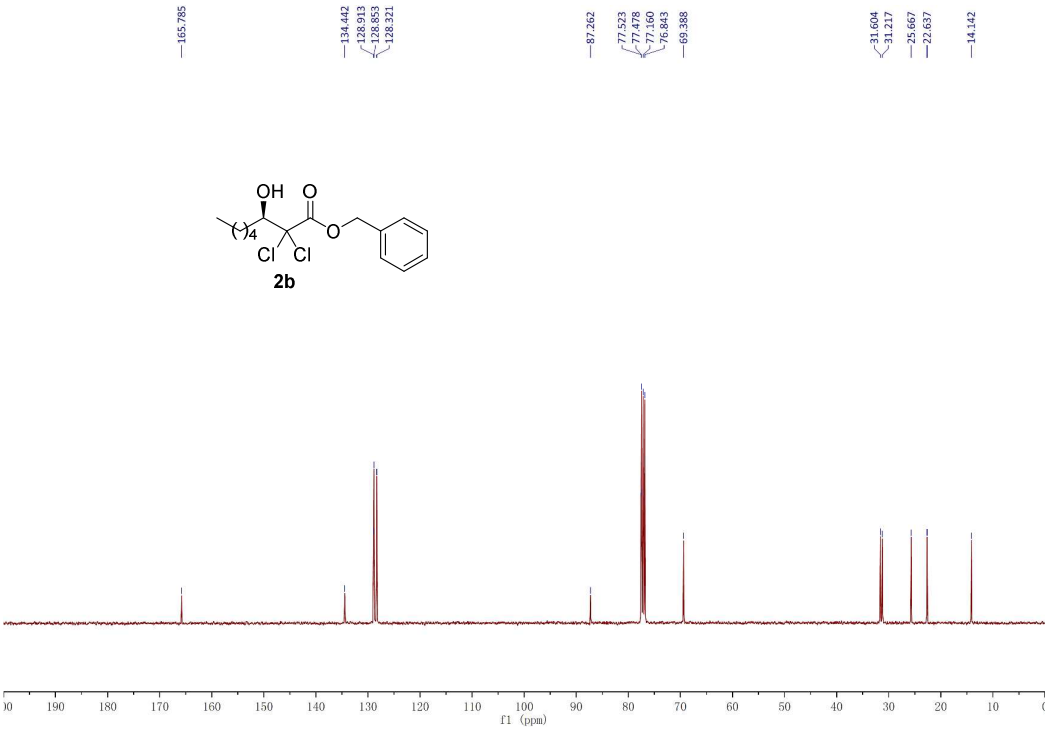
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.56	8.86	9.35	0.00	49.79	223.4	48.5	49.790
2	UNKNOWN	9.51	9.86	10.42	0.00	50.21	159.3	48.9	50.210
Total						100.00	382.7	97.4	100.000

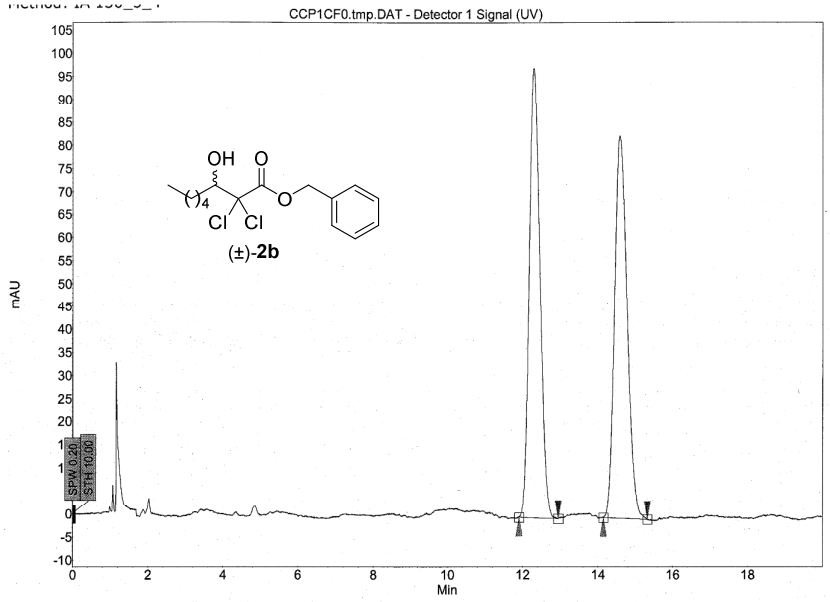


Results Table:

Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.53	8.88	9.38	0.00	100.00	258.3	56.7	100.000
Total						100.00	258.3	56.7	100.000

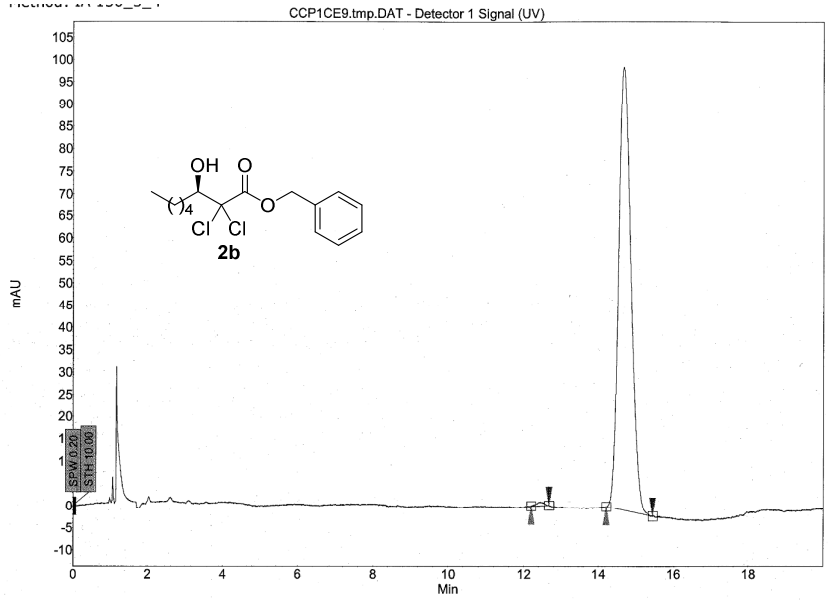

7.400
7.395
7.389
7.379
7.371
7.358
7.351
7.260
5.356
5.336
5.311
5.280
4.233
4.227
4.214
4.208
4.204
4.190
4.185
2.448
2.430
2.173
1.837
1.812
1.806
1.801
1.796
1.796
1.791
1.782
1.782
1.772
1.762
1.757
1.657
1.642
1.632
1.625
1.614
1.599
1.591
1.588
1.574
1.563
1.553
1.541
1.529
1.437
1.413
1.401
1.390
1.382
1.370
1.352
1.323
1.306
1.301
1.287
1.271
1.261
1.229
1.217
0.909
0.892
0.875
OH
O
O
Cl
Cl
2b
4.45
2.00
1.03
0.97
1.09
2.18
5.09
2.99
f1 (ppm)


165.785
134.442
128.913
128.853
128.321
87.262
77.523
77.478
77.160
76.843
69.388
31.604
31.217
25.667
22.637
14.142
OH
O
O
Cl
Cl
2b
f1 (ppm)



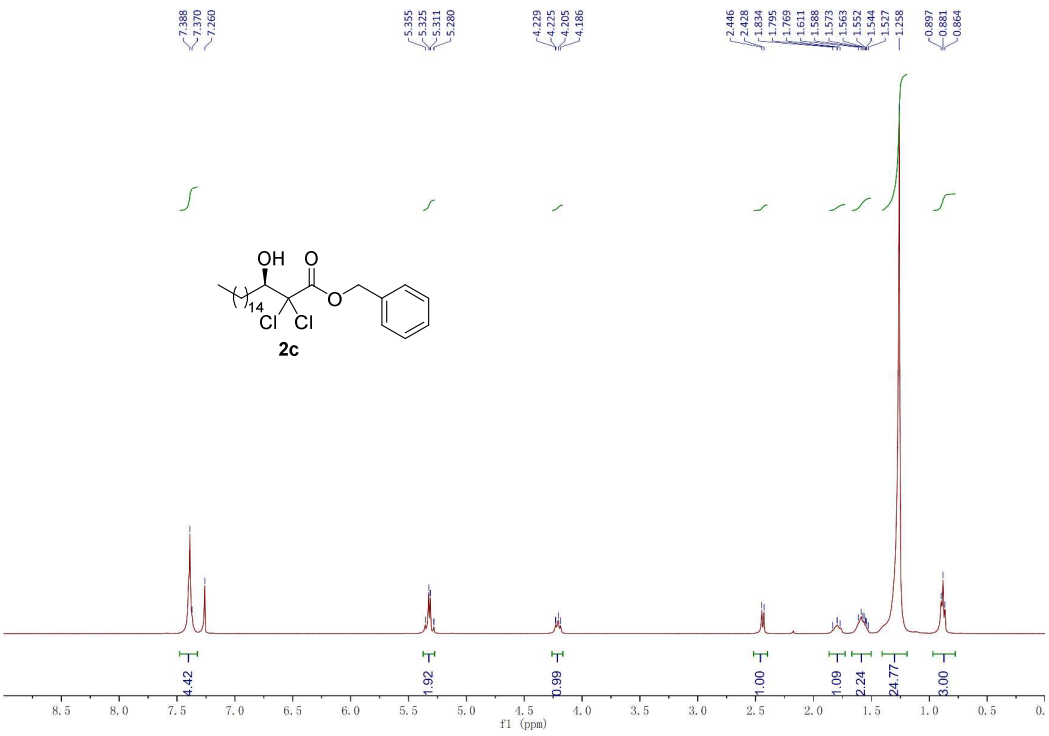
Results Table:

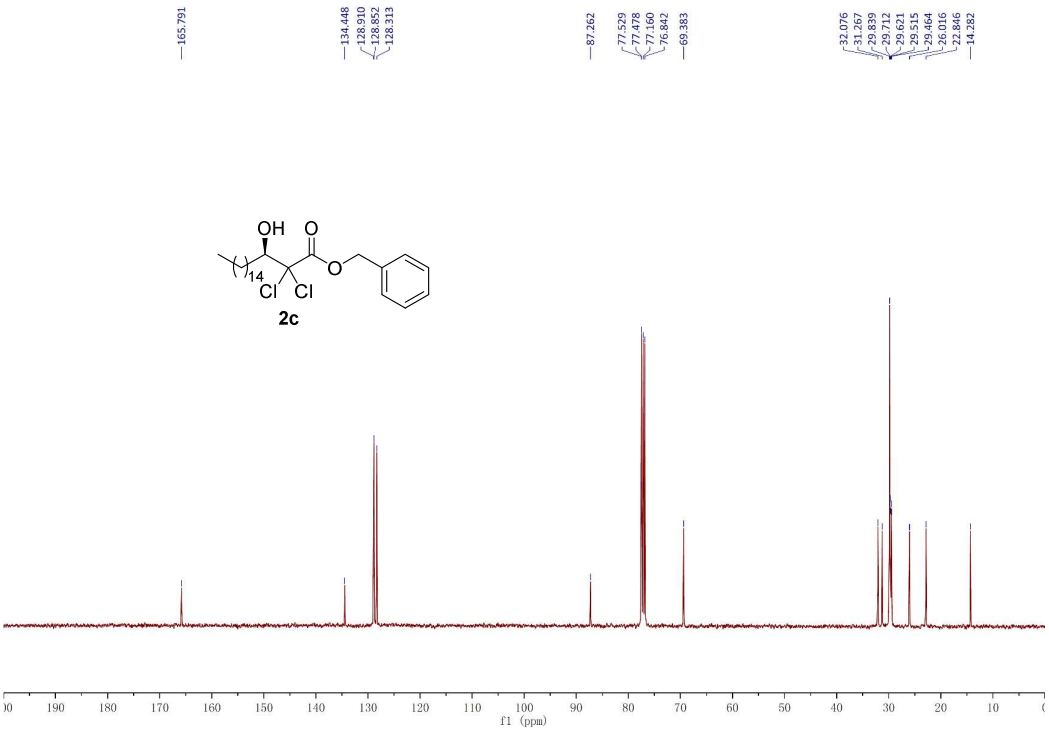
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	11.91	12.30	12.95	0.00	49.72	97.6	32.0	49.719
2	UNKNOWN	14.14	14.58	15.32	0.00	50.28	83.0	32.3	50.281
Total						100.00	180.5	64.3	100.000

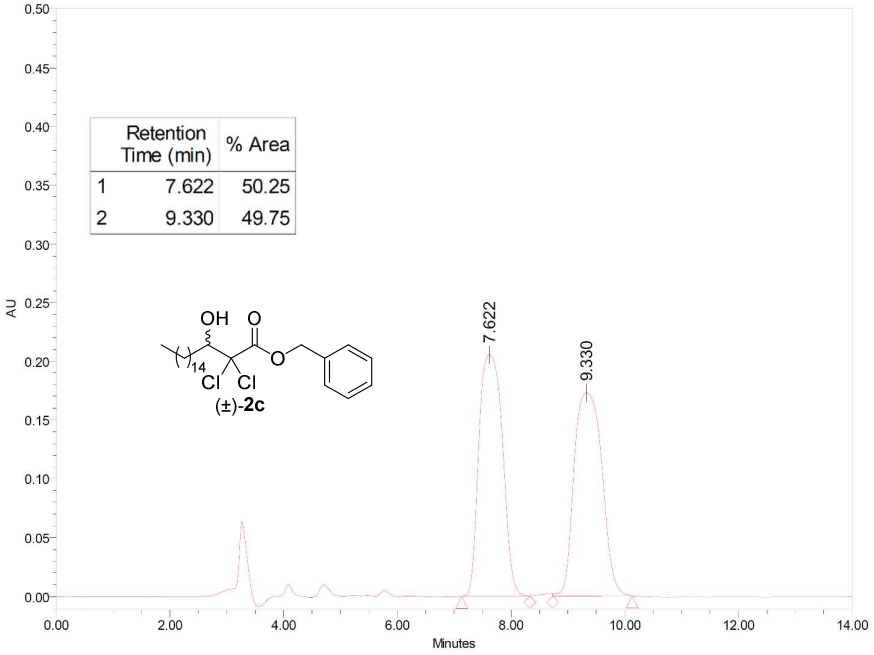


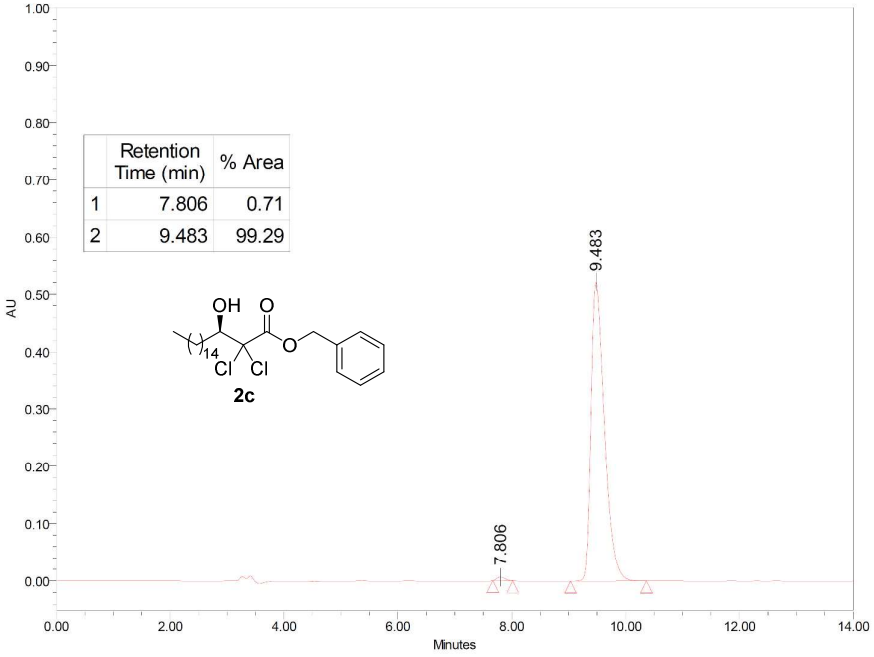
Results Table:

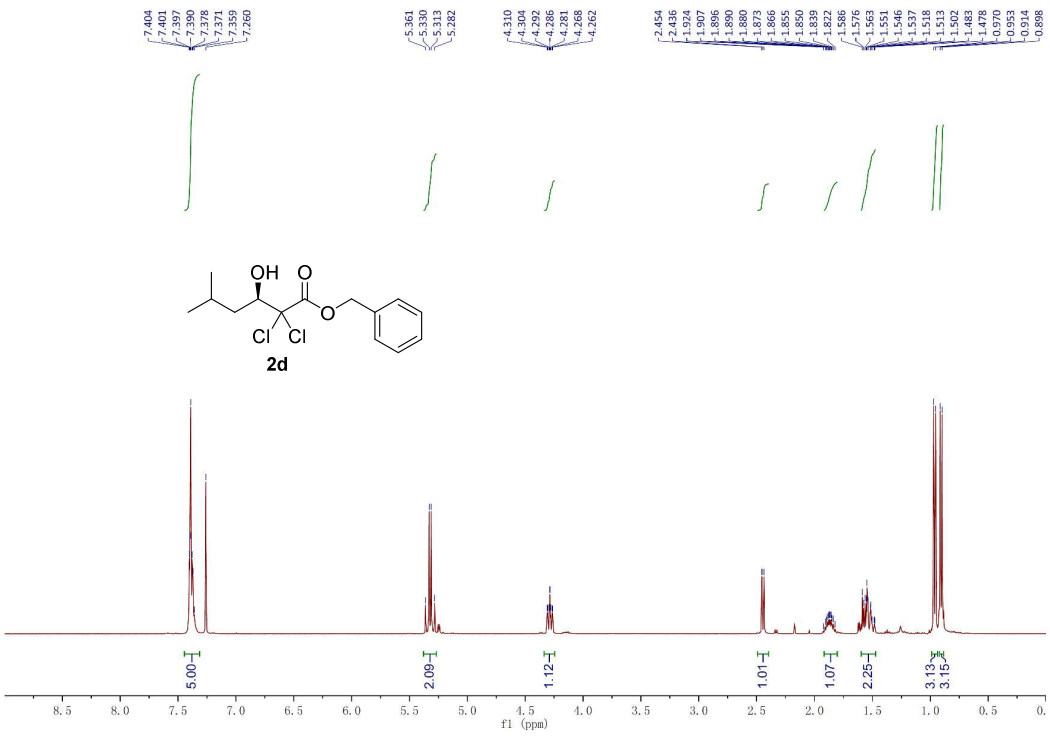
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	12.20	12.44	12.68	0.00	0.52	0.9	0.2	0.520
1	UNKNOWN	14.21	14.67	15.45	0.00	99.48	99.2	37.8	99.480
Total						100.00	100.1	38.0	100.000

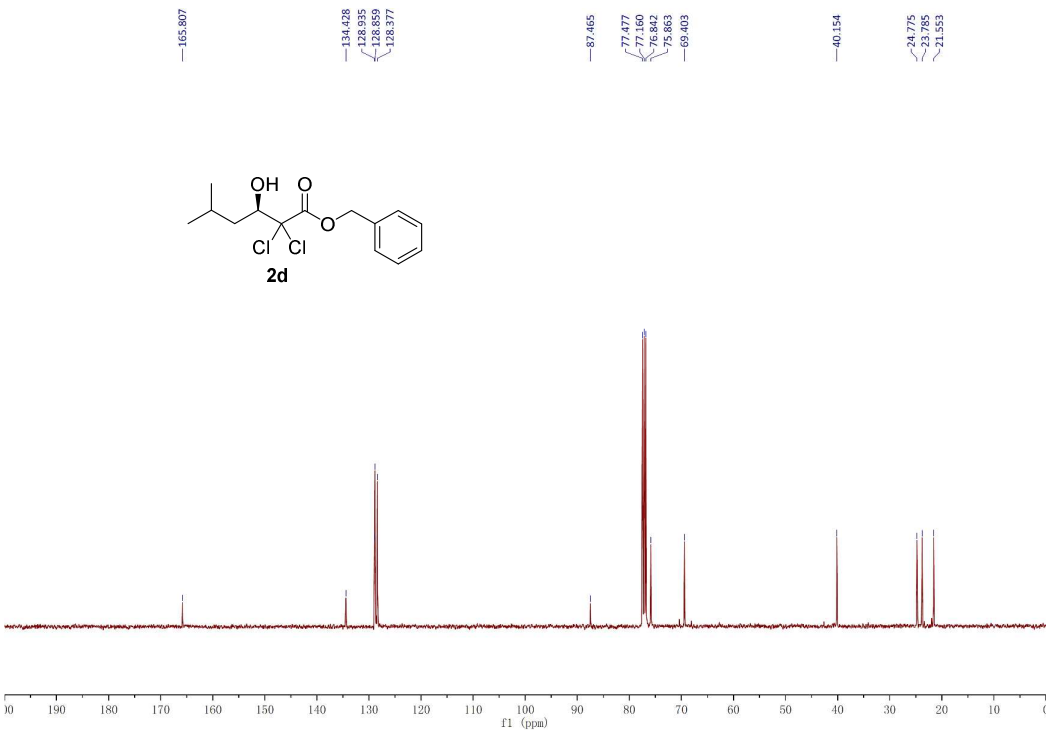

7.388
7.370
7.260
5.355
5.325
5.311
5.280
4.229
4.225
4.205
4.186
2.446
2.428
1.834
1.795
1.769
1.611
1.588
1.573
1.563
1.552
1.544
1.527
1.258
0.897
0.881
0.864
OH
O
14
Cl
Cl
O
2c
4.42
1.92
0.99
1.00
1.09
2.24
24.77
3.00
f1 (ppm)

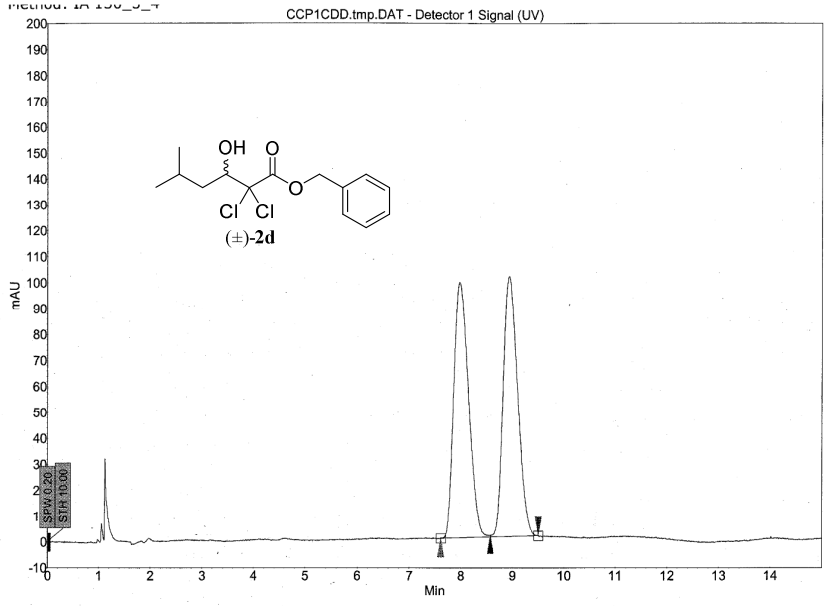

165.791
134.448
128.910
128.852
128.313
87.262
77.529
77.478
77.160
76.842
69.383
32.076
31.267
29.839
29.712
29.621
29.515
29.464
26.016
22.846
14.282
OH
O
14
Cl
Cl
O
2c
f1 (ppm)


Retention Time (min) % Area
1 7.622 50.25
2 9.330 49.75
OH O
14
Cl Cl
(±)-2c
7.622
9.330
AU
Minutes


Retention Time (min) % Area
1 7.806 0.71
2 9.483 99.29
OH O
14
Cl Cl
2c
9.483
7.806
AU
Minutes

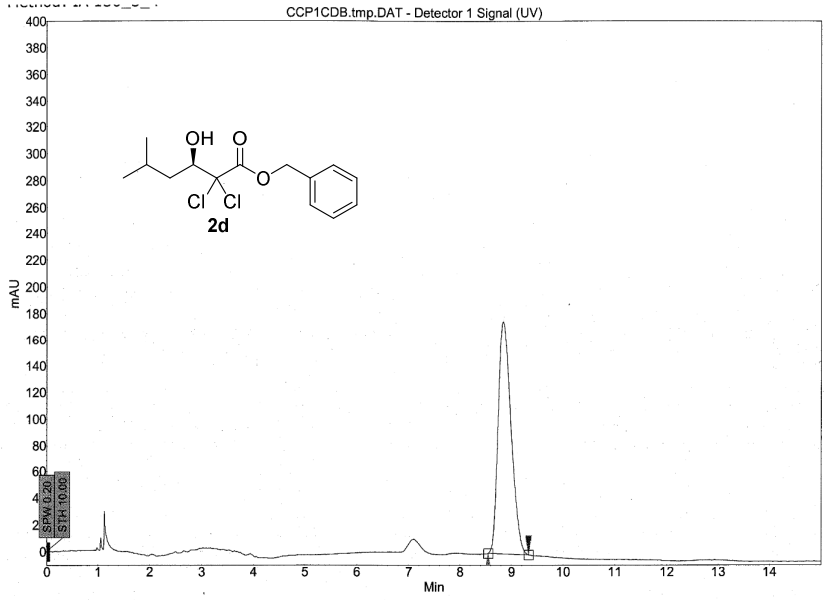

7.404
7.401
7.397
7.390
7.378
7.371
7.359
7.260
5.361
5.330
5.313
5.282
4.310
4.304
4.292
4.286
4.281
4.268
4.262
2.454
2.436
1.924
1.907
1.896
1.890
1.880
1.873
1.866
1.855
1.850
1.839
1.822
1.586
1.576
1.563
1.551
1.546
1.537
1.518
1.513
1.502
1.483
1.478
0.970
0.953
0.914
0.898
OH
O
Cl
Cl
O
2d
5.00
2.09
1.12
1.01
1.07
2.25
3.13
3.15
f1 (ppm)


165.807
134.428
128.935
128.859
128.377
87.465
77.477
77.160
76.842
75.863
69.403
40.154
24.775
23.785
21.553
OH
O
Cl
Cl
O
2d
f1 (ppm)



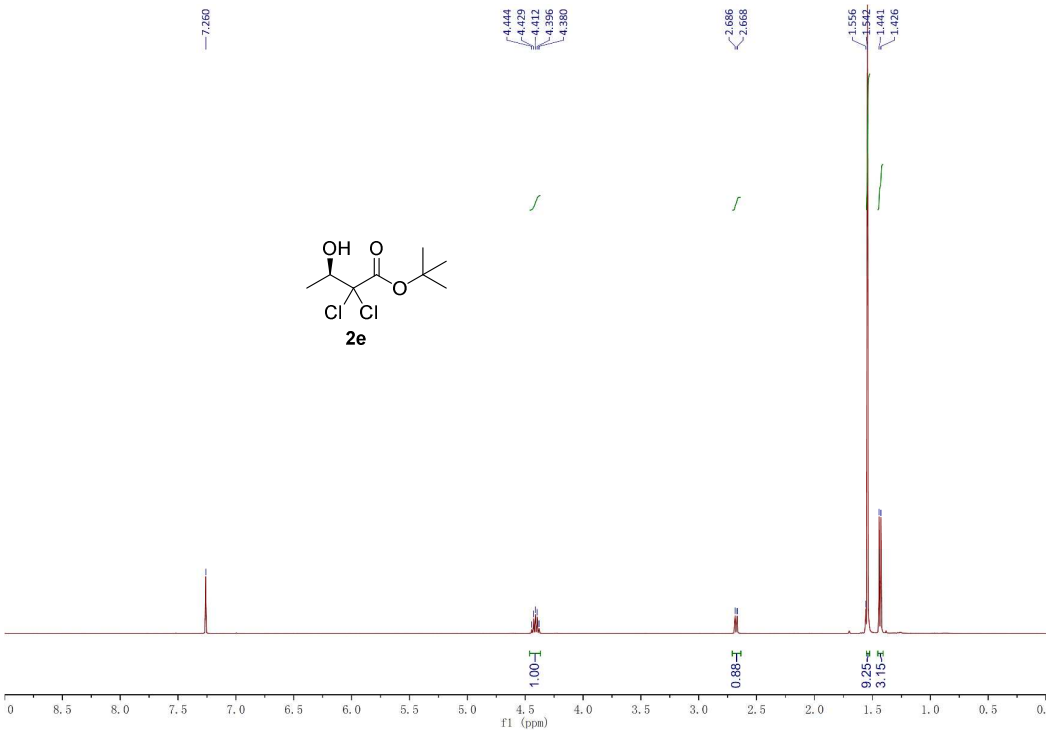
Results Table:

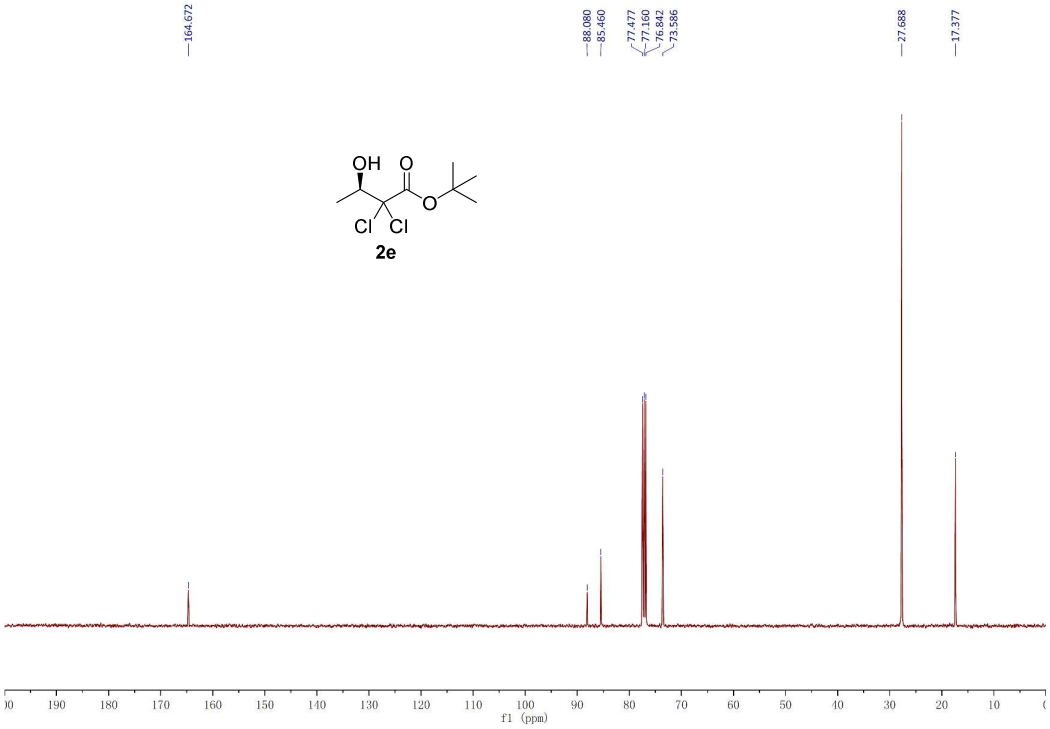
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	7.61	7.98	8.58	0.00	50.01	98.5	32.7	50.006
2	UNKNOWN	8.58	8.94	9.51	0.00	49.99	100.3	32.7	49.994
Total						100.00	198.8	65.4	100.000

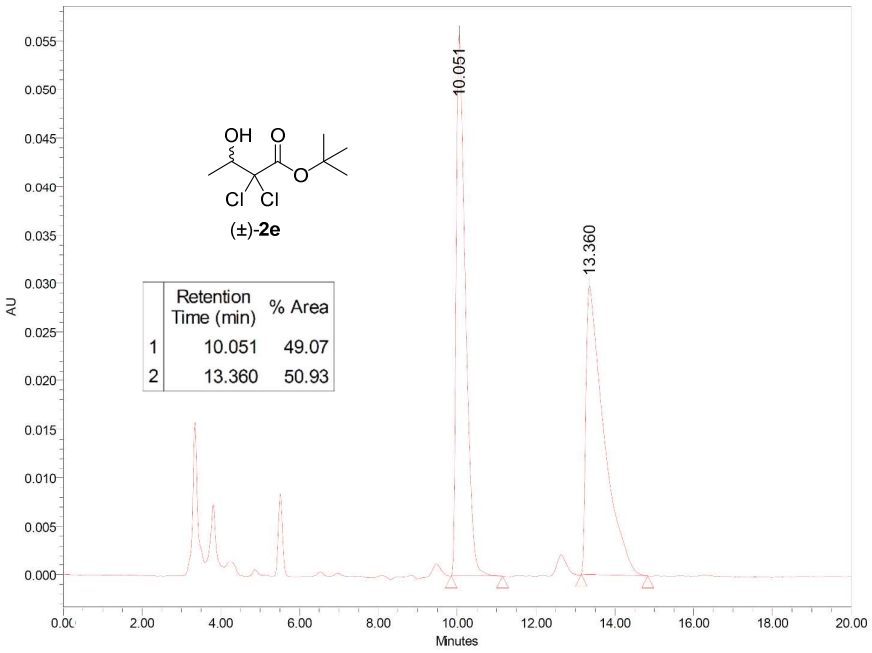


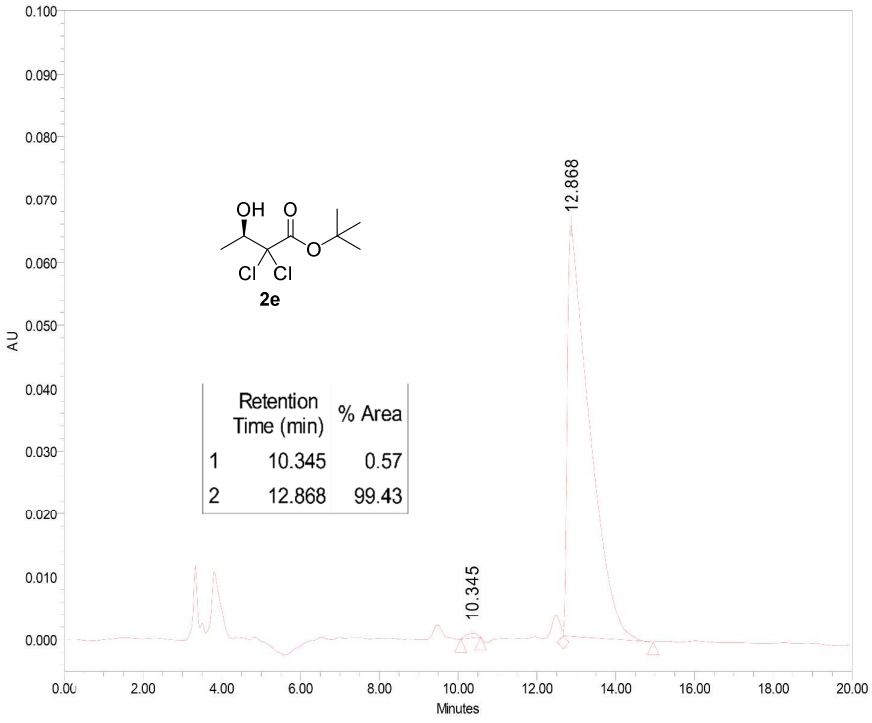
Results Table:

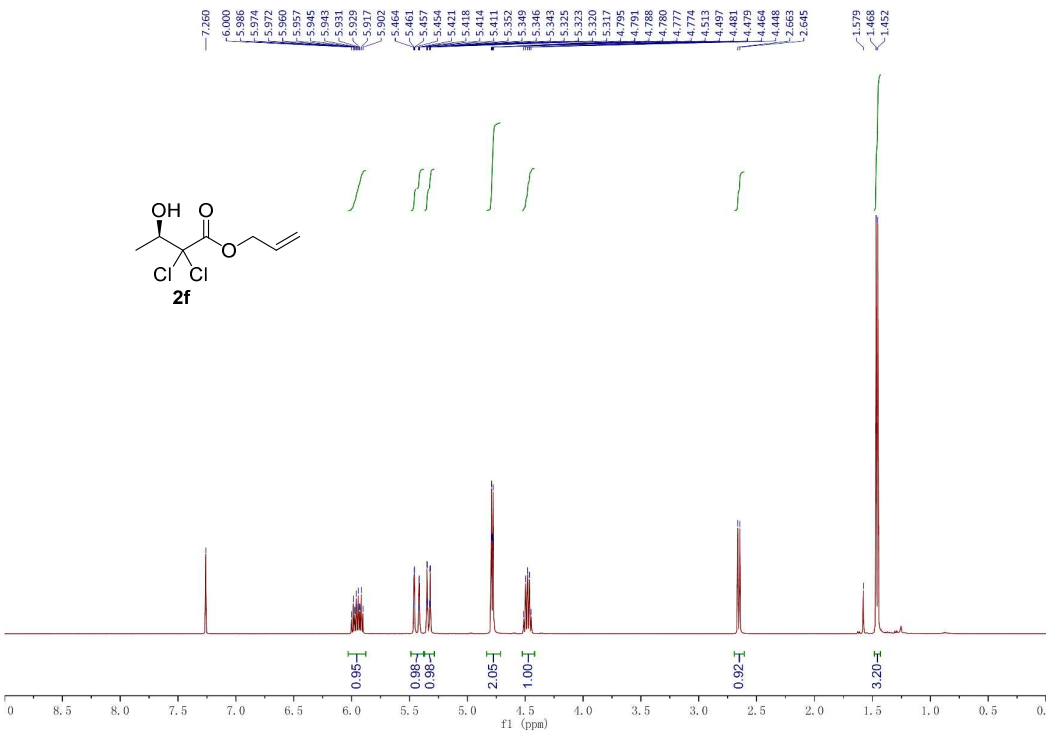
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.55	8.84	9.34	0.00	100.00	175.4	51.1	100.000
Total						100.00	175.4	51.1	100.000

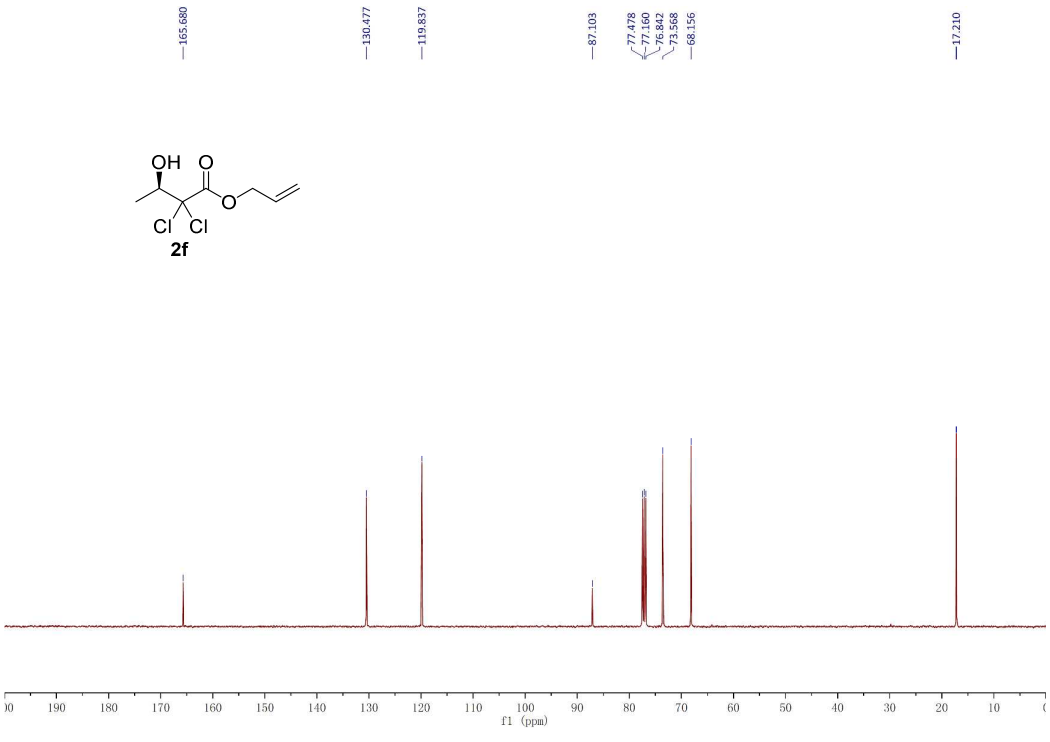

7.260
4.444
4.429
4.412
4.396
4.380
2.686
2.668
1.556
1.542
1.441
1.426
OH
O
O
Cl
Cl
2e
1.00
0.88
9.25
3.15
f1 (ppm)

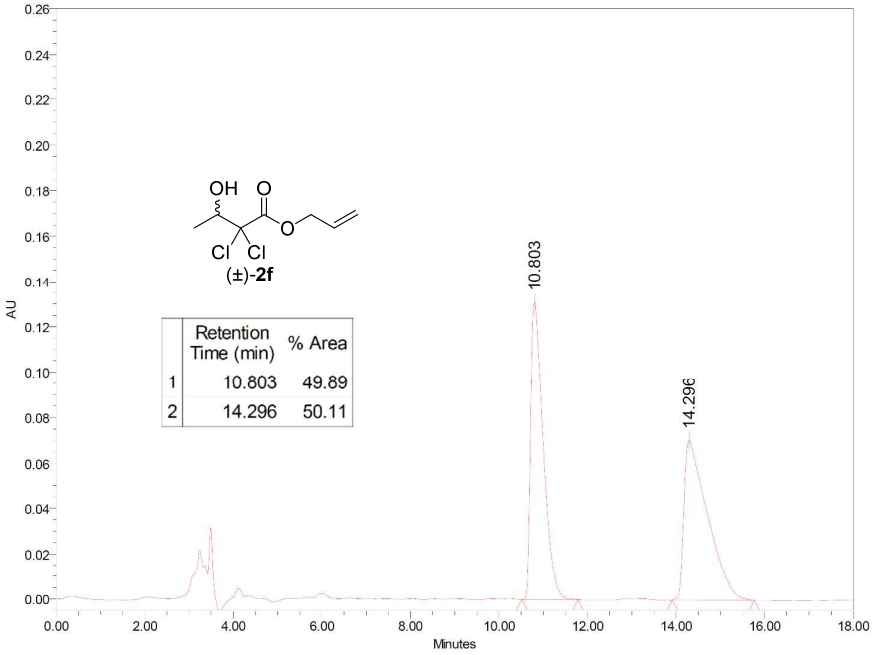

164.672
88.080
85.460
77.477
77.160
76.842
73.586
27.688
17.377
OH
O
O
Cl
Cl
2e
f1 (ppm)

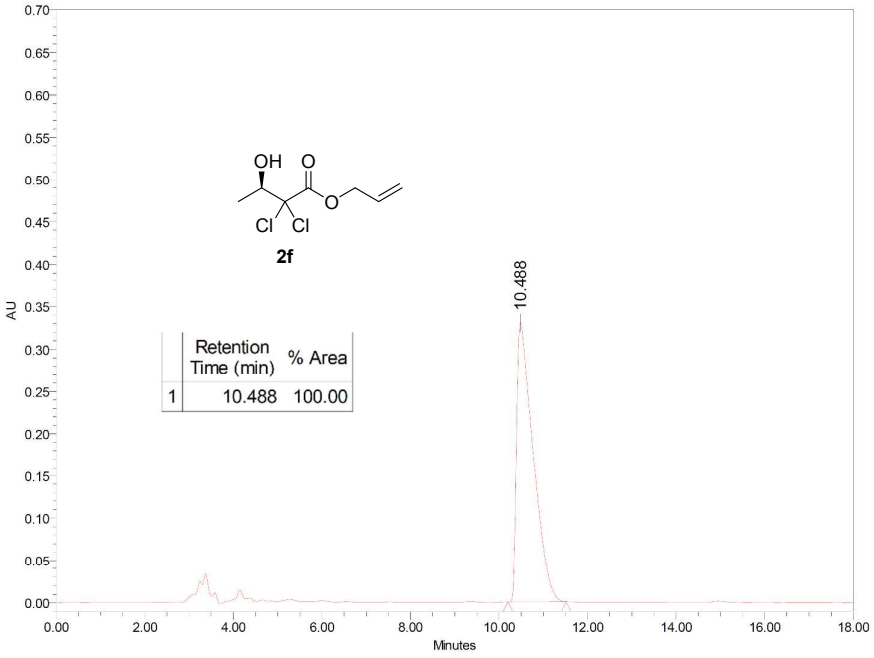

10.051
13.360
OH O
Cl Cl
(±)-2e
Retention Time (min) % Area
1 10.051 49.07
2 13.360 50.93
AU
Minutes

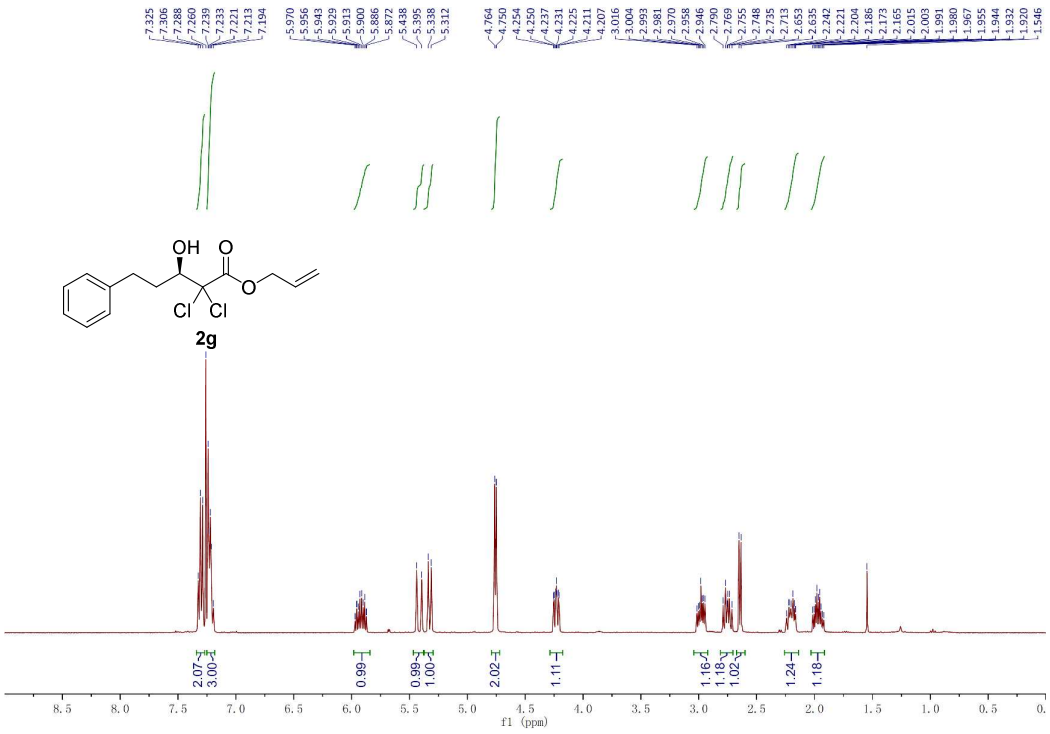

12.868
10.345
OH O
Cl Cl
2e
Retention Time (min) % Area
1 10.345 0.57
2 12.868 99.43
AU
Minutes

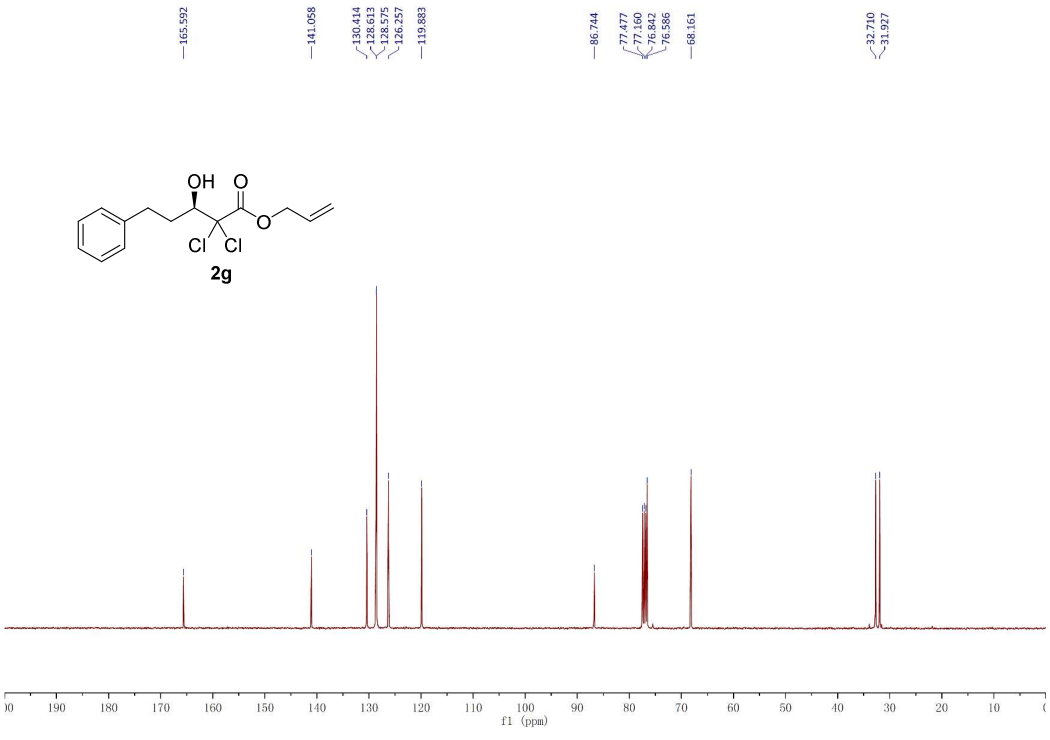

7.260
6.000
5.986
5.974
5.972
5.960
5.957
5.945
5.943
5.931
5.929
5.917
5.902
5.464
5.461
5.457
5.454
5.421
5.418
5.414
5.411
5.352
5.349
5.346
5.343
5.325
5.323
5.320
5.317
4.795
4.791
4.788
4.780
4.777
4.774
4.513
4.497
4.481
4.479
4.464
4.448
2.663
2.645
1.579
1.468
1.452
OH
O
O
Cl
Cl
2f
0.95
0.98
0.98
2.05
1.00
0.92
3.20
f1 (ppm)

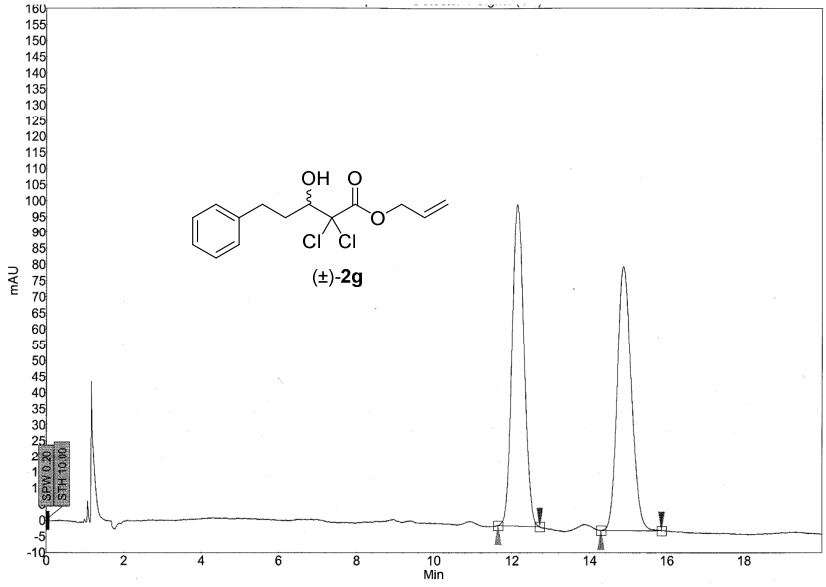

165.680
130.477
119.837
87.103
77.478
77.160
76.842
73.568
68.156
17.210
OH
O
O
Cl
Cl
2f
f1 (ppm)


OH
O
O
Cl
Cl
(±)-2f
10.803
14.296
AU
Minutes
Retention Time (min) % Area
1 10.803 49.89
2 14.296 50.11


OH
O
O
Cl
Cl
2f
10.488
AU
Minutes
Retention Time (min) % Area
1 10.488 100.00

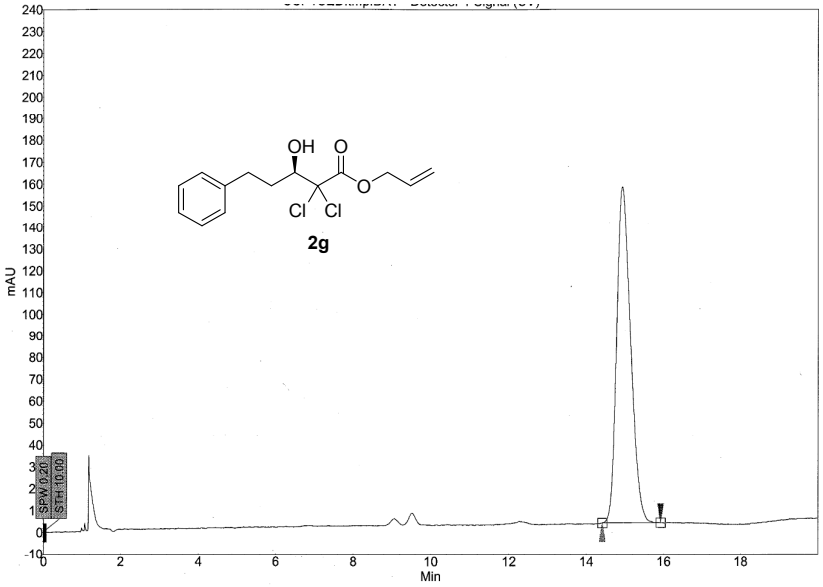

7.325
7.306
7.288
7.260
7.239
7.233
7.221
7.213
7.194
5.970
5.956
5.943
5.929
5.913
5.900
5.886
5.872
5.438
5.395
5.338
5.312
4.764
4.750
4.254
4.250
4.237
4.231
4.225
4.211
4.207
3.016
3.004
2.993
2.981
2.970
2.958
2.946
2.790
2.769
2.755
2.748
2.735
2.713
2.653
2.635
2.242
2.221
2.204
2.186
2.173
2.165
2.015
2.003
1.991
1.980
1.967
1.955
1.944
1.932
1.920
1.546
OH
O
O
Cl
Cl
2g
2.07
3.00
0.99
0.99
1.00
2.02
1.11
1.16
1.18
1.02
1.24
1.18
f1 (ppm)


165.592
141.058
130.414
128.613
128.575
126.257
119.883
86.744
77.477
77.160
76.842
76.586
68.161
32.710
31.927
OH
O
O
Cl
Cl
2g
f1 (ppm)



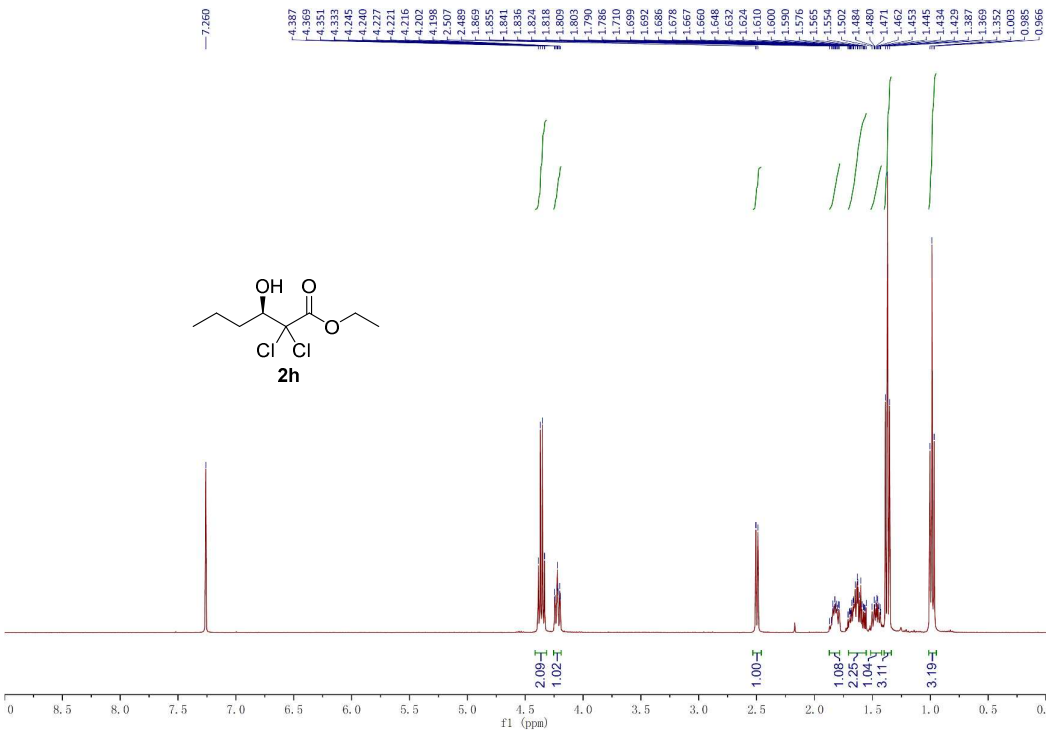
Results Table:

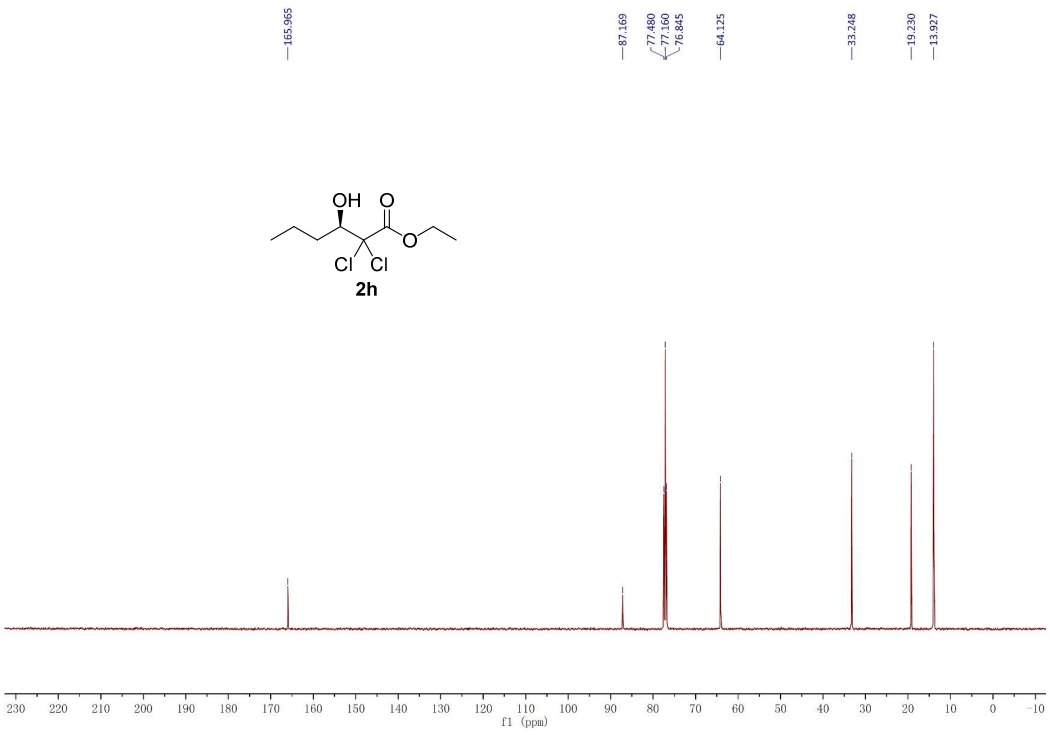
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	11.64	12.14	12.72	0.00	50.56	100.6	36.0	50.561
2	UNKNOWN	14.29	14.87	15.86	0.00	49.44	82.5	35.2	49.439
Total						100.00	183.2	71.2	100.000

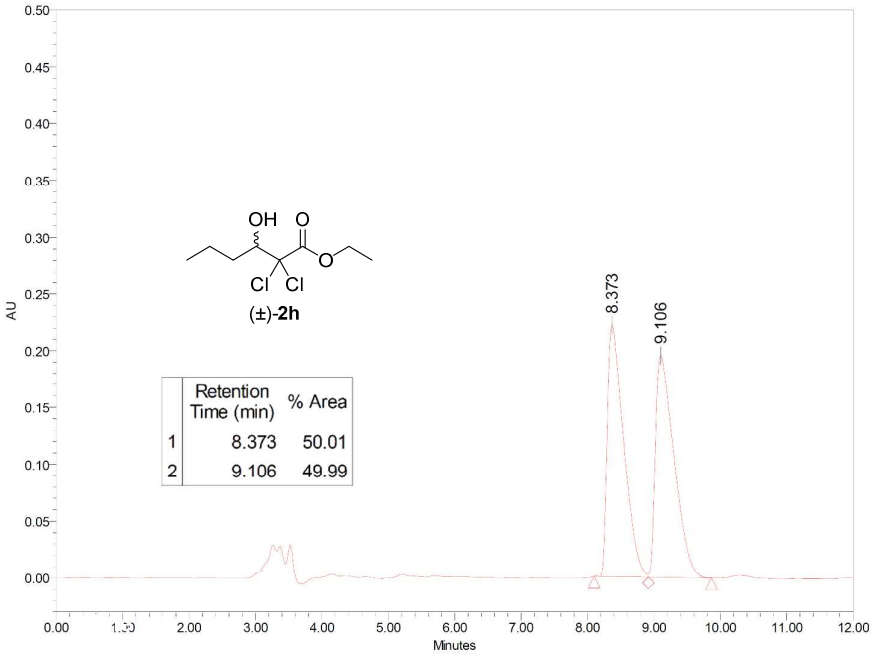


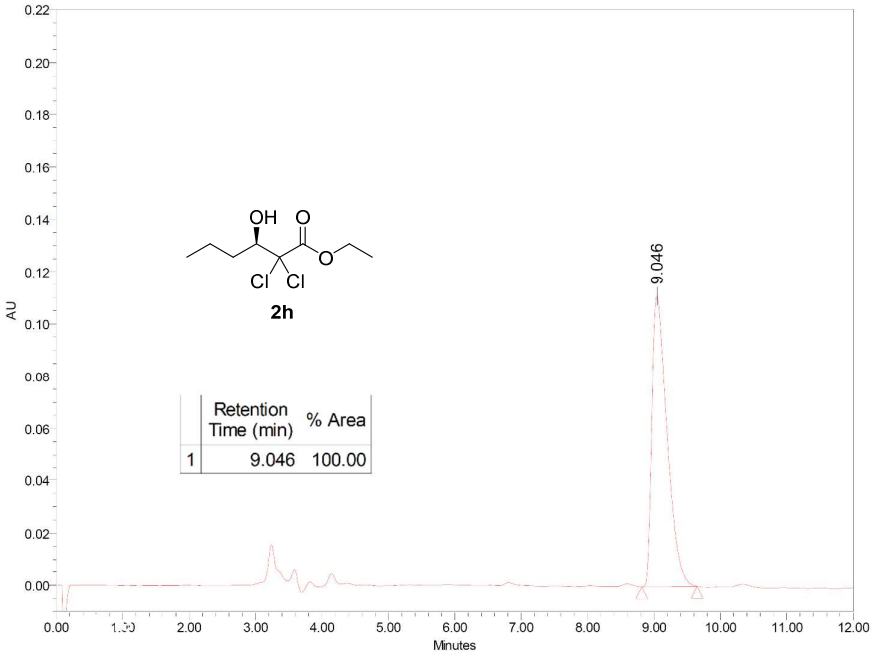
Results Table:

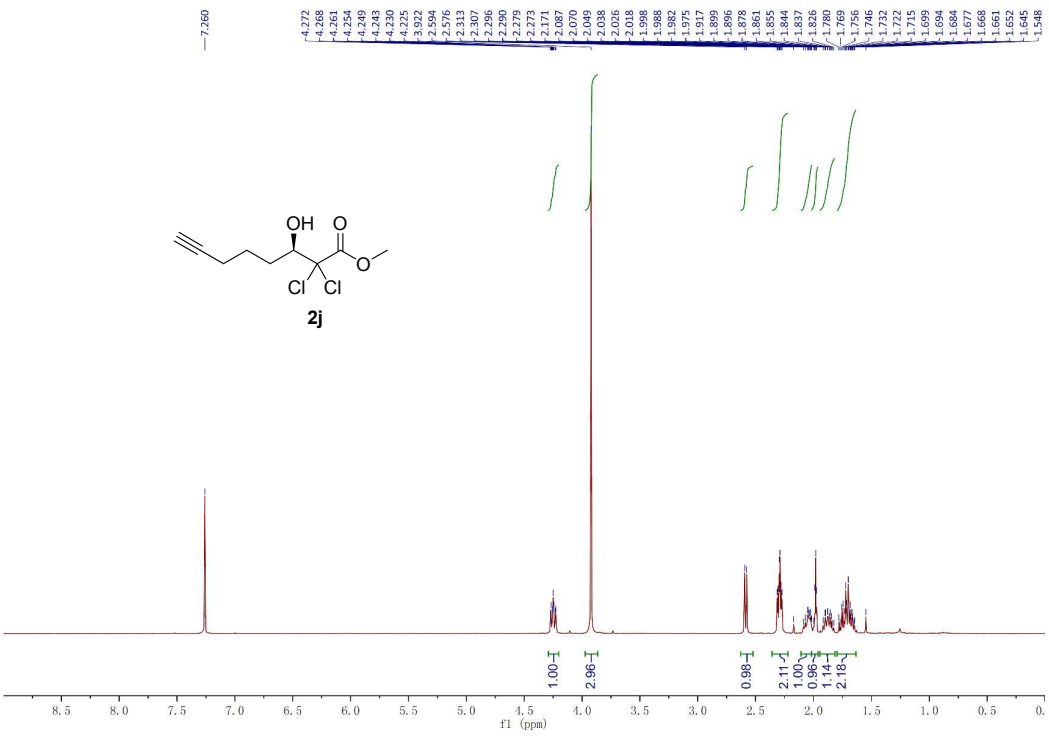
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	14.41	14.93	15.92	0.00	100.00	154.2	64.0	100.000
Total						100.00	154.2	64.0	100.000


7.260
4.387
4.369
4.351
4.333
4.245
4.240
4.227
4.221
4.216
4.202
4.198
2.507
2.489
1.869
1.855
1.841
1.836
1.824
1.818
1.809
1.803
1.790
1.786
1.710
1.699
1.692
1.686
1.678
1.667
1.660
1.648
1.632
1.624
1.610
1.600
1.590
1.576
1.565
1.554
1.502
1.484
1.480
1.471
1.462
1.453
1.445
1.434
1.429
1.387
1.369
1.352
1.003
0.985
0.966
OH
O
O
Cl
Cl
2h
2.09
1.02
1.00
1.08
2.25
1.04
3.11
3.19
f1 (ppm)

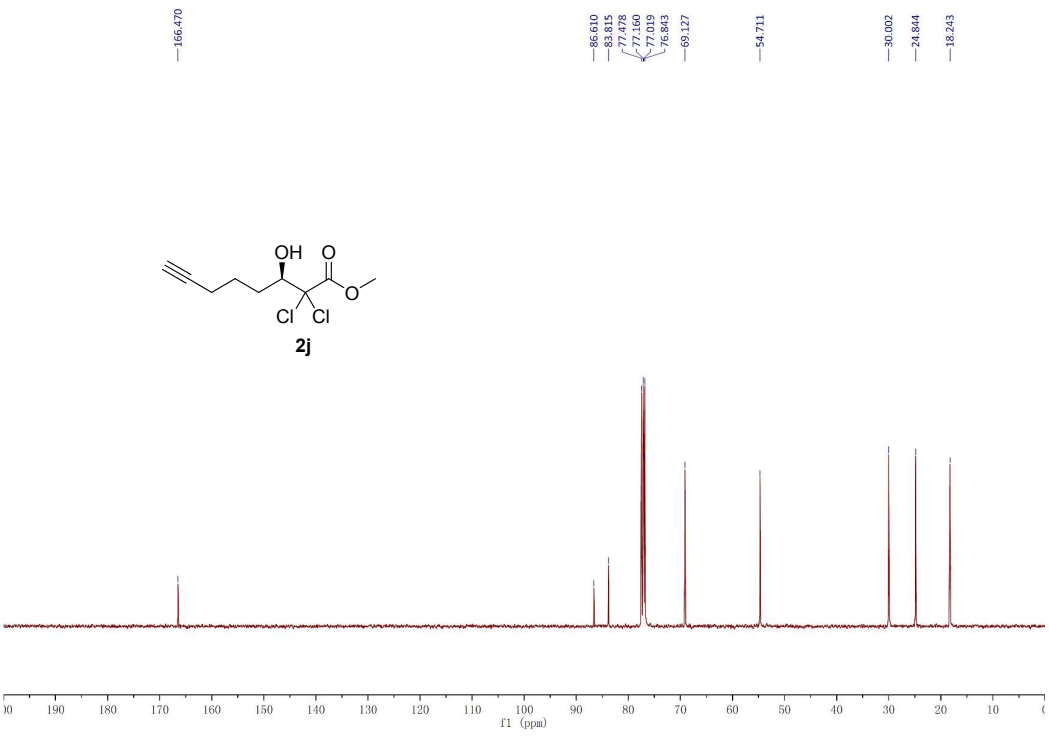

165.965
87.169
77.480
77.160
76.845
64.125
33.248
19.230
13.927
OH
O
O
Cl
Cl
2h
f1 (ppm)


OH O
Cl Cl
O
(±)-2h
8.373
9.106
AU
Minutes
Retention Time (min) % Area
1 8.373 50.01
2 9.106 49.99

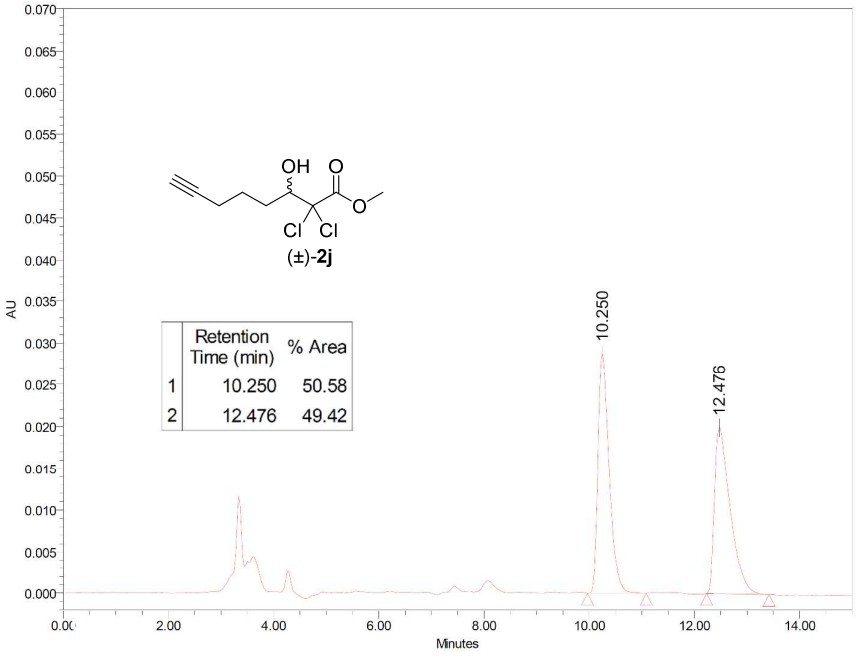

OH O
Cl Cl
O
2h
9.046
AU
Minutes
Retention Time (min) % Area
1 9.046 100.00

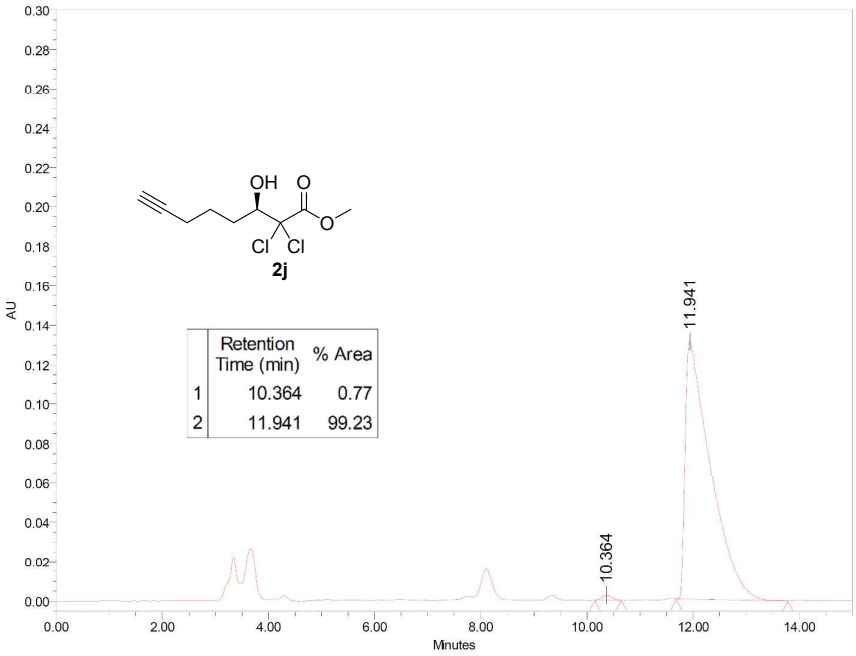

7.260
4.272
4.268
4.261
4.254
4.249
4.243
4.230
4.225
3.922
2.594
2.576
2.313
2.307
2.296
2.290
2.279
2.273
2.171
2.087
2.070
2.049
2.038
2.026
2.018
1.998
1.988
1.982
1.975
1.917
1.899
1.896
1.878
1.861
1.855
1.844
1.837
1.826
1.780
1.769
1.756
1.746
1.732
1.722
1.715
1.699
1.694
1.684
1.677
1.668
1.661
1.652
1.645
1.548
OH
O
O
Cl
Cl
1.00
2.96
0.98
2.11
1.00
0.96
1.14
2.18
f1 (ppm)

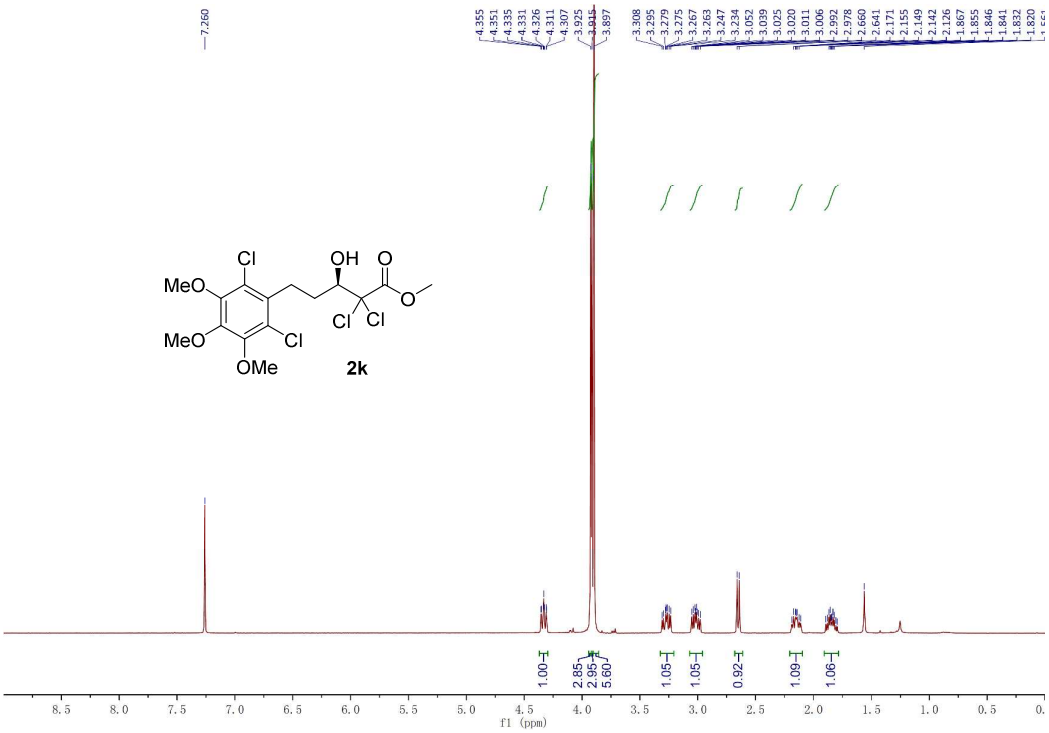
2j

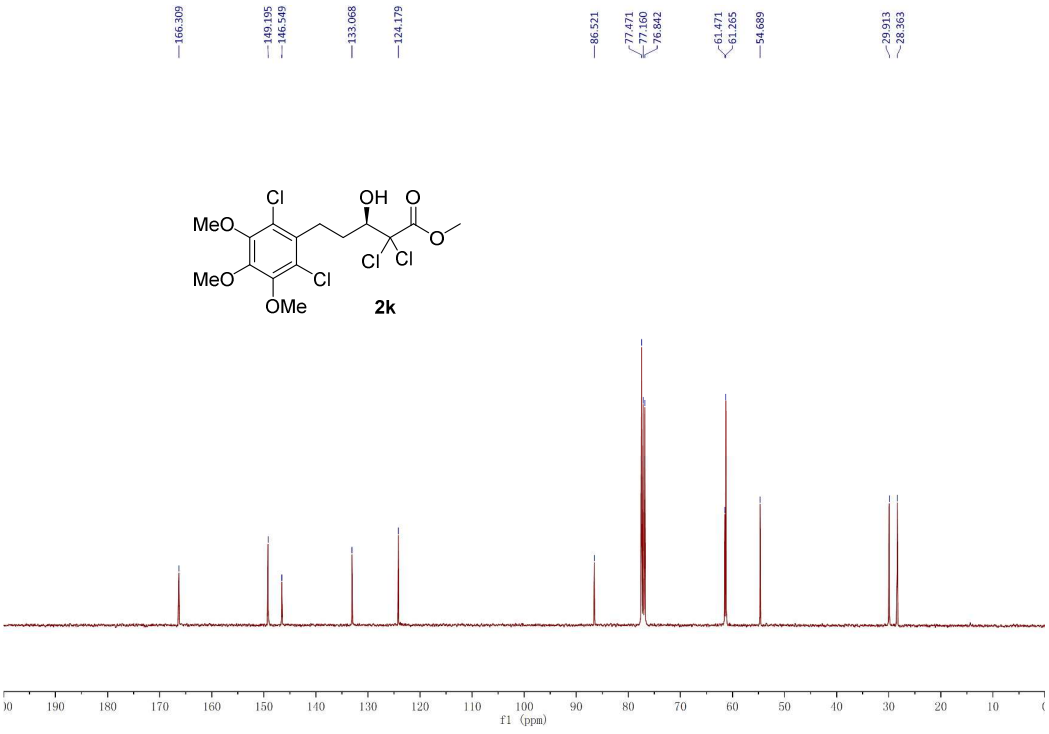

166.470
86.610
83.815
77.478
77.160
77.019
76.843
69.127
54.711
30.002
24.844
18.243
OH
O
O
Cl
Cl
f1 (ppm)

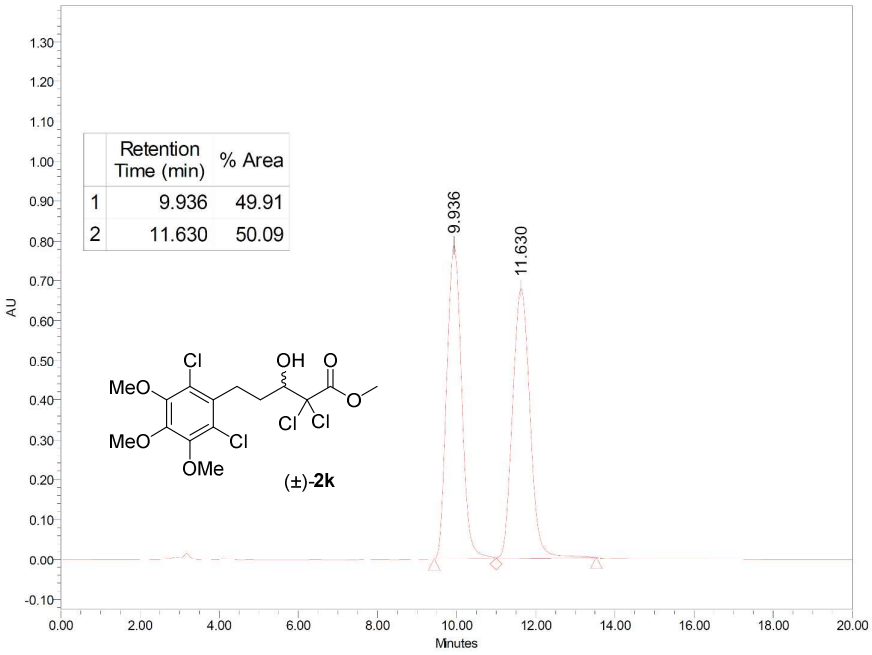
2j

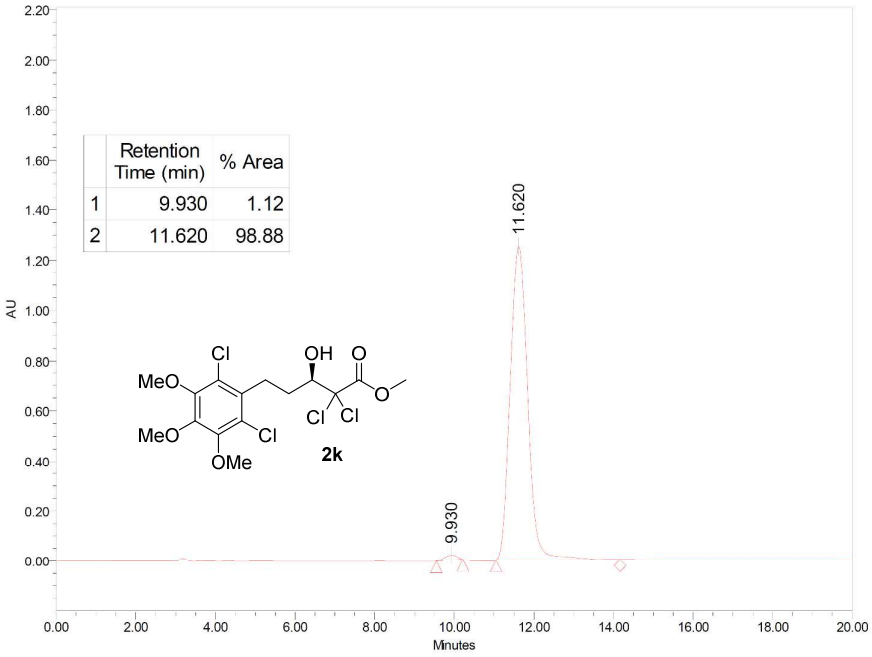

OH
O
O
Cl
Cl
(±)-2j
Retention Time (min) % Area
1 10.250 50.58
2 12.476 49.42
10.250
12.476
AU
Minutes

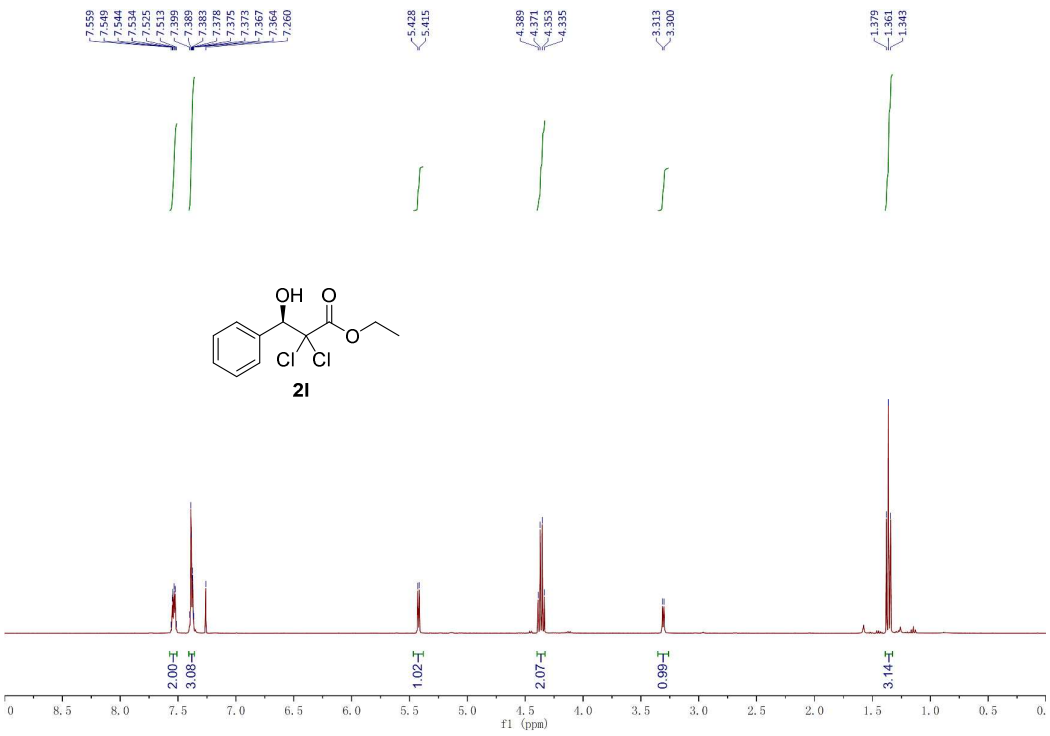

OH
O
O
Cl
Cl
2j
Retention Time (min) % Area
1 10.364 0.77
2 11.941 99.23
11.941
10.364
AU
Minutes


7.260
4.355
4.351
4.335
4.331
4.326
4.311
4.307
3.925
3.915
3.897
3.308
3.295
3.279
3.275
3.267
3.263
3.247
3.234
3.052
3.039
3.025
3.020
3.011
3.006
2.992
2.978
2.660
2.641
2.171
2.155
2.149
2.142
2.126
1.867
1.855
1.846
1.841
1.832
1.820
Cl
OH
O
MeO
O
Cl
Cl
MeO
Cl
OMe
2k
1.00
2.85
2.95
5.60
1.05
1.05
0.92
1.09
1.06
f1 (ppm)

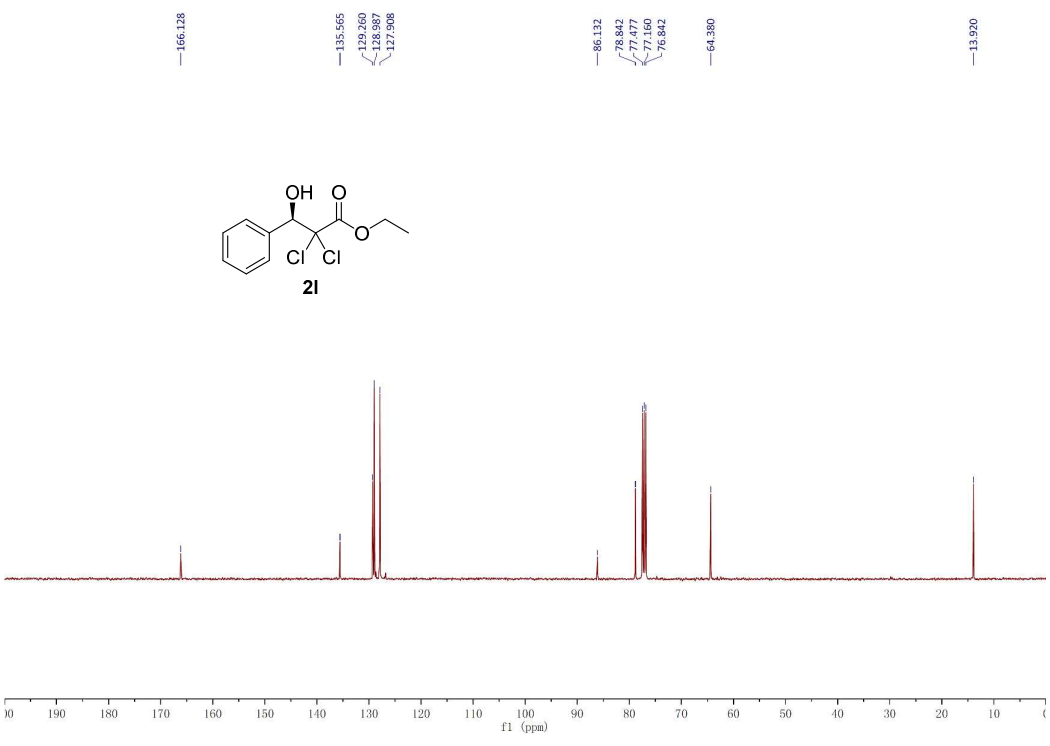

166.309
149.195
146.549
133.068
124.179
86.521
77.471
77.160
76.842
61.471
61.265
54.689
29.913
28.363
Cl
OH
O
MeO
O
Cl
Cl
MeO
Cl
OMe
2k
f1 (ppm)


Retention Time (min) % Area
1 9.936 49.91
2 11.630 50.09
9.936
11.630
AU
Minutes
(±)-2k

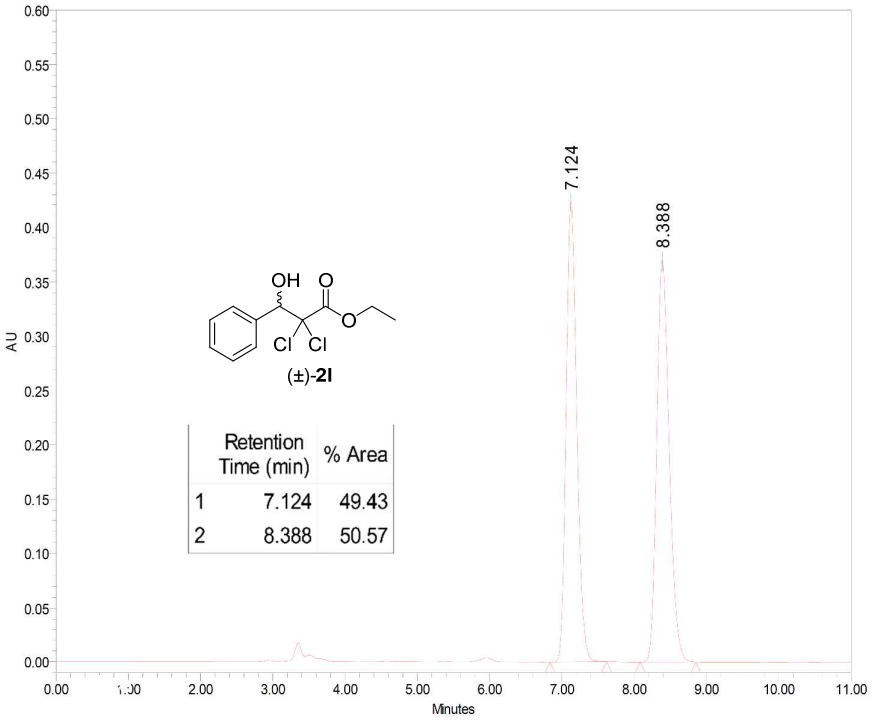

Retention Time (min) % Area
1 9.930 1.12
2 11.620 98.88
11.620
9.930
AU
Minutes
2k


7.559
7.549
7.544
7.534
7.525
7.513
7.399
7.389
7.383
7.378
7.375
7.373
7.367
7.364
7.260
5.428
5.415
4.389
4.371
4.353
4.335
3.313
3.300
1.379
1.361
1.343
OH
O
Cl
Cl
O
2.00
3.08
1.02
2.07
0.99
3.14
f1 (ppm)

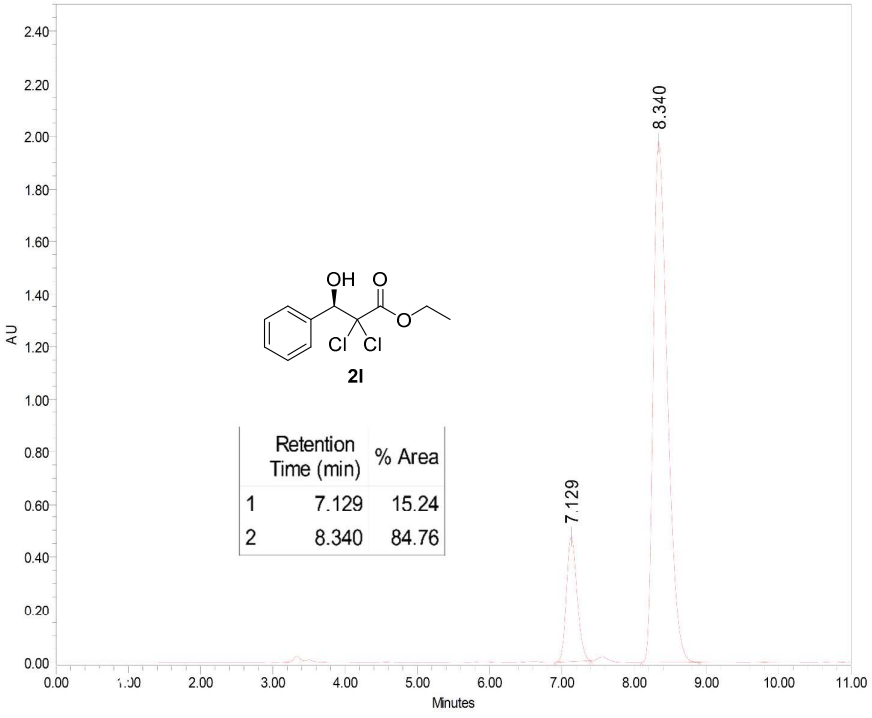
2l


166.128
135.565
129.260
128.987
127.908
86.132
78.842
77.477
77.160
76.842
64.380
13.920
OH
O
Cl
Cl
O
f1 (ppm)

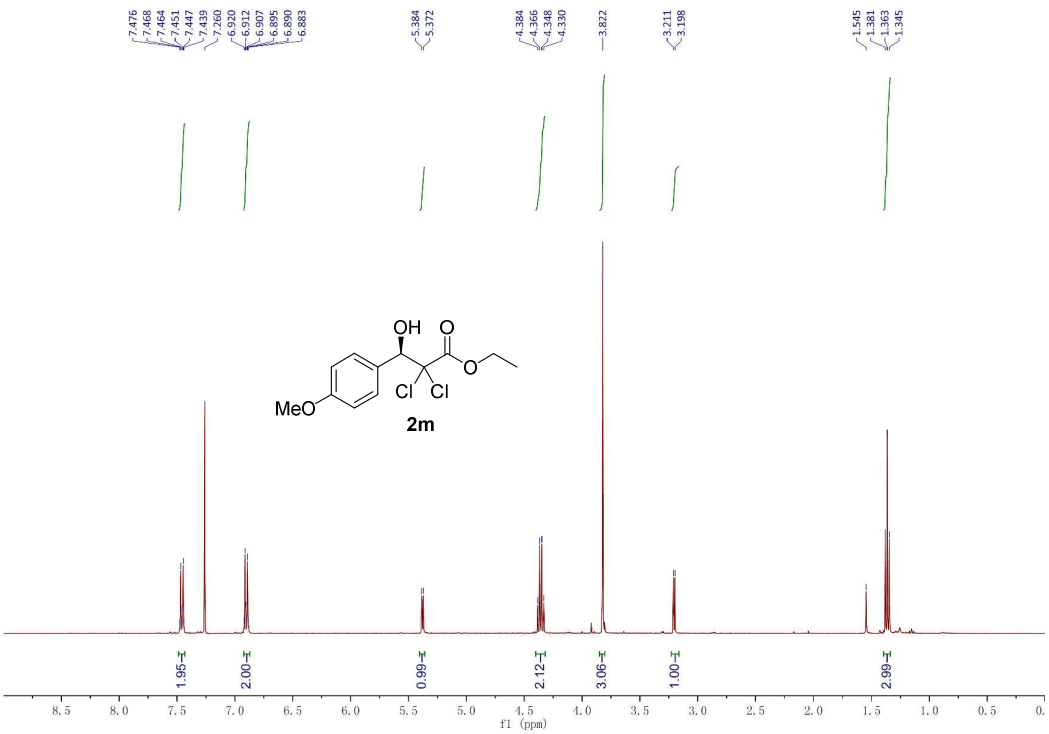
2l

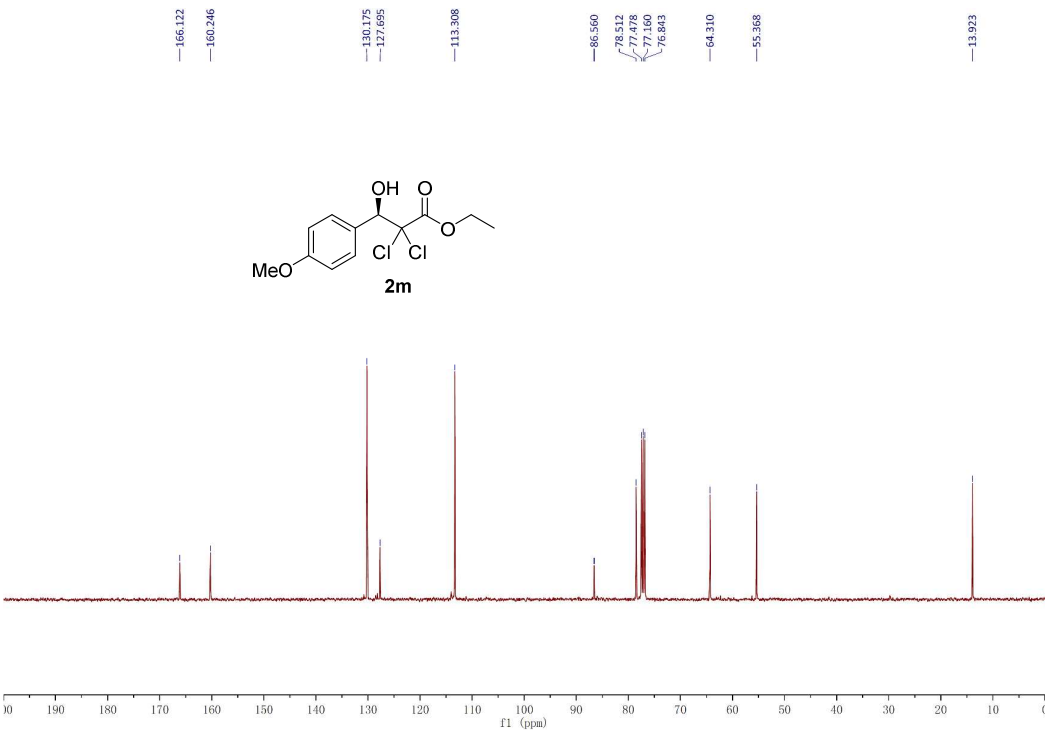


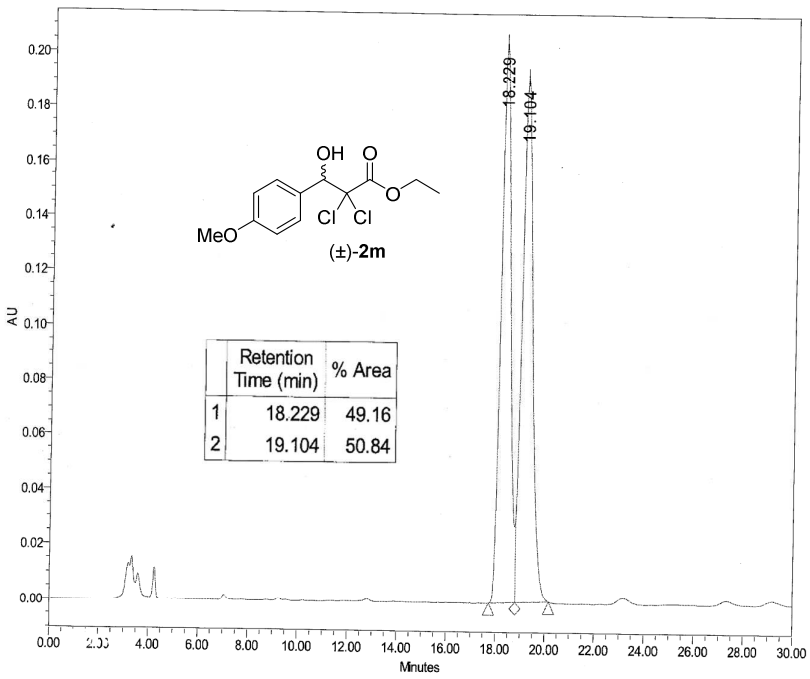
	Retention Time (min)	% Area
1	7.124	49.43
2	8.388	50.57



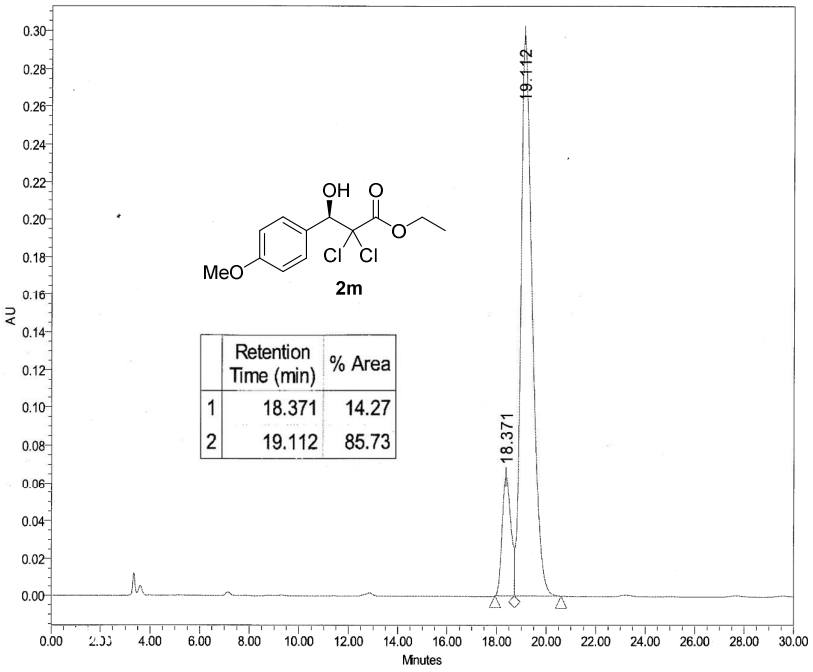
	Retention Time (min)	% Area
1	7.129	15.24
2	8.340	84.76


7.476
7.468
7.464
7.451
7.447
7.439
7.260
6.920
6.912
6.907
6.895
6.890
6.883
5.384
5.372
4.384
4.366
4.348
4.330
3.822
3.211
3.198
1.545
1.381
1.363
1.345
OH
O
O
Cl
Cl
MeO
2m
1.95
2.00
0.99
2.12
3.06
1.00
2.99
f1 (ppm)

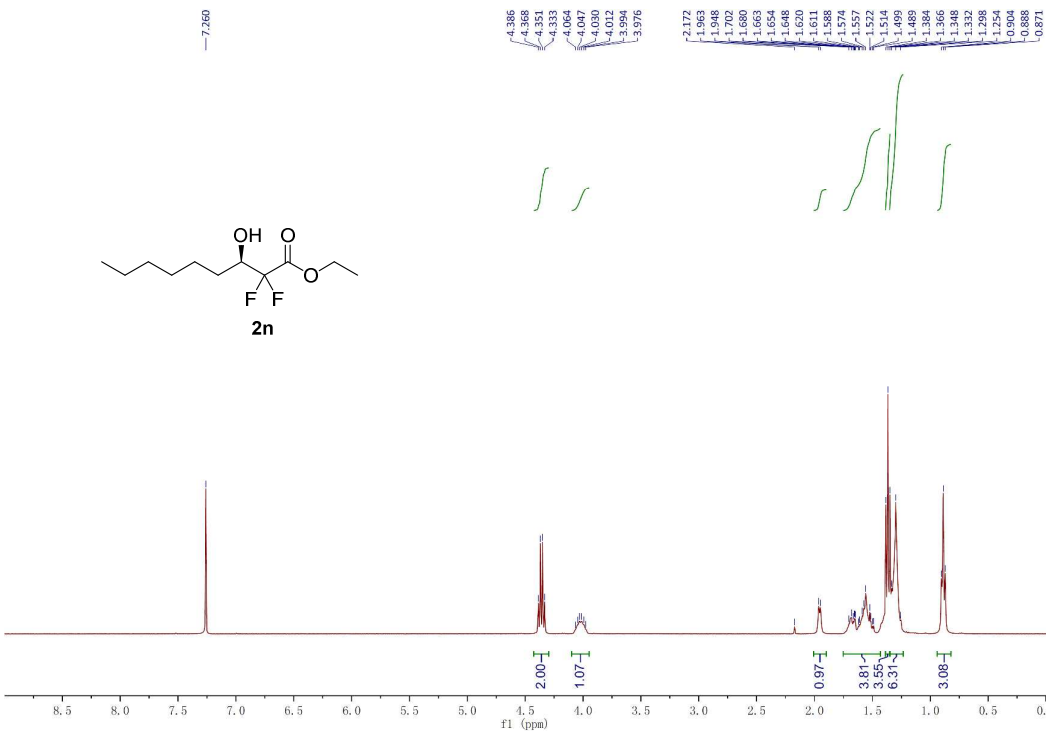

166.122
160.246
130.175
127.695
113.308
86.560
78.512
77.478
77.160
76.843
64.310
55.368
13.923
OH
O
O
Cl
Cl
MeO
2m
f1 (ppm)

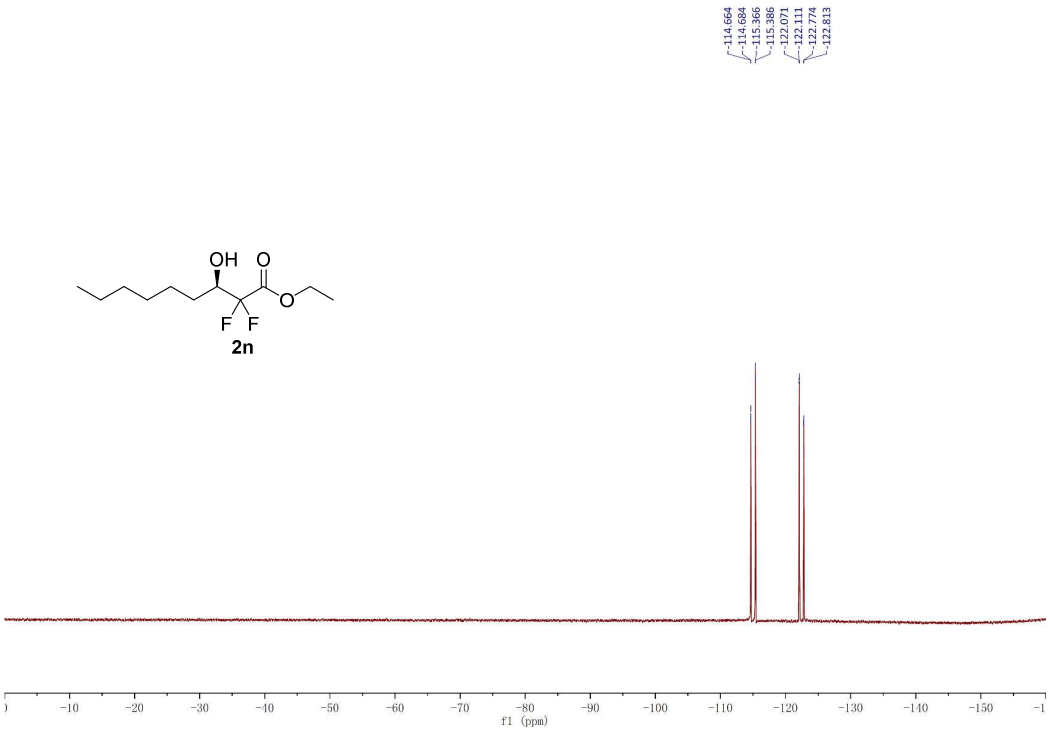


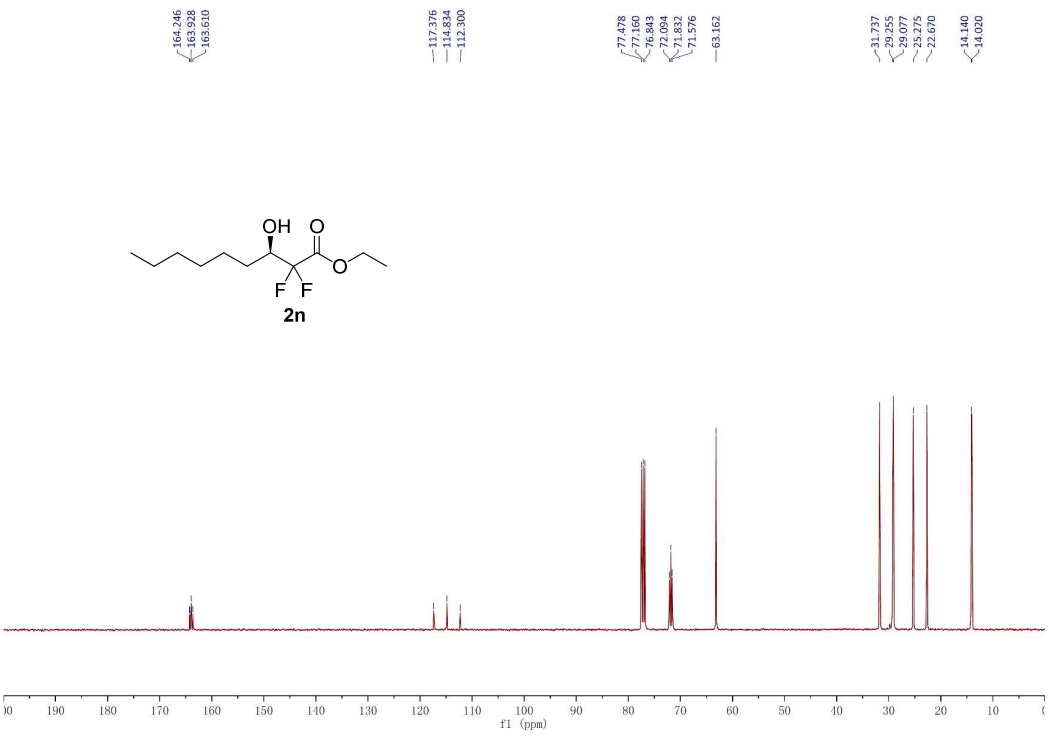
	Retention Time (min)	% Area
1	18.229	49.16
2	19.104	50.84

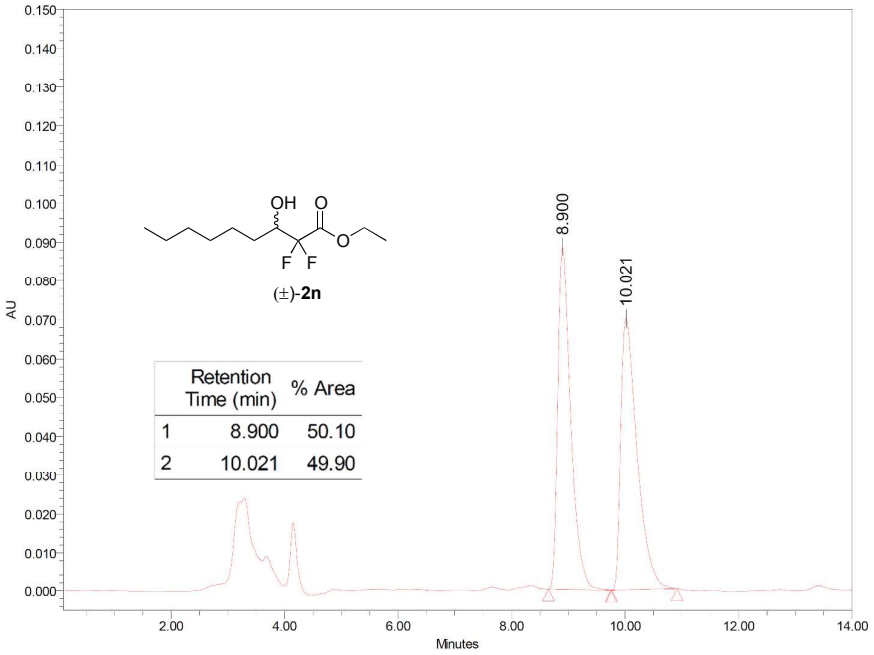


	Retention Time (min)	% Area
1	18.371	14.27
2	19.112	85.73

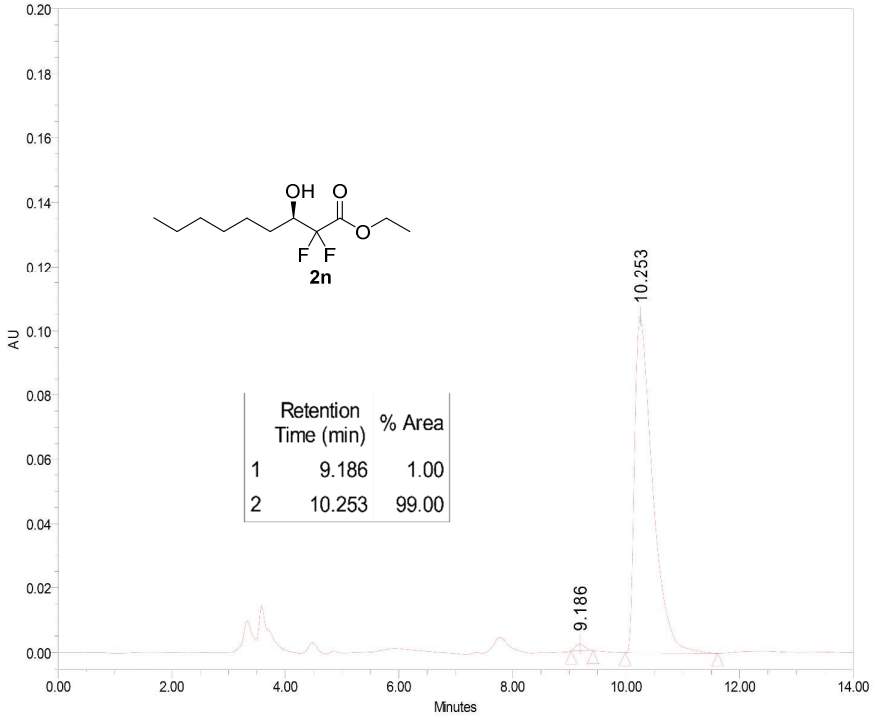

7.260
4.386
4.368
4.351
4.333
4.064
4.047
4.030
4.012
3.994
3.976
2.172
1.963
1.948
1.702
1.680
1.663
1.654
1.648
1.620
1.611
1.588
1.574
1.557
1.522
1.514
1.499
1.489
1.384
1.366
1.348
1.332
1.298
1.254
0.904
0.888
0.871
OH
O
F F
O
2n
2.00
1.07
0.97
3.81
3.55
6.31
3.08
f1 (ppm)


-114.664
-114.684
-115.366
-115.386
-122.071
-122.111
-122.774
-122.813
OH
O
F F
O
2n
f1 (ppm)

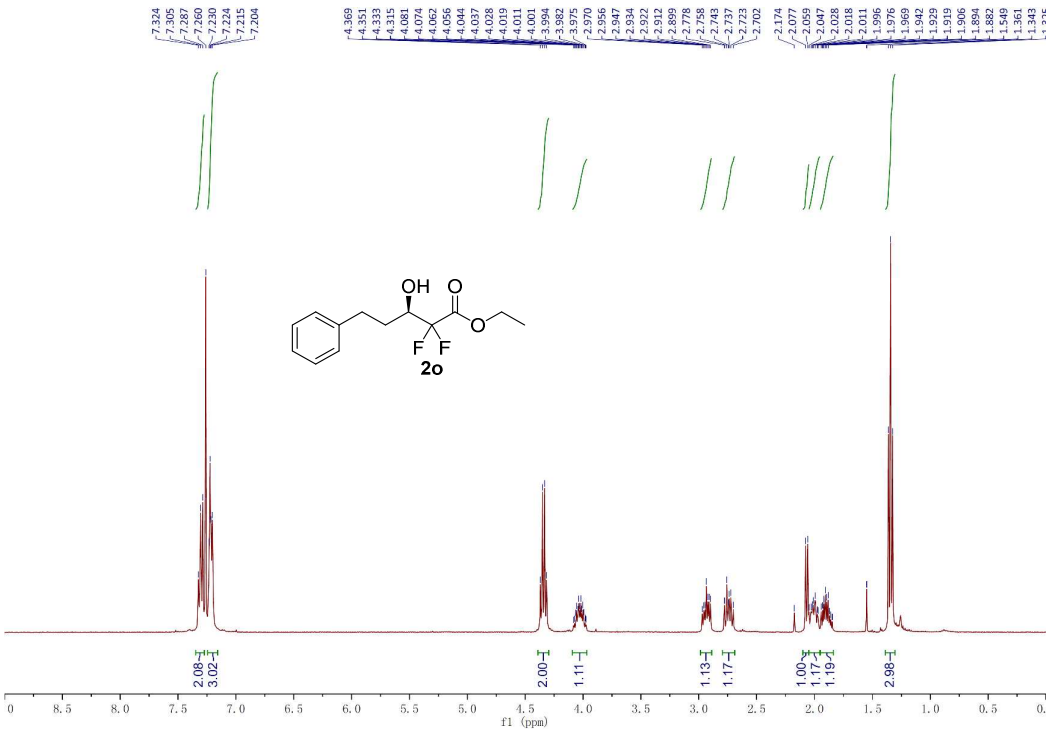

164.246
163.928
163.610
117.376
114.834
112.300
77.478
77.160
76.843
72.094
71.832
71.576
63.162
31.737
29.255
29.077
25.275
22.670
14.140
14.020
OH
O
O
F
F
2n
f1 (ppm)

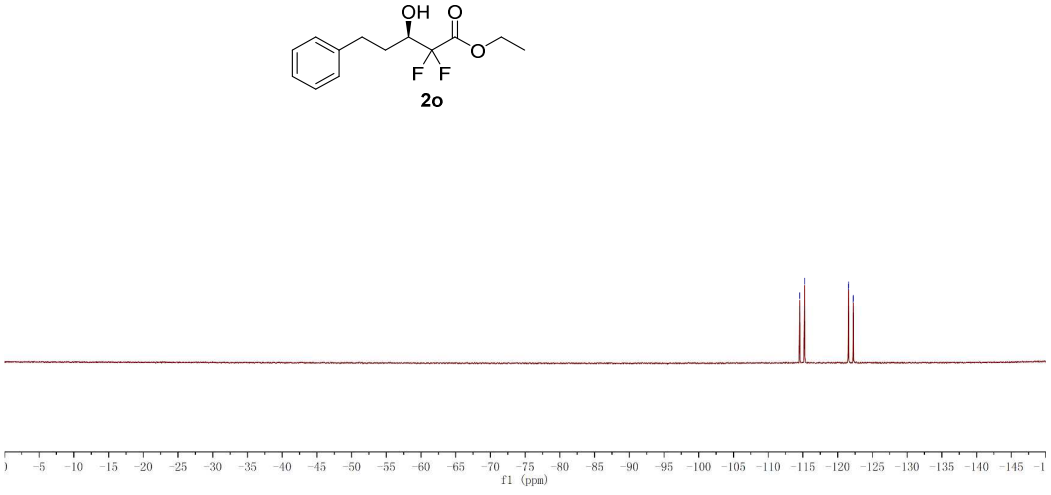


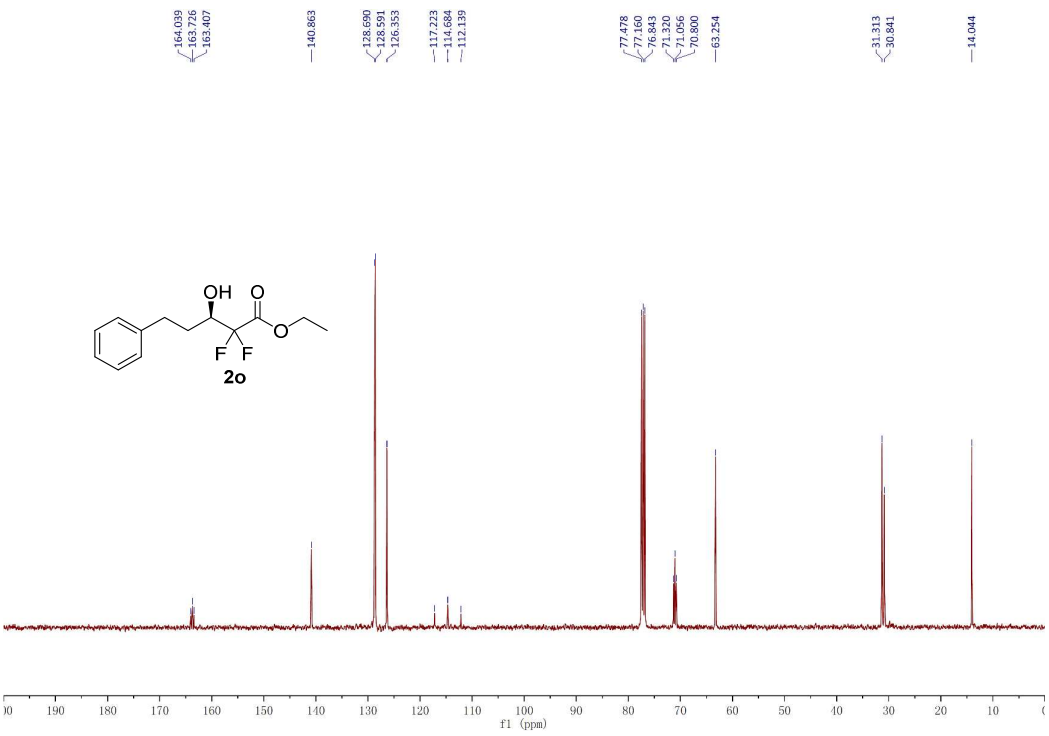
	Retention Time (min)	% Area
1	8.900	50.10
2	10.021	49.90

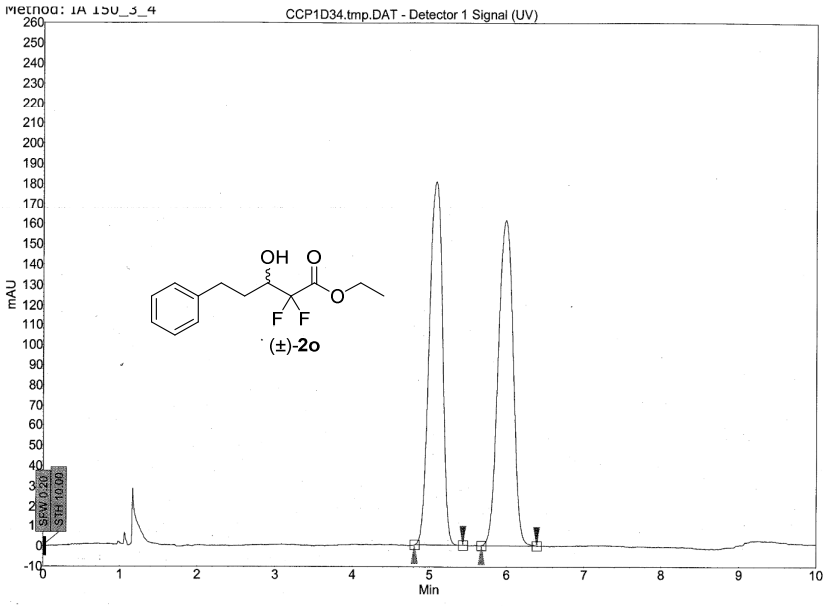


	Retention Time (min)	% Area
1	9.186	1.00
2	10.253	99.00


OH
O
O
F F
2o
f1 (ppm)

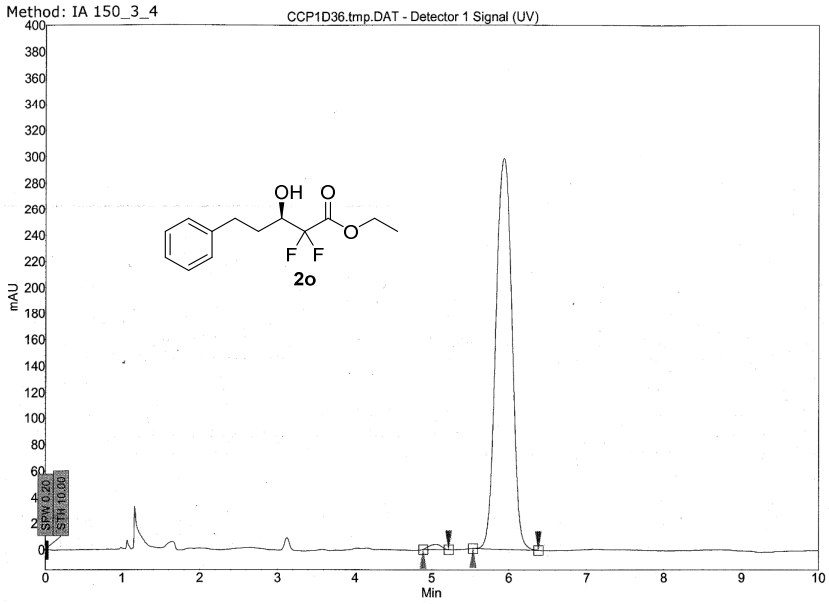

OH
O
O
F F
2o
f1 (ppm)


164.039
163.726
163.407
140.863
128.690
128.591
126.353
117.223
114.684
112.139
77.478
77.160
76.843
71.320
71.056
70.800
63.254
31.313
30.841
14.044
OH
O
O
F
F
2o
f1 (ppm)



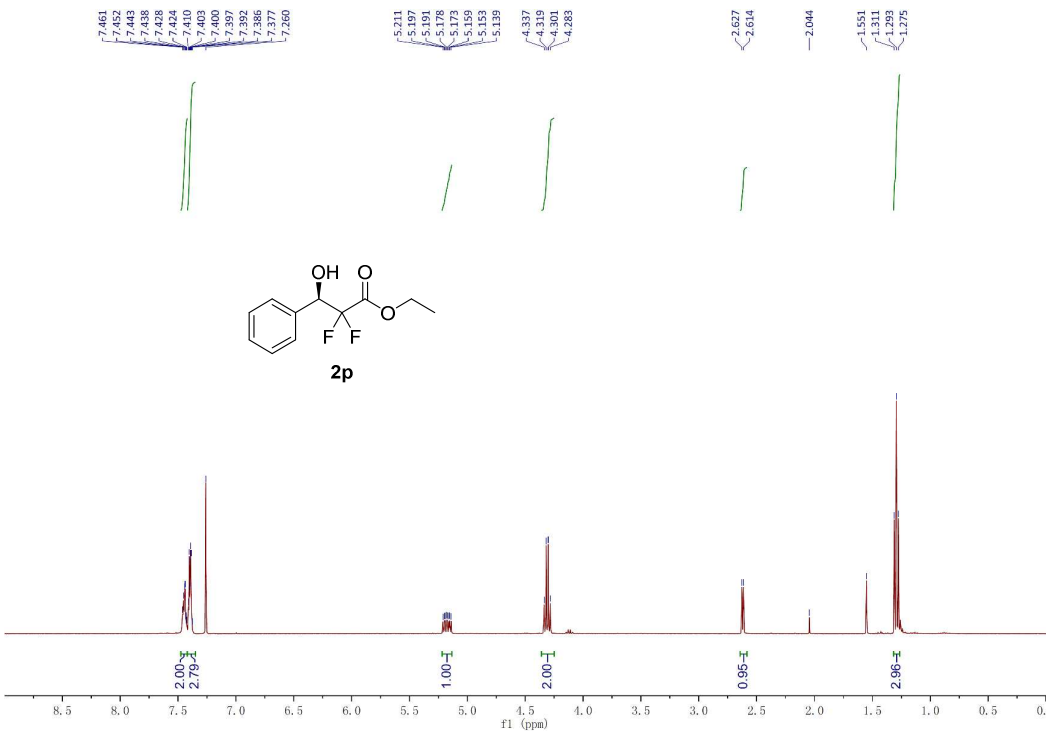
Results Table:

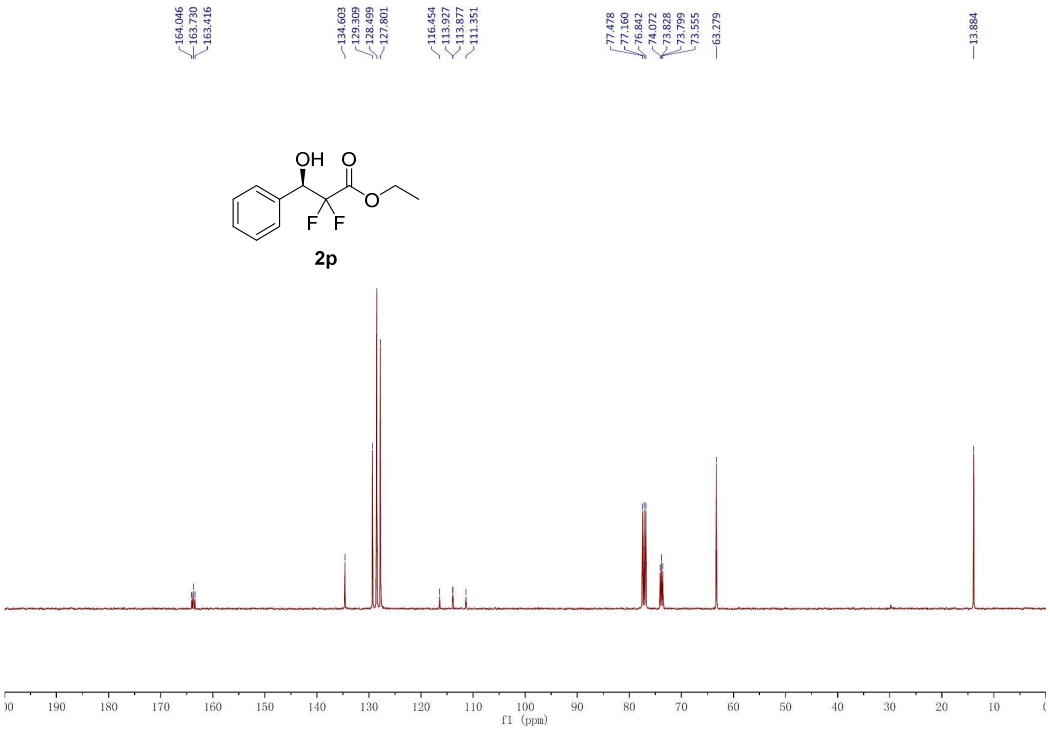
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	4.81	5.09	5.44	0.00	49.55	180.5	35.8	49.552
2	UNKNOWN	5.67	5.98	6.39	0.00	50.45	161.3	36.5	50.448
Total						100.00	341.8	72.3	100.000

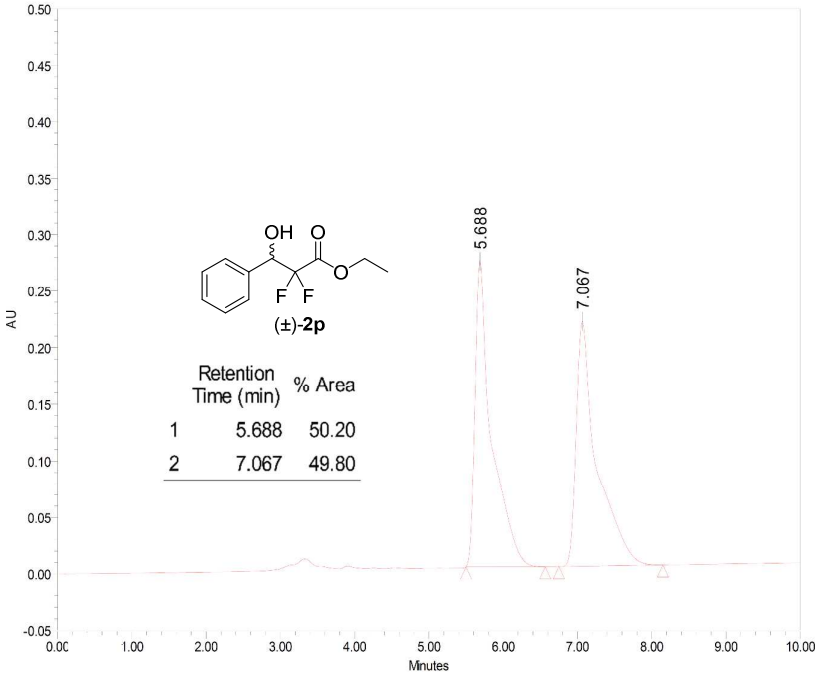


Results Table:

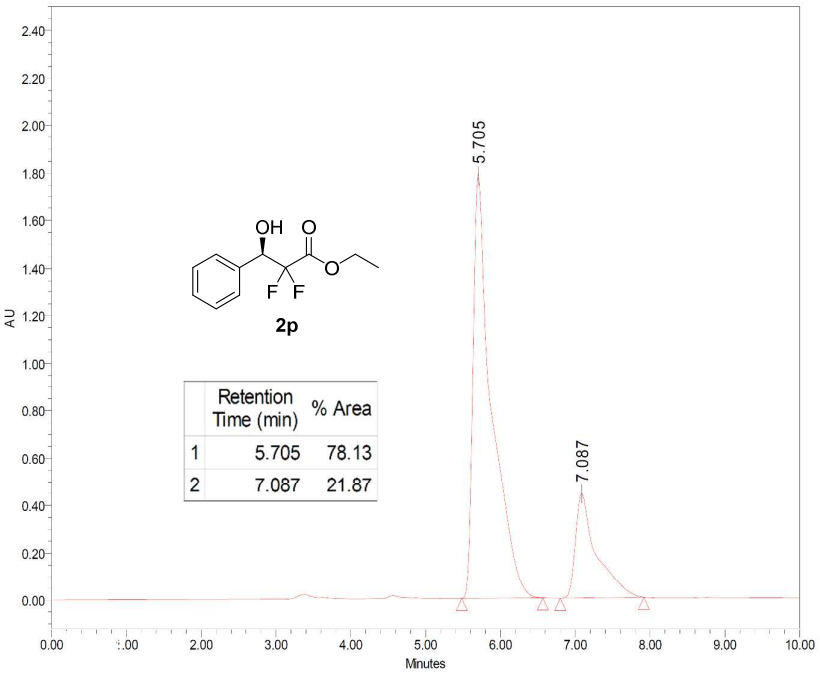
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	4.89	5.06	5.22	0.00	0.96	3.7	0.7	0.964
1	UNKNOWN	5.54	5.94	6.38	0.00	99.04	298.4	71.6	99.036
Total						100.00	302.1	72.3	100.000


7.461
7.452
7.443
7.438
7.428
7.424
7.410
7.403
7.400
7.397
7.392
7.386
7.377
7.260
5.211
5.197
5.191
5.178
5.173
5.159
5.153
5.139
4.337
4.319
4.301
4.283
2.627
2.614
2.044
1.551
1.311
1.293
1.275
OH
O
O
F
F
2p
2.00
2.79
1.00
2.00
0.95
2.96
f1 (ppm)

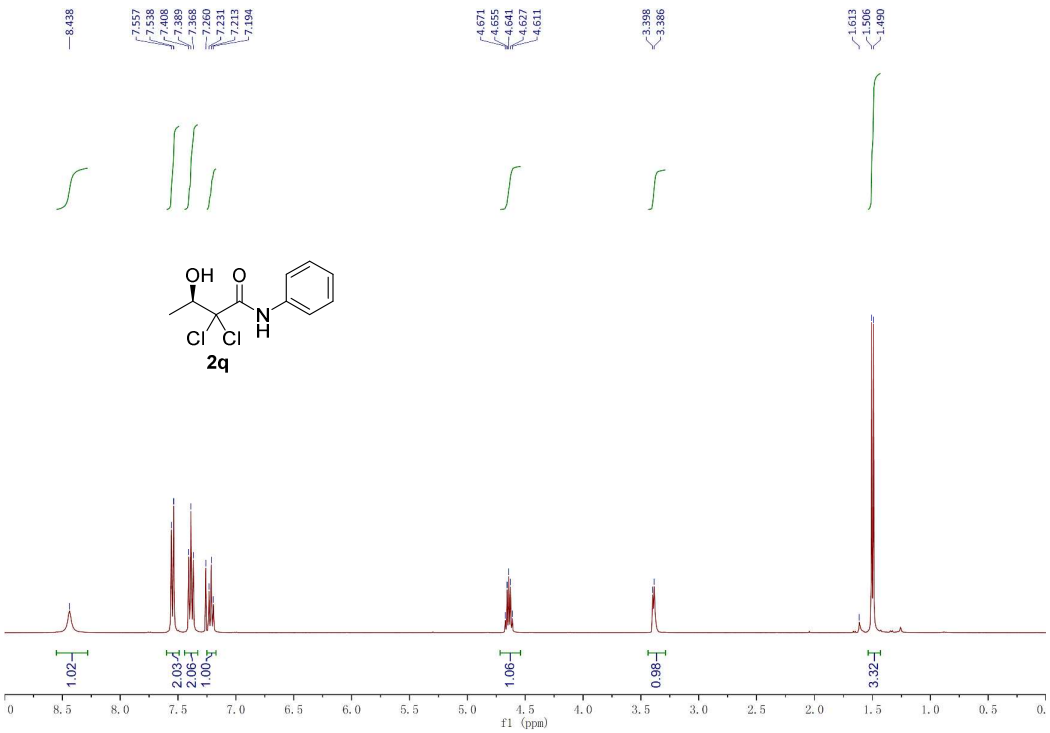

164.046
163.730
163.416
134.603
129.309
128.499
127.801
116.454
113.927
113.877
111.351
77.478
77.160
76.842
74.072
73.928
73.799
73.555
63.279
13.884
OH
O
O
F
F
2p
f1 (ppm)

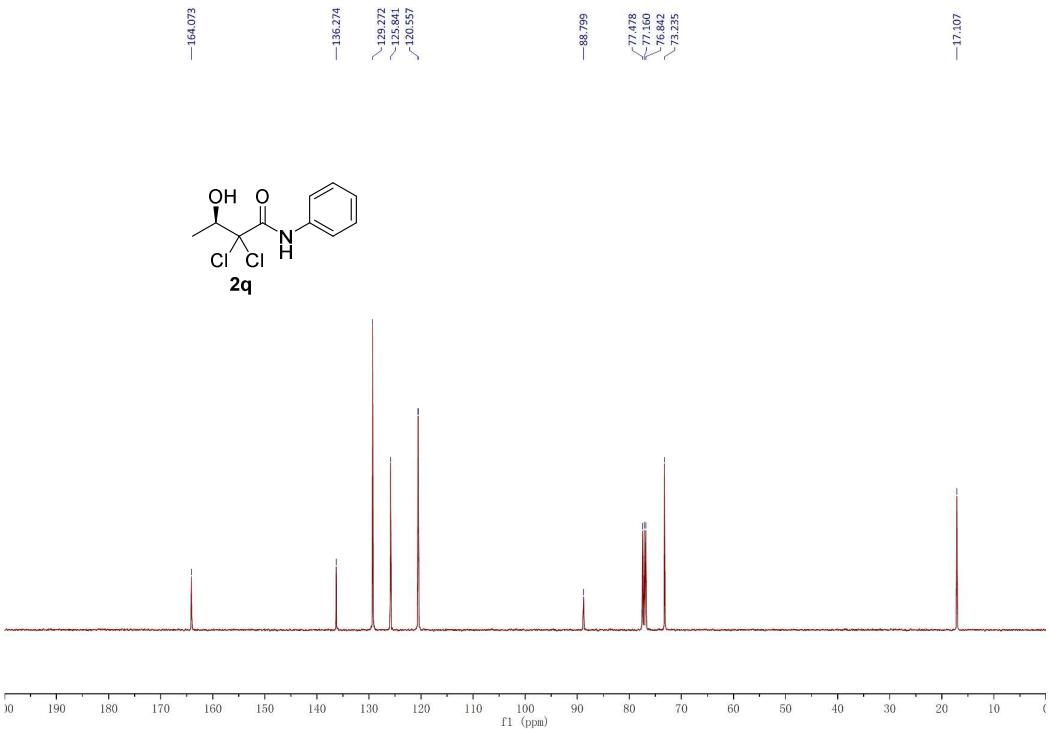


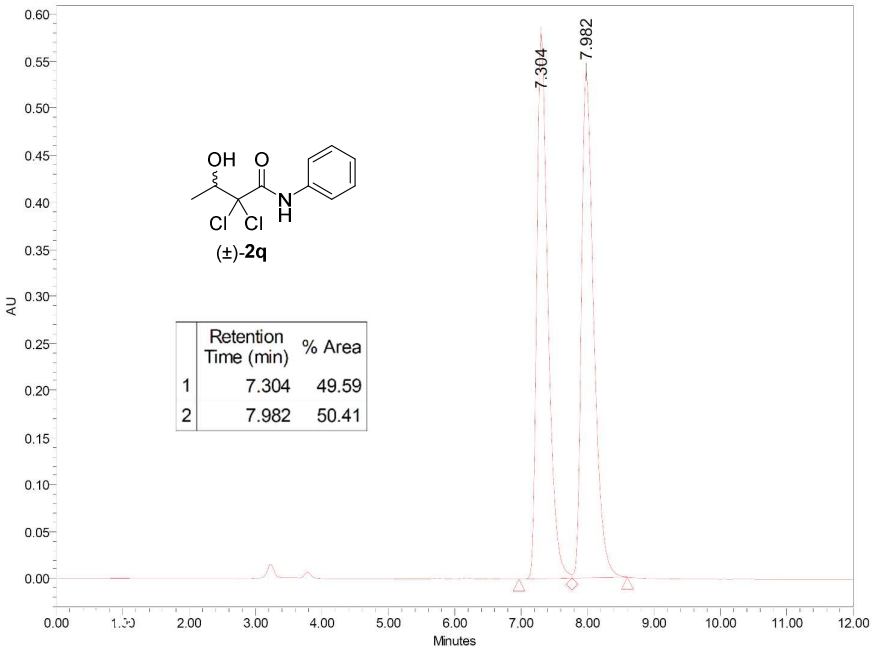
	Retention Time (min)	% Area
1	5.688	50.20
2	7.067	49.80

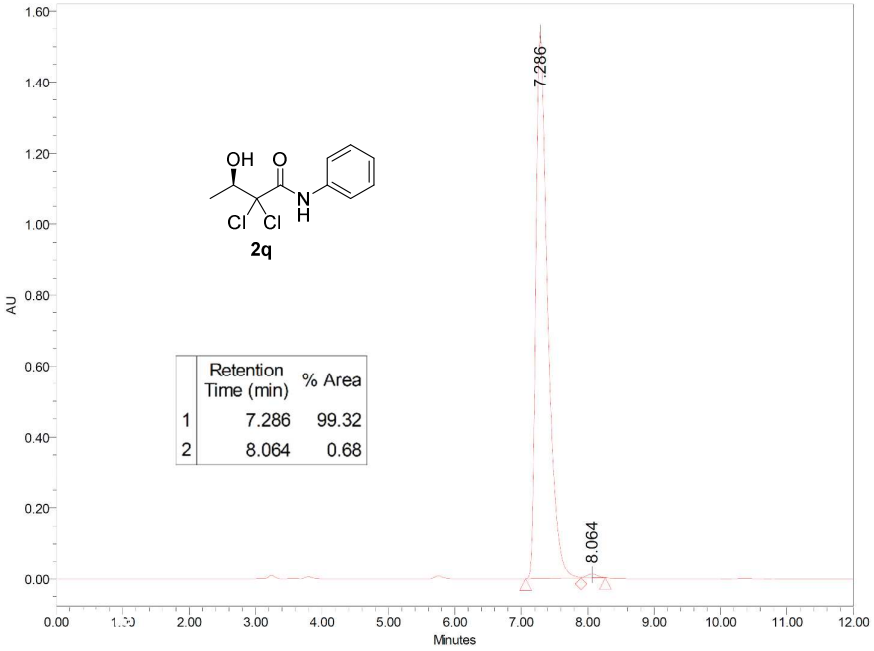


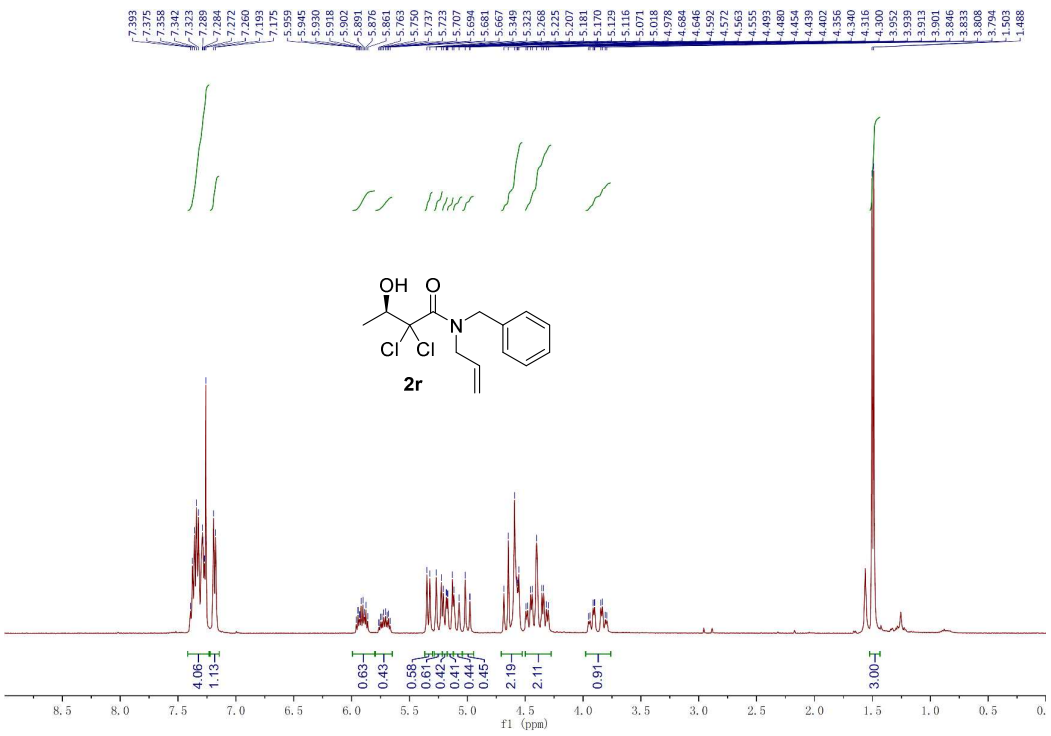
	Retention Time (min)	% Area
1	5.705	78.13
2	7.087	21.87

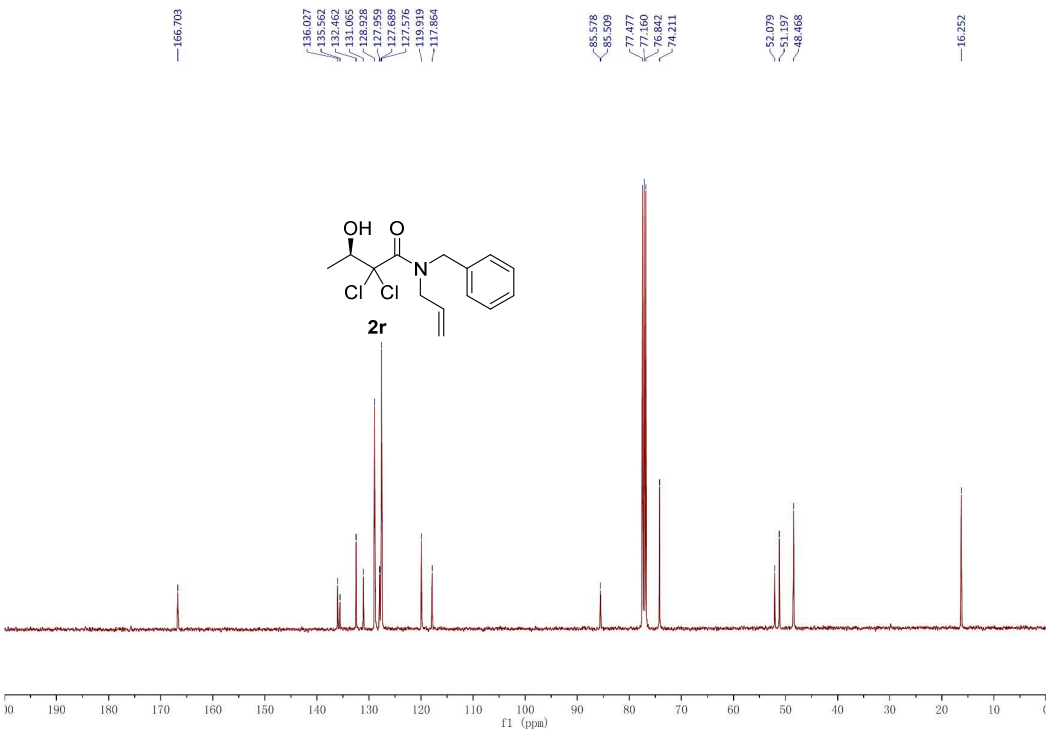

8.438
7.557
7.538
7.408
7.389
7.368
7.260
7.231
7.213
7.194
4.671
4.655
4.641
4.627
4.611
3.398
3.386
1.613
1.506
1.490
OH
O
N
H
Cl
Cl
2q
1.02
2.03
2.06
1.00
1.06
0.98
3.32
f1 (ppm)

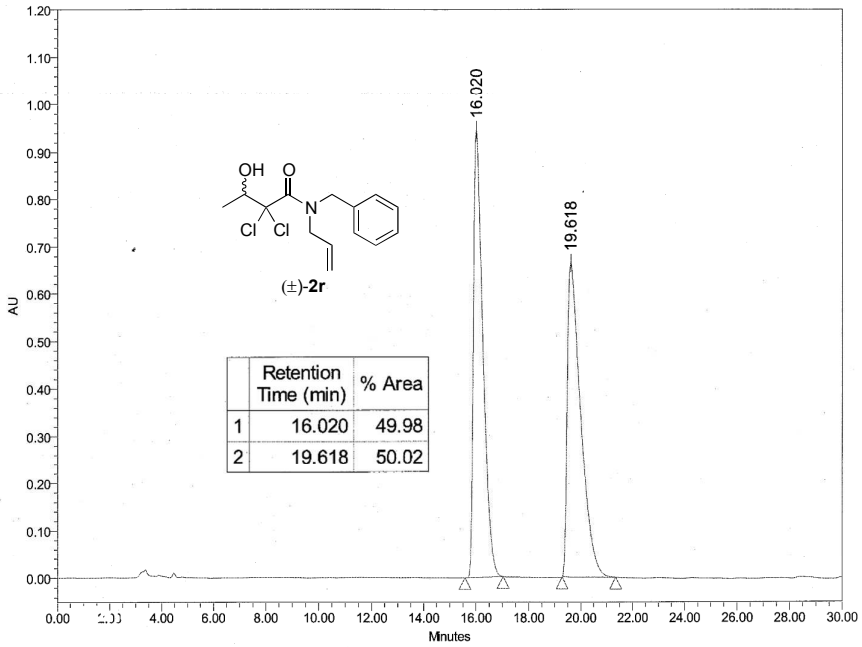

164.073
136.274
129.272
125.841
120.557
88.799
77.478
77.160
76.842
73.235
17.107
OH
O
N
H
Cl
Cl
2q
f1 (ppm)


7.304
7.982
OH
O
N
H
Cl
Cl
(±)-2q
AU
Minutes
Retention Time (min) % Area
1 7.304 49.59
2 7.982 50.41

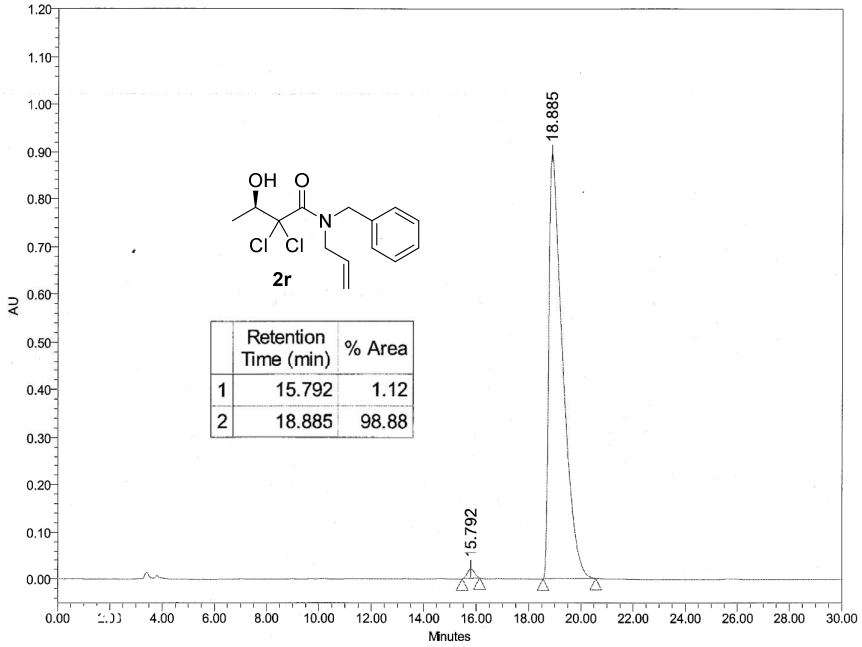

7.286
8.064
OH
O
N
H
Cl
Cl
2q
AU
Minutes
Retention Time (min) % Area
1 7.286 99.32
2 8.064 0.68


7.393
7.375
7.358
7.342
7.323
7.289
7.284
7.272
7.260
7.193
7.175
5.959
5.945
5.930
5.918
5.902
5.891
5.876
5.861
5.763
5.750
5.737
5.723
5.707
5.694
5.681
5.667
5.349
5.323
5.268
5.225
5.207
5.181
5.170
5.129
5.116
5.071
5.018
4.978
4.684
4.646
4.592
4.572
4.563
4.555
4.493
4.480
4.454
4.439
4.402
4.356
4.340
4.316
4.300
3.952
3.939
3.913
3.901
3.846
3.833
3.808
3.794
1.503
1.488
OH
O
N
Cl
Cl
2r
4.06
1.13
0.63
0.43
0.58
0.61
0.42
0.41
0.44
0.45
2.19
2.11
0.91
3.00
f1 (ppm)


166.703
136.027
135.562
132.462
131.065
128.928
127.959
127.689
127.576
119.919
117.864
85.578
85.509
77.477
77.160
76.842
74.211
52.079
51.197
48.468
16.252
OH
O
N
Cl
Cl
2r
f1 (ppm)

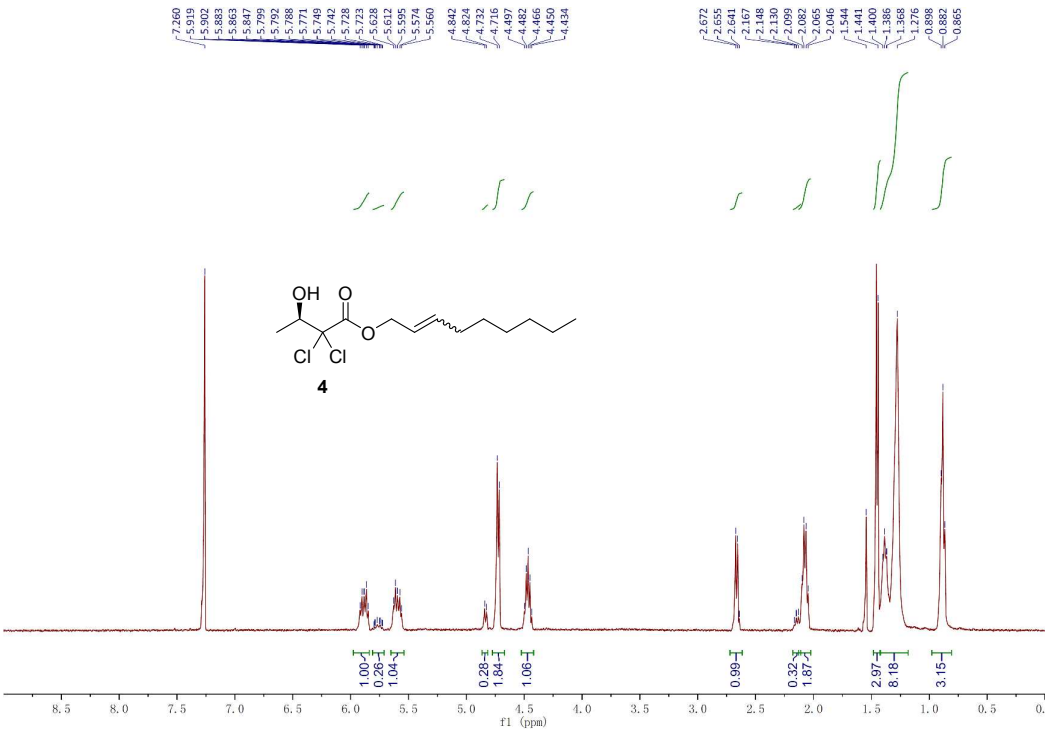


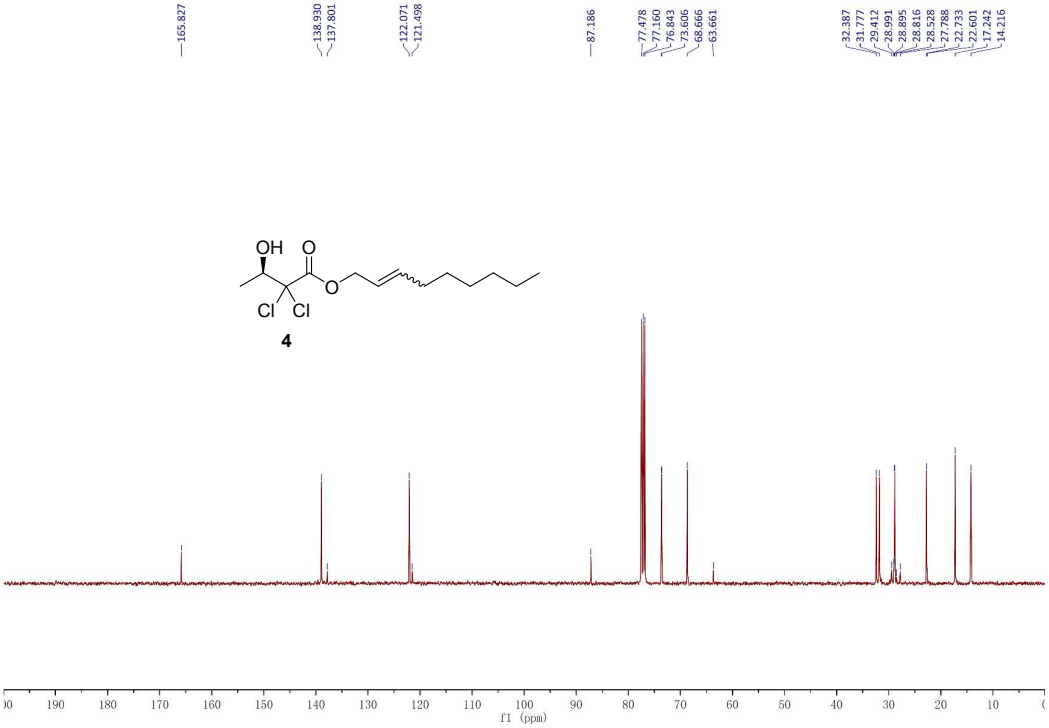
	Retention Time (min)	% Area
1	16.020	49.98
2	19.618	50.02

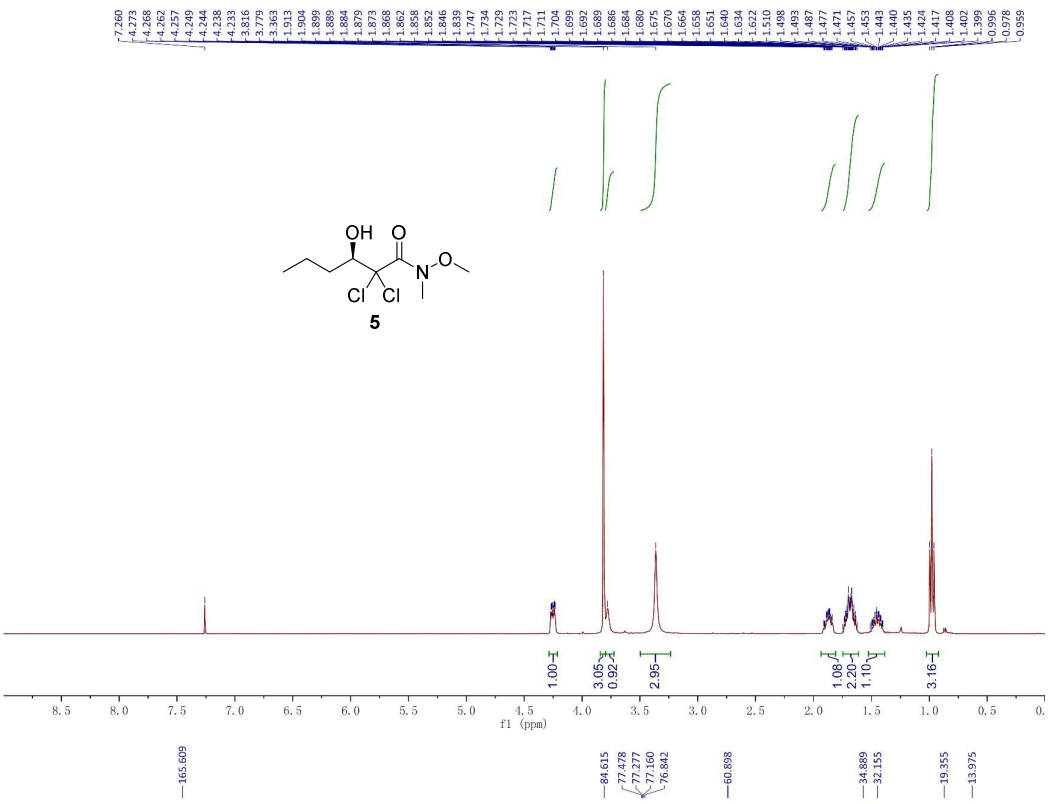


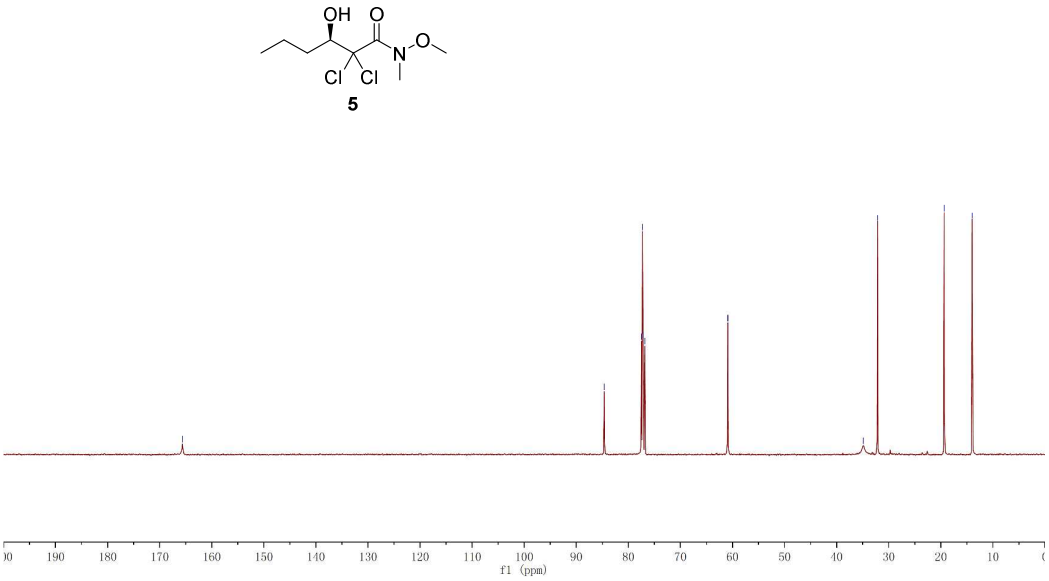
	Retention Time (min)	% Area
1	15.792	1.12
2	18.885	98.88

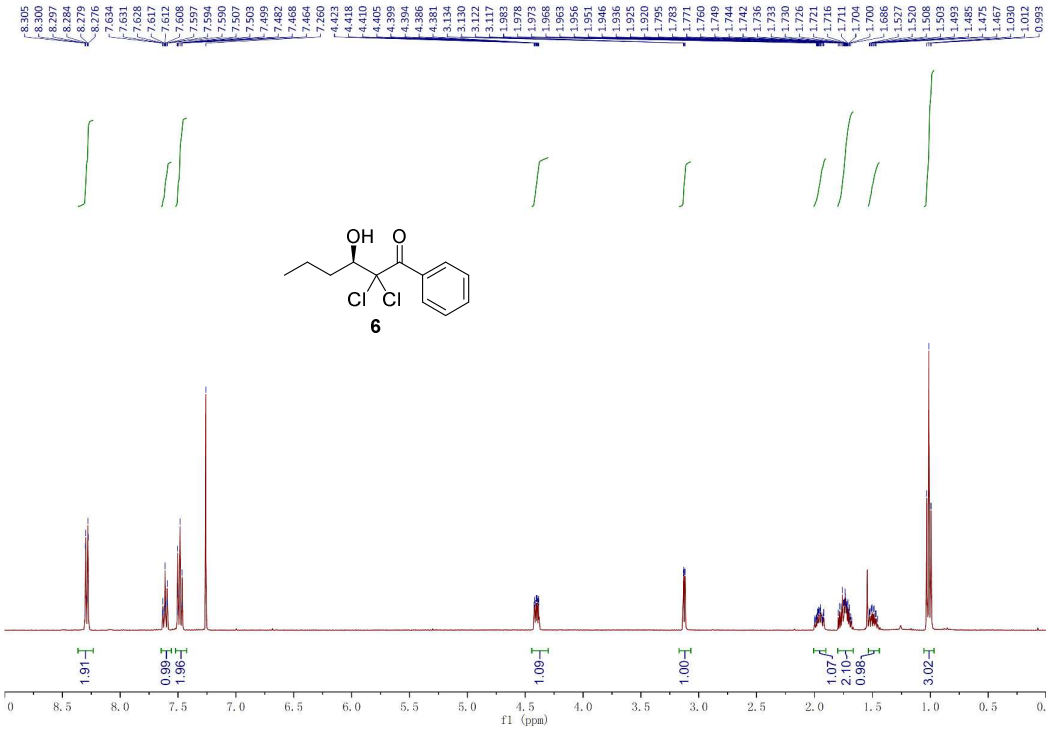
9. NMR spectra of compounds 4–6.

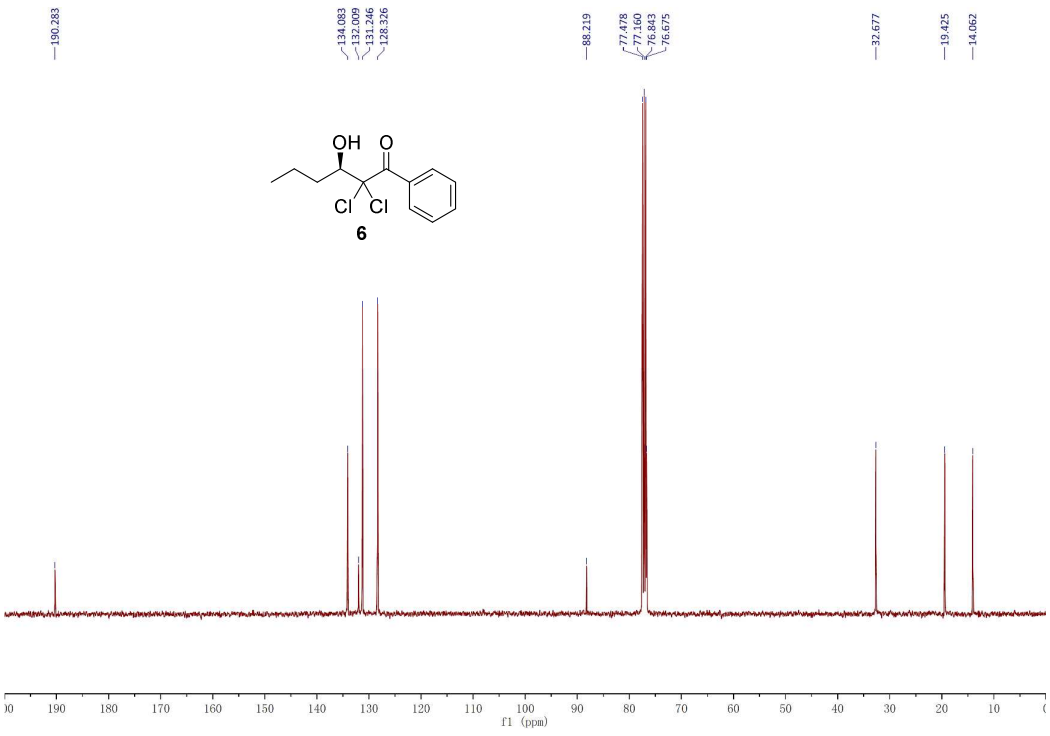





OH
O
N
O
Cl
Cl
5
1.00
3.05
0.92
2.95
1.08
2.20
1.10
3.16
f1 (ppm)

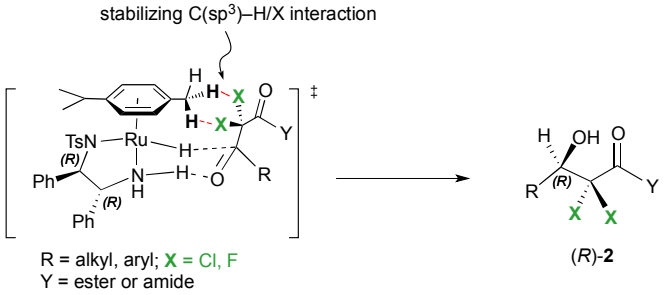

OH
O
N
O
Cl
Cl
5
f1 (ppm)


8.305
8.300
8.297
8.284
8.279
8.276
7.634
7.631
7.628
7.617
7.612
7.608
7.597
7.594
7.590
7.507
7.503
7.499
7.482
7.468
7.464
7.260
4.423
4.418
4.410
4.405
4.399
4.394
4.386
4.381
3.134
3.130
3.122
3.117
1.983
1.978
1.973
1.968
1.963
1.956
1.951
1.946
1.936
1.925
1.920
1.795
1.783
1.771
1.760
1.749
1.744
1.742
1.736
1.733
1.730
1.726
1.721
1.716
1.711
1.704
1.700
1.686
1.527
1.520
1.508
1.503
1.493
1.485
1.475
1.467
1.030
1.012
0.993
OH
O
Cl
Cl
6
1.91
0.99
1.96
1.09
1.00
1.07
2.10
0.98
3.02
f1 (ppm)


190.283
134.083
132.009
131.246
128.326
88.219
77.478
77.160
76.843
76.675
32.677
19.425
14.062
OH
O
Cl
Cl
6
f1 (ppm)

10. Proposed rationale for the stereochemical outcome of the ATH.

For alkyl substrates, a stabilizing C(sp^3)-H/X interaction favors the transition state shown below, leading to very high enantioselectivities in favor of the (*R*)-alcohol.



For aryl substrates, a competitive C(sp^3)-H/π interaction (shown below), which would favor formation of the (*S*)-alcohol, would explain the lower enantioselectivity observed for the (*R*)-alcohol.