catalysts

MDPI

Contents

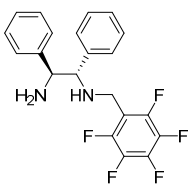
1. General

Dry solvents were purchased from commercial suppliers and used without further purification. Analytical thin–layer chromatography (TLC) was performed on glass plates coated with 0.25 mm 230–400 mesh silica gel containing a fluorescent indicator (Merck, #1.05715.0009). Silica gel column chromatography was performed on Kanto silica gel 60 (spherical, 100–210 μm). IR spectra were recorded on JASCO FT/IR–4100 using ATR. ^{1}H–NMR spectra were recorded on JEOL ECS–400 (400 MHz) spectrometer. Chemical shifts of ^{1}H–NMR spectra were reported relative to tetramethylsilane (δ 0). ^{13}C–NMR spectra were recorded on JEOL ECA–400 (100 MHz) spectrometer. Chemical shifts of ^{13}C–NMR spectra were reported relative to $CDCl_3$ (δ 77.0). Splitting patterns were reported as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.

β-keto esters were synthesized according to known procedure [1,2]. The chiral bis(imidazolidine)pyridine ligands were synthesized according to known procedure [3].

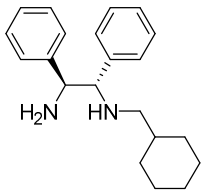
2. Analytical data of Diamine and Ligands

2.1. (1S,2S)-N1-((perfluorophenyl)methyl)-1,2-diphenylethane-1,2-diamine



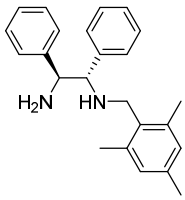
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.82 (br, 3H), 3.64 (d, *J* = 13.6 Hz, 1H), 3.66 (d, *J* = 6.7 Hz, 1H), 3.77 (d, *J* = 13.6Hz, 1H), 3.96 (d, *J* = 6.7Hz, 1H), 7.07-7.25 (m, 10H); **{^{19}F}^{13}C NMR** (100 MHz, $CDCl_3$): δ 145.1, 142.9, 140.5, 140.2, 137.1, 128.1, 128.1, 127.7, 127.3, 127.0, 126.6, 113.5, 68.8, 61.7, 38.8; **HRMS** calcd for $C_{21}H_{18}N_2F_5$ $(M+H)^+$: 393.1385, found: 393.1370; **[α]** $_D^{22.5}$ = +6.1 (*c* = 1.0, $CHCl_3$); **IR** (neat) 1520, 1502, 1123, 959, 931 cm^{-1}.

2.2. (1S,2S)-N1-(cyclohexylmethyl)-1,2-diphenylethane-1,2-diamine



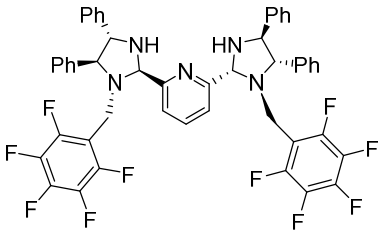
^{1}H NMR (400M Hz, $CDCl_3$) δ 0.74-0.85 (m, 2H), 1.10-1.20 (m, 3H), 1.34-1.36 (m, 1H), 1.63-1.65 (br, 5H), 1.74 (br, 3H), 2.15-2.26 (m, 2H), 3.67 (d, *J* = 6.9 Hz, 1H), 3.97 (d, *J* = 6.9 Hz, 1H), 7.08-7.23 (m, 10H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.4, 141.6, 128.0, 127.8, 127.8, 127.6, 126.8, 126.7, 126.6, 126.6, 69.7, 61.7, 54.3, 38.0, 31.3, 31.1, 26.5, 25.9, 25.9; **HRMS** calcd for $C_{21}H_{29}N_2$ $(M+H)^+$: 309.2325, found: 309.2319; **[α]$_D^{22}$** = -17.5 (*c* = 1.0, $CHCl_3$); **IR** (neat) 3270, 3082, 3060, 1600, 1406, 1368, 1348, 1250, 1181, 1092, 1067, 646, 606, 593 cm^{-1}.

2.3. (1S,2S)-1,2-diphenyl-N^1-(2,4,6-trimethylbenzyl) ethane-1,2-diamine



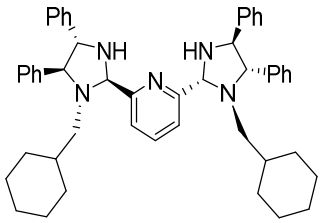
^{1}H NMR (400 MHz, $CDCl_3$) δ 1.72 (br, 3H), 2.12 (s, 6H), 2.23 (s, 3H), 3.39 (d, *J* = 11.4 Hz, 1H), 3.52 (d, *J* = 11.4 Hz, 1H), 3.77 (d, *J* = 6.9 Hz, 1H), 3.97 (d, *J* = 6.9 Hz, 1H), 6.79 (s, 2H), 7.13-7.30 (m, 10H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.3, 141.6, 137.0, 136.2, 133.6, 128.7, 128.0, 127.7, 126.9, 126.8, 126.8, 70.4, 61.6, 46.0, 20.8, 19.1; **HRMS** calcd for $C_{24}H_{29}N_2$ $(M+H)^+$: 345.2325, found: 345.2318; **[α]$_D^{22}$** = +2.4 (*c* = 1.0, $CHCl_3$); **IR** (neat) 1579, 1375, 1222, 1028 cm^{-1}.

2.4. N-Pentafluorobenzyl pyBidine



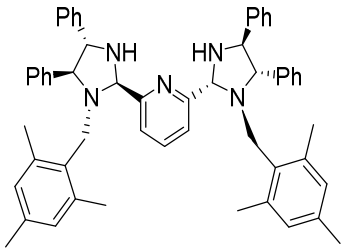
^{1}H NMR (400 MHz, $CDCl_3$) δ 3.79 (d, *J* = 7.8 Hz, 2H), 3.85 (s, 4H), 4.37 (d, *J* = 7.8 Hz, 2H), 5.04 (s, 2H), 7.16-7.29 (m, 20H), 7.79-7.89 (m, 3H); **{^{19}F}^{13}C NMR** (100 MHz, $CDCl_3$): δ 160.9, 145.0, 141.0, 140.1, 139.6, 137.5, 136.8, 128.3, 128.0, 127.6, 127.5, 127.4, 126.9, 121.0, 111.4, 83.1, 77.8, 69.9, 42.6; **HRMS** calcd for $C_{49}H_{36}N_5F_{10}$ $(M+H)^+$: 884.2806, found: 884.2783; **[α]$_D^{20.0}$** = -93.4 (*c* = 1.0, $CHCl_3$); **IR** (neat) 3063, 1656, 1590, 1574, 1356, 1249, 1205, 1074, 817, 648, 613 cm^{-1}.

2.5. N-cyclohexylmethyl pyBidine



^{1}H NMR (400 MHz, $CDCl_3$) δ 0.44-0.55 (m, 4H), 0.64-0.81 (m, 4H), 0.85-0.93 (m, 4H), 1.32-1.43 (m, 4H), 1.49-1.64 (m, 6H), 2.38-2.54 (m, 4H), 3.72 (d, *J* = 8.0 Hz, 2H), 4.39 (d, *J* = 8.0 Hz, 2H), 4.93 (s, 2H), 7.19-7.35 (m, 20H), 7.78-7.88 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 162.8, 141.4, 141.1, 136.9, 128.1, 128.0, 127.2, 127.1, 121.0, 84.4, 79.1, 69.6, 61.5, 36.6, 31.5, 31.4, 26.4, 25.7; **HRMS** calcd for $C_{49}H_{58}N_5$ $(M+H)^+$: 716.4687, found: 716.4673; **[α]$_D^{19.7}$** = -143.1 (*c* = 1.0, $CHCl_3$); **IR** (neat) 3308, 2972, 2923, 2848, 1451, 1378, 1315, 1153, 1088, 1047, 695 cm^{-1}.

2.6. N-trimethylbenzyl pyBidine



^{1}H NMR (400 MHz, $CDCl_3$) δ 2.02 (s, 6H), 2.09 (s, 12H), 3.65 (d, *J* = 12.7 Hz, 2H), 3.75 (d, *J* = 8.5 Hz, 2H), 3.78 (d, *J* = 13.4 Hz, 2H), 4.55 (d, *J* = 8.0 Hz, 2H), 4.89 (s, 2H), 6.40 (s, 4H), 6.76 (d, *J* = 7.6 Hz, 2H), 7.08 (t, *J* = 7.6 Hz, 1H), 7.13-7.32 (m, 20H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 160.6, 141.9, 140.3, 137.4, 136.0, 135.3, 131.5, 128.4, 128.2, 128.1, 127.8, 127.1, 127.0, 126.9, 120.5, 82.4, 79.5, 69.4, 51.1, 20.6, 20.3; **HRMS** calcd for $C_{55}H_{58}N_5$ $(M+H)^+$: 788.4687, found: 788.4670; **[α]$_D^{19.5}$** = -153.1 (*c* = 1.0, $CHCl_3$); **IR** (neat) 3061, 3027, 2915, 2852, 1494, 1453, 1125, 1027, 755, 698 cm^{-1}.

3. General Procedure of Asymmetric Chlorination Reaction

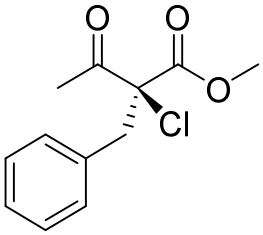
N-PFB PyBidine (0.022 mmol) and $Zn(OAc)_2$ (0.02 mmol) were added to a glass tube equipped with a magnetic stirrer bar under Ar. DCM (1.0 mL) was added to the glass tube and the mixture was stirred overnight. After removal of the solvent under reduced pressure, cyclohexane (2.0 mL) was

added. Then the *β*-ketoesters (0.2 mmol) was added at 25°C followed by the addition of $NaHCO_3$ (0.02 mmol) and *N*-chlorosuccinimide (0.22 mmol). After stirring for 24 h, the reaction was directly purified by silica-gel column chromatography to afford the product. The enantiomeric excesses of the products were determinded by chiral stationary phase HPLC by using Daicel Chiralcel OJ-H, and Chiralpak AS-H and IC-3 columns.

Absolute configurations of **2a** and **2e** were determined to be (*S*) through comparison of optical rotations with reported values [4]. Absolute configurations of the other compounds were determined by analogy.

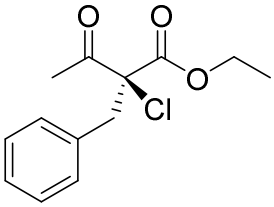
4. Analytical Data of Chlorinated Products

4.1. Methyl (S)-2-benzyl-2-chloro-3-oxobutanoate



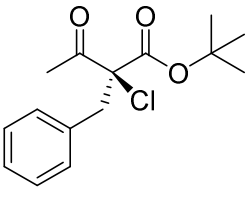
The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (90% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.24 (s, 3H), 3.44 (d, *J* = 14.5 Hz, 1H), 3.53 (d, *J* = 14.5 Hz, 1H), 3.77 (s, 3H), 7.19-7.21 (m, 2H), 7.25-7.32 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.8, 167.5, 133.7, 130.5, 128.2, 127.5, 75.1, 53.6, 42.2, 26.5; **HRMS** calcd for $C_{12}H_{13}O_3ClNa$ $(M+Na)^+$: 263.0445, found: 263.0447; **Enantiomeric excess** was determined by HPLC with a Chiralcel OJ-H column (hexane:2-propanol 98:2, 1.0 mL/min, 210 nm), minor enantiomer t_r = 20.6 min, major enantiomer t_r = 24.7 min, 76% ee; **$[\alpha]_D^{18.4}$** = -2.2 (*c* = 1.0, $CHCl_3$, 76% ee); **IR** (neat) 2955, 1729 1495, 1455, 1356, 1322, 1251, 1183, 1170, 1084, 1032, 994, 951, 932, 838, 758, 700, 582, 556 cm^{-1}.

4.2. Ethyl (S)-2-benzyl-2-chloro-3-oxobutanoate



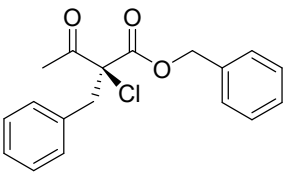
The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (99% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.24 (t, *J* = 7.2 Hz, 3H), 2.24 (s, 3H), 3.44 (d, *J* = 14.2 Hz, 1H), 3.53 (d, *J* = 14.2 Hz, 1H), 4.16-4.28 (m, 2H), 7.16-7.22 (m, 2H), 7.26-7.32 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.8, 166.9, 133.9, 130.5, 128.1, 127.9, 127.4, 75.2, 63.0, 42.1, 26.4, 13.7; **HRMS** calcd for $C_{13}H_{15}O_3ClNa$ $(M+Na)^+$: 277.0602, found: 277.0605; **Enantiomeric excess** was determined by HPLC with a Chiralcel OJ-H column (hexane:2-propanol 90:10, 0.5 mL/min, 210 nm), major enantiomer t_r = 17.7 min, minor enantiomer t_r = 20.9 min, 78% ee; **$[\alpha]_D^{17}$** = -7.0 (*c* = 1.0, $CHCl_3$, 78% ee); **IR** (neat) 2983, 2937, 2362, 2340, 1729, 1604, 1585, 1496, 1455, 1429, 1392, 1356, 1320, 1247, 1190, 1084, 1032, 1015 cm^{-1}.

4.3. tert-butyl (S)-2-benzyl-2-chloro-3-oxobutanoate



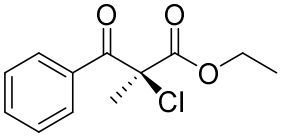
The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 10:1) to give colorless oil (72% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.43 (s, 9H), 2.24 (s, 3H), 3.42 (d, *J* = 14.5 Hz, 1H), 3.48 (d, *J* = 14.5Hz, 1H), 7.22-7.30 (m, 5H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.0, 165.6, 134.2, 130.7, 128.0, 127.8, 127.3, 84.3, 75.9, 41.8, 27.5, 26.4; **HRMS** calcd for $C_{15}H_{19}O_3ClNa$ $(M+Na)^+$: 305.0915, found: 305.0916; **Enantiomeric excess** was determined by HPLC with a Chiralpak AD-3 column (hexane:2-propanol 500:1, 0.5 mL/min, 210 nm), major enantiomer t_r = 17.8 min, minor enantiomer t_r = 19.6 min, 76% ee; **$[\alpha]_D^{18.4}$** = -6.5 (*c* = 1.0, $CHCl_3$, 76% ee); **IR** (neat) 2979, 2934, 1729, 1496, 1475, 1455, 1428, 1395, 1370, 1355, 1328, 1256, 1182, 1145, 1079, 1030 cm^{-1}.

4.4. Benzyl (S)-2-benzyl-2-chloro-3-oxobutanoate



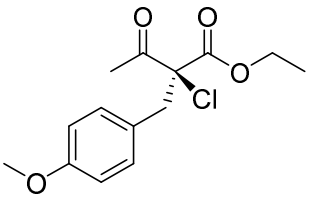
The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (66% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.17 (s, 3H), 3.43 (d, *J* = 14.3 Hz, 1H), 3.53 (d, *J* = 14.3 Hz, 1H), 5.15-5.2 (m, 2H), 7.14-7.15 (m, 2H), 7.18-7.25 (m, 3H), 7.29-7.30 (m, 2H), 7.35-7.37 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.5, 166.8, 134.3, 133.7, 130.5, 128.9, 128.7, 128.6, 128.4, 128.3, 128.1, 127.4, 75.2, 68.5, 42.1, 26.4; **HRMS** calcd for $C_{18}H_{18}O_3Cl$ $(M+H)^+$: 317.0939, found: 317.0939; **Enantiomeric excess** was determined by HPLC with a Chiralpak AS-H column (hexane:2-propanol 99:1, 0.3 mL/min, 254 nm), minor enantiomer t_r = 22.6 min, major enantiomer t_r = 26.6 min, 61% ee; **$[\alpha]_D^{15.4}$** = -5.2 (*c* = 1.0, $CHCl_3$, 61% ee); **IR** (neat) 2953, 2884, 1950, 1883, 1813, 1603, 1494, 1423, 1378, 1353, 1321, 1303, 1211, 1082, 1025 cm^{-1}.

4.5. Ethyl (S)-2-chloro-2-methyl-3-oxo-3-phenylpropanoate



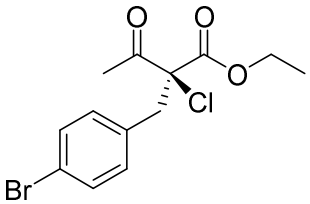
The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (86% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.08 (t, *J* = 7.2 Hz, 3H), 2.01 (s, 3H), 4.14-4.26 (m, 2H), 7.42-7.46 (m, 2H), 7.52-7.58 (m, 1H), 7.98-8.01 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 189.2, 169.2, 133.4, 133.1, 129.4, 128.4, 68.5, 63.1, 26.0, 13.6; **HRMS** calcd for $C_{12}H_{13}O_3ClNa$ $(M+Na)^+$: 263.0445, found: 263.0449; **Enantiomeric excess** was determined by HPLC with a Chiralcel OJ-H column (hexane:2-propanol 90:10, 1.0 mL/min, 254 nm), major enantiomer t_r = 7.0 min, minor enantiomer t_r = 9.9 min, 30% ee; **$[\alpha]_D^{16.2}$** = -17.3 (*c* = 1.0, $CHCl_3$, 30% ee); **IR** (neat) 2991, 2939, 1597, 1584, 1447, 1375, 1186, 1067, 1012 cm^{-1}.

4.6. Ethyl (S)-2-chloro-2-(4-methoxybenzyl)-3-oxobutanoate



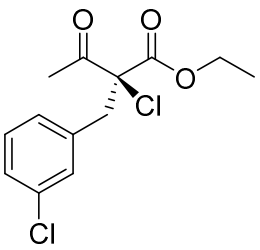
The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (93% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.26 (t, *J* = 7.2Hz, 3H), 2.24 (s, 3H), 3.39 (d, *J* = 14.5 Hz, 1H), 3.47 (d, *J* = 14.7 Hz, 1H), 3.78 (s, 3H), 4.17-4.29 (m, 2H), 6.79-6.83 (m, 2H), 7.10-7.15 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.1, 167.0, 158.9, 131.6, 125.7, 113.5, 75.4, 63.0, 55.1, 41.3, 26.6, 13.8; **HRMS** calcd for $C_{14}H_{17}O_4ClNa$ $(M+Na)^+$: 307.0708, found: 307.0708; **Enantiomeric excess** was determined by HPLC with a Chiralcel OJ-H column (hexane:2-propanol 95:05, 0.5 mL/min, 210 nm), minor enantiomer t_r = 39.9 min, major enantiomer t_r = 45.5 min, 75% ee; **$[\alpha]_D^{17.5}$** = -0.5 (*c* = 1.0, $CHCl_3$, 75% ee); **IR** (neat) 2982, 2936, 2837, 2361, 1729, 1611, 1512, 1464, 1443, 1429, 1356, 1321, 1301, 1245, 1177, 1111, 1094, 1081, 1033 cm^{-1}.

4.7. Ethyl (S)-2-(4-bromobenzyl)-2-chloro-3-oxobutanoate



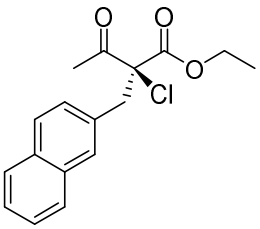
The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (71% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.25 (t, *J* = 7.1Hz, 3H), 2.26 (s, 3H), 3.39 (d, *J* = 14.5 Hz, 1H), 3.47 (d, *J* = 14.5Hz, 1H), 4.14-4.29 (m, 2H), 7.08-7.10 (m, 2H), 7.40-7.42 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.5, 166.8, 132.9, 132.3, 131.7, 131.4, 131.3, 121.7, 74.8, 63.2, 41.4, 26.4, 13.8; **HRMS** calcd for $C_{13}H_{15}O_3BrCl$ $(M+H)^+$: 332.9888, found: 332.9882; **Enantiomeric excess** was determined by HPLC with a Chiralcel OJ-H column (hexane:2-propanol 98:02, 0.3 mL/min, 210 nm), major enantiomer t_r = 41.0 min, minor enantiomer, t_r = 43.6 min, 82% ee; **$[\alpha]_D^{15.7}$** = -2.4 (*c* = 1.0, $CHCl_3$, 82% ee); **IR** (neat) 2984, 2935, 1487, 1430, 1405, 1356, 1321, 1287, 1176, 1105, 1072, 1034 cm^{-1}.

4.8. Ethyl (S)-2-chloro-2-(3-chlorobenzyl)-3-oxobutanoate



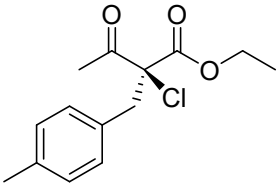
The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (94% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.26 (t, *J* = 7.0 Hz, 3H), 2.28 (s, 3H), 3.39 (d, *J* = 14.5 Hz, 1H), 3.50 (d, *J* = 14.5 Hz, 1H), 4.20-4.28 (m, 2H), 7.09-7.11 (m, 1H), 7.19-7.30 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.2, 166.7, 135.9, 133.9, 130.6, 129.3, 128.7, 128.1, 127.6, 74.8, 63.2, 41.5, 26.2, 13.8; **HRMS** calcd for $C_{13}H_{14}O_3Cl_2Na$ $(M+Na)^+$: 311.0212, found: 311.0213; **Enantiomeric excess** was determined by HPLC with a Chiralcel OJ-H column (hexane:2-propanol 95:05, 0.5 mL/min, 210 nm), minor enantiomer t_r = 16.4 min, major enantiomer t_r = 17.8 min, 70% ee; **[α]$_D^{17.2}$** = -4.3 (*c* = 1.0, $CHCl_3$, 70% ee); **IR** (neat) 2985, 2938, 1731, 1597, 1573, 1507, 1476, 1431, 1392, 1357, 1321, 1298, 1246, 1188, 1174, 1080, 1034, 1014 cm^{-1}.

4.9. Ethyl (S)-2-chloro-2-(naphthalen-2-ylmethyl)-3-oxobutanoate



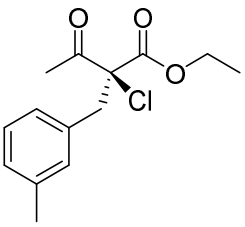
The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (65% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.22 (t, *J* = 7.0 Hz, 3H), 2.25 (s, 3H), 3.61 (d, *J* = 14.3 Hz, 1H), 3.70 (d, *J* = 14.3 Hz, 1H), 4.14-4.30 (m, 2H), 7.29-7.35 (m, 1H), 7.39-7.54 (m, 2H), 7.68 (s, 1H), 7.75-7.88 (m, 3H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.0, 167.0, 133.1, 132.6, 131.4, 129.6, 128.4, 127.7, 127.7, 127.5, 126.0, 125.9, 75.3, 63.1, 42.2, 26.5, 13.8; **HRMS** calcd for $C_{17}H_{18}O_3Cl$ $(M+H)^+$: 305.0939, found: 305.0912; **Enantiomeric excess** was determined by HPLC with a Chiralpak IC-3 column (hexane:2-propanol 90:10, 0.5 mL/min, 254 nm), major enantiomer t_r = 10.0 min, minor enantiomer t_r = 11.0 min, 78% ee; **[α]$_D^{15.9}$** = -1.5 (*c* = 1.0, $CHCl_3$, 78% ee); **IR** (neat) 2992, 1600, 1508, 1464, 1428, 1356, 1319, 1246, 1227, 1174, 1094, 1080, 1035, 1014 cm^{-1}.

4.10. Ethyl (S)-2-chloro-2(4-methylbenzyl)-3-oxobutanoate



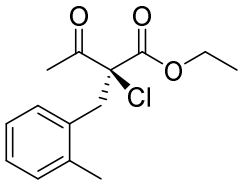
The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (81% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.25 (t, *J* = 7.3 Hz, 3H), 2.24 (s, 3H), 2.31 (s, 3H), 3.40 (d, *J* = 14.5Hz, 1H), 3.48 (d, *J* = 14.5Hz, 1H), 4.19-4.27 (m, 2H), 7.07-7.11 (m, 4H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.9, 167.0, 137.1, 130.7, 130.4, 128.8, 75.4, 62.9, 41.7, 26.5, 21.0, 13.8; **HRMS** calcd for $C_{14}H_{17}O_3ClNa$ $(M+Na)^+$: 291.0758, found: 291.0755; **Enantiomeric excess** was determined by HPLC with a Chiralcel OJ-H column (hexane:2-propanol 90:10, 1.0 mL/min, 210 nm), major enantiomer t_r = 8.6 min, minor enantiomer t_r = 13.2 min, 74% ee; **[α]$_D^{16.8}$** = -5.0 (*c* = 1.0, $CHCl_3$, 74% ee); **IR** (neat) 2982, 2928, 1729, 1515, 1445, 1429, 1391, 1356, 1319, 1294, 1246, 1176, 1112, 1081, 1035, 1015 cm^{-1}.

4.11. Ethyl (S)-2-chloro-2-(3-methylbenzyl)-3-oxobutanoate



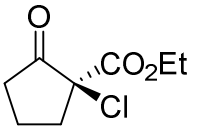
The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (84% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.25 (t, *J* = 7.0 Hz, 3H), 2.25 (s, 3H), 2.31 (s, 3H), 3.39 (d, *J* = 14.5 Hz, 1H), 3.49 (d, *J* = 14.2 Hz, 1H), 4.18-4.27 (m, 2H), 6.99-7.01 (m, 2H), 7.06-7.08 (m, 1H), 7.15-7.21 (m, 1H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 198.8, 167.0, 137.7, 133.7, 131.3, 128.2, 128.0, 127.5, 75.2, 62.9, 42.0, 26.4, 21.3, 13.8; **HRMS** calcd for $C_{14}H_{17}O_3ClNa$ $(M+Na)^+$: 291.0758, found: 291.0760; **Enantiomeric excess** was determined by HPLC with a Chiralcel OJ-H column (hexane:2-propanol 90:10, 1.0 mL/min, 210 nm), minor enantiomer t_r = 11.5 min, major enantiomer t_r = 16.2 min, 74% ee; **[α]$_D^{17.0}$** = -3.8 (*c* = 1.0, $CHCl_3$, 74% ee); **IR** (neat) 2983, 2935, 1730, 1607, 1590, 1521, 1506, 1488, 1445, 1430, 1391, 1356, 1322, 1297, 1246, 1221, 1188, 1096, 1036, 1015 cm^{-1}.

4.12. Ethyl (S)-2-chloro-2-(2-methylbenzyl)-3-oxobutanoate



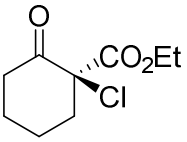
The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (92% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.25 (t, *J* = 7.2 Hz, 3H), 2.27 (s, 3H), 2.34 (s, 3H), 2.96 (s, 3H), 3.56 (d, *J* = 15.0 Hz, 1H), 3.60 (d, *J* = 15.0 Hz, 1H), 4.17-4.31 (m, 2H), 7.07-7.13 (m, 2H), 7.15-7.19 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.0, 167.3, 137.7, 132.6, 130.6, 130.1, 127.4, 125.6, 75.5, 63.1, 37.8, 26.4, 20.1, 13.7; **HRMS** calcd for $C_{14}H_{17}O_3ClNa$ $(M+Na)^+$: 291.0758, found: 291.0762; **Enantiomeric excess** was determined by HPLC with a Chiralcel OJ-H column (hexane:2-propanol 90:10, 1.0 mL/min, 210 nm), major enantiomer t_r = 7.4 min, minor enantiomer t_r = 13.6 min, 79% ee; **[α]$_D^{17.9}$** = +27.6 (*c* = 1.0, $CHCl_3$, 79% ee); **IR** (neat) 3022, 2982, 2936, 1730, 1494, 1462, 1445, 1356, 1323, 1249, 1232, 1196, 1173, 1113, 1095, 1078, 1055, 1015 cm^{-1}.

4.13. Ethyl (S)-1-chloro-2-oxocyclopentane-1-carboxylate



The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (53% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.31 (t, *J* = 7.1 Hz, 3H), 2.11-2.22 (m, 2H), 2.35-2.45 (m, 2H), 2.53-2.60 (m, 1H), 2.71-2.79 (m, 1H), 4.29 (q, *J* = 7.1 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 206.2, 167.2, 63.1, 38.3, 35.3, 19.0, 13.9; HRMS calcd for $C_8H_{11}O_3ClNa$ $(M+Na)^+$: 213.0289, found: 213.0291; **Enantiomeric excess** was determined by HPLC with a Chiralpak AS-H column (hexane:2-propanol 90:10, 0.5 mL/min, 210 nm), major enantiomer t_r = 12.7 min, minor enantiomer t_r = 13.7 min, 53% ee; **[α]$_D^{16.0}$** = -2.7 (*c* = 1.0, $CHCl_3$, 76% ee); **IR** (neat) 1767, 1720, 1279, 1243, 1147, 1020, 1002 cm^{-1}.

4.14. Ethyl (S)-1-chloro-2-oxocyclohexane-1-carboxylate



The title compound was prepared according to the general procedure and purified by column chromatography (Hexane:AcOEt = 20:1) to give colorless oil (61% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 1.32 (t, *J* = 7.3 Hz, 3H), 1.73-1.96 (m, 4H), 2.10-2.17 (m, 1H), 2.40-2.47 (m, 1H), 2.77-2.88 (m, 2H), 4.28 (q, *J* = 7.0 Hz, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 199.7, 167.2, 73.4, 62.8, 39.5, 38.8, 26.6, 22.1, 13.8; **HRMS** calcd for $C_9H_{14}O_3Cl$ $(M+H)^+$: 205.0626, found: 205.0627; **Enantiomeric excess** was determined by HPLC with a Chiralpak IC-3 column (hexane:2-propanol 95:05, 0.5 mL/min, 210 nm), minor enantiomer t_r = 29.9 min, major enantiomer t_r = 31.5 min, 61% ee; **[α]$_D^{16.1}$** = -1.5 (*c* = 1.0, $CHCl_3$, 61% ee); **IR** (neat) 2946, 2868, 1450, 1366, 1289, 1141, 1123, 1095, 1071, 1039, 1014 cm^{-1}.

5. Cyano-epoxidation of ⚜-chloro-⚜-ketoester 2a

5.1. Stepwise synthesis

To◎a solution of◎◎-chloro-◎-ketoester **2a** (0.1 mmol, 75% ee) in DMSO (1.5 mL) in a glass test tube equipped with a magnetic stirrer bar was added potassium cyanide (0.24 mmol) under Ar. The mixture was stirred for 4 h. After completion of the reaction, $NaHCO_3$aq was added and the mixture was extracted by Et_2O. Combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by preparative thin layer chromatography (Hexane:AcOEt = 10:1) to afford the epoxide **3** in 83% yield (dr = 65/35, major diastereomer:74% ee, minor diastereomer:73% ee).

5.2. One-pot synthesis

N-PFB PyBidine (0.022 mmol) and $Zn(OAc)_2$ (0.02 mmol) were added to a glass tube equipped with a magnetic stirrer bar under Ar. DCM (1.0 mL) was added to the glass tube and the mixture was stirred overnight. After removal of the solvent under reduced pressure, cyclohexane (2.0 mL) was added. Then the *β*-ketoesters (0.2 mmol) was added at rt followed by the addition of $NaHCO_3$ (0.02

mmol) and *N*-chlorosuccinimide (0.22 mmol). After stirring for 24 h, the solvent was removed under reduced pressure. To the residue were added DMSO (3 mL) and potassium cyanide (0.48 mmol) under Ar. The mixture was stirred for 5 h. After completion of the reaction, $NaHCO_3$aq was added and the mixture was extracted by Et_2O. Combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure. The crude residue was purified by preparative thin layer chromatography (Hexane:AcOEt = 10:1) to afford the epoxide **3** in 87% yield (dr = 65/35, major diastereomer:71% ee, minor diastereomer:51% ee).

Diastereomeric ratios were determined through analysis of crude ^{1}H NMR spectra.

Relative configurations of the products were determined through difference nOe experiments of the major diastereomer.

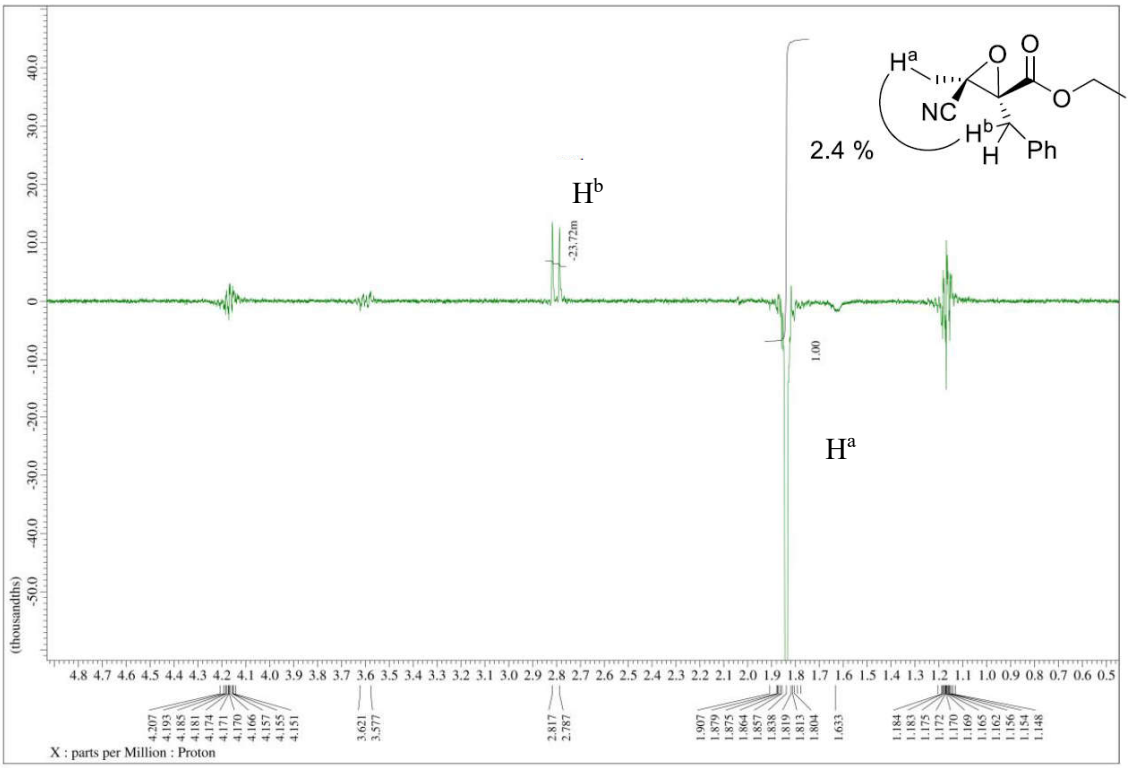
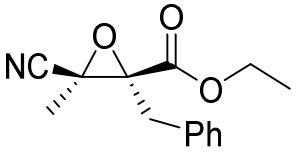


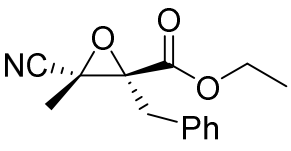
Figure S1. nOe experiment of major epoxide **3**.

5.3. Ethyl (2R,3R)-2-benzyl-3-cyano-3-methyloxirane-2-carboxylate (major diastereomer)



^{1}H NMR (500 MHz, $CDCl_3$) δ 1.17 (t, *J* = 7.2 Hz, 3H), 1.84 (s, 3H), 2.81 (d, *J* = 14.9 Hz, 1H), 3.61 (d, *J* = 14.9 Hz, 1H), 4.13-4.23 (m, 2H), 7.24-7.32 (m, 5H) ; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 166.3, 133.8, 129.2, 128.7, 127.5, 116.6, 66.9, 62.6, 52.1, 34.4, 17.6, 13.8; **HRMS** calcd for $C_{14}H_{16}NO_3$ $(M+H)^+$: 246.1125, found: 246.1126; **Enantiomeric excess** was determined by HPLC with a Chiralcel OZ-3 column (hexane:2-propanol 100:1, 0.5 mL/min, 210 nm), major enantiomer t_r = 37.1 min, minor enantiomer t_r = 35.2 min, 74% ee; **$[\alpha]_D^{26.1}$**=+4.4 (*c* = 1.0, $CHCl_3$, 74% ee); **IR** (neat) 2985, 2937, 2360, 1737, 1300, 1194, 1086, 1038, 750, 700 cm^{-1}.

5.4. Ethyl (2R,3S)-2-benzyl-3-cyano-3-methyloxirane-2-carboxylate (minor diastereomer)



^{1}H NMR (400 MHz, $CDCl_3$) δ 1.13 (t, *J* = 7.2 Hz, 3H), 1.68 (s, 3H), 3.07 (d, *J* = 15.0 Hz, 1H), 3.73 (d, *J* = 14.7 Hz, 1H), 4.08-4.16 (m, 2H), 7.26-7.33 (m, 5H); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 165.7, 133.9, 129.3, 128.7, 127.5, 116.6, 67.4, 62.3, 53.0, 38.0, 17.4, 14.0; **HRMS** calcd for $C_{14}H_{16}NO_3$ $(M+H)^+$:

246.1125, found: 246.1125; **Enantiomeric excess** was determined by HPLC with a Chiralcel OZ-3 column (hexane:2-propanol 100:1, 0.5 mL/min, 210 nm), major enantiomer t_r = 16.5 min, minor enantiomer t_r = 19.6 min, 73% ee; $[\alpha]_D^{26.3}$ =-20.6 (*c* = 0.5, $CHCl_3$, 73% ee); **IR** (neat) 2983, 2935, 2359, 1751, 1281, 1198, 1080, 1047, 754, 700 cm^{-1}.

6. Mechanistic study

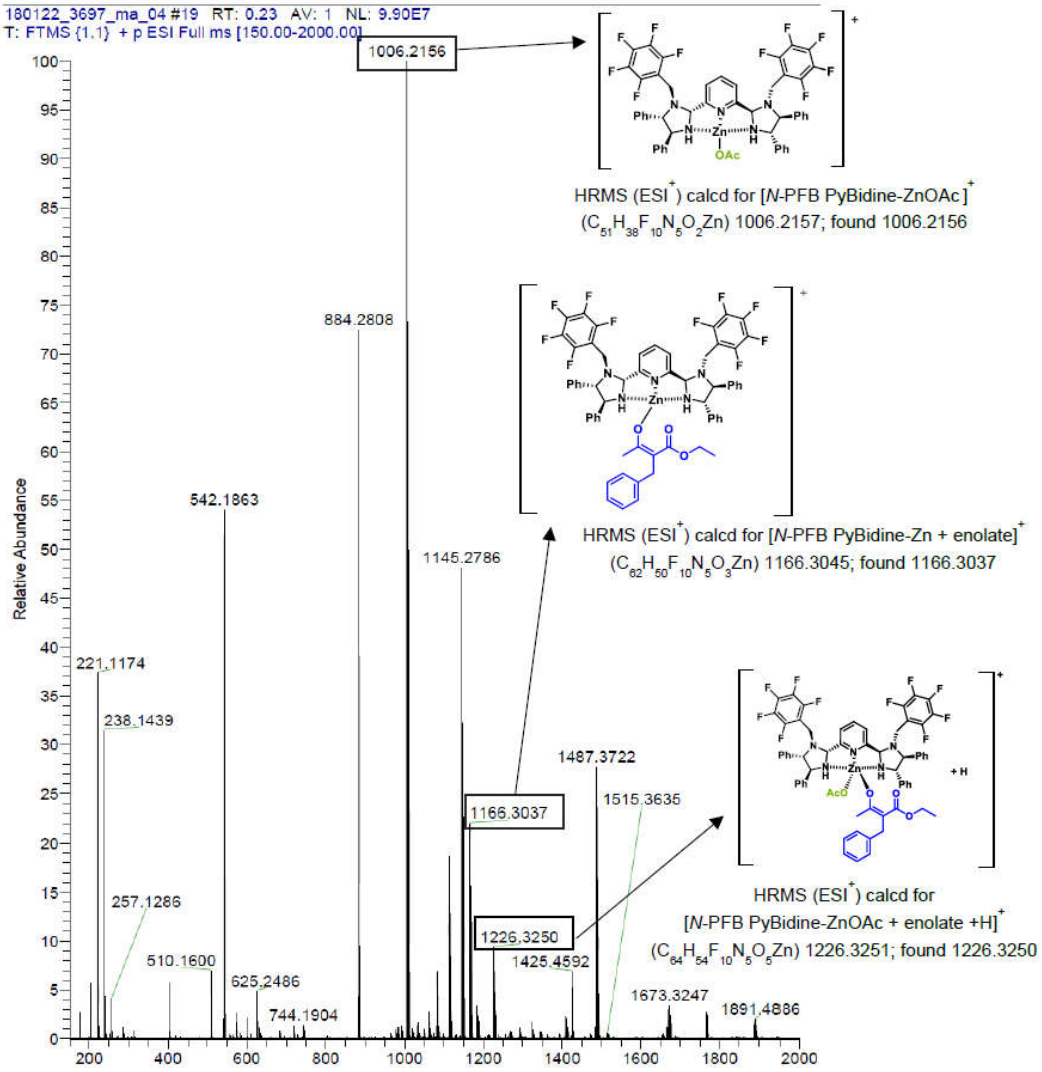


Figure S2. ESI-MS analysis of a mixture of *N*-PFB-PyBidine (**L10**)-Zn(OAc)$_2$ complex, **1a** (1 eq) and $NaHCO_3$ (1 eq) in CH_2Cl_2.

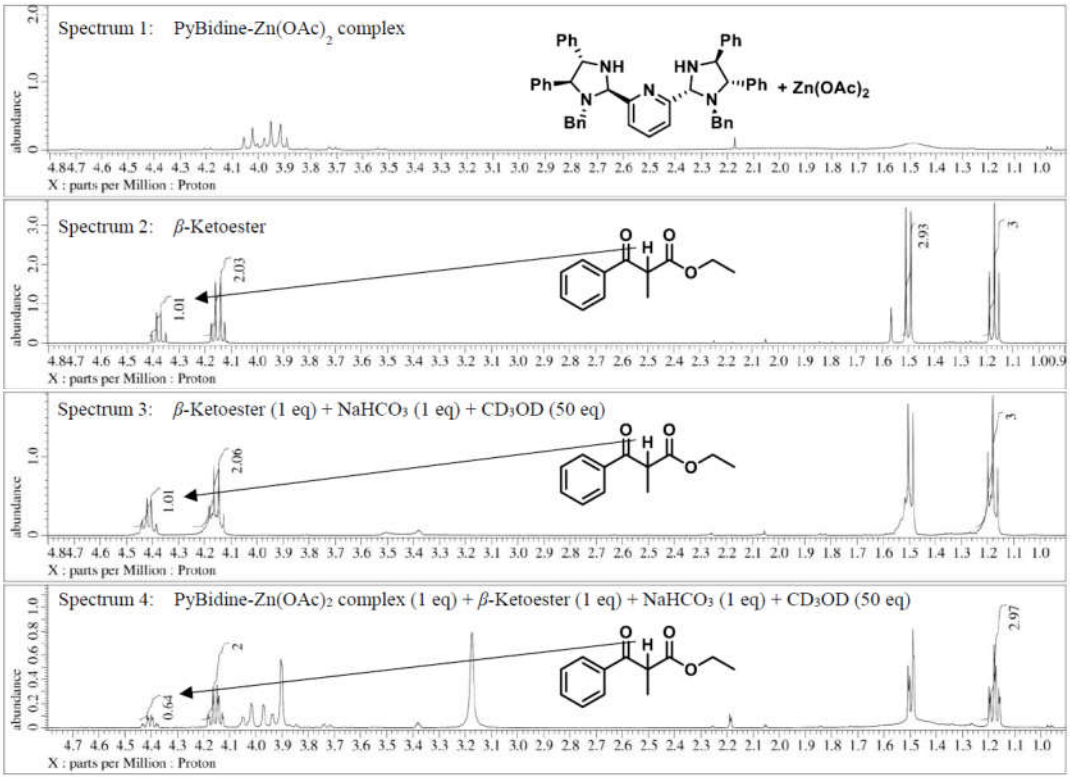
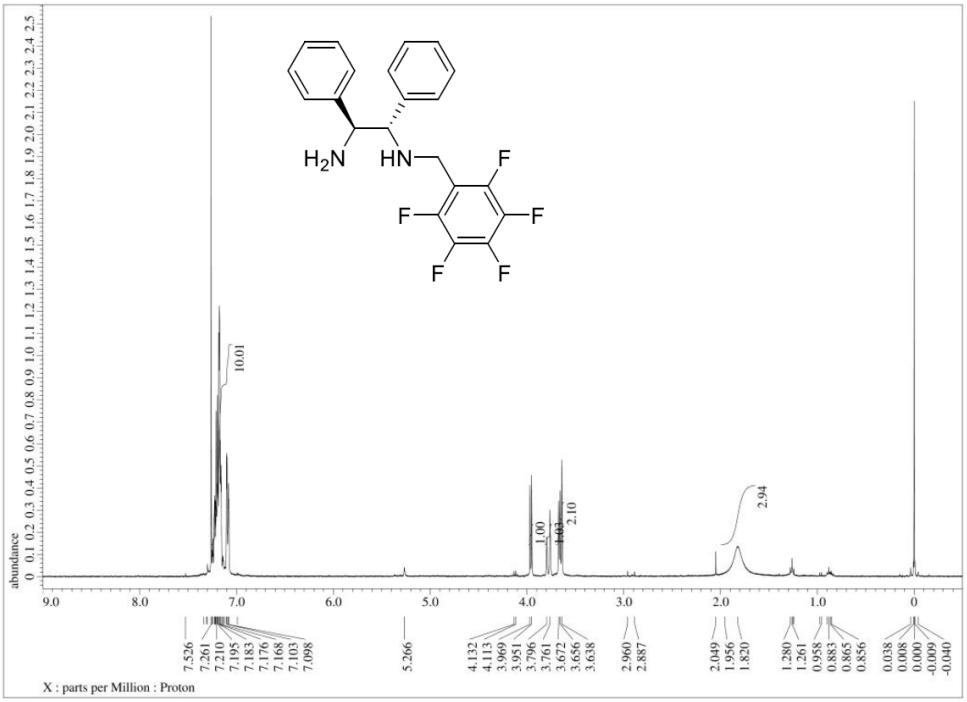
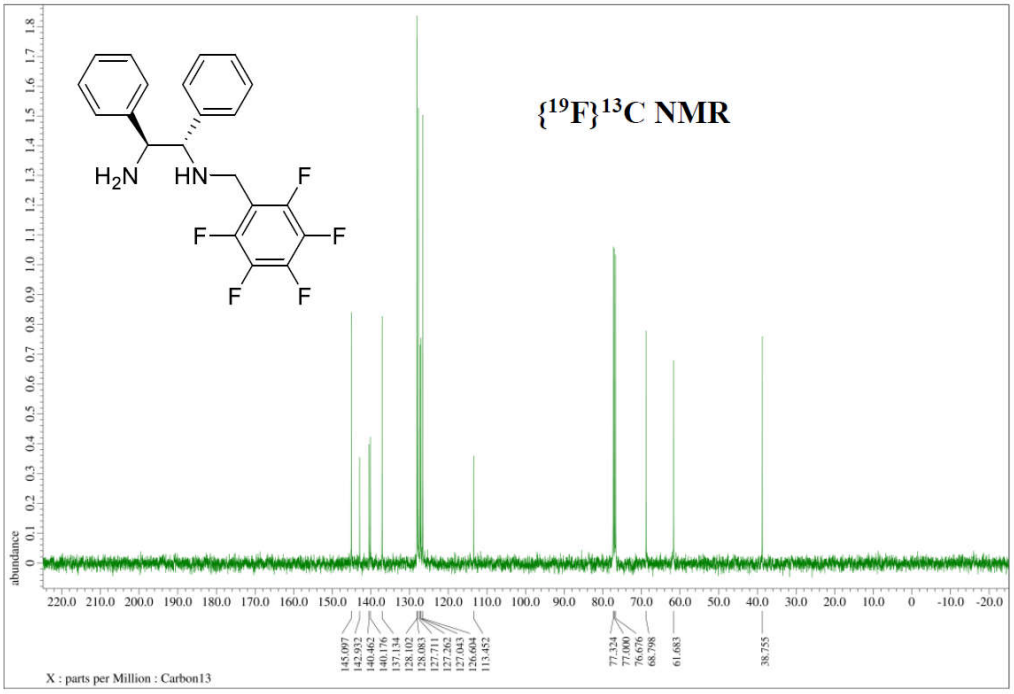
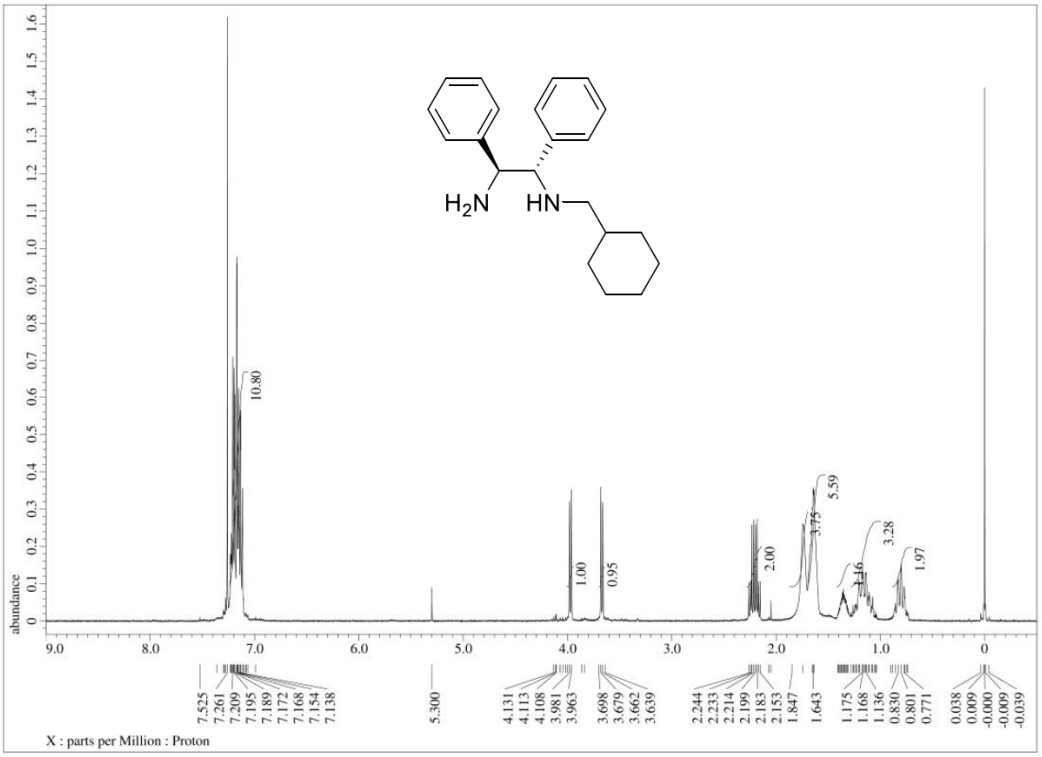


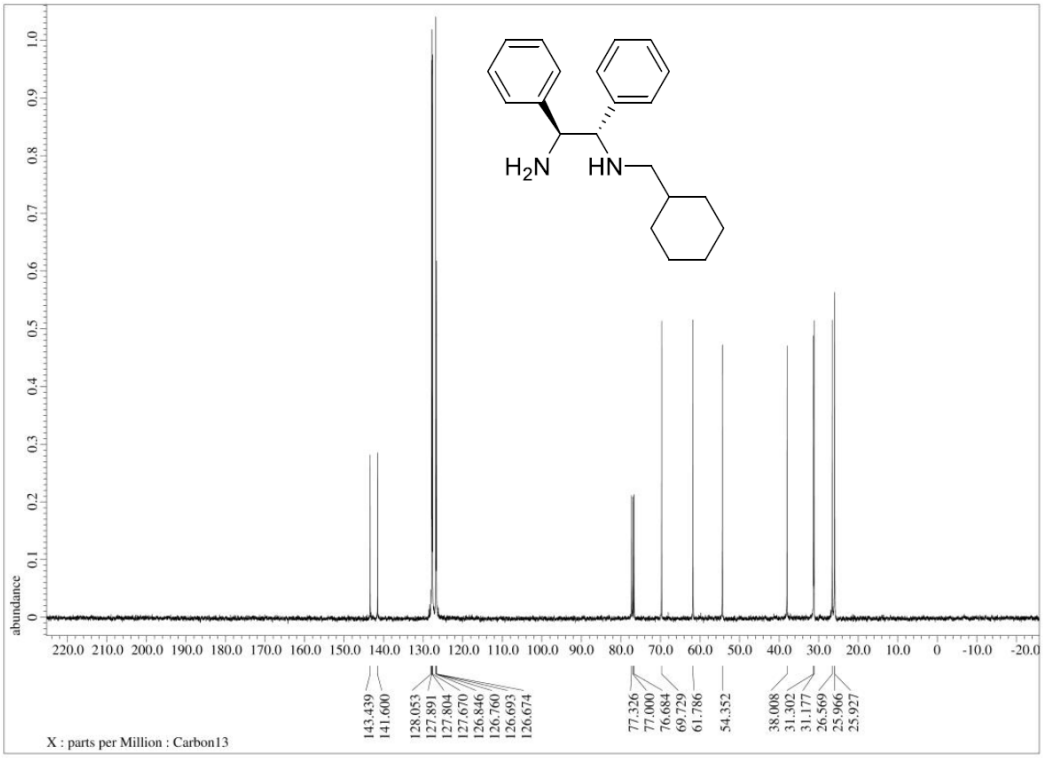
Figure S3. ^{1}H-NMR study of **L10**-Zn(OAc)$_2$ complex, **1a** (1 eq), NaHCO$_3$ (1 eq), and CD$_3$OD (50 eq) in CDCl$_3$.

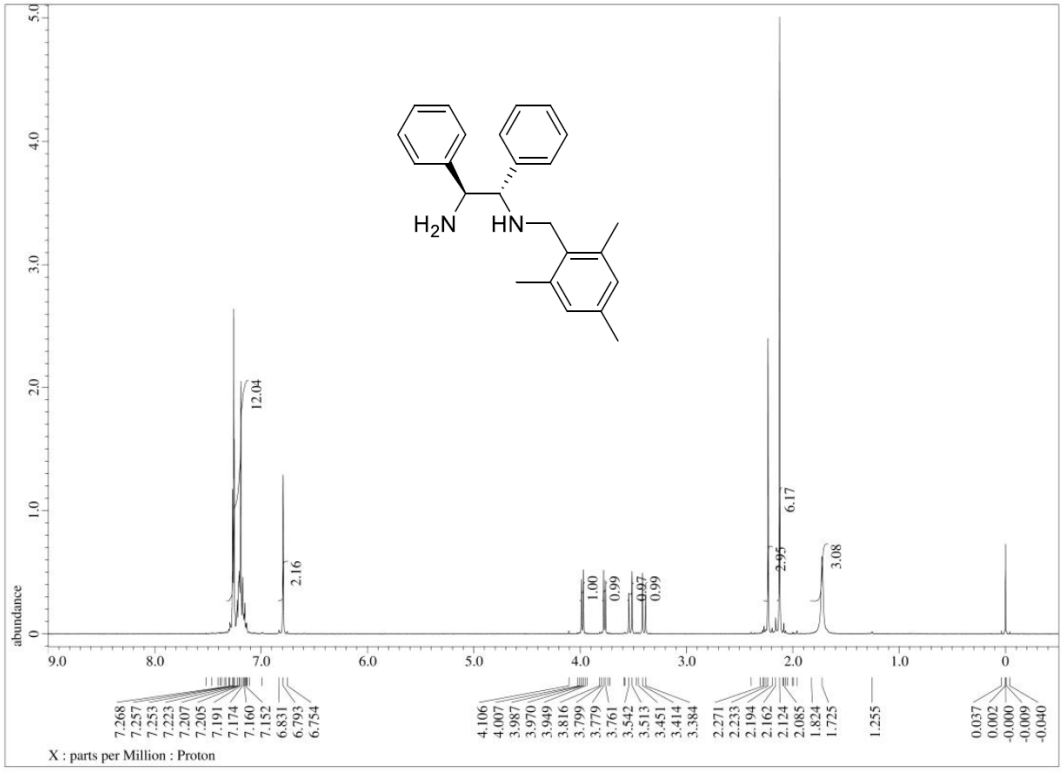
7. ^{1}H-NMR and ^{13}C-NMR spectra

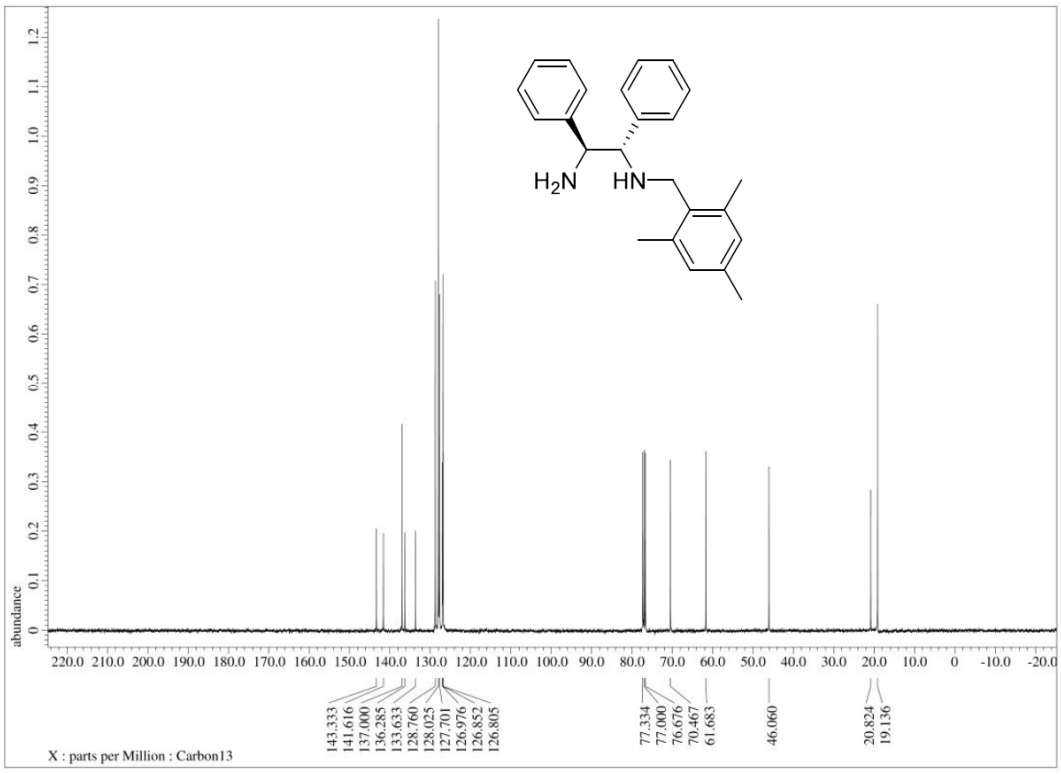


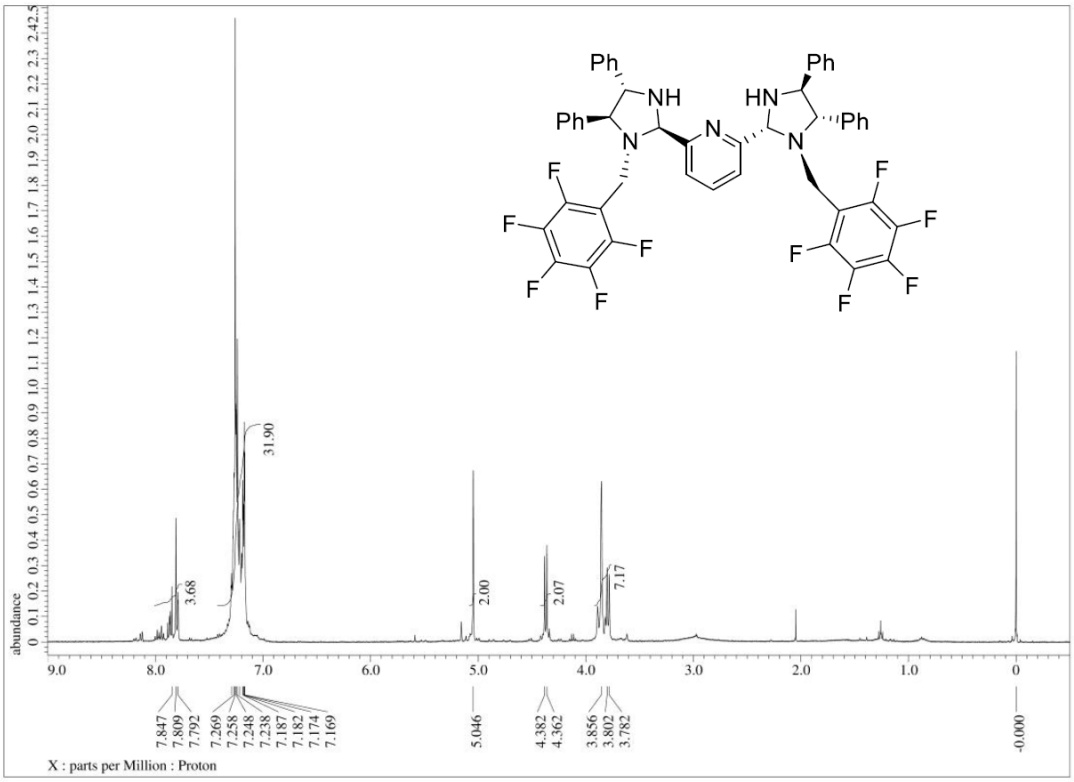

{19F}13C NMR
H2N
HN
F
F
F
F
F
abundance
X : parts per Million : Carbon13

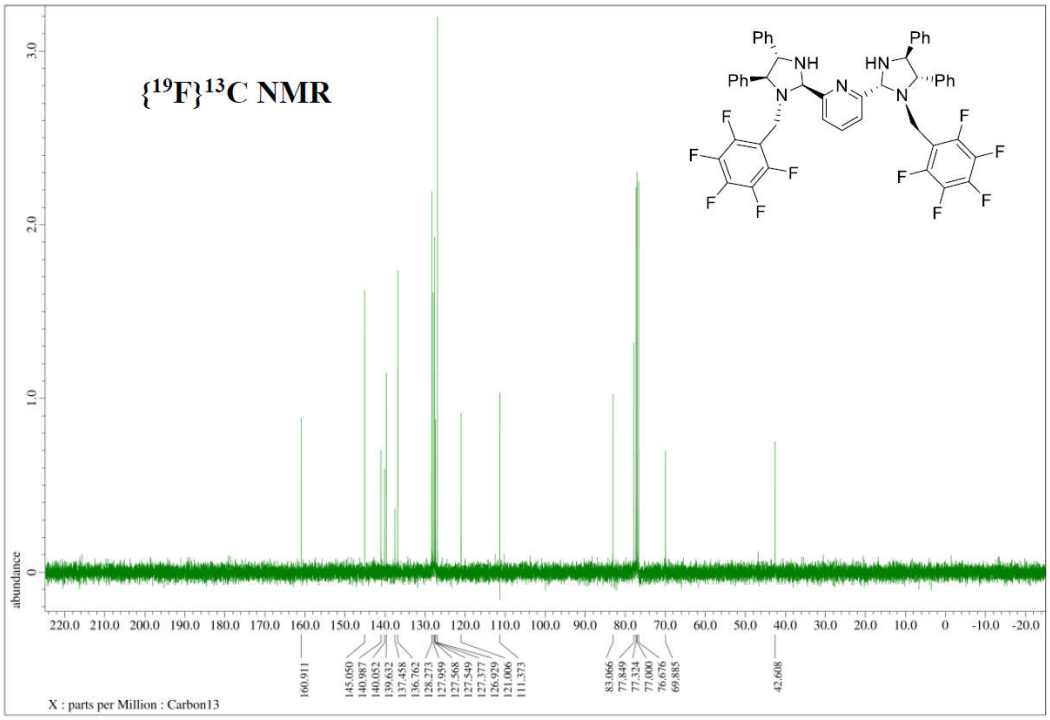

H2N
HN
10.80
1.00
0.95
2.00
3.75
5.59
1.16
3.28
1.97
abundance
X : parts per Million : Proton

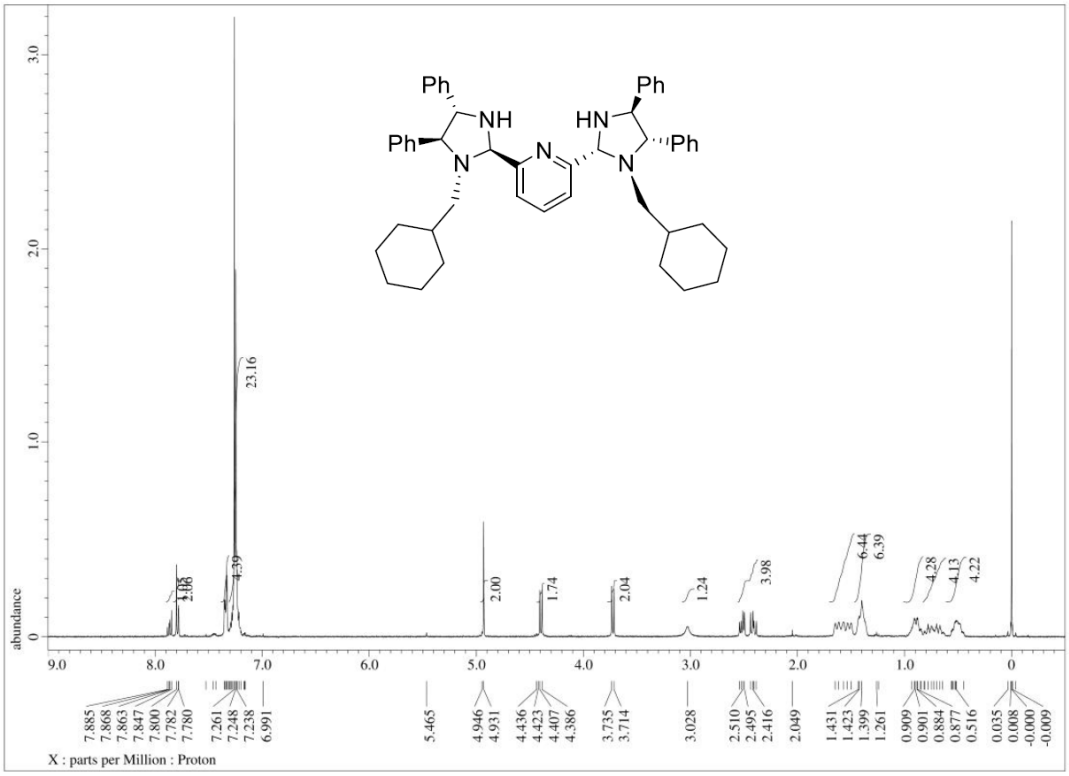

abundance
X : parts per Million : Carbon13
143.439
141.600
128.053
127.891
127.804
127.670
126.846
126.760
126.693
126.674
77.326
77.000
76.684
69.729
61.786
54.352
38.008
31.302
31.177
26.569
25.966
25.927

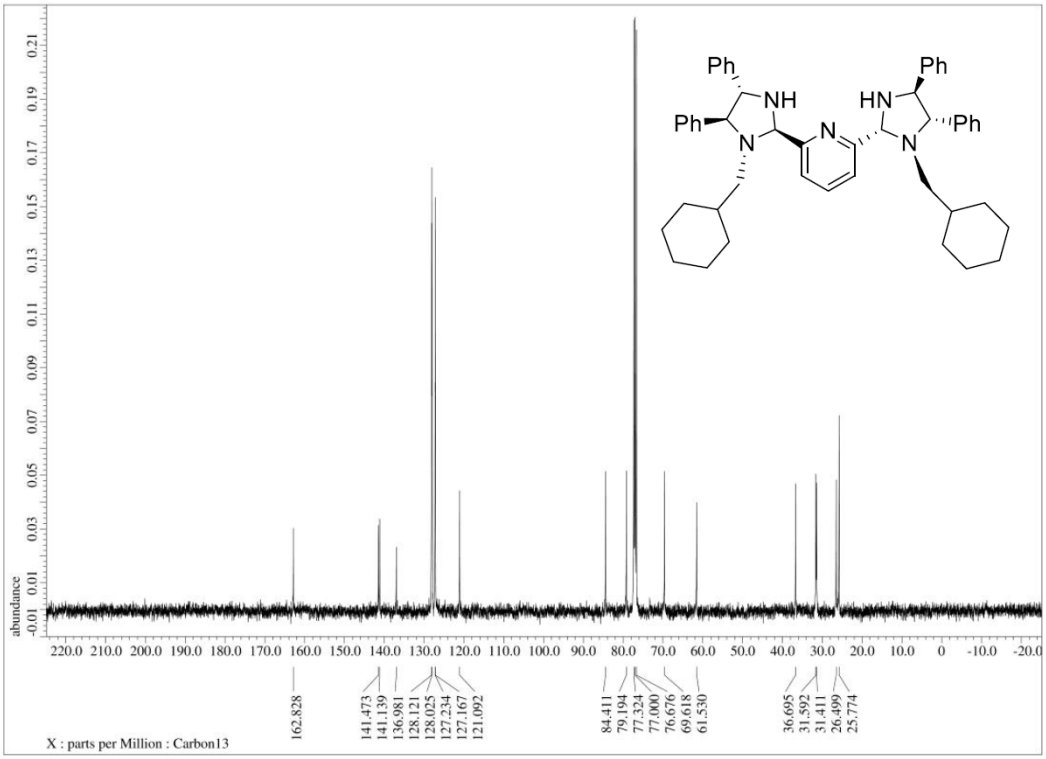

abundance
X : parts per Million : Proton
12.04
2.16
1.00
0.99
0.97
0.99
2.95
6.17
3.08
7.268
7.257
7.253
7.223
7.207
7.205
7.191
7.174
7.160
7.152
6.831
6.793
6.754
4.106
4.007
3.987
3.970
3.949
3.816
3.799
3.779
3.761
3.542
3.513
3.451
3.414
3.384
2.271
2.233
2.194
2.162
2.124
2.085
1.824
1.725
1.255
0.037
0.002
-0.000
-0.009
-0.040

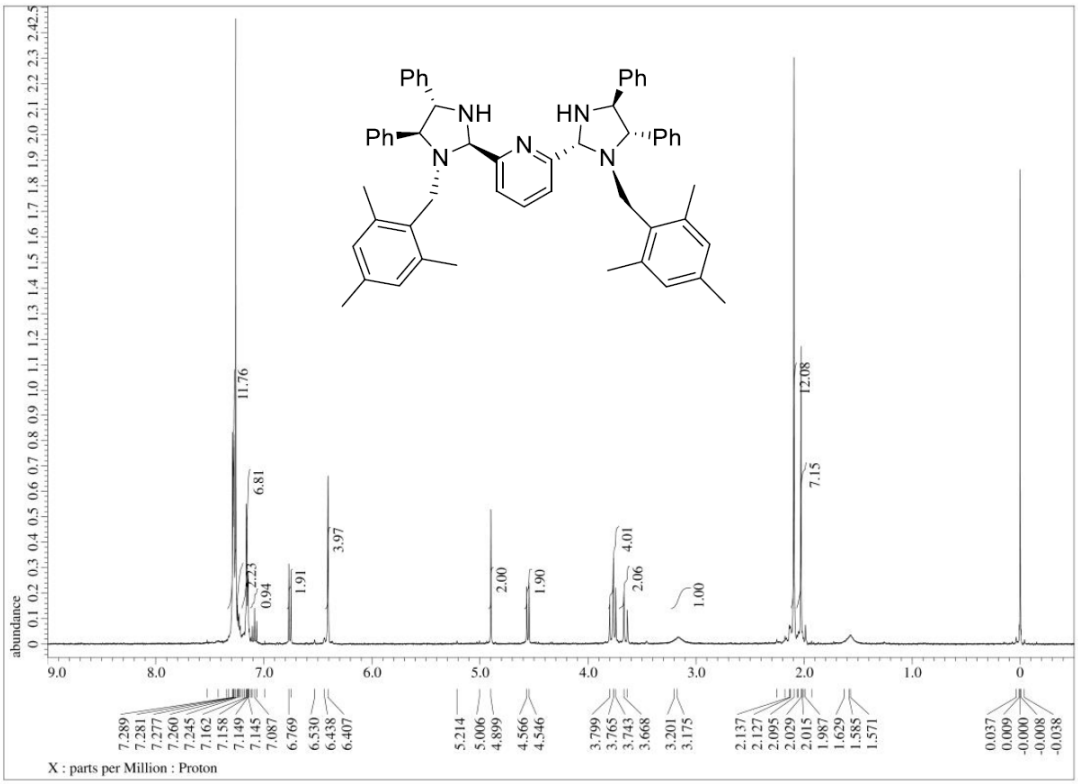

abundance
X : parts per Million : Carbon13
143.333
141.616
137.000
136.285
133.633
128.760
128.025
127.701
126.976
126.852
126.805
77.334
77.000
76.676
70.467
61.683
46.060
20.824
19.136

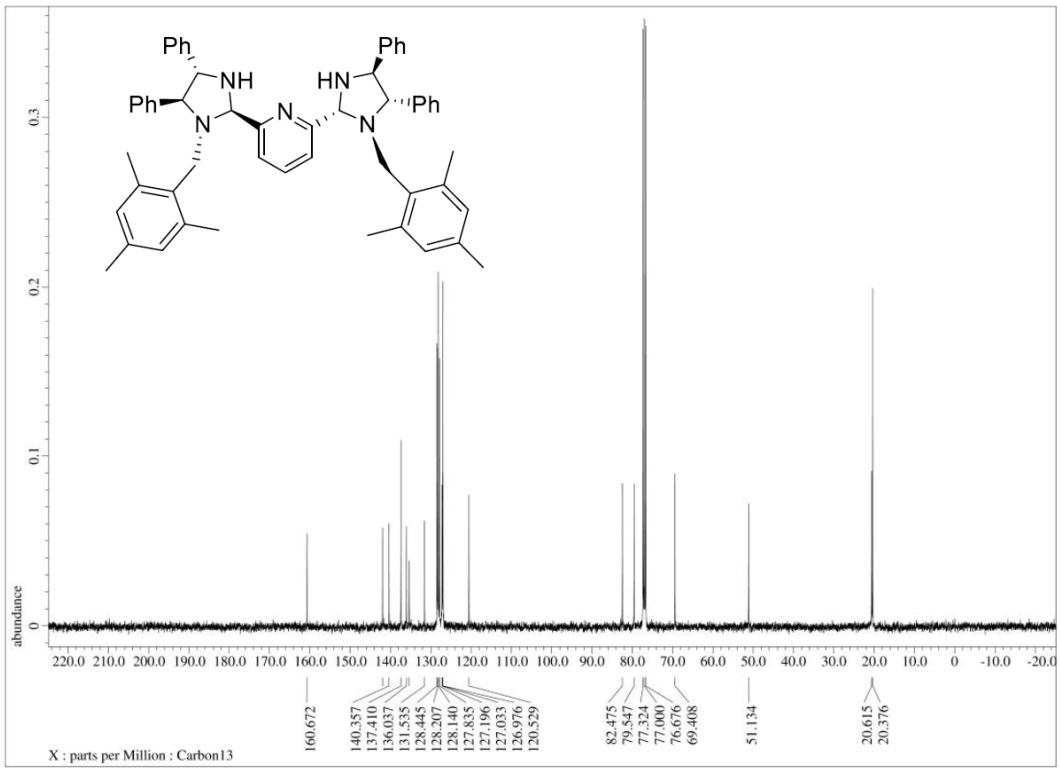

abundance
X : parts per Million : Proton
31.90
3.68
2.00
2.07
7.17
7.847
7.809
7.792
7.269
7.258
7.248
7.238
7.187
7.182
7.174
7.169
5.046
4.382
4.362
3.856
3.802
3.782
-0.000

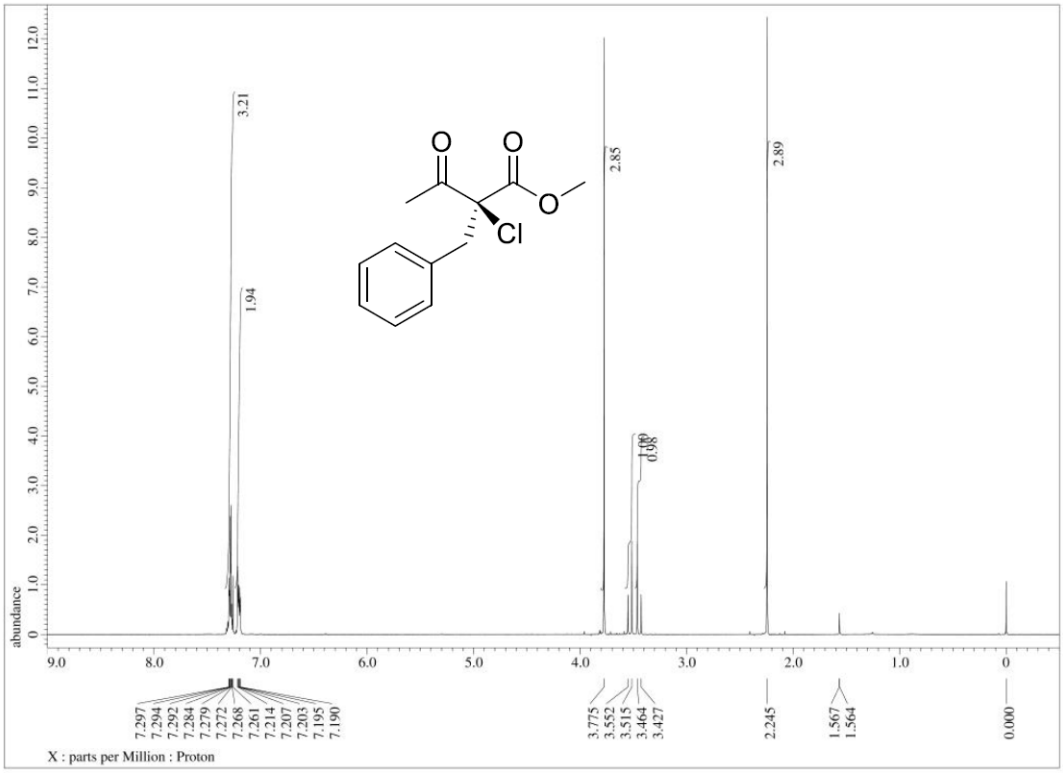

{19F}13C NMR
Ph
NH
HN
Ph
N
F
abundance
X : parts per Million : Carbon13

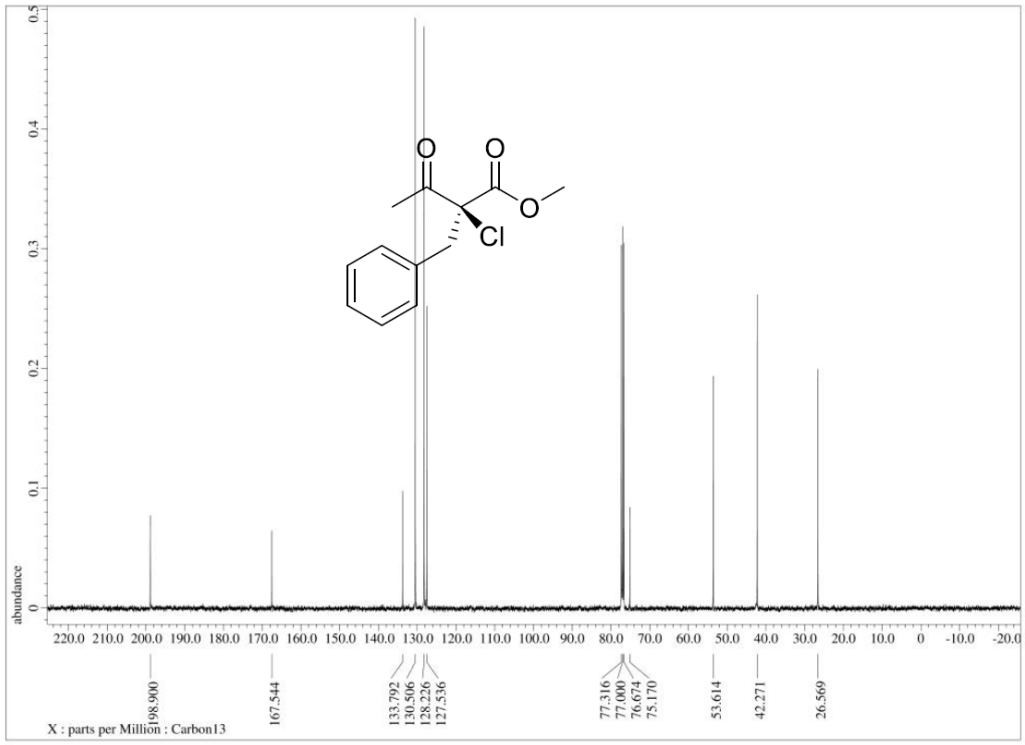

Ph
NH
HN
Ph
N
abundance
23.16
X : parts per Million : Proton

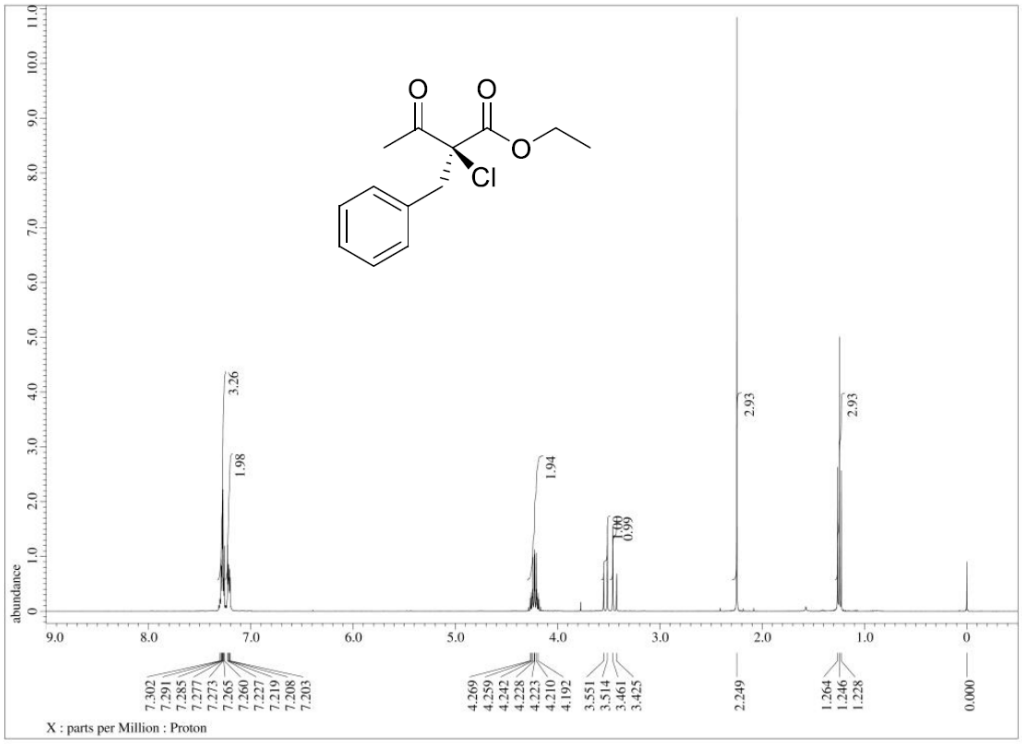

Ph
NH
Ph
N
N
HN
Ph
Ph
N
abundance
X : parts per Million : Carbon13
162.828
141.473
141.139
136.981
128.121
128.025
127.234
127.167
121.092
84.411
79.194
77.324
77.000
76.676
69.618
61.530
36.695
31.592
31.411
26.499
25.774

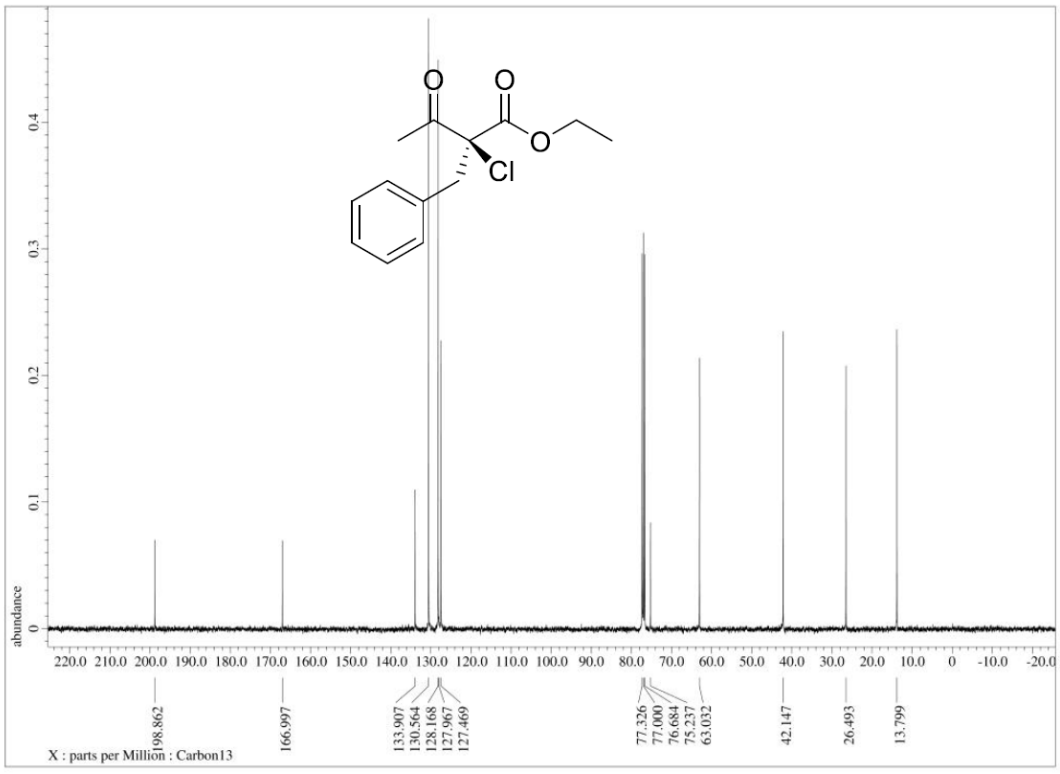

Ph
NH
Ph
N
N
HN
Ph
Ph
N
abundance
X : parts per Million : Proton
11.76
6.81
2.23
0.94
1.91
3.97
2.00
1.90
4.01
2.06
1.00
12.08
7.15
7.289
7.281
7.277
7.260
7.245
7.162
7.158
7.149
7.145
7.087
6.769
6.530
6.438
6.407
5.214
5.006
4.899
4.566
4.546
3.799
3.765
3.743
3.668
3.201
3.175
2.137
2.127
2.095
2.029
2.015
1.987
1.629
1.585
1.571
0.037
0.009
-0.000
-0.008
-0.038

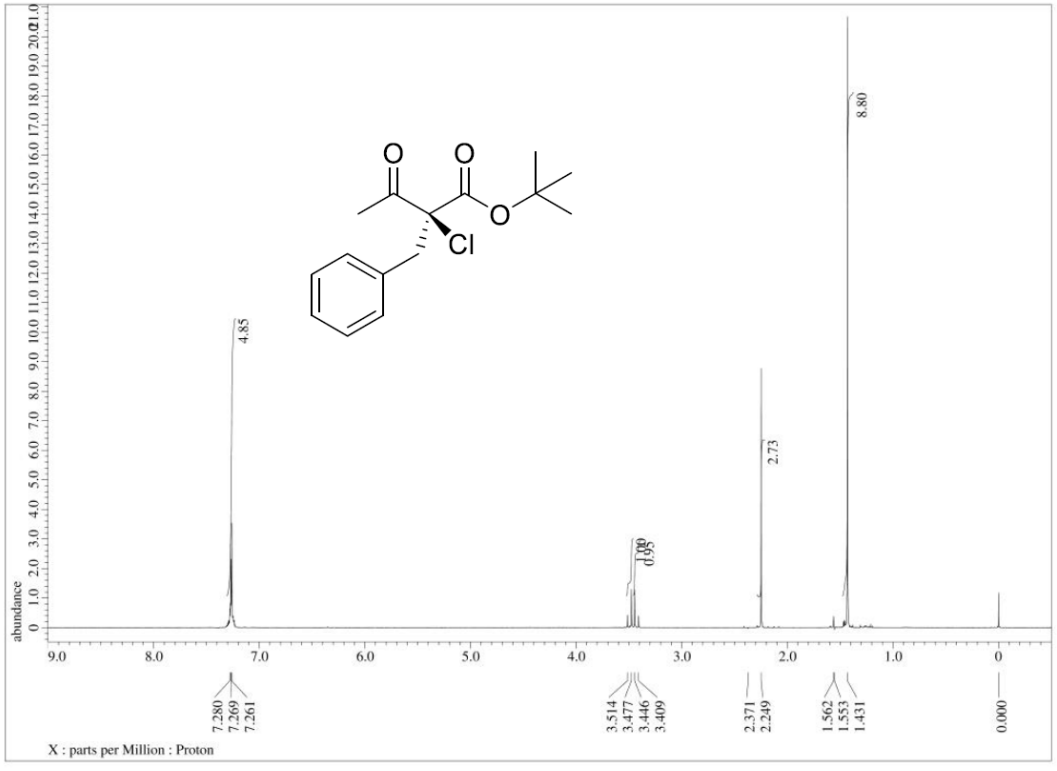

Ph
NH
Ph
N
N
HN
Ph
N
Ph
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
160.672
140.357
137.410
136.037
131.535
128.445
128.207
128.140
127.835
127.196
127.033
126.976
120.529
82.475
79.547
77.324
77.000
76.676
69.408
51.134
20.615
20.376
X : parts per Million : Carbon13

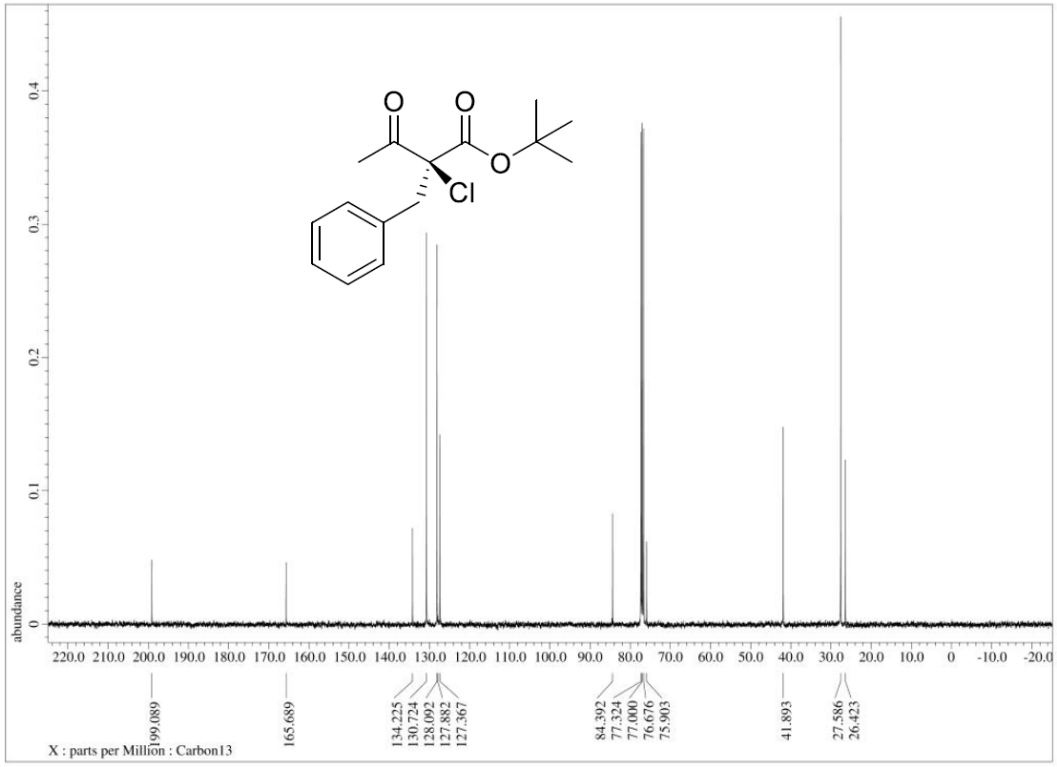

O
O
O
Cl
3.21
1.94
2.85
2.89
1.09
1.08
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.297
7.294
7.292
7.284
7.279
7.272
7.268
7.261
7.214
7.207
7.203
7.195
7.190
3.775
3.552
3.515
3.464
3.427
2.245
1.567
1.564
0.000
X : parts per Million : Proton

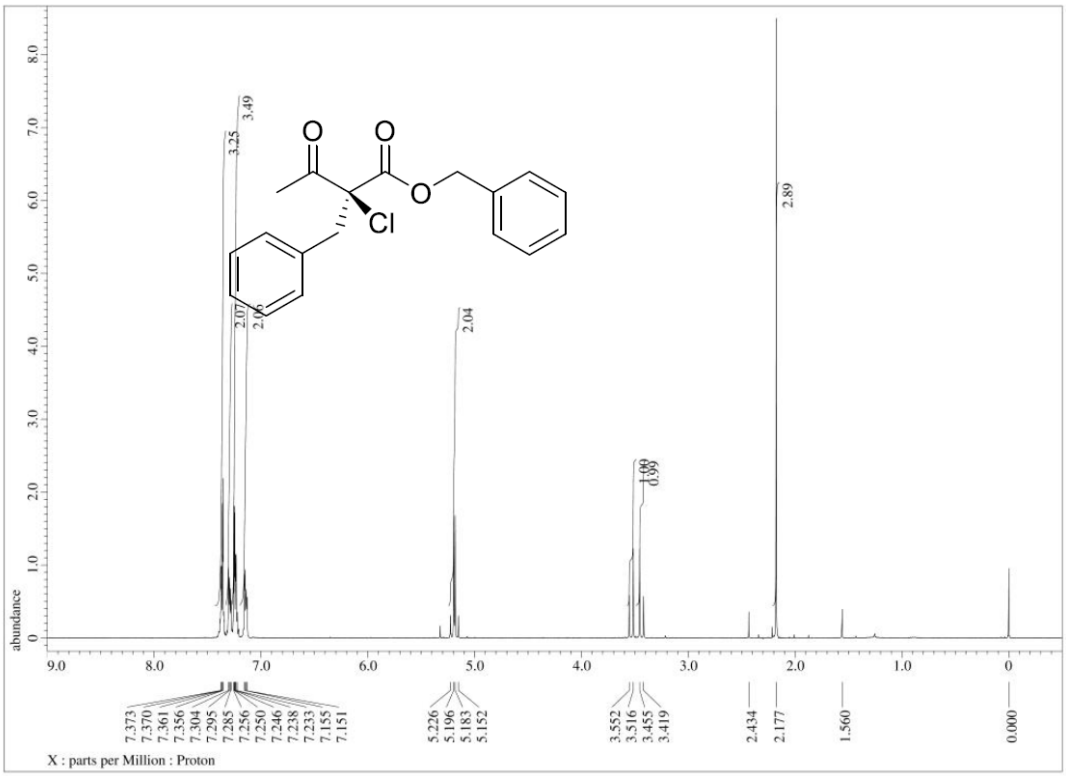

O
O
O
Cl
abundance
198.900
167.544
133.792
130.506
128.226
127.536
77.316
77.000
76.674
75.170
53.614
42.271
26.569
X : parts per Million : Carbon13

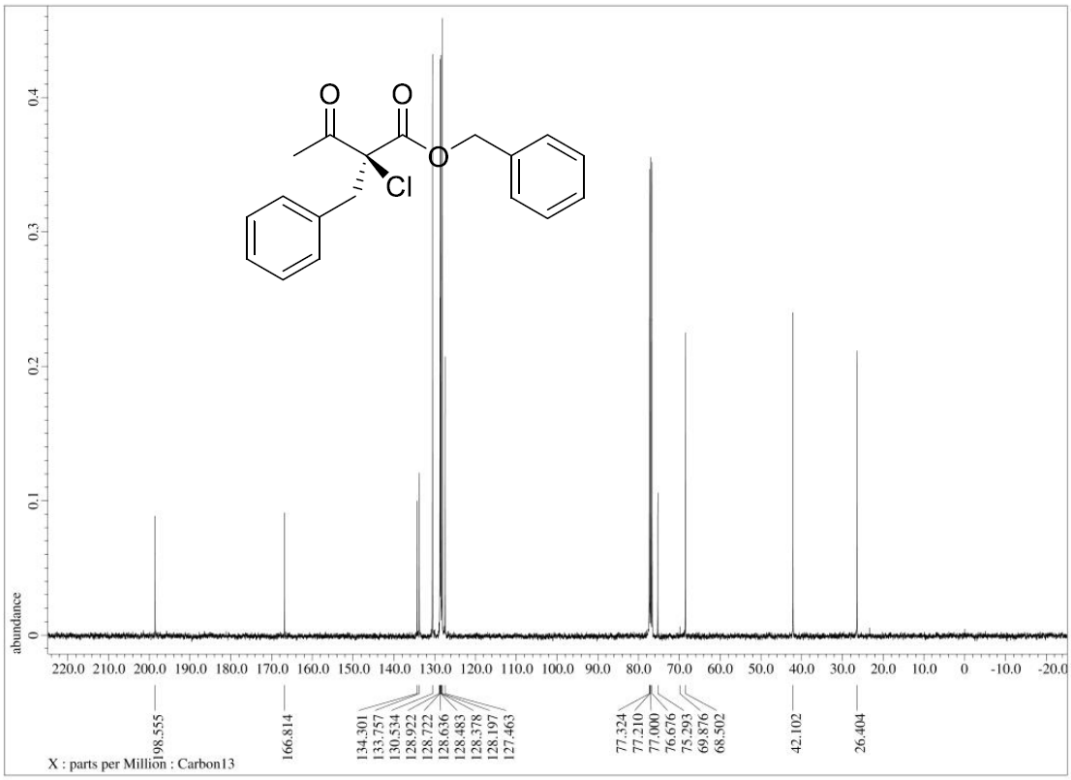

O
O
O
Cl
abundance
3.26
1.98
1.94
1.00
0.99
2.93
2.93
7.302
7.291
7.285
7.277
7.273
7.265
7.260
7.227
7.219
7.208
7.203
4.269
4.259
4.242
4.228
4.223
4.210
4.192
3.551
3.514
3.461
3.425
2.249
1.264
1.246
1.228
0.000
X : parts per Million : Proton

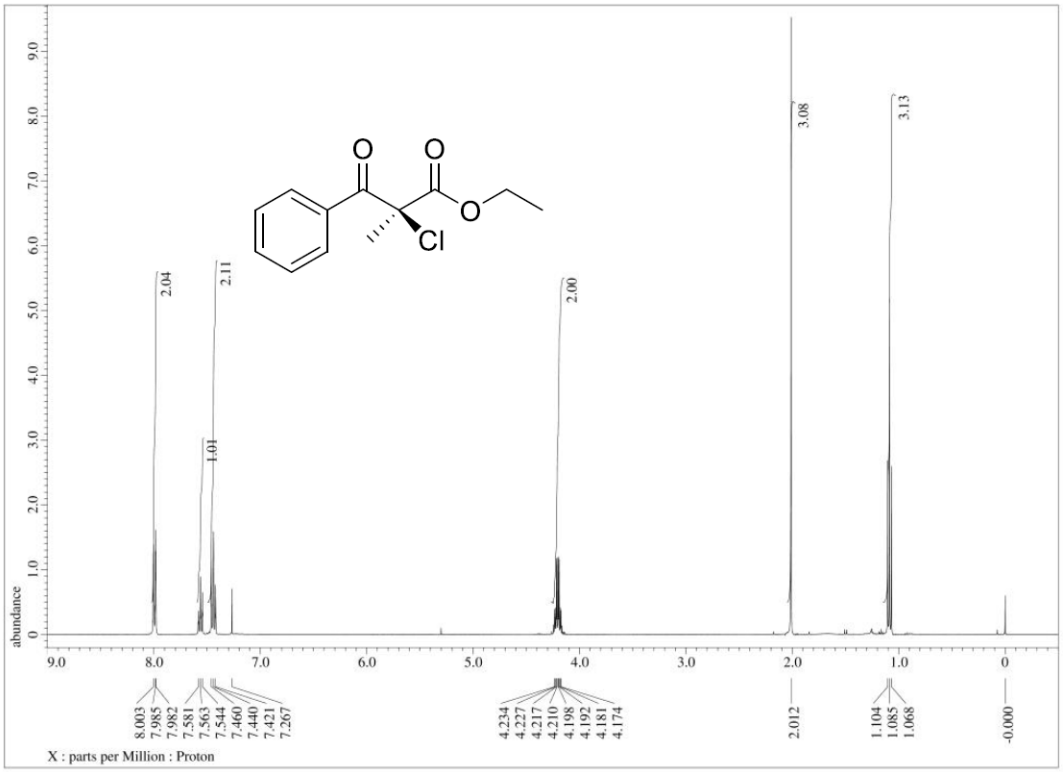

O
O
O
Cl
abundance
0
0.1
0.2
0.3
0.4
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
198.862
166.997
133.907
130.564
128.168
127.967
127.469
77.326
77.000
76.684
75.237
63.032
42.147
26.493
13.799
X : parts per Million : Carbon13

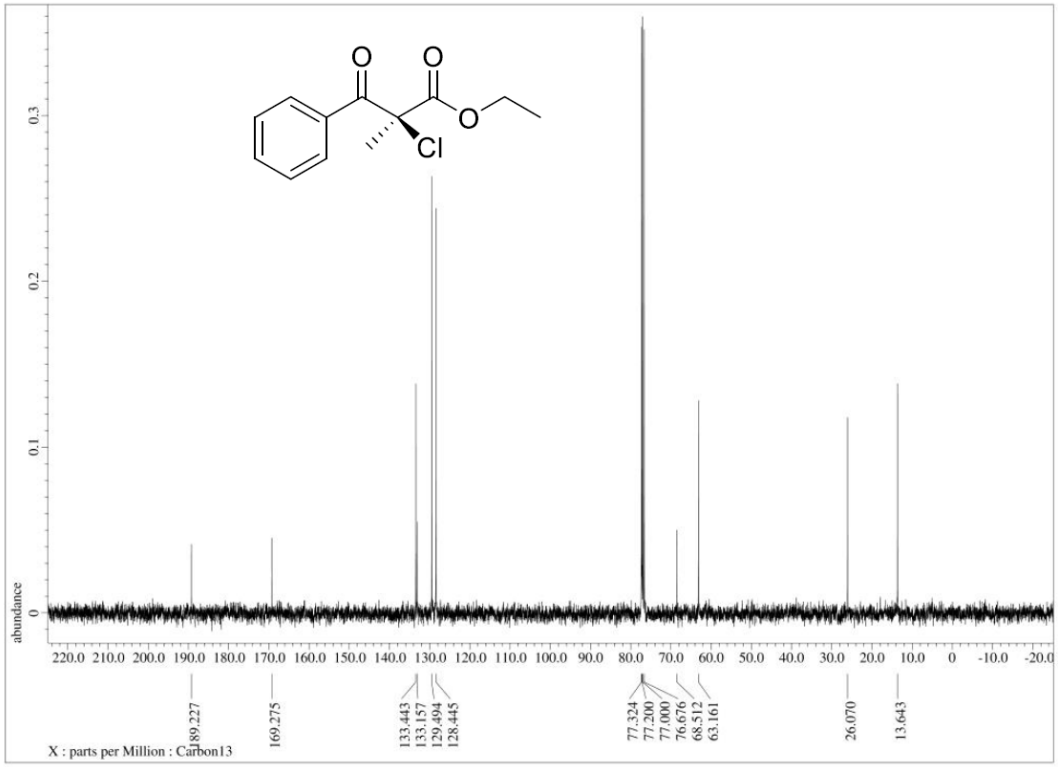

O
O
O
Cl
4.85
2.73
8.80
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
10.0
11.0
12.0
13.0
14.0
15.0
16.0
17.0
18.0
19.0
20.0
21.0
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.280
7.269
7.261
3.514
3.477
3.446
3.409
2.371
2.249
1.562
1.553
1.431
0.000
X : parts per Million : Proton

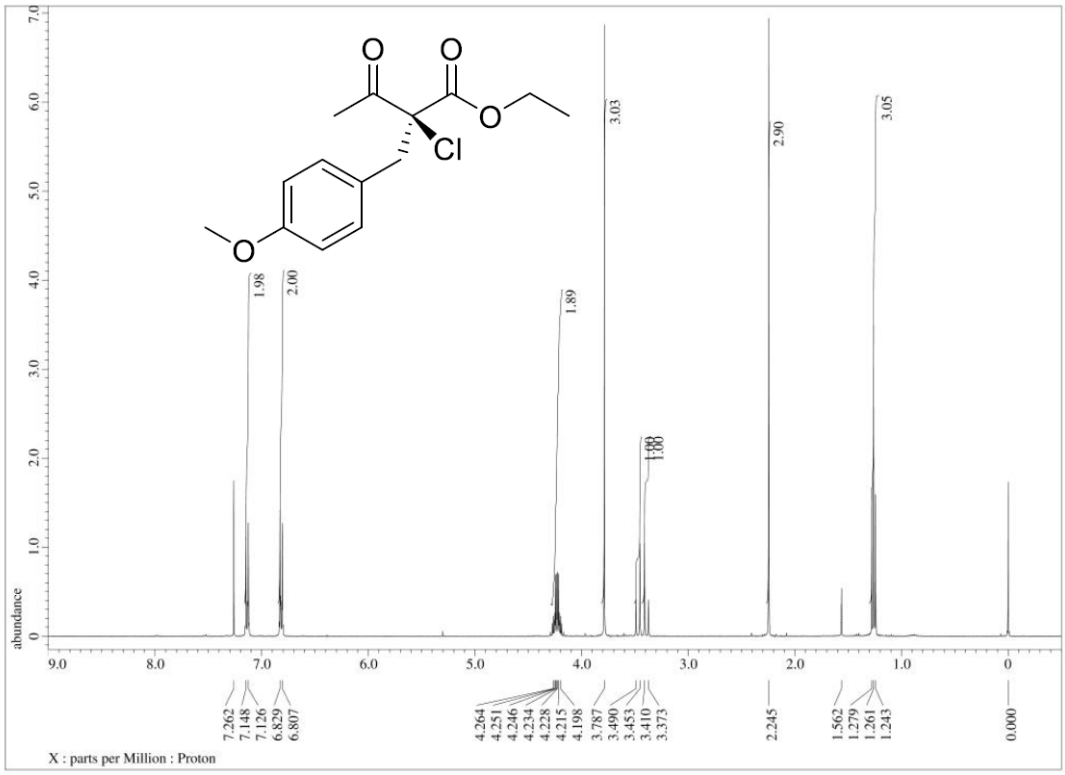

O
O
O
Cl
abundance
0.4
0.3
0.2
0.1
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
199.089
165.689
134.225
130.724
128.092
127.882
127.367
84.392
77.324
77.000
76.676
75.903
41.893
27.586
26.423
X : parts per Million : Carbon13

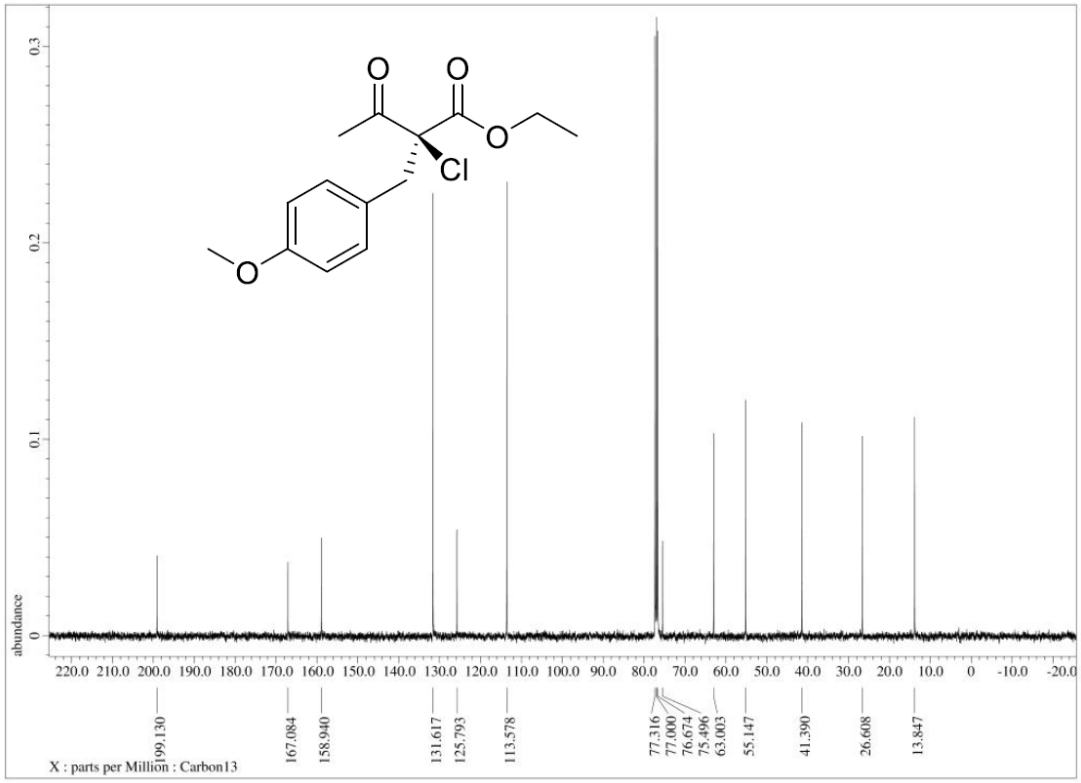

O
O
O
Cl
3.49
3.25
2.89
2.07
2.06
2.04
1.09
0.99
abundance
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.373
7.370
7.361
7.356
7.304
7.295
7.285
7.256
7.250
7.246
7.238
7.233
7.155
7.151
5.226
5.196
5.183
5.152
3.552
3.516
3.455
3.419
2.434
2.177
1.560
0.000
X : parts per Million : Proton

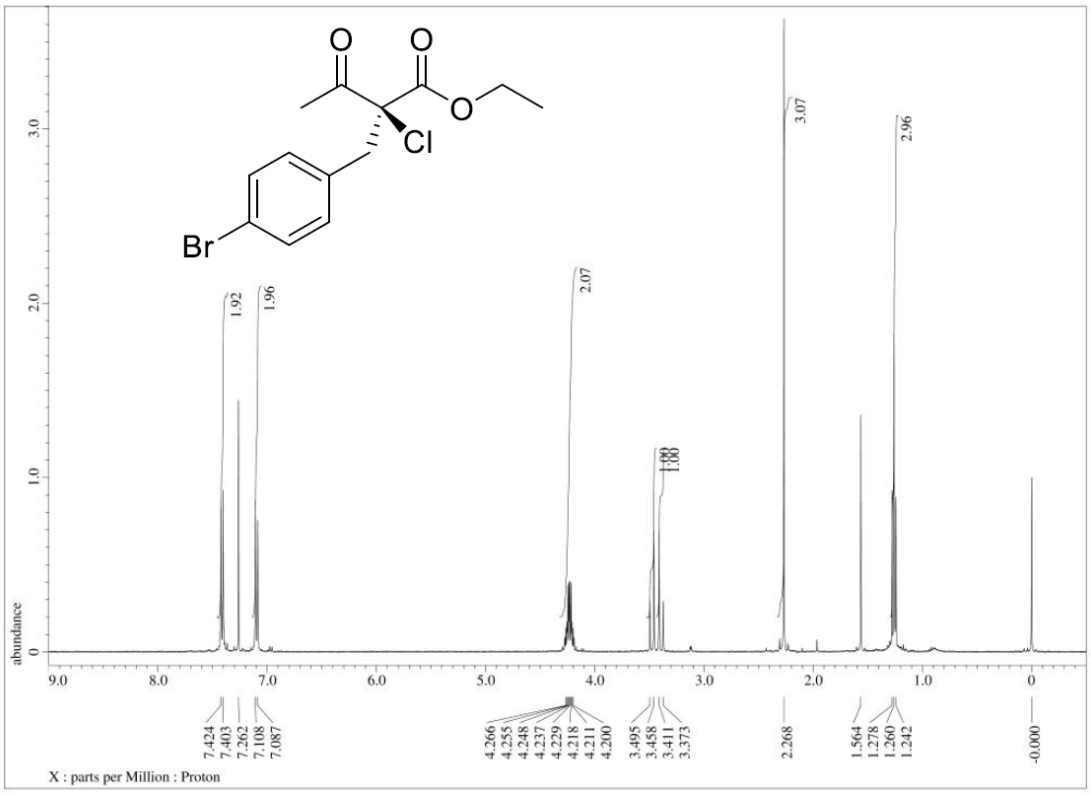

O
O
O
Cl
abundance
0
0.1
0.2
0.3
0.4
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
198.555
166.814
134.301
133.757
130.534
128.922
128.722
128.636
128.483
128.378
128.197
127.463
77.324
77.210
77.000
76.676
75.293
69.876
68.502
42.102
26.404
X : parts per Million : Carbon13

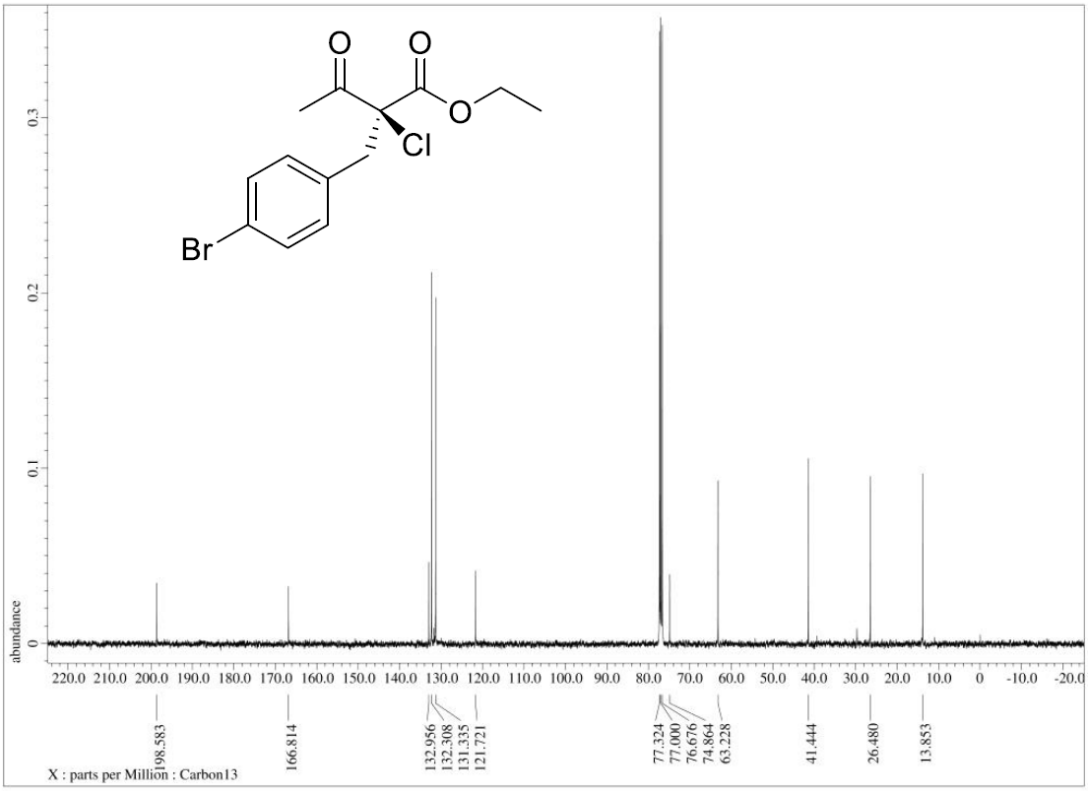

O
O
O
Cl
2.04
2.11
1.01
2.00
3.08
3.13
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
9.0
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
8.003
7.985
7.982
7.581
7.563
7.544
7.460
7.440
7.421
7.267
4.234
4.227
4.217
4.210
4.198
4.192
4.181
4.174
2.012
1.104
1.085
1.068
-0.000
X : parts per Million : Proton

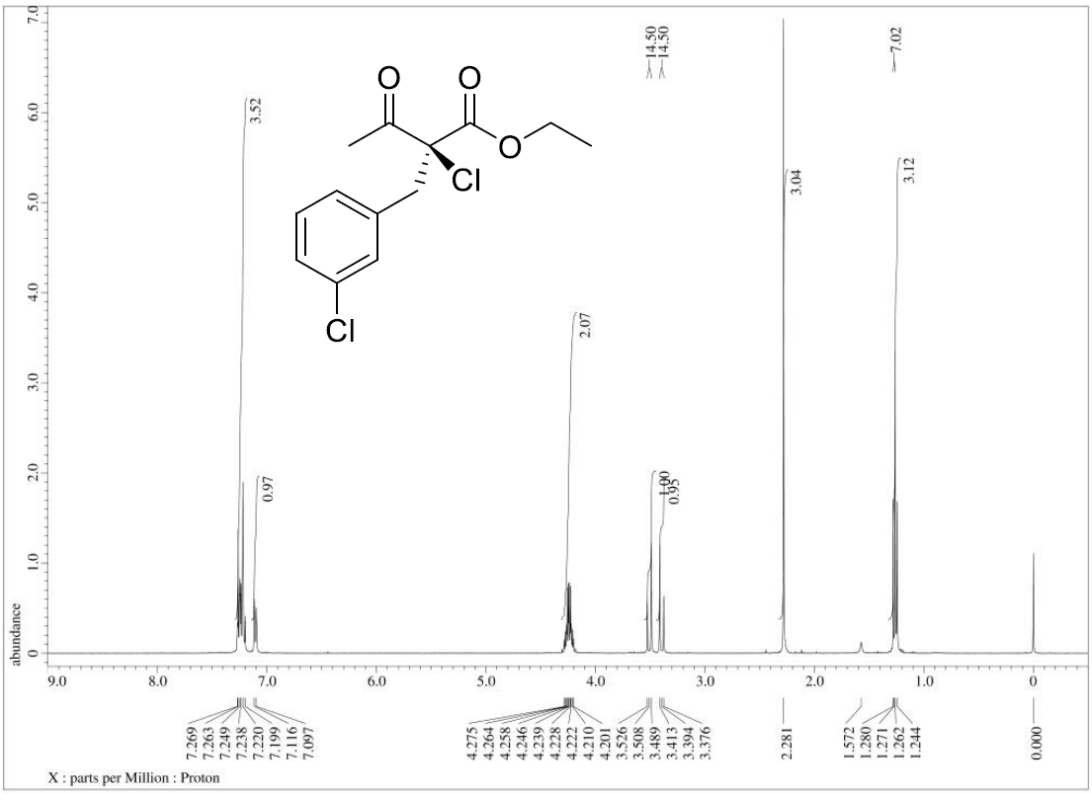

O
O
O
Cl
abundance
0.3
0.2
0.1
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
189.227
169.275
133.443
133.157
129.494
128.445
77.324
77.200
77.000
76.676
68.512
63.161
26.070
13.643
X : parts per Million : Carbon13

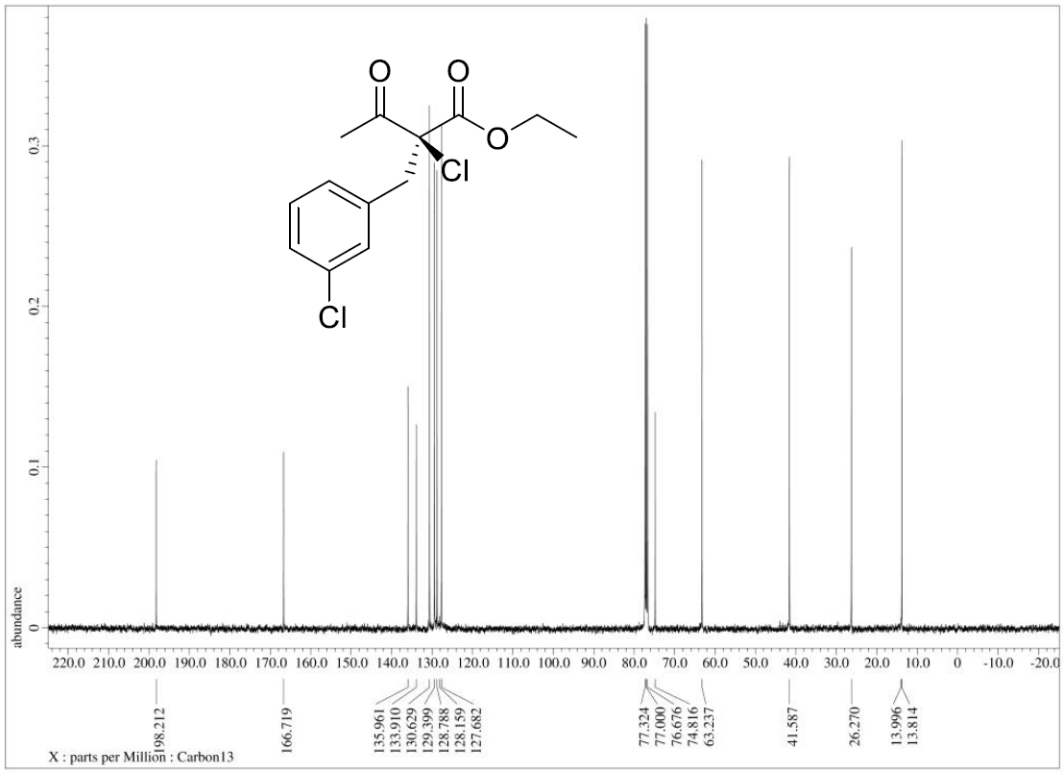

O
O
O
Cl
O
1.98
2.00
1.89
3.03
2.90
3.05
abundance
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.262
7.148
7.126
6.829
6.807
4.264
4.251
4.246
4.234
4.228
4.215
4.198
3.787
3.490
3.453
3.410
3.373
2.245
1.562
1.279
1.261
1.243
0.000
X : parts per Million : Proton

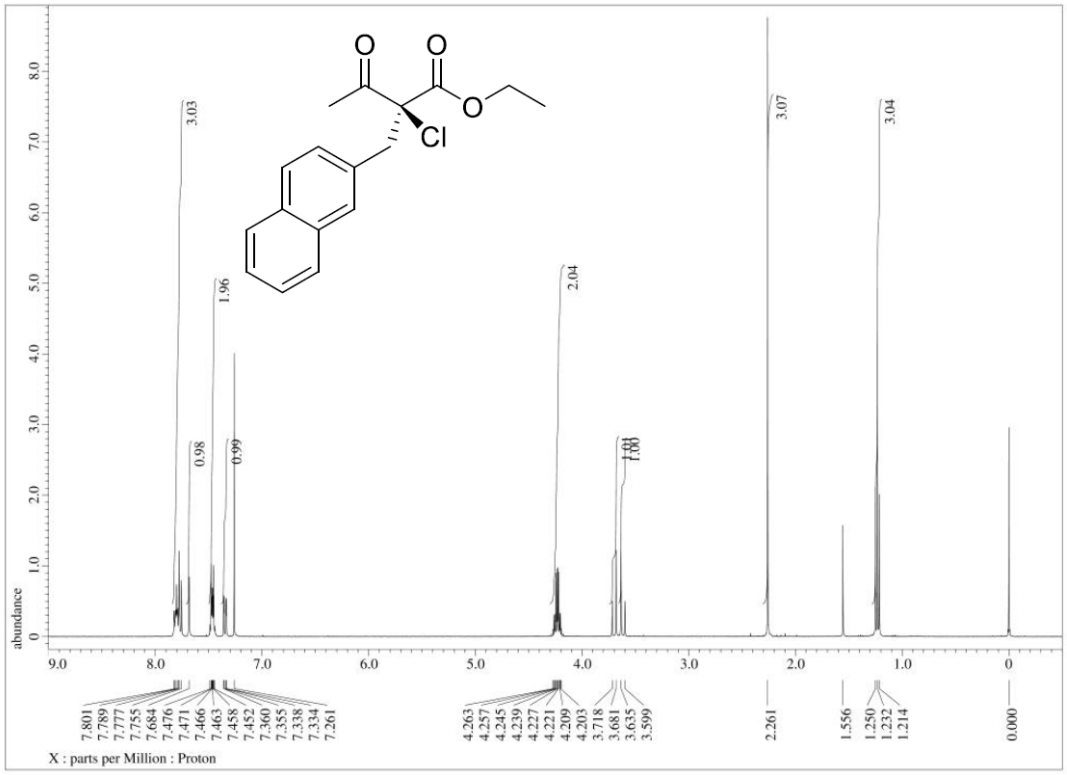

O
O
O
Cl
O
abundance
0.3
0.2
0.1
0
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
199.130
167.084
158.940
131.617
125.793
113.578
77.316
77.000
76.674
75.496
63.003
55.147
41.390
26.608
13.847
X : parts per Million : Carbon13

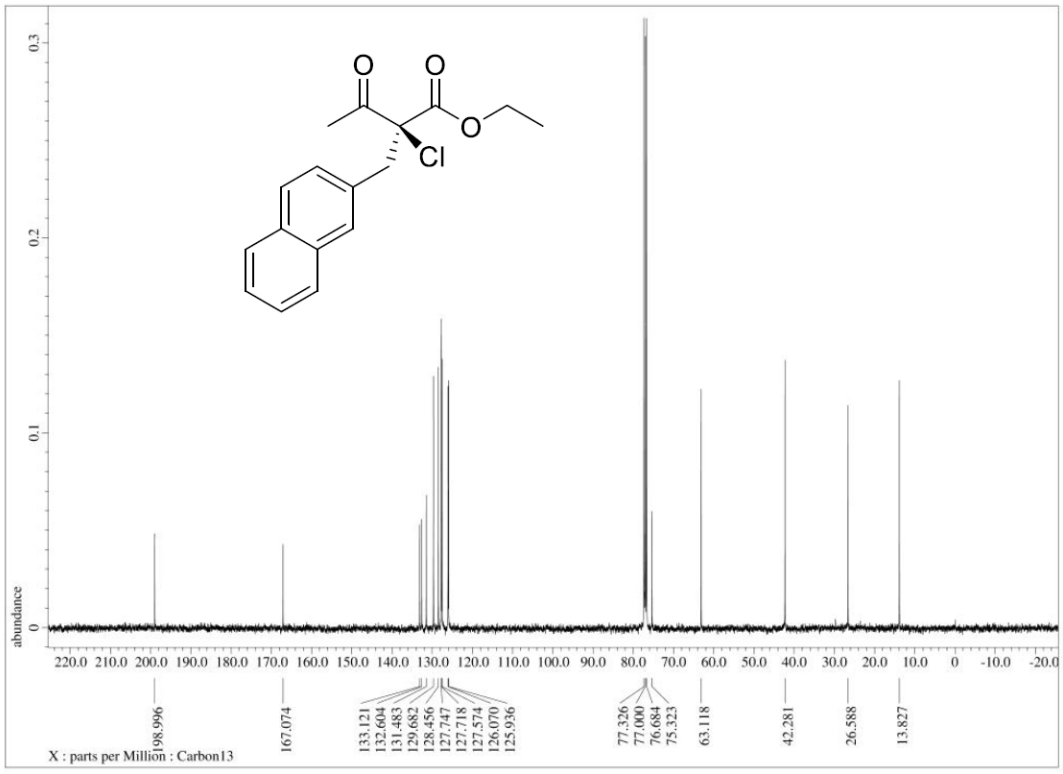

O
O
O
Cl
Br
abundance
3.0
2.0
1.0
0
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
1.92
1.96
2.07
3.07
2.96
7.424
7.403
7.262
7.108
7.087
4.266
4.255
4.248
4.237
4.229
4.218
4.211
4.200
3.495
3.458
3.411
3.373
2.268
1.564
1.278
1.260
1.242
-0.000
X : parts per Million : Proton

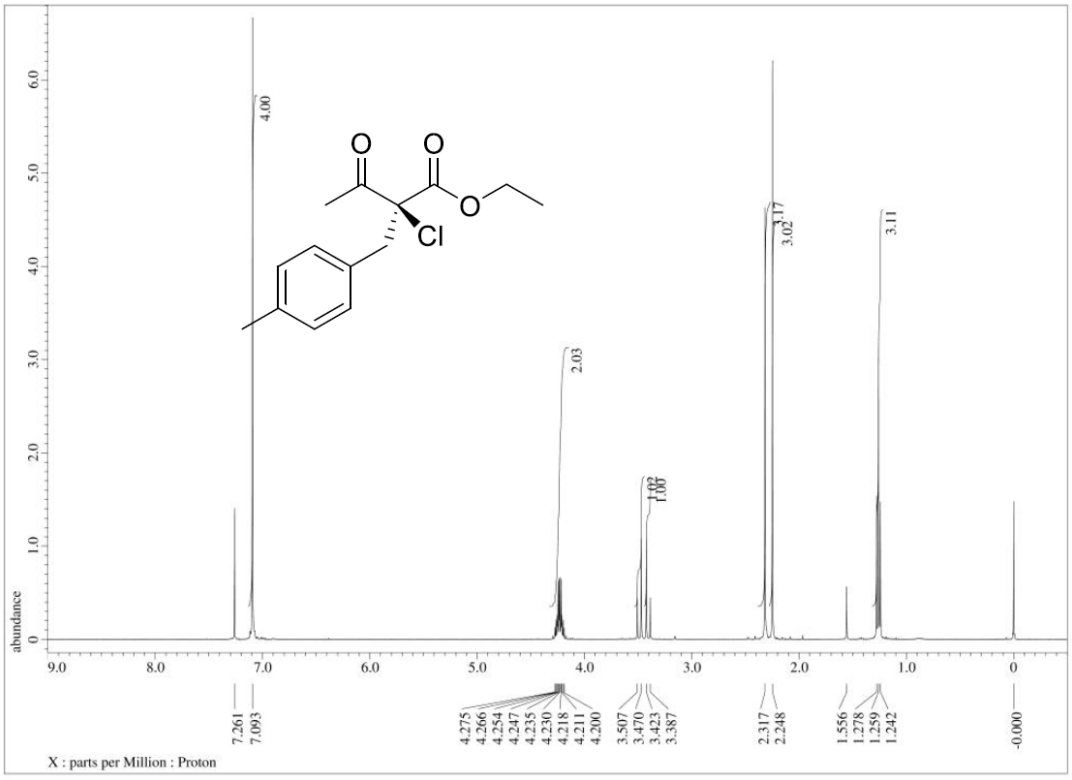

O
O
O
Cl
Br
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
198.583
166.814
132.956
132.308
131.335
121.721
77.324
77.000
76.676
74.864
63.228
41.444
26.480
13.853
X : parts per Million : Carbon13

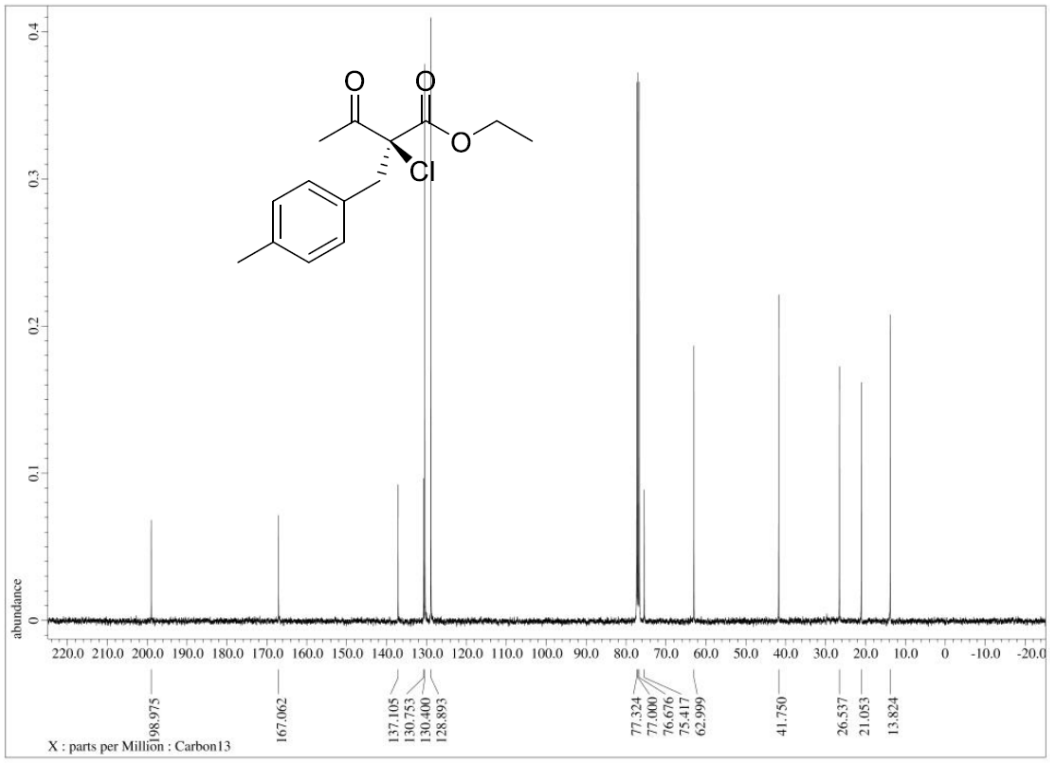

O
O
O
Cl
Cl
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
3.52
0.97
2.07
14.50
14.50
1.00
0.95
3.04
7.02
3.12
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.269
7.263
7.249
7.238
7.220
7.199
7.116
7.097
4.275
4.264
4.258
4.246
4.239
4.228
4.222
4.210
4.201
3.526
3.508
3.489
3.413
3.394
3.376
2.281
1.572
1.280
1.271
1.262
1.244
0.000
X : parts per Million : Proton

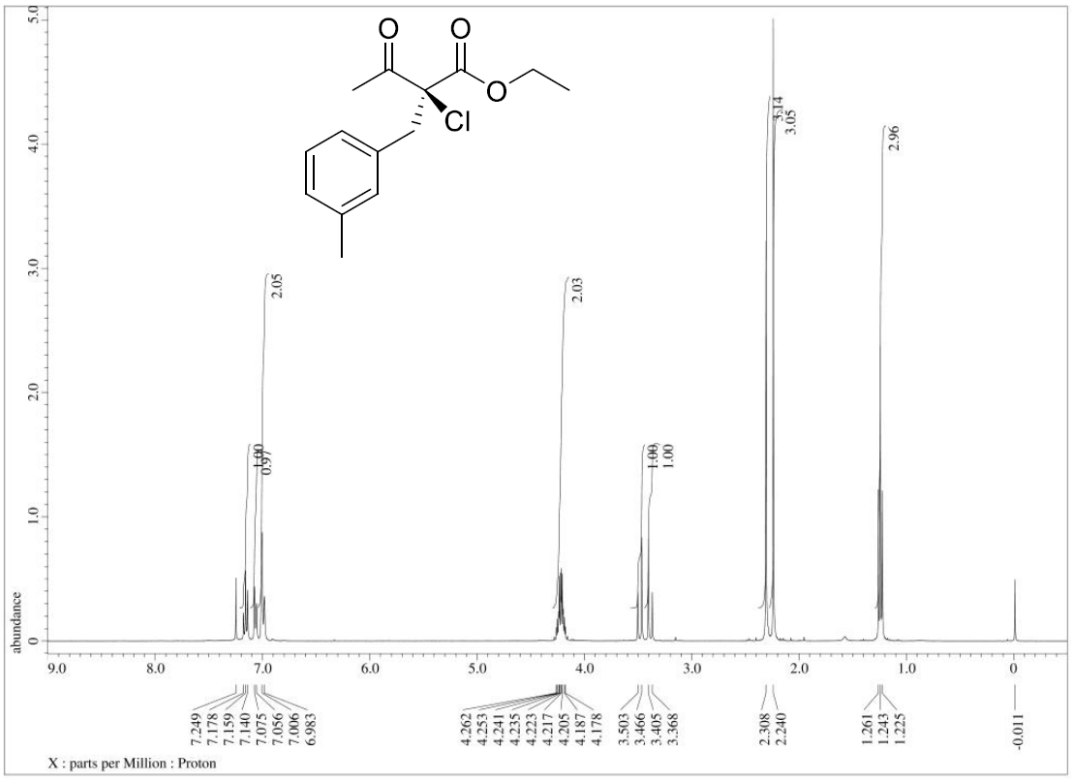

O
O
O
Cl
Cl
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
198.212
166.719
135.961
133.910
130.629
129.399
128.788
128.159
127.682
77.324
77.000
76.676
74.816
63.237
41.587
26.270
13.996
13.814
X : parts per Million : Carbon13

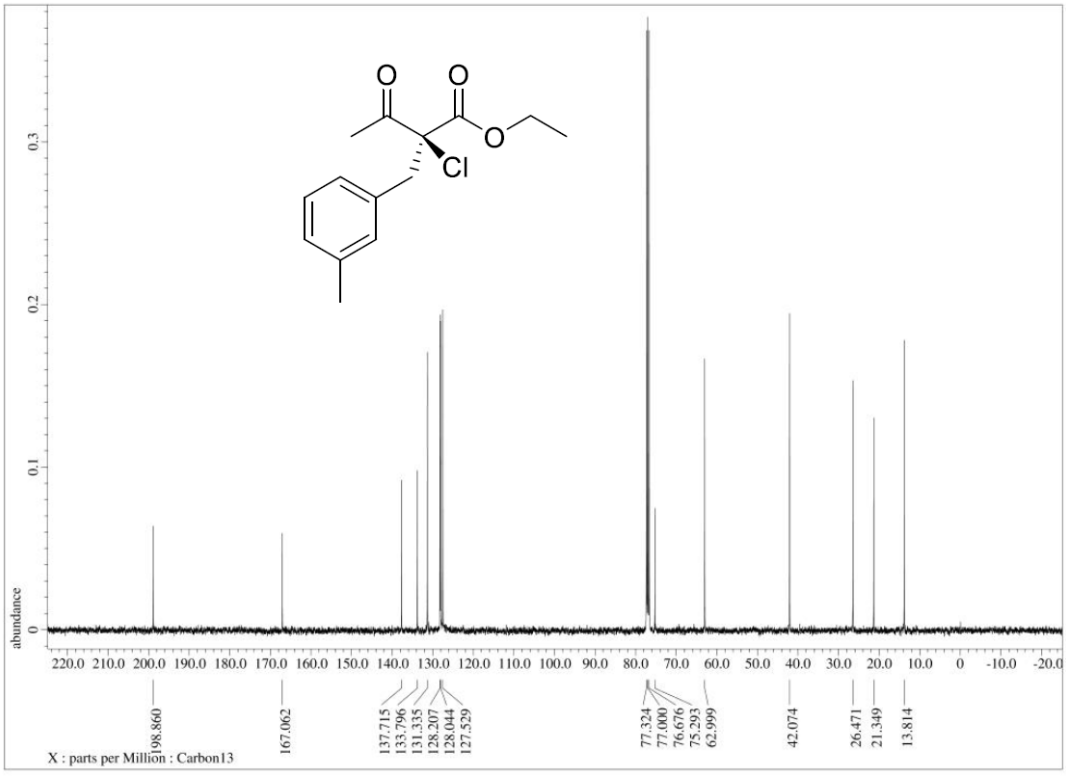

O
O
O
Cl
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
3.03
1.96
0.98
0.99
2.04
1.01
1.00
3.07
3.04
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.801
7.789
7.777
7.755
7.684
7.476
7.471
7.466
7.463
7.458
7.452
7.360
7.355
7.338
7.334
7.261
4.263
4.257
4.245
4.239
4.227
4.221
4.209
4.203
3.718
3.681
3.635
3.599
2.261
1.556
1.250
1.232
1.214
0.000
X : parts per Million : Proton

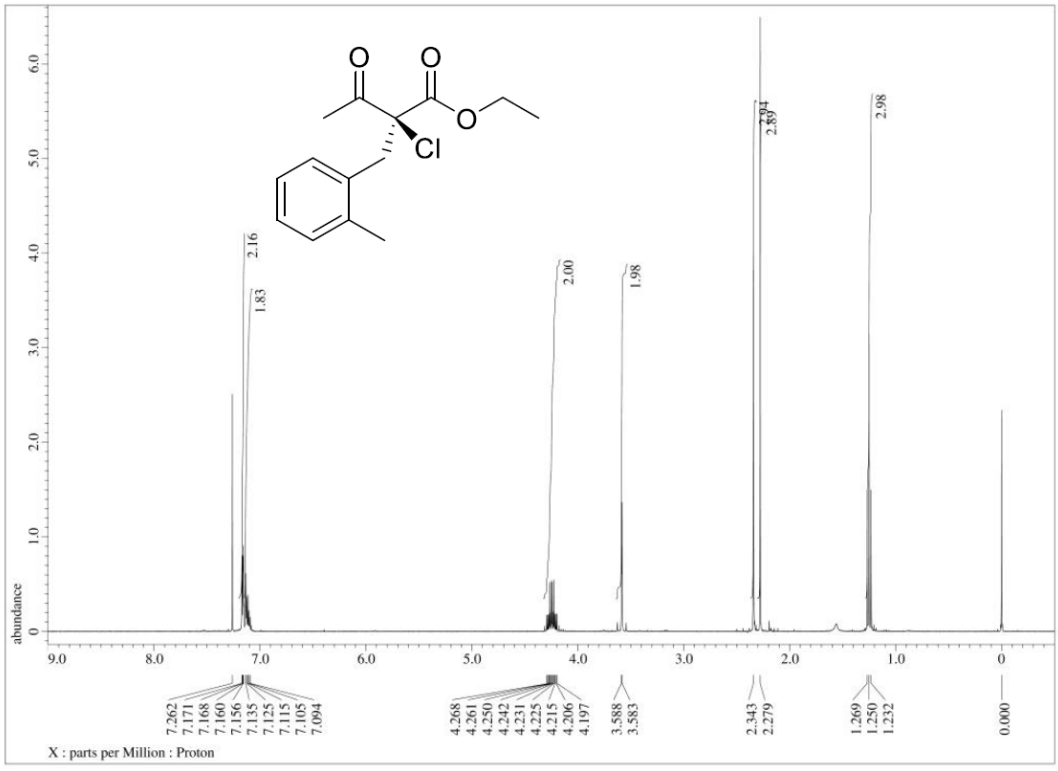

O
O
O
Cl
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
198.996
167.074
133.121
132.604
131.483
129.682
128.456
127.747
127.718
127.574
126.070
125.936
77.326
77.000
76.684
75.323
63.118
42.281
26.588
13.827
X : parts per Million : Carbon13

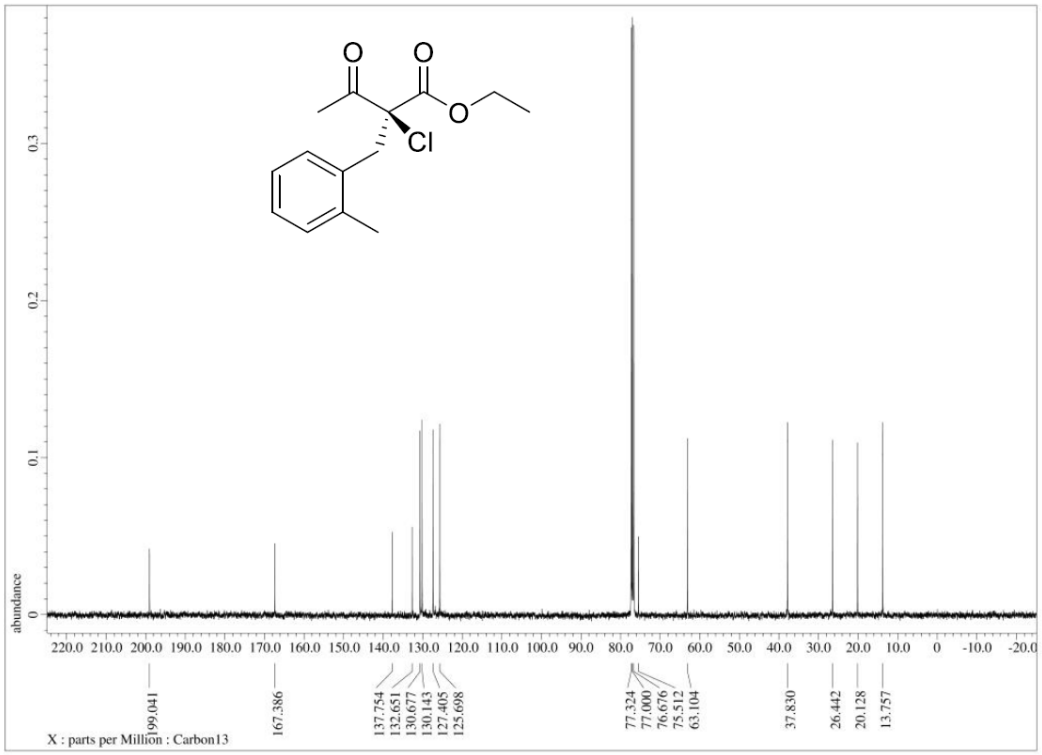

O
O
O
Cl
4.00
2.03
3.17
3.02
3.11
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.261
7.093
4.275
4.266
4.254
4.247
4.235
4.230
4.218
4.211
4.200
3.507
3.470
3.423
3.387
2.317
2.248
1.556
1.278
1.259
1.242
-0.000
X : parts per Million : Proton

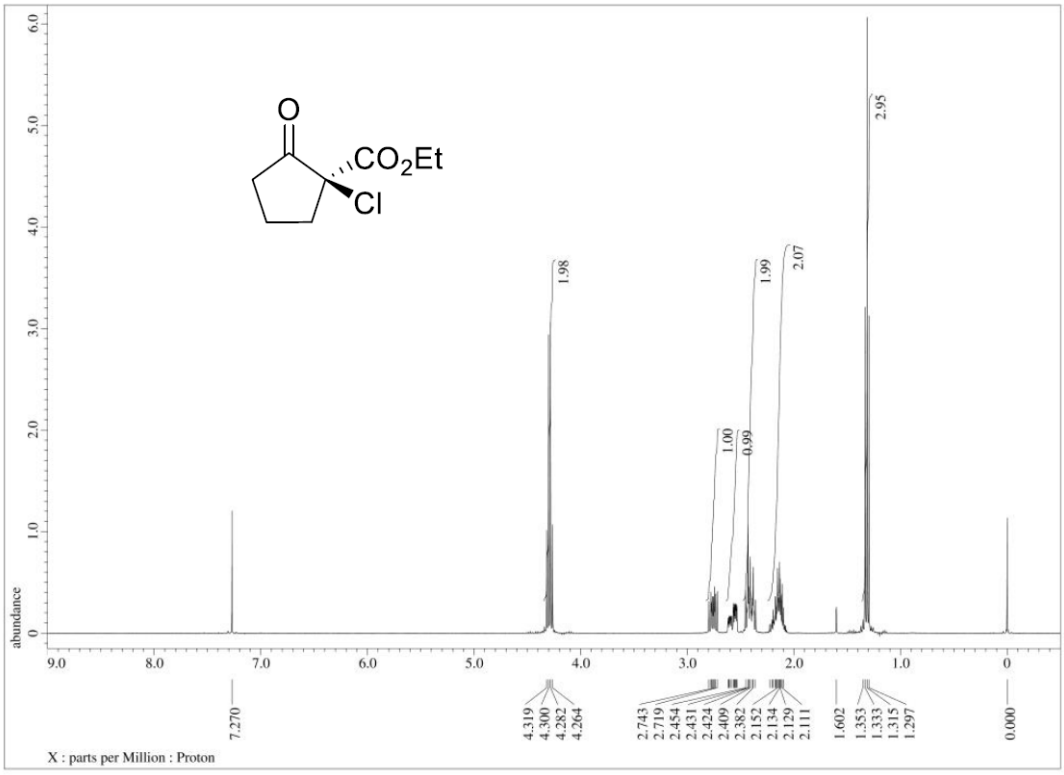

O
O
O
Cl
abundance
0
0.1
0.2
0.3
0.4
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
198.975
167.062
137.105
130.753
130.400
128.893
77.324
77.000
76.676
75.417
62.999
41.750
26.537
21.053
13.824
X : parts per Million : Carbon13

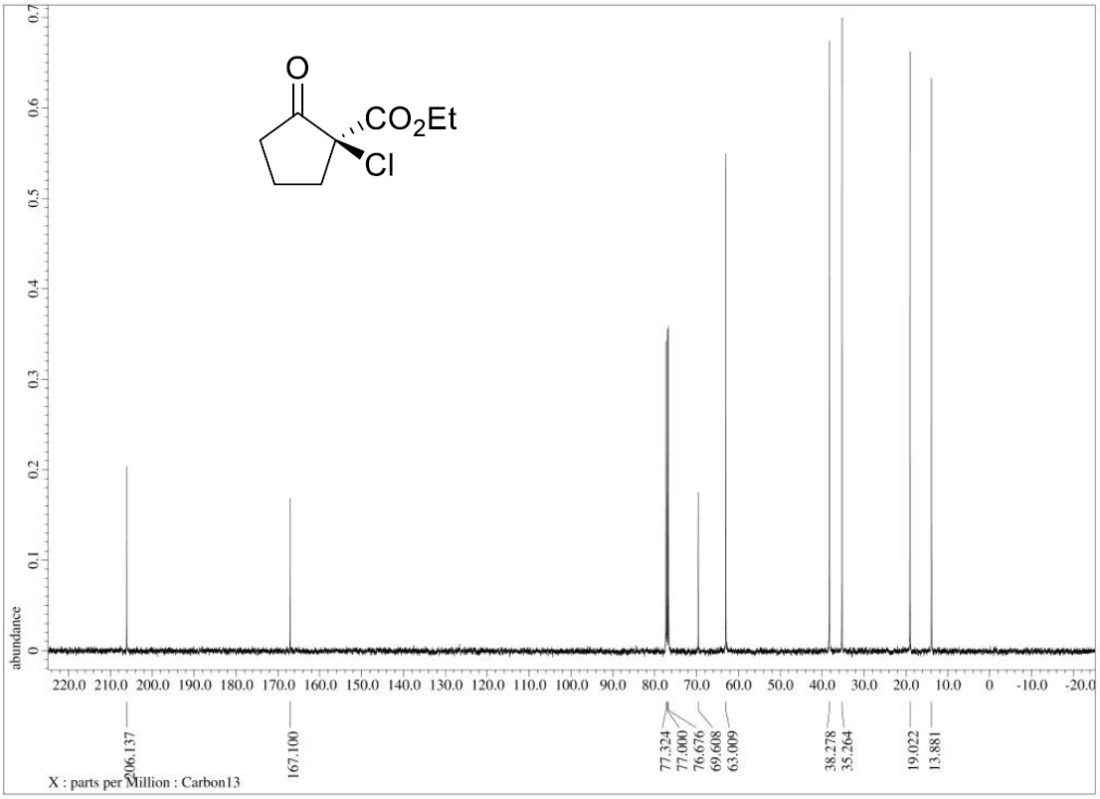

O
O
O
Cl
abundance
0
1.0
2.0
3.0
4.0
5.0
2.05
0.90
0.97
2.03
1.00
1.00
3.14
3.05
2.96
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.249
7.178
7.159
7.140
7.075
7.056
7.006
6.983
4.262
4.253
4.241
4.235
4.223
4.217
4.205
4.187
4.178
3.503
3.466
3.405
3.368
2.308
2.240
1.261
1.243
1.225
-0.011
X : parts per Million : Proton

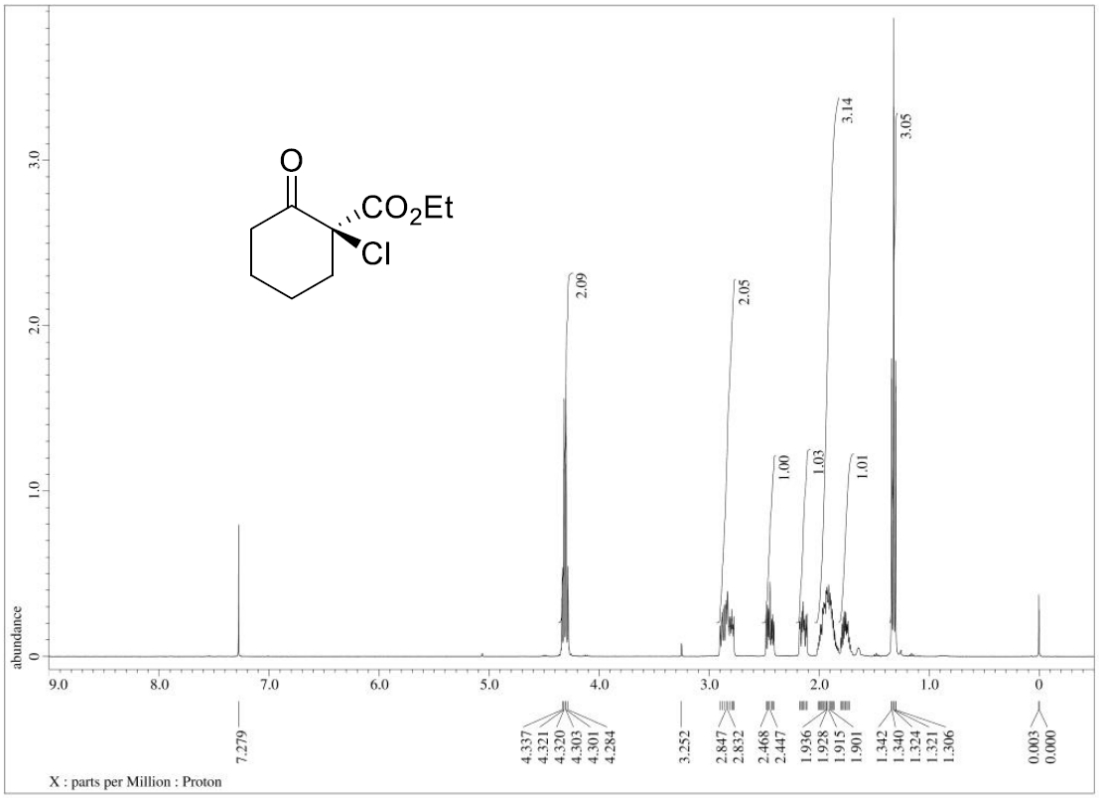

O
O
O
Cl
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
198.860
167.062
137.715
133.796
131.335
128.207
128.044
127.529
77.324
77.000
76.676
75.293
62.999
42.074
26.471
21.349
13.814
X : parts per Million : Carbon13

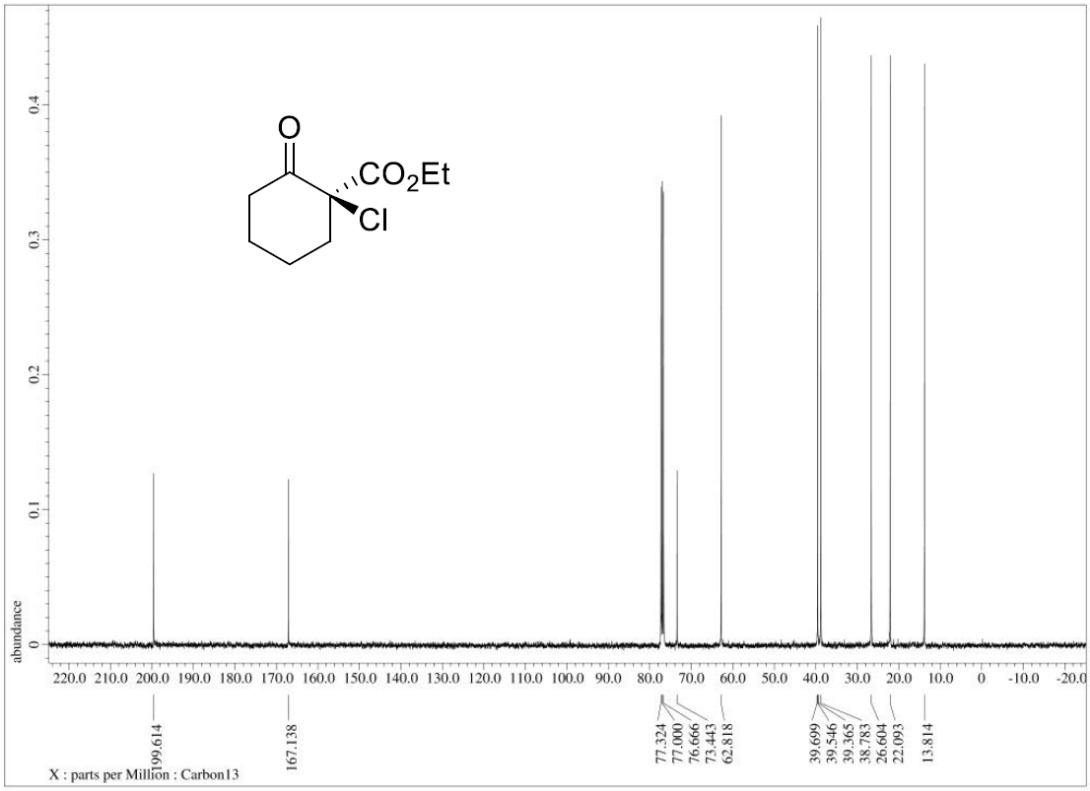

O
O
O
Cl
2.16
1.83
2.00
1.98
2.94
2.89
2.98
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.262
7.171
7.168
7.160
7.156
7.135
7.125
7.115
7.105
7.094
4.268
4.261
4.250
4.242
4.231
4.225
4.215
4.206
4.197
3.588
3.583
2.343
2.279
1.269
1.250
1.232
0.000
X : parts per Million : Proton

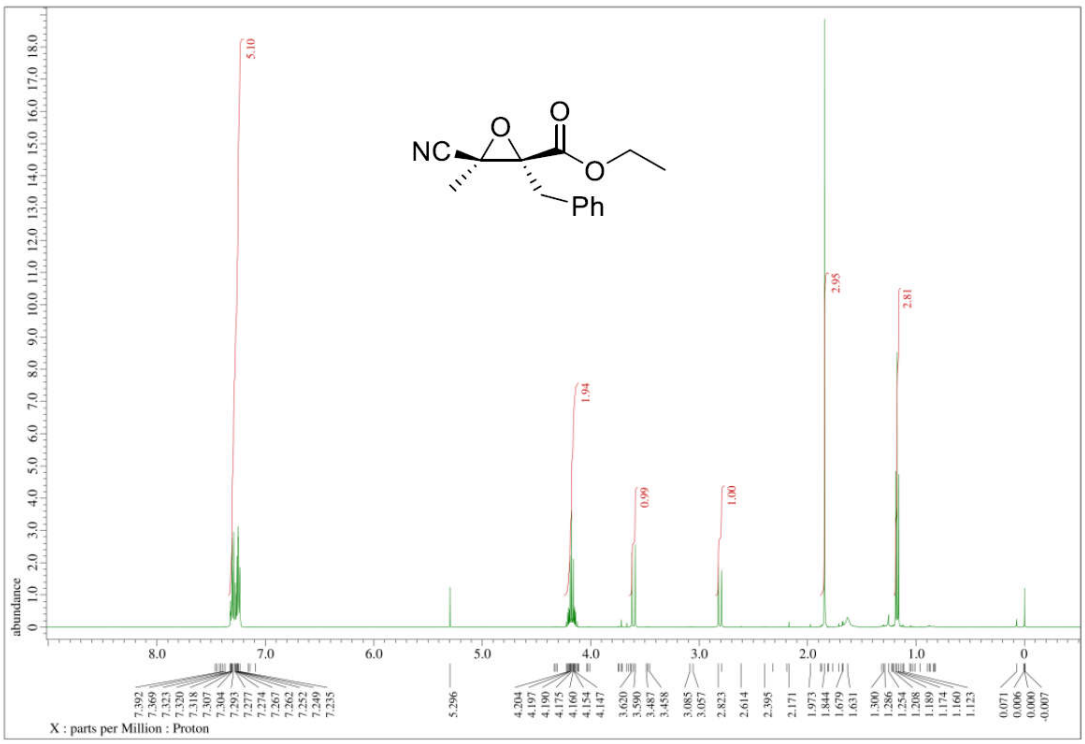

O
O
O
Cl
abundance
0
0.1
0.2
0.3
220.0 210.0 200.0 190.0 180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0 -10.0 -20.0
199.041
167.386
137.754
132.651
130.677
130.143
127.405
125.698
77.324
77.000
76.676
75.512
63.104
37.830
26.442
20.128
13.757
X : parts per Million : Carbon13

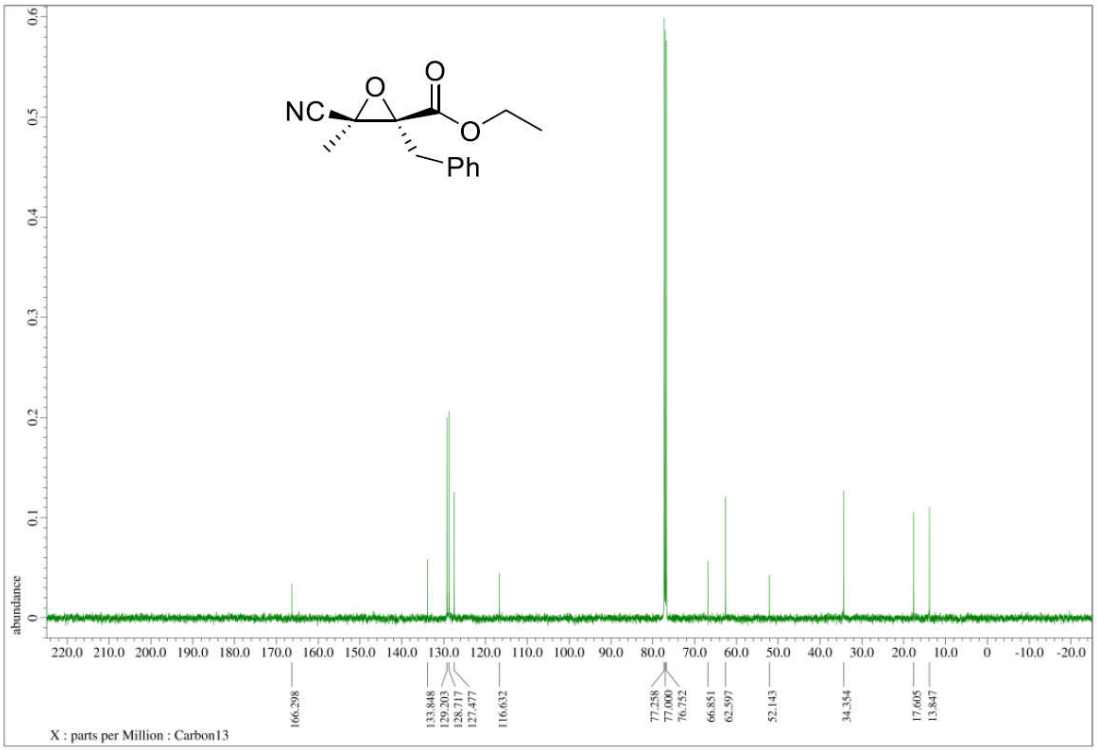

O
CO2Et
Cl
1.98
1.99
2.07
2.95
1.00
0.99
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0
9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.270
4.319
4.300
4.282
4.264
2.743
2.719
2.454
2.431
2.424
2.409
2.382
2.152
2.134
2.129
2.111
1.602
1.353
1.333
1.315
1.297
0.000
X : parts per Million : Proton

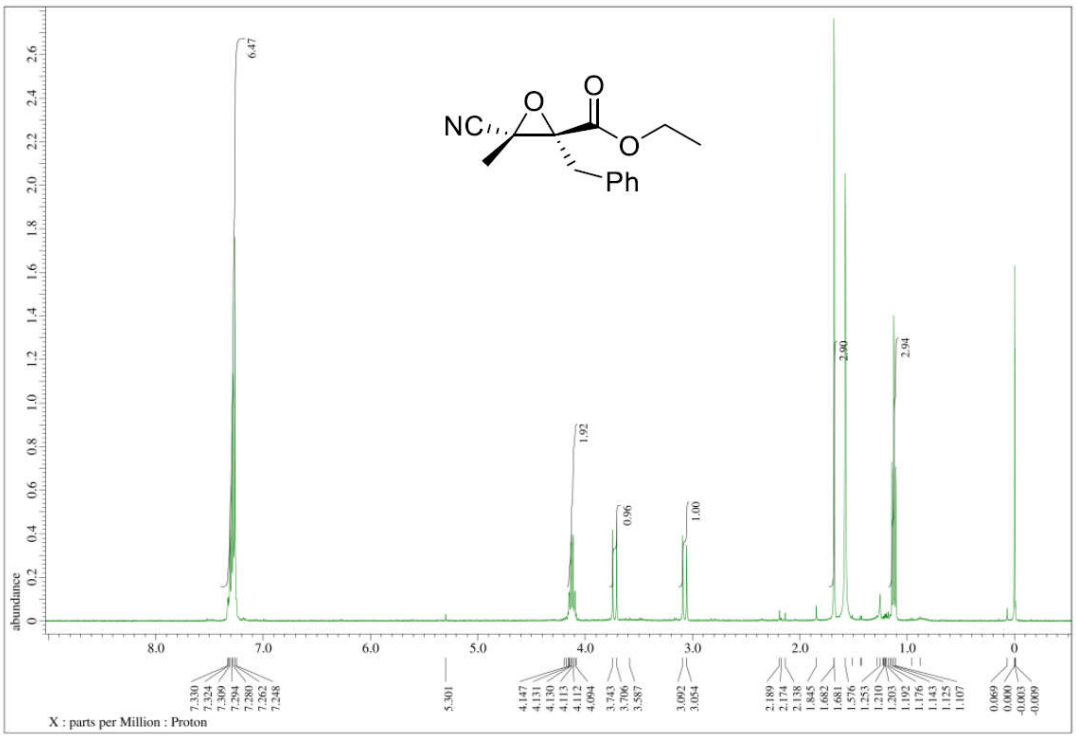

O
CO2Et
Cl
abundance
206.137
167.100
77.324
77.000
76.676
69.608
63.009
38.278
35.264
19.022
13.881
X : parts per Million : Carbon13

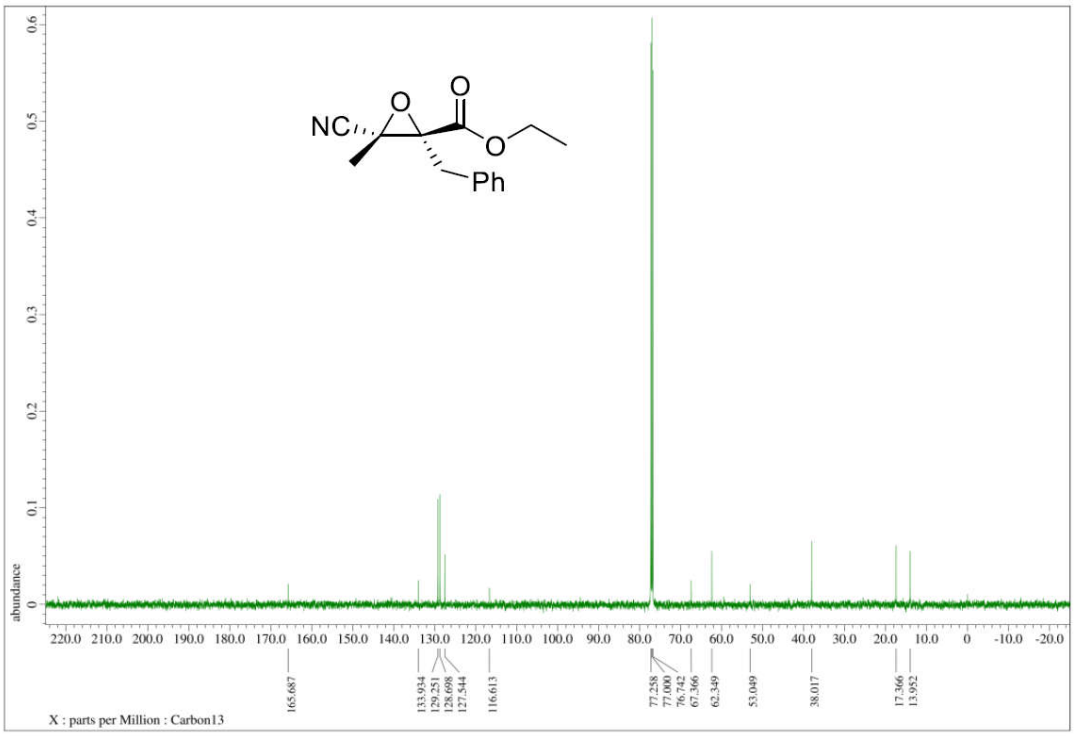

O
CO2Et
Cl
abundance
7.279
4.337
4.321
4.320
4.303
4.301
4.284
3.252
2.847
2.832
2.468
2.447
1.936
1.928
1.915
1.901
1.342
1.340
1.324
1.321
1.306
0.003
0.000
2.09
2.05
1.00
1.03
1.01
3.14
3.05
X : parts per Million : Proton


O
CO2Et
Cl
abundance
X : parts per Million : Carbon13
199.614
167.138
77.324
77.000
76.666
73.443
62.818
39.699
39.546
39.365
38.783
26.604
22.093
13.814

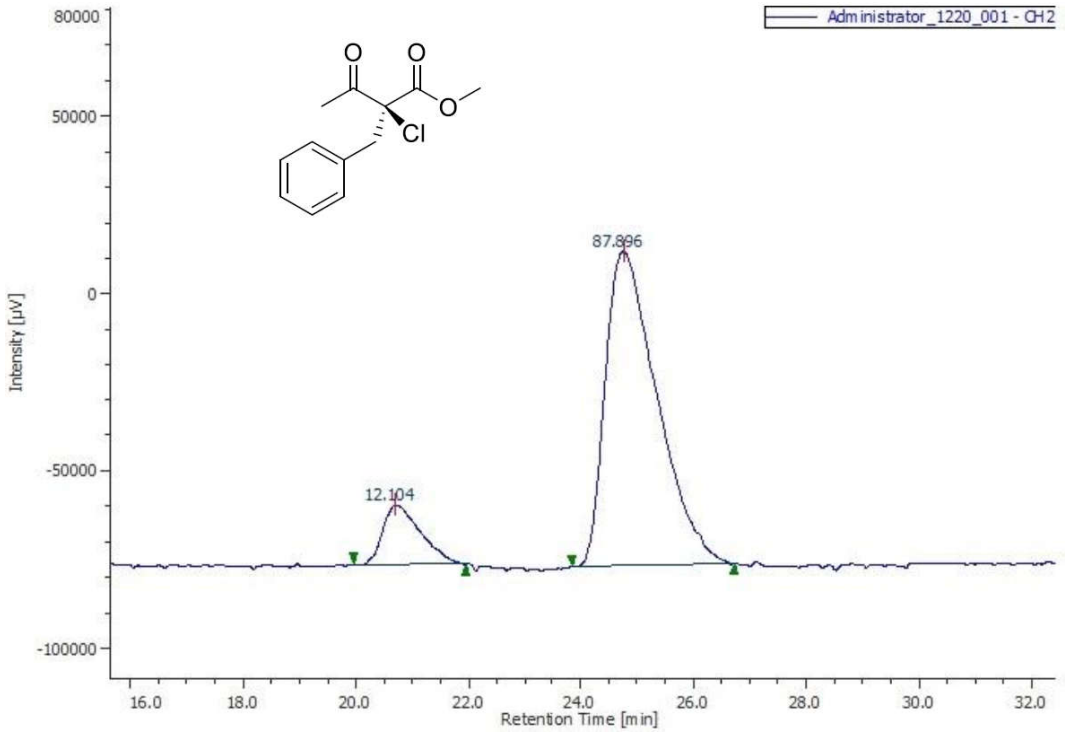

NC
O
O
O
Ph
abundance
X : parts per Million : Proton
5.10
1.94
0.99
1.00
2.95
2.81

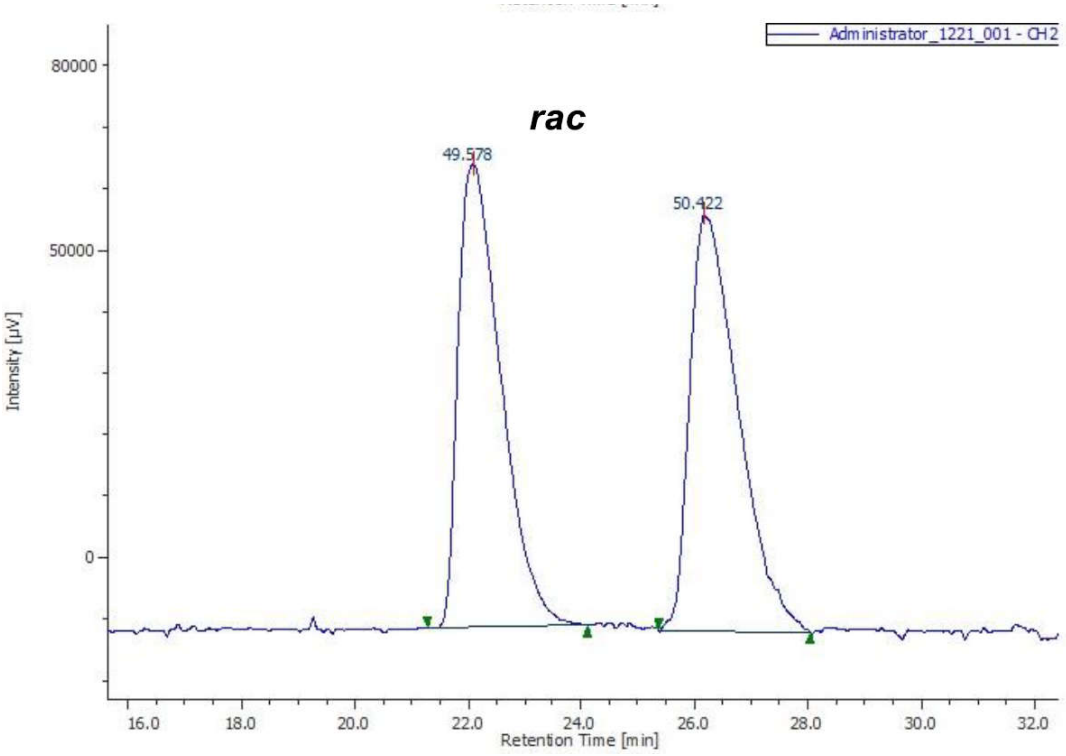

NC
O
O
O
Ph
abundance
X : parts per Million : Carbon13
166.298
133.848
129.203
128.717
127.477
116.632
77.258
77.000
76.752
66.851
62.597
52.143
34.354
17.605
13.847


NC
O
O
O
Ph
6.47
1.92
0.96
1.00
2.90
2.94
abundance
X : parts per Million : Proton

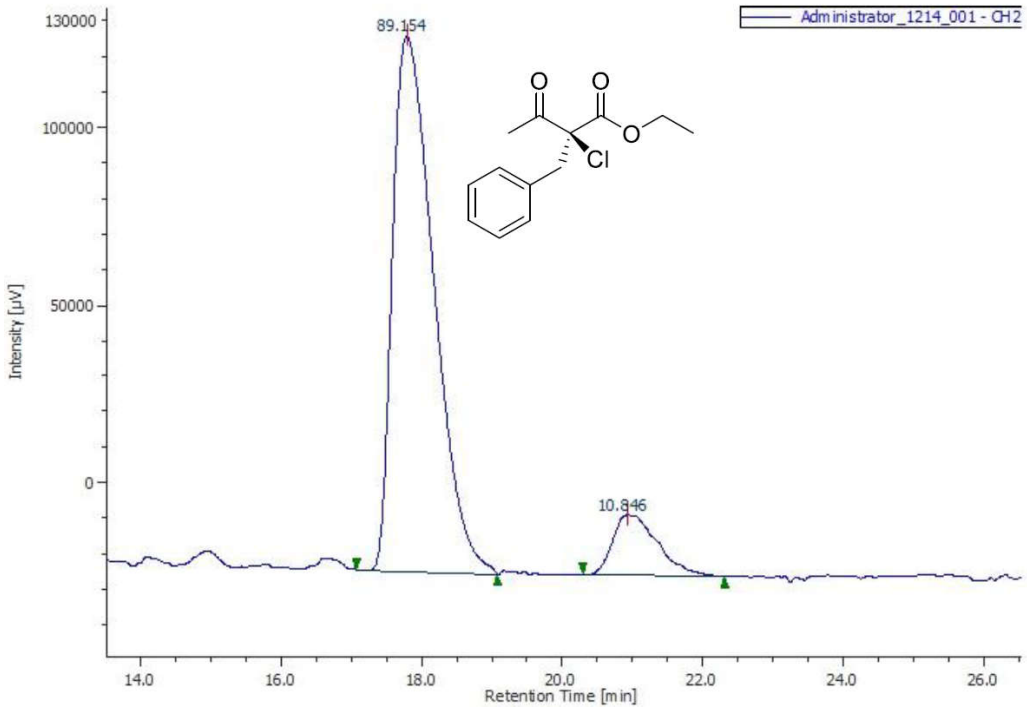


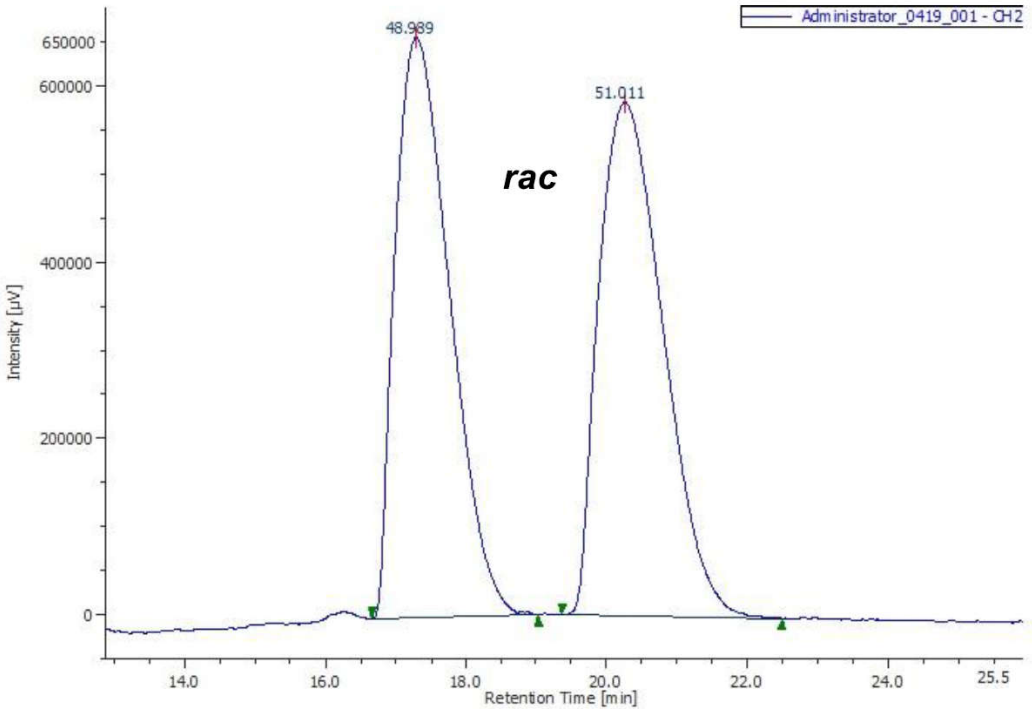
8. HPLC spectra



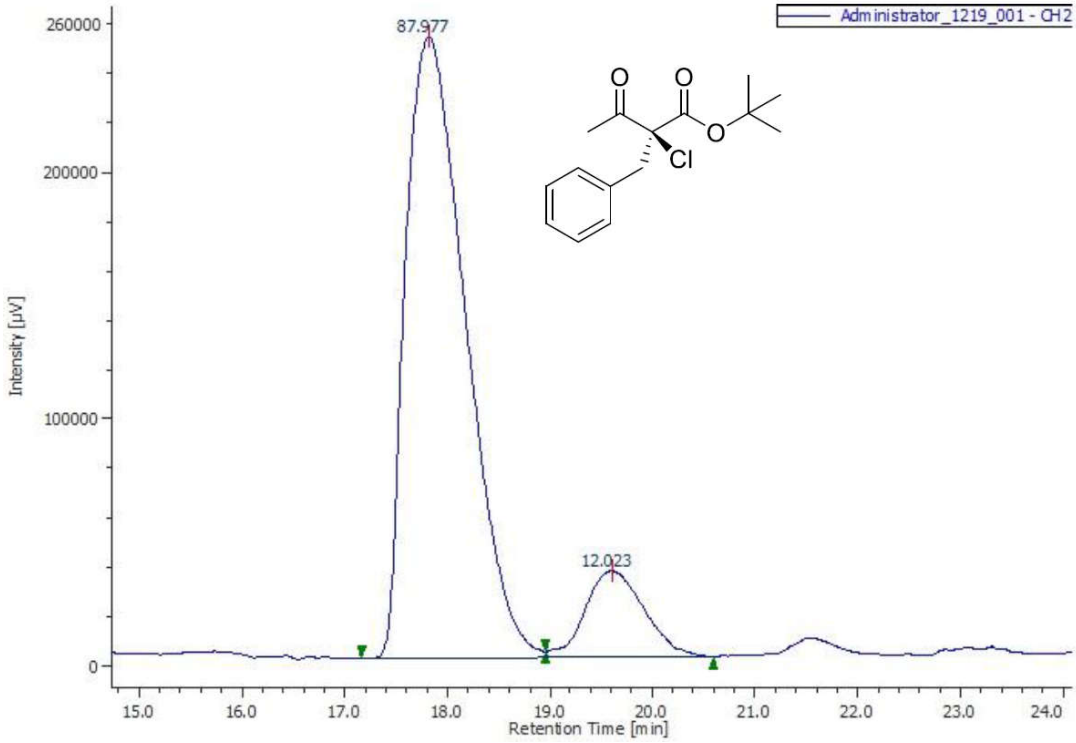


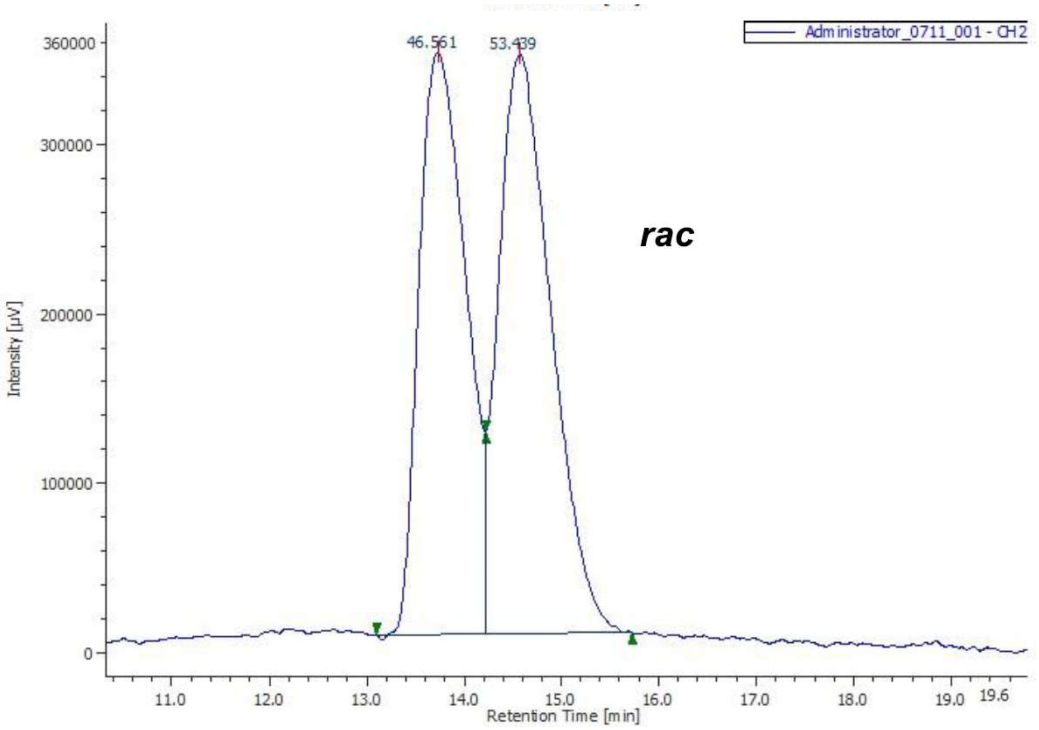
Chiralcel OJ-H column (hexane:2-propanol= 98:2, 1.0 mL/min, 210 nm)



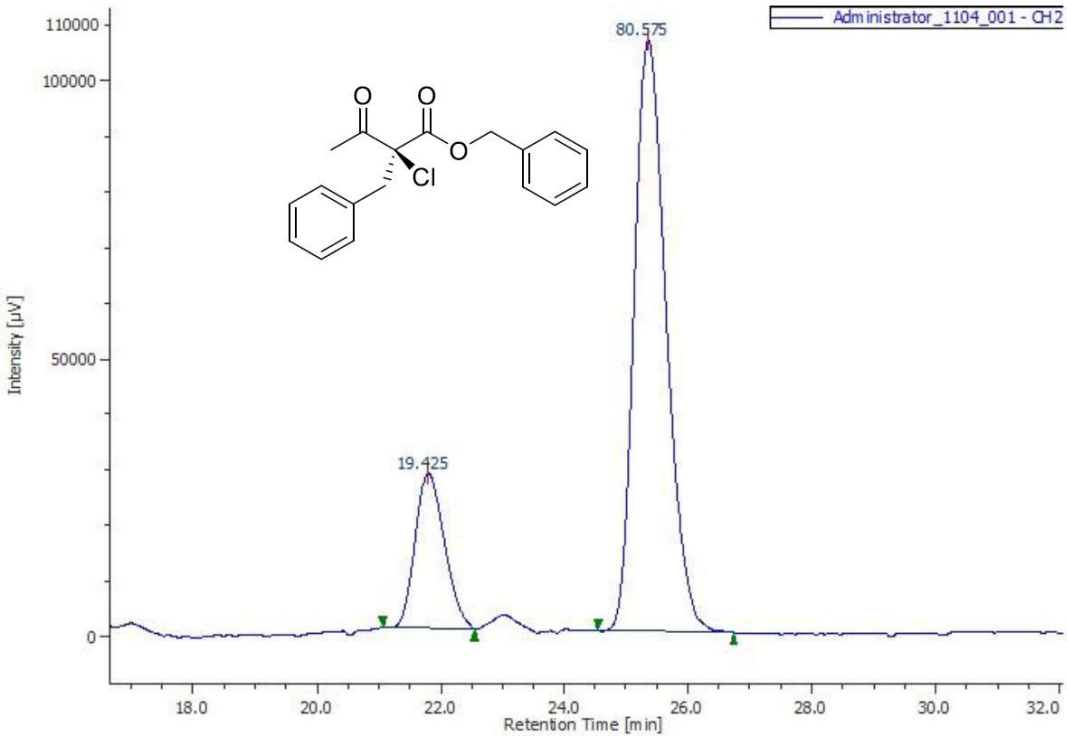


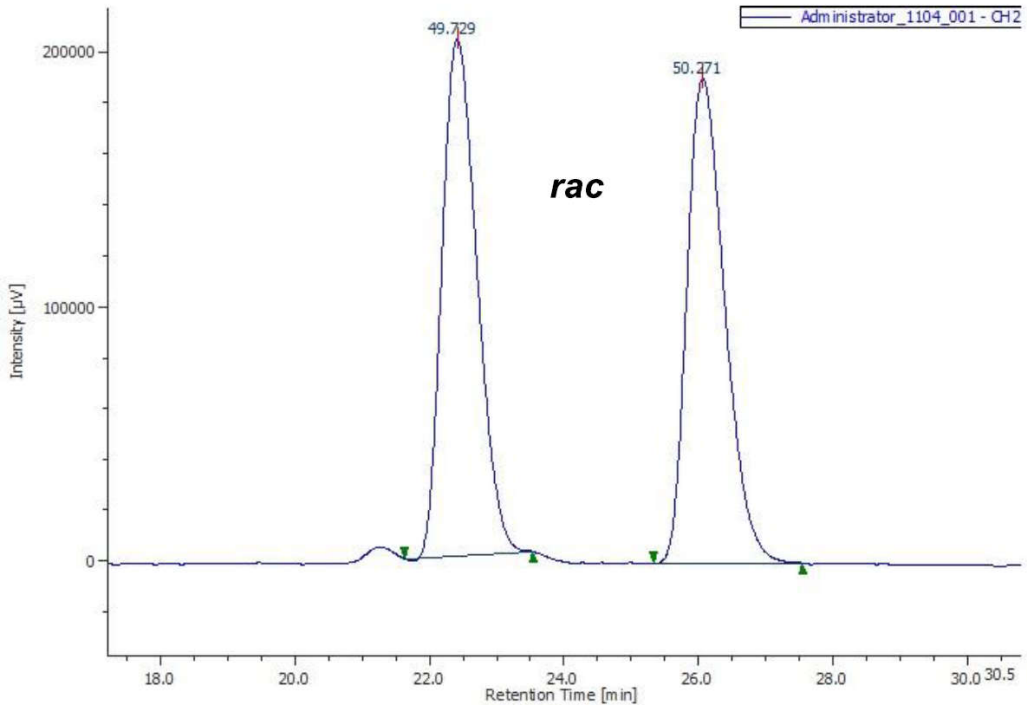
Chiralcel OJ-H column (hexane:2-propanol= 90:10, 0.5 mL/min, 210 nm)



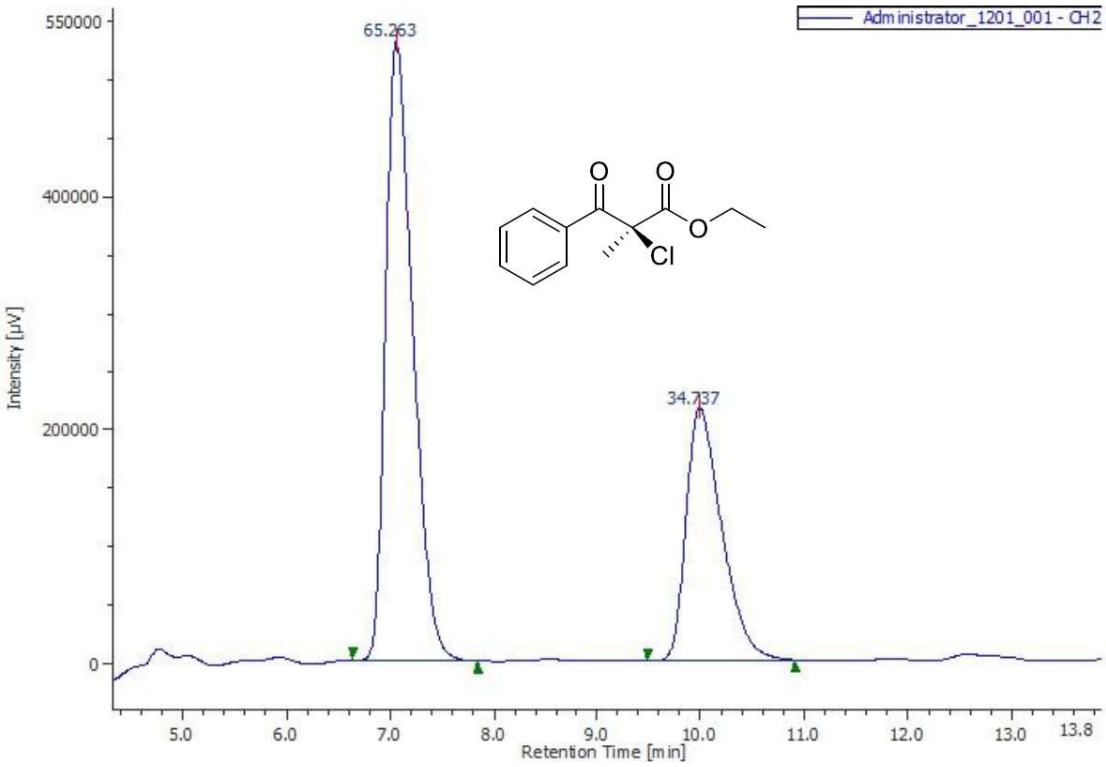


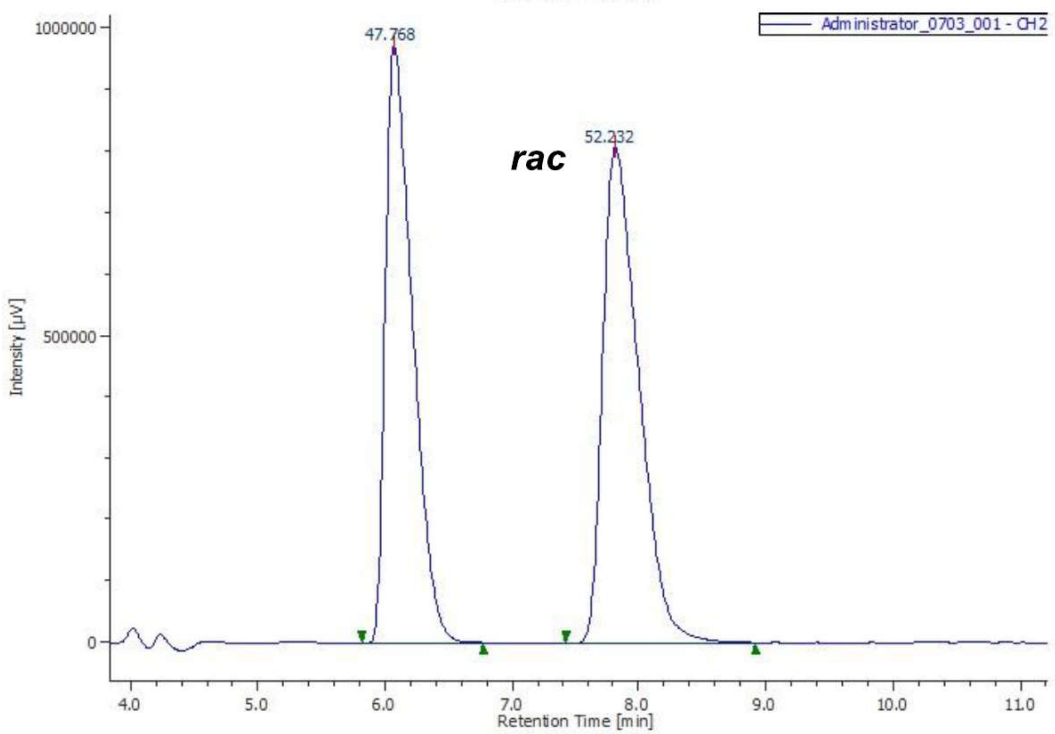
Chiralpak AD-3 column (hexane:2-propanol= 500:1, 0.5 mL/min, 210 nm)



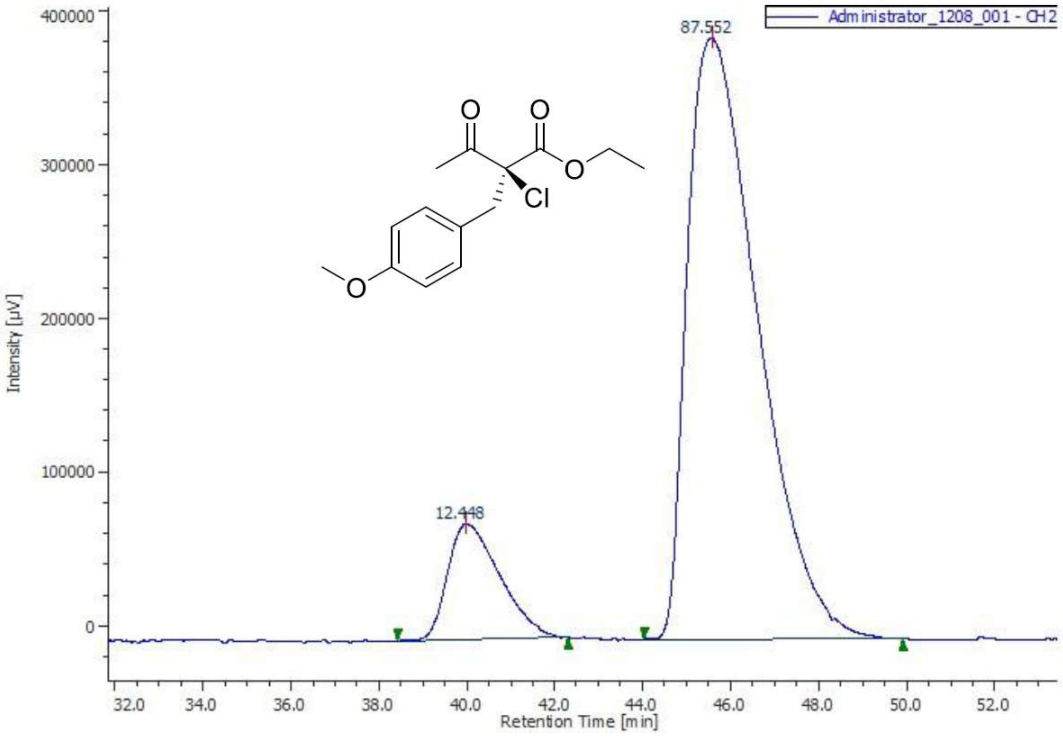


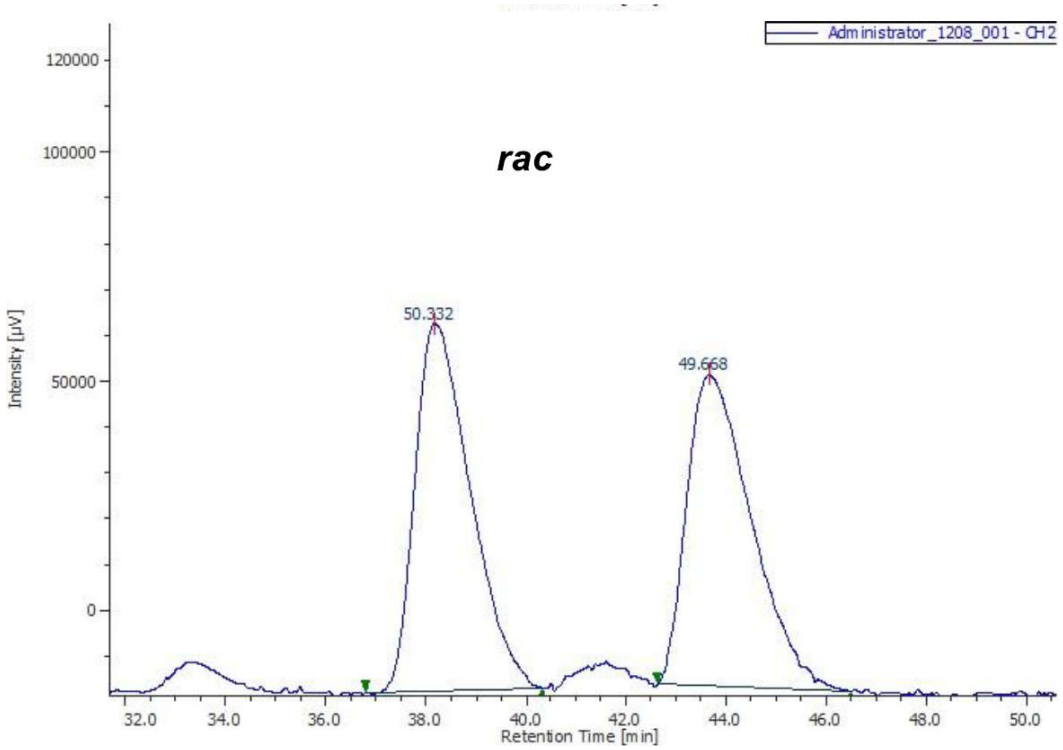
Chiralpak AS-H column (hexane:2-propanol= 99:1, 0.3 mL/min, 254 nm)



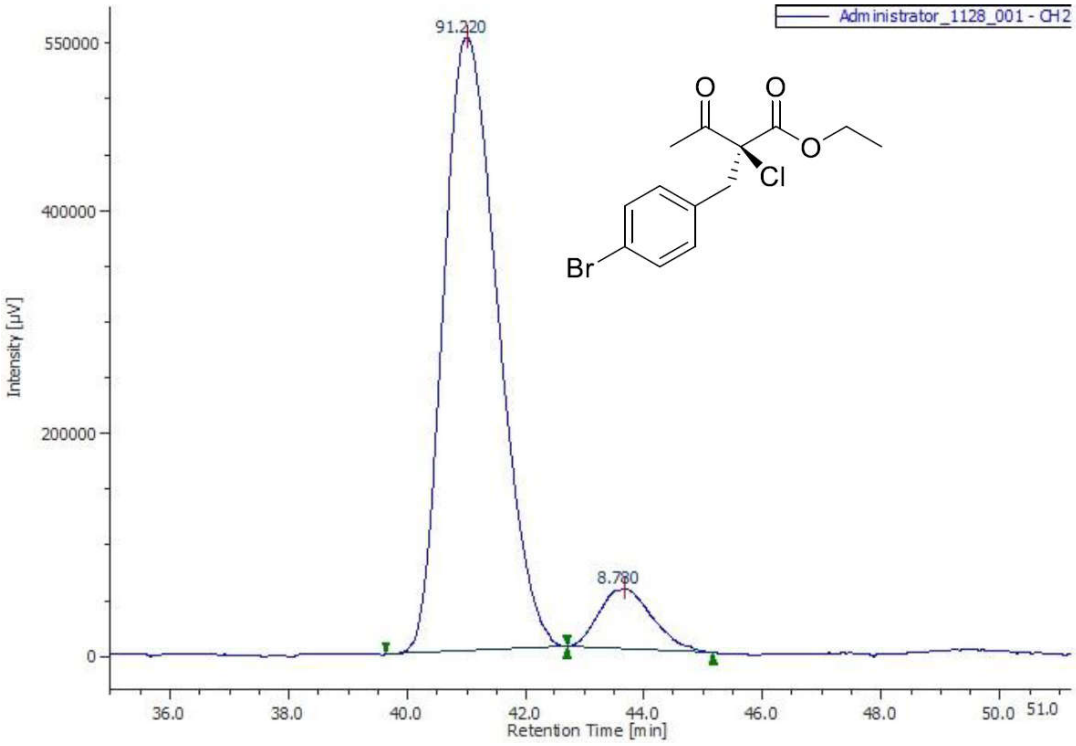


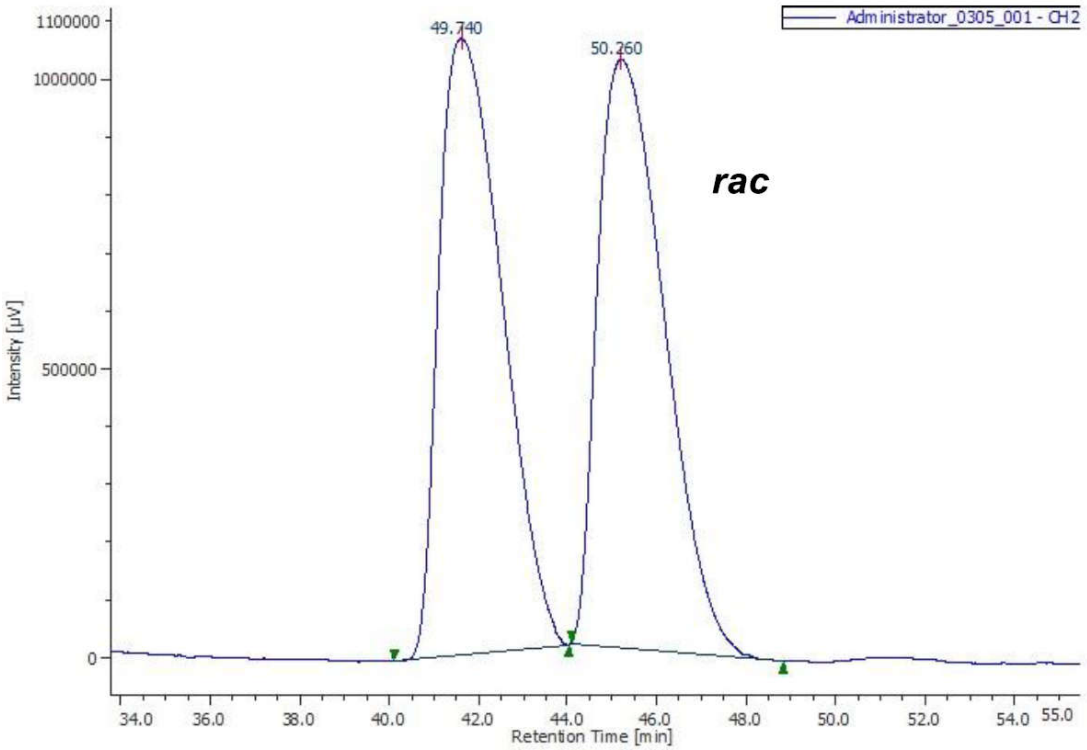
Chiralcel OJ-H column (hexane:2-propanol= 90:10, 1.0 mL/min, 254 nm).



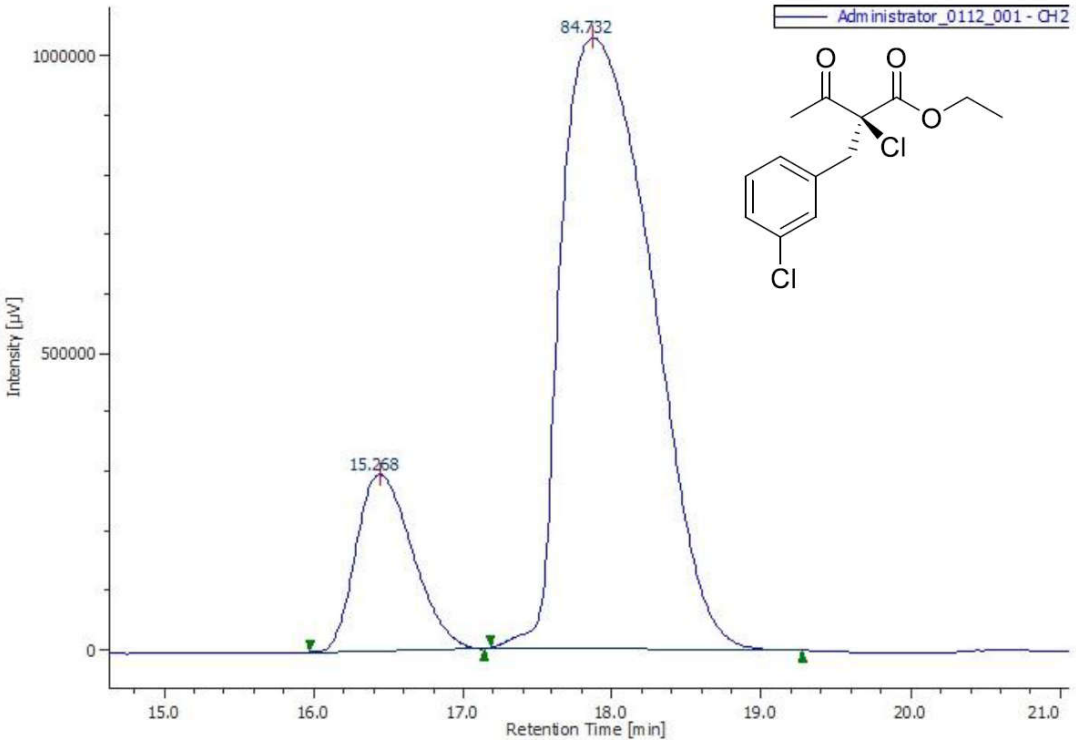


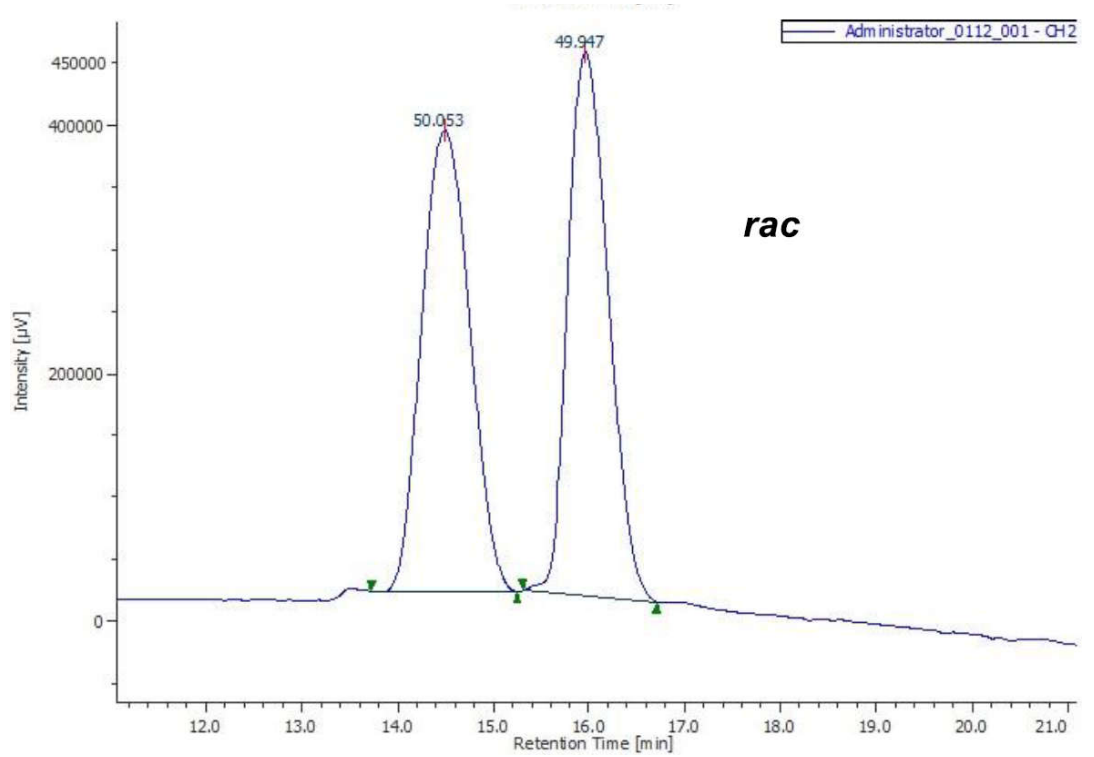
Chiralcel OJ-H column (hexane:2-propanol= 95:5, 0.5 mL/min, 210 nm)

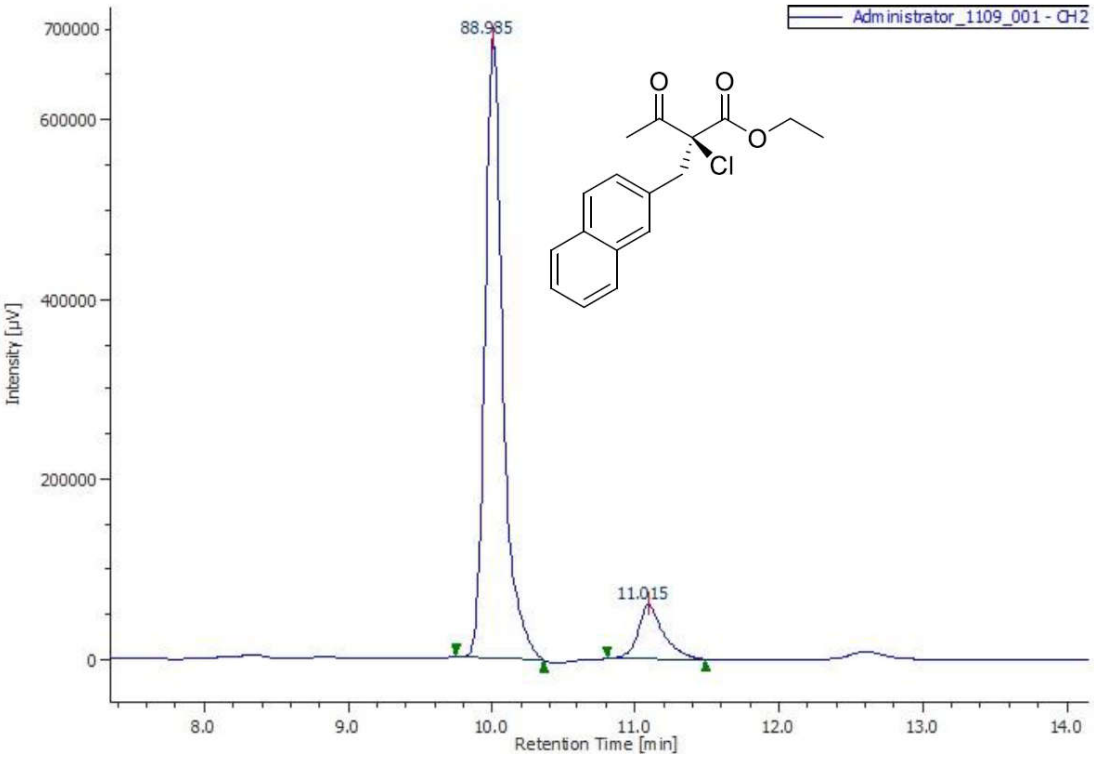


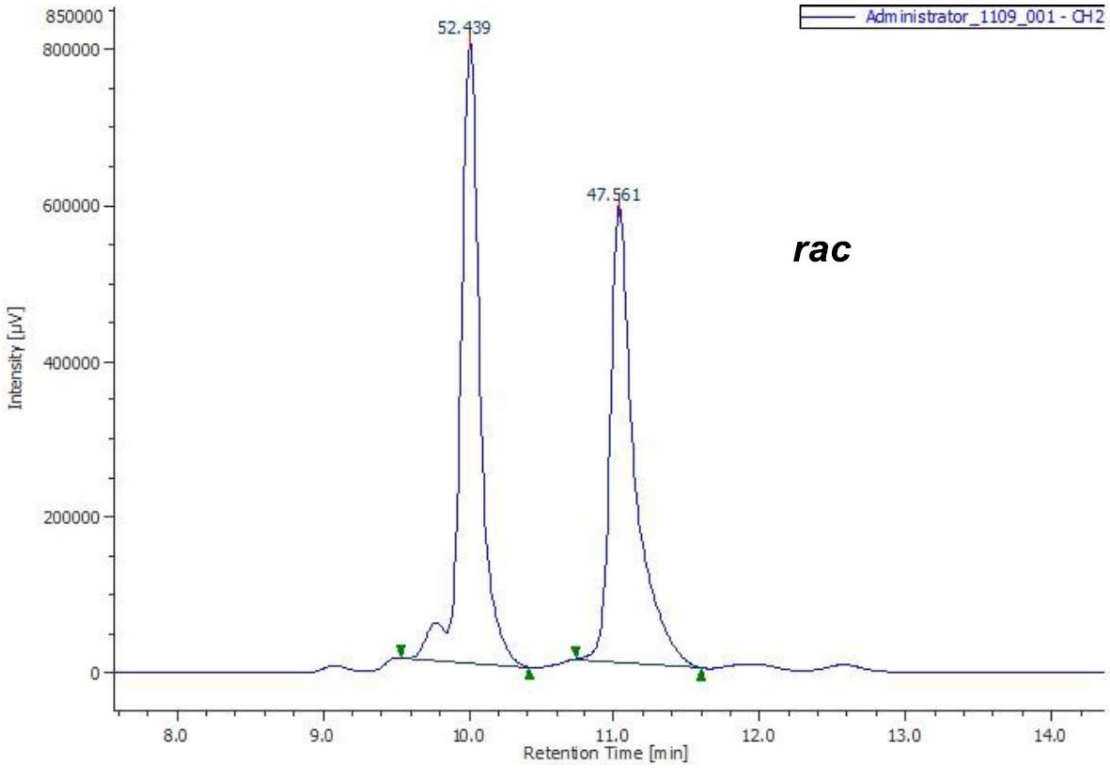


Chiralcel OJ-H column (hexane:2-propanol= 98:2, 0.3 mL/min, 210 nm)

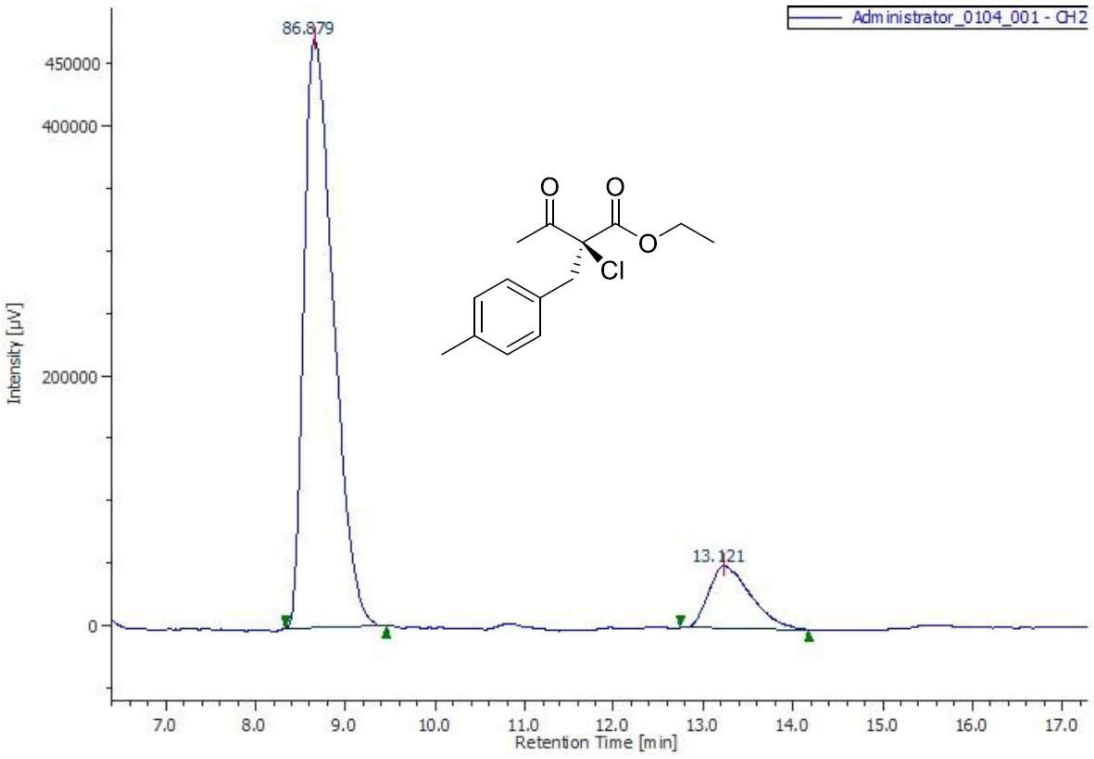


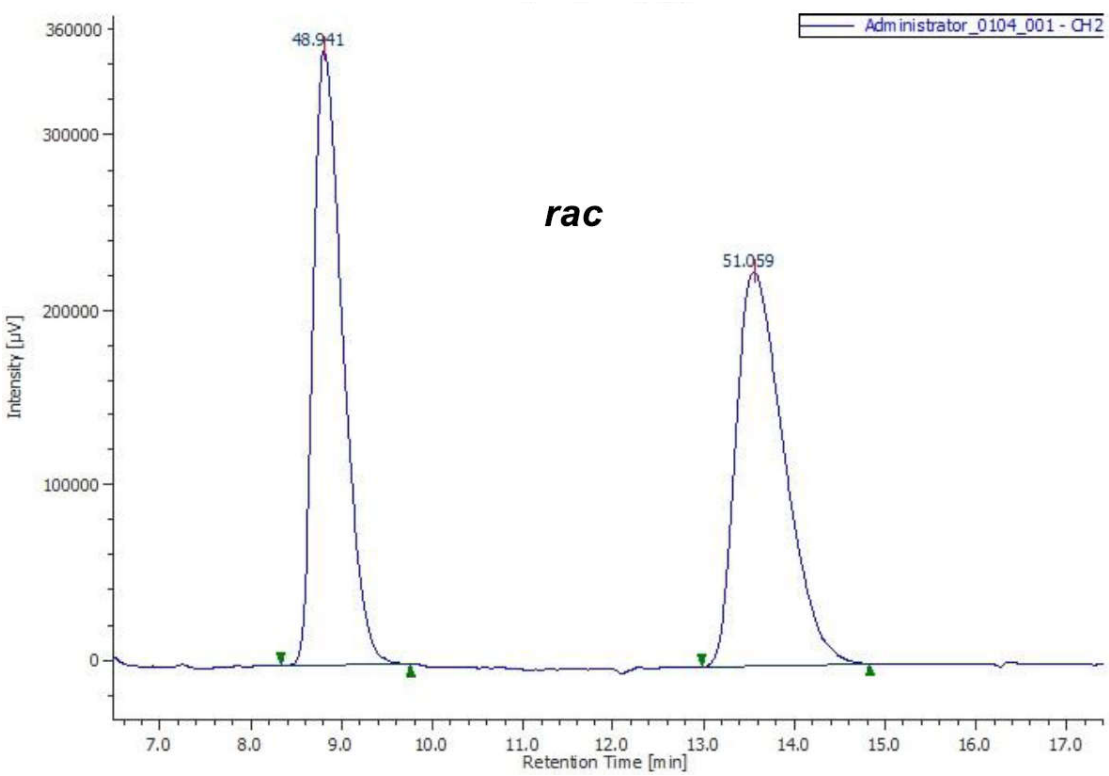

Administrator_0112_001 - CH2
49.947
50.053
rac
Intensity [µV]
Retention Time [min]


Administrator_1109_001 - CH2
88.985
11.015
O
O
O
Cl
Intensity [µV]
Retention Time [min]

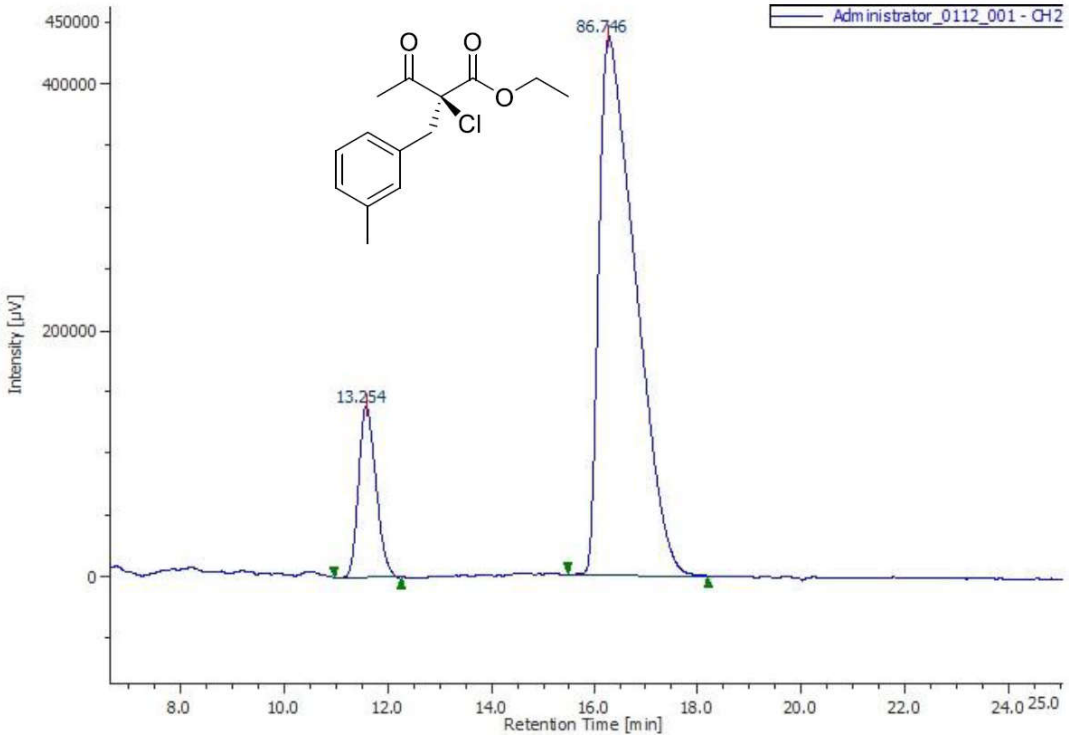


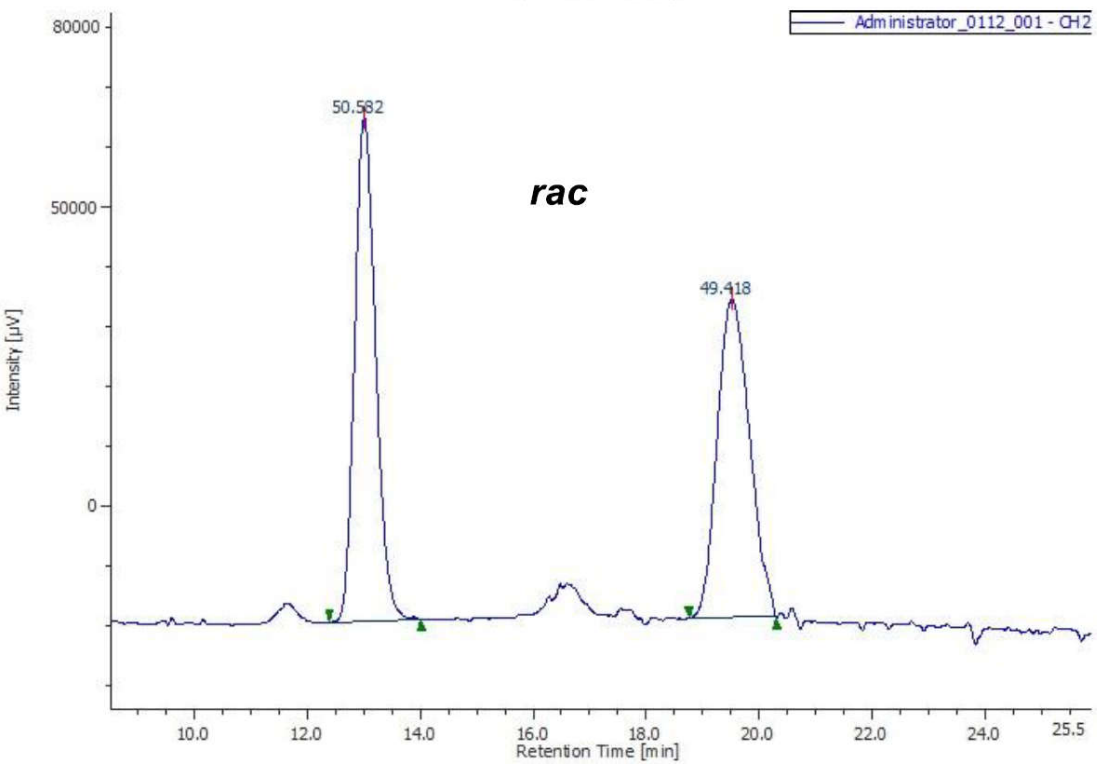
Chiralpak IC-3 column (hexane:2-propanol= 90:10, 0.5 mL/min, 254 nm)



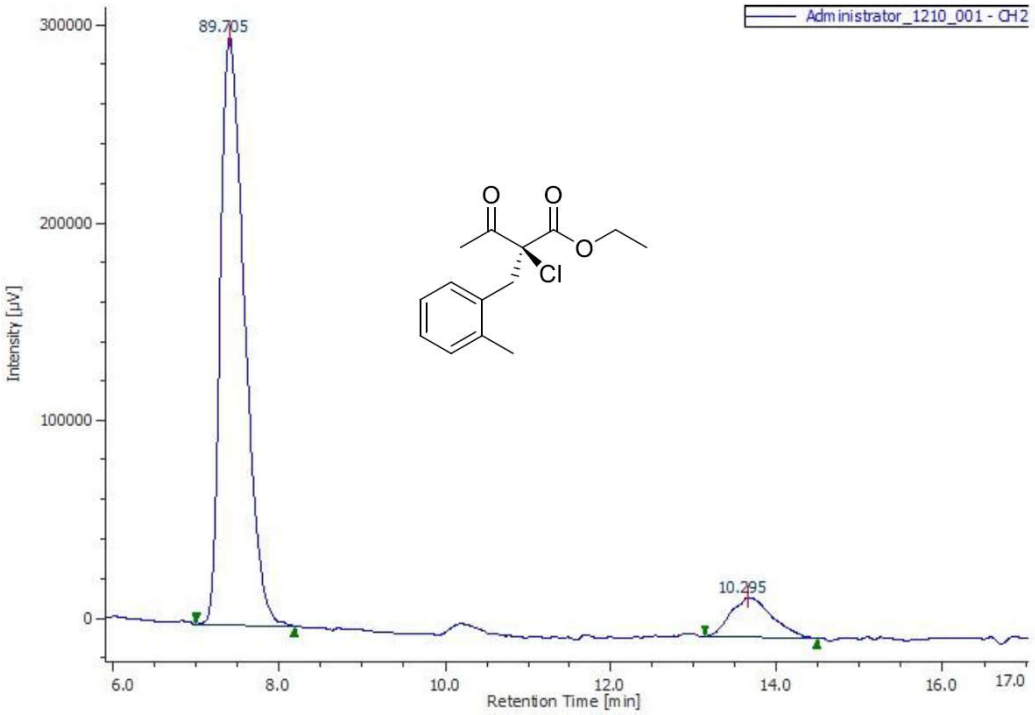


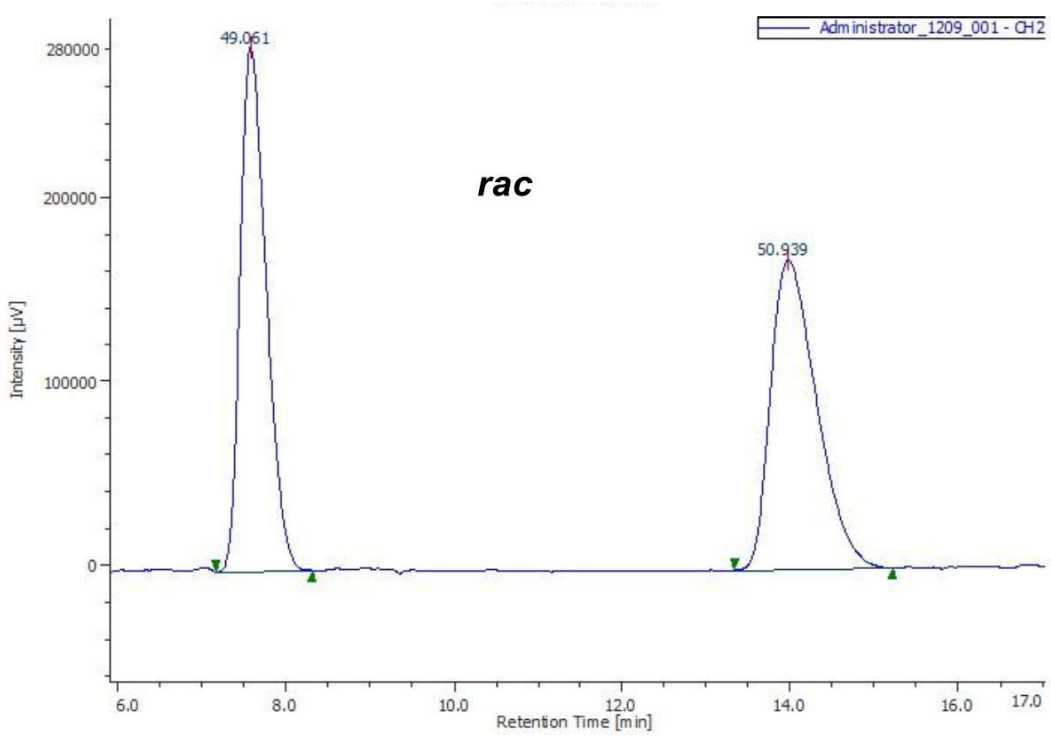
Chiralcel OJ-H column (hexane:2-propanol= 90:10, 1.0 mL/min, 210 nm)



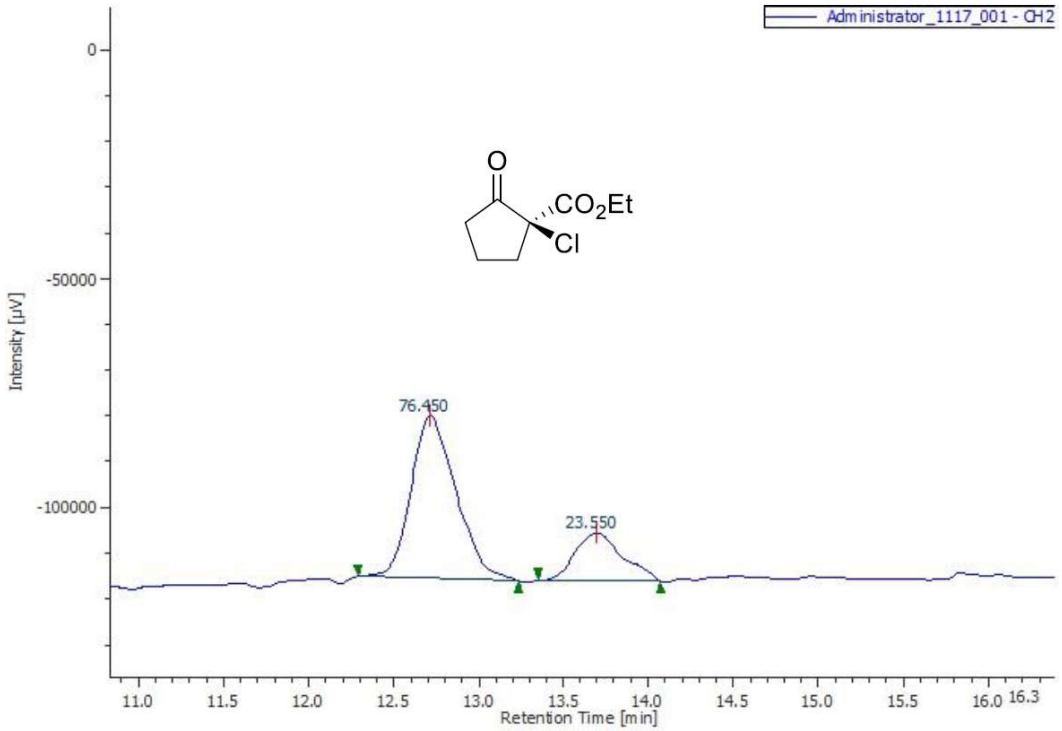


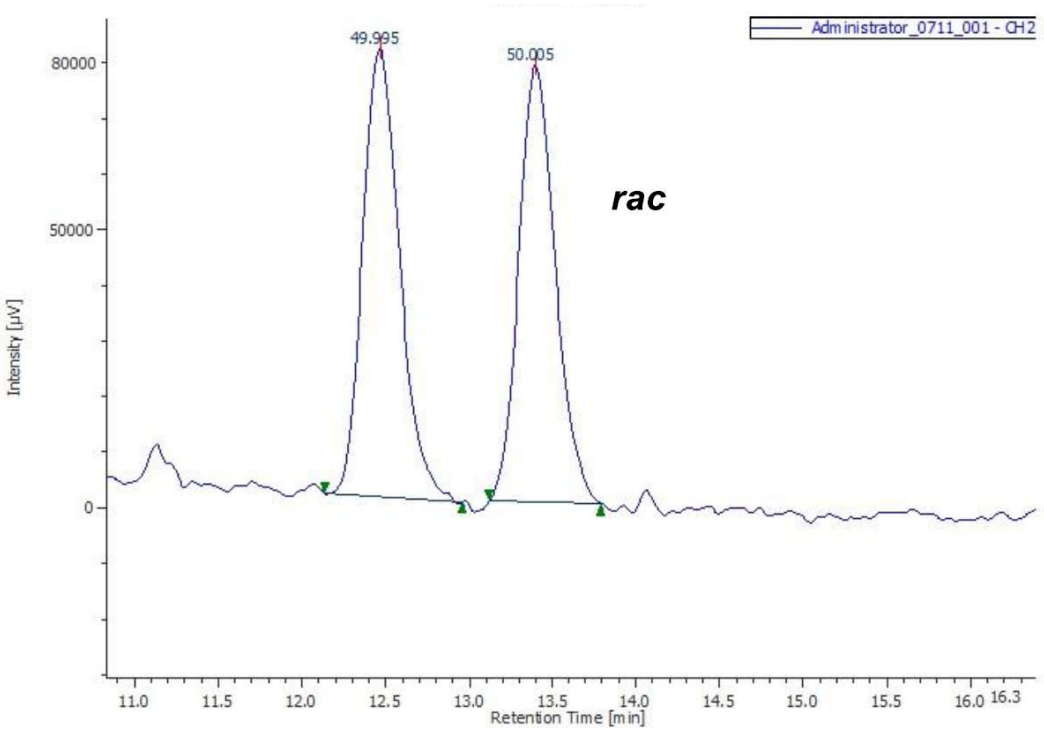
Chiralcel OJ-H column (hexane:2-propanol= 90:10, 1.0 mL/min, 210 nm)



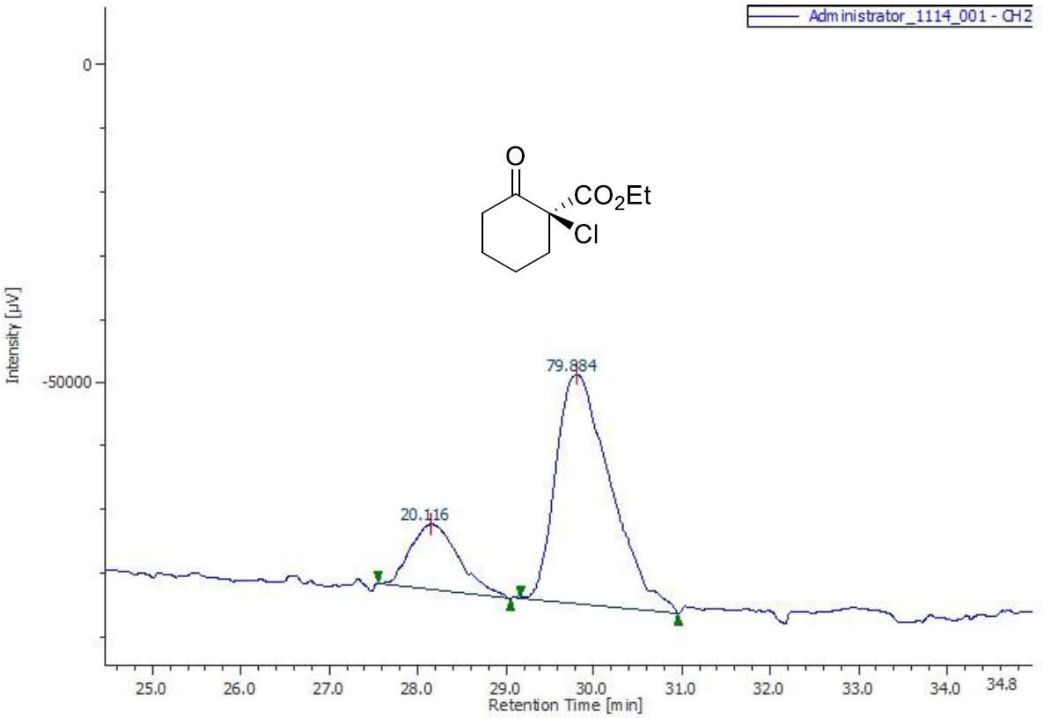


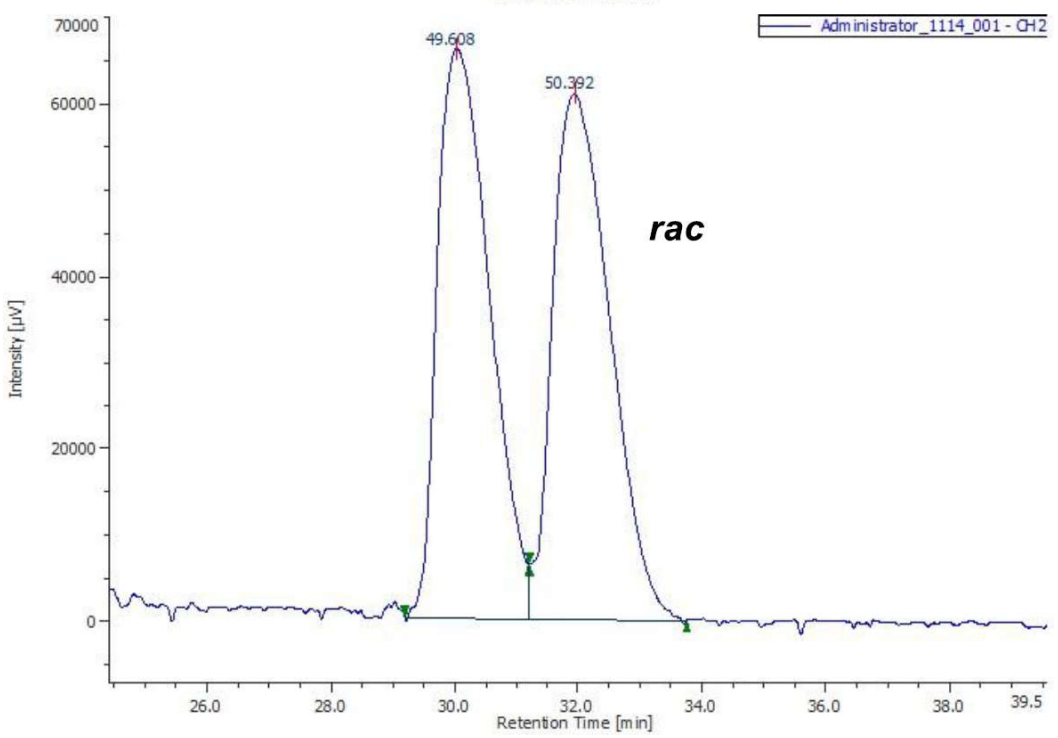
Chiralcel OJ-H column (hexane:2-propanol= 90:10, 1.0 mL/min, 210 nm)



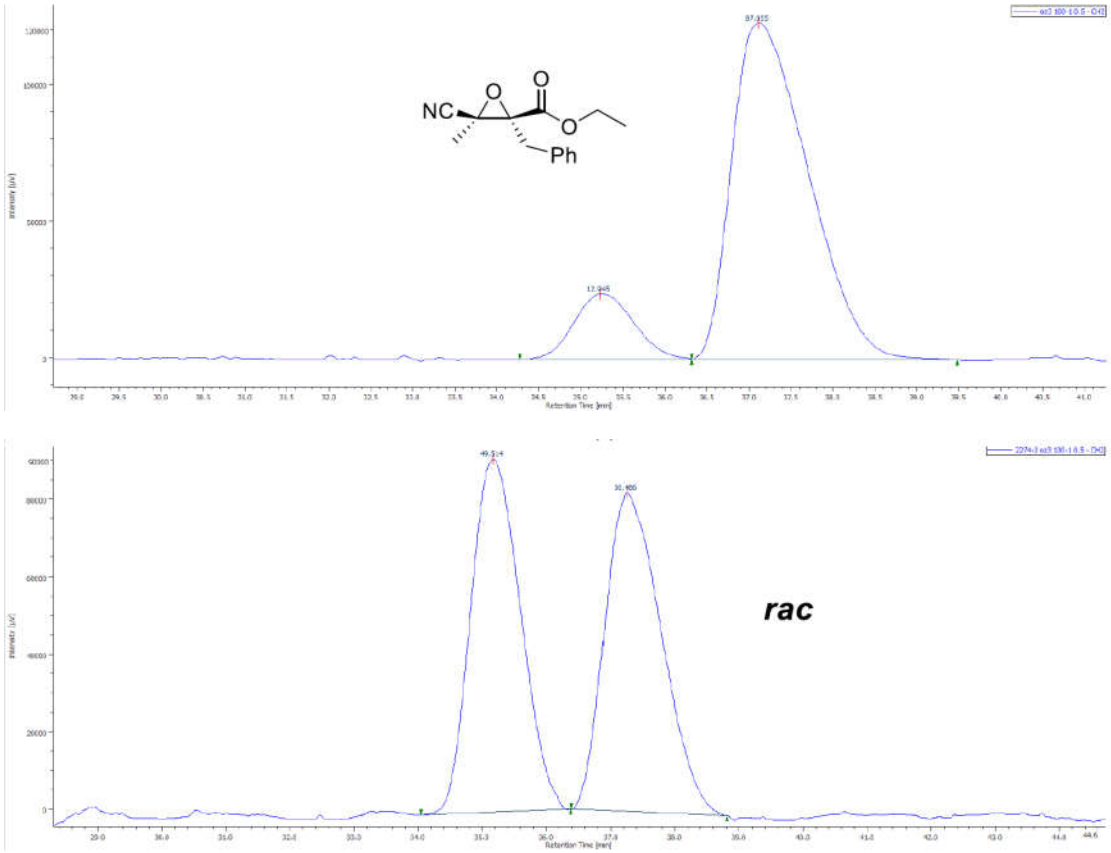


Chiralpak AS-H column (hexane:2-propanol= 90:10, 0.5 mL/min, 210 nm)

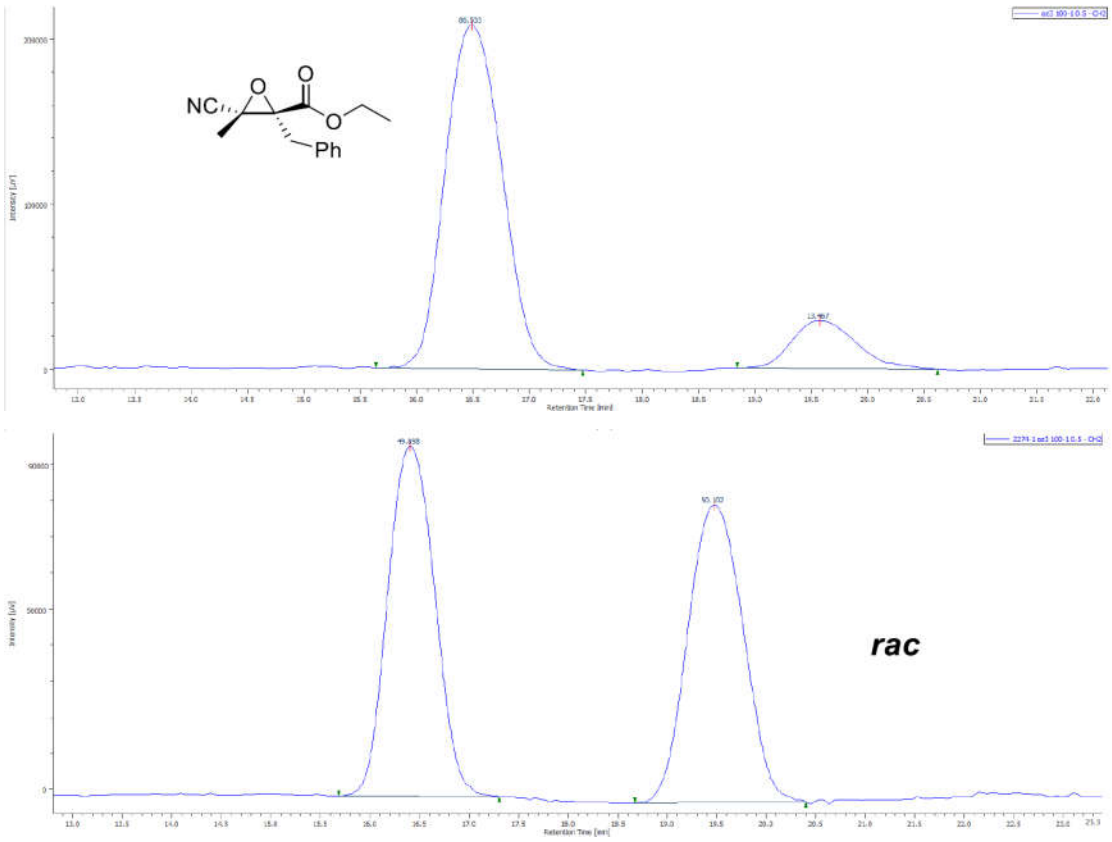




Chiralpak IC-3 column (hexane:2-propanol= 95:5, 0.5 mL/min, 210 nm).



Chiralcel OZ-3 column (hexane:2-propanol= 100:1, 0.5 mL/min, 210 nm)



Chiralcel OZ-3 column (hexane:2-propanol= 100:1, 0.5 mL/min, 210 nm)

References

1. Kamlar, M.; Císařová, I.; Veselý, J. *Org. Biomol. Chem.* **2015**, *13*, 2884.
2. Hong, S.; Shin, Y.; Jung, M.; Ha, M. W.; Park, Y.; Lee Y. J.; Shin, J.; Oh, K. B.; Lee, S. K.; Park, H. G. *Eur. J. Med. Chem.* **2015**, *96*, 218.
3. Arai, T.; Mishiro, A.; Yokoyama, N.; Suzuki, K.; Sato, H. *J. Am. Chem. Soc.* **2010**, *132*, 5338.
4. Marigo, M. Kumaragurubaran, N. Jϕrgensen, K. A. *Chem. Eur. J.* **2004**, *10*, 2133.