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Supporting Information

Peptide-Catalyzed Kinetic Resolution of Planar-Chiral Metallocenes

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General information.

^{1}H and ^{13}C NMR spectra were recorded at 400 and 100 MHz respectively on a JEOL JNM-LA400 spectrometer, and chemical shifts were referenced to internal tetramethylsilane (TMS, $\delta = 0.0$ ppm) for ^{1}H and the central line of $CDCl_3$ ($\delta = 77.0$ ppm) for ^{13}C. High-resolution FAB mass measurements were performed on a JEOL JMS-600H mass spectrometer in a positive-ionization mode using 3-nitrobenzyl alcohol as a matrix. Polyethylene glycol 400 was added to the matrix as an internal mass calibrant. HPLC traces were recorded on a Shimadzu CLASS-VP system with a Chiralcel OD-H column (25 cm) and OD-H guard (1 cm), Chiralcel OJ-H column (25 cm) and OJ-H guard (1 cm), or Chiralpak AS-H column (25 cm) and AS-H guard (1 cm). For the peptide-catalyzed kinetic resolution, solvents were degassed by a repeated cycle of freeze-pump-thaw immediately before the reaction.

Preparation of peptide catalyst 9.

The resin-supported peptide was synthesized according to the previous report.[1] As a resin, TentaGel S-NH_2 (AnaSpec, Inc., product number: 22798, 0.29 mmol/g amine loading) was used. The coupling reaction of an amino acid was performed with 3.0 equiv each of an *N*-α-9-fluorenylmethoxycarbonyl (Fmoc) amino acid, *O*-(7-azabenzotriazol-1-yl)-*N*,*N*,*N*',*N*'-tetramethyluronium hexafluorophosphate (HATU), and 1-hydroxy-7-azabenzotriazole (HOAt) along with 6.0 equiv of diisopropylethylamine in *N*,*N*-dimethylformamide (DMF) for 60 min. After washing the resin with DMF, the completion of the peptide bond formation was confirmed by the Kaiser test or the chloranil test. To remove the Fmoc group, the resin was soaked in 20% piperidine/DMF solution for 20 min and washed with DMF. This cycle, the coupling of an Fmoc-protected amino acid and removal of the Fmoc group, was repeated until an intended sequence was introduced on the resin. After the Fmoc group on the terminal prolyl residue was removed, the resin was washed with DMF and dichloromethane (DCM), and dried under reduced pressure. To convert the supported peptide to the salt of hydrogen chloride (HCl), the resin was soaked in 1,4-dioxane solution of HCl (4 M) for a few minutes. Then, the resin was washed successively with DCM, DMF, and DCM, and dried under reduced pressure.

Typical procedure for the kinetic resolution by hydrogenation (Tables 1 and 2).

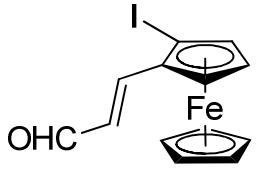
Water (666 μL) was added slowly at room temperature to a two-necked round-bottom flask that contained aldehyde **1a** (25 μmol), Hantzsch ester **3** (75 μmol), 20 mol% of resin-supported peptide, and THF (333 μL) with stirring by a magnetic stirrer under argon atmosphere. The mixture was stirred for 24 h at 30 °C. Then, the peptide catalyst was filtered off and washed with chloroform. After removal of the solvent under reduced pressure, the residue was purified by preparative TLC (hexanes/ethyl acetate 4:1) to afford starting material **1a** and product **2a**.

Typical procedure for the kinetic resolution by the addition of nitromethane (Table 3).

Water (0.40 mL) was added dropwise over 10 min at 30 °C to a two-necked round-bottom flask that contained aldehyde **1** (30 μmol), resin-supported peptide **9** (30 mg, 6.0 μmol of the terminal prolyl group), and 1,4-dioxane (0.20 mL) with stirring at 180 rpm by a magnetic stirrer under argon atmosphere. Nitromethane (150 μmol) was added, and the resulting mixture was stirred for the given time. Then, the peptide catalyst was filtered off and washed with methanol and chloroform. After removal of the solvent under reduced pressure, the residue was purified by preparative TLC under nitrogen atmosphere using dichloromethane as eluent to afford starting material **1** and product **10**. The minor diastereomer of **10** was removed by preparative TLC using hexanes/ethyl acetate (4:1) as eluent for an HPLC analysis.

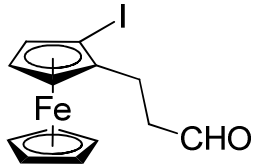
In Scheme 1, methanol was used instead of 1,4-dioxane as an organic co-solvent. The reaction was performed at 20 °C for 2 h.

Spectroscopic data for the compounds obtained by the kinetic resolution.



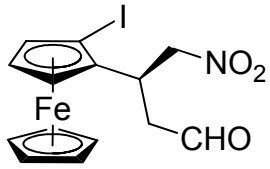
(S_p)-3-(2-Iodoferrocenyl)prop-2-enal (1a).

^{1}H NMR ($CDCl_3$) δ 9.66 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 15.6 Hz, 1H), 6.46 (dd, J = 15.6, 8.0 Hz, 1H), 4.81–4.77 (m, 1H), 4.71–4.67 (m, 1H), 4.65–4.61 (m, 1H), 4.23–4.13 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 193.11, 153.93, 127.55, 78.72, 78.21, 72.97, 72.42, 65.64, 46.45; HRMS (FAB) m/z: calculated for $C_{13}H_{11}FeIO$ $[M]^+$: 365.9204, found 365.9209. Enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, hexane/2-propanol 90:10, 1.0 mL min^{-1}): t_R = 10.6 min (minor), 12.6 min (major).



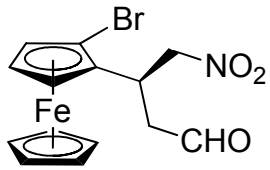
(R_p)-3-(2-Iodoferrocenyl)propanal (2a).

^{1}H NMR ($CDCl_3$) δ 9.81 (s, 1H), 4.41–4.39 (m, 1H), 4.16–4.12 (m, 7H), 2.82–2.55 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 201.53, 88.14, 74.22, 71.58, 68.21, 67.10, 45.06, 44.75, 22.82; HRMS (FAB) m/z: calculated for $C_{13}H_{13}FeIO$ $[M]^+$: 367.9361, found 367.9360. Enantiomeric excess was determined by HPLC analysis (Chiralpak AS-H, hexane/2-propanol 90:10, 1.0 mL min^{-1}): t_R = 11.2 min (minor), 12.1 min (major).



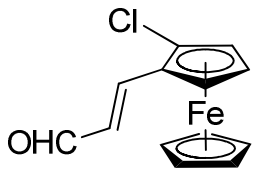
(*S*,*R*$_p$)-3-(2-Iodoferrocenyl)-4-nitrobutanal (10a).

^{1}H NMR ($CDCl_3$) δ 9.97 (s, 1H), 4.65 (dd, *J* = 12.2, 3.8 Hz, 1H), 4.55–4.53 (m, 1H), 4.51 (dd, *J* = 12.2, 6.8 Hz, 1H), 4.26 (brt, *J* = 2.0 Hz 1H), 4.17–4.14 (m, 5H), 4.07–4.05 (m, 1H), 3.88–3.81 (m, 1H), 3.31 (dd, *J* = 18.8, 9.2 Hz, 1H), 3.22 (dd, *J* = 18.8, 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 199.21, 87.59, 78.42, 75.07, 71.79, 69.07, 65.95, 45.23, 43.28, 32.61; HRMS (FAB) *m*/*z*: calculated for $C_{14}H_{14}FeINO_3$ $[M]^+$: 426.9368, found 426.9374. Enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, hexane/2-propanol 70:30, 1.0 mL min^{-1}): t_R = 49.5 min (major), 57.6 min (minor).



(*S*,*R*$_p$)-3-(2-Bromoferrocenyl)-4-nitrobutanal (10b).

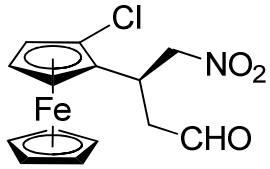
^{1}H NMR ($CDCl_3$) δ 9.96 (s, 1H), 4.69 (dd, *J* = 11.9, 3.8 Hz, 1H), 4.55 (dd, *J* = 11.9, 6.8 Hz, 1H), 4.54–4.52 (m, 1H), 4.20–4.17 (m, 5H), 4.15 (brt, *J* = 2.6 Hz 1H), 3.98–3.91 (m, 1H), 3.88–3.81 (m, 1H), 3.28 (dd, *J* = 18.8, 8.8 Hz, 1H), 3.20 (dd, *J* = 18.8, 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 199.22, 85.17, 78.61, 78.15, 71.36, 70.64, 66.53, 65.44, 45.07, 31.29; HRMS (FAB) *m*/*z*: calculated for $C_{14}H_{14}BrFeNO_3$ $[M]^+$: 378.9506, found 378.9504. Enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, hexane/2-propanol 70:30, 1.0 mL min^{-1}): t_R = 47.8 min (major), 52.9 min (minor).



(*S*$_p$)-3-(2-Chloroferrocenyl)prop-2-enal (1c).

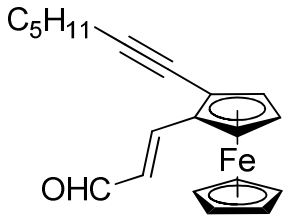
^{1}H NMR ($CDCl_3$) δ 9.65 (d, *J* = 8.0 Hz, 1H), 7.62 (d, *J* = 15.6 Hz, 1H), 6.49 (dd, *J* = 15.6, 8.0 Hz, 1H), 4.77–4.73 (m, 1H), 4.59–4.55 (m, 1H), 4.47–4.43 (m, 1H), 4.30–4.19 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 193.23, 151.11, 127.53, 94.65, 74.99, 72.22, 71.26, 68.49, 64.77; HRMS (FAB) *m*/*z*: calculated for $C_{13}H_{11}ClFeO$ $[M]^+$: 273.9848, found 273.9842. Enantiomeric excess was determined

by HPLC analysis (Chiralcel OD-H, hexane/2-propanol 90:10, 1.0 mL min^{-1}): t_R = 34.3 min (minor), 37.1 min (major).



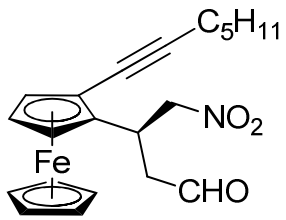
(*S*,*R*$_p$)-3-(2-Chloroferrocenyl)-4-nitrobutanal (10c).

^{1}H NMR ($CDCl_3$) δ 9.95 (s, 1H), 4.70 (dd, *J* = 12.2, 3.8 Hz, 1H), 4.56 (dd, *J* = 12.2, 6.8 Hz, 1H), 4.51–4.49 (m, 1H), 4.21–4.18 (m, 5H), 4.08 (brt, *J* = 2.6 Hz 1H), 3.98–3.81 (m, 2H), 3.25 (dd, *J* = 18.8, 8.4 Hz, 1H), 3.18 (dd, *J* = 18.8, 4.8 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 199.15, 91.86, 83.87, 78.06, 71.00, 68.36, 65.09, 64.96, 45.11, 30.65; HRMS (FAB) *m*/*z*: calculated for $C_{14}H_{14}ClFeNO_3$ $[M]^+$: 335.0012, found 335.0015. Enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, hexane/2-propanol 70:30, 1.0 mL min^{-1}): t_R = 48.9 min (major), 53.7 min (minor).



(*S*$_p$)-3-(2-Heptyn-1-ylferrocenyl)prop-2-enal (1d).

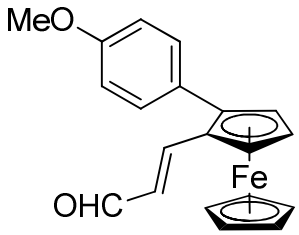
^{1}H NMR ($CDCl_3$) δ 9.63 (d, *J* = 8.0 Hz, 1H), 7.61 (d, *J* = 16.0 Hz, 1H), 6.57 (dd, *J* = 16.0, 8.0 Hz, 1H), 4.72–4.70 (m, 1H), 4.62–4.60 (m, 1H), 4.51–4.49 (m, 1H), 4.19–4.16 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 193.55, 153.63, 126.74, 91.29, 78.55, 75.89, 74.47, 71.74, 70.96, 69.70, 67.28, 31.13, 28.47, 22.21, 19.59, 14.04; HRMS (FAB) *m*/*z*: calculated for $C_{20}H_{22}FeO$ $[M]^+$: 334.1020, found 334.1020. Enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, hexane/2-propanol 90:10, 1.0 mL min^{-1}): t_R = 6.6 min (minor), 7.4 min (major).



(*S*,*R*$_p$)-3-(2-Heptyn-1-ylferrocenyl)-4-nitrobutanal (10d).

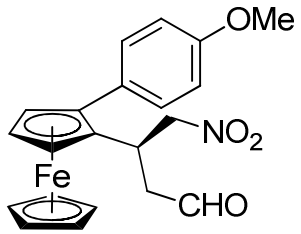
^{1}H NMR ($CDCl_3$) δ 9.93 (s, 1H), 4.79 (dd, *J* = 12.0, 3.6 Hz, 1H), 4.60 (dd, *J* = 12.0, 7.4 Hz, 1H), 4.44–4.41 (m, 1H), 4.17–4. 12 (m, 6H), 4.05–3.95 (m, 2H), 3.15 (d, *J* = 6.4 Hz, 2H), 2.33 (t, *J* = 7.2

Hz, 2H), 1.64–1.57 (m, 2H), 1.48–1.34 (m, 4H), 0.64 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 199.55, 90.68, 88.17, 78.70, 76.11, 71.41, 70.48, 67.32, 67.10, 66.14, 45.42, 31.95, 31.16, 28.50, 22.21, 19.55, 14.02; HRMS (FAB) *m*/*z*: calculated for $C_{21}H_{25}FeNO_3$ $[M]^+$: 395.1184, found 395.1187. Enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, hexane/2-propanol 70:30, 1.0 mL min^{-1}): t_R = 18.9 min (minor), 26.3 min (major).



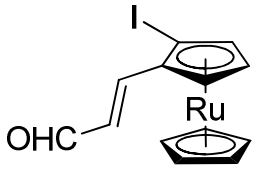
(S_p)-3-[2-(4-Methoxyphenyl)ferrocenyl]prop-2-enal (1e).

^{1}H NMR ($CDCl_3$) δ 9.56 (d, J = 8.0 Hz, 1H), 7.67 (d, J = 15.6 Hz, 1H), 7.66–40 (m, 2H), 6.96–92 (m, 2H), 6.43 (dd, J = 15.6, 8.0 Hz, 1H), 4.76–4.71 (m, 2H), 4.62–4.60 (m, 1H), 4.16–4.13 (m, 5H), 3.86 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 193.43, 158.84, 154.24, 130.79, 128.55, 126.66, 113.85, 91.73, 75.86, 73.14, 71.27, 70.55, 66.46, 55.36; HRMS (FAB) *m*/*z*: calculated for $C_{20}H_{18}FeO_2$ $[M]^+$: 346.0656, found 346.0656. Enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, hexane/2-propanol 90:10, 1.0 mL min^{-1}): t_R = 15.2 min (major), 23.6 min (minor).



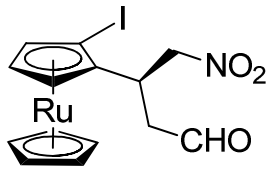
(S,R_p)-3-[2-(4-Methoxyphenyl)ferrocenyl]-4-nitrobutanal (10e).

^{1}H NMR ($CDCl_3$) δ 10.01 (s, 1H), 7.48–7.44 (m, 2H), 6.94–6.90 (m, 2H), 4.43–4.41 (m, 1H), 4.27 (brt, J = 2.6 Hz, 1H), 4.22 (dd, J = 11.7, 4.2 Hz, 1H), 4.18–4.12 (m, 6H), 4.05–4.03 (m, 1H), 4.01 (dd, J = 11.7, 6.8 Hz, 1H), 3.85 (s, 3H), 3.23 (dd, J = 18.8, 5.6 Hz, 1H), 3.18 (dd, J = 18.8, 8.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 199.66, 158.74, 130.64, 128.65, 113.85, 87.98, 84.89, 78.62, 70.00, 69.35, 67.28, 66.26, 55.30, 45.67, 30.49; HRMS (FAB) *m*/*z*: calculated for $C_{21}H_{21}FeNO_4$ $[M]^+$: 407.0820, found 407.0833. Enantiomeric excess was determined by HPLC analysis (Chiralpak AS-H, hexane/2-propanol 70:30, 1.0 mL min^{-1}): t_R = 21.7 min (major), 32.3 min (minor).



(S_p)-3-(2-Iodoruthenocenyl)prop-2-enal (1f).

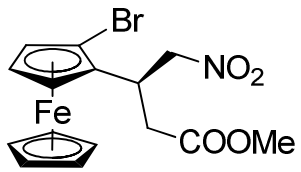
^{1}H NMR ($CDCl_3$) δ 9.60 (d, J = 8.0 Hz, 1H), 7.41 (d, J = 15.6 Hz, 1H), 6.39 (dd, J = 15.6, 8.0 Hz, 1H), 5.11–5.09 (m, 1H), 4.99–4.97 (m, 1H), 4.83–4.81 (m, 1H), 4.60–4.56 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 193.41, 152.44, 126.85, 83.80, 80.24, 74.75, 74.00, 68.12, 41.19; HRMS (FAB) m/z: calculated for $C_{13}H_{11}IORu$ $[M]^+$: 411.8898, found 411.8900. Enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H, hexane/2-propanol 90:10, 1.0 mL min^{-1}): t_R = 9.4 min (minor), 10.6 min (major).



(S,R_p)-3-(2-Iodoruthenocenyl)-4-nitrobutanal (10f).

^{1}H NMR ($CDCl_3$) δ 9.85 (s, 1H), 4.90–4.88 (m, 1H), 4.69 (dd, J = 12.2, 4.0 Hz, 1H), 4.61 (dd, J = 12.2, 6.8 Hz, 1H), 4.55–4.54 (m, 6H), 4.43–4.41 (m, 1H), 3.74–3.65 (m, 1H), 3.12 (dd, J = 18.6, 7.6 Hz, 1H), 2.97 (dd, J = 18.6, 5.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 199.14, 92.07, 78.63, 77.78, 73.96, 71.82, 69.39, 46.28, 39.14, 32.72; HRMS (FAB) m/z: calculated for $C_{13}H_{11}INO_3Ru$ $[M]^+$: 472.9062, found 472.9060. Enantiomeric excess was determined by HPLC analysis (Chiralcel OJ-H, hexane/2-propanol 70:30, 1.0 mL min^{-1}): t_R = 56.0 min (major), 72.0 min (minor).

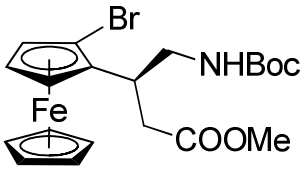
Procedure for the transformation into planar-chiral derivatives.



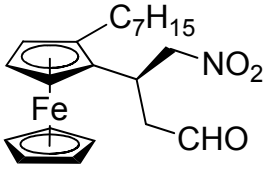
(S,R_p)-3-(2-Bromoferrocenyl)-4-nitrobutanoic acid methyl ester (11).

To a solution of compound **10b** (6.3 mg) in *t*-butyl alcohol (1.2 mL) and water (0.3 mL), 16 equiv of 2-methyl-2-butene, 5.0 equiv of sodium dihydrogen phosphate dihydrate, and 3.0 equiv of sodium chlorite were added successively under argon atmosphere. After stirring the mixture for 10 min, brine (5 mL) was added. The resulting mixture was extracted with ethyl acetate. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. After removal of the solvent under reduced pressure, the residue was dissolved in methanol (0.5 mL) and toluene (3.5 mL). To

this solution, 1.2 equiv of trimethylsilyldiazomethane (0.6 M in *n*-hexane) was added. After stirring the mixture for 10 min, the solvent was removed under the reduced pressure. The residue was purified by preparative TLC (hexanes/dichloromethane 4:1) to afford **11** (5.9 mg, 87%). ^{1}H NMR ($CDCl_3$) δ 4.72 (dd, *J* = 12.4, 3.8 Hz, 1H), 4.62 (dd, *J* = 12.4, 6.4 Hz, 1H), 4.53–4.50 (m, 1H), 4.23–4.18 (m, 5H), 4.16–4.13 (m, 1H), 4.03–4.00 (m, 1H), 3.80 (s, 3H), 3.12 (dd, *J* = 16.8, 4.2 Hz, 1H), 3.02 (dd, *J* = 16.8, 9.4 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 171.89, 85.41, 78.71, 78.05, 71.38, 70.51, 66.48, 65.29, 52.14, 35.60, 33.63; HRMS (FAB) *m*/*z*: calculated for $C_{15}H_{16}BrFeNO_4$ $[M]^+$: 408.9612, found 408.9602.



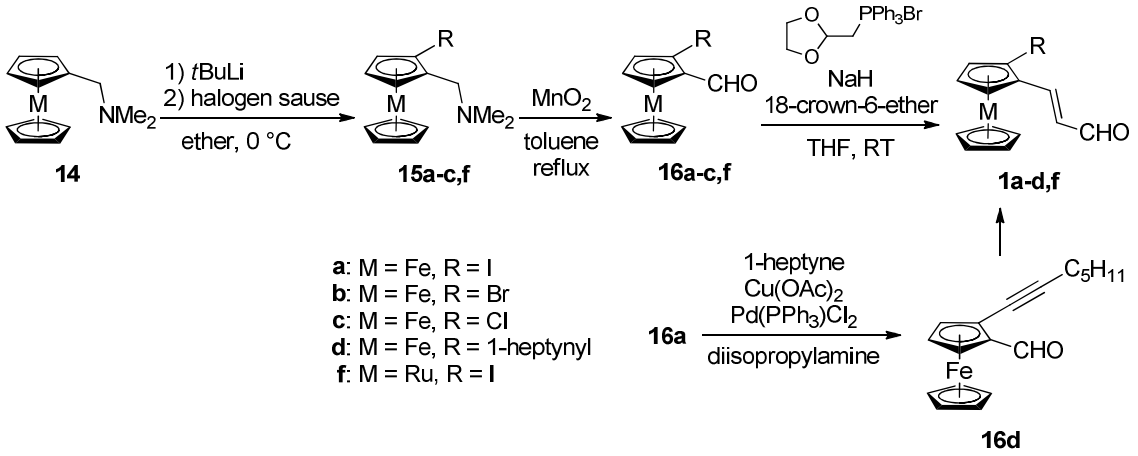
(*S*,*R*$_p$)-3-(2-Bromoferrocenyl)-4-(*N*-*tert*-butoxycarbonyl)aminobutanoic acid methyl ester (12).
To a solution of **11** (5.0 mg) in THF (50 μL) and acetic acid (50 μL), 15 equiv of Zn powder was added three times with 5 min intervals under argon atmosphere. The resulting mixture was stirred for 1 h at room temperature. This was cooled to 0 °C, and THF (50 μL) and water (100 μL) were added. To this solution, sodium hydrogen carbonate (183 mg) was added in four portions. Then, the mixture was warmed to room temperature and 1.5 equiv of di-*tert*-butyl dicarbonate was added. After stirring the mixture for 1 h, water was added. The mixture was extracted with ethyl acetate, and the organic layer was washed with water two times and dried over anhydrous magnesium sulfate. After removal of the solvent under reduced pressure, the residue was purified by preparative TLC (dichloromethane) to afford **12** (5.2 mg, 89%). ^{1}H NMR ($CDCl_3$) δ 4.50 (brs, 1H), 4.46–4.44 (m, 1H), 4.20–4.15 (m, 5H), 4.11–4.08 (m, 1H), 3.95–3.92 (m, 1H), 3.79 (s, 3H), 3.38–3.26 (m, 2H), 3.23–3.13 (m, 1H), 2.97 (dd, *J* = 15.6, 2.8 Hz, 1H), 2.67 (dd, *J* = 15.6, 9.8 Hz, 1H), 1.39 (s, 9H); ^{13}C NMR ($CDCl_3$) δ 173.06, 155.80, 88.56, 79.15, 79.08, 71.16, 70.02, 66.05, 64.50, 51.96, 44.77, 36.82, 34.71, 28.36; HRMS (FAB) *m*/*z*: calculated for $C_{20}H_{26}BrFeNO_4$ $[M]^+$: 479.0395, found 479.0405.



(*S*,*R*$_p$)-3-(2-Heptylferrocenyl)-4-nitrobutanal (13).
To a solution of **10d** (5.8 mg) in ethyl acetate (0.5 mL), palladium on carbon (10 w%, 2.6 mg) was added. This mixture was stirred under hydrogen atmosphere for 30 min at room temperature. The resulting mixture was purified by preparative TLC (dichloromethane) to afford **13** (5.1 mg, 87%). ^{1}H

NMR ($CDCl_3$) δ 9.96 (s, 1H), 4.48 (dd, J = 11.6, 4.0 Hz, 1H), 4.35 (dd, J = 11.6, 7.4 Hz, 1H), 4.19–4.16 (m, 1H), 4.08–4.02 (m, 6H), 3.91–3.81 (m, 2H), 3.32 (dd, J = 19.0, 4.8 Hz, 1H), 3.25 (dd, J = 19.0, 8.4 Hz, 1H), 2.45–2.35 (m, 1H), 2.33–2.24 (m, 1H), 1.62–1.50 (m, 2H), 1.43–1.28 (m, 8H), 0.91 (t, J = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$) δ 199.67, 87.75, 85.55, 79.38, 69.24, 68.30, 66.38, 65.65, 46.48, 31.84, 30.64, 30.45, 29.99, 29.22, 27.62, 22.65, 14.13; HRMS (FAB) *m/z*: calculated for $C_{21}H_{21}FeNO_3$ $[M]^+$: 399.1497, found 399.1496.

Preparation of substrates 1a-f.

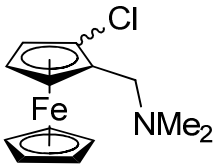


Typical procedure for the conversion of 14 to 15.[2]

To a solution of dimethylaminomethylferrocene (**14**, 1.2 mL) in diethyl ether (10 mL), 0.85 equiv of *t*-butyllithium (1.64 M in *n*-pentane) was added dropwise at 0 °C under argon atmosphere. After stirring the solution for 10 min, 1.05 equiv of 1,2-diiodoethane was added. This solution was stirred for 10 min, warmed to room temperature, and stirred for 30 min. Then, water (10 mL) was added, and the resulting mixture was extracted with diethyl ether. The organic layer was washed with water and dried over anhydrous magnesium sulfate. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexanes/ethyl acetate/triethylamine 50:46:4) to afford 1-dimethylaminomethyl-2-iodoferrocene (**15a**, 1.3 g, 59% yield).

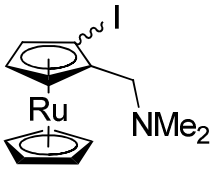
For the synthesis of 1-bromo-2-dimethylaminomethylferrocene (**15b**), 1.5 equiv of *t*-butyllithium and 2.0 equiv of 1,1,2,2-tetrabromoethane instead of 1,2-diiodoethane were used. For the synthesis of 1-chloro-2-dimthylaminomethyl ferrocene (**15c**), 2.0 equiv of *t*-butyllithium and 1.5 equiv of hexachloroethane instead of 1,2-diiodoethane were used.

The spectroscopic data for **15a**[3] and **15b**[4] were reported.



1-Chloro-2-dimethylaminomethylferrocene (15c).

^{1}H NMR ($CDCl_3$) δ 4.42–4.39 (m, 1H), 4.21–4.10 (m, 6H), 4.06–4.03 (m, 1H), 3.53 (d, J = 13.0 Hz, 1H), 3.69 (d, J = 13.0 Hz, 1H), 2.22 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 93.67, 80.80, 70.73, 67.86, 64.96, 56.12, 44.85; HRMS (FAB) *m*/*z*: calculated for $C_{13}H_{16}ClFeN$ $[M + H]^+$: 278.0394, found 278.0412.



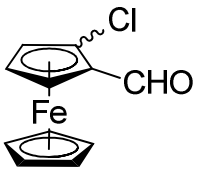
1-Dimethylaminomethyl-2-iodoruthenocene (15f).

^{1}H NMR ($CDCl_3$) δ 4.85–4.82 (m, 1H), 4.65–4.62 (m, 1H), 4.56–4.50 (m, 6H), 3.24 (d, J = 13.2 Hz, 1H), 3.19 (d, J = 13.2 Hz, 1H), 2.28 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 89.17, 77.62, 73.43, 71.66, 71.58, 58.58, 45.15, 41.50; HRMS (FAB) *m*/*z*: calculated for $C_{13}H_{16}INRu$ $[M]^+$: 414.9371, found 414.9377.

Typical procedure for the conversion of 15 to 16.[5]

To a solution of 1-dimethylaminomethyl-2-iodoferrocene (**15a**, 0.59 g) in toluene (15 mL), manganese dioxide (3.2 g) was added. The resulting mixture was refluxed for 90 min under argon atmosphere. After cooling to room temperature, the solid was filtered off, and washed with chloroform. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (hexanes/ethyl acetate 4:1) to afford 1-formyl-2-iodoferrocene (**16a**, 0.26 g, 48%).

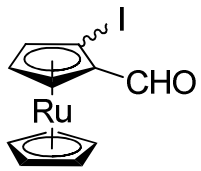
The spectroscopic data for **16a** and **16b** were reported.[6]



1-Chloro-2-formylferrocene (16c).

^{1}H NMR ($CDCl_3$) δ 10.22 (s, 1H), 4.82–4.78 (m, 2H), 4.56–4.51 (m, 1H), 4.39–4.30 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 192.24, 95.08, 74.73, 72.72, 71.93, 69.81, 65.97; HRMS (FAB) *m*/*z*: calculated for

$C_{11}H_9ClFeO$ $[M]^+$: 247.9691, found 247.9679.



1-Formyl-2-iodoruthenocene (16f).

^1H NMR ($CDCl_3$) δ 9.84 (s, 1H), 5.15–5.11 (m, 2H), 4.90–4.88 (m, 1H), 4.68–4.66 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 191.30, 82.54, 81.42, 75.16, 74.71, 69.75, 65.97; HRMS (FAB) *m*/*z*: calculated for $C_{11}H_9IORu$ $[M]^+$: 385.8742, found 385.8743.

1-Formyl-2-heptyn-1-ylferrocene (**16d**) was synthesized from 1-formyl-2-iodoferrocene (**16a**) by a known procedure.[7]

Typical procedure for the conversion of 16 to 1.[8]

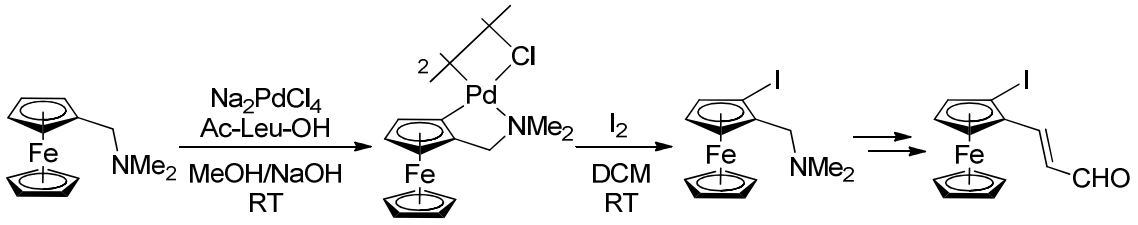
To a solution of 1-formyl-2-iodoferrocene (**16a**, 110 mg) in THF (7 mL), 2.0 equiv of (1,3-dioxolan-2-yl)methyltriphenylphosphonium bromide, 4.2 equiv of sodium hydride (dispersion in paraffin liquid, 60%), and 18-crown-6-ether (1.2 mg) were added. The resulting mixture was stirred overnight at room temperature under argon atmosphere. After adding water (10 mL) slowly, the mixture was extracted with diethyl ether. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. After removal of the solvent under reduced pressure, the residue was dissolved in THF (5 mL). An aqueous solution of HCl (1 N, 1 mL) was added to the solution, and this mixture was stirred for 10 min at room temperature. After adding a saturated aqueous solution of sodium hydrogen carbonate, the mixture was extracted with chloroform two times. The combined organic layer was dried over anhydrous magnesium sulfate. After removal of the solvent under reduced pressure, the residue was purified by silica-gel column chromatography (dichloromethane) followed by preparative TLC (hexanes/ethyl acetate 4:1) to afford 3-(2-iodoferrocenyl)prop-2-enal (**1a**, 62.9 mg, 58%).

Preparation of 1e.[9]

To a solution of **1a** (8.5 mg) in THF (0.75 mL) and water (0.25 mL), 20 mol% of palladium(II) acetate, 1.3 equiv of *p*-methoxyphenylbenzeneboronic acid, and 2.5 equiv of barium(II) hydroxide were added. The resulting mixture was refluxed for 3 h under argon atmosphere. After cooling to room temperature, the mixture was extracted with diethyl ether. The organic layer was washed with water and dried over anhydrous magnesium sulfate. After removal of the solvent under reduced pressure, the residue was purified by preparative TLC (hexanes/ethyl acetate 4:1) to afford **1e** (5.5

mg, 72%).

Determination of the absolute configurations of the obtained compounds.



(R_p)-**17** (R_p)-**15a** (R_p)-**1a**

(R_p)-Bis(μ-chloro)bis(2-dimethylaminomethylferrocenyl)-N-dipalladium (**17**) was synthesized by a known procedure.[10] To a solution of (R_p)-**17** (48.6 mg) in dichloromethane (5 mL) 16 equiv of iodine was added. After stirring the mixture for 3 h at room temperature, the solid was filtered off. The solution was washed with aqueous sodium thiosulfate, and the organic layer was dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure and the residue was purified by preparative TLC (hexanes/ethyl acetate/triethylamine 76:20:4) to afford (R_p)-1-dimethylaminomethyl-2-iodoferrocene (**15a**, 19.8 mg, 43%).[11] By the method described above, (R_p)-**1a** was synthesized from (R_p)-**15a** as noted above (78% ee). By comparing the retention time on the HPLC analysis, the absolute configuration of the major enantiomer obtained by the peptide-catalyzed hydrogenation was determined as S_p for **1a**. Based on the mechanistic similarity for the peptide-catalyzed reaction with other substrates, the major configurations of all compounds were assigned as the same ones.

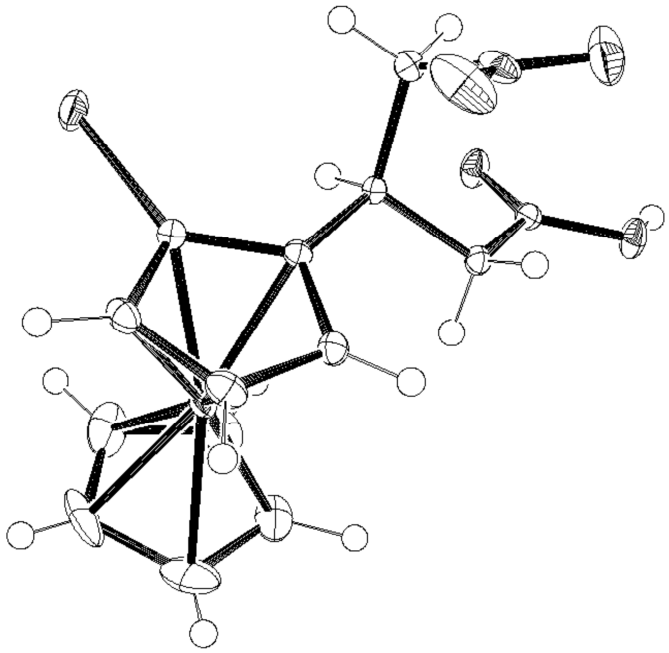
In the peptide-catalyzed kinetic resolution by the addition of nitromethane, the absolute configuration of the major enantiomer for the recovered starting material **1a** was determined as S_p by comparing with the above-mentioned sample. Accordingly, the major configuration of the planar-ferrocenyl part of product **10a** was assigned as R_p. The relative configurations of the major diastereomer for **10a** were determined by an X-ray crystallographic analysis of the corresponding carboxylic form of racemic **10a**. Thus, the absolute configurations of the major product obtained by the peptide catalyst was assigned as S,R_p.

To a solution of racemic compound **10a (**3.2 mg) in *t*-butyl alcohol (800 μL) and water (200 μL), 10 equiv of 2-methyl-2-butene, 5.0 equiv of sodium dihydrogen phosphate dihydrate, and 3.0 equiv of sodium chlorite were added successively. After stirring the mixture at 0 °C for 30 min, brine (5 mL) was added. The resulting mixture was extracted with chloroform. The organic layer was washed with brine and dried over anhydrous magnesium sulfate. After removal of the solvent under reduced pressure, the residue was purified by preparative TLC (hexanes/ethyl acetate/acetic acid 76:20:4) to afford 3-(2-iodoferrocenyl)-4-nitrobutanoic acid (2.2 mg, 66%). ^{1}H NMR ($CDCl_3$) δ 4.72 (dd, J =

12.4, 3.6 Hz, 1H), 4.60 (dd, *J* = 19.0, 6.4 Hz, 1H), 4.54–4.52 (m, 1H), 4.26 (brt, *J* = 2.4 Hz, 1H), 4.20–4.17 (m, 5H), 4.09–4.08 (m, 1H), 3.74–3.67 (m, 1H), 3.23 (dd, *J* = 17.4, 4.0 Hz, 1H), 3.15 (dd, *J* = 17.4, 9.0 Hz, 1H). A crystal suitable for an X-ray diffraction analysis was obtained by recrystallization from chloroform.The X-Ray diffraction analysis was performed on a Rigaku Mercury–CCD diffractometer equipped with a graphite monochromatized Mo Kα source (λ = 0.71075 Å). Data were processed using the CrystalClear program package[12] and corrected for absorption. Structure solution and refinements were performed by using the CrystalStructure program package.[13] The positions of non-hydrogen atoms were determined by direct methods (SIR2008[14]) and refined with anisotropic thermal parameters by full-matrix least-squares techniques (SHELXL97[15]). All hydrogen atoms were found in Fourier maps and refined isotropically. Crystallographic data in CIF format is deposited at the Cambridge Crystallographic Data Centre (CCDC 996655).

formula	C14 H14 Fe I N O4
fw	443.02
T (K)	113
cryst syst	Triclinic
space group	P -1
a, (Å)	6.997(3)
b, (Å)	7.231(3)
c, (Å)	15.311(6)
α, (°)	93.523(5)
β, (°)	97.073(4)
γ, (°)	101.321(6)
Volume, ($Å^3$)	750.9(5)
Dx, (g/cm^{-3})	1.959
Z	2
μ, (mm^{-1})	3.073
F(000)	432.0
crystal size (mm^3)	0.400 x 0.350 x 0.030
Transmission factor	0.690–0.912
Number of unique reflections	3556
R_{int}	0.0264
Number of variables	246
2θ	6°<2θ <55°

GOF on F^2	0.967
R_1 [I>2σ(I)] , wR_2 [all data]	0.0214, 0.0484
Residual electron density (e Å^{-3})	0.740 (–0.570)



(50% thermal ellipsoids, hydrogen atoms are omitted for clarity)

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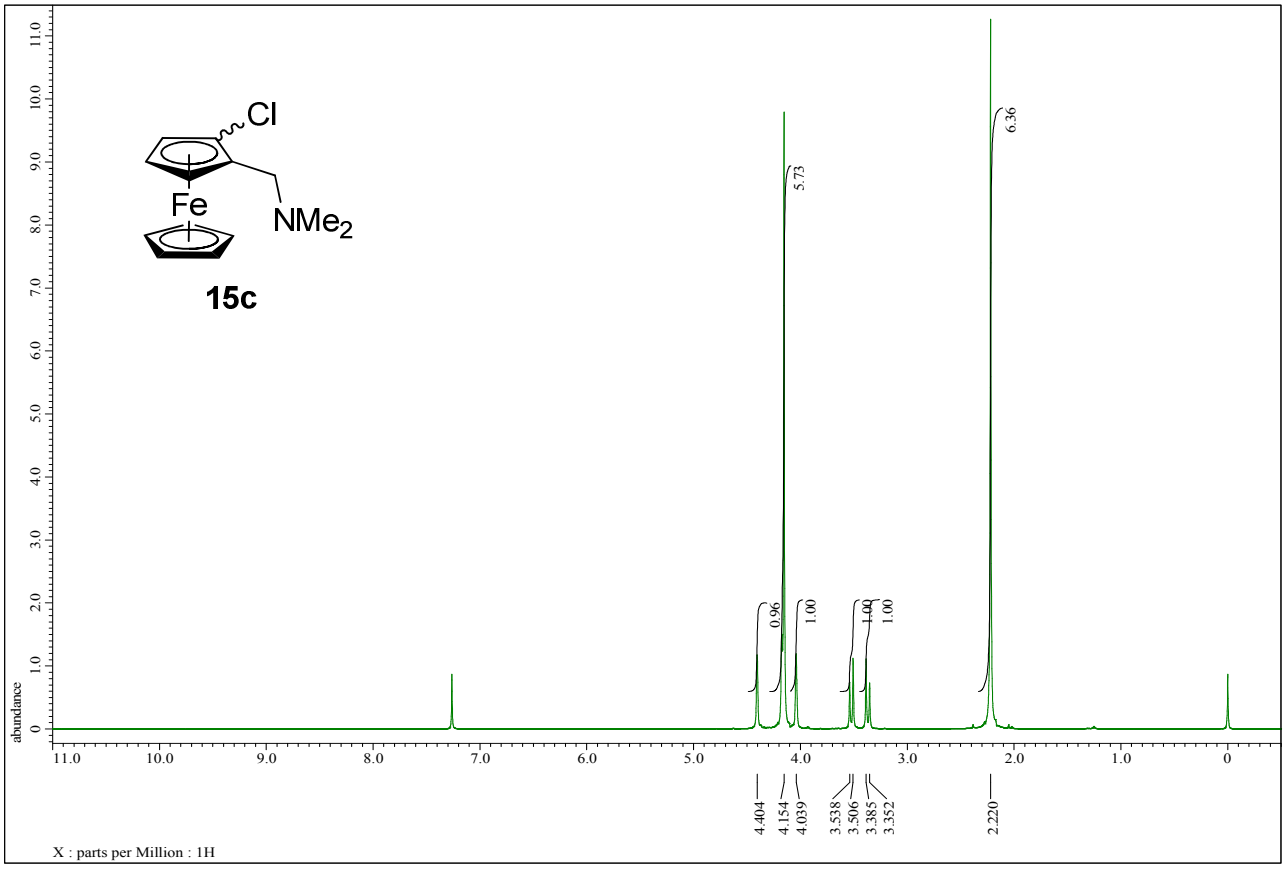
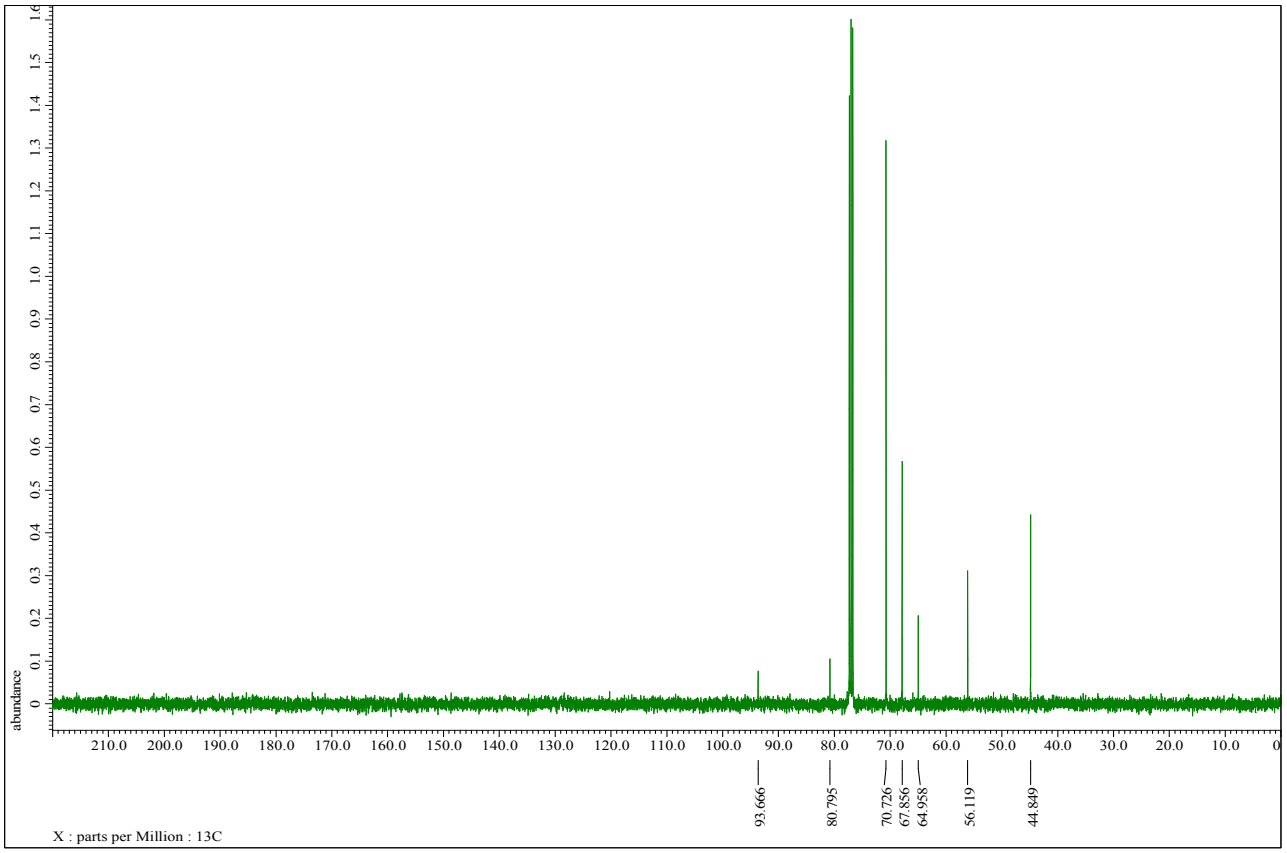
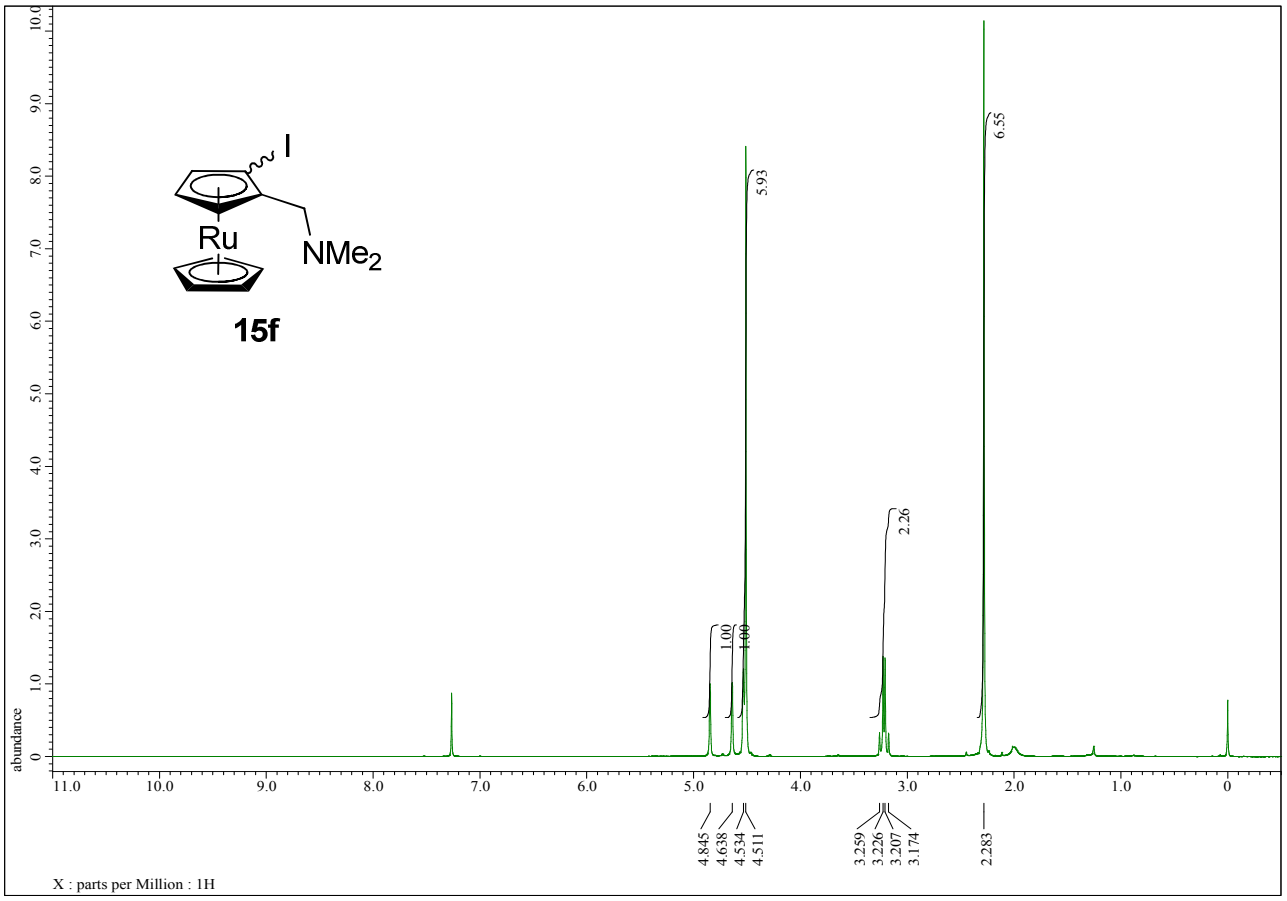
^{1}H and ^{13}C NMR spectra.



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8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
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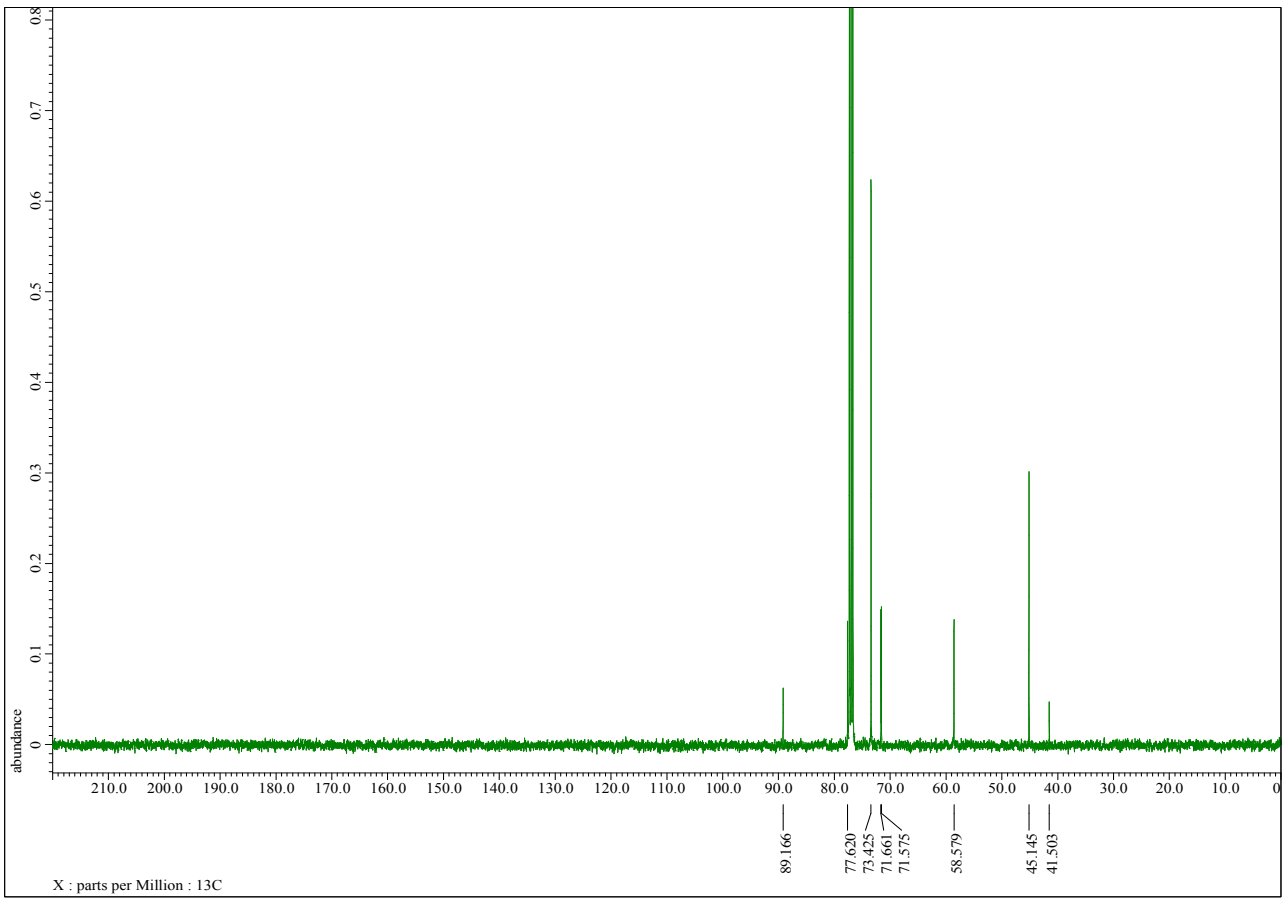
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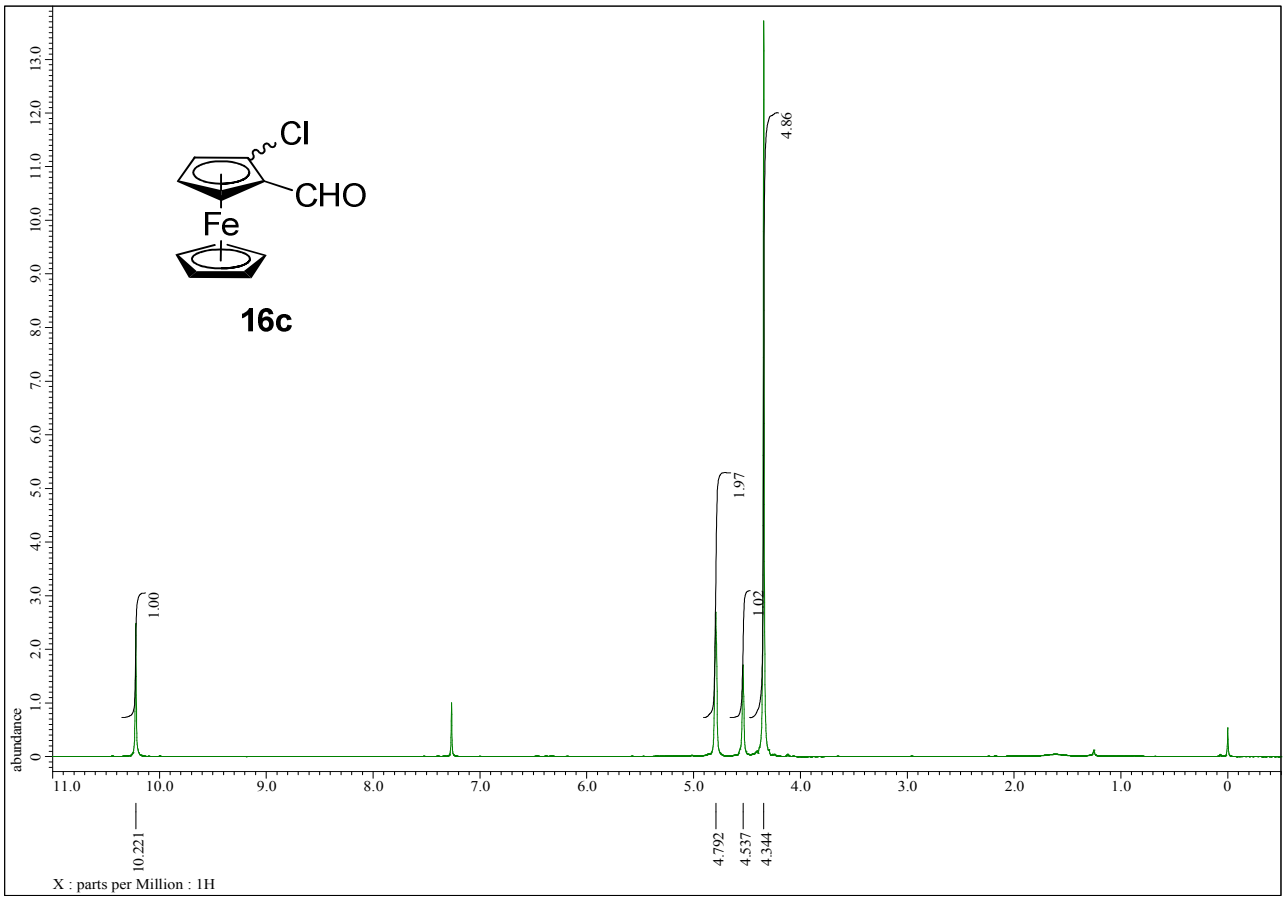
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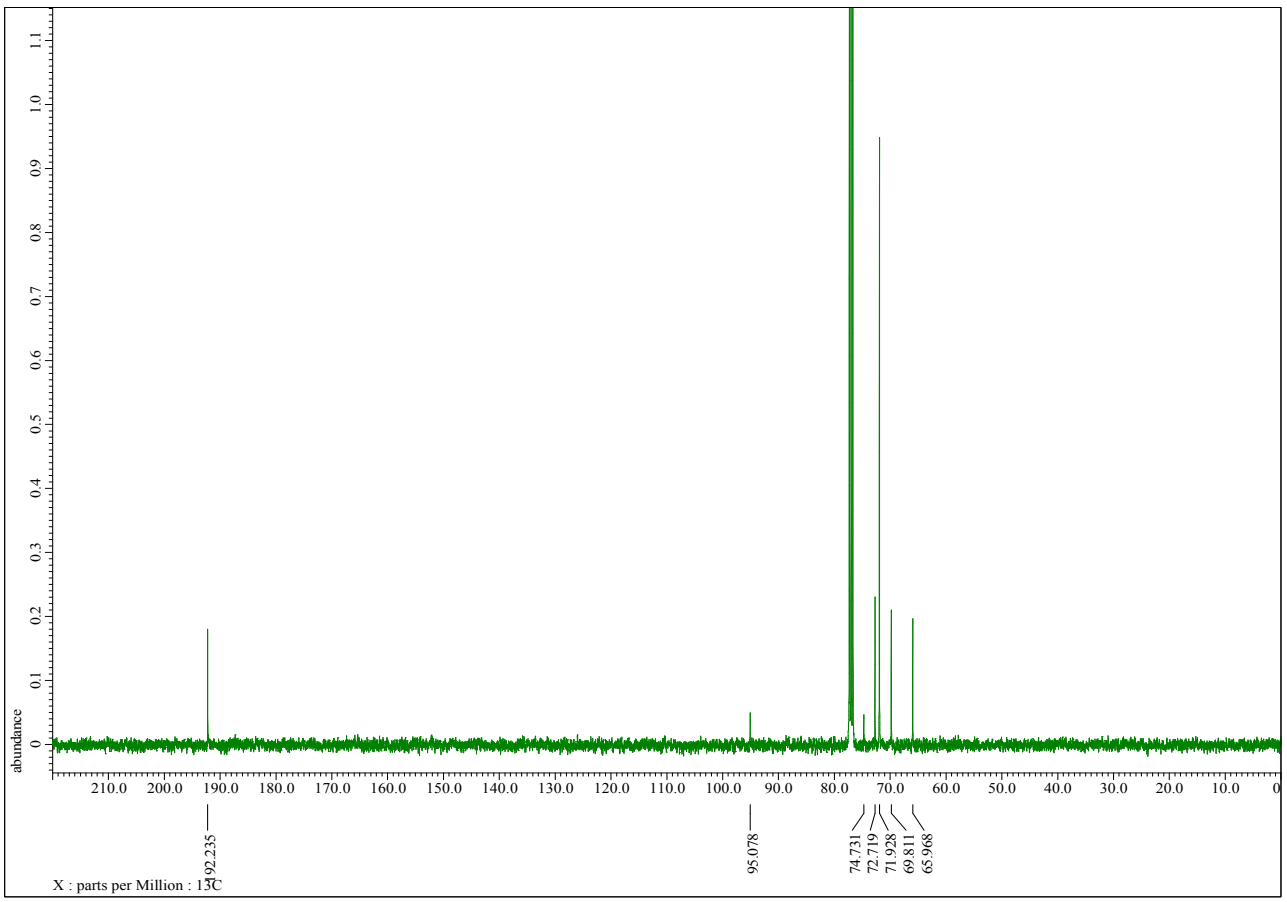
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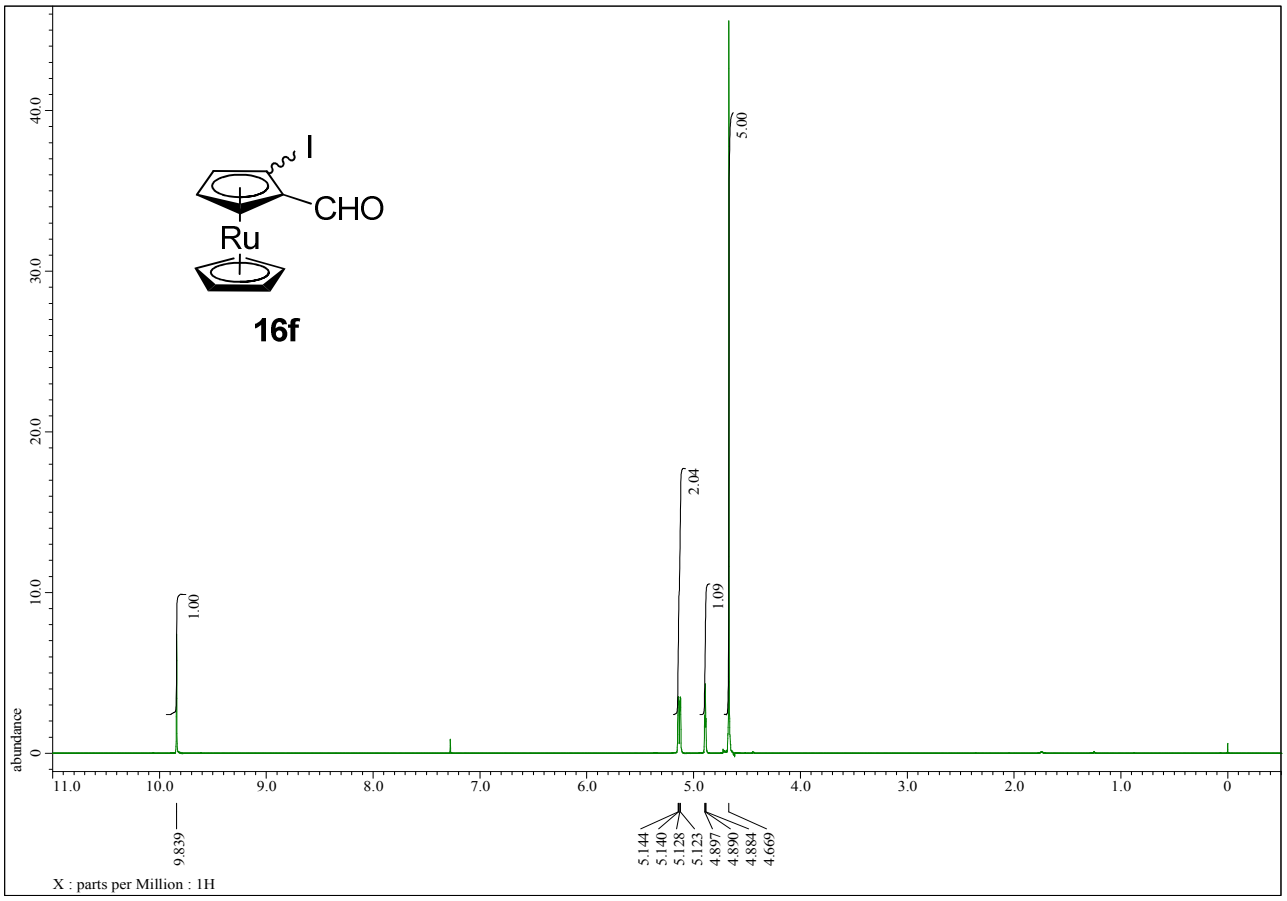
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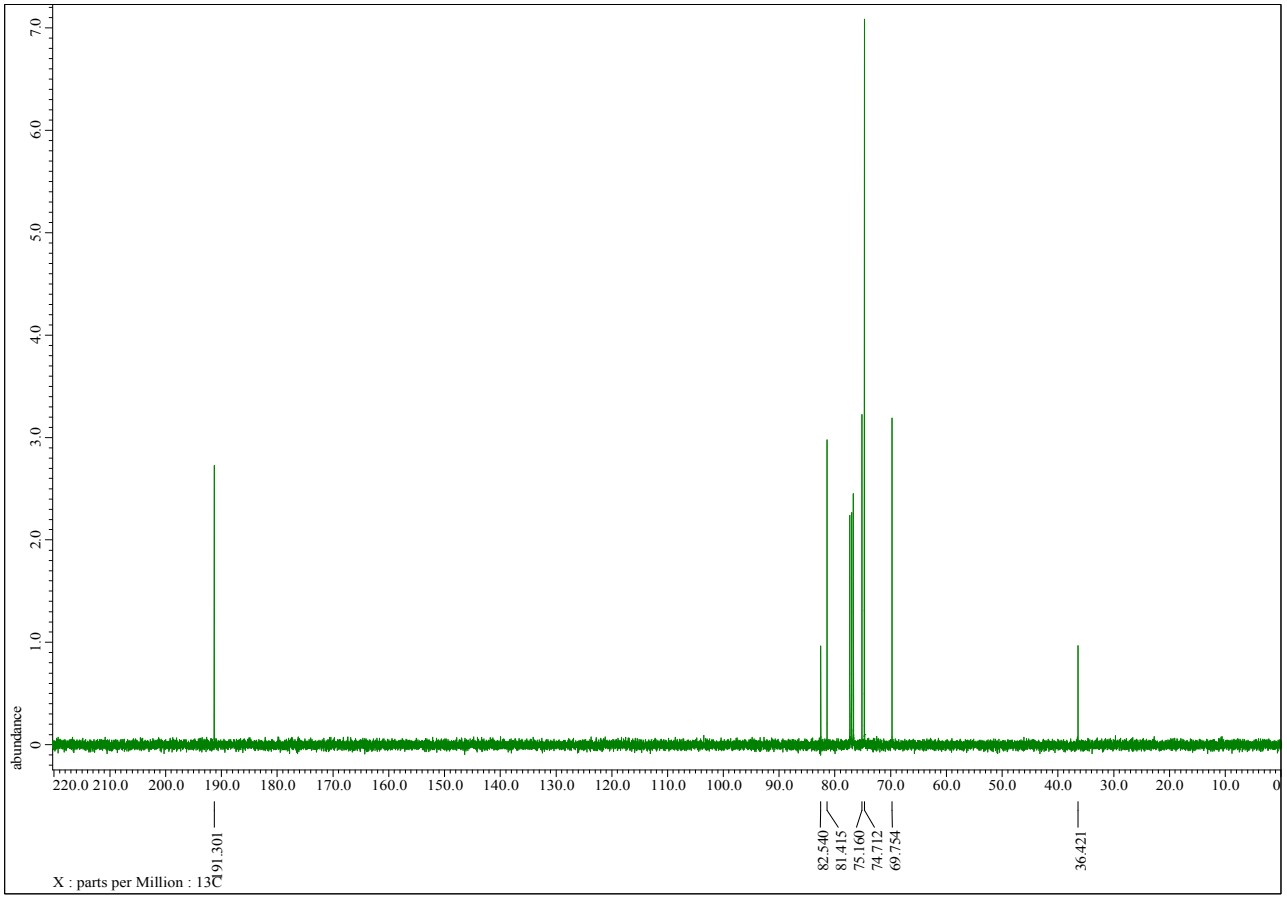
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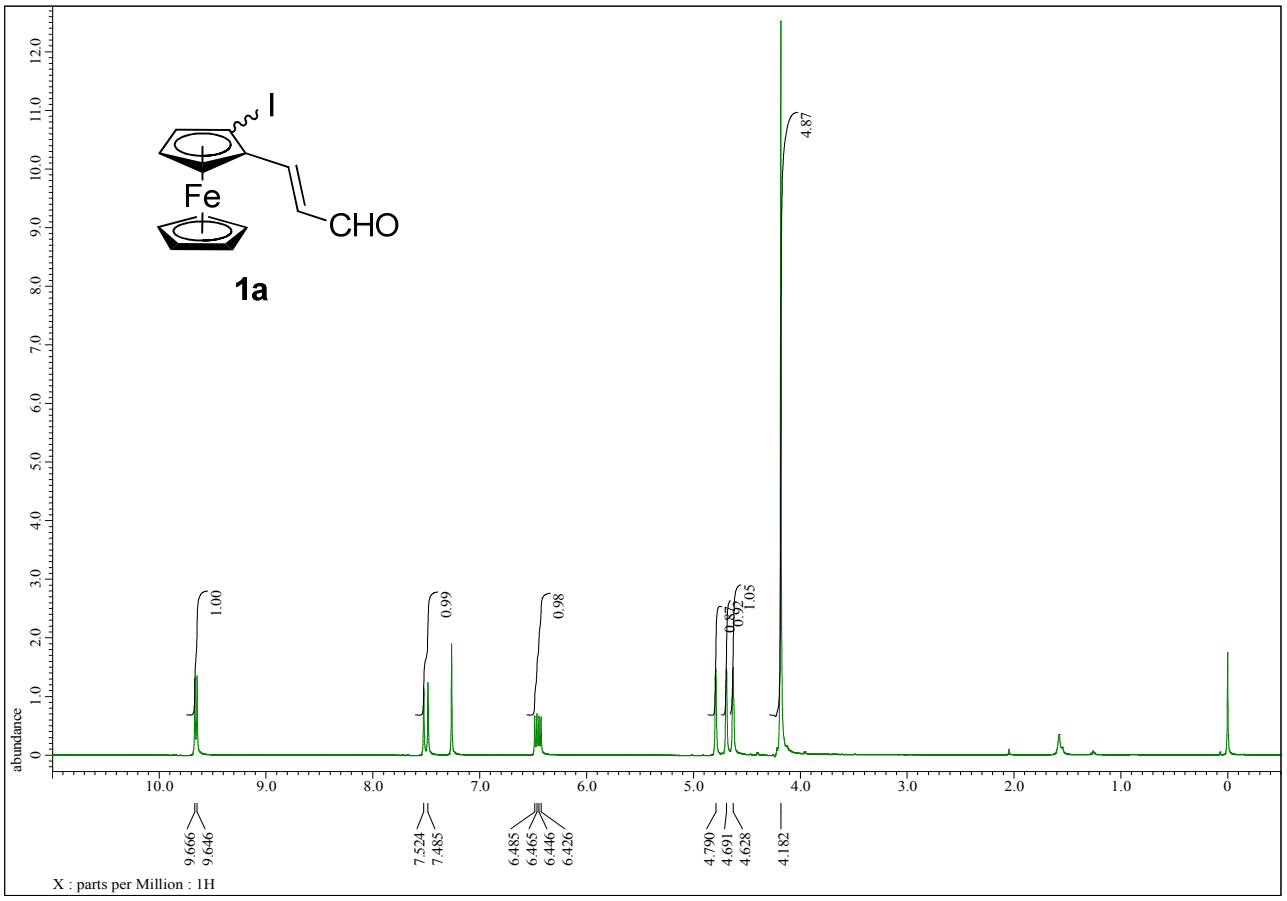
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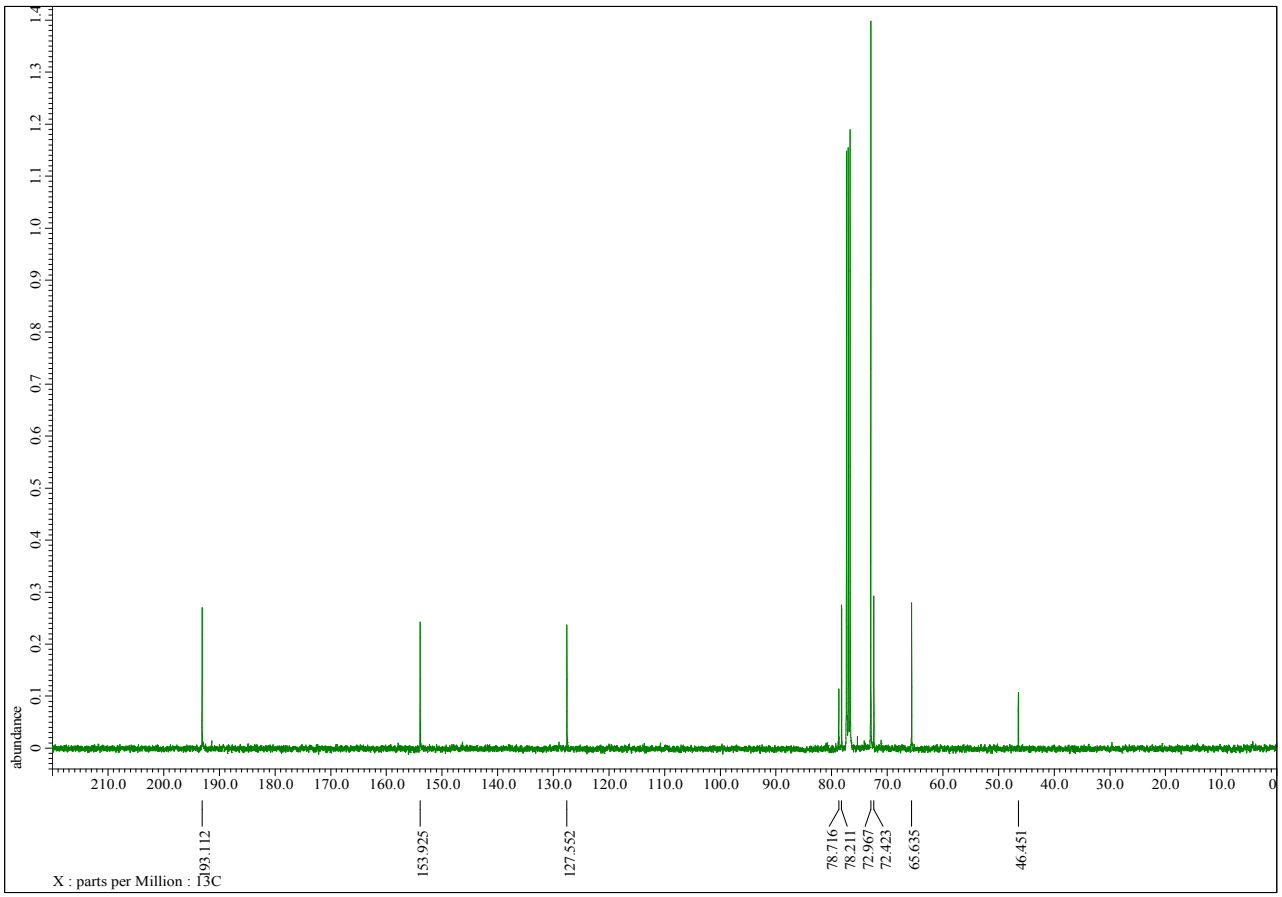
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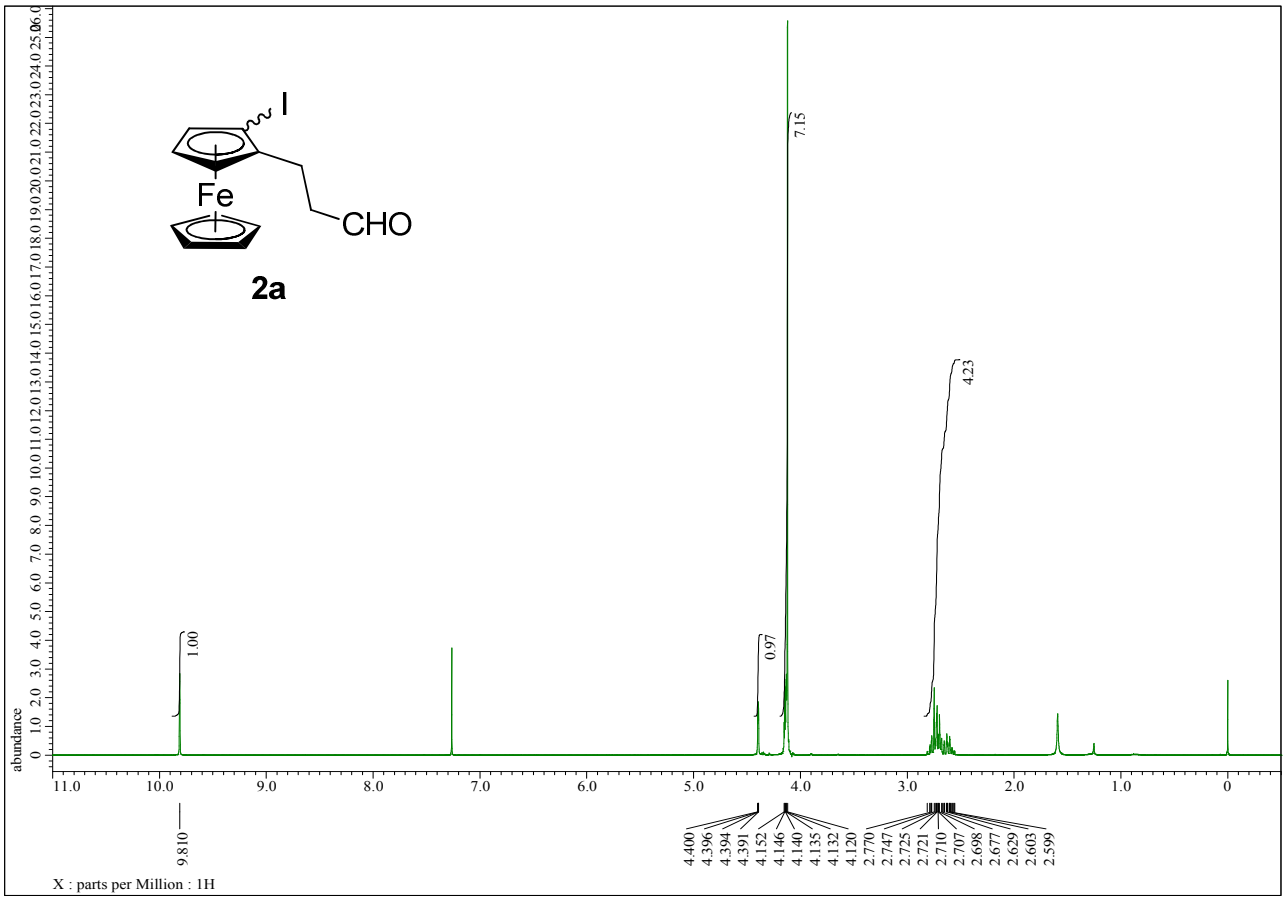
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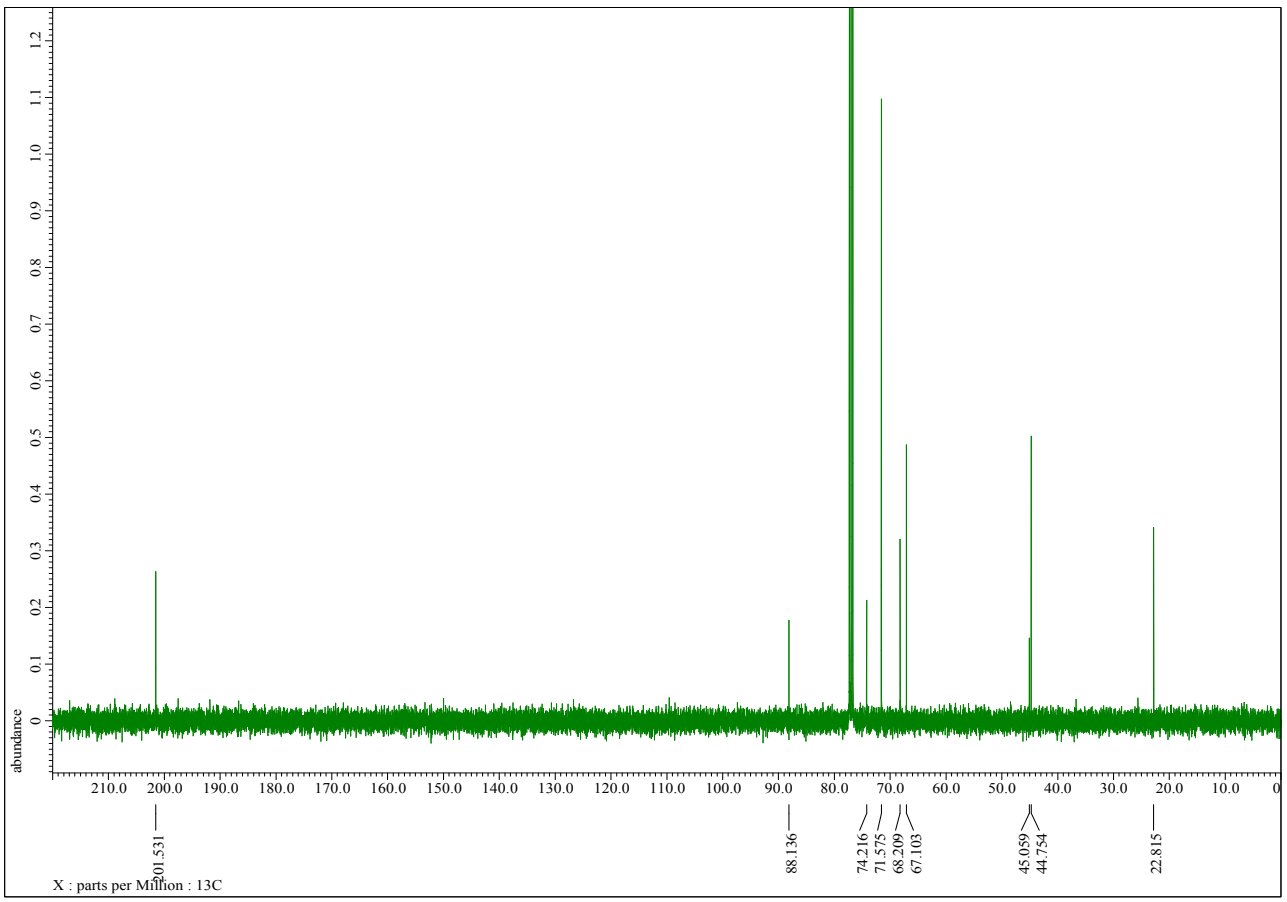
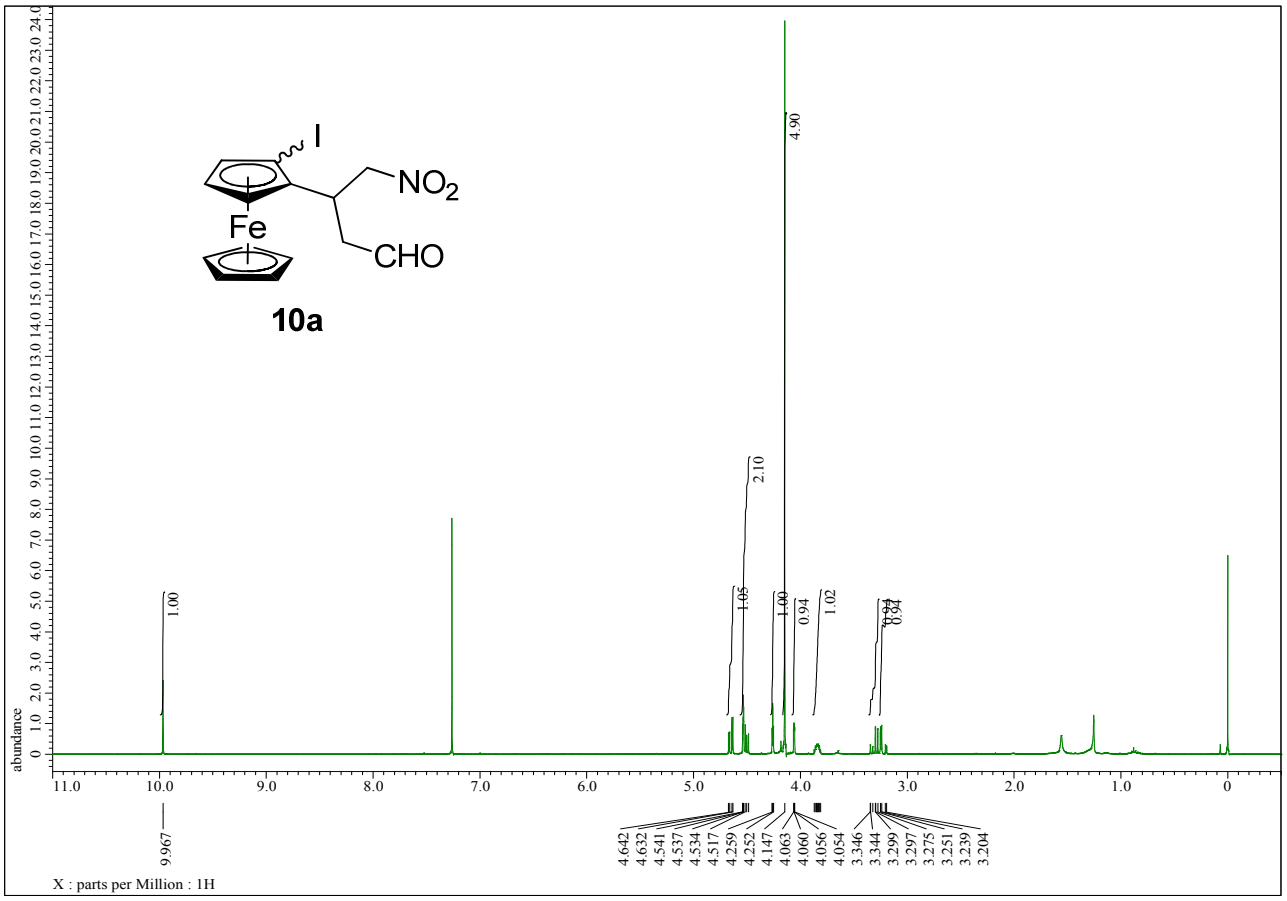
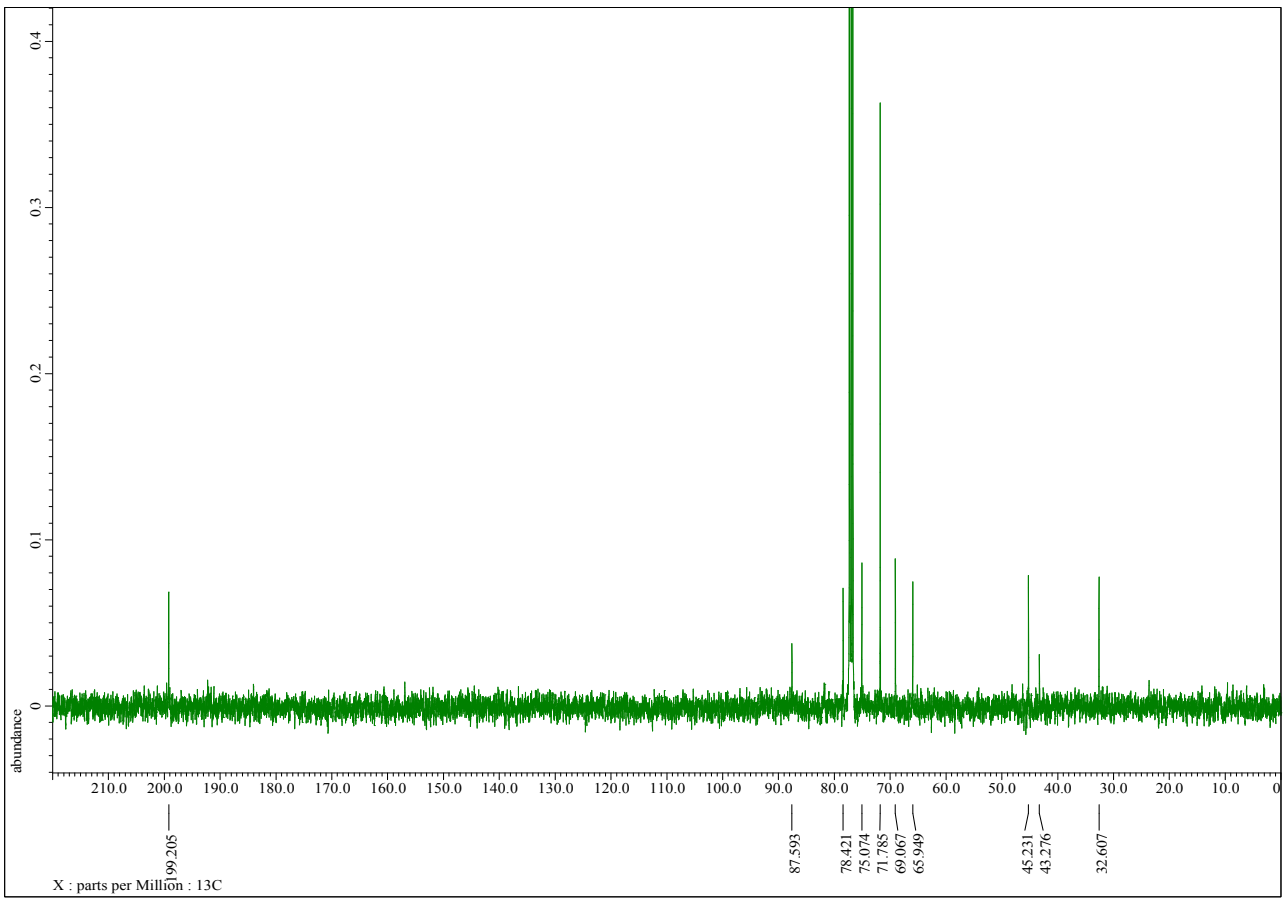
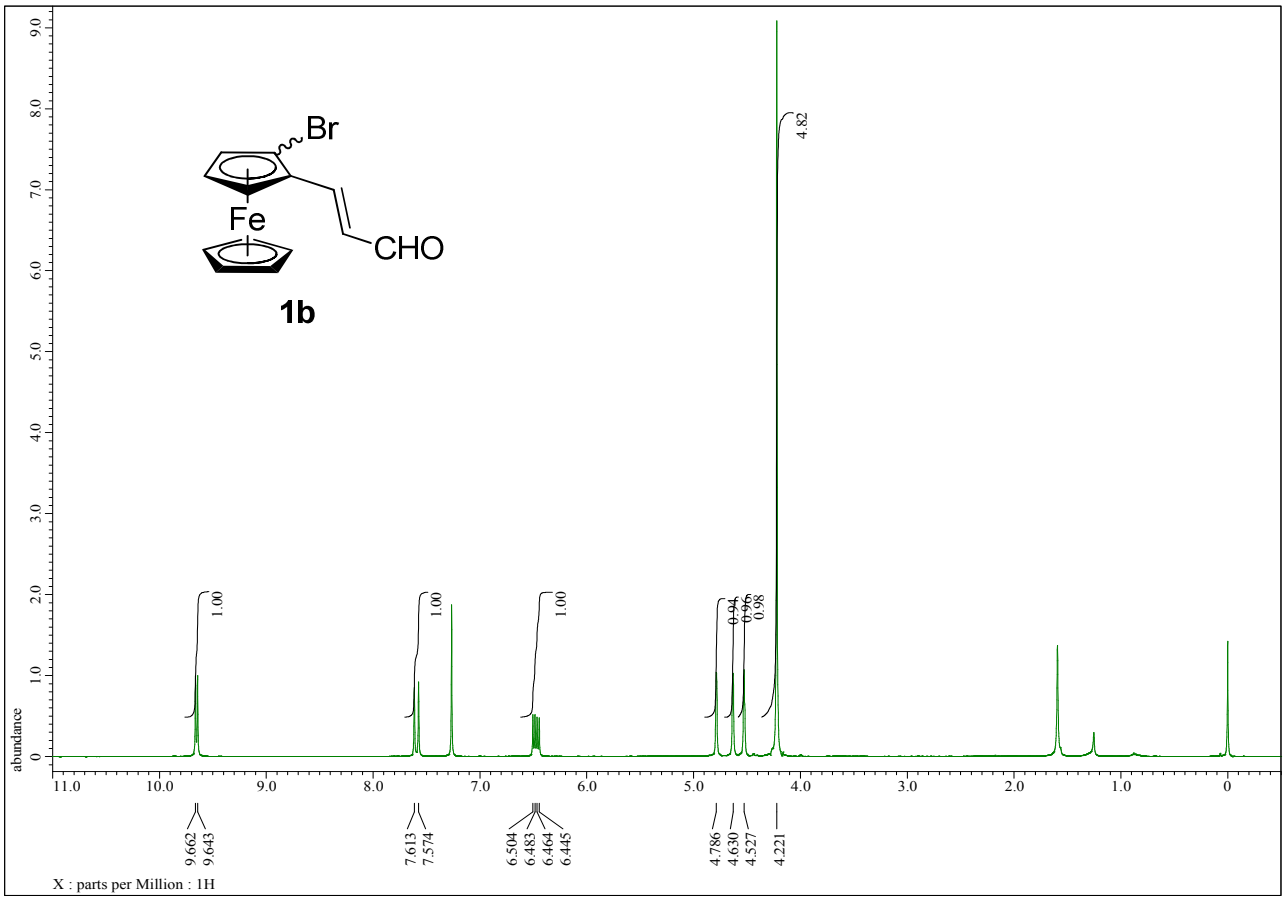
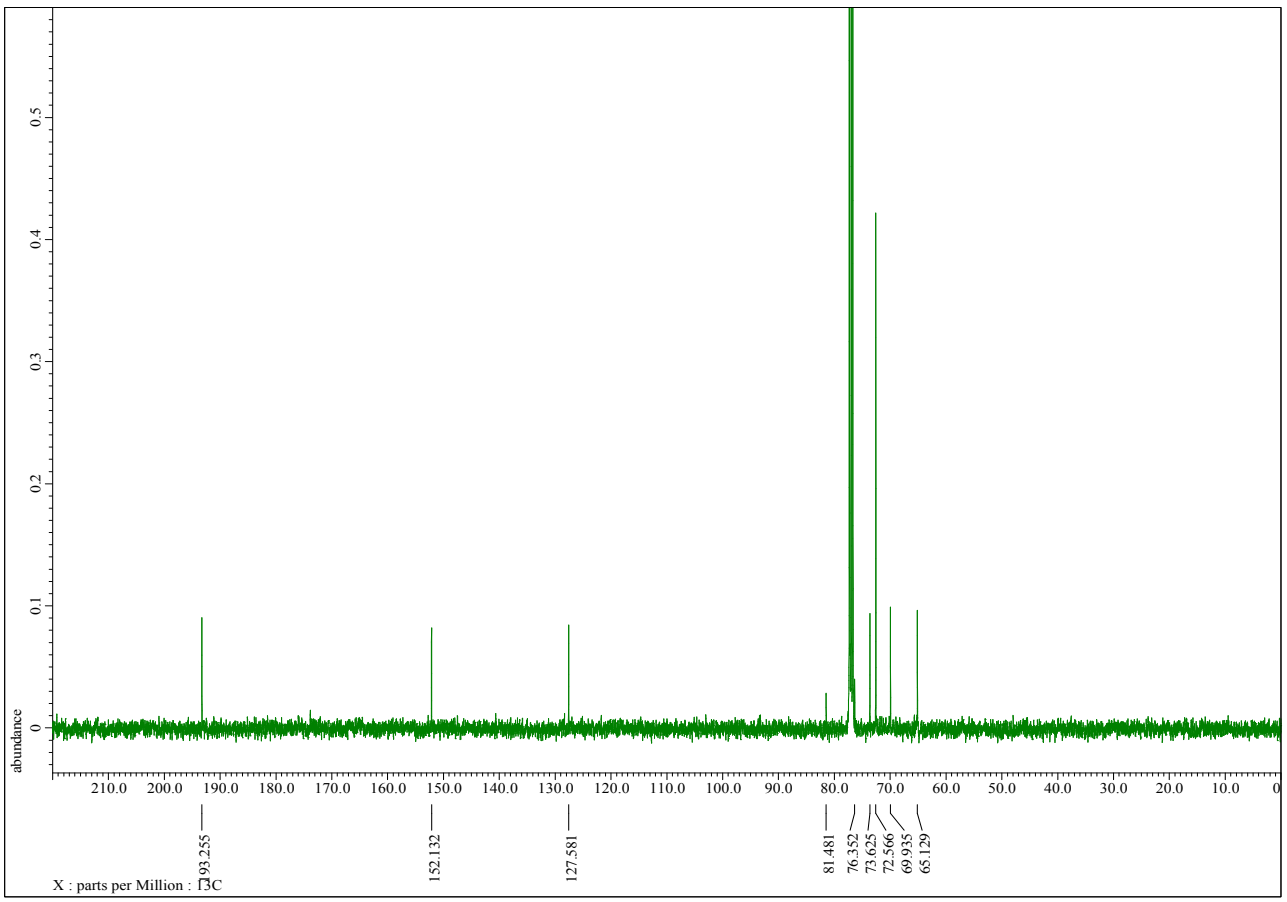
4.120
2.770
2.747
2.725
2.721
2.710
2.707
2.698
2.677
2.629
2.603
2.599
X : parts per Million : 1H

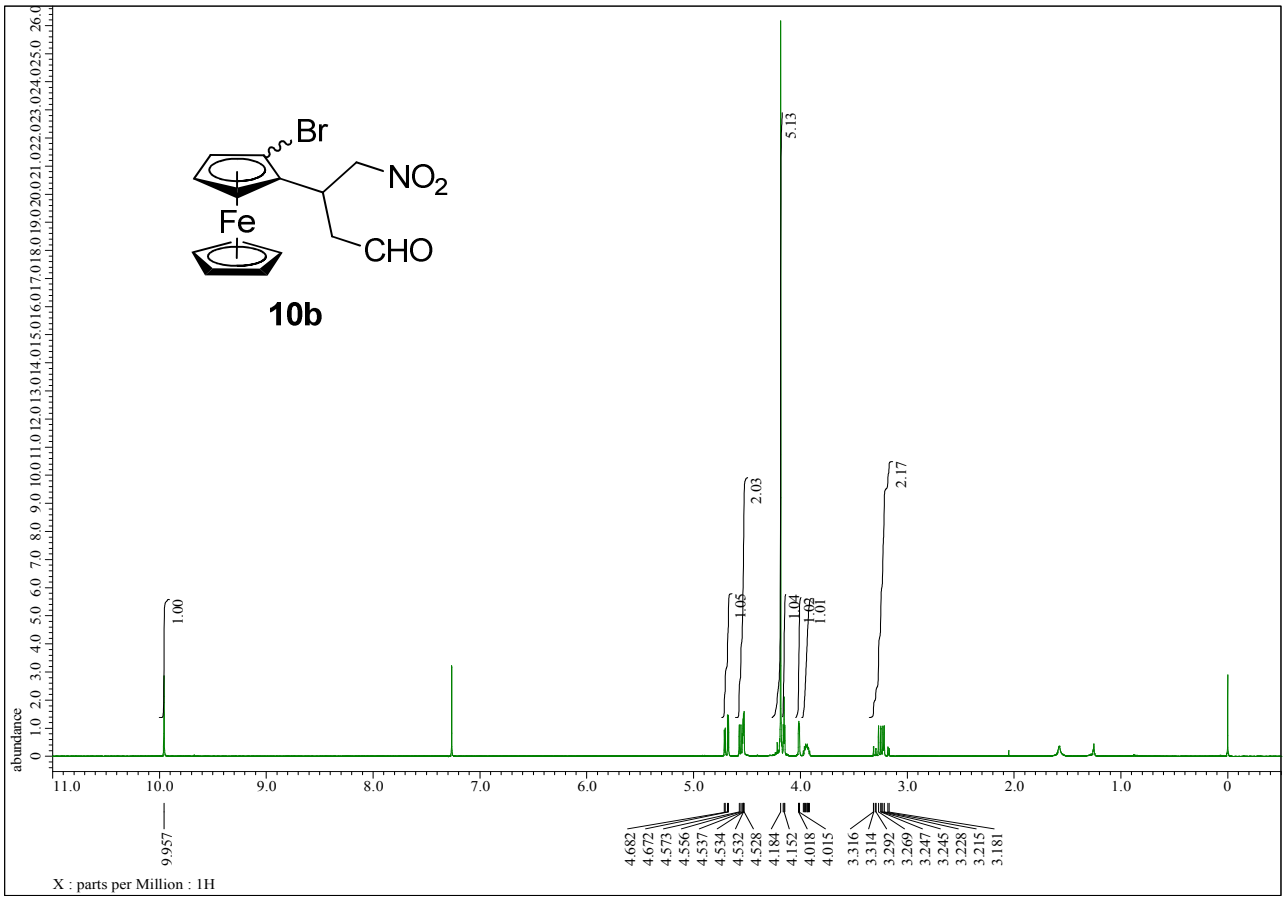

abundance
201.531
88.136
74.216
71.575
68.209
67.103
45.059
44.754
22.815
X : parts per Million : 13C

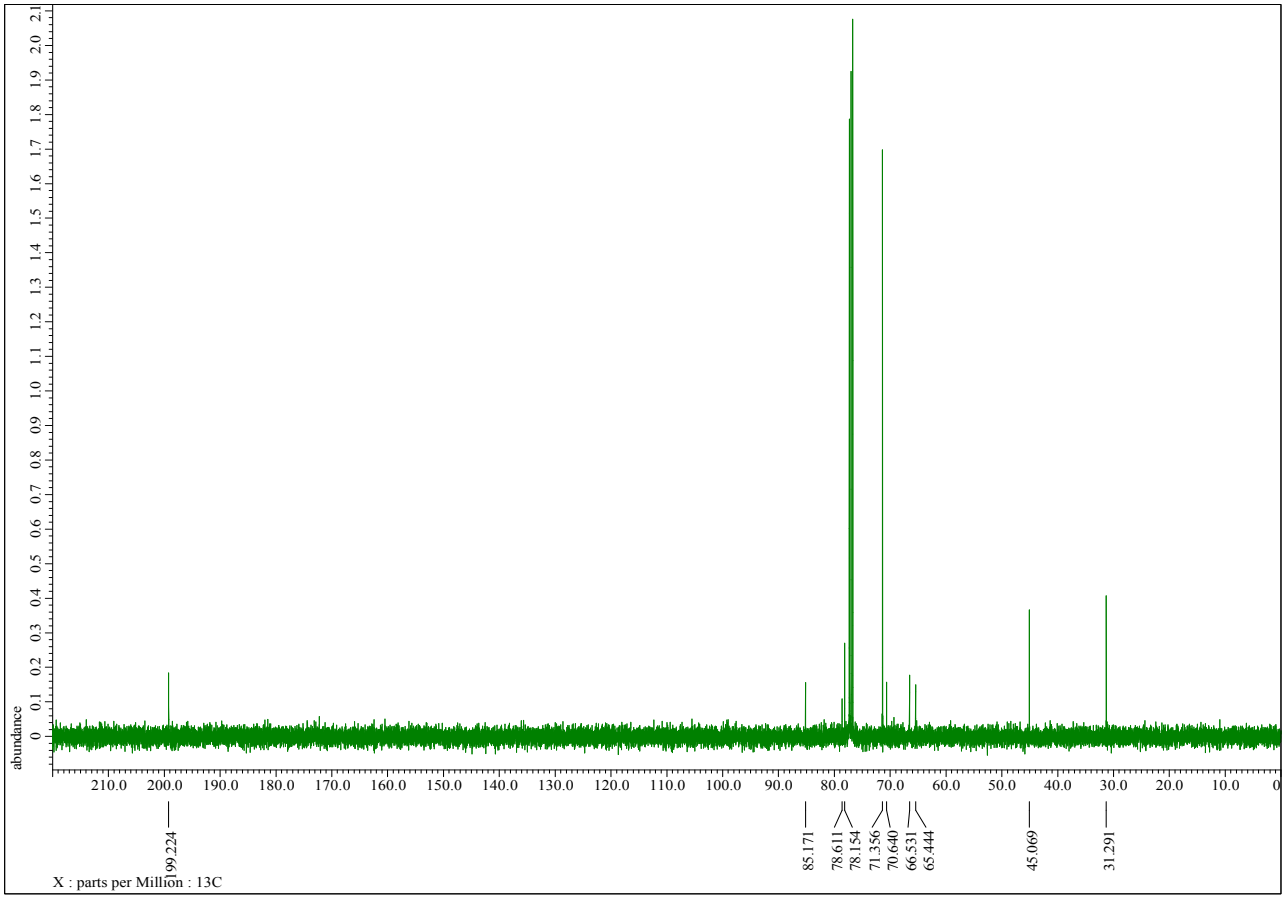

I
NO2
Fe
CHO
10a
abundance
X : parts per Million : 1H

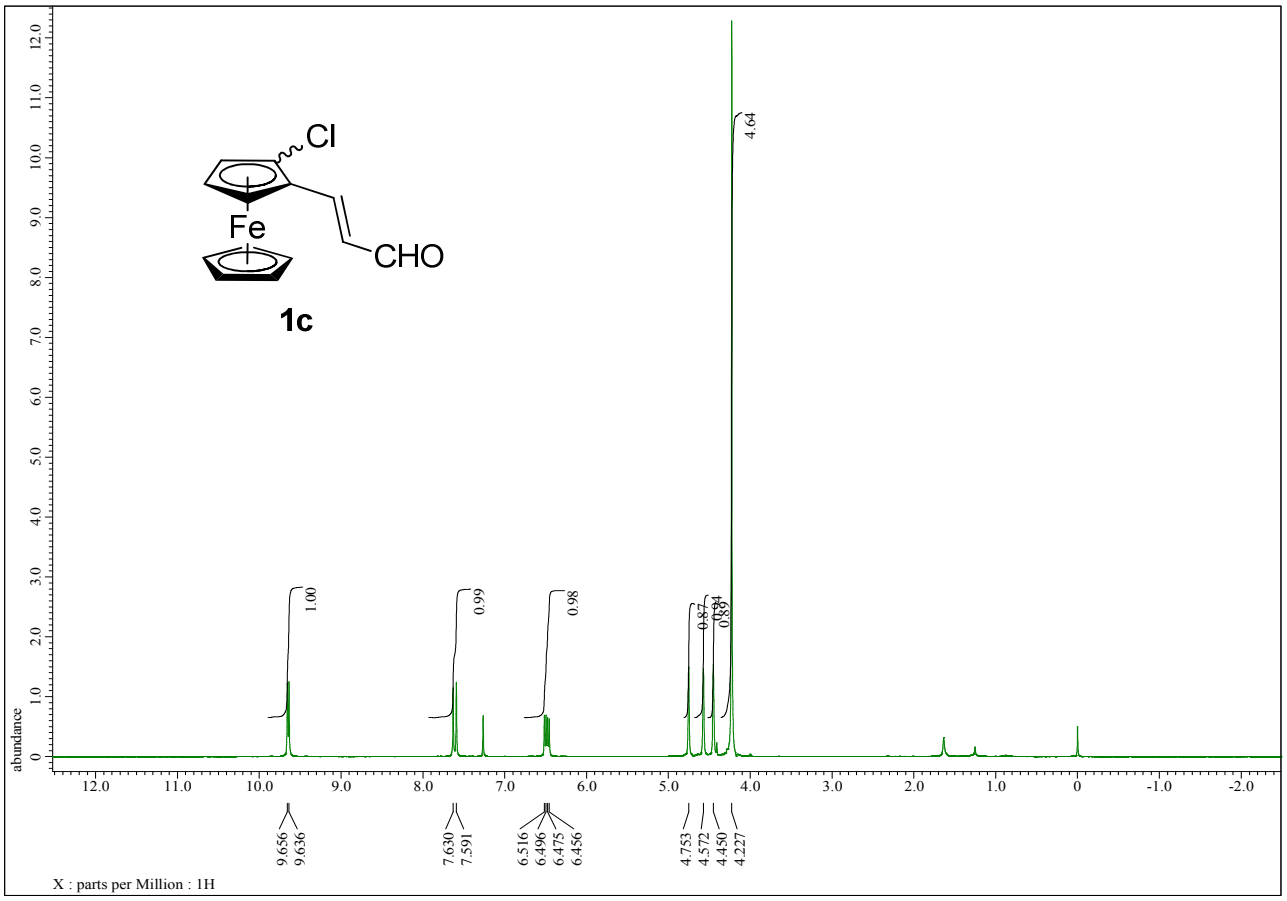

abundance
X : parts per Million : 13C

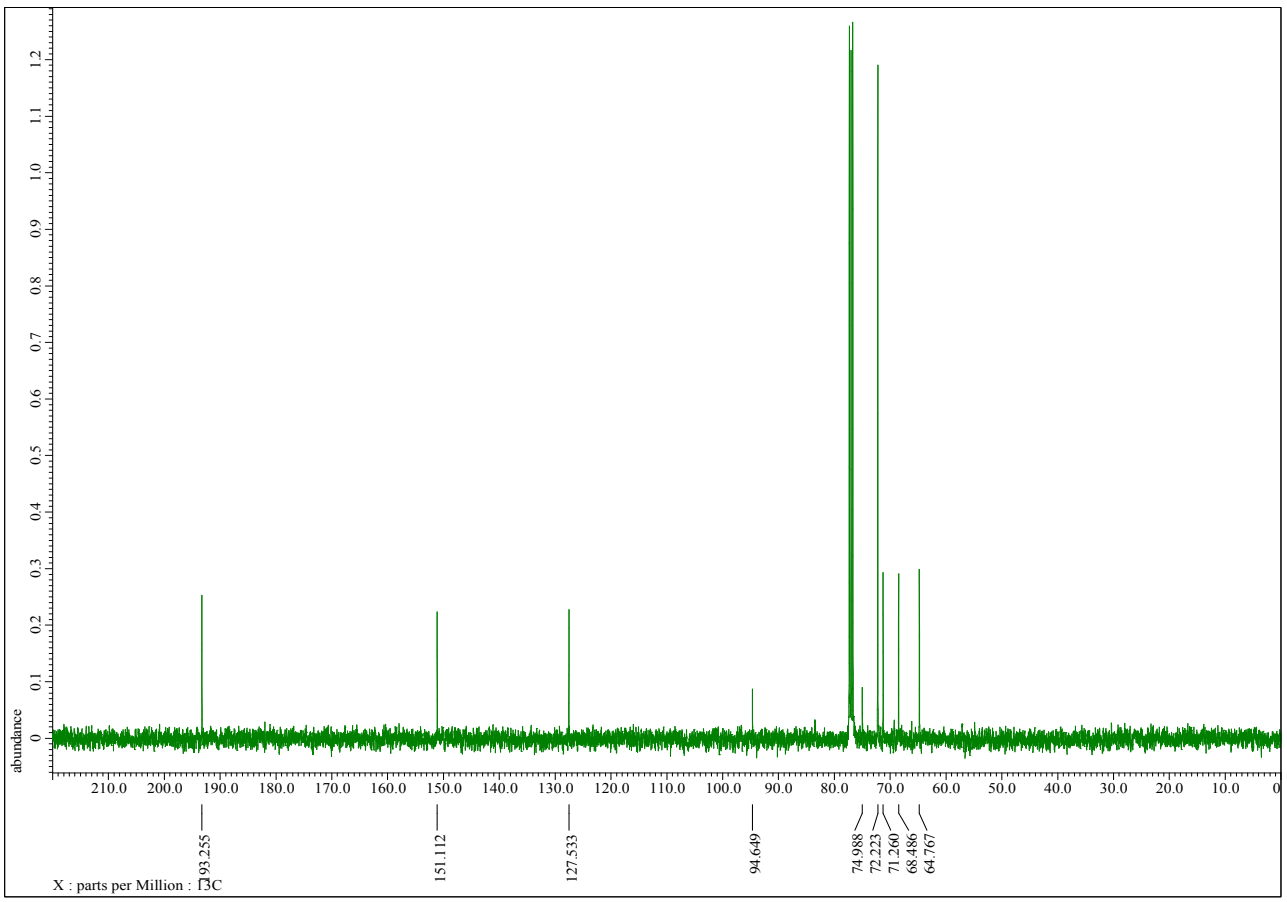

Br
Fe
CHO
1b
4.82
1.00
1.00
1.00
0.94
0.96
0.98
abundance
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
9.662
9.643
7.613
7.574
6.504
6.483
6.464
6.445
4.786
4.630
4.527
4.221
X : parts per Million : 1H

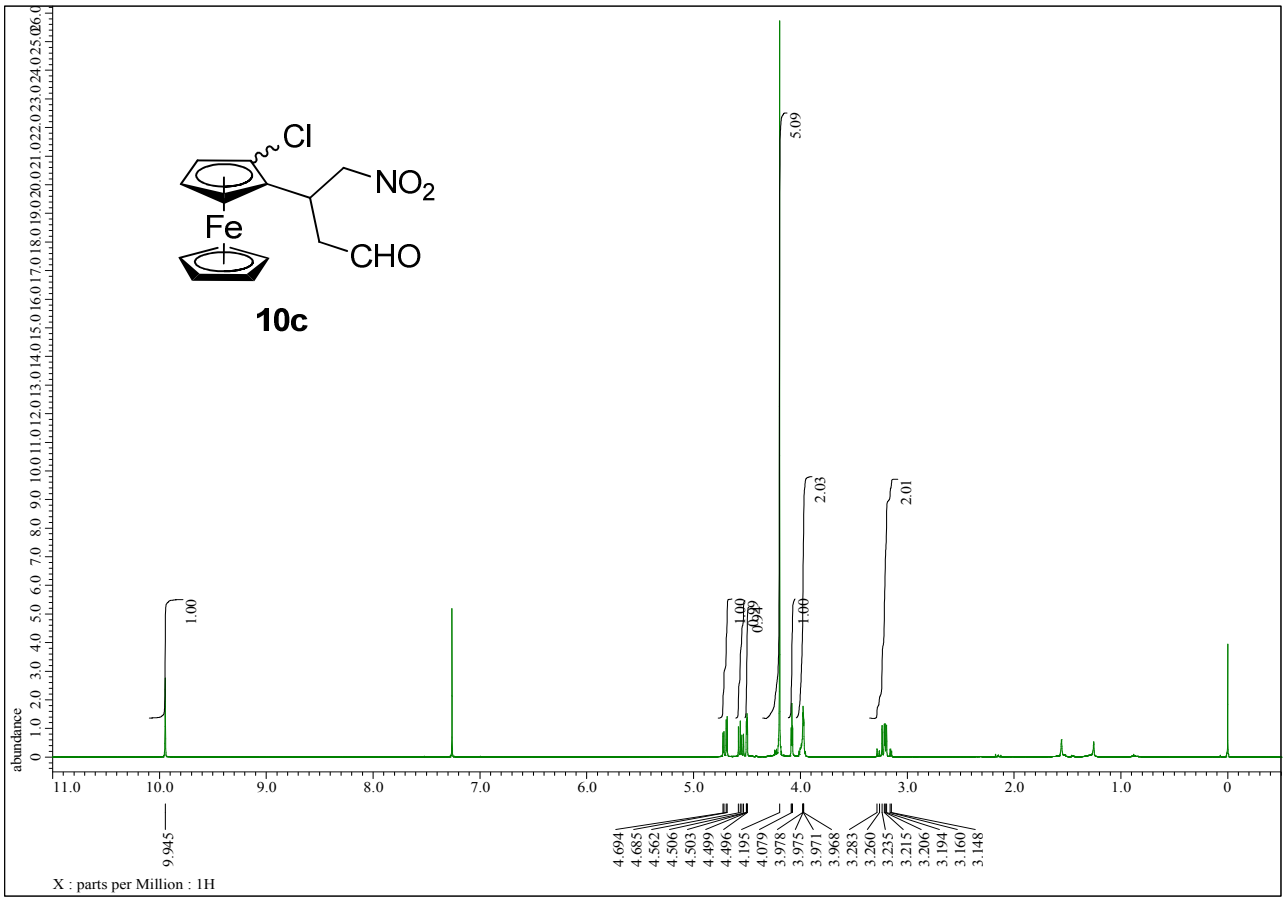

abundance
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
193.255
152.132
127.581
81.481
76.352
73.625
72.566
69.935
65.129
X : parts per Million : 13C

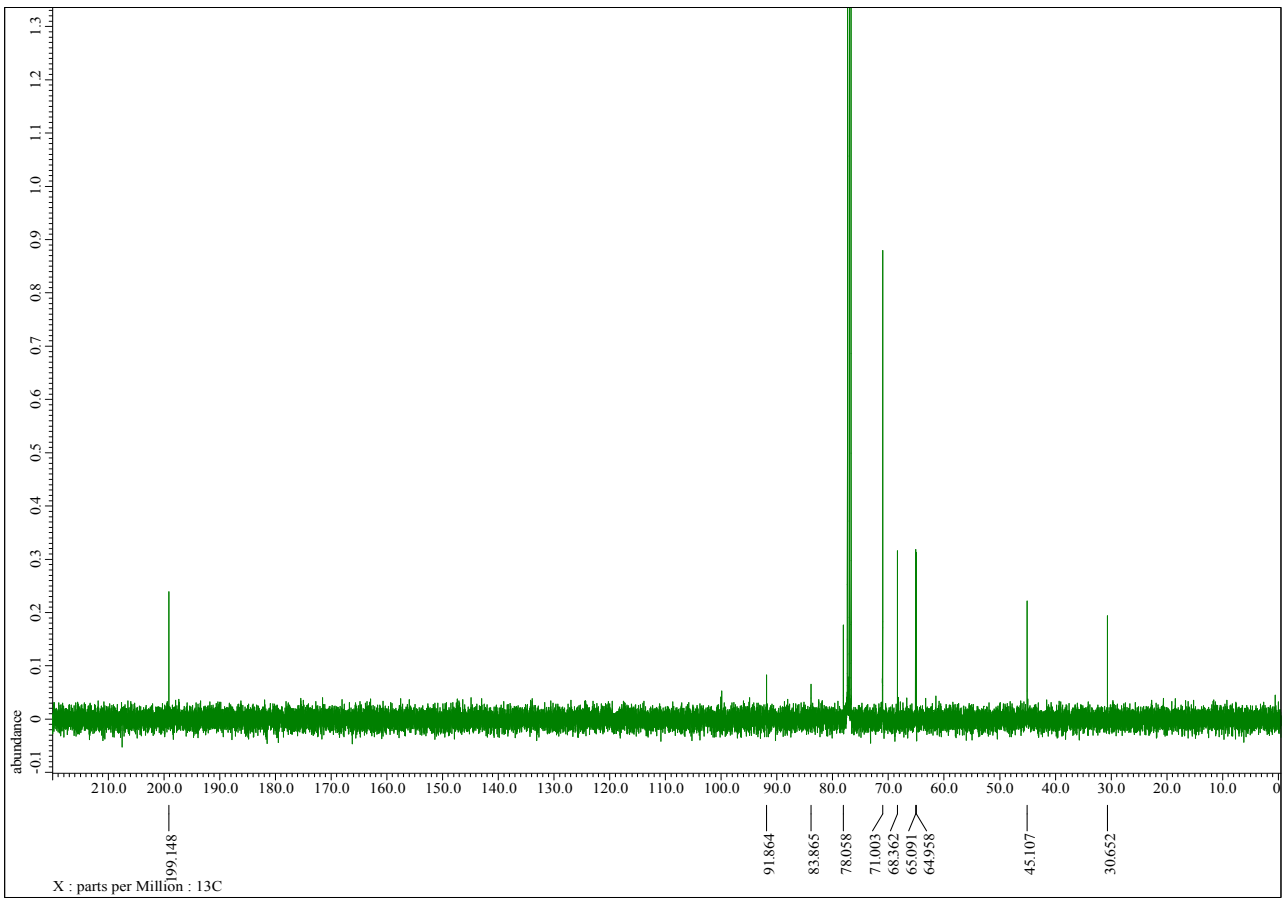

Br
NO2
Fe
CHO
10b
abundance
X : parts per Million : 1H

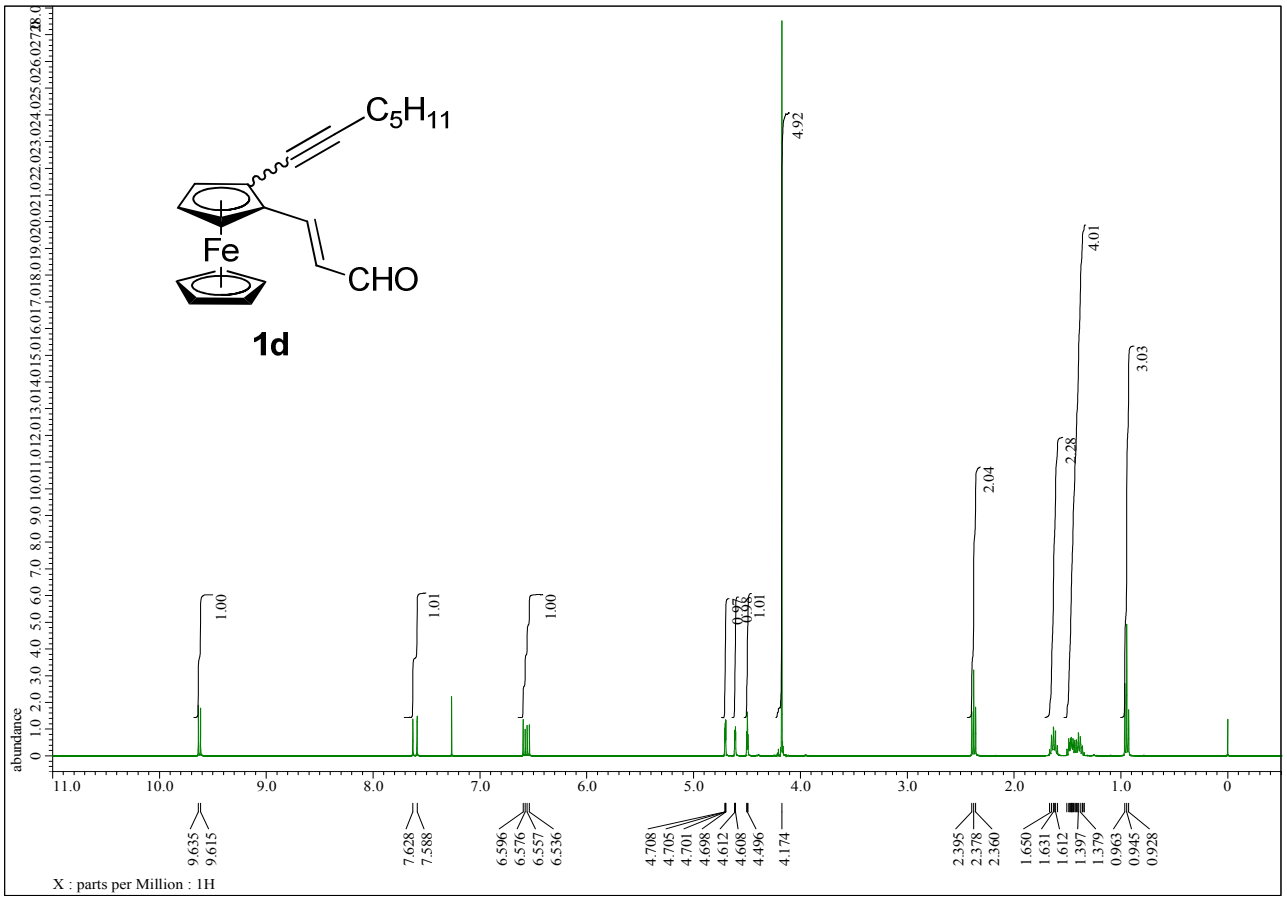

abundance
X : parts per Million : 13C

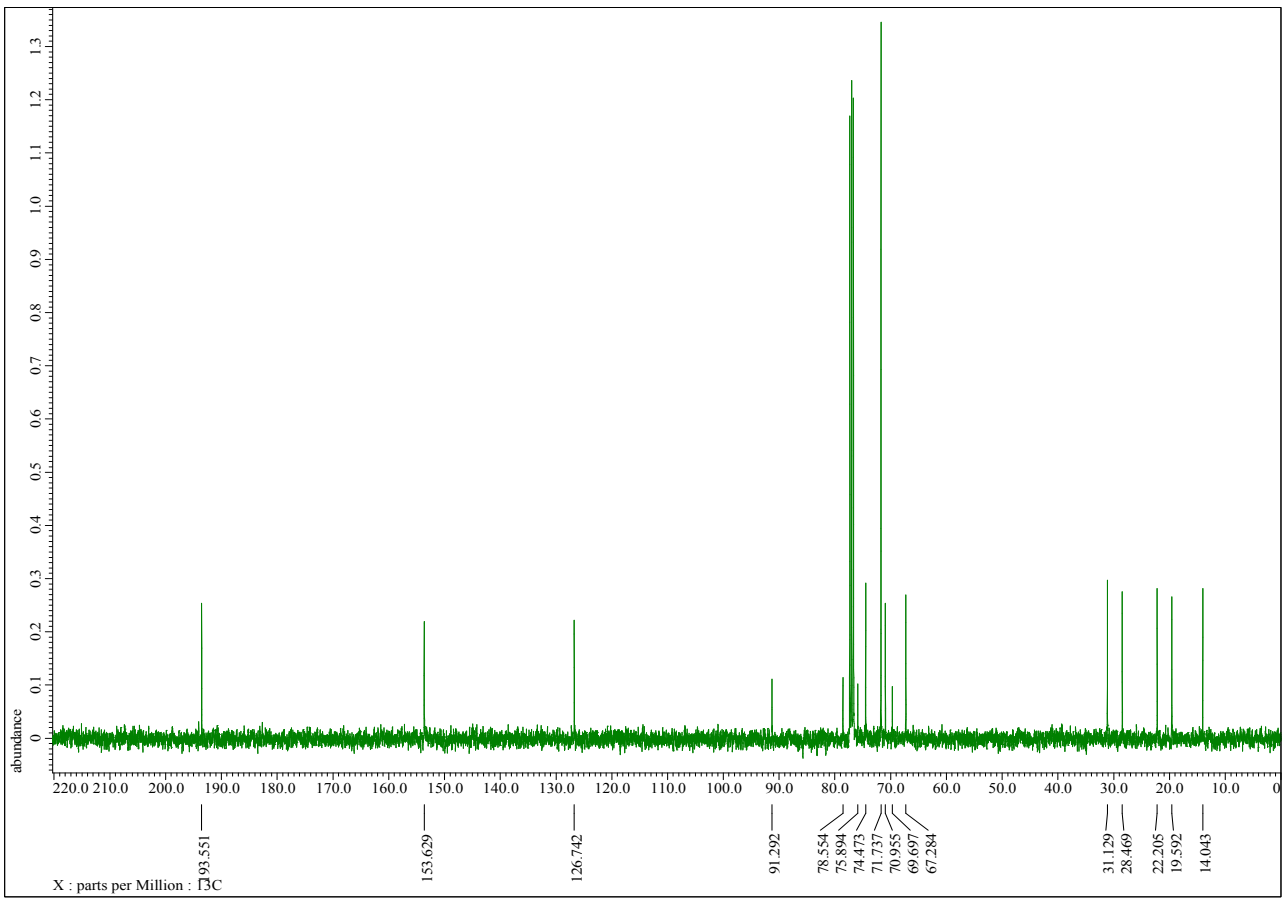

Cl
Fe
CHO
1c
abundance
X : parts per Million : 1H
9.656
9.636
7.630
7.591
6.516
6.496
6.475
6.456
4.753
4.572
4.450
4.227
1.00
0.99
0.98
0.87
0.84
0.80
4.64

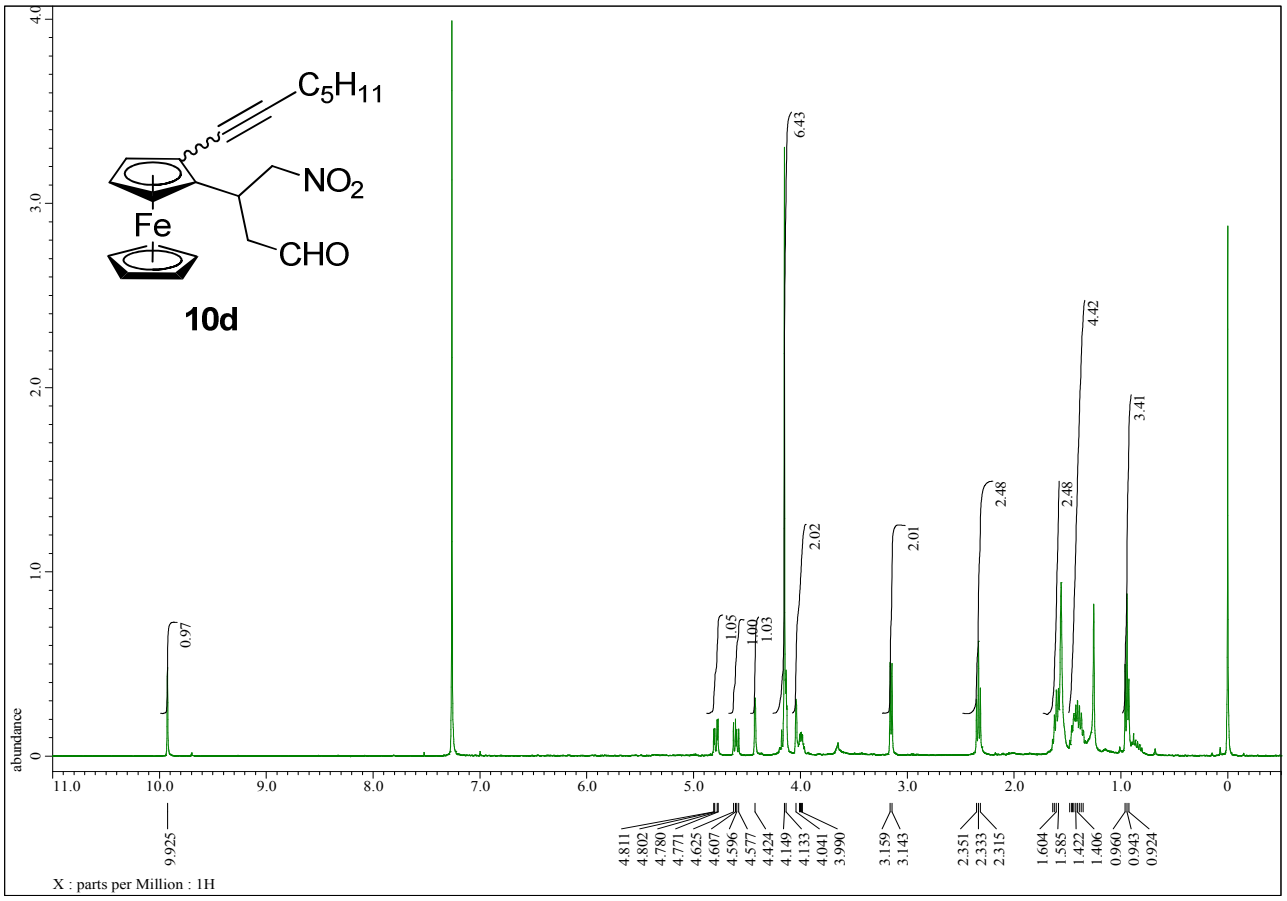

abundance
X : parts per Million : 13C
93.255
151.112
127.533
94.649
74.988
72.223
71.260
68.486
64.767

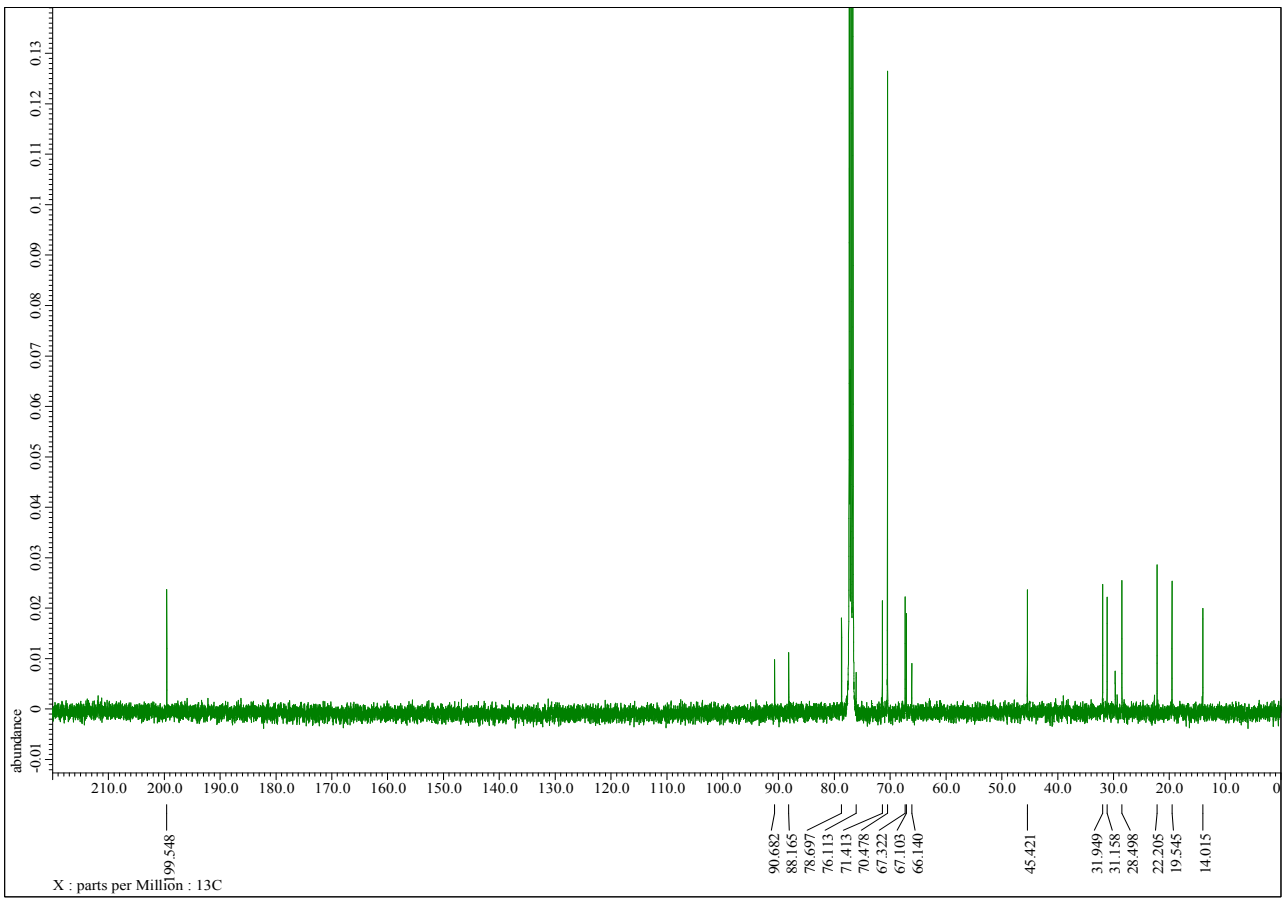

Cl
NO2
Fe
CHO
10c
abundance
X : parts per Million : 1H

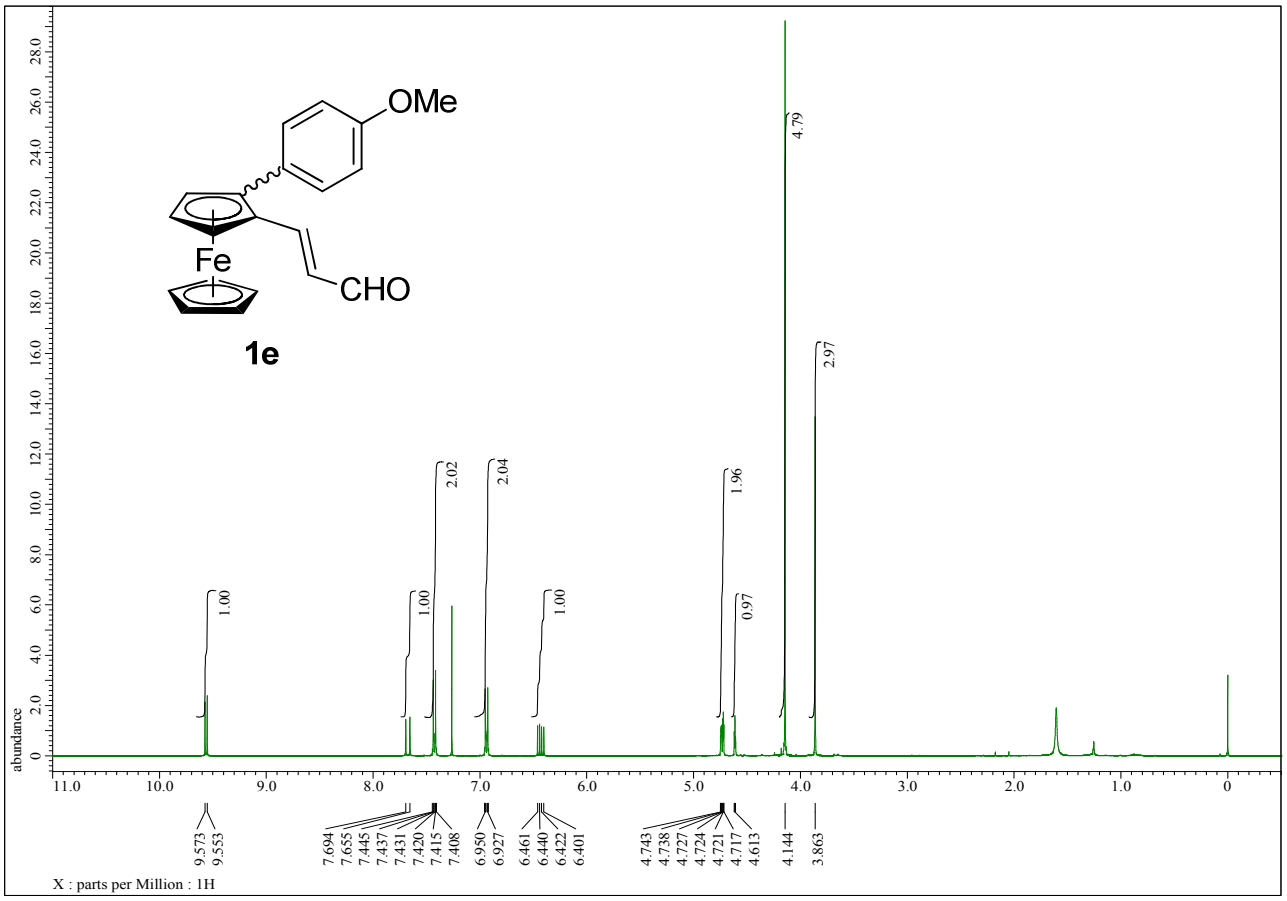

abundance
X : parts per Million : 13C

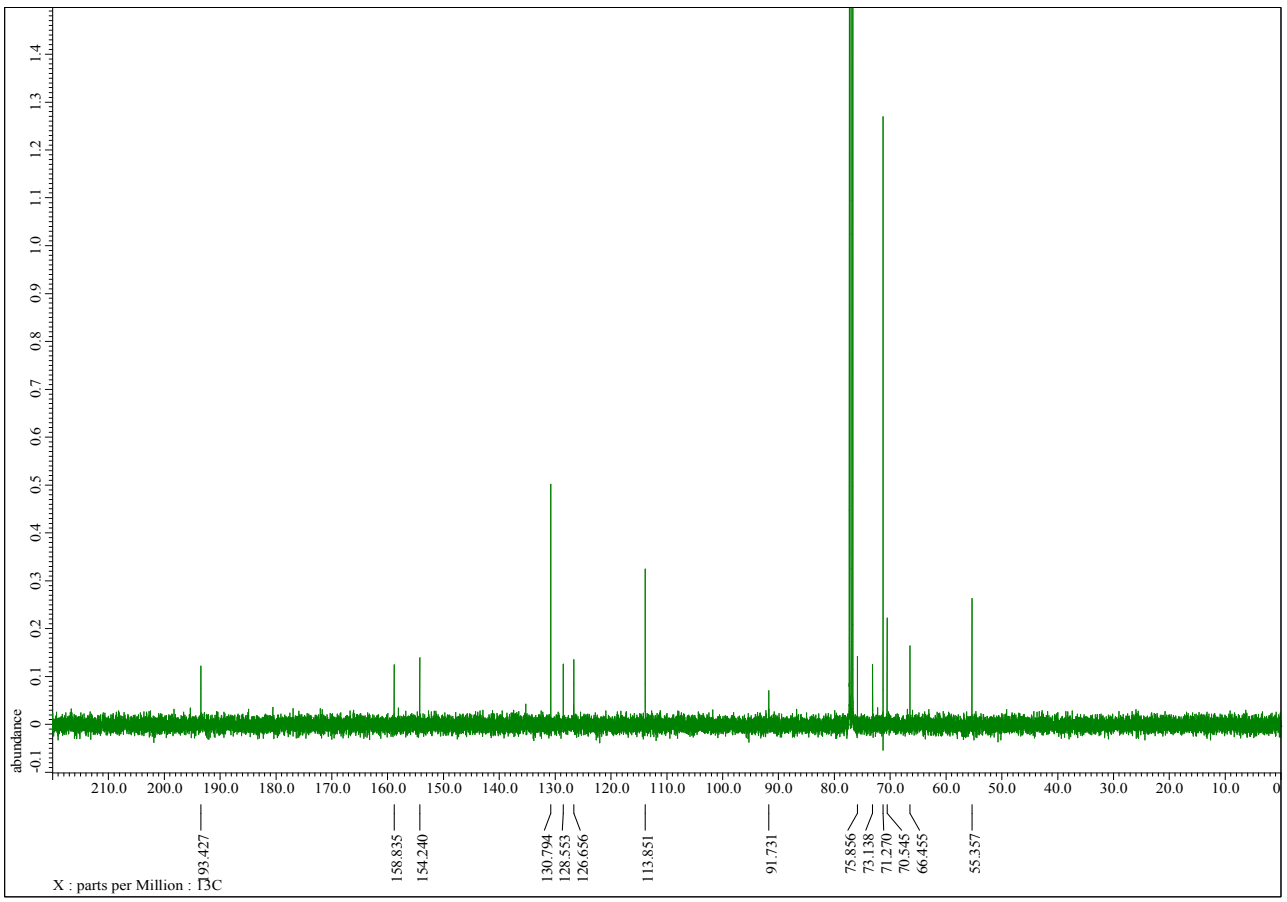

C5H11
Fe
CHO
1d
abundance
X : parts per Million : 1H

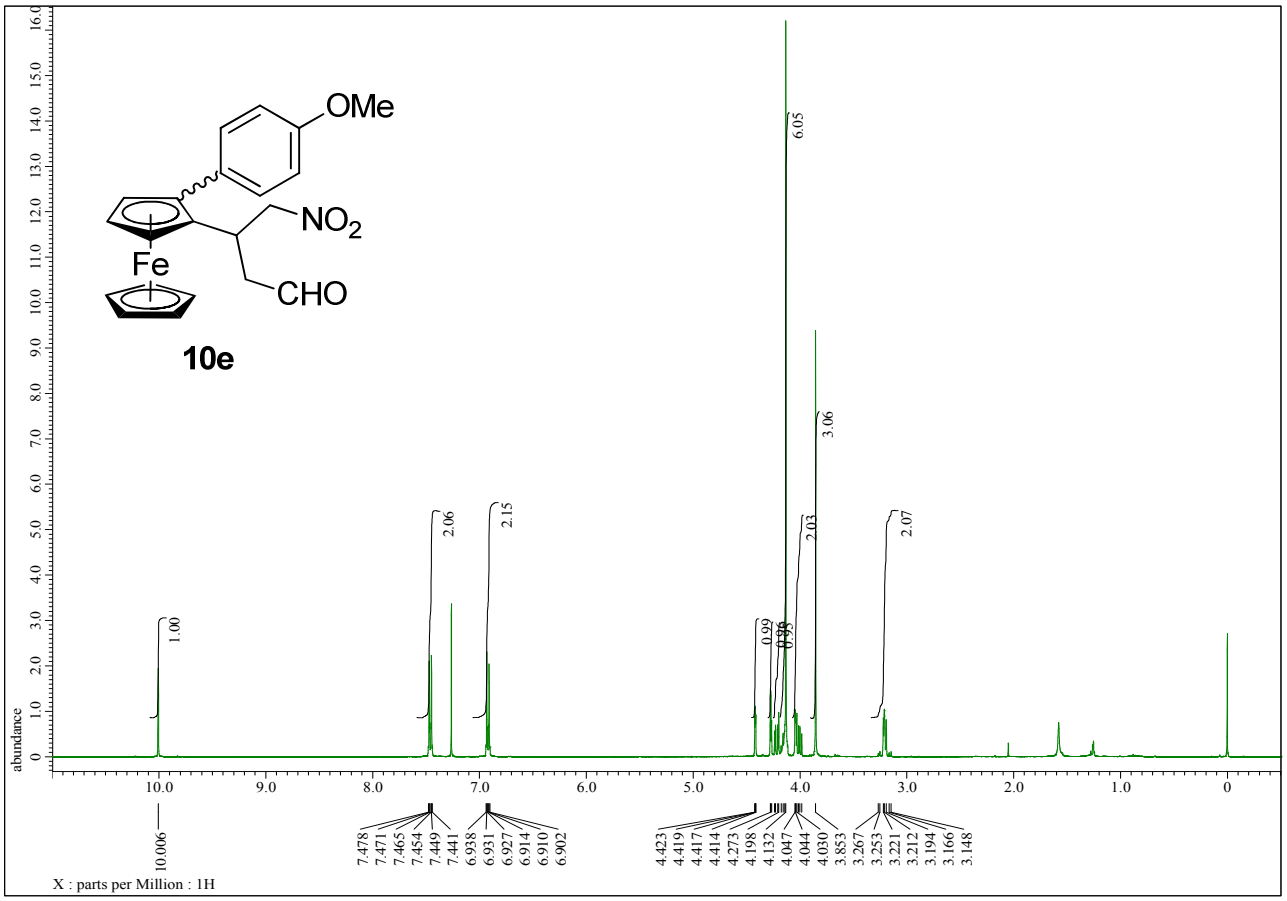

abundance
X : parts per Million : 13C

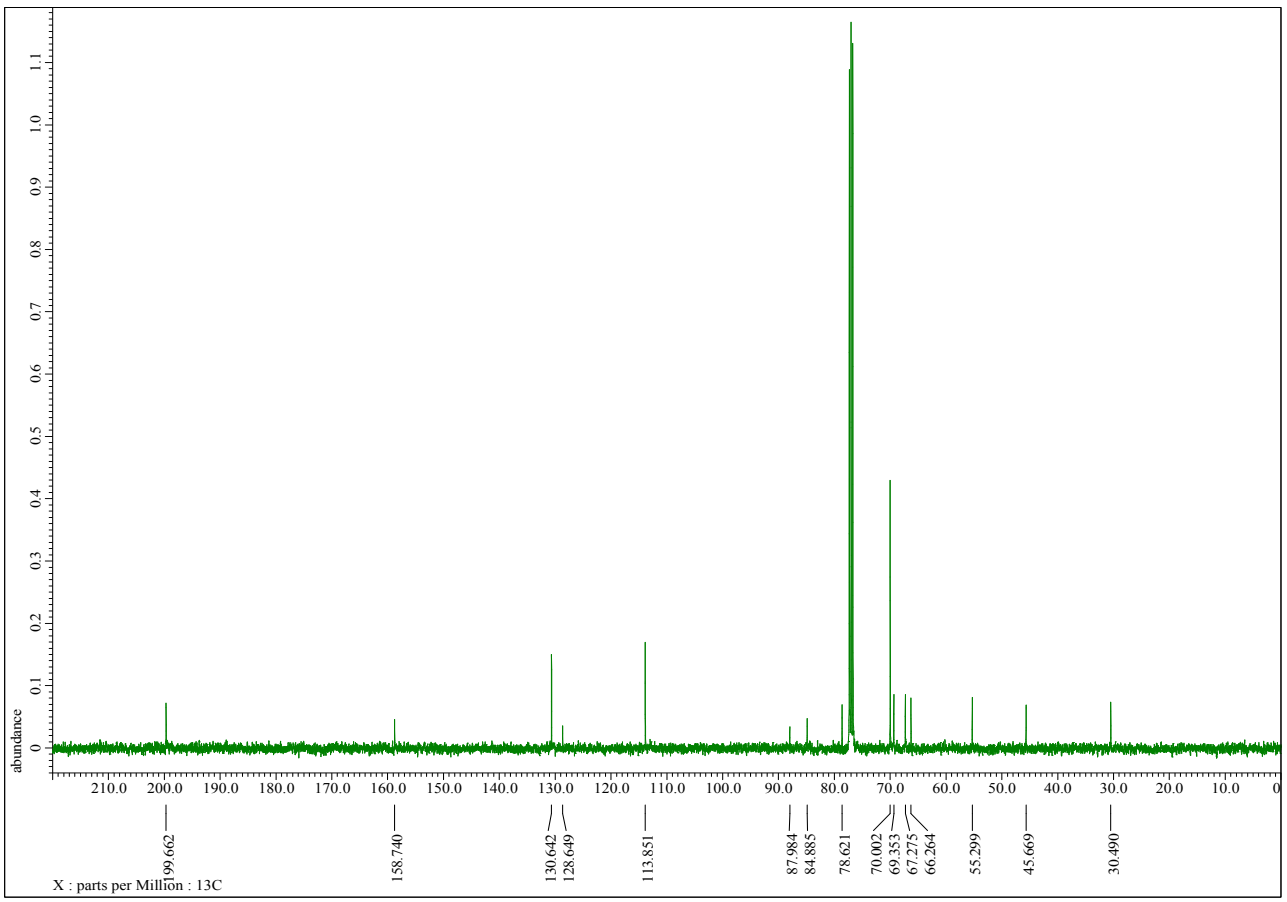

C_5H_{11}
NO_2
Fe
CHO
10d
abundance
X : parts per Million : 1H

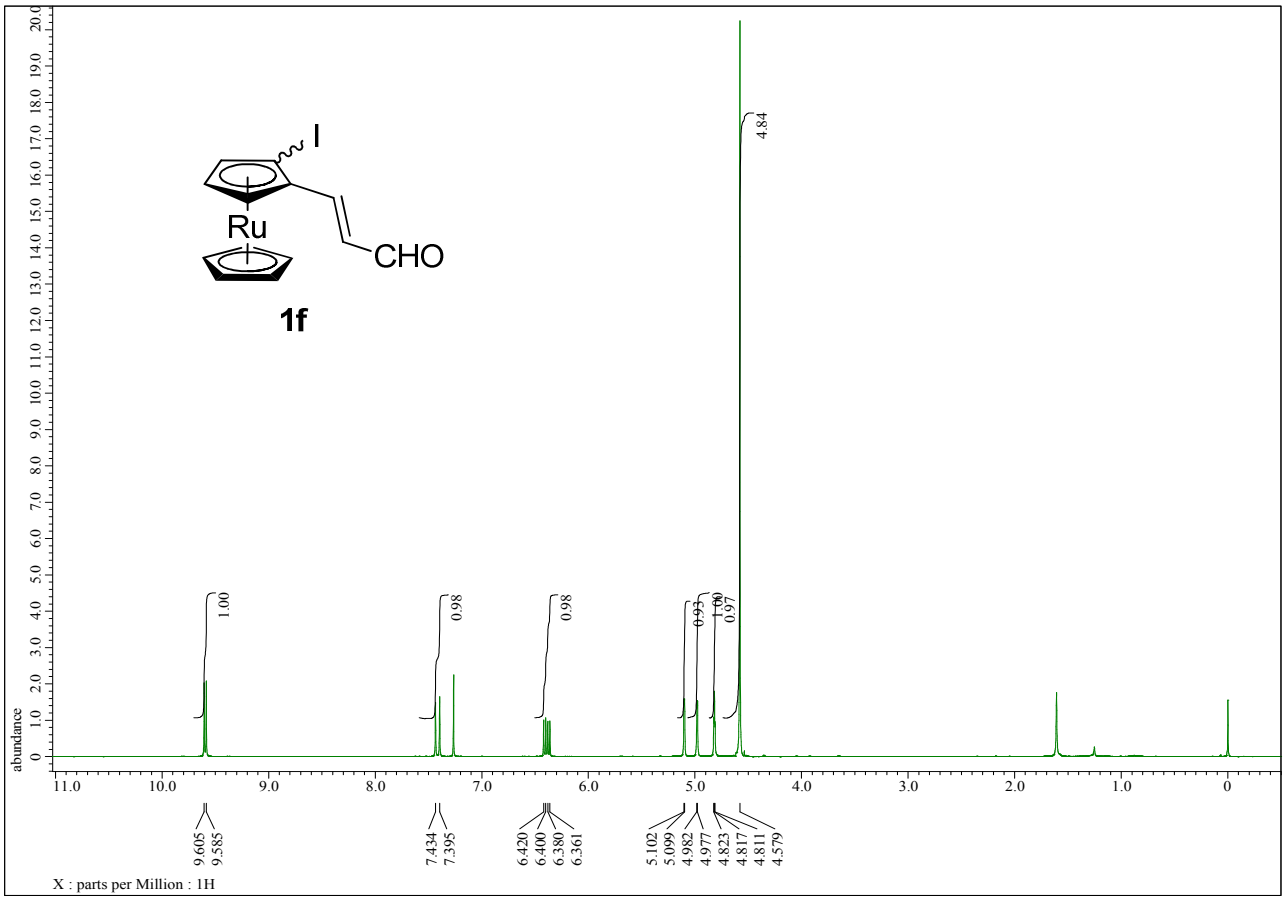

abundance
X : parts per Million : 13C

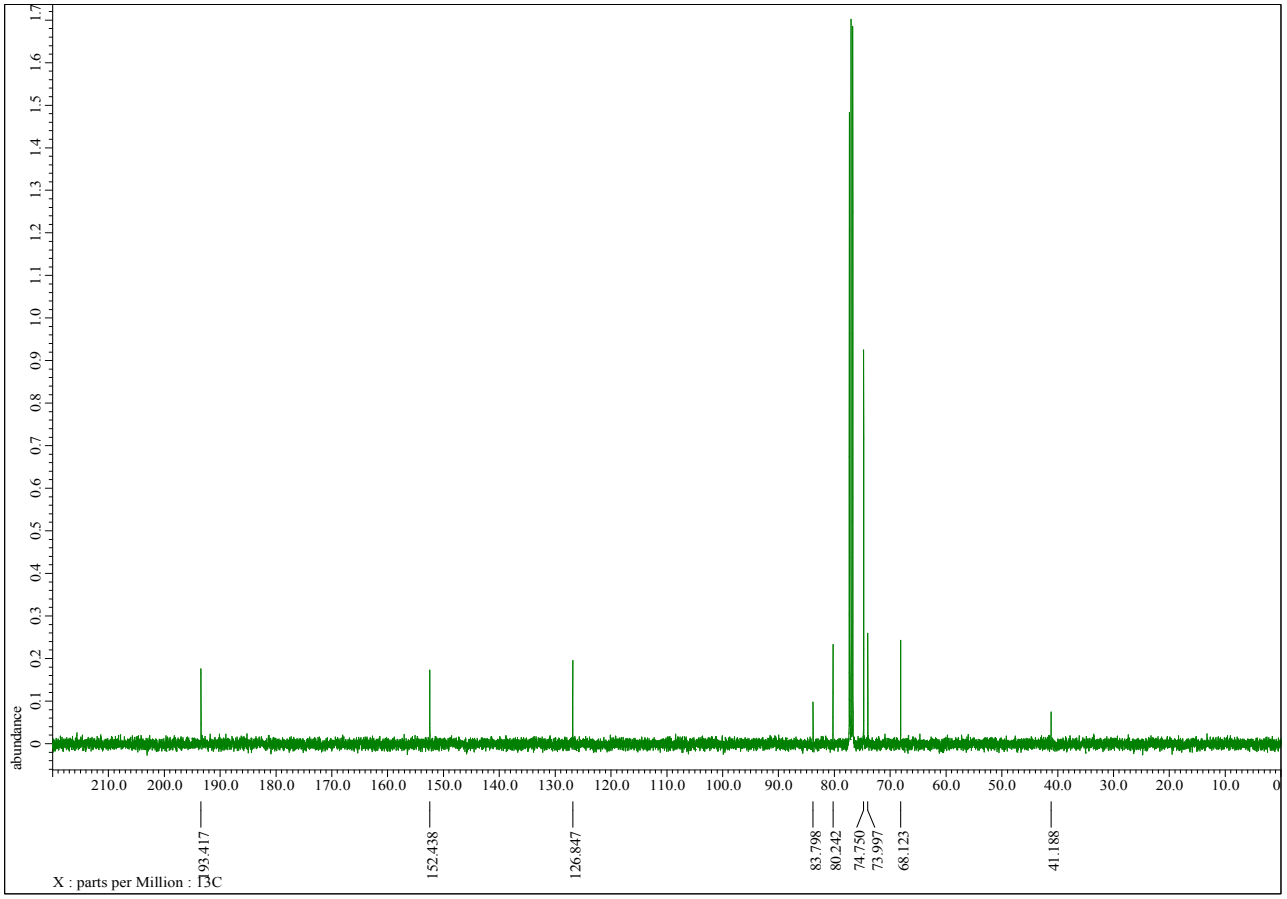

OMe
Fe
CHO
1e
abundance
X : parts per Million : 1H

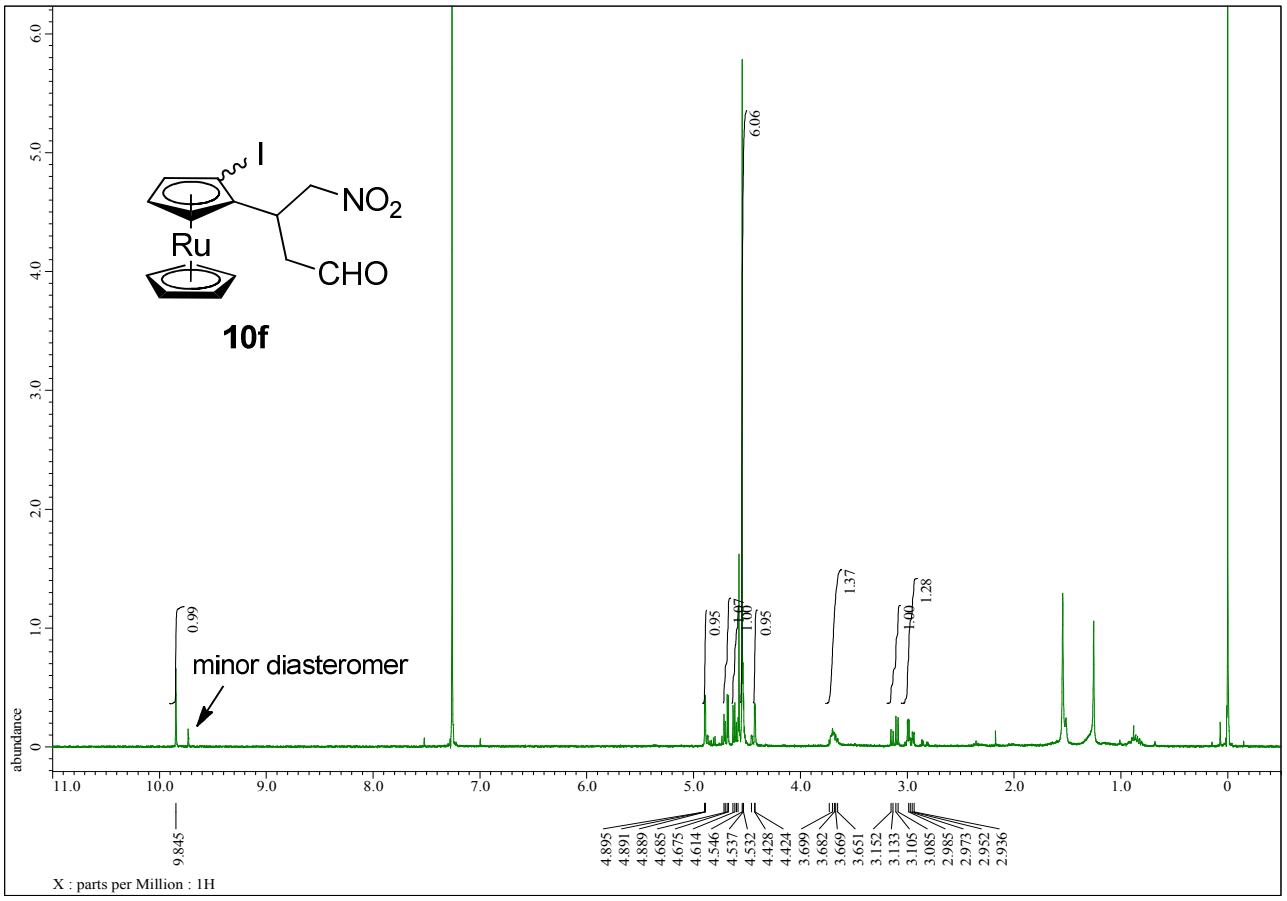

abundance
X : parts per Million : 13C

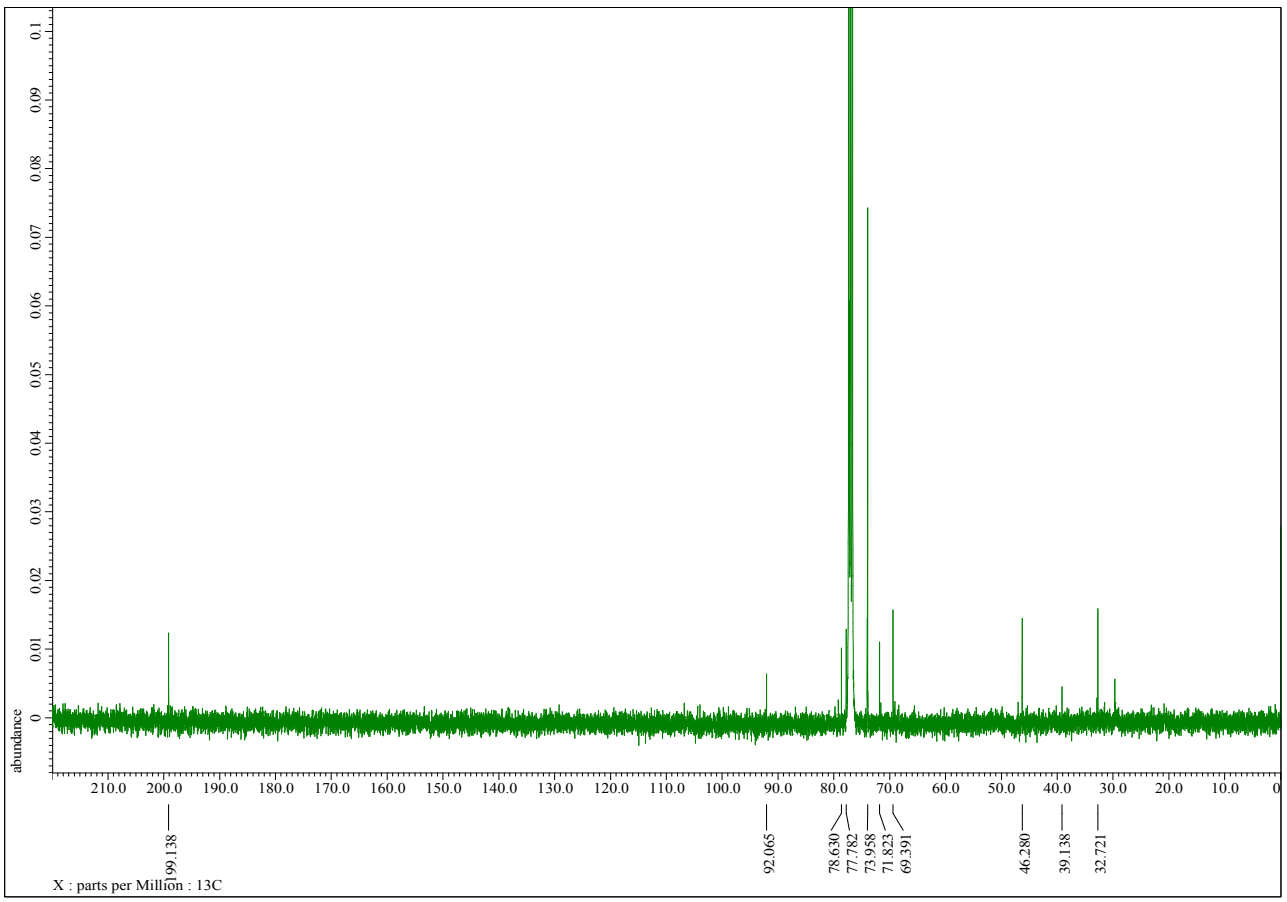

OMe
NO2
Fe
CHO
10e
abundance
X : parts per Million : 1H

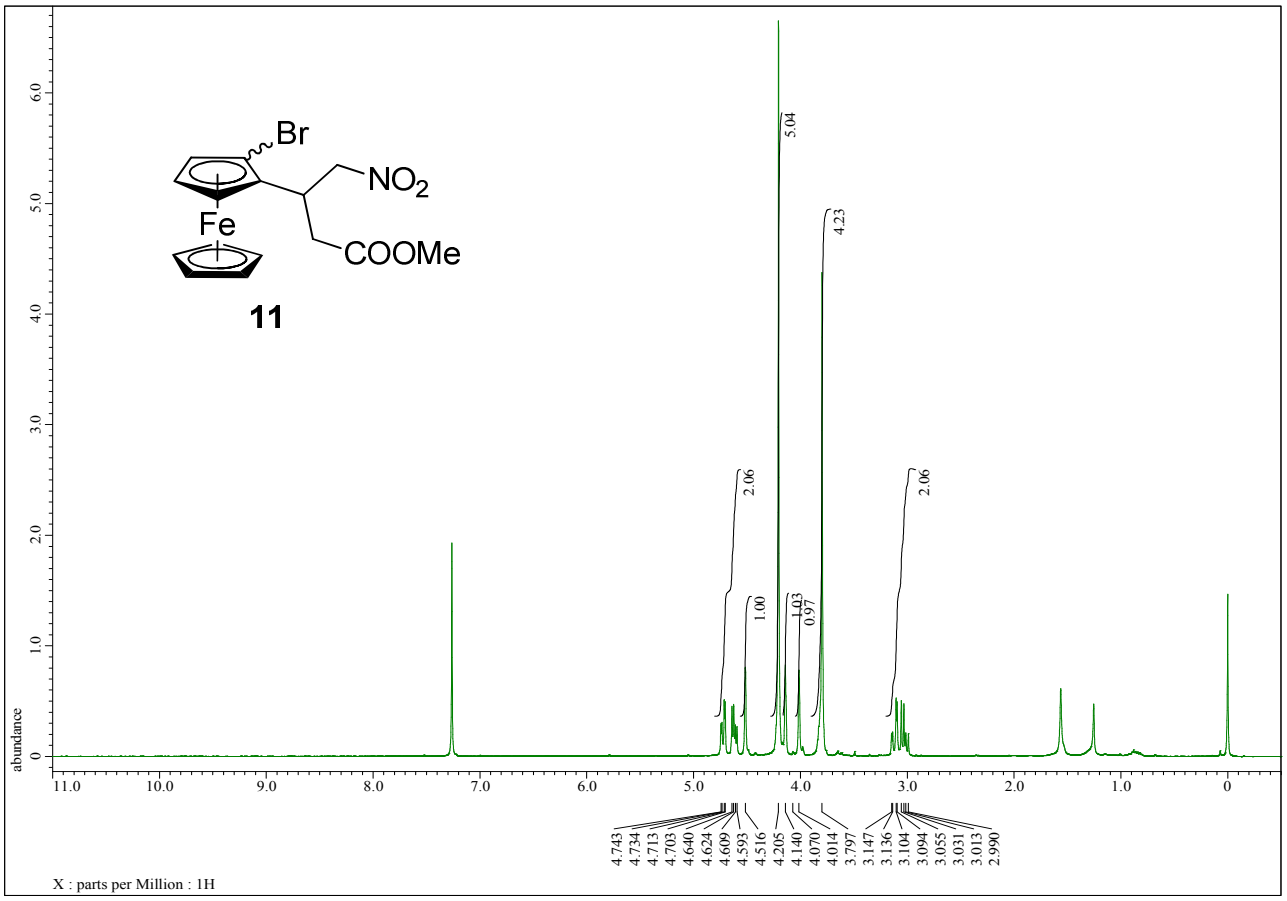

abundance
X : parts per Million : 13C

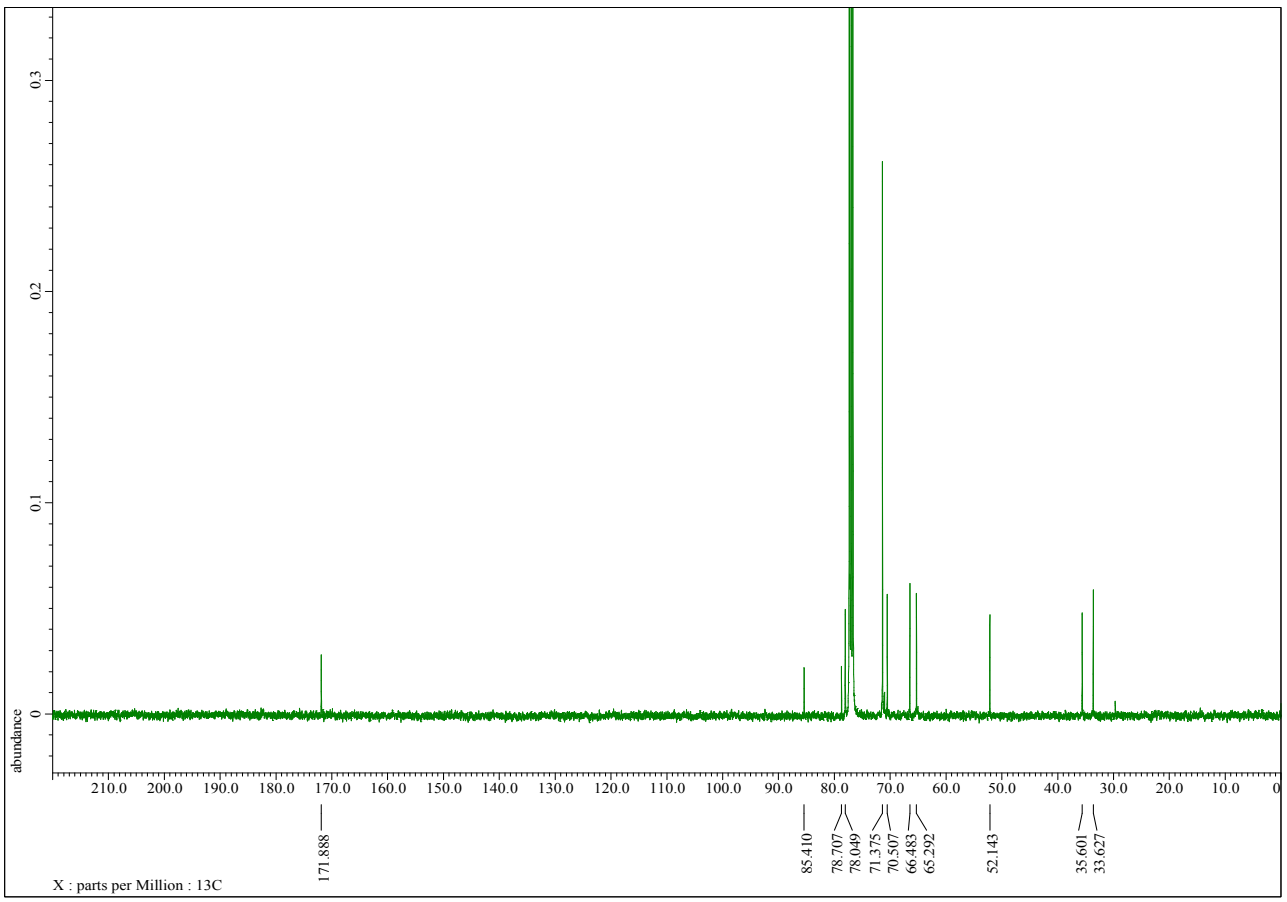

I
Ru
CHO
1f
abundance
1.00
0.98
0.98
0.93
1.00
0.97
4.84
9.605
9.585
7.434
7.395
6.420
6.400
6.380
6.361
5.102
5.099
4.982
4.977
4.823
4.817
4.811
4.579
X : parts per Million : 1H

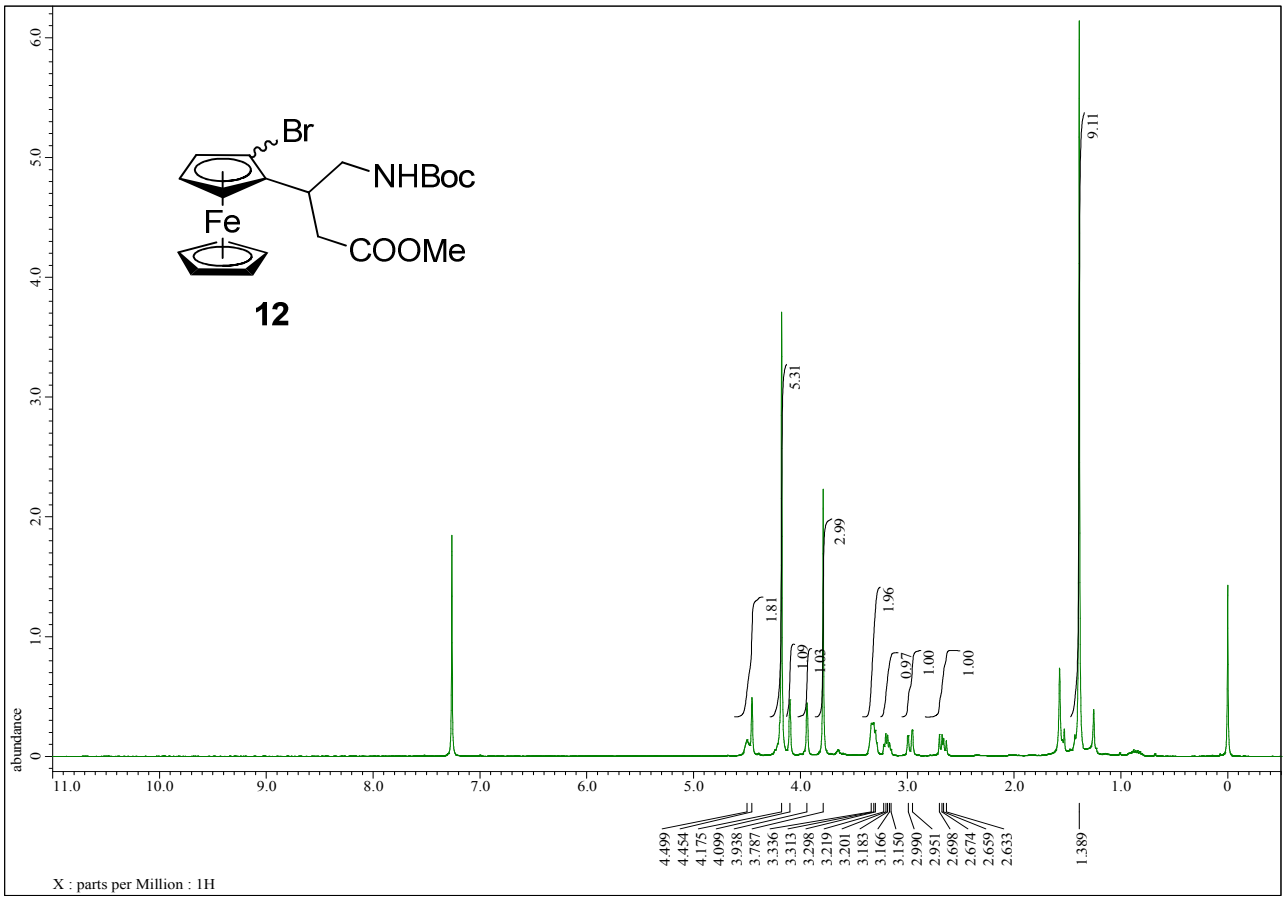

abundance
193.417
152.438
126.847
83.798
80.242
74.750
73.997
68.123
41.188
X : parts per Million : 13C

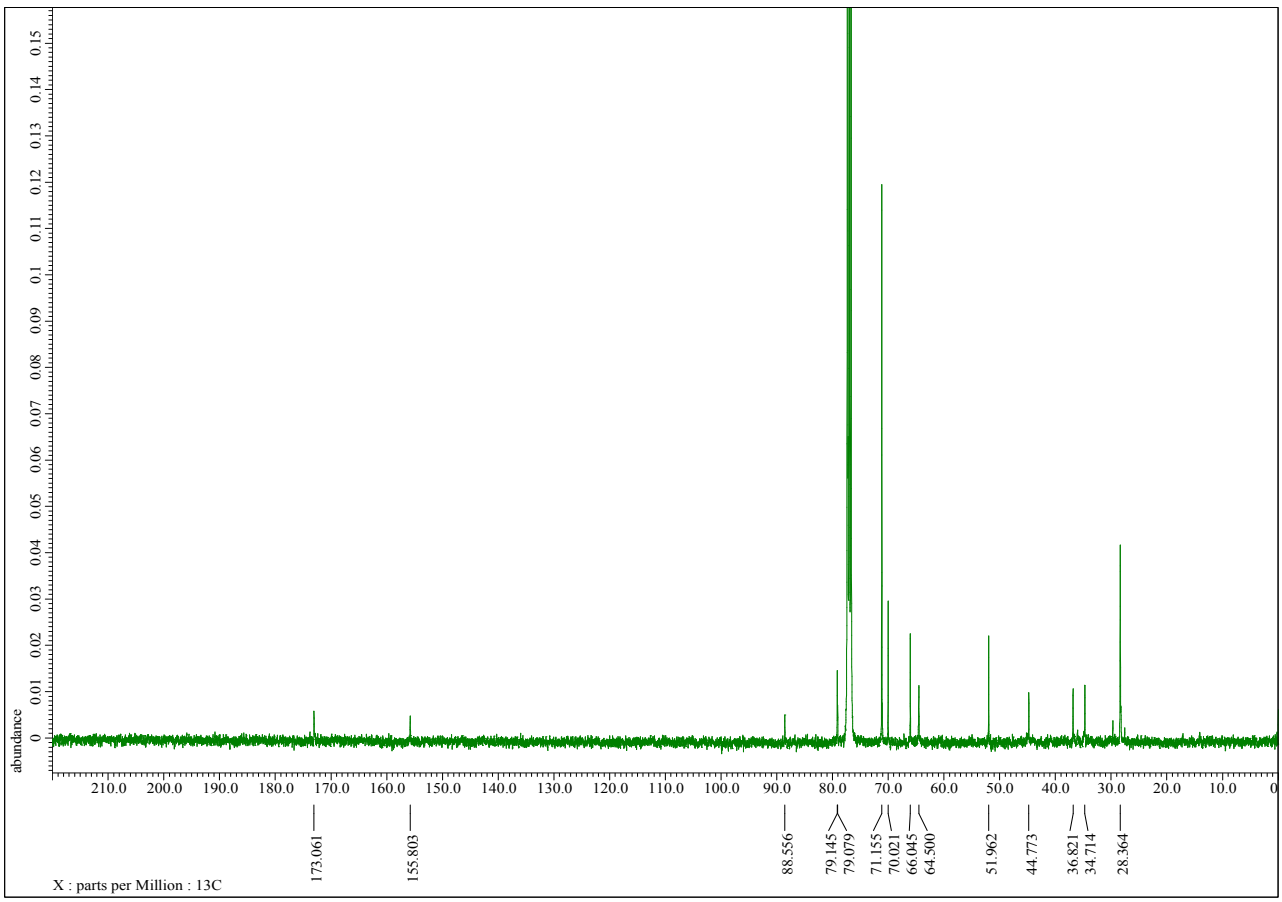

I
NO2
Ru
CHO
10f
minor diasteromer
abundance
X : parts per Million : 1H

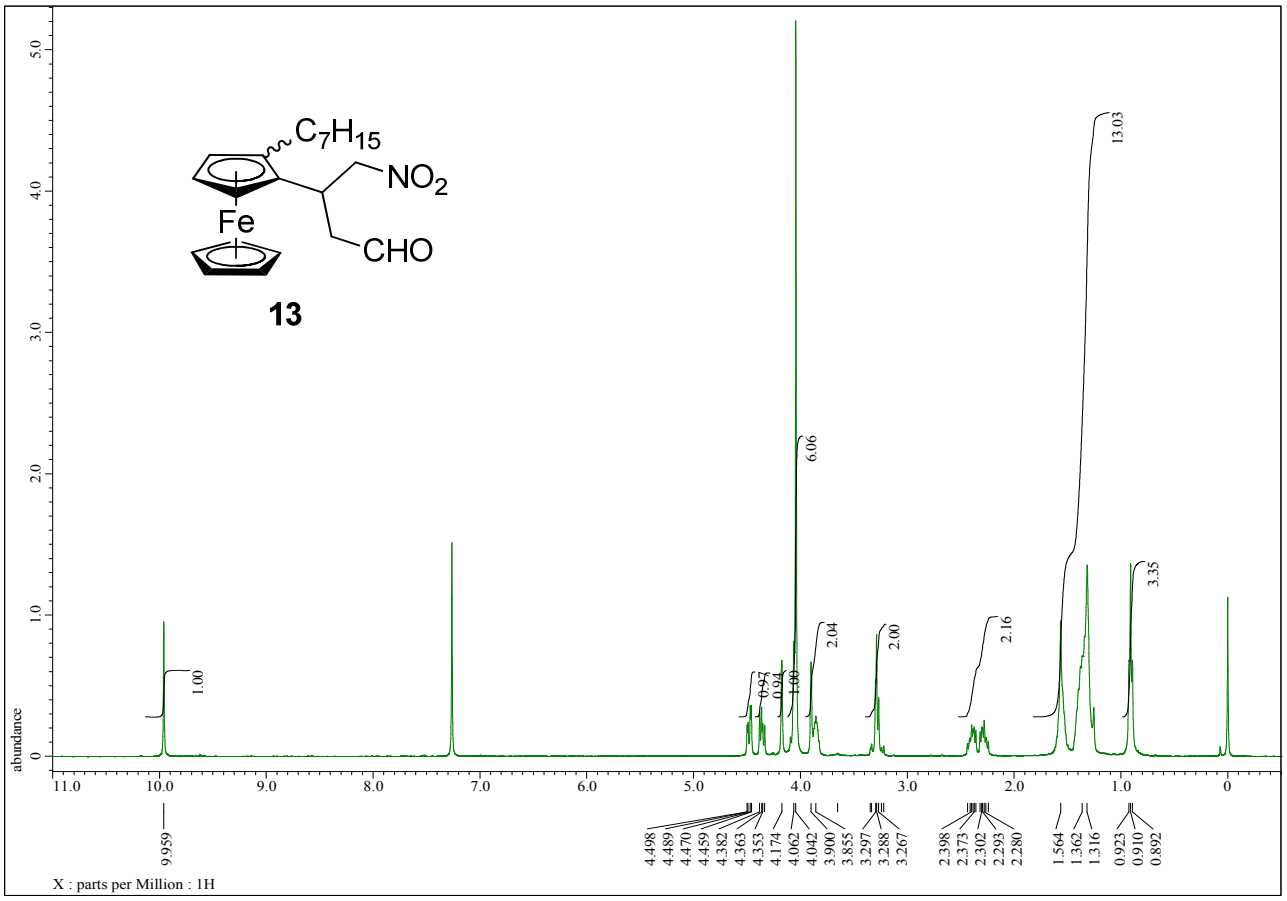

abundance
X : parts per Million : 13C

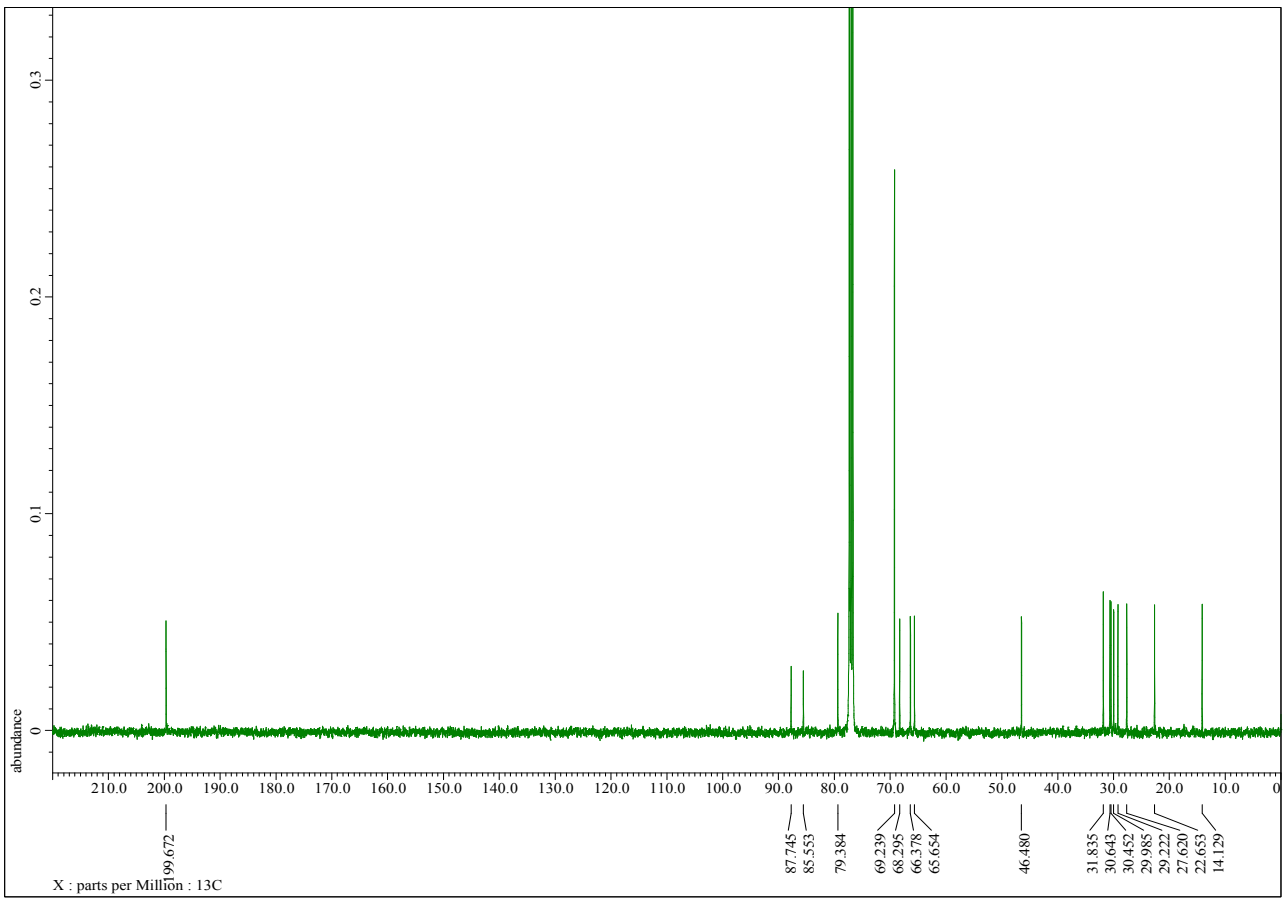

Br
NO2
Fe
COOMe
11
abundance
X : parts per Million : 1H


abundance
X : parts per Million : 13C


Br
NHBoc
Fe
COOMe
12
abundance
X : parts per Million : 1H
9.11
5.31
2.99
1.81
1.96
1.09
1.03
0.97
1.00
1.00
4.499
4.454
4.175
4.099
3.938
3.787
3.336
3.313
3.298
3.219
3.201
3.183
3.166
3.150
2.990
2.951
2.698
2.674
2.659
2.633
1.389

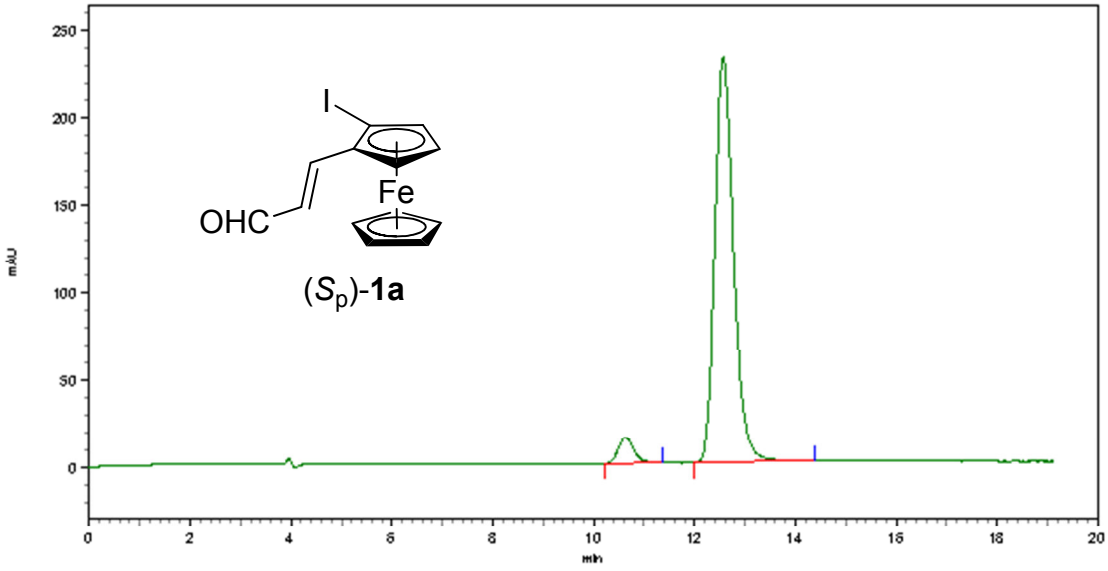

abundance
X : parts per Million : 13C
173.061
155.803
88.556
79.145
79.079
71.155
70.021
66.045
64.500
51.962
44.773
36.821
34.714
28.364


C7H15
NO2
Fe
CHO
13
abundance
X : parts per Million : 1H


abundance
X : parts per Million : 13C

HPLC traces.

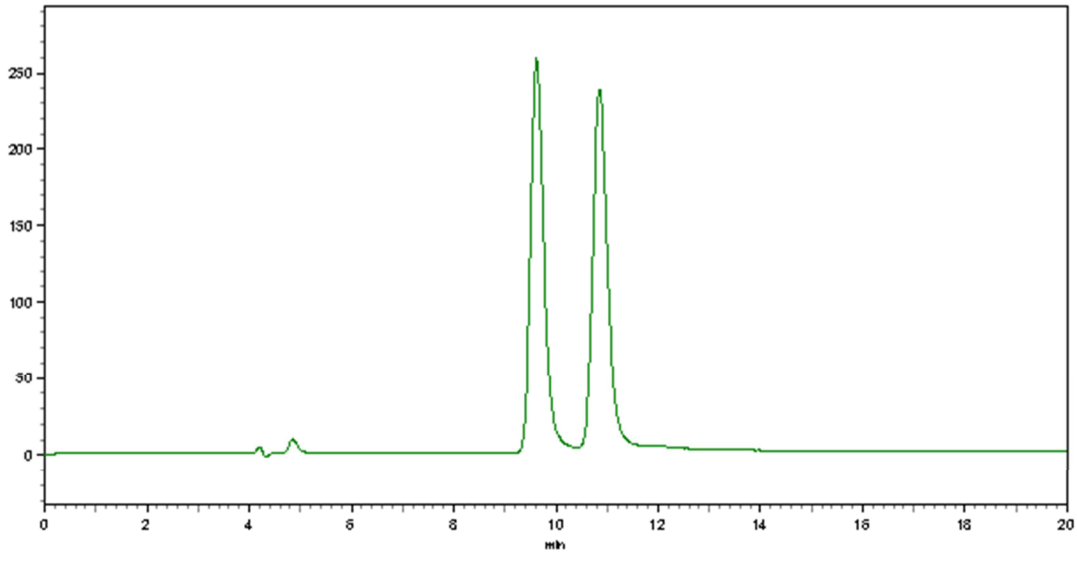
Chiralcel OD-H column, hexane/2-propanol = 90:10, 1.0 mL min^{-1}



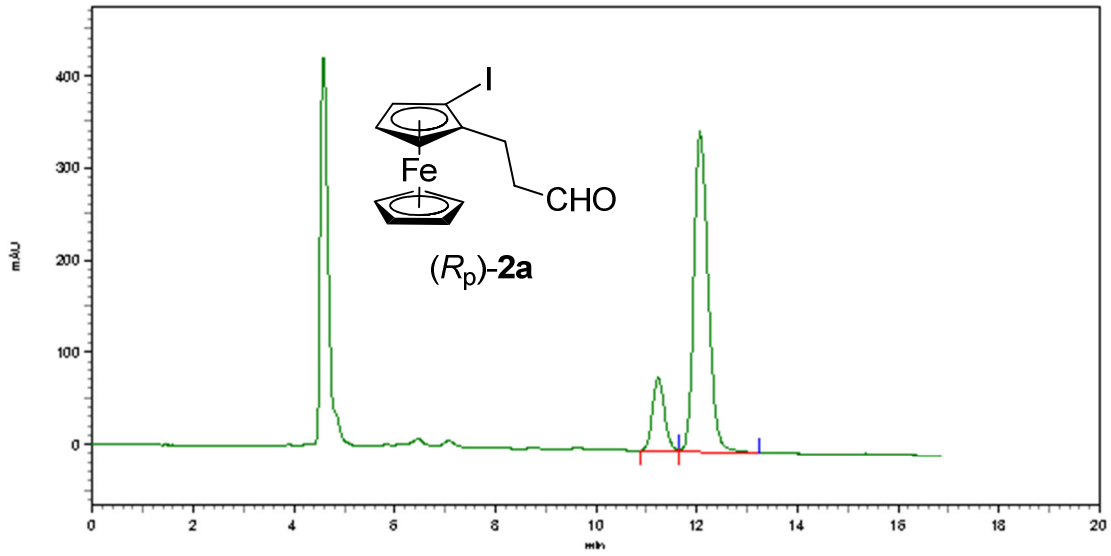
4: 310 nm, 8 nm

retention time	area	area%
10.624	327764	5.17
12.564	6017898	94.83
Total	6345662	100.00

racemic sample



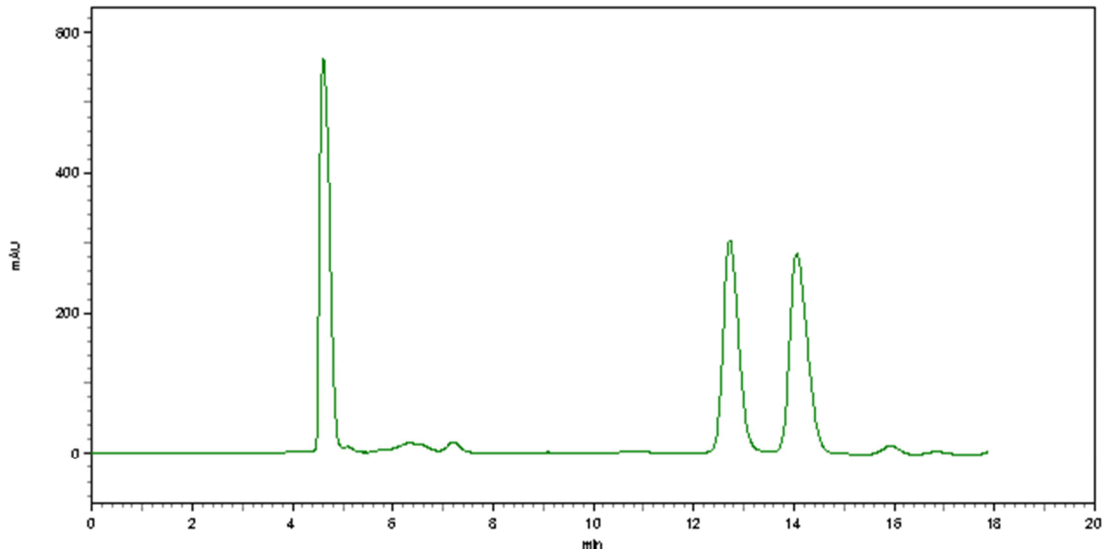
Chiralpak AS-H column, hexane/2-propanol = 90:10, 1.0 mL min^{-1}



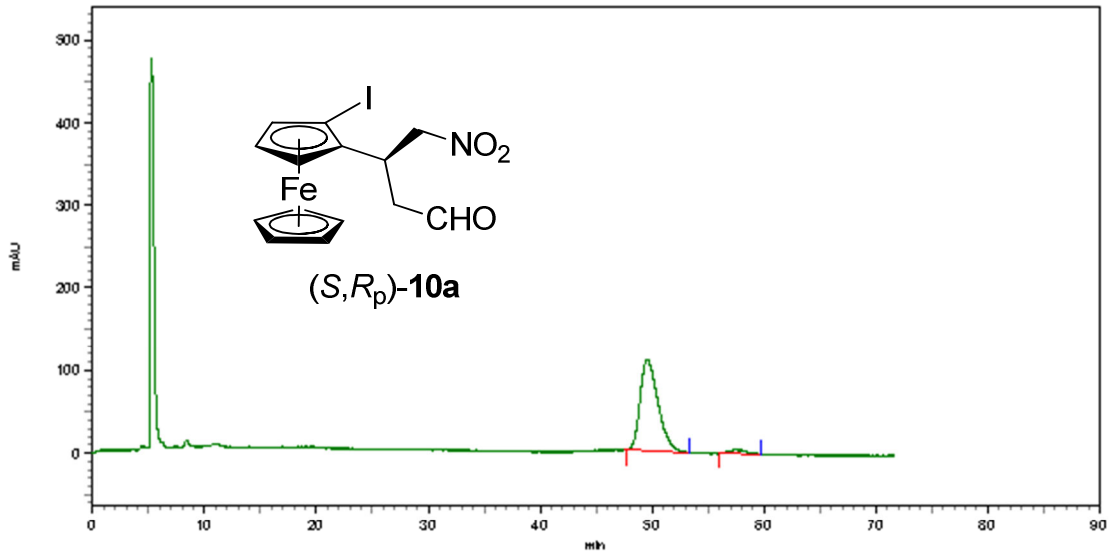
1: 220 nm, 8 nm

retention time	area	area%
11.230	1297543	16.05
12.056	6784999	83.95
Total	8082543	100.00

racemic sample



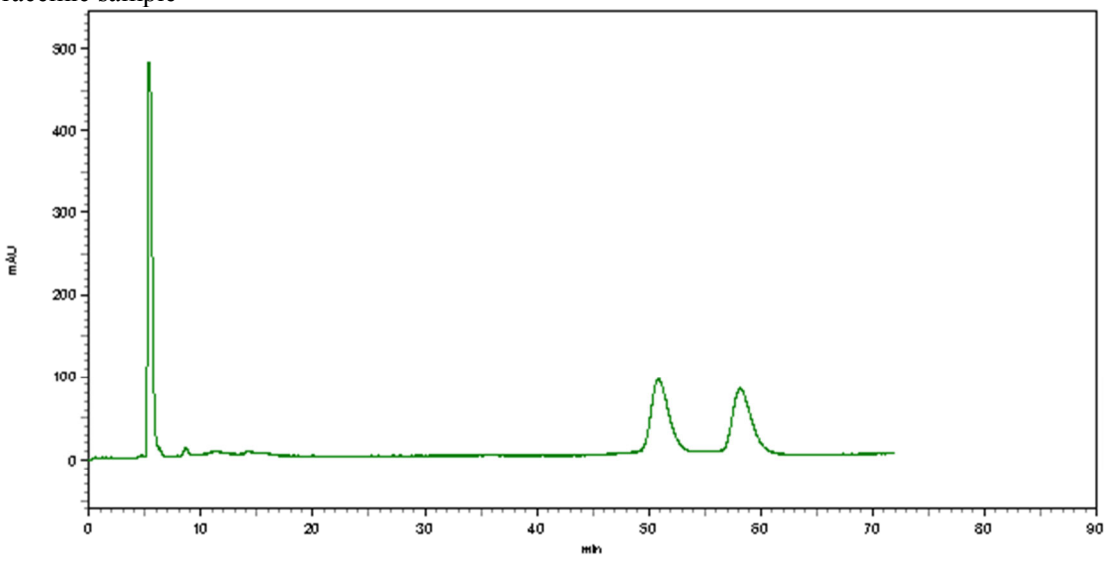
Chiralcel OJ-H column, hexane/2-propanol = 70:30, 0.8 mL min^{-1}



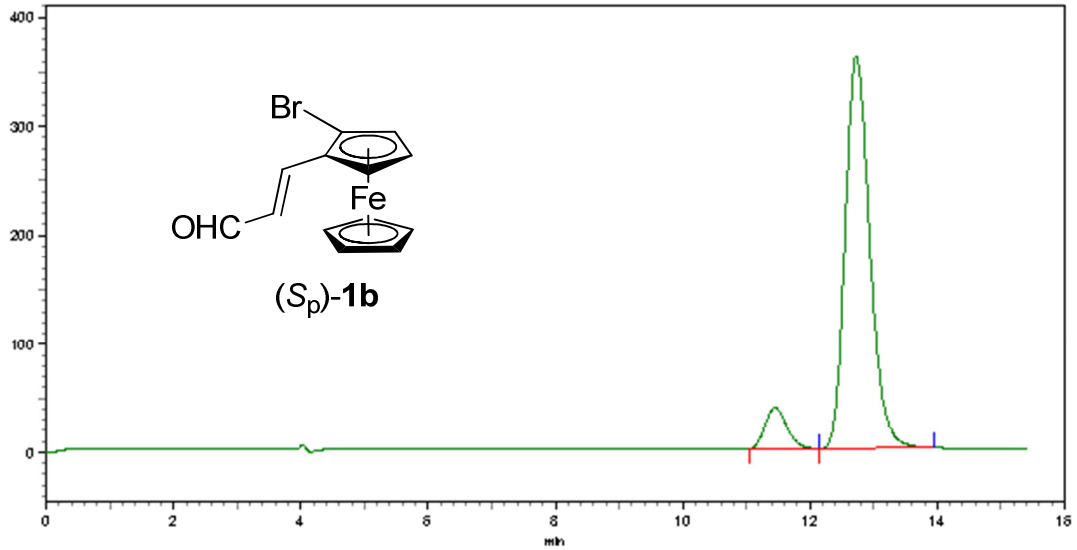
3: 210 nm, 8 nm

retention time	area	area%
49.525	12529310	95.94
57.611	530033	4.06
Total	13059343	100.00

racemic sample



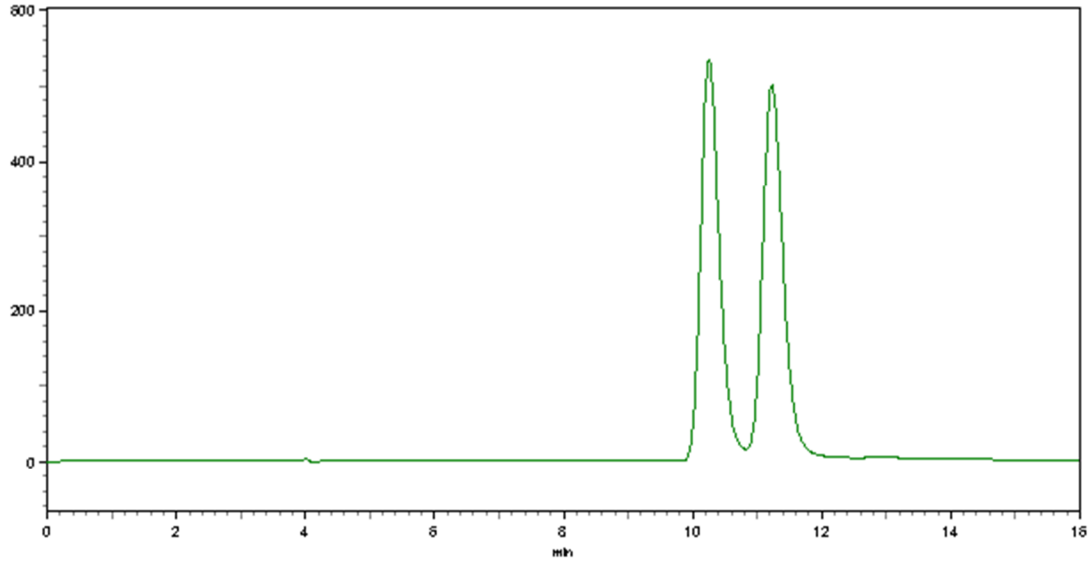
Chiralcel OD-H column, hexane/2-propanol = 90:10, 1.0 mL min^{-1}



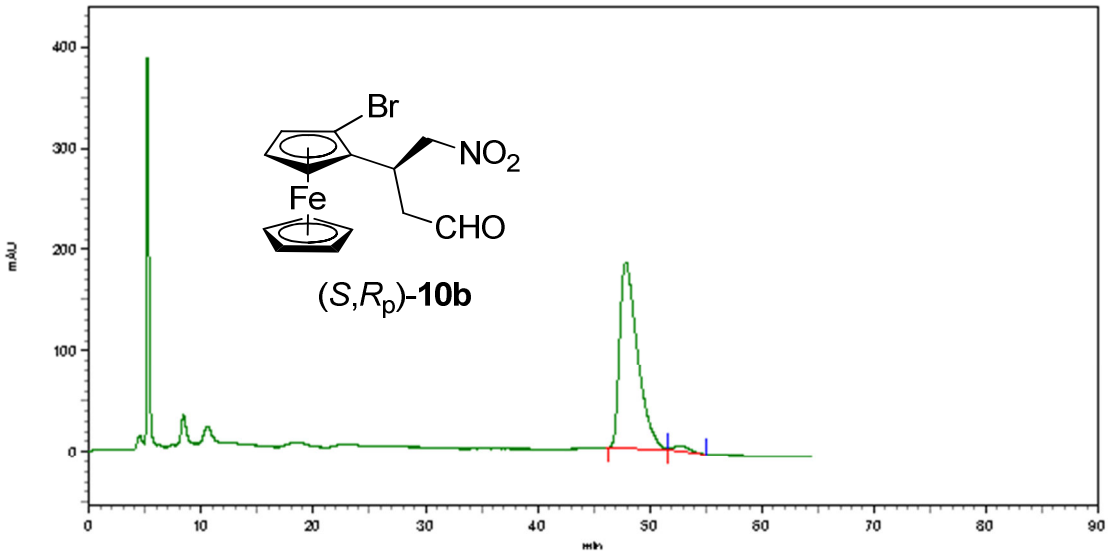
3: 310 nm, 8 nm

retention time	area	area%
11.445	907730	8.56
12.723	9698606	91.44
Total	10606335	100.00

racemic sample



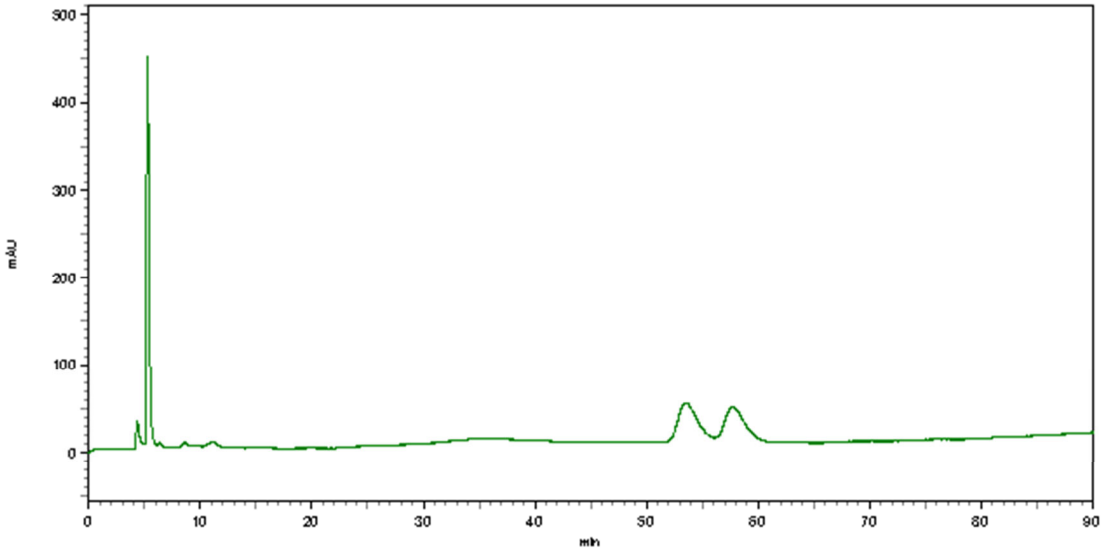
Chiralcel OJ-H column, hexane/2-propanol = 70:30, 0.8 mL min^{-1}



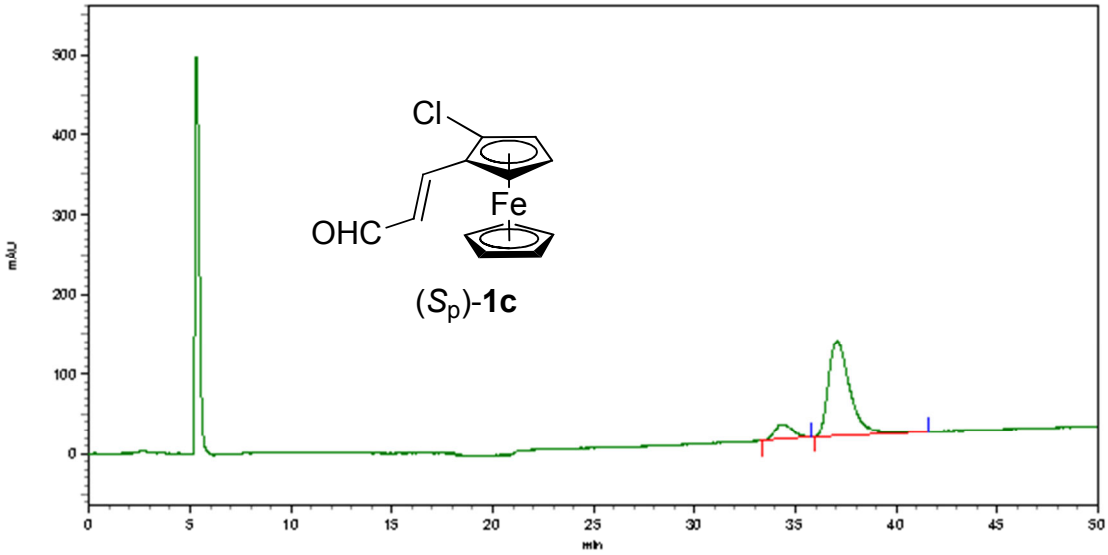
1: 220 nm, 8 nm

retention time	area	area%
47.847	20273331	97.86
52.853	443006	2.14
Total	20716337	100.00

racemic sample



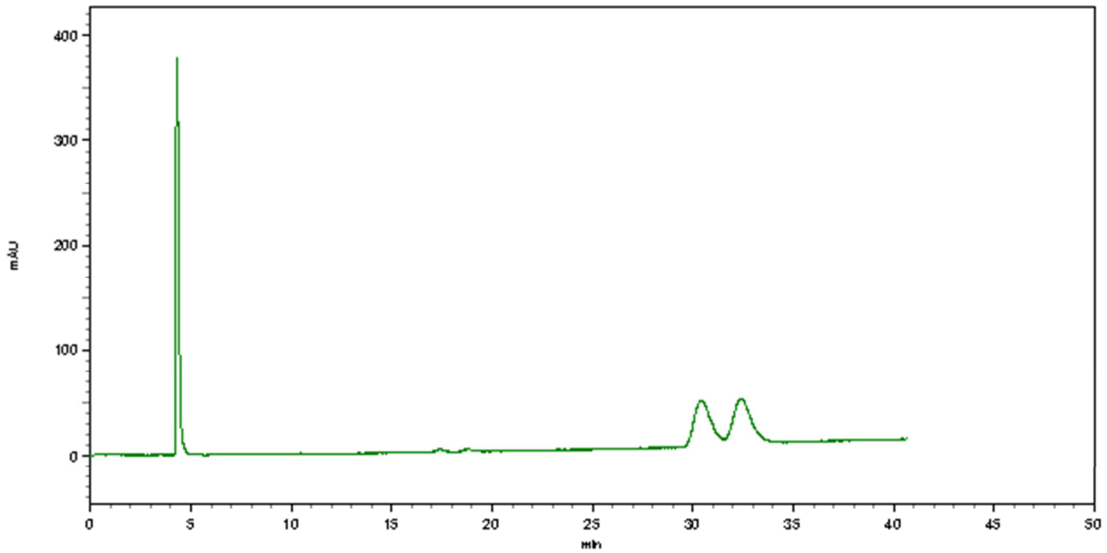
Chiralcel OD-H column, hexane/2-propanol = 90:10, 1.0 mL min^{-1}



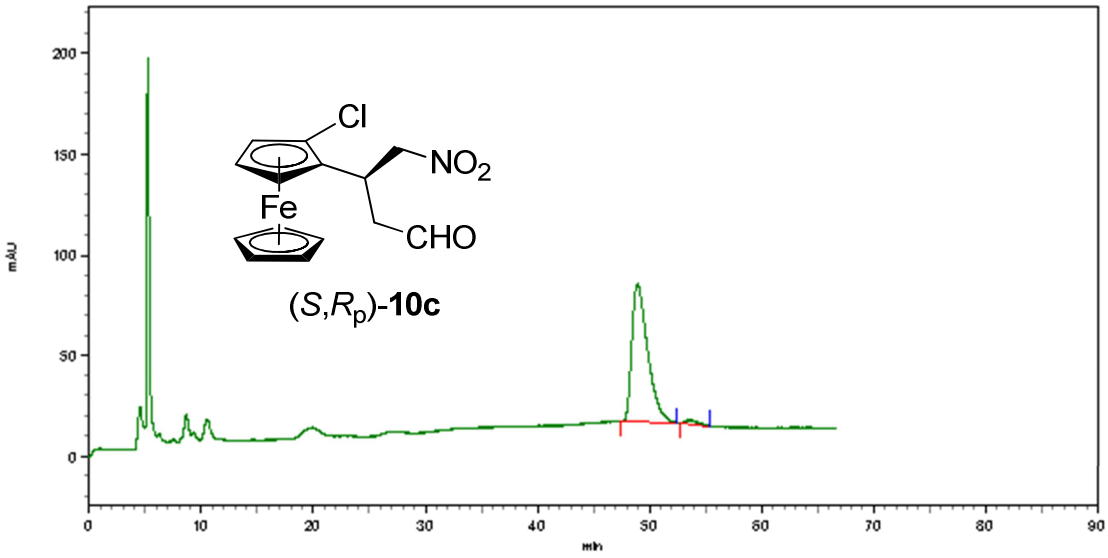
3: 210 nm, 8 nm

retention time	area	area%
34.338	1203082	12.10
37.077	8742391	87.90
Total	9945472	100.00

racemic sample



Chiralcel OJ-H column, hexane/2-propanol = 70:30, 0.8 mL min^{-1}

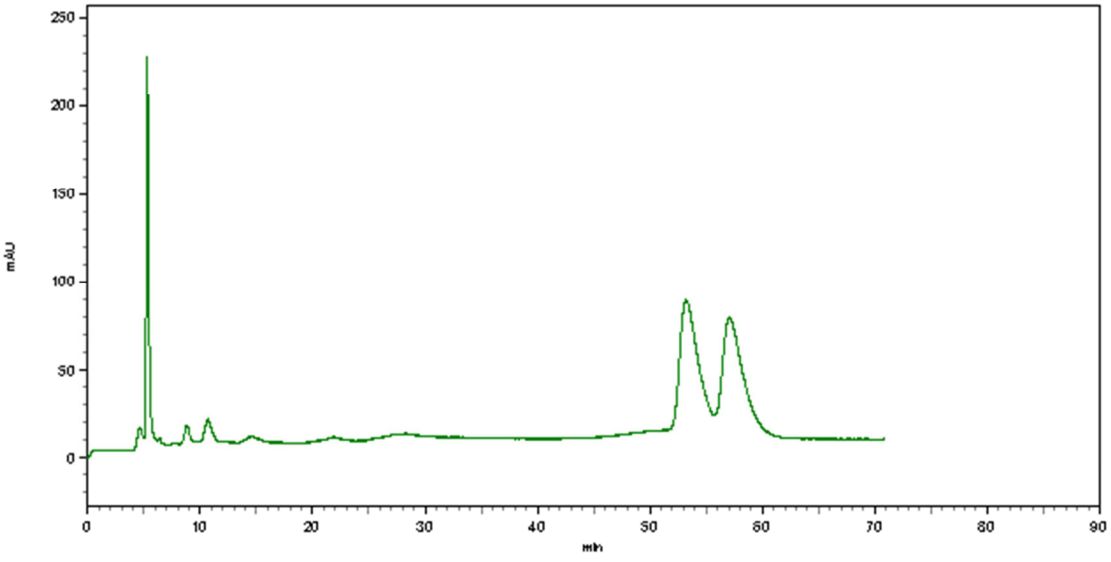


1: 225 nm, 8 nm

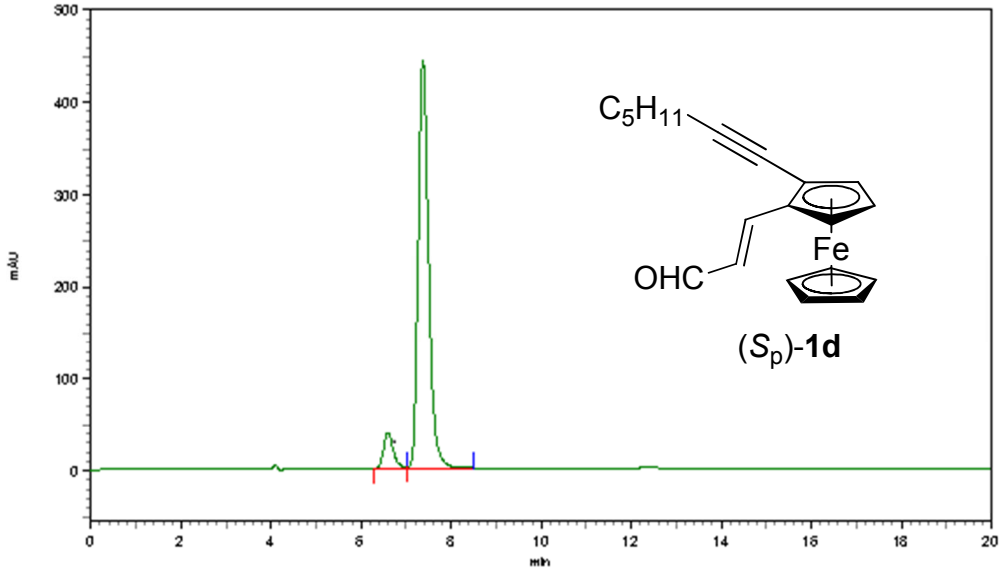
retention time	area	area%
48.939	6695638	97.54
53.728	168933	2.46

Total	6864571	100.00

racemic sample



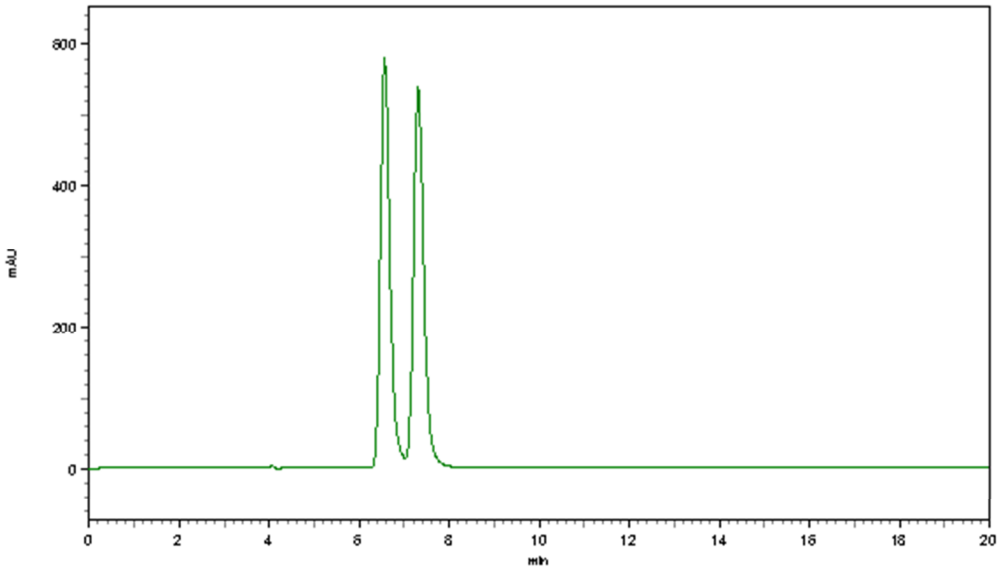
Chiralcel OD-H column, hexane/2-propanol = 90:10, 1.0 mL min^{-1}



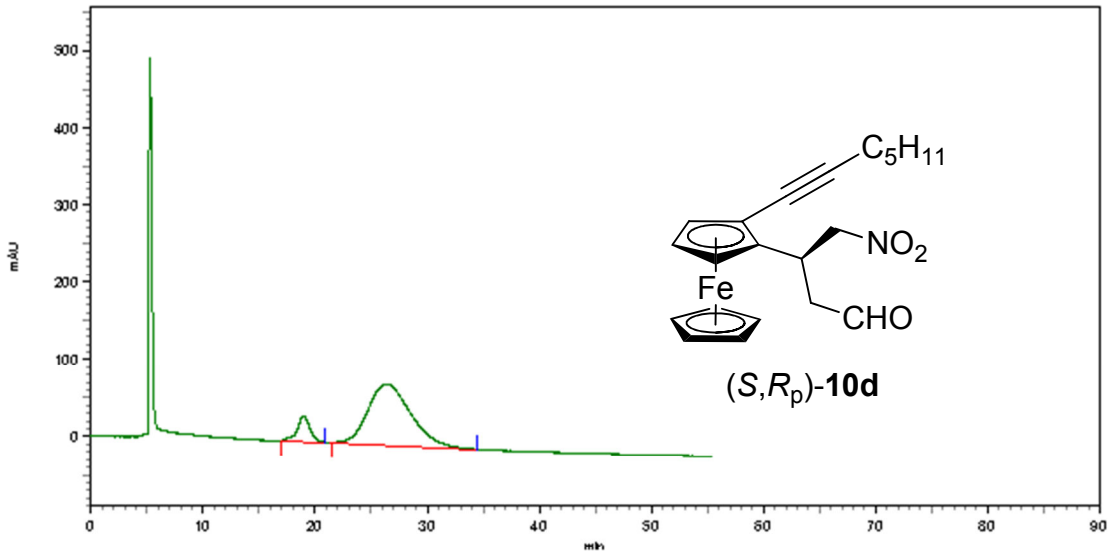
4: 310 nm, 8 nm

retention time	area	area%
6.590	565904	7.32
7.368	7162226	92.68
Total	7728131	100.00

racemic sample



Chiralcel OJ-H column, hexane/2-propanol = 70:30, 0.8 mL min^{-1}



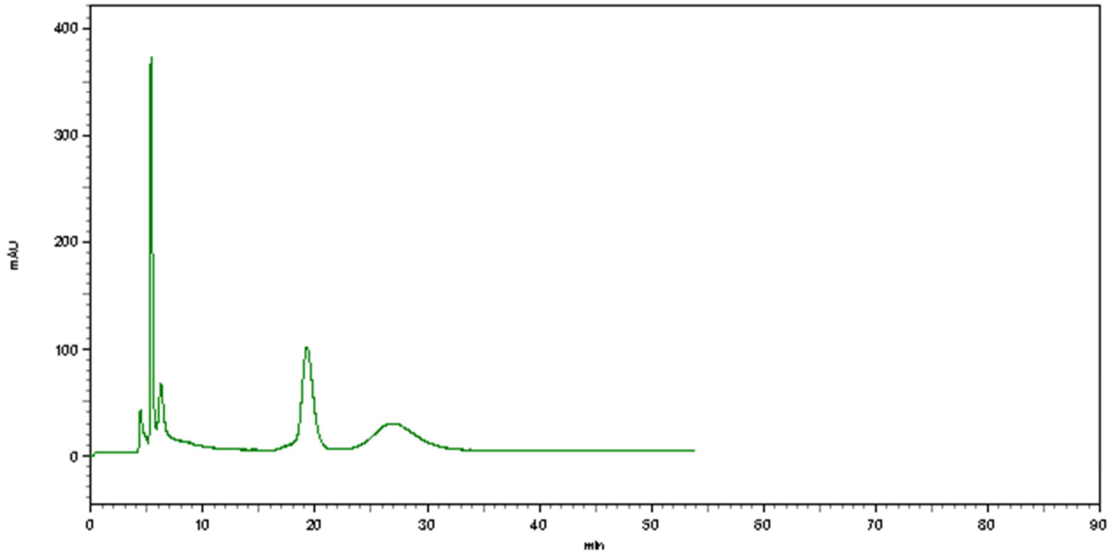
(S,R_p)-**10d**

1: 220 nm, 8 nm

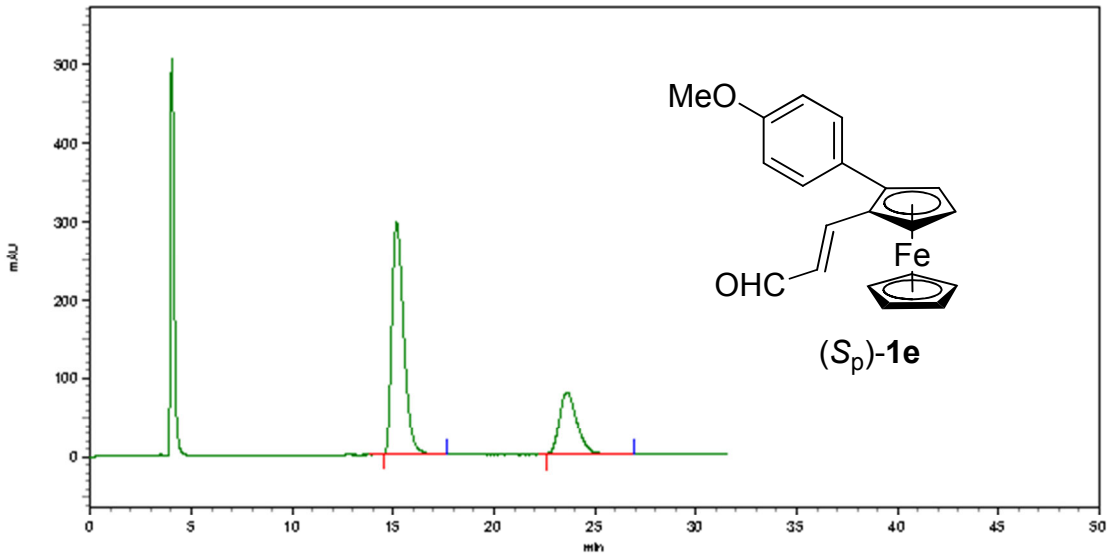
retention time	area	area%
18.944	2542313	10.81
26.347	20976662	89.19

Total	23518975	100.00

racemic sample



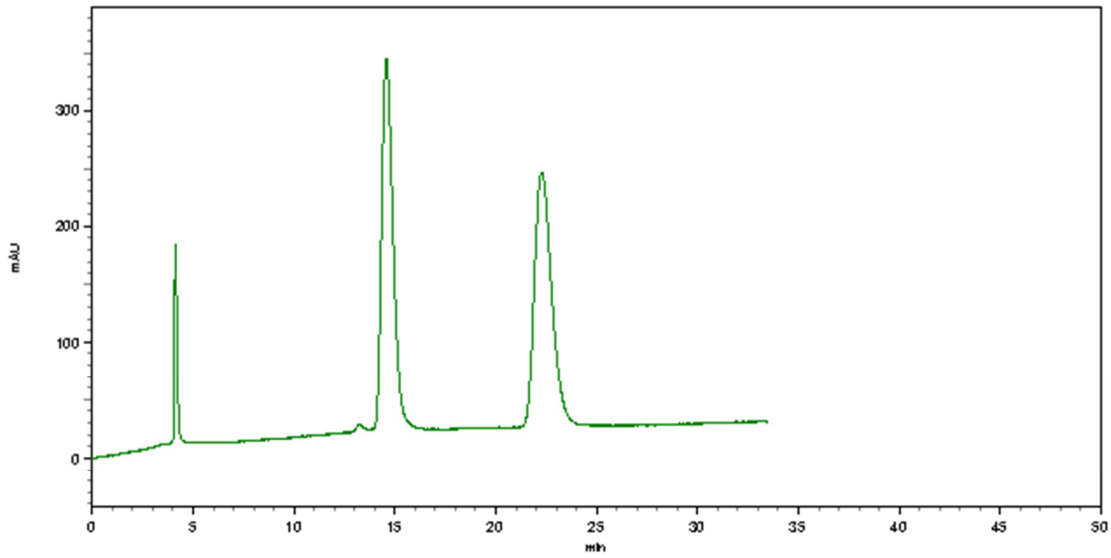
Chiralcel OD-H column, hexane/2-propanol = 90:10, 1.0 mL min^{-1}



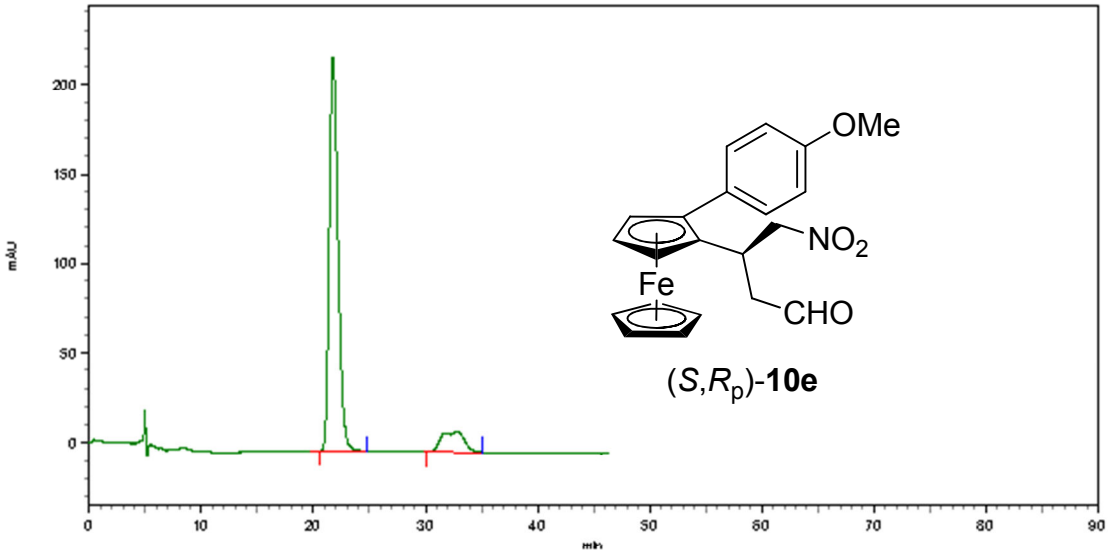
3: 210 nm, 8 nm

retention time	area	area%
15.165	12127471	71.55
23.592	4822672	28.45
Total	16950143	100.00

racemic sample



Chiralpak AS-H column, hexane/2-propanol = 70:30, 0.8 mL min^{-1}



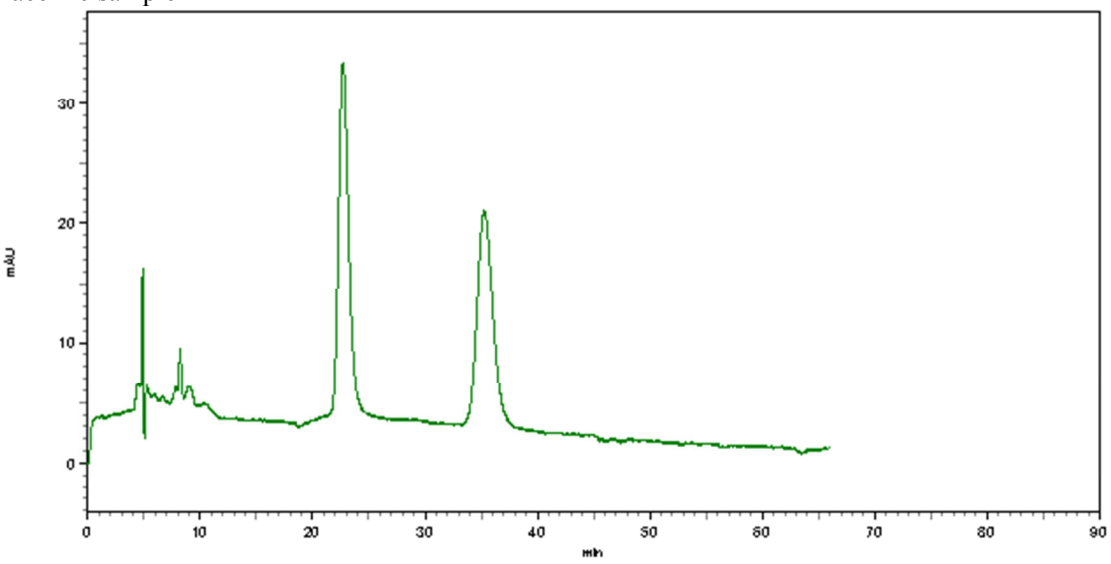
(S,R_p)-**10e**

1: 254 nm, 8 nm

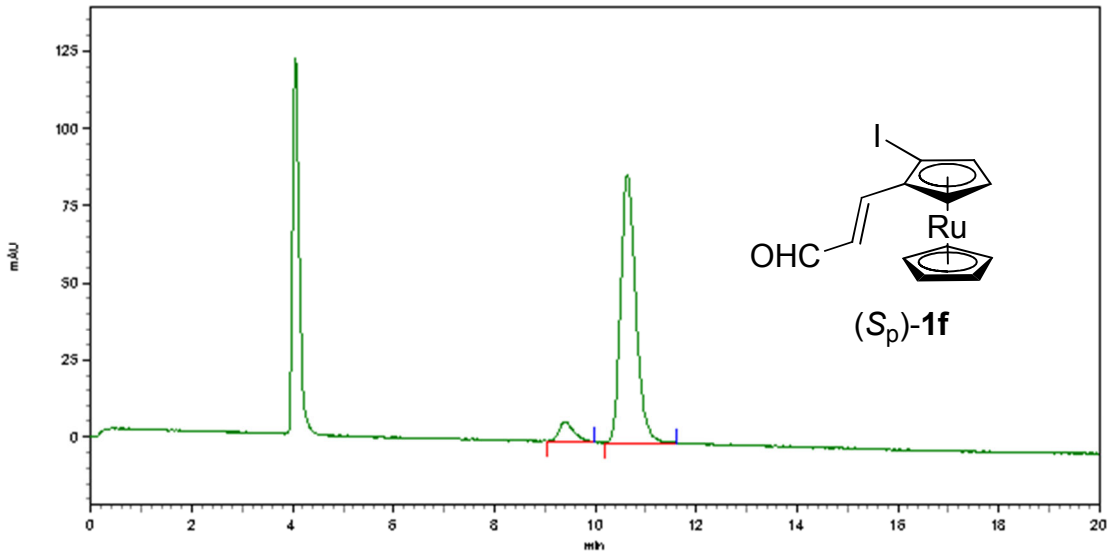
retention time	area	area%
21.749	11963065	88.03
32.835	1626596	11.97
Total	13589660	100.00

The minor diastereomer could not be removed for this compound, and its peak overlapped with that of the minor enantiomer at around 32.8 min. The ee value was calculated based on the diastereomeric ratio determined by ^{1}H NMR analysis.

racemic sample



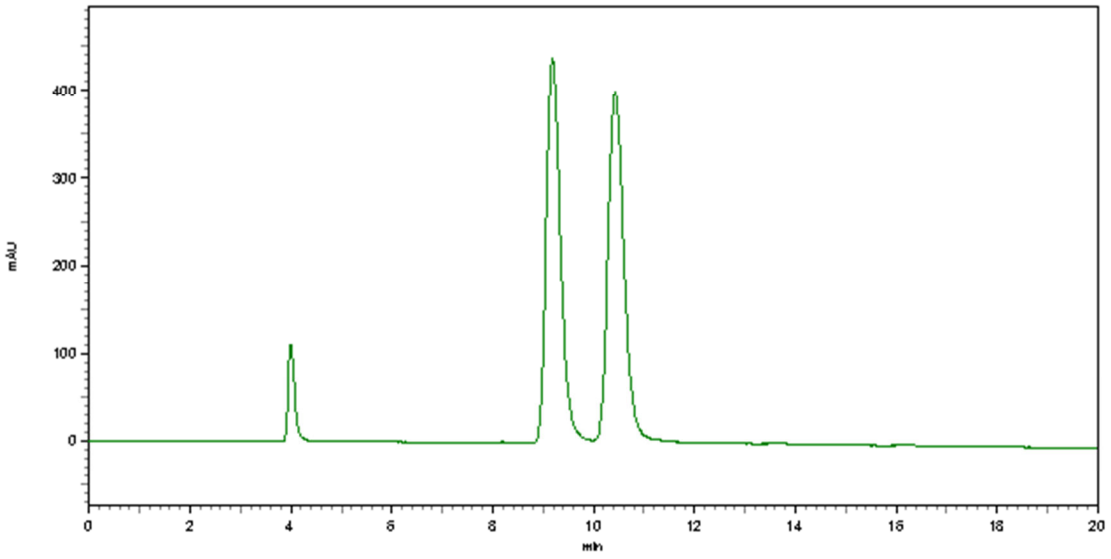
Chiralcel OD-H column, hexane/2-propanol = 90:10, 1.0 mL min^{-1}



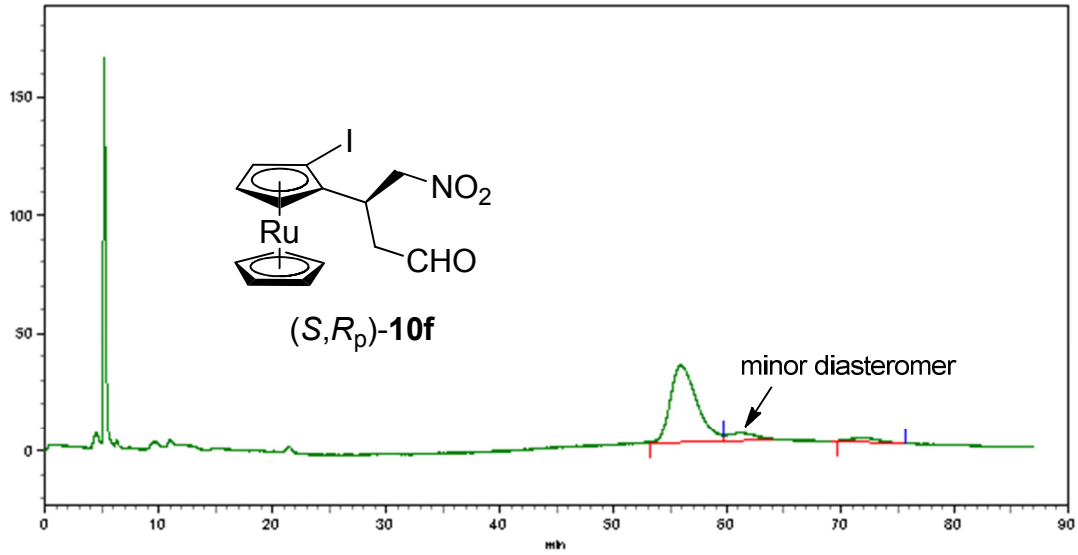
1: 225 nm, 8 nm

retention time	area	area%
9.384	132254	6.72
10.629	1837154	93.28
Total	1969408	100.00

racemic sample



Chiralcel OJ-H column, hexane/2-propanol = 70:30, 0.8 mL min^{-1}



1: 225 nm, 8 nm

retention time	area	area%
55.973	5247547	93.70
72.032	352653	6.30

Total	5600200	100.00

racemic sample