Activated Alkene Dependent One-Pot, Three Component aza-Morita-Baylis-Hillman Reaction of Ferrocenealdehyde: Synthesis of highly functionalized diverse ferrocene derivatives

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Contents

(1) General remarks

All the reactions were carried out in oven-dried glassware. Progress of reactions was monitored by Thin Layer Chromatography (TLC) while purification of crude compounds was done by column chromatography using silica gel (100-200 mesh). NMR spectra were recorded at 500 and 300 MHz (based on availability of instruments) 125 and 75 MHz (for ^{13}C) respectively on Brucker Avance DPX-500 MHz. and Bruker Avance DPX-300 MHz. Chemical shifts are reported in δ (ppm) relative to TMS (^{1}H) or $CDCl_3$ (^{13}C) as internal standards. Integrals are in accordance with assignments; coupling constants are given in Hz. All ^{13}C spectra are proton-decoupled. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), dt (doublet triplet), td (triplet of doublet), ddd (doublet of doublet of doublet), br s (broad singlet). For detailed peak assignments 2D spectra were measured (COSY, HMQC, HMBC, NOESY and 1D-NOE if necessary). LRMS and HRMS analyses were recorded using JEOL JMS 600H and Q-Tof Micro mass spectrometers. IR spectra were recorded on Bruker Alpha FT-IR spectrometer; absorbencies are reported in cm^{-1}. Yields refer to quantities obtained after chromatography.

(2) General experimental procedure:

(a) Synthesis of Nitrile aza-MBH adduct 4

A mixture of ferrocenealdehyde (100 mg, 0.47mmol), 4 A^0 molecular sieves (100 mg, 100 % w/w), Tosyl amine (96.0 mg, 0.56 mmol) and Lewis Acid (2 mol %) in dry solvent (0.5 ml) was stirred at room temperature for 10 minutes. Then, acrylonitrile (0.06 ml, 0.93 mmol) and Lewis base (50 mol %) was added and the reaction mixture was stirred at RT for 12h. After the completion of the reaction (monitored by TLC), evaporation of excess of acrylonitrile and solvent under reduced pressure followed by purification by silica gel column chromatography using EtOAc: hexane (10:90) as eluent afforded the nitrile aza-MBH adduct in moderate to good yields (52-76%).

(b) **Synthesis of ester aza-MBH adducts 7 and 8:**

A mixture of ferrocenealdehyde (100 mg, 0.47mmol), 4 A^0 molecular sieves (100 mg, 100 % w/w), Tosyl amine (96.0 mg, 0.56 mmol) and $Yb(OTf)_3$ as Lewis acid(2 mol %) in dry THF (0.5 ml) was stirred at room temperature for 10 minutes. Then methyl/ethyl acrylate (1.5 eq.) and DABCO (26.5 mg, 50 mol %) was added and the reaction mixture was stirred at RT for 24h. After the completion of the reaction (monitored by TLC), evaporation of excess of acrylates and solvent under reduced pressure followed by purification by silica gel column chromatography using EtOAc: hexane (10:90) as eluent afforded the ester aza-MBH adduct **7** and isomerised product **8** in 35-36% and 42-45% yields.

(c) **Synthesis of unusual MVK aza-MBH adduct 12:**

A mixture of ferrocenealdehyde (100 mg, 0.47mmol), 4 A^0 molecular sieves (100 mg, 100 % w/w), and Tosyl amine (120.0 mg, 0.70 mmol) in dry THF (0.5 ml) was stirred at room temperature for 10 minutes. Then MVK (0.07 ml, 0.94 mmol) and base (20 mol %) was added and the reaction mixture was stirred at RT for 24h. After the completion of the reaction (monitored by TLC), evaporation of excess of MVK and solvent under reduced pressure followed by purification by silica gel column chromatography using EtOAc: hexane (15:85) as eluent afforded the ferrocenyl piperidine product **12** in excellent yields (15-99 %).

(d) **Synthesis of piperidine derivative 13:**

To a mixture of ferrocenyl piperidine product **12** (100 mg, 0.19 mmol) and diethyl malonate (44 mg, 0.28 mmol) in dry dichloromethane (1 ml) anhydrous K_2CO_3 (54.5, 0.39 mmol) was added and stirred at room temperature for 6 hours or microwave irradiation, 450W, 5 minutes yielded the Michael addition product **13** after purification by silica gel column chromatography using EtOAc: hexane (10:90) as eluent in 98% yield.

(e) **Synthesis of usual MVK aza-MBH adduct 14**

A mixture of ferrocenealdehyde (100 mg, 0.47mmol), 4 A^0 molecular sieves (100 mg, 100 % w/w), Tosyl amine (96.0 mg, 0.56 mmol) in dry THF (0.5 ml) was stirred at room temperature for 10 minutes. Then, MVK (0.07 ml, 0.94 mmol), base (20 mol %) and Proline (21.4 mg, 40 mol %) was added and the reaction mixture was stirred at RT for 24h. After the completion of the reaction (monitored by TLC), evaporation of excess MVK and solvent

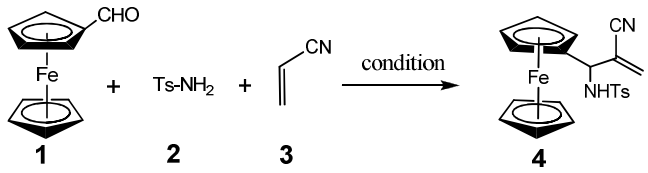
under reduced pressure followed by purification by silica gel column chromatography using EtOAc: hexane (10:90) as eluent afforded usual MVK adduct **14** in good yield (72-80 %).

(f) **Synthesis of γ- ketoester derivative 16:**

A mixture of ferrocenealdehyde (100 mg, 0.47mmol), 4 A^0 molecular sieves (100 mg, 100 % w/w), Tosyl amine (96.0 mg, 0.56 mmol) in dry dichloromethane solvent (0.5 ml) was stirred at room temperature for 10 minutes. Then allenes **15** (2.2 eq.) and Lewis base (20 mol %) was added and the reaction mixture was stirred at RT for 36 h. After the completion of the reaction (monitored by TLC), evaporation of excess solvent under reduced pressure followed by purification by silica gel column chromatography using EtOAc: hexane (5:95) as eluent afforded the γ-ketoester derivative **16** in good yield (92%).

(3) Reaction optimization for the preparation of aza-MBH adduct 4

Table 1

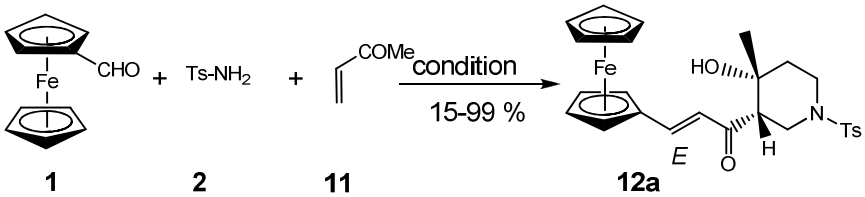


Entry	Solvent	Base	Lewis acid	Yield
1	2-PrOH	DABCO	-	52
2	-	DABCO	-	polymerised
3	THF	DABCO	-	Traces
4	THF	DABCO	$Yb(OTf)_3$	73
5	THF	DABCO	$Sc(OTf)_3$	70
6	**THF**	**DABCO**	**$Ti(OPr)_3Cl$**	**76**
7	MeOH	DABCO	$Yb(OTf)_3$	69
8	CH_3CN	DABCO	$Yb(OTf)_3$	70
9	THF	Cinchonidine	$Yb(OTf)_3$	64
10	THF	DBU	$Yb(OTf)_3$	-
11	THF	PPh_3	$Yb(OTf)_3$	-

Condition: 50 mol% Base, 2 mol% Lewis acid, 4Å MS, rt, 12 h

(4) Reaction optimization for the preparation of piperidine derivative 12a

Table 2

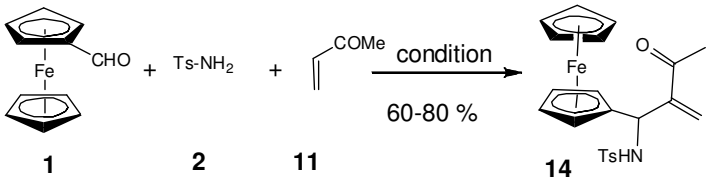


1 **2** **11** **12a**

Entry	Catalyst	Yield (**12**)
1	DABCO	15
2	DBU	95
3	$P(Cy)_3$	75
4	DMAP	40
5	PMe_3	96
6	**Tris(2,6-dimethoxyphenyl phosphine)**	**99**
7	Tris(pentafluorophenyl phosphine)	-
8	Tris(o-tolylphenyl phosphine)	20
9	PPh_3	-
10	$P(Bu)_3$	98

Condition: 20 mol% catalyst, 4Å MS, rt, 24 h

(5) Reaction optimization for preparation of aza-MBH adduct 14



1 **2** **11** **14**

Table 3

Entry	Co-catalyst	Yield
1	**DABCO**	**80**
2	DBU	78
3	PPh_3	-
4	DMAP	60
5	Tris(o-tolylphenyl phosphine)	75

Condition: 40 mol% Proline, 20 mol% co-catalyst, 4Å MS, rt, 24 h

Scheme 1 Synthesis of piperidine derivative 12a and aza-MBH adduct **14**

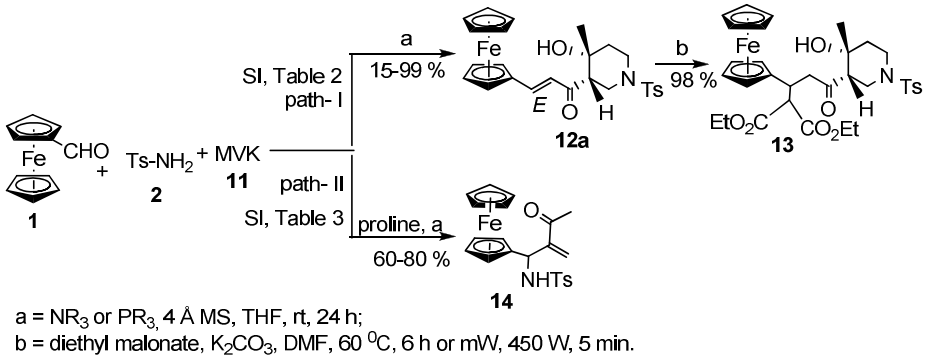
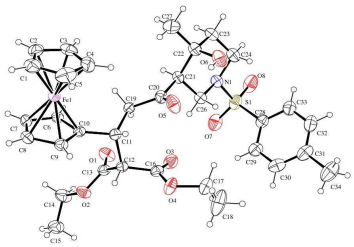
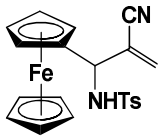
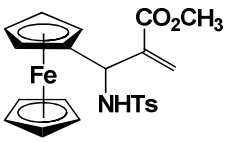
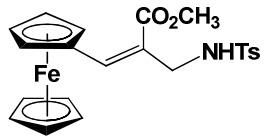
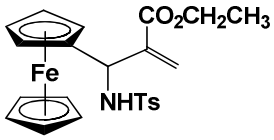
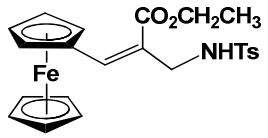
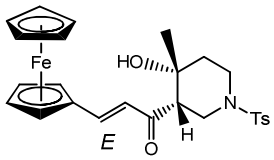
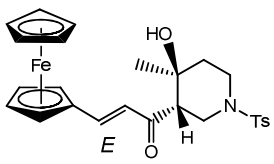


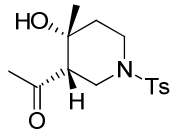
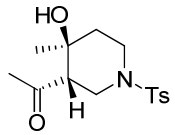
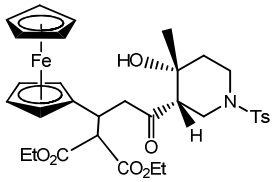
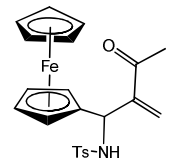
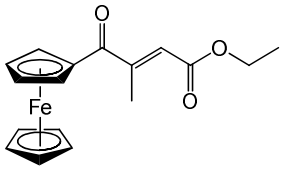
Figure 1 ORTEP diagram of compound 13



(6) Characterization data for Compounds

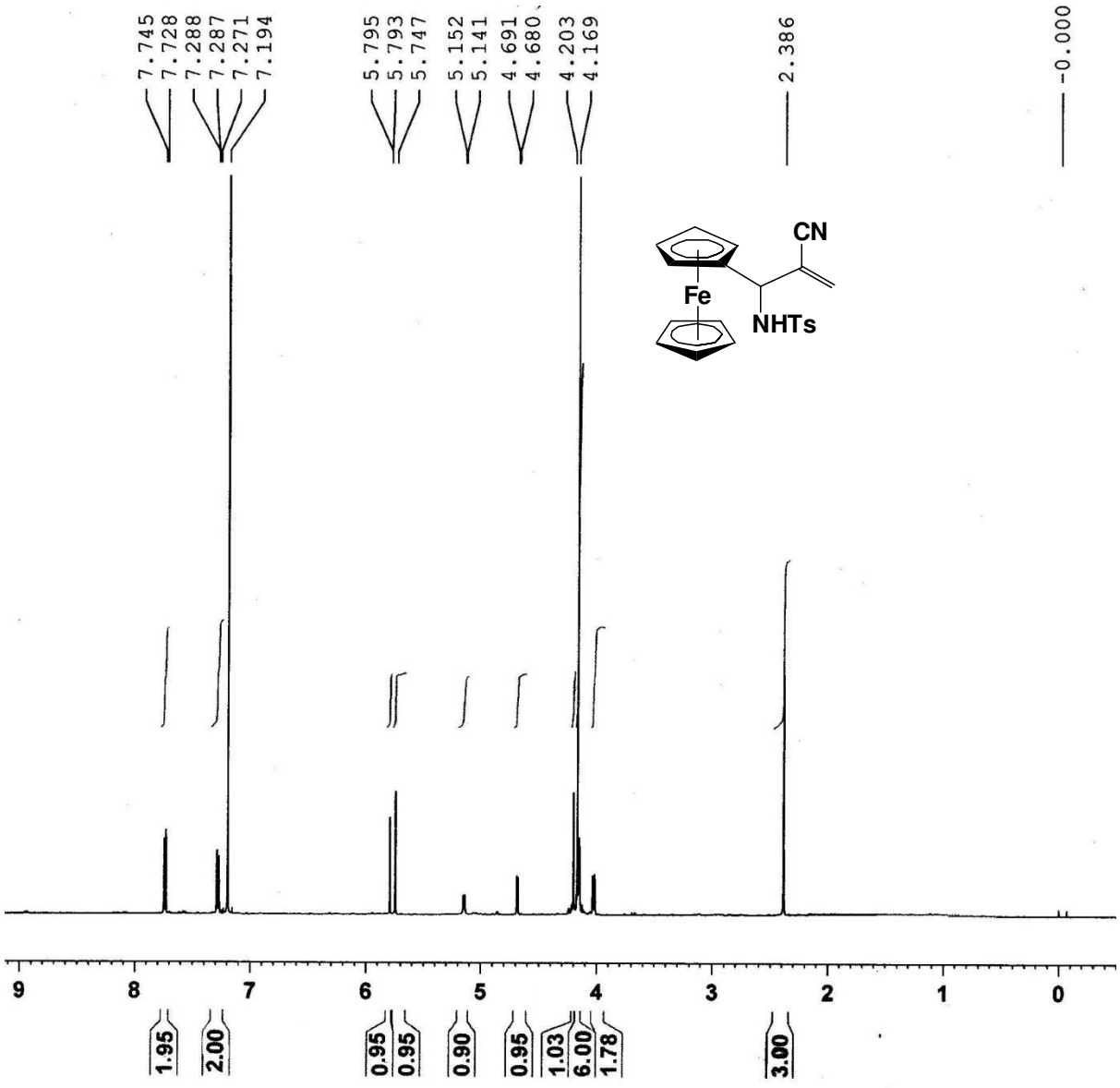
 **4**	IR (neat): 3273, 2925, 2211, 1645 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.5 Hz, 2H), 7.27 (d, *J* = 8.5 Hz, 2H), 5.79 (s, 1H), 5.74 (s, 1H), 5.14 (d, *J* = 5.5 Hz, 1H), 4.68 (d, *J* = 5.5 Hz, 1H), 4.23-4.01 (m, 9H), 2.38 (s, 3H) ; ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 149.4, 144.1, 131.5, 129.9, 129.8, 127.6, 127.3, 123.7, 86.6, 71.5, 69.9, 69.8, 69.2, 68.8, 68.7, 66.4, 55.7, 21.6; HRMS: calcd for $C_{21}H_{20}FeN_2O_2S$ $[M]^+$: 420.0595, found: 420.0191.
 **7**	IR (neat): 3273, 2924, 1741, 1645, 1161 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.0 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.01 (s, 1H), 5.73 (d, *J* = 8.5 Hz, 1H), 5.70 (s, 1H), 5.05 (d, *J* = 8.5 Hz, 1H), 4.14 (s, 5H), 4.09-4.07 (m, 3H), 3.93 (s, 1H), 3.64 (s, 3H), 2.42 (s, 3H) ; ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 166.0, 143.3, 139.0, 137.7, 129.7, 129.5, 127.6, 127.3, 126.6, 88.9, 74.6, 71.33, 70.7, 70.2, 68.9, 68.0, 67.9, 67.0, 55.1, 51.9, 21.5 ; LRMS: calcd for $C_{22}H_{23}FeNO_4S$ $[M]^+$: 453.3323, found: 453.42.

 **8**	IR (neat): 3273, 2926, 1741, 1600, 1161 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8 Hz, 2H), 7.51 (s, 1H) , 7.28 (d, *J* = 8.0 Hz, 2H), 5.19 (s, 1H), 4.59 (s, 2H), 4.45 (s, 2H), 4.16 (s, 5H), 3.90 (d, *J* = 5 Hz, 2H), 3.68 (s, 3H), 2.41 (s, 3H) ; ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 167.7, 144.3, 143.3, 136.5, 129.6, 129.4, 127.2, 120.9, 71.6, 70.9, 69.7, 52.0, 40.7, 21.5 ; HRMS: calcd for $C_{22}H_{23}FeNO_4S$ $[M]^+$: 453.3323, found: 453.0612
 **9**	IR (neat): 3273, 2924, 1741, 1645, 1161 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 7.8 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 5.97 (s, 1H), 5.78 (d, *J* = 8.5 Hz, 1H), 5.66 (s, 1H), 5.04 (d, *J* = 8.1 Hz, 1H), 4.18-4.07 (m, 10H), 3.92 (s, 1H), 2.42 (s, 3H), 1.20 (t, *J* = 6.9 Hz, 1H) ; ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 165.5, 143.3, 139.2, 137.8, 129.4, 127.3, 126.4, 89.0, 69.0, 68.0, 67.9, 67.1, 67.0, 60.9, 55.3, 21.5, 14.0 ; HRMS: calcd for $C_{23}H_{25}FeNO_4S$ [M+Na]: 490.0751, found: 490.0746.
 **10**	IR (neat): 3273, 2924, 1741, 1600, 1161 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.77 (d, *J* = 8 Hz, 2H), 7.5 (s, 1H) , 7.32 (d, *J* = 8.0 Hz, 2H), 4.98 (s, 1H), 4.68 (s, 2H), 4.52 (s, 2H), 4.27 (s, 5H), 4.17 (q, *J* = 7, 14 Hz, 2H), 3.92 (d, *J* = 6 Hz, 2H), 2.44 (s, 3H), 1.28 (t, *J* = 7 Hz, 3H) ; ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 171.2, 143.6, 139.1, 136.0, 129.7, 129.4, 127.2, 126.4, 71.6, 70.9, 69.7, 68.9, 67.9, 66.9, 60.7, 55.2, 44.9, 21.5, 14.1 ; LRMS: calcd for $C_{23}H_{25}FeNO_4S$ $[M]^+$: 467.3589, found: 467.71.
 **12a** **Major Diastereomer**	IR (neat): 3506, 2978, 1695, 1596 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 8 Hz, 2H), 7.57 (d, *J* = 16 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 6.51 (d, *J* = 16 Hz, 1H), 4.55 (s, 2H), 4.49 (s, 2H), 4.18 (s, 5H), 3.73 (dd, *J* = 2, 12 Hz, 1H), 3.66 (d, *J* = 12 Hz, 1H), 3.10 (dd, *J* = 4, 10.5 Hz, 1H), 2.74 (t, *J* = 12 Hz, 1H), 2.52 (td, *J* = 3, 11.5Hz, 1H), 2.44 (s, 3H), 2.04 (s, 1H), 1.91 (td, *J* = 4, 12.5 Hz, 1H), 1.82 (dt, *J* = 3, 13Hz, 1H), 1.10 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.2, 146.3, 143.7, 133.2, 129.8, 127.6, 123.2, 78.4, 71.7, 70.6, 69.9, 69.5, 68.9, 55.5, 45.3, 43.7, 39.5, 22.5, 21.5 ; HRMS: calcd for $C_{26}H_{29}FeNO_4S$ $[M]^+$: 507.4228, found: 507.0873.
 **12b** **Minor Diastereomer**	IR (neat): 3506, 2978, 1695, 1596 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 8.0 Hz, 2H), 7.56 (d, *J* = 15.5 Hz, 1H), 7.33 (d, *J* = 8.0 Hz, 2H), 6.52 (d, *J* = 15.5 Hz, 1H), 4.54 (s, 2H), 4.47 (s, 2H), 4.17 (s, 5H), 3.71 (dd, *J* = 1.5, 10 Hz, 1H), 3.65-3.62 (m, 1H), 3.10 (dd, *J* = 4.5, 10.5 Hz, 1H), 2.76 (t, *J* = 11 Hz, 1H), 2.53 (td, *J* = 3, 11 Hz, 1H), 2.44 (s, 3H), 2.04 (s, 1H), 1.87-1.82 (m, 2H), 1.09 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.3, 146.2, 143.7, 133.2, 129.8, 129.7, 127.6, 127.0, 123.3, 78.4, 71.6, 70.5, 69.9, 69.5, 68.8, 55.5, 45.3, 43.8, 39.5, 22.5, 21.5 ; LRMS: calcd for $C_{26}H_{29}FeNO_4S$ $[M]^+$: 507.4228, found: 508.41.

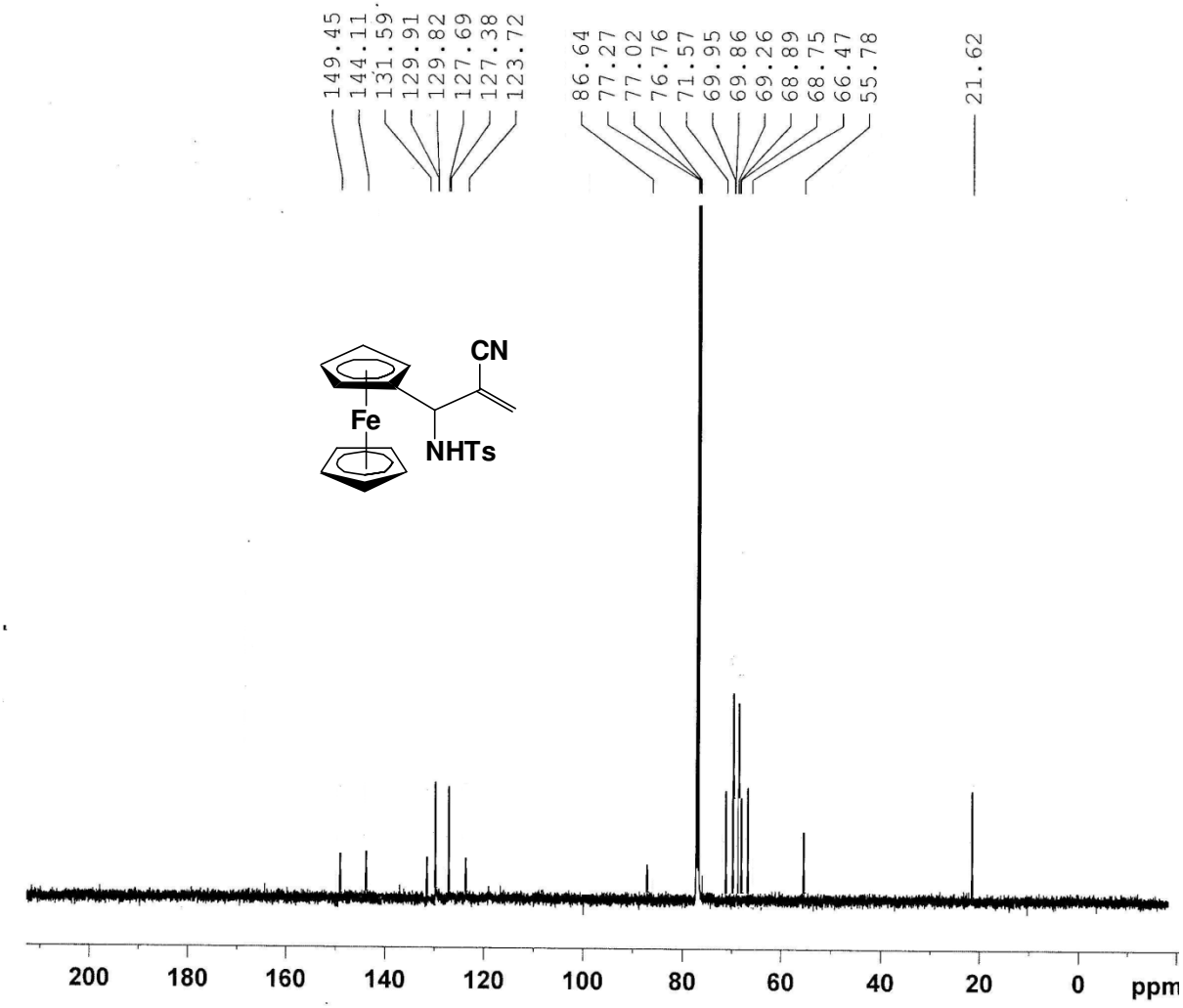
 **C1** **Intermediate-1**	IR (neat): 3506, 2978, 1745 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.62 (d, *J* = 8.0 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 3.69 (d, *J* = 6 Hz, 1H), 3.67 (d, *J* = 2 Hz, 1H), 3.54 (dt, *J* = 2, 9.5 Hz, 1H), 2.90 (dd, *J* = 4.5, 11.5 Hz, 1H), 2.67 (td, *J* = 3.5, 11.5 Hz, 1H), 2.62 (t, J= 11.5 Hz, 1H), 2.41 (s, 3H), 2.29 (s, 3H), 1.66-1.59 (m, 2H), 1.18 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ =212.6, 143.7, 132.9, 129.7, 129.5, 127.5, 126.2, 67.8, 55.5, 43.7, 42.0, 37.2, 31.9, 28.2, 21.4; LRMS: calcd for $C_{15}H_{21}NO_4S$ $[M]^+$: 311.3965, found[M+1]: 312.69.
 **C2** **Intermediate-2**	IR (neat): 3506, 2978, 1745 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.0 Hz, 2H), 7.34 (d, *J* = 8.0 Hz, 2H), 3.63-3.61 (m, 1H), 3.55-3.51 (m, 1H), 2.86 (dd, *J* = 4, 10 Hz, 1H), 2.73 (t, *J* = 10.5, 1H), 2.55-2.54 (m, 2H), 2.44 (s, 3H), 2.29 (s, 3H), 1.85-1.83 (m, 2H), 1.05 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ =209.1, 143.9, 132.9, 129.8, 127.5, 70.0, 57.7, 44.9, 43.7, 39.5, 32.0, 22.3, 21.5; LRMS: calcd for $C_{15}H_{21}NO_4S$ $[M]^+$: 311.3965, found[M+1]: 312.78.
 **13**	IR (neat): 3506, 2978, 1747, 1726, 1161 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 7.0 Hz, 2H), 7.31 (d, *J* = 7.0 Hz, 2H), 4.24- 4.12 (m, 13H), 3.82-3.78 (m, 2H), 3.60-3.52 (m, 3H), 3.49 (s, 1H), 3.00-2.97(m, 1H), 2.84 (s, 1H), 2.68 (t, J= 9.5, 1H), 2.57 (s, 1H), 2.43 (s, 3H), 1.64-1.61(m, 2H), 1.25 (t, *J* = 7.0 Hz, 6H), 1.15 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 212.8, 168.2, 143.6, 133.1, 129.7, 127.6, 90.1, 68.6, 68.2, 67.9, 67.8, 67.3, 61.5, 61.4, 56.8, 55.4, 48.5, 44.0, 41.9, 37.4, 32.4, 30.9, 28.4, 21.5, 14.0; HRMS: calcd for $C_{33}H_{42}FeNO_8S$ $[M]^+$: 668.1981, found: 668.1987.
 **14**	IR (neat): 3273, 2925, 1747, 1645 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$): δ = 7.69 (s, 2H), 7.27 (d, *J* = 4.5 Hz, 2H), 5.89 (s, 2H), 5.74 (s, 1H), 4.93 (s, 1H), 4.19-3.95 (m, 9H), 2.41 (s, 3H), 2.11(s, 3H) ; ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 198.9, 146.9, 143.4, 137.4, 129.5, 127.5, 127.4, 89.9, 69.6, 68.4, 67.8, 67.2, 54.5, 26.2, 21.5; HRMS: calcd for $C_{22}H_{23}FeNO_3S$ [M+Na]: 460.0646, found: 460.0642.
 **16**	IR (neat): 1695, 1592, 1156 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.45 (s, 1H), 4.48 (d, *J* = 6.3 Hz, 4H), 4.37 (q, *J* = 7.2, 14 Hz, 2H), 4.21 (s, 5H), 2.34 (s, 3H), 1.37 (t, *J* = 7.0 Hz, 3H) ; ^{13}C-NMR (125 MHz, $CDCl_3$): δ = 193.8, 168.5, 143.2, 130.1, 72.3, 70.7, 70.0, 61.4, 26. 5, 14.1; LRMS: calcd for $C_{17}H_{18}FeO_3$ $[M]^+$: 326.1680, found: 326.45.

(7) Scanned copies of spectra

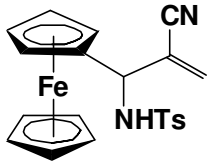
^{1}H NMR of Compound 4

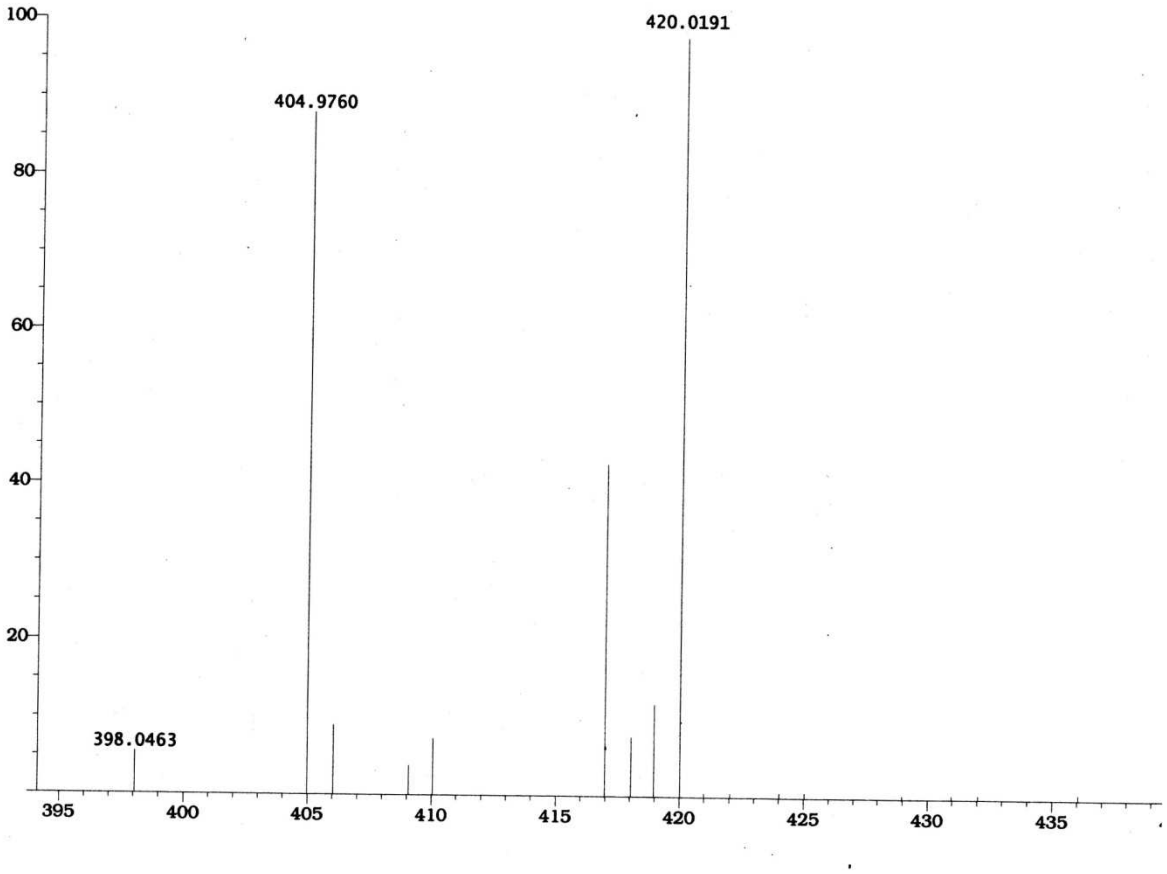


^{13}C NMR of Compound 4

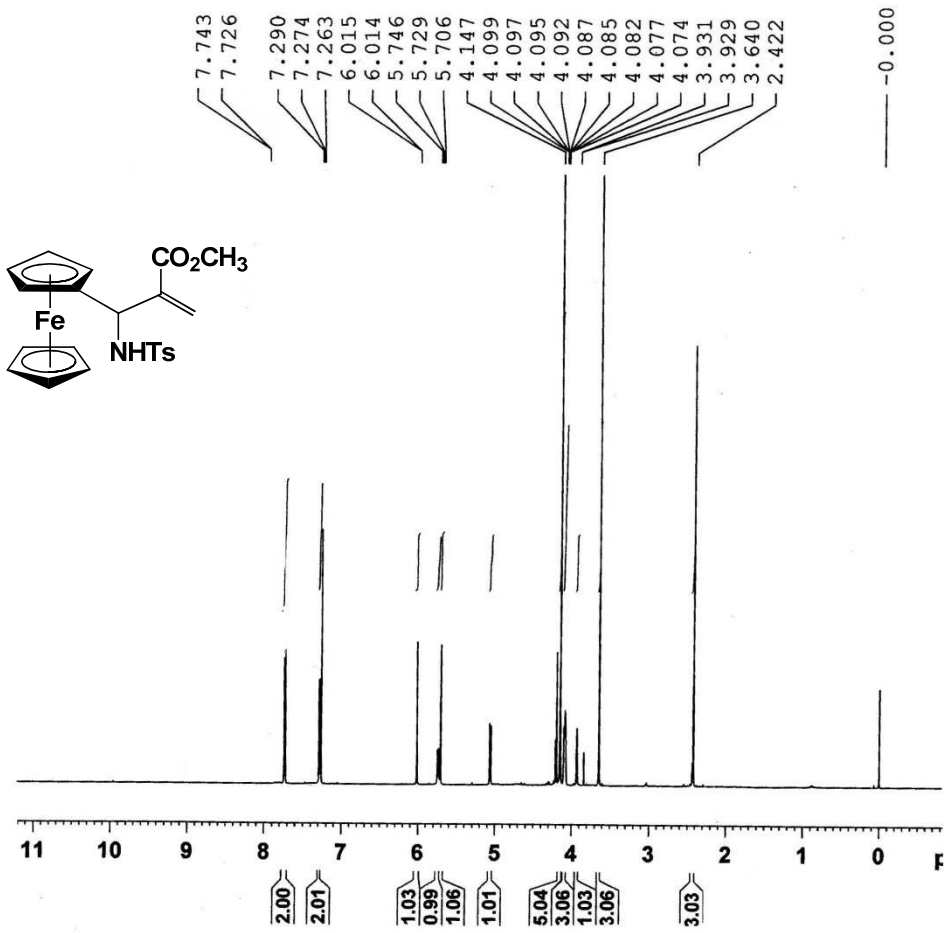


Mass of Compound 4

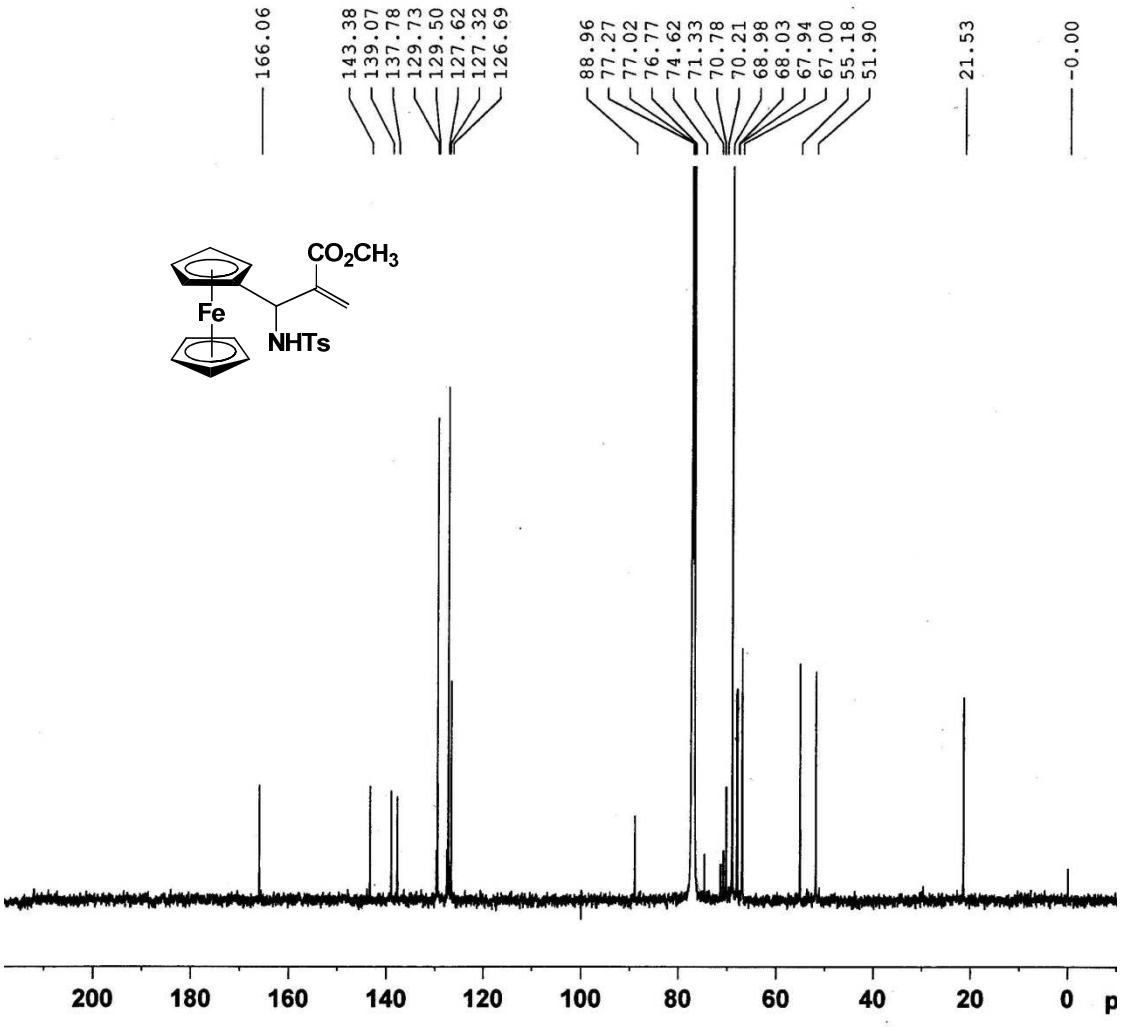




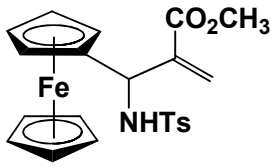
^{1}H NMR of Compound 7

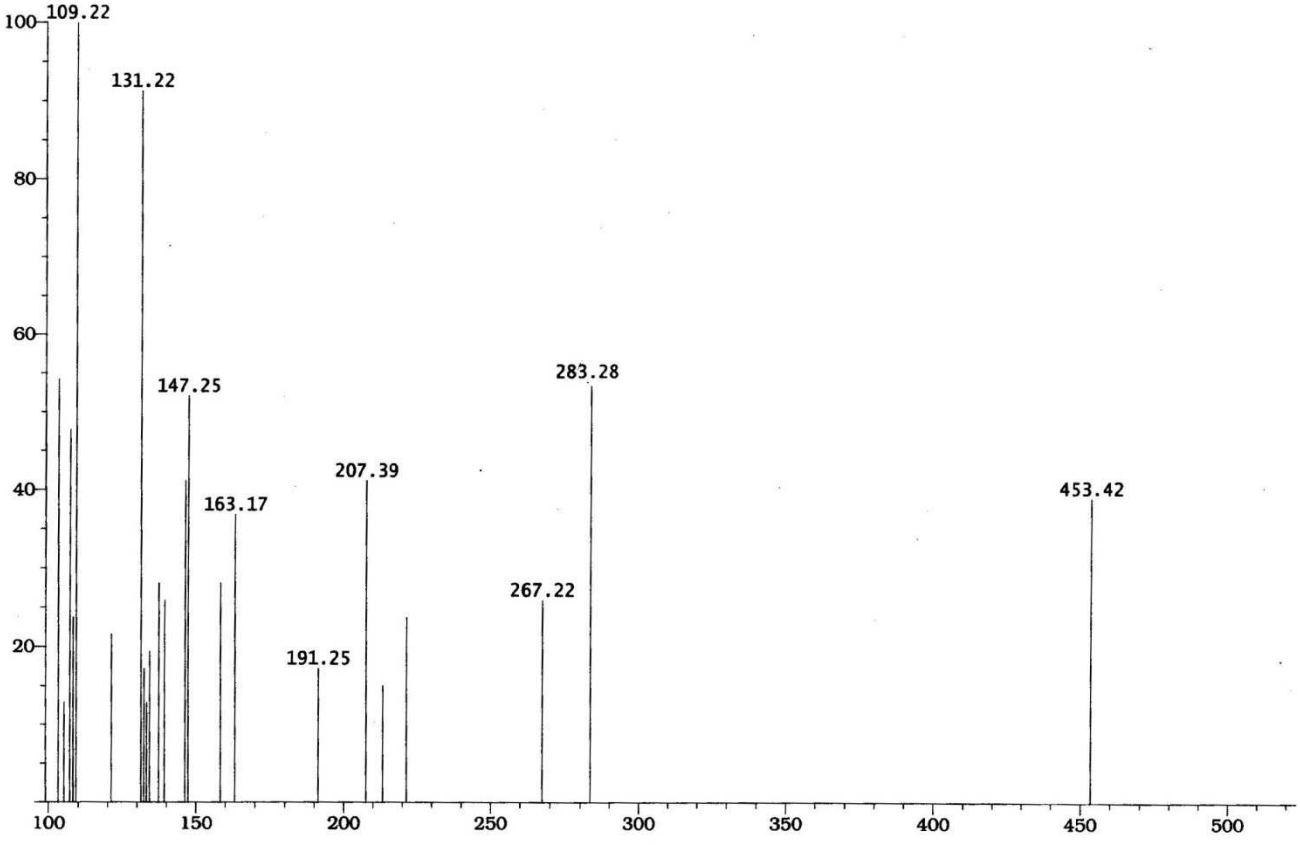


^{13}C NMR of Compound 7

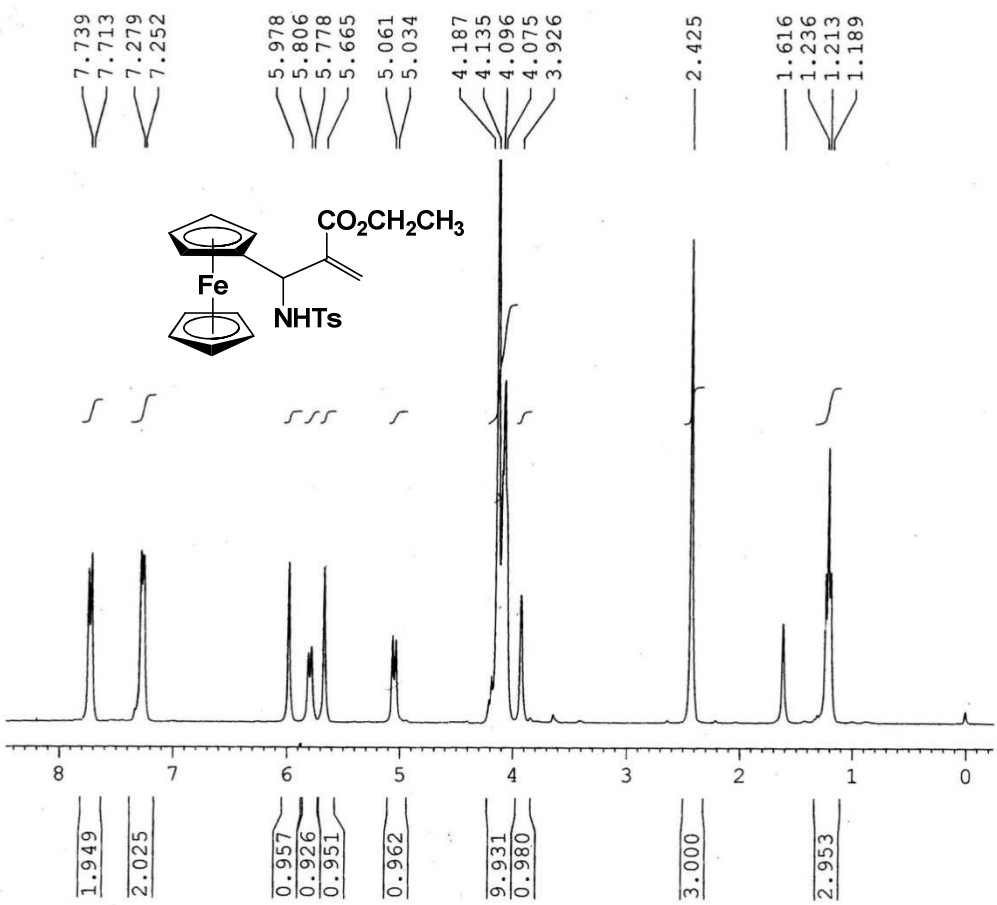


Mass of Compound 7

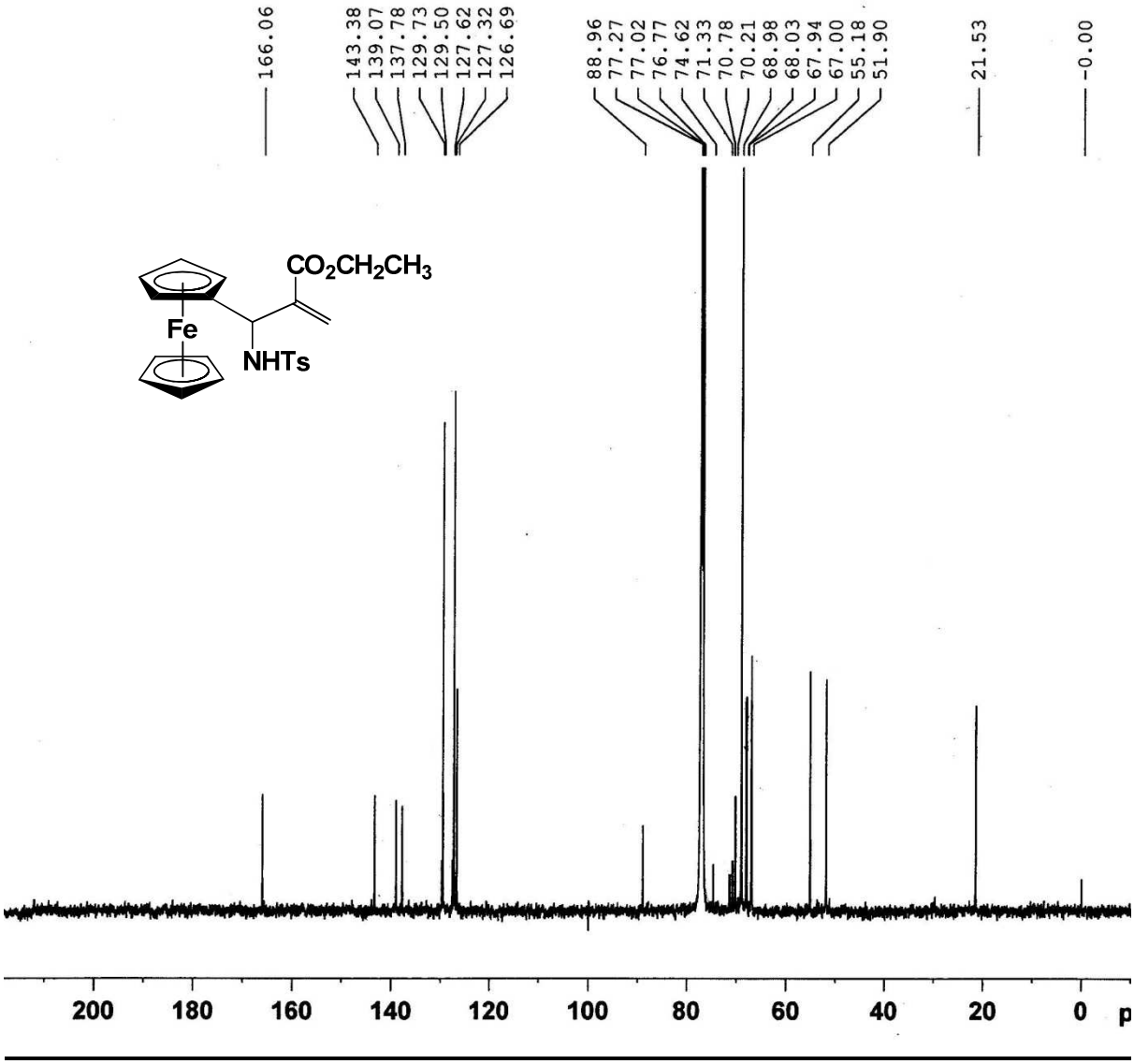




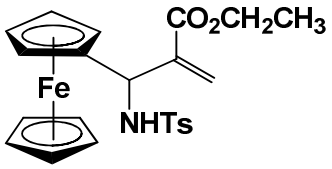
^{1}H NMR of Compound 9



^{13}C NMR of Compound 9



HRMS Mass of Compound 9

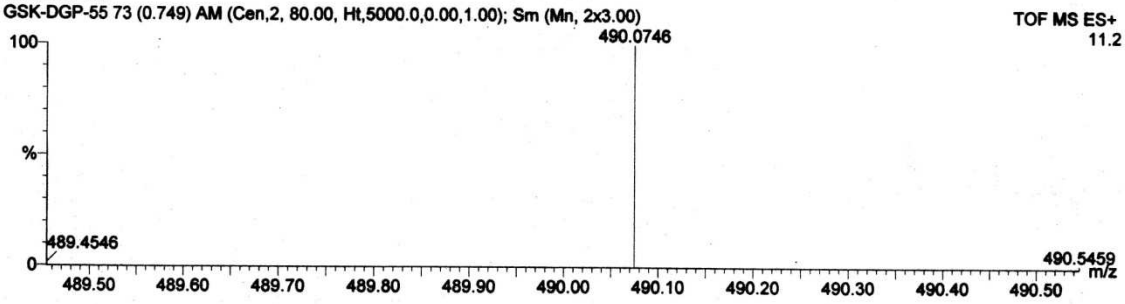


Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 200.0 mDa / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

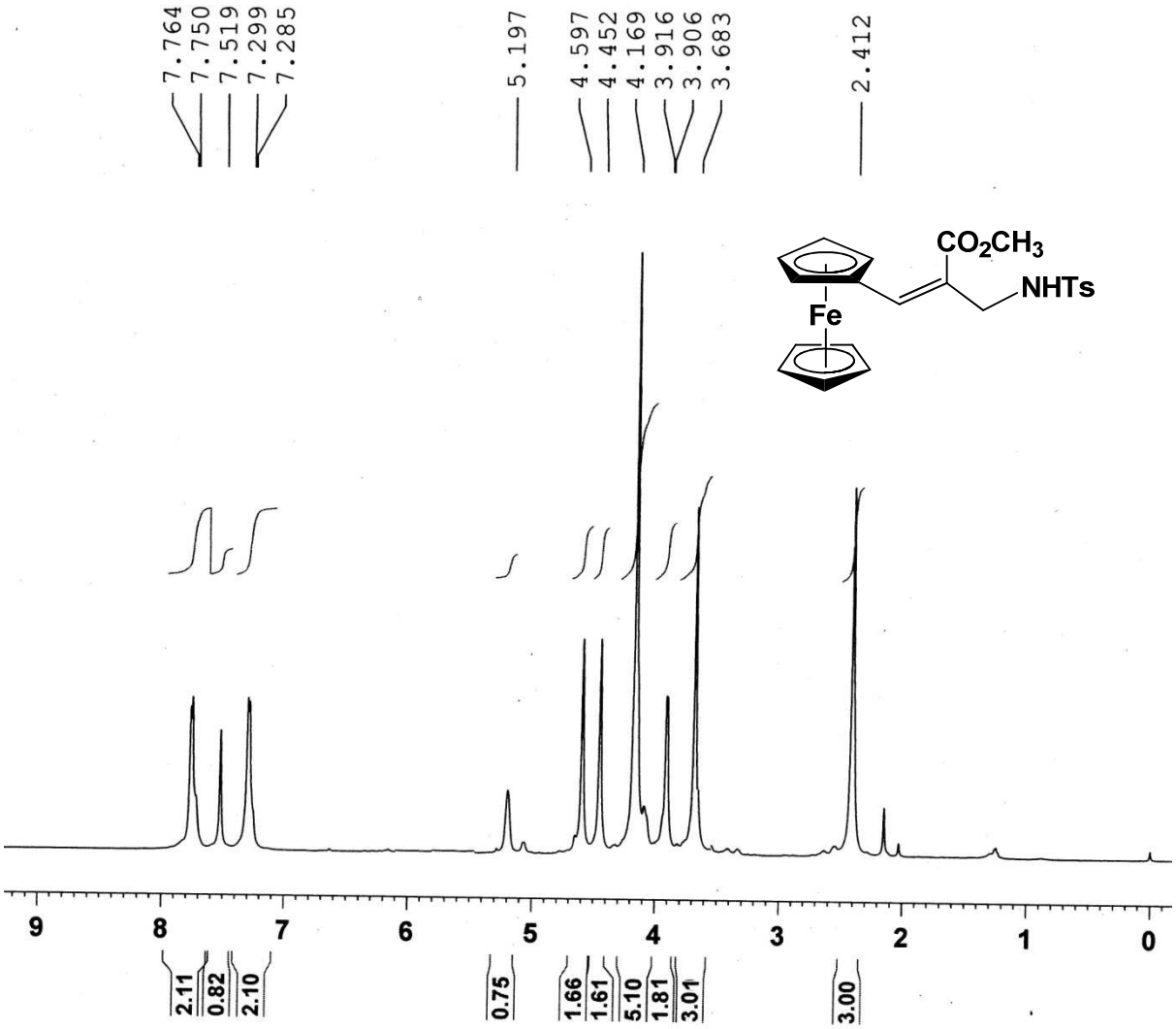
Monoisotopic Mass, Odd and Even Electron Ions
74 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

GSK-DGP-55
GSK-DGP-55 73 (0.749) AM (Cen,2, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00) TOF MS ES+ 11.2

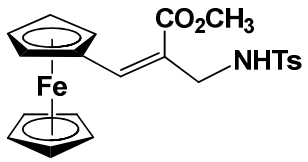


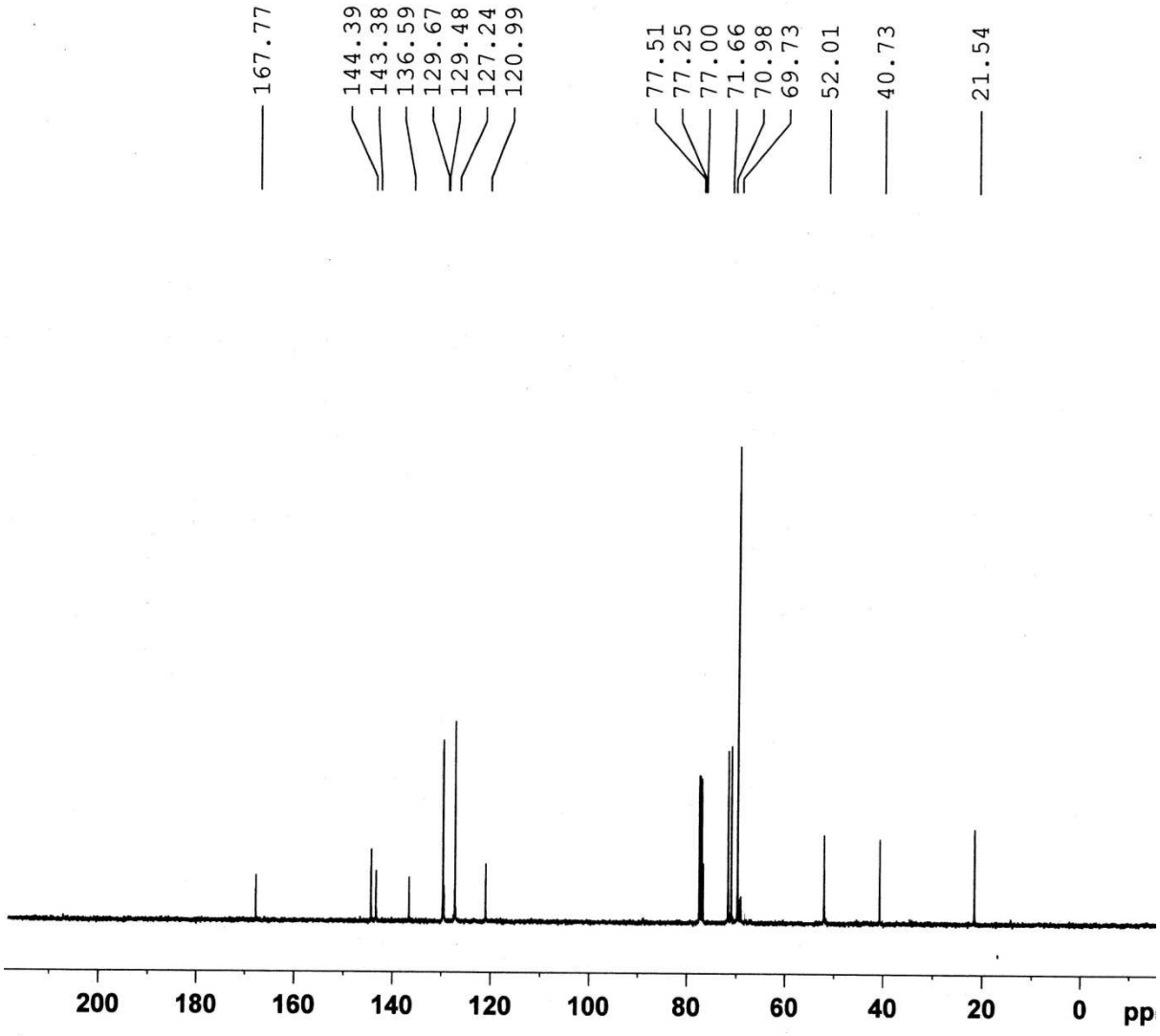
Minimum:				-1.5		
Maximum:		200.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
490.0746	490.0751	-0.5	-1.1	11.5	1	C23 H25 N O4 S Fe Na

^{1}H NMR of Compound 8

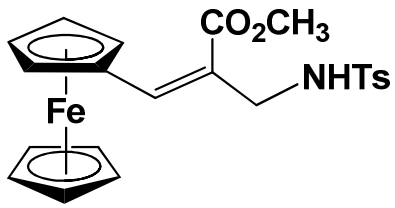


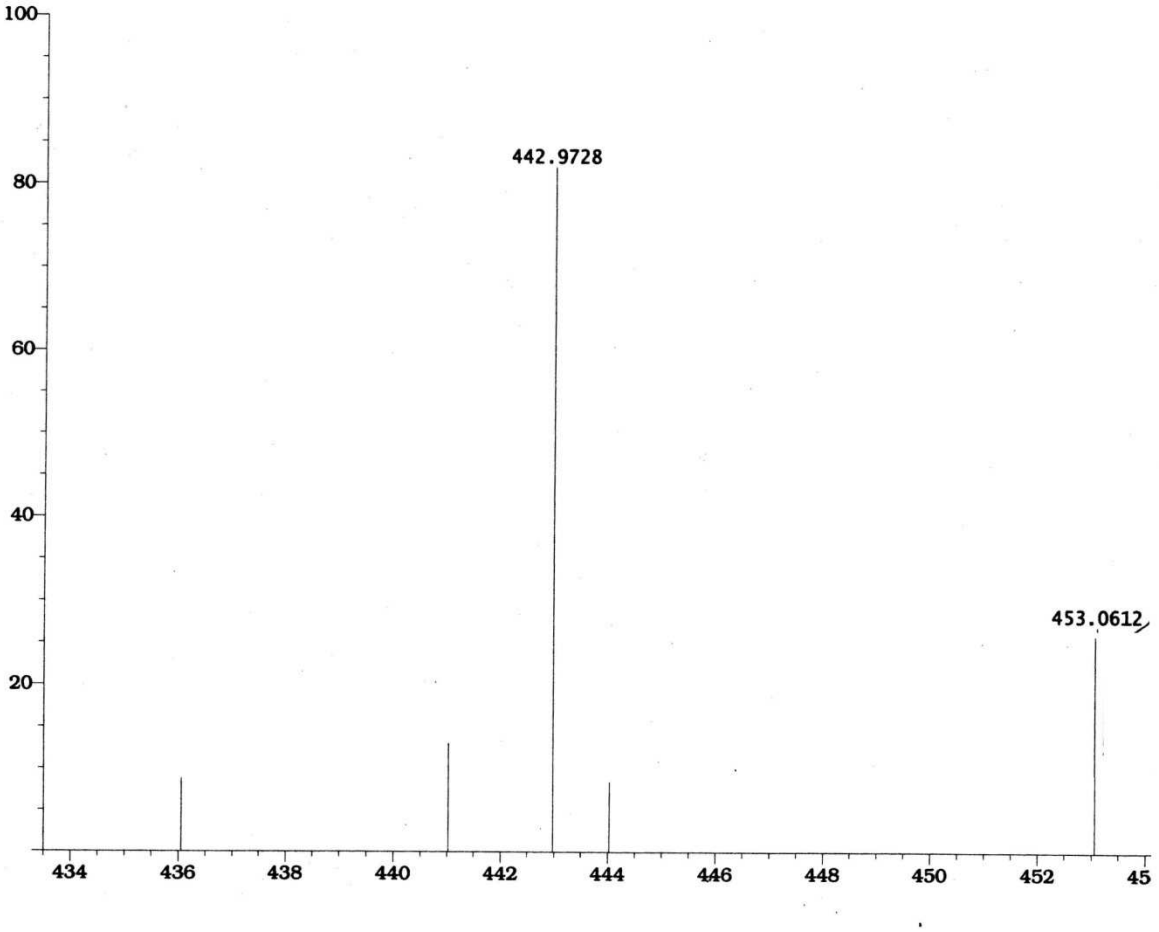
^{13}C NMR of Compound 8



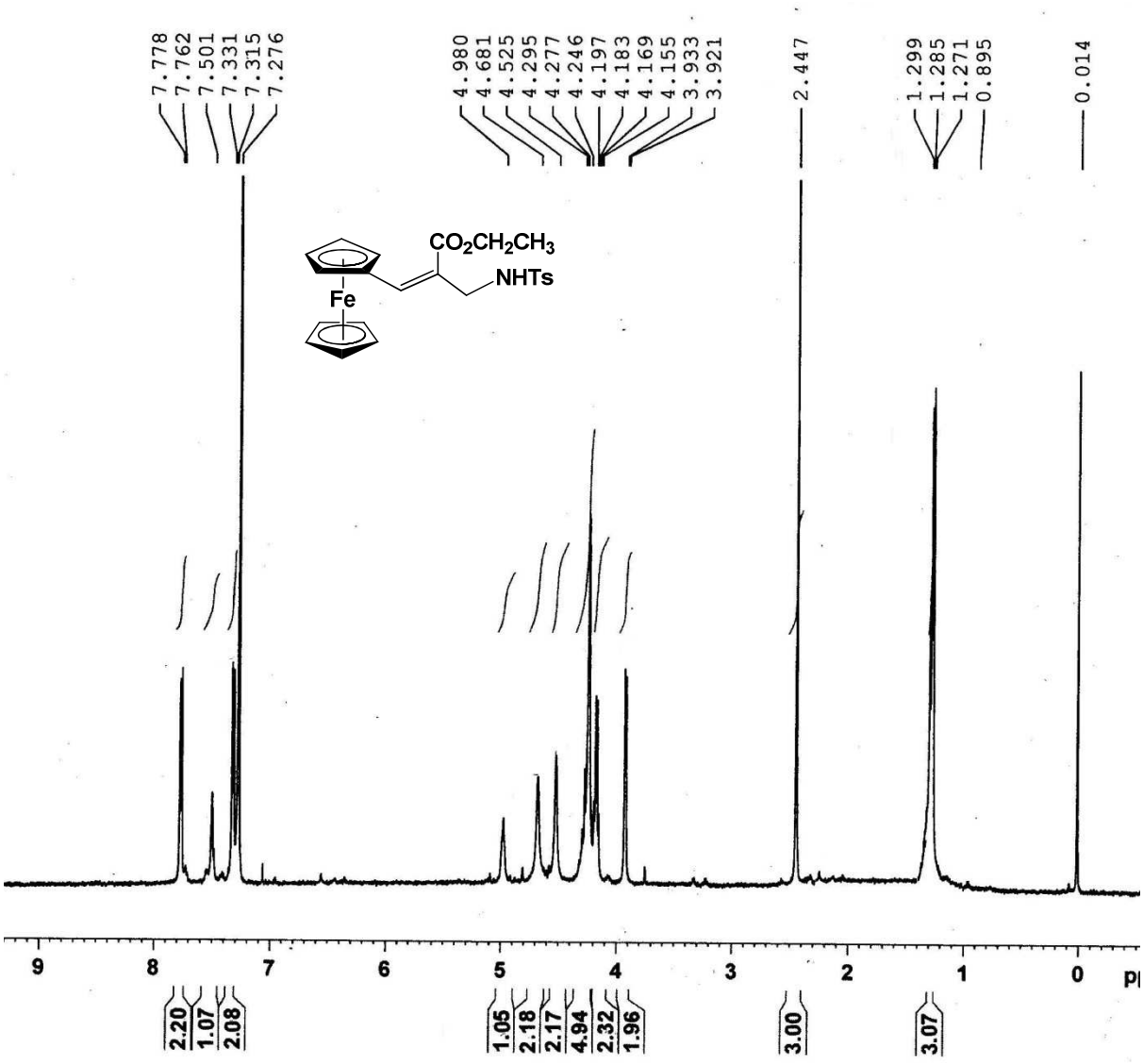


HRMS of Compound 8

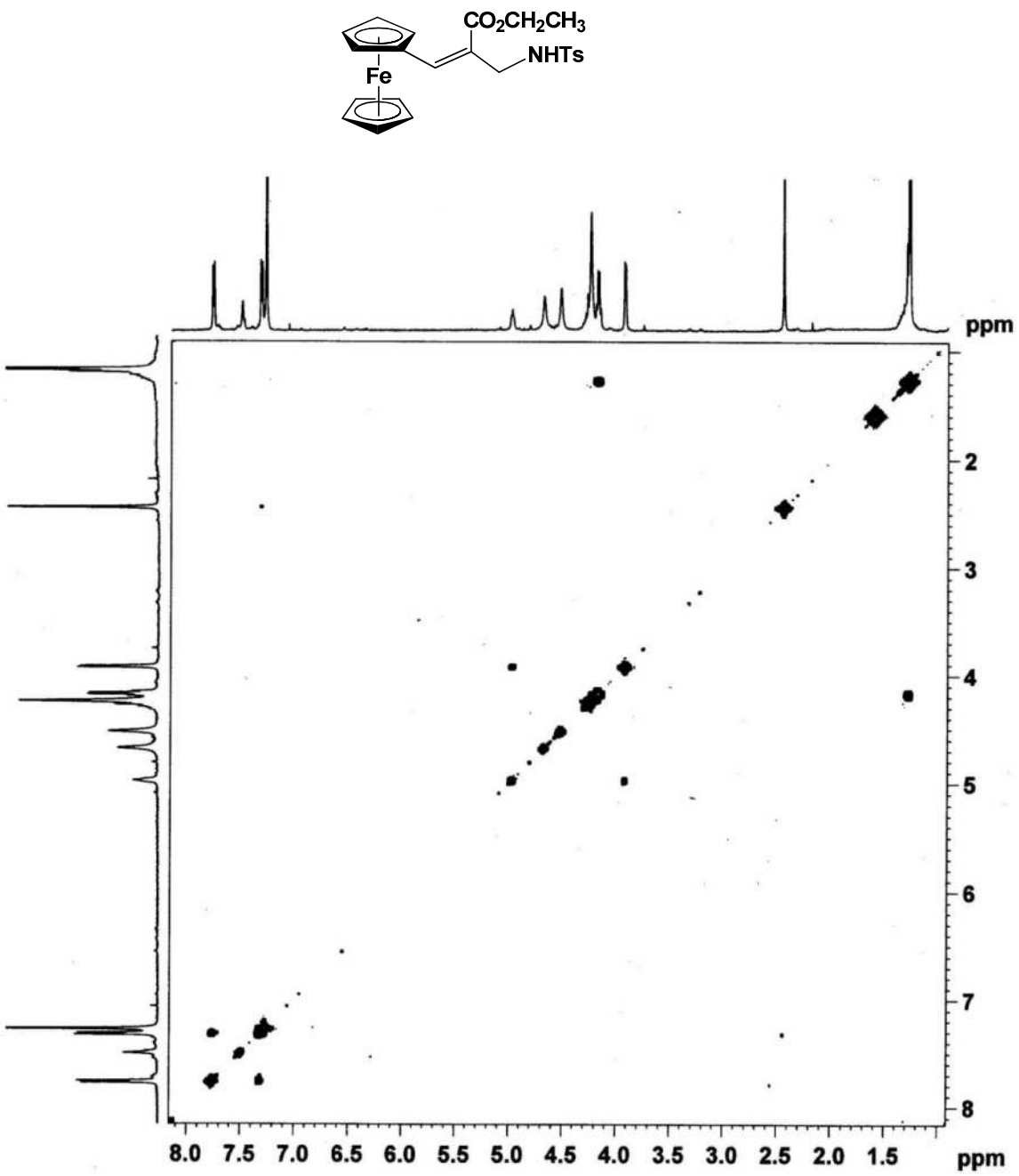




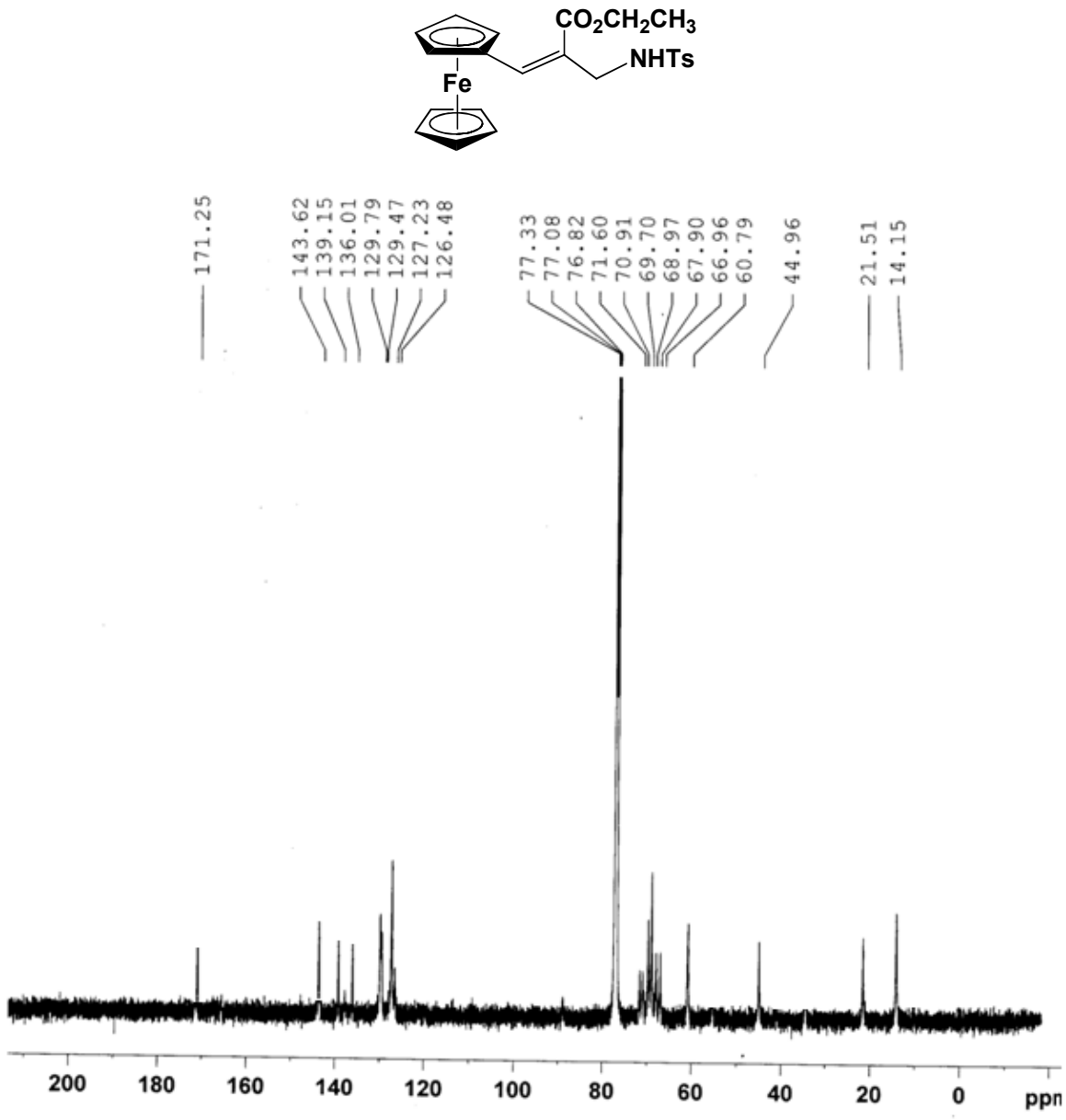
^{1}H NMR of Compound 10



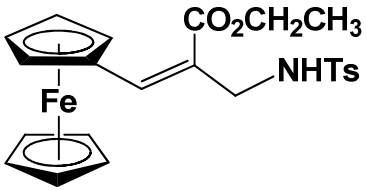
COSY of Compound 10

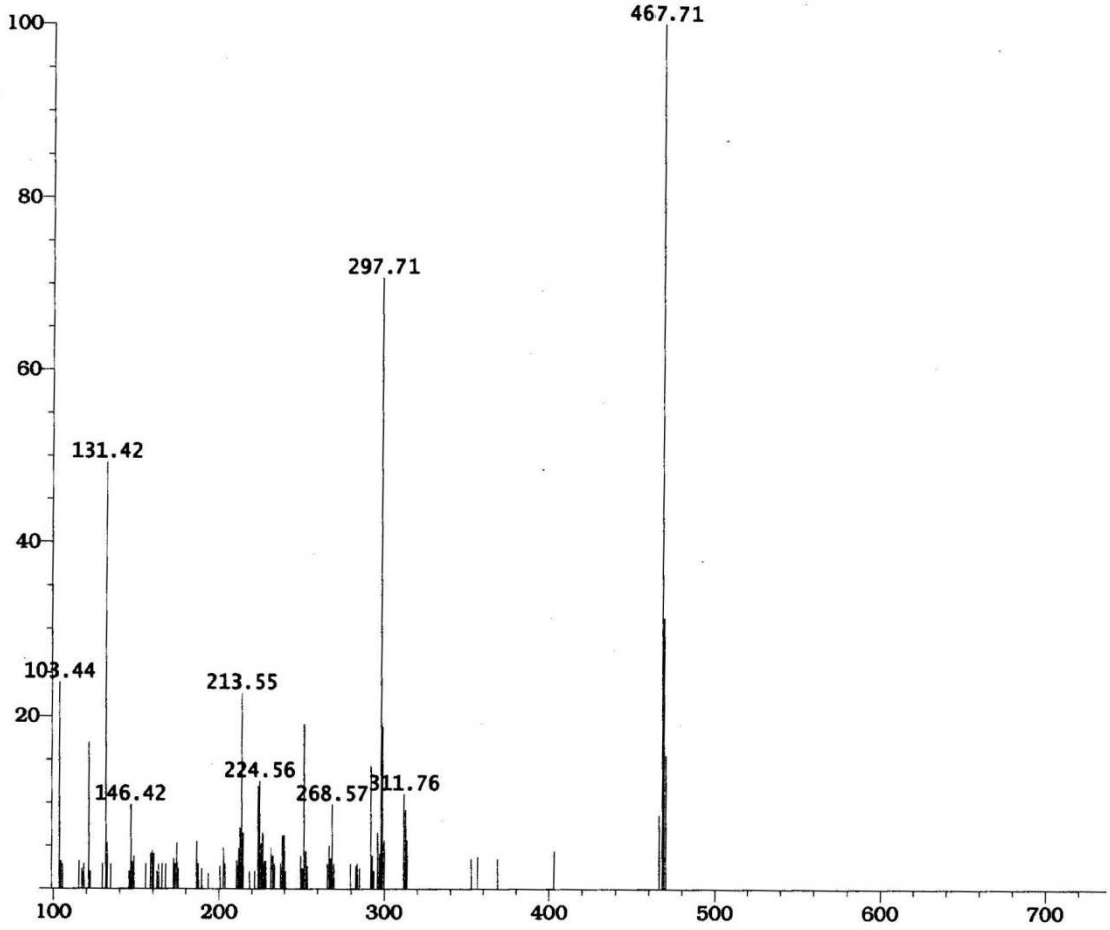


^{13}C NMR of Compound 10

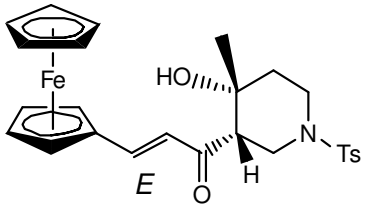


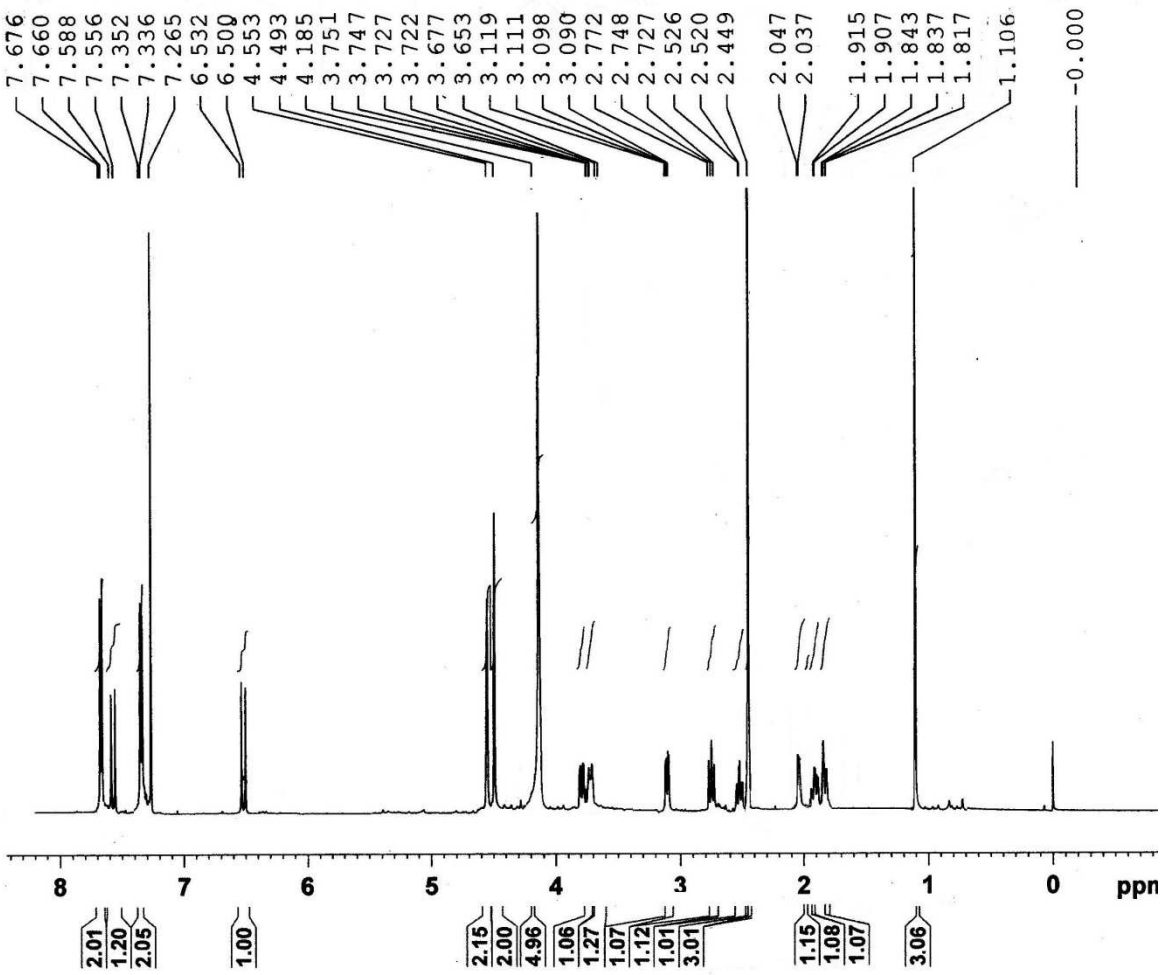
FAB mass of Compound 10



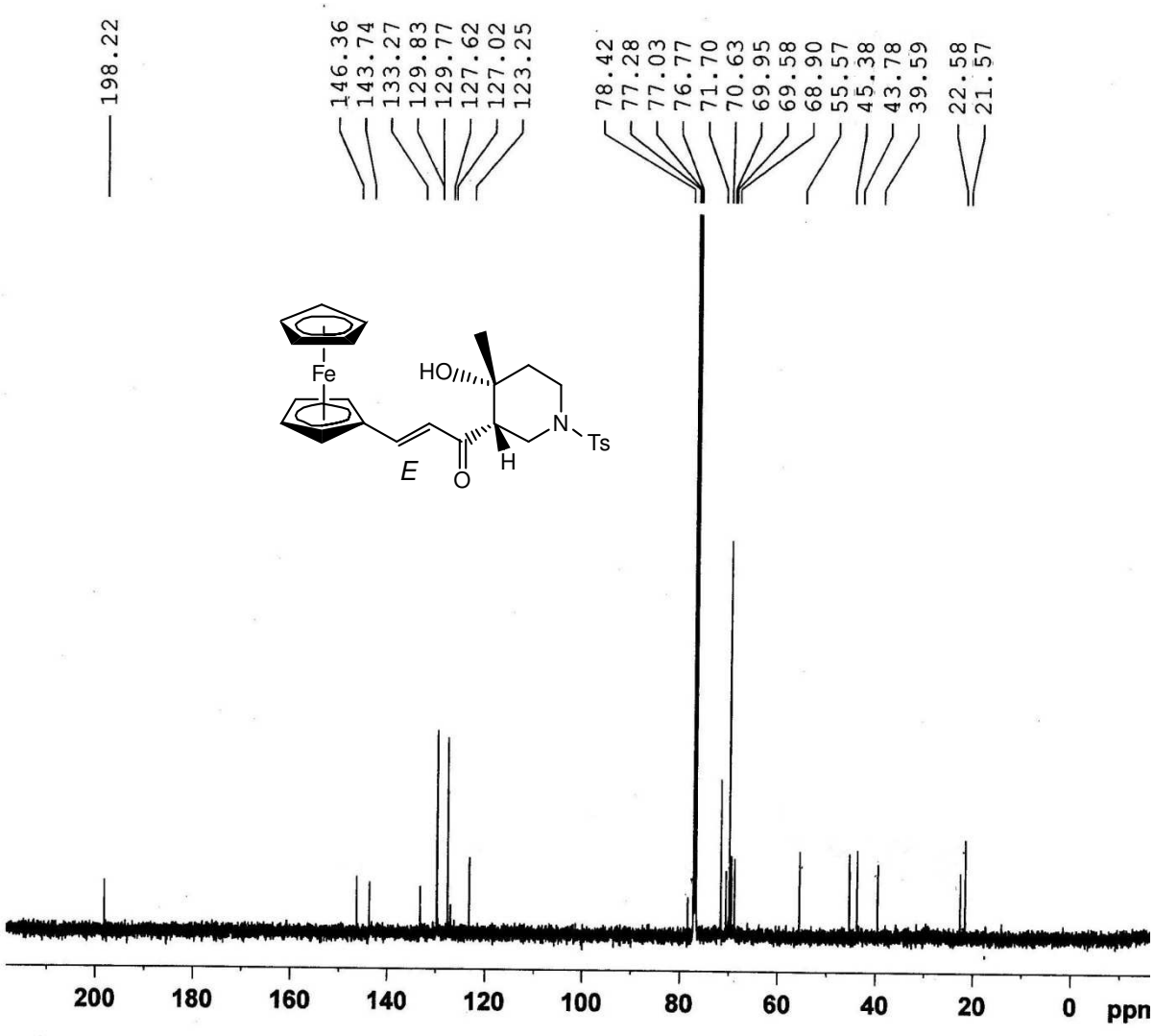


^{1}H NMR of Compound 12a

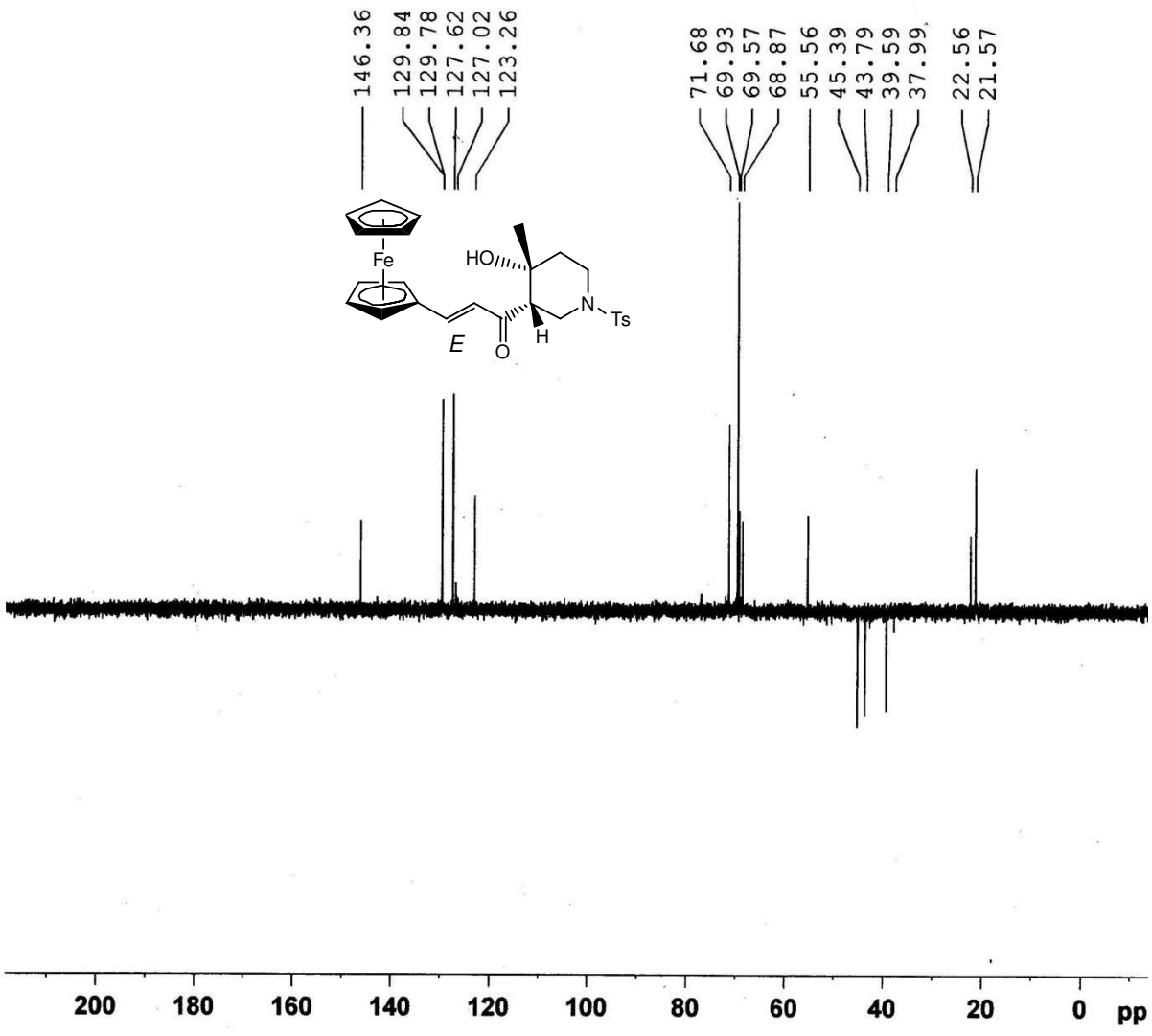




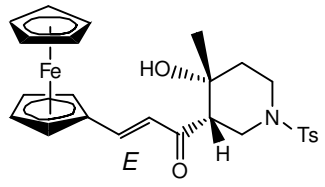
^{13}C NMR of Compound 12a

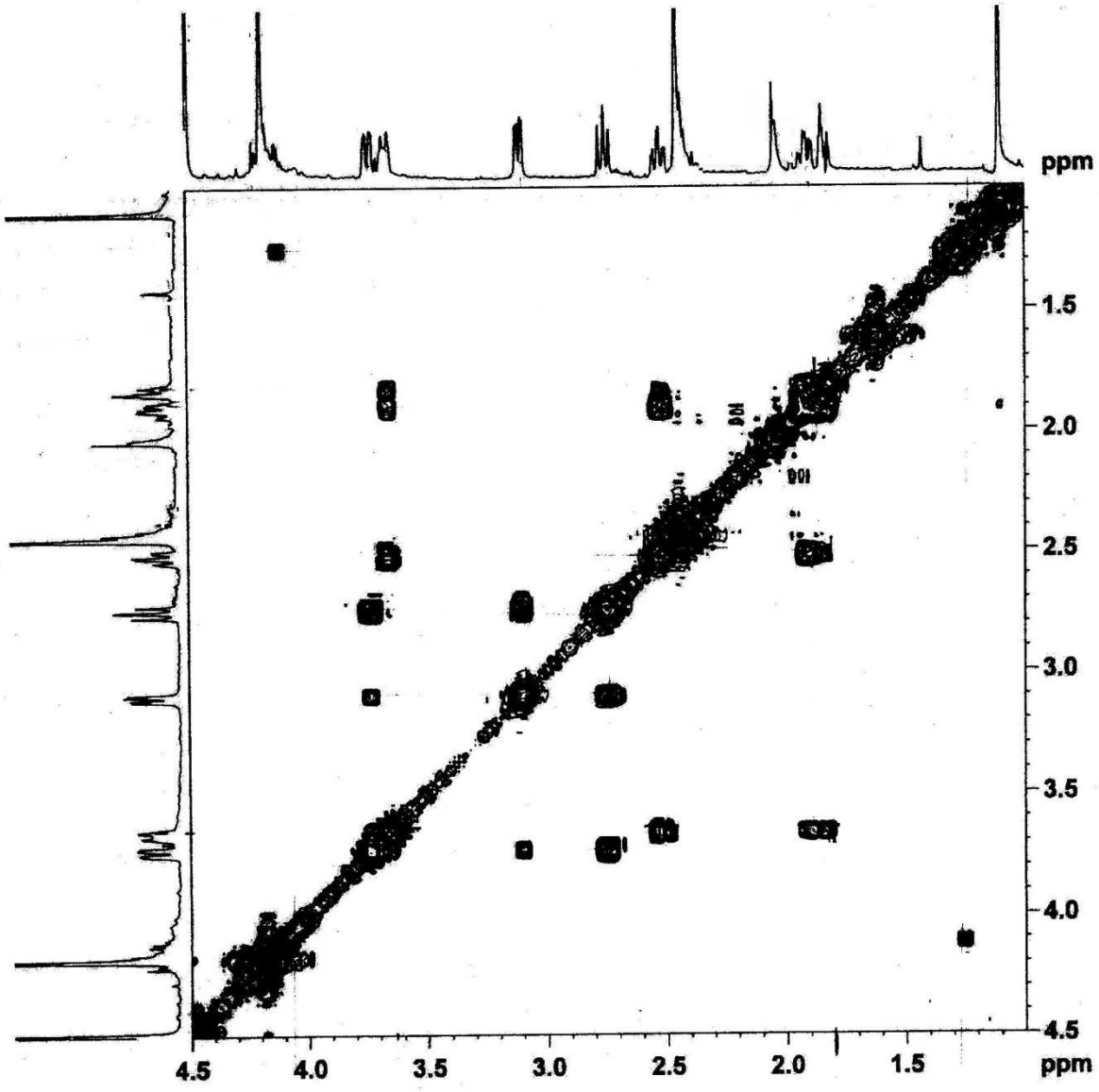


DEPT 135 NMR of Compound 12a

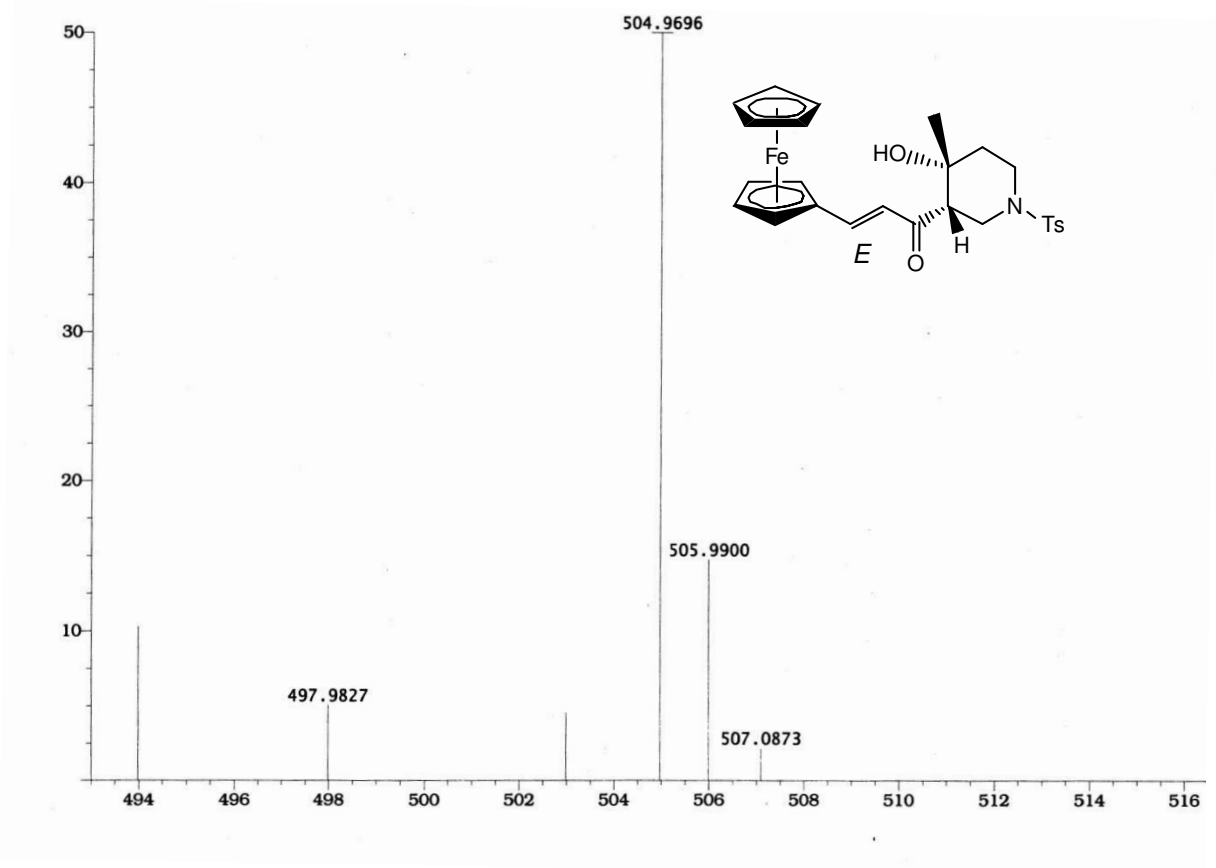


Expansion of COSY Compound 12a

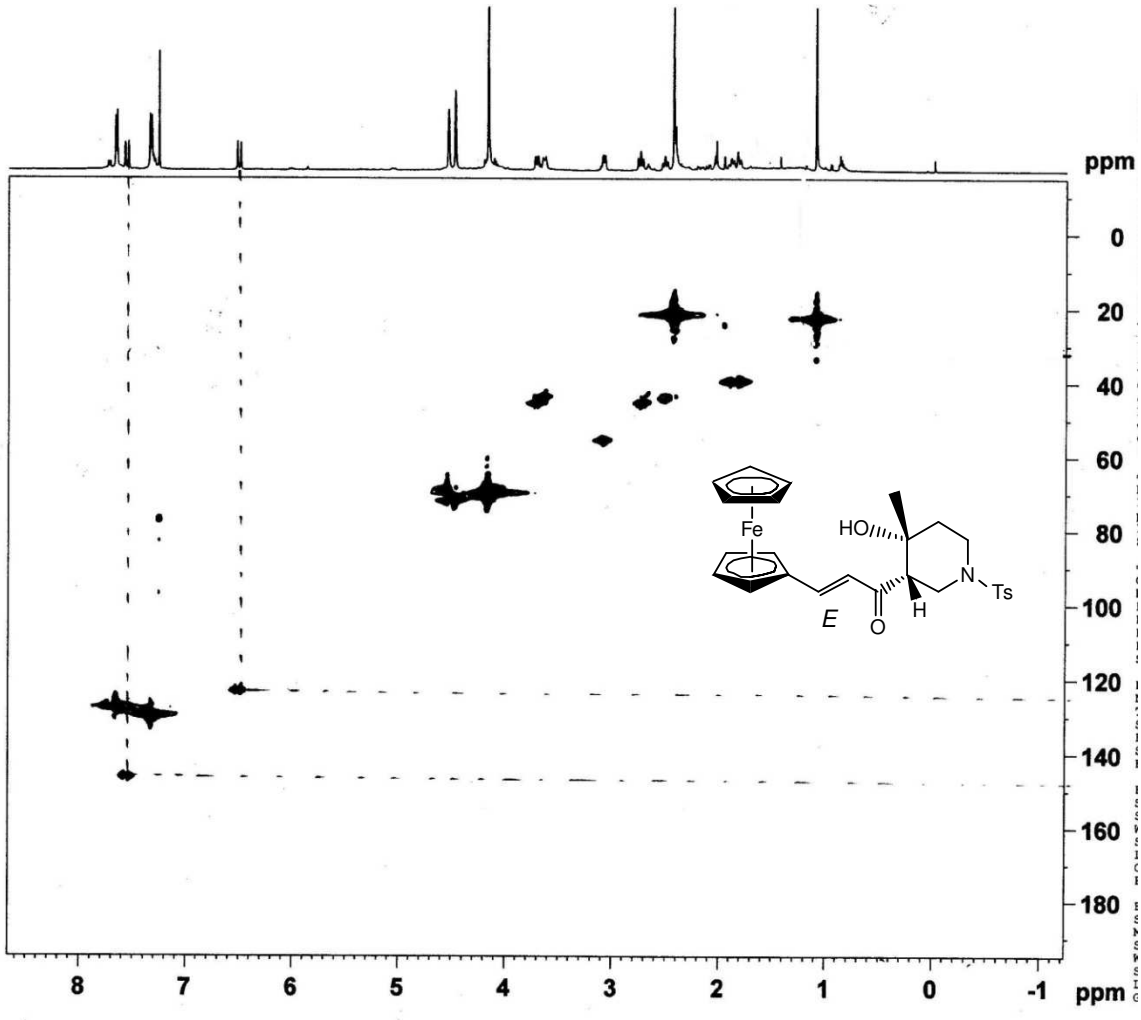




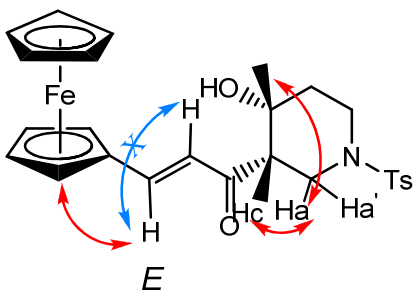
HRMS of Compound 12a



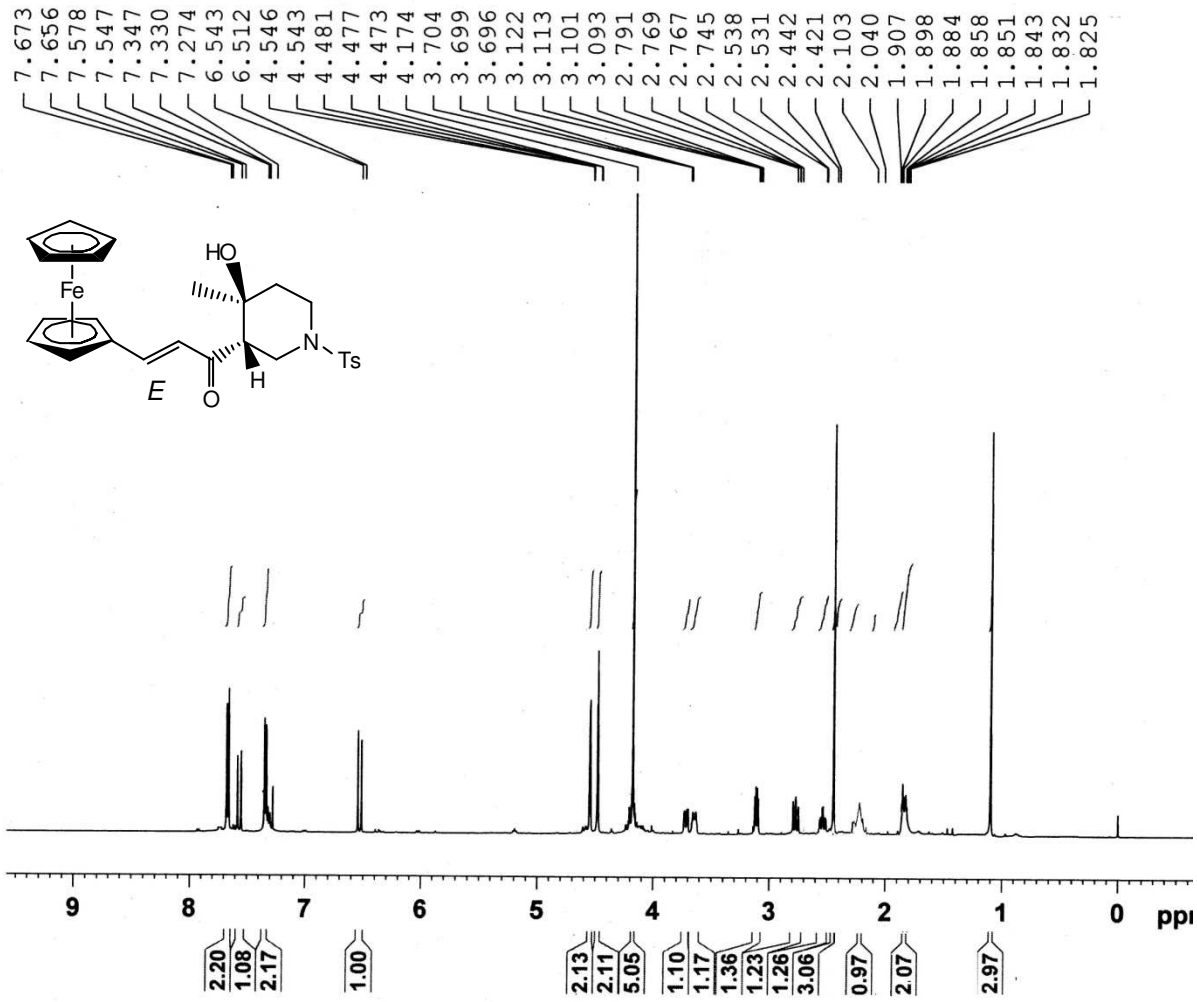
HMQC of Compound 12a



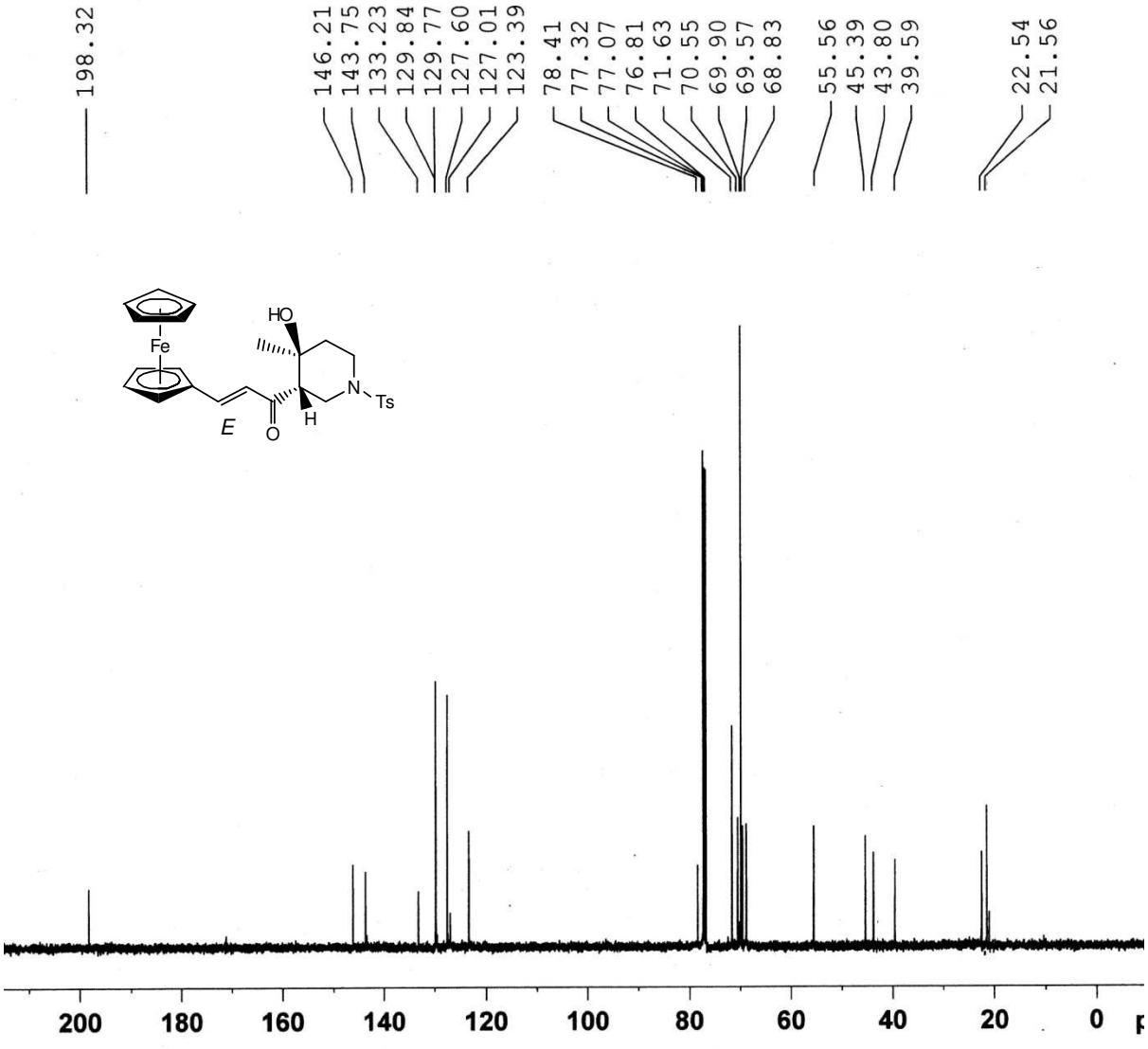
NOE Correlations for compound 12



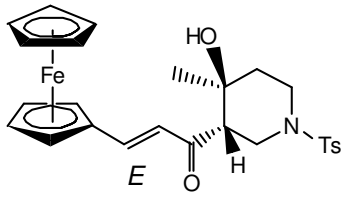
^{1}H NMR of compound 12b (minor isomer)

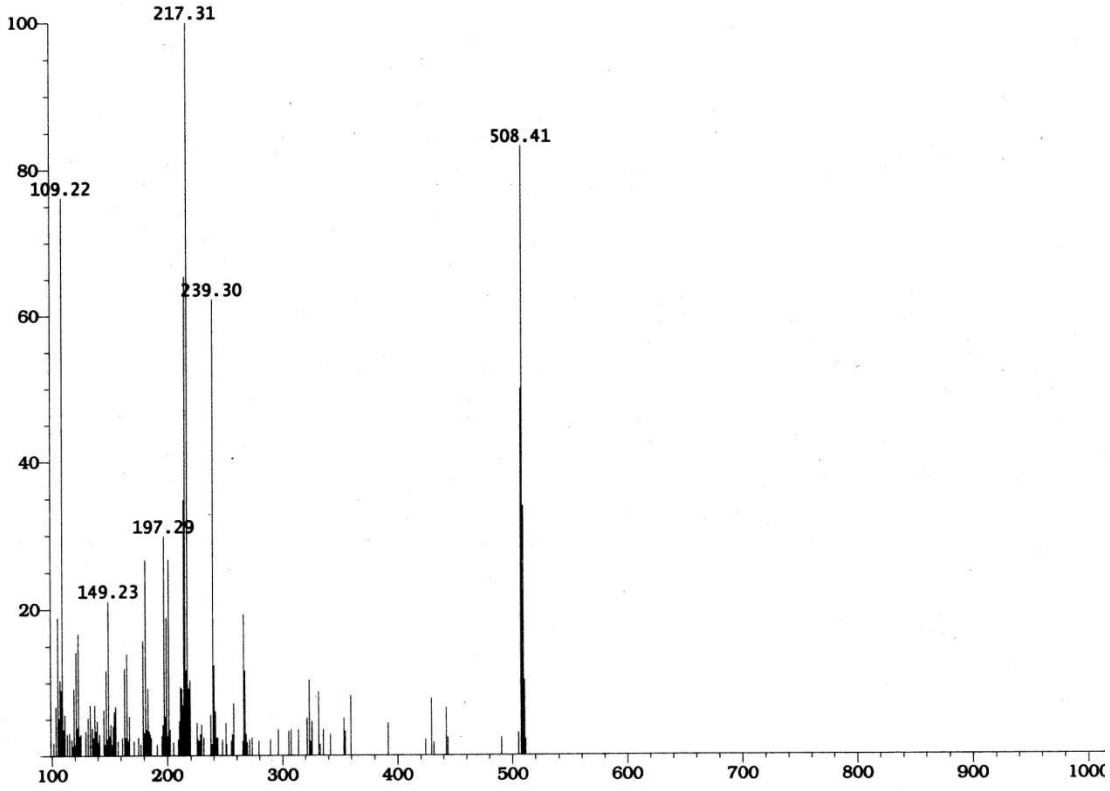


^{13}C NMR of compound 12b (minor isomer)

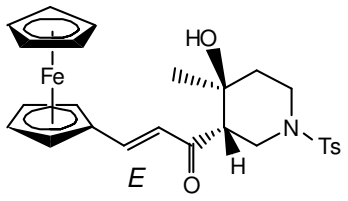


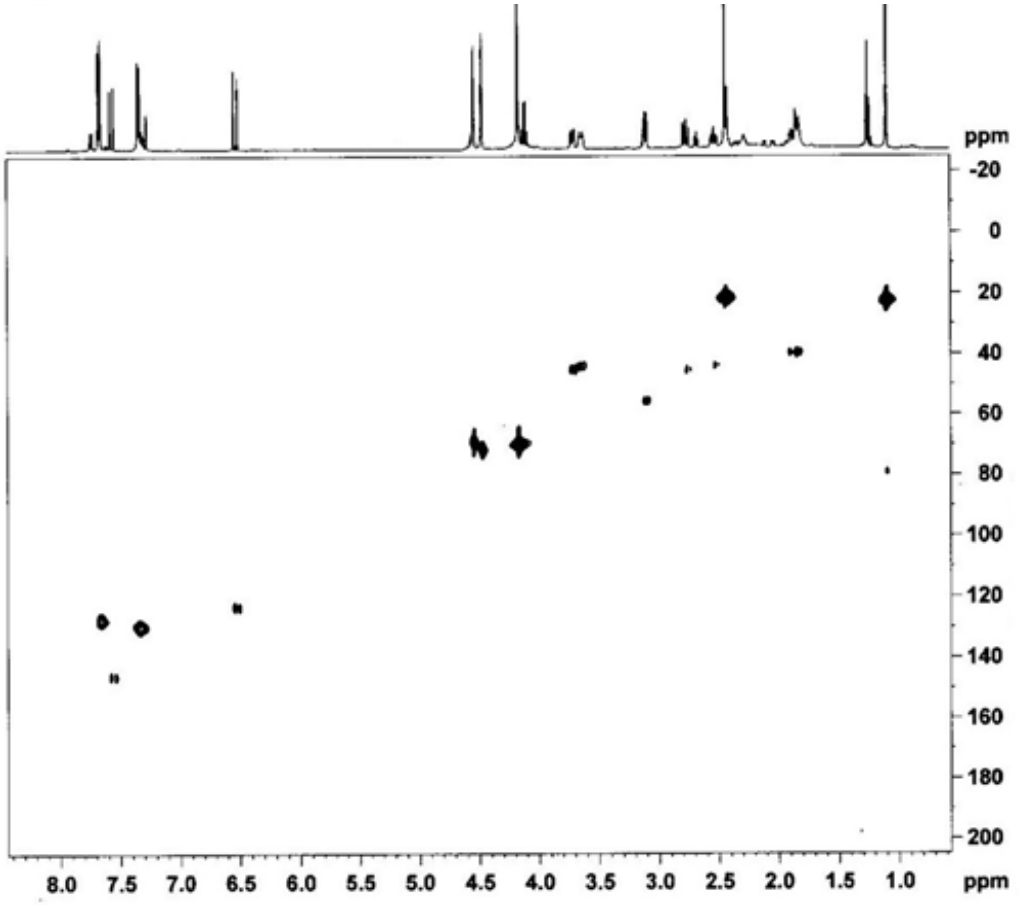
FAB Mass of compound 12b (minor isomer)



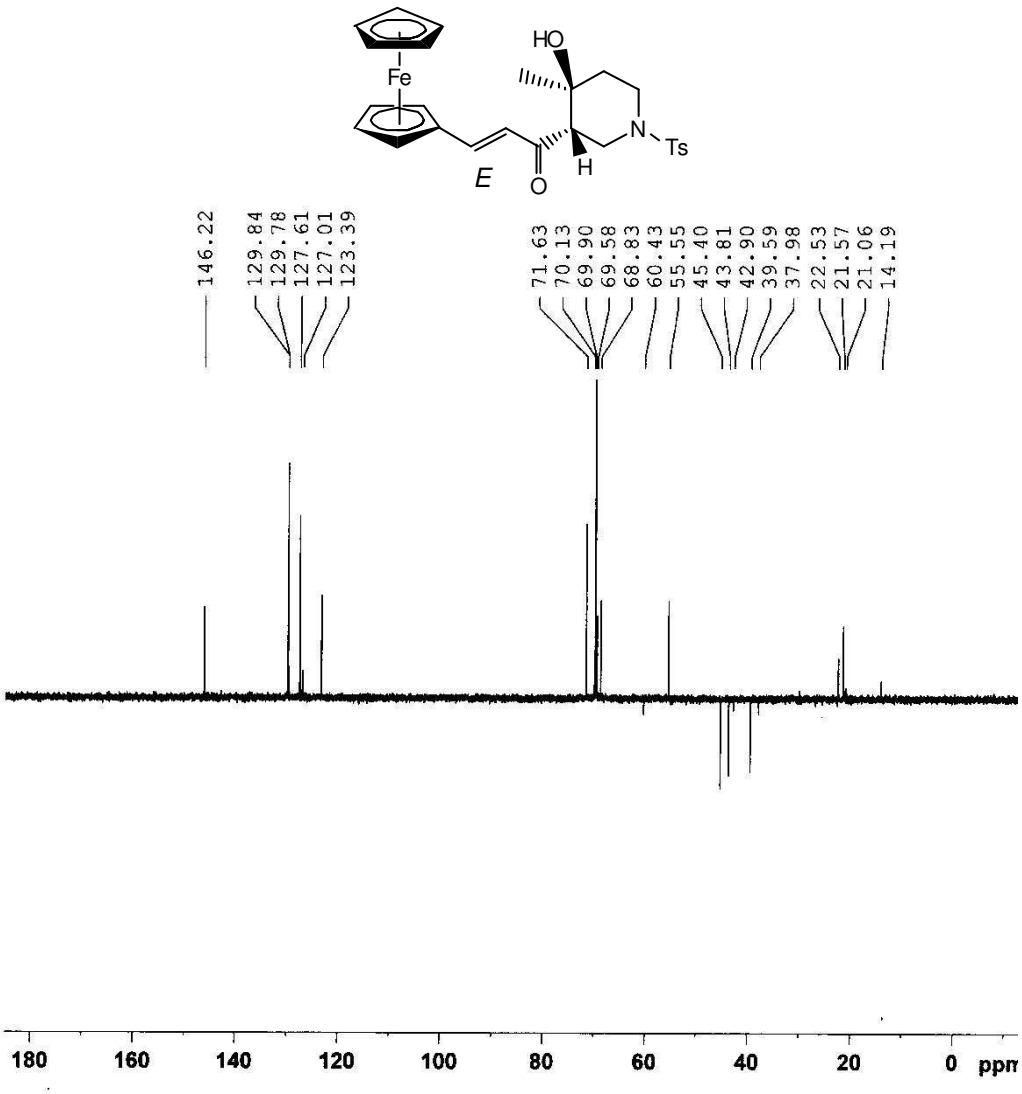


HMQC spectrum of compound 12b (minor isomer)

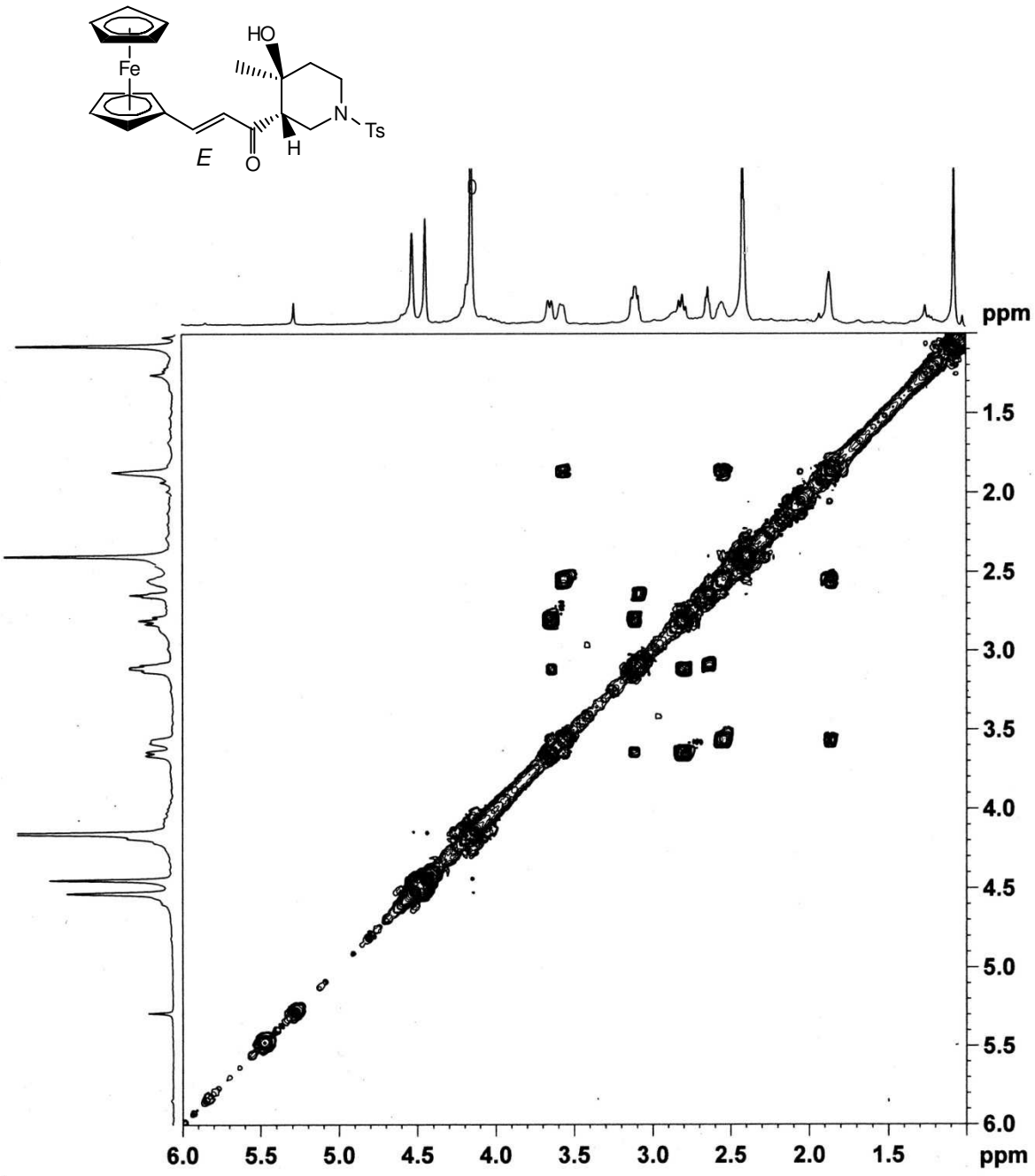




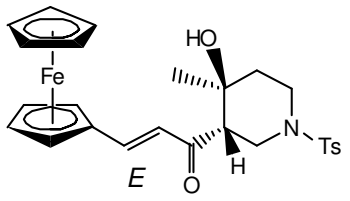
DEPT-135 of compound 12b (minor isomer)

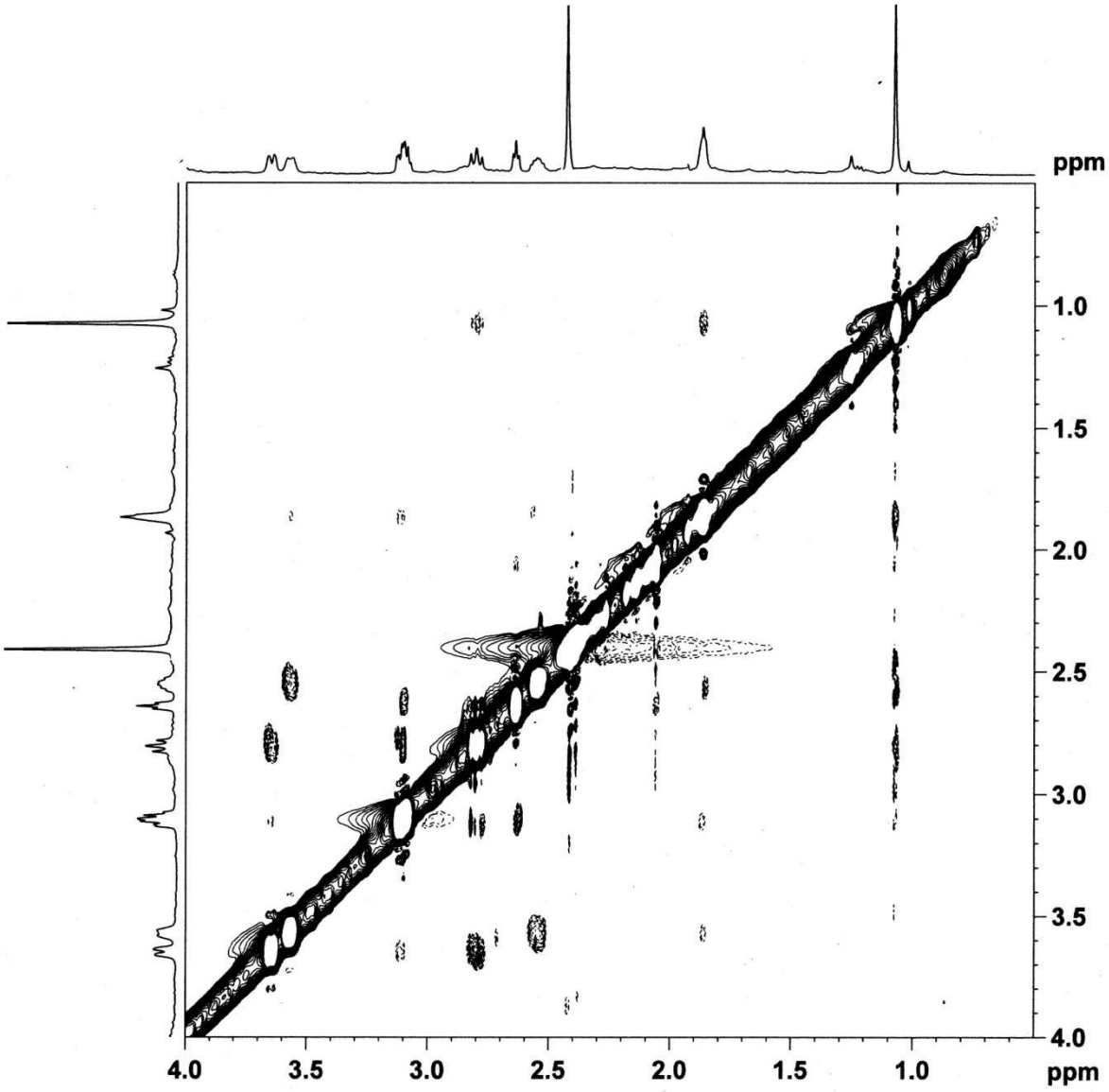


Expansion of COSY of Compound 12b

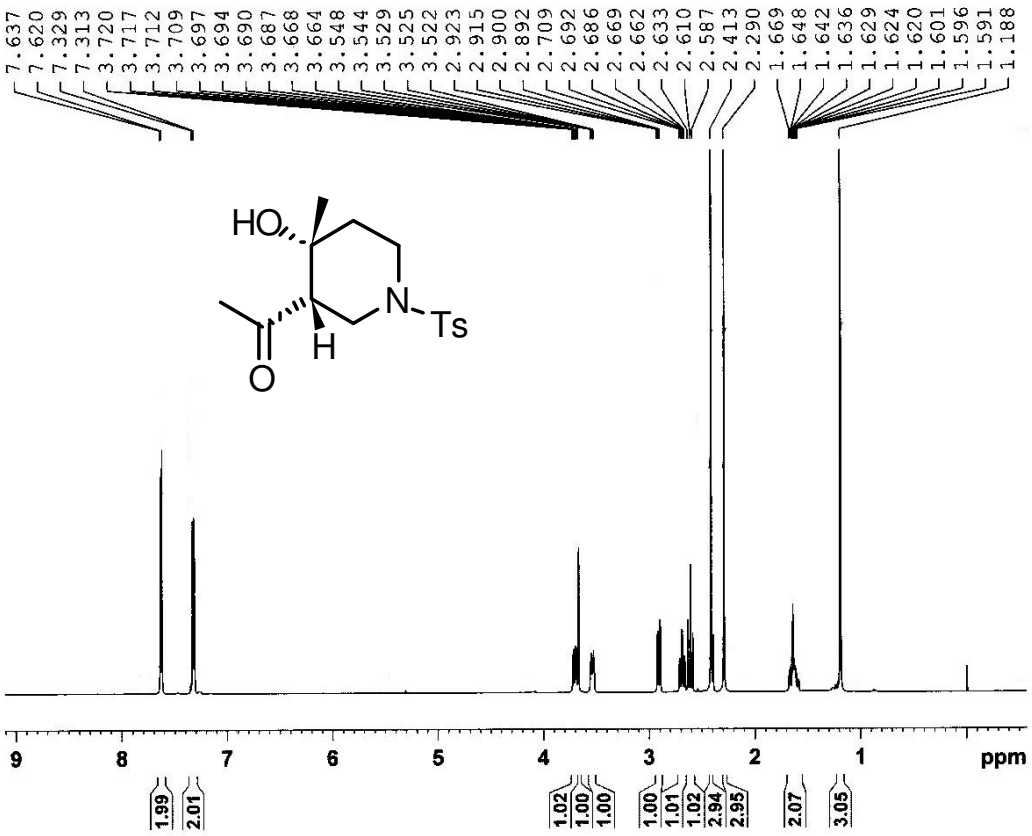


Expansion of NOESY of Compound 12b

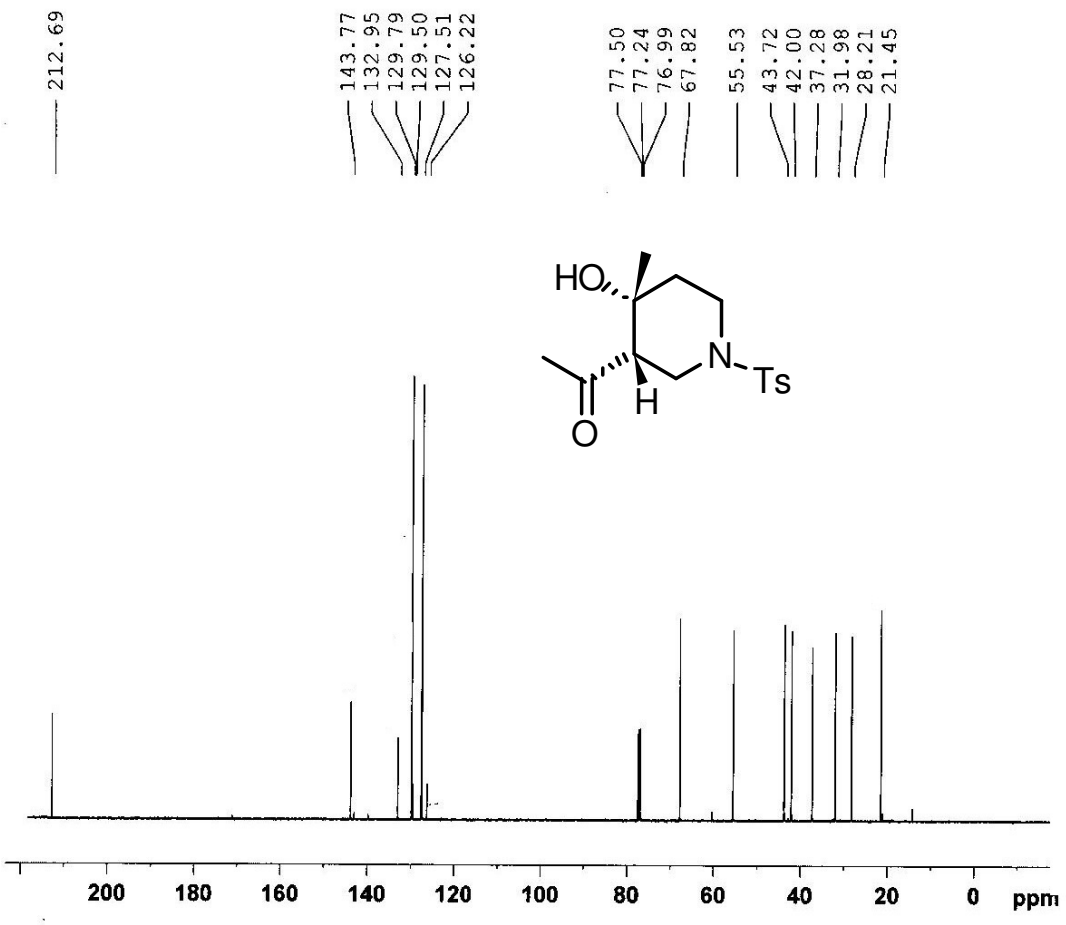




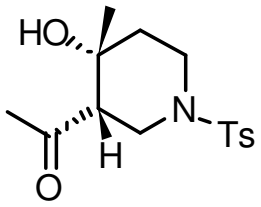
[1]HNMR of Intermediate C (diastereomer-1)

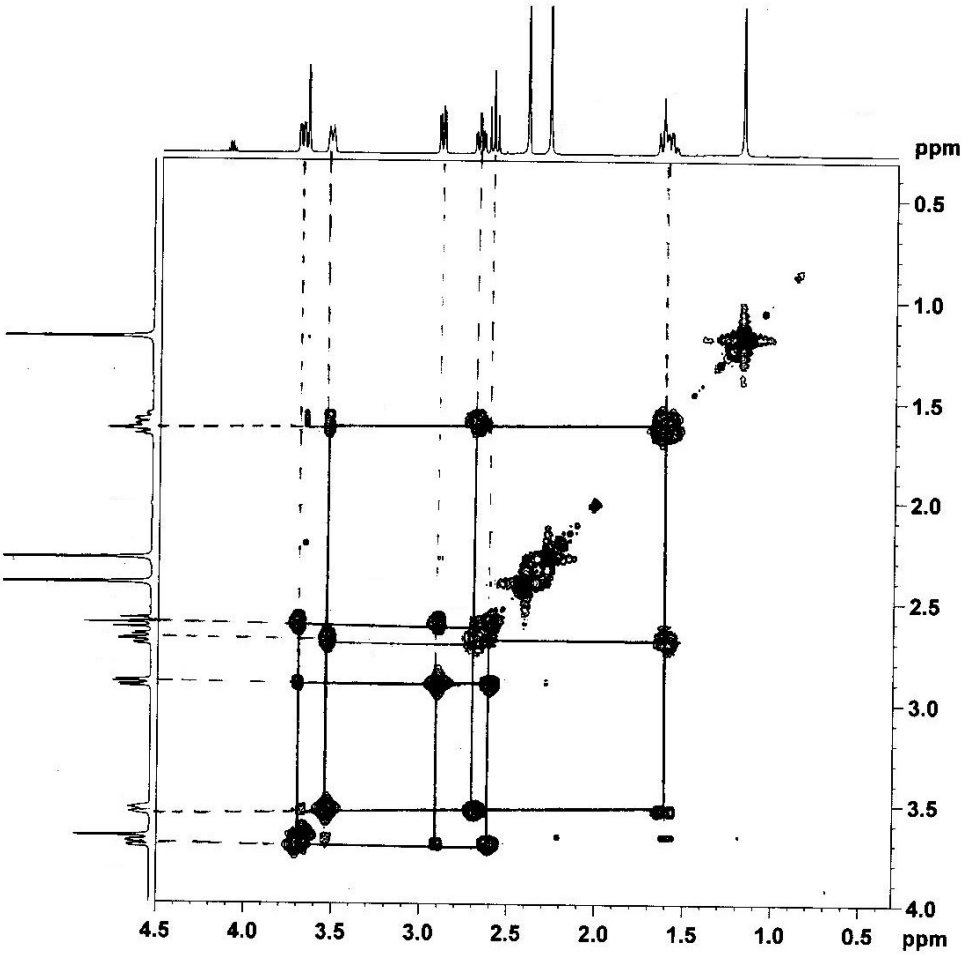


^{13} C NMR of Intermediate C (diastereomer-1)

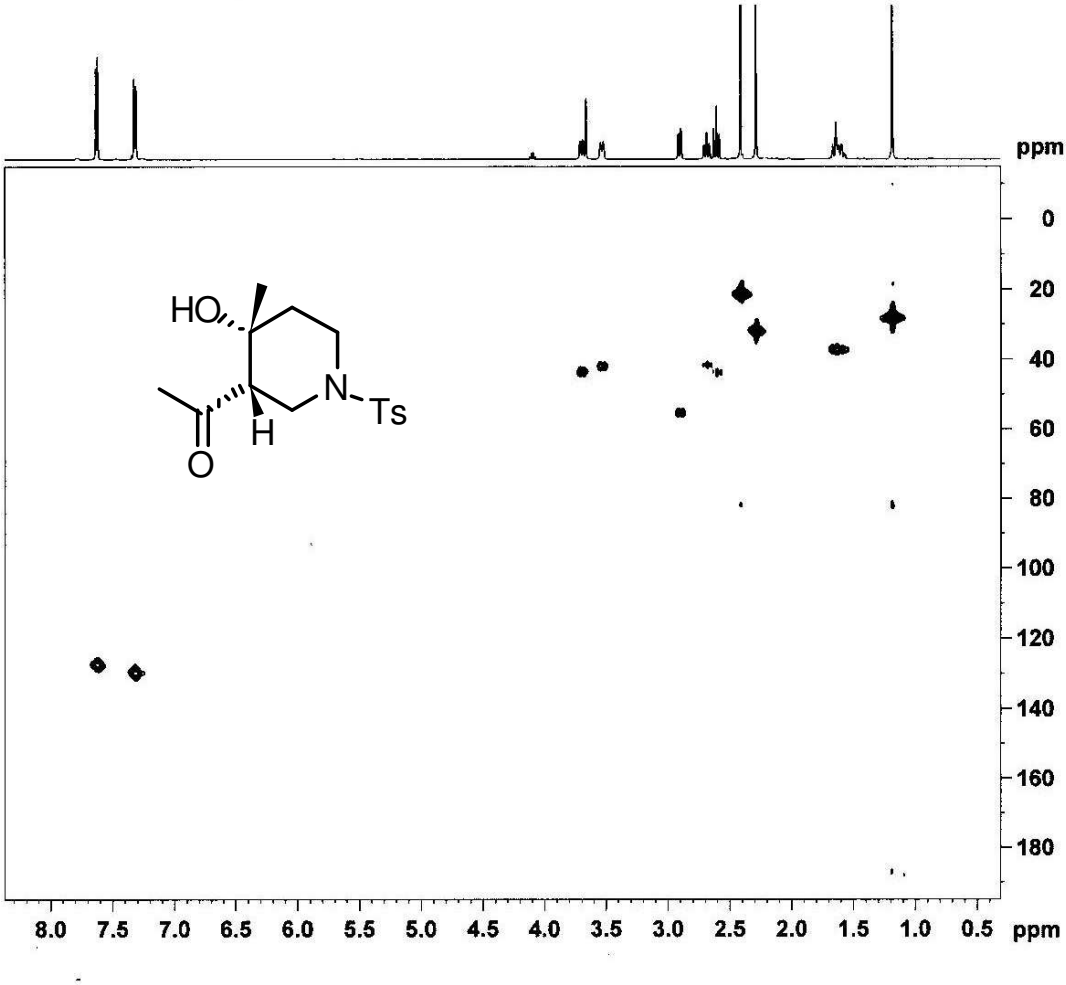


Expansion of COSY of Intermediate C (diastereomer-1)

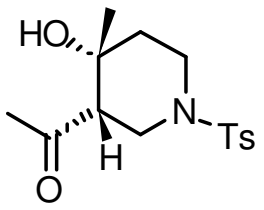


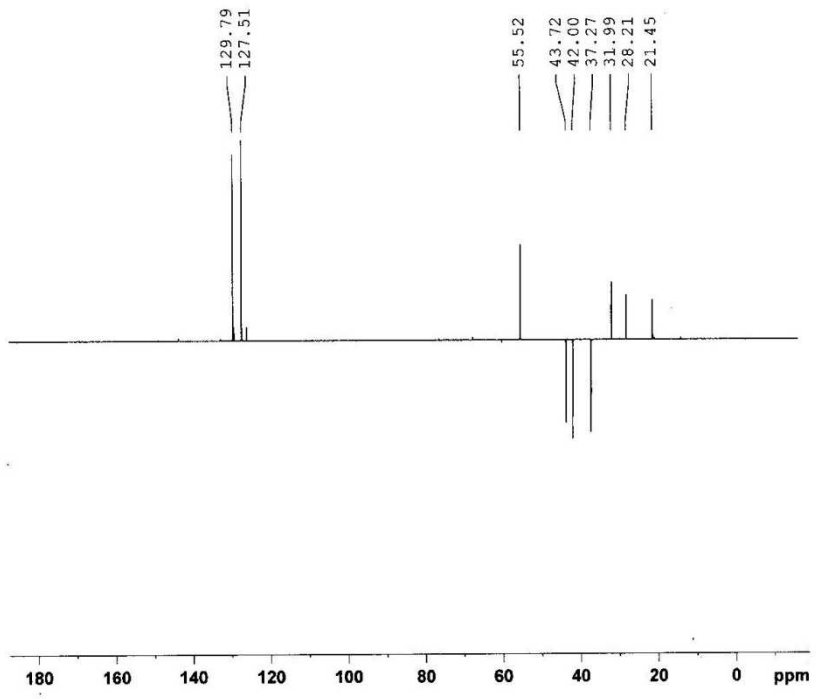


HMQC of Intermediate C (diastereomer-1)

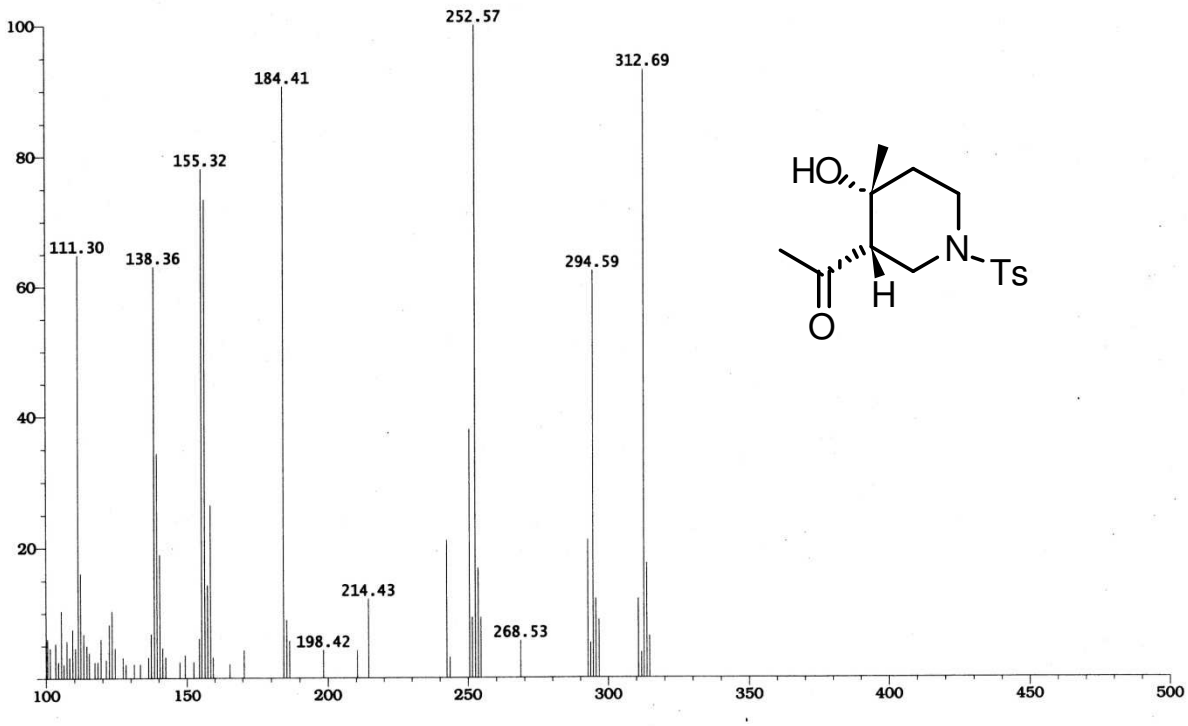


DEPT-135 of Intermediate C (diastereomer-1)

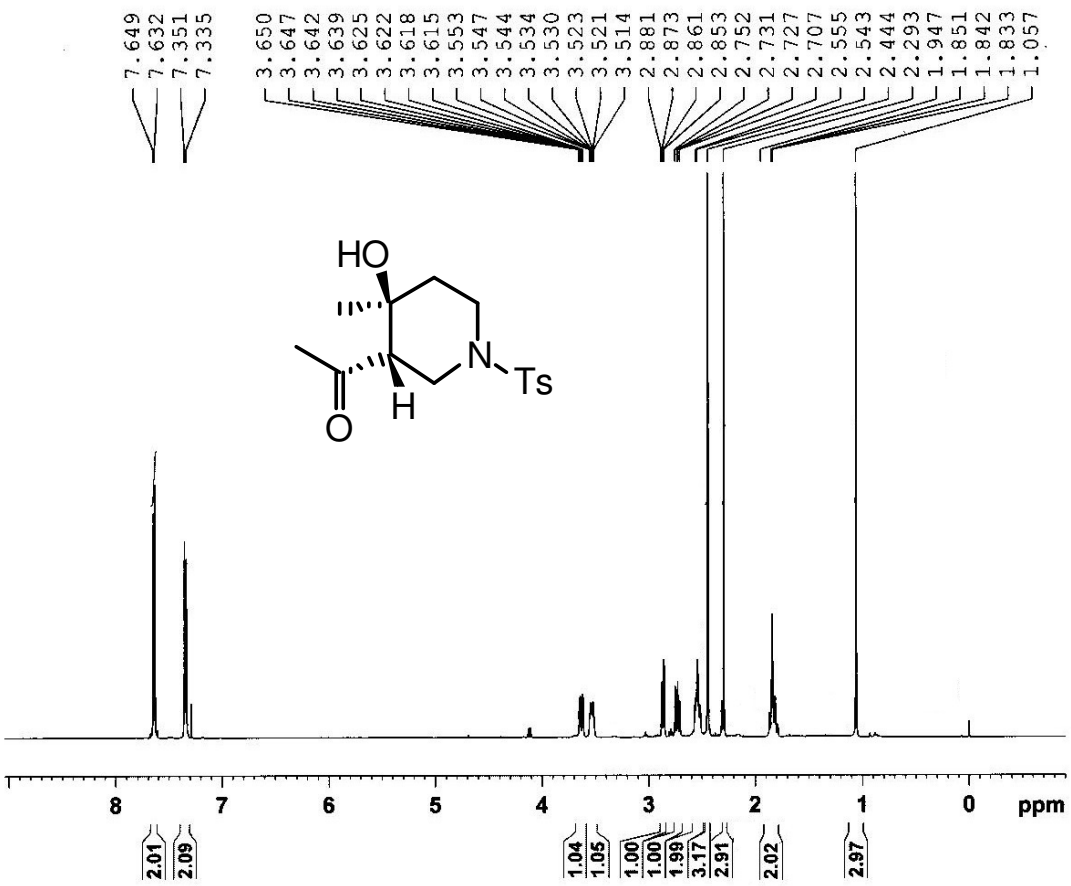




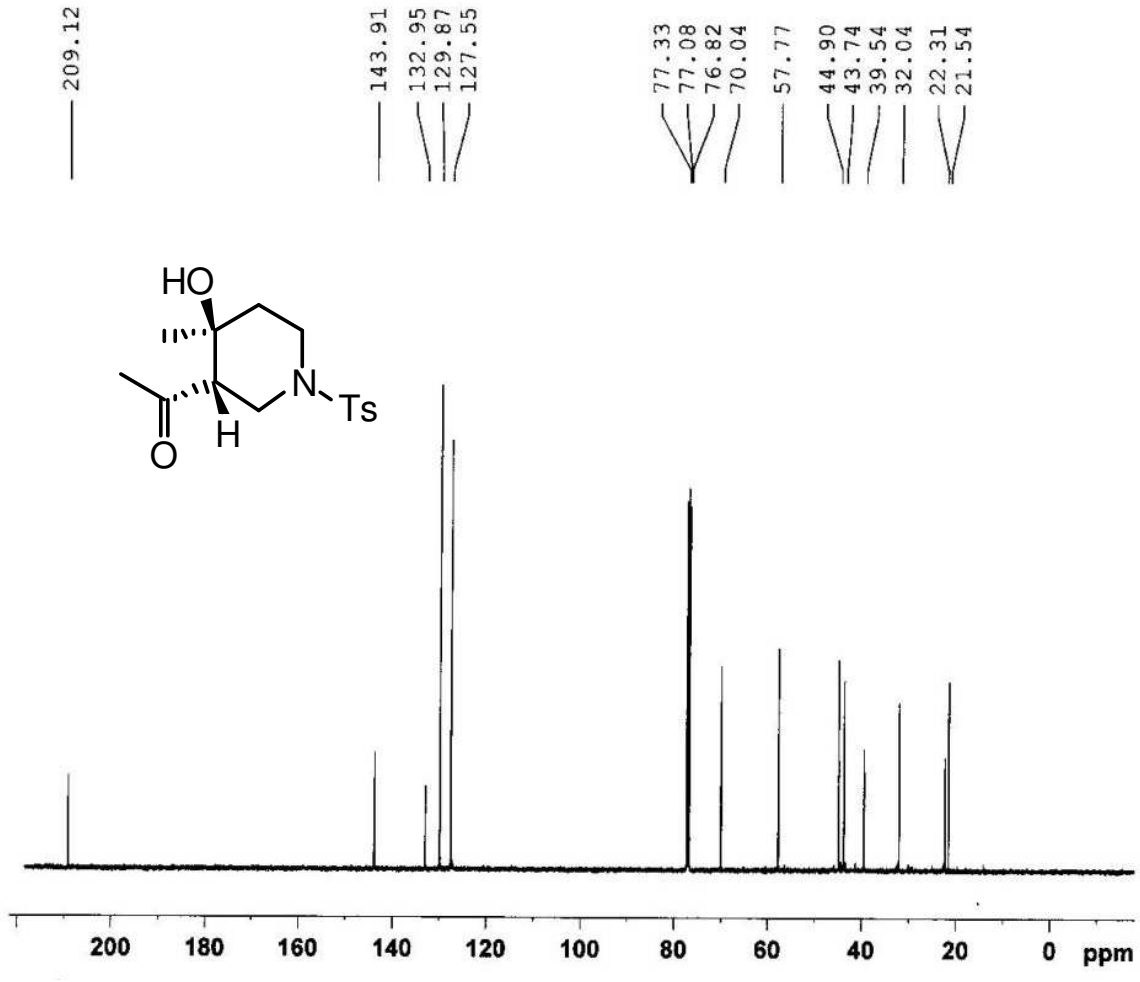
FAB Mass **of Intermediate C (diastereomer-1)**



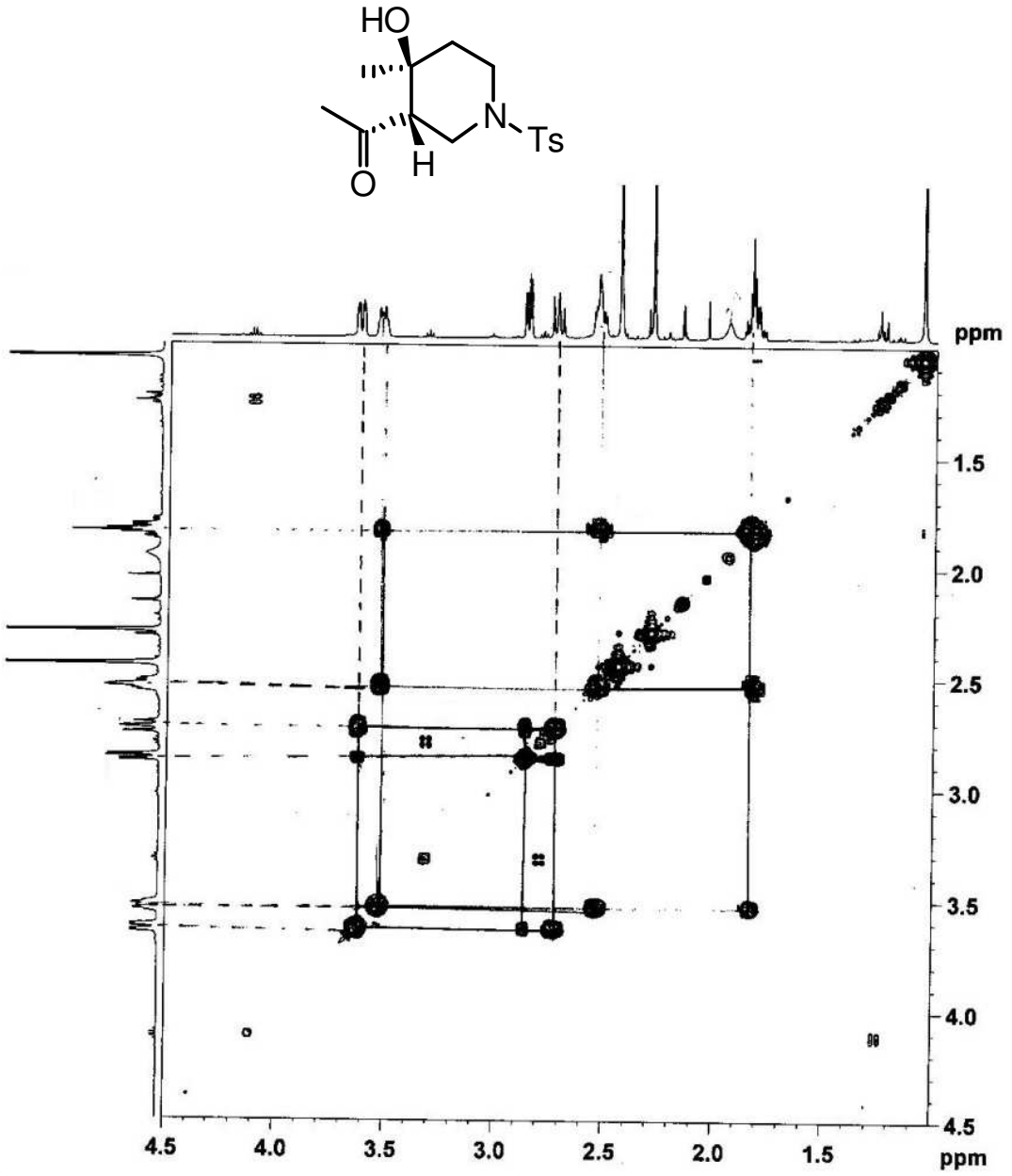
^{1}H NMR of Intermediate C (diastereomer-2)



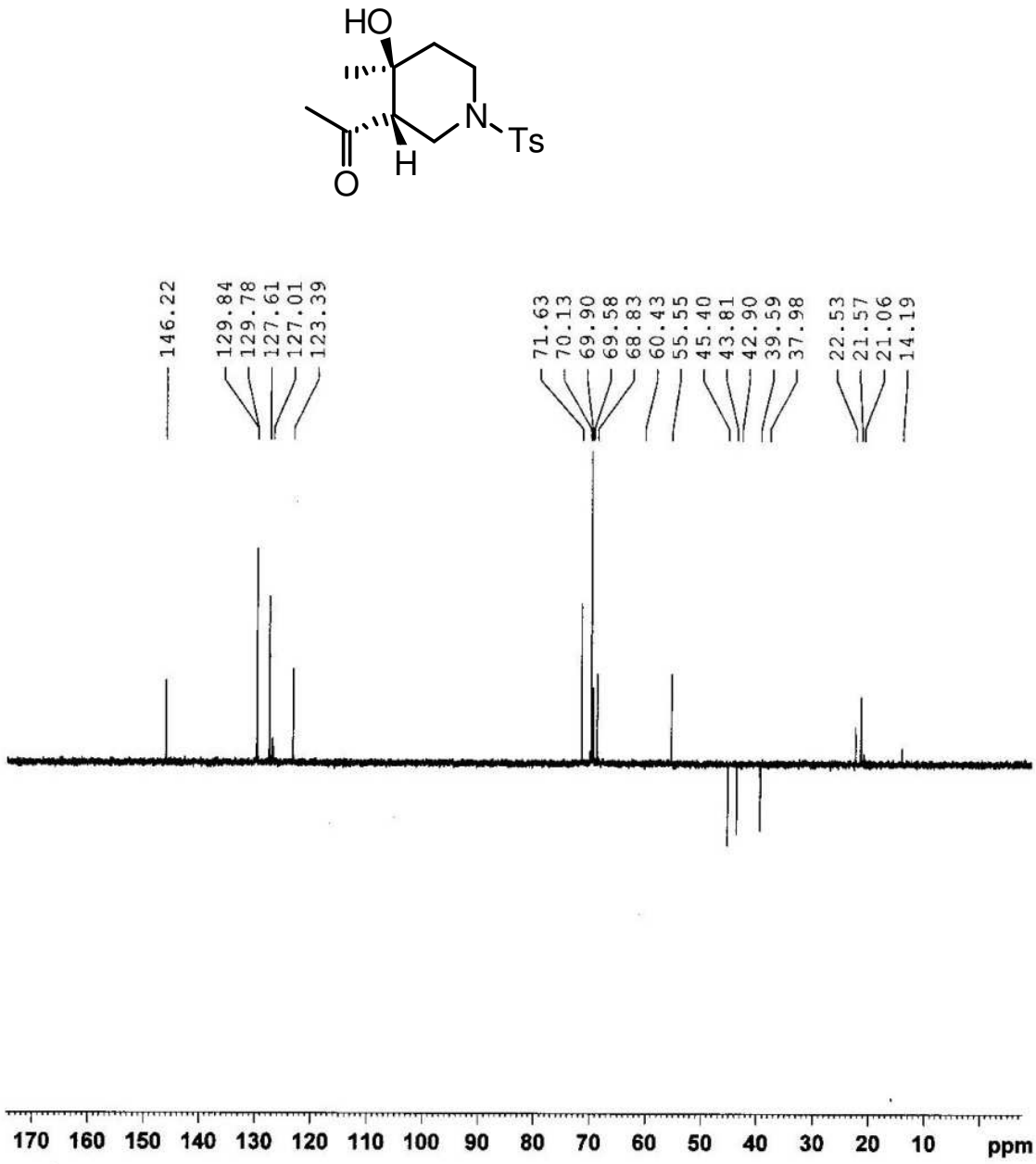
^{13}C NMR of Intermediate C (diastereomer-2)



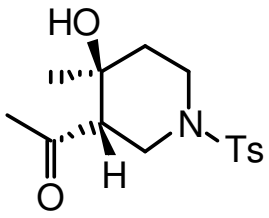
COSY of Intermediate C (diastereomer-2)

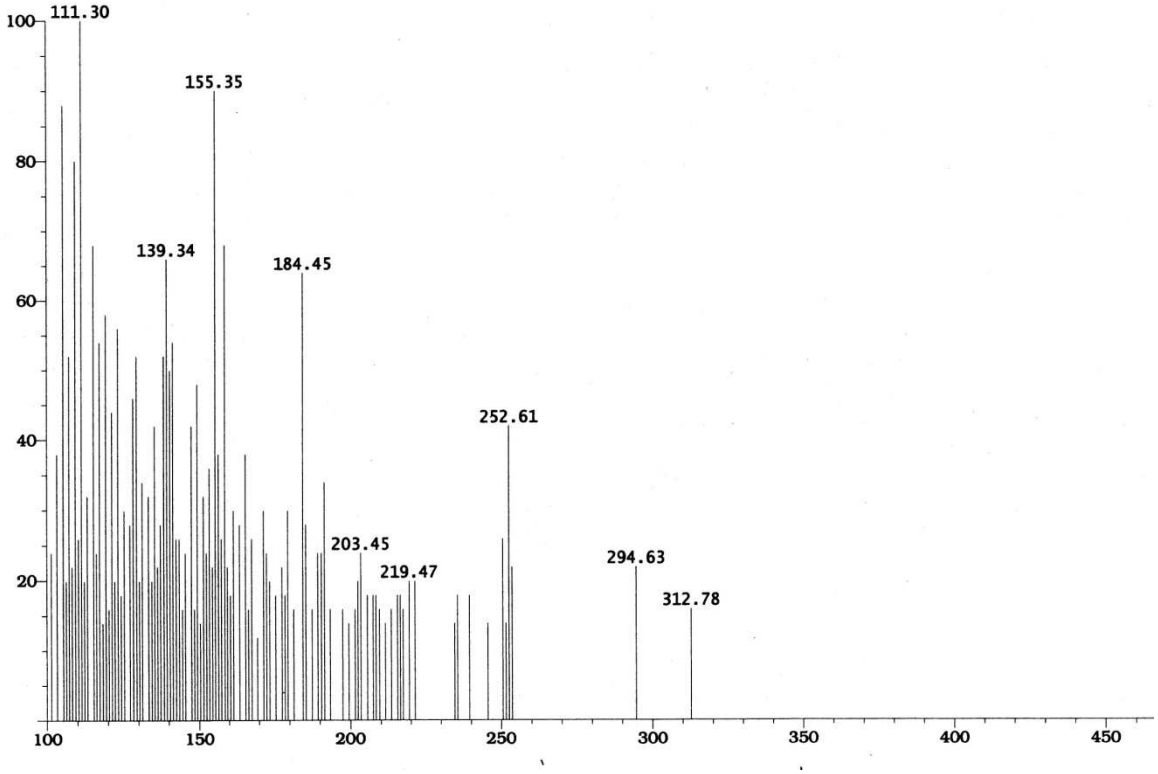


DEPT-135 NMR of Intermediate C (diastereomer-2)

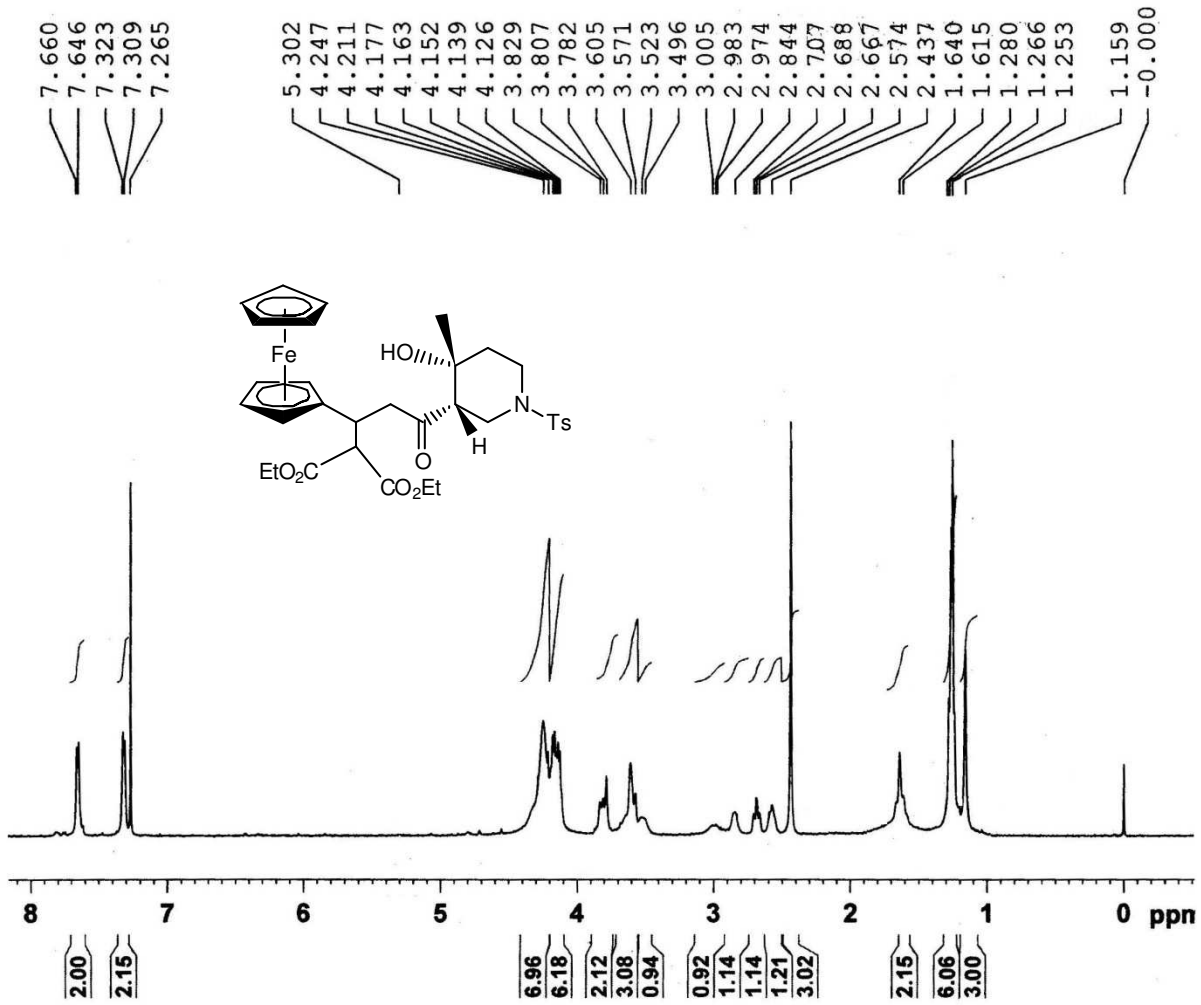


FAB Mass of Intermediate C (diastereomer-1)

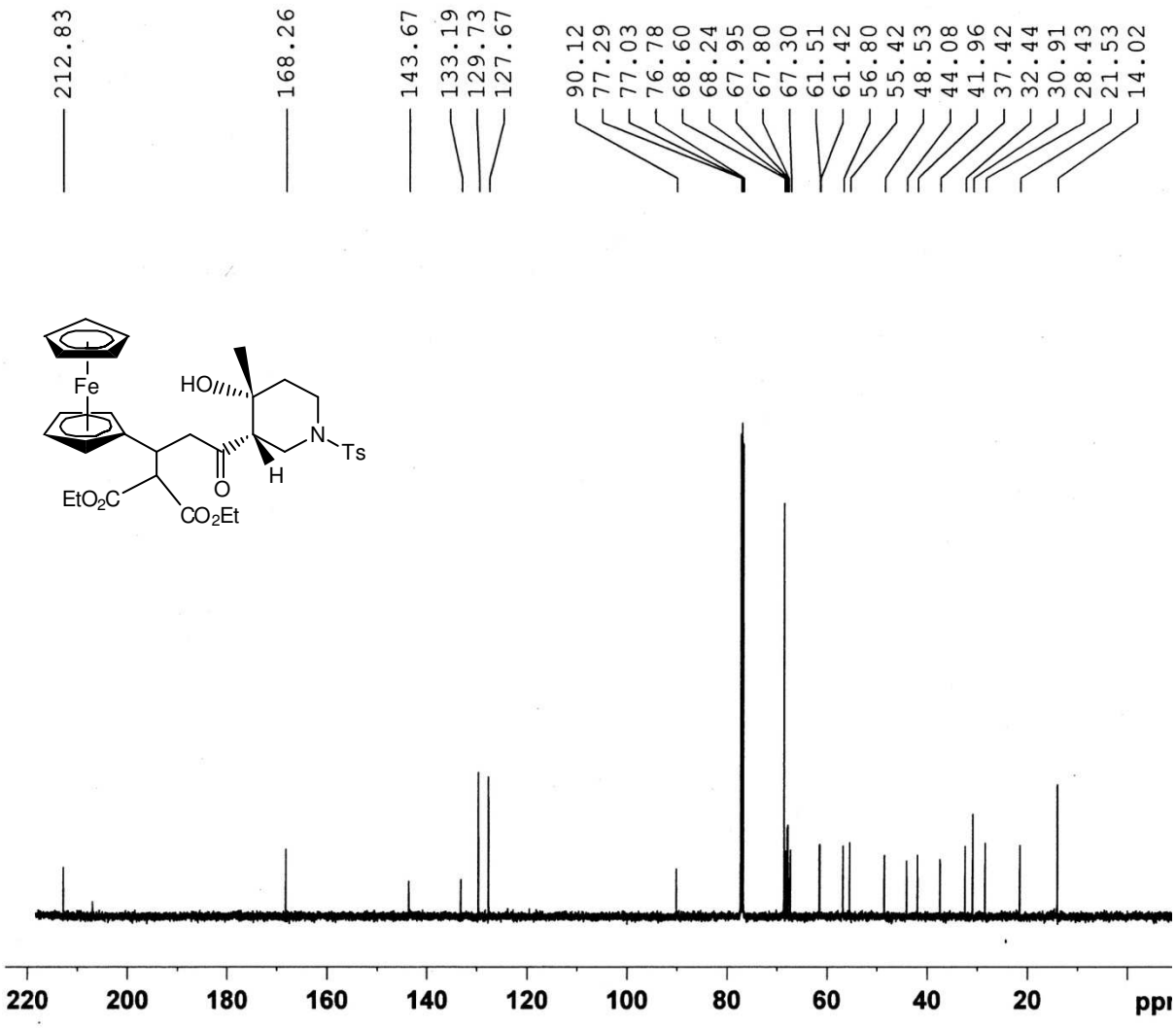




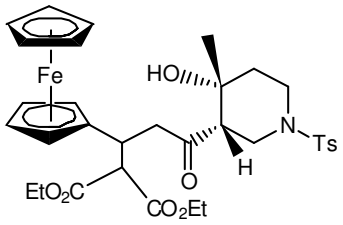
^{1}H NMR Compound 13



^{13}C NMR of Compound 13



HRMS of Compound 13

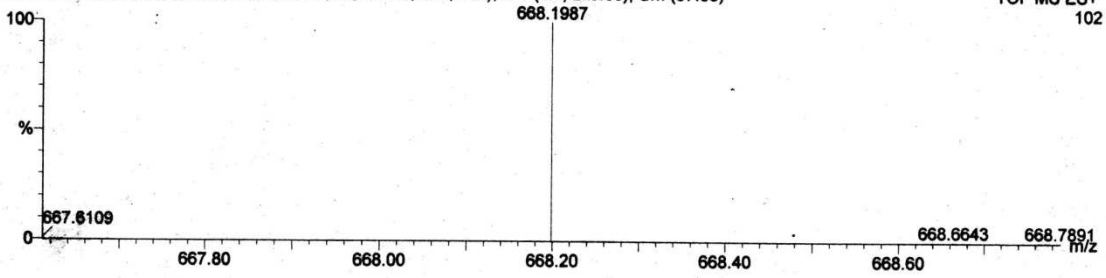


Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 200.0 mDa / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

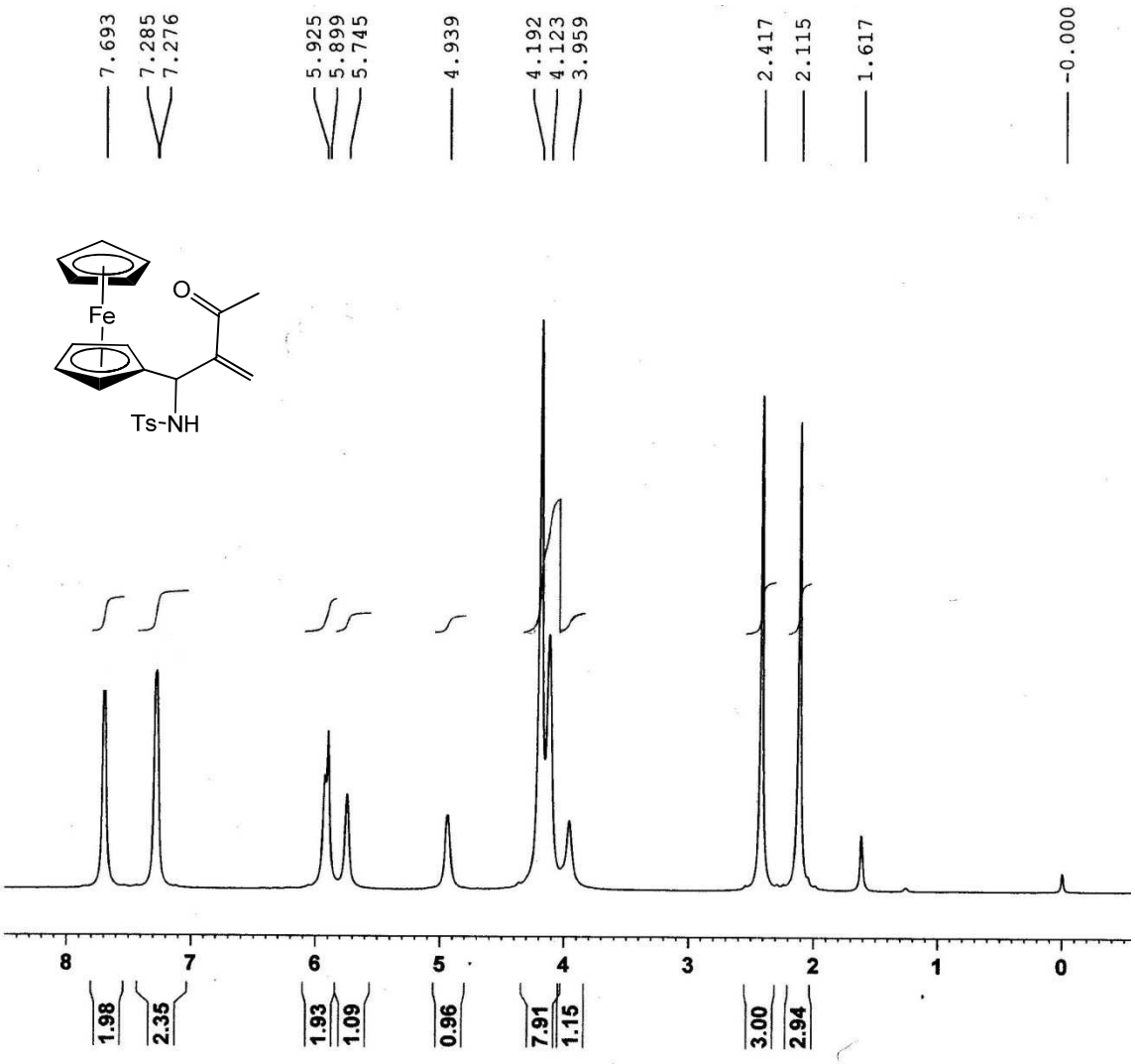
Monoisotopic Mass, Odd and Even Electron Ions
67 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

GSK-DGP-51
GSK-DGP-51 37 (0.371) AM (Cen,2, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00); Cm (37:38) TOF MS ES+ 102

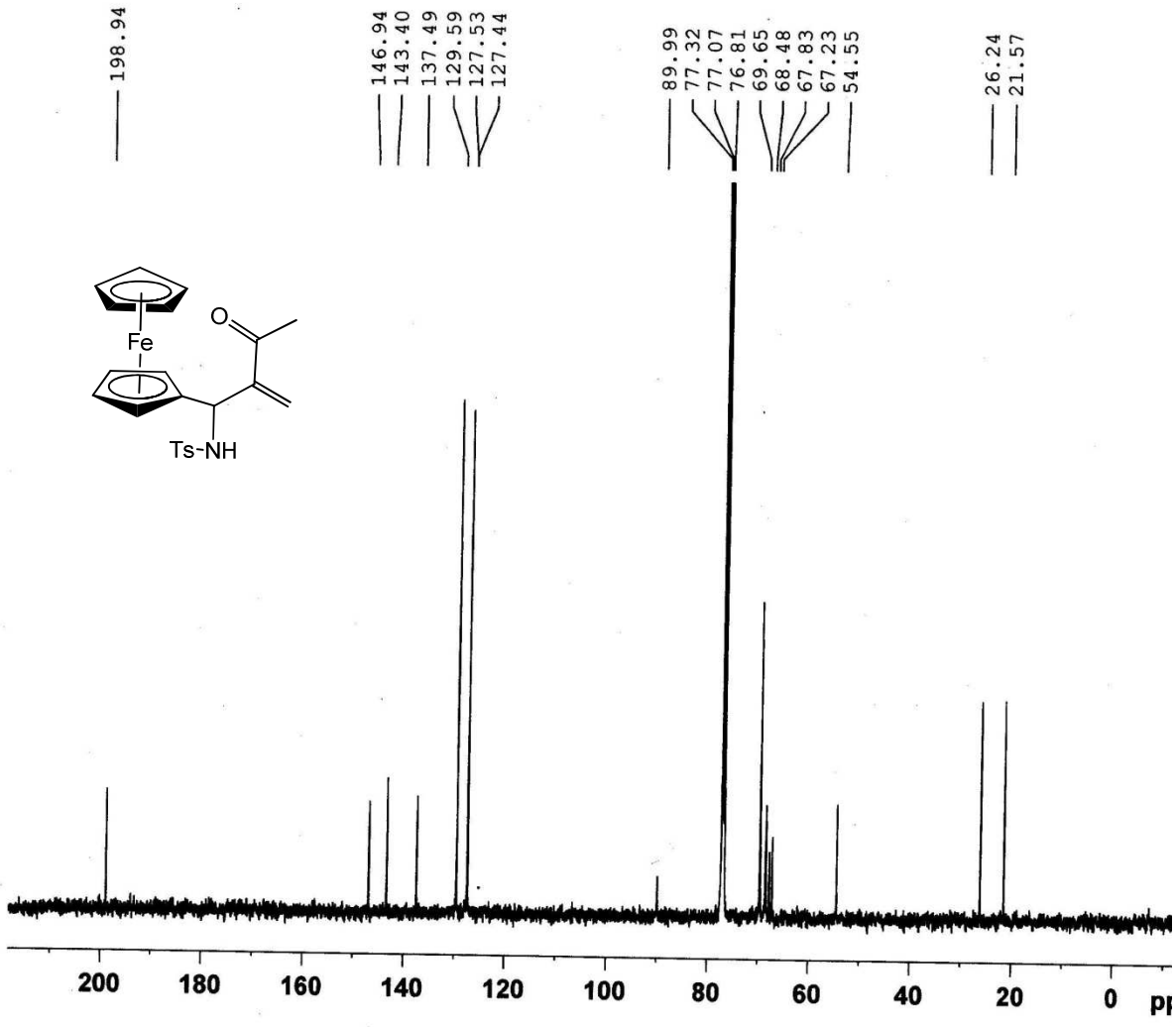


Minimum:				-1.5		
Maximum:		200.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
668.1987	668.1981	0.7	1.0	13.5	1	C33 H42 N O8 S Fe

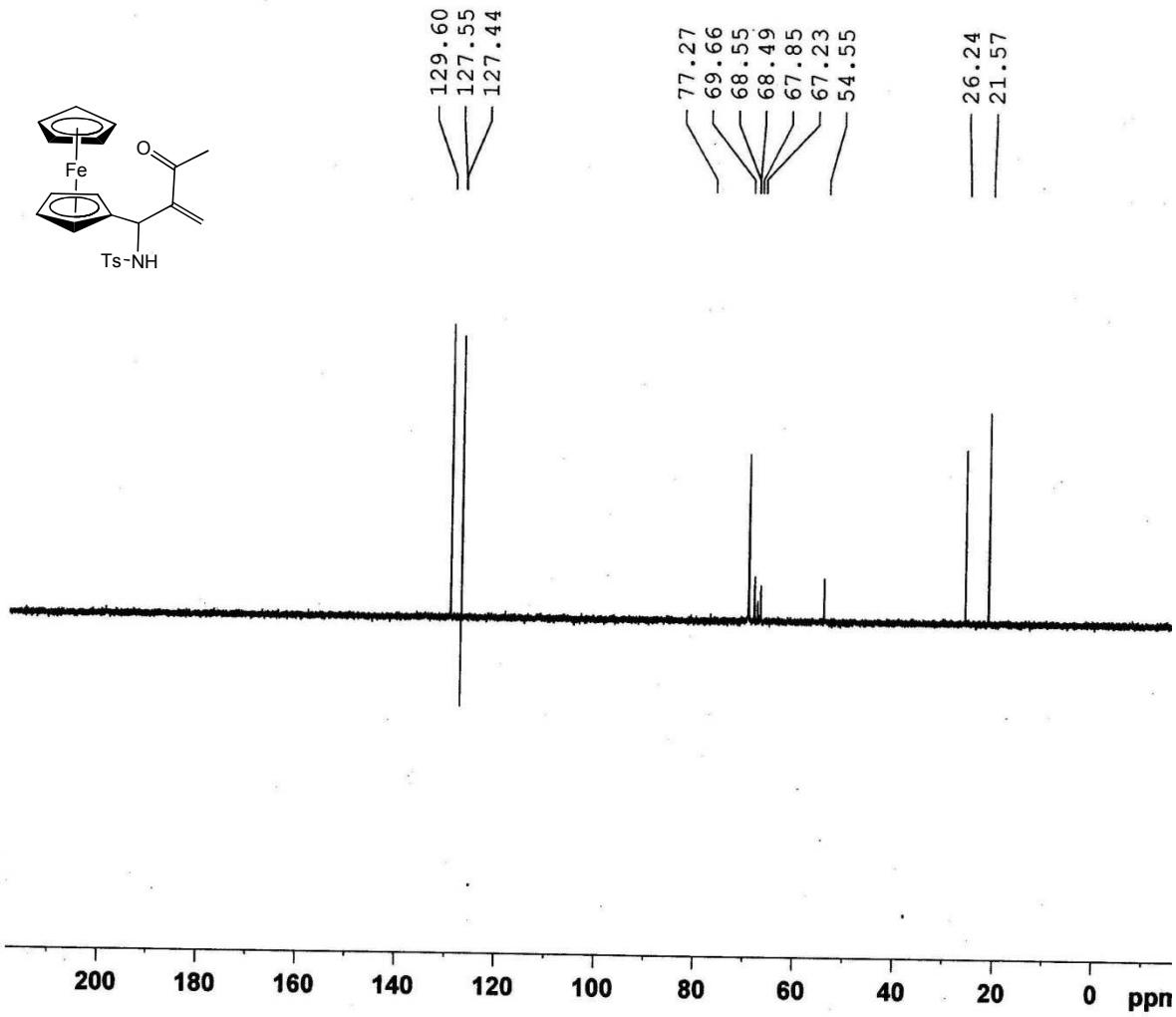
^{1}H NMR Compound 14



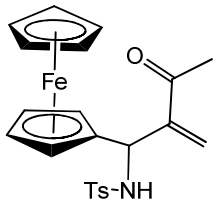
^{13}C NMR Compound 14



DEPT-135 NMR Compound 14



HRMS of Compound 14

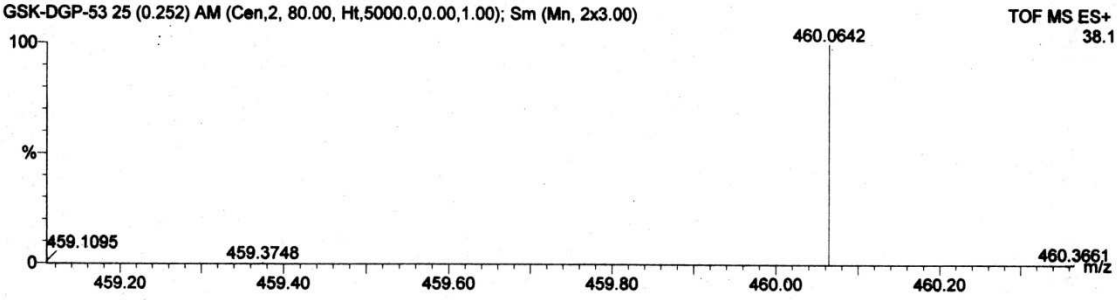


Elemental Composition Report **Page 1**

Single Mass Analysis
Tolerance = 200.0 mDa / DBE: min = -1.5, max = 50.0
Isotope cluster parameters: Separation = 1.0 Abundance = 1.0%

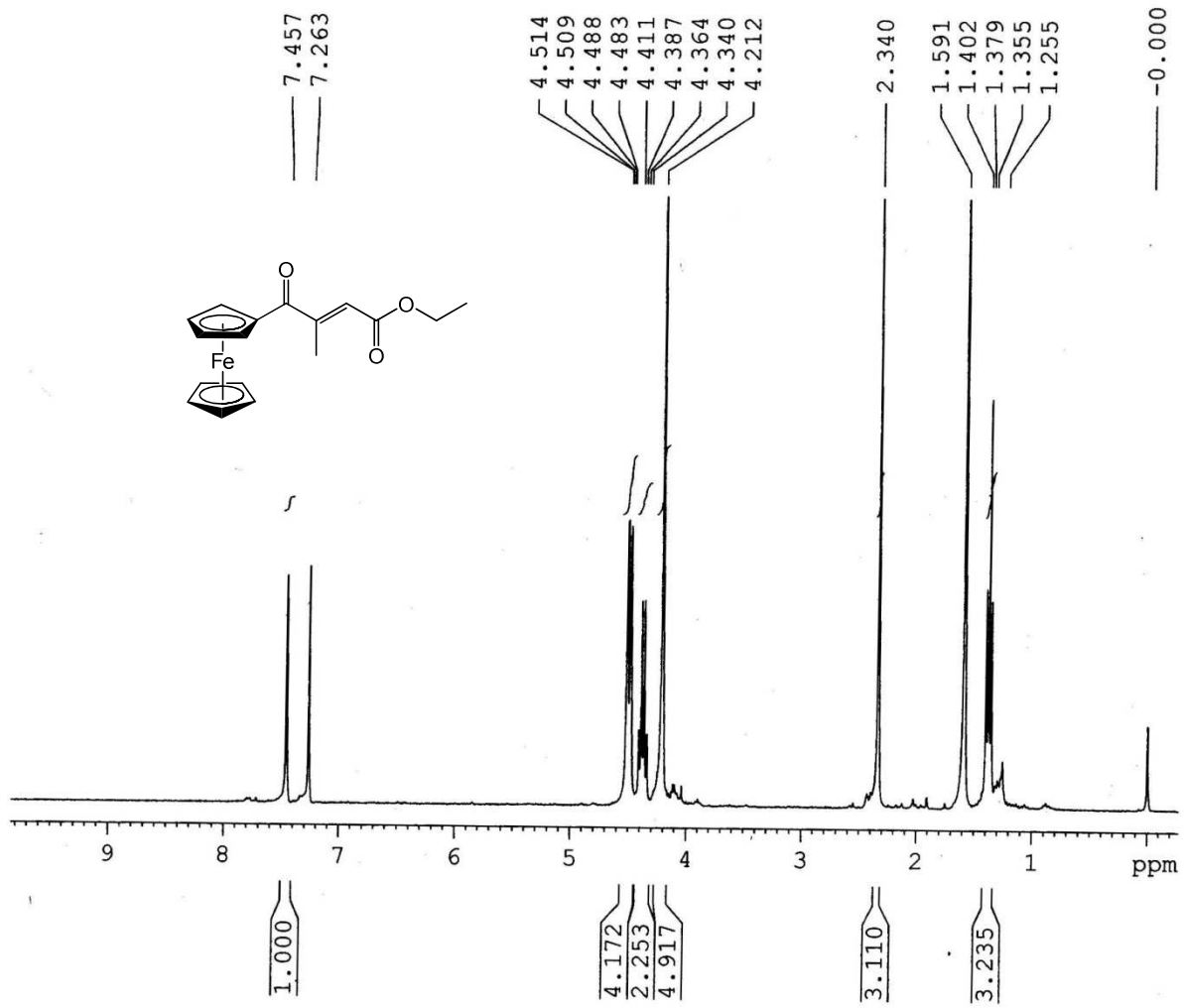
Monoisotopic Mass, Odd and Even Electron Ions
58 formula(e) evaluated with 1 results within limits (all results (up to 1000) for each mass)

GSK-DGP-53
GSK-DGP-53 25 (0.252) AM (Cen,2, 80.00, Ht,5000.0,0.00,1.00); Sm (Mn, 2x3.00) TOF MS ES+ 38.1

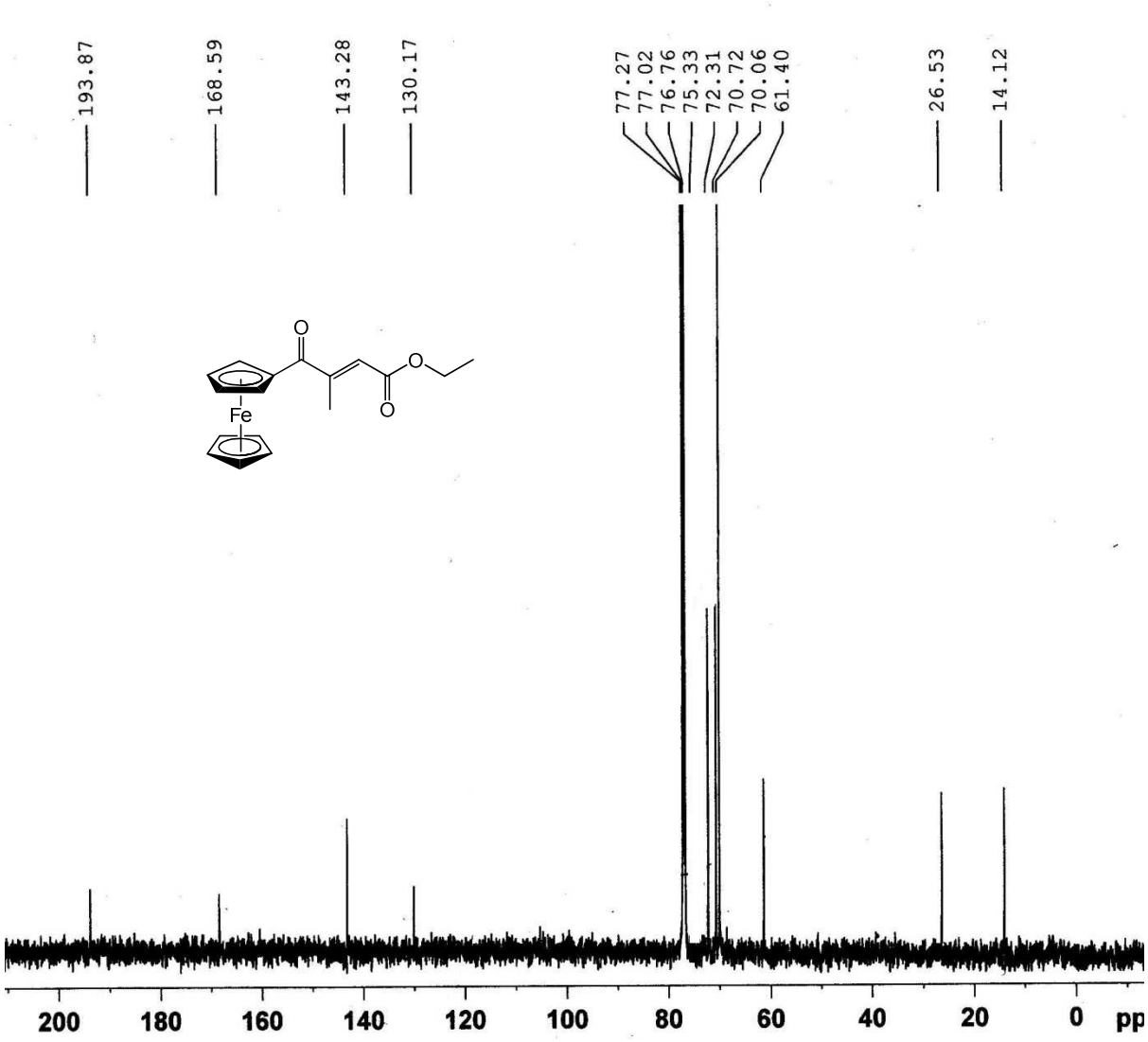


Minimum:				-1.5		
Maximum:		200.0	5.0	50.0		
Mass	Calc. Mass	mDa	PPM	DBE	Score	Formula
460.0642	460.0646	-0.3	-0.7	11.5	1	C22 H23 N O3 S Fe Na

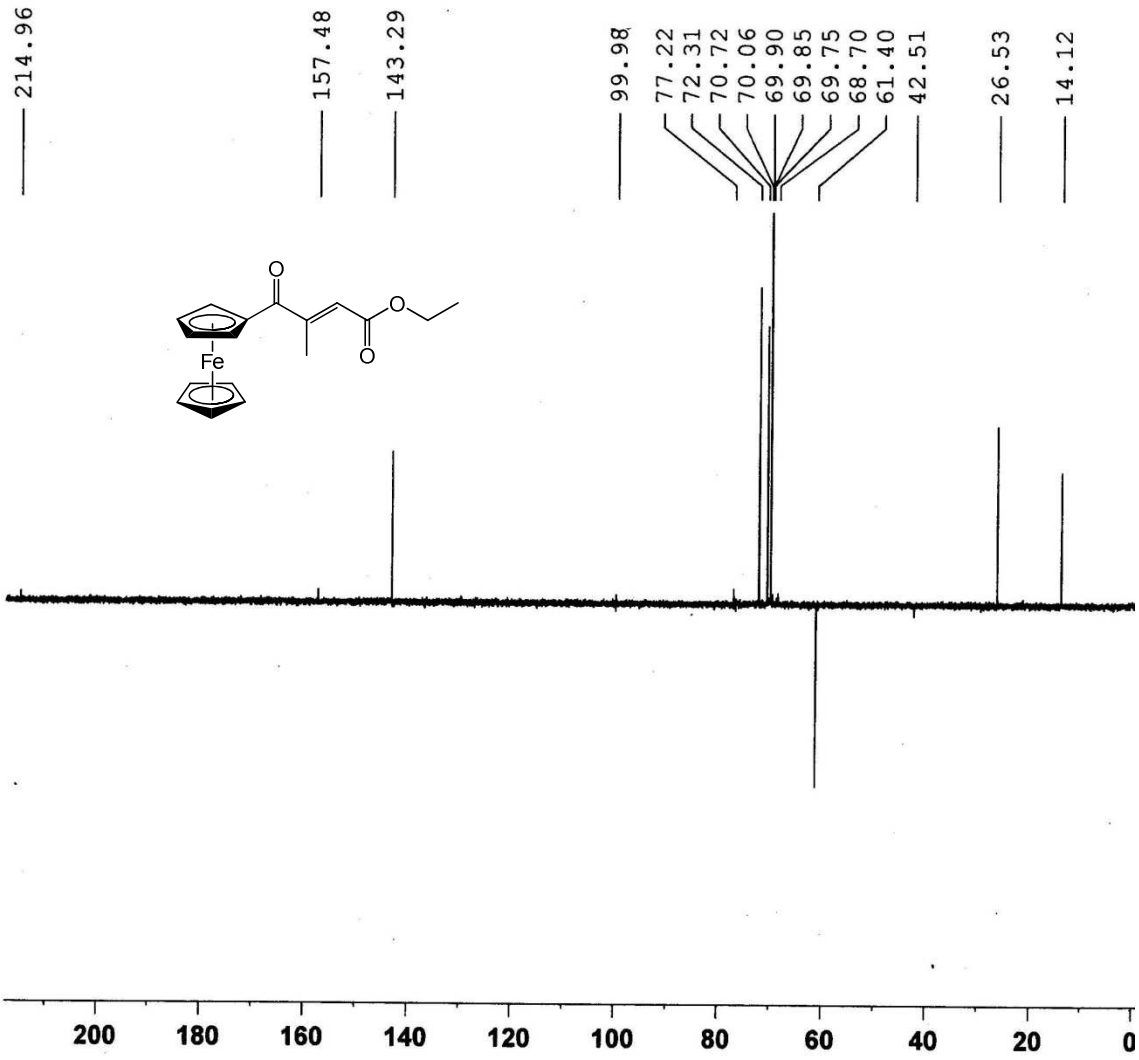
^{1}H NMR of Compound 16



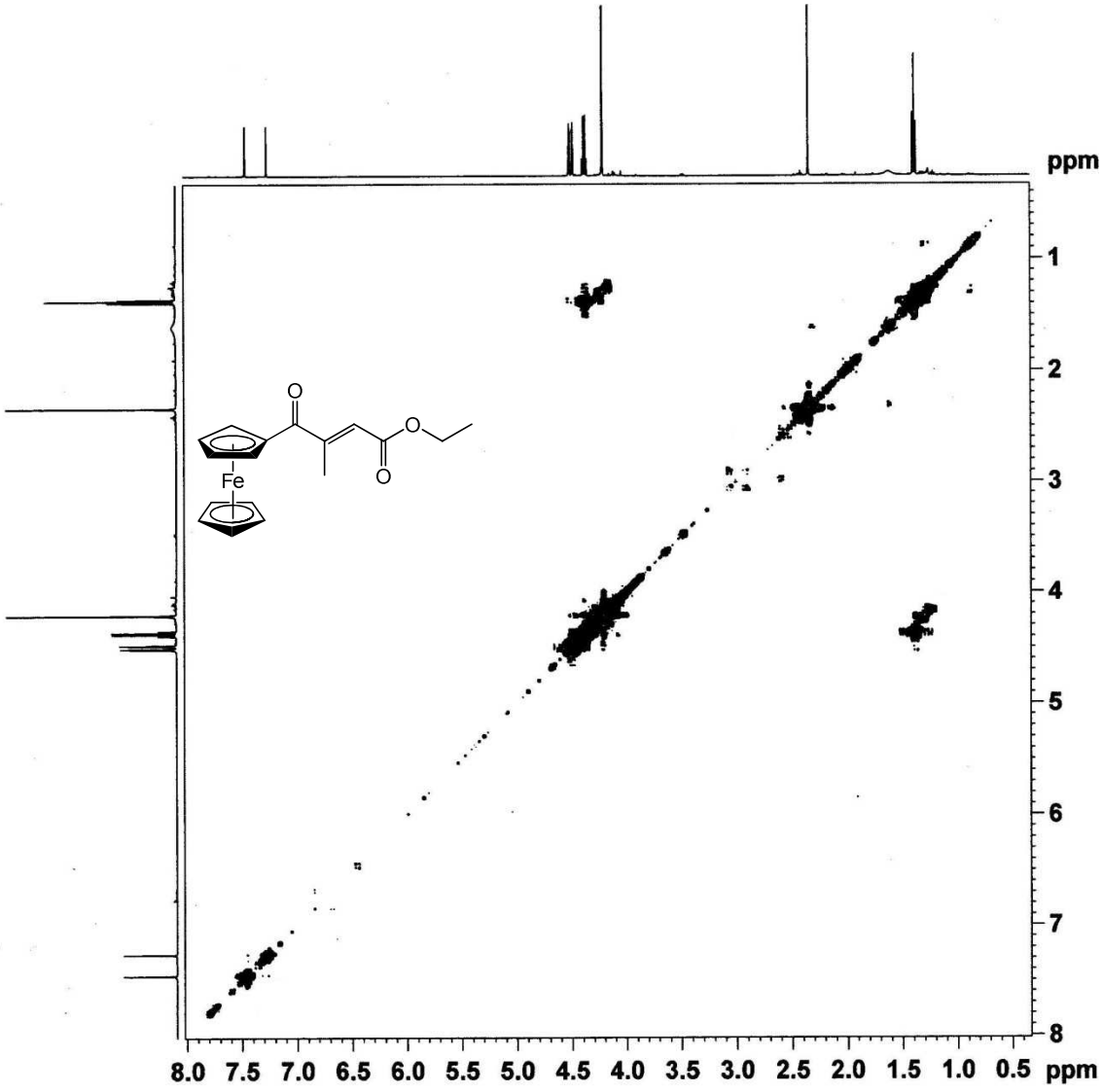
^{13}C NMR of Compound 16



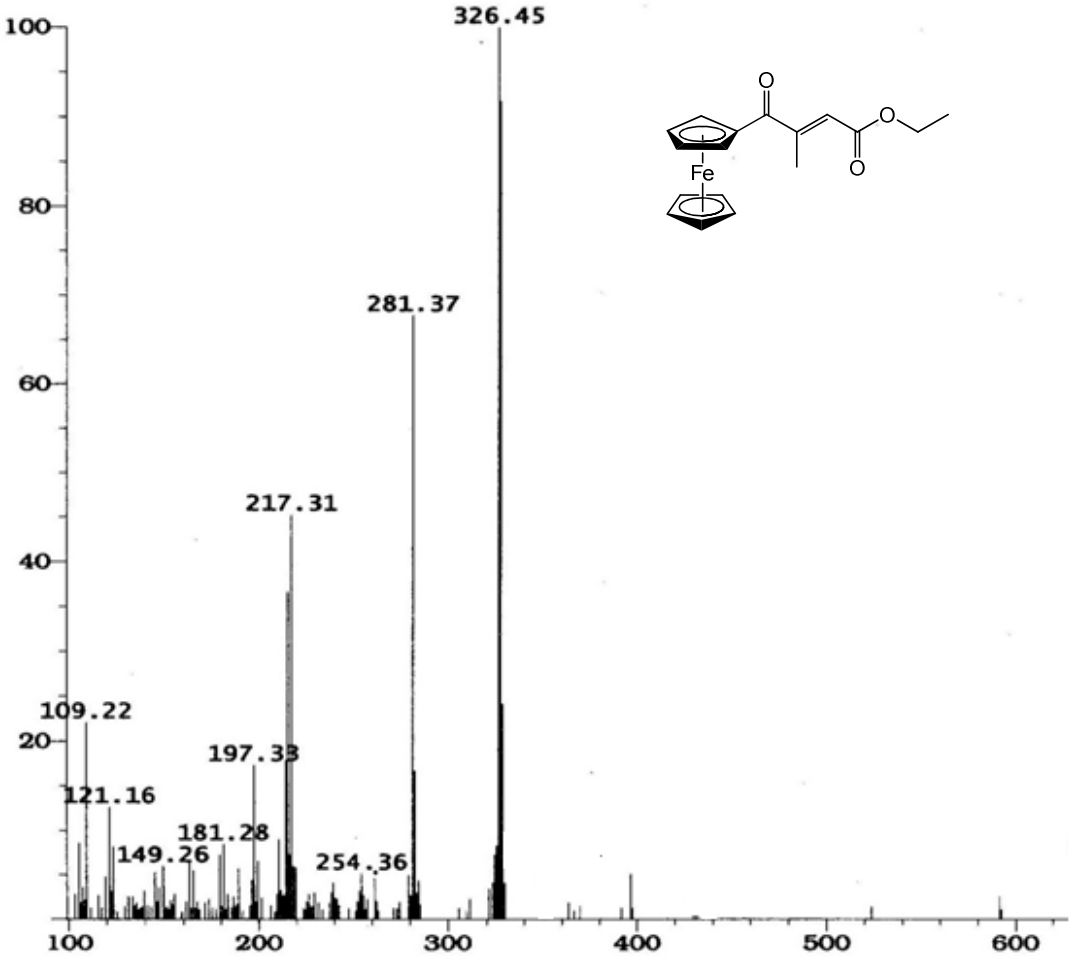
DEPT- 135 of Compound 16



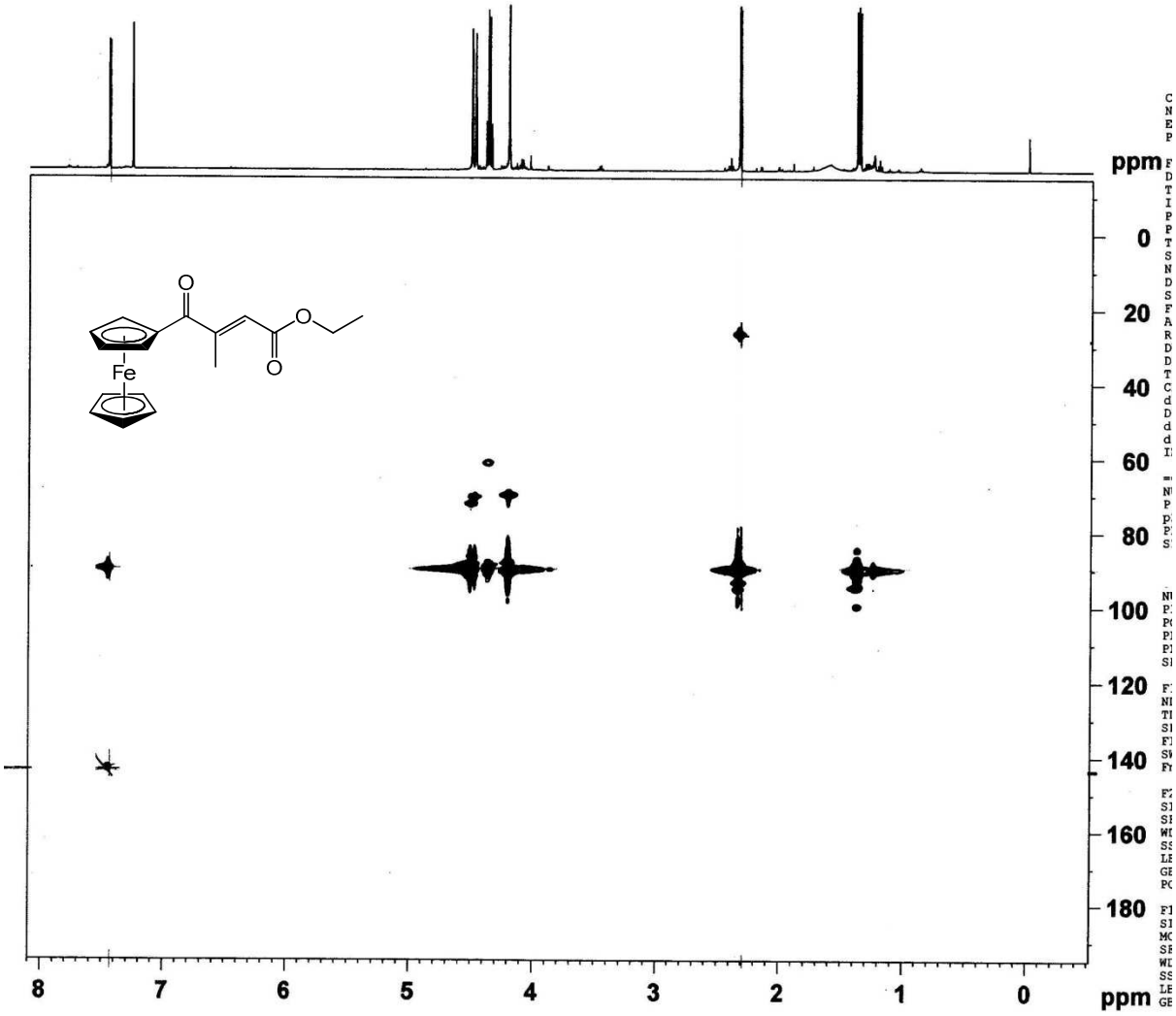
^{1}H-^{1}H COSY of Compound 16



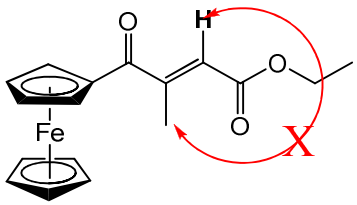
FAB mass of compound 16



HMQC compound 16



NOE Correlations for compound 16



(8) CIF file fo the crystal

Table 1. Crystal data and structure refinement for sham.

Identification code	shelxl
Empirical formula	C33 H41 Fe N O8 S
Formula weight	667.58
Temperature	293(2) K
Wavelength	1.54180 A
Crystal system, space group	Monoclinic, P21/c
Unit cell dimensions	a = 13.268(2) A alpha = 90 deg.
	b = 11.3892(10) A beta = 99.826(9) deg.
	c = 22.2817(16) A gamma = 90 deg.
Volume	3317.7(6) A^3
Z, Calculated density	4, 1.337 Mg/m^3
Absorption coefficient	4.650 mm^-1
F(000)	1408
Crystal size	0.20 x 0.10 x 0.10 mm
Theta range for data collection	3.38 to 64.93 deg.
Limiting indices	0<=h<=15, 0<=k<=13, -26<=l<=25
Reflections collected / unique	5906 / 5641 [R(int) = 0.0286]
Completeness to theta = 64.93	100.0 %
Absorption correction	Psi-scan
Max. and min. transmission	0.7423 and 0.5581
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5641 / 5 / 409
Goodness-of-fit on F^2	1.038
Final R indices [I>2sigma(I)]	R1 = 0.0529, wR2 = 0.1127
R indices (all data)	R1 = 0.1002, wR2 = 0.1314

Extinction coefficient **0.00361(19)**

Largest diff. peak and hole **0.399 and -0.258 e.A^-3**