

[Rh₂(phesp)₂]: a Bulkier [Rh₂(esp)₂] Analog to Tune the Site-Selectivity in Carbene C–H Insertion Reactions

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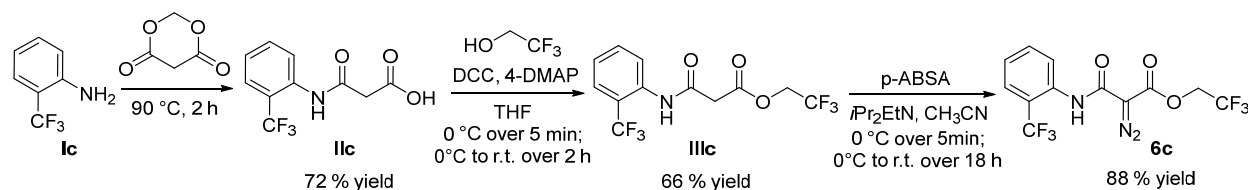
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Synthesis of 2,2,2-Trifluoroethyl 2-diazo-3-oxo-3-[[2-(trifluoromethyl)phenyl]amino]propanoate 6c



Synthesis of 3-oxo-3-((2-trifluoromethyl)phenylamino)propanoic acid (IIc)

The procedure has been adapted from the literature.^[1] A mixture of 2-trifluoromethylaniline **1c** (5.0g, 33.1 mmol, 1.0 equiv.) and Meldrum's acid (8.95g, 62 mmol, 1.9 equiv.) was heated in a round bottom flask and stirred for 2h at 90 °C. After cooling, the residue was purified by recrystallization from chloroform (25 mL) to give **IIc** as a white solid (5.5 g, 72% yield).

HMRS (DCI-CH₄) m/z [M+H]⁺ calcd for C₁₀H₉NO₃F₃ 248.0546, found: 248.0536; m/z [M]⁺ calcd for C₁₀H₈NO₃F₃ 247.0456, found: 247.0467.

¹H NMR (300 MHz, DMSO-*d*₆) δ 12.66 (s, 1H), 9.84 (s, 1H), 7.77 – 7.57 (m, 3H), 7.44 (t, *J* = 7.6 Hz, 1H), 3.43 (s, 2H). ¹⁹F NMR (282 MHz, DMSO-*d*₆) δ -59.37. ¹³C NMR (75 MHz, DMSO-*d*₆) δ 168.44, 165.55, 135.13 (q, *J* = 2.0 Hz), 133.06, 129.04, 126.46, 126.27 (q, *J* = 5.2 Hz), 123.76 (q, *J* = 30.9, 29.4 Hz), 123.57 (q, *J* = 272.2 Hz), 41.98.

Synthesis of 2,2,2-trifluoroethyl-3-oxo-3-((2-trifluoromethyl)phenylamino)propanoate (IIIc)

The procedure has been adapted from the literature.^[2] To a solution of acid **IIc** (5.5g, 22.3 mmol, 1 equiv.), trifluoroethanol (2.4 mL, 33.4 mmol, 1.5 equiv.) and 4-DMAP (4-dimethylaminopyridine) (408 mg, 3.34 mmol, 0.15 equiv.) in anhydrous THF (70 mL) was added DCC (N,N'-Dicyclohexylcarbodiimide) (5.5 g, 26.8 mmol, 1.2 equiv.) over 5 min at 0 °C. The mixture was allowed to warm to room temperature, stirred for another 2h then concentrated *in vacuo*. Diethyl ether was added (100 mL) and the mixture was filtered. The yellow filtrate was washed with 0.5 M aq. HCl (2x80 mL), aq. sat. NaHCO₃ (2x80 mL), brine (80 mL), dried (MgSO₄) and the solvent was evaporated *in vacuo*. The organic residue was redissolved in dichloromethane (2 mL) and purified by CombiFlash® (120g silica column, eluent: dichloromethane) to give product **IIIc** as a white crystalline solid (4.9 g, 66% yield).

HMRS (DCI-CH₄) m/z [M+H]⁺ calcd for C₁₂H₁₀NO₃F₆ 330.0565, found: 330.0580; m/z [M]⁺ calcd for C₁₂H₉NO₃F₆ 329.0487, found: 329.0499.

¹H NMR (400 MHz, CDCl₃) δ 9.13 (s, 1H), 8.16 (d, *J* = 8.3 Hz, 1H), 7.67 – 7.60 (m, 1H), 7.57 (t, *J* = 7.9 Hz, 1H), 7.27 (t, *J* = 7.7 Hz, 1H), 4.60 (q, *J* = 8.2 Hz, 2H), 3.66 (s, 2H). ¹⁹F NMR (376 MHz, Chloroform-*d*) δ -61.09, -73.67 (t, *J* = 8.2 Hz). ¹³C NMR (101 MHz, CDCl₃) δ 167.95, 162.40, 134.57, 132.95, 126.28 (q, *J* = 5.3 Hz), 125.28, 125.10, 123.92 (q, *J* = 272.6 Hz), 122.62 (q, *J* = 277.3 Hz), 121.24 (q, *J* = 29.8 Hz), 61.29 (q, *J* = 37.2 Hz), 41.28.

Synthesis of 2,2,2-trifluoroethyl-2-diazo-3-oxo-3-((2-trifluoromethyl)phenylamino)propanoate (6c)

The procedure has been adapted from the literature.^[2] To a Schlenk tube charged with a solution of ester **IIIc** (4.8 g, 14.6 mmol, 1 equiv.) in anhydrous acetonitrile was added *p*-ABSA (4-acetamidobenzenesulfonyl azide) (3.67 g, 15.3 mmol, 1.1 equiv.) and DIPEA (N,N-Diisopropylethylamine) (3.81 mL, 21.9 mmol, 1.5 equiv.) over 5 minutes at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 18h. It was then concentrated *in vacuo*, the

residue was dissolved in dichloromethane (200 mL) and filtered. The filtrate was stirred with 1M aq. HCl (100 mL) for 1h. The phases were separated, the organic layer was washed with aq. sat. NaHCO₃ (2x100 mL), brine (100 mL), dried (MgSO₄) and concentrated *in vacuo*. The resulting yellow residue was purified by CombiFlash® (12g silica column, hexane/DCM;40/60) to give **6c** as a white crystalline solid (3.85 g, 75% yield).

HMRS (DCI-CH₄) m/z [M+H]⁺ calcd for C₁₂H₈N₃O₃F₆ 356.0470, found: 356.0481; m/z [M]⁺ calcd for C₁₂H₇N₃O₃F₆ 355.0392, found: 355.0403.

¹H NMR (400 MHz, CDCl₃) δ 9.72 (s, 1H, NH), 8.23 (d, *J*_{HH} = 8.3 Hz, 1H, CH arom.), 7.63 (d, *J*_{HH} = 7.8 Hz, 1H, CH arom.), 7.56 (t, *J*_{HH} = 7.9 Hz, 1H, CH arom.), 7.25 (t, *J*_{HH} = 7.7 Hz, 1H, CH arom.), 4.68 (q, *J*_{HF} = 8.2 Hz, 2H, CH₂CF₃). ¹⁹F NMR (377 MHz, CDCl₃) δ -61.35 (s, CF₃ arom.), -73.92 (t, *J*_{FF} = 7.8 Hz, CF₃CH₂). ¹³C NMR (101 MHz, CDCl₃) δ 162.47 (C(=O) ester), 158.29 (C(=O) amide), 134.90 (q, *J* = 1.7 Hz, C_{quat} arom.), 132.92 (d, *J* = 1.3 Hz, CH arom.), 126.28 (q, *J* = 5.4 Hz, CH arom.), 124.83 (CH arom.), 124.47 (CH arom.), 123.91 (q, *J* = 272.9 Hz, CF₃ arom.), 122.57 (q, *J* = 277.4 Hz, CF₃CH₂), 120.88 (q, *J* = 30.0 Hz, C_{quat} arom.), 61.03 (q, *J* = 37.5 Hz, CH₂CF₃).

NMR characterisation of products 12c-14c (¹H, ¹³C) in CDCl₃

¹H NMR (400 MHz, CDCl₃) C1-H functionalization product **12c**: δ 8.66 (s, 1H, NH), 8.15 (d, *J*_{HH} = 8.3 Hz, 1H, CH arom.), 7.66 (app. d, *J*_{HH} = 7.9 Hz, 1H, CH arom.), 7.62 – 7.56 (m, 1H, CH arom.), 7.32 – 7.26 (m, 1H, CH arom.), 4.76 – 4.47 (m, 2H, CH₂CF₃), 3.54 (t, *J*_{HH} = 7.3 Hz, 1H, C(O)CHC(O)), 2.11 – 2.03 (m, 2H, C(O)CHCH₂CH₂-), 1.49 – 1.25 (m, 6H, (CH₂)₃CH₃), 0.95 – 0.88 (m, 3H, CH₃). C2-H functionalization product **13c**: δ 8.88, 8.81 (s, 2x1H, NH, dia1+dia2), 8.18-8.15 (m, 1H, CH arom.), 7.63 (app. d, *J*_{HH} = 7.9 Hz, 1H, CH arom.), 7.55 (t, *J*_{HH} = 7.9 Hz, 1H, CH arom.), 7.25 (t, *J*_{HH} = 7.7 Hz, 1H, CH arom.), 4.73 – 4.67 (m, 1H, CH₂CF₃), 4.51 – 4.45 (m, 1H, CH₂CF₃), 3.43 (d, *J*_{HH} = 8.2 Hz, 1H, C(O)CHC(O), dia 1), 3.39 (d, *J*_{HH} = 8.6 Hz, 1H, C(O)CHC(O), dia 2), 2.33-2.29 (m, 1H, CH₃CHCH₂-), 1.51 – 1.40 (m, 2H, CHCH₂CH₂CH₃), 1.34 – 1.24 (m, 2H, CHCH₂CH₂CH₃), 1.07 (d, *J*_{HH} = 6.8 Hz, 3H, dia2), 1.04 (d, *J*_{HH} = 6.7 Hz, 3H, dia1), 0.92 – 0.88 (m, 3H, -CH₂CH₃). C3-H functionalization product **14c**: δ 8.85 (s, 1H, NH); CH arom., CH₂CF₃: not assigned due to superimposition; 3.57-3.54 (1H, C(O)CHC(O)), 2.16-2.09 (m, 1H, -CH₂CHCH₂-), 1.55 – 1.40 (m, 4H, -CH₂CHCH₂-), 0.95 – 0.91 (m, 6H, CH₃CH₂CH).

¹³C NMR (101 MHz, CDCl₃) C1-H functionalization product **12c**: δ 170.79 (C(=O) ester), 166.09 (C(=O) amide), 53.44 ((CO)CH(CO)), 31.46 (C(O)CHCH₂CH₂-) (other signals not assigned). C2-H functionalization product **13c**: 170.97, 170.85 (2xC(=O) ester, dia1+dia2), 165.68, 165.39 (2xC(=O) amide, dia1+dia2), 134.78 (C_{quat} arom.), 132.96 (C-H arom.), 126.25 (q, *J* = 5.3 Hz, C-H arom.), 125.01 (C-H arom.), 124.72 (d, *J* = 4.4 Hz, C-H arom.), (other C_{quat} arom. not assigned), 60.99 (q, *J* = 37.1, 3.0 Hz, 2xCH₂CF₃), 59.72, 59.43 (2x(CO)CH(CO), dia1+dia2), 36.86, 36.72 (2xCHCH₂, dia1+dia2), 36.60, 36.42 (2xCHCH₂, dia1+dia2), 19.91, 19.82 (2xCH₂CH₃, dia1+dia2), 16.91, 16.85 (2xCHCH₃, dia1+dia2), 13.99 (2xCH₂CH₃, dia1+dia2). C3-H functionalization product **14c**: δ 171.15 (C(=O) ester), 165.63 (C(=O) amide), 56.89 ((CO)CH(CO)), 44.18 (-CH₂CHCH₂-) (other signals not assigned).

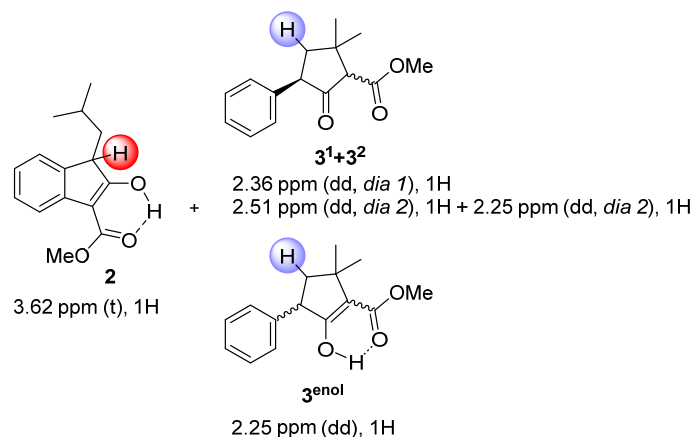
References:

- [1] W. Gao, W. Hou, M. Zheng, in *Huaxue Yanjiu*, Vol. 19, Huaxue Yanjiu Bianjibu, **2008**, pp. 37-41.
- [2] S. Yuan, E. J. McLaren, S. France, *ChemCatChem* **2022**, *14*, e202101977.

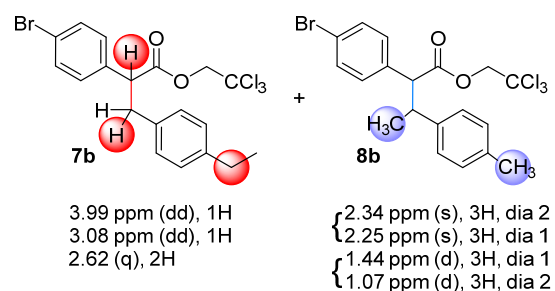
Procedure for Determining Product Ratios

To measure the product ratios, the mixtures obtained were analysed by ^1H NMR. The data was processed using MestReNova software. The ratios were measured by integration of the characteristic NMR peaks resulting from the indicated hydrogens below:

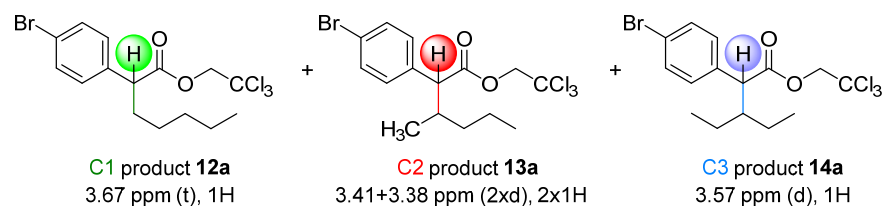
Intramolecular decomposition of diazo compound 1 to give products 2 and 3 (^1H NMR in CDCl_3 , 30s relaxation delay):



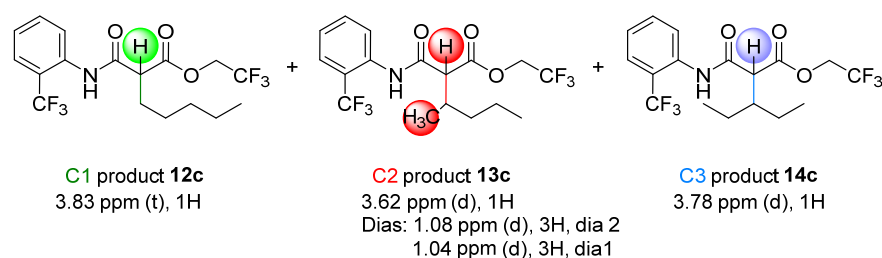
Intermolecular reaction of donor-acceptor diazo compound 5b with 4-ethyltoluene (^1H NMR in CDCl_3 , 30s relaxation delay):



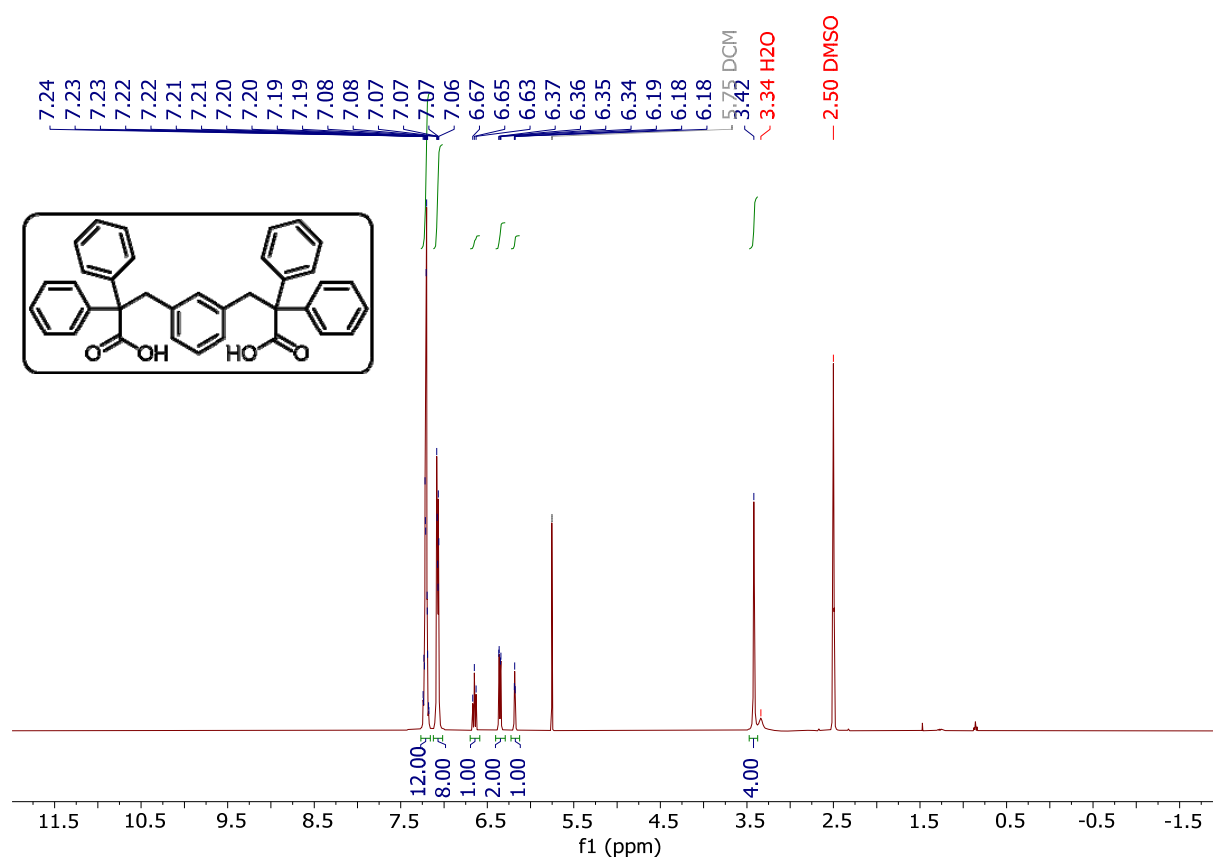
Intermolecular reaction of donor-acceptor diazo compound 5b with pentane (^1H NMR in CDCl_3 , 30s relaxation delay):



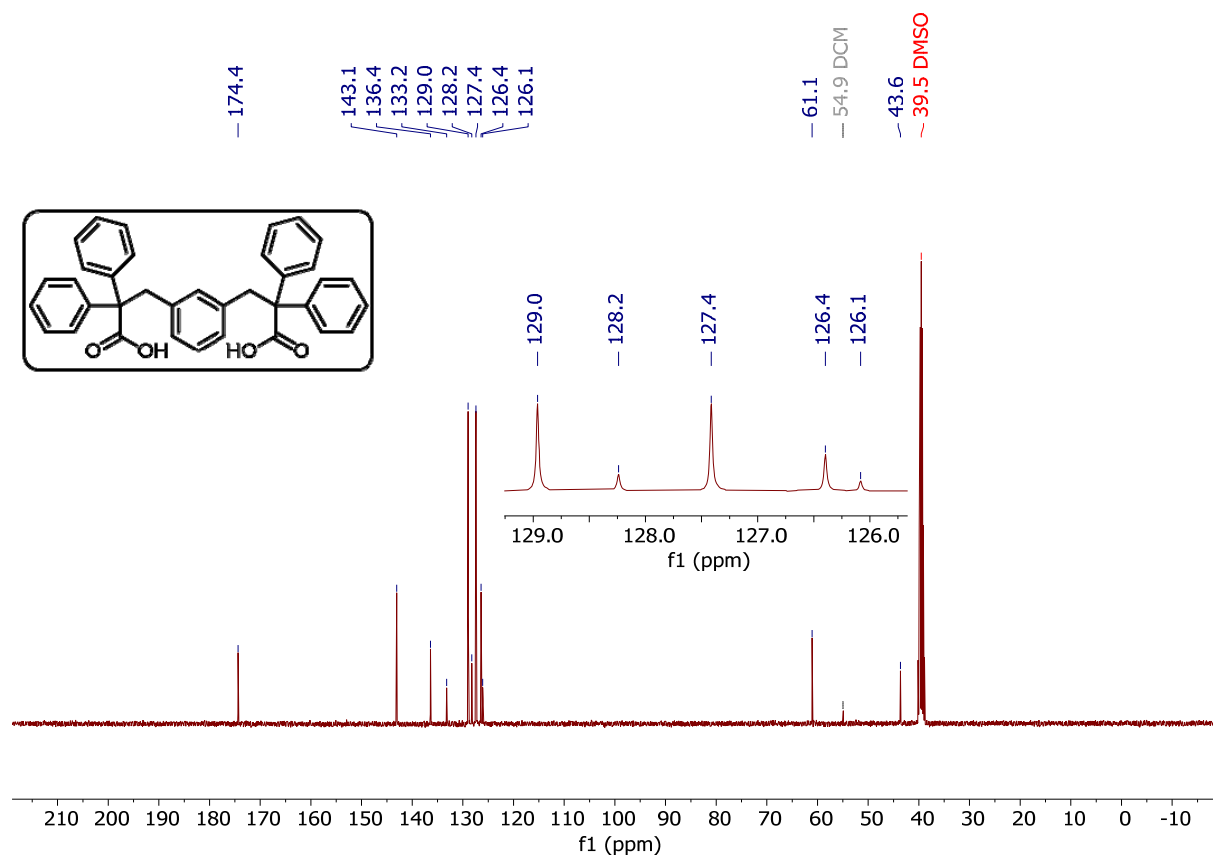
Intermolecular reaction of acceptor-acceptor diazo compound 6c with pentane (^1H NMR in $\text{acetone-}d_6$, 30s relaxation delay):



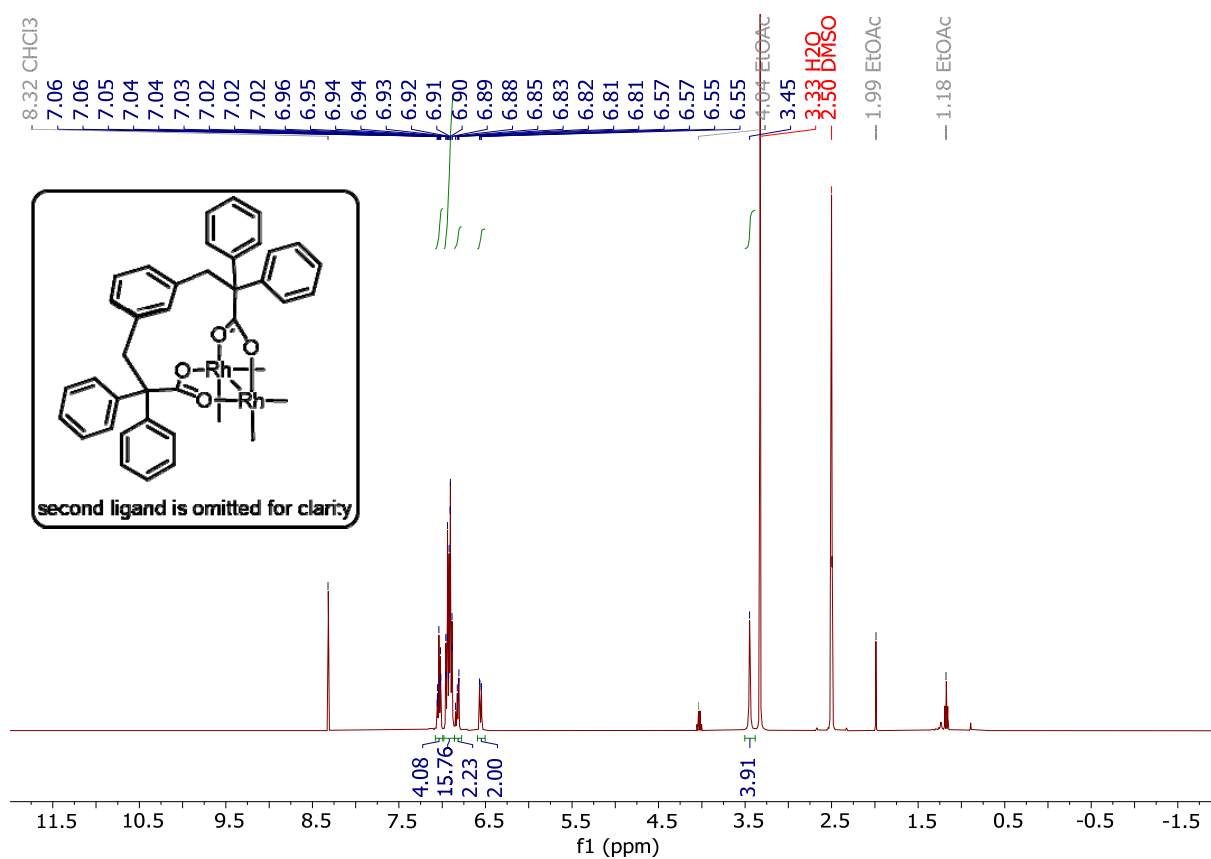
^1H NMR spectrum of H_2phesp ligand 15 (400 MHz, $\text{DMSO-}d_6$)



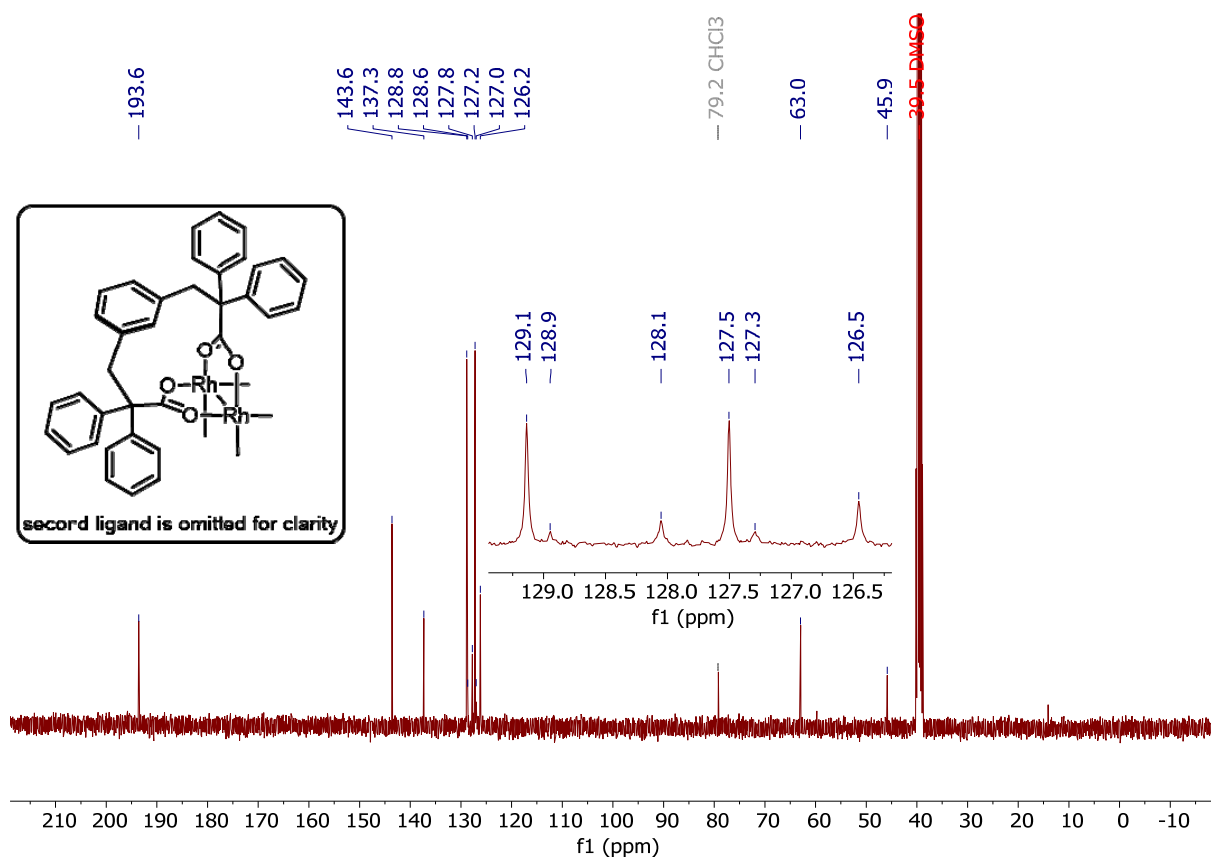
^{13}C NMR spectrum of H_2phesp ligand 15 (101 MHz, $\text{DMSO-}d_6$)



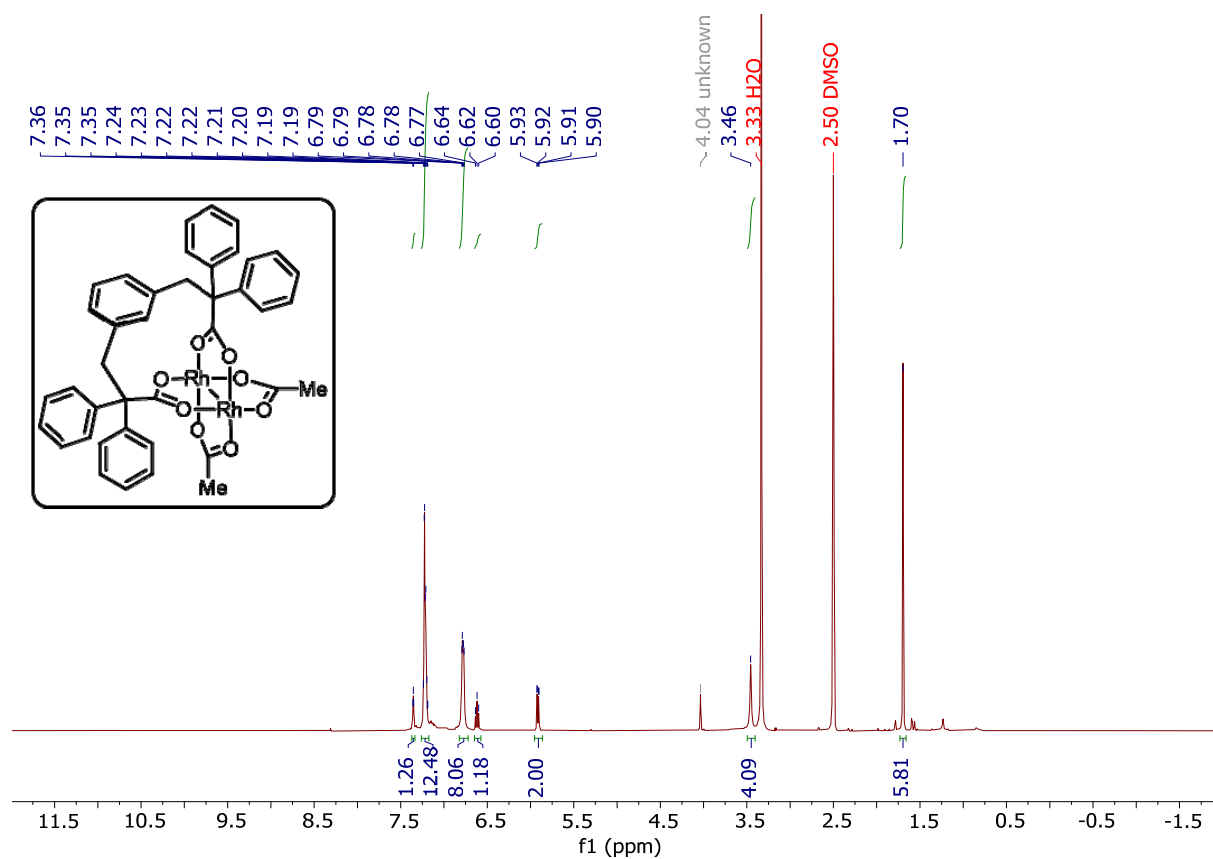
^1H NMR spectrum of $[\text{Rh}_2(\text{phesp})_2]$ complex 16 (400 MHz, $\text{DMSO-}d_6$)



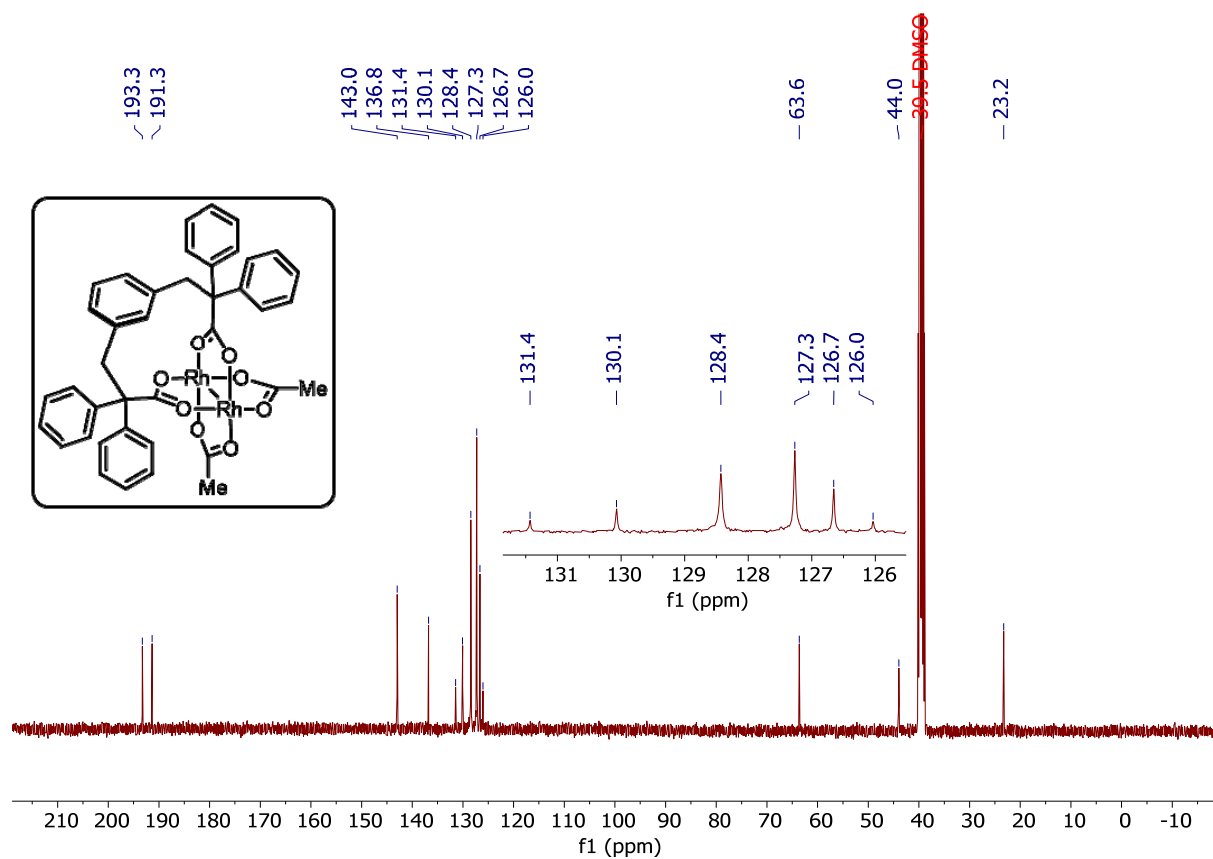
^{13}C NMR spectrum of $[\text{Rh}_2(\text{phesp})_2]$ complex 16 (101 MHz, $\text{DMSO-}d_6$)



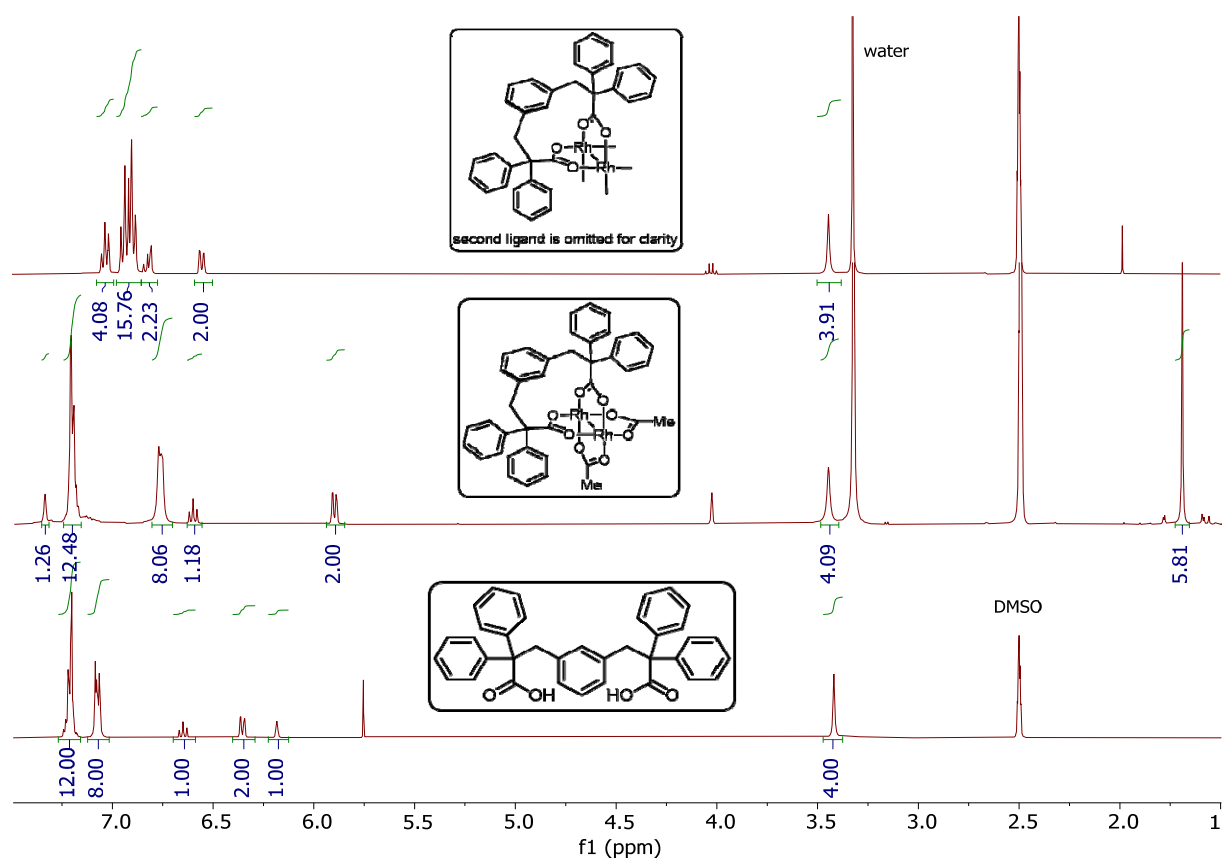
^1H NMR spectrum of $[\text{Rh}_2(\text{phesp})(\text{OAc})_2]$ complex 17 (400 MHz, $\text{DMSO-}d_6$)



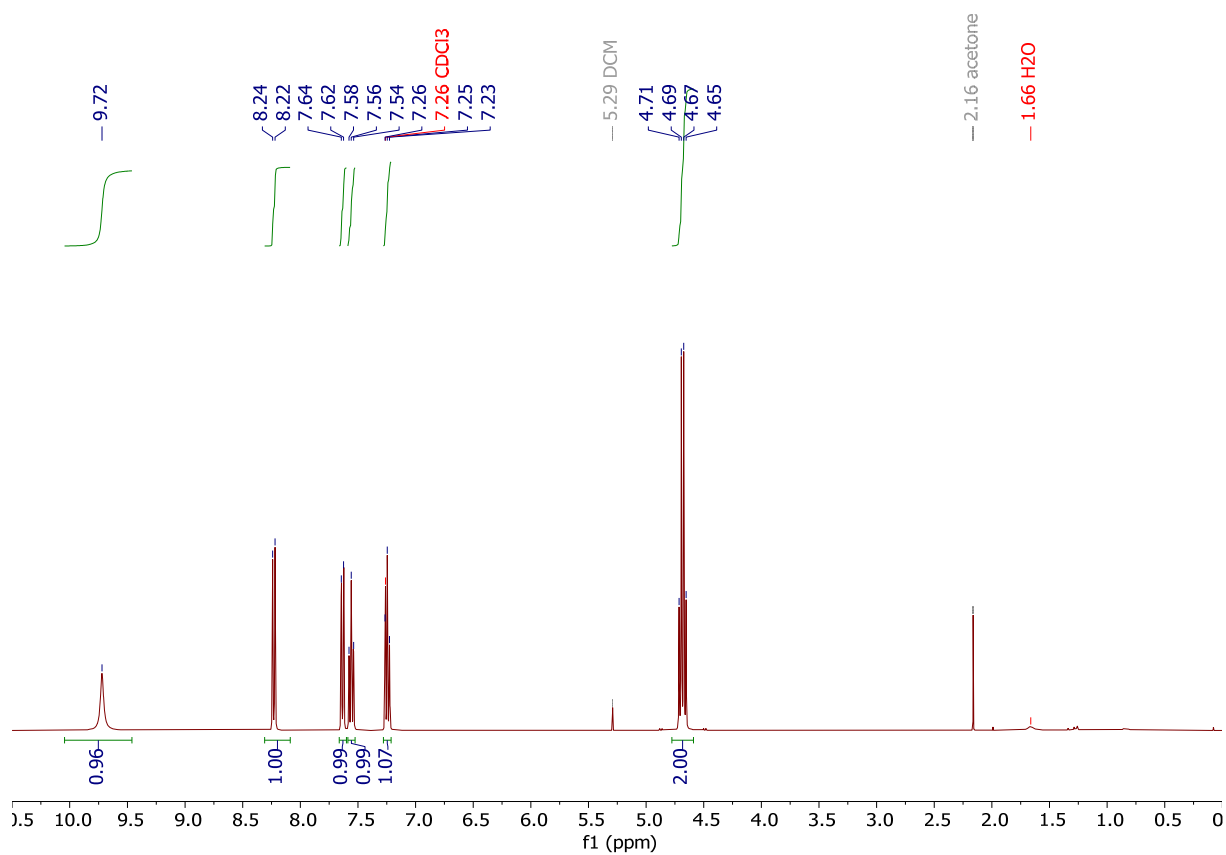
^{13}C NMR spectrum of $[\text{Rh}_2(\text{phesp})(\text{OAc})_2]$ complex 17 (101 MHz, $\text{DMSO-}d_6$)



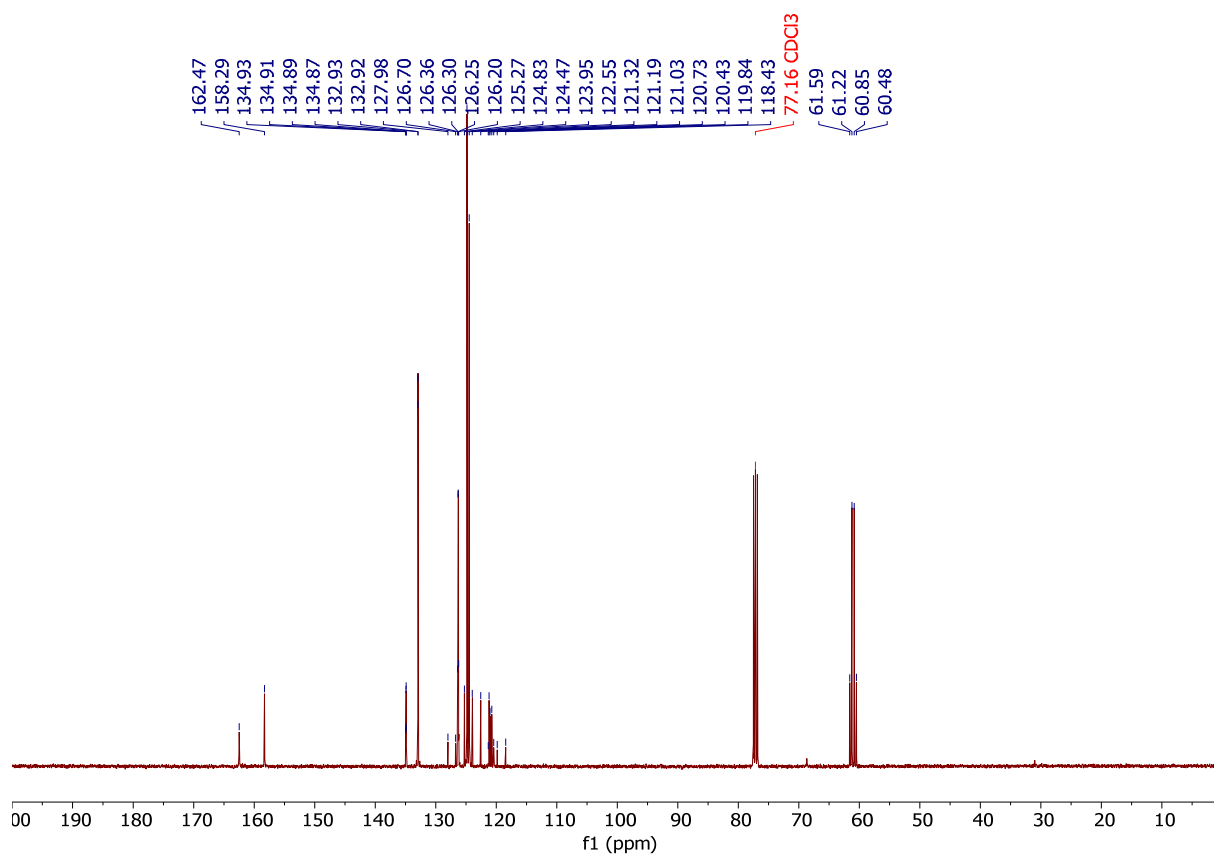
Comparison of ^1H NMR spectra of H_2phesp ligand **15** (bottom), $[\text{Rh}_2(\text{phesp})_2]$ complex **16** (top) and $[\text{Rh}_2(\text{phesp})(\text{OAc})_2]$ complex **17** (middle) (400 MHz, $\text{DMSO-}d_6$)



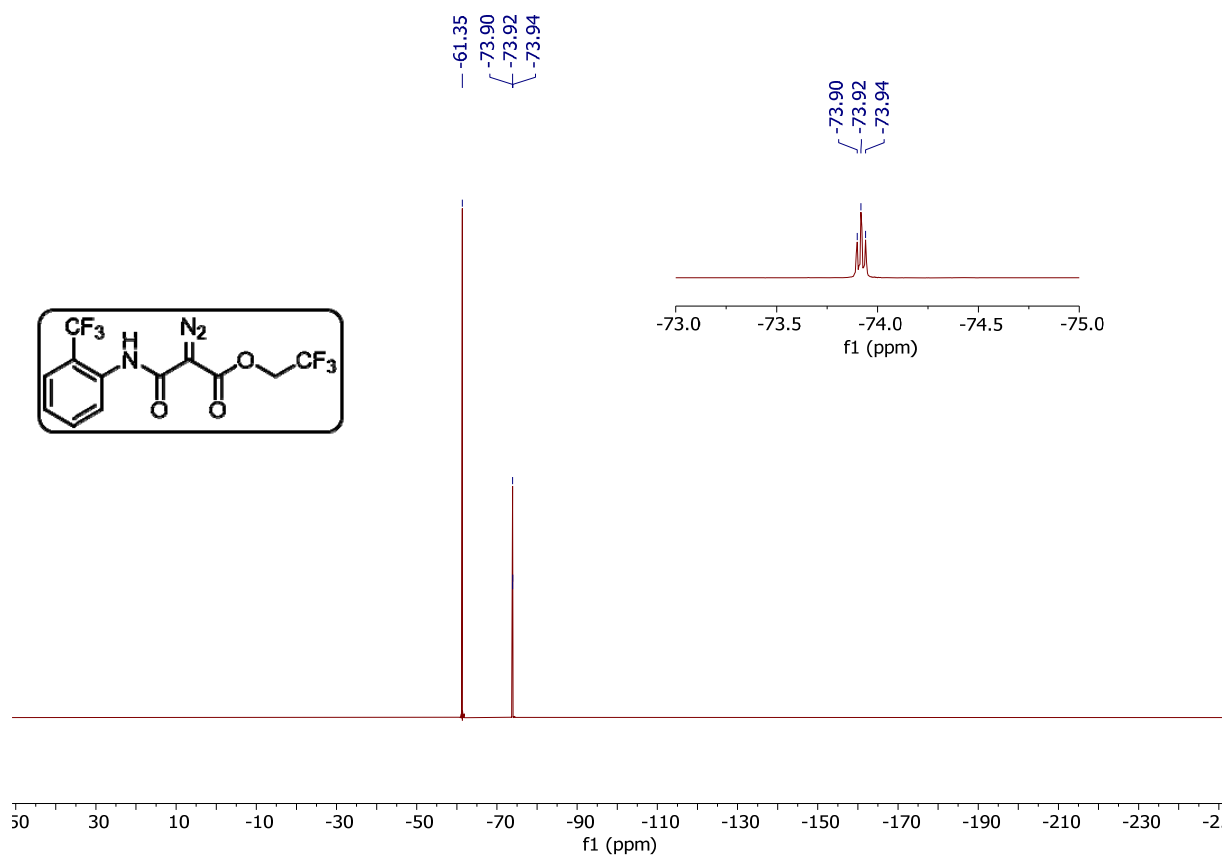
^1H NMR spectrum of diazo compound **6c** (400 MHz, CDCl_3)



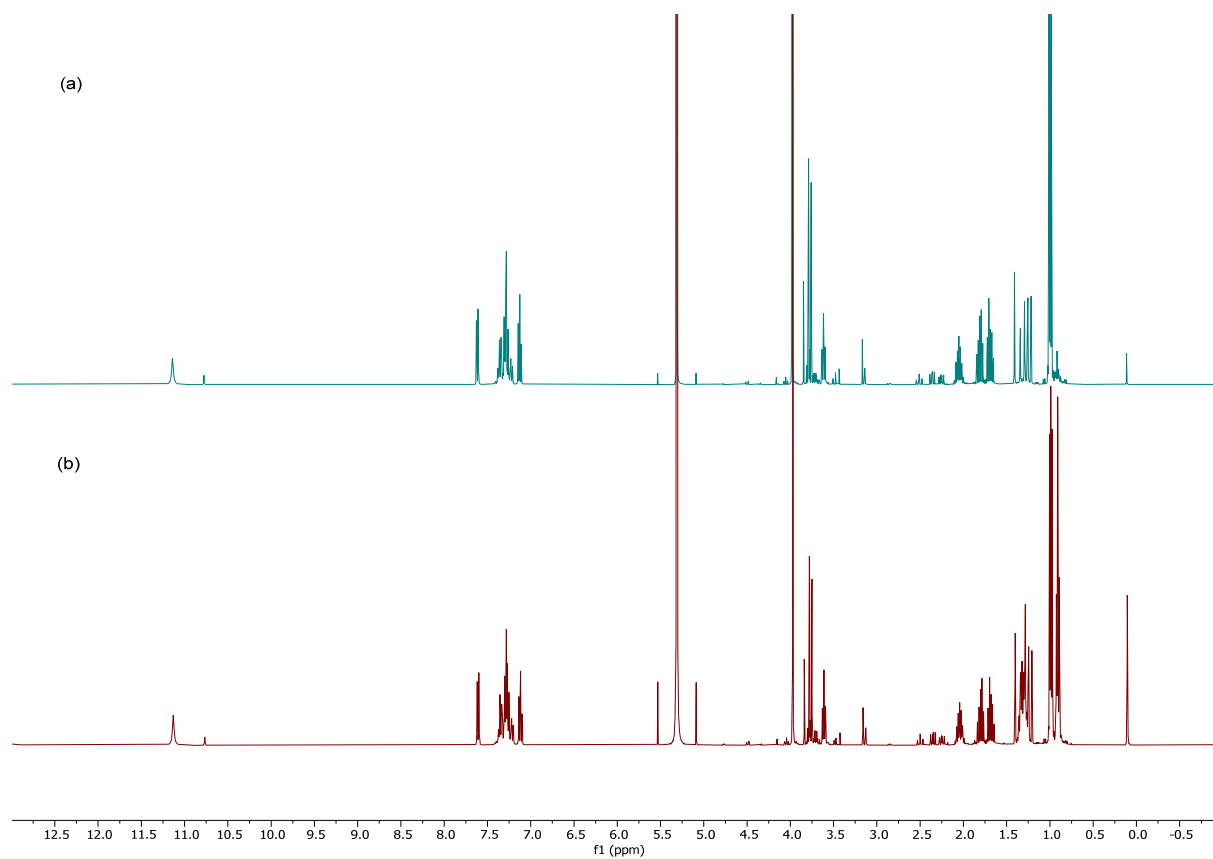
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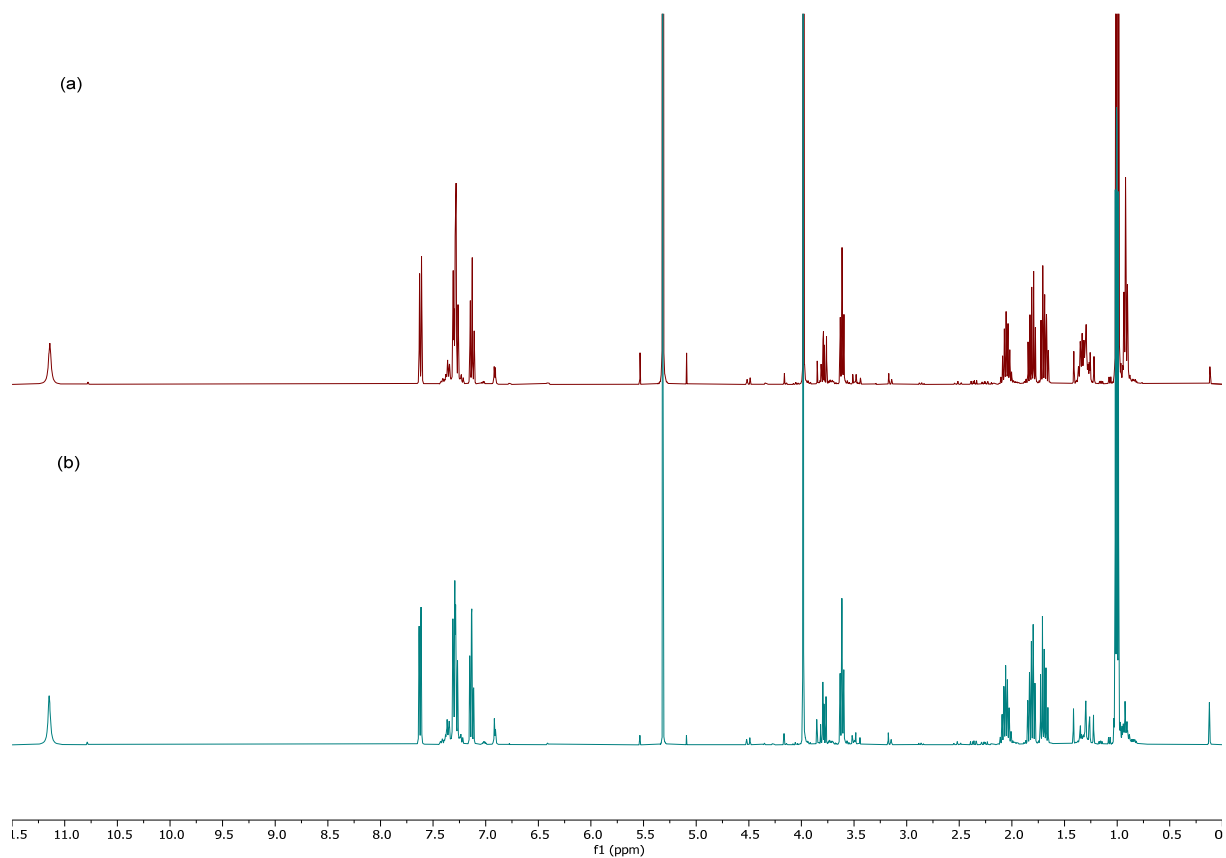
^{19}F NMR spectrum of diazo compound **6c** (376.5 MHz, CDCl_3)



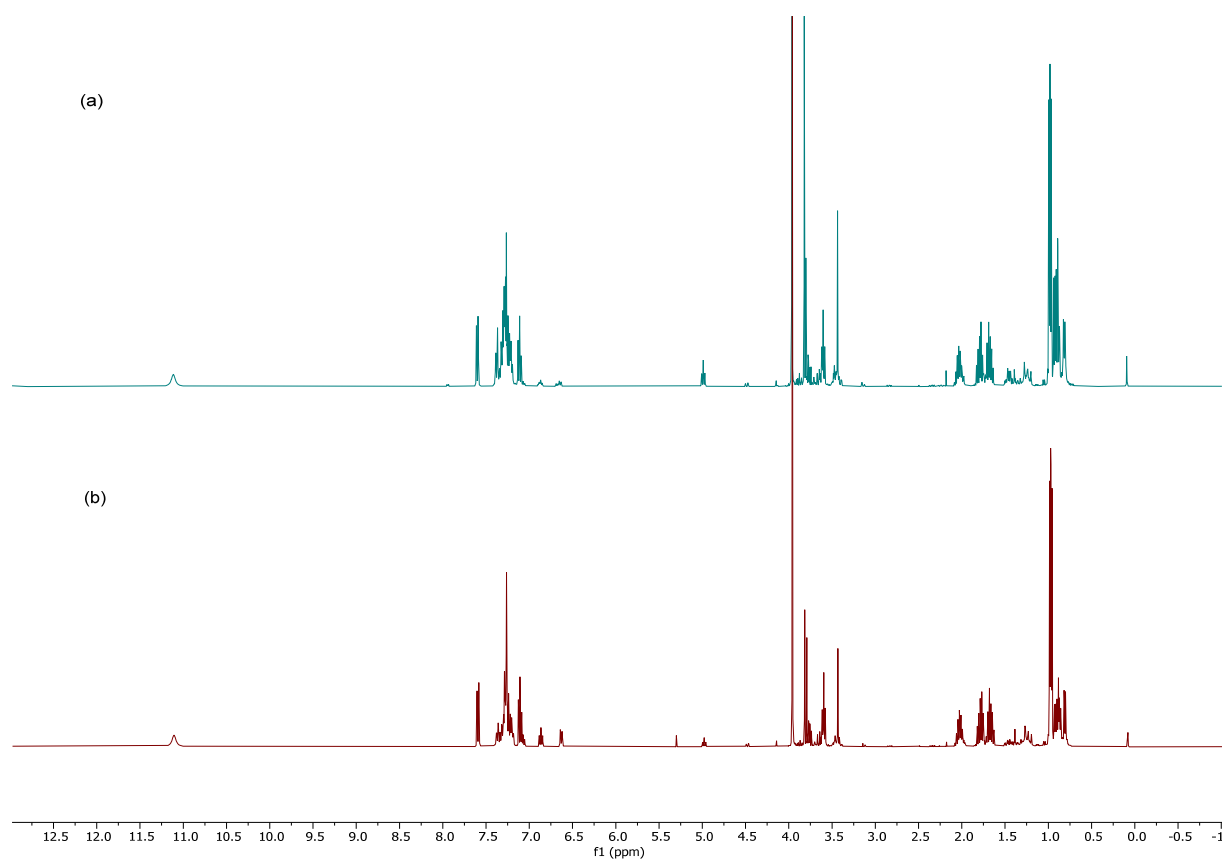
^1H NMR spectra of products 2+3 from the reaction of 1 with $[\text{Rh}_2(\text{esp})_2]$ (400 MHz, CDCl_3)



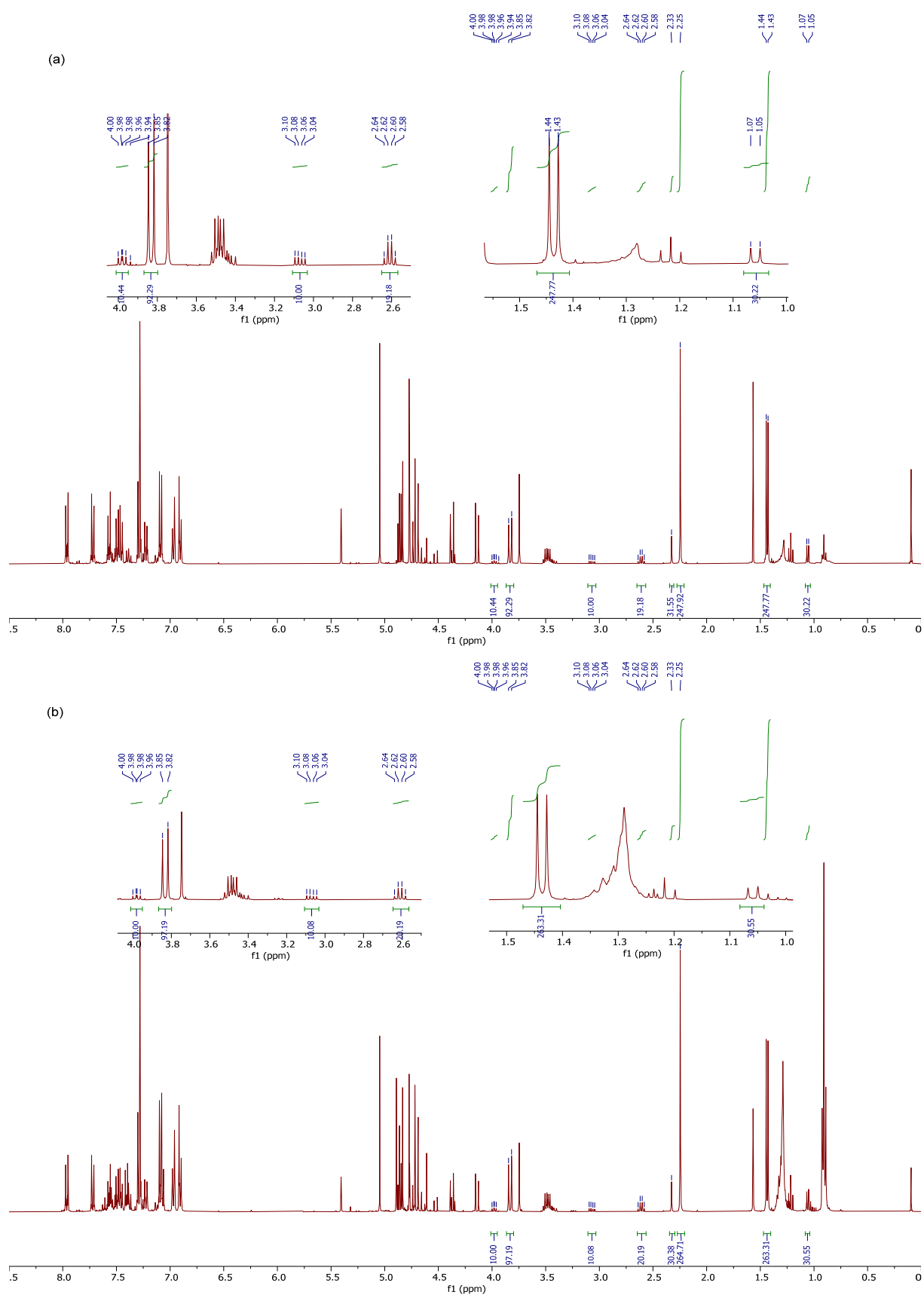
^1H NMR spectra of products 2+3 from the reaction of 1 with $[\text{Rh}_2(\text{phesp})_2]$ (400 MHz, CDCl_3)



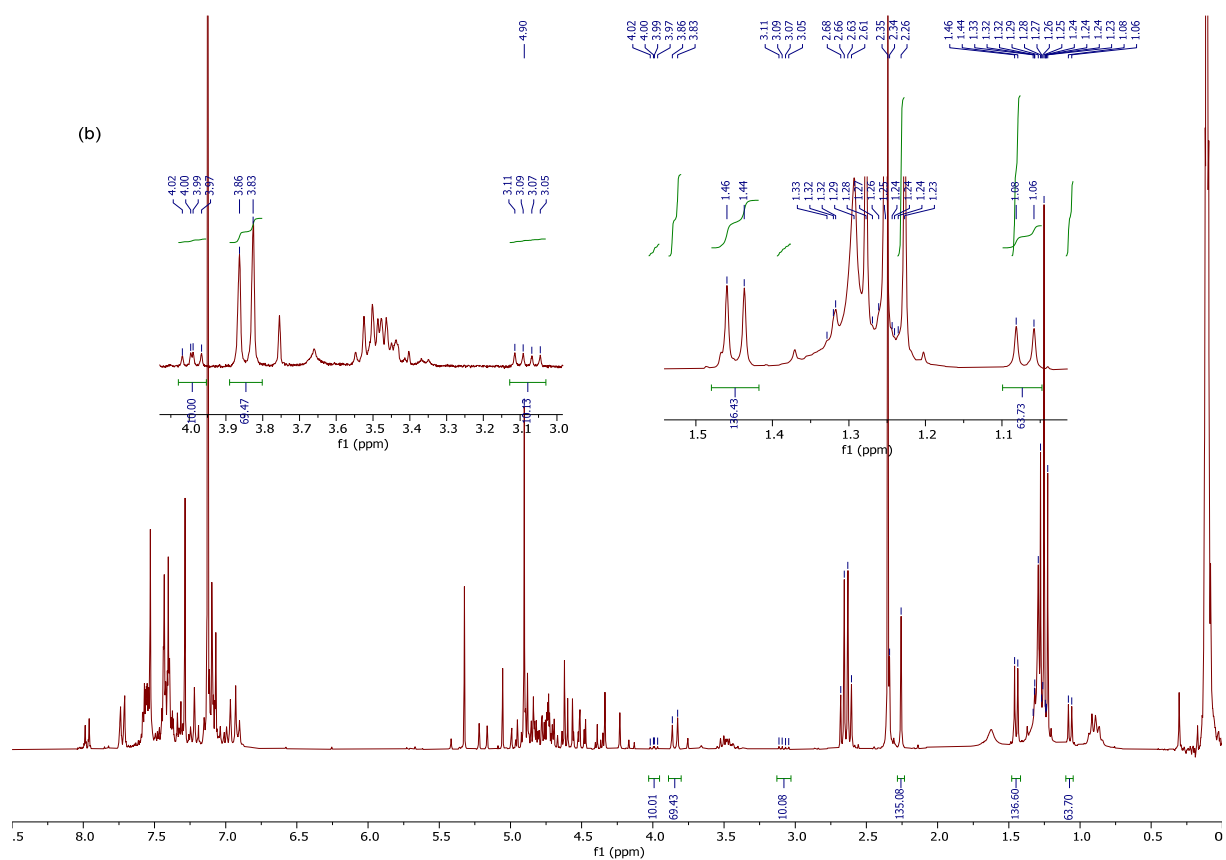
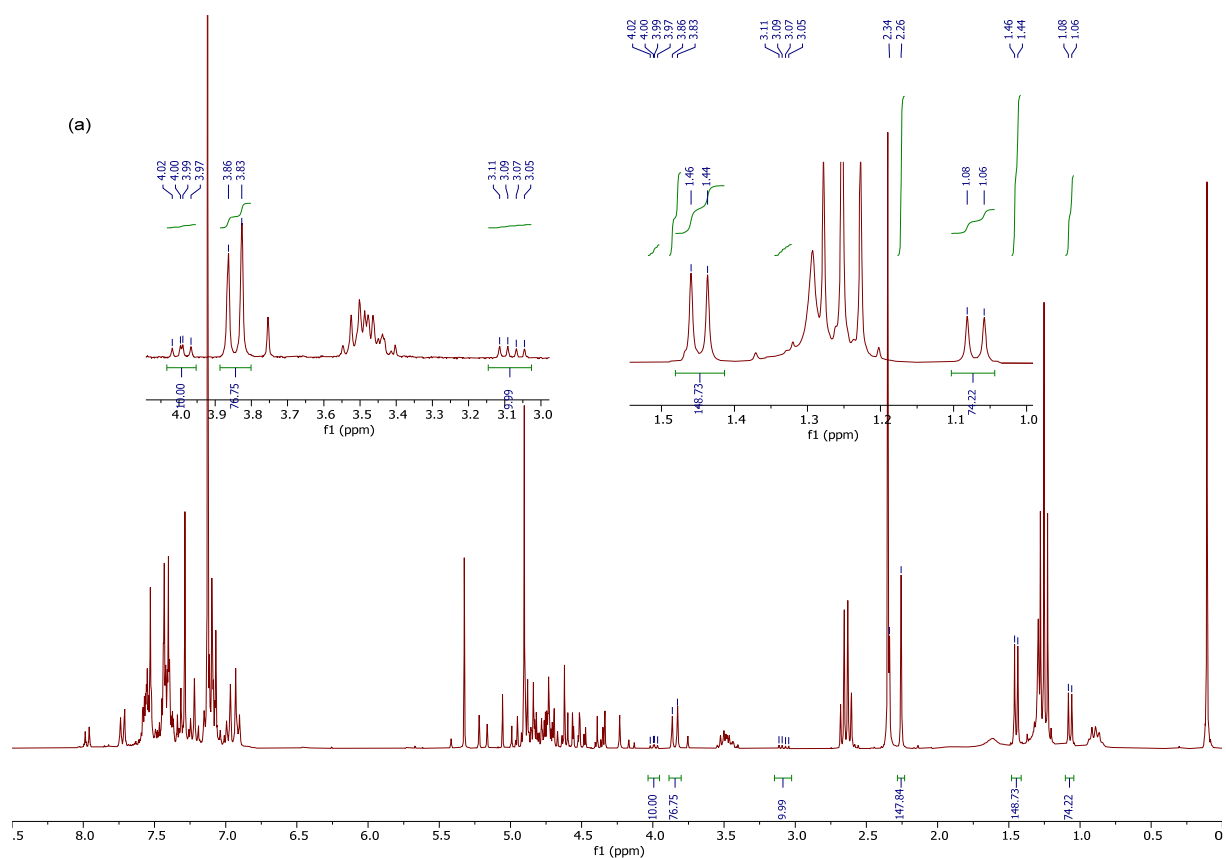
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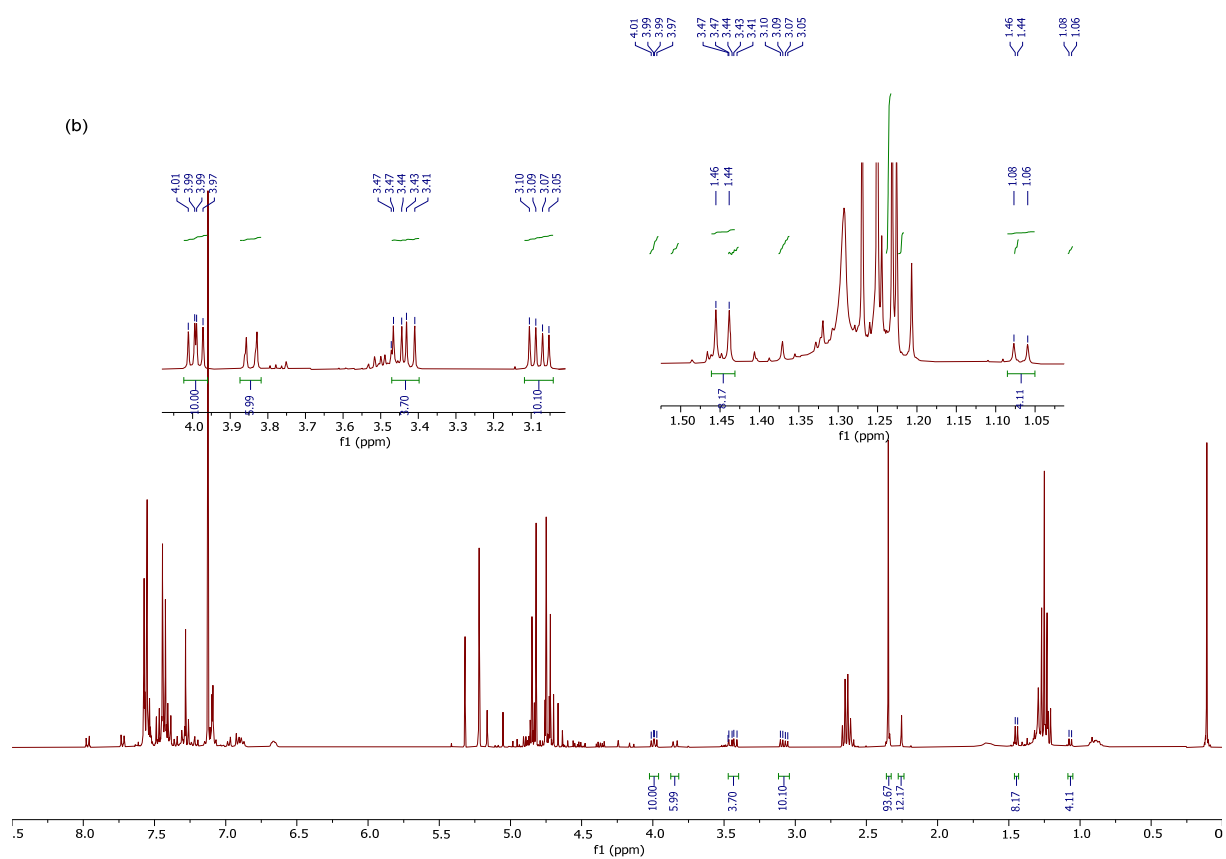
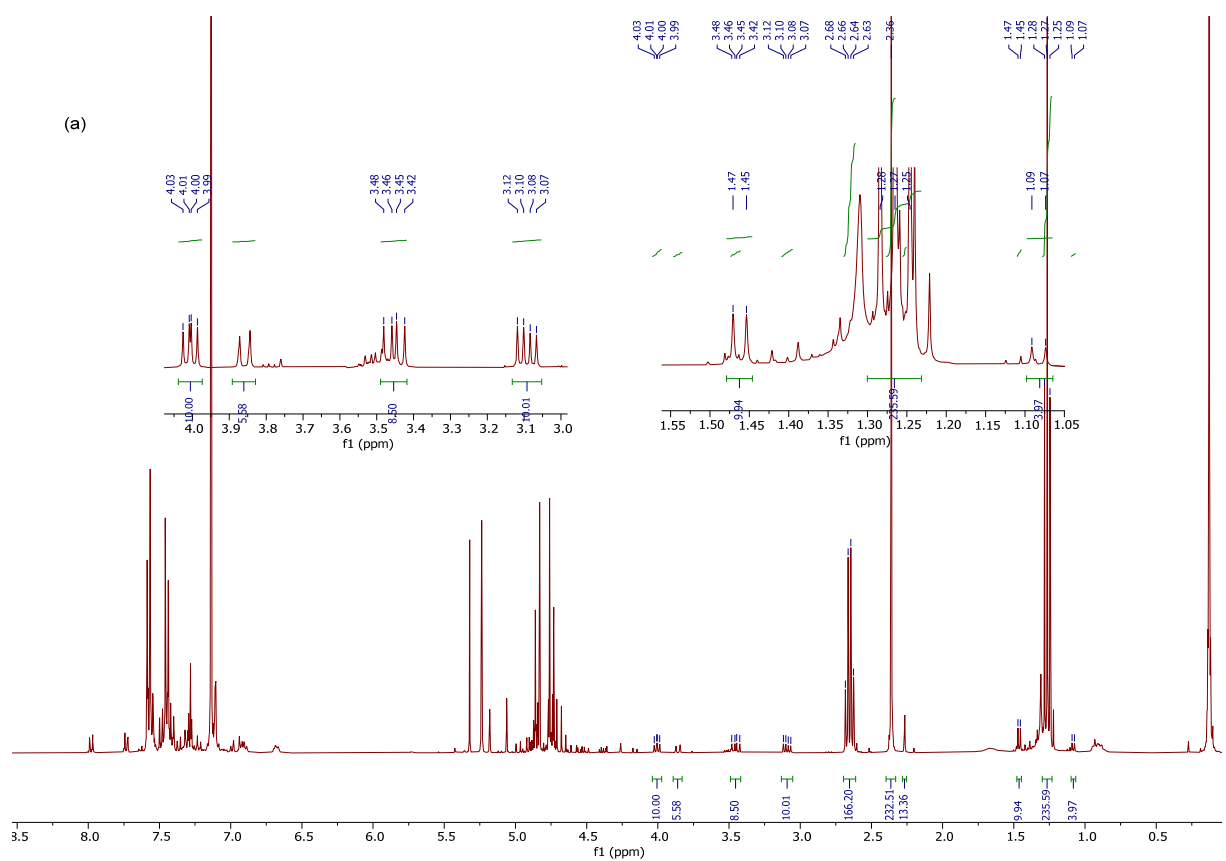
^1H NMR spectra of products 7b+8b from the reaction of 5b with $[\text{Rh}_2(\text{esp})_2]$ (400 MHz, CDCl_3)



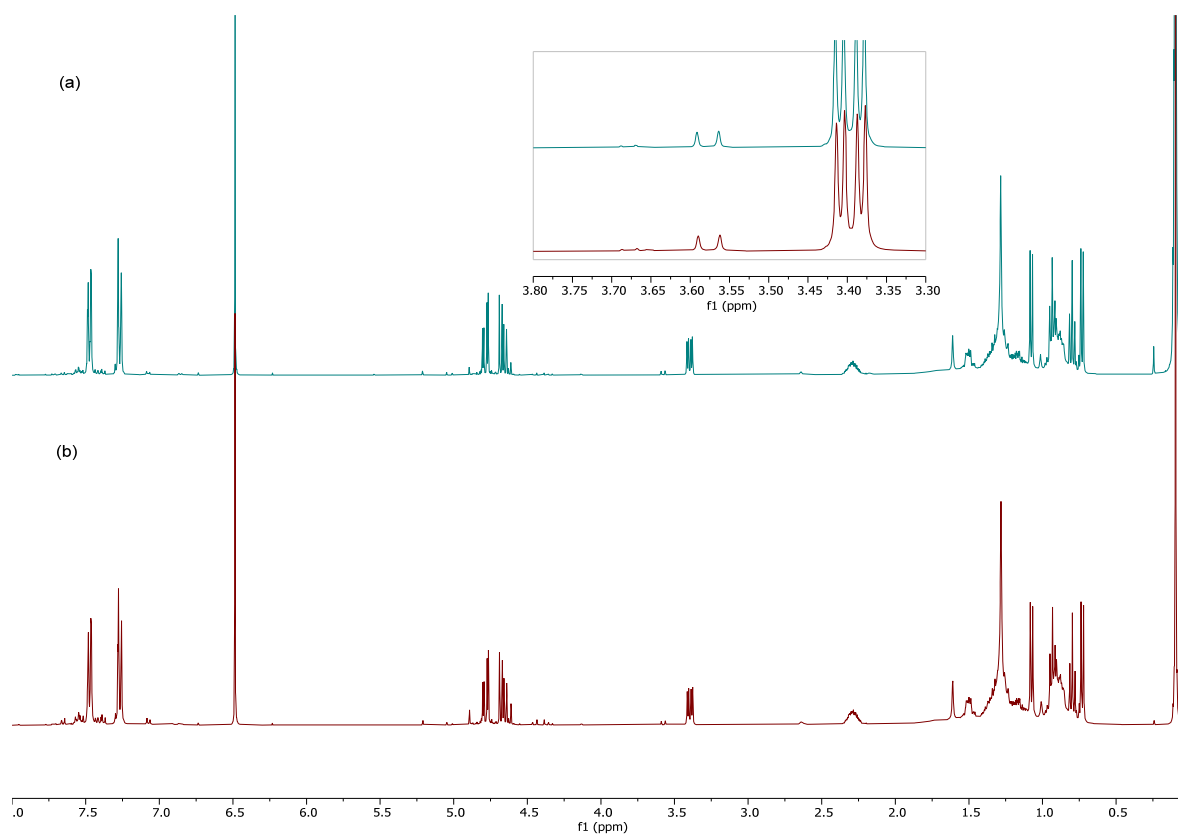
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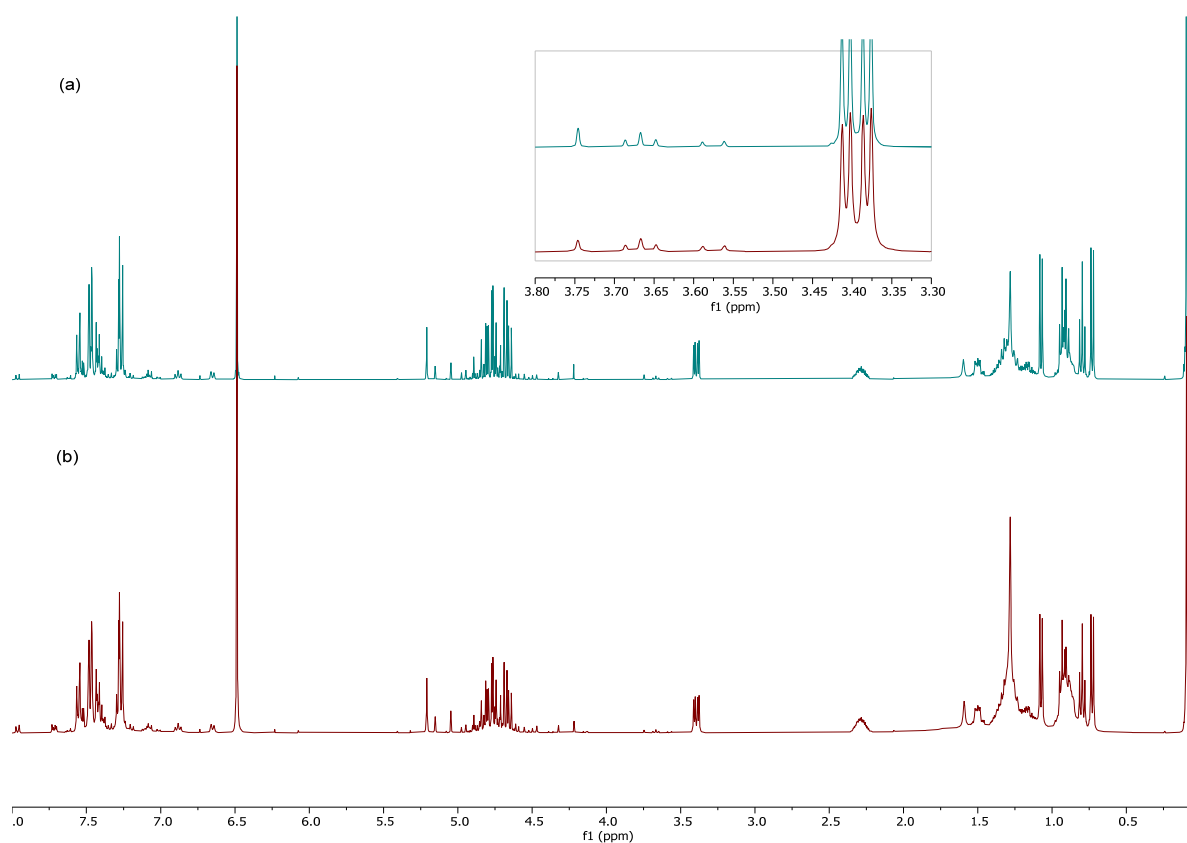
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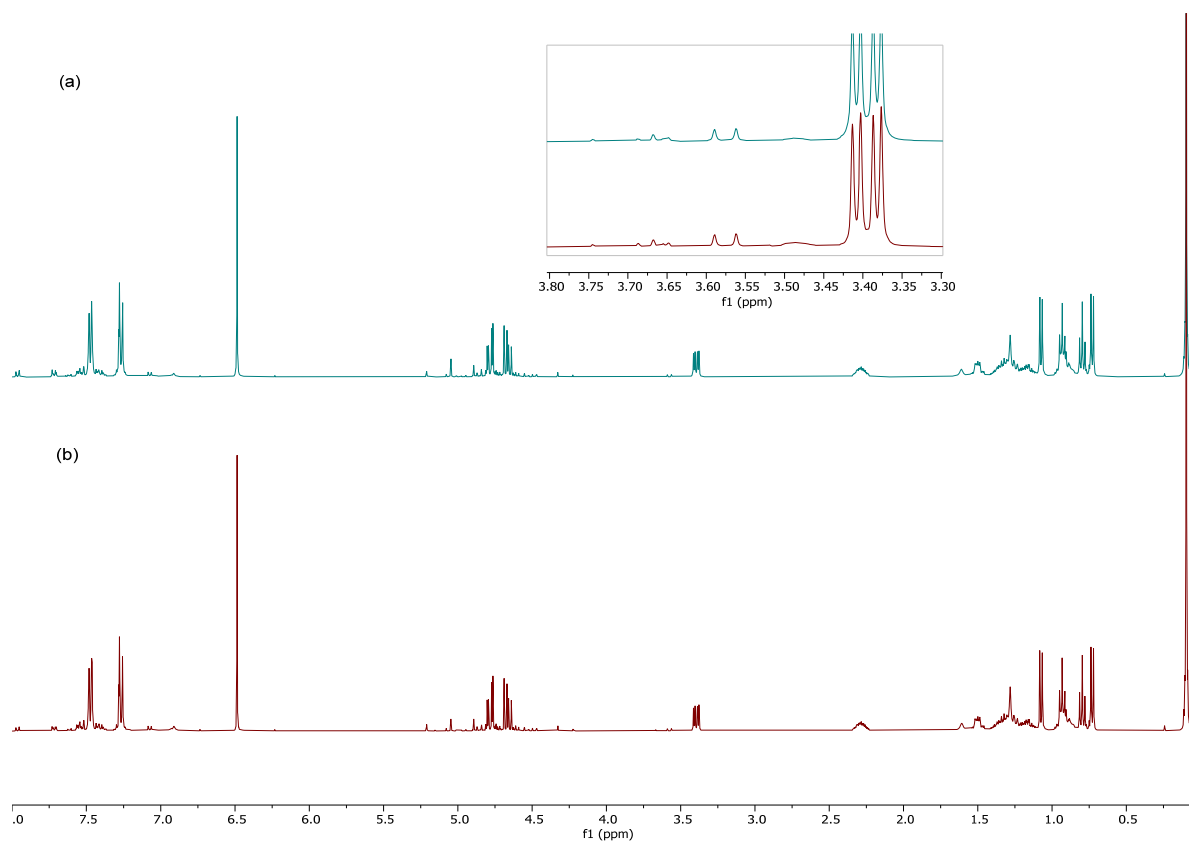
^1H NMR spectra of products 12a+13a+14a from the reaction of 5b with $[\text{Rh}_2(\text{esp})_2]$ (400 MHz, CDCl_3)



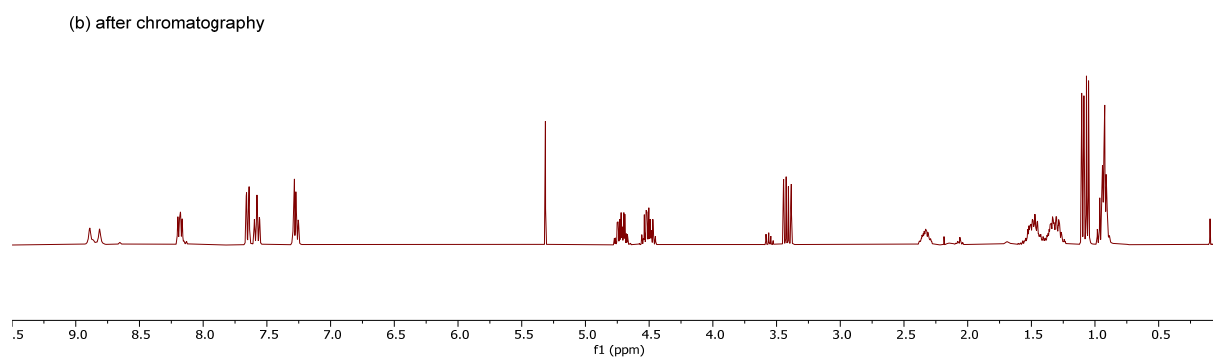
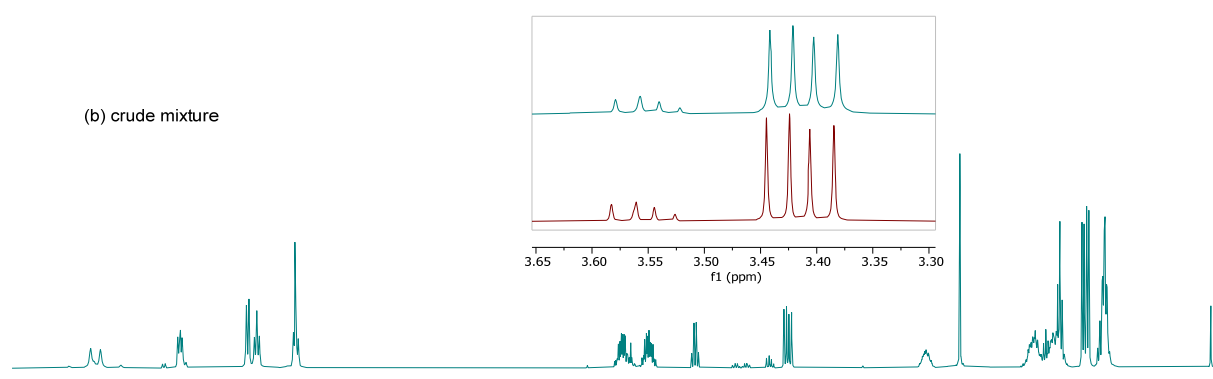
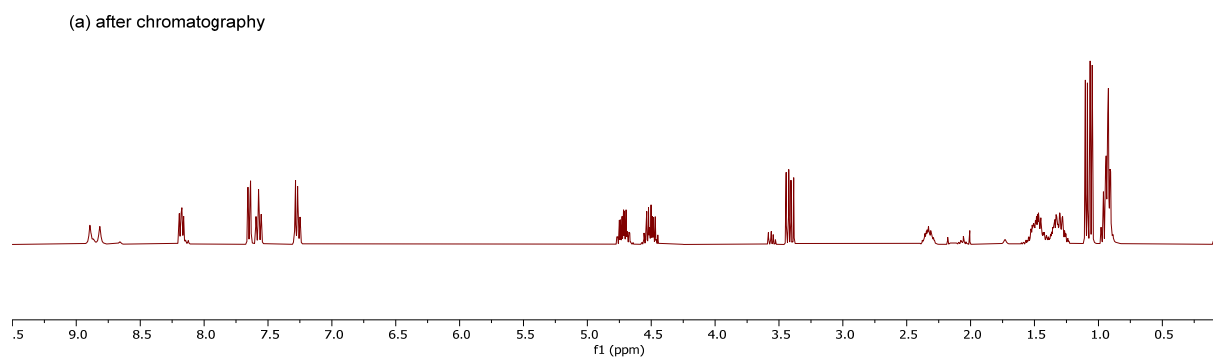
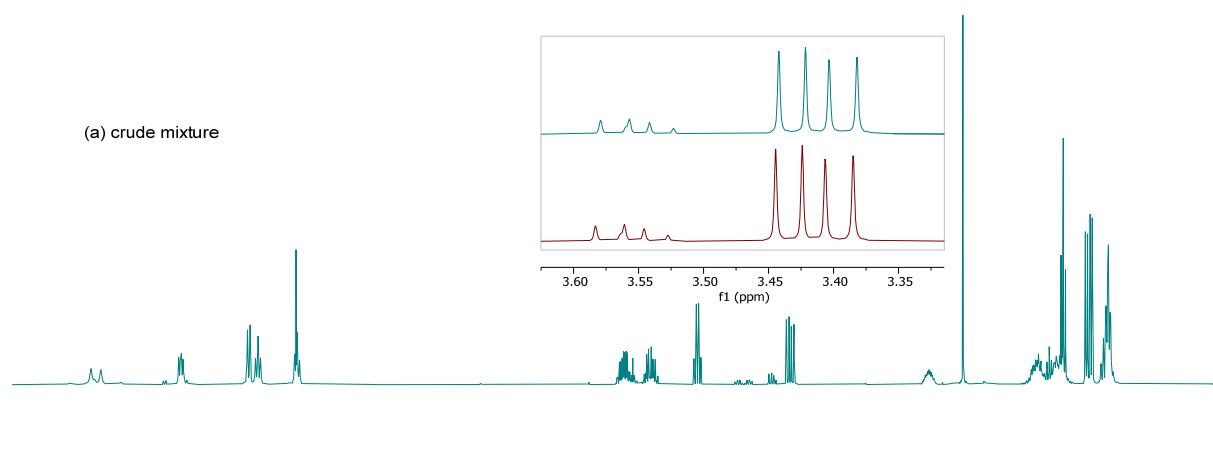
^1H NMR spectra of products 12a+13a+14a from the reaction of 5b with $[\text{Rh}_2(\text{phesp})_2]$ (400 MHz, CDCl_3)



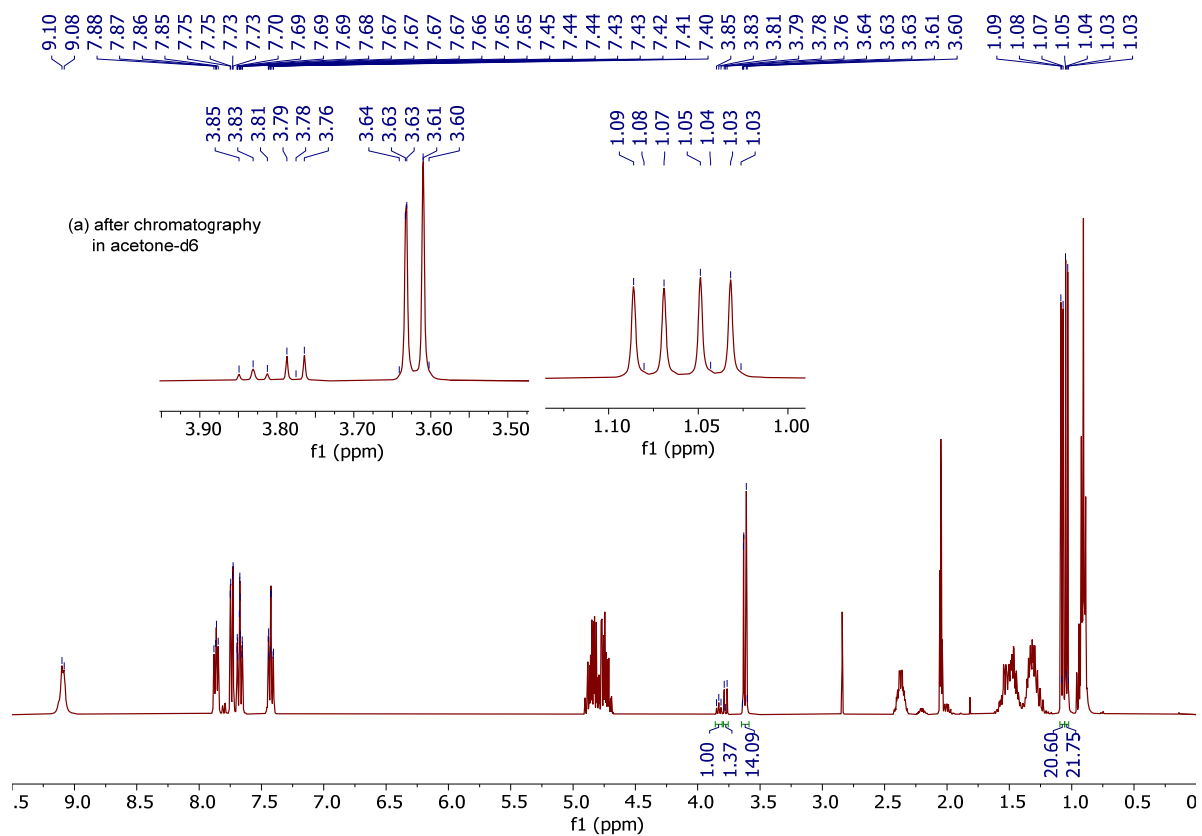
¹H NMR spectra of products 12a+13a+14a from the reaction of 5b with [Rh₂(tpa)₄] (400 MHz, CDCl₃)



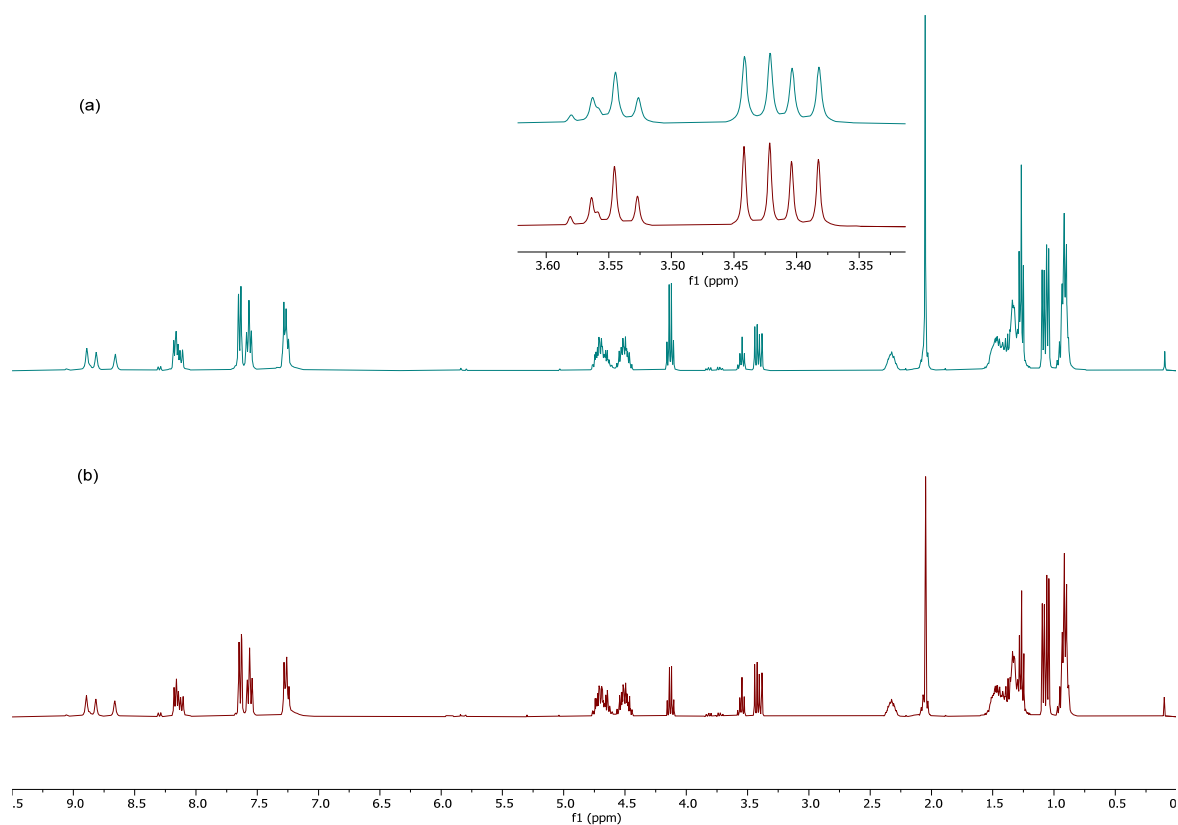
¹H NMR spectra of products 12c+13c+14c from the reaction of 6c with [Rh₂(esp)₂] (400 MHz, CDCl₃)



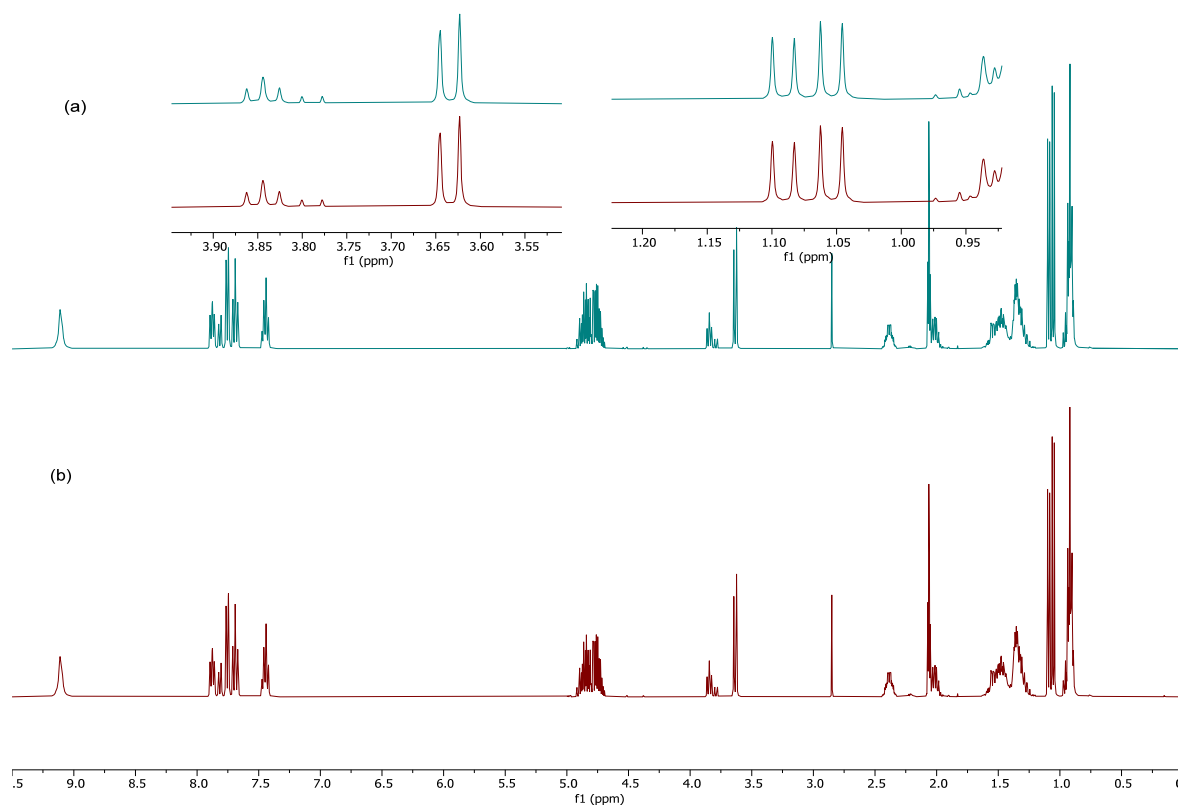
^1H NMR spectra of products 12c+13c+14c from the reaction of 6c with $[\text{Rh}_2(\text{esp})_2]$ (400 MHz, acetone- d_6): after column chromatography



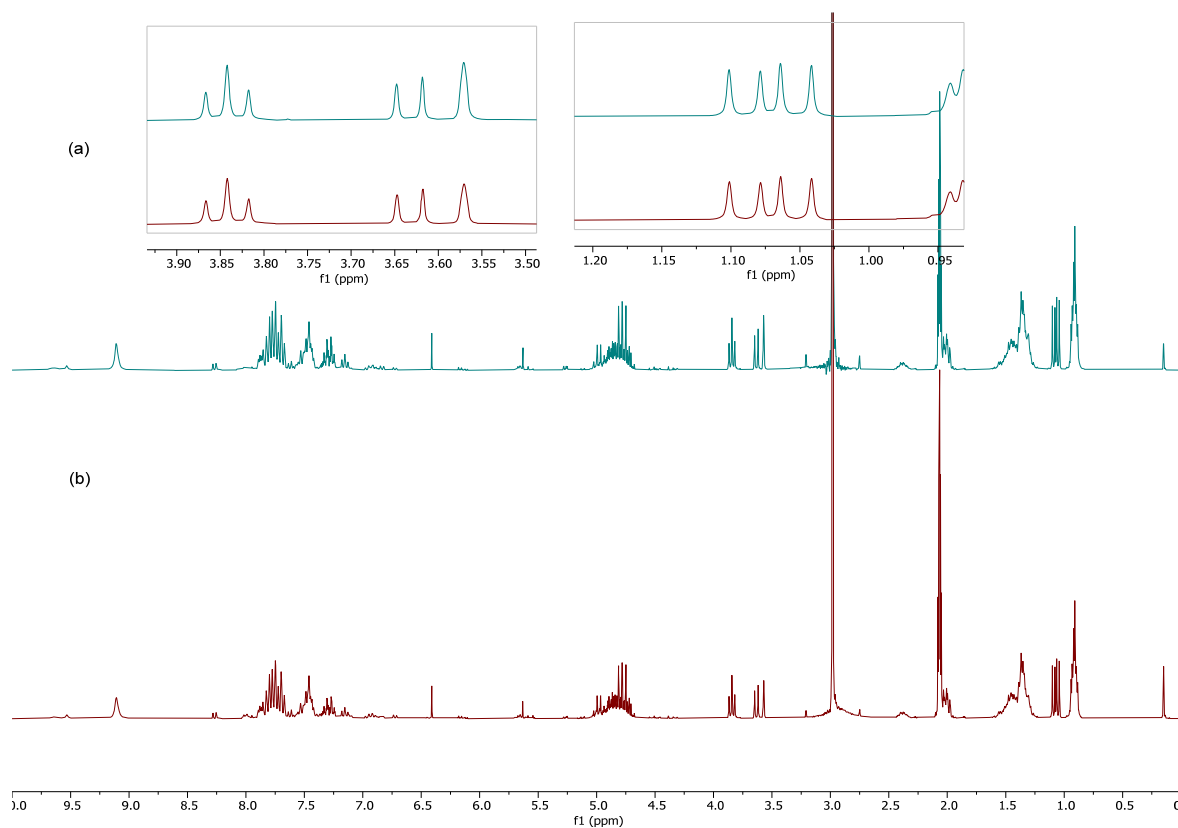
^1H NMR spectra of products 12c+13c+14c from the reaction of 6c with $[\text{Rh}_2(\text{phesp})_2]$ (400 MHz, CDCl_3): crude mixture



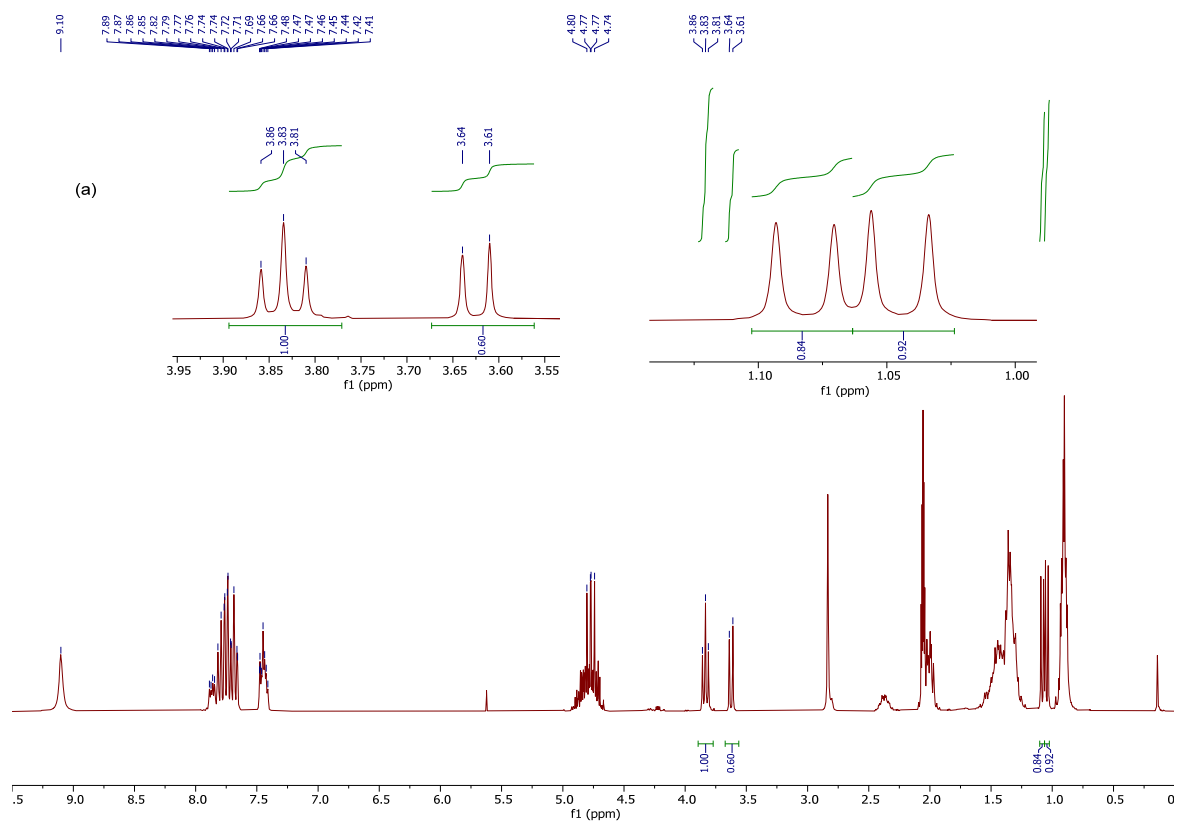
^1H NMR spectra of products 12c+13c+14c from the reaction of 6c with $[\text{Rh}_2(\text{phesp})_2]$ (400 MHz, $\text{acetone-}d_6$): after chromatography



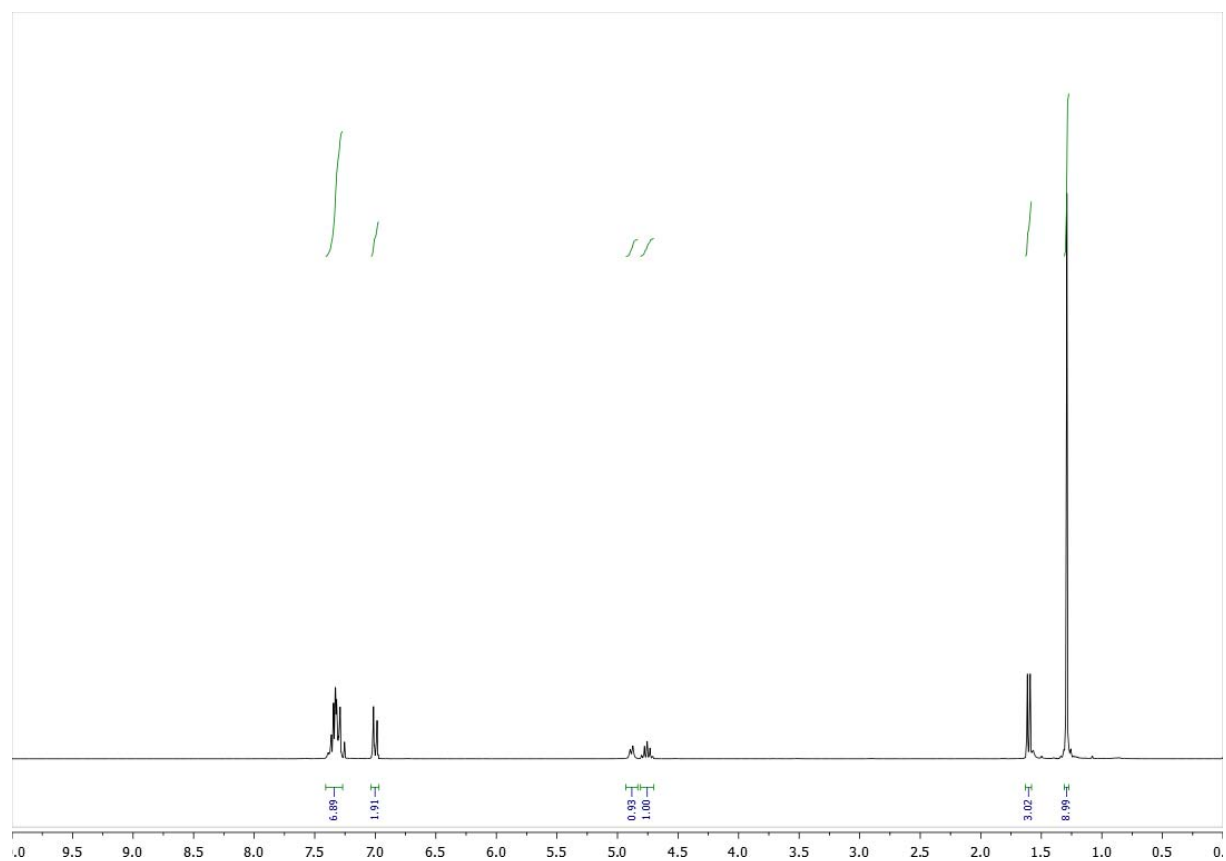
^1H NMR spectra of products 12c+13c+14c from the reaction of 6c with $[\text{Rh}_2(\text{tpa})_2]$ (400 MHz, acetone- d_6) : crude mixture



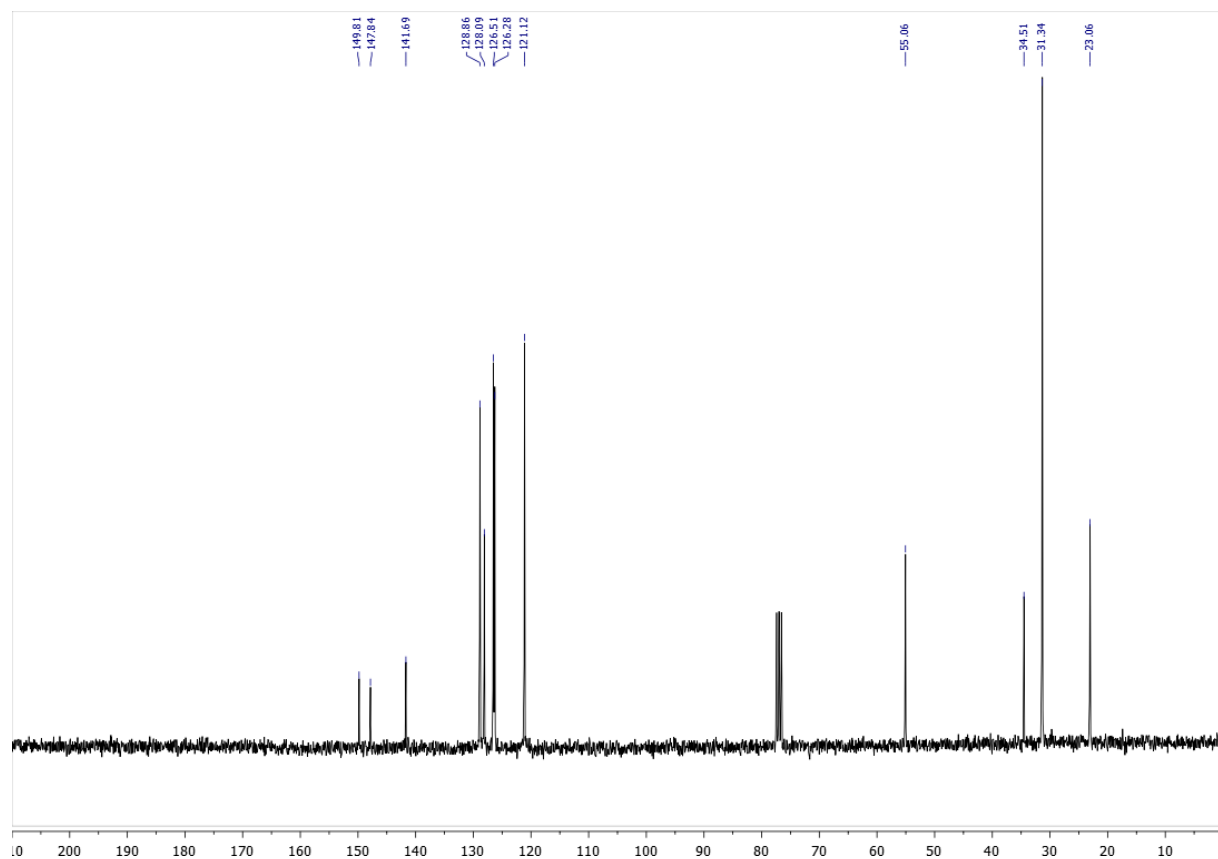
^1H NMR spectra of products 12c+13c+14c from the reaction of 6c with $[\text{Rh}_2(\text{tpa})_2]$ (400 MHz, acetone- d_6) : after chromatography



¹H NMR spectrum of 4-(*tert*-butyl)phenyl (1-phenylethyl)sulfamate 20 (300 MHz, CDCl₃)



¹³C NMR spectrum of 4-(*tert*-butyl)phenyl (1-phenylethyl)sulfamate 20 (75 MHz, CDCl₃)



Crystal Data, Data Collection, and Structure Refinement for 16 and 17.

ID	16	17
formula	C ₇₄ H ₆₄ O ₁₀ Rh ₂ , CH ₄ O	C ₄₄ H ₄₆ O ₁₀ Rh ₂ S ₂ , 2(C ₂ H ₆ OS)
<i>M_r</i>	1351.12	1161
crystal system	triclinic	triclinic
space group	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$
<i>a</i> (Å)	8.98750(10)	9.79690(10)
<i>b</i> (Å)	15.83990(10)	13.12620(10)
<i>c</i> (Å)	23.58660(10)	20.36700(10)
α (°)	92.04	92.1020(10)
β (°)	95.28	98.0640(10)
γ (°)	94.49	108.7910(10)
<i>V</i> (Å ³)	3330.21(4)	2445.62(4)
<i>Z</i>	2	2
ρ_{calc} (g cm ⁻³)	1.347	1.577
μ (mm ⁻¹)	4.488	7.563
<i>F</i> (000)	1392	1192
crystal size (mm ³)	0.20 x 0.20 x 0.20	0.10 x 0.08 x 0.02
<i>T</i> /K	100(2)	100(2)
measd reflns	117856	64578
Unique reflns (Rint)	14232 (0.0356)	10457 (0.0545)
Data/restraints/parameters	14232 / 228 / 864	10457 / 320 / 715
GOF on F ²	1.064	1.081
R ₁ ^a [I>2 σ (I)]	0.0386	0.0413
wR ₂ ^b [all data]	0.1030	0.1032

^a $R_1 = \sum ||F_o| - |F_c|| / \sum |F_o|$. ^b $wR_2 = [\sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_o^2)^2]]^{1/2}$.