Enantioselective organocatalytic formal allylation of α-branched aldehydes

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Supplementary information

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1.- General methods

NMR spectra were acquired using $CDCl_3$ as the solvent, running at 300 and 75 MHz for ^1H and ^{13}C respectively. Chemical shifts (δ) are reported in ppm relative to residual solvent signals ($CHCl_3$, 7.26 ppm for ^1H NMR, $CDCl_3$, and 77.0 ppm for ^{13}C NMR). In all ^1H NMR spectra, multiplicity is indicated as follows: bs (broad singlet), s (singlet), d (doublet), t (triplet), q (quartet) or m (multiplet). Coupling constant values (in Hertz) and number of protons for each signal are also indicated.

Melting points were measured using *Gallenkamp melting point apparatus* in open capillary tubes. Optical rotation was recorded in cells with 10 cm path length on a Perkin-Elmer 241 MC polarimeter.

For thin layer chromatography (TLC) Supelco silica gel plates with fluorescence indicator 254 nm were used and compounds were visualized by irradiation with UV light and/or by treatment with a solution of $KMnO_4$ (1.5 g), K_2CO_3 (10g), and 10% NaOH (1.25 mL) in H_2O (200 mL) or a solution of phosphomolybdic acid (12 g), in EtOH (250 mL) followed by heating. Flash column chromatography (FCC) was performed using Fluka pore 60 Å, 40-63 μm silica gel and compressed air.

Mass spectra were obtained in a *VG AutoSpec Spectrometer* in positive electrospray ionisation (ESI+) or electron impact ionisation (EI). Obtained data are expressed in mass/charge (m/z) units. Values between parentheses indicate relative intensities with regard to the base peak.

Hexane and EtOAc were supplied by *Scharlau* and were used without previous purification. *m*-Chloroperbenzoic acid (77%) was bought in *Aldrich* and was used without drying. All the other reactants were bought in *Aldrich, Fluka* or *Alfa Aesar* and were also used without any previous treatment.

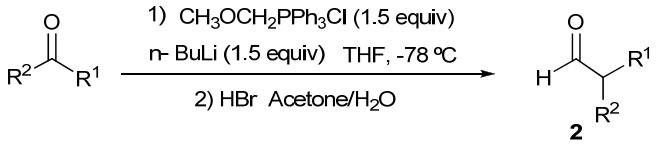
2.- Determination of enantiomeric excesses

Enantiomeric excesses (*ee*) were determined by chiral-phase HPLC using an Agilent-1100 instrument in the indicated column and conditions in each case. Synthesis of racemic compounds is detailed for every reaction.

3.- Preparation of aldehydes 2

Commercially available aldehydes **2a, 2i** and **2j** were purchased and used without any previous treatment.

The rest of the aldehydes were prepared in a two step process from the corresponding ketones following the procedure described in the literature.[1] Spectroscopic data are in agreement with the literature.

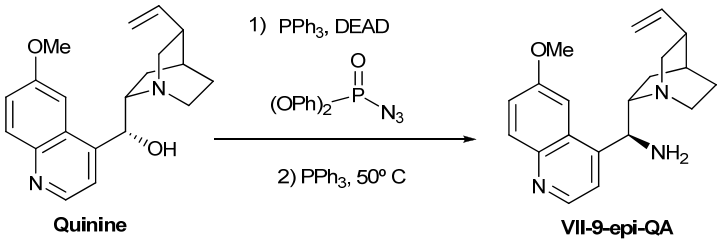


1. a) S. Hoffmann, M. Nicoletti, B. List, *J. Am. Chem. Soc.*, 2006, **128**, 13074.

4.- Preparation of catalyst VI, VII and VIII

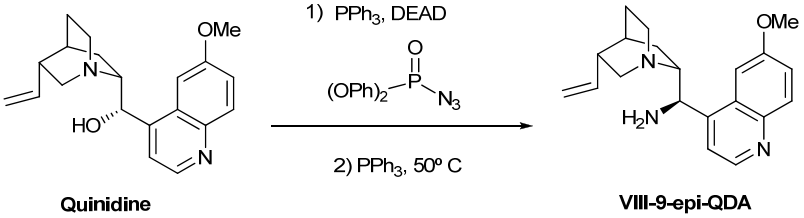
Catalyst **VI-9-epi-DHQA** was prepared from dihydroquinine according to the procedure described in the literature[2].

Catalyst **VII-9-epi-QA** was prepared following the procedure described in the literature[3].



Quinine **VII-9-epi-QA**

Catalyst **VIII 9-epi-QDA** was prepared following the same procedure described for catalyst **VII** using Quinidine.

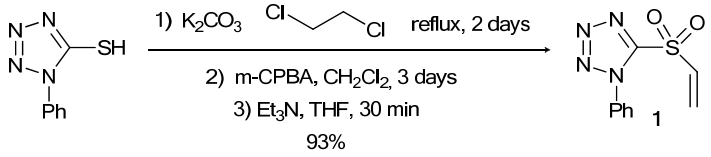


Quinidine **VIII-9-epi-QDA**

All spectroscopic data are in agreement with the literature.

2. S. H. McCooey, S. J. Connon, *Org. Lett.*, 2007, **9**, 599.
3. B. Vakulya, S.Varga, A. Csámpai, T. Soós, *Org. Lett.*, 2005, **7**, 1967.

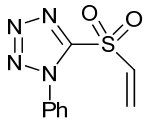
5.- Preparation of heteroaryl vinylsulfone 1



1-Phenyl-1*H*-tetrazole-5-thiol (10.7 g, 60 mmol) was placed in a 500 ml flask equipped with a magnetic stirring bar and 1,2-dichloroethane (250 ml) followed by K_2CO_3 (20.1 g, 150 mmol) were added. The suspension was stirred and heated under reflux during 2 days. After cooling to room temperature, 200 ml of water were added and the mixture was extracted with CH_2Cl_2 (2 x 100 ml). The organic layers were combined, washed with water (200 ml) and brine (200 ml), dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford 13.9 g (Yield for this step: 97%) of 5-(2-chloroethylthio)-1-phenyl-1*H*-tetrazole as a pale yellow solid that was used in the next step without previous purification.

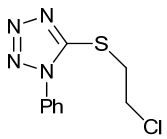
The crude compound (4.8 g, 20 mmol) was placed in a 500 ml flask equipped with a magnetic stirring bar and dissolved in CH_2Cl_2 (50 ml). A solution of *m*-chloroperbenzoic acid (17.2 g, 100 mmol) in CH_2Cl_2 (200 ml) was added and the reaction mixture was stirred at room temperature for 3 days, whereupon it was filtered. The filtrate was transferred into a separatory funnel, washed with 150 ml of a $NaHSO_3$ solution 40% w/v, a sat. aq. $NaHCO_3$ solution (2 x 150 ml) and brine (150 ml). The organic phase was dried over $MgSO_4$, filtered and concentrated under vacuum. The obtained crude was dissolved in THF (100 mL) in a 250 ml flask equipped with a magnetic stirring bar and triethylamine (4.1 ml, 30 mmol) was added dropwise. The clear solution turned to a clouded suspension which was stirred for 30 min. Solid triethlyamine hydrochloride was filtered and the solvent removed under reduced pressure. The residue was purified by flash column chromatography (hexane/EtOAc = 4:1) to afford 4.53 g (Yield over two last steps: 96%) of compound **1** as a white solid.

1-Phenyl-5-(vinylsulfonyl)-1*H*-tetrazole (1)



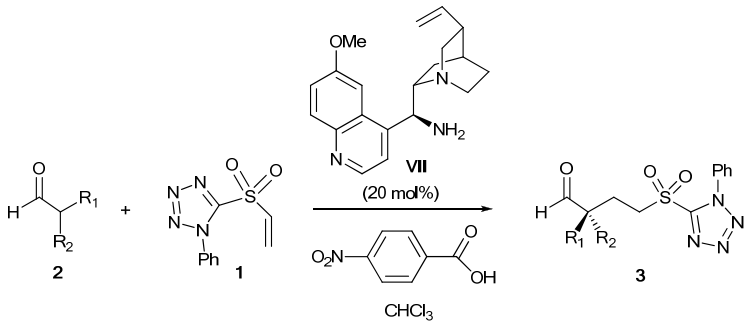
White solid. **Mp:** 63-64 ºC. **^{1}H NMR** (300 MHz): δ 7.72-7.57 (m, 5H), δ 7.14 (dd, *J* = 10.0, 16,5 Hz, 1H), δ 6.67 (d, *J* = 16,5 Hz, 1H), δ 6.49 (d, *J* = 10 Hz, 1H). **^{13}C NMR** (75 MHz): δ 154.2 (C), 135.3 (CH), 134.5 (CH), 133.0 (C), 131.6 (CH_2), 129.8 (2 CH), 125.2 (2 CH). **MS** (ESI): m/z 237 (M^++1, 48), 149 (13), 118 (100). **HRMS** (ESI): calculated for $C_9H_9N_4O_2S$ (M^++1): 237.0440; found: 237.0450.

5-(2-chloroethylthio)-1-Phenyl-1*H*-tetrazole



Yellow solid. **Mp:** 57-58 ºC. **^{1}H NMR** (300 MHz): δ 7.52 (bs, 5H), 3.90 (t, *J* = 6.9 Hz, 2H), 3.67 (t, *J* = 6.9 Hz, 2H). **^{13}C NMR** (75 MHz): δ 153.3 (C), 133.4 (C), 130.4 (CH), 129.9 (2 CH), 123.8 (2 CH), 42.2 (CH_2), 35.2 (CH_2). **MS** (ESI): m/z 241 (M^++1, 43), 149 (100), 79 (35). **HRMS** (ESI): calculated for $C_9H_{10}N_4SCl$ (M^++1): 241.0309; found: 241.0316.

6.- General procedure for the conjugate addition of α,α-disubtituted aldehydes 2 to heteroaryl vinylsulfone 1.



Catalyst **VII** (9-amino-(9-deoxi)-*epi*quinine) (9.6 mg, 0.03 mmol) was dissolved in $CHCl_3$ (1 ml) and the indicated equivalents in each case of the corresponding aldehyde **2** were added to the solution. The mixture was stirred for 5 minutes before sulfone **1** (35 mg, 0.15 mmol) and *p*-nitrobenzoic acid were added. The reaction mixture was stirred at room temperature until completion (TLC) (see table 2). The solvent was removed under reduced pressure and the crude was purified by flash column chromatography (hexane/EtOAc = 10:1 to 8:1 to 6:1) to afford the corresponding Michael adduct **3**.

Racemics:

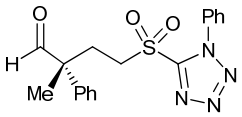
Method A: A mixture of (*S*)-methylbenzylamine (2 µl, 0.01 mmol) and (*R*)-methylbenzylamine (2 µl, 0.01 mmol) were dissolved in $CHCl_3$ (0.5 ml) and the corresponding aldehyde **2** (30 equiv, 2.25 mmol) was added to the solution. The mixture was stirred for 5 minutes before sulfone **1** (17.8 mg, 0.075 mmol) was added. The reaction mixture was stirred at room temperature until completion (TLC). The solvent was removed under reduced pressure and the crude was purified by flash column chromatography (hexane/EtOAc = 10:1 to 8:1 to 6:1) to afford the corresponding racemic aldehyde **3**.

Method B[4]: A mixture of 9-amino-(9-deoxi)-*epi*quinine **VII** (2.4 mg, 0.0075 mmol) and 9-amino-(9-deoxi)-*epi*quinidine (2.4 mg, 0.0075 mmol) were dissolved in $CHCl_3$ (0.5 ml) and the indicated equivalents in each case of the corresponding aldehyde **2** were added to the solution. The mixture was stirred for 5 minutes before sulfone **1** (17.8 mg, 0.075 mmol) and and *p*-nitrobenzoic acid were added. The reaction mixture was stirred at room temperature until completion (TLC). The solvent was removed under reduced pressure and the crude was purified by flash column chromatography (hexane/EtOAc = 10:1 to 8:1 to 6:1) to afford the corresponding racemic aldehyde **3**.

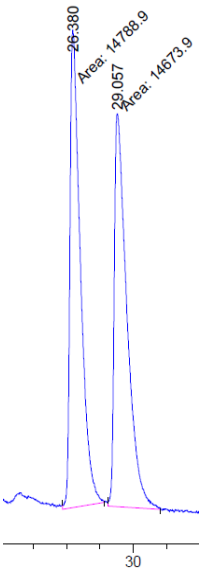
4. It is important to note that, as the catalysts used are not enantiomers but pseudoenantiomers, adducts **3** are not obtained as racemates.

7.- Data of Michael adducts 3

(*R*)-2-Methyl-2-phenyl-4-(1-phenyl-1*H*-tetrazol-5-ylsulfonyl) butanal (3a).



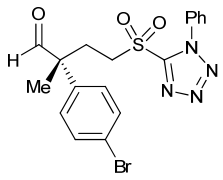
Adduct **3a** was obtained following the general method using 5 equiv of aldehyde **2a** and 20 mol % of *p*-nitrobenzoic acid. Yield: 76%.
White solid. **Mp:** 83-84 ºC. $[\alpha]^{30}_{D}$ -32.1º (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (300 MHz): δ 9.41 (s, 1H), 7.71-7.53 (m, 5H), 7.49-7.21 (m, 5H), 3.61 (ddd, *J* = 4.4, 12.6, 14.4 Hz, 1H), 3.43 (ddd, *J* = 4.4, 12.5, 14.4 Hz, 1H), 2.61 (ddd, *J* = 4.5, 12.5, 13.7 Hz, 1H), 2.36 (ddd, *J* = 4.4, 12.6, 13.7 Hz, 1H), 1.60 (s, 3H). **^{13}C NMR** (75 MHz): δ 199.9 (CHO), 153.2 (C), 136.9 (C), 133.0 (C), 131.5 (CH), 129.7 (2 CH), 129.6 (2 CH), 128.4 (CH), 127.0 (2 CH), 125.1 (2 CH), 52.9 (C), 52.3 (CH_2), 28.8 (CH_2) 18.5 (CH_3). **MS** (ESI): m/z 371 (M^++1, 71), 149 (100), 143 (37), 64 (22). **HRMS** (ESI): calculated for $C_{18}H_{19}N_4O_3S$ (M^++1): 371.1172; found: 371.1166. **IR** (film): 3026, 1723 (CHO), 1497, 1342, 1155 cm^{-1}.
The procedure to obtain this product has been scaled up until 500 mg of sulfone **1**. Yield: 70%.
Racemic aldehyde was obtained using **Method A**.
The enantiomeric excess was determined by HPLC using a Chiralpak IB column [hexane/iPrOH = 90:10]; flow rate 1.0 ml/min. ***ee* = 94%**, τ_{major} = 23.6 min; τ_{minor} = 26.9 min.



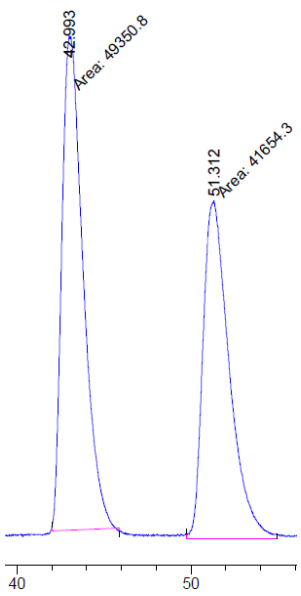
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.380	MM	0.7269	1.47889e4	339.06662	50.1951
2	29.057	MM	0.8770	1.46739e4	278.87228	49.8049

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.625	MM	0.7483	3.08794e4	687.78094	96.8793
2	26.931	MM	0.7189	994.70233	23.06037	3.1207

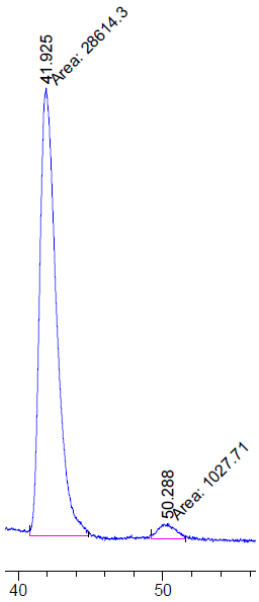
(*R*)-2-(4-bromophenyl)-2-methyl-4-(1-phenyl-1H-tetrazol-5-ylsulfonyl) butanal (3b)



Adduct **3b** was obtained following the general method using 5 equiv of aldehyde **2b** and 20 mol % of *p*-nitrobenzoic acid. Yield: 71%.
Colourless oil. $[\alpha]^{30}_{D}$ -3.3° (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (300 MHz): δ 9.45 (s, 1H), 7.69-7.53 (m, 7H), 7.17-7.11 (m, 2H), 3.61 (ddd, *J* = 4.4, 12.4, 14.5 Hz, 1H), 3.42 (ddd, *J* = 4.4, 12.6, 14.5 Hz, 1H), 2.60 (ddd, *J* = 4.5, 12.6, 13.8 Hz, 1H), 2.29 (ddd, *J* = 4.5, 12.4, 13.8 Hz, 1H), 1.59 (s, 3H). **^{13}C NMR** (75 MHz): δ 199.2 (CHO), 153.1 (C), 136.0 (C), 132.9 (C), 132.7 (2 CH), 131.5 (CH), 129.7 (2 CH), 128.7 (2 CH), 125.0 (2 CH), 122.7 (CH), 52.6 (C) 52.1 (CH_2) 28.7 (CH_2) 18.5 (CH_3). **MS** (ESI): 449 (M^++1, 28), 149 (100), 79 (30). **HRMS** (ESI): calculated $C_18H_{18}BrN_4O_3S$ (M^++1): 449.0243; found: 449.0268. **IR** (film): 2926, 1725 (CHO), 1497, 1347, 1154 cm^{-1}.
Racemic aldehyde was obtained using **Method B**.
The enantiomeric excess was determined by HPLC using a Chiralpak IC column [hexane/iPrOH = 90:10]; flow rate 1.0 ml/min. ***ee* = 93%,** τ_{major} = 41.9 min; τ_{minor} = 50.2 min.

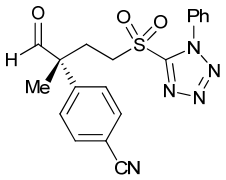


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	42.993	MM	1.4119	4.93508e4	582.56677	54.2287
2	51.312	MM	1.7463	4.16543e4	397.53754	45.7713

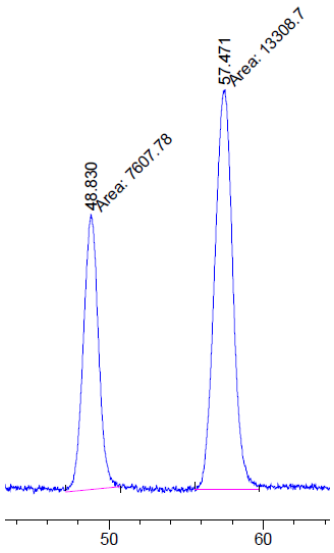


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.925	MM	1.3416	2.86143e4	355.47931	96.5329
2	50.288	MM	1.3833	1027.70532	12.38245	3.4671

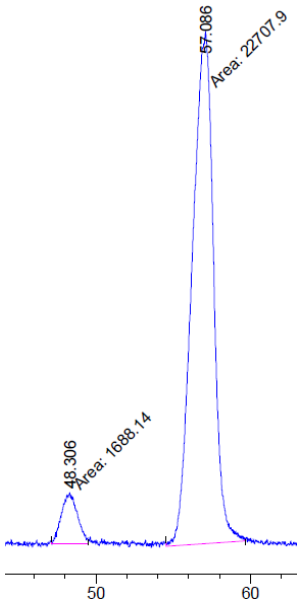
(*R*)-4-(2-methyl-1-oxo-4-(1-phenyl-1H-tetrazol-5-ylsulfonyl)butan-2-yl)benzonitrile (3c)



Adduct **3c** was obtained following the general method using 5 equiv of aldehyde **2c** and 20 mol % of *p*-nitrobenzoic acid. Yield: 65%.
Colourless oil. $[\alpha]^{25}_{D}$ -10.5º (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (300 MHz): δ 9.49 (s, 1H), 7.75 (d, *J* = 8.5 Hz, 2H), 7.70- 7.55 (m, 5H), 7.41 (d, *J* = 8.5 Hz, 2H), 3.62 (ddd, *J* = 4.8, 12.4, 14.6 Hz, 1H), 3.45 (ddd, *J* = 4.4, 12.3, 14.6 Hz, 1H), 2.62 (ddd, *J* = 4.4, 12.3, 13.9 Hz, 1H), 2.46 (ddd, *J* = 4.8, 12.4, 13.9 Hz, 1H), 1.64 (s, 3H). **^{13}C NMR** (75 MHz): δ 198.7 (CHO), 153.1 (C), 142.6 (C), 133.2 (2 CH), 132.8 (C), 131.6 (CH), 129.8 (2 CH), 127.9 (2 CH), 124.9 (2 CH), 117.9 (C), 112.6 (CN), 53.3 (C), 51.9 (CH_2), 28.8 (CH_2), 18.6 (CH_3). **MS** (ESI): 396 (M^++1, 28), 280 (64), 149 (100). **HRMS** (ESI): calculated for $C_{19}H_{18}N_5O_3S$ (M^++1): 396.1124; found: 396.1118. **IR** (film): 3021, 2233 (CN), 1728 (CHO), 1216, 1155 cm^{-1}.
Racemic aldehyde was obtained using **Method B**.
The enantiomeric excess was determined in the corresponding acetal by HPLC using a Chiralpak IA column [hexane/iPrOH = 90:10]; flow rate 1.0 ml/min. ***ee* = 86%,** τ_{major} = 57.1 min; τ_{minor} = 48.3 min.

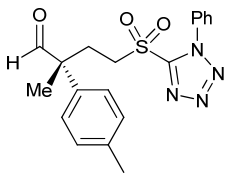


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	48.830	MM	1.1319	7607.77637	112.02406	36.3721
2	57.471	MM	1.3622	1.33087e4	162.83296	63.6279

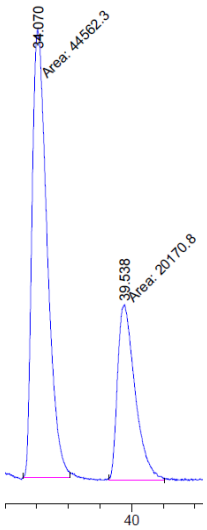


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	48.306	MM	1.1859	1688.13538	23.72432	6.9197
2	57.086	MM	1.5876	2.27079e4	238.38347	93.0803

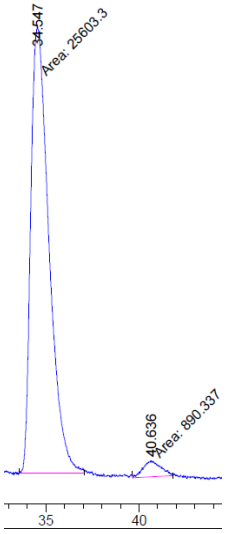
(*R*)-2-methyl-4-(1-phenyl-1H-tetrazol-5-ylsulfonyl)-2-p-tolylbutanal (3d)



Adduct **3d** was obtained following the general method using 5 equiv of aldehyde **2d** and 20 mol % of *p*-nitrobenzoic acid. Yield: 60%.
Colourless oil. $[\alpha]^{30}_{D}$ - 30.7° (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (300 MHz): δ 9.44 (s, 1H), 7.69-7.54 (m, 5H), 7.24 (d, *J* = 8.3 Hz, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 3.59 (ddd, *J* = 4.5, 12.6, 14.5 Hz, 1H), 3.42 (ddd, *J* = 4.4, 12.3, 14.5 Hz, 1H), 2.59 (ddd, *J* = 4.3, 12.6, 13.5 Hz, 1H), 2.36 (s, 3H), 2.35 (ddd, *J* = 4.5, 12.5, 13.6 Hz, 1H), 1.57 (s, 3H). **^{13}C NMR** (75 MHz): δ 200.0 (CHO), 153.4 (C), 138.3 (C), 133.8 (C), 133.1 (C), 131.5 (CH), 130.3 (2 CH), 129.7 (2 CH), 126.9 (2 CH), 125.1 (2 CH), 52.6 (C), 52.3 (CH_2), 28.8 (CH_2), 21.0 (CH_3), 18.5 (CH_3). **MS** (ESI): 385 (M^++1, 53), 157 (55), 149 (100). **HRMS** (ESI): calculated for $C_{19}H_{21}N_4O_3S$ (M^++1): 385.1328; found: 385.1314. **IR** (film): 2921, 2714, 2360, 1773 (CHO) cm^{-1}.
Racemic aldehyde was obtained using **Method B**.
The enantiomeric excess was determined by HPLC using a Chiralpak IC column [hexane/iPrOH = 90:10]; flow rate 1.0 ml/min. ***ee* = 93%,** τ_{major} = 34.5 min; τ_{minor} = 40.6 min.

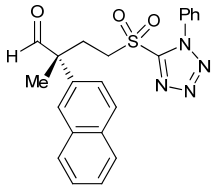


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.070	MM	1.1046	4.45623e4	672.34747	68.8400
2	39.538	MM	1.2820	2.01708e4	262.23016	31.1600

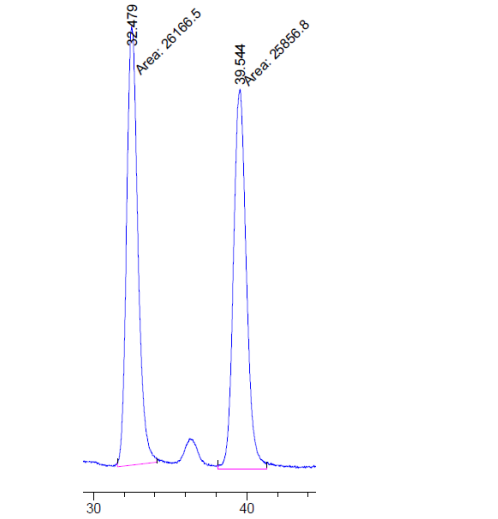


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.547	MM	1.1266	2.56033e4	378.78482	96.6394
2	40.636	MM	1.0819	890.33734	13.71532	3.3606

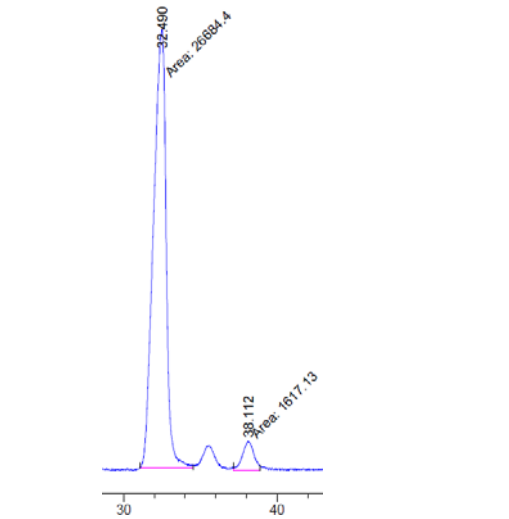
(*R*)-2-methyl-2-(naphthalen-2-yl)-4-(1-phenyl-1H-tetrazol-5-ylsulfonyl) butanal (3e)



Adduct **3e** was obtained following the general method using 5 equiv of aldehyde **2e** and 20 mol % of *p*-nitrobenzoic acid. Yield: 83%.
Colourless oil. $[\alpha]^{30}_{D}$ -1.7º (*c* = 0.9, $CHCl_3$). **^{1}H NMR** (300 MHz): δ 9.55 (s, 1H), 7.94-7.83 (m, 3H), 7.72 (d, *J* = 1.8 Hz, 1H), 7.63-7.52 (m, 7H), 7.32 (dd, *J* = 2.0, 8.7 Hz, 1H), 3.62 (ddd, *J* = 4.4, 12.6, 14.5 Hz, 1H), 3.43 (ddd, *J* = 4.4, 12.5, 14.5 Hz, 1H), 2.74 (ddd, *J* = 4.4, 12.7, 13.9 Hz, 1H), 2.45 (ddd, *J* = 4.4, 12.6, 13.9 Hz, 1H), 1.71 (s, 3H). **^{13}C NMR** (75 MHz): δ 200.1 (CHO), 153.3 (C), 134.3 (C), 133.4 (C), 132.9 (C), 132.8 (C), 131.5 (CH), 129.7 (2 CH), 129.6 (CH), 128.1 (CH), 127.8 (CH), 126.9 (CH), 126.8 (CH), 126.5 (CH), 125.1 (2 CH), 124.1 (CH), 53.1 (C), 52.3 (CH_2), 28.7 (CH_2), 18.6 (CH_3). **MS** (ESI): 421 (M^++1, 78), 149 (100), 119 (16). **HRMS** (ESI): calculated for $C_{22}H_{21}N_4O_3S$ (M^++1): 421.1328; found: 421.1310. **IR** (film): 2921, 1724 (CHO), 1345, 1215 cm^{-1}.
Racemic aldehyde was obtained using **Method A**.
The enantiomeric excess was determined by HPLC using a Chiralpak IA column [hexane/iPrOH = 90:10]; flow rate 1.0 ml/min. ***ee* = 89%,** τ_{major} = 32.4 min; τ_{minor} = 38.1 min.

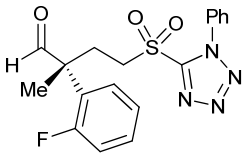


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.479	MM	0.8539	2.61665e4	510.75183	50.2977
2	39.544	MM	0.9732	2.58568e4	442.79239	49.7023



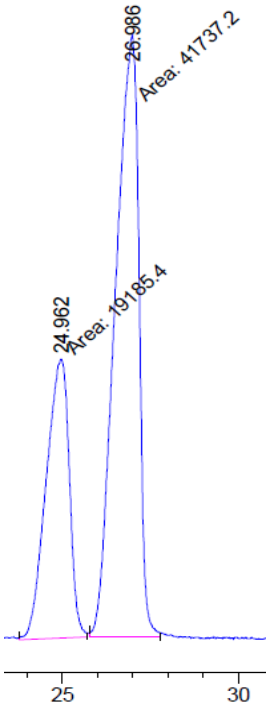
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	32.490	MM	0.9549	2.66844e4	465.76666	94.2861
2	38.112	MM	0.8580	1617.13196	31.41435	5.7139

(*R*)-2-(2-fluorophenyl)-2-methyl-4-(1-phenyl-1H-tetrazol-5-ylsulfonyl) butanal (3f)

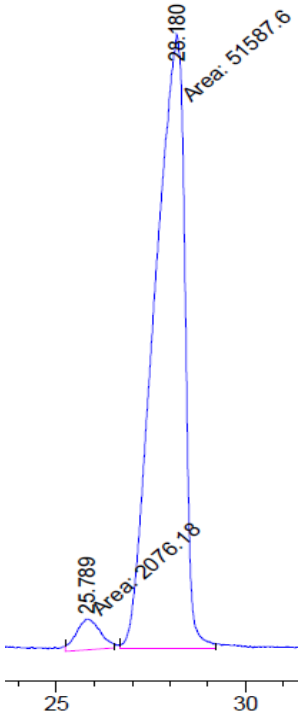


(*R*)-2-(2-fluorophenyl)-2-methyl-4-(1-phenyl-1*H*-tetrazol-5-ylsulfonyl)butanal

Adduct **3f** was obtained following the general method using 5 equiv of aldehyde **2f** and 20 mol % of *p*-nitrobenzoic acid. Yield bsmr: 30%.
Colourless oil. Data obtained from a mixture which contained a 25% of sulfone **1**. **^{1}H NMR** (300 MHz): δ 9.65 (d, *J* = 5.5 Hz, 1H), 7.71-7.56 (m, 5H), 7.43-7.34 (m, 1H), 7.32-7.27 (m, 2H), 7.19-7-10 (m, 1H), 3.62 (ddd, *J* = 4.5, 12.6, 14.4 Hz, 1H), 3.48 (ddd, *J* = 4.7, 12.4, 14.4 Hz, 1H), 2.61 (ddd, *J* = 4.6, 12.4, 13.6 Hz, 1H), 2.42 (ddd, *J* = 4.8, 12.3, 13.8 Hz, 1H), 1.65 (s, 3H). **^{13}C NMR** (75 MHz): δ 199.4 (d, *J* = 2.4 Hz, CHO), 160.75 (d, *J* = 246.8 Hz, C-F), 153.2 (C), 134.9 (d, *J* = 59.3 Hz, CH), 132.9 (C), 131.5 (CH), 130.6 (d, *J* = 5.5 Hz, CH), 129.7 (2CH), 128.4 (d, *J* = 4.4 Hz, CH), 125.3 (d, J = 3.4 Hz, C), 125.1 (2 CH), 52.3 (CH_2), 51.1 (C), 27.6 (CH_2), 19.5 (CH_3).
Racemic aldehyde was obtained using **Method B**.
The enantiomeric excess was determined by HPLC using a Chiralpak IA column [hexane/iPrOH = 90:10]; flow rate 1.0 ml/min. ***ee* = 92%,** τ_{major} = 28.1 min; τ_{minor} = 25.7 min.

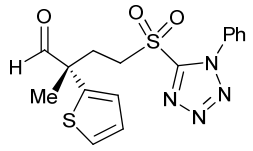


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.962	MM	0.7627	1.91854e4	419.25598	31.4915
2	26.986	MM	0.7702	4.17372e4	903.11981	68.5085



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.789	MM	0.7351	2076.18115	47.07070	3.8689
2	28.180	MM	0.9165	5.15876e4	938.15649	96.1311

(*S*)-2-methyl-4-(1-phenyl-1H-tetrazol-5-ylsulfonyl)-2-(thiophen-2-yl) butanal (3g).



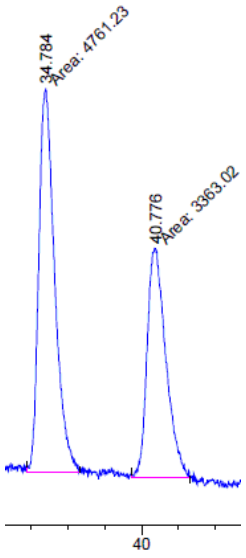
(*S*)-2-methyl-4-(1-phenyl-1*H*-tetrazol-5-ylsulfonyl)-2-(thiophen-2-yl)butanal

Adduct **3g** was obtained following the general method using 5 equiv of aldehyde **2g** and 20 mol % of *p*-nitrobenzoic acid. Yield: 68%.

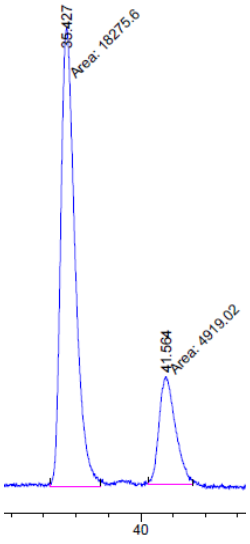
Colourless oil. $[\alpha]^{30}_{D}$ -7.3º (*c* = 0.5, $CHCl_3$). **^{1}H NMR** (300 MHz): δ 9.45 (s, 1H), 7.72-7.56 (m, 5H), 7.36 (dd, *J* = 1.1, 5.1 Hz, 1H), 7.07 (dd, *J* = 3.6, 5.1 Hz, 1H), 6.95 (dd, *J* = 1.1, 3.6 Hz, 1H), 3.75-3.54 (m, 2H), 2.63 (ddd, *J* = 4.5, 12.1, 13.8 Hz, 1H), 2.42 (ddd, *J* = 5.1, 12.1, 13.8 Hz, 1H), 1.65 (s, 3H). **^{13}C NMR** (75 MHz): δ 197.6 (CHO), 153.2 (C), 141.3 (C), 132.9 (C), 131.6 (CH), 129.8 (2 CH), 128.0 (CH), 126.5 (CH), 126.2 (CH), 125.1 (2 CH), 52.2 (CH_2), 51.3 (C), 29.2 (CH_2), 20.2 (CH_3). **MS** (ESI): 377 (M^++1, 30), 149 (100). **HRMS** (ESI): calculated for $C_{16}H_{17}N_4O_3S_2$ (M^++1): 377.0736; found: 377.0735. **IR** (film): 2922, 2851, 1725 (CHO), 1342 cm^{-1}.

Racemic aldehyde was obtained using **Method B**.

The enantiomeric excess was determined by HPLC using a Chiralpak IC column [hexane/iPrOH = 90:10]; flow rate 1.0 ml/min. ***ee* = 58%,** τ_{major} = 35.4 min; τ_{minor} = 41.5 min.

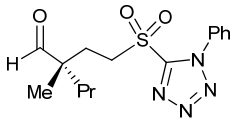


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	34.784	MM	0.9987	4761.23242	79.45654	58.6052
2	40.776	MM	1.1806	3363.01880	47.47803	41.3948



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	35.427	MM	1.0271	1.82756e4	296.57071	78.7924
2	41.564	MM	1.1788	4919.01953	69.55045	21.2076

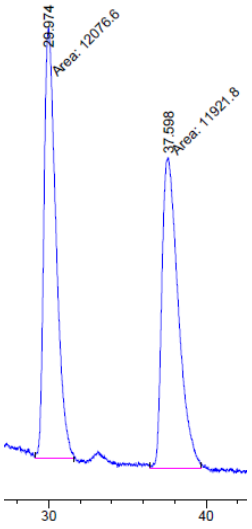
(*S*)-2-Methyl-2-isopropyl-4-(1-phenyl-1*H*-tetrazol-5-ylsulfonyl) butanal (3h)



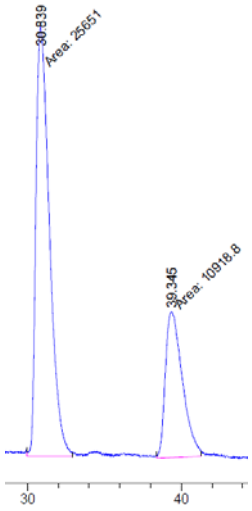
Adduct **3h** was obtained following the general method using 10 equiv of aldehyde **2h** and 50 mol % of *p*-nitrobenzoic acid. Yield: 48%. Colourless oil. **^{1}H NMR** (300 MHz): δ 9.44 (s, 1H), 7.70-7.55 (m, 5H), 3.71-3.51 (m, 2H), 2.23-1.98 (m, 2H), 1.55-1.47 (m, 2H), 1.40-1.06 (m, 5H), 0.93 (t, *J* = 7.2 Hz, 3H). **^{13}C NMR** (75 MHz): δ 204.1 (CHO), 153.2 (C), 133.0 (C), 131.5 (CH), 129.7 (2 CH), 125.1 (2 CH), 52.0 (CH_2), 48.2 (C), 37.3 (CH_2), 26.4 (CH_2), 18.8 (CH_3), 17.1 (CH_2), 14.5 (CH_3).

Racemic aldehyde was obtained using **Method A**.

The enantiomeric excess was determined by HPLC using a Chiralpak IC column [hexane/iPrOH = 90:10]; flow rate 1.0 ml/min. ***ee* = 40%,** τ_{major} = 30.8 min; τ_{minor} = 39.3 min.

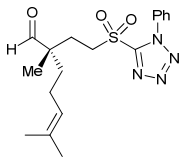


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.974	MM	0.8828	1.20766e4	227.99025	50.3226
2	37.598	MM	1.2081	1.19218e4	164.47237	49.6774

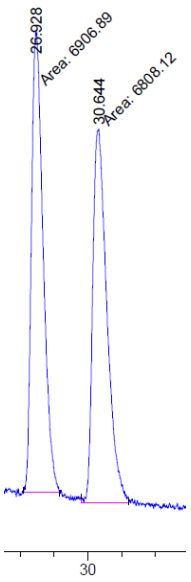


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	30.839	MM	1.0198	2.56510e4	419.20572	70.1425
2	39.345	MM	1.2779	1.09188e4	142.41057	29.8575

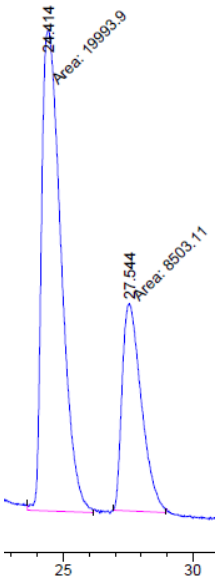
(*S*)-2-Methyl-2-isopropyl-4-(1-phenyl-1*H*-tetrazol-5-ylsulfonyl) butanal (3i).



Adduct **3i** was obtained following the general method using 10 equiv of aldehyde **2i** and 50 mol % of *p*-nitrobenzoic acid. Yield: 46%
Colourless oil. **^{1}H NMR** (300 MHz): δ 9.45 (s, 1H), 7.76-7.54 (m, 5H), 5.08-4.95 (m, 1H), 3.73-3.62 (m, 2H), 2.27-1.83 (m, 4H), 1.71-1.48 (m, 8H), 1.17 (s, 3H). **^{13}C NMR** (75 MHz): δ 203.8 (CHO), 153.2 (C), 133.2 (C), 133.0 (C), 131.5 (CH), 129.7 (2 CH), 125.0 (2 CH), 122.7 (CH) 51.9 (CH_2), 48.1 (C), 35.6 (CH_2), 26.3 (CH_2), 25.6 (CH_3), 22.4 (CH_2), 18.7 (CH_3), 17.7 (CH_3). **MS** (ESI): m/z: 377 (M^++1, 44), 359 (100), 149 (55), 147 (38), 121 (19). **HRMS** (ESI): calculated for $C_{18}H_{25}N_4O_3S$ (M^++1): 377.1641; found: 377.1629.
Racemic aldehyde was obtained using **Method A**
The enantiomeric excess was determined by HPLC using a Chiralpak IC column [hexane/iPrOH = 90:10]; flow rate 1.0 ml/min. ***ee* = 42%,** τ_{major} = 24.4 min; τ_{minor} = 27.5 min.

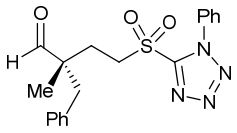


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.928	MM	0.7959	6906.89209	144.63930	50.3601
2	30.644	MM	0.9672	6808.11865	117.31634	49.6399



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.414	MM	0.8711	1.99939e4	382.53430	70.1614
2	27.544	MM	0.8584	8503.11035	165.09218	29.8386

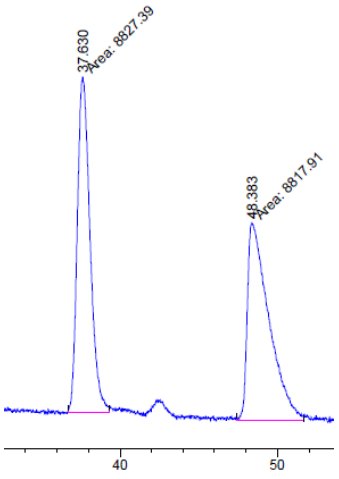
(*R*)-2-benzyl-2-methyl-4-(1-phenyl-1H-tetrazol-5-ylsulfonyl) butanal (3j)



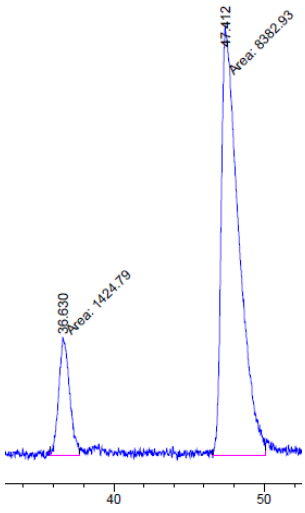
Adduct **3j** was obtained following the general method using 5 equiv of aldehyde **2j** and 20 mol % of *p*-nitrobenzoic acid. Yield: 62%. Colourless oil. $[\alpha]^{30}_{D}$ -1.2º (*c* = 1.0, $CHCl_3$). **^{1}H NMR** (300 MHz): δ 9.58 (s, 1H), 7.70-7.55 (m, 5H), 7.33-7.23 (m, 3H), 7.11-7.04 (m, 2H), 3.76-3.63 (m, 2H), 2.95-2.79 (m, 2H), 2.30-2.15 (m, 1H), 2.11-1.96 (m, 1H), 1.17 (s, 3H). **^{13}C NMR** (75 MHz): δ 203.9 (CHO), 153.3 (C), 135.0 (C), 132.9 (C), 131.5 (CH), 130.1 (2 CH), 129.7 (2 CH), 128.6 (2 CH), 127.2 (CH), 125.1 (2 CH), 52.0 (CH_2), 49.2 (C), 42.4 (CH_2), 26.8 (CH_2), 18.6 (CH_3). **MS** (ESI): 385 (M^++1, 80), 149 (100). **HRMS** (ESI): calculated for $C_{19}H_{21}N_4O_3S$ (M^++1): 385.1328; found: 385.1321. **IR** (film): 2928, 1739 (CHO), 1345, 1149 cm^{-1}.

Racemic aldehyde was obtained using **Method A.**

The enantiomeric excess was determined by HPLC using a Chiralpak IC column [hexane/iPrOH = 90:10]; flow rate 1.0 ml/min. ***ee* = 71%** τ_{major} = 47.4 min; τ_{minor} = 36.6 min.

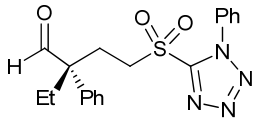


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	37.630	MM	0.9320	8827.38867	157.84938	50.0268
2	48.383	MM	1.5819	8817.91406	92.90266	49.9732



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.630	MM	0.8367	1424.79260	28.38234	14.5272
2	47.412	MM	1.3512	8382.93262	103.39736	85.4728

(*R*)-2-ethyl-2-phenyl-4-(1-phenyl-1H-tetrazol-5-ylsulfonyl)butanal (3k)



Adduct **3k** was obtained in 50 % yield (ca. 70 % purity) following the general method using 10 equiv aldehyde **2k** and 50 mol % of *p*-nitrobenzoic acid. Colourless oil.

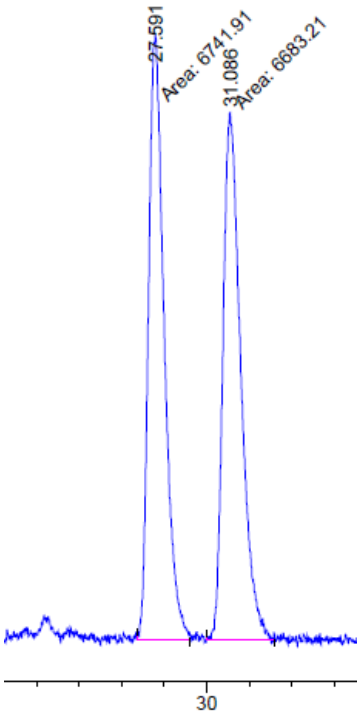
^{1}H-NMR (300 MHz): δ 9.44 (s, 1H) 7.62-7.44 (m, 5H), 7.41-7.10 (m, 5H), 3.41 (ddd, *J* = 4.4, 12.5 and 14.5 Hz, 1H), 3.27 (ddd, *J* = 4.4 12.5 and 14.5 Hz, 1H), 2.50 (ddd, *J* = 4.6, 12.5 and 13.9 Hz, 1H), 2.36 (ddd, *J* = 4.6, 12.5 and 13.9 Hz, 1H), 2.20-1.90 (m, 2H), 0.89 (t, *J* = 7.5 Hz, 3H).

^{13}C NMR (75 MHz): δ 200.9 (CHO), 153.1 (C), 136.8 (C), 132.9 (C), 131.5 (CH), 129.7 (2 CH), 129.5 (2 CH), 128.3 (CH), 127.2 (2 CH), 125.1 (2 CH), 56.6 (C), 52.0 (CH_2), 25.0 (CH_2), 24.9 (CH_2), 8.4 (CH_3).

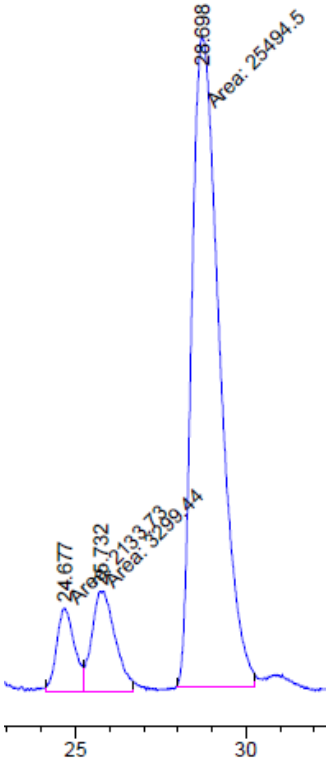
Racemic aldehyde was obtained using **Method A.**

Both enantiomers from the racemic sample could be separated by HPLC using a Chiralpak IC column [hexane/iPrOH = 90:10]; flow rate 1.0 ml/min. τ_1 = 27.5 min; τ_2 = 31.0 min.

The enantiomeric excess of the Michael adduct obtained using catalyst **VII** could not be determined accurately due to presence of impurities (see ^{1}H NMR, page 33) which could not be removed after several attemps. ***ee* = 75 - 80%** (Estimated *ee* according to the chromatogram).



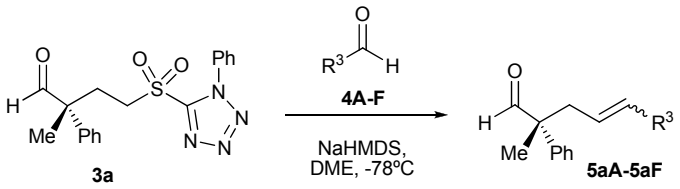
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.591	MM	0.8507	6741.91455	132.09225	50.2186
2	31.086	MM	0.9692	6683.21094	114.92384	49.7814



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	24.677	MM	0.6117	2133.72900	58.14014	6.8991
2	25.732	MM	0.7887	3299.43774	69.72473	10.6682
3	28.698	MM	0.9362	2.54945e4	453.85382	82.4327

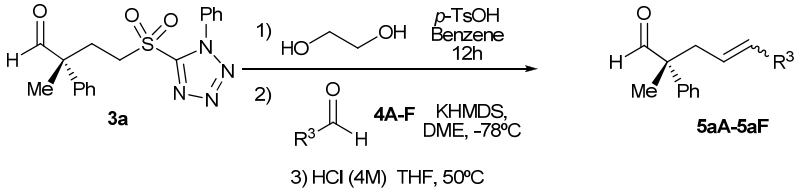
8.- General procedure for the Julia-Kocienski olefination

Method A



Sulfone **3a** (37 mg, 0.1 mmol) was placed in a 10 ml flask equipped with a magnetic stirring bar. Dry DME (1 ml) and the corresponding aldehyde **4A-F** (1.2 equiv, 0.12 mmol) were added subsequently under argon atmosphere. After stirring the mixture at -78 ºC for 5 min, NaHMDS 1M in THF (1.2 equiv, 0.12 ml, 0.12 mmol) was added and the reaction mixture was stirred at –78 ºC for 15 min whereupon it was allowed to reach to room temperature removing the cooling bath. After 5 minutes, the reaction was quenched with a sat. aq. NH_4Cl solution (10 ml) and extracted with EtOAc (3 x 10 ml). The combined organic layers were washed with water (10 ml) and brine (10 ml), dried over $MgSO_4$, filtered and concentrated under vacuum. The crude was purified by flash column chromatography (hexane/EtOAc = 30:1) to afford the corresponding aldehyde.

Method B



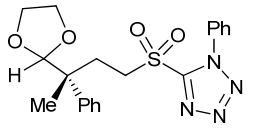
Aldehyde **3a** (185 mg, 0.5 mmol) was placed in a 25 ml flask equipped with a magnetic stirring bar, a Dean-Stark apparatus and a reflux condenser. Benzene (5 ml), *p*-toluene sulfonic acid (9.5 mg, 0.05 mmol) and 1,2-ethanodiol (0.14 ml, 2.5 mmol) were sequentially added. The reaction mixture was heated under reflux overnight. After cooling to room temperature, the reaction was quenched with a sat. aq. $NaHCO_3$ solution (10 ml), extracted with EtOAc (3 x 10 ml). The combined organic layers were washed with water (10 ml) and brine (10 ml), dried over $MgSO_4$, filtered and concentrated under vacuum to afford the corresponding acetal as colourless oil used in the next step without purification.

The crude acetal (41 mg, 0.1 mmol) was placed in a 10 ml flask equipped with a magnetic stirring bar. Dry DME (1 ml) and the corresponding aldehyde **4A-F** were subsequently added under argon atmosphere. After stirring the mixture at -78 ºC for 5 min, KHMDS 0.5 M in toluene (1.25 equiv, 0.25 ml, 0.125 mmol) was added and the reaction mixture was stirred at –78 ºC for 15 min whereupon it was allowed to reach to room temperature by removing the bath until the colour of the solution disappeared. Then the reaction was quenched with a sat. aq. NH_4Cl solution (10 ml) and extracted with EtOAc (3 x10 ml). The combined organic layers were washed with water (10 ml) and brine (10 ml), dried over $MgSO_4$, filtered and concentrated under vacuum.

The corresponding resulting acetal was dissolved in a mixture of THF (1.5 ml) and HCl 4 M (1.5 ml) and stirred at 50 ºC overnight, whereupon the reaction was quenched with a sat. aq. $NaHCO_3$ solution (10 ml) and extracted with EtOAc (3 x 10 ml). The combined organic layers were washed with water (10 ml) and brine (10 ml), dried over $MgSO_4$, filtered and concentrated under vacuum. The crude was purified by flash column chromatography (hexane/EtOAc = 30:1) to afford the corresponding aldehyde **5aA-5aF**.

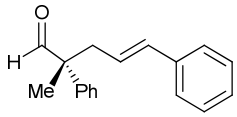
9.- Data of the allylated aldehydes 5aA-5aF

-Data of (*R*)-5-(3-(1,3-dioxolan-2-yl)-3-Phenylbutylsulfonyl)-1-phenyl-1H-tetrazole.



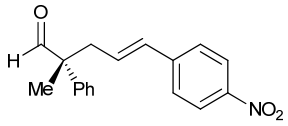
This compound was prepared as specified in the first part of the general **method B**.
^{1}H NMR (300 MHz): δ 7.75-7.22 (m, 10H), 4.95 (s, 1H), 3.84 (bs, 4H), 3.64 (ddd, *J* = 4.4, 12.6, 14.4 Hz,1H), 3.47 (ddd, *J* = 4.4, 12.5, 14.4 Hz, 1H), 2.68 (ddd, *J* = 4.5, 12.5, 13.8 Hz, 1H), 2.34 (ddd, *J* = 4.4, 12.6, 13.7 Hz, 1H), 1.47 (s, 3H). **^{13}C NMR** (75 MHz): δ 153.2 (C), 140.8 (C), 132.9 (C), 131.3 (CH), 129.6 (2 CH), 128.5 (2 CH), 127.1 (2 CH), 127.0 (CH), 125.0 (2 CH), 108.6 (CH), 65.3 (CH_2), 65.2 (CH_2), 52.5 (CH_2), 44.7 (C), 28.2 (CH_2), 19.3 (CH_3).

(*R,E*)-2-Methyl-2,5-diphenylpent-4-enal (5aA)



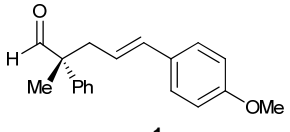
Aldehyde **5aA** was obtained using Julia-Kocienski olefination following general **methods A and B.** Method A. Yield: 48%. E/Z = 10:1
Method B. Yield: 72%. E/Z > 10/1
Colorless oil. $[\alpha]^{30}_{D}$ - 88.8º (*c* = 1.0, $CHCl_3$). Data of the mayor stereomer: **^{1}H NMR** (300 MHz): δ 9.58 (s, 1H), 7.46-7.17 (m, 10H), 6.42 (d, *J* = 15.5 Hz, 1H), 5.95 (dt, *J* = 7.4 and 15.5 Hz, 1H), 2.88-2.78 (m, 2H), 1.51 (s, 3H). **^{13}C NMR** (75 MHz): δ 201.9 (CHO), 139.5 (C), 137.2 (C), 133.6 (CH), 128.9 (2 CH), 128.4 (2 CH), 127.4 (CH), 127.2 (CH), 127.1 (2 CH), 126.1 (2 CH), 124.9 (CH), 54.1 (C), 39.9 (CH_2), 18.9 (CH_3). **MS** (Gc/EI): 250 (M^+, 0.1), 117 (100), 115 (69), 91 (25). **HRMS** (EI): calculated for $C_{18}H_{18}O$ (M^+): 250.1358; found: 250.1348. **IR** (film): 3027, 2929, 1724 (CHO), 1495, 1446 cm^{-1}.

***(R,E)*-2-Methyl-5-(4-nitrophenyl)-2-phenylpent-4-enal (5aB)**



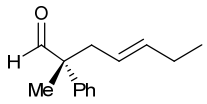
Aldehyde **5aB** was obtained using Julia-Kocienski olefination following the general **method B**. Yield: 77 %. E/Z = 9/1.
Yellow oil. $[\alpha]^{25}_{D}$ - 77.5º (*c* = 1.0, $CHCl_3$). Data of the mayor stereomer. **^{1}H NMR** (300 MHz): δ 9.56 (s, 1H), 8.13 (d, *J* = 8.9 Hz, 2H), 7.46-7.18 (m, 7H), 6.46 (d, *J* = 15.8 Hz, 1H), 6.15 (dt, *J* = 7.5 and 15.8 Hz, 1H), 2.95-2.78 (m, 2H), 1.52 (s, 3H). **^{13}C NMR** (75 MHz): δ 201.4 (CHO), 146.7 (C), 143.5 (C), 138.9 (C), 131.6 (CH), 130.6 (CH), 129.0 (2 CH), 127.7 (CH), 127.1 (2 CH), 126.6 (2 CH), 123.9 (2 CH), 54.1 (C), 40.1 (CH_2), 18.9 (CH_3).

(*R,E*)-5-(4-methoxyphenyl)-2-Methyl-2-phenylpent-4-enal (5aC)



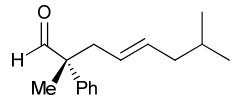
Aldehyde **5aC** was obtained using Julia-Kocienski olefination following the general **method B.** Yield: 60 %. E/Z > 10/1.
Orange oil. $[\alpha]^{25}_{D}$ - 39.4º (*c* = 1.0, $CHCl_3$). Data of the mayor stereomer. **^{1}H NMR** (300 MHz): δ 9.58 (s, 1H), 7.0 (m, 2H), 7.30 (m, 3H), 7.19 (d, *J* = 8.7 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 6.35 (d, *J* = 15.6 Hz, 1H), 5.79 (dt, *J* = 7.5 and 15.6 Hz, 1H), 3.79 (s, 3H), 2.79 (m, 2H), 1.49 (s, 3H). **^{13}C NMR** (75 MHz): δ 202.1 (CHO), 158.9 (C), 139.6 (C), 133.0 (CH), 130.1 (C), 128.9 (2 CH), 127.3 (CH), 127.2 (2 CH), 127.1 (2 CH), 122.6 (CH), 113.9 (2 CH), 55.3 (CH_3), 54.2 (C), 39.9 (CH_2), 19.0 (CH_3).

(*R,E*)-2-Methyl-2-phenylhept-4-enal (5aD)



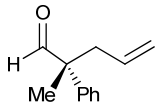
Aldehyde **5aD** was obtained using Julia-Kocienski olefination following general **methods A and B**. Method A. Yield: 15%. E/Z = 2:1
Method B. Yield: 45%. E/Z= 8/1
Yellowish oil. $[\alpha]^{25}_{D}$ - 22.0 º (*c* = 0.7, $CHCl_3$). Data of the mayor stereomer. **^{1}H NMR** (300 MHz): δ 9.54 (s, 1H), 7.44-7.23 (m, 5H), 5.57-5.44 (m, 1H), 5.24-5.10 (m, 1H), 2.61 (m, 2H), 2.03-1.90 (m, 2H), 1.41 (s, 3H), 0.91 (t, *J* = 7.5 Hz, 3H).**^{13}C NMR** (75 MHz): δ 202.4 (CHO), 140.0 (C), 136.6 (CH), 134.7 (CH), 128.8 (2 CH), 127.2 (2 CH), 123.2 (CH), 54.0 (C), 39.3 (CH_2), 25.6 (CH_2), 19.4 (CH_3), 13.9 (CH_3).
MS (Gc/EI): 202 (M^+, 0.9), 134 (100), 105 (91), 91 (49). **HRMS** (EI): calculated for $C_{14}H_{18}O$ (M^+): 202.1358; found: 202.1351. **IR** (film): 2926, 1724 (CHO), 1216, 899 cm^{-1}.

(*R,E*)-2,7-Dimethyl-2-phenyloct-4-enal (5aE)



Aldehyde **5aE** was obtained using Julia-Kocienski olefination following the general **method B**. Yield: 48%. E/Z = 7/1
Colourless oil. $[\alpha]^{25}_{D}$ -14.7º (c = 0.9, $CHCl_3$). Data of the mayor stereomer. **^{1}H NMR** (300 MHz): δ 9.54 (s, 1H), 7.42-7.22 (m, 5H), 5.53-5.38 (m, 1H), 5.26-5.09 (m, 1H), 2.62 (m, 2H), 1.75 (m, 2H), 1.60-1.48 (m, 1H), 1.43 (s, 3H), 0.81 (dd, *J* = 4.1 and 6.6 Hz, 6H). **^{13}C NMR** (75 MHz): δ 202.3 (CHO), 139.9 (C), 133.7 (CH), 128.8 (2 CH), 127.1 (3 CH), 125.2 (CH), 53.9 (C), 41.9 (CH_2), 39.5 (CH_2), 28.3 (CH), 22.1 (2 CH_3), 19.0 (CH_3). **MS** (EI): 230 (M^+, 0.2), 134 (100), 105 (38). **HRMS** (EI): calculated for $C_{16}H_{22}O$ (M^+): 230.1671; found: 230.1680. **IR** (film): 2925.74, 1723.94 (CHO), 1358.03, 999.58 cm^{-1}.

(*R*)-2-Methyl-2-phenylpent-4-enal (5aF)

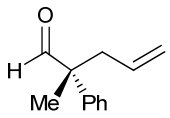


Aldehyde **5aF** was obtained using Julia-Kocienski olefination following the general **method B** adding 30 equiv of formaldehyde. Yield: 30%
$[\alpha]^{25}_{D}$ -54.2º (*c* = 1.0, MeOH).
^{1}H-NMR (300 MHz): *δ* 9.52 (s, 1H), 7.42-7.34 (m, 2H), 7.32-7.22 (m, 3H), 5.61-5.47 (m, 2H), 5.08-5.01 (m, 1H), 2.73-2.59 (m, 2H), 1.44 (s, 3H).

10.- Assignation of the absolute stereochemistry

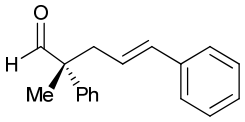
Configuration of compounds **5aA** and **5aF** was assigned by comparison with the literature data and the configurations of the rest of compounds were assigned by analogy.

(*R*)-2-Methyl-2-phenylpent-4-enal (5aF)

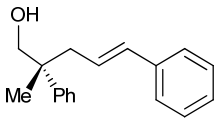


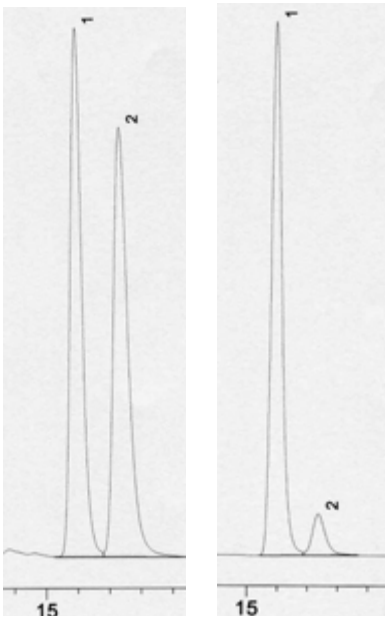
$[\alpha]^{25}_{D}$ -54.2º (*c* = 1.0, MeOH). [Lit.[5] -38º (MeOH) for the (*R*) enantiomer]; [Lit.[6] +84.8º (*c* = 1.08, MeOH) for the (*S*) enantiomer]. Comparing to the $[\alpha]^{25}_{D}$ values reported in the literature, the configuration of **5aF** was assigned as (*R*).

(*R,E*)-2-Methyl-2,5-diphenylpent-4-enal (5aA)



The enantiomeric excess of compound **5aA** was determined and checked to remain the same after the whole process without erosion of the *ee* value by comparison with the HPLC data reported by List[6] for the corresponding alcohol of known configuration after reduction with $NaBH_4$ in EtOH at 0 ºC. (Chiralpak AS-H column [95:5 *n*-heptane/*i*-PrOH, 0.5 ml/min]. Major enantiomer: t_R= 15.94 min, minor enantiomer: t_R = 17.36 min).





Detector A Ch1 220nm			
Peak #	Ret. Time	Area %	
1	15.93	49.09	
2	17.32	50.91	
Total		100.00	

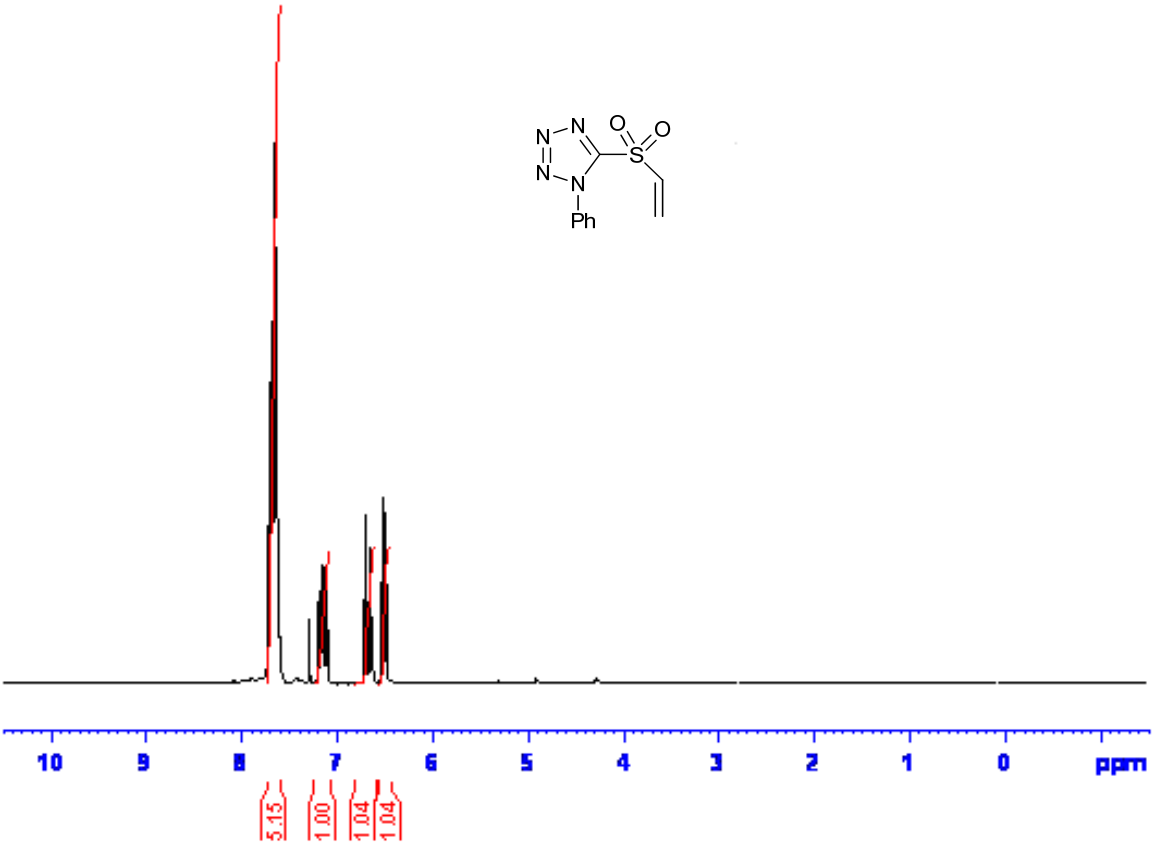
Detector A Ch1 220nm			
Peak #	Ret. Time	Area %	
1	15.94	91.01	
2	17.36	8.99	
Total		100.00	

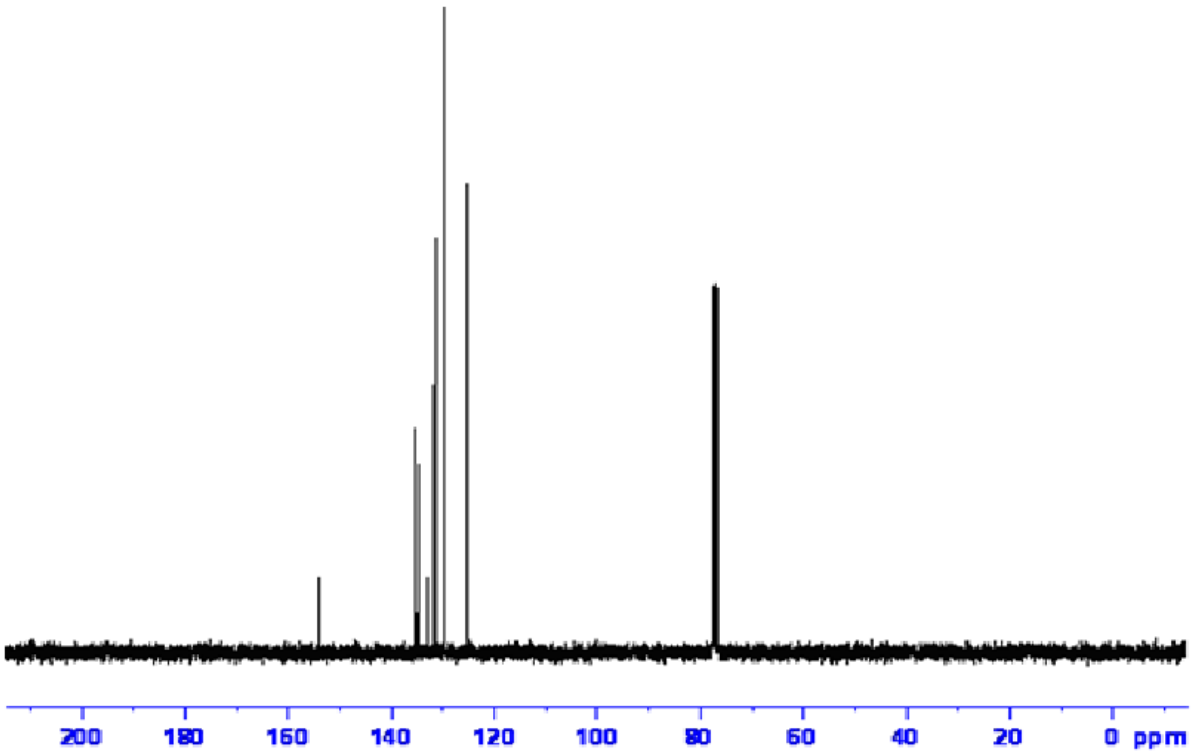
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	20.931	MM	0.6472	5.23385e4	1347.74902	95.7794
2	23.711	MM	0.6504	2306.34204	59.09829	4.2206

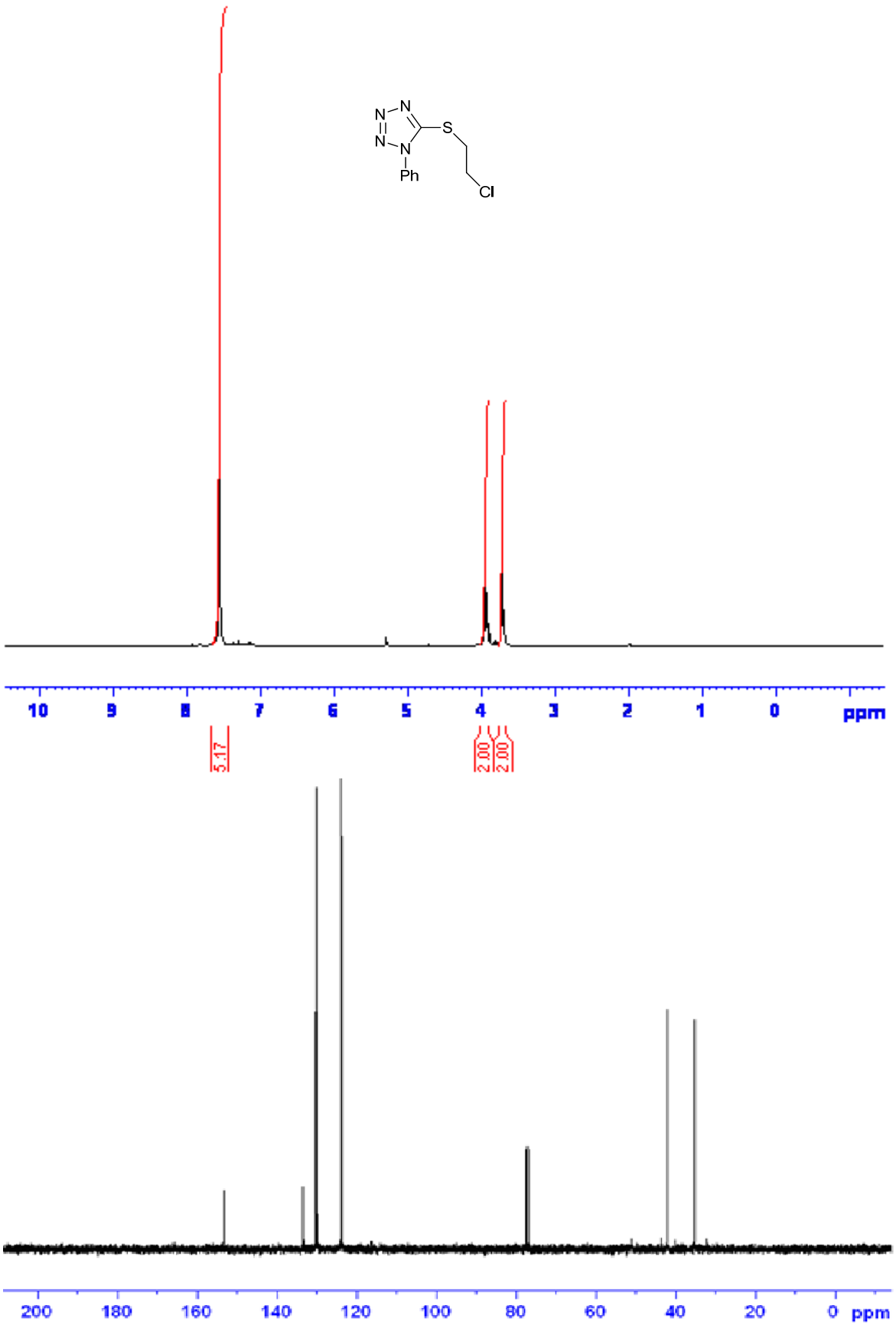
The (*R*) configuration deduced from the chromatogram is in agreement with the configuration deduced for the compound **5aF** from the value of the optical rotatory power.

5. K. Hiroi, J. Abe, K. Suya, S. Sato, *Tetrahedron Lett.,* 1989, **30**, 1543.
6. S. Mukherjee, B. List, *J. Am. Chem. Soc.*, 2007, **129**, 11336.

11.- NMR Spectra of the Products



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Ph
Cl
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7
6
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2.00
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140
120
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20
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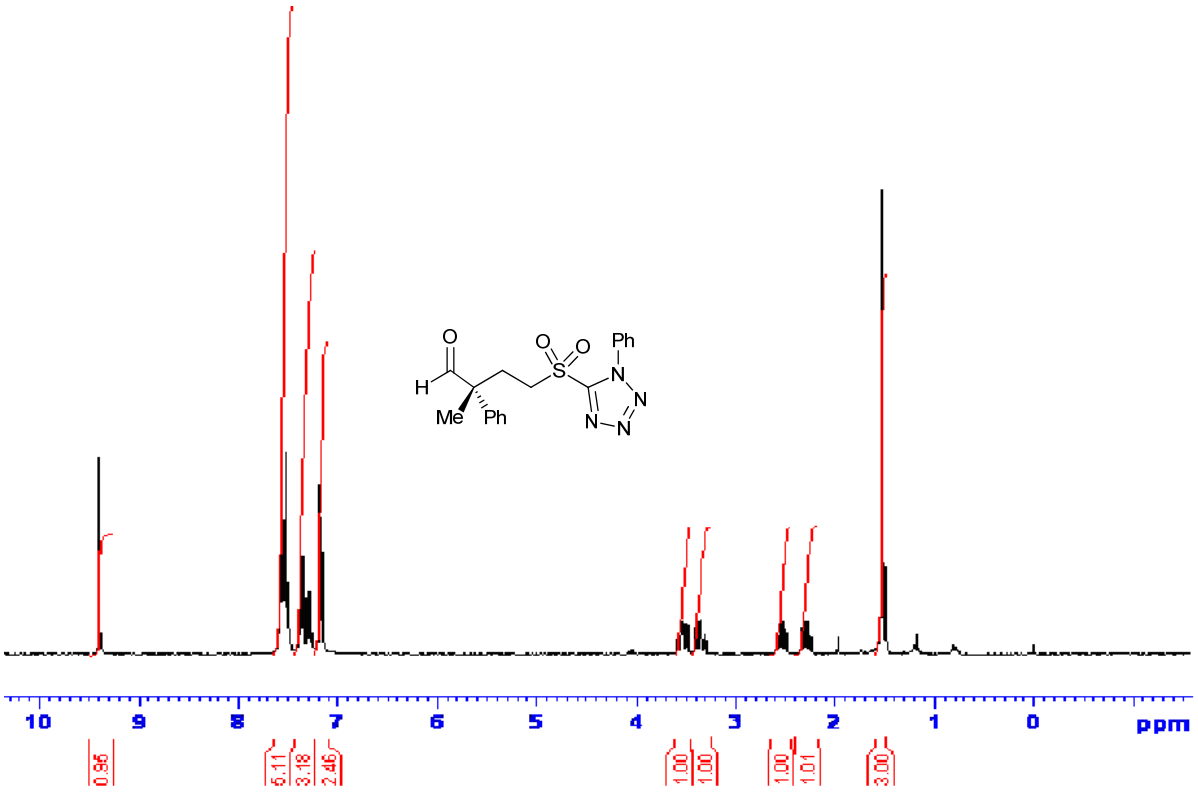
ppm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Me
Ph
O
S
O
Ph
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10
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8
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6
5
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1.00
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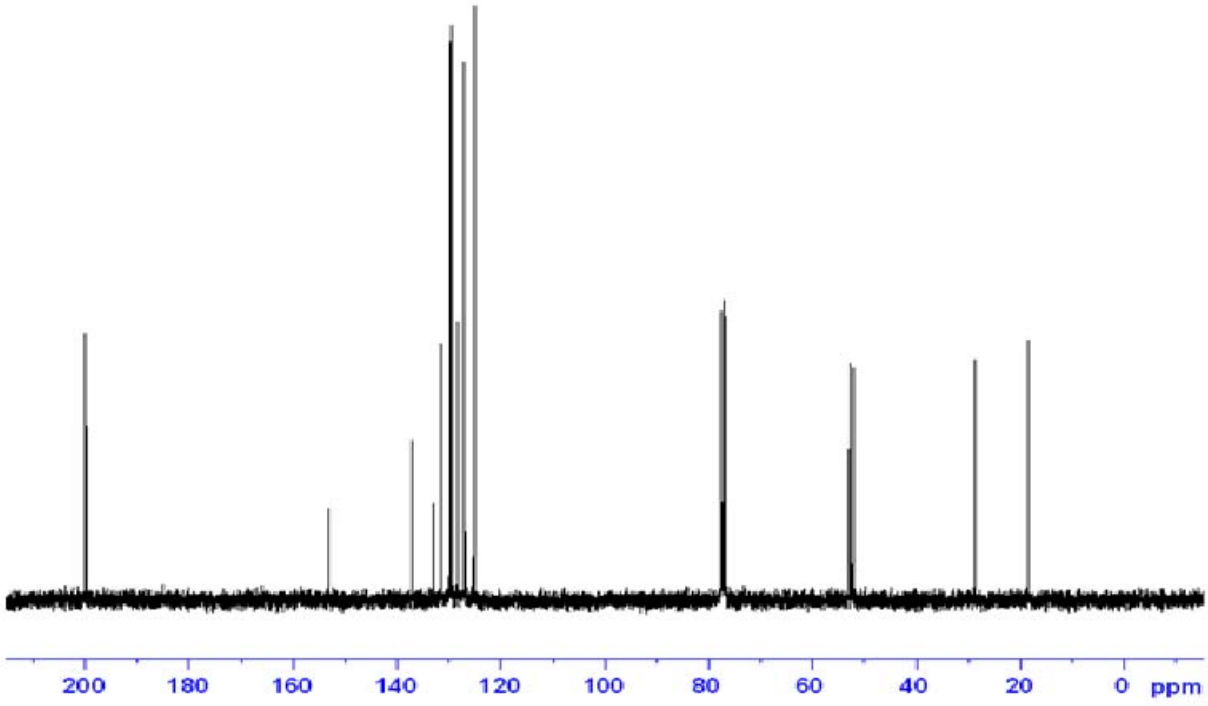
1.00
1.01
3.00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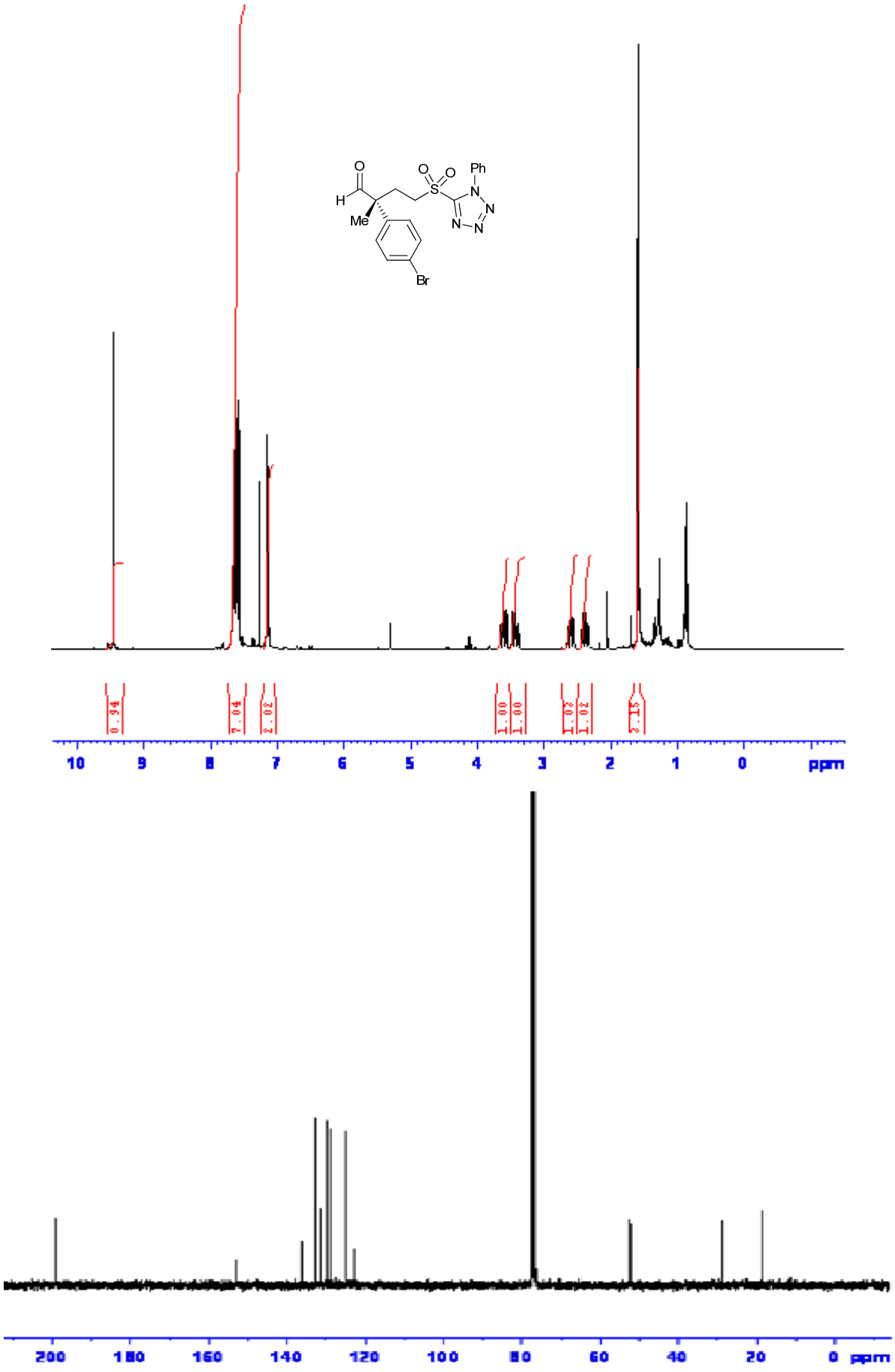
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2.02
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1.02
1.01
2.15
10
9
8
7
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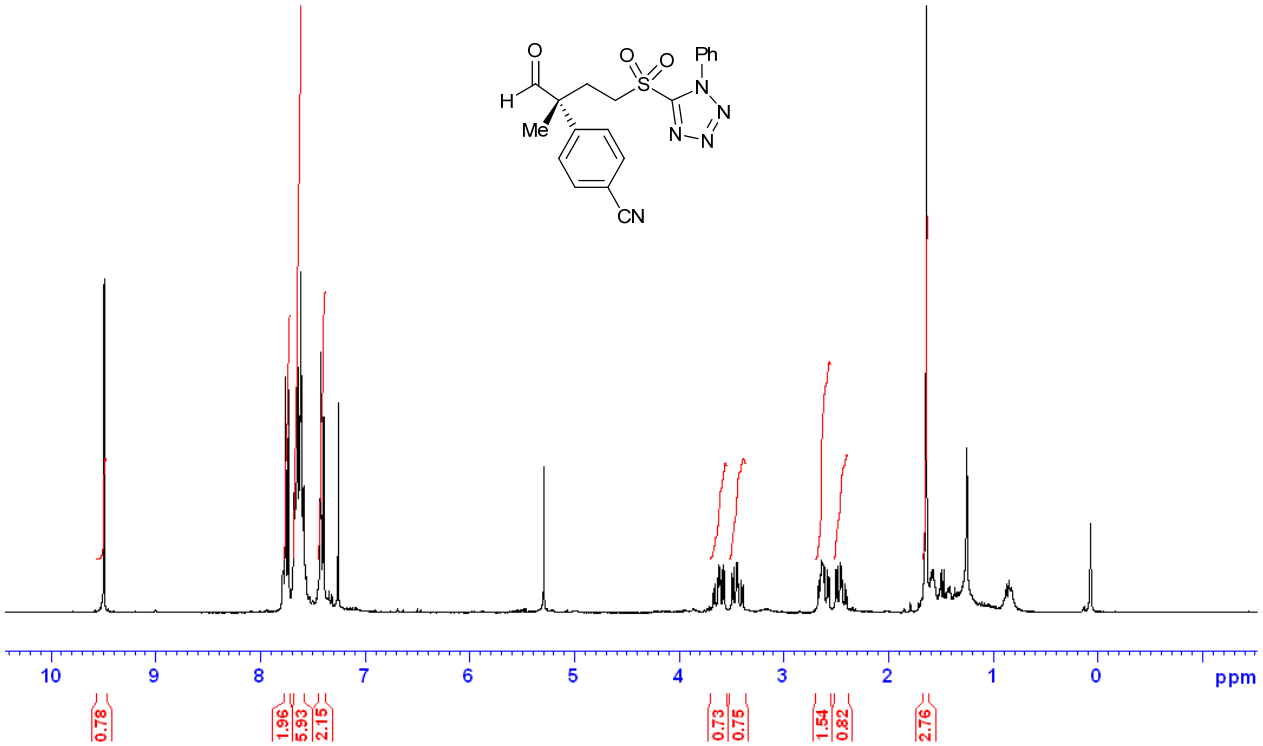
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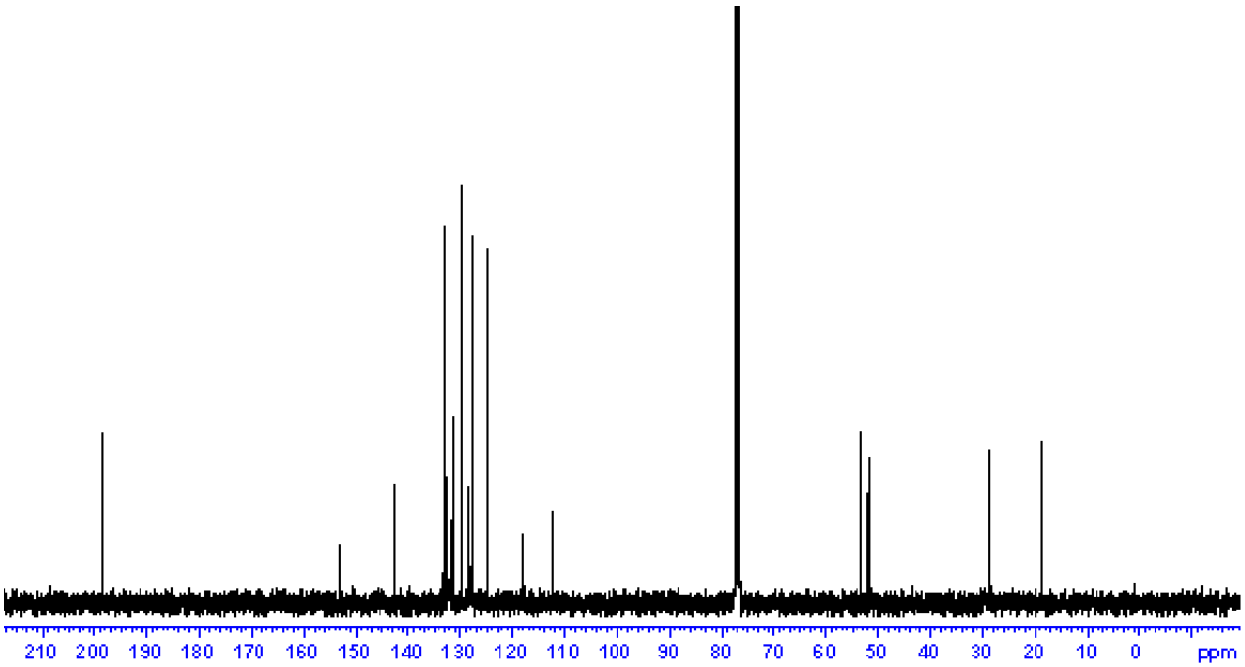
1.54
0.82
2.76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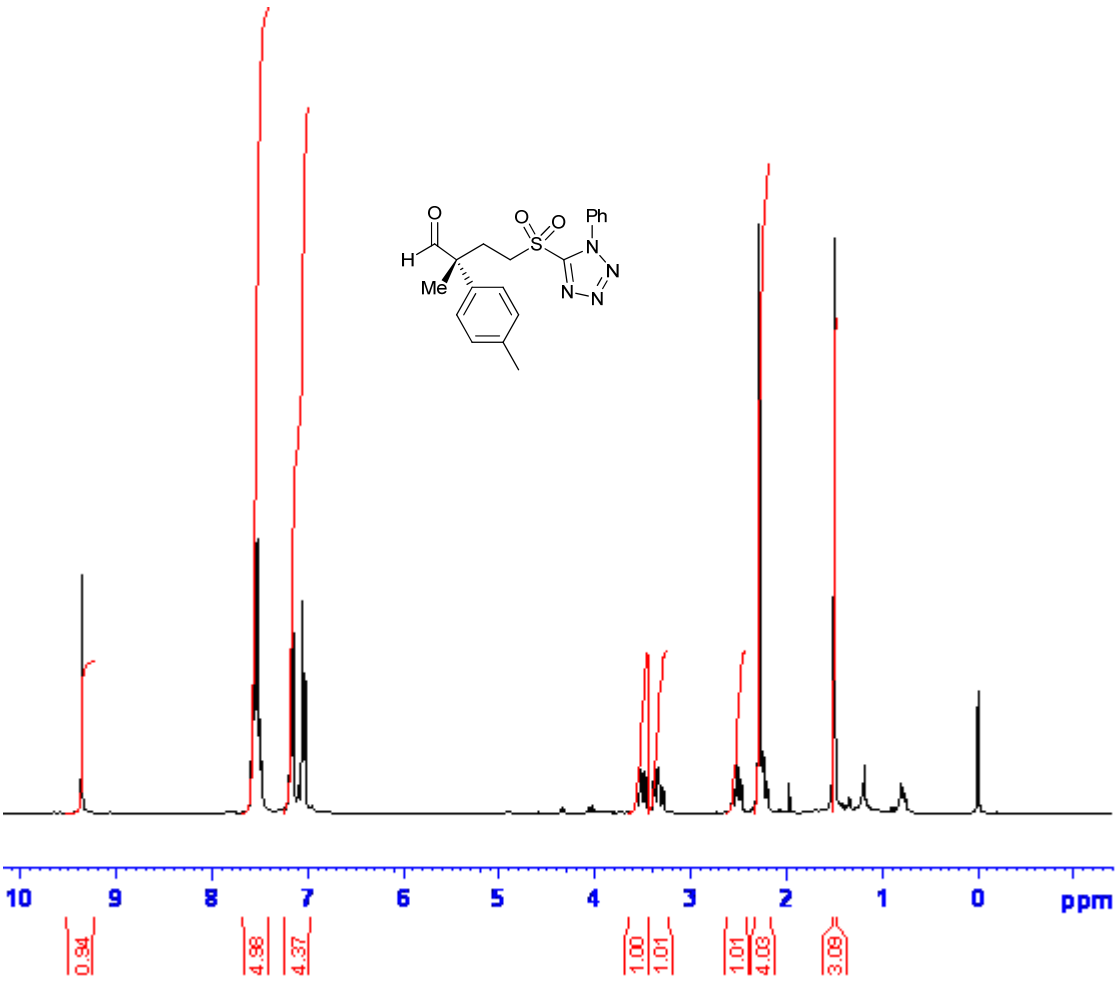
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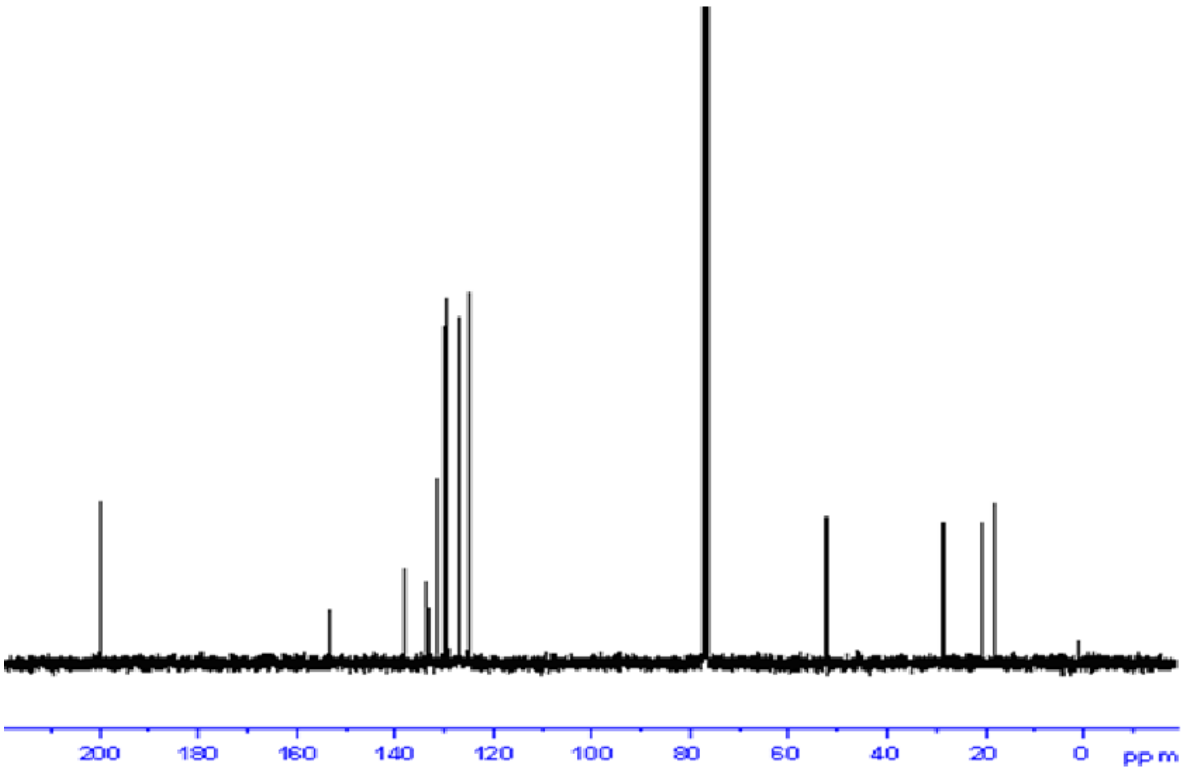
4.03
3.09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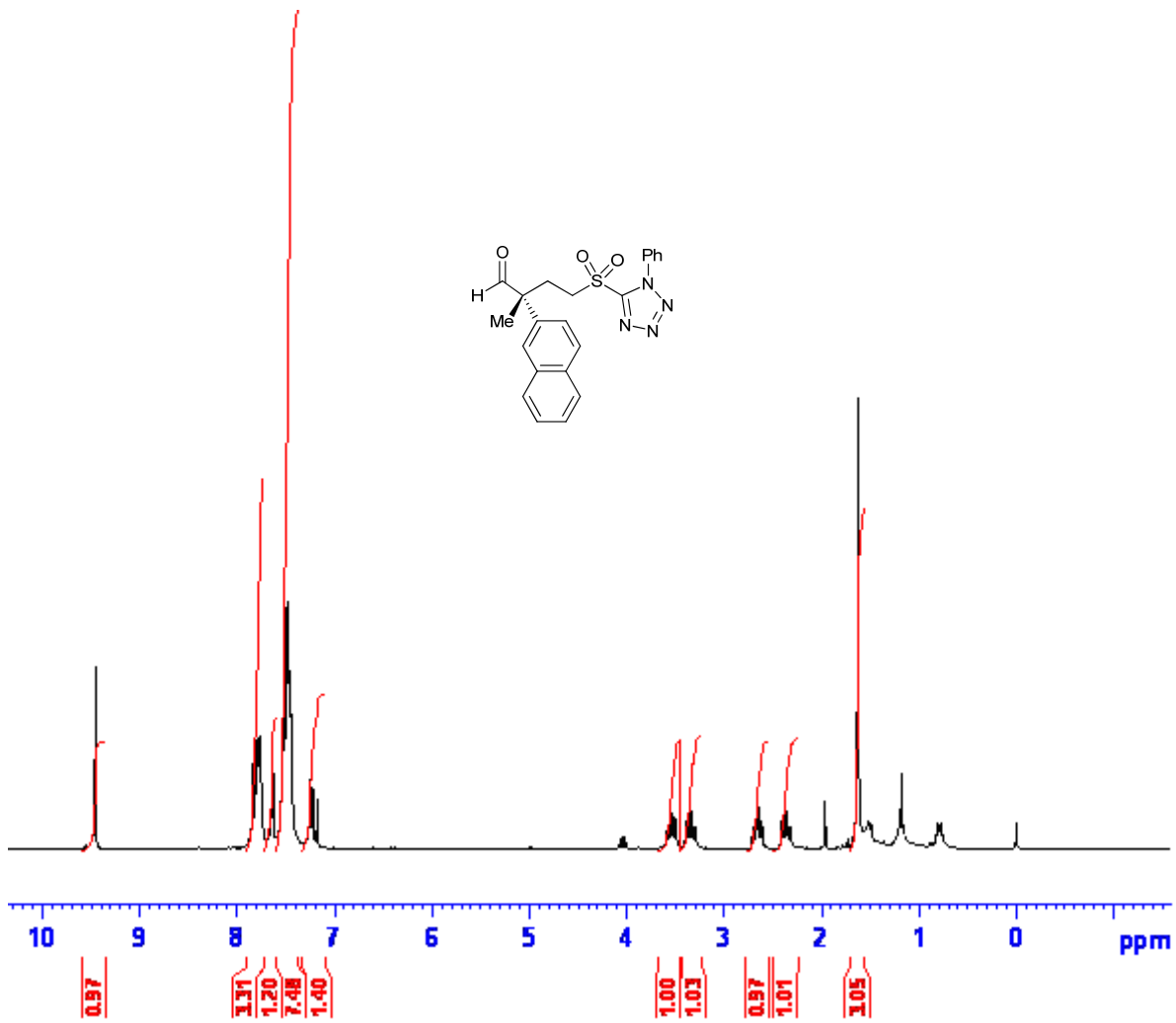
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1.00
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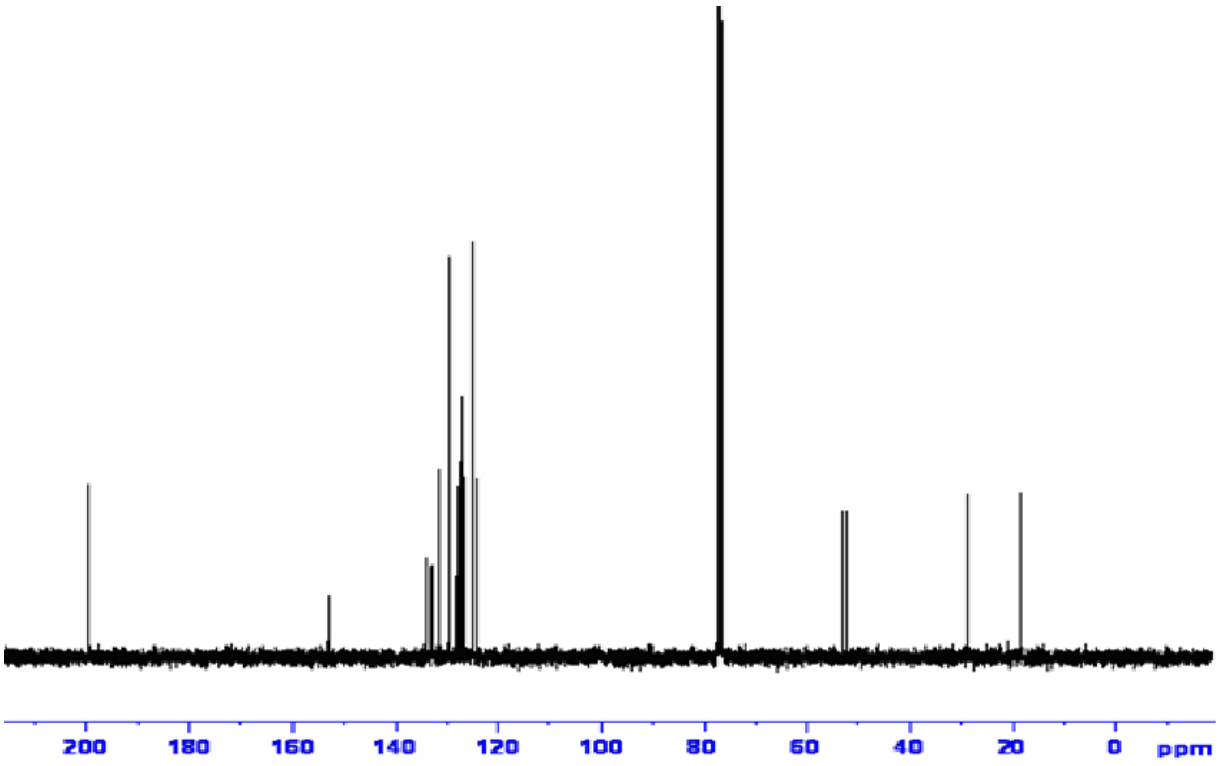
0.97
1.01
3.05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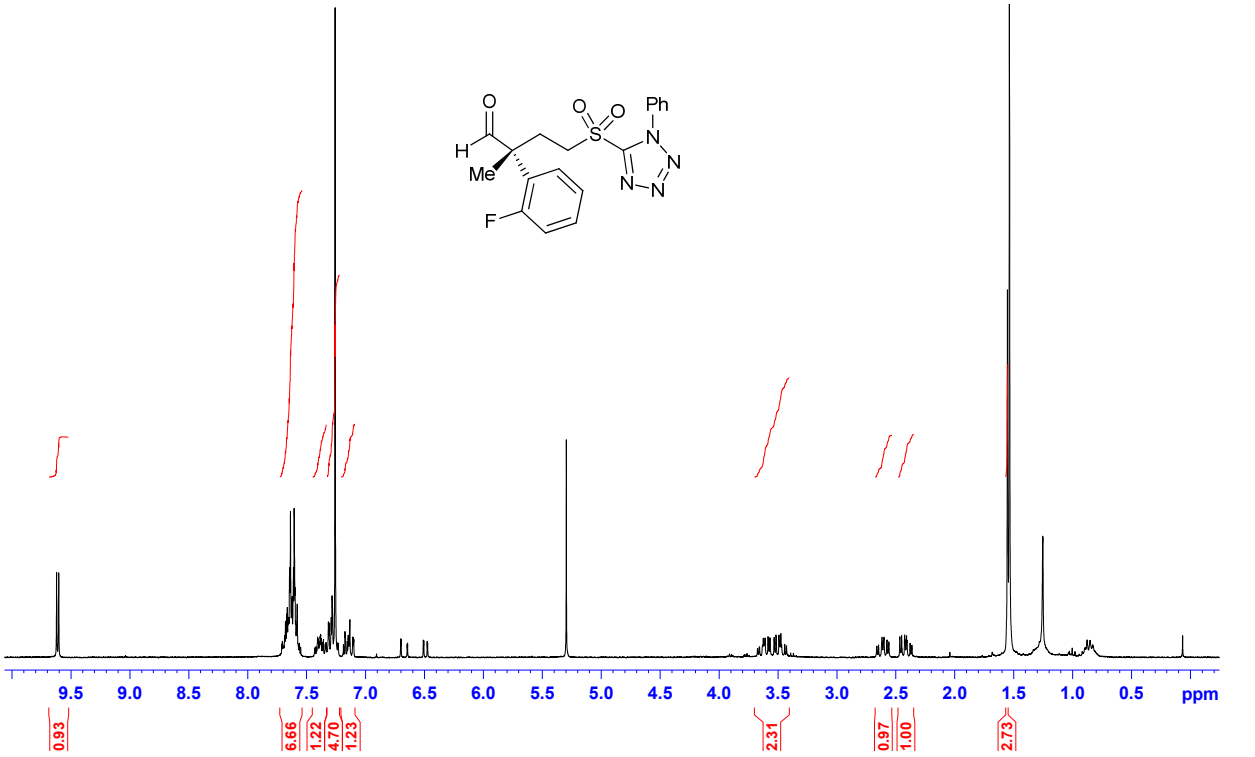
ppm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Me
F
O
O
S
Ph
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N
N
N
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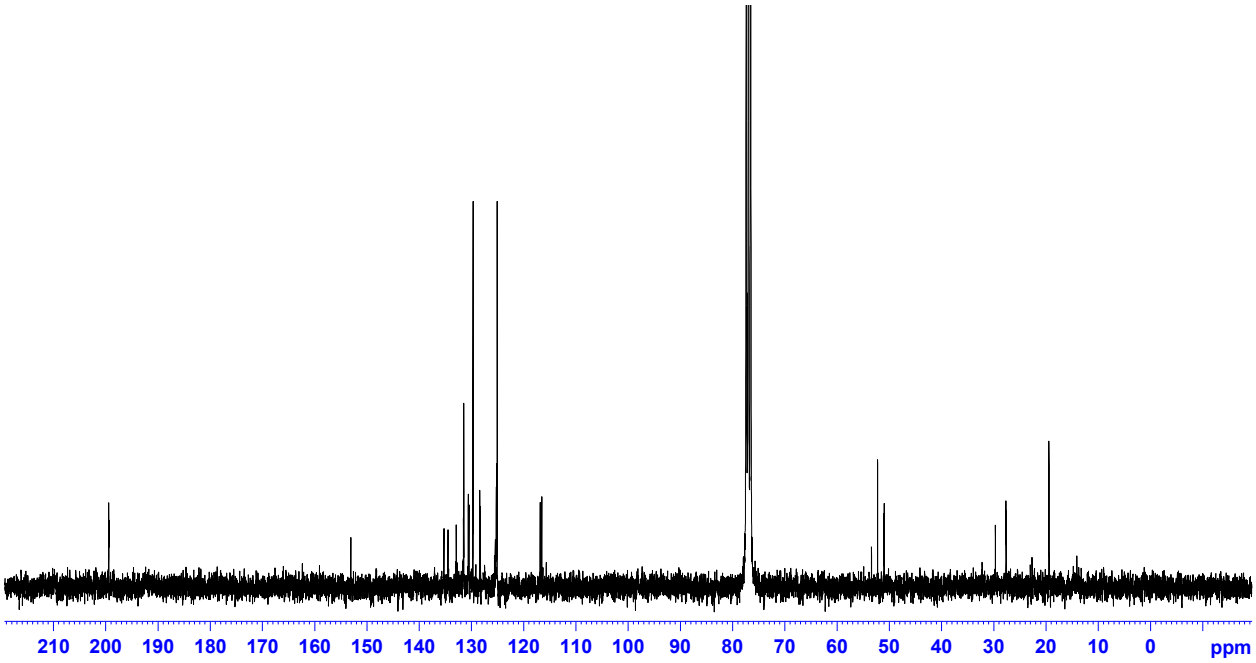
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm
0.93
6.66
1.22
4.70
1.23
2.31
0.97
1.00
2.73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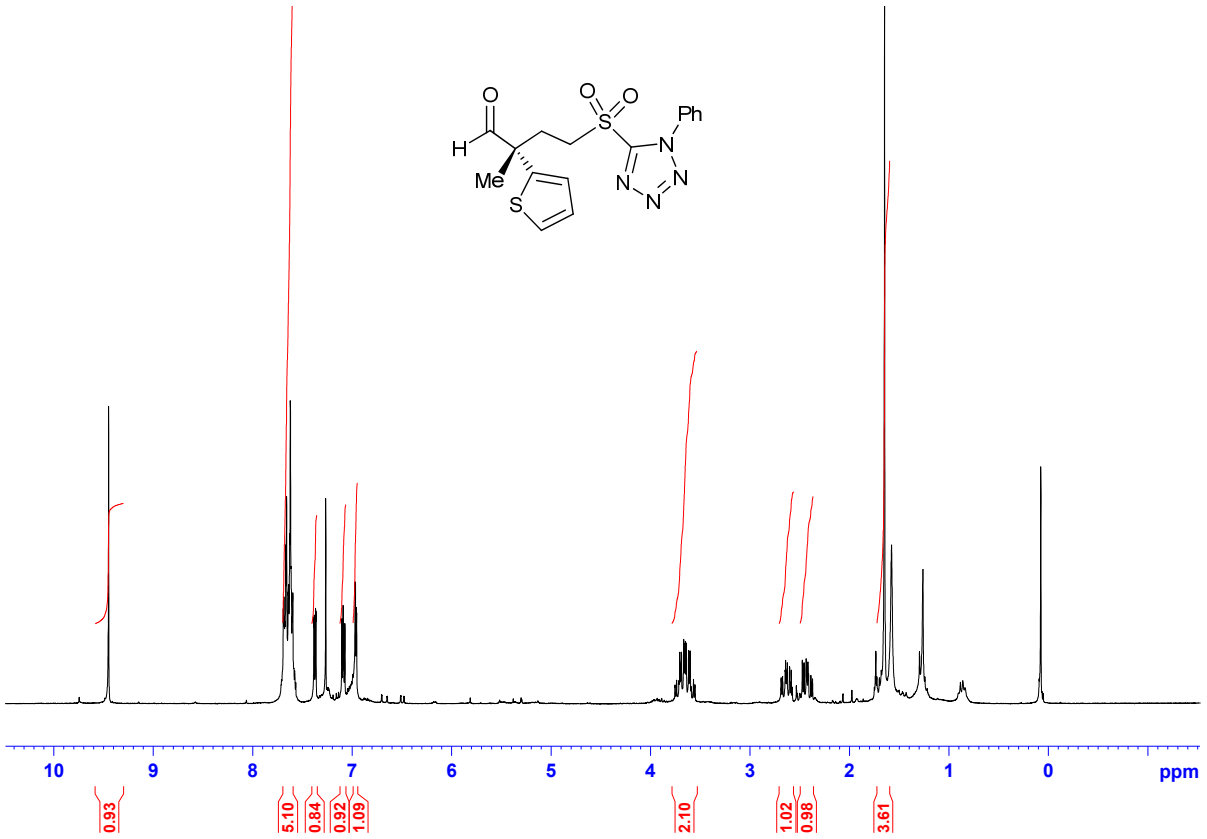
ppm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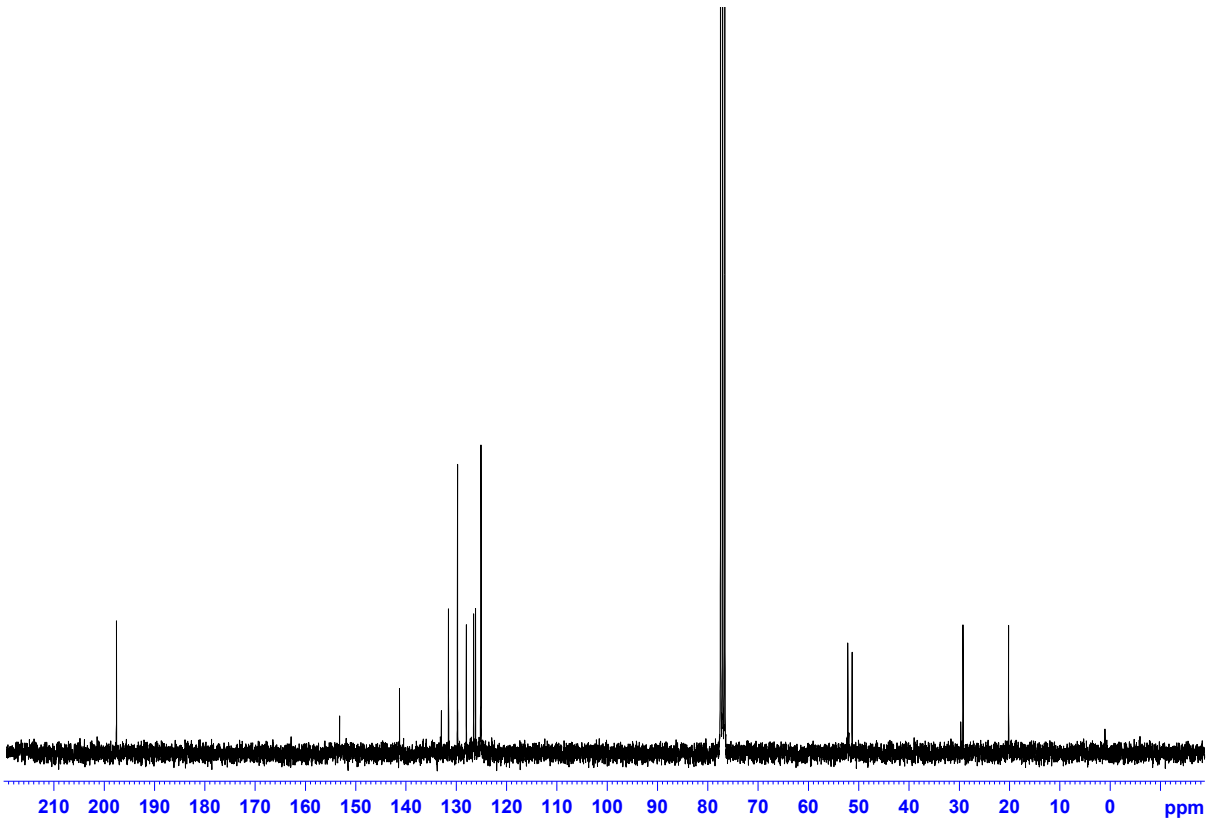
O
O
S
Ph
H
N
Me
N
N
S
10
9
8
7
6
5
4
3
2
1
0
ppm
0.93
5.10
0.84
0.92
1.09
2.10
1.02
0.98
3.61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200
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170
160
150
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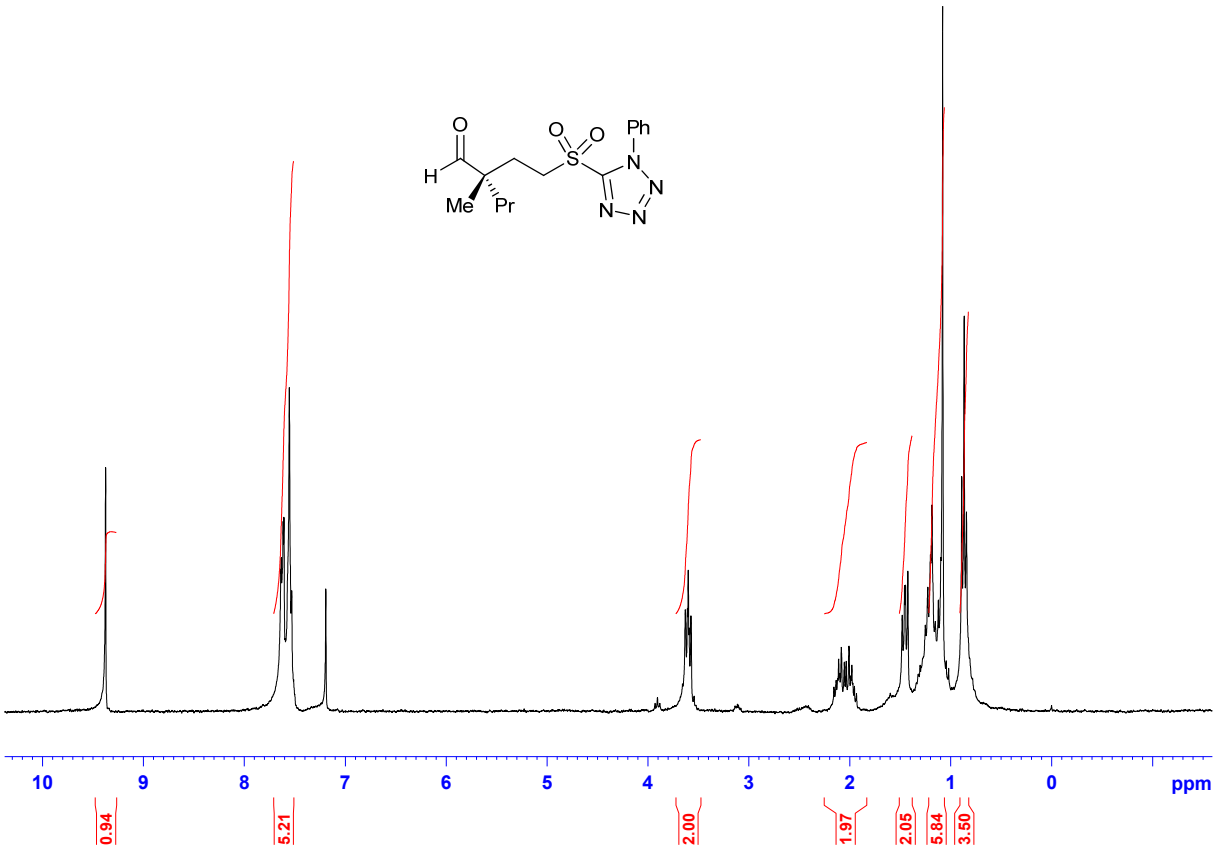
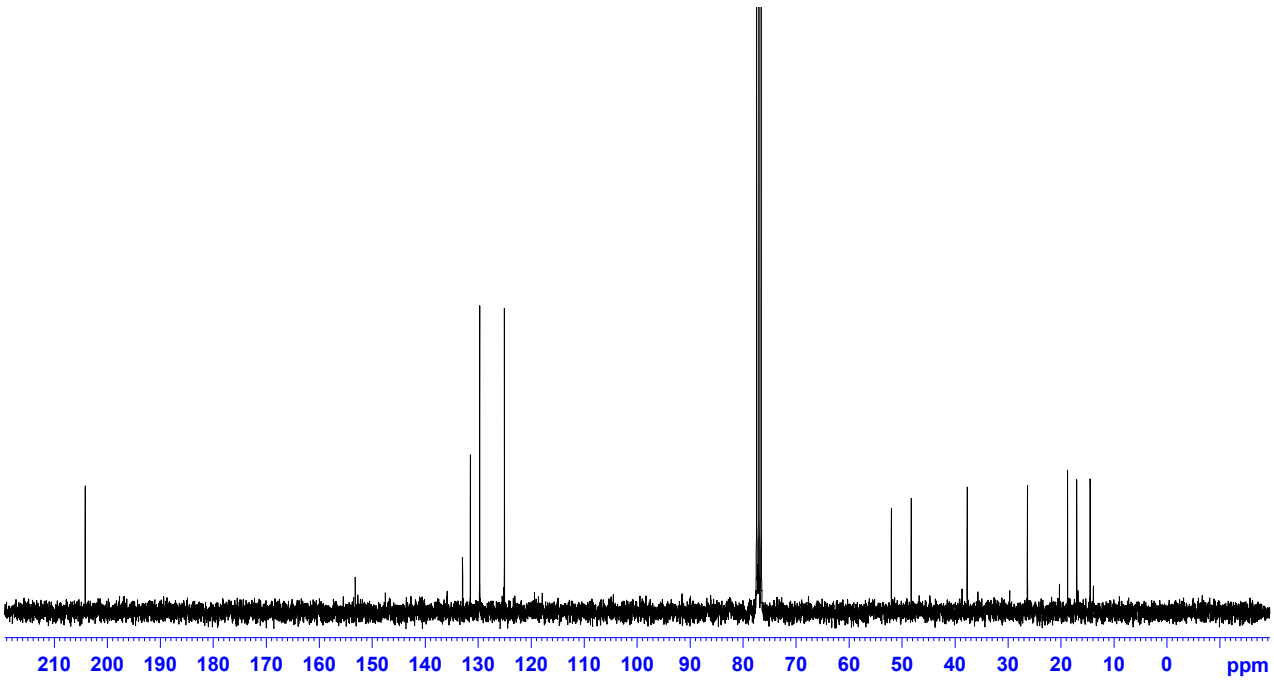
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


O
H
Me
Pr
O
O
S
Ph
N
N
N
N
10
9
8
7
6
5
4
3
2
1
0
ppm
0.94
5.21
2.00
1.97
2.05
5.84
3.50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200
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170
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150
140
130
120
110
100
90
80
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60
50
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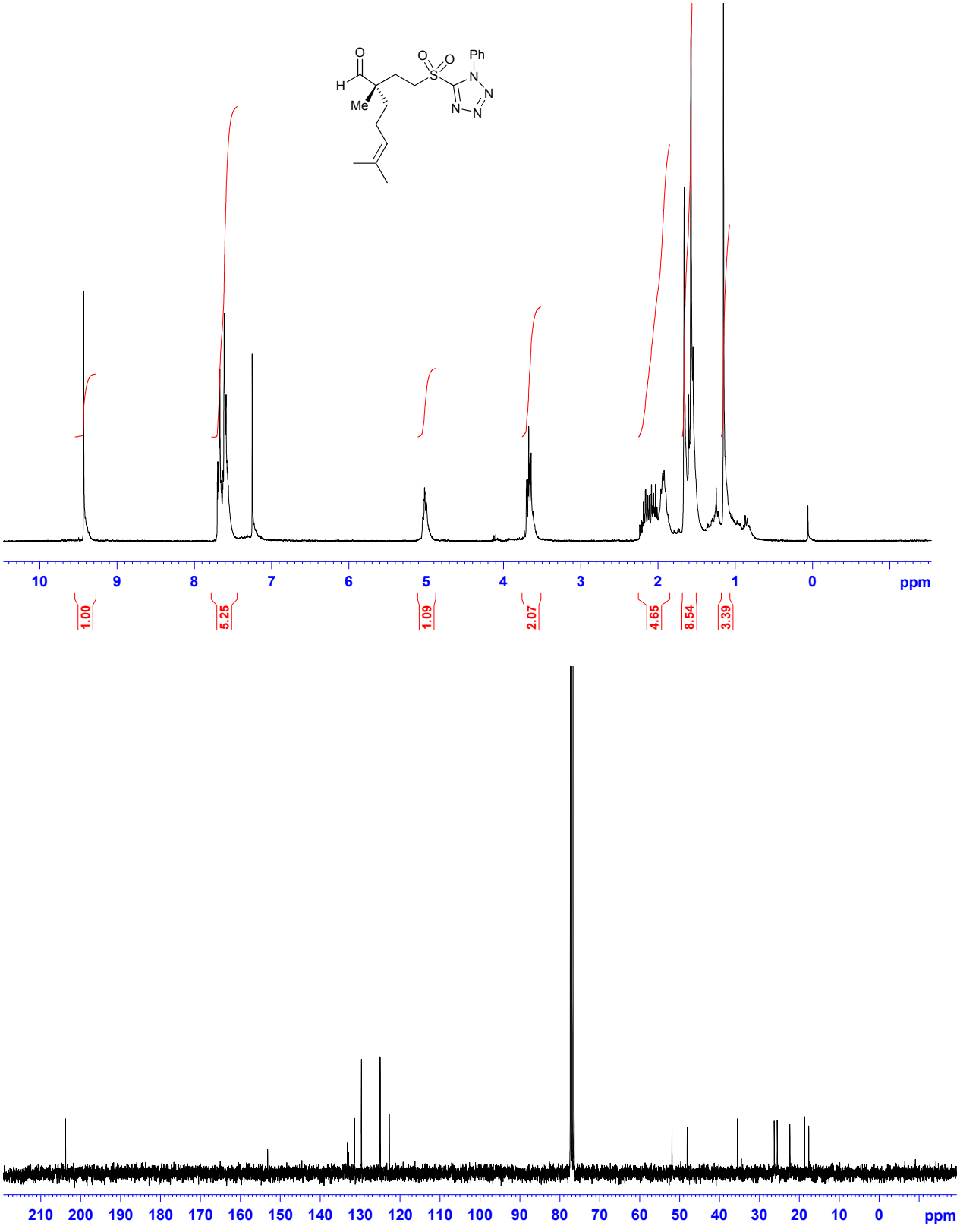
30
20
10
0
ppm


O
H
Me
O
O
S
Ph
N
N
N
N
10
9
8
7
6
5
4
3
2
1
0
ppm
1.00
5.25
1.09
2.07
4.65
8.54
3.39
210
200
190
180
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140
130
120
110
100
90
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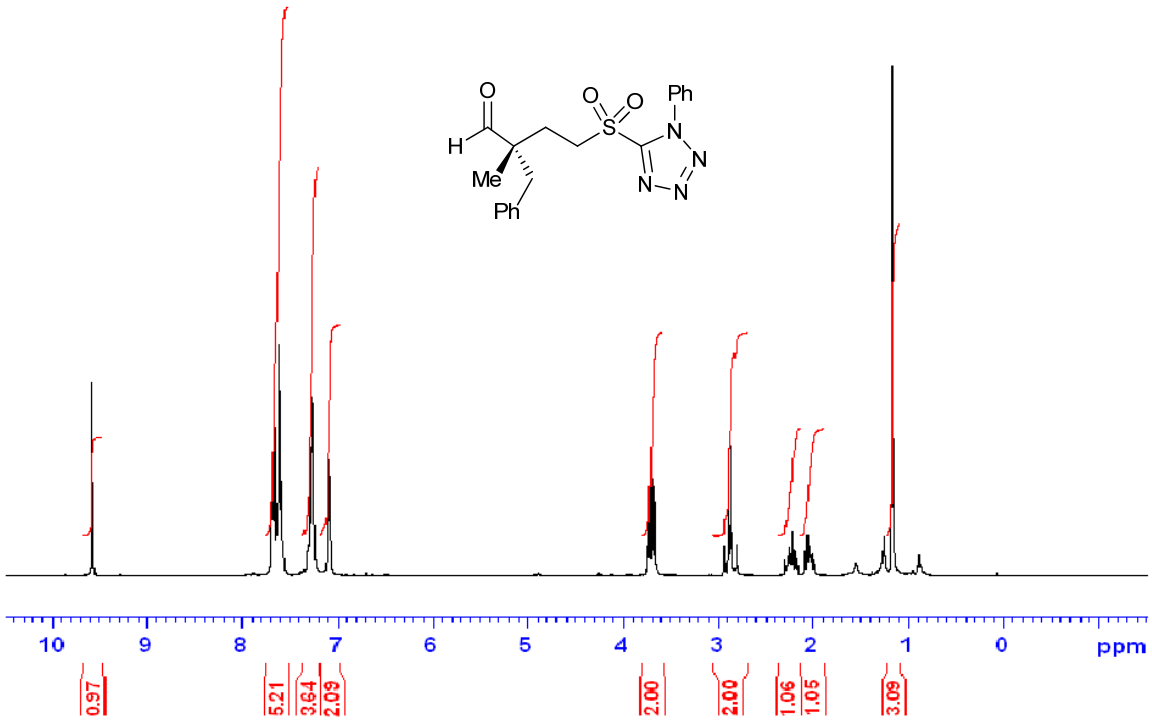
60
50
40
30
20
10
0
ppm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H
Me
Ph
O
O
S
Ph
N
N
N
N
10
9
8
7
6
5
4
3
2
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ppm
0.97
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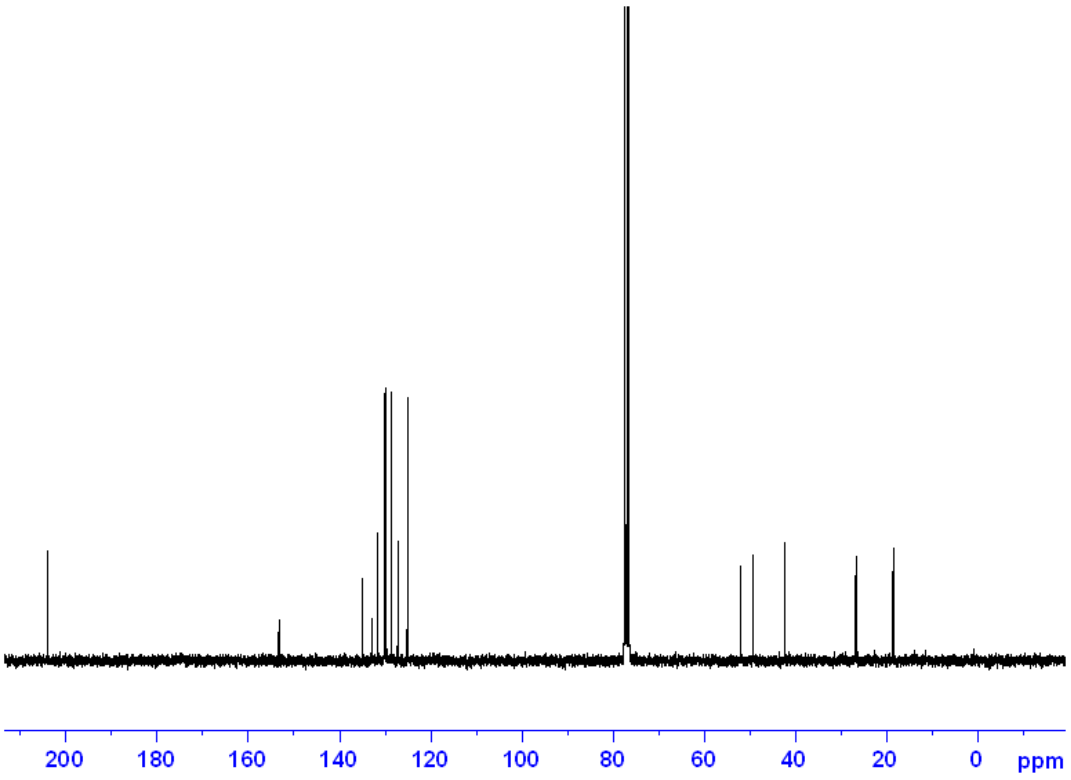
3.64
2.09
2.00
2.00
1.06
1.05
3.09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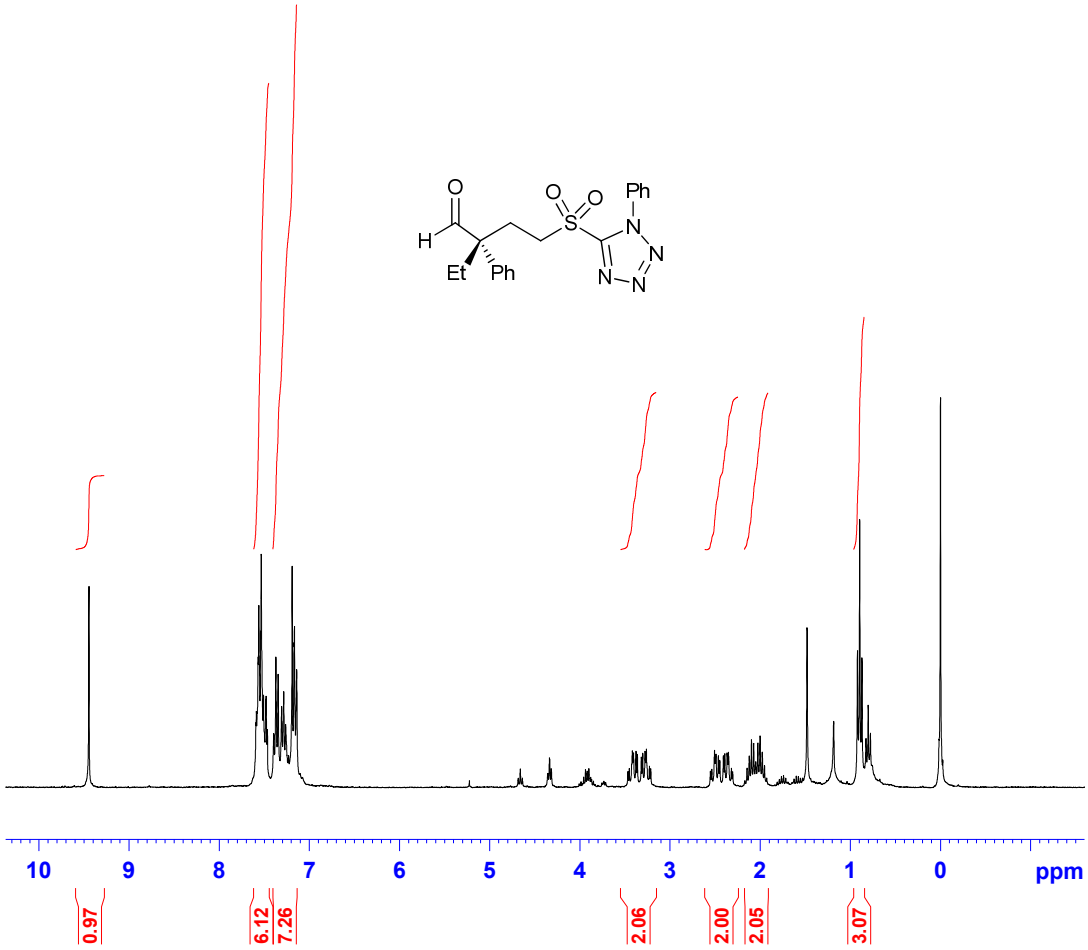
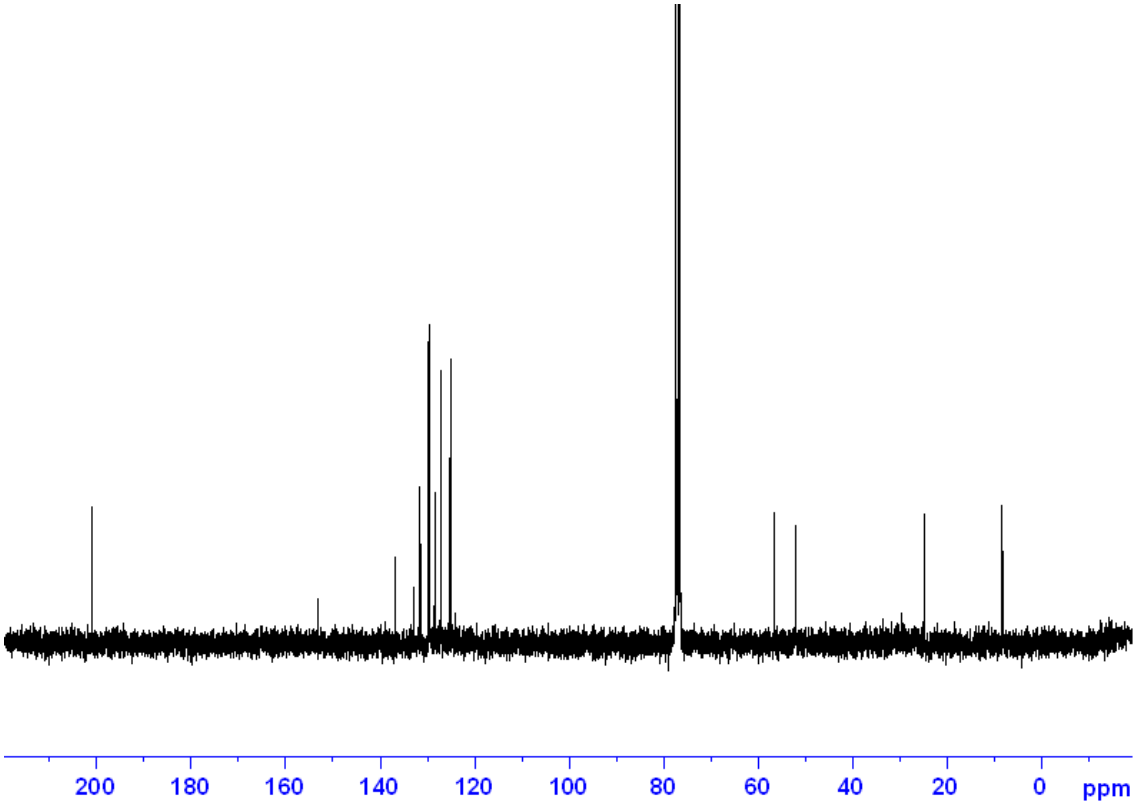
160
140
120
100
80
60
40
20
0
ppm


O
H
Et
Ph
O
O
S
Ph
N
N
N
N
10
9
8
7
6
5
4
3
2
1
0
ppm
0.97
6.12
7.26
2.06
2.00
2.05
3.07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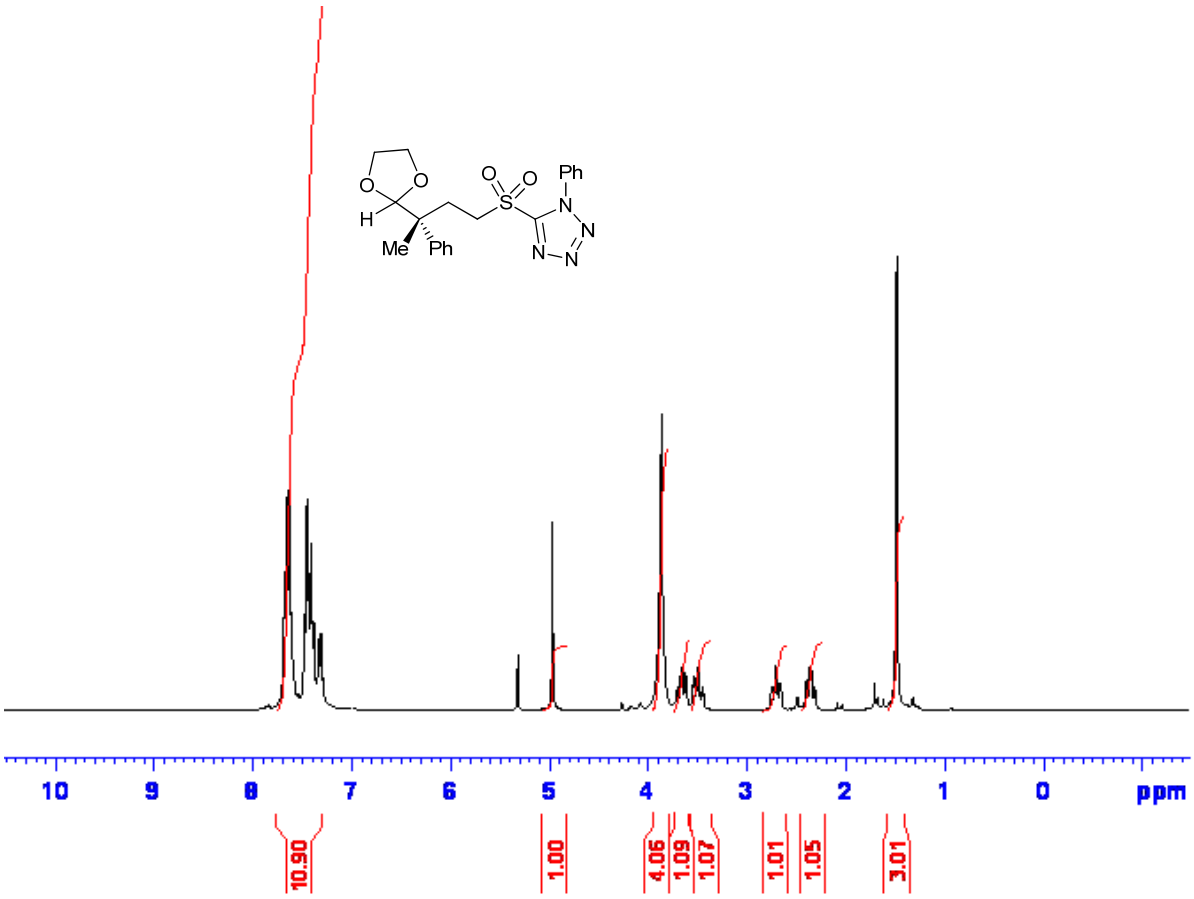
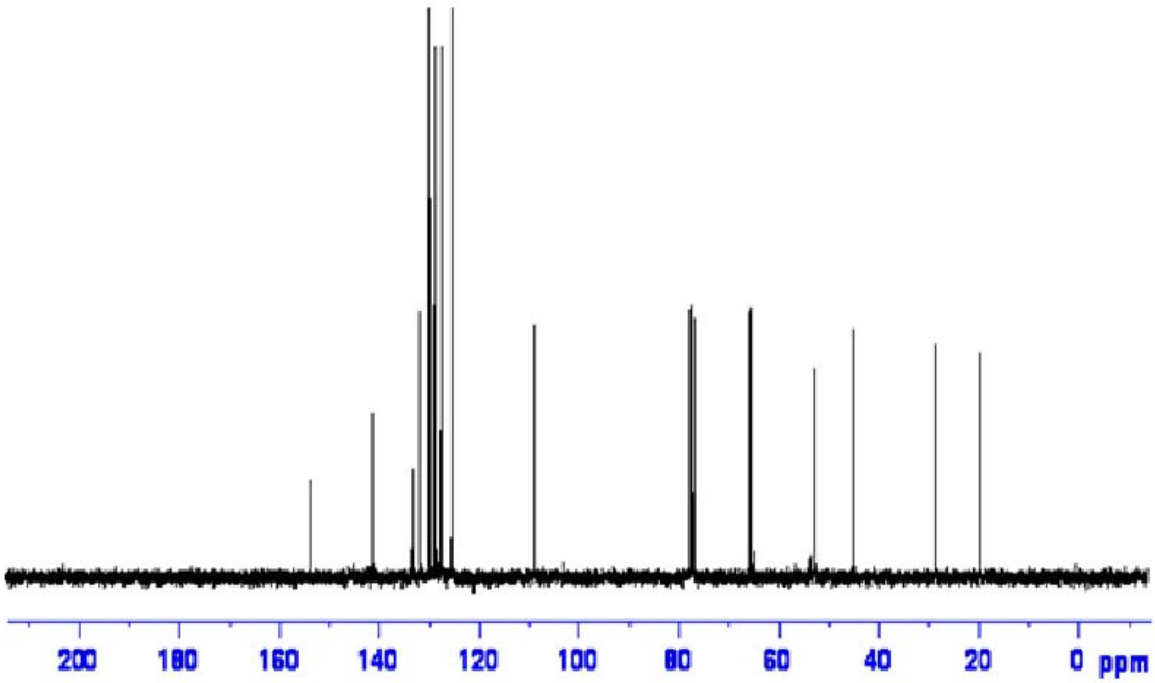
140
120
100
80
60
40
20
0
ppm


O
O
H
Me
Ph
O
O
S
Ph
N
N
N
N
10
9
8
7
6
5
4
3
2
1
0
ppm
10.90
1.00
4.06
1.09
1.07
1.01
1.05
3.01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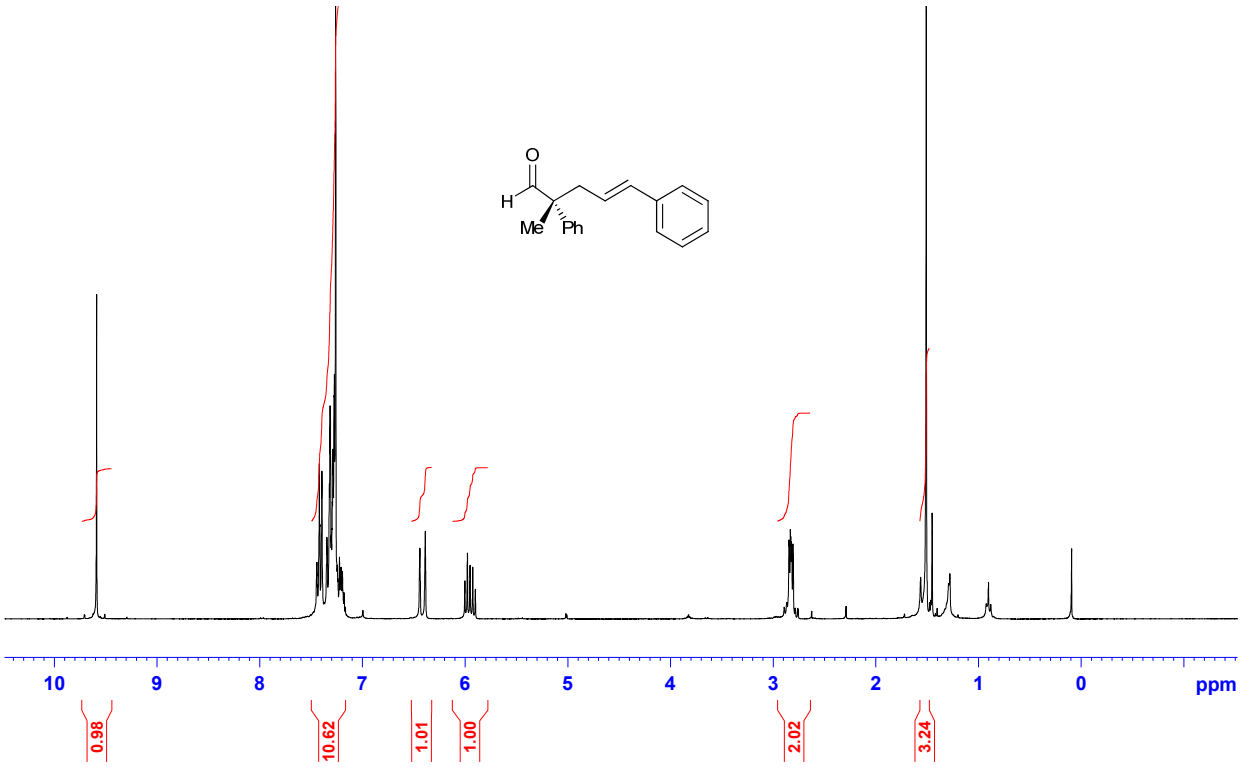
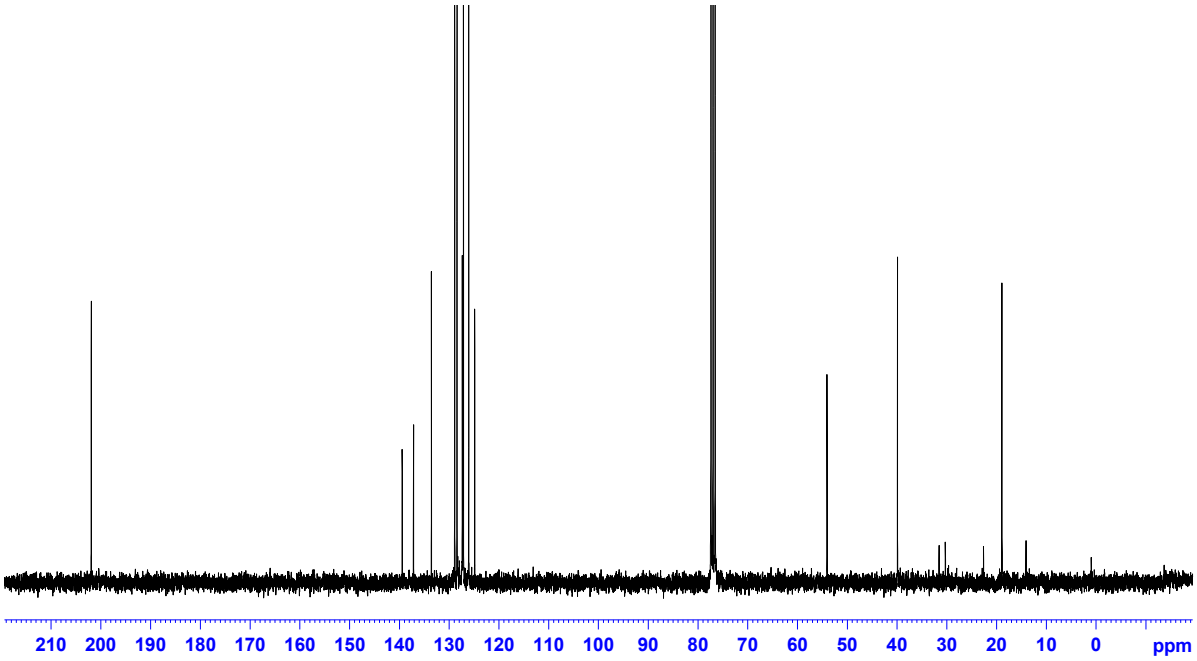
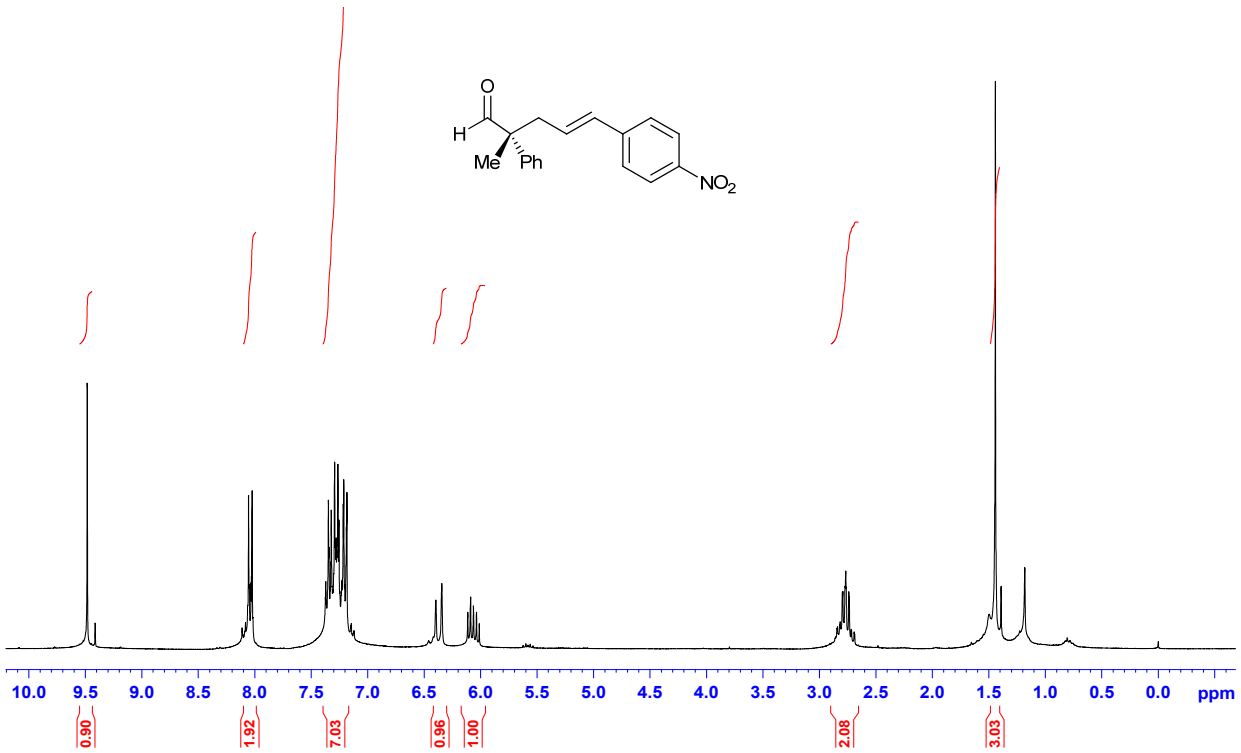
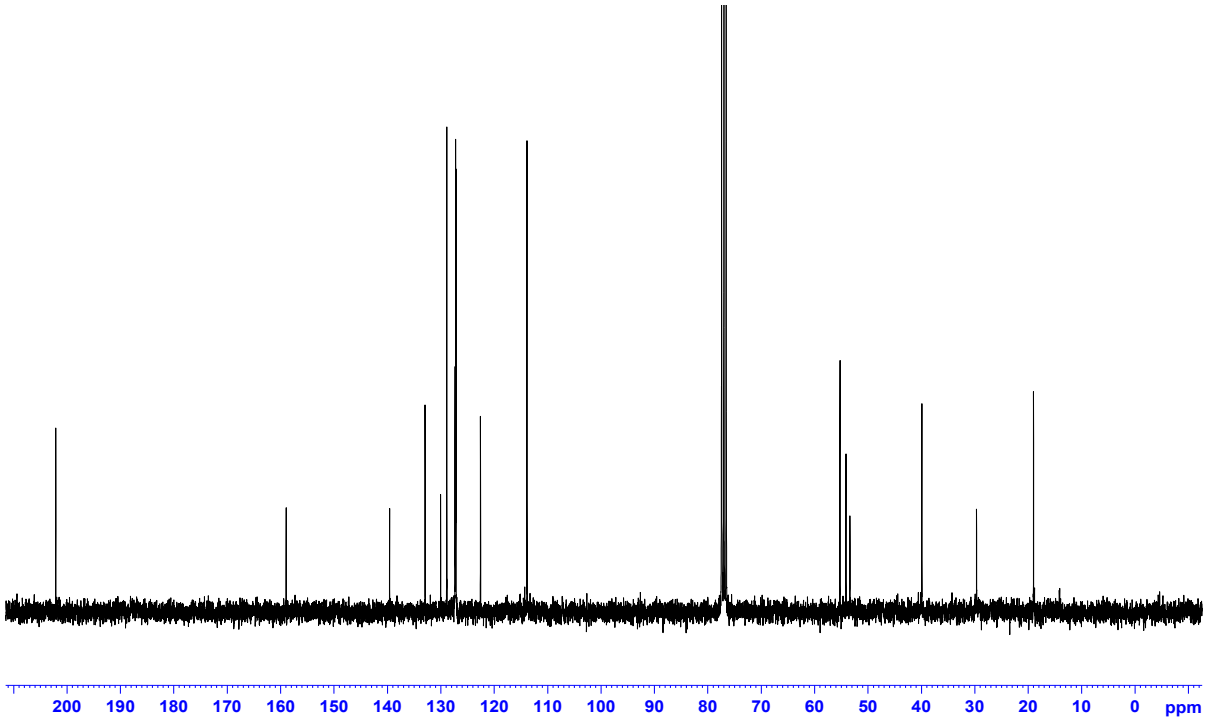
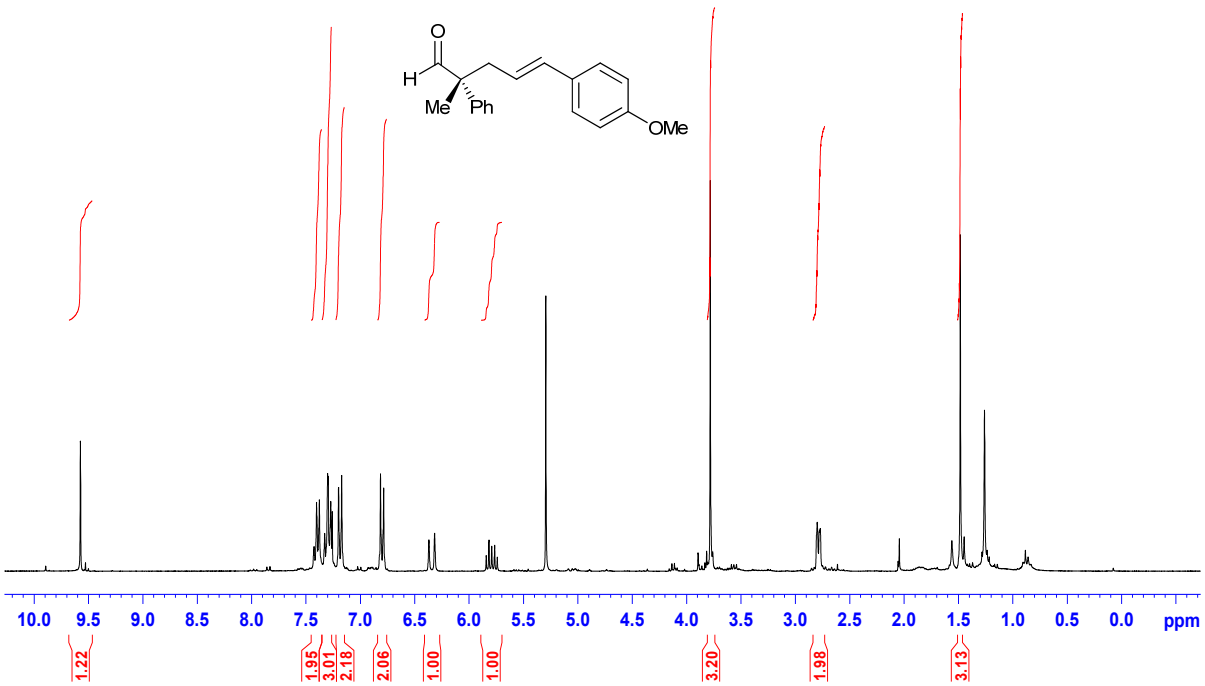
180
160
140
120
100
80
60
40
20
0
ppm

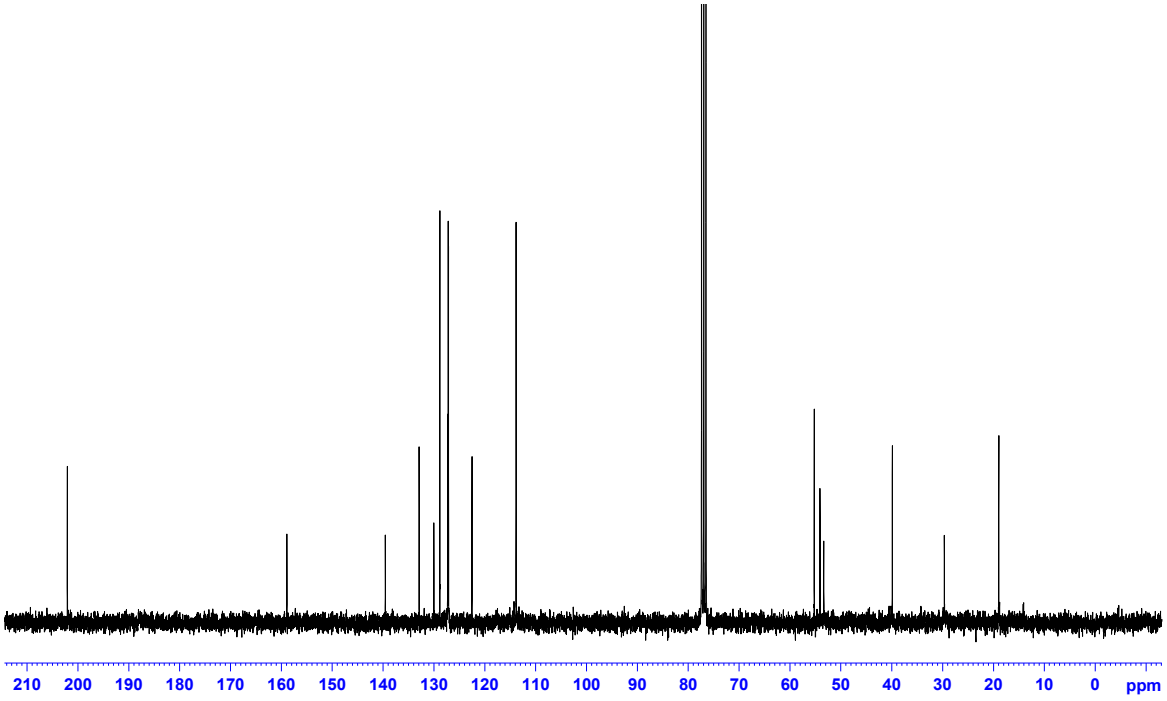

O
H
Me
Ph
10
9
8
7
6
5
4
3
2
1
0
ppm
0.98
10.62
1.01
1.00
2.02
3.24

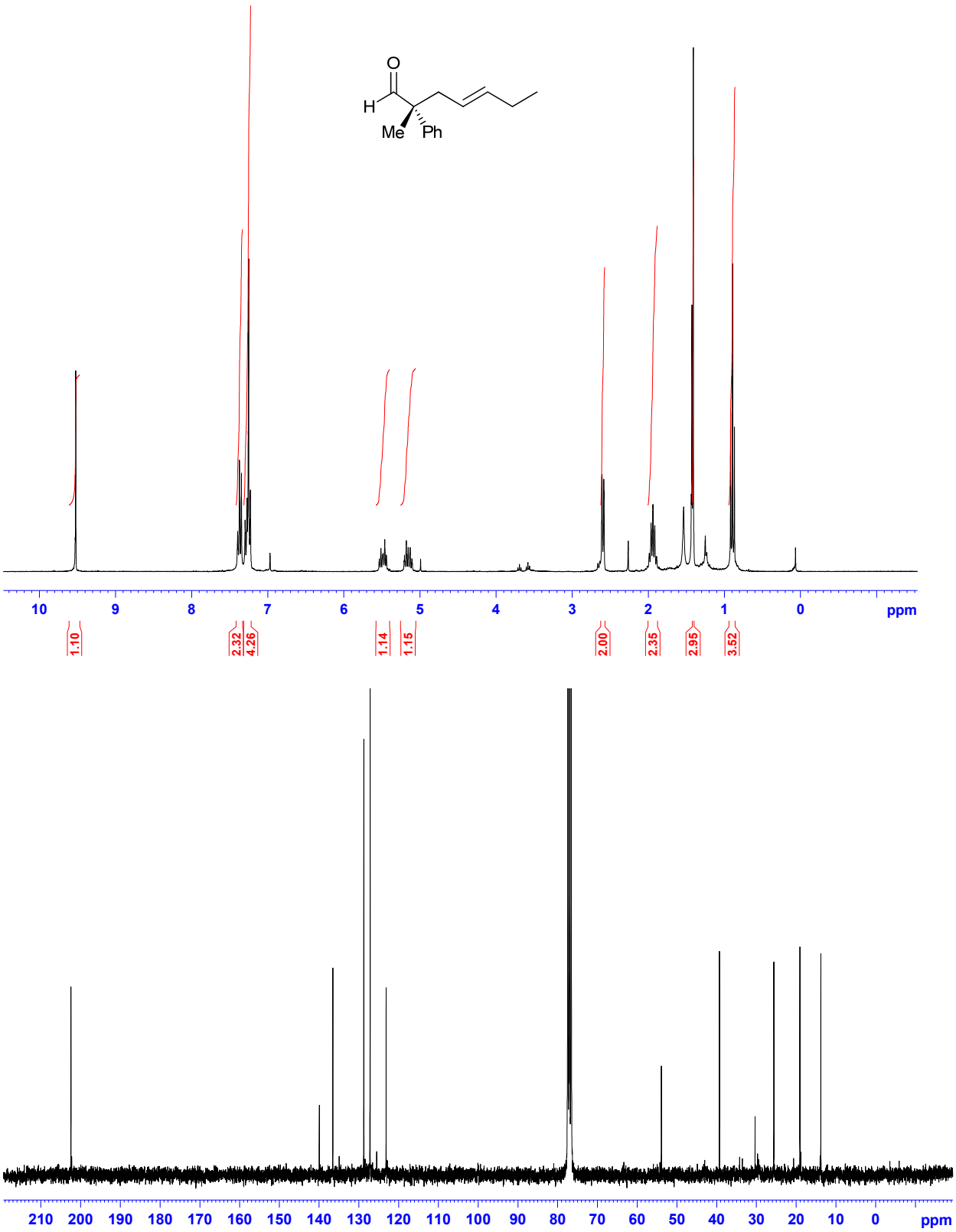

210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

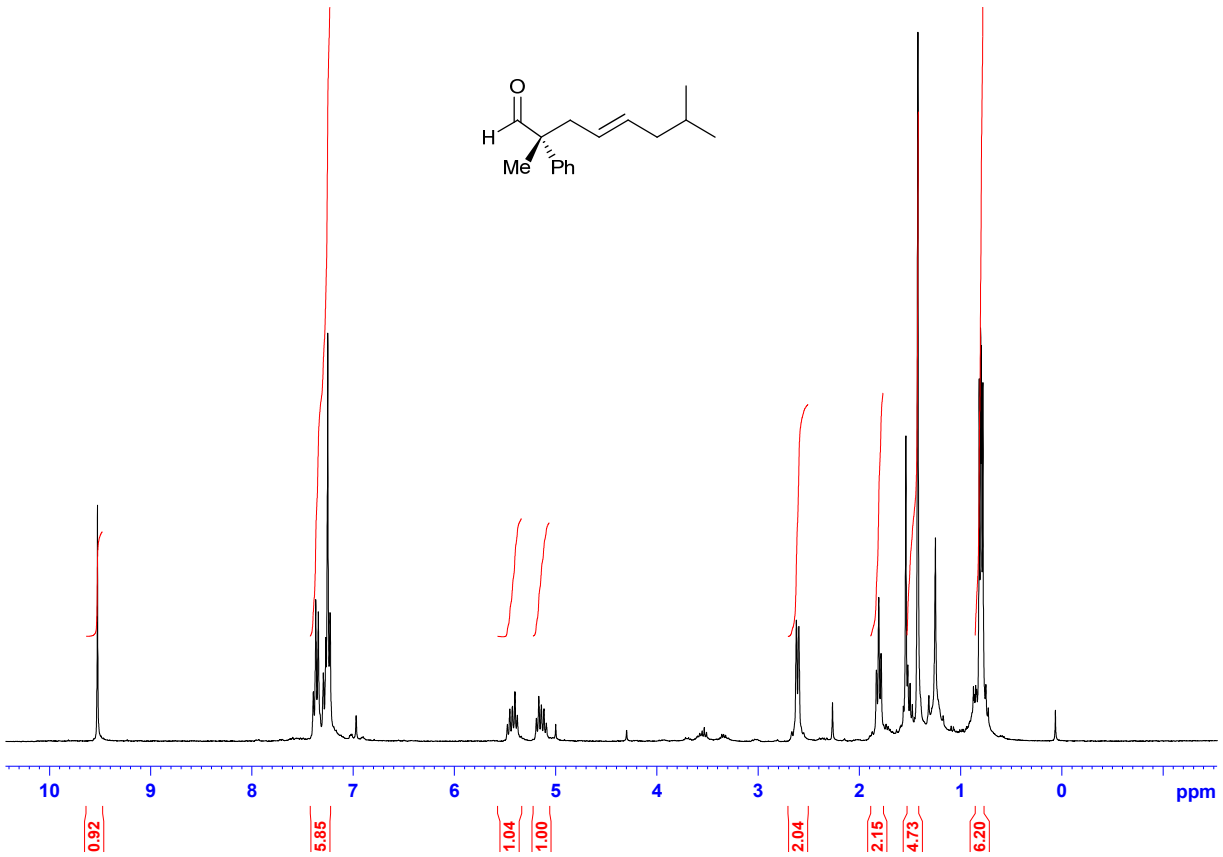

O
H
Me
Ph
NO2
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
0.90
1.92
7.03
0.96
1.00
2.08
3.03

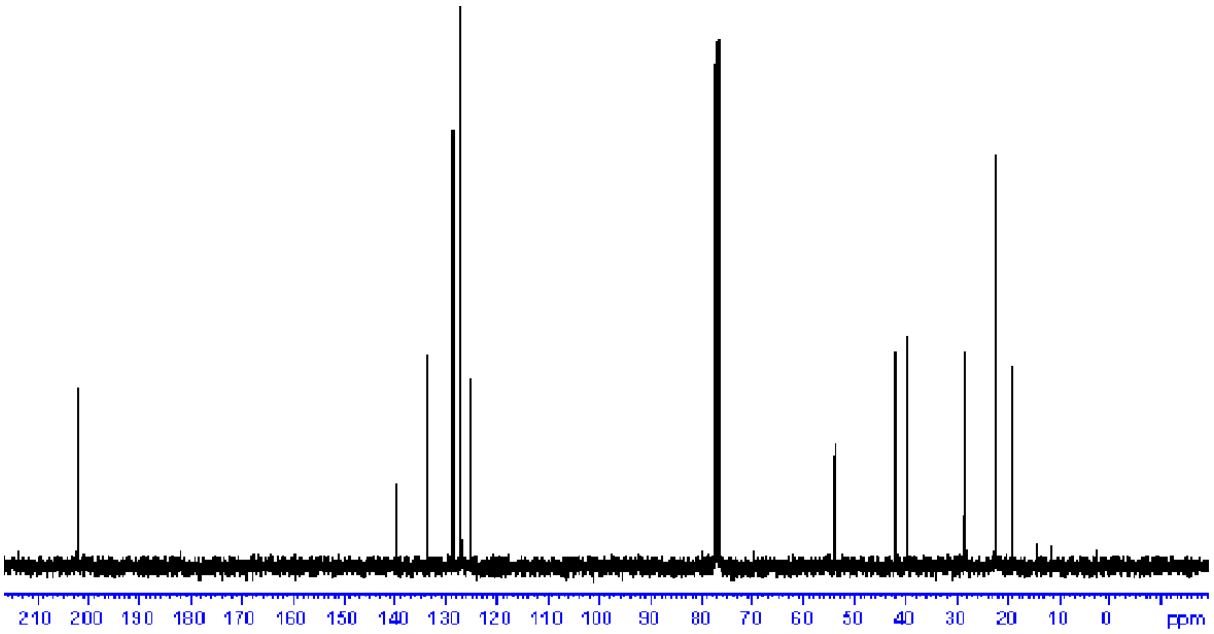

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


O
H
Me
Ph
OMe
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm
1.22
1.95
3.01
2.18
2.06
1.00
1.00
3.20
1.98
3.13


210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm


O
H
Me
Ph
10
9
8
7
6
5
4
3
2
1
0
ppm
1.10
2.32
4.26
1.14
1.15
2.00
2.35
2.95
3.52
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


O
H
Me
Ph
10
9
8
7
6
5
4
3
2
1
0
ppm
0.92
5.85
1.04
1.00
2.04
2.15
4.73
6.20


210
200
190
180
170
160
150
140
130
120
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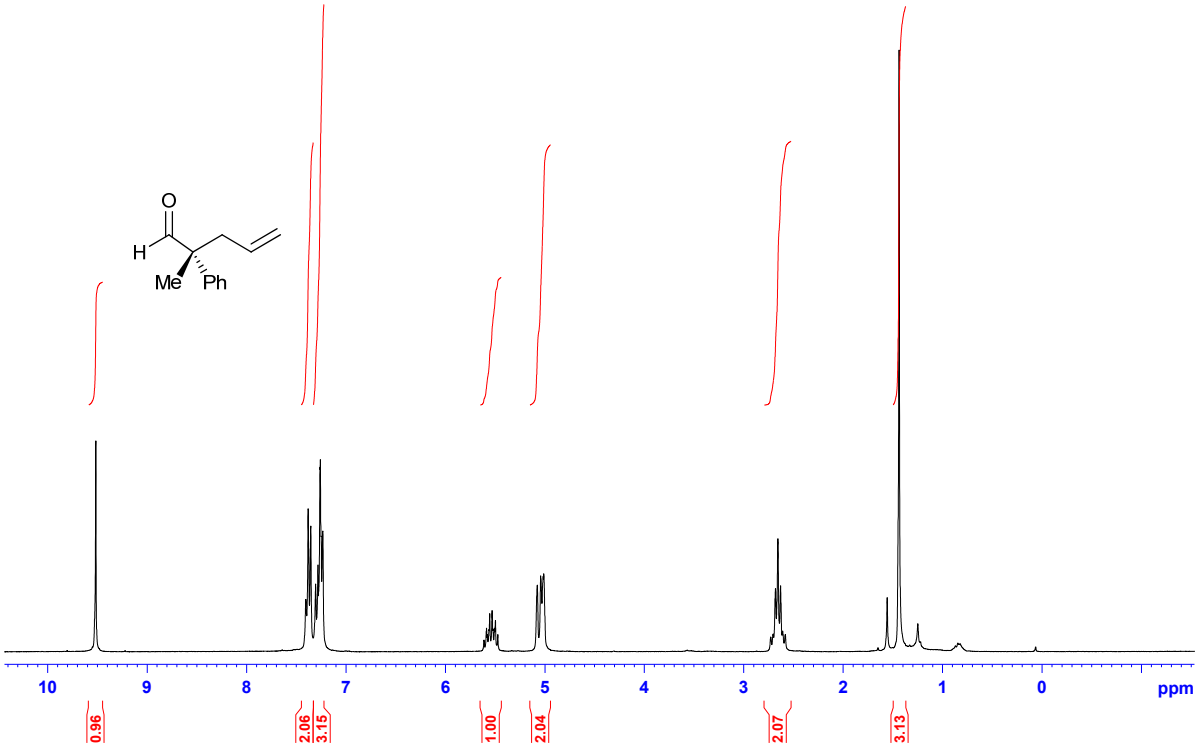
100
90
80
70
60
50
40
30
20
10
0
ppm



- Literature ^{1}H NMR spectrum for compound **5aF**:
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