Asymmetric addition of α-hetero-disubstituted aldehydes to vinyl sulfones; formation of highly functionalized tetra-substituted carbon centres.

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General Remarks:

^{1}H (400 MHz or 300 MHz), ^{13}C (75 MHz) NMR spectra were recorded on a Bruker 400 FT or Bruker 300 FT NMR in $CDCl_3$, and chemical shift (δ) are given in ppm relative to residual $CHCl_3$. Multiplicity is indicated as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), dd (doublet of doublet), dt (doublet of triplet), ddd (doublet of doublet of doublet), brs (broad singlet). Coupling constants are reported in Hertz (Hz). Mass spectra (MS) were obtained by ESI and High resolution mass spectra HRMS by Electrospray Ionisation (ESI). Optical rotations were recorded on a Perkin-Elmer 241 polarimeter at 20°C in a 10 cm cell in $CHCl_3$; $[\alpha]_D$ values are given in 10^{-1} $deg.cm^{2}$ g^{-1} (concentration c given as g/100 mL). Enantiomeric excesses were determined by chiral-SFC measurement on a Berger SFC with the stated column. Gradient programs are described as follows: initial methanol concentration (%) - initial time (min) - percent gradient of methanol (% / min) - final methanol concentration (%); retention times (R_T) are given in min. Flash chromatography was performed using silica gel 60 Å. All the organocatalysed reactions were conducted in non-dried solvents.

Catalyst **4c** and **4d** were prepared according to procedures developped in our group.[1] Oxygenated aldehyde **9**,[2] aminated aldehyde **10**,[3] were prepared according to known procedures. Chlorinated aldehydes were prepared on 10mmol scale according to known procedures using DL-Proline as catalyst in CH_2Cl_2, followed by simple filtration after precipitation of the impurities by addition of pentane.[4] These chlorinated aldehydes are relatively sensitive and should not be stored more then 2-3 days before use. If non-specified, other products were purchased directly from commercial sources.

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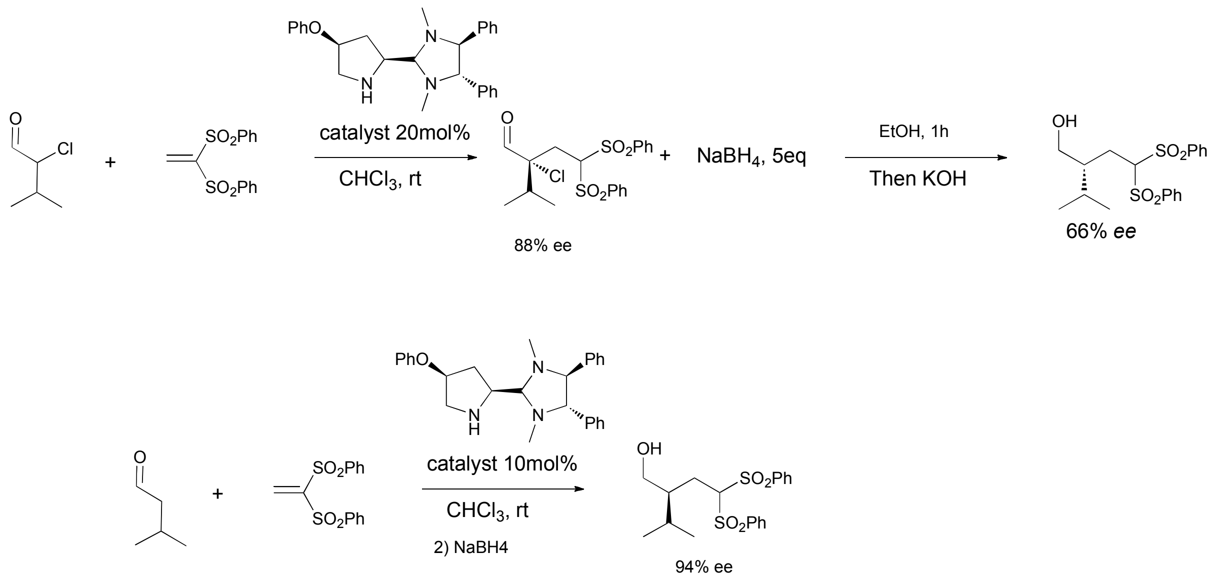
[1] A. Quintard, S. Belot, E. Marchal, A. Alexakis, *Eur. J. Org. Chem.* DOI: 10.1002/ejoc.200901283.
[2] U. Chiacchio, A. Corsaro, G. Gumina, A. Rescifina, D. Iannazzo, A. Piperno, G. Romeo, R. Romeo, *J. Org. Chem.* 1999, **64**, 9321.
[3] A. Bogevig, K. Juhl, N. Kumaragurubaran, W. Zhuang, K. A. Jørgensen, *Angew. Chem. Int. Ed.* **2002**, *41*, 1790.
[4] N. Halland, A. Braunton, M. Marigo, K. A. Jørgensen, *J. Am. Chem. Soc.* 2004, **126**, 4790.

Determination of the absolute configuration of the Michael adducts:

The absolute configuration of the Michael adducts was obtained by over-reduction of the Chlorinated Michael adduct in the presence of an excess of $NaBH_4$ in Ethanol (scheme 1). Despite the loss of enantioselectivity due to a partial SN1 reaction favoured in protic solvent, the obtained compound was then compared to an original sample.[5] Indeed, the obtained alcohol had already been prepared in our group by direct Michael addition of 3-Methylbutyraldehyde to vinyl sulfone.



Scheme 1: Determination of the absolute configuration of the Michael adducts

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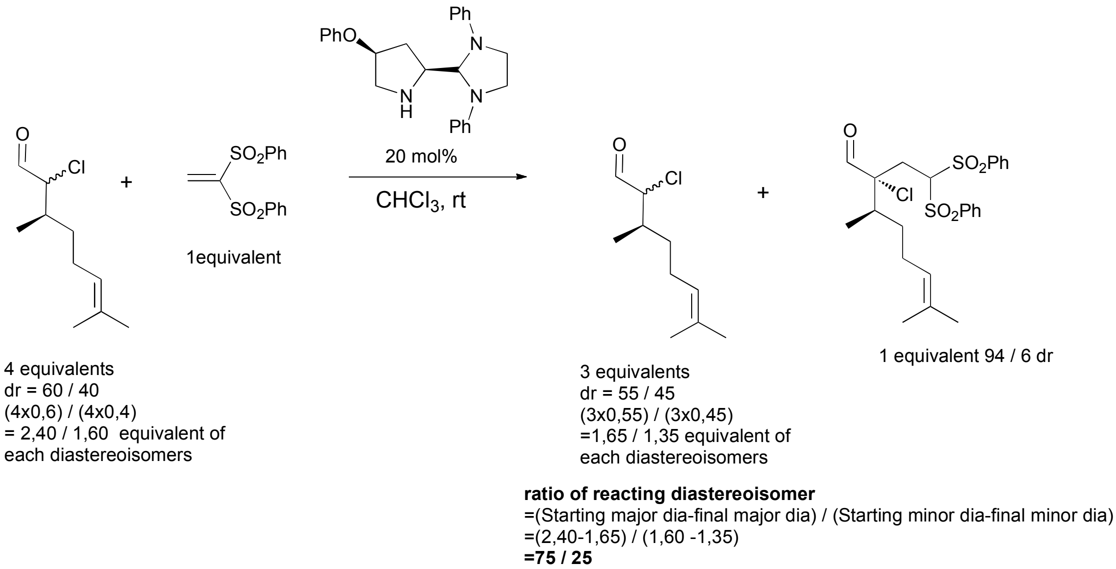
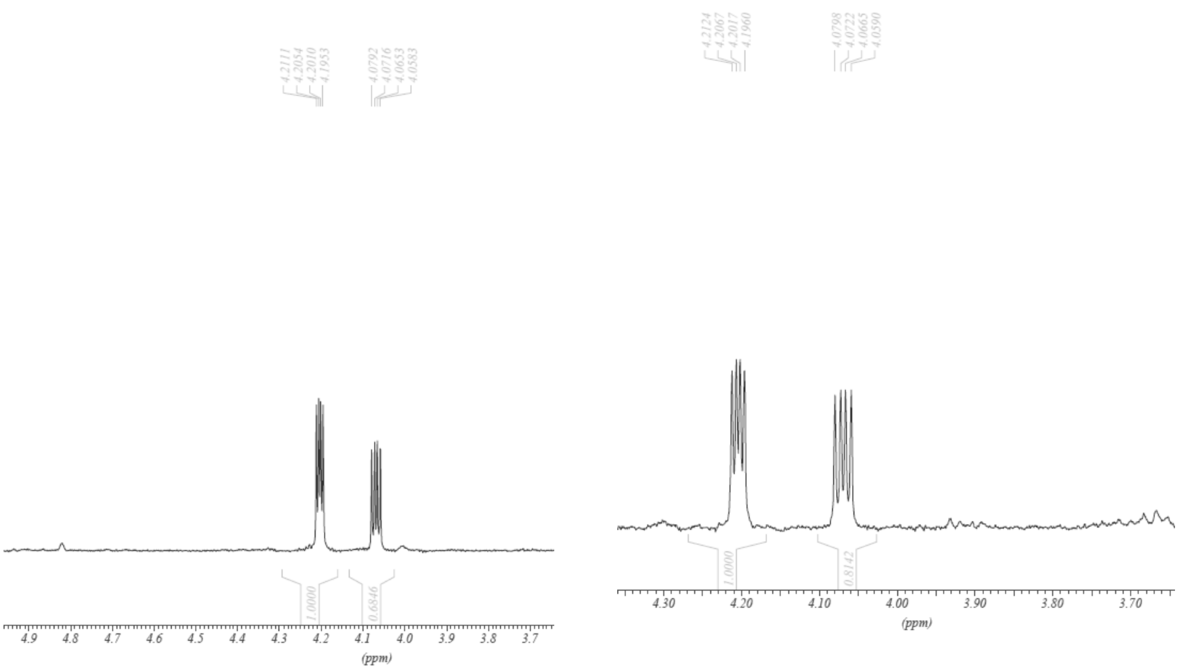
[5] a) S. Mossé, A. Alexakis, *Org. Lett*. 2005, **7**, 4361; b) S. Sulzer-Mossé, A. Alexakis, J. Mareda, G. Bollot, G. Bernardinelli, Y. Filinchuk, *Chem. Eur. J.* 2009 **15**, 3204 ; c) A. Quintard, S. Belot, E. Marchal, A. Alexakis, *Eur. J. Org. Chem.* 2009, accepted manuscript.

Observation of kinetic resolution using chlorinated (-)-citronellal:

The kinetic resolution mechanism was confirmed by using (-)-citronellal derivative (**scheme 2**). Observing the evolution of the diastereomeric ratio of the starting material by ^{1}H NMR (major diastereoisomer 4,19 ppm, minor diastereoisomer 4,05 ppm) confirmed this mechanism (scheme 3). Indeed, the 60 / 40 dr of the starting material evolved to a 55 / 45 dr (**scheme 2**). Considering that 4 equivalent of starting material at dr = 60 / 40 corresponds to a ratio of 2,40 / 1,60 equivalent of each diastereoisomers, and that the final mixture now contains 3 equivalents of the two diastereoisomers in a 55 / 45 ratio that means 1,65 / 1,35 equivalent of each diastereoisomers. This indicates that the starting material has reacted with a 75 / 25 selectivity (2,40-1,65 / 1,60-1,35) corroborating the major kinetic resolution pathway.



Scheme 2: observation of the kinetic resolution mechanism



Scheme 3: Chlorinated aldehyde before reaction and after.

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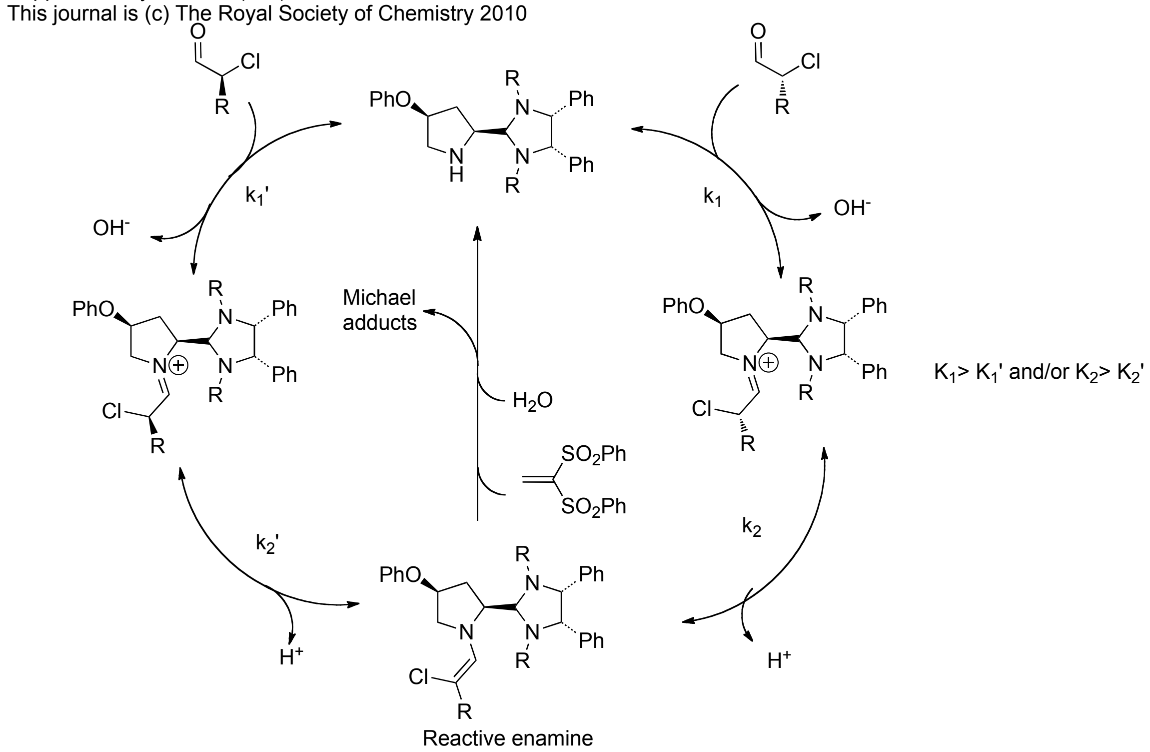
Postulated mechanism:



Scheme 4: mechanism of the Michael addition

From all these observations, a catalytic cycle can easily be drawn (**scheme 4**). The reaction starts with the amine addition on the chlorinated aldehyde to form the iminium cation who can then abstract the hydrogen in α position to form the reactive enamine intermediate. This enamine thus react on the vinyl sulfone and after addition of water, releases the Michael adduct and the catalyst who can re-enter the catalytic cycle.

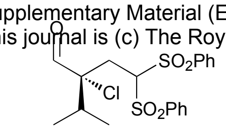
To explain the observed kinetic resolution, a different rate of iminium and/or enamine formation has to be taken in account. The enamine formation is prevented if the big R group is placed on the same face than the bulky groups coming from the pyrolidine backbone.

This stability of one enantiomer toward enamine formation is usual and explains the chiral stability of tertiary stereogenic centers in enamine catalysis.

Organocatalytic addition to vinyl sulfones:

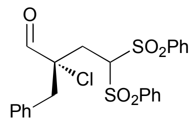
General procedure for the conjugate addition to1,1-vinyl sulfones:

To a solution of 0,4 mmol (4 eq) of disubsituted aldehyde in 0,4 ml of chloroform at room temperature is added successively 31,0 mg of the vinyl sulfone (0,1 mmol, 1 eq) and finally 0,02 mmol (20mol%) of the aminal-pyrrolidine catalyst. The mixture is stirred at room temperature and conversion is controlled by TLC. When conversion is completed, the reaction is quenched by addition of 1,5 ml of 1M HCl, the reaction mixture exctracted by three times 3 ml of dichloromethane, dried over Na_2SO_4 and the solvent evaporated. Purification by flash chromatography using a cyclohexane / ethyl acetate mixture affords the corresponding Michael adduct.



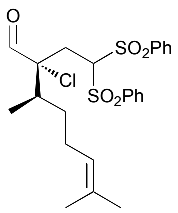
Chemical Formula: $C_{19}H_{21}ClO_5S_2$
Exact Mass: 428.05
Molecular Weight: 428.95

According to general procedure on 62,4 mg (0,2 mmol) of starting vinyl sulfone. m = 68 mg (0,158 mmol) of a white powder. Yield = 79%. The enantiomeric excess was determined by SFC (chiralcel OJ column, 2 ml / min, 200 bar, MeOH, 5% during 2 minutes, then 2%/min. 30 °C). R_t (maj): 7,0 R_t : 7,5. $[\alpha]^{20}_D$ = -57,9 ($CHCl_3$, c = 1,0, 93 % *ee*). ^1H NMR (400 MHz, $CDCl_3$): δ = 0,93 (d, 3H, *J* = 6,8 Hz), 1,03 (d, 3H, *J* = 6,8 Hz), 2,29-2,41 (m, 1H), 2,82 (dd, 1H, *J* = 14,4. 2,0 Hz), 3,03 (dd, 1H, *J* = 10,0. 6,0 Hz), 4,71 (dd, 1H, *J* = 4,8. 2,0 Hz), 7,50-7,92 (m, 10H), 9,46 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 16,6 (CH_3), 18,1 (CH_3), 31,3 (CH_2), 35,4 (CH), 79,4 (CH), 81,4 (Cquat), 129,2 (CH), 129,7 (CH), 134,8 (CH), 137,2 (Cquat), 138,0 (Cquat), 196,7 (CH). MS ESI: *m/z* = 439,3 $[M+NH_4]^+$, HRMS ESI $[M+H]^+$ calcd for $C_{19}H_{22}ClO_5S_2$ 429,0591, found 429,0587.



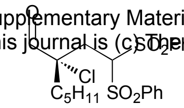
Chemical Formula: $C_{23}H_{21}ClO_5S_2$
Exact Mass: 476.05
Molecular Weight: 476.99

According to general procedure on 31,2 mg (0,1 mmol) of starting vinyl sulfone. m = 36 mg (0,075 mmol) of a white powder. Yield = 75%. The enantiomeric excess was determined by SFC (chiralcel OJ column, 2 ml / min, 200 bar, MeOH, 5% during 2 minutes, then 2%/min. 30 °C). R_t : 12,8 R_t (maj): 13,1. $[\alpha]^{20}_D$ = -16,9 ($CHCl_3$, c = 0,88. 91 % *ee*). ^1H NMR (300 MHz, $CDCl_3$): δ = 2,73 (dd, 1H, *J* = 14,4. 2,4 Hz), 3,04 (dd, 1H, *J* = 9,9. 6,9 Hz), 3,28 (AB, 2H, *J* = 14,4 Hz), 4,76 (dd, 1H, *J* = 4,2. 2,4 Hz), 7,17-7,95 (m, 15H), 9,50 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 32,8 (CH_2), 44,5 (CH_2), 75,7 (CH), 79,5 (Cquat), 127,8 (CH), 128,5 (CH), 129,2 (CH), 129,7 (CH), 131,3 (CH), 132,7 (CH), 134,7 (CH), 136,8 (Cquat), 137,8 (Cquat), 195,1 (CH). MS ESI: *m/z* = 494,3 $[M+NH_4]^+$, HRMS ESI $[M+H]^+$ calcd for $C_{23}H_{22}ClO_5S_2$ 477,0594, found 477,0591.



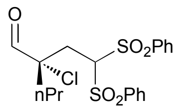
Chemical Formula: $C_{24}H_{29}ClO_5S_2$
Exact Mass: 496.11
Molecular Weight: 497.07

According to general procedure on 31,2 mg (0,1 mmol) of starting vinyl sulfone. m = 36 mg (0,072 mmol) of pale oil. Yield = 72%. The diastereomeric ratio was determined by ^1H NMR by comparison of the ^1H α-to the sulfone at 4,75 ppm for the major diastereoisomer and 4,69 ppm for the minor diastereoisomer. ^1H NMR of the major diastereoisomer (300 MHz, $CDCl_3$): δ = 0,95 (d, 3H, *J* = 6,6 Hz), 1,14-1,21 (m, 1H), 1,62-1,72 (m, 7H), 1,92-2,12 (m, 3H), 2,87 (dd, 1H, *J* = 6,6. 3,0 Hz), 3,04 (dd, 1H, *J* = 9,9. 6,6 Hz), 4,75 (dd, 1H, *J* = 6,6. 4,2 Hz), 5,03-5,09 (m, 1H), 7,49-7,70 (m, 6H), 7,80 (d, 1H, *J* = 7,2 Hz), 7,90 (d, 1H, *J* = 7,5 Hz), 9,44 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 14,8 (CH_3), 17,8 (CH_3), 25,3 (CH_2), 25,8 (CH_3), 30,7 (CH_2), 30,8 (CH_2), 40,1 (CH), 79,6 (CH), 81,2 (Cquat), 123,1 (CH), 129,1 (CH), 129,3 (CH), 129,7 (CH), 132,9 (Cquat), 134,7 (CH), 134,8 (CH), 137,3 (Cquat), 138,0 (Cquat), 196,4 (CH). MS ESI: *m/z* = 514 $[M+NH_4]^+$, HRMS ESI $[M+H]^+$ calcd for $C_{24}H_{30}ClO_5S_2$ 497,1217, found 497,1199.



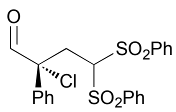
Chemical Formula: $C_{21}H_{25}ClO_5S_2$
Exact Mass: 456.08
Molecular Weight: 457.00

According to general procedure on 30,9 mg (0,1 mmol) of starting vinyl sulfone. m = 41 mg (0,090 mmol). Yield = 90%. The enantiomeric excess was determined by SFC (chiralcel OJ column, 2 ml / min, 200 bar, MeOH, 5% during 2 minutes, then 2%/min. 30 °C). R_t: 5,3 R_t (maj): 5,8. $[\alpha]^{20}_D$ = -17,5 ($CHCl_3$, c = 0,82. 82 % *ee*). ^1H NMR (300 MHz, $CDCl_3$): δ = 0,85-0,90 (m, 3H), 1,25-1,44 (m, 6H), 1,71-1,79 (m, 1H), 1,98-2,09 (m, 1H), 2,81 (dd, 1H, *J* = 13,5. 3,3 Hz), 2,98 (dd, 1H, *J* = 10,8. 6,6 Hz), 4,73 (dd, 1H, *J* = 3,3. 2,4 Hz), 7,53-7,91 (m, 10H), 9,45 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13,9 (CH_3), 22,3 (CH_2), 23,7 (CH_2), 31,5 (CH_2), 33,1 (CH_2), 33,8 (CH_2), 76,4 (Cquat), 79,5 (CH), 129,2 (CH), 129,3 (CH), 129,9 (CH), 134,8 (CH), 137,4 (Cquat), 195,8 (CH). MS ESI: *m/z* = 474,1 $[M+NH_4]^+$, HRMS ESI $[M+H]^+$ calcd for $C_{21}H_{26}ClO_5S_2$ 457,0904, found 457,0885.



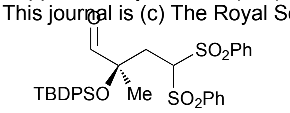
Chemical Formula: $C_{19}H_{21}ClO_5S_2$
Exact Mass: 428.05
Molecular Weight: 428.95

According to general procedure on 31,4 mg (0,1 mmol) of starting vinyl sulfone. m = 33 mg (0,076 mmol) of a white powder. Yield = 76%. The enantiomeric excess was determined by SFC (chiralcel OJ column, 2 ml / min, 200 bar, MeOH, 2% during 2 minutes, then 2%/min. 30 °C). R_t : 7,6 R_t (maj): 8,0. $[\alpha]^{20}_D$ = -14,0 ($CHCl_3$, c = 0,74. 75 % *ee*). ^1H NMR (300 MHz, $CDCl_3$): δ = 0,91(t, 3H, *J* = 7,5 Hz), 1,19-1,51 (m, 2H), 1,79-1,77 (m, 1H), 1,98-2,04 (m, 1H), 2,82 (dd, 1H, *J* = 13,5. 3,3 Hz), 2,99 (dd, 1H, *J* = 10,0. 5,7 Hz), 4,73 (dd, 1H, *J* = 3,3. 2,1 Hz), 7,53-7,91 (m, 10H), 9,46 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 13,9 (CH_3), 17,6 (CH_2), 33,1 (CH_2), 40,8 (CH_2), 76,2 (Cquat), 79,5 (CH), 129,2 (CH), 129,7 (CH), 134,8 (CH), 137,4 (Cquat), 195,7 (CH). MS ESI: *m/z* = 429,1 $[M+H]^+$, HRMS ESI $[M+H]^+$ calcd for $C_{19}H_{22}ClO_5S_2$ 429,0600, found 429,0591.



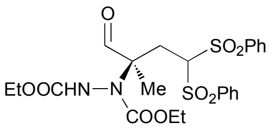
Chemical Formula: $C_{22}H_{19}ClO_5S_2$
Exact Mass: 462.04
Molecular Weight: 462.97

According to general procedure on 31,2mg (0,1 mmol) of starting vinyl sulfone. m = 26 mg (0,056 mmol) of a white powder. Yield = 56%. The enantiomeric excess was determined by SFC (chiralcel AS column, 2 ml / min, 200 bar, MeOH, 10% during 2 minutes, then 2%/min. 30 °C). R_t : 5,8 R_t (maj): 6,5. $[\alpha]^{20}_D$ = -10,6 ($CHCl_3$, c = 0,6. 58 % *ee*). ^1H NMR (300 MHz, $CDCl_3$): δ = 3,29 (dd, 1H, *J* = 13,2. 3,3 Hz), 3,43 (dd, 1H, *J* = 11,4. 5,4 Hz), 4,70 (dd, 1H, *J* = 3,3. 2,1 Hz), 7,45-7,93 (m, 15H), 9,40 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 33,5 (CH_2), 79,9 (Cquat), 127,4 (CH), 129,2 (CH), 129,7 (CH), 129,9 (CH), 134,7 (CH), 134,8 (Cquat), 190,0 (CH). MS ESI: *m/z* = 480,3 $[M+NH_4]^+$, HRMS ESI $[M+H]^+$ calcd for $C_{22}H_{20}ClO_5S_2$ 463,0435, found 463,0412.



Chemical Formula: $C_{33}H_{36}O_6S_2Si$
Exact Mass: 620.17
Molecular Weight: 620.85

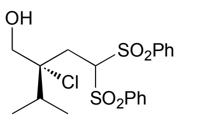
According to general procedure on 30,6 mg (0,1 mmol) of starting vinyl sulfone. m = 36 mg (0,058 mmol). Yield = 58%. The enantiomeric excess was determined by SFC (chiralcel OD column, 2 ml / min, 200 bar, MeOH, 5% during 2 minutes, then 2%/min. 30 °C). R_t : 12,3 R_t (maj): 13,2. $[\alpha]^{20}_D$ = -0,82 ($CHCl_3$, c = 0,45. 97 % *ee*). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0,98-1,09 (m, 12H), 2,55 (dd, 1H, *J* = 9,9. 6,0 Hz), 2,84 (dd, 1H, *J* = 12,6. 3,6 Hz), 4,89-4,92 (m, 1H), 7,29-7,89 (m, 10H), 9,62 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 19,5 (Cquat), 24,2 (CH_3), 27,2 (CH_3), 34,3 (CH_2), 78,7 (Cquat), 79,2 (CH), 127,8 (CH), 129,1 (CH), 129,7 (CH), 130,2 (CH), 133,6 (CH), 134,5 (Cquat), 136,9 (Cquat), 202,9 (CH). MS ESI: *m/z* = 638,5 $[M+NH_4]^+$, HRMS ESI $[M+Na]^+$ calcd for $C_{33}H_{36}O_6NaSiS_2$ 643,1621, found 643,1614.



Chemical Formula: $C_{23}H_{28}N_2O_9S_2$
Exact Mass: 540.12
Molecular Weight: 540.61

According to general procedure on 15,4 mg (0,05 mmol) of starting vinyl sulfone. The remaining aldehyde starting material was removed prior to flash chromatography by distillation under reduced pressure (bp = 145°C). m = 14mg (0,026mmol). Yield = 52%. The enantiomeric excess was determined by SFC (chiralcel OJ column, 2 ml / min, 200 bar, MeOH, 5% during 2 minutes, then 2%/min. 30 °C). R_t (maj): 5,8 R_t: 6,8. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1,12-1,32 (m, 9H), 2,71-2,89 (m, 2H), 4,11-4,29 (m, 4H), 4,91-4,95 (m, 1H), 6,89 (brs, 1H), 7,52-7,96 (m, 10H), 9,37(brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$). A long acquisition time was needed to obtain the spectrum due to the presence of carbamates conformers: δ = 14,5 (CH_3), 14,6 (CH_3), 19,2 (CH_3), 27,8 (CH_2), 62,6 (CH_2), 63,7 (CH_2), 68,0 (CH), 79,1 (Cquat), 129,1 (CH), 129,6 (CH), 129,9 (CH), 130,1 (CH), 134,9 (CH), 135,2 (CH), 137,0 (Cquat), 157,5 (Cquat), 194,7 (CH). MS ESI: *m/z* = 541,3 $[M+H]^+$, HRMS ESI $[M+H]^+$ calcd for $C_{33}H_{29}N_2O_9S_2$ 541,1311, found 541,13039.

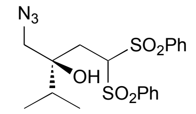
Derivatisation of the Michael adducts:



Chemical Formula: $C_{19}H_{23}ClO_5S_2$
Exact Mass: 430.07
Molecular Weight: 430.97

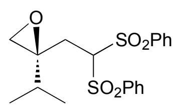
To a solution of Michael adduct **3a** (68 mg, 0,158 mmol) in 1 ml of methanol is added 13 mg (0,3 mmol, 2 eq) of $NaBH_4$ and the mixture stirred at room temperature for 15 minutes. 5 ml of 1M HCl are then added, and the resulting aqueous layer extracted by 3 times 10 ml of CH_2Cl_2, the organic layer dried on Na_2SO_4, filtered and the solvent evaporated to give 64 mg (0,148 mmol) of pur alcohol as a white powder. Yield = 94%. $[\alpha]^{20}_D$ = -49,4 ($CHCl_3$, c = 0,65. 93 % *ee*). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0,97-1,03 (m, 6H), 2,11-2,21 (m, 1H), 2,72-2,91 (m, 2H), 3,30-3,35 (m, 1H), 3,62-3,81 (m, 2H), 4,86-4,89 (m, 1H), 7,46-7,81 (m, 8H), 8,03-8,06 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17,8 (CH_3), 30,2 (CH_2), 32,8 (CH_2), 34,5 (CH), 64,9

(CH$_2$), 77,9 (Cquat), 80,9 (CH), 129,2 (CH), 129,7 (CH), 130,0 (CH), 134,8 (CH), 137,9 (Cquat). ESI: *m/z* = 431,3 [M+H]$^+$. HRMS ESI [M+H]$^+$ calcd for $C_{19}H_{24}ClO_5S_2$ 431,0748, found 431,0745.



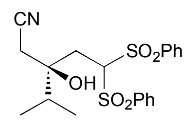
Chemical Formula: $C_{19}H_{23}N_3O_5S_2$
Exact Mass: 437.11
Molecular Weight: 437.53

To a solution of alcohol **5** (21 mg, 0,05 mmol) in 0,5 ml of DMF is added 26 mg (0,3 mmol, 6 eq) of NaN_3 and the resulting mixture stirred at 60°C for 3 days. 3 ml of water are then added, and the resulting aqueous layer extracted by 3 times 15 ml of ethyl acetate, the organic layer is then washed by 3 times 5 ml of water, dried on Na_2SO_4, filtered and the solvent evaporated to give 16 mg (0,036 mmol) of the azide **6** with >95% purity. Yield = 72%. $[\alpha]^{20}_D$ = -28,8 ($CHCl_3$, c = 0,80. 88 % *ee*). The enantiomeric excess was determined by SFC (chiralcel AD column, 2 ml / min, 200 bar, MeOH, 5% during 2 minutes, then 2%/min. 30 °C). R_t : 12,6 R_t (maj): 14,4. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0,92-1,03 (m, 6H), 2,05-2,12 (m, 1H), 2,42-2,60 (m, 2H), 3,80 (AB, 2H, *J* = 12,3 Hz), 5,06-5,09 (m, 1H), 7,48-8,04 (m, 10H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17,4 (CH$_3$), 27,0 (CH$_2$), 34,1 (CH), 65,0 (CH$_2$), 67,1 (Cquat), 79,6 (CH), 129,1 (CH), 129,5 (CH), 129,9 (CH), 134,8 (CH), 138,1 (Cquat). ESI: *m/z* = 455,3 [M+NH$_4$]$^+$. HRMS ESI [M+H]$^+$ calcd for $C_{19}H_{24}N_3O_5S_2$ 438,1151, found 438,1155.



Chemical Formula: $C_{19}H_{22}O_5S_2$
Exact Mass: 394.09
Molecular Weight: 394.50

To a solution of alcohol **5** (21 mg, 0,05 mmol) in 0,5 ml of DMF is added 72 mg (0,2 mmol, 4 eq) of Cs_2CO_3 and the resulting mixture stirred at room temperature for 14h. 3 ml of water are then added, and the resulting aqueous layer extracted by 3 times 15 ml of ethyl acetate, the organic layer is then washed by 3 times 5 ml of water, dried on Na_2SO_4, filtered and the solvent evaporated to give 16 mg (0,040 mmol) of the epoxide with >95% purity. Yield = 81%. $[\alpha]^{20}_D$ = -20,8 ($CHCl_3$, c = 0,65. 92 % *ee*). The enantiomeric excess was determined by SFC (chiralcel AD column, 2 ml / min, 200 bar, MeOH, 5% during 2 minutes, then 2%/min. 30 °C). R_t : 8,7 R_t (maj): 9,4. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0,87 (t, 6H, *J* = 7,2 Hz), 1,58-1,67 (m, 1H), 2,53-2,61 (m, 3H), 2,75 (dd, 1H, *J* = 12,8. 3,6 Hz), 4,26 (dd, 1H, *J* = 3,6. 1,6 Hz), 7,51-7,69 (m, 6H), 7,86-7,91 (m, 2H), 7,94-7,99 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17,3 (CH$_3$), 17,7 (CH$_3$), 24,0 (CH$_2$), 33,3 (CH), 48,5 (CH$_2$), 59,1 (Cquat), 78,0 (CH), 129,1 (CH), 129,3 (CH), 130,0 (CH), 134,4 (CH), 134,7 (CH), 137,6 (Cquat), 138,2 (Cquat). ESI: *m/z* = 395,3 [M+H]$^+$. HRMS ESI [M+H]$^+$ calcd for $C_{19}H_{23}O_5S_2$ 395,0981, found 395,0976.



Chemical Formula: $C_{20}H_{23}NO_5S_2$
Exact Mass: 421.10
Molecular Weight: 421.53

To a solution of alcohol **5** (21 mg, 0,05 mmol) in 0,5 ml of DMF is added 24 mg (0,3 mmol, 6 eq) of KCN and the resulting mixture stirred at 60°C for 3 days. 3 ml of water are then added, and the resulting aqueous layer extracted by 3 times 15 ml of ethyl acetate, the organic layer is then washed by 3 times 5 ml of water, dried on Na_2SO_4, filtered and the solvent evaporated. The crude is then purified by flash chromatography on silica gel using a cyclohexane / ethyl acetate mixture (8/2) to give 14 mg (0,033 mmol) of the cyanide. Yield = 67%. $[\alpha]^{20}_D$ = -2,32 ($CHCl_3$, c = 0,50. 92 % *ee*). The enantiomeric excess was determined by SFC (chiralcel IC column, 2 ml / min, 200 bar, MeOH, 5% during 2 minutes, then 2%/min. 30 °C). R_t (maj): 12,9 R_t : 13,3. ^1H NMR (300 MHz, $CDCl_3$): δ = 1,01-1,04 (m, 6H), 2,05-2,09 (m, 1H), 2,42 (dd, 1H, *J* = 14,1. 2,7 Hz), 2,56 (s, 2H), 2,71 (dd, 1H, *J* = 11,4. 5,7 Hz), 4,98 (dd, 1H, *J* = 3,0. 2,7 Hz), 7,51-7,70 (m, 6H), 7,85-7,89 (m, 2H), 7,94-7,99 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 16,6 (CH_3), 16,8 (CH_3), 26,1 (CH_2), 36,6 (CH), 73,3 (Cquat), 78,8 (CH), 117,3 (CN), 129,2 (CH), 130,2 (CH), 134,8 (CH), 135,0 (CH), 136,2 (Cquat), 137,5 (Cquat). ESI: *m/z* = 439,3 $[M+NH_4]^+$. HRMS ESI $[M+H]^+$ calcd for $C_{20}H_{24}NO_5S_2$ 422,1090, found 422,1088.

Supplementary Material (ESI) for Chemical Communications
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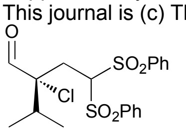
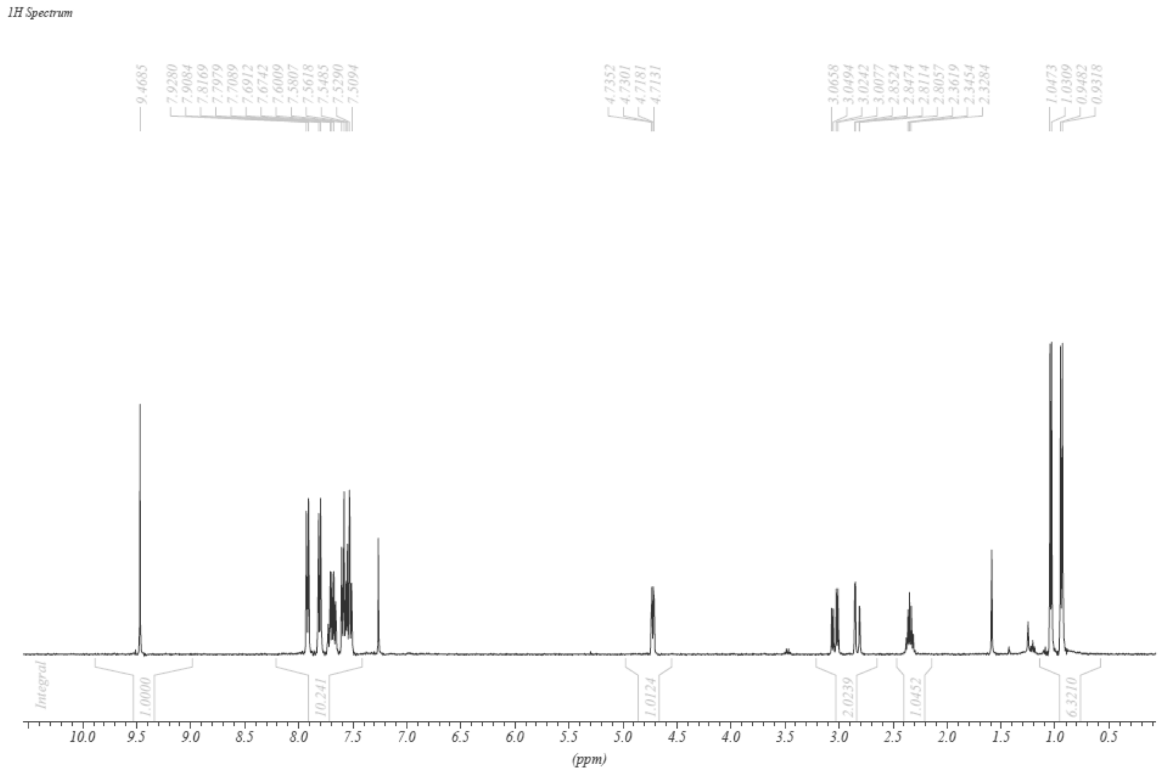
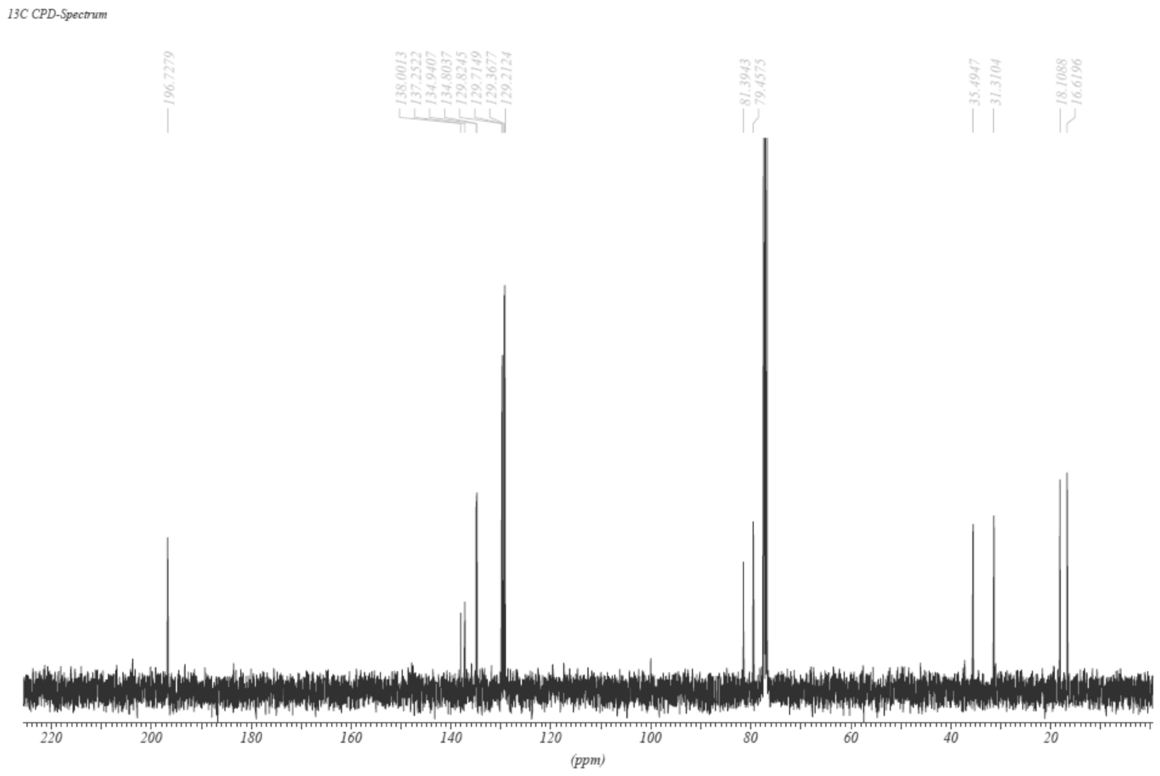
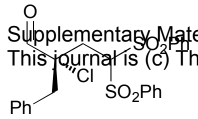
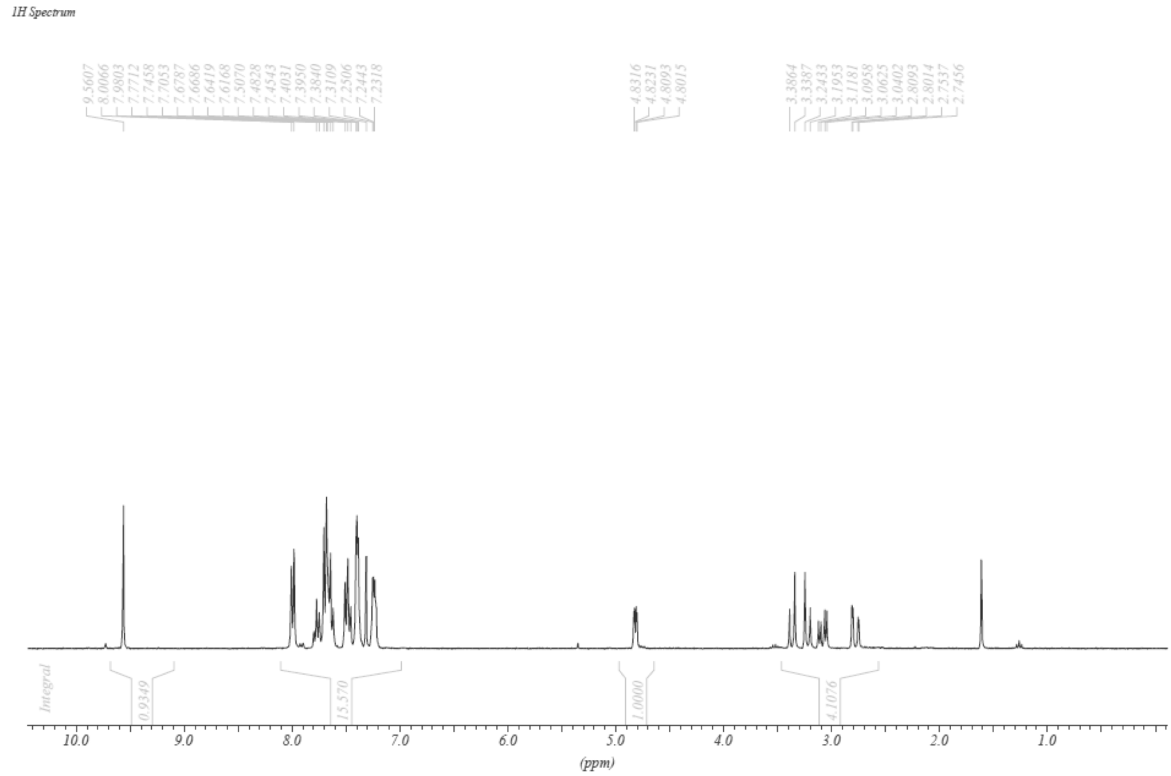
NMR Spectra:

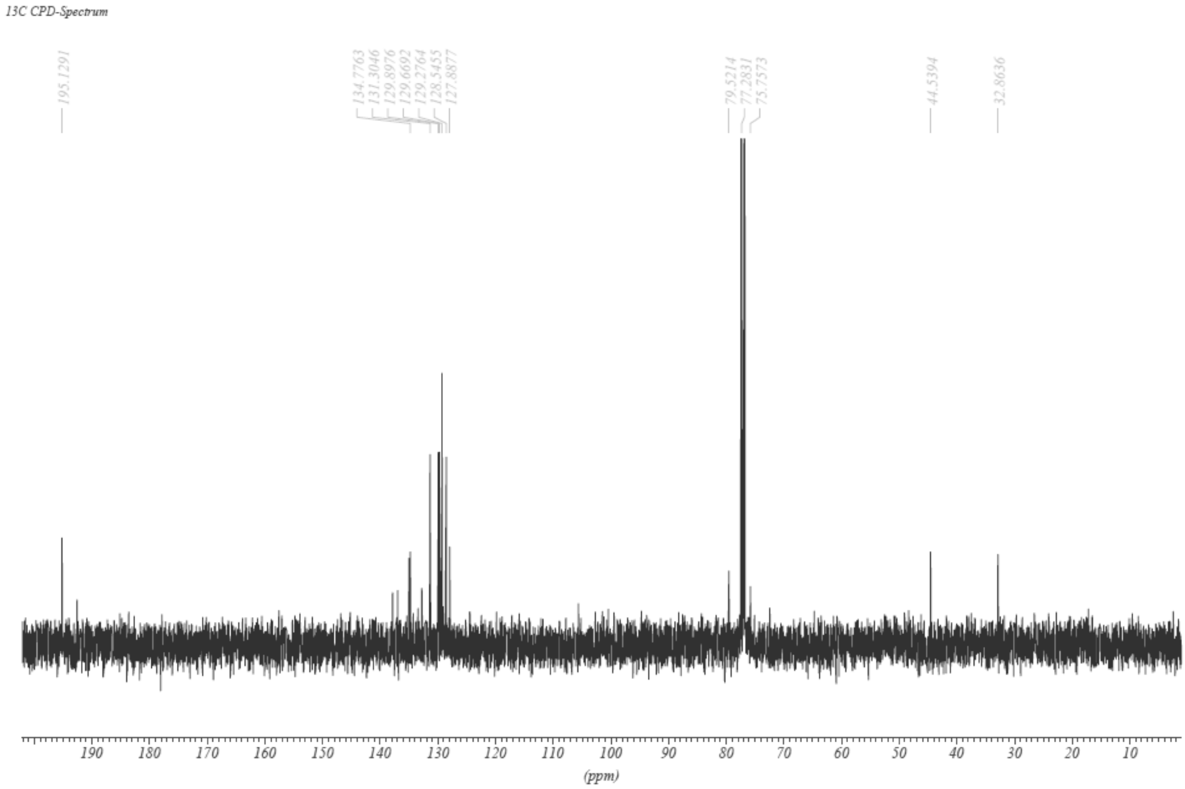


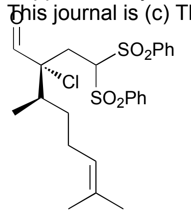




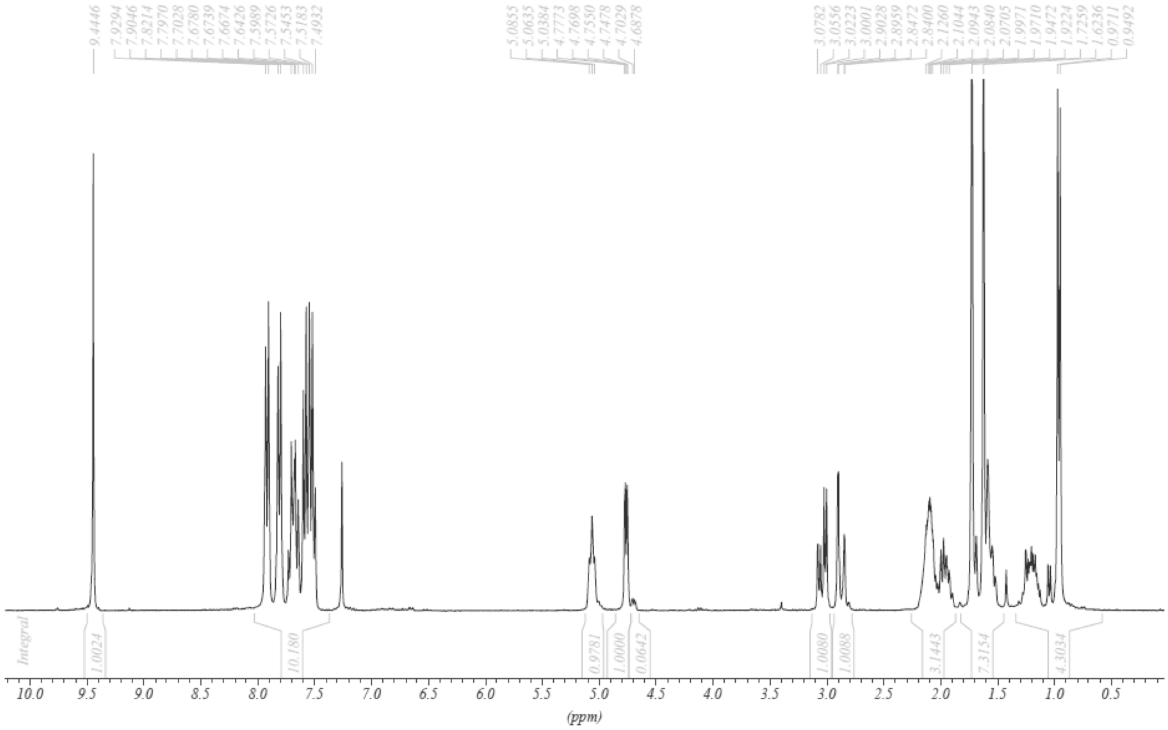

O
SO2Ph
Cl
SO2Ph
Ph


1H Spectrum
Integral
(ppm)

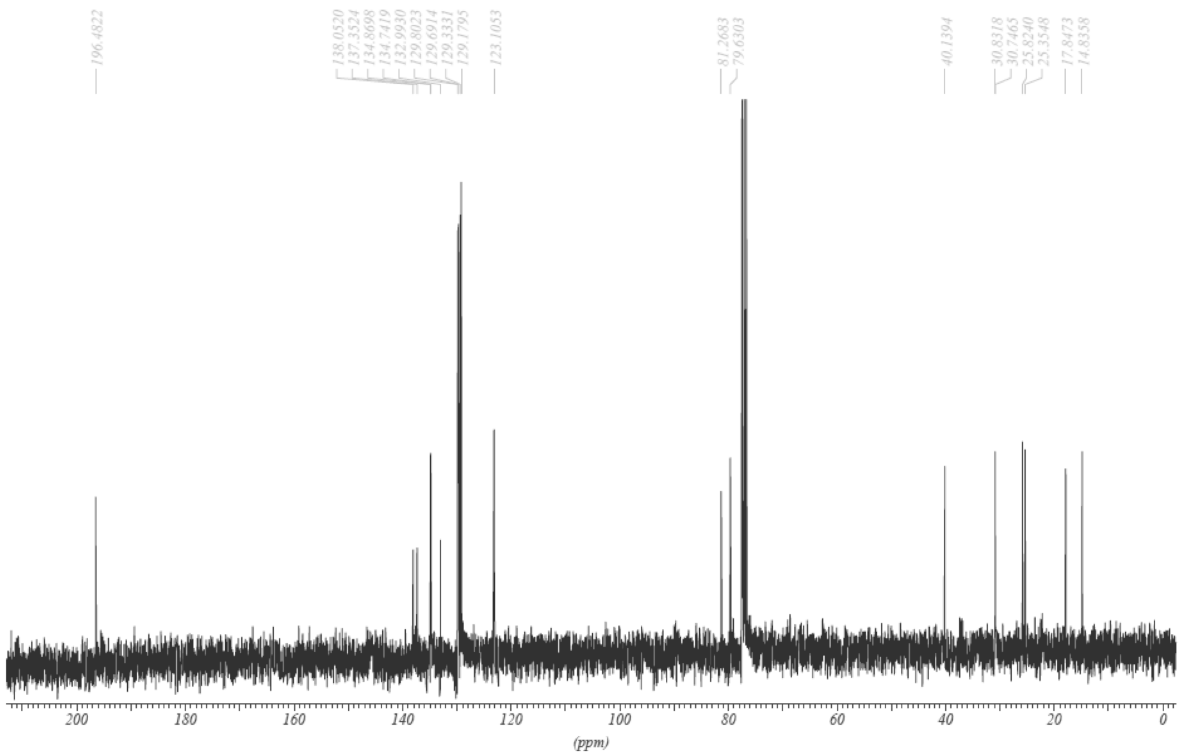

13C CPD-Spectrum
(ppm)

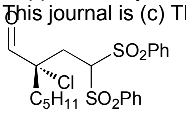


1H Spectrum



C13 Spectrum





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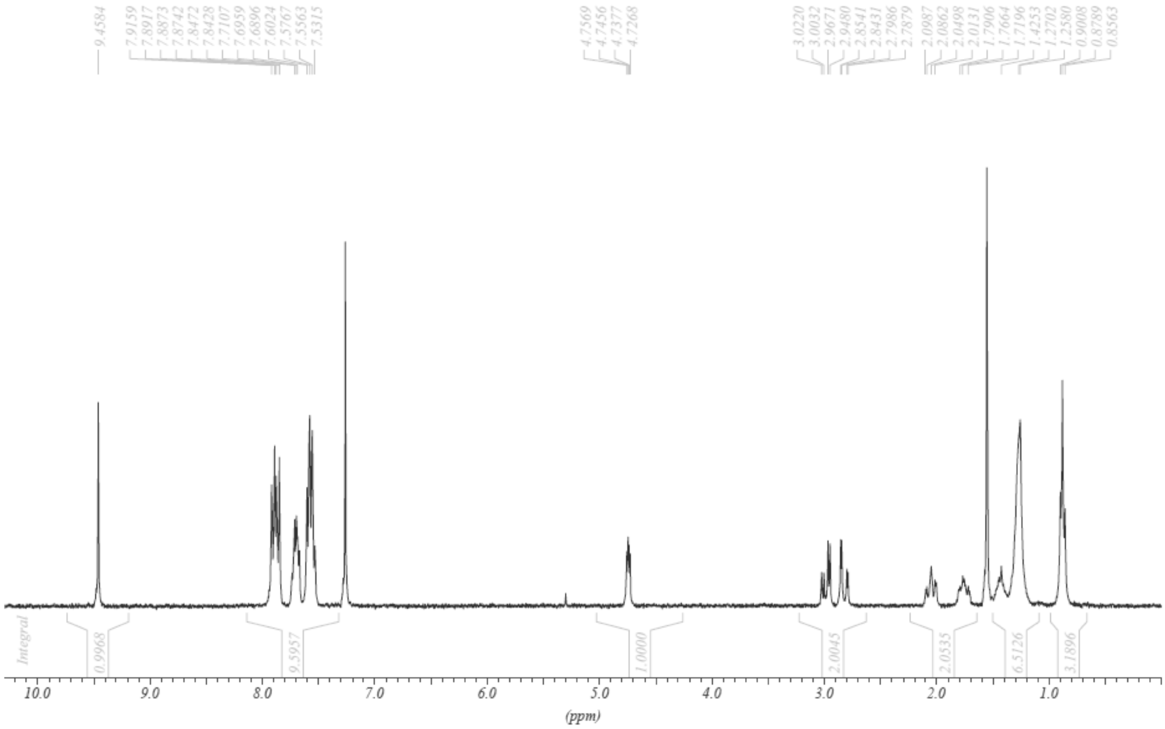
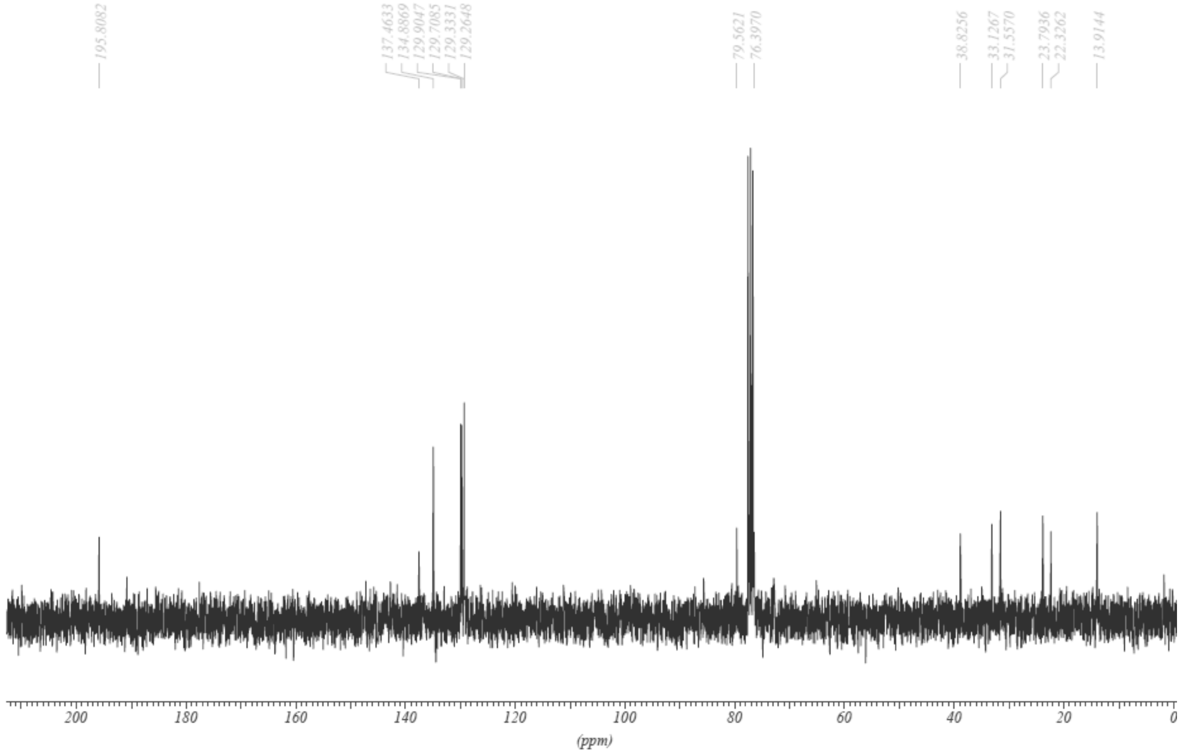
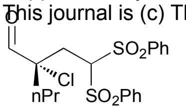


C13 Spectrum





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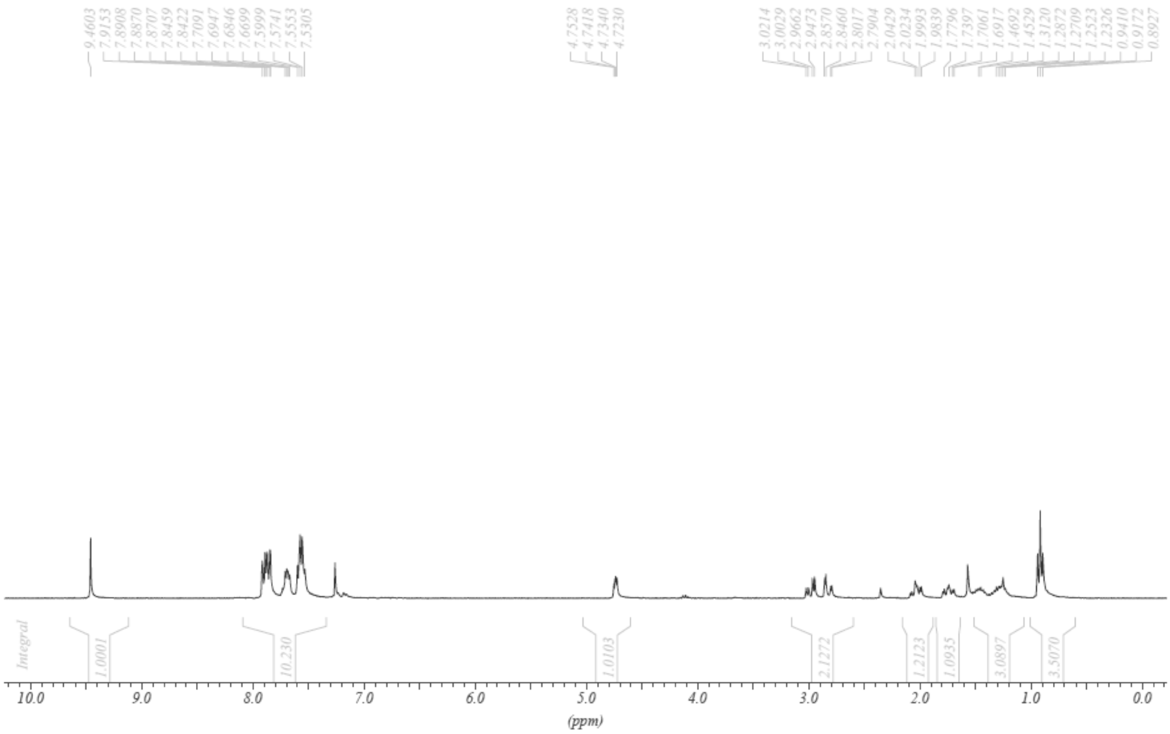

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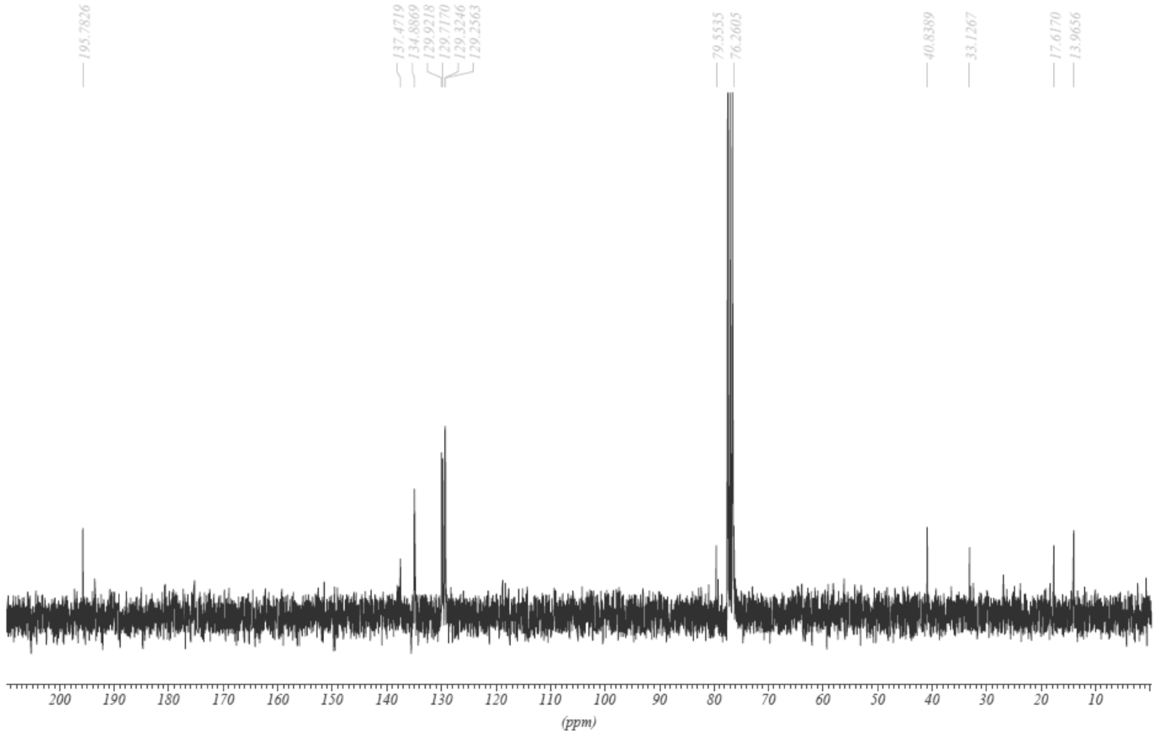
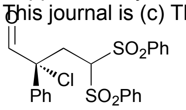
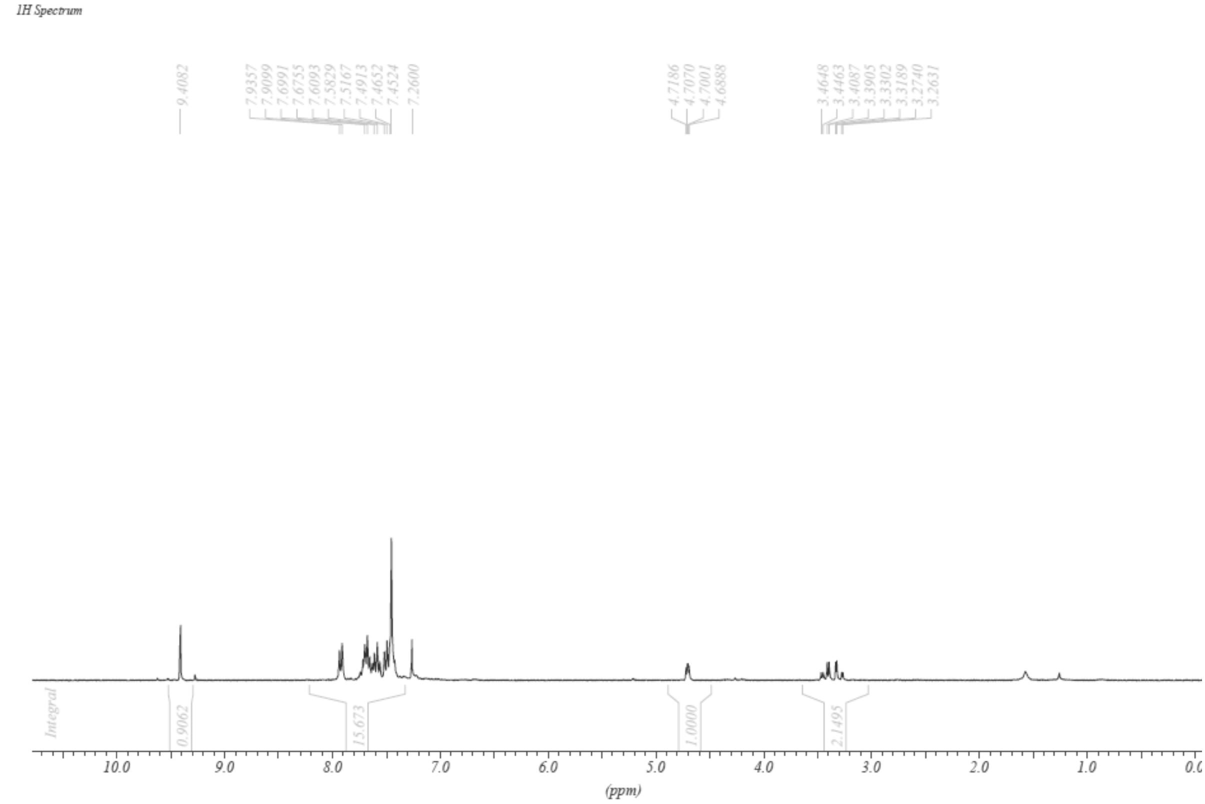



O
SO2Ph
Cl
Ph
SO2Ph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7.9099
7.6991
7.6755
7.6093
7.5829
7.5167
7.4913
7.4652
7.4524
7.2600
4.7186
4.7070
4.7001
4.6888
3.4648
3.4463
3.4087
3.3905
3.3302
3.3189
3.2740
3.2631
Integral
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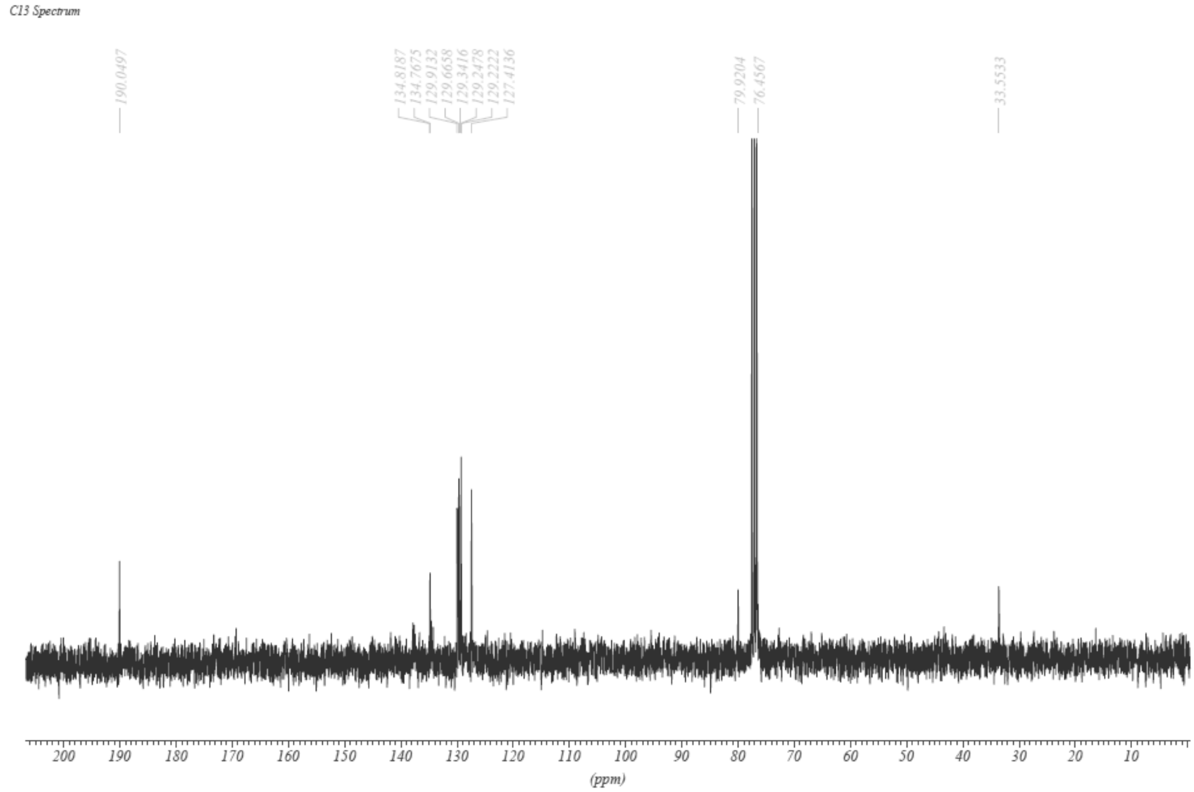
1.0000
2.1495
(ppm)


C13 Spectrum
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134.7675
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129.3416
129.2478
129.2222
127.4136
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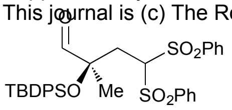
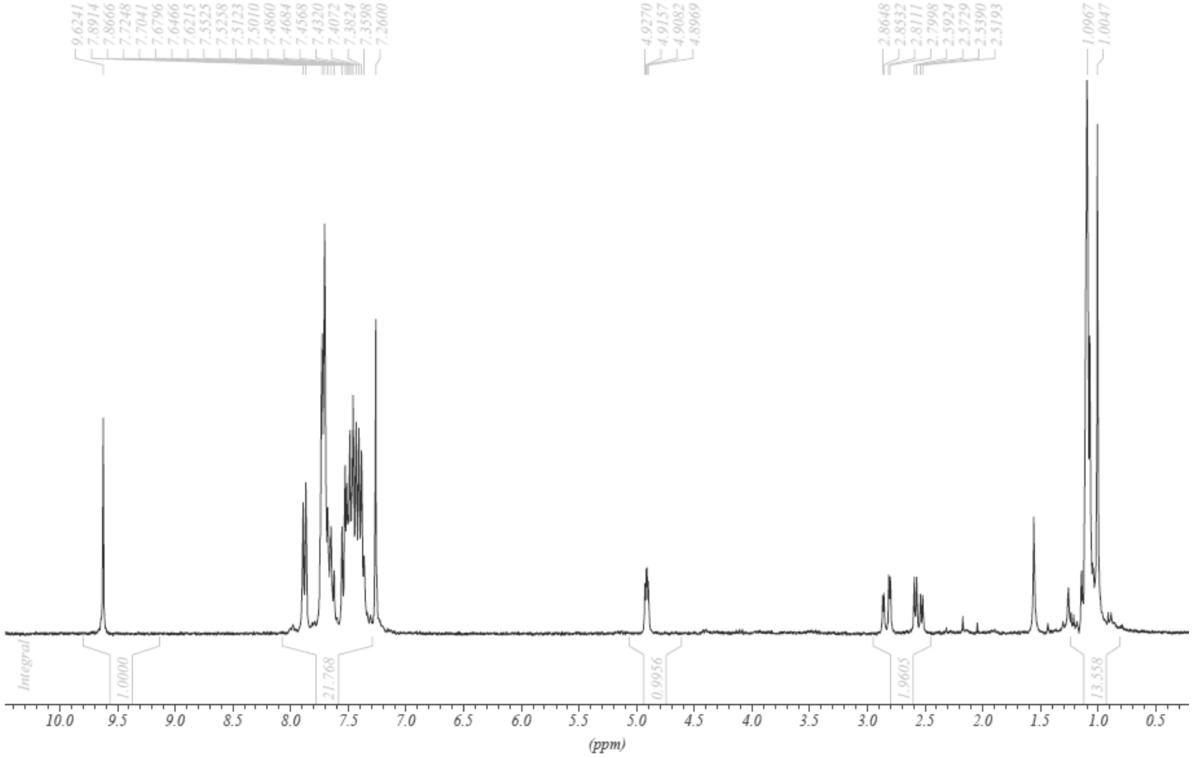
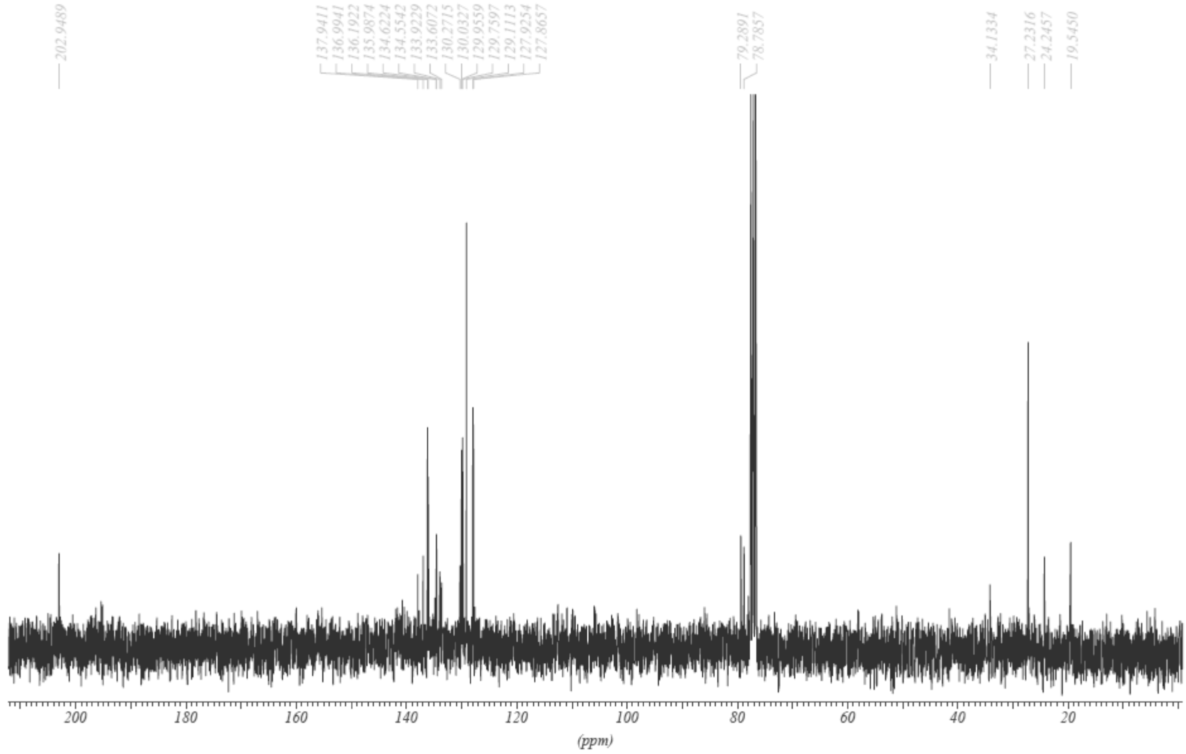
76.4567
33.5533
(ppm)

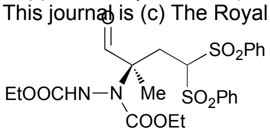


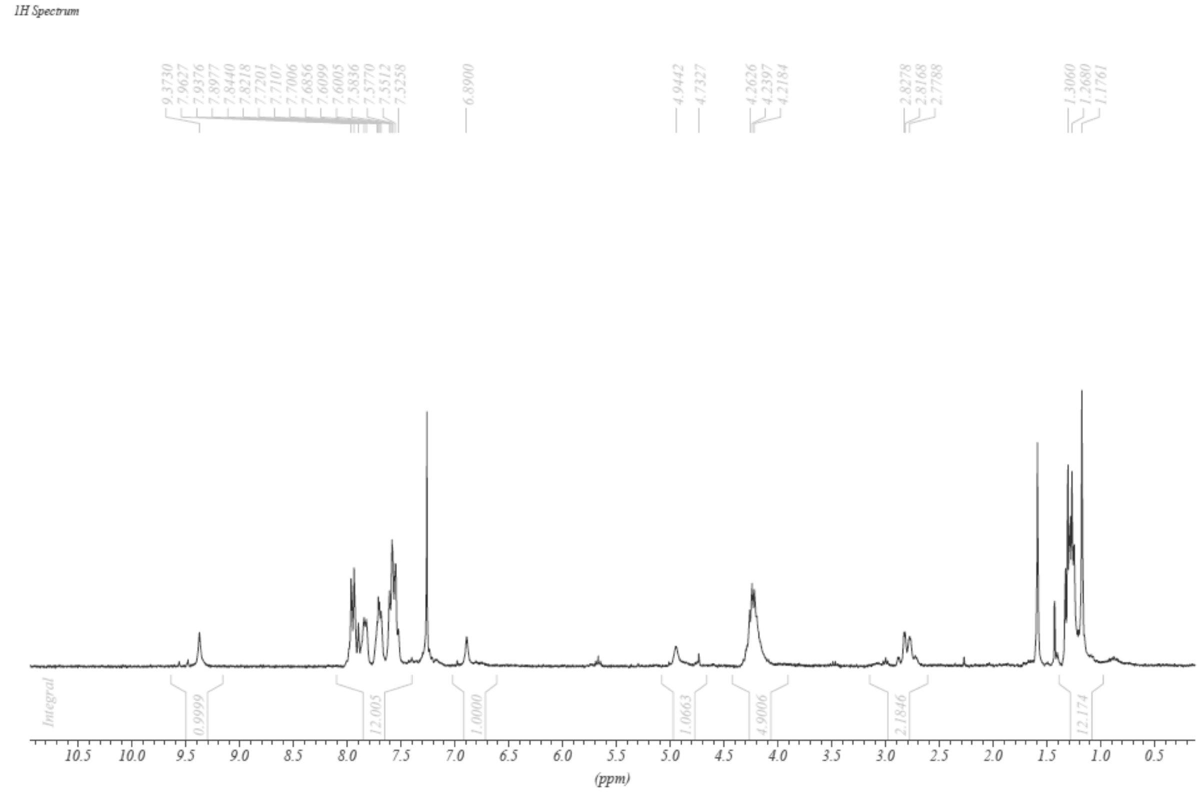
1H Spectrum



C13 Spectrum




O
SO2Ph
EtOOCHN
N
Me
SO2Ph
COOEt


1H Spectrum
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7.8977
7.8440
7.8218
7.7201
7.7107
7.7006
7.6856
7.6099
7.6005
7.5836
7.5770
7.5512
7.5258
6.8900
4.9442
4.7327
4.2626
4.2397
4.2184
2.8278
2.8168
2.7788
1.3060
1.2680
1.1761
Integral
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1.0000
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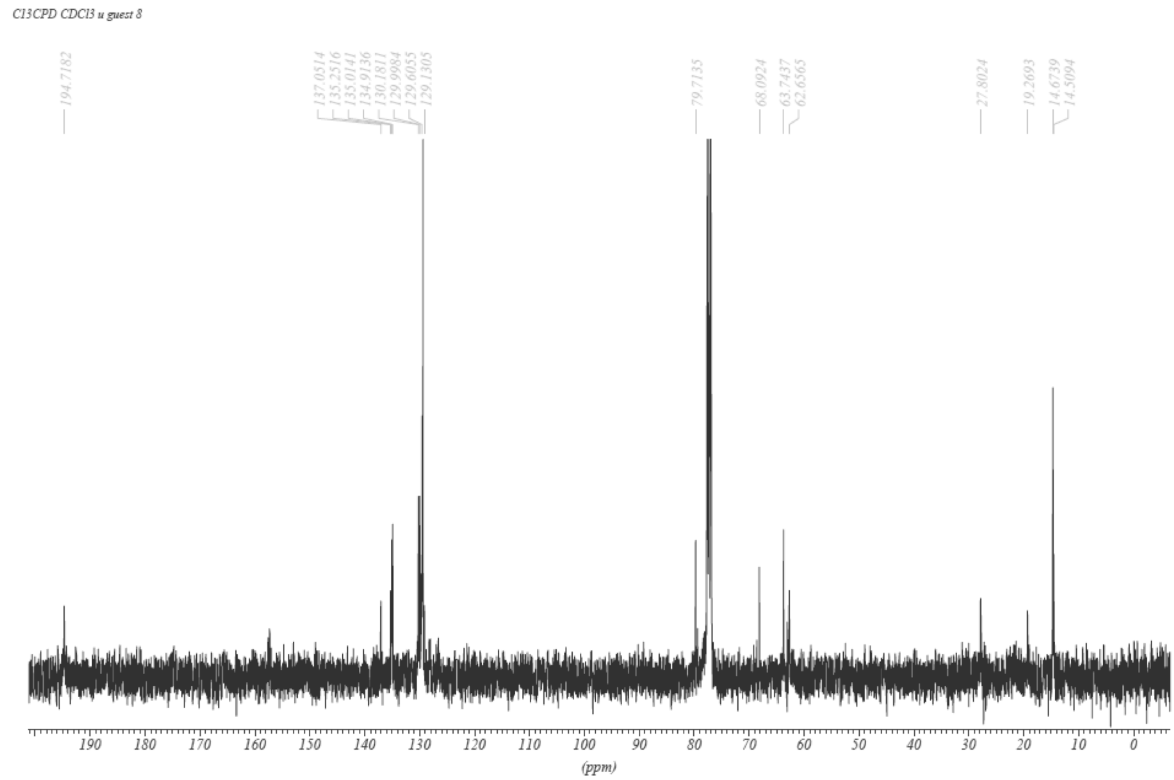
4.9006
2.1846
12.174
(ppm)


C13CPD CDCl3 u guest 8
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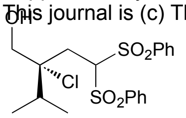
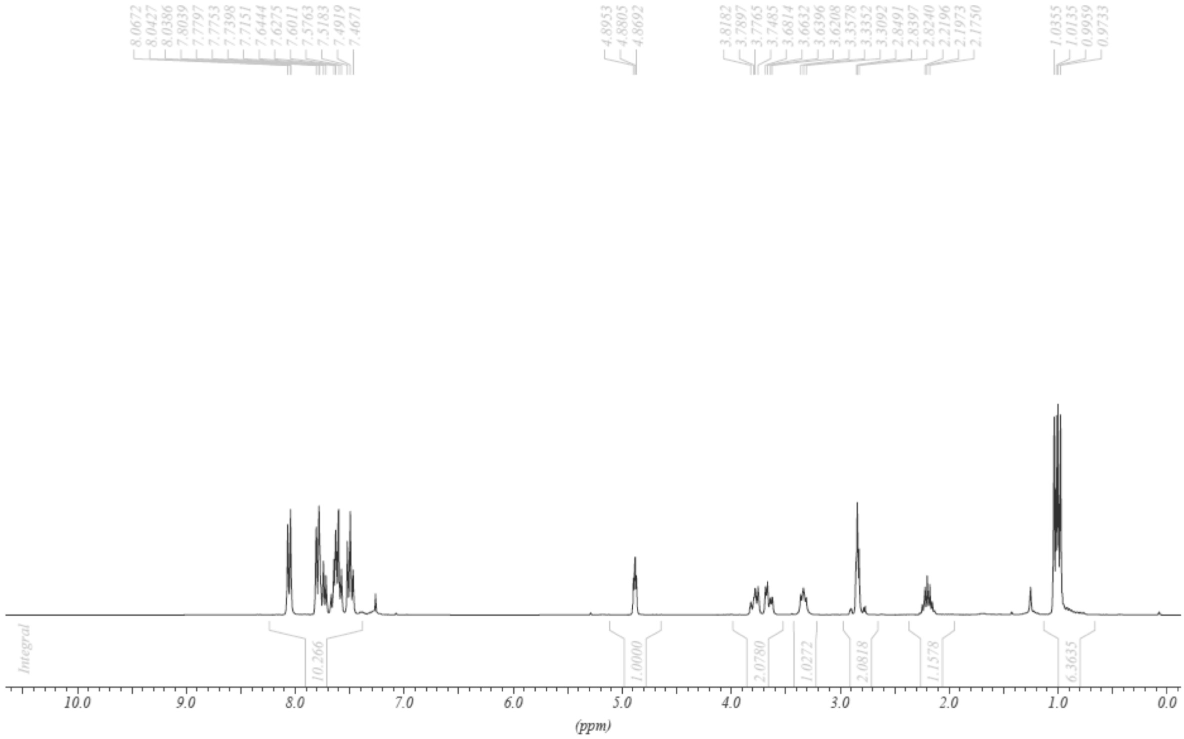
137.0514
135.2516
135.0141
134.9136
130.1811
129.9984
129.6055
129.1305
79.7135
68.0924
63.7437
62.6565
27.8024
19.2693
14.6739
14.5094
(ppm)

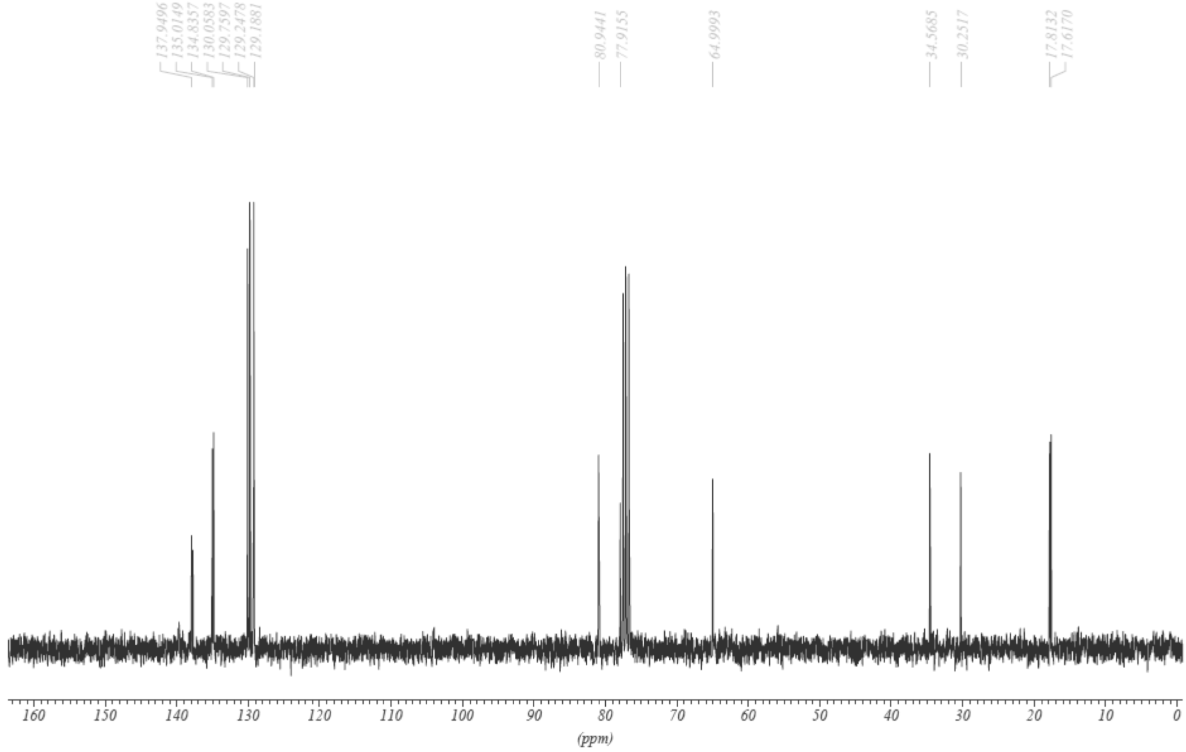
Supplementary Material (ESI) for Chemical Communications

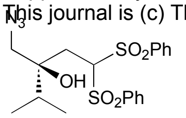


1H Spectrum



C13 Spectrum





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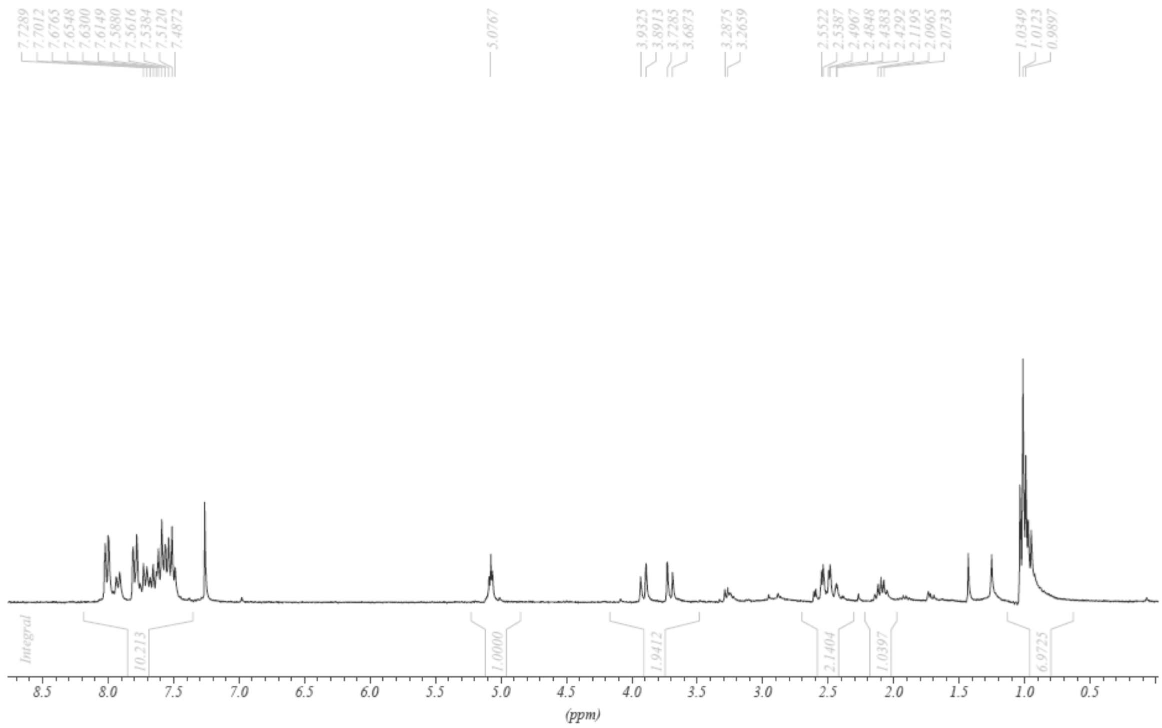

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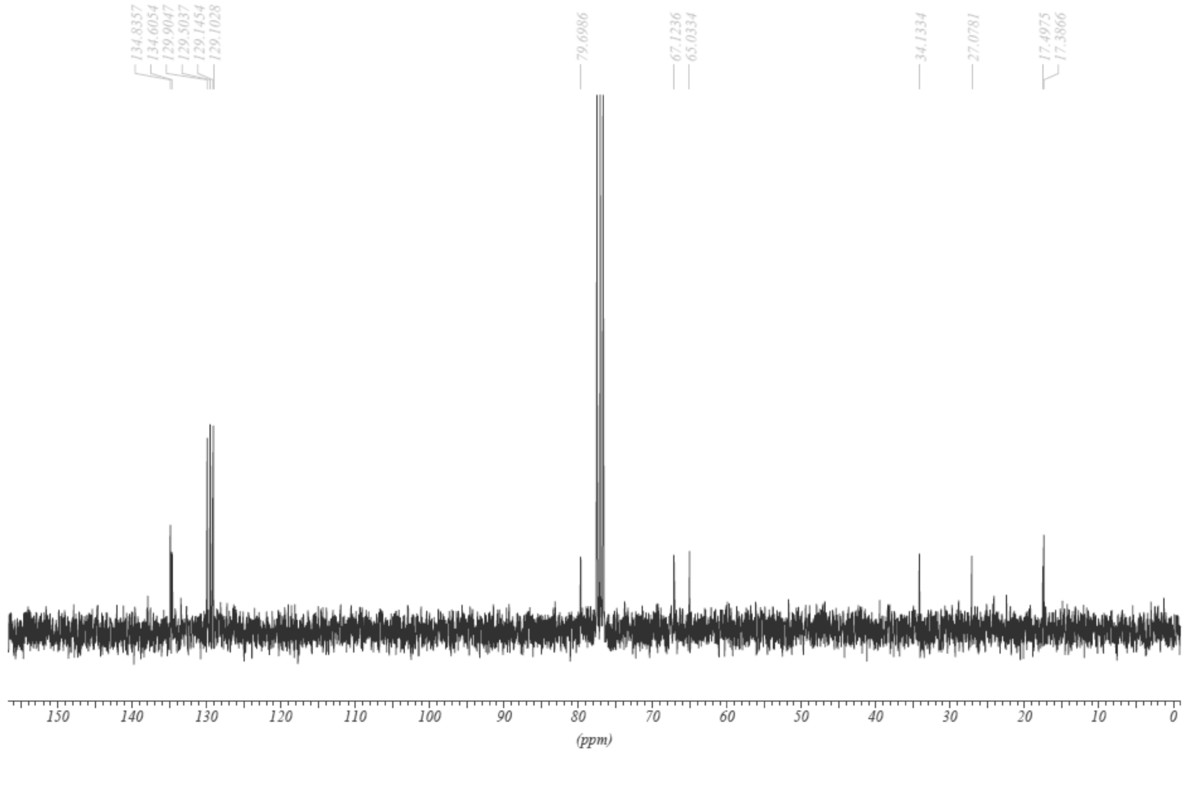

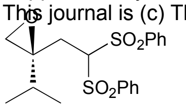

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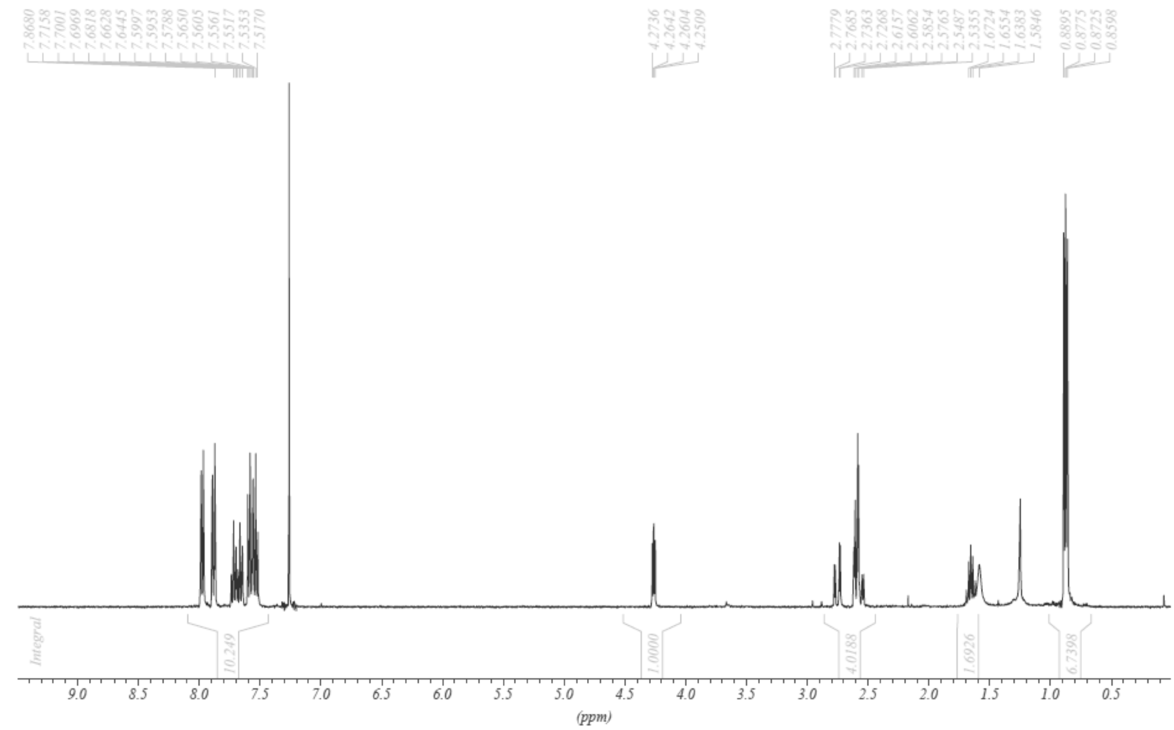
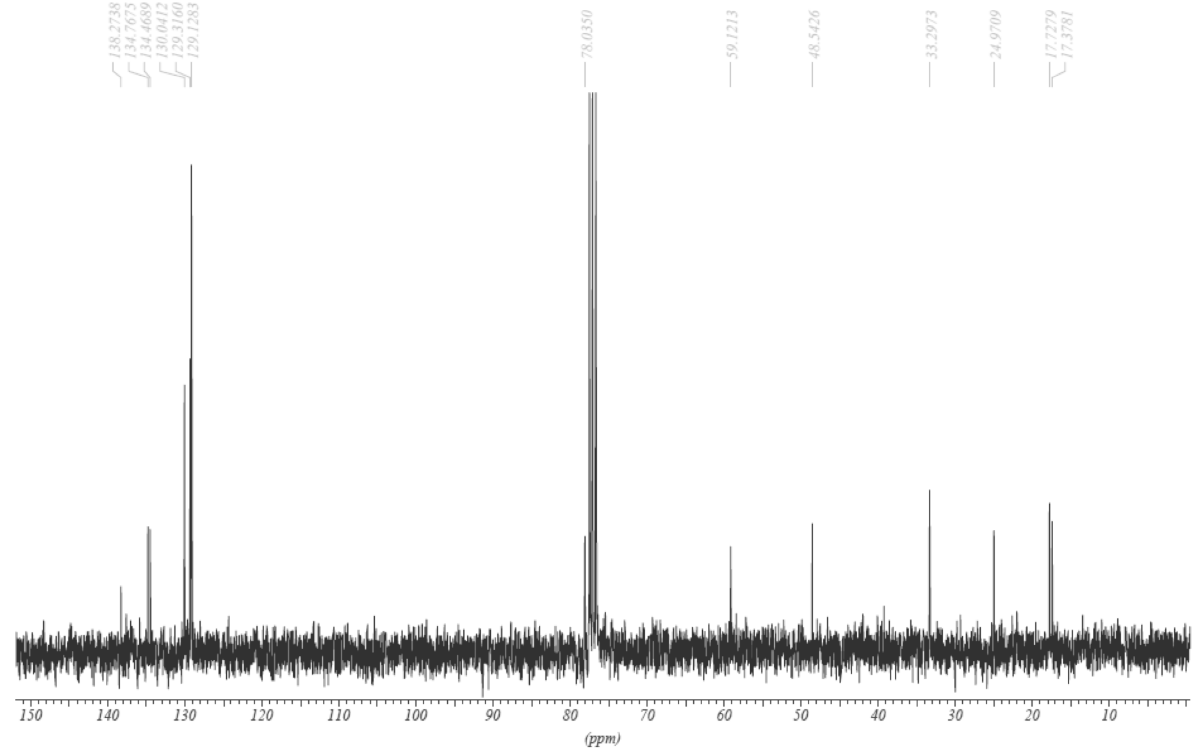
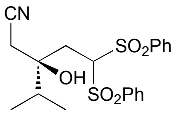
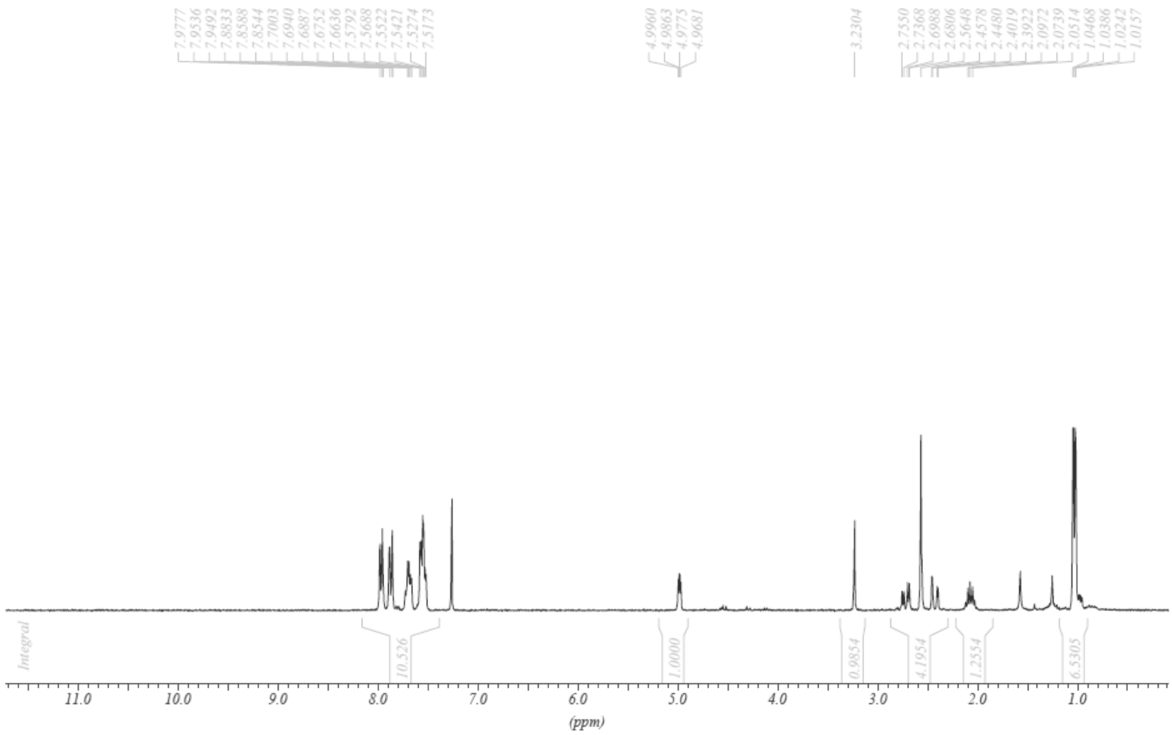


C13 Spectrum

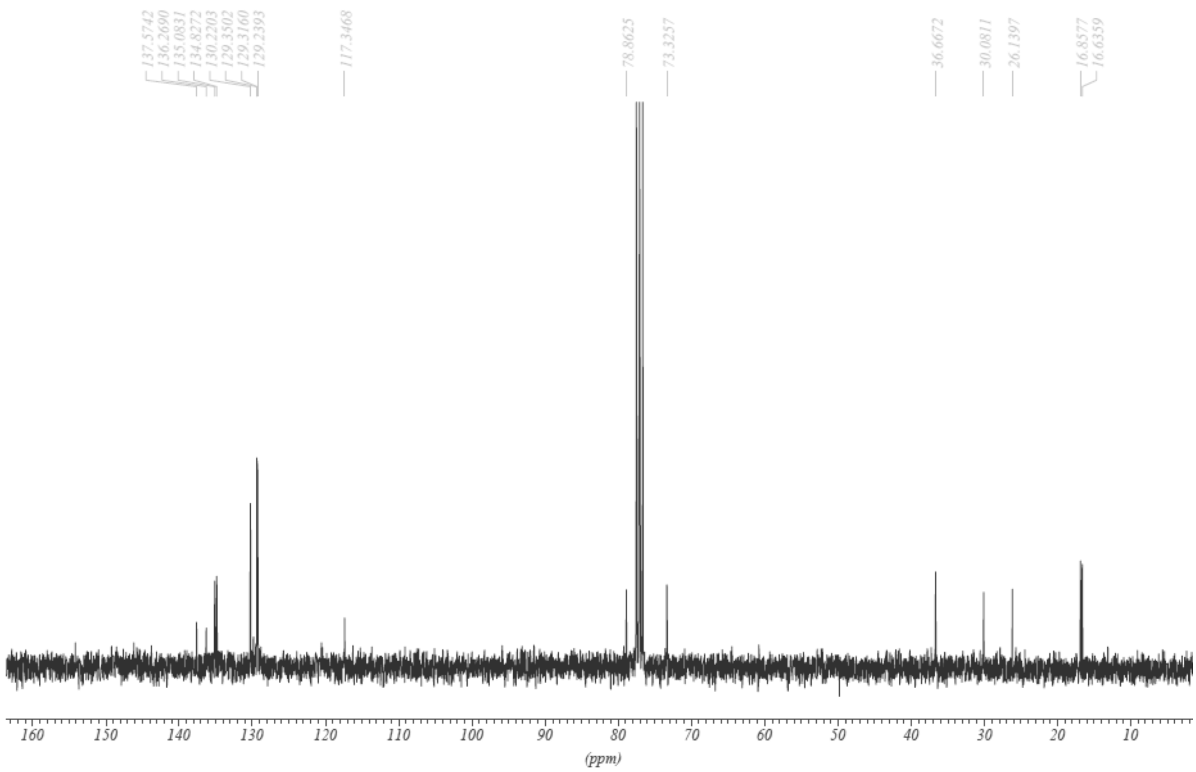




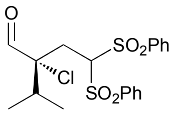
1H Spectrum

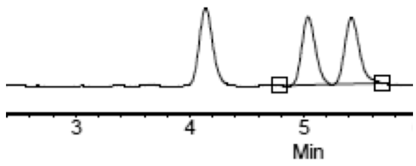


C13 Spectrum



Chiral separation:





Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
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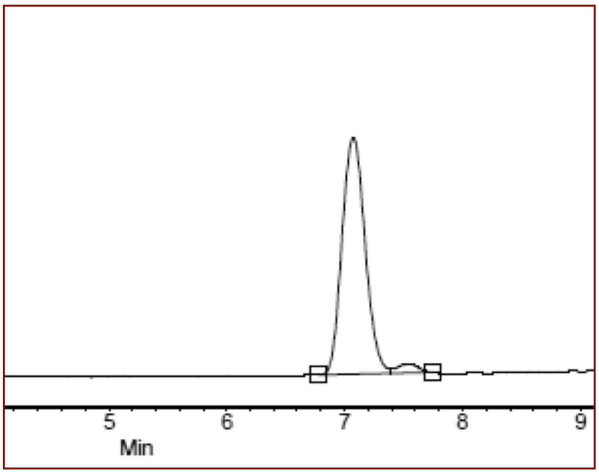
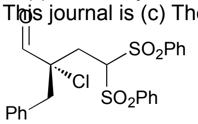
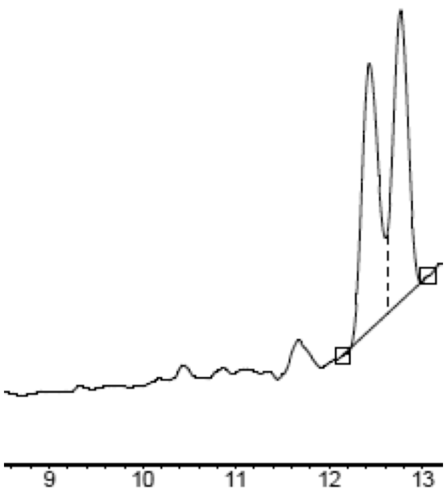
1	UNKNOWN	4.79	5.03	5.24	0.00	48.74	229.6	31.5	48.739
2	UNKNOWN	5.24	5.41	5.68	0.00	51.26	223.4	33.1	51.261
Total						100.00	453.0	64.6	100.000



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.78	7.07	7.39	0.00	96.58	740.8	167.7	96.581
2	UNKNOWN	7.39	7.54	7.75	0.00	3.42	28.8	5.9	3.419
Total						100.00	769.6	173.6	100.000





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1	UNKNOWN	12.15	12.43	12.62	0.00	50.04	164.1	33.8	50.038
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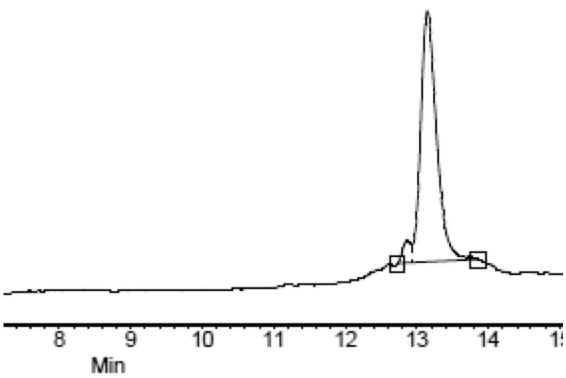
Total						100.00	343.2	67.5	100.000



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
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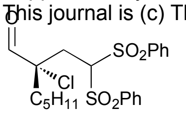
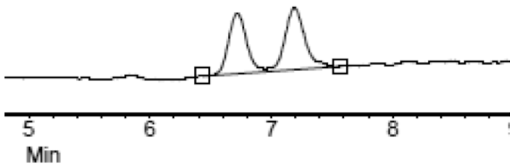
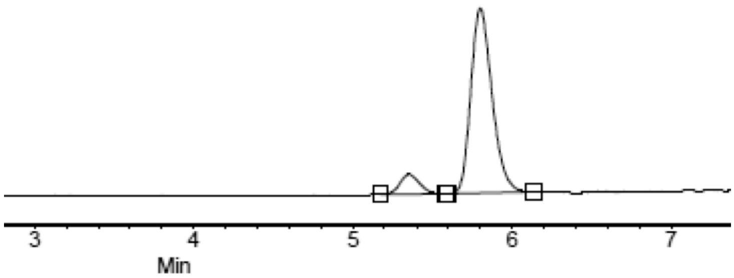
1	UNKNOWN	12.73	12.86	12.94	0.00	4.79	70.6	10.3	4.786
2	UNKNOWN	12.94	13.14	13.85	0.00	95.21	806.7	204.9	95.214
Total						100.00	877.3	215.2	100.000

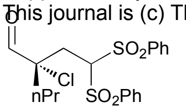


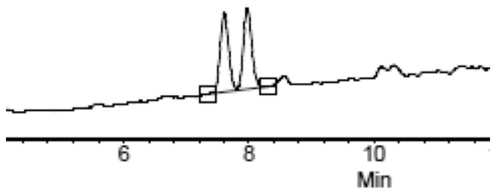


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	6.43	6.72	6.96	0.00	46.80	68.8	11.8	46.801
2	UNKNOWN	6.96	7.19	7.57	0.00	53.20	70.5	13.4	53.199
Total						100.00	139.3	25.2	100.000

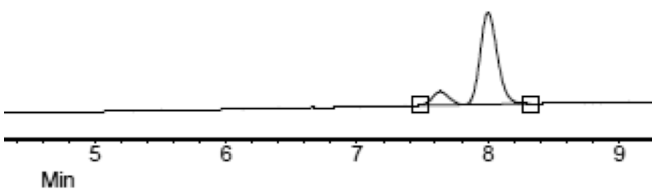


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.17	5.35	5.59	0.00	8.87	60.0	8.6	8.869
2	UNKNOWN	5.59	5.80	6.13	0.00	91.13	571.4	88.2	91.131
Total						100.00	631.3	96.8	100.000

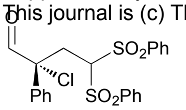


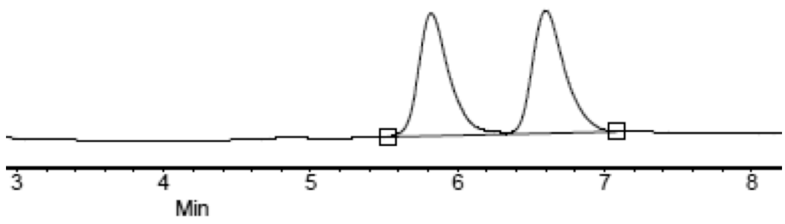


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	7.36	7.61	7.79	0.00	48.51	83.1	12.6	48.506
2	UNKNOWN	7.79	7.97	8.30	0.00	51.49	84.2	13.3	51.494
Total						100.00	167.3	25.9	100.000

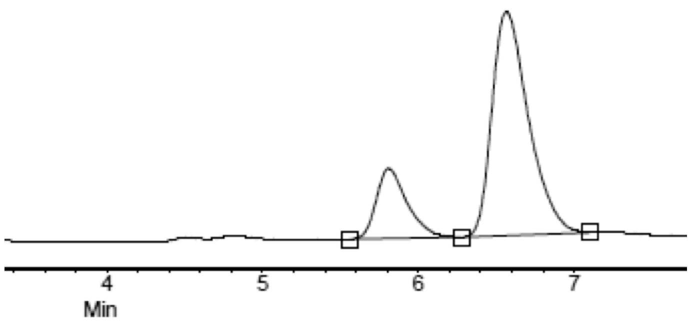


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[μV]	[μV.Min]	[%]
1	UNKNOWN	7.48	7.63	7.84	0.00	12.41	43.2	6.4	12.414
2	UNKNOWN	7.84	8.00	8.33	0.00	87.59	295.4	44.9	87.586
Total						100.00	338.7	51.3	100.000

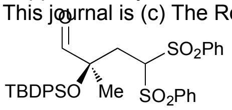


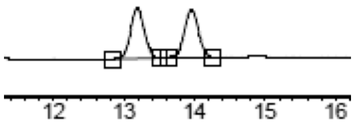


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.52	5.82	6.33	0.00	48.63	245.9	59.5	48.631
2	UNKNOWN	6.33	6.60	7.08	0.00	51.37	246.3	62.8	51.369
Total						100.00	492.1	122.3	100.000

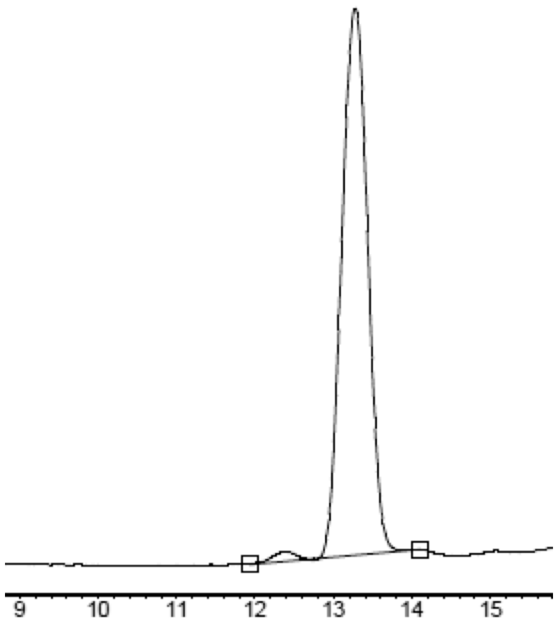


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.56	5.81	6.27	0.00	20.86	204.2	46.7	20.860
2	UNKNOWN	6.28	6.57	7.09	0.00	79.14	651.5	177.2	79.140
Total						100.00	855.6	224.0	100.000

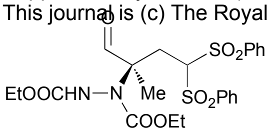


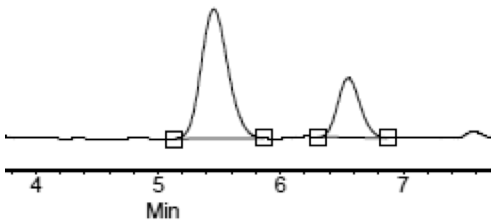


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	12.85	13.19	13.50	0.00	50.37	137.0	30.9	50.367
2	UNKNOWN	13.62	13.96	14.26	0.00	49.63	130.5	30.4	49.633
Total						100.00	267.5	61.3	100.000



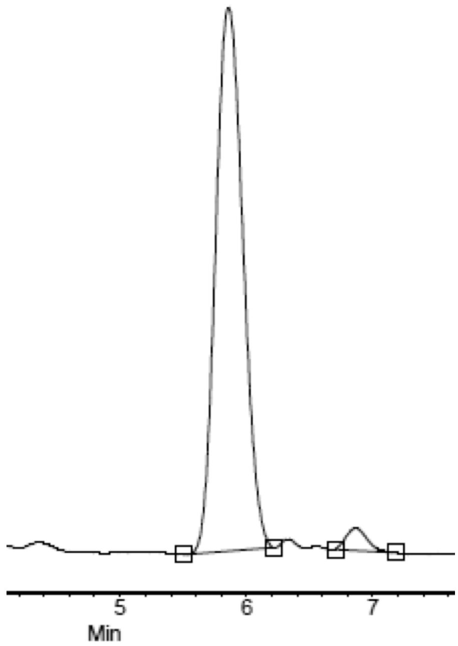
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	11.93	12.37	12.75	0.00	1.46	13.2	4.5	1.463
2	UNKNOWN	12.75	13.27	14.11	0.00	98.54	786.3	301.1	98.537
Total						100.00	799.5	305.5	100.000



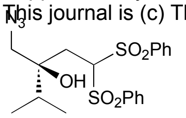


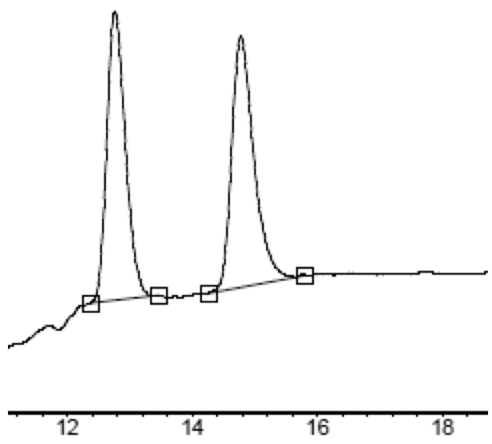
Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.13	5.45	5.87	0.00	72.21	311.9	79.6	72.205
2	UNKNOWN	6.31	6.55	6.88	0.00	27.79	143.3	30.7	27.795
Total						100.00	455.2	110.3	100.000

compound with 44% ee.

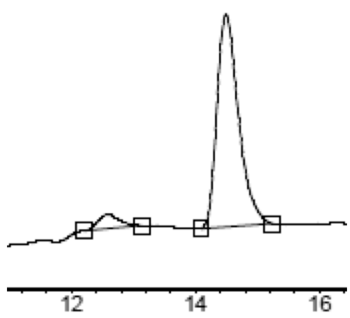


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	5.50	5.86	6.21	0.00	96.95	1126.7	282.6	96.946
2	UNKNOWN	6.70	6.87	7.19	0.00	3.05	46.3	8.9	3.054
Total						100.00	1173.0	291.5	100.000

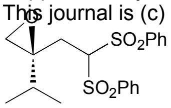


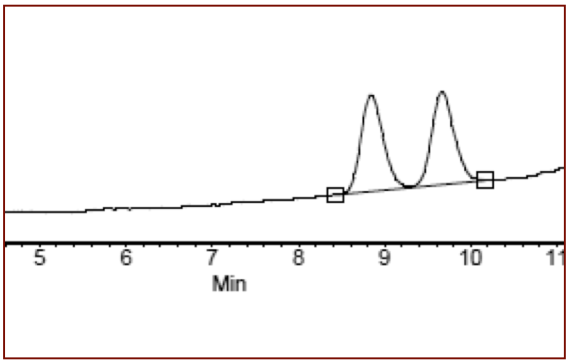


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	12.36	12.76	13.46	0.00	49.00	402.0	138.9	48.999
2	UNKNOWN	14.26	14.77	15.81	0.00	51.00	349.6	144.6	51.001
Total						100.00	751.6	283.4	100.000

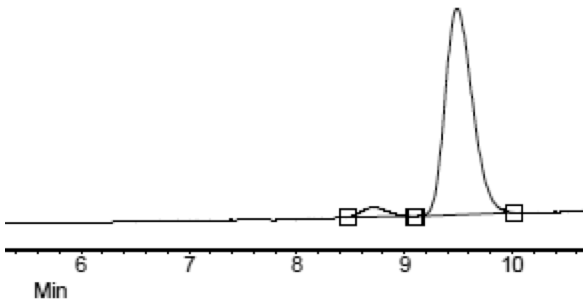


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
2	UNKNOWN	12.20	12.59	13.12	0.00	6.25	41.2	16.8	6.249
1	UNKNOWN	14.08	14.49	15.24	0.00	93.75	627.4	251.5	93.751
Total						100.00	668.6	268.3	100.000

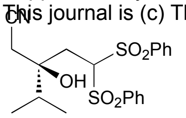


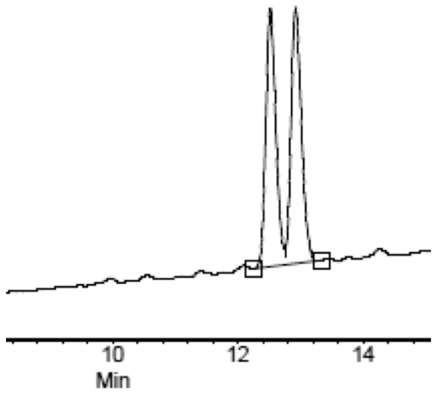


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.43	8.85	9.32	0.00	50.81	113.2	34.4	50.806
2	UNKNOWN	9.32	9.67	10.17	0.00	49.19	108.9	33.3	49.194
Total						100.00	222.0	67.6	100.000

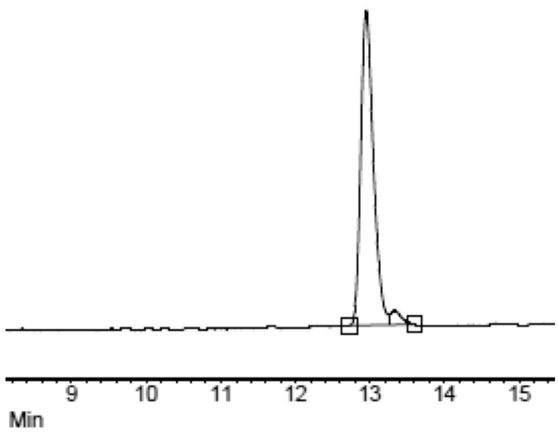


Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	8.48	8.71	9.09	0.00	4.09	20.9	5.8	4.085
2	UNKNOWN	9.10	9.49	10.01	0.00	95.91	464.0	136.7	95.915
Total						100.00	484.8	142.5	100.000





Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	12.24	12.51	12.75	0.00	49.63	396.8	73.7	49.633
2	UNKNOWN	12.75	12.92	13.34	0.00	50.37	392.7	74.8	50.367
Total						100.00	789.5	148.4	100.000



Index	Name	Start	Time	End	RT Offset	Quantity	Height	Area	Area
		[Min]	[Min]	[Min]	[Min]	[% Area]	[µV]	[µV.Min]	[%]
1	UNKNOWN	12.73	12.95	13.25	0.00	96.16	326.8	64.2	96.156
2	UNKNOWN	13.25	13.33	13.60	0.00	3.84	14.6	2.6	3.844
Total						100.00	341.5	66.8	100.000