

Supporting Information for:

On the Mechanism of Cu-Catalyzed Enantioselective Extended Conjugate Additions: a Structure-Based Approach

Tim den Hartog, Yange Huang, Martín Fañanás-Mastral, Anne Meuwese, Alena Rudolph, Manuel Pérez, Adriaan J. Minnaard* and Ben L. Feringa*

Stratingh Institute for Chemistry,
University of Groningen,
Nijenborgh 4, 9797 AG, Groningen, The Netherlands.
Fax: +31 50 363 4278;
Tel: +31 50 363 8569;
E-mail: B.L.Feringa@rug.nl; A.J.Minnaard@rug.nl

Table of contents

Footnotes	p 4
Conditions for Table 1	p 6
Conditions for Table 2	
Conditions for Table 3	
Conditions for Table 4	
Conditions for Table 5	
Conditions for Table 6	
Scheme S1. Alternative depiction of the mechanism of the enantioselective 1,6-addition.	p 7
Scheme S2. Alternative depiction of the mechanisms for the enantioselective 1,8-addition.	
Scheme S3. Alternative depiction of the mechanism for the catalytic formation of the 1,4-addition product in dienoates.	p 8
Figure S1. Graphical depiction of the transfer of chirality from the hypothetical Cu ^{III} - σ -intermediate at the β -position (39) to the Cu ^{III} - σ -intermediate at the δ -position (37).	
General experimental procedures	p 9
1. <u>Halide dependency: experimentals</u>	p 9
(2 <i>E</i> ,4 <i>E</i>)-ethyl undeca-2,4-dienoate (10)	
2. <u>Ester size dependency: experimentals</u>	
General procedure for the synthesis of $\alpha,\beta,\gamma,\delta$ -bis-unsaturated esters from $\alpha,\beta,\gamma,\delta$ -bis-unsaturated carboxylic acids	p 9

(2 <i>E</i> ,4 <i>E</i>)-methyl hexa-2,4-dienoate (13a)	
(2 <i>E</i> ,4 <i>E</i>)-ethyl hexa-2,4-dienoate (13b)	
(2 <i>E</i> ,4 <i>E</i>)- <i>iso</i> -propyl hexa-2,4-dienoate (13c)	
(2 <i>E</i> ,4 <i>E</i>)- <i>tert</i> -butyl hexa-2,4-dienoate (13d)	
3. Michael acceptor dependency: experimentals	p 10
(2 <i>E</i> ,4 <i>E</i>)- <i>S</i> -ethyl nona-2,4-dienethioate (15b)	
(3 <i>E</i> ,5 <i>E</i>)-deca-3,5-dien-2-one (15c)	
2-([1 <i>E</i> ,3 <i>E</i>]-octa-1,3-dienylsulfonyl)pyridine (15d)	
3-(2 <i>E</i> ,4 <i>E</i>)-hexa-2,4-dienoyloxazolidin-2-one (15e)	
(2 <i>E</i> ,4 <i>E</i>)-1-(1-methyl-1 <i>H</i> -imidazol-2-yl)hexa-2,4-dien-1-one (15f)	
4. Influence of the olefin substitution pattern: experimentals	p 11
General procedure for the synthesis of α -Me-substituted $\alpha,\beta,\gamma,\delta$ -bis-unsaturated esters from α,β -unsaturated aldehydes via Horner-Wadsworth-Emmons reaction	p 11
(2 <i>E</i> ,4 <i>E</i>)-ethyl 2-methylnona-2,4-dienoate (25a)	
(2 <i>E</i> ,4 <i>E</i>)-ethyl 3-methylnona-2,4-dienoate (25b)	
General procedure for the synthesis of $\alpha,\beta,\gamma,\delta$ -bis-unsaturated esters from α,β -unsaturated aldehydes via Horner-Wadsworth-Emmons reaction	p 12
(2 <i>E</i> ,4 <i>E</i>)-ethyl 4-methylhexa-2,4-dienoate (25c)	
<i>E</i> -ethyl 5-methylhexa-2,4-dienoate (25d)	
5. Olefin geometry dependency: experimentals	p 12
(2 <i>Z</i> ,4 <i>E</i>)-ethyl undeca-2,4-dienoate (28a)	
(2 <i>E</i> ,4 <i>Z</i>)-ethyl undeca-2,4-dienoate (28b)	
(2 <i>Z</i> ,4 <i>Z</i>)-ethyl undeca-2,4-dienoate (28c)	
6. Enantioselective 1,8- and 1,10-addition: experimentals	p 13
(2 <i>E</i> ,4 <i>E</i> ,6 <i>E</i>)-ethyl undeca-2,4,6-trienoate (29a)	
Synthesis of <i>S</i> -ethyl 2-(diethoxyphosphoryl)ethanethioate	p 13
General procedure for the synthesis of $\alpha,\beta,\gamma,\delta,\epsilon,\zeta$ -triple unsaturated thioesters from $\alpha,\beta,\gamma,\delta$ -bis-unsaturated aldehydes via Horner-Wadsworth-Emmons reaction	p 13
(2 <i>E</i> ,4 <i>E</i> ,6 <i>E</i>)- <i>S</i> -ethyl undeca-2,4,6-trienethioate (29b)	
Synthesis of (2 <i>E</i> ,4 <i>E</i> ,6 <i>E</i> ,8 <i>E</i>)-ethyl trideca-2,4,6,8-tetraenoate (29c) from	p 14
(2 <i>E</i> ,4 <i>E</i> ,6 <i>E</i>)-ethyl undeca-2,4,6-trienoate	
Synthesis of (2 <i>E</i> ,4 <i>E</i> ,6 <i>E</i> ,8 <i>E</i>)- <i>S</i> -ethyl trideca-2,4,6,8-tetraenethioate (29d)	p 14
from (2 <i>E</i> ,4 <i>E</i> ,6 <i>E</i>)-ethyl undeca-2,4,6-trienoate	
7. Halide dependency: spectra	p 15
<i>E</i> -Ethyl 5-ethylundec-3-enoate (11)	
8. Ester size dependency: spectra	p 17
(2 <i>E</i> ,4 <i>E</i>)- <i>iso</i> -propyl hexa-2,4-dienoate (13c)	
(2 <i>E</i> ,4 <i>E</i>)- <i>tert</i> -butyl hexa-2,4-dienoate (13d)	
(<i>S</i> , <i>E</i>)-methyl 5-methylhept-3-enoate (14a)	
(<i>S</i> , <i>E</i>)- <i>iso</i> -propyl 5-methylhept-3-enoate (14c)	
(<i>S</i> , <i>E</i>)- <i>tert</i> -butyl 5-methylhept-3-enoate (14d)	
(<i>S</i> , <i>E</i>)- <i>tert</i> -butyl 5-methylundec-3-enoate (14e)	
(<i>S</i> , <i>E</i>)- <i>tert</i> -butyl 5,8-dimethylnon-3-enoate (14f)	
(<i>S</i> , <i>E</i>)- <i>tert</i> -butyl 5-methyl-7-phenylhept-3-enoate (14g)	
9. Michael acceptor dependency: spectra	p 32
(2 <i>E</i> ,4 <i>E</i>)- <i>S</i> -ethyl nona-2,4-dienethioate (15b)	
2-([1 <i>E</i> ,3 <i>E</i>]-octa-1,3-dienylsulfonyl)pyridine (15d)	
3-(2 <i>E</i> ,4 <i>E</i>)-hexa-2,4-dienoyloxazolidin-2-one (15e)	
(2 <i>E</i> ,4 <i>E</i>)-1-(1-methyl-1 <i>H</i> -imidazol-2-yl)hexa-2,4-dien-1-one (15f)	
<i>E</i> -2-(4-ethyloct-2-enylsulfonyl)pyridine (16d)	
<i>E</i> -3-(5-methylhept-3-enoyl)oxazolidin-2-one (16e)	
<i>E</i> -1-(1-methyl-1 <i>H</i> -imidazol-2-yl)-3-phenethylhex-4-en-1-one (17f)	
(<i>S</i> , <i>E</i>)- <i>S</i> -ethyl 5-methylnon-3-enethioate (16i)	
10. Influence of the olefin substitution pattern: spectra	p 45
(2 <i>E</i> ,4 <i>E</i>)-ethyl 2-methylnona-2,4-dienoate (25a)	
(2 <i>E</i> ,4 <i>E</i>)-ethyl 3-methylnona-2,4-dienoate (25b)	
(2 <i>E</i> ,4 <i>E</i>)-ethyl 4-methylhexa-2,4-dienoate (25c)	

E-ethyl 5-methylhexa-2,4-dienoate (**25d**)
(5*R*,*E*)-ethyl 5-ethyl-2-methylnon-3-enoate (**26a**)
E/Z-ethyl 4,5-dimethylhept-3-enoate (**26c**)

11. Enantioselective 1,8- and 1,10-addition: spectra

p 53

(2*E*,4*E*,6*E*)-ethyl undeca-2,4,6-trienoate (**29a**)
(2*E*,4*E*,6*E*)-*S*-ethyl undeca-2,4,6-trienethioate (**29b**)
(2*E*,4*E*,6*E*,8*E*)-ethyl trideca-2,4,6,8-tetraenoate (**29c**)
(2*E*,4*E*,6*E*,8*E*)-*S*-ethyl trideca-2,4,6,8-tetraenethioate (**29d**)
(*R*,3*E*,5*E*)-ethyl 7-ethylundeca-3,5-dienoate (**30a**)
(*R*,3*E*,5*E*)-*S*-ethyl 7-methylundeca-3,5-dienethioate (**30b**)
(*R*,3*E*,5*E*,7*E*)-ethyl 9-ethyltrideca-3,5,7-trienoate (**30c**)
(*R*,3*E*,5*E*,7*E*)-*S*-ethyl 9-methyltrideca-3,5,7-trienethioate (**30d**)

12. References

p 65

Footnotes

- (F1) Performing 1,6-ECA to substrate **25c** at slightly higher temperature (−60 °C) for 40 h gave full conversion to the 1,6-addition product **26c** in 94% conversion, 59% yield, regioselectivity 1,6 : 1,4 = >92 : 8, but as a racemic mixture (0% ee).
- (F2) When the 1,6-ECA to substrate **25d** was performed at −60 °C, a mixture of 1,4- and 1,6-addition product (**27d** : **26d** = 43 : 57) was obtained with slightly higher conversion (≈ 40% conv., ≈ 40% of **25d** was recovered). The ee of the 1,4-addition product **27d** was 35%.
- (F3) In ref 15a the 1,4-ECA of EtMgBr to *Z*-methyl hex-2-enoate using a Cu-**L1** complex is described; for this reaction no isomerization of the olefin is observed under the reaction conditions. We consider it more appropriate to compare the 1,6-ECA in Table 5 with 1,4-ECA results for which the same catalyst (Cu-**L2**) is used.
- (F4) We presume only one Cu-complex is involved in the reaction mechanism. We have never observed the drastic effect of dilution on the 1,6-ECA that should be expected for a reaction that is 2nd order in catalyst. However, kinetic studies are required to confirm the 1st order dependency on catalyst.
- (F5) An immediate coordination to the remote olefin seems less likely in view of our results, however it cannot be excluded.
- (F6) This is in contrast to the mechanism we had proposed on literature precedent in ref 7b.
- (F7) The fact that the opposite enantiomer of the 1,6-addition product is obtained in excess using either the 2*E*,4*E*-substrate **10** or the 2*E*,4*Z*-substrate **28a** (Table 6, entry 1 vs. 2), further supports that, if the hypothetical Cu^{III}-σ-complex **39** at the β-position would be involved in the mechanism, the stereochemical information would be transferred from the β- to the δ-position.
- (F8) Alternatively, the 1,6-addition product would be formed with a lower enantiomeric excess than the 1,4-addition product, if (partial) racemization occurs in the transfer of the Cu-complex from the β-position to the δ-position.
- (F9) An initial formation of hypothetical Cu^{III}-σ-complex **39** at the β-position, followed by a kinetic resolution to give the 1,6-addition products in high ee, and the 1,4-addition products in low ee, seems unlikely due to the disparity between the enantioselectivity for the addition to 2*E*,4*Z*-substrate **28b** (ee 12%; *S*-isomer) and the addition to the 2*Z*,4*Z*-substrate **28c** (ee 66%; *R*-isomer). If the isomerization at the *re* and *si* face would proceed with different rates it is expected that the product from the 2*E*,4*Z*-substrate **28b** and the 2*Z*,4*Z*-substrate **28c** would have been obtained with the same amount of enantioselectivity, but with an opposite sign.
- (F10) Due to the better Michael acceptor properties of the bisunsaturated thioester and ketone substrates, the mechanism for 1,6-ECA to these substrates might proceed via consecutive thioester or ketone analogues of Cu^I-π-complex **35**, Cu^{III}-σ-complex **39** (instead of Cu^I-π-complex **36**) and Cu^{III}-σ-complex **37**.
- (F11) Please note that the absence of isomerization is in contrast to the 1,4-addition to *Z*-methyl cinnamate using Cu-**L2** (Table 5, entry 6, far right columns);^{15a} here, a (partial) isomerization was observed from the *Z*- to the *E*-substrate.^{15a} For this isomerization during the 1,4-addition we previously proposed a reversible formation of a Cu^{III}-σ-intermediate.

- (F12) Preliminary computational results indicate that instead of previously drawn Br coordination to Cu in intermediates **33**, **35** and **36**, it would be more appropriate to draw a coordination of the electronrich alkylCu intermediate to the electron poor Mg. In SI, Scheme S1-S3 the alternative depictions of the mechanism can be found.
- (F13) This is in sharp contrast to the 1,4-addition, the use of the CO-oxazolidinone EWG in combination with Cu-**L1** as catalyst gave 99% conversion and 50% ee, see ref 3c.
- (F14) The mechanism for 1,8-ECA to thioester substrates might involve instead of intermediate **44**, a first Cu^I- π -complex (analogous to **42**), and only then a first Cu^{III}- σ -complex in which the Cu would be coordinated to the δ -position.
- (F15) A coordination of the Cu-catalyst to the SEt seems unlikely due to steric reasons, but cannot be excluded.

Conditions for Table 1:

1,6-addition: a solution of **10** in CH₂Cl₂ was added to a solution of EtMgCl, EtMgBr or EtMgI (3.0 M in Et₂O, 2.0 equiv), (–)-(R,S)-**L2** (5.25 mol%) and CuCl, CuBr•SMe₂ or CuI (5 mol%) in CH₂Cl₂ (0.2 M final concentration in **10**).

1,4-addition: a solution of methyl crotonate in *t*BuOMe was added in 1 h to a solution of EtMgCl, EtMgBr or EtMgI (3.0 M solution in Et₂O, 1.5 equiv), and (–)-(R,S)-**L1**-CuCl, (–)-(R,S)-**L1**-CuBr, or (–)-(R,S)-**L1**-CuI complex (5 mol%) in *t*BuOMe (0.35 M final concentration in substrate) at –78 °C, 5 h total reaction time.

Conditions for Table 2:

1,6-addition: a solution of **13** in CH₂Cl₂ was added in 2 h to a solution of R¹MgBr (solution in Et₂O, 2.0 equiv), (–)-(R,S)-**L2** (5.25 mol%) and CuBr•SMe₂ (5 mol%) in CH₂Cl₂ (0.2 M final concentration in **13**) at –70 °C, 16 h total reaction time.

1,4-addition: a solution of methyl crotonate, ethyl crotonate, *iso*-propyl crotonate, or *tert*-butyl crotonate in *t*BuOMe was added in 1 h to a solution of EtMgBr (3.0 M solution in Et₂O, 1.15 equiv), (–)-(R,S)-**L2** (6 mol%), and CuBr•SMe₂ (5 mol%) in *t*BuOMe (0.5 M final concentration in substrate) at –75 °C, 2 h total reaction time.

Conditions for Table 3:

1,6-addition: a solution of substrate in CH₂Cl₂ was added in 2 h to a solution of R²MgBr (solution in Et₂O, 2.0 equiv), (–)-(R,S)-**L2** (5.25 mol%) and CuBr•SMe₂ (5 mol%) in CH₂Cl₂ (0.2 M final concentration in substrate) at –70 °C, 16 h total reaction time.

Conditions for Table 4:

1,6-addition: a solution of **25** in CH₂Cl₂ was added in 2 h to a solution of EtMgBr (solution in Et₂O, 2.0 equiv), (–)-(R,S)-**L2** (5.25 mol%) and CuBr•SMe₂ (5 mol%) in CH₂Cl₂ (0.2 M final concentration in **25**) at –70 °C, 16 h total reaction time.

1,4-addition to the α-Me-substituted ester substrate: a solution of ethyl tiglate in CH₂Cl₂ was added in 2 h to a solution of EtMgBr (solution in Et₂O, 2.0 equiv), (–)-(R,S)-**L2** (5.25 mol%) and CuBr•SMe₂ (5 mol%) in CH₂Cl₂ (0.2 M final concentration in substrate) at –70 °C, 16 h total reaction time.

1,4-addition to the β-Me-substituted ester substrate: a solution of ethyl 3-methyl-2-butenate in CH₂Cl₂ was added in 2 h to a solution of EtMgBr (solution in Et₂O, 2.0 equiv), (–)-(R,S)-**L2** (5.25 mol%) and CuBr•SMe₂ (5 mol%) in CH₂Cl₂ (0.2 M final concentration in substrate) at –70 °C, 16 h total reaction time.

Conditions for Table 5:

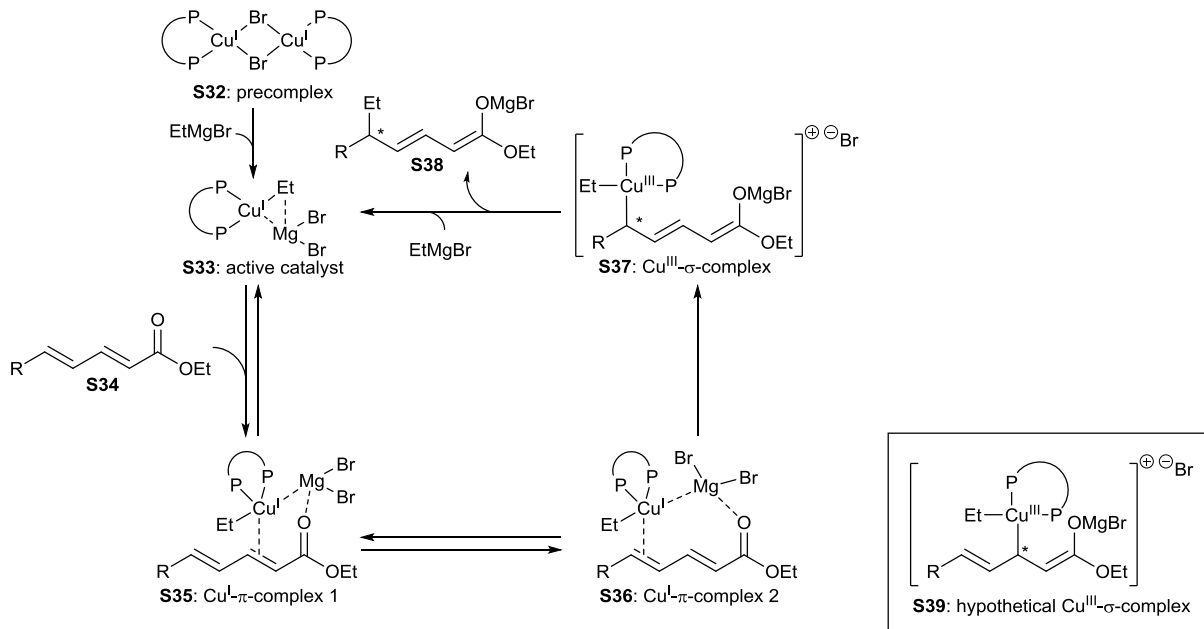
1,6-addition: Conditions: a solution of substrate in CH₂Cl₂ was added in 2 h to a solution of EtMgBr (solution in Et₂O, 2.0 equiv), (–)-(R,S)-**L2** (5.25 mol%) and CuBr•SMe₂ (5 mol%) in CH₂Cl₂ (0.2 M final concentration in substrate) at –70 °C, 16 h total reaction time.

1,4-addition: a solution of substrate in *t*BuOMe was added in 1 h to a solution of EtMgBr (3.0 M solution in Et₂O, 1.5 equiv), and (+)-(S,R)-**L2**-CuBr (5 mol%) in *t*BuOMe (0.35 M final concentration in substrate) at –78 °C, 5 h total reaction time.

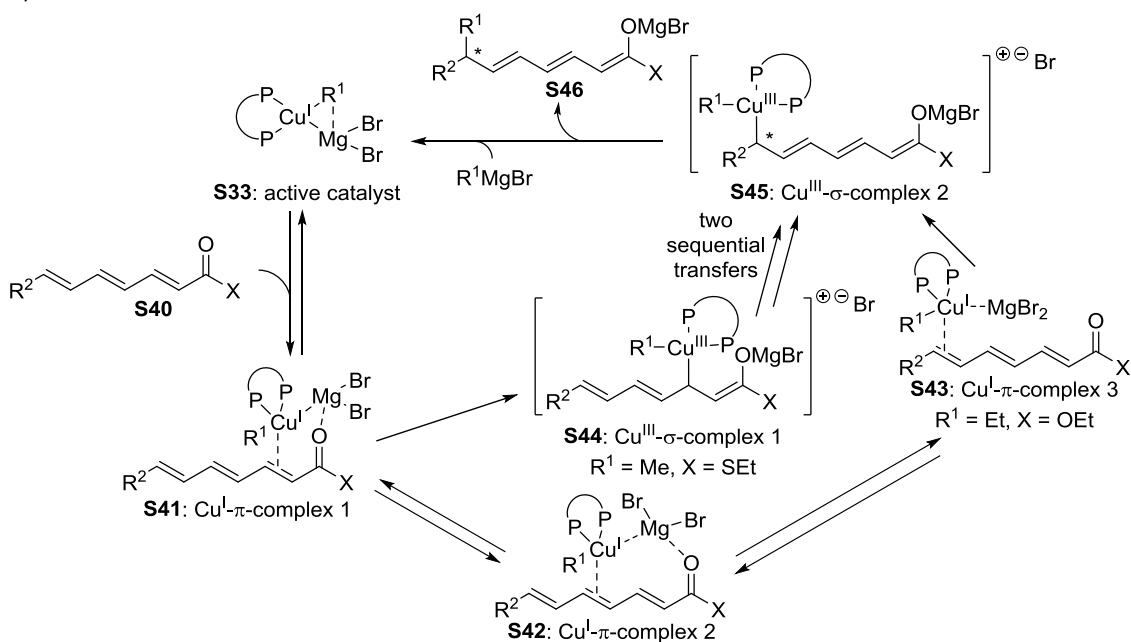
Conditions for Table 6:

Conditions: a solution of **29** in CH₂Cl₂ was added in 2 h to a solution of EtMgBr (solution in Et₂O, 2.0 equiv), (–)-(R,S)-**L2** (5.25 mol%, 7.88 mol% or 10.5 mol%) and CuBr•SMe₂ (5 mol%, 7.5 mol% or 10 mol%) in CH₂Cl₂ (0.2 M final concentration in **29**) at –70 °C, 48 h total reaction time.

Scheme S1. Alternative depiction of the mechanism of the enantioselective 1,6-addition.^[S1]



Scheme S2. Alternative depiction of the mechanisms for the enantioselective 1,8-addition.



Scheme S3. Alternative depiction of the mechanism for the catalytic formation of the 1,4-addition product in dienates.

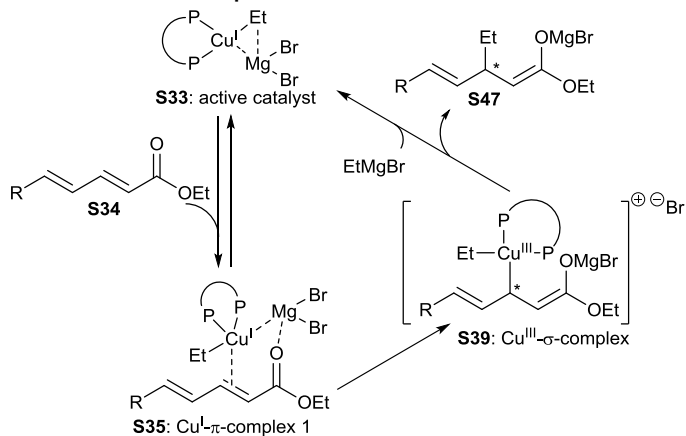
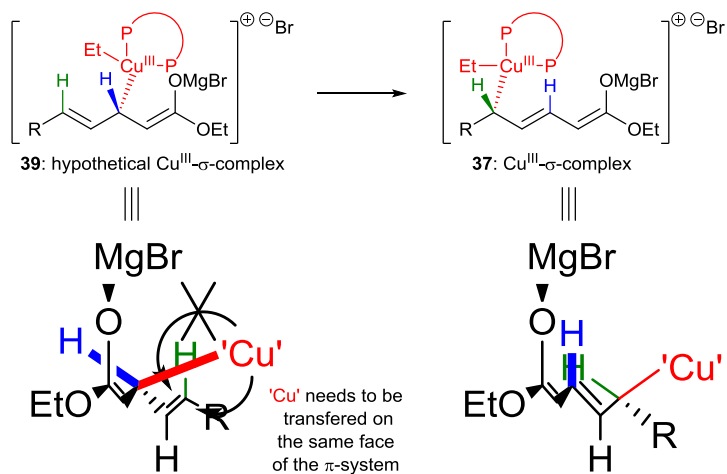


Figure S1. Graphical depiction of the transfer of chirality from the hypothetical Cu^{III} - σ -intermediate at the β -position (**39**) to the Cu^{III} - σ -intermediate at the δ -position (**37**).



General experimental procedures:

Thin-layer chromatography (TLC) was performed on commercial Kieselgel 60 F₂₅₄ silica gel plates and compounds were visualized with KMnO₄ reagent. Flash chromatography was performed on silica gel. Drying of solutions was performed with MgSO₄. Concentration of solutions was conducted with a rotary evaporator. Progress of the reactions and conversion was determined by TLC or GC-MS (GC, HP6890; MS, HP5973) with an HP5 column (Agilent Technologies, Palo Alto, CA). *Ee* and regioselectivities were determined by chiral GC (CP-Chiraldex-B-PM (30 m x 0.25 mm)) using flame ionization detection or HPLC analysis ((*R,R*)-Whelk-01, 4.6 x 250 mm, 5 m, 40 °C, 0.5 mL/min, 210 nm; chiralcel OD-H, 4.6 x 250 mm, 5 m, 40 °C, 0.5 mL/min, 215 nm; chiralcel OJ-H, 4.6 x 250 mm, 5 m, 40 °C, 0.5 mL/min, 275 nm) (in comparison to authentic samples of racemates of the products). Optical rotations were measured in CH₂Cl₂ or CHCl₃ on a Schmidt + Haensch polarimeter (Polartronic MH8) with a 10 cm cell (c given in g/100 mL), [α]_D values are given in 10⁻¹ deg cm² g⁻¹. ¹H NMR spectra were recorded at 400 MHz with CDCl₃ as solvent (Varian AMX400 spectrometer). ¹³C NMR spectra were obtained at 100.59 MHz in CDCl₃. The nature of the carbon was determined from APT ¹³C NMR experiments. Chemical shifts were determined relative to the residual solvent peaks (CHCl₃, δ = 7.26 for hydrogen atoms, δ = 77.16 for carbon atoms). The following abbreviations were used to indicate signal multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; p, pentet; br, broad; m, multiplet. High resolution mass spectra were determined on a FTMS Orbitrap FischerScientific mass spectrometer by ESI measurements in positive mode. Fragmentation patterns were determined by GC-MS (GC, HP6890; MS, HP5973) with an HP5 column (Agilent Technologies, Palo Alto, CA).

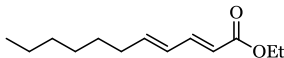
All reactions under a N₂ atmosphere were conducted using standard Schlenk techniques. CH₂Cl₂ was distilled from CaH₂ under a N₂ atmosphere prior to use. Et₂O was distilled from Na using benzophenone as indicator under a N₂ atmosphere prior to use. THF was distilled from Na using benzophenone as indicator under a N₂ atmosphere prior to use. CuBr·SMe₂ was purchased from Sigma-Aldrich. (-)-(*R,S*)-reversed Josiphos and (+)-(*S,R*)-reversed Josiphos were purchased from Sigma-Aldrich. Grignard reagents were purchased from Sigma-Aldrich (EtMgBr and hexylMgBr) or prepared from the corresponding alkyl bromides and magnesium turnings in anhydrous Et₂O following standard procedures. Grignard reagents were titrated using sBuOH and catalytic amounts of 1,10-phenanthroline before use.

Sorbic acid, oxalyl chloride (2 M solution in CH₂Cl₂), NaH (60% dispersion in mineral oil), diethyl (2-oxopropyl)phosphonate, oxazolidin-2-one, triethyl phosphonopropionate, triethyl phosphonoacetate, (2*E*,4*E*)-nona-2,4-dienal (85% technical grade) and DIBAL-H (1.0 M in CH₂Cl₂) were purchased from Sigma-Aldrich. DMF, *E*-hept-2-enal, *n*BuLi in hexanes, *E*-2-methylbut-2-enal and 3-methylbut-2-enal were purchased from ACROS. MeOH and *i*PrOH were purchased from Lab-Scan. *t*BuOH was purchased from Boom. 1-Methyl-1H-imidazole was purchased from Janssen Chimica.

S-ethyl 2-(triphenylphosphoranylidene)ethanethioate was prepared as described in ref S2. IBX was prepared as described in ref S3.

1. Halide dependency: experimentals

(2*E*,4*E*)-ethyl undeca-2,4-dienoate (**10**) was prepared according to the procedure given in ref S4, reaction time 16 h. [5.0 mmol scale, 80% yield, colorless oil]



Data were in accordance to those given in ref S4.

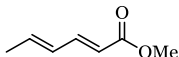
2. Ester size dependency: experimentals

General procedure for the synthesis of $\alpha,\beta,\gamma,\delta$ -bis-unsaturated esters from $\alpha,\beta,\gamma,\delta$ -bis-unsaturated carboxylic acids:^[S5]

In a dried two necked flask equipped with septum and stirring bar under a N₂ atmosphere, sorbic acid (1 equiv) was dissolved in CH₂Cl₂ (4.0 mL/mmol substrate) and DMF (1 equiv) was added. Then oxalyl chloride (3 equiv, 2 M solution in CH₂Cl₂) was added slowly (over 30 min) with the formation of CO and CO₂ gas. After stirring for 1 h (after addition) at room temperature the alcohol (6 equiv) was added and the reaction mixture was stirred for an additional 4 h. The reaction mixture was quenched with a saturated aq. NaHCO₃ solution (4 mL/mmol substrate) and the layers were separated. The organic layer was washed with an aq. NaHCO₃ solution (2x 4 mL/mmol substrate) and the resulting combined aqueous layers were washed with CH₂Cl₂ (4 mL/mmol substrate). Then the combined organic extracts were dried and carefully concentrated to a yellow oil. Flash column chromatography (1:49 Et₂O:pentane) yielded the product as a colorless oil.

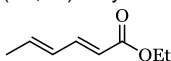
(2*E*,4*E*)-methyl hexa-2,4-dienoate (**13a**) was prepared via the general procedure for the synthesis of $\alpha,\beta,\gamma,\delta$ -bis-unsaturated esters from $\alpha,\beta,\gamma,\delta$ -bis-unsaturated carboxylic acids using MeOH.

[5.0 mmol scale, 77% yield, colorless oil]



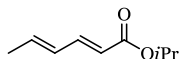
Data were in accordance to those given in ref S6; additional data: MS (m/z) 126 (49) [*M*⁺], 111 (100) [*M*⁺-Me], 95 (59) [*M*⁺-OMe], 67 (85) [C₄H₃O⁺]; HRMS calcd. for C₇H₁₀O₂Na⁺ 149.0578, found 149.0578.

(2*E*,4*E*)-ethyl hexa-2,4-dienoate (**13b**) was purchased.



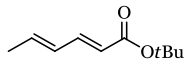
(2*E*,4*E*)-*iso*-propyl hexa-2,4-dienoate (**13c**) was prepared via the general procedure for the synthesis of $\alpha,\beta,\gamma,\delta$ -bis-unsaturated esters from $\alpha,\beta,\gamma,\delta$ -bis-unsaturated carboxylic acids using *i*PrOH.

[5.0 mmol scale, 83% yield, colorless oil]



¹H NMR (400 MHz, CDCl₃, 25 °C, TMS): δ= 7.16 (dd, *J* = 15.3, 9.8 Hz, 1H), 6.18–5.98 (m, 2H), 5.68 (d, *J* = 15.4 Hz, 1H), 5.08–4.94 (m, 1H), 1.78 (d, *J* = 6.0 Hz, 3H), 1.20 ppm (dd, *J* = 6.3, 1.5 Hz, 6H); ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ= 166.7 (C), 144.6 (CH), 138.9 (CH), 129.8 (CH), 119.6 (CH), 67.4 (CH), 21.9 (CH₃), 18.6 ppm (CH₃); MS (*m/z*) 154 (21) [*M*⁺], 112 (40) [*M*⁺-*i*Pr+H], 97 (100) [C₅H₅O₂⁺], 95 (93) [*M*⁺-O*i*Pr], 67 (69) [C₄H₃O⁺]; HRMS calcd. for C₉H₁₄O₂Na⁺ 177.0886, found 177.0881.

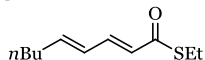
(2*E*,4*E*)-*tert*-butyl hexa-2,4-dienoate (**13d**) was prepared via the general procedure for the synthesis of α,β,γ,δ-bis-unsaturated esters from α,β,γ,δ-bis-unsaturated carboxylic acids using *t*BuOH. [4.5 mmol scale, 83% yield, colorless oil]



Data were in accordance to those given in ref S7; additional data: ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ= 166.7 (C), 143.9 (CH), 138.4 (CH), 129.9 (CH), 121.1 (CH), 80.0 (C), 28.2 (CH₃), 18.6 ppm (CH₃); MS (*m/z*) 168 (36) [*M*⁺], 113 (49), 112 (40) [*M*⁺-*t*Bu+H], 97 (85) [C₅H₅O₂⁺], 95 (76) [*M*⁺-O*t*Bu], 67 (56) [C₄H₃O⁺], 57 (100) [C₂HO₂⁺]; HRMS calcd. for C₁₀H₁₆O₂⁺ 168.1151, found 168.1150.

3. Michael acceptor dependency: experimentals

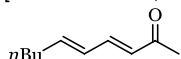
(2*E*,4*E*)-*S*-ethyl nona-2,4-dienethioate (**15b**) was prepared according to the procedure in ref S8 (procedure D; the reaction of aldehydes with Ph₃PCHCOSEt, 24 h reaction time) using *E*-hept-2-enal. [14.9 mmol scale, 61% yield, colorless oil]



¹H NMR (400 MHz, CDCl₃, 25 °C, TMS): δ= 7.16 (dd, *J* = 15.2, 10.1 Hz, 1H), 6.22–6.09 (m, 2H), 6.05 (d, *J* = 15.2 Hz, 1H), 2.93 (*J* = 7.4 Hz, 2H), 2.16 (dd, *J* = 13.9, 6.7 Hz, 2H), 1.39 (dt, *J* = 14.4, 7.2 Hz, 2H), 1.34–1.29 (m, 2H), 1.26 (td, *J* = 7.4, 0.5 Hz, 3H), 0.88 ppm (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ= 190.3 (C), 146.6 (CH), 141.1 (CH), 128.4 (CH), 126.6 (CH), 33.1 (CH₂), 31.0 (CH₂), 23.4 (CH₂), 22.4 (CH₂), 15.1 (CH₃), 14.1 ppm (CH₃); MS (*m/z*) 198 (14) [*M*⁺], 137 (100) [*M*⁺-SEt], 81 (39) [C₅H₅O⁺]; HRMS calcd. for C₁₁H₁₈OS⁺ 198.1078, found 198.1083.

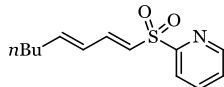
(3*E*,5*E*)-deca-3,5-dien-2-one (**15c**):^[S9]

In a roundbottom flask equipped with stirring bar under a N₂ atmosphere, NaH (60% solution in mineral oil, 2.7 equiv) was vigorously stirred in anhydrous THF (10 mL/mmol aldehyde) and cooled to –20 °C. Diethyl (2-oxopropyl)phosphonate (neat, 3.0 equiv) was added dropwise and the mixture was stirred for 30 min. Subsequently, *E*-hept-2-enal (1 equiv) dissolved in anhydrous THF (2.0 mL/mmol aldehyde) was added dropwise. After addition, the solution was stirred for 20 min at –20 °C and was subsequently stirred at room temperature for 30 min. The reaction mixture was diluted with Et₂O (2 mmol/mmol aldehyde) and the solution was subsequently washed with NH₄Cl (saturated aq. solution, 2 mL/mmol aldehyde), Na₂CO₃ (saturated aq. solution, 2 mL/mmol aldehyde) and brine (2 mL/mmol aldehyde). The combined organic extracts were dried and concentrated. Flash column chromatography (1:99 Et₂O:pentane) yielded the product. [7.6 mmol scale, 65% yield, colorless oil]



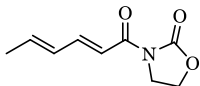
Colorless oil; data were in accordance with those given in ref S10.

2-([1*E*,3*E*]-octa-1,3-dienylsulfonyl)pyridine (**15d**) was prepared analogous to the general procedure for the synthesis of α,β-unsaturated sulfones in ref S11 using *E*-hept-2-enal. [3.0 mmol scale, 27% yield (2 steps), slightly yellow viscous oil]



¹H NMR (400 MHz, CDCl₃, 25 °C, TMS): δ= 8.70 (d, *J* = 4.3 Hz, 1H), 8.06 (d, *J* = 7.8 Hz, 1H), 7.91 (td, *J* = 7.8, 1.5 Hz, 1H), 7.48 (dd, *J* = 7.1, 4.9 Hz, 1H), 7.33 (dd, *J* = 14.9, 10.7 Hz, 1H), 6.45 (d, *J* = 14.9 Hz, 1H), 6.32–6.22 (m, 1H), 6.15 (dd, *J* = 15.1, 10.8 Hz, 1H), 2.17 (q, *J* = 7.0 Hz, 2H), 1.46–1.21 (m, 4H), 0.87 ppm (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ= 158.9 (C), 150.4 (CH), 148.8 (CH), 145.8 (CH), 138.2 (CH), 127.1 (CH), 126.3 (CH), 124.7 (CH), 121.8 (CH), 32.9 (CH₂), 30.6 (CH₂), 22.3 (CH₂), 13.9 ppm (CH₃); MS (*m/z*) 251 (1) [*M*⁺], 130 (100) [C₅H₆O₂S⁺], 80 (44) [C₆H₆⁺], 79 (38), 78 (29) [C₅H₅N⁺]; HRMS calcd. for C₁₃H₁₇NO₂SN⁺ 274.0886, found 274.0868.

3-(2*E*,4*E*)-hexa-2,4-dienoyloxazolidin-2-one (**15e**) was prepared analogous to the general coupling procedure (as illustrated for 3-(*E*-3-(methoxycarbonyl)propenoyl)-1,3-oxazolidin-2-one **7**) in ref S12 using sorbic acid and oxazolidin-2-one; Flash column chromatography (1:1 Et₂O:pentane) yielded the product.
[5.0 mmol scale, 17% yield, white solid, mp: 119.7-119.8 °C]

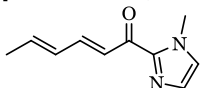


¹H NMR (400 MHz, CDCl₃, 25 °C, TMS): δ = 7.42 (dd, *J* = 15.0, 10.5 Hz, 1H), 7.17 (d, *J* = 15.1 Hz, 1H), 6.44–6.10 (m, 2H), 4.39 (t, *J* = 8.0 Hz, 2H), 4.05 (t, *J* = 8.0 Hz, 2H), 1.86 ppm (d, *J* = 6.3 Hz, 3H); ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ = 165.6 (C), 153.6 (C), 146.6 (CH), 141.1 (CH), 130.4 (CH), 117.5 (CH), 62.1 (CH₂), 42.8 (CH₂), 18.8 ppm (CH₃); MS (*m/z*) 281 (1) [*M*⁺], 119 (53) [C₄H₇O₂S⁺], 83 (66), 79 (51), 69 (53) [C₅H₉⁺], 55 (100) [C₃H₃O⁺]; HRMS calcd. for C₉H₁₁NO₃Na⁺ 204.0631, found 204.0629; Elemental analysis calcd. (%) for C₉H₁₁NO₃: C, 58.93; H, 5.97; N, 7.71, Found: C, 58.78, H, 5.97; N, 7.63.

(2*E*,4*E*)-1-(1-methyl-1H-imidazol-2-yl)hexa-2,4-dien-1-one (**15f**):

In a two necked flask equipped with septum and stirring bar under a N₂ atmosphere, 1-methyl-1H-imidazole (2.2 equiv) was dissolved in anhydrous THF (4.0 mL/mmol substrate) and the solution was cooled to –78 °C and stirred for 30 min. Then *n*BuLi (2.0 equiv, 1.6 M in hexanes) was added dropwise (in 30 min) and the mixture was stirred for 5 min after addition. Then the reaction mixture was allowed to warm up to room temperature in 30 min, cooled down again to –78 °C and stirred for 20 min. A solution of sorbic acid (1 equiv) in anhydrous THF (0.5 mL/mmol substrate) was added and the reaction mixture was stirred for 10 min after addition. Then the reaction mixture was allowed to warm up to room temperature in 40 min, and was slowly quenched with a saturated aq. NaHCO₃ solution (1 mL/mmol substrate). EtOAc (2 mL/mmol substrate) was added and the layers were separated. The aqueous layer was washed with EtOAc (2x 4 mL/mmol substrate). The combined organic extracts were dried and carefully concentrated to a brown solid. Flash column chromatography (1:1 Et₂O:pentane) yielded the product.

[20 mmol scale, 38% yield, white solid, mp: 88.1-88.4 °C]



¹H NMR (400 MHz, CDCl₃, 25 °C, TMS): δ = 7.35–7.20 (m, 2H), 7.03 (d, *J* = 2.8 Hz, 1H), 6.91 (d, *J* = 2.7 Hz, 1H), 6.27–6.05 (m, 2H), 3.91 (d, *J* = 3.6 Hz, 3H), 1.76 ppm (dd, *J* = 6.4, 2.4 Hz, 3H); ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ = 180.9 (C), 143.9 (C), 143.8 (CH), 140.9 (CH), 130.7 (CH), 129.0 (CH), 127.0 (CH), 124.2 (CH), 36.2 (CH₃), 18.9 ppm (CH₃); MS (*m/z*) 176 (29) [*M*⁺], 161 (60) [*M*⁺-Me], 147 (45) [C₈H₆N₂O⁺], 133 (100) [C₇H₅N₂O⁺], 82 (53) [C₄H₆N₂⁺]; HRMS calcd. for C₁₀H₁₃N₂O⁺ 177.1022, found 177.1020; Elemental analysis calcd. (%) for C₁₀H₁₂N₂O: C, 68.17; H, 6.90; N, 15.91, Found: C, 68.03, H, 6.85; N, 15.86.

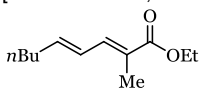
4. Influence of the olefin substitution pattern: experimentals

General procedure for the synthesis of α-Me-substituted α,β,γ,δ-bis-unsaturated esters from α,β-unsaturated aldehydes via Horner-Wadsworth-Emmons reaction.^[S13]

In a roundbottom flask equipped with stirring bar under a N₂ atmosphere, triethyl phosphonopropionate (1.2 equiv) was dissolved in anhydrous THF (4 mL/mmol aldehyde) and cooled to –78 °C. *n*BuLi (1.6 M solution in hexanes, 1.15 equiv) was added dropwise and the mixture was stirred for 30 min. Subsequently, the aldehyde (1 equiv) dissolved in anhydrous THF (1 mL/mmol aldehyde) was added dropwise. After addition, the solution was allowed to warm up to room temperature and stirred for 16 h. The reaction mixture was diluted with Et₂O (5 mL/mmol aldehyde) and the solution was subsequently washed with NH₄Cl (saturated aq. solution, 5 mL/mmol aldehyde), Na₂CO₃ (saturated aq. solution, 5 mL/mmol aldehyde) and brine (5 mL/mmol aldehyde). The combined organic extracts were dried and concentrated. Flash column chromatography (1:99 Et₂O:pentane) yielded the product.

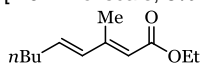
(2*E*,4*E*)-ethyl 2-methylnona-2,4-dienoate (**25a**) was prepared via the general procedure for the synthesis of α-Me-substituted α,β,γ,δ-bis-unsaturated esters from α,β-unsaturated aldehydes via Horner-Wadsworth-Emmons reaction using *E*-hept-2-enal.

[10 mmol scale, 90% yield, *E*:*Z* = 16:1, colorless oil]



¹H NMR (400 MHz, CDCl₃, 25 °C, TMS): δ = 7.13 (d, *J* = 11.3 Hz, 1H), 6.37–6.24 (m, 1H), 6.12–5.97 (m, 1H), 4.16 (q, *J* = 7.1 Hz, 2H), 2.15 (q, *J* = 7.0 Hz, 2H), 1.89 (d, *J* = 0.8 Hz, 3H), 1.46–1.20 (m, 7H), 0.87 ppm (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ = 168.6 (C), 143.1 (CH), 138.6 (CH), 126.0 (CH), 125.1 (C), 60.4 (CH₂), 33.0 (CH₂), 31.2 (CH₂), 22.3 (CH₂), 14.4 (CH₃), 13.9 (CH₃), 12.6 ppm (CH₃); MS (*m/z*) 196 (47) [*M*⁺], 151 (30) [*M*⁺-OEt], 139 (100) [C₈H₁₀O₂⁺], 112 (35), 111 (85) [C₆H₇O₂⁺]; HRMS calcd. for C₁₂H₂₀O₂Na⁺ 219.1356, found 219.1355.

(2*E*,4*E*)-ethyl 3-methylnona-2,4-dienoate (**25b**) was prepared via the procedure described in ref S14.
[4.9 mmol scale, 8% yield, colorless oil]



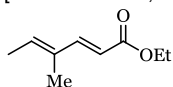
Data were in accordance to those given in ref S14; additional data: MS (m/z) 196 (10) [*M*⁺], 139 (96) [C₈H₁₀O₂⁺], 111 (100) [C₆H₇O₂⁺]; HRMS calcd. for C₁₂H₂₁O₂⁺ 197.1536, found 197.1536.

General procedure for the synthesis of $\alpha,\beta,\gamma,\delta$ -bis-unsaturated esters from α,β -unsaturated aldehydes via Horner-Wadsworth-Emmons reaction:^[S15]

In a roundbottom flask equipped with stirring bar under a N₂ atmosphere, NaH (1.75 equiv, 60% dispersion in mineral oil) was vigorously stirred in anhydrous THF (1 mL/mmol aldehyde) and cooled to -20 °C. Triethyl phosphonoacetate (neat, 1.75 equiv) was added dropwise and the mixture was stirred for 30 min. Subsequently, the aldehyde (1 equiv) dissolved in anhydrous THF (0.1 mL/mmol aldehyde), was added dropwise. After addition, the solution was stirred for 20 min at -20 °C and subsequently stirred at room temperature for 30 min. The reaction mixture was diluted with Et₂O (2 mL/mmol aldehyde) and the solution was subsequently washed with NH₄Cl (saturated aq. solution, 2 mL/mmol aldehyde), Na₂CO₃ (saturated aq. solution, 2 mL/mmol aldehyde) and brine (2 mL/mmol aldehyde). The combined organic extracts were dried and concentrated. Flash column chromatography (1:99 Et₂O:pentane) yielded the product.

(2*E*,4*E*)-ethyl 4-methylhexa-2,4-dienoate (**25c**) was prepared via the general procedure for the synthesis of $\alpha,\beta,\gamma,\delta$ -bis-unsaturated esters from α,β -unsaturated aldehydes via Horner-Wadsworth-Emmons reaction using *E*-2-methylbut-2-enal.

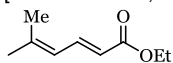
[10 mmol scale, 89% yield, *Z*-isomer not observed, colorless oil]



Data were in accordance to those given in ref S16; additional data: ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ = 167.8 (C), 149.6 (CH), 136.4 (CH), 133.9 (C), 115.4 (CH), 60.2 (CH₂), 14.7 (CH₃), 14.5 (CH₃), 11.9 ppm (CH₃); MS (m/z) 154 (69) [*M*⁺], 139 (47) [*M*⁺-CH₃], 111 (86) [C₆H₇O₂⁺], 109 (54) [*M*⁺-OEt], 83 (58) [C₄H₃O₂⁺], 81 (100) [*M*⁺-CO₂Et]; HRMS calcd. for C₉H₁₄O₂⁺ 154.0994, found 154.0987.

E-ethyl 5-methylhexa-2,4-dienoate (**25d**) was prepared via the general procedure for the synthesis of $\alpha,\beta,\gamma,\delta$ -bis-unsaturated esters from α,β -unsaturated aldehydes via Horner-Wadsworth-Emmons reaction using 3-methylbut-2-enal.

[10 mmol scale, 84% yield, *Z*-isomer not observed, colorless oil]

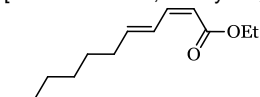


Data were in accordance to those given in ref S17; additional data: ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ = 167.5 (C), 146.0 (C), 140.8 (CH), 123.7 (CH), 118.6 (CH), 60.0 (CH₂), 26.4 (CH₃), 18.8 (CH₃), 14.3 ppm (CH₃); HRMS calcd. for C₉H₁₄O₂Na⁺ 177.0886, found 177.0884.

5. Olefin geometry dependency: experimentals

(2*Z*,4*E*)-ethyl undeca-2,4-dienoate (**28a**) was prepared according to the procedure given in ref S4, reaction time 6 h.

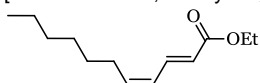
[1.0 mmol scale, 72% yield, colorless oil]



Data were in accordance to those given in ref S4.

(2*E*,4*Z*)-ethyl undeca-2,4-dienoate (**28b**) was prepared according to the procedure given in ref S4, reaction time 3 h, reaction temperature 0 °C.

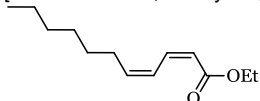
[1.0 mmol scale, 67% yield, colorless oil]



Data were in accordance to those given in ref S4.

(2*Z*,4*Z*)-ethyl undeca-2,4-dienoate (**28c**) was prepared according to the procedure given in ref S4, reaction time 1 h, reaction temperature -20 °C.

[1.0 mmol scale, 63% yield, 2*Z*,4*Z*:2*Z*,4*E* = 92:8, colorless oil]

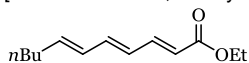


Data were in accordance to those given in ref S4.

6. Enantioselective 1,8- and 1,10-addition: experimentals

(2*E*,4*E*,6*E*)-ethyl undeca-2,4,6-trienoate (**29a**) was prepared via the general procedure for the synthesis of $\alpha,\beta,\gamma,\delta$ -bis-unsaturated esters from α,β -unsaturated aldehydes via Horner-Wadsworth-Emmons reaction using (2*E*,4*E*)-nona-2,4-dienal.

[10.0 mmol scale, 75% yield, 6:1 all-*E*:mono-*Z*, slightly yellow oil]



¹H NMR (400 MHz, CDCl₃, 25 °C, TMS): δ = 7.27 (dd, *J* = 14.8, 11.3 Hz, 1H), 6.50 (dd, *J* = 14.8, 10.7 Hz, 1H), 6.14 (ddd, *J* = 29.4, 14.6, 11.0 Hz, 2H), 5.96–5.85 (m, 1H), 5.81 (d, *J* = 15.3 Hz, 1H), 4.17 (qd, *J* = 7.1, 1.3 Hz, 2H), 2.12 (q, *J* = 7.0 Hz, 2H), 1.44–1.22 (m, 7H), 0.88 ppm (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ = 167.2 (C), 144.9 (CH), 141.2 (CH), 140.6 (CH), 129.9 (CH), 127.8 (CH), 120.1 (CH), 60.2 (CH₂), 32.7 (CH₂), 31.2 (CH₂), 22.3 (CH₂), 14.4 (CH₃), 14.0 ppm (CH₃); MS (*m/z*) 208 (43) [*M*⁺], 119 (36) [C₈H₇O₂⁺], 91 (76) [C₇H₇⁺], 79 (100) [C₅H₃O⁺], 77 (42), 57 (42) [C₄H₅⁺]; HRMS (APCI+) calcd. for C₁₃H₂₁O₂⁺ 209.1536, found 209.1528.

Synthesis of *S*-ethyl 2-(diethoxyphosphoryl)ethanethioate:

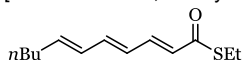
In a dried roundbottom two necked flask equipped with septum and stirring bar under a N₂ atmosphere, 2-(diethoxyphosphoryl)acetic acid (1.0 equiv) and DMAP (0.1 equiv) were dissolved in anhydrous CH₂Cl₂ (1.5 mL/mmol substrate). After 5 min stirring at room temperature the mixture was cooled to 0 °C and subsequently EtSH (1.05 equiv) and DCC (1.05 equiv) in anhydrous CH₂Cl₂ (0.5 mL/mmol substrate) were added. After stirring for 4 h (0 °C to room temperature) the solution was filtered over celite. The filtrate was washed with pentane and then the organic extract were dried and concentrated to a yellow oil. Flash column chromatography (gradient 20% EtOAc/pentane to 100% EtOAc/automated column) yielded the product in ~60% as a colorless oil (with traces of OPPH₃).

General procedure for the synthesis of $\alpha,\beta,\gamma,\delta,\epsilon,\zeta$ -triple unsaturated thioesters from $\alpha,\beta,\gamma,\delta$ -bis-unsaturated aldehydes via Horner-Wadsworth-Emmons reaction:

In a round bottom flask equipped with stirring bar *S*-ethyl 2-(diethoxyphosphoryl)ethanethioate (1.5 equiv) is dissolved in anhydrous THF (20.0 mL/mmol substrate) and cooled to 0 °C. *n*BuLi (1.6 M in Et₂O, 1.4 equiv) is added dropwise and the reaction mixture is stirred for 30 min and then cooled to –78 °C. Then, the aldehyde substrate (1 equiv) dissolved in anhydrous THF (2.0 mL/mmol substrate) was added dropwise. After addition, the solution was allowed to warm to room temperature and stirred in total for 16 h. Then a solution of aqueous NH₄Cl (1 M, 1 mL) was added and the mixture extracted with Et₂O (3x 2 mL). The combined organic extracts were dried and concentrated. Flash column chromatography (1:99 Et₂O:pentane) yielded the product.

(2*E*,4*E*,6*E*)-*S*-ethyl undeca-2,4,6-trienethioate (**29b**) was prepared via the general procedure for the synthesis of $\alpha,\beta,\gamma,\delta,\epsilon,\zeta$ -triple unsaturated thioesters from $\alpha,\beta,\gamma,\delta$ -bis-unsaturated aldehydes via Horner-Wadsworth-Emmons reaction using (2*E*,4*E*)-nona-2,4-dienal.

[6.0 mmol scale, 61% yield, 9:1 all-*E*:mono-*Z*, yellow oil]



¹H NMR (400 MHz, CDCl₃, 25 °C, TMS): δ = 7.19 (dd, *J* = 15.1, 11.4 Hz, 2H), 6.55 (dd, *J* = 14.8, 10.7 Hz, 2H), 6.22–5.98 (m, 6H), 5.98–5.82 (m, 2H), 2.92 (qd, *J* = 7.4, 1.2 Hz, 4H), 2.11 (q, *J* = 7.1 Hz, 4H), 1.43–1.12 (m, 15H), 0.87 ppm (t, *J* = 7.2 Hz, 7H); ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ = 189.6 (C), 142.6 (CH), 141.1 (CH), 140.6 (CH), 130.0 (CH), 127.6 (CH), 127.1 (CH), 32.8 (CH₂), 31.1 (CH₂), 23.2 (CH₂), 22.3 (CH₂), 14.9 (CH₃), 13.9 ppm (CH₃); MS (*m/z*) 224 (11) [*M*⁺], 163 (80) [*M*⁺-SEt], 107 (100) [C₇H₆O⁺], 91 (31) [C₇H₇⁺], 91 (45) [C₅H₉⁺]; HRMS calcd. for C₁₃H₂₀OSNa⁺ 247.1127, found 247.1124.

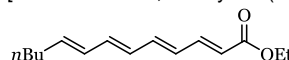
Synthesis of (2*E*,4*E*,6*E*,8*E*)-ethyl trideca-2,4,6,8-tetraenoate (**29c**) from (2*E*,4*E*,6*E*)-ethyl undeca-2,4,6-trienoate:

1) General procedure for the reduction of an unsaturated ester to the allylic alcohol:

In a dried Schlenk tube equipped with septum and stirring bar under a N₂ atmosphere the ester was dissolved in anhydrous CH₂Cl₂ (5 mL). After 5 min stirring at room temperature the mixture was cooled to -70 °C and DIBAL-H (1.0 M solution in CH₂Cl₂, 2.1 equiv) was added. The reaction mixture was stirred for 16 h at -70 °C. Subsequently the reaction mixture was poured into a roundbottom flask with aq. Rochelle's salt-solution (saturated, 10 mL), stirred for 1 h at room temperature and the layers were separated. After extraction with CH₂Cl₂ (2x 5 mL), the combined organic extracts were washed with the aq. Rochelle's salt solution (2x 5 mL), dried and carefully concentrated. The alcohol was used without further purification in the subsequent IBX oxidation.

2) IBX oxidation of the allylic alcohol was performed according to ref S18. The aldehyde was used without further purification for the HWE reaction.

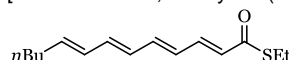
3) The product was prepared via the general procedure for the synthesis of $\alpha,\beta,\gamma,\delta$ -bis-unsaturated esters from α,β -unsaturated aldehydes via Horner-Wadsworth-Emmons reaction.
[6.0 mmol scale, 20% yield (3 steps), 7:1 all-*E*:mono-*Z*, white solid]


¹H NMR (400 MHz, CDCl₃, 25 °C, TMS): δ = 7.29 (dd, *J* = 15.2, 11.4 Hz, 1H), 6.54 (dd, *J* = 14.7, 11.0 Hz, 1H), 6.40–6.04 (m, 4H), 5.88–5.76 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.11 (q, *J* = 7.0 Hz, 2H), 1.44–1.21 (m, 7H), 0.88 ppm (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ = 167.2 (C), 144.6 (CH), 141.1 (CH), 138.8 (CH), 137.7 (CH), 130.3 (CH), 129.6 (CH), 129.1 (CH), 120.2 (CH), 60.2 (CH₂), 32.7 (CH₂), 31.3 (CH₂), 22.3 (CH₂), 14.4 (CH₃), 14.0 ppm (CH₃); MS (*m/z*) 234 (38) [*M*]⁺, 131 (31) [C₁₀H₁₁]⁺, 117 (73) [C₉H₉]⁺, 105 (55) [C₈H₇]⁺, 91 (100) [C₇H₇]⁺, 79 (32) [C₆H₇]⁺; HRMS calcd. for C₁₅H₂₃O₂⁺ 235.1693, found 235.1694.

Synthesis of (2*E*,4*E*,6*E*,8*E*)-S-ethyl trideca-2,4,6,8-tetraenethioate (**29d**) from (2*E*,4*E*,6*E*)-ethyl undeca-2,4,6-trienoate:

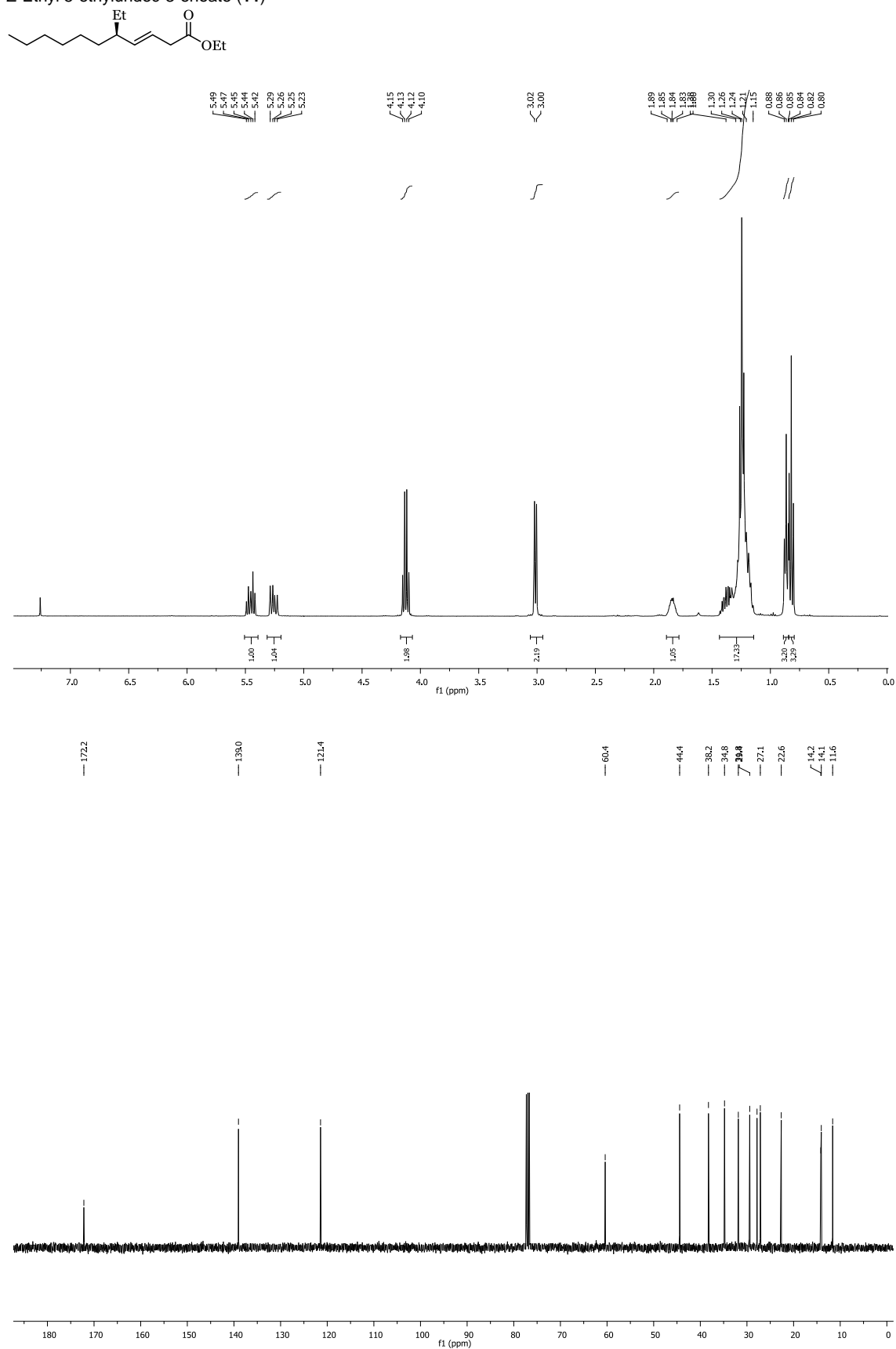
Step 1) and 2) are according to the synthesis of (2*E*,4*E*,6*E*,8*E*)-ethyl trideca-2,4,6,8-tetraenoate from (2*E*,4*E*,6*E*)-ethyl undeca-2,4,6-trienoate.

3) The product was prepared via the general procedure for the synthesis of $\alpha,\beta,\gamma,\delta,\epsilon,\zeta$ -triple unsaturated thioesters from $\alpha,\beta,\gamma,\delta$ -bis-unsaturated aldehydes via Horner-Wadsworth-Emmons reaction.
[6.0 mmol scale, 23% yield (3 steps), 8:1 all-*E*:mono-*Z*, yellow solid]

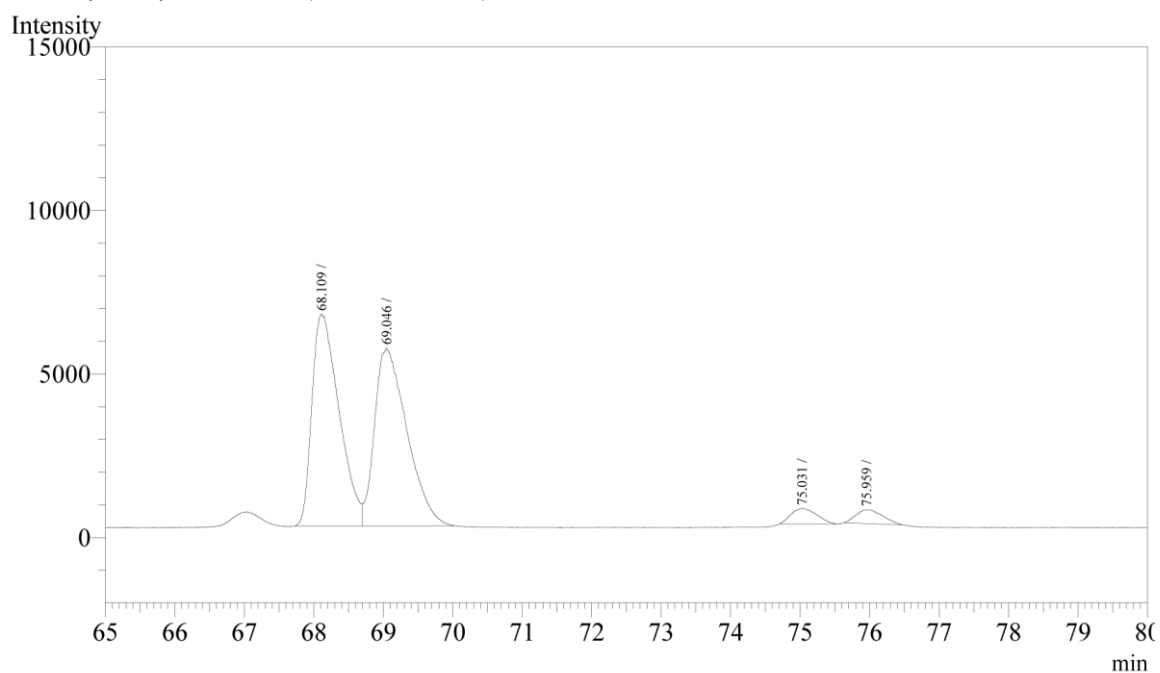

¹H NMR (400 MHz, CDCl₃, 25 °C, TMS): δ = 7.32–7.13 (m, 1H), 6.61 (dd, *J* = 14.5, 11.2 Hz, 1H), 6.37 (dd, *J* = 14.8, 10.7 Hz, 1H), 6.31–6.00 (m, 4H), 5.90–5.79 (m, 1H), 2.94 (qd, *J* = 7.4, 1.2 Hz, 2H), 2.12 (q, *J* = 7.0 Hz, 2H), 1.45–1.13 (m, 7H), 0.88 ppm (t, *J* = 7.1 Hz, 3H); ¹³C NMR (100.59 MHz, CDCl₃, 25 °C, TMS): δ = 189.6 (C), 142.6 (CH), 140.4 (CH), 139.3 (CH), 138.2 (CH), 130.3 (CH), 129.7 (CH), 129.0 (CH), 127.2 (CH), 32.8 (CH₂), 31.3 (CH₂), 23.3 (CH₂), 22.3 (CH₂), 15.0 (CH₃), 14.0 ppm (CH₃); MS (*m/z*) 250 (22) [*M*]⁺, 189 (55) [*M*⁺-SEt], 133 (100) [C₉H₉O]⁺, 107 (66) [C₇H₆O]⁺, 91 (78) [C₇H₇]⁺; HRMS calcd. for C₁₅H₂₃OS⁺ 251.1464, found 251.1457.

7. Halide dependency: spectra

E-Ethyl 5-ethylundec-3-enoate (**11**)

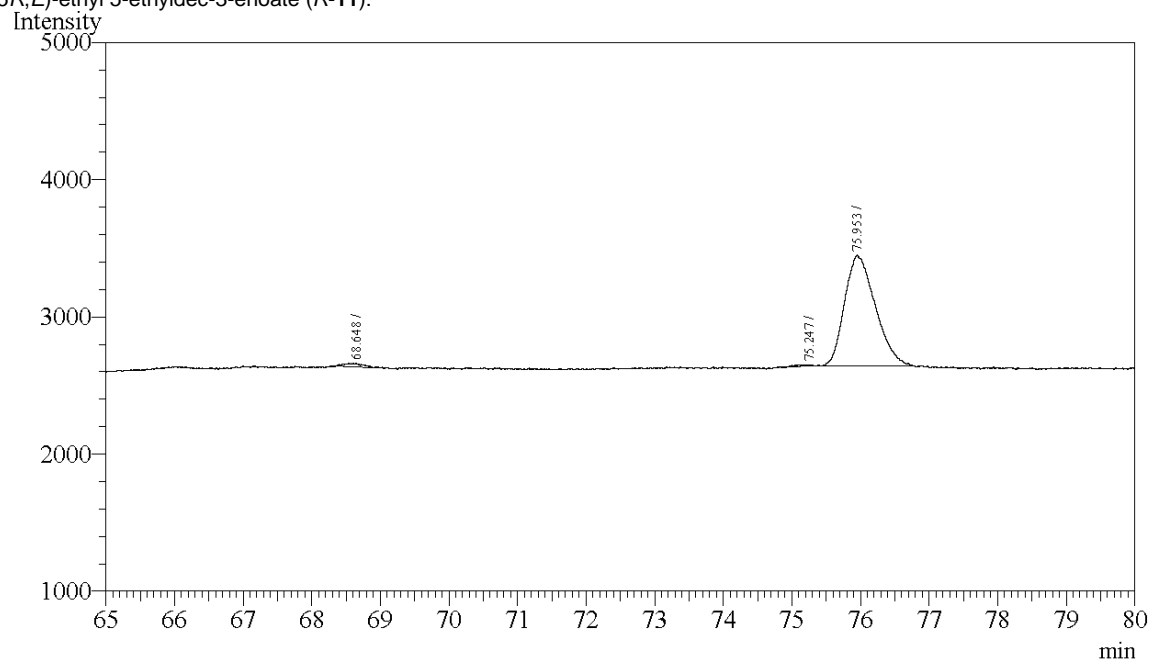


rac *E*-ethyl 5-ethyldec-3-enoate (*rac*-11 and *rac*-12):



Peak#	Ret.Time	Area	Height	Conc.	Unit Mark	ID#	Cmpd Name	Area%
1	68.109	175938	6487	0.000				46.8346
2	69.046	176034	5449	0.000	V			46.8603
3	75.031	12240	477	0.000				3.2583
4	75.959	11445	428	0.000				3.0468
Total		375657	12841					100.0000

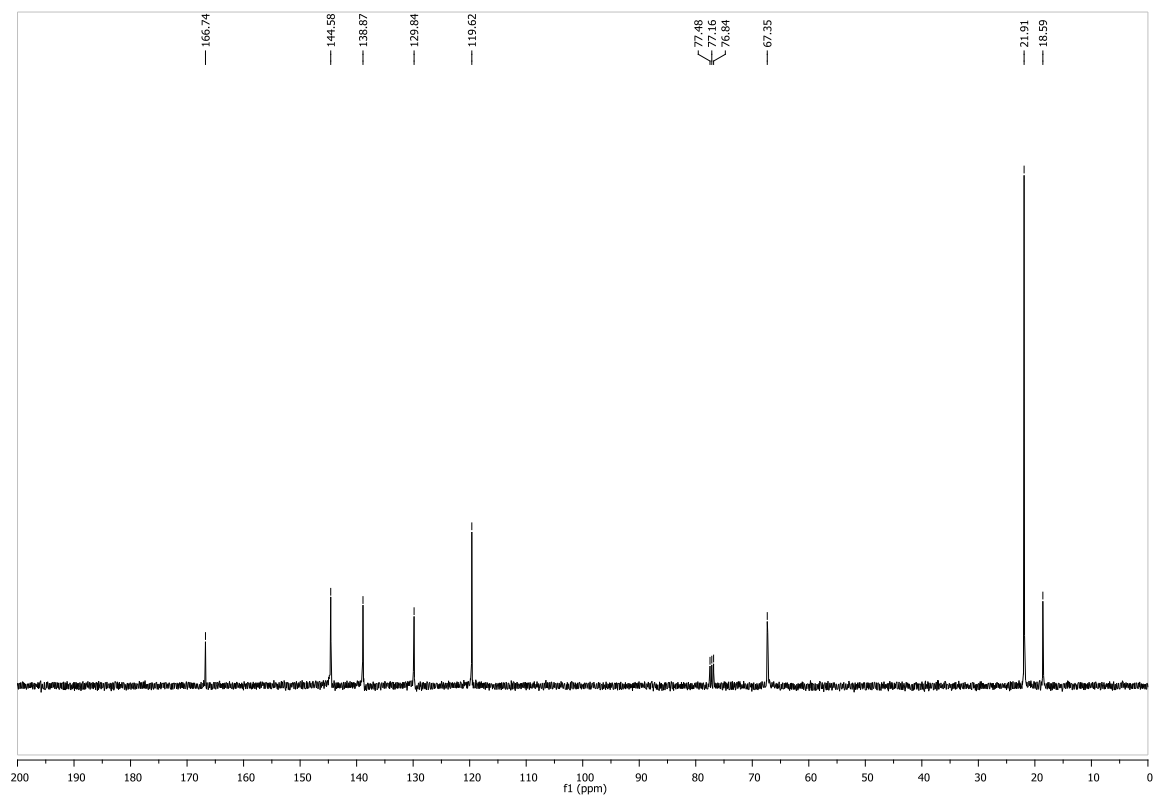
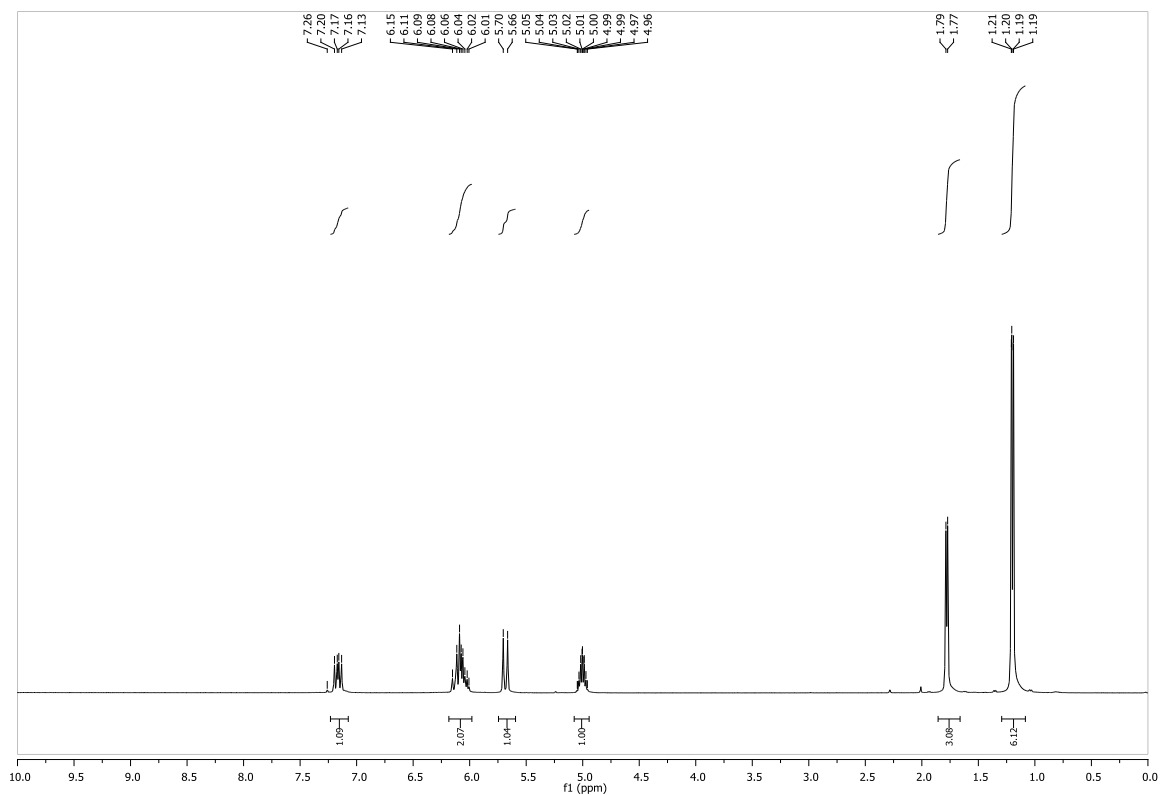
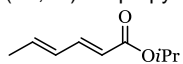
(5*R,E*)-ethyl 5-ethyldec-3-enoate (*R*-11):



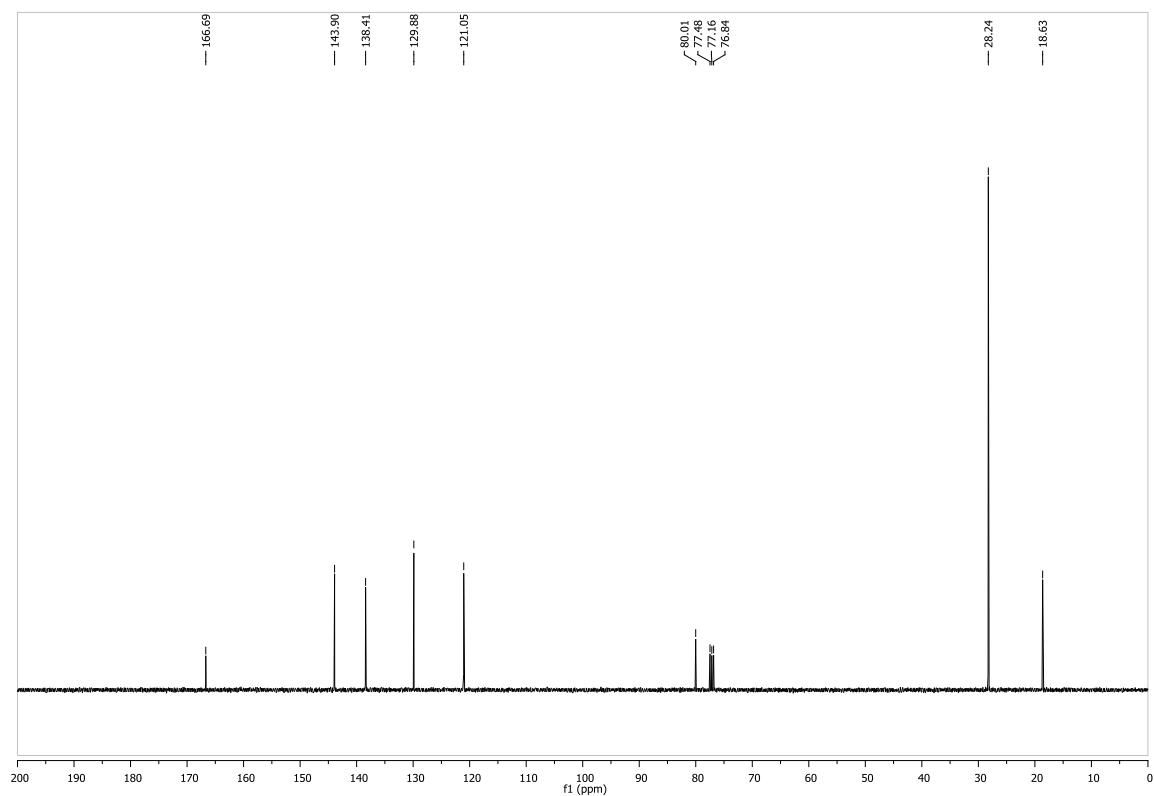
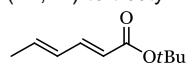
Peak#	Ret.Time	Area	Height	Conc.	Unit Mark	ID#	Cmpd Name	Area%
1	68.648	526	28	0.000				2.0452
2	75.247	156	12	0.000				0.6077
3	75.953	25029	808	0.000				97.3471
Total		25711	848					100.0000

8. Ester size dependency: spectra

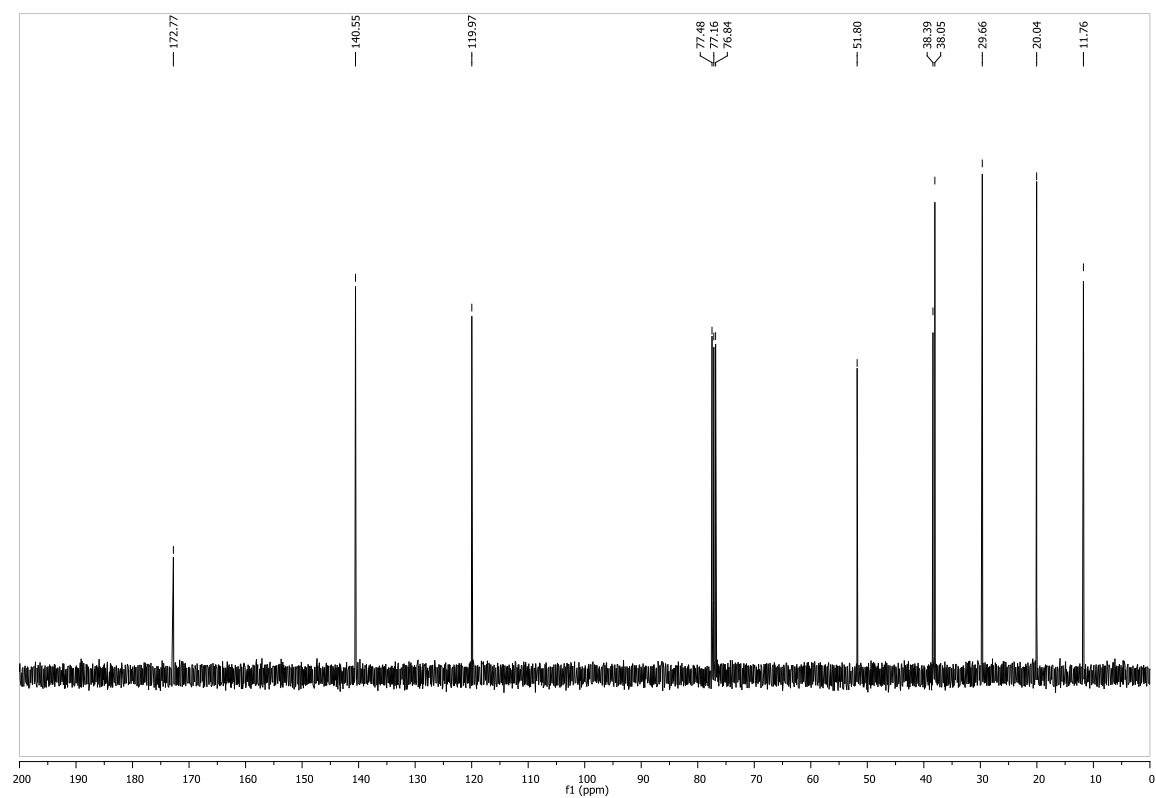
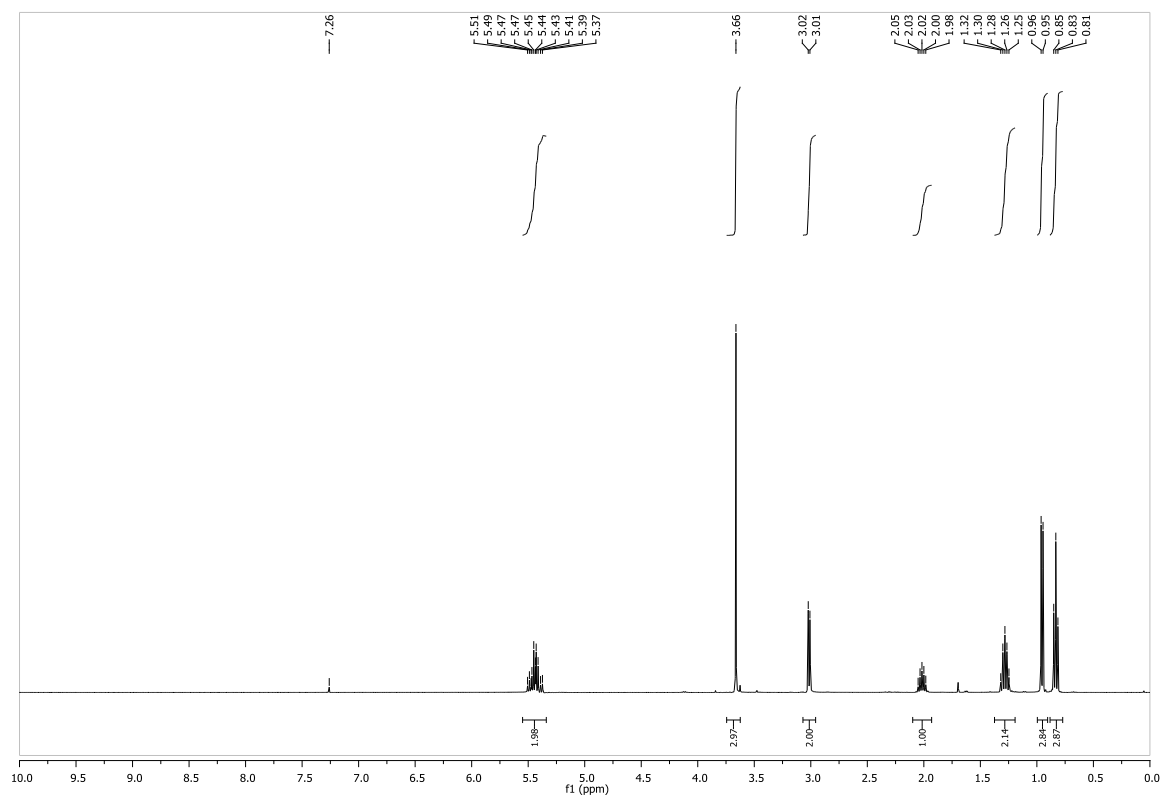
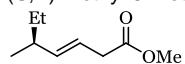
(2E,4E)-iso-propyl hexa-2,4-dienoate (**13c**)



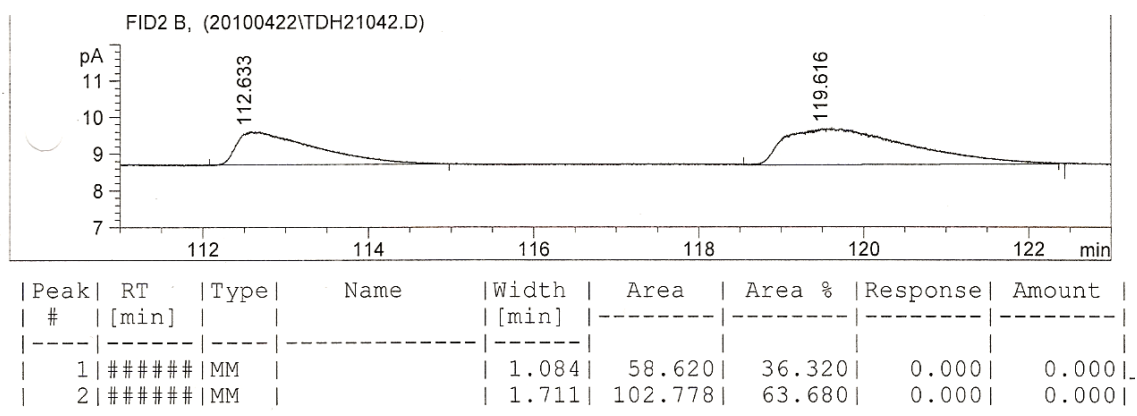
(2*E*,4*E*)-*tert*-butyl hexa-2,4-dienoate (**13d**)



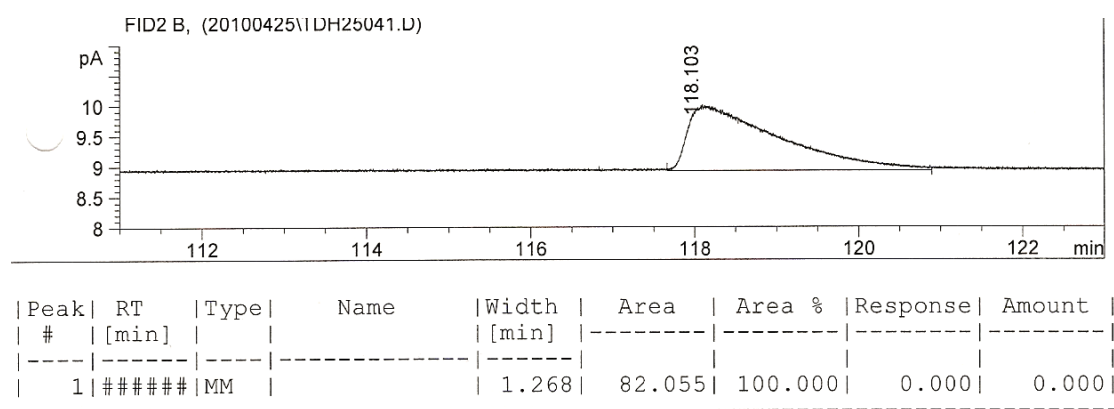
(*S,E*)-methyl 5-methylhept-3-enoate (**14a**)



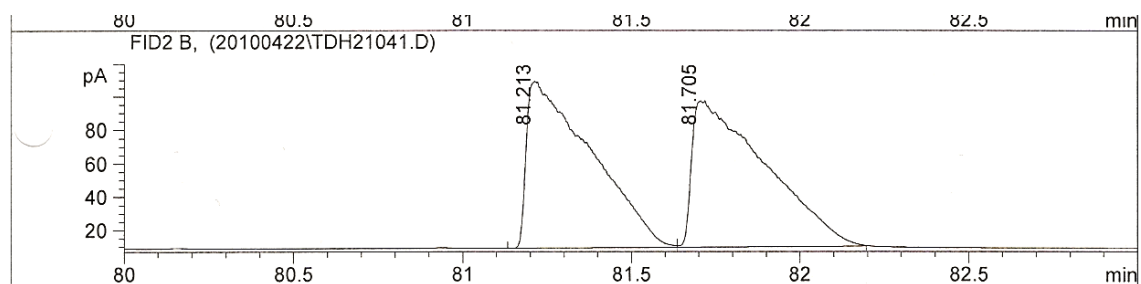
Regioselectivity: *rac*-*E*-methyl 5-methylhept-3-enoate (*rac*-**14a** and *rac*-1,4-addition product):



Regioselectivity: (*S,E*)-methyl 5-methylhept-3-enoate (**S-14a**):

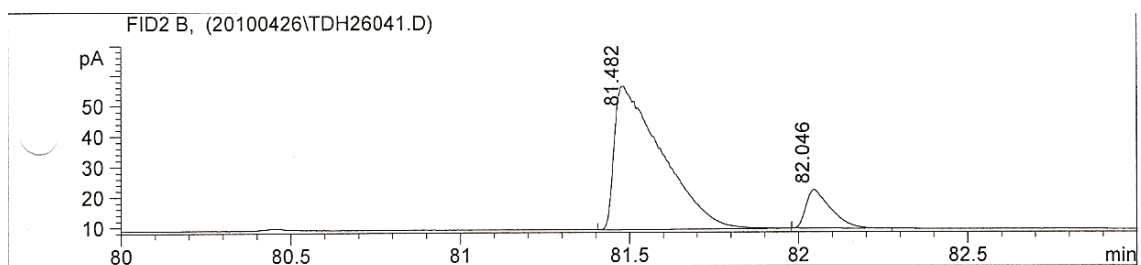


Enantioselectivity: *rac*-2-methylbutanoic acid:



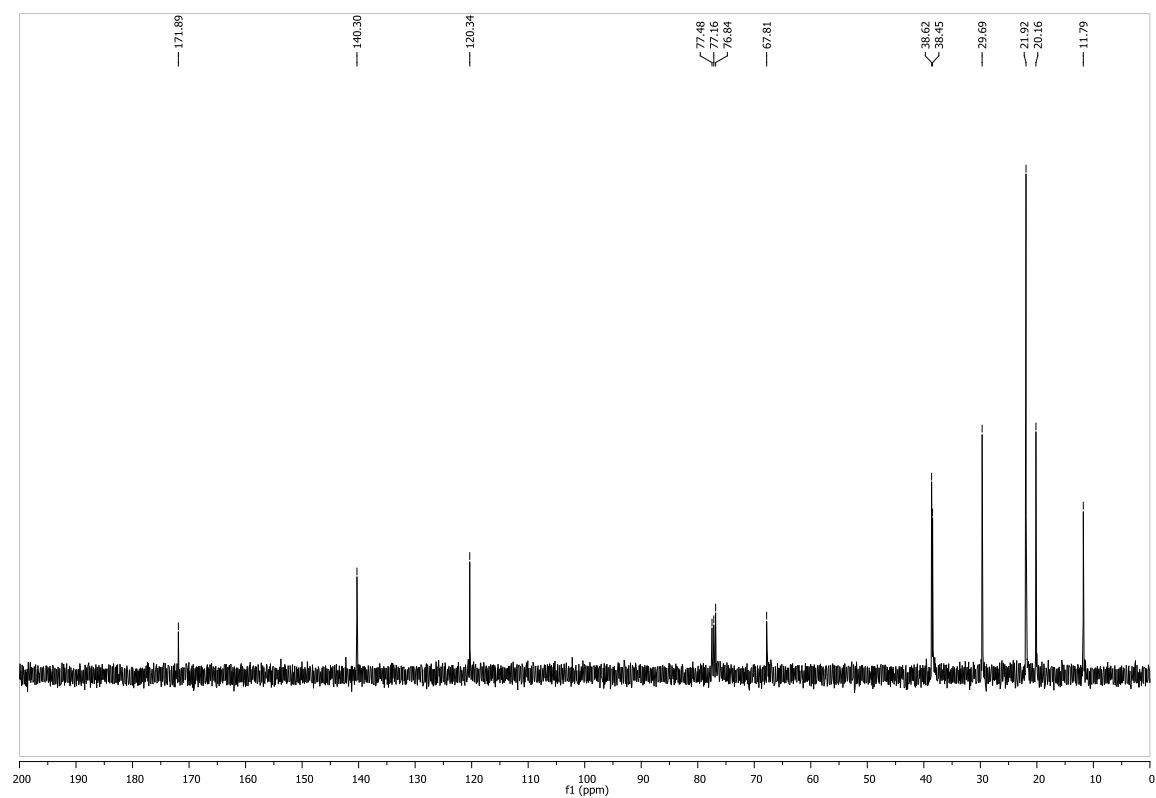
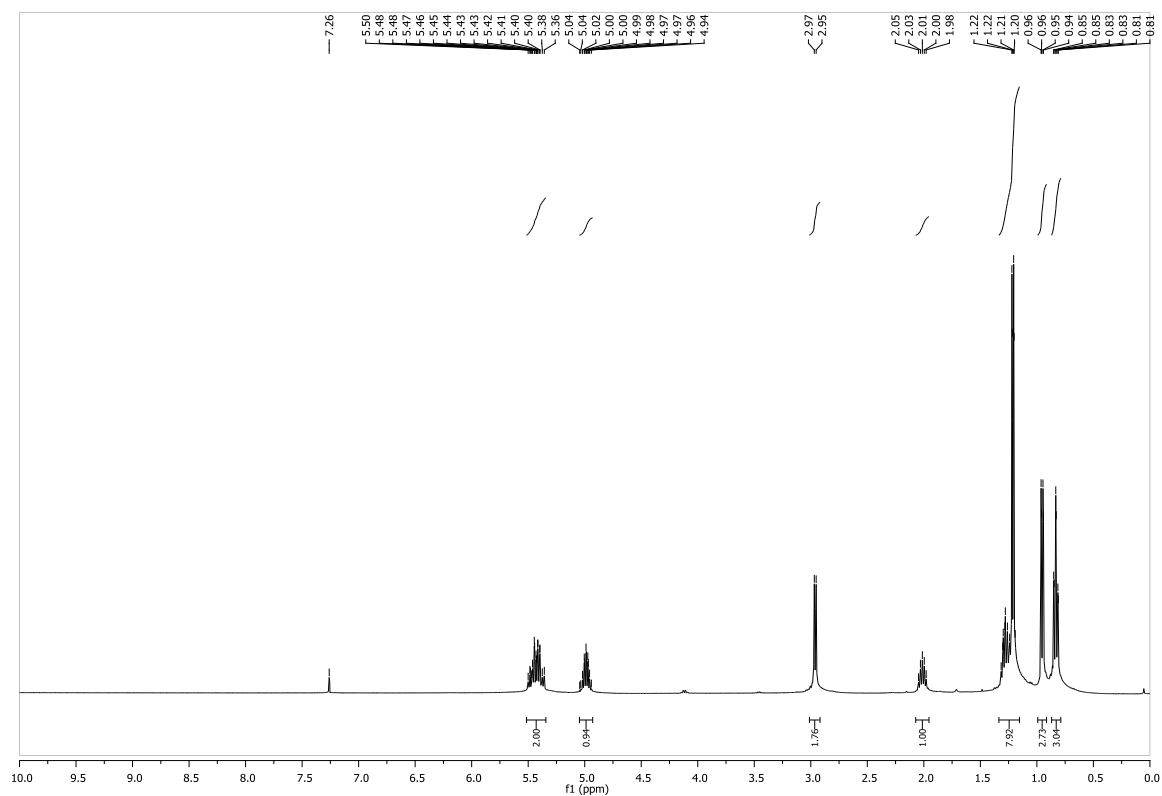
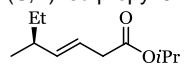
Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	81.213	PB		0.168	1337.457	50.187	0.000	0.000
2	81.705	BB		0.186	1327.511	49.813	0.000	0.000

Enantioselectivity: *S*-2-methylbutanoic acid: {obtained after derivatisation}

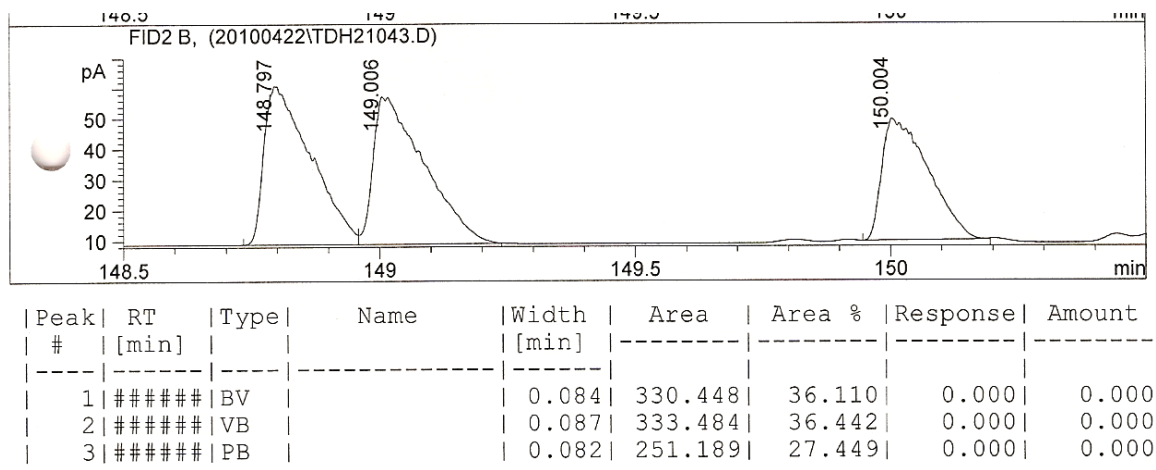


Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	81.482	MM		0.163	462.534	87.672	0.000	0.000
2	82.046	MM		0.084	65.040	12.328	0.000	0.000

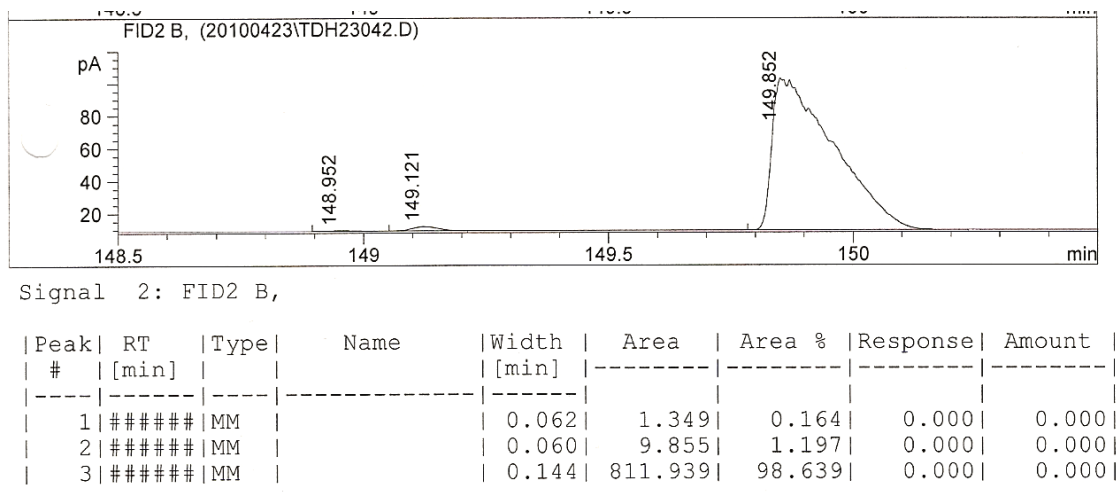
(*S,E*)-*iso*-propyl 5-methylhept-3-enoate (**14c**)



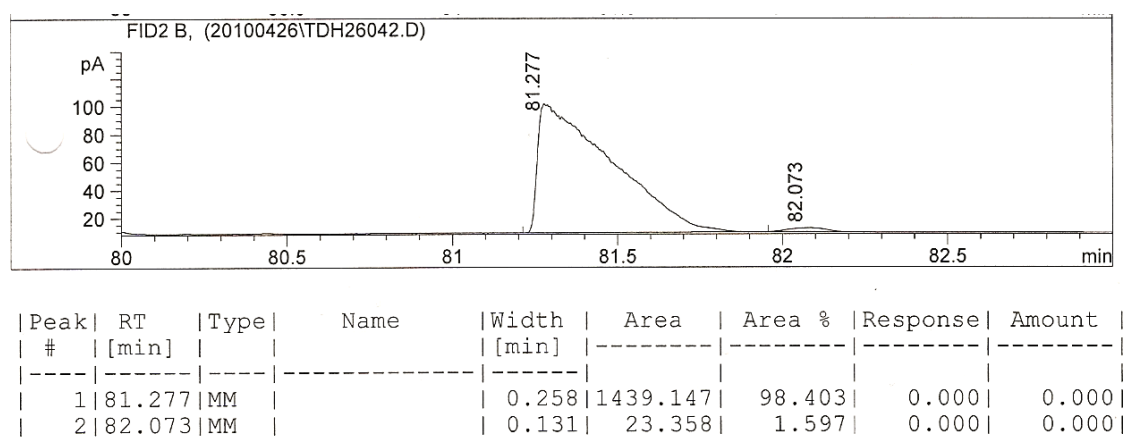
Regioselectivity: *rac*-*E*-iso-propyl 5-methylhept-3-enoate (*rac*-**14c** and *rac*-1,4-addition product):



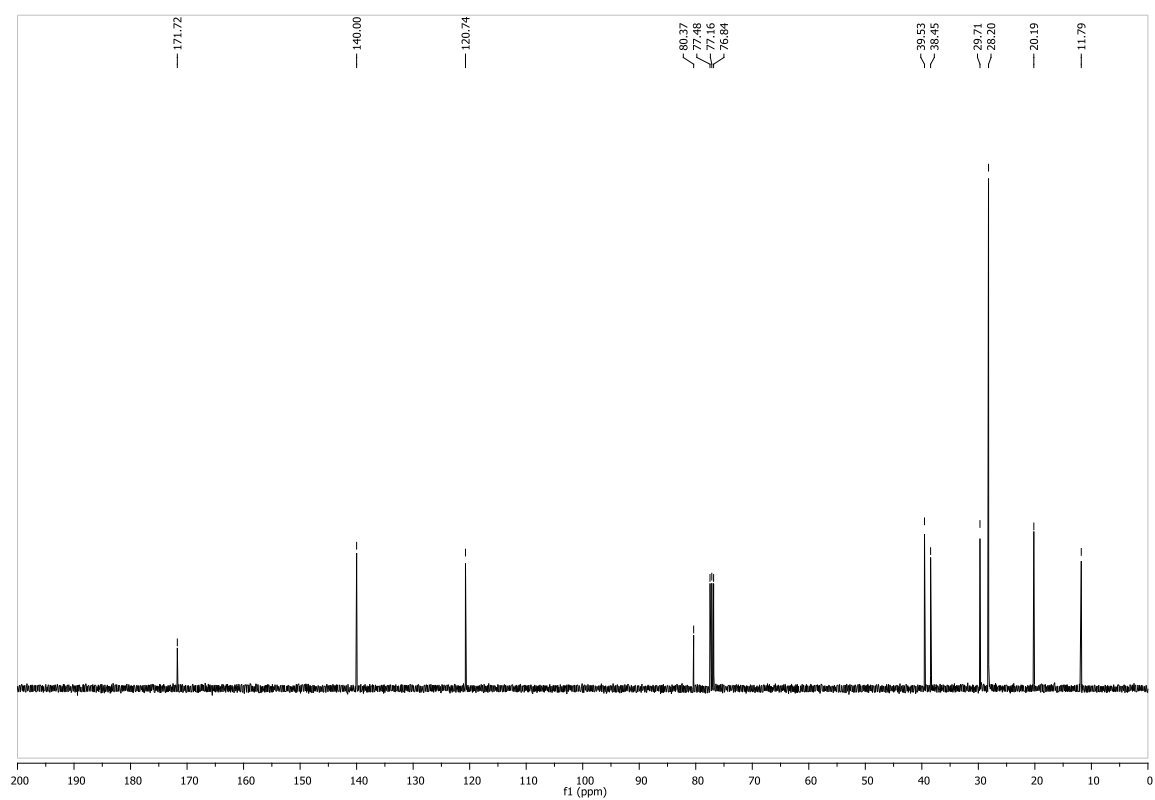
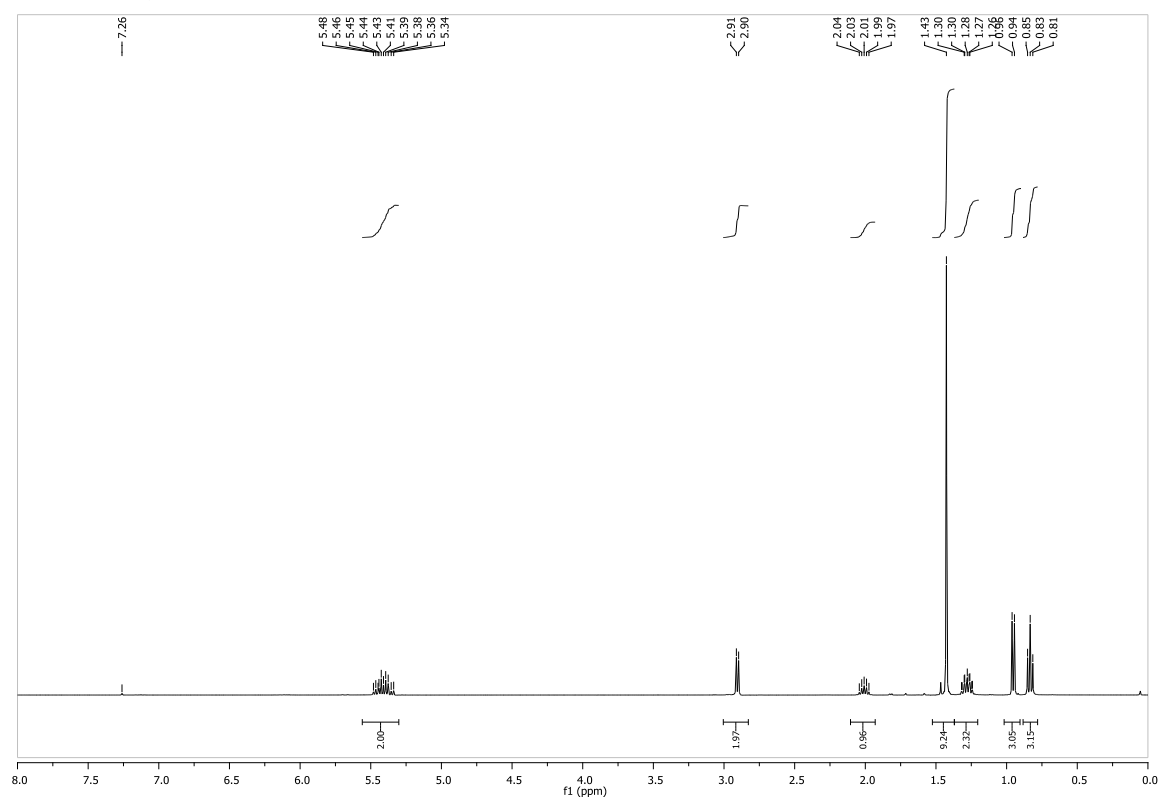
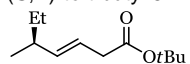
(*S,E*)-iso-propyl 5-methylhept-3-enoate (*S*-**14c**):



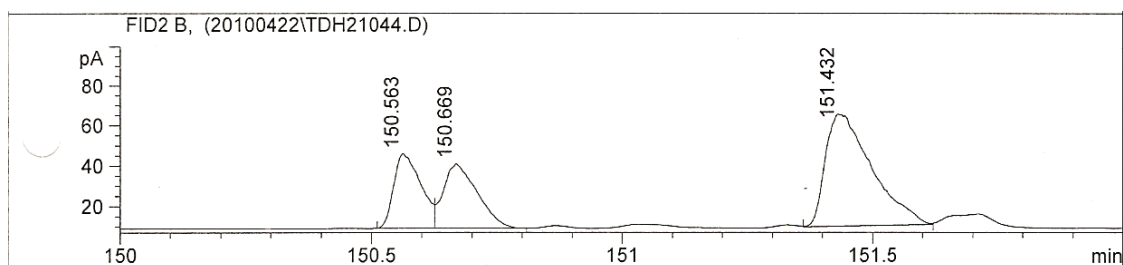
Enantioselectivity *S*-2-methylbutanoic acid: {obtained after derivatisation}



(*S,E*)-*tert*-butyl 5-methylhept-3-enoate (**14d**)

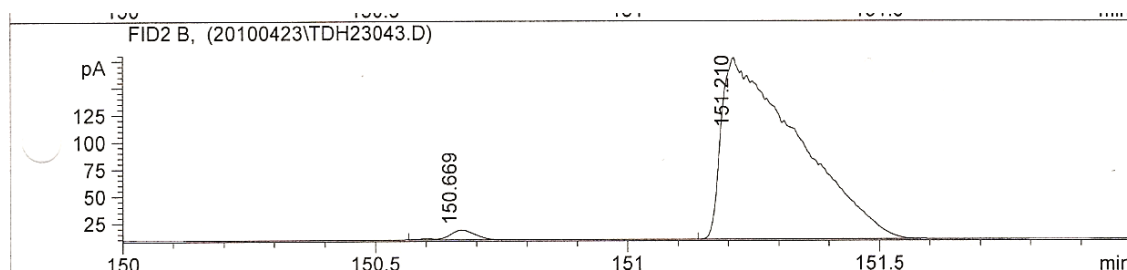


Regioselectivity: *rac-E-tert*-butyl 5-methylhept-3-enoate (*rac-14d* and *rac-1,4*-addition product):



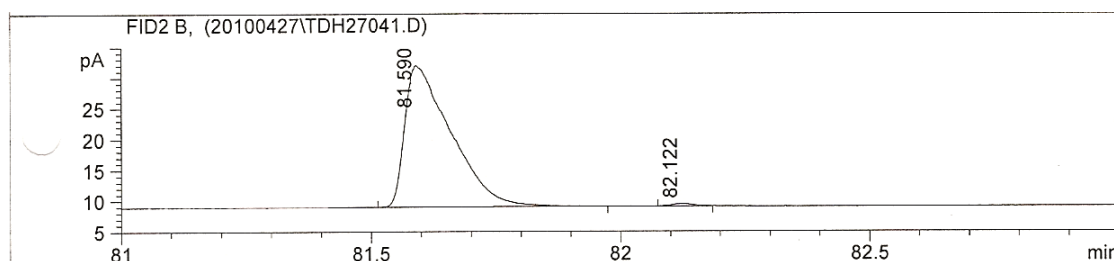
Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	150.563	BV		0.053	138.495	21.521	0.000	0.000
2	150.669	VP		0.065	149.070	23.165	0.000	0.000
3	151.432	MM		0.107	355.961	55.314	0.000	0.000

Regioselectivity: (*S,E*)-*tert*-butyl 5-methylhept-3-enoate (*S-14d*):



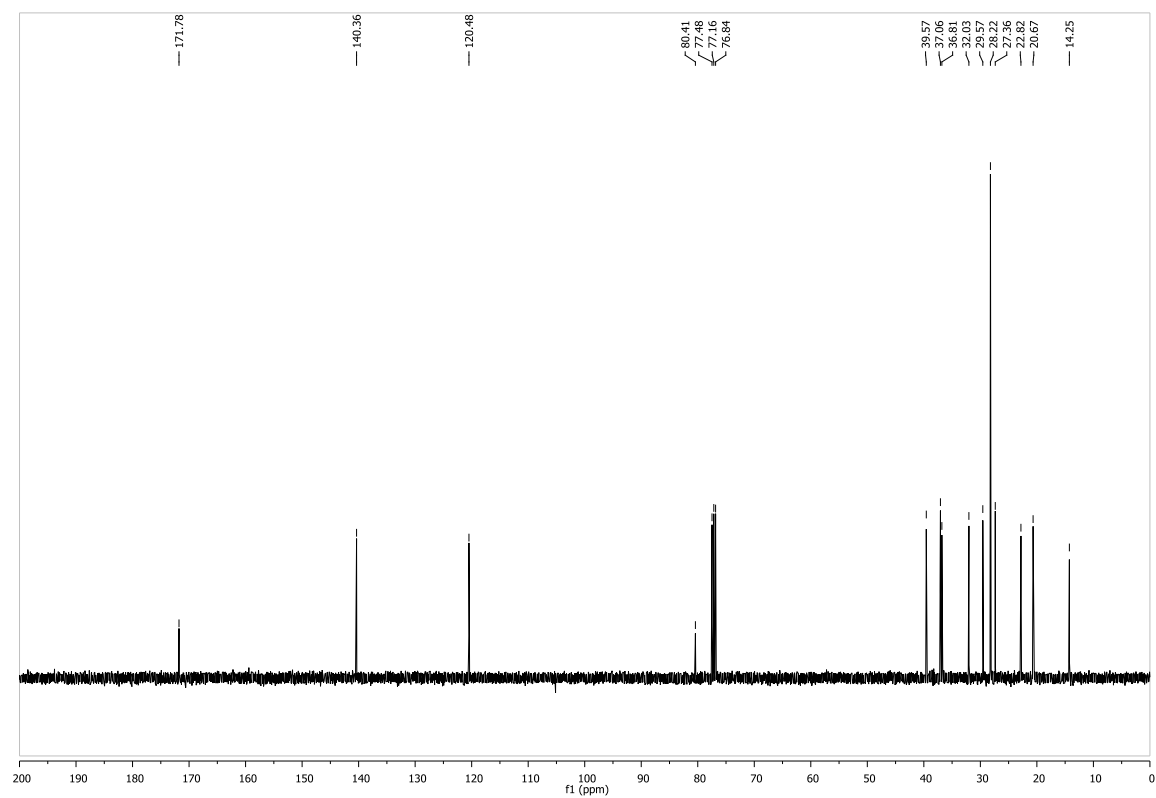
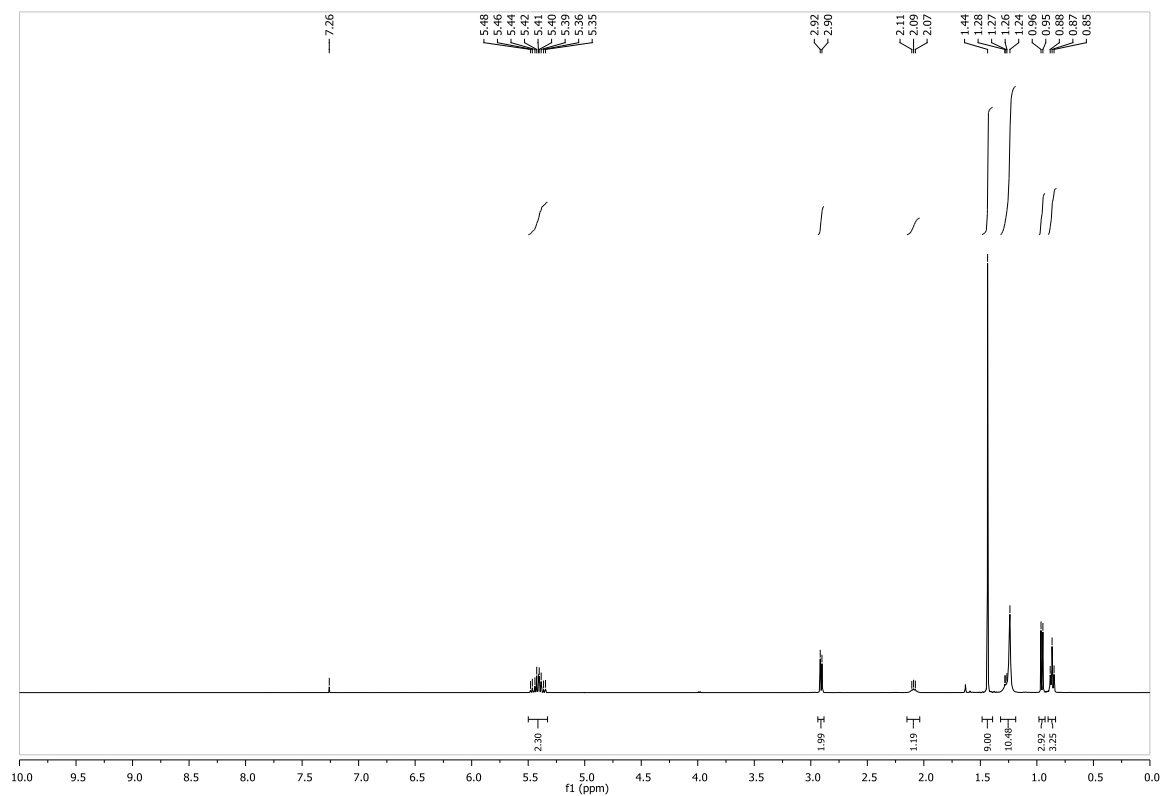
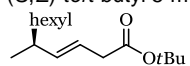
Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	150.669	MM		0.059	31.968	1.776	0.000	0.000
2	151.210	PB		0.135	1768.346	98.224	0.000	0.000

Enantioselectivity: *S*-2-methylbutanoic acid: {obtained after derivatisation}

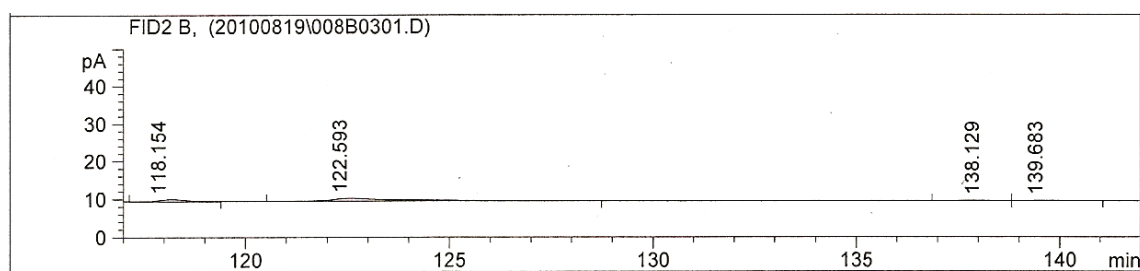


Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	81.590	MM		0.108	148.553	99.152	0.000	0.000
2	82.122	MM		0.055	1.270	0.848	0.000	0.000

(*S,E*)-*tert*-butyl 5-methylundec-3-enoate (**14e**)

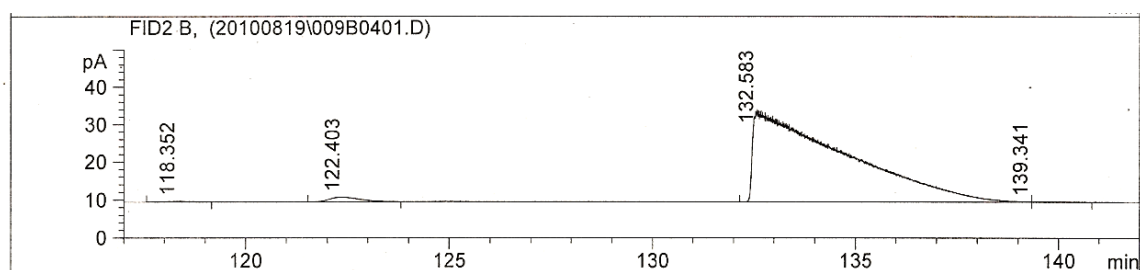


Regio- and enantioselectivity: *rac*-*E*-ethyl 5-methylundec-3-enoate (*rac*-**14e** and 1,4-addition product):



Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	118.154	MM		0.845	27.517	19.041	0.000	0.000
2	122.593	MM		2.283	106.217	73.500	0.000	0.000
3	138.129	MF		0.818	5.402	3.738	0.000	0.000
4	139.683	FM		0.822	5.377	3.721	0.000	0.000

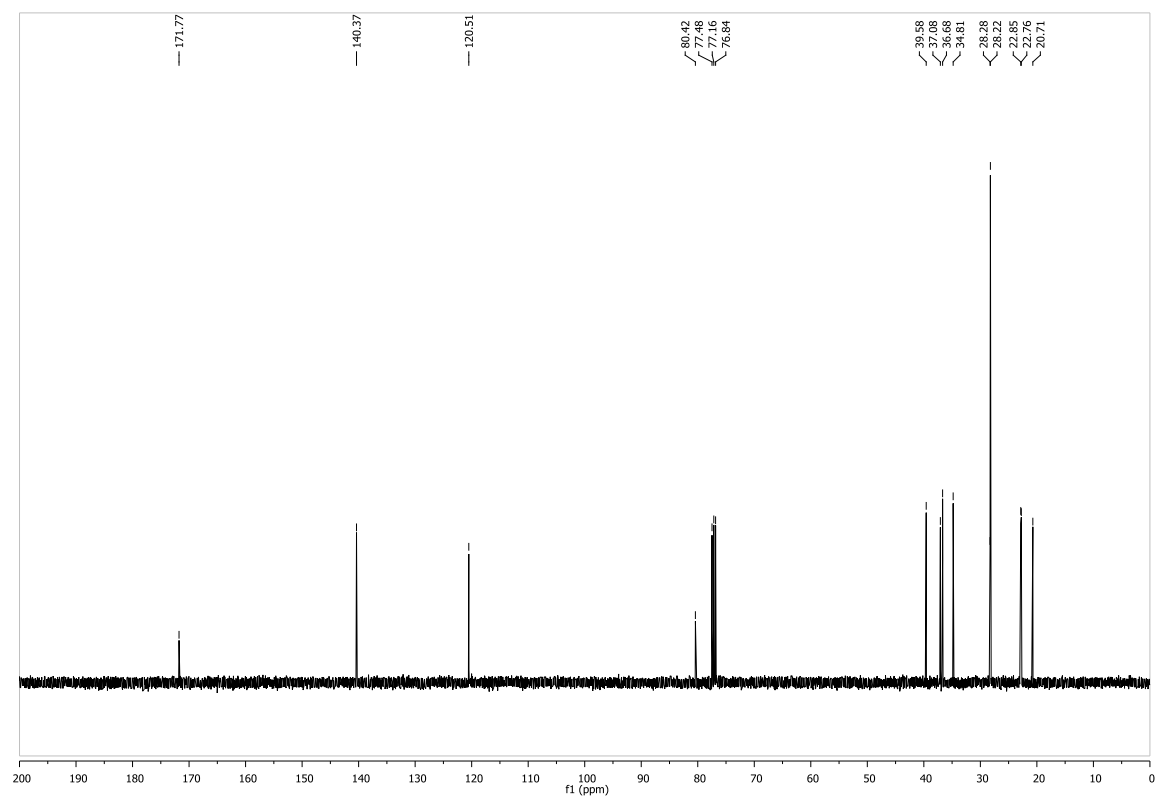
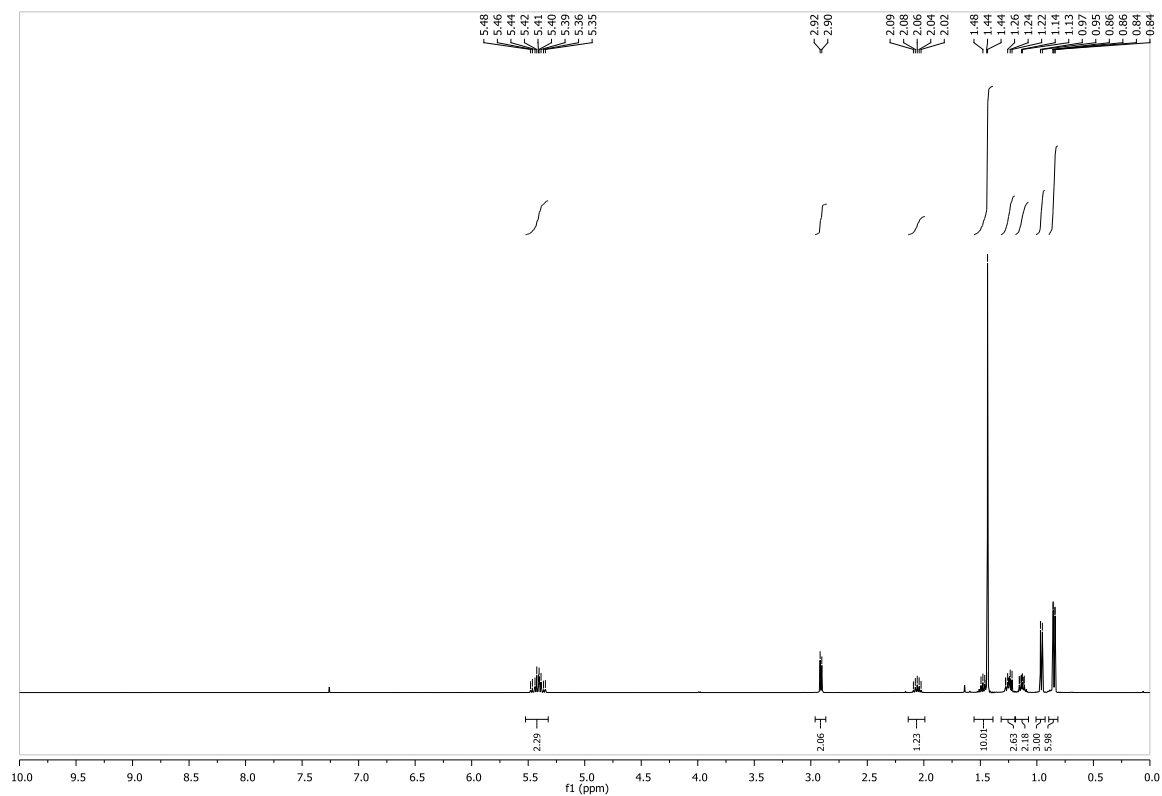
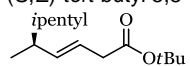
Regio- and enantioselectivity: (*S,E*)-ethyl 5-methylundec-3-enoate (*S*-**14e**): {obtained after derivatisation}



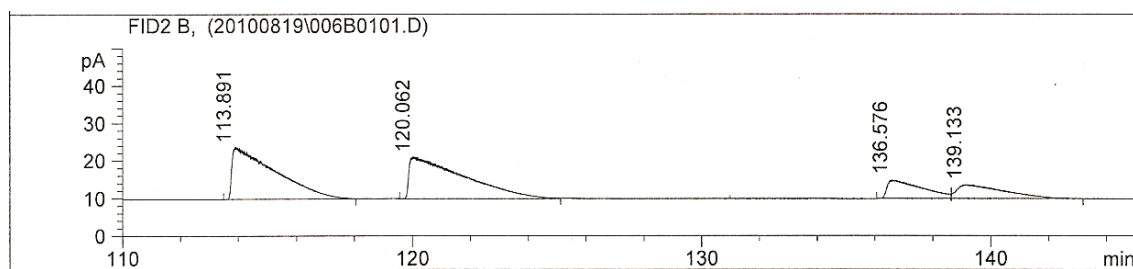
Signal 2: FID2 B,

Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	118.352	MM		0.737	10.140	0.264	0.000	0.000
2	122.403	MM		0.862	62.479	1.628	0.000	0.000
3	132.583	MF		2.587	3760.799	97.970	0.000	0.000
4	139.341	MM		0.708	5.297	0.138	0.000	0.000

(*S,E*)-*tert*-butyl 5,8-dimethylnon-3-enoate (**14f**)



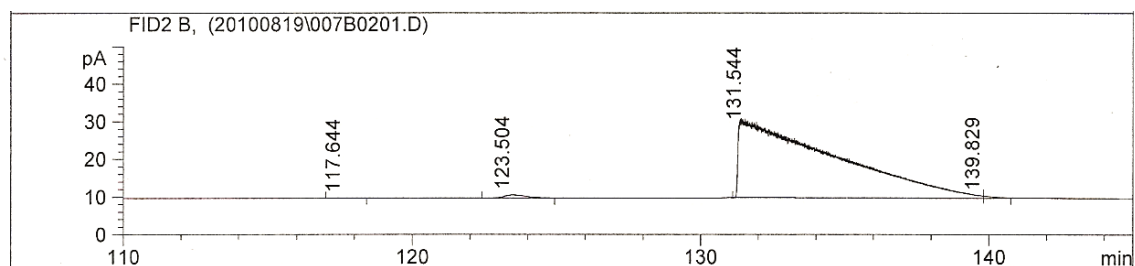
Regio- and enantioselectivity: *rac*-*E*-ethyl 5,8-dimethylnon-3-enoate (*rac*-**14f** and 1,4-addition product):



Signal 2: FID2 B,

Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	113.891	MM		1.754	1421.558	38.946	0.000	0.000
2	120.062	MM		2.204	1432.883	39.257	0.000	0.000
3	136.576	MF		1.368	396.848	10.872	0.000	0.000
4	139.133	FM		1.850	398.759	10.925	0.000	0.000

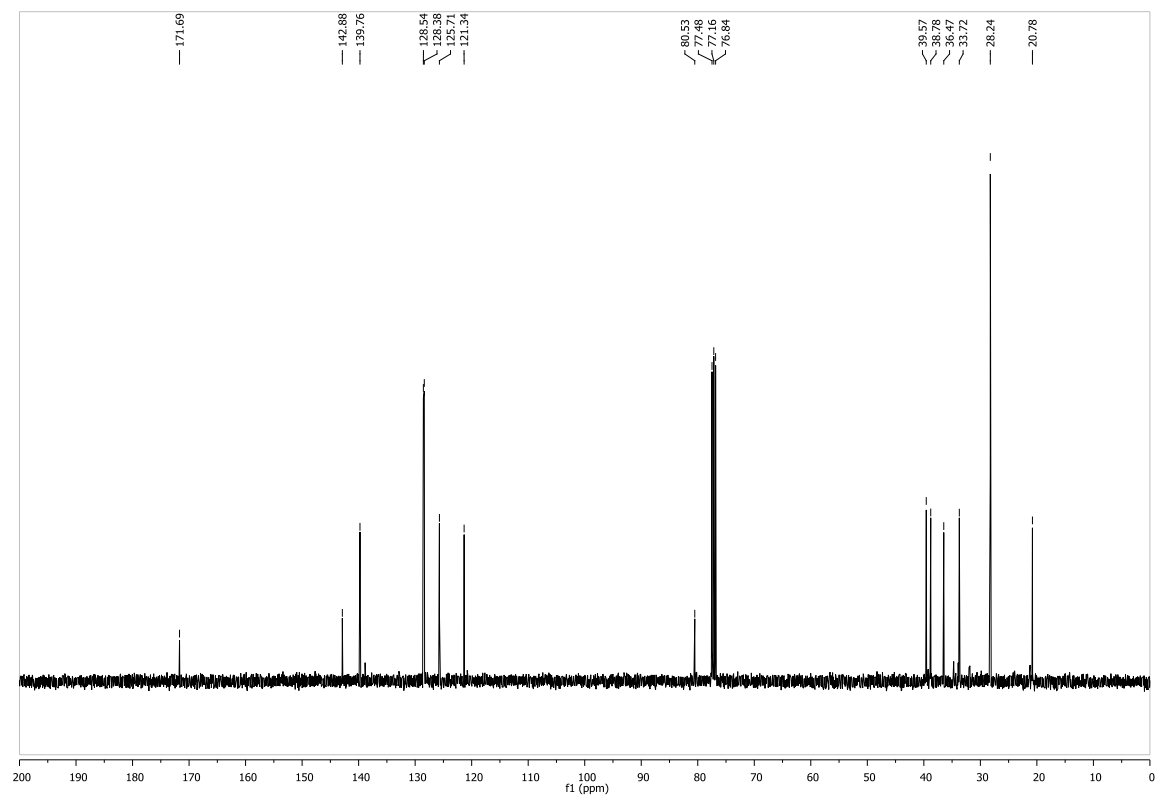
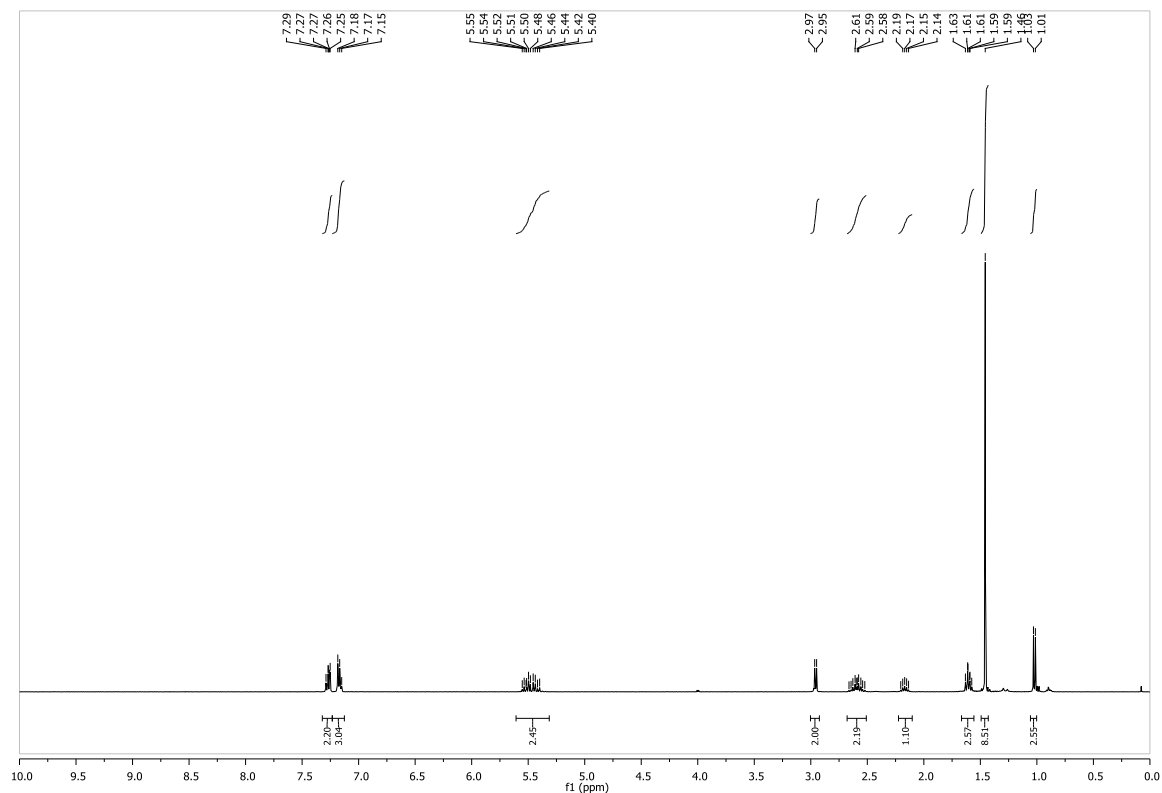
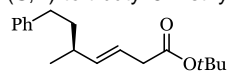
Regio- and enantioselectivity: (*S,E*)-ethyl 5,8-dimethylnon-3-enoate (*S*-**14f**): {obtained after derivatisation}



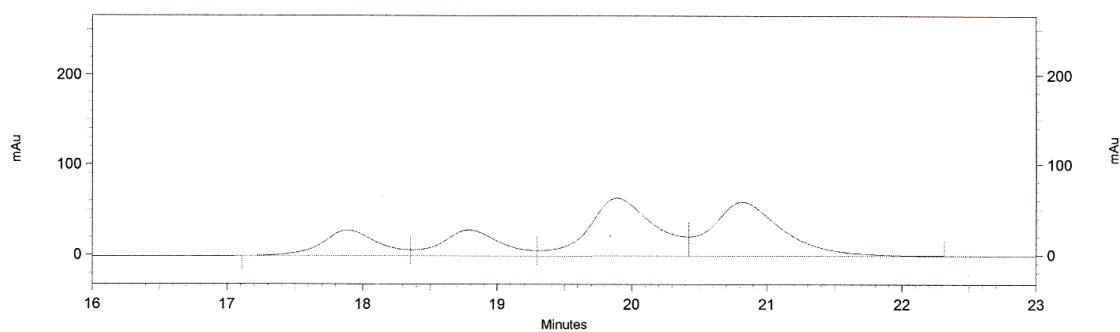
Signal 2: FID2 B,

Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	117.644	MM		0.972	5.601	0.117	0.000	0.000
2	123.504	MM		0.956	50.020	1.044	0.000	0.000
3	131.544	MF		3.815	4719.896	98.488	0.000	0.000
4	139.829	FM		0.486	16.816	0.351	0.000	0.000

(*S,E*)-*tert*-butyl 5-methyl-7-phenylhept-3-enoate (**14g**)



Regio- and enantioselectivity: *rac-E-tert*-butyl 5-methyl-7-phenylhept-3-enoate (*rac-14g* and 1,4-addition product):



1: 210

nm, 2 nm

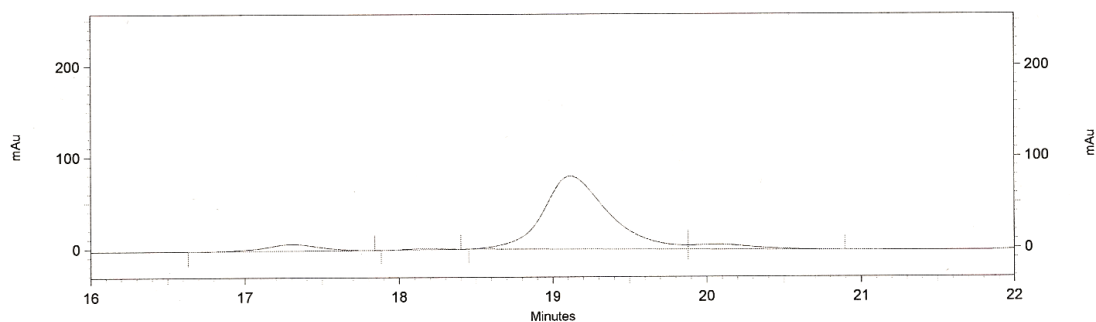
Results

Pk #	Name	Retention Time	Area	Area Percent
1	Peak @ 17,888 Minutes	17,888	823562	13,599
2	Peak @ 18,788 Minutes	18,788	881439	14,554
3	Peak @ 19,892 Minutes	19,892	2184832	36,076
4	Peak @ 20,816 Minutes	20,816	2166413	35,772

Totals			6056246	100,000
--------	--	--	---------	---------

Regio- and enantioselectivity: (*S,E-tert*-butyl 5-methyl-7-phenylhept-3-enoate (*S-14g*):

Chromatogram



1: 210

nm, 2 nm

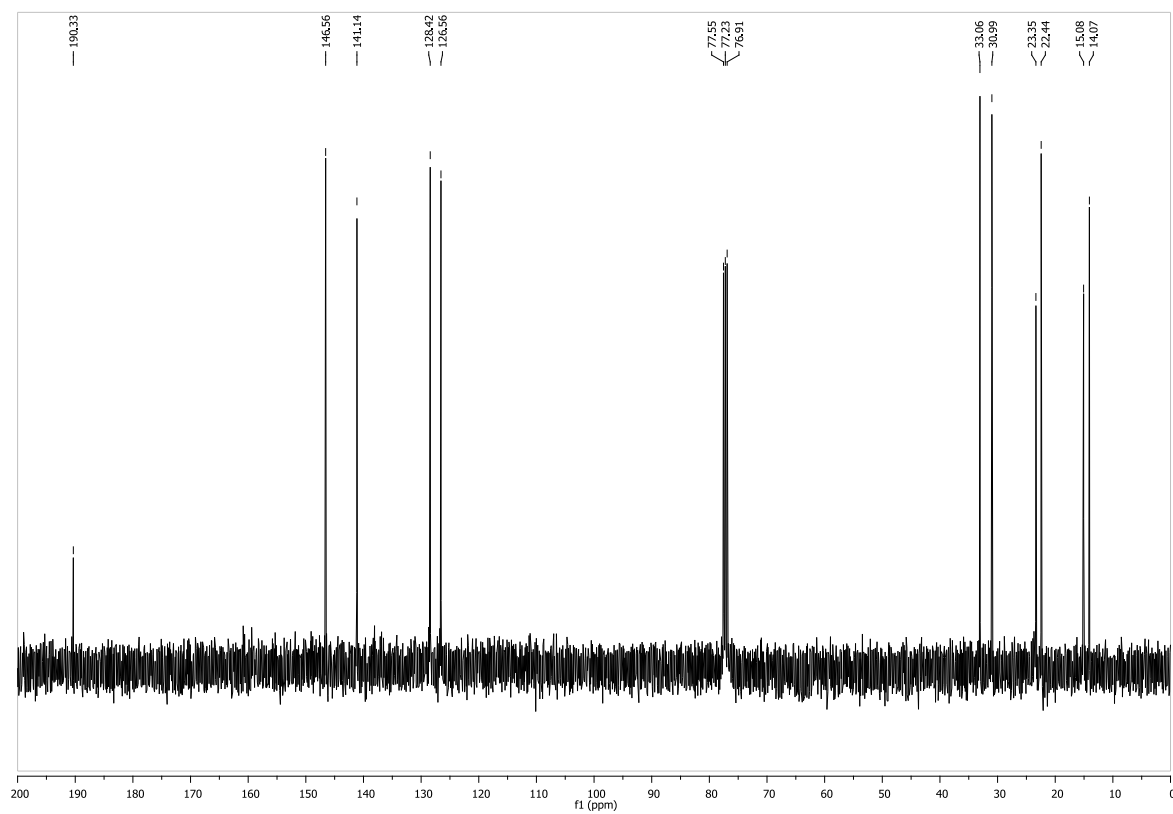
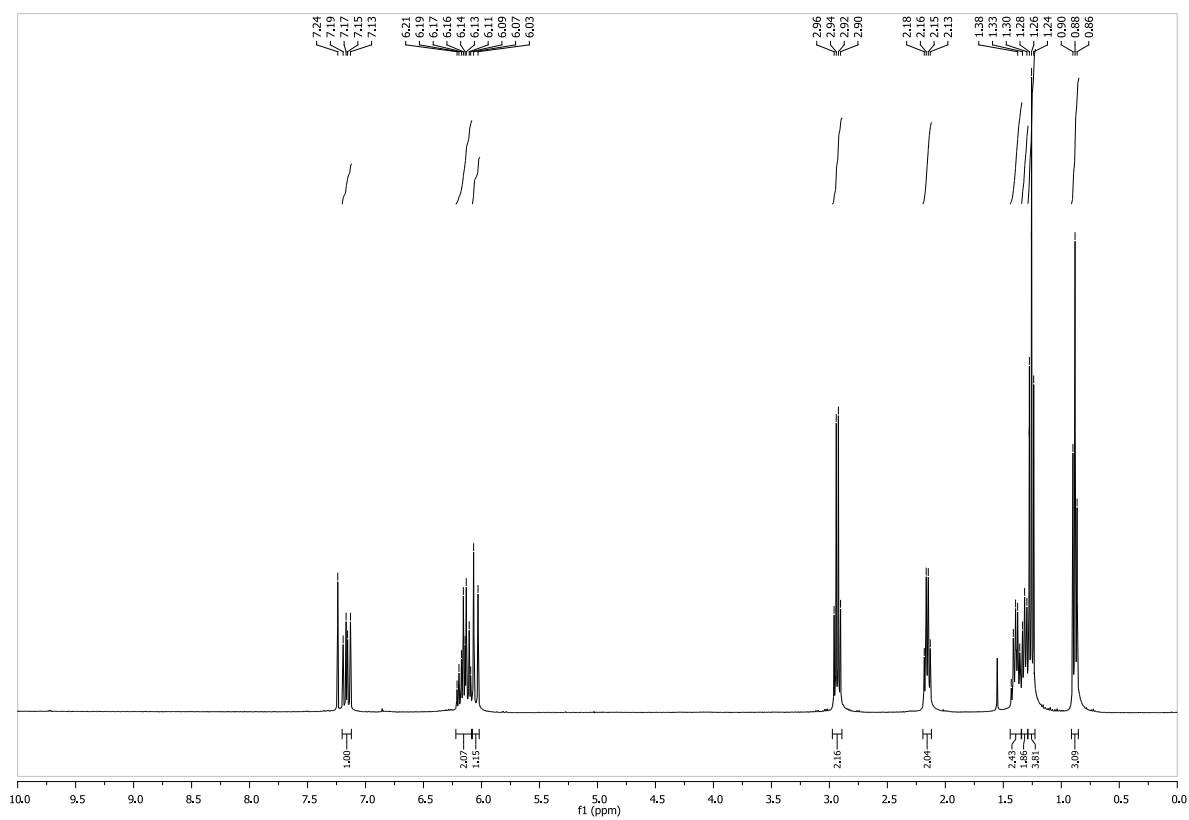
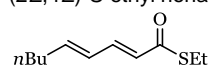
Results

Pk #	Name	Retention Time	Area	Area Percent
1	Peak @ 17,308 Minutes	17,308	176434	6,513
2	Peak @ 18,192 Minutes	18,192	18968	0,700
3	Peak @ 19,116 Minutes	19,116	2367403	87,386
4	Peak @ 20,052 Minutes	20,052	146336	5,402

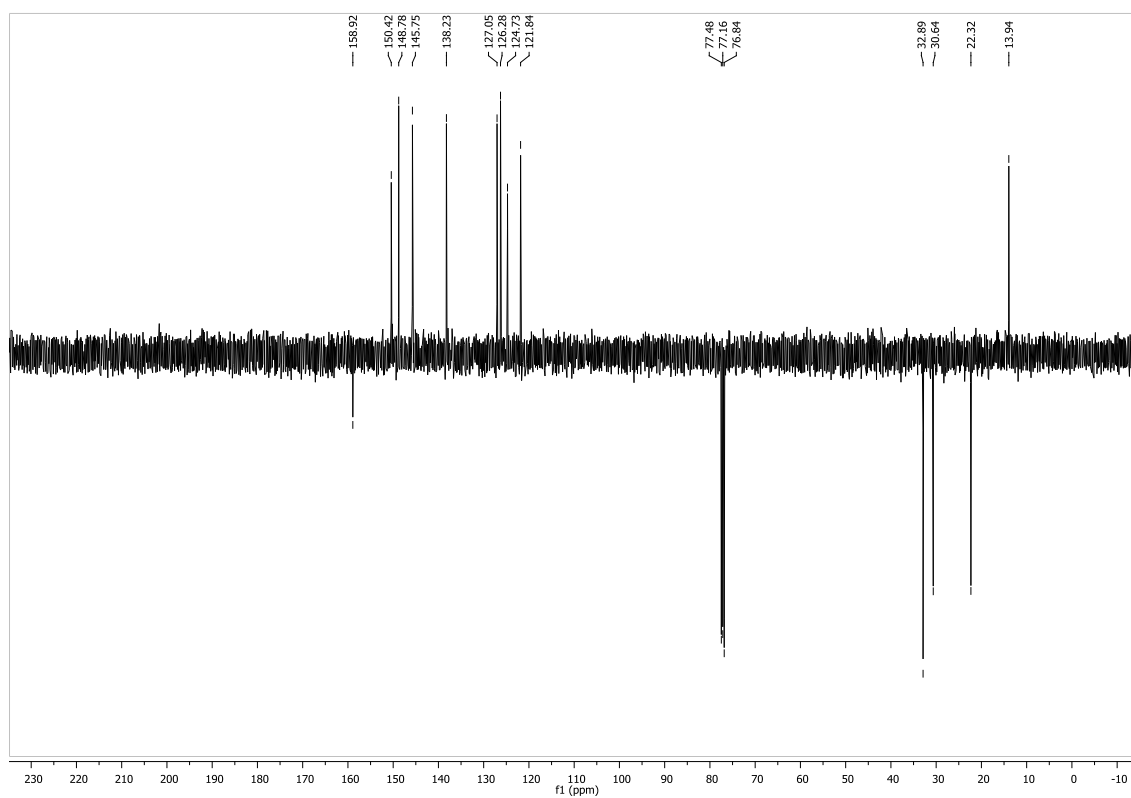
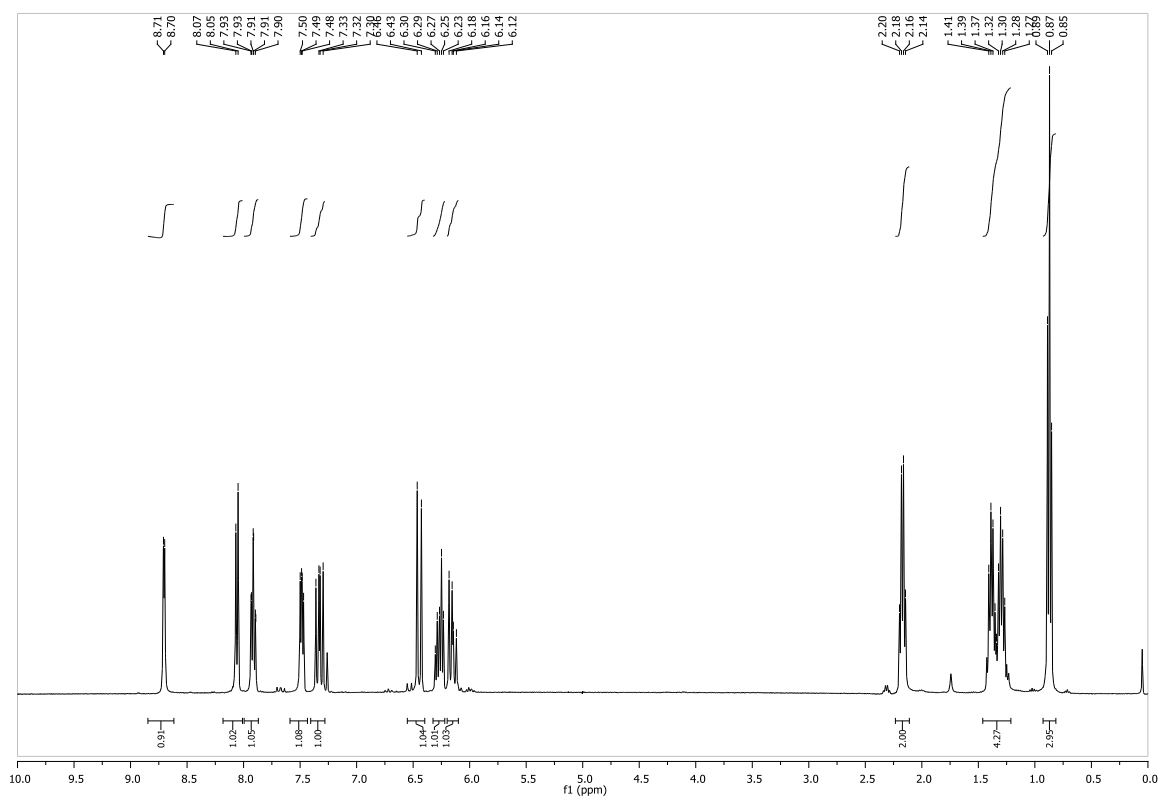
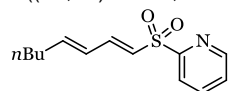
Totals			2709141	100,000
--------	--	--	---------	---------

9. Michael acceptor dependency: spectra

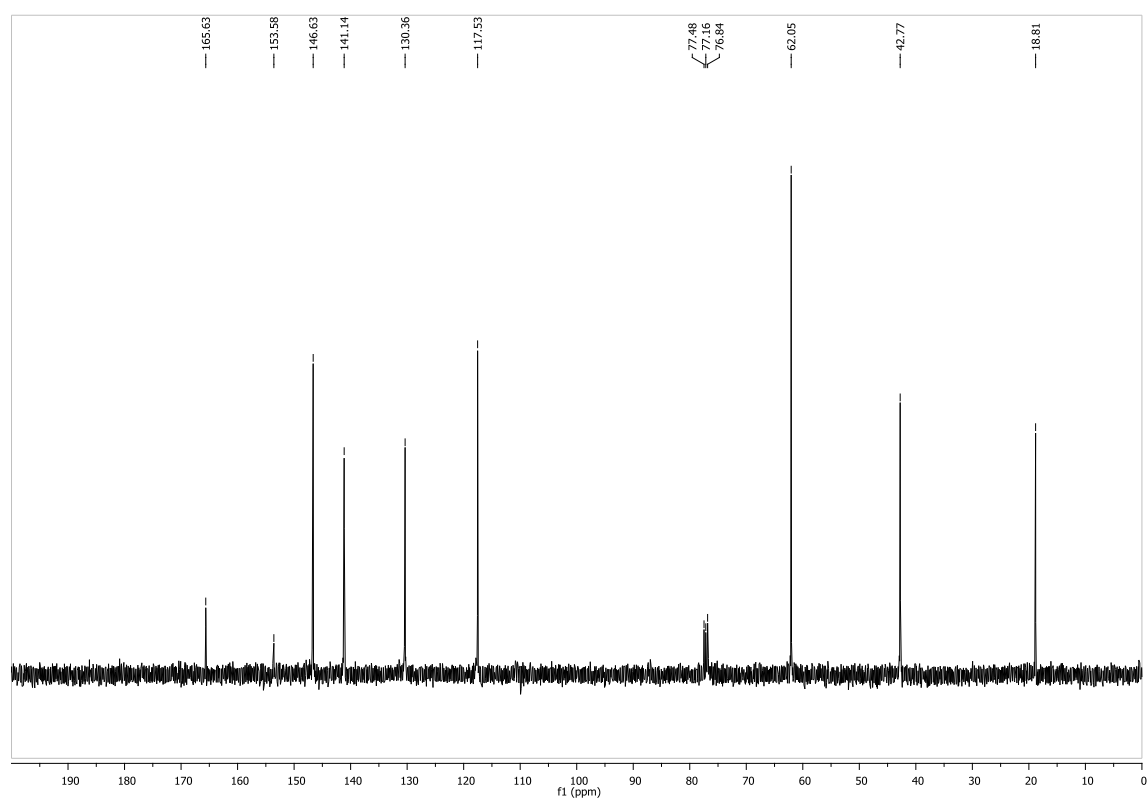
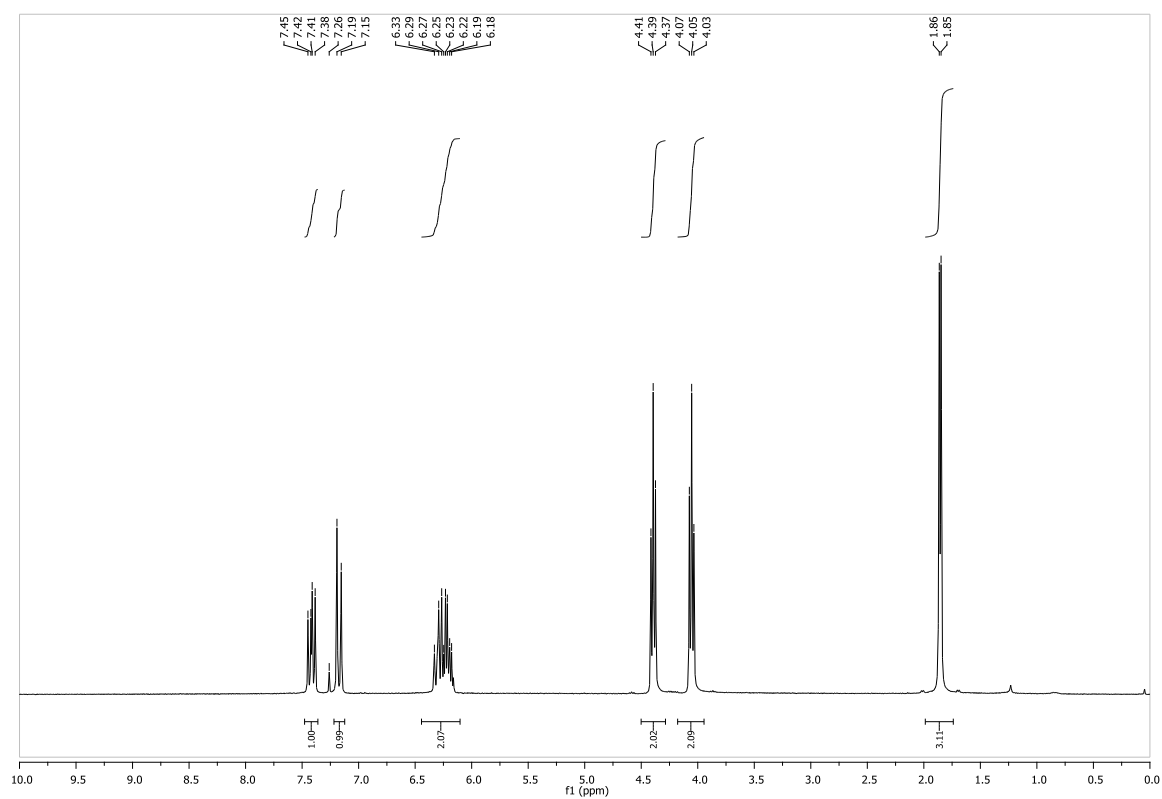
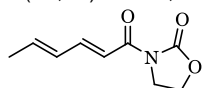
(2*E*,4*E*)-*S*-ethyl nona-2,4-dienethioate (**15b**)



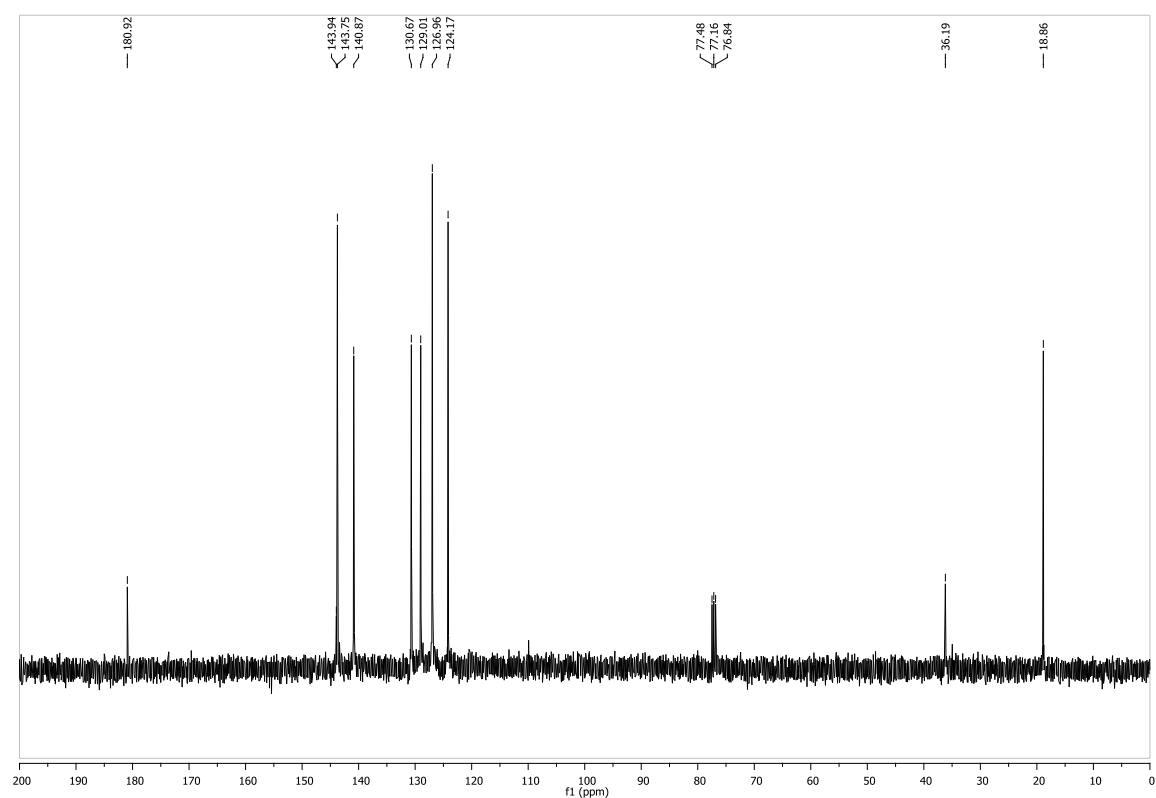
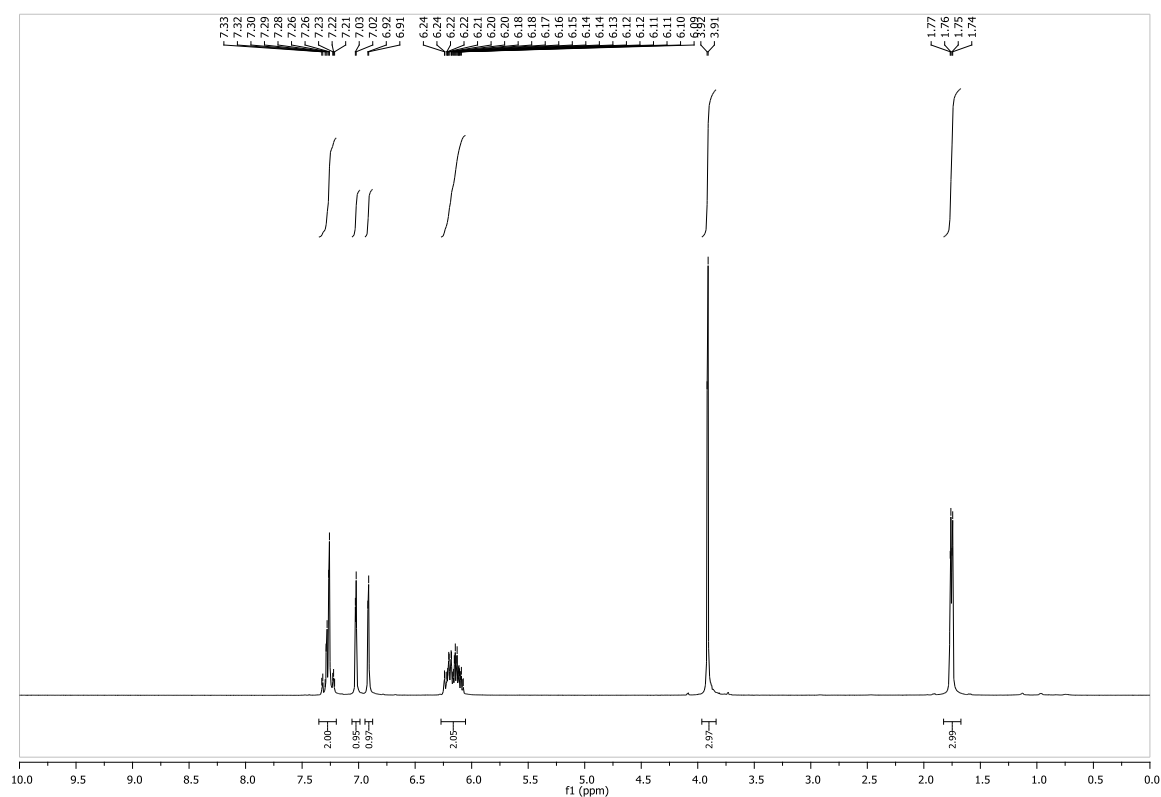
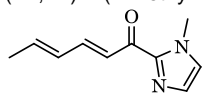
2-((1*E*,3*E*)-octa-1,3-dienylsulfonyl)pyridine (**15d**)



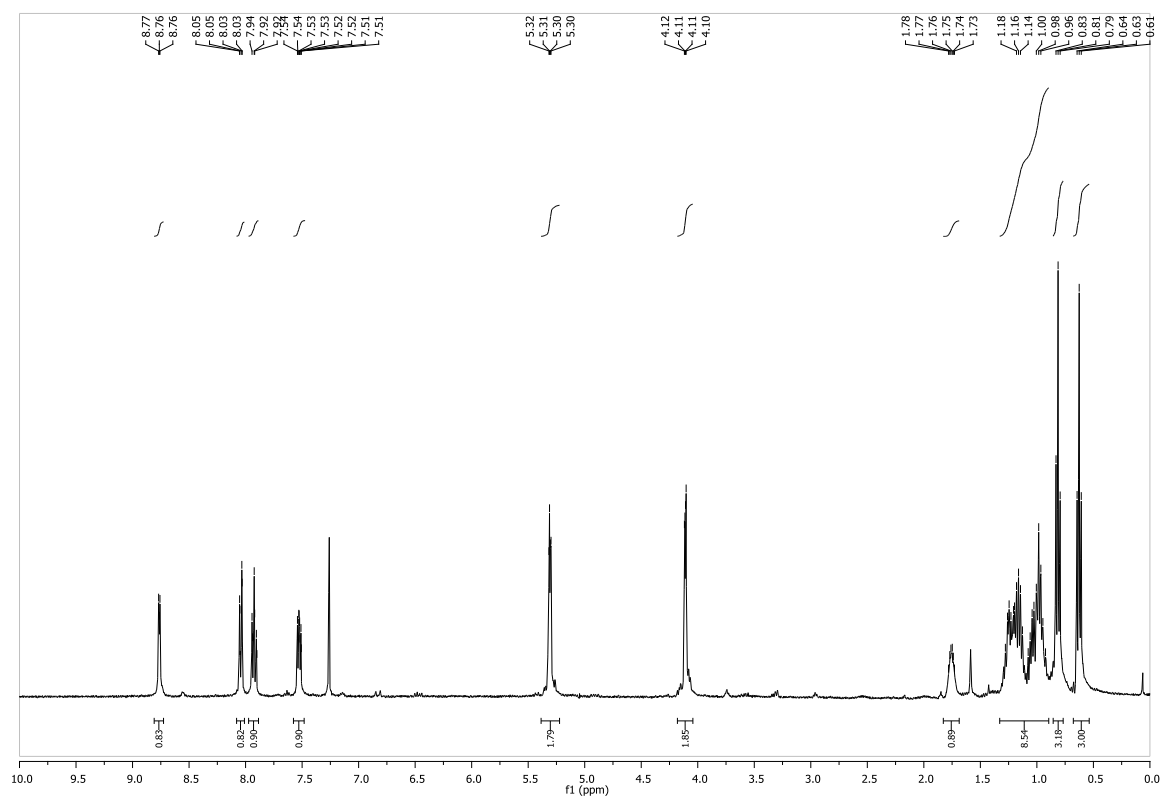
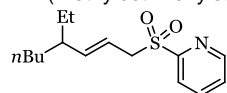
3-(2*E*,4*E*)-hexa-2,4-dienyloxazolidin-2-one (**15e**)



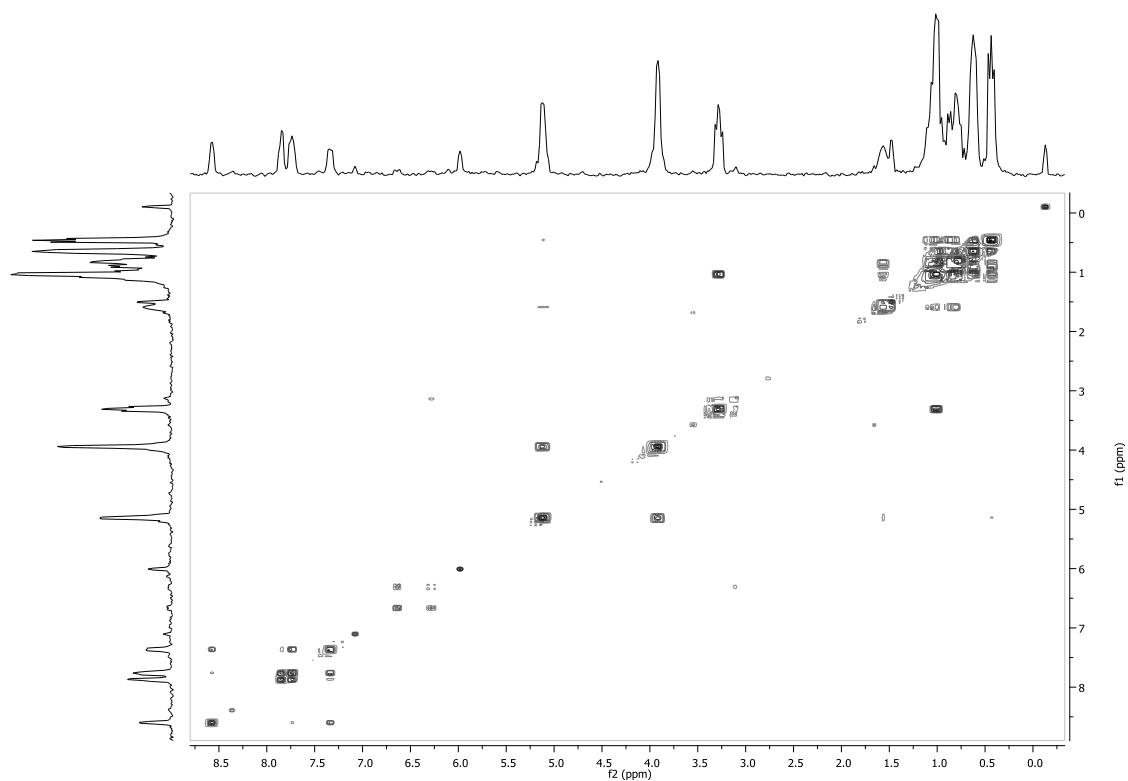
(2*E*,4*E*)-1-(1-methyl-1*H*-imidazol-2-yl)hexa-2,4-dien-1-one (**15f**)



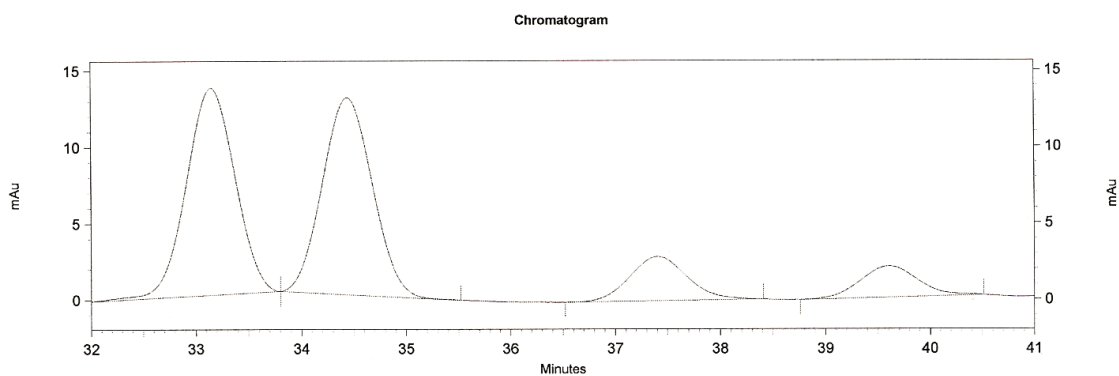
E-2-(4-ethyloct-2-enylsulfonyl)pyridine (**16d**)



GCOSY spectrum contains Et₂O: Coupling between the NMR signals at δ = 5.31 and 4.11 ppm indicate 1,6-addition product.



Regio- and enantioselectivity: *rac*-*E*-2-(4-ethyloct-2-enylsulfonyl)pyridine (*rac*-**16d** and *rac*-**17d**):

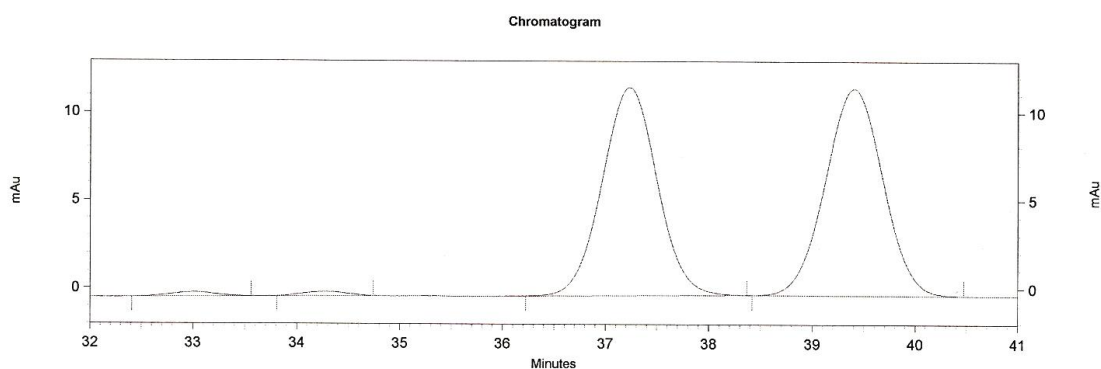


1: 215 nm,
2 nm Results

Pk #	Name	Retention Time	Area	Area Percent
1	Peak @ 33,152 Minutes	33,152	436846	41,595
2	Peak @ 34,444 Minutes	34,444	425521	40,517
3	Peak @ 37,400 Minutes	37,400	110105	10,484
4	Peak @ 39,620 Minutes	39,620	77757	7,404

Totals			1050229	100,000
--------	--	--	---------	---------

Regio- and enantioselectivity: Selective reaction with *E*-2-(4-ethyloct-2-enylsulfonyl)pyridine (**16d**):

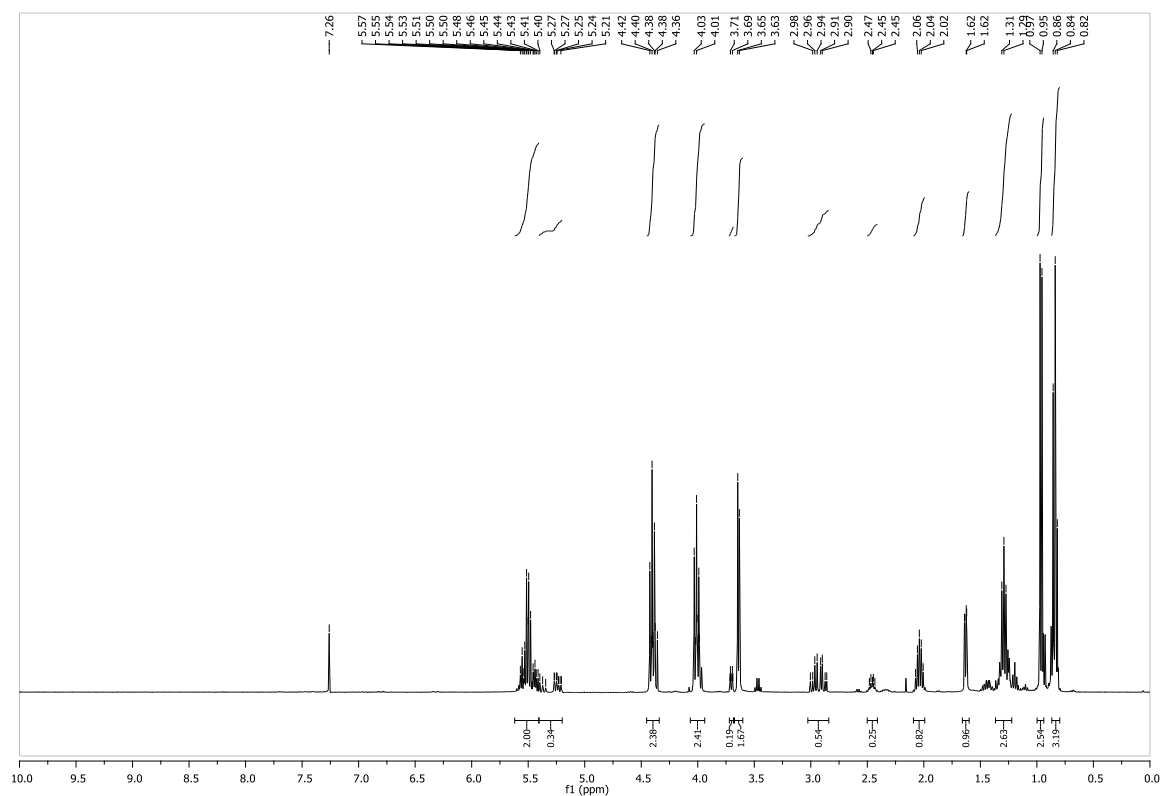
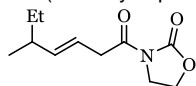


1: 215 nm,
2 nm Results

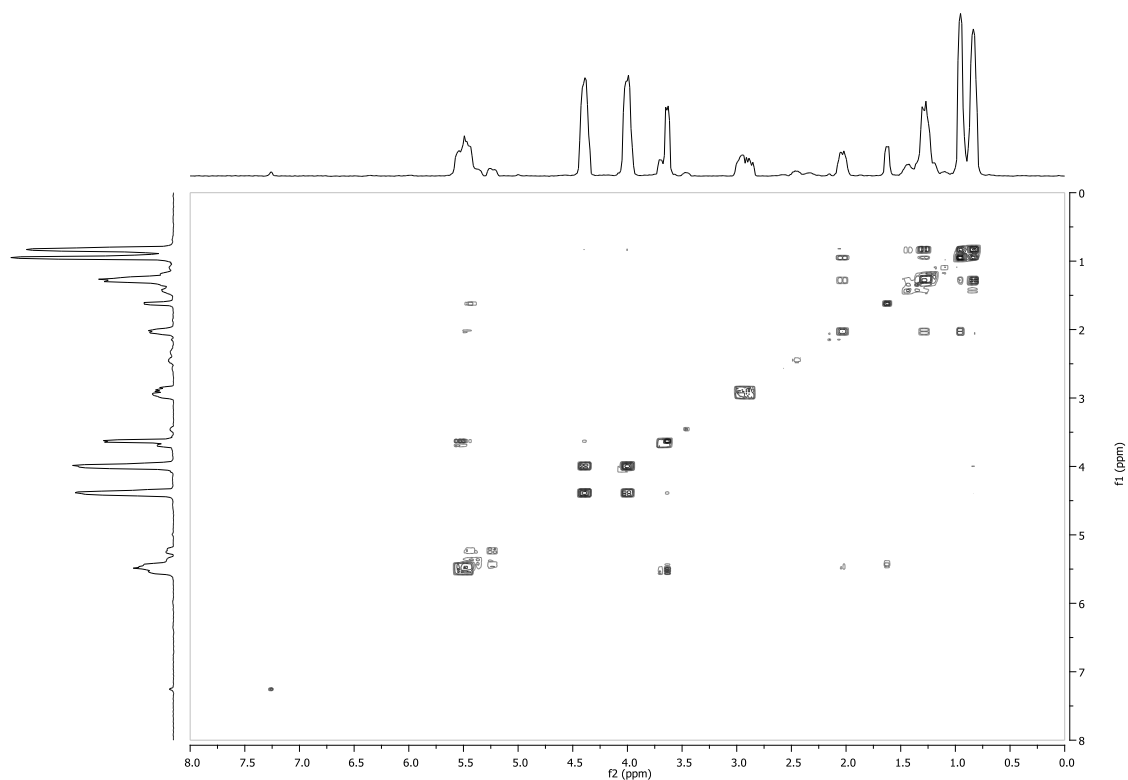
Pk #	Name	Retention Time	Area	Area Percent
1	Peak @ 33,028 Minutes	33,028	7830	0,859
2	Peak @ 34,284 Minutes	34,284	7293	0,801
3	Peak @ 37,232 Minutes	37,232	439233	48,213
4	Peak @ 39,408 Minutes	39,408	456672	50,127

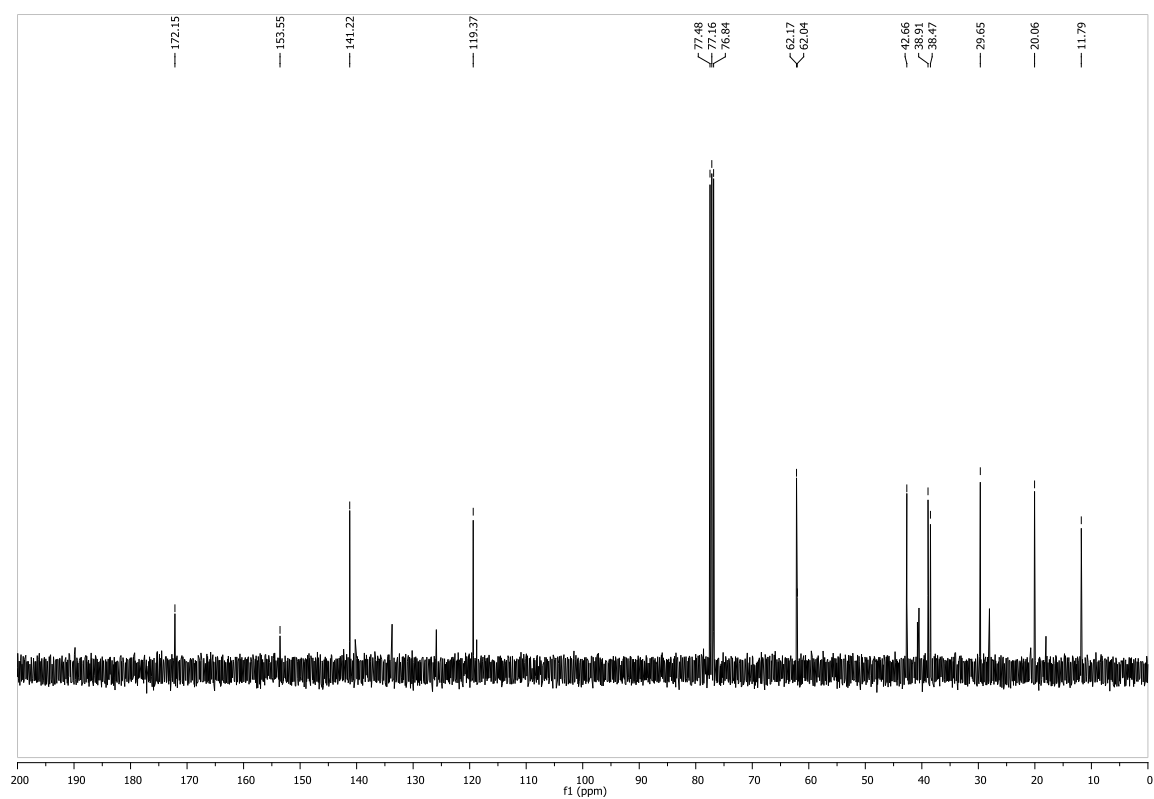
Totals			911028	100,000
--------	--	--	--------	---------

E-3-(5-methylhept-3-en-1-yn-1-yl)oxazolidin-2-one (**16e**)

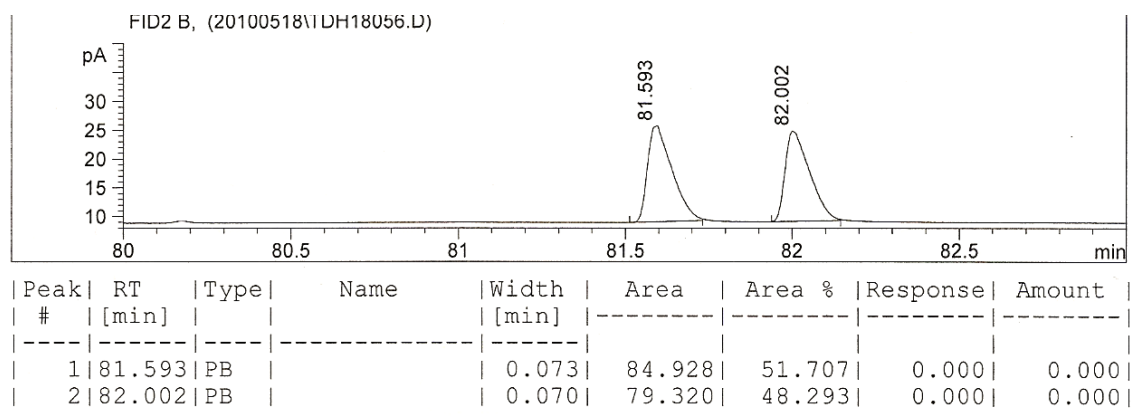


Coupling between the NMR signals at $\delta = 5.30$ and 3.64 ppm indicate 1,6-addition product.

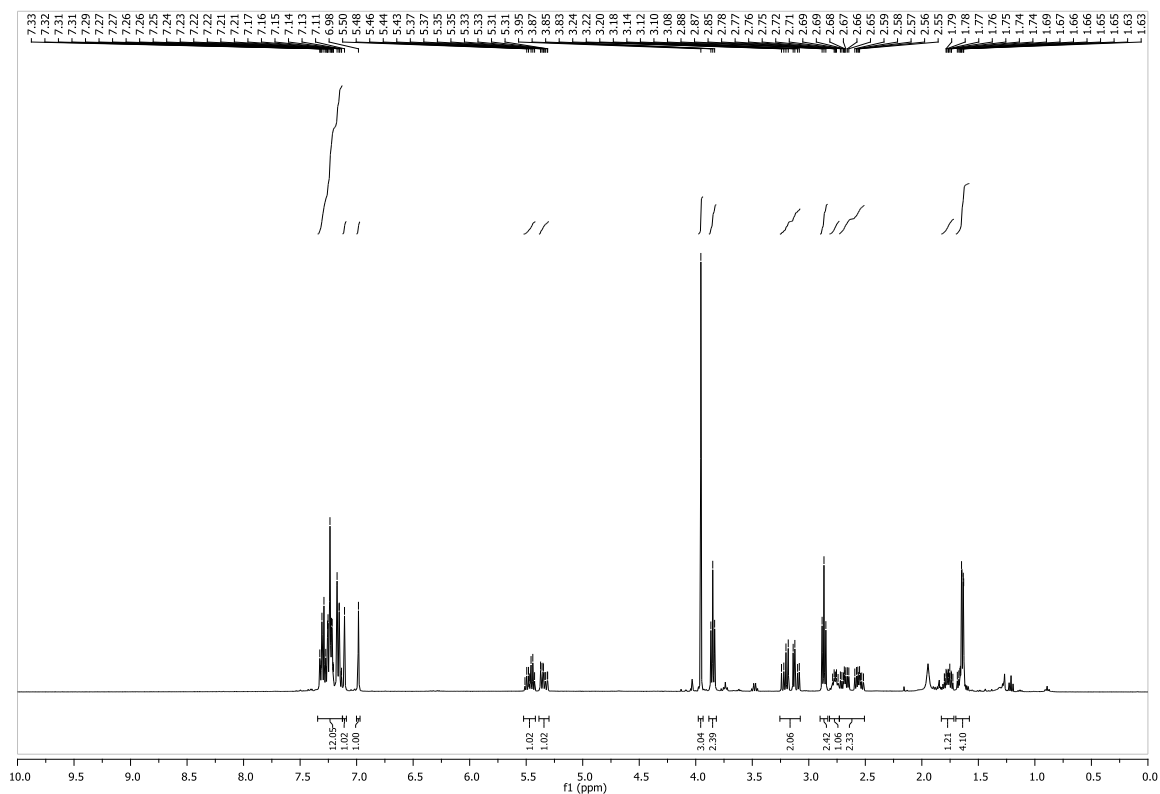
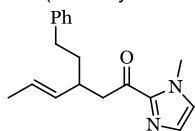




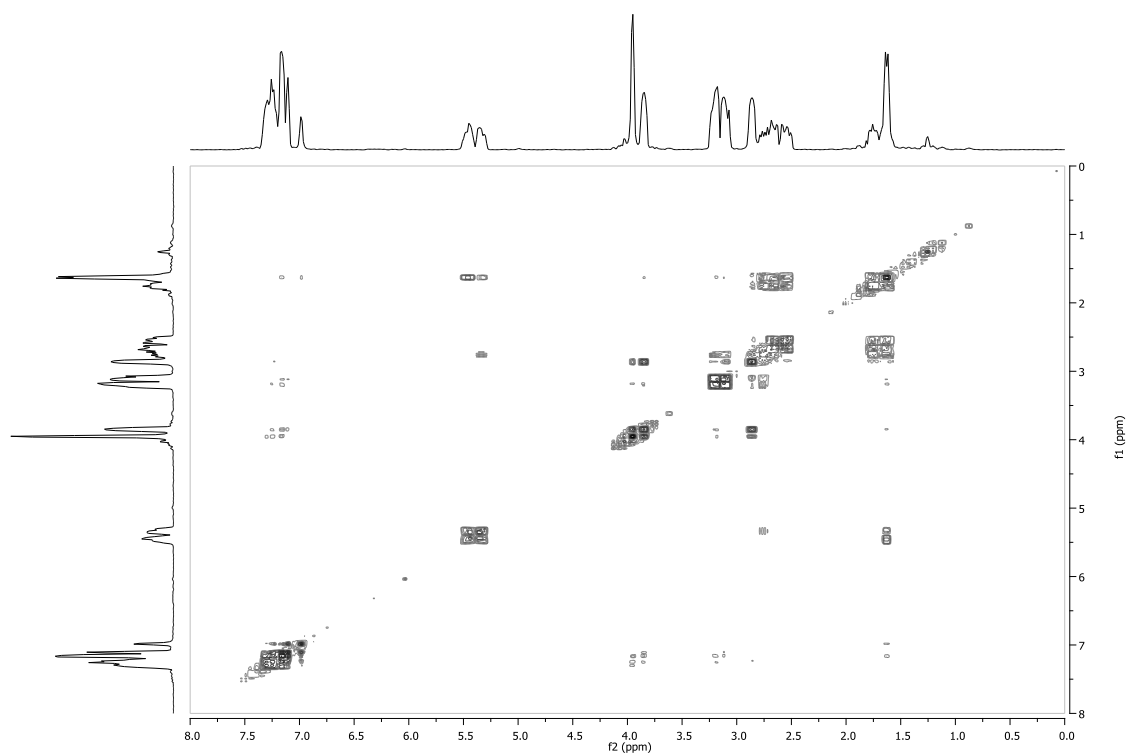
Enantioselectivity: selective-2-methylbutanoic acid: {obtained after derivatisation}

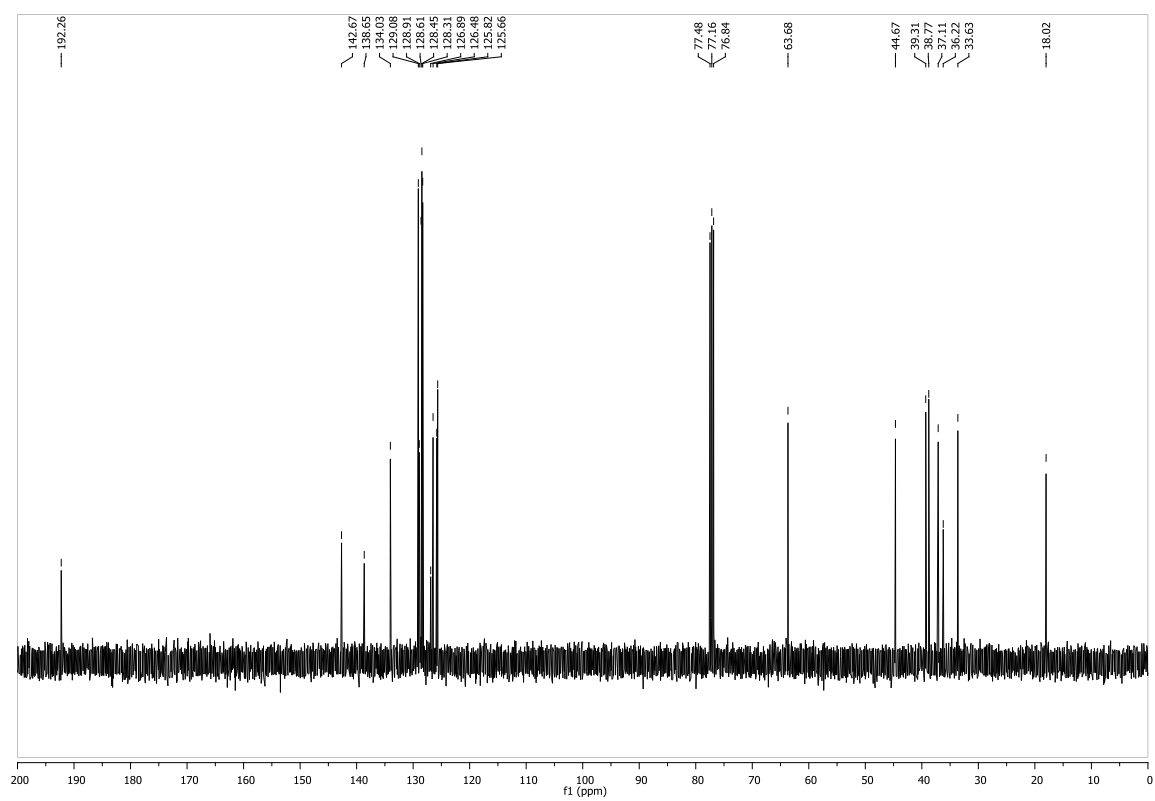


E-1-(1-methyl-1H-imidazol-2-yl)-3-phenethylhex-4-en-1-one (**17f**): spectra contain ~1 equiv. phenethyl alcohol.

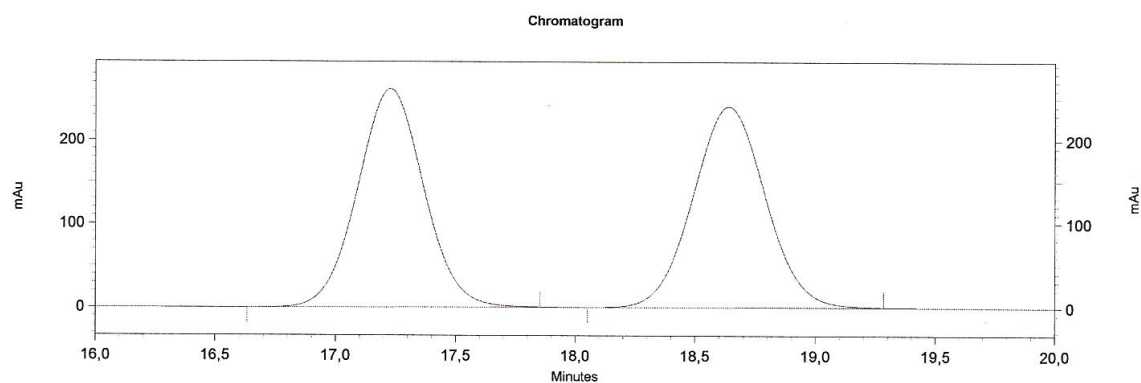


Coupling between the NMR signals at $\delta = 3.85$ and 1.65 ppm and the coupling between the NMR signals at $\delta = 3.16$ and 2.77 ppm indicate 1,4-addition product





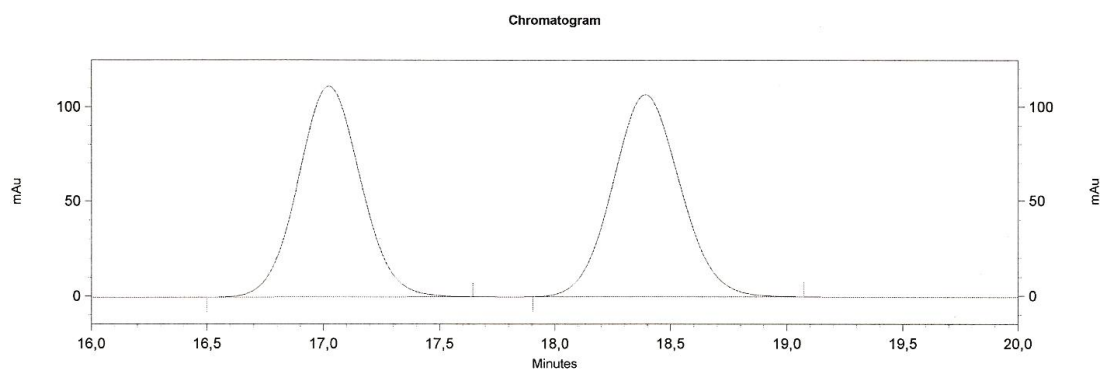
Enantioselectivity: *rac*-*E*-1-(1-methyl-1H-imidazol-2-yl)-3-phenethylhex-4-en-1-one (*rac*-**17f**):



1: 275
nm, 2 nm
Results

Pk #	Name	Retention Time	Area	Area Percent
1	Peak @ 17,224 Minutes	17,224	5023150	49,953
2	Peak @ 18,640 Minutes	18,640	5032625	50,047
Totals			10055775	100,000

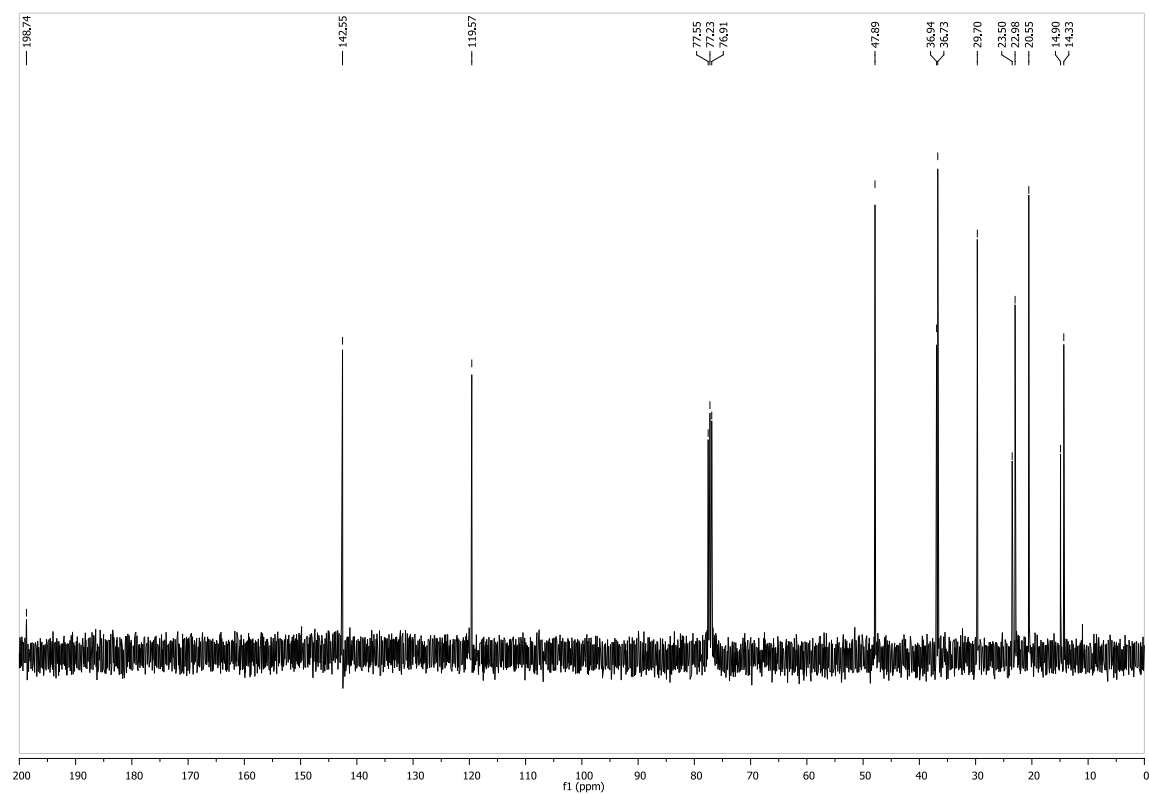
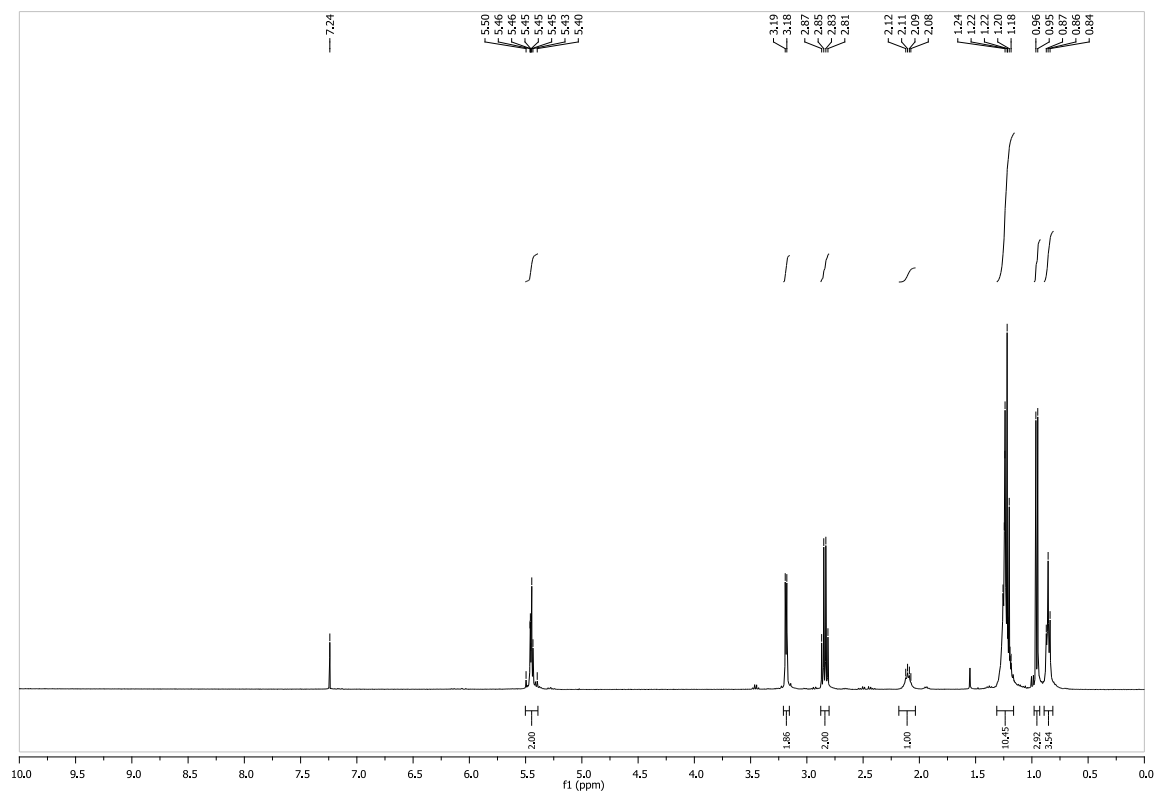
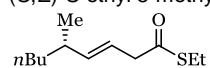
Enantioselectivity: selective *E*-1-(1-methyl-1H-imidazol-2-yl)-3-phenethylhex-4-en-1-one (**17f**):



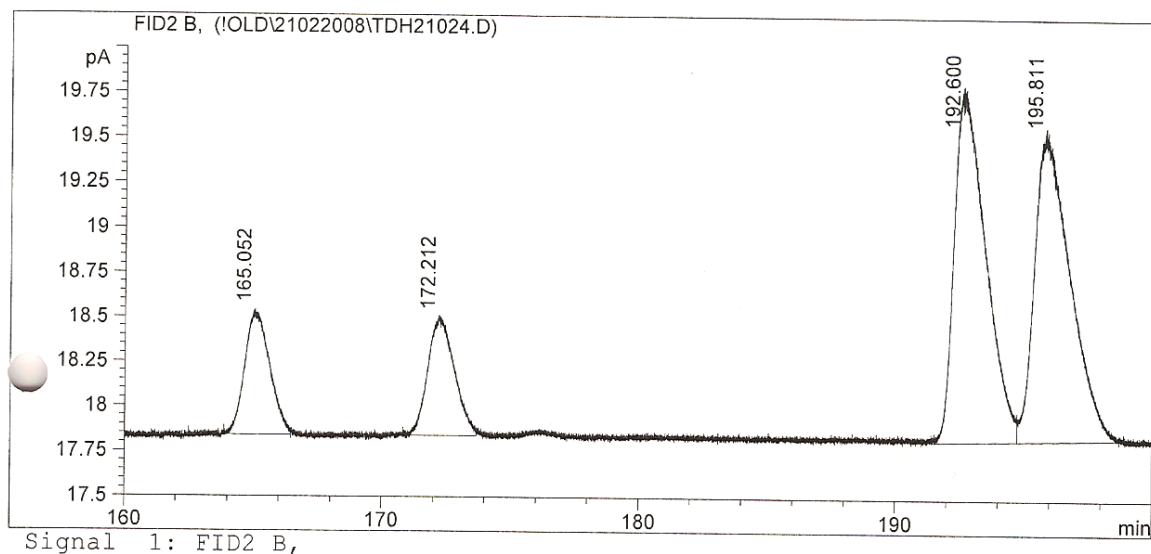
1: 254
nm, 2 nm
Results

Pk #	Name	Retention Time	Area	Area Percent
1	Peak @ 17,024 Minutes	17,024	2101142	49,129
2	Peak @ 18,392 Minutes	18,392	2175614	50,871
Totals			4276756	100,000

(*S,E*)-*S*-ethyl 5-methylnon-3-enethioate (**16i**): spectrum contains traces of 1,4-addition product.

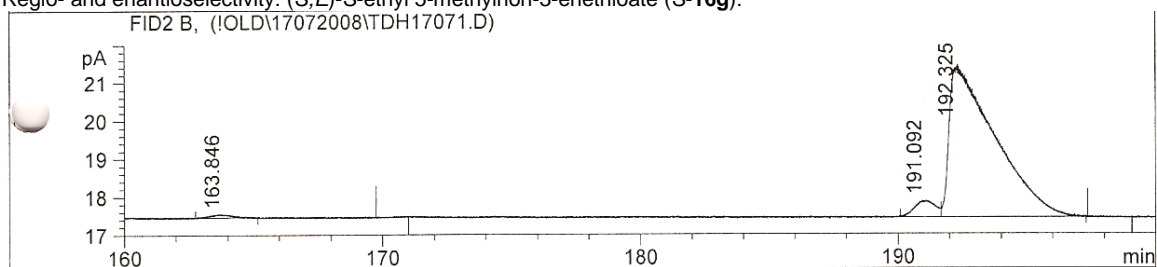


Regio- and enantioselectivity: *rac-E-S*-ethyl 5-methylnon-3-enethioate (*rac-16i* and *rac-17i*):



Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	165.052	MM		1.100	46.873	10.954	0.000	0.000
2	172.212	MM		1.174	47.529	11.107	0.000	0.000
3	192.600	MF		1.402	167.207	39.075	0.000	0.000
4	195.811	FM		1.589	166.305	38.864	0.000	0.000

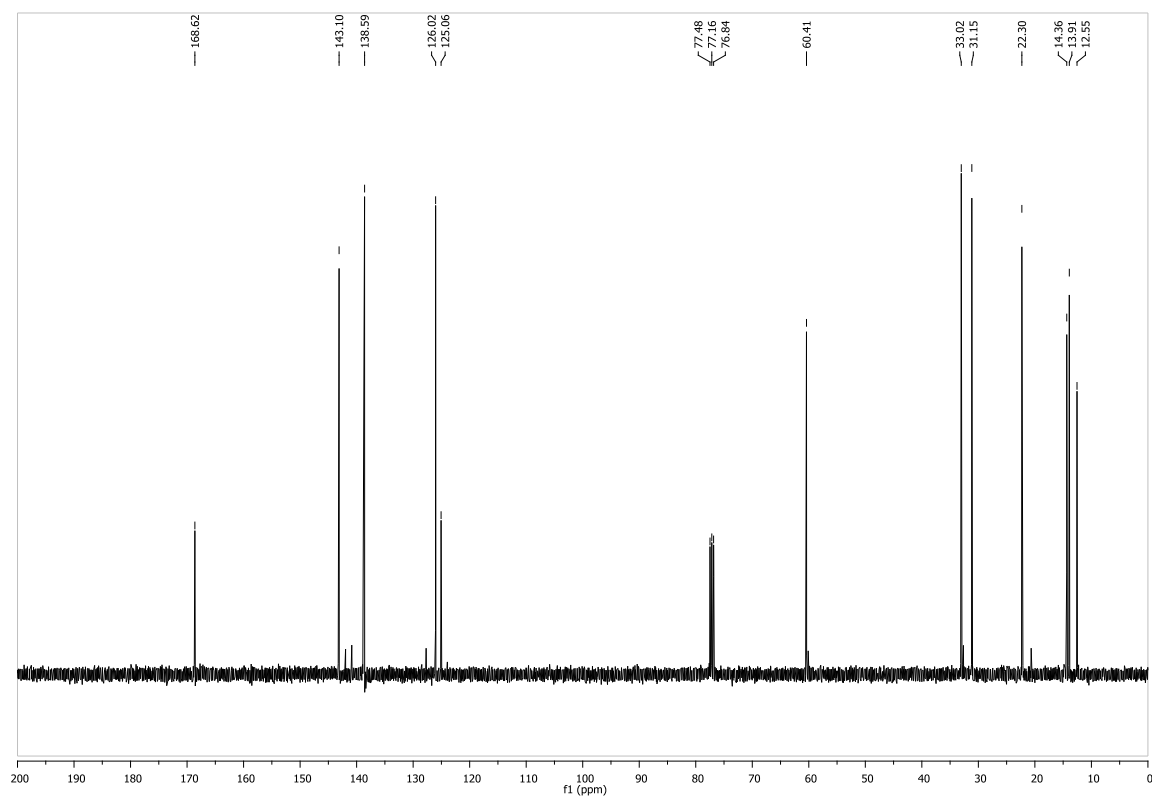
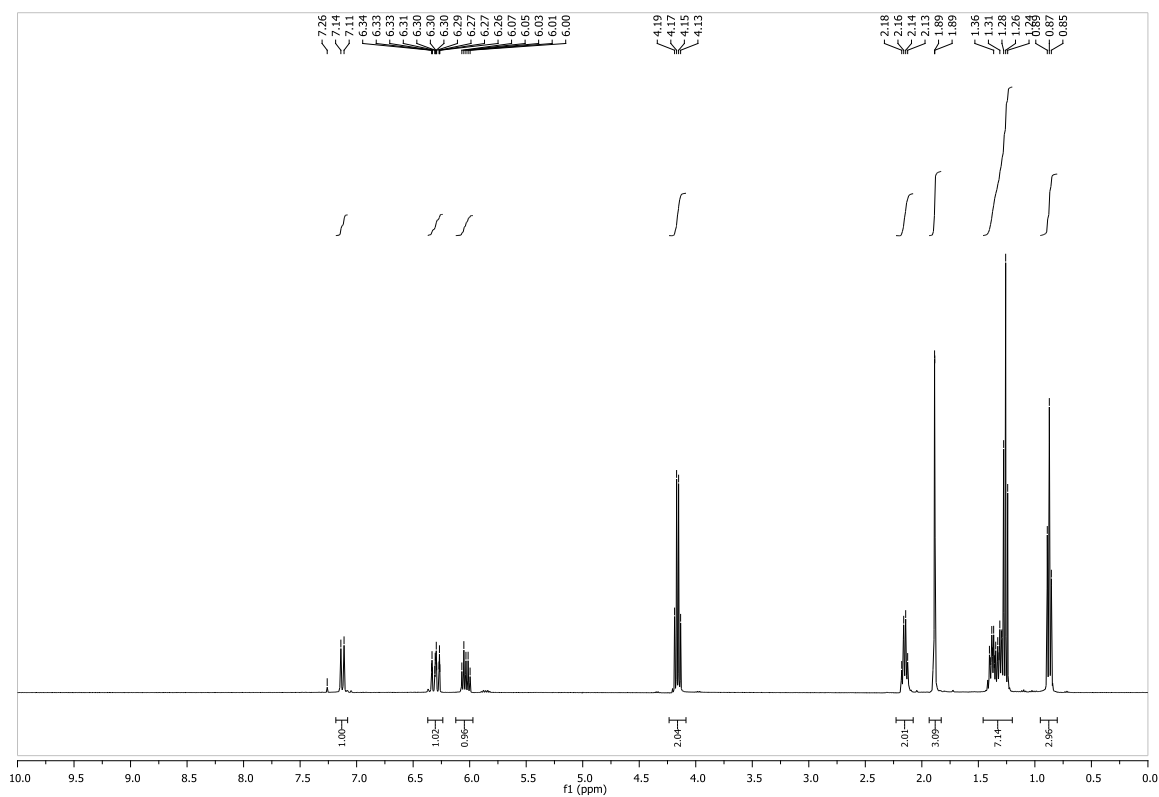
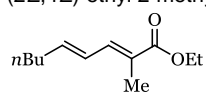
Regio- and enantioselectivity: (*S,E*)-*S*-ethyl 5-methylnon-3-enethioate (*S-16g*):



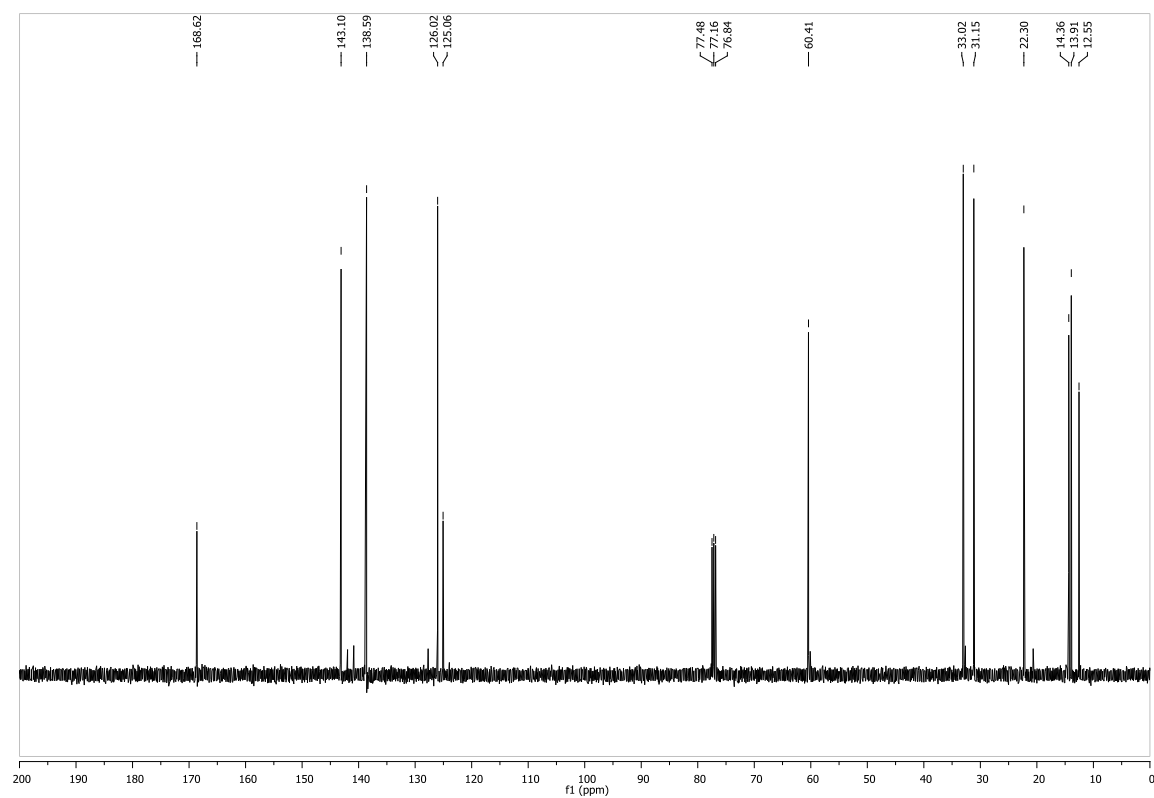
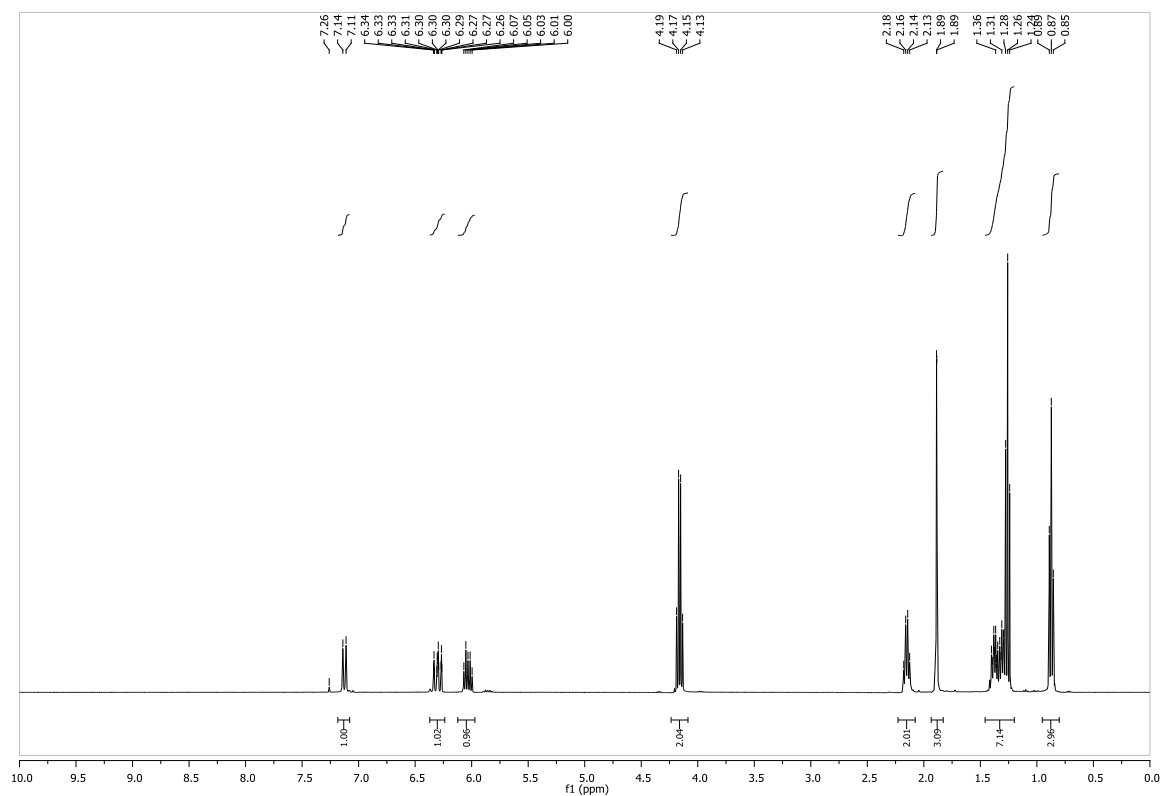
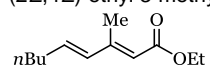
Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	163.846	MM		0.894	5.622	1.089	0.000	0.000
2	191.092	MF		0.914	24.058	4.661	0.000	0.000
3	192.325	FM		2.022	486.417	94.249	0.000	0.000

10. Influence of the olefin substitution pattern: spectra

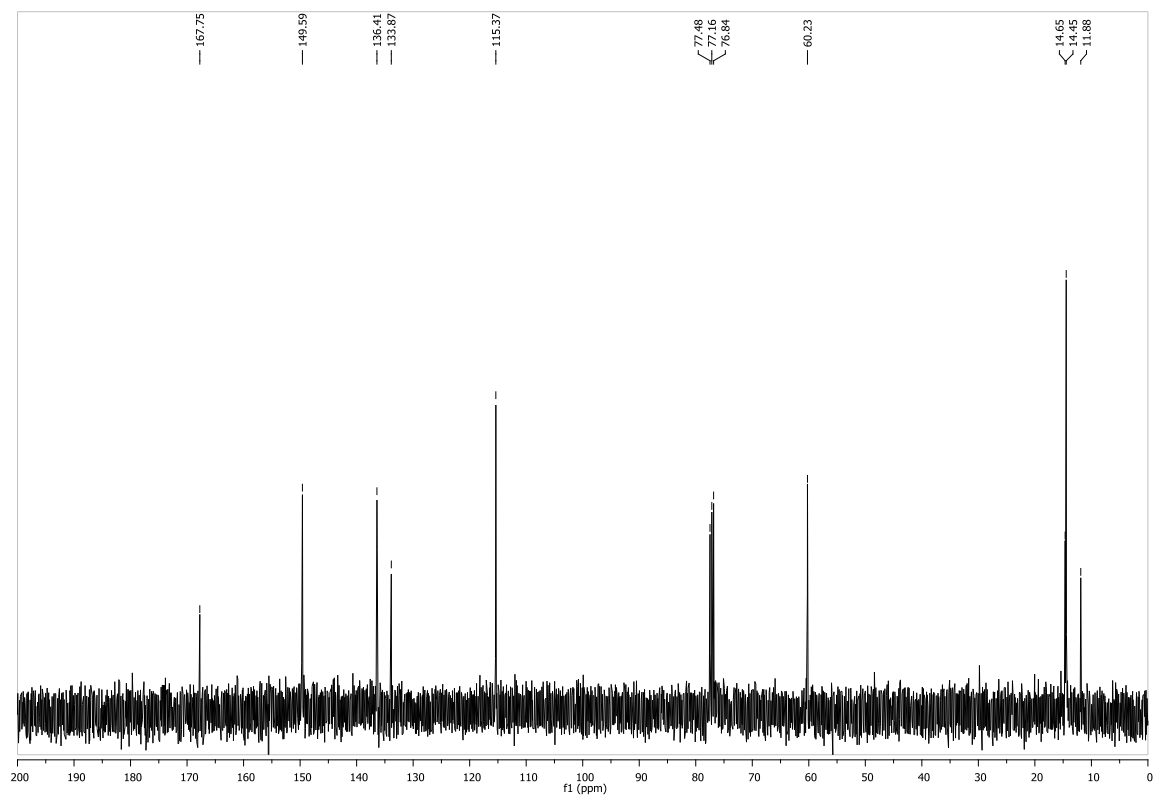
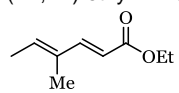
(2*E*,4*E*)-ethyl 2-methylnona-2,4-dienoate (**25a**): spectrum contains traces of (2*Z*,4*E*)-ethyl 2-methylnona-2,4-dienoate.



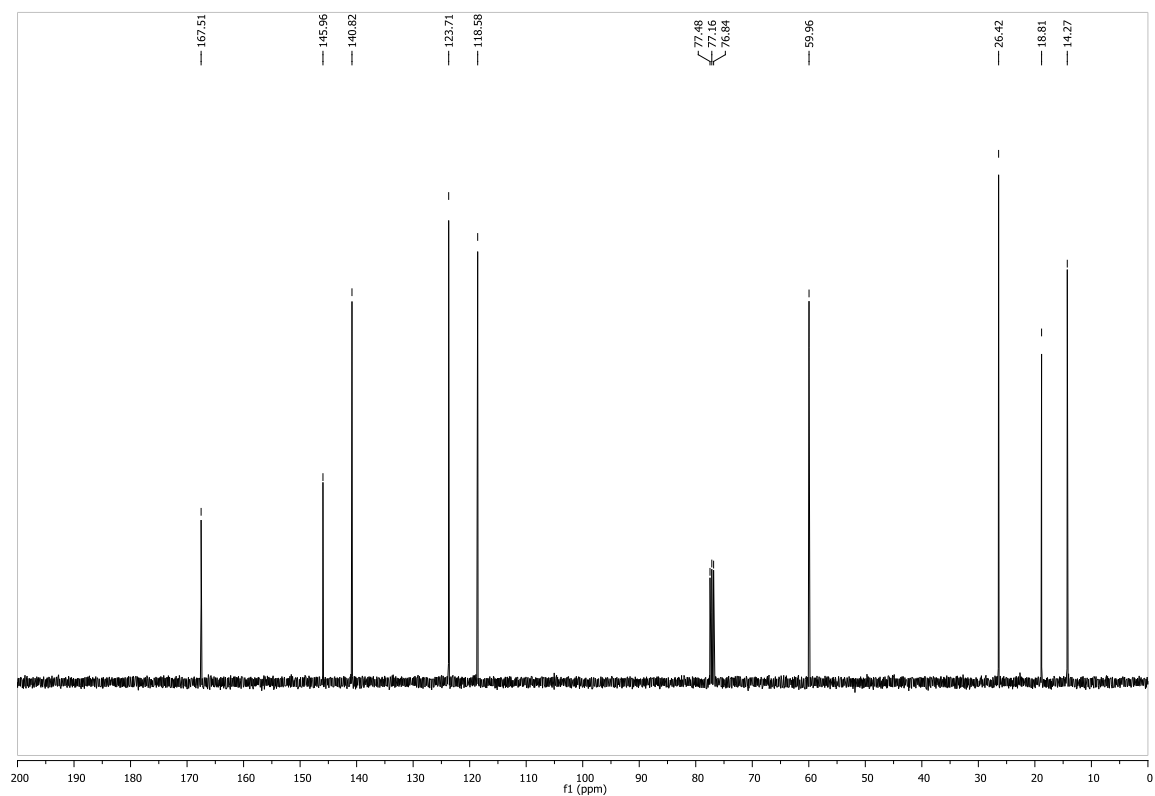
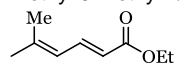
(2*E*,4*E*)-ethyl 3-methylnona-2,4-dienoate (**25b**): spectrum contains traces of (2*Z*,4*E*)-ethyl 3-methylnona-2,4-dienoate.



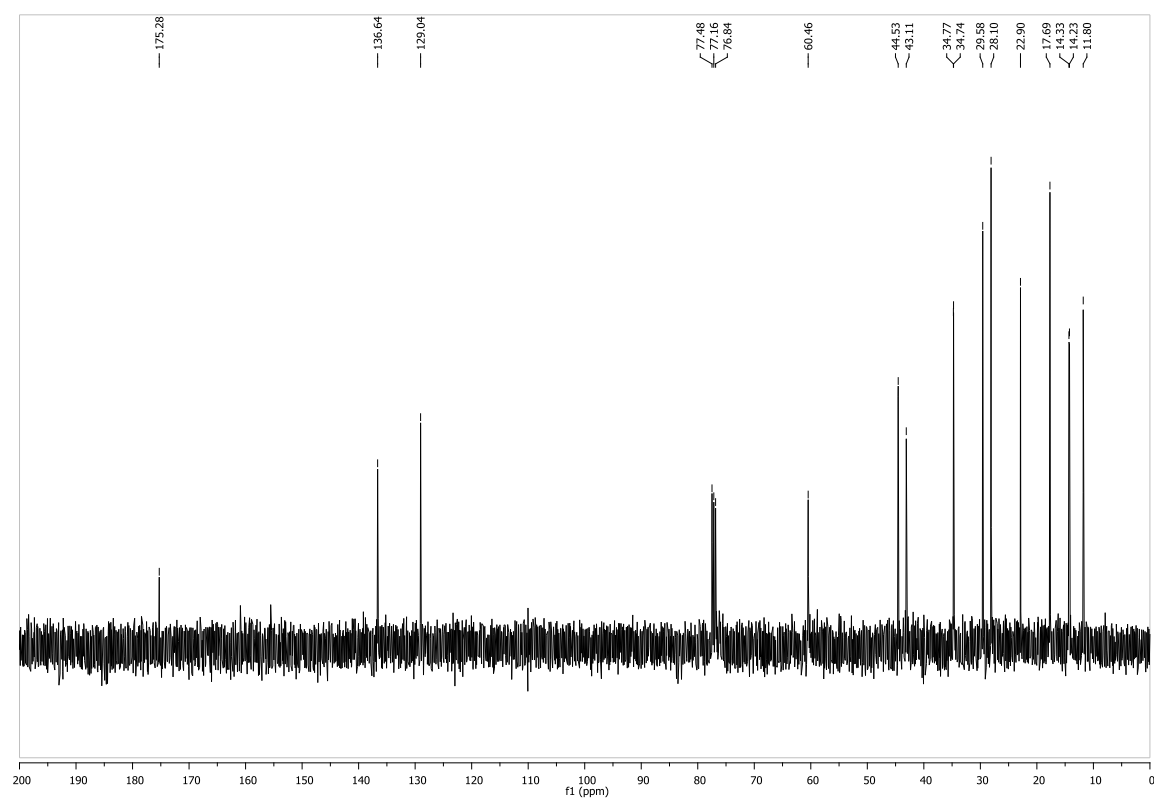
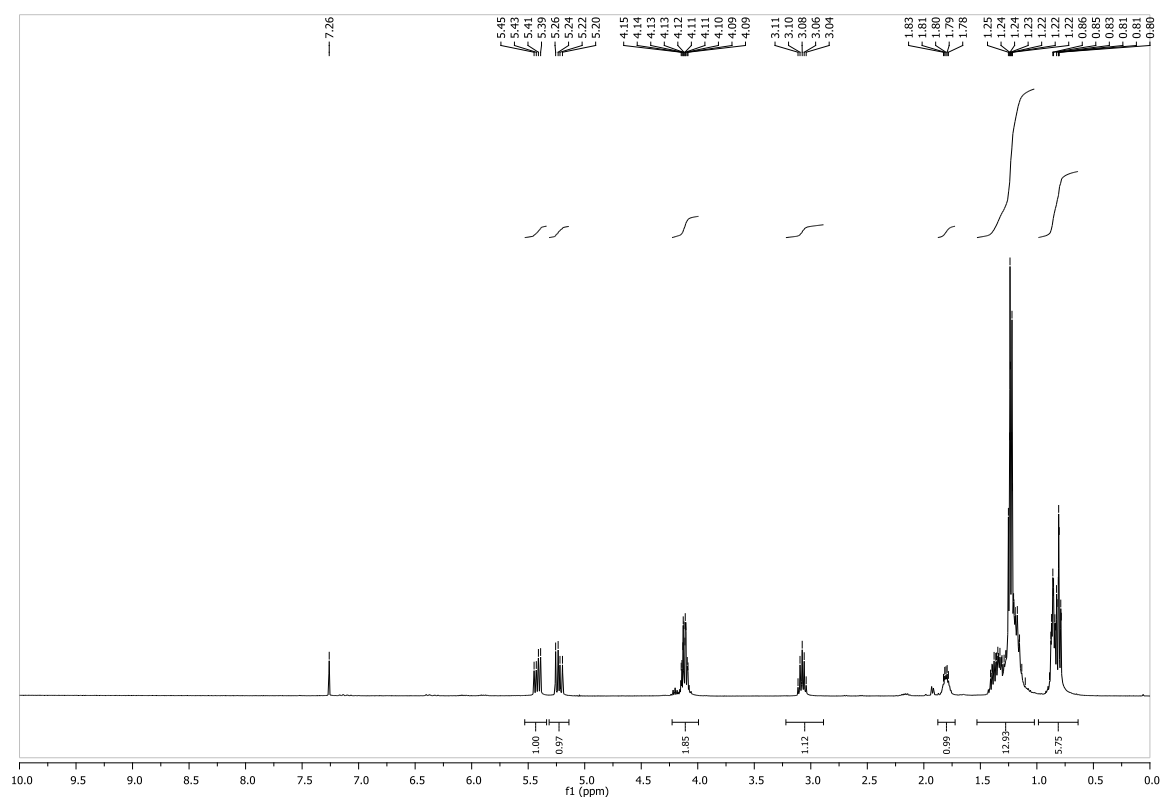
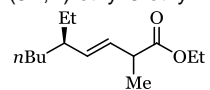
(2*E*,4*E*)-ethyl 4-methylhexa-2,4-dienoate (**25c**)



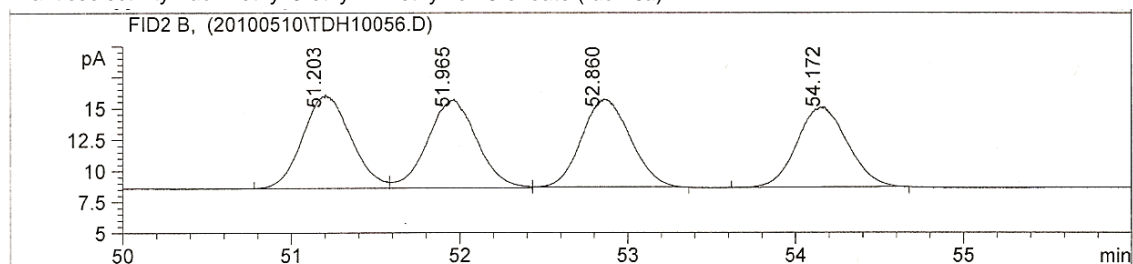
E-ethyl 5-methylhexa-2,4-dienoate (**25d**)



(5*R*,*E*)-ethyl 5-ethyl-2-methylnon-3-enoate (**26a**): spectrum contains traces starting material.

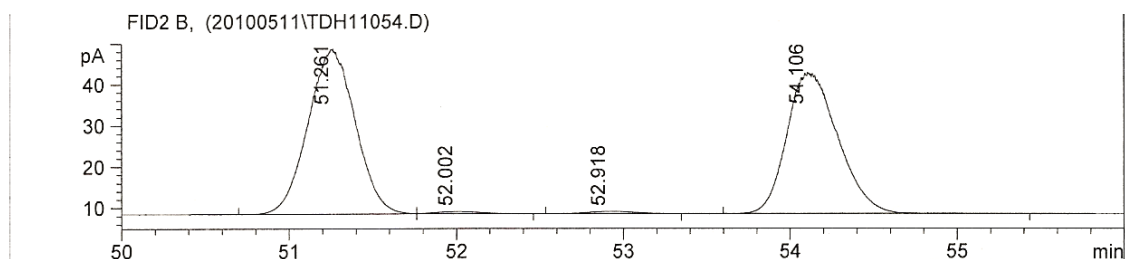


Enantioselectivity: *rac-E*-ethyl 5-ethyl-2-methylnon-3-enoate (*rac-26a*):



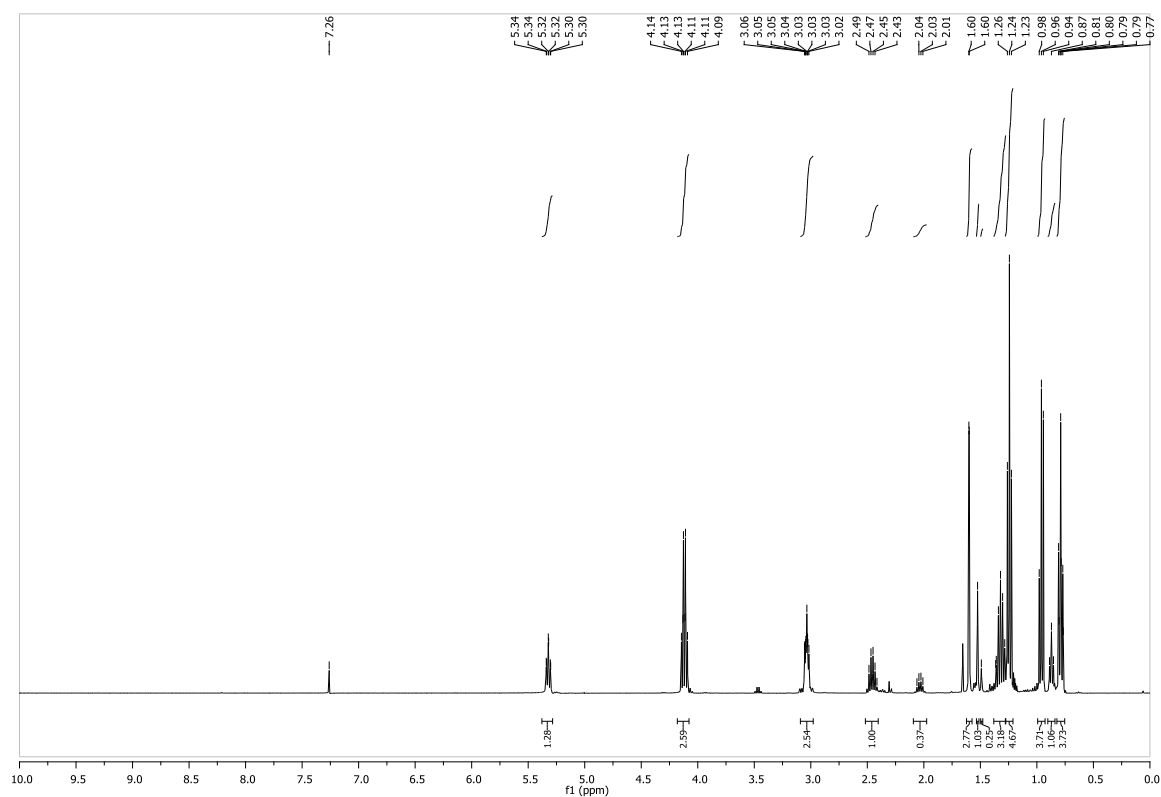
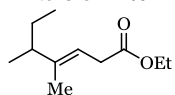
Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	37.204	MM		0.225	2.262	0.396	0.000	0.000
2	38.378	MM		0.188	2.666	0.467	0.000	0.000
3	51.203	MF		0.325	147.182	25.801	0.000	0.000
4	51.965	FM		0.336	142.870	25.045	0.000	0.000
5	52.860	MM		0.335	141.464	24.798	0.000	0.000
6	54.172	MM		0.347	134.014	23.492	0.000	0.000

Enantioselectivity: (*5R,E*)-ethyl 5-ethyl-2-methylnon-3-enoate (*R-26a*):

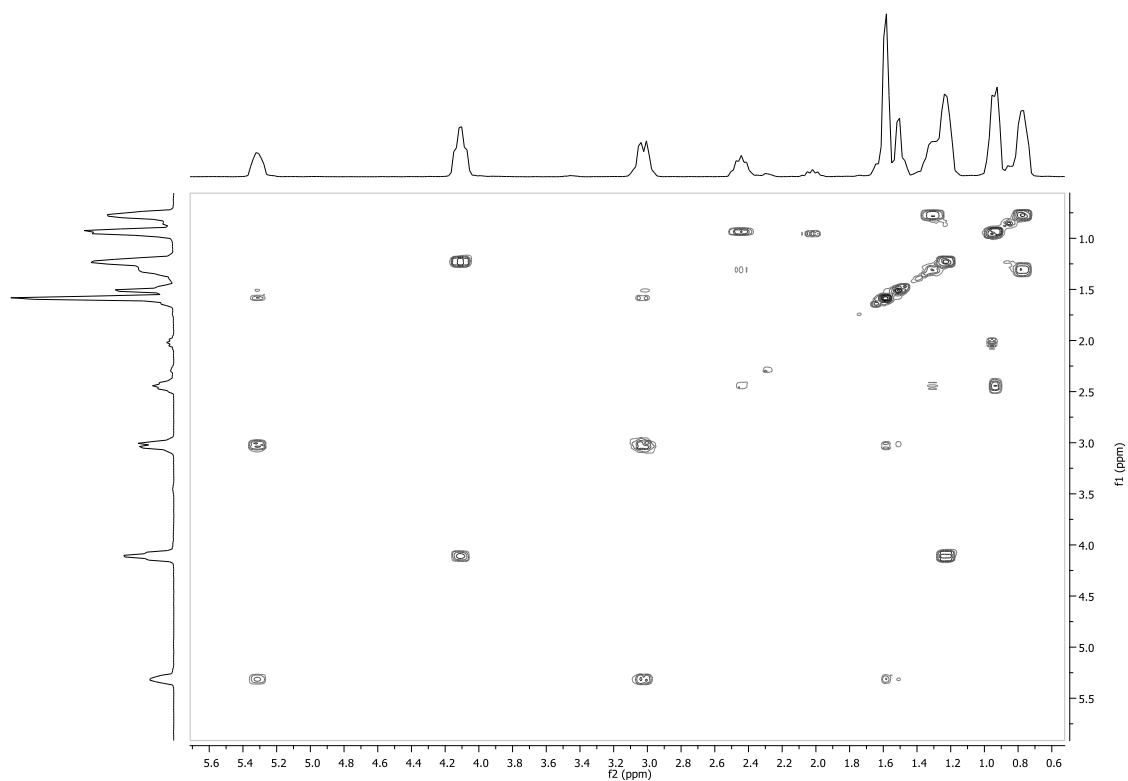


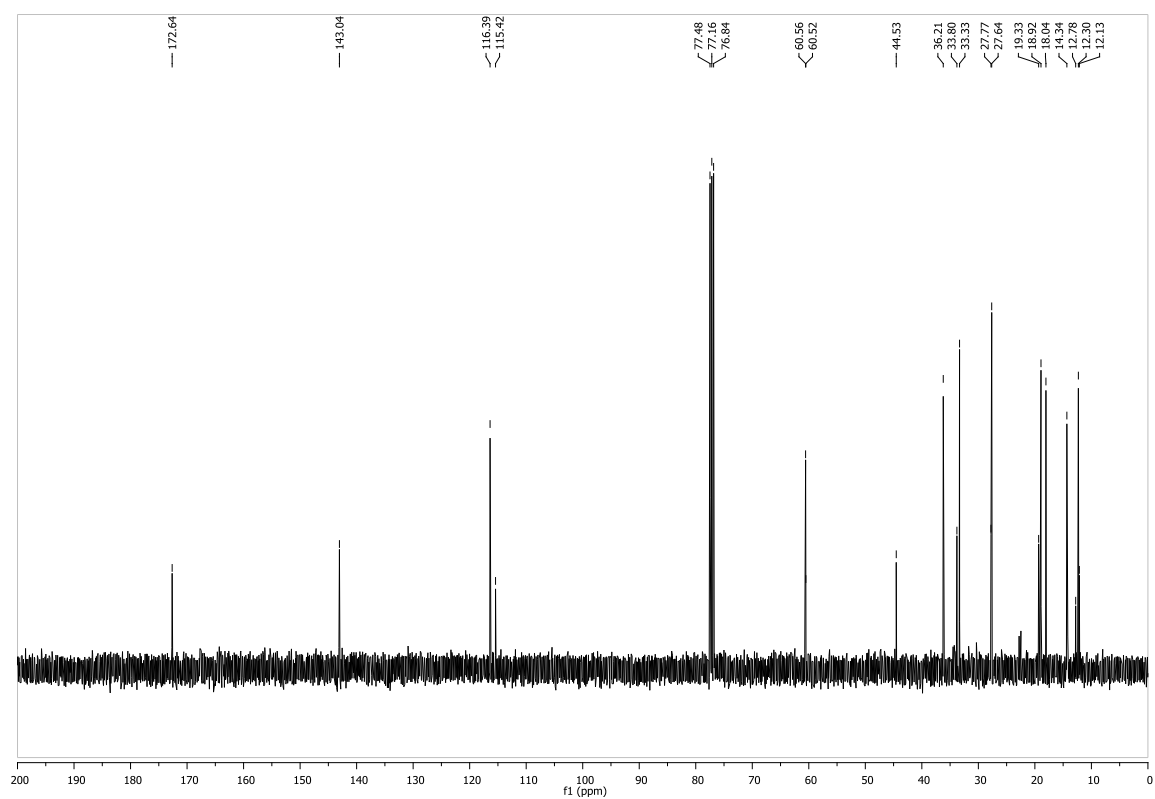
Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	38.397	MM		0.225	1.447	0.094	0.000	0.000
2	51.261	MF		0.325	784.522	51.074	0.000	0.000
3	52.002	FM		0.331	10.651	0.693	0.000	0.000
4	52.918	MM		0.332	11.294	0.735	0.000	0.000
5	54.106	MM		0.353	728.137	47.403	0.000	0.000

mixture of 27% *Z*-ethyl 4,5-dimethylhept-3-enoate and 73% *E*-ethyl 4,5-dimethylhept-3-enoate (**26c**)

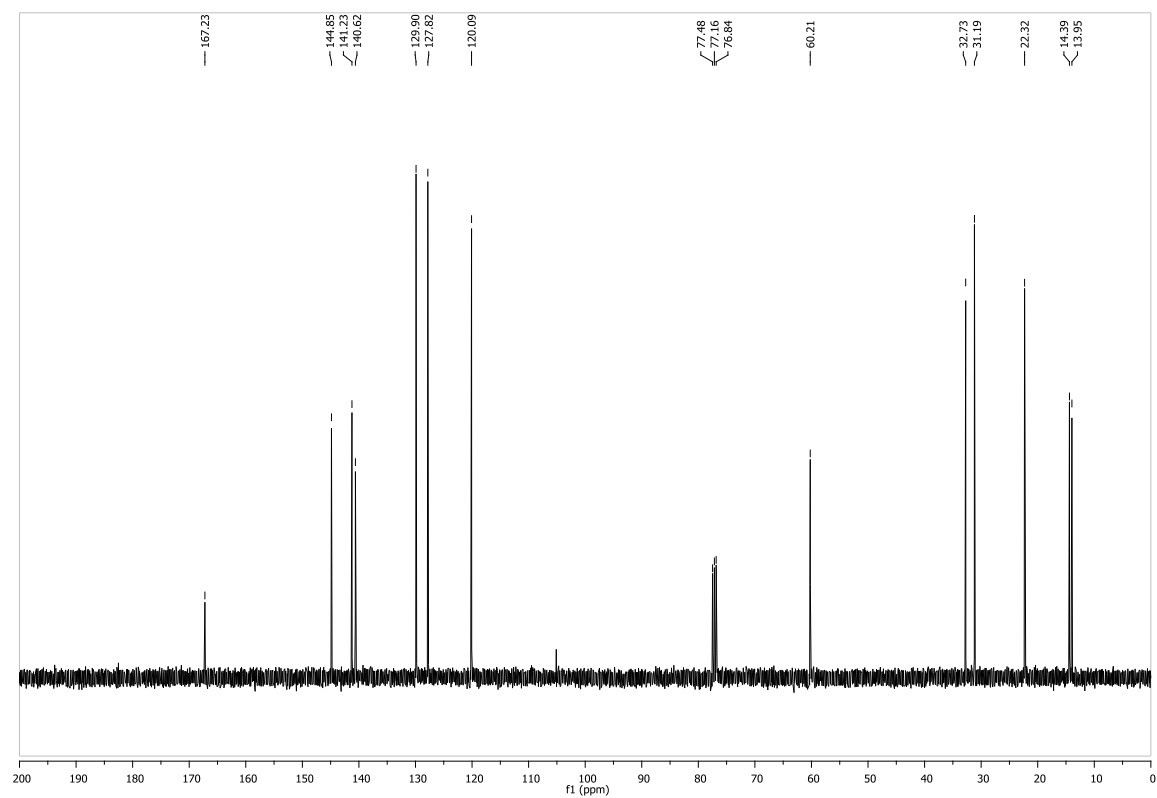
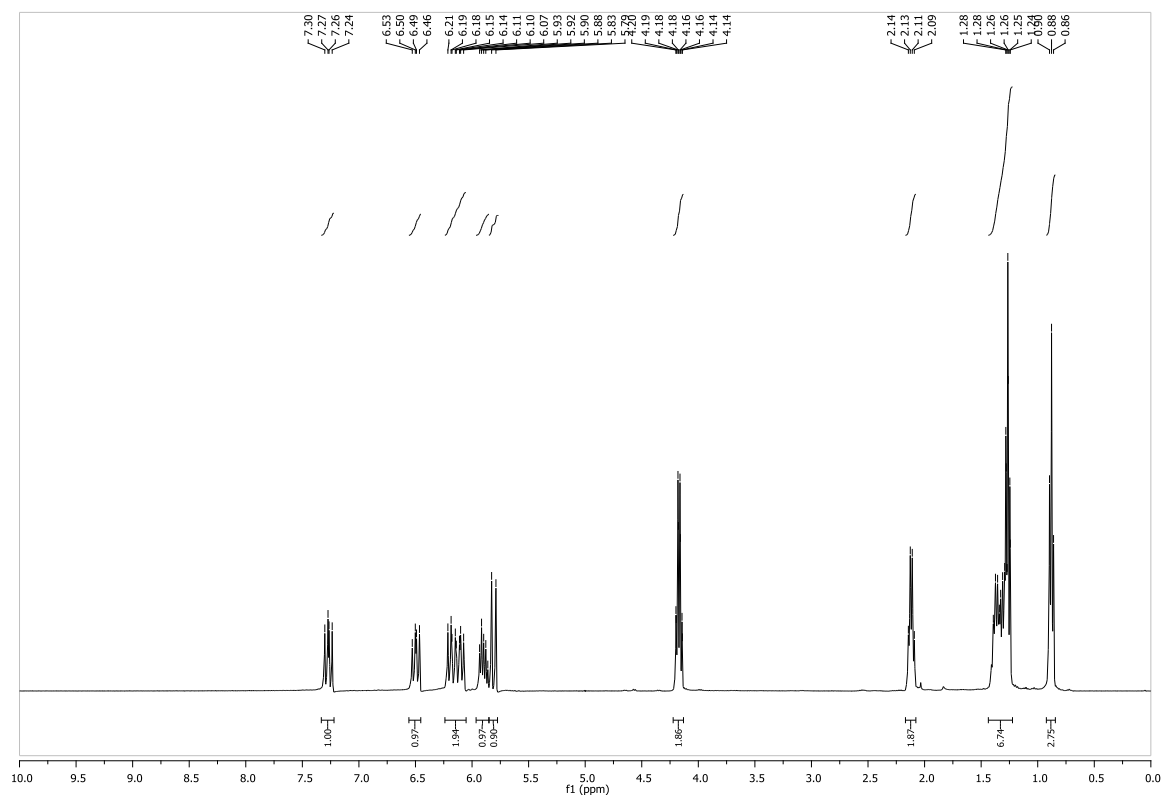
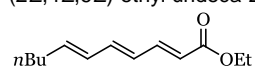


Coupling of the overlapping NMR signals for both the *E*- and *Z*-product at δ = 5.38-5.28 and 3.09-2.98 ppm indicate *Z*- and *E*-1,6-addition product

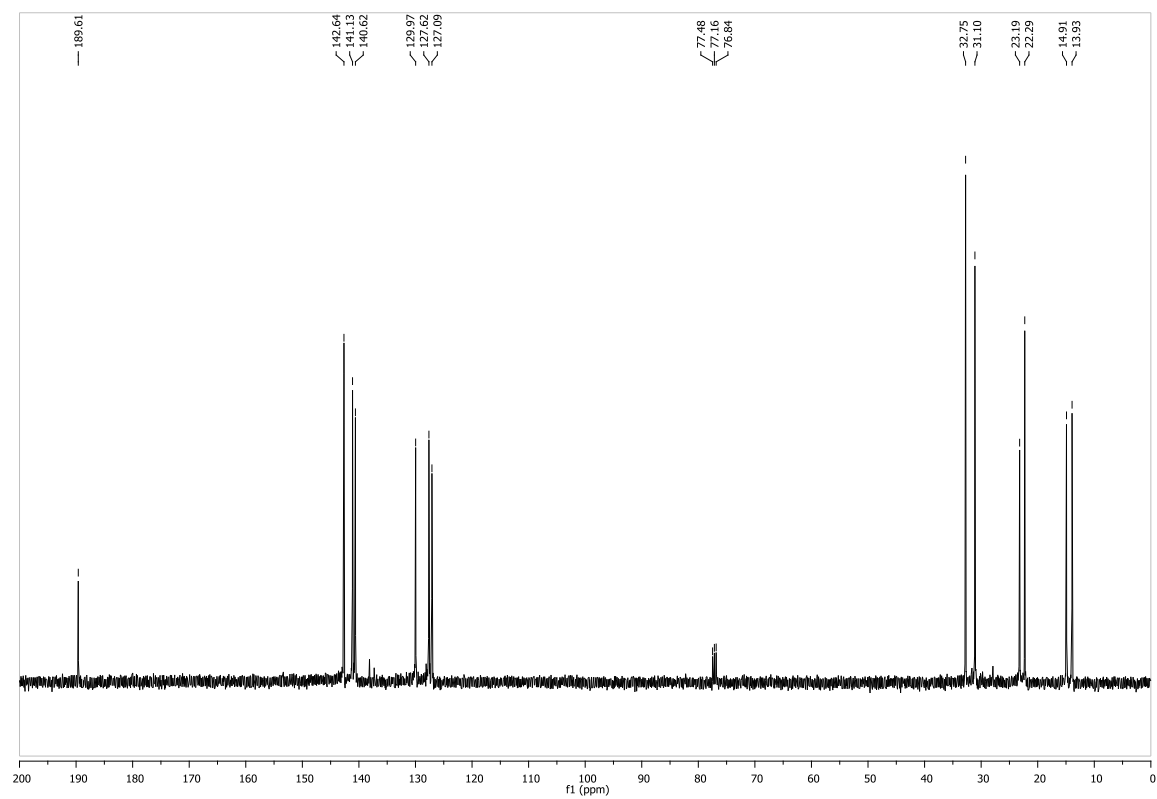
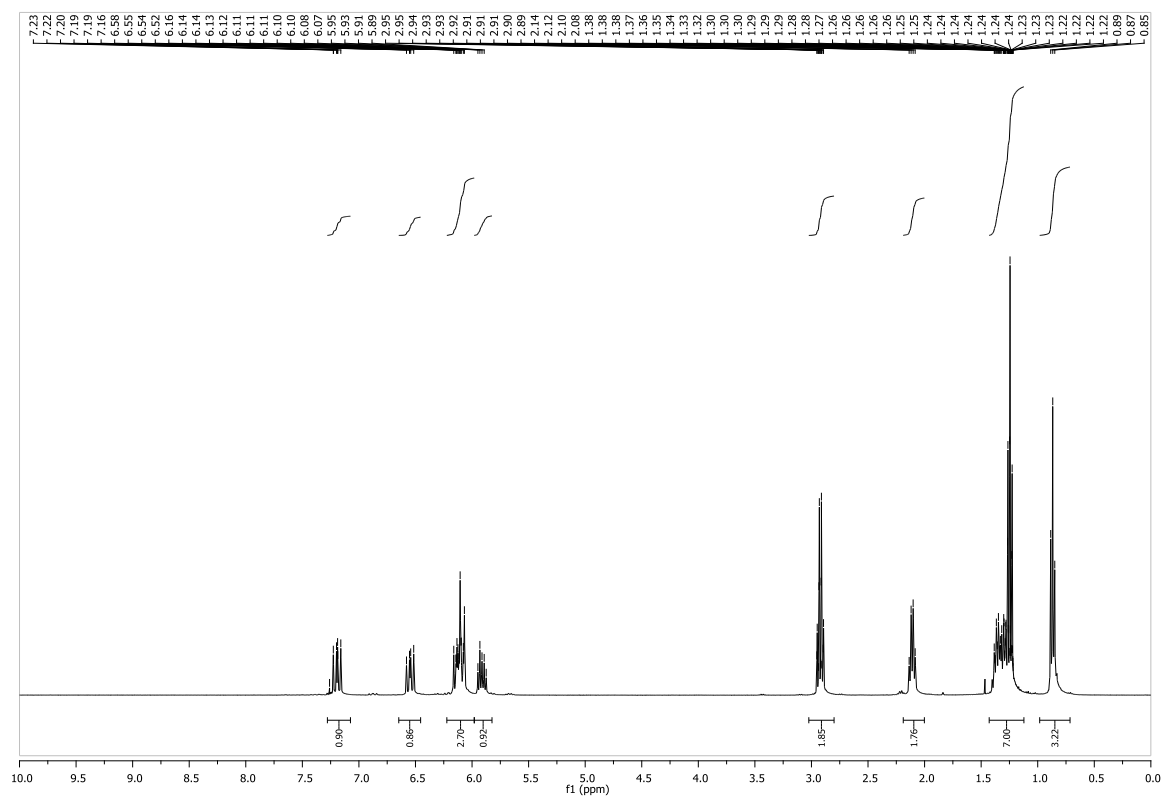
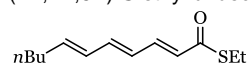




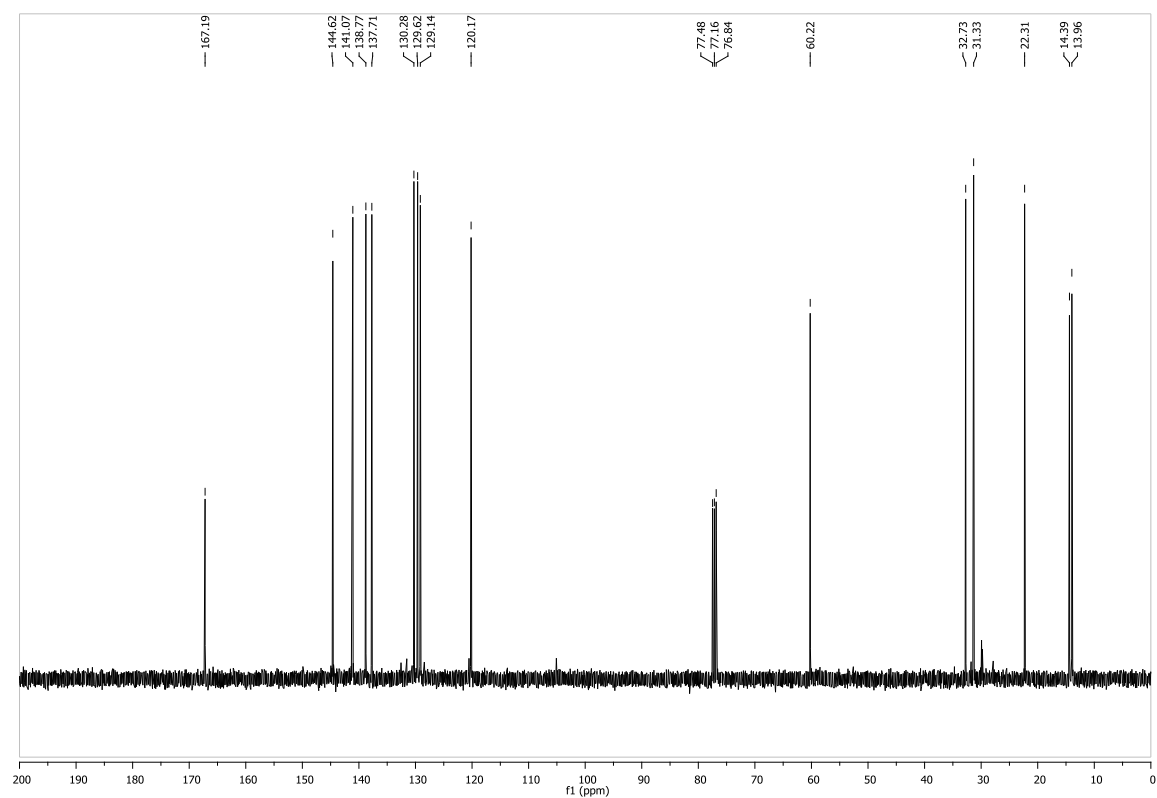
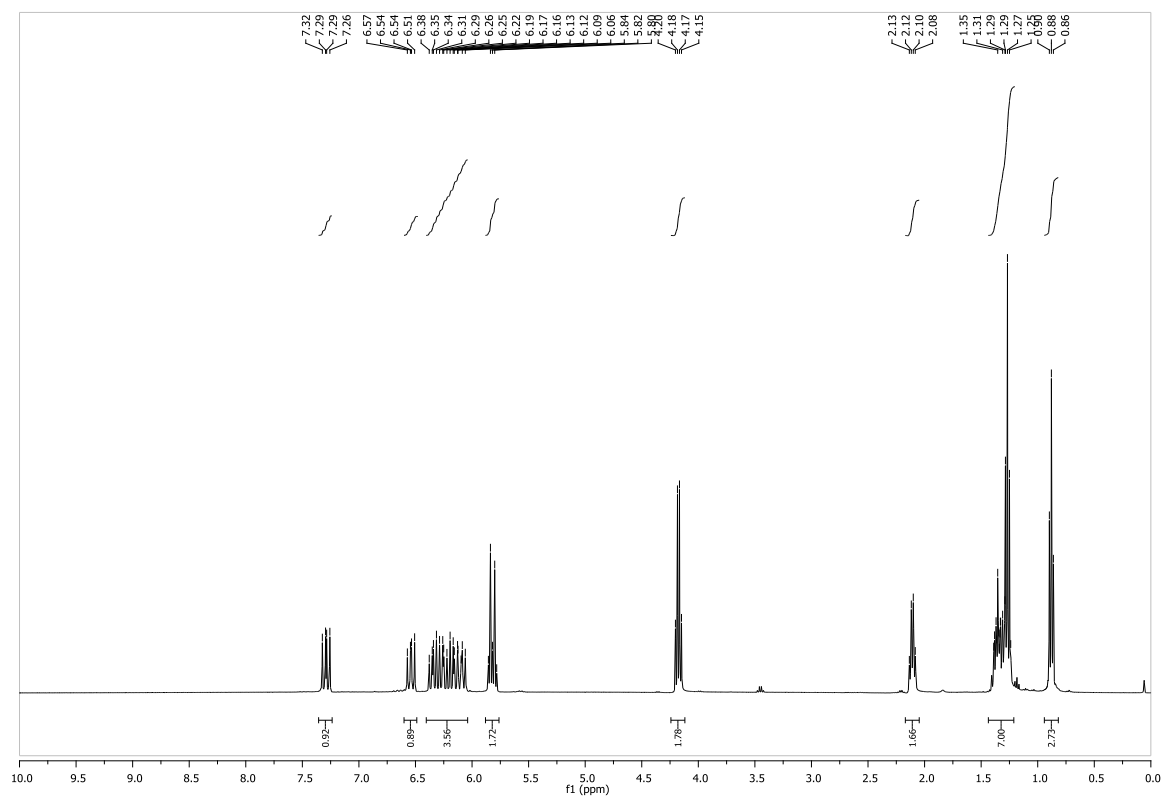
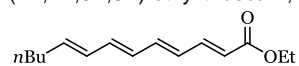
11. Enantioselective 1,8- and 1,10-addition: spectra (2*E*,4*E*,6*E*)-ethyl undeca-2,4,6-trienoate (**29a**)



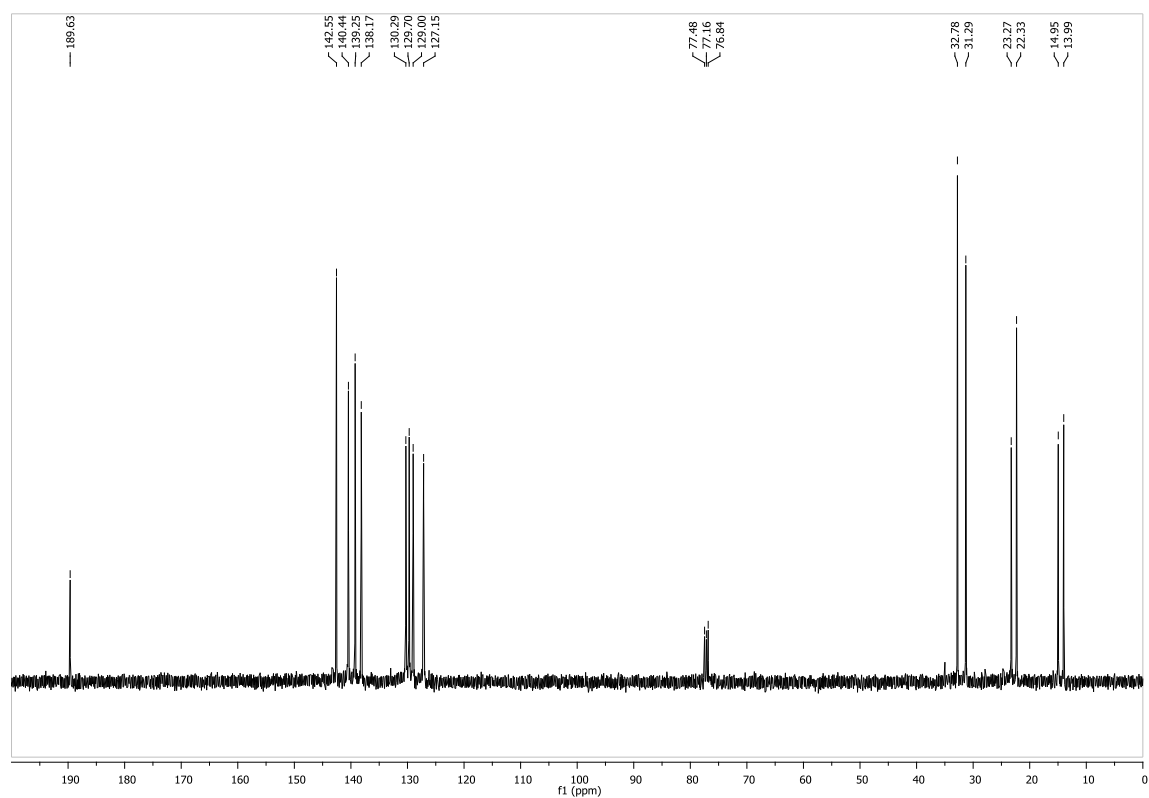
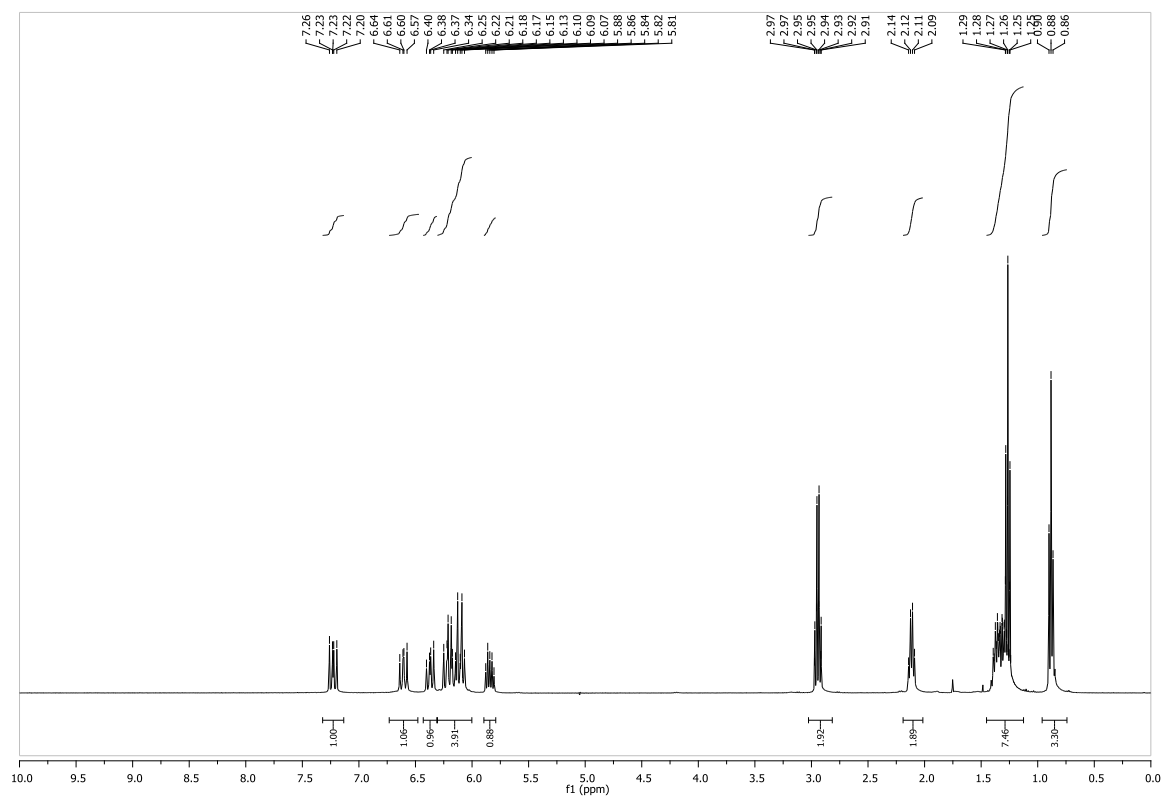
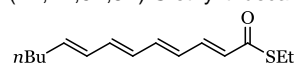
(2*E*,4*E*,6*E*)-*S*-ethyl undeca-2,4,6-trienethioate (**29b**): spectrum contains traces of (2*Z*,4*E*,4*E*)-product.



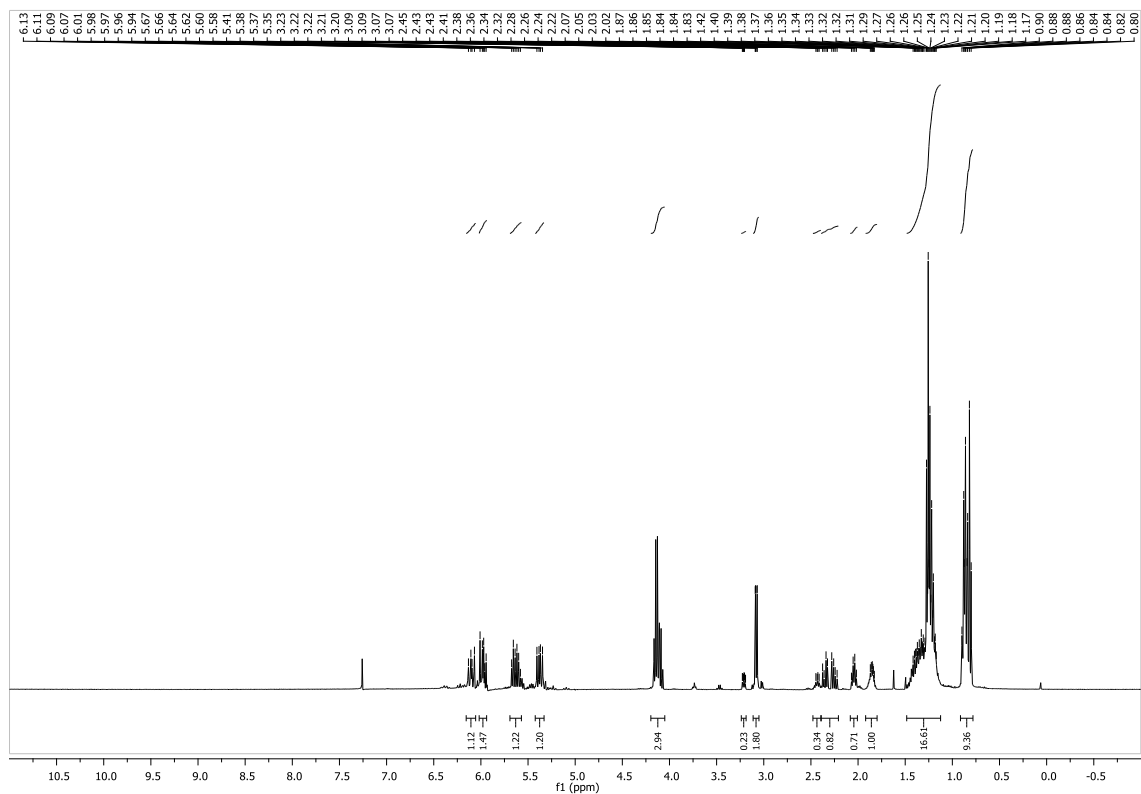
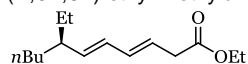
(2*E*,4*E*,6*E*,8*E*)-ethyl trideca-2,4,6,8-tetraenoate (**29c**)



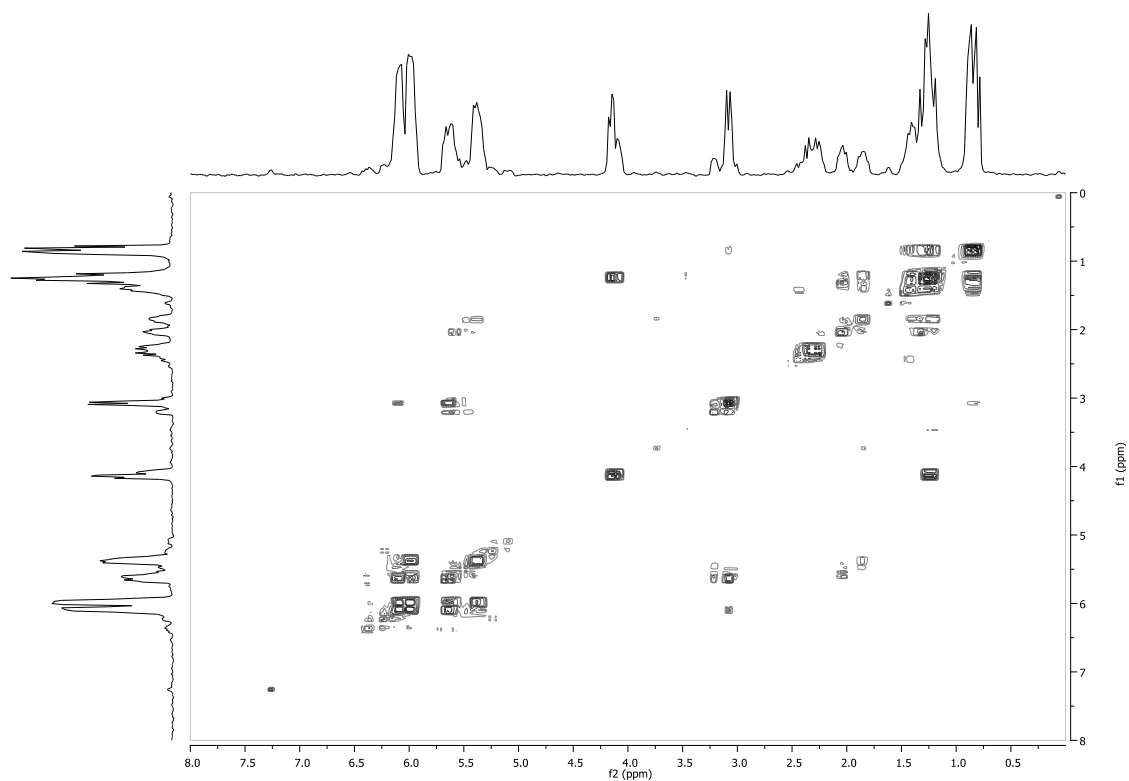
(2*E*,4*E*,6*E*,8*E*)-*S*-ethyl trideca-2,4,6,8-tetraenethioate (**29d**)

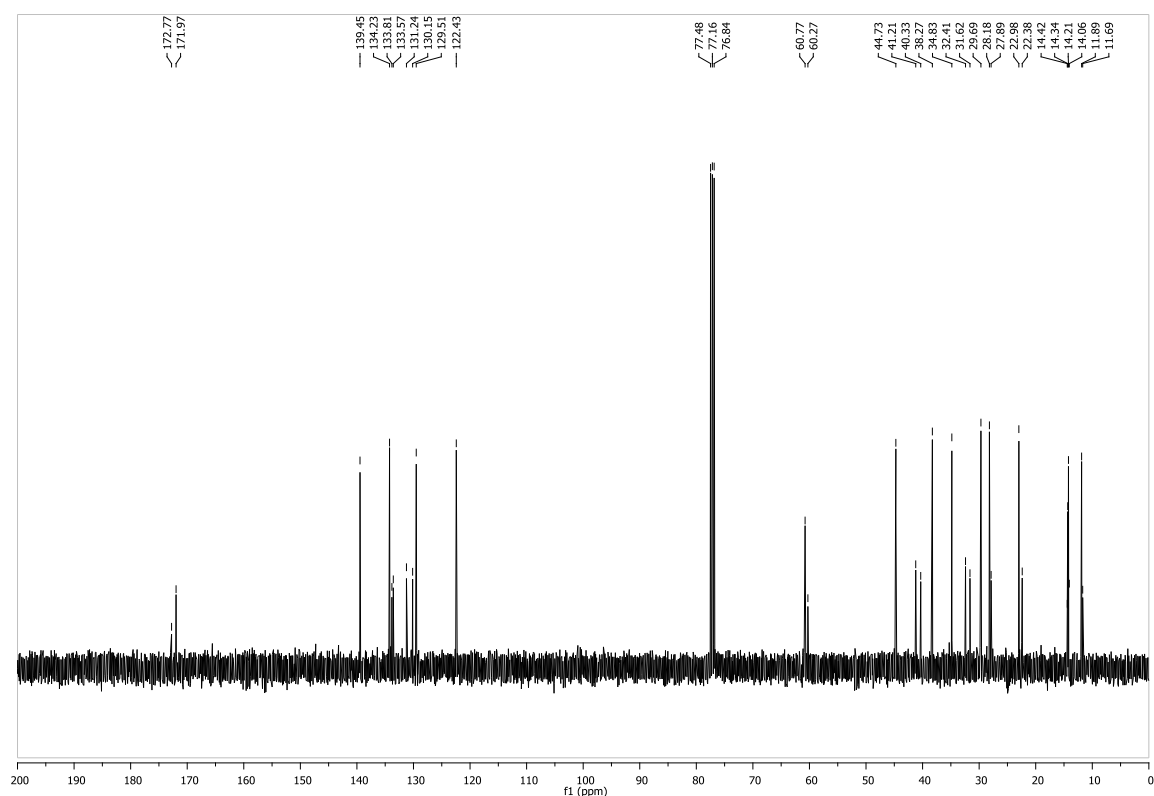


(*R*,3*E*,5*E*)-ethyl 7-ethylundeca-3,5-dienoate (**30a**): spectrum contains traces of Et₂O.

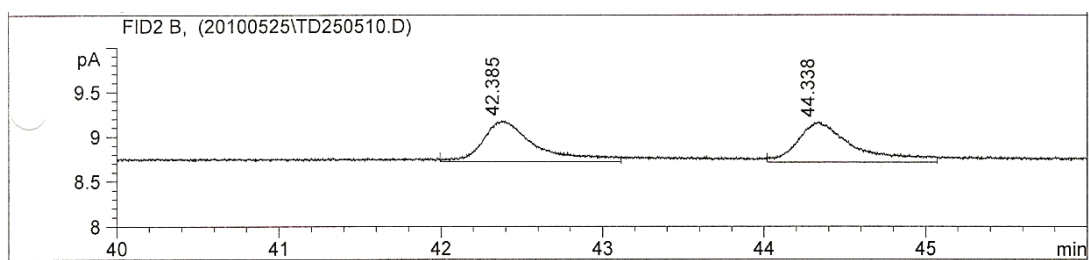


Coupling between the NMR signals at $\delta = 2.25$ and 2.05 ppm and the coupling between the NMR signals at $\delta = 5.58$ and 2.05 ppm indicate 1,4-addition product, Coupling between the NMR signals at $\delta = 5.63$ and 3.08 ppm and the coupling between the NMR signals at $\delta = 5.39$ and 1.85 ppm indicate 1,8-addition product



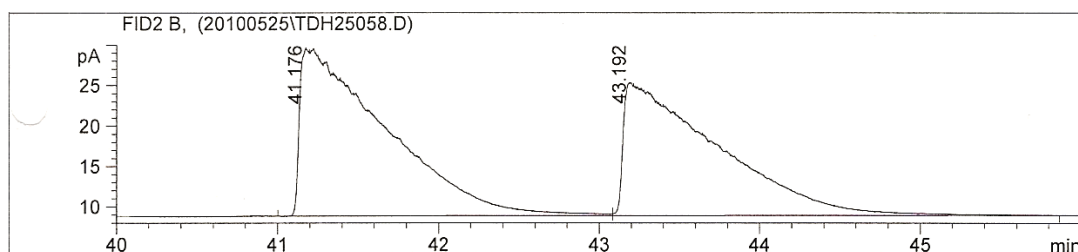


Enantioselectivity: *rac*-2-ethylhexanoic acid:



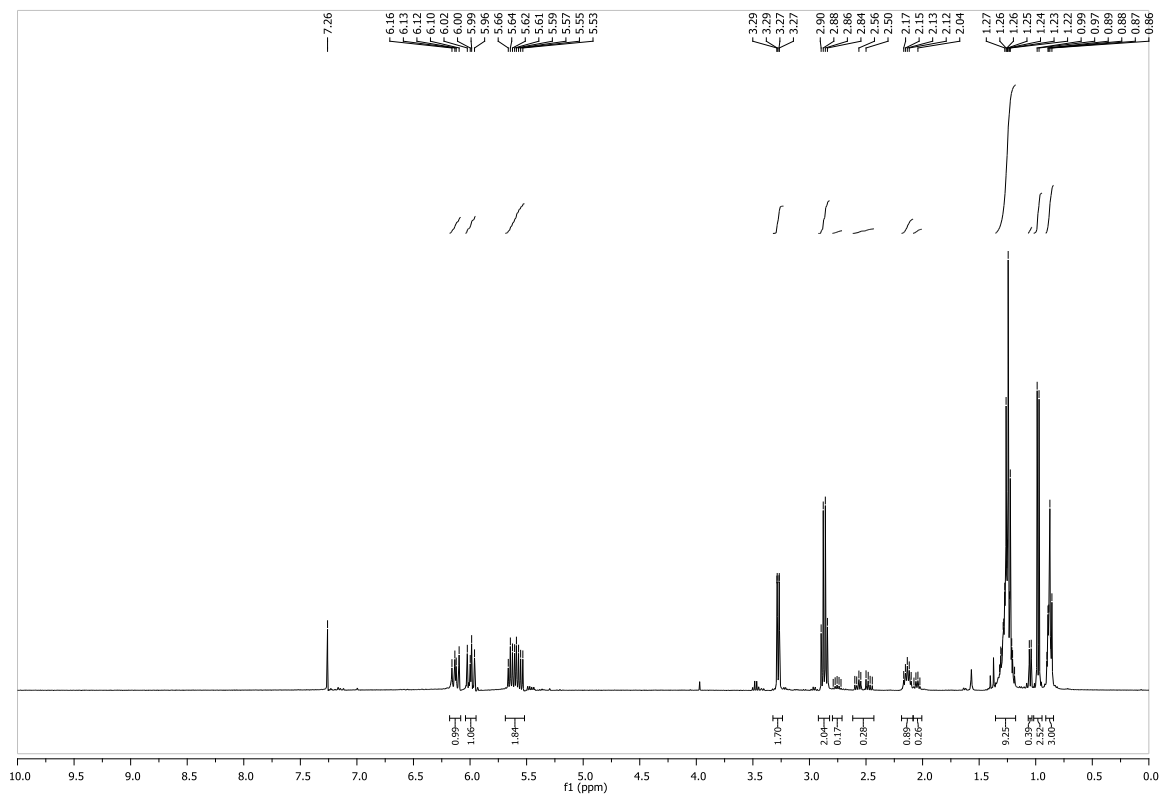
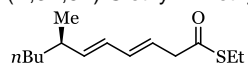
Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	42.385	MM		0.382	10.469	49.293	0.000	0.000
2	44.338	MM		0.404	10.769	50.707	0.000	0.000

Enantioselectivity: (*R*)-2-ethylhexanoic acid: {obtained after derivatisation}

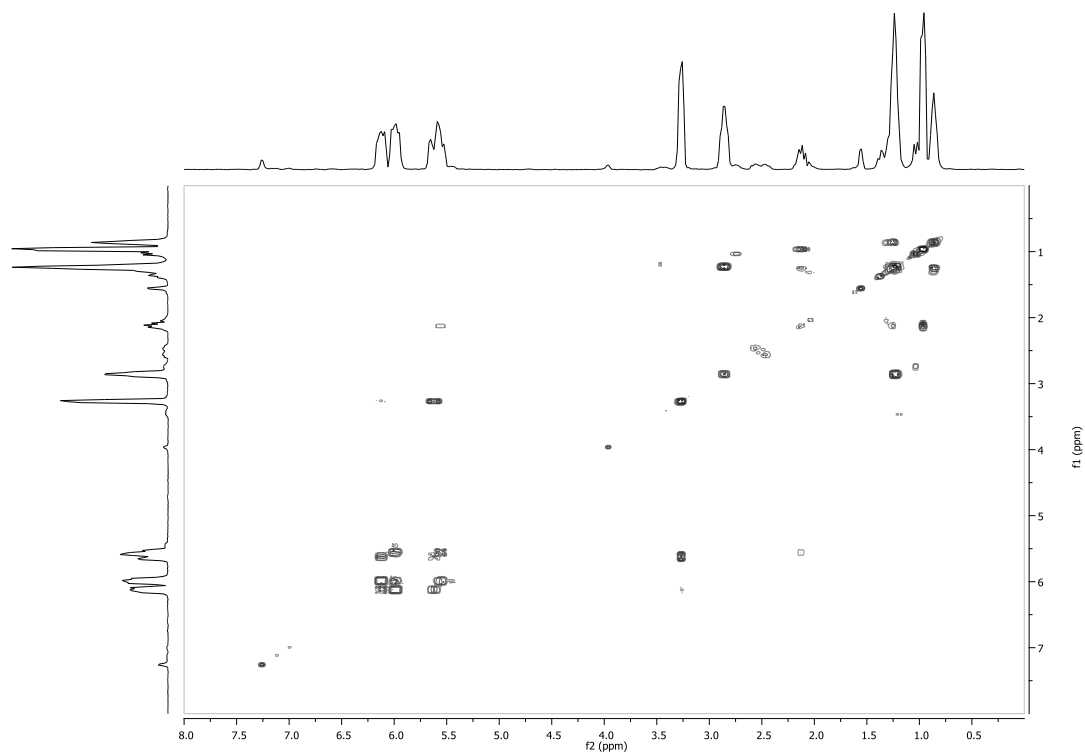


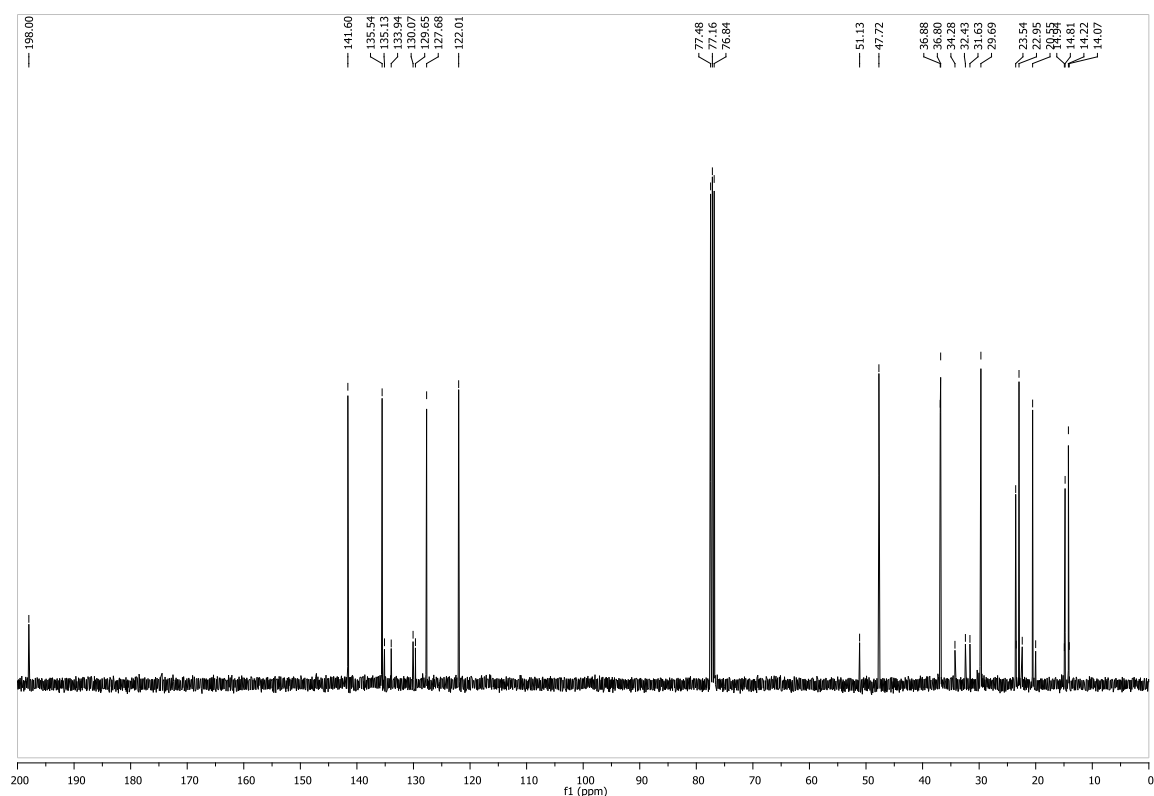
Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	41.176	MF		0.617	769.433	53.528	0.000	0.000
2	43.192	FM		0.681	668.012	46.472	0.000	0.000

(*R*,3*E*,5*E*)-*S*-ethyl 7-methylundeca-3,5-dienethioate (**30b**): spectrum contains traces of Et₂O.

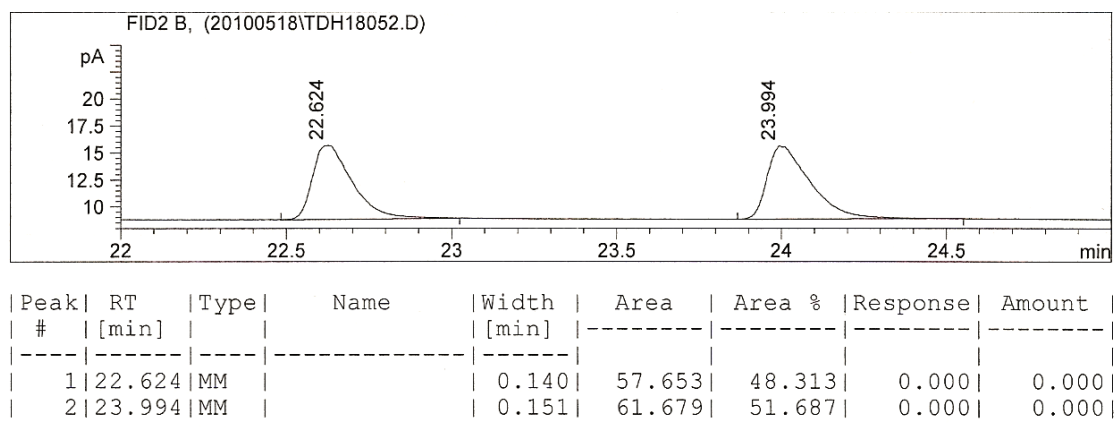


Coupling between the NMR signals at δ = 2.75 and 2.53 ppm and the coupling between the NMR signals at δ = 5.48 and 2.75 ppm indicate 1,4-addition product, coupling between the NMR signals at δ = 5.60 and 3.27 ppm and the coupling between the NMR signals at δ = 5.56 and 2.12 ppm indicate 1,8-addition product.

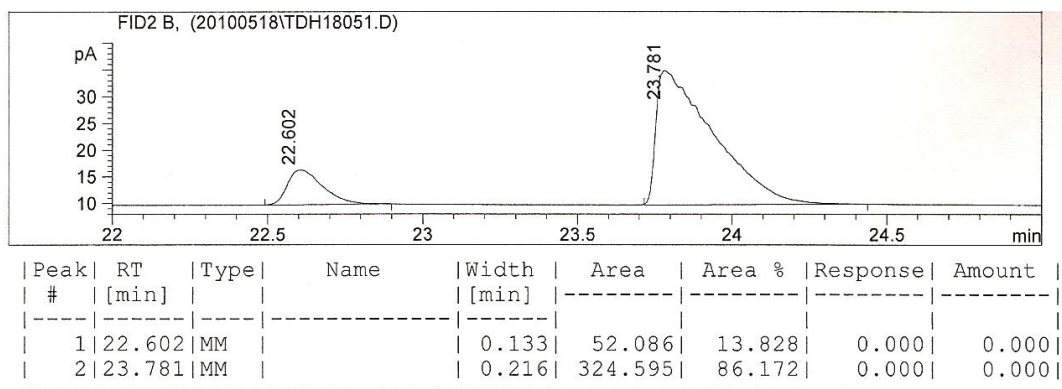




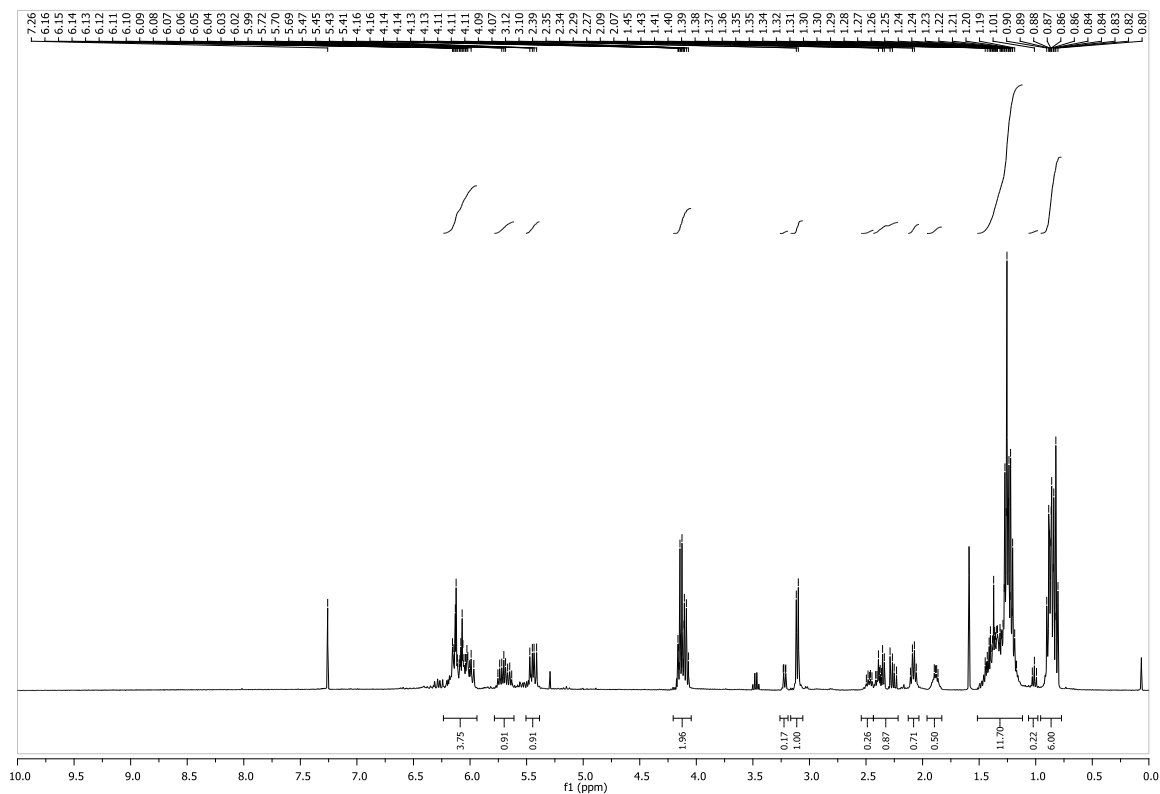
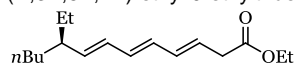
Enantioselectivity: *rac*-2-methylhexanoic acid:



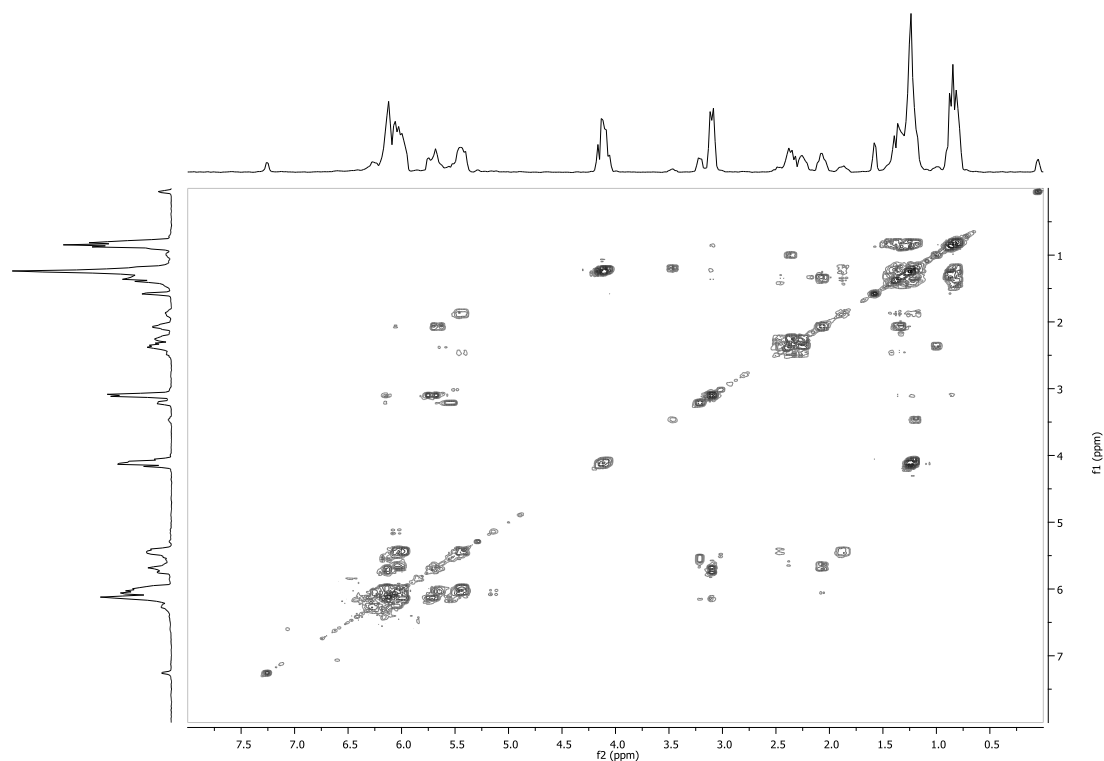
Enantioselectivity: (*R*)-2-methylhexanoic acid: {obtained after derivatisation}

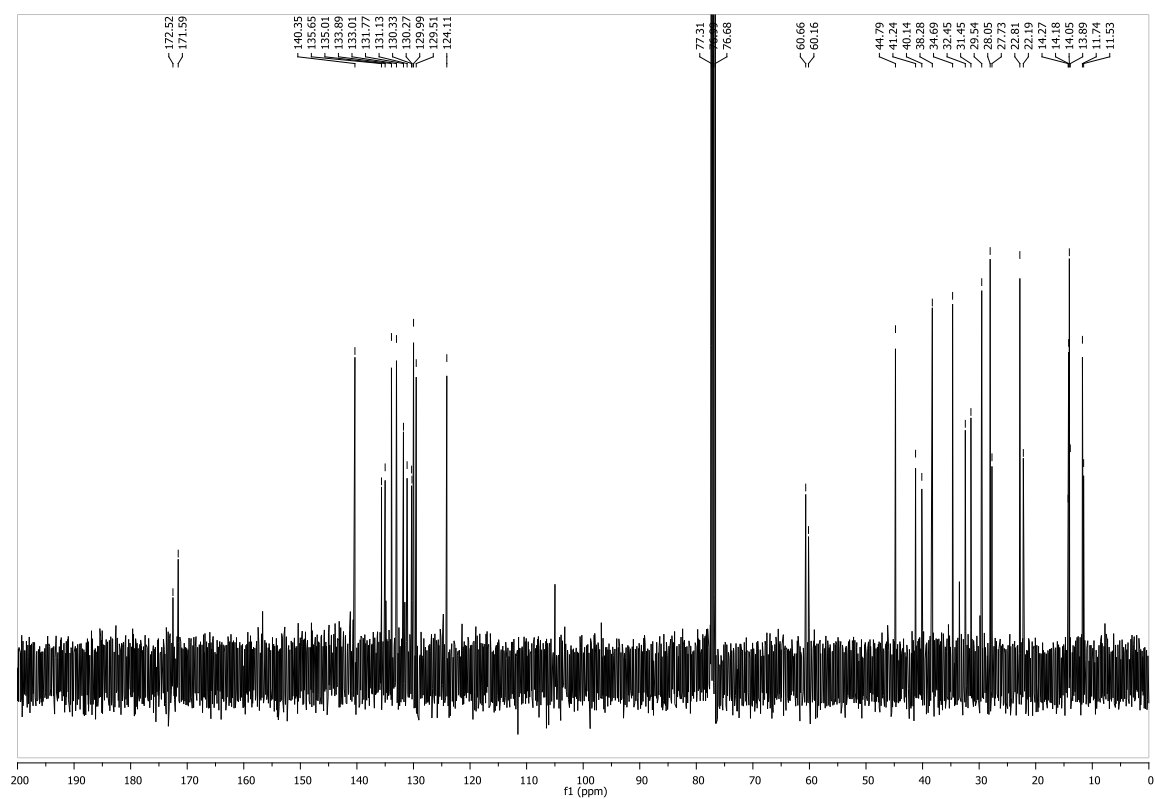


(*R*,3*E*,5*E*,7*E*)-ethyl 9-ethyltrideca-3,5,7-trienoate (**30c**): spectrum contains traces of Et₂O and CH₂Cl₂.

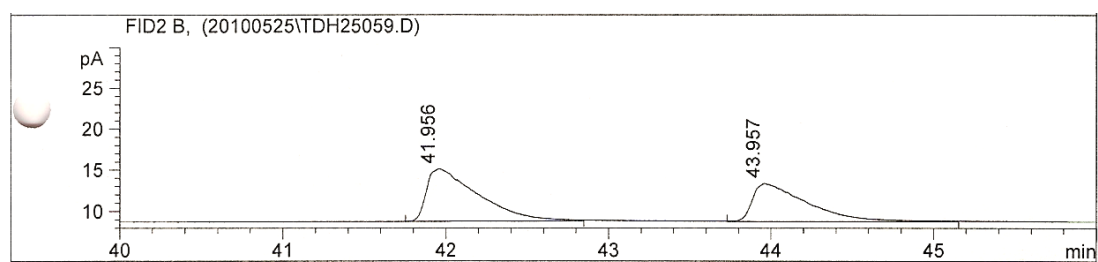


Coupling between the NMR signals at δ = 2.52 and 2.30 ppm and the coupling between the NMR signals at δ = 5.43 and 2.52 ppm indicate 1,4-addition product, Coupling between the NMR signals at δ = 5.55 and 3.21 ppm indicate either 1,6- or 1,8-addition product, Coupling between the NMR signals at δ = 5.44 and 1.80 ppm and the coupling between the NMR signals at δ = 5.77 and 3.10 ppm indicate 1,10-addition product.



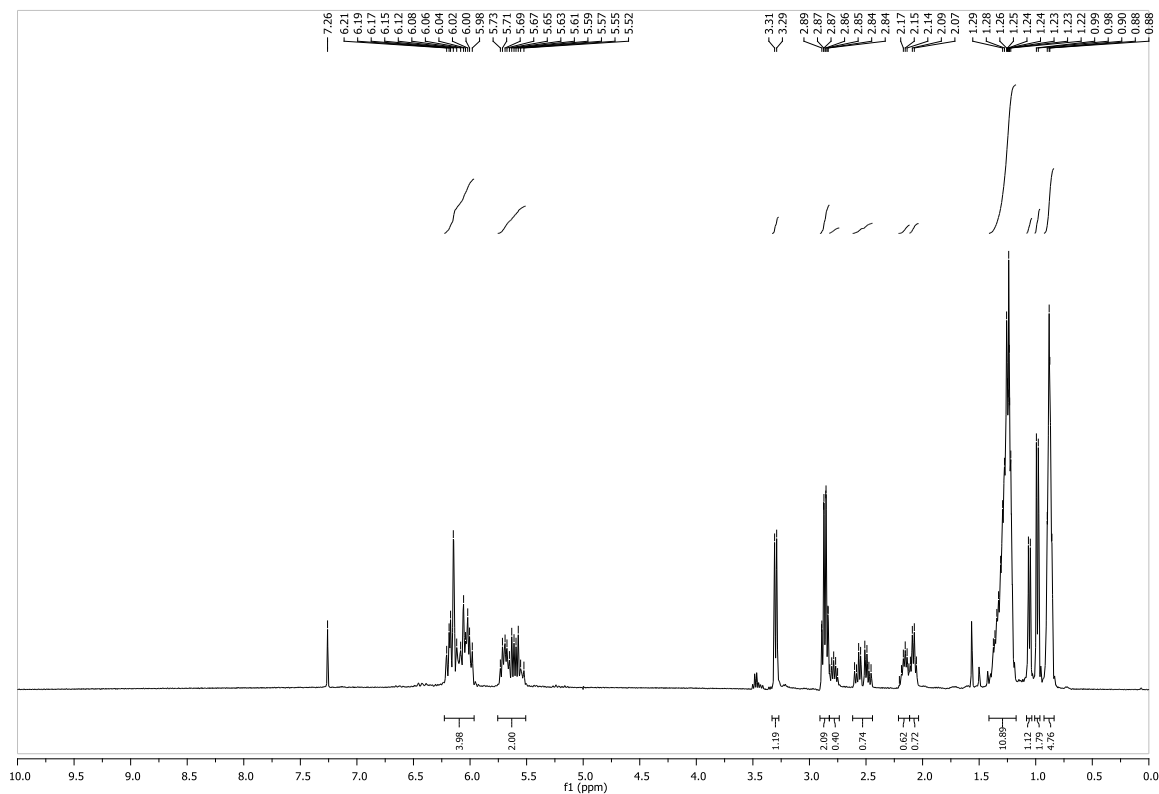
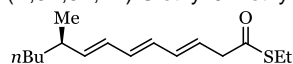


Enantioselectivity: (*R*)-2-ethylhexanoic acid: {obtained after derivatisation}

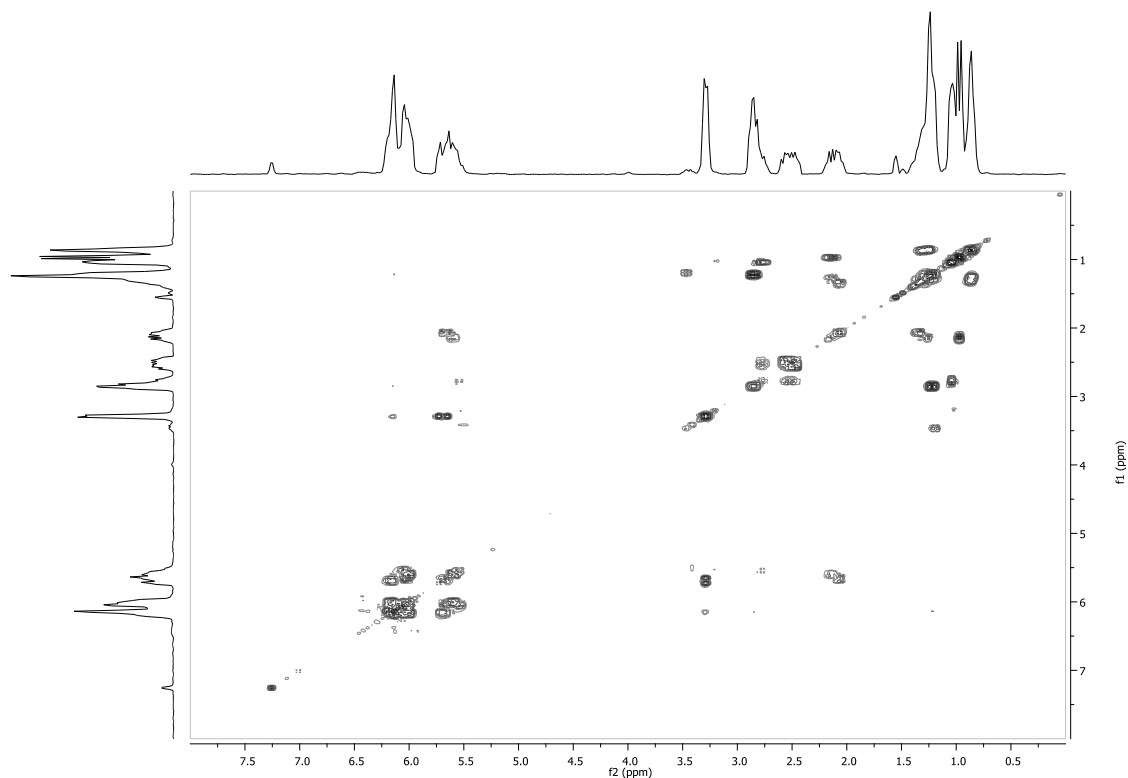


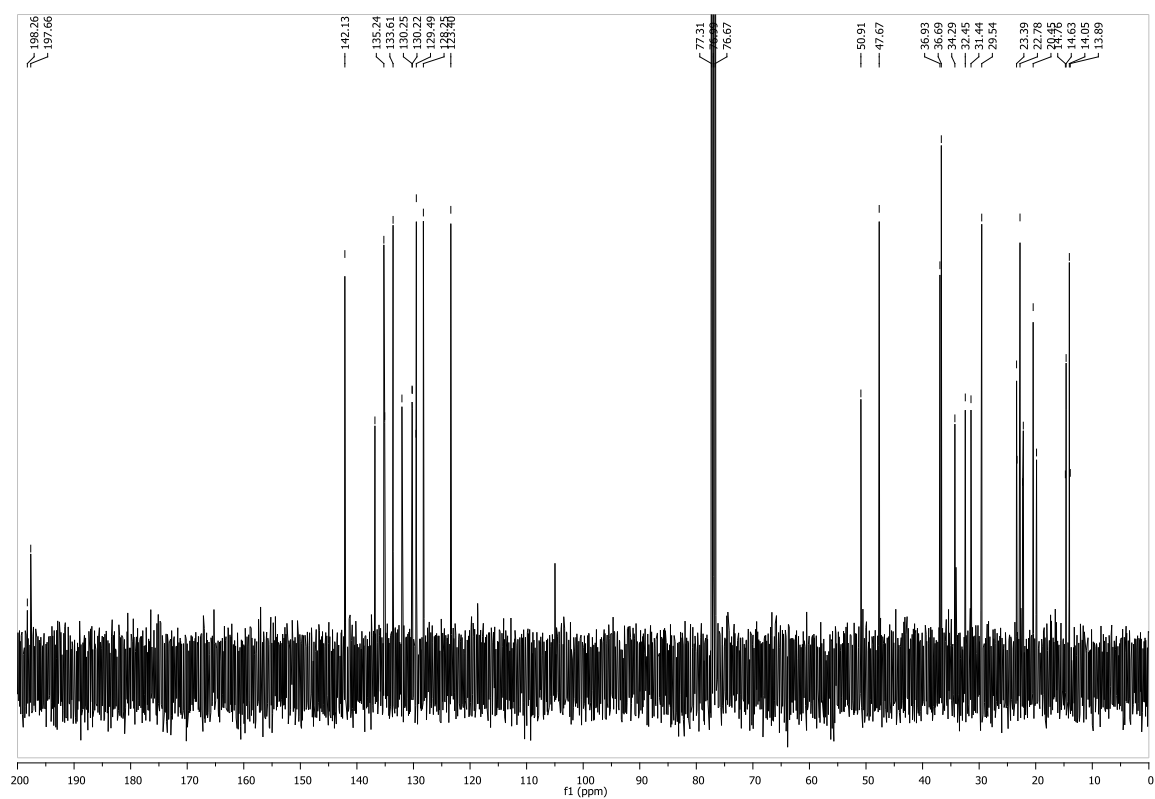
Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	41.956	MM		0.365	138.863	56.184	0.000	0.000
2	43.957	MM		0.389	108.296	43.816	0.000	0.000

(*R*,3*E*,5*E*,7*E*)-*S*-ethyl 9-methyltrideca-3,5,7-trienethioate (**30d**): spectrum contains traces of Et₂O and CH₂Cl₂

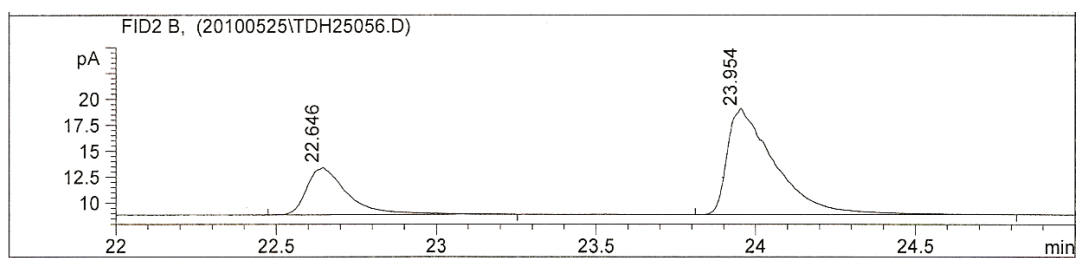


Coupling between the NMR signals at $\delta=2.78$ and 2.52 ppm and the coupling between the NMR signals at $\delta=5.54$ and 2.78 ppm indicate 1,4-addition product, coupling between the NMR signals at $\delta=5.61$ and 2.16 ppm and the coupling between the NMR signals at $\delta=5.65$ and 3.30 ppm indicate 1,10-addition product.





Enantioselectivity: (*R*)-2-methylhexanoic acid: {obtained after derivatisation}



Peak #	RT [min]	Type	Name	Width [min]	Area	Area %	Response	Amount
1	22.646	MM		0.149	40.325	27.442	0.000	0.000
2	23.954	MM		0.174	106.621	72.558	0.000	0.000

12. References

- ^{S1} a) Blake, M. P.; Kaltsoyannis, N.; Mountford, P. *Chem. Commun.* **2013**, 49, 3315-3317; b) Hicks, J.; Hoyer, C. E.; Moubarak, B.; Manni, G. L.; Carter, E.; Murphy, D. M.; Murray, K. S.; Gagliardi, L.; Jones, C. *J. Am. Chem. Soc.* **2014**, 136, 5283-5286.
- ^{S2} Keck, G. E.; Boden, E. P.; Mabury, S. A. *J. Org. Chem.* **1985**, 50, 709-710.
- ^{S3} Frigerio, M.; Santagostino, M.; Sputore, S. *J. Org. Chem.* **1999**, 64, 4537-4538.
- ^{S4} Wang, G.; Mohan, S.; Negishi, E.-i. *Proc. Natl. Acad. Sci. U.S.A.* **2011**, 108, 11344-11349.
- ^{S5} Inoue, M.; Yokota, W.; Muruges, M. G.; Izuhara, T.; Katoh, T. *Angew. Chem., Int. Ed.* **2004**, 43, 4207-4209.
- ^{S6} Bollans, L.; Bacsa, J.; Iggo, J. A.; Morris, G. A.; Stachulski, A. V. *Org. Biomol. Chem.* **2009**, 7, 4531-4538.
- ^{S7} Nishimura, T.; Yasuhara, Y.; Hayashi, T. *Angew. Chem., Int. Ed.* **2006**, 45, 5164-5166.
- ^{S8} Des Mazery, R.; Pullez, M.; López, F.; Harutyunyan, S. R.; Minnaard, A. J.; Feringa, B. L. *J. Am. Chem. Soc.* **2005**, 127, 9966-9967.
- ^{S9} Mann, S.; Carillon, S.; Breyne, O.; Duhayon, C.; Hamon, L.; Marquet, A. *Eur. J. Org. Chem.* **2002**, 736-744.
- ^{S10} Yoo, K. S.; Yoon, C. H.; Jung, K. W. *J. Am. Chem. Soc.* **2006**, 128, 16384-16393.
- ^{S11} Bos, P. H.; Minnaard, A. J.; Feringa, B. L. *Org. Lett.* **2008**, 10, 4219-4222.
- ^{S12} Knol, J.; Feringa, B. L. *Synth. Commun.* **1996**, 26, 261-268.
- ^{S13} Evans, D. A.; Gage, J. R.; Leighton, J. L. *J. Am. Chem. Soc.* **1992**, 114, 9434-9453.
- ^{S14} Yoon, C. H.; Yoo, K. S.; Yi, S. W.; Mishra, R. K.; Jung, K. W. *Org. Lett.* **2004**, 6, 4037-4039.
- ^{S15} Mann, S.; Carillon, S.; Breyne, O.; Duhayon, C.; Hamon, L.; Marquet, A. *Eur. J. Org. Chem.* **2002**, 736-744.
- ^{S16} Shing, T. K. M.; Tang, Y. *Tetrahedron* **1990**, 46, 2187-2194.
- ^{S17} Huang, Y.; Shen, Y.; Zheng, J.; Zhang, S. *Synthesis* **1985**, 57-58.
- ^{S18} Harutyunyan, S. R.; Zhao, Z.; den Hartog, T.; Bouwmeester, K.; Minnaard, A. J.; Feringa, B. L.; Govers, F. *Proc. Natl. Acad. Sci. U.S.A.* **2008**, 105, 8507-8512 (4-(*tert*-butyldimethylsilyloxy)but-2-enethioic acid S-ethyl ester).