Experimental section

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Experimental Procedures

General Remarks

NMR spectra were recorded on Bruker AV400 and AVII500 spectrometers. Proton and carbon chemical shifts (δ_H, δ_C) are quoted in ppm and referenced to tetramethylsilane with residual protonated solvent as internal standard. For chloroform-*d*, solvent residuals are 7.26 ppm and 77.16 ppm for proton and carbon respectively. Resonances are described as s (singlet), d (doublet), t (triplet), q (quartet) and combinations thereof. Coupling constants (*J*) are given in Hz and rounded to nearest 0.1 Hz. For diastereotopic protons, no particular stereochemistry is implied.

Mass spectra (low resolution) were recorded on a Micromass ZMD (ES). High resolution spectra were recorded by the Mass Spectrometry service at the Chemical Research Laboratory, University of Oxford using a Bruker Daltronics microTOF (ES) or a Micromass GCT (FI). *m/z* values are reported in Daltons with their percentage abundance and, where known, the relevant fragment ions in parentheses. High resolution values are calculated to 4 d.p. from the molecular formula, all found values being within 5 ppm tolerance.

TLC was performed on Merck DC-Alufolien 60 F_{254} 0.2 mm precoated plates and visualised using an acidic vanillin or basic potassium permanganate dip. Retention factors (R_f) are reported with the solvent system used in parentheses. Flash column chromatography was performed on Merck 60 silica (particle size 40–63 μm, pore diameter 60 Å) and the solvent system used is recorded in parentheses.

Infrared spectra were recorded using a Bruker Tensor 27 Fourier Transform spectrophotometer using thin films on a diamond ATR.

Melting points were determined using a Leica Galen III Compound Microscope and are uncorrected.

All non-aqueous reactions were carried out in oven-dried glassware under an inert atmosphere of nitrogen and employing standard techniques for handling air-sensitive materials. Solvents and commercially available reagents were dried and purified before use, as appropriate. In particular DCM and THF were distilled from CaH_2 and stored over 3 Å molecular sieves. 'PE' refers to the fraction of light petroleum ether boiling in the range 40–60 °C unless otherwise stated. All water used experimentally was distilled.

pH 2 sulfate buffer was prepared by dissolving $NaHSO_4$ (213 g, 1.50 mol) and H_2SO_4 (28.0 mL, 0.500 mol) in water (2.00 L).

Assignment of relative configuration The relative configuration of the product [3.3.0]-bicyclic γ-lactones was assigned on the basis of ^{1}H NMR nOe experiments or by analogy. In only a few cases was the relative configuration of the minor diastereomer(s) assigned. Where nOe data were not obtained, it was assumed that the [3.3.0]-bicyclic γ-lactones were *cis*-configured in keeping with those [3.3.0]-bicyclic γ-lactones for which nOe data was readily obtained and from previous precedent.[1, 2]

Synthesis and Compounds Characterisation

General procedure

General procedure 1 : Rh(II)-catalysed OH-insertion on diazomalonate[3]

To a solution of alcohol (1 eq.) in benzene (0.3 M) were added diazomalonate (1.05 eq.) and $Rh_2(OAc)_4$ (0.5 mol%). The reaction mixture was heated at 60 °C for 2 h. After cooling down at room temperature, the solvent was evaporated to give the crude product. The residue was purified by Flash Chromatography using the indicated solvent system.

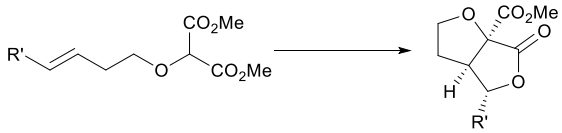
General procedure 2: one pot alkylation/reduction of 3-enoic acids

To a solution of 3-enoic acid derivative (1.0 eq.) in THF (0.4 M) at -78 °C was added (30 sec/mmol) a solution of *n*-BuLi in hexanes (2.5 M, 2.20 eq.). The mixture was stirred at -78 °C and the corresponding alkyl halide (3.0 eq.) was added (20 sec/mmol). After 5 min stirring the reaction was warmed to room temperature outside the cooling bath and stirred at this temperature for the indicated period. The reaction mixture was then cooled to 0 °C and $LiAlH_4$ (1.25 eq.) was added portionwise (about 1 mmol every 20 seconds). The reaction mixture was stirred at this temperature for 30 min before careful addition of aqueous HCl (2.0 M, 175 eq.). During the addition, Et_2O (2 × initial volume of THF) was also progressively added to maintain good stirring. At the end of the addition, the mixture was vigorously stirred for 30 min and layers were separated. The aqueous layer was extracted with more Et_2O (1 × initial volume of THF). The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered and carefully evaporated (mind the volatility of some alcohols). The residue was purified by Flash Chromatography using the indicated solvent system.

General procedure 3: oxidative radical cyclisation of the alkoxymalonates

Copper(II) triflate (1.0 eq.) and manganese(III) acetate dihydrate (2.0 eq.) were placed under vacuum and heated to 40 °C for 10 minutes and then quenched to N_2. A solution of alkoxymalonate (1.0 eq.) in MeCN (0.15 M) was then added rapidly and the solution stirred for 6h (unless otherwise stated). After cooling down to room temperature, the reaction mixture was diluted with a saturated aqueous solution of NH_4Cl and the aqueous phase was extracted with ethyl acetate three times. The combined extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum to give the crude product. The residue was purified by Flash Chromatography using the indicated solvent system.

Control experiments

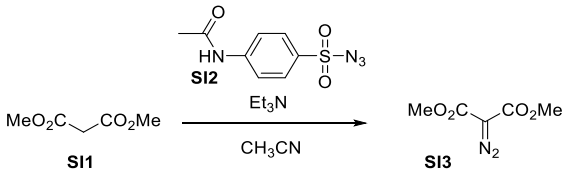


Entry	T(°C)	Substrate	R'	$Mn(OAc)_3$ (eq.)	$Cu(OTf)_2$ (eq.)	Yield lactone (%)	% SM recovered
1	40 °C	**7a**	H	3	0	0	100[a]
2	40 °C	**7a**	H	2	0	0	100[a]
3	40 °C	**7a**	H	0	1	0	100[a]
4	40 °C	**7a**	H	0	2	0	100[a]
5	40 °C	**7a**	H	0	3	0	100[a]
6	40 °C	**7c**	Ph	3	0	0	100[a]
7	40 °C	**7c**	Ph	2	0	0	100[a]
8	40 °C	**7c**	Ph	0	1	0	100[a]
9	40 °C	**7c**	Ph	0	2	0	100[a]
10	40 °C	**7c**	Ph	0	3	0	100[a]
11	80 °C	**7a**	H	3	0	63	36
12	80 °C	**7a**	H	2	0	41	28
13	80 °C	**7a**	H	0	1	34	45
14	80 °C	**7a**	H	0	2	31	6
15	80 °C	**7a**	H	0	3	26	24
16	80 °C	**7c**	Ph	3	0	66	17
17	80 °C	**7c**	Ph	2	0	54	26
18	80 °C	**7c**	Ph	0	1	54	29
20	80 °C	**7c**	Ph	0	3	23	19

[a] Only starting material, based on crude ^{1}H NMR.

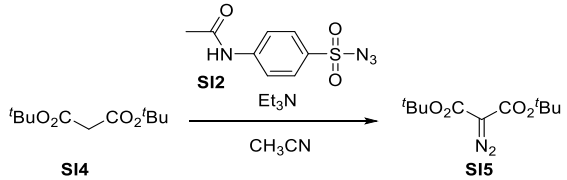
Synthetic Procedures

Dimethyl 2-diazomalonate (SI3)[4]



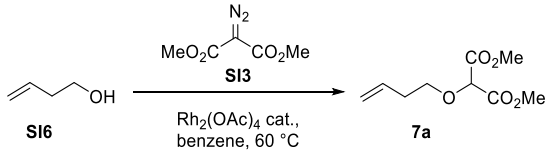
To a solution of dimethylmalonate (6.0 mL, 52.5 mmol) and *p*-acetamidobenzensulfonyl azide (12.9 g, 53.8 mmol, 1.02 eq.) in acetonitrile (130 mL) at 0 °C was added triethylamine (22 mL). The solution was allowed to warm to room temperature and sirred for 12 h. The solvent was then evaporated under reduced pressured and the residue was triturated with ether/petroleum ether (1:1) and filtered. The solvent was evaporated under reduced pressured. The crude product was then purified by flash chromatography ($PE_{40\text{-}60}/Et_2O$ 4:1 to 2:1) to give **SI3** as a yellow oil (6.3 g, 40 mmol, 76 %). $\mathbf{R_f}$ 0.49 ($PE_{40\text{-}60}$/EtOAc 5:5); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 3.83 (6H, s, CO_2Me), **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 161.4 (2×*C*=O), 52.5 (2×CO_2Me) *Note: the diazo carbon was not detected*; $\mathbf{\nu_{max}}$ 2133 (s,C=N_2), 1735 (s, C=O); **m/z** (ESI$^+$) 159.0 ([M+H]$^+$, 9%), 339.0 ([2M+Na]$^+$, 100 %). NMR data are in accordance with literature.[5]

Di-*tert*-butyl 2-diazomalonate (SI5)



To a solution of di-*tert*-butylmalonate (5.38 mL, 24 mmol) and *p*-acetamidobenzensulfonyl azide (6.34 g, 26.4 mmol, 1.02 eq.) in acetonitrile (55 mL) at 0 °C was added triethylamine (10 mL). The solution was allowed to warm to room temperature and sirred for 12 h. The solvent was then evaporated under reduced pressured and the residue was triturated with ether/petroleum ether (1:1) and filtered. The solvent was evaporated under reduced pressured. The crude product was then purified by flash chromatography ($PE_{40\text{-}60}$/Diethyl ether 4:1 to 2:1) to give **SI5** as a yellow oil (5.4 g, 22.3 mmol, 93 %). $\mathbf{R_f}$ 0.73 ($PE_{40\text{-}60}$/EtOAc 6:4); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 1.47 (18H, s, ^{t}Bu); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 160.4 (2×*C*=O), 82.8 (O*C*^{t}Bu), 28.3 (^{t}Bu) *Note: the diazo carbon was not detected*; **m/z** (ESI$^+$) 507.3 ([2M+Na]$^+$, 100 %). NMR data are in agreement with literature.[6]

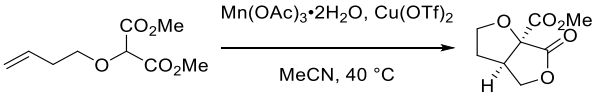
Dimethyl 2-(but-3-en-1-yloxy)malonate (7a)



The title compound was prepared according to the general procedure 1 using buten-3-ol (0.3 mL, 3.5 mmol) and dimethyl 2-diazomalonate (550 mg, 3.48 mmol, 1.05 eq.). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 9:1) gave the title compound **7a** as a colourless oil (590 mg, 2.92 mmol, 84%). $\mathbf{R_f}$ 0.40 ($PE_{40\text{-}60}$/EtOAc 8:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.82 (1H, tdd, *J* = 6.7, 10.1, 17.1 Hz, CH=CH_2), 5.12 (1H, dd, *J* = 17.1, 1.2 Hz, C*H*H'=CH), 5.06 (1H, dd, *J* = 10.1, 1.2 Hz, CH*H'*=CH), 4.53 (1H,

s, C*H*($CO_2Me)_2$), 3.81 (6H, s, CO_2*Me*), 3.64 (2H, t, *J* = 6.9 Hz, OCH_2CH_2), 2.43 (2H, q, *J* = 6,9 Hz, OCH_2CH_2); **^{13}C NMR ($CDCl_3$, 100 MHz)** *δ* 166.9 (2×*C*=O), 134.1 (CH_2=*C*H), 117.0 (*C*H_2=CH), 79.0 (*C*H($CO_2Me)_2$), 70.8 (*C*H_2O), 52.9 (2×CO_2*Me*), 33.8 (OCH_2CH_2); **ν_{max}** 2957 (w, C-H), 1744 (s, C=O), 1201 (m), 1131 (s), 1019 (m), 919 (w); **m/z** (ESI$^+$) 225.1 ([M+Na]$^+$, 100%), 427.2 ([2M+Na]$^+$, 17%); **HRMS-ESI** calculated for $C_9H_{14}NaO_5$: *m/z* 225.0733 ([M+Na]$^+$), found: *m/z* 225.0742 ([M+Na]$^+$).

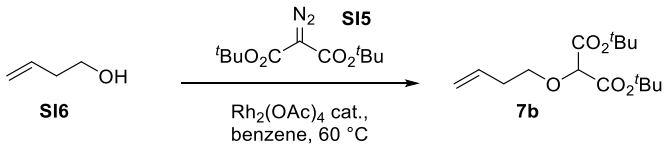
(3a*R**,6a*S**)-Methyl 6-oxohexahydrofuro[3,4-*b*]furan-6a-carboxylate (8a)



7a **8a**

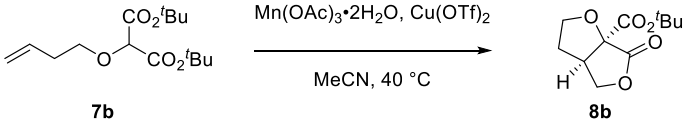
The title compound was prepared according to the general procedure 3 using **7a** (55 mg, 0.27 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 8:2 to 6:4) gave the title compound **8a** as a colourless oil (41 mg, 0.22 mmol, 81%). **R_f** 0.10 ($PE_{40\text{-}60}$/EtOAc 6:4); **^{1}H NMR ($CDCl_3$, 400 MHz)** *δ* 4.58 (1H, dd, *J* = 9.6, 7.2 Hz, OC*H*H'CH), 4.21 (1H, dd, *J* = 9.6, 2.7 Hz, OCH*H*'CH), 4.15 (1H, dt, *J* = 9.0, 6.8 Hz, OC*H*H'CH_2), 4.07 (1H, dddd, *J* = 9.0, 7.0, 6.3, 0.6 Hz, OCH*H*'CH_2), 3.83 (3H, s, CO_2Me), 3.31 (1H, ddddd, *J* = 8.7, 7.2, 6.0, 2.7, 0.6 Hz, CH_2*C*HCH_2), 2.39 (1H, dddd, *J* = 12.9, 8.7, 6.8, 6.3 Hz, C*H*H'CHCH_2), 1.96 (dtd, *J* = 12.9, 6.9, 6.0 Hz, 1H, CH*H*'CHCH_2). **^{13}C NMR ($CDCl_3$, 100 MHz)** *δ* 171.9 (*C*=O), 168.4 (*C*=O), 86.7 (C_{quat}), 70.9 (O*C*H_2CH_2), 70.8 (O*C*H_2CH), 53.4, 45.5 (CH_2*C*HCH_2), 32.9 (CH_2*C*H_2CH); **ν_{max}** 2961 (w, C-H), 1776 (s, C=O), 1758 (s, C=O), 1223 (s), 1115 (s), 1032 (m); **m/z** (ESI$^+$) 209.1 ([M+Na]$^+$, 40%), 395.1 ([2M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_8H_{10}NaO_5$: *m/z* 209.0420 ([M+Na]$^+$), found: *m/z* 209.0415 ([M+Na]$^+$).

Di-*tert*-Butyl 2-(but-3-en-1-yloxy)malonate (7b)



The title compound was prepared according to the general procedure 1 using 3-buten-1-ol (0.86 mL, 10 mmol) and di-*tert*-butyl 2-diazomalonate (2.54 g, 10.5 mmol). Flash Chromatography purification (PE/Et_2O 9:1) gave the product **7b** as a colourless oil (1.91 g, 6.66 mmol, 66%); **R_f** 0.37 (PE/Et_2O 9:1); **^{1}H NMR ($CDCl_3$, 400 MHz)** *δ* 5.78 (1H, ddt, *J* = 17.1, 10.3, 6.8 Hz, CH_2=C*H*), 5.04 (1H, ddt, *J* = 17.1, 2.0, 1.3 Hz, C*H*H'=CH), 4.99 (1H, ddt, *J* = 10.3, 2.0, 1.3 Hz, CH*H*'=CH), 4.19 (1H, s, O*CH*), 3.55 (1H, t, *J* = 7.0 Hz, O*C*H_2), 2.36 (2H, qt, *J* = 7.0, 1.3 Hz, =CHCH_2), 1.42 (9H, OC($CH_3)_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** *δ* 166.0 (*C*=O), 134.6 (CH_2=*C*H), 116.9 (*C*H_2=CH), 82.7 (C_{quat}), 80.4 (O*C*H), 70.4 (O*C*H_2), 34.0 (=CH-*C*H_2), 28.0 (OC(*C*$H_3)_3$); **ν_{max}** 2980 (w, C-H), 1758 (m, C=O), 1737 (s, C=O), 1394 (w), 1248 (m), 1137 (s), 848 (=C-H); **m/z** (ESI$^+$) 309.2 ([M+Na]$^+$, 100%), 595.4 ([2M+Na]$^+$, 29%); **HRMS-ESI** calculated for $C_{15}H_{26}NaO_5$: *m/z* 309.1672 ([M+Na]$^+$), found: *m/z* 309.1674 ([M+Na]$^+$).

(3a*R**,6a*R**)-*tert*-Butyl 6-oxotetrahydrofuro[3,4-*b*]furan-6a(6*H*)-carboxylate (8b)

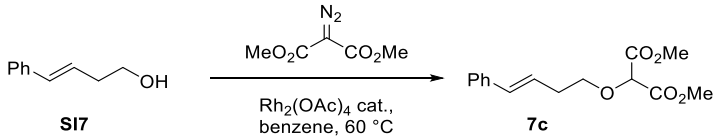


7b **8b**

The title compound was prepared according to the general procedure 3 using di-*tert*-butyl 2-(but-3-en-1-yloxy)malonate (1.28 g, 4.46 mmol). Flash Chromatography purification (PE/EtOAc 1:1) gave

the desired product **8b** as a white solid (841 mg, 3.69 mmol, 83%). $\mathbf{R_f}$ 0.38 (PE/EtOAc 1:1); **m.p.** 116-118 °C; **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 4.54 (1H, dd, *J* = 9.5, 6.7 Hz, CO_2CHH'), 4.21 (1H, dd, *J* = 9.5, 2.3 Hz, CO_2CHH'), 4.11 (1H, ddd, *J* = 9.0, 7.2, 6.7 Hz, $OCHH'$), 4.05 (1H, ddd, *J* = 9.0, 7.2, 6.3, Hz, $OCHH'$), 3.22 (1H, dtd, *J* = 9.0, 6.7, 2.3 Hz, CH_2CHCH_2), 2.38 (1H, dddd, *J* = 12.7, 9.0, 6.7, 6.3 Hz, OCH_2CHH'), 1.92 (1H, dq, *J* = 12.7, 6.7 Hz, OCH_2CHH'), 1.49 (9H, s, $OC(CH_3)_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 172.4 (*C*=O), 166.7 (*C*=O), 86.8 (C_{quat}), 84.2 (C_{quat}), 70.8 (CO_2CH_2), 45.6 (*C*H), 33.0 (OCH_2CH_2), 28.0 ($OC(CH_3)_3$); $\mathbf{\nu_{max}}$ 2986 (w, C-H), 1767 (m, C=O), 1748 (s, C=O), 1158 (m), 1116 (s); **m/z** (ESI^+) 251.1 ($[M+Na]^+$, 100%), 479.2 ($[2M+Na]^+$, 34%); **HRMS-ESI** calculated for $C_{11}H_{16}NaO_5$: *m/z* 251.0890 ($[M+Na]^+$), found: *m/z* 251.0901 ($[M+Na]^+$).

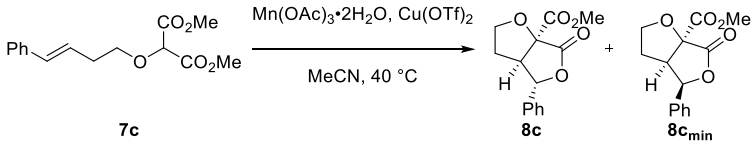
(*E*)-Dimethyl 2-((4-phenylbut-3-en-1-yl)oxy)malonate (7c)



SI7 **7c**

The title compound was prepared according to the general procedure 1 using the alcohol **SI7** and dimethyl 2-diazomalonate (520 mg, 3.29 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 9:1) gave the title compound **7c** as a yellow oil (480 mg, 1.73 mmol, 53%). $\mathbf{R_f}$ 0.36 ($PE_{40\text{-}60}$/EtOAc 8:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.32-7.17 (5H, m, Ar*H*), 6.44 (1H, dt, *J* = 15.9, 1.4 Hz, PhC*H*=CH), 6.19 (1H, td, *J* = 5.9, 15.9 Hz, PhCH=C*H*), 4.53 (1H, s, $CH(CO_2Me)_2$), 3.78 (6H, s, CO_2Me), 3.69 (2H, t, *J* = 6.9 Hz, OCH_2), 2.56 (2H, qd, *J* = 6.9, 1.4 Hz, $CHCH_2CH_2O$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 167.0 (2×*C*=O), 137.4 (C_{Ar}), 132.3 (Ph*C*H=CH), 128.6 (2×C_{Ar}), 127.3 (C_{Ar}), 126.2 (2×C_{Ar}), 125.8 (PhCH=*C*H), 79.2 ($CH(CO_2Me)_2$), 71.1 (CH_2O), 53.0 (2×OCH_3), 33.2 ($CHCH_2CH$); $\mathbf{\nu_{max}}$ 2954 (w, C-H), 1741 (w, C=O), 1200 (m), 1133 (m), 745 (s), 694 (s); **m/z** (ESI^+) 301.1 ($[M+Na]^+$, 100%); **HRMS-ESI** calculated for $C_{15}H_{18}NaO_5$: *m/z* 301.1046 ($[M+Na]^+$), found: *m/z* 301.1039 ($[M+Na]^+$).

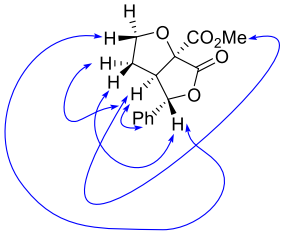
(3a*R**,4*S**,6a*S**)-Methyl 6-oxo-4-phenylhexahydrofuro[3,4-*b*]furan-6a-carboxylate (8c)



7c **8c** **$8c_{min}$**

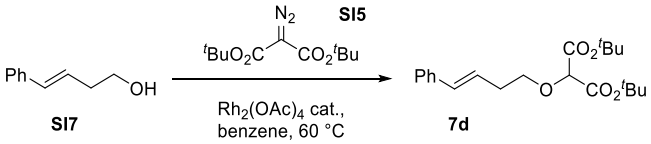
Crude d.r. = 14:1 (**8c**:**$8c_{min}$**)

The title compound was prepared according to the general procedure 3 using **7c** (68 mg, 0.25 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 8:2 to 6:4) gave the title compound **8c** as a colourless oil (48 mg, 0.18 mmol, 72%). Characterisation is given for the major diastereoisomer. $\mathbf{R_f}$ 0.23 ($PE_{40\text{-}60}$/EtOAc 6:4); **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 7.43-7.36 (5H, Ar*H*), 5.19 (1H, d, *J* = 5.7 Hz, OC*H*Ph), 4.36 (1H, ddd, *J* = 9.0, 7.9, 3.9 Hz, OC*H*H'), 4.20 (1H, tdd, *J* = 9.0, 6.3, 0.53 Hz, OCH*H'*), 3.81 (3H, s, CO_2Me), 3.36 (1H, ddd, *J* = 7.9, 5.7, 2.4 Hz, CH_2CHCH), 2.35 (1H, ddt, *J* = 13.0, 9.0, 7.9 Hz, $CH_2CHH'CH$), 2.18 (1H, dddd, 13.0, 6.3, 3.9, 2.4 Hz, $CH_2CHH'CH$); **^{13}C NMR ($CDCl_3$, 125 MHz)** δ 170.9 (*C*=O), 168.7 (*C*=O), 138.3 (C_{Ar}), 129.2 (C_{Ar}), 129.1 (2×C_{Ar}), 125.8 (2×C_{Ar}), 88.0 (C_{quat}), 84.9 (O*C*HPh), 70.8 (OCH_2), 54.5 (CH_2CHCH), 53.4 (CO_2Me), 31.9 (CH_2CH_2CH) ; $\mathbf{\nu_{max}}$ 2956 (w, C-H), 1780 (s, C=O), 1761 (s, C=O), 1254 (w), 1216 (w), 1090 (m), 1022 (s), 1050 (m), 699 (s); **m/z** (ESI^+) 263.1 ($[M+H]^+$, 40%), 285.1 ($[M+Na]^+$, 74%), 547.2 ($[2M+Na]^+$, 100%); **HRMS-ESI** calculated for $C_{14}H_{14}NaO_5$: *m/z* 285.0733 ($[M+Na]^+$), found: *m/z* 285.0727 ($[M+Na]^+$).



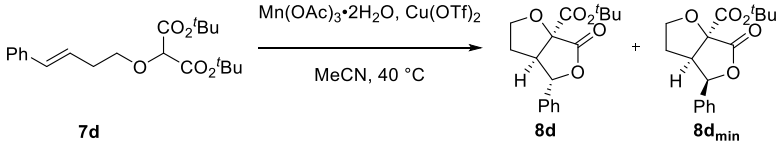
Key nOe interactions

(*E*)-di-*tert*-Butyl 2-((4-phenylbut-3-en-1-yl)oxy)malonate (7d)



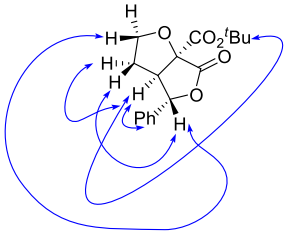
The title compound was prepared according to the general procedure 1 using (*E*)-4-phenylbut-3-en-1-ol (400 mg, 2.7 mmol) and di-*tert*-butyl 2-diazomalonate (680 mg, 2.81 mmol, 1.05 eq.). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 9:1) gave the title compound **7d** as a colourless oil (860 mg, 2.37 mmol, 88%). $\mathbf{R_f}$ 0.57 ($PE_{40\text{-}60}$/EtOAc 8:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.32-7.17 (m, 5H, Ar*H*), 6.44 (1H, d, *J* = 15.9 Hz, PhC*H*=CH), 6.21 (1H, td, *J* = 7.0, 15.9 Hz, PhCH=C*H*), 4.27 (1H, s, $CH(CO_2{}^tBu)_2$), 3.67 (2H, t, *J* = 7.0 Hz, OCH_2), 2.60-2.54 (2H, m, $CHCH_2CH_2O$), 1.47 (18H, $CO_2(CH_3)_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 165.9 (2×*C*=O), 137.5 (C_{Ar}), 132.1 (Ph*C*H=CH), 128.6 (C_{Ar}), 128.5 (2×C_{Ar}), 127.2 (PhCH=*C*H), 126.2 (2×C_{Ar}), 82.7 ($OCH(CO_2tBu)_2$), 80.4 (2×C_{quat}), 70.6 (OCH_2), 33.3 ($CHCH_2CH_2O$), 27.9 (6×C^tBu); $\mathbf{\nu_{max}}$ 2978 (w), 1735 (s, C=O), 1393 (s), 1247 (s), 1134 (w), 744 (s), 693 (s); **m/z** (ESI^+) 385.2 ($[M+Na]^+$, 100%); **HRMS-ESI** calculated for $C_{21}H_{30}NaO_5$: *m/z* 385.1985 ($[M+Na]^+$), found: *m/z* 385.1990 ($[M+Na]^+$).

(3*aR**,4*S**,6a*R**)-*tert*-Butyl 6-oxo-4-phenylhexahydrofuro[3,4-*b*]furan-6a-carboxylate (8d)



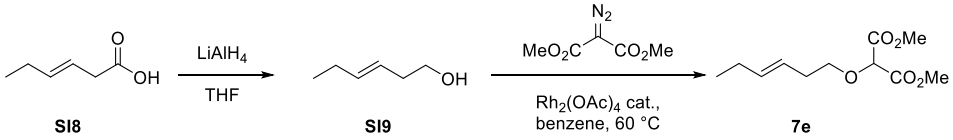
Crude d.r. = 16:1 (**8d**:**8d$_{min}$**)

The title compound was prepared according to the general procedure 3 using **7d** (93 mg, 0.26 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 8:2 to 6:4) gave the title compound **8d** as a colourless oil (48 mg, 0.16 mmol, 62%). Characterisation is given for the major diastereoisomer. $\mathbf{R_f}$ 0.49 ($PE_{40\text{-}60}$/EtOAc 5:5); **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 7.43-7.23 (5H, Ar*H*), 5.19 (1H, d, *J* = 5.1 Hz, CO_2CHPh), 4.33 (1H, ddd, *J* = 8.9, 7.6, 4.2 Hz, $OCHH'CH_2$), 4.14 (1H, dt, *J* = 6.3, 8.9 Hz, $OCHH'CH_2$), 3.28 (1H, dddd, *J* = 8.1, 5.1, 2.8, 0.6 Hz, $CHCHCH_2$), 2.36 (1H, dddd, *J* = 12.9, 8.9, 8.1, 7.6 Hz, $CH_2CHH'CH$), 2.15 (1H, ddddd, *J* = 12.9, 6.3, 4.2. 2.8, 0.4 Hz, $CH_2CHH'CH$), 1.42 (s, 9H, $CO_2C(CH_3)_3$); **^{13}C NMR ($CDCl_3$, 125 MHz)** δ 171.5 (*C*=O), 166.9 (*C*=O), 138.9 (C_{Ar}), 129.0 (2×C_{Ar}), 128.9 (C_{Ar}), 125.6 (2×C_{Ar}), 87.8 (C_{quat}), 84.8 (OCH_2), 84.2 ($CO_2C(CH_3)_3$), 70.6 (O*C*HPh), 54.2 (CH_2CH_2CH), 32.5 ($CH_2CHCHPh$), 27.8 (3×CH_3); $\mathbf{\nu_{max}}$ 2979 (w, C-H), 1781 (s, C=O), 1751 (s, C=O), 1155 (s), 1103 (s), 1050 (m), 969 (s); **m/z** (ESI^+) 327.1 ($[M+Na]^+$, 67%), 631.3 ($[2M+Na]^+$, 100%),; **HRMS-ESI** calculated for $C_{17}H_{20}NaO_5$: *m/z* 327.1203 ($[M+Na]^+$), found: *m/z* 327.1209 ($[M+Na]^+$).



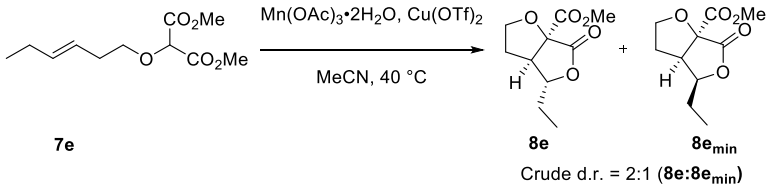
Key nOe interactions

(*E*)-Dimethyl 2-(hex-3-en-1-yloxy)malonate (7e)



To a solution of trans-hexenoic acid (0.4 mL, 3.37 mmol) in THF (15 mL) was added portionwise $LiAlH_4$ (175 mg, 4.6 mmol) at 0 °C. The reaction mixture was stirred for 1 h and hydrolysed with water (0.22 mL) followed by addition of an aqueous solution of NaOH 3M (0.65 mL), and water (0.22 mL). The solution was stirred overnight and filtered over Celite. The solvent was evaporated under reduced pressure and the crude alcohol **SI9** was used without further purification to prepare the title compound according to the general procedure 1. Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 9:1) gave **7e** as a colourless oil (194 mg, 0.84 mmol, 25% over two steps). **R_f** 0.38 (PE/EtOAc 8:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.54 (1H, dtt, *J* = 15.3, 6.2, 1.2 Hz, CH_2CH=C*H*CH_2), 5.36 (1H, dtt, *J* = 15.3, 7.0, 1.5 Hz, CH_2CH=*CH*CH_2), 4.52 (1H, s, C*H*$(CO_2Me)_2$), 3.80 (6H, s, CO_2*Me*), 3.58 (2H, t, *J* = 7.1 Hz, O*C*H_2), 2.35 (1 H, qq, *J* = 7.0, 1.2 Hz, CHCH_2CH_2O), 1.99 (1 H, qdq, *J* = 7.5, 6.2, 1.2 Hz, CH_2CH_3), 0.95 (3H, t, *J* = 7.5 Hz, CH_3) ; **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 167.1 (2×*C*=O), 135.0 (CH_3CH_2*C*H=CH), 124.1 (CH_3CH_2CH=*C*H), 79.1 (*C*H$(CO_2Me)_2$), 71.6 (O*C*H_2CH_2), 53.0 (2×CO_2*Me*), 32.7 (CH*C*H_2CH_2O), 25.7 (*C*H_2CH_3), 13.8 (CH_2*C*H_3); **ν_{max}** 2959 (w, C-H), 1744 (w, C=O), 1201 (m), 1131 (m), 1028 (w), 969 9 (s); **m/z** (ESI$^+$) 253.1 ([M+Na]$^+$, 100%), 483.3 ([2M+Na]$^+$, 31%); **HRMS-ESI** calculated for $C_{11}H_{18}NaO_5$: *m/z* 253.1046 ([M+Na]$^+$), found: *m/z* 253.1050 ([M+Na]$^+$).

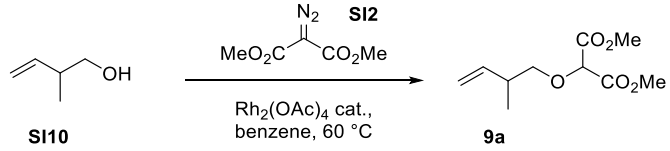
(3*aR**,4*R**,6*aS**)-Methyl 4-ethyl-6-oxohexahydrofuro[3,4-b]furan-6a-carboxylate (8e)



The title compound was prepared according to the general procedure 3 using **7e** (56 mg, 0.24 mmol). Characterisation is given for the major diastereoisomer. Flash Chromatography purification (PE40-60/EtOAc 8:2 to 6:4) gave the title compound **8e** (25 mg, 0.12 mmol, 50%) as a mixture of two diastereoisomers. **R_f** 0.15 (PE/EtOAc 6:4); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 4.63 (1H, dt, *J* = 8.2, 5.9 Hz, OC*H*CH_2 maj), 4.24 (1H, ddd, *J* = 9.0, 7.6, 4.4 Hz, OC*H*H, min), 4.16 (1 H, ddd, *J* = 7.6, 5.8, 4.7 Hz, OC*H*CH_2, min), 4.11-4.05 (2H, m, CH_2O, maj), 4.04-4.00 (1H, m, OCH*H*, min), 3.84 (3H, s, CO_2Me, maj), 3.83 (3H, s, CO_2Me, min), 3.18 (1H, td, *J* = 8.7, 5.9 Hz, CH_2*C*HCH maj), 3.00 (1 H, ddd, *J* = 8.1, 4.7, 3.2 Hz, CH_2*C*HCH maj), 2.31 (1H, dtd, *J* = 12.8, 8.4, 7.7 Hz CH_2C*H*HCH, min), 2.20-2.02 (2H, m, CH_2*C*H_2CH, maj), 1.98-1.92 (1H, m, CH_2CH*H*CH, min), 1.93-1.83 (1H, m, CH*H*CH_3, maj), 1.58-1.69 (1H, m, C*H*HCH_3,

maj), 1.06 (1H, t, *J* = 7.4 Hz, CH_3 maj), 1.04 (1H, t, *J* = 7.4 Hz, CH_3 min). **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 194.8 (C=O), 171.8 (C=O), 168.9 (C=O), 168.6 (C=O), 88.5 (C_{quat} maj), 86.0 (O*C*HCH, min), 80.5 (OCHCH, maj), 71.4 (O*C*H_2CH_2, maj), 70.7 (O*C*H_2CH_2, min), 53.4 (CO_2Me), 50.8 (CH_2*C*HCH, min) 49.3 (CH_2*C*HCH), 32.7 (*C*H_2, min), 28.9 (*C*H_2, min), 26.7 (CH_2, maj), 24.3 (CH_2, maj), 10.3 (CH_3, maj), 9.6 (CH_3, min); **ν_{max}** 2971 (w), 1776 (s, C=O), 1760 (s, C=O), 1113 (m), 1021 (m); **m/z** (ESI$^+$) 327.1 ([M+Na]$^+$, 451.2 ([2M+Na]$^+$, 100%), 71%); **HRMS-ESI** calculated for $C_{10}H_{14}NaO_5$: *m/z* 237.0733 ([M+Na]$^+$), found: *m/z* 237.0742 ([M+Na]$^+$).

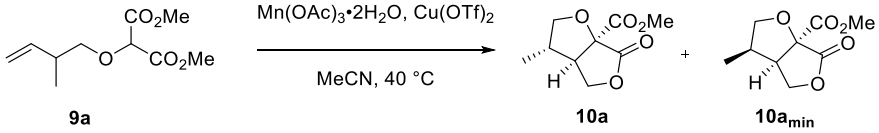
Dimethyl 2-((2-methylbut-3-en-1-yl)oxy)malonate (9a)



SI10 **9a**

The title compound was prepared according to the general procedure 1 using 2-methylbut-3-en-1-ol (258 mg, 3.00 mmol) and dimethyl 2-diazomalonate (501 mg, 3.17 mmol). Flash Chromatography purification ($PE_{30\text{-}40}$/Et_2O 4:1) gave the compound **9a** as a colourless oil (216 mg, 1.0 mmol, 33%). **R_f** 0.36 (PE/Et_2O 7:3); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.78 (1H, ddd, *J* = 17.3, 10.4, 7.0 Hz, CH_2=C*H*), 5.08 (1H, d, *J* = 17.3 Hz, C*H*H'=CH_2), 5.03 (1H, d, *J* = 10.4 Hz, CH*H'*=CH_2), 4.51 (1H, s, OC*H*(CO_2CH_3)$_2$), 3.80 (6H, s, (CO_2CH_3)$_2$), 3.51 (1H, dd, *J* = 8.9, 7.0 Hz, CHC*H*H'O), 3.41 (1H, dd, *J* = 8.9, 7.0 Hz, CHCH*H'*O), 2.60-2.51 (1H, m, C*H*CH_3), 1.05 (3H, d, *J* = 7.0 Hz, *Me*); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 167.1 (*C*=O), 140.3 (CH_2=*C*H), 114.9 (*C*H_2=CH), 79.3 (O*C*H), 796.1 (O*C*H_2), 53.0 (CO_2*C*H $_3$), 37.6 (*C*HCH_3), 16.4 (CH*C*H_3); **ν_{max}** 2958 (w, C-H), 1744 (s, C=O), 1200 (m), 1128 (s), 1026 (m), 917 (w); **m/z** (ESI$^+$) 239.1 ([M+Na]$^+$, 100%), 455.1 ([2M+Na]$^+$, 11%); **HRMS-ESI** calculated for $C_{10}H_{16}NaO_5$: *m/z* 239.0890 ([M+Na]$^+$), found: *m/z* 239.0894 ([M+Na]$^+$).

Methyl (3*S**,3a*S**,6a*S**)-3-methyl-6-oxotetrahydrofuro[3,4-*b*]furan-6a(6*H*)-carboxylate (10a)

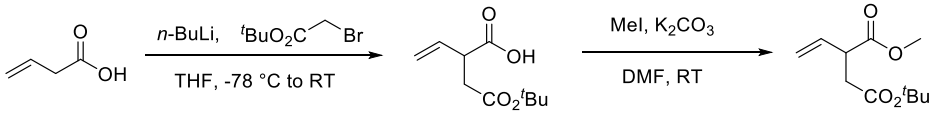


9a **10a** **10a$_{min}$**

Crude d.r. 3:1 (**10a:10a$_{min}$**)

The title compound was prepared according to the general procedure 3 using dimethyl 2-((2-methylbut-3-en-1-yl)oxy)malonate (55 mg, 0.254 mmol). Flash Chromatography purification ($PE_{30\text{-}40}$/Et_2O 1:2 to 1:4) gave the title compound **10a** (37 mg, 0.185 mmol, 73%). A second purification ($PE_{30\text{-}40}$/Et_2O 1:2 to 1:4) gave the clean major diastereoisomer. Characterisation is given for the major diastereoisomer only. **R_f** 0.38 (PE/Et_2O 1:4); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 4.56 (1H, dd, *J* = 9.7, 6.8 Hz, CO_2C*H*H'), 4.25 (1H, dd, *J* = 9.7, 1.8 Hz, CO_2CH*H'*), 4.18 (1H, dd, *J* = 8.6, 6.6 Hz, OC*H*H'), 3.83 (3H, s, CO_2CH_3), 3.74 (1H, t, *J* = 8.6, Hz, OCH*H'*), 2.82 (1H, td, *J* = 6.8, 1.8 Hz, CO_2CHH'C*H*), 2.37-2.24 (1H, m, CH_2C*H*CH_3), 1.12 (3H, d, *J* = 6.9 Hz, CHC*H*$_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 172.0 (*C*=O), 168.6 (*C*=O), 86.7 (*C*$_{quat}$), 77.3 (O*C*H_2CHCH_3), 69.5 (CO_2*C*H_2CH), 53.3 (CO_2*C*H_3), 53.1 (CO_2CH_2*C*H), 41.1 (CH_2*C*HCH_3), 15.4 (CH_2CH*C*H_3); **ν_{max}** 2962 (w, C-H), 1778 (s, C=O), 1760 (s, C=O), 1728 (m, C=O), 1194 (m); **m/z** (ESI$^+$) 201.1 ([M+H]$^+$, 20%), 223.1 ([M+Na]$^+$, 50%), 423.1 ([2M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_9H_{12}NaO_5$: *m/z* 223.0577 ([M+Na]$^+$), found: *m/z* 223.0578 ([M+Na]$^+$).

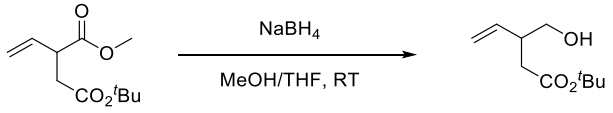
4-(*tert*-Butyl) 1-methyl 2-vinylsuccinate (SI13)



SI11 **SI12** **SI13**

To a solution of 3-butenoic acid (0.796 mL, 9.37 mmol) in THF (24 mL) at -78 °C was added a solution of *n*-BuLi in hexanes (2.5 M, 8.14 mL, 20.4 mmol) over 5 min. The mixture was stirred for 10 min and *tert*-butyl bromoacetate (4.1 mL, 28 mmol) was added over 5 min. The reaction was warmed to room temperature outside the cooling bath and stirred for 8 h. The mixture was quenched at 0° C with aqueous NaOH (0.5 M, 40 mL) and Et_2O was added (40 mL). The layers were separated and the organic phase was extracted with more aqueous NaOH (0.5 M, 20 mL). The combined aqueous layers were treated with pH 2 sulphate buffer (15 mL) and acidified by dropwise addition of concentrated aqueous HCl until pH 2. The acidified aqueous layer was extracted with Et_2O and the combined layers were dried (Na_2SO_4), filtered and evaporated to give the crude carboxylic acid **SI12** (2.16 g). The residual oil was dissolved in dry DMF and treated upon stirring at room temperature with K_2CO_3 (3.83 g, 27.8 mmol) and MeI (1.43 mL, 23.1 mmol). The reaction was stirred for 4 h at room temperature and was then diluted with Et_2O (50 mL) and pentane (50 mL). The mixture was washed with H_2O (2 x 100 mL) and brine (50 mL), dried (Na_2SO_4), filtered and evaporated. The residue was purified by Flash Chromatography ($PE_{30\text{-}40}/Et_2O$ 9:1) to give the title compound **SI13** as a colourless oil (473 mg, 2.21 mmol, 24%). **R_f** 0.48 (PE/Et_2O 6:1); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.84 (1H, ddd, *J* = 17.2, 10.2, 7.8 Hz, CH_2=*C*H), 5.20 (1H, dt, *J* = 17.2, 1.1 Hz, C*H*H'=CH), 5.16 (1H, dt, *J* = 10.2, 1.0 Hz, CH*H*'=CH), 3.70 (3H, s, OCH_3), 3.48 (1H, dddt, *J* = 8.8, 7.8, 5.9, 1.0, Hz, C*H*CH_2), 2.76 (1H, dd, *J* = 16.4, 8.8 Hz, C*H*H'$CO_2{}^t$Bu), 2.47 (1H, dd, *J* = 16.4, 5.9 Hz, CH*H*'$CO_2{}^t$Bu), 1.42 (9H, OC(CH_3)$_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 173.4 (*C*=O), 170.6 (*C*=O), 134.4 (CH_2=*C*H_2), 117.9 (*C*H_2=CH), 81.1 (C_{quat}), 52.3 (O*C*H_3), 45.8 (*C*H), 37.3 (*C*H2), 28.2 (OC(*C*H_3)$_3$); **ν_{max}** 2980 (w, C-H), 1730 (s, C=O), 1150 (s), 924 (w, =C-H), 845 (w, =C-H); **m/z** (ESI$^+$) 237.1 ([M+Na]$^+$, 100%), 451.2 ([2M+Na]$^+$, 20%); **HRMS-ESI** calculated for $C_{11}H_{18}NaO_4$: *m/z* 237.1097 ([M+Na]$^+$), found: *m/z* 237.1102 ([M+Na]$^+$).

tert-Butyl 3-(hydroxymethyl)pent-4-enoate (SI14)

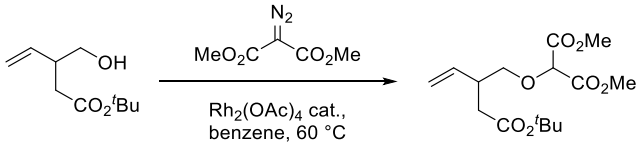


SI13 **SI14**

To a vigorously stirred solution of 4-(*tert*-butyl) 1-methyl 2-vinylsuccinate (457 mg, 2.13 mmol) in THF/MeOH (1:1, 15 mL), was added every 30 min $NaBH_4$ (4 additions, each addition: 457 mg, 12 mmol) and the reaction was stirred for another hour. The reaction mixture was quenched with saturated aqueous NH_4Cl (20 mL) and water was added (20 mL). The mixture was extracted with Et_2O (3 x 25 mL). The combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by Flash Chromatography ($PE_{30\text{-}40}/Et_2O$ 3:2) to give desired product **SI14** as a colourless oil (224 mg, 1.20 mmol, 56%); **R_f** 0.30 (PE/Et_2O 3:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.70 (1H, ddd, *J* = 17.0, 10.5, 7.8 Hz, CH_2=C*H*), 5.16 (2H, m, C*HH*'=CH), 3.56 (2H, d, *J* = 6.1 Hz, CH_2OH), 2.71 (1H, m, C*H*(CH_2)$_2$), 2.40 (1H, dd, *J* = 15.0, 6.6 Hz, C*H*H'$CO_2{}^t$Bu), 2.29 (1H, dd, *J* = 15.0, 7.6 Hz, CH*H*'$CO_2{}^t$Bu), 1.43 (9H, s, OC(CH_3)$_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 172.1 (*C*=O), 138.0 (CH_2=*C*H), 117.2 (*C*H_2=CH), 80.9 (C_{quat}), 65.4 (*C*H_2OH), 43.0 (*C*H), 37.5 (*C*$H_2CO_2{}^t$Bu), 28.2 (OC(*C*H_3)$_3$); **ν_{max}** 3428 (br, O-H), 2979 (w, C-H), 1727 (s, C=O), 1368 (w), 1153 (s), 918 (=C-H), 842 (=C-H); **m/z** (ESI$^+$) 209.1 ([M+Na]$^+$, 100%),

395.3 ([2M+Na]$^+$, 15%); **HRMS-ESI** calculated for $C_{10}H_{18}NaO_3$: *m/z* 209.1148 ([M+Na]$^+$), found: *m/z* 209.1158 ([M+Na]$^+$).

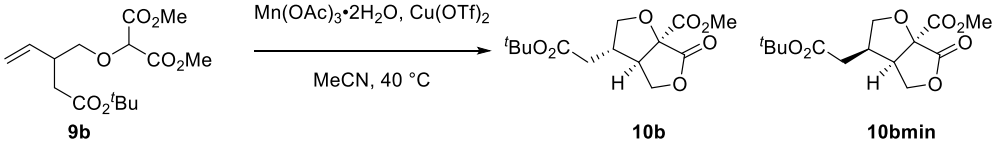
Dimethyl 2-((2-(2-(tert-butoxy)-2-oxoethyl)but-3-en-1-yl)oxy)malonate (9b)



SI14 **9b**

The title compound was prepared according to the general procedure 1 using *tert*-butyl 3-(hydroxymethyl)pent-4-enoate (210 mg, 1.13 mmol) and dimethyl 2-diazomalonate (134 mg, 0.840 mmol). Flash Chromatography purification ($PE_{30\text{-}40}/Et_2O$ 3:1 to 2:1) gave the desired product **9b** as a colourless oil (217 mg, 0.686 mmol, 61%); $\mathbf{R_f}$ 0.38 (PE/Et_2O 2:1); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.65, (1H, ddd, *J* = 17.3, 10.3, 7.6 Hz, CH_2=C*H*), 5.09 (1H, dt, *J* = 17.3, 1.2 Hz, C*H*H'=CH), 5.05 (1H, ddd, *J* = 10.3, 1.4, 1.0 Hz, CH*H'*=CH), 4.45 (1H, s, OC*H*), 3.74 (6H, s, OCH_3), 3.55 (1H, dd, *J* = 9.1, 5.9 Hz, OC*H*H'), 3.45 (1H, dd, *J* = 9.1, 7.1 Hz, OCH*H'*), 2.93-2.83 (1H, m, C*H*(CH_2)$_2$), 2.51 (1H, dd, *J* = 15.4, 5.6 Hz, C*H*H'$CO_2{}^t$Bu), 2.20 (1H, dd, *J* = 15.4, 8.6 Hz, CH*H'*$CO_2{}^t$Bu), 1.36 (9H, s, OC(CH_3)$_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 171.5 (*C*=O), 166.9 (*C*=O), 137.3 (CH_2=*C*H), 116.8 (*C*H_2=CH), 80.5 (C_{quat}), 79.2 (O*C*H), 73.8 (O*C*H_2), 53.0 (O*C*H_3), 40.2 (*C*H(CH_2)$_2$), 37.3 (*C*$H_2CO_2{}^t$Bu), 28.2 (OC(*C*H_3)$_3$); $\boldsymbol{\nu_{max}}$ 2979 (w, C-H) 1740 (C=O), 1727 (s, C=O), 1243 (m), 1138 (s), 1027 (m), 921 (w, =C-H); **m/z** (ESI$^+$) 339.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{15}H_{24}NaO_7$: *m/z* 339.1414 ([M+Na]$^+$), found: *m/z* 339.1413 ([M+Na]$^+$).

(3*S**,3a*S**,6a*S**)-Methyl 3-(2-(*tert*-butoxy)-2-oxoethyl)-6-oxotetrahydrofuro[3,4-*b*]furan-6a(6*H*)-carboxylate (10b)

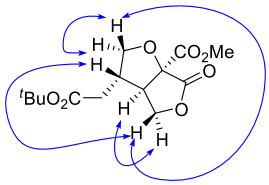


9b **10b** **10bmin**

Crude d.r. = 3.6:1 (**10b:10b$_{min}$**)

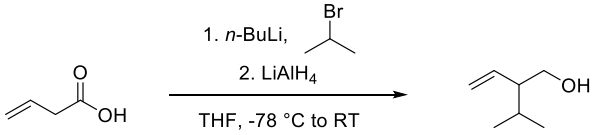
The title compound was prepared according to the general procedure 3 using dimethyl 2-((2-(2-(*tert*-butoxy)-2-oxoethyl)but-3-en-1-yl)oxy)malonate (94.9 mg, 0.300 mmol). Flash Chromatography purification ($PE_{30\text{-}40}/Et_2O$ 1:4) gave an inseparable mixture (3.6:1) of the two diastereosiomers (68.0 mg, 0.226 mmol, 76%) as a white solid. For analytical purposes, two successive recrystallisations from Hexane/EtOAc (4:1) gave the title compound **10b** in higher diastereomeric purity (15:1, 42 mg). Characterisation was performed on the recrystallised mixture and is given for the major diastereoisomer only. $\mathbf{R_f}$ 0.59 (PE/Et_2O 1:4); **m.p.** 98-99 °C; **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 4.54 (1H, dd, *J* = 9.8, 7.1 Hz, CO_2C*H*H'), 4.33 (1H, dd, *J* = 9.8, 2.5 Hz, CO_2CH*H'*), 4.17 (1H, dd, *J* = 9.1, 6.9 Hz, OC*H*H'), 3.80 (1H, dd, *J* = 9.1, 7.2 Hz, OCH*H'*), 3.80 (3H, s, OCH_3), 2.94 (1H, ddd, *J* = 7.2, 6.2, 2.5 Hz, CO_2CH_2C*H*), 2.55 (1H, dqn, *J* = 8.3, 6.7 Hz, C*H*$CH_2CO_2{}^t$Bu), 2.41 (1H, dd, *J* = 16.4, 6.7 Hz, C*H*H'$CO_2{}^t$Bu), 2.29 (1H, dd, *J* = 16.4, 8.3 Hz, CH*H'*$CO_2{}^t$Bu), 1.38 (9H, s, OC(CH_3)$_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 171.7 (*C*=O), 170.6 (*C*=O), 168.5 (*C*=O), 86.9 (C_{quat}), 81.8 (C_{quat}), 75.5 (O*C*H_2), 70.6 (CO_2*C*H_2), 53.5 (O*C*H_3), 51.3 (CO_2CH_2*C*H), 43.1 (*C*H$CH_2CO_2{}^t$Bu), 37.4 (*C*$H_2CO_2{}^t$Bu), 28.2 (OC(*C*H_3)$_3$); $\boldsymbol{\nu_{max}}$ 2980 (w, C-H), 1783 (s, C=O), 1763 (m, C=O), 1724 (s, C=O), 1256 (m), 1155 (s); **m/z** (ESI$^+$) 323.1 ([M+Na]$^+$, 100%), 623.2 ([2M+Na]$^+$, 35%); **HRMS-ESI** calculated for $C_{14}H_{20}NaO_7$: *m/z* 323.1101 ([M+Na]$^+$), found: *m/z* 323.1099 ([M+Na]$^+$).

nOe analysis was performed in MeOD. ^{1}H NMR (MeOD, 400 MHz) δ 4.55 (1H, dd, *J* = 9.8, 7.2 Hz, CO_2CHH'), 4.41 (1H, dd, *J* = 9.8, 2.4 Hz, CO_2CHH'), 4.17 (1H, dd, *J* = 8.9, 6.6 Hz, $OCHH'$), 3.79 (3H, s, OCH_3), 3.75 (1H, dd, *J* = 8.9, 7.8 Hz, $OCHH'$), 3.10 (1H, dt, *J* = 2.4, 6.9 Hz, CO_2CH_2CH), 2.55 (1H, sext, *J* = 7.0 Hz, $CHCH_2CO_2{}^t$Bu), 2.45 (1H, dd, *J* = 7.2, 16.6 Hz, $CH_2CO_2{}^t$Bu), 2.40 (1H, dd, *J* = 7.9, 16.6 Hz, $CH_2CO_2{}^t$Bu), 1.41 (9H, s, $OC(CH_3)_3$)).



Key nOe interactions

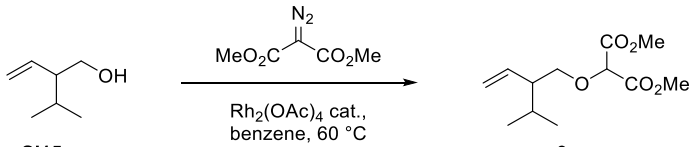
2-Isopropylbut-3-en-1-ol (SI15)



SI11 **SI15**

The title compound was prepared according to the general procedure 2 using vinyl acetic acid (1.00 g, 11.7 mmol) and 2-bromopropane (3.30 mL, 35.1 mmol). The stirring period at room temperature was 6 h. Flash Chromatography purification ($PE_{30\text{-}40}/Et_2O$ 7:3) gave the title compound **SI15** as a colourless oil (635 mg, 5.56 mmol, 48%). $\mathbf{R_f}$ 0.32 (PE/Et_2O 7:3); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.65 (1H, ddd, *J* = 17.1, 10.3, 9.3 Hz, CH_2=C*H*), 5.23 (1H, dd, *J* = 10.3, 2.4 Hz, C*H*H'=CH), 5.15 (1H, ddd, *J* = 17.1, 2.4, 0.5 Hz, CH*H'*=CH), 3.70 (1H, dd, *J* = 10.5, 4.9 Hz, C*H*H'OH), 3.47 (1H, dd, *J* = 10.5, 9.1 Hz, CH*H'*OH), 2.08-1.99 (1H, m, C*H*CH_2OH), 1.69 (1H, m, C*H*$(CH_3)_2$), 0.94 (1H, d, *J* = 6.9 Hz, CHC*H*$_3$), 0.89 (1H, d, *J* = 6.9 Hz, CHC*H*$_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 138.3 (CH_2=*C*H), 118.5 (CH_2), 63.9 (CH_2OH), 53.9 (*C*HCH_2), 28.7 (*C*H$(CH_3)_2$), 20.9 (CH_3), 19.7 (CH_3); $\mathbf{\nu_{max}}$ 3335 (br, O-H), 2958 (m, C-H), 1044 (m), 913 (s). NMR data are in agreement with literature.[7]

Dimethyl 2-((2-isopropylbut-3-en-1-yl)oxy)malonate (9c)

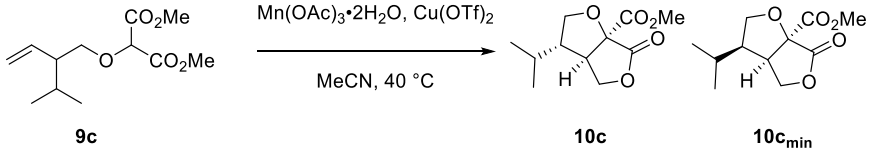


SI15 **9c**

The title compound was prepared according to the general procedure 1 using 2-isopropylbut-3-en-1-ol (343 mg, 3.0 mmol) and dimethyl 2-diazomalonate (501 mg, 3.15 mmol). Flash Chromatography purification ($PE_{30\text{-}40}/Et_2O$ 9:1) gave the compound **9c** as a colourless oil (590 mg, 2.42 mmol, 81%). $\mathbf{R_f}$ 0.20 (PE/Et_2O 9:1); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.69 (1H, ddd, *J* = 17.1, 10.5, 9.1 Hz, CH_2=C*H*), 5.13 (1H, dd, *J* = 10.5, 2.0 Hz, C*H*H'=CH), 5.09 (1H, dd, *J* = 17.1, 2.0 Hz, CH*H'*=CH), 4.52 (1H, s, OC*H*), 3.82 (6H, s, CO_2CH_3), 3.63 (1H, dd, *J* = 9.1, 6.6 Hz, C*H*H'O), 3.59 (1H, dd, *J* = 9.1, 6.6 Hz, CH*H'*O), 2.31-2.21 (1H, m, C*H*$CH(CH_3)_2$), 1.88 (1H, m, C*H*$(CH_3)_2$), 0.93 (1H, d, *J* = 6.6 Hz, CHC*H*$_3$), 0.86 (1H, d, *J* = 6.6 Hz, CHC*H*$_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 167.2 (*C*=O), 167.1 (*C*=O), 137.0 (CH_2=C*H*), 117.3 (CH_2=CH), 79.3 (O*C*H), 73.2 (O*C*H_2), 52.9 (CO_2CH_3), 49.9 (*C*HCH$(CH_3)_2$), 28.1 (*C*H$(CH_3)_2$), 20.8 (CH*C*H_3), 18.4 (CH*C*H_3);

ν_{max} 2958 (w, C-H), 1746 (s, C=O), 1129 (m), 1028 (m), 917 (w); **m/z** (ESI$^+$) 267.1 ([M+Na]$^+$, 100%), 511.0 ([2M+Na]$^+$, 20%); **HRMS-ESI** calculated for $C_{12}H_{20}NaO_5$: *m/z* 267.1203 ([M+Na]$^+$), found: *m/z* 267.1205 ([M+Na]$^+$).

(3*S**,3a*R**,6a*S**)-*tert*-Butyl 3-isopropyl-6-oxotetrahydrofuro[3,4-*b*]furan-6a(6H)-carboxylate (10c)

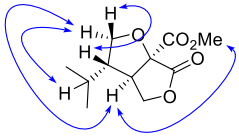


9c **10c** **10c$_{min}$**

Crude d.r. = 22:1 (**10c:10c$_{min}$**)

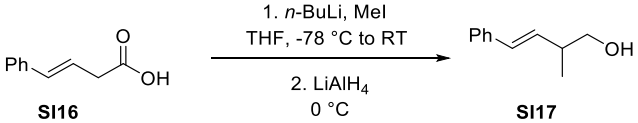
The title compound was prepared according to the general procedure 3 using dimethyl 2-((2-isopropylbut-3-en-1-yl)oxy)malonate (70.0 mg, 0.287 mmol). Flash Chromatography purification (PE_{30-40}/Et_2O 2:3) gave the title compound as a coulourless oil (48 mg, 0.211 mmol, 73%). **R_f** 0.50 (PE_{30-40}/Et_2O 3:7); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 4.52 (1H, dd, *J* = 9.5, 6.7 Hz, CO_2CHH'), 4.22 (1H, ddd, *J* = 9.5, 1.7, 0.4 Hz, CO_2CH*H'*), 4.19 (1H, ddd, *J* = 8.8, 7.3, 0.5 Hz, C*H*H'O), 3.80 (3H, s, OCH_3), 3.79 (1H, m, CH*H'*O), 2.90 (1H, ddd, *J* = 8.2, 6.7, 1.7 Hz, CO_2CH_2CH), 2.05-1.97 (1H, m, C*H*CH(CH_3)$_2$), 1.60 (1H, dsep, *J* = 8.8, 6.7 Hz, C*H*(CH_3)$_2$), 0.91 (3H, d, *J* = 6.7 Hz, CHCH_3), 0.84 (3H, d, *J* = 6.7 Hz, CHCH_3); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 172.0 (*C*=O), 168.8 (*C*=O), 87.1 (C_{quat}), 75.6 (OCH_2), 70.7 (CO_2CH_2), 54.0 (*C*HCH(CH_3)$_2$), 53.3 (OCH_3), 50.4 (CO_2CH_2CH), 30.9 (C*H*(CH_3)$_2$), 21.4 (CH*C*H$_3$), 21.2 (CH*C*H$_3$); **ν_{max}** 2960 (w, C-H), 1783 (s, C=O), 1762 (m, C=O), 1730 (w, C=O), 1028 (m); **m/z** (ESI$^+$) 251.0 ([M+Na]$^+$, 100%), 479.0 ([2M+Na]$^+$, 80%); **HRMS-ESI** calculated for $C_{11}H_{16}NaO_5$: *m/z* 251.0890 ([M+Na]$^+$), found: *m/z* 251.0892 ([M+Na]$^+$).

nOe analysis was performed in C_6D_6. ^{1}H NMR (C_6D_6, 400 MHz) δ 3.94 (1H, dd, *J* = 9.3, 6.9 Hz, CO_2CHH'), 3.80 (1H, dd, *J* = 8.5, 7.3 Hz, C*H*H'O), 3.55 (1H, dd, *J* = 9.3, 1.8 Hz, CO_2CH*H'*), 3.48 (1H, t, *J* = 9.2 Hz, CH*H'*O), 3.24 (3H, s, CO_2Me), 2.31 (1H, ddd, *J* = 8.5, 6.9, 1.8 Hz, $COOCH_2CH$), 1.26-1.19 (1H, m, C*H*i*Pr*), 0.92 (1H, septd, *J* = 6.7, 8.9 Hz, C*H*(CH_3)$_2$), 0.38 (6H, d, *J* = 6.7 Hz, CH(CH_3)$_2$).



Key nOe interactions

(*E*)-2-Methyl-4-phenylbut-3-en-1-ol (SI17)

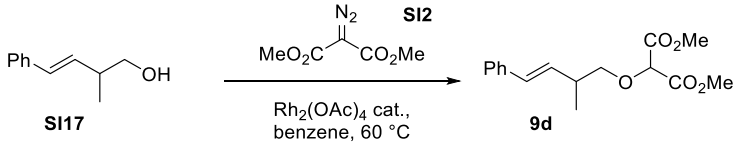


SI16 **SI17**

The title compound was prepared according to the general procedure 2 using trans-styrylacetic acid (1.00 g, 6.17 mmol) and iodomethane (1.18 mL, 19 mmol, 3.0 eq). The stirring period at room temperature was one hour. Flash Chromatography purification (PE_{30-40}/Et_2O 3:2) gave the product **SI17** as an orange oil (302 mg, 1.86 mmol, 30%). **R_f** 0.52 (PE/Et_2O 1:1); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.40-7.35 (2H, m, Ar*H*), 7.34-7.27 (2H, m, Ar*H*), 7.25-7.19 (1H, m, Ar*H*), 6.49 (1H, d, *J* = 15.9 Hz, Ar-C*H*=CH), 6.10 (1H, dd, *J* = 15.9, 8.1 Hz, Ar-CH=C*H*), 3.60 (1H, dd, *J* = 10.6, 5.6 Hz, C*H*H'OH), 3.52 (1H, dd, *J* = 10.6, 7.6 Hz, CH*H'*OH), 2.61-2.48 (1H, m, C*H*CH$_3$), 1.11 (1H, d, *J* = 6.6 Hz, CHCH_3); **^{13}C NMR**

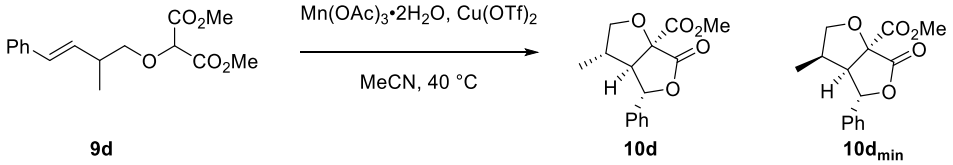
($CDCl_3$, 100 MHz) δ 137.3 (Ar-CH=*C*H), 132.6 (Ar-*C*H=CH), 131.1 (*Ar*), 128.7 (*Ar*), 127.4 (*Ar*), 126.3 (*Ar*), 67.5 (CH_2), 40.3 ($CHCH_3$), 16.6 (CH_3); **ν_{max}** 3342 (br, O-H), 2960 (w, C-H), 1031 (m), 476 (s), 693 (s); **m/z** (ESI^+) 185.1 ($[M+Na]^+$, 100%). NMR data are in agreement with literature.[8]

Dimethyl (*E*)-2-((2-methyl-4-phenylbut-3-en-1-yl)oxy)malonate (9d)



The title compound was prepared according to the general procedure 1 using (*E*)-2-Methyl-4-phenylbut-3-en-1-ol (286 mg, 1.76 mmol) and dimethyl 2-diazomalonate (294 mg, 1.85 mmol). Flash Chromatography purification (PE_{30-40}/Et_2O 3:1) gave the title compound **9d** as a colourless oil (285 mg, 0.975 mmol, 55%). **R_f** 0.47 (PE/Et_2O 3:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.37-7.32 (2H, m, Ar*H*), 7.32-7.26 (2H, m, Ar*H*), 7.23-7.17 (1H, m, Ar*H*), 6.45 (1H, d, *J* = 16.0 Hz, Ar-C*H*=CH), 6.16 (1H, dd, *J* = 16.0, 7.3 Hz, Ar-CH=C*H*), 4.54 (1H, s, OC*H*(CO_2Me)$_2$), 3.80 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 3.59 (1H, dd, *J* = 9.0, 6.9, Hz C*H*H'OCH), 3.51 (1H, dd, *J* = 9.0, 6.9 Hz, CH*H'*OCH), 2.80-2.67 (1H, dsep, *J* = 1.1, 6.9 Hz C*H*CH_3), 1.16 (3H, d, *J* = 6.9 Hz, CHCH_3); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 167.1 (*C*=O), 167.1 (*C*=O), 137.6 (Ar-CH=*C*H), 132.0 (Ar-*C*H=CH), 130.2 (*Ar*), 128.6 (*Ar*), 127.3 (*Ar*), 126.3 (*Ar*), 79.4 (O*C*H(CO_2Me)$_2$), 76.3 (CH_2-O-CH), 53.0 (CO_2CH_3), 37.2 (*C*HCH_3), 17.0 (CHCH_3); **ν_{max}** 2957 (w, C-H), 1764 (m, C=O), 1746 (s, C=O), 1139 (m), 1028 (w), 750 (w), 695 (w); **m/z** (ESI^+) 315.1 ($[M+Na]^+$, 100%); **HRMS-ESI** calculated for $C_{16}H_{20}NaO_5$: *m/z* 315.1203 ($[M+Na]^+$), found: *m/z* 315.1203 ($[M+Na]^+$).

(3*S**,3a*R**,4*S**,6a*S**)-Methyl 3-methyl-6-oxo-4-phenyltetrahydrofuro[3,4-*b*]furan-6a(6*H*)-carboxylate (10d)

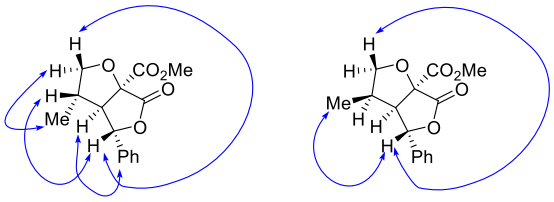


Crude d.r. 4.6:1 (**10d:10d$_{min}$**)

The title compound was prepared according to the general procedure 3 using dimethyl (*E*)-2-((2-methyl-4-phenylbut-3-en-1-yl)oxy)malonate **9d** (75 mg, 0.257 mmol). Flash Chromatography purification (PE/Et_2O 2:3) gave the product **10d** as a mixture of two diastereoisomers (65 mg, 0.236 mmol, 92%). A second purification (PE/Et_2O 2:3) gave the major diastereoisomer and a small amount of the minor diastereoisomer. **R_f** 0.24 (3:2 PE/Et_2O); **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 7.46-7.50 (3H, m, Ar*H*), 7.40-7.34 (2H, m, Ar*H*), 5.26 (1H, d, *J* = 4.6 Hz, C*H*Ph), 4.29 (1H, dd, *J* = 9.1, 6.0 Hz, OC*H*H'), 3.97 (1H, *J* = 9.1, 4.7 Hz, OCH*H'*), 3.78 (3H, s, CO_2CH_3), 2.96 (1H, dd, *J* = 4.6, 3.7 Hz, PhCHC*H*), 2.59-2.52 (1H, m, CHCH_3), 1.15 (3H, d, *J* = 6.9 Hz, CH_3); **^{13}C NMR ($CDCl_3$, 125 MHz)** δ 171.4 (*C*=O), 169.0 (*C*=O), 138.6 (*Ar*), 129.1 (*Ar*), 129.0 (*Ar*), 122.5 (*Ar*), 87.5 (C_{quat}), 84.5 (Ph*C*H), 66.0 (CH_2), 61.4 (PhCH*C*H), 53.4 (O*C*H_3), 41.2 (*C*HCH_3), 17.5 (CH*C*H_3); **ν_{max}** 2959 (w, C-H), 1780 (s, C=O), 1732 (s, C=O), 725 (w), 699 (w); **m/z** (ESI^+) 299.0 ($[M+Na]^+$, 100%), 575.0 ($[2M+Na]^+$, 75%); **HRMS-ESI** calculated for $C_{15}H_{16}NaO_5$: *m/z* 299.0890 ($[M+Na]^+$), found: *m/z* 299.0886 ($[M+Na]^+$).

The clean sample of minor diastereoisomer **10d$_{min}$** (3 mg) was submitted for NMR and NOESY analysis: **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 7.44-7.34 (5H, m, ArH), 5.43 (1H, d, *J* = 6.2, C*H*Ph), 4.38 (1H, dd, *J* = 8.7, 7.1, OC*H*H'), 3.84 (3H, s, OCH_3), 3.75 (1H, dd, *J* = 10.7, 8.7, OCH*H'*), 3.36 (1H, dd, *J* = 7.1, 6.2, C*H*CHPh), 2.63—2.52 (1H, dsex, *J* = 10.7, 7.1 Hz, C*H*CH_3), 1.05 (3H, d, *J* = 7.1, $CHCH_3$); **^{13}C NMR ($CDCl_3$,**

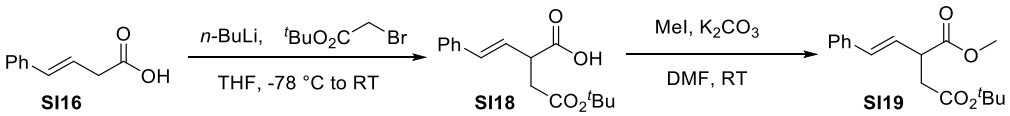
125 MHz) δ 171.2 (*C*=O), 168.7 (*C*=O), 138.7 (*Ar*), 129.2 (*Ar*), 129.2 (*Ar*), 126.5 (*Ar*), 88.4 (C_{quat}), 79.3 (Ph*C*H), 75.8 (CH_2), 57.4 (PhCH*C*H), 53.5 (OCH_3), 36.9 ($CHCH_3$), 10.9 ($CHCH_3$).



Key nOe interactions
Major diastereoisomer

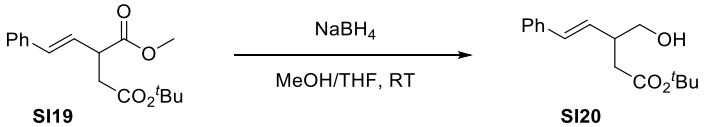
Key nOe interactions
Minor diastereoisomer

4-(*tert*-Butyl) 1-methyl (*E*)-2-styrylsuccinate (SI19)



To a solution of trans-styrylacetic acid (1.50 g, 9.25 mmol) in THF (24 mL) at -78 °C was added a solution of *n*-BuLi in hexanes (2.5 M, 8.14 mL, 20.4 mmol) over 5 min. The mixture was stirred for 10 min and *tert*-butyl bromoacetate (4.1 mL, 28 mmol) was added over 5 min. The reaction mixture was warmed to room temperature outside the cooling bath and stirred for 3 h. The mixture was quenched at 0° C with aqueous NaOH (0.5 M, 40 mL), Et_2O was added (40 mL). Layers were separated and the organic phase was extracted with more aqueous NaOH (0.5 M, 20 mL). The combined aqueous layers were treated with pH 2 sulphate buffer (15 mL) and acidified by dropwise addition of conc. aqueous HCl until pH 2. The acidified aqueous layers was extracted with Et_2O. The combined layers were dried (Na_2SO_4), filtered and evaporated to give the crude carboxylic acid **SI18** (3.07 g). The residual oil was dissolved in dry DMF and treated upon stirring at room temperature with K_2CO_3 (3.83 g, 27.8 mmol) and MeI (1.43 mL, 23.1 mmol). The reaction was stirred for 16 h at room temperature and was then diluted with EtOAc (50 mL) and PE (50 mL). The mixture was washed with H_2O (2 x 100 mL) and brine (50 mL), dried (Na_2SO_4), filtered and evaporated. The residue was purified 2 times by Flash Chromatography ($PE_{30\text{-}40}/Et_2O$ 9:1) to give the titled compound **SI19** as a colourless oil (520 mg, 1.79 mmol, 19% over 2 steps). **R_f** 0.32 (PE/Et_2O 8:1); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.36-7.28 (4H, m, Ar*H*), 7.27-7.20 (1H, m, Ar*H*), 6.53 (1H, d, *J* = 15.9 Hz, PhC*H*=CH), 6.18 (1H, dd, *J* = 15.9, 8.6 Hz, PhCH=C*H*), 3.73 (3H, s, CO_2CH_3), 3.64 (1H, tdd, *J* = 8.6, 6.0, 1.0 Hz, C*H*CH_2), 2.86 (1H, *J* = 16.4, 8.6 Hz, C*H*H'), 2.56 (1H, dd, *J* = 16.4, 6.0 Hz, CH*H*'), 1.6 (9H, s, $OC(CH_3)_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ) 173.5 (*C*=O), 170.6 (*C*=O), 136.6 (*Ar*), 133.1 (Ph*C*H=CH), 128.7 (*Ar*), 127.9 (*Ar*), 126.5 (*Ar*), 125.7 (PhCH=C*H*), 81.2 (C_{quat}), 52.3 (CH_3), 45.4 (*C*H), 37.8 (CH_2), 28.2 ($OC(CH_3)_3$); **ν_{max}** 2978 (w, C-H), 1729 (s, C=O), 1254 (w), 1148 (s), 745 (w, =C-H), 694 (w, =C-H); **m/z** (ESI^+) 313.1 ($[M+Na]^+$, 100%); **HRMS-ESI** calculated for $C_{17}H_{22}NaO_4$: *m/z* 313.1410 ($[M+Na]^+$), found: *m/z* 313.1417 ($[M+Na]^+$).

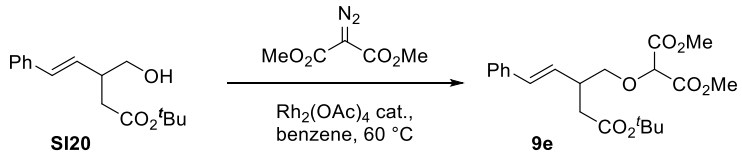
tert-Butyl (*E*)-3-(hydroxymethyl)-5-phenylpent-4-enoate (SI20)



To a solution 4-(*tert*-butyl) 1-methyl (*E*)-2-styrylsuccinate (418 mg, 1.44 mmol) in THF/MeOH (1:1, 10 mL) was added $NaBH_4$ (272 mg) in three portions. The reaction mixture was stirred for 30 min and

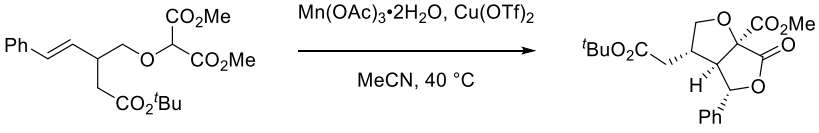
quenched with aqueous NH_4Cl (2.0 M, 30 mL), the mixture was extracted with Et_2O (3 x 20 mL) and the combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by Flash Chromatography ($PE_{30\text{-}40}/Et_2O$ 1:2) to give desired product **SI20** as colourless oil (334 mg, 1.27 mmol, 88%); $\mathbf{R_f}$ 0.38 ($PE_{30\text{-}40}/Et_2O$ 1:1); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.37-7.27 (4H, m, Ar*H*), 7.25-7.18 (1H, m, Ar*H*), 6.52 (1H, d, *J* = 16.0 Hz, PhC*H*=CH), 6.08 (1H, dd, *J* = 16.0, 8.5 Hz, PhCH=C*H*), 3.65 (2H, d, *J* = 5.9 Hz, CH_2OH), 2.94-2.84 (1H, m, C*H*), 2.50 (1H, dd, *J* = 14.9, 6.6 Hz, C*H*H'$CO_2{}^t$Bu), 2.37 (1H, dd, *J* = 14.9, 7.6 Hz, CH*H'*$CO_2{}^t$Bu), 1.99 (1H, br, OH), 1.43 (9H, s, OC(CH_3)$_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 172.0 (*C*=O), 137.0 (*Ar*), 132.4 (Ph*C*H=CH), 129.4 (PhCH=*C*H), 128.7 (*Ar*), 127.6 (*Ar*), 126.3 (*Ar*), 80.9 (C_{quat}), 65.7 (*C*H_2OH), 42.7 (*C*H), 38.0 (*C*$H_2CO_2{}^t$Bu), 28.2 (OC(*C*H_3)$_3$); $\mathbf{\nu_{max}}$ 3248 (br, OH), 2978 (w, C-H), 1724 (m, C=O), 1148 (s), 748 (w, =C-H); **m/z** (ESI$^+$) 285.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{16}H_{22}NaO_3$: *m/z* 285.1461 ([M+Na]$^+$), found: *m/z* 285.1460 ([M+Na]$^+$).

(*E*)-Dimethyl 2-((2-(2-(*tert*-butoxy)-2-oxoethyl)-4-phenylbut-3-en-1-yl)oxy)malonate (9e)



The title compound was prepared according to the general procedure 1 using *tert*-butyl (*E*)-3-(hydroxymethyl)-5-phenylpent-4-enoate **SI20** (370 mg, 1.42 mmol) and dimethyl 2-diazomalonate (237.2 mg, 1.49 mmol). Flash Chromatography purification ($PE_{30\text{-}40}/Et_2O$ 3:1) gave the desired product **9e** as a colourless oil (284 mg, 0.724 mmol, 51%). $\mathbf{R_f}$ 0.42 (PE/Et_2O 3:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.37-7.25 (4H, m, Ar*H*), 7.25-7.16 (1H, m, Ar*H*), 6.50 (1H, d, *J* = 16.0 Hz, PhC*H*=CH), 6.11 (1H, dd, *J* = 16.0, 8.3 Hz, PhCH=C*H*), 4.54 (1H, s, OC*H*), 3.80 (3H, s, OCH_3), 3.79 (3H, s, OCH_3), 3.69 (1H, dd, *J* = 9.1, 5.6 Hz, C*H*H'O), 3.60 (1H, dd, *J* = 9.1, 5.6 Hz, CH*H'*O), 3.05 (1H, m, *CH*CH_2), 2.67 (1H, dd, *J* = 15.2, 5.4 Hz, C*H*H'$CO_2{}^t$Bu), 2.36 (1H, dd, *J* = 15.2, 8.8 Hz, CH*H'*$CO_2{}^t$Bu), 1.40 (9H, s, OC(CH_3)$_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 171.4 (*C*=O), 166.9 (*C*=O), 137.1 (*Ar*), 131.9 (Ph*C*H=CH), 128.7 (PhCH=*C*H), 128.5 (*Ar*), 127.4 (*Ar*), 126.3 (*Ar*), 80.5 (C_{quat}), 79.1 (O*C*H), 73.9 (O*C*H_2), 52.9 (O*C*H_3), 39.8 (*C*H(CH_2)$_2$), 37.8 (*C*$H_2CO_2{}^t$Bu), 28.1 (OC(*C*H_3)$_3$); $\mathbf{\nu_{max}}$ 2977 (w, C-H), 1747 (s, C=O), 1723 (s, C=O), 1240 (m), 1149 (s), 751 (w, =C-H); **m/z** (ESI$^+$) 415.2 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{21}H_{28}NaO_7$: *m/z* 415.1727 ([M+Na]$^+$), found: *m/z* 415.1732 ([M+Na]$^+$).

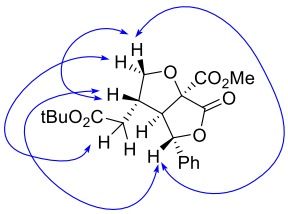
(3*S**,3a*R**,4*S**,6a*S**)-Methyl 3-(2-(*tert*-butoxy)-2-oxoethyl)-6-oxo-4-phenyltetrahydrofuro[3,4-*b*]furan-6a(6*H*)-carboxylate (10e)



Crude d.r. = 6.7:1:0.7:0.4

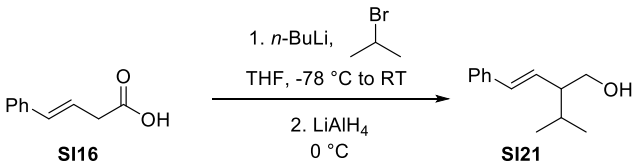
The title compound was prepared according to the general procedure 3 using dimethyl (*E*)-2-((2-(2-(*tert*-butoxy)-2-oxoethyl)-4-phenylbut-3-en-1-yl)oxy)malonate (62 mg, 0.158 mmol). Flash Chromatography purification ($PE_{30\text{-}40}/Et_2O$ 3:2) gave the desired product **10e** as a colourless oil (41 mg, 0.109 mmol, 69%) as a mixture of diastereoisomers. As second purification gave the clean major diasteroisomer **10e**. $\mathbf{R_f}$ 0.32 (PE/Et_2O 3:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.44-7.32 (5H, m, Ar*H*), 5.36

(1H, d, *J* = 4.8 Hz, PhC*H*), 4.30 (1H, dd, *J* = 9.3, 6.1 Hz, OC*H*H'), 4.05 (1H, dd, *J* = 9.3, 4.0 Hz, OCH*H'*), 3.79 (3H, s, OCH_3), 3.04 (1H, dd, *J* = 4.8, 3.0 Hz, CHC*H*CH), 2.86 (1H, tddd, *J* = 7.6, 6.1, 4.0, 3.0 Hz, C*H*$CH_2CO_2{}^t$Bu), 2.46 (1H, dd, *J* = 16.4, 7.6 Hz, C*H*H'$CO_2{}^t$Bu), 2.33 (1H, dd, *J* = 16.4, 7.6 Hz, CH*H'*$CO_2{}^t$Bu), 1.36 (9H, s, OC(CH_3)$_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 171.1 (*C*=O), 170.5 (*C*=O), 168.7 (*C*=O), 138.5 (*Ar*), 129.1 (*Ar*), 129.0 (*Ar*), 125.8 (*Ar*), 87.6 (C_{quat}), 84.6 (Ph*C*H), 81.7 (C_{quat}), 75.2 (OCH_2), 59.4 (CH*C*HCH), 53.5 (OCH_3), 43.0 (*C*H$CH_2CO_2{}^t$Bu), 38.0 (*C*$H_2CO_2{}^t$Bu), 28.1 (OC(*C*H_3)$_3$); **ν_{max}** 2978 (w, C-H), 1783 (s, C=O), 1761 (m, C=O), 1722 (m, C=O), 1152 (s), 726 (w, =C-H); **m/z** (ESI$^+$) 399.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{20}H_{24}NaO_7$: *m/z* 399.1414 ([M+Na]$^+$), found: *m/z* 399.1421 ([M+Na]$^+$).



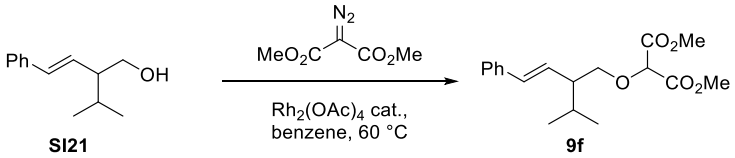
Key nOe interactions

(*E*)-2-isopropyl-4-phenylbut-3-en-1-ol (SI21)



The title compound was prepared according to the general procedure 2 using trans-styrylacetic acid (1.50 g, 9.25 mmol) and 2-bromopropane (2.77 mL, 29.5 mmol, 3 eq.). The stirring period at room temperature was 3 h. Two successive Flash Chromatography purifications (PE_{30-40}/ Et_2O 3:1) gave the titled compound **SI21** as a colourless oil (540 mg, 2.84 mmol, 31%). **R_f** 0.27 (PE/Et_2O 3:1); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.42-7.38 (2H, m, Ar*H*), 7.36-7.30 (2H, m, Ar*H*), 7.26-7.22 (1H, m, Ar*H*), 6.50 (1H, d, *J* = 15.8 Hz, Ar-C*H*=CH), 6.05 (1H, dd, *J* = 15.8, 9.3 Hz, Ar-CH=C*H*), 3.76 (1H, dd, *J* = 10.7, 4.9 Hz, C*H*H'OH), 3.56 (1H, dd, *J* = 10.7, 9.1 Hz, CH*H'*OH), 2.25-2.14 (1H, m, C*H*CH(CH_3)$_2$), 1.84-1.72 (1H, m, CHC*H*(CH_3)$_2$), 0.97 (3H, d, *J* = 6.9 Hz, CH_3), 0.84 (3H, d, *J* = 6.9 Hz, CH_3); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 137.2 (Ar-*C*H=CH), 133.6 (Ar-CH=*C*H), 129.8 (*Ar*), 128.7 (*Ar*), 127.5 (*Ar*), 126.3 (*Ar*), 64.4 (*C*H_2OH), 53.1 (*C*HCH(CH_3)$_2$), 29.3 (CHC*H*(CH_3)$_2$), 21.1 (*C*H_3), 19.8 (*C*H_3); **ν_{max}** 3349 (br, OH), 2957 (m, C-H), 967 (m), 746 (s, =C-H), 693 (s, =C-H); **m/z** (ESI$^+$) 213.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{13}H_{18}NaO$: *m/z* 213.1250 ([M+Na]$^+$), found: *m/z* 213.1248 ([M+Na]$^+$). Data are in agreement with literature.[9]

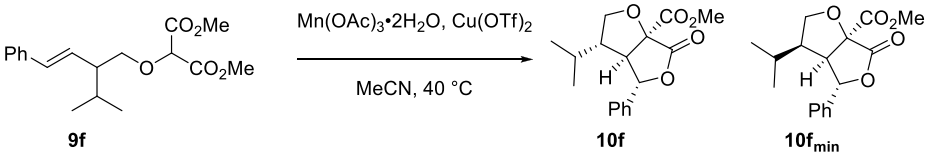
(*E*)-Dimethyl 2-((2-isopropyl-4-phenylbut-3-en-1-yl)oxy)malonate (9f)



The title compound was prepared according to the general procedure 1 using (*E*)-2-isopropyl-4-phenylbut-3-en-1-ol (476 mg, 2.50 mmol) and dimethyl 2-diazomalonate (418 mg, 2.63 mmol). Flash Chromatography purification (PE_{30-40}/Et_2O 4:1 to 3:1) gave the compound **9f** as a colourless oil (590 mg, 1.84 mmol, 74%). **R_f** 0.38 (PE/Et_2O 7:3); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.40-7.30 (2H, m, Ar*H*), 7.28-7.21 (2H, m, Ar*H*), 7.20-7.16 (1H, m, Ar*H*), 6.44 (1H, d, *J* = 15.8 Hz, Ar-C*H*=CH), 6.09 (1H, dd, *J* =

15.8, 9.1 Hz, Ar-CH=C*H*), 4.52 (1H, s, OC*H*(CO_2Me)$_2$), 3.79 (3H, s, OCH_3), 3.77 (3H, s, OCH_3), 3.70 (1H, dd, *J* = 9.2, 6.4 Hz, C*H*H'OCH), 3.65 (1H, dd, *J* = 9.2, 6.4 Hz, CH*H*'OCH), 2.46-2.36 (1H, dtdd, *J* = 9.1, 6.4, 5.5, 0.9 Hz, C*H*CH(CH_3)$_2$), 1.97 (1H, qnd, *J* = 6.8 and 5.5, C*H*(CH_3)$_2$), 0.96 (3H, d, *J* = 6.8 Hz, CH_3), 0.91 (3H, d, *J* = 6.8 Hz, CH_3); **^{13}C NMR ($CDCl_3$, 100 MHz)** *δ* 167.2 (*C*=O), 167.1 (*C*=O), 137.7 (Ar-*C*H=CH), 132.5 (Ar-CH=*C*H), 128.9 (*Ar*), 128.6 (*Ar*), 127.2 (*Ar*), 126.3 (*Ar*), 79.4 (CH_2*O*CH), 73.4 (*C*H_2OCH), 52.9 (O*C*H_3), 49.4 (*C*HCH(CH_3)$_2$), 28.7 (CH*C*H(CH_3)$_2$), 21.0 (*C*H_3), 18.7 (*C*H_3); **ν_{max}** 2957 (w, C-H), 1748 (s, C=O), 1139 (m), 749 (w, =C-H), 695 (w, =C-H); **m/z** (ESI$^+$) 343.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{18}H_{24}NaO_5$: *m/z* 343.1516 ([M+Na]$^+$), found: *m/z* 343.1531 ([M+Na]$^+$).

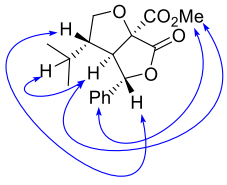
(3*S**,3a*R**,4*S**,6a*S**)-Methyl 3-isopropyl-6-oxo-4-phenyltetrahydrofuro[3,4-*b*]furan-6a(6*H*)-carboxylate (10f)



9f **10f** **10f$_{min}$**

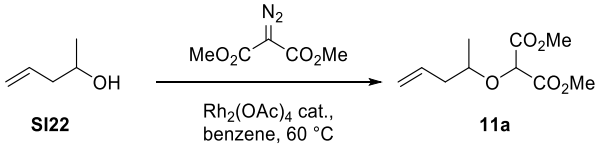
Crude d.r. = 28:1 (**10f**:**10f$_{min}$**)

The title compound was prepared according to the general procedure 2 using dimethyl (*E*)-2-((2-isopropyl-4-phenylbut-3-en-1-yl)oxy)malonate (84.0 mg, 0.26 mmol). Flash Chromatography purification (PE/Et_2O 2:3) gave the product **10f** (73.0 mg, 0.24 mmol, 92%). Characterisation is given for the major diastereoisomer only. **R_f** 0.24 (3:2 PE/ Et_2O); **^{1}H NMR ($CDCl_3$, 400 MHz)** *δ* 7.44-7.34 (5H, m, Ar*H*), 5.28 (1H, d, *J* = 4.7 Hz, C*H*Ph), 4.33 (1H, dd, *J* = 9.1, 7.1 Hz, OC*H*H'), 4.02 (1H, dd, *J* = 9.1, 7.1 Hz, OCH*H*'), 3.78 (3H, s, CO_2CH_3), 3.11 (1H, t, *J* = 4.7 Hz, PhCHC*H*), 2.23 (1H, dtd, *J* = 8.9, 7.1, 4.7 Hz, C*H*CH(CH_3)$_2$), 1.60 (1H, dsep, *J* = 8.9, 6.7 Hz, C*H*(CH_3)$_2$), 0.88 (3H, d, *J* = 6.7 Hz, CHCH_3), 0.83 (3H, d, *J* = 6.7 Hz, CHCH_3); **^{13}C NMR ($CDCl_3$, 100 MHz)** *δ* 170.9 (*C*=O), 169.2 (*C*=O), 138.2 (*Ar*), 129.1 (*Ar*), 129.0 (*Ar*), 126.1 (*Ar*), 88.3 (C_{quat}), 86.2 (*C*HPh), 75.2 (OCH_2), 58.1 (PhCHC*H*), 55.2 (*C*HCH(CH_3)$_2$), 53.3 (CO_2*C*H_3), 30.4 (*C*H(CH_3)$_2$), 21.4 (CH*C*H_3), 21.0 (CH*C*H_3); **ν_{max}** 2959 (w, C-H), 1782 (s, C=O), 1760 (m, C=O), 1731 (w, C=O), 699 (w); **m/z** (ESI$^+$) 327.1 ([M+Na]$^+$, 100%), 631.3 ([2M+Na]$^+$, 80%); **HRMS-ESI** calculated for $C_{17}H_{20}NaO_5$: *m/z* 327.1203 ([M+Na]$^+$), found: *m/z* 327.1212 ([M+Na]$^+$). The relative configuration of the minor diastereomer was assigned by comparison with the diastereomers of **10d.**



Key nOe interactions

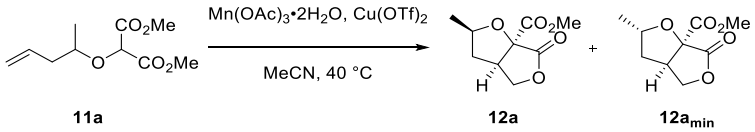
Dimethyl 2-(pent-4-en-2-yloxy)malonate (11a)



SI22 **11a**

The title compound was prepared according to the general procedure 1 using **SI22** (0.3 mL, 2.91 mmol) and dimethyl 2-diazomalonate (500 mg, 3.16 mmol). Flash Chromatography purification (PE40-60/EtOAc 9:1) gave the title compound **11a** as a colourless oil (420 mg, 1.94 mmol, 67%). $\mathbf{R_f}$ 0.40 (PE40-60/EtOAc 8:2); **^{1}H NMR (CDCl3, 400 MHz)** δ 5.77 (1H, ddt, *J* = 17.2, 10.1, 7.1 Hz, CH_2=C*H*), 5.05 (1H, dd, *J* = 17.2, 1.9 Hz, C*H*H=CH), 5.02 (1H, dd, *J* = 10.1, 1.9 Hz, CH*H*=CH), 4.57 (3H, s, CO_2Me), 3.76 (3H, s, CO_2Me), 3.60 (1 H, sex, *J* = 6.2 Hz, OC*H*CH_3), 2.37 (1 H, dddt, *J* = 14.1, 6.9, 5.7, 1.3 Hz, CHC*H*HCH), 2.20 (1H, dddt, *J* = 14.1, 7.5, 6.5, 1.1 Hz, CHCH*H*CH), 1.18 (3H, d, *J* = 6.2 Hz, CH_3); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 167.6 (*C*=O), 167.4 (*C*=O), 134.1 (CH_2=*C*H), 117.5 (*C*H_2=CH), 77.3 (O*C*H(CO_2Me)$_2$), 77.1 (O*C*H(CO_2Me)$_2$), 52.9 (CO_2*Me*), 52.8 (CO_2*Me*), 40.6 (CH*C*H_2), 19.4 (CH*C*H_3); $\mathbf{\nu_{max}}$ 2957 (w, C-H), 1747 (s, C=O), 1120 (m), 1022 (m), 917 (w); **m/z (ESI$^+$)** 239.1 ([M+Na]$^+$, 100%), 455.2 ([2M+Na]$^+$, 12 %); **HRMS-ESI** calculated for $C_{10}H_{16}NaO_5$: *m/z* 239.0890 ([M+Na]$^+$), found: *m/z* 239.0901 ([M+Na]$^+$).

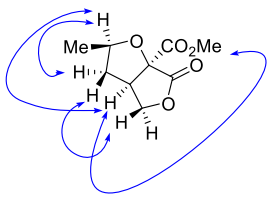
(2*R**,3a*R**,6a*)-Methyl 2-methyl-6-oxohexahydrofuro[3,4-*b*]furan-6a-carboxylate (12a)



11a **12a** **12a$_{min}$**

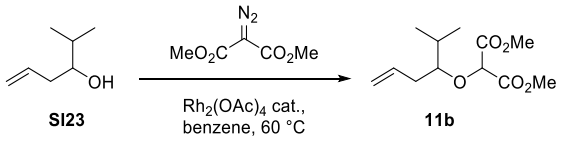
Crude d.r. = 6.1:1 (**12a:12a$_{min}$**)

The title compound was prepared according to the general procedure 3 using **11a** (50 mg, 0.23 mmol). The reaction mixture was stirred overnight at 40 °C. Flash Chromatography purification (PE_{40-60}/EtOAc 8:2 to 6:4) gave the title compound **12a** as a colourless oil (45 mg, 0.22 mmol, 96%). Characterisation is given for the major diastereoisomer. $\mathbf{R_f}$ 0.10 (PE_{40-60}/EtOAc 6:4); **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 4.52 (1H, dd, *J* = 9.4, 6.6 Hz, CO_2C*H*'CH), 4.38 (1H, dqd, *J* = 10.6, 6.0, 4.6 Hz, OC*H*CH_2), 4.23 (1H, dd, *J* = 9.4, 1.6 Hz, CO_2CH*H*'CH), 3.82 (s, CO_2Me), 3.31 (1H, dddd, *J* = 9.9, 8.3, 6.6, 1.6 Hz, CH_2C*H*CH_2), 2.48 (1H, ddd, *J* = 12.6, 8.3, 4.6 Hz, CHC*H*H'CH), 1.56 (1H, dt, *J* = 12.6, 10.1 Hz, CHCH*H*'CH), 1.36 (3H, d, *J* = 6.0 Hz, CH_3) ; **^{13}C NMR ($CDCl_3$, 125 MHz)** δ 172.1 (*C*=O), 169.1 (*C*=O), 86.3 (C_{quat}), 80.8 (O*C*HCH_2), 70.2 (CO_2*C*H_2CH), 53.3 (CO_2Me), 46.9 (CO_2CH_2*C*H), 40.6 (CH*C*H_2CH), 19.9 (CH_3); $\mathbf{\nu_{max}}$ 2978 (w), 1779 (s, C=O), 1760 (s, C=O), 1114 (m), 1037 (s); **m/z** (ESI$^+$) 201.1 ([M+H]$^+$, 16%), 223.1 ([M+Na]$^+$, 62%), 423.1 ([2M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_9H_{12}NaO_5$: *m/z* 223.0577 ([M+Na]$^+$), found: *m/z* 223.0585 ([M+Na]$^+$).



Key nOe interactions

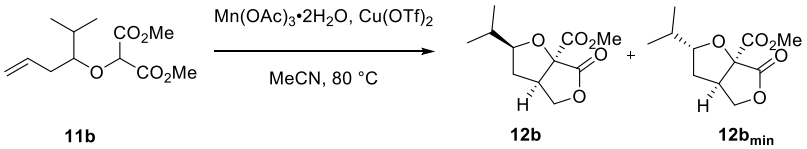
Dimethyl 2-((2-methylhex-5-en-3-yl)oxy)malonate (11b)



SI23 11b

The title compound was prepared according to the general procedure 1 using 2-methyl-5-hexen-3-ol (300 mg, 2.62 mmol) and dimethyl 2-diazomalonate (440 mg, 2.78 mmol, 1.06 eq.). Flash Chromatography purification (PE_{40-60}/EtOAc 80:20) gave the title compound **11b** as a colourless oil (435 mg, 1.78 mmol, 68%). $\mathbf{R_f}$ 0.52 (PE/EtOAc 8:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.84 (1H, ddt, *J* = 17.2, 10.1, 7.1 Hz, CH_2=C*H*), 5.05 (1H, dd, *J* = 17.2, 0.9 Hz, C*H*'=CH), 5.02 (1H, dd, *J* = 10.1, 0.9 Hz, CH*H'*=CH), 4.55 (1H, s, OC*H*(CO_2Me)$_2$), 3.76 (6H, s, OC*H*$_3$), 3.24 (1H, q, *J* = 5.5 Hz, C*H*CH(CH_3)$_2$), 2.33-2.21 (2H, m, C*H*$_2$CHO), 1.91-1.80 (1H, m, C*H*(CH_3)$_2$), 0.92 (3H, d, *J* = 6.8 Hz, CHC*H*$_3$), 0.89 (3H, d, *J* = 6.8 Hz, CHC*H*$_3$). **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 167.6 (2×*C*=O), 134.8 (CH_2=*C*H), 117.2 (*C*H_2=CH), 86.9 (O*C*H(CO_2Me)$_2$), 78.7 (O*C*HCH$_2$), 52.8 (2×CO_2Me), 35.1 (OCH*C*H$_2$), 31.0 (*C*H(CH_3)$_2$), 18.1 (CH_3), 18.0 (CH_3); $\mathbf{\nu_{max}}$ 2958 (w, C-H), 1746 (s, C=O), 1118 (m), 1022 (m), 916 (w); **m/z** (ESI$^+$) 267.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{12}H_{20}NaO_5$: *m/z* 267.1203 ([M+Na]$^+$), found: *m/z* 267.1211 ([M+Na]$^+$).

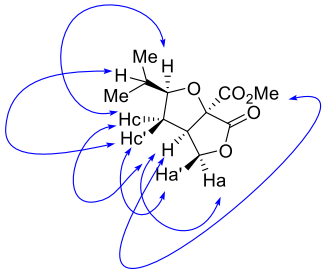
(2*S**,3a*R**,6a*S**)-Methy 2-isopropyl-6-oxohexahydrofuro[3,4-*b*]furan-6a-carboxylate (12b)



11b 12b 12b$_{min}$

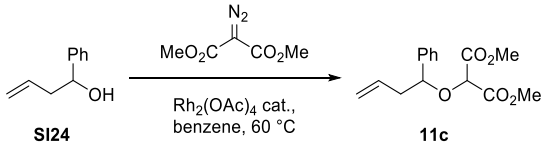
Crude d.r. = 5.7:1 (**12b:12bmin**)

The title compound was prepared according to the general procedure 3 using **11b** (61 mg, 0.25 mmol). The reaction mixture was stirred overnight at 40 °C. Flash Chromatography purification (PE_{40-60}/EtOAc 8:2 to 6:4) gave the clean compound **12b** as a colourless oil (23 mg, 0.10 mmol, 40%) and a mixture of the two diastereoisomers (31 mg, 0.136 mmol, 54%). Characterisation is given for the major diastereoisomer only. $\mathbf{R_f}$ 0.23 (PE/EtOAc 6:4); **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 4.52 (1H, dd, *J* = 9.4, 6.4 Hz, CO_2C*H*H'), 4.22 (1H, dd, *J* = 9.4, 1.2 Hz, CO_2CH*H'*), 4.03 (1H, ddd, *J* = 11.0, 6.8, 4.7 Hz, OC*H*CH(CH_3)$_2$), 3.82 (3H, s, CO_2*Me*), 3.29 (1H, m, CO_2CHH'C*H*), 2.38 (1H, ddd, *J* = 12.7, 8.3, 4.7 Hz, CHCH*H'*CH), 1.87 (1H, oct, *J* = 6.8 Hz, OCHC*H*(CH_3)$_2$), 1.63 (1H, m, CHC*H*H'CH), 1.00 (3H, d, *J* = 6.8 Hz, CH(*CH*$_3$)$_2$), 0.89 (3H, d, *J* = 6.8 Hz, CH(*CH*$_3$)$_2$); **^{13}C NMR ($CDCl_3$, 125 MHz)** δ 172.1 (*C*=O), 169.2 (*C*=O), 89.7 (O*C*HCH(CH_3)$_2$), 86.2 (C_{quat}), 70.2 (CO_2CH_2CH), 53.3 (CO_2*Me*), 46.5 (CO_2CHH'*C*H), 35.7 (CH*C*HH'CH), 32.1 (*C*H(CH_3)$_2$), 19.2 (CH*C*H$_3$), 17.9 (CH*C*H$_3$); $\mathbf{\nu_{max}}$ 2961 (w), 1780 (s, C=O), 1760 (s, C=O); 1117 (m), 1033 (s), 982 (s); **m/z** (ESI$^+$) 479.2([2M+Na]$^+$, 100%); 251.1 ([M+Na]$^+$, 75%); 229.1 ([M+H]$^+$, 21%); **HRMS-ESI** calculated for $C_{11}H_{16}NaO_5$: *m/z* 251.0890 ([M+Na]$^+$), found: *m/z* 251.0895 ([M+Na]$^+$).



Key nOe interactions

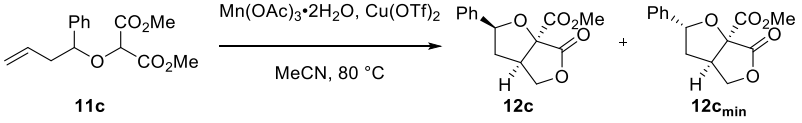
Dimethyl 2-((1-phenylbut-3-en-1-yl)oxy)malonate (11c)



SI24 **11c**

The title compound was prepared according to the general procedure 1 using 4-phenyl-1-butene-4-ol 0.4 mL, 2.68 mmol) and dimethyl 2-diazomalonate (450 mg, 2.85 mmol, 1.05 eq.). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 80:20) gave the title compound **11c** as a colourless oil (635 mg, 2.28 mmol, 85%). $\mathbf{R_f}$ 0.40 (PE/EtOAc 8:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.32-7.23 (5H, Ar*H*), 5.73 (1H, tdd, *J* = 7.0, 10.2, 17.1 Hz, CH_2=C*H*), 5.00 (1H, dd, *J* = 17.1, 1.5 Hz, C*H*H'=CH), 4.96 (1H, dd, *J* = 10.2, 1.5 Hz, CH*H'*=CH), 4.41 (1H, t, *J* = 6.8 Hz, OC*H*CH_2), 4.35 (1H, s, C*H*$(CO_2Me)_2$), 3.74 (3H, s, CO_2*Me*), 3.63 (3H, s, CO_2*Me*), 2.72 (1H, m, C*H*H'CHO), 2.44 (1H, m, CH*H'*CHO); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 167.6 (*C*=O), 166.7 (*C*=O), 139.5 (C_{quat}), 134.0 (CH_2=*C*H), 128.7 (2×C_{Ar}), 128.5 (C_{Ar}), 127.3 (2×C_{Ar}), 117.5 (CH_2=CH), 82.9 (OCH$(CO_2Me)_2$), 76.6 (OCHPh), 52.8 (2×CO_2Me), 42.2 (CH*C*H2); $\mathbf{\nu_{max}}$ 2955 (w, C-H), 1745 (s, C=O), 1117 (m), 1022 (m), 918 (w), 702 (s); **m/z** (ESI$^+$) 301.1 ([M+Na]$^+$, 100%), 579 ([2M+Na]$^+$, 17%); **HRMS-ESI** calculated for $C_{15}H_{18}NaO_5$: *m/z* 301.1046 ([M+Na]$^+$), found: *m/z* 301.1045 ([M+Na]$^+$).

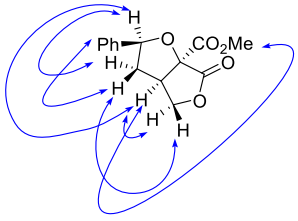
(2*S**,3a*R**,6a*S**)-Methyl 6-oxo-2-phenylhexahydrofuro[3,4-*b*]furan-6a-carboxylate (12c)



11c **12c** **12c$_{min}$**

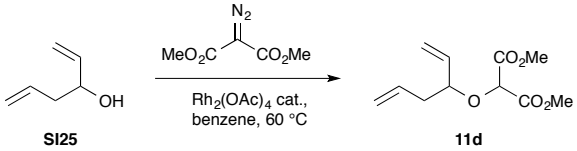
Crude d.r. = 7.5:1 (**12c:12c$_{min}$**)

The title compound was prepared according to the general procedure 3 using **11c** (70 mg, 0.25 mmol). The reaction mixture was stirred overnight at 40 °C. Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 8:2 to 6:4) gave the title compound **12c** as a mixture of two diastereoisomers (52 mg, 0.19 mmol, 80%). A second purification led to the pure major diastereoisomer as a white solid. Characterisation is given for the major diastereoisomer only. $\mathbf{R_f}$ 0.15 ($PE_{40\text{-}60}$/EtOAc 6:4); **m. p.** 98-102 °C; **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 7.27-7.19 (5H, Ar*H*), 5.24 (1H, dd, *J* = 10.6, 5.1 Hz, OC*H*Ph), 4.49 (1H, dd, *J* = 9.5, 6.4 Hz, CO_2C*H*H'), 4.17 (1H, dd, *J* = 9.5, 1.6 Hz, CO_2CH*H'*), 3.79 (3H, s, CO_2*Me*), 3.89 (1H, dddd, *J* = 10.1, 6.4, 8.1, 1.6 Hz, CH_2*C*HCH_2), 2.69 (ddd, *J* = 12.9, 8.1, 5.1 Hz, CHC*H*H'CH), 1.83 (1H, td, *J* = 10.1, 12.9 Hz, CHCH*H'*CH); **^{13}C NMR ($CDCl_3$, 125 MHz)** δ 171.8 (*C*=O), 168.9 (*C*=O), 138.9 (C_{quat}), 128.7 (2×C_{Ar}), 128.4 (C_{Ar}), 125.8 (2×C_{Ar}), 86.5 (*C*$_{quat}$), 85.6 (OCHPh), 69.8 (CO_2*C*H_2CH), 53.4 (CO_2*Me*), 46.8 (CO_2CHH'*C*H), 41.7 (CH*C*HH'CH); $\mathbf{\nu_{max}}$ 2920 (w), 1782 (s, C=O), 1743 (s), 1275 (m), 1106 (w), 761 (s), 714 (s) ; **m/z** (ESI$^+$) 285.1 ([M+Na]$^+$, 47%), 547.2 ([2M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{14}H_{14}O_5Na$: *m/z* 285.0733 ([M+Na]$^+$), found: *m/z* 285.0736 ([M+Na]$^+$).



Key nOe interactions

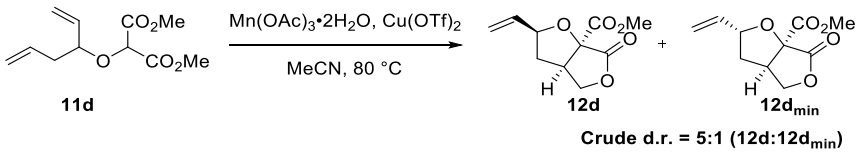
Dimethyl 2-(hexa-1,5-dien-3-yloxy)malonate (11d)



SI25 11d

The title compound was prepared according to the general procedure 1 using 1,5 hexadien-3-ol (0.3 mL, 2.68 mmol) and dimethyl 2-diazomalonate (460 mg, 2.91 mmol, 1.09 eq.). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 80:20) gave the title compound **11d** as a yellow oil (460 mg, 2.02 mmol, 75%). $\mathbf{R_f}$ 0.43 (PE/EtOAc 8:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.79 (1H, ddt, *J* = 17.2, 10.1, 7.0 Hz, CH_2=C*H*-CH_2), 5.65 (1H, ddd, *J* = 17.2, 10.3, 8.3 Hz, CH_2=C*H*-CH), 5.25 (1H, ddd, *J* = 10.3, 1.3, 0.6 Hz, C*H*H'=CH-CH), 5.20 (1H, ddd, *J* = 17.2, 1.5, 0.8 Hz, CH*H'*=CH-CH), 5.06 (1H, dd, *J* = 17.2, 1.8 Hz, C*H*H'=CHCH_2), 5.03 (1H, dd, *J* = 10.1, 1.8 Hz, CH*H'*=CH-CH_2), 4.55 (1H, s, OC*H*(CO_2Me)), 3.83 (1H, td, *J* = 6.6, 8.3 Hz, OC*H*CH_2), 3.77 (3H, s, CO_2*Me*), 3.74 (3H, s, CO_2*Me*), 2.51 (1H, dtt, *J* = 14.3, 6.6, 1.3 Hz, CHC*H*H'CH), 2.33 (1H, dddt, *J* = 14.2, 7.1, 6.7, 1.3, Hz, CH-CH*H'*-CH); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 167.5 (*C*=O), 167.1 (*C*=O), 136.5 (CH_2=*C*H), 133.7 (CH_2=*C*H), 119.6 (*C*H_2=CH), 117.5 (*C*H_2=CH), 82.3 (OCHCH_2), 76.4 (OC*H*(CO_2Me)$_2$), 52.9 (CO_2Me), 52.8 (CO_2Me), 39.6 (OCH*C*H_2); $\mathbf{\nu_{max}}$ 2956 (w, C-H), 1747 (s, C=O), 1123 (m), 1022 (m), 925 (w); **m/z** (ESI$^+$) 251.1 ([M+Na]$^+$, 100%), 479.2 ([2M+Na]$^+$, 12 %); **HRMS-ESI** calculated for $C_{11}H_{16}NaO_5$: *m/z* 251.0890 ([M+Na]$^+$), found: *m/z* 251.0897 ([M+Na]$^+$).

(2*S**,3a*R**,6a*S**)-Methyl 6-oxo-2-vinylhexahydrofuro[3,4-*b*]furan-6a-carboxylate (12d)

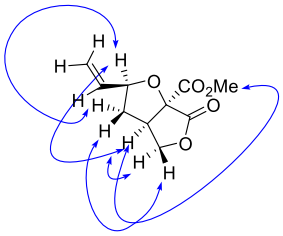


11d 12d 12d$_{min}$

Crude d.r. = 5:1 (12d:12d$_{min}$)

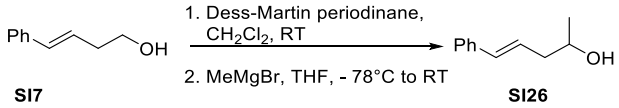
The title compound was prepared according to the general procedure 3 using **11d** (50 mg, 0.22 mmol). The reaction mixture was stirred overnight at 40 °C. Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 8:2 to 6:4) gave the title compound **12d** as a colourless oil (40 mg, 0.19 mmol, 86%). $\mathbf{R_f}$ 0.27 ($PE_{40\text{-}60}$/EtOAc 5:5); **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 5.86 (1H, ddd, *J* = 17.1, 10.5, 6.4 Hz, CH_2=C*H*), 5.37 (1H, dd, *J* = 17.1, 1.0 Hz, C*H*H'=CH), 5.21 (1H, dd, *J* = 10.5, 1.0 Hz, CH*H'*=CH), 4.75 (1H, dddt, *J* = 9.5, 6.4, 5.4, 1.1 Hz, OC*H*CH_2), 4.54 (1H, dd, *J* = 9.5, 6.7 Hz, CO_2C*H*H'), 4.24 (1H, dd, *J* = 9.5, 2.0 Hz, CO_2CH*H'*), 3.84 (3H, s, CO_2*Me*), 3.35 (1H, ddt, *J* = 6.7, 2.0, 8.5 Hz, CH_2C*H*CH_2), 2.54 (1H, ddd, *J* = 12.7, 8.5, 5.4 Hz, CHC*H*H'CH), 1.77 (1H, td, *J* = 9.5, 12.7 Hz, CHCH*H'*CH); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 171.8 (*C*=O), 168.9 (*C*=O), 135.7 (CH_2=*C*H), 118.1 (*C*H_2=CH), 86.3 (C_{quat}), 84.8 (OCHCH_2), 70.1 (CO_2*C*H_2CH), 53.4 (CO_2*Me*), 46.5 (CO_2CHH'*C*H), 38.9 (CH*C*HH'CH); $\mathbf{\nu_{max}}$ 2950 (w, C-H), 1779 (s, C=O), 1760 (s, C=O),

1264 (s), 1126 (m), 1035 (s) ; **m/z** (ESI$^+$) 235.1 ([M+Na]$^+$, 83%); 479.2 ([2M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{10}H_{12}NaO_5$: *m/z* 235.0577 ([M+Na]$^+$), found: *m/z* 235.0578 ([M+Na]$^+$).



Key nOe interactions

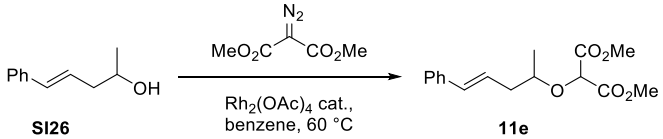
(*E*)-5-Phenylpent-4-en-2-ol (SI26)



SI7 **SI26**

To a solution of (*E*)-4-phenylbut-3-en-1-ol (270 mg, 1.82 mmol) in CH_2Cl_2 (9.5 mL) was added Dess-Martin periodinane (1.16 g, 2.73 mmol, 1.5 eq.). After stirring for 2 h, the reaction mixture was hydrolysed with a saturated aqueous solution of sodium hydrogen carbonate. The aqueous phase was extracted three times with diethyl ether. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was engaged in the next step without further purification. To a solution of the previous crude product in THF (9 mL) at - 78 °C was added dropwise MeMgBr (1.20 mL, 3 M in Et_2O, 3.60 mmol, 1.7 eq.). The solution was stirred for 30 min at - 78 °C and warmed up to room temperature overnight. The reaction mixture was hydrolysed with a saturated aqueous solution of ammonium chloride. The aqueous phase was extracted three times with diethyl ether. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography ($PE_{40\text{-}60}$/EtOAc 7:3) to give **11e** as a yellow oil (149 mg, 0.92 mmol, 51% over 2 steps). **R_f** 0.33 ($PE_{40\text{-}60}$/EtOAc 7:3); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.33-7.16 (5H, m, Ar*H*), 6.44 (1H, d, *J* = 15.9 Hz, PhC*H*=CH), 6.19 (1H, ddd, *J* = 15.9, 7.8, 6.8 Hz, PhCH=C*H*), 3.89 (1H, dqd, *J* = 7.3, 6.2, 5.0 Hz, C*H*CH_3), 2.37 (1H, dddd, *J* = 13.5, 6.8, 5.0, 1.4 Hz, C*H*H'), 2.29 (1H, *J* = 13.5, 8.7, 7.8, 1.2 Hz, C*H*H'), 1.21 (1H, d, *J* = 6.2 Hz, CH_3).

(*E*)-Dimethyl 2-(5-phenylpent-4-en-2-yloxy)malonate (11e)

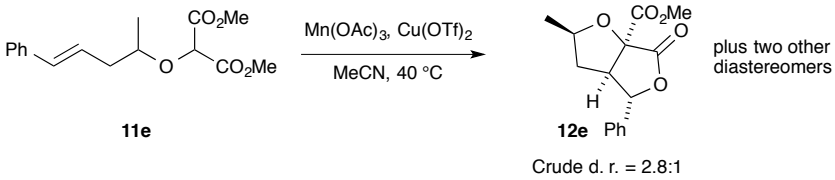


SI26 **11e**

The title compound was prepared according to the general procedure 1 using the alcohol **SI26** (115 mg, 0.71 mmol) and dimethyl 2-diazomalonate (127 mg, 0.80 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 9:1) gave the title compound **11e** as a yellow oil (172 mg, 0.59 mmol, 83%). **R_f** 0.31 ($PE_{40\text{-}60}$/EtOAc 8:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.33-7.15 (5H, m, Ar*H*), 6.41 (1H, d, *J* = 15.9 Hz, PhC*H*=CH), 6.21 (1H, td, *J* = 7.2, 15.9 Hz, PhCH=C*H*), 4.60 (1H, s, C*H*(CO_2Me)$_2$), 3.77 (3H, s, CO_2*Me*), 3.72 (3H, s, CO_2*Me*), 3.68 (1H, tq, *J* = 7.2, 6.2 Hz, OC*H*CH_3), 2.54 (1H, dddd, *J* = 14.1, 7.2, 6.2,

1.2 Hz, C*H*H'), 2.37 (1H, dddd, *J* = 14.1, 7.2, 6.2 1.2 Hz, CH*H'*), 1.24 (3H, d, *J* = 6.2 Hz, C*H*$_3$); **^{13}C NMR (CDCl$_3$, 100 MHz)** δ 167.6 (*C*=O), 167.4 (*C*=O), 137.5 (C_{Ar}), 132.7 (PhCH=CH), 128.6 (2×C_{Ar}), 127.2 (C_{Ar}), 126.1 (2×C_{Ar}), 125.8 (PhCH=*C*H), 77.6 (CH_3CHO), 77.5 ($CH(CO_2Me)_2$), 52.9 (2×CO_2*Me*), 39.9 ($CHCH_2CH$), 19.6 ($CHCH_3$); **ν_{max}** 2955 (w, C-H), 1742 (w, C=O), 1201 (m), 1121 (s), 732 (s), 694 (s); **m/z** (ESI$^+$) 315.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{16}H_{20}NaO_5$: *m/z* 315.1203 ([M+Na]$^+$), found: 315.1199 *m/z* ([M+Na]$^+$).

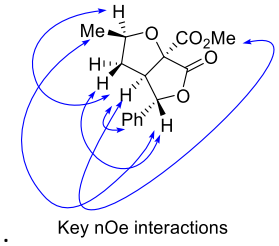
(2*R**,3a*R**,4*S**,6a*S**)-Methyl 2-methyl-6-oxo-4-phenylhexahydrofuro[3,4-*b*]furan-6a-carboxylate (12e)



11e **12e**

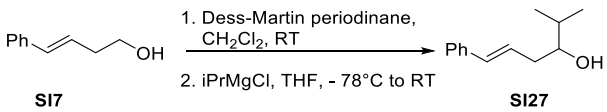
Crude d. r. = 2.8:1

The title compound was prepared according to the general procedure 3 using **11e** (52 mg, 0.18 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 8:2) gave the title compound **12e** as a colourless oil, as a mixture of three diastereoisomers (32 mg, 0.12 mmol, 66%). Characterisation is given for the major diastereoisomer. **R_f** 0.18 ($PE_{40\text{-}60}$/EtOAc 7:3); **^{1}H NMR (CDCl$_3$, 500 MHz)** δ 7.42-7.34 (5H, m, Ar*H*), 5.33 (1H, d, *J* = 4.5 Hz, OC*H*Ph), 4.53 (1H, qnd, *J* = 6.1, 8.9 Hz, OC*H*CH_3), 3.74 (3H, s, CO_2*Me*), 3.36 (1H, ddd, *J* = 8.9, 6.2, 4.5 Hz, OCHC*H*CH_2), 2.60 (1H, ddd, *J* = 12.8, 8.9, 6.2 Hz, C*H*H'), 1.80 (1H, ddd, *J* = 12.8, 8.9, 6.2 Hz, CH*H'*), 1.46 (1H, d, *J* = 6.1 Hz, C*H*$_3$); **^{13}C NMR (CDCl$_3$, 125 MHz)** δ 170.5 (*C*=O), 169.3 (*C*=O), 138.5 (C_{Ar}), 129.0 (2×C_{Ar}), 128.9 (C_{Ar}), 125.6 (2×C_{Ar}) 88.0 (C_{quat}), 86.0 (O*C*HPh), 80.9 (O*C*H_2), 55.1 (CH_2CHCH), 53.2 (CO_2*Me*), 40.5 (CH_2), 20.6 (CH_3); **ν_{max}** 2976 (w, C-H), 1782 (s, C=O), 1760 (s, C=O), 1219 (m), 1109 (w), 1068 (m), 1022 (s), 1050 (m); 700 (s); **m/z** (ESI$^+$) 575.2 299.1 ([M+Na]$^+$, 62%), ([2M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{15}H_{16}NaO_5$: *m/z* 299.0890 ([M+Na]$^+$), found: *m/z* 299.0889 ([M+Na]$^+$)



Key nOe interactions

(*E*)-2-Methyl-6-phenylhex-5-en-3-ol (SI27)

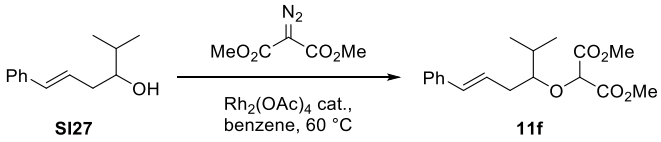


SI7 **SI27**

To a solution of (*E*)-4-phenylbut-3-en-1-ol (308 mg, 2.08 mmol) in CH_2Cl_2 (9.5 mL) was added Dess-Martin periodinane (1.32 g, 3.11 mmol, 1.5 eq.). After stirring for 2h, the reaction mixture was

hydrolysed with a saturated aqueous solution of sodium hydrogen carbonate. The aqueous phase was extracted three times with diethyl ether. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was engaged in the next step without further purification. To a solution of the previous crude product in THF (10 mL) at - 78 °C was added dropwise *i*PrMgCl (3.1 mL, 2 M in Et_2O, 6.2 mmol, 3 eq.). The solution was stirred for 30 min at - 78 °C and warmed up to room temperature overnight. The reaction mixture was hydrolysed with a saturated aqueous solution of ammonium chloride. The aqueous phase was extracted three times with diethyl ether. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography ($PE_{40\text{-}60}$/EtOAc 7:3) to give **SI27** as a yellow oil (130 mg, 0.68 mmol, 33% over 2 steps). **R_f** 0.5 ($PE_{40\text{-}60}$/EtOAc 7:3); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.39-7.19 (5H, m, Ar*H*), 6.50 (1H, d, *J* = 15.9 Hz, PhC*H*=CH), 6.26 (1H, ddd, *J* = 15.9, 7.9, 6.7 Hz, PhCH=C*H*), 3.49 (1H, ddd, *J* = 8.6, 5.5, 3.8 Hz, CH_2CHOH), 2.46 (1H, dddd, *J* = 14.0, 6.7, 3.8, 1.5 Hz, C*H*H'), 2.31 (1H, dddd, *J* = 14.0, 8.6, 7.9, 1.2 Hz CH*H*'), 1.75 (1H, dtd, *J* = 12.4, 6.8, 5.5 Hz, C*H*$(CH_3)_2$), 0.99 (1H, d, *J* = 6.8 Hz, CH$(CH_3)_2$), 0.97 (1H, d, *J* = 6.8 Hz, CH$(CH_3)_2$).

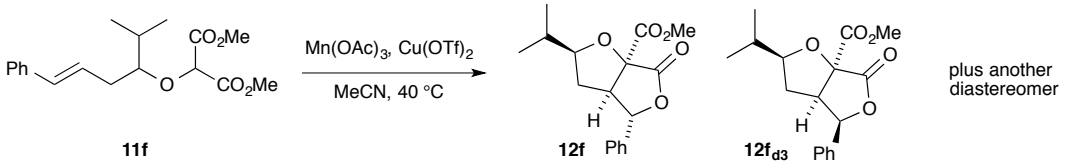
(*E*)-Dimethyl 2-(2-methyl-6-phenylhex-5-en-3-yloxy)malonate (11f)



SI27 11f

The title compound was prepared according to the general procedure 1 using the alcohol **SI27** (64 mg, 0.337 mmol) and dimethyl 2-diazomalonate (61 mg, 0.39 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 9:1) gave the title compound **11f** as a yellow oil (74 mg, 0.23 mmol, 68%). **R_f** 0.42 ($PE_{40\text{-}60}$/EtOAc 8:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.36-7.17 (5H, m, Ar*H*), 6.43 (1H, d, *J* = 15.9 Hz, PhC*H*=CH), 6.29 (1H, td, *J* = 7.0, 15.9 Hz, PhCH=C*H*), 4.59 (1H, s, C*H*$(CO_2Me)_2$), 3.79 (3H, s, CO_2Me), 3.68 (3H, s, CO_2Me), 3.34 (1H, dt, *J* = 6.4, 5.3 Hz, OC*H*iPr), 2.46 (2H, m, CH_2), 1.93 (1H, septd, *J* = 6.8, 5.3 Hz, C*H*$(CH_3)_2$), 0.98 (3H, d, *J* = 6.8 Hz, C*H*$_3$), 0.96 (3H, d, *J* = 6.8 Hz, C*H*$_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 167.7 (2×*C*=O), 137.6 (C_{Ar}), 132.4 (Ph*C*H=CH), 128.6 (2×C_{Ar}), 127.2 (C_{Ar}), 126.5 (2×C_{Ar}), 126.2 (2×C_{Ar}), 87.4 (*C*HiPr), 79.0 (O*C*H$(CO_2Me)_2$), 52.9 (2×CO_2*Me*), 34.4 (CH_2), 31.3 (*C*H$(CH_3)_2$), 18.2 (*C*H$_3$), 18.1 (*C*H$_3$); **ν_{max}** 2956 (w, C-H), 1743 (s, C=O), 1285 (m), 1124 (m), 746 (m), 695 (m); **m/z** (ESI$^+$) 343.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{18}H_{24}NaO_5$: *m/z* 343.1516 ([M+Na]$^+$), found: *m/z* 301.1514 ([M+Na]$^+$).

(2*S**,3a*R**,4*S**,6a*S**)-Methyl 2-isopropyl-6-oxo-4-phenylhexahydrofuro[3,4-*b*]furan-6a-carboxylate (12f)



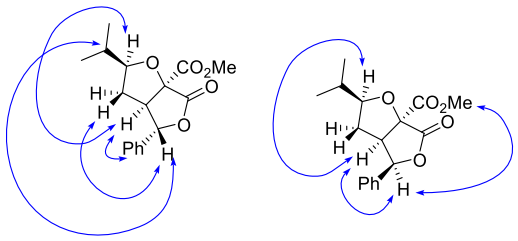
11f 12f 12f$_{d3}$

Crude d. r. =5.4:0.7:1

The title compound was prepared according to the general procedure 3 using **11f** (58 mg, 0.18 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 8:2) gave the title compound **12f** as a

colourless oil (34 mg, 0.11 mmol, 61%) as a mixture of three diastereoisomers. Characterisation is given for the major diastereoisomer. **R_f** 0.34 ($PE_{40\text{-}60}$/EtOAc 7:3); **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 7.42-7.35 (5H, m, Ar*H*), 5.30 (1H, d, *J* = 4.6 Hz, OC*H*Ph), 4.12 (1H, ddd, *J* = 9.0, 7.0, 6.5 Hz, OC*H*CH_2), 3.72 (3H, s, CO_2*Me*), 3.35 (1H, ddd, *J* = 9.0, 6.0, 4.6 Hz, OCHC*H*CH_2), 2.48 (1H, ddd, *J* = 12.8, 8.9, 6.5 Hz, C*H*H'), 1.93 (1H, oct, *J* = 7.0 Hz, C*H*$(CH_3)_2$), 1.86 (2H, ddd, *J* = 12.8, 9.0, 6.0 Hz, CH*H'*), 1.05 (3H, d, *J* = 7.0 Hz, CH_3), 0.95 (3H, d, *J* = 7.0 Hz, CH_3); **^{13}C NMR ($CDCl_3$, 125 MHz)** δ 170.6 (*C*=O), 169.4 (*C*=O), 138.5 (C_{Ar}), 129.0 (2×C_{Ar}), 128.9 (C_{Ar}), 125.5 (2×C_{Ar}), 90.0 (O*C*HCH_2), 87.8 (C_{quat}), 85.7 (O*C*HPh), 54.6 (OCH*C*HCH_2), 53.1 (CO_2*Me*), 36.0 (*C*H_2), 32.6 (*C*H$(CH_3)_2$), 19.3 (CH_3), 18.3 (*C*H_3); **ν_{max}** 2959 (w, C-H), 1782 (s, C=O), 1760 (s, C=O), 1219 (w), 1112 (w), 1026 (w), 699 (m); **m/z** (ESI$^+$) 327.1 ([M+Na]$^+$, 100%), 631.3 ([2M+Na]$^+$, 28%); **HRMS-ESI** calculated for $C_{17}H_{20}NaO_5$: *m/z* 327.1203 ([M+Na]$^+$), found: *m/z* 327.1201 ([M+Na]$^+$)

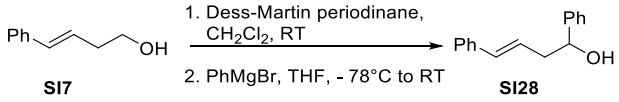
Minor diastereomer: **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 7.43-7.23 (5H, m, Ar*H*), 5.86 (1H, d, *J* = 5.9 Hz, OC*H*Ph), 3.97 (1H, ddd, *J* = 11.1, 6.7, 4.5 Hz, OC*H*CH_2), 3.90 (3H, s, CO_2*Me*), 3.58 (1H, ddd, *J* = 11.0, 8.1, 5.9 Hz, OCHC*H*CH_2), 1.81 (1H, oct, *J* = 6.7 Hz, C*H*$(CH_3)_2$), 1.65 (1 H, ddd, *J* = 12.9, 8.1, 4.5 Hz, C*H*H'), 1.34 (1 H, dt, *J* = 12.9, 11.1 Hz, CH*H'*), 0.94 (1 H, d, *J* = 6.7 Hz, CH_3), 0.79 (1H, d, *J* = 6.7 Hz, CH_3).



Key nOe interactions
Major diastereoisomer (**12f**)

Key nOe interactions
Minor diastereoisomer (**12f$_{d3}$**)

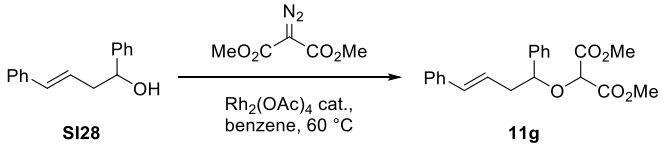
(*E*)-1,4-diphenylbut-3-en-1-ol (SI28)



To a solution of (*E*)-4-phenylbut-3-en-1-ol (331 mg, 2.24 mmol) in CH_2Cl_2 (12 mL) was added Dess-Martin periodinane (1.5 g, 3.54 mmol, 1.5 eq.). After stirring for 2 h, the reaction mixture was hydrolysed with a saturated aqueous solution of sodium hydrogen carbonate. The aqueous phase was extracted three times with diethyl ether. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was engaged in the next step without further purification. To a solution of the previous crude product in THF (10 mL) at - 78 °C was added dropwise PhMgBr (2.3 mL, 3 M in diethyl ether, 6.9 mmol, 2.9 eq.). The solution was stirred for 30 min at - 78 °C and warmed up to room temperature overnight. The reaction mixture was hydrolysed with a saturated aqueous solution of ammonium chloride. The aqueous phase was extracted three times with diethyl ether. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography ($PE_{40\text{-}60}$/EtOAc 8:2) to give **SI28** as a yellow oil (142 mg, 0.63 mmol, 28% over 2 steps). **R_f** 0.45 ($PE_{40\text{-}60}$/EtOAc 7:3); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.41-7.22

(10H, m, Ar*H*), 6.51 (1H, d, *J* = 15.9 Hz, PhC*H*=CH), 6.21 (1H, td, *J* = 15.9, 7.3 Hz, PhCH=C*H*), 4.82 (1H, dd, *J* = 7.3, 5.6 Hz, CH_2CHPh), 2.67 (2H, m, CH_2).

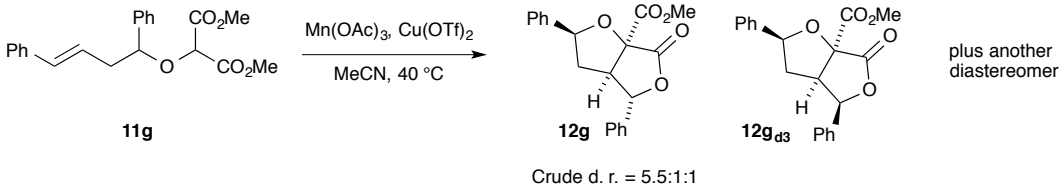
(*E*)-Dimethyl 2-(1,4-diphenylbut-3-enyloxy)malonate (11g)



SI28 **11g**

The title compound was prepared according to the general procedure 1 using the alcohol **SI28** (115 mg, 0.51 mmol) and dimethyl 2-diazomalonate (93 mg, 0.58 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 9:1) gave the title compound **11g** as a yellow oil (147 mg, 0.41 mmol, 80%). $\mathbf{R_f}$ 0.33 ($PE_{40\text{-}60}$/EtOAc 8:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.35-7.15 (10H, m, Ar*H*), 6.38 (1H, d, *J* = 15.9 Hz, PhC*H*=CH), 6.18 (1H, ddd, *J* = 15.9, 7.4, 6.8 Hz, PhCH=C*H*), 4.49 (1H, dd, *J* = 7.4, 6.1 Hz, OC*H*Ph), 4.40 (1H, s, $CH(CO_2Me)_2$), 3.74 (3H, s, CO_2Me), 3.67 (3H, s, CO_2Me), 2.88 (1H, dddd, *J* = 14.4, 7.4, 6.8, 1.3 Hz, CH*H'*CHO), 2.61 (1H, dddd, *J* = 14.4, 7.4, 6.1, 1.2 Hz, CH*H'*CHO); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 167.6 (*C*=O), 166.8 (*C*=O), 139.6 (C_{Ar}), 137.6 (C_{Ar}), 132.6 (Ph*C*H=CH), 128.8 (2×C_{Ar}), 128.6 (2×C_{Ar}), 127.6 (2×C_{Ar}), 127.3 (C_{Ar}), 127.2 (C_{Ar}), 126.2 (2×C_{Ar}), 125.9 (PhCH=*C*H), 83.3 (O*C*HPh), 76.8 ($CH(CO_2Me)_2$), 52.9 (2×CO_2Me), 41.5 (CH_2); $\boldsymbol{\nu_{max}}$ 2954 (w, C-H), 1743 (s, C=O), 1230 (m), 1163 (m), 745 (s), 699 (s); **m/z** (ESI$^+$) 377.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{21}H_{22}NaO_5$: *m/z* 377.1359 ([M+Na]$^+$), found: *m/z* 377.1363 ([M+Na]$^+$).

(2*S**,3a*R**,4*S**,6a*S**)-Methyl 6-oxo-2,4-diphenylhexahydrofuro[3,4-*b*]furan-6a-carboxylate (12g)

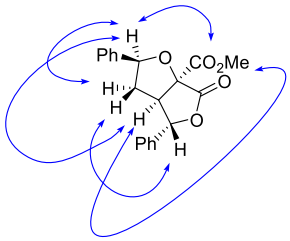


11g **12g** **12g$_{d3}$**

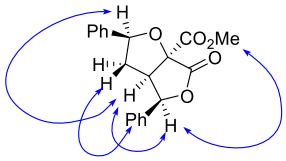
Crude d. r. = 5.5:1:1

The title compound was prepared according to the general procedure 3 using **11g** (54 mg, 0.14 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 8:2) gave the title compound **12g** as a colourless oil as a mixture of three diastereoisomers (29 mg, 0.09 mmol, 60%). Characterisation is given for the major diastereoisomer. $\mathbf{R_f}$ 0.23 ($PE_{40\text{-}60}$/EtOAc 7:3); **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 7.42-7.32 (10H, Ar*H*), 5.52 (1H, t, *J* = 7.4 Hz, OC*H*CH_2), 5.21 (1H, d, *J* = 5.0 Hz, OC*H*CH), 3.79 (3H, s, CO_2Me), 3.48 (1H, td, *J* = 5.0, 8.5 Hz, OCHC*H*CH_2), 2.89 (1H, ddd, *J* = 13.1, 8.5, 6.9 Hz, C*H*H'), 2.23 (1H, ddd, *J* = 13.1, 7.9, 5.6, CH*H'*); **^{13}C NMR ($CDCl_3$, 125 MHz)** δ 170.4 (C=O), 169.1 (C=O), 139.7 (C_{Ar}), 138.3 (C_{Ar}), 129.0 (2×C_{Ar}), 128.9 (2×C_{Ar}), 128.3 (2×C_{Ar}), 125.6 (2×C_{Ar}), 125.5 (2×C_{Ar}), 88.2(C_{quat}), 85.2 (O*C*HCH_2), 85.0 (O*C*HCH), 54.9 (O*C*H*C*HCH_2), 53.4 (CO_2Me), 40.8 (CH_2); $\boldsymbol{\nu_{max}}$ 2955 (w, C-H), 1782 (s, C=O), 1760 (s, C=O), 1259 (w), 1222 (w), 1117 (m), 1026 (m), 668 (s); **m/z** (ESI$^+$) %), 361.1 ([M+Na]$^+$, 76%), 699.2 ([2M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{20}H_{18}NaO_5$: *m/z* 361.1046 ([M+Na]$^+$), found: *m/z* 361.1044 ([M+Na]$^+$).

Minor diastereomer: **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 7.39-7.27 (10H, Ar*H*), 5.94 (1H, d, *J* = 5.8 Hz, OC*H*CH), 5.24 (1H, dd, *J* = 11.4, 4.5 Hz, OC*H*CH_2), 3.95 (3H, s, CO_2*Me*), 3.76 (1H, ddd, *J* = 11.4, 7.6, 5.9 Hz, OCHC*H*CH_2), 2.05 (1H, ddd, *J* = 12.8, 7.6, 4.5 Hz, C*H*H'), 1.60 (1H, td, *J* = 11.4, 12.8 Hz, CH*H'*).

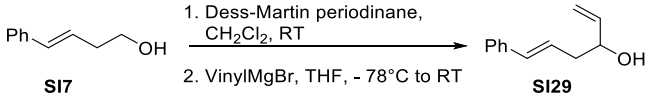


Key nOe interactions
Major diastereoisomer (**12g**)



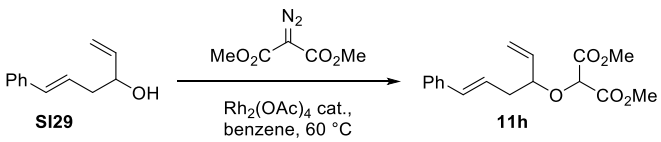
Key nOe interactions
Minor diastereoisomer (**12g$_{d3}$**)

(*E*)-6-Phenylhexa-1,5-dien-3-ol (SI29)



To a solution of (*E*)-4-phenylbut-3-en-1-ol (368 mg, 2.48 mmol) in CH_2Cl_2 (12 mL) was added Dess-Martin periodinane (1.5 g, 3.54 mmol, 1.4 eq.). After stirring for 2h, the reaction mixture was hydrolysed with a saturated aqueous solution of sodium hydrogen carbonate. The aqueous phase was extracted three times with diethyl ether. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was engaged in the next step without further purification. To a solution of the previous crude product in THF (10 mL) at - 78 °C was added dropwise vinylmagnesium bromide (5 mL, 1 M in THF, 5 mmol, 2 eq.). The solution was stirred for 30 min at - 78 °C and warmed up to room temperature overnight. The reaction mixture was hydrolysed with a saturated aqueous solution of ammonium chloride. The aqueous phase was extracted three times with diethyl ether. The combined organic phases were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by flash chromatography ($PE_{40\text{-}60}$/EtOAc 8:2) to give **SI29** as a yellow oil (156 mg, 0.90 mmol, 36%). **R_f** 0.43 ($PE_{40\text{-}60}$/EtOAc 7:3); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.37-7.20 (5H, m, Ar*H*), 6.50 (1H, d, *J* = 15.9 Hz, PhC*H*=CH), 6.22 (1H, dt, *J* = 15.9, 7.3 Hz, PhCH=C*H*), 5.95 (1H, ddd, *J* = 17.2, 10.5, 5.8 Hz, CHC*H*=CH_2), 5.29 (1H, td, *J* = 17.2, 1.4 Hz, C*H*H'=CHCHOH), 5.16 (1H, td, *J* = 10.5, 1.3 Hz, CH*H'*=CHCHOH), 4.31-4.21 (1H, m, C*H*CH=CH_2), 2.55-2.41 (2H, m, CH_2).

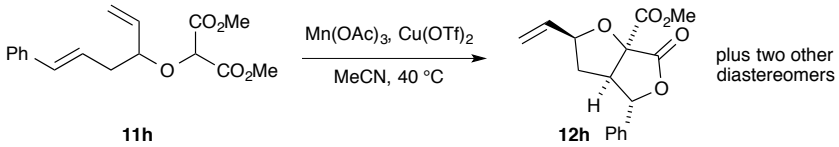
(*E*)-Dimethyl 2-(6-phenylhexa-1,5-dien-3-yloxy)malonate (11h)



The title compound was prepared according to the general procedure 1 using the alcohol **SI29** (156 mg, 0.90 mmol) and dimethyl 2-diazomalonate (162 mg, 1.01 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 9:1) gave the title compound **11h** as a yellow oil (189 mg, 0.62 mmol, 69%). **R_f** 0.33 ($PE_{40\text{-}60}$/EtOAc 8:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.36-7.18 (5H, m, Ar*H*), 6.45 (1H, d, *J* =

15.9 Hz, PhC*H*=CH), 6.24 (1H, dt, *J* = 15.9, 7.2 Hz, PhCH=C*H*), 5.74 (1H, ddd, *J* = 17.2, 10.3, 8.2 Hz, CHC*H*=CH_2), 5.29 (1H, dt, *J* = 10.3, 1.4 Hz, C*H*H'=CHCHO), 5.27 (1H, dd, *J* = 17.2, 1.4 Hz, CH*H'*CHCHO), 4.61 (1H, s, C*H*(CO_2Me)$_2$), 3.96-3.90 (1H, m, OC*H*CH_2), 3.79 (3H, s, CO_2Me), 3.77 (3H, s, CO_2Me), 2.70 (1H, dddd, *J* = 14.2, 8.2, 7.2, 1.3 Hz, C*H*H'), 2.52 (1H, dddd, *J* = 14.2, 7.2, 6.6, 1.3 Hz, CH*H'*); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 167.4 (*C*=O), 167.0 (*C*=O), 137.4 (C_{Ar}), 136.5 (CH_2=*C*H), 132.5 (Ph*C*H=CH), 128.4(2×C_{Ar}), 127.1 (C_{Ar}), 126.1(2×C_{Ar}), 125.4 (PhCH=*C*H), 119.6 (*C*H_2=CH), 82.5 (O*C*HCH_2), 76.4 (*C*H(CO_2Me)$_2$), 52.8 (2×CO_2*Me*), 38.8 (*C*H_2); **ν_{max}** 2954 (w, C-H), 1746 (s, C=O), 1286 (m), 1125 (m), 747 (m), 694 (m); **m/z** (ESI$^+$) 327.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{17}H_{20}NaO_5$: *m/z* 327.1203 ([M+Na]$^+$), found: *m/z* 327.1201 ([M+Na]$^+$).

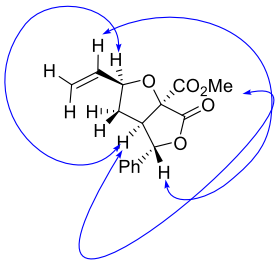
(2*S**,3a*R**,4*S**,6a*S**)-Methyl 6-oxo-4-phenyl-2-vinylhexahydrofuro[3,4-b]furan-6a-carboxylate (12h)



11h **12h** Ph

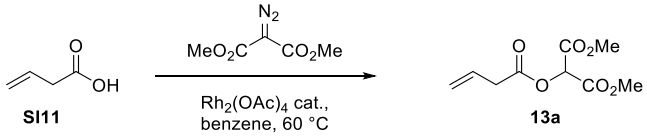
Crude d. r. = 2.8:1

The title compound was prepared according to the general procedure 3 using **11h** (60 mg, 0.20 mmol). Flash Chromatography purification (PE_{40-60}/EtOAc 8:2) gave the title compound **12h** as a colourless oil as a mixture of three diastereoisomers (40 mg, 0.14 mmol, 70%). Characterisation is given for the major diastereoisomer. **R_f** 0.20 (PE_{40-60}/EtOAc 7:3); **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 7.43-7.33 (5H, Ar*H*), 5.97 (1H, ddd, *J* = 17.2, 10.6, 5.5 Hz, CH_2=C*H*), 5.42 (1H, dt, *J* = 17.2, 1.3 Hz, C*H*H'=CH), 5.32 (1H, d, *J* = 5.0 Hz, OC*H*Ph), 5.26 (1H, dt, *J* = 1.3, 10.6 Hz, CH*H'*=CH), 4.96 (1H, tdt, *J* = 7.0, 5.5, 1.3 Hz, OC*H*CH_2), 3.78 (3H, s, CO_2*Me*), 3.37 (td, *J* = 5.0, 8.6 Hz, OCHC*H*CH_2), 2.60 (1H, ddd, *J* = 13.0, 8.6, 7.0 Hz, C*H*H'), 2.05 (1H, ddd, *J* = 13.0, 7.0, 5.0 Hz, CH*H'*); **^{13}C NMR ($CDCl_3$, 125 MHz)** δ 170.4 (*C*=O), 169.0 (*C*=O), 138.2 (C_{Ar}), 136.4 (CH_2=*C*H), 129.1 (C_{Ar}), 129.0 (2×C_{Ar}), 125.7 (2×C_{Ar}), 117.6 (*C*H_2=CH), 88.2 (C_{quat}), 85.3 (O*C*HPh), 84.4 (OC*H*CH_2), 54.8 (OCH*C*HCH_2), 53.3 (CO_2*Me*), 37.8 (*C*H_2); **ν_{max}** 2956 (w, C-H), 1781 (s, C=O), 1761 (s, C=O), 1260 (s), 1115 (s), 986 (s), 699 (s); **m/z** (ESI$^+$) 599.2 ([2M+Na]$^+$, 100%), 311.1 ([M+Na]$^+$, 73%); **HRMS-ESI** calculated for $C_{16}H_{16}NaO_5$: *m/z* 311.0890 ([M+Na]$^+$), found: *m/z* 311.0887 ([M+Na]$^+$).



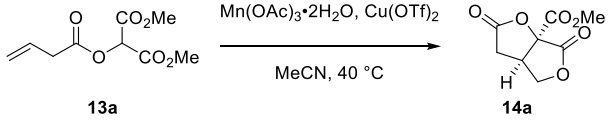
Key nOe interactions

Dimethyl 2-(but-3-enoyloxy)malonate (13a)



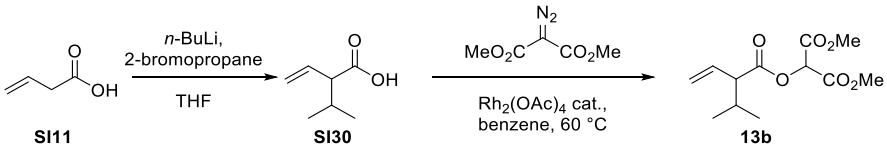
The title compound was prepared according to the general procedure 1 using 3-butenoic acid (0.3 mL, 3.50 mmol) and dimethyl 2-diazomalonate (600 mg, 3.80 mmol, 1.09 eq.). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 8:2) gave the title compound **13a** as a colourless oil (750 mg, 3.47 mmol, 99%). **R_f** 0.57 (PE/EtOAc 7:3); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.92 (1H, m, CH_2=C*H*), 5.56 (1H, s, C*H*($CO_2Me)_2$), 5.28-5.22 (1H, m, C*H*H'=CH), 5.26-5.22 (1H, m, CH*H'*=CH), 3.82 (6H, s, CO_2*Me*), 3.33-3.3-2 (1H, m, C*H*H'), 3.29-3.28 (1H, m, CH*H'*); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 170.2 (*C*=O), 164.8 (*C*=O), 129.1 (CH_2=*C*H), 119.6 (*C*H_2=CH), 71.6 (CH($CO_2Me)_2$), 53.4 (CO_2*Me*), 38.3 (CH_2); **ν_{max}** 1745 (s, C=O), 1437 (s), 1150 (m), 1024 (s), 928 (w) ; **m/z** (ESI$^+$) 239.1 ([M+Na]$^+$, 100%), 455.0 ([2M+Na]$^+$, 7%); **HRMS-ESI** calculated for $C_9H_{12}NaO_6$: *m/z* 239.0526 ([M+Na]$^+$), found: *m/z* 239.0522 ([M+Na]$^+$).

(3a*R**,6a*S**)-Methyl 2,6-dioxohexahydrofuro[3,4-*b*]furan-6a-carboxylate (14a)



The title compound was prepared according to the general procedure 3 using **13a** (56 mg, 0.26 mmol). Flash Chromatography purification (PE/EtOAc 1:1 to 1:4) gave the title compound **14a** as a white solid (40 mg, 0.20 mmol, 77%). **R_f** 0.14 (PE/EtOAc 5:5); **m.p** 127-130 °C; **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 4.74 (1H, dd, *J* = 9.8, 7.5 Hz, OC*H*H'), 4.25 (1H, dd, *J* = 9.8, 3.9 Hz, OCH*H'*), 3.92 (3H, s, CO_2*Me*), 3.57 (1H, dddd, *J* = 9.6, 7.5, 5.5, 3.9 Hz, CH_2C*H*CH_2), 3.06 (1H, dd, *J* = 18.5, 9.6 Hz, C*H*H'CH), 2.65 (1H, dd, *J* = 18.5, 5.5 Hz, CH*H'*CH) ; **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 171.8 (*C*=O), 167.7 (*C*=O), 165.8 (*C*=O), 83.2 (C_{quat}), 70.8 (O*C*H_2CH), 54.1 (CO_2*Me*), 40.0 (OCH_2*C*H), 33.2 (*C*H_2CH) ; **ν_{max}** 2922 (w, C-H), 1786 (m, C=O), 1198 (m), 1113 (m) ; **HRMS-ESI** calculated for $C_8H_8NaO_6$: *m/z* 223.0213 ([M+Na]$^+$), found: *m/z* 223.0209 ([M+Na]$^+$).

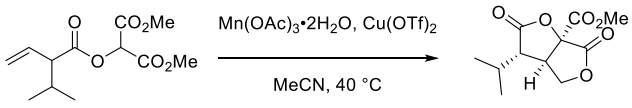
Dimethyl 2-((2-*iso*propylbut-3-enoyl)oxy)malonate (13b)



To a solution of but-3-enoic acid (1 mL, 11.8 mmol) in THF (30 mL) was added slowly *n*-BuLi (11.8 mL, 2.5 M in hexanes) at -78 °C. The mixture was stirred for 20 min and 2-bromopropane (3.36 mL, 35.8 mmol, 3 eq.) was added. The solution was allowed to warm to room temperature and stirred for 1 h. The reaction mixture was hydrolysed at 0 °C with aqueous NaOH (0.5 M). The layers were separated with Et_2O and the organic phase was extracted with more aqueous NaOH (0.5 M). The combined aqueous layers were acidified slowly by addition of conc. HCl until pH 2. After three extractions of the aqueous layer with Et_2O, the combined organic layers were dried, filtered and concentrated under reduced pressure to give the crude carboxylic acid **SI30**, which was used without further purification. The title compound was prepared according to the general procedure 1 using the previous carboxylic acid (345 mg, 2.69 mmol) and dimethyl 2-diazomalonate (450 mg, 2.85 mmol,

1.06 eq.). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 9:1) gave the title compound **13b** as a colourless oil (290 mg, 1.12 mmol, 42 %). **R_f** 0.64 (PE/EtOAc 7:3); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.82 (1H, ddd, *J* = 17.1, 10.2, 9.4 Hz, CH_2=C*H*CH), 5.55 (1H, s, C*H*($CO_2Me)_2$), 5.20 (1H, dd, *J* = 10.2, 1.3 Hz, C*H*H'=CH), 5.17 (1H, dd, *J* = 17.1, 1.3 Hz, CH*H'*=CH), 3.82 (6H, s, CO_2*Me*), 2.91 (ddt, *J* = 9.4, 8.0 and 0.6 Hz, C*H*CH($CH_3)_2$), 2.10 (1H, septd, *J* = 6.7, 8.0 Hz, CHC*H*($CH_3)_2$), 0.98 (3H, d, *J* = 6.7 Hz, CH_3), 0.92 (3H, d, *J* = 6.7 Hz, CH_3); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 172.4 (*C*=O), 165.0 (*C*=O), 164.9 (*C*=O), 133.9 (CH_2=*C*H), 119.1 (*C*H_2=CH), 71.5 (CH($CO_2Me)_2$), 57.3 (*C*HCH($CH_3)_2$), 53.4 (2×CO_2*Me*), 30.8 (CH*C*H($CH_3)_2$), 20.6 (*C*H_3), 19.5 (*C*H_3) ; **ν_{max}** 2960 (w, C-H), 1745 (m, C=O), 1437 (s), 1207 (m), 1118 (m), 1025 (s); **m/z** (ESI^+) 281.1 ([M+Na]$^+$, 100%).

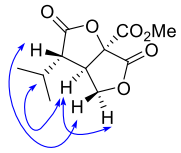
(3*S**,3a*R**,6a*S**)-Methyl 3-isopropyl-2,6-dioxohexahydrofuro[3,4-*b*]furan-6a-carboxylate (14b)



13b **14b**

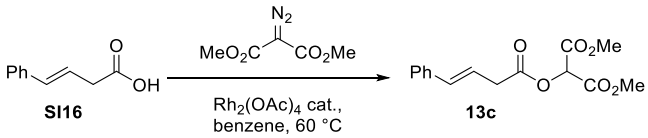
Crude d.r. > 24:1

The title compound was prepared according to the general procedure 3 using **13b** (68 mg, 0.26 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 6:4 to 4:6) gave the title compound **14b** as a colourless oil (46 mg, 0.19 mmol, 73%). **R_f** 0.38 (PE/EtOAc 4:6); **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 4.72 (1H, dd, *J* = 9.7, 6.7 Hz, OC*H*H'CH), 4.28 (1H, dd, *J* = 9.7, 2.0 Hz, OCH*H'*CH), 3.90 (3H, s, CO_2*Me*), 3.27 (1H, dt, *J* = 2.0, 7.1 Hz, CH_2*C*HCH), 2.64, (1H, dd, *J* = 7.6, 5.0 Hz, C*H*CH($CH_3)_2$), 2.30 (1H, septd, *J* = 6.8, 5.0 Hz, CHC*H*($CH_3)_2$), 1.05 (3H, d, *J* = 6.8 Hz, *C*H_3), 0.95 (3H, d, *J* = 6.8 Hz, CH_3); **^{13}C NMR ($CDCl_3$, 125 MHz)** δ 173.6 (*C*=O), 168.5 (*C*=O), 166.0 (*C*=O), 81.7 (C_{quat}), 71.3 (O*C*H_2CH), 54.1 (CO_2*Me*), 51.5 (*C*HCH($CH_3)_2$), 42.5 (CH_2*C*HCH), 28.5 (CH*C*H($CH_3)_2$), 20.1 (*C*H_3), 18.4 (*C*H_3); **ν_{max}** 2964 (w, C-H), 1787 (m, C=O), 1173 (m), 1104 (m), 997 (s), 731 (m) ; **HRMS-ESI** calculated for $C_{11}H_{14}NaO_6$: *m/z* 265.683 ([M+Na]$^+$), found: *m/z* 265.0679 ([M+Na]$^+$).



Key nOe interactions

(*E*)-Dimethyl 2-((4-phenylbut-3-enoyl)oxy)malonate (13c)

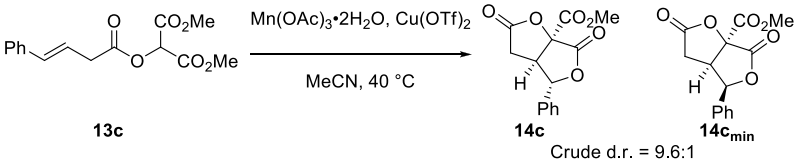


SI16 **13c**

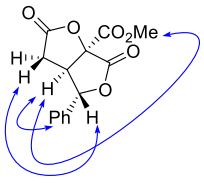
The title compound was prepared according to the general procedure 1 using (*E*)-4-phenylbut-3-enoic acid (300 mg, 1.85 mmol) and dimethyl 2-diazomalonate (300 mg, 1.90 mmol, 1.03 eq.). Flash Chromatography purification ($PE_{40\text{-}60}$/ EtOAc 9:1) gave the title compound **13c** as a colourless oil (385 mg, 1.32 mmol, 71%). **R_f** 0.55 ($PE_{40\text{-}60}$/EtOAc 7:3); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.34-7.17 (5H, m, Ar*H*), 6.50 (1H, *J* = 15.9 Hz, PhC*H*=CH), 6.24 (td, *J* = 15.9, 7.0 Hz, PhCH=C*H*), 5.56 (1H, s, CH($CO_2Me)_2$), 3.79 (6H, s, CO_2*Me*), 3.89 (2H, dd, *J* = 7.0, 1.4 Hz, CHCH_2) ; **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 170.3 (*C*=O), 164.8

(*C*=O), 136.7 (C_{Ar}), 134.4 (Ph*C*H=CH), 128.7 (2×C_{Ar}), 127.8 (C_{Ar}), 126.5 (2×C_{Ar}), 120.4 (PhCH=*C*H), 71.7 (O*C*H(CO_2Me)$_2$), 53.5 (2×CO_2*Me*), 37.6 (*C*H$_2$); **ν_{max}** 1745 (s, C=O), 1436 (s), 1140 (m), 1024 (s), 967 (s), 743 (s), 693 (s) ; **m/z** (ESI$^+$) 293.1 ([M+H]$^+$, 29 %), 315.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{15}H_{16}NaO_6$: *m/z* 315.0839 ([M+Na]$^+$), found: *m/z* 315.0832 ([M+Na]$^+$).

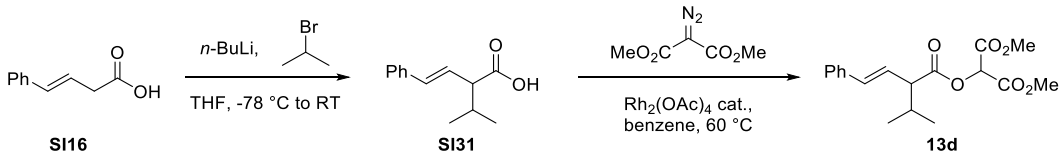
(3a*R**,4*S**,6a*S**)-Methyl 2,6-dioxo-4-phenylhexahydrofuro[3,4-*b*]furan-6a-carboxylate (14c)



The title compound was prepared according to the general procedure 3 using **13c** (76 mg, 0.26 mmol). Flash Chromatography purification (PE_{40-60}/EtOAc 6:4 to 3:7) gave the title compound **14c** as a white solid (43 mg, 0.16 mmol, 62%). **R_f** 0.43 (PE/EtOAc 4:6); **m.p.** 124-132 °C; **NMR ($CDCl_3$, 500 MHz)** δ 7.46-7.35 (5H, Ar*H*), 5.23 (1H, d, *J* = 7.1 Hz, OC*H*Ph), 3.91 (3H, s, CO_2*Me*), 3.46 (1H, ddd, *J* = 8.8, 7.1, 1.8 Hz, OCHC*H*CH$_2$), 2.98 (1H, dd, *J* = 18.5, 8.7 Hz, CH*H*'CHCH), 2.79 (1H, dd, *J* = 18.5, 1.8 Hz, C*H*H'CHCH); **^{13}C NMR ($CDCl_3$, 125 MHz)** δ 172.3 (*C*=O), 166.6 (*C*=O), 166.3 (*C*=O), 136.1 (C_{Ar}), 130.0 (C_{Ar}), 129.5 (2×C_{Ar}), 126.0 (2×C_{Ar}), 85.3 (O*C*HPh), 84.9 (C_{quat}), 54.3 (CO_2*Me*), 48.6 (OCH*C*HCH$_2$), 32.5 (CH$_2$) ; **ν_{max}** 2958 (w, C-H), 1744 (m, C=O), 1223 (m), 1160 (m), 1084 (m); **HRMS-ESI** calculated for $C_{14}H_{12}NaO_6$: *m/z* 299.526 ([M+Na]$^+$), found: *m/z* 299.0523 ([M+Na]$^+$).



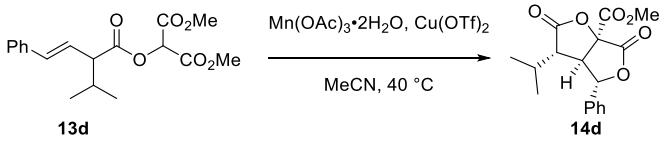
(*E*)-Dimethyl 2-((2-isopropyl-4-phenylbut-3-enoyl)oxy)malonate (13d)



To a solution of (*E*)-4-phenylbut-3-enoic acid (1 g, 6.17 mmol) in THF (15.5 mL) was added slowly *n*-BuLi (5.4 mL, 2.5 M in hexanes) at – 78 °C. The mixture was stirred for 20 min and 2-bromopropane (3.36 mL, 35.8 mmol, 3 eq.) was added. The solution was allowed to come to room temperature and stirred for 1 h. The reaction mixture was hydrolysed at 0 °C with aqueous NaOH (0.5 M). The layers were separated with Et_2O and the organic phase was extracted with more aqueous NaOH (0.5 M). The combined aqueous layers were acidified slowly by addition of conc. HCl until pH 2. After three extraction of the aqueous layer with Et_2O, the combined organic layers were dried, filtered and concentrated under reduced pressure to give the crude carboxylic acid **SI31** which was used without further purification. **m/z** (ESI$^+$) 205.2 ([M+H]$^+$, 37 %), 227.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{13}H_{16}NaO_2$: *m/z* 227.1043 ([M+Na]$^+$), found: *m/z* 227.1048 ([M+Na]$^+$). The title compound was

prepared according to the general procedure 1 using (*E*)-2-isopropyl-4-phenylbut-3-enoic acid (550 mg, 2.70 mmol) and dimethyl 2-diazomalonate (450 mg, 2.85 mmol, 1.06 eq.). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 9:1 to 7:3) gave the compound **13d** as a colourless oil (570 mg, 1.71 mmol, 63%). **R_f** 0.61 (PE/EtOAc 7:3); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.39-7.37 (m, 2H, Ar*H*), 7.33-7.29 (m, 3H, Ar*H*), 6.51 (1H, d, *J* = 15.9 Hz, Ar-C*H*=CH), 6.21 (1H, dd, *J* = 15.9, 9.6 Hz, Ar-CH=C*H*), 5.59 (1H, s, OC*H*(CO_2Me)$_2$), 3.83 (3H, s, OCH_3), 3.82 (3H, s, OCH_3), 3.07 (1H, dd, *J* = 9.6, 8.6 Hz, C*H*CH(CH_3)$_2$), 2.21 (1H, m, C*H*(CH_3)$_2$), 1.04 (3H, d, *J* = 6.7 Hz, CH_3), 0.97 (3H, d, *J* = 6.7 Hz, CH_3); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 172.5 (*C*=O), 165.0 (*C*=O), 164.9 (*C*=O), 136.8 (C_{Ar}), 134.0 (PhCH=CH), 128.7 (C_{Ar}), 128.2 (C_{Ar}), 127.8 (C_{Ar}), 126.5 (C_{Ar}), 125.5 (PhCH=*C*H), 71.5 (OCH(CO_2Me)$_2$), 56.5 (*C*HCH(CH_3)$_2$), 53.4 (CO_2Me), 31.5 (CH*C*H(CH_3)$_2$, 20.8 (CH_3), 19.7 (CH_3); **ν_{max}** 2959 (m, C-H), 1743 (w, C=O), 1132 (m), 746 (s, =C-H), 693 (s, =C-H); **m/z** (ESI$^+$) 335.1 ([M+H]$^+$, 56%), 357.1 ([M+Na]$^+$, 100%); **HRMS-ESI** calculated for $C_{18}H_{22}NaO_6$: *m/z* 357.1309 ([M+Na]$^+$), found: *m/z* 357.1309 ([M+Na]$^+$).

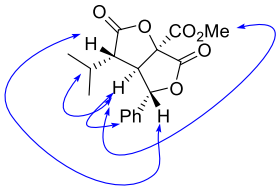
(3*S**,3a*R**,4*S**,6a*S**)-Methyl 3-isopropyl-2,6-dioxo-4-phenylhexahydrofuro[3,4-*b*]furan-6a-carboxylate (14d)



13d **14d**

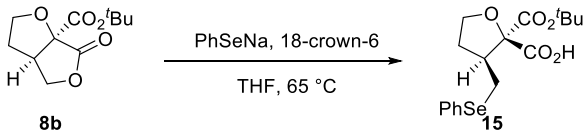
Crude d.r. = 9.6:1

The title compound was prepared according to the general procedure 3 using **13d** (86 mg, 0.26 mmol). Flash Chromatography purification ($PE_{40\text{-}60}$/EtOAc 6:4 to 3:7) gave the title compound **14d** as a colourless oil (64 mg, 0.20 mmol, 77%). **R_f** 0.65 (PE/EtOAc 4:6); **^{1}H NMR ($CDCl_3$, 500 MHz)** δ 7.45-7.37 (5H, Ar*H*), 5.31 (1H, d, *J* = 5.4 Hz, OC*H*Ph), 3.86 (3H, s, CO_2*Me*), 3.23 (1H, dd, *J* = 5.4, 3.5 Hz, OCHC*H*CH_2), 2.81 (1H, dd, *J* = 5.4, 3.5 Hz, C*H*CH(CH_3)$_2$), 2.20 (1H, m, CHC*H*(CH_3)$_2$), 0.95 (3H, d, *J* = 6.8 Hz, CH_3), 0.82 (3H, d, *J* = 6.8 Hz, CH_3); **NMR ($CDCl_3$, 125 MHz)** δ 174.4 (*C*=O), 167.7 (*C*=O), 166.8 (*C*=O), 136.8 (C_{Ar}), 129.7 (2×C_{Ar}), 129.4 (C_{Ar}), 125.7 (2×C_{Ar}), 86.5 (O*C*HPh), 83.7 (C_{quat}), 54.1 (CO_2*Me*), 53.2 (*C*HCH(CH_3)$_2$), 50.7 (OCH*C*HCH_2), 29.4 (CH*C*H(CH_3)$_2$), 20.5 (CH_3), 18.8 (CH_3); **ν_{max}** 2972 (w, C-H), 1791 (m, C=O), 1200 (m), 1173 (m), 1111 (m), 753 (m), 699 (s); **HRMS-ESI** calculated for $C_{17}H_{18}NaO_6$: *m/z* 341.0996 ([M+Na]$^+$), found: *m/z* 341.0992 ([M+Na]$^+$).



Key nOe interactions

(2*R**,3*S**)-2-(*tert*-Butoxycarbonyl)-3-((phenylselanyl)methyl)tetrahydrofuran-2-carboxylic acid (15)

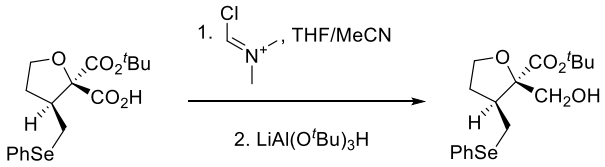


8b **15**

To $(PhSe)_2$ (749 mg, 2.4 mmol) and NaH (60% dispersion, 160 mg, 4.00 mmol) was added nitrogen sparged THF (4.1 mL) at room temperature under argon. The mixture was then stirred at 65 °C for 90

min. The mixture was cooled to 0 °C and a solution of *tert*-butyl (3a*S*,6a*S*)-6-oxotetrahydrofuro[3,4-*b*]furan-6a(6*H*)-carboxylate **8b** (456 mg, 2.0 mmol) and 18-crown-6 (132 mg, 0.50 mmol) in nitrogen sparged THF (4 mL) was added to the mixture. The mixture was then stirred at room temperature for 90 min, aqueous NaOH (0.5 M, 15 mL) and Et_2O (15 mL) were then carefully added. The organic layer was extracted with more aqueous NaOH (0.5 M, 2 x 10 mL). A solution of pH 2 sulphate buffer (10 mL) was added and conc. aqueous HCl was added until pH 2. The aqueous layer was then extracted with Et_2O (3 x 25 mL). The combined organic extracts were dried (Na_2SO_4), filtered, and evaporated to give the crude title compound **15** as a yellow oil (416 mg, 1.07 mmol, 54%). $\mathbf{R_f}$ is not given as compounds streaks even in presence of AcOH; **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 9.12-8.50 (1H, br, CO_2H), 7.56-7.50 (2H, m, Ar*H*), 7.32-7.24 (3H, m, Ar*H*), 4.22 (1H, td, *J* = 8.3, 3.4 Hz, OC*H*H'), 3.96 (1H, q, *J* = 8.3 Hz, OCH*H'*), 3.39 (1H, dd, *J* = 12.2, 3.4 Hz, C*H*H'Se), 3.07-2.96 (1H, m, C*H*CH_2Se), 2.71 (1H, t, *J* = 12.2 Hz, CH*H'*Se), 2.40-2.30 (1H, m, OCH_2CHH'), 2.00-1.90 (1H, m, OCH_2CH*H'*), 1.45 (1H, s, $OC(CH_3)_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 171.2 (*C*=O), 167.8 (*C*=O), 132.9 (*Ar*), 129.5 (*Ar*), 129.4 (*Ar*), 127.3 (*Ar*), 88.8 (C_{quat}), 83.9 (C_{quat}), 69.1 (OCH_2), 46.8 (*C*H), 31.9 (OCH_2CH_2), 27.8 ($OC(CH_3)_3$), 27.6 (CH_2Se); $\mathbf{\nu_{max}}$ 3200 (br, CO_2-H), 2979 (w, C-H), 1734 (s, C=O), 1158 (m), 1122 (m), 737 (m); **m/z** (ESI^+) 409.1 ($[M+Na]^+$, 100%); **HRMS-ESI** calculated for $C_{17}H_{21}Na_2O_5Se$: *m/z* 431.0345 ($[M-H+2Na]^+$) , found: *m/z* 431.0359 ($[M-H+2Na]^+$).

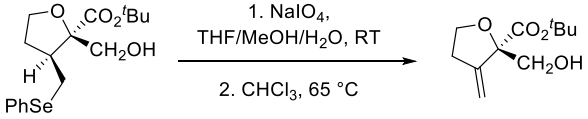
(2*R**,3*S**)-*tert*-Butyl 2-(hydroxymethyl)-3-((phenylselanyl)methyl)tetrahydrofuran-2-carboxylate (16)



To a solution of DMF (96.0 µL) in DCM (14 mL) was added oxalyl chloride dropwise (0.32 mL) at room temperature. The mixture was stirred for 20 min and all volatiles were removed. The residual salt was dissolved in dry THF/MeCN (1:1, 15 mL). A solution of (2*S*,3*R*)-2-(*tert*-butoxycarbonyl)-3-((phenylselanyl)methyl)tetrahydrofuran-2-carboxylic acid **15** (239 mg, 0.62 mmol) was added over 2 min at 0 °C. The mixture was stirred for 20 min and cooled to -78 °C. A solution of LiAl(O^{t}Bu)$_3$H in THF (1.0 M, 6.2 mL, 6.2 mmol) was added over 5 min. The mixture was warmed to room temperature outside the cooling bath, and stirred at room temperature for 90 min. Water (20 mL), saturated aqueous NH_4Cl (20 mL), saturated aqueous Rochelle salt solution (20 mL) and EtOAc (50 mL) were successively added. The mixture was vigorously stirred for two hours and the layers were separated. The aqueous layer was extracted with more EtOAc (30 mL). The combined organic layers were dried (Na_2SO_4), filtered and evaporated. The residue was purified by Flash Chromatography (PE/EtOAc 3:2) to give the desired product **16** as a colourless oil (176 mg, 0.473 mmol, 76%). $\mathbf{R_f}$ 0.34 (PE/EtOAc 3:2); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 7.55-7.48 (2H, m, Ar*H*), 7.31-7.22 (3H, m, Ar*H*), 4.08 (1H, td, *J* = 8.1, 2.6 Hz, OC*H*H'), 3.90 (1H, ddd, *J* = 10.1, 8.1, 5.9 Hz, OCH*H'*), 3.77 (2H, s, CH_2OH), 3.35 (1H, dd, *J* = 11.9, 3.7 Hz, C*H*H'Se), 2.90 (1H, t, *J* = 11,9 Hz, CH*H'*Se), 2.54 (1H, dddd, *J* = 11.9, 10.1, 7.5, 3.7 Hz, C*H*), 2.30 (1H, dddd, *J* = 11.9. 7.5, 5.9, 2.6 Hz, OCH_2CHH'), 2.24 (1H, br, O*H*), 1.79 (1H, dtd, *J* = 11.9, 10.1, 8.1 Hz, OCH_2CH*H'*), 1.40 (9H, s, $OC(CH_3)_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 177.2 (*C*=O), 133.0 (*Ar*), 129.6 (*Ar*), 129.3 (*Ar*), 127.3 (*Ar*), 86.7 (C_{quat}), 82.1 (C_{quat}), 68.0 (OCH_2), 63.8 (CH_2OH), 46.6 (*C*H), 33.6 (OCH_2CH_2), 28.0 ($OC(CH_3)_3$), 27.7 (CH_2Se); $\mathbf{\nu_{max}}$ 3468 (br, O-H), 2976 (w, C-H), 1742 (s, C=O), 1368 (m),

1148 (s), 1036 (s), 737 (s); **m/z** (ESI^+) 395.0 ($[M+Na]^+$, 100%), 767.1 ($[2M+Na]^+$, 8%); **HRMS-ESI** calculated for $C_{17}H_{24}NaO_4Se$: *m/z* 395.0732 ($[M+Na]^+$), found: *m/z* 395.0740 ($[M+Na]^+$).

tert-Butyl 2-(hydroxymethyl)-3-methylenetetrahydrofuran-2-carboxylate (17)



16 **17**

To a vigorously stirred solution of *tert*-butyl (2*S*,3*R*)-2-(hydroxymethyl)-3-((phenylselanyl)methyl)tetrahydrofuran-2-carboxylate **16** (218 mg, 0.586 mmol) in THF/MeOH/H_2O (1:1:1, 12 mL) at room temperature were added successively $NaHCO_3$ (198 mg, 2.35 mmol) and $NaIO_4$ (503 mg, 2.35, mmol). The mixture was stirred for 30 min. Water (35 mL) and $CHCl_3$ (20 mL) were added. Stirring was continued for 5 min and the mixture was filtered through celite, which was further eluted with $CHCl_3$ (15 mL). The layers were separated and the aqueous phase was extracted with more $CHCl_3$ (20 mL). The combined organic layers were dried (Na_2SO_4), filtered and refluxed for 2 h at 65 °C. Solvent was evaporated and the residue was purified by Flash Chromatography (PE/Et_2O 3:2 to 2:3) to give the desired compound **17** as a colourless oil (116 mg, 0.541 mmol, 92%); $\mathbf{R_f}$ 0.40 (PE/Et_2O 2:3); **^{1}H NMR ($CDCl_3$, 400 MHz)** δ 5.22 (1H, t, *J* = 2.2 Hz, C*H*H'=C), 5.19 (1H, t, *J* = 2.2 Hz, CH*H'*=C), 4.10 (2H, t, *J* = 7.0 Hz, OCH_2), 3.90 (1H, d, *J* = 11.5 Hz, C*H*H'OH), 3.68 (1H, d, *J* = 11.5 Hz, CH*H'*OH), 2.67-2.63 (2H, m, OCH_2CH_2), 2.13 (1H, br, O*H*), 1.47 (1H, s, $OC(CH_3)_3$); **^{13}C NMR ($CDCl_3$, 100 MHz)** δ 170.6 (*C*=O), 147.5 (CH_2=*C*), 108.4 (*C*H_2=C), 87.2 (C_{quat}), 82.2 (C_{quat}), 68.1 (OCH_2), 67.0 (*C*H_2OH), 33.3 (*C*H), 28.0 ($O(CH_3)_3$); $\mathbf{\nu_{max}}$ 3468 (br, O-H), 2977 (w, C-H), 1725 (s, C=O), 1163 (s), 1031 (s), 899 (w), 846 (w); **m/z** (ESI^+) 237.1 ($[M+Na]^+$, 47%), 451.0 ($[2M+Na]^+$, 100%); **HRMS-ESI** calculated for $C_{11}H_{18}NaO_4$: *m/z* 237.1097 ($[M+Na]^+$), found: *m/z* 237.1102 ($[M+Na]^+$).

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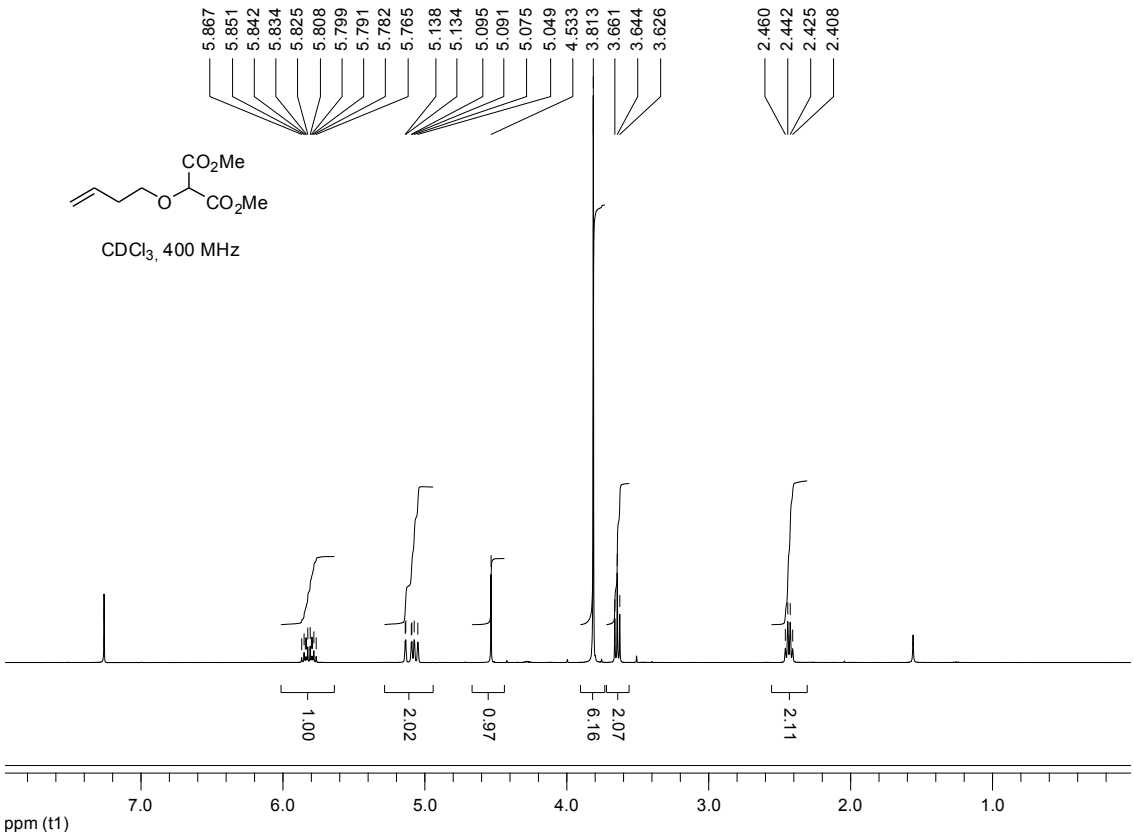
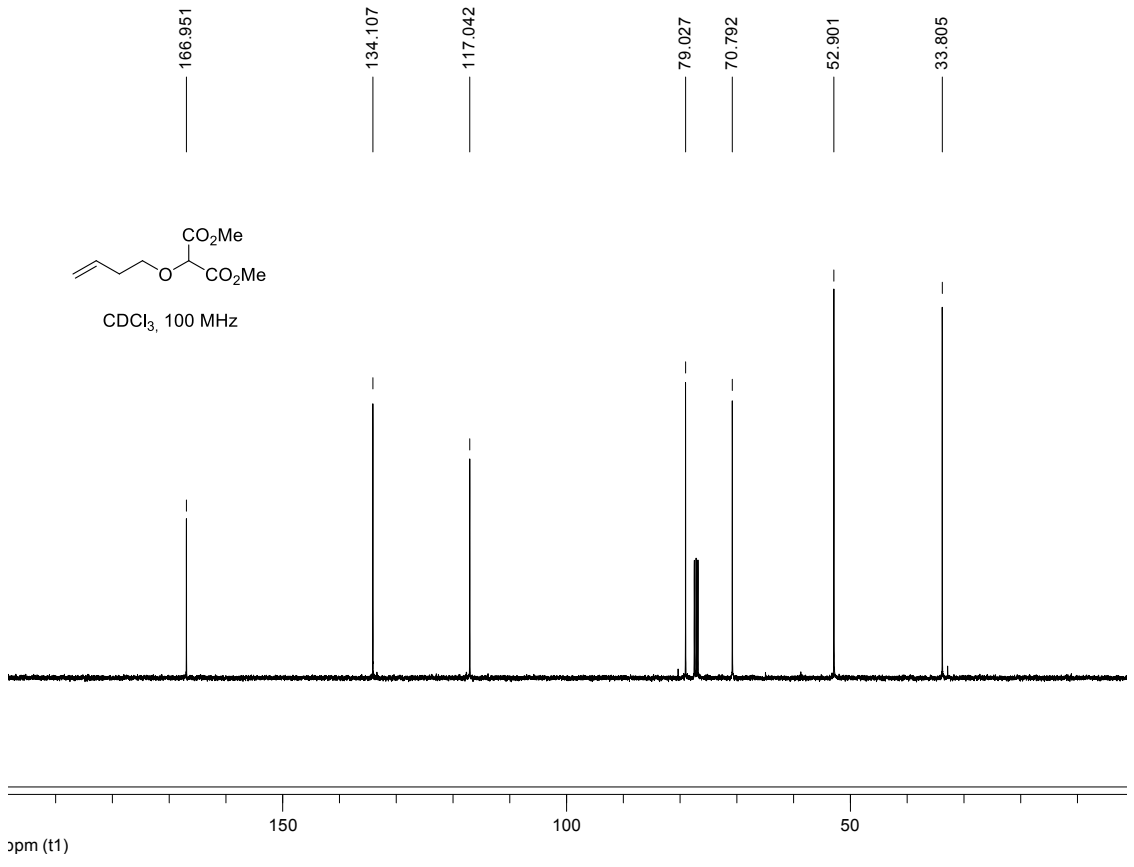
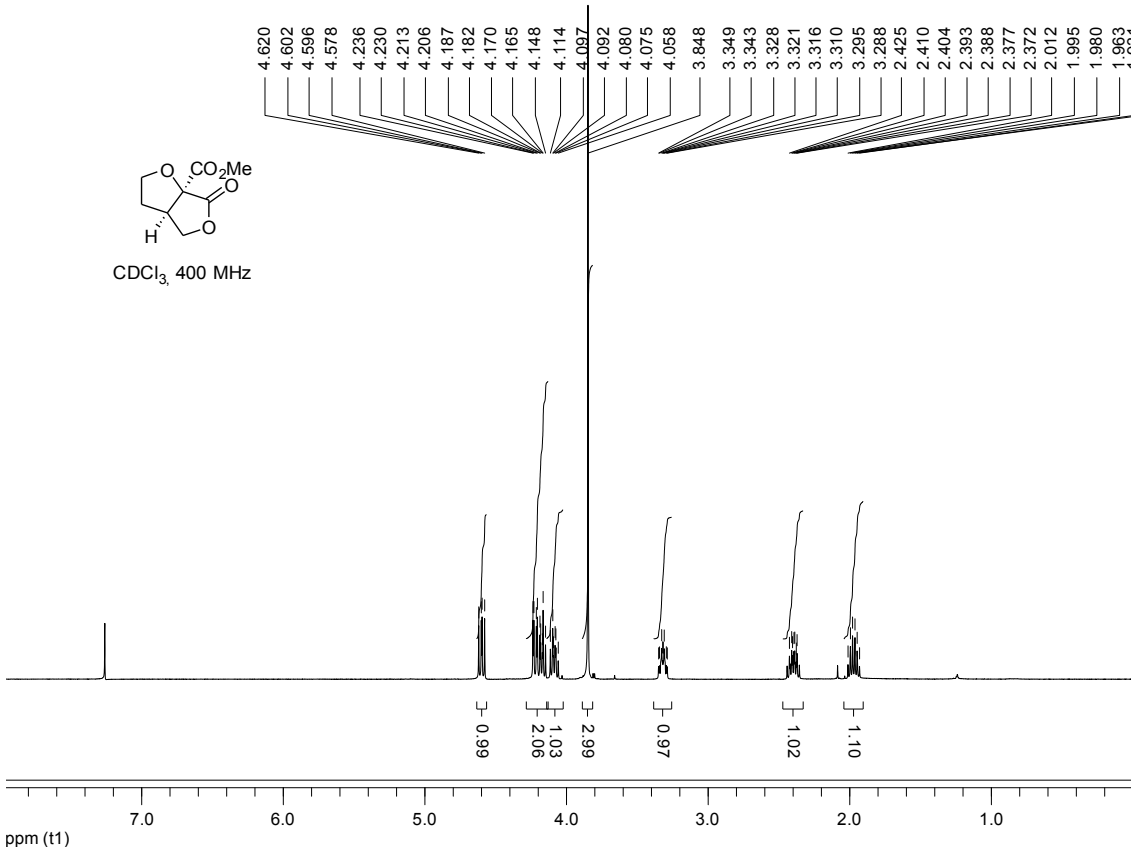
NMR Spectra

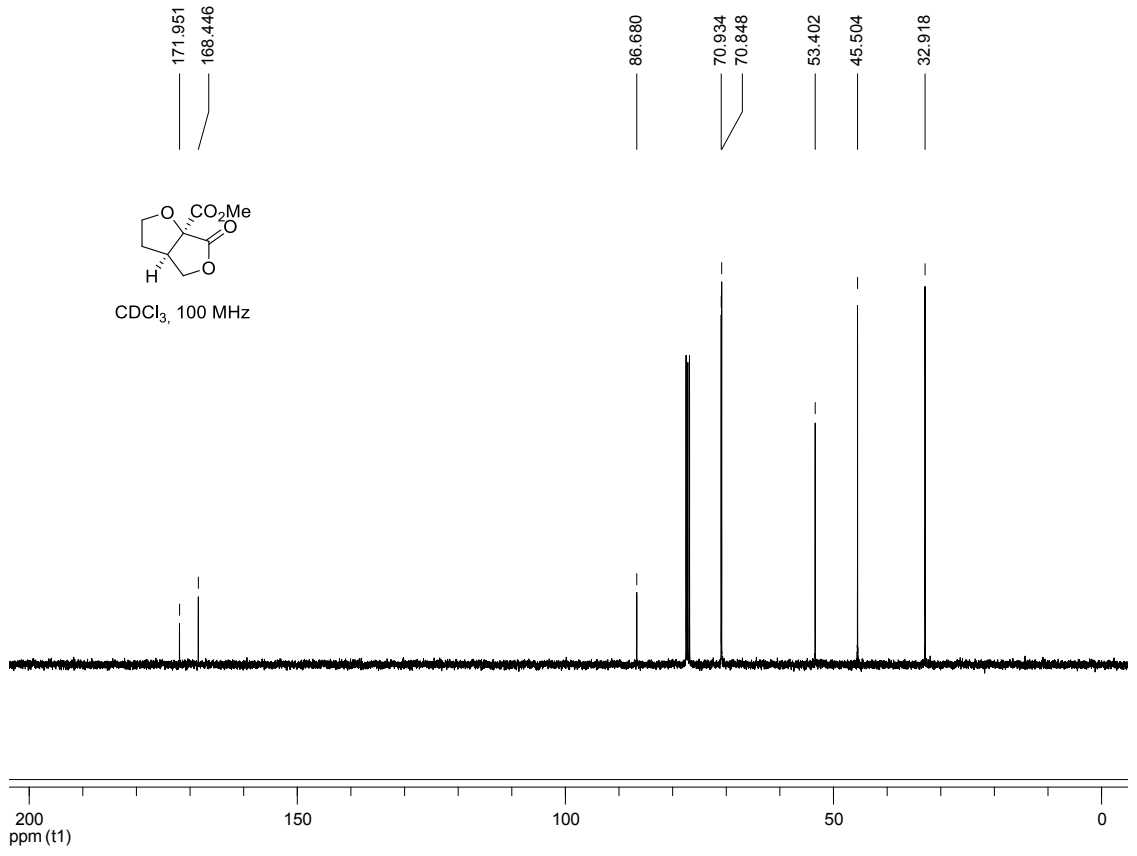
Spectra for compound **7a**



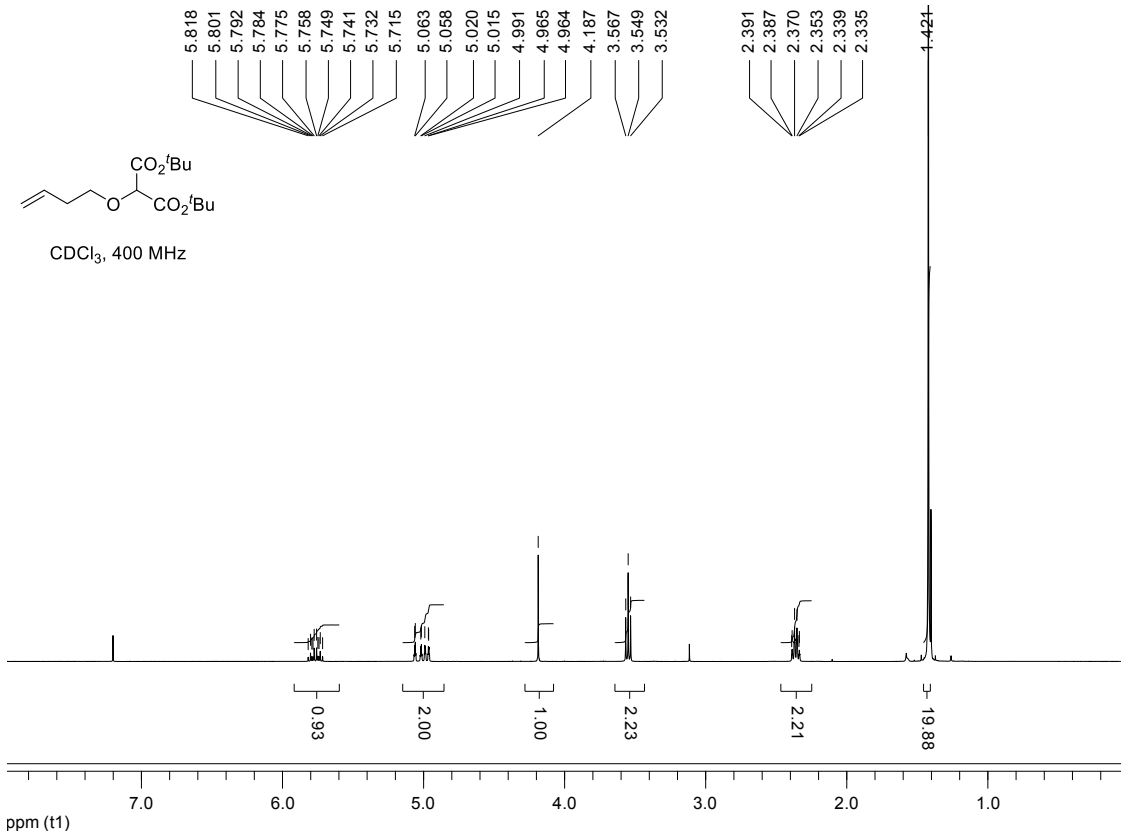


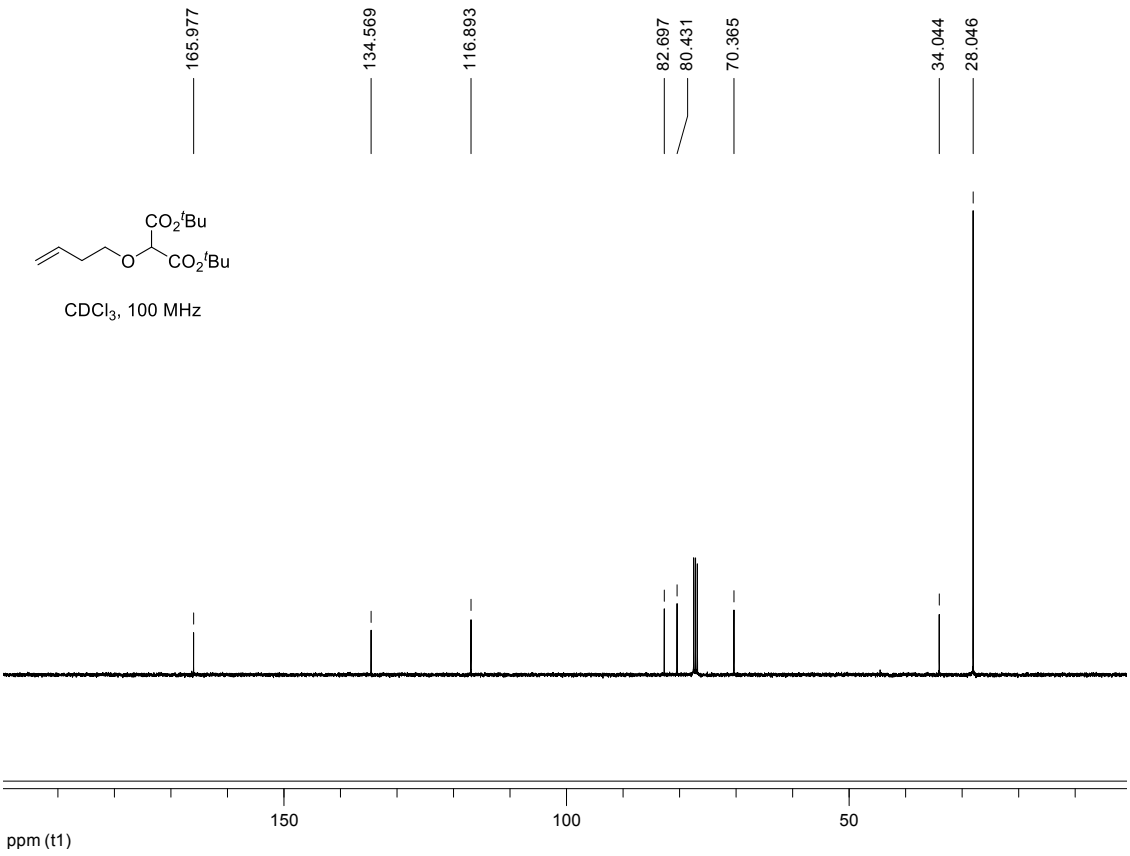
Spectra for compound **8a**



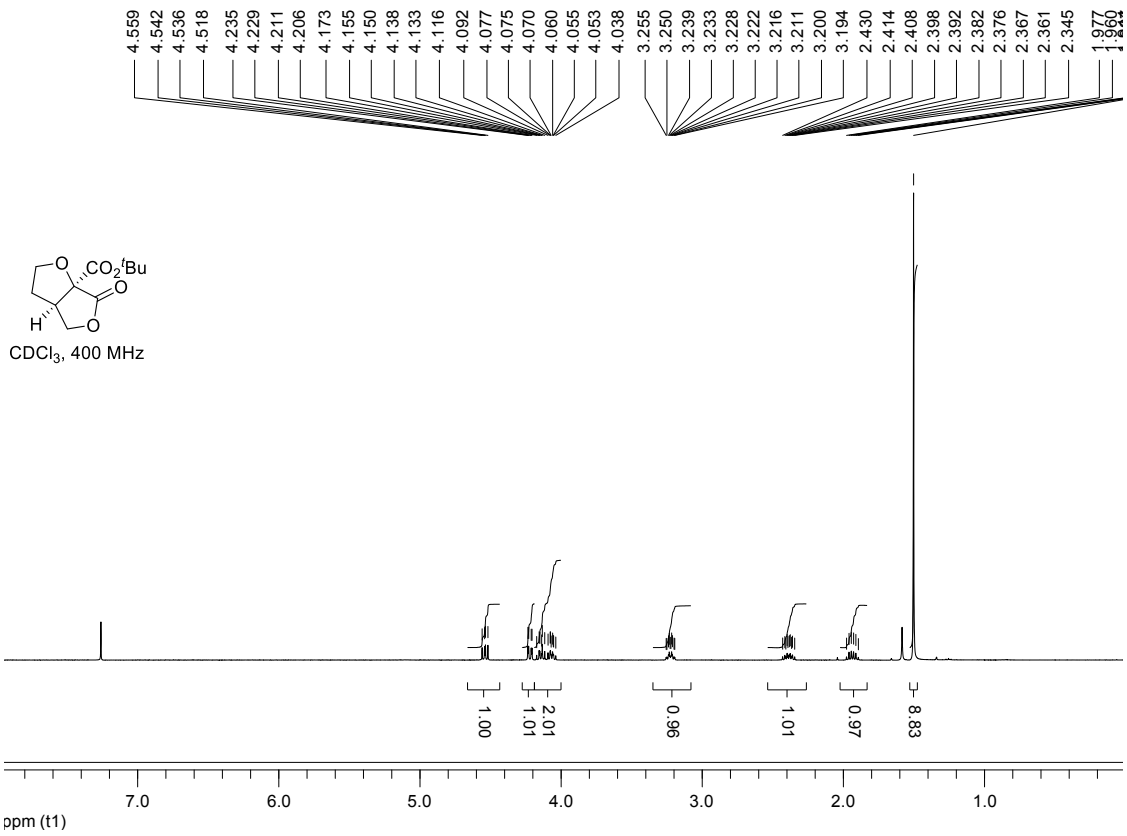


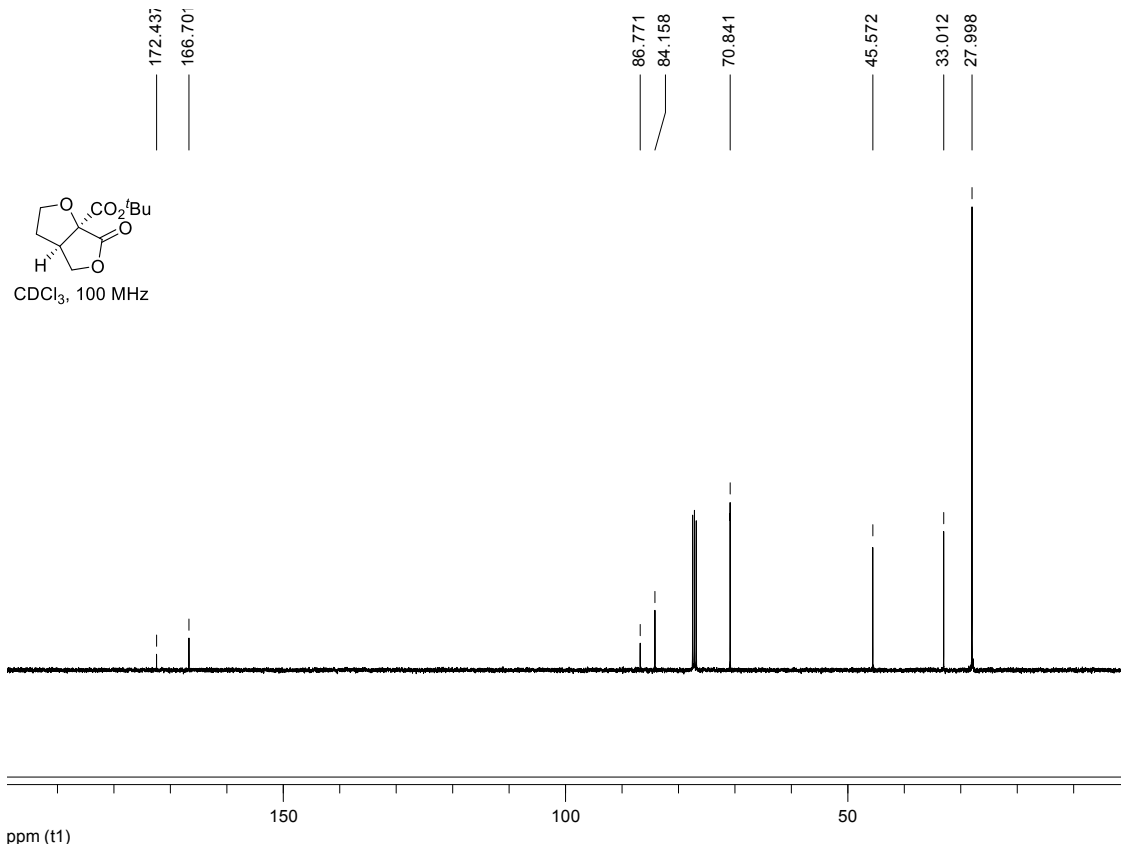
Spectra for compound **7b**



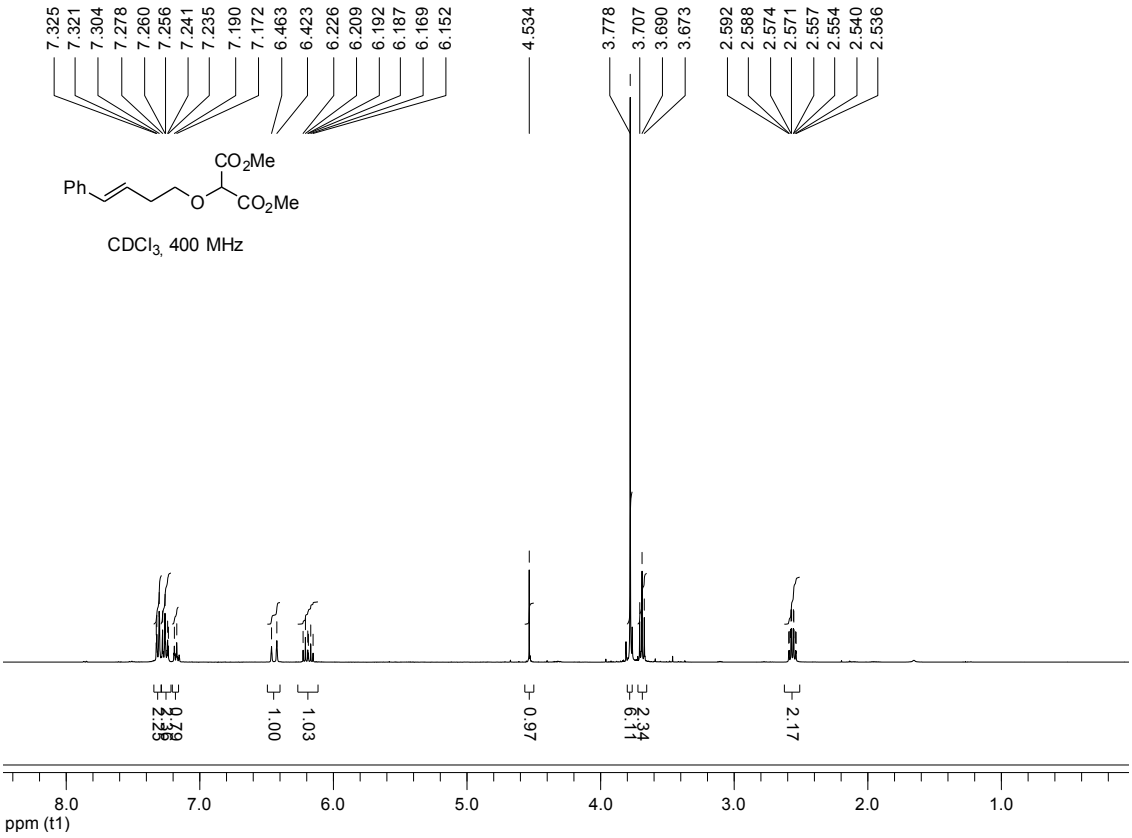


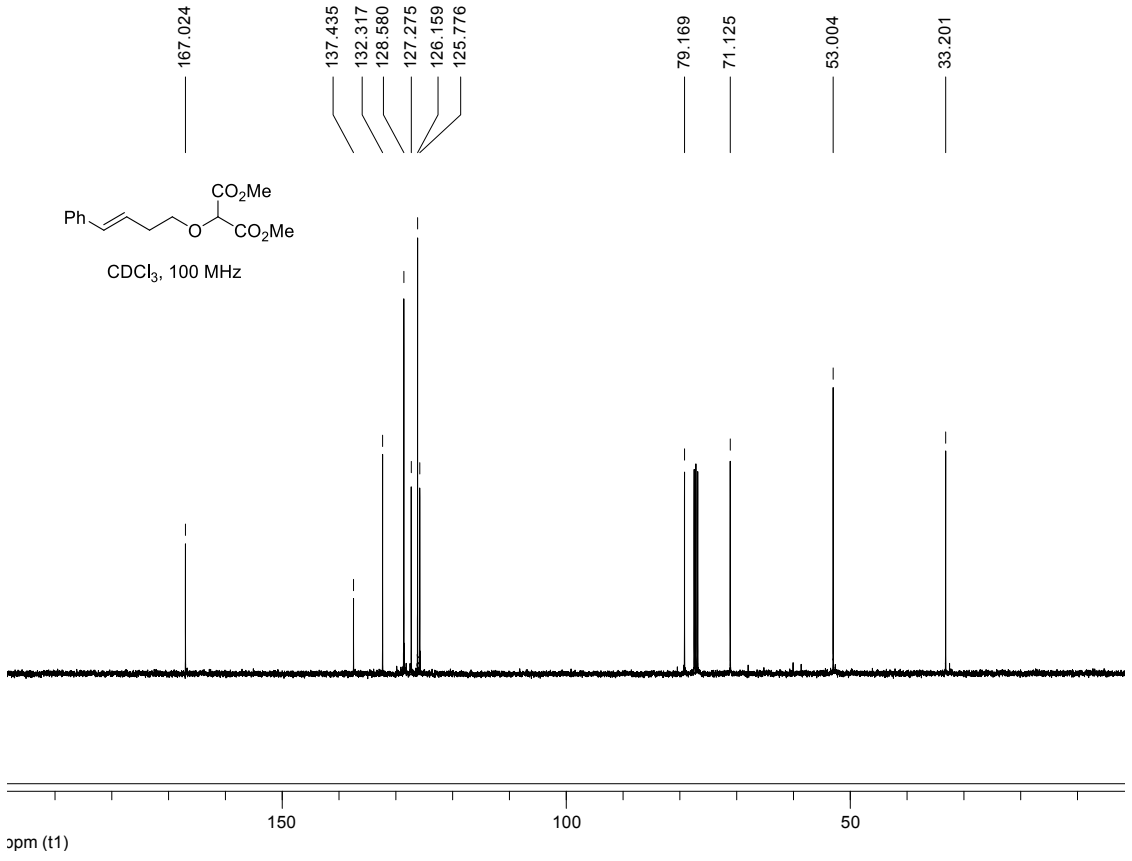
Spectra for compound **8b**



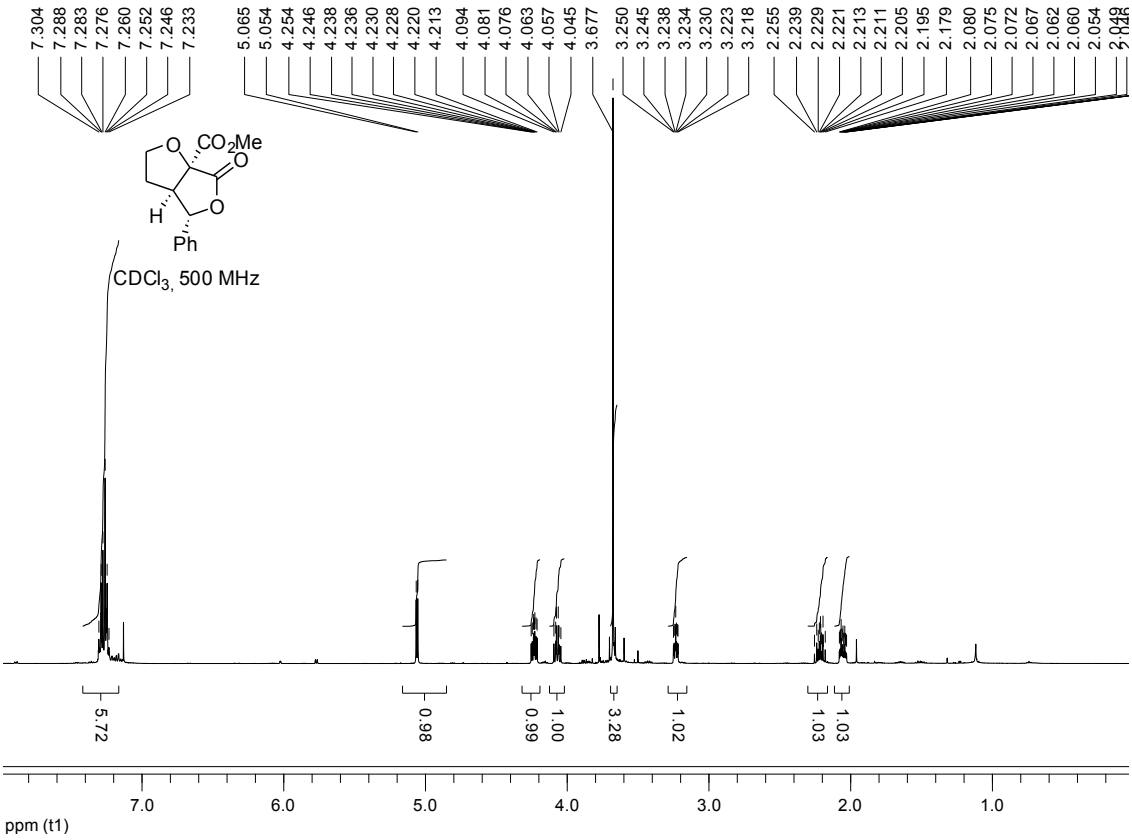


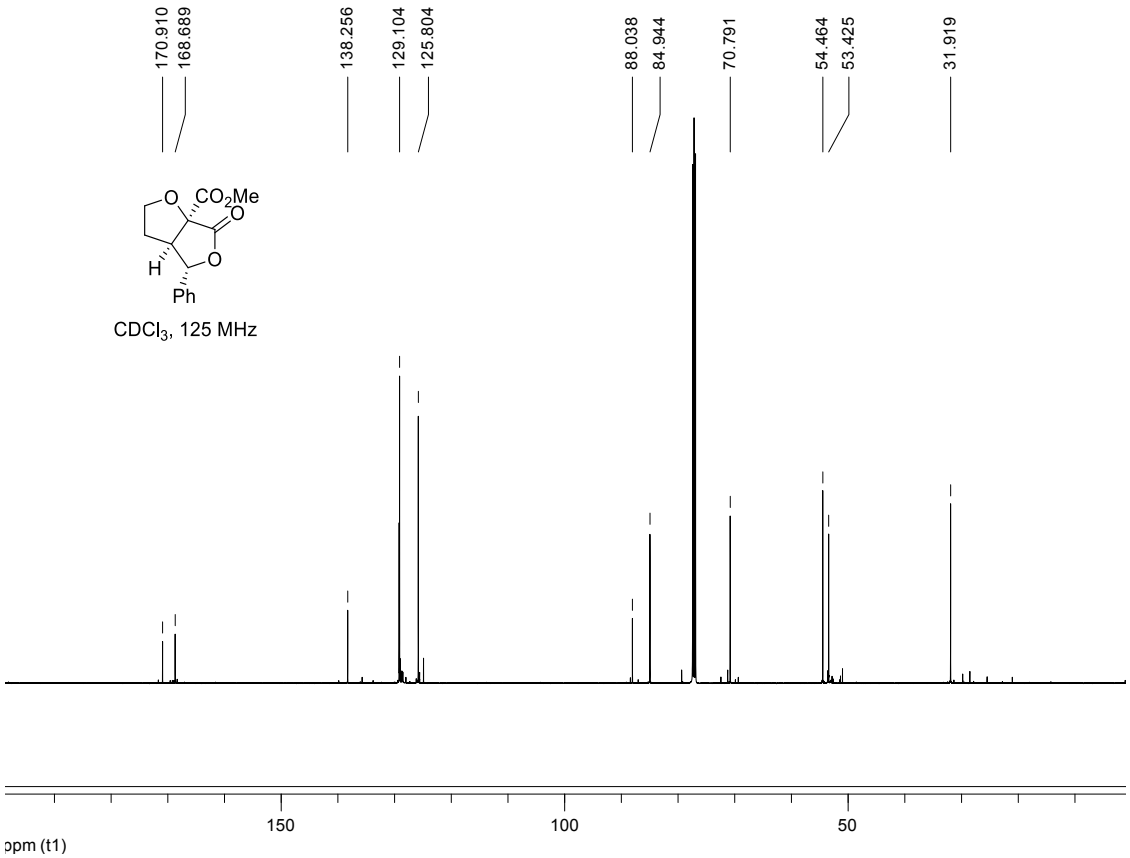
Spectra for compound **7c**



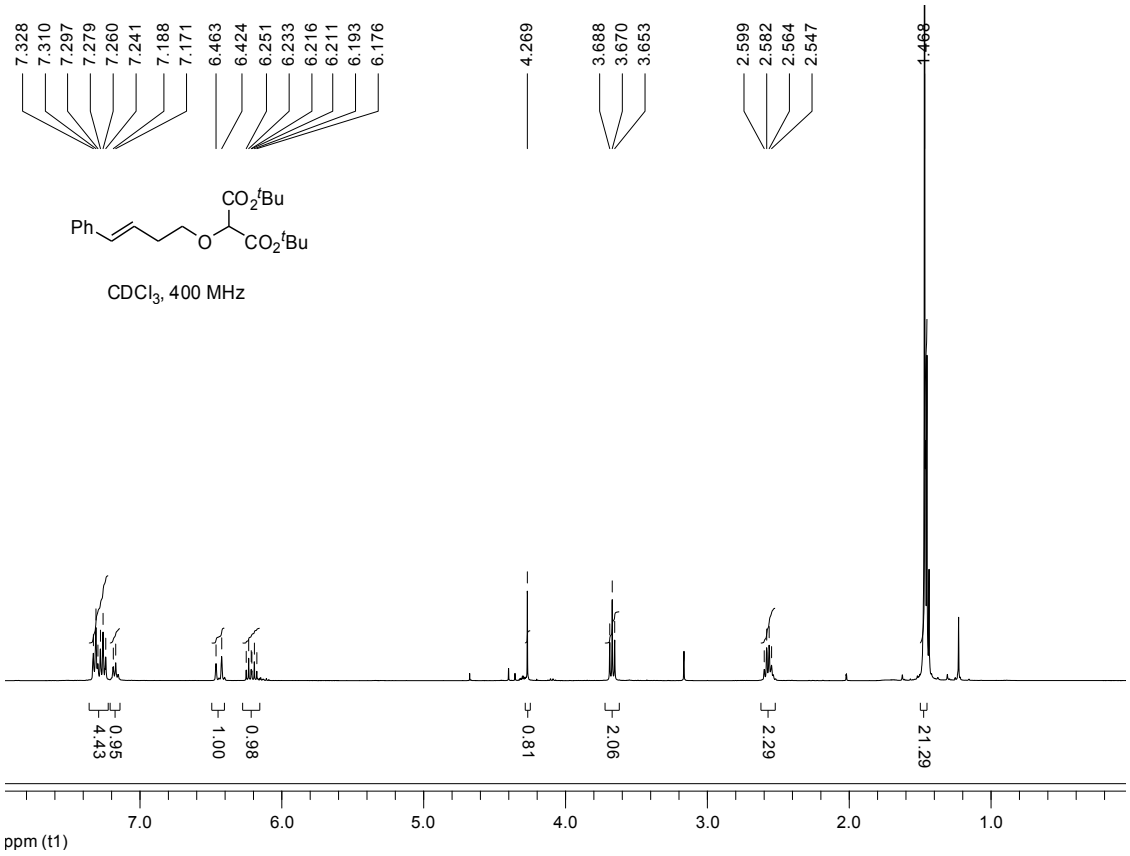


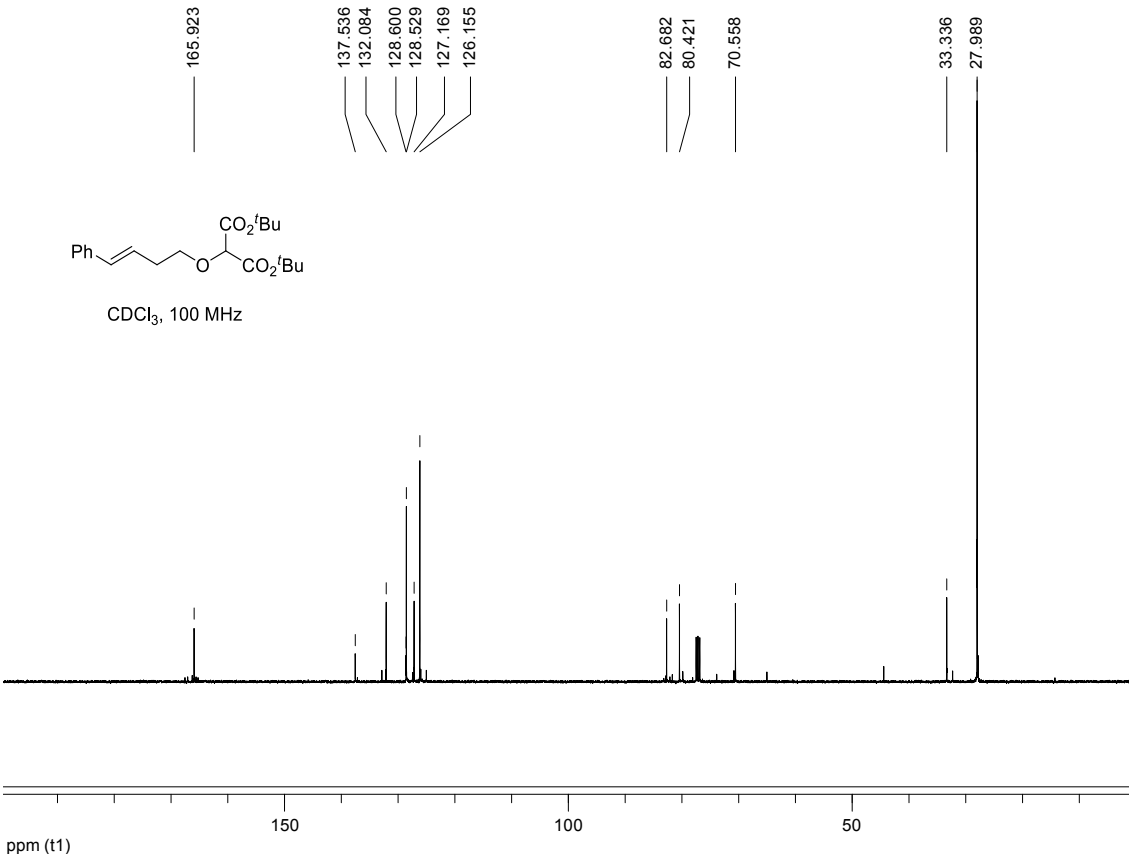
Spectra for compound **8c**



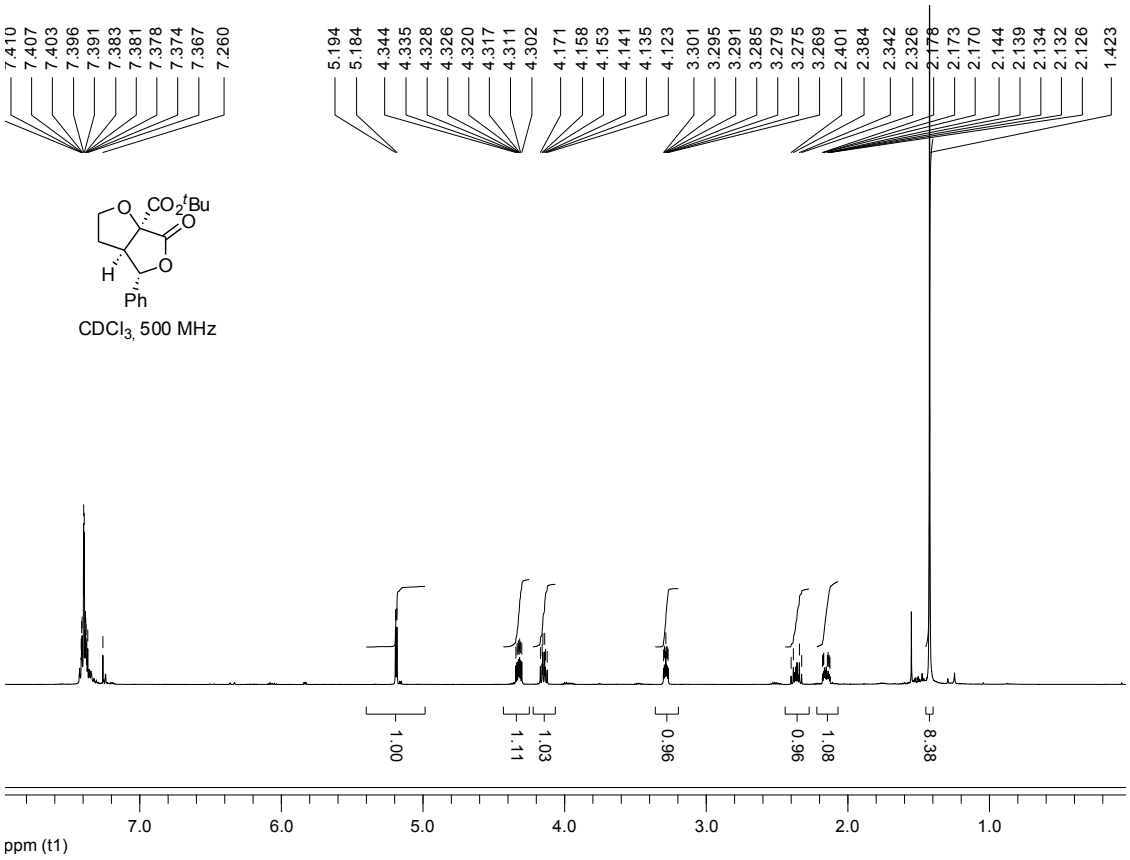


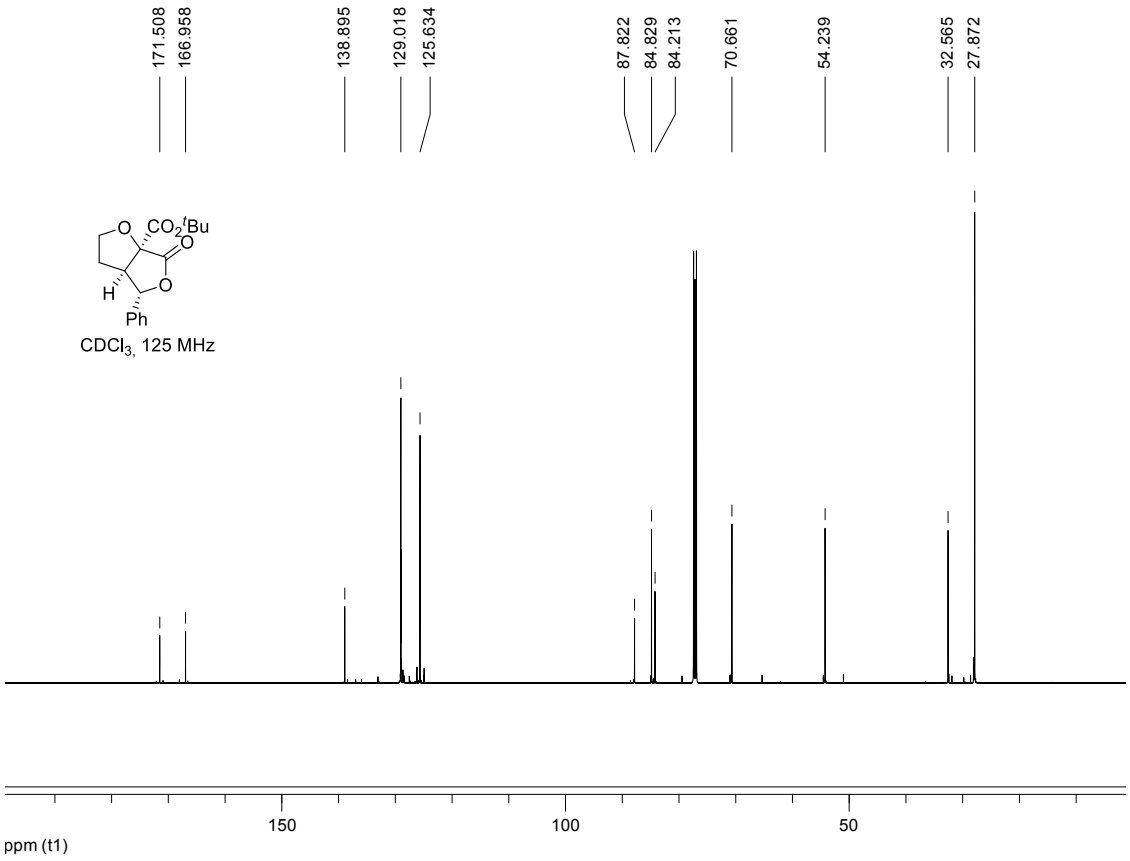
Spectra for compound **7d**



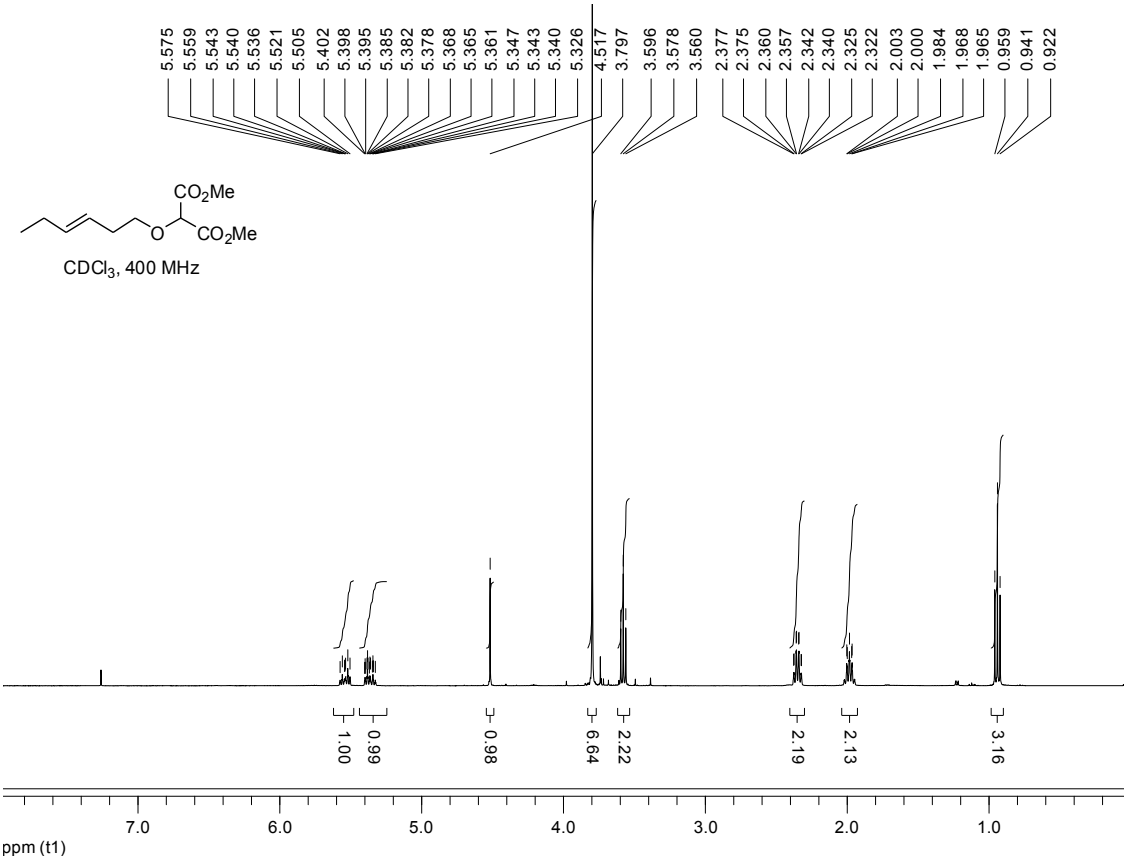


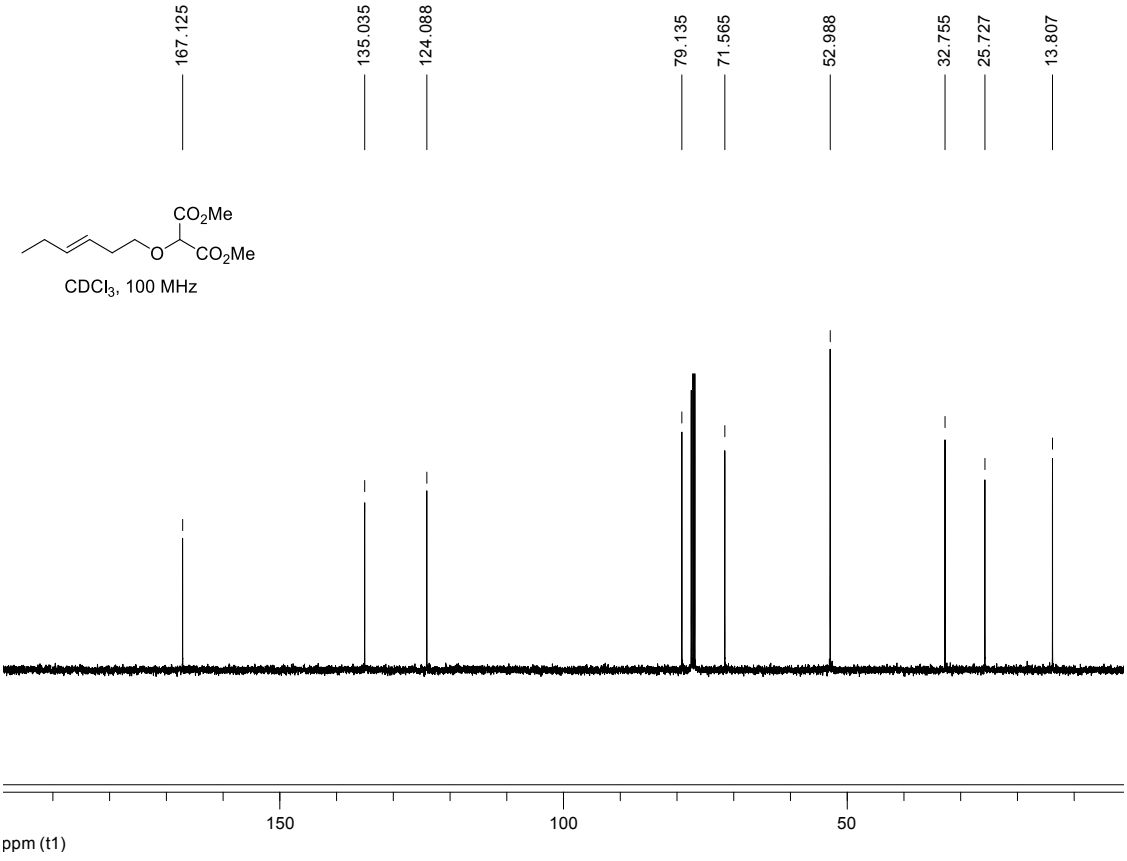
Spectra for compound **8d**



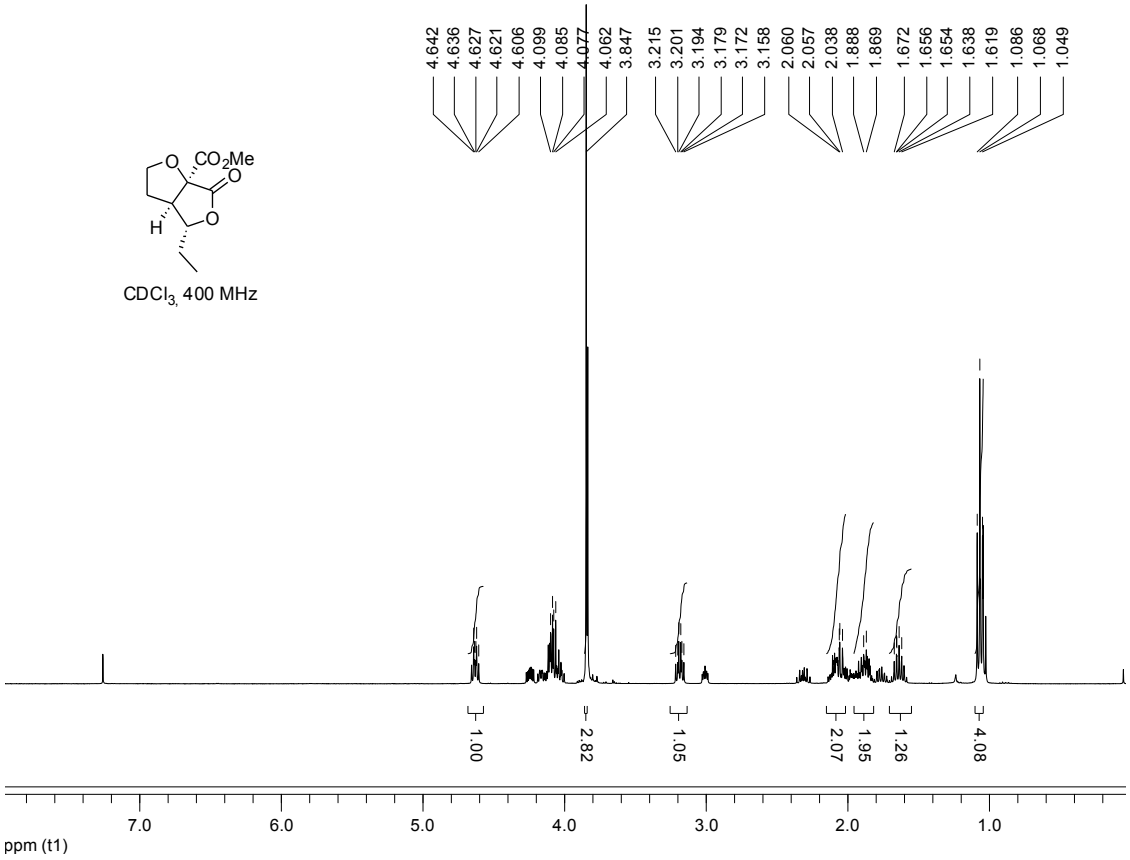


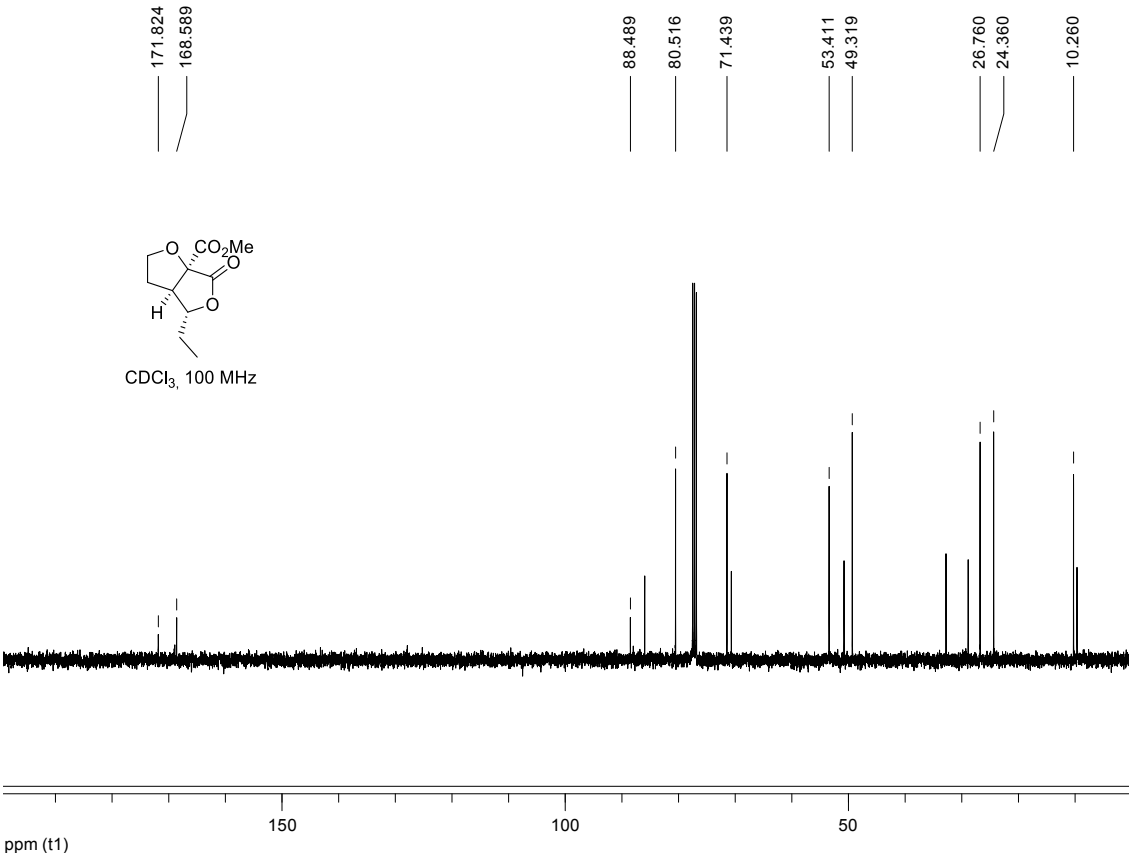
Spectra for compound **7e**



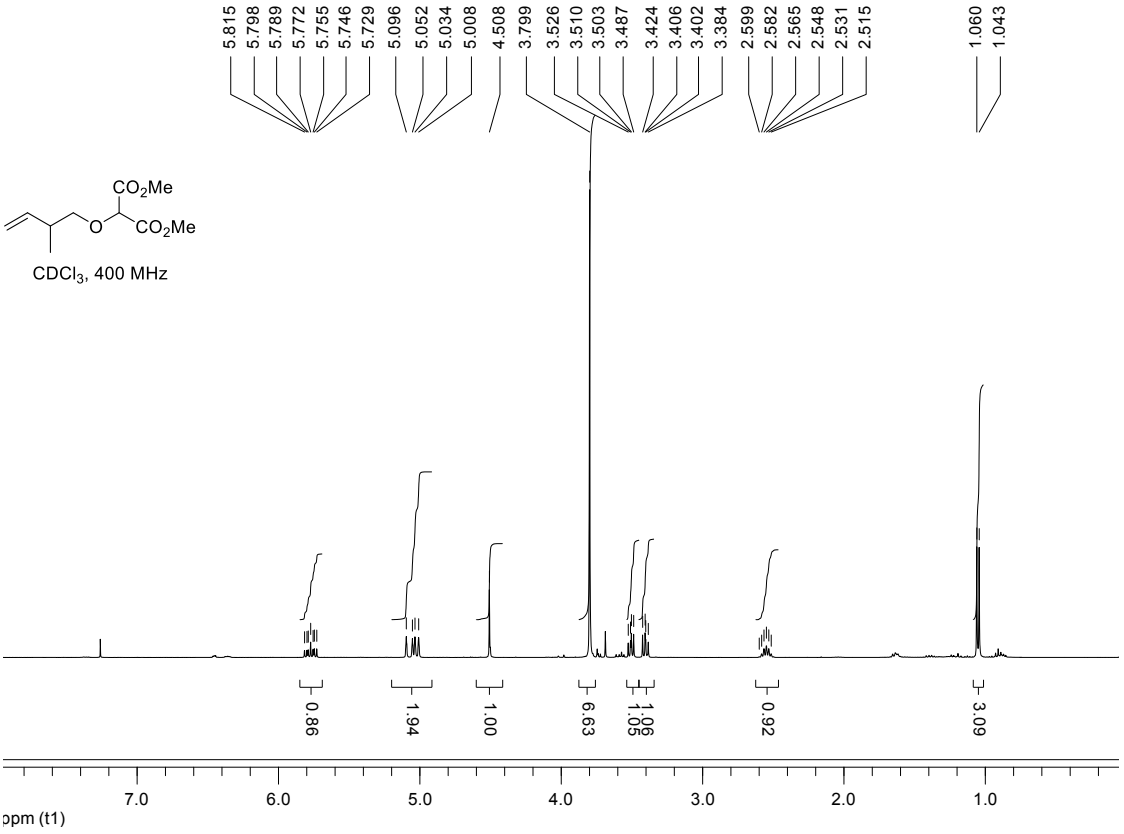


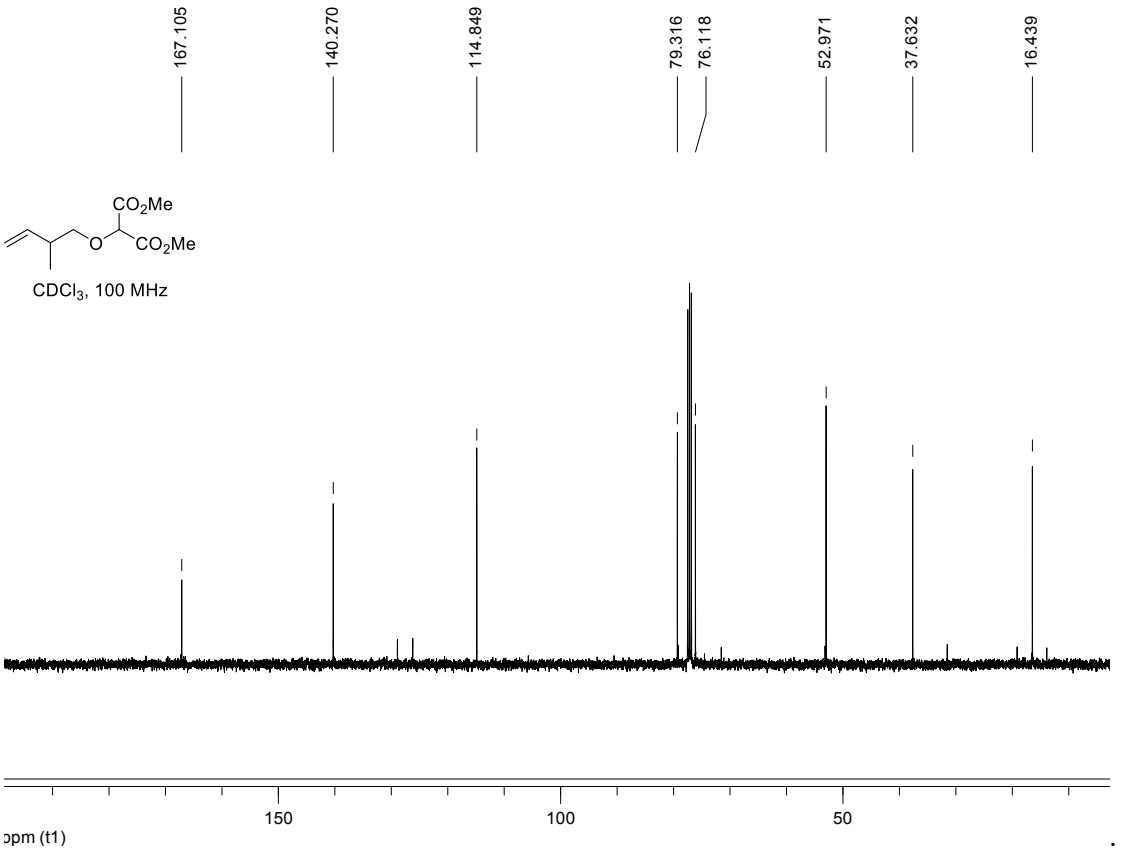
Spectra for compound **8e** (mixture of diastereoisomers after purification d. r. = 2.1:1)



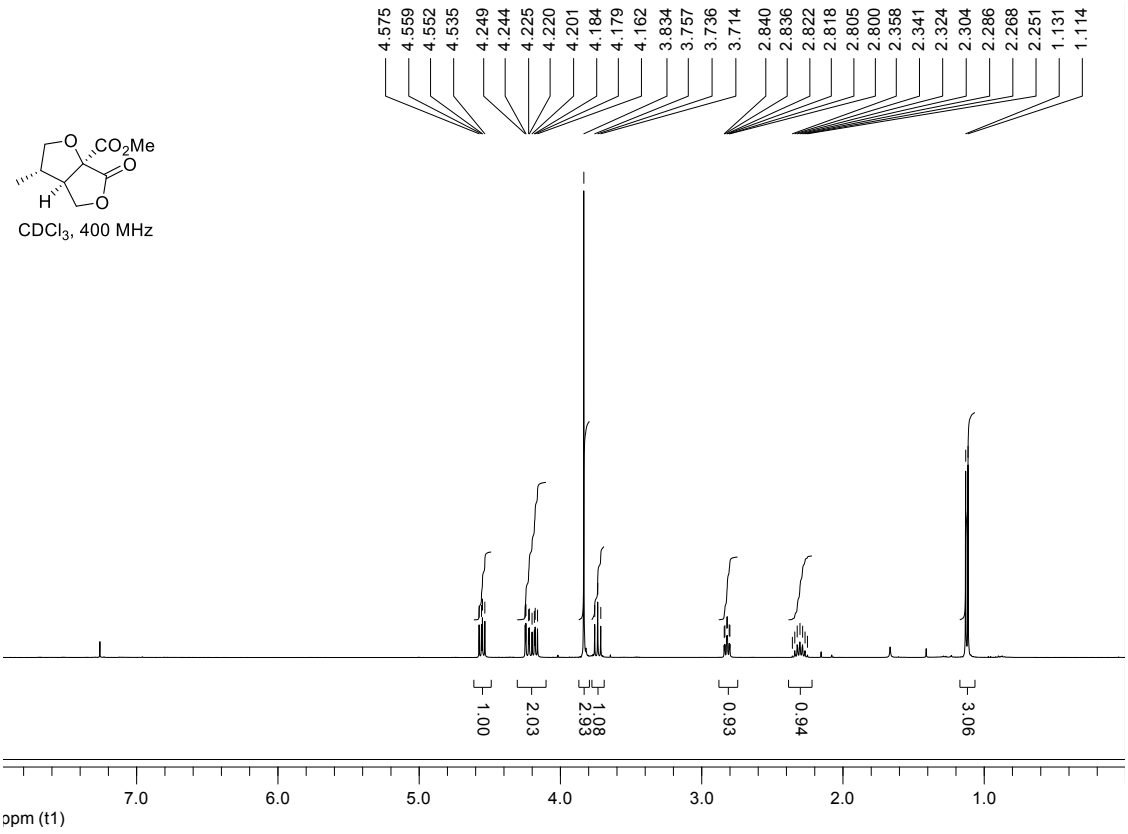


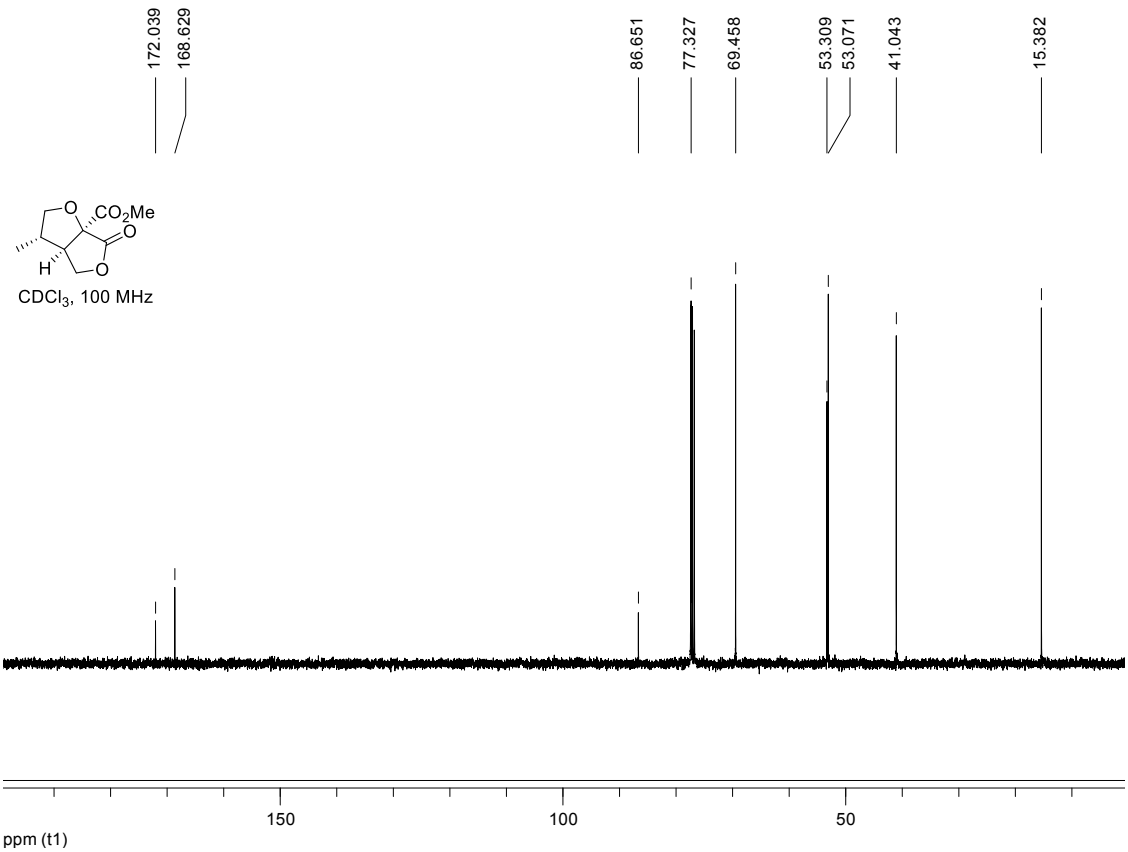
Spectra for compound **9a**



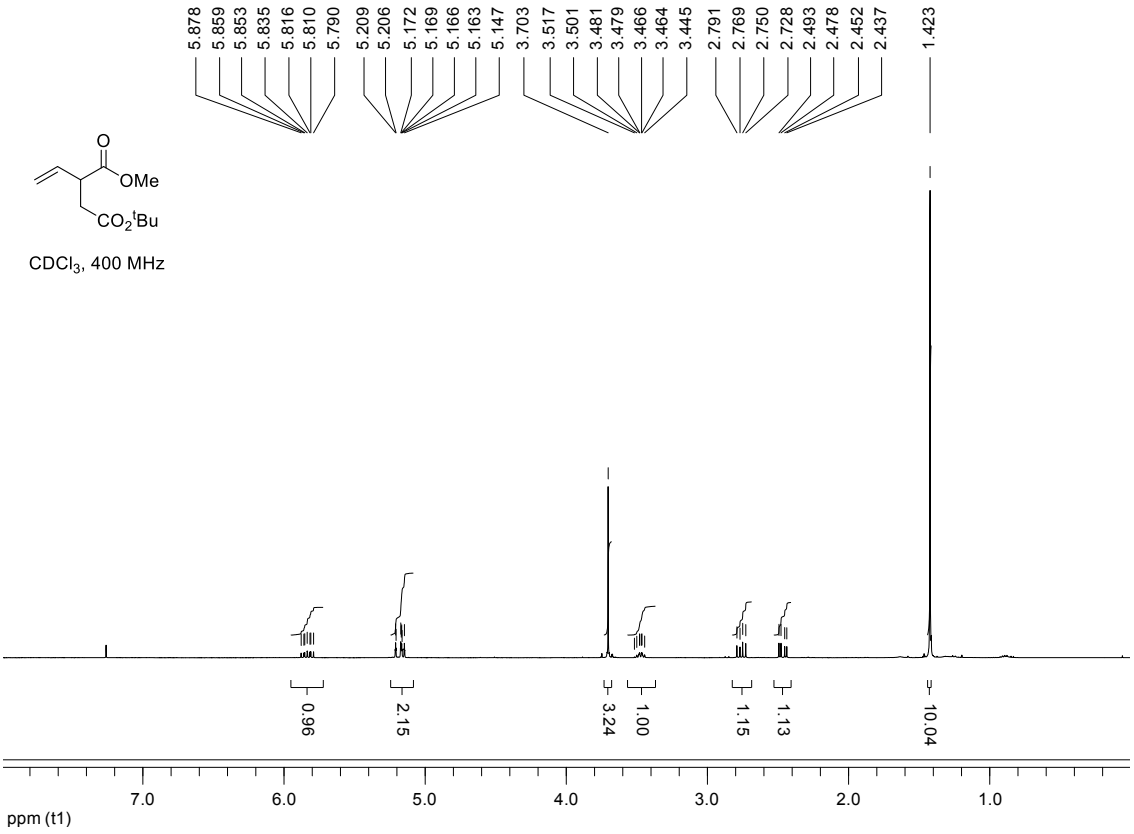


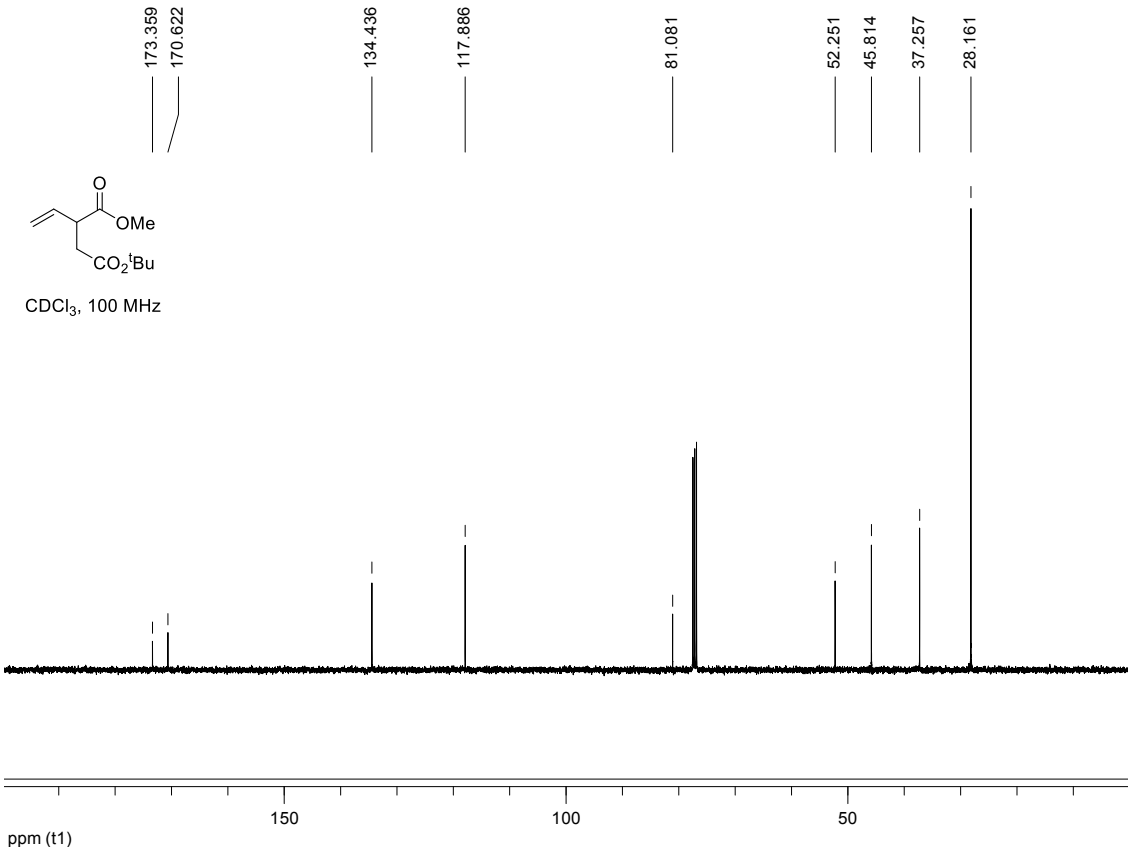
Spectra for compound **10a**



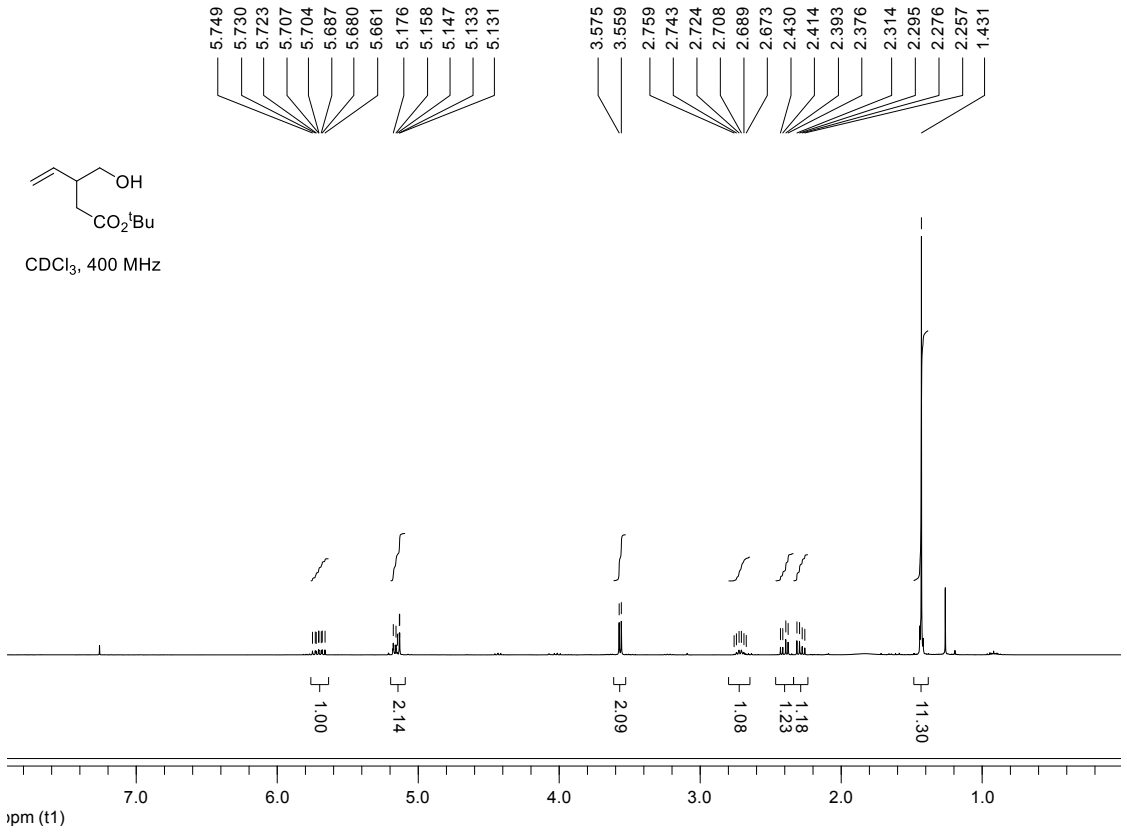


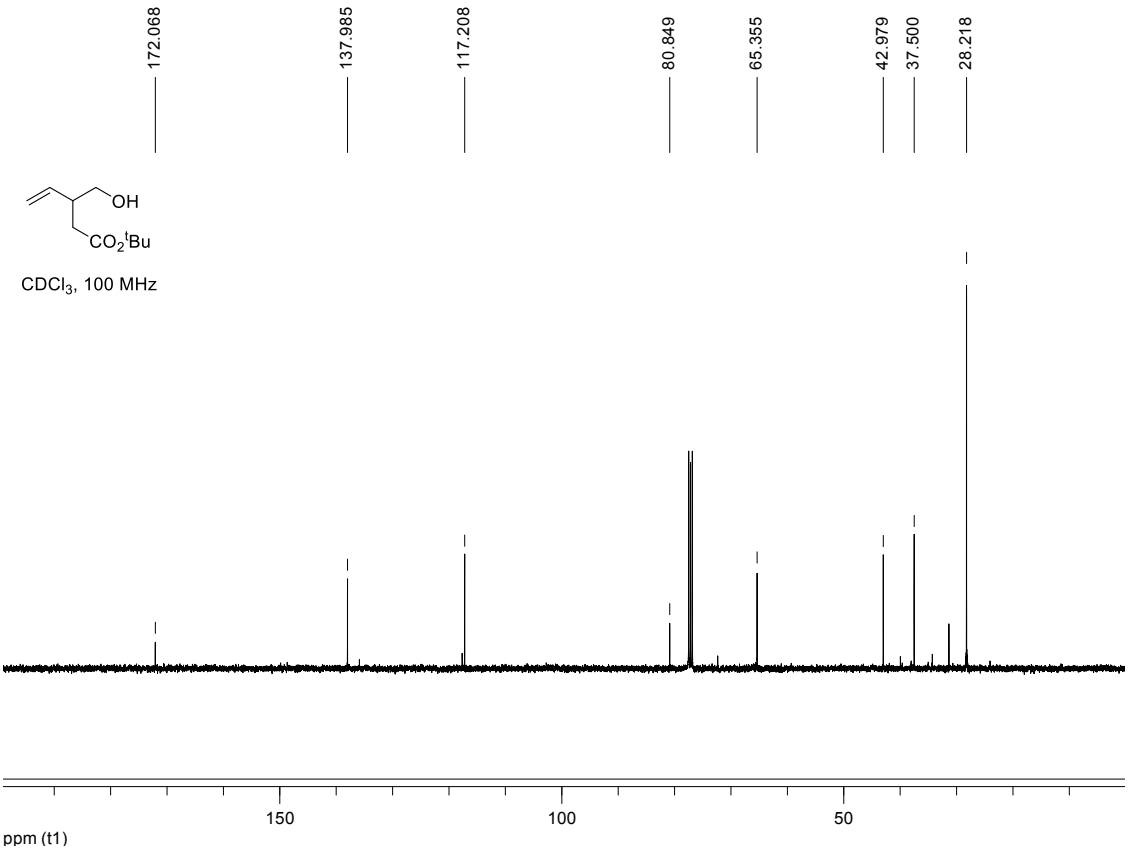
Spectra for compound **SI13**



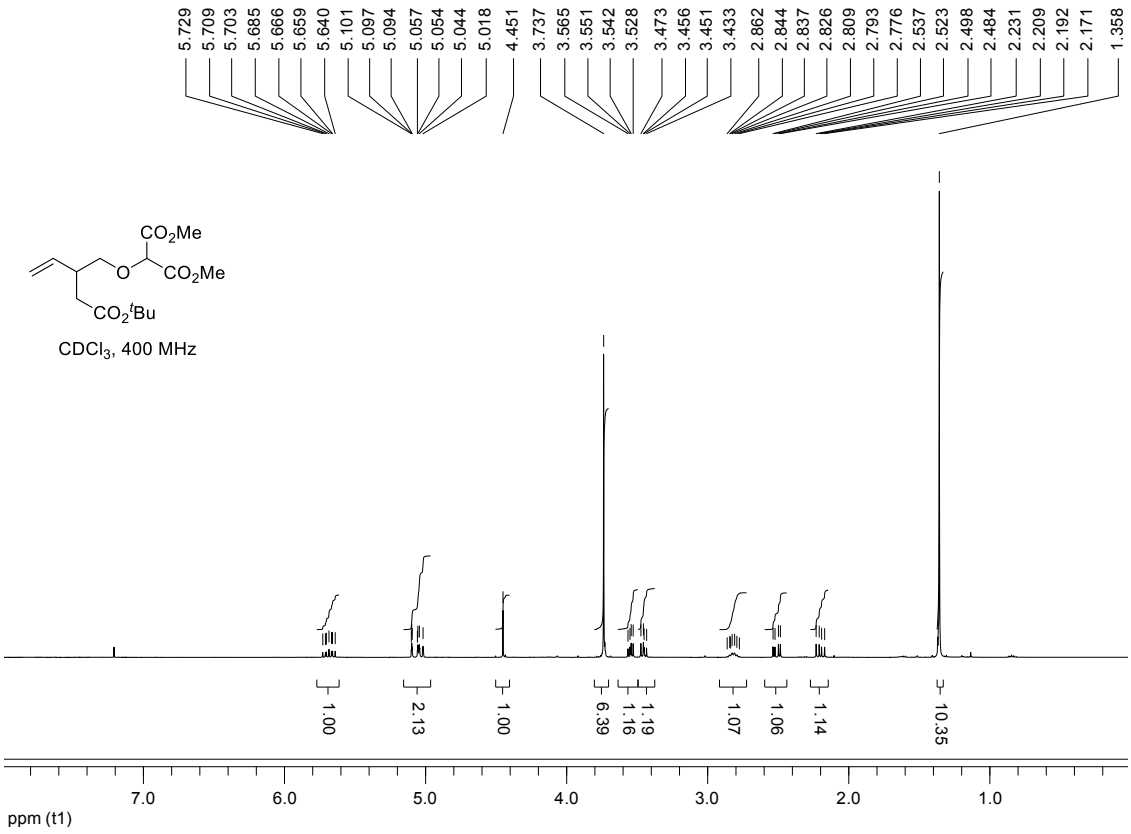


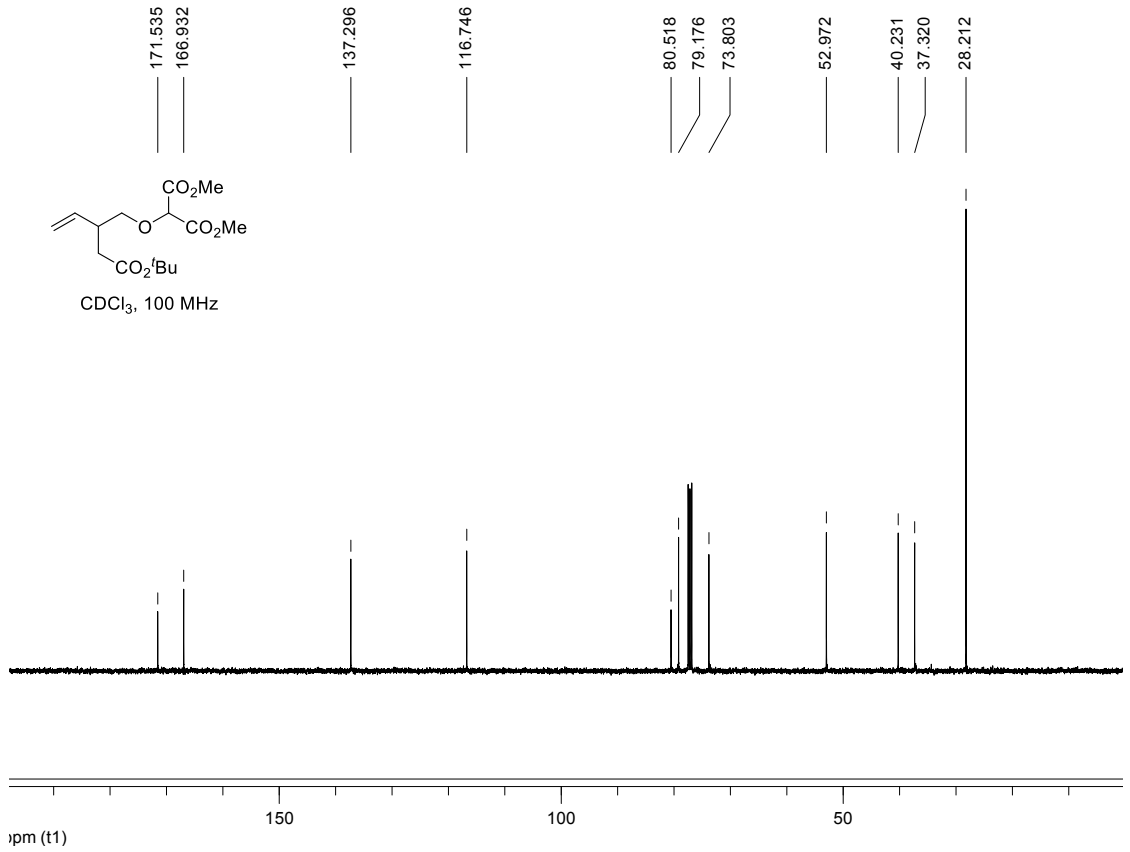
Spectra for compound **SI14**



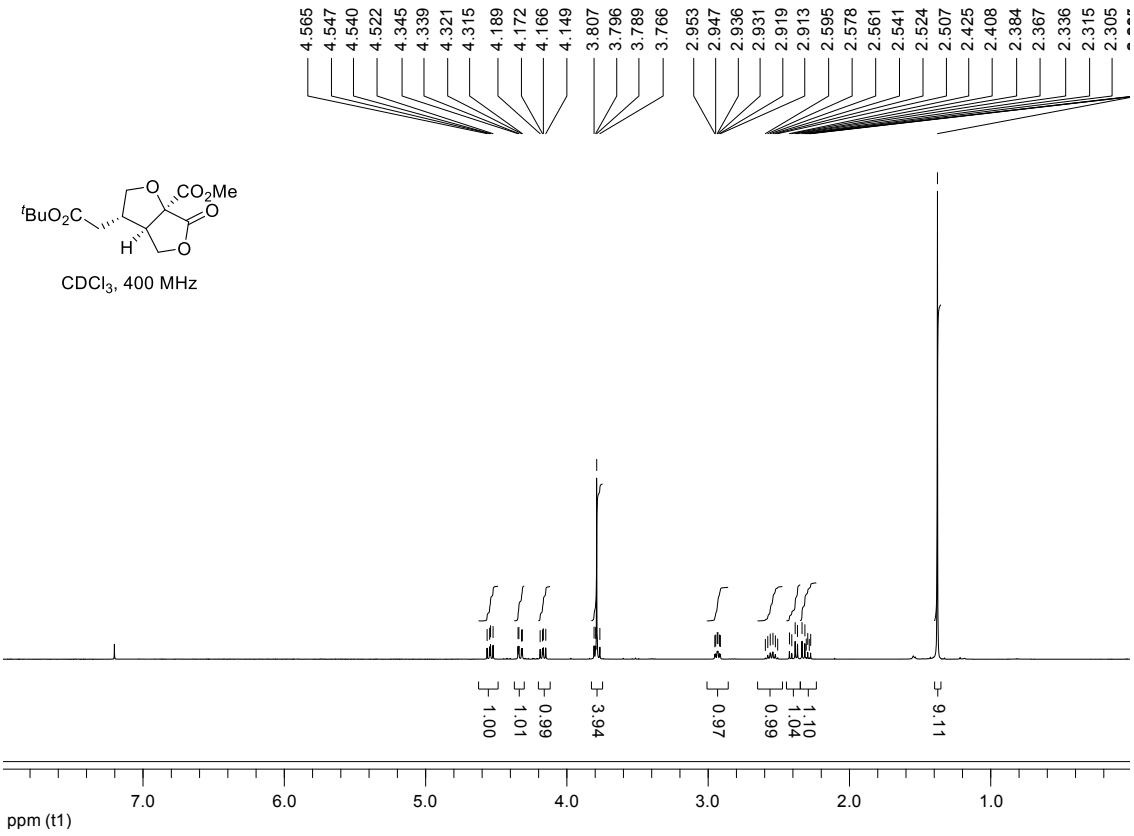


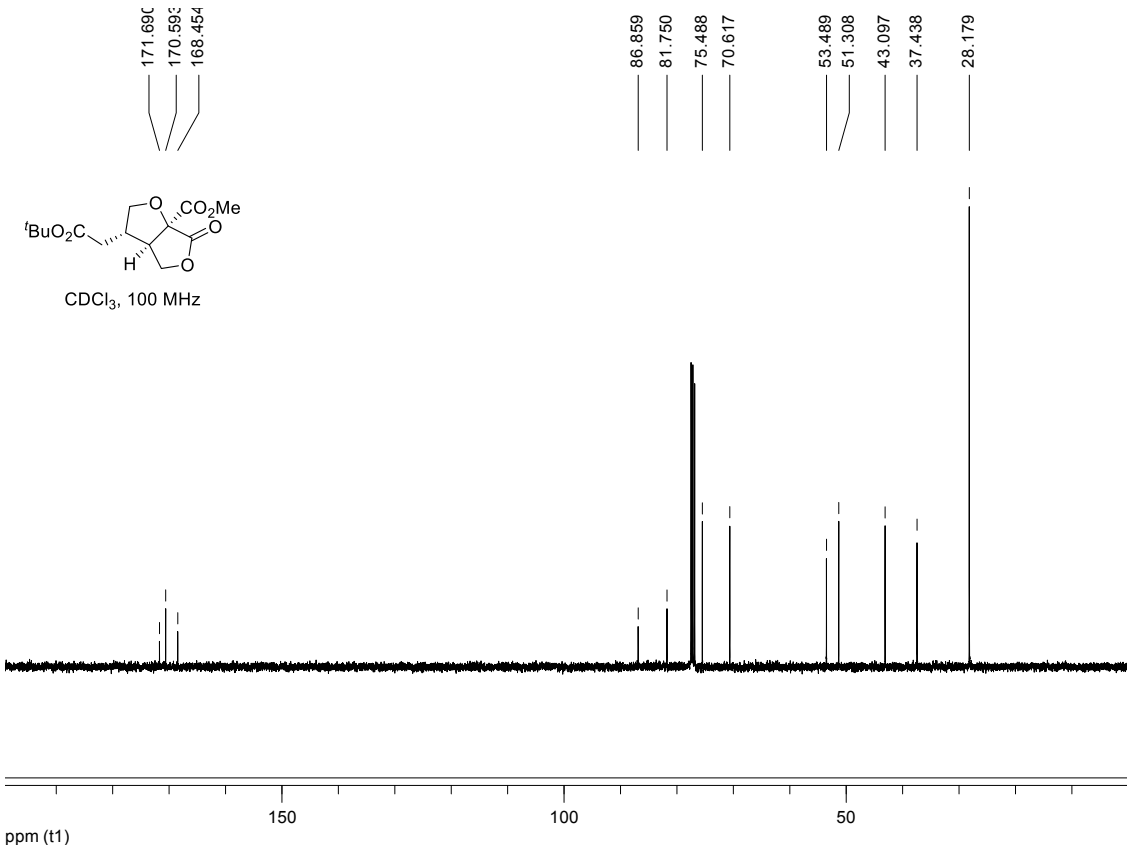
Spectra for compound **9b**



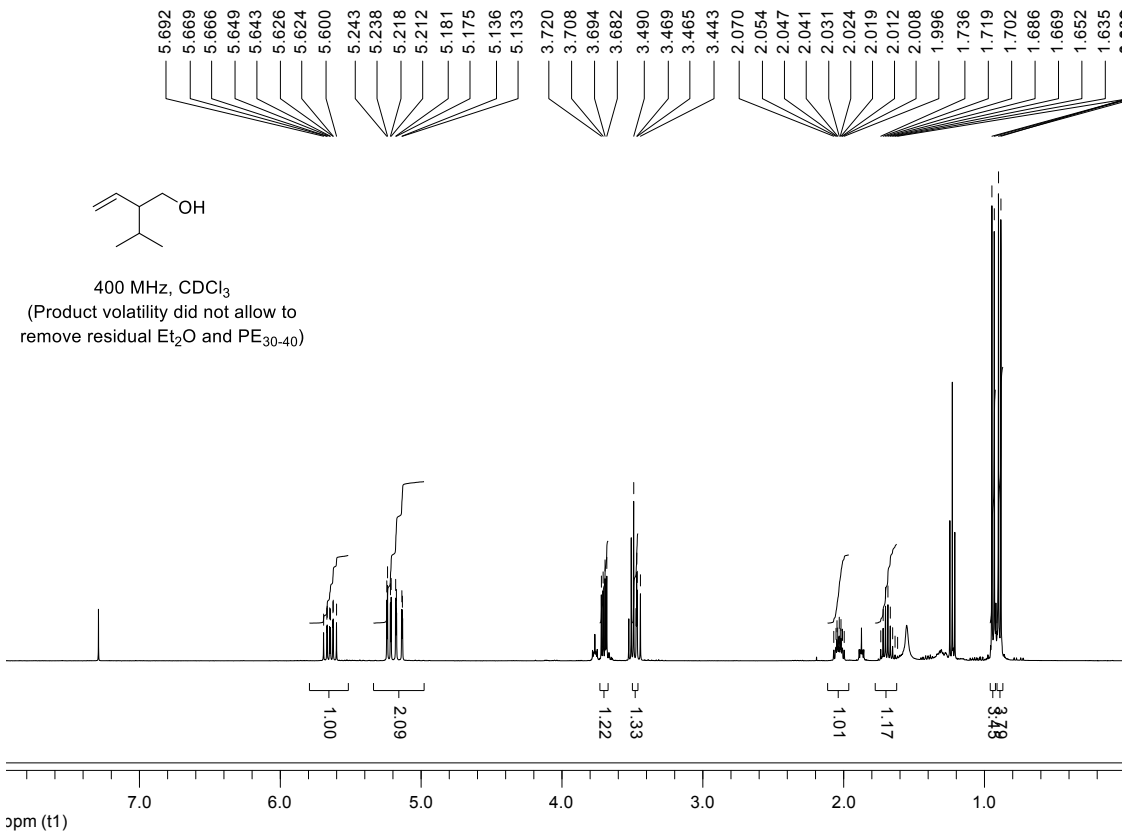


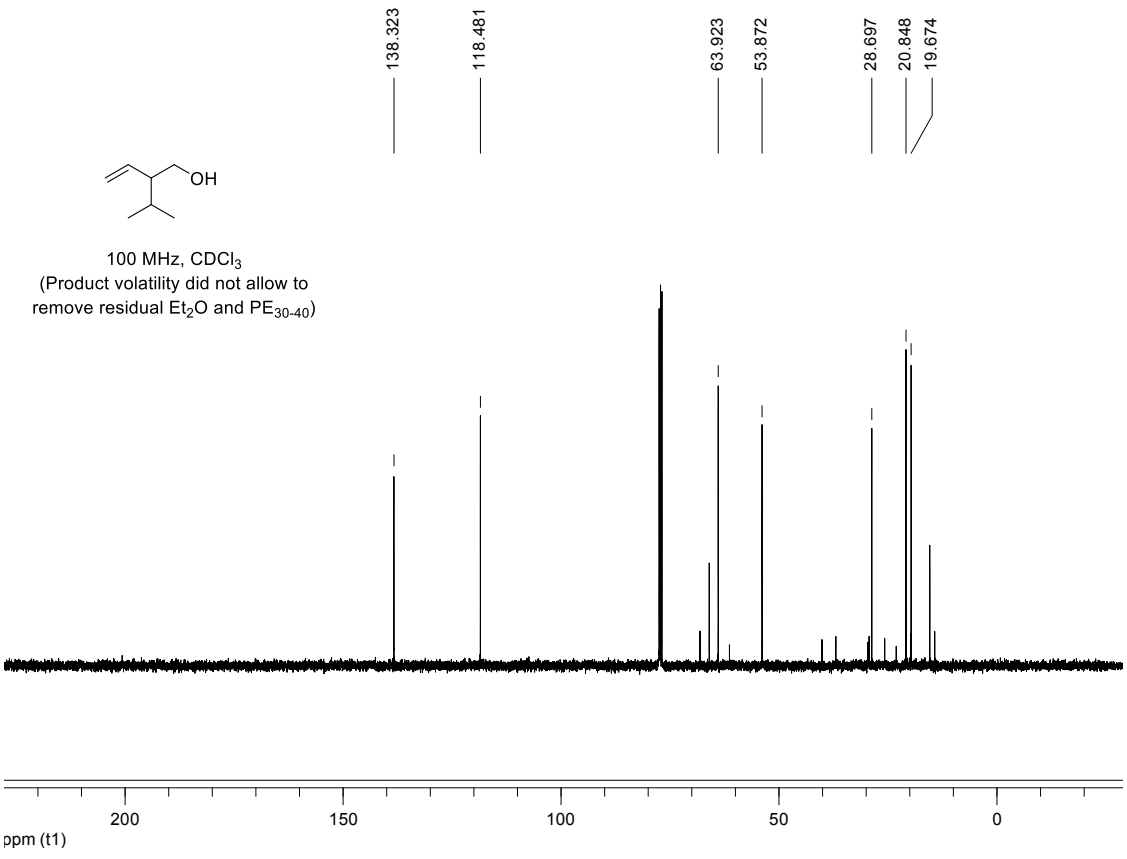
Spectra for compound **10b**



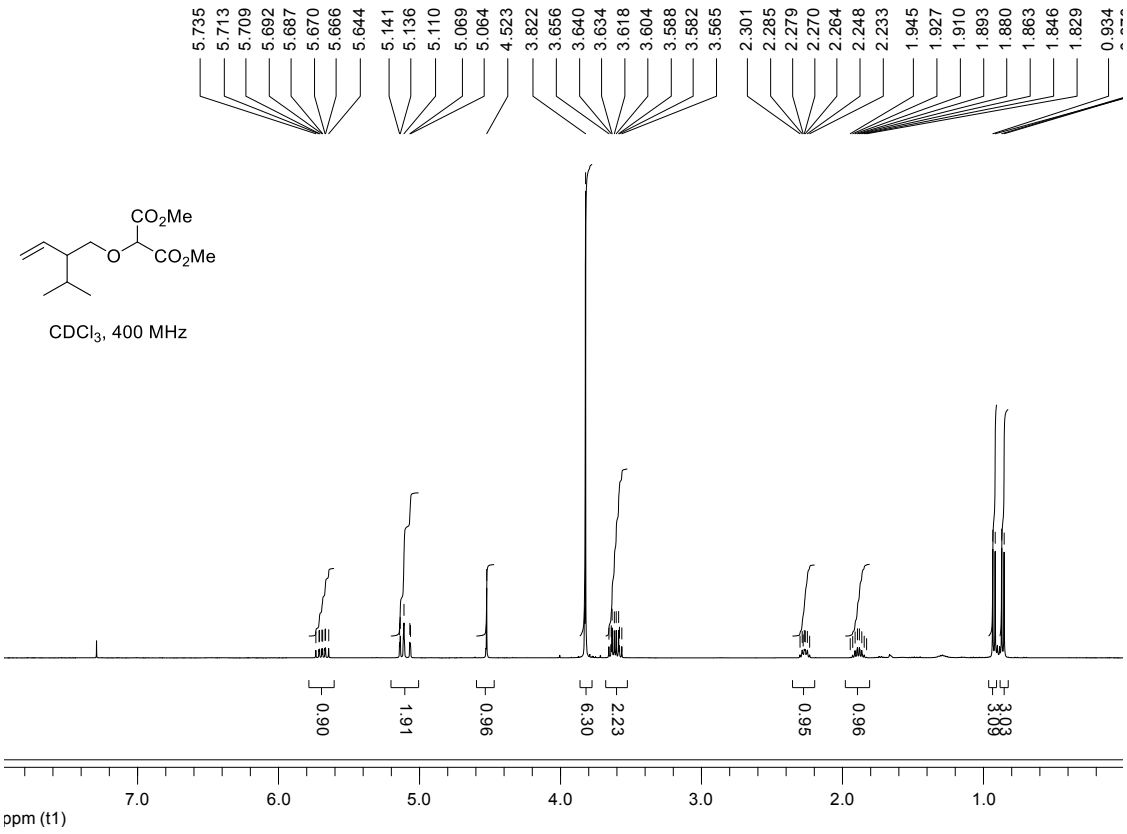


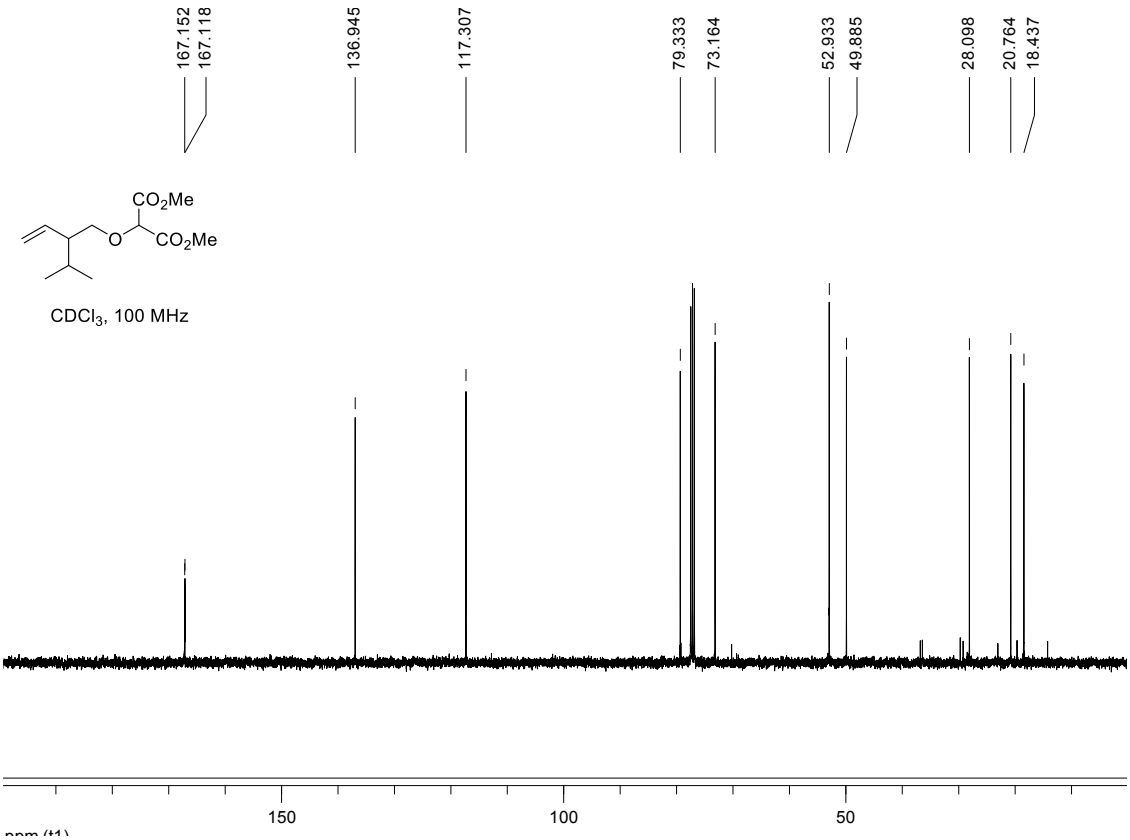
Spectra for compound **SI15**



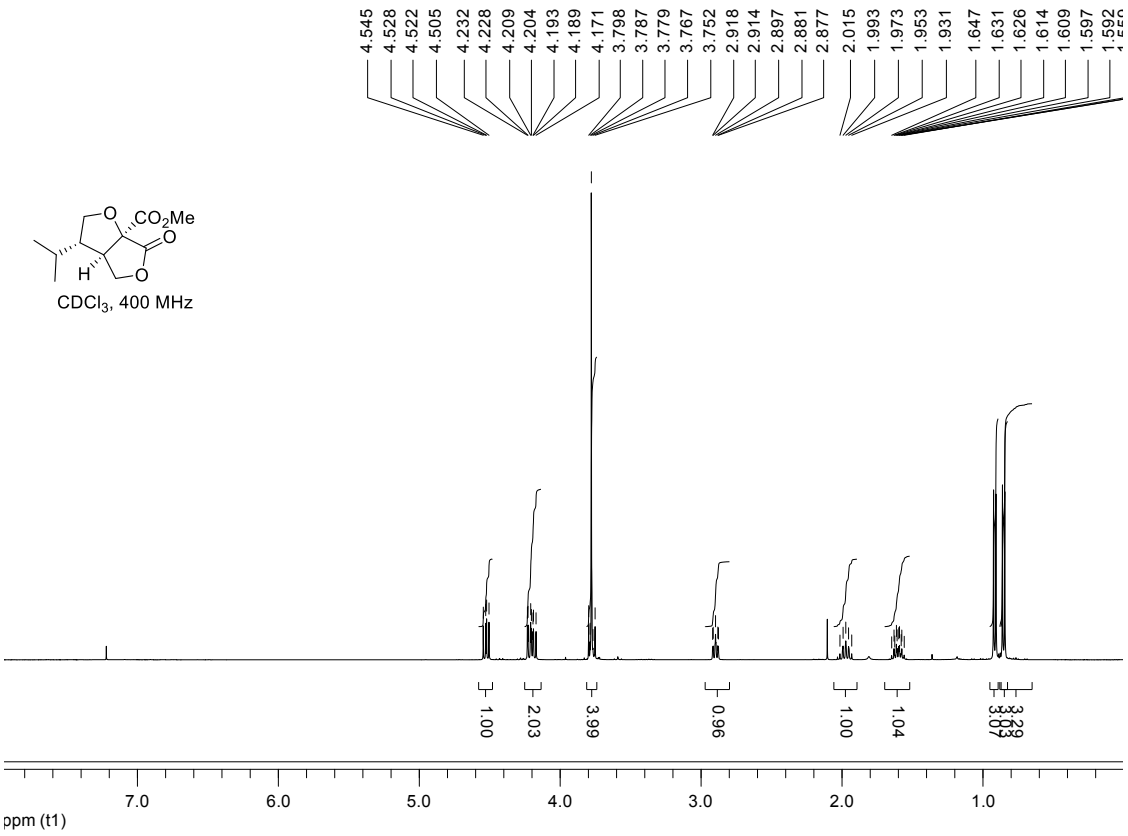


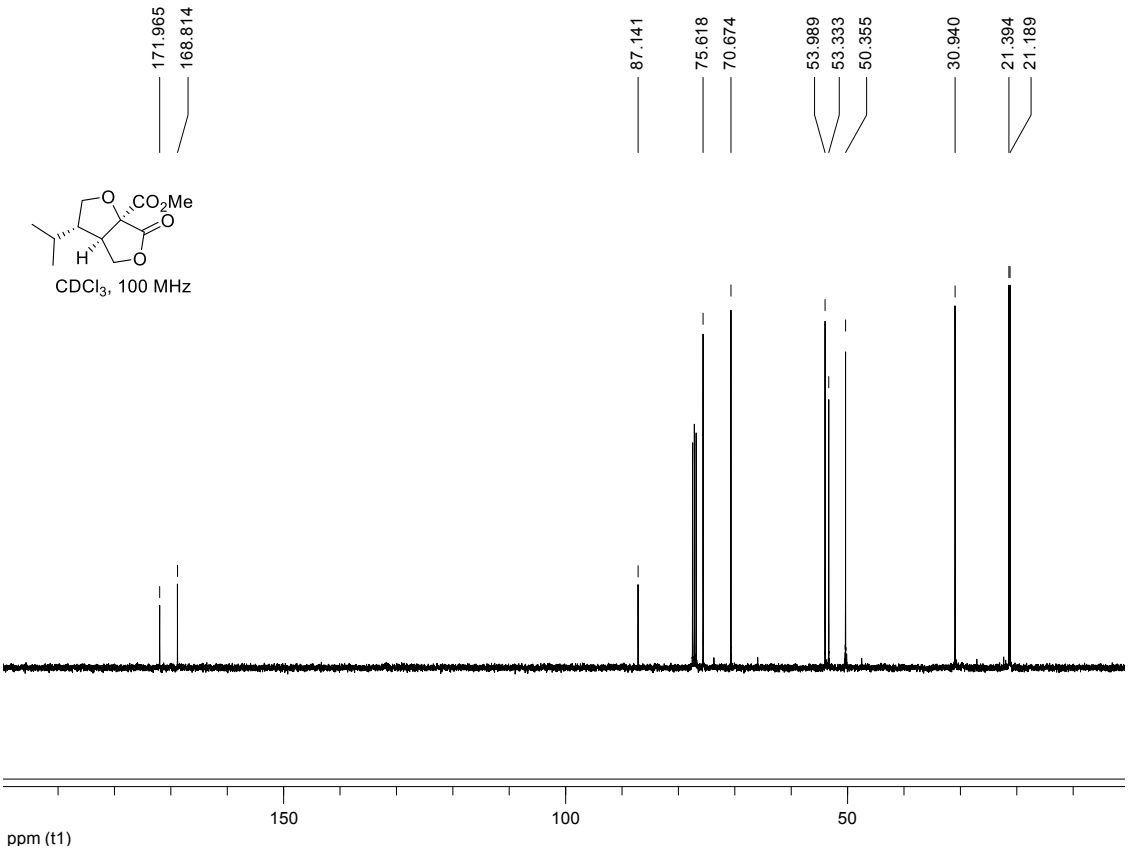
Spectra for compound **9c**



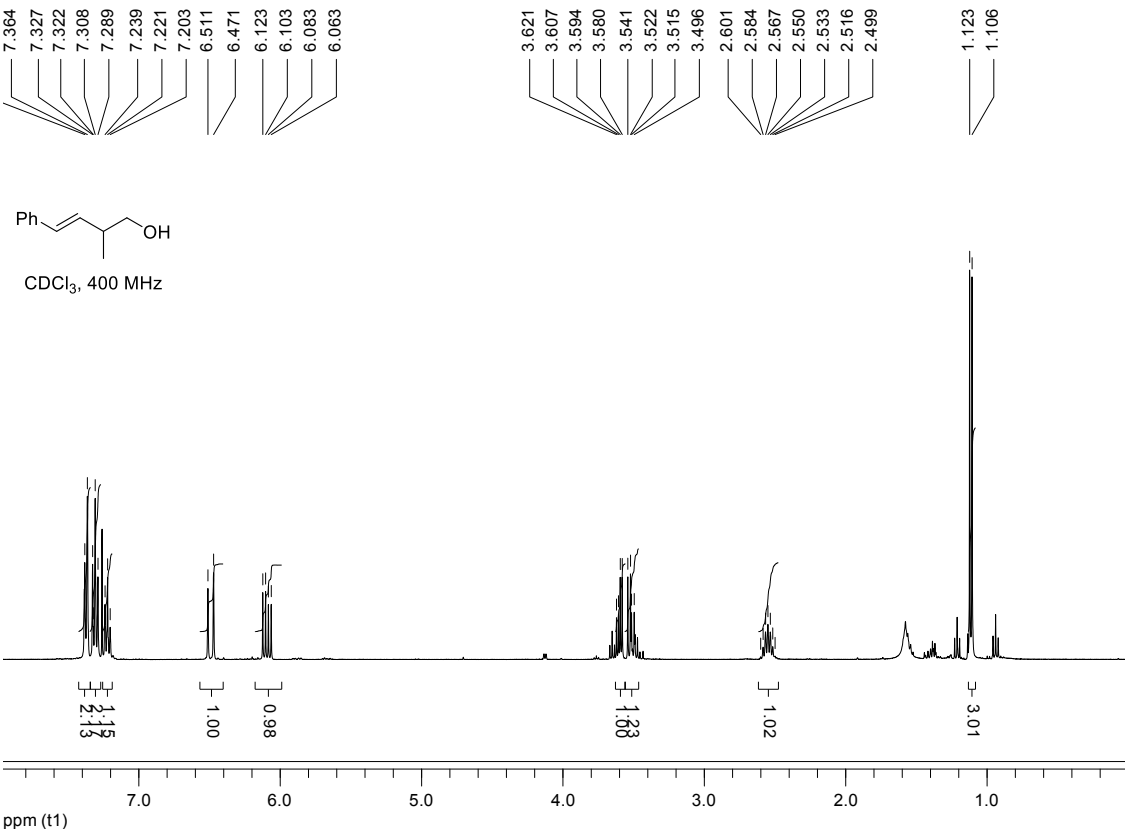


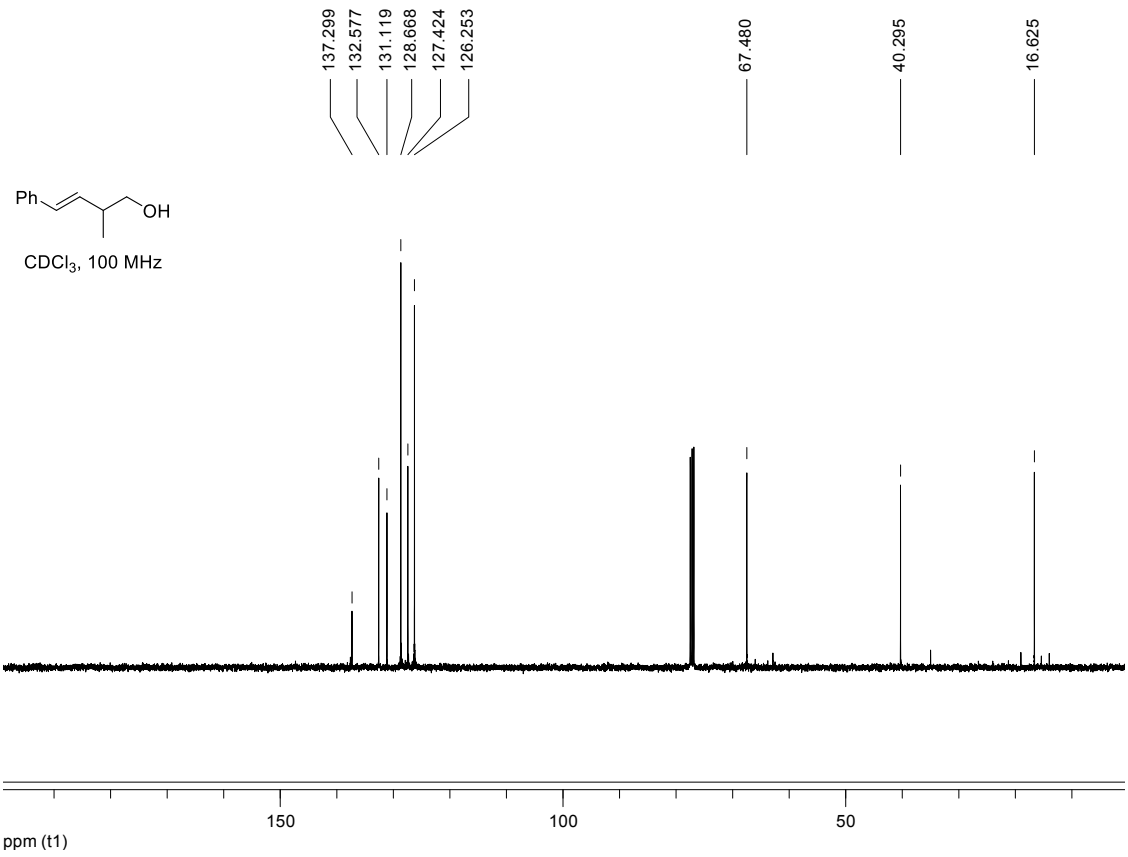
Spectra for compound **10c**



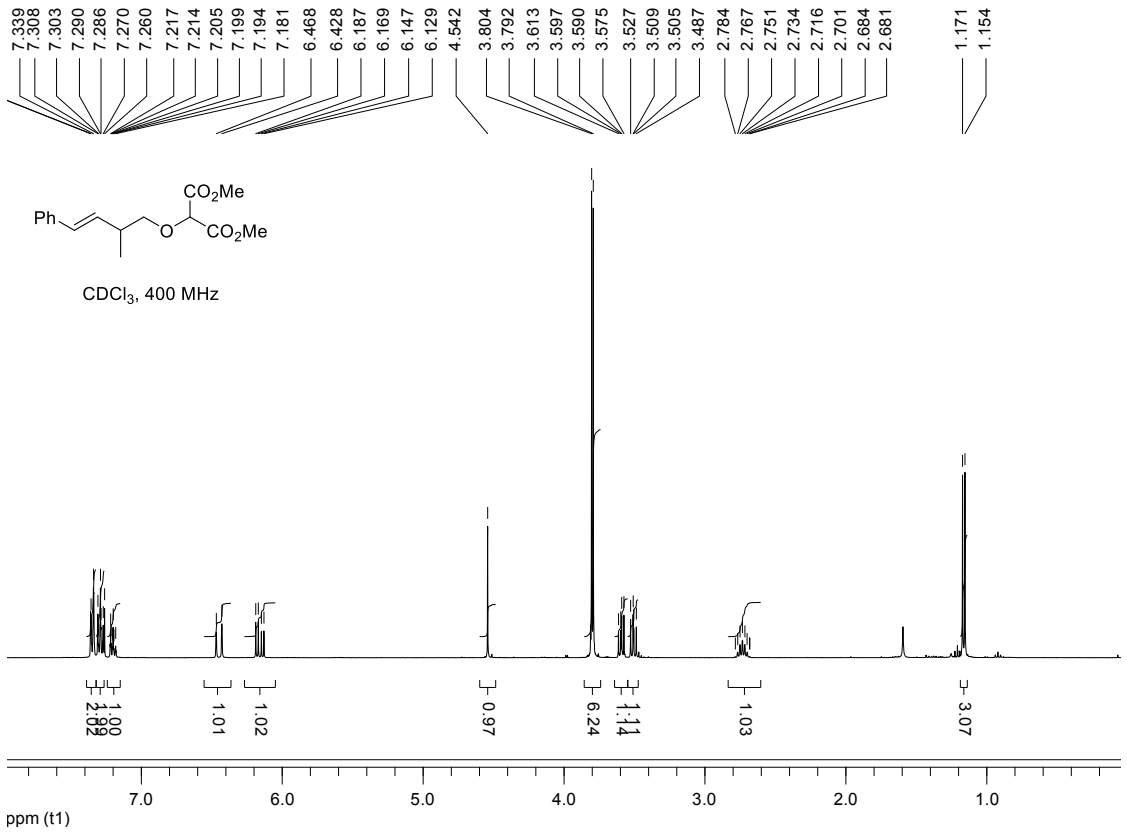


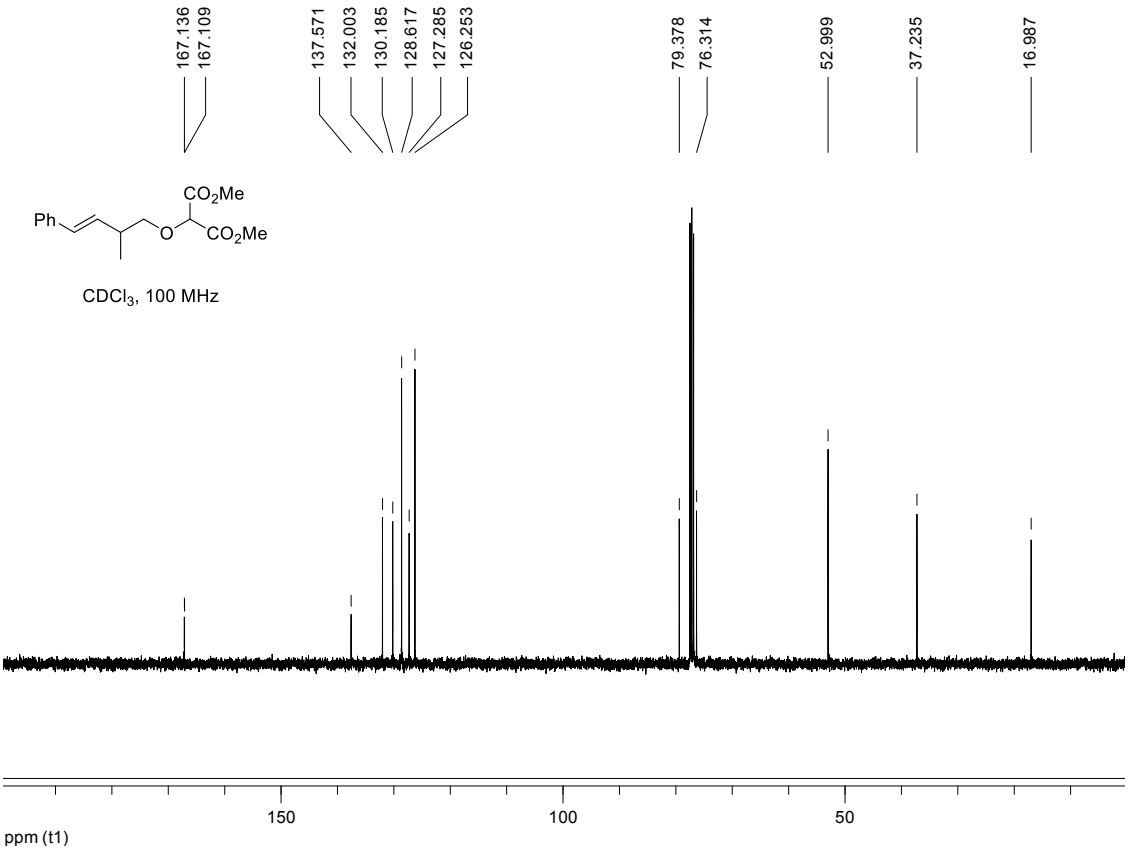
Spectra for compound **SI17**



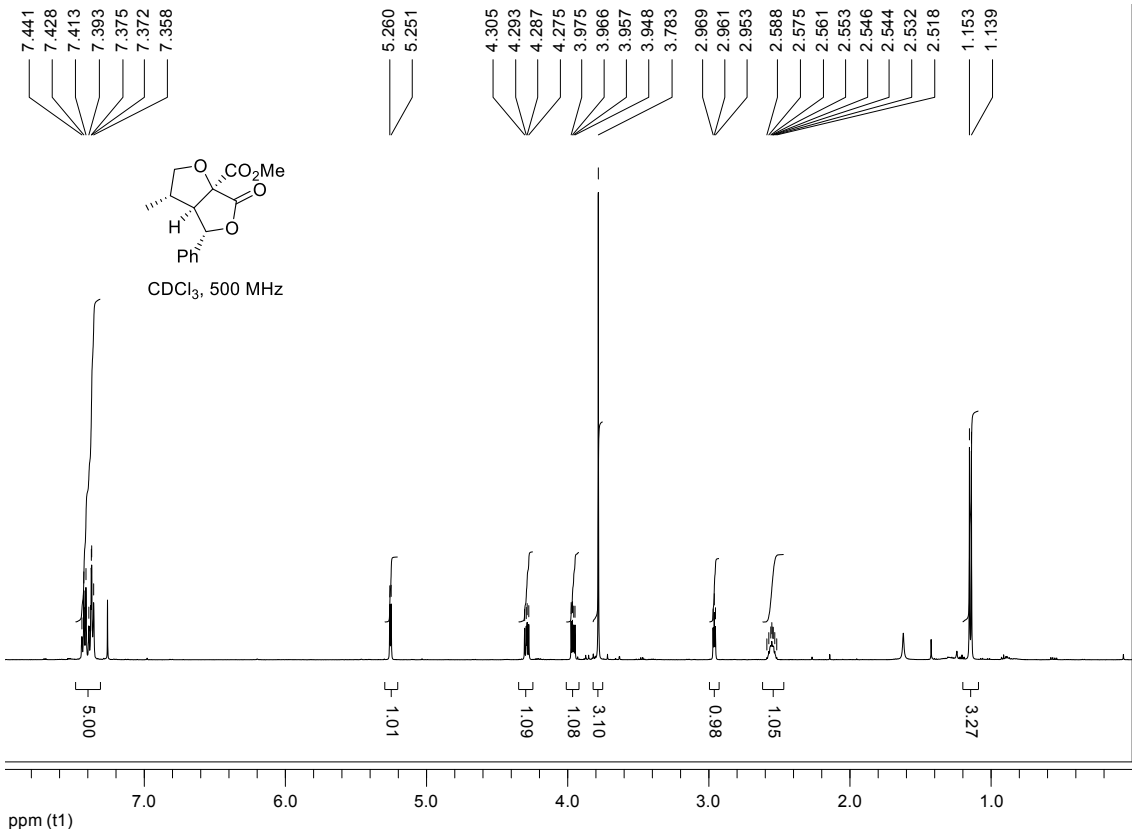


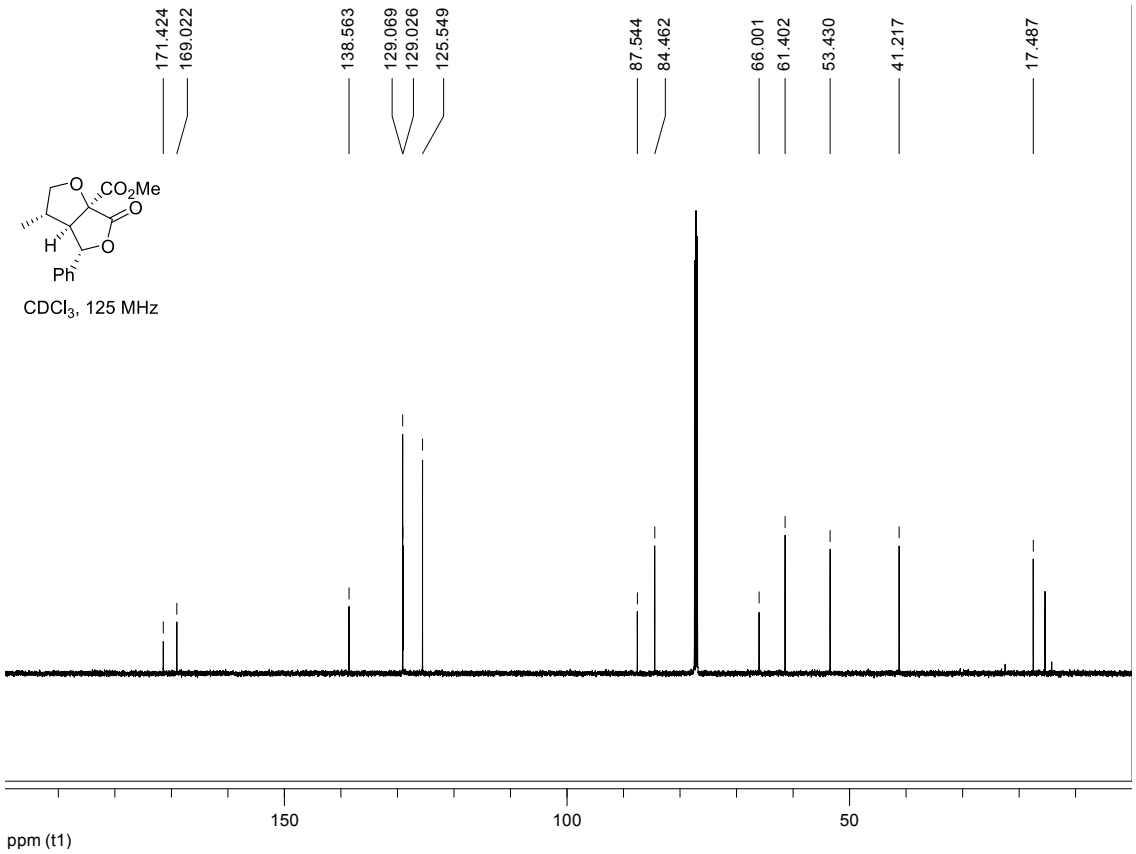
Spectra for compound **9d**



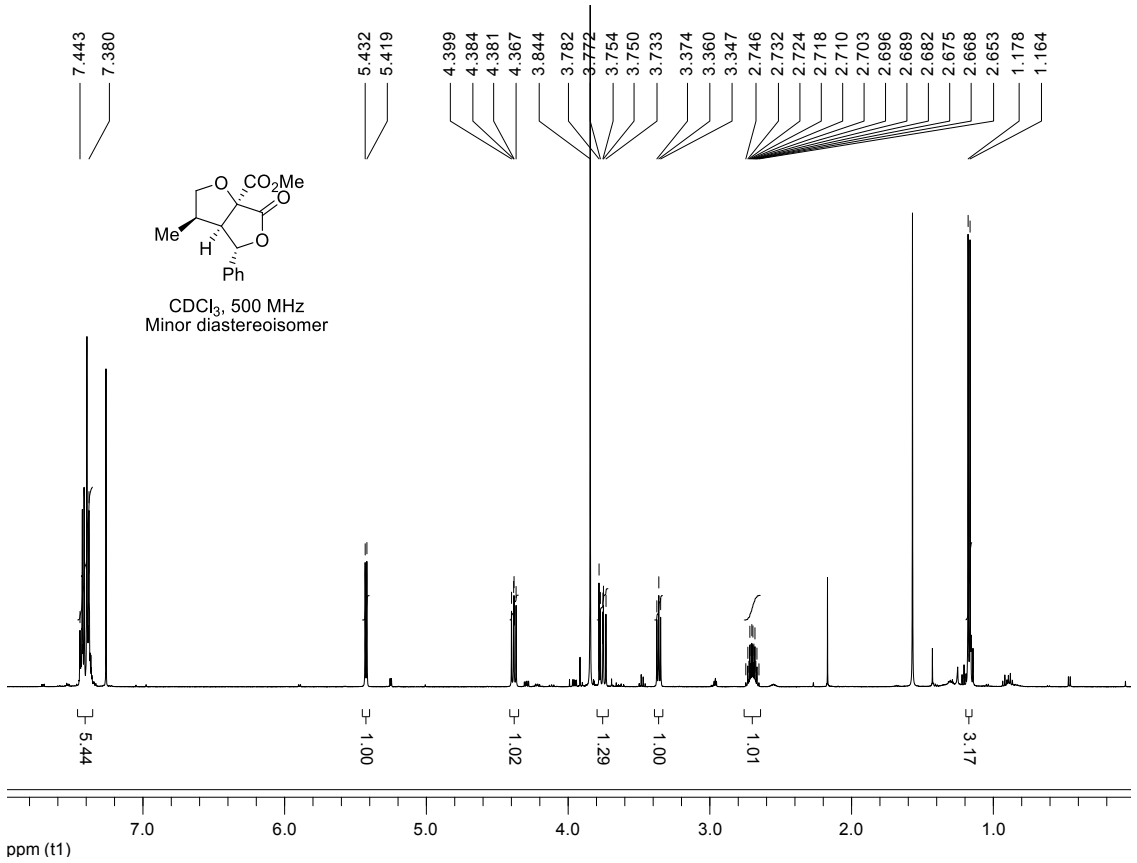


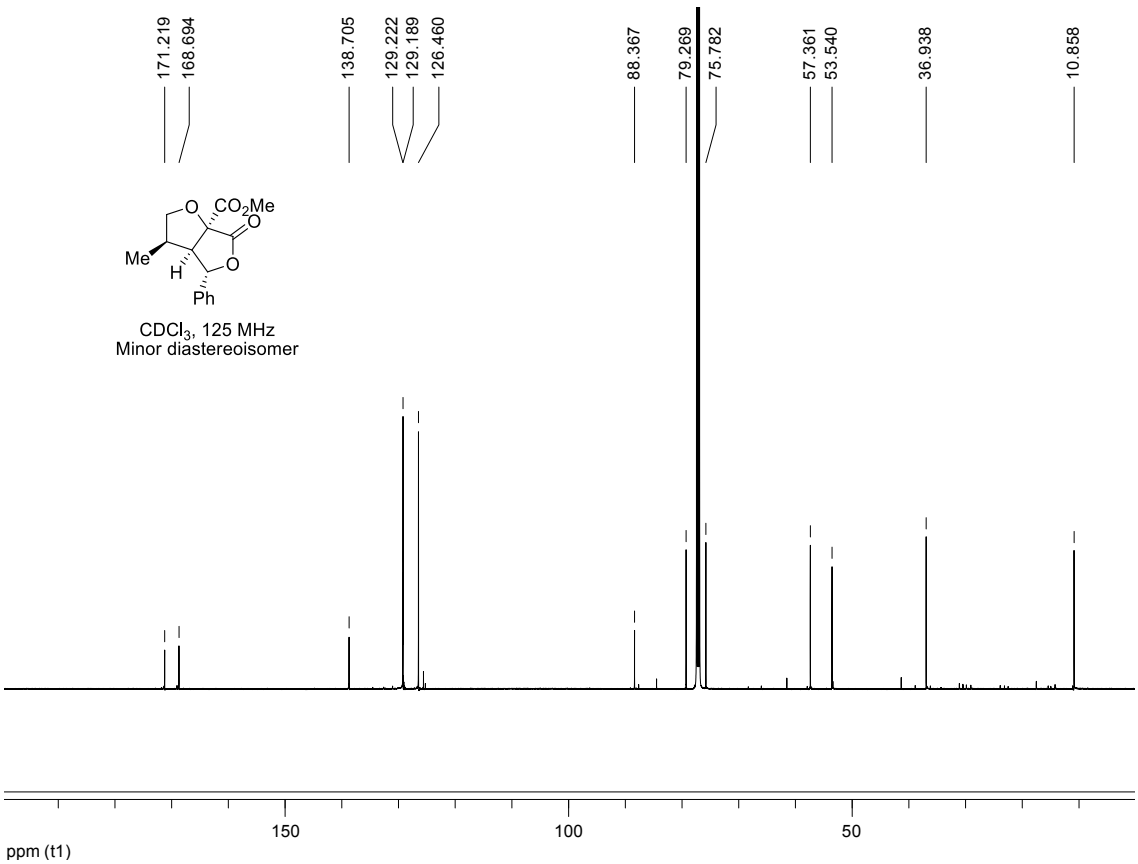
Spectra for compound **10d**



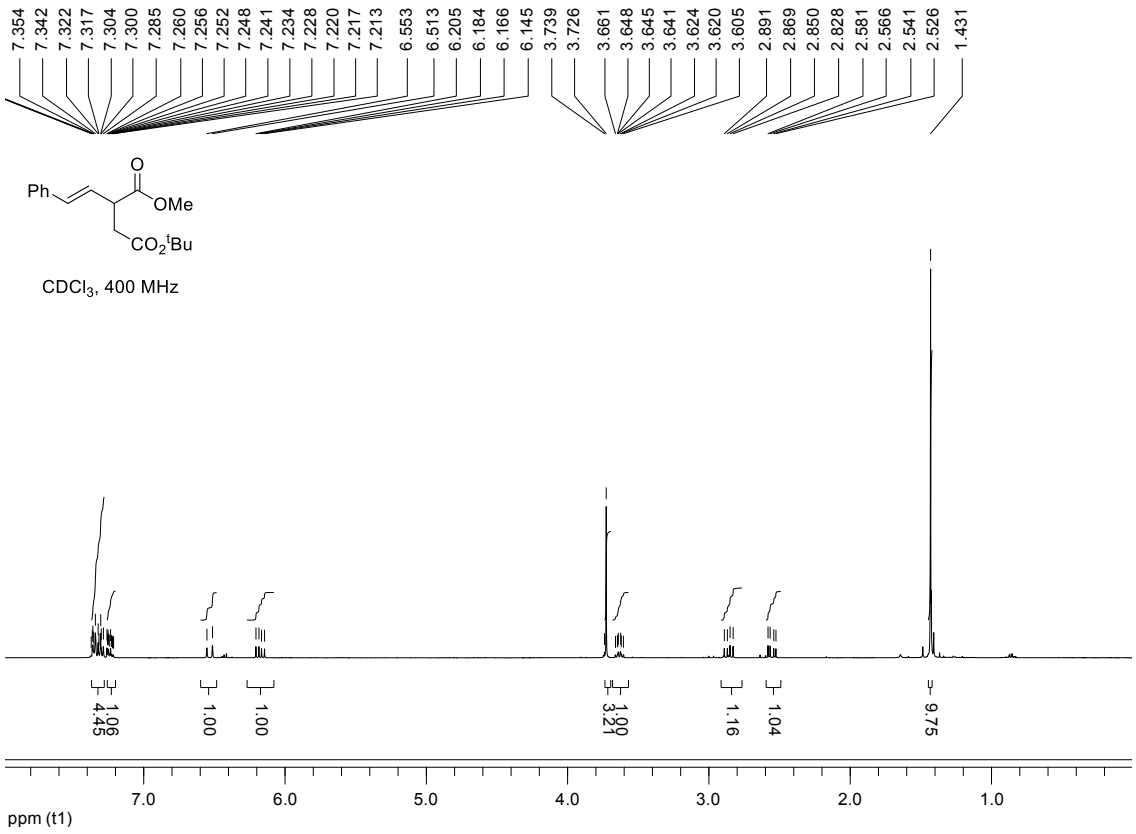


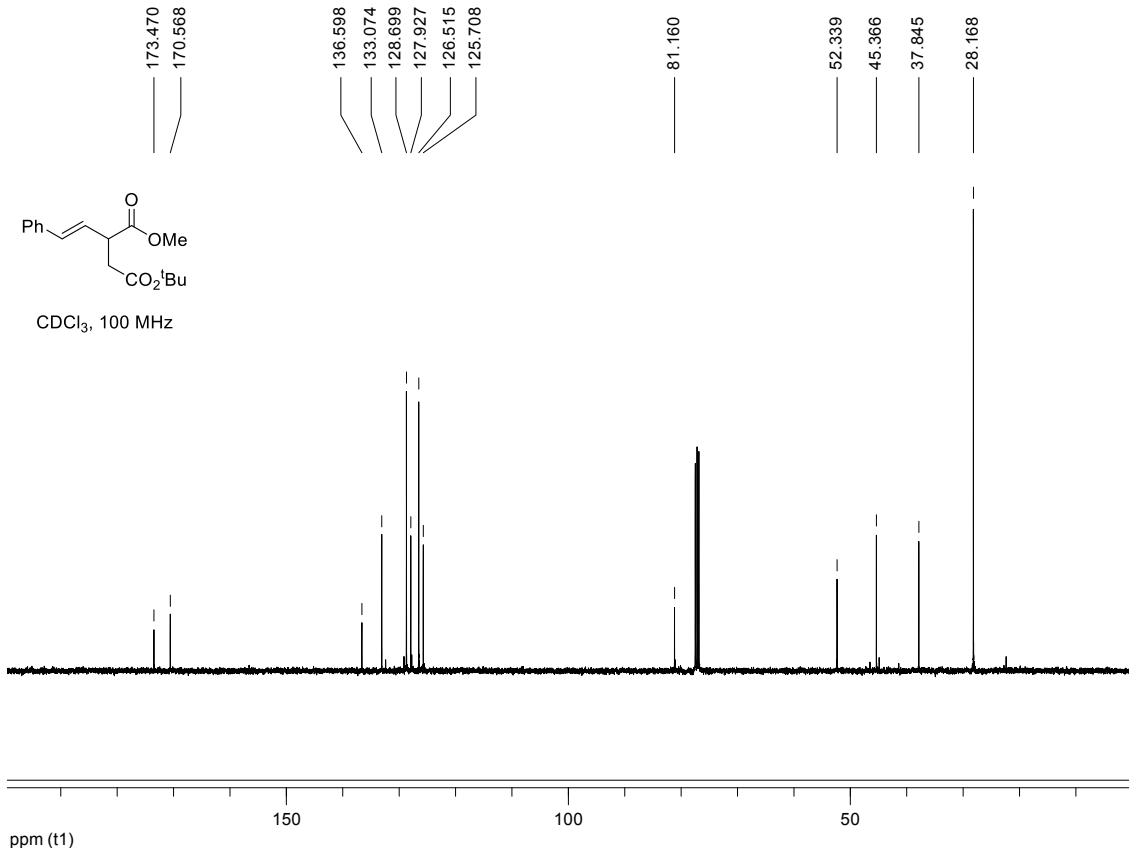
Spectra for compound **10d$_{min}$**



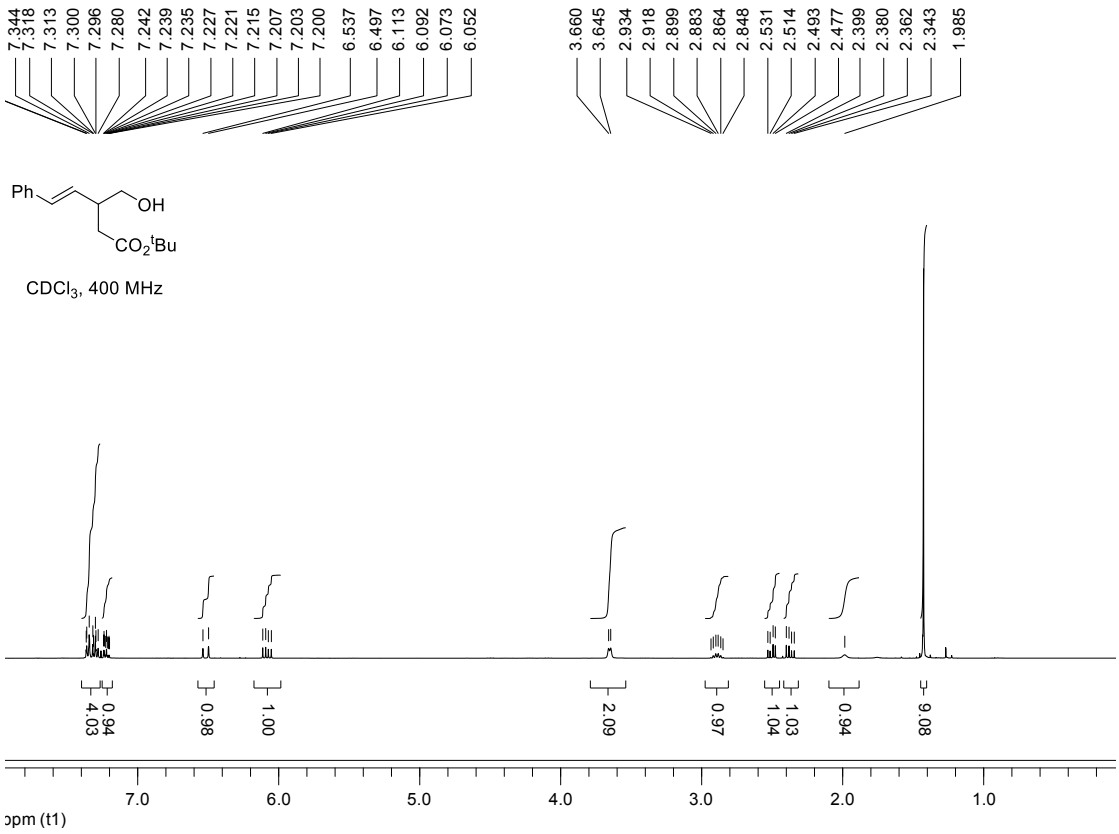


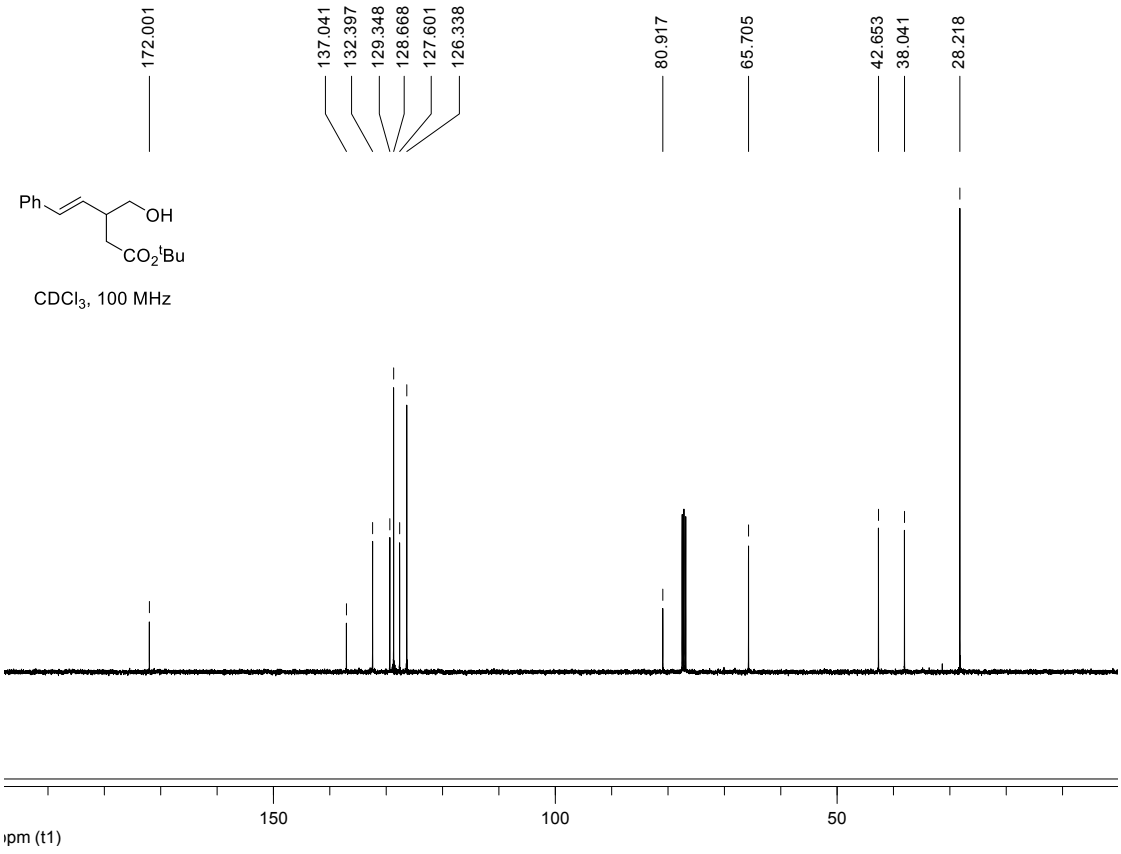
Spectra for compound **SI19**



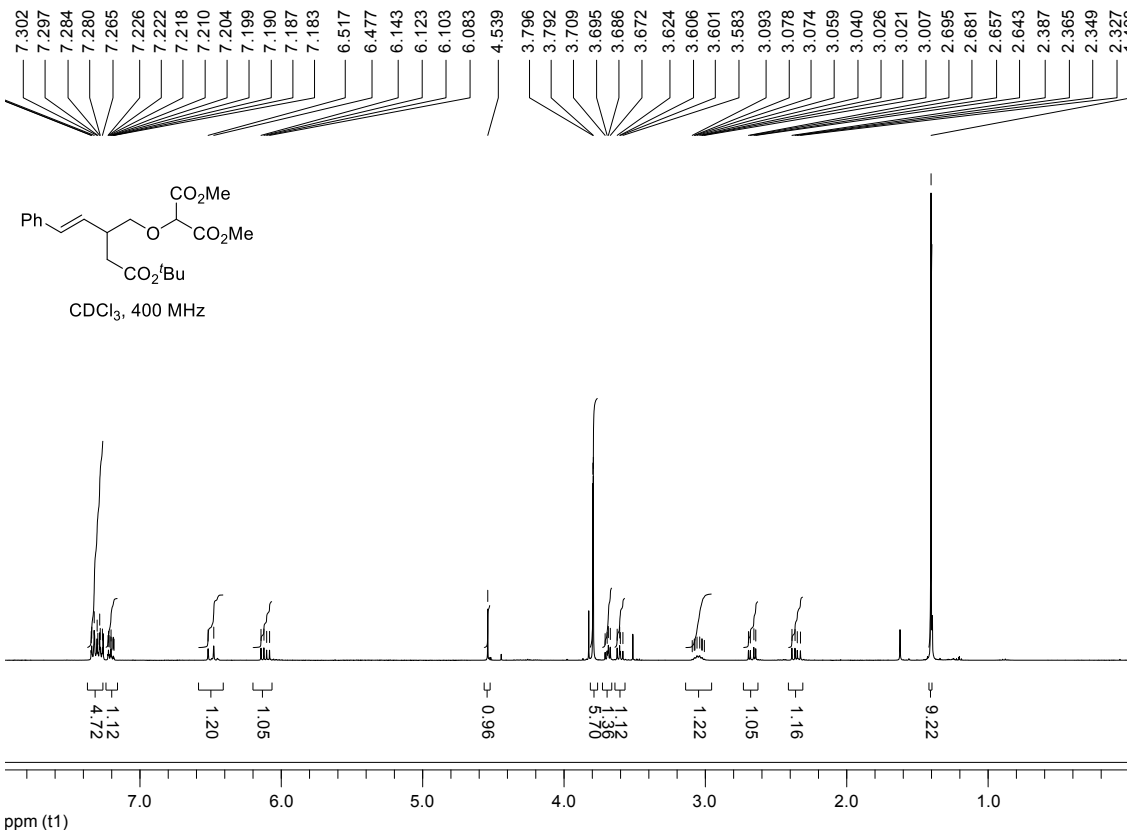


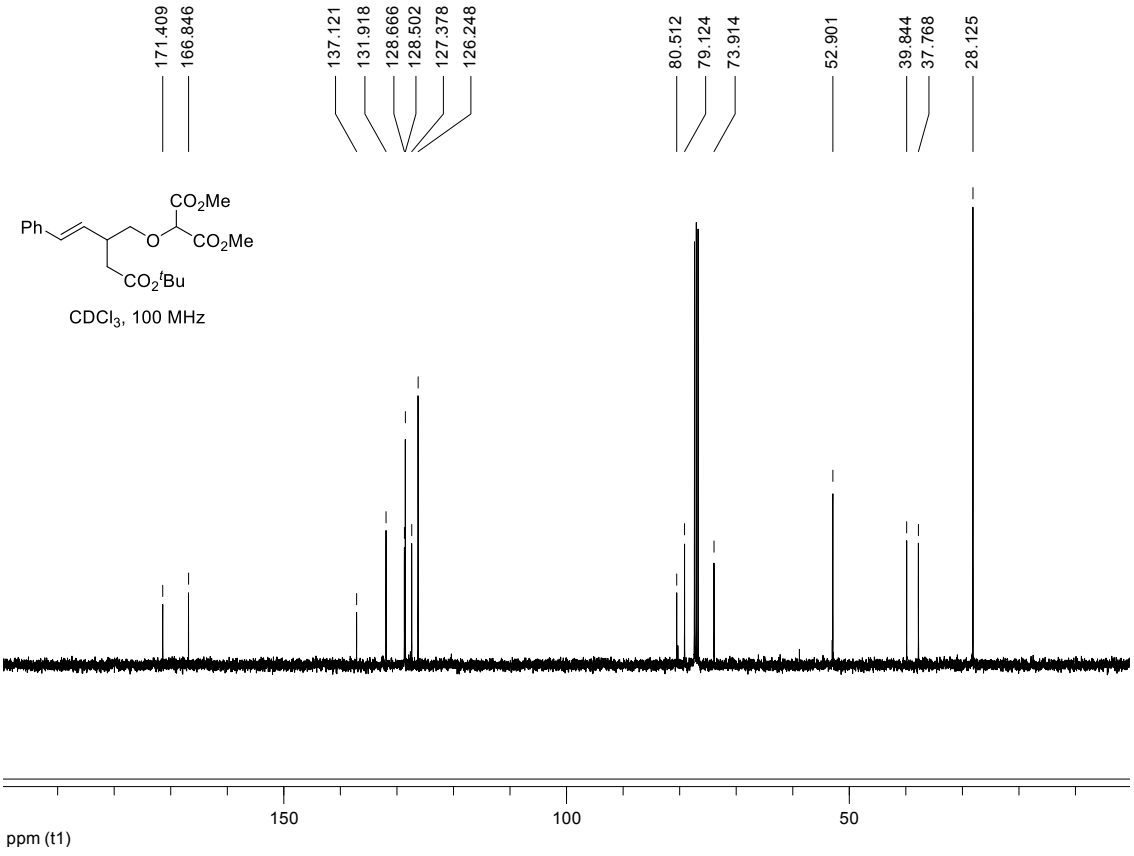
Spectra for compound **SI20**



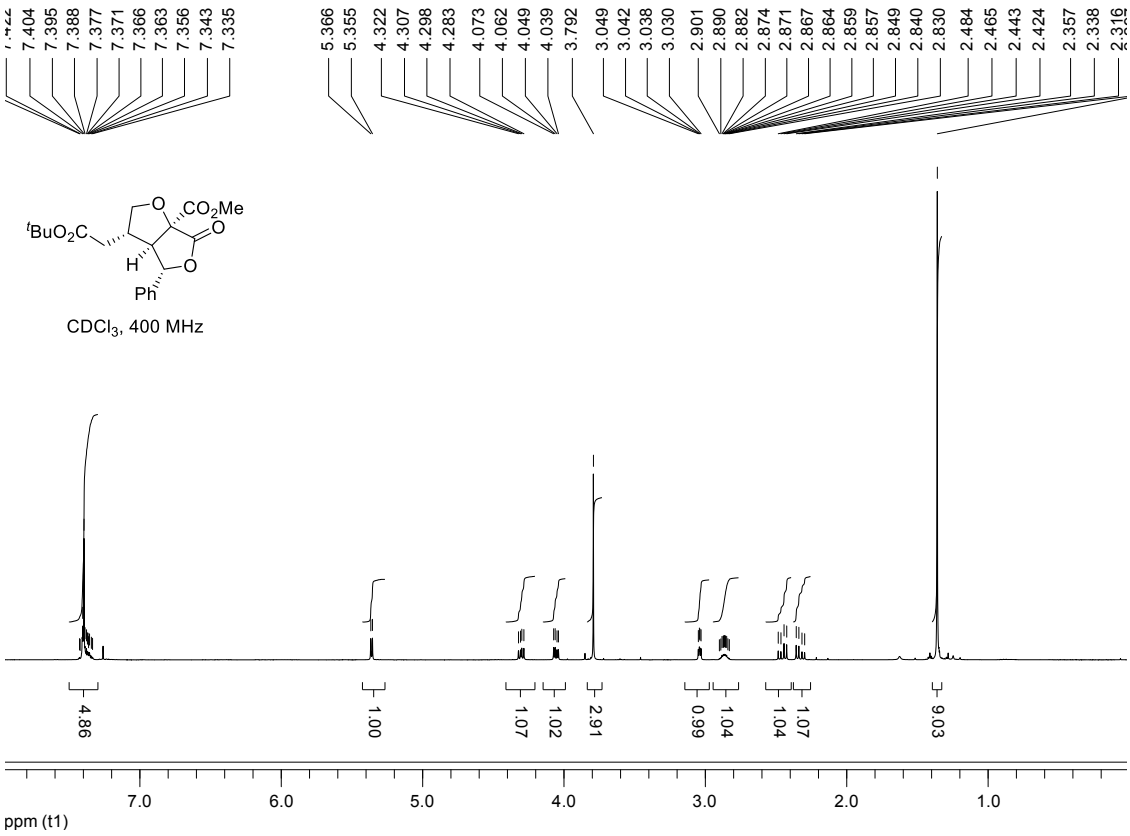


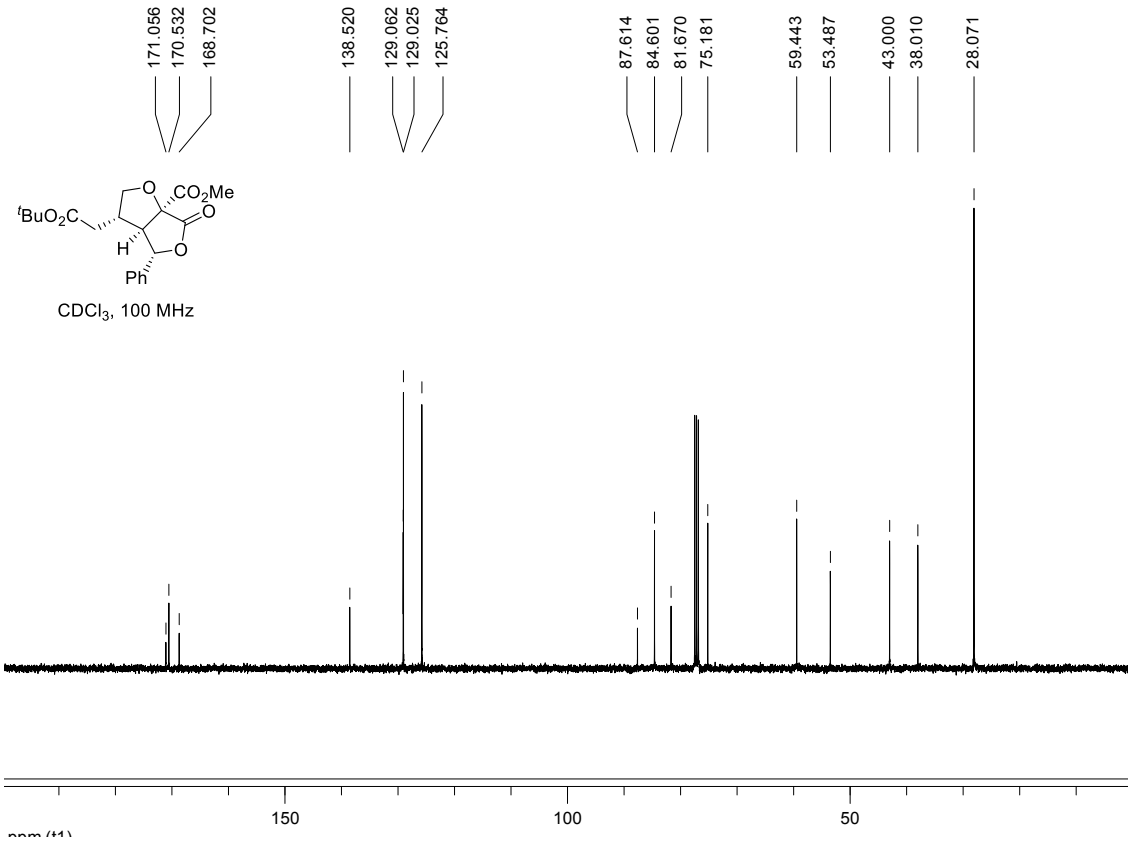
Spectra for compound **9e**



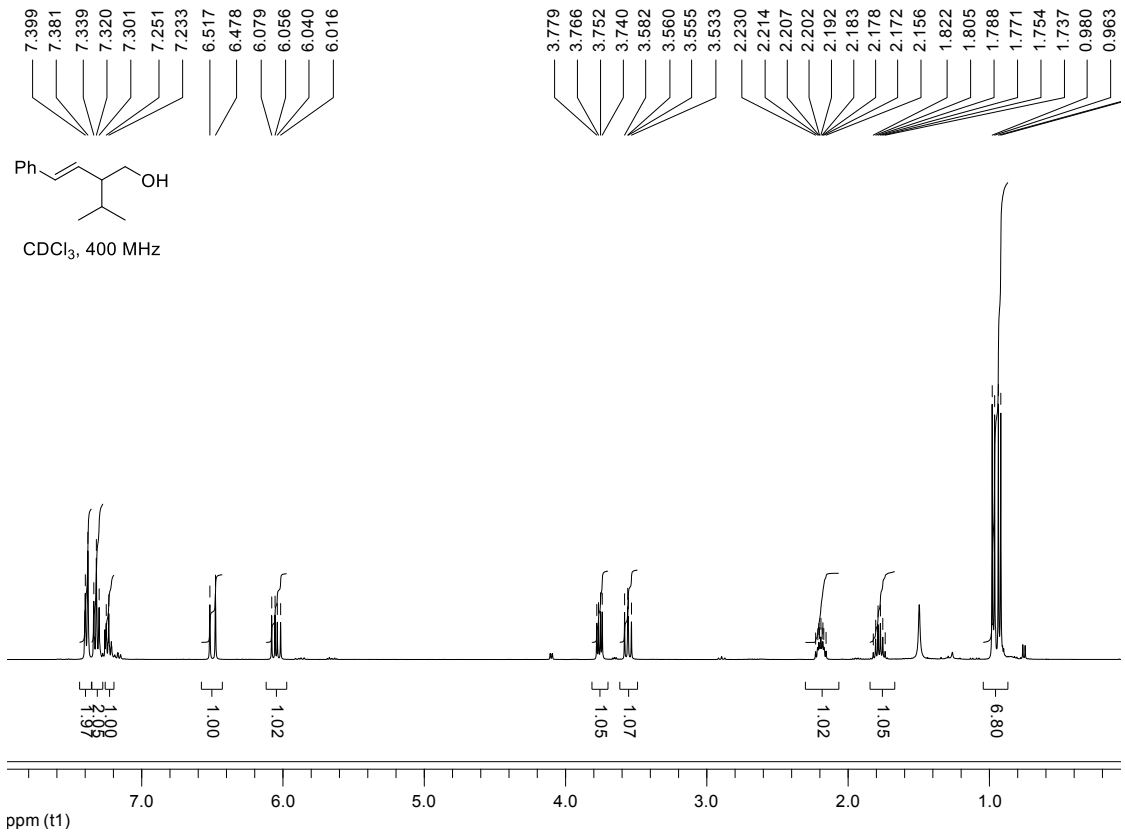


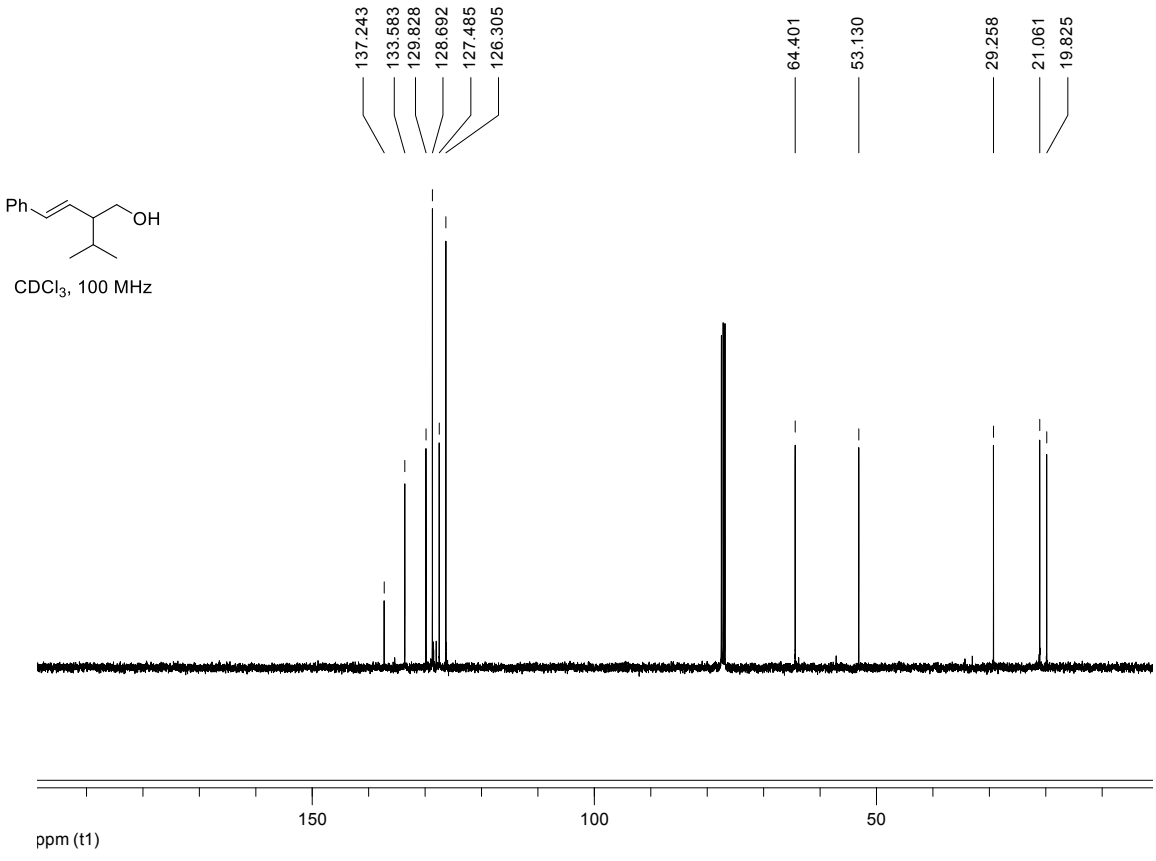
Spectra for compound **10e**



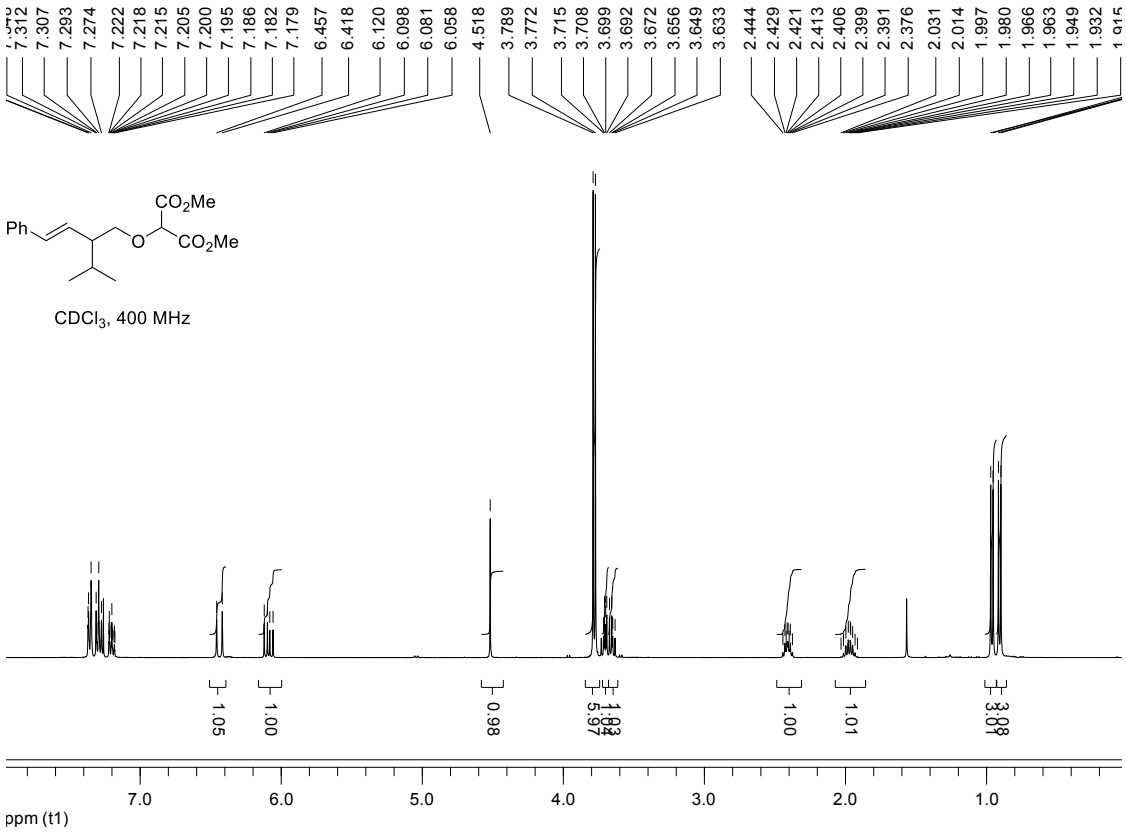


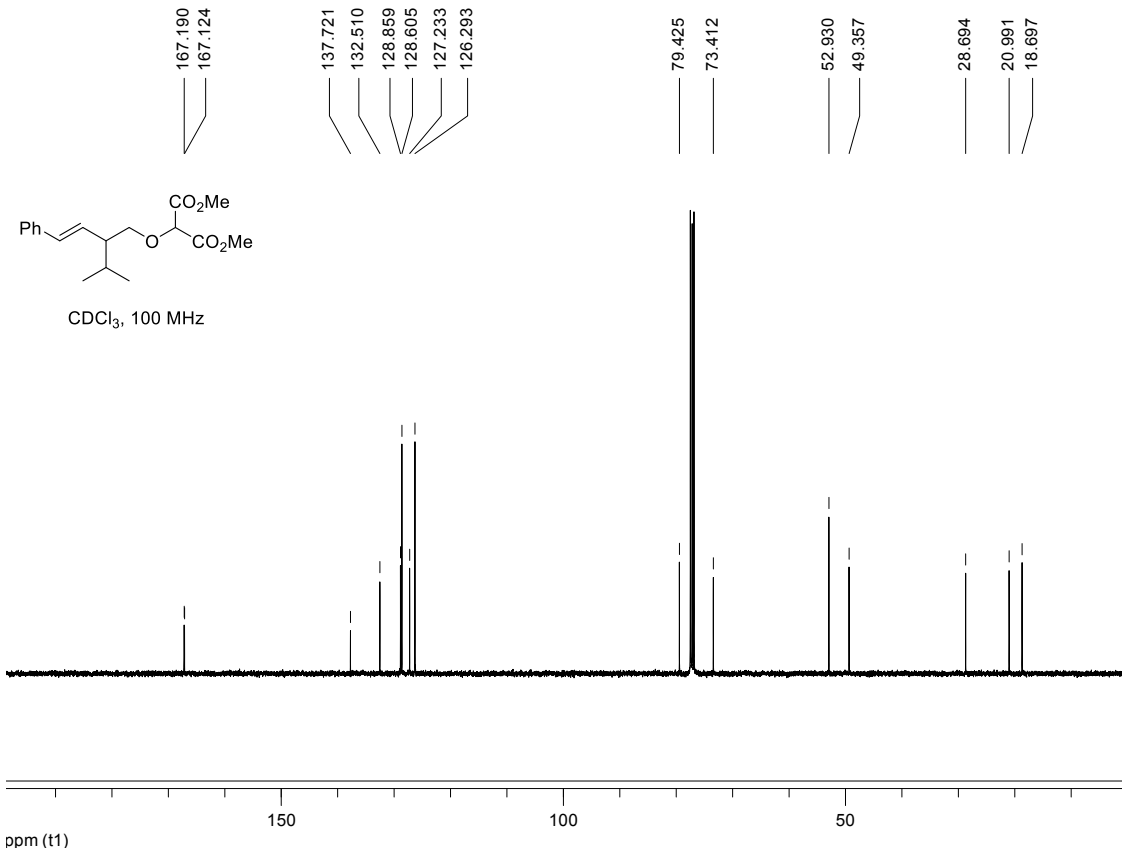
Spectra for compound **SI21**



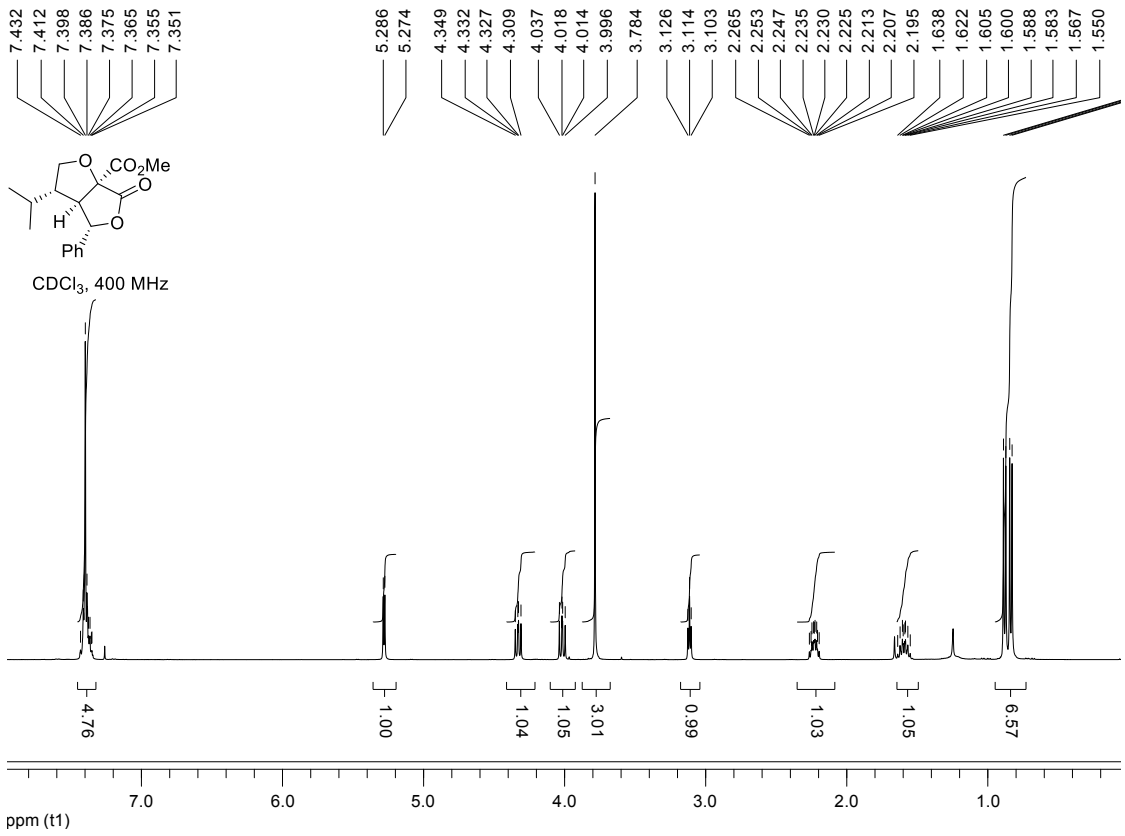


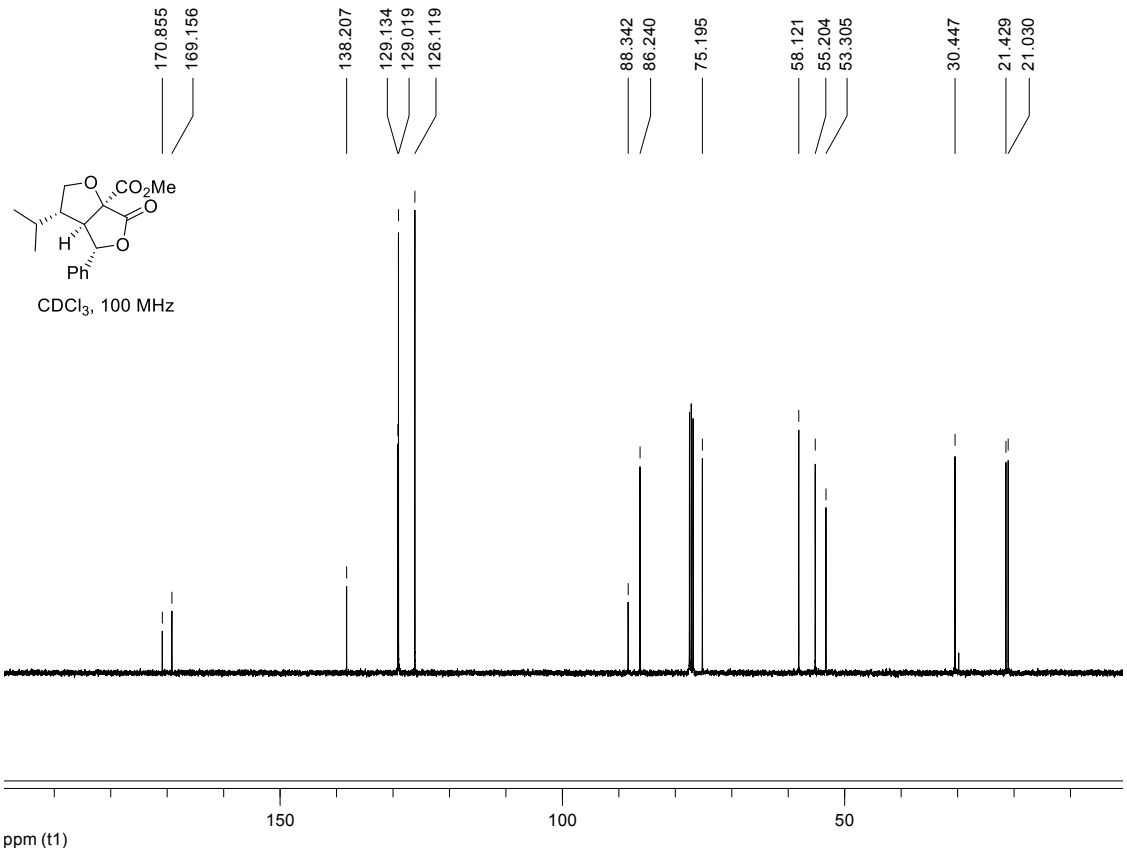
Spectra for compound **9f**



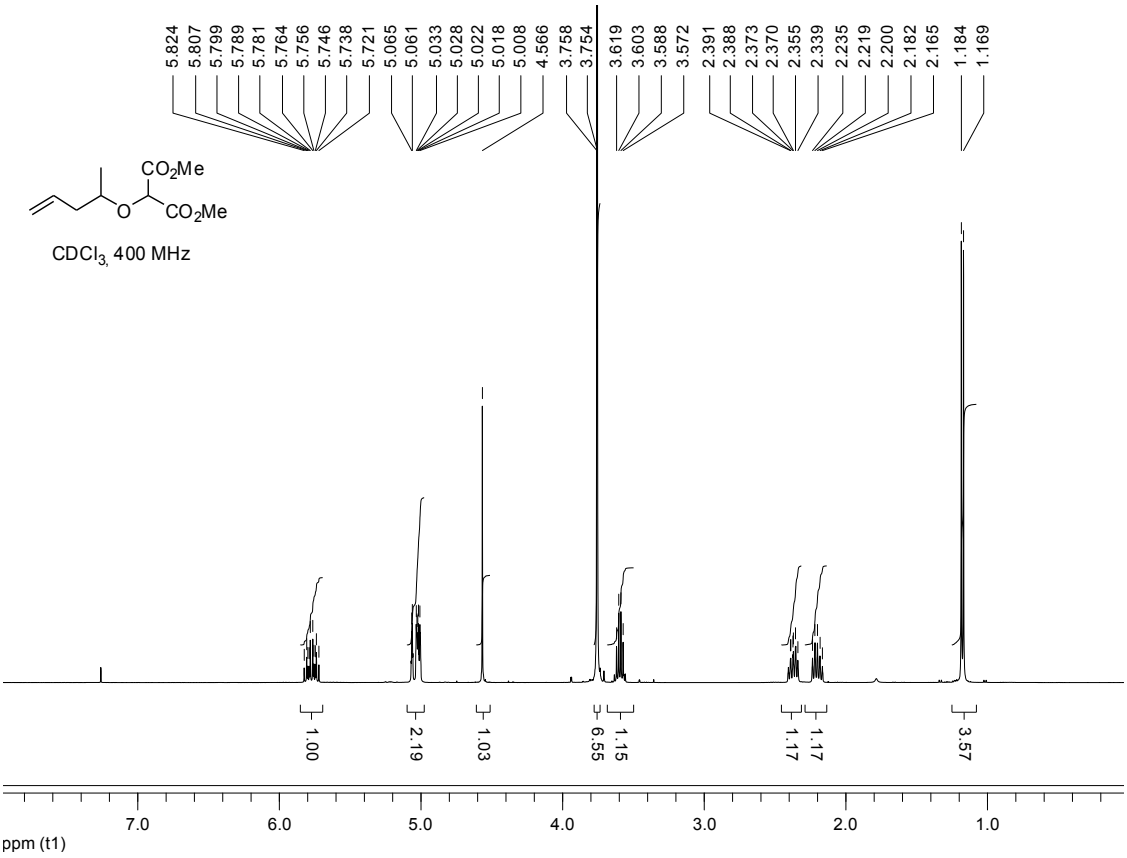


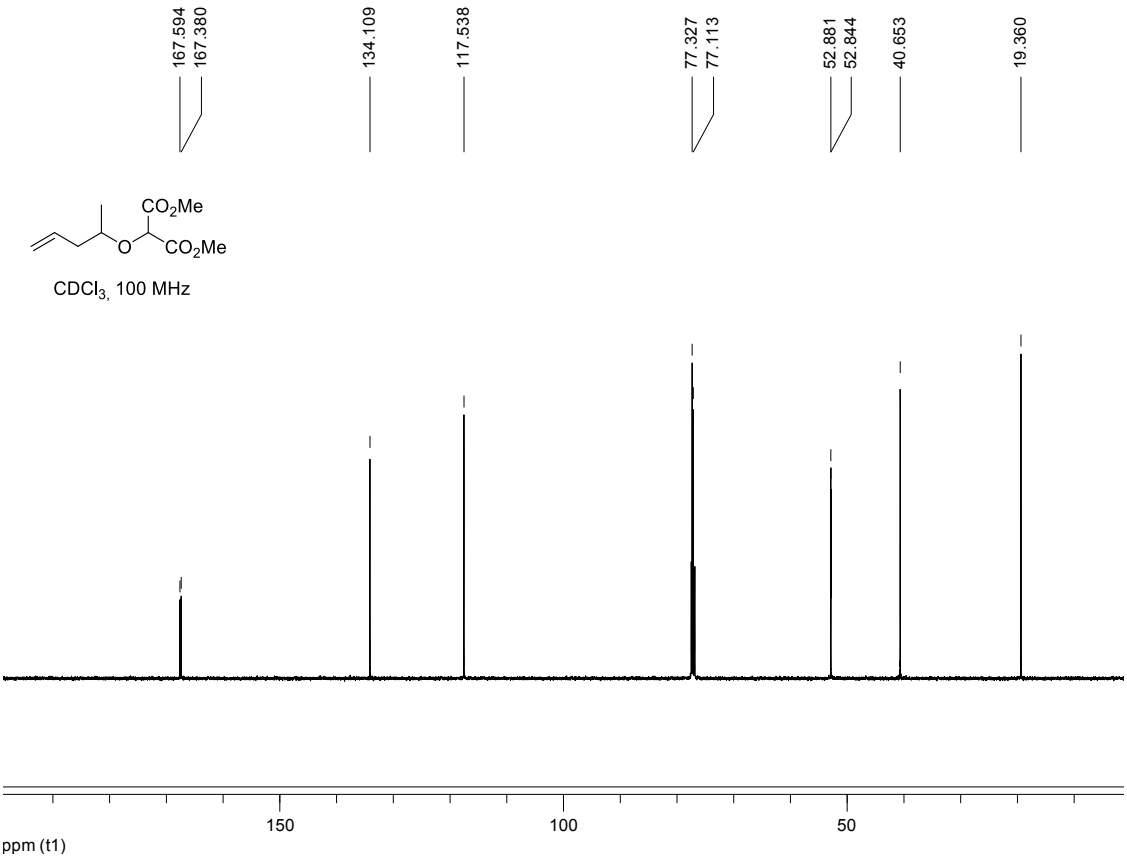
Spectra for compound **10f**



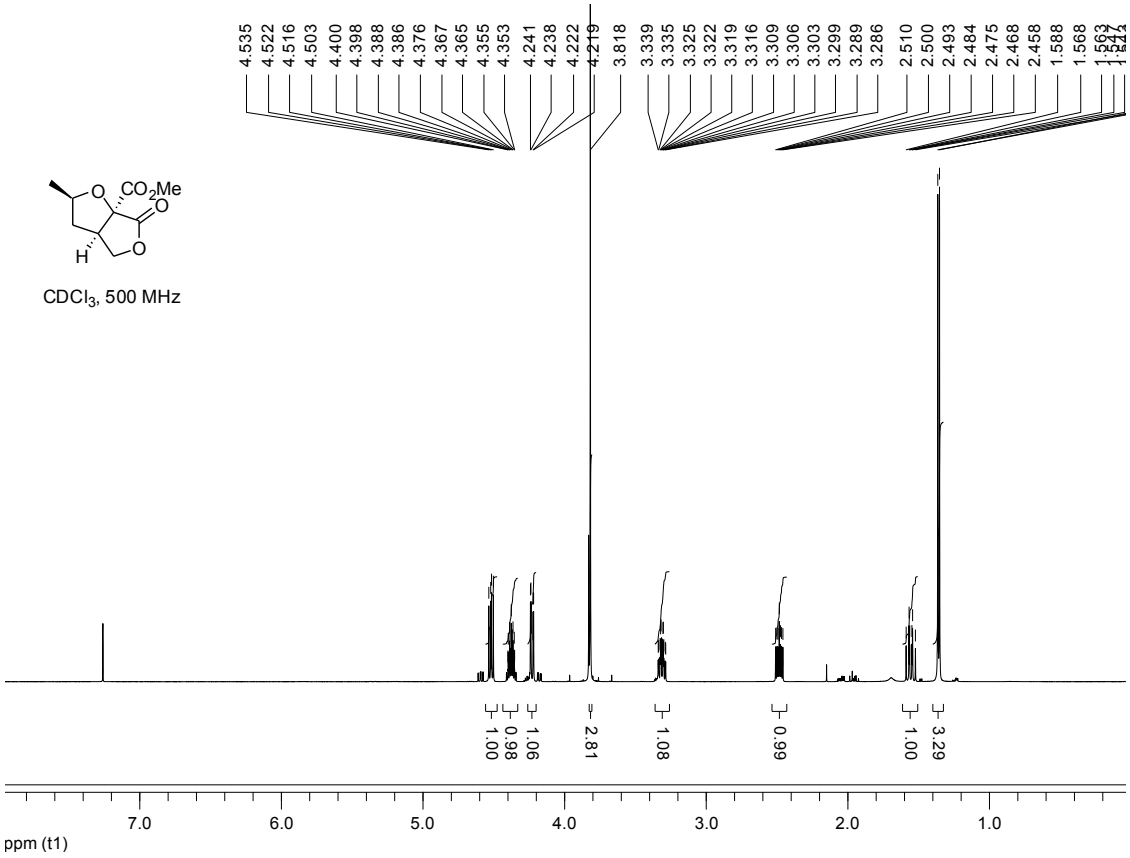


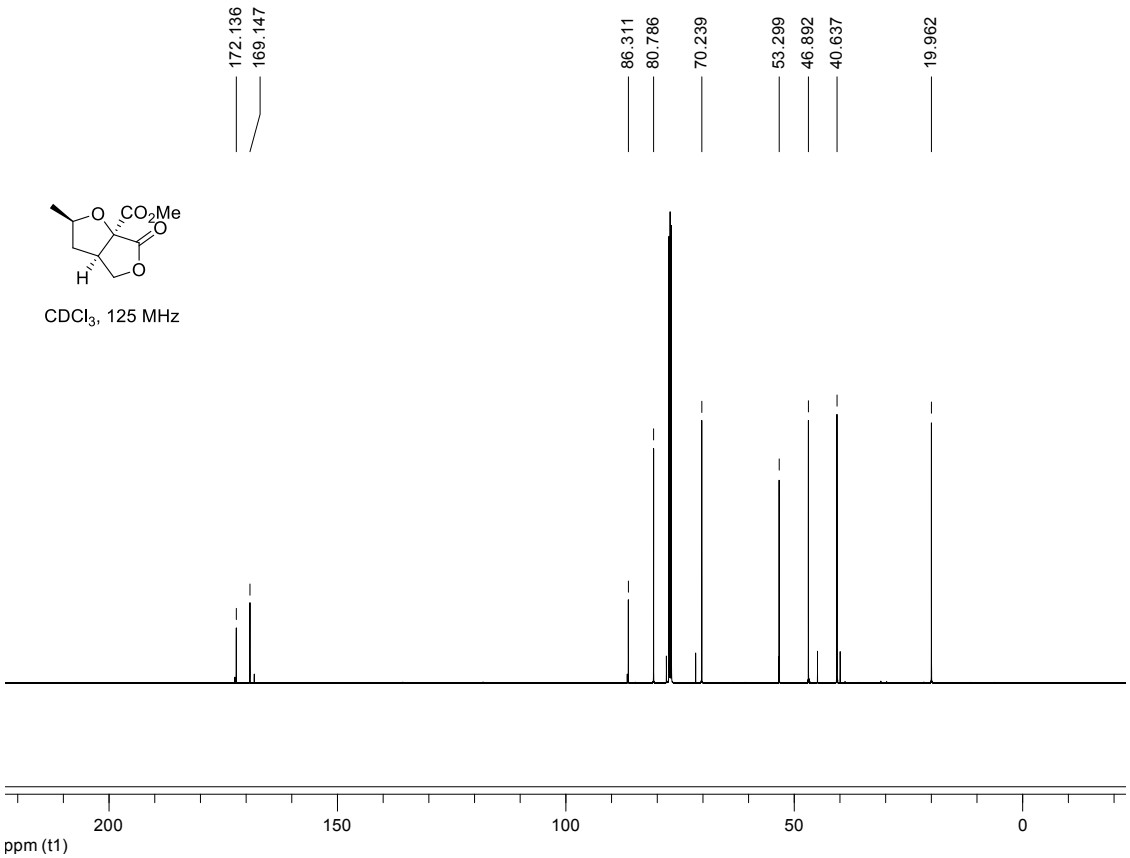
Spectra for compound **11a**



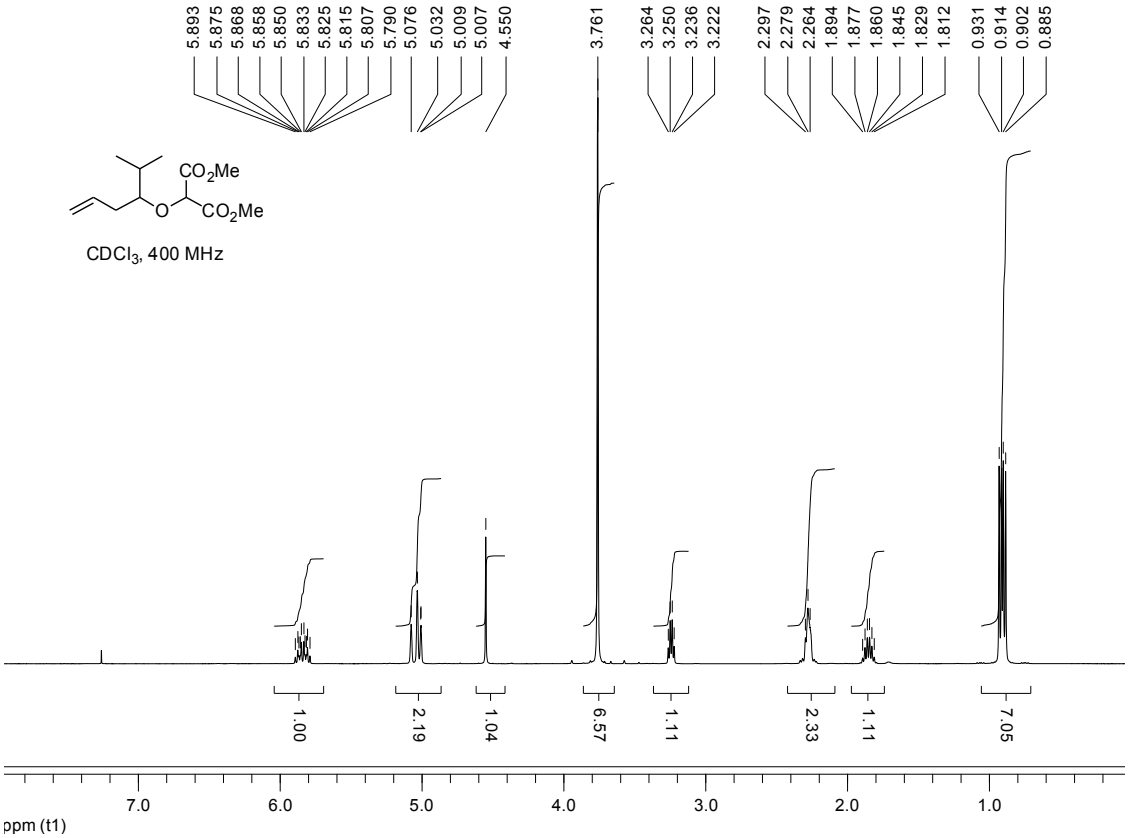


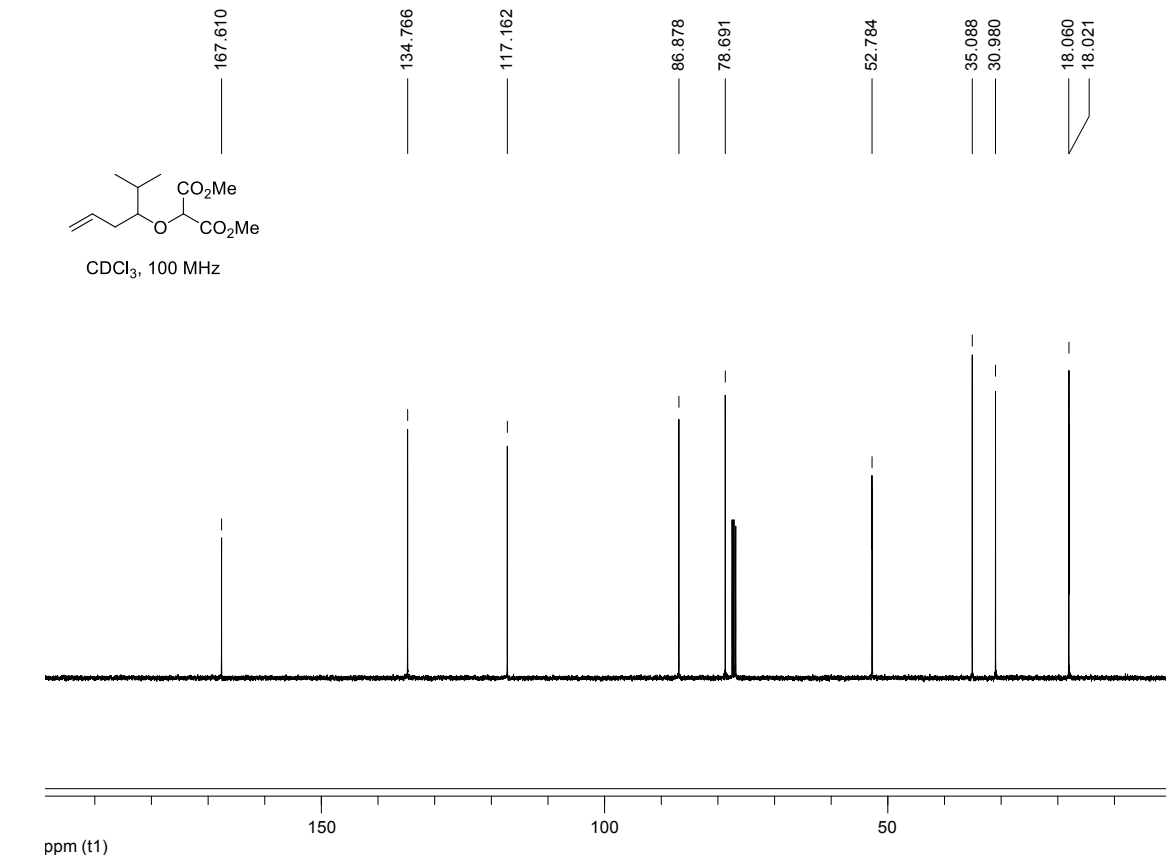
Spectra for compound **12a** (mixture of diastereoisomers after purification d. r. = 8.5:1)



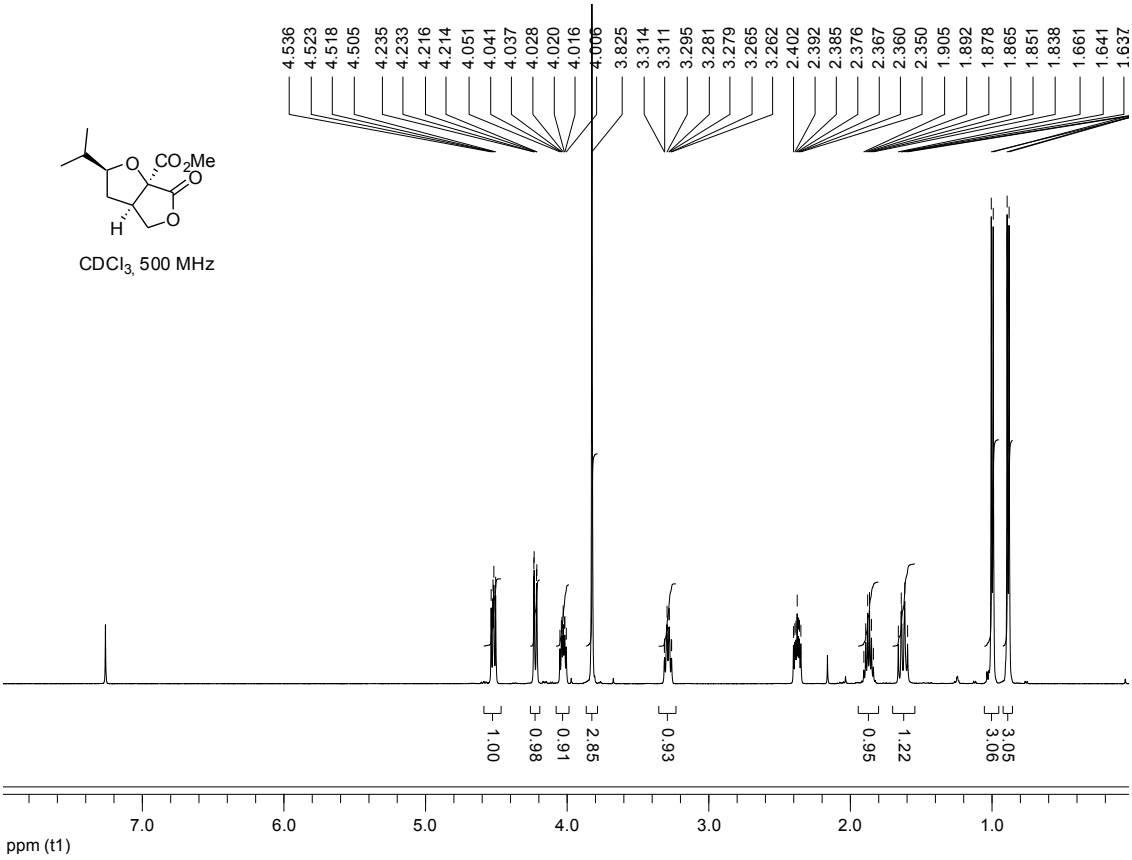


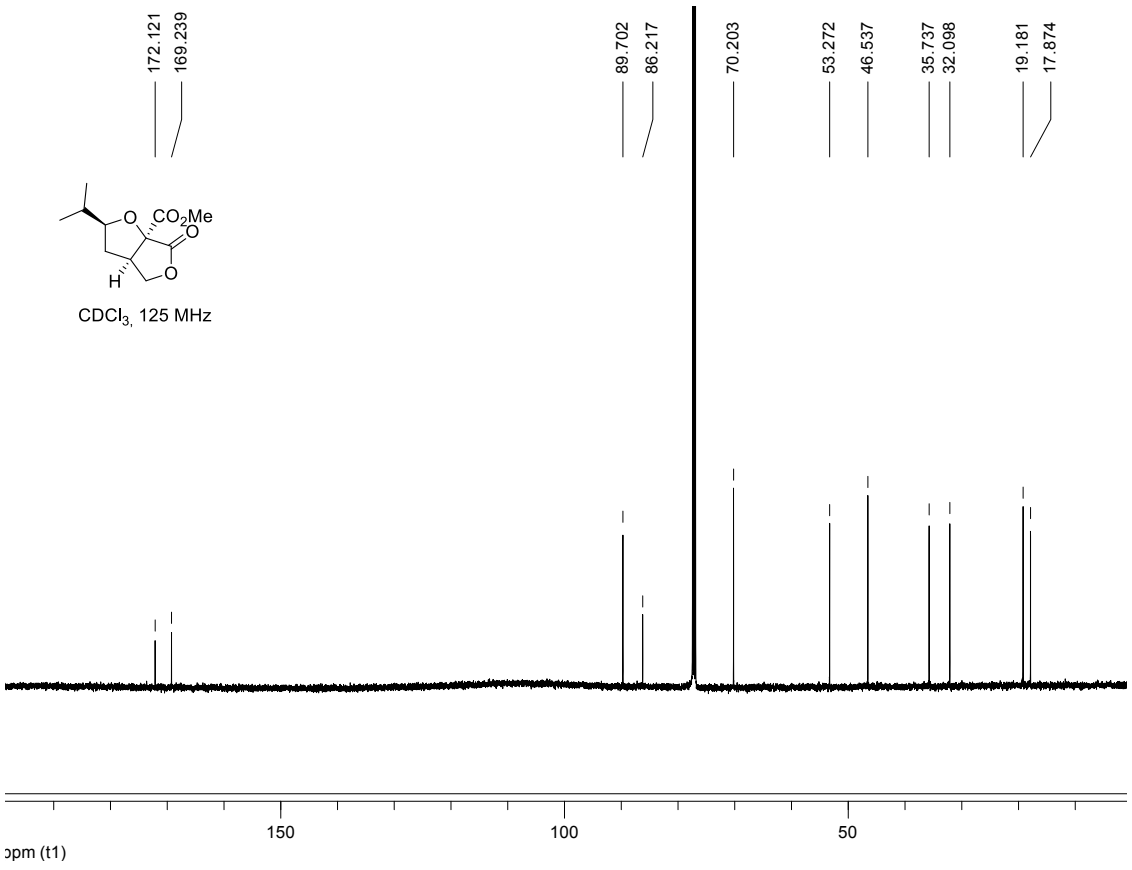
Spectra for compound **11b**



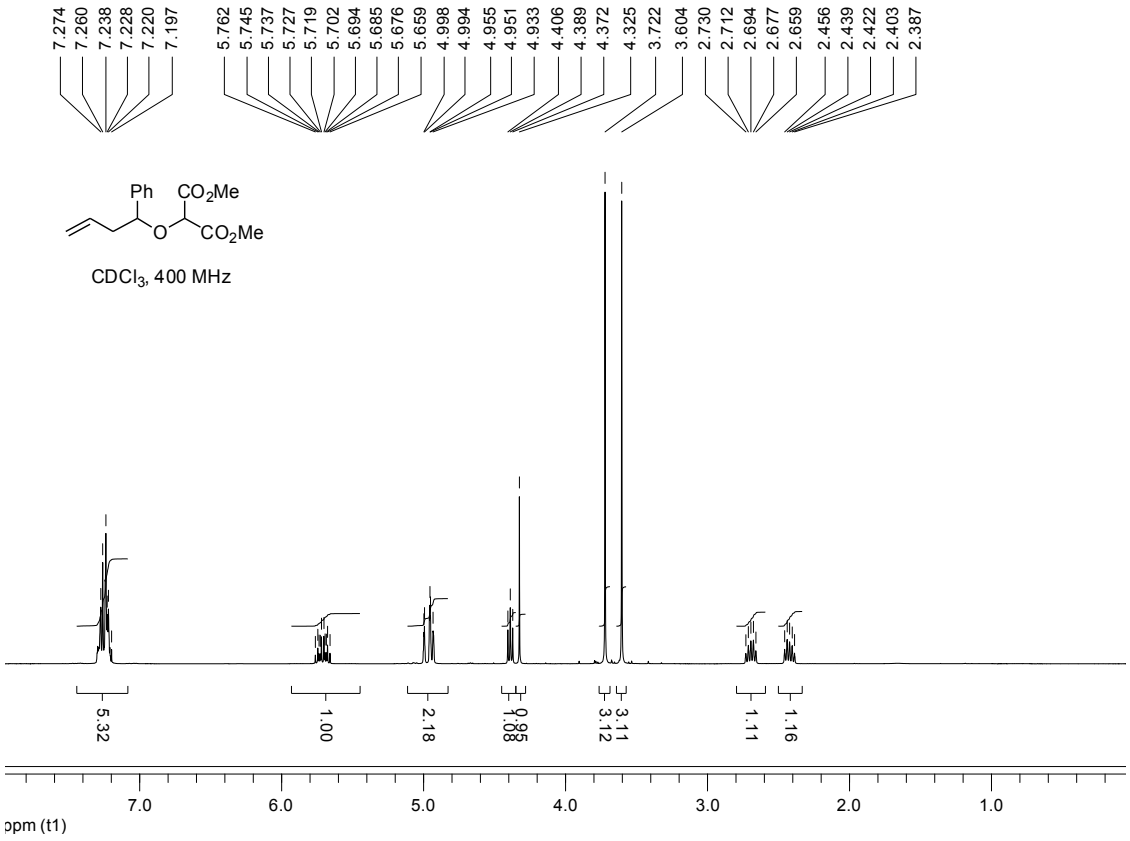


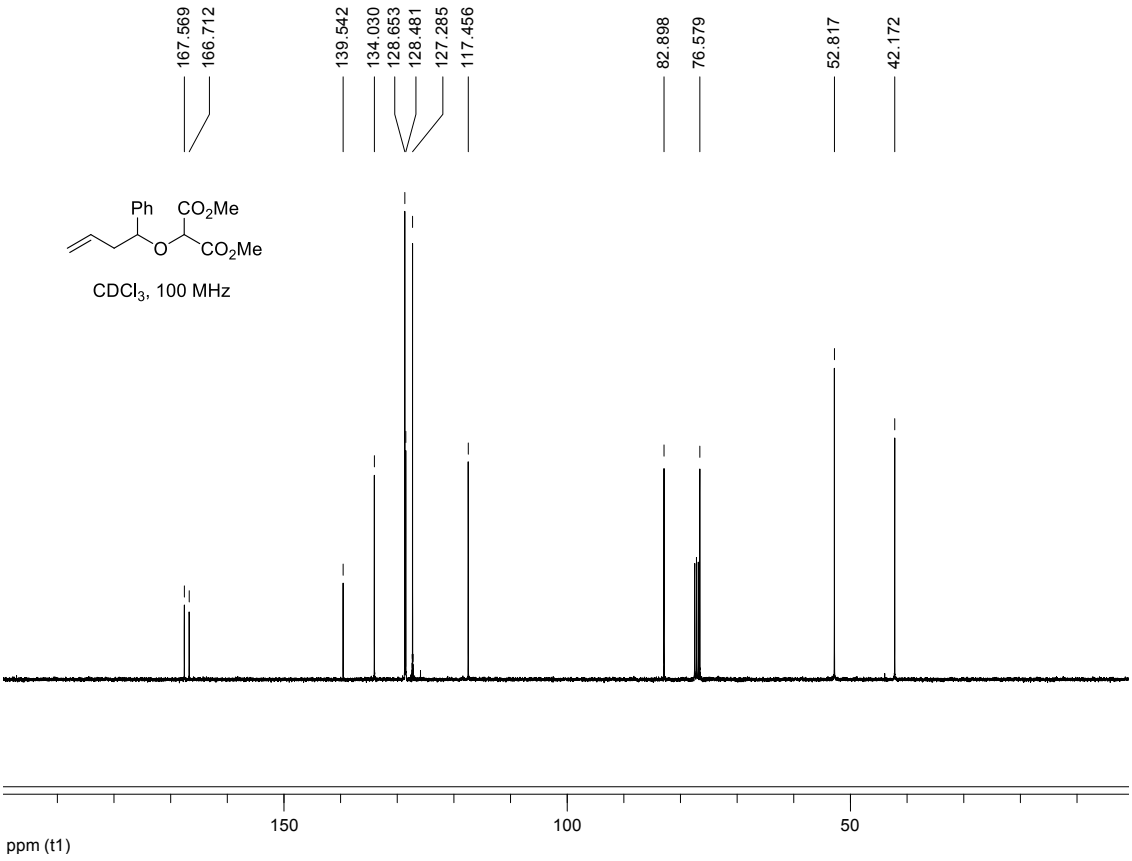
Spectra for compound **12b**



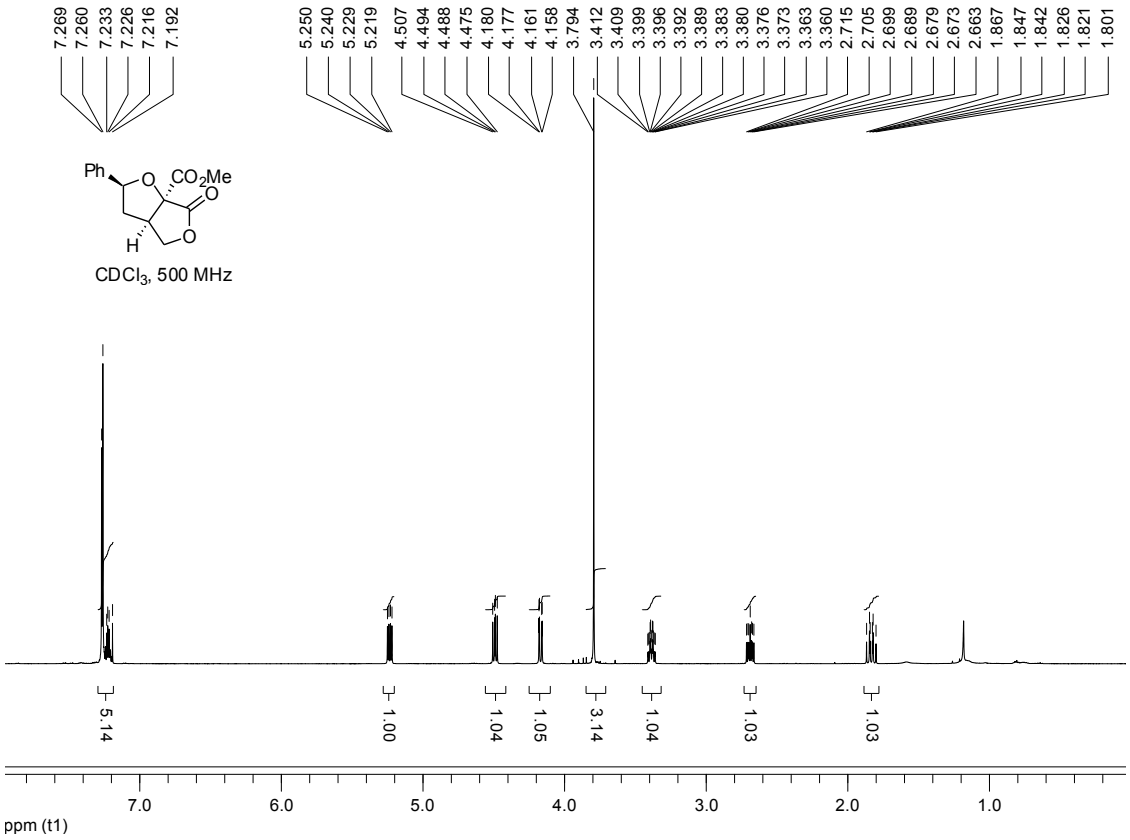


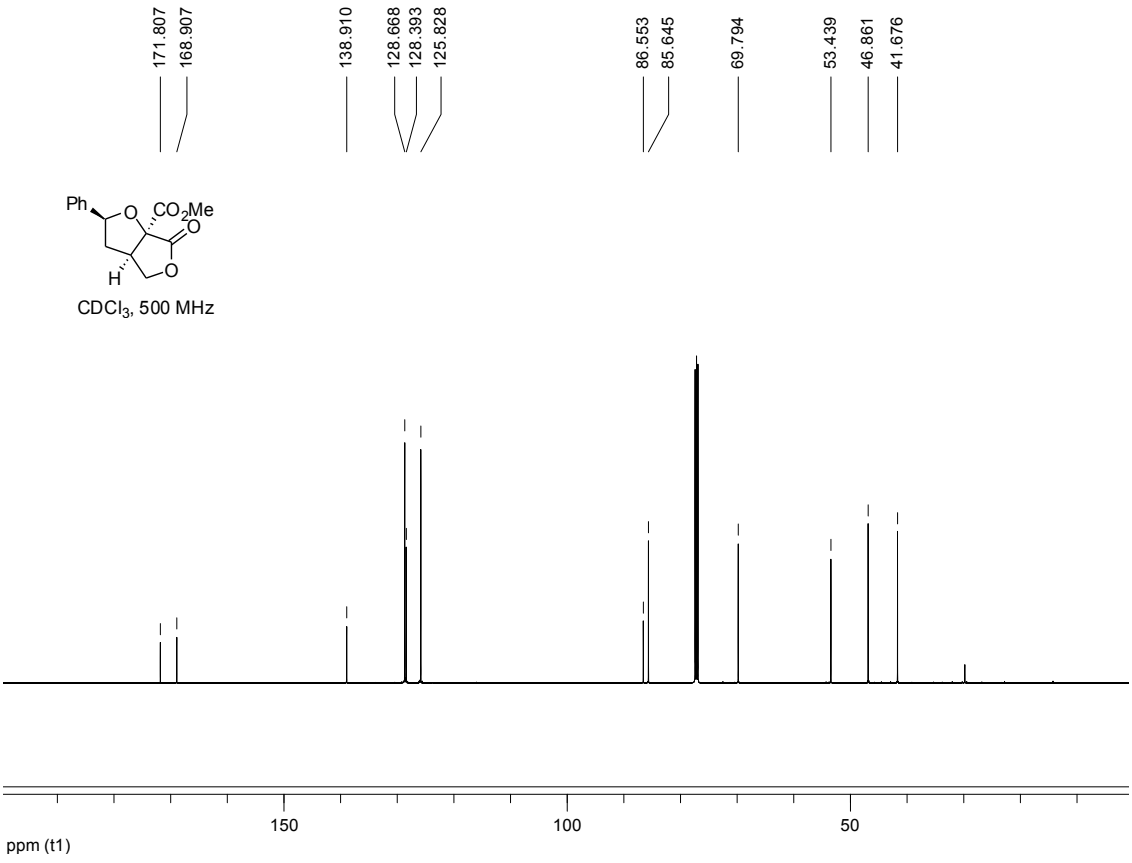
Spectra for compound **11c**



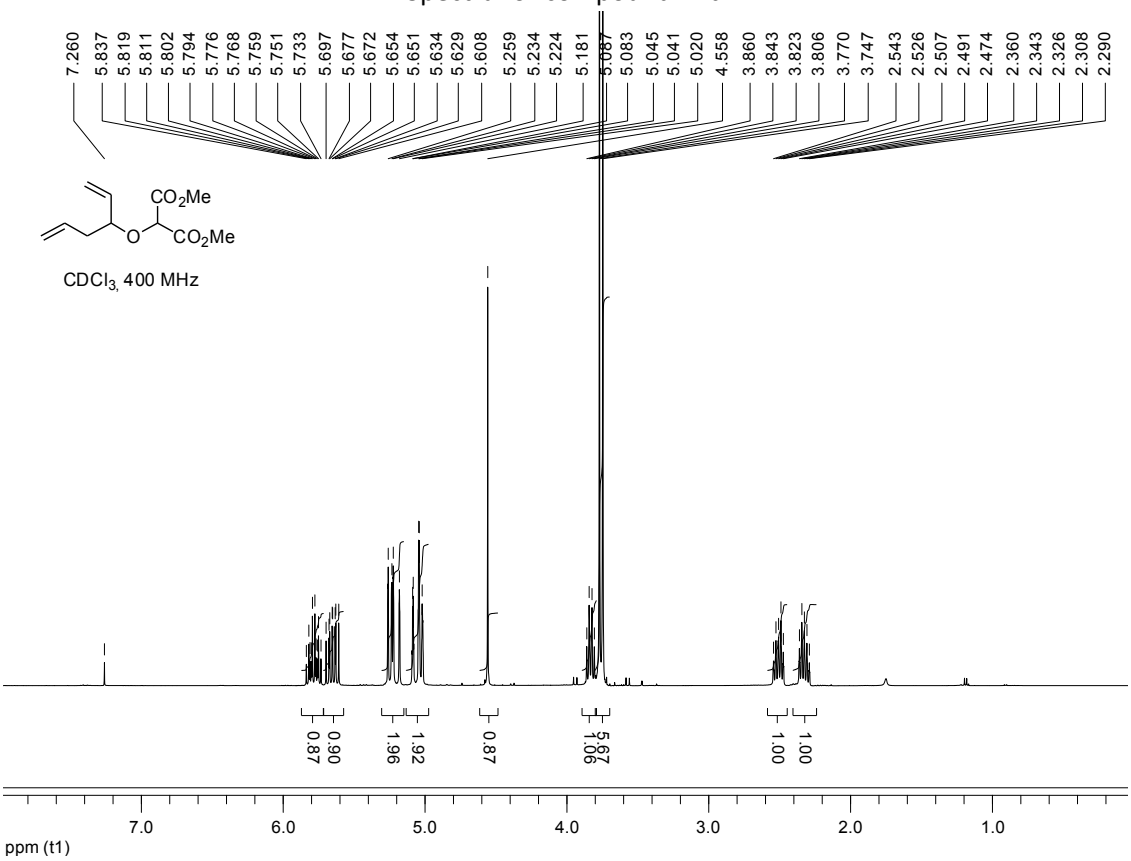


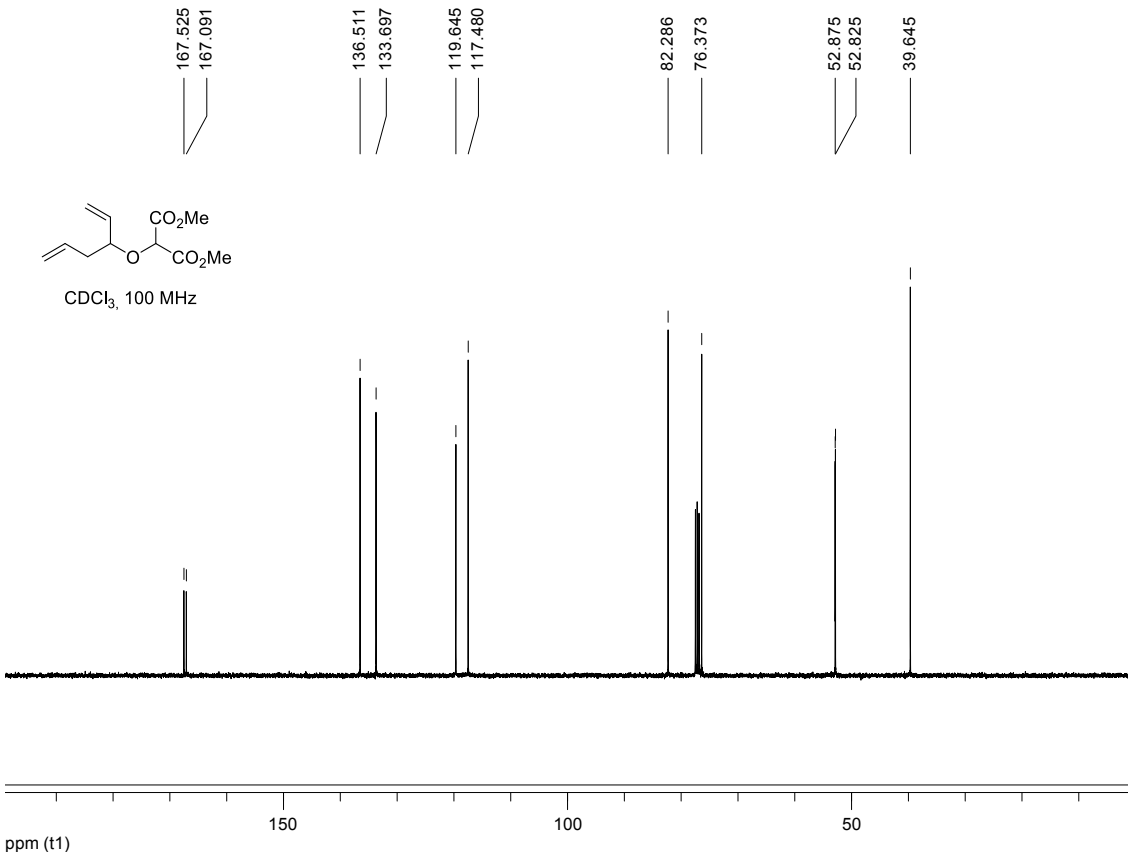
Spectra for compound **12c**



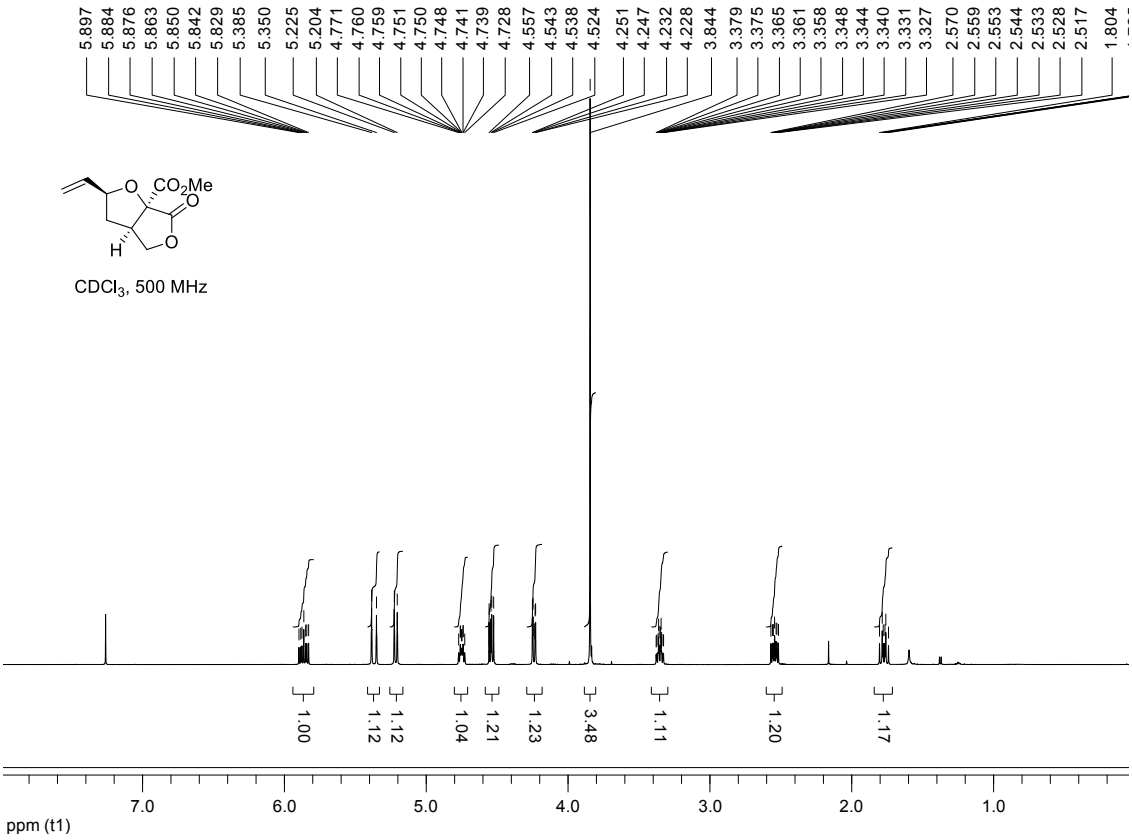


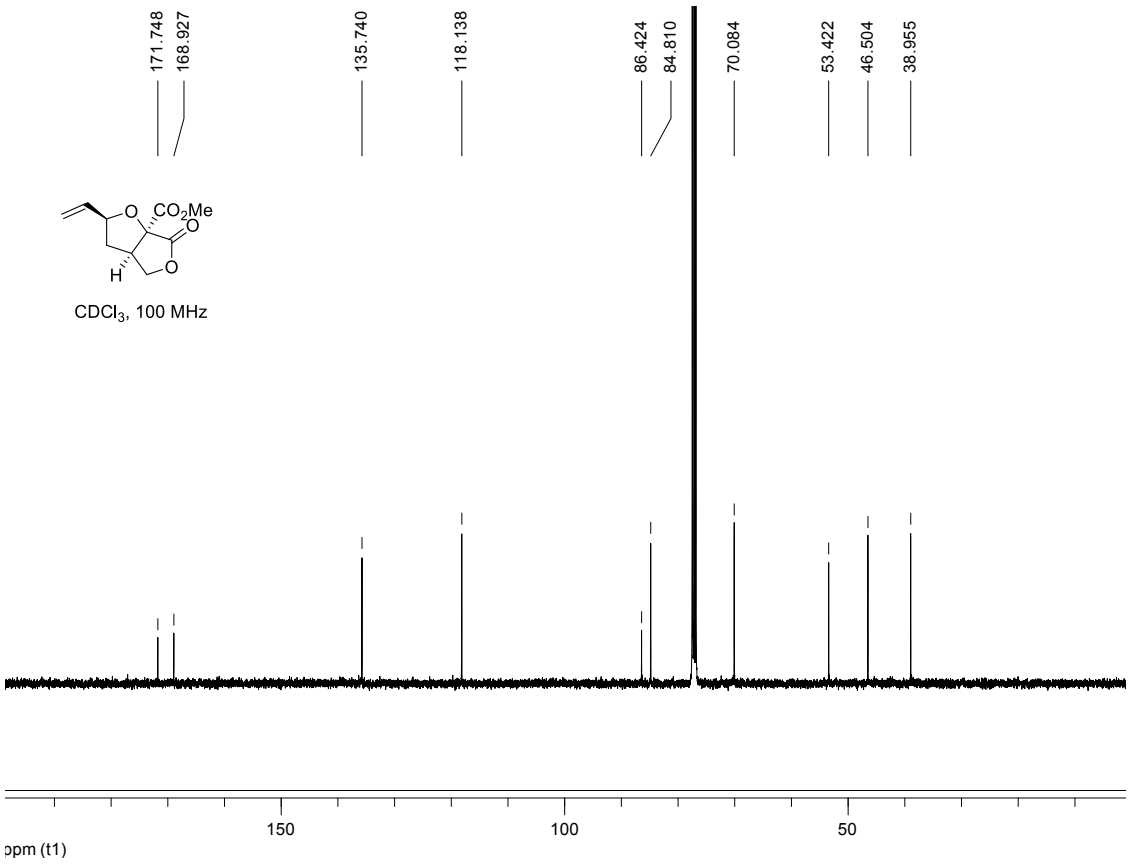
Spectra for compound **11d**



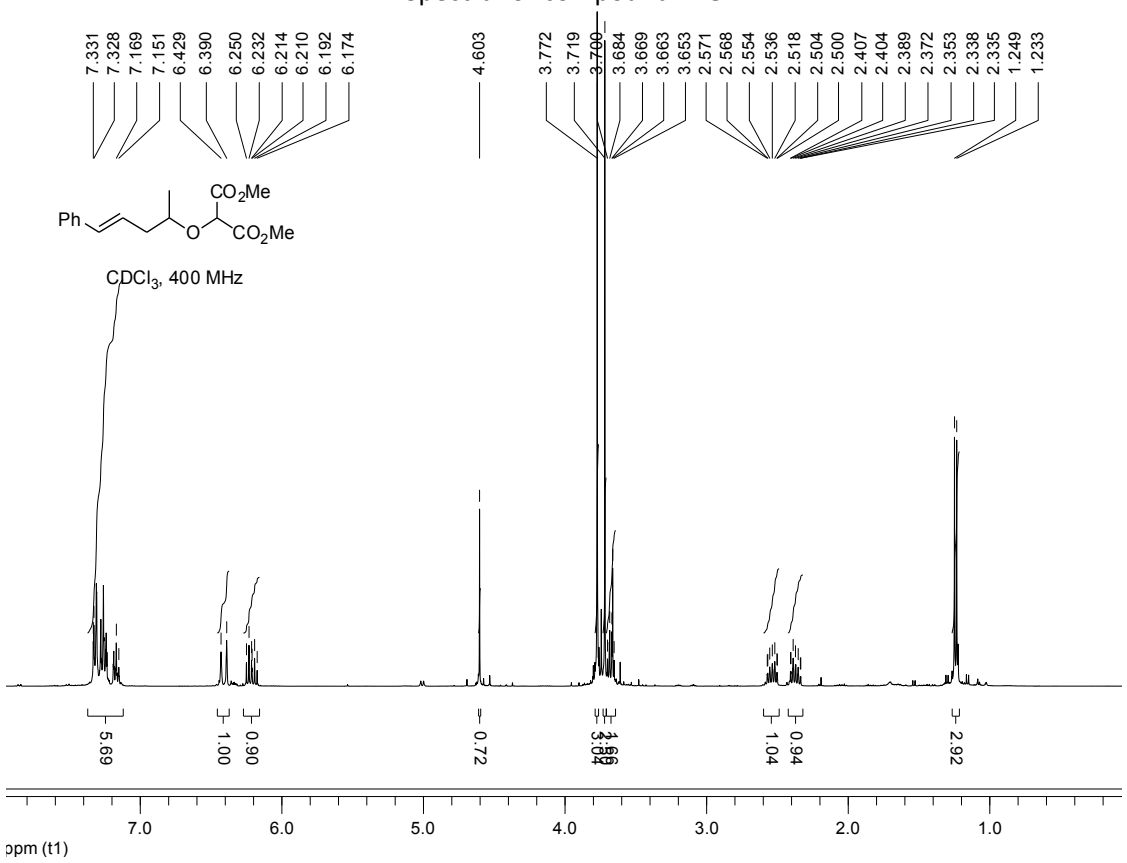


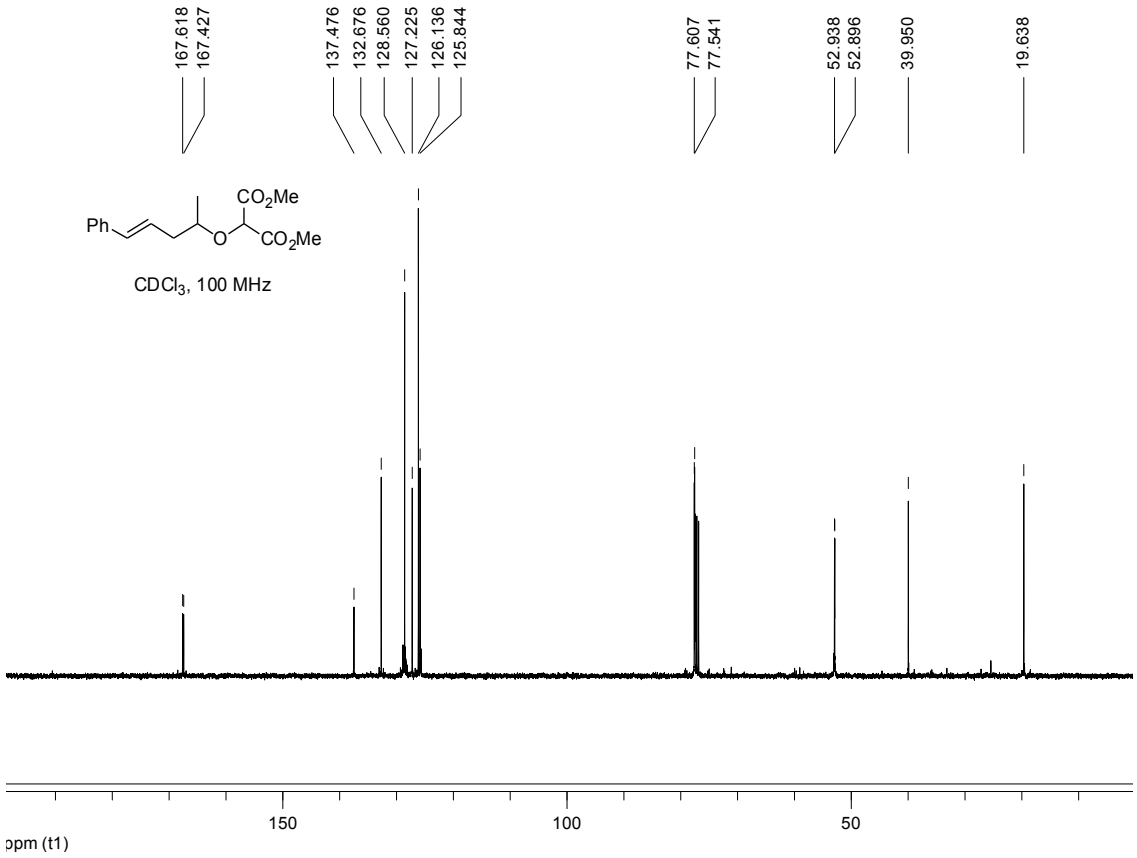
Spectra for compound **12d**



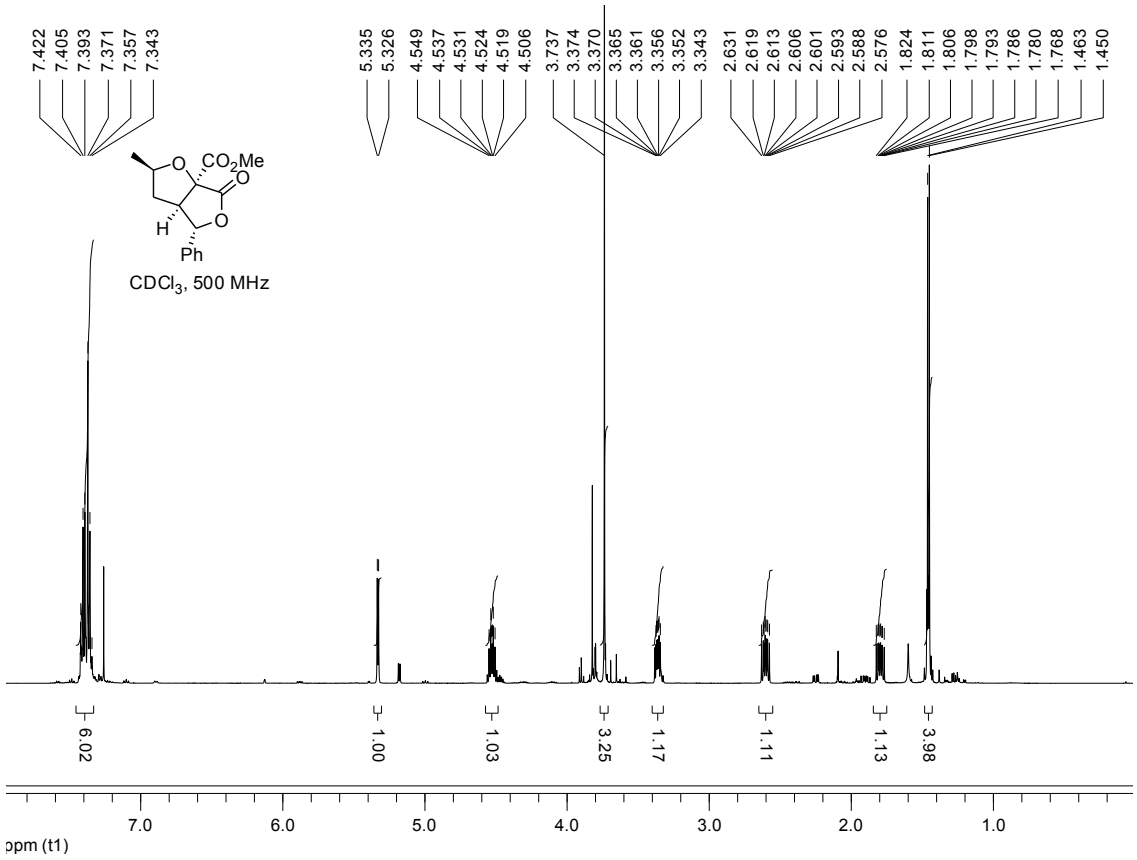


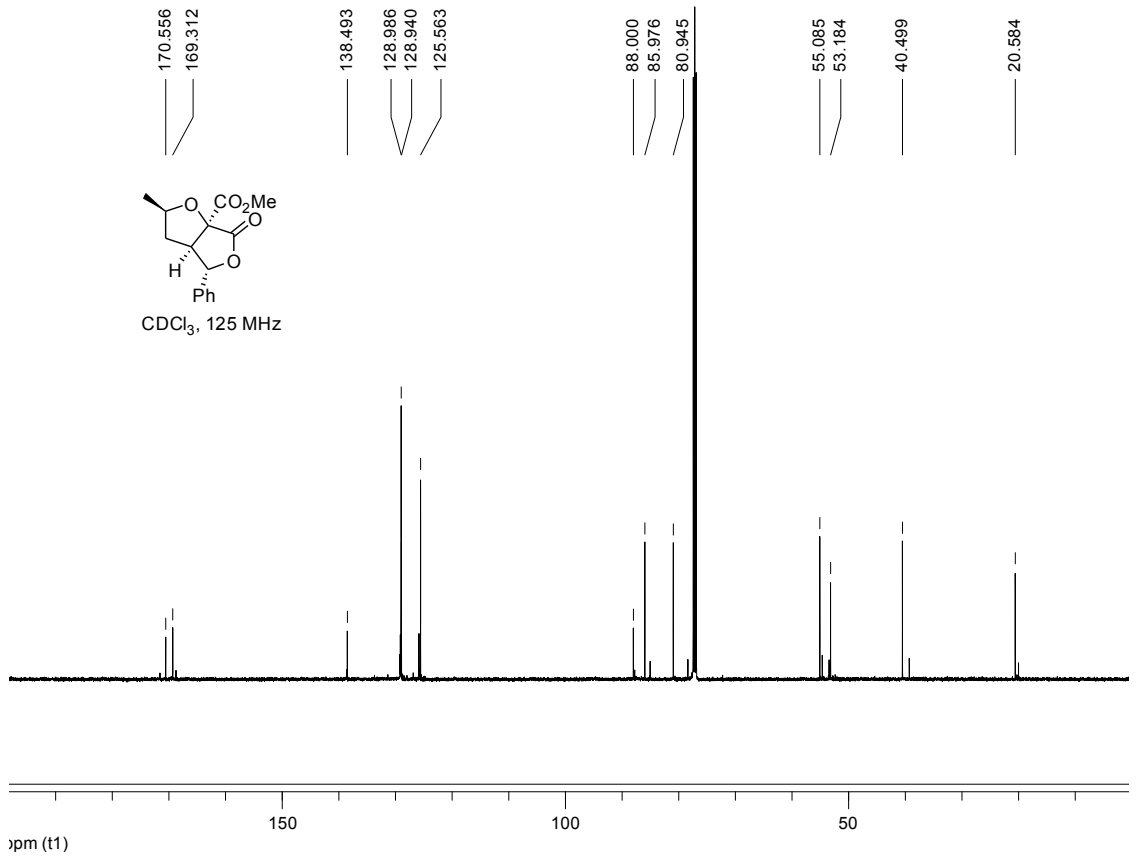
Spectra for compound **11e**



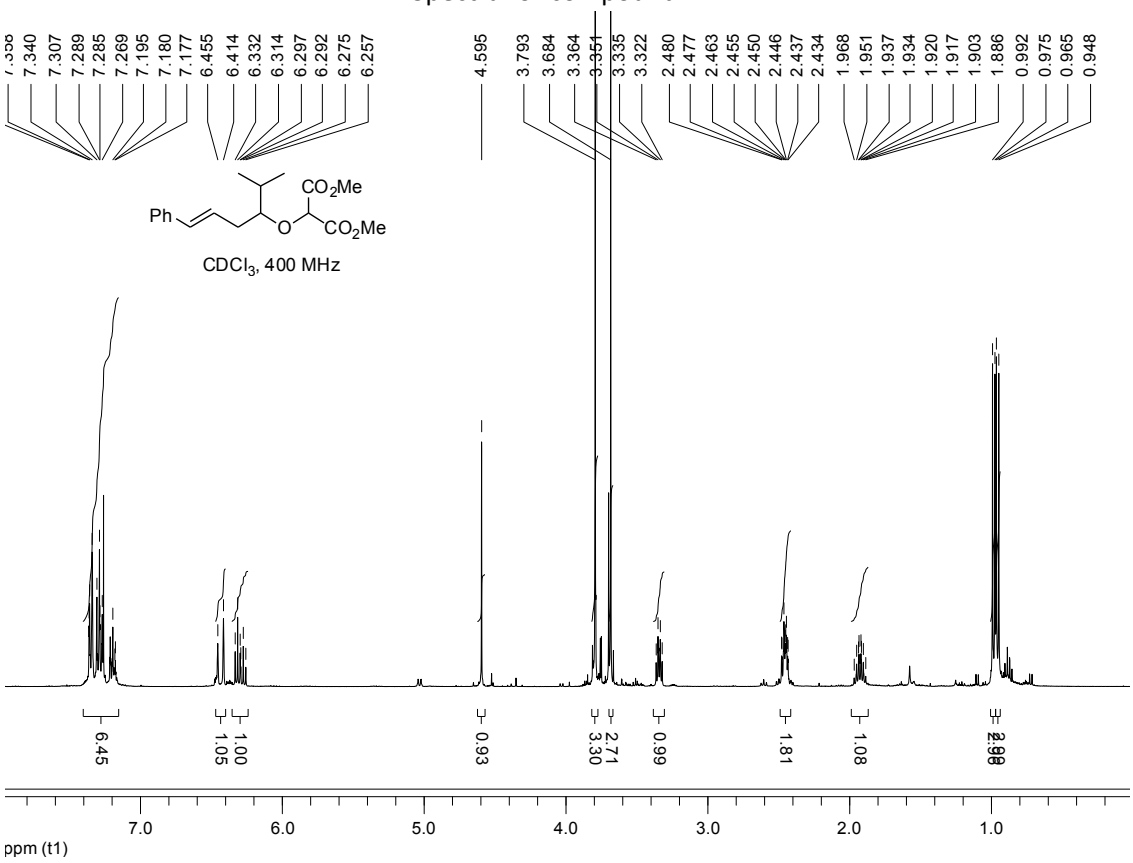


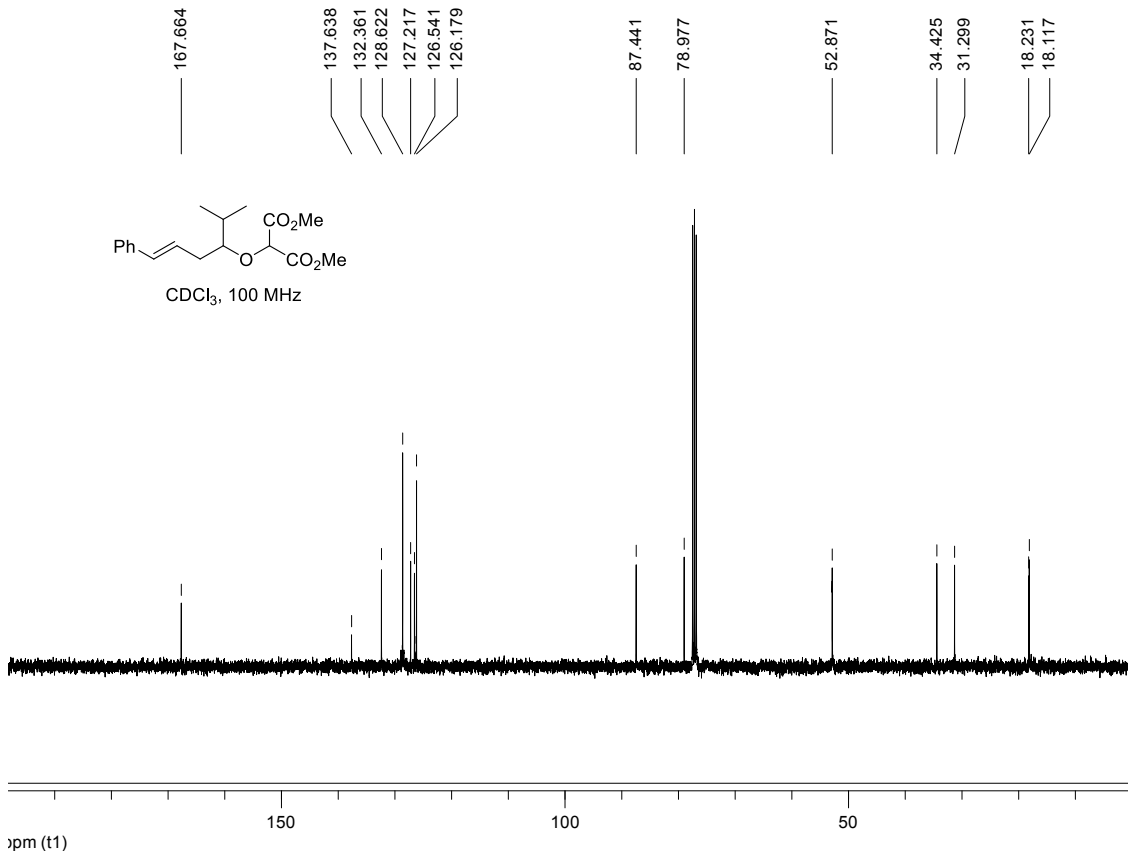
Spectra for compound **12e** (mixture of diastereoisomers after purification d. r. = 5.6:1)



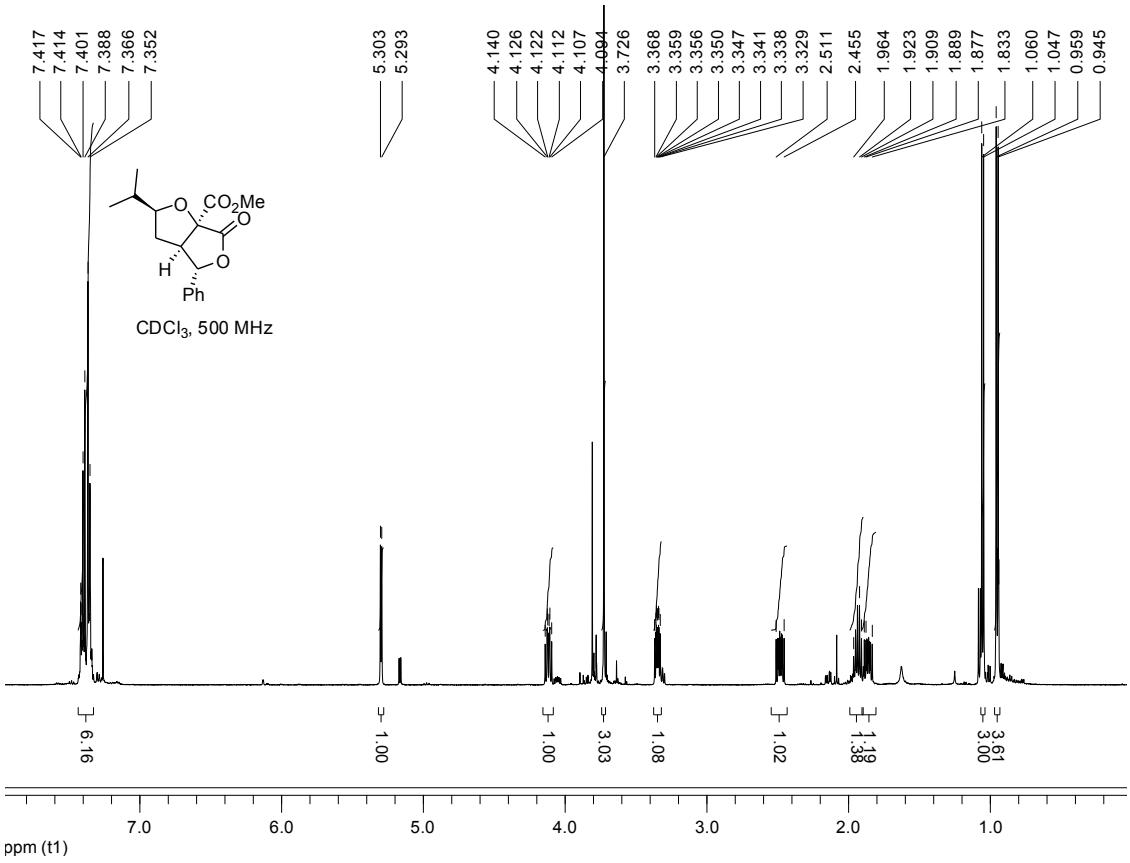


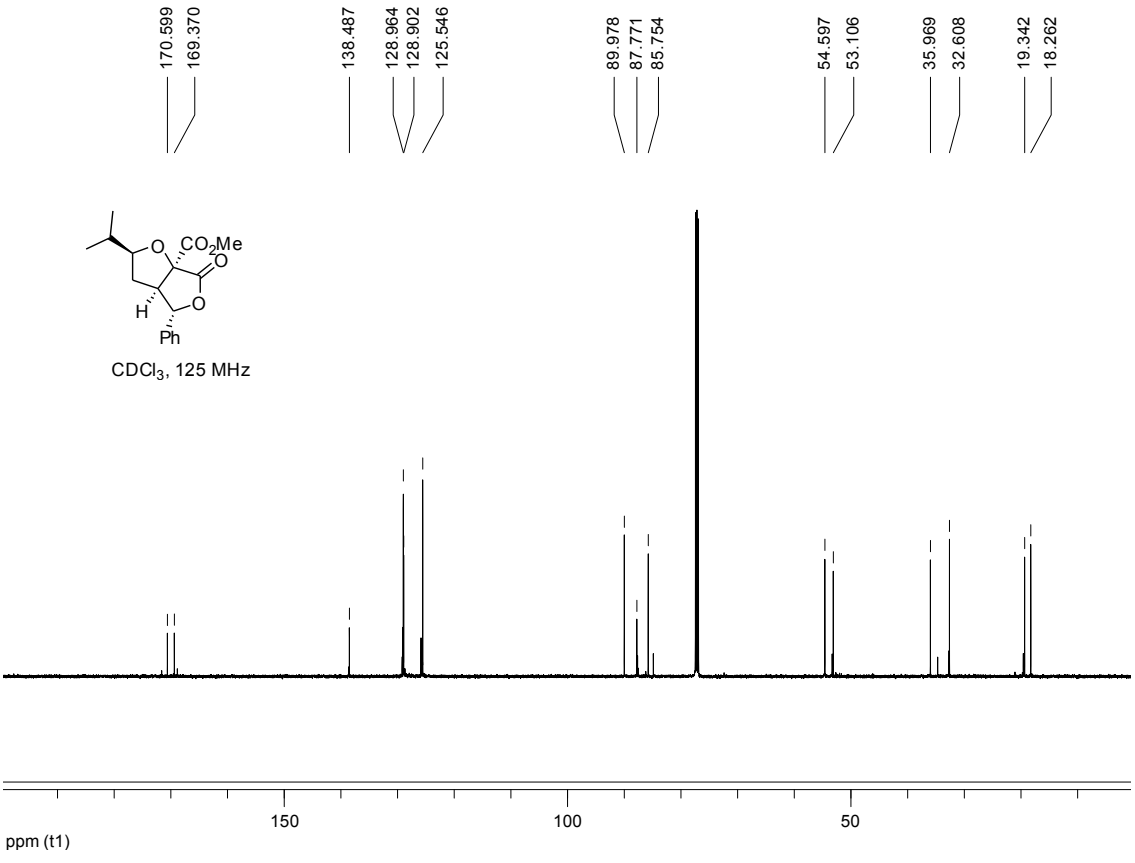
Spectra for compound **11f**



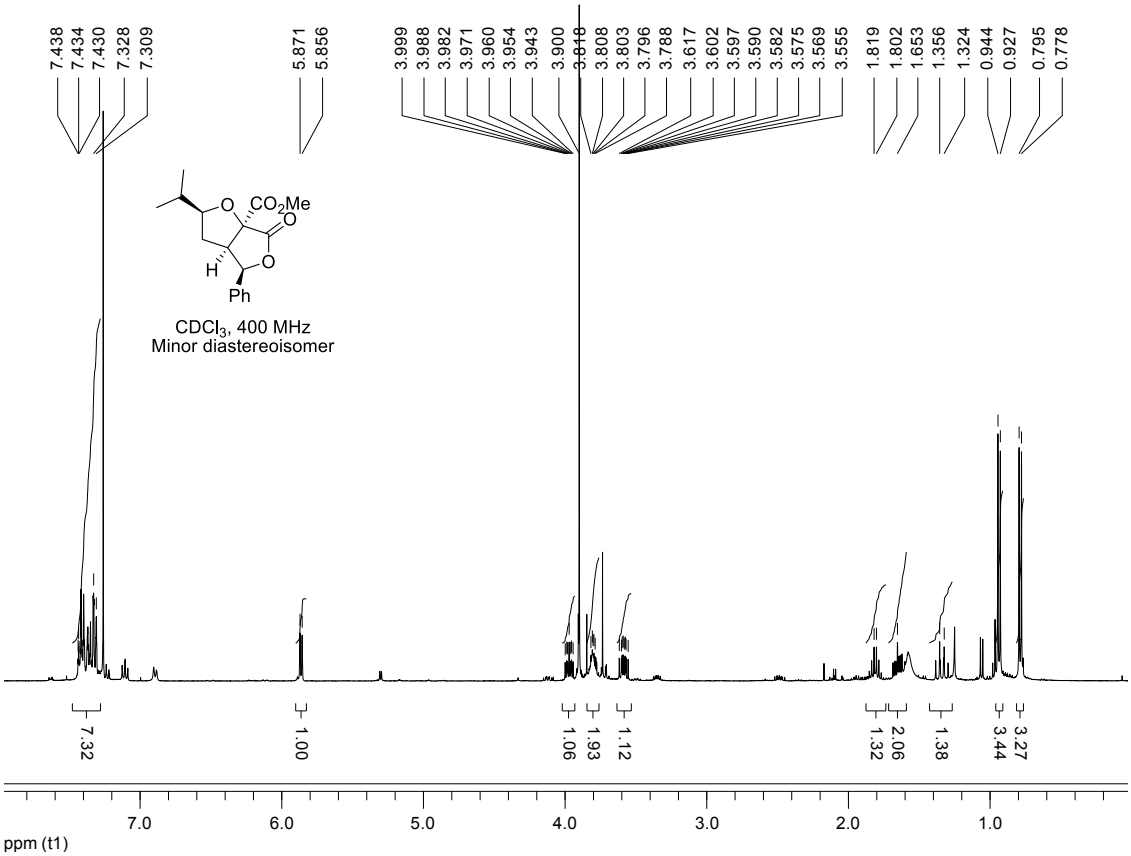


Spectra for compound **12f** (mixture of diastereoisomers after purification d. r. = 5.7:1)

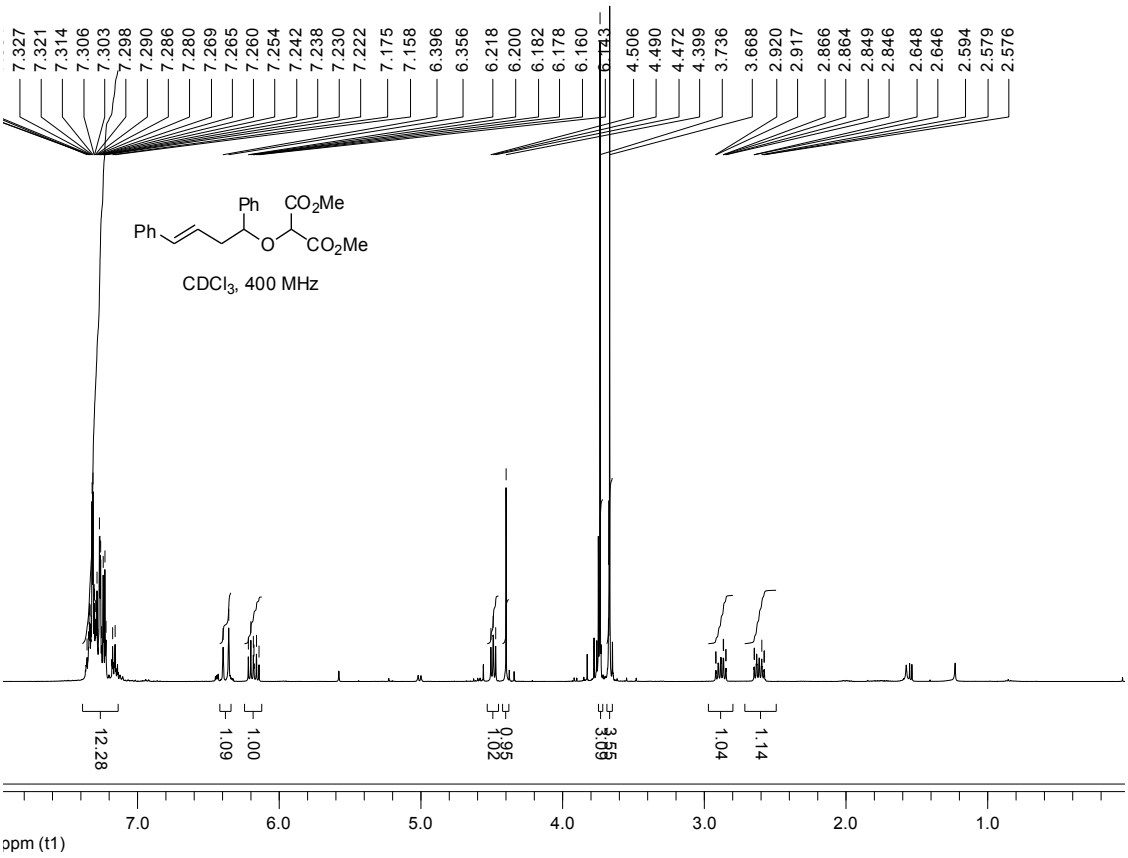


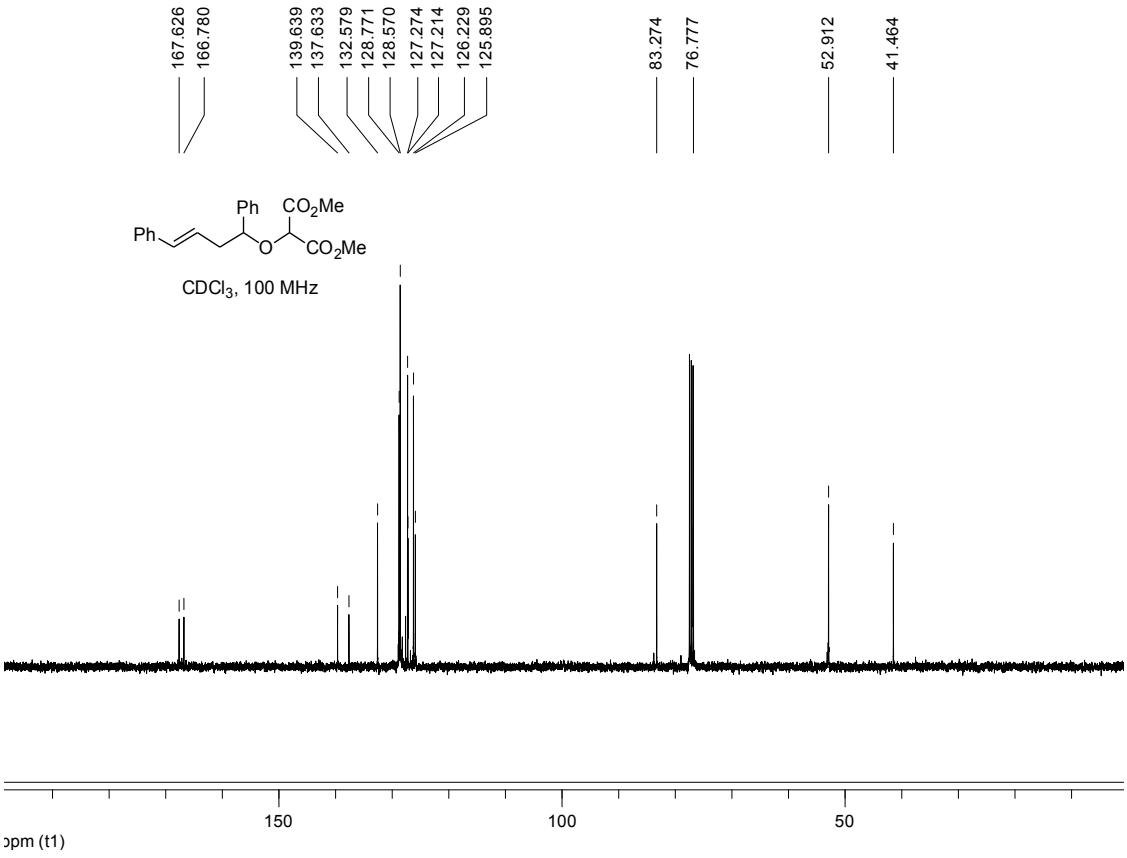


Spectra for compound **12f$_{d3}$** (mixture of diastereoisomers after purification d. r. = 5.5:1)

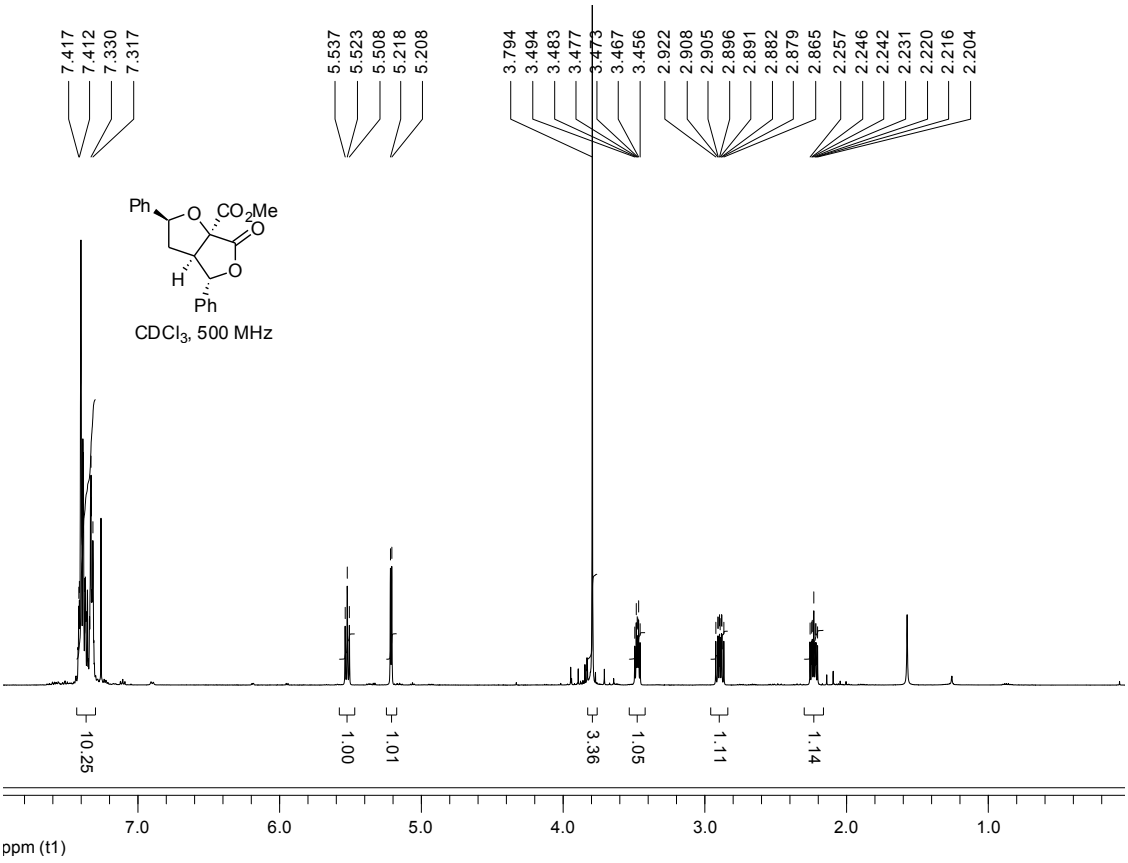


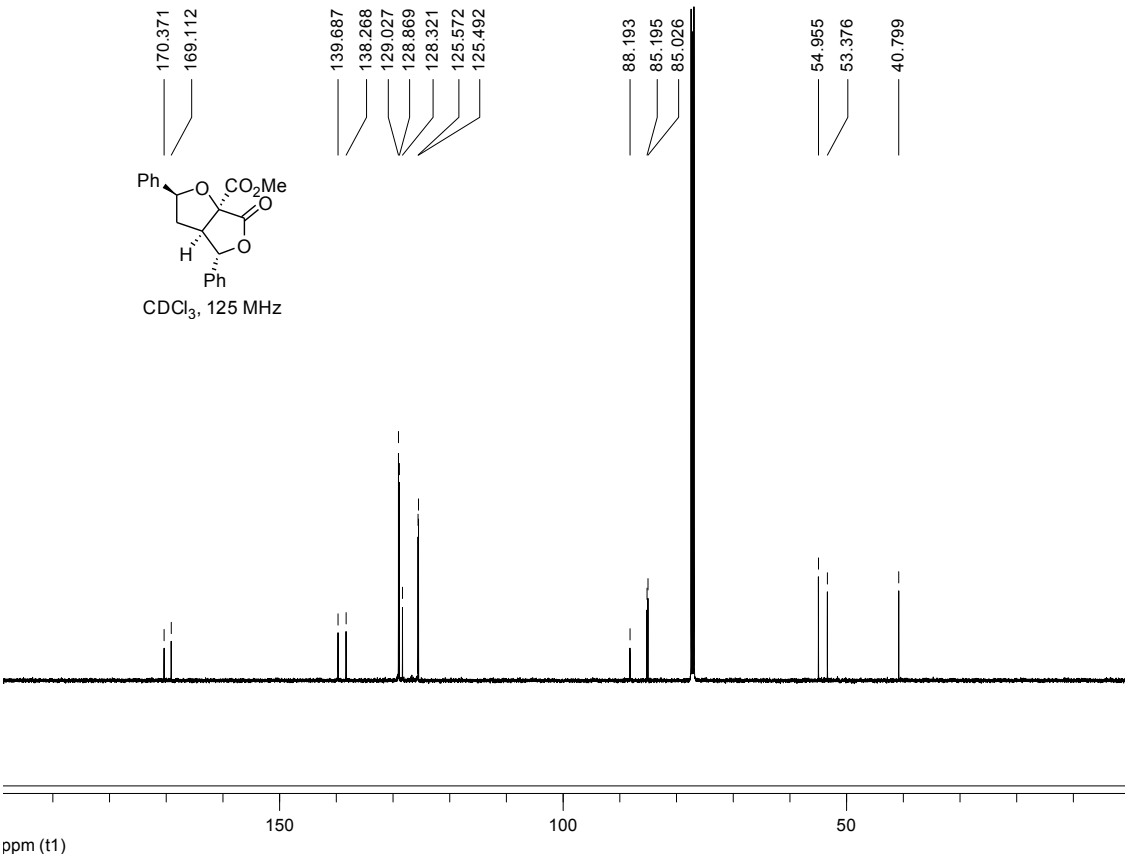
Spectra for compound **11g**



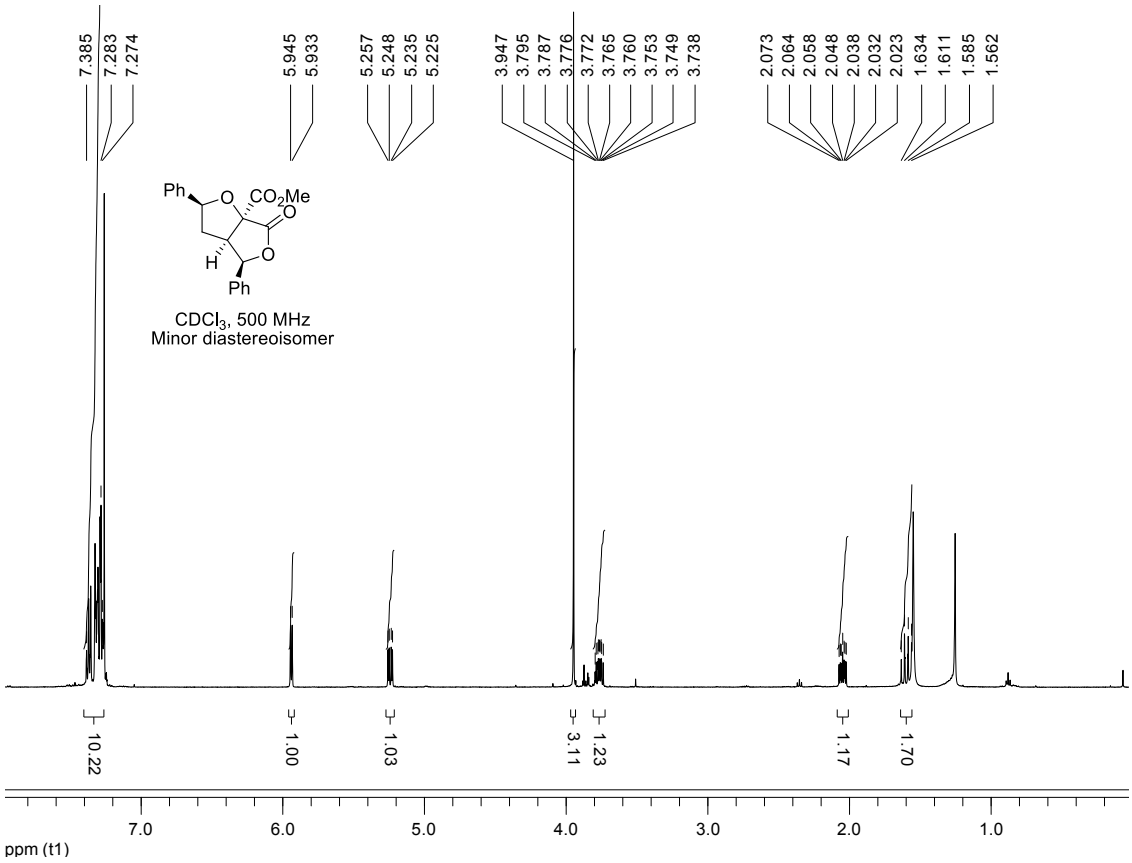


Spectra for compound **12g**

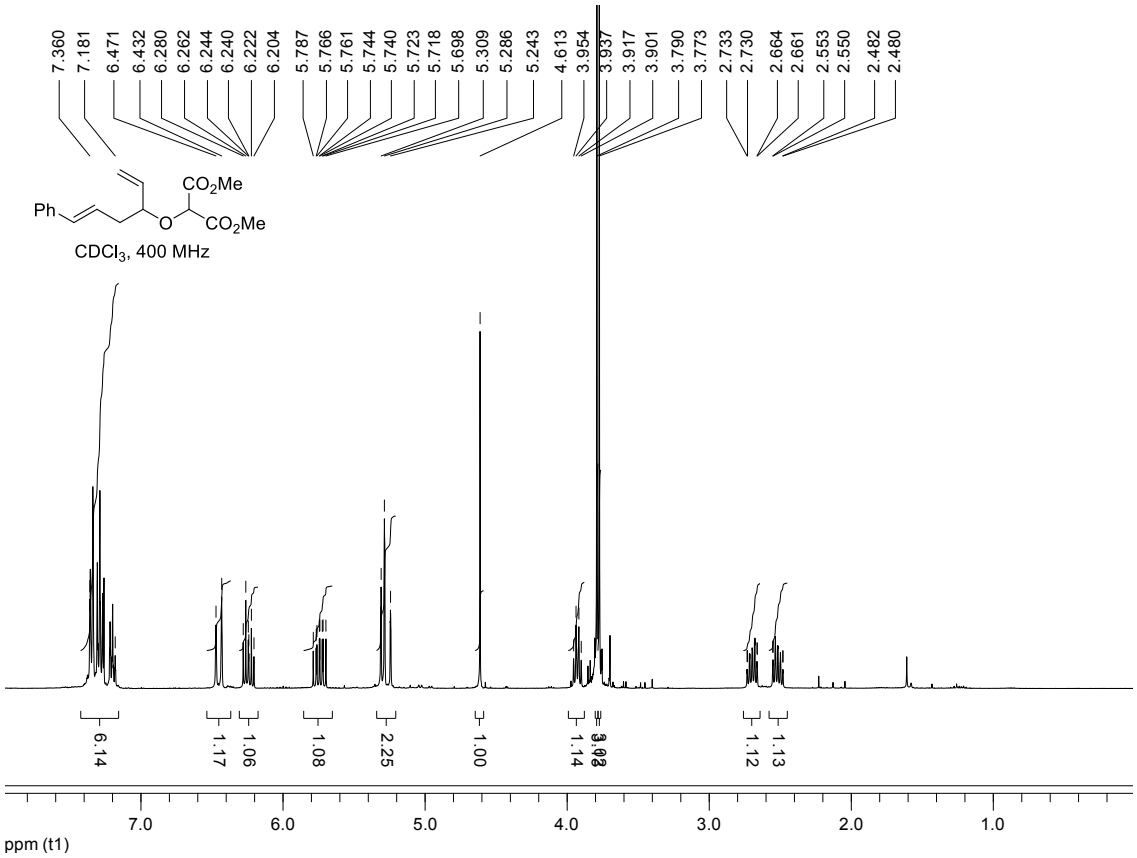


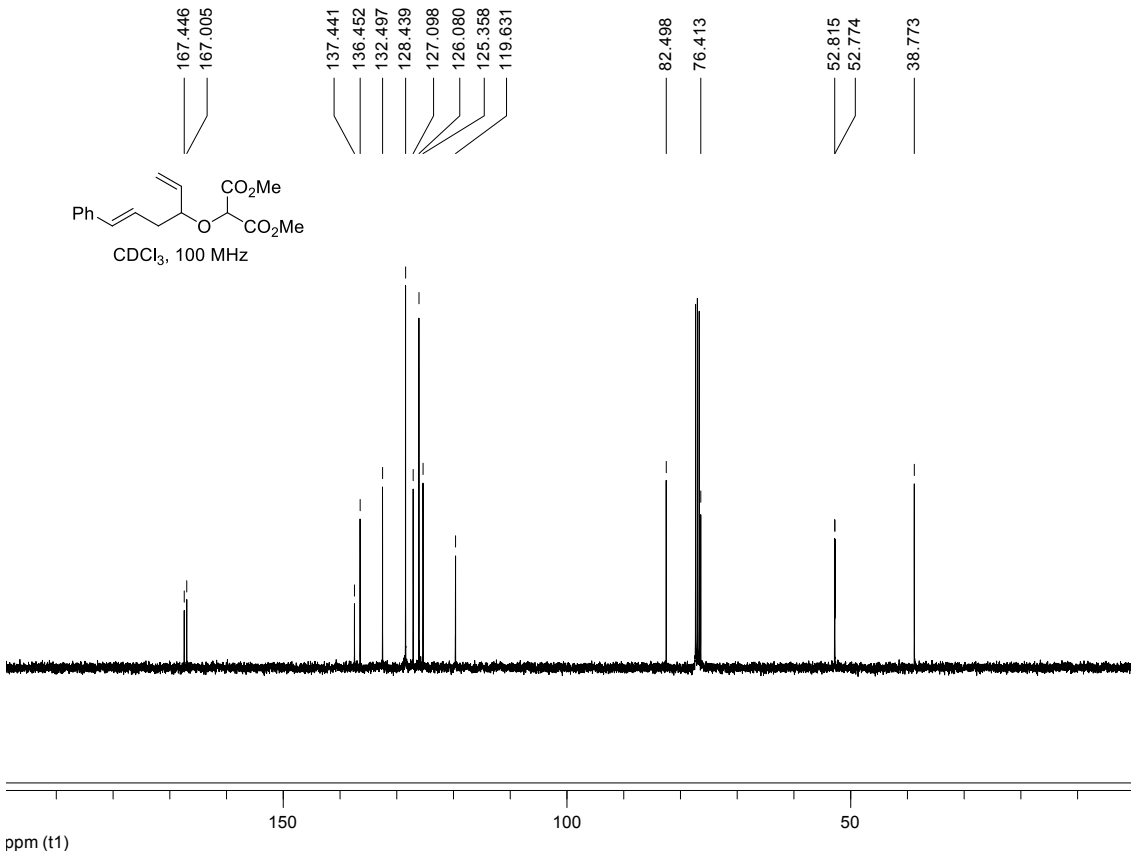


Spectra for compound **12g$_{d3}$**

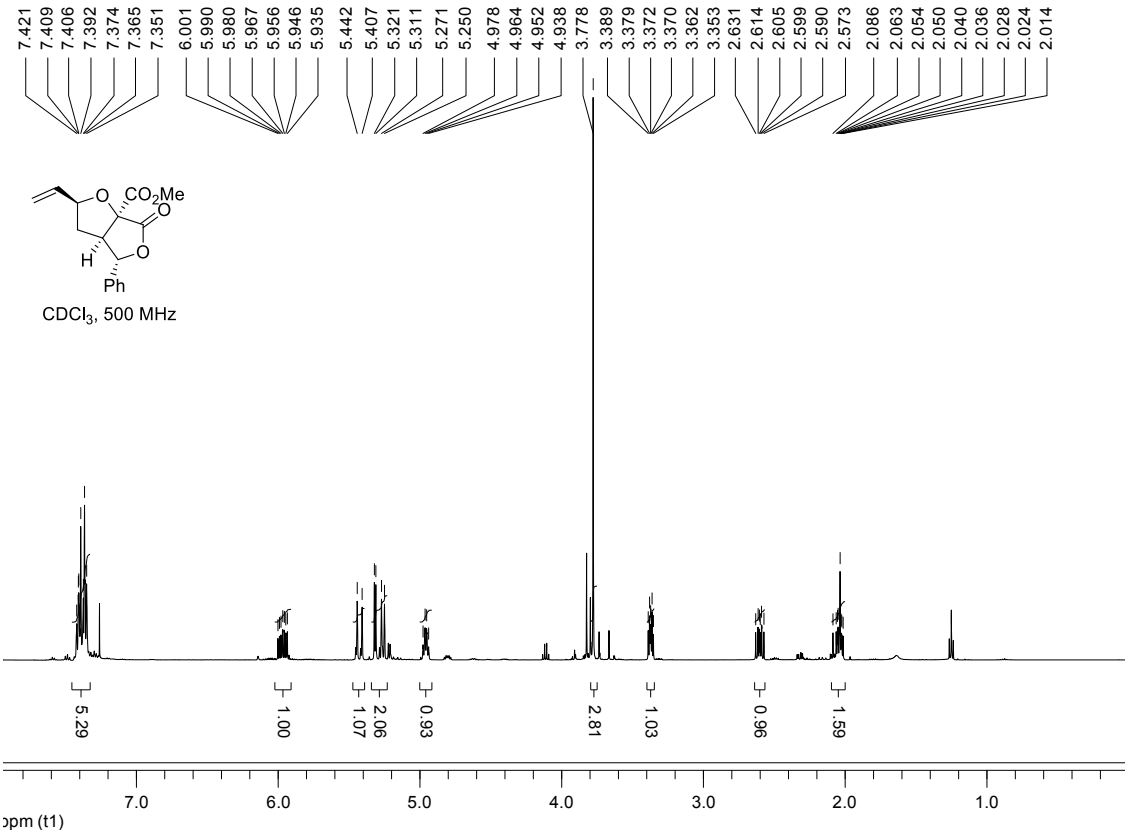


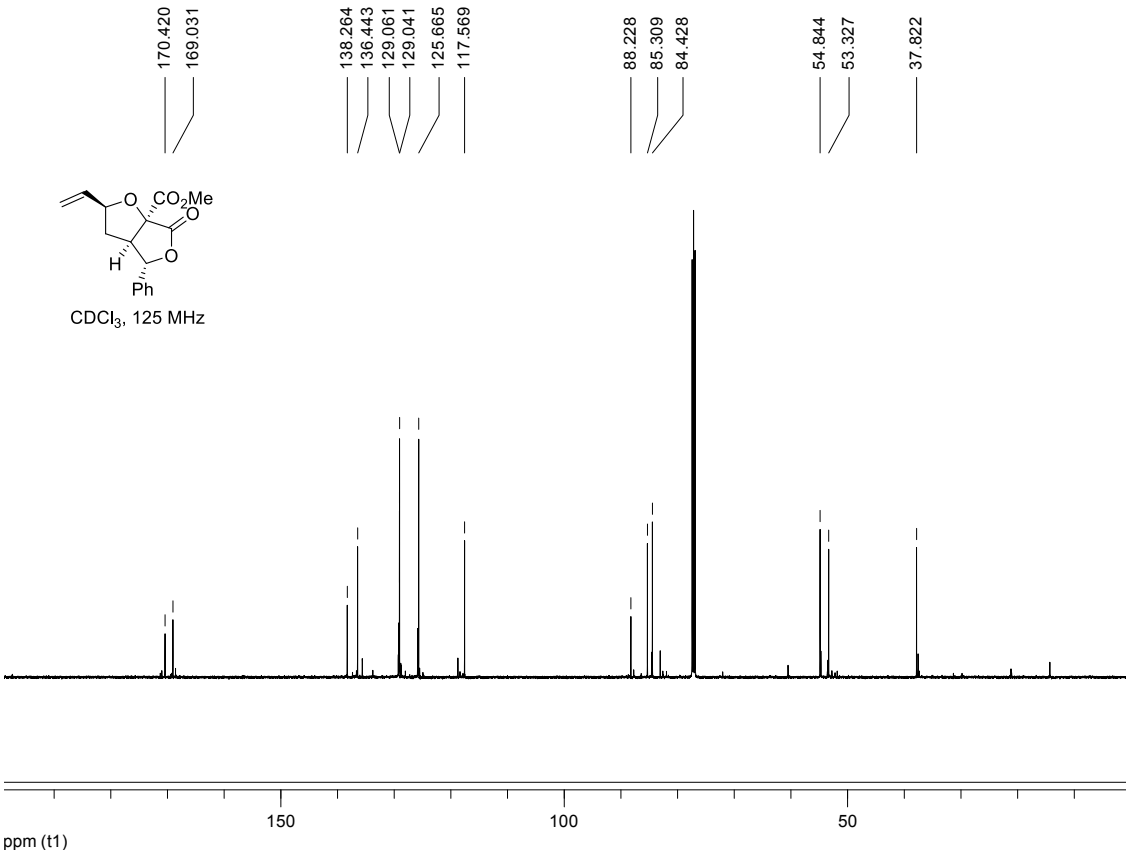
Spectra for compound **11h**



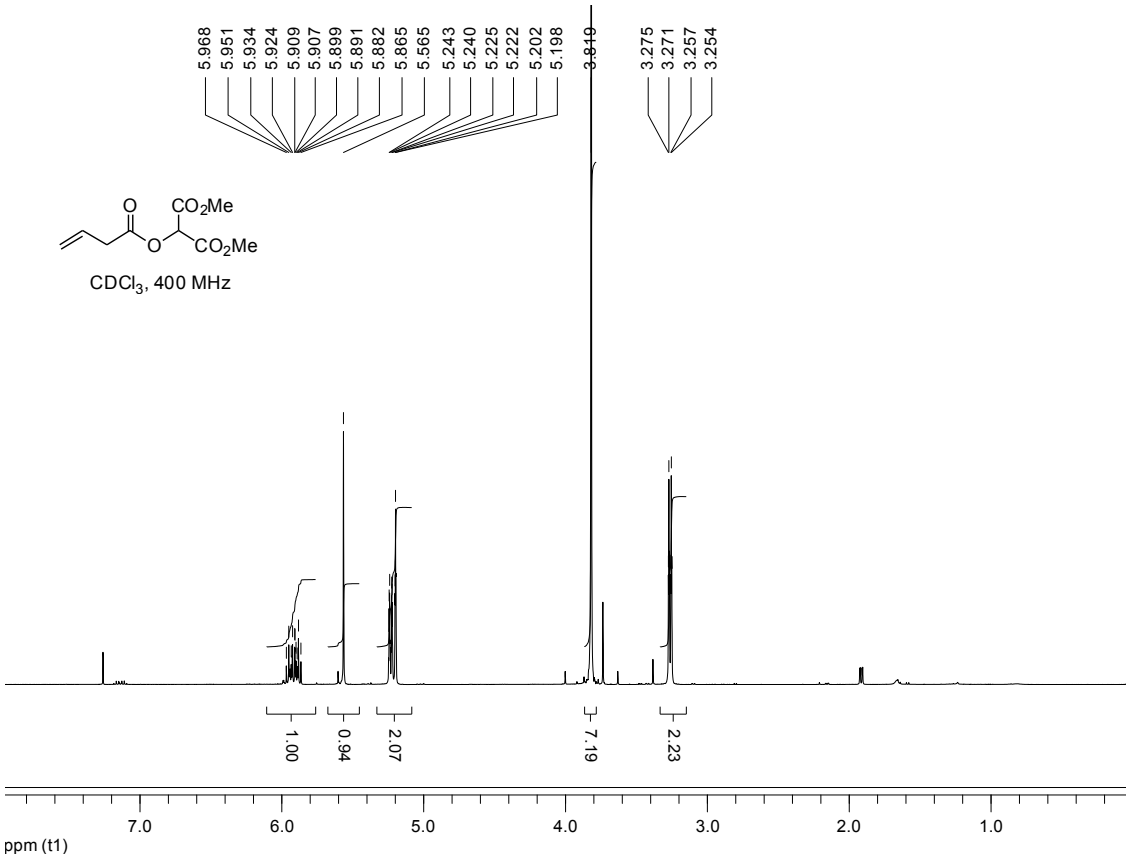


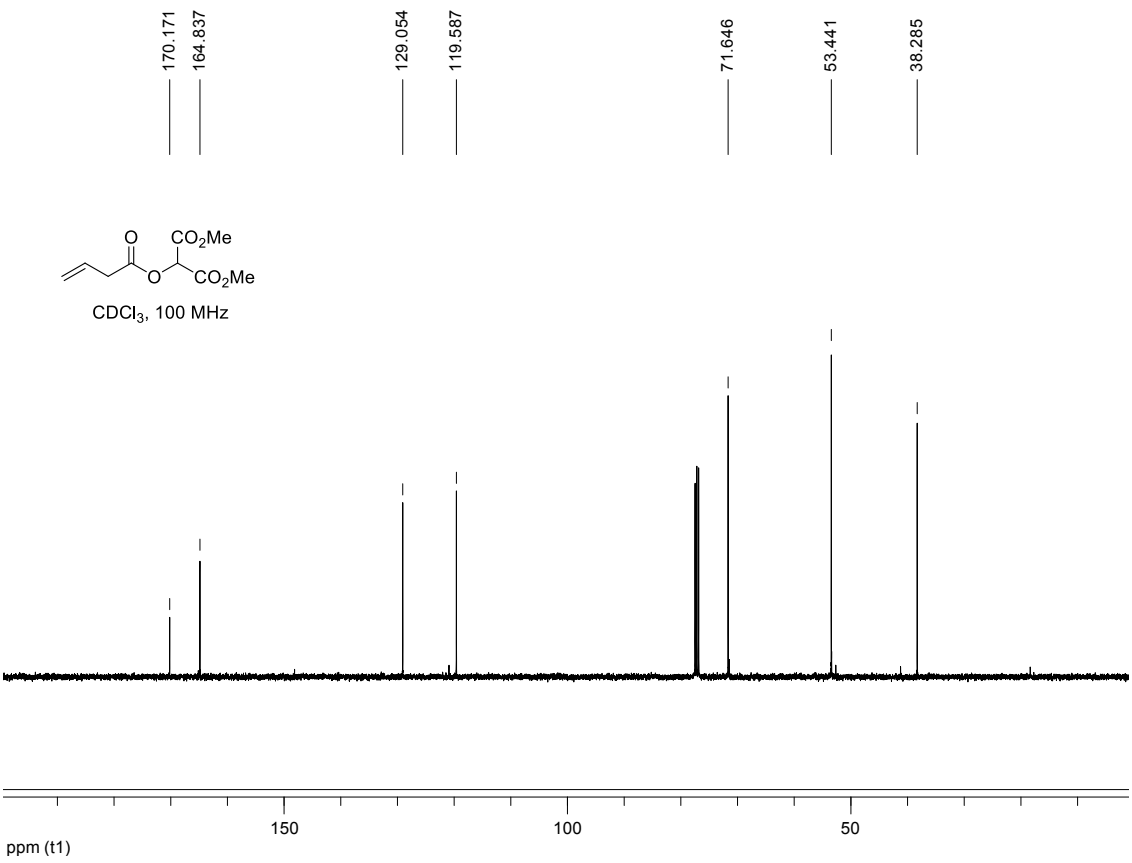
Spectra for compound **12h** (mixture of diastereoisomers after purification d. r. = 5.5:1)



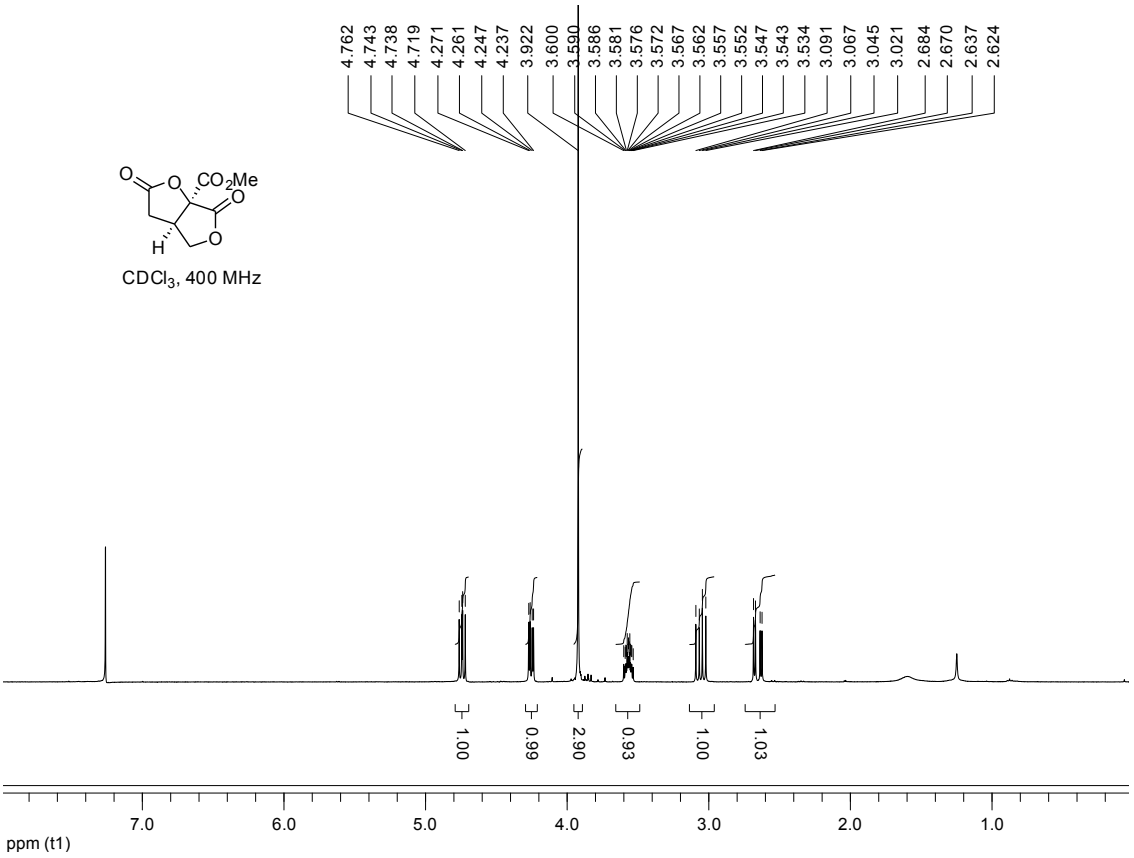


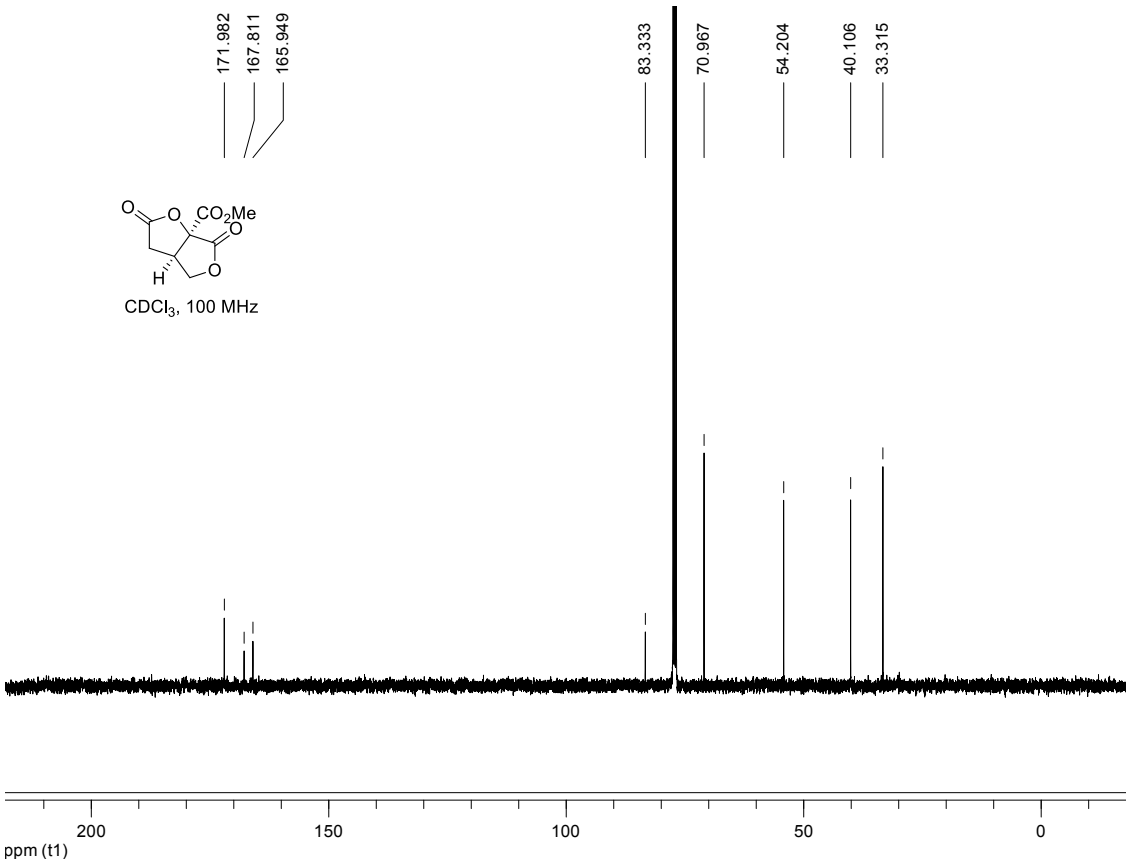
Spectra for compound **13a**



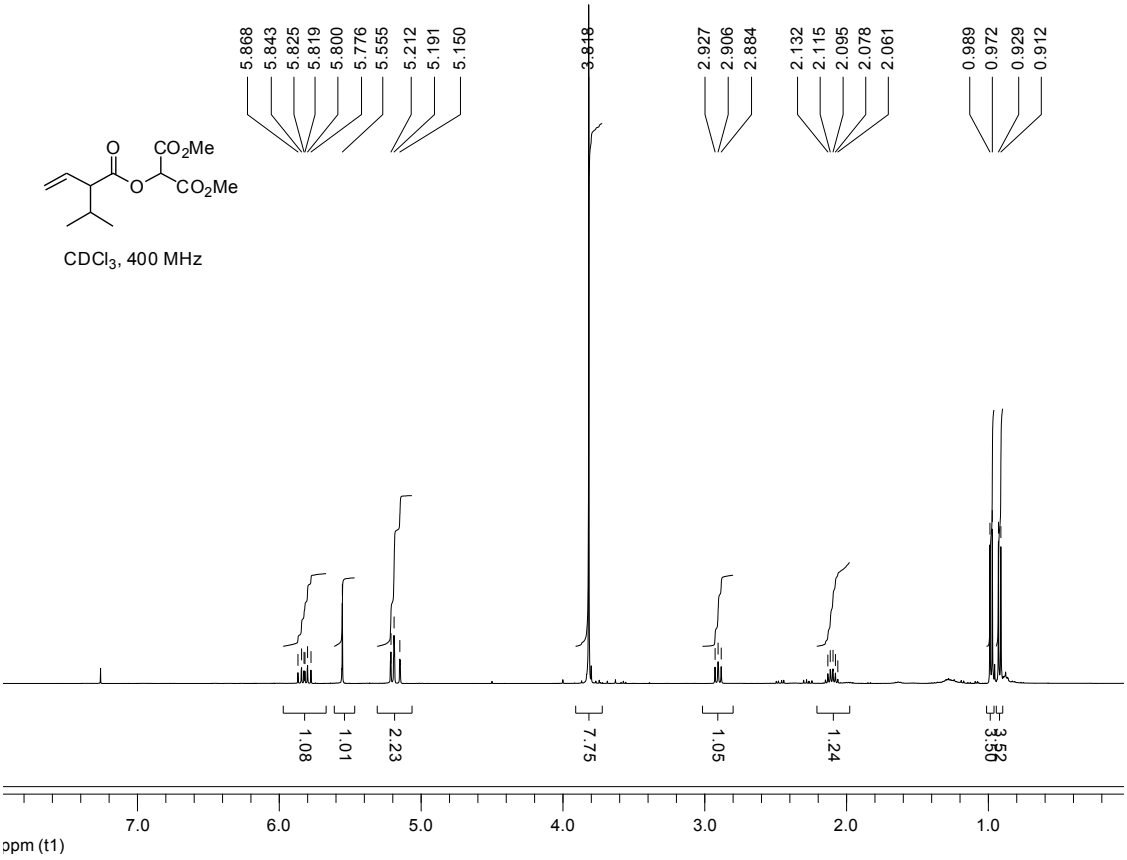


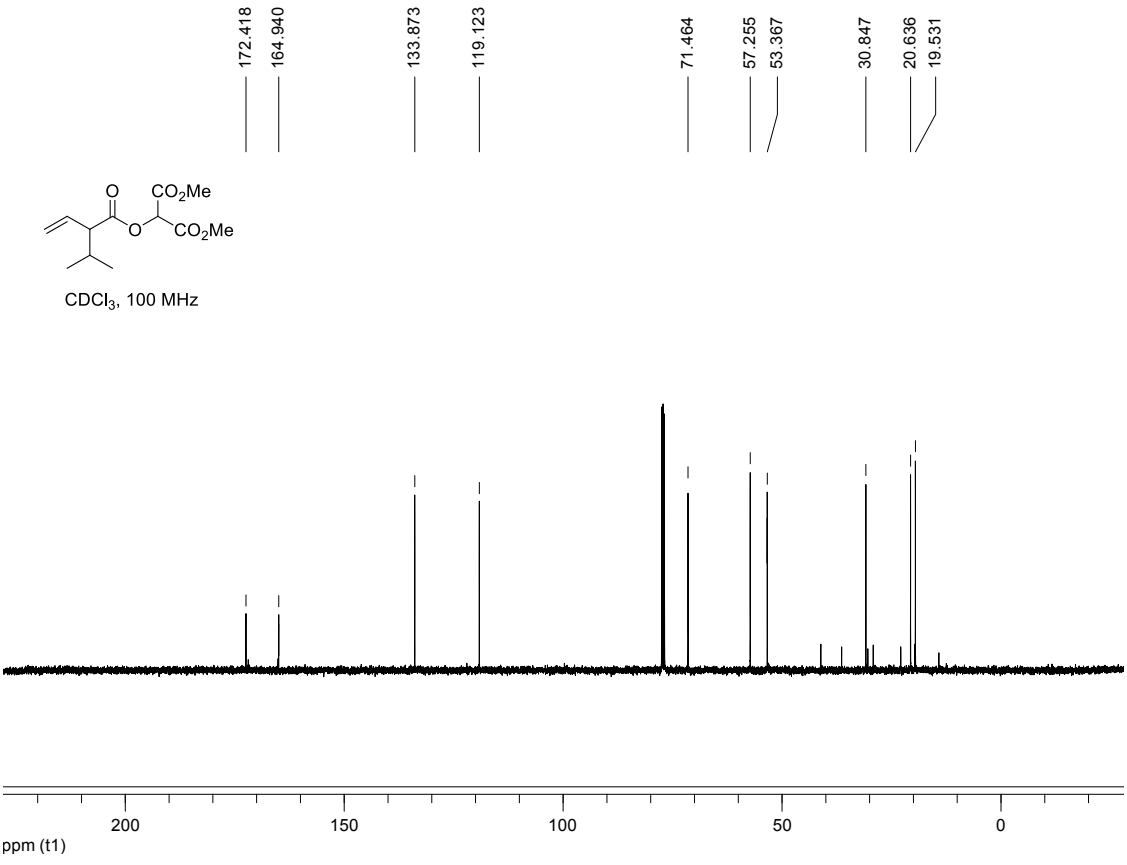
Spectra for compound **14a**



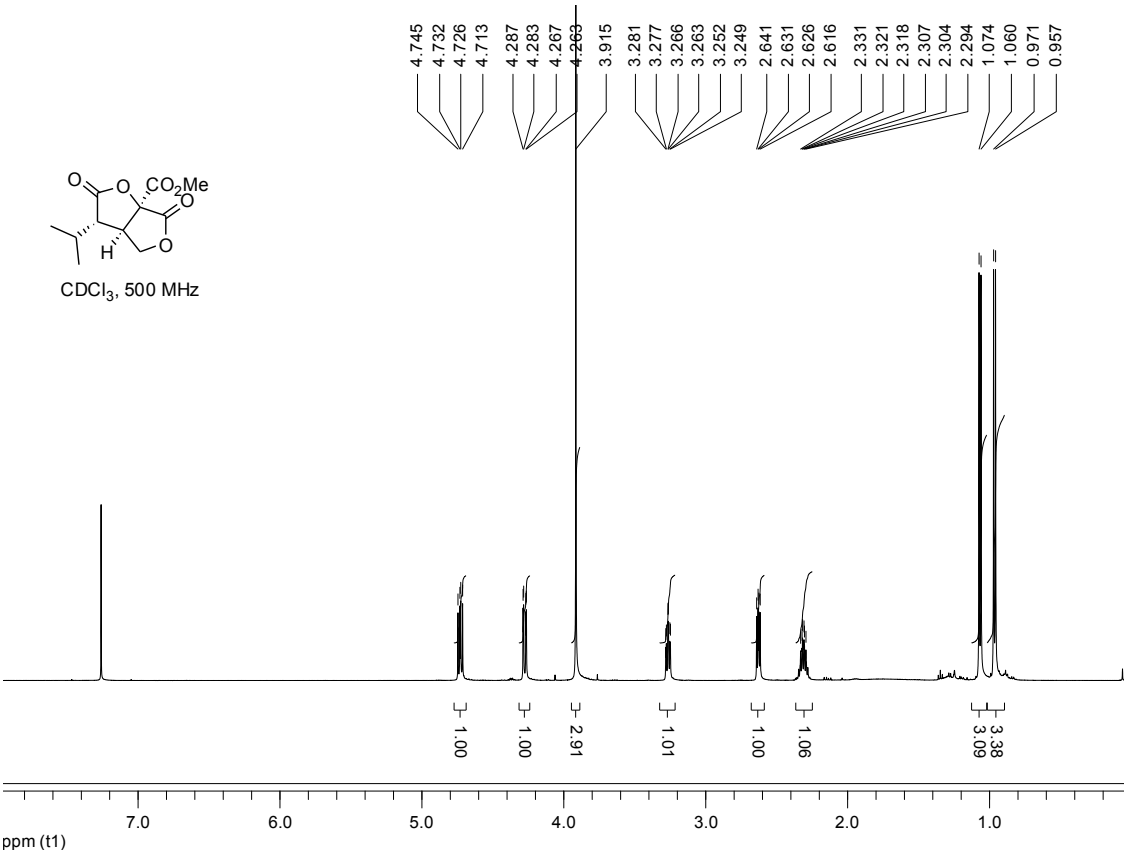


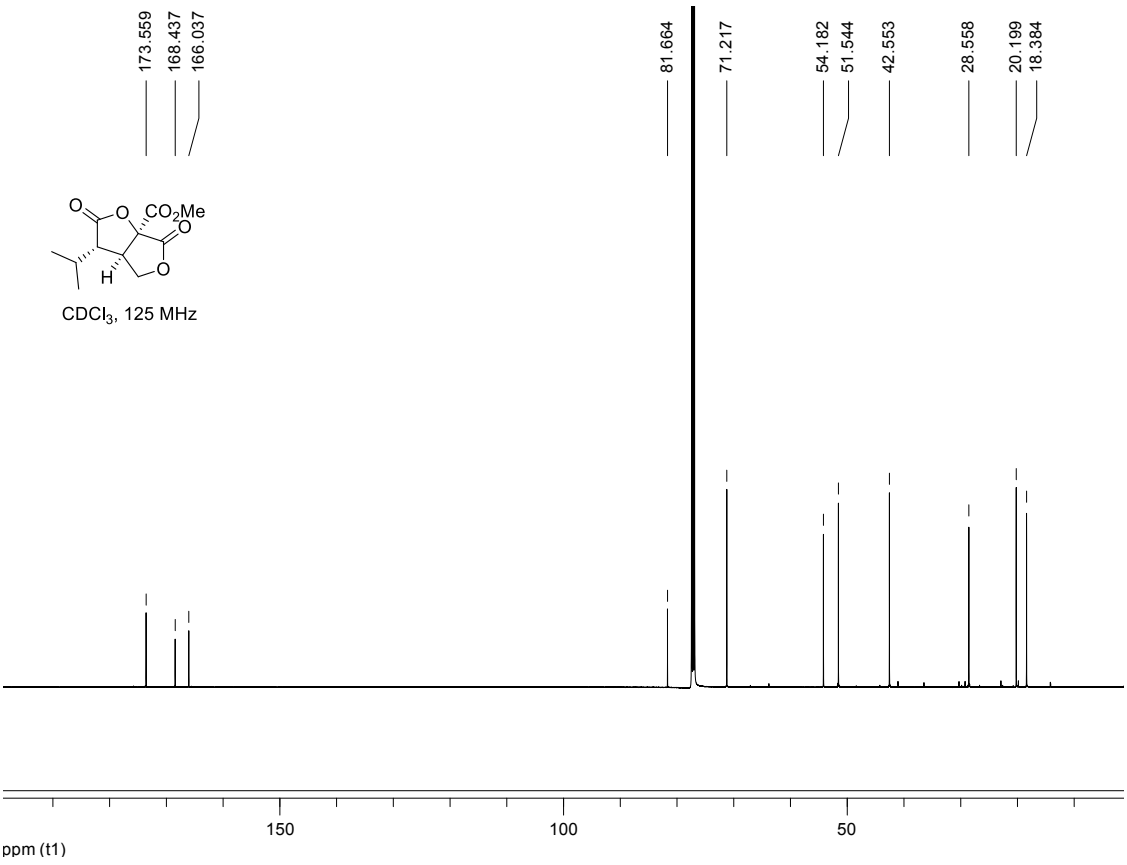
Spectra for compound **13b**



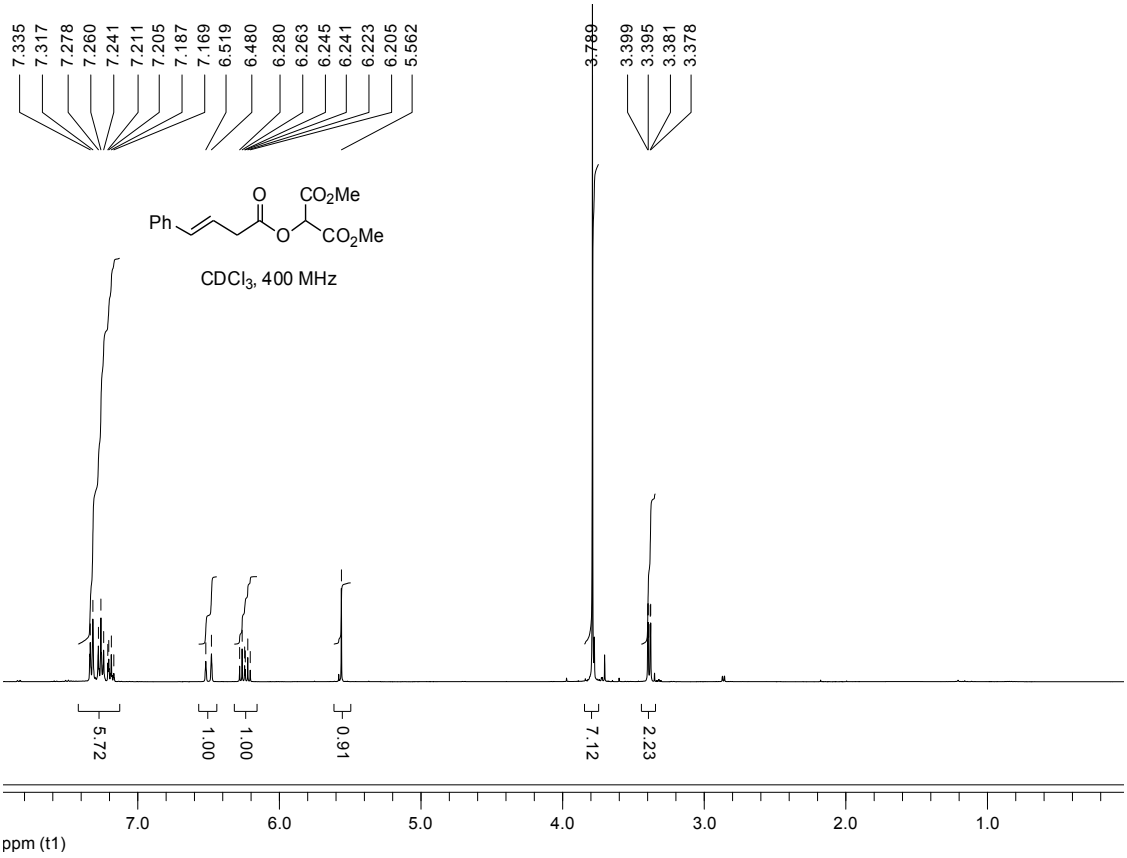


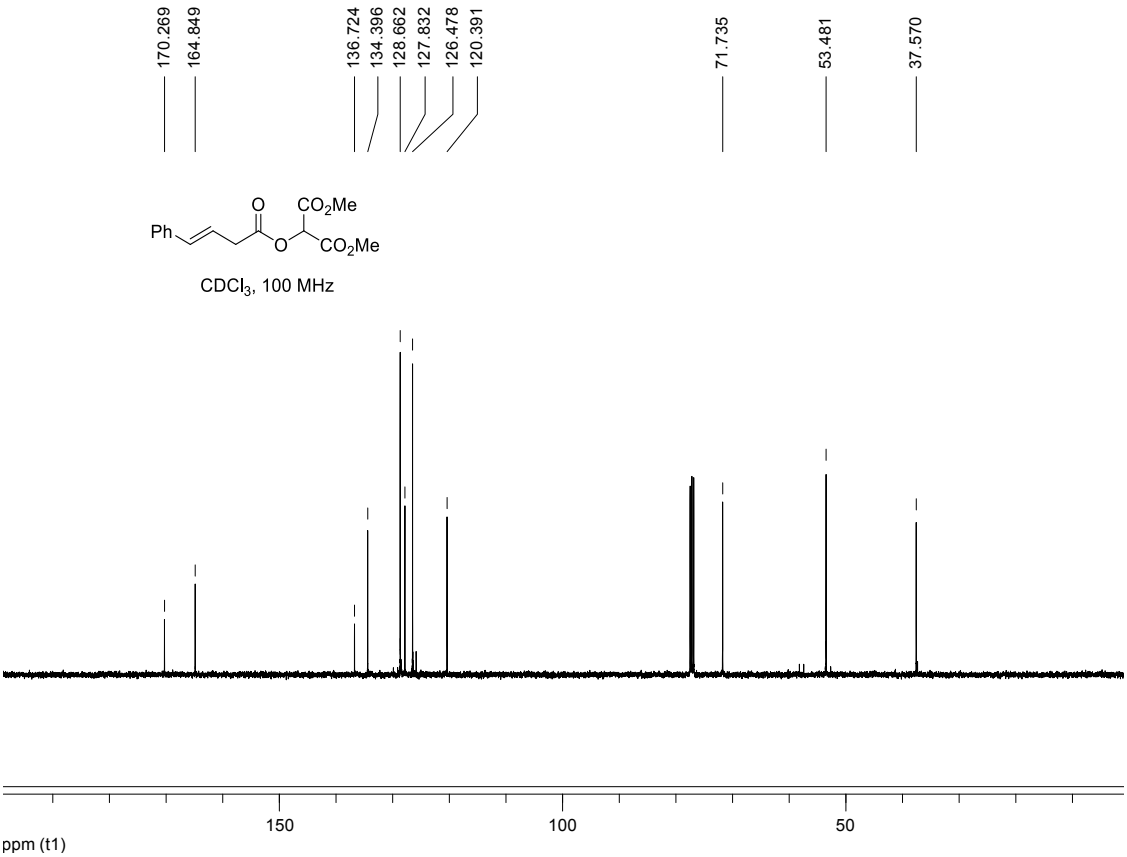
Spectra for compound **14b**



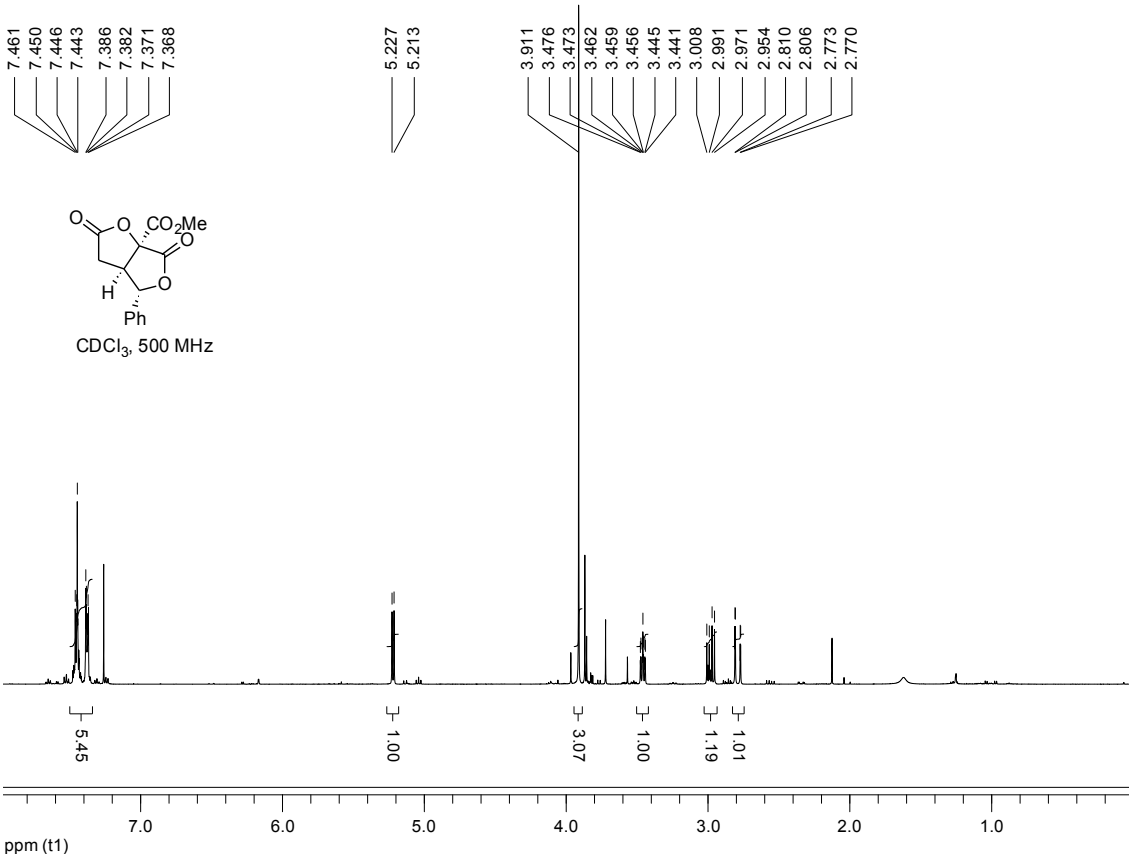


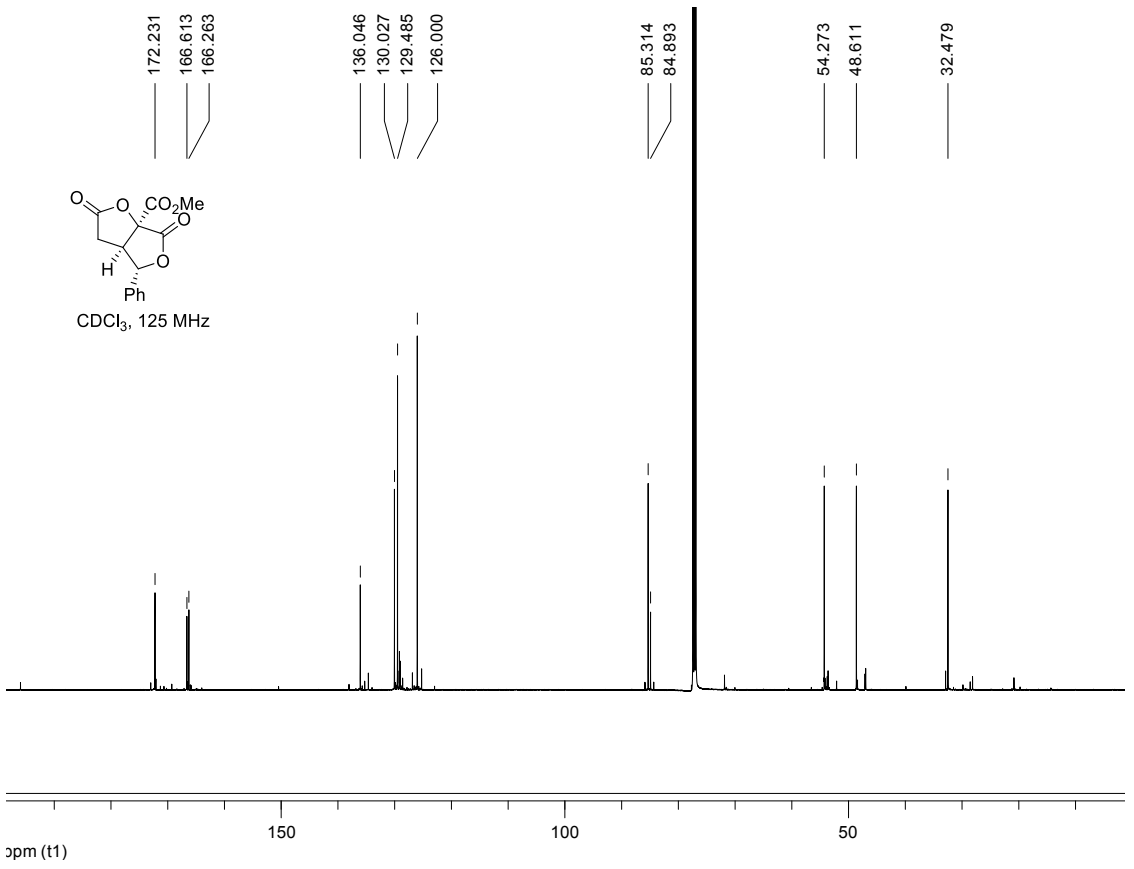
Spectra for compound **13c**



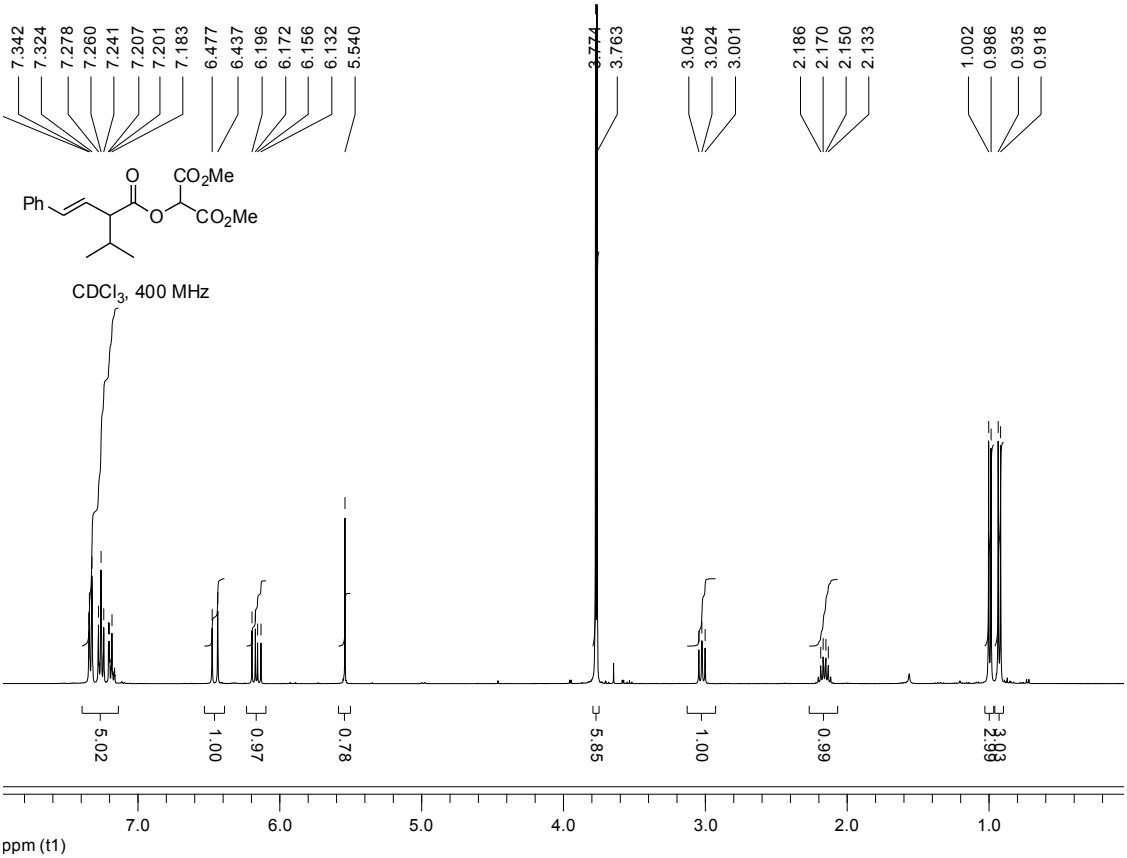


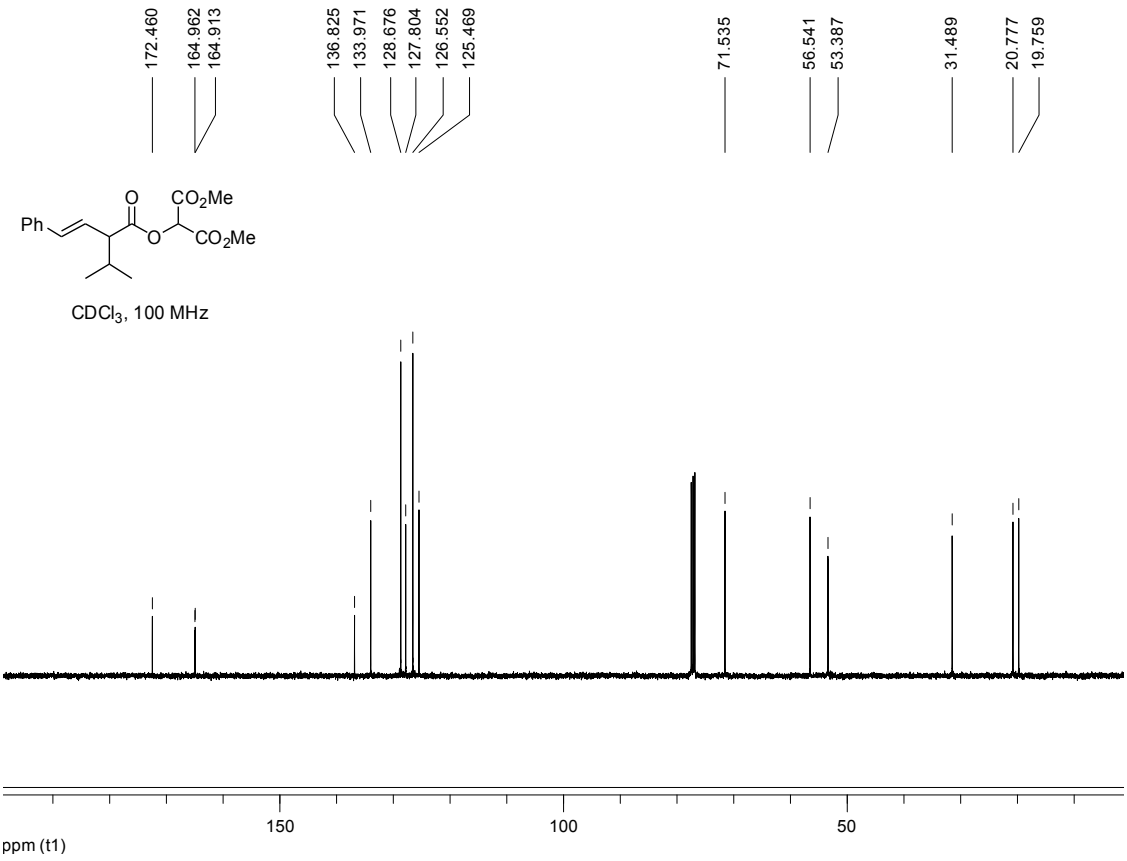
Spectra for compound **14c**



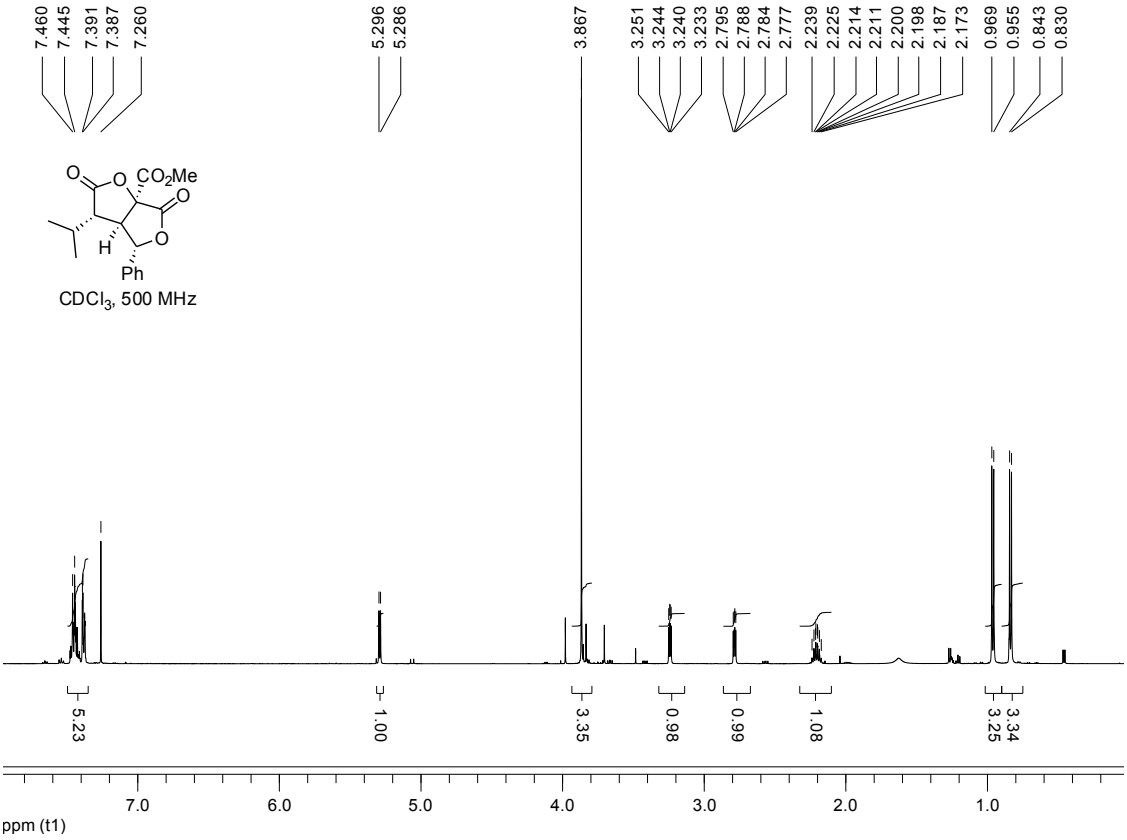


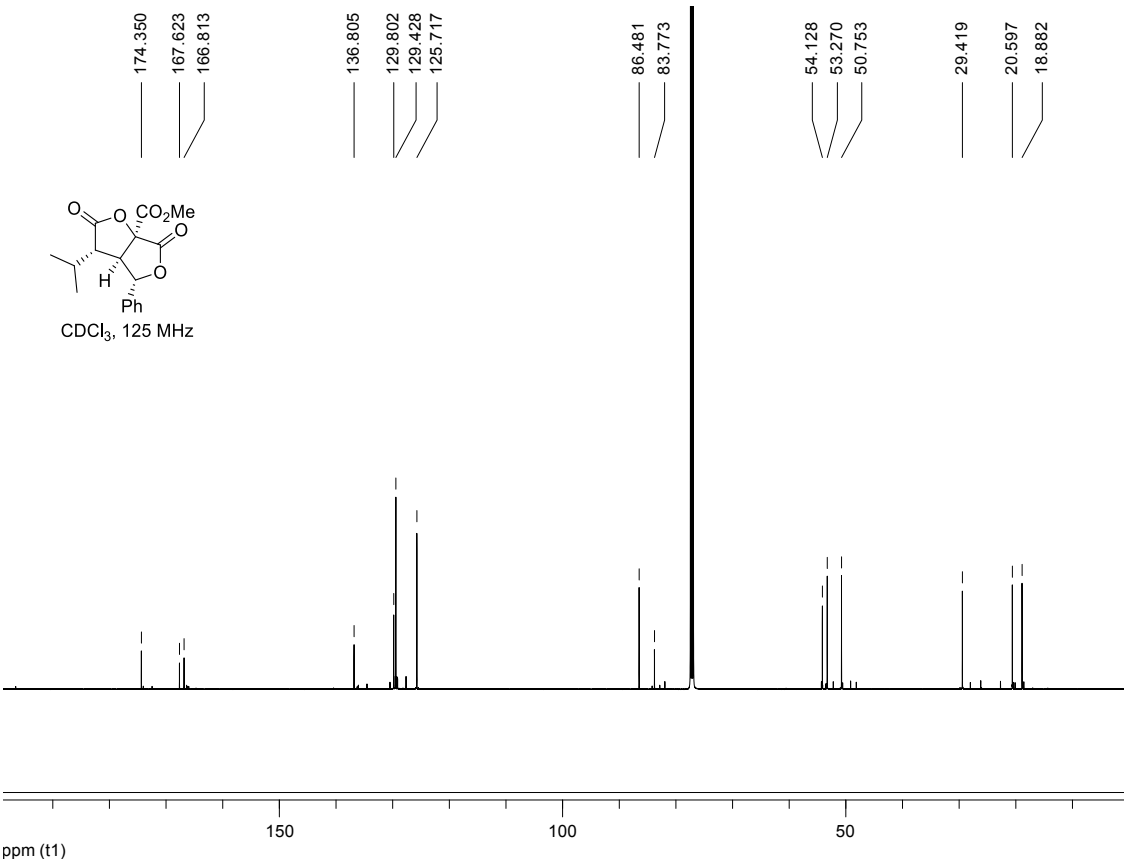
Spectra for compound **13d**



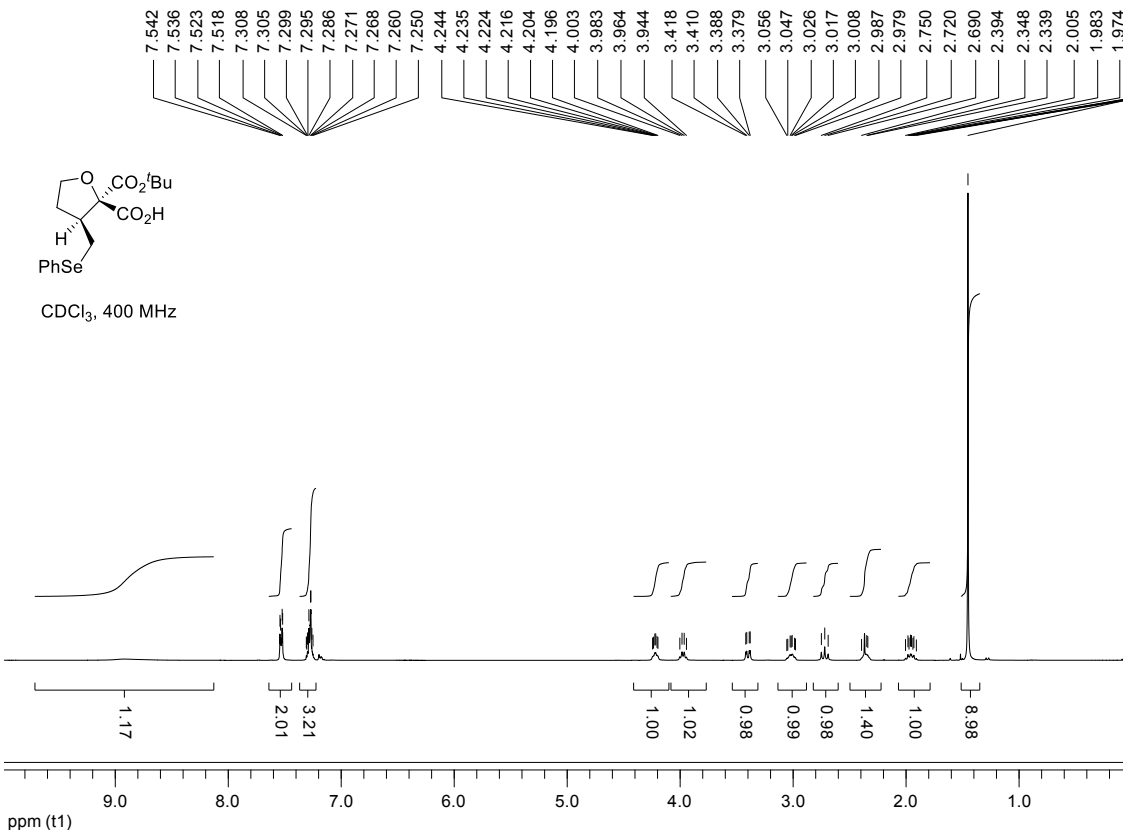


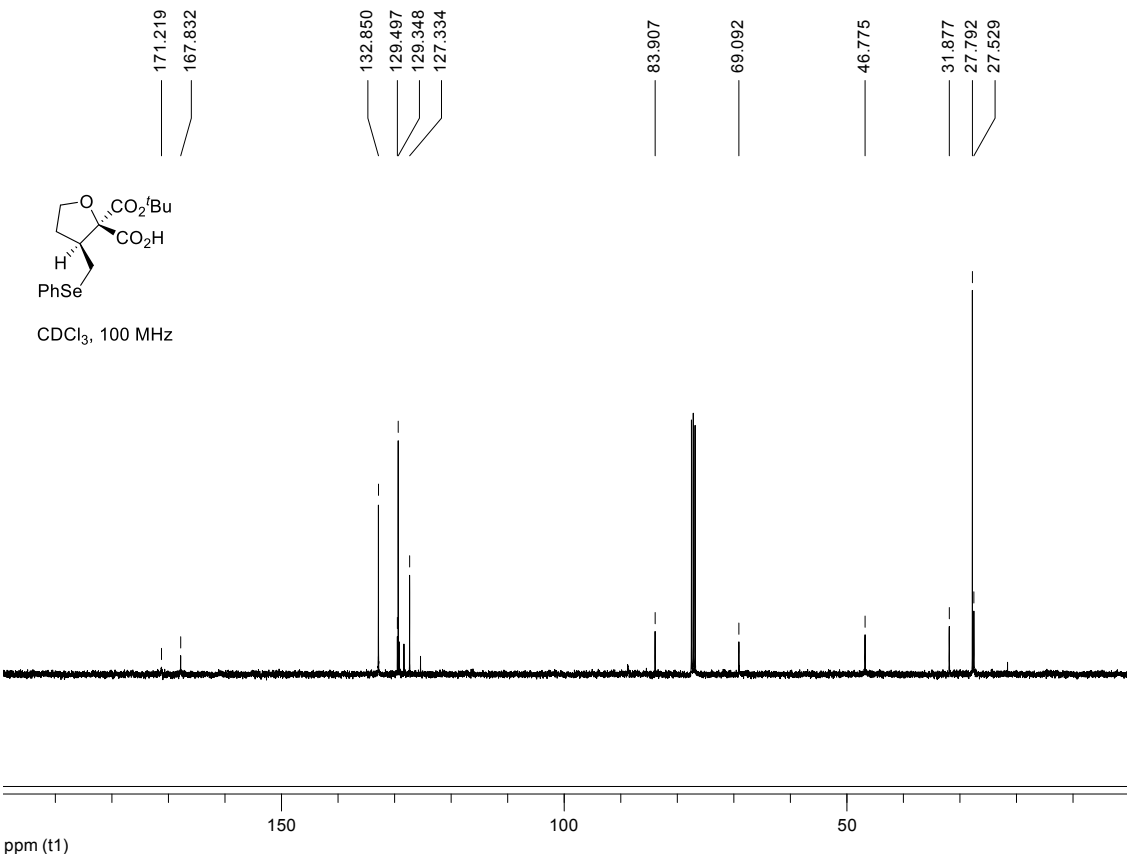
Spectra for compound **14d** (mixture of diastereoisomers after purification d. r. = 15.7:1)



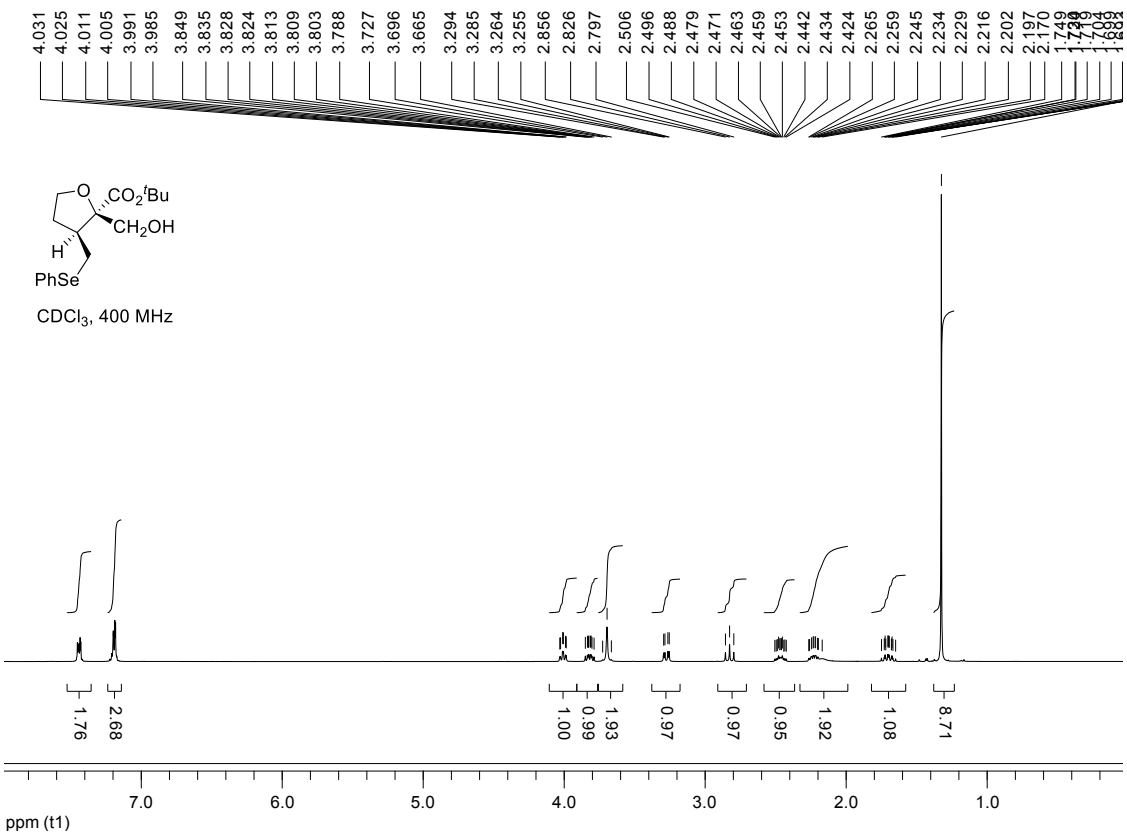


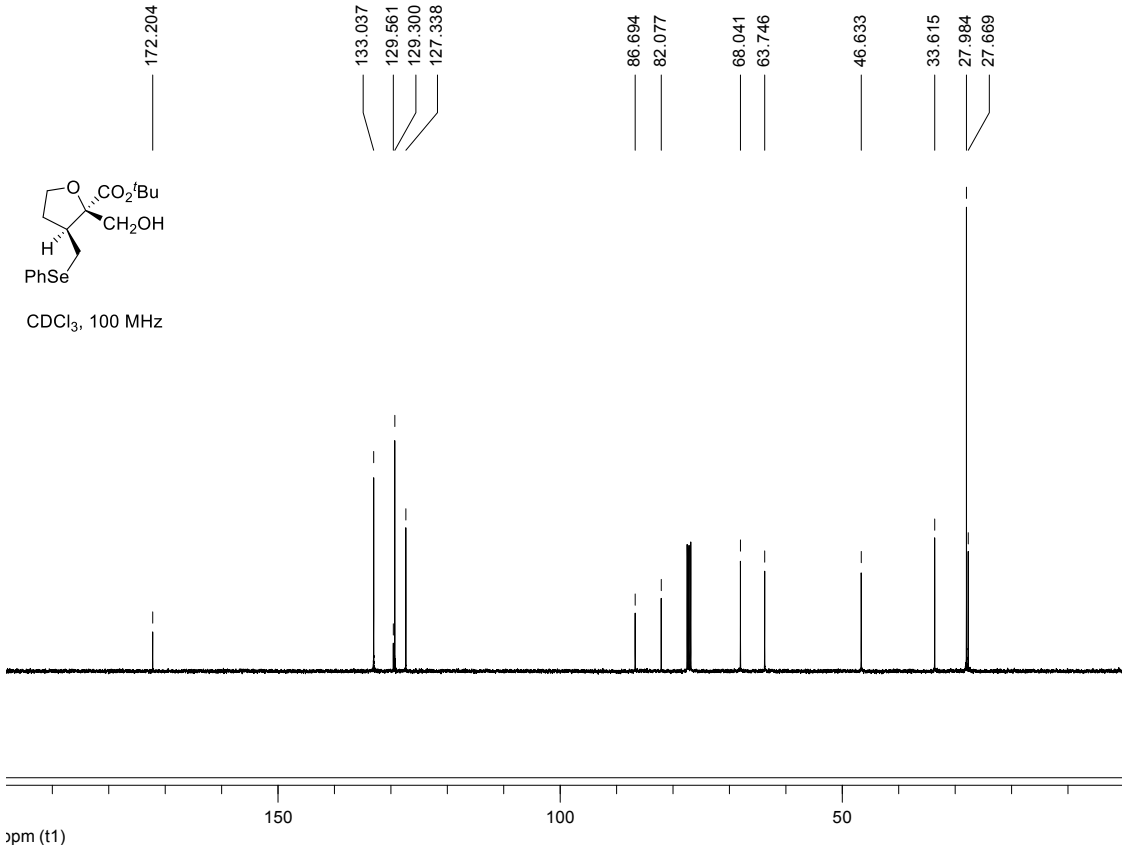
Spectra for compound **15**





Spectra for compound **16**





Spectra for compound **17**