Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Enantioselective Vinylogous-Mukaiyama-Dearomatisation by Anion-Binding Catalysis

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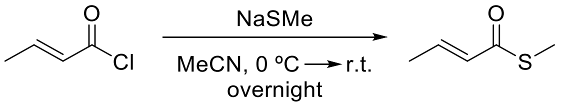
1. General Information and Materials

^{1}H- and ^{13}C-NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 (reference signal:[1] ^{1}H = 7.26 ppm, ^{13}C = 77.16 ppm for $CDCl_3$; ^{1}H = 2.50 ppm, ^{13}C = 39.52 ppm for DMSO-d_6) on a Bruker Advance 300 ,400, 500 or 600 MHz. Chemical shifts (δ) are given in ppm and spin-spin coupling constants (J) are given in Hz. X-Ray diffraction data sets for compound **4j** were collected with a Bruker D8 Venture PHOTON III diffractometer. Programs used: data collection: APEX3 V2016.1-0[2] (Bruker AXS Inc., 2016); cell refinement: SAINT V8.37A (Bruker AXS Inc., 2015); data reduction: SAINT V8.37A (Bruker AXS Inc., 2015); absorption correction, SADABS V2014/7 (Bruker AXS Inc., 2014); structure solution SHELXT-2015[3] (Sheldrick, G. M. *Acta Cryst.,* **2015**, A71, 3-8); structure refinement SHELXL-2015[4] (Sheldrick, G. M. *Acta Cryst.,* **2015**, C71, 3-8) and graphics, XP[5] (Version 5.1, Bruker AXS Inc., Madison, Wisconsin, USA, 1998). R-values are given for observed reflections, and *w*R^2 values are given for all reflections. Analytical thin layer chromatography was performed using silica gel 60 F254 and a solution of $KMnO_4$ or phosphomolybdic acid served as staining agent. Column chromatography was performed on silica gel 60 (0.040-0.063 mm). Preparative TLC plates were performed using silica gel 60PF254 containing gypsum. Exact masses (HRMS) were performed using electrospray ionization techniques (ESI+) and recorded on an Agilent Q-TOF 6540 UHD or a Bruker Daltonics MicroTof spectrometer. The enantiomeric ratios were determined by supercritical fluid chromatography (SFC) analysis on an Agilent SFC-LC 1260 series using a chiral chiralpack Daicel IG, IC, IA, OD-H or OJ-H column. TetrakisTriazoles **1a–d** were synthetised according to procedures already described by our research group.[6] The quinazoline derivatives **2h**–**2l**,[7] **2n**–**2q**[8] and **2r**[9] were synthetised following described procedures reported in the literature. The silyl vinylketene acetals **3a**, **3b**, **3e**, **3f** and **3g** were synthesised following described procedures reported in the literature,[10] while the synthesis of **3c** and **3d** is described in the following document. The employed solvents such as methyl-*tert*-butylether (MTBE), diethyl ether (Et_2O), and toluene were distilled in a solvent purification system (SPS) and dried over 3 or 4 Å molecular sieve (MS).

2. Synthesis and Analytical Data of S-Methyl (*E*)-But-2-enethioate

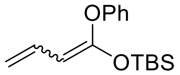


In a round-bottom flask, crotonyl chloride (3.19 mL, 30 mmol, 1.5 equiv.) was dissolved in dry MeCN. The solution was cooled to 0 °C in an ice-bath and sodium methylthiolate (1.557 g, 20 mmol, 1 equiv.) was added portion-wise. The reaction was then warmed up to room temperature and stirred overnight. The acetonitrile was removed under reduce pressure and the crude was dissolved in diethyl ether. The organic phase was washed with water, $NaHCO_3$ (sat) and brine. The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was purified by vacuum distillation using a Kugelrohr apparatus. Observed boiling point: 42-45 °C (2.3 mbar). The product was obtained as a colourless oil (yield 61%). **^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.91 (dq, *J* = 15.5, 6.9 Hz, 1H), 6.16 (dd, *J* = 15.5, 1.7 Hz, 1H), 2.34 (s, 3H), 1.88 (dd, *J* = 6.9, 1.7 Hz, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 190.4, 140.6, 130.2, 18.0, 11.4. **ESI-HRMS:** *m/z* calculated for $[C_5H_9OS]^+$: 117.0374; found 117.0372.

3. General Procedure for the Synthesis and Analytical Data of 3c and 3d

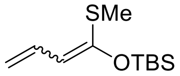
In a flame-dry Schlenk flask, diisopropylamine (1.1 equiv., 11 mmol, 1.5 mL) was dissolved in dry THF (2 mL/ mmol of ester, 20 mL) under Ar atmosphere. The reaction was cooled to -78 °C. Then, *n*BuLi 2.5 M (1.1 equiv., 11 mmol, 4.4 mL) was added dropwise at -78 °C. The reaction was stirred for 30 min. Subsequently, DMPU (1.2 equiv., 12 mmol, 1.45 mL) was added and some turbidity was appreciated. The reaction was stirred for another 30 min at -78 °C. After this time, the corresponding ester (or thioester) (1 equiv., 10 mmol) was added dropwise, and the reaction was stirred for 30 min observing loss of the turbidity. Then, TBSCl (1.1 equiv., 11 mmol, 1.658 g) was added in one portion. The reaction was then stirred for 2-3 h while reaching room temperature. After this time, pentane was added to the reaction and the organic phase was washed three times with cold water to remove the insoluble salts. The organic phase was dried over $MgSO_4$ and filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and the residue is purified by vacuum distillation using a Kugelrohr apparatus.

***tert*-Butyldimethyl((1-phenoxybuta-1,3-dien-1-yl)oxy)silane (3c)**



Following the general procedure, the phenyl (*E*)-but-2-enoate (10 mmol, 1.62 g) gave the corresponding dienolate as a colourless oil. Observed boiling point: 106 °C (1.7 mbar). Yield 34%. *E/Z* ratio: 4:1. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.34 (app. t, *J* = 8.0 Hz, 2H major), 7.31 – 7.27 (app t, *J* = 7.9 Hz, 2H minor), 7.23 (app t, *J* = 7.9 Hz, 1H minor), 7.14 (app. d, *J* = 8.0 Hz, 1H major), 7.05 (app d, *J* = 7.5, 1.0 Hz, 2H major), 7.00 (app. d, *J* = 7.7 Hz, 2H minor), 6.56 – 6.41 (m, 1H major + 1H minor), 5.03 (d, *J* = 10.6 Hz, 1H minor), 4.98 (dd, *J* = 17.1, 2.1 Hz, 1H minor), 4.81 (dd, *J* = 17.2, 1.9 Hz, 1H major), 4.74 (dd, *J* = 10.5, 2.2 Hz, 1H minor), 4.69 (dd, *J* = 10.5, 1.7 Hz, 1H major), 4.54 (d, *J* = 10.4 Hz, 1H major), 0.98 (s, 9H major), 0.81 (s, 9H minor), 0.23 (s, 6H major), 0.12 (s, 6H minor); **^{13}C NMR** (125 MHz, $CDCl_3$) δ 156.2, 154.5, 131.7, 131.5, 129.7, 129.5, 129.5, 124.3, 122.9, 121.8, 119.8, 117.3, 110.8, 109.5, 95.0, 88.7, 25.8, 25.4, 18.3, -4.1, -4.8; **ESI-HRMS:** *m/z* calculated for $[C_{16}H_{25}O_2Si]^+$: 231.1624; found 231.1623.

***tert*-Butyldimethyl((1-(methylthio)buta-1,3-dien-1-yl)oxy)silane (3d)**



Following the general procedure, the S-methyl (*E*)-but-2-enethioate (10 mmol, 1.16 g) gave the corresponding dienolate as a yellowish oil. Observed boiling point: 88-93 °C (2.4 mbar). Yield 50%. *E/Z* ratio: 3:1.**^{1}H NMR** (300 MHz, $CDCl_3$) δ 6.71 – 6.50 (m, 1H major + 1H minor), 5.63 minor (d, *J* = 10.7 Hz, 1H minor), 5.43 (d, *J* = 10.6, 1H major), 5.01 (ddd, *J* = 16.9, 2.0, 0.8 Hz, 1H minor), 4.99 (ddd, *J* = 17.2, 2.0, 0.7 Hz, 1H major), 4.87 (ddd, *J* = 10.4, 2.0, 0.8 Hz, 1H minor), 4.81 (ddd, *J* = 10.3, 2.0, 0.8 Hz, 1H major), 2.27 (s, 3H major), 2.24 (s, 3H minor), 0.99 (s, 9H major), 0.97 (s, 9H minor), 0.24 (s, 6H major + 6H minor); **^{13}C NMR** (75 MHz, $CDCl_3$) δ 150.0, 150.0, 133.4, 131.0, 114.0, 112.8, 111.7, 111.1, 77.6, 77.2, 76.7, 25.9, 25.8, 18.4, 15.8, 14.1, -4.1, -4.5; **ESI-HRMS:** *m/z* calculated for $[C_{11}H_{23}OSSi]^+$: 231.1239; found 231.1240.

4. Reaction conditions screening for the different *N*- and *O*-heteroarenes

Employed H-donor catalysts:

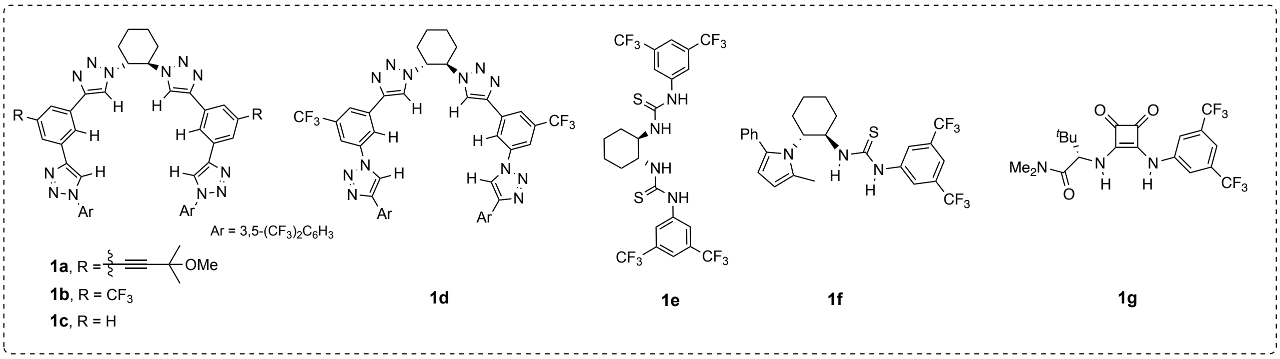
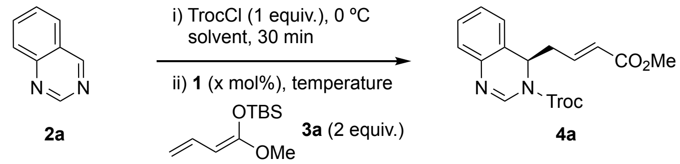


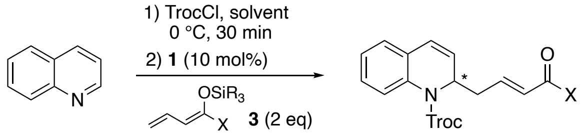
Table S1: Screening of the vinylogous addition reaction with quinazoline



Entry	Catalyst (mol%)	Solvent	Conc.	T (°C)	Yield (%)[a]	e.r.[b]
1	**1a** (10)	MTBE	0.1 M	-78	69	84:16
2	**1b** (10)	MTBE	0.1 M	-78	69	82:18
3	**1c** (10)	MTBE	0.1 M	-78	46	77:23
4	**1d** (10)	MTBE	0.1 M	-78	58	75:25
5	**1e** (10)	MTBE	0.1 M	-78	48	52:48
6	**1f** (10)	MTBE	0.1 M	-78	50	51:49
7	**1a** (15)	MTBE	0.1 M	-78	75	82:18
8	**1a** (5)	MTBE	0.1 M	-78	70	86:14
9	**1a** (3)	MTBE	0.1 M	-78	73	90:10
10	**1a** (1)	MTBE	0.1 M	-78	63	88:12
11	**1a** (3)	Et_2O	0.1 M	-78	54	87:13
12	**1a** (3)	C_6F_6	0.1 M	6	35	54:46
13	**1a** (3)	Et_2O:C_6F_6 (3:1)	0.1 M	-30	66	69:31
14	**1d** (3)	Et_2O:C_6F_6 (3:1)	0.1 M	-30	70	70:30
15	**1a** (3)	Toluene	0.1 M	-78	57	95.5:4.5
16	**1a** (1)	Toluene	0.1 M	-78	71	93:7
17	**1a** (3)	Toluene	0.1 M	-78	35[c]	97.5:3.5
18	**1a** (3)	Toluene	0.2 M	-78	81[c]	96:4
19	**1a** (3)	Toluene	0.2 M	-78	83[d]	96:4

Conditions: i) Quinazoline (0.1 mmol, 1 equiv.) and TrocCl (1 equiv.) in the appropriate solvent at 0 °C, 30 min; ii) at the corresponding temperature, catalyst **1** (10 mol%) and **3a** (2 equiv.) were added and the reaction stirred for 18 h. [a] Isolated yield after column chromatography. [b] E.r. determined by chiral SFC. [c] 0.5 mmol scale reaction. [d] 1.0 mmol scale reaction.

Table S2: Screening of the reaction with quinoline



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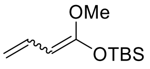
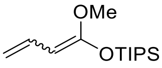
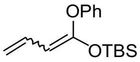
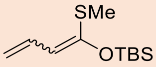
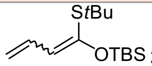
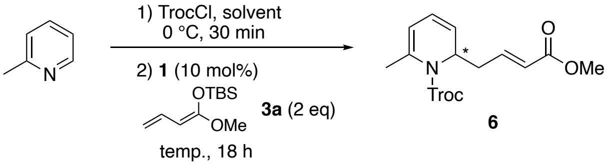
Entry	Catalyst	Dienolate **3**	Solvent	T (°C)	Yield (%)[a]	e.r.[b]
1	**1a**	 **3a**	Et_2O	-78	56	76:24
2	**1b**	**3a**	Et_2O	-78	49	77:23
3	**1c**	**3a**	Et_2O	-78	47	80:20
4	**1d**	**3a**	Et_2O	-78	53	80:20
5	**1e**	**3a**	Et_2O	-78	16	45:55
6	**1f**	**3a**	Et_2O	-78	76	54:46
7	**1g**	**3a**	Et_2O	-78	11	46:54
8	**1d**	**3a**	toluene	-78	53	65:35
9	**1d**	**3a**	C_6F_6	6	n.d.	75:25
10	**1d**	**3a**	Et_2O:C_6F_6 (3:1)	-30	81	82:18
11	**1d**	**3a**	Et_2O:C_6F_6 (3:1)[c]	-30	86	76:24
12	**1d**[d]	**3a**	Et_2O:C_6F_6 (3:1)	-30	65	78:22
13	**1d**	**3a**	Et_2O:C_6F_6 (3:1) + 5 mol% H_2O	-30	58	82:18
14	**1d**	 **3a'**	Et_2O:C_6F_6 (3:1)	-30	86	75:25
15	**1d**	 **3c**	Et_2O:C_6F_6 (3:1)	-30	n.d.	78:22
16	**1d**	 **3d**	Et_2O:C_6F_6 (3:1)	-30	80	84:16
17	**1d**	 **3d'**	Et_2O:C_6F_6 (3:1)	-30	32	50:50

Conditions: i) Quinoline (0.1 mmol, 1 equiv.) and TrocCl (1 equiv.) in the appropriate solvent (0.1 M) at 0 °C, 30 min; ii) at the corresponding temperature, catalyst **1** (10 mol%) and **3** (2 equiv.) were added and the reaction stirred for 18 h. [a] Isolated yield after column chromatography. [b] E.r. determined by chiral SFC. [c] 0.3 M concentration. [d] 5 mol% of **1d** was used.

Table S3: Screening of the reaction with picoline



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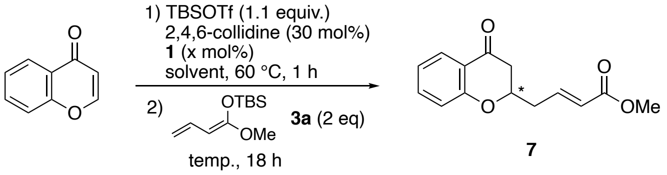
Entry	Catalyst (mol%)	Solvent	T (°C)	Yield (%)[a]	e.r.[b]
1	OMe-TetraTri	Et_2O	–78	39	55:45
2	CF_3-TetraTri isomer	Et_2O	–78	47	56:44
3	CF_3-TetraTri isomer	toluene	–78	30	56:44
4	CF_3-TetraTri isomer	Et_2O/C_6F_6 2:1	–30	41	68:32
5	CF_3-TetraTri isomer	C_6F_6	6	46	70:30
6	–	C_6F_6	6	–	–

Conditions: i) Picoline (0.1 mmol, 1 equiv.) and TrocCl (1 equiv.) in the appropriate solvent (0.1 M) at 0 °C, 30 min; ii) at the corresponding temperature, catalyst **1** (10 mol%) and **3a** (2 equiv.) were added and the reaction stirred for 18 h. [a] Isolated yield after column chromatography. [b] E.r. determined by chiral SFC.

Table S4: Screening of the reaction with 4-chromenone



Entry	Catalyst (mol%)	Solvent	T (°C)	Yield (%)[a]	e.r.[b]
1	–	Et_2O/C_6F_6 (2:1)[c]	–30	69	50:50
2	**1d** (10)	Et_2O/C_6F_6 (2:1)[c]	–30	65	68:32
3	**1d** (10)	C_6F_6	6	58	54:46
4	**1a** (10)	toluene	–78	70	79:21
5	**1a** (5)	toluene	–78	66	79:21
6	**1a** (2)	toluene	–78	46	78:22
7	**1a** (5)	toluene[d]	–78	n.d.	76:24
8	**1a** (5)	Et_2O	–78	61	65:35
9	**1c** (5)	toluene	–78	77	61:39

Conditions: i) Chromenone (0.1 mmol, 1 equiv.), TBSOTf (1.1 equiv.), collidine (0.3 equiv.) and catalyst **1** in the appropriate solvent (0.25 M) at 60 °C, 1 h; ii) at the corresponding temperature, **3a** (2 equiv.) was added and the reaction stirred for 18 h. [a] Isolated yield after column chromatography. [b] E.r. determined by chiral SFC. [c] 0.1 M solution. [d] 0.5 M solution.

5. General Procedures for the Anion-Binding Catalysed Vinylogous-Mukaiyama Dearomatisation Reaction

General procedure A: Reaction with quinazoline derivatives

In a flame-dried 5 mL Schlenk pressure tube, the quinazoline derivative **2** (0.10 mmol, 1.0 equiv.) was dissolved in anhydrous toluene (1 mL) and cooled to 0 °C. 2,2,2-Trichloroethoxycarbonyl chloride (14 µL, 0.10 mmol, 1.0 equiv.) was added and the reaction was stirred at 0 °C for 30 min. Subsequently, catalyst **1a** (3.36 mg, 3.00 µmol, 3 mol%) was added and the reaction was cooled to –78 °C. Dienolate **3** (0.20 mmol, 2.0 equiv.) was added and the reaction was stirred at –78 °C overnight. The solvent was then removed under reduced pressure and the desired product was obtained after purification by flash column chromatography on silica gel using *n*-pentane/EtOAc.

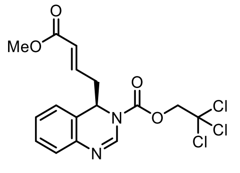
The racemic versions were prepared without catalyst, following the general procedure described above. Both possible regioisomers (C-2 and C-4 substitution) were formed in the racemic reactions. In some cases, the C-2 regioisomer could not be completely separated from the C-4 isomer and appear in the SFC chromatograms.

General procedure B: Reaction with quinoline derivatives

In a flame-dry Schlenk flask, the quinoline derivative (0.10 mmol, 1.0 equiv.) was dissolved in a 3:1 mixture of anhydrous Et_2O/C_6F_6 (1 mL) and cooled to 0 °C. TrocCl (14 µL, 0.10 mmol, 1.0 equiv.) was added and the reaction was stirred at 0 °C for 30 min. Subsequently, catalyst **1d** (10.6 mg, 0.10 mmol, 10 mol%) was added and the reaction cooled to –30 °C. Then, dienolate **3** (0.2 mmol, 2 equiv.) was added and the reaction was stirred at –30 °C overnight. The solvent was then removed under reduced pressure and the crude was purified by flash column chromatography on silica gel using *n*-pentane or cyclohexane/EtOAc.

6. Analytical Data for 4a–4s

(*R*,*E*)-2,2,2-Trichloroethyl 4-(4-methoxy-4-oxobut-2-en-1-yl)quinazoline-3(4*H*)-carboxylate (4a)



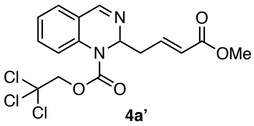
4a

According to the general procedure A, the reaction of quinazoline (**2a**) (13.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 10:1) the desired product **4a** (23.1 mg, 0.057 mmol, 57%) as a white solid. The enantiomeric ratio was determined as 95.5:4.5 e.r. by chiral SFC (Chiralcel IG, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 290 nm): *tr* (major): 14.1 min, *tr* (minor): 15.1 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-*d*$_6$): δ = 7.96 (s, 1H), 7.36–7.32 (m, 1H), 7.30–7.26 (m, 2H), 7.25 (d, ^3J = 7.1 Hz, 1H), 6.70 (dt, $^3J_{trans}$ = 15.3 Hz, ^3J = 7.6 Hz, 1H), 5.78 (dt, $^3J_{trans}$ = 15.5, ^4J = 1.3 Hz, 1H), 5.48 (t, ^3J = 5.7 Hz, 1H), 5.08 (d, ^3J = 12.2 Hz, 1H), 5.04 (d, ^3J = 12.2 Hz, 1H), 3.63 (s, 3H), 2.74–2.67 (m, 1H), 2.63–2.57 (m, 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-*d*$_6$): δ = 164.9, 150.4, 141.9, 140.0, 138.5, 128.3, 126.9, 125.9, 125.1, 124.9, 124.0, 94.5, 74.8, 54.2, 52.1, 50.6 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{16}H_{15}Cl_3N_2O_4]^+$: 405.0170; found 405.0169.

The same reaction with the TIPS-dienolate **3a’** provided the product **4a** in 96:4 e.r. (26.5 mg, 0.065 mmol, 65%).

The reaction with **3a’** was also successfully scaled up to 1.0 mmol, leading to **4a** in 96:4 e.r. (334.7 mg, 0.825 mmol, 83%).

2,2,2-Trichloroethyl (*E*)-2-(4-methoxy-4-oxobut-2-en-1-yl)quinazoline-1(2H)-carboxylate (*rac*-4a')



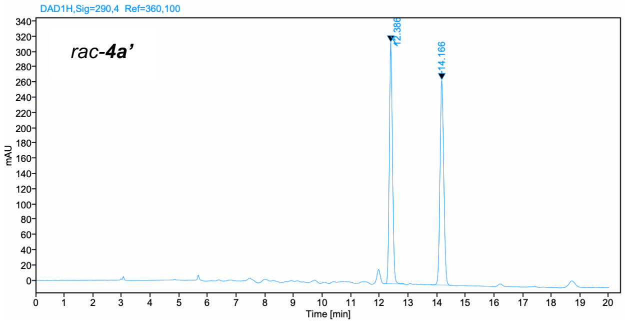
4a'

According to the general procedure A without catalyst for the preparation of the racemic sample, the reaction of quinazoline (**2a**) (26.0 mg, 0.200 mmol, 1.0 equiv.) with dienolate **3a** (94.2 µL, 0.400 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 10:1) the desired product **rac-4a** (25.3 mg, 0.062 mmol, 31%) and its regioisomer **rac-4a'** (14.5 mg, 0.036 mmol, 18%) as white solids. The separation of the enantiomers was conducted by chiral SFC (Chiralcel IG, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 290 nm): **4a'** *tr* (1): 12.4 min, *tr* (2): 14.2 min; **4a** *tr* (1): 17.7 min, *tr* (2): 18.2 min).

***rac*-4a': ^{1}H NMR** (500 MHz, 90 °C, DMSO-*d*$_6$): δ = 7.95 (s, 1H), 7.36 (td, *J* = 7.6, 1.4 Hz, 1H), 7.25 (t, *J* = 7.5 Hz, 2H), 7.10 (d, *J* = 7.5 Hz, 1H), 5.76 (d, *J* = 5.0 Hz, 1H), 5.59 (dt, *J* = 17.6, 9.9 Hz, 1H), 5.14 – 5.04 (m, 4H), 3.67 (s, 3H), 3.50 (dd, *J* = 9.7, 5.0 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-*d*$_6$): δ = 169.4, 150.2, 140.4, 139.0, 130.0, 128.8, 126.8, 126.4, 125.1, 121.8, 120.7, 94.5, 74.9, 55.1, 54.4, 51.5 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{16}H_{14}Cl_3N_2O_4Na]^+$: 426.9990; found 426.9988.

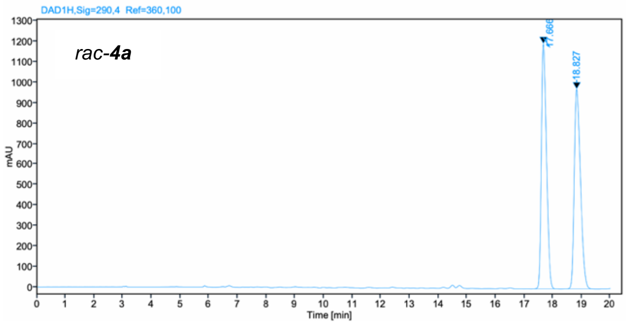
Chiral-phase SFC: Chiralcel IG, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm)

Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

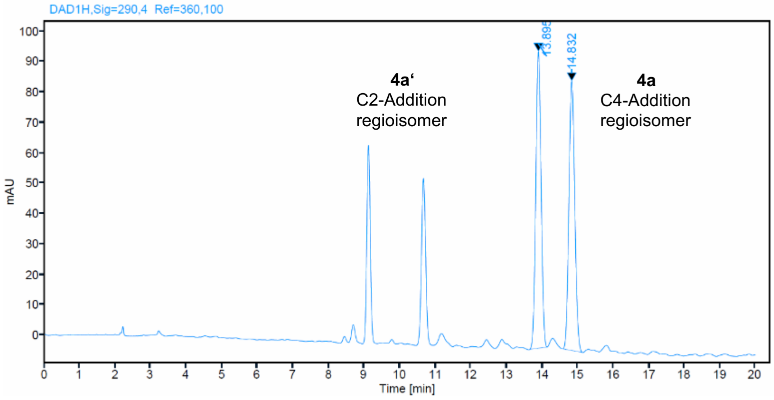
RT [min]	Type	Width [min]	Area	Height	Area%
12.386	MM m	0.1193	2423.4588	316.6658	49.7607
14.166	MM m	0.1422	2446.7681	268.8261	50.2393
		Sum	4870.2269		



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
17.666	MM m	0.1905	14844.9812	1198.8582	50.0353
18.827	MM m	0.2331	14824.0635	976.7200	49.9647
		Sum	29669.0447		

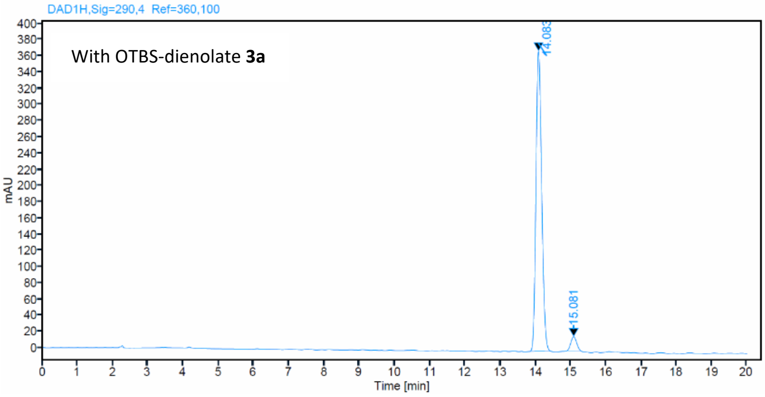
*Mixture of regioisomers rac-**4a** and rac-**4a'**:*



Signal: DAD1H,Sig=290,4 Ref=360,100

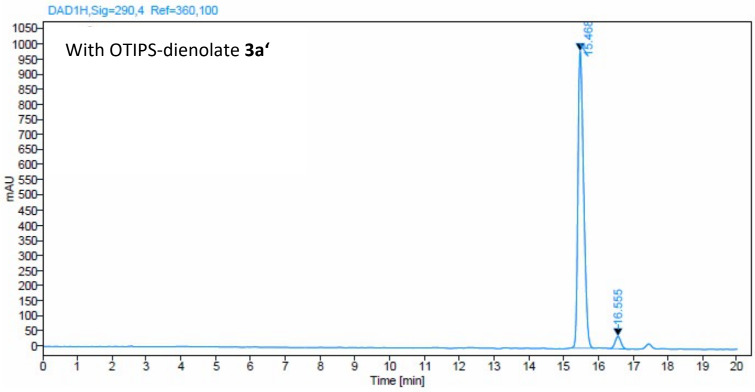
RT [min]	Type	Width [min]	Area	Height	Area%
13.895	MM m	0.1621	1005.7256	97.6678	49.8058
14.832	MM m	0.1774	1013.5683	88.6748	50.1942
		Sum	2019.2939		

Enantioselective:



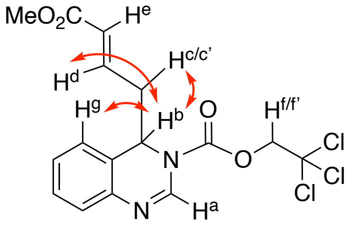
Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
14.083	MM m	0.1754	4172.7217	370.5436	95.5376
15.081	MM m	0.1791	194.8990	17.3482	4.4624
		Sum	4367.6207		

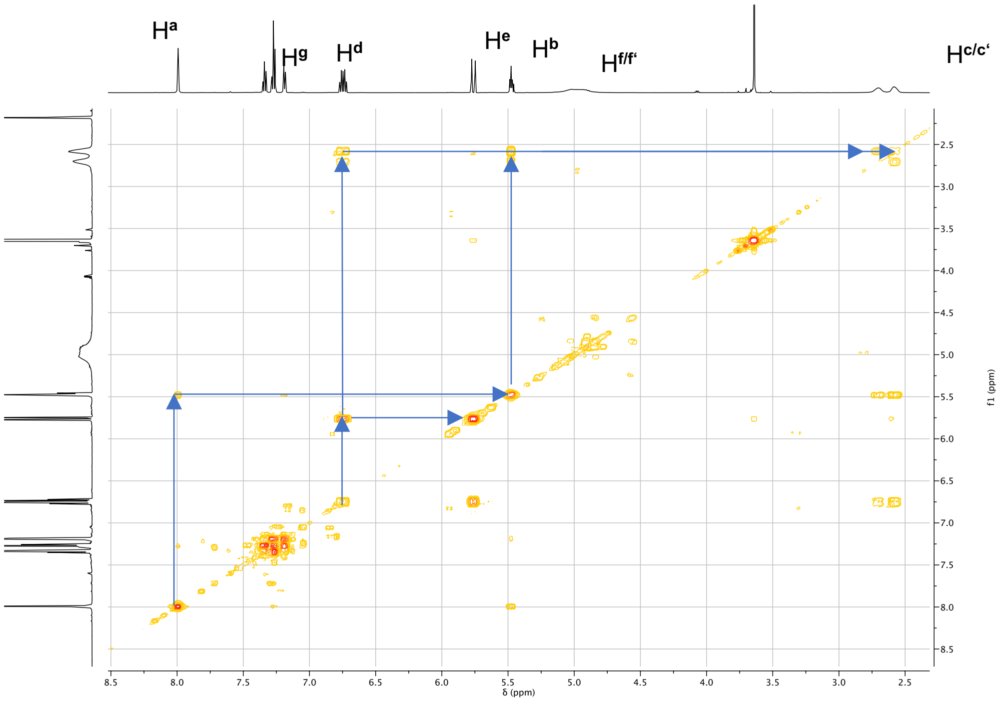


Signal: DAD1H,Sig=290,4 Ref=360,100

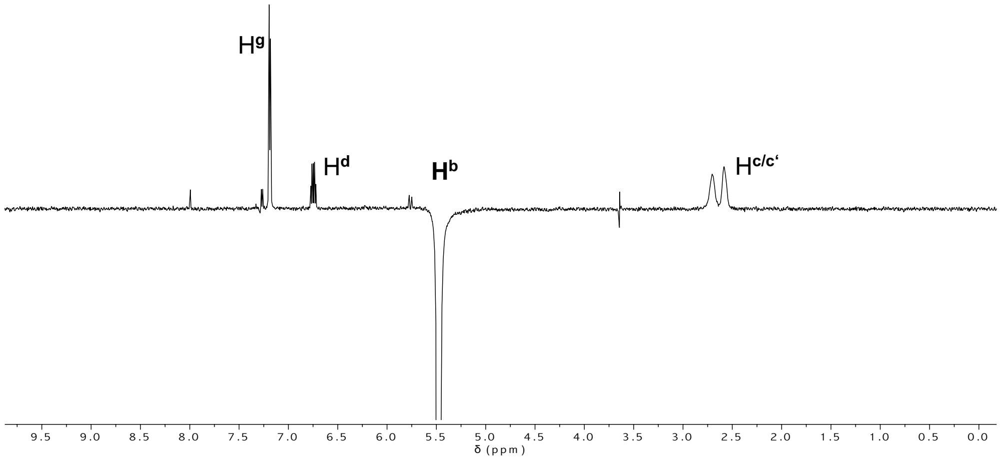
RT [min]	Type	Width [min]	Area	Height	Area%
15.468	MM m	0.1768	11170.2253	981.6381	95.9698
16.555	MM m	0.1800	469.0905	40.8489	4.0302



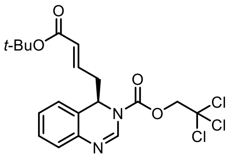
COSY-spectrum of 4a: measurement in MeCN-d₃ @ 25 °C (instead of DMSO-d6 @ 90 °C)



1D-NOESY-spectrum of 4a: saturation of peak @ 5.48 ppm (**H^b**)



(*R*,*E*)-2,2,2-Trichloroethyl 4-(4-(*tert*-butoxy)-4-oxobut-2-en-1-yl)quinazoline-3(4*H*)-carboxylate (4b)

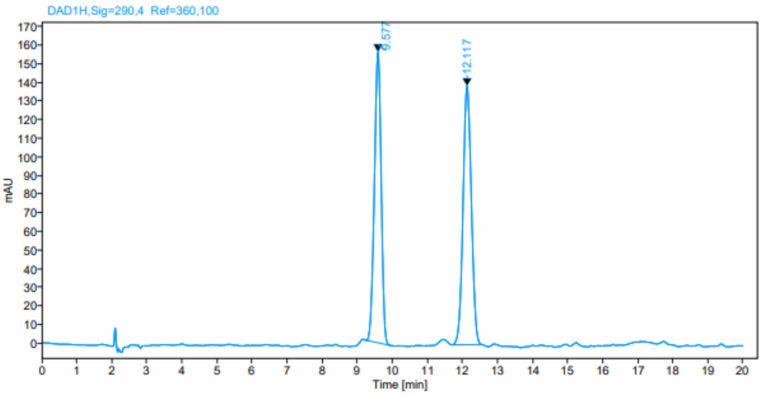


4b

According to the general procedure A, the reaction of quinazoline (**2a**) (13.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3b** (60.3 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 5:1) the desired product **4b** (36.6 mg, 0.082 mmol, 82%) as a colourless viscous liquid. The enantiomeric ratio was determined as 96:4 e.r. by chiral SFC (Daicel IC, CO_2/MeOH (90:10), 2.0 mL/min, (λ = 290 nm): *tr* (major): 7.5 min, *tr* (minor): 9.8 min). **^{1}H NMR** (500 MHz, 363 K, DMSO-d_6): δ = 7.95 (s, 1H), 7.38–7.30 (m, 1H), 7.30–7.23 (m, 3H), 6.60 (dt, $^3J_{trans}$ = 15.4 Hz, ^3J = 7.2 Hz, 1H), 5.67 (t, $^3J_{trans}$ = 15.4 Hz, 1H), 5.46 (t, ^3J = 5.7 Hz, 1H), 5.09 (d, ^2J = 12.2 Hz, 1H), 5.02 (d, ^2J = 12.2 Hz, 1H), 2.66 (dt, ^2J = 13.9 Hz, ^3J = 7.2 Hz, 1H), 2.55 (dt, ^2J = 13.9 Hz, ^3J = 7.2 Hz, 1H), 1.41 (s, 9H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-d_6): δ = 163.9, 150.4, 140.7, 139.9, 138.5, 128.3, 126.9, 126.1, 125.9, 125.1, 125.0, 94.5, 79.3, 74.8, 52.2, 38.8, 27.4 ppm; **ESI-HRMS**: m/z calculated for $[C_{21}H_{17}Cl_3N_2O_4Na]^+$: 469.0465; found 469.0463.

Chiral-phase SFC: Daicel IC, CO_2/MeOH (90:10) 2.0 mL/min, (λ= 290 nm)

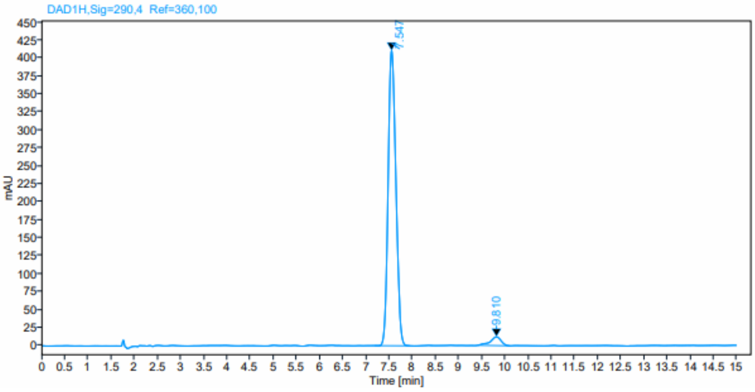
Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
9.577	MM m	0.2115	2105.7600	155.9635	47.9308
12.117	MM m	0.2564	2287.5704	138.6878	52.0692
		Sum	4393.3304		

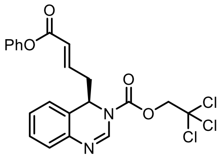
Enantioselective:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
7.547	MM m	0.1800	4713.5194	410.4543	96.0445
9.810	MM m	0.2365	194.1242	12.1414	3.9555
		Sum	4907.6436		

(*R*,*E*)-2,2,2-Trichloroethyl 4-(4-oxo-4-phenoxybut-2-en-1-yl)quinazoline-3(4*H*)-carboxylate (4c)

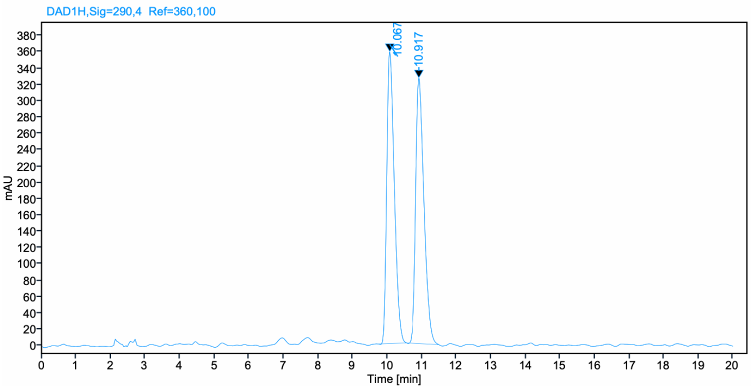


4c

According to the general procedure A, the reaction of quinazoline (**2a**) (13.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3c** (57.0 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 5:1) the desired product **4c** (30.3 mg, 0.065 mmol, 65%) as a colourless viscous liquid. The enantiomeric ratio was determined as 94:6 e.r. by chiral SFC (Chiralcel OJ-H, CO_2/MeOH (80:20), 2.0 mL/min, (λ = 290 nm): *tr* (major): 10.1 min, *tr* (minor): 10.9 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-d_6): δ = 8.00 (s, 1H), 7.41 (t, ^3J = 7.8 Hz, 3H), 7.36 (td, J = 7.2 Hz, 2.4 Hz, 1H), 7.32 (d, J = 2.4 Hz, 1H), 7.27 (dt, J = 14.2 Hz, ^3J = 7.5 Hz, 2H), 7.10 (d, ^3J = 7.8 Hz, 2H), 6.93 (dt, $^3J_{\text{trans}}$ = 15.5 Hz, ^3J = 7.0 Hz, 1H), 6.01 (d, $^3J_{\text{trans}}$ = 15.5 Hz, 1H), 5.54 (t, ^3J = 5.8 Hz, 1H), 5.11 (d, ^3J = 12.2 Hz, 1H), 5.06 (d, ^3J = 12.1 Hz, 1H), 2.79 (dt, ^2J = 13.9 Hz, ^3J = 7.0 Hz, 1H), 2.70 (dt, ^2J = 13.9 Hz, ^3J = 7.0 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-d_6): δ = 163.0, 150.4, 150.1, 144.4, 140.0, 138.5, 128.9, 128.4, 127.0, 126.0, 125.2, 125.1, 124.9, 123.4, 121.0, 94.6, 74.8, 52.1, 40.1 ppm; **ESI-HRMS**: m/z calculated for $[C_{21}H_{17}Cl_3N_2O_4Na]^+$: 489.0152; found 489.0145.

Chiral-phase SFC: Chiralcel OJ-H, CO_2/MeOH (80:20) 2.0 mL/min, (λ= 290 nm)

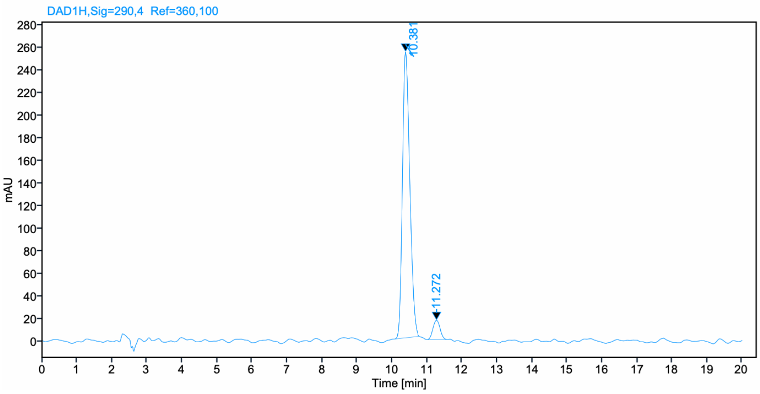
Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
10.067	MM m	0.2352	5430.8266	357.4894	49.9264
10.917	MM m	0.2573	5446.8285	325.2968	50.0736
		Sum	10877.6551		

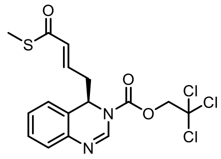
Enantioselective:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
10.381	MM m	0.2240	3697.3976	253.6727	93.9102
11.272	MM m	0.2202	239.7644	17.0344	6.0898
		Sum	3937.1620		

(*R*,*E*)-2,2,2-trichloroethyl 4-(4-(methylthio)-4-oxobut-2-en-1-yl)quinazoline-3(4*H*)-carboxylate (4d)

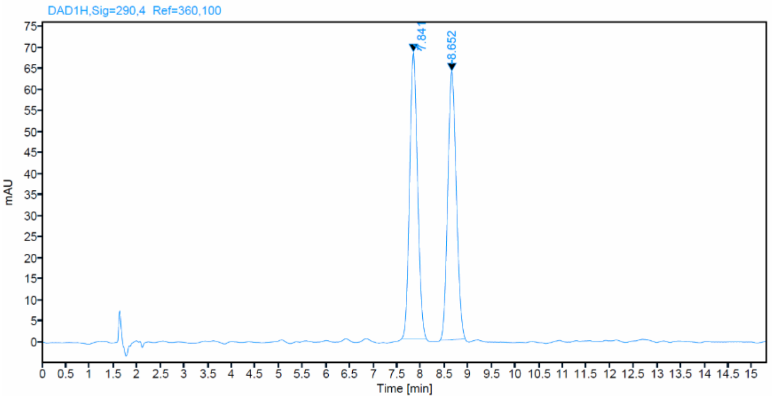


4d

According to the general procedure A, the reaction of quinazoline (**2a**) (13.0 mg, 0.100 mmol, 1.0 equiv.) with thioester dienolate **3d** (54.2 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 5:1) the desired product **4d** (27.0 mg, 0.064 mmol, 64%) as a colourless oil. The enantiomeric ratio was determined as 82:18 e.r. by chiral SFC (Chiralcel IC, CO_2/MeOH (90:10), 2.0 ml/min, (λ = 290 nm): *tr* (minor): 8.0 min, *tr* (major): 8.8 min). **^{1}H NMR** (500 MHz, CD_3CN): δ = 7.98 (s, 1H), 7.34 (td, ^3J = 7.5 Hz, ^4J = 1.6 Hz, 1H), 7.30–7.24 (m, 2H), 7.19 (d, ^3J = 7.1 Hz, 1H), 6.67 (dt, $^3J_{trans}$ = 15.5 Hz, ^3J = 7.8 Hz, 1H), 6.06 (dt, $^3J_{trans}$ = 15.4 Hz, ^4J = 1.3 Hz, 1H), 5.49 (t, ^3J = 5.6 Hz, 1H), 5.00 (s, 2H), 2.68 (*br*s, 1H), 2.57 (*br*s, 1H), 2.28 (*br*s, 2H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-*d*$_6$): δ = 189.4, 151.3, 140.9, 139.0, 132.1, 129.3, 127.9, 126.9, 126.1, 125.7, 95.5, 75.7, 53.0, 39.8, 11.2 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{21}H_{17}Cl_3N_2O_3NaS]^+$: 422.9912; found 422.9903.

Chiral-phase SFC: Chiralcel IC, CO_2/MeOH 90:10, 2.0 ml/min, (λ = 290 nm)

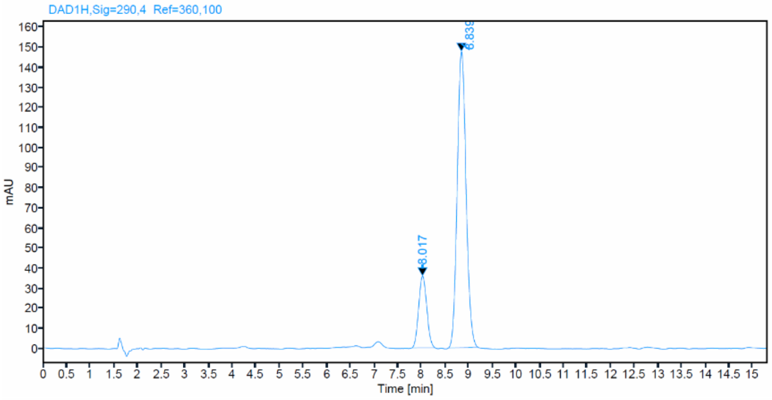
Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
7.841	MM m	0.1863	807.3391	68.1163	49.8321
8.652	MM m	0.2006	812.7805	63.8140	50.1679
		Sum	1620.1196		

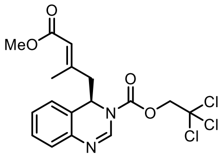
Enantioselective:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
8.017	MM m	0.1862	422.5513	35.6826	18.0420
8.839	MM m	0.2039	1919.4958	147.4455	81.9580
		Sum	2342.0471		

(*R*,*E*)-2,2,2-Trichloroethyl 4-(4-methoxy-2-methyl-4-oxobut-2-en-1-yl)quinazoline-3(4*H*)-carboxylate (4e)

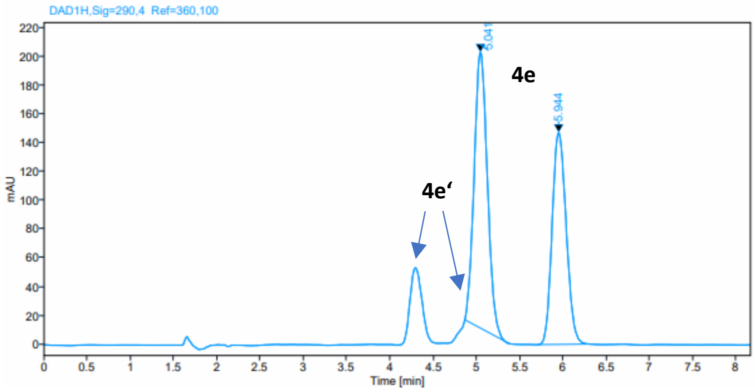


4e

According to the general procedure A, the reaction of quinazoline (**2a**) (13.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3e** (51.9 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 5:1) the desired product **4e** (24.7 mg, 0.059 mmol, 59%) as a colourless viscous liquid. The enantiomeric ratio was determined as 90:10 e.r. by chiral SFC (Chiralcel OD-H, CO_2/MeOH (90:10), 2.0 mL/min, (λ = 290 nm): *tr* (minor): 5.0 min, *tr* (major): 5.8 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-d_6): 7.97 (s, 1H), 7.34 (t, ^3J = 7.4 Hz, 1H), 7.26 (t, ^3J = 7.4 Hz, 2H), 7.21 (d, ^3J = 7.4 Hz, 1H), 5.49–5.44 (m, 2H), 5.08 (d, ^2J = 12.2 Hz, 1H), 5.01 (d, ^2J = 12.2 Hz, 1H), 3.59 (s, 3H), 2.55–2.50 (m, 1H), 2.46 (dd, ^2J = 12.9 Hz, ^3J = 6.5 Hz, 1H), 2.09 (s, 3H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-d_6): δ = 165.1, 152.8, 150.3, 139.9, 138.4, 128.3, 126.75 , 125.9, 125.2, 125.0, 118.6, 94.5, 74.8, 51.7, 50.0, 46.5, 18.5 ppm; **ESI-HRMS**: m/z calculated for $[C_{17}H_{17}Cl_3N_2O_4Na]^+$: 441.0146; found 441.0142.

Chriral-phase SFC: Chiralcel OD-H, CO_2/MeOH (90:10) 2.0 mL/min, (λ= 290 nm)

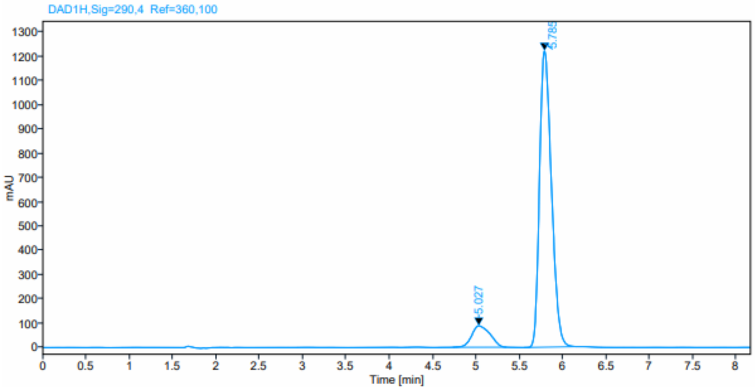
Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
5.041	MM m	0.1635	2030.4766	191.8430	54.9621
5.944	MM m	0.1778	1663.8444	147.3299	45.0379
		Sum	3694.3210		

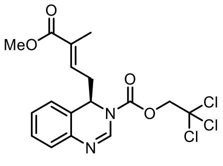
Enantioselective:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
5.027	MM m	0.2454	1298.3457	88.3666	10.0270
5.785	MM m	0.1493	11650.1195	1221.0578	89.9730
		Sum	12948.4652		

(*R*,*E*)-2,2,2-Trichloroethyl 4-(4-methoxy-3-methyl-4-oxobut-2-en-1-yl)quinazoline-3(4*H*)-carboxylate (4f)

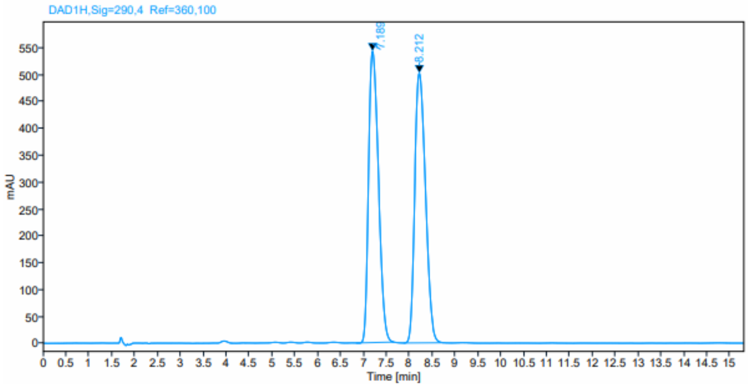


4f

According to the general procedure A, the reaction of quinazoline (**2a**) (13.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3f** (53.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 5:1) the desired product **4f** (16.2 mg, 0.039 mmol, 39%) as a colourless viscous liquid. The enantiomeric ratio was determined as 78:22 e.r. by chiral SFC (Chiralcel OD-H, CO_2/MeOH (92:8), 2.0 mL/min, (λ = 290 nm): *tr* (minor): 7.1 min, *tr* (major): 8.1 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-d_6): δ = 7.96 (s, 1H), 7.36–7.32 (m, 1H), 7.28–7.23 (m, 3H), 6.57 (t, ^3J = 7.6 Hz, 1H), 5.45 (t, ^3J = 6.2 Hz, 1H), 5.08 (d, ^2J = 12.2 Hz, 1H), 5.05 (d, ^2J = 12.2 Hz, 1H), 3.65 (s, 3H), 2.69 (dt, ^2J = 14.3 Hz, ^3J = 7.6 Hz, 1H), 2.59 (dt, ^2J = 14.3 Hz, ^3J = 6.2 Hz, 1H), 1.59 (s, 3H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-d_6): δ = 166.6, 150.4, 139.9, 138.5, 134.3, 130.2, 128.2, 126.8, 125.9, 125.0, 124.9, 94.5, 74.8, 52.0, 51.0, 35.2, 11.5 ppm; **ESI-HRMS**: m/z calculated for $[C_{17}H_{17}Cl_3N_2O_4Na]^+$: 441.0146; found 441.0146.

Chriral-phase SFC: Chiralcel OD-H, CO_2/MeOH (92:8) 2.0 mL/min, (λ= 290 nm)

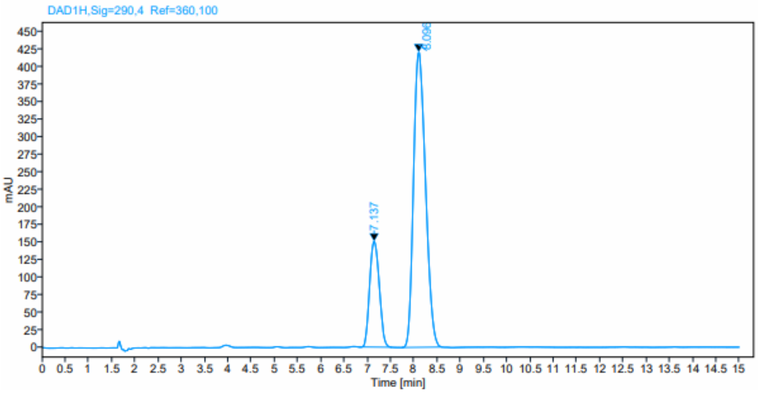
Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
7.189	MM m	0.2407	8118.7835	542.0486	49.7331
8.212	MM m	0.2609	8205.9231	501.6272	50.2669
		Sum	16324.7065		

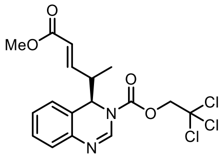
Enantioselective:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
7.137	MM m	0.2313	2151.7859	150.0689	22.1738
8.096	MM m	0.2859	7552.3748	419.6948	77.8262
		Sum	9704.1608		

(*R*,*E*)-2,2,2-Trichloroethyl 4-(5-methoxy-5-oxopent-3-en-2-yl)quinazoline-3(4*H*)-carboxylate (4g)

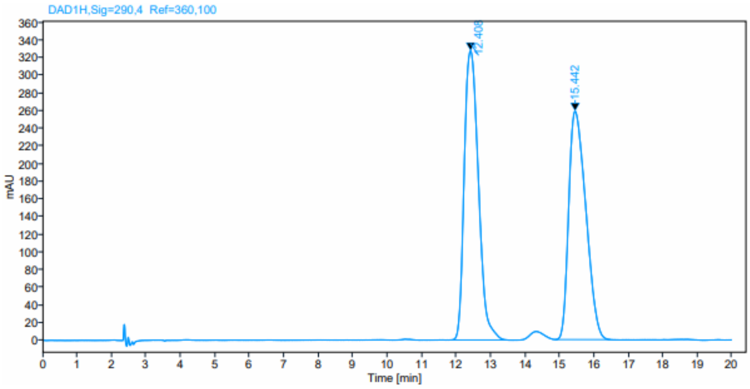


4g

According to the general procedure A, the reaction of quinazoline (**2a**) (13.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3g** (49.7 µL, 0.200 mmol, 2.0 equiv.) led to the desired product **4g** as a mixture of two diastereomers (d.r.: 6/1, 77% combined NMR yield). The major isomer (26.8 mg, 0.064 mmol, 64%) was isolated after flash column chromatography (*n*-pent/EtOAc 10:1) as a colourless viscous liquid. The enantiomeric ratio of the major product **4g** was determined as 97.5:2.5 e.r. by chiral SFC (Chiralcel OD-H, CO_2/MeOH (92:8), 2.0 mL/min, (λ = 290 nm): *tr* (minor): 12.1 min, *tr* (major): 15.2 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-*d*$_6$): δ =7.98 (s, 1H), 7.39 – 7.35 (m, 1H), 7.30 – 7.23 (m, 3H), 6.61 (dd, $^3J_{trans}$ = 15.6 Hz, ^3J = 8.5 Hz, 1H), 5.72 (d, $^3J_{trans}$ = 15.6 Hz, z1H), 5.33 (d, ^3J = 4.6 Hz, 1H), 5.09 (d, ^2J = 12.2 Hz, 2H), 5.05 (d, ^2J = 12.2 Hz, 2H), 3.62 (s, 3H), 2.86 – 2.77 (m, 1H), 1.04 (d, ^3J = 7.0 Hz, 3H). ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-*d*$_6$): δ = 165.1, 150.5, 147.5, 140.5, 139.2, 128.5, 126.9, 126.6, 125.0, 122.6, 121.7, 94.6, 74.8, 56.6, 50.6, 42.6, 14.5 ppm; **ESI-HRMS**: m/z calculated for $[C_{17}H_{17}Cl_3N_2O_4Na]^+$: 441.0146; found 441.0146.

Chriral-phase SFC: Chiralcel OD-H, CO_2/MeOH (92:8) 2.0 mL/min, (λ= 290 nm)

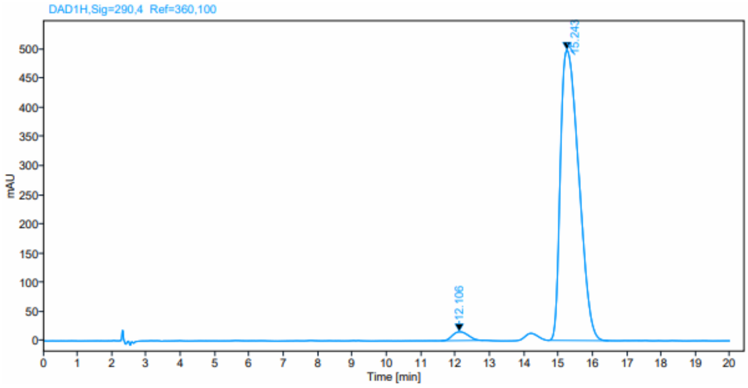
Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
12.408	MM m	0.4625	9384.2481	327.2875	51.2410
15.442	MM m	0.5430	8929.7055	258.4865	48.7590
		Sum	18313.9536		

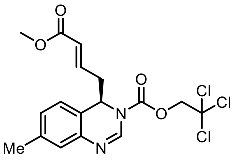
Enantioselective:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
12.106	MM m	0.3894	481.4279	15.0412	2.5424
15.243	MM m	0.5805	18454.7822	497.8417	97.4576
		Sum	18936.2101		

(*R*,*E*)-2,2,2-Trichloroethyl 4-(4-methoxy-4-oxobut-2-en-1-yl)-7-methylquinazoline-3(4*H*)-carboxylate (4h)

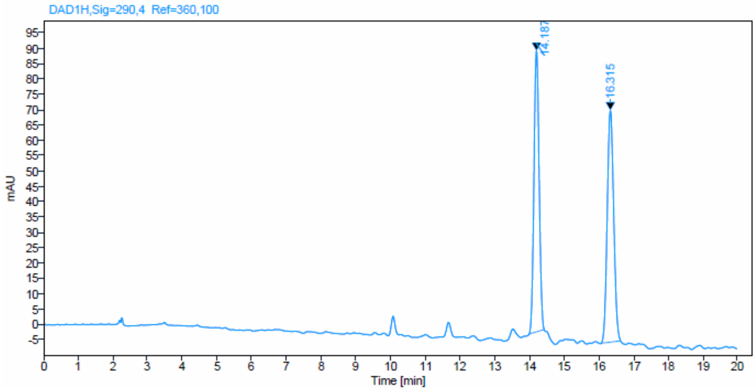


4h

According to the general procedure A, the reaction of 7-methylquinazoline (**2h**) (14.4 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 4:1) the desired product **4h** (27.2 mg, 0.065 mmol, 65%) as a white solid. The enantiomeric ratio was determined as 95.5:4.5 e.r. by chiral SFC (Chiralcel IG, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 290 nm): *tr* (major): 14.2 min, *tr* (minor): 16.4 min.). **^{1}H NMR** (500 MHz, 90 °C, DMSO-*d*$_6$): δ = 7.94 (s, 1H), 7.14 (d, ^3J = 7.5 Hz, 1H), 7.09 (d, ^3J = 8.8 Hz, 2H), 6.69 (dt, $^3J_{trans}$ = 15.4 Hz, ^3J = 7.6 Hz, 1H), 5.79 (d, $^3J_{trans}$ = 15.6 Hz, 1H), 5.43 (t, ^3J = 5.6 Hz, 1H), 5.08 (d, ^2J = 12.2 Hz, 1H), 5.04 (d, ^2J = 12.2 Hz, 1H), 3.63 (s, 3H), 2.68 (dt, ^2J = 13.8 Hz, ^3J = 7.0 Hz, 1H), 2.58 (dt, ^2J = 14.1 Hz, ^3J = 6.5 Hz, 1H), 2.32 (s, 3H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-*d*$_6$): δ = 164.9, 150.4, 142.0, 139.9, 138.3, 137.8, 127.6, 125.7, 125.6, 123.9, 121.9, 94.5, 74.8, 52.0, 50.6, 39.0, 20.0 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{17}H_{17}N_2O_4Cl_3Na]^+$: 441.0146; found 441.0144.

Chiral-phase SFC: Chiralcel IG, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm)

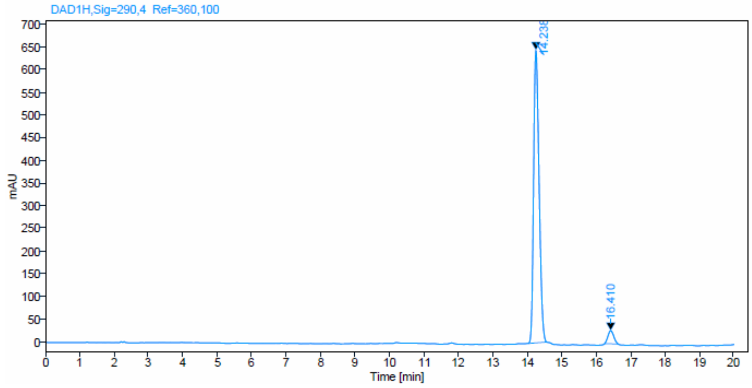
Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
14.187	MM m	0.1619	940.8143	91.5548	49.2648
16.315	MM m	0.2017	968.8957	75.5144	50.7352
		Sum	1909.7100		

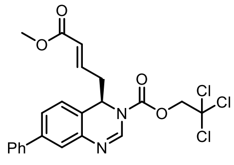
Enantioselective:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
14.238	MM m	0.1708	7120.5043	645.0129	95.5052
16.410	MM m	0.1853	335.1150	28.8979	4.4948
		Sum	7455.6193		

(*R*,*E*)-2,2,2-Trichloroethyl 4-(4-methoxy-4-oxobut-2-en-1-yl)-7-phenylquinazoline-3(4*H*)-carboxylate (4i)

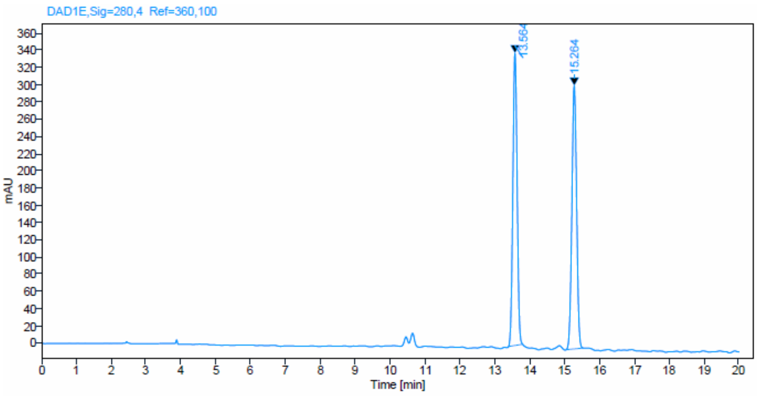


4i

According to the general procedure A, the reaction of 7-phenylquinazoline (**2i**) (20.6 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 4:1) the desired product **4i** (46.3 mg, 0.096 mmol, 96%) as a slightly yellow solid. The enantiomeric ratio was determined as 94:6 e.r. by chiral SFC (Chiralcel IG, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 280 nm): *tr* (major): 13.6 min, *tr* (minor): 15.3 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-d_6): δ = 8.02 (s, 1H), 7.68 (d, ^3J = 7.7 Hz, 2H), 7.58 (dd, ^3J = 7.9 Hz, ^4J = 2.0 Hz, 1H), 7.52 (d, ^4J = 1.9 Hz, 1H), 7.47 (t, ^3J = 7.6 Hz, 2H), 7.38 (td, ^3J = 7.8 Hz, ^4J = 1.9 Hz, 2H), 6.75 (dt, $^3J_{trans}$ = 15.4 Hz, ^3J = 7.6 Hz, 1H), 5.83 (d, $^3J_{trans}$ = 15.5 Hz, 1H), 5.53 (t, ^3J = 5.7 Hz, 1H), 5.10 (d, ^2J = 12.2 Hz, 1H), 5.06 (d, ^2J = 12.1 Hz, 1H), 3.63 (s, 3H), 2.75 (dt, ^2J = 13.8 Hz, ^3J = 6.7 Hz, 1H), 2.65 (dt, ^2J = 14.0 Hz, ^3J = 6.5 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-d_6): δ = 165.0, 150.4, 142.0, 140.6, 140.4, 139.0, 138.8, 128.4, 127.2, 126.5, 126.1, 125.2, 124.0, 124.0, 123.1, 94.5, 74.8, 52.0, 50.6, 38.9 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{22}H_{19}N_2O_4Cl_3Na]^+$: 503.0303; found 503.0302.

Chiral-phase SFC: Chiralcel IG, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 280 nm)

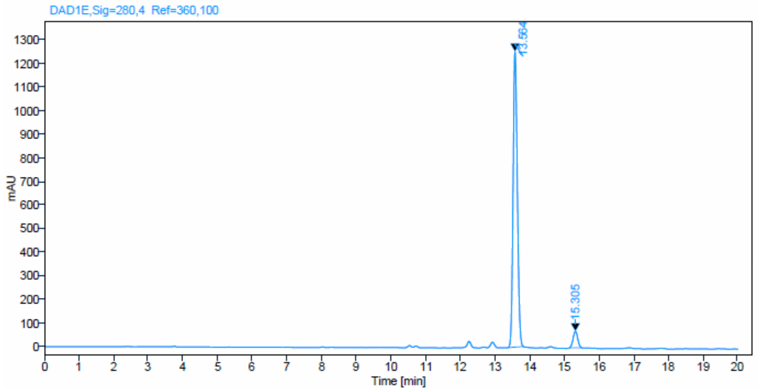
Racemic:



Signal: DAD1E,Sig=280,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
13.564	MM m	0.1328	2874.8804	339.3811	49.9305
15.264	MM m	0.1481	2882.8873	305.5036	50.0695
		Sum	5757.7677		

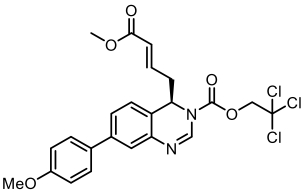
Enantioselective:



Signal: DAD1E,Sig=280,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
13.564	MM m	0.1305	10591.9876	1254.3664	94.2857
15.305	MM m	0.1457	641.9407	69.5077	5.7143
		Sum	11233.9283		

(*R*,*E*)-2,2,2-Trichloroethyl 4-(4-methoxy-4-oxobut-2-en-1-yl)-7-(4-methoxyphenyl)-quinazoline-3(4*H*)-carboxylate (4j)

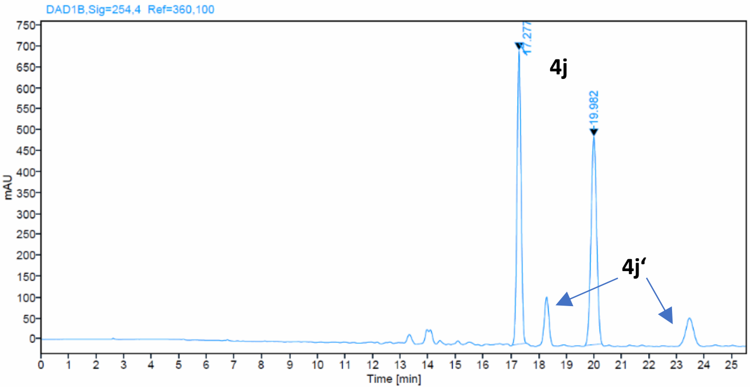


4j

According to the general procedure A, the reaction of 7-(4-methoxyphenyl)quinazoline (**2j**) (23.6 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 2:1) the desired product **4j** (54.1 mg, 0.99 mmol, 99%) as a slightly yellow solid. The enantiomeric ratio was determined as 95:5 e.r. by chiral SFC (Chiralcel IC, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 254 nm): *tr* (major): 16.7 min, *tr* (minor): 19.5 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-*d*$_6$): δ = 8.01 (s, 1H), 7.64–7.60 (m, 2H), 7.52 (dd, ^3J = 7.9 Hz, ^4J = 1.9 Hz, 1H), 7.47 (d, ^4J = 1.7 Hz, 1H), 7.32 (d, ^3J = 7.9 Hz, 1H), 7.03 (d, ^3J = 8.7 Hz, 2H), 6.74 (dt, $^3J_{trans}$ = 15.4 Hz, ^3J = 7.6 Hz, 1H), 5.83 (d, $^3J_{trans}$ = 15.6 Hz, 1H), 5.51 (t, ^3J = 5.7 Hz, 1H), 5.09 (d, ^2J = 12.2 Hz, 1H), 5.05 (d, ^2J = 12.1 Hz, 1H), 3.82 (s, 3H), 3.63 (s, 3H), 2.74 (dt, ^2J = 13.8 Hz, ^3J = 6.8 Hz, 1H), 2.64 (dt, ^2J = 13.8 Hz, ^3J = 6.5 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-*d*$_6$): δ = 165.0, 158.9, 150.4, 142.0, 140.3, 138.9, 131.3, 127.2, 126.4, 124.7, 124.0, 123.2, 122.7, 114.1, 94.5, 74.8, 54.9, 52.0, 50.6, 39.0 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{23}H_{21}N_2O_5Cl_3Na]^+$: 533.0408; found 533.0411.

Chiral-phase SFC: Chiralcel IC, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 254 nm)

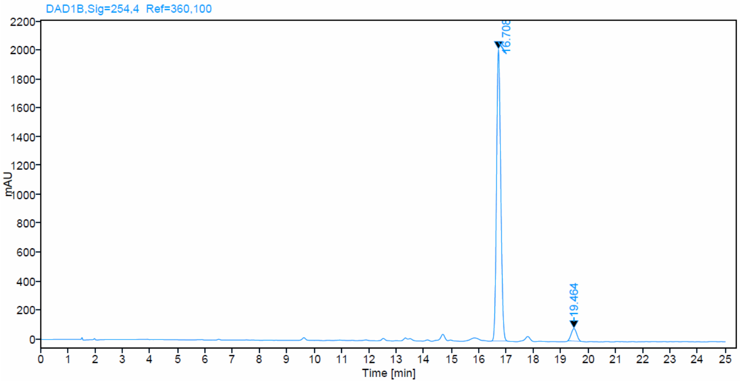
Racemic:



Signal: DAD1B,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
17.277	MM m	0.1588	7135.4020	700.9590	50.2602
19.982	MM m	0.2220	7061.5263	496.3362	49.7398
		Sum	14196.9283		

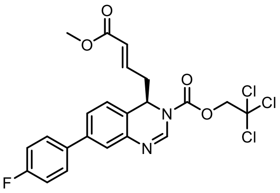
Enantioselective:



Signal: DAD1B,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
16.708	MM m	0.1683	21479.9306	2016.4916	94.7239
19.464	MM m	0.2223	1196.4188	86.0171	5.2761
		Sum	22676.3493		

(*R*,*E*)-2,2,2-Trichloroethyl 7-(4-fluorophenyl)-4-(4-methoxy-4-oxobut-2-en-1-yl)-quinazoline-3(4*H*)-carboxylate (4k)

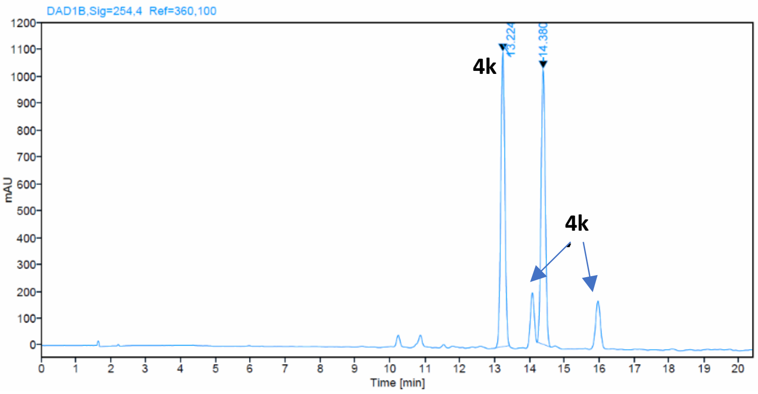


4k

According to the general procedure A, the reaction of 7-(4-fluorophenyl)quinazoline (**2k**) (22.4 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 3:1) the desired product **4k** (22.1 mg, 0.044 mmol, 44%) as a white solid. The enantiomeric ratio was determined as 96:4 e.r. by chiral SFC (Chiralcel IC, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 254 nm): *tr* (major): 12.9 min, *tr* (minor): 14.1 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-d_6): δ = 8.01 (s, 1H), 7.74–7.70 (m, 2H), 7.55 (dd, ^3J = 7.9 Hz, ^4J = 1.9 Hz, 1H), 7.50 (d, ^4J = 1.7 Hz, 1H), 7.36 (d, ^3J = 7.9 Hz, 1H), 7.29–7.23 (m, 2H), 6.74 (dt, $^3J_{trans}$ = 15.3 Hz, ^3J = 7.7 Hz, 1H), 5.83 (d, $^3J_{trans}$ = 15.6 Hz, 1H), 5.52 (t, ^3J = 5.7 Hz, 1H), 5.10 (d, ^2J = 12.2 Hz, 1H), 5.06 (d, ^2J = 12.1 Hz, 1H), 3.63 (s, 3H), 2.75 (dt, ^2J = 13.7 Hz, ^3J = 6.8 Hz, 1H), 2.64 (dt, ^2J = 14.2 Hz, ^3J = 6.6 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-d_6): δ = 164.9, 161.7 (d, $^1J_{C,F}$ = 245.1 Hz), 150.4, 141.9, 140.5, 139.5, 139.0, 135.3 (d, $^4J_{C,F}$ = 3.0 Hz), 128.2 (d, $^3J_{C,F}$ = 8.2 Hz), 126.6, 125.1, 124.0, 124.0, 123.1, 115.2 (d, $^3J_{C,F}$ = 21.5 Hz), 94.5, 74.8, 52.0, 50.6, 38.9 ppm; **^{19}F NMR** (600 MHz, 25 °C, DMSO-d_6): -113.79, -114.89 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{22}H_{18}N_2O_4Cl_3Na]^+$: 521.0208; found 521.0214.

Chiral-phase SFC: Chiralcel IC, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 254 nm)

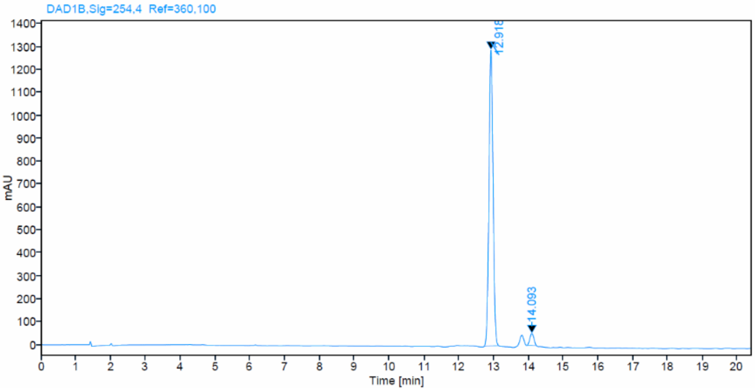
Racemic:



Signal: DAD1B,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
13.224	MM m	0.1267	8905.2204	1096.9883	51.0111
14.380	MM m	0.1314	8552.1962	1024.7603	48.9889
		Sum	17457.4165		

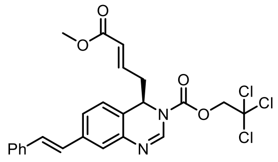
Enantioselective:



Signal: DAD1B,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
12.918	MM m	0.1281	10651.2852	1293.0522	96.3346
14.093	MM m	0.1275	405.2672	51.6692	3.6654
		Sum	11056.5523		

(*R*)-2,2,2-Trichloroethyl 4-((*E*)-4-methoxy-4-oxobut-2-en-1-yl)-7-((*E*)-styryl)quinazoline-3(4*H*)-carboxylate (4l)

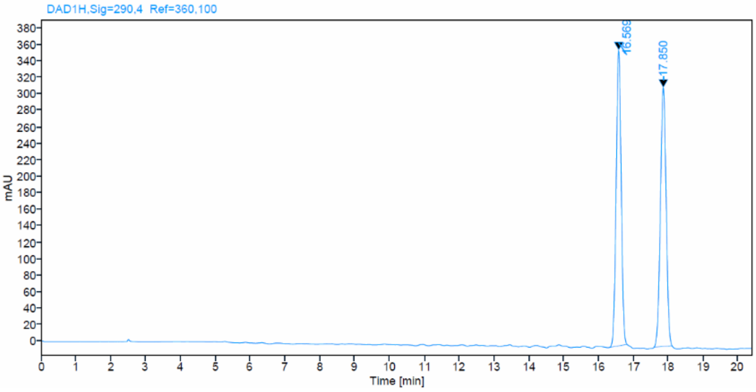


4l

According to the general procedure A, the reaction of 7-((*E*)-styryl)quinazoline (**2l**) (23.2 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 3:1) the desired product **4l** (37.8 mg, 0.074 mmol, 74%) as a slightly yellow solid. The enantiomeric ratio was determined as 92:8 e.r. by chiral SFC (Chiralcel IC, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 290 nm): *tr* (major): 17.4 min, *tr* (minor): 18.8 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-*d*$_6$): δ = 8.00 (s, 1H), 7.60 (d, ^3J = 8.1 Hz, 2H), 7.50 (dd, ^3J = 7.9 Hz, ^4J = 1.8 Hz, 1H), 7.47 (d, ^4J = 1.7 Hz, 1H), 7.38 (t, ^3J = 7.7 Hz, 2H), 7.27 (dd, $^3J_{trans}$ = 12.2 Hz, ^3J = 4.5 Hz, 3H), 7.21 (d, $^3J_{trans}$ = 16.4 Hz, 1H), 6.72 (dt, $^3J_{trans}$ = 15.3 H, ^3J = 7.6 Hz, 1H), 5.81 (d, $^3J_{trans}$ = 15.6 Hz, 1H), 5.48 (t, ^3J = 5.6 Hz, 1H), 5.09 (d, ^2J = 12.2 Hz, 1H), 5.05 (d, ^2J = 12.0 Hz, 1H), 3.63 (s, 3H), 2.73 (dt, ^2J = 13.8 Hz, ^3J = 6.7 Hz, 1H), 2.62 (dt, ^2J = 14.2 Hz, ^3J = 6.8 Hz 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-*d*$_6$): δ = 165.3, 150.4, 141.9, 140.3, 138.8, 137.6, 136.5, 129.0, 128.1, 127.3, 127.2, 126.3, 126.1, 125.0, 124.0, 124.0, 123.0, 94.5, 73.6, 52.1, 50.6, 38.9 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{24}H_{21}N_2O_4Cl_3Na]^+$: 529.0459; found 529.0465.

Chiral-phase SFC: Chiralcel IC, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm)

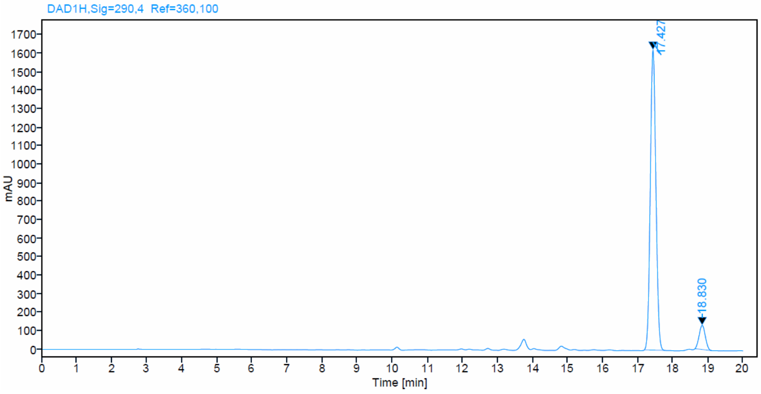
Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
16.569	MM m	0.1567	3583.1632	358.2538	50.0575
17.850	MM m	0.1790	3574.9374	313.5922	49.9425
		Sum	7158.1007		

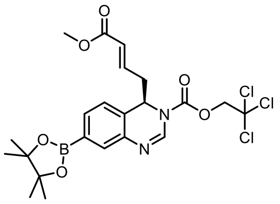
Enantioselective:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
17.427	MM m	0.1732	17965.8228	1622.5569	91.8335
18.830	MM m	0.1930	1597.6471	130.3562	8.1665
		Sum	19563.4699		

(*R*,*E*)-2,2,2-Trichloroethyl 4-(4-methoxy-4-oxobut-2-en-1-yl)-7-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)quinazoline-3(4*H*)-carboxylate (4m)

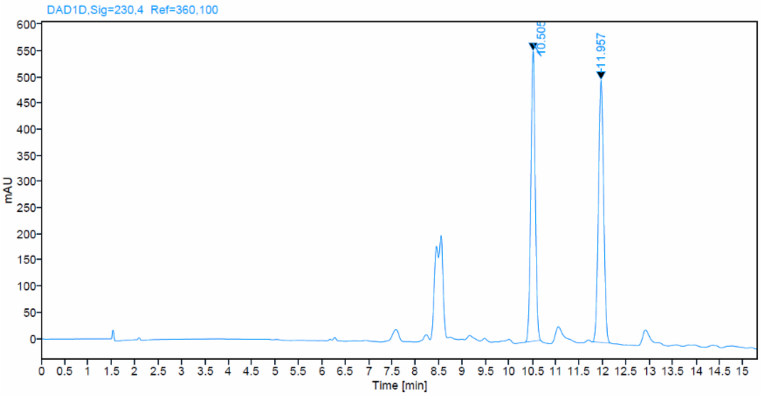


4m

According to the general procedure A, the reaction of benzo[*f*]quinazoline (**2m**) (25.6 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 3:1) the desired product **4m** (32.3 mg, 0.061 mmol, 61%) as a slightly yellow solid. The enantiomeric ratio was determined as 96:4 e.r. by chiral SFC (Chiralcel IC, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 230 nm): *tr* (major): 11.0 min, *tr* (minor): 12.6 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-*d*$_6$): δ = 7.97 (s, 1H), 7.56 (d, ^3J = 7.5 Hz, 1H), 7.51 (s, 1H), 7.28 (d, ^3J = 7.5 Hz, 1H), 6.69 (dt, $^3J_{\mathrm{trans}}$ = 15.3 Hz, ^3J = 7.6 Hz, 1H), 5.79 (d, $^3J_{\mathrm{trans}}$ = 15.5 Hz, 1H), 5.49 (t, ^3J = 5.6 Hz, 1H), 5.08 (d, ^2J = 12.1 Hz, 1H), 5.04 (d, ^2J = 12.1 Hz, 1H), 3.63 (s, 2H), 2.71 (dt, ^2J = 13.9 Hz, ^3J = 6.7 Hz,1H), 2.60 (dt, ^2J = 14.1 Hz, ^3J = 6.5 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-*d*$_6$): δ = 164.9, 150.4, 141.8, 140.2, 138.0, 132.8, 130.9, 127.9, 125.6, 124.0, 94.5, 83.4, 74.8, 52.2, 50.6, 38.8, 24.2 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{22}H_{26}N_2O_6BCl_3Na]^+$: 533.0846; found 553.0850.

Chiral-phase SFC: Chiralcel IC, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 230 nm)

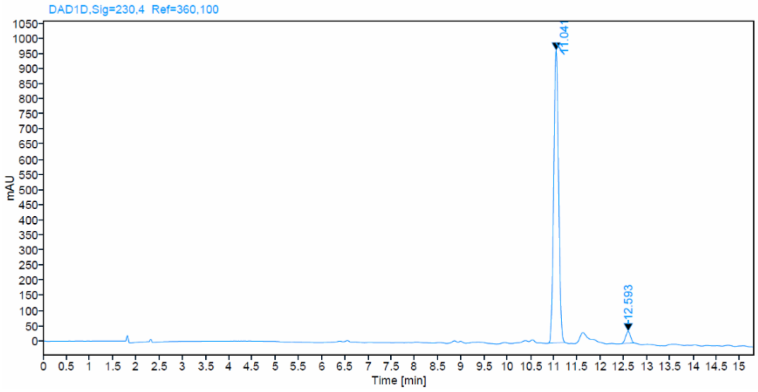
Racemic:



Signal: DAD1D,Sig=230,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
10.505	MM m	0.1072	3760.2351	553.7421	49.4994
11.957	MM m	0.1194	3836.2972	500.6729	50.5006
		Sum	7596.5323		

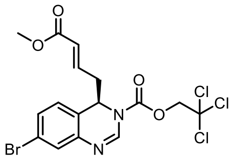
Enantioselective:



Signal: DAD1D,Sig=230,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
11.041	MM m	0.1133	6895.9789	965.4881	96.1119
12.593	MM m	0.1162	278.9724	38.6424	3.8881
		Sum	7174.9513		

(R,E)-2,2,2-Trichloroethyl 7-bromo-4-(4-methoxy-4-oxobut-2-en-1-yl)quinazoline-3(4H)-carboxylate (4o)



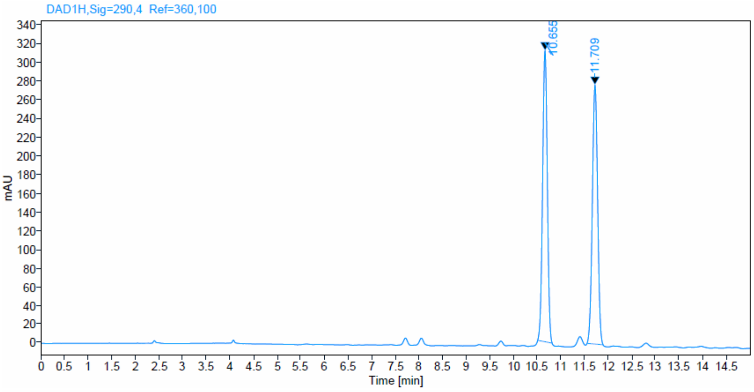
4o

According to the general procedure A, the reaction of 7-bromoquinazoline (**2o**) (20.9 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 5:1) the desired product **4o** (38.2 mg, 0.079 mmol, 79%) as a white solid. The enantiomeric ratio was determined as 94:6 e.r. by chiral SFC (Chiralcel IG, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 290 nm): *tr* (major): 10.8 min, *tr* (minor): 11.8 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-d_6): δ = 8.00 (s, 1H), 7.45 (dd, ^3J = 8.1 Hz, ^4J = 1.9 Hz, 1H), 7.41 (d, ^4J = 2.1 Hz, 1H), 7.26 (d, ^3J = 8.1 Hz, 1H), 6.70 (dt, $^3J_{trans}$ = 15.3 Hz, ^3J = 7.6 Hz, 1H), 5.80 (d, $^3J_{trans}$ = 15.6 Hz, 1H), 5.49 (t, ^3J = 5.7 Hz, 1H), 5.08 (d, ^2J = 12.2 Hz, 1H), 5.05 (d, ^2J = 12.2 Hz, 1H), 3.63 (s, 3H), 2.70 (dt, ^2J = 13.8 Hz, ^3J = 6.7 Hz, 1H), 2.60 (dt, ^2J = 14.3 Hz, ^3J = 6.6 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-d_6): δ = 164.9, 150.2, 141.6, 141.5, 140.2, 129.5, 127.9, 127.5, 124.2, 120.7, 94.4, 74.9, 51.8, 50.6, 38.7 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{16}H_{14}BrCl_3N_2O_4Na]^+$: 506.9072; found 506.9071.

The same reaction with the TIPS-dienolate **3a'** led to the product **4o** in a 97:3 e.r. (27.9 mg, 0.058 mmol, 58%).

Chiral-phase SFC: Chiralcel IC, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm)

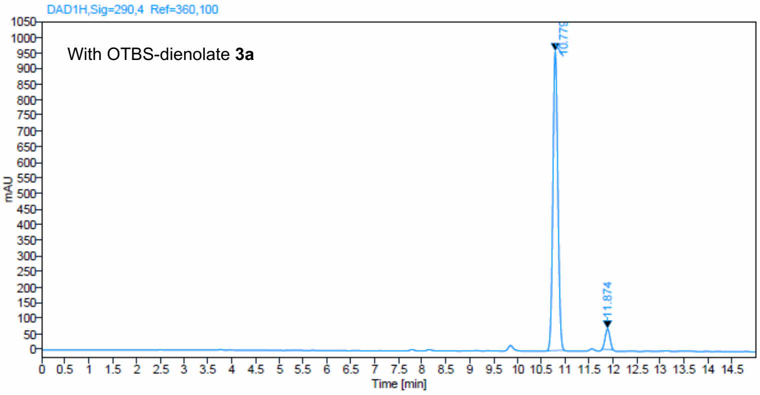
Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

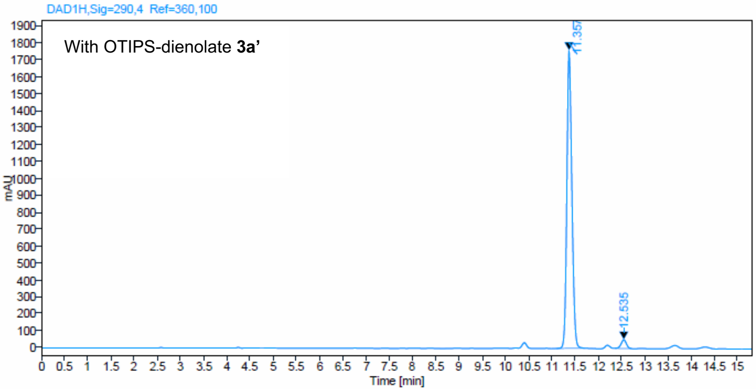
RT [min]	Type	Width [min]	Area	Height	Area%
10.655	MM m	0.1067	2153.4663	311.4700	50.1555
11.709	MM m	0.1201	2140.1139	277.1224	49.8445
		Sum	4293.5803		

Enantioselective:



Signal: DAD1H,Sig=290,4 Ref=360,100

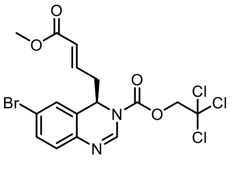
RT [min]	Type	Width [min]	Area	Height	Area%
10.779	MM m	0.1125	6951.7443	959.3486	93.8276
11.874	MM m	0.1110	457.3156	65.8975	6.1724
		Sum	7409.0599		



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
11.357	MM m	0.1182	13604.0003	1760.4501	97.0698
12.535	MM m	0.1229	410.6589	51.5707	2.9302

(*R*,*E*)-2,2,2-Trichloroethyl 6-bromo-4-(4-methoxy-4-oxobut-2-en-1-yl)quinazoline-3(4*H*)-carboxylate (4p)

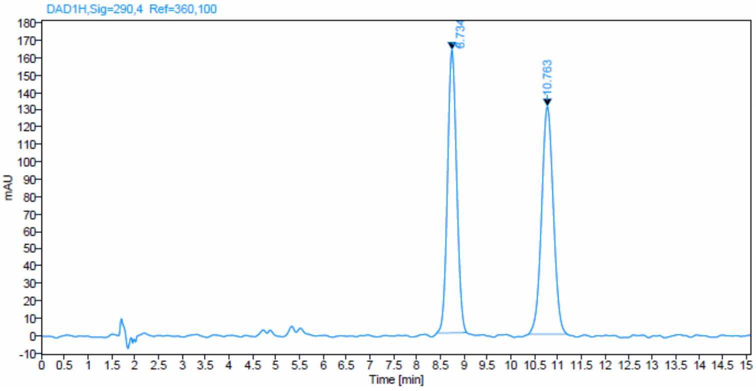


4p

According to the general procedure A, the reaction of 6-bromoquinazoline (**2p**) (20.9 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 5:1) the desired product **4p** (36.5 mg, 0.075 mmol, 75%) as a white solid. The enantiomeric ratio was determined as 80:20 e.r. by chiral SFC (Chiralcel IG, CO_2/MeOH (70:30), 2.0 ml/min, (λ = 290 nm): *tr* (major): 8.6 min, *tr* (minor): 10.6 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-d_6): δ = 7.98 (s, 1H), 7.55 (d, ^4J = 2.2 Hz, 1H), 7.50 (dd, ^3J = 8.4 Hz, ^4J = 2.1 Hz, 1H), 7.18 (d, ^3J = 8.3 Hz, 1H), 6.70 (dt, $^3J_{trans}$ = 15.4 Hz, ^3J = 7.6 Hz, 1H), 5.80 (d, $^3J_{trans}$ = 15.5 Hz, 1H), 5.52 (t, ^3J = 5.7 Hz, 1H), 5.08 (d, ^2J = 12.2 Hz, 1H), 5.04 (d, ^2J = 12.1 Hz, 1H), 3.63 (s, 3H), 2.74–2.66 (m, 1H), 2.70 (dt, ^2J = 12.8 Hz, ^3J = 6.4 Hz, 1H), 2.61 (dt, ^2J = 14.0 Hz, ^3J = 6.4 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-d_6): δ = 164.9, 150.3, 141.7, 140.7, 137.8, 131.3, 128.8, 127.2, 127.0, 124.2, 119.1, 94.4, 74.9, 51.5, 50.6, 38.8 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{16}H_{14}BrCl_3N_2O_4Na]^+$: 506.9072; found 506.9071.

Chiral-phase SFC: Chiralcel IC, CO_2/MeOH 70:30, 2.0 ml/min, (λ = 290 nm)

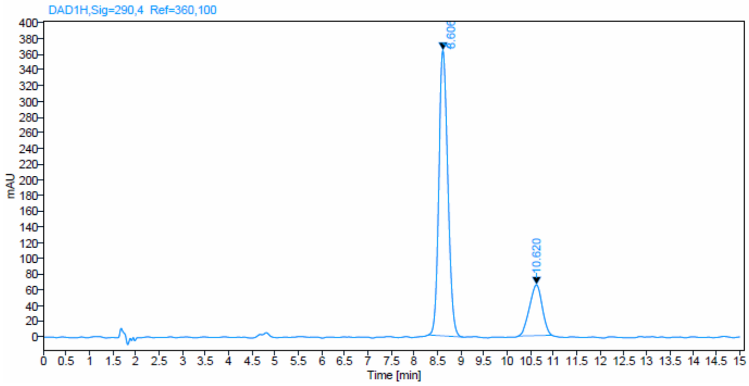
Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
8.734	MM m	0.2092	2192.9035	162.7958	49.1694
10.763	MM m	0.2679	2266.9880	130.9887	50.8306
		Sum	4459.8915		

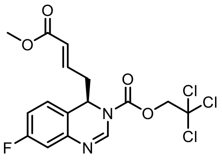
Enantioselective:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
8.606	MM m	0.2133	4962.8559	363.4314	80.1297
10.620	MM m	0.2984	1230.6740	64.5591	19.8703
		Sum	6193.5298		

(*R*,*E*)-2,2,2-Trichloroethyl 7-fluoro-4-(4-methoxy-4-oxobut-2-en-1-yl)quinazoline-3(4*H*)-carboxylate (4q)

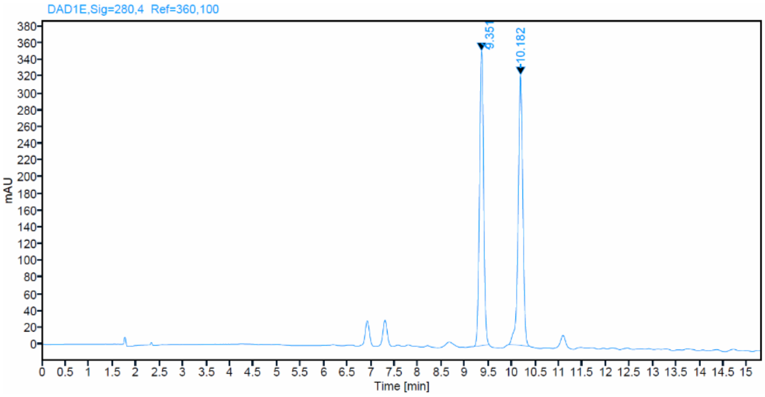


4q

According to the general procedure A, the reaction of 7-fluoroquinazoline (**2q**) (14.8 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 4:1) the desired product **4q** (30.1 mg, 0.071 mmol, 71%) as a white solid. The enantiomeric ratio was determined as 94:6 e.r. by chiral SFC (Chiralcel IC, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 280 nm): *tr* (major): 8.6 min, *tr* (minor): 9.3 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-d_6): δ = 8.01 (s, 1H), 7.33 (dd, ^3J = 8.4 Hz, ^4J = 6.0 Hz, 1H), 7.10 (td, ^3J = 8.6 Hz, ^4J = 2.7 Hz, 1H), 7.03 (dd, ^3J = 9.8 Hz, ^4J = 2.7 Hz, 1H), 6.70 (dt, $^3J_{trans}$ = 15.4 Hz, ^3J = 7.6 Hz, 1H), 5.78 (d, $^3J_{trans}$ = 15.6 Hz, 1H), 5.50 (t, ^3J = 5.6 Hz, 1H), 5.08 (d, ^2J = 12.1 Hz, 1H), 5.05 (d, ^2J = 12.2 Hz, 1H), 3.63 (s, 3H), 2.69 (dt, ^2J = 14.2 Hz, ^3J = 6.9 Hz, 1H), 2.59 (dt, ^2J = 14.1 Hz, ^3J = 6.9 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-d_6): δ = 164.9, 161.7 (d, $^1J_{C,F}$ = 243.9 Hz), 149.4, 141.7, 141.3, 140.2 (d, $^3J_{C,F}$ = 11.2 Hz), 127.7 (d, $^3J_{C,F}$ = 9.3 Hz), 124.1, 121.1 (d, $^4J_{C,F}$ = 3.3 Hz), 113.6 (d, $^2J_{C,F}$ = 21.9 Hz), 111.5 (d, $^2J_{C,F}$ = 22.4 Hz), 94.5, 74.9, 51.7, 50.6, 38.9 ppm; **^{19}F NMR** (600 MHz, 25 °C, DMSO-d_6): -112.50, -112.93 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{16}H_{14}N_2O_4Cl_3FNa]^+$: 444.9895; found 444.9893.

Chiral-phase SFC: Chiralcel IC, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 280 nm)

Racemic:

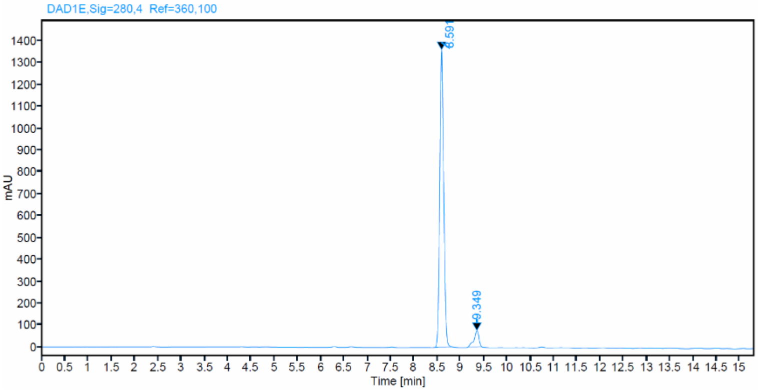


p = 192 bar

Signal: DAD1E,Sig=280,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
9.351	MM m	0.0970	2203.2209	351.9509	48.8337
10.182	MM m	0.1094	2308.4610	322.8546	51.1663
		Sum	4511.6820		

Enantioselective:

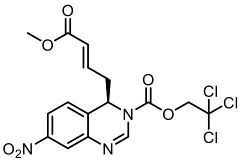


p = 207 bar

Signal: DAD1E,Sig=280,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
8.591	MM m	0.0960	8378.4026	1358.4816	93.8034
9.349	MM m	0.1118	553.4724	73.5797	6.1966
		Sum	8931.8749		

(*R*,*E*)-2,2,2-Trichloroethyl 4-(4-methoxy-4-oxobut-2-en-1-yl)-7-nitroquinazoline-3(4*H*)-carboxylate (4r)

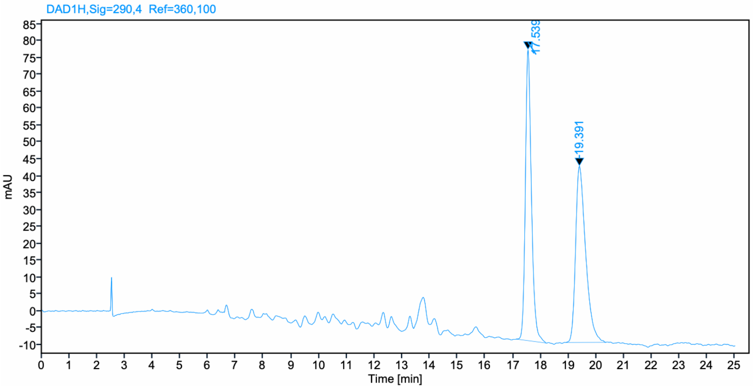


4r

According to the general procedure A, the reaction of 7-nitroquinazoline (**2r**) (17.5 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 3:1) the desired product **4r** (26.3 mg, 0.058 mmol, 58%) as a yellow solid. The enantiomeric ratio was determined as 77:23 e.r. by chiral SFC (Chiralcel IA, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 290 nm): *tr* (major): 17.5 min, *tr* (minor): 19.4 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-*d*$_6$): δ = 8.12–8.09 (m, 2H), 7.95 (d, ^4J = 2.4 Hz, 1H), 7.60 (d, ^3J = 8.4 Hz, 1H), 6.71 (dt, $^3J_{trans}$ = 15.4 Hz, ^3J = 7.6 Hz, 1H), 5.81 (d, $^3J_{trans}$ = 15.5 Hz, 1H), 5.68–5.64 (m, 1H), 5.49 (t, ^3J = 5.7 Hz, 1H), 5.10 (d, ^2J = 12.1 Hz, 1H) 5.07 (d, ^2J = 12.3 Hz, 1H), 3.63 (s, 3H), 2.76 (dt, ^2J = 13.6 Hz, ^3J = 6.7 Hz, 1H), 2.65 (dt, ^2J = 14.5 Hz, ^3J = 7.1 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-*d*$_6$): δ = 164.8, 150.1, 147.8, 142.5, 141.2, 139.6, 131.9, 127.6, 124.5, 121.3, 119.2, 94.4, 75.0, 51.9, 50.7, 38.6 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{16}H_{14}N_3O_6Cl_3Na]^+$: 471.9840; found 471.9842.

Chiral-phase SFC: Chiralcel IA, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm)

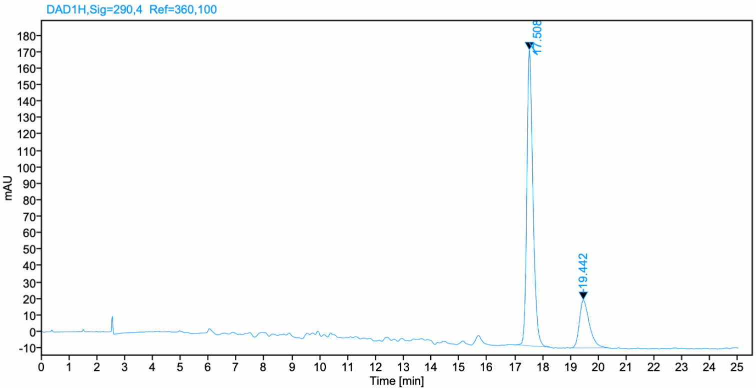
Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
17.539	MM m	0.2286	1301.9116	86.0154	49.7931
19.391	MM m	0.3858	1312.7314	52.1198	50.2069
		Sum	2614.6430		

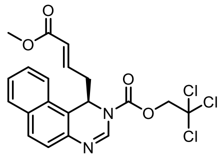
Enantioselective:



Signal: DAD1G,Sig=270,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
14.311	MM m	0.1845	9026.6008	728.9978	76.6839
15.689	MM m	0.2357	2744.5745	178.2053	23.3161
		Sum	11771.1753		

(*R*,*E*)-2,2,2-Trichloroethyl 1-(4-methoxy-4-oxobut-2-en-1-yl)benzo[*f*]quinazoline-2(1*H*)-carboxylate (4s)

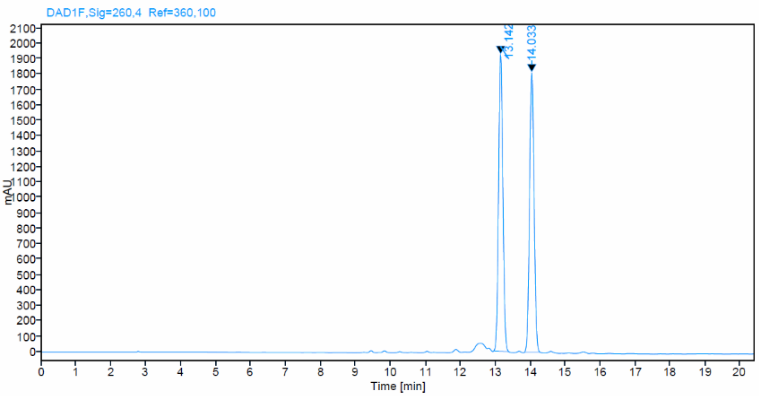


4s

According to the general procedure A, the reaction of benzo[*f*]quinazoline (**2s**) (18.0 mg, 0.100 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.200 mmol, 2.0 equiv.) afforded after flash column chromatography (*n*-pent/EtOAc 3:1) the desired product **4s** (38.5 mg, 0.084 mmol, 84%) as a brown solid. The enantiomeric ratio was determined as 84:16 e.r. by chiral SFC (Chiralcel IC, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 260 nm): *tr* (major): 12.2 min, *tr* (minor): 13.1 min). **^{1}H NMR** (500 MHz, 90 °C, DMSO-*d*$_6$): δ = 8.09 (s, 1H), 8.04 (d, ^3J = 8.5 Hz, 1H), 7.95 (d, ^3J = 8.1 Hz, 1H), 7.92 (d, ^3J = 8.6 Hz, 1H), 7.63 (t, ^3J = 7.7 Hz, 1H), 7.54 (t, ^3J = 7.5 Hz, 1H), 7.45 (d, ^3J = 8.6 Hz, 1H), 6.79 (dt, $^3J_{trans}$ = 15.5 Hz, ^3J = 7.7 Hz, 1H), 6.18 (t, ^3J = 5.6 Hz, 1H), 5.78 (d, $^3J_{trans}$ = 15.5 Hz, 1H), 5.13 (d, ^2J = 12.2 Hz, 1H), 5.05 (d, ^2J = 12.1 Hz, 1H), 3.61 (s, 2H), 2.76 (dt, ^2J = 14.5 Hz, ^3J = 6.6 Hz,1H), 2.69 (dt, ^2J = 14.6 Hz, ^3J = 7.4 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, 90 °C, DMSO-*d*$_6$): δ = 164.9, 150.4, 142.2, 140.6, 136.8, 132.3, 128.6, 128.2, 128.1, 126.8, 125.3, 124.2, 123.9, 121.8, 118.4, 94.5, 74.9, 50.6, 49.2, 37.1 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{20}H_{17}N_2O_4Cl_3Na]^+$: 477.0146; found 477.0145.

Chiral-phase SFC: Chiralcel IC, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 260 nm)

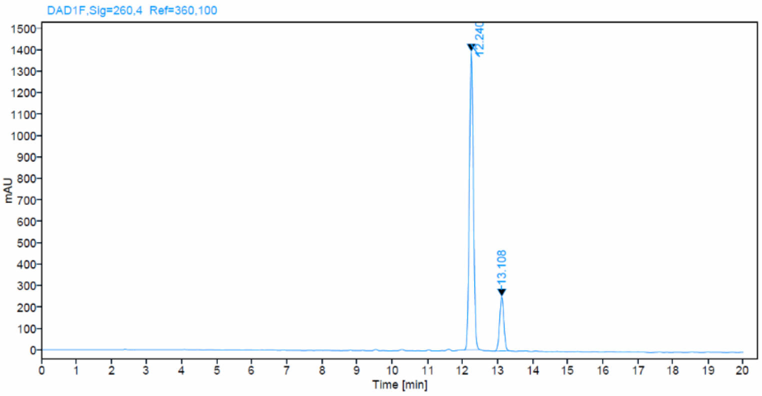
Racemic:



Signal: DAD1F,Sig=260,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
13.142	MM m	0.1333	16406.2878	1926.9833	50.0617
14.033	MM m	0.1412	16365.8537	1814.6854	49.9383
		Sum	32772.1415		

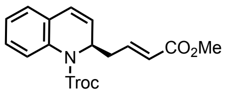
Enantioselective:



Signal: DAD1F,Sig=260,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
12.240	MM m	0.1231	11124.5350	1394.7752	84.0257
13.108	MM m	0.1318	2114.9148	252.1910	15.9743
		Sum	13239.4498		

(*R*,*E*)-2,2,2-Trichloroethyl 2-(4-methoxy-4-oxobut-2-en-1-yl)quinoline-1(2*H*)-carboxylate (5a)

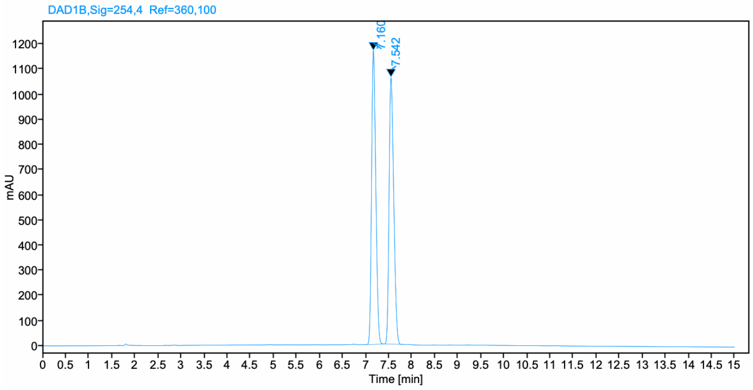


5a

According to the general procedure B, the reaction of quinoline (12.3 µL, 0.10 mmol, 1.0 equiv.) with dienolate **3a** (47.1 µL, 0.20 mmol, 2.0 equiv.) gave after flash column chromatography (*n*-pent/EtOAc 20:1) the desired product **5a** as a colourless oil (32.8 mg, 0.081 mmol, 81%). The enantiomeric ratio was found to be 82:18 by chiral SFC (Daicel IG, CO_2/MeOH (gradient 98:2 → 65:35) 2.0 mL/min, λ= 290 nm, *tr* (major): 8.1 min, *tr* (minor): 8.5 min). ^{1}**H NMR** (400 MHz, $CDCl_3$): δ 7.66 (bs, 1H), 7.30 – 7.22 (m, 1H), 7.15 – 7.09 (m, 2H), 6.88 (dt, *J* = 15.4, 7.6 Hz, 1H), 6.55 (d, *J* = 9.6 Hz, 1H), 6.06 (dd, *J* = 8.9, 6.0 Hz, 1H), 5.76 (dt, *J* = 15.4, 1.3 Hz, 1H), 5.27 – 5.14 (m, 1H), 4.82 (bs, 1H), 4.49 (bs, 1H), 3.69 (s, 3H), 2.52 – 2.15 (m, 2H); ^{13}**C NMR** (100 MHz, $CDCl_3$): δ 166.4, 152.5, 143.4, 133.0, 128.1, 128.0, 127.1, 126.5, 125.8, 125.2, 124.0, 95.2, 75.4, 52.0, 51.5, 35.8 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{17}H_{16}Cl_3NO_4Na]^+$: 426.0037; found 426.0035.

Chiral-phase SFC: Chiralpak IG, CO_2/MeOH 95:5 → 65:35, 2.0 ml/min, (λ = 254 nm)

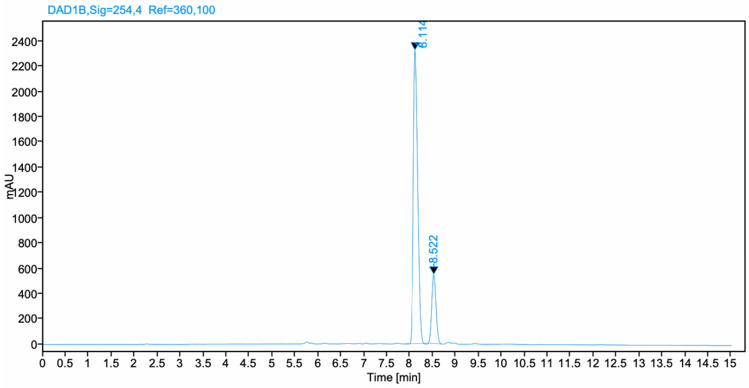
Racemic:



Signal: DAD1B,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
7.160	MM m	0.0991	7330.4754	1169.7724	50.0443
7.542	MM m	0.1083	7317.4962	1062.5755	49.9557
		Sum	14647.9716		

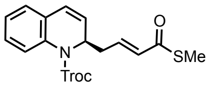
Enantioselective:



Signal: DAD1B,Sig=254,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
8.114	MM m	0.1055	15399.5697	2318.5058	81.6838
8.522	MM m	0.1000	3453.0824	544.0569	18.3162
		Sum	18852.6521		

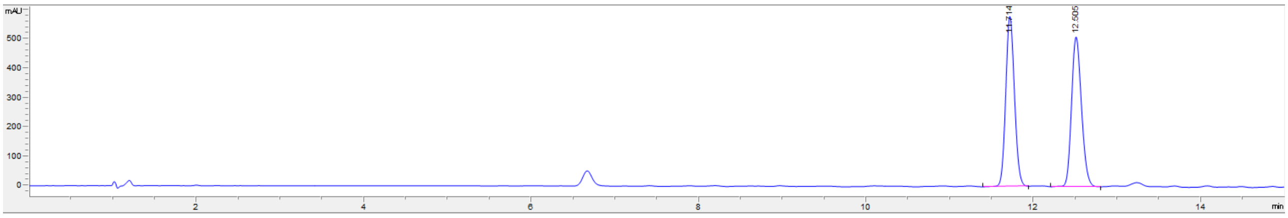
(*R*,*E*)-2,2,2-Trichloroethyl 2-(4-(methylthio)-4-oxobut-2-en-1-yl)quinoline-1(2*H*)-carboxylate (5b)



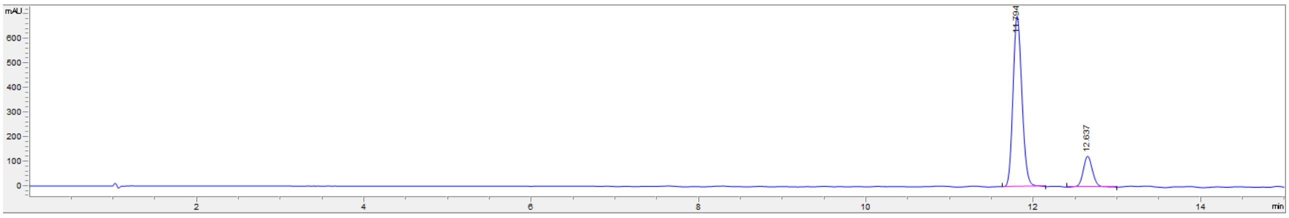
5b

According to the general procedure B, the reaction of quinoline (12.3 µL, 0.10 mmol, 1.0 equiv.) with dienolate **3d** (54.2 µL, 0.20 mmol, 2.0 equiv.) gave after flash column chromatography (cyclohexane/EtOAc 20:1) the desired product **5b** as a white oil (33.6 mg, 0.08 mmol, 80% yield). The enantiomeric ratio was determined as 84:16 e.r. by chiral SFC (Chiralpak IG, CO_2/MeOH (95:5 → 65:35), 2.0 ml/min in 15 min, (λ = 254 nm): tr (major): 11.8 min, tr (minor): 12.6 min). ^{1}**H NMR** (300 MHz, $CDCl_3$) δ 7.66 (bs, 1H), 7.32 – 7.20 (m, 1H), 7.12 (m, 2H), 6.80 (dt, *J* = 15.4, 8.3 Hz 1H), 6.55 (d, *J* = 10.2 Hz, 1H), 6.14 – 5.95 (m, 2H), 5.22 (app. q, *J* = 6.7 Hz, 1H), 4.67 (bs, 2H), 2.47 – 2.23 (m, 5H) ppm; ^{13}**C NMR** (75 MHz, $CDCl_3$) δ 190.0, 152.6, 139.2, 133.4, 131.4 (2C), 128.2, 127.2, 126.6 (2C), 126.0, 125.3, 95.3, 75.6, 52.2, 35.9, 11.5 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{17}H_{20}Cl_3N_2O_3S\,NH_4]^+$: 437.0255; found 437.0256.

Chiral-phase SFC: Chiralpak IG, CO_2/MeOH 95:5 → 65:35, 2.0 ml/min, (λ = 254 nm)

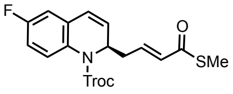


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	11.714	BB	4222.8	582.9	0.1125	49.924	0.874
2	12.505	BB	4235.6	513.6	0.1282	50.076	0.809



#	Time	Type	Area	Height	Width	Area%	Symmetry
1	11.794	BB	5178.5	697.5	0.1166	84.104	0.811
2	12.637	BB	978.7	126.3	0.1184	15.896	0.877

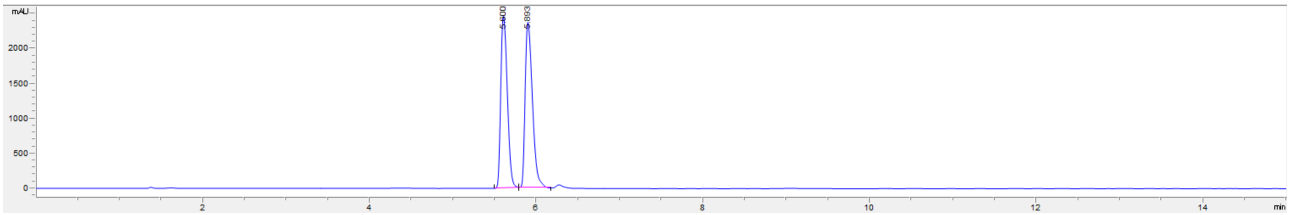
(*R*,*E*)--2,2,2-Trichloroethyl 6-fluoro-2-(4-(methylthio)-4-oxobut-2-en-1-yl)quinoline-1(2*H*)-carboxylate (5c)



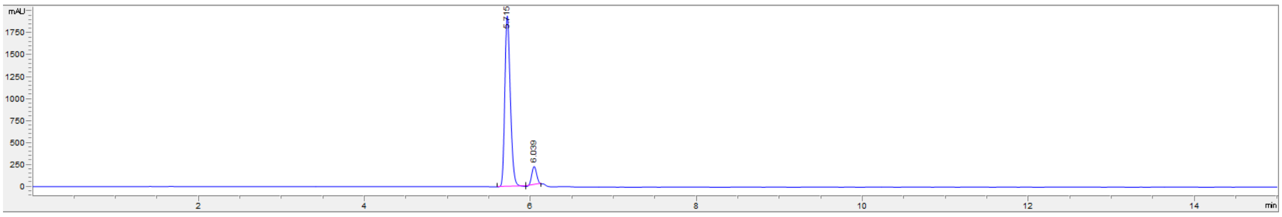
5c

According to the general procedure B, the reaction of 6-fluoroquinoline (12.2 µL, 0.10 mmol, 1.0 equiv.) with dienolate **3d** (54.2 µL, 0.20 mmol, 2.0 equiv.) gave after flash column chromatography (cyclohexane/EtOAc 20:1) the desired product **5b** as a yellowish oil (25.1 mg, 0.057 mmol, 57% yield). The enantiomeric ratio was determined as 91:9 e.r. by chiral SFC (Chiralpak IA, CO_2/MeOH (95:5 → 60:40), 3.0 ml/min in 15 min, (λ = 254 nm): tr (major): 5.7 min, tr (minor): 6.0 min). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 7.61 (bs, 1H), 6.96 (td, *J* = 8.6, 3.1 Hz, 1H), 6.84 (dd, *J* = 8.4, 3.1 Hz, 1H), 6.81 – 6.69 (m, 1H), 6.51 (d, *J* = 9.6 Hz, 1H), 6.12 (dd, *J* = 9.6, 5.9 Hz, 1H), 6.04 (d, *J* = 15.5 Hz, 1H), 5.30 – 5.18 (m, 1H), 4.84 (bs, 1H), 4.49 (bs, 1H), 2.53 – 2.16 (m, 2H), 2.33 (s, 3H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$) δ 190.0, 160.0 (d, $^1J_{C,F}$ = 242.3 Hz), 152.6, 138.9, 131.5, 130.0, 128.9 (d, $^3J_{C,F}$ = 7.5 Hz), 127.3, 125.4, 125.3, 114.8 (d, $^2J_{C,F}$ = 23.3 Hz), 112.9 (d, $^2J_{C,F}$ = 23.2 Hz), 95.2, 75.6, 52.2, 35.5, 11.5 ppm; **^{19}F NMR** (282 MHz, $CDCl_3$): -116.88, -117.34; **ESI-HRMS**: *m/z* calculated for $[C_{17}H_{19}Cl_3FN_2O_3S\ NH_4]^+$: 455.0161; found 455.0106.

Chiral-phase SFC: Chiralpak IA, CO_2/MeOH 95:5 → 60:40, 3.0 ml/min, (λ = 254 nm)

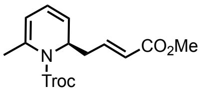


#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.6	BB	13471.8	2466.6	0.0877	48.390	0.655
2	5.893	BB	14368.4	2371.3	0.0947	51.610	0.563



#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.715	BB	9031.9	1952.7	0.072	91.044	0.727
2	6.039	BB	888.5	213.3	0.0666	8.956	0.96

(*R*,*E*)--2,2,2-Trichloroethyl 2-(4-methoxy-4-oxobut-2-en-1-yl)-6-methylpyridine-1(2*H*)-carboxylate (6)

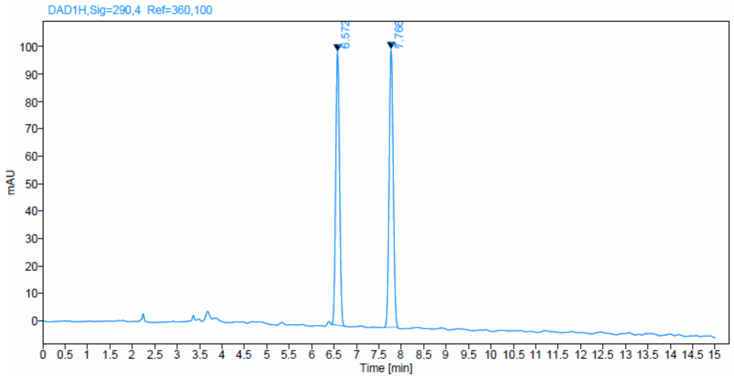


6

In a flame-dried 5 mL Schlenk pressure tube, 2-picoline (9.88 µL, 0.10 mmol, 1.0 equiv.) was dissolved in hexafluorobenzene (1 mL) and cooled to 6 °C. 2,2,2-Trichloroethoxycarbonyl chloride (14 µL, 0.10 mmol, 1.0 equiv.) was added and the reaction was stirred at 6 °C for 30 min. Subsequently, catalyst **1d** (10.6 mg, 0.01 mmol, 10 mol%) and dienolate **3a** (47.1 µL, 0.20 mmol, 2.0 equiv.) were added and the reaction was stirred at 6 °C overnight. The solvent was then removed under reduced pressure and the desired product was obtained as a colourless oil (17.0 mg, 0.046 mmol, 46%) after purification by column chromatography (*n*-pent/EtOAc 10:1). The enantiomeric ratio was determined as 70:30 *e.r.* by chiral SFC (Chiralcel IG, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 290 nm): *tr* (minor): 6.5 min, *tr* (major): 7.7 min). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.89 (dt, $^3J_{trans}$ = 15.5 Hz, ^3J = 7.7 Hz, 1H), 5.95 (dd, ^3J = 9.3 Hz, ^3J = 5.3 Hz, 1H), 5.81 (dt, $^3J_{trans}$ = 15.6 Hz, ^3J = 1.4 Hz, 1H), 5.68 (dd, ^3J = 9.4 Hz, ^3J = 5.9 Hz, 1H), 5.50 (dp, ^3J = 5.2 Hz, ^3J = 1.2 Hz, 1H), 5.04 – 4.96 (m, 1H), 4.94 (bs, 1H), 4.68 (bs, 1H), 3.70 (s, 3H), 2.44 – 2.33 (m, 2H), 2.19 (s, 3H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$) δ 166.6, 152.6, 144.0, 133.8, 123.7, 123.13, 123.0, 112.6, 93.0, 75.5, 52.3, 51.6, 35.3, 21.7 ppm; **ESI-HRMS**: *m/z* calculated for $[C_{14}H_{16}NO_4Cl_3Na]^+$: 390.0037; found 390.0054.

Chiral-phase SFC: Chiralcel IC, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 290 nm)

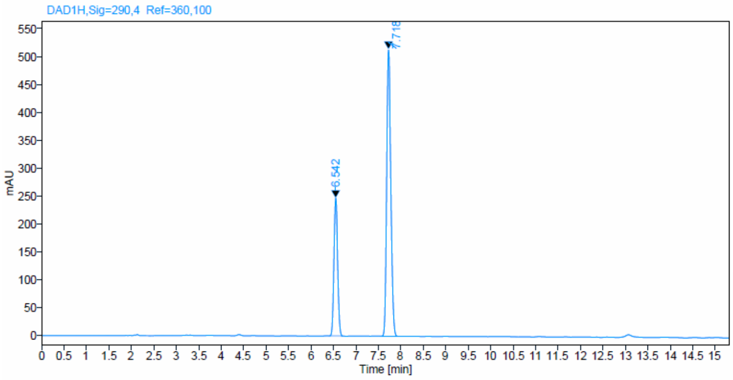
Racemic:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
6.572	MM m	0.0922	583.0129	99.6783	47.9993
7.766	MM m	0.0968	631.6147	101.2784	52.0007
		Sum	1214.6276		

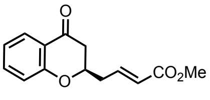
Enantioselective:



Signal: DAD1H,Sig=290,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
6.542	MM m	0.0923	1445.9645	247.0109	29.8968
7.718	MM m	0.1030	3390.5540	513.9692	70.1032
		Sum	4836.5185		

(*R*,*E*)-Methyl 4-(4-oxochroman-2-yl)but-2-enoate (7)

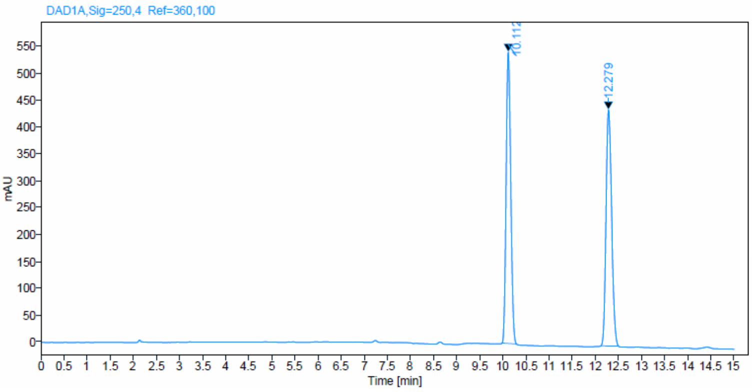


7

In a flame-dried 5 mL Schlenk pressure tube, 4*H*-chromenone (15 mg, 0.10 mmol, 1.0 equiv.) and catalyst **1a** (5.6 mg, 0.005 mmol, 5.0 mol%) were dissolved in anhydrous toluene (0.4 mL). 2,4,6-Collidine (4.0 µL, 0.03 mmol, 0.30 equiv.) and TBSOTf (25 µL, 0.11 mmol, 1.1 equiv.) were added and the mixture was stirred at 60 °C for 1 h. Subsequently, the reaction was cooled to –78 °C and dienolate **3a** (47.1 µL, 0.20 mmol, 2.0 equiv.) was added. After stirring for 18 h at –78 °C, the reaction was quenched with aq. HCl (6.0 equiv., 3 M) and was allowed to warm to room temperature for 1 h. The solution was diluted with water (5 mL), the aq. phase extracted with EtOAc (3 x 3 mL) and the combined organic phases dried over $MgSO_4$. After removing the solvent under reduced pressure, the residue was purified *via* column chromatography (SiO_2, *n*-pent/EtOAc 5:1) to give the desired product as a white solid (16 mg, 0.066 mmol, 66%). The enantiomeric ratio was determined as 79:21 *e.r.* by chiral SFC (Chiralcel IG, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min, (λ = 250 nm): *tr* (minor): 10.4 min, *tr* (major): 12.6 min). **^{1}H NMR** (400 MHz, $CDCl_3$): δ = 7.87 (dd, ^3J = 7.9 Hz, ^4J = 1.7 Hz, 1H), 7.48 (ddd, ^3J = 8.3 Hz, ^3J = 7.2 Hz, ^4J = 1.8 Hz, 1H), 7.08–6.96 (m, 3H), 5.99 (dt, $^3J_{trans}$ = 15.7 Hz, ^4J = 1.5 Hz, 1H), 4.63–4.55 (m, 1H), 3.75 (s, 3H), 2.80–2.63 (m, 4H) ppm; **^{13}C NMR** (100 MHz, $CDCl_3$): δ = 190.7, 166.5, 161.3, 143.2, 135.6, 127.1, 124.6, 121.8, 121.0, 116.7, 73.8, 50.7, 41.8, 38.5 pm; **ESI-HRMS:** calculated for $[C_{14}H_{14}O_4Na]^+$: 269.0795; found 269.0784.

Chiral-phase SFC: Chiralcel IC, CO_2/MeOH 98:2 → 65:35, 2.0 ml/min, (λ = 250 nm)

Racemic:



Signal: DAD1A,Sig=250,4 Ref=360,100

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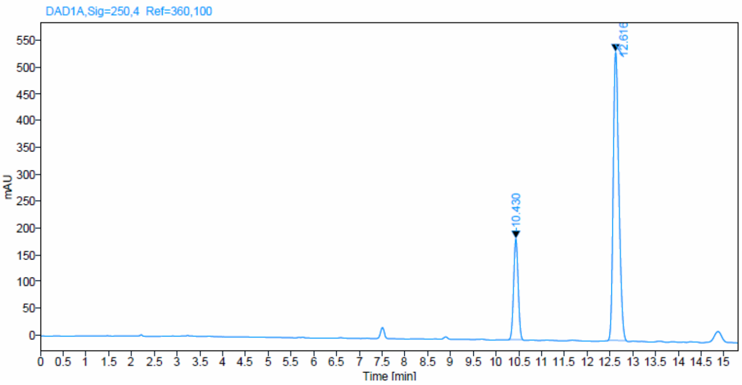
12.279	MM m	0.1328	3724.1396	439.9180	50.1543
		Sum	7425.3650		

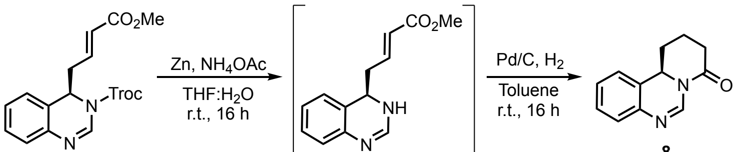
Enantioselective:



Signal: DAD1A,Sig=250,4 Ref=360,100

RT [min]	Type	Width [min]	Area	Height	Area%
10.430	MM m	0.1047	1267.3173	187.8117	21.2211
12.616	MM m	0.1361	4704.6529	537.4452	78.7789
		Sum	5971.9702		

7. Derivatization of 4a: Synthesis of 8



4a
96:4 e.r.

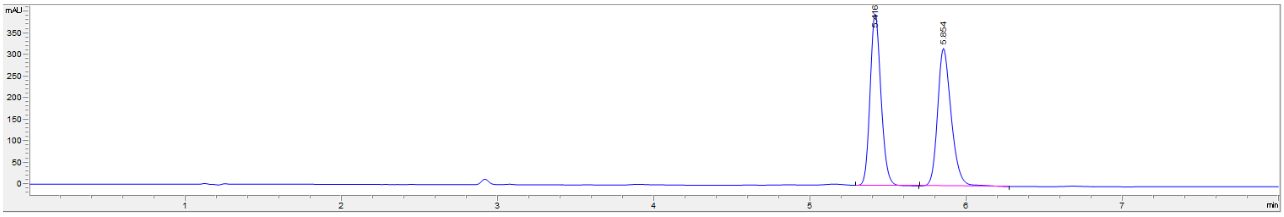
8
47% overall yield
94:6 e.r.

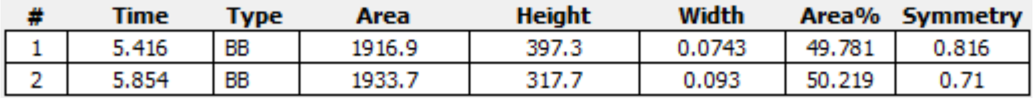
In a vial, **4a** (202.8 mg, 0.5 mmol, 1 equiv.), activated Zn powder (326.9 mg, 5.0 mmol, 10 equiv.) and NH_4OAc (385.4 mg, 5.0 mmol, 10 equiv.) were dissolved in 1.5 mL of a mixture 3:1 of THF:H_2O and stirred overnight at r.t. Then, a 5 mL of a saturated aqueous solution of Na_2CO_3 was added, followed by an extraction with $CHCl_3$ (4x3 mL). The organic phases were combined, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude was used in the next step without further purifications.

In a flame-dry sealed vial, Pd/C (5.4 mg, 0,05 mmol, 0.1 equiv.) was suspended in 0.5 mL of dry toluene and the suspension was purged with a H_2 balloon for 15 min. Subsequently, a solution of the previous crude mixture (0.5 mmol, 1 equiv.) in 0.5 mL of dry toluene was added to the suspension and the reaction was stirred overnight. Then, EtOAc was added and the crude was filtered through a pad of Celite. The filtrate was concentrated under reduced pressure and purified by flash chromatography using silica gel (cyclohexane/EtOAc, 1:3), affording the tricyclic product **8** as a white solid (470.6 mg, 2.35 mmol, 47% overall yield). $[\alpha]^{20}_D$ = 59.1 (c 6.9, $CHCl_3$). The enantiomeric ratio was determined as 94:6 *e.r.* by chiral SFC (Chiralcel IA, CO_2/MeOH (95:5 → 60:40), 3.0 ml/min, (λ = 280 nm): *tr* (minor): 5.4 min, *tr* (major): 5.8 min). **^{1}H NMR** (300 MHz, $CDCl_3$): δ 8.41 (s, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.32 (t, *J* = 7.5 Hz, 1H), 7.25 – 7.19 (m, 1H), 7.16 (d, *J* = 7.8 Hz, 1H), 4.94 (dd, *J* = 10.6, 4.1 Hz, 1H), 2.84 – 2.50 (m, 3H), 2.28 – 1.82 (m, 3H); **^{13}C NMR** (75 MHz, $CDCl_3$): δ 170.2, 142.2, 140.1, 129.0, 127.6, 126.6, 126.2, 123.4, 53.9, 32.2, 27.3, 18.9; **ESI-HRMS:** *m/z* calculated for $[C_{12}H_{13}N_2O]^+$: 201.1022; found: 201.1020.

Chiral-phase SFC: Chiralcel IA, CO_2/MeOH 95:5 → 60:40, 3.0 ml/min, (λ = 280 nm)

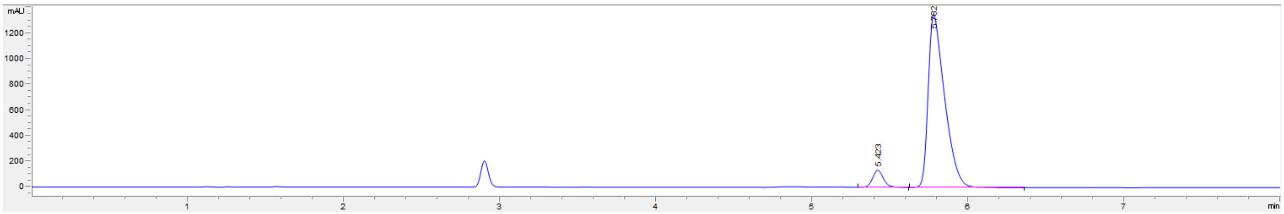
Racemic:

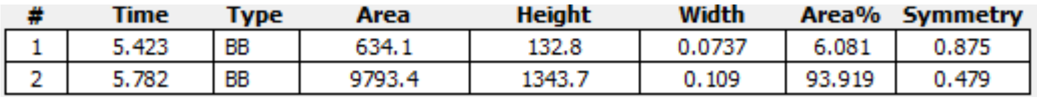




#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.416	BB	1916.9	397.3	0.0743	49.781	0.816
2	5.854	BB	1933.7	317.7	0.093	50.219	0.71

Enantioselective:

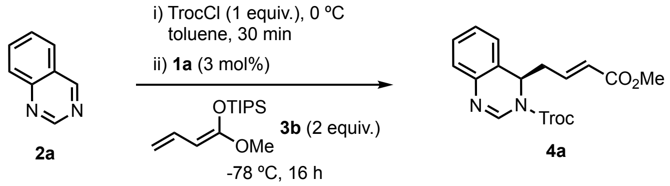


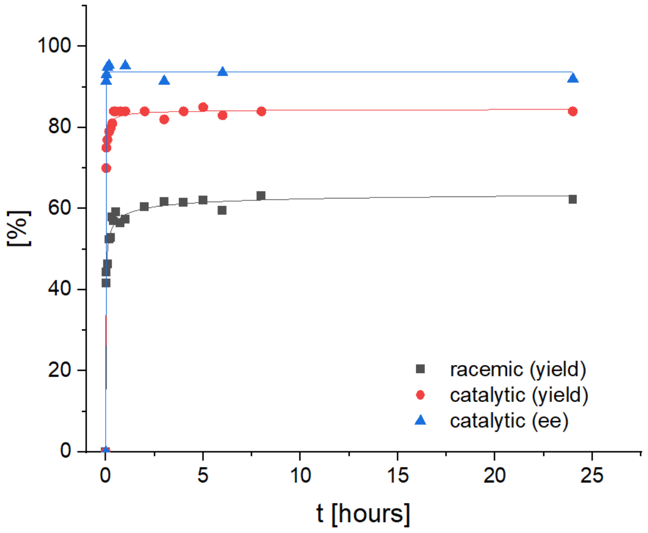


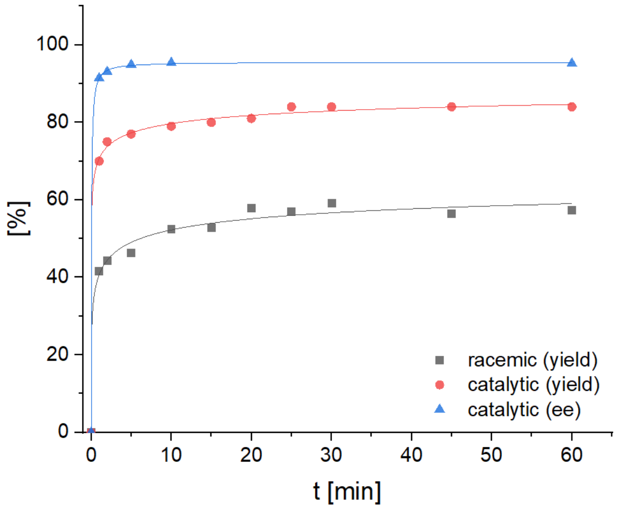
#	Time	Type	Area	Height	Width	Area%	Symmetry
1	5.423	BB	634.1	132.8	0.0737	6.081	0.875
2	5.782	BB	9793.4	1343.7	0.109	93.919	0.479

8. Kinetic Study

The kinetic study was carried out for the model reaction between quinazoline (**2a**) (130.0 mg, 1.00 mmol, 1.0 equiv.) and dienolate **3a** (471.0 µL, 2.00 mmol, 2.0 equiv.) in presence and absence of catalyst **1a** (33.6 mg, 0.03 mmol, 3 mol%). The aliquots were quenched by addition of aq. HCl (1 M), extracted with EtOAc and dried over $MgSO_4$. After removal of the solvent under reduced pressure, the yield was determined by ^1H NMR analysis using 1,3,5-trimethoxybenzene as internal standard, and the enantiomeric excess was determined by chiral SFC using Chiralcel IG, CO_2/MeOH (98:2 → 65:35), 2.0 ml/min.

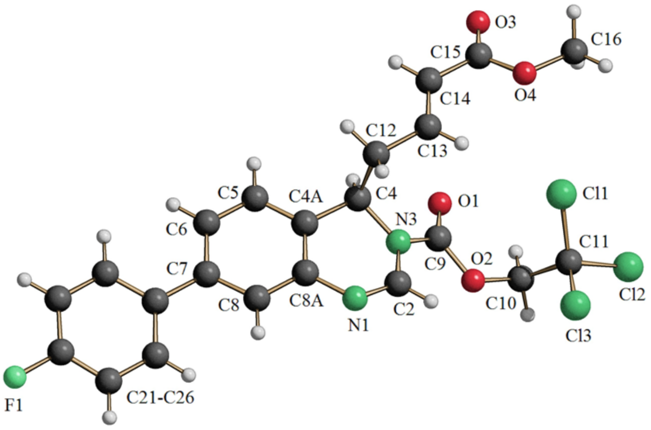






9. X-Ray Crystal Structure Analysis of 4k

CCDC Nr.: 2069596



Chemical formula	$C_{22}H_{18}Cl_3FN_2O_4$	
Formula weight	499.73 g/mol	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal size	0.053 x 0.102 x 0.192 mm	
Crystal habit	colorless plate	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 6.0314(3) Å	α = 90°
	b = 7.4369(3) Å	β = 92.818(2)°
	c = 23.9241(10) Å	γ = 90°
Volume	1071.82(8) $Å^3$	
Z	2	
Density (calculated)	1.548 g/cm^3	
Absorption coefficient	0.470 mm^{-1}	
F(000)	512	

A colourless plate-like specimen of $C_{22}H_{18}Cl_3FN_2O_4$, approximate dimensions 0.053 mm x 0.102 mm x 0.192 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured on a Bruker D8 Venture Bruker D8 Venture Photon III Diffractometer system equipped with a micro focus tube MoKα (MoKα, λ = 0.71073 Å) and a MX mirror monochromator.

A total of 510 frames were collected. The total exposure time was 3.54 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 20681 reflections to a maximum θ angle of 26.78° (0.79 Å resolution), of which 4559 were independent (average redundancy 4.536, completeness = 99.6%, R_{int} = 3.92%, R_{sig} = 2.97%) and 4388 (96.25%) were greater than $2\sigma(F^2)$. The final cell constants of a = 6.0314(3) Å, b = 7.4369(3) Å, c = 23.9241(10) Å, β = 92.818(2)°, volume = 1071.82(8) $Å^3$, are based upon the refinement of the XYZ-centroids of 9738 reflections above 20 σ(I) with 5.114° < 2θ < 53.52°. Data were corrected for absorption effects using the multi-scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.939. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.9150 and 0.9760.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group $P2_1$, with Z = 2 for the formula unit, $C_{22}H_{18}Cl_3FN_2O_4$. The final anisotropic full-matrix least-squares refinement on F^2 with 290 variables converged at R1 = 2.44%, for the observed data and wR^2 = 5.67% for all data. The goodness-of-fit was 1.031. The largest peak in the final difference electron density synthesis was 0.207 $e^-/Å^3$ and the largest hole was -0.195 $e^-/Å^3$ with an RMS deviation of 0.039 $e^-/Å^3$. On the basis of the final model, the calculated density was 1.548 g/cm^3 and F(000), 512 e^-.

Flack parameter was refined to -0.026(19).

10. References

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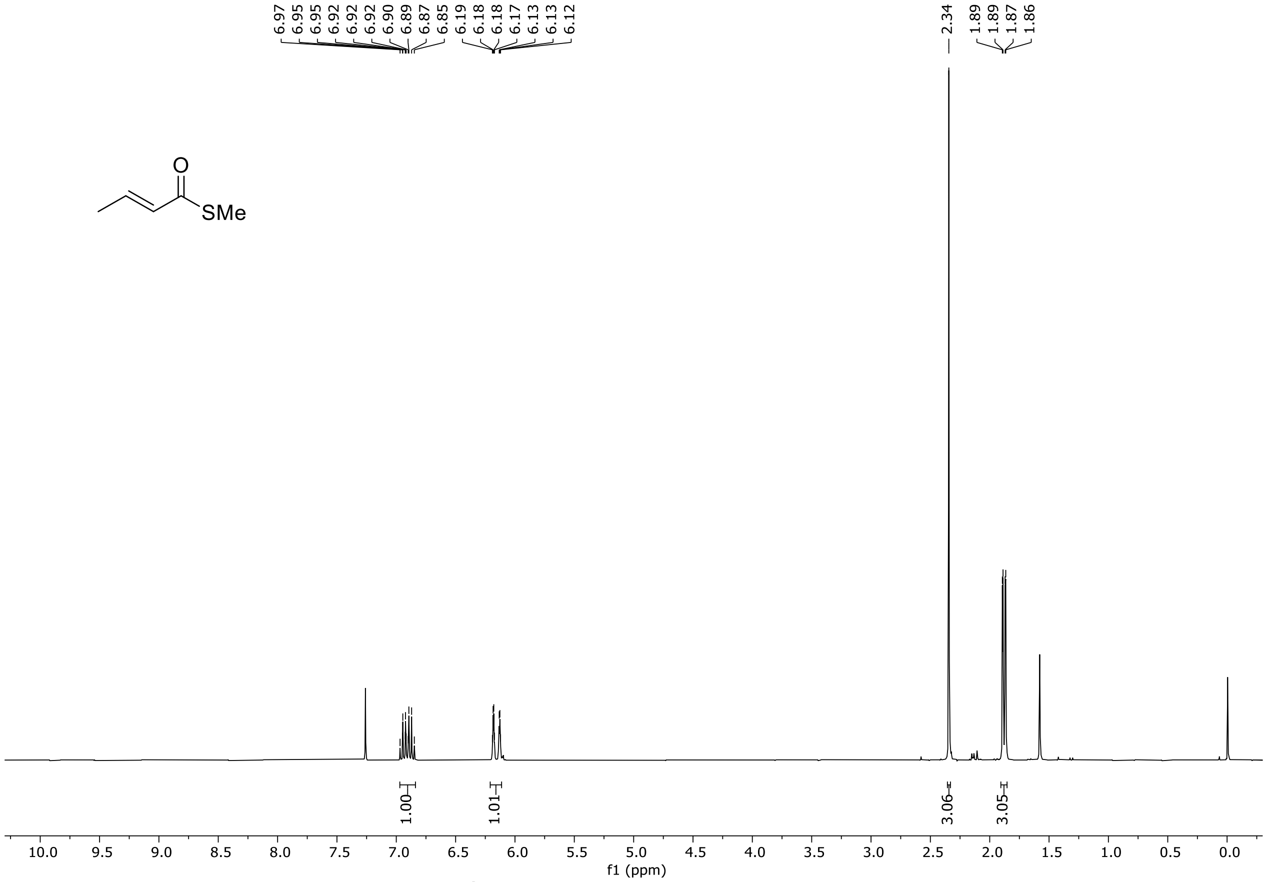
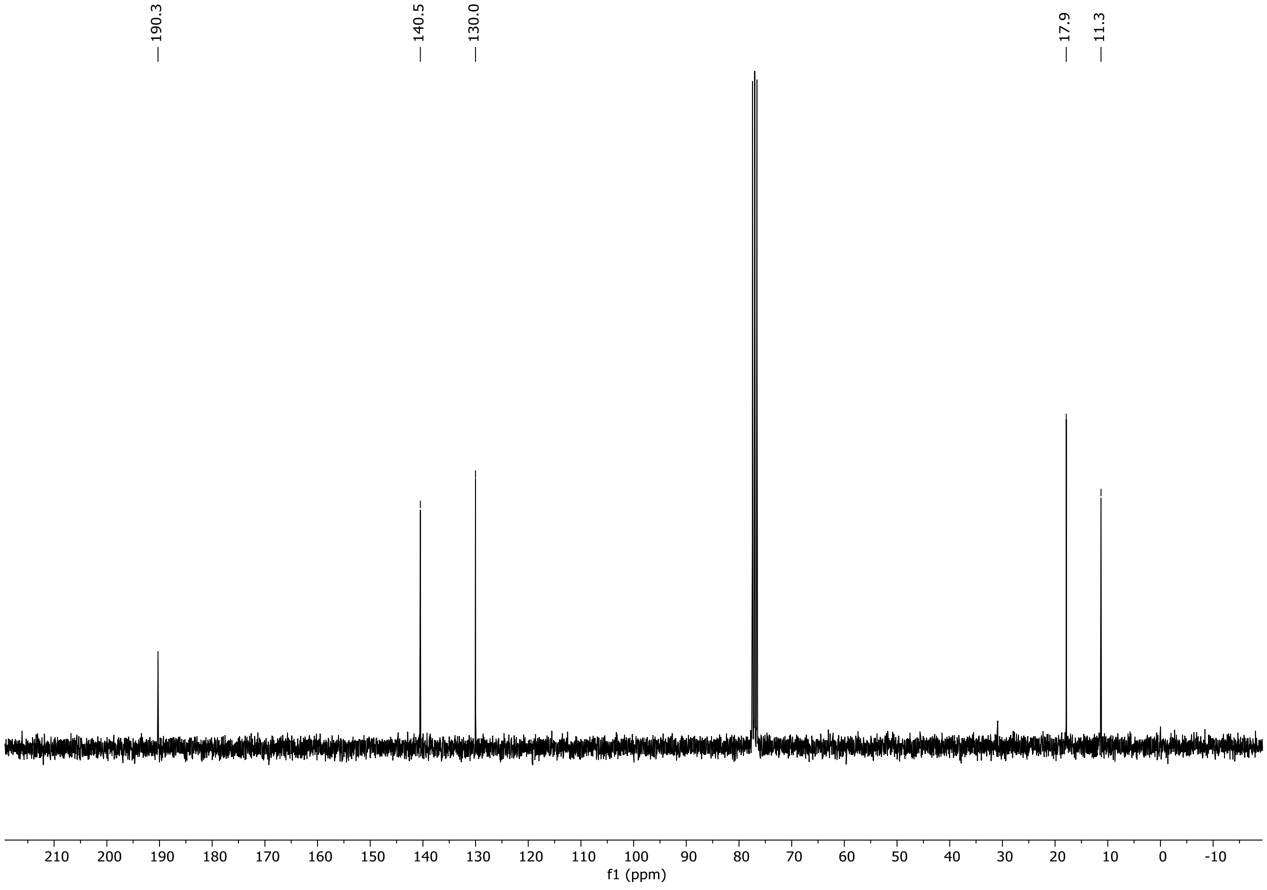
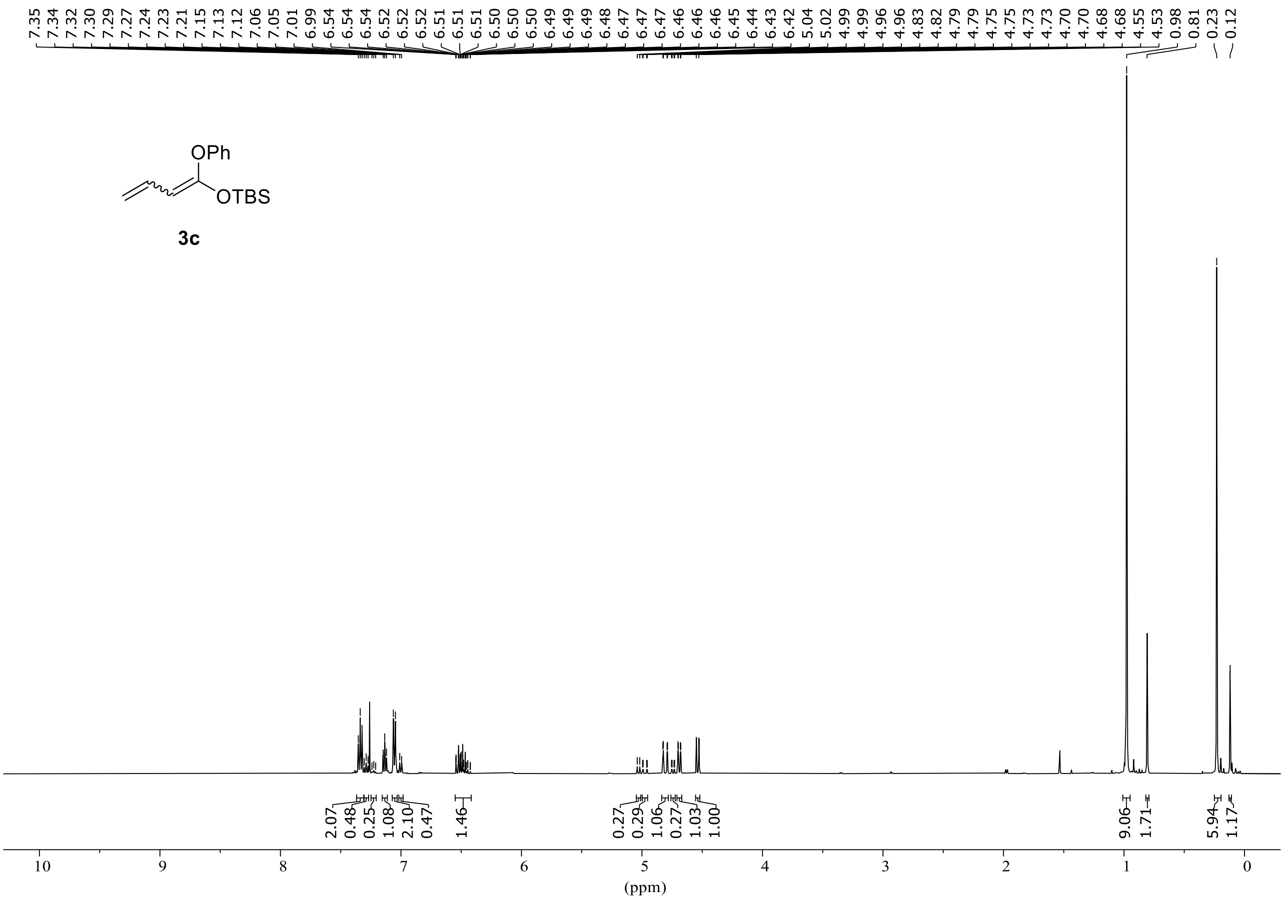
11. NMR Collection



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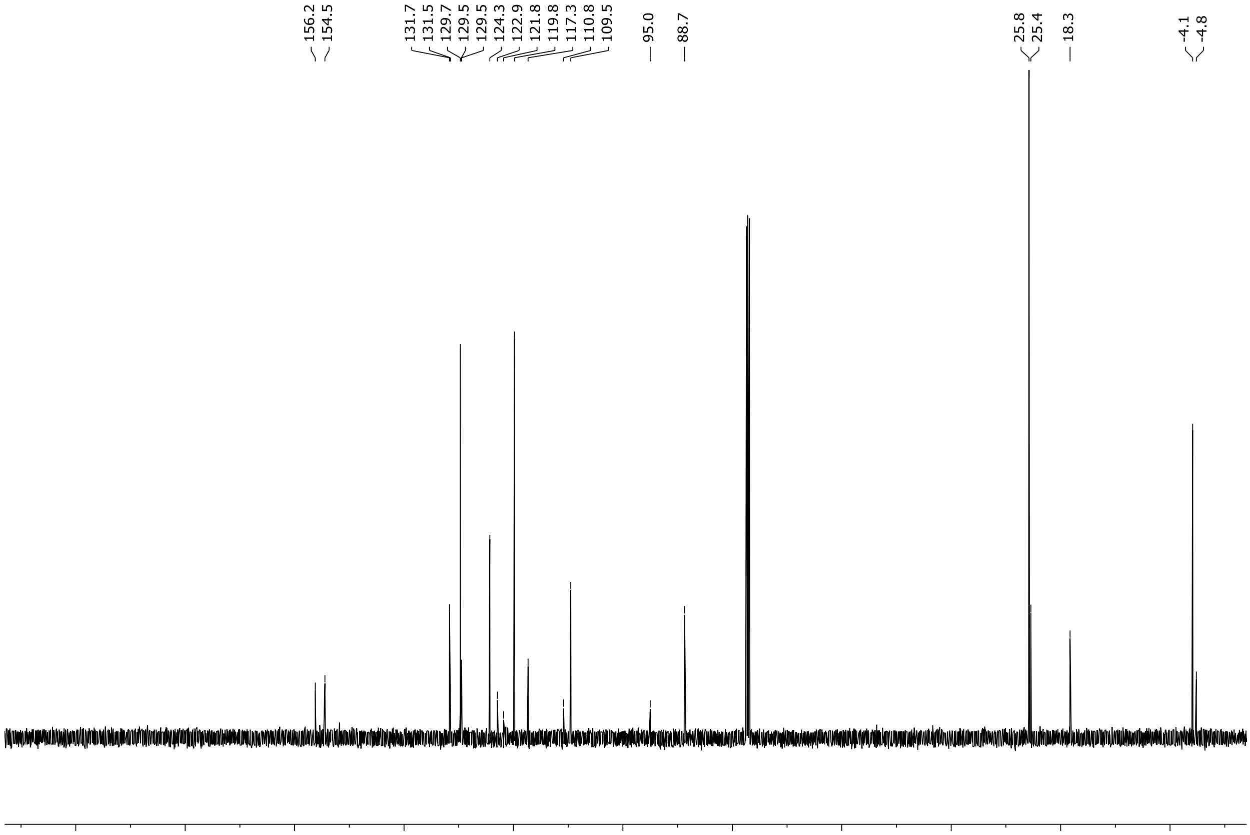
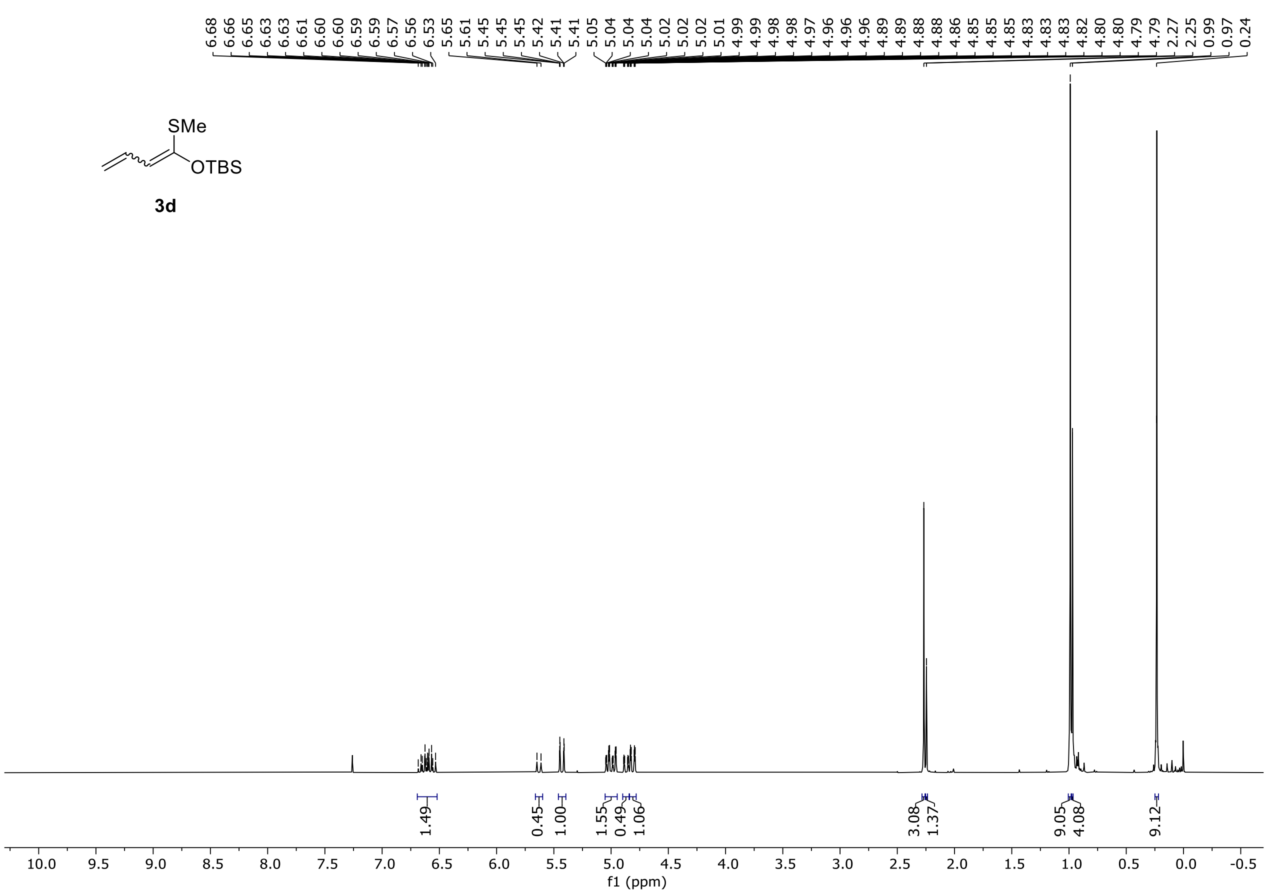
OTBS
3c
7.35 7.34 7.32 7.30 7.29 7.27 7.24 7.23 7.21 7.15 7.13 7.12 7.06 7.05 7.01 6.99 6.54 6.54 6.54 6.52 6.52 6.51 6.51 6.51 6.50 6.50 6.49 6.49 6.48 6.47 6.47 6.47 6.46 6.46 6.46 6.45 6.44 6.43 6.42 5.04 5.02 4.99 4.99 4.96 4.96 4.83 4.82 4.79 4.79 4.75 4.75 4.73 4.73 4.70 4.70 4.68 4.68 4.55 4.53 0.98 0.81 0.23 0.12
2.07 0.48 0.25 1.08 2.10 0.47 1.46 0.27 0.29 1.06 0.27 1.03 1.00 9.06 1.71 5.94 1.17
10 9 8 7 6 5 4 3 2 1 0
(ppm)


156.2 154.5 131.7 131.5 129.7 129.5 129.5 124.3 122.9 121.8 119.8 117.3 110.8 109.5 95.0 88.7 25.8 25.4 18.3 -4.1 -4.8
200 180 160 140 120 100 80 60 40 20 0
(ppm)


SMe
OTBS

3d

6.68
6.66
6.65
6.63
6.63
6.61
6.60
6.60
6.59
6.59
6.57
6.56
6.53
5.65
5.61
5.45
5.45
5.45
5.42
5.41
5.41
5.05
5.04
5.04
5.04
5.02
5.02
5.02
5.01
4.99
4.99
4.98
4.98
4.97
4.96
4.96
4.96
4.89
4.89
4.88
4.88
4.86
4.85
4.85
4.85
4.83
4.83
4.83
4.82
4.80
4.80
4.79
4.79
2.27
2.25
0.99
0.97
0.24
1.49
0.45
1.00
1.55
0.49
1.06
3.08
1.37
9.05
4.08
9.12
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
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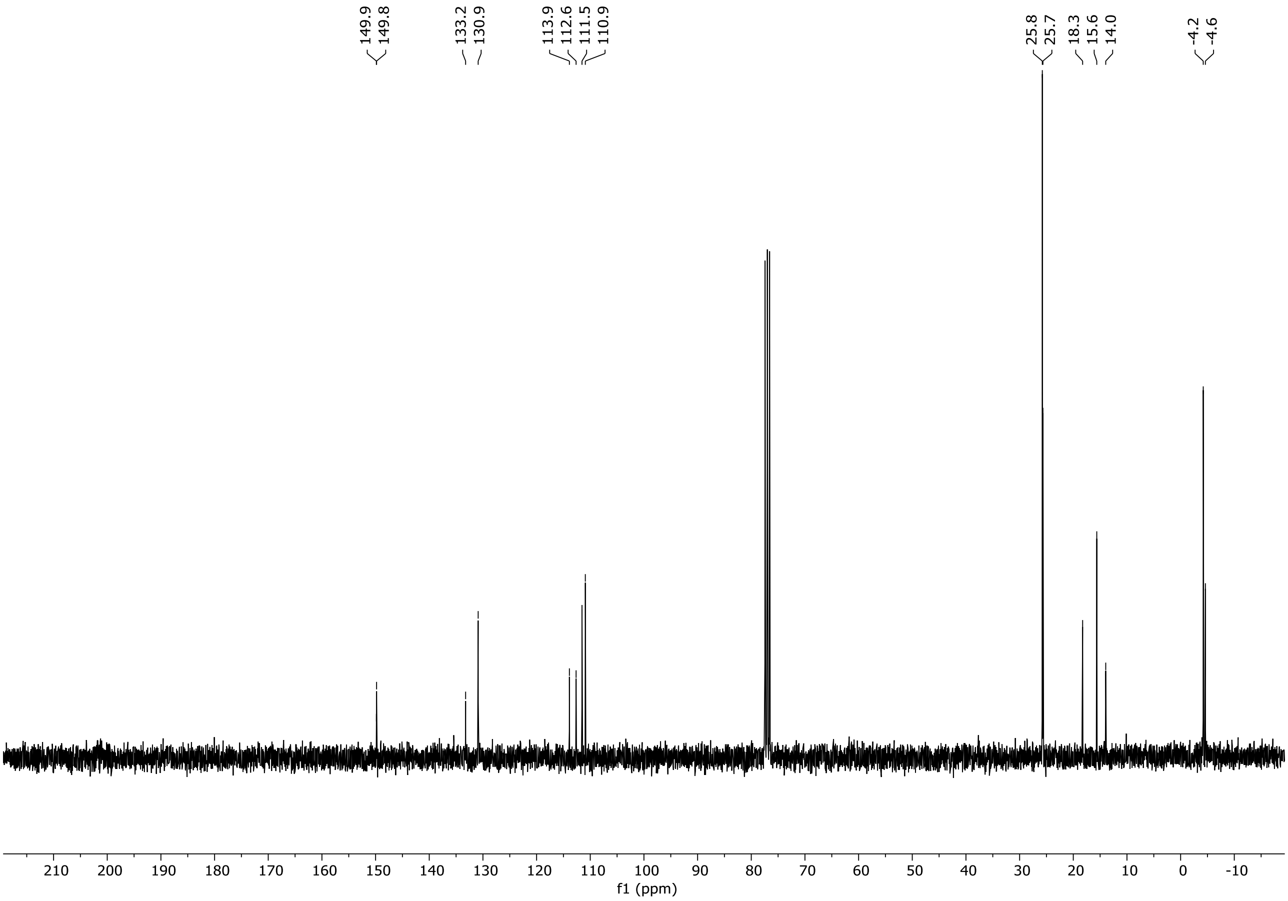
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)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110.9
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25.7
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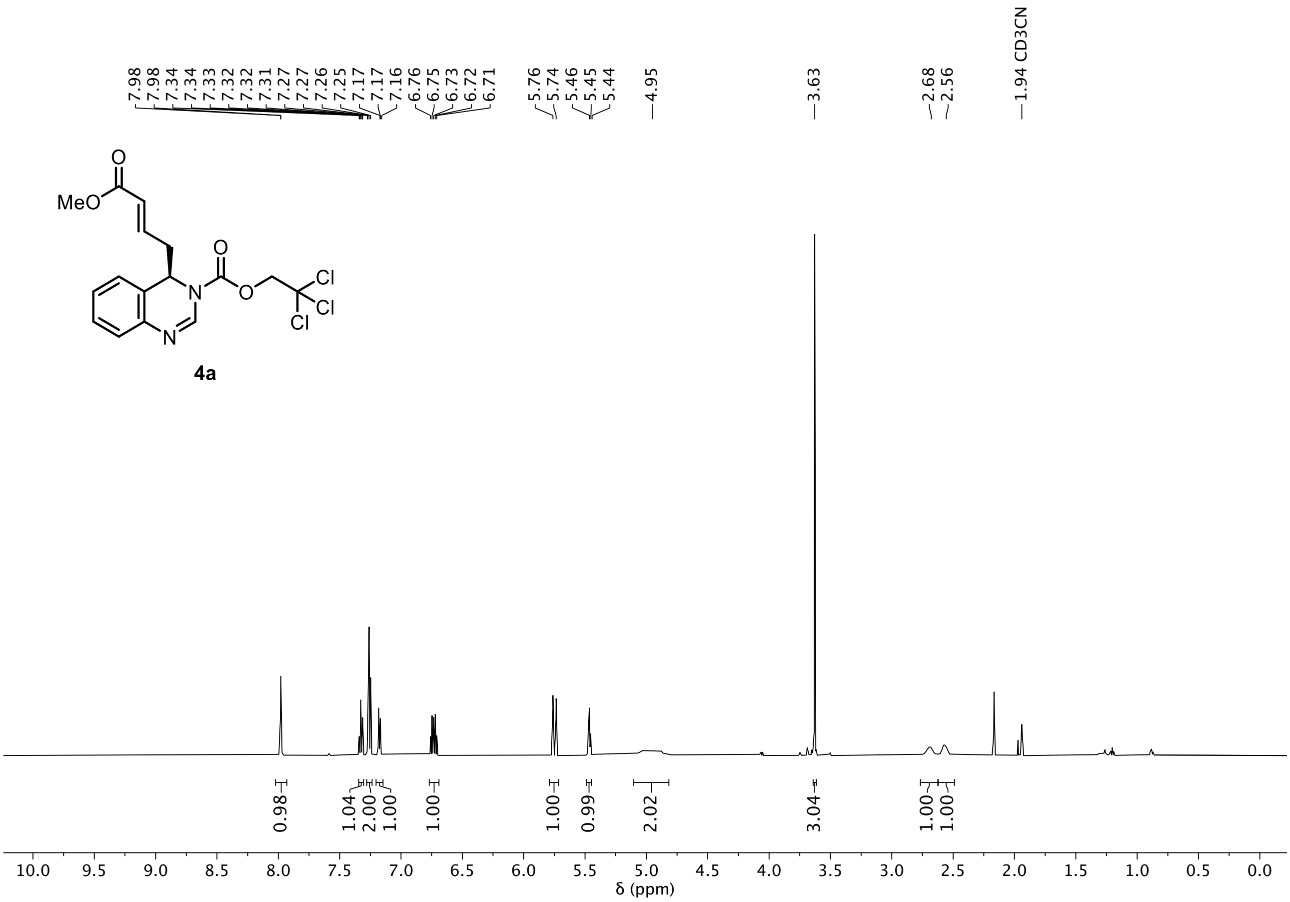
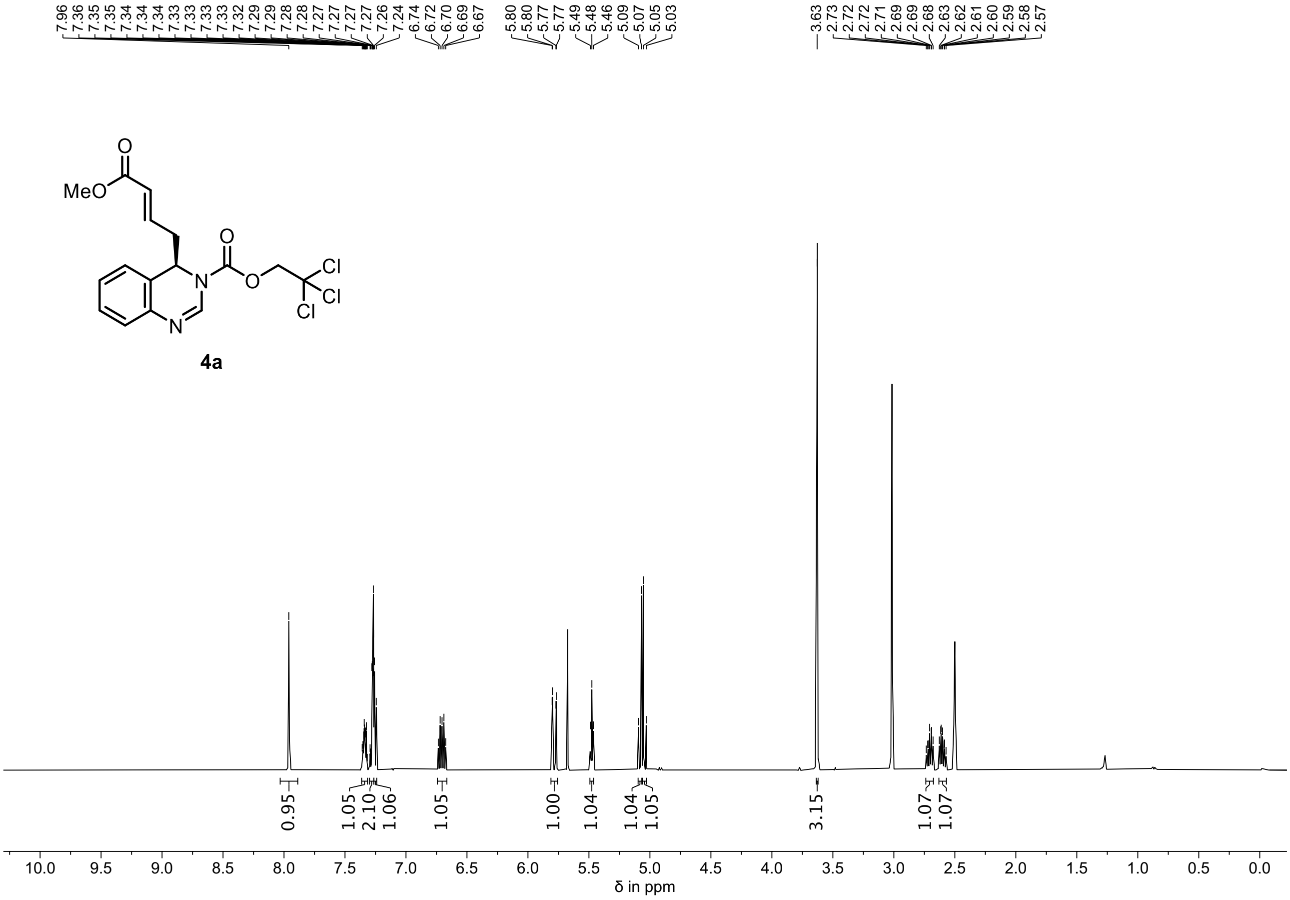
14.0
-4.2
-4.6
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

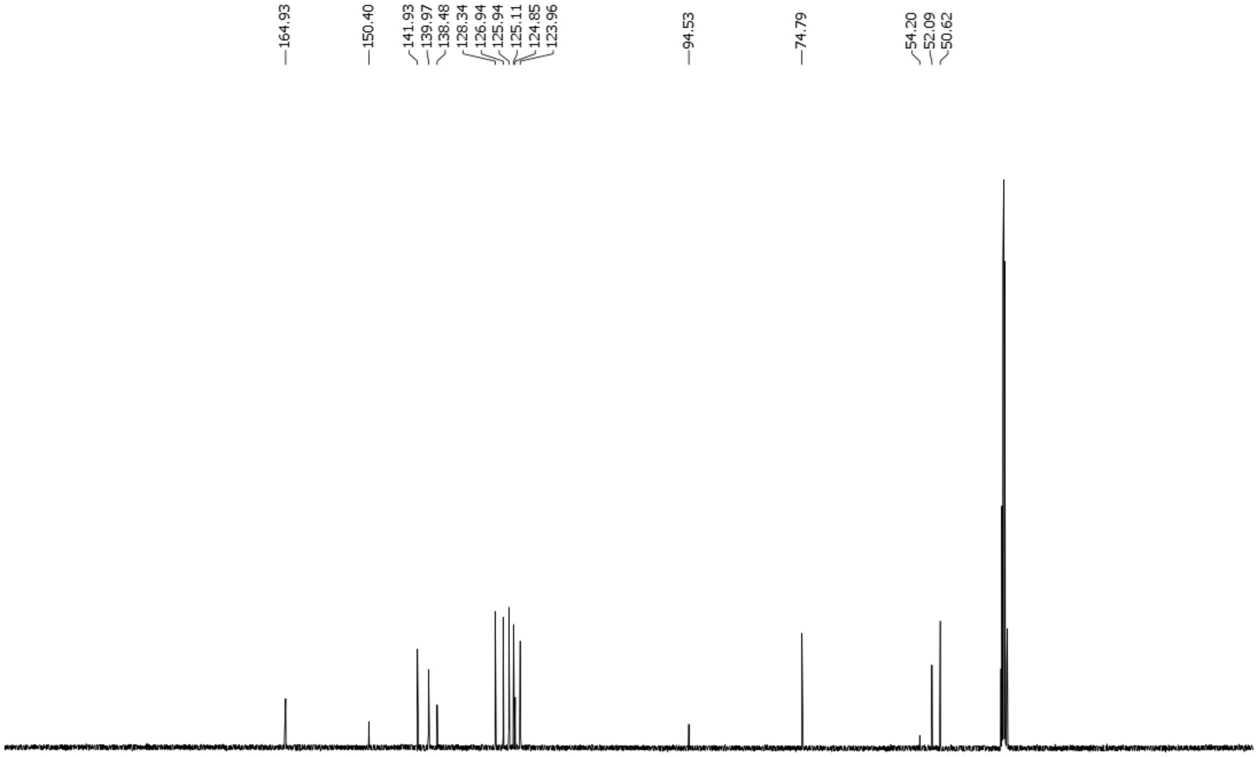
4a (MeCN-d_3, 25 °C):



Due to the presence of Troc-rotamers, broad signals in ^1H NMR and ^{13}C NMR were observed, which hampered the characterization of the products. In order to get more defined signals, most of the NMRs were later on measured and given in DMSO-d_6 at 90 °C (^1H NMR residual solvent peaks DMSO ~ 2.50 ppm, H_2O ~ 3.00 ppm), unless a strong and/or fast decomposition of the products takes place at this temperature during the NMR measurements. However, in some cases rotamer species are still present at 90 °C, leading to low intensity signals, in particular in ^{13}C NMR for the Troc C=O group at ~ 150-152 ppm, and the side chain and $Ar_{C\text{-}H}$ bonds close to this group.

4a (DMSO-d_6, 90 °C):





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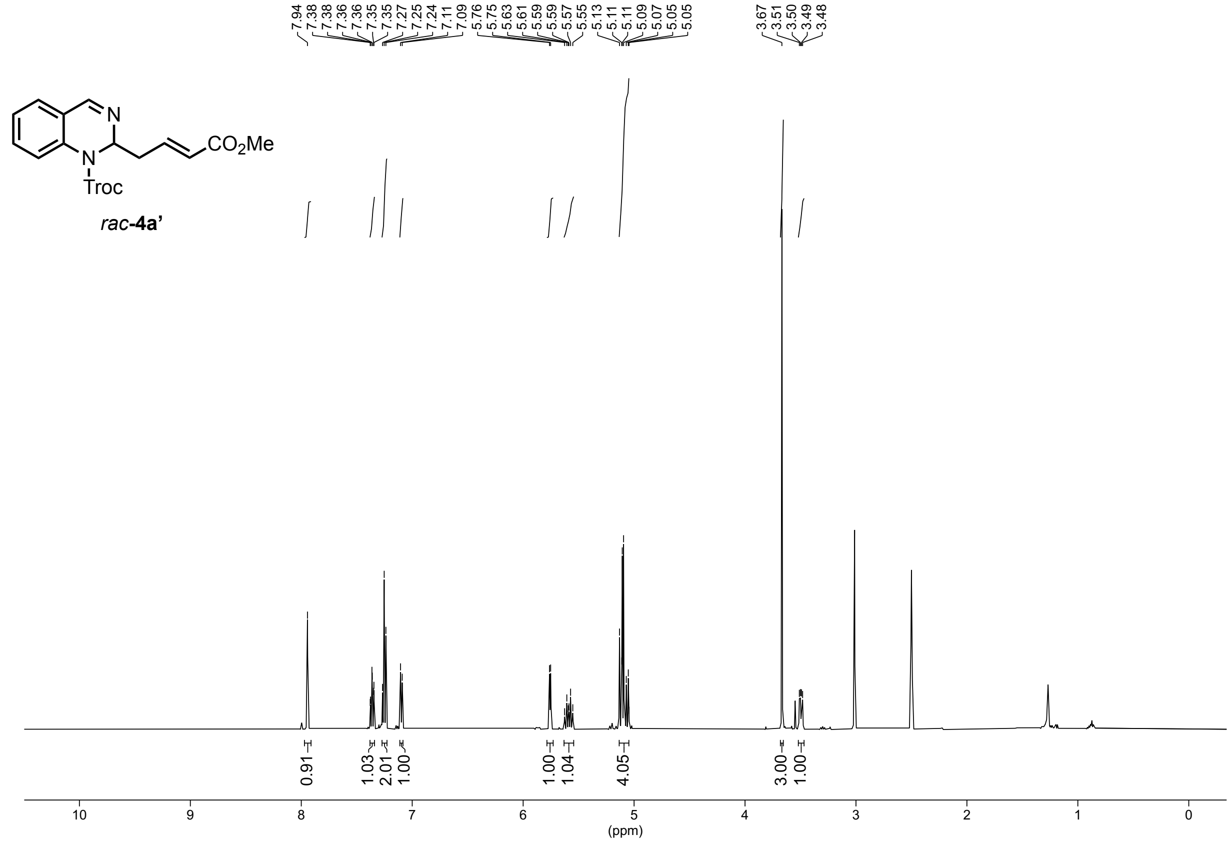
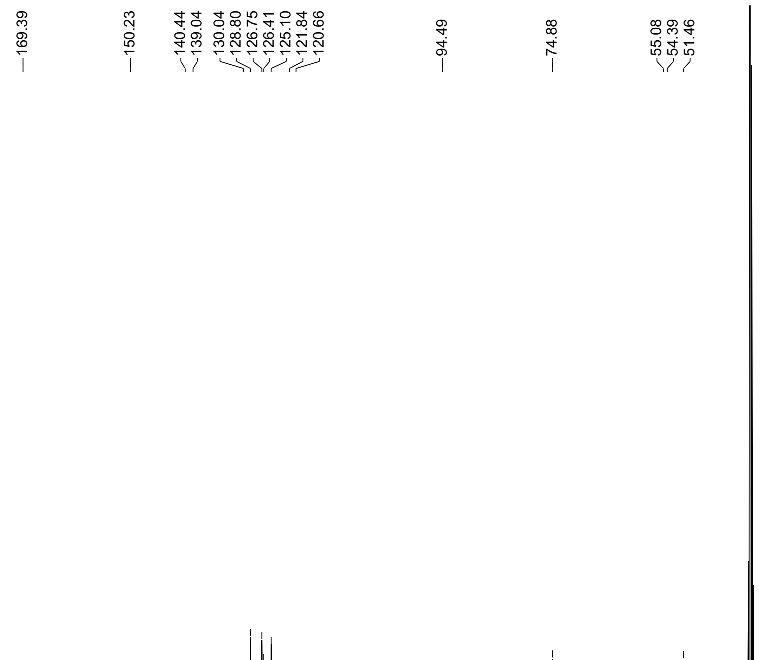
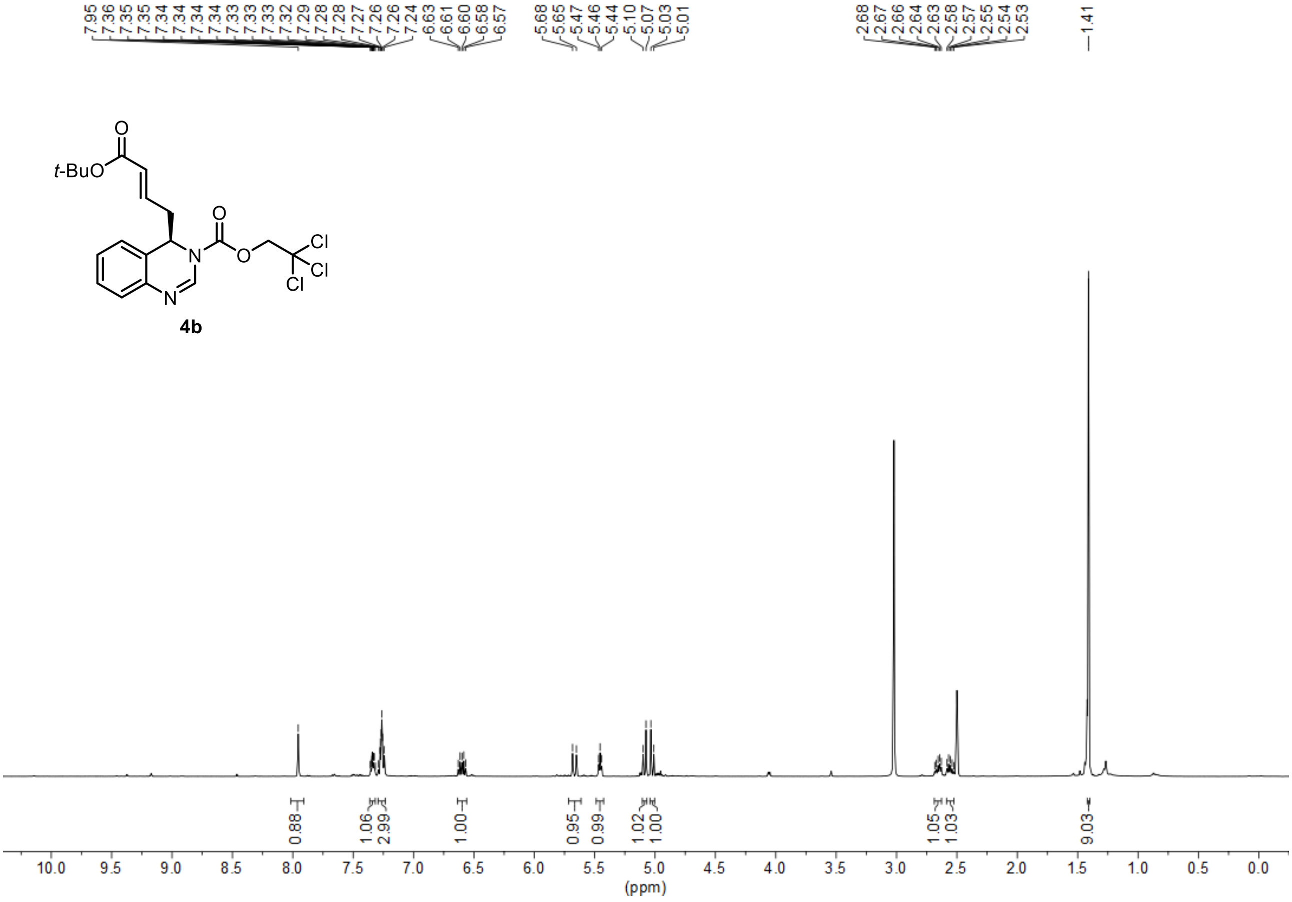
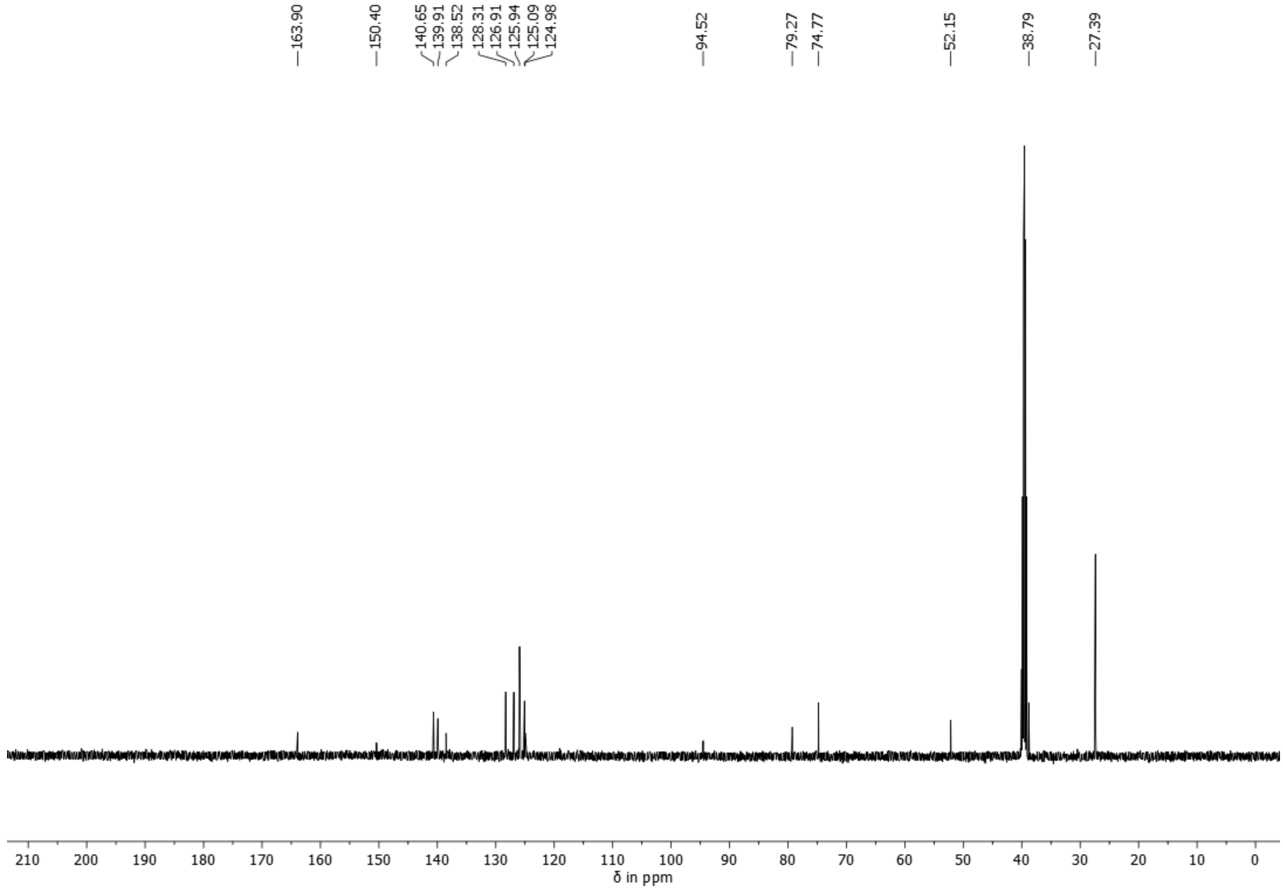


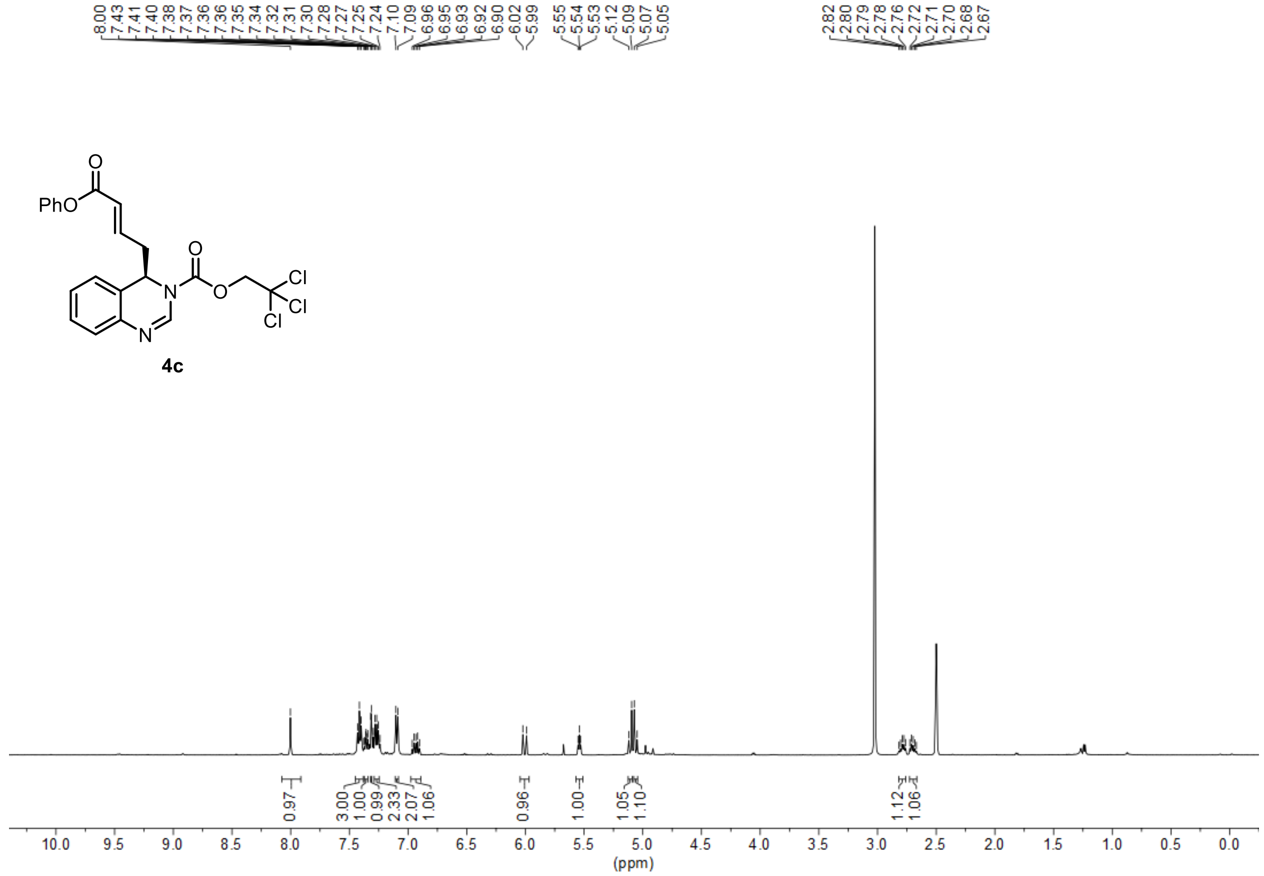


4b (DMSO-d$_6$, 90 °C):

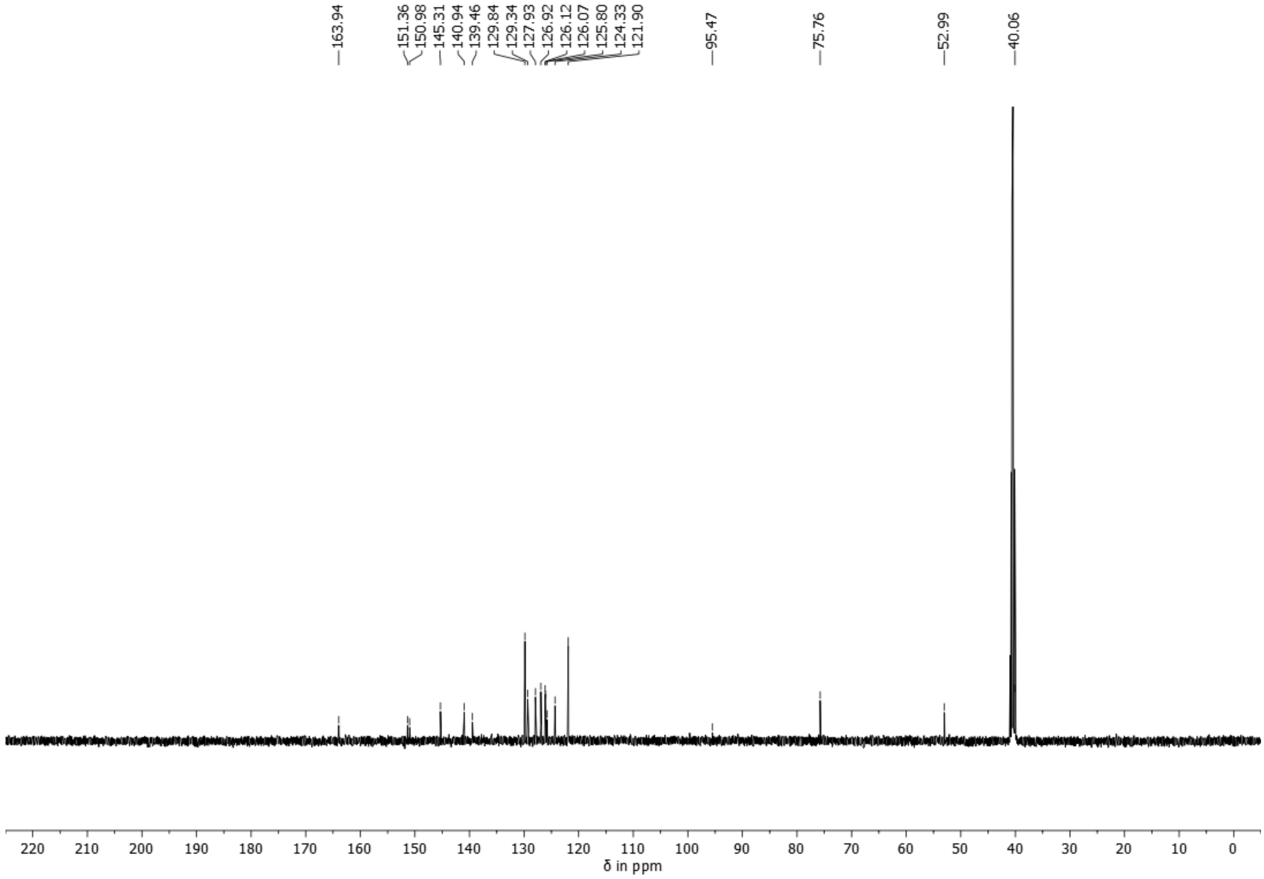




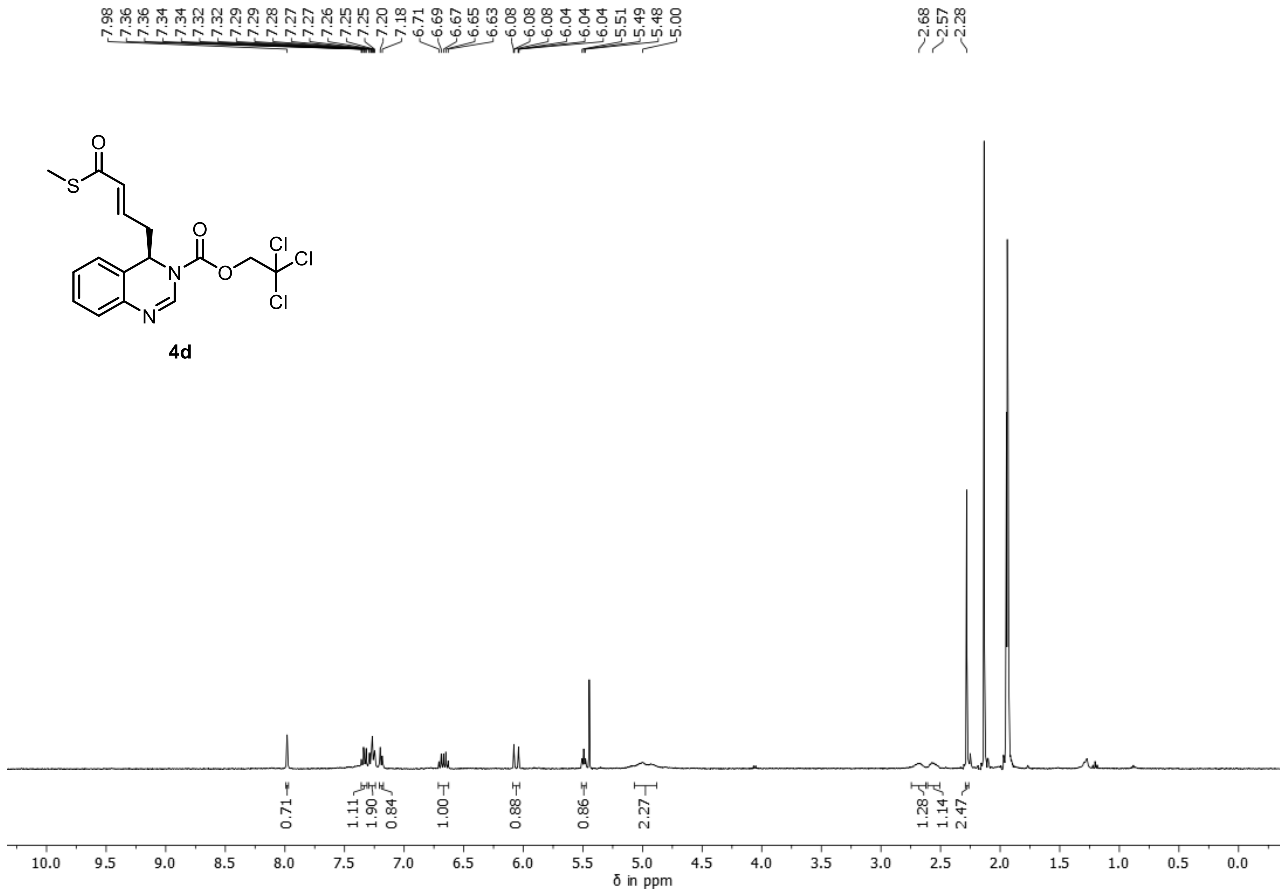
4c (DMSO-d_6, 90 °C):

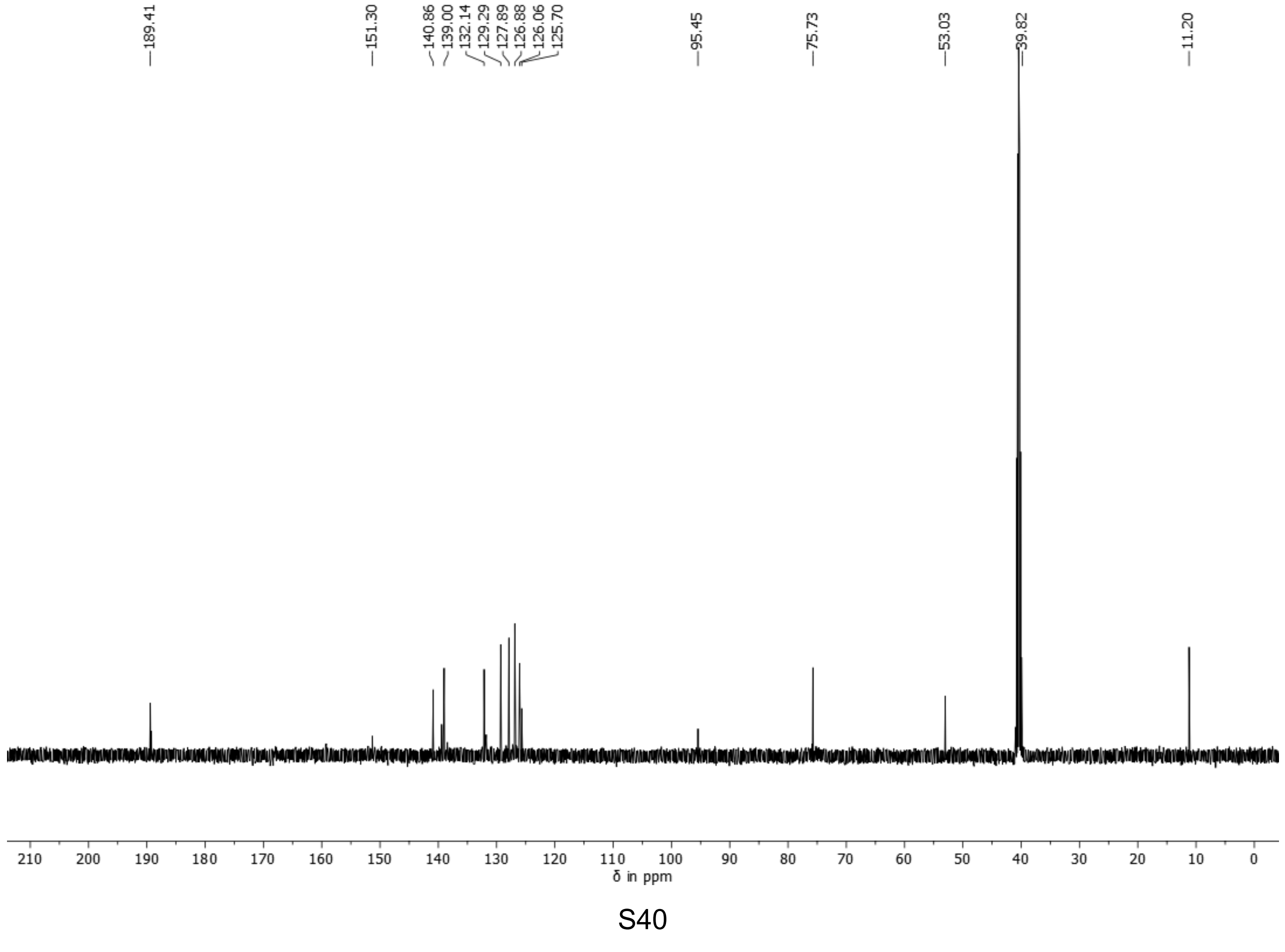


4c



4d (MeCN-d_3, 25 °C): broad signals due Troc-rotamers





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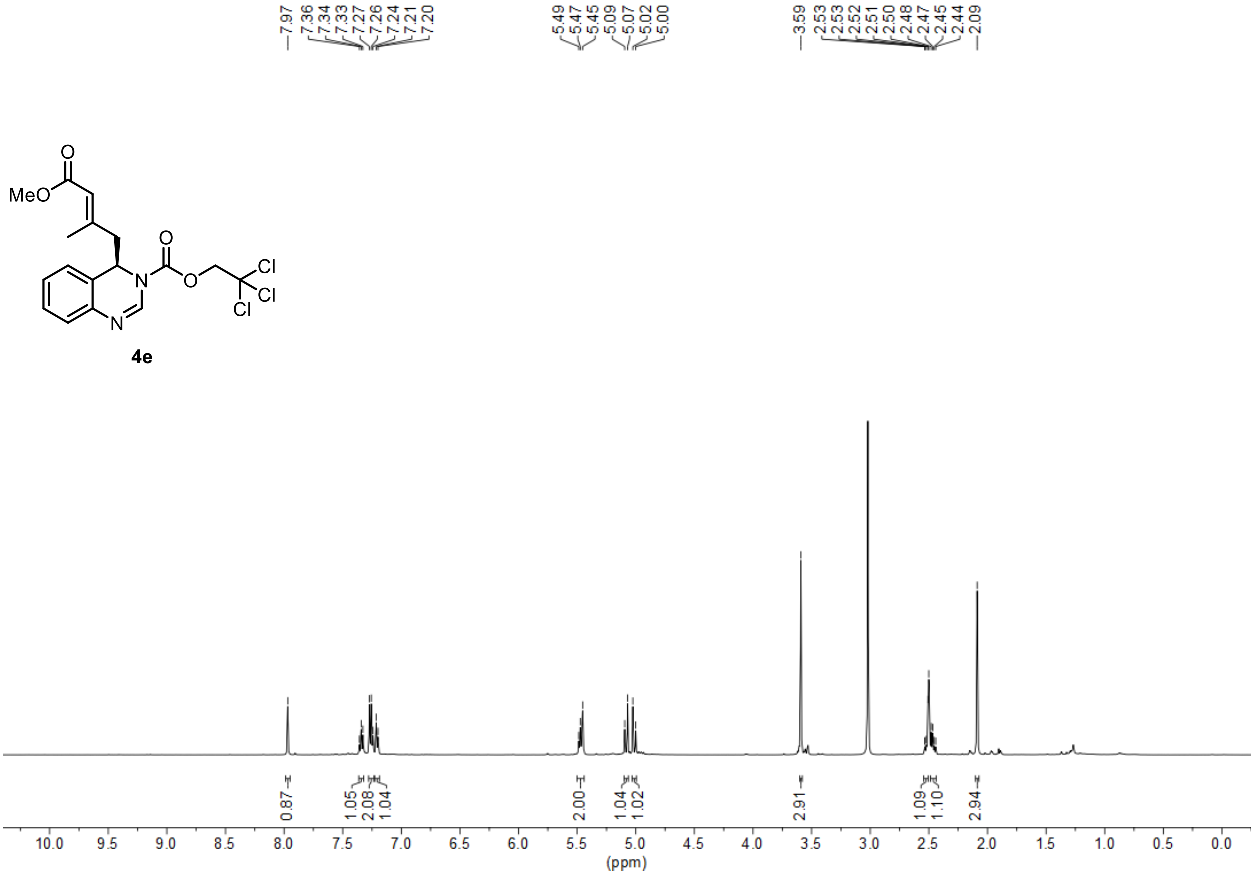
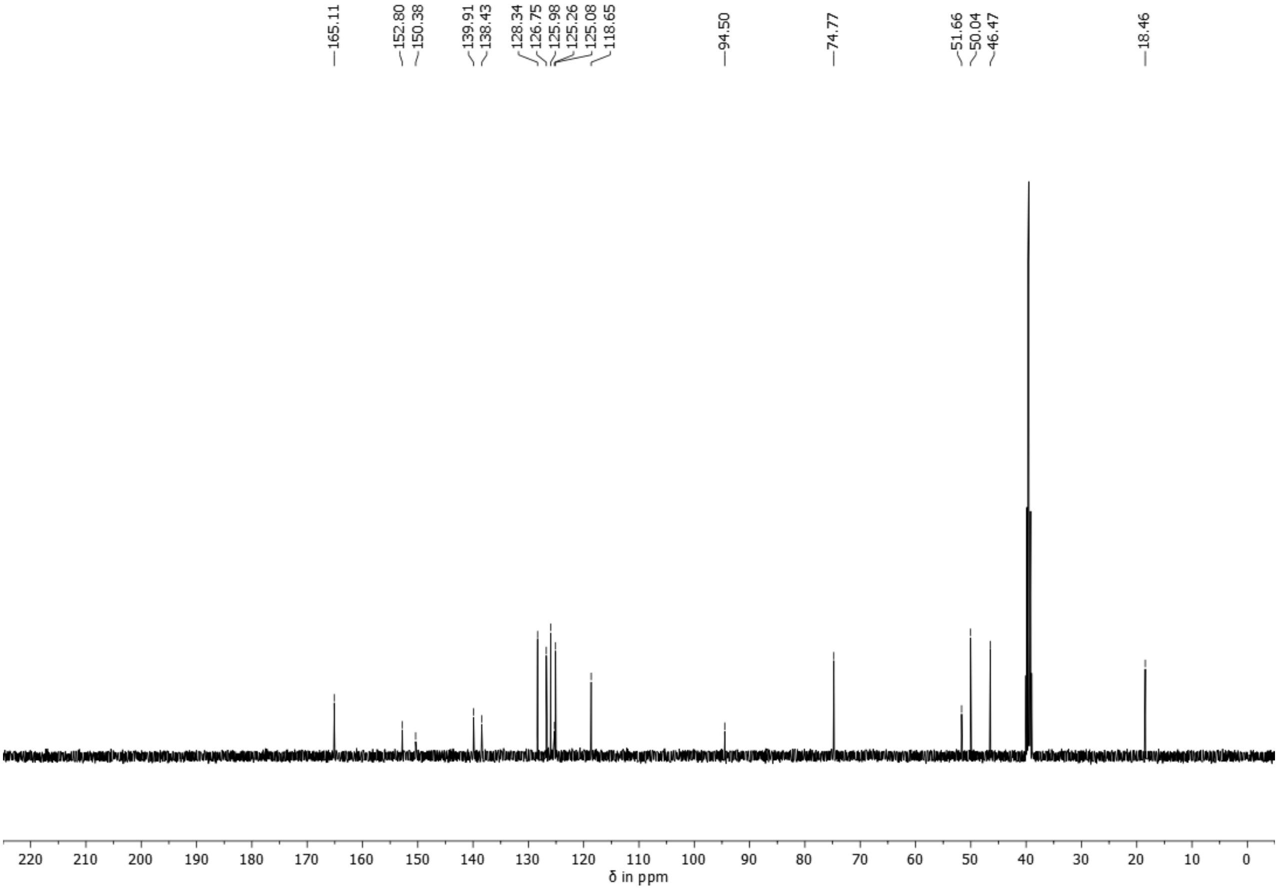


4e



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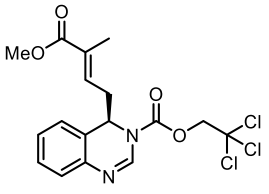
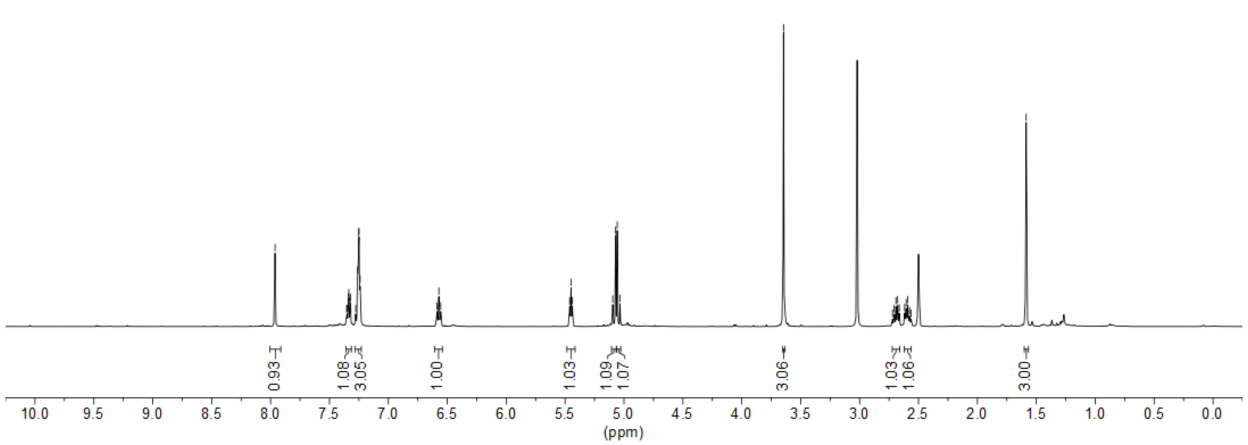
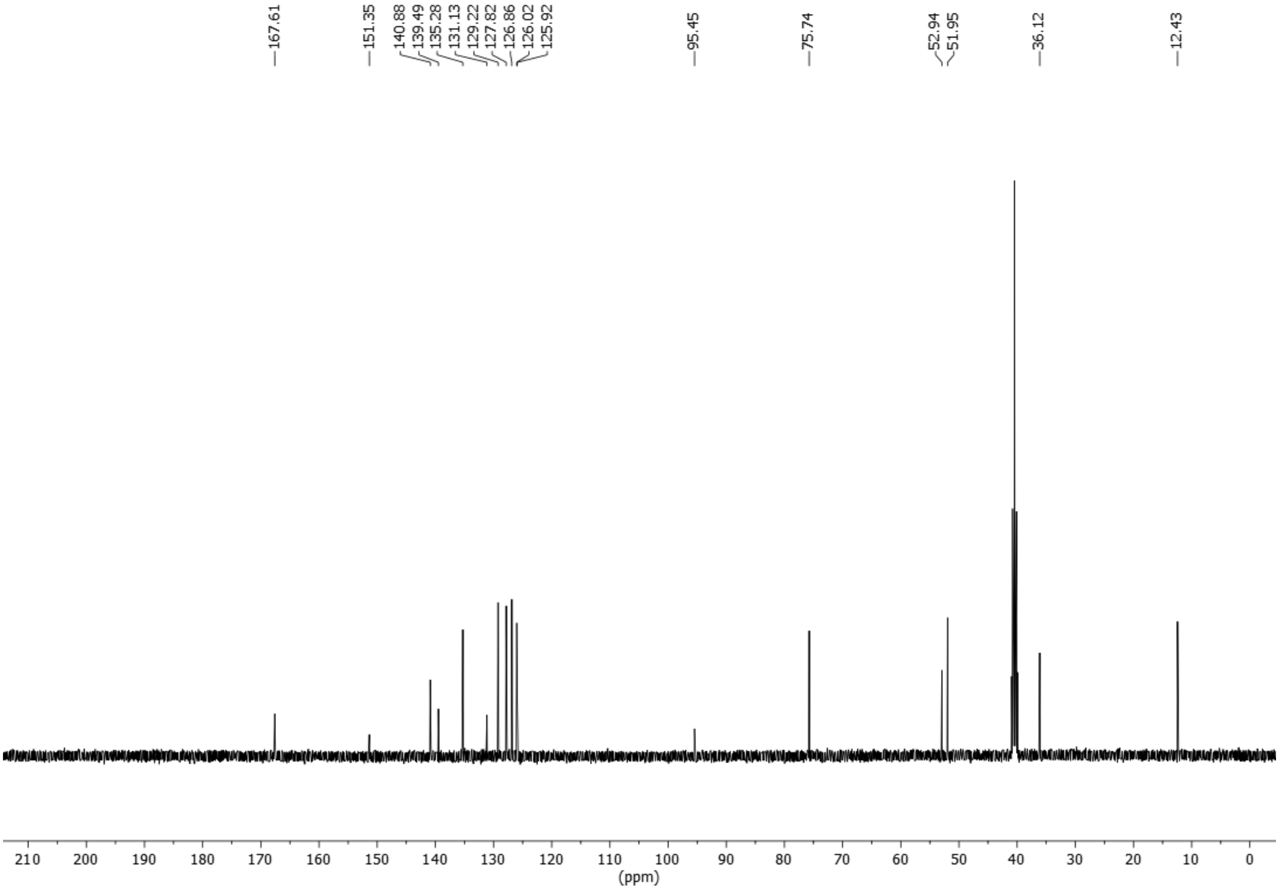


4f





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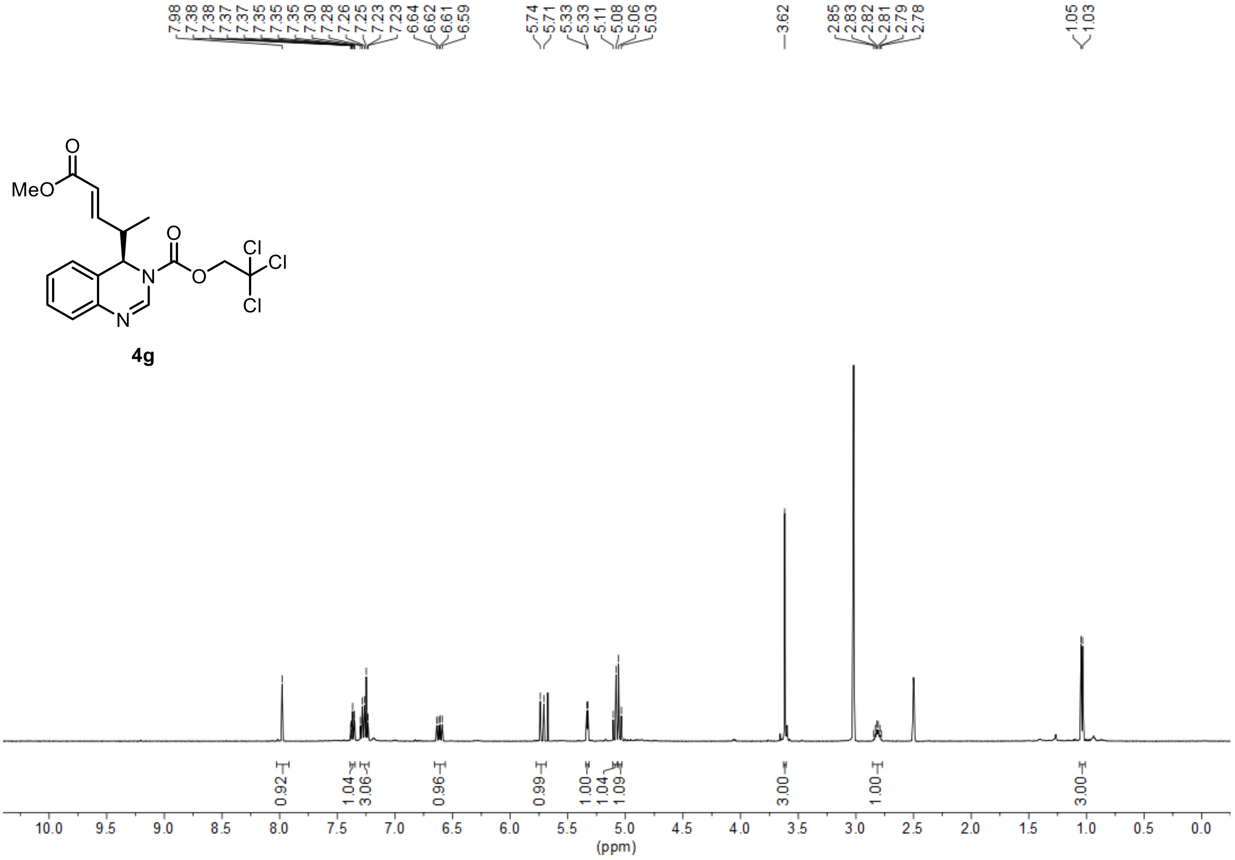

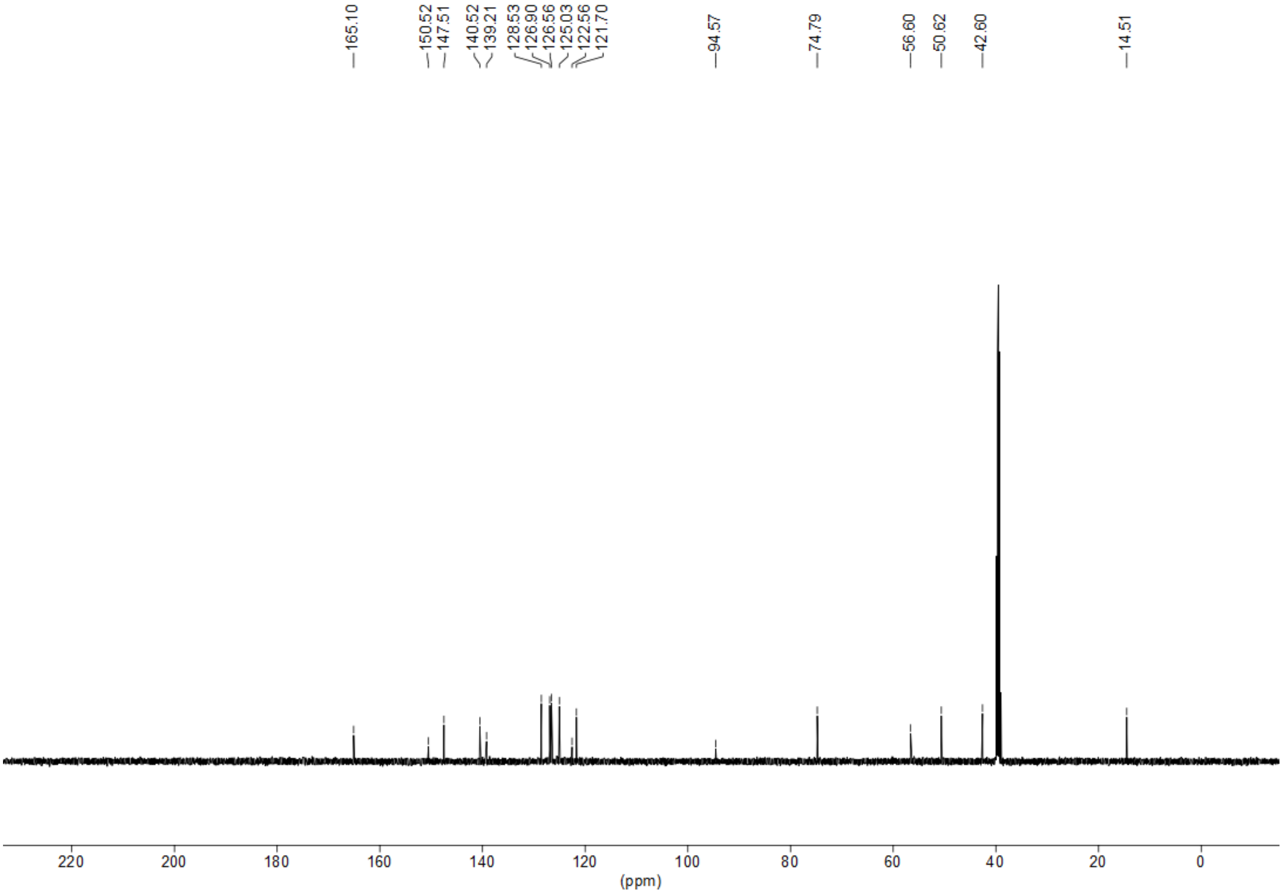

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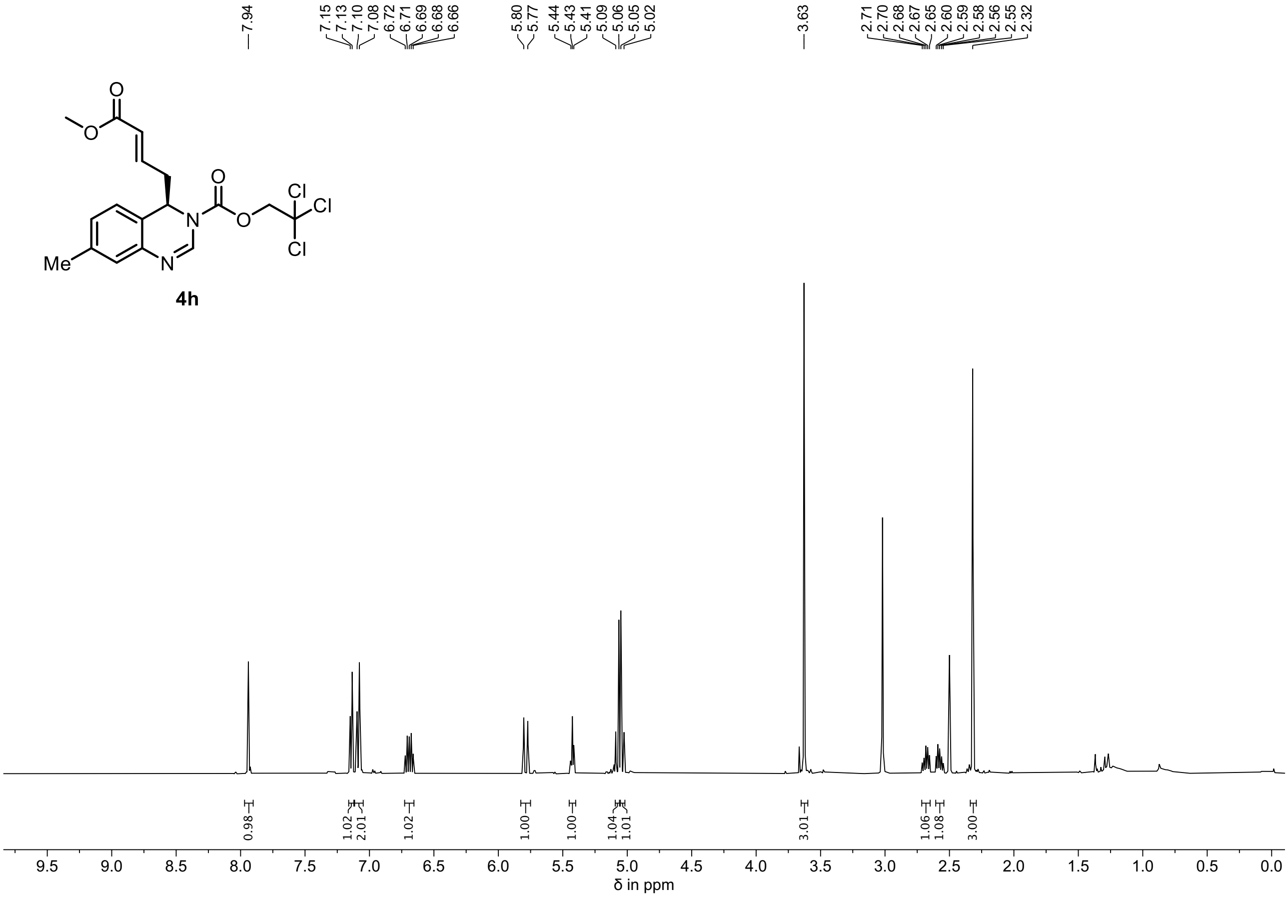

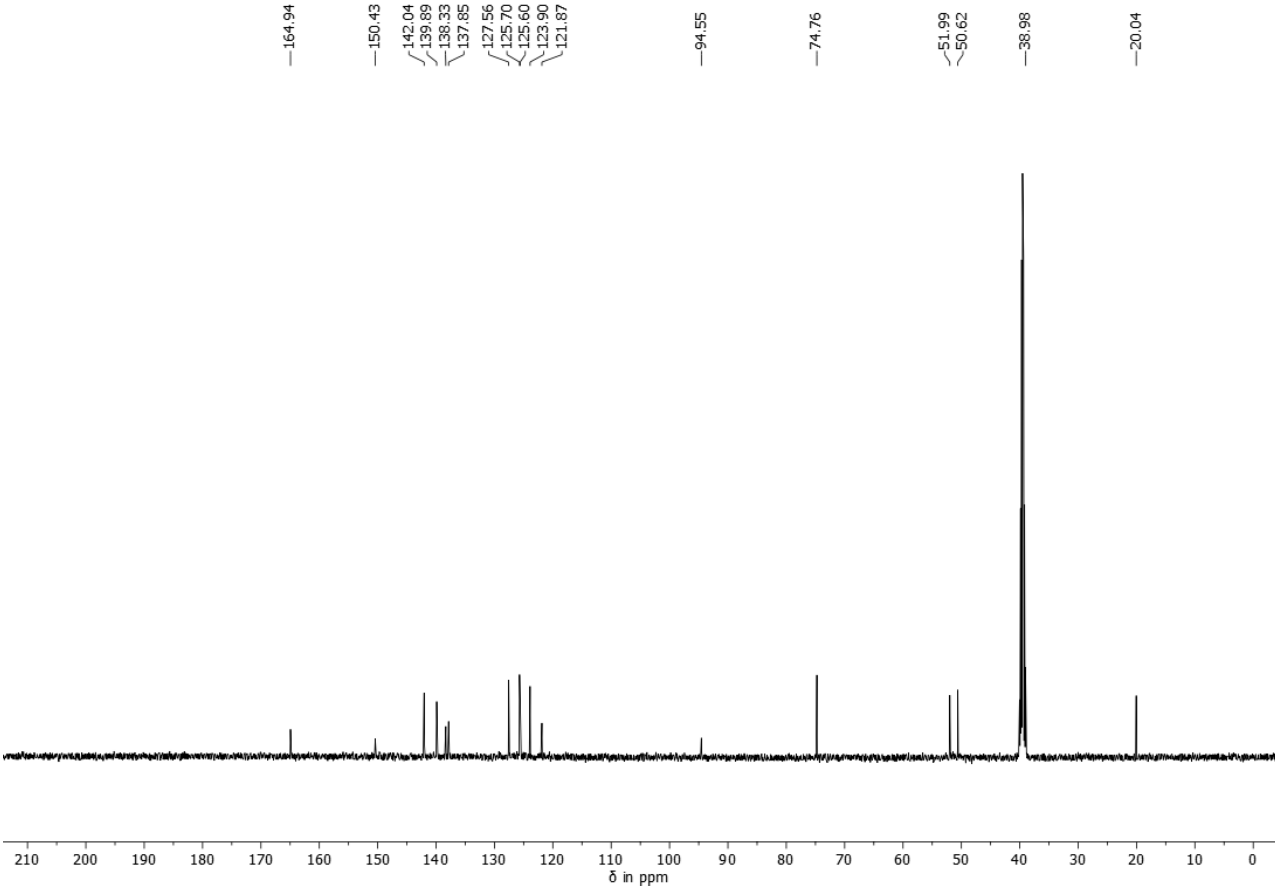

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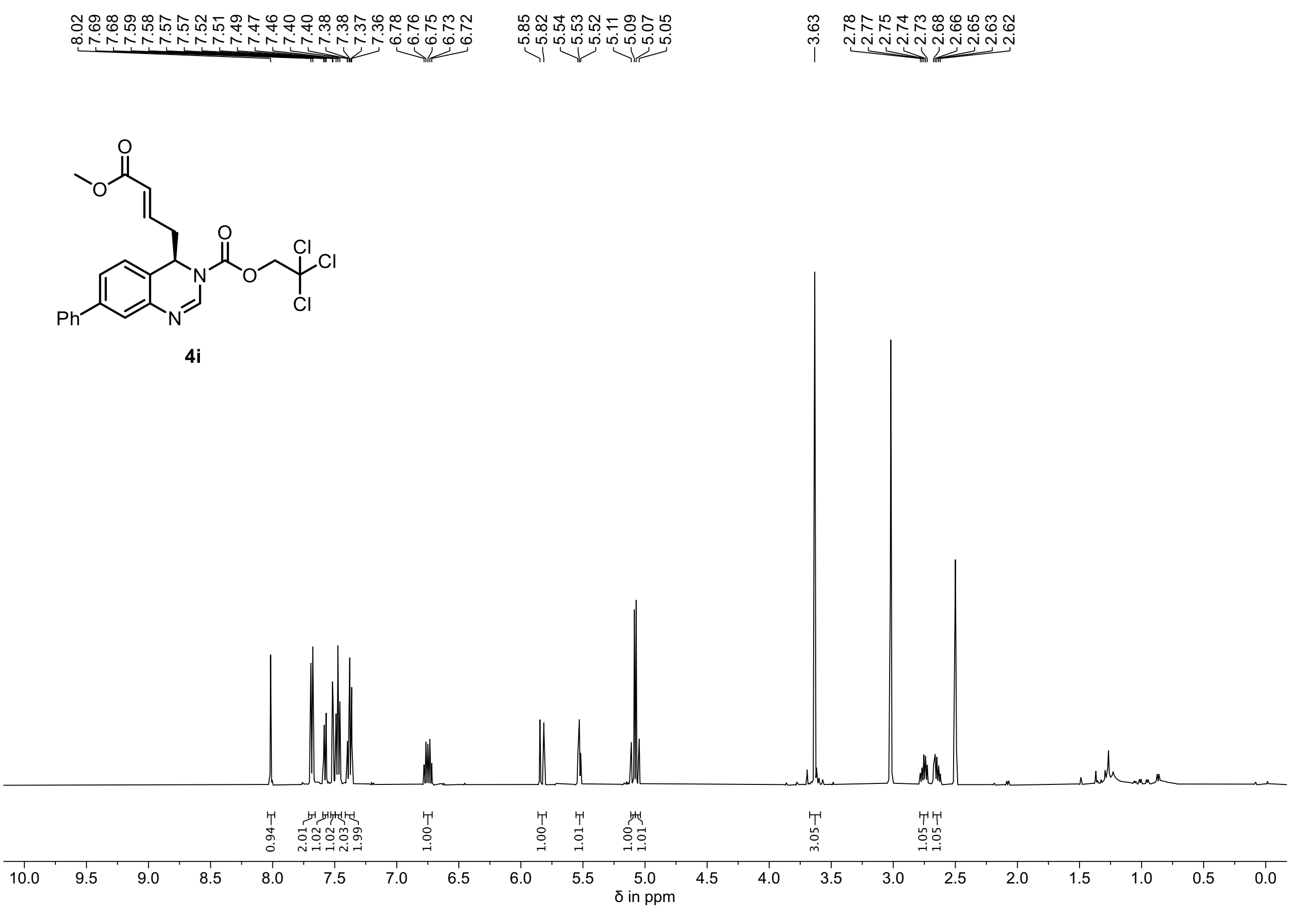

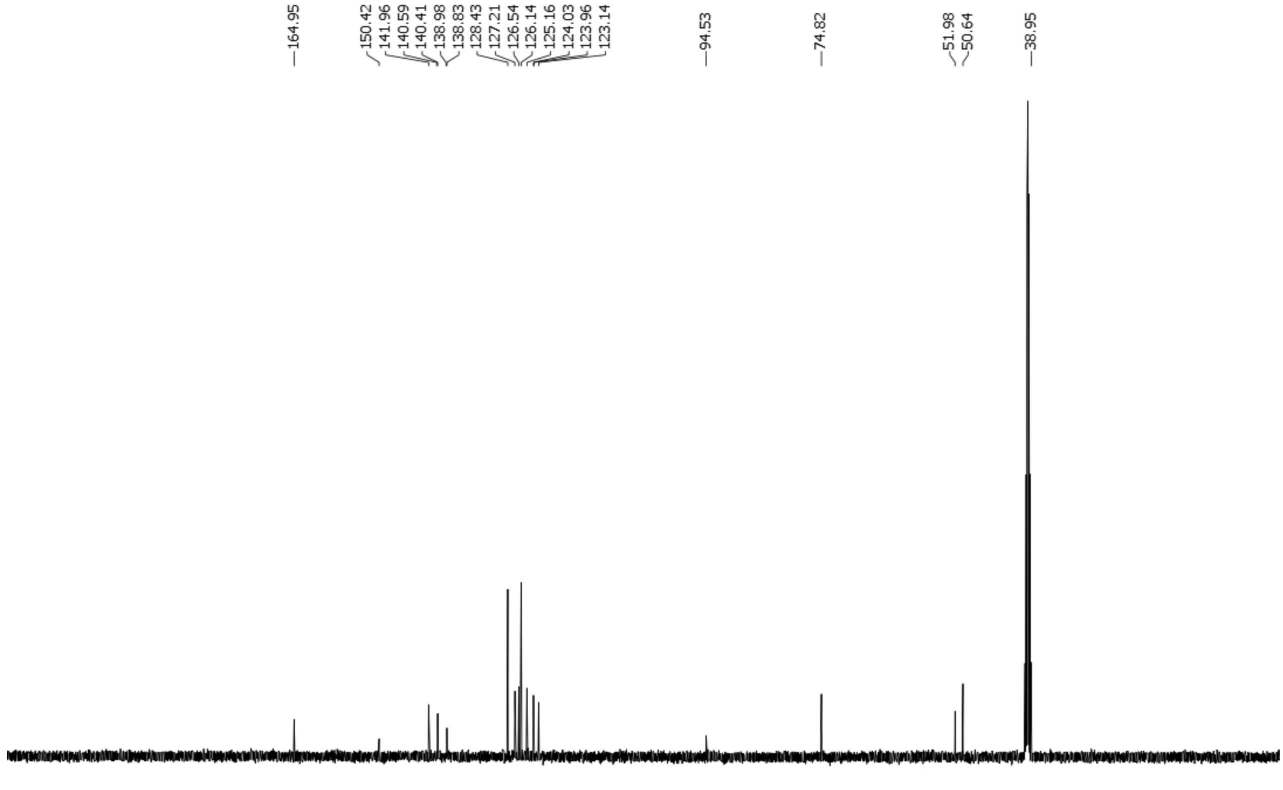

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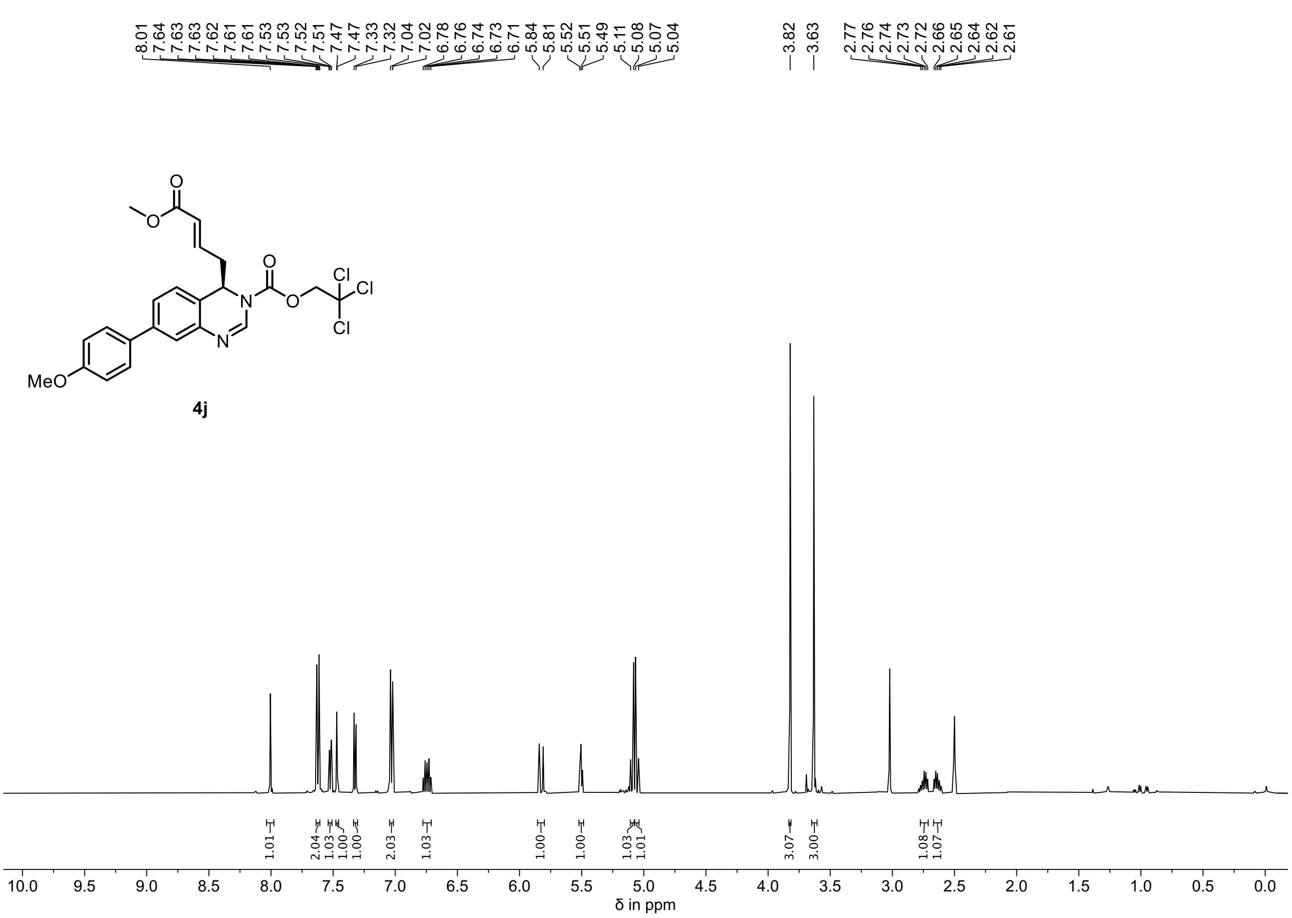

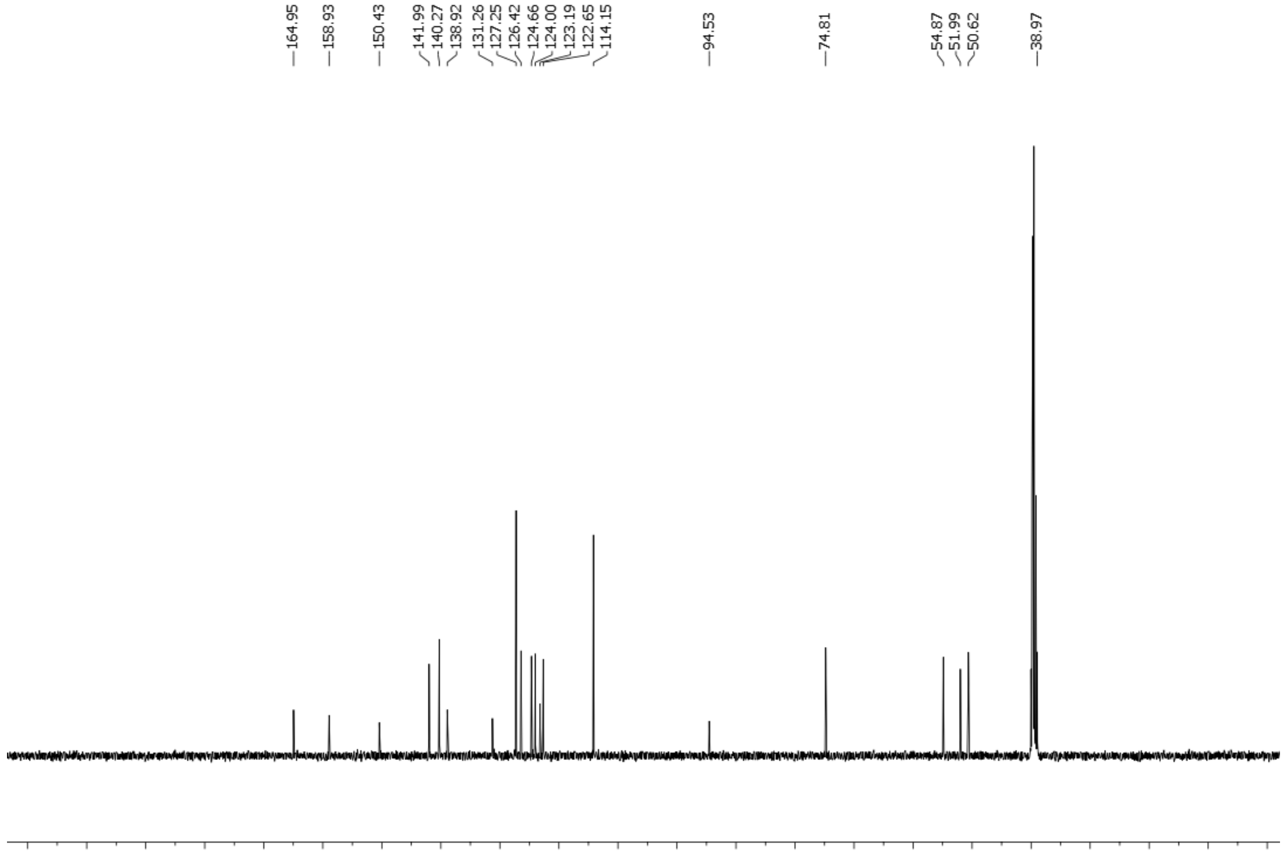

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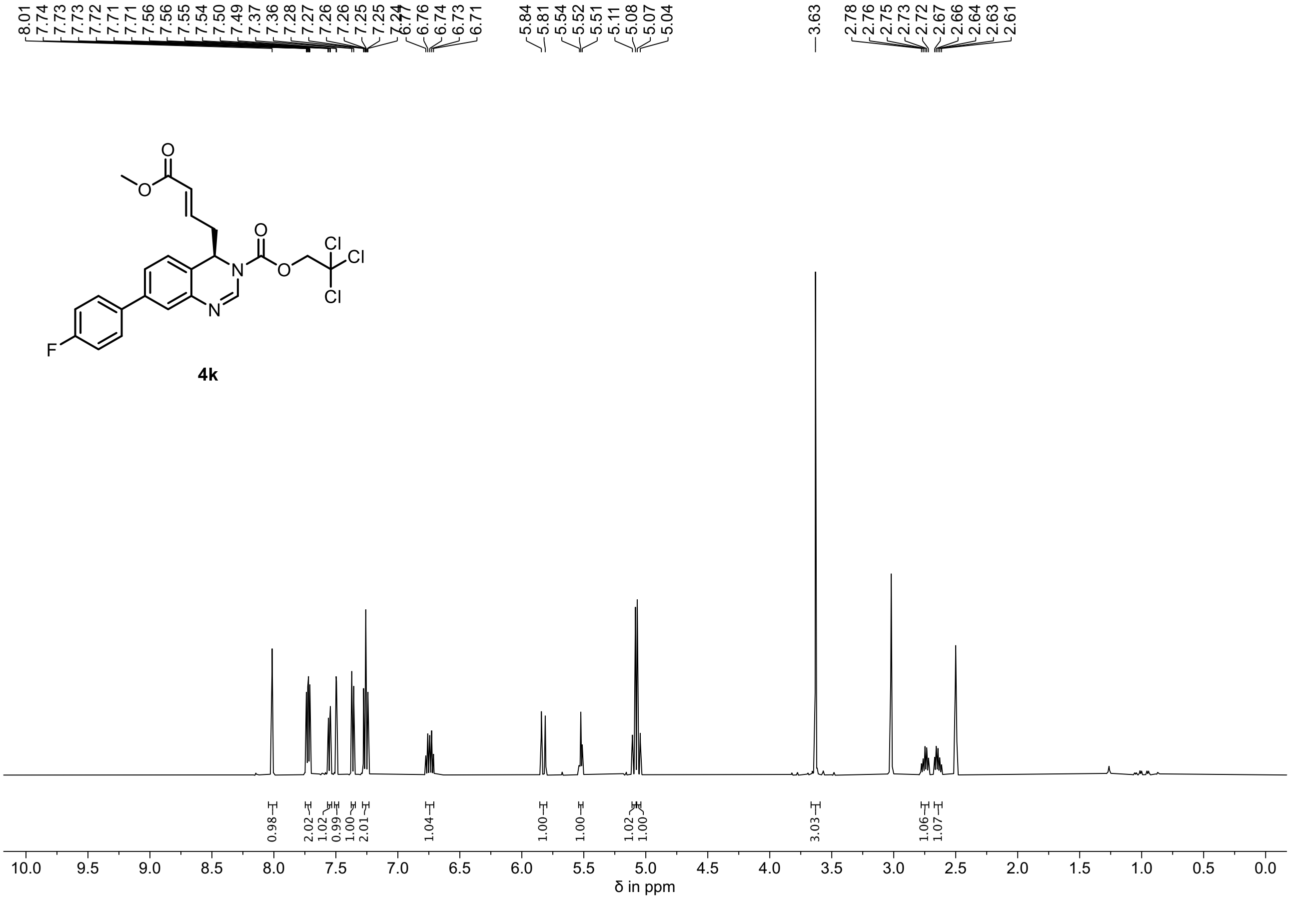

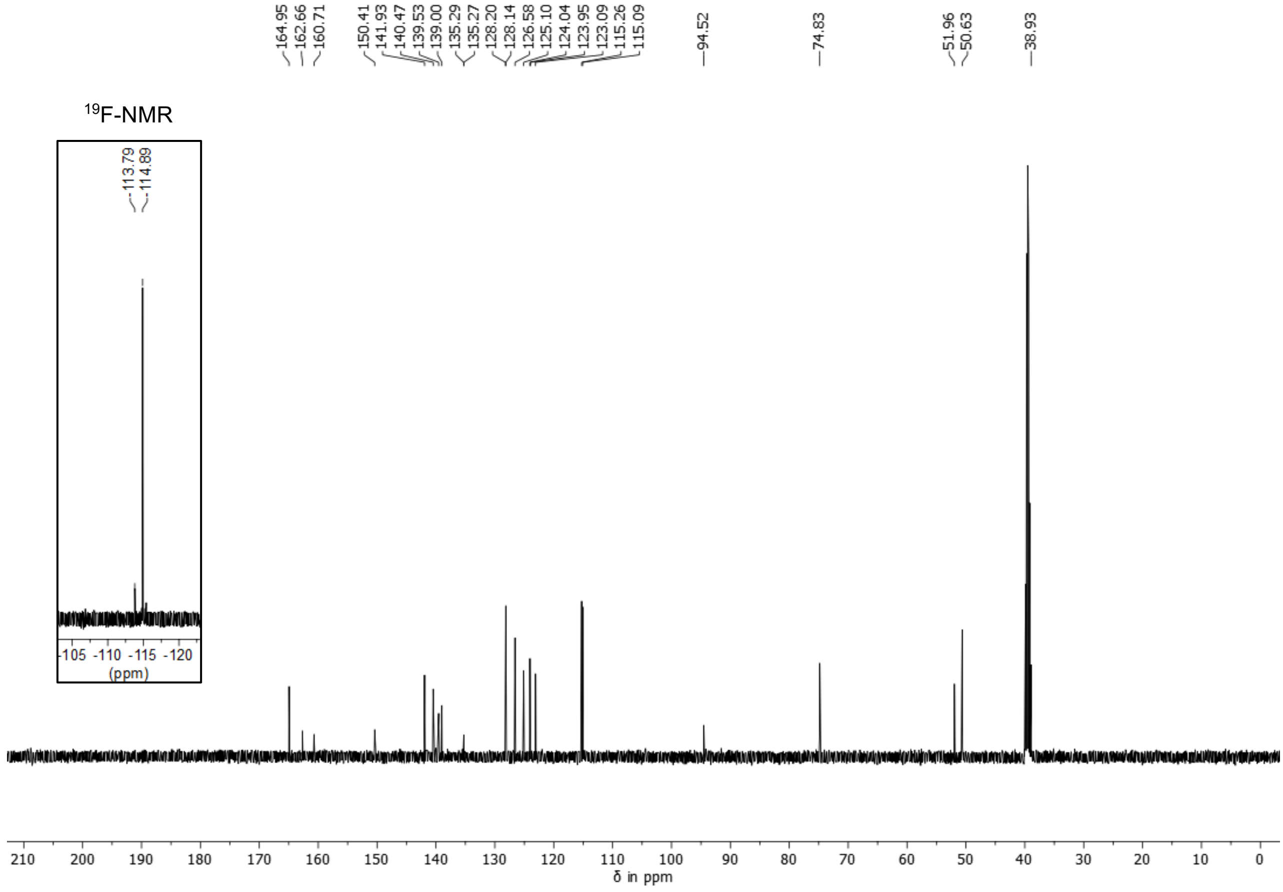

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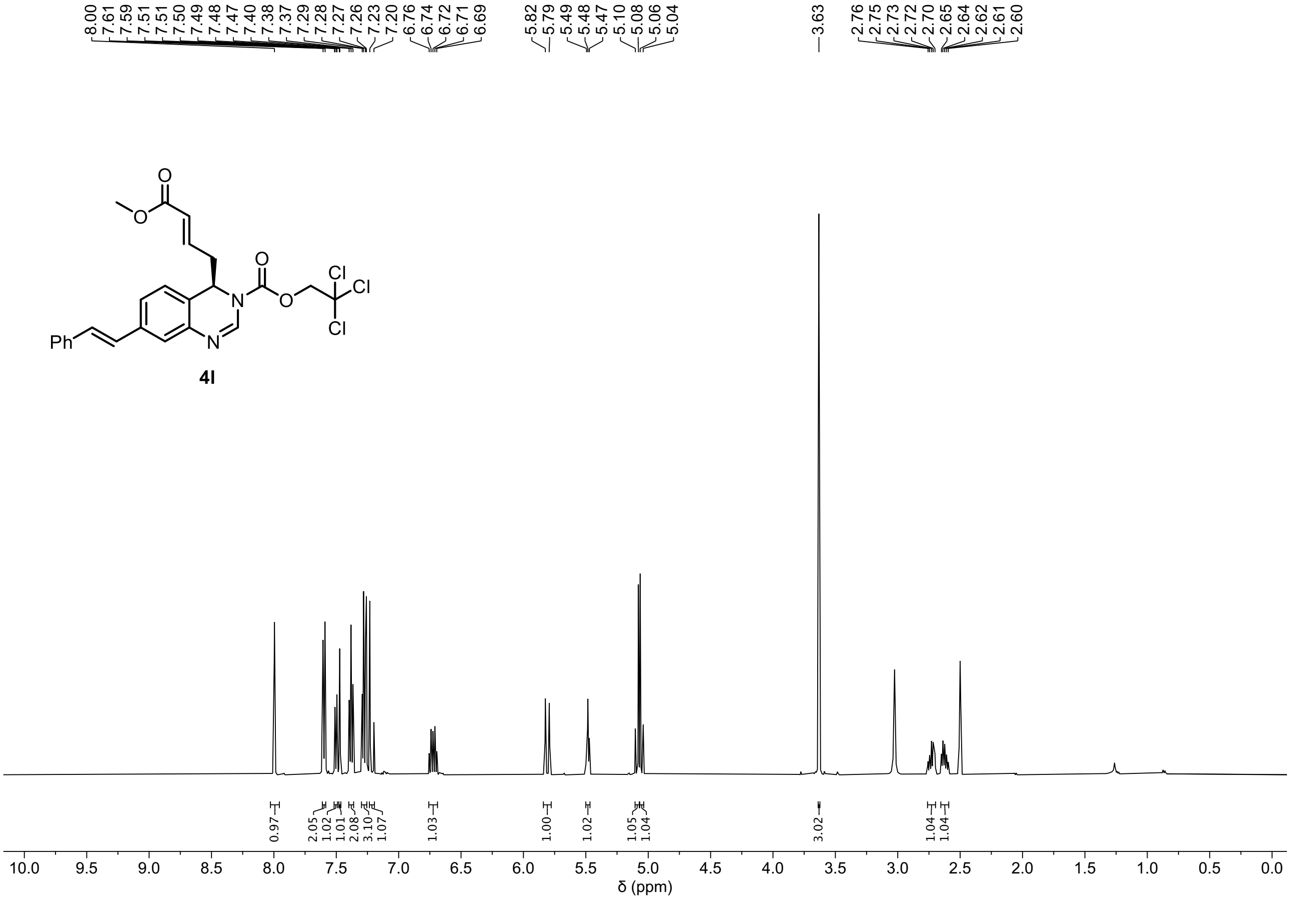

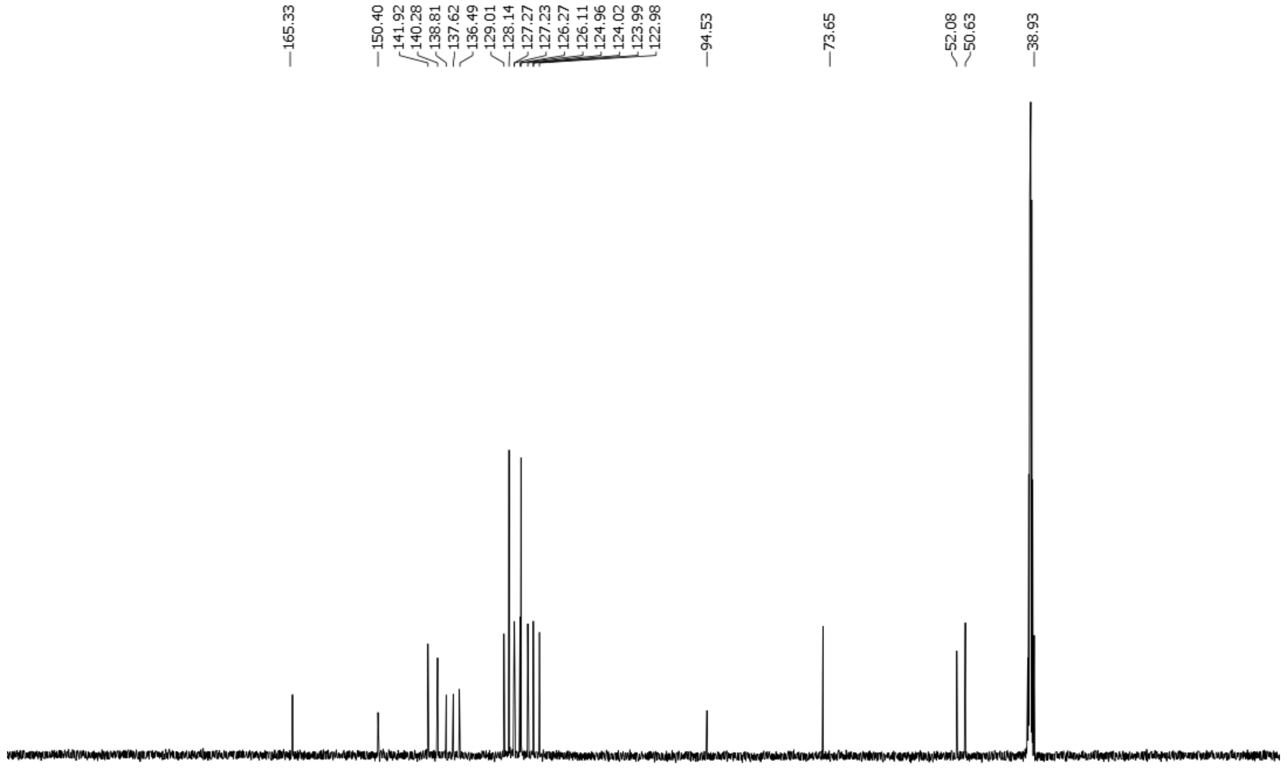

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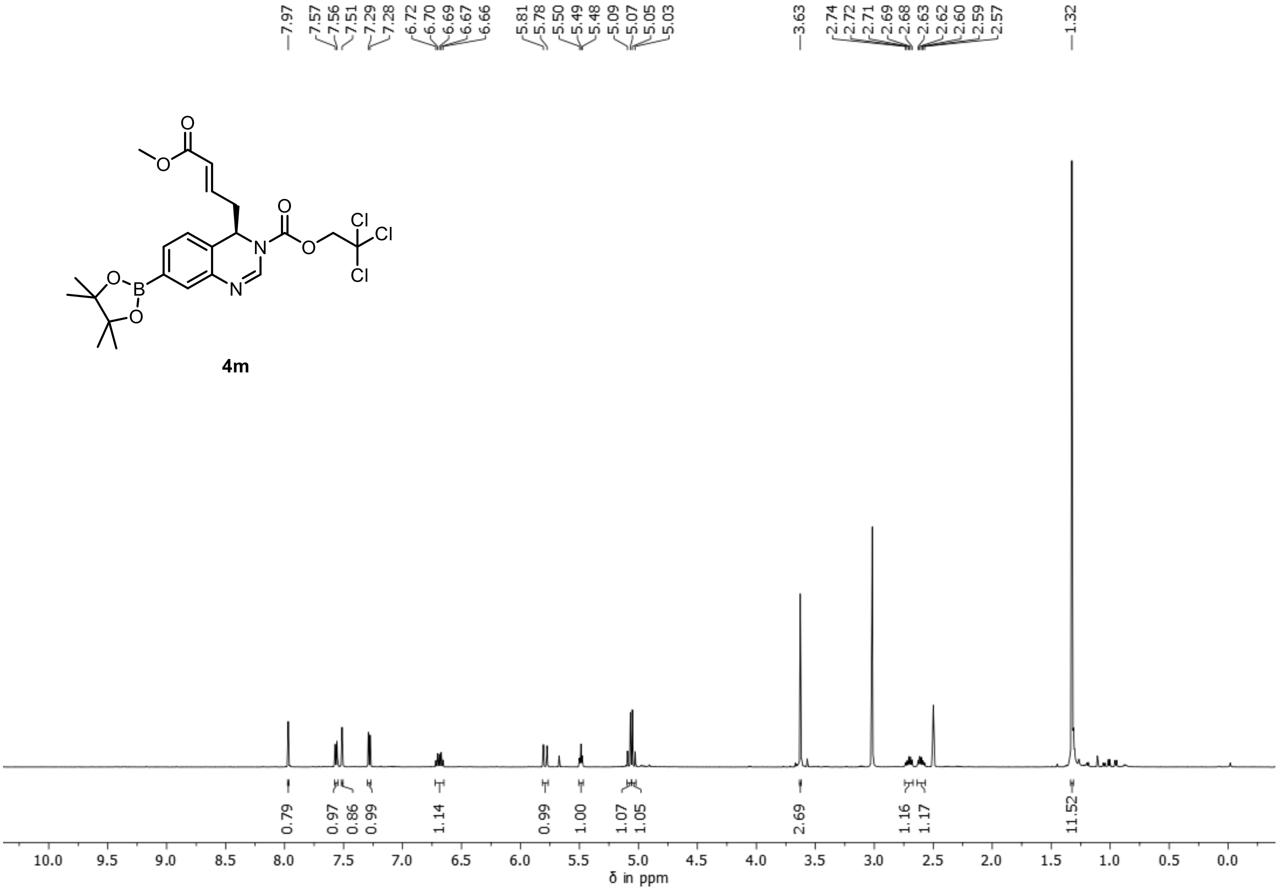

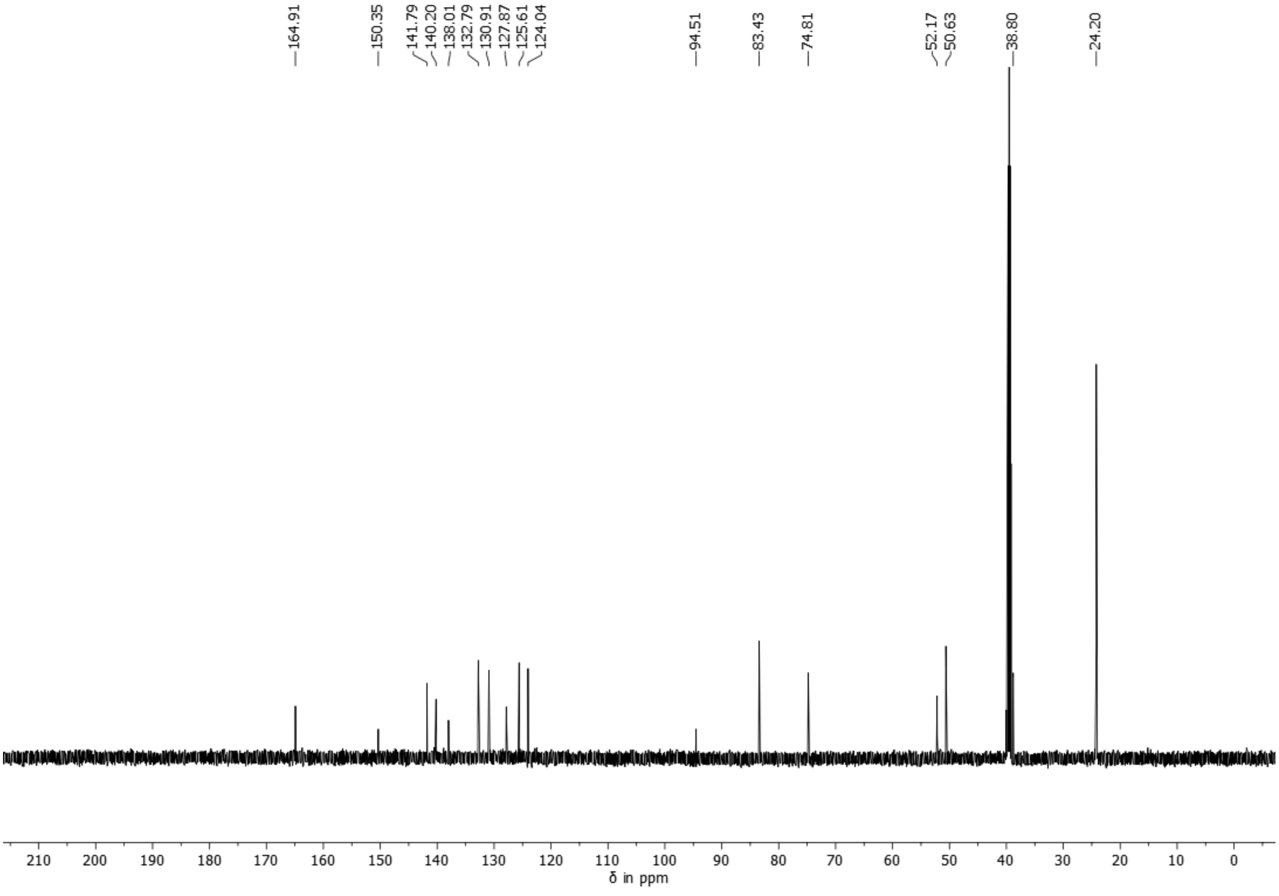

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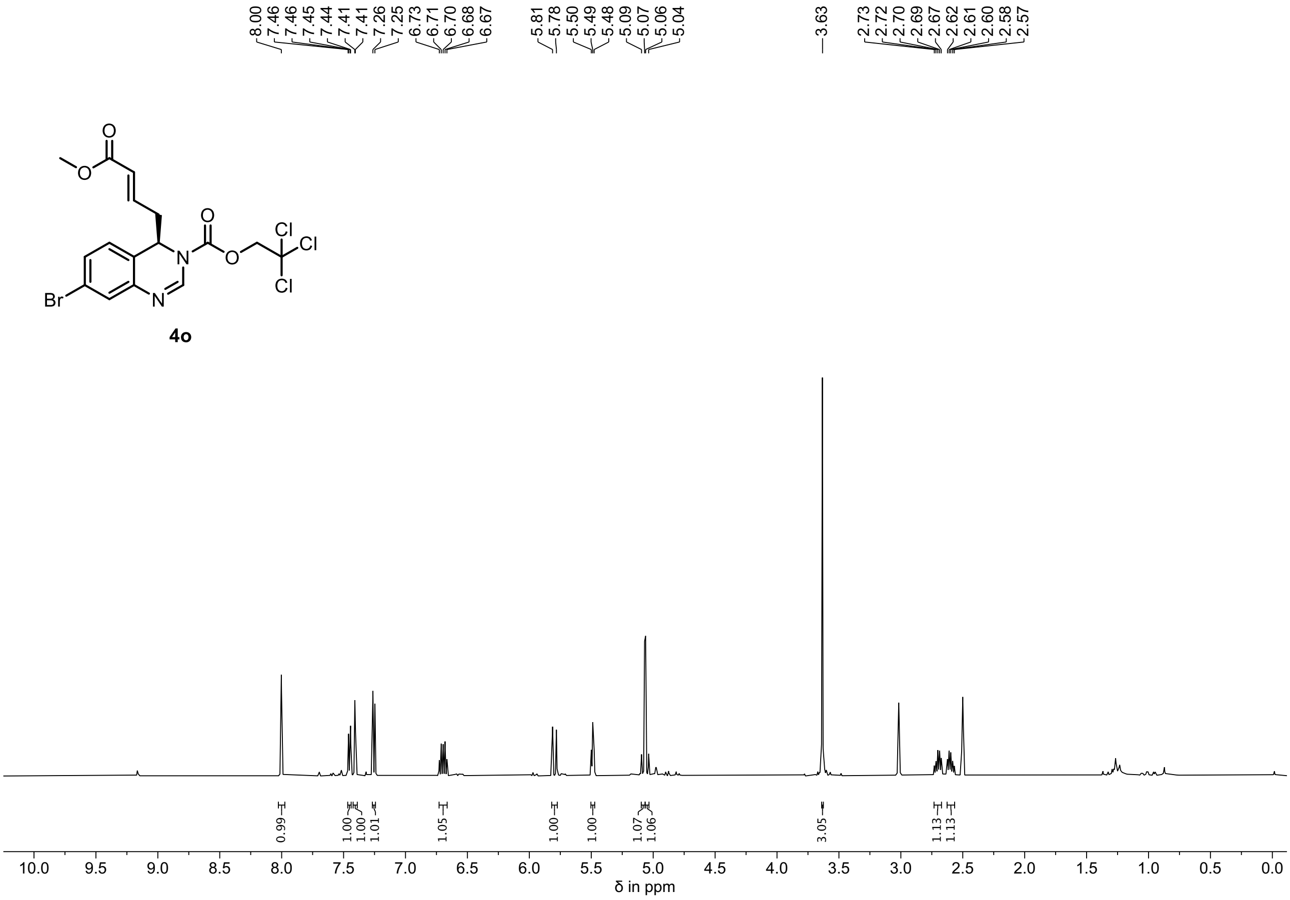

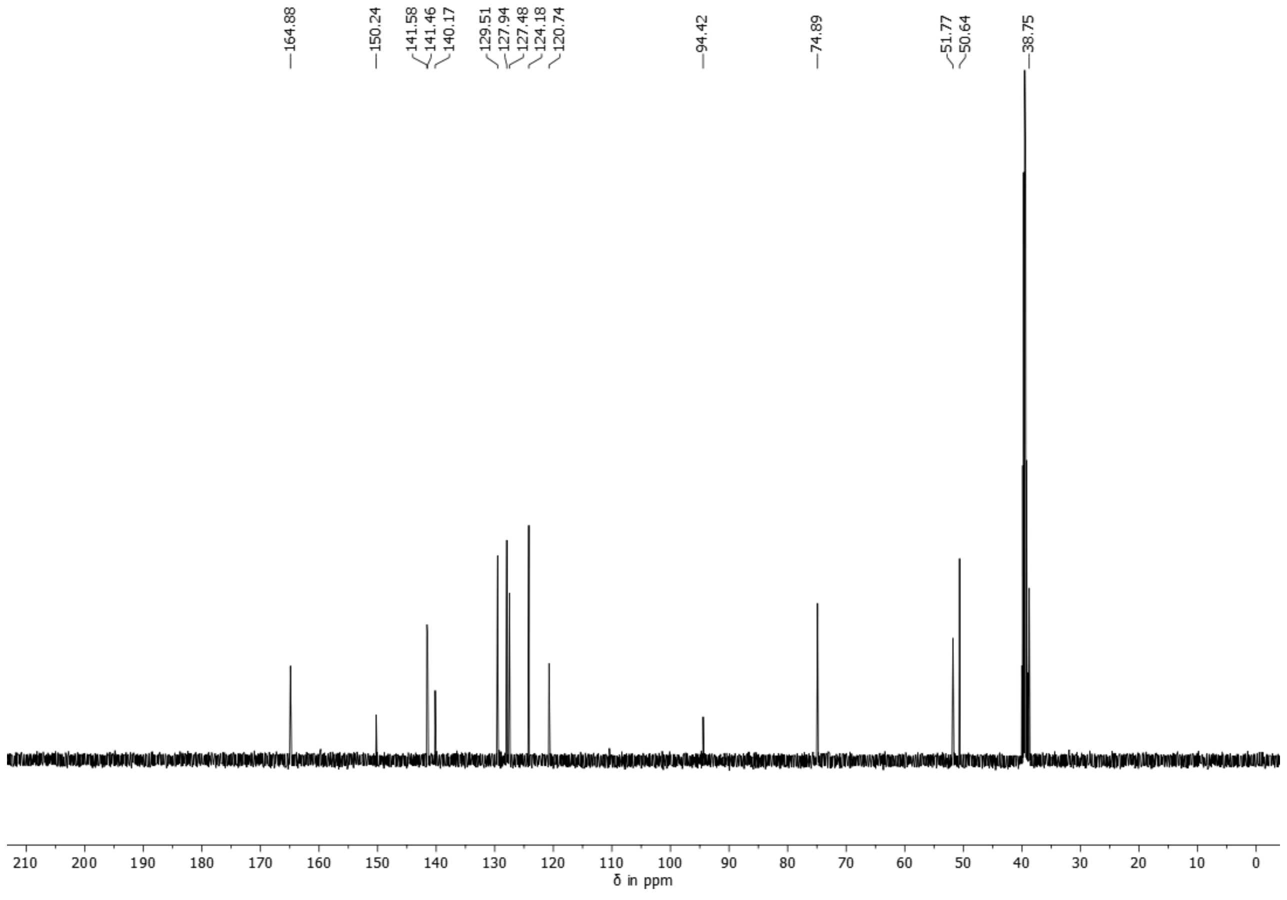

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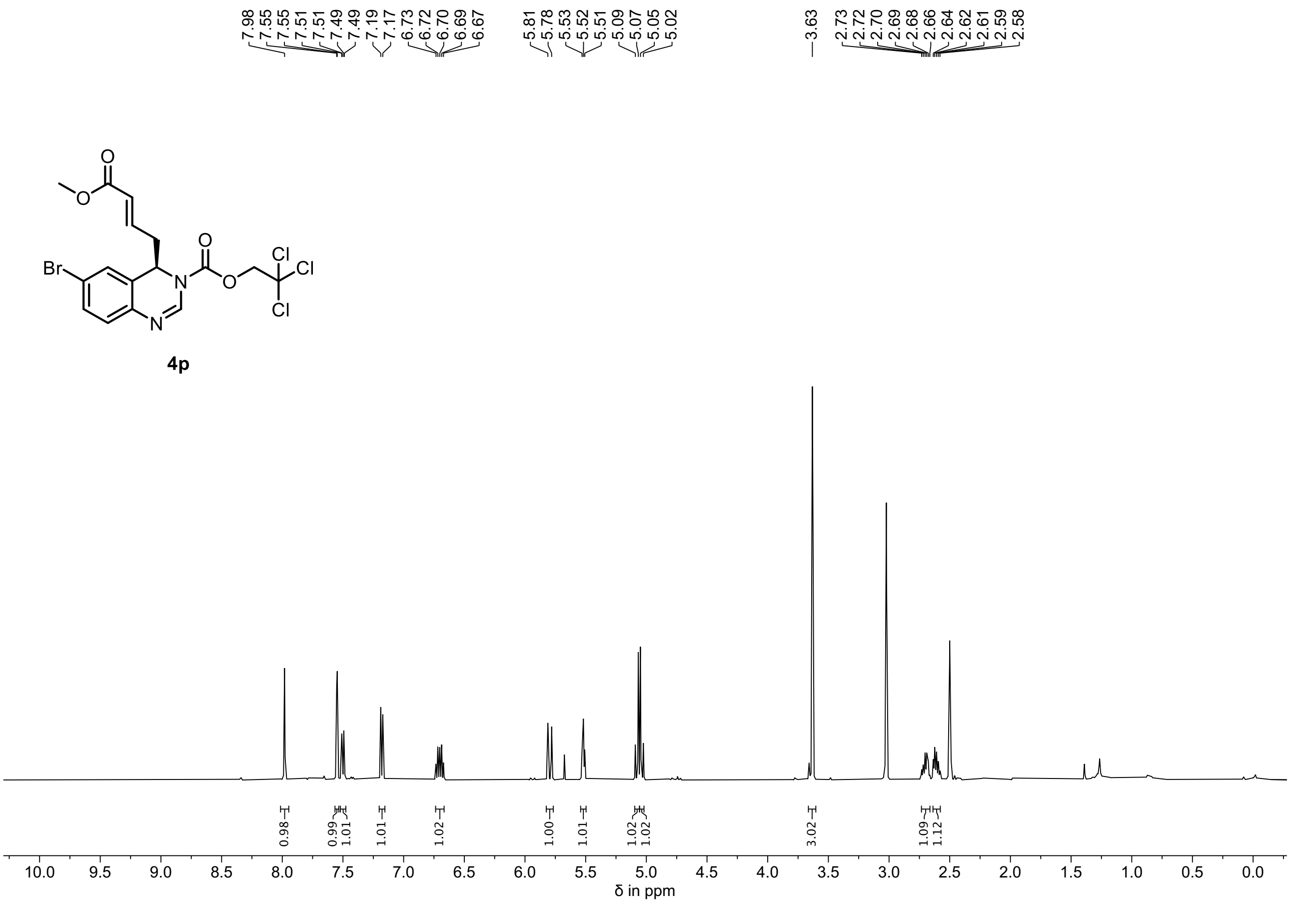

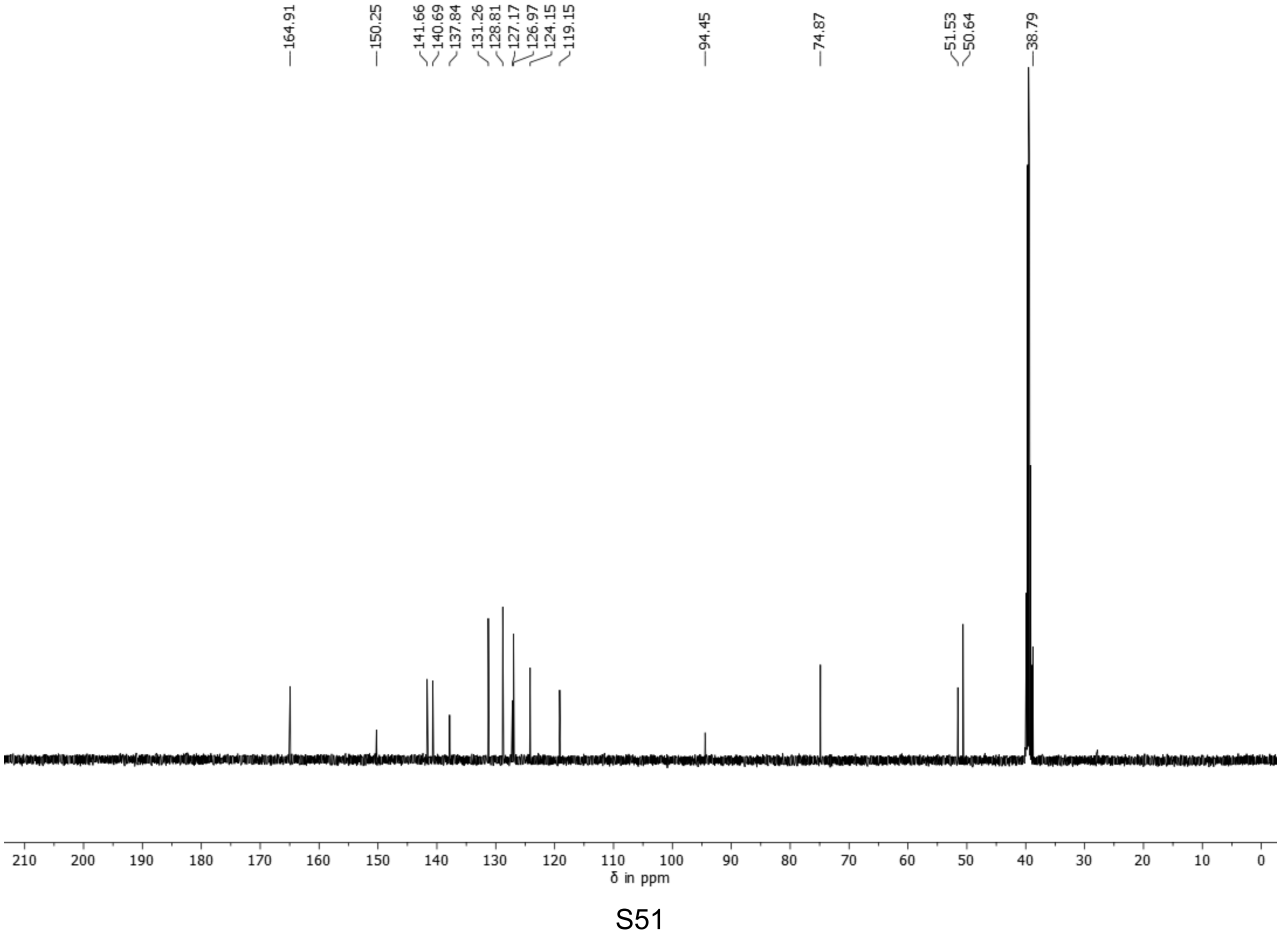

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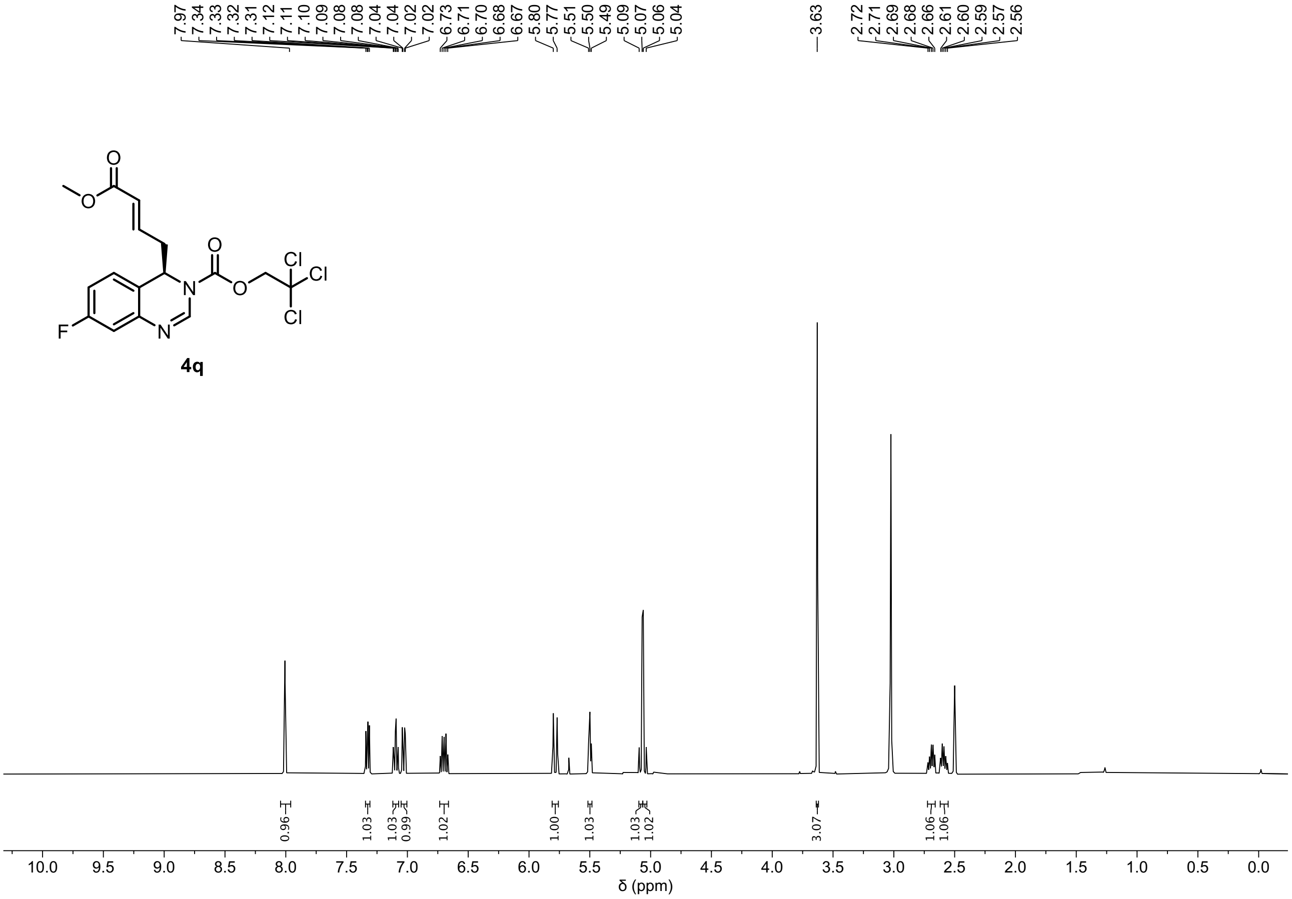
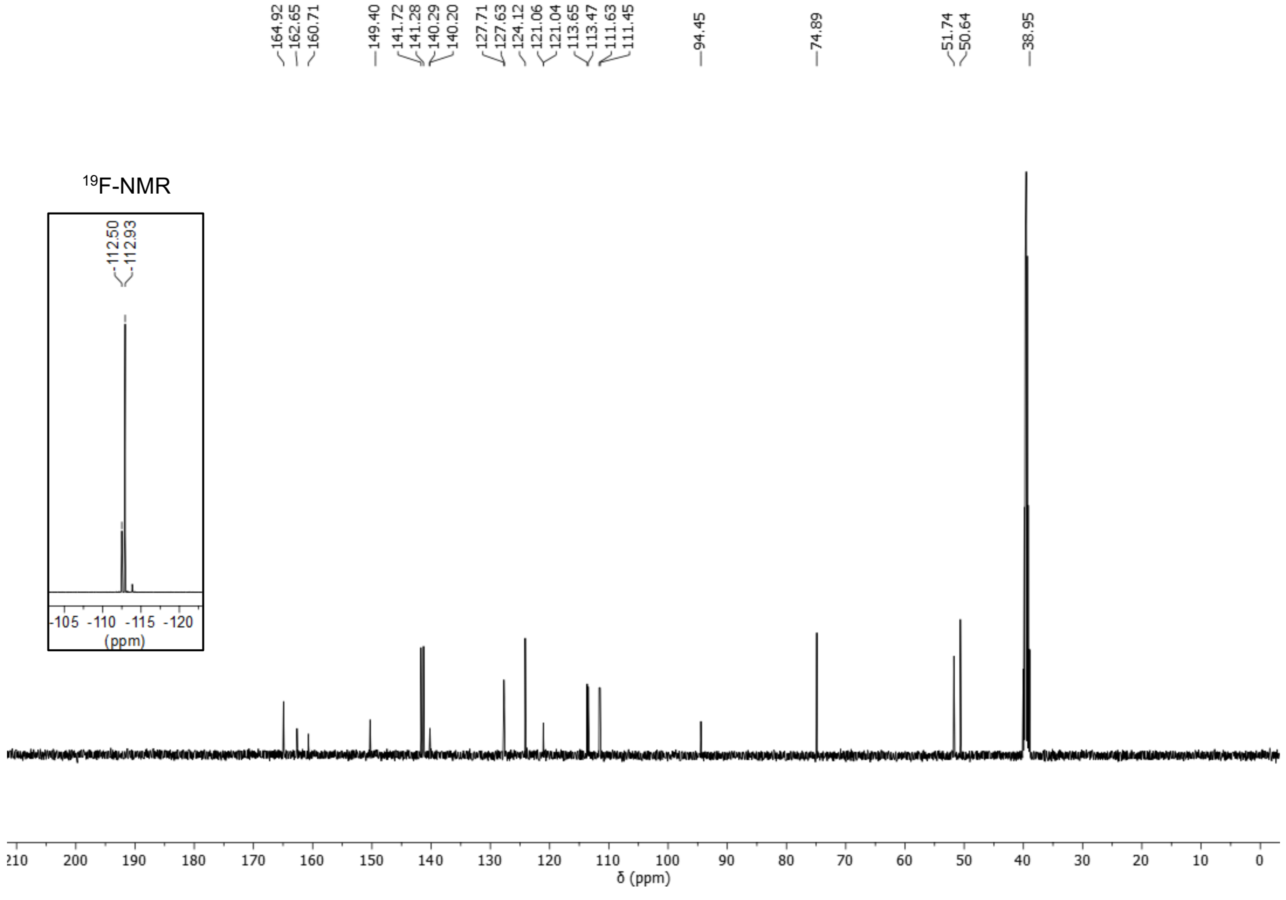
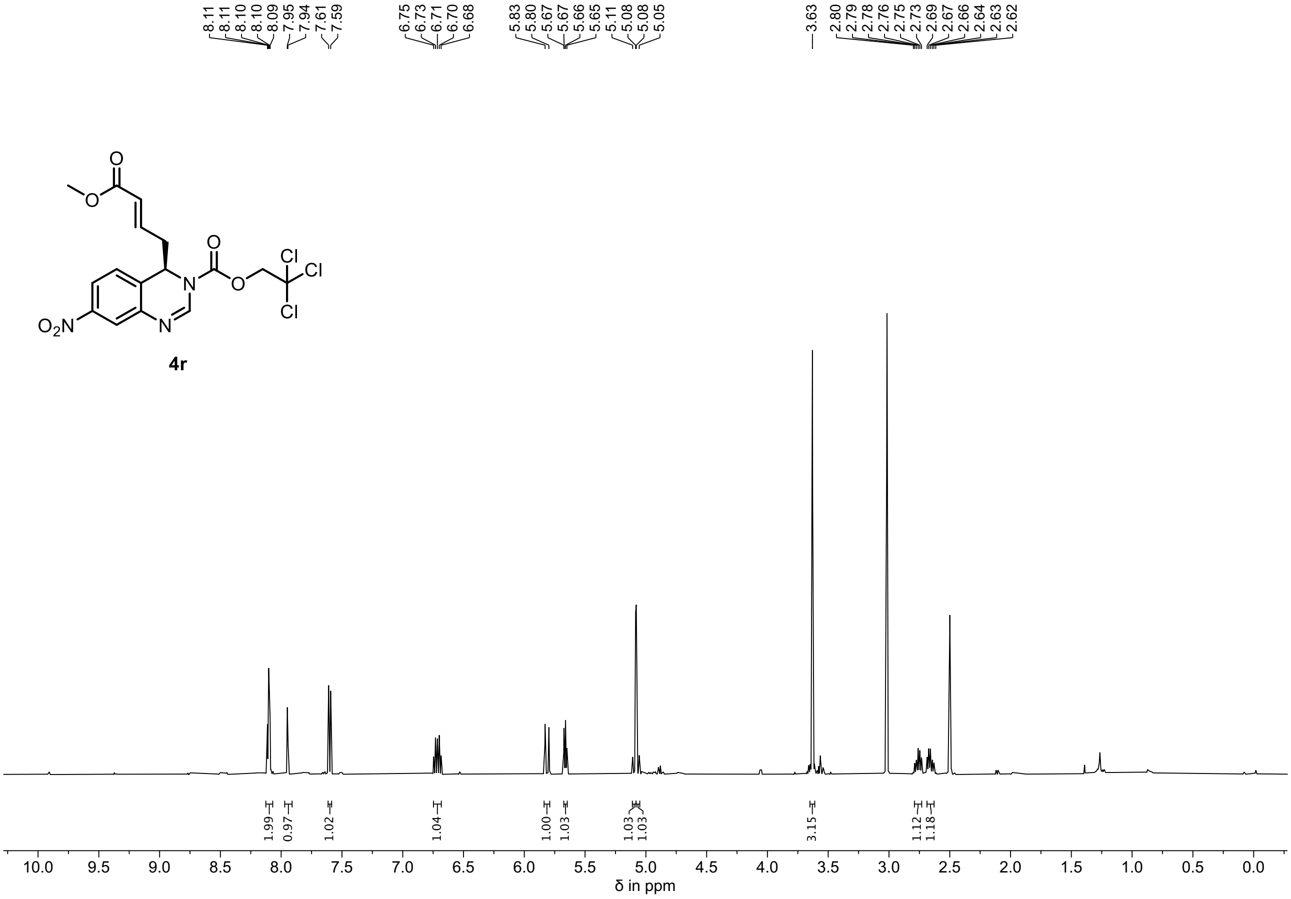
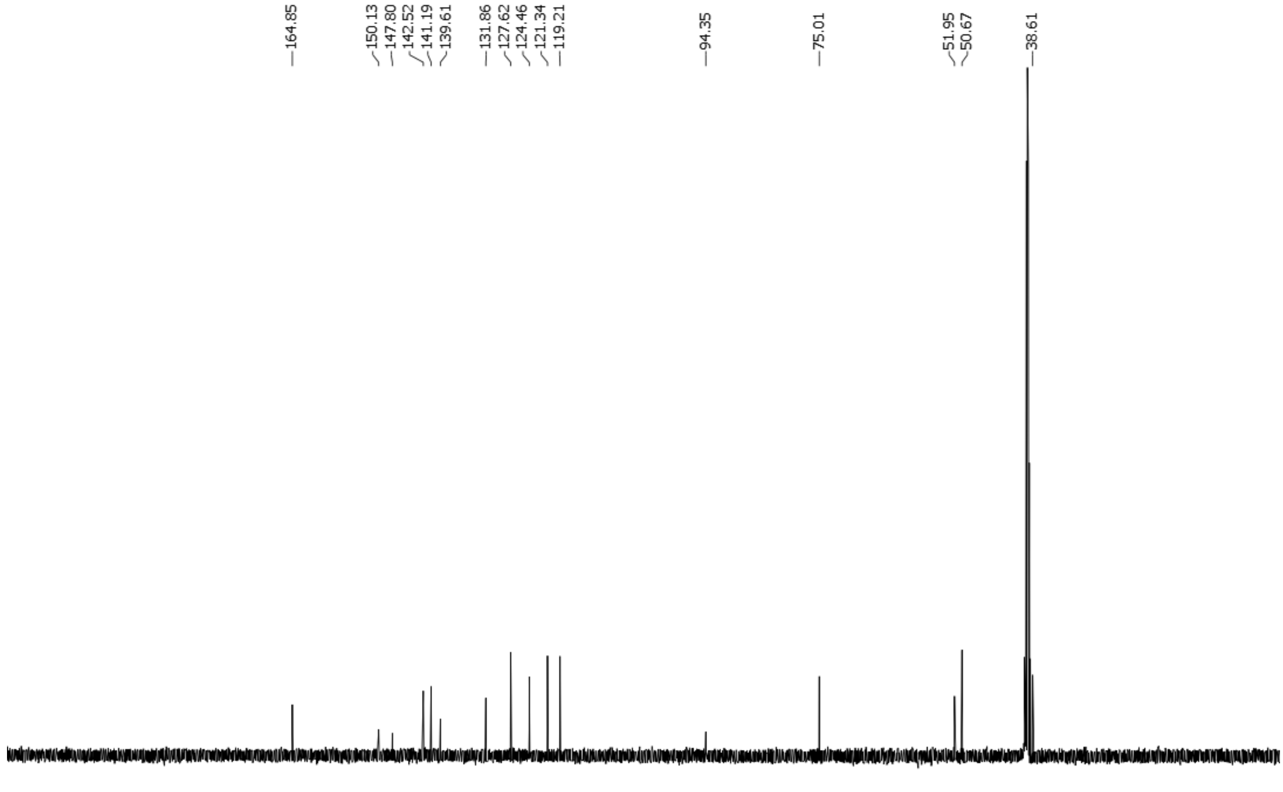




4r (DMSO-d$_6$, 90 °C):

4r





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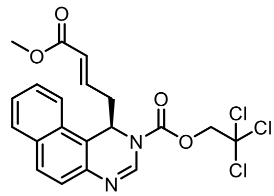

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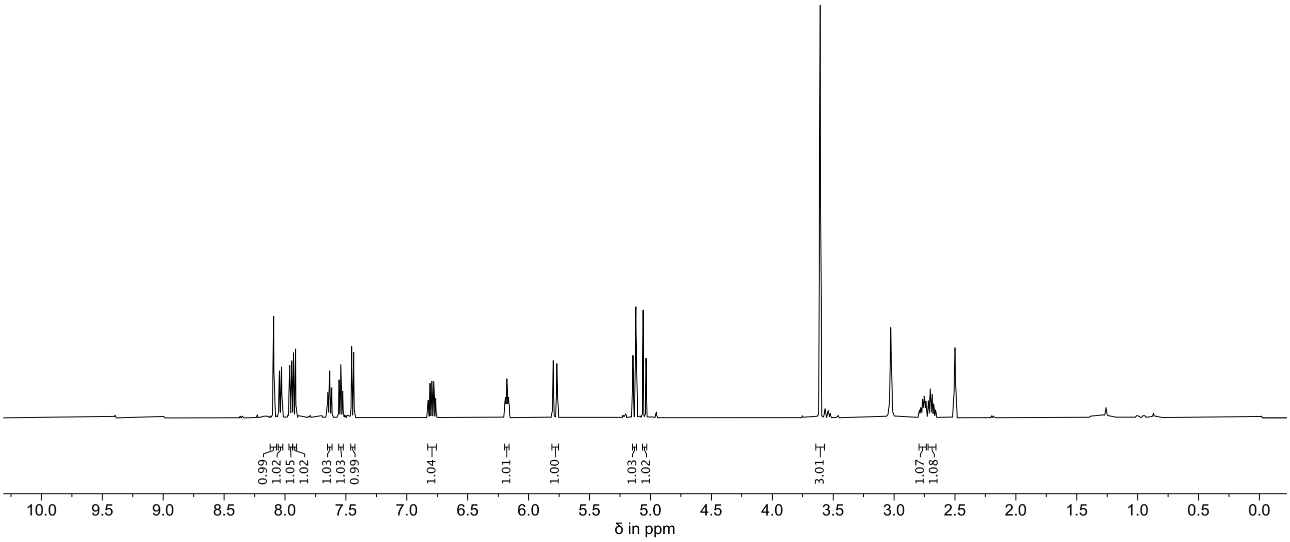
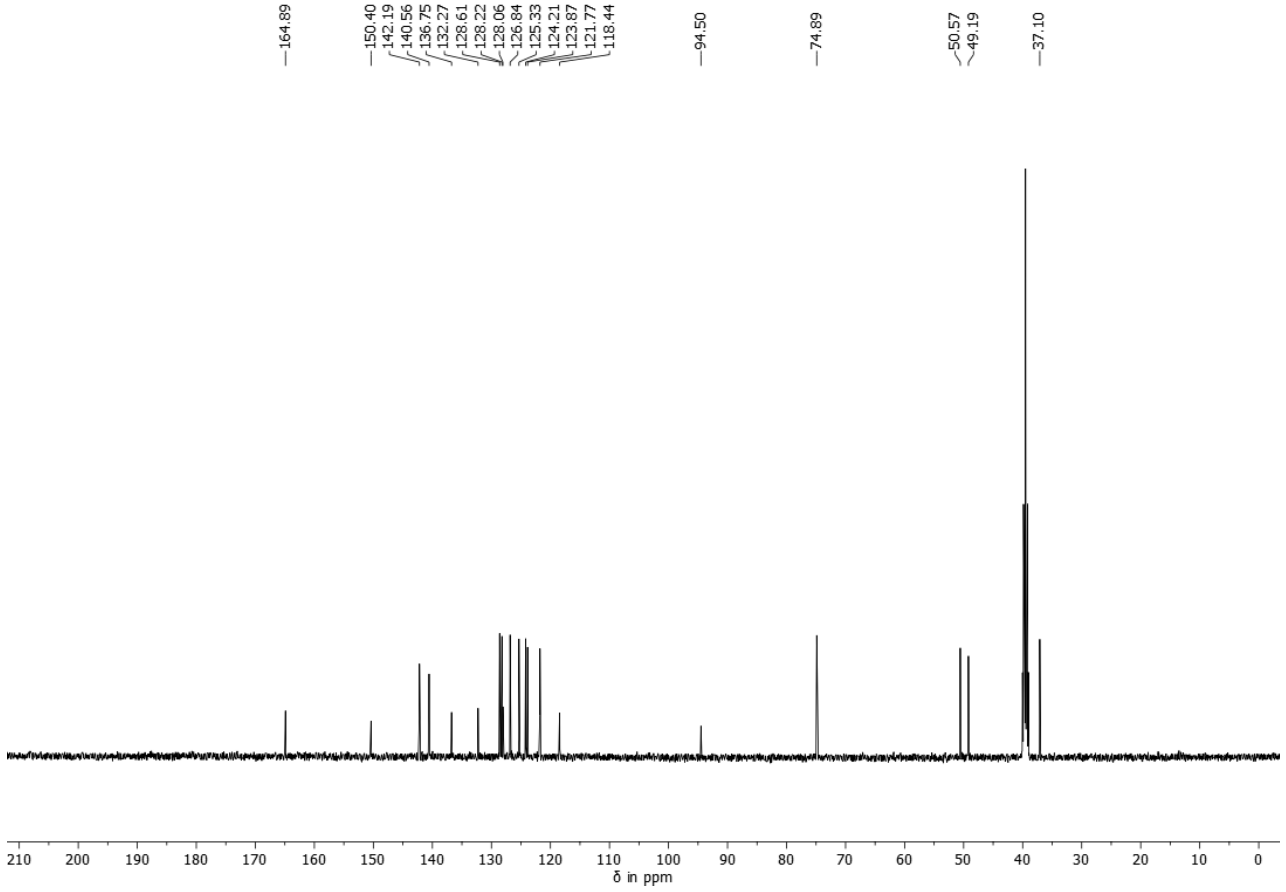
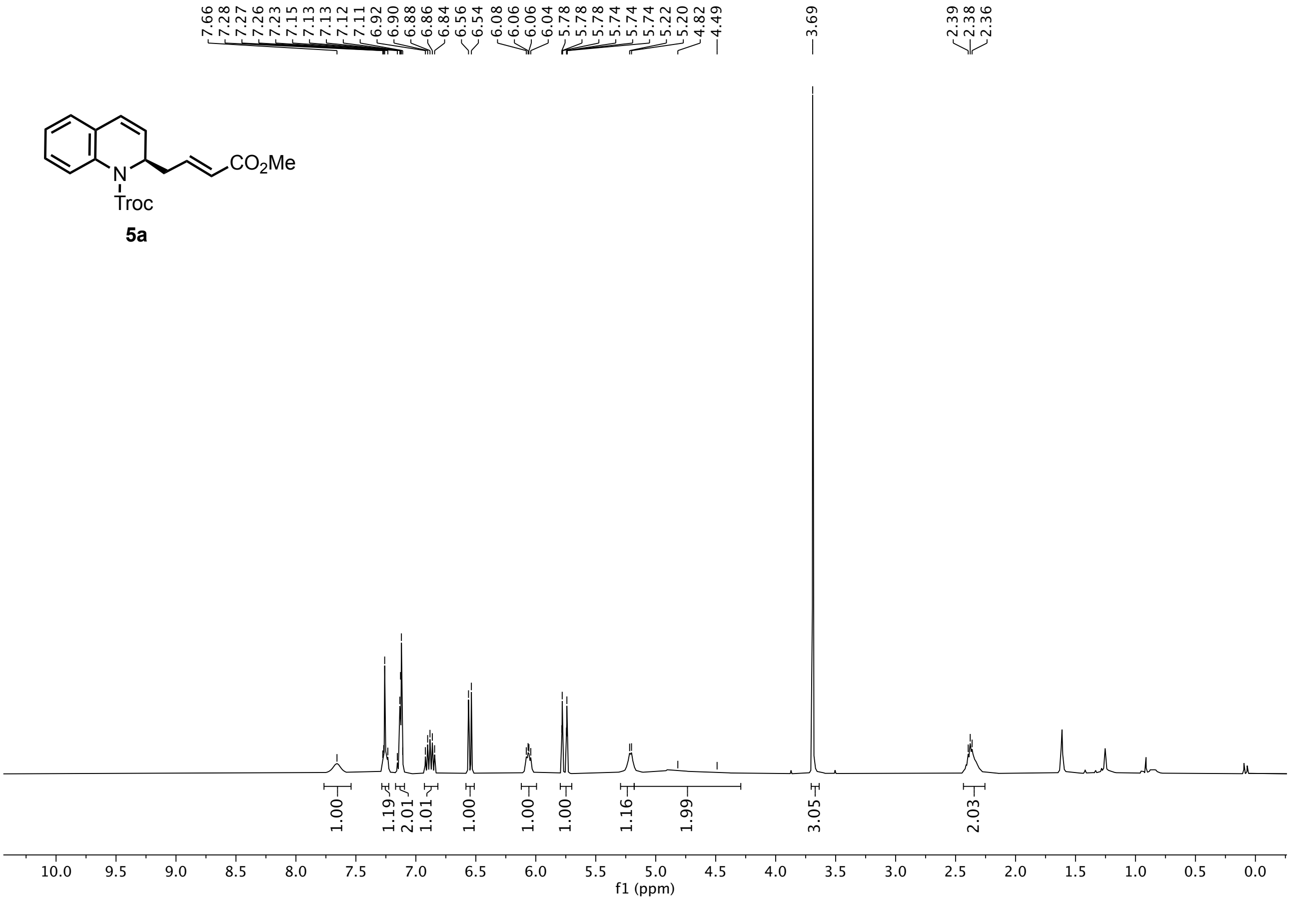
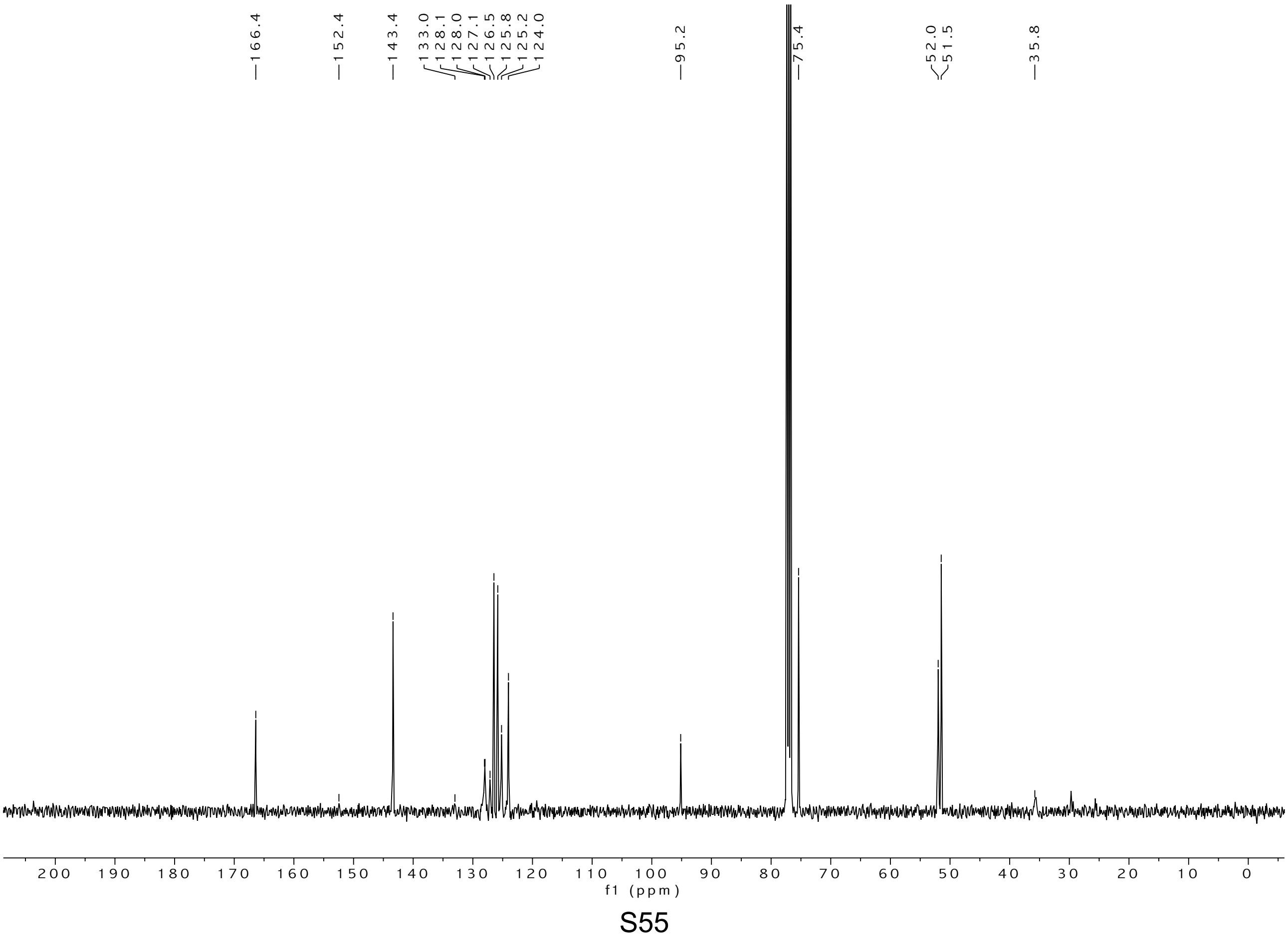




5a (CDCl$_3$, 25 °C): broad signals due Troc-rotamers

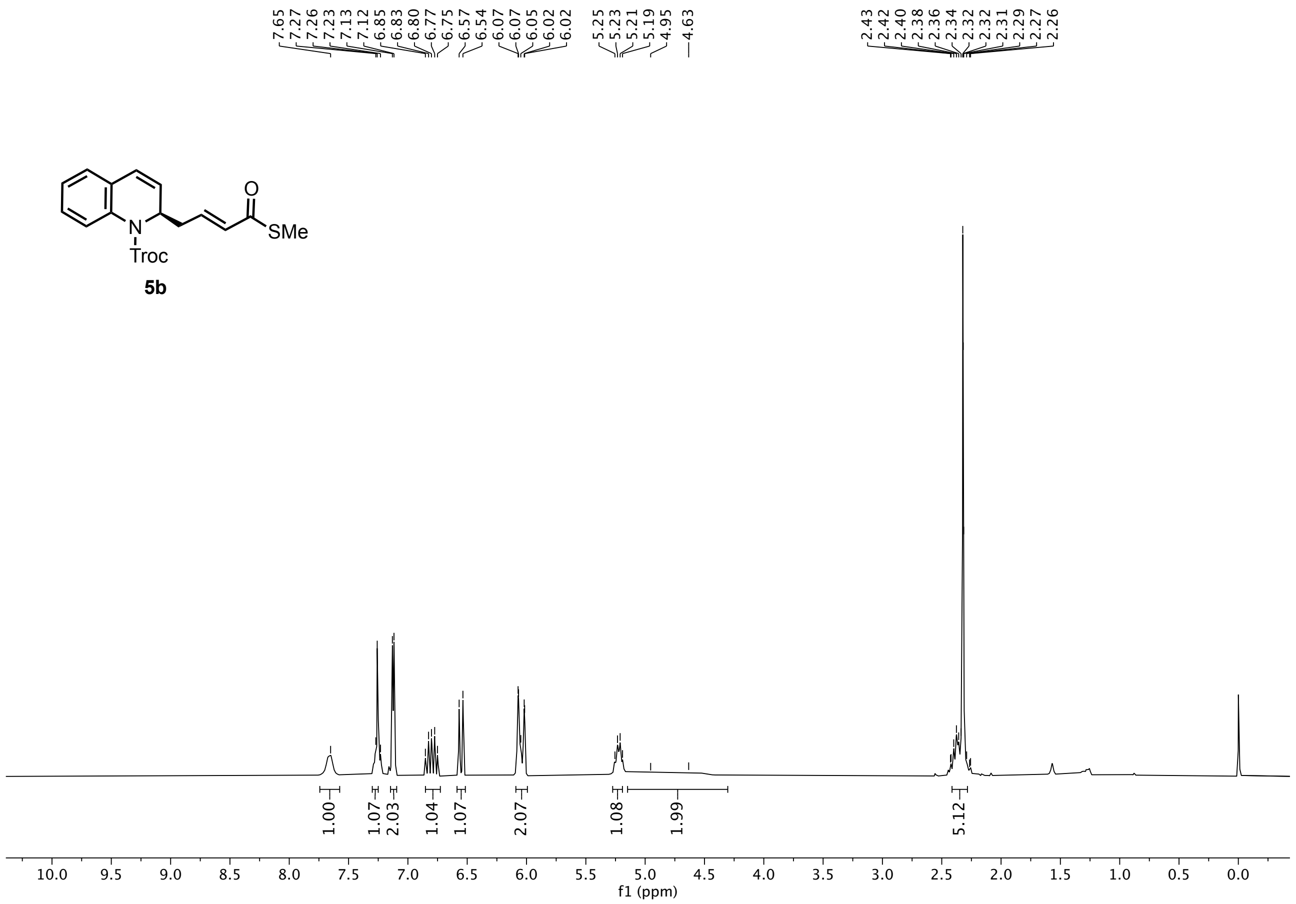


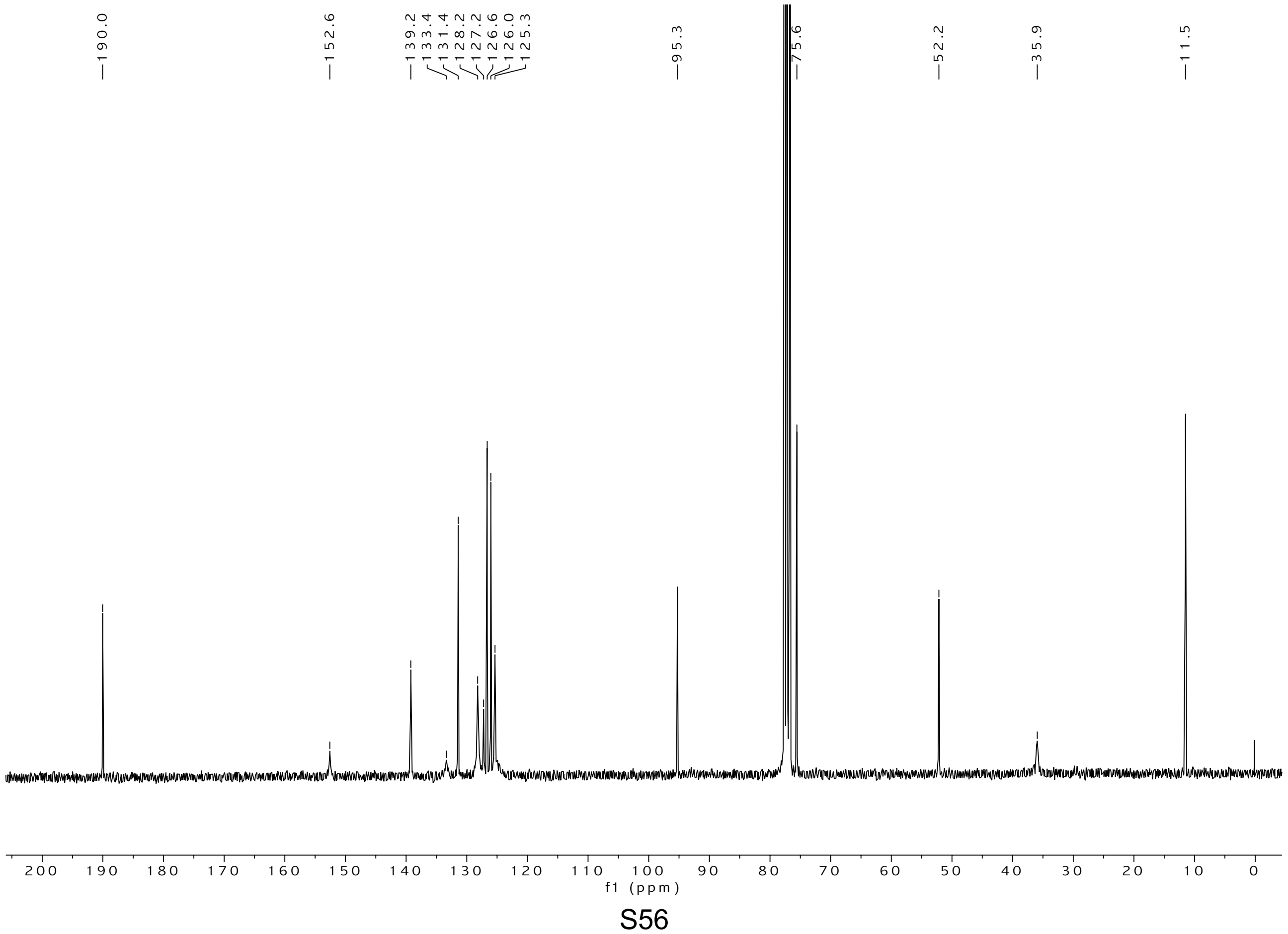
5a



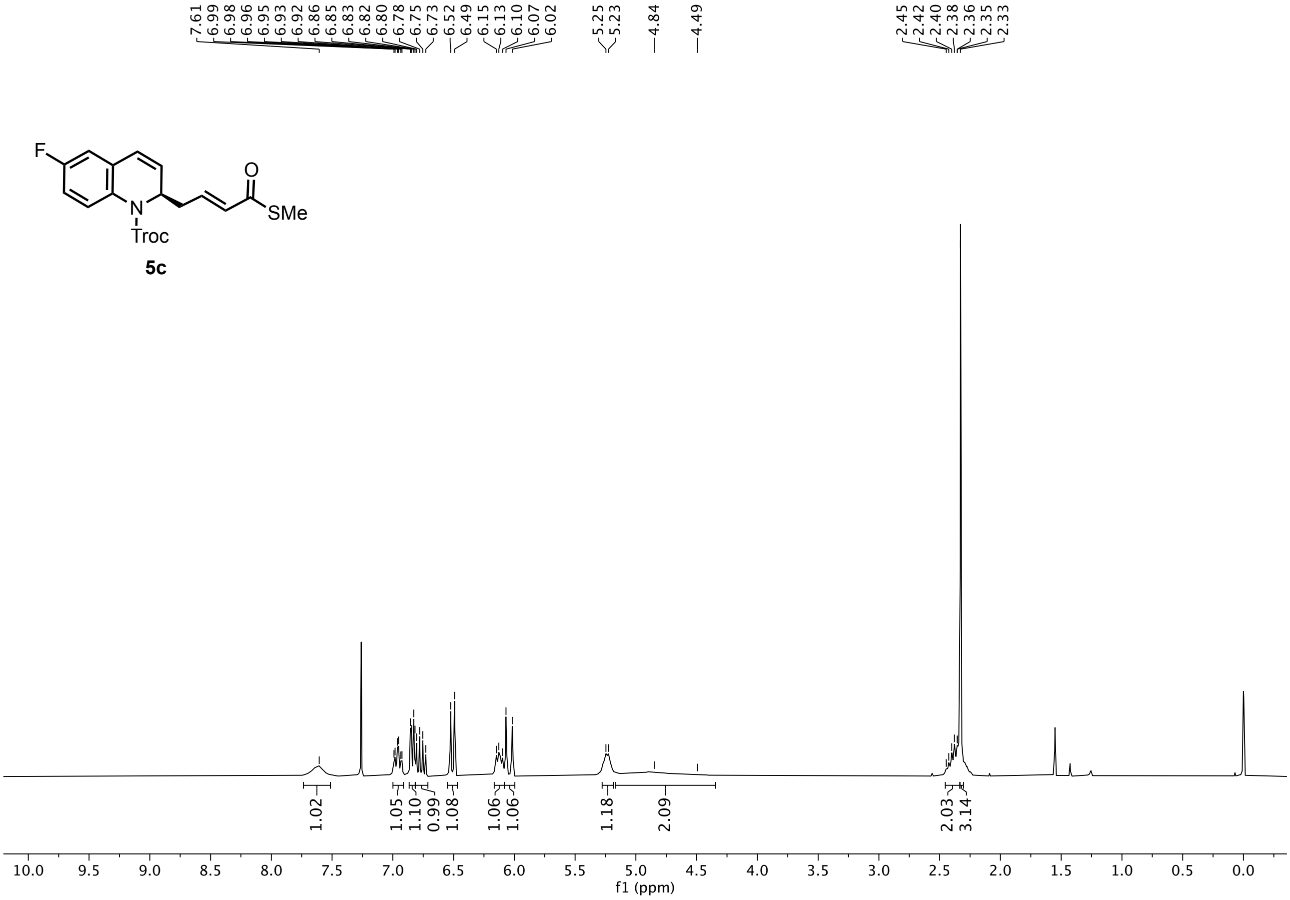
5b (CDCl$_3$, 25 °C): broad signals due Troc-rotamers

5b

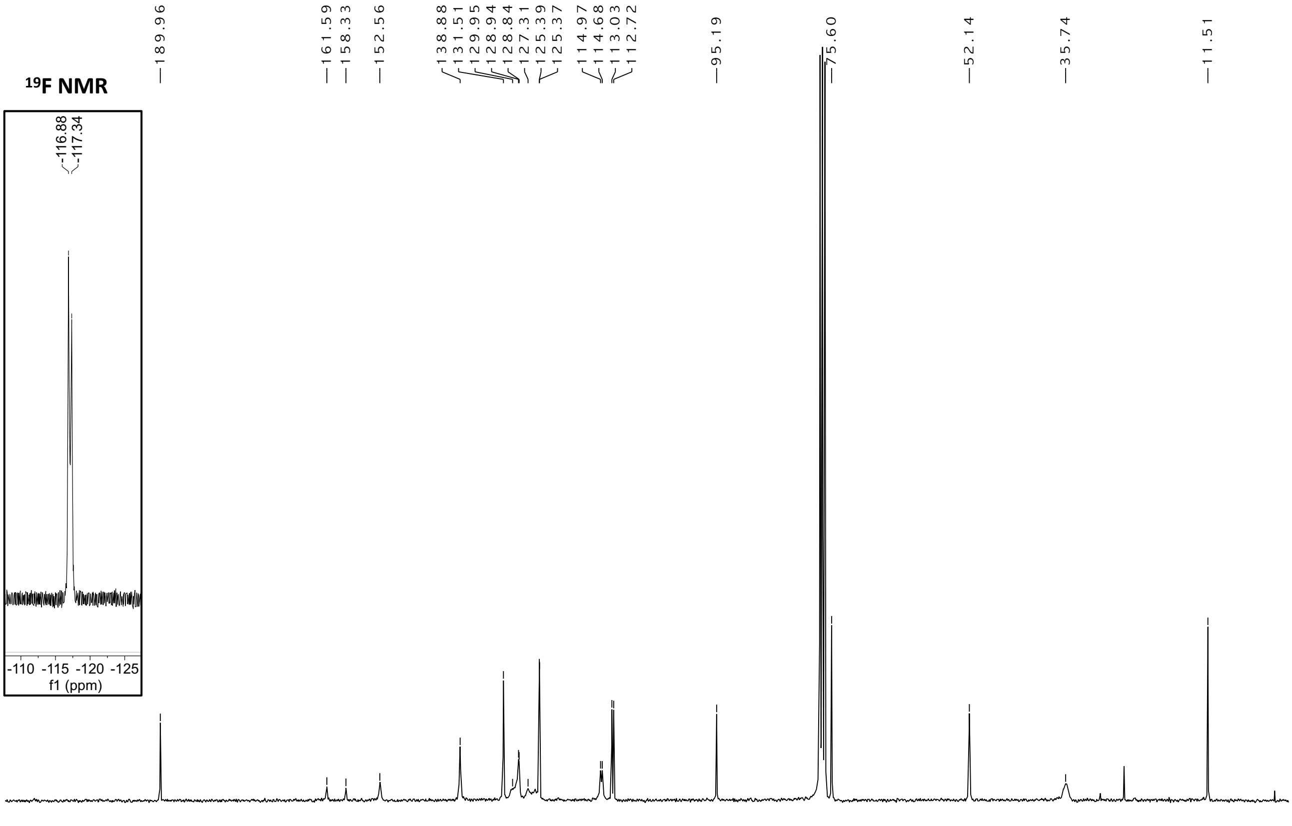




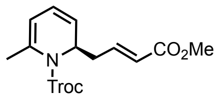
5c (CDCl$_3$, 25 °C): broad signals due Troc-rotamers



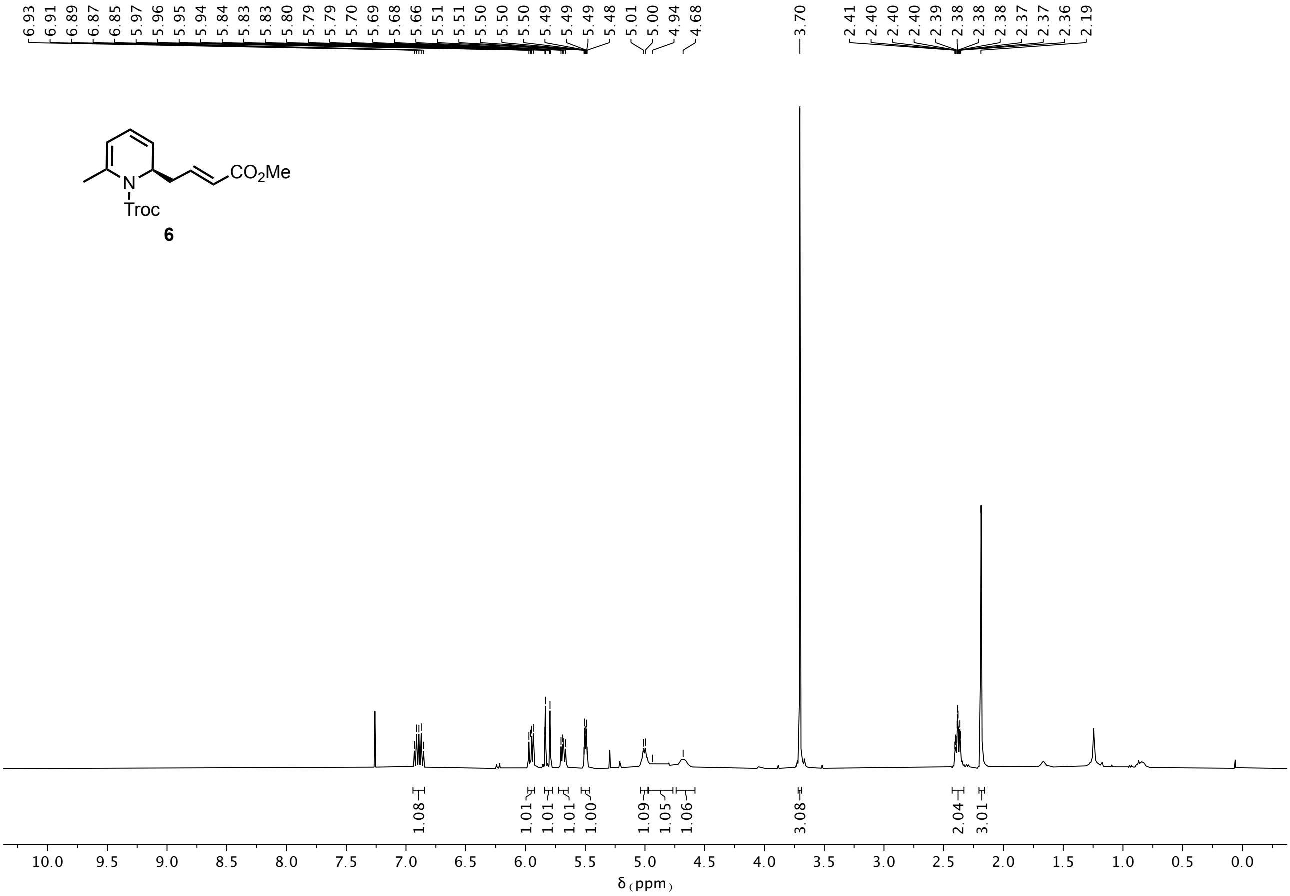
5c

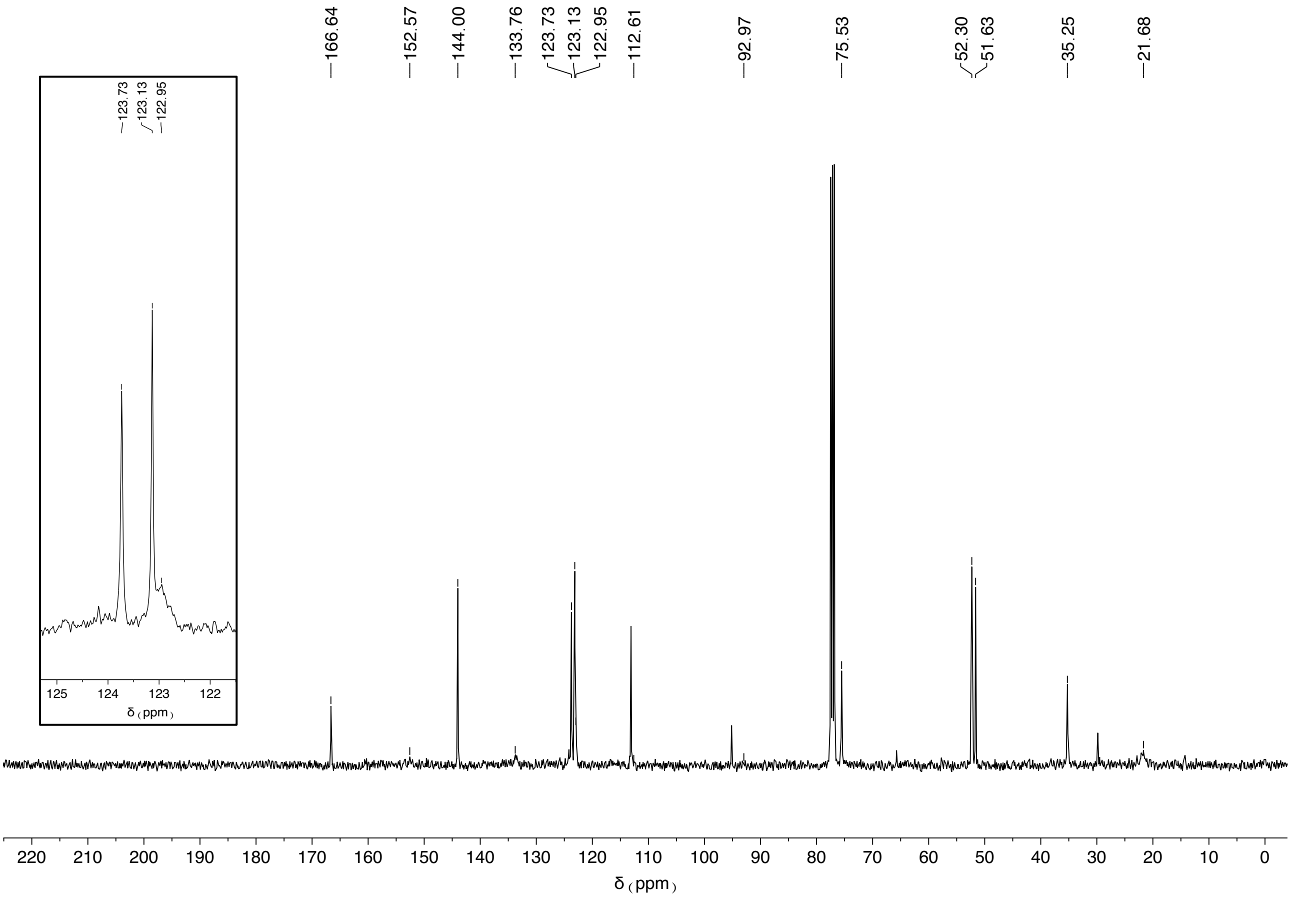


6 ($CDCl_3$, 25 °C): broad signals due Troc-rotamers (compound instable in solution; it decomposes partially in the NMR tube within the time)

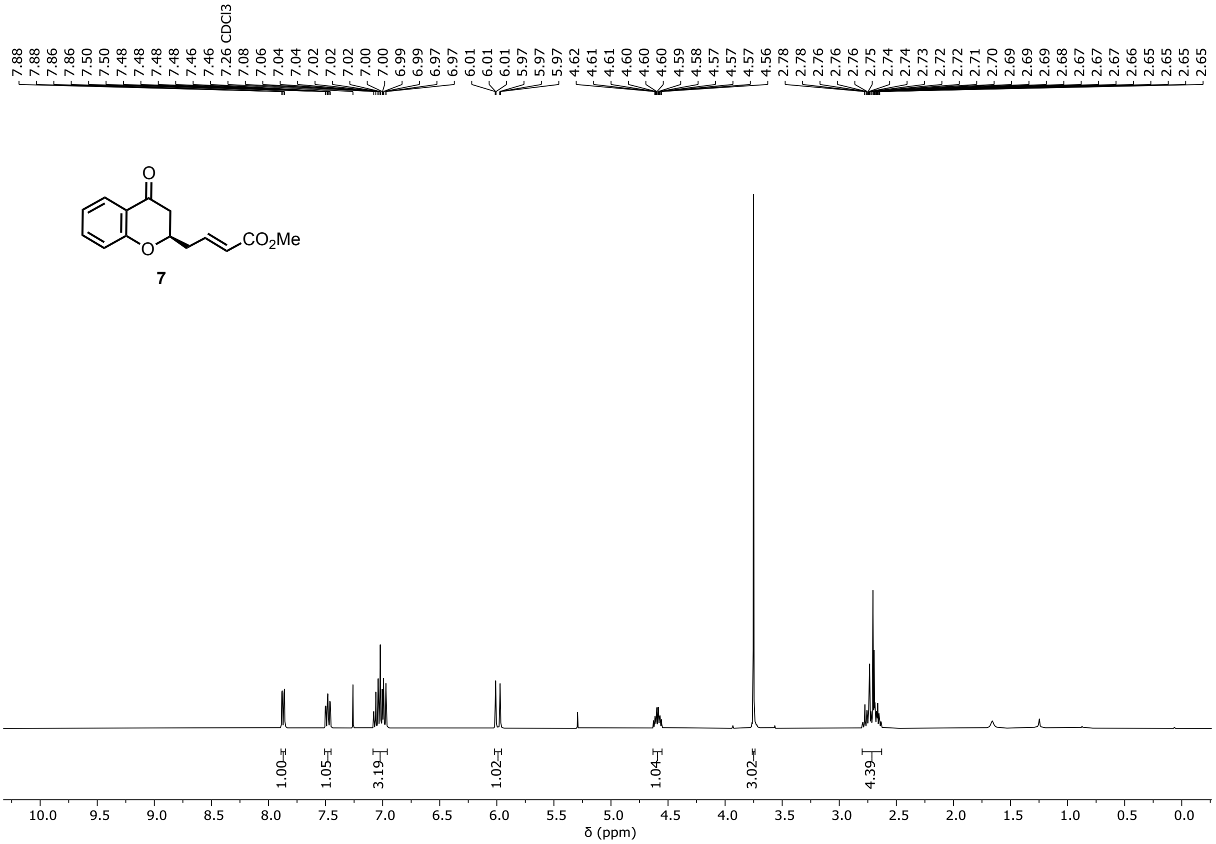


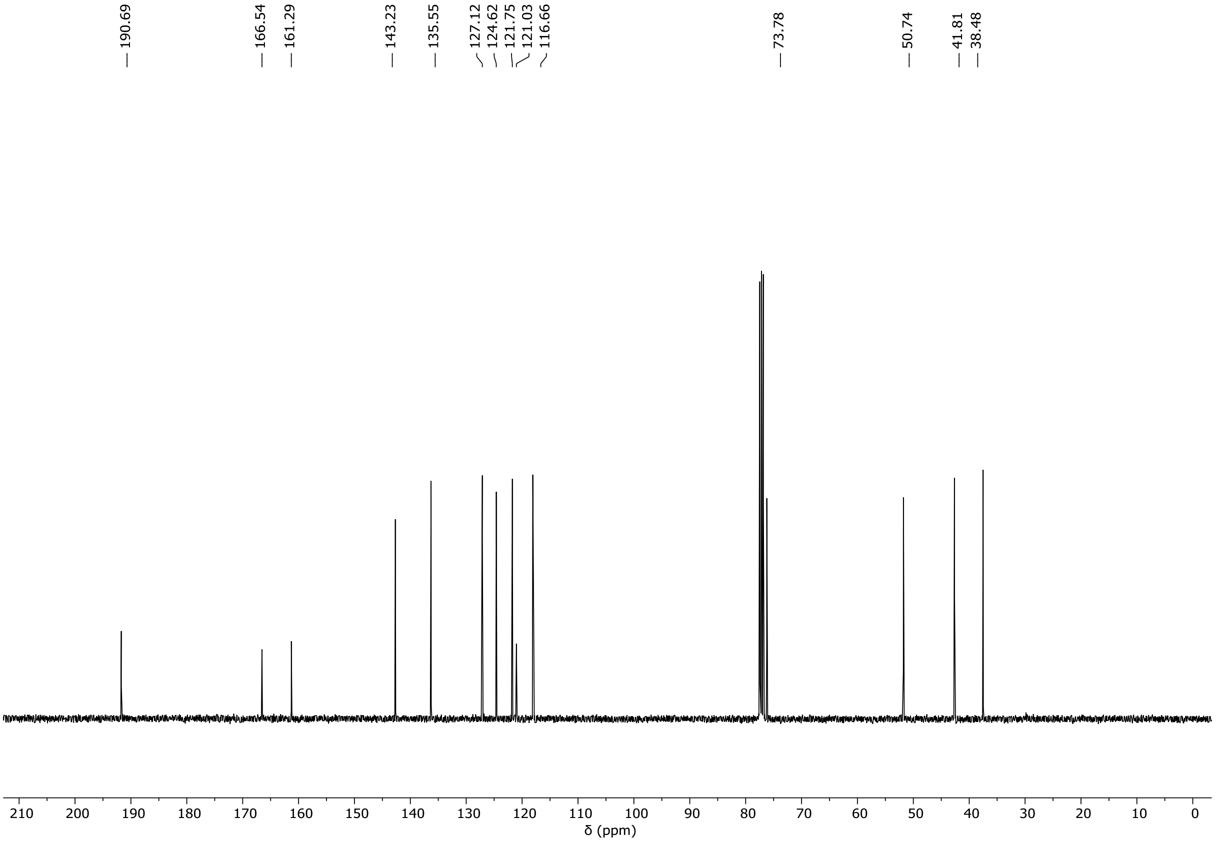
6



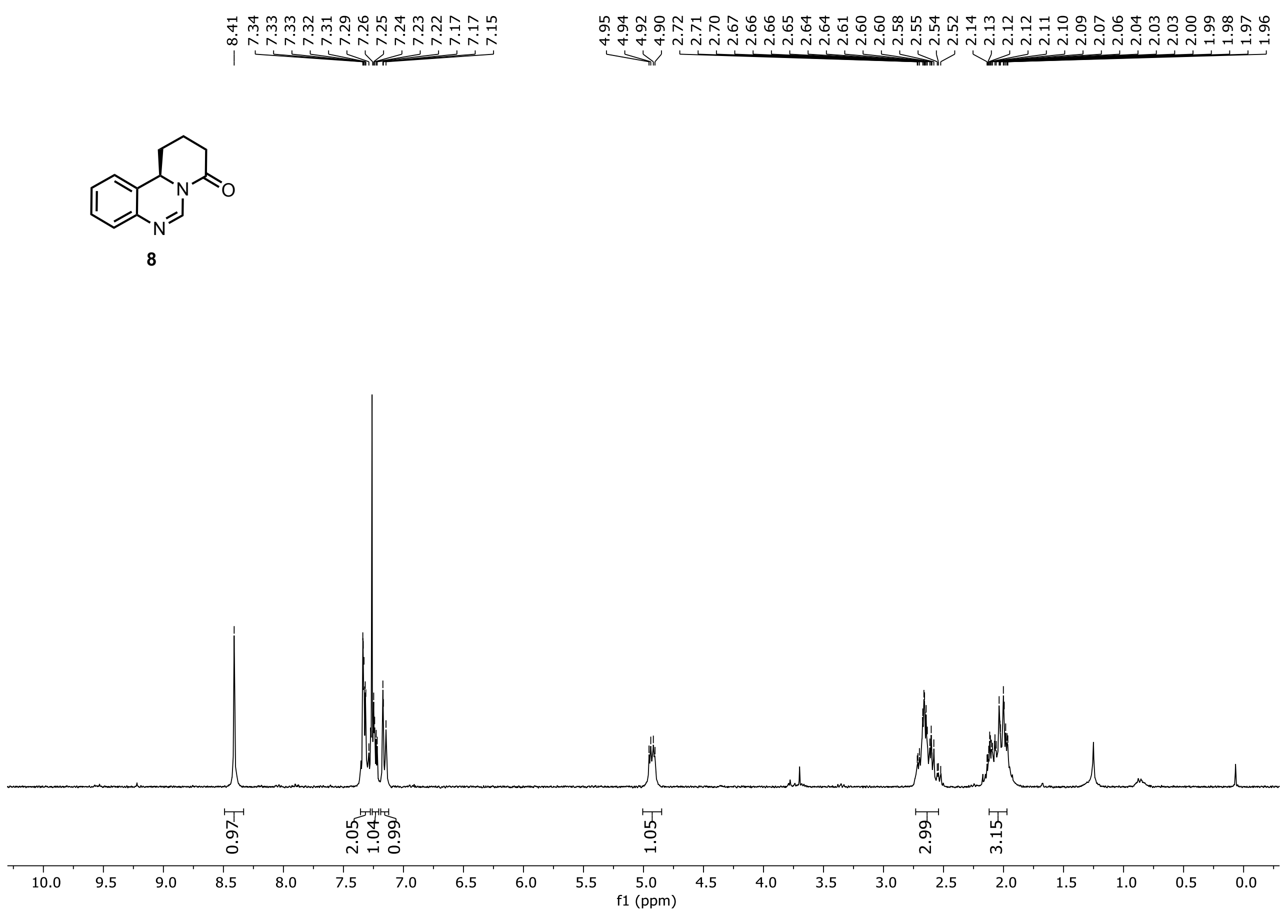


7 (CDCl$_3$, 25 °C):

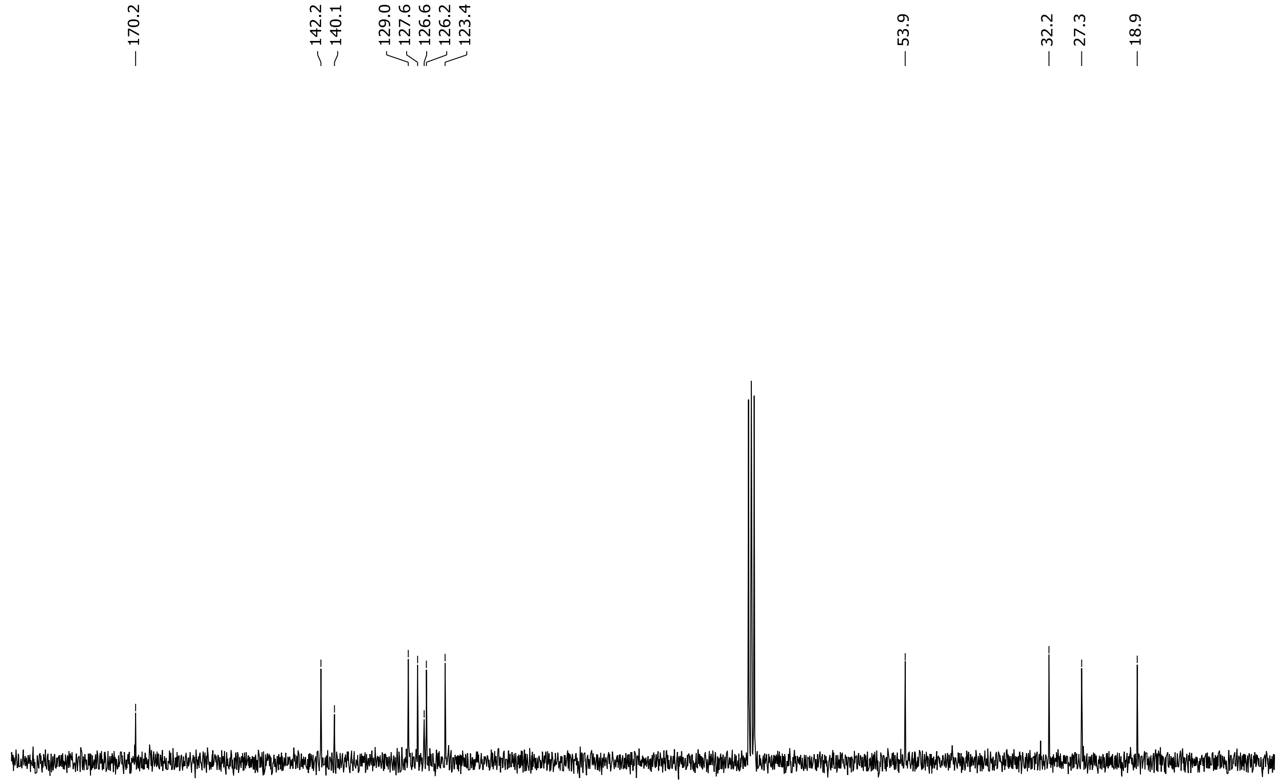

7.88
7.88
7.86
7.86
7.50
7.50
7.48
7.48
7.48
7.48
7.46
7.26 CDCl3
7.08
7.06
7.04
7.04
7.02
7.02
7.02
7.00
7.00
6.99
6.99
6.97
6.97
6.01
6.01
5.97
5.97
4.62
4.61
4.60
4.60
4.59
4.58
4.57
4.57
4.56
2.78
2.78
2.76
2.76
2.75
2.74
2.74
2.73
2.72
2.72
2.71
2.70
2.69
2.69
2.68
2.67
2.67
2.67
2.66
2.65
2.65
2.65
2.65
O
O
CO2Me
7
1.00
1.05
3.19
1.02
1.04
3.02
4.39
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
δ (ppm)


190.69
166.54
161.29
143.23
135.55
127.12
124.62
121.75
121.03
116.66
73.78
50.74
41.81
38.48
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
δ (ppm)

8 (CDCl$_3$, 25 °C):


8.41
7.34
7.33
7.33
7.32
7.31
7.29
7.26
7.25
7.24
7.23
7.22
7.17
7.17
7.15
4.95
4.94
4.92
4.90
2.72
2.71
2.70
2.67
2.66
2.66
2.65
2.64
2.64
2.61
2.60
2.60
2.58
2.55
2.54
2.52
2.14
2.13
2.12
2.12
2.11
2.10
2.09
2.07
2.06
2.04
2.03
2.03
2.00
1.99
1.98
1.97
1.96
N
N
O
0.97
2.05
1.04
0.99
1.05
2.99
3.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

8


170.2
142.2
140.1
129.0
127.6
126.6
126.2
123.4
53.9
32.2
27.3
18.9
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)