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Supporting Information

Highly Stereoselective [4+2] and [3+2] Spiroannulations of 2-(2-Oxoindolin-3-ylidene)acetic Esters Catalyzed by Bifunctional Thioureas

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Supporting Information

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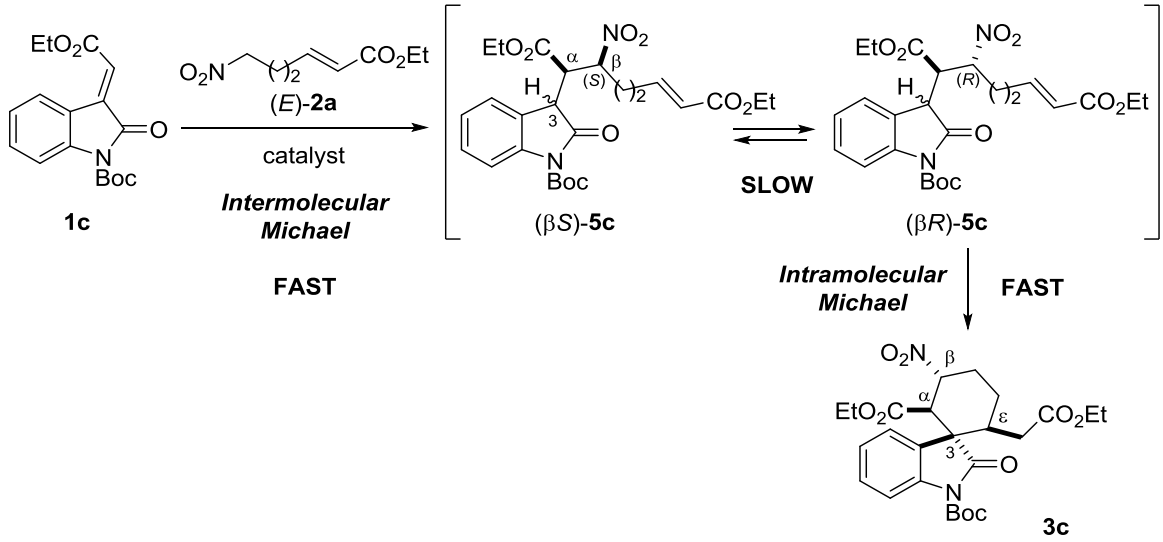
A. Mechanistic Studies.

6-membered β-nitro spirooxindoles.

For 6-membered spirooxindoles (Scheme S1), the ^{1}H NMR spectrum of the crude mixture recorded after three hours showed very low levels of both starting 3-ylidene oxindole **1c** and spirocyclohexane indolinone **3c**. The main component was the acyclic intermediate (β*S*)-**5c**, whose α,β-*anti* relationship was deduced comparing the ^{1}H NMR spectrum of the crude mixture recorded at low conversion of **3c** with the previously reported[1] spectra of **16a** and **16b** (Figure S1). Since the X-ray crystallographic analysis assigned to spirocyclic product **3c** the α,β-*trans* relative configuration, we assume that the bifunctional organocatalyst first promotes the Cβ epimerization of (β*S*)-**5c**, followed by a selective spirocyclization of (β*R*)-**5c**, only.



Scheme S1.

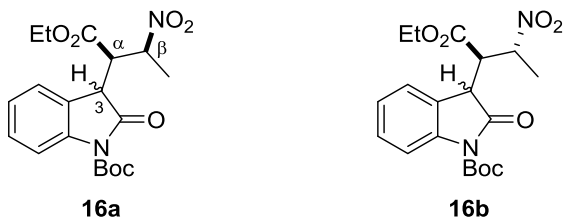


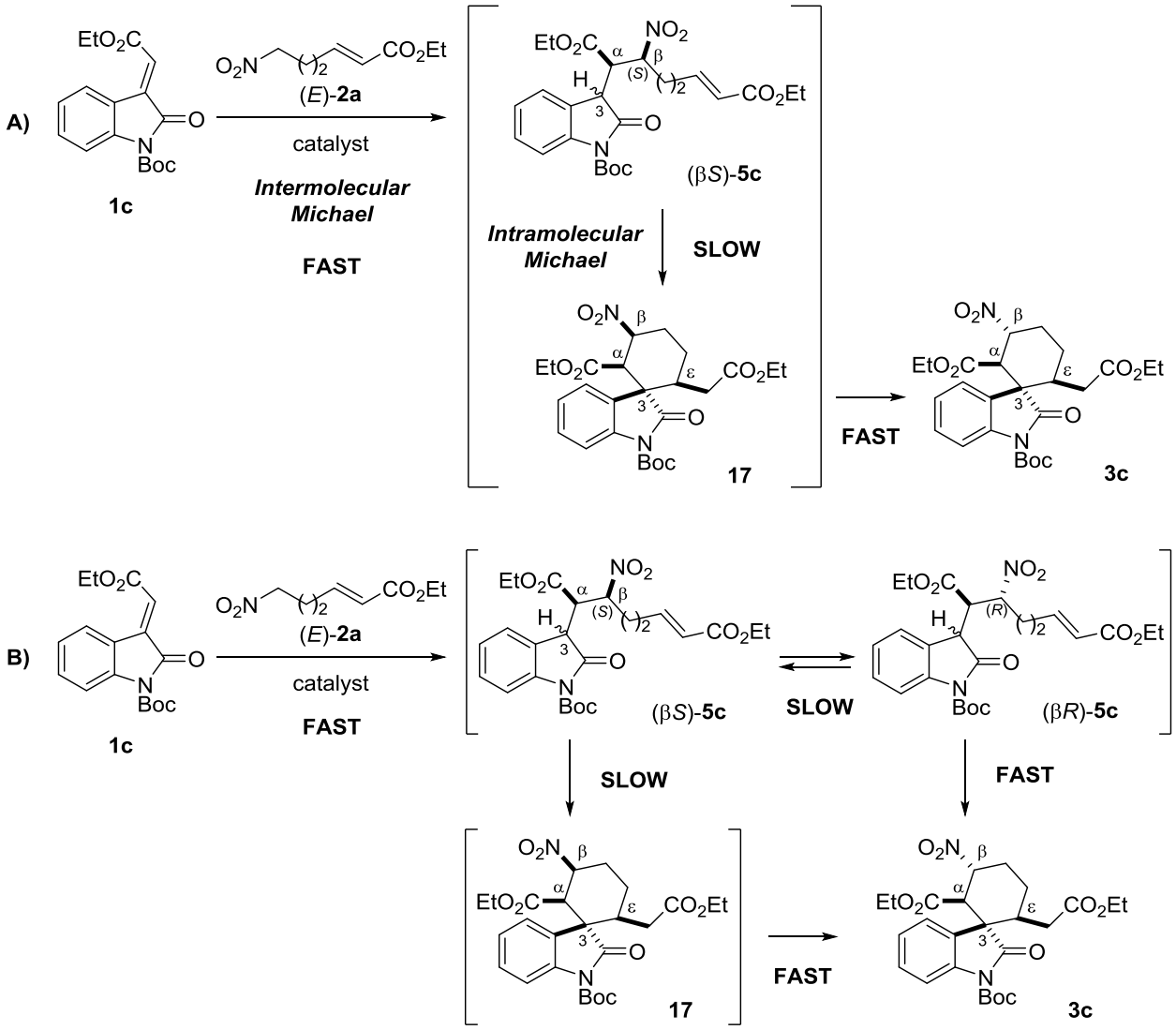
Figure S1.

The claimed organocatalyst-promoted Cβ epimerization was already observed for compounds **16a**, **16b** and analogues.[1] According to this mechanistic hypothesis, the rate determining step of the overall cascade reaction is the epimerization of (β*S*)-**5c** to (β*R*)-**5c**, which is then followed by a fast

[1] A. Quintavalla, F. Lanza, E. Montroni, M. Lombardo, C. Trombini, *J. Org. Chem.* **2013**, *78*, 12049-12064.

cyclization of the latter to **3c**. As an evidence, (β*R*)-**5c** was not detected during the reaction progress.

Alternative mechanistic hypotheses could involve the formation of the final product **3c** through the Cβ epimerization of the spirocyclic product **17** (Scheme S2). In the first case (Scheme S2**A**), the acyclic intermediate (β*S*)-**5c** undergoes a slow spirocyclization to **17**, followed by a fast catalyst-promoted Cβ epimerization to **3c**. The rate determining step should be the ring closure reaction, since **17** was not detected during the reaction progress. Alternatively, a stereoconvergent mechanism (Scheme S2**B**) could entail that the intermediate (β*S*)-**5c** is slowly epimerized to (β*R*)-**5c**, which quickly cyclizes to **3c**. At the same time, (β*S*)-**5c** slowly undergoes ring closure reaction to **17**, which is quickly epimerized to **3c**.

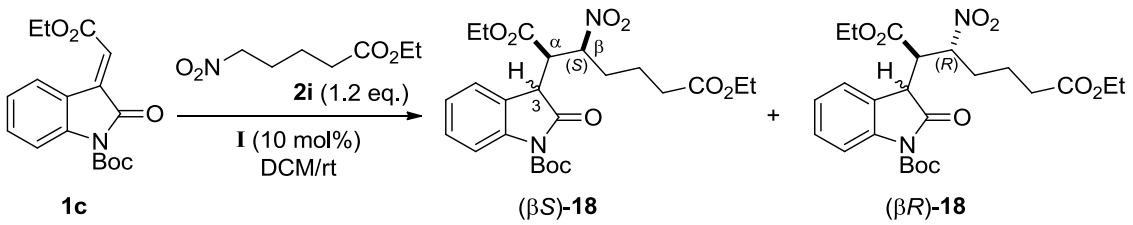


Scheme S2.

In our opinion these mechanistic hypotheses are unlikely on the following grounds:

i) The catalyst-promoted Cβ epimerization of intermediate (β*S*)-**5c** cannot be excluded, because it was already observed on **16a** and analogues[1] and at room temperature it was detectable after a few hours.

ii) When the same reaction protocol was applied to nitroester **2i** (Scheme S3), unable to provide spirocyclization, after a few hours the Cβ epimerized product (β*R*)-**18** was observed and after 22 hours the two Cβ epimers were present in almost equimolar amount.



3h: (β*S*)-**18**/(β*R*)-**18** = 75/25
22h: (β*S*)-**18**/(β*R*)-**18** = 55/45

Scheme S3.

iii) Three different diastereoisomers of **3c** (obtained by the DBU[2]-promoted racemic cascade reaction, see Section E) were subjected to catalyst **I** (10 mol%) in DCM at room temperature for 24 hours. No epimerization was observed. In particular, one of these isomers (**19**, Figure S2) is characterized by an α,β-*cis* relationship (as shown by ^{1}H NMR signals and 1D NOESY experiments, see p. S39 and pp. S52-S53) similar to that present in the spirocycle **17**.

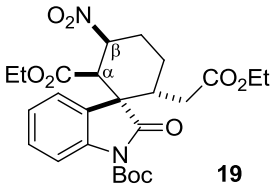


Figure S2.

iv) Spirocyclohexane oxindole **14'** (Figure S3, obtained applying the organocatalyzed cascade reaction to 3-ylidene oxindole **1c** and chiral nitroenoate *syn*-**2g**, see p. S37 and p. S52) was subjected to catalyst **I** (20 mol%) in DCM at room temperature for 24 hours. No epimerization was observed.

[2] DBU = 1,8-Diazabiciclo[5.4.0]undec-7-ene.

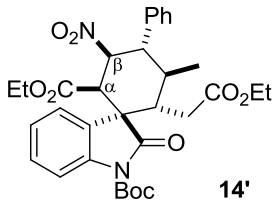


Figure S3.

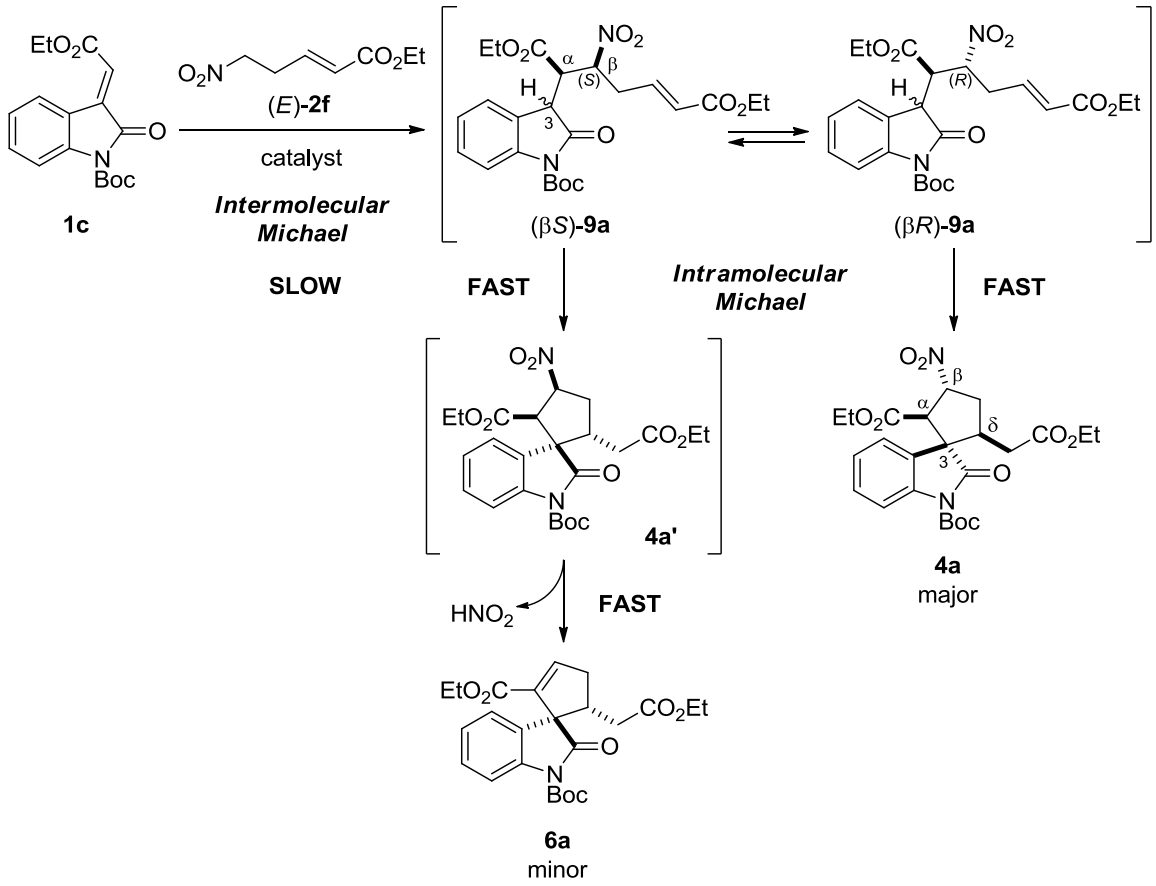
These last two results suggest that the Cβ epimerization transforming α,β-*cis* spirocycles (such as **17**) into α,β-*trans* spirocycles (such as **3c**) is not favored and/or the organocatalyst is unable to promote it.

Lastly, in support of the proposed mechanism (Scheme S1), it is interesting to note that most of the organocatalytic syntheses of β-nitro spirocyclohexane oxindoles provide products with α,β-*cis* relative configurations (such as **17**), but the epimerization of the β position is not observed.[3,4]

5-membered β-nitro spirooxindoles.

In the case of 5-membered spirooxindoles (Scheme S4), the acyclic intermediates **9a** were not detected during the reaction progress. Thus, we hypothesize that both the intermediates (β*S*)-**9a** and (β*R*)-**9a** are able to cyclize. In the presence of bifunctional organocatalyst **I**, (β*S*)-**9a** is formed more rapidly, then it equilibrates to (β*R*)-**9a**. The intramolecular Michael reaction on (β*R*)-**9a** is kinetically favored, being spirocyclopentane **4a** the major product. However, in contrast to 6-membered rings, (β*S*)-**9a** also undergoes cyclization followed by loss of HNO_2 to get spirocyclopentene **6a**. According to this mechanistic hypothesis, the rate determining step of the cascade process is the intermolecular Michael addition. From a stereochemical point of view, the two isomers **4a** and **4a'** differ for all the absolute configurations other than Cα, concluding that the simple inversion of configuration at Cβ determines the inversion of both C3 and Cδ configurations during the ring-closure step.

[3] a) K. Jiang, Z.-J. Jia, S. Chen, L. Wu, Y.-C. Chen, *Chem. Eur. J.* **2010**, *16*, 2852-2856; b) K. Jiang, Z.-J. Jia, X. Yin, L. Wu, Y.-C. Chen, *Org. Lett.* **2010**, *12*, 2766-2769.
[4] B. Zhou, Y. Yang, J. Shi, Z. Luo, Y. Li, *J. Org. Chem.* **2013**, *78*, 2897-2907.



Scheme S4.

Our mechanistic hypothesis states that **6a** does not derive from **4a**, but from a different diastereoisomer formed during the cascade process. The grounds of this assumption are the following: *i)* the **4a**/**6a** ratio was constant during the reaction progress; *ii)* the purified compound **4a** subjected to catalyst **I** (10 mol%) in DCM at room temperature for 21 hours did not yield **6a** nor epimerized products.

We propose the stereochemistry of **4a'** as indicated in Scheme S4 relying on the following observations: *i)* the opposite C3,Cδ-*trans* relationship of **4a** and **6a** was demonstrated by X-ray crystallographic analysis of **6d** (see Section H) and by the formation of *ent*-**6a** through base-promoted HNO_2 elimination from **4a** (Scheme 3); *ii)* only **4a'** presents the correct *trans* orientation of H and NO_2 required by a base-promoted E2 elimination of HNO_2 (Figure S4).

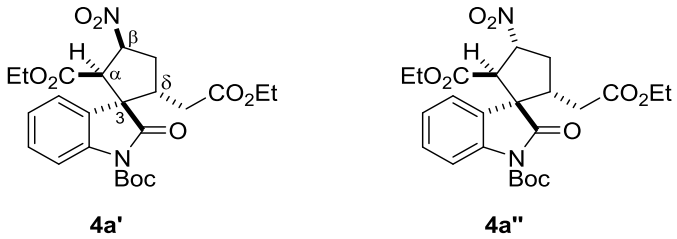


Figure S4.

As a further confirmation of the proposed mechanism (Scheme S4) and of the stereochemistry proposed for **4a'**, stereoisomer **4a''** was isolated from the DBU-promoted racemic cascade reaction (see Section E and p. S39).

The relative stereochemistry of **4a''** was established as follows: *i)* the Hα-Hβ coupling constant (*J*) is 10 Hz, similar to that of α,β-*trans* spirocyclopentanes (**4a-d** and **4f**); *ii)* the isolated **4a''**, subjected to quinuclidine (1.2 eq.) in DCM at room temperature, provided **6a**, thus confirming a C3,Cδ-*trans* relationship. The only diastereoisomer of **4a**, whose structure is compatible with these experimental findings, is **4a''** (Figure S4).

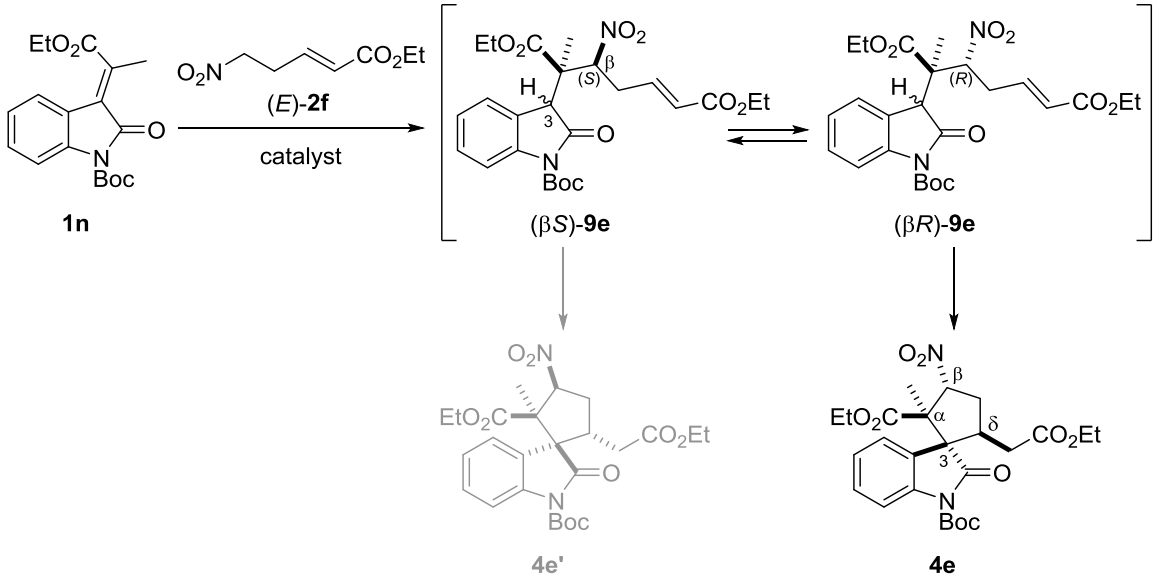
In conclusion, the spirocycle **4a''** was exposed to catalyst **I** (15 mol%) in DCM at room temperature for 22 hours without providing **6a**. This finding indirectly confirms the proposed structure of **4a'** and our mechanistic hypothesis.

We wish to mention that the minor isomer obtained employing *Cinchona*-derived catalysts **VII** and **IX** was **4a''** (Table 5). Conversely, Takemoto's catalyst **I** yielded **4a'** as minor isomer (isolated as **6a**). This finding demonstrates that the catalyst structure significantly affects both the rate and the stereoselectivity of the spirocyclization step.

Concerning the synthesis of the α-methyl β-nitro spirooxindole **4e**, according to the mechanism proposed in Scheme S4, the organocascade sequence carried out on substrate **1n** should provide the product as mixture of the two diastereoisomers **4e** and **4e'** (Scheme S5), since the HNO_2 elimination cannot take place. We observed that **4e** was the only spirocyclic product, even if the isolated yield was low.

The relative stereochemistry of **4e** shown in Scheme S5 was confirmed as follows: *i)* 1D NOESY experiments (see Section H); *ii)* the ^{1}H NMR spectrum of **4e** displays the same signals trend of α-methyl β-nitro cyclohexane spirooxindole **3n**.

The experimental evidences regarding the formation of **4e** led us to propose a mechanism (Scheme S5) analogous to that suggested for **3n** and **3c** (Scheme S1), characterized by the exclusive spirocyclization of the intermediate (β*R*)-**9e**.

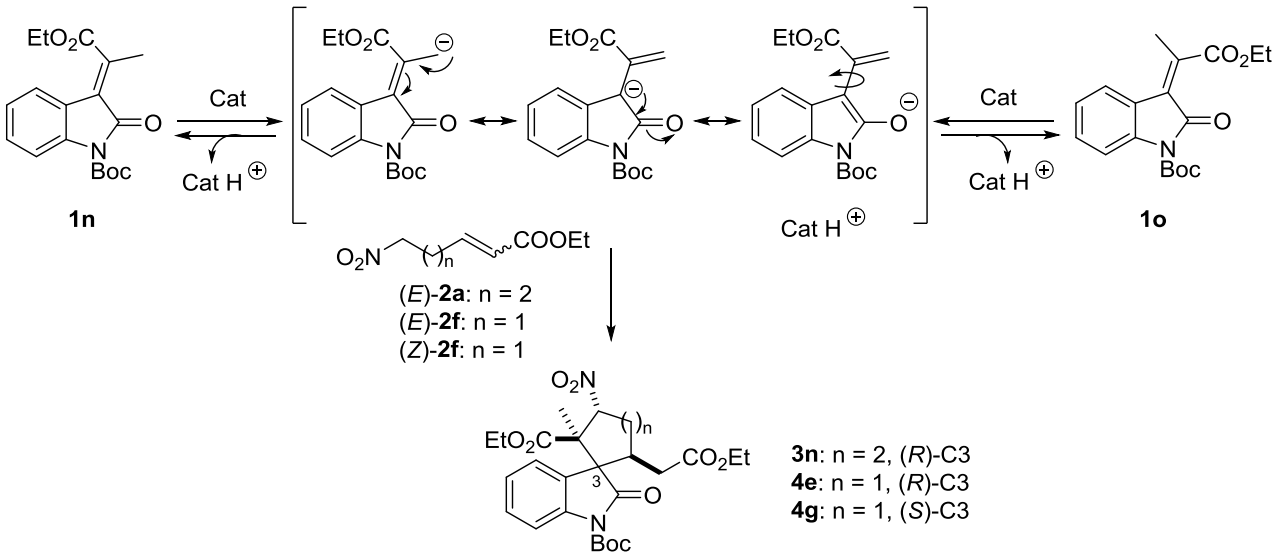

EtO2C
O2N
CO2Et
(E)-2f
catalyst
1n
NO2
(S)
(R)
H
3
O
N
Boc
(βS)-9e
(βR)-9e
4e'
4e
α
β
δ

Scheme S5.

*Stereoconvergent formation of α-methyl spirooxindoles **3n**, **4e** and **4g**.*

The synthetic approach to β-nitro spirooxindoles was extended to the construction of a second quaternary stereocenter on the Cα position, contiguous to the quaternary spiro carbon (C3). To this purpose, the protocol was applied to substrates **1n-o**, that present a tetrasubstituted double bond. The reactivity of these 3-ylidene oxindoles was much lower, therefore two equivalents of nitro compound and 20 mol% of catalyst **I** were required to obtain acceptable yields (30-40% yields; Table 2, entries 12-13; Table 6, entries 5-6 and 8-9). However, the process retained an excellent stereoselectivity, allowing the isolation of spiroindolinones **3n**, **4e** and **4g**, characterized by two adjacent quaternary stereocenters, as single diastereoisomers in 92-99% *ee*.

A possible explanation for the low yields might lie in the reactivity of the allylic position, already demonstrated for 3-ylidene oxindoles in the presence of bifunctional organocatalysts. In our reaction conditions, the alkylidene indolinones **1n** and **1o** could undergo deprotonation to an intermediate dienolate (Scheme S6), which was likely responsible of a variety of side reactions. Furthermore, the α-methyl spirooxindoles were formed with high *ee* and the same absolute stereochemistry, regardless of the starting *Z*/*E* double bond configuration. The observed stereoconvergence suggests that only one of the two isomeric 3-ylidene-indolin-2-ones participates as acceptor to the first intermolecular Michael reaction.

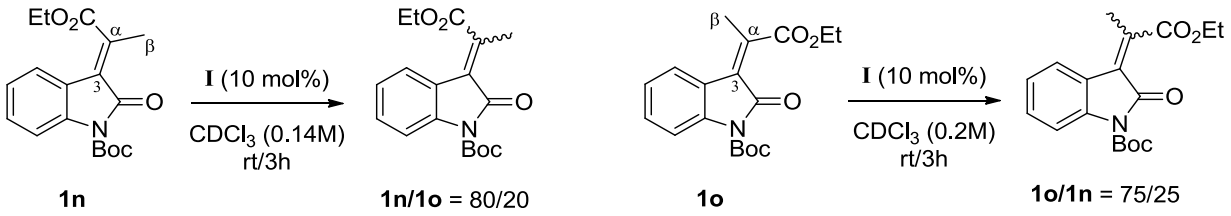


Scheme S6.

Our hypothesis is supported by the following experimental findings:

i) Setting the organocascade reaction on pure **1n** or **1o**, after two hours we observed the presence of both the isomers in the crude mixture (^{1}H NMR spectrum). It demonstrates that the starting material isomerization occurs in our reaction conditions and it is faster than the intermolecular Michael addition.

ii) Subjecting substrates **1n** and **1o** to catalyst **I** (10 mol%) in $CDCl_3$ at room temperature, we observed (^{1}H NMR spectra) a significant amount of isomerized substrate in both the reactions after three hours (Scheme S7).



Scheme S7.

iii) 1D NOESY experiments on products **3n**, **4e** and **4g** showed the same relative stereochemistry of spirooxindoles **3c**, **4a** and **4f**, respectively, leading us to hypothesize that the (*E*)-configured 3-ylidene indolinone **1n** was the reactive species.

B. Optimization Study.

Table S1. Reaction conditions optimization for the asymmetric Michael-Michael organocascade reaction between 3-ylidene oxindole **1c** and nitroester (*E*)-**2a**.[a]

Entry	**I** [mol%]	Solvent	Time [d]	Conversion [**3c**%][b]	*ee* [%][c]
1	10	DCM	3	90	98
2	5	DCM	4	61	98
3	10	Toluene	3	70	>99
4	10	Hexane	3	90	94
5	10	Et_2O	3	90	97
6	10	THF	4	73	98
7	10	CH_3CN	4	62	96
8	10	DMF	3	76	81
9	10	H_2O	2	72	94
10	5	H_2O	2	66	90

[a] Reaction conditions: **1c** (0.1 mmol), (*E*)-**2a** (0.12 mmol), catalyst **I**, solvent (0.15 mL), rt. [b] Determined by ^{1}H NMR of the crude mixture. Spirooxindole **3c** was detected as single diastereoisomer. [c] Determined by CSP-HPLC of isolated **3c**. DCM = dichloromethane, THF = tetrahydrofuran, DMF = dimethylformamide, d = days.

As expected, the lowering of catalyst loading caused a significant conversion decrement (Table S1, entry 2), therefore the solvents screening was carried out employing 10 mol% of catalyst **I**. The best results in terms of both reaction rate and stereoselectivity were obtained in less polar media (entries 1, 3-5), yielding conversions up to 90% and *ee* up to >99%. More polar solvents, such as THF and CH_3CN, required longer reaction times, while maintaining a high level of enantiocontrol (entries 6-7). Conversely, the very polar DMF showed a good conversion, but poor *ee* (entry 8), likely because its ability as hydrogen-bonding acceptor affected the catalyst-substrate interaction. An interesting and unexpected behavior was observed carrying out the organocascade reaction in water. We obtained a good conversion and an excellent enantiomeric excess after only 48 hours (entry 9). Assuming that the reaction acceleration was due to micelles formation, we tried to exploit this phenomenon to reduce the catalyst loading, but the reaction rate decreased in turn (entry 10). The

optimal conditions, representing the best balance between reaction rate, stereocontrol and solvent toxicity, were identified in 10 mol% of catalyst **I** and DCM as the reaction medium.

C. General Information.

^{1}H and ^{13}C NMR spectra were recorded on Varian Gemini 200 or Inova 400 NMR instruments with a 5 mm probe. All chemical shifts are quoted relative to deuterated solvent signal, chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are reported in Hz.

HPLC-MS analyses were performed on an Agilent Technologies HP1100 instrument coupled with an Agilent Technologies MSD1100 single-quadrupole mass spectrometer. A Phenomenex Gemini C18 3 μm (100 x 3 mm) column was employed for the chromatographic separation: mobile phase H_2O/CH_3CN, gradient from 30% to 80% of CH_3CN in 8 min, 80% of CH_3CN until 22 min, then up to 90% of CH_3CN in 2 min, flow rate 0.4 mL min^{-1}. Mass spectrometric detection was performed in full-scan mode from m/z 50 to 2500, scan time 0.1 s in positive ion mode, ESI spray voltage 4500 V, nitrogen gas 35 psi, drying gas flow rate 11.5 mL min^{-1}, fragmentor voltage 30 V.

High-resolution MS (HRMS) ESI analyses were performed on a LTQ Orbitrap XL (Thermo Scientific) mass spectrometer.

CSP-HPLC analyses were performed on an Agilent Technologies Series 1200 instrument using Daicel® chiral columns and *n*-hexane/2-propanol (*n*-Hex/IPA) mixtures.

Optical rotation measurements were performed on a polarimeter Schmidt+Haensch UniPol L1000.

Melting point measurements were performed on a Bibby Stuart Scientific SMP3 apparatus.

Flash chromatography purifications were carried out using Merck silica gel 60 (230-400 mesh particle size). Thin-layer chromatography was performed on Merck 60 F254 plates.

Commercial reagents were used as received without additional purification.

Catalysts **II-IX** are known and prepared according to the literature procedures.[5]

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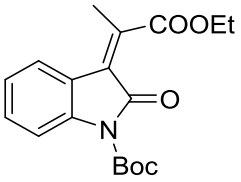
D. Preparation and Characterization of the Starting Materials.

3-Yliden oxindoles **1a**,[6] **1b-c**,[7] **1d-h**,[8] **1i**,[9] **1j**,[10] **1k**,[11] **1l**,[12] **1m**,[13] and **1n**[1] are known and prepared according to the literature procedures. Nitro compounds (*E*)-**2a**,[14] (*E*)-**2c** and (*E*)-**2f**,[15] (*E*)-**2e**[16] and **13b**[17] are known and prepared according to the literature procedures. Nitro compounds *anti*-**13a**,[18] *syn*-**13a**[19] and **2i**[20] are known, but they are prepared following a modified procedure.



1o

tert*-butyl (*Z*)-3-(1-ethoxy-1-oxopropan-2-ylidene)-2-oxoindoline-1-carboxylate:** Obtained as the major isomer from the synthesis of **(E*)-isomer **1n**. Yield = 33%; dark red syrup.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.1 Hz, 1H), 7.59 (d, *J* = 7.7 Hz, 1H), 7.36 (t, *J* = 8.0 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 4.42 (q, *J* = 7.2 Hz, 2H), 2.45 (s, 3H), 1.64 (s, 9H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 163.7, 148.9, 140.6, 139.9, 129.8, 124.1, 123.9, 123.7, 121.7, 115.1, 84.3, 61.8, 28.0, 18.3, 13.8. HPLC-MS (ESI) t_r = 11.1 min; $[M+Na]^+$ = 354.2 *m/z*, $[2M+Na]^+$ = 685.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{18}H_{21}NO_5Na$ 354.1312 found 354.1307.

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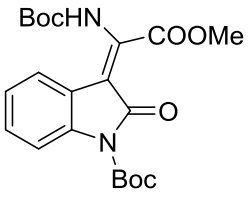
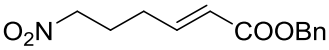


1p

***tert*-butyl (*E*)-3-(1-((*tert*-butoxycarbonyl)amino)-2-methoxy-2-oxoethylidene)-2-oxoindoline-1-carboxylate**: Indolin-2-one (1 mmol, 133 mg) is dissolved in THF (5 mL), DMAP (4-dimethylaminopyridine, 5 mol%) is added to the solution, and finally, Boc_2O (di-*tert*-butyl dicarbonate, 1.1 mmol) is added. The reaction mixture is stirred at room temperature for 1 h. Then the solvent is removed under reduced pressure and the crude mixture is used as such.

To a suspension of NaH (1.2 mmol) in THF (0.2 M) at 0 °C a solution of methyl 2-((*tert*-butoxycarbonyl)amino)-2-(dimethoxyphosphoryl)acetate (1.2 mmol) in THF (2 mL) is added dropwise. This solution is left to stir for 15 minutes, or until effervescence ceased, before the dropwise addition of a solution of crude *N*-Boc indolin-2-one in THF (2 mL). The mixture is left to warm to room temperature overnight. The reaction is then quenched with a saturated solution of NH_4Cl, extracted with diethyl ether (3 x 10 mL), the combined organic layers are dried over Na_2SO_4, filtered and concentrated under reduced pressure. The mixture is purified by column chromatography on silica gel (ethyl acetate/cyclohexane 1/9) providing product **1p** as single diastereoisomer in 70% yield (292 mg).

Pale yellow crystals; m.p. = 115-117 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.90 (bs, 1H), 7.88 (d, *J* = 8.0, 1H), 7.28 – 7.24 (m, 1H), 7.18 – 7.09 (m, 2H), 4.06 (s, 3H), 1.68 (s, 9H), 1.52 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.0, 162.9, 150.7, 148.7, 139.8, 136.5, 127.5, 124.1, 120.2, 119.2, 114.9, 101.9, 84.5, 83.3, 53.3, 28.0, 27.9. HPLC-MS (ESI) t_r = 13.9 min; $[M+Na]^+$ = 441.0 *m/z*, $[2M+Na]^+$ = 859.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{21}H_{26}N_2O_7Na$ 441.1632 found 441.1633.



(*E*)-**2b**

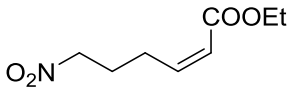
benzyl (*E*)-6-nitrohex-2-enoate: Obtained using the same procedure employed for (*E*)-**2a**. Yield = 74%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.29 (m, 5H), 6.95 (td, *J* = 15.6, 6.9 Hz, 1H), 5.95 (td, *J* = 15.7, 1.6 Hz, 1H), 5.20 (s, 2H), 4.41 (t, *J* = 6.8 Hz, 2H), 2.42 – 2.29 (m, 2H), 2.26 – 2.13 (m, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 165.7, 146.0, 135.8, 128.5, 128.14, 128.11, 122.8, 74.3, 66.1, 28.5, 25.4. HPLC-MS (ESI) t_r = 9.4 min; $[M+Na]^+$ = 272.0 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{13}H_{15}NO_4Na$ 272.0893 found 272.0896.

(*E*)-**2d** (*Z*)-**2d**

(*E*)-6-nitrohex-2-enenitrile and (*Z*)-6-nitrohex-2-enenitrile: To a solution of (cyanomethyl)triphenylphosphonium chloride (2.4 mmol, 853.4 mg) in THF (10 mL) at 0 °C NaH (2.4 mmol, 96 mg) is added and the mixture is stirred at this temperature for 15 min. 4-Bromobutanal (302 mg, 2 mmol) in 10 mL of THF is slowly added and the reaction is left stirring at room temperature overnight. It is then quenched with a saturated solution of NH_4Cl and the aqueous phase is extracted with diethyl ether (3 x 10 mL). The combined organic layers are dried over Na_2SO_4, filtered and concentrated. The mixture is purified by column chromatography on silica gel (diethyl ether/cyclohexane 1/9) providing the product in quantitative yield as a mixture of *E* and *Z* isomers (*E*/*Z* = 2/1) as colourless oil. The mixture of the two isomers is dissolved in 20 mL of anhydrous DMF. Then, $NaNO_2$ (3 mmol, 207 mg) is added and the reaction is stirred at room temperature for 22 h. Cold water is added to the reaction and the water phase is extracted with diethy ether (3 x 15 mL). The organic phases are collected, dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel (diethyl ether/cyclohexane from 1/9 to 3/7) allows the separation of *E* and *Z* isomers, affording (*E*)-**2d** (35% yield) and (*Z*)-**2d** (18% yield) as colourless oils.

(*E*)-**2d**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 – 6.52 (m, 1H), 5.44 (d, *J* = 16.4 Hz, 1H), 4.42 (t, *J* = 6.7 Hz, 2H), 2.38 (q, *J* = 7.2 Hz, 2H), 2.29 – 2.06 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 116.7, 102.0, 74.1, 29.8, 25.2. HPLC-MS (ESI) t_r = 4.7 min; $[M+H]^+$ = 141.0 *m/z*, $[M+Na]^+$ = 163.0 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_6H_8N_2O_2Na$ 163.0478 found 163.0476.

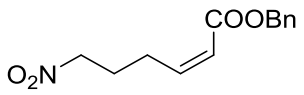
(*Z*)-**2d**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.57 – 6.38 (m, 1H), 5.45 (d, *J* = 10.8 Hz, 1H), 4.44 (t, *J* = 7.0 Hz, 2H), 2.57 (q, *J* = 7.7 Hz, 2H), 2.23 (p, *J* = 7.4 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 151.3, 115.2, 101.9, 74.3, 28.5, 25.7. HPLC-MS (ESI) t_r = 4.5 min; $[M+H]^+$ = 141.0 *m/z*, $[M+Na]^+$ = 163.0 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_6H_8N_2O_2Na$ 163.0478 found 163.0473.



(*Z*)-**2a**

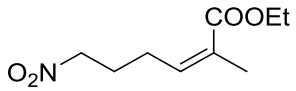
ethyl (*Z*)-6-nitrohex-2-enoate: Obtained as the minor isomer from the synthesis of **(*E*)-2a**. Yield = 13%; colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.25 – 6.12 (m, 1H), 5.88 (d, *J* = 11.6 Hz, 1H), 4.42 (t, *J* = 7.2 Hz, 2H), 4.18 (q, *J* = 7.1 Hz, 2H), 2.78 (q, *J* = 7.7 Hz, 2H), 2.19 (p, *J* = 7.3 Hz, 2H), 1.30 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 146.3, 121.9, 74.7, 60.1, 26.4, 25.4,

14.1. HPLC-MS (ESI) t_r = 7.5 min; $[M+H]^+$ = 188.0 *m/z*, $[M+Na]^+$ = 210.0 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_8H_{13}NO_4Na$ 210.0737 found 210.0741.



(*Z*)-**2b**

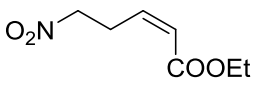
benzyl (*Z*)-6-nitrohex-2-enoate: Obtained as the minor isomer from the synthesis of **(*E*)-2b**. Yield = 10%; colourless oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.61 – 7.22 (m, 5H), 6.36 – 6.09 (m, 1H), 5.93 (d, *J* = 11.2 Hz, 1H), 5.17 (s, 2H), 4.39 (t, *J* = 7.1 Hz, 2H), 2.79 (q, *J* = 7.8 Hz, 2H), 2.19 (p, *J* = 7.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 147.0, 135.8, 128.6, 128.3, 121.6, 74.7, 66.0, 26.3, 25.5. HPLC-MS (ESI) t_r = 9.7 min; $[M+Na]^+$ = 272.0 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{13}H_{15}NO_4Na$ 272.0893 found 272.0889.



(*Z*)-**2e**

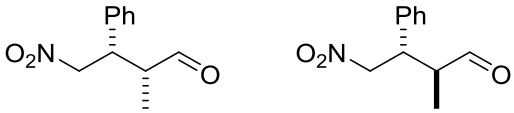
ethyl (*Z*)-2-methyl-6-nitrohex-2-enoate: KHMDS (2 mmol, 4 mL, 0.5 M in toluene) is added dropwise to a solution of triethyl 2-phosphonopropionate (2 mmol, 0.438 mL) and 18-crown-6 (3.6 mmol, 950 mg) in anhydrous THF (18 mL) at -78 °C and the reaction is stirred for 20 min at this temperature. Then a solution of 4-bromobutanal (2 mmol, 302 mg) in anhydrous THF (4.5 mL) is added dropwise and the reaction is stirred at -78 °C for 1 h and then at room temperature for 1 h. The reaction is quenched with a saturated solution of NH_4Cl and extracted with diethyl ether (3 x 15 mL). The organic phases are collected, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The purification by column chromatography on silica gel (ethyl acetate/cyclohexane 1/9) provides the product in 69% yield as a mixture of *E* and *Z* isomers (*E*/*Z* = 1/3.3). The obtained ethyl 6-bromo-2-methylhex-2-enoate is dissolved in anhydrous DMF (13 mL) and $NaNO_2$ (2.06 mmol, 141.7 mg) is added. The reaction is stirred overnight at room temperature. Then cold water is added and the water phase is extracted with diethyl ether (3 x 15 mL). The organic phases are collected, dried over Na_2SO_4, filtered and concentrated under reduced pressure. Purification by column chromatography on silica gel (diethyl ether/cyclohexane 5/95) allows the separation of *E* and *Z* isomers, affording (*Z*)-**2e** in 35% yield as colourless oil (*E* + *Z* isomers yield = 58%).

^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (t, *J* = 7.5 Hz, 1H), 4.39 (t, *J* = 7.1 Hz, 2H), 4.19 (q, *J* = 7.3 Hz, 2H), 2.55 (q, *J* = 7.6 Hz, 2H), 2.14 (p, *J* = 7.1 Hz, 2H), 1.91 (s, 3H), 1.29 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 138.9, 129.7, 74.8, 60.3, 26.8, 26.0, 20.6, 14.3. HPLC-MS (ESI) t_r = 8.6 min; $[M+Na]^+$ = 224.0 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_9H_{15}NO_4Na$ 224.0893 found 224.0899.



(*Z*)-**2f**

ethyl (*Z*)-5-nitropent-2-enoate: Obtained as the minor isomer from the synthesis of (*E*)-**2f**. Yield = 10%; colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.24 (td, *J* = 11.5, 7.5 Hz, 1H), 5.96 (d, *J* = 11.6 Hz, 1H), 4.53 (t, *J* = 6.7 Hz, 2H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.33 (q, *J* = 6.4 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 142.1, 123.5, 74.3, 60.3, 26.4, 14.2. HPLC-MS (ESI) t_r = 6.3 min; $[M+H]^+$ = 174.0 *m/z*, $[M+Na]^+$ = 196.0 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_7H_{11}NO_4Na$ 196.0580 found 196.0576.



syn-**13a** *anti*-**13a**

(2*R*,3*S*)-2-methyl-4-nitro-3-phenylbutanal (*syn*-13a) and (2*S*,3*S*)-2-methyl-4-nitro-3-phenylbutanal (*anti*-13a): Propanal (0.5 mmol, 36 µL) is added to a solution of (*S*)-2-(diphenyl((trimethylsilyl)oxy)methyl)pyrrolidine (10 mol%, 8 mg) and *trans*-β-nitrostyrene (0.25 mmol, 37.5 mg) in DCM (1 mL). The reaction is stirred for 3 h at room temperature. Then, it is quenched at 0 °C with HCl (1M) and extracted with DCM (3 x 5 mL). The organic phases are collected, dried over Na_2SO_4, filtered and concentrated under reduced pressure. The purification by column chromatography on silica gel (ethyl acetate/cyclohexane 5/95) provides a mixture of *syn*-**13a** and *anti*-**13a** (*syn*-**13a**/*anti*-**13a** = 65/35) as colourless oil in 80% yield.

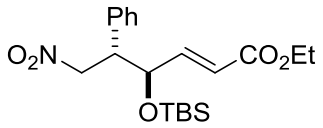
syn-**2g** *anti*-**2g**

ethyl (4*S*,5*S*,*E*)-4-methyl-6-nitro-5-phenylhex-2-enoate (*syn*-2g) and ethyl (4*R*,5*S*,*E*)-4-methyl-6-nitro-5-phenylhex-2-enoate (*anti*-2g): The mixture of *syn*-**13a** and *anti*-**13a** is subjected to the Wittig reaction, following the procedure reported for (*E*)-**2a**, which provides a mixture of *syn*-**2g** and *anti*-**2g** (*syn*-**2g**/*anti*-**2g** = 65/35) in 77% yield. The separation of *syn*-**2g** and *anti*-**2g** is carried out by means of CSP-HPLC on a semi-preparative Daicel® IC column, 90:10 *n*-Hex/IPA for 7 min, then to 80:20 in 20 min, 80:20 for 10 min, then to 70:30 in 10 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r (*anti*) = 23.8 min (major); t_r (*syn*) = 28.3 min (major).

syn-**2g**: pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 – 7.27 (m, 3H), 7.18 (d, *J* = 6.8 Hz, 2H), 6.86 (dd, *J* = 15.6, 9.2 Hz, 1H), 5.93 (d, *J* = 15.6 Hz, 1H), 4.70 – 4.55 (m, 2H), 4.23 (q, *J* = 7.2

Hz, 2H), 3.38 (dt, *J* = 9.6, 4.8 Hz, 1H), 2.67 – 2.59 (m, 1H), 1.32 (t, *J* = 7.2 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 149.9, 137.3, 129.0, 128.0, 128.0, 122.8, 79.2, 60.6, 49.0, 40.3, 18.2, 14.1. HPLC-MS (ESI) t_r = 10.2 min; $[M+H]^+$ = 278.0 *m/z*, $[M+Na]^+$ = 300.0 *m/z*, $[M+K]^+$ = 316.0 *m/z*. $[\alpha]_D^{20}$ = -18 (c = 0.84, DCM). HRMS (ESI) $[M+Na]^+$ calcd for $C_{15}H_{19}NO_4Na$ 300.1206 found 300.1201.

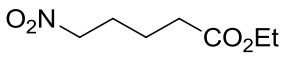
anti-**2g**: pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.27 (m, 3H), 7.12 (d, *J* = 7.6 Hz, 2H), 6.73 (dd, *J* = 16.0, 8.8 Hz, 1H), 5.80 (d, *J* = 15.2 Hz, 1H), 4.75 – 4.65 (m, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 3.61 – 3.56 (m, 1H), 2.76 – 2.70 (m, 1H), 1.29 (t, *J* = 6.8 Hz, 3H), 1.08 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0, 148.7, 136.1, 128.8, 128.4, 127.9, 122.7, 77.9, 60.5, 48.6, 39.1, 17.4, 14.1. HPLC-MS (ESI) t_r = 9.8 min; $[M+H]^+$ = 278.0 *m/z*, $[M+Na]^+$ = 300.0 *m/z*, $[M+K]^+$ = 316.0 *m/z*. $[\alpha]_D^{20}$ = -3 (c = 0.89, DCM). HRMS (ESI) $[M+Na]^+$ calcd for $C_{15}H_{19}NO_4Na$ 300.1206 found 300.1210.



2h

ethyl (4*R*,5*S*,*E*)-4-((*tert*-butyldimethylsilyl)oxy)-6-nitro-5-phenylhex-2-enoate: Nitroaldehyde **13b** (0.2 mmol, *dr* = 98:2, 98% *ee*) is subjected to the Wittig reaction, following the procedure reported for (*E*)-**2a**, which provides **2h** as pale yellow oil in 89% yield (70 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 3H), 7.21 (d, *J* = 8.0 Hz, 2H), 6.87 (dd, *J* = 12.0, 4.0 Hz, 1H), 5.93 (d, *J* = 16.0 Hz, 1H), 4.87 – 4.76 (m, 2H), 4.48 (t, *J* = 4.0 Hz, 1H), 4.19 (q, *J* = 7.2 Hz, 2H), 3.73 – 3.65 (m, 1H), 1.29 (t, *J* = 6.4 Hz, 3H), 0.92 (s, 9H), -0.09 (s, 3H), -0.24 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7, 147.3, 136.6, 128.8, 128.4, 128.1, 128.1, 122.5, 75.4, 74.3, 60.7, 49.5, 25.8, 18.0, 14.2, -4.5, -5.6. HPLC-MS (ESI) t_r = 16.2 min; $[M+H]^+$ = 394.2 *m/z*, $[M+Na]^+$ = 416.0 *m/z*. $[\alpha]_D^{20}$ = -11 (c = 1.21, DCM). HRMS (ESI) $[M+Na]^+$ calcd for $C_{20}H_{31}NO_5SiNa$ 416.1864 found 416.1866.



2i

ethyl 5-nitropentanoate: Ethyl 5-bromopentanoate (2.5 mmol, 396 μL) is dissolved in anhydrous DMF (20 mL) and $NaNO_2$ (3.75 mmol, 259 mg) is added. The reaction is stirred overnight at room temperature. Then cold water is added and the water phase is extracted with diethyl ether (3 x 20 mL). The organic phases are collected, dried over Na_2SO_4, filtered and concentrated under reduced

pressure. Purification by column chromatography on silica gel (diethyl ether/cyclohexane 1/9) provides **2i** in 60% yield as colourless oil.

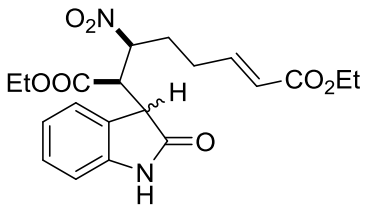
E. Typical Procedures for the Michael/Michael Cascade Reactions.

Typical procedure for the enantioselective synthesis of spirocyclohexane oxindoles: The nitro compound **2** (0.12 mmol) is added to a solution of catalyst (10 mol%) and 3-ylidene oxindole **1** (0.1 mmol) in DCM (0.15 mL). The reaction is stirred at room temperature for the reported time. The conversion is monitored by TLC and ^{1}H NMR. The crude mixture is directly purified by flash chromatography on silica gel (cyclohexane/ethyl acetate 9/1).

Typical procedure for the enantioselective synthesis of spirocyclopentane oxindoles: The nitro compound **2** (0.12 mmol) is added to a solution of catalyst (10 mol%) and 3-ylidene oxindole **1** (0.1 mmol) in DCM (0.15 mL). The reaction is stirred at the reported temperature for the reported time. The conversion is monitored by TLC and ^{1}H NMR. The reactions carried out below room temperature are quenched at 0 °C with HCl (1M), extracted with DCM, and concentrated under reduced pressure before the ^{1}H NMR analysis and/or the chromatographic purification. The reactions carried out at room temperature are directly purified by flash chromatography on silica gel (cyclohexane/ethyl acetate from 9/1 to 8/2).

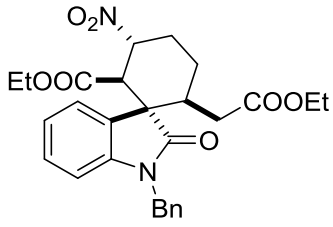
Typical procedure for the synthesis of racemic spirooxindoles: The racemic cascade reactions products are synthesized employing DBU instead of the bifunctional organocatalyst. The typical procedure is as follows: DBU (10 mol%) is added to a solution of 3-ylidene oxindole **1** (0.1 mmol) and nitro compound **2** (0.12 mmol) in DCM (150 μL). The mixture is stirred at room temperature overnight, then the crude is directly purified by flash chromatography on silica gel. The racemic spirooxindoles are obtained as mixture of diastereoisomers.

F. Characterization of the Cascade Reactions Products.



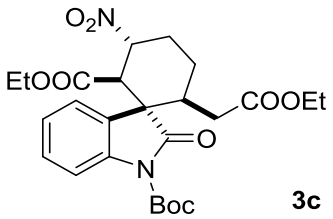
5a

diethyl (6*S*,7*R*,*E*)-6-nitro-7-(2-oxoindolin-3-yl)oct-2-enedioate: Mixture of two diastereoisomers (1/1). Yield = 70%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (bs, 1H), 7.91 (bs, 1H), 7.36 – 7.19 (m, 6H), 7.14 – 6.99 (m, 2H), 6.98 – 6.83 (m, 2H), 5.96 – 5.75 (m, 2H), 5.62 – 5.53 (m, 1H), 5.32 – 5.21 (m, 1H), 4.26 – 4.13 (m, 2H), 4.13 – 3.90 (m, 2H), 3.84 – 3.74 (m, 1H), 3.73 (dd, *J* = 9.3, 4.2 Hz, 1H), 3.60 (d, *J* = 4.2 Hz, 1H), 3.50 (d, *J* = 4.1 Hz, 1H), 2.40 – 2.00 (m, 6H), 1.73 – 1.53 (m, 2H), 1.36 – 1.22 (m, 6H), 1.05 – 0.90 (m, 6H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 187.0, 182.9, 176.1, 175.9, 168.5, 166.2, 145.2, 145.1, 129.1, 129.0, 125.2, 125.2, 124.5, 123.2, 123.1, 122.8, 122.6, 109.8, 103.9, 86.4, 83.7, 61.8, 60.4, 49.8, 49.7, 49.3, 45.0, 44.0, 30.9, 30.5, 28.6, 28.0, 25.6, 14.2, 13.7, 13.6. HPLC-MS (ESI) t_r = 8.83 min, 9.01 min; $[M+H]^+$ = 405.2 *m/z*, $[M+Na]^+$ = 427.2 *m/z*, $[2M+H]^+$ = 809.4 *m/z*, $[2M+Na]^+$ = 831.4 *m/z*.



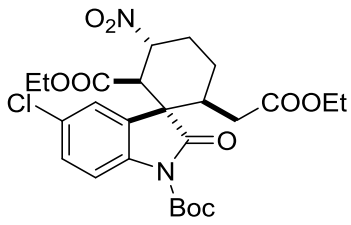
3b

ethyl (1*S*,2*R*,3*R*,6*S*)-1'-benzyl-6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-2-carboxylate: Yield = 50%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.39 (m, 2H), 7.38 – 7.21 (m, 5H), 7.04 (t, *J* = 7.7 Hz, 1H), 6.87 (d, *J* = 7.9 Hz, 1H), 5.26 (dt, *J* = 12.2, 4.7 Hz, 1H), 5.09 (d, *J* = 15.3 Hz, 1H), 4.79 (d, *J* = 15.0 Hz, 1H), 4.10 – 3.98 (m, 2H), 3.94 (d, *J* = 11.7 Hz, 1H), 3.67 (q, *J* = 7.1 Hz, 2H), 2.79 – 2.59 (m, 2H), 2.25 – 2.02 (m, 2H), 1.87 (dd, *J* = 16.0, 2.8 Hz, 1H), 1.80 – 1.63 (m, 1H), 1.55 – 1.45 (m, 1H), 1.19 (t, *J* = 7.2 Hz, 3H), 0.67 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 171.0, 168.3, 143.4, 135.6, 129.4, 128.8, 128.1, 127.9, 125.9, 125.2, 122.6, 109.6, 82.3, 61.4, 60.7, 53.9, 49.9, 44.7, 40.1, 34.7, 30.7, 25.8, 14.1, 13.4. HPLC-MS (ESI) t_r = 10.7 min; $[M+H]^+$ = 495.4 *m/z*, $[2M+Na]^+$ = 1011.7 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{27}H_{30}N_2O_7Na$ 517.1945 found 517.1939. CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 20 min, 80:20 for 25 min, then up to 70:30 in 10 min; flow rate = 0.7 mL/min; *T* = 40 °C; λ = 214 nm; t_r = 63.3 min (minor), t_r = 65.2 min (major).



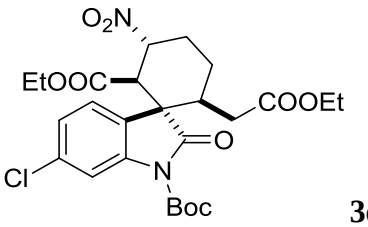
3c

1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,6*S*) 6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 73%; white crystals; m.p. = 123-125 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.2 Hz, 1H), 7.39 (t, *J* = 7.8, 1H), 7.25 (d, *J* = 6.3 Hz, 1H), 7.18 (t, *J* = 7.5, 1H), 5.23 (dt, *J* = 12.3, 4.7 Hz, 1H), 4.13 – 3.99 (m, 2H), 3.95 (d, *J* = 11.7 Hz, 1H), 3.76 (q, *J* = 7.2, 2H), 2.78 – 2.66 (m, 1H), 2.67 – 2.57 (m, 1H), 2.23 – 2.02 (m, 2H), 1.97 (dd, *J* = 16.1, 3.0 Hz, 1H), 1.68 (s, 9H), 1.56 – 1.46 (m, 2H), 1.20 (t, *J* = 7.1, 3H), 0.87 (t, *J* =7.2 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.5, 170.7, 168.2, 148.8, 140.1, 129.7, 125.0, 124.61, 124.58, 115.6, 85.0, 81.9, 61.7, 60.8, 54.4, 50.3, 40.6, 35.1, 30.6, 28.1, 25.3, 14.1, 13.3. HPLC-MS (ESI) t_r = 11.0 min; $[M+Na]^+$ = 527.5 *m/z*, $[2M+Na]^+$ = 1031.8 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{25}H_{32}N_2O_9Na$ 527.2000 found 527.1993. $[\alpha]_D^{20}$ = 19 (c = 1.57, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 254 nm; t_r = 49.5 min (minor), t_r = 74.1 min (major).



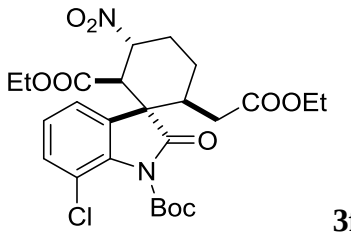
3d

1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,6*S*)-5'-chloro-6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 82%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.8 Hz, 1H), 7.37 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.20 (d, *J* = 2.1 Hz, 1H), 5.23 – 5.10 (m, 1H), 4.07 (q, *J* = 7.2 Hz, 2H), 3.94 (d, *J* = 11.8 Hz, 1H), 3.87 – 3.72 (m, 2H), 2.80 – 2.68 (m, 1H), 2.69 – 2.56 (m, 1H), 2.24 – 2.01 (m, 2H), 1.95 (dd, *J* = 16.1, 3.1 Hz, 1H), 1.67 (s, 9H), 1.61 – 1.48 (m, 2H), 1.21 (t, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 170.4, 168.0, 148.6, 138.7, 130.1, 129.8, 126.9, 124.7, 116.8, 85.5, 81.6, 61.9, 60.9, 54.4, 50.1, 40.6, 35.0, 30.5, 28.1, 25.3, 14.1, 13.3. HPLC-MS (ESI) t_r = 11.5 min; $[M+Na]^+$ = 561.0 *m/z*, $[2M+Na]^+$ = 1099.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{25}H_{31}ClN_2O_9Na$ 561.1610 found 561.1608. $[\alpha]_D^{20}$ = 19 (c = 0.6, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 8 min, then up to 80:20 in 8 min, 80:20 for 8 min, then up to 70:30 in 8 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 214 nm; t_r = 47.5 min (minor), t_r = 50.2 min (major).



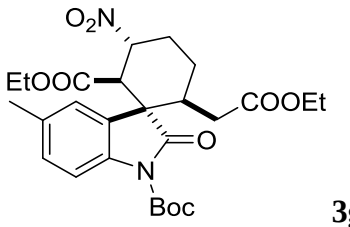
3e

1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,6*S*)-6'-chloro-6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 63%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.98 (m, 1H), 7.22 – 7.13 (m, 2H), 5.23 – 5.10 (m, 1H), 4.13 – 4.01 (m, 2H), 3.93 (d, *J* = 11.6 Hz, 1H), 3.80 (q, *J* = 7.3 Hz, 2H), 2.77 – 2.66 (m, 1H), 2.67 – 2.56 (m, 1H), 2.22 – 2.00 (m, 2H), 1.94 (dd, *J* = 15.9, 2.4 Hz, 1H), 1.68 (s, 9H), 1.63 – 1.47 (m, 2H), 1.20 (t, *J* = 7.2 Hz, 3H), 0.92 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.1, 170.5, 168.1, 148.5, 141.1, 135.8, 125.4, 124.6, 123.4, 116.4, 85.6, 81.7, 61.9, 60.9, 54.2, 50.2, 40.6, 35.0, 30.5, 28.0, 25.3, 14.1, 13.4. HPLC-MS (ESI) t_r = 12.1 min; $[M+Na]^+$ = 561.2 *m/z*, $[2M+Na]^+$ = 1099.7 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{25}H_{31}ClN_2O_9Na$ 561.1610 found 561.1602. $[\alpha]_D^{20}$ = 13 (c = 0.56, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r = 41.5 min (minor), t_r = 57.2 min (major).



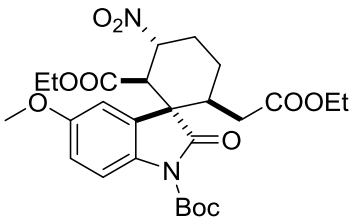
3f

1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,6*S*)-7'-chloro-6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 42%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 7.0 Hz, 1H), 7.23 – 7.04 (m, 2H), 5.20 (dt, *J* = 12.3, 4.7 Hz, 1H), 4.15 – 3.99 (m, 2H), 3.93 (d, *J* = 11.7 Hz, 1H), 3.87 (q, *J* = 7.2 Hz, 2H), 2.78 – 2.66 (m, 1H), 2.66 – 2.55 (m, 1H), 2.22 – 1.98 (m, 3H), 1.66 (s, 9H), 1.61 – 1.44 (m, 2H), 1.20 (t, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 170.6, 168.1, 147.6, 137.5, 131.3, 128.3, 125.0, 123.2, 119.3, 86.1, 81.7, 62.3, 60.9, 55.0, 49.6, 40.6, 34.7, 30.5, 27.7, 25.3, 14.1, 13.3. HPLC-MS (ESI) t_r = 12.1 min; $[M-Boc+H]^+$ = 439.0 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{25}H_{31}ClN_2O_9Na$ 561.1610 found 561.1611. CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 254 nm; t_r = 40.0 min (major), t_r = 42.8 min (minor).



3g

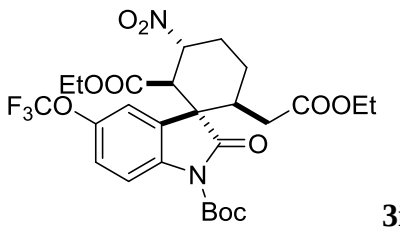
1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,6*S*)-6-(2-ethoxy-2-oxoethyl)-5'-methyl-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 77%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 1H), 7.17 (d, *J* = 8.3 Hz, 1H), 7.01 (s, 1H), 5.23 (dt, *J* = 12.3, 4.7 Hz, 1H), 4.15 – 4.00 (m, 2H), 3.93 (d, *J* = 11.7 Hz, 1H), 3.77 (q, *J* = 7.2 Hz, 2H), 2.78 – 2.66 (m, 1H), 2.67 – 2.55 (m, 1H), 2.37 (s, 3H), 2.20 – 2.01 (m, 2H), 1.96 (dd, *J* = 16.1, 3.0 Hz, 1H), 1.67 (s, 9H), 1.59 – 1.46 (m, 2H), 1.20 (t, *J* = 7.2 Hz, 3H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 170.8, 168.3, 148.8, 137.7, 134.3, 130.2, 125.1, 125.0, 115.3, 84.8, 81.9, 61.7, 60.8, 54.4, 50.2, 40.6, 35.1, 30.6, 28.1, 25.3, 21.3, 14.1, 13.3. HPLC-MS (ESI) t_r = 11.5 min; $[M+Na]^+$ = 541.4 *m/z*, $[2M+Na]^+$ = 1059.9 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{26}H_{34}N_2O_9Na$ 541.2157 found 541.2150. $[\alpha]_D^{20}$ = 20 (c = 1.08, $CHCl_3$). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 254 nm; t_r = 58.9 min (minor), t_r = 73.0 min (major).



3h

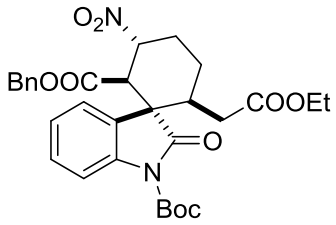
1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,6*S*)-6-(2-ethoxy-2-oxoethyl)-5'-methoxy-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 76%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.9 Hz, 1H), 6.88 (dd, *J* = 9.1, 2.6 Hz, 1H), 6.78 (d, *J* = 2.6 Hz, 1H), 5.19 (dt, *J* = 12.3, 4.7 Hz, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 3.94 (d, *J* = 11.7 Hz, 1H), 3.86 – 3.74 (m, 5H), 2.75 – 2.65 (m, 1H), 2.66 – 2.57 (m, 1H), 2.20 – 2.01 (m, 2H), 1.96 (dd, *J* = 16.1, 3.0 Hz, 1H), 1.67 (s, 9H), 1.61 – 1.49 (m, 2H), 1.20 (t, *J* = 7.1 Hz, 3H), 0.89 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 170.7, 168.2, 156.5, 148.8, 133.3, 126.3, 116.3, 112.9, 112.3, 84.8, 81.8, 61.7, 60.8, 55.7, 54.5, 50.1, 40.5, 35.0, 30.5, 28.1, 25.2, 14.1, 13.3. HPLC-MS (ESI) t_r = 10.9 min; $[M-HNO_2-Boc+H]^+$ = 388.3 *m/z*, $[M-Boc+H]^+$ = 435.4 *m/z*, $[M-HNO_2+Na]^+$ = 510.4 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{26}H_{34}N_2O_{10}Na$ 557.2106 found 557.2099. $[\alpha]_D^{20}$ = 24 (c = 0.55, $CHCl_3$). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min,

then up to 70:30 in 10 min; flow rate = 0.5 mL/min; T = 40 °C; λ = 254 nm; t_r = 48.0 min (minor), t_r = 77.0 min (major).



3i

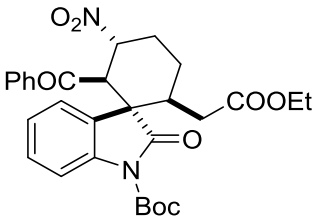
1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,6*S*)-6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxo-5'-(trifluoromethoxy)spiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 78%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 9.0 Hz, 1H), 7.33 – 7.16 (m, 1H), 7.13 – 7.03 (m, 1H), 5.14 (dt, J = 12.5, 4.8 Hz, 1H), 4.18 – 3.99 (m, 2H), 3.96 (d, J = 11.8 Hz, 1H), 3.79 (q, J = 7.1 Hz, 2H), 2.79 – 2.70 (m, 1H), 2.70 – 2.57 (m, 1H), 2.26 – 2.01 (m, 2H), 1.95 (dd, J = 16.1, 3.1 Hz, 1H), 1.67 (s, 9H), 1.63 – 1.47 (m, 2H), 1.21 (t, J = 7.1 Hz, 3H), 0.88 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 170.4, 167.9, 148.6, 145.5, 138.8, 126.8, 122.3, 120.4 (q, J = 256 Hz), 118.1, 116.7, 85.6, 81.6, 61.9, 61.0, 54.5, 50.2, 40.5, 35.0, 30.5, 28.1, 25.4, 14.1, 13.3. HPLC-MS (ESI) t_r = 12.0 min; $[M+Na]^+$ = 611.3 *m/z*, $[2M+Na]^+$ = 1199.7 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{26}H_{31}F_3N_2O_{10}Na$ 611.1823 found 611.1819. $[\alpha]_D^{20}$ = 16 (c = 0.88, $CHCl_3$). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min; flow rate = 0.5 mL/min; T = 40 °C; λ = 230 nm; t_r = 26.5 min (minor), t_r = 49.0 min (major).



3j

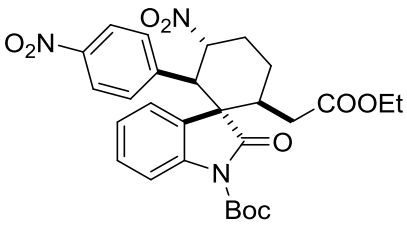
2-benzyl 1'-(*tert*-butyl) (1*S*,2*R*,3*R*,6*S*)-6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 74%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, J = 8.4 Hz, 1H), 7.32 – 7.16 (m, 6H), 7.11 (t, J = 7.2 Hz, 1H), 6.97 – 6.90 (m, 1H), 5.25 (dt, J = 12.4, 4.8 Hz, 1H), 4.84 – 4.67 (m, 2H), 4.16 – 3.93 (m, 3H), 2.79 – 2.66 (m, 1H), 2.66 – 2.54 (m, 1H), 2.21 – 1.99 (m, 2H), 1.91 (dd, J = 16.1, 3.1 Hz, 1H), 1.73 – 1.44 (m, 11H), 1.18 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.3, 170.7, 168.3, 148.5, 139.9, 134.3, 129.6, 128.5, 128.33, 128.30, 124.6, 124.38, 124.36, 115.7, 84.8, 81.9, 67.4, 60.8, 54.3, 50.1, 40.8, 34.9, 30.6, 28.1, 25.3, 14.1. HPLC-MS (ESI) t_r = 12.0 min; $[M+Na]^+$ = 589.4 *m/z*. HRMS

(ESI) $[M+Na]^+$ calcd for $C_{30}H_{34}N_2O_9Na$ 589.2157 found 589.2151. $[\alpha]_D^{20}$ = 12 (c = 0.72, $CHCl_3$). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r = 42.0 min (minor), t_r = 69.6 min (major).



3k

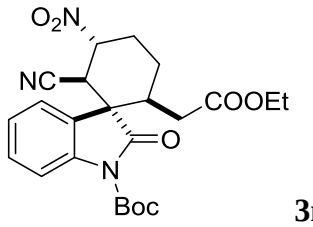
***tert*-butyl (1*S*,2*R*,3*R*,6*S*)-2-benzoyl-6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1'-carboxylate:** Yield = 19%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.0 Hz, 1H), 7.64 – 7.45 (m, 2H), 7.45 – 7.29 (m, 2H), 7.29 – 7.14 (m, 4H), 5.51 (dt, *J* = 12.1, 4.4 Hz, 1H), 4.74 (d, *J* = 11.3 Hz, 1H), 4.05 (q, *J* = 6.7 Hz, 2H), 2.94 – 2.83 (m, 1H), 2.83 – 2.70 (m, 1H), 2.39 – 2.14 (m, 2H), 1.89 – 1.77 (m, 1H), 1.72 – 1.50 (m, 11H), 1.19 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.1, 174.8, 170.7, 147.7, 139.1, 136.4, 133.6, 129.5, 128.6, 128.3, 125.5, 124.7, 115.4, 110.0, 84.5, 82.2, 60.8, 55.3, 52.1, 40.3, 35.5, 30.5, 27.8, 25.9, 14.1. HPLC-MS (ESI) t_r = 12.0 min; $[M+Na]^+$ = 559.2 *m/z*; $[2M+Na]^+$ = 1095.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{29}H_{32}N_2O_8Na$ 559.2051 found 559.2055. $[\alpha]_D^{20}$ = 13 (c = 0.18, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r = 41.3 min (major), t_r = 60.0 min (minor).



3l

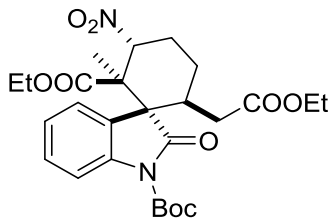
***tert*-butyl (1*S*,2*R*,3*R*,6*S*)-6-(2-ethoxy-2-oxoethyl)-3-nitro-2-(4-nitrophenyl)-2'-oxospiro[cyclohexane-1,3'-indoline]-1'-carboxylate:** Yield = 83%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (bt, *J* = 6.8 Hz, 2H), 7.57 (t, *J* = 6.8 Hz, 2H), 7.43 – 7.26 (m, 2H), 6.88 (bs, 2H), 5.37 (dt, *J* = 12.2, 4.2 Hz, 1H), 4.15 – 4.03 (m, 2H), 4.00 (d, *J* = 12.2 Hz, 1H), 3.01 – 2.85 (m, 1H), 2.80 – 2.67 (m, 1H), 2.49 – 2.31 (m, 2H), 2.10 – 1.84 (m, 2H), 1.79 – 1.65 (m, 1H), 1.50 (s, 9H), 1.21 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.8, 170.7, 147.63, 147.55, 140.5, 140.1, 129.9, 124.8, 124.7, 124.6, 123.0, 122.9, 115.7, 85.2, 84.8, 60.8, 57.9, 53.5, 39.1, 36.3, 31.2,

27.9, 25.8, 14.1. HPLC-MS (ESI) t_r = 11.4 min; $[M+Na]^+$ = 576.3 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{28}H_{31}N_3O_9Na$ 576.1953 found 576.1946. CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 254 nm; t_r = 40.4 min (minor), t_r = 42.1 min (major).



3m

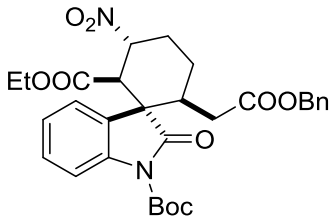
***tert*-butyl (1*S*,2*R*,3*R*,6*S*)-2-cyano-6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1'-carboxylate:** Yield = 47%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.3 Hz, 1H), 7.55 – 7.45 (m, 1H), 7.38 – 7.27 (m, 2H), 5.03 (dt, *J* = 12.2, 4.4 Hz, 1H), 4.15 – 3.98 (m, 2H), 3.88 (d, *J* = 11.9 Hz, 1H), 2.81 – 2.67 (m, 1H), 2.68 – 2.55 (m, 1H), 2.33 – 2.08 (m, 2H), 1.95 (dd, *J* = 16.2, 3.2 Hz, 1H), 1.89 – 1.72 (m, 1H), 1.72 – 1.56 (m, 10H), 1.20 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 170.2, 148.1, 140.4, 130.7, 125.1, 124.4, 123.7, 116.5, 114.3, 85.9, 82.1, 61.0, 54.7, 39.7, 38.8, 35.4, 30.3, 28.0, 25.0, 14.1. HPLC-MS (ESI) t_r = 10.1 min; $[M+Na]^+$ = 480.0 *m/z*, $[2M+Na]^+$ = 937.4 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{23}H_{27}N_3O_7Na$ 480.1741 found 480.1750. CSP-HPLC: IC 90:10 *n*-Hex/IPA for 8 min, then up to 80:20 in 8 min, 80:20 for 8 min, then up to 70:30 in 8 min, 70:30 for 8 min, then up to 1:1; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r = 31.0 min (major), t_r = 36.3 min (minor).



3n

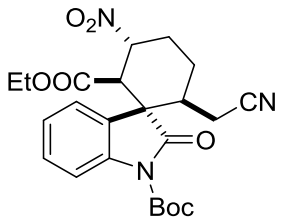
1'-(*tert*-butyl) 2-ethyl (1*R*,2*R*,3*R*,6*S*)-6-(2-ethoxy-2-oxoethyl)-2-methyl-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 40%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.4 Hz, 1H), 7.46 – 7.36 (m, 2H), 7.23 (t, *J* = 7.4 Hz, 1H), 4.93 (dd, *J* = 13.4, 4.9 Hz, 1H), 4.42 – 4.31 (m, 2H), 4.12 – 3.95 (m, 2H), 3.59 – 3.46 (m, 1H), 3.26 (dq, *J* = 13.3, 5.5 Hz, 1H), 2.54 – 2.39 (m, 1H), 2.38 – 2.21 (m, 1H), 1.93 – 1.72 (m, 2H), 1.64 (s, 9H), 1.58 – 1.43 (m, 1H), 1.38 (t, *J* = 7.1 Hz, 3H), 1.20 (t, *J* = 7.2 Hz, 3H), 0.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 170.9, 169.5, 148.4, 140.3, 129.6, 125.6, 124.7, 124.5, 115.6, 90.2, 85.2, 61.7, 60.7, 59.1, 49.7, 36.5, 35.0, 28.1, 27.3, 25.0, 19.2, 14.1, 13.9. HPLC-MS (ESI) t_r = 12.6min;

$[M+Na]^+$ = 541.2 *m/z*; $[2M+Na]^+$ = 1059.4 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{26}H_{34}N_2O_9Na$ 541.2157 found 541.2163. $[\alpha]_D^{20}$ = 42 (c = 0.15, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r = 22.1 min (major), t_r = 26.8 min (minor).



3q

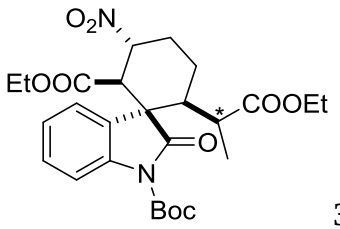
1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,6*S*)-6-(2-(benzyloxy)-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 65%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.3 Hz, 1H), 7.42 – 7.20 (m, 7H), 7.17 (t, *J* = 7.7 Hz, 1H) 5.22 (dt, *J* = 12.4, 8 Hz, 1H), 5.05 (d, *J* = 12.1 Hz, 1H), 5.00 (d, *J* = 12.1 Hz, 1H), 3.94 (d, *J* = 11.7 Hz, 1H), 3.76 (q, *J* = 7.2 Hz, 2H), 2.74 – 2.58 (m, 2H), 2.17 – 1.95 (m, 3H), 1.67 (s, 9H), 1.62 1.52 (m, 2H), 0.86 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 170.5, 168.2, 148.7, 140.1, 135.3, 129.7, 128.6, 128.51, 128.48, 124.9, 124.6, 115.6, 85.1, 81.8, 66.7, 61.8, 54.3, 50.2, 40.6, 35.0, 30.6, 28.1, 25.3, 13.3. HPLC-MS (ESI) t_r = 12.8 min; $[M+Na]^+$ = 589.2 *m/z*; $[2M+Na]^+$ = 1155.4 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{30}H_{34}N_2O_9Na$ 589.2157 found 589.2161. $[\alpha]_D^{20}$ = 17 (c = 0.81, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r = 51.8 min (minor), t_r = 58.9 min (major).



3s

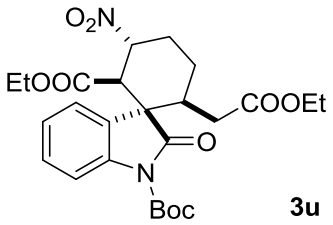
1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,6*S*)-6-(cyanomethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 32% (major diastereoisomer); pale yellow oil. ^{1}H NMR (400 MHz, CDCl3) δ 7.97 (d, *J* = 8.3 Hz, 1H), 7.49 – 7.37 (m, 1H), 7.32 – 7.18 (m, 2H), 5.24 (dt, *J* = 12.3, 4.8 Hz, 1H), 3.92 (d, *J* = 11.7 Hz, 1H), 3.87 – 3.67 (m, 2H), 2.88 – 2.75 (m, 1H), 2.57 – 2.44 (m, 1H), 2.35 – 2.23 (m, 1H), 2.19 – 2.00 (m, 2H), 1.84 (ddd, *J* = 27.1, 13.7, 3.4 Hz, 1H), 1.75 – 1.51 (m, 10H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 167.7, 148.5, 140.2, 130.4, 125.0, 124.8, 123.3, 116.6, 115.8, 85.5, 81.4, 62.0, 54.0, 50.1, 40.7, 30.2, 28.0, 25.2, 19.1,

13.3. HPLC-MS (ESI) t_r = 10.2min; $[M+Na]^+$ = 480.0 *m/z*; $[2M+Na]^+$ = 937.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{23}H_{27}N_3O_7Na$ 480.1741 found 480.1738. $[\alpha]_D^{20}$ = 24 (c = 1.5, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 8 min, then up to 80:20 in 8 min, 80:20 for 8 min, then up to 70:30 in 8 min, 70:30 for 8 min, then up to 1:1 in 8 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r = 56.8 min (major), t_r = 65.5 min (minor).



3t

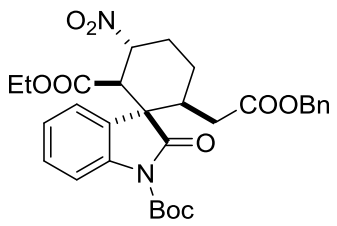
(1*R*,2*R*,3*R*,6*S*)-1'-*tert*-butyl 2-ethyl 6-((*S*)-1-ethoxy-1-oxopropan-2-yl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 40%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.79 (m, 1H), 7.41 – 7.29 (m, 2H), 7.23 – 7.13 (m, 1H), 5.73 (dt, *J* = 11.9, 4.4 Hz, 1H), 4.28 – 4.10 (m, 2H), 3.75 (q, *J* = 7.1 Hz, 1H), 3.74 (q, *J* = 7.1 Hz, 1H), 3.42 (d, *J* = 11.5 Hz, 1H), 2.75 – 2.59 (m, 2H), 2.45 (dd, *J* = 12.5, 3.3 Hz, 1H), 2.13 – 1.99 (m, 1H), 1.64 (s, 9H), 1.61 – 1.45 (m, 2H), 1.29 (t, *J* = 7.1 Hz, 3H), 0.82 (t, *J* = 7.2 Hz, 3H), 0.65 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 173.8, 167.9, 149.3, 140.1, 129.4, 128.3, 124.0, 123.9, 115.7, 84.1, 81.5, 62.4, 61.5, 55.6, 51.9, 51.0, 30.4, 28.2, 26.4, 21.8, 14.0, 13.4. HPLC-MS (ESI) t_r = 7.0 min; $[M+K]^+$ = 557.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{26}H_{34}N_2O_9Na$ 541.2157 found 541.2149. $[\alpha]_D^{20}$ = 16 (c = 0.74, $CHCl_3$). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min, 70:3 for 15 min, then up to 1:1 in 2 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r = 53.7 min (major), t_r = 86.4 min (minor).



3u

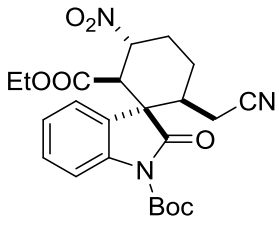
1'-(*tert*-butyl) 2-ethyl (1*R*,2*R*,3*R*,6*S*)-6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 79%; white crystals; m.p. = 129-131 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 1H), 7.39 – 7.20 (m, 3H), 5.63 (dt, *J* = 11.7, 6.0 Hz, 1H), 4.07 – 3.90 (m, 2H), 3.80 (q, *J* = 7.2 Hz, 2H), 3.45 (d, *J* = 11.4 Hz, 1H), 2.73 – 2.55 (m, 1H), 2.54 – 2.39 (m, 1H), 2.35 – 2.19 (m, 1H), 2.19 – 1.89 (m, 3H), 1.90 – 1.78 (m, 1H), 1.65 (s, 9H), 1.17 (t, *J* = 7.1 Hz, 3H), 0.84 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 171.3, 168.3, 148.7, 140.0,

129.4, 127.5, 125.0, 122.6, 115.0, 84.8, 81.8, 61.6, 60.8, 53.8, 53.0, 41.2, 34.6, 30.6, 28.1, 24.3, 14.0, 13.4. HPLC-MS (ESI) t_r = 11.5 min; $[M-Boc+H]^+$ = 405.2 *m/z*; $[M+Na]^+$ = 527.2 *m/z*; $[2M+Na]^+$ = 1031.6 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{25}H_{32}N_2O_9Na$ 527.2000 found 527.2001. $[\alpha]_D^{20}$ = 16 (c = 0.91, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 10 min, then up to 80:20 in 10 min, 80:20 for 10 min, then up to 70:30; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 254 nm; t_r = 29.1 min (minor), t_r = 30.5 min (major).



3v

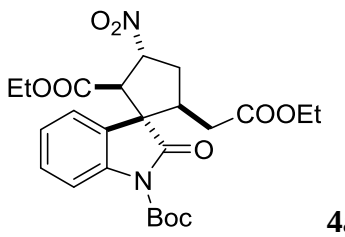
1'-(*tert*-butyl) 2-ethyl (1*R*,2*R*,3*R*,6*S*)-6-(2-(benzyloxy)-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 75%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.4 Hz, 1H), 7.41 – 7.20 (m, 8H), 5.63 (dt, *J* = 11.8, 4.3 Hz, 1H), 5.00 (d, *J* = 12.2 Hz, 1H), 4.94 (d, *J* = 12.2 Hz, 1H), 3.80 (q, *J* = 7.1 Hz, 2H), 3.45 (d, *J* = 11.5 Hz, 1H), 2.68 – 2.57 (m, 1H), 2.55 – 2.42 (m, 1H), 2.34 – 2.18 (m, 1H), 2.16 – 2.01 (m, 2H), 1.99 – 1.84 (m, 2H), 1.64 (s, 9H), 0.84 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.6, 171.2, 168.3, 148.7, 140.0, 135.3, 129.5, 128.6, 128.4, 128.2, 127.4, 125.0, 122.6, 115.1, 84.8, 81.8, 66.7, 61.6, 53.8, 52.9, 41.3, 34.6, 30.5, 28.1, 24.2, 13.4. HPLC-MS (ESI) t_r = 12.1 min; $[M+Na]^+$ = 589.0 *m/z*, $[2M+Na]^+$ = 1155.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{30}H_{34}N_2O_9Na$ 589.2157 found 589.2154. $[\alpha]_D^{20}$ = 15 (c = 0.73, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 8 min, then up to 80:20 in 8 min, 80:20 for 8 min, then up to 70:30 in 8 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 254 nm; t_r = 27.3 min (minor), t_r = 32.2 min (major).



3w

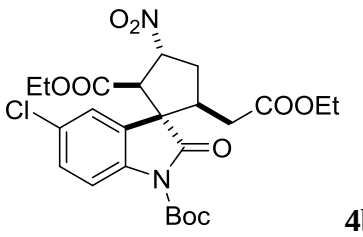
1'-(*tert*-butyl) 2-ethyl (1*R*,2*R*,3*R*,6*S*)-6-(cyanomethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 83%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 1H), 7.47 – 7.38 (m, 1H), 7.35 – 7.27 (m, 2H), 5.64 (dt, *J* = 11.9, 4.4 Hz, 1H), 3.82 (q, *J* = 7.0 Hz, 2H), 3.44 (d, *J* = 11.5 Hz, 1H), 2.80 – 2.67 (m, 1H), 2.49 – 2.33 (m, 1H), 2.33 – 1.91 (m, 5H), 1.65 (s, 9H), 0.85 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 167.9, 148.4,

139.9, 130.1, 126.5, 125.4, 122.2, 117.0, 115.4, 85.3, 81.4, 61.9, 53.5, 52.6, 42.0, 30.1, 28.1, 24.0, 18.8, 13.4. HPLC-MS (ESI) t_r = 9.9 min; $[M+Na]^+$ = 480.0 *m/z*, $[2M+Na]^+$ = 937.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{23}H_{27}N_3O_7Na$ 480.1741 found 480.1748. $[\alpha]_D^{20}$ = 4 (c = 0.65, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 8 min, then up to 80:20 in 8 min, 80:20 for 8 min, then up to 70:30 in 8 min, 70:30 for 8 min, then up to 1:1; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r = 50.7 min (minor), t_r = 53.1 min (major).



4a

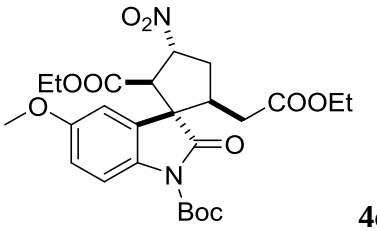
1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,5*S*)-5-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-1',2-dicarboxylate: Yield = 73%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.2 Hz, 1H), 7.38 (t, *J* = 7.9 Hz, 1H), 7.21 – 7.12 (m, 1H), 6.97 (d, *J* = 7.9 Hz, 1H), 5.68 (ddd, *J* = 10.8, 7.6, 3.0 Hz, 1H), 4.44 (d, *J* = 7.7 Hz, 1H), 4.10 – 3.95 (m, 2H), 3.87 – 3.65 (m, 2H), 3.37 – 3.20 (m, 1H), 3.03 – 2.92 (m, 1H), 2.54 – 2.42 (m, 1H), 2.01 (dd, *J* = 16.2, 5.5 Hz, 1H), 1.90 (dd, *J* = 16.2, 9.3 Hz, 1H), 1.67 (s, 9H), 1.18 (t, *J* = 7.2 Hz, 3H), 0.75 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.6, 170.3, 167.7, 148.9, 140.3, 129.7, 124.61, 124.58, 123.4, 115.7, 84.9, 84.3, 61.6, 60.9, 60.4, 57.6, 44.4, 36.4, 34.6, 28.1, 14.0, 13.2. HPLC-MS (ESI) t_r = 10.7 min; $[2M+Na]^+$ = 1003.7 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{24}H_{30}N_2O_9Na$ 513.1844 found 513.1845. $[\alpha]_D^{20}$ = 18 (c = 0.96, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r = 48.5 min (minor), t_r = 58.6 min (major).



4b

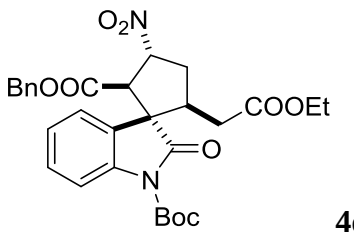
1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,5*S*)-5'-chloro-5-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-1',2-dicarboxylate: Yield = 57%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.8 Hz, 1H), 7.37 (d, *J* = 8.9 Hz, 1H), 6.94 (s, 1H), 5.65 (ddd, *J* = 10.9, 7.7, 2.9 Hz, 1H), 4.45 (d, *J* = 7.7 Hz, 1H), 4.12 – 3.98 (m, 2H), 3.90 – 3.73 (m, 2H), 3.35 – 3.22 (m, 1H), 3.04 – 2.93 (m, 1H), 2.47 (dt, *J* = 15.4, 11.5 Hz, 1H), 2.08 – 1.89 (m, 2H), 1.66 (s,

9H), 1.18 (t, J = 7.1 Hz, 3H), 0.81 (t, J = 7.2 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.0, 170.1, 167.4, 148.8, 139.0, 130.1, 129.8, 126.5, 123.4, 116.9, 85.3, 84.0, 61.8, 61.0, 60.4, 57.6, 44.4, 36.3, 34.5, 28.0, 14.0, 13.3. HPLC-MS (ESI) t_r = 11.8 min; $[M+H]^+$ = 525.2 *m/z*, $[M+Na]^+$ = 547.0 *m/z*, $[2M+Na]^+$ = 1071.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{24}H_{29}ClN_2O_9Na$ 547.1454 found 547.1450. $[\alpha]_D^{20}$ = 17 (c = 0.54, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 8 min, then up to 80:20 in 8 min, 80:20 for 8 min, then up to 70:30 in 8 min; flow rate = 0.5 mL/min; T = 40 °C; λ = 230 nm; t_r = 36.8 min (minor), t_r = 44.8 min (major).



4c

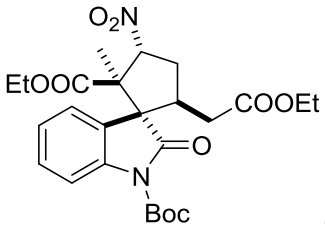
1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,5*S*)-5-(2-ethoxy-2-oxoethyl)-5'-methoxy-3-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-1',2-dicarboxylate: Yield = 65%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, J = 9.0 Hz, 1H), 6.87 (d, J = 7.9 Hz, 1H), 6.51 (s, 1H), 5.65 (ddd, J = 11.0, 7.7, 3.3 Hz, 1H), 4.44 (d, J = 7.8 Hz, 1H), 4.10 – 3.90 (m, 2H), 3.88 – 3.69 (m, 2H), 3.79 (s, 3H), 3.37 – 3.21 (m, 1H), 2.97 (ddd, J = 15.3, 8.3, 2.8 Hz, 1H), 2.46 (dt, J = 15.5, 11.7 Hz, 1H), 2.03 (dd, J = 16.1, 5.4 Hz, 1H), 1.91 (dd, J = 16.2, 9.7 Hz, 1H), 1.66 (s, 9H), 1.18 (t, J = 7.2 Hz, 3H), 0.79 (t, J = 7.2 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.6, 170.3, 167.6, 156.7, 149.0, 133.6, 125.9, 116.5, 113.2, 110.6, 84.7, 84.2, 61.6, 60.9, 60.7, 57.4, 55.7, 44.3, 36.2, 34.5, 28.0, 14.0, 13.3. HPLC-MS (ESI) t_r = 11.0 min; $[M+Na]^+$ = 543.4 *m/z*, $[2M+Na]^+$ = 1063.8 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{25}H_{32}N_2O_{10}Na$ 543.1949 found 543.1948. $[\alpha]_D^{20}$ = 12 (c = 0.34, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 8 min, then up to 80:20 in 8 min, 80:20 for 8 min, then up to 70:30 in 8 min, 70:30 for 10 min, then up to 1:1 in 8 min; flow rate = 0.5 mL/min; T = 40 °C; λ = 230 nm; t_r = 46.5 min (minor), t_r = 53.8 min (major).



4d

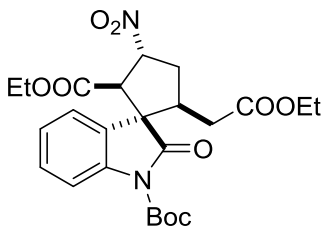
2-benzyl 1'-(*tert*-butyl) (1*S*,2*R*,3*R*,5*S*)-5-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-1',2-dicarboxylate: Yield = 63%; white crystals; m.p. = 122-124 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, J = 8.2 Hz, 1H), 7.33 – 7.18 (m, 4H), 7.12 (t, J

= 7.5 Hz, 1H), 6.93 (d, *J* = 7.5 Hz, 1H), 6.90 – 6.81 (m, 2H), 5.72 (ddd, *J* = 10.8, 7.6, 2.9 Hz, 1H), 4.70 (s, 2H), 4.51 (d, *J* = 7.6 Hz, 1H), 4.08 – 3.95 (m, 2H), 3.32 – 3.18 (m, 1H), 2.98 (ddd, *J* = 15.4, 8.4, 2.8 Hz, 1H), 2.46 (dt, *J* = 15.3, 11.6 Hz, 1H), 1.96 (dd, *J* = 16.4, 5.6 Hz, 1H), 1.83 (dd, *J* = 16.2, 9.4 Hz, 1H), 1.60 (s, 9H), 1.16 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 170.3, 167.8, 148.6, 140.0, 134.1, 129.7, 128.5,128.4, 128.4, 124.5, 124.2, 123.1, 115.9, 84.7, 84.4, 67.6, 60.9, 60.4, 57.0, 44.8, 36.2, 34.4, 28.0, 14.0. HPLC-MS (ESI) t_r = 12.2 min; $[M+Na]^+$ = 575.4 *m/z*, $[2M+Na]^+$ = 1127.8 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{29}H_{32}N_2O_9Na$ 575.2000 found 575.2007. $[\alpha]_D^{20}$ = 5 (c = 0.48, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 8 min, then up to 80:20 in 8 min, 80:20 for 8 min, then up to 70:30 in 8 min, 70:30 for 8 min, then up to 1:1 in 8 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 214 nm; t_r = 39.2 min (minor), t_r = 40.2 min (major).



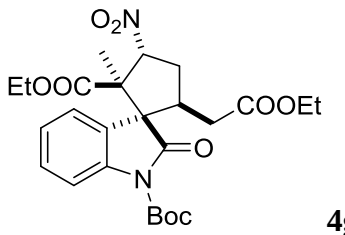
4e

1'-(*tert*-butyl) 2-ethyl (1*R*,2*R*,3*R*,5*S*)-5-(2-ethoxy-2-oxoethyl)-2-methyl-3-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-1',2-dicarboxylate: Yield = 31%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.3 Hz, 1H), 7.41 (t, *J* = 8.0 Hz, 1H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.03 (d, *J* = 7.5 Hz, 1H), 4.92 (dd, *J* = 11.7, 6.5 Hz, 1H), 4.33 – 4.15 (m, 2H), 4.02 (q, *J* = 7.2 Hz, 2H), 3.72 – 3.62 (m, 1H), 3.61 – 3.46 (m, 1H), 2.54 – 2.39 (m, 1H), 2.06 (dd, *J* = 15.5, 9.4 Hz, 1H), 1.96 (dd, *J* = 15.8, 5.8 Hz, 1H), 1.64 (s, 9H), 1.31 (t, *J* = 7.1 Hz, 3H), 1.19 (s, 3H), 1.17 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 172.2, 170.8, 170.2, 148.7, 140.3, 129.6, 124.9, 124.6, 123.9, 115.9, 90.5, 84.9, 64.9, 62.1, 60.8, 60.7, 38.6, 36.1, 34.6, 28.0, 19.7, 14.1, 13.7. HPLC-MS (ESI) t_r = 11.7 min; $[M+Na]^+$ = 527.4 *m/z*, $[2M+Na]^+$ = 1031.6 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{25}H_{32}N_2O_9Na$ 527.2000 found 527.1994. $[\alpha]_D^{20}$ = 11 (c = 1.1, DCM). CSP-HPLC: AD 90:10 *n*-Hex/IPA for 8 min, then up to 80:20 in 8 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 214 nm; t_r = 17.6 min (major), t_r = 20.5 min (minor).



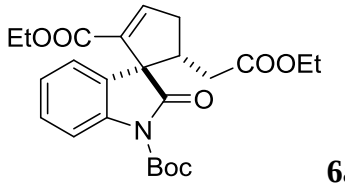
4f

1'-(*tert*-butyl) 2-ethyl (1*R*,2*R*,3*R*,5*S*)-5-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-1',2-dicarboxylate: Yield = 52%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.0 Hz, 1H), 7.42 – 7.33 (m, 2H), 7.26 (t, *J* = 7.5 Hz, 1H), 5.68 (ddd, *J* = 9.7, 6.9, 2.5 Hz, 1H), 4.29 (d, *J* = 6.9 Hz, 1H), 4.14 – 4.01 (m, 1H), 4.03 – 3.84 (m, 3H), 3.12 – 3.00 (m, 1H), 2.84 – 2.72 (m, 1H), 2.71 – 2.60 (m, 1H), 2.23 (dd, *J* = 15.9, 10.3 Hz, 1H), 2.04 (dd, *J* = 15.9, 4.4 Hz, 1H), 1.65 (s, 9H), 1.16 (t, *J* = 7.2 Hz, 3H), 1.05 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.6, 170.6, 168.1, 148.7, 140.4, 129.4, 127.1, 125.1, 122.0, 115.1, 86.0, 84.8, 61.9, 60.9, 59.8, 57.3, 45.9, 35.9, 33.3, 28.1, 14.0, 13.5. HPLC-MS (ESI) t_r = 11.5 min; $[M+H]^+$ = 491.0 *m/z*, $[M+Na]^+$ = 513.2 *m/z*, $[2M+Na]^+$ = 1003.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{24}H_{30}N_2O_9Na$ 513.1844 found 513.1841. $[\alpha]_D^{20}$ = 23 (c = 0.15, DCM). CSP-HPLC: IC 95:5 *n*-Hex/IPA for 40 min, then up to 90:10 in 2 min, 90:10 for 9 min, then up to 80:20 in 4 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r = 51.4 min (minor), t_r = 53.1 min (major).



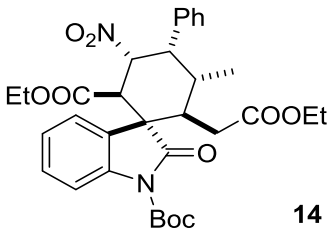
4g

1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,5*S*)-5-(2-ethoxy-2-oxoethyl)-2-methyl-3-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-1',2-dicarboxylate: Yield = 36%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.2 Hz, 1H), 7.43 – 7.33 (m, 1H), 7.30 (d, *J* = 6.5 Hz, 1H), 7.21 (td, *J* = 7.6, 1.1 Hz, 1H), 6.17 (dd, *J* = 10.1, 3.9 Hz, 1H), 4.23 – 3.88 (m, 4H), 3.25 (qd, *J* = 10.5, 4.2 Hz, 1H), 2.93 (ddd, *J* = 14.5, 9.1, 3.9 Hz, 1H), 2.62 – 2.49 (m, 1H), 2.25 (dd, *J* = 15.7, 10.3 Hz, 1H), 1.94 (dd, *J* = 15.7, 4.2 Hz, 1H), 1.64 (s, 9H), 1.51 (s, 3H), 1.17 (t, *J* = 7.2 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.7, 171.6, 171.0, 148.6, 140.7, 129.4, 125.24, 125.20, 124.3, 114.9, 89.6, 84.8, 63.8, 62.1, 60.8, 59.5, 42.7, 34.3, 32.3, 28.1, 18.5, 14.0, 13.5. HPLC-MS (ESI) t_r = 11.9 min; $[M+Na]^+$ = 527.4 *m/z*, $[2M+Na]^+$ = 1031.6 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{25}H_{32}N_2O_9Na$ 527.2000 found 527.1994. $[\alpha]_D^{20}$ = 1 (c = 0.79, DCM). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 8 min, then up to 80:20 in 8 min, 80:20 for 8 min, then up to 70:30 in 8 min, 70:30 for 10 min, then up to 1:1 in 1 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 214 nm; t_r = 25.6 min (minor), t_r = 36.7 min (major).



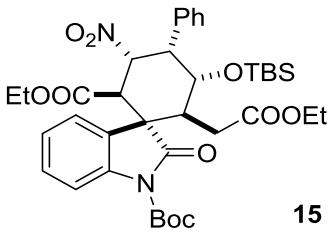
6a

1'-(*tert*-butyl) 2-ethyl (1*S*,5*R*)-5-(2-ethoxy-2-oxoethyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-1',2-dicarboxylate: Yield = 33%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.1 Hz, 1H), 7.31 (t, *J* = 7.9 Hz, 1H), 7.17 (bt, *J* = 2.4 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.95 (d, *J* = 7.5 Hz, 1H), 4.11 – 3.82 (m, 4H), 3.53 – 3.38 (m, 1H), 3.05 (ddd, *J* = 18.7, 8.5, 3.0 Hz, 1H), 2.51 (ddd, *J* = 18.6, 9.5, 2.2 Hz, 1H), 2.25 (dd, *J* = 16.4, 8.5 Hz, 1H), 2.13 (dd, *J* = 16.4, 7.3 Hz, 1H), 1.67 (s, 9H), 1.13 (t, *J* = 7.1 Hz, 3H), 1.05 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 171.1, 162.2, 149.3, 146.3, 140.0, 138.6, 128.9, 127.4, 124.0, 123.8, 115.4, 84.0, 62.6, 60.6, 60.5, 45.1, 38.4, 35.7, 28.1, 14.0, 13.6. HPLC-MS (ESI) t_r = 10.3 min; $[M+Na]^+$ = 466.4 *m/z*, $[2M+Na]^+$ = 909.7 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{24}H_{29}NO_7Na$ 466.1836 found 466.1830. $[\alpha]_D^{20}$ = -32 (c = 1.12, $CHCl_3$). CSP-HPLC: IC 90:10 *n*-Hex/IPA for 15 min, then up to 80:20 in 10 min, 80:20 for 15 min, then up to 70:30 in 10 min; flow rate = 0.5 mL/min; *T* = 40 °C; λ = 230 nm; t_r = 68.2 min (major), t_r = 83.5 min (minor).



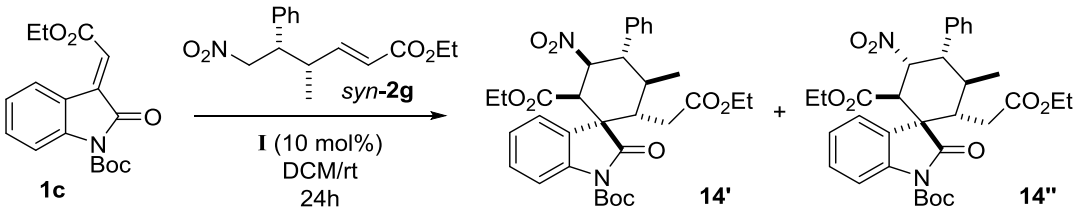
14

1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,4*S*,5*R*,6*R*)-6-(2-ethoxy-2-oxoethyl)-5-methyl-3-nitro-2'-oxo-4-phenylspiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Yield = 75%; pale yellow syrup. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.4 Hz, 1H), 7.52 (d, *J* = 7.2, 1H), 7.42 – 7.30 (m, 6H), 7.20 (t, *J* = 7.6, 1H), 5.61 (dd, *J* = 12.4, 6.4 Hz, 1H), 4.44 (d, *J* = 12.8 Hz, 1H), 3.94 – 3.66 (m, 5H), 3.26 (m, 1H), 1.86 – 1.76 (m, 2H), 1.70 (s, 9H), 1.08 (t, *J* = 7.2 Hz, 3H), 0.89 (t, *J* = 7.2 Hz, 3H), 0.80 (d, *J* = 6.8, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.3, 171.0, 168.6, 148.9, 140.4, 134.0, 130.8, 129.8, 129.0, 128.9, 128.6, 128.3, 125.2, 125.2, 124.5, 115.6, 85.0, 84.5, 61.7, 60.7, 55.2, 51.1, 47.0, 40.7, 36.1, 34.5, 28.1, 17.8, 13.8, 13.4. HPLC-MS (ESI) t_r = 13.2 min; $[M-Boc+H]^+$ = 495.2 *m/z*, $[M+Na]^+$ = 617.2 *m/z*, $[2M+Na]^+$ = 1211.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{32}H_{38}N_2O_9Na$ 617.2470 found 617.2476. $[\alpha]_D^{20}$ = 31 (c = 0.88, DCM).



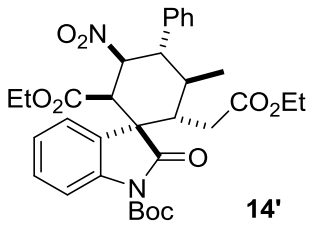
1'-(*tert*-butyl) 6-ethyl (1*S*,2*S*,3*R*,4*S*,5*R*,6*R*)-3-((*tert*-butyldimethylsilyl)oxy)-2-(2-ethoxy-2-oxoethyl)-5-nitro-2'-oxo-4-phenylspiro[cyclohexane-1,3'-indoline]-1',6-dicarboxylate: Yield = 78%; pale yellow syrup. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 (d, *J* = 8.0 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 2H), 7.44 – 7.21 (m, 6H), 5.58 (dd, *J* = 12.8, 6 Hz, 1H), 4.39 – 4.32 (m, 2H), 4.19 (t, *J* = 6 Hz, 1H), 3.98 – 3.83 (m, 2H), 3.78 – 3.70 (m, 1H), 3.68 – 3.57 (m, 2H), 2.17 (dd, *J* = 16.0, 4.8 Hz, 1H), 1.69 (s, 9H), 1.11 (t, *J* = 7.6, 3H), 0.88 (t, *J* =7.2 Hz, 3H), 0.58 (s, 9H), 0.18 (s, 3H), 0.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 170.7, 168.4, 148.9, 140.5, 132.7, 131.1, 129.9, 128.6, 128.2, 124.9, 124.8, 124.6, 115.8, 84.8, 83.5, 71.3, 61.7, 60.5, 54.1, 51.2, 46.7, 42.2, 33.6, 28.1, 25.3, 17.6, 13.8, 13.3, -3.6, -4.9. HPLC-MS (ESI) t_r = 21.6 min; $[M\text{-}Boc+H]^+$ = 611.2 *m/z*, $[M+Na]^+$ = 733.2 *m/z*, $[2M+Na]^+$ = 1443.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{37}H_{50}N_2O_{10}SiNa$ 733.3127 found 733.3123. $[\alpha]_D^{20}$ = 53 (c = 1.26, DCM).

Applying the developed organocascade protocol to 3-ylidene oxindole **1c** and nitro compound *syn*-**2g**, we obtained two new spirocyclohexane oxindoles (**14'** and **14''**, Scheme S8), diastereoisomers of product **14**.



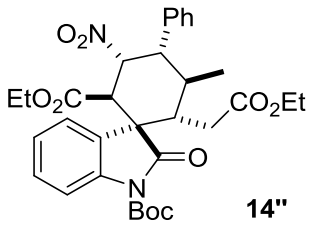
Scheme S8.

The nitro compound *syn*-**2g** (0.12 mmol, 33 mg) is added to a solution of catalyst **I** (10 mol%, 4 mg) and 3-ylidene oxindole **1c** (0.1 mmol, 32 mg) in DCM (0.15 mL). The reaction is stirred at room temperature for 24 h. The conversion is monitored by ^{1}H NMR analysis. The crude mixture is directly purified by flash chromatography on silica gel (cyclohexane/ethyl acetate 9/1), affording the separated spirooxindoles **14'** and **14''** (*dr* = 1:1) as pale yellow syrups in 79% total yield.



14'

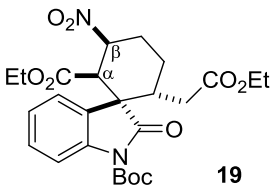
1'-(*tert*-butyl) 2-ethyl (1*R*,2*R*,3*S*,4*S*,5*S*,6*S*)-6-(2-ethoxy-2-oxoethyl)-5-methyl-3-nitro-2'-oxo-4-phenylspiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.8 Hz, 1H), 7.65 (d, *J* = 8.0, 1H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.43 – 7.27 (m, 6H), 5.42 (dd, *J* = 12.4, 4.8 Hz, 1H), 4.30 – 4.18 (m, 3H), 3.95 – 3.87 (m, 1H), 3.80 – 3.72 (m, 1H), 3.40 – 3.33 (m, 1H), 3.18 (d, *J* = 4.4 Hz, 1H), 2.53 – 2.43 (m, 1H), 2.03 (dd, *J* = 16.0, 5.6 Hz, 1H), 1.94 (dd, *J* = 15.6, 4.4 Hz, 1H), 1.64 (s, 9H), 1.29 (t, *J* = 6.8, 3H), 1.10 (t, *J* = 7.2 Hz, 3H), 0.96 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 171.3, 167.3, 148.7, 139.8, 138.9, 129.8, 129.0, 128.9, 128.3, 128.0, 127.4, 125.1, 124.4, 115.9, 87.8, 85.0, 61.7, 60.6, 54.9, 50.6, 47.6, 39.5, 38.2, 35.3, 28.0, 17.5, 13.9, 13.9. HPLC-MS (ESI) t_r = 14.4 min; $[M\text{-}Boc+H]^+$ = 495.2 *m/z*, $[M+Na]^+$ = 617.2 *m/z*, $[2M+Na]^+$ = 1211.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{32}H_{38}N_2O_9Na$ 617.2470 found 617.2472. $[\alpha]_D^{20}$ = -2 (c = 0.60, DCM).



14''

1'-(*tert*-butyl) 2-ethyl (1*R*,2*R*,3*R*,4*S*,5*S*,6*S*)-6-(2-ethoxy-2-oxoethyl)-5-methyl-3-nitro-2'-oxo-4-phenylspiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.0 Hz, 1H), 7.47 (d, *J* = 7.6, 1H), 7.40 (t, *J* = 8.0 Hz, 1H), 7.36 – 7.26 (m, 6H), 5.93 (dd, *J* = 12.4, 10.0 Hz, 1H), 3.93 (d, *J* = 12.4 Hz, 1H), 3.88 – 3.76 (m, 4H), 3.67 (t, *J* = 10.8 Hz, 1H), 2.86 – 2.80 (m, 1H), 2.60 – 2.52 (m, 1H), 2.28 (dd, *J* = 16.8, 6.0 Hz, 1H), 2.04 (dd, *J* = 16.8, 7.6 Hz, 1H), 1.65 (s, 9H), 1.06 (t, *J* = 7.2, 3H), 0.91 – 0.87 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 171.0, 168.4, 148.9, 140.3, 137.0, 129.4, 129.0, 128.9, 128.6, 128.5, 128.4, 127.9, 124.6, 123.9, 115.3, 84.7, 83.6, 61.6, 60.7, 52.9, 51.0, 49.5, 42.3, 36.5, 35.7, 28.0, 18.1, 13.9, 13.4. HPLC-MS (ESI) t_r = 13.2 min; $[M\text{-}Boc+H]^+$ = 495.2 *m/z*, $[M+Na]^+$ = 617.2 *m/z*, $[2M+Na]^+$ = 1211.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{32}H_{38}N_2O_9Na$ 617.2470 found 617.2465. $[\alpha]_D^{20}$ = 23 (c = 1.12, DCM).

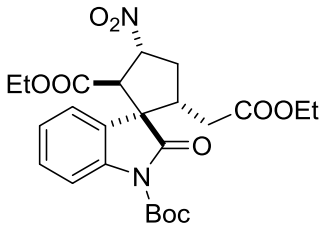
Applying the DBU-mediated protocol to 3-ylidene oxindole **1c** and nitro compound (*E*)-**2a**, we obtained the corresponding β-nitro spirocyclohexane as mixture of four diastereoisomers, including **19**.



19

(1*S*,2*R*,3*S*,6*R*)-1'-*tert*-butyl 2-ethyl 6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.4 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.17 – 7.14 (m, 2H), 5.51 (dt, *J* = 12.8, 4.8 Hz, 1H), 4.20 – 4.10 (m, 1H), 4.06 – 3.93 (m, 3H), 3.40 (d, *J* = 5.2 Hz, 1H), 3.15 – 3.06 (m, 1H), 2.90 (dq, *J* = 12.8, 4.4 Hz, 1H), 2.53 – 2.45 (m, 1H), 2.19 (dq, *J* = 12.8, 4.4 Hz, 1H), 2.11 – 2.03 (m, 1H), 1.95 (dd, *J* = 15.2, 10.4 Hz, 1H), 1.77 (dd, *J* = 15.2, 3.6 Hz, 1H), 1.67 (s, 9H), 1.17 (t, *J* = 7.2 Hz, 3H), 1.09 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 171.3, 168.7, 148.6, 139.5, 129.6, 126.8, 124.7, 124.0, 115.1, 85.3, 80.7, 61.2, 60.7, 52.4, 47.5, 35.6, 34.9, 28.1, 24.9, 24.6, 14.1, 13.7. HPLC-MS (ESI) t_r = 12.3 min; $[M\text{-}Boc+H]^+$ = 405.0 *m/z*, $[M+Na]^+$ = 527.0 *m/z*, $[2M+Na]^+$ = 1031.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{25}H_{32}N_2O_9Na$ 527.2000 found 527.1995.

Applying the DBU-mediated protocol to 3-ylidene oxindole **1c** and nitro compound (*E*)-**2f**, we obtained the corresponding β-nitro spirocyclopentane as mixture of three diastereoisomers, including **4a''**.

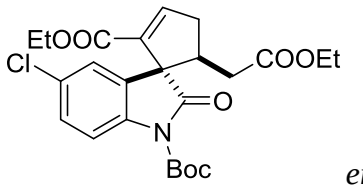


4a''

(1*R*,2*R*,3*R*,5*R*)-1'-*tert*-butyl 2-ethyl 5-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-1',2-dicarboxylate: Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 7.6 Hz, 1H), 7.31 – 7.23 (m, 2H), 5.64 – 5.56 (m, 1H), 4.09 (d, *J* = 9.6 Hz, 1H), 4.04 – 3.86 (m, 4H), 3.09 – 2.98 (m, 2H), 2.54 – 2.43 (m, 1H), 2.32 (dd, *J* = 16.8, 7.6 Hz, 1H), 2.21 (dd, *J* = 16.8, 5.2 Hz, 1H), 1.64 (s, 9H), 1.13 – 1.07 (m, 6H).

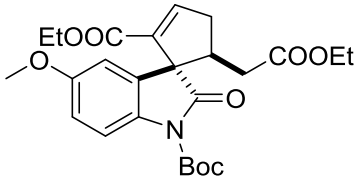
G. Further Transformations: Procedures and Products Characterization.

Typical procedure for spirocyclopentene oxindoles synthesis: Quinuclidine (1.2 equivalents, 7 µL) is added to a solution of spirocyclopentane oxindole **4** (0.05 mmol) in DCM (0.3 mL). The reaction is stirred at room temperature for 2 h. The conversion is monitored by TLC and ^{1}H NMR. The crude mixture is directly purified by flash chromatography on silica gel (cyclohexane/ethyl acetate 8/2).



ent-**6b**

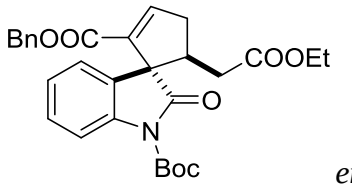
1'-(*tert*-butyl) 2-ethyl (1*R*,5*S*)-5'-chloro-5-(2-ethoxy-2-oxoethyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-1',2-dicarboxylate: Yield = 88%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.7 Hz, 1H), 7.29 (d, *J* = 8.4 Hz, 1H), 7.18 (s, 1H), 6.92 (s, 1H), 4.16 – 3.86 (m, 4H), 3.44 (p, *J* = 8.2 Hz, 1H), 3.06 (ddd, *J* = 18.1, 8.3, 2.9 Hz, 1H), 2.52 (dd, *J* = 18.6, 9.6 Hz, 1H), 2.30 (dd, *J* = 16.6, 8.2 Hz, 1H), 2.15 (dd, *J* = 16.5, 7.6 Hz, 1H), 1.66 (s, 9H), 1.14 (t, *J* = 7.1 Hz, 3H), 1.08 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 176.5, 171.0, 162.1, 149.2, 146.6, 138.7, 138.3, 129.4, 129.3, 129.0, 123.9, 116.7, 84.4, 62.6, 60.8, 60.6, 45.1, 38.4, 35.5, 28.1, 14.0, 13.6. HPLC-MS (ESI) t_r = 11.7 min; $[M\text{-}Boc+H]^+$ = 378.0 *m/z*, $[M+Na]^+$ = 500.0 *m/z*, $[2M+Na]^+$ = 977.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{24}H_{28}ClNO_7Na$ 500.1447 found 500.1440. $[\alpha]_D^{20}$ = 56 (c = 0.53, DCM).



ent-**6c**

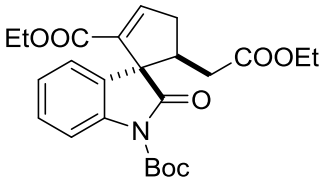
1'-(*tert*-butyl) 2-ethyl (1*R*,5*S*)-5-(2-ethoxy-2-oxoethyl)-5'-methoxy-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-1',2-dicarboxylate: Yield = 82%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J* = 8.8 Hz, 1H), 7.16 (t, *J* = 2.4 Hz, 1H), 6.82 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.50 (d, *J* = 2.8 Hz, 1H), 4.04 – 3.90 (m, 4H), 3.79 (s, 3H), 3.43 (quintet, *J* = 8.0 Hz, 1H), 3.04 (ddd, *J* = 11.2, 8.4, 2.8 Hz, 1H), 2.49 (ddd, *J* = 12.0, 9.6, 2.4 Hz, 1H), 2.26 (dd, *J* = 16.4, 8.8 Hz, 1H), 2.15 (dd, *J* = 16.4, 6.8 Hz, 1H), 1.65 (s, 9H), 1.14 (t, *J* = 7.2 Hz, 3H), 1.07 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3, 171.1, 162.2, 156.4, 149.4, 146.3, 138.6, 133.4, 128.8, 116.2, 112.9, 110.6, 83.9, 62.9, 60.7, 60.5, 55.6, 45.1, 38.4, 35.6, 28.1, 14.0, 13.6. HPLC-MS (ESI) t_r = 10.4 min; [M-

Boc+H]$^+$ = 374.2 *m/z*, [M+Na]$^+$ = 496.0 *m/z*, [2M+Na]$^+$ = 969.2 *m/z*. HRMS (ESI) [M+Na]$^+$ calcd for $C_{25}H_{31}NO_8Na$ 496.1942 found 496.1943. $[\alpha]_D^{20}$ = 22 (c = 0.72, DCM).



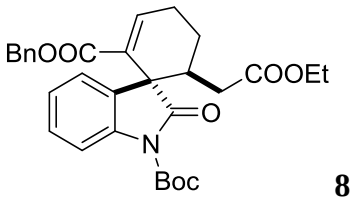
ent-**6d**

2-benzyl 1'-(*tert*-butyl) (1*R*,5*S*)-5-(2-ethoxy-2-oxoethyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-1',2-dicarboxylate: Yield = 85%; white crystals; m.p. = 156-158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 1H), 7.31 (t, *J* = 7.9 Hz, 1H), 7.28 – 7.21 (m, 4H), 7.12 (t, *J* = 7.5 Hz, 1H), 7.04 – 6.98 (m, 2H), 6.95 (d, *J* = 6.2 Hz, 1H), 5.04 (d, *J* = 12.4 Hz, 1H), 4.88 (d, *J* = 12.5 Hz, 1H), 4.01 – 3.88 (m, 2H), 3.50 – 3.39 (m, 1H), 3.05 (ddd, *J* = 18.6, 8.4, 3.0 Hz, 1H), 2.51 (ddd, *J* = 18.6, 9.6, 2.2 Hz, 1H), 2.24 (dd, *J* = 16.5, 8.4 Hz, 1H), 2.12 (dd, *J* = 16.5, 7.4 Hz, 1H), 1.61 (s, 9H), 1.12 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 171.1, 162.1, 149.2, 147.2, 140.0, 138.1, 135.2, 128.9, 128.4, 128.0, 127.7, 127.3, 124.0, 123.8, 115.6, 84.0, 66.5, 62.6, 60.5, 45.3, 38.4, 35.7, 28.1, 14.0. HPLC-MS (ESI) t_r = 11.7 min; [M+Na]$^+$ = 528.2 *m/z*, [2M+Na]$^+$ = 1033.6 *m/z*. HRMS (ESI) [M+Na]$^+$ calcd for $C_{29}H_{31}NO_7Na$ 528.1993 found 528.1996. $[\alpha]_D^{20}$ = 20 (c = 0.04, DCM).



6f

1'-(*tert*-butyl) 2-ethyl (1*S*,5*S*)-5-(2-ethoxy-2-oxoethyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-1',2-dicarboxylate: Yield = 89%; pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.4 Hz, 1H), 7.31 – 7.24 (m, 1H), 7.19 (t, *J* = 2.4 Hz, 1H), 7.14 – 7.10 (m, 2H), 3.96 – 3.84 (m, 4H), 3.12 – 3.03 (m, 1H), 2.93 (ddd, *J* = 11.2, 8.4, 3.2 Hz, 1H), 2.61 (ddd, *J* = 11.6, 9.6, 2.4 Hz, 1H), 2.54 (dd, *J* = 16.0, 10.0 Hz, 1H), 2.30 (dd, *J* = 16.0, 5.2 Hz, 1H), 1.62 (s, 9H), 1.13 (t, *J* = 7.2 Hz, 3H), 0.93 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 171.7, 162.8, 149.2, 148.2, 140.4, 137.7, 130.7, 128.6, 124.7, 122.7, 114.7, 84.2, 62.8, 60.6, 60.4, 47.8, 37.6, 34.4, 28.1, 14.0, 13.6. HPLC-MS (ESI) t_r = 11.1 min; [M-Boc+H]$^+$ = 344.2 *m/z*, [M+Na]$^+$ = 466.0 *m/z*, [2M+Na]$^+$ = 909.2 *m/z*. HRMS (ESI) [M+Na]$^+$ calcd for $C_{24}H_{29}NO_7Na$ 466.1836 found 466.1834. $[\alpha]_D^{20}$ = 42 (c = 0.25, DCM).

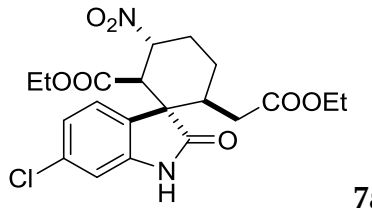


8

2-benzyl 1'-(*tert*-butyl) (1*R*,6*S*)-6-(2-ethoxy-2-oxoethyl)-2'-oxospiro[cyclohexane-1,3'-indolin]-2-ene-1',2-dicarboxylate: Quinuclidine (2.5 equivalents, 9 µL) is added to a solution of spirocyclohexane oxindole **3j** (0.03 mmol) in DCM (0.25 mL). The reaction is stirred at room temperature for 24 h. The conversion is monitored by TLC and ^{1}H NMR. The crude mixture is directly purified by flash chromatography on silica gel (cyclohexane/ethyl acetate 8/2) affording spirocyclohexene oxindole **8** in 77% yield (12 mg) as pale yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.4 Hz, 1H), 7.51 (t, *J* = 3.6 Hz, 1H), 7.34 – 7.21 (m, 5H), 7.11 (t, *J* = 7.2 Hz, 1H), 7.08 – 7.01 (m, 2H), 5.05 (d, *J* = 12.4 Hz, 1H), 4.86 (d, *J* = 12.4 Hz, 1H), 4.10 – 3.99 (m, 2H), 2.75 – 2.63 (m, 1H), 2.59 – 2.47 (m, 2H), 2.07 (dd, *J* = 16.0, 3.2 Hz, 1H), 2.01 – 1.92 (m, 1H), 1.73 – 1.62 (m, 1H), 1.63 (s, 9H), 1.19 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.6, 171.4, 164.4, 149.1, 144.9, 140.2, 135.4, 129.9, 129.4, 128.6, 128.4, 128.3, 128.3, 128.0, 127.9, 124.0, 123.9, 115.3, 84.3, 66.7, 60.5, 53.5, 39.7, 35.1, 28.1, 25.4, 22.7, 14.1. HPLC-MS (ESI) t_r = 13.1 min; $[M\text{-}Boc+H]^+$ = 420.0 *m/z*, $[M+Na]^+$ = 542.0 *m/z*, $[2M+Na]^+$ = 1061.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{30}H_{33}NO_7Na$ 542.2149 found 542.2154. $[\alpha]_D^{20}$ = 44 (c = 0.71, DCM).

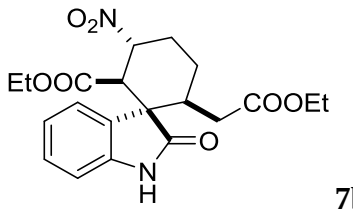
Typical procedure for *N*Boc-deprotection: Trifluoroacetic acid (TFA, 18 equivalents, 69 µL) is added to a solution of spirooxindole (**3** or **4** or **6**, 0.05 mmol) in DCM (0.5 mL). The reaction is stirred at room temperature for 2 h. The conversion is monitored by TLC. The mixture is quenched with aqueous phosphate buffer (pH = 7, 1M) and extracted with DCM (3 x 3 mL). The combined organic layers are dried over Na_2SO_4, filtered and concentrated. The mixture is purified by a short column chromatography on silica gel (cyclohexane/ethyl acetate 7/3) providing the corresponding NH-indolinone in quantitative yield.



7a

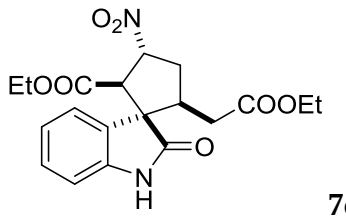
ethyl (1*S*,2*R*,3*R*,6*S*)-6'-chloro-6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-2-carboxylate: Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.02 (bs, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.05 (dd, *J* = 8.0, 2.0 Hz, 1H), 7.01 (d, *J* = 2.0 Hz, 1H), 5.20 (dt, *J* = 12.0, 4.4 Hz, 1H),

4.06 (q, *J* = 6.8 Hz, 1H), 4.05 (q, *J* = 7.2 Hz, 1H), 3.88 (d, *J* = 11.6 Hz, 1H), 3.87 – 3.79 (m, 2H), 2.75 – 2.68 (m, 1H), 2.62 – 2.54 (m, 1H), 2.22 – 2.15 (m, 1H), 2.13 – 2.02 (m, 2H), 1.70 – 1.59 (m, 1H), 1.58 (dd, *J* = 16.0, 10.8 Hz, 1H), 1.19 (t, *J* = 7.2 Hz, 3H), 0.88 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9, 170.9, 168.1, 142.5, 135.6, 126.2, 124.6, 122.7, 111.4, 82.0, 61.8, 60.8, 54.6, 49.8, 39.7, 34.7, 30.6, 25.7, 14.1, 13.5. HPLC-MS (ESI) t_r = 9.1 min; $[M+H]^+$ = 439.2 *m/z*, $[M+Na]^+$ = 461.2 *m/z*, $[M+K]^+$ = 477.0 *m/z*, $[2M+H]^+$ = 877.4 *m/z*, $[2M+Na]^+$ = 899.4 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{20}H_{23}ClN_2O_7Na$ 461.1091 found 461.1086. $[\alpha]_D^{20}$ = -3 (c = 1.2, DCM).



7b

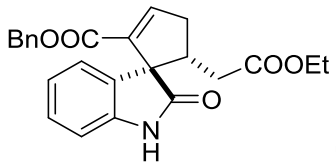
ethyl (1*R*,2*R*,3*R*,6*S*)-6-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclohexane-1,3'-indoline]-2-carboxylate: Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (bs, 1H), 7.30 – 7.24 (m, 2H), 7.11 (t, *J* = 7.6 Hz, 1H), 6.84 (d, *J* = 7.6 Hz, 1H), 5.74 (dt, *J* = 12.0, 4.4 Hz, 1H), 4.02 – 3.91 (m, 2H), 3.83 – 3.72 (m, 2H), 3.48 (d, *J* = 11.2 Hz, 1H), 2.71 – 2.61 (m, 1H), 2.55 – 2.45 (m, 1H), 2.32 (dq, *J* = 13.2, 3.6 Hz, 1H), 2.14 – 2.03 (m, 1H), 2.05 (dd, *J* = 16.4, 11.2 Hz, 1H), 1.99 – 1.91 (m, 1H), 1.90 (dd, *J* = 16.0, 3.6 Hz, 1H), 1.16 (t, *J* = 6.8 Hz, 3H), 0.78 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 171.6, 169.0, 140.7, 129.2, 128.9, 123.6, 123.0, 109.7, 81.5, 61.3, 60.7, 53.1, 53.0, 40.5, 34.8, 30.7, 24.4, 14.0, 13.4. HPLC-MS (ESI) t_r = 8.7 min; $[M+H]^+$ = 405.2 *m/z*, $[M+K]^+$ = 443.2 *m/z*, $[2M+Na]^+$ = 831.4 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{20}H_{24}N_2O_7Na$ 427.1476 found 427.1473. $[\alpha]_D^{20}$ = 64 (c = 0.13, DCM).



7c

ethyl (1*R*,2*R*,3*R*,5*S*)-5-(2-ethoxy-2-oxoethyl)-3-nitro-2'-oxospiro[cyclopentane-1,3'-indoline]-2-carboxylate: White crystals; m.p. = 149-151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (bs, 1H), 7.35 (d, *J* = 7.5 Hz, 1H), 7.31 – 7.24 (m, 1H), 7.13 (t, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 5.70 (ddd, *J* = 10.0, 7.2, 2.6 Hz, 1H), 4.28 (d, *J* = 7.2 Hz, 1H), 4.13 – 3.90 (m, 4H), 3.13 – 3.01 (m, 1H), 2.85 – 2.72 (m, 1H), 2.65 (ddd, *J* = 14.6, 8.4, 2.8 Hz, 1H), 2.27 (dd, *J* = 15.9, 10.2 Hz, 1H), 2.08 (dd, *J* = 15.7, 3.5 Hz, 1H), 1.16 (t, *J* = 6.9 Hz, 3H), 1.07 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (50 MHz,

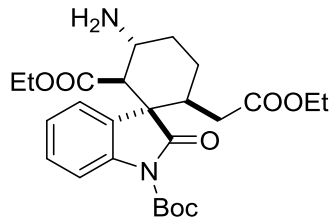
$CDCl_3$) δ 179.4, 170.9, 168.3, 140.9, 129.3, 128.5, 123.6, 122.6, 110.2, 85.8, 61.9, 60.9, 59.9, 56.3, 44.6, 35.7, 33.5, 14.0, 13.6. HPLC-MS (ESI) t_r = 8.2 min; $[M+H]^+$ = 391.2 *m/z*, $[M+Na]^+$ = 413.4 *m/z*, $[2M+Na]^+$ = 803.4 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{19}H_{22}N_2O_7Na$ 413.1319 found 413.1317.



7d

benzyl (1*S*,5*R*)-5-(2-ethoxy-2-oxoethyl)-2'-oxospiro[cyclopentane-1,3'-indolin]-2-ene-2-carboxylate: Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (bs, 1H), 7.28 – 7.20 (m, 5H), 7.08 – 7.04 (m, 1H), 7.00 (dt, *J* = 7.6, 1.2 Hz, 1H), 6.96 (t, *J* = 6.8 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 5.06 (d, *J* = 12.4 Hz, 1H), 4.91 (d, *J* = 12.4 Hz, 1H), 3.99 (q, *J* = 7.2 Hz, 1H), 3.99 (q, *J* = 7.2 Hz, 1H), 3.45 – 3.37 (m, 1H), 3.07 (ddd, *J* = 11.2, 8.4, 2.8 Hz, 1H), 2.52 (ddd, *J* = 11.6, 9.6, 2.0 Hz, 1H), 2.21 (dd, *J* = 16.4, 9.2 Hz, 1H), 2.13 (dd, *J* = 16.4, 6.4 Hz, 1H), 1.15 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.1, 171.4, 162.3, 147.4, 140.8, 137.5, 135.4, 128.9, 128.8, 128.4, 128.0, 127.9, 124.4, 122.2, 109.9, 66.4, 62.6, 60.5, 44.4, 38.5, 35.7, 14.1. HPLC-MS (ESI) t_r = 8.5 min; $[M+H]^+$ = 406.2 *m/z*, $[2M+H]^+$ = 811.4 *m/z*, $[2M+Na]^+$ = 833.4 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{24}H_{23}NO_5Na$ 428.1468 found 428.1474. $[\alpha]_D^{20}$ = -22 (c = 0.61, DCM).

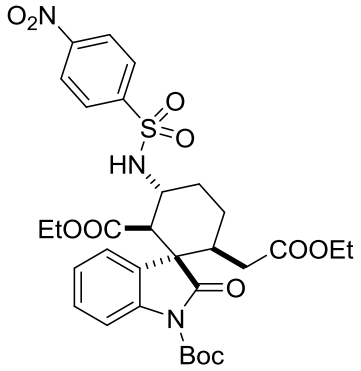
Typical procedure for NO_2-reduction: β-nitro spirooxindole (**3** or **4**, 0.1 mmol) is dissolved in anhydrous EtOH (2 mL), Raney® nickel (6 drops of the commercially available suspension in water) is added, and the mixture is stirred overnight at room temperature under H_2 atmosphere (balloon). The conversion is monitored by TLC. The mixture is filtered and washed with ethyl acetate (1 x 3 mL) and DCM (2 x 3 mL). The solvent is removed under reduced pressure and the corresponding β-amino spirooxindole is quantitatively obtained pure.



10

1'-(*tert*-butyl) 2-ethyl (1*R*,2*R*,3*R*,6*S*)-3-amino-6-(2-ethoxy-2-oxoethyl)-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 1H), 7.32 – 7.22 (m, 2H), 7.19 – 7.15 (m, 1H), 4.30 (bt, *J* = 10.8 Hz, 1H), 4.03 – 3.92 (m, 3H), 3.90 – 3.79 (m, 1H), 3.23 (d, *J* = 11.2 Hz, 1H), 2.57 – 2.46 (m, 1H), 2.46

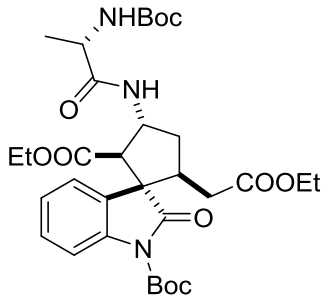
– 2.35 (m, 1H), 2.20 – 2.10 (m, 1H), 2.03 – 1.89 (m, 2H), 1.88 – 1.74 (m, 2H), 1.64 (s, 9H), 1.16 (t, *J* = 7.2 Hz, 3H), 0.83 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 171.3, 168.9, 149.0, 140.0, 129.0, 128.4, 124.9, 122.5, 114.7, 84.5, 62.2, 60.7, 54.7, 52.4, 47.9, 41.4, 34.9, 30.0, 28.1, 24.0, 14.1, 13.3. HPLC-MS (ESI) t_r = 2.1 min; $[M\text{-}Boc+H]^+$ = 375.0 *m/z*, $[M+H]^+$ = 475.2 *m/z*, $[M+Na]^+$ = 497.2 *m/z*, $[2M+H]^+$ = 949.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{25}H_{34}N_2O_7Na$ 497.2258 found 497.2251. $[\alpha]_D^{20}$ = 7 (c = 0.77, DCM).



11a

1'-(*tert*-butyl) 2-ethyl (1*R*,2*R*,3*R*,6*S*)-6-(2-ethoxy-2-oxoethyl)-3-((4-nitrophenyl)sulfonamido)-2'-oxospiro[cyclohexane-1,3'-indoline]-1',2-dicarboxylate: The crude **10** (0.128 mmol, 61 mg) is dissolved in anhydrous DCM (3.5 mL), then 4-nitrobenzenesulfonyl chloride (1.5 equivalents, 43 mg) and TEA (2 equivalents, 36 µL) are sequentially added. The reaction is stirred at room temperature overnight. The conversion is monitored by TLC and ^{1}H NMR. The solvent is removed under reduced pressure and the mixture is purified by column chromatography on silica gel (cyclohexane/ethyl acetate 8/2) providing product **11a** as white syrup in 83% yield (70 mg).

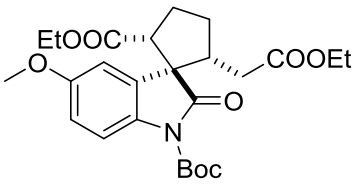
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (d, *J* = 9.2 Hz, 2H), 8.06 (d, *J* = 8.4 Hz, 2H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.19 – 7.14 (m, 2H), 4.82 (d, *J* = 8.8 Hz, 1H), 4.53 – 4.43 (m, 1H), 4.02 – 3.87 (m, 2H), 3.60 – 3.52 (m, 1H), 3.46 – 3.38 (m, 1H), 2.76 (d, *J* = 11.6 Hz, 1H), 2.33 – 2.10 (m, 3H), 1.95 (dd, *J* = 15.6, 10.0 Hz, 1H), 1.75 (dd, *J* = 15.6, 3.2 Hz, 1H), 1.65 (s, 9H), 1.59 – 1.50 (m, 1H), 1.14 (t, *J* = 7.2 Hz, 3H), 0.73 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 171.6, 169.1, 149.9, 148.7, 146.6, 139.8, 129.2, 128.4, 127.8, 124.8, 124.2, 122.2, 114.8, 84.6, 61.2, 60.7, 58.0, 52.4, 49.8, 41.3, 34.6, 33.9, 28.1, 24.9, 14.0, 13.3. HPLC-MS (ESI) t_r = 11.4 min; $[M\text{-}Boc+H]^+$ = 560.0 *m/z*, $[M+Na]^+$ = 682.0 *m/z*, $[2M+Na]^+$ = 1341.2 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{31}H_{37}N_3O_{11}SNa$ 682.2041 found 682.2038. $[\alpha]_D^{20}$ = 15 (c = 1.12, DCM).



11b

1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,5*S*)-3-((*S*)-2-((*tert*-butoxycarbonyl)amino)propanamido)-5-(2-ethoxy-2-oxoethyl)-2'-oxospiro[cyclopentane-1,3'-indoline]-1',2-dicarboxylate: The crude 1'-(*tert*-butyl) 2-ethyl (1*S*,2*R*,3*R*,5*S*)-3-amino-5-(2-ethoxy-2-oxoethyl)-2'-oxospiro[cyclopentane-1,3'-indoline]-1',2-dicarboxylate (0.05 mmol, 23 mg), obtained as reported for compound **10**, is dissolved in anhydrous DCM (2.5 mL), then (*tert*-butoxycarbonyl)-L-alanine (1.2 equivalents, 11.5 mg) and *N*,*N*'-dicyclohexylcarbodiimide (1.2 equivalents, 12.4 mg) are sequentially added. The reaction is stirred at room temperature overnight. The conversion is monitored by TLC and ^{1}H NMR. The solvent is removed under reduced pressure and the mixture is purified by column chromatography on silica gel (cyclohexane/ethyl acetate 8/2) providing product **11b** as white syrup in 70% yield (22 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.0 Hz, 1H), 7.36 – 7.29 (m, 1H), 7.18 – 7.11 (m, 2H), 6.72 (bs, 1H), 5.03 – 4.89 (m, 2H), 4.17 (bs, 1H), 4.01 – 3.92 (m, 2H), 3.74 – 3.63 (m, 2H), 3.51 (d, *J* = 8.0 Hz, 1H), 3.26 – 3.17 (m, 1H), 2.37 – 2.22 (m, 2H), 2.08 – 1.89 (m, 2H), 1.66 (s, 9H), 1.45 (s, 9H), 1.37 (d, *J* = 7.2 Hz, 3H), 1.13 (t, *J* = 7.2 Hz, 3H), 0.74 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 172.2, 170.9, 168.9, 149.0, 140.2, 129.1, 125.5, 124.4, 124.2, 115.3, 84.6, 60.8, 60.6, 60.0, 59.5, 50.6, 43.9, 38.5, 35.3, 31.9, 28.3, 28.1, 22.7, 14.0, 13.3. HPLC-MS (ESI) t_r = 10.2 min; $[M\text{-}Boc+H]^+$ = 532.2 *m/z*, $[M+H]^+$ = 632.2 *m/z*, $[2M+H]^+$ = 1263.4 *m/z*, $[2M+Na]^+$ = 1285.4 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{32}H_{45}N_3O_{10}Na$ 654.2997 found 654.2995. $[\alpha]_D^{20}$ = -4 (c = 0.39, DCM).



12

1'-(*tert*-butyl) 2-ethyl (1*R*,2*R*,5*R*)-5-(2-ethoxy-2-oxoethyl)-5'-methoxy-2'-oxospiro[cyclopentane-1,3'-indoline]-1',2-dicarboxylate: Spirocyclopentene oxindole **6c** (0.03 mmol, 14 mg) is dissolved in anhydrous MeOH (1.5 mL) and Pd on C (20% w/w) is added. The mixture is stirred overnight at room temperature under H_2 atmosphere (balloon). The conversion is

monitored by TLC and ^{1}H NMR. The mixture is filtered and washed with ethyl acetate (1 x 3 mL) and DCM (2 x 3 mL). The solvent is evaporated under reduced pressure and the crude is purified by column chromatography on silica gel (cyclohexane/ethyl acetate 9/1) providing product **12** as pale yellow oil in 77% yield (11 mg).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.9 Hz, 1H), 6.83 (dd, *J* = 8.9, 2.7 Hz, 1H), 6.67 (d, *J* = 2.6 Hz, 1H), 4.02 (q, *J* = 7.1 Hz, 1H), 4.01 (q, *J* = 7.1 Hz, 1H), 3.80 (s, 3H), 3.77 – 3.57 (m, 3H), 3.07 – 2.95 (m, 1H), 2.55 – 2.21 (m, 3H), 2.00 (dd, *J* = 15.9, 5.3 Hz, 1H), 1.88 (dd, *J* = 15.9, 9.5 Hz, 1H), 1.84 – 1.73 (m, 1H), 1.66 (s, 9H), 1.18 (t, *J* = 7.1 Hz, 3H), 0.78 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.1, 171.3, 170.8, 156.5, 149.2, 133.5, 128.0, 115.9, 112.6, 111.0, 84.1, 60.6, 60.5, 55.6, 53.7, 46.5, 35.3, 29.7, 28.1, 24.4, 14.1, 13.3. HPLC-MS (ESI) t_r = 10.7 min; $[M-Boc+H]^+$ = 376.2 *m/z*, $[M+H]^+$ = 476.2 *m/z*, $[M+Na]^+$ = 498.2 *m/z*, $[2M+Na]^+$ = 973.6 *m/z*. HRMS (ESI) $[M+Na]^+$ calcd for $C_{25}H_{33}NO_8Na$ 498.2098 found 498.2096.

H. Determination of the Relative and Absolute Stereochemistry.

X-ray crystallographic analyses.

Single crystal X-ray diffraction for 3c, 3u, 4d, 6d and **7c.** The X-ray intensity data for **3c, 3u, 6d** and **7c** were measured at room temperature on a Bruker SMART Apex II CCD area detector diffractometer using Mo-Kα radiation, whereas **4d** was collected using Cu-Kα radiation on a Bruker X8 Prospector diffractometer. Data were reduced with empirical absorption correction and all structures were solved by direct methods and subsequent Fourier syntheses and refined by full-matrix least-squares on F^2 (SHELXTL),[21] using anisotropic thermal parameters for all non-hydrogen atoms. The hydrogen atoms were added in calculated positions, included in the final stage of refinement with isotropic thermal parameters, U(H) = 1.2 U_{eq}(C) [U(H) = 1.5 U_{eq}(C-Me)], and allowed to ride on their carrier carbons. Two independent conformers are present in **3c**. In the unit cell of **4d** disordered solvent molecules are present and a calculation using the SQUEEZE routine of PLATON[22] revealed that the potential total solvent accessible volume is 272 Å^3. The absolute structure configuration for **4d** was determined from X-ray data. The molecular diagrams of the structures were generated using Mercury.[23]

3c: Empirical formula: $C_{25}H_{32}N_2O_9$; crystal system: triclinic; space group: *P 1*; *a* = 8.9314(11), *b* = 11.2207(15), *c* = 13.6038(17) Å, α = 92.405(9), β = 96.213(9), γ = 90.958(9)°; V = 1353.8(3) Å^3; *Z* = 2; μ = 0.094 mm^{-1}; ρ_{cald} = 1.238 Mg m^{-3}; crystal dimensions (ca.) 0.30 x 0.20 x 0.10 mm^3; 296 K; 2ϑ_{max} = 50.00; 18189 reflections; 8160 independent (Rint = 0.0764); R1 = 0.1355 (I > 2σ(I)); and wR2 = 0.3636 (all data); max/min residual electron density 0.607/-0.369 e Å^{-3} .

3u: Empirical formula: $C_{25}H_{32}N_2O_9$; crystal system: orthorhombic; space group: *Pna2$_1$*; *a* = 11.720(3), *b* = 11.071(2), *c* = 20.346(4) Å, V = 2640(1) Å^3; *Z* = 4; μ = 0.097 mm^{-1}; ρ_{cald} = 1.269 Mg m^{-3}; crystal dimensions (ca.) 0.30 x 0.22 x 0.10 mm^3; 296 K; 2ϑ_{max} = 50.34; 14177 reflections; 4590 independent (Rint = 0.0220); R1 = 0.0471 (I > 2σ(I)); and wR2 = 0.1296 (all data); max/min residual electron density 0.195/-0.147 e Å^{-3}.

4d: Empirical formula: $C_{29}H_{32}N_2O_9$; crystal system: monoclinic; space group: *P2$_1$*; *a* = 13.0851(9), *b* = 8.8314(6), *c* = 14.1924(10) Å, β = 100.413(9)°; V = 1613.1(2) Å^3; *Z* = 2; μ = 0.708 mm^{-1}; ρ_{cald} = 1.138 Mg m^{-3}; crystal dimensions (ca.) 0.25 x 0.18 x 0.07 mm^3; 296 K; 2ϑ_{max} = 54.89;

[21] G. M. Sheldrick, SHELXTL*plus* (*Windows NT Version*) *Structure Determination Package*, Version 5.1. Bruker Analytical X-ray Instruments Inc.: Madison, WI, USA, 1998.
[22] A. L. Spek, *PLATON A Multipurpose Crystallographic Tool*. Utrecht University, Utrecht, The Netherlands, 2003.
[23] C. F. Macrae, I. J. Bruno, J. A. Chisholm, P. R. Edgington, P. McCabe, E. Pidcock, L. Rodriguez-Monge, R. Taylor, J. van de Streek, P. A. Wood, *J. Appl. Crystallogr*. **2008**, *41*, 466–470.

7248 reflections; 2673 independent (Rint = 0.0278); R1 = 0.0378 (I > 2σ(I)); and wR2 = 0.1139 (all data); Absolute structure parameter = -0.1(3); max/min residual electron density 0.128/-0.142 e $Å^{-3}$.

6d: Empirical formula: $C_{29}H_{31}NO_7$; crystal system: orthorhombic; space group: $P2_12_12_1$; a = 9.9133(16), b = 10.7889(18), c = 24.981(4) Å; V = 2.671.8(8) $Å^3$; Z = 4; μ = 0.090 mm^{-1}; ρ_{cald} = 1.257 Mg m^{-3}; crystal dimensions (ca.) 0.28 x 0.25 x 0.10 mm^3; 296 K; $2\vartheta_{max}$ = 48.05; 28893 reflections; 4201 independent (Rint = 0.0251); R1 = 0.0382 (I > 2σ(I)); and wR2 = 0.0894 (all data); max/min residual electron density 0.215/-0.139 e $Å^{-3}$.

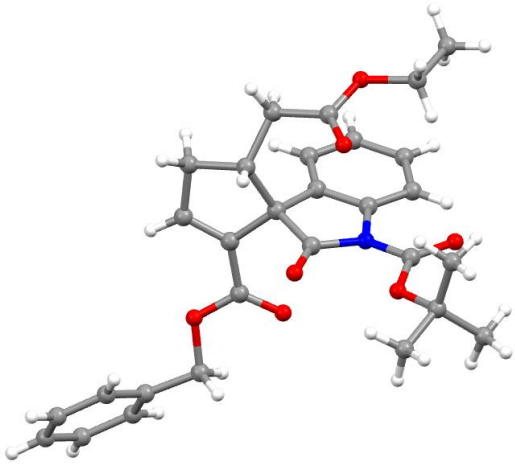


Figure S5.

7c: Empirical formula: $C_{19}H_{22}N_2O_7$; crystal system: monoclinic; space group: $P2_1/c$; a = 21.8507(6), b = 10.6820(3), c = 16.6118(4) Å, β = 100.992(2)°; V = 3806.21(18) $Å^3$; Z = 4; μ = 0.105 mm^{-1}; ρ_{cald} = 1.363 Mg m^{-3}; crystal dimensions (ca.) 0.32 x 0.25 x 0.10 mm^3; 296 K; $2\vartheta_{max}$ = 50.00; 47558 reflections; 6700 independent (Rint = 0.1165); R1 = 0.0754 (I > 2σ(I)); and wR2 = 0.1823 (all data); max/min residual electron density 0.356/-0.306 e $Å^{-3}$.

1D NOESY experiments.

1D NOESY experiments on compounds **3c**, **3u**, **4a**, and **4f** confirm the relative stereochemistry established by X-ray crystallographic analysis on products **3c**, **3u**, **4d**, and **7c**, respectively. The most relevant and diagnostic nOe signals are shown in Figure S6.

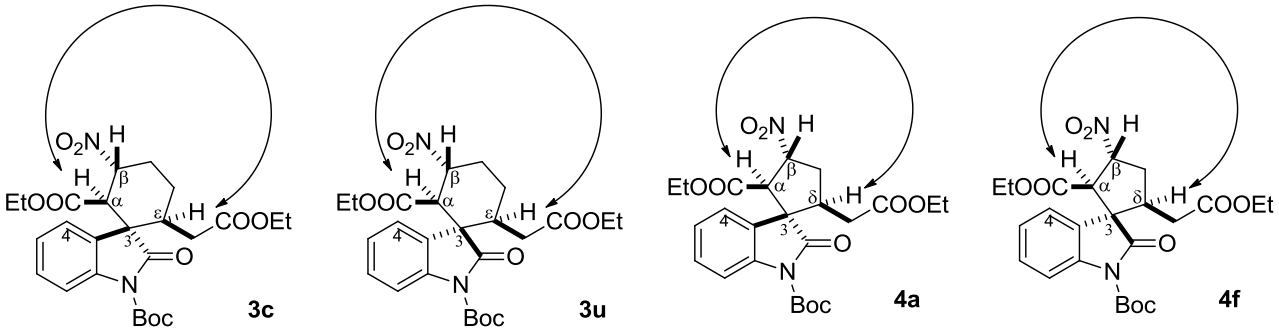


Figure S6.

The presence of a nOe correlation between Hβ and the aromatic proton at C4 allows us to infer the C3-configuration of products **3c** and **4a**. The presence of a nOe correlation between Hα (and Hε or Hδ) and the aromatic proton at C4 allows us to infer the C3-configuration of products **3u** and **4f**.

Identified the diagnostic nOe signals for cyclohexane- and cyclopentane-spirooxindoles, we have performed 1D NOESY experiments on a series of particularly substituted compounds.

1D NOESY experiments on α-methyl derivatives **3n**, **4e** and **4g** allow us to establish the *relative* configuration of the four stereocenters, two of them quaternary centers (Figure S7).

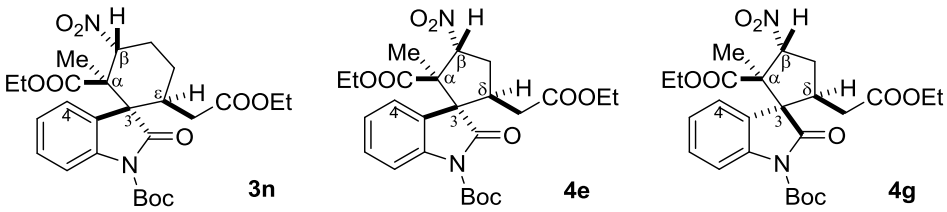


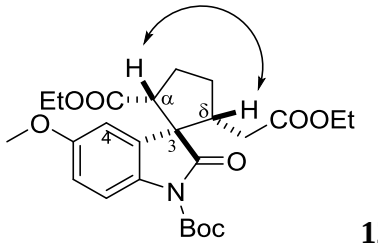
Figure S7.

The nOe correlation between αMe and Hε (or Hδ) is not detectable for compounds **3n** and **4e**, but the presence of a strong nOe signal correlating Hβ and the aromatic proton at C4 allows us to infer the C3-configuration. Moreover, the absence of nOe signals correlating: *i)* αMe (and Hε or Hδ) with the aromatic proton at C4, and *ii)* Hε (or Hδ) with Hβ, suggests the configuration of the Cα and Cε (or Cδ) stereocenters.

The relative stereochemistry of **4g** has been confirmed thanks to: *i)* the presence of nOe signals correlating Hδ with αMe and the aromatic proton at C4, *ii)* the absence of nOe signals correlating Hβ with Hδ and the aromatic proton at C4.

On the basis of the absolute stereochemistry established for compound **4d** (X-ray crystallographic analysis), we propose the *absolute* stereochemistry of compounds **3n**, **4e** and **4g** shown in Figure S7.

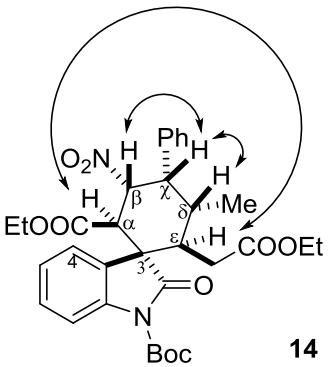
1D NOESY experiments on compound **12** allow us to establish the *relative* configuration of the three stereocenters. The most relevant nOe signal is shown in Figure S8. The absence of a nOe correlation between Hα (or Hδ) and the aromatic proton at C4 allows us to infer the C3-configuration. On the basis of the absolute stereochemistry established for compound **4d** (X-ray crystallographic analysis) and for the couple *ent*-**6a**/**6a** (CSP-HPLC analysis), we propose the *absolute* stereochemistry of compound **12** (Figure S8).



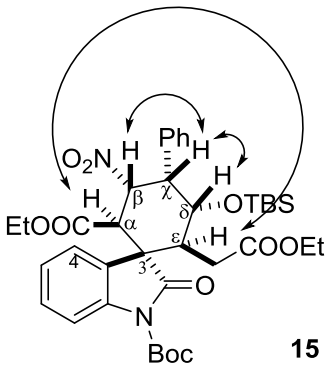
12

Figure S8.

1D NOESY experiments on compounds **14** and **15** allow us to establish the *relative* configuration of the six stereocenters. The most relevant nOe signals are shown in Figure S9. The presence of a nOe correlation between Hβ (and Hδ) and the aromatic proton at C4 allows us to infer the C3-configuration. On the basis of the absolute stereochemistry established for compound **4d** (X-ray crystallographic analysis), we propose the *absolute* stereochemistry of compounds **14** and **15** shown in Figure S9.



14



15

Figure S9.

To further confirm the reliability of the results obtained by 1D NOESY experiments on product **14**, we have subjected also **14'** and **14''** (diastereoisomers of spiroindolinone **14**) to 1D NOESY experiments, which allow us to establish the *relative* configuration of the six stereocenters. The most relevant nOe signals are shown in Figure S10. The presence of a nOe correlation between Hβ (and Hδ) and the aromatic proton at C4 in **14'**, and between Hα (and Hδ) and the aromatic proton at C4 in **14''**, allows us to infer the C3-configuration. On the basis of the absolute stereochemistry established for compound **4d** (X-ray crystallographic analysis), we propose the *absolute* stereochemistry of compounds **14'** and **14''** shown in Figure S10.

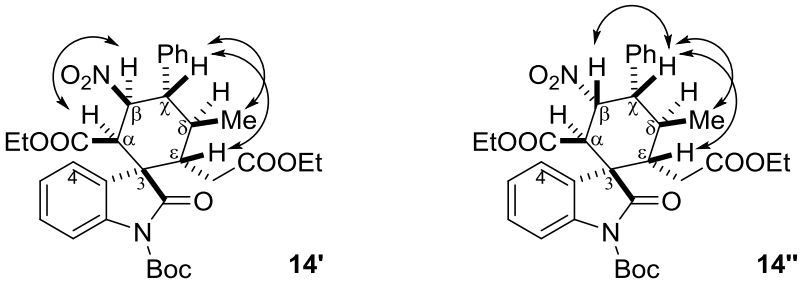


Figure S10.

The relative stereochemistry established for products **14**, **14'**, **14''** and **15** allows us to make some comments on the use of chiral nitroenoates **2g** and **2h** in the developed Michael-Michael organocascade reaction:

- *anti* nitro compounds (*anti*-**2g** and **2h**) provide the corresponding spirooxindoles (**14** and **15**) with high diastereoselectivity. Conversely, *syn*-**2g** affords a couple of Cβ-epimers, suggesting that the different Cδ configuration enables the cyclization of both the Cβ-configured acyclic intermediates;
- as previously mentioned for the synthesis of spiroindolinones **3** and **4**, (*E*)-nitroenoates invariably provide spirooxindoles with a C3,Cε-*trans* relationship, even if *anti*-**2g** and *syn*-**2g** yield products with opposite C3 and Cε configurations.

To investigate the cascade reaction mechanism, we isolated and characterized the racemic spirocyclohexane oxindole **19** (Figure S11), diastereoisomer of compound **3c**. 1D NOESY experiments on compound **19** allow us to establish the *relative* configuration of the four stereocenters. The most relevant nOe signal is shown in Figure S11. The presence of a nOe correlation between Hε and the aromatic proton at C4 allows us to infer the C3-configuration.

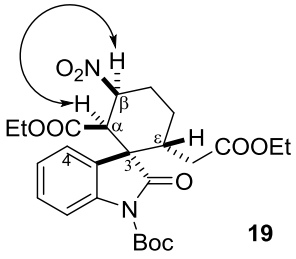
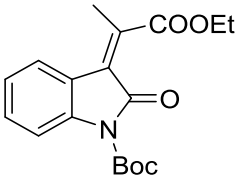
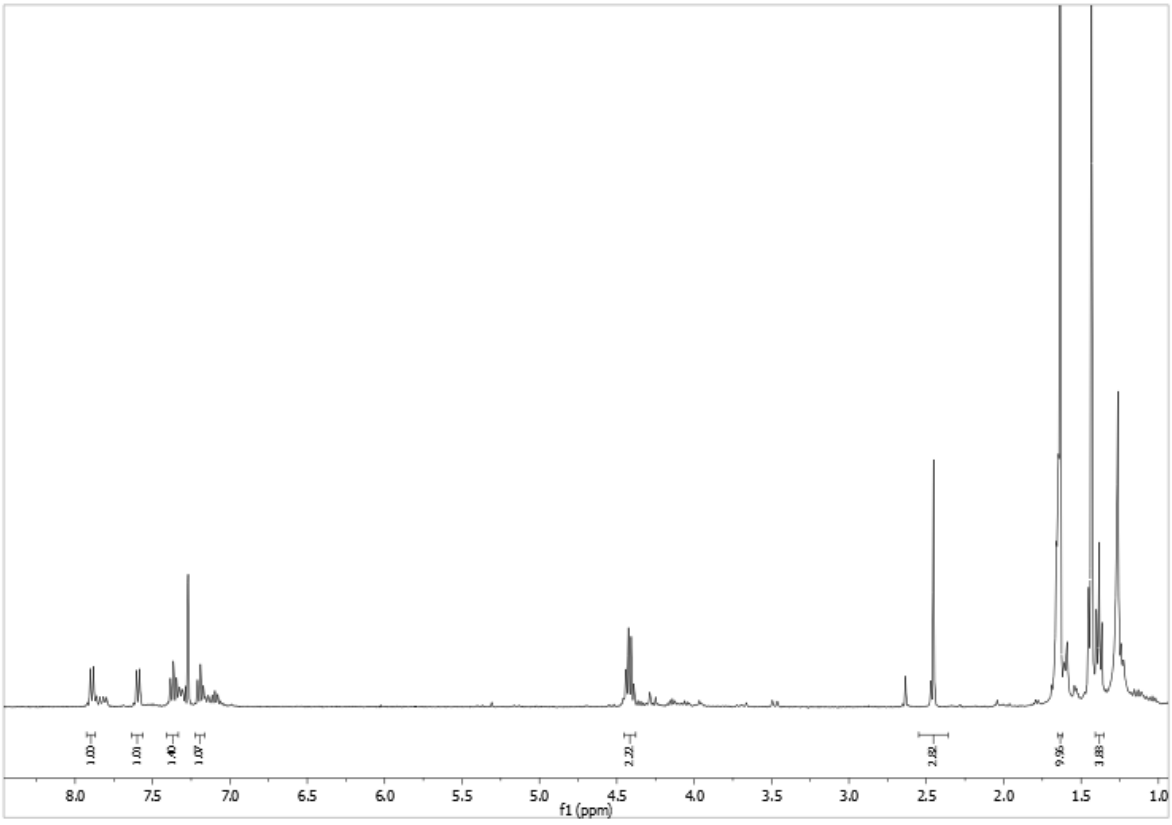


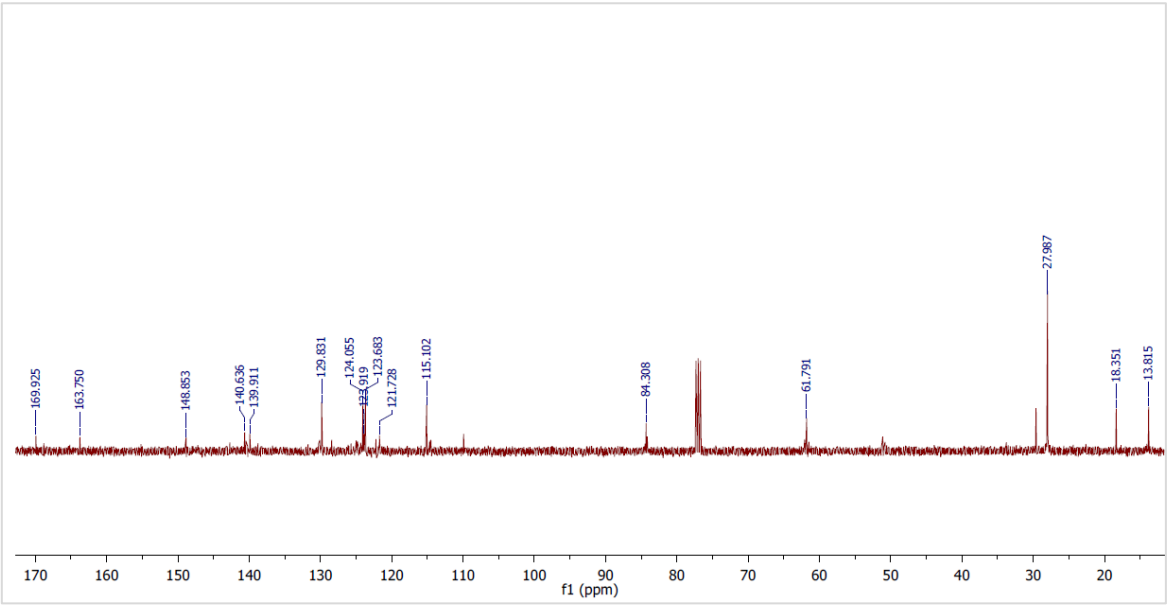
Figure S11.

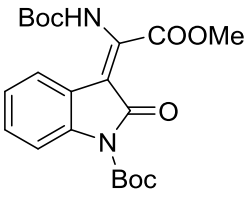
I. NMR Spectra.



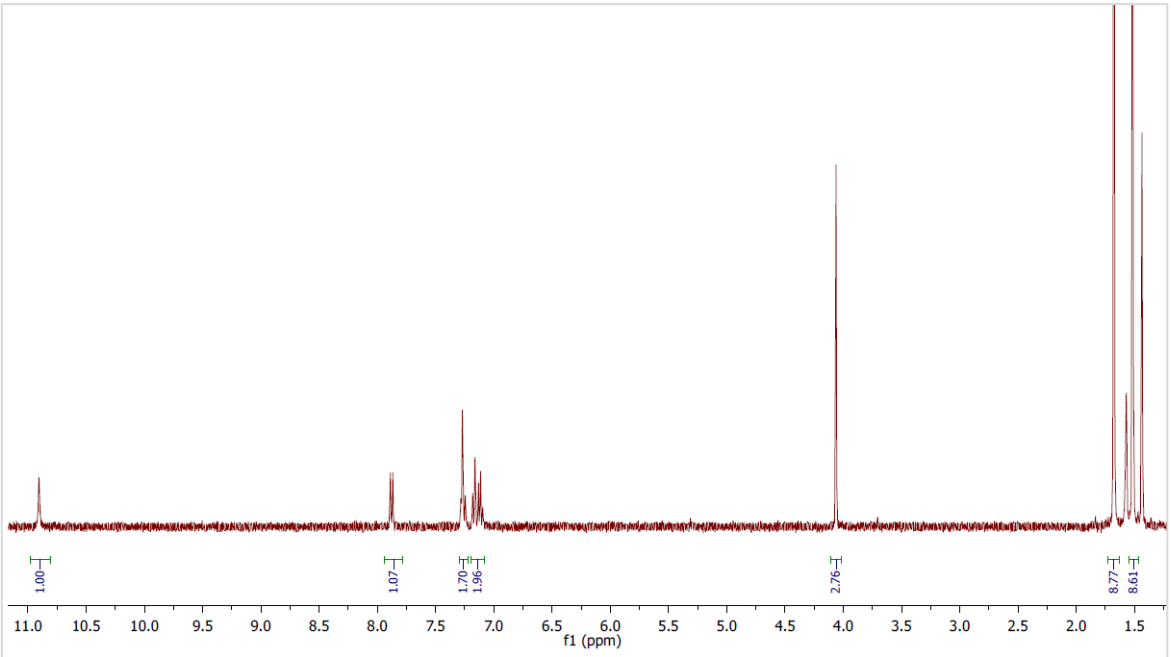
1o

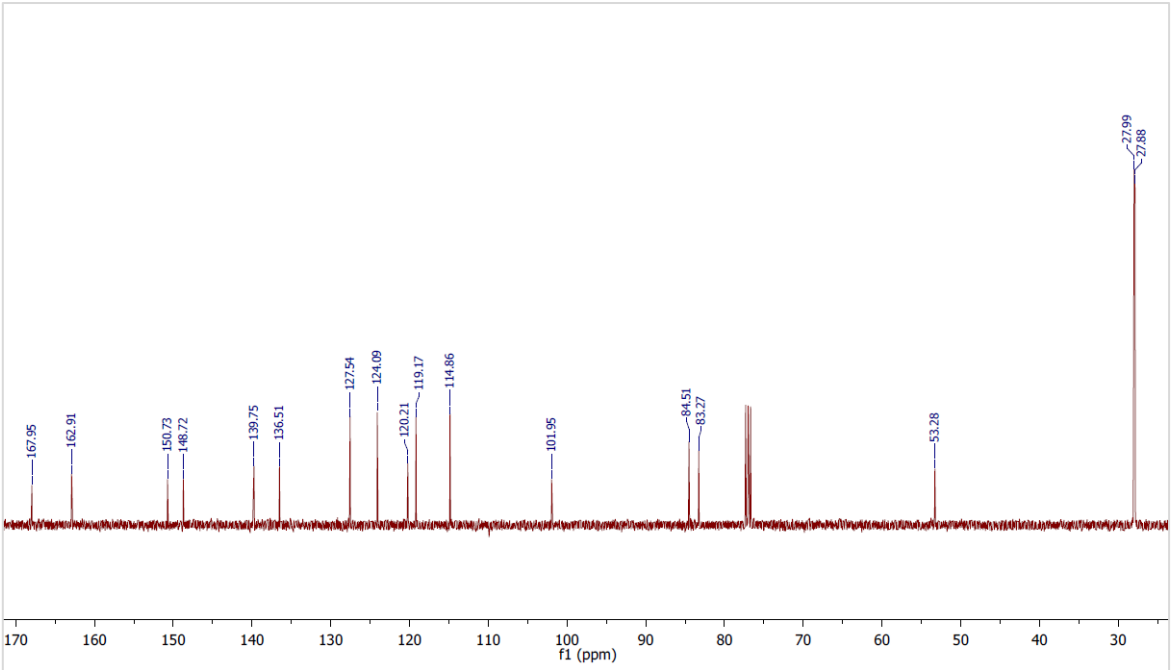





BocHN
COOMe
O
N
Boc

1p


1.00
1.07
1.70
1.96
2.76
8.77
8.61
11.0 10.5 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
f1 (ppm)


167.95
162.91
150.73
148.72
139.75
136.51
127.54
124.09
120.21
119.17
114.86
101.95
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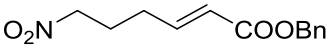
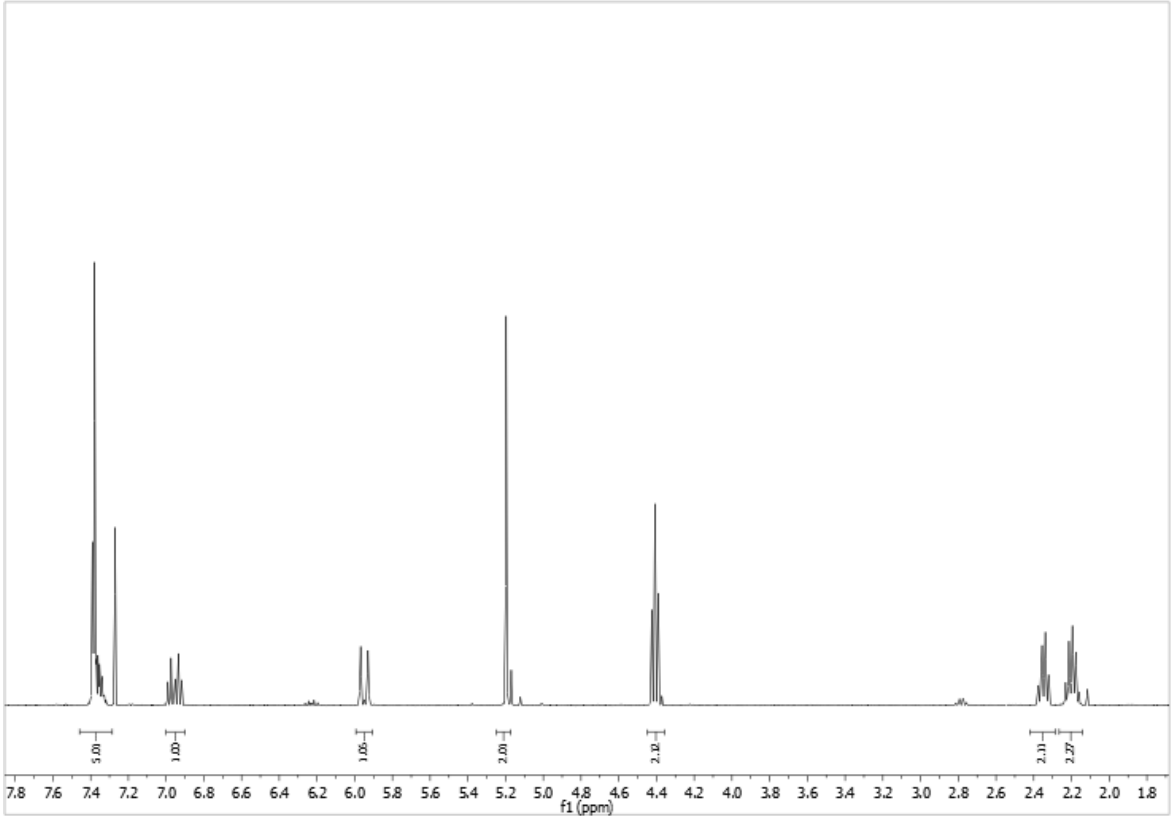
53.28
27.99
27.88
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30
f1 (ppm)


O2N
COOBn

(*E*)-**2b**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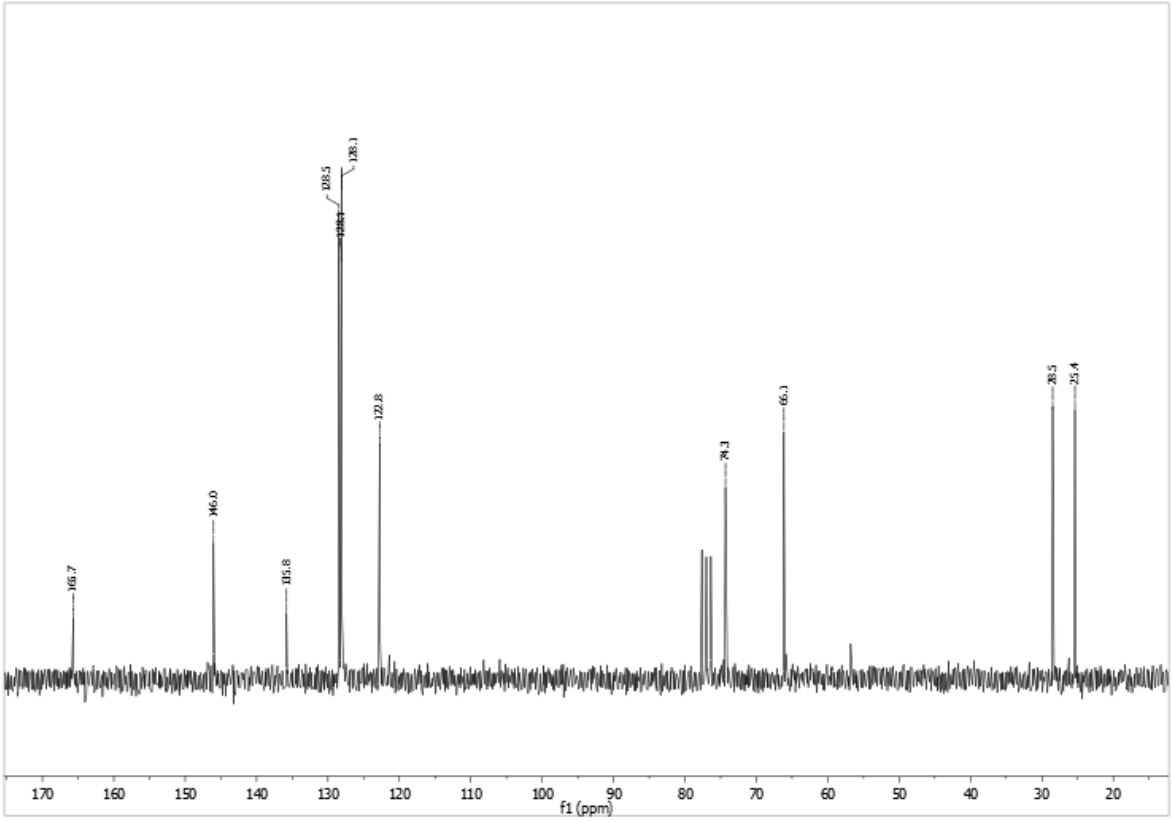
1.00
1.05
2.00
2.10
2.11
2.27
7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8
f1 (ppm)


166.7
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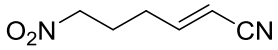
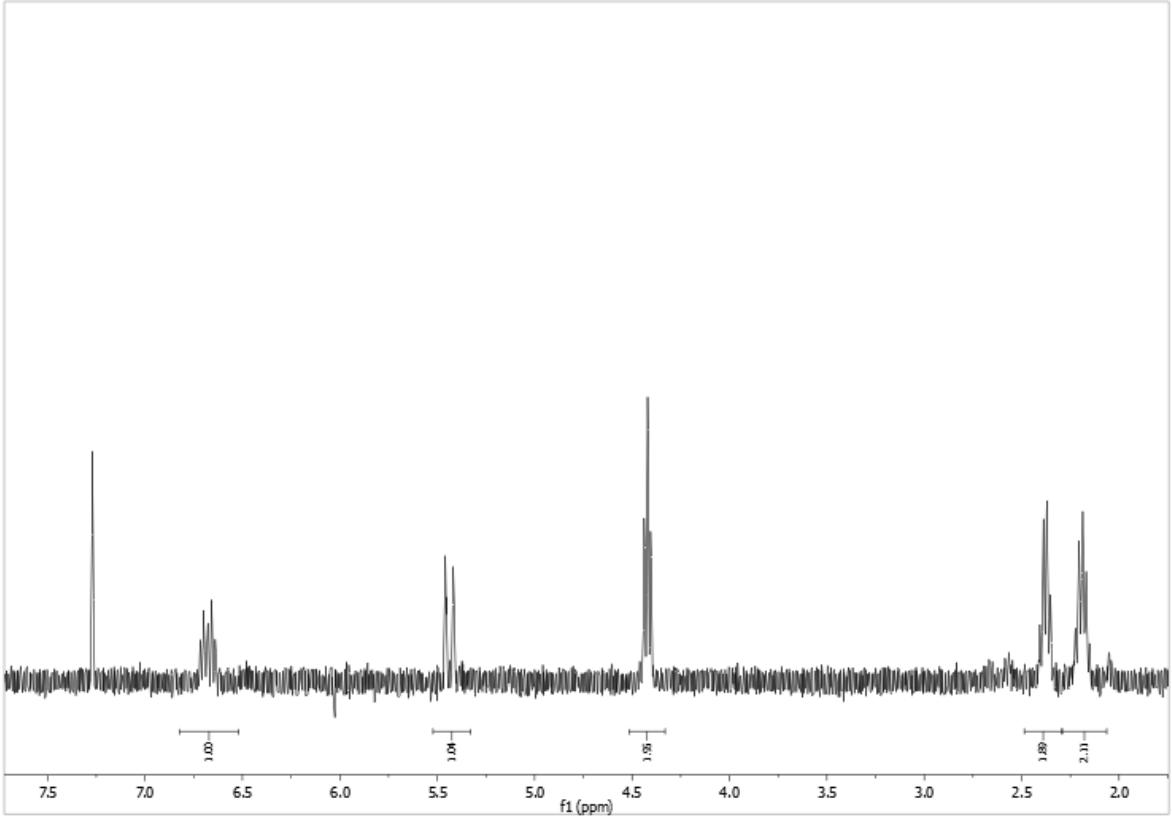
135.8
129.5
128.1
122.8
74.3
66.1
28.5
25.4
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)



(*E*)-**2d**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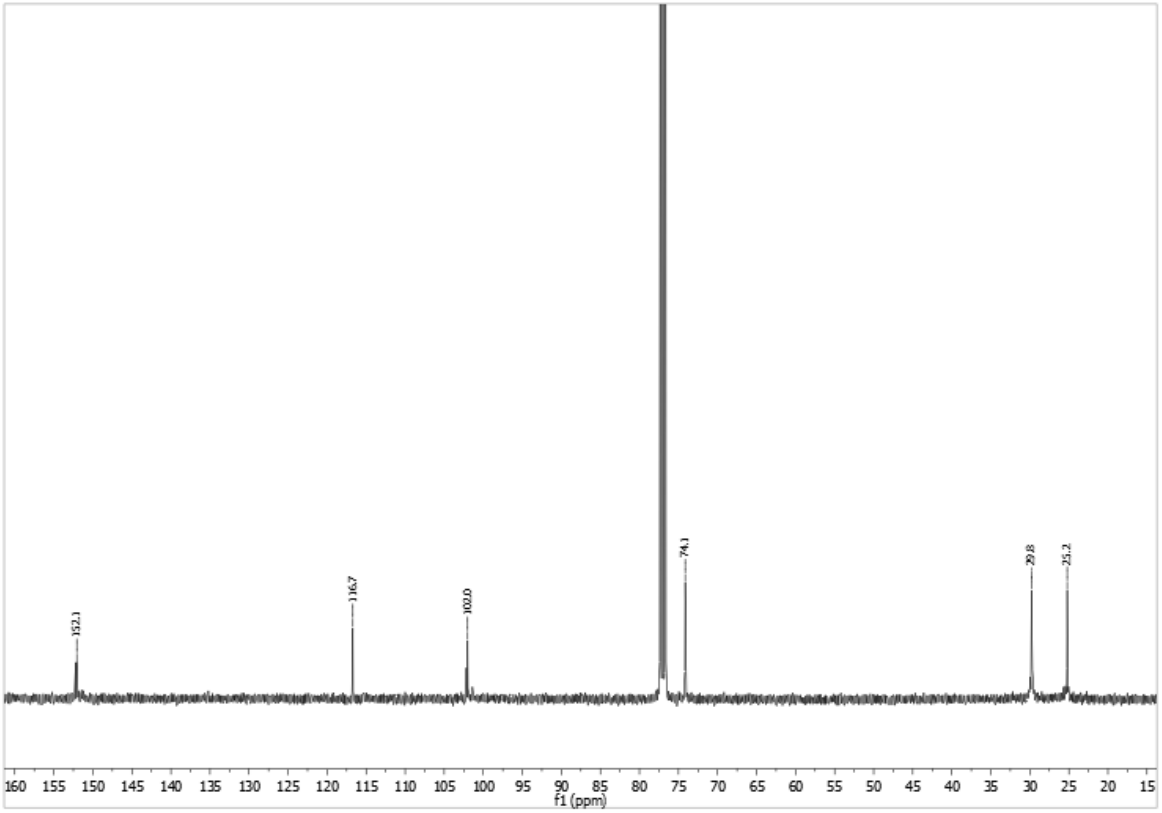
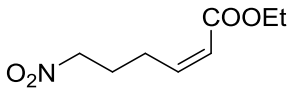
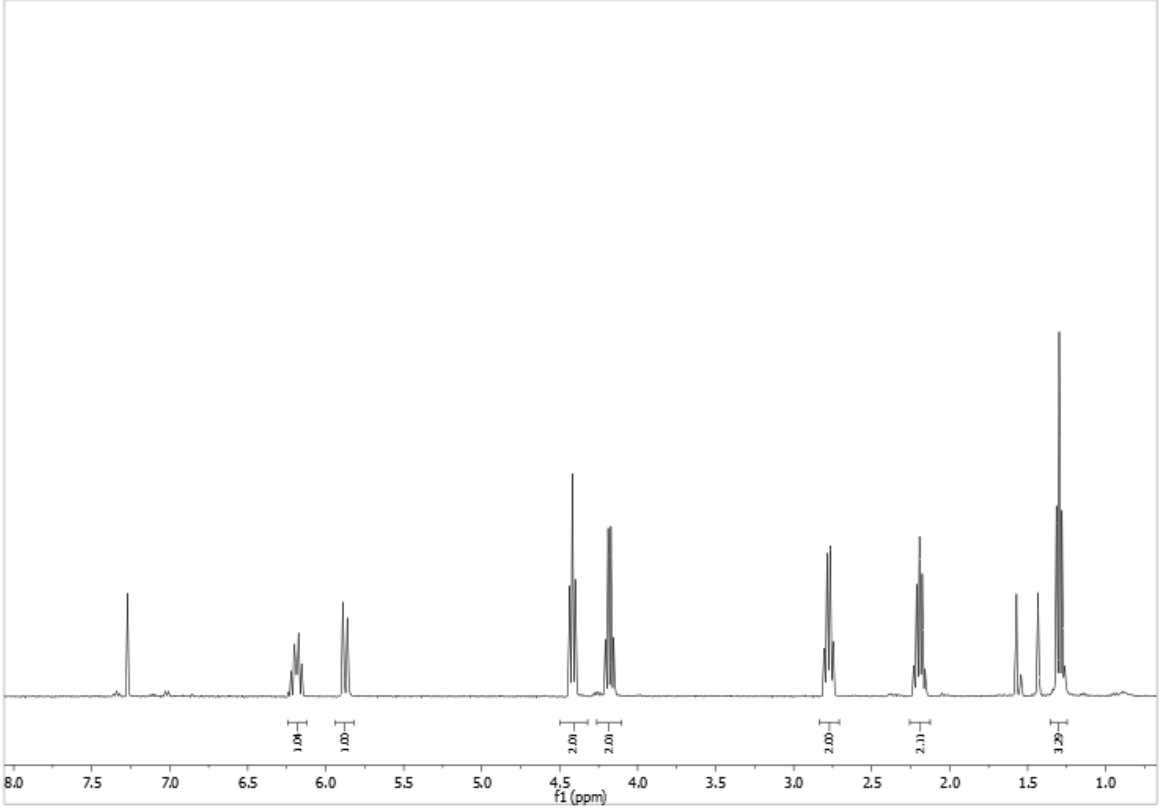
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
f1 (ppm)


152.1
116.7
102.0
74.1
29.8
25.2
160
155
150
145
140
135
130
125
120
115
110
105
100
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
f1 (ppm)


COOEt
O2N

(*Z*)-**2a**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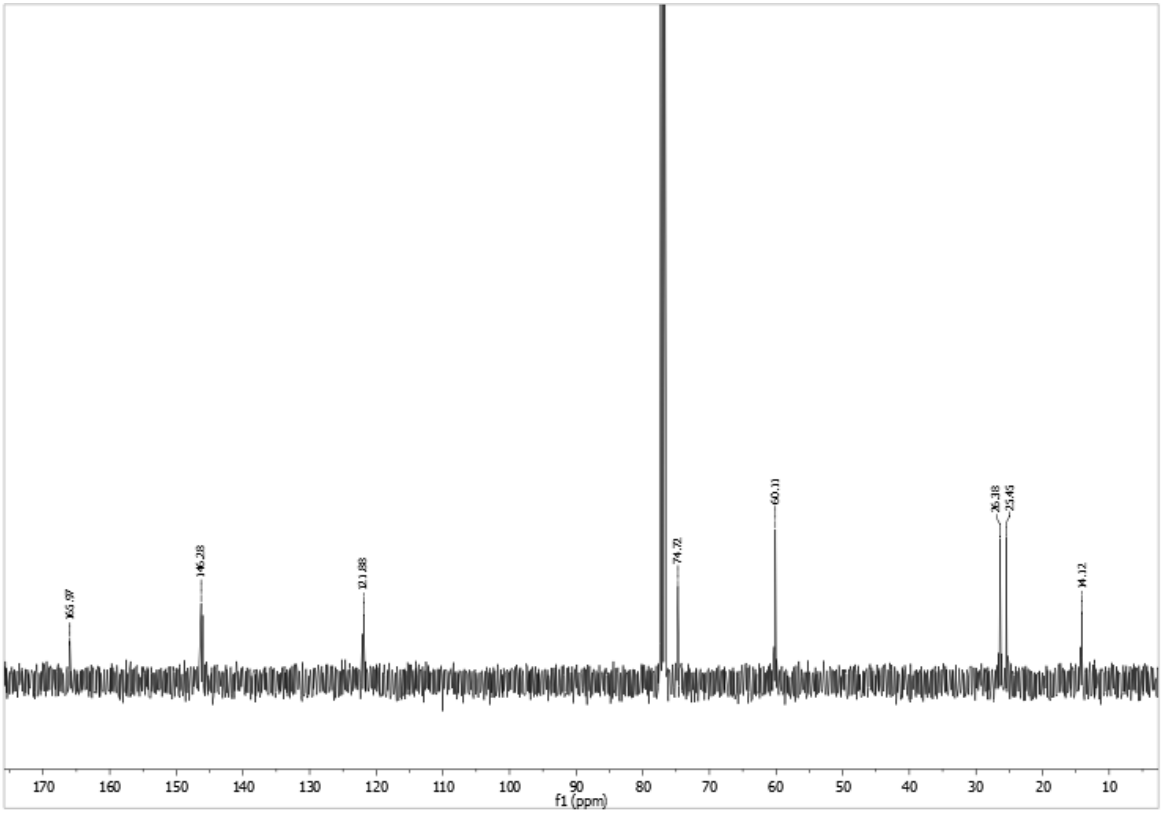
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)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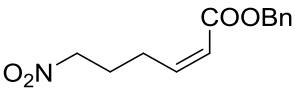
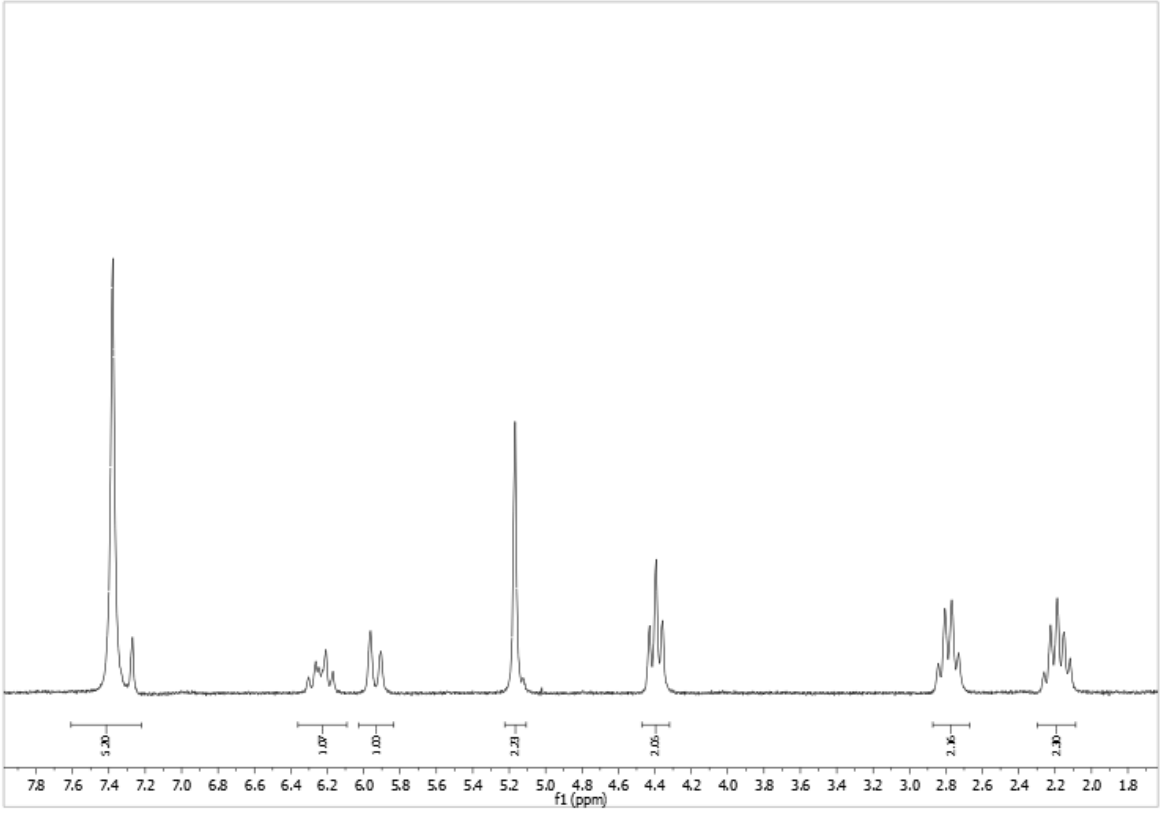
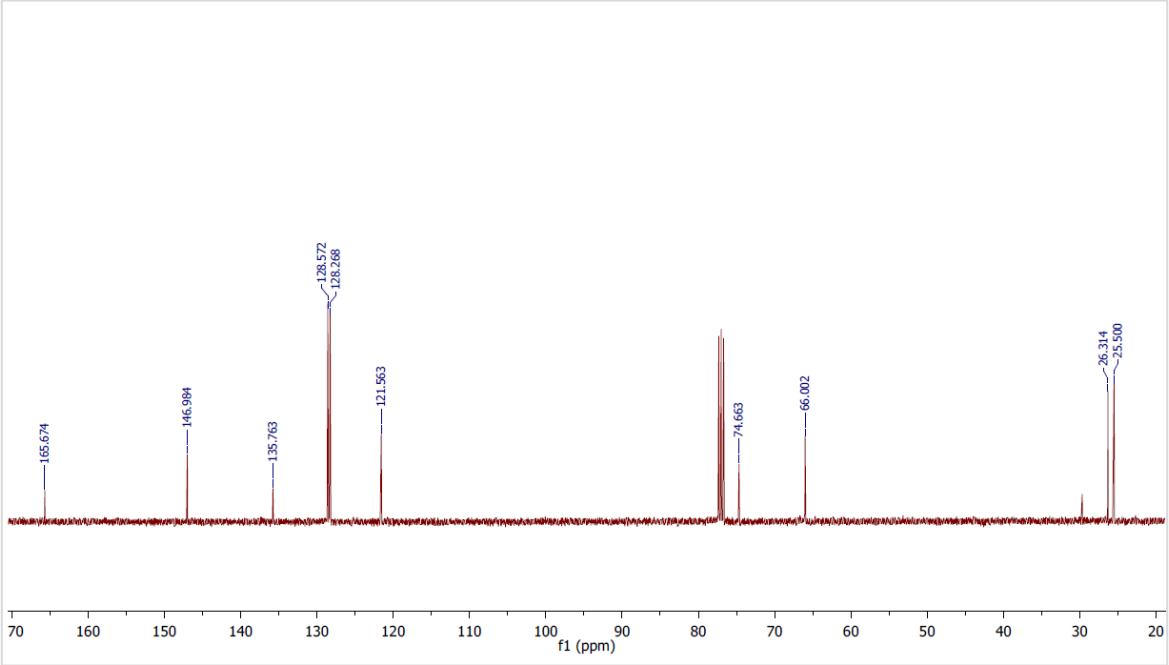
146.218
121.188
74.72
60.31
36.318
25.45
14.12
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


COOBn
O_2N

(*Z*)-**2b**


5.00
1.07
1.03
2.23
2.06
2.16
2.00
7.8 7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8
f1 (ppm)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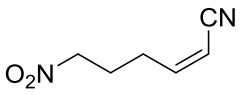
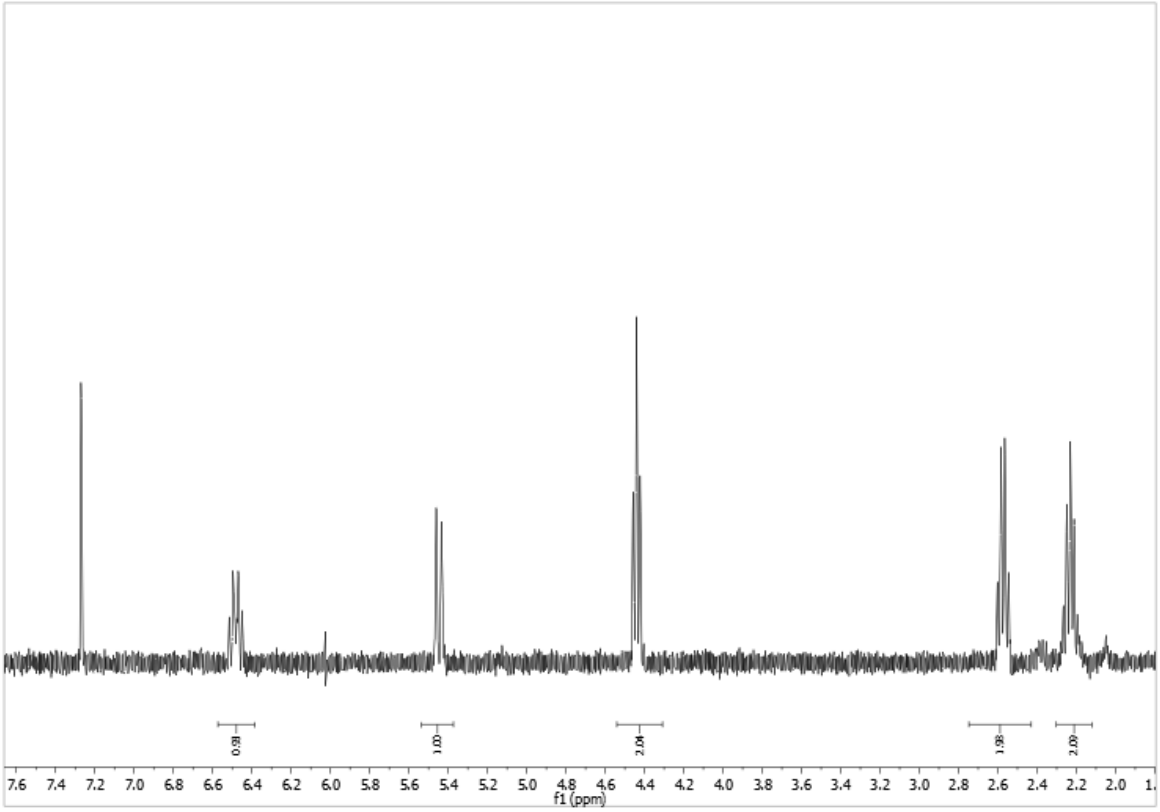
146.984
135.763
128.572
128.268
121.563
74.663
66.002
26.314
25.500
70 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20
f1 (ppm)



(*Z*)-**2d**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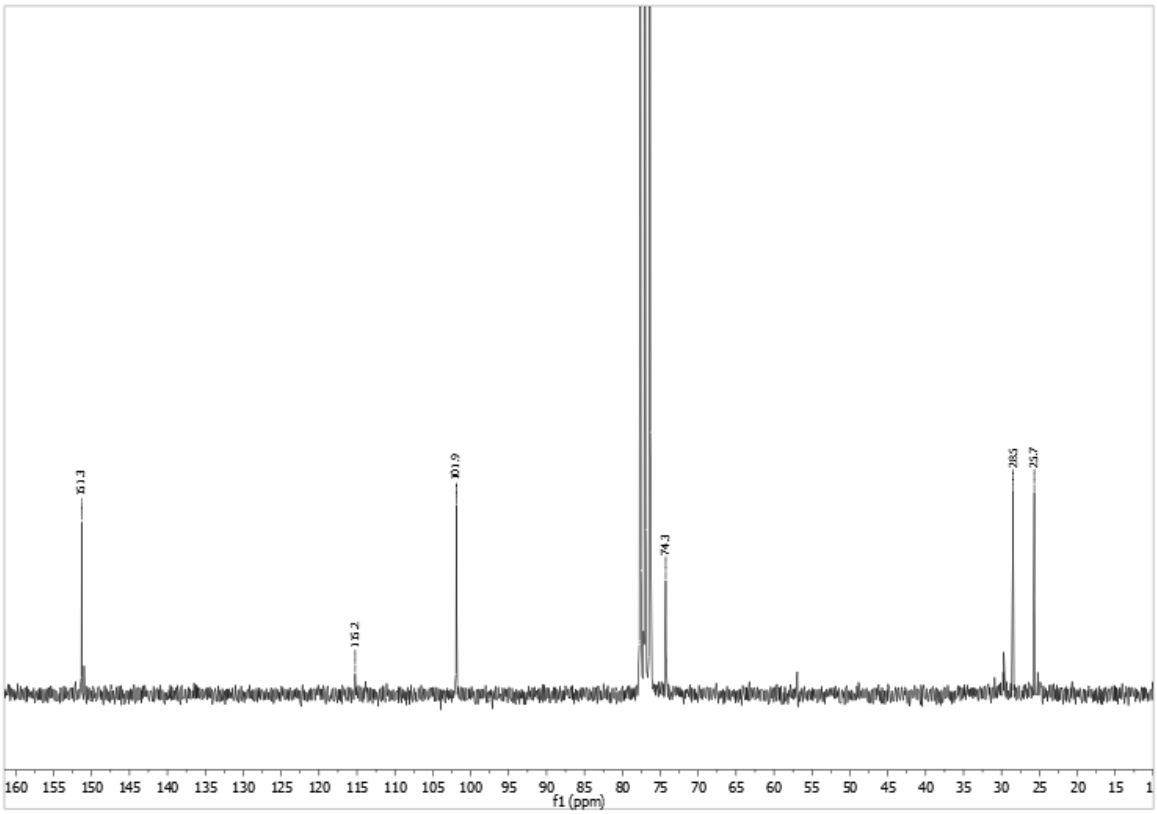
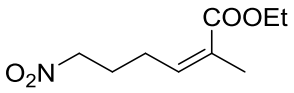
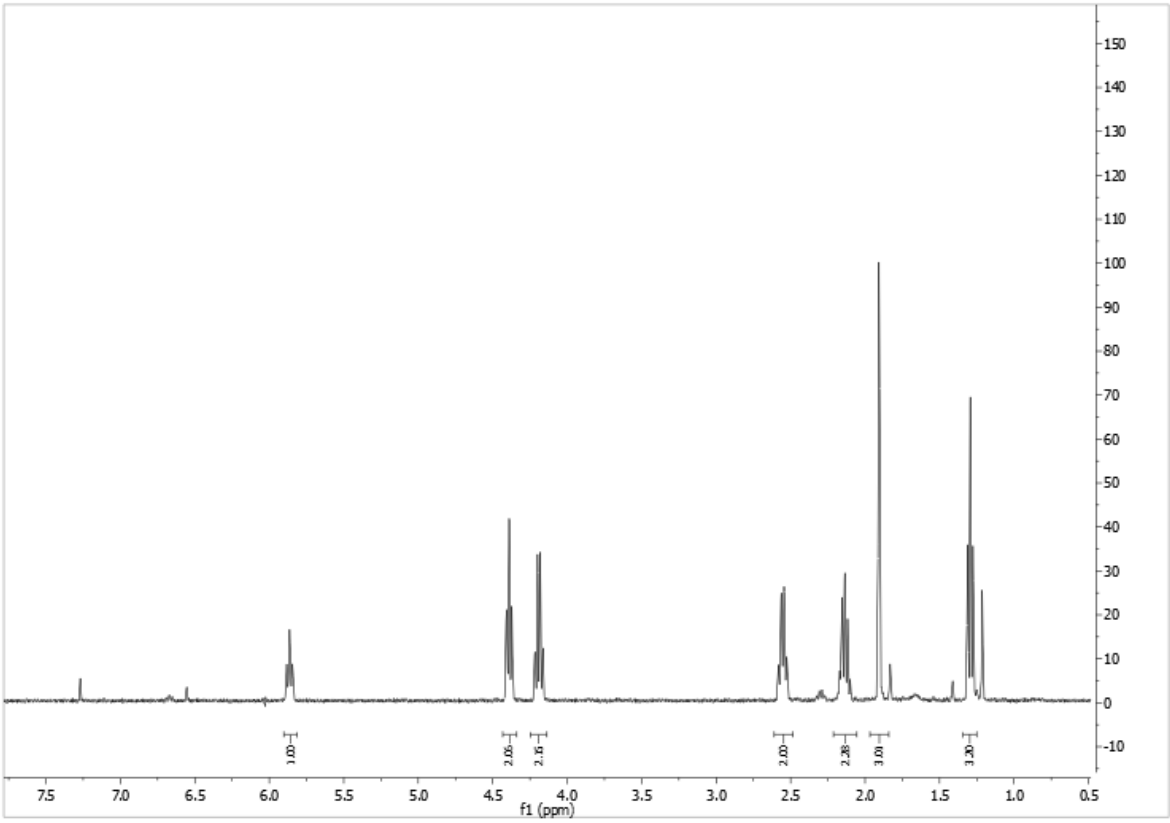
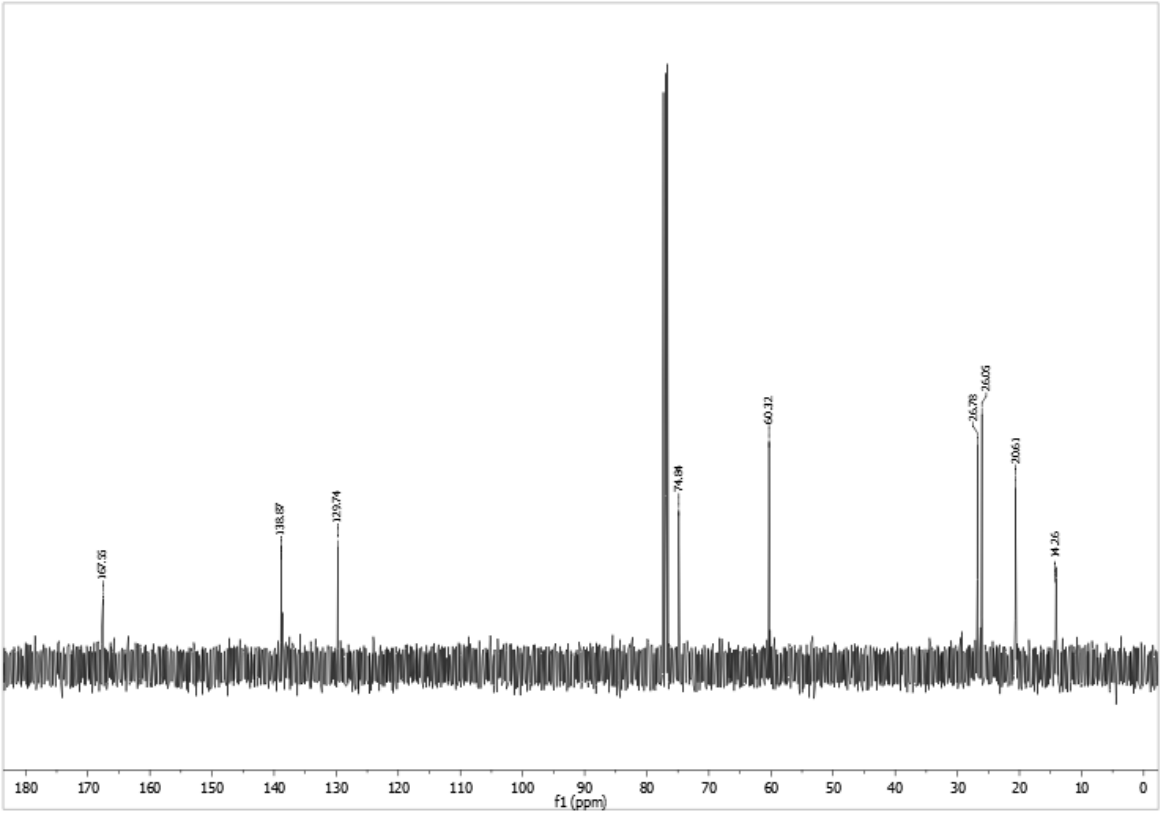
2.04
1.98
2.09
7.6 7.4 7.2 7.0 6.8 6.6 6.4 6.2 6.0 5.8 5.6 5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0
f1 (ppm)

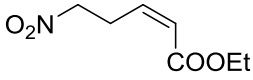

151.3
116.2
101.9
74.3
28.5
25.7
160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15
f1 (ppm)


COOEt
O2N

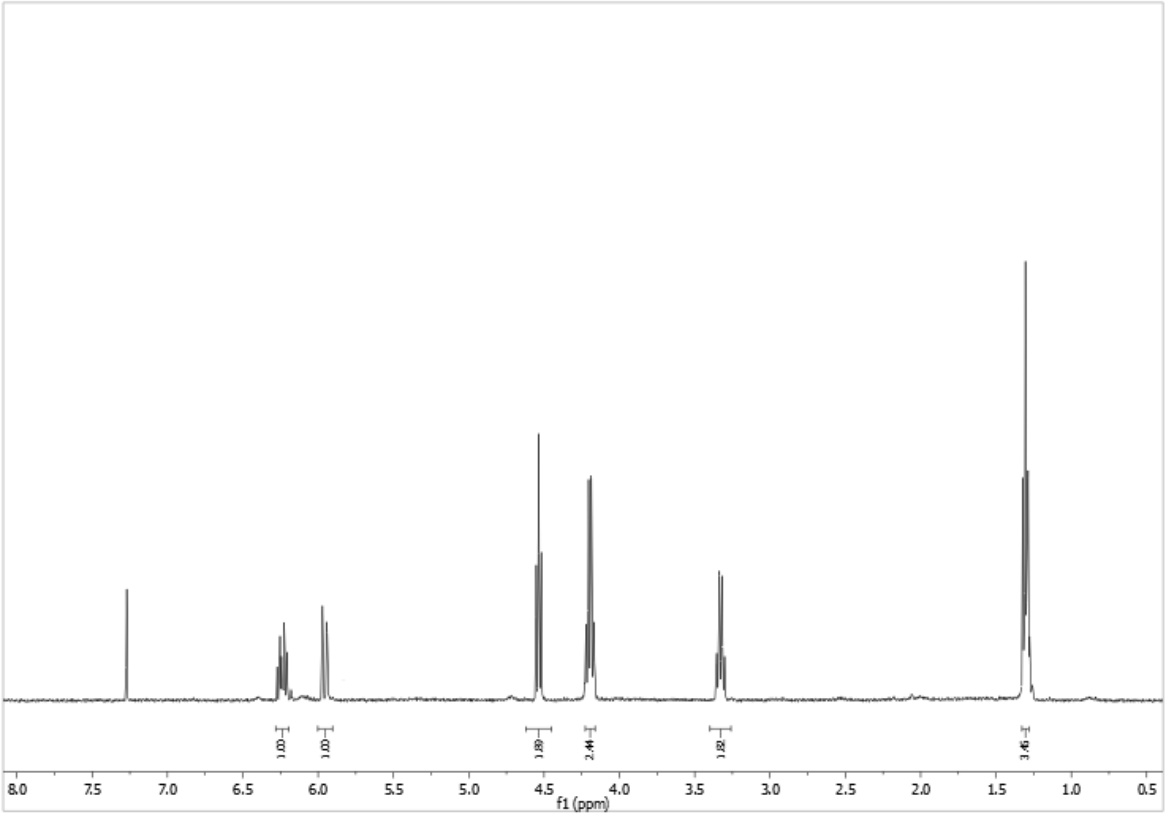
(*Z*)-**2e**


f1 (ppm)


167.55
138.87
129.74
74.84
60.32
26.78
26.05
20.61
14.26
f1 (ppm)


O2N
COOEt

(*Z*)-**2f**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7.5
7.0
6.5
6.0
5.5
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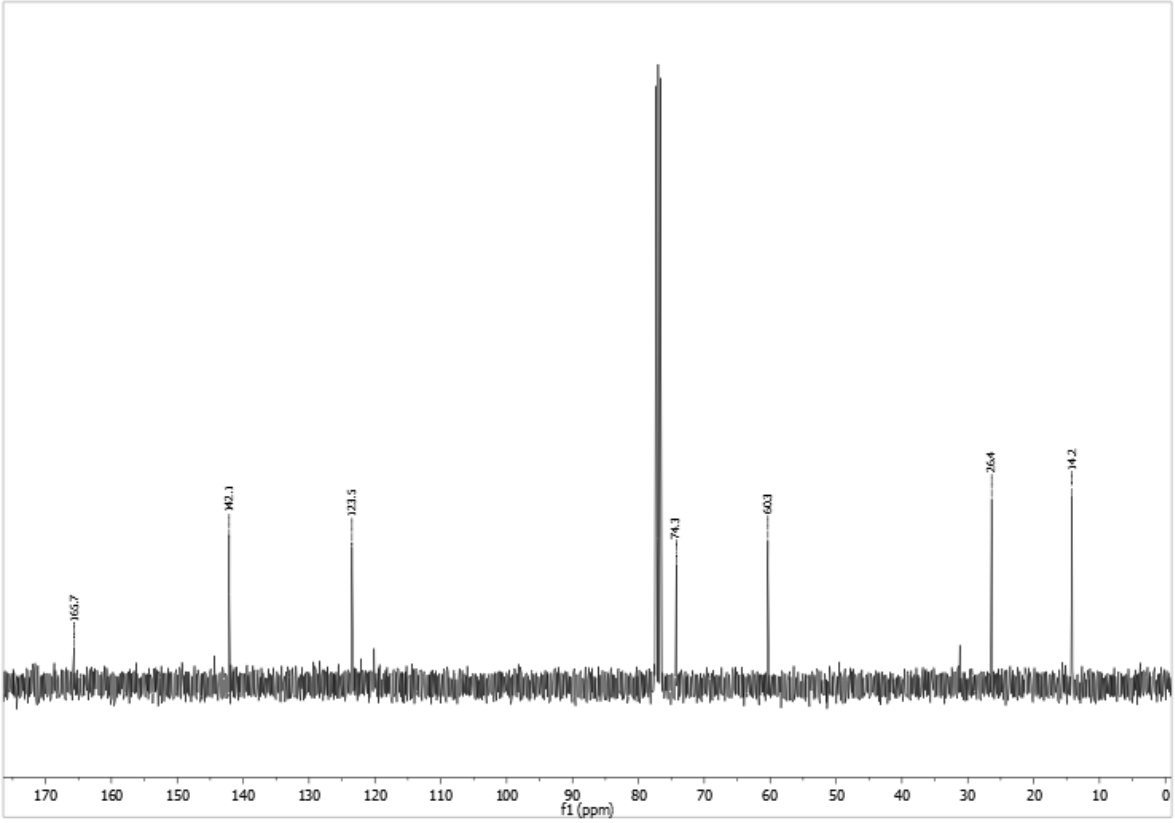
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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142.1
123.5
74.3
60.3
26.4
14.2
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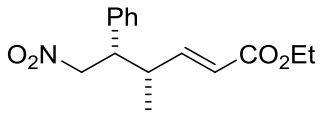
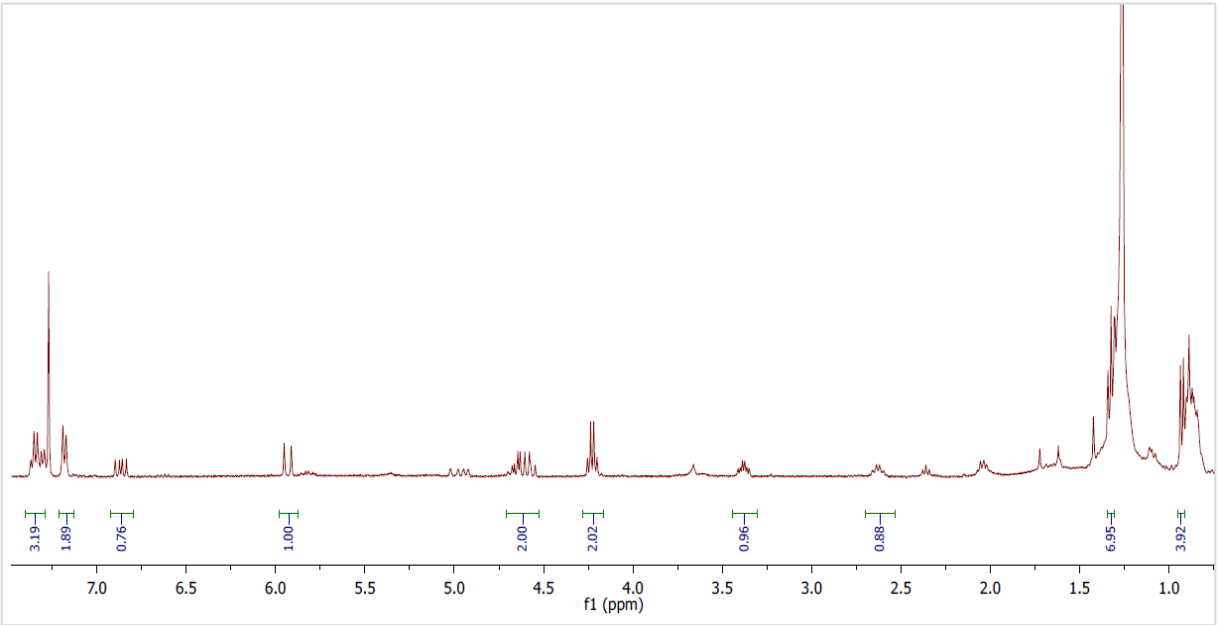
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Ph
O2N
CO2Et

syn-**2g**


3.19
1.89
0.76
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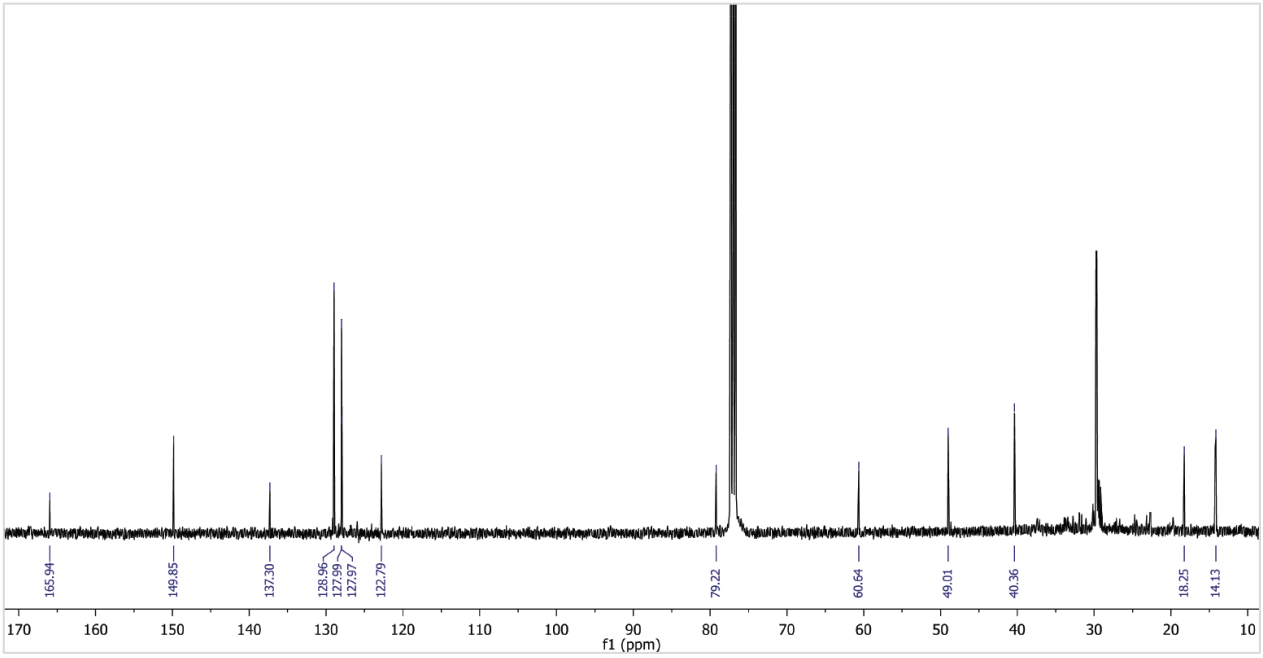
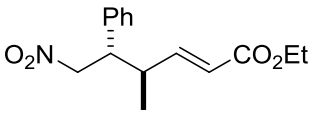
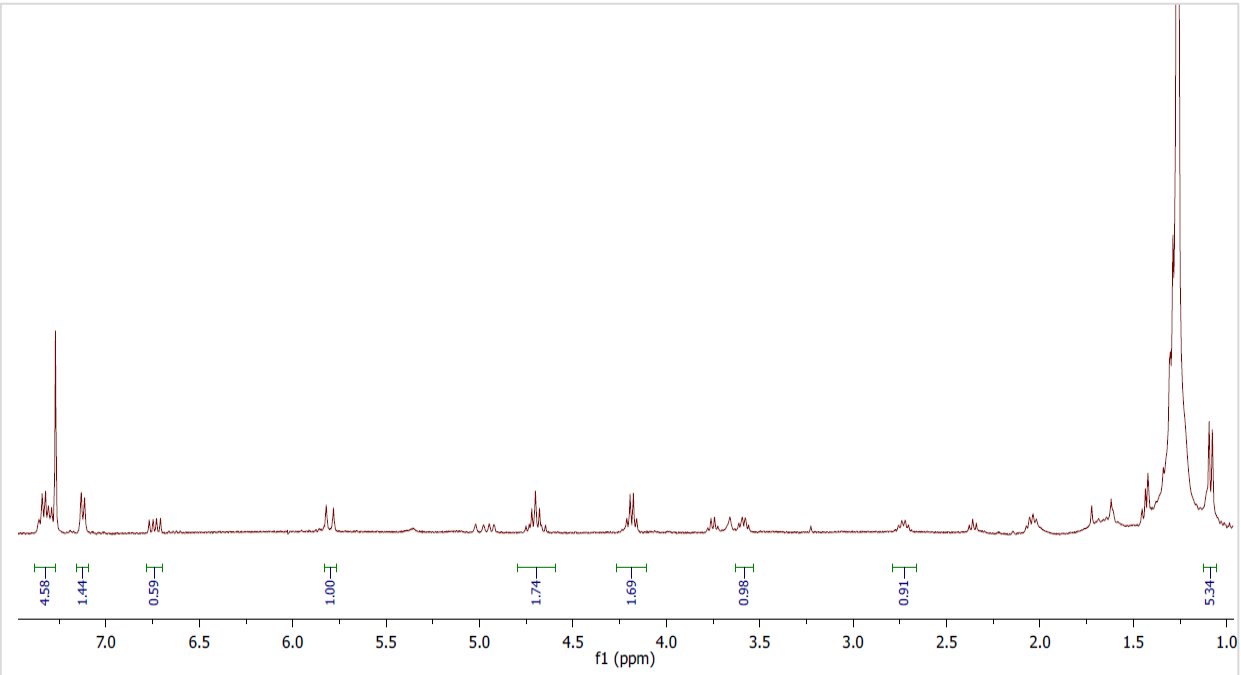
2.00
2.02
0.96
0.88
6.95
3.92
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)


165.94
149.85
137.30
128.96
127.99
127.97
122.79
79.22
60.64
49.01
40.36
18.25
14.13
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


Ph
O2N
CO2Et

anti-**2g**


4.58
1.44
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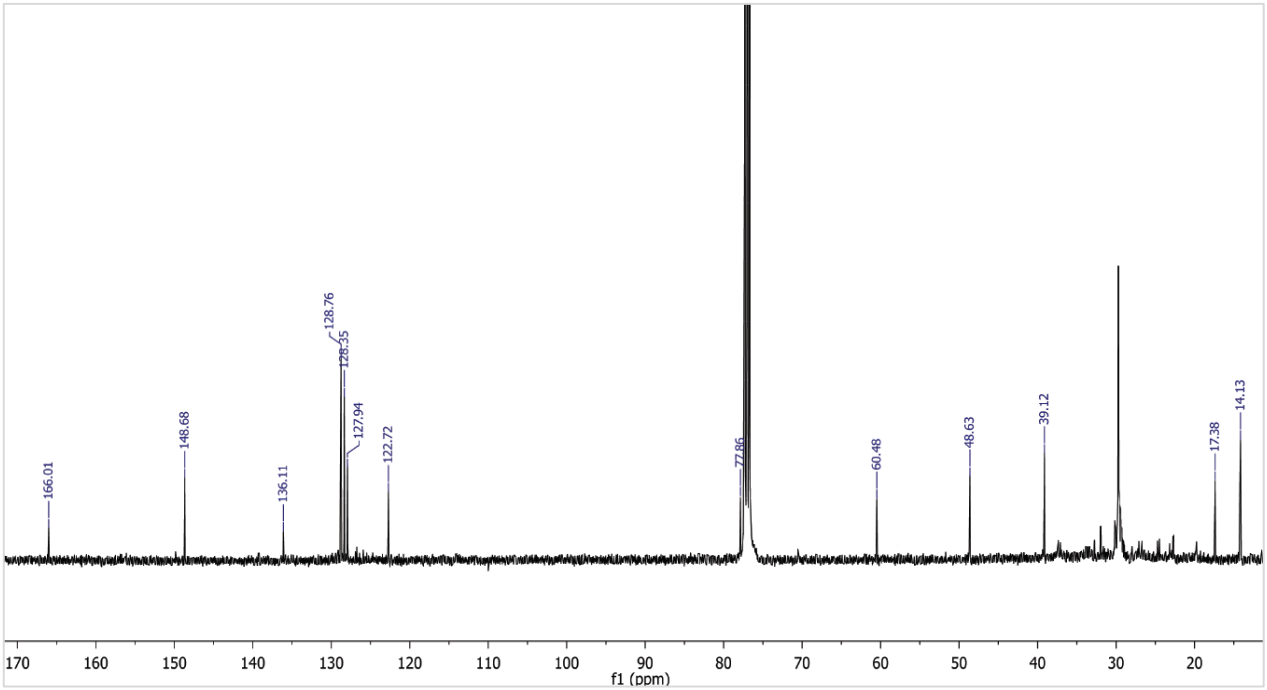
1.00
1.74
1.69
0.98
0.91
5.34
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)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148.68
136.11
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128.55
127.94
122.72
77.86
60.48
48.63
39.12
17.38
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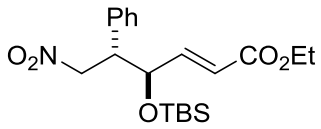
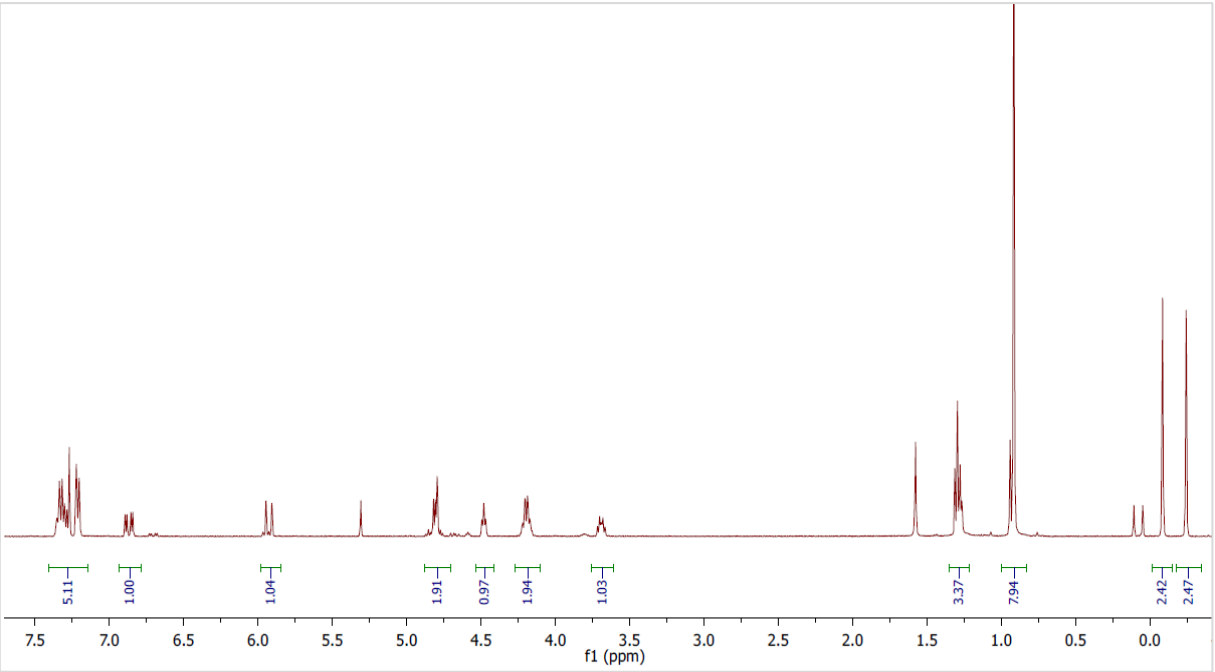
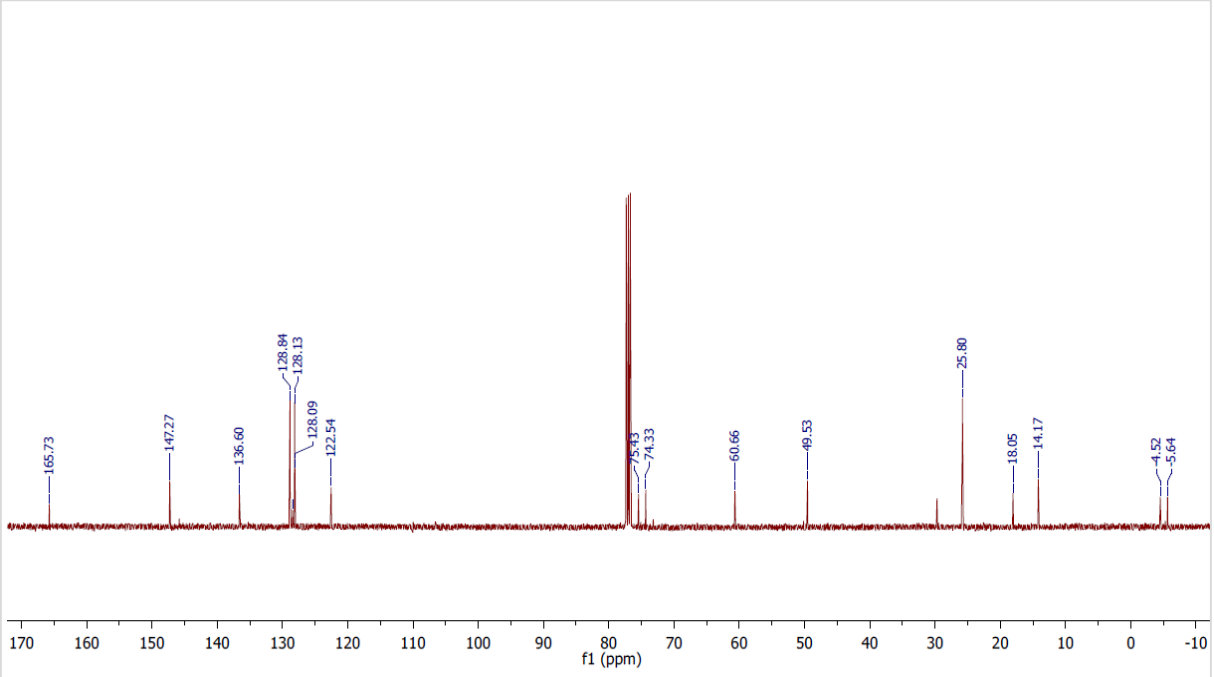
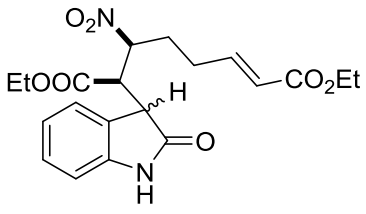
80
70
60
50
40
30
20
f1 (ppm)


Ph
O2N
CO2Et
OTBS

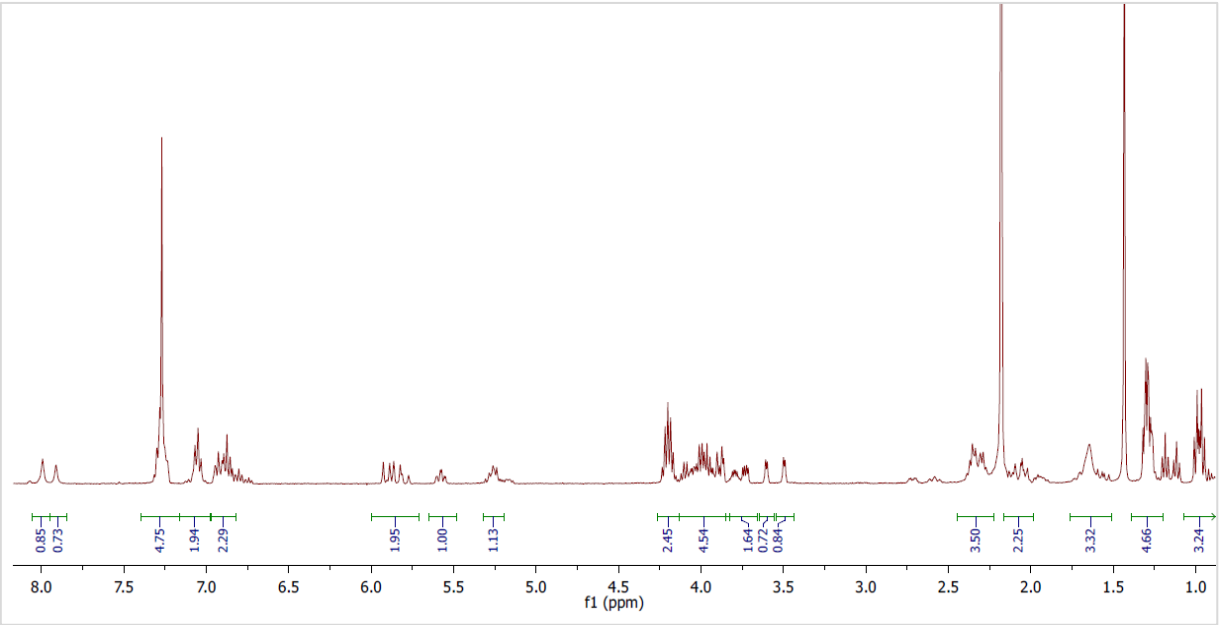
2h

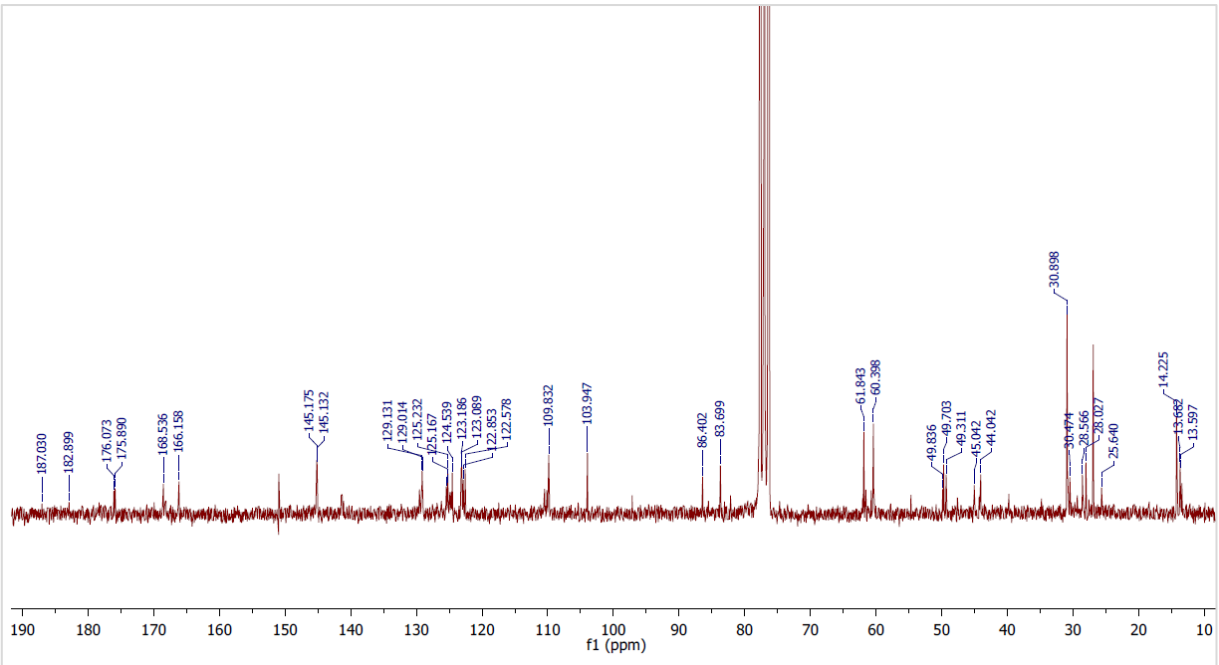

5.11
1.00
1.04
1.91
0.97
1.94
1.03
3.37
7.94
2.42
2.47
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

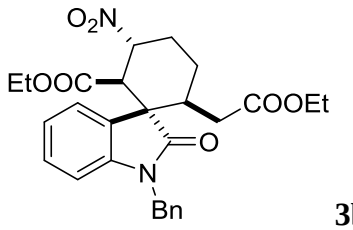

165.73
147.27
136.60
128.84
128.13
128.09
122.54
75.43
74.33
60.66
49.53
25.80
18.05
14.17
-4.52
-5.64
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


O2N
EtOOC
H
CO2Et
O
N
H

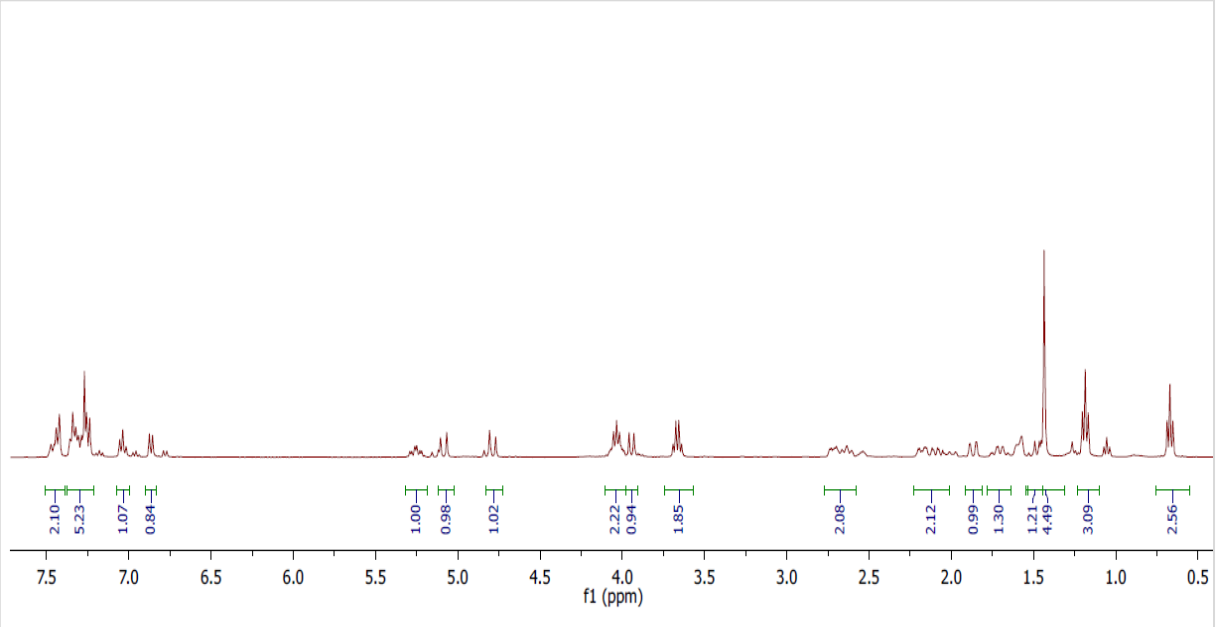
5a

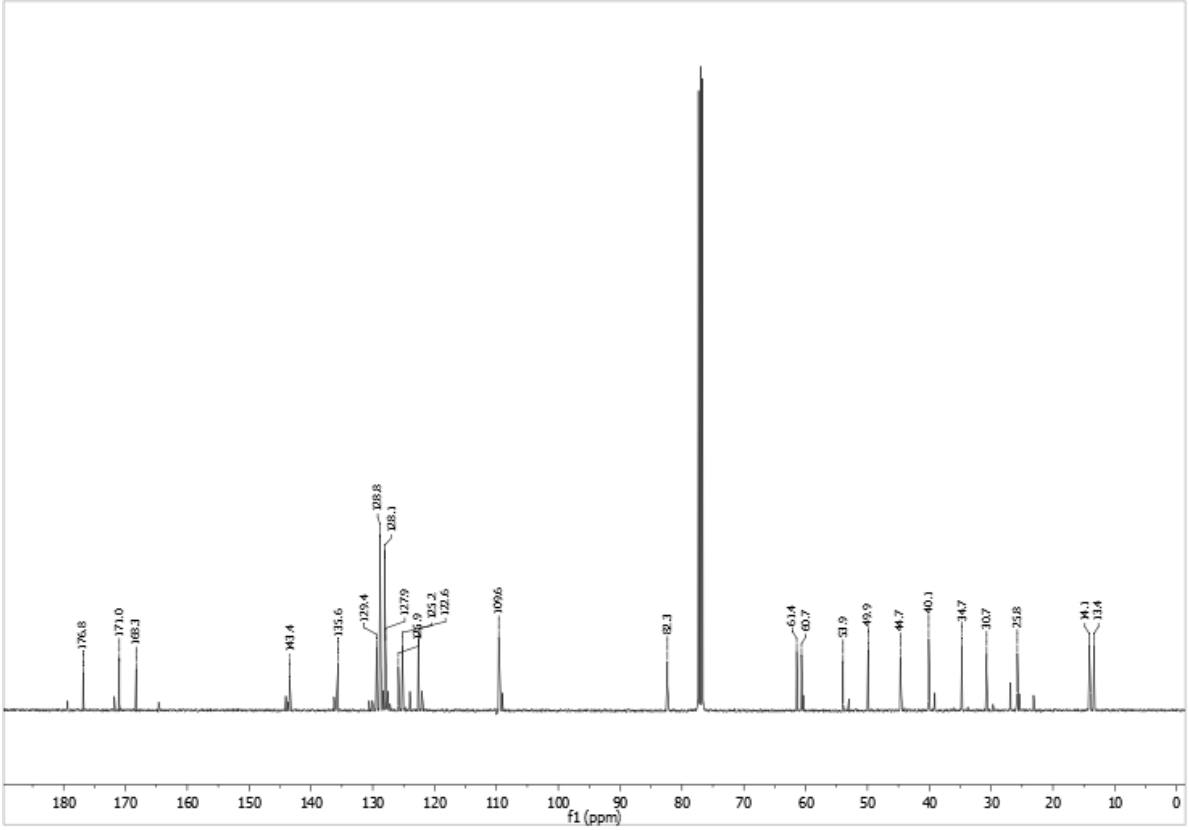

0.85
0.73
4.75
1.94
2.29
1.95
1.00
1.13
2.45
4.54
1.64
0.72
0.84
3.50
2.25
3.32
4.66
3.24
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

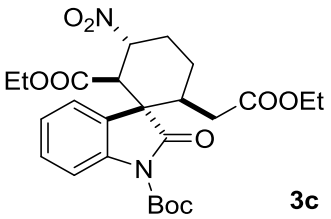

187.030
182.899
176.073
175.890
168.536
166.158
145.175
145.132
129.131
129.014
125.232
125.167
124.539
123.186
123.089
122.853
122.578
109.832
103.947
86.402
83.699
61.843
60.398
49.836
49.703
49.311
45.042
44.042
30.898
30.474
28.566
28.027
25.640
14.225
13.662
13.597
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
COOEt
O
N
Bn

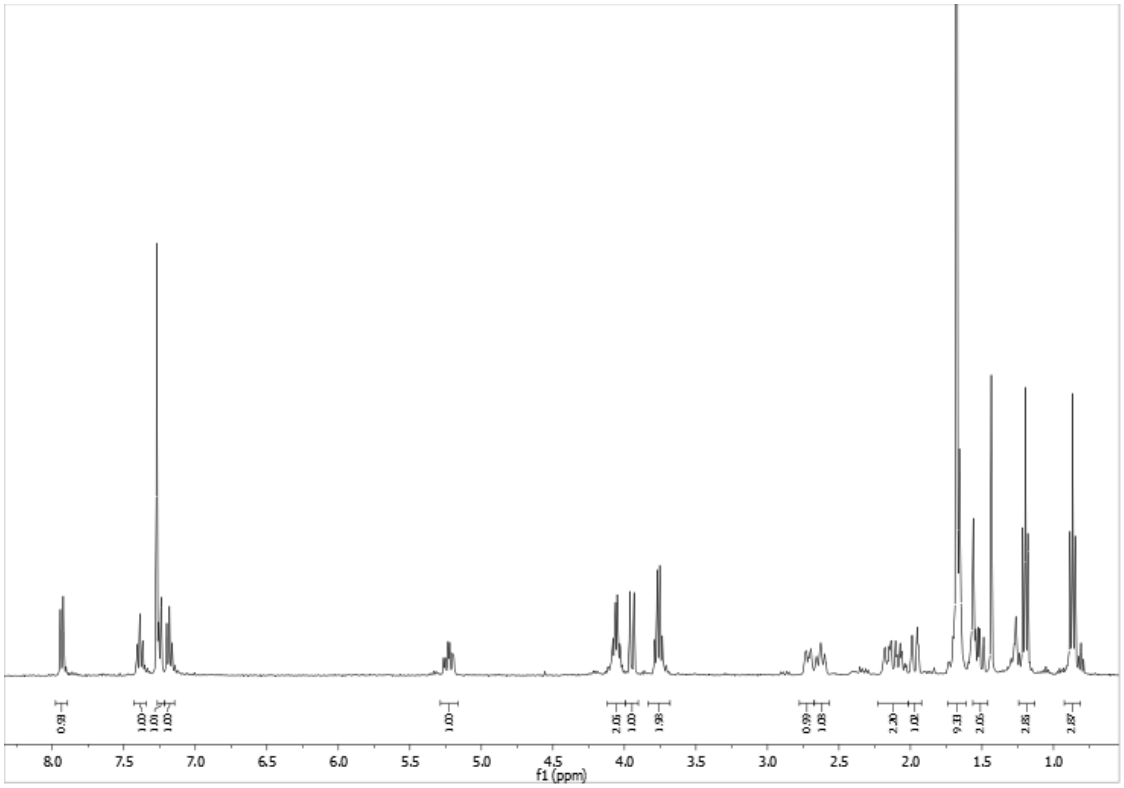
3b

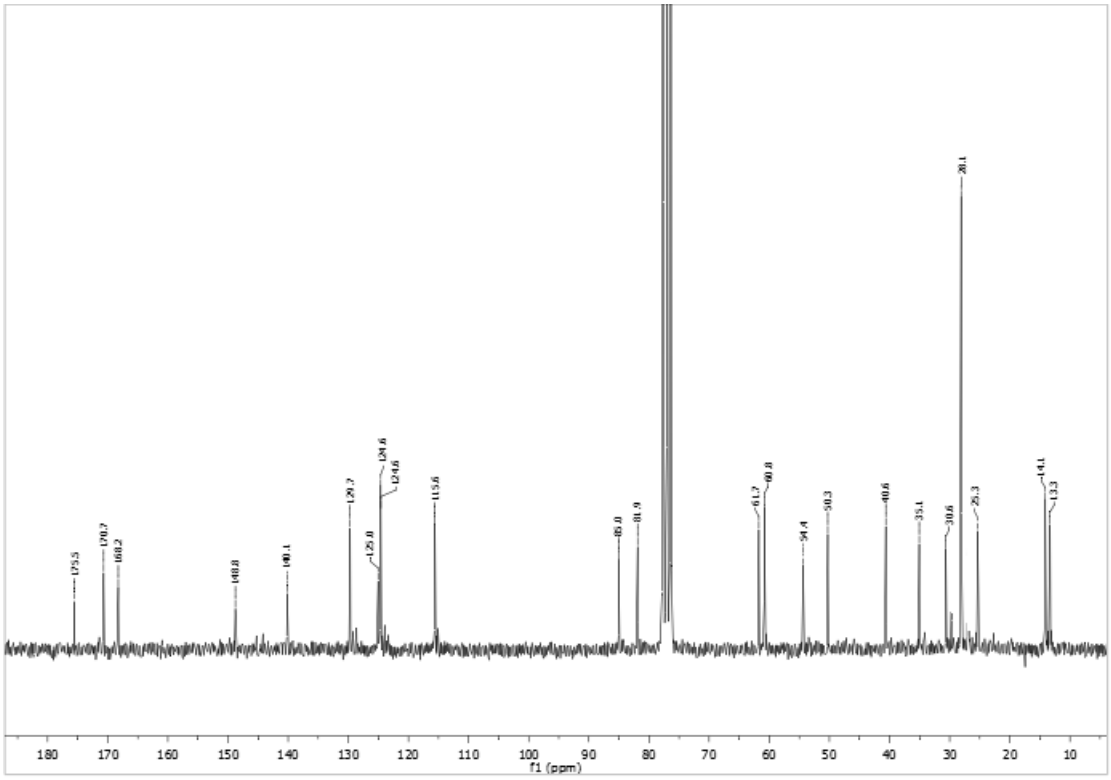

2.10
5.23
1.07
0.84
1.00
0.98
1.02
2.22
0.94
1.85
2.08
2.12
0.99
1.30
1.21
4.49
3.09
2.56
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

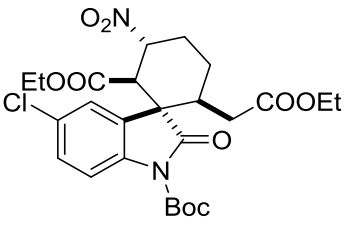

176.8
171.0
168.3
143.4
135.6
129.4
128.8
128.1
127.9
126.9
125.2
122.6
109.6
82.3
61.4
60.7
51.9
49.9
44.7
40.1
34.7
30.7
25.8
14.1
13.4
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



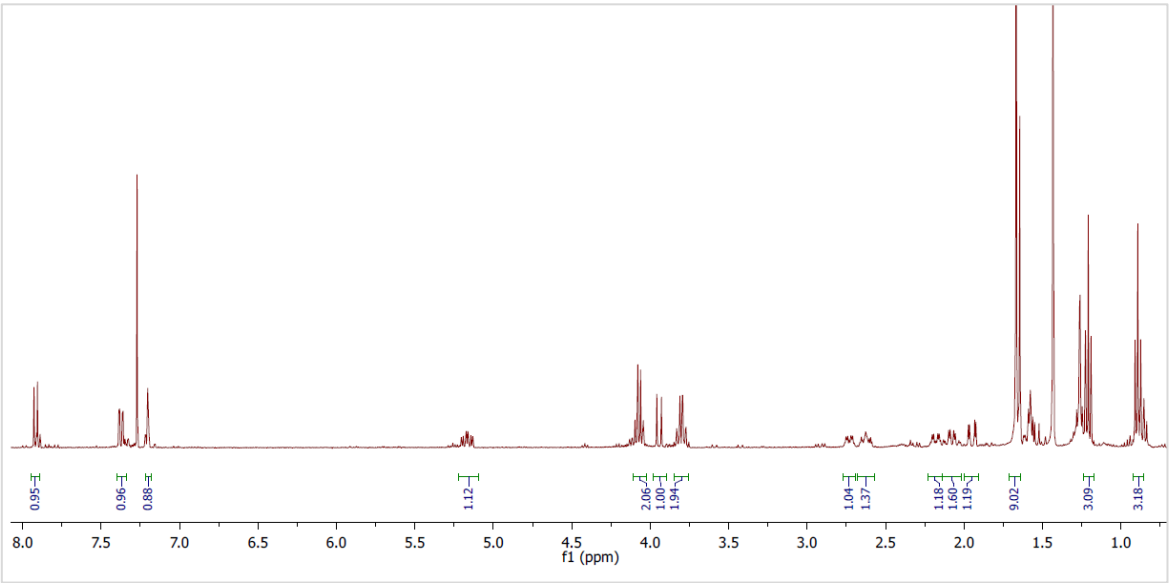
3c

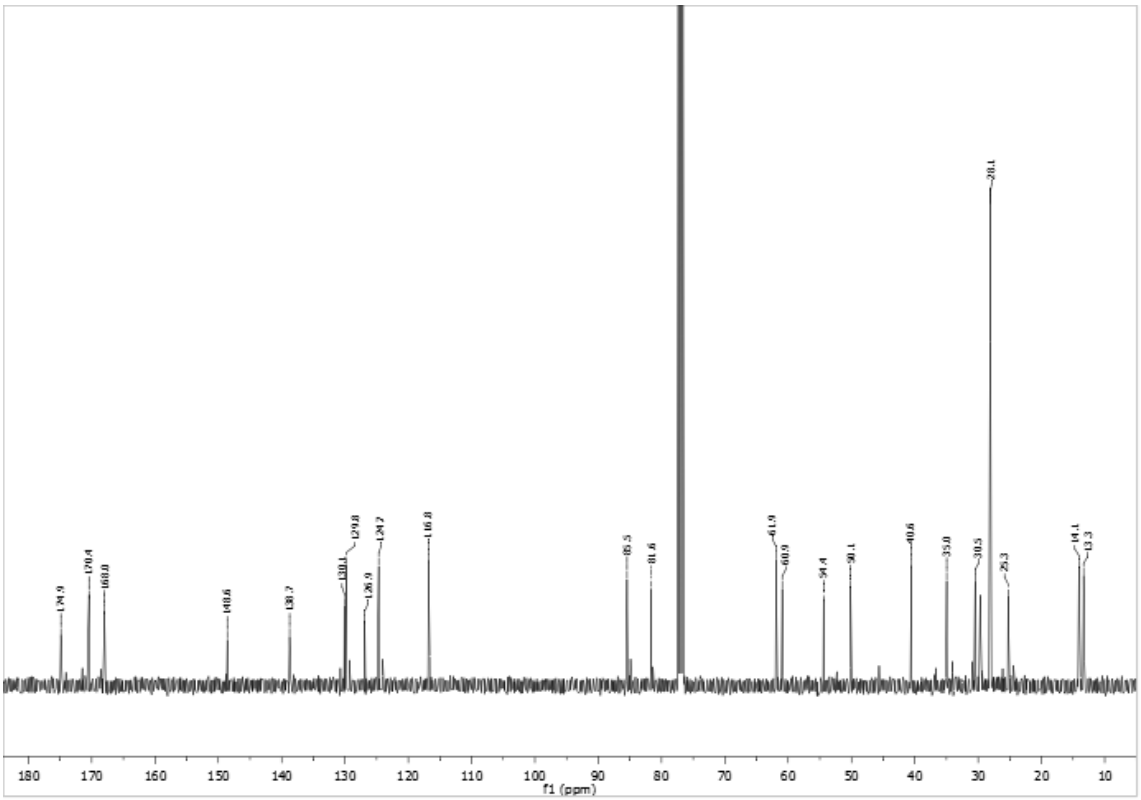


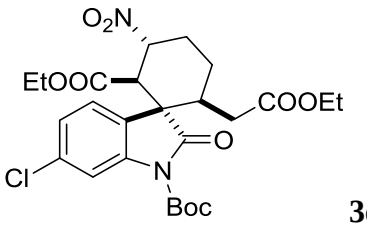



O2N
EtOOC
Cl
COOEt
O
N
Boc

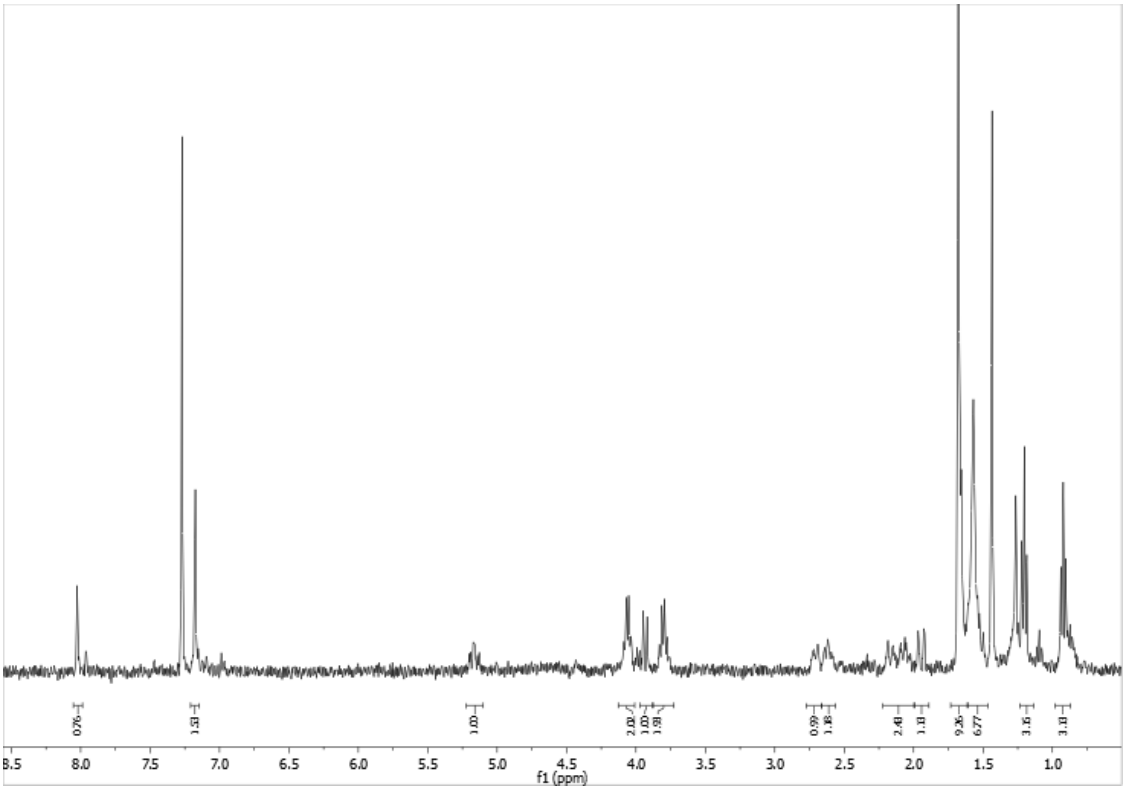
3d

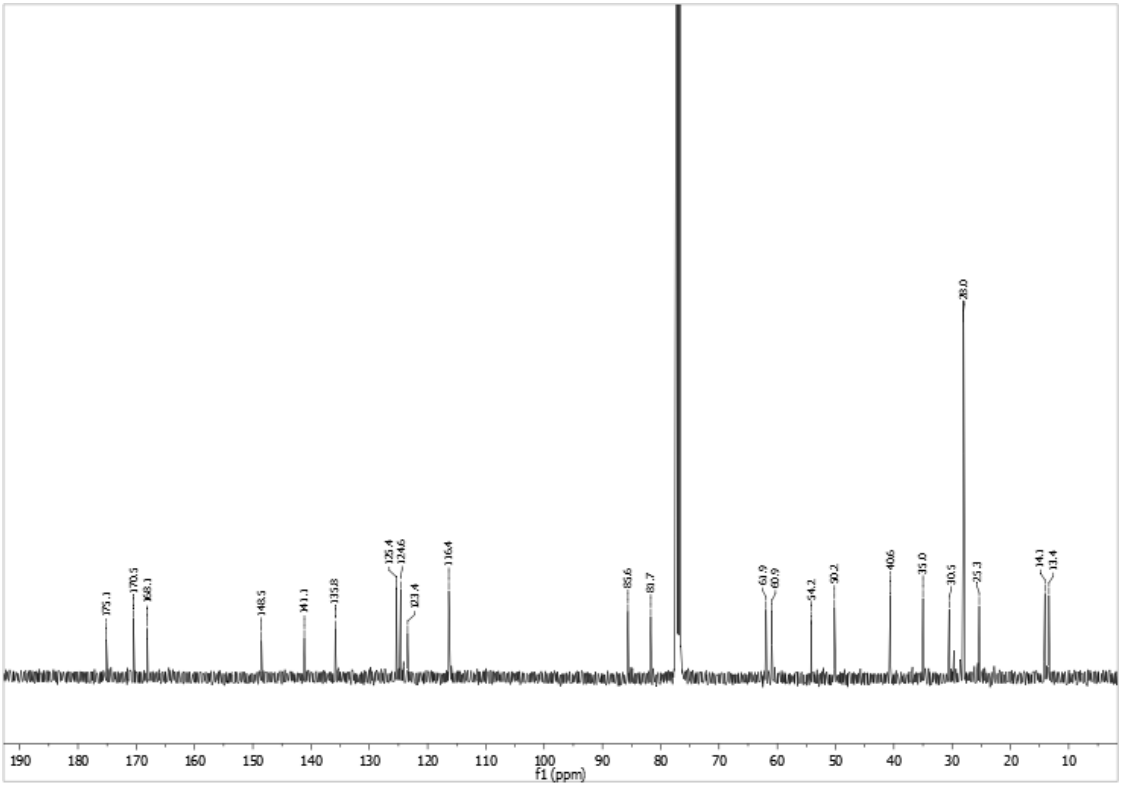

0.95
0.96
0.88
1.12
2.06
1.00
1.94
1.04
1.37
1.18
1.60
1.19
9.02
3.09
3.18
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

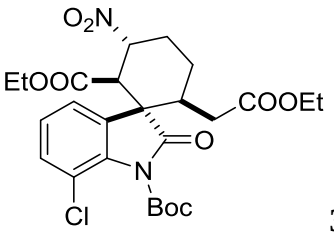

174.9
170.4
169.0
148.6
138.7
130.1
129.8
126.9
124.7
116.8
85.5
81.6
61.9
60.9
54.4
50.1
40.6
35.0
30.5
28.1
25.3
14.1
13.3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



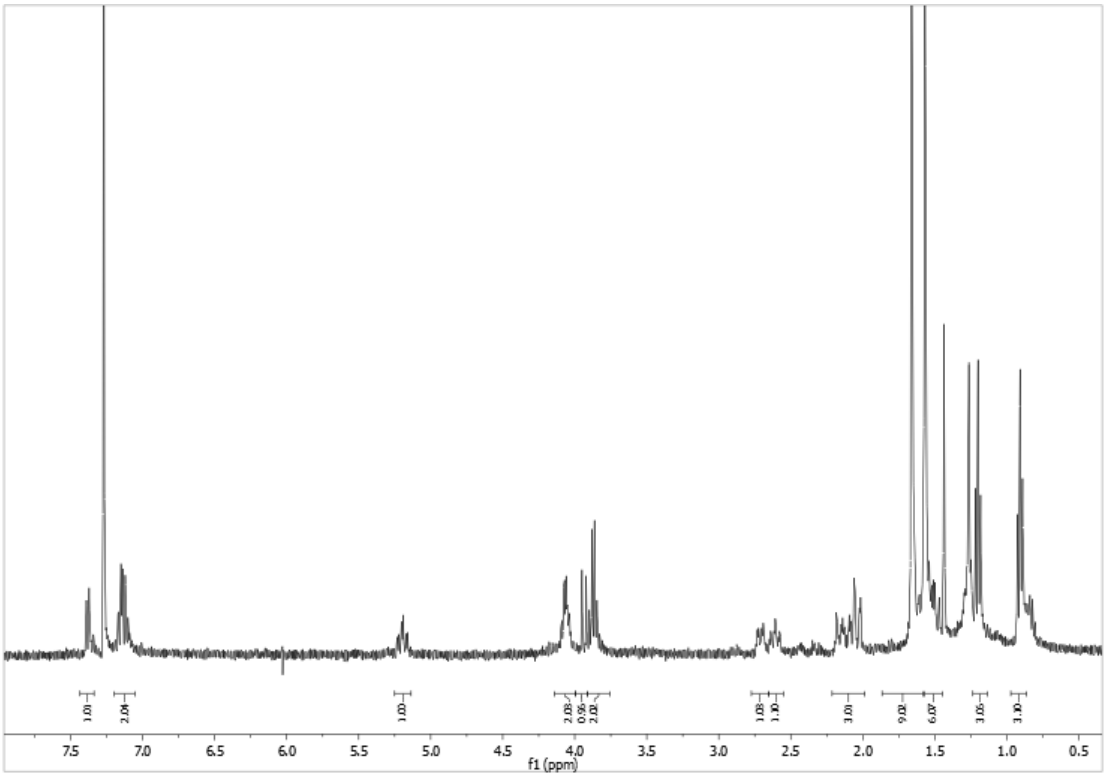
3e

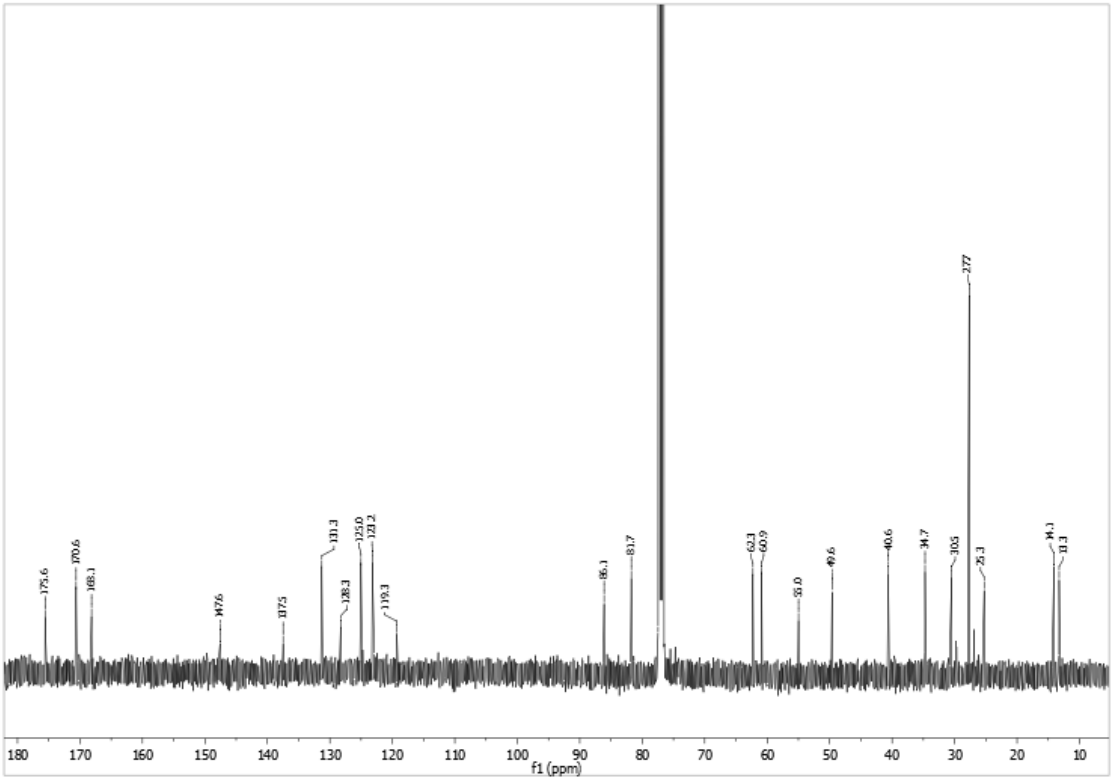


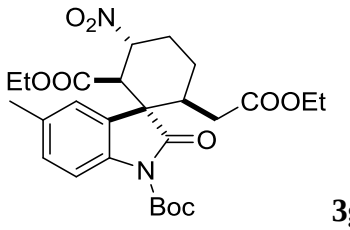



O2N
EtOOC
COOEt
O
N
Cl
Boc

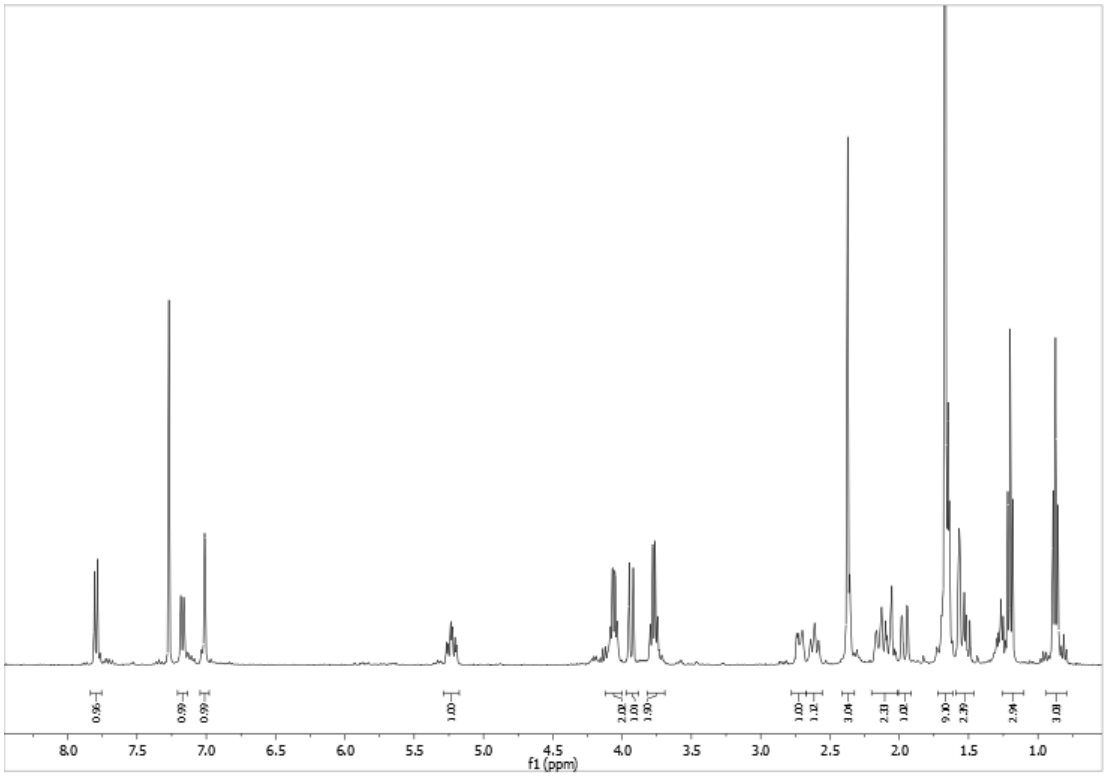
3f

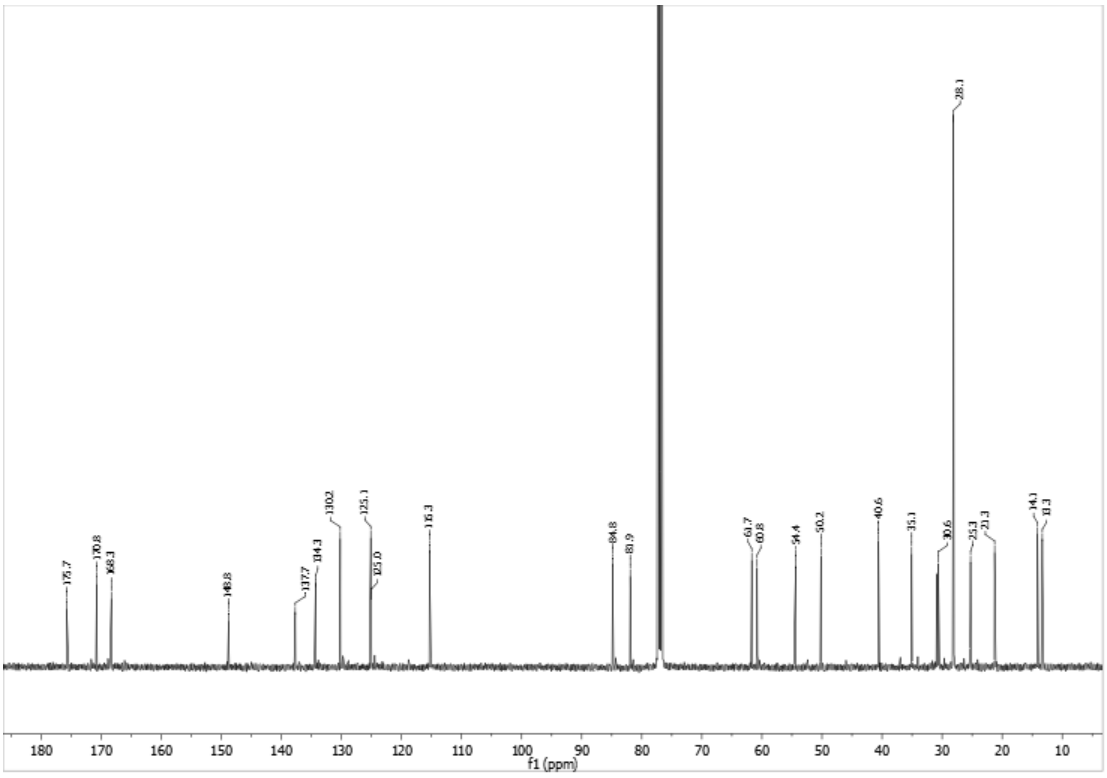

7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

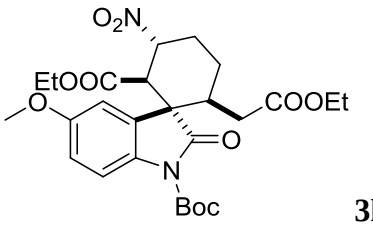

175.6
170.6
168.1
147.6
137.5
131.3
128.3
125.0
123.2
119.3
86.1
81.7
62.3
60.9
55.0
49.6
40.6
34.7
30.5
27.7
25.3
14.1
13.3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



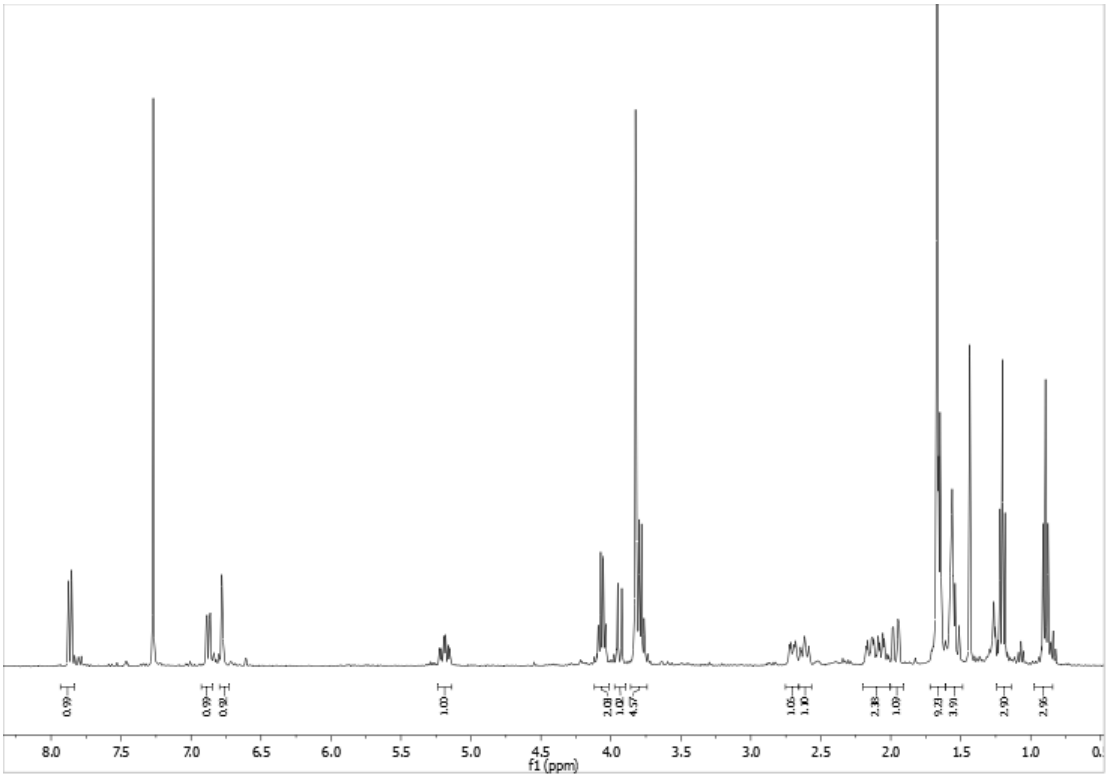
3g

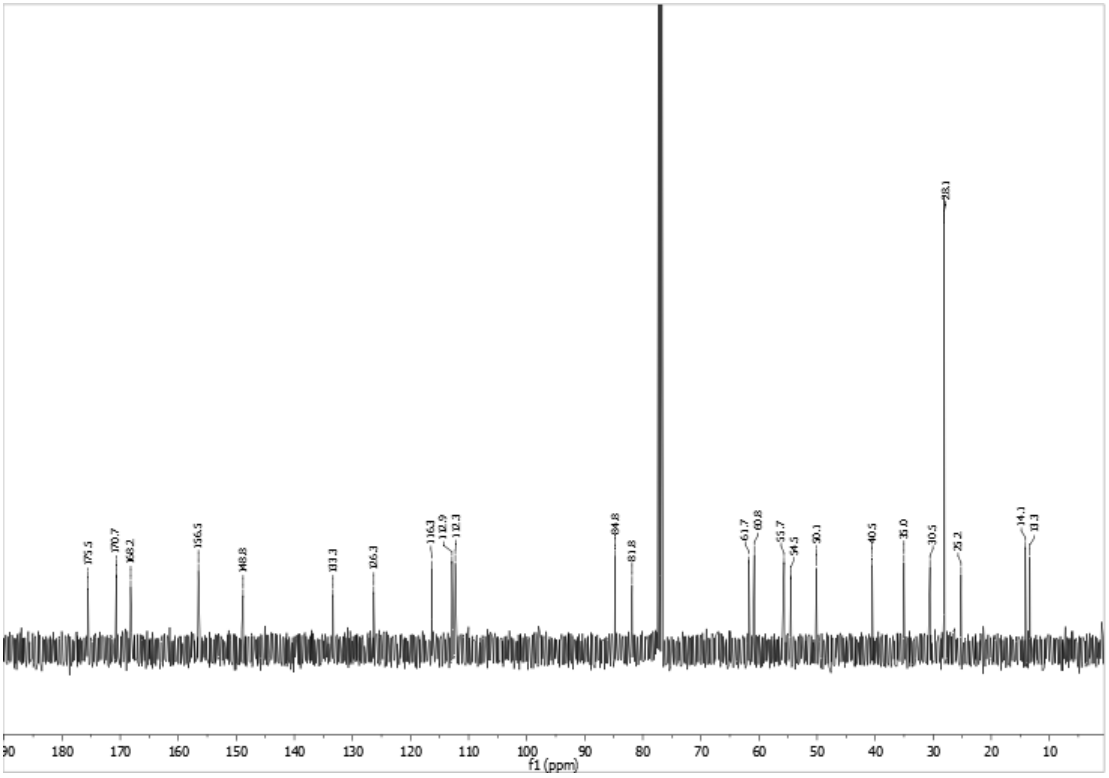


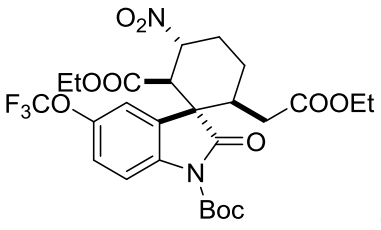




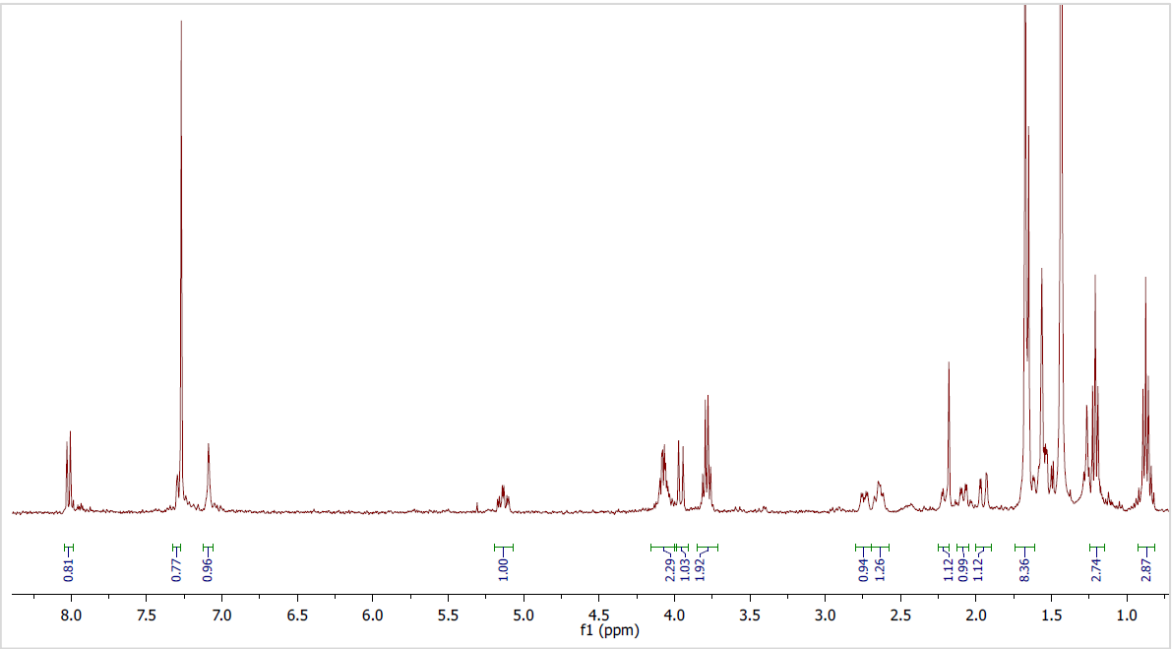
3h

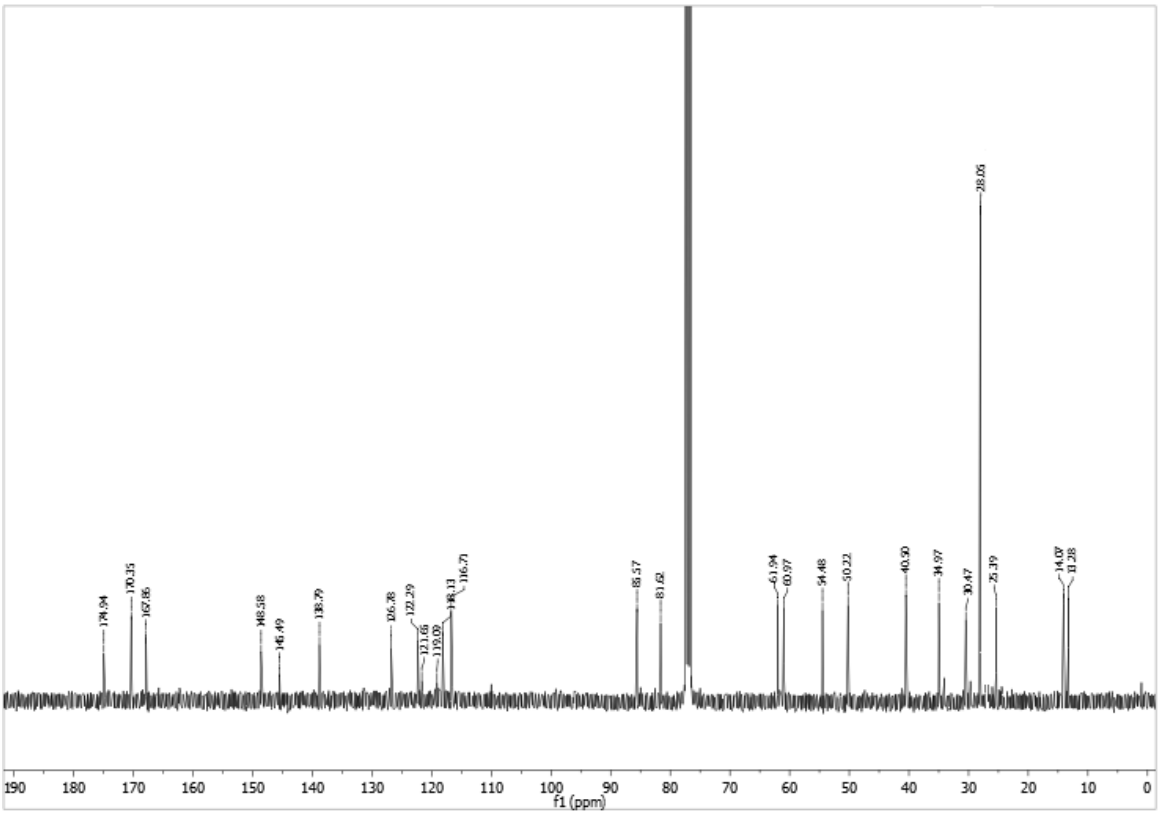


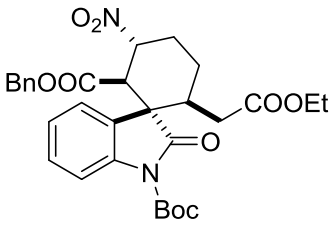



O2N
EtOOC
F3CO
COOEt
O
N
Boc

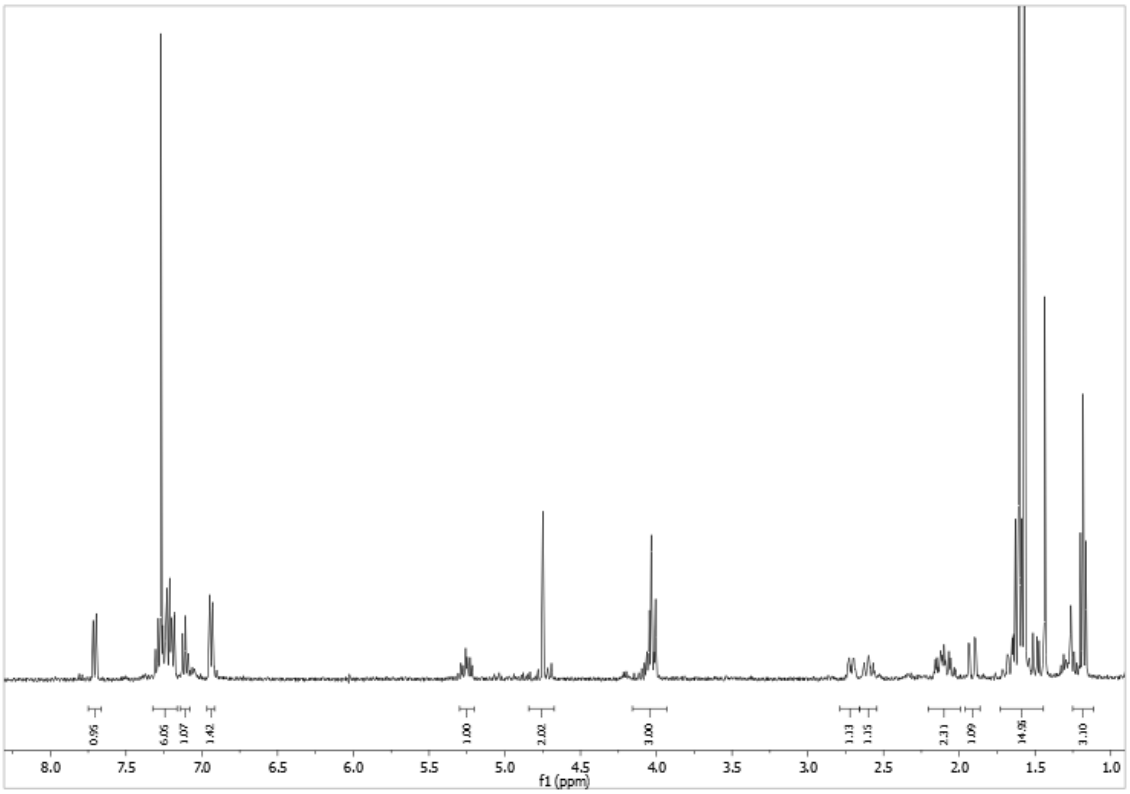
3i

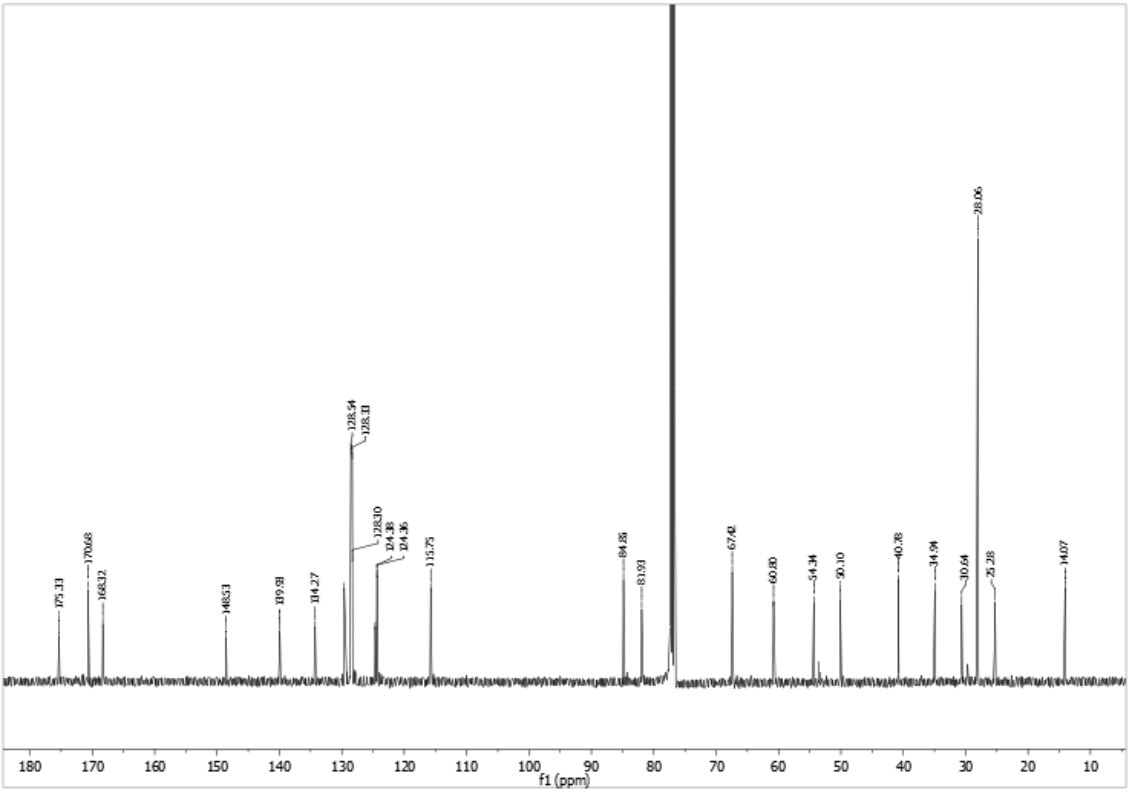

0.81
0.77
0.96
1.00
2.29
1.03
1.92
0.94
1.26
1.12
0.99
1.12
8.36
2.74
2.87
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

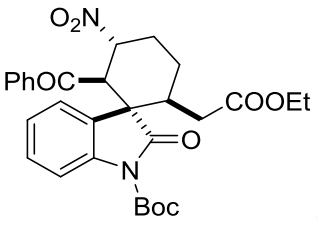

174.94
170.35
167.86
148.58
146.49
138.79
126.78
122.29
121.66
119.00
118.13
116.73
85.57
81.62
61.94
60.97
54.48
50.22
40.50
34.97
30.47
28.05
25.39
14.07
13.28
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


O2N
BnOOC
COOEt
O
N
Boc

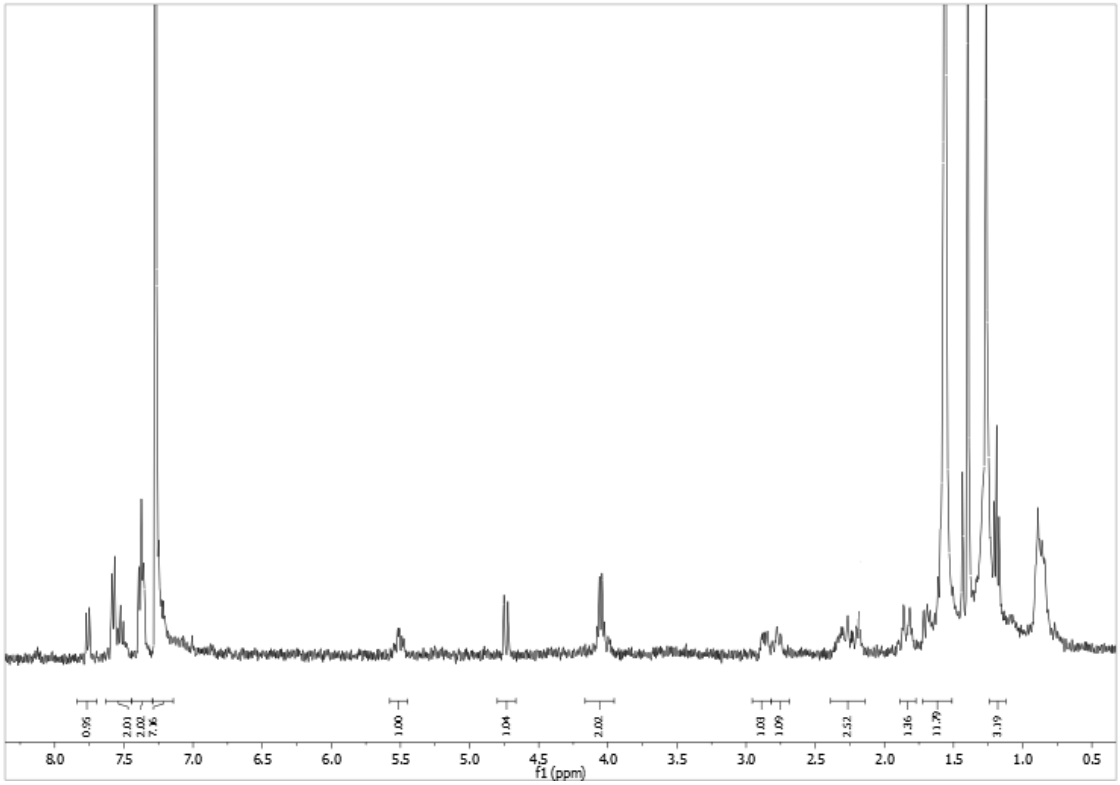
3j

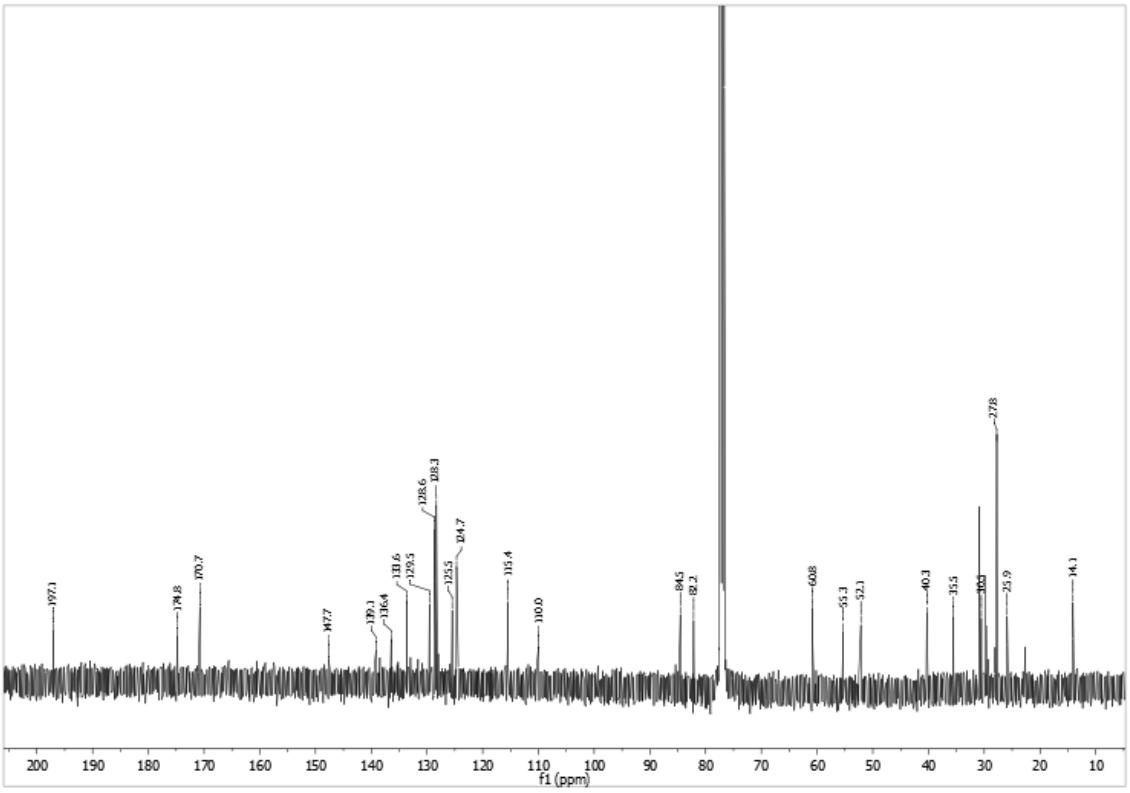

0.95
6.06
1.07
1.42
1.00
2.02
3.00
1.13
1.15
2.31
1.09
14.58
3.10
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

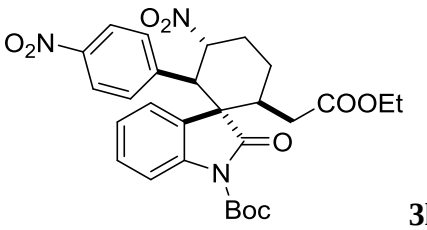

175.33
170.68
168.12
148.53
139.91
134.27
128.54
128.31
128.10
124.38
124.36
115.75
84.85
81.93
67.42
60.80
54.34
50.10
40.78
34.94
30.64
28.06
25.28
14.07
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



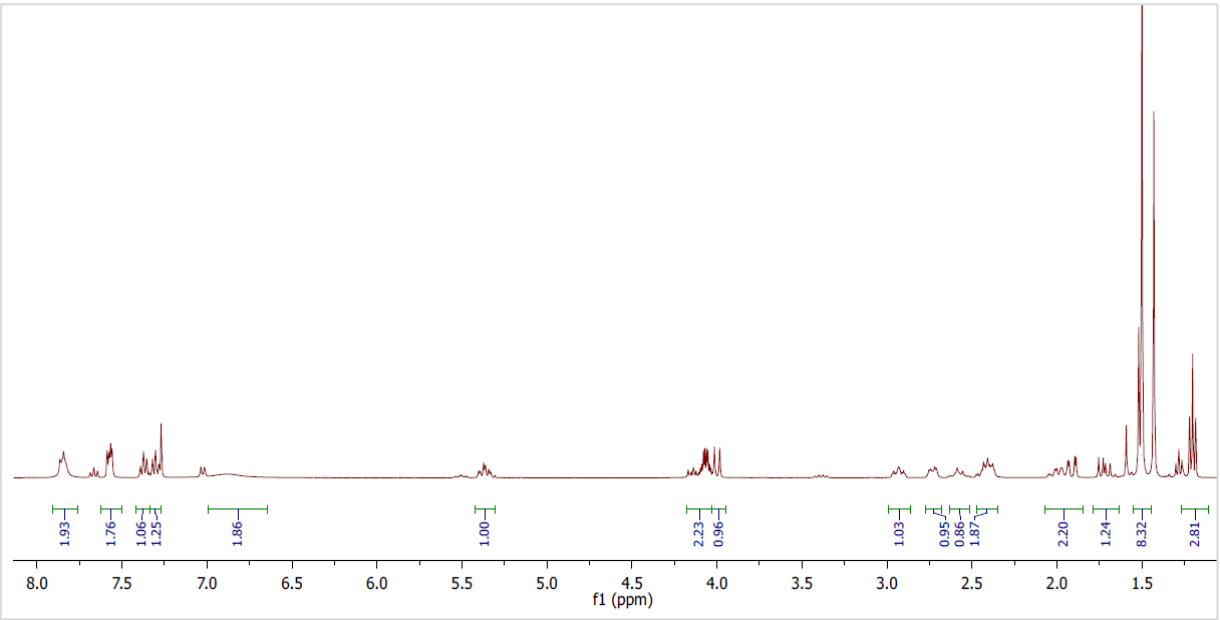
3k

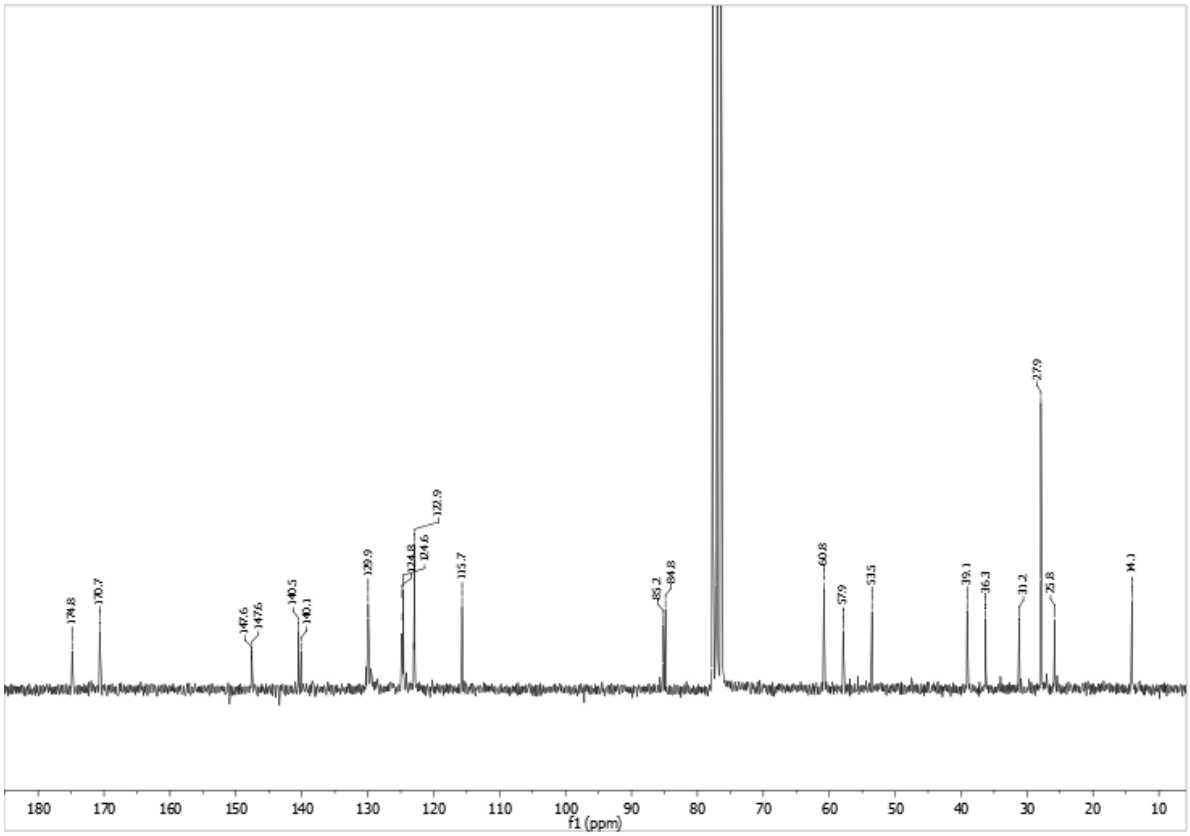


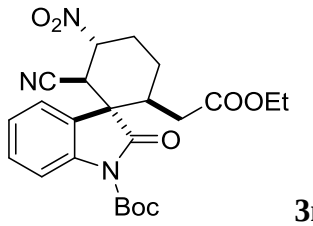



O2N
O2N
COOEt
O
N
Boc

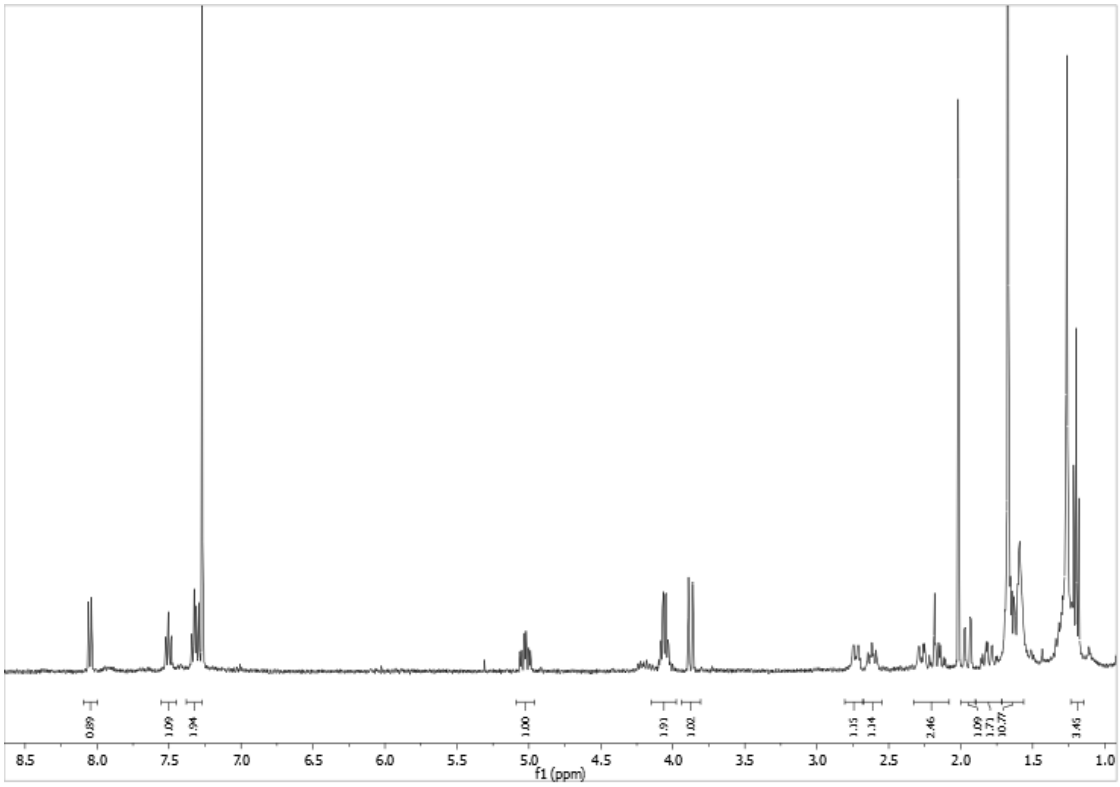
3l

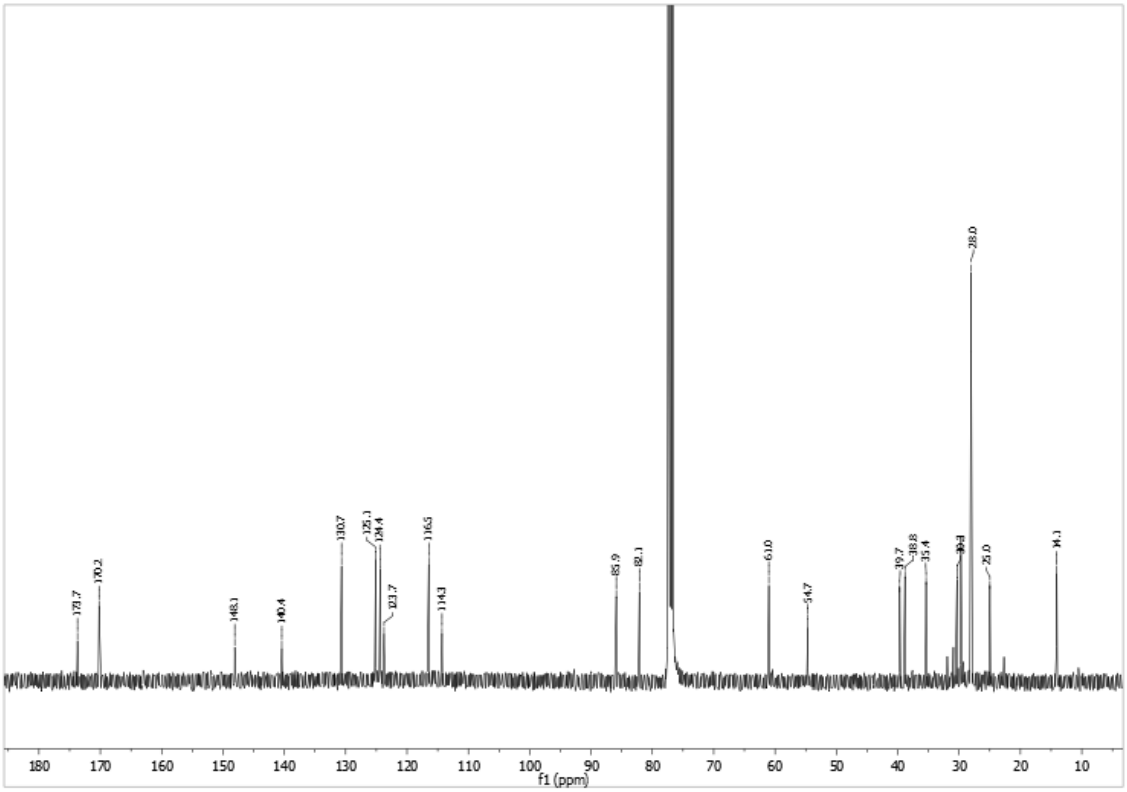

1.93
1.76
1.06
1.25
1.86
1.00
2.23
0.96
1.03
0.95
0.86
1.87
2.20
1.24
8.32
2.81
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

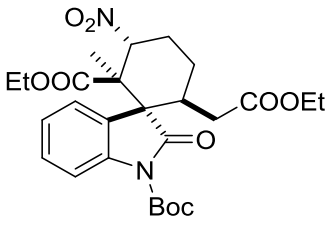

174.8
170.7
147.6
147.6
140.5
140.1
129.9
124.8
124.6
122.9
115.7
85.2
84.8
60.8
57.9
53.5
39.1
36.3
31.2
27.9
25.8
14.1
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



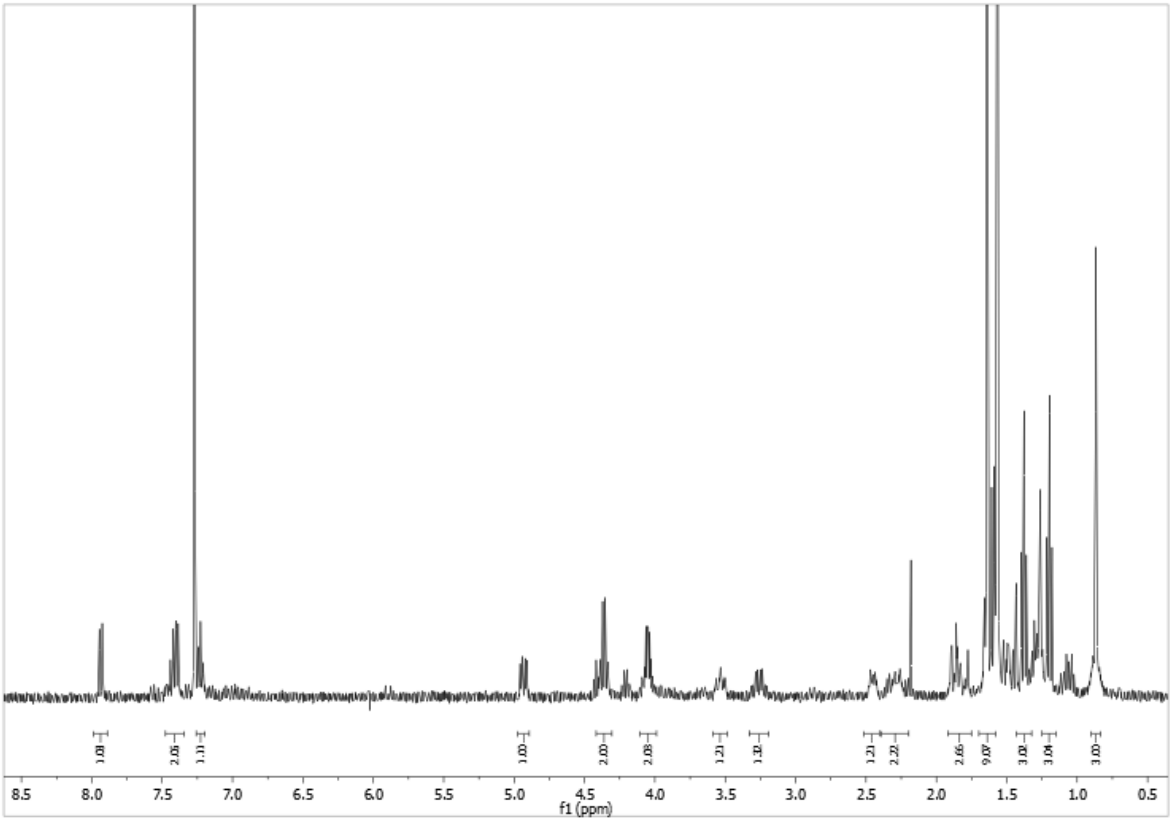
3m






O2N
EtOOC
COOEt
O
N
Boc

3n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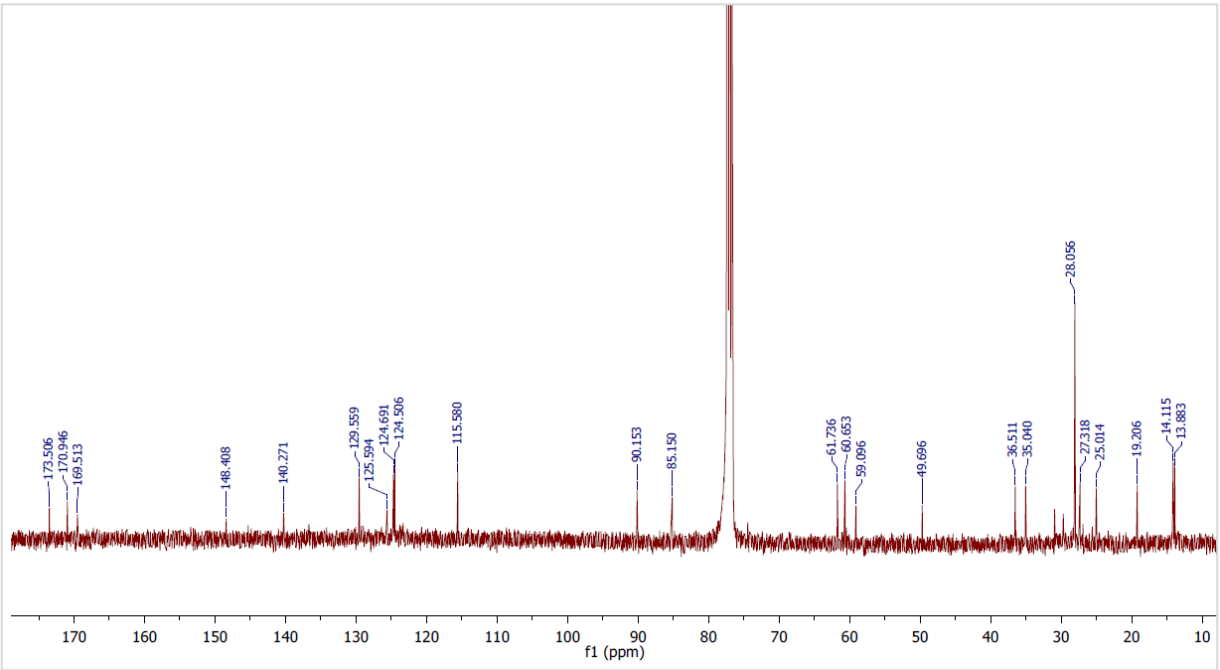
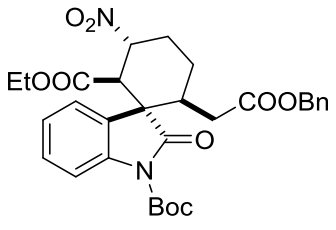
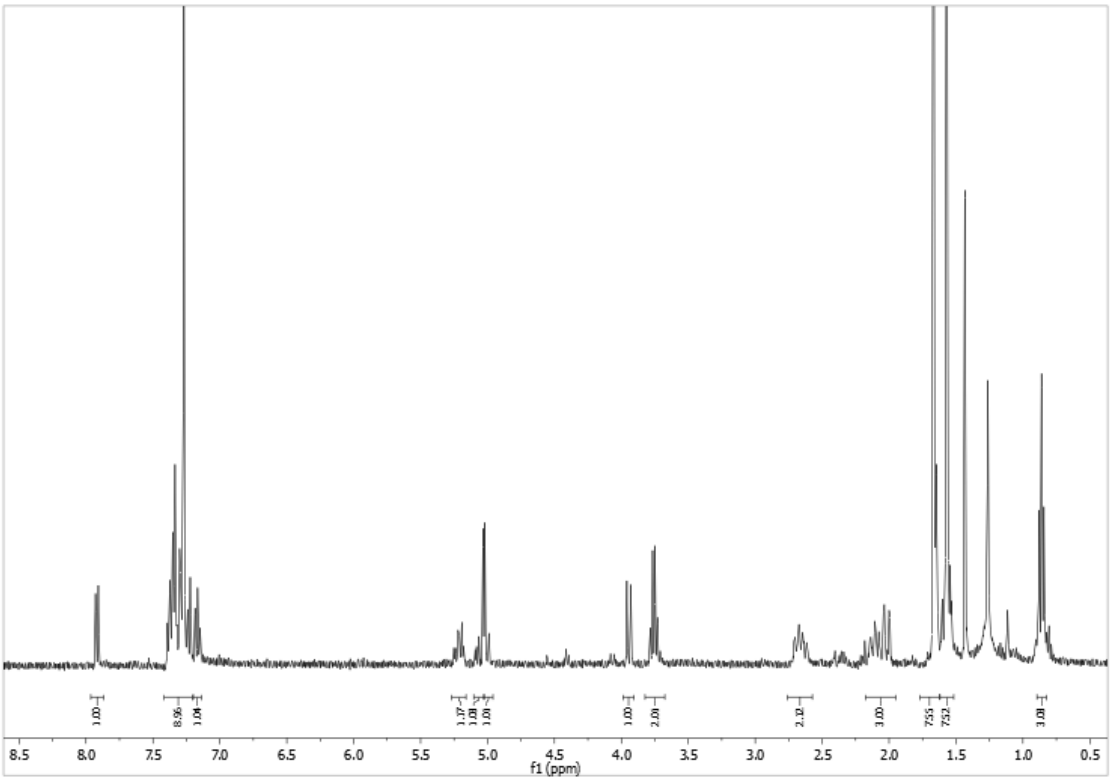
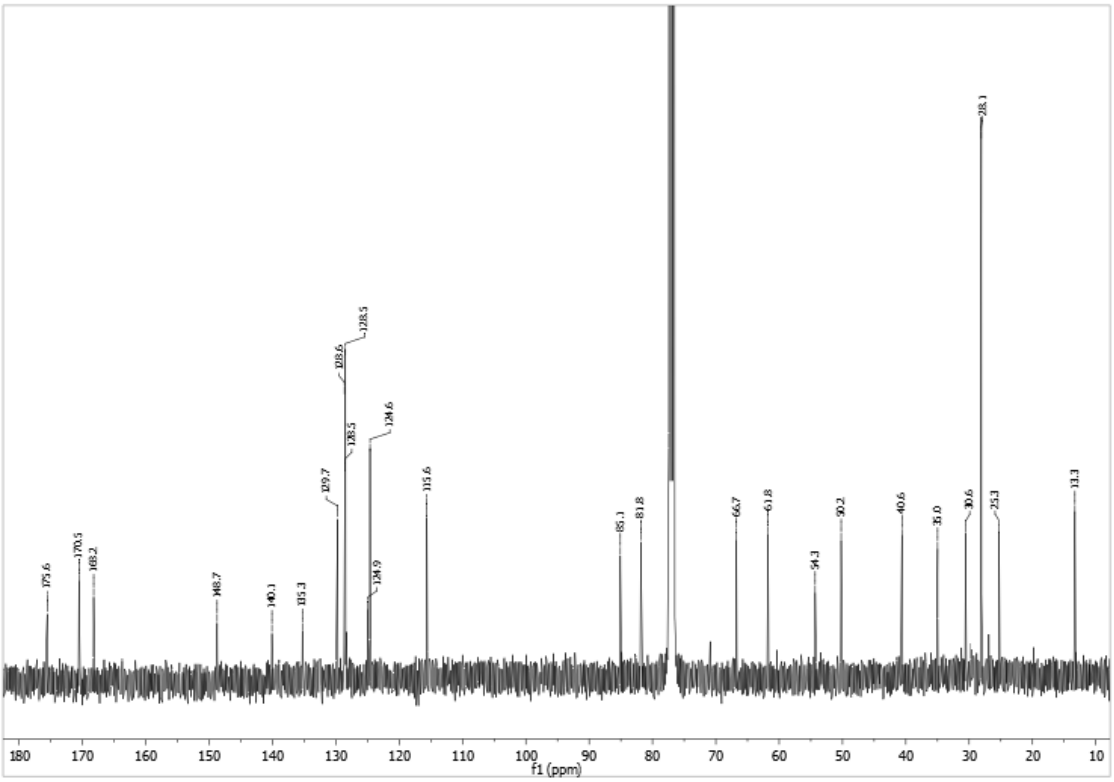
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

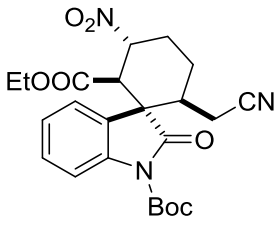

173.506
170.946
169.513
148.408
140.271
129.559
125.594
124.691
124.506
115.580
90.153
85.150
61.736
60.653
59.096
49.696
36.511
35.040
28.056
27.318
25.014
19.206
14.115
13.883
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
COOBn
O
N
Boc

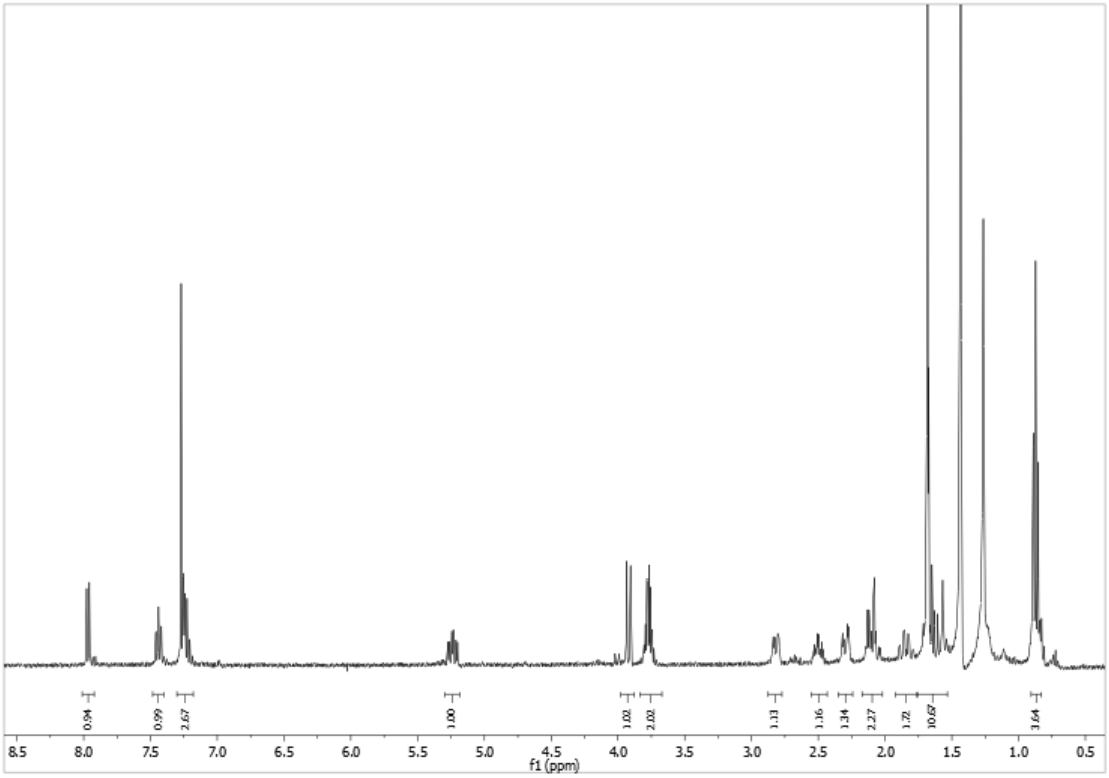
3q


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
f1 (ppm)


175.6
170.5
168.2
148.7
140.1
135.3
129.7
128.6
128.5
128.3
124.6
124.9
115.6
85.1
81.8
66.7
61.8
54.3
50.2
40.6
35.0
30.6
28.1
25.3
13.3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
CN
O
N
Boc

3s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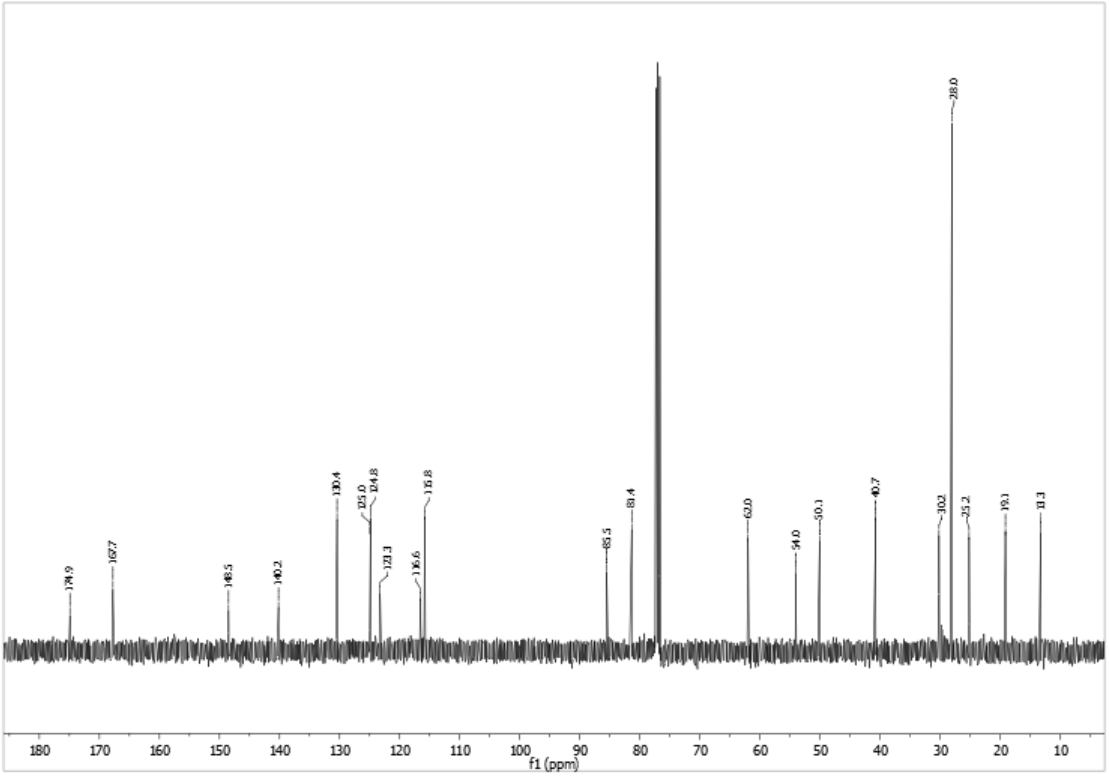
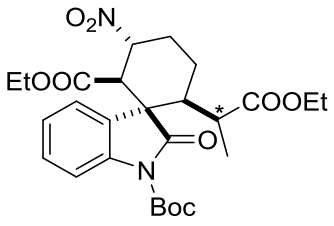
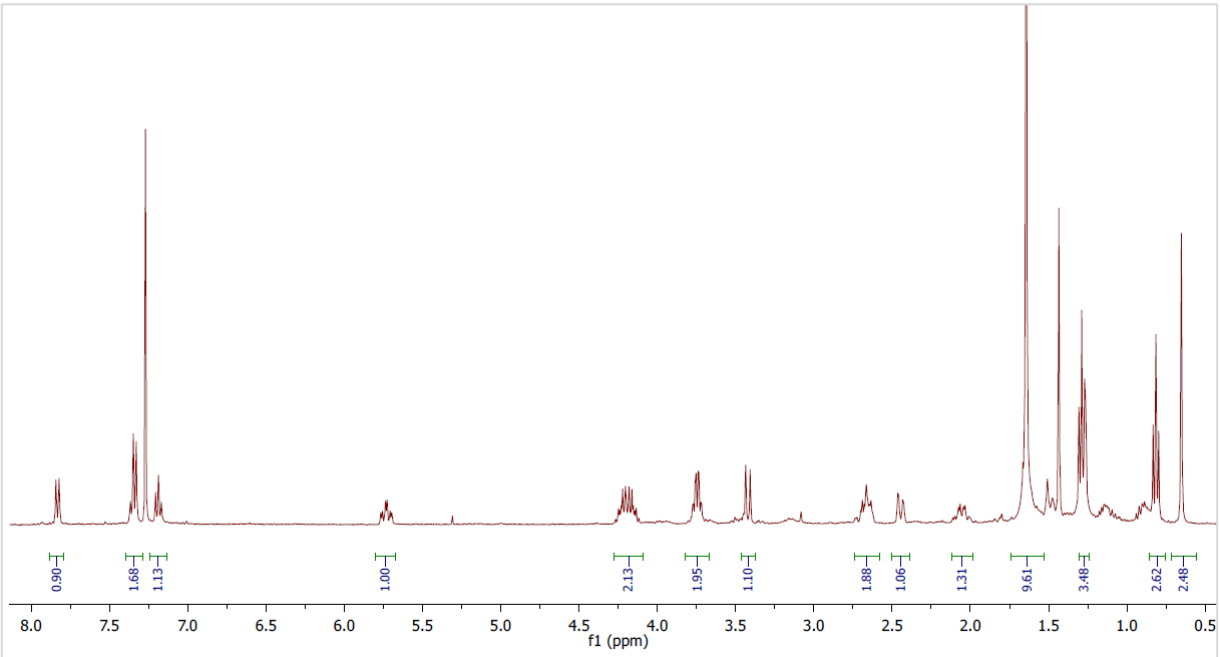
2.67
1.00
1.02
2.02
1.13
1.16
1.34
2.27
1.22
10.69
3.64
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


174.9
167.7
148.5
140.2
130.4
125.0
124.8
123.3
116.6
116.8
85.5
81.4
62.0
54.0
50.1
40.7
30.2
28.0
25.2
19.1
13.3
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
COOEt
*
O
N
Boc

3t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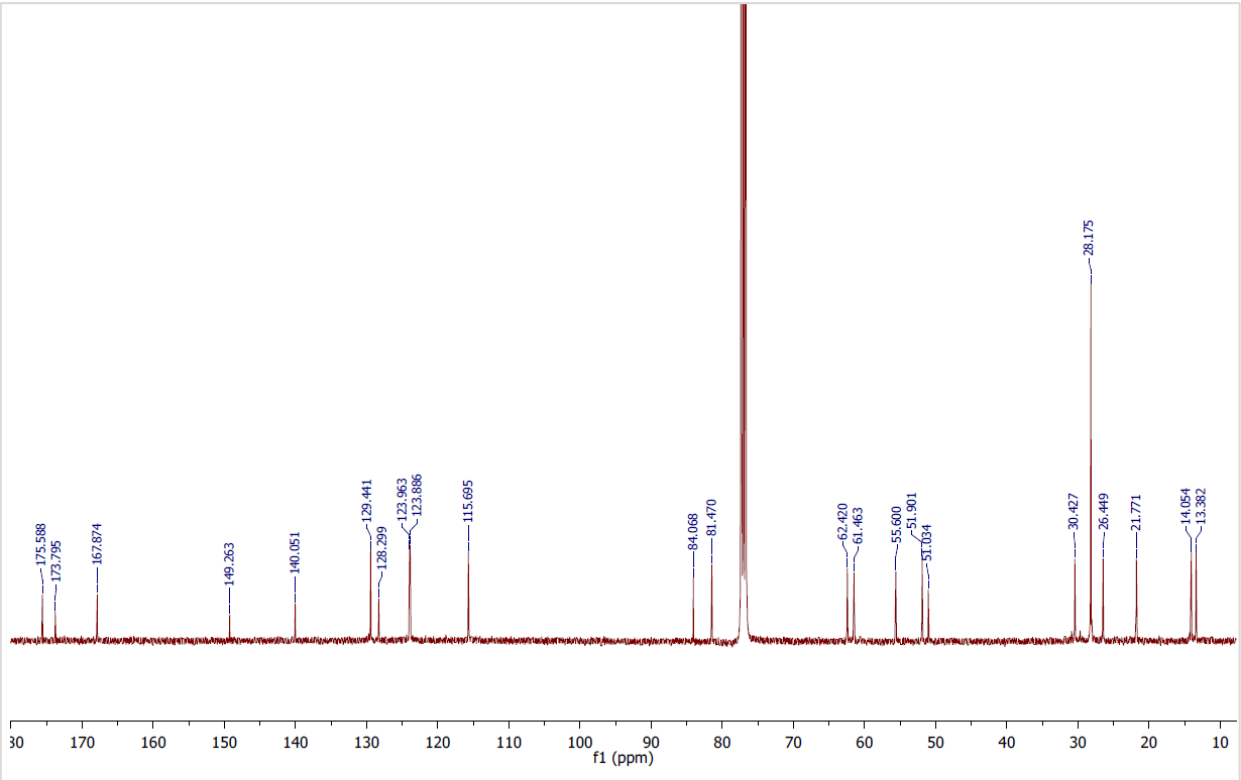
1.13
1.00
2.13
1.95
1.10
1.88
1.06
1.31
9.61
3.48
2.62
2.48
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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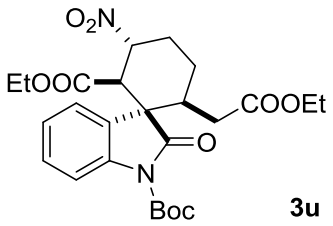
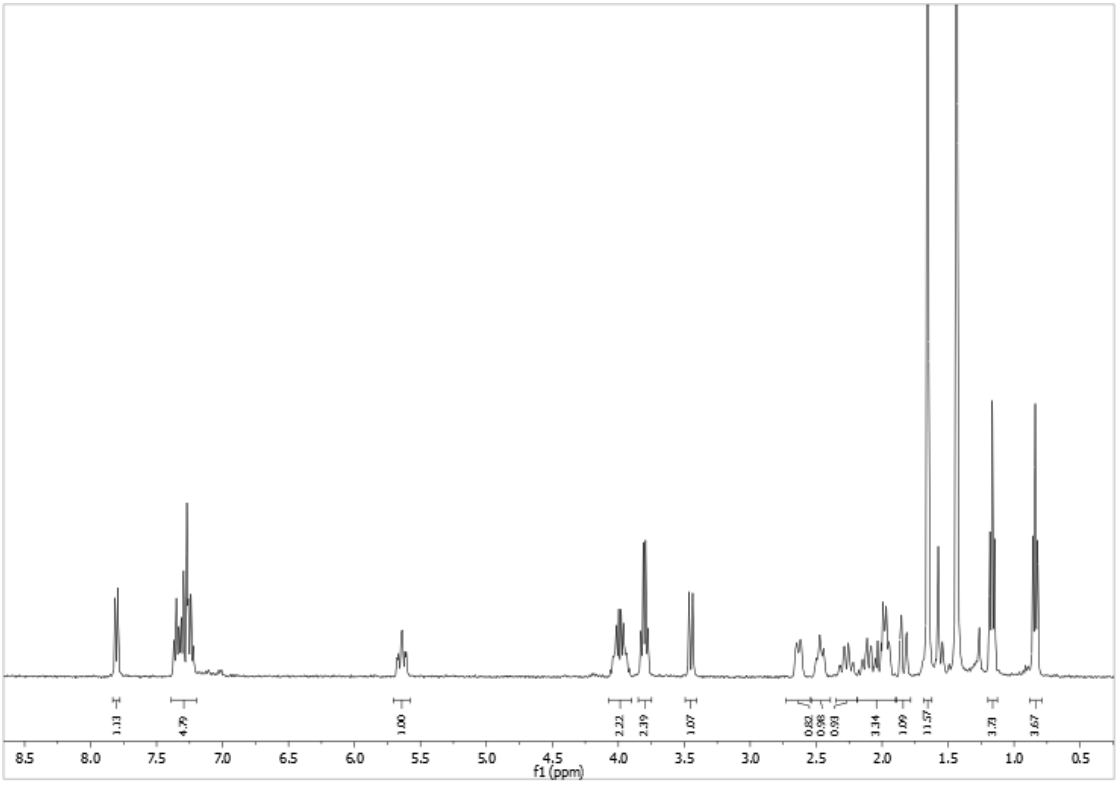
167.874
149.263
140.051
129.441
128.299
123.963
123.886
115.695
84.068
81.470
62.420
61.463
55.600
51.901
51.034
30.427
28.175
26.449
21.771
14.054
13.382
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
COOEt
O
N
Boc

3u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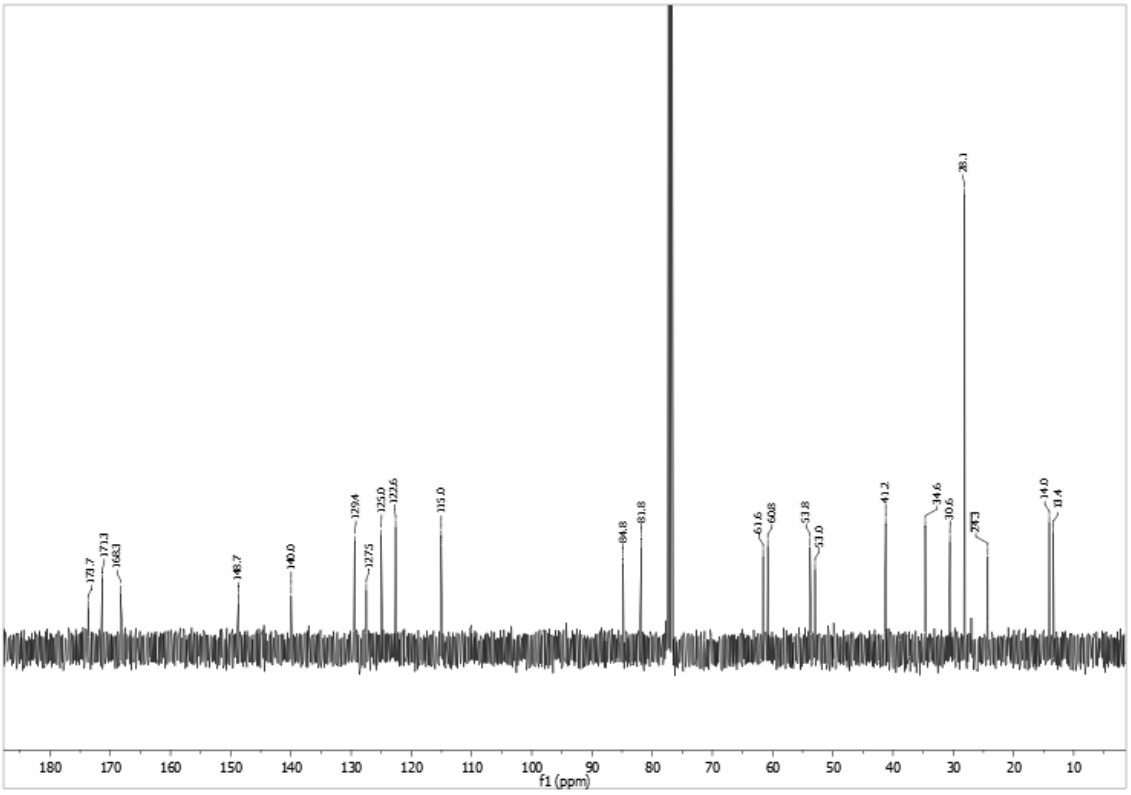
4.79
1.00
2.22
2.19
1.07
0.82
0.98
0.93
3.34
1.09
11.57
3.21
3.67
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)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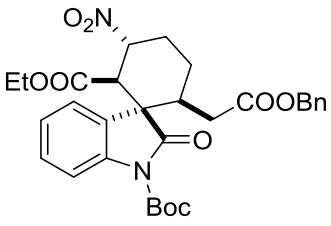
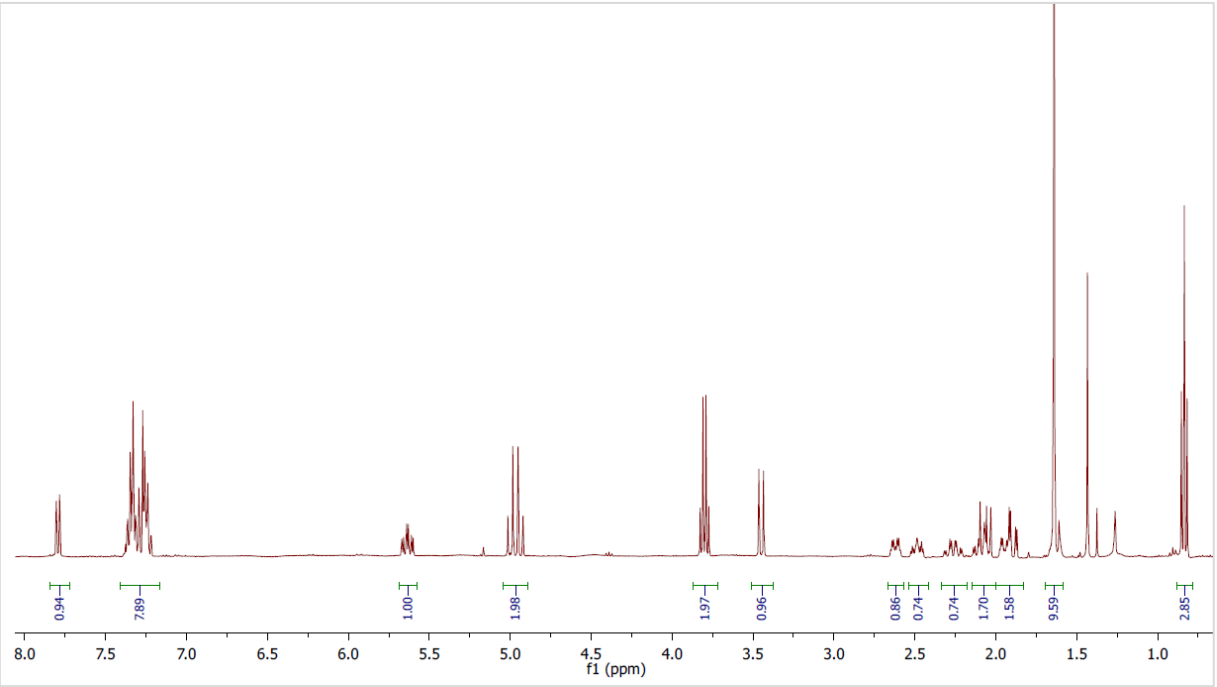
171.3
168.3
148.7
140.0
129.4
127.5
125.0
123.6
115.0
84.8
81.8
61.6
60.8
53.8
53.0
41.2
34.6
30.6
28.1
23.3
14.0
13.4
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
COOBn
O
N
Boc

3v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7.89
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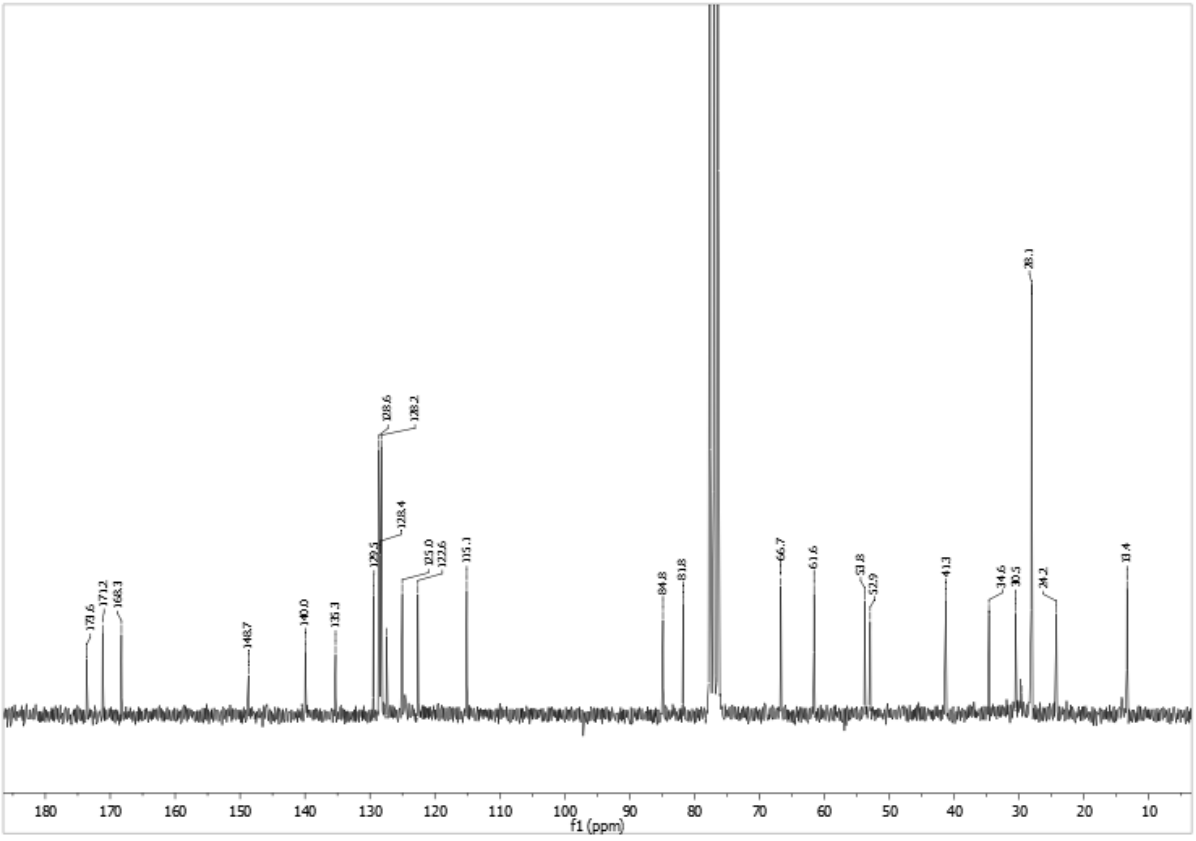
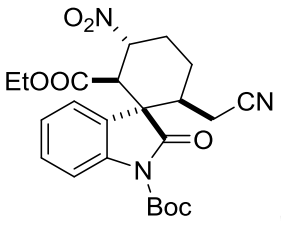
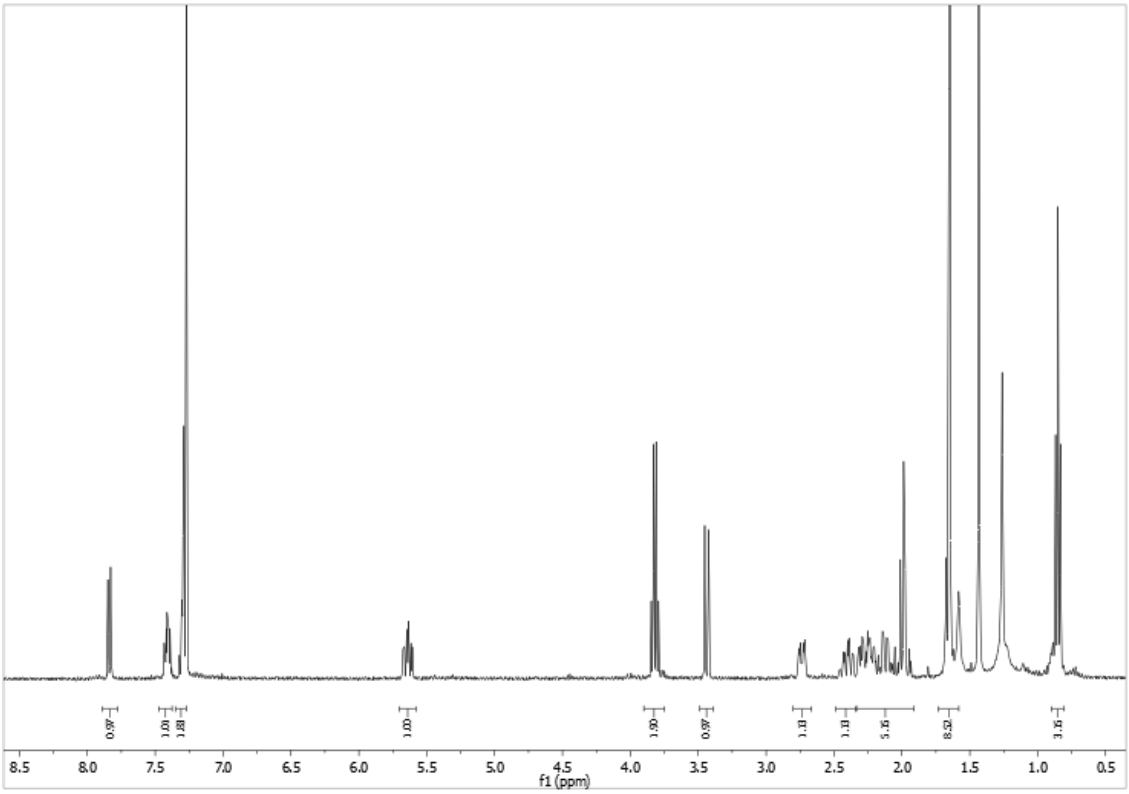
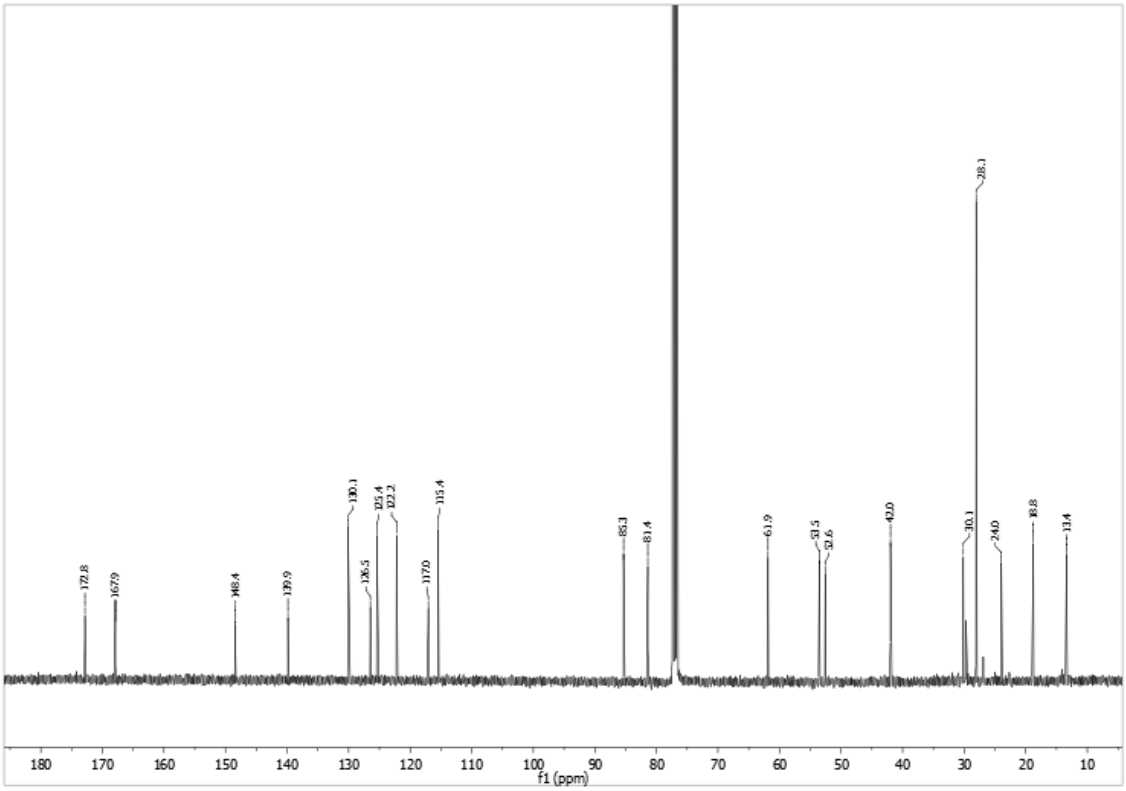
1.97
0.96
0.86
0.74
0.74
1.70
1.58
9.59
2.85
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

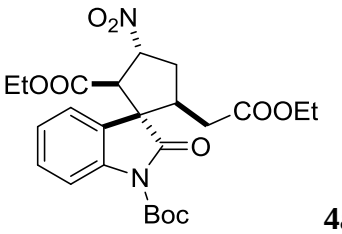

173.6
171.2
168.3
148.7
140.0
135.3
129.5
128.6
128.2
128.4
125.0
122.6
115.1
84.8
81.8
66.7
61.6
53.8
52.9
41.3
34.6
30.5
28.1
24.2
11.4
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
CN
O
N
Boc

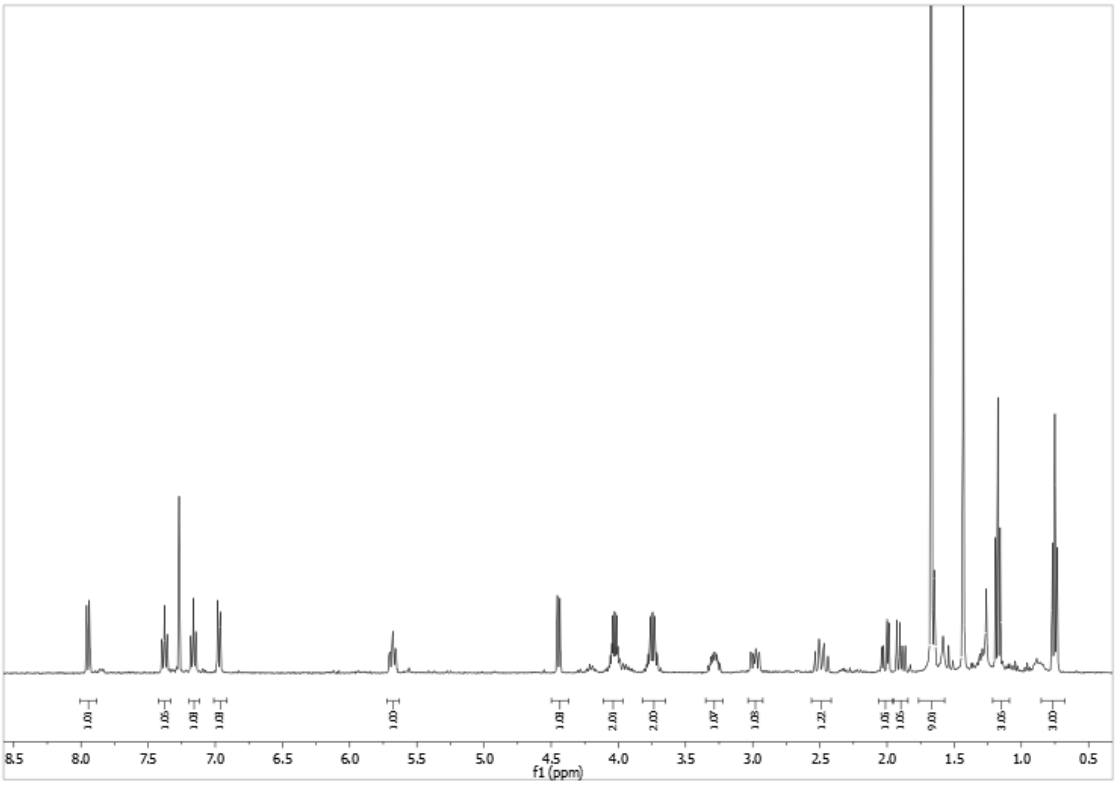
3w

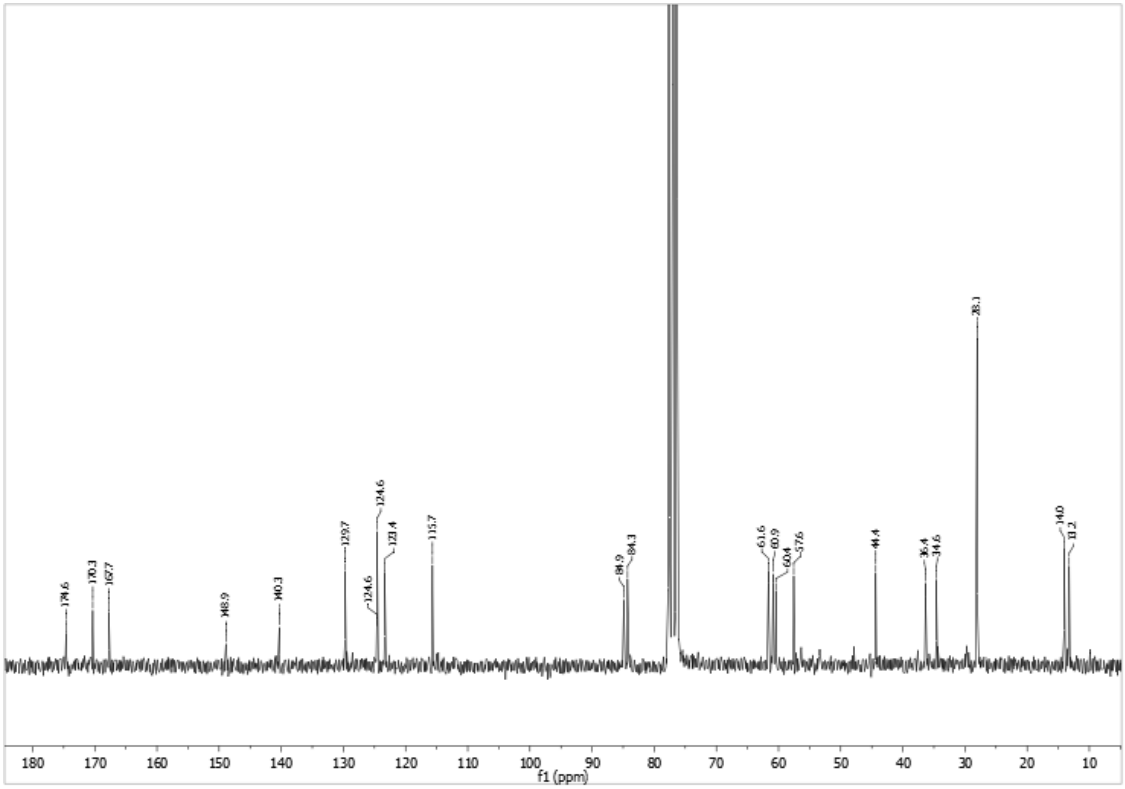

0.97
1.00
1.88
1.00
1.90
0.97
1.10
1.10
5.16
8.52
3.16
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

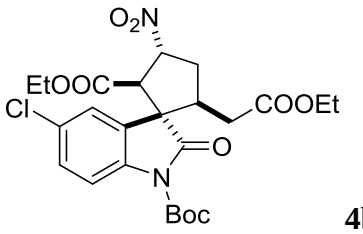

28.3
130.1
125.4
122.2
115.4
85.3
81.4
61.9
53.5
52.6
42.0
30.1
24.0
18.8
13.4
172.8
167.9
148.4
139.9
126.5
117.0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
COOEt
O
N
Boc

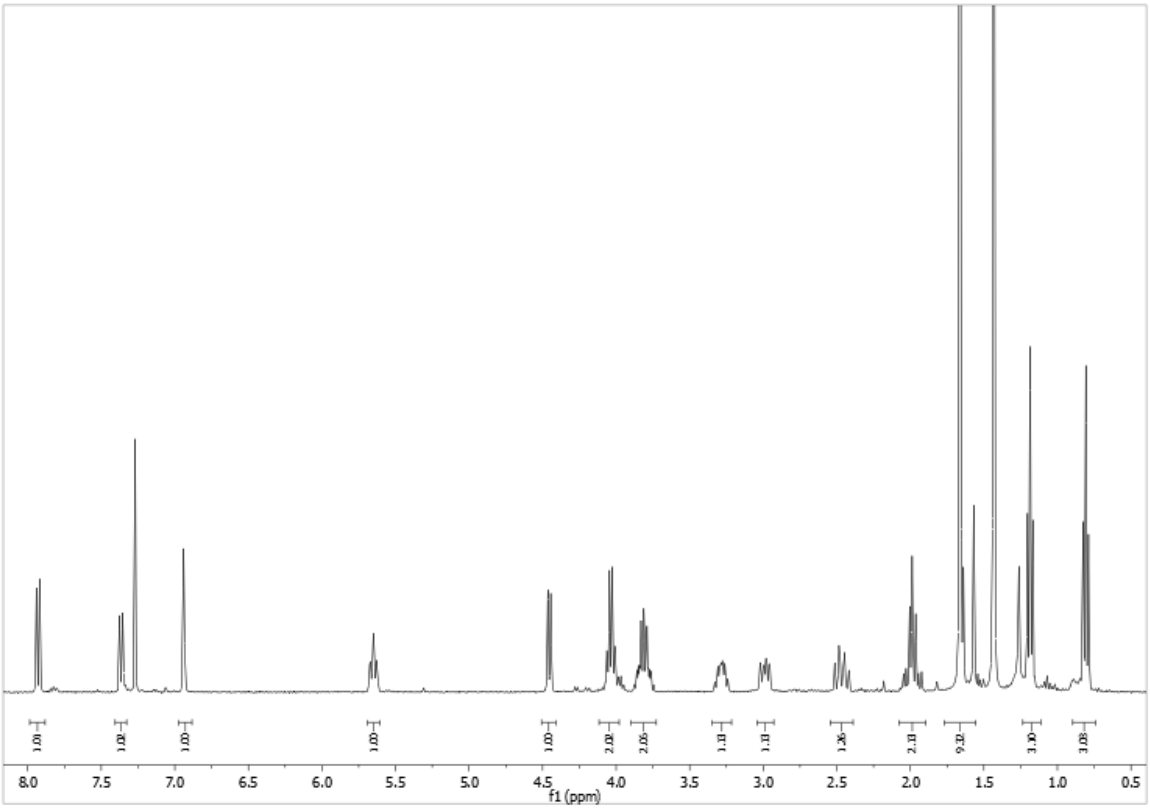
4a

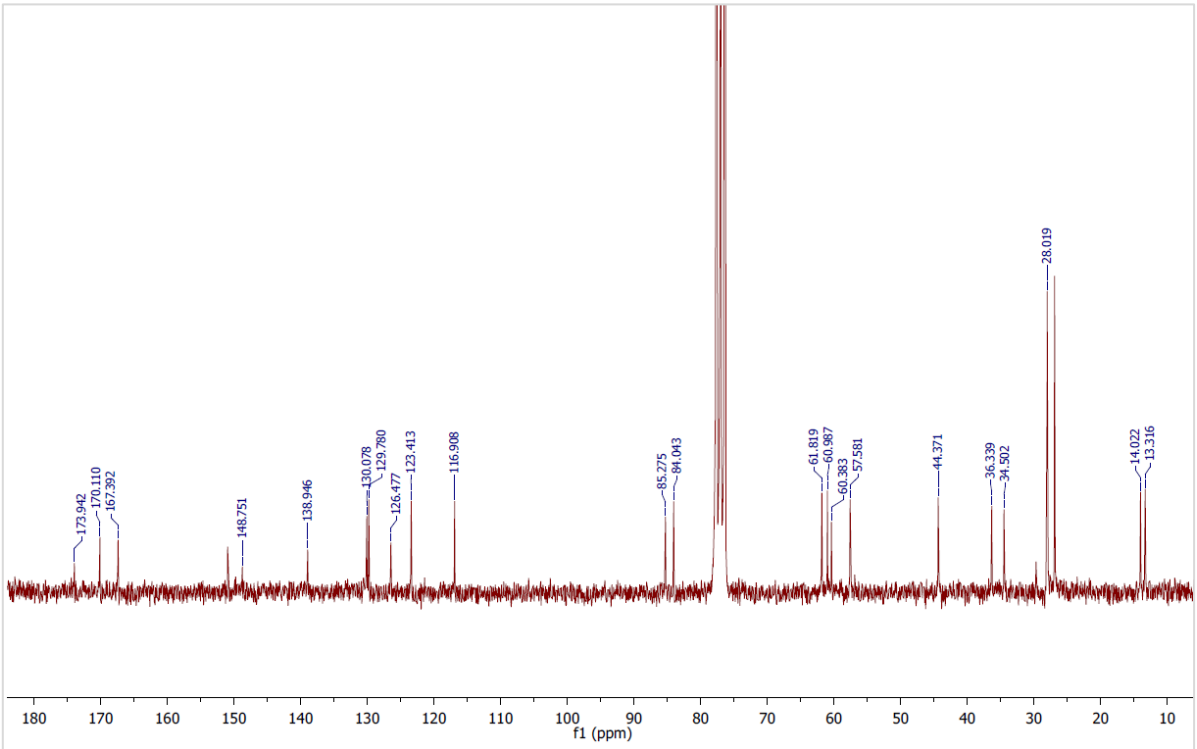

8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


174.6
170.3
167.7
148.9
140.3
129.7
124.6
124.4
123.4
115.7
84.9
84.3
61.6
60.9
60.4
57.6
44.4
36.4
34.6
28.1
14.0
13.2
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
COOEt
Cl
O
N
Boc

4b


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
f1 (ppm)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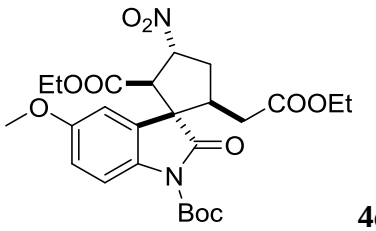
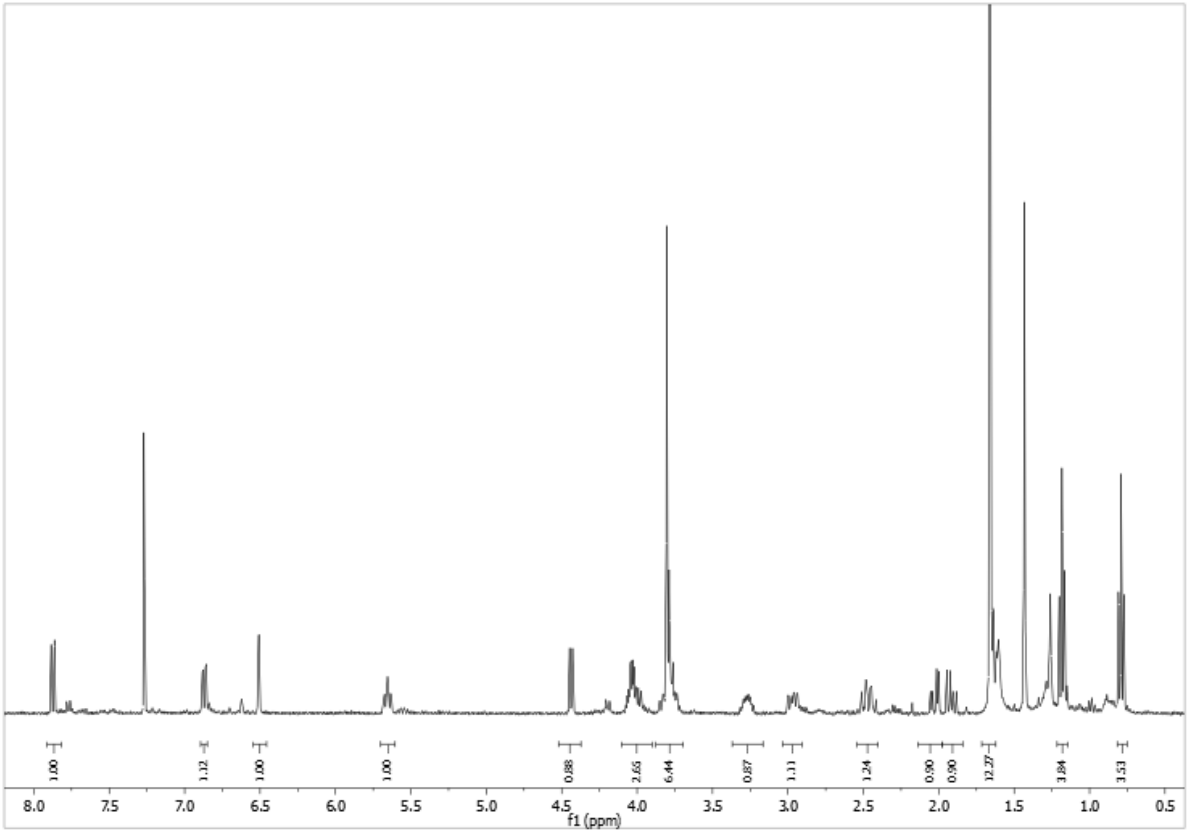
138.946
130.078
129.780
126.477
123.413
116.908
85.275
84.043
61.819
60.987
60.383
57.581
44.371
36.339
34.502
28.019
14.022
13.316
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
COOEt
O
O
N
Boc

4c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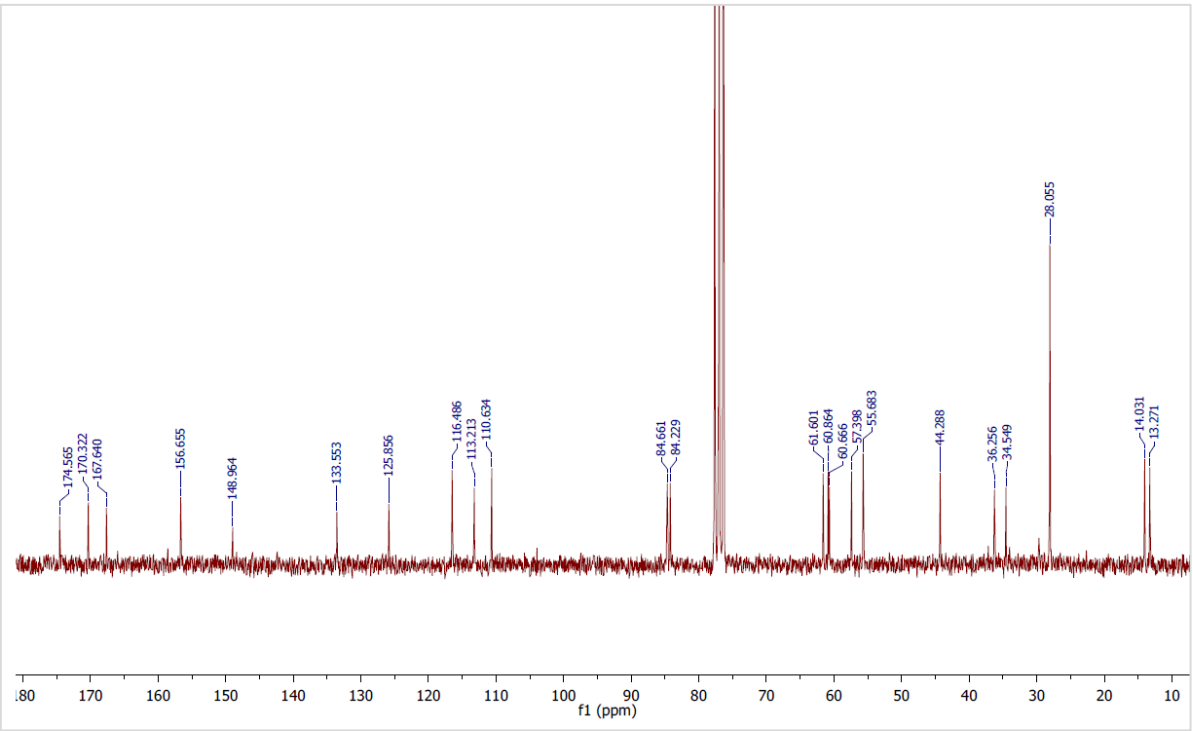
1.12
1.00
1.00
0.88
2.65
6.44
0.87
1.11
1.24
0.90
0.90
12.27
3.84
3.53
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)


174.565
170.322
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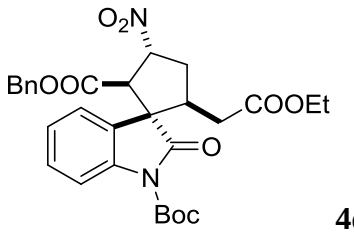
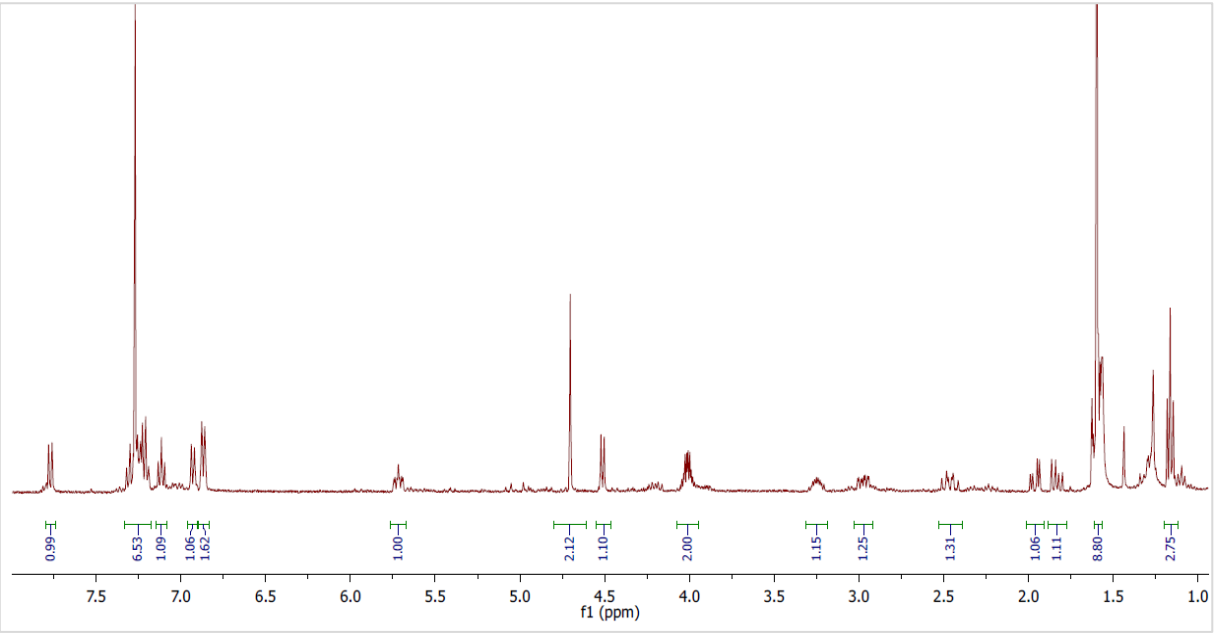
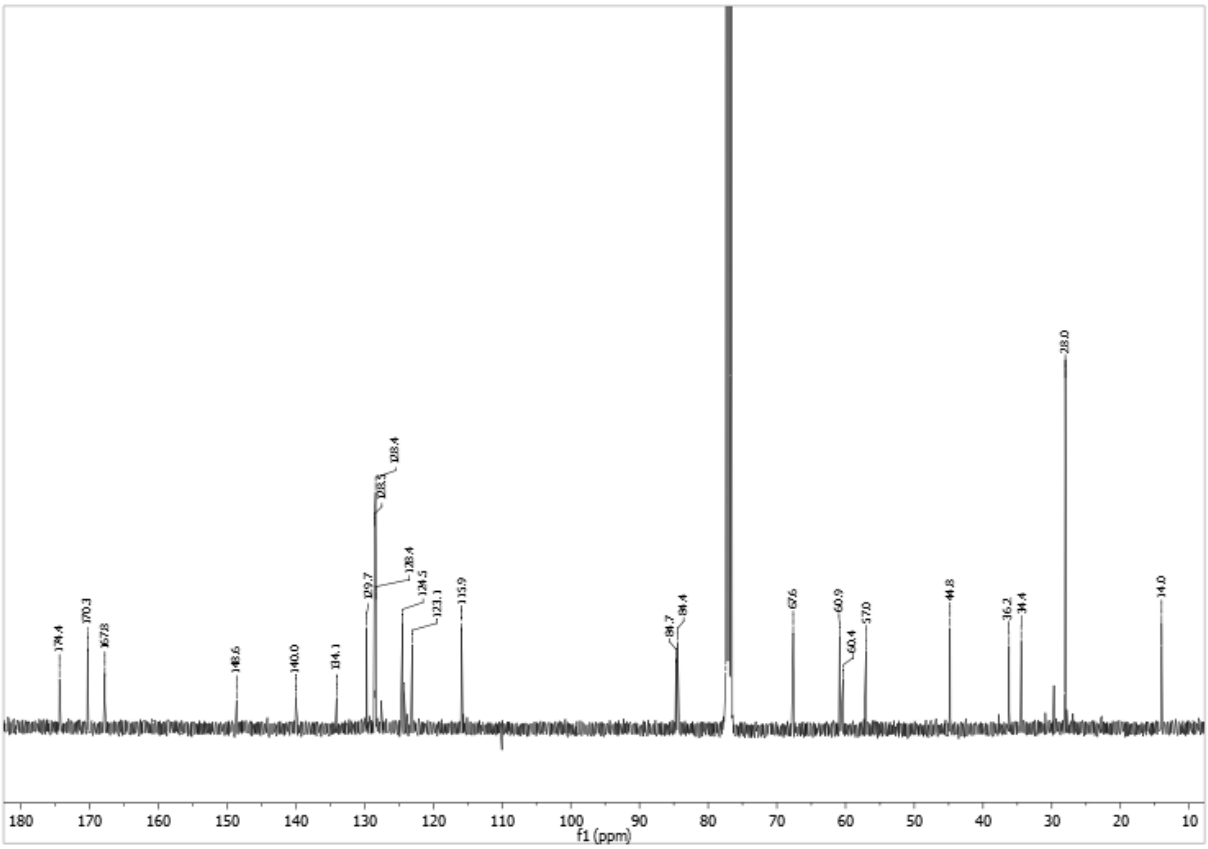
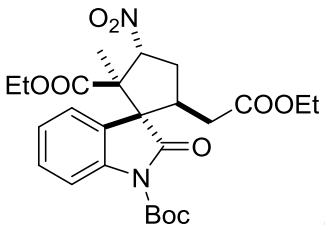
156.655
148.964
133.553
125.856
116.486
113.213
110.634
84.661
84.229
61.601
60.864
60.666
57.398
55.683
44.288
36.256
34.549
28.055
14.031
13.271
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
BnOOC
COOEt
O
N
Boc

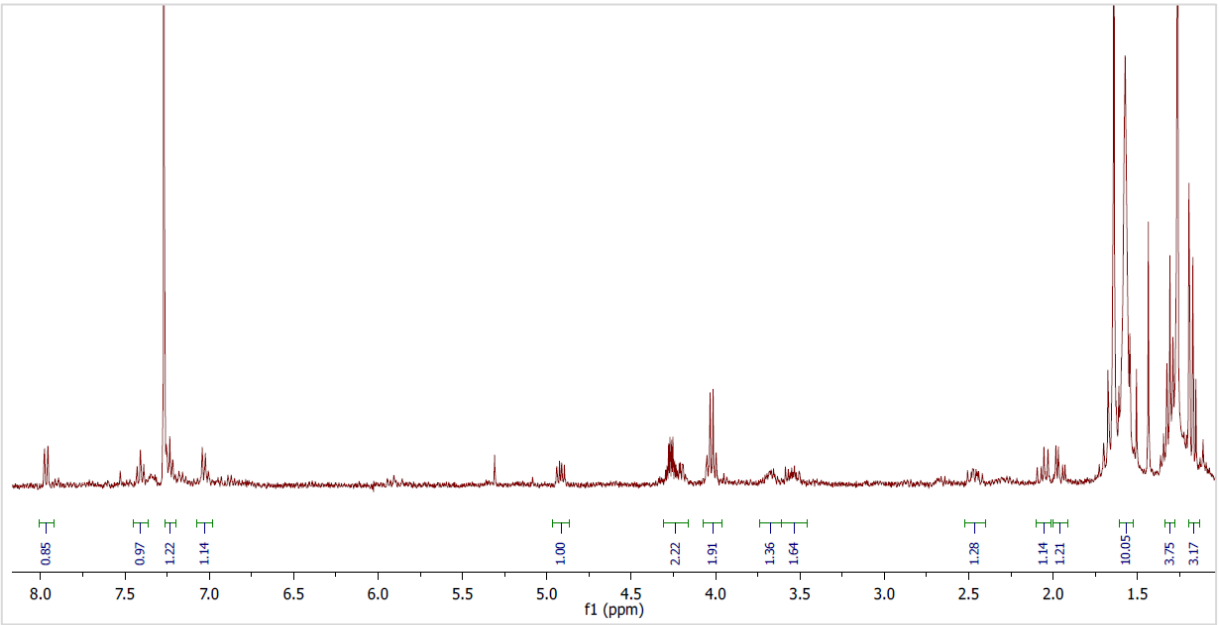
4d

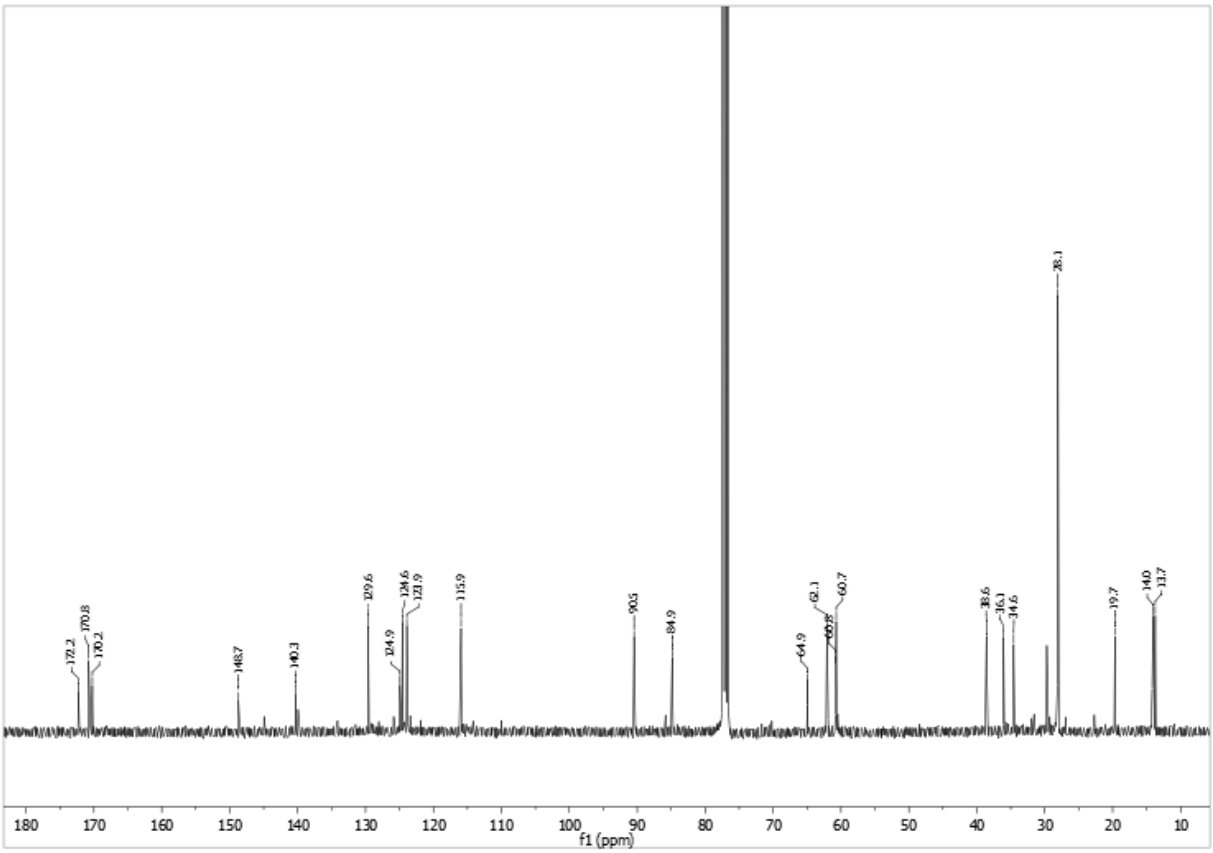

0.99
6.53
1.09
1.06
1.62
1.00
2.12
1.10
2.00
1.15
1.25
1.31
1.06
1.11
8.80
2.75
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

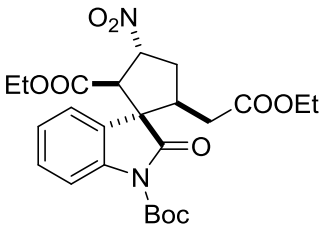

174.4
170.1
167.8
148.6
140.0
134.1
129.7
128.4
128.3
128.4
124.5
123.1
115.9
84.7
84.4
67.6
60.9
60.4
57.0
44.8
36.2
34.4
28.0
14.0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
COOEt
O
N
Boc

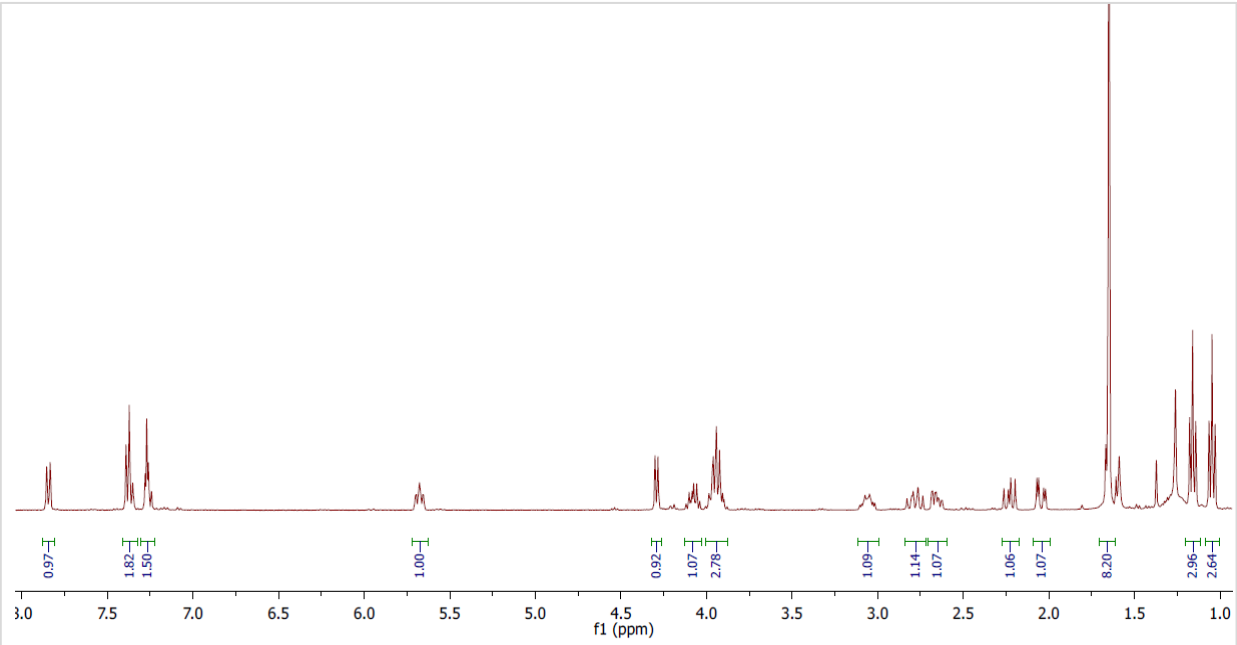
4e

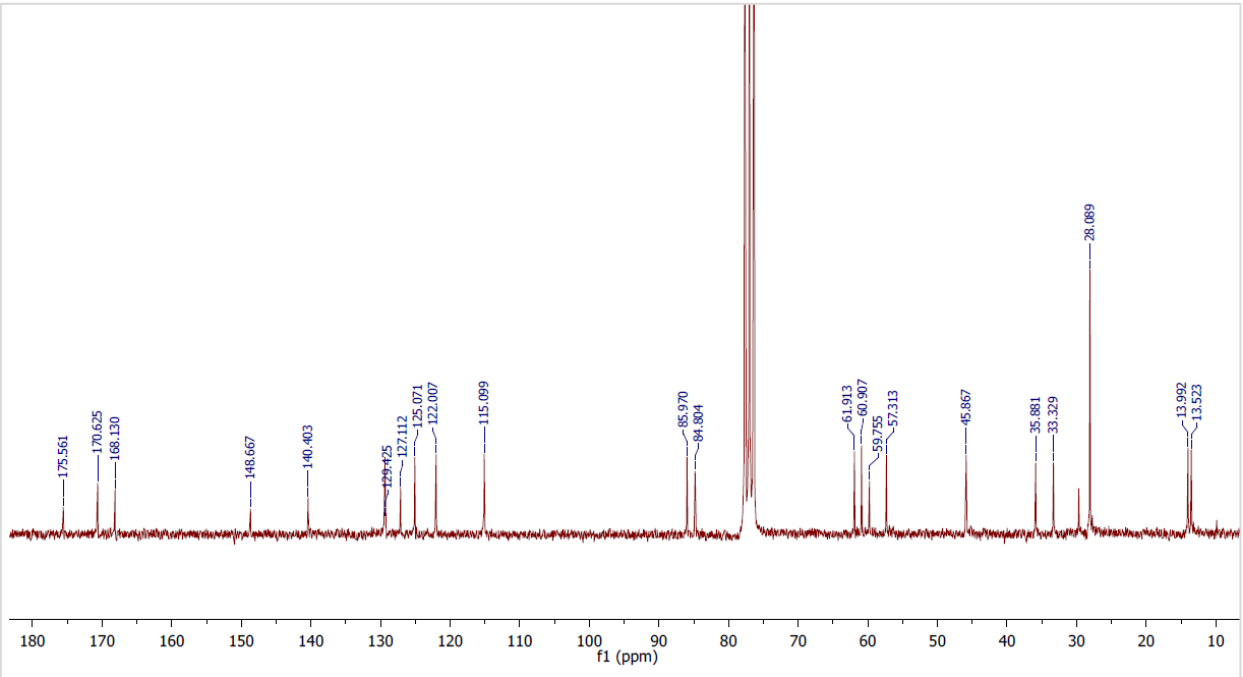

0.85
0.97
1.22
1.14
1.00
2.22
1.91
1.36
1.64
1.28
1.14
1.21
10.05
3.75
3.17
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

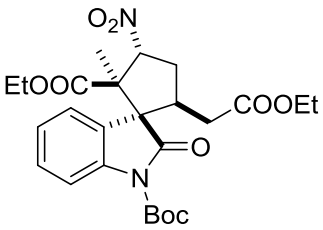

172.2
170.8
170.2
148.7
140.3
129.6
124.9
124.6
122.9
115.9
90.5
84.9
64.9
62.1
60.7
38.6
36.1
34.6
28.1
19.7
14.0
13.7
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
COOEt
O
N
Boc

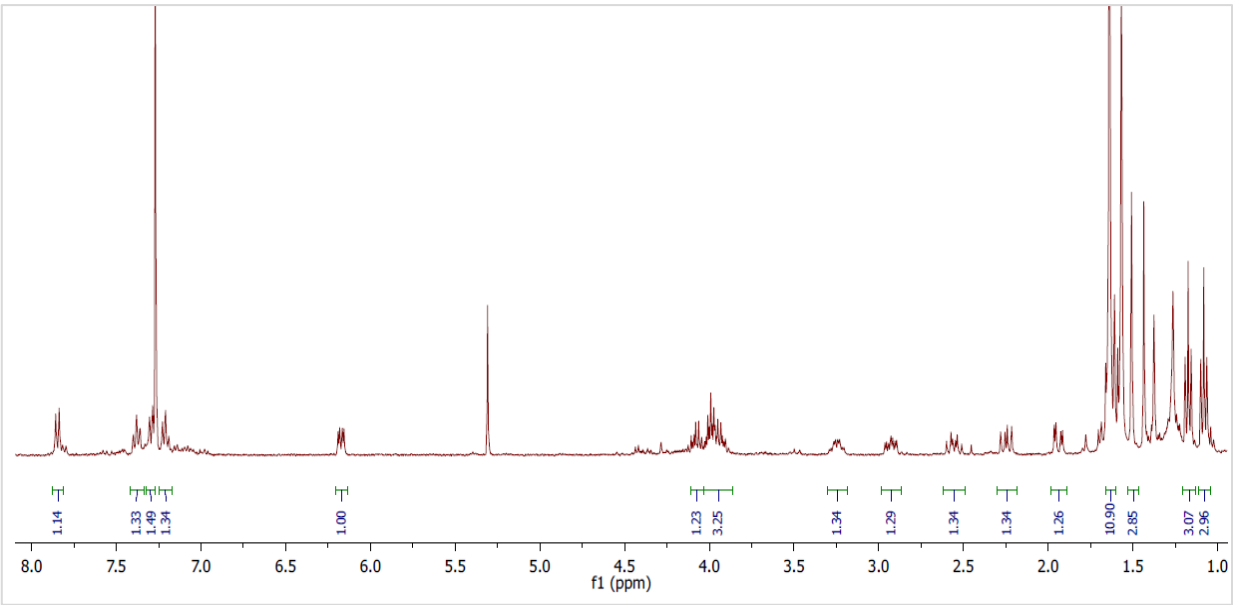
4f

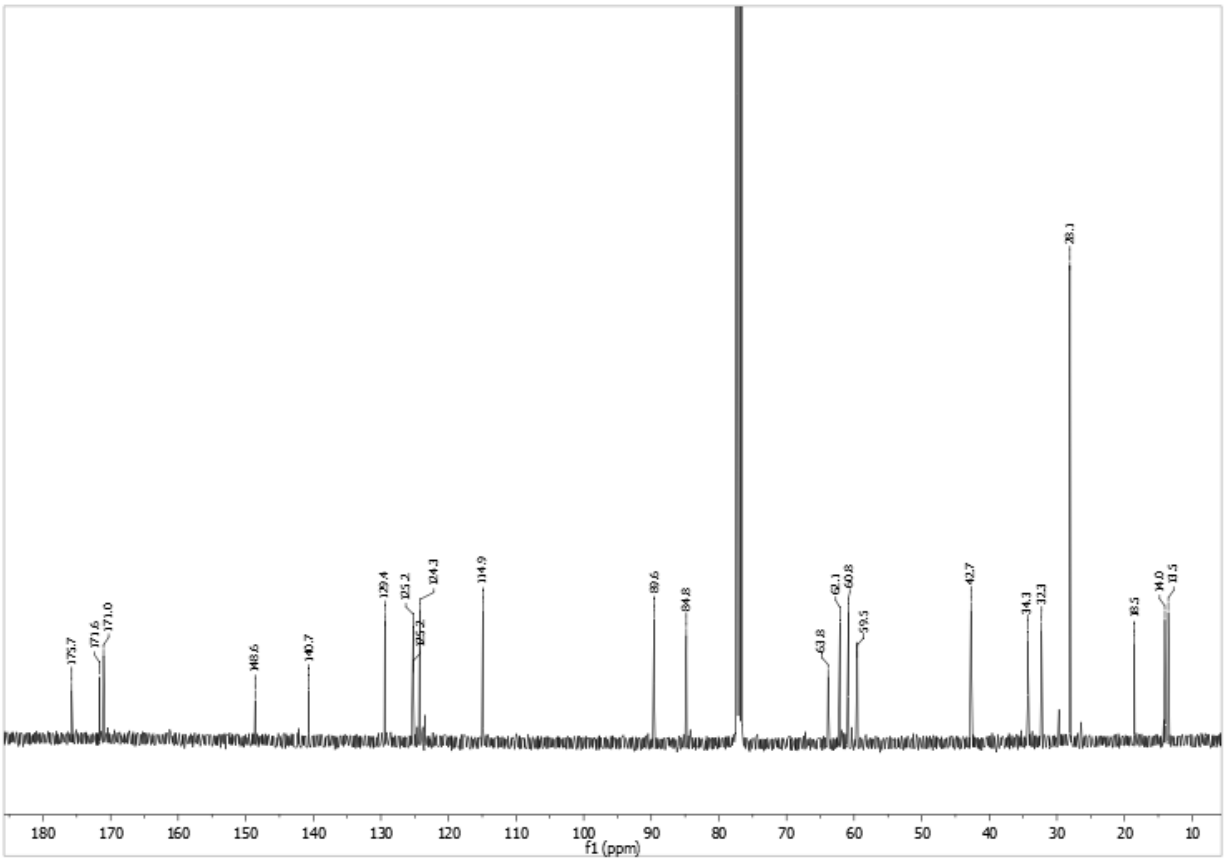

0.97
1.82
1.50
1.00
0.92
1.07
2.78
1.09
1.14
1.07
1.06
1.07
8.20
2.96
2.64
f1 (ppm)

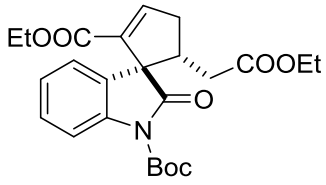

175.561
170.625
168.130
148.667
140.403
129.425
127.112
125.071
122.007
115.099
85.970
84.804
61.913
60.907
59.755
57.313
45.867
35.881
33.329
28.089
13.992
13.523
f1 (ppm)


O2N
EtOOC
COOEt
O
N
Boc

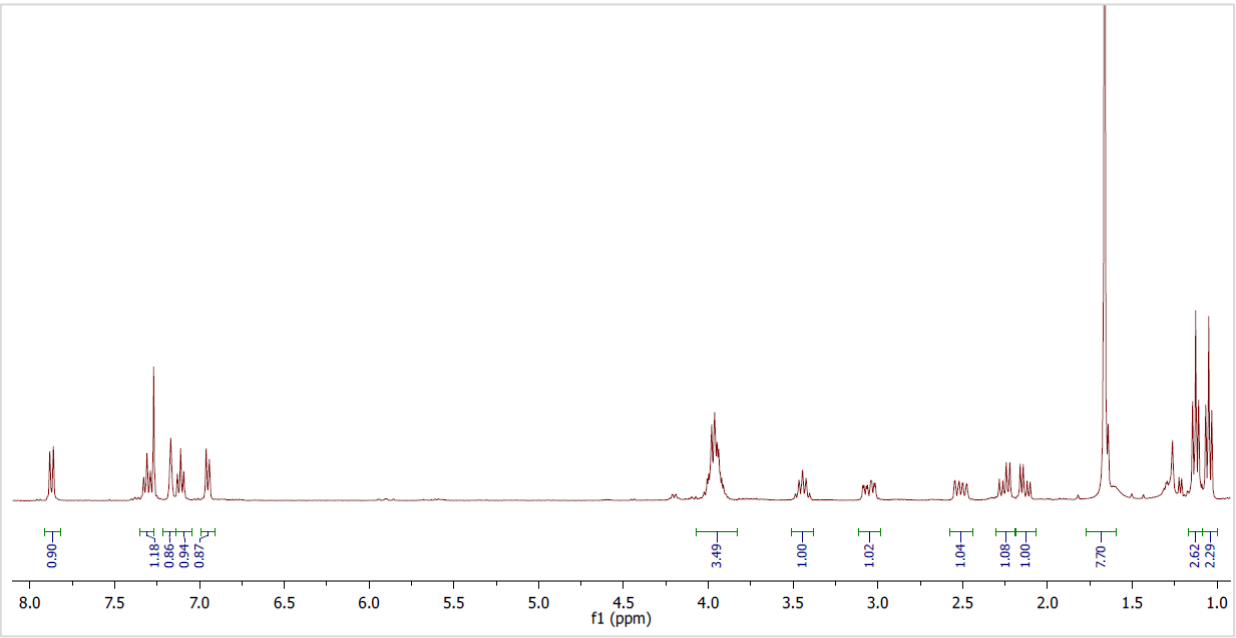
4g

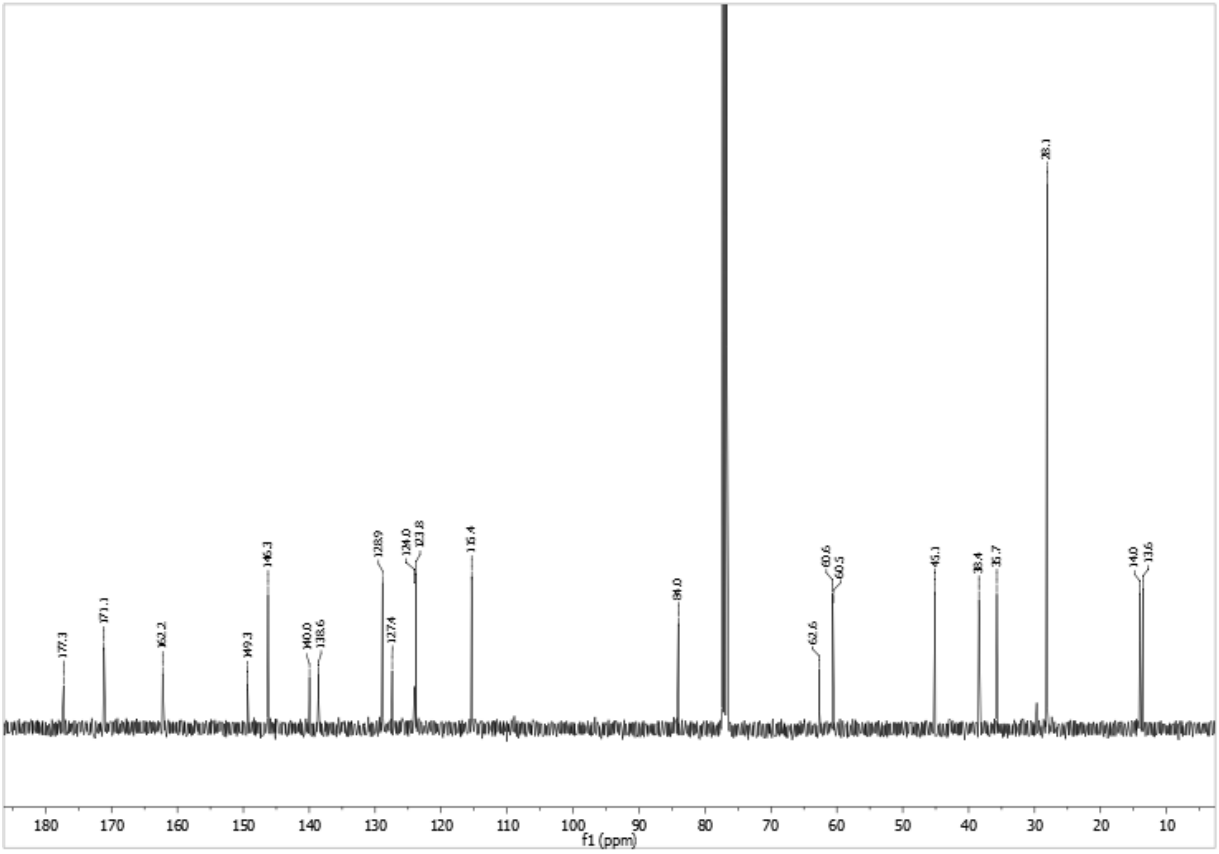

1.14
1.33
1.49
1.34
1.00
1.23
3.25
1.34
1.29
1.34
1.34
1.26
10.90
2.85
3.07
2.96
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

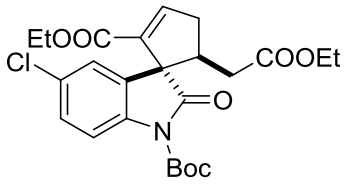

175.7
171.6
171.0
148.6
140.7
129.4
125.2
124.3
114.9
89.6
84.8
63.8
62.1
60.8
59.5
42.7
34.3
32.3
28.1
18.5
14.0
13.5
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


EtOOC
COOEt
O
N
Boc

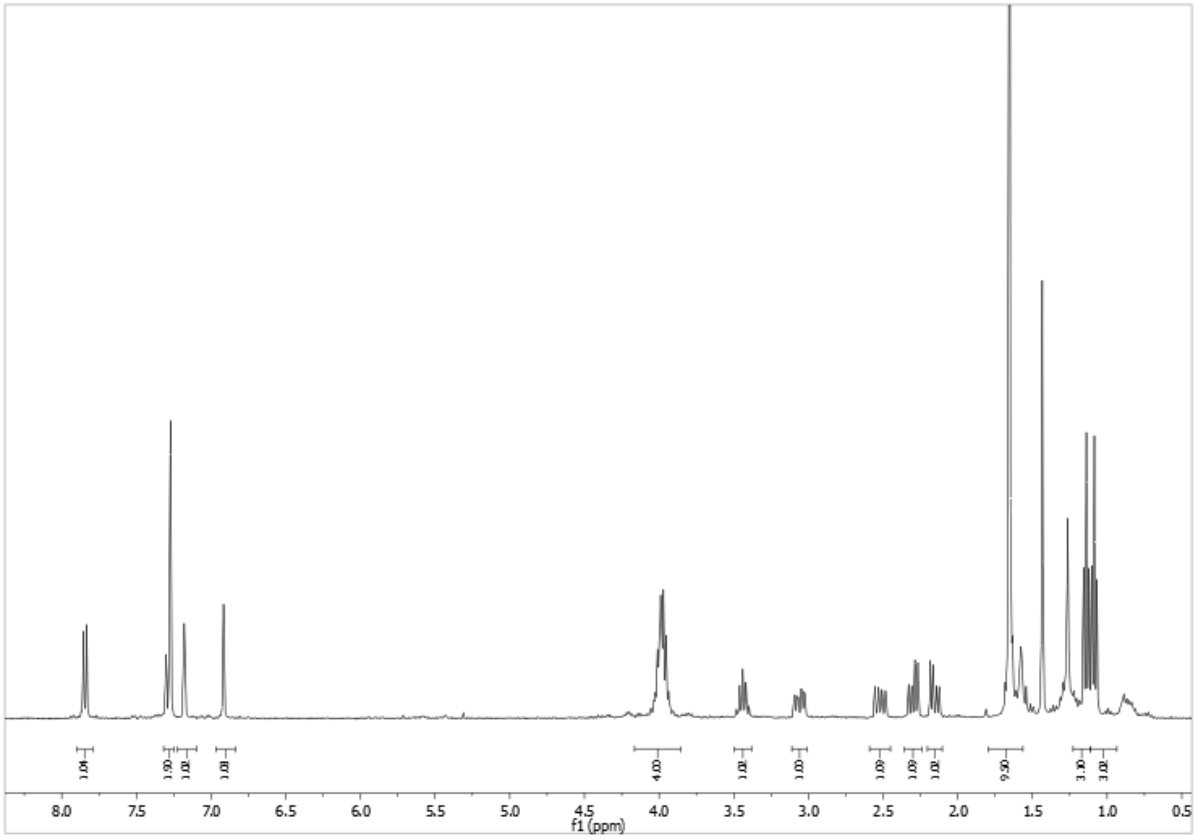
6a

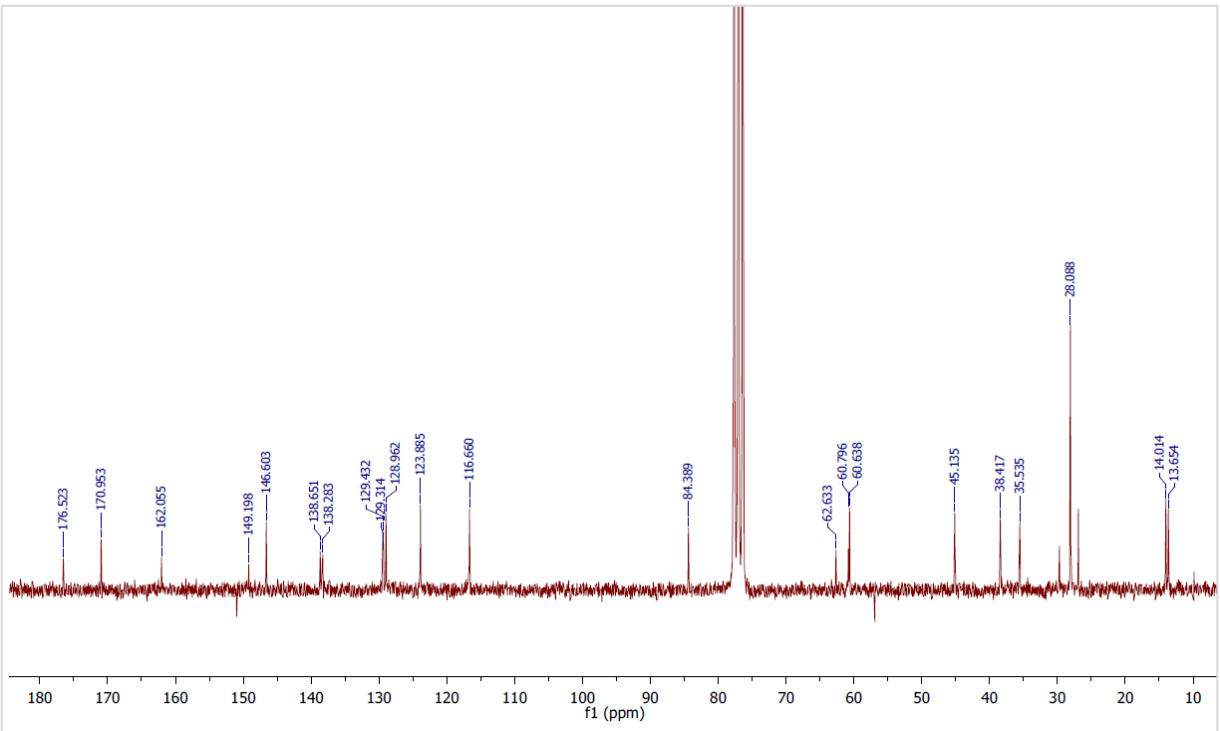

0.90
1.18
0.86
0.94
0.87
3.49
1.00
1.02
1.04
1.08
1.00
7.70
2.62
2.29
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

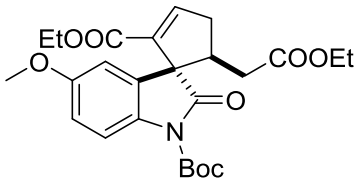

177.3
171.1
162.2
149.3
146.3
140.0
138.6
128.9
127.4
124.0
123.8
116.4
84.0
62.6
60.6
60.5
45.1
38.4
35.7
28.1
14.0
13.6
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


EtOOC
Cl
COOEt
O
N
Boc

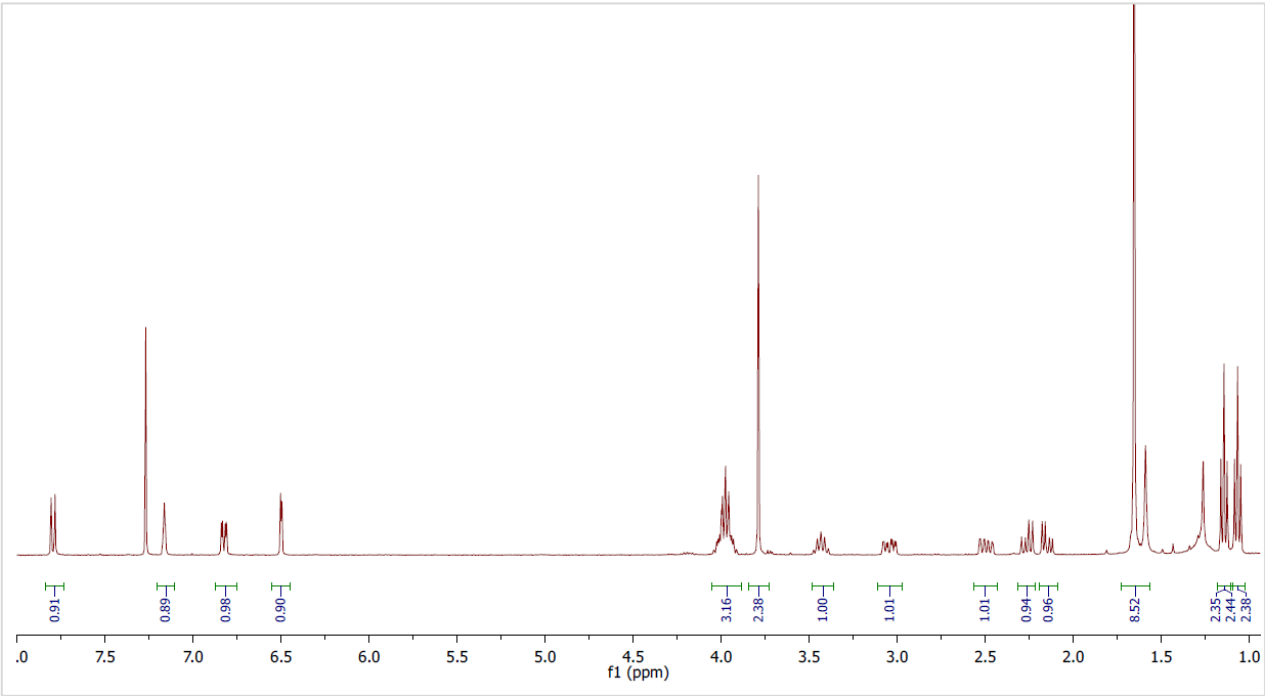
ent-**6b**

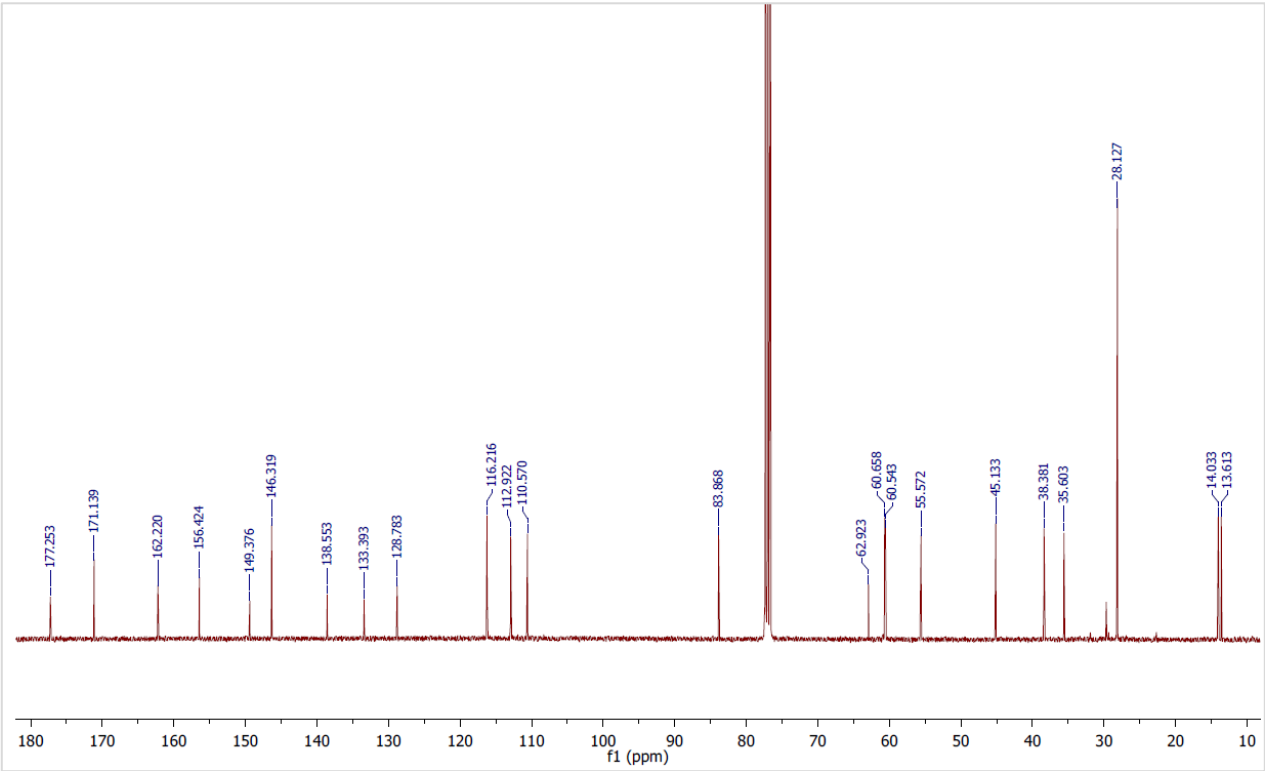

8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

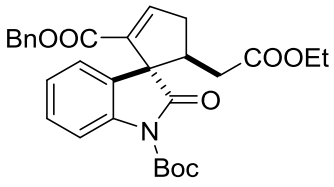

176.523
170.953
162.055
149.198
146.603
138.651
138.283
129.432
129.314
128.962
123.885
116.660
84.389
62.633
60.796
60.638
45.135
38.417
35.535
28.088
14.014
13.654
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


EtOOC
COOEt
O
O
N
Boc

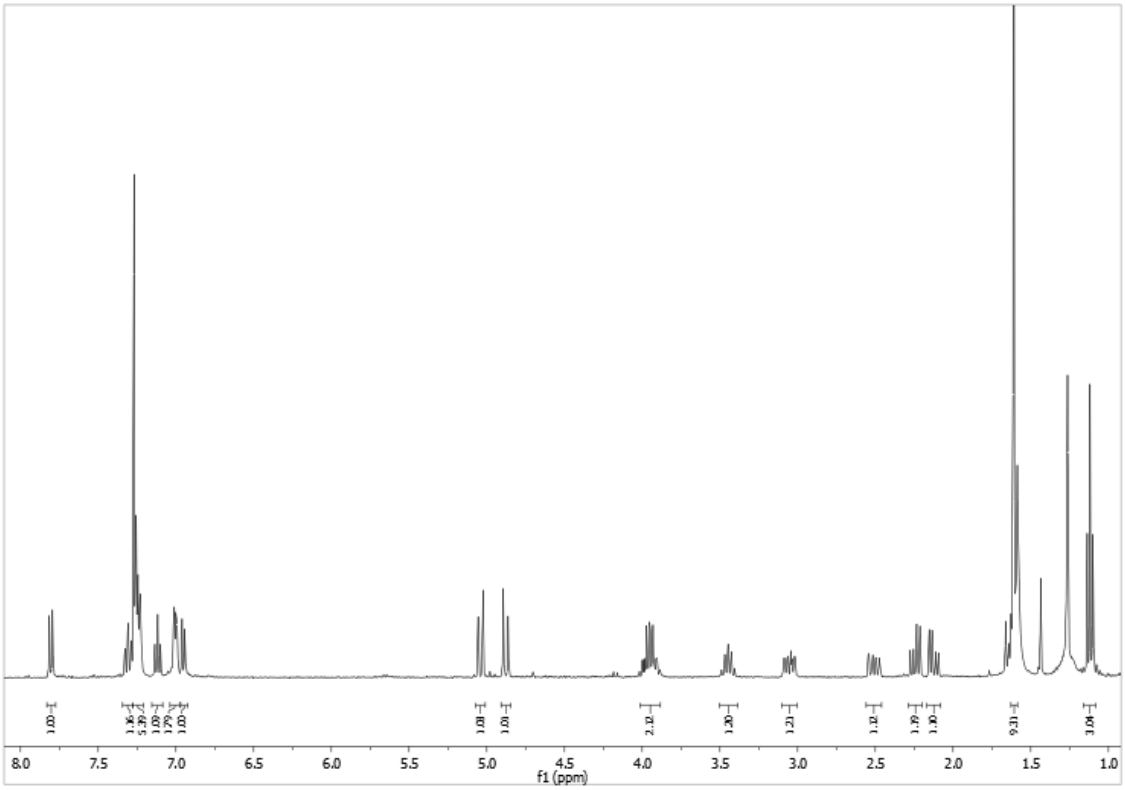
ent-**6c**

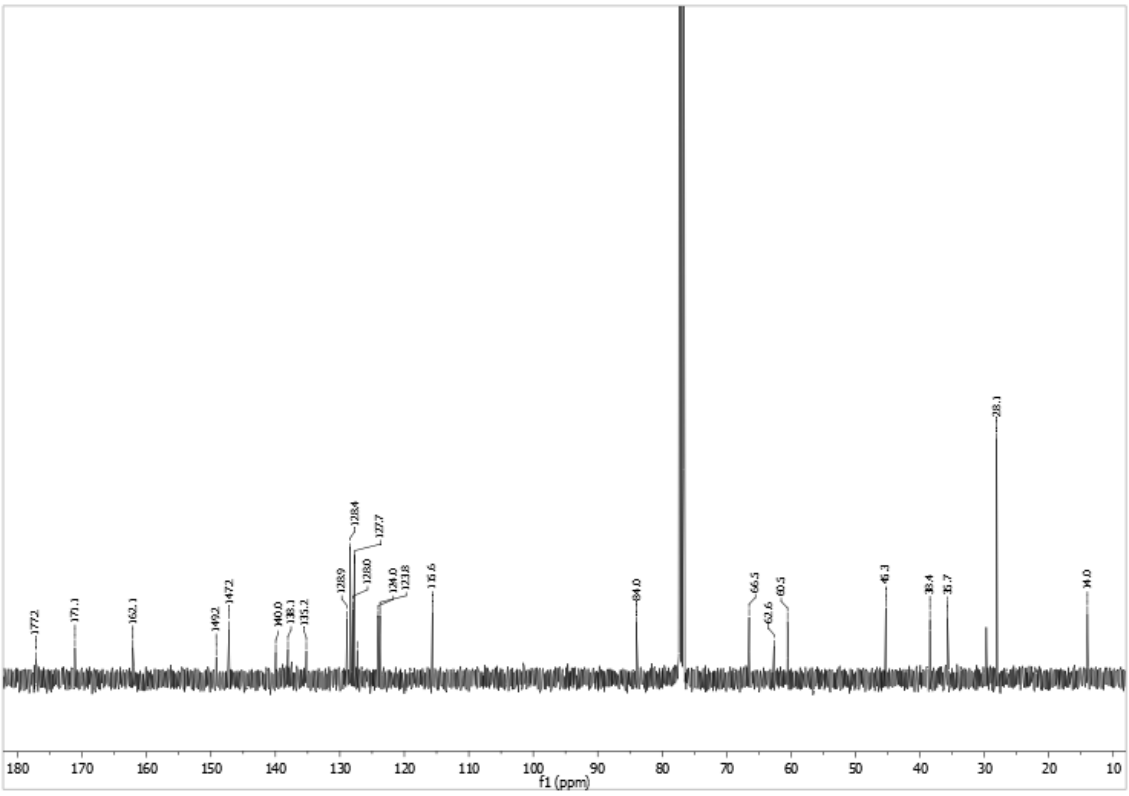

0.91
0.89
0.98
0.90
3.16
2.38
1.00
1.01
1.01
0.94
0.96
8.52
2.35
2.44
2.38
.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

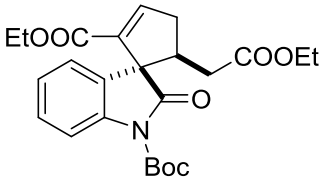

177.253
171.139
162.220
156.424
149.376
146.319
138.553
133.393
128.783
116.216
112.922
110.570
83.868
62.923
60.658
60.543
55.572
45.133
38.381
35.603
28.127
14.033
13.613
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



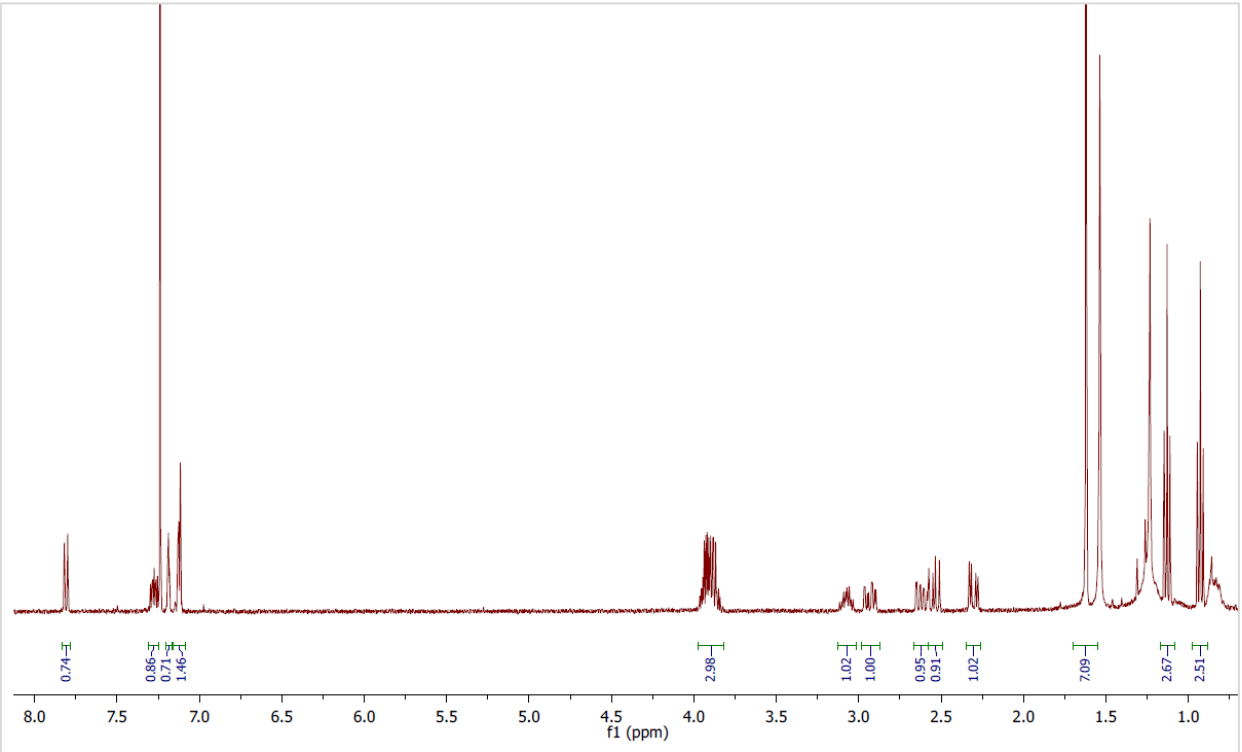
ent-**6d**

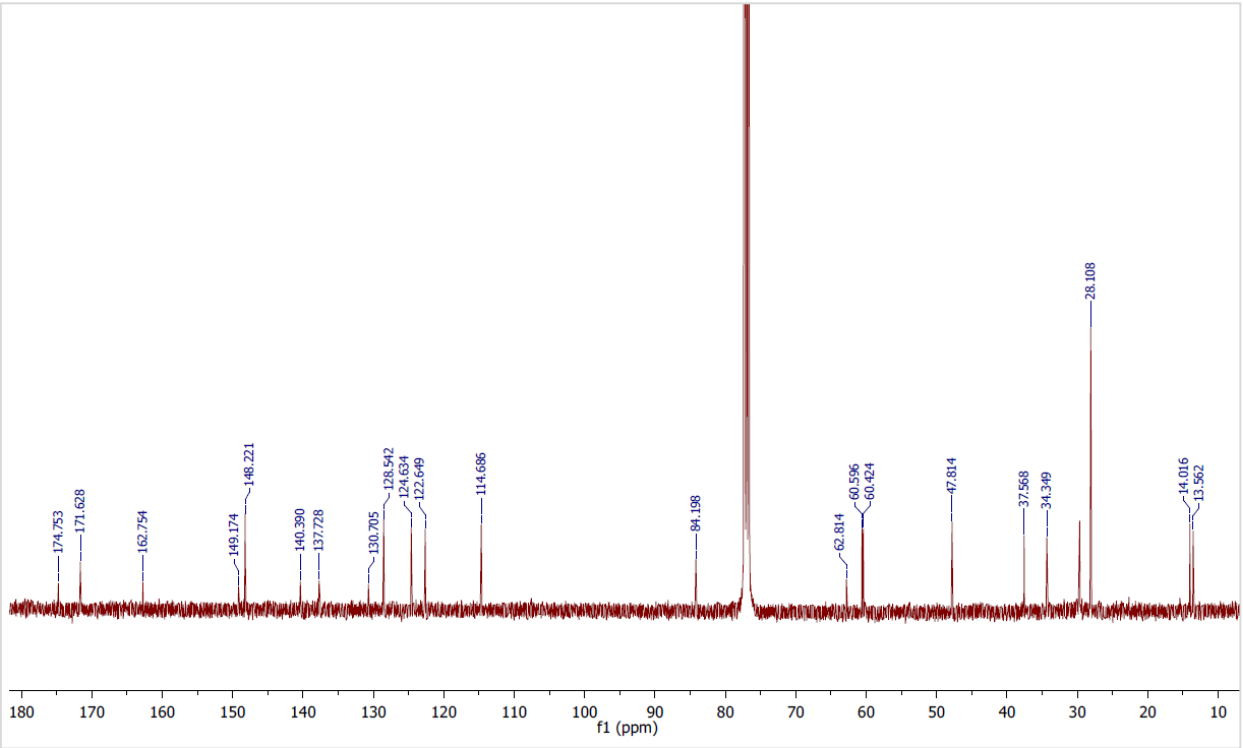


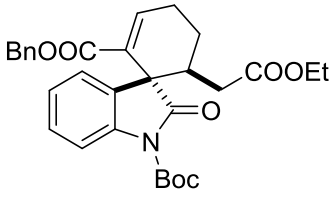



EtOOC
COOEt
O
N
Boc

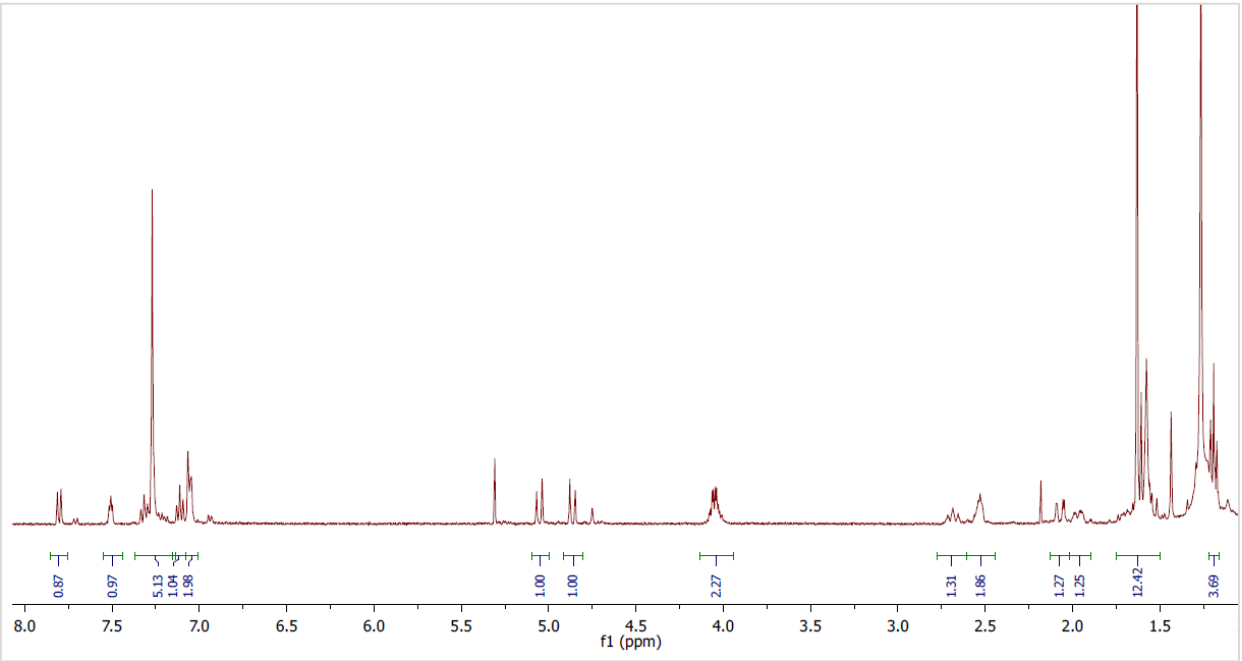
6f

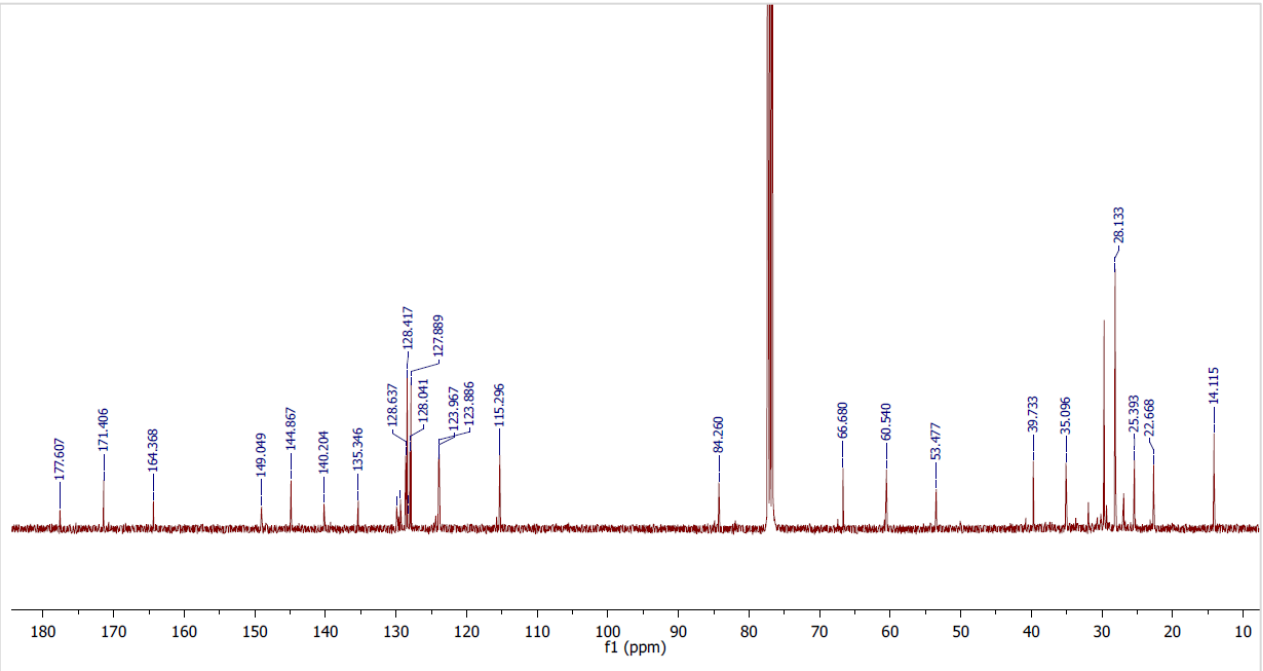

0.74
0.86
0.71
1.46
2.98
1.02
1.00
0.95
0.91
1.02
7.09
2.67
2.51
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

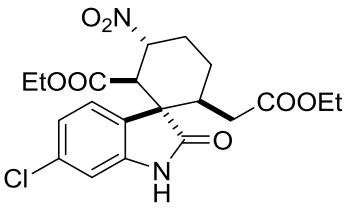

174.753
171.628
162.754
149.174
148.221
140.390
137.728
130.705
128.542
124.634
122.649
114.686
84.198
62.814
60.596
60.424
47.814
37.568
34.349
28.108
14.016
13.562
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


BnOOC
COOEt
O
N
Boc

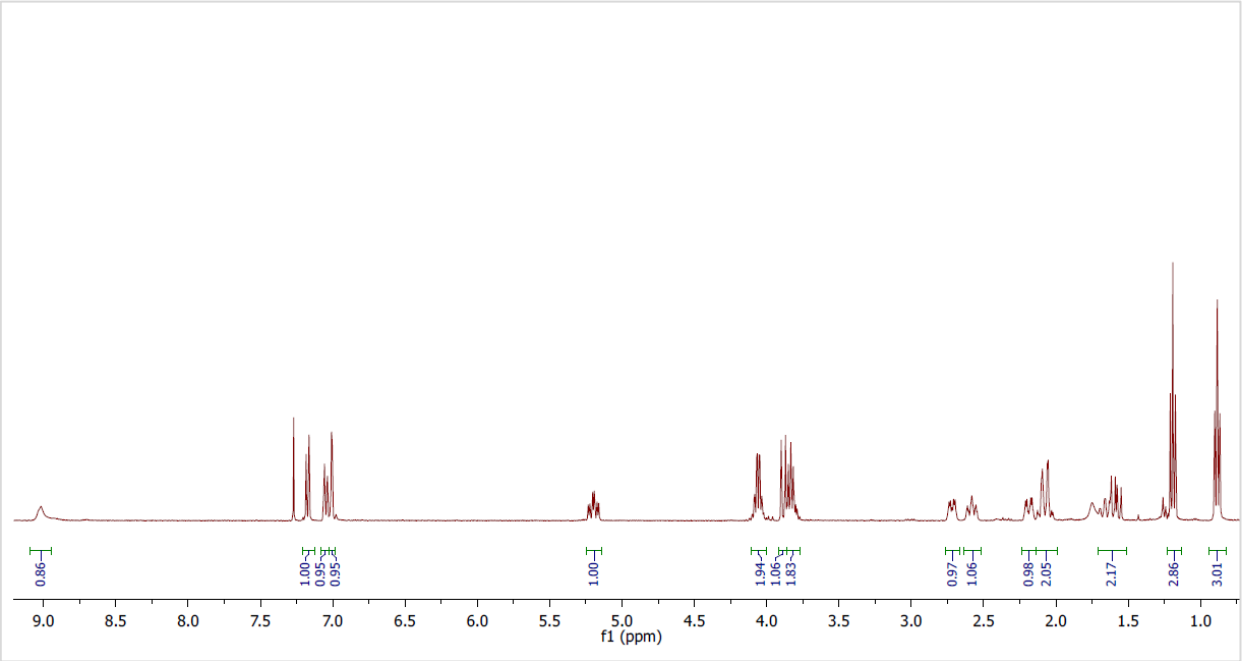
8

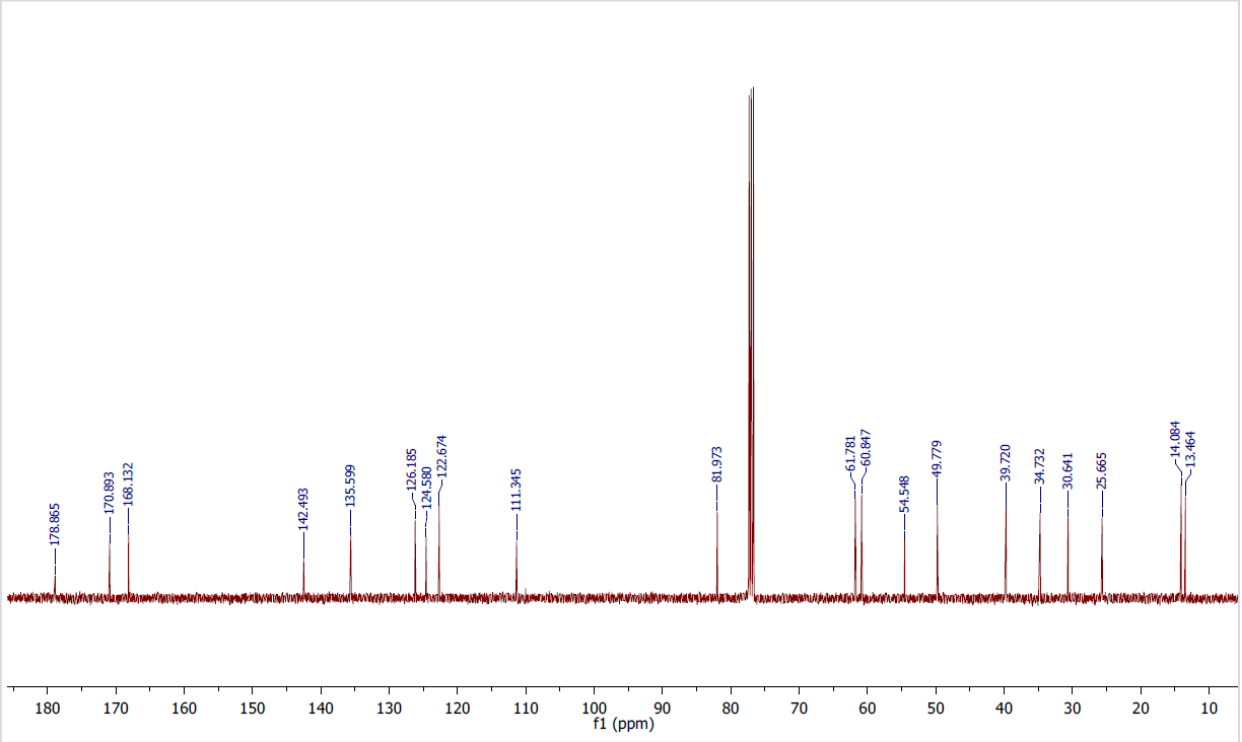

0.87
0.97
5.13
1.04
1.98
1.00
1.00
2.27
1.31
1.86
1.27
1.25
12.42
3.69
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

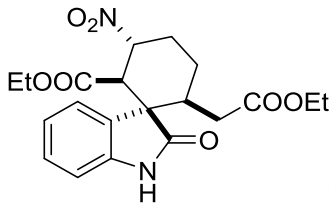

177.607
171.406
164.368
149.049
144.867
140.204
135.346
128.637
128.417
128.041
127.889
123.967
123.886
115.296
84.260
66.680
60.540
53.477
39.733
35.096
28.133
25.393
22.668
14.115
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
COOEt
O
Cl
N
H

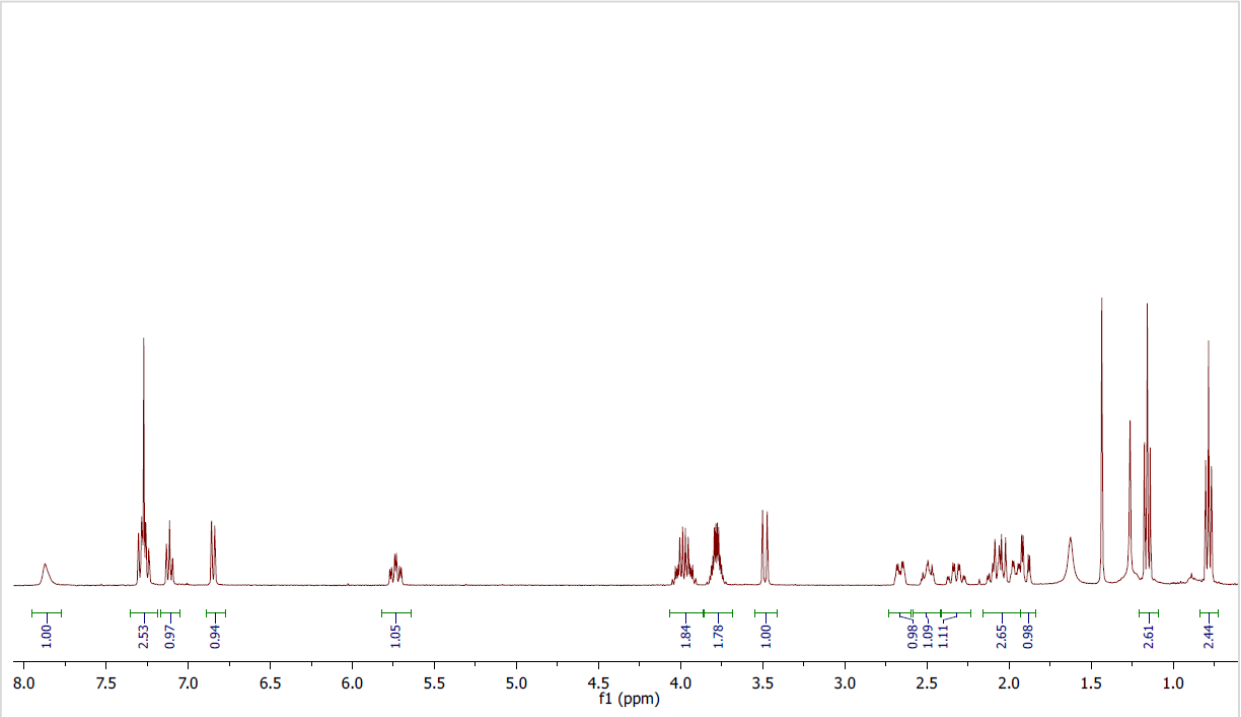
7a

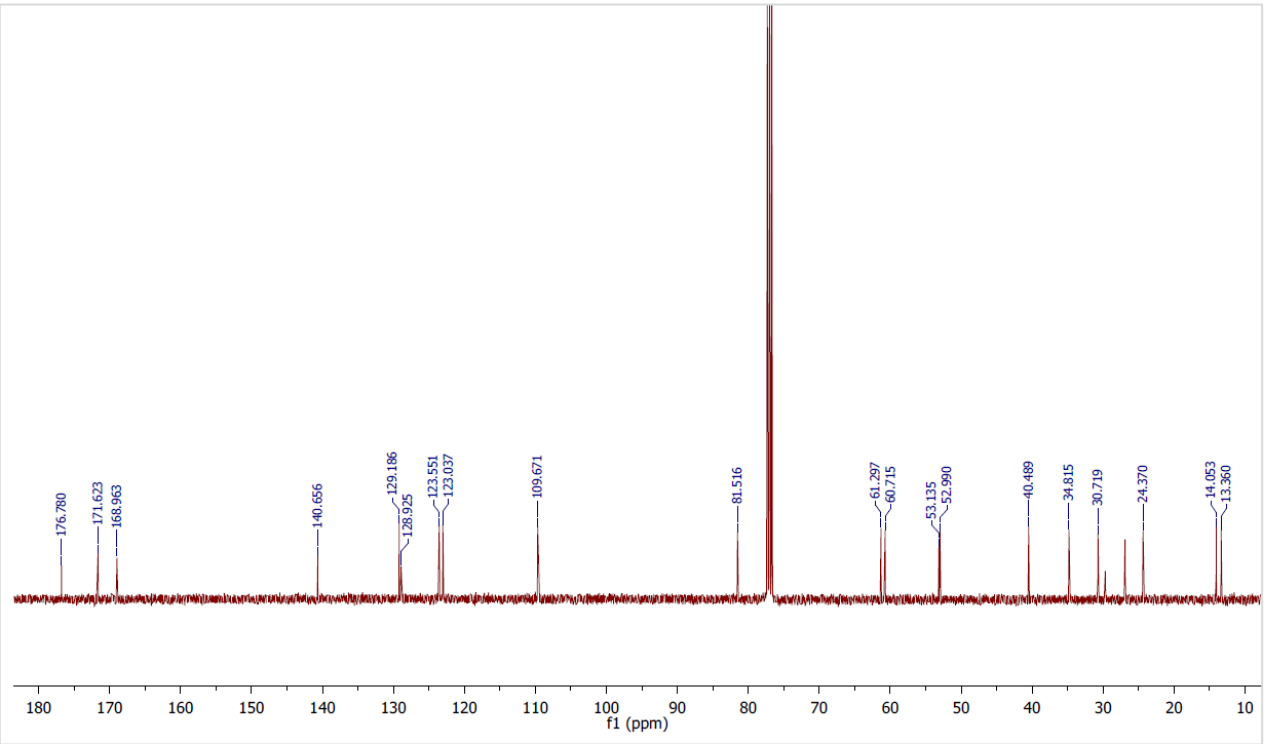

0.86
1.00
0.95
0.95
1.00
1.94
1.06
1.83
0.97
1.06
0.98
2.05
2.17
2.86
3.01
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)

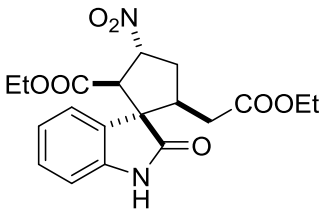

178.865
170.893
168.132
142.493
135.599
126.185
124.580
122.674
111.345
81.973
61.781
60.847
54.548
49.779
39.720
34.732
30.641
25.665
14.084
13.464
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


O2N
EtOOC
COOEt
O
N
H

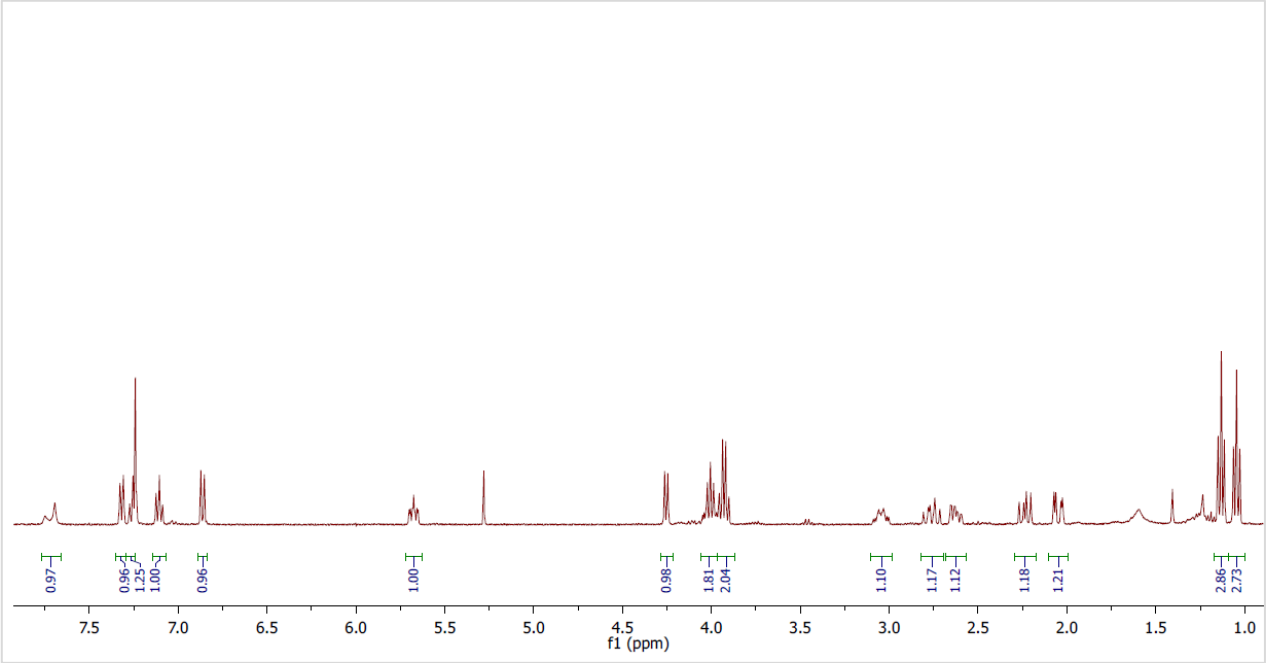
7b

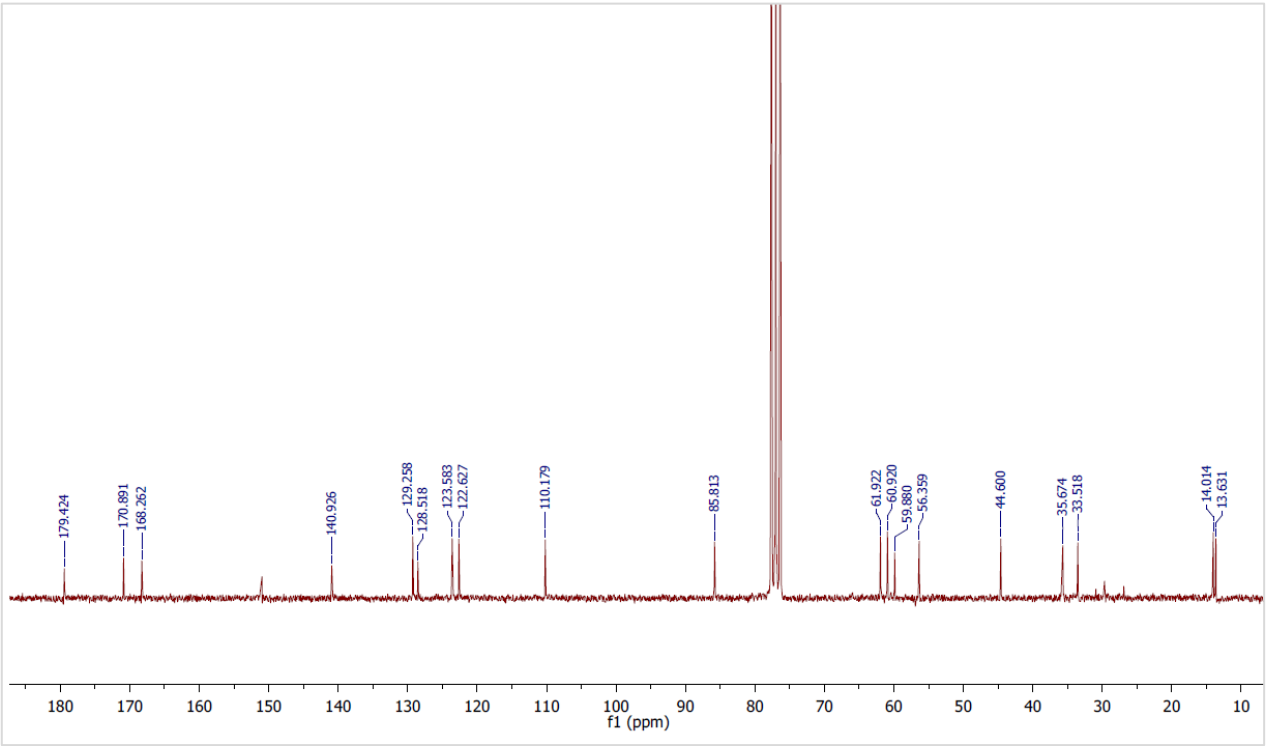

1.00
2.53
0.97
0.94
1.05
1.84
1.78
1.00
0.98
1.09
1.11
2.65
0.98
2.61
2.44
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

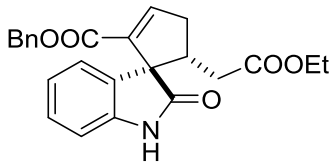

176.780
171.623
168.963
140.656
129.186
128.925
123.551
123.037
109.671
81.516
61.297
60.715
53.135
52.990
40.489
34.815
30.719
24.370
14.053
13.360
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtOOC
COOEt
O
N
H

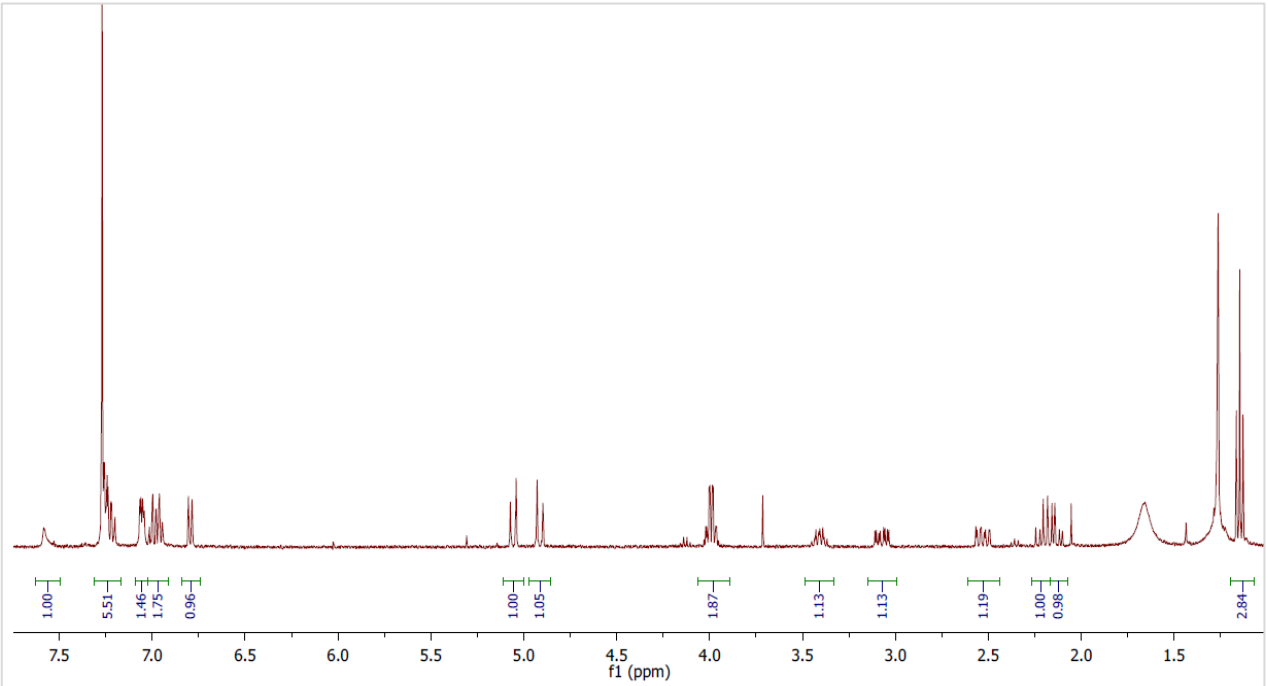
7c

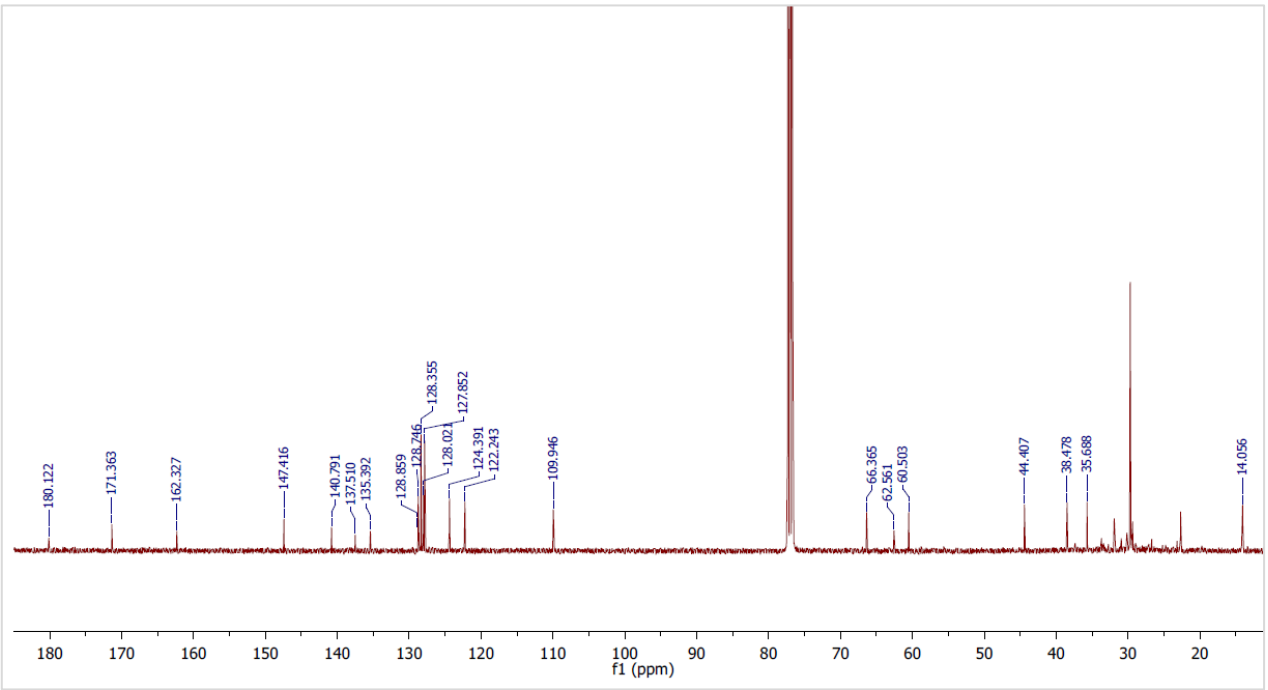

0.97
0.96
1.25
1.00
0.96
1.00
0.98
1.81
2.04
1.10
1.17
1.12
1.18
1.21
2.86
2.73
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

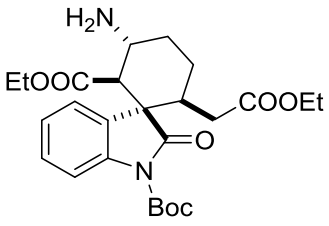

179.424
170.891
168.262
140.926
129.258
128.518
123.583
122.627
110.179
85.813
61.922
60.920
59.880
56.359
44.600
35.674
33.518
14.014
13.631
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


BnOOC
COOEt
O
N
H

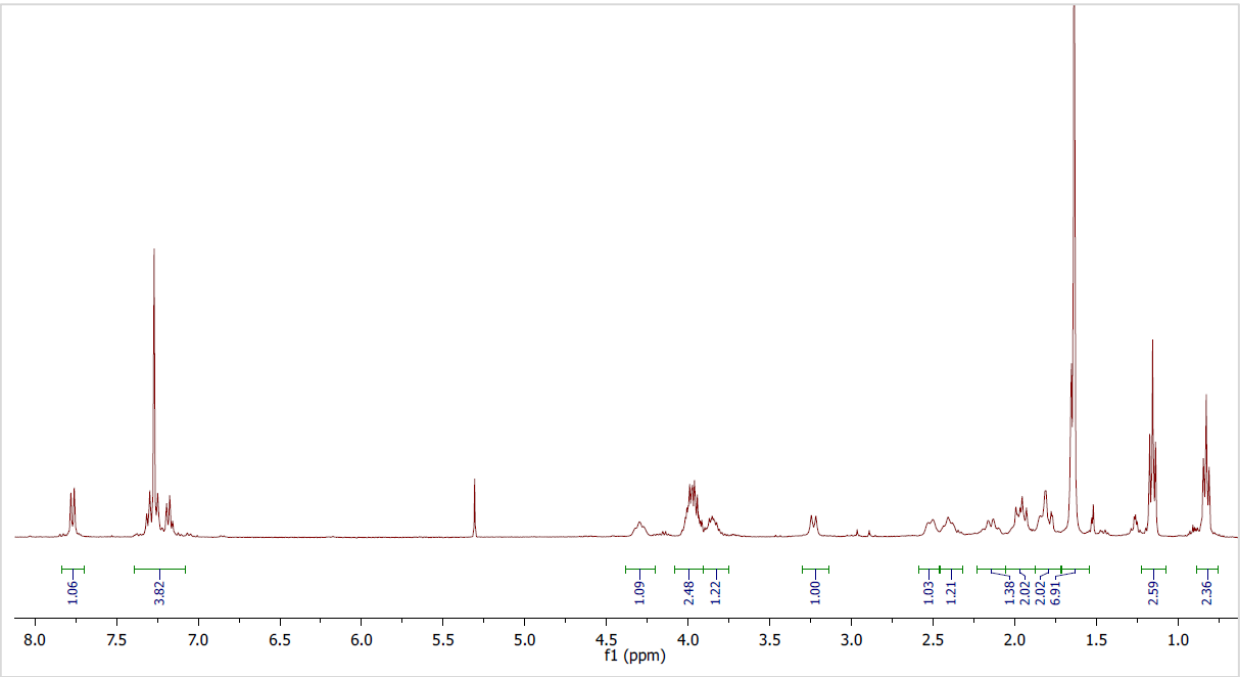
7d

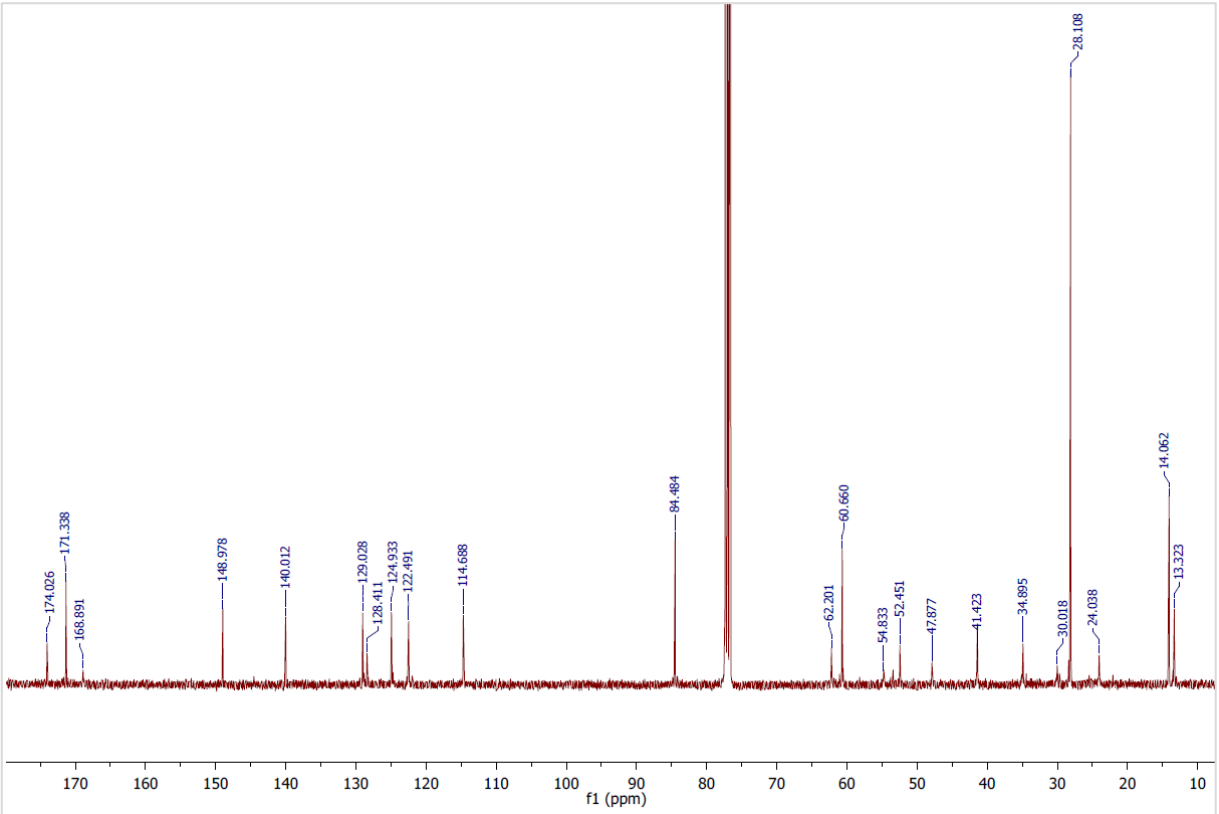

1.00
5.51
1.46
1.75
0.96
1.00
1.05
1.87
1.13
1.13
1.19
1.00
0.98
2.84
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
f1 (ppm)

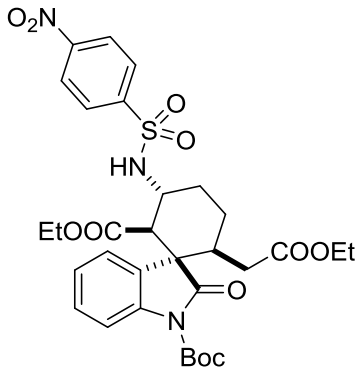

180.122
171.363
162.327
147.416
140.791
137.510
135.392
128.859
128.746
128.355
128.021
127.852
124.391
122.243
109.946
66.365
62.561
60.503
44.407
38.478
35.688
14.056
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
f1 (ppm)


H2N
EtOOC
COOEt
O
N
Boc

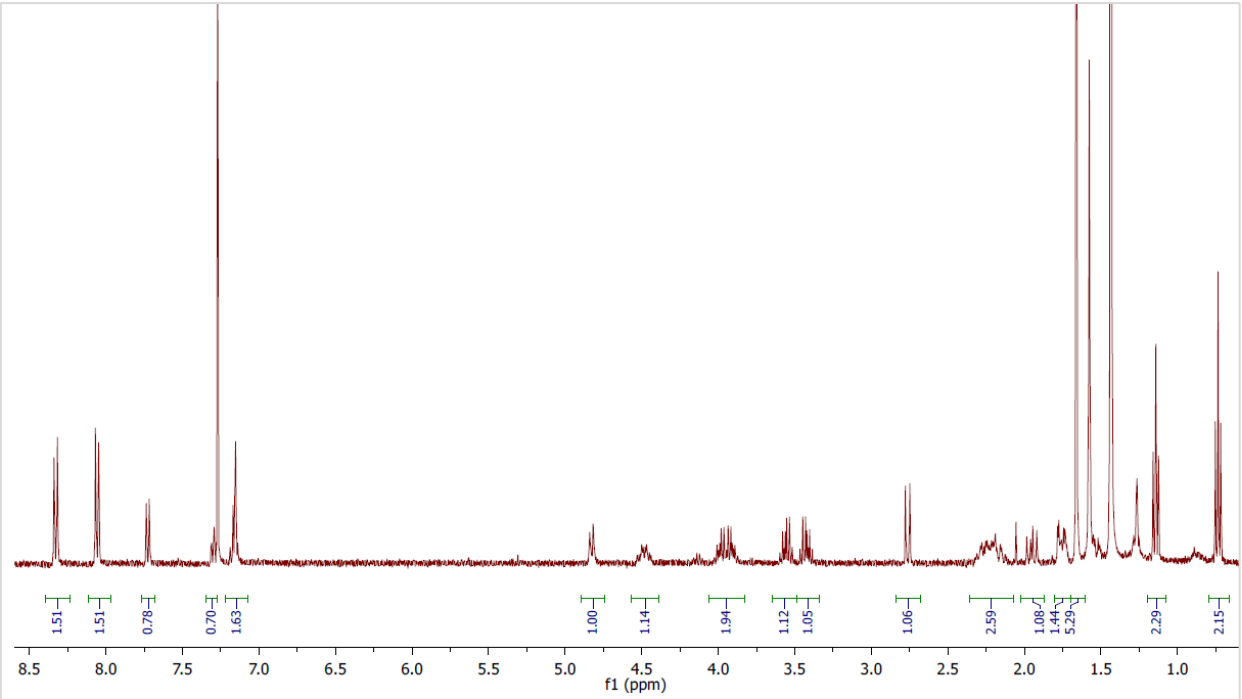
10

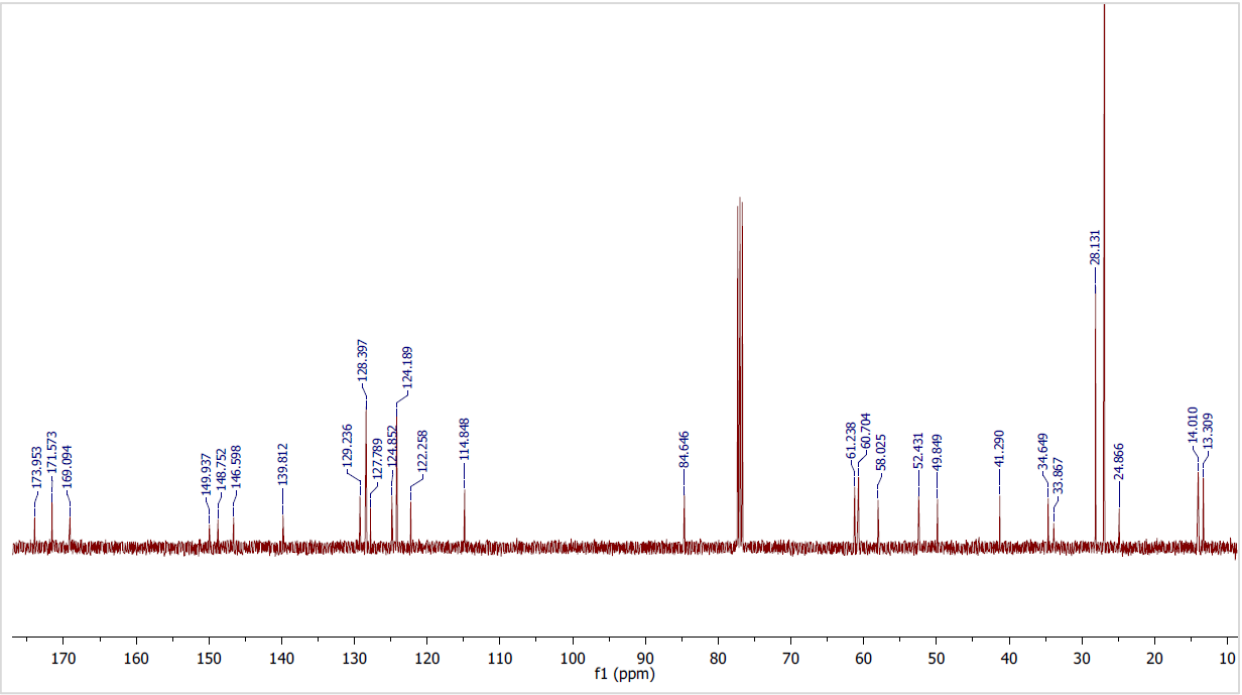

1.06
3.82
1.09
2.48
1.22
1.00
1.03
1.21
1.38
2.02
2.02
6.91
2.59
2.36
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

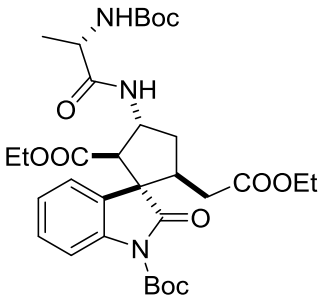

174.026
171.338
168.891
148.978
140.012
129.028
128.411
124.933
122.491
114.688
84.484
62.201
60.660
54.833
52.451
47.877
41.423
34.895
30.018
28.108
24.038
14.062
13.323
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
O
S
O
HN
EtOOC
COOEt
O
N
Boc

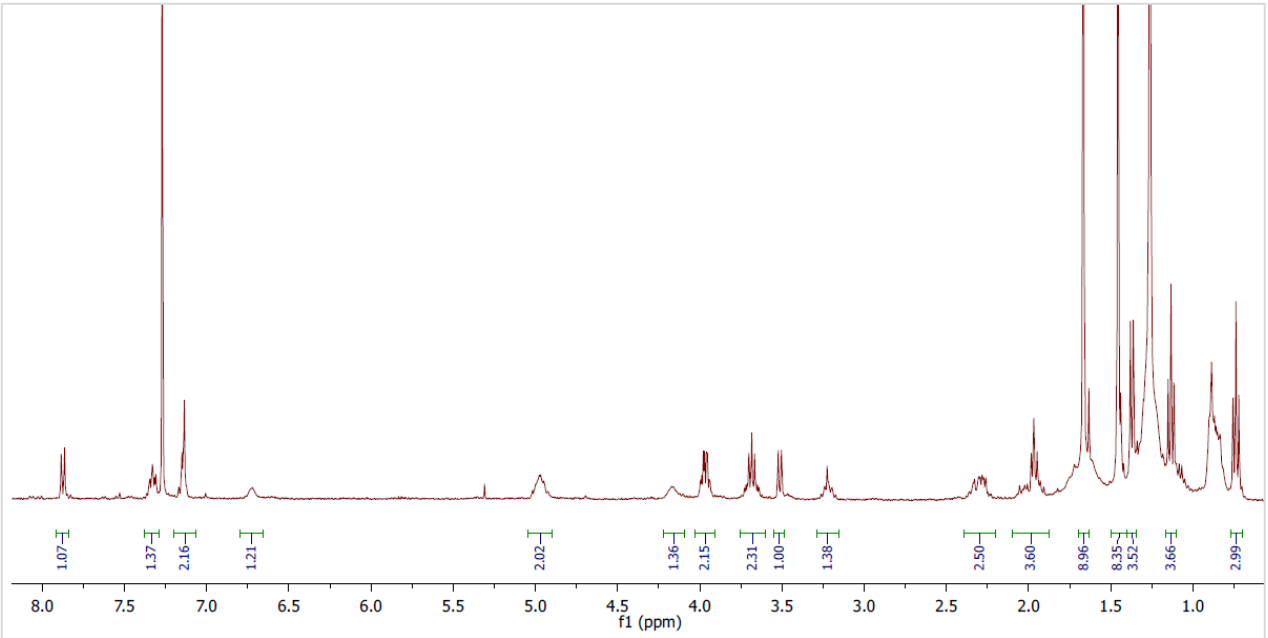
11a

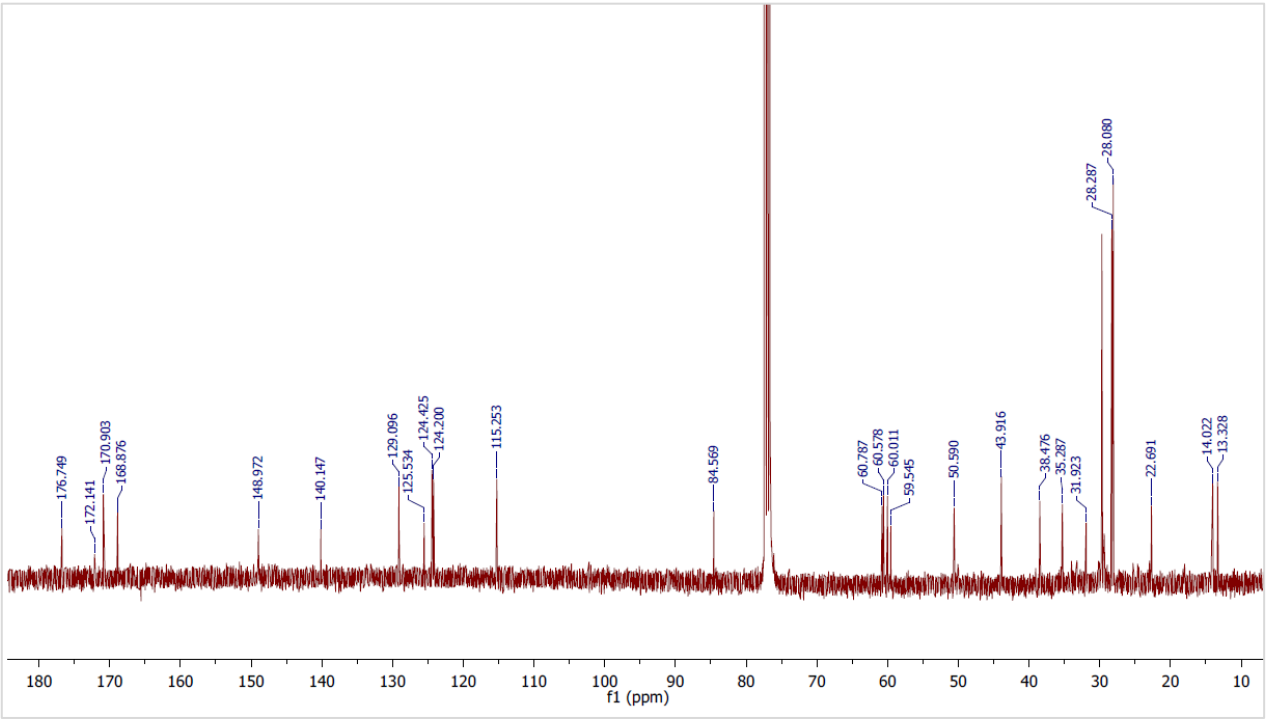

1.51
1.51
0.78
0.70
1.63
1.00
1.14
1.94
1.12
1.05
1.06
2.59
1.08
1.44
5.29
2.29
2.15
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

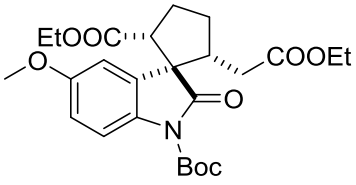

173.953
171.573
169.094
149.937
148.752
146.598
139.812
129.236
128.397
127.789
124.852
124.189
122.258
114.848
84.646
61.238
60.704
58.025
52.431
49.849
41.290
34.649
33.867
28.131
24.866
14.010
13.309
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


NHBoc
NH
O
EtOOC
COOEt
O
N
Boc

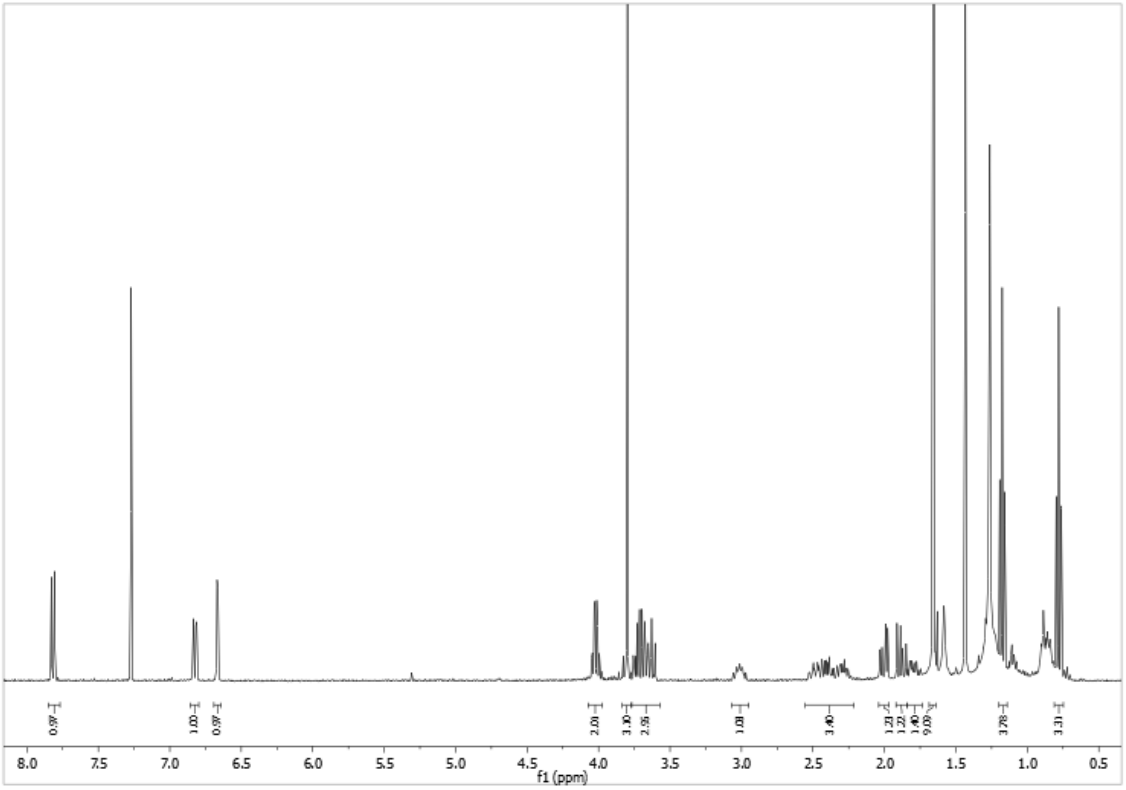
11b

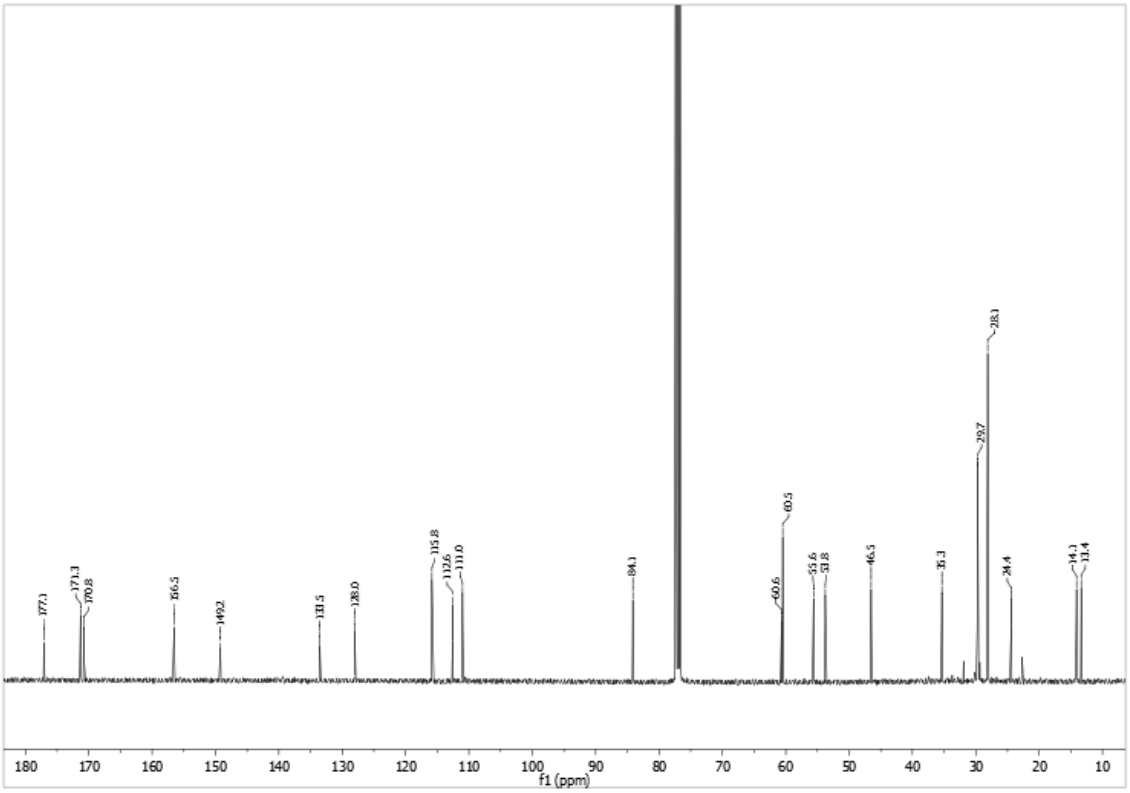

1.07
1.37
2.16
1.21
2.02
1.36
2.15
2.31
1.00
1.38
2.50
3.60
8.96
8.35
3.52
3.66
2.99
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

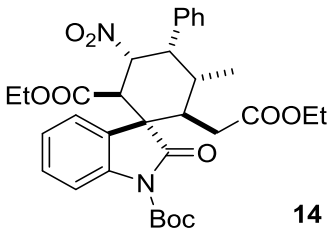

176.749
172.141
170.903
168.876
148.972
140.147
129.096
125.534
124.425
124.200
115.253
84.569
60.787
60.578
60.011
59.545
50.590
43.916
38.476
35.287
31.923
28.287
28.080
22.691
14.022
13.328
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)



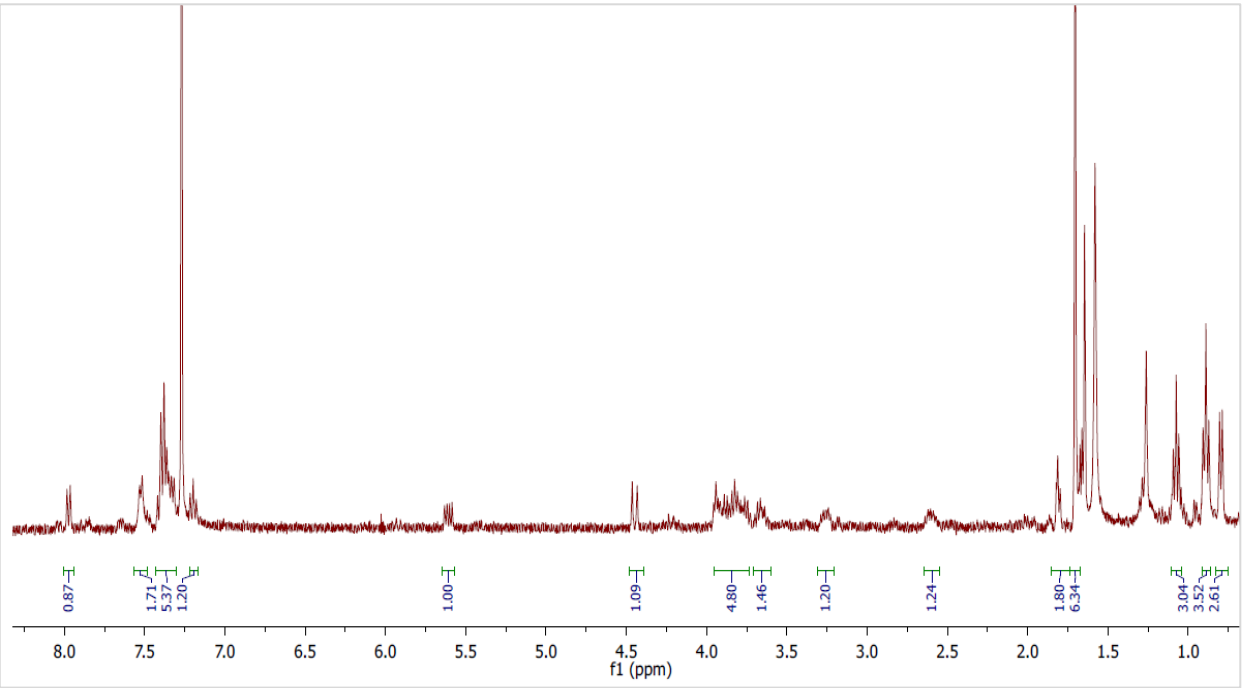
12

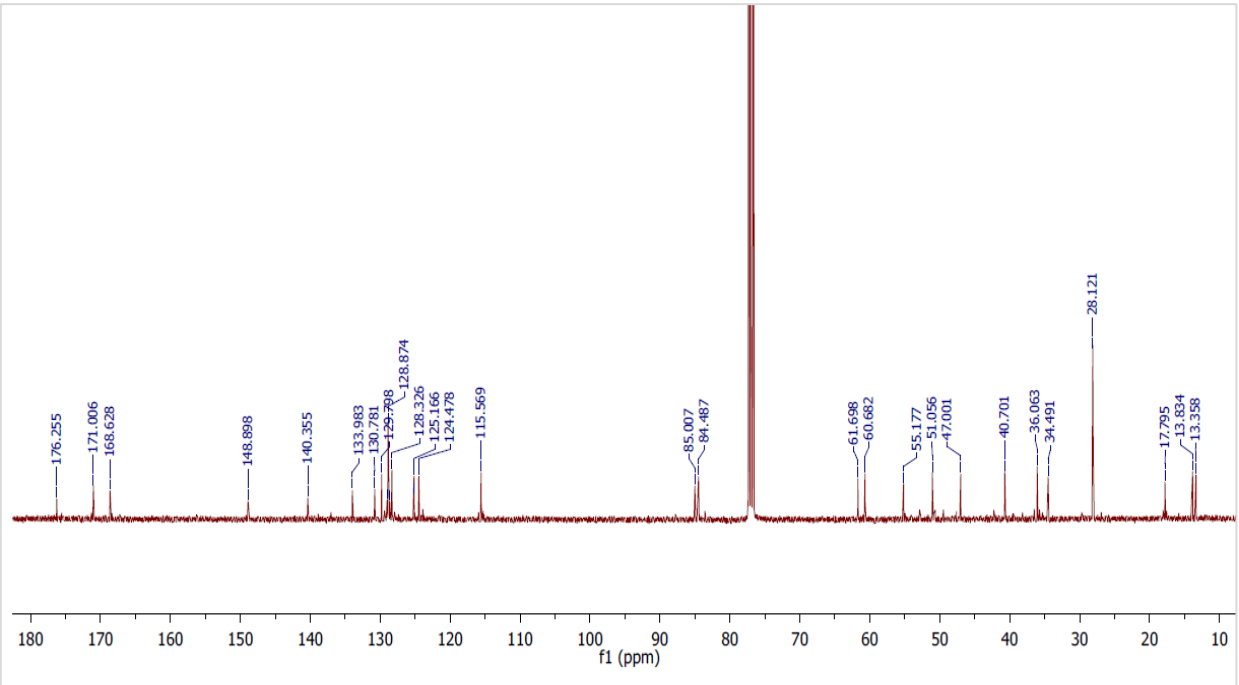


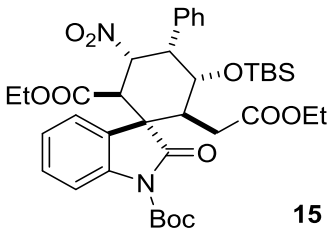



O2N
Ph
EtOOC
COOEt
O
N
Boc

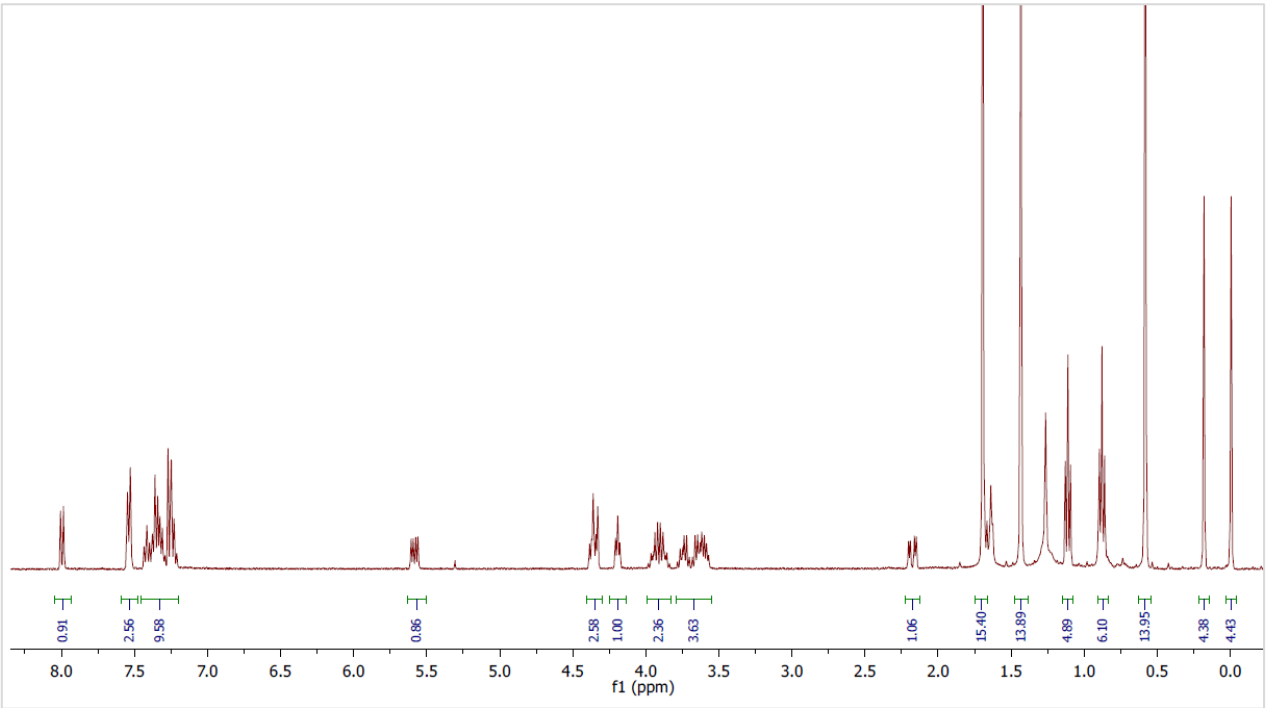
14

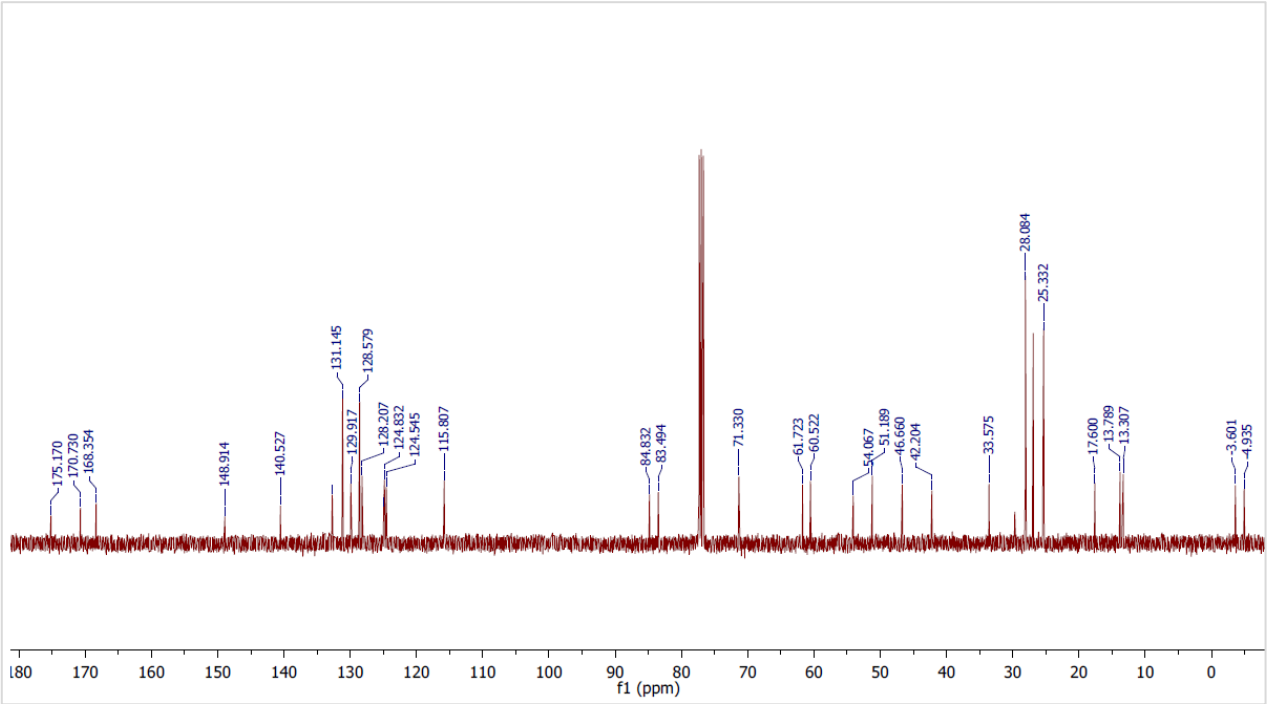

0.87
1.71
5.37
1.20
1.00
1.09
4.80
1.46
1.20
1.24
1.80
6.34
3.04
3.52
2.61
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
f1 (ppm)

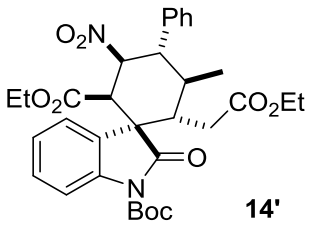

176.255
171.006
168.628
148.898
140.355
133.983
130.781
129.798
128.874
128.326
125.166
124.478
115.569
85.007
84.487
61.698
60.682
55.177
51.056
47.001
40.701
36.063
34.491
28.121
17.795
13.834
13.358
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)


O2N
Ph
OTBS
EtOOC
COOEt
O
N
Boc

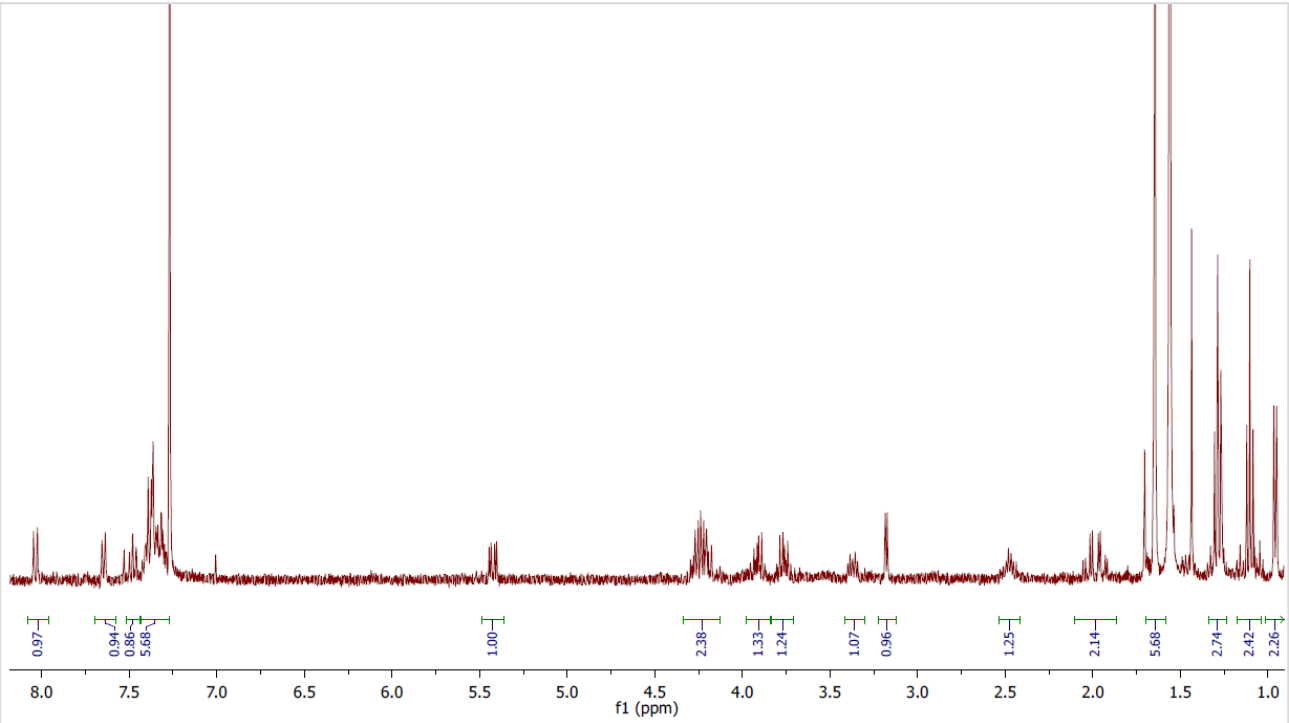
15

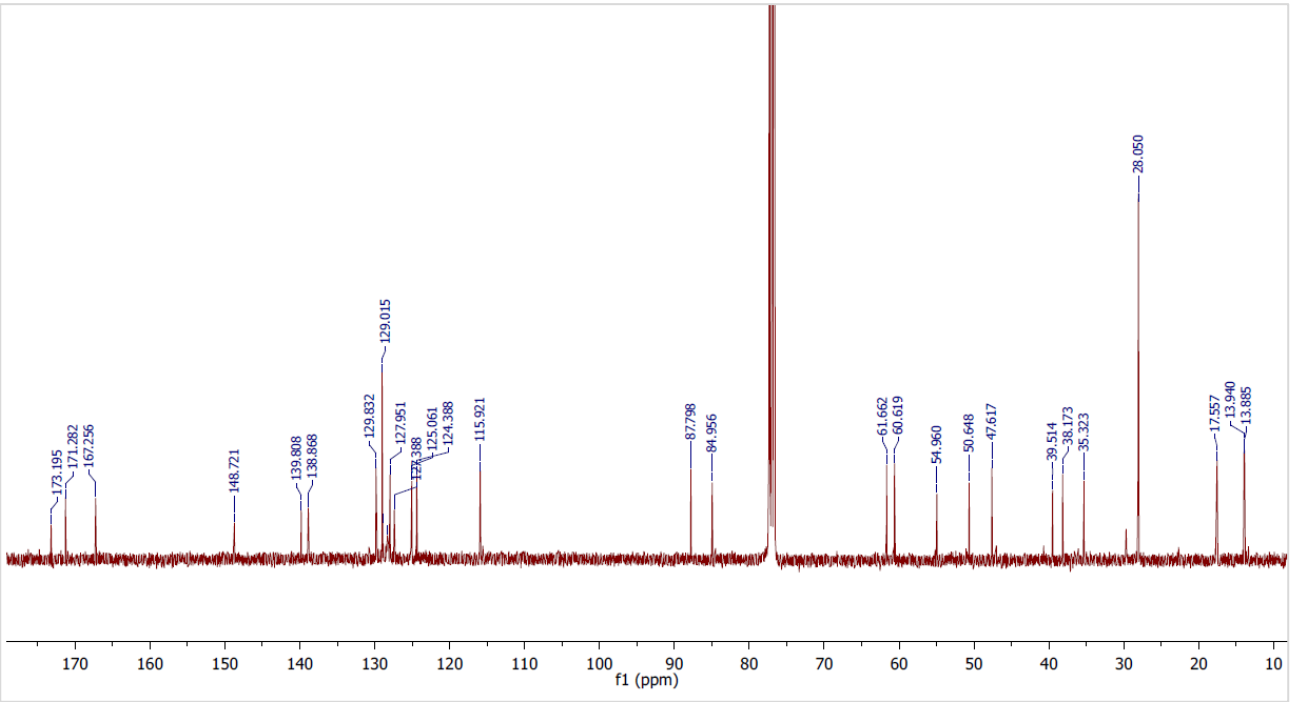

0.91
2.56
9.58
0.86
2.58
1.00
2.36
3.63
1.06
15.40
13.89
4.89
6.10
13.95
4.38
4.43
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

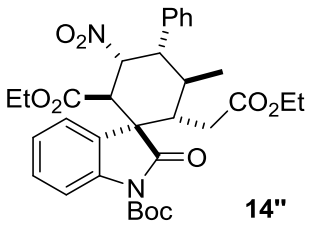

175.170
170.730
168.354
148.914
140.527
131.145
129.917
128.579
128.207
124.832
124.545
115.807
84.832
83.494
71.330
61.723
60.522
54.067
51.189
46.660
42.204
33.575
28.084
25.332
17.600
13.789
13.307
3.601
4.935
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Ph
O2N
EtO2C
CO2Et
O
N
Boc

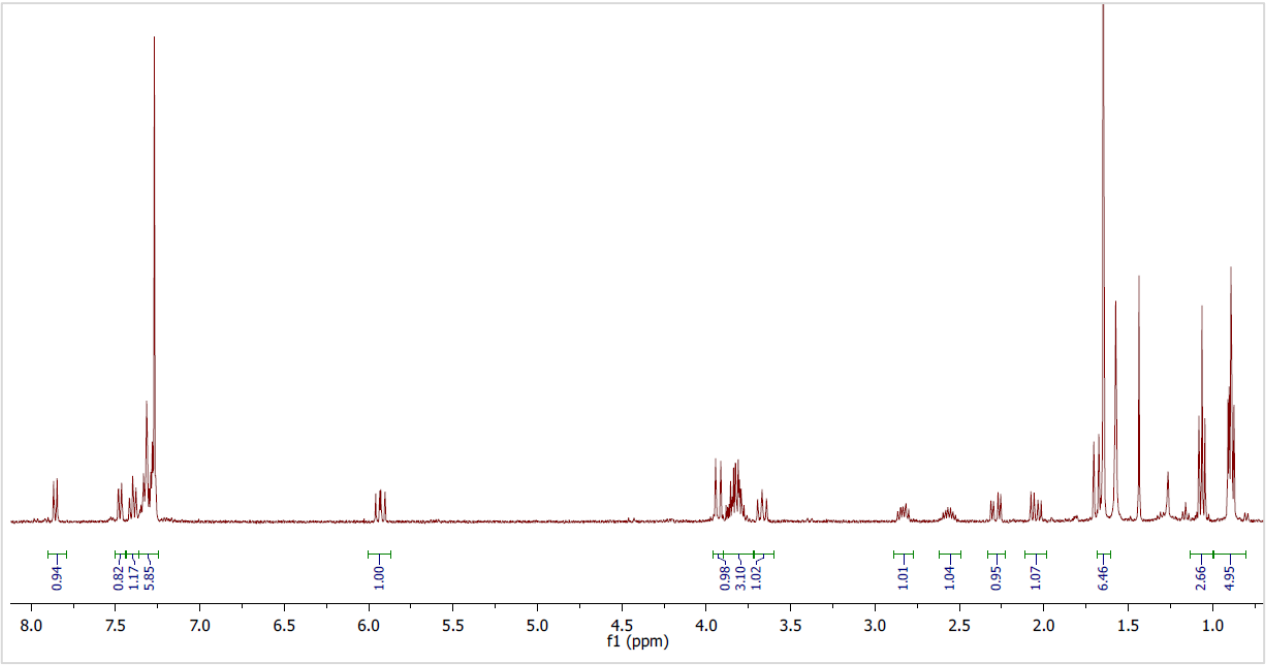
14'

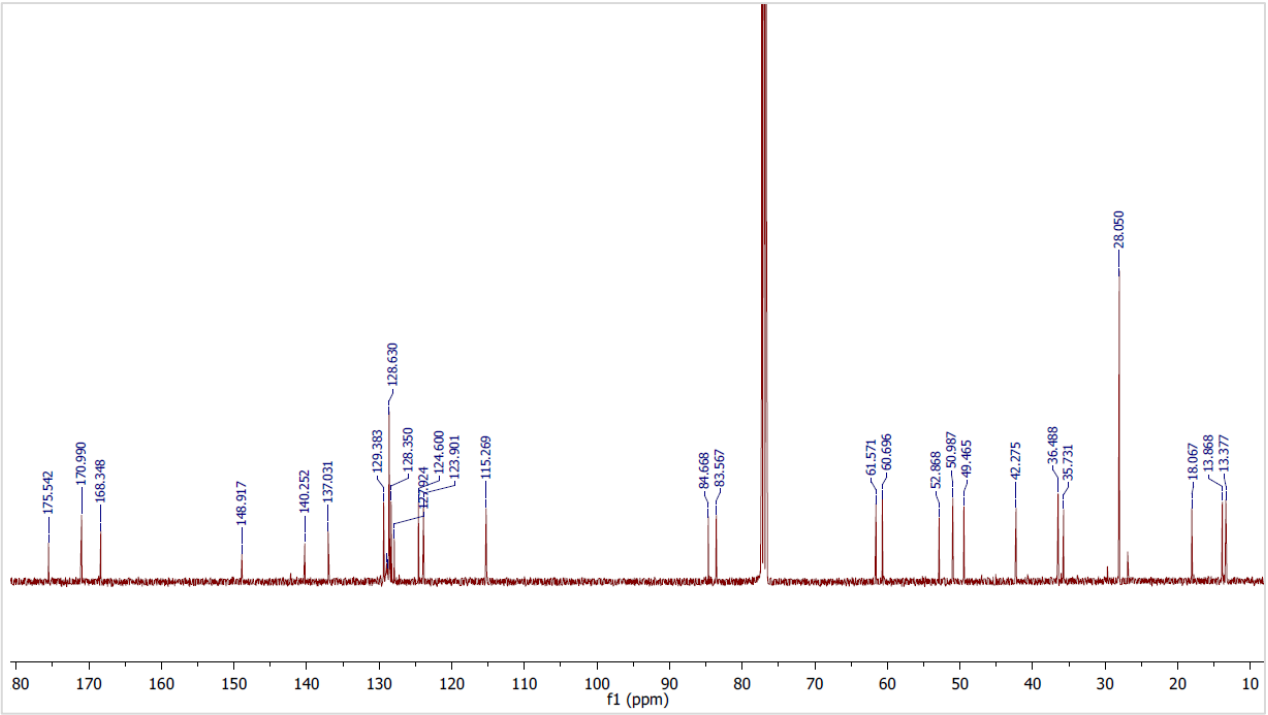

0.97
0.94
0.86
5.68
1.00
2.38
1.33
1.24
1.07
0.96
1.25
2.14
5.68
2.74
2.42
2.26
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

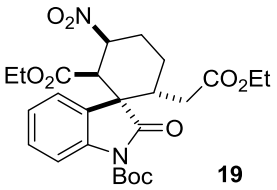

173.195
171.282
167.256
148.721
139.808
138.868
129.832
129.015
127.951
125.061
124.388
115.921
87.798
84.956
61.662
60.619
54.960
50.648
47.617
39.514
38.173
35.323
28.050
17.557
13.940
13.885
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


Ph
O2N
EtO2C
CO2Et
O
N
Boc

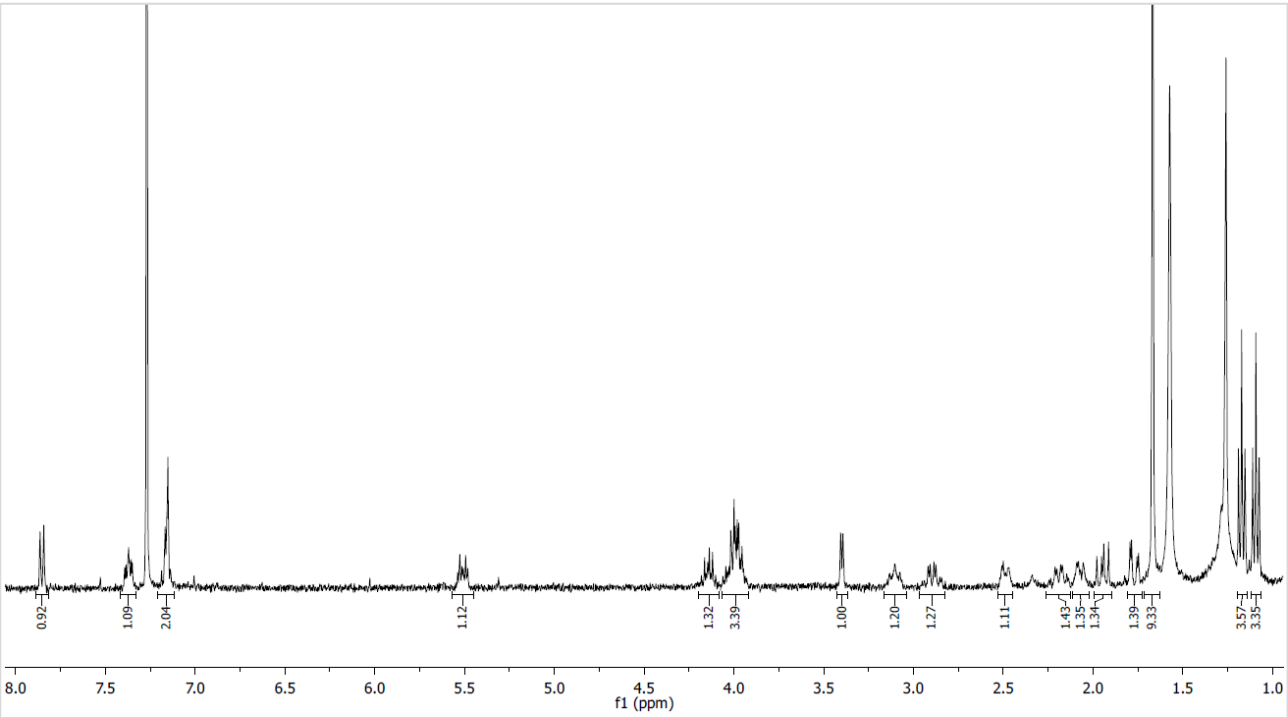
14''

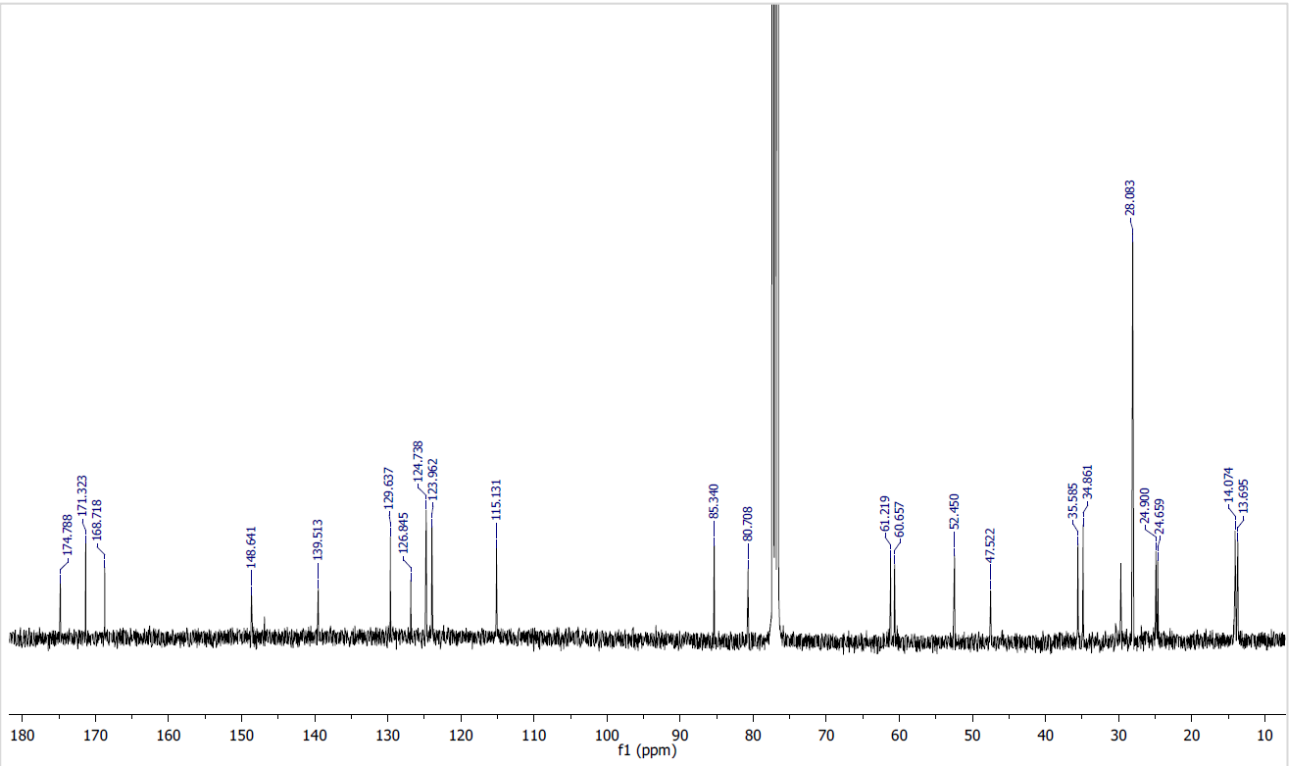

0.94
0.82
1.17
5.85
1.00
0.98
3.10
1.02
1.01
1.04
0.95
1.07
6.46
2.66
4.95
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

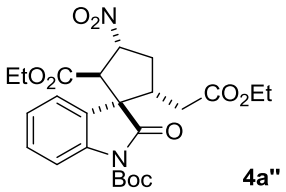

175.542
170.990
168.348
148.917
140.252
137.031
129.383
128.630
128.350
127.924
124.600
123.901
115.269
84.668
83.567
61.571
60.696
52.868
50.987
49.465
42.275
36.488
35.731
28.050
18.067
13.868
13.377
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


O2N
EtO2C
CO2Et
O
N
Boc

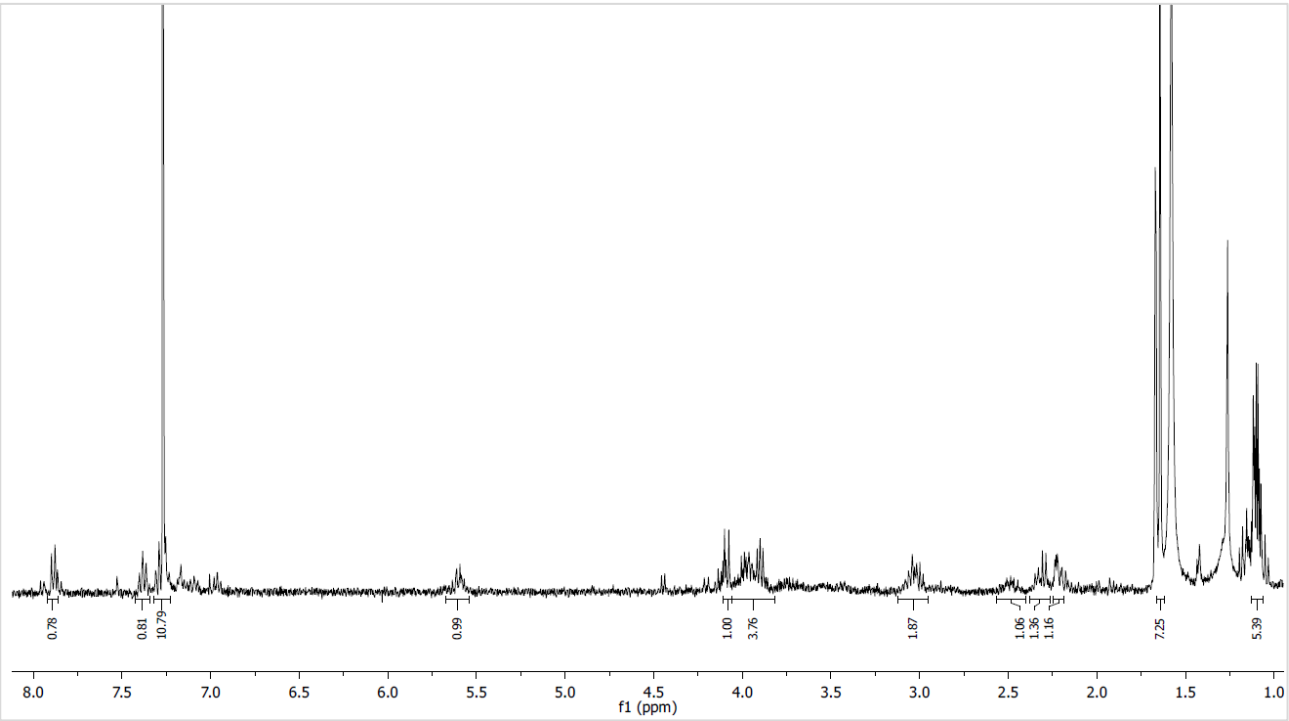
19


0.92
1.09
2.04
1.12
1.32
3.39
1.00
1.20
1.27
1.11
1.43
1.35
1.34
1.39
9.33
3.57
3.35
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
f1 (ppm)


174.788
171.323
168.718
148.641
139.513
129.637
126.845
124.738
123.962
115.131
85.340
80.708
61.219
60.657
52.450
47.522
35.585
34.861
28.083
24.900
24.659
14.074
13.695
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)

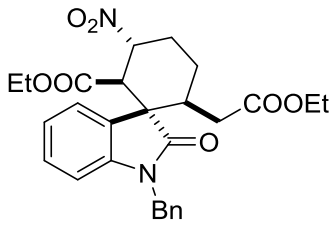

O2N
EtO2C
CO2Et
O
N
Boc

4a''


0.78
0.81
10.79
0.99
1.00
3.76
1.87
1.06
1.36
1.16
7.25
5.39
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
f1 (ppm)

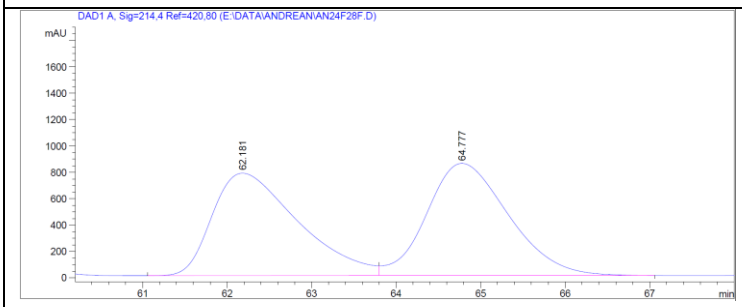
J. CSP-HPLC Traces.

The racemic cascade reactions products are synthesized employing DBU instead of the bifunctional organocatalyst. The typical procedure is described in Section E (p. S21).



3b

Racemic mixture

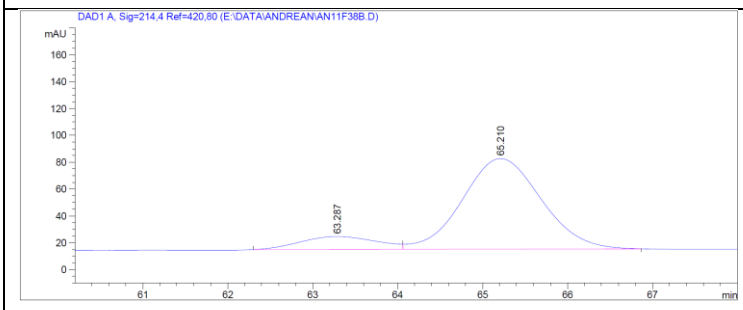


Signal 1: DAD1 A, Sig=214,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	62.181	BV	1.0729	5.48162e4	777.12354	48.8762
2	64.777	VB	1.0424	5.73369e4	850.61334	51.1238

Totals : 1.12153e5 1627.73688

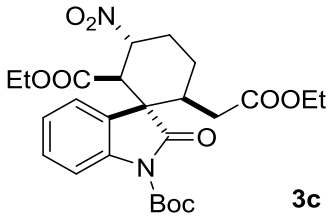
Table 1, entry 2



Signal 1: DAD1 A, Sig=214,4 Ref=420,80

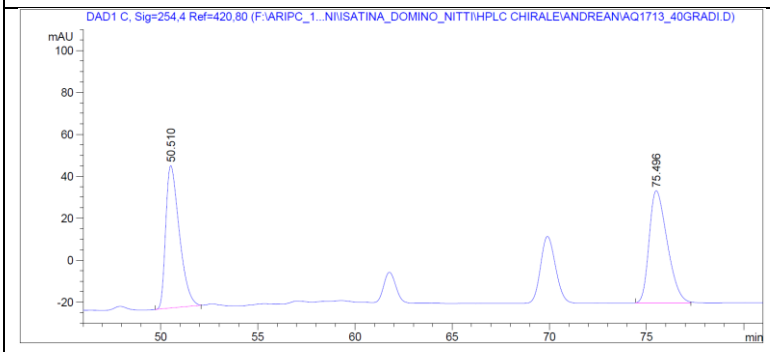
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	63.287	BV	0.9440	617.09894	9.75581	12.3453
2	65.210	VB	1.0043	4381.57129	67.58851	87.6547

Totals : 4998.67023 77.34432



3c

Racemic mixture

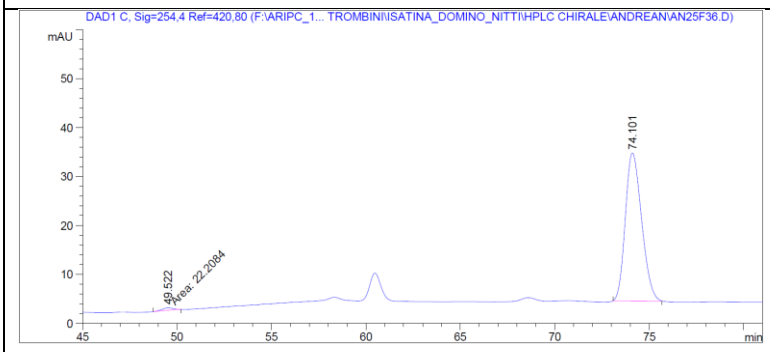


Signal 1: DAD1 C, Sig=254,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	50.510	BB	0.7475	3304.32080	67.92823	48.8208
2	75.496	BB	1.0033	3463.93823	53.50592	51.1792

Totals : 6768.25903 121.43415

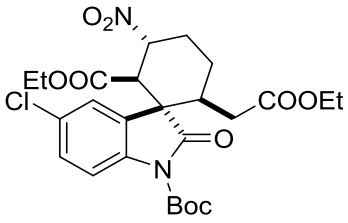
Table 1, entry 3



Signal 1: DAD1 C, Sig=254,4 Ref=420,80

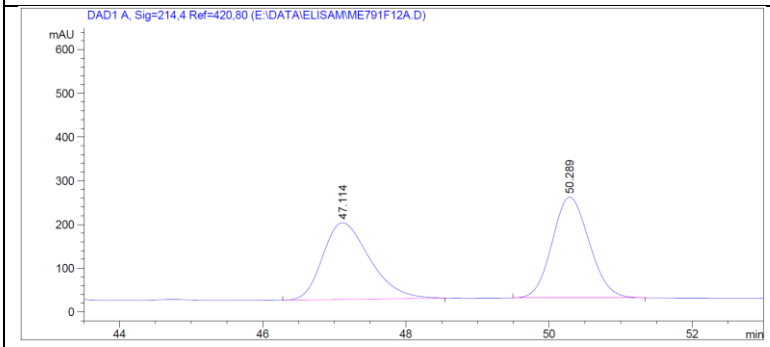
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	49.522	MM	0.6977	22.20839	5.30546e-1	1.2076
2	74.101	BB	0.9082	1816.84949	30.27356	98.7924

Totals : 1839.05787 30.80410



3d

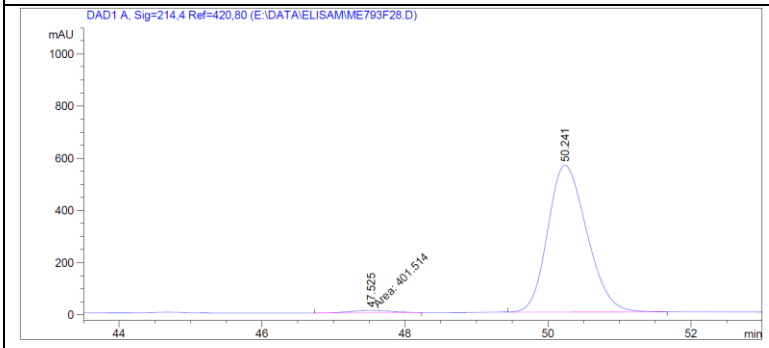
Racemic mixture



Signal 1: DAD1 A, Sig=214,4 Ref=420,80

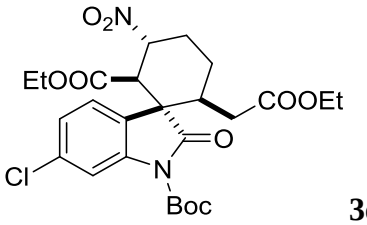
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	47.114	BB	0.7025	8025.21973	175.82608	49.0257
2	50.289	BB	0.5657	8344.18652	230.87202	50.9743
Totals :				1.63694e4	406.69810	

Table 2, entry 2



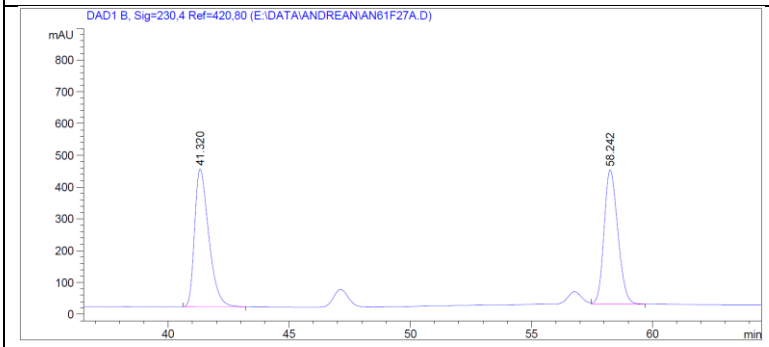
Signal 1: DAD1 A, Sig=214,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	47.525	MF	0.7121	401.51447	9.39717	1.8346
2	50.241	BB	0.5891	2.14845e4	563.16174	98.1654
Totals :				2.18860e4	572.55891	



3e

Racemic mixture

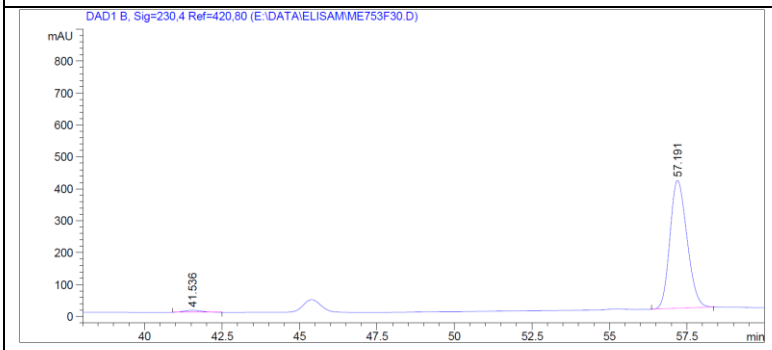


Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.320	BB	0.6243	1.76999e4	433.57635	51.3841
2	58.242	VB	0.6142	1.67464e4	422.74994	48.6159

Totals : 3.44463e4 856.32629

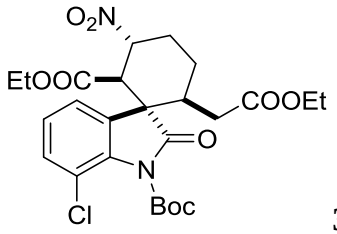
Table 2, entry 3



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

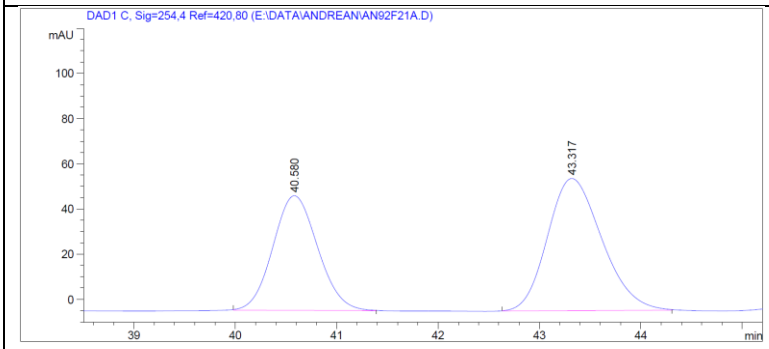
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.536	BB	0.5880	262.22717	6.62228	1.6749
2	57.191	BB	0.6000	1.53941e4	400.93152	98.3251

Totals : 1.56563e4 407.55379



3f

Racemic mixture

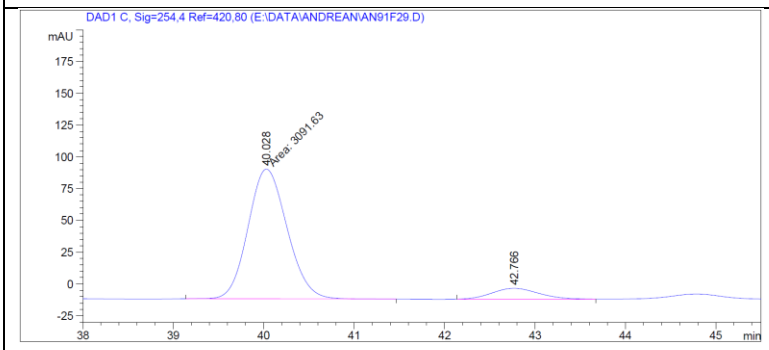


Signal 1: DAD1 C, Sig=254,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.580	BB	0.4792	1565.59338	50.84852	41.6777
2	43.317	BB	0.5801	2190.83521	58.61187	58.3223

Totals : 3756.42859 109.46040

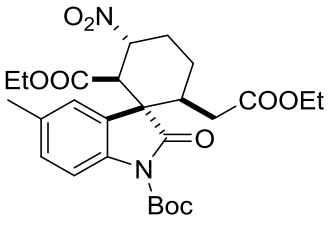
Table 2, entry 4



Signal 1: DAD1 C, Sig=254,4 Ref=420,80

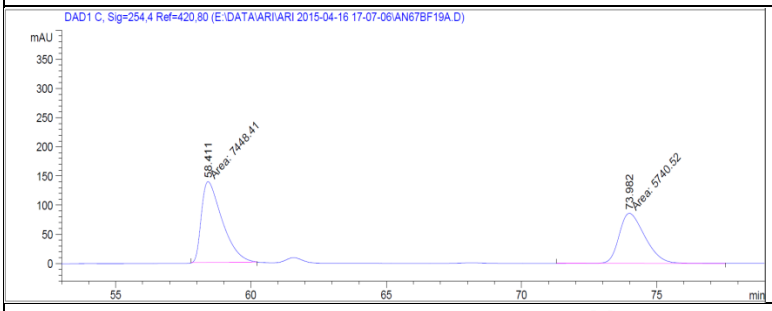
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.028	MM	0.5039	3091.62720	102.25825	91.0527
2	42.766	BB	0.5510	303.79907	8.49889	8.9473

Totals : 3395.42627 110.75714



3g

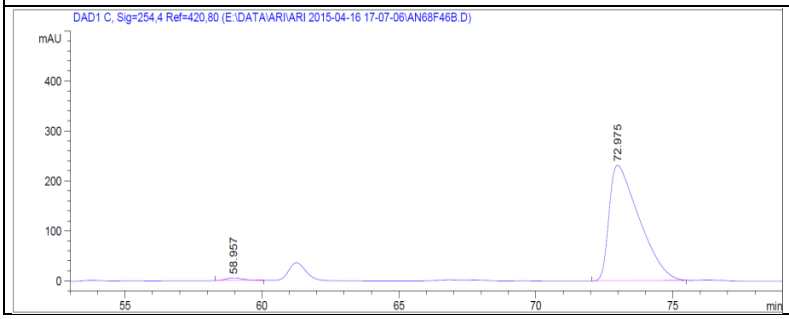
Racemic mixture



Signal 1: DAD1 C, Sig=254,4 Ref=420,80

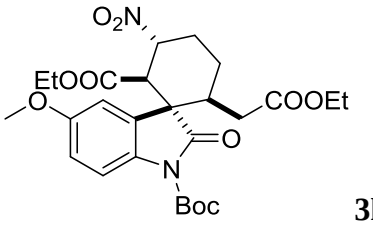
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	58.411	MM	0.8930	7448.40967	139.00792	56.4747
2	73.982	MM	1.1122	5740.52246	86.02360	43.5253

Table 2, entry 5



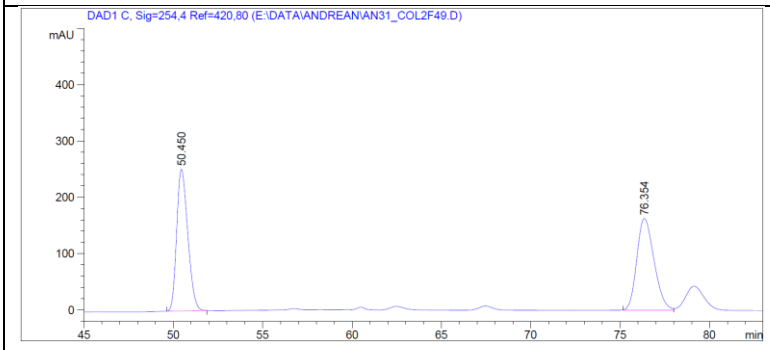
Signal 1: DAD1 C, Sig=254,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	58.957	BB	0.6425	226.70717	5.08169	1.2662
2	72.975	BB	1.1206	1.76782e4	231.56744	98.7338



3h

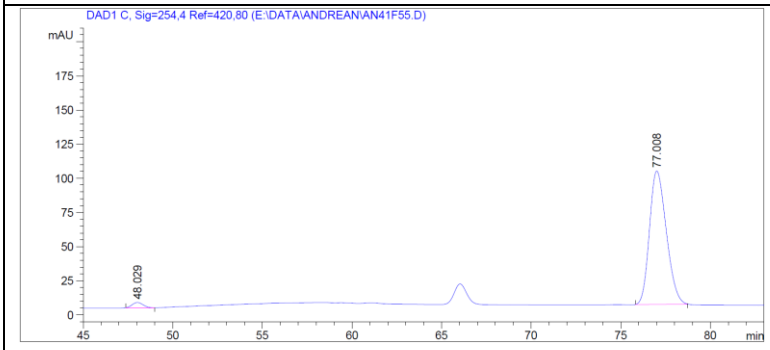
Racemic mixture



Signal 1: DAD1 C, Sig=254,4 Ref=420,80

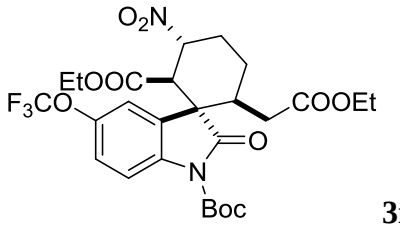
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	50.450	BB	0.6778	1.09170e4	251.79955	49.8877
2	76.354	BV	1.0404	1.09661e4	163.10132	50.1123
Totals :				2.18831e4	414.90086	

Table 2, entry 6



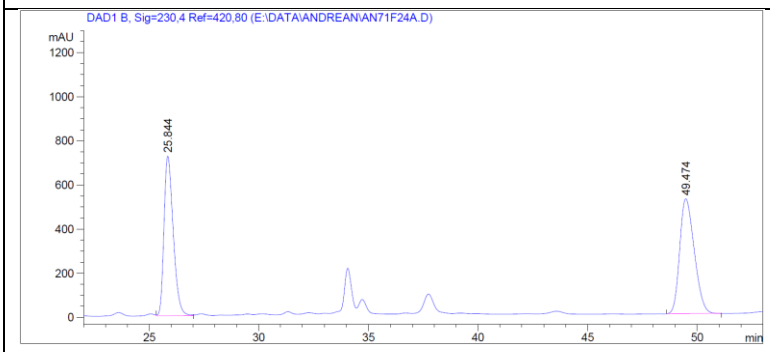
Signal 1: DAD1 C, Sig=254,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	48.029	BB	0.5848	160.09785	3.86870	2.4356
2	77.008	BB	1.0169	6413.08154	97.81683	97.5644
Totals :				6573.17940	101.68553	



3i

Racemic mixture

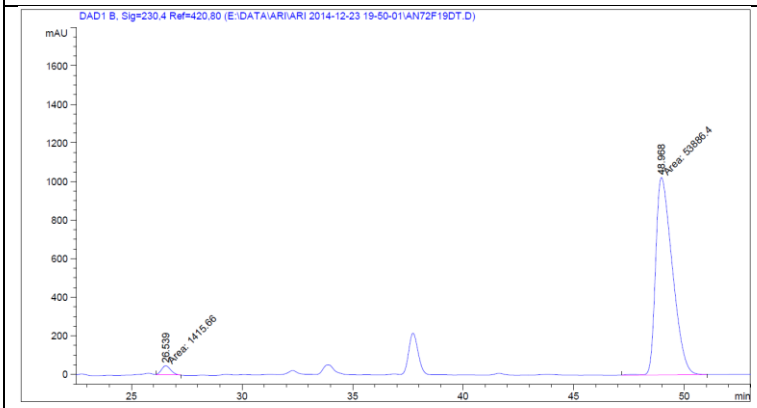


Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.844	VV	0.4540	2.11960e4	723.10144	46.8688
2	49.474	BB	0.7228	2.40281e4	520.26886	53.1312

Totals : 4.52240e4 1243.37030

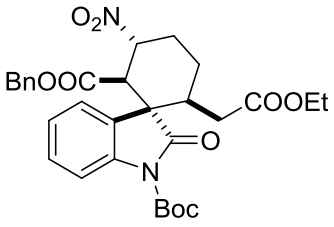
Table 2, entry 7



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

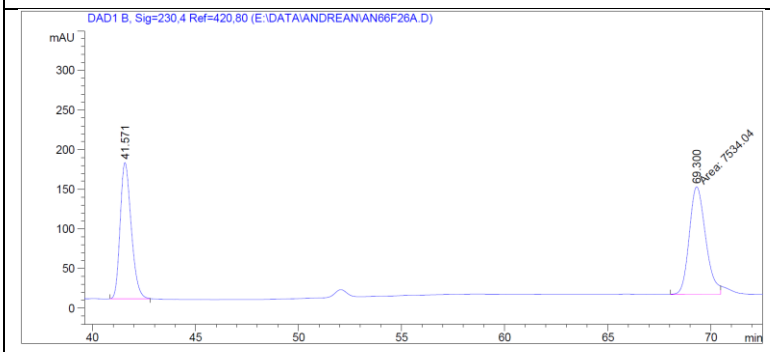
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.539	FM	0.4925	1415.65833	47.91178	2.5599
2	48.968	MM	0.8769	5.38864e4	1024.18713	97.4401

Totals : 5.53021e4 1072.09891



3j

Racemic mixture

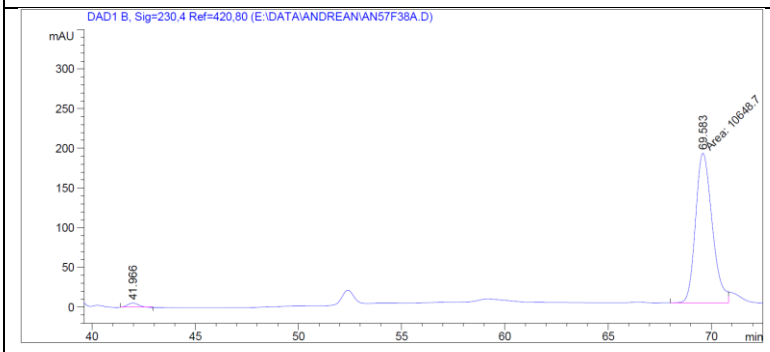


Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.571	BB	0.5763	6435.22754	172.06778	46.0671
2	69.300	MF	0.9239	7534.03564	135.91295	53.9329

Totals : 1.39693e4 307.98073

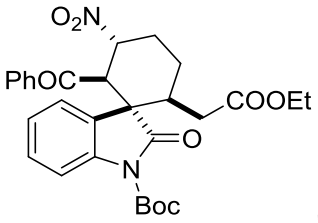
Table 2, entry 8



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

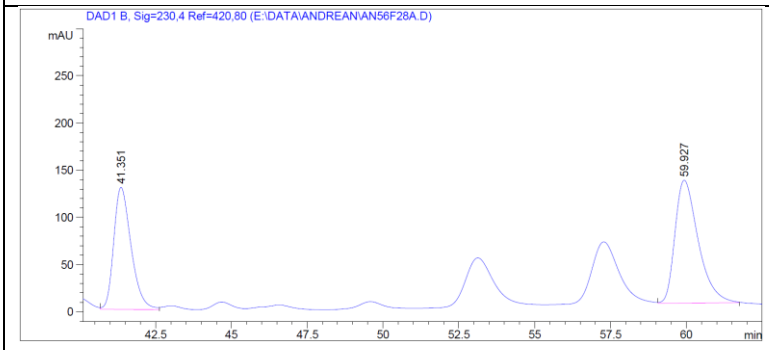
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.966	BB	0.5989	207.85841	5.37872	1.9146
2	69.583	MF	0.9393	1.06487e4	188.95111	98.0854

Totals : 1.08565e4 194.32983



3k

Racemic mixture

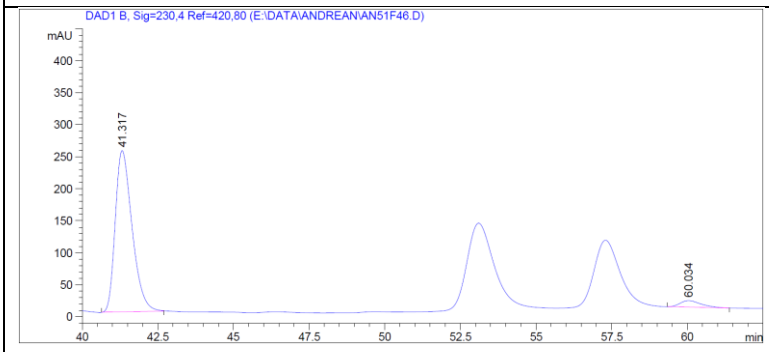


Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.351	BB	0.6090	5162.80469	129.54561	42.4722
2	59.927	BB	0.8152	6992.91846	130.49910	57.5278

Totals : 1.21557e4 260.04471

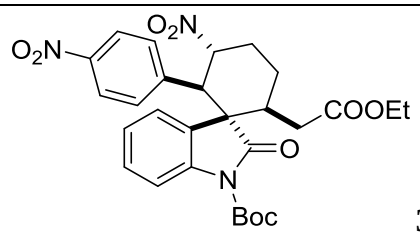
Table 2, entry 9



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

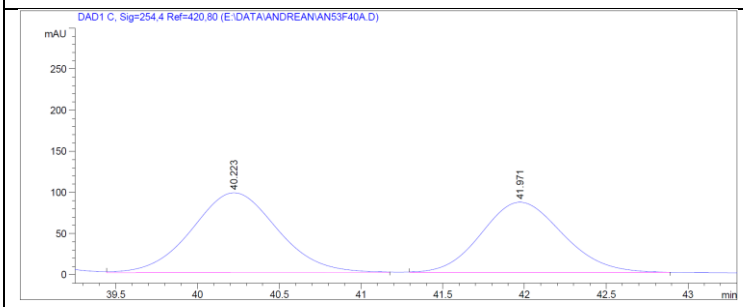
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	41.317	BB	0.5914	9752.44727	252.03749	95.2053
2	60.034	BB	0.7134	491.15125	10.27927	4.7947

Totals : 1.02436e4 262.31677



3l

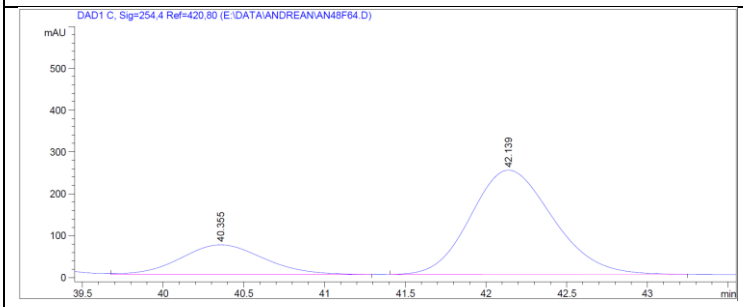
Racemic mixture



Signal 1: DAD1 C, Sig=254,4 Ref=420,80

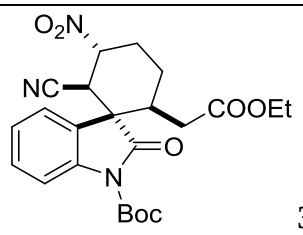
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.223	VB	0.5630	3558.83521	97.22609	54.4330
2	41.971	BB	0.5380	2979.17529	85.60295	45.5670
Totals :				6538.01050	182.82904	

Table 2, entry 10



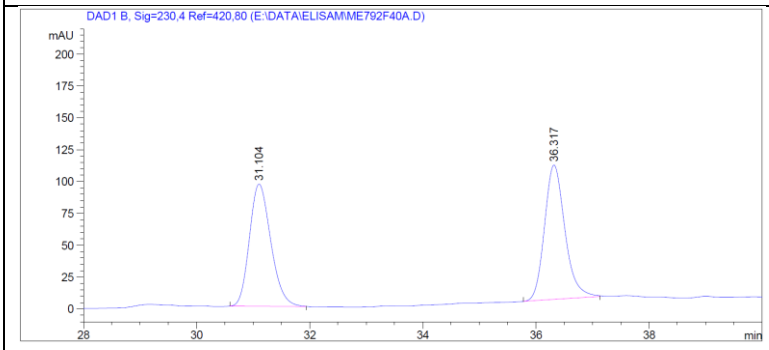
Signal 1: DAD1 C, Sig=254,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.355	VB	0.5565	2579.74292	71.24366	22.5477
2	42.139	BB	0.5523	8861.50488	249.53363	77.4523
Totals :				1.14412e4	320.77729	



3m

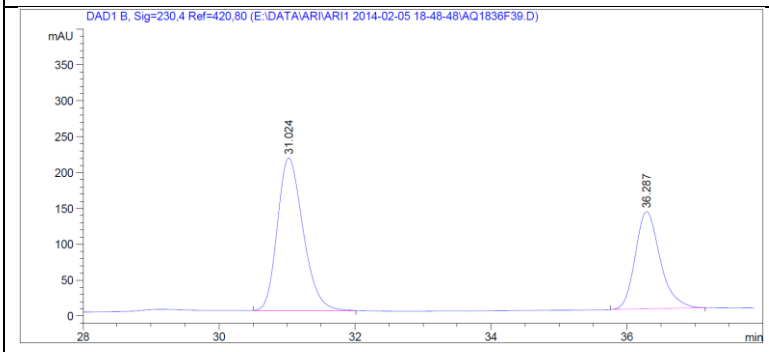
Racemic mixture



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

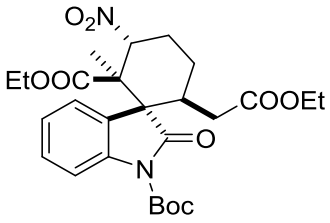
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.104	BB	0.4097	2537.50024	96.19913	48.9172
2	36.317	BB	0.3849	2649.84204	105.54355	51.0828
Totals :				5187.34229	201.74268	

Table 2, entry 11



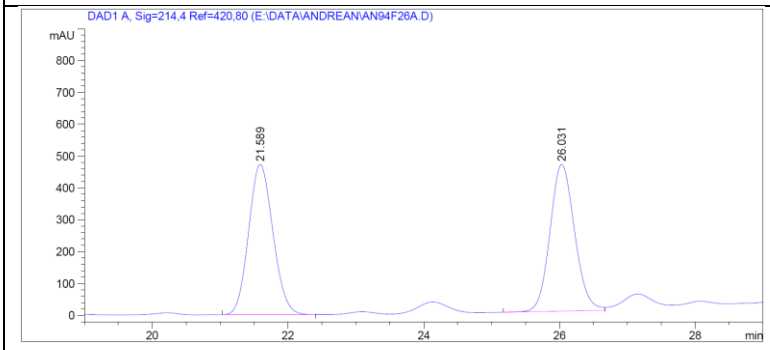
Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.024	BB	0.4069	5597.02100	212.74551	61.6823
2	36.287	BB	0.3905	3476.93140	135.90718	38.3177
Totals :				9073.95239	348.65269	



3n

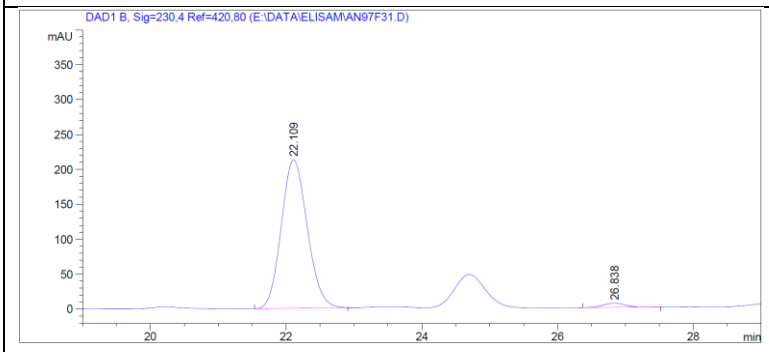
Racemic mixture



Signal 1: DAD1 A, Sig=214,4 Ref=420,80

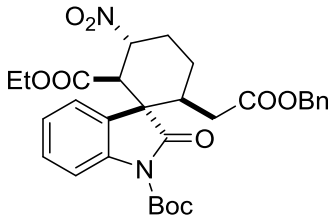
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	21.589	BB	0.3887	1.17543e4	471.77542	50.2367
2	26.031	BV	0.3927	1.16436e4	460.91568	49.7633
Totals :				2.33979e4	932.69110	

Table 2, entry 12



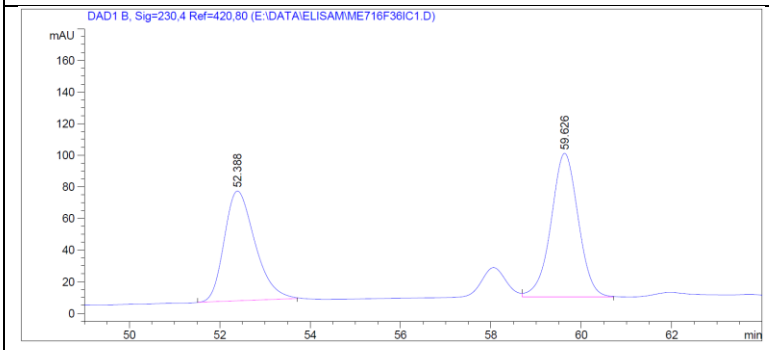
Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.109	BB	0.4145	5661.67725	212.73070	97.5825
2	26.838	BB	0.3729	140.26007	6.04088	2.4175
Totals :				5801.93732	218.77157	



3q

Racemic mixture

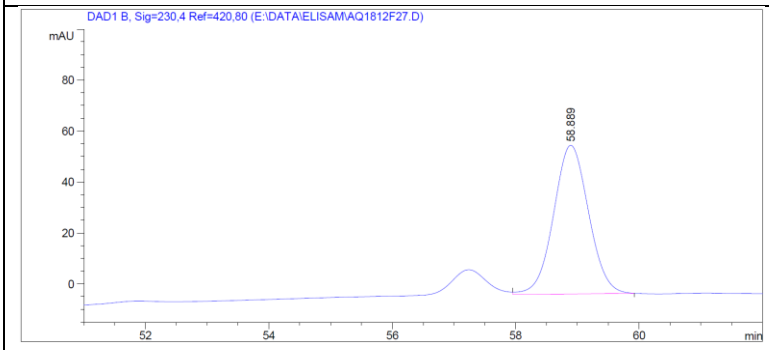


Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	52.388	BB	0.7259	3289.01709	69.52522	46.4409
2	59.626	VB	0.6395	3793.13599	90.78068	53.5591

Totals : 7082.15308 160.30589

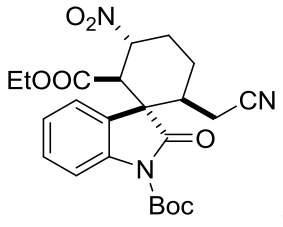
Table 3, entry 2



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

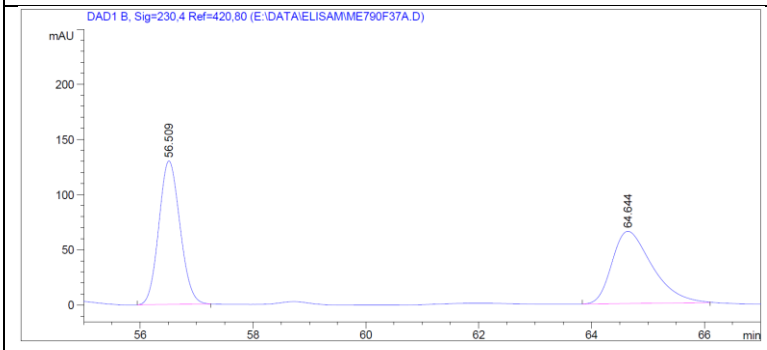
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	58.889	VB	0.6087	2307.31177	58.42599	100.0000

Totals : 2307.31177 58.42599



3s

Racemic mixture

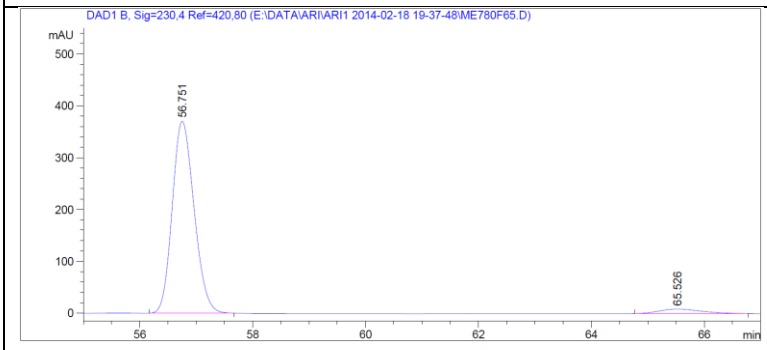


Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	56.509	BB	0.4065	3399.89990	130.24654	51.1767
2	64.644	BB	0.7558	3243.55762	65.48833	48.8233

Totals : 6643.45752 195.73486

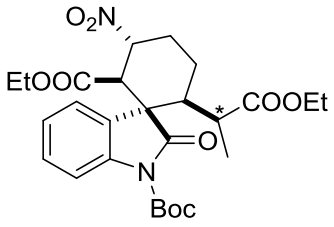
Table 3, entry 4



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

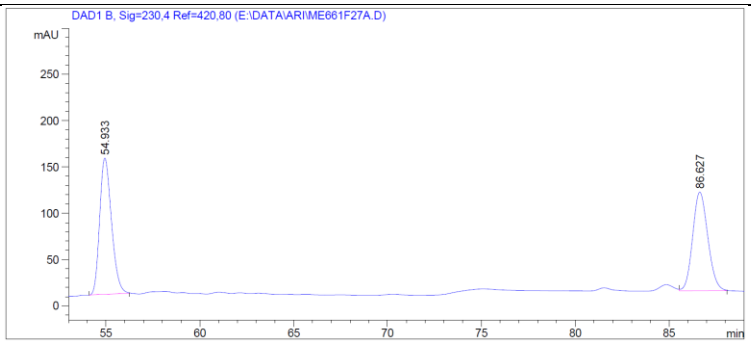
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	56.751	BB	0.4198	9967.78711	370.59311	95.6126
2	65.526	BB	0.7678	457.39960	8.75102	4.3874

Totals : 1.04252e4 379.34413



3t

Racemic mixture

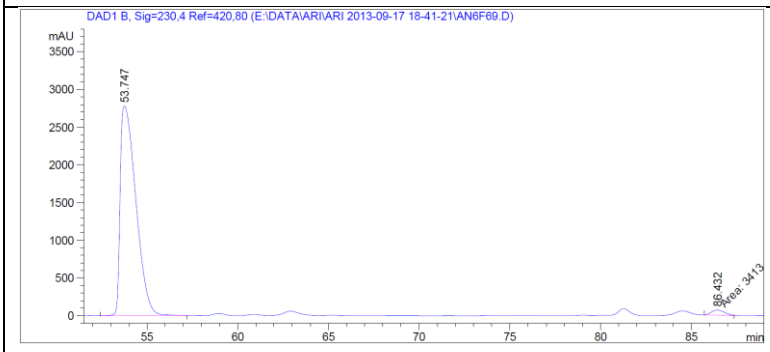


Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	54.933	BB	0.6799	6461.71973	147.27621	51.9552
2	86.627	VB	0.8701	5975.37988	106.58411	48.0448

Totals : 1.24371e4 253.86032

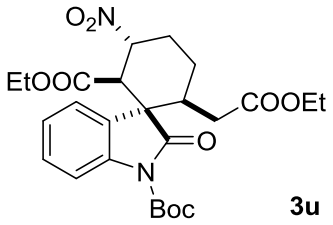
Table 3, entry 5



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

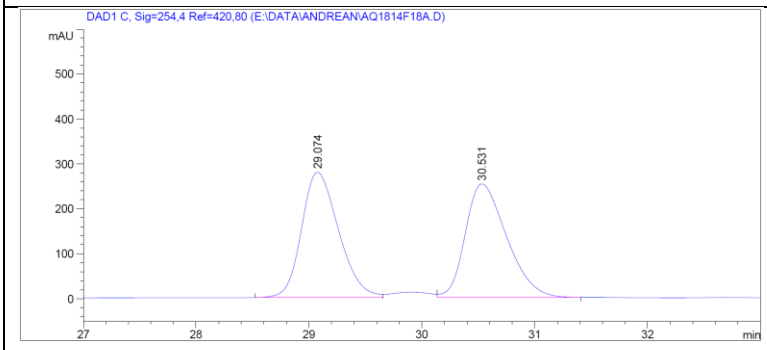
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	53.747	VB	0.9371	1.67070e5	2780.04248	97.9978
2	86.432	MM	0.8421	3413.42798	67.55979	2.0022

Totals : 1.70483e5 2847.60227



3u

Racemic mixture

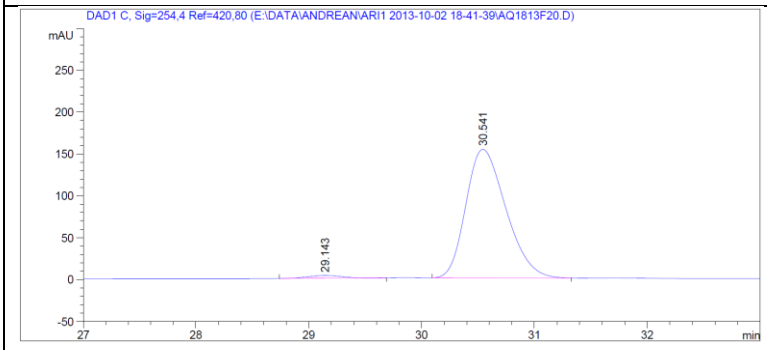


Signal 1: DAD1 C, Sig=254,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.074	BV	0.3500	6360.90918	278.93909	49.7328
2	30.531	VB	0.3927	6429.26465	252.79912	50.2672

Totals : 1.27902e4 531.73820

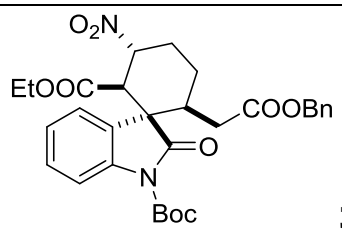
Table 4, entry 1



Signal 1: DAD1 C, Sig=254,4 Ref=420,80

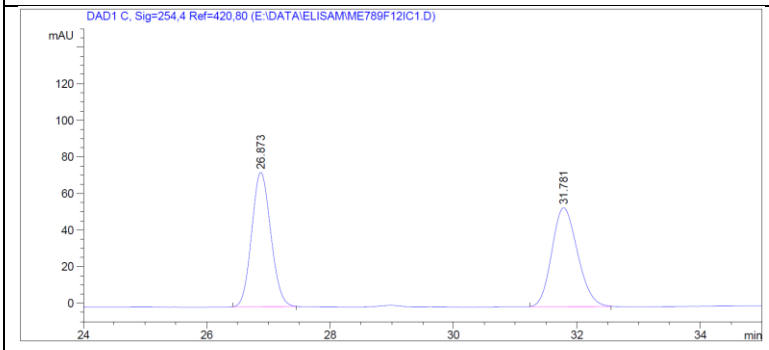
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	29.143	BB	0.3092	65.45360	3.33142	1.6978
2	30.541	BB	0.3818	3789.81738	153.63638	98.3022

Totals : 3855.27098 156.96781



3v

Racemic mixture

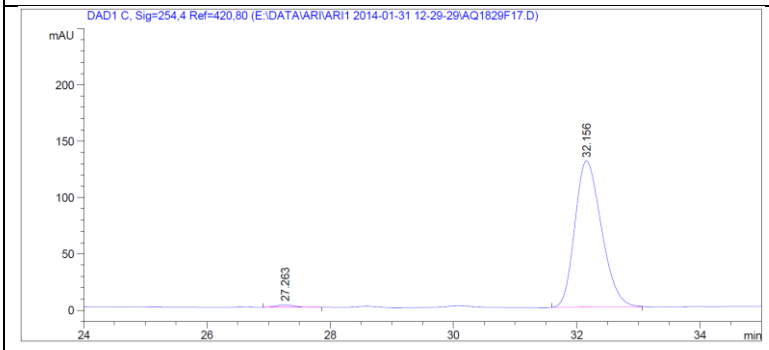


Signal 1: DAD1 C, Sig=254,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.873	BB	0.3378	1586.56702	73.49847	50.3042
2	31.781	BB	0.4505	1567.37598	54.02652	49.6958

Totals : 3153.94299 127.52499

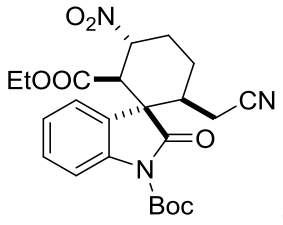
Table 4, entry 2



Signal 1: DAD1 C, Sig=254,4 Ref=420,80

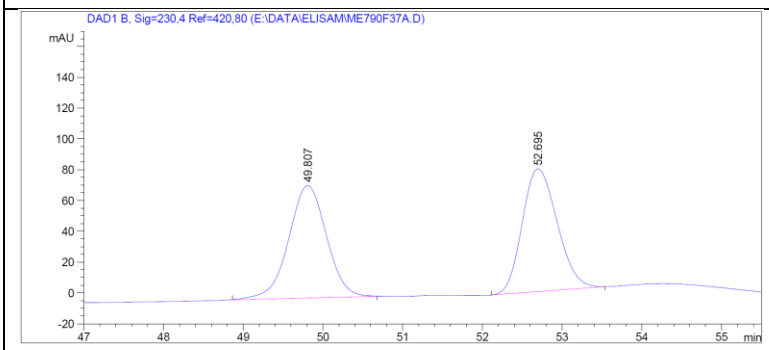
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.263	BB	0.3261	47.54875	2.21820	1.2038
2	32.156	BB	0.4689	3902.30029	129.75706	98.7962

Totals : 3949.84904 131.97526



3w

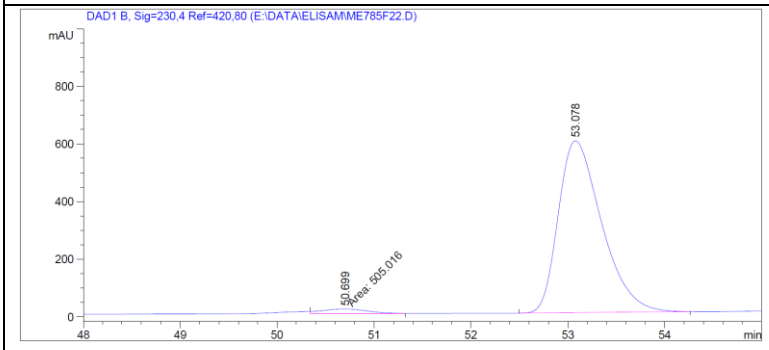
Racemic mixture



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

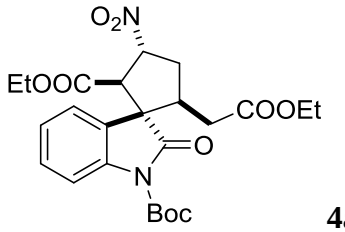
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	49.807	BB	0.5076	2416.33105	73.11047	49.8054
2	52.695	BB	0.4798	2435.21021	79.84827	50.1946
Totals :				4851.54126	152.95874	

Table 4, entry 3



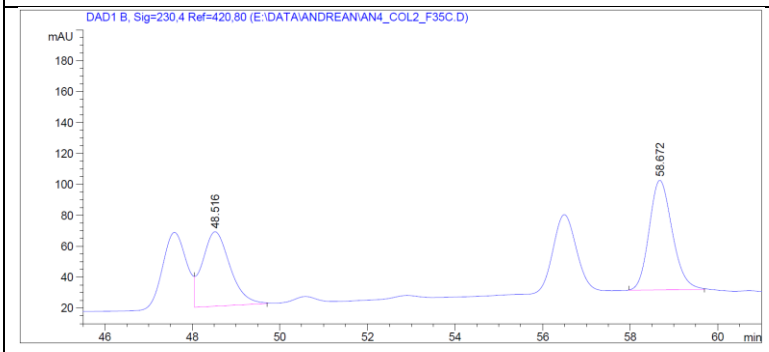
Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	50.699	MF	0.5335	505.01645	15.77704	2.6506
2	53.078	BB	0.4787	1.85481e4	596.55768	97.3494
Totals :				1.90531e4	612.33472	



4a

Racemic mixture

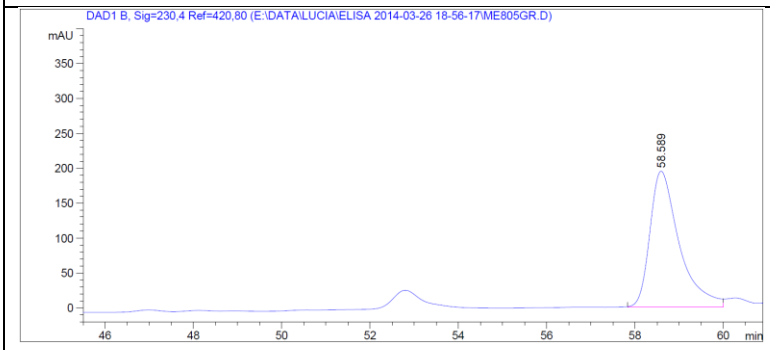


Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	48.516	VB	0.6654	2120.53003	48.18478	44.7331
2	58.672	BB	0.5700	2619.87183	71.07971	55.2669

Totals : 4740.40186 119.26450

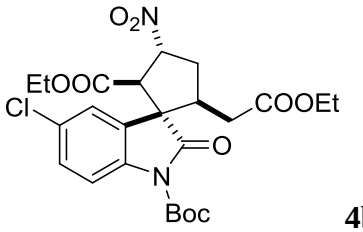
Table 5, entry 10



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

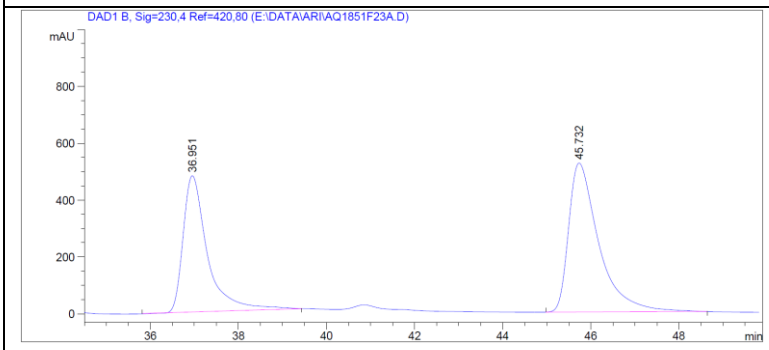
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	58.589	BV	0.6886	9024.55176	194.77315	100.0000

Totals : 9024.55176 194.77315



4b

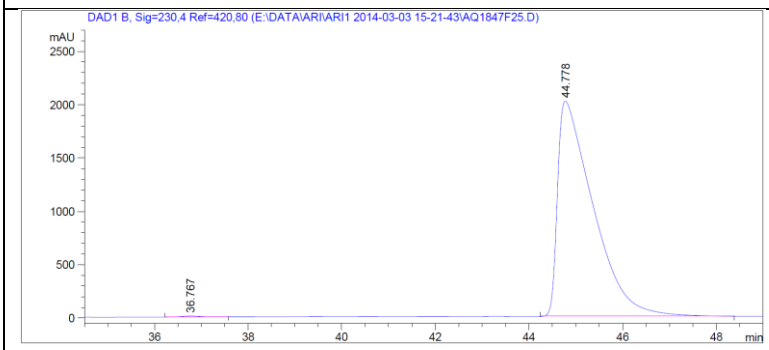
Racemic mixture



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

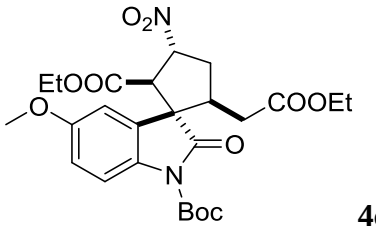
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.951	BB	0.5752	1.85792e4	480.36093	42.6339
2	45.732	BB	0.7104	2.49993e4	524.23322	57.3661
Totals :				4.35786e4	1004.59415	

Table 6, entry 2



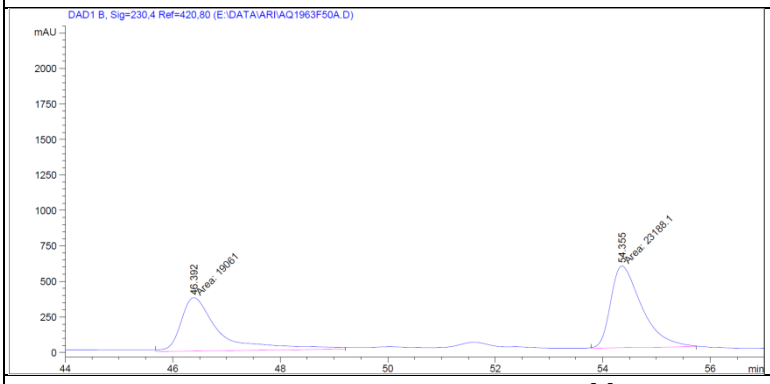
Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	36.767	BB	0.4641	279.91803	9.17108	0.2618
2	44.778	BB	0.7680	1.06655e5	2019.89539	99.7382
Totals :				1.06935e5	2029.06646	



4c

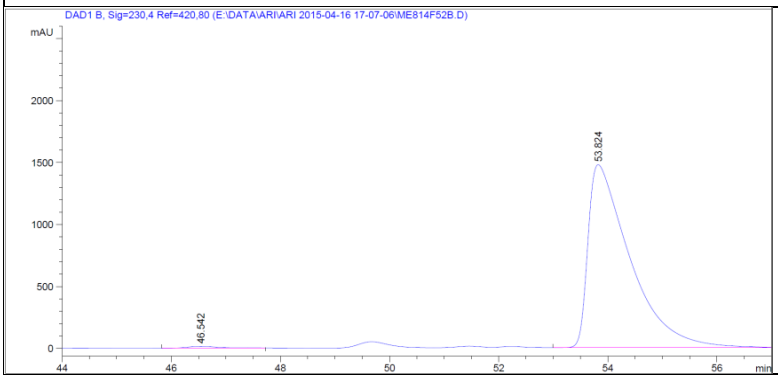
Racemic mixture



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

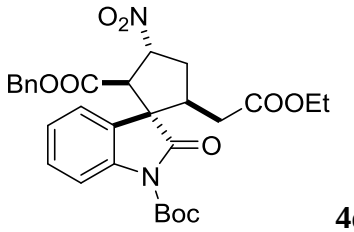
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	46.392	MM	0.8429	1.90610e4	376.88806	45.1157
2	54.355	MM	0.6713	2.31881e4	575.67932	54.8843

Table 6, entry 3



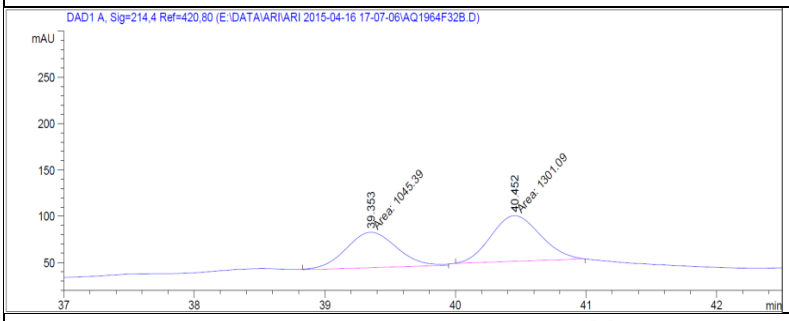
Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	46.542	BB	0.6694	681.44373	15.13303	0.8472
2	53.824	VB	0.7894	7.97519e4	1478.40015	99.1528



4d

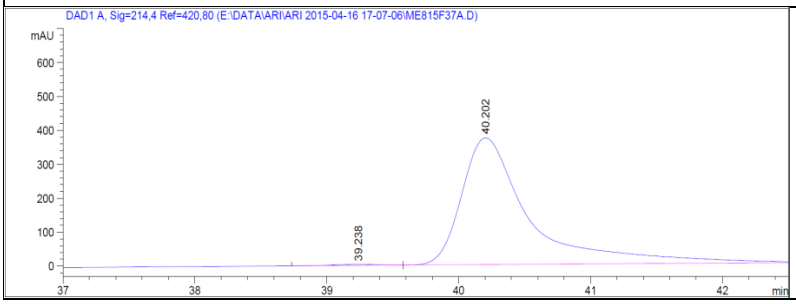
Racemic mixture



Signal 1: DAD1 A, Sig=214,4 Ref=420,80

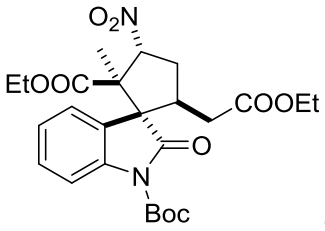
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	39.353	MM	0.4534	1045.39221	38.42723	44.5514
2	40.452	MM	0.4393	1301.09448	49.36071	55.4486

Table 6, entry 4



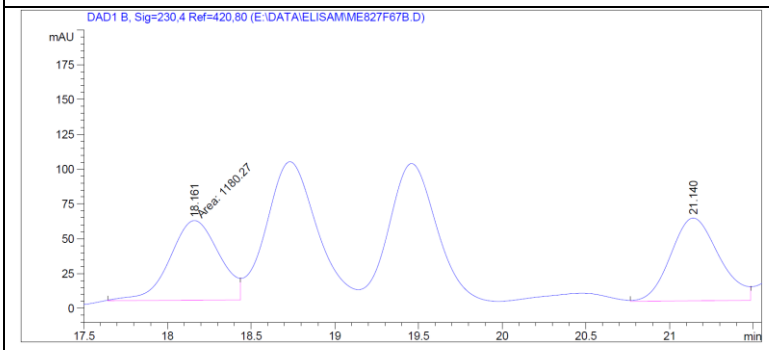
Signal 1: DAD1 A, Sig=214,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	39.238	BV	0.3863	86.66928	3.50727	0.6385
2	40.202	VB	0.5249	1.34880e4	373.83939	99.3615



4e

Racemic mixture

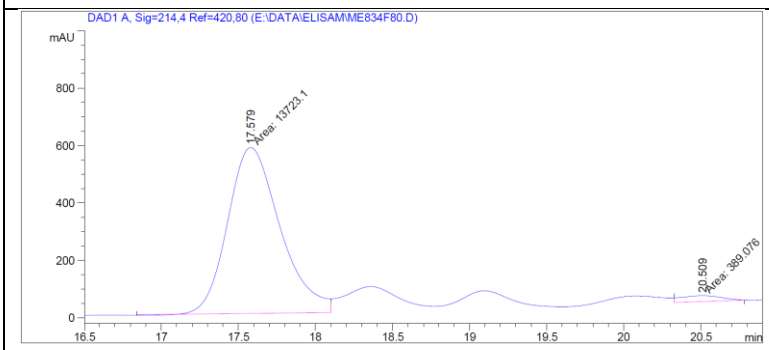


Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.161	MF	0.3433	1180.27441	57.30660	99.2181
2	21.140	VV	0.3106	1198.87781	59.61024	100.7819

Totals : 2379.15222 116.91684

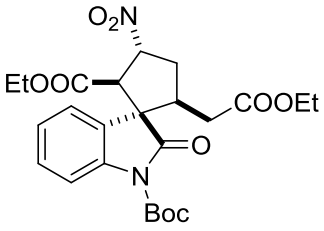
Table 6, entry 6



Signal 1: DAD1 A, Sig=214,4 Ref=420,80

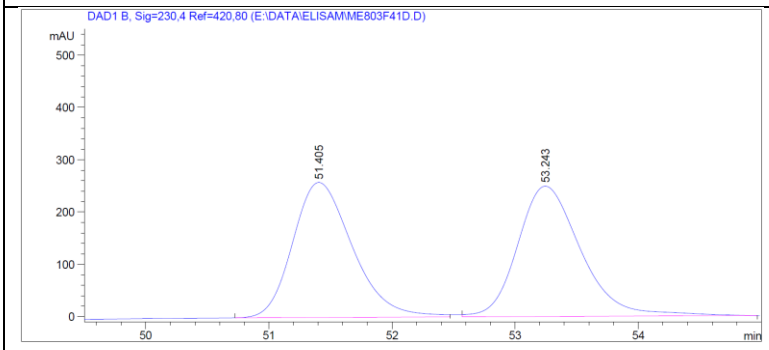
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.579	FM	0.3953	1.37231e4	578.52142	97.2430
2	20.509	FM	0.3048	389.07565	21.27705	2.7570

Totals : 1.41122e4 599.79848



4f

Racemic mixture

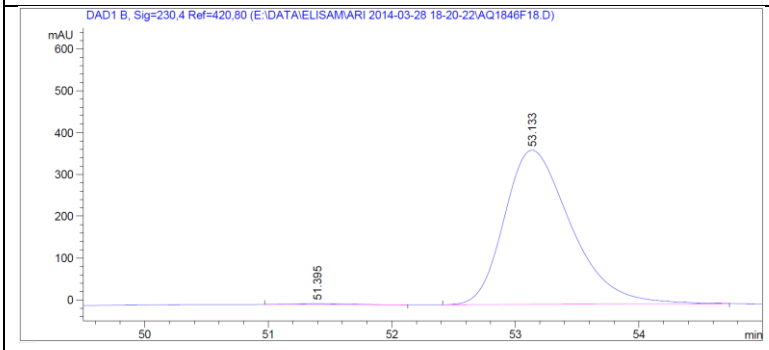


Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	51.405	BB	0.5213	8711.48047	258.39941	49.3762
2	53.243	BB	0.5498	8931.58008	249.38127	50.6238

Totals : 1.76431e4 507.78069

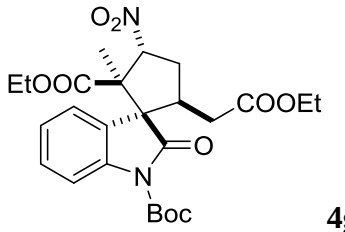
Table 6, entry 7



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

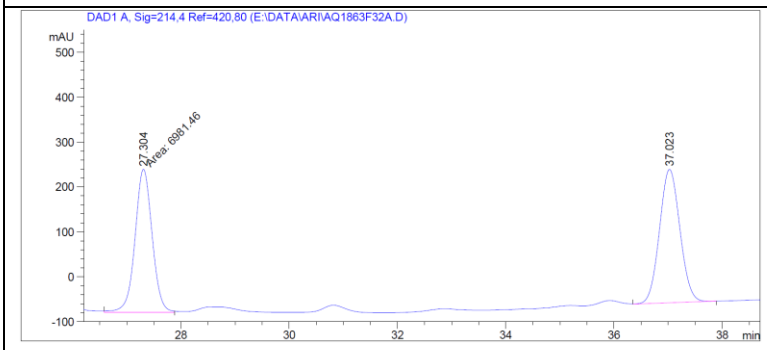
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	51.395	BB	0.3874	75.08672	2.34573	0.5414
2	53.133	BB	0.5746	1.37938e4	368.57339	99.4586

Totals : 1.38689e4 370.91912



4g

Racemic mixture

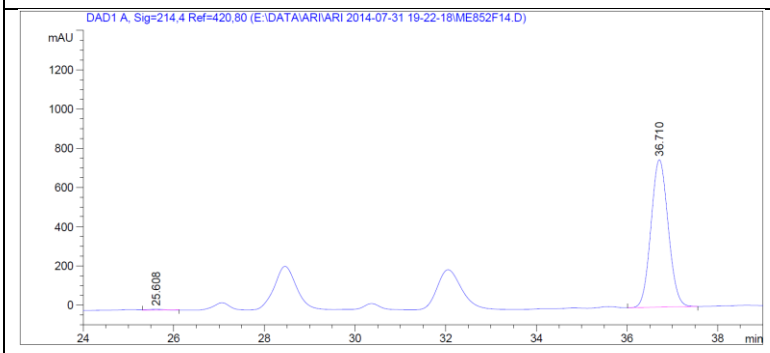


Signal 1: DAD1 A, Sig=214,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	27.304	MM	0.3654	6981.46045	318.44336	47.1382
2	37.023	VB	0.4106	7829.17432	297.91049	52.8618

Totals : 1.48106e4 616.35385

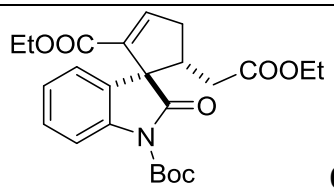
Table 6, entry 8



Signal 1: DAD1 A, Sig=214,4 Ref=420,80

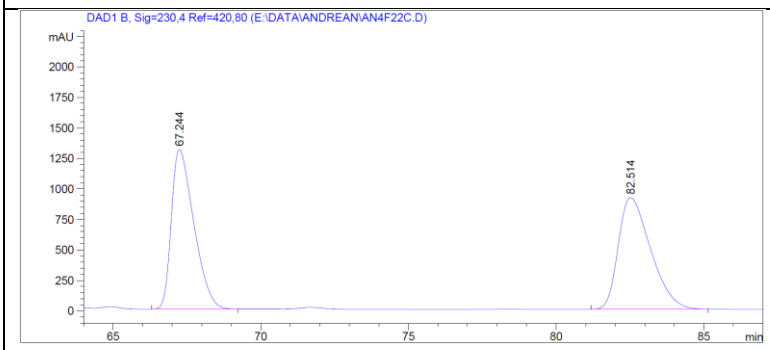
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	25.608	VB	0.3589	121.38121	5.00622	0.6066
2	36.710	VB	0.4125	1.98890e4	752.19196	99.3934

Totals : 2.00103e4 757.19817



6a

Racemic mixture

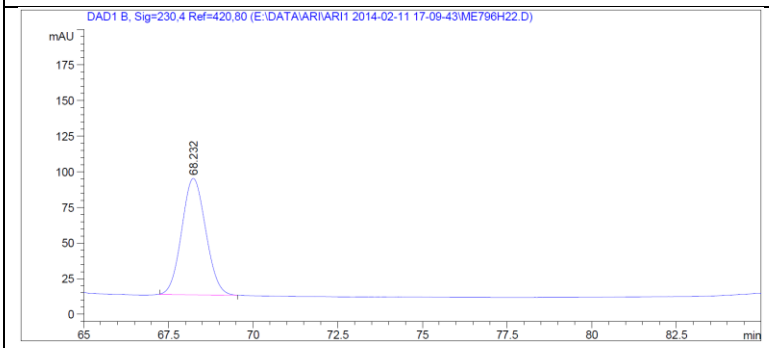


Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	67.244	BB	0.8059	6.91031e4	1308.91687	49.8243
2	82.514	BB	1.1694	6.95904e4	914.88745	50.1757

Totals : 1.38693e5 2223.80432

Table 5, entry 3



Signal 1: DAD1 B, Sig=230,4 Ref=420,80

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	68.232	BB	0.7660	4058.19189	81.90925	100.0000

Totals : 4058.19189 81.90925