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Facile dearomatization of nitroaromatic compounds using lithium enolates of unsaturated ketones in conjugate additions and (4+2) formal cycloadditions

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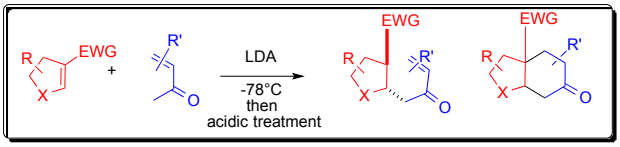
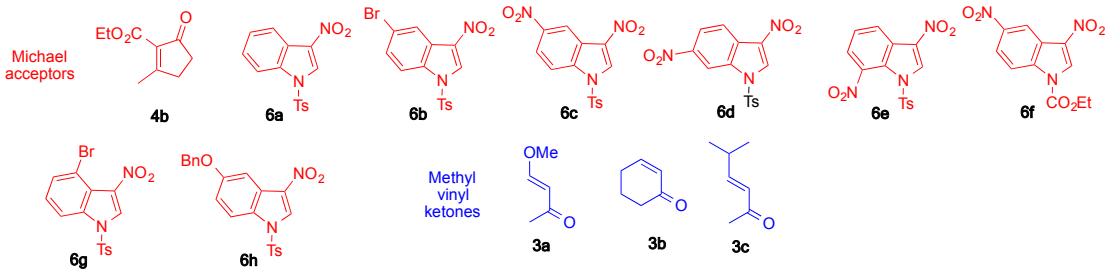
Supporting information

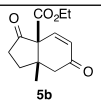
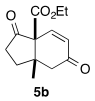
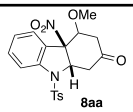
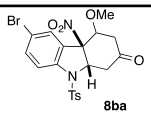
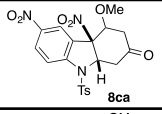
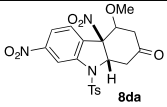
- Optimization of the reaction conditions
- Reaction in organocatalyzed conditions
- Procedures and analytical data for compounds **8aa, 8ba, 8ca, 8da, 8ea, 8fa, 7ga, 7ha, 8ab, 7ac, 8ac, 9, 8ia, 10a, 10b, 11, 13, 14a, 14b.**
- X-Ray structure of compound **8fa**, **7ga**, **8ab**, **8ac, 9.**
- Calculated distances and coupling constants for cis and trans 1,4-adduct **10a**.
- Cartesian coordinates for compounds **10a** and its cis diastereomer.
- Stereochemistry assignment for **14a**/**14b**
- ^{1}H and ^{13}C NMR Spectra for compounds **8aa, 8ba, 8ca, 8da, 8ea, 8fa, 7ga, 7ha, 8ab, 7ac, 8ac, 9, 8ia, 10a, 10b, 11, 13, 14a, 14b.**

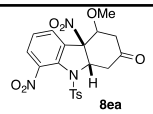
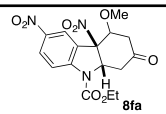
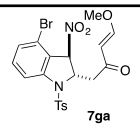
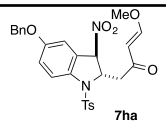
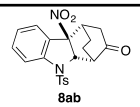
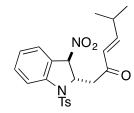
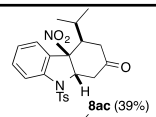
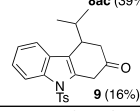
Optimization of the reaction conditions

The reaction conditions were first optimized in the presence of the model tetrasubstituted Michael acceptor **4b**. We tried to generate the lithium dienolate **2a** from butenone **3a** directly, avoiding the use of the more expensive silyloxydiene. **3a** was slowly added to a preformed LDA solution, at –78°C, in order to prevent the usual condensation of the dienolate on the butenone precursor, behaving as a Michael acceptor. Reaction of a slight excess of this preformed lithium dienolate on the model tetrasubstituted ketone **4b**, led to results similar to those reported by Danishefsky from methoxytrimethylsilyloxybutadiene, after TFA treatment. The reaction proved efficient when performed in THF only, thus avoiding the use of solvent mixtures or different temperatures reported in the literature[10,11] (entries 1-3). This led us to use the methoxybutenone **3a** as dienolate precursor in standard conditions (THF, at –78°C) for the subsequent dearomatization study, (entries 4-19). The conversion of the aromatic compound was followed by TLC and confirmed by ^{1}H NMR on the crude mixture, after acidic quenching.





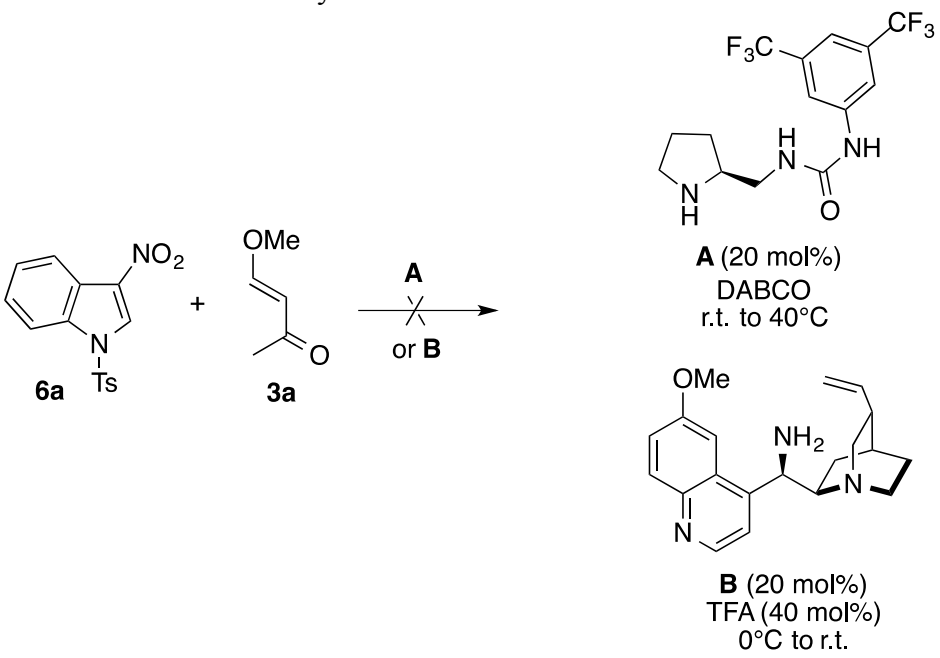
Entry	Michael acceptor	Methyl vinyl ketone	Solvent	Number of enolate equivalent	time	Conv (%)	d.r.	Yield (%)	Product
1	**4b**	**3a**	DME/THF[a]	1.2	2h[b]	100[c]	100 :0	55	 **5b**
2	**4b**	**3a**	DME[d]	1.2	2h	0	-	-	
3	**4b**	**3a**	THF	1.2	2h[b]	100	100 :0[c]	-	 **5b**
4	**6a**	**3a**	THF	1.2	4h[b]	95[e]	85 :15	83	 **8aa**
5	**6b**	**3a**	THF	1.2	4h[b]	62[e]	77 :23	-	
6	**6b**	**3a**	THF	2.4	5h[b]	100[e]	77 :23	61	 **8ba**
7	**6c**	**3a**	THF	1.2	6h[b]	100[e]	89 :11	87	 **8ca**
8	**6d**	**3a**	THF	1.2	6h[b]	100[e]	84 :16	86	 **8da**

9	**6e**	**3a**	THF	1.2	6h[b]	100[e]	78 :22	89	 **8ea**
10	**6f**	**3a**	THF	1.2	6h[b]	100[e]	81 :19	94	 **8fa**
11	**6g**	**3a**	THF	1.2	4h	56	100 :0	n.d.	 **7ga**
12	**6g**	**3a**	THF	1.6	4h	72	100 :0	n.d.	
13	**6g**	**3a**	THF	2.4	5h[b]	100[e]	100 :0	80	
14	**6h**	**3a**	THF	1.2	2h	56	100 :0	n.d.	 **7ha**
15	**6h**	**3a**	THF	1.2	4h	100[e]	100 :0	77	
16	**6a**	**3b**	THF	1.2	6h[b]	100[f]	53 :47	60	 **8ab**
17	**6a**	**3c**	THF	1.2	3h	59	100 :0	n.d.	
18	**6a**	**3c**	THF	1.8	24h[b]	95[e]	100 :0	95	 **7ac**
19	**6a**	**3c**	THF	1.8	24h[b]	95[f]		55	 **8ac** (39%)  **9** (16%)

[a] in the solvent conditions reported by Danishefsky, using a mixture of DME and THF. See ref 11 of the manuscript [b] TLC control. [c] after TFA treatment, under the conditions described by Danishefsky. See ref 11 of the manuscript. [d] in the solvent conditions reported by Baker, see ref 10 of the manuscript. [e] after hydrolysis using aqueous NH_4Cl. [f] hydrolysis using aqueous NH_4Cl, then treatment on SiO_2. n.d. : not determined

Reactions in organocatalyzed conditions:

We envisaged an activation of the methoxybutenne **3a** by involvement of the corresponding dienamine. Considering the reported enantioselective formal [4+2] cycloadditions to 3-nitroindoles by trienamine catalysis reported by Jorgensen et coll.,[1] we considered the reaction of **6a** with **3a** in the presence of the aminourea catalyst **A** and DABCO. Unfortunately, no reaction was observed and the substrates were recovered after 24h. Similarly, when considering the reaction with the cinchona-based primary amine **B**, for a more favorable ketone activation,[2] no reaction was observed in the presence of an acid co-catalyst.



[1] Y. Li, F. Tur, R. P. Nielsen, H. Jiang, F. Jensen and K. A. Jørgensen, *Angew. Chem. Int. Ed.*, 2016, **55**, 1020–1024 (ref 5e of the manuscript).

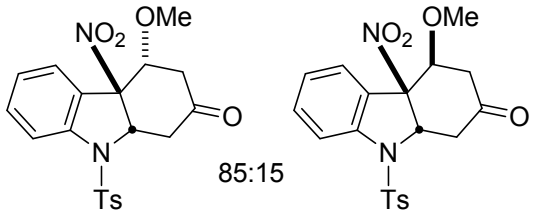
[2] P. Melchiorre, *Angew. Chem. Int. Ed.*, 2012, **51**, 9748–9770.

General. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in deuterated chloroform relative to $(CH_3)_4Si$ and $CDCl_3$ respectively. Chemical shifts are expressed in parts per million (ppm). NOESY spectra were recorded using a mixing time of 300ms and a relaxation delay of 2s. Low and high resolution mass spectra were recorded in either EI, CI or FAB operating in positive or negative ion mode.

General procedure for the reactions with 3-nitroindoles and 3-nitrobenzofuran.
A solution of LDA was prepared at -78˚C under inert atmosphere: to a solution of diisopropylamine (DiPA) (0.6 or 1.2 mmol) in 1 or 2 mL of dry THF cooled to -78˚C was added *n*BuLi (0.6 or 1.2 mmol, 2.4 M in hexane). The dienolate precursor (0.6 or 1.2 mmol) was then added slowly. The resultant mixture was stirred at this temperature for 30 min before adding the nitroaromatic compound (0.5 mmol) dissolved in dry THF. The reaction mixture was then stirred at -78˚C for the requisite time before being quenched with 10 mL of a saturated aqueous NH_4Cl solution. The resulting mixture was extracted with EtOAc (3*10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. When required, the residue was purified by flash chromatography on silica (cyclohexane or petroleum ether (P.E)/ EtOAc or acetone).

General procedure for the reactions with 1,5-dinitronaphthalene and 3-nitropyridine
A solution of LDA was prepared at -78°C under inert atmosphere: to a solution of DiPA (0.6 or 1.2 mmol) in 1 or 2 mL of dry THF cooled to -78°C was added *n*BuLi (0.6 or 1.2 mmol, 2.4 M in hexane). The dienolate precursor (0.6 or 1.2 mmol) was then added dropwise. The resultant mixture was stirred at this temperature for 30 min. Then, freshly distilled HMPA (1.2, 2.4 or 4.8 equiv) was added and the mixture was stirred for the requisite time. A solution of the nitroaromatic compound (0.5 mmol) in dry THF was added and then stirred at -78°C for the requisite time. The mixture was quenched with 5 mL saturated aqueous NH_4Cl solution. The resulting mixture was extracted with EtOAc or DCM (3*10 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The residue was then purified by flash chromatography on silica (cyclohexane/ EtOAc).

4-Methoxy-4-nitro-9-tosyl-4,4,9,9-tetrahydro-1H-carbazol-2(3H)-one - (4S*,4aR*,9aS*) and (4R*,4aR*,9aS*) diastereomers (8aa)[3]



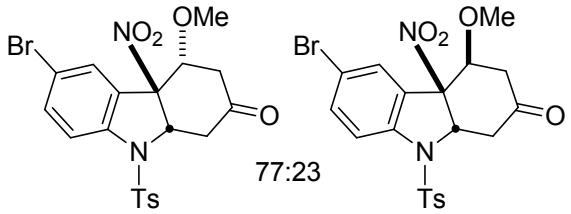
8aa was prepared according to the general procedure using 1.2 eq LDA and trans-4-methoxy-3-buten-2-one **3a** (68 µL, 0.6 mmol) in 1 mL THF and a solution of 3-nitro-1-tosyl-1*H*-indole **6a** (158 mg, 0.5 mmol) in 2 mL THF. The reaction mixture was stirred at -78°C for 4 h. Flash chromatography of the residue (Cyclohexane/EtOAc : 80/20) afforded **8aa** (172 mg, 83%) in a 85 : 15 diastereomeric ratio.

[3] Biolatto, B. ; Kneeteman, M. ; Paredes, E. ; Mancini, P. M. E. *J. Org. Chem*. **2001**, *66*, p 3906-3912

(4R, 4aR*,9aS*) major diastereomer:*
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.2 Hz, 1H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.49-7.43 (m, 3H), 7.20 – 7.13 (m, 3H), 5.08 (dd≈t, *J* = 6.2, 4.9 Hz, 1H), 4.67 (dd, *J* = 10.1, 4.5 Hz, 1H), 3.35 (s, 3H), 3.12 (dd, *J* = 16.2, 6.2 Hz, 1H), 3.05 (dd, J = 16.2, 4.9 Hz, 1H), 2.71 (dd, *J* = 18.6, 4.5 Hz, 1H), 2.35 (s, 3H), 2.07 (dd, *J* = 18.6, 10.1 Hz, 1H).^{13}C NMR (75 MHz, $CDCl_3$) : δ = 202.97, 145.32, 143.20, 132.79, 132.51, 129.96 (2C), 129.61, 127.15 (2C), 125.21, 123.58, 116.86, 96.88, 77.99, 63.54, 58.21, 44.57, 40.14, 21.62.
(4S, 4aR*,9aS*) minor diastereomer :*
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.73 (d, *J* = 8.2, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.55 (d, *J* = 7.9 Hz, 1H), 7.49-7.43 (m, 2H), 7.20 – 7.05 (m, 3H), 5.78 (dd, *J* = 4.9, 3.5 Hz, 1H), 4.65 (m, 1H), 3.35 (s, 3H), 3.28-3.22 (m, 2H), 2.67-2.60 (m, 1H), 2.35 (s, 3H), 1.91 (dd, *J* = 18.9, 2.5 Hz, 1H).^{13}C NMR (75 MHz, $CDCl_3$) : δ = 204.22, 145.22, 142.54, 133.11, 132.90, 129.90 (2C), 129.61, 127.64 (2C), 125.46, 125.03, 116.61, 95.66, 80.35, 61.60, 44.14, 37.5, 30.9, 26.93.

HRMS (ESI^+) m/z Calcd for $C_{20}H_{24}N_3O_6S$ $[M+NH_4]^+$: 434.1389; Found : 434.1386.
IR (neat) ν cm^{-1} = 1726, 1550, 1477, 1357, 1167, 1087, 1014, 659, 571.

6-Bromo-4-methoxy-4a-nitro-9-tosyl-1,3,4,4a,9,9a-hexahydro-2*H*-carbazol-2-one - (4S*,4aR*,9aS*) and(4R*,4aR*,9aS*) diastereomers (8ba)

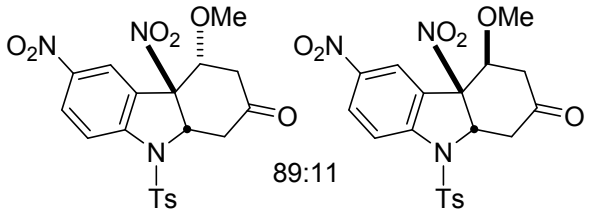


8ba was prepared according to the general procedure using 2.4 eq LDA and **3a** (123 µL, 1.2 mmoL) in 2 mL THF and a solution of 5-bromo-3-nitro-1-tosyl-1*H*-indole **6b** (198 mg, 0.5 mmoL) in 4 mL THF. The reaction mixture was stirred at -78 ˚C for 5 h. Flash chromatography of the residue (Cyclohexane/EtOAc : 95/5) afforded **8ba** (135 mg, 61%) in a 77 : 23 diastereomeric ratio (white solid). From this mixture, the cis cycloadduct could be isolated as a pure compound m.p.=155°C.

(4R,4aR*,9aS*) major diastereomer:*
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.71 (dd, *J* = 1.9, 0.5 Hz, 1H), 7.65-7.58 (m, 2H), 7.46 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 5.04 (dd≈t, *J* = 5.3, 5.3 Hz, 1H), 4.64 (dd, *J* = 10.5, 4.6 Hz, 1H), 3.34 (s, 3H), 3.11 – 3.06 (m, 2H), 2.76 (dd, *J* = 18.7, 4.6 Hz, 1H), 2.36 (s, 3H), 2.04 (dd, *J* = 18.7, 10.5 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 202.46, 145.70, 142.47, 135.63, 132.56, 132.52 (2C), 130.18, 127.17 (2C), 125.36, 118.28, 118.01, 96.33, 77.93, 63.91, 58.32, 44.49, 40.11, 21.71.
(4S,4aR*,9aS*) minor diastereomer:*
^{1}H-NMR (300 MHz, $CDCl_3$): δ= 7.68 (d, *J* = 2.0 Hz, 1H), 7.63 (m, 3H), 7.56 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.24 (d, *J* = 8.0 Hz, 2H), 5.75 (dd≈t, *J* = 4.3, 4.3 Hz, 1H), 4.59 (dd, *J* = 3.5, 2.5 Hz, 1H), 3.35 (s, 3H), 3.31-3.19 (m, 2H), 2.70 (dd, *J* = 18.9, 3.5 Hz, 1H), 2.37 (s, 3H), 1.94 (dd, *J* = 18.9, 2.5 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 203.70, 145.66, 141.90, 136.25, 132.66, 130.18 (2C), 128.60, 127.75 (2C), 126.90, 118.20, 117.82, 95.10, 80.47, 61.99, 58.38, 43.93, 37.68, 21.78.

HRMS (ESI$^-$) m/z Calcd for $C_{20}H_{18}BrN_2O_6S$ [M-H]$^-$: 493.0069; Found: 493.0061. IR (neat) ν (cm^{-1}) = 1733, 1555, 1467, 1362, 1168, 1101, 1086, 666, 576.

4-Methoxy-4a,6-dinitro-9-tosyl-1,3,4,4a,9,9a-hexahydro-2*H*-carbazol-2-one – (4S*,4aR*,9aS*) and (4R*,4aR*,9aS*) diastereomers (8ca)

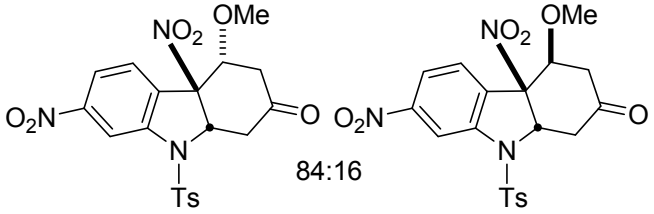


8ca was prepared according to the general procedure with 1.2 eq LDA and **3a** (68 µL, 0.6 mmoL) in 1 mL dry THF and a solution of 3,5-dinitro-1-tosyl-1*H*-indole **6c** (181 mg, 0.5 mmoL) in 4 mL THF. The reaction mixture was stirred at -78 ˚C for 6 h. **8ca** was obtained without further purification (126 mg, 87%) as an oil in a 89 : 11 diastereomeric ratio. Part of this mixture could furnish the pure trans and cis cycloadducts as solids m.p. (trans) = 168°C, m.p. (cis) = 199°C.

(4R,4aR*,9aS*) major diastereomer:*
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.45 (d, *J* = 2.3 Hz, 1H), 8.36 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.85 (d, *J* = 9.1 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 5.19 (dd, *J* = 6.1, 5.0 Hz, 1H), 4.72 (dd, *J* = 9.8, 4.4 Hz, 1H), 3.40 (s, 3H), 3.18 (dd, *J* = 15.4, 6.1 Hz, 1H), 3.11 (dd, *J* = 15.4, 5.0 Hz, 1H), 2.80 (dd, *J* = 18.7, 4.4 Hz, 1H), 2.38 (s, 3H), 2.14 (dd, *J* = 18.7, 9.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 201.92, 148.25, 146.34, 144.88, 132.71, 130.45 (2C), 128.50, 127.12 (2C), 126.02, 124.48, 116.22, 95.75, 77.66, 64.57, 58.41, 44.08, 40.07, 21.78.
(4*S**,4a*R**,9a*S**) minor *diastereomer:*
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.45 (d, *J* = 2.3 Hz, 1H), 8.35 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.84 (d, *J* = 9.1 Hz, 1H), 7.69 (d, *J* = 8.5Hz, 2H), 7.27 (d, *J* = 8.5Hz, 2H), 5.90 (dd, *J* = 5.4, 3.5 Hz, 1H), 4.73 (dd ≈t, *J* = 3.4, 2.6 Hz, 1H), 3.40 (s, 3H), 3.33-3.28 (m, 2H), 2.79 (dd, *J* = 19.1, 3.4 Hz, 1H), 2.38 (s, 3H), 1.97 (dd, *J* = 19.1, 2.6 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 203.07, 147.71, 146.34, 144.66, 132.68, 130.44 (2C), 129.18, 127.62 (2C), 125.71, 122.11, 116.13, 94.45, 80.17, 62.93, 58.53, 43.74, 37.62, 21.83.

HRMS (ESI$^-$) m/z Calcd for $C_{20}H_{18}N_3O_8S$ [M-H]$^-$: 460.0815; Found: 460.0818. IR (neat) ν cm^{-1} = 1734, 1557, 1529, 1371, 1345, 1171, 1096, 1087, 725, 665.

4-Methoxy-4a-7-dinitro-9-tosyl-1,3,4,4a,9,9a-hexahydro-2*H*-carbazol-2-one- (4*S,4a*R**,9a*S**) and (4*R**,4a*R**,9a*S**) diastereomers (8da)**



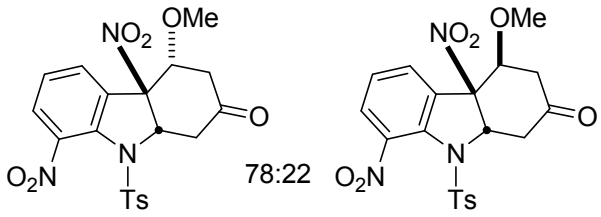
8da was prepared according to the general procedure using 1.2 eq LDA and **3a** (68 µL, 0.6 mmoL) in 1 mL dry THF and a solution of 3,6-dinitro-1-tosyl-1*H*-indole **6d** (181 mg, 0.5 mmoL) in 4 mL THF. The reaction was stirred at -78 ˚C for 6 h. **8da** was

obtained without further purification (132mg, 86%) in a 84 : 16 diastereomeric ratio. Part of this mixture could furnish the trans cycloadduct as a pure solid m.p. (trans) = 173°C.

(4R,4aR*,9aS*) major diastereomer:*
^{1}H-NMR (300 MHz, $CDCl_3$): δ= 8.51 (d, *J* = 2.0 Hz, 1H), 8.01 (dd, *J* = 8.6, 2.0 Hz, 1H), 7.78 (d, *J* = 8.6 Hz, 1H), 7.53 (d, *J* = 8.3 Hz, 2H), 7.22 (d, *J* = 8.3 Hz, 2H), 5.18 (dd ≈t, *J* = 5.5, 5.5 Hz, 1H), 4.72 (dd, *J* = 9.9, 4.4 Hz, 1H), 3.37 (s, 3H), 3.25 – 3.01 (m, 2H), 2.79 (dd, *J* = 18.7, 4.4 Hz, 1H), 2.37 (s, 3H), 2.08 (dd, *J* = 18.7, 9.9 Hz, 1H).
^{13}C NMR (75 MHz, $CDCl_3$): δ= 202.00, 151.01, 146.17, 144.32, 132.41, 130.73, 130.40 (2C), 129.47, 127.22 (2C), 119.91, 111.55, 95.84, 77.72, 64.27, 58.33, 44.20, 39.96, 21.75.
(4S,4aR*,9aS*) minor diastereomer:*
^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.50 (d, *J* = 2.0 Hz, 1H), 7.96 (dd, *J* = 8.5, 2.0 Hz, 1H), 7.76 (d, *J* = 8.5 Hz, 1H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.27 (d, *J* = 8.4 Hz, 2H), 5.87 (dd ≈t, *J* = 4.4, 4.4 Hz, 1H), 4.66 (dd, *J* = 3.6, 2.5 Hz, 1H), 3.39 (s, 3H), 3.17-3.00 (m, 2H), 2.74 (dd, *J* = 18.9, 3.6 Hz, 1H), 2.37 (s, 3H), 1.93(dd, *J* = 18.9, 2.5 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ= 203.05, 151.10, 146.19, 144.39, 132.54, 130.71, 130.42, 129.46 (2C), 127.75 (2C), 120.00, 111.47, 94.79, 80.31, 62.57, 58.47, 43.78, 37.62, 29.82.

HRMS (ESI$^-$) m/z Calcd for $C_{20}H_{18}N_3O_8S$ $[M-H]^-$: 460.0815; Found: 460.0817. IR (neat) ν cm^{-1} = 1728, 1558, 1530, 1347, 1168, 1088, 664.

4-Methoxy-4a-8-dinitro-9-tosyl-1,3,4,4a,9,9a-hexahydro-2*H*-carbazol-2-one - (4S*,4aR*,9aS*) and (4R*,4aR*,9aS*) diastereomers (8ea)



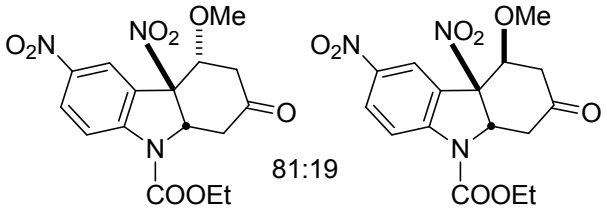
8ea was prepared according to the general procedure with 1.2 eq LDA and **3a** (68 μL, 0.6 mmoL) in 1 mL dry THF and a solution of 3,7-dinitro-1-tosyl-1*H*-indole **6e** (181 mg, 0.5 mmoL) in 4 mL THF. The reaction was stirred at -78 ˚C for 6 h. **8ea** was obtained without further purification (106 mg, 89%) in a 78 : 22 diastereomeric ratio. Part of this mixture could furnish the trans cycloadduct as a pure solid m.p. (trans) = 162°C.

(4R,4aR*,9aS*) major diastereomer:*
^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.01 (dd, *J* = 8.1, 0.9 Hz, 1H), 7.94 (dd, *J* = 7.8, 0.9 Hz, 1H), 7.52 (d, *J* = 8.3 Hz, 2H), 7.45 (dd≈t, *J* = 8.1, 7.8 Hz, 1H), 7.26 (d, *J* = 8.3 Hz, 2H), 5.27 (dd, *J* = 7.0, 4.6 Hz, 1H), 4.61 (dd, *J* = 9.9, 4.7 Hz, 1H), 3.34 (s, 3H), 2.95 (dd, *J* = 16.1, 7.0 Hz, 1H), 2.82 (dd, *J* = 18.3, 4.7 Hz, 1H), 2.74 (dd, *J* = 16.1, 4.6 Hz, 1H), 2.43 (s, 3H), 2.00 (dd, *J* = 18.3, 9.9 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ= 201.58, 146.35, 142.17, 135.77, 134.54, 132.67 (2C), 130.38, 129.39, 128.15, 128.07 (2C), 126.84, 96.49, 78.31, 64.35, 58.41, 43.86, 40.28, 21.85.

(4S,4aR*,9aS*) minor diastereomer:*
^{1}H NMR (300 MHz, $CDCl_3$): δ= 8.02 (dd, *J* = 8.1, 1.2 Hz, 1H), 7.94 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.55 (d, *J* = 8.3 Hz, 2H), 7.43 (dd≈t, *J* = 8.1, 7.8 Hz, 1H), 7.29 (d, *J* = 8.3 Hz, 2H), 5.78 (dd, *J* = 6.8, 3.6 Hz, 1H), 4.46 (dd, *J* = 4.3, 3.0 Hz, 1H), 3.35 (s, 3H), 3.14 (dd, *J* = 16.6, 6.8 Hz, 1H), 2.92 (d, *J* = 18.4, 4.3 Hz, 1H), 2.68 (dd, *J* = 16.6, 3.6 Hz, 1H), 2.43 (s, 3H), 1.98 (dd, *J* = 18.4, 3.0 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ= 202.52, 146.24, 145.20, 141.90, 135.02, 132.78 (2C), 131.10, 130.56, 128.53, 128.13 (2C), 127.02, 94.66, 80.69, 62.78, 58.41, 43.24, 37.89, 21.83.

HRMS (ESI$^-$) m/z Calcd for $C_{20}H_{23}N_4O_8S$ $[M+NH_4^+]^-$: 479.1237; Found: 479.1236. IR (neat) ν cm^{-1} = 1728, 1558, 1539, 1356, 1167, 1088, 660.

Ethyl-4-methoxy-4a,7-dinitro-2-oxo-1,2,3,4,4a-9a-hexahydro-9H-carbazole-9-carboxylate –(4*S, 4a*R**, 9a*S**) and (4*R**, 4a*R**, 9a*S**) diastereomers (8fa)**

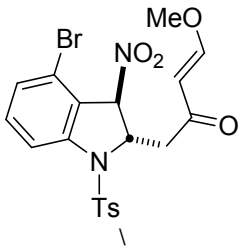


8fa was prepared according to the general procedure using 1.2 eq LDA and **3a** (68 μL, 0.6 mmoL) in 1 mL dry THF and a solution of ethyl-3,5-dinitro-1*H*-indole-1-carboxylate **6f** (139.60 mg, 0.5 mmoL) in 4 mL THF. The reaction was stirred at -78 ˚C for 6 h. Flash chromatography of the residue (P.E./EtOAc = 60/40) afforded **8fa** (178mg, 94%) in a 81 : 19 diastereomeric ratio. Part of this mixture could furnish the pure trans and cis cycloadducts as solids m.p. (trans) = 155°C, m.p. (cis) = 136°C.

(4*R**, 4a*R**, 9a*S**) major diastereomer:
^{1}H-NMR (300 MHz, $CDCl_3$): δ= 8.59 (d, *J* = 2.4 Hz, 1H), 8.35 (dd, *J* = 9.1, 2.4 Hz, 1H), 7.93 (m, 1H), 5.39 (dd, *J* = 6.1, 4.7 Hz, 1H), 4.84 (dd, *J* = 10.0, 4.6 Hz, 1H), 4.36 (m, 2H), 3.47 (s, 3H), 3.09 (dd, *J* = 16.3, 6.1 Hz, 1H), 2.96 (dd, *J* = 16.3, 4.7 Hz, 1H), 2.88 (dd, *J* = 18.6, 4.6 Hz, 1H), 2.20 (dd, *J* = 18.6, 10.0 Hz, 1H), 1.40 (t, *J* = 7.2 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 202.71, 151.34, 148.25, 143.74, 128.58, 125.92, 122.77, 115.68, 95.58, 77.95, 63.75, 62.47, 58.51, 41.97, 40.47, 14.49.
(4*S**, 4a*R**, 9a*S**) minor diastereomer:
^{1}H-NMR (300 MHz, $CDCl_3$): δ= 8.53 (d, *J* = 2.3 Hz, 1H), 8.34 (dd, *J* = 9.1, 2.3 Hz, 1H), 7.95 (m, 1H), 6.08 (dd, *J* = 6.8, 1.8 Hz, 1H), 4.88 (dd≈t, *J* = 2.9, 2.9 Hz, 1H), 4.39 (m, 2H), 3.46 (s, 3H), 3.29 (dd, *J* = 16.8, 6.8 Hz, 1H), 2.98 (d, *J* = 16.8, 1.8 Hz, 1H), 2.78 (dd, *J* = 19.1, 2.9 Hz, 1H), 2.07 (dd, *J* = 19.1, 2.9 Hz, 1H), 1.42 (t, *J* = 7.1 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 203.96, 151.60, 147.93, 143.80, 129.24, 124.63, 121.70, 116.22, 94.30, 80.09, 63.78, 61.03, 58.56, 42.00, 38.12, 14.50.

HRMS (ESI$^-$) m/z Calcd for $C_{16}H_{16}N_3O_8$ $[M-H]^-$: 378.0937; Found: 378.0931. IR (neat) ν cm^{-1} = 1716, 1600, 1445, 1400, 1248, 1173, 1093, 734.

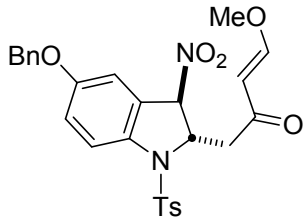
(E)-1-((2S*,3R*)-4-bromo-3-nitro-1-tosylindolin-2-yl)-5-methylhex-3-en-2-one (7ga)



7ga was prepared according to the general procedure using 2.4 eq LDA and **3a** (123 µL, 1.2 mmoL) in 2 mL dry THF and a solution of 4-bromo-3-nitro-1-tosyl-1*H*-indole **6g** (198 mg, 0.5 mmoL) in 4 mL THF. The reaction was stirred at -78 ˚C for 5 h. Flash chromatography of the residue (cyclohexane/EtOAc = 95/5) afforded **7ga** as an oil (198 mg, 80%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ= 7.77 (dd, *J* = 8.0, 0.6 Hz, 1H), 7.70 (d, *J* = 12.7 Hz, 1H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.34 (dd t, *J* = 8.0, 8.0 Hz, 1H), 7.28 (dd, *J* = 8.0, 0.6 Hz, 1H), 7.25 (d, *J* = 8.3 Hz, 2H), 5.65 (d, *J* = 12.7 Hz, 1H), 5.62 (d, *J* = 1.8 Hz, 1H), 4.97 (ddd, *J* = 10.1, 3.3, 1.8 Hz, 1H), 3.76 (s, 3H), 3.42 (dd, *J* = 17.1, 3.3 Hz, 1H), 3.04 (dd, *J* = 17.1, 10.1 Hz, 1H), 2.40 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 195.17, 164.27, 145.31, 144.69, 133.56, 133.45, 129.99 (2C), 128.11, 127.30 (2C), 124.69, 121.81, 115.07, 105.38, 89.38, 63.78, 57.97, 45.05, 21.64. HRMS (ESI$^+$) m/z Calcd for $C_{20}H_{20}BrN_2O_6S$ $[M+H]^+$: 495.0225; Found: 495.0221. IR (neat) ν cm^{-1} = 1620, 1594, 1556, 1361, 1165, 577.

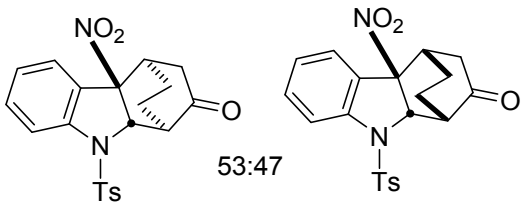
(E)-1-((2*S,3*R**)-5-(benzyloxy)-3-nitro-1-tosylindolin-2-yl)-4-methoxybut-3-en-2-one (7ha)**



7ha was prepared according to the general procedure with 1.2 eq LDA and **3a** (13 µL, 0.12 mmoL) in 0.5 mL dry THF and a solution of 5-(benzyloxy)-3-nitro-1-tosyl-1H-indole **6h** (44 mg, 0.1 mmoL) in 2 mL THF. The reaction was stirred at -78 ˚C for 4 h. After washing with pentane, **7ha** was isolated as an oil (42 mg, 77%).

^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.91 (d, *J* = 9.1 Hz, 1H), 7.64 (d, *J* = 12.7 Hz, 1H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.44 – 7.28 (m, 7H), 7.21 (d, *J* = 8.1 Hz, 2H), 5.91 (d, *J* = 1.5 Hz, 1H), 5.60 (d, *J* = 12.7 Hz, 1H), 5.23 (d, *J* = 11.6 Hz, 1H), 5.17 (d, *J* = 11.6 Hz, 1H), 5.06 (ddd, *J* = 9.1, 2.3, 1.5 Hz, 1H), 3.74 (s, 3H), 3.34 (dd, *J* = 17.0, 2.3 Hz, 1H), 3.11 (dd, *J* = 17.0, 9.1 Hz, 1H), 2.37 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ= 195.10, 164.52, 149.31, 145.81, 137.75, 137.62, 135.31, 133.00, 130.35 (2C), 129.00 (2C), 128.70, 127.73, 127.39 (3C), 121.19, 120.09, 119.84, 105.53, 86.90, 72.48, 63.80, 58.18, 44.93, 21.86. HRMS (ESI$^+$) m/z Calcd $C_{27}H_{25}N_2O_7S$ for $[M-H_2+H]^+$ (oxidized compound): 521.1382; Found: 521.1391. IR (neat) ν cm^{-1} = 1656, 1561, 1534, 1357, 1161, 661, 584, 543.

4a-Nitro-9-tosyl-4,4a,9,9a-tetrahyro-1*H*-1,4-ethanocarbazol-2(*3H*)-one – (*1S*,4S*,4aR*,9aS) and (*1R*,4R*,4aR*,9aS**) diastereomers (8ab)**

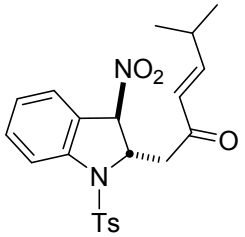


8ab was prepared according to the general procedure using 1.2 eq LDA and cyclohex-2-enone **3b** (60 µL, 0.6 mmoL) in 1 mL dry THF and a solution of **6a** (158 mg, 0.5 mmoL) in 2 mL THF. The reaction mixture was stirred at -78 ˚C for 6 h. The crude mixture was dissolved in EtOH (5 mL) and heated at 40 ˚C with silica gel for 48 hrs. It was filtered over celite and purified by flash chromatography on silica (cyclohexane/EtOAc = 70/30) to afford **8ab** (124 mg, 60%) in a 53 : 47 diastereomeric ratio as a yellow solid. Part of this mixture could furnish the pure trans and cis cycloadducts as solids m.p. (trans) = 96°C, m.p. (cis) = 198°C.

(*1S*,4S*,4aR*,9aS**) major diastereomer :
^{1}H-NMR (300 MHz, $CDCl_3$): δ= 7.72 – 7.61 (m, 3H), 7.48 (dd, *J* = 7.7, 0.8 Hz, 1H), 7.45 – 7.35 (m, 1H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.11 (ddd≈td, *J* = 7.7, 7.7, 0.9 Hz, 1H), 5.49 (d, *J* = 3.6 Hz, 1H), 3.39 – 3.16 (m, 2H), 2.35 (s, 3H), 2.16 (dd, *J* = 19.4, 3.2 Hz, 1H), 2.09 – 1.65 (m, 5H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 208.64, 145.17, 142.57, 133.27, 132.66, 129.95 (2C), 127.71 (2C), 126.68, 125.27, 125.25, 116.51, 96.56, 66.36, 48.19, 40.34, 37.38, 21.71, 20.09, 19.34.
(*1R*,4R*,4aR*,9aS**) minor diastereomer:
^{1}H-NMR (300 MHz, $CDCl_3$): δ= 7.83 (d, *J*=8.6 Hz, 1H), 7.67 (d, *J* = 8.1 Hz, 2H), 7.52 – 7.42 (m, 2H), 7.21 (d, *J* = 8.1 Hz, 2H), 7.15 (dd, *J* = 7.7, 0.9 Hz, 1H), 5.32 (d, *J* = 3.5 Hz, 1H), 3.36-3.28 (m, 1H), 3.25-3.17 (m, 1H), 2.45-2.36 (m, 1H), 2.35 (s, 3H), 2.24 (dd≈t, *J* = 2.7, 2.7 Hz, 1H), 2.02 – 1.83 (m, 1H), 1.74-1.48 (m, 2H), 1.44-1.23 (m, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 209.39, 145.26, 143.33, 133.13, 132.59, 130.00 (2C), 127.76 (2C), 127.10, 125.4, 125.07, 116.24, 96.69, 63.50, 48.51, 41.26, 36.70, 21.73, 21.69, 15.29.

HRMS (ESI$^-$) m/z Calcd. for $C_{21}H_{19}N_2O_5S$ $[M-H]^-$: 411.1093; Found: 411.1091.
IR (neat) ν (cm^{-1}) = 1724, 1551, 1168, 1079, 949, 765.

(E)-5-methyl-1-((2*S,3*R**)-3-nitro-1-tosylindolin-2-yl)hex-3-en-2-one (7ac)**



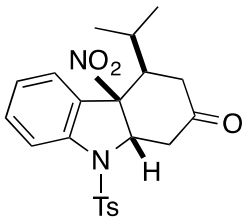
7ac was prepared according to the general procedure using 1.8 eq. LDA and 5-methyl-3-hexen-2-one **3c** (47.5 µL, 0.36 mmol) in 2 mL dry THF and a solution of **6a** (63 mg, 0.2 mmoL) in 2 mL THF. The reaction was stirred at -78 ˚C for 24 h. The crude was washed with pentane, the solid was removed and the filtrate was evaporated to afford

crude oily **7ac,** as a mixture with 5% of unreacted 3-nitro-1-tosyl-1*H*-indole (86 mg, 95% conversion).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 8.9, 0.9 Hz, 1H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.51 (m, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 7.17 (ddd≈td, *J* = 7.6, 7.6, 0.9 Hz, 1H), 6.96 (dd, *J* = 16.1, 6.7 Hz, 1H), 6.12 (dd, *J* = 16.1, 1.3 Hz, 1H), 5.57 (d, *J* = 2.1 Hz, 1H), 5.32 (ddd, *J* = 11.0, 3.5, 2.1 Hz 1H), 3.70 (dd, *J* = 17.9, 3.5 Hz, 1H), 3.13 (dd, *J* = 17.9, 11.0 Hz, 1H), 2.57 (m, 1H), 2.43 (s, 3H), 1.15 (dd, *J* = 6.8, 1.3 Hz, 6H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 197.90, 156.25, 145.07, 142.54, 133.53, 132.39, 129.93 (2C), 127.62 (2C), 127.57, 126.62, 124.78, 124.57, 116.26, 89.04, 62.05, 44.19, 31.46, 21.75, 21.29, 19.21. HRMS (ESI$^+$) m/z Calcd. for $C_{22}H_{26}N_2O_5S$ $[M+H]^+$: 429.1484; Found: 429.1489. IR (neat) ν cm^{-1} = 1718, 166.8, 1557, 1464, 1167, 1089, 757, 573.

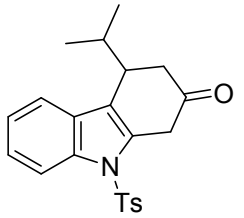
The crude mixture of **7ac** (62 mg, theoretically 0.144 mmol) was dissolved in EtOAc and stirred on silica at room temperature. The crude was then purified by chromatography (98: 2/ Cyclohexane : EtOAc) to afford **8ac** and **9** as oils (24 mg, and 9 mg, 39 % and 16% yield respectively).

(4*S,4a*R**,9a*S**)-4-isopropyl-4-nitro-9-tosyl-1,3,4,4a,9,9a-tetrahydro-1*H*-carbazol-2(3*H*)-one (8ac)**



^{1}H-NMR (300 MHz, $CDCl_3$): δ= 7.78 (d, *J* = 8.2 Hz, 1H), 7.63 (d, *J* = 7.7 Hz, 1H), 7.54-7.46 (m, 1H), 7.5 (d, *J* = 8.1 Hz, 2H) 7.35-7.25 (m, 1H), 7.16 (d, *J* = 8.1 Hz, 2H), 5.48 (dd, *J* = 10.7, 6.1 Hz, 1H), 3.19 (dd, *J* = 17.4, 6.1 Hz, 1H), 2.69 – 2.50 (m, 3H), 2.39 – 2.28 (m, 5H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.70 (d, *J* = 7.0 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 205.72, 145.21, 141.18, 134.03, 132.56, 129.99 (2C), 128.63, 127.21, 127.11 (2C), 125.74, 117.54, 96.22, 64.35, 45.02, 43.71, 36.64, 27.45, 23.98, 21.75, 16.70 . HRMS (ESI$^-$) m/z Calcd. for $C_{22}H_{23}N_2O_5S$ $[M-H]^-$: 427.1328; Found: 427.1332. IR (neat) ν cm^{-1} =1723, 1601, 1544, 1479, 1360, 1167, 765, 573, 539.

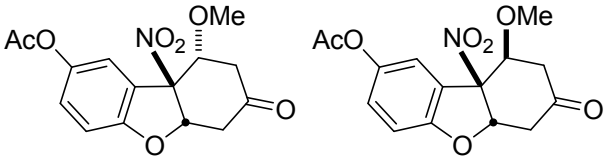
4-isopropyl-9-tosyl-3,4-dihydro-1H-carbazol-2(9H)-one (9)



^{1}H-NMR (300 MHz, $CDCl_3$): δ= 8.19 (d, *J* = 7.7 Hz, 1H), 7.63 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 7.5 Hz, 1H), 7.37 – 7.24 (m, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 3.88 (d, *J* = 22.7 Hz, 1H), 3.79 (d, *J* = 22.7 Hz, 1H), 3.21 (ddd, *J* = 6.9, 5.2, 1.8 Hz, 1H), 2.78 (dd, *J* = 15.3, 1.8 Hz, 1H), 2.58 (dd, *J* = 15.3, 6.9 Hz, 1H), 2.33 (s, 3H), 2.03 – 1.84 (m, 1H), 0.89 (d,

J = 6.8 Hz, 3H), 0.71 (d, *J* = 6.8 Hz, 3H).^{13}C-NMR (75 MHz, $CDCl_3$): δ = 208.07, 145.16, 137.12, 135.79, 131.69, 130.10 (2C), 129.22, 126.41 (2C), 124.70, 123.74, 121.24, 119.17, 114.89, 41.34, 40.09, 38.04, 33.40, 21.67, 20.74, 18.92. HRMS (ESI^-) m/z Calcd. for $C_{22}H_{22}NO_3S$ $[M-H]^-$: 380.1320; Found : 380.1327. IR (neat) ν cm^{-1} = 3664, 2957, 2923, 1712, 1602, 1367, 1166, 1087, 567, 540.

9-methoxy-9a-nitro-7-oxo-5a,6,7,8,9,9a-hexahyrodibenzo[*b,d*]furan-2-yl acetate - (5a*R, 9*R**, 9a*R**) and (5a*R**, 9*S**, 9a*R**) diastereomers (8ia)**

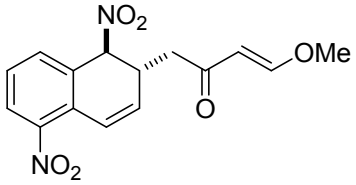


75:25

8ia was prepared according to the general procedure with 1.2 eq LDA and **3a** (68 µL, 0.6 mmoL) in 1 mL dry THF and a solution of 3-nitrobenzofuran-5-yl-acetate **6i** (111 mg, 0.5 mmoL) in 4 mL THF. The reaction was stirred at -78 ˚C for 6 h. Flash chromatography of the residue (Cyclohexane/Acetone = 80/20) afforded solid **8ia** (127 mg, 79%) in a 75 : 25 diastereomeric ratio. Part of this mixture could furnish the pure trans and cis cycloadducts as solids m.p. (trans) = 98°C, m.p. (cis) = 103°C.

(5a*R**, 9*S**, 9a*R**) major diastereomer:
^{1}H- NMR (300 MHz, $CDCl_3$): δ= 7.43 (d, *J* = 2.6 Hz, 1H), 7.12 (dd, *J* = 8.8, 2.6 Hz, 1H), 6.83 (d, *J* = 8.8 Hz, 1H), 5.44 – 5.40 (m, 1H), 4.64 (dd, *J* = 12.2, 4.4 Hz, 1H), 3.42 (s, 3H), 3.04 – 2.89 (m, 2H), 2.82 (dd, *J* = 18.4, 4.4 Hz, 1H), 2.30 (s, 3H), 1.97 (dd, *J* = 18.4, 12.2 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 203.01, 169.66, 158.04, 145.03, 126.37, 123.44, 119.19, 110.84, 98.24, 83.09, 78.85, 58.30, 42.56, 40.39, 21.18.
(5a*R**, 9*R**, 9a*R**) minor diastereomer:
^{1}H-NMR (300 MHz, $CDCl_3$): δ= 7.44 (d, *J* = 2.5 Hz, 1H), 7.09 (dd, *J* = 8.8, 2.5 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.16 (ddd, *J* = 4.5, 2.5, 1.1 Hz, 1H), 4.53 (ddd, *J* = 3.7, 2.0, 1.1 Hz, 1H), 3.37 (s, 3H), 3.13 (dd, *J* = 17.5, 4.5 Hz, 1H), 2.95 (dd, *J* = 17.5, 2.5 Hz, 1H), 2.76 (dd, *J* = 18.4, 3.7 Hz, 1H), 2.29 (s, 3H), 2.05 (dd, *J* = 18.4, 2.0 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ= 203.71, 169.61, 157.10, 145.23, 126.77, 122.28, 118.73, 111.59, 96.07, 81.57, 80.69, 58.36, 41.65, 38.19, 21.12.

HRMS (ESI^-) m/z Calcd. $C_{13}H_{12}NO_6$ for $[M-C_2H_3O]^-$: 278.0665; Found: 278.0667. IR (neat) ν cm^{-1} = 1757, 1726, 1618, 1554, 1480, 1178, 499.
(*E*)-1-((1*R,2*R**)-1,5-dinitro-1,2-dihydronaphthalen-2-yl)-4-methoxybut-3-en-2-one (10a)**

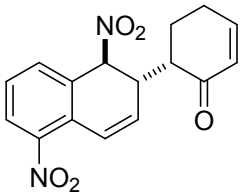


10a was prepared according to general procedure using **3a** (68 µL, 0.6 mmol) in 1 mL dry THF. The mixture was stirred at -78°C for 30 min. To this mixture was added HMPA (418 µL, 2.4 mmol) and the whole was stirred for 5 min. Then a solution of 1,5-

dinitronaphthalene **9** (109 mg, 0.5 mmol) in 5 mL THF was added dropwise. The reaction mixture was stirred at -78°C for 4 h. After hydrolysis, extraction and concentration, flash chromatography of the residue (Cyclohexane/EA = 80/20) afforded **10a** (130 mg, 82%).

^{1}H-NMR (300 MHz, $CDCl_3$): 8.02 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.62 (d, *J* = 7.5 Hz, 1H), 7.58 (d, *J* = 12.7 Hz, 1H), 7.45 (t, *J* = 8.0 Hz, 1H), 7.12 (d, *J* = 10.1 Hz, 1H), 6.39 (ddd, *J* = 10.1, 5.9, 1.0 Hz, 1H), 5.58 (d, *J* = 2.1 Hz 1H), 5.53 (d, *J* = 12.7 Hz, 1H), 4.10 – 4.00 (m, 1H), 3.70 (s, 3H), 2.62 (dd, *J* = 17.0, 6.0 Hz, 1H), 2.40 (dd, *J* = 17.0, 8.8 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.41, 163.93, 136.47, 133.95, 128.33, 128.17, 127.52, 126.99, 121.45, 120.08, 105.04, 85.78, 58.07, 41.15, 33.46. HRMS (ESI^-) m/z Calcd for $C_{15}H_{13}N_2O_6$ $[M-H]^-$: 317.0779; Found: 317.0770.

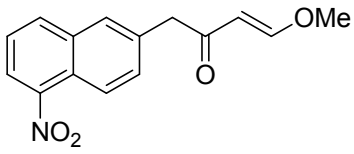
(S)-6-((1R,2S)-1,5-dinitro-1,2-dihydronaphthalen-2-yl)cyclohex-2-enone (10b)



10b was prepared according to general procedure using **3b** (68 μL, 0.6 mmol) in 1 mL dry THF. The mixture was stirred at -78°C for 30 min. To this mixture was added HMPA (418 μL, 2.4 mmol) and the whole was stirred for 5 min. Then a solution of **9** (109 mg, 0.5 mmol) in 5 mL THF was added. The reaction mixture was stirred at -78°C for 14 h. After hydrolysis, extraction and concentration, flash chromatography of the residue (Cyclohexane/EA= 80/20 then 70/30) afforded **10b** (113 mg, 72%).

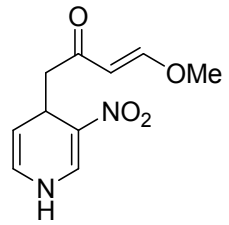
^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.03 (d, *J* = 8.3 Hz, 1H), 7.65 (d, *J* = 7.5 Hz, 1H), 7.46 (dd, *J* = 8.3, 7.5 Hz, 1H), 7.23 (d, *J* = 10.3 Hz, 1H), 7.06 – 6.93 (m, 1H), 6.29 (dd, *J* = 10.3, 5.9 Hz, 1H), 6.04 (d, *J* = 10.1 Hz, 1H), 5.87 (bs, 1H), 4.00 - 3.96 (m, 1H), 2.43 – 2.26 (m, 3H), 2.04 – 1.80 (m, 2H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 198.96, 150.58, 146.80, 136.41, 131.86, 129.41, 128.92, 128.41, 127.48, 126.85, 122.86, 85.69, 47.20, 36.52, 25.76, 25.06. HRMS (ESI^-) m/z Calcd for $C_{16}H_{13}N_2O_5$ $[M-H]^-$: 313.0824; Found: 313.0823.

(*E*)-4-methoxy-1-(5-nitronaphthalen-2-yl)but-3-en-2-one (11)



^{1}H-NMR (300 MHz, $CDCl_3$): δ = 8.53 (d, *J* = 8.9 Hz, 1H), 8.20 (dd, *J* = 7.6, 1.1 Hz, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.80 (m, 1H), 7.68 (d, *J* = 12.6 Hz, 1H), 7.60 – 7.49 (m, 2H), 5.66 (d, *J* = 12.6 Hz, 1H), 3.94 (s, 2H), 3.69 (s, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 195.99, 163.89, 146.56, 134.70, 134.55, 134.49, 131.41, 128.78, 124.57, 124.21, 123.95, 123.66, 104.73, 57.93, 48.36. HRMS (ESI^+) m/z Calcd. $C_{15}H_{14}NO_4$ for $[M+H]^+$: 272.0923; Found: 272.0921. IR (neat) ν cm^{-1} = 1634, 1582, 1513, 1331, 1190, 774.

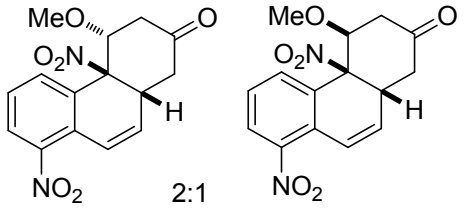
(*E*)-4-methoxy-1-(3-nitro-1,4-dihydropyridin-4-yl)but-3-en-2-one (13)



13 was prepared according to general procedure using **3a** (136 µL, 1.2 mmol) in 2 mL dry THF. The mixture was stirred at -78°C for 30 min. To this mixture was added HMPA (418 µL, 2.4 mmol) and the whole was stirred for 15 min. Then a solution of nitropyridine **12** (62 mg, 0.5 mmol) in 0.5 mL THF was added. The reaction mixture was stirred at -78°C for 3 h. After hydrolysis, extraction and concentration, flash chromatography of the residue (Cyclohexane/EA = 70/30, 50/50 then 100% EA) afforded **13** (80 mg, 71%).

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 7.95 (d, *J* = 6.5 Hz, 1H), 7.64 (d, *J* = 12.7 Hz, 1H), 7.16 (bs, 1H), 6.05 (dd, *J* = 7.8, 4.1 Hz, 1H), 5.56 (d, *J* = 12.7 Hz, 1H), 5.28 (ddd, *J* = 7.8 , 4.9, 1.4, 1H), 4.33 – 4.25 (m, 1H), 3.71 (s, 3H), 2.98 (dd, *J* = 15.0, 3.1 Hz, 1H), 2.64 (dd, *J* = 15.0, 9.1 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ = 197.73, 163.72, 137.98, 124.67, 122.86, 111.01, 106.20, 57.82, 47.06, 31.34. HRMS (ESI$^+$) m/z Calcd for $C_{10}H_{13}N_2O_4$ $[M+H]^+$: 225.0870; Found: 225.0875.

4-methoxy-4a,8-dinitro-1,4,4a,10a-tetrahydrophenanthren-2(3H)-one - (4R*,4aR*,10aR*) and (4R*,4aR*,10aS*) diastereomers (14a, 14b)



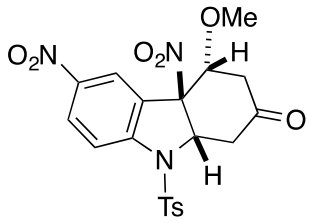
14a and **14b** were prepared according to general procedure using **3a** (68 µL, 0.6 mmol) in 1 mL dry THF. The mixture was stirred at -78°C for 30 min. To this mixture was added HMPA (104 µL, 0.6 mmol) and the whole was stirred for 5 min. Then a solution of **9** (109 mg, 0.5 mmol) in 5 mL THF was added. The reaction mixture was stirred at -78°C for 4 h. After hydrolysis, extraction and concentration, the mixture was left at r.t. for 36 h. Flash chromatography of the residue (Cyclohexane/EA = 80/20, 70/30 then 50/50) afforded **14a** and **14b** (55 mg (**14a**), 30 mg (**14b**), 53% overall yield).

(4R*,4aR*,10aR*) major diastereomer **14a**:
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 8.63 (d, *J* = 7.9 Hz, 1H), 8.04 (dd, *J* = 8.2, 0.8 Hz, 1H), 7.55 (dd, *J* = 8.2, 7.9 Hz, 1H), 7.10 (d, *J* = 10.0 Hz, 1H), 6.30 (dd, *J* = 10.0, 6.2 Hz, 1H), 4.55 (dd, *J* = 13.2, 4.6 Hz, 1H), 3.53 (ddd, *J* = 13.6, 6.2, 4.8 Hz, 1H), 3.46 (s, 3H), 3.06 (ddd, *J* = 14.6, 4.6, 2.0 Hz, 1H), 2.73 (ddd, *J* = 14.6, 13.2, 0.8 Hz, 1H), 2.65 (ddd, *J* = 15.6, 4.6, 2.1 Hz, 1H), 1.95 (dd, *J* = 15.6, 13.6 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm) 201.93, 147.75, 135.45, 130.60, 128.53, 128.47, 128.31, 126.39, 122.99, 93.63, 83.07, 59.03, 42.98, 42.43, 37.63.
(4R*,4aR*,10aS*) minor diastereomer **14b**:

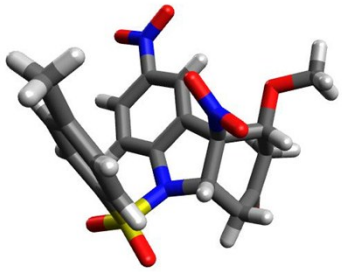
^{1}H-NMR (300 MHz, $CDCl_3$): δ (ppm) 7.97 (dd, *J* = 8.2, 1.1 Hz, 1H), 7.92 (d, *J* = 7.9 Hz, 1H), 7.56 (dd, *J* = 8.2, 7.9 Hz, 1H), 6.93 (d, *J* = 10.1 Hz, 1H), 6.53 (dd, *J* = 10.1, 6.1 Hz, 1H), 4.98 (dd, *J* = 3.7, 2.5 Hz, 1H), 4.18 (ddd, *J* = 13.2, 6.1, 5.6 Hz, 1H), 3.42 (s, 3H), 2.91 (ddd, *J* = 15.3, 3.7, 2.6Hz, 1H), 2.73 – 2.65 (m, 2H), 2.02 (dd, *J* = 15.1, 13.2 Hz, 1H). ^{13}C-NMR (75 MHz, $CDCl_3$): δ (ppm) 202.85, 147.92, 135.47, 132.52, 129.19, 128.79, 127.69, 126.83, 119.43, 91.37, 81.69, 58.11, 41.97, 40.13, 33.85.

HRMS (ESI^-) m/z Calcd for $C_{15}H_{13}N_2O_6$ $[M - H]^-$: 317.0852; Found: 317.0767.
IR (neat) ν cm^{-1} = 1728, 1549, 1522, 1342, 1101, 1077.

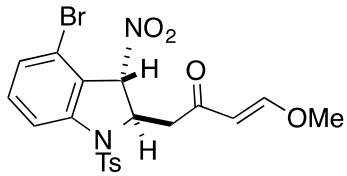
X-Ray structure of 8fa (major diastereomer)



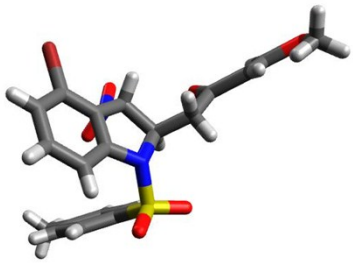
8fa major



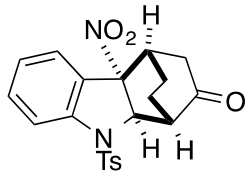
X-Ray structure of 7ga



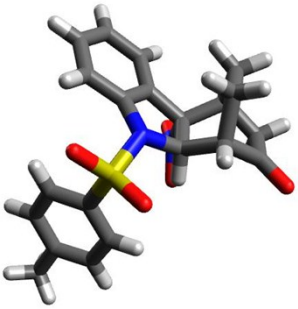
7ga



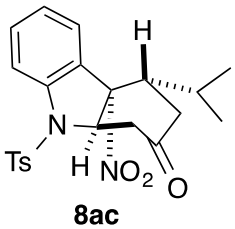
X-Ray structure of 8ab (major diastereomer)



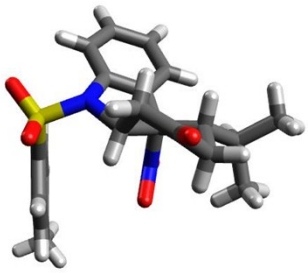
8ab



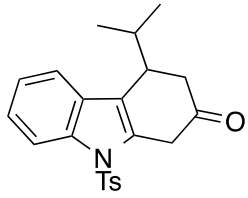
X-Ray structure of 8ac.



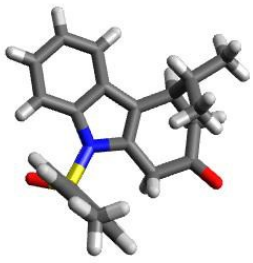
8ac



X-Ray structure of 9.



9



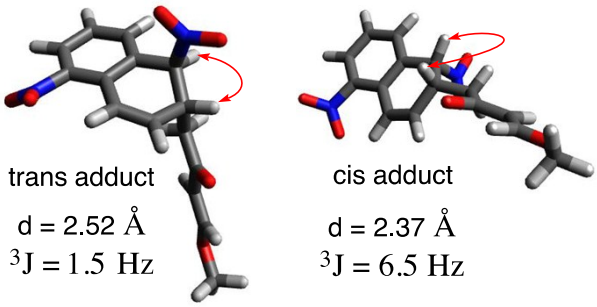
Stereochemistry of compound 10a

Optimization of the structures were effected using Gaussian 09, Revision D.01, set of programs.[4] Full geometry optimizations were carried out in the absence of symmetry constraints at the M062X/6-311++G(d,p) level of theory applying the conductor polarizable continuum model ($CHCl_3$).

NMR calculations were effected on the optimized structures at the M062X/6-311++G(d,p) level of theory

The 1,2-trans stereochemistry of the adduct **10a** was assigned by ^{1}H NMR ^3J coupling constant between the two vicinal protons borne by the tetrahedral carbon atoms, by comparing the experimental figures with the values estimated by DFT calculations. The experimental scalar coupling is indeed small, 2.1 Hz, in global accord with the 1.5 Hz calculated one for the trans diastereomer. The calculated coupling for the cis diastereomer is significantly larger (6.5 Hz). Note that this stereochemical characteristic could not be assigned on the sole basis of NOE effects. Indeed, a NOE effect was observed between these two protons that are close-by, even in the trans structure: the DFT optimized distance is 2.52 Å in the trans and 2.37 Å in the cis.

Calculated distances and coupling constants for cis and trans 1,4-adduct



[4] Gaussian 09, Revision D.01, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Men- nucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Ko- bayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyen- gar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Knox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, R. L. Martin, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, Ö. Farkas, J. B. Foresman, J. V. Ortiz, J. Cio- slowski, D. J. Fox, Gaussian, Inc., Wallingford CT, 2009.

Cartesian coordinates for the cis adduct :

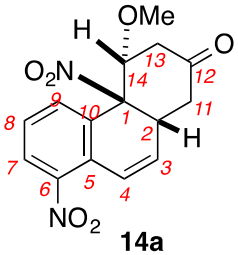
C	0.13332	-0.89013	1.24413
C	0.80751	-1.53941	2.26983
C	2.18169	-1.40180	2.36741
C	2.85617	-0.63546	1.42216
C	2.16823	-0.01728	0.38685
C	0.76863	-0.11915	0.26400
H	0.24683	-2.13328	2.97944
H	2.72165	-1.88642	3.16991
H	3.93168	-0.51484	1.48745
C	2.93189	0.82602	-0.61043
C	0.09542	0.49423	-0.89133
N	-1.33119	-1.06408	1.24045
O	-2.02303	-0.10455	0.97137
O	-1.76185	-2.15815	1.53876
C	0.80270	0.93627	-1.93180
C	2.30270	0.84514	-1.99415
N	3.03104	2.22555	0.01035
O	3.94916	2.40403	0.78016
O	2.18901	3.04733	-0.26762
C	2.93000	1.87871	-2.92733
C	2.66360	1.57601	-4.39407
O	2.09383	0.55285	-4.73207
C	3.14691	2.58699	-5.33854
C	2.96475	2.40201	-6.65494
O	3.37865	3.27976	-7.56299
C	3.11433	2.94014	-8.92675
H	3.50387	3.75815	-9.52601
H	3.62436	2.01216	-9.19069
H	2.03998	2.84039	-9.09032
H	-0.98186	0.55305	-0.89999
H	0.29331	1.34043	-2.79966
H	3.64469	3.47443	-4.96704
H	2.46116	1.50957	-7.02389
H	2.56400	2.88605	-2.70930
H	4.01897	1.91154	-2.79861
H	2.53316	-0.14451	-2.41404
H	3.97216	0.50816	-0.65751

Cartesian coordinates for the trans adduct (10a):

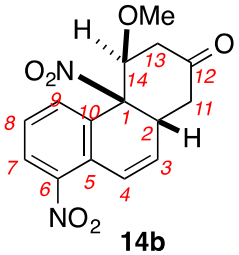
C	-0.00927	-0.21172	0.64004
C	0.13424	0.52633	1.80791
C	1.39356	0.96697	2.17864
C	2.48349	0.67654	1.36354
C	2.31831	-0.04119	0.18826
C	1.05477	-0.51457	-0.21574
H	-0.73847	0.73749	2.41142
H	1.52449	1.52848	3.09417
H	3.47543	1.01231	1.64531
C	3.49708	-0.35344	-0.68436
C	0.93721	-1.19996	-1.51304
N	-1.38115	-0.65907	0.33512
O	-1.53324	-1.76387	-0.14207
O	-2.28692	0.10119	0.60617
C	1.90753	-1.09596	-2.42710
C	3.16369	-0.30479	-2.17190
H	4.35052	0.28622	-0.45325
C	2.99500	1.15310	-2.61996
C	2.85274	1.28445	-4.12786
O	2.97451	0.31573	-4.85667
C	2.58320	2.64040	-4.61498
C	2.45227	2.85422	-5.93308
O	2.20903	4.05815	-6.44066
C	2.09064	4.12324	-7.86447
H	1.89431	5.16369	-8.10720
H	3.02083	3.80193	-8.33620
H	1.26075	3.50100	-8.20338
H	0.03750	-1.75330	-1.73423
H	1.79014	-1.54727	-3.40420
H	2.48967	3.45658	-3.90899
H	2.54268	2.02960	-6.63877
H	2.12231	1.61333	-2.14372
H	3.86410	1.75245	-2.32230
H	3.99375	-0.73855	-2.73065
N	4.02942	-1.76502	-0.35865
O	4.96222	-2.14814	-1.02826
O	3.51687	-2.39102	0.53692

Stereochemistry assignment for **14a**/**14b**

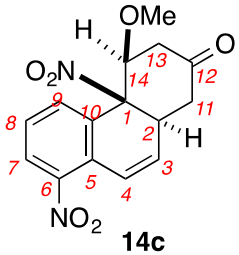
The cyclization of the crude adduct **10a** can theoretically lead to four cycloadducts **14a**, **14b**, **14c** and **14d**.



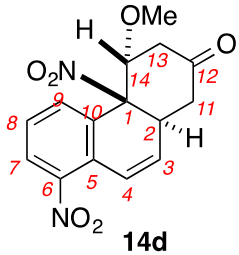
14a



14b



14c



14d

Two of these four compounds were isolated and characterized by 2D ^{1}H-^{1}H NOESY NMR. In NOESY spectra, correlations are expected between protons separated by a distance of less than 3Å, the intensity of the NOE being inversely proportional to the distance between the correlated protons. In order to identify the isolated structures, the geometries of the four isomers were optimized by DFT calculations (M062X/6-31G) and the interatomic H-H distances were estimated to be compared to the observed NOE (table 1).

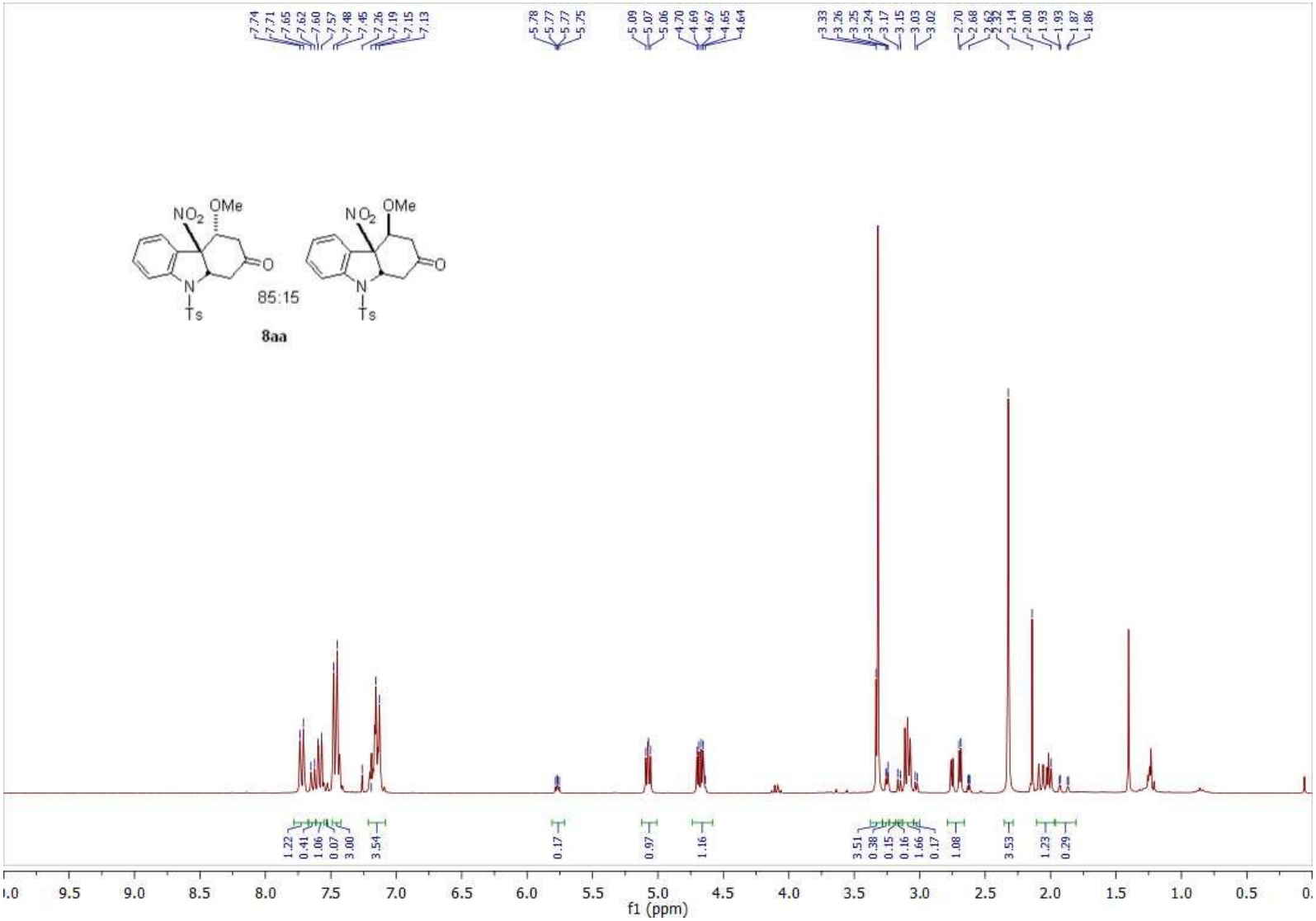
On the 2D NOESY spectrum of the main form, a strong NOE was observed between H2

(3.53 ppm) and H14 (4.55 ppm), excluding the isomers **14b** and **14d** in which H2 and H14 are directed on either side of the molecule plane. Another strong NOE correlation appeared between H9 (8.63 ppm) and one of the H13 (2.73 ppm). In **14c** $d_{H9\text{-}H13a}$ and $d_{H9\text{-}H13b}$ were estimated to 4.39Å and 4.51Å, respectively, whereas in **14a** $d_{H9\text{-}H13a}$ and $d_{H9\text{-}H13b}$ were 2.41Å and 3.58Å, respectively. Consequently the main cycloadduct was assigned to **14a**. The absence of correlation between H9 and H14 confirmed this conclusion. Actually, $d_{H9\text{-}H14}$ was 3.71 in **14a** and 2.33 in **14c** for which a strong NOE would therefore be expected.

The same method was used to determine the structure of the minor cycloadduct. No correlation appeared between H2 (4.18 ppm) and H14 (4.98 ppm) in the 2D NOESY spectrum, excluding the structures **14a** and **14c**. The mean NOE observed between H9 and H13 (2.70 ppm) was in favour of the isomer **14b**.

Table 1: H-H distances (Å) estimated on the calculated structures and expected/observed NOEs

$d_{H\text{-}H}$ (Å)			Expected NOE	Observed NOE
	14a	**14c**		
H2-H14	2.31	2.65	Strong/mean	Strong
H9-H13a	2.41	4.39	Strong/-	Strong
H9-H13b	3.58	4.51	- / -	No NOE
H9-H14	3.71	2.33	- / strong	No NOE
	14b	**14d**		
H2-H14	3.71	3.69	- / -	No NOE
H9-H13a	2.59	4.44	Mean/-	Mean
H9-H13b	3.57	4.42	- / -	
H9-H11a	4.35	5.65	- / -	
H9-H11b	5.61	5.98	- / -	
H9-H14	2.02	2.06	Strong/strong	Strong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7.62
7.60
7.57
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7.45
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7.19
7.15
7.13
5.78
5.77
5.77
5.75
5.09
5.07
5.06
4.70
4.69
4.67
4.65
4.64
3.33
3.26
3.25
3.24
3.17
3.15
3.03
3.02
2.70
2.68
2.62
2.32
2.14
2.00
1.93
1.93
1.87
1.86
NO2
OMe
O
N
Ts
85:15
NO2
OMe
O
N
Ts
8aa
1.22
0.41
1.06
0.07
3.00
3.54
0.17
0.97
1.16
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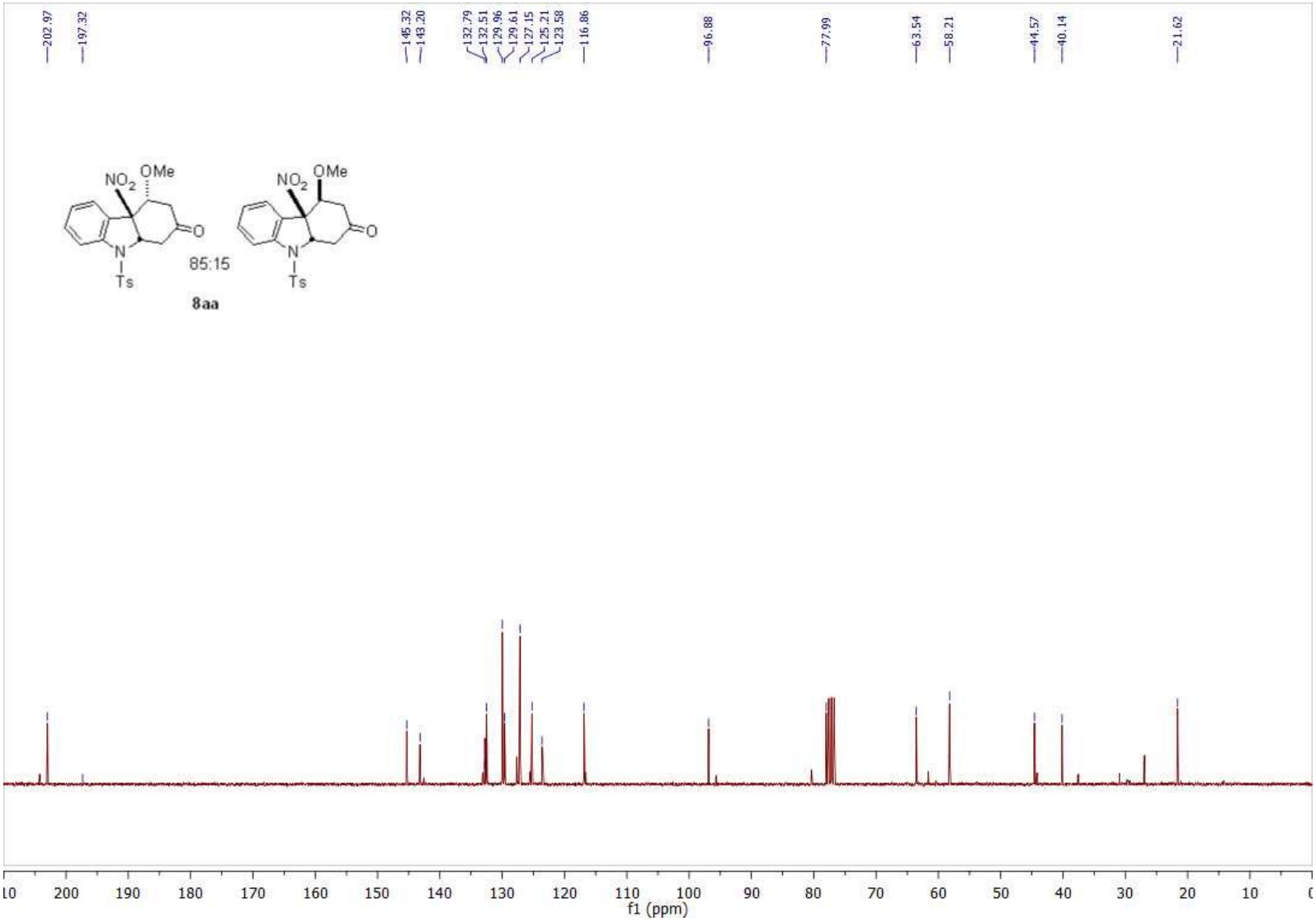
f1 (ppm)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132.51
129.96
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127.15
125.21
123.58
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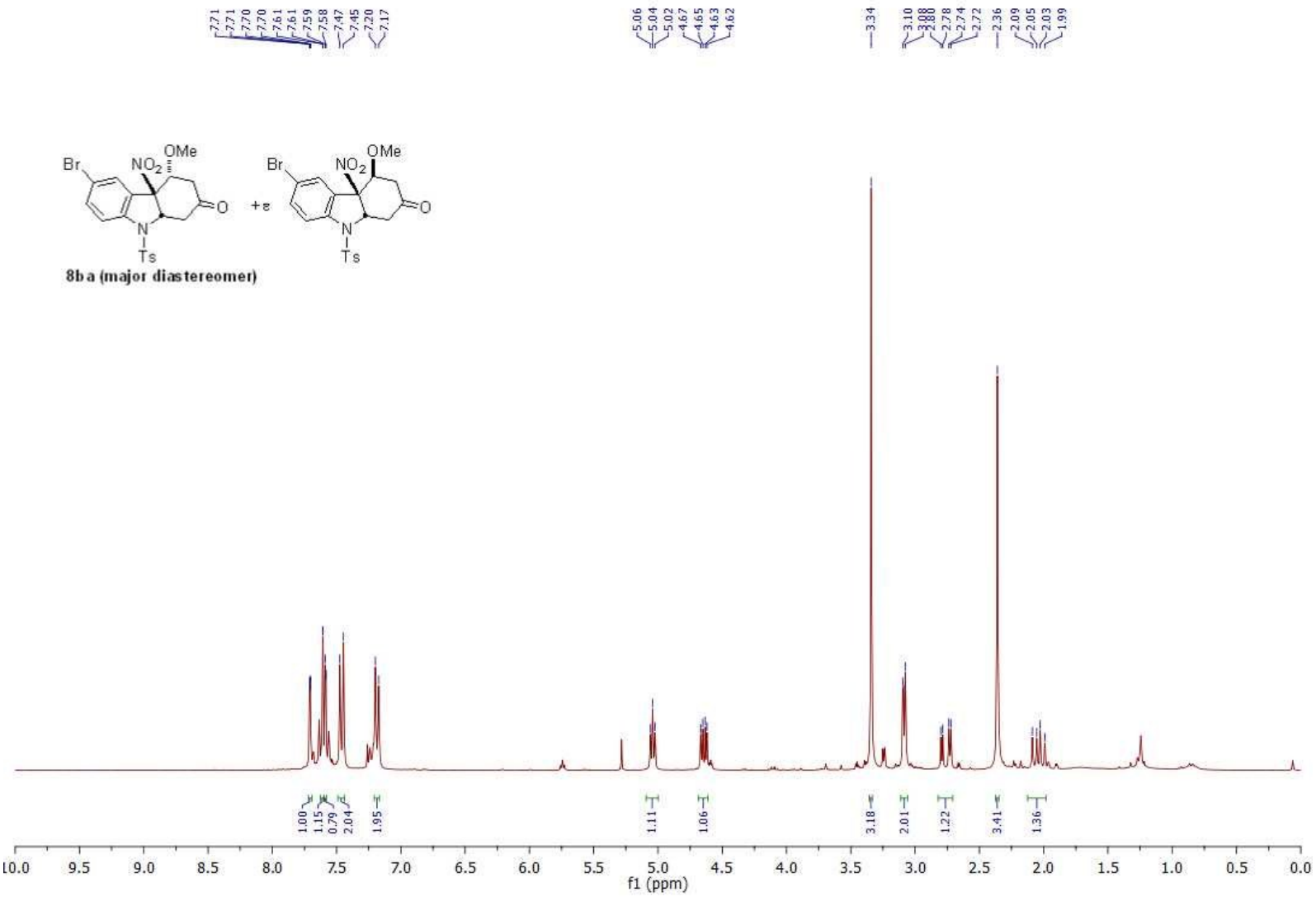
96.88
77.99
63.54
58.21
44.57
40.14
21.62
NO2
OMe
O
N
Ts
85:15
8aa
f1 (ppm)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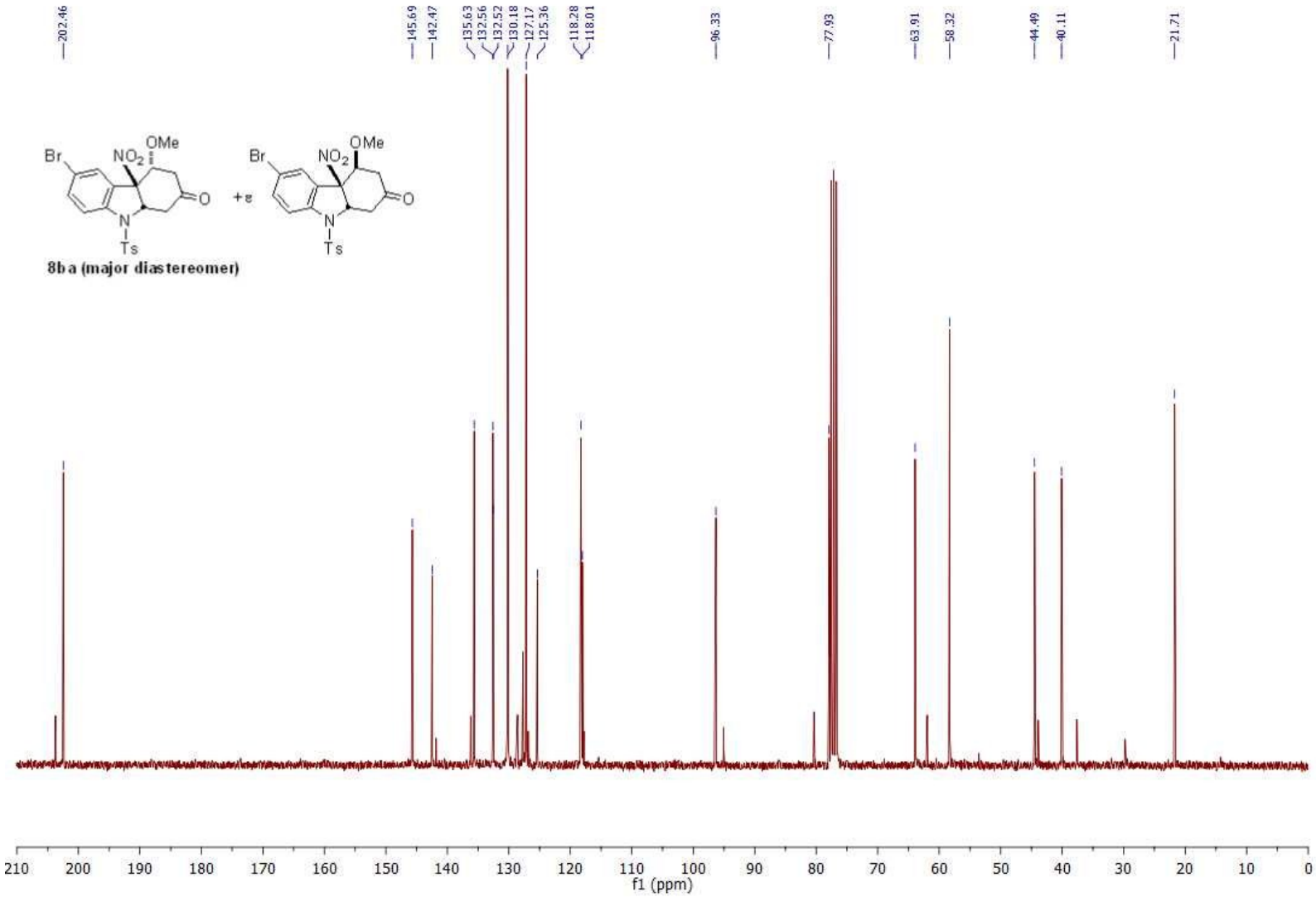
7.71
7.70
7.70
7.70
7.61
7.61
7.59
7.58
7.47
7.45
7.20
7.17
5.06
5.04
5.02
4.67
4.65
4.63
4.62
3.34
3.10
2.78
2.74
2.72
2.36
2.09
2.05
2.03
1.99
Br
NO2
OMe
O
N
Ts
+ε
8ba (major diastereomer)
1.00
1.15
0.79
2.04
1.95
1.11
1.06
3.18
2.01
1.22
3.41
1.36
f1 (ppm)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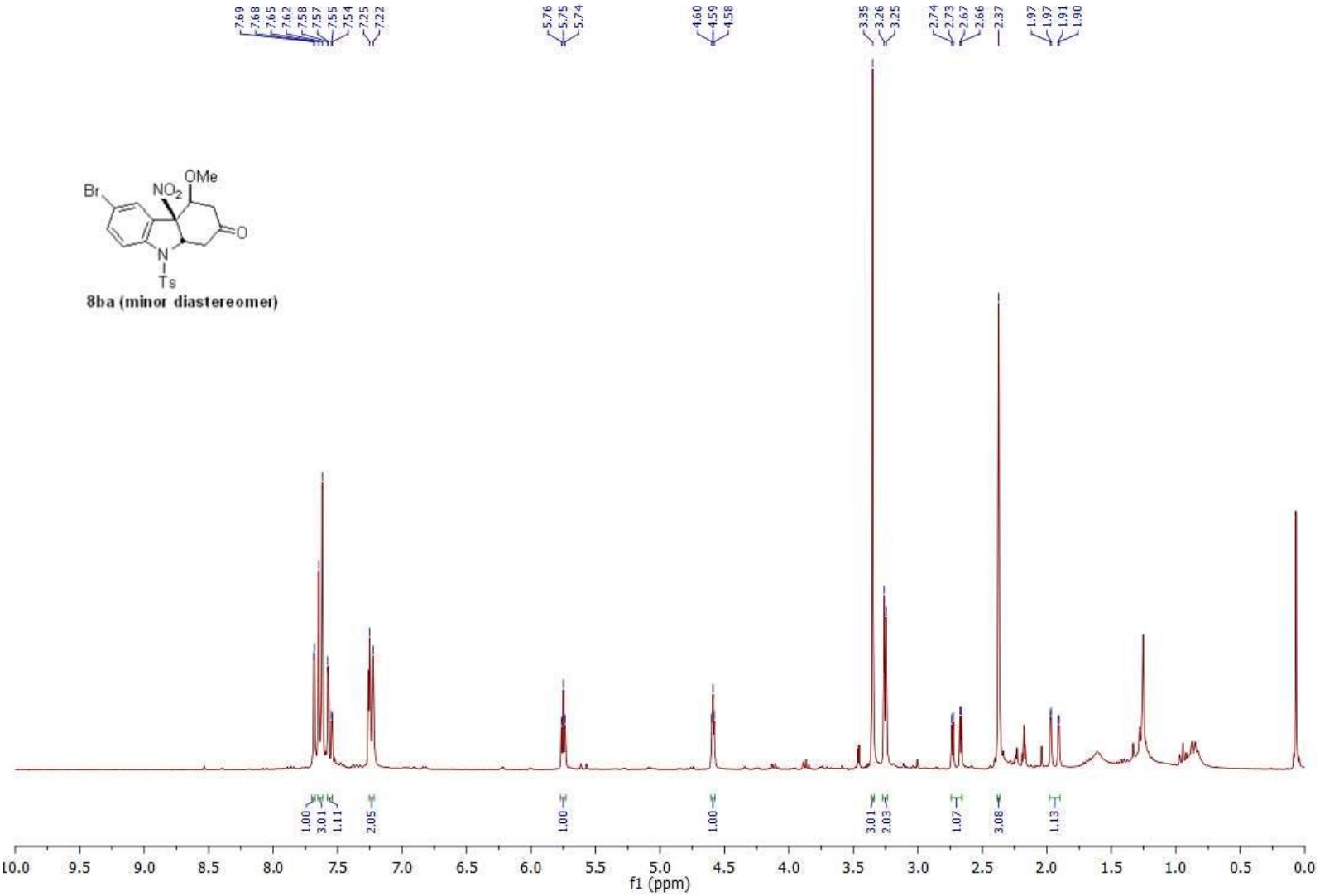
130.18
127.17
125.36
118.28
118.01
96.33
77.93
63.91
58.32
44.49
40.11
21.71
Br
NO2
OMe
O
N
Ts
+ε
8ba (major diastereomer)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.55
7.54
7.25
7.22
5.76
5.75
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4.60
4.59
4.58
3.35
3.26
3.25
2.74
2.73
2.67
2.66
2.37
1.97
1.97
1.91
1.90
Br
NO2
OMe
O
N
Ts
8ba (minor diastereomer)
1.00
3.01
1.11
2.05
1.00
1.00
3.01
2.03
1.07
3.08
1.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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3.0
2.5
2.0
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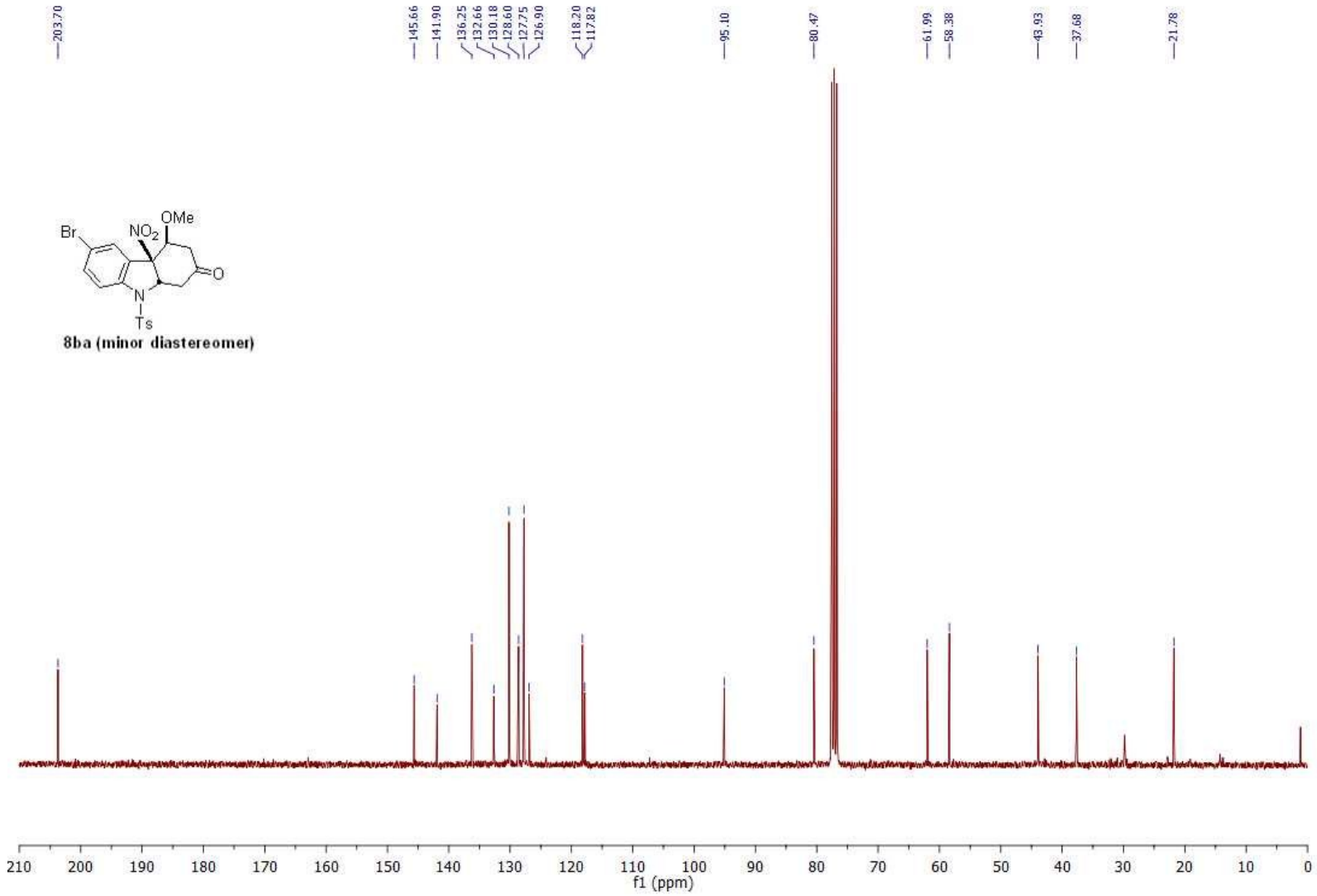
f1 (ppm)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130.18
128.60
127.75
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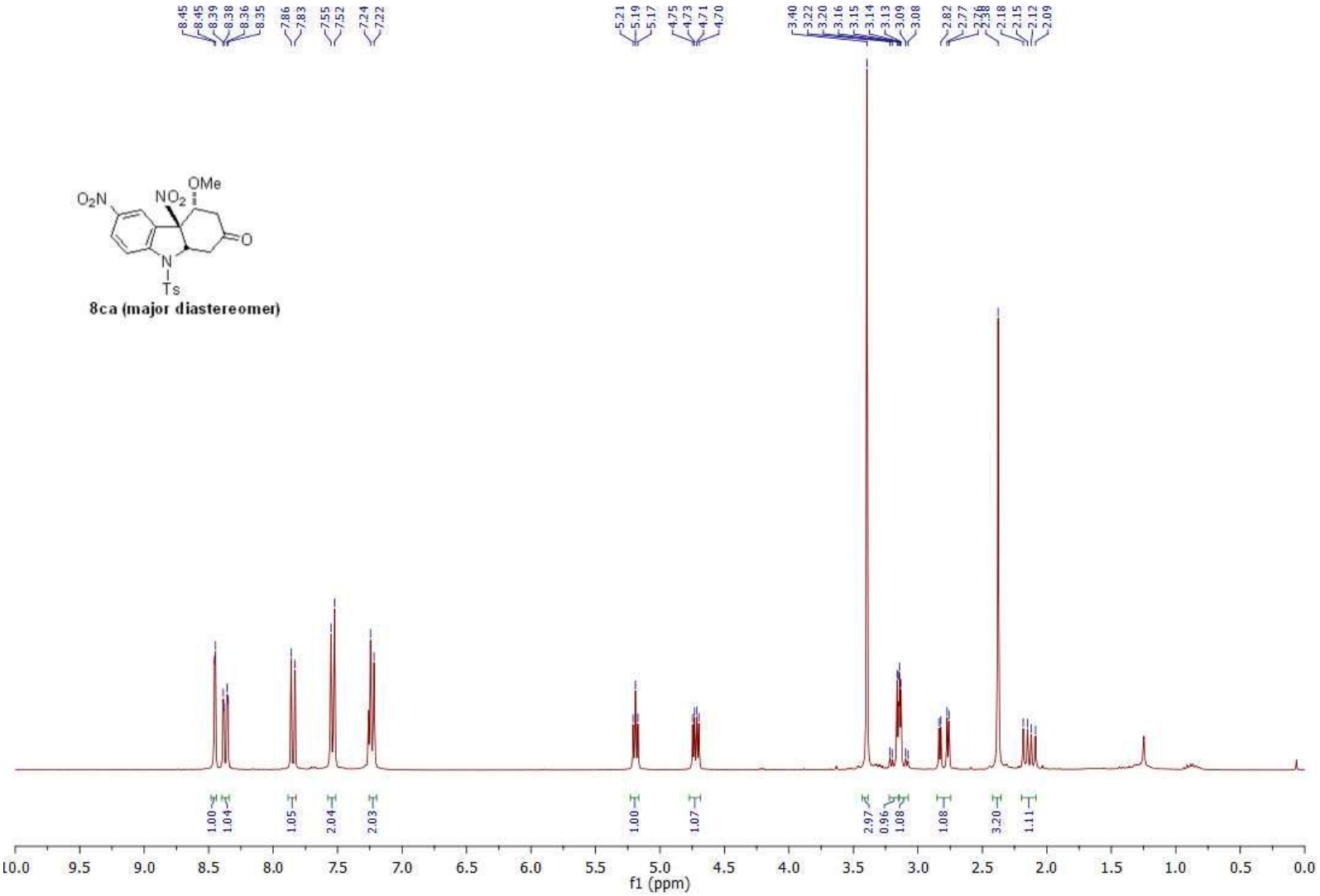
118.20
117.82
95.10
80.47
61.99
58.38
43.93
37.68
21.78
Br
NO2
OMe
O
N
Ts
8ba (minor diastereomer)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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7.52
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5.21
5.19
5.17
4.75
4.73
4.71
4.70
3.40
3.22
3.20
3.16
3.15
3.14
3.13
3.09
3.08
2.82
2.77
2.18
2.15
2.12
2.09
O2N
NO2
OMe
O
N
Ts
8ca (major diastereomer)
1.00
1.04
1.05
2.04
2.03
1.00
1.07
2.97
0.96
1.08
1.08
3.20
1.11
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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3.0
2.5
2.0
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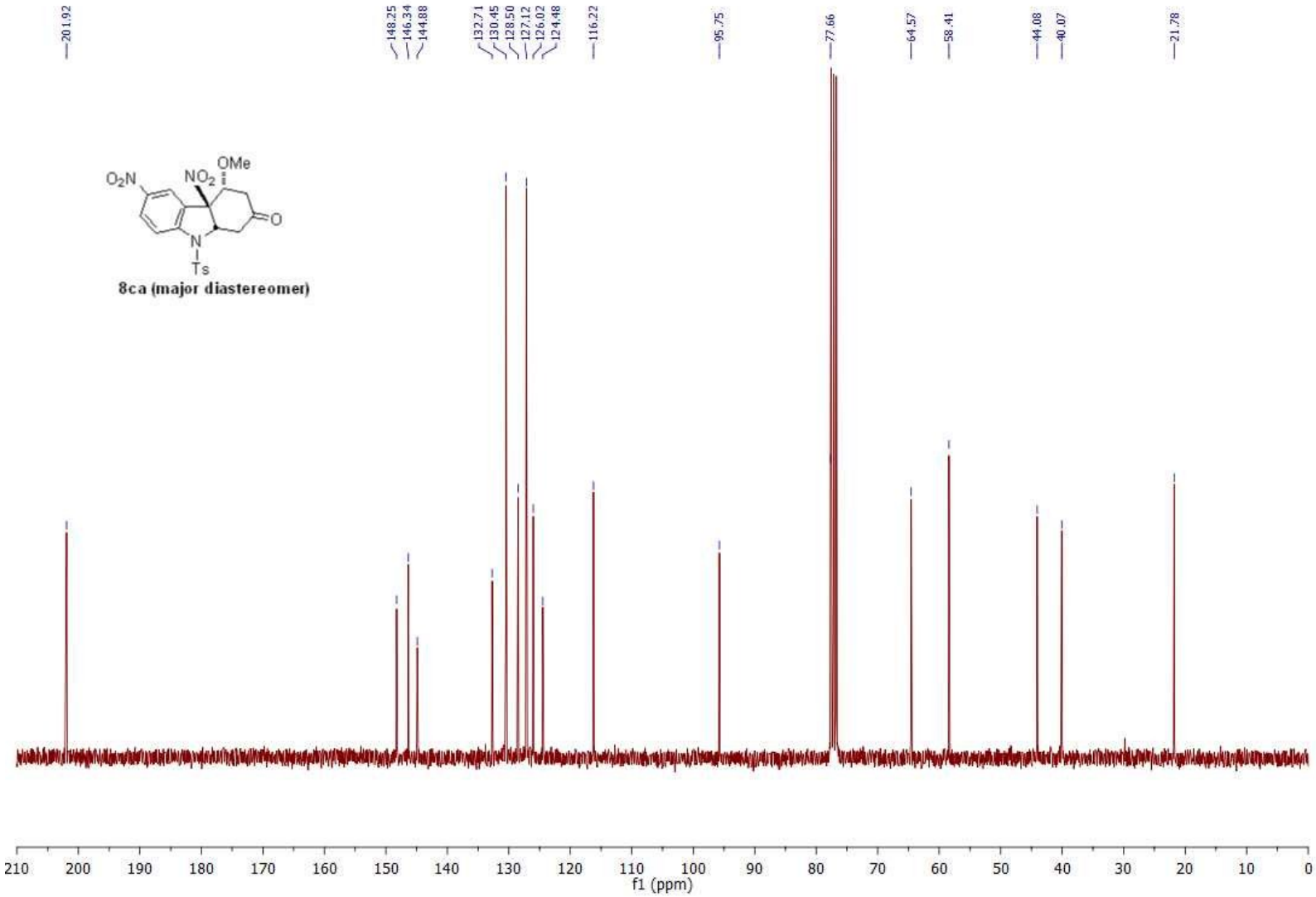
0.0
f1 (ppm)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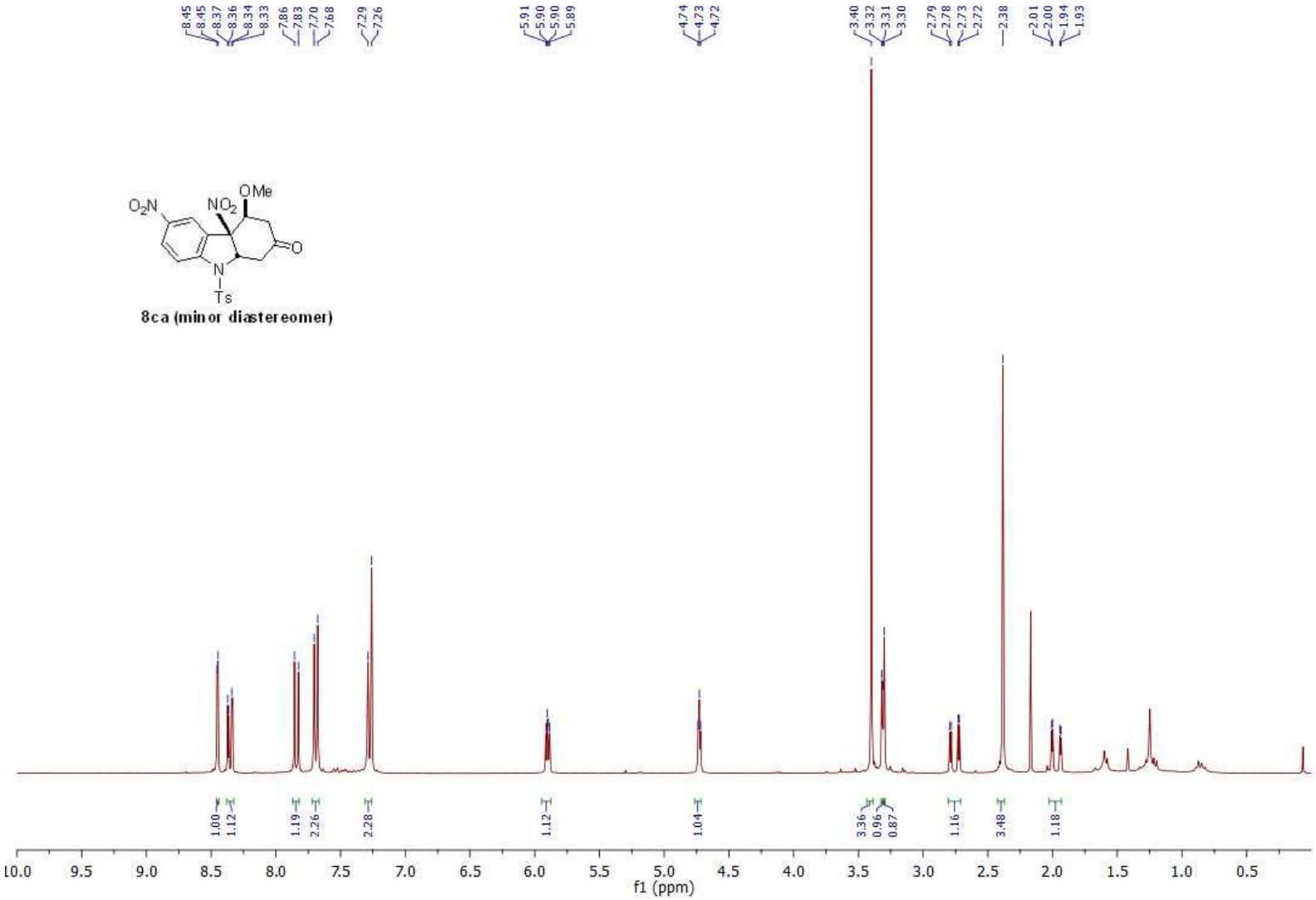
132.71
130.45
128.50
127.12
126.02
124.48
116.22
95.75
77.66
64.57
58.41
44.08
40.07
21.78
O2N
NO2
OMe
O
N
Ts
8ca (major diastereomer)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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8.45
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8.33
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7.70
7.68
7.29
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5.90
5.90
5.89
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4.73
4.72
3.40
3.32
3.31
3.30
2.79
2.78
2.73
2.72
2.38
2.01
2.00
1.94
1.93
O2N
NO2
OMe
O
N
Ts
8ca (minor diastereomer)
1.00
1.12
1.19
2.26
2.28
1.12
1.04
3.36
0.96
0.87
1.16
3.48
1.18
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
3.5
3.0
2.5
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1.5
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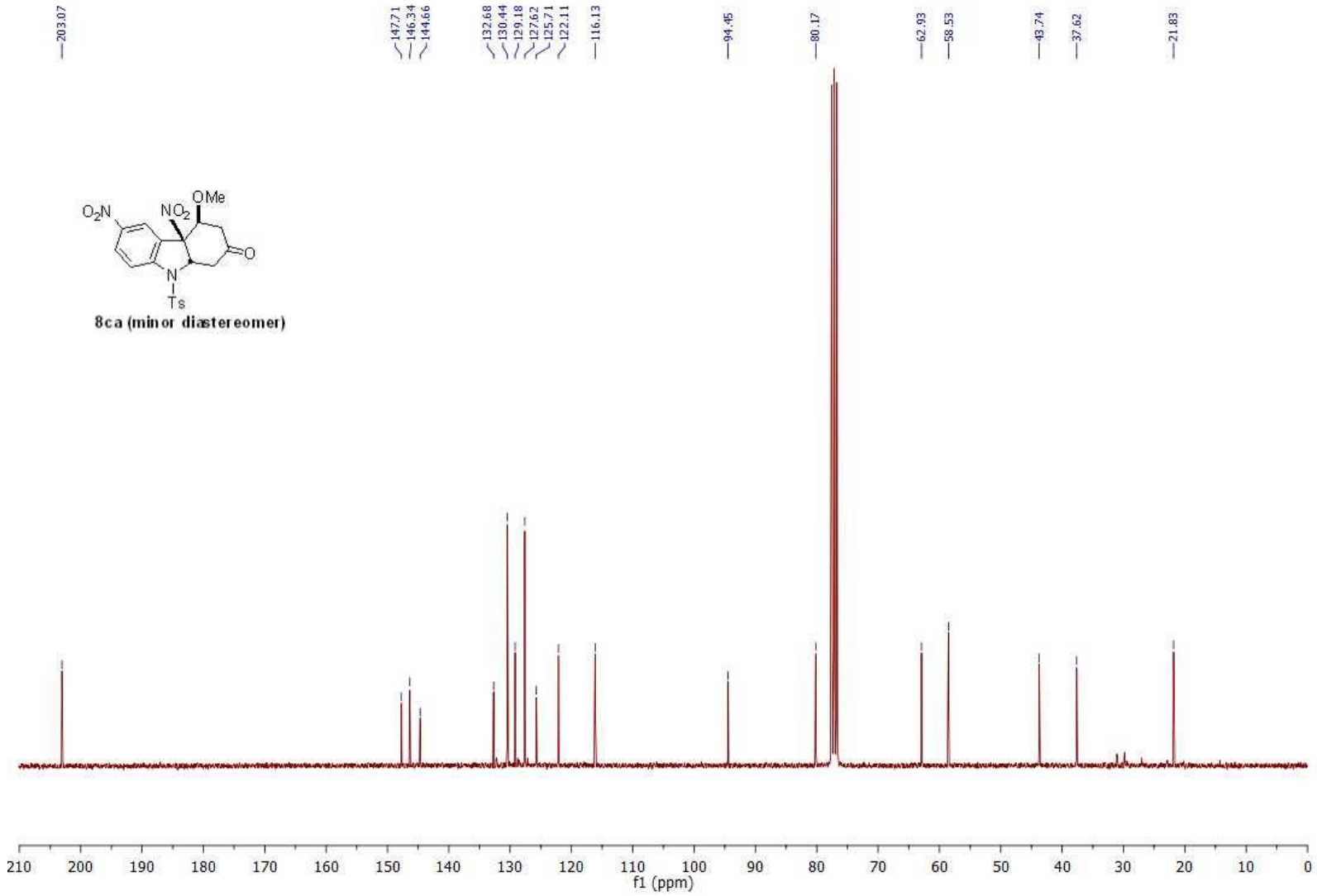
f1 (ppm)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132.68
130.44
129.18
127.62
125.71
122.11
116.13
94.45
80.17
62.93
58.53
43.74
37.62
21.83
O2N
NO2
OMe
O
N
Ts
8ca (minor diastereomer)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
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10
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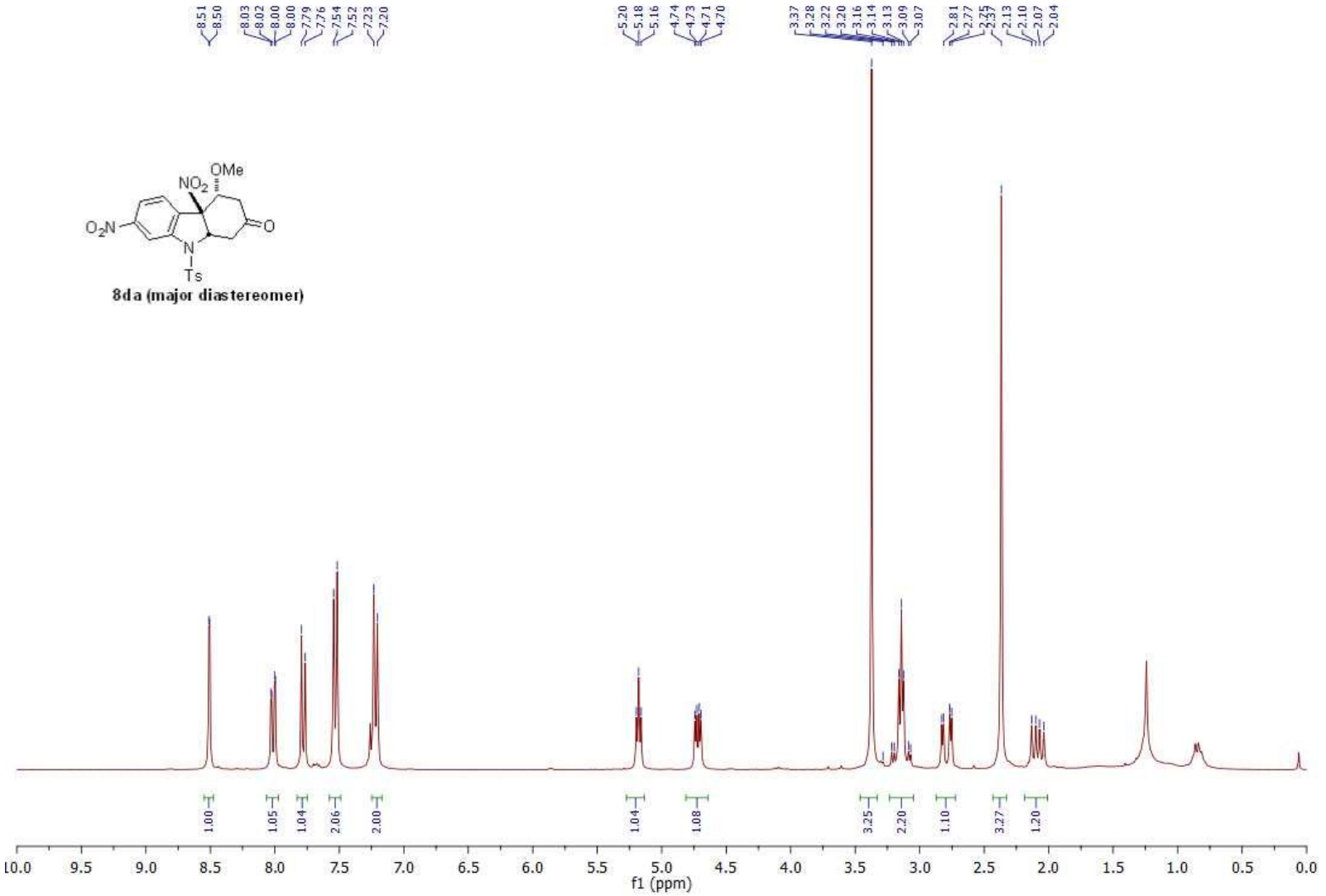
f1 (ppm)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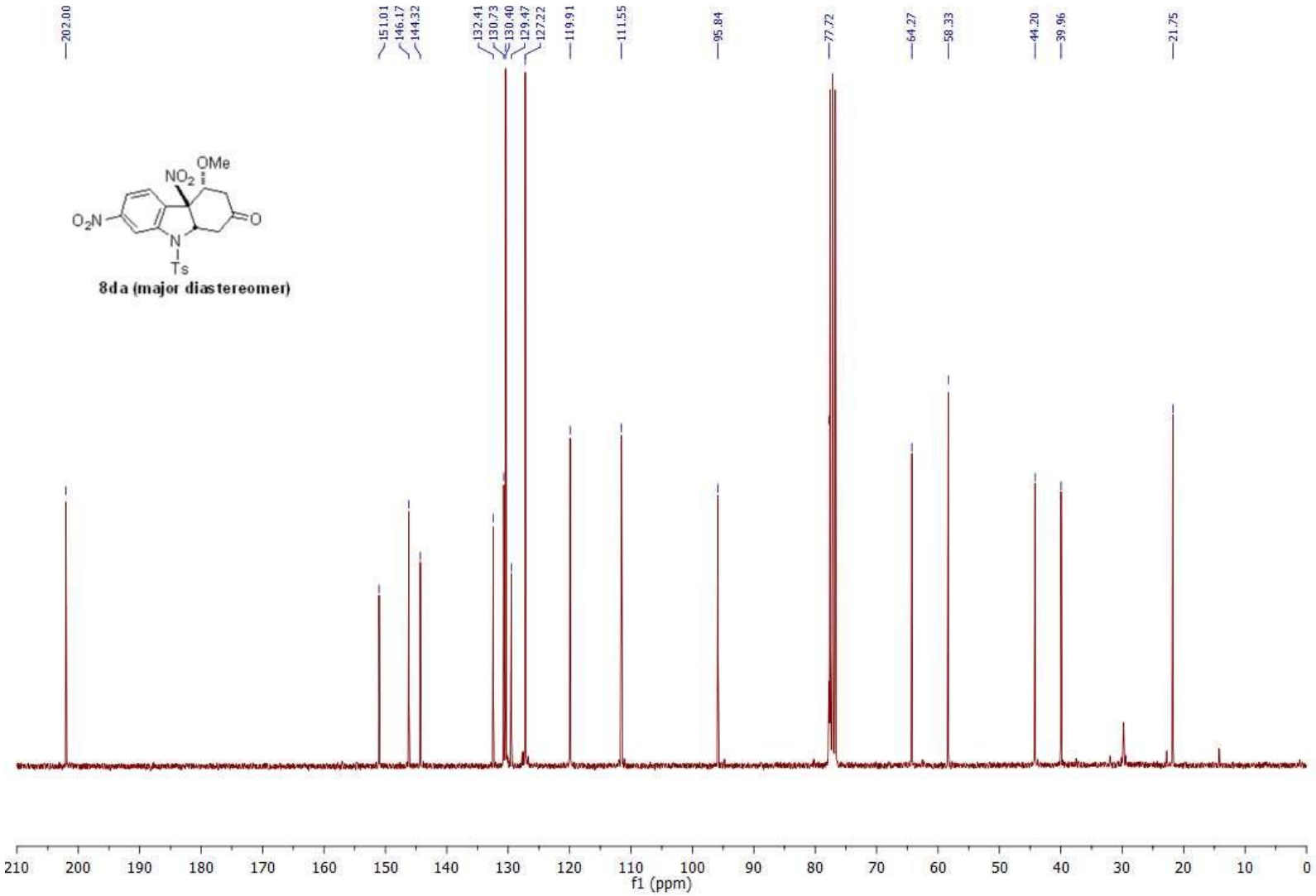
3.22
3.20
3.16
3.14
3.13
3.09
3.07
2.81
2.77
2.13
2.10
2.07
2.04
OMe
NO2
O2N
O
N
Ts
8da (major diastereomer)
1.00
1.05
1.04
2.06
2.00
1.04
1.08
3.25
2.20
1.10
3.27
1.20
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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132.41
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130.40
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127.22
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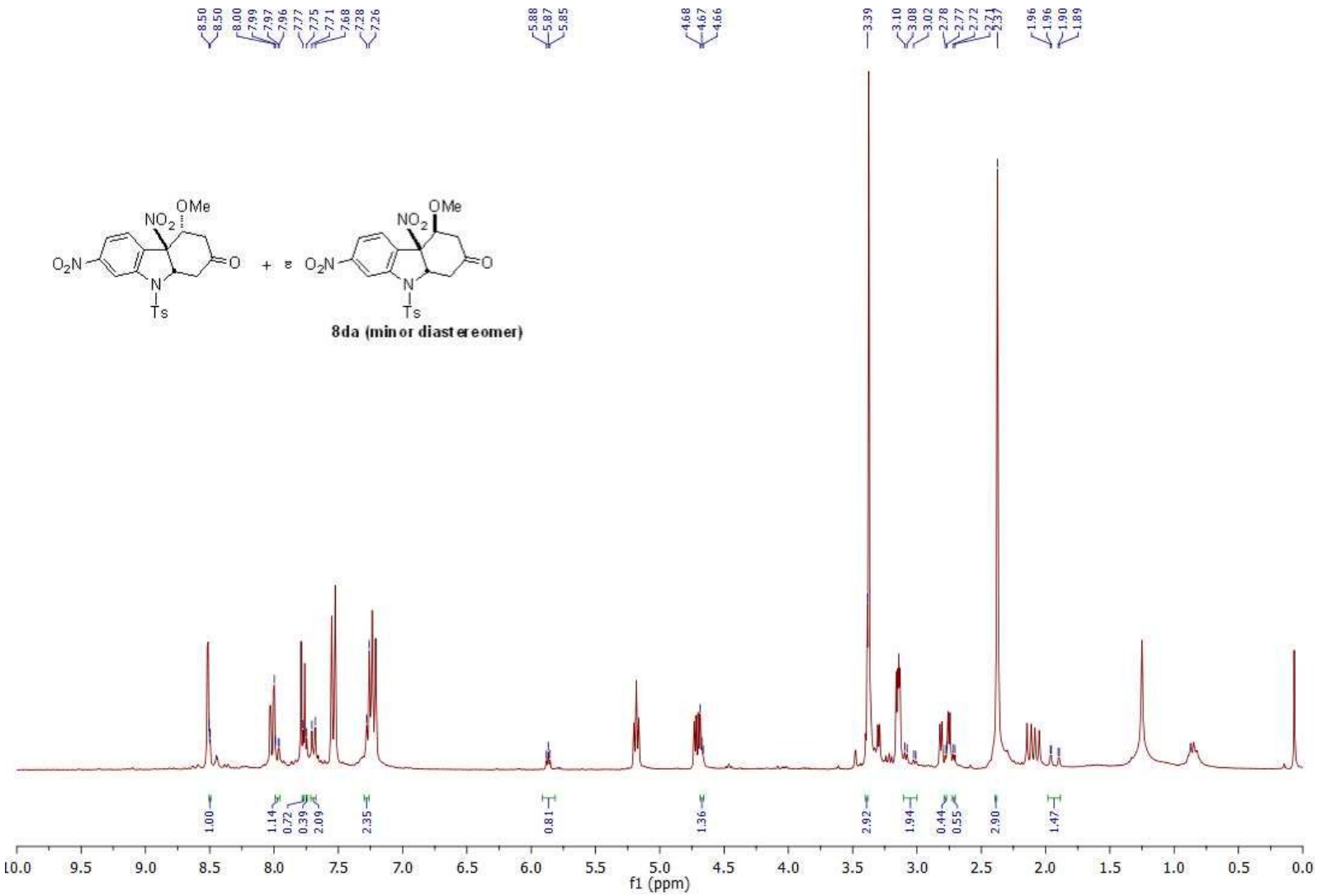
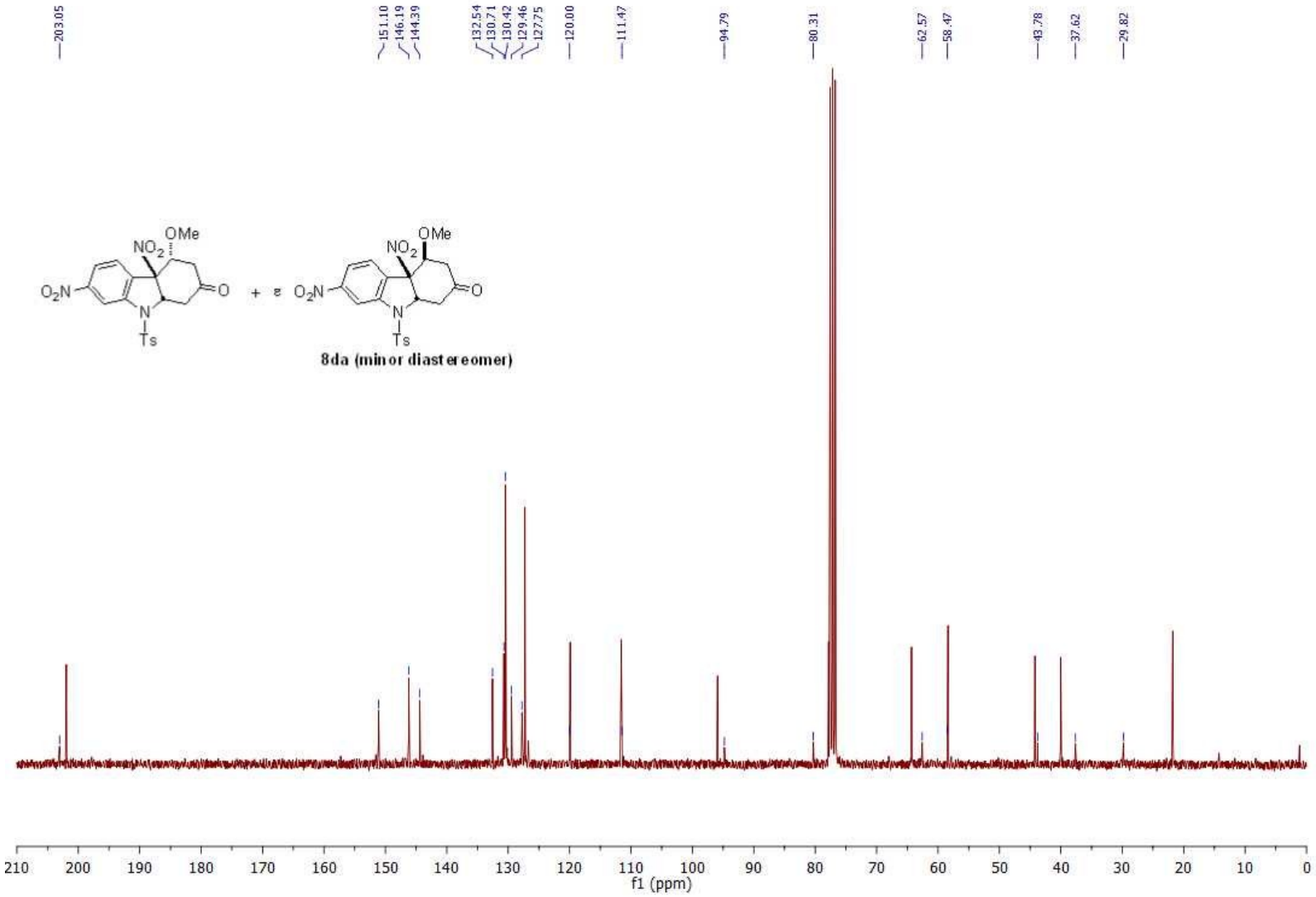
95.84
77.72
64.27
58.33
44.20
39.96
21.75
OMe
NO2
O2N
O
N
Ts
8da (major diastereomer)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.50
8.50
8.00
7.99
7.97
7.96
7.77
7.75
7.71
7.68
7.28
7.26
5.88
5.87
5.85
4.68
4.67
4.66
3.39
3.10
3.08
3.02
2.78
2.77
2.72
2.71
2.31
1.96
1.96
1.90
1.89
OMe
NO2
O2N
O
N
Ts
+
OMe
NO2
O2N
O
N
Ts
8da (minor diastereomer)
1.00
1.14
0.72
0.39
2.09
2.35
0.81
1.36
2.92
1.94
0.44
0.55
2.90
1.47
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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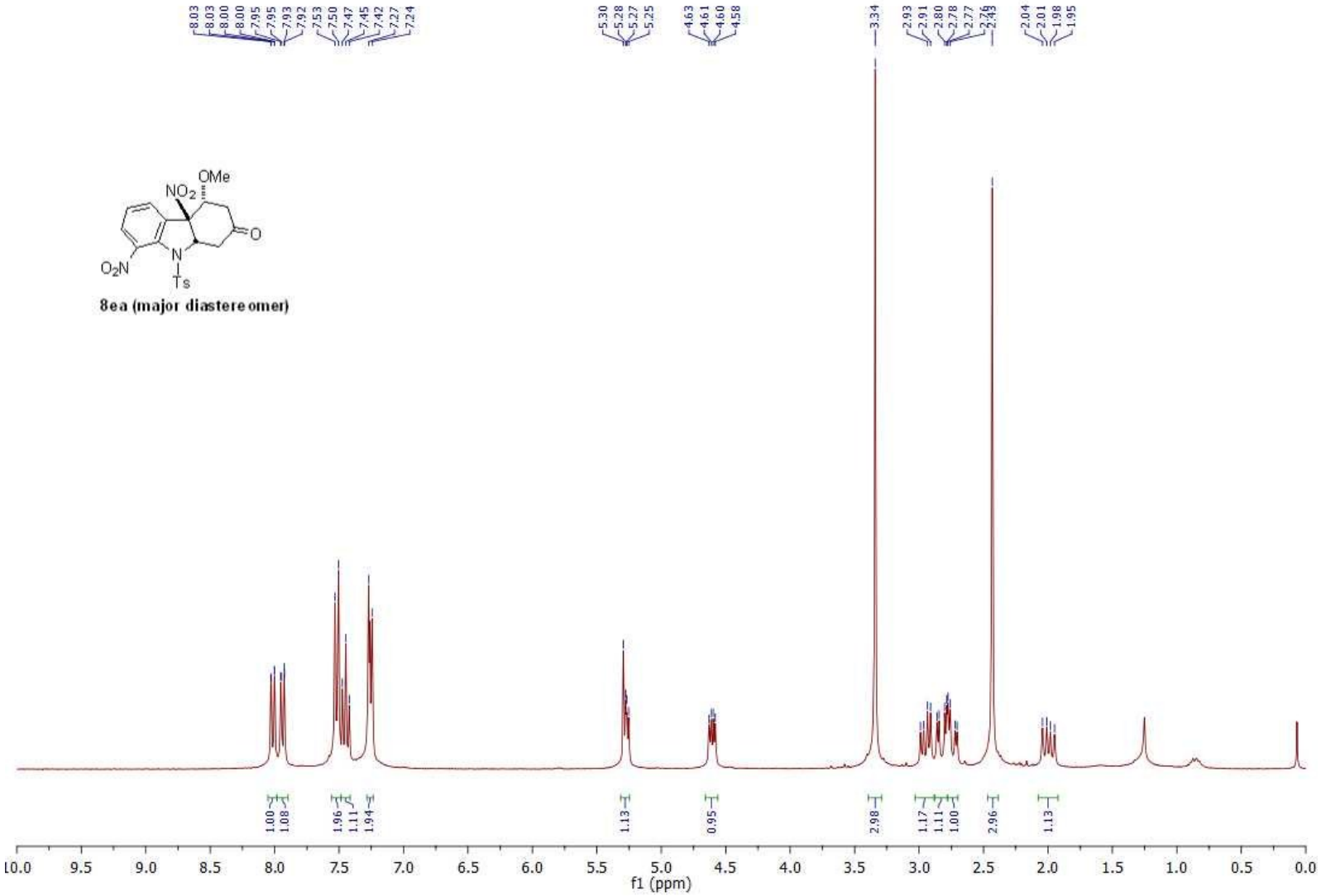
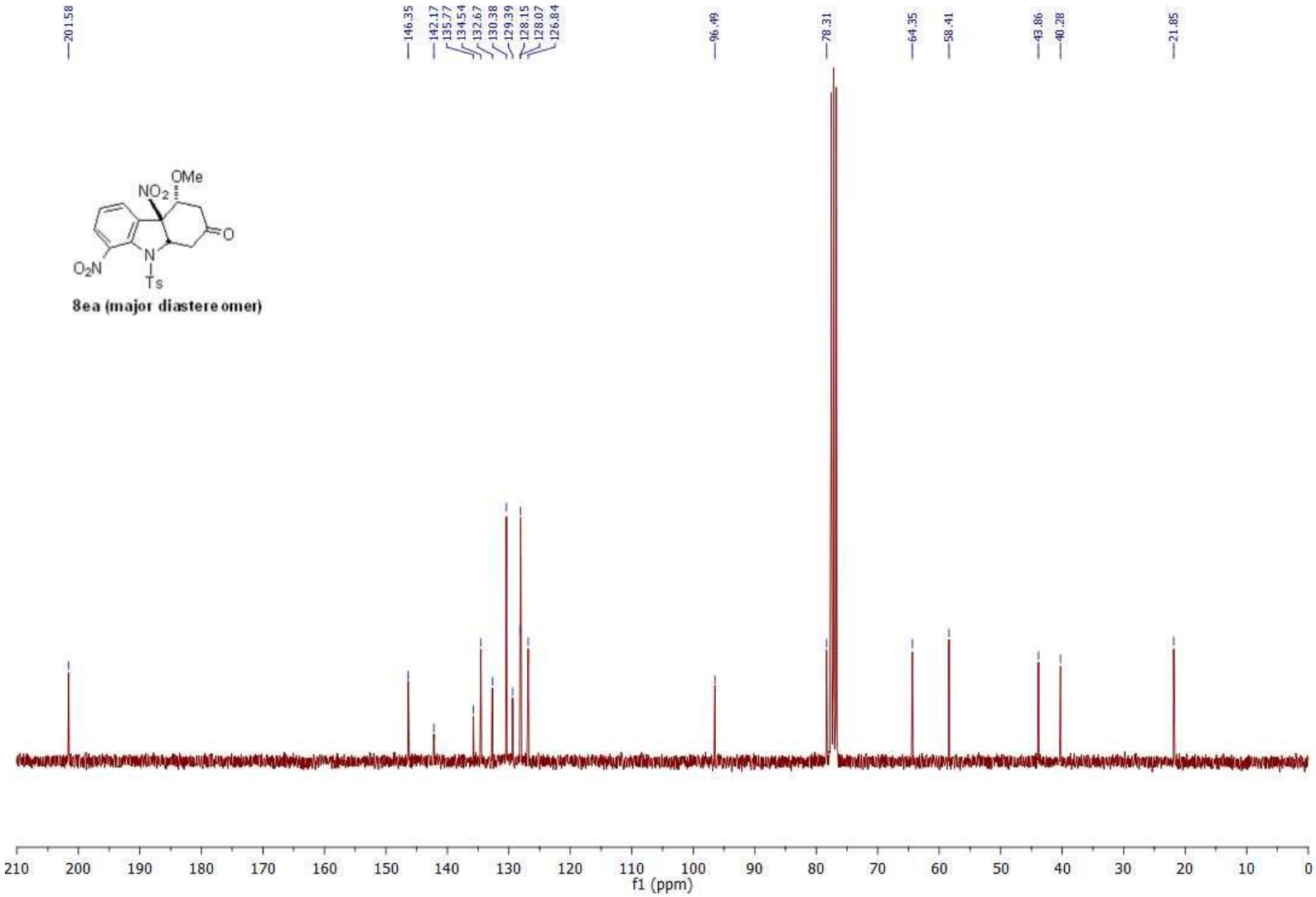
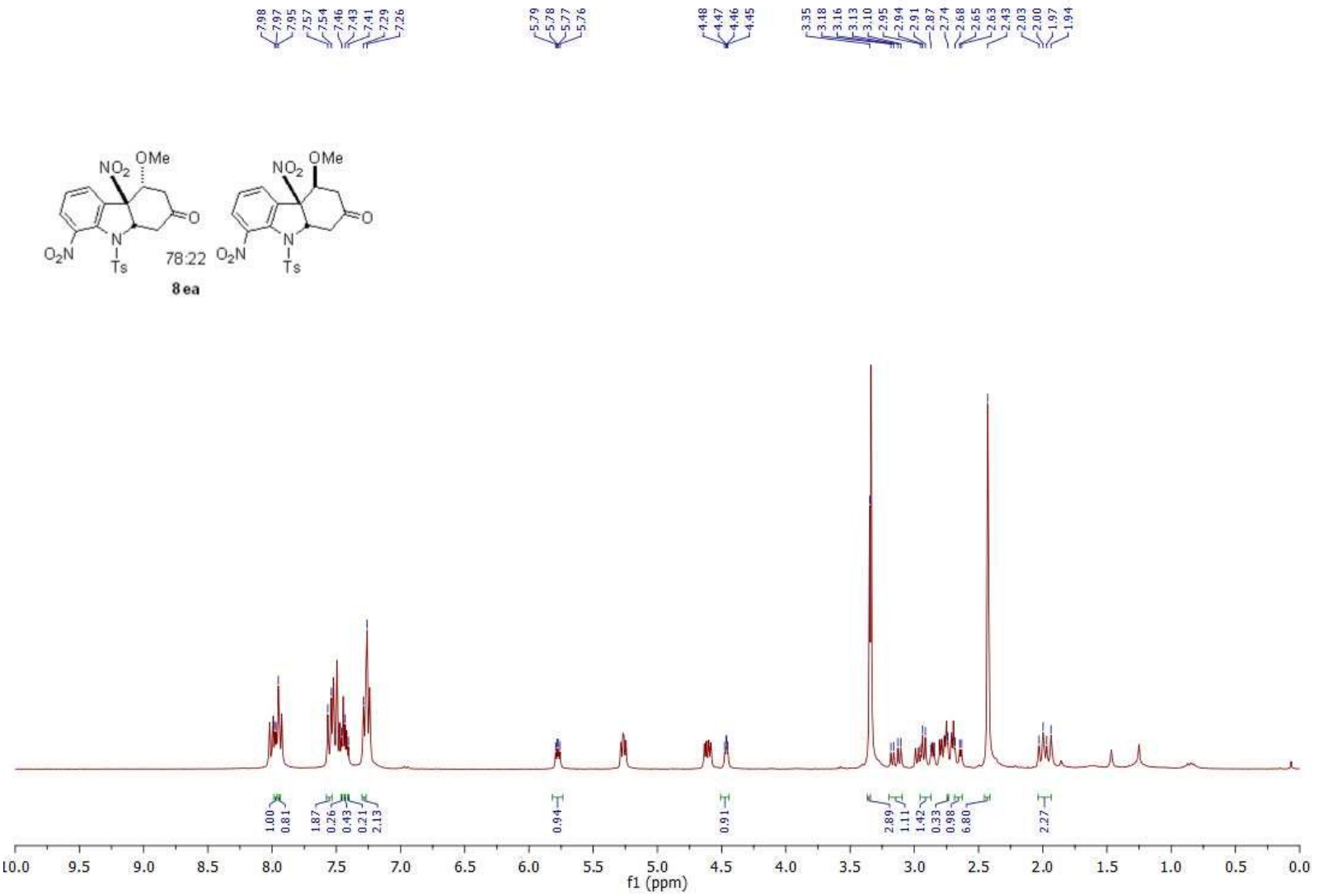
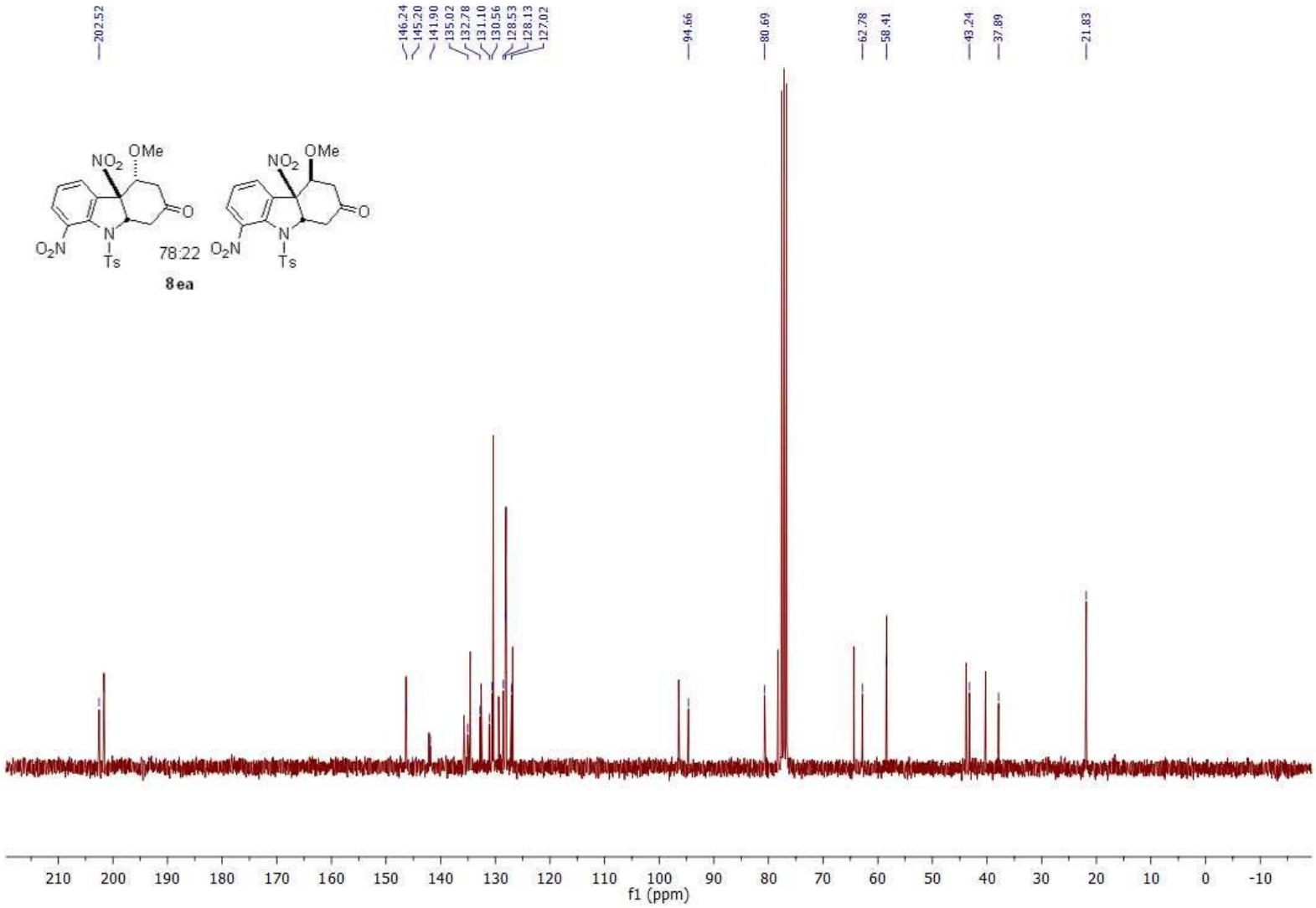
151.10
146.19
144.39
132.54
130.71
130.42
129.46
127.75
120.00
111.47
94.79
80.31
62.57
58.47
43.78
37.62
29.82
OMe
NO2
O2N
O
N
Ts
+ a
8da (minor diastereomer)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.03
8.03
8.00
8.00
7.95
7.95
7.93
7.92
7.53
7.50
7.47
7.45
7.42
7.27
7.24
5.30
5.28
5.27
5.25
4.63
4.61
4.60
4.58
3.34
2.93
2.91
2.80
2.78
2.77
2.04
2.01
1.98
1.95
OMe
NO2
O
O2N
N
Ts
8ea (major diastereomer)
1.00
1.08
1.96
1.11
1.94
1.13
0.95
2.98
1.17
1.11
1.00
2.96
1.13
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


201.58
146.35
142.17
135.77
134.54
132.67
130.38
129.39
128.15
128.07
126.84
96.49
78.31
64.35
58.41
43.86
40.28
21.85
OMe
NO2
O
O2N
N
Ts
8ea (major diastereomer)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.98
7.97
7.95
7.57
7.54
7.46
7.43
7.41
7.29
7.26
5.79
5.78
5.77
5.76
4.48
4.47
4.46
4.45
3.35
3.18
3.16
3.13
3.10
2.95
2.94
2.91
2.87
2.74
2.68
2.65
2.63
2.43
2.03
2.00
1.97
1.94
NO2
OMe
O
O2N
N
Ts
78:22
8ea
1.00
0.81
1.87
0.26
0.43
0.21
2.13
0.94
0.91
2.89
1.11
1.42
0.33
0.98
6.80
2.27
f1 (ppm)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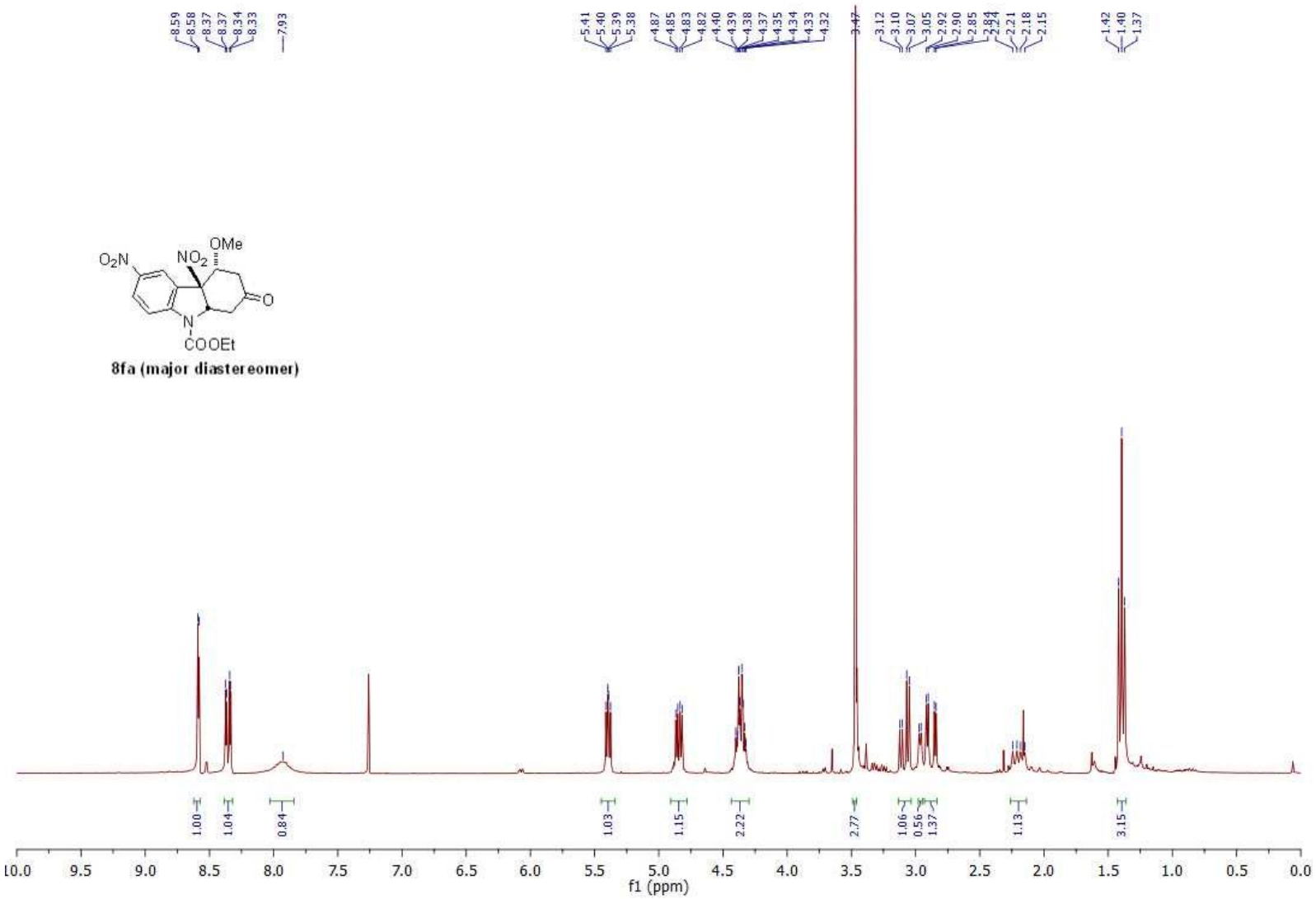
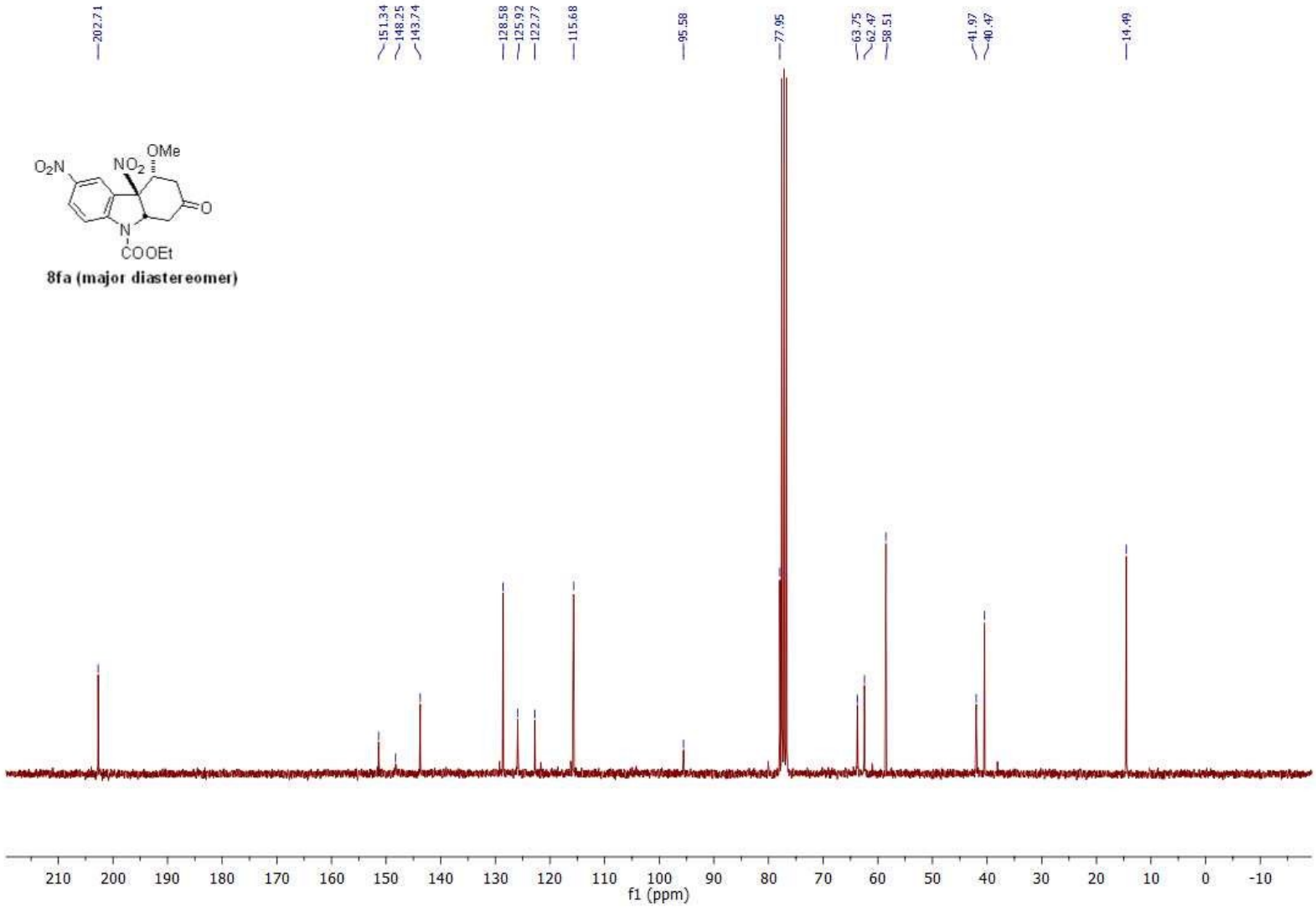
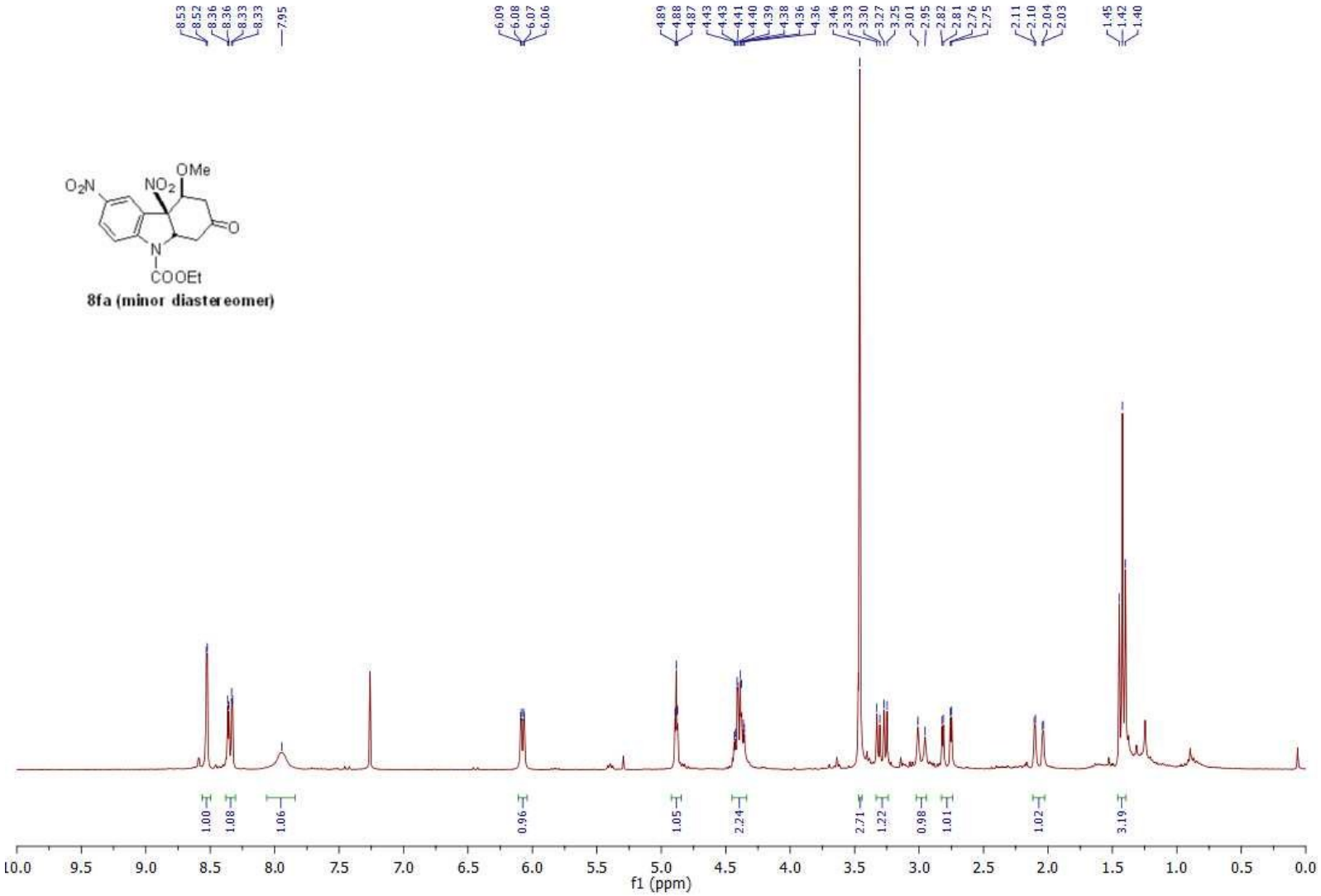
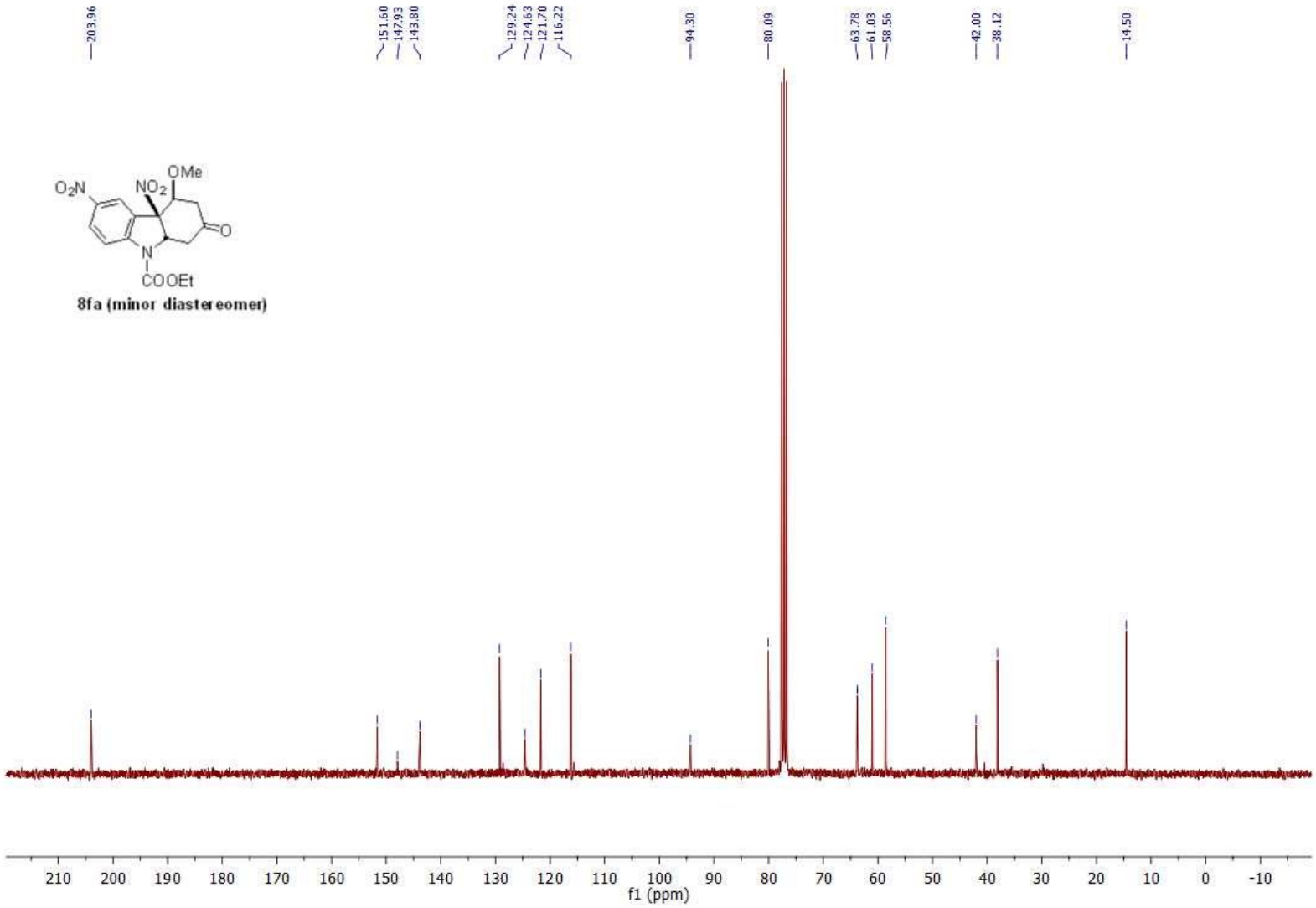
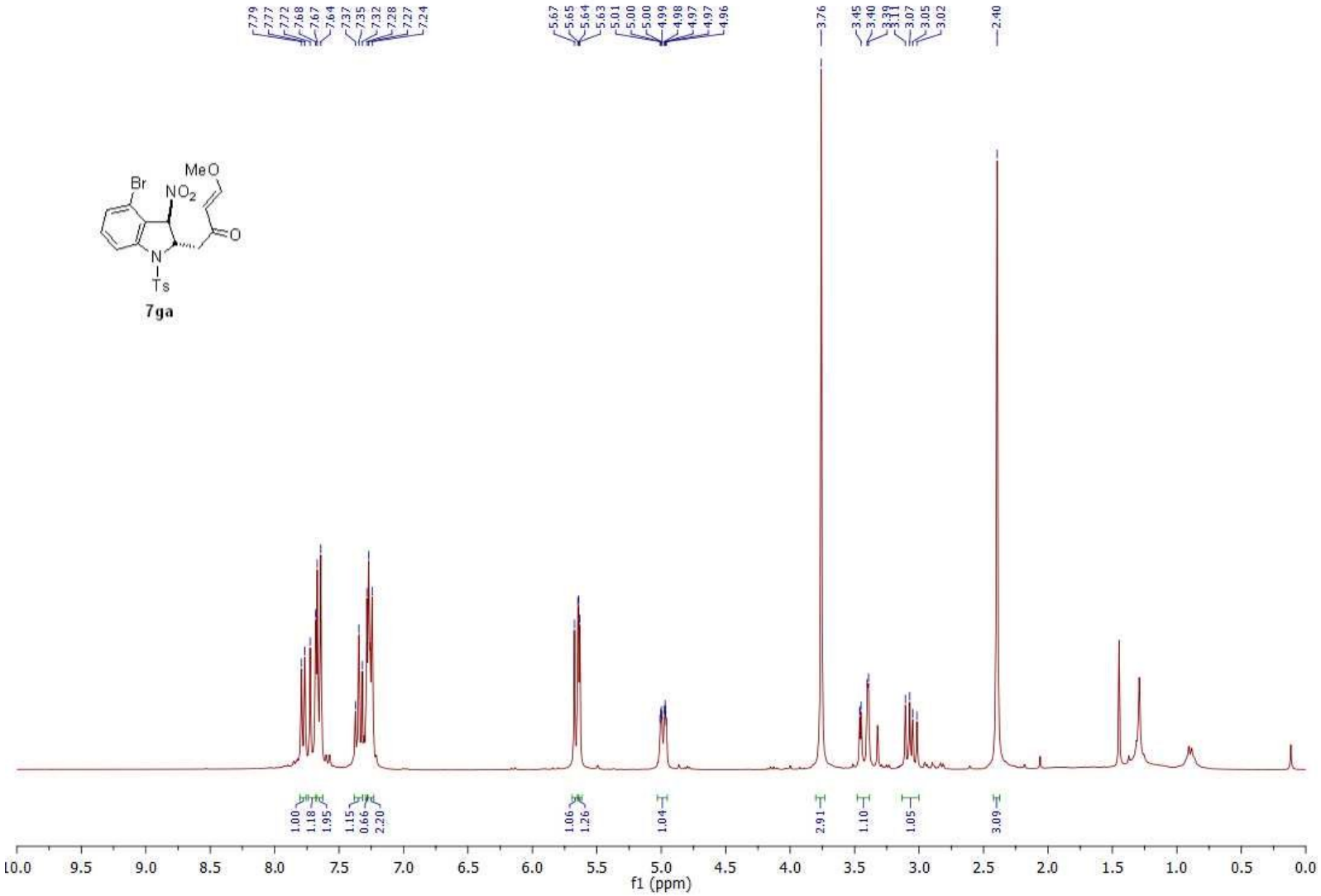
146.24
145.20
141.90
135.02
132.78
131.10
130.56
128.53
128.13
127.02
94.66
80.69
62.78
58.41
43.24
37.89
21.83
NO2
OMe
O
O2N
N
Ts
78:22
8ea
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

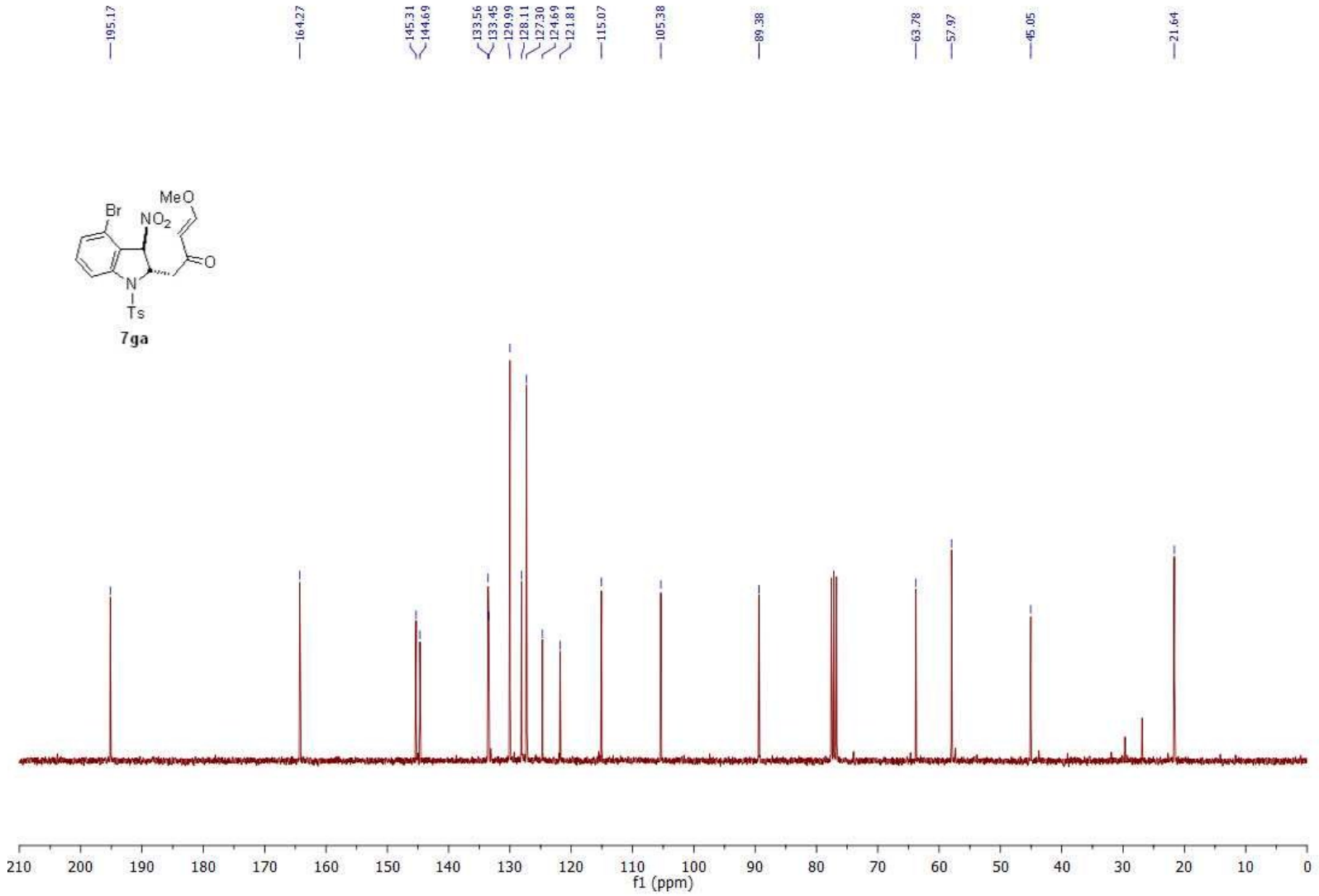

8.59
8.58
8.37
8.37
8.34
8.33
7.93
5.41
5.40
5.39
5.38
4.87
4.85
4.83
4.82
4.40
4.39
4.38
4.37
4.35
4.34
4.33
4.32
3.47
3.12
3.10
3.07
3.05
2.92
2.90
2.85
2.84
2.21
2.18
2.15
1.42
1.40
1.37
O2N
NO2
OMe
O
N
COOEt
8fa (major diastereomer)
1.00
1.04
0.84
1.03
1.15
2.22
2.77
1.06
0.56
1.37
1.13
3.15
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

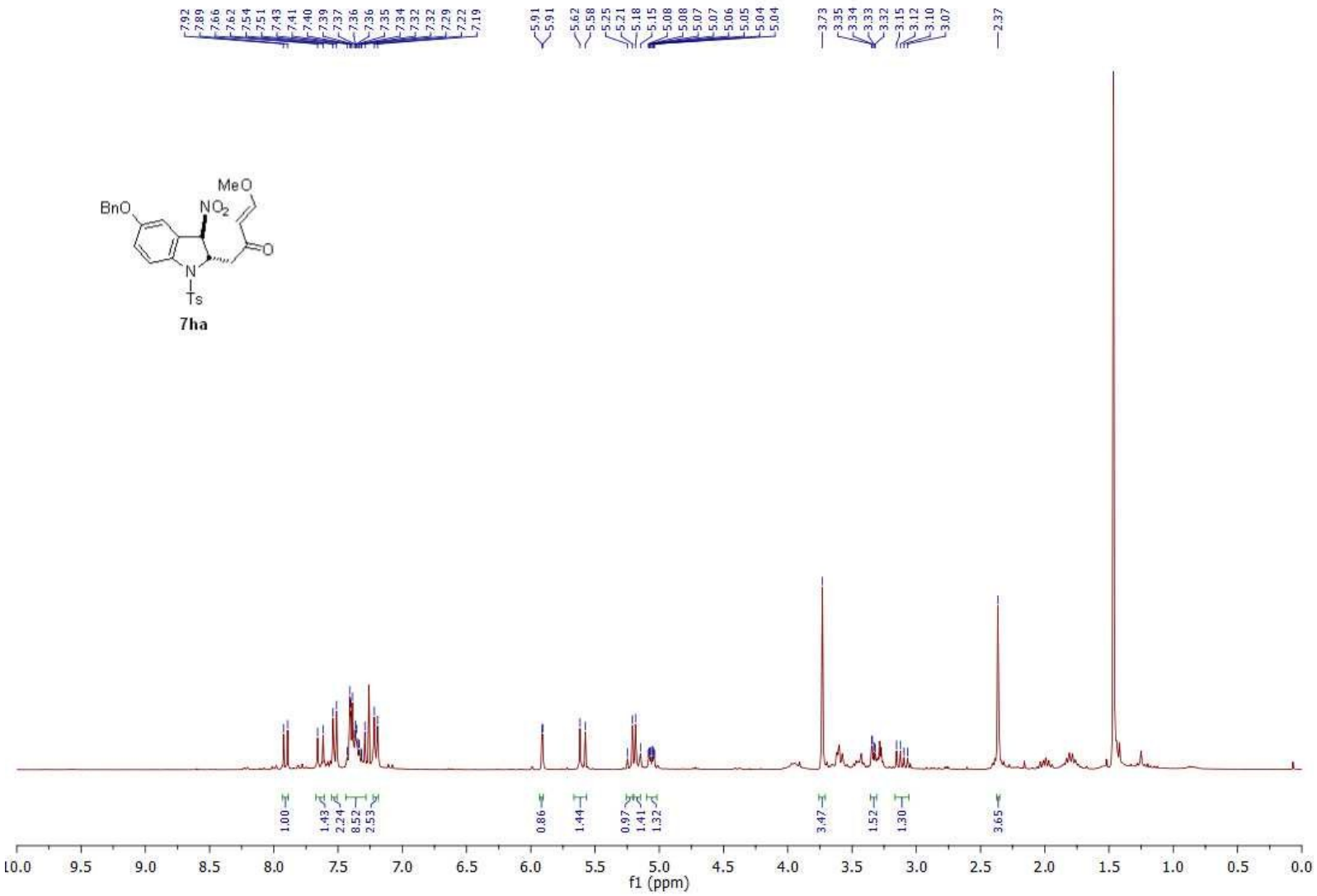

202.71
151.34
148.25
143.74
128.58
125.92
122.77
115.68
95.58
77.95
63.75
62.47
58.51
41.97
40.47
14.49
O2N
NO2
OMe
O
N
COOEt
8fa (major diastereomer)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

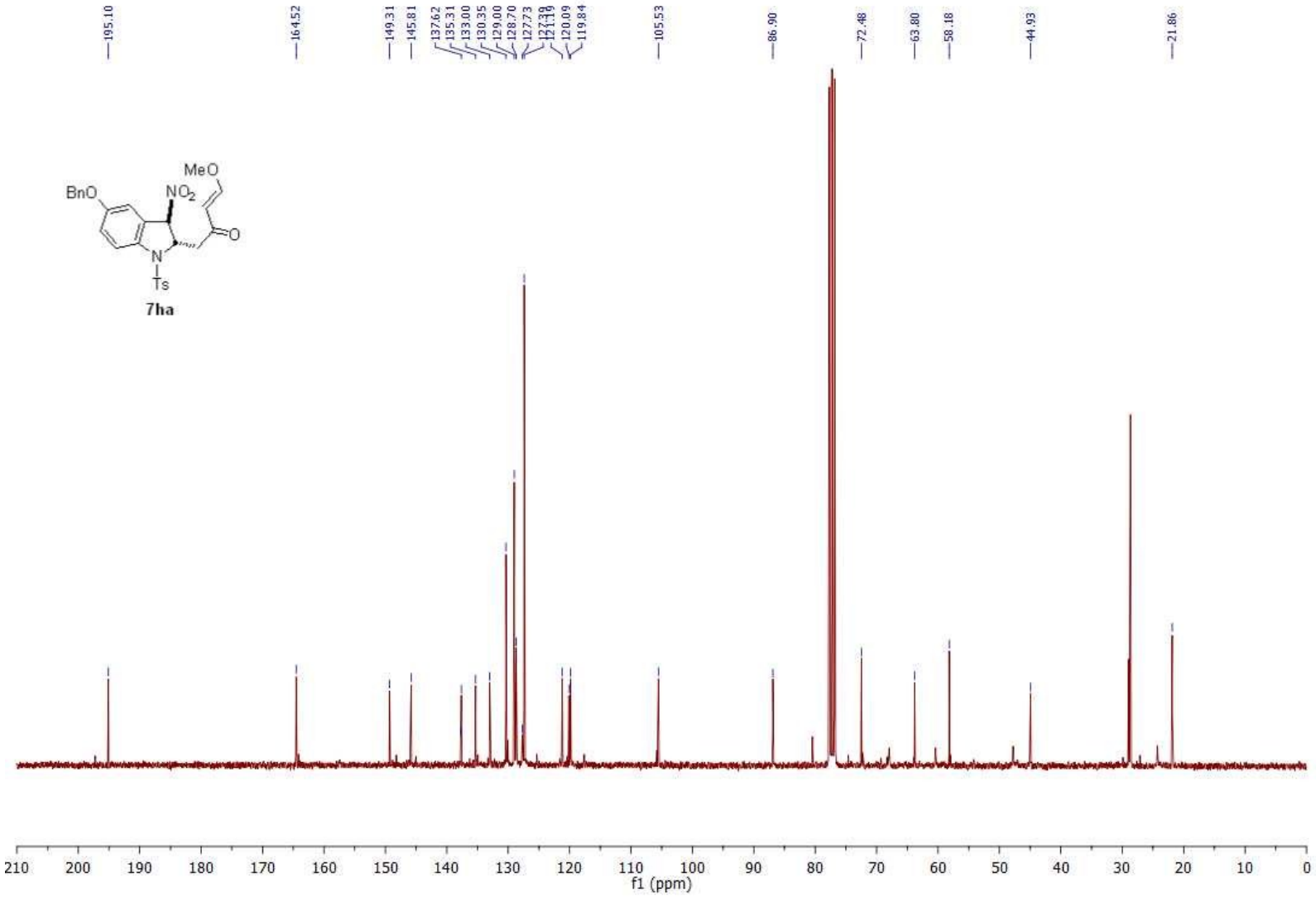

8.53
8.52
8.36
8.36
8.33
8.33
7.95
6.09
6.08
6.07
6.06
4.89
4.88
4.87
4.43
4.43
4.41
4.40
4.39
4.38
4.36
4.36
3.46
3.33
3.30
3.27
3.25
3.01
2.95
2.82
2.81
2.76
2.75
2.11
2.10
2.04
2.03
1.45
1.42
1.40
O2N
NO2
OMe
O
N
COOEt
8fa (minor diastereomer)
1.00
1.08
1.06
0.96
1.05
2.24
2.71
1.22
0.98
1.01
1.02
3.19
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

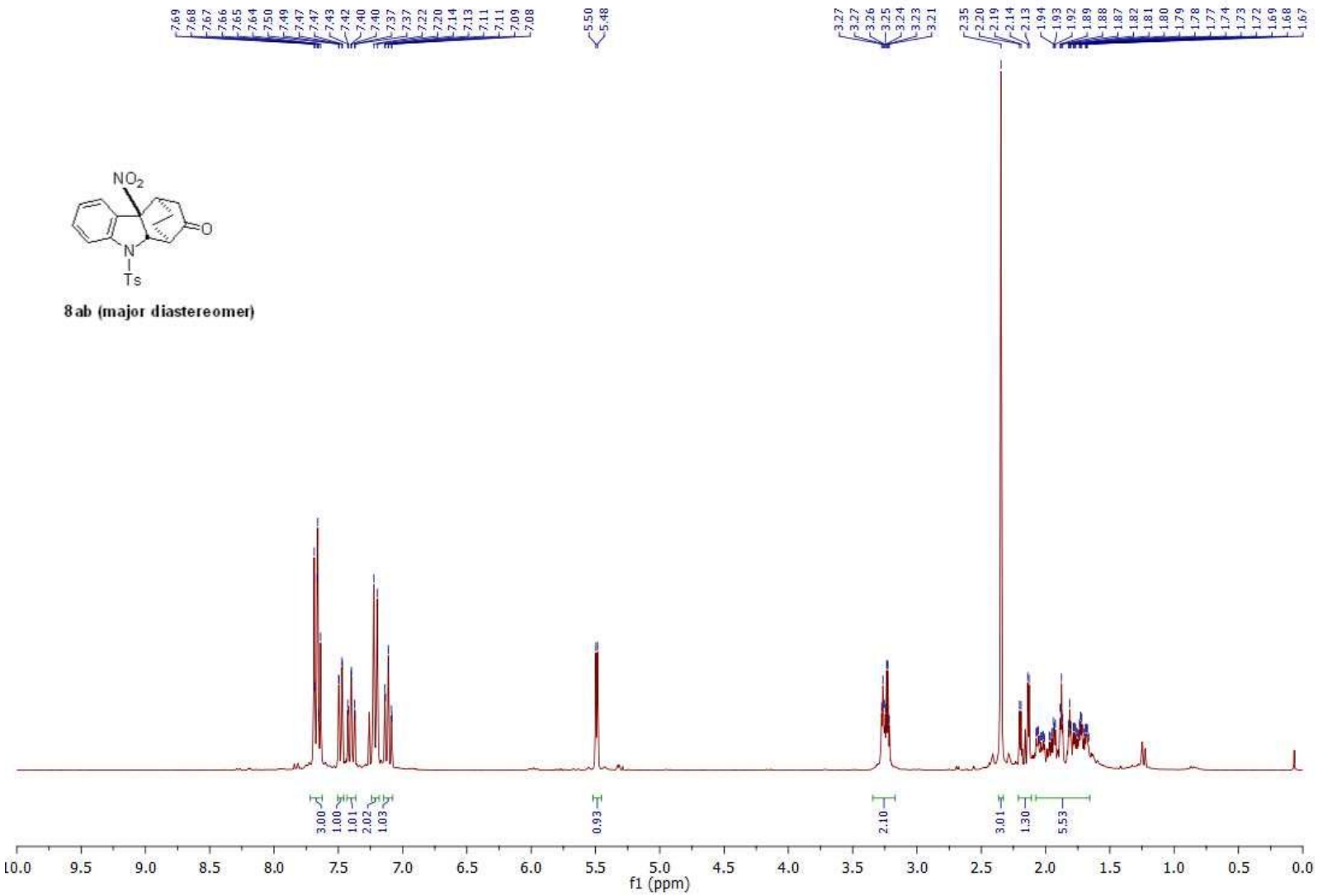

203.96
151.60
147.93
143.80
129.24
124.63
121.70
116.22
94.30
80.09
63.78
61.03
58.56
42.00
38.12
14.50
OMe
O2N
NO2
O
N
COOEt
8fa (minor diastereomer)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

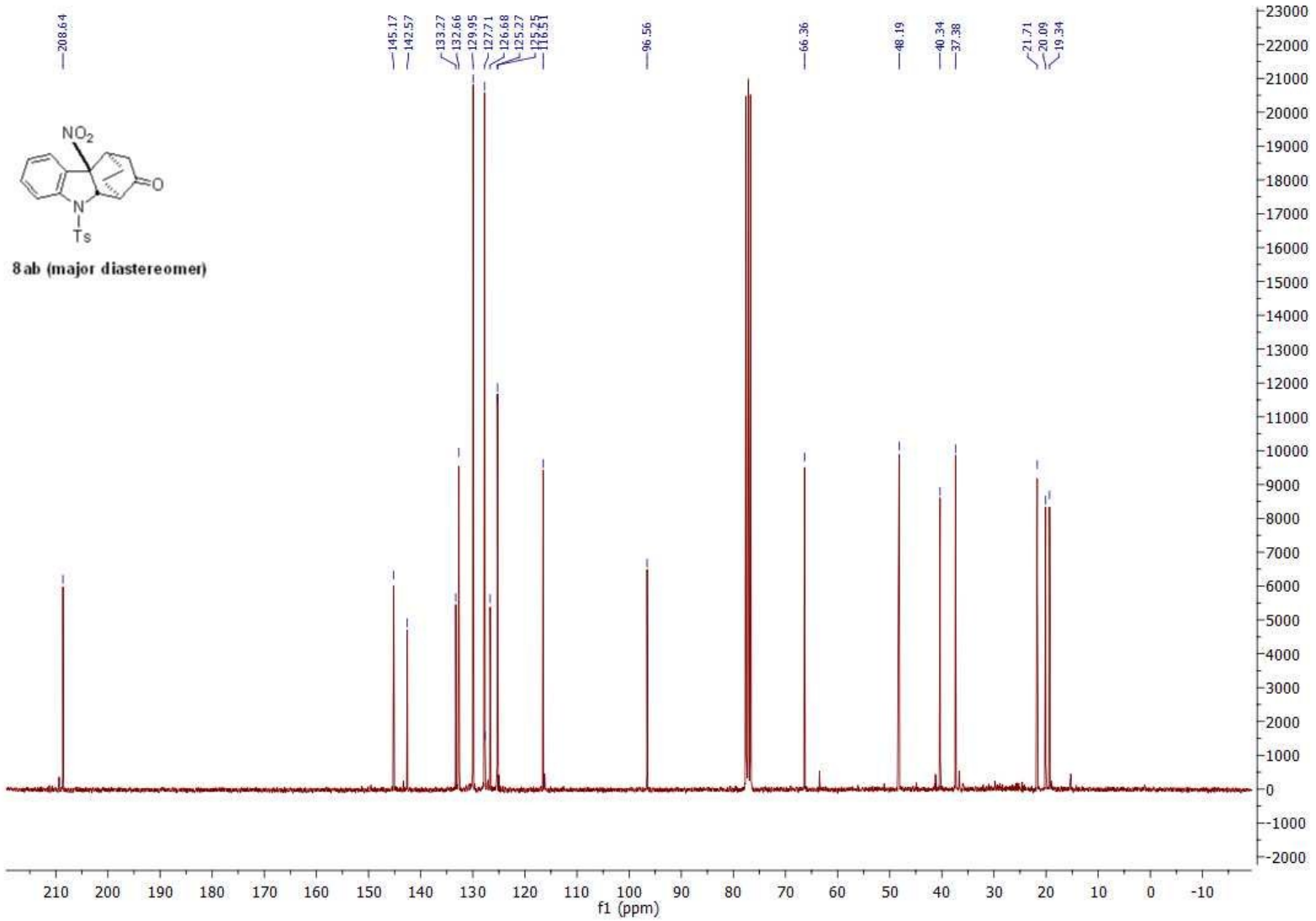

7.79
7.77
7.72
7.68
7.67
7.64
7.37
7.35
7.32
7.28
7.27
7.24
5.67
5.65
5.64
5.63
5.01
5.00
5.00
4.99
4.98
4.97
4.97
4.96
3.76
3.45
3.40
3.39
3.11
3.07
3.05
3.02
2.40
Br
MeO
NO2
O
N
Ts
7ga
1.00
1.18
1.95
1.15
0.66
2.20
1.06
1.26
1.04
2.91
1.10
1.05
3.09
f1 (ppm)

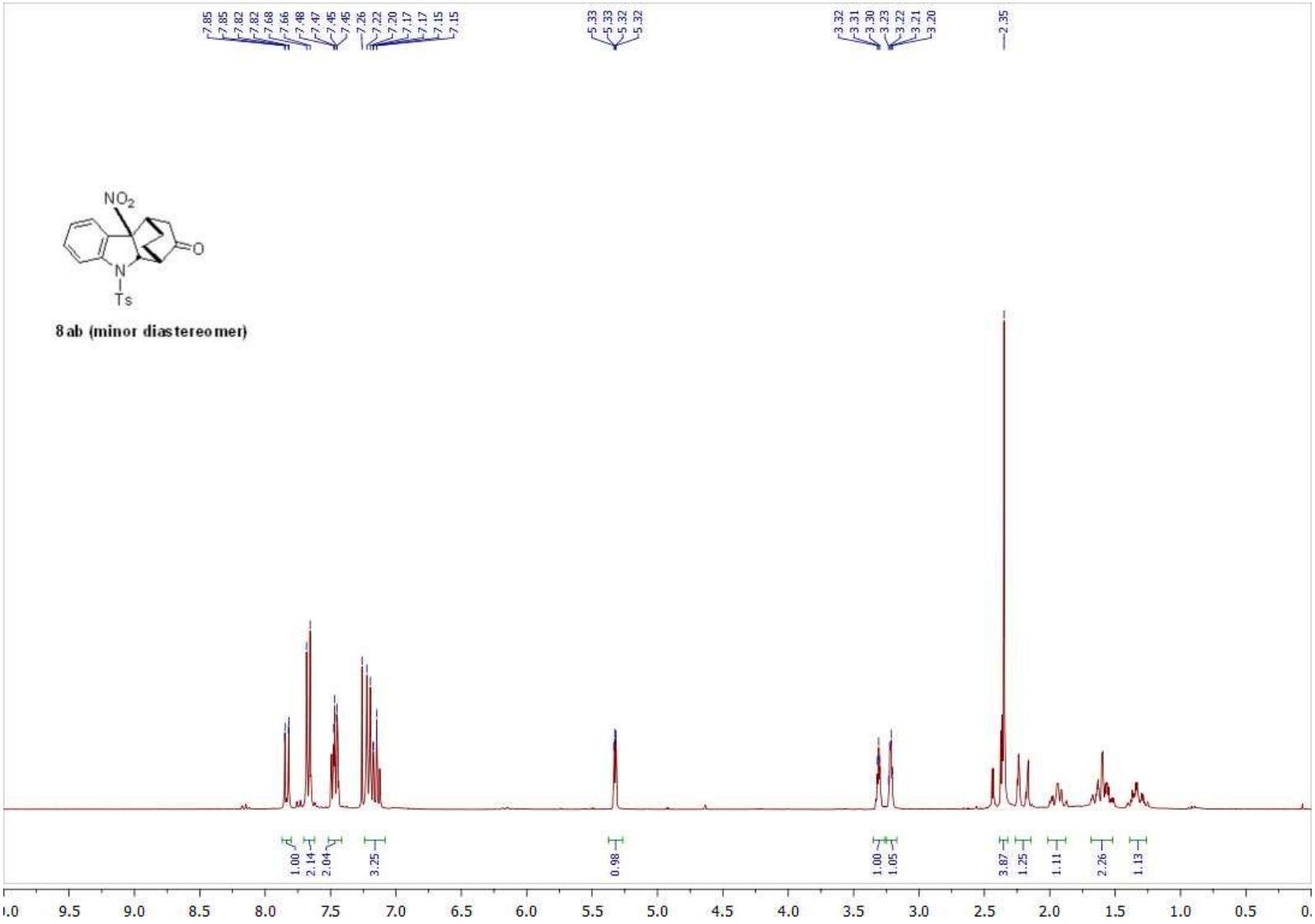

195.17
164.27
145.31
144.69
133.56
133.45
129.99
128.11
127.30
124.69
121.81
115.07
105.38
89.38
63.78
57.97
45.05
21.64
MeO
Br
NO2
O
N
Ts
7ga
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

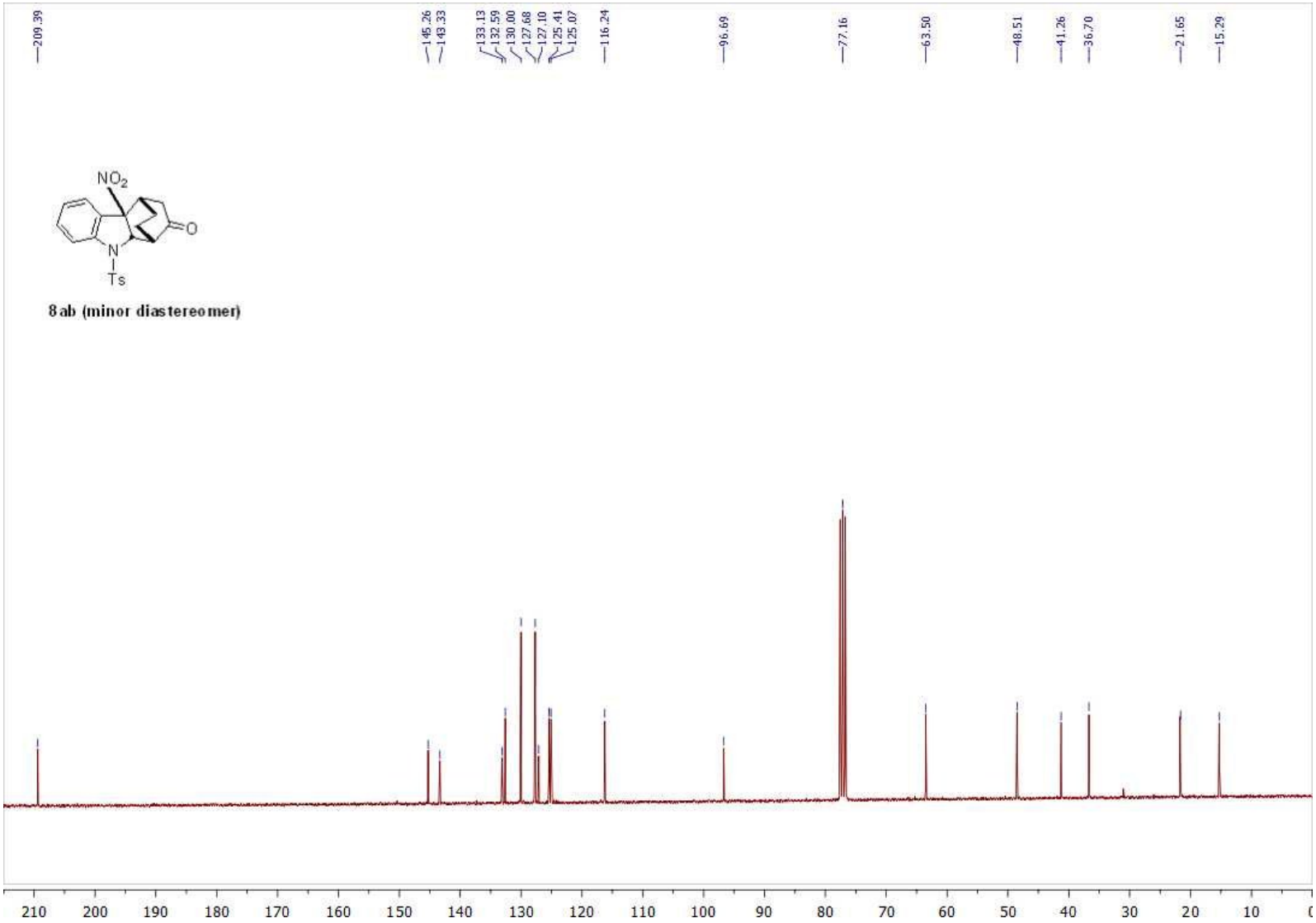

7.92
7.89
7.66
7.62
7.54
7.51
7.43
7.41
7.40
7.39
7.37
7.36
7.36
7.35
7.34
7.32
7.32
7.29
7.22
7.19
5.91
5.91
5.62
5.58
5.25
5.21
5.18
5.15
5.08
5.08
5.07
5.07
5.06
5.05
5.04
5.04
3.73
3.35
3.34
3.33
3.32
3.15
3.12
3.10
3.07
2.37
MeO
NO2
BnO
O
N
Ts
7ha
1.00
1.43
2.24
8.52
2.53
0.86
1.44
0.97
1.41
1.32
3.47
1.52
1.30
3.65
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

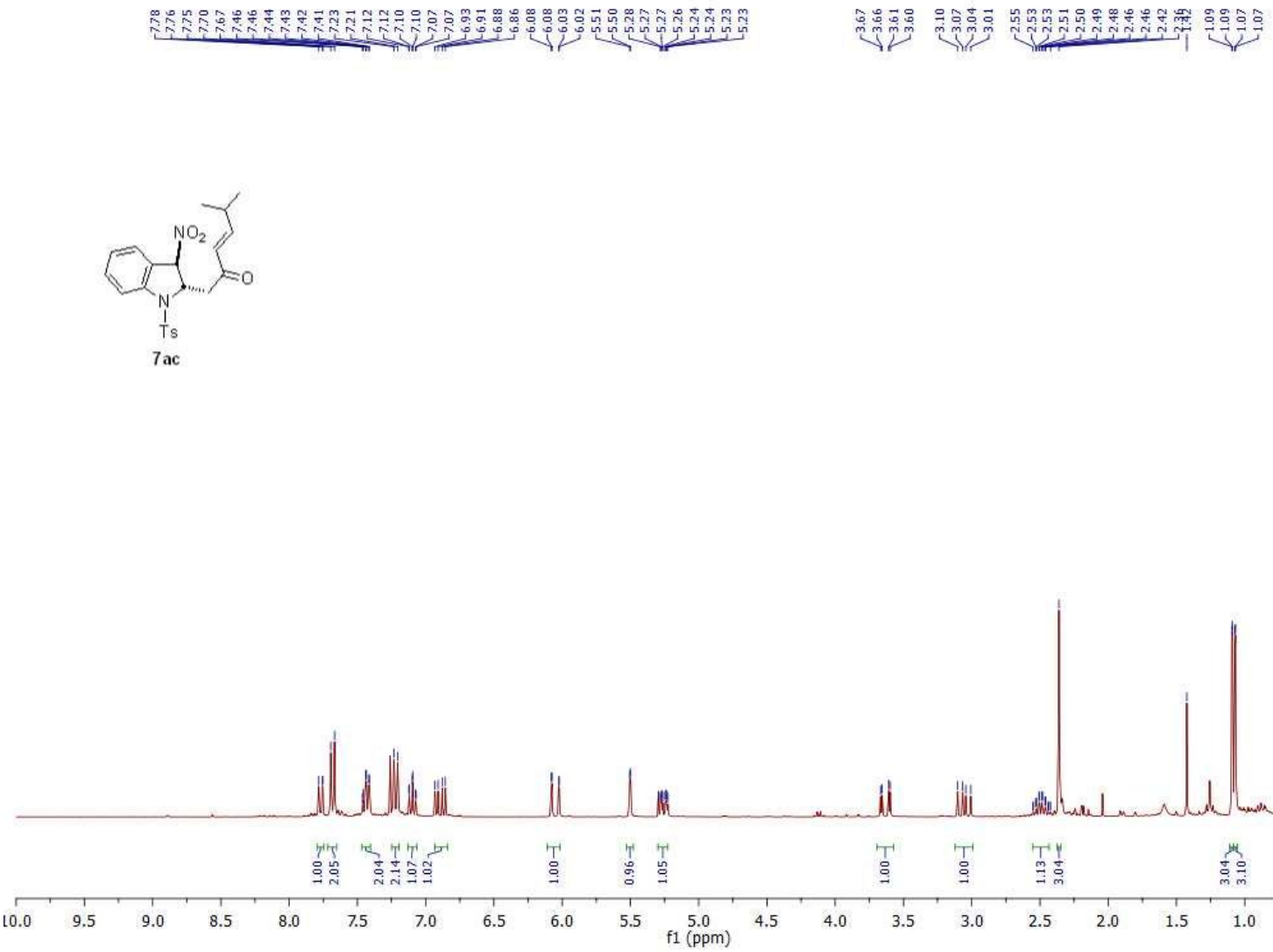

195.10
164.52
149.31
145.81
137.62
135.31
133.00
130.35
129.00
128.70
127.73
120.09
119.84
105.53
86.90
72.48
63.80
58.18
44.93
21.86
MeO
BnO
NO2
O
N
Ts
7ha
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

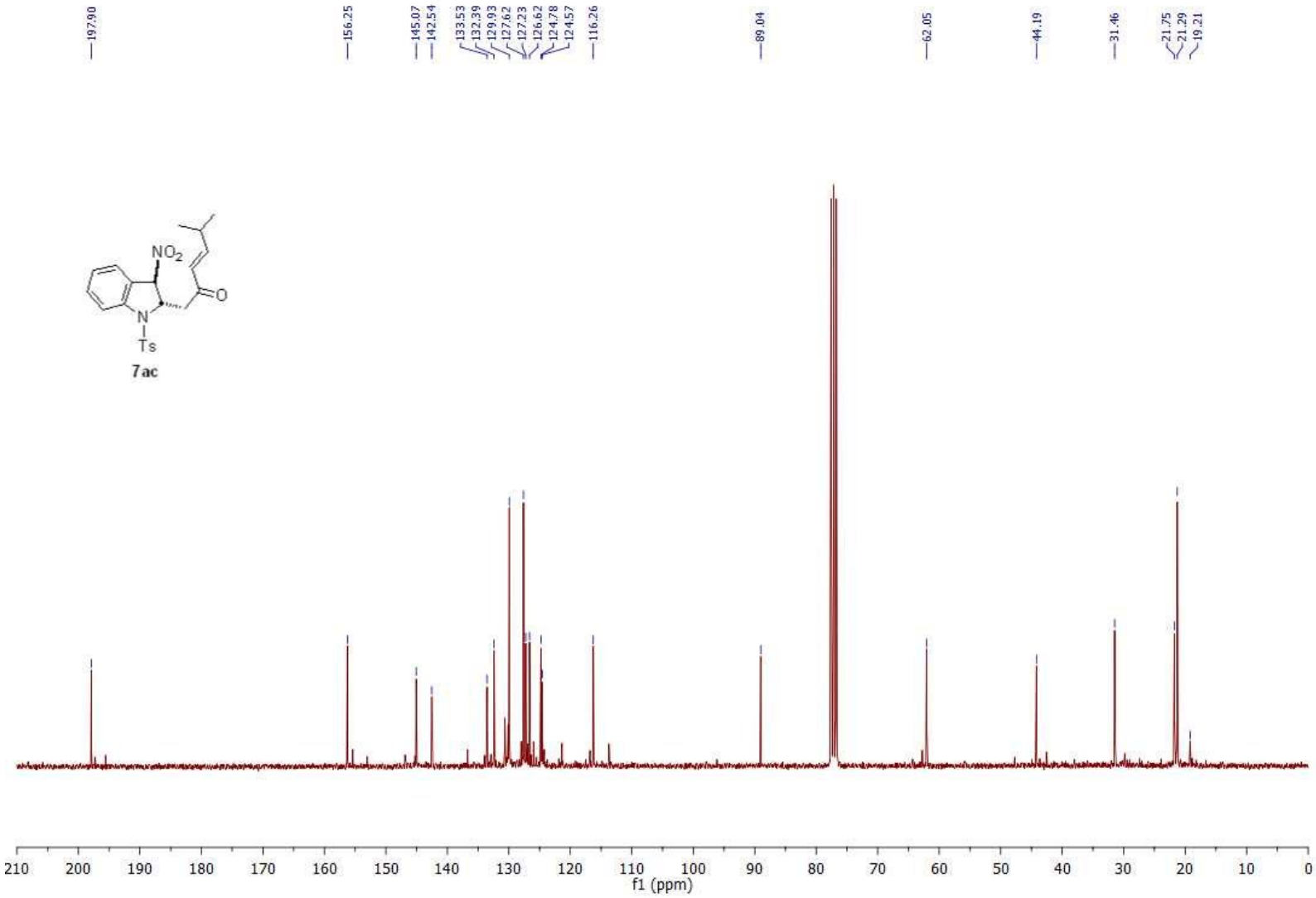

7.69
7.68
7.67
7.66
7.65
7.64
7.50
7.49
7.47
7.47
7.43
7.42
7.40
7.40
7.37
7.37
7.22
7.20
7.14
7.13
7.11
7.11
7.09
7.08
5.50
5.48
3.27
3.27
3.26
3.25
3.24
3.23
3.21
2.35
2.20
2.19
2.14
2.13
1.94
1.93
1.92
1.89
1.88
1.87
1.82
1.81
1.80
1.79
1.78
1.77
1.74
1.73
1.72
1.69
1.68
1.67
NO2
O
N
Ts
8ab (major diastereomer)
3.00
1.00
1.01
2.02
1.03
0.93
2.10
3.01
1.30
5.53
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

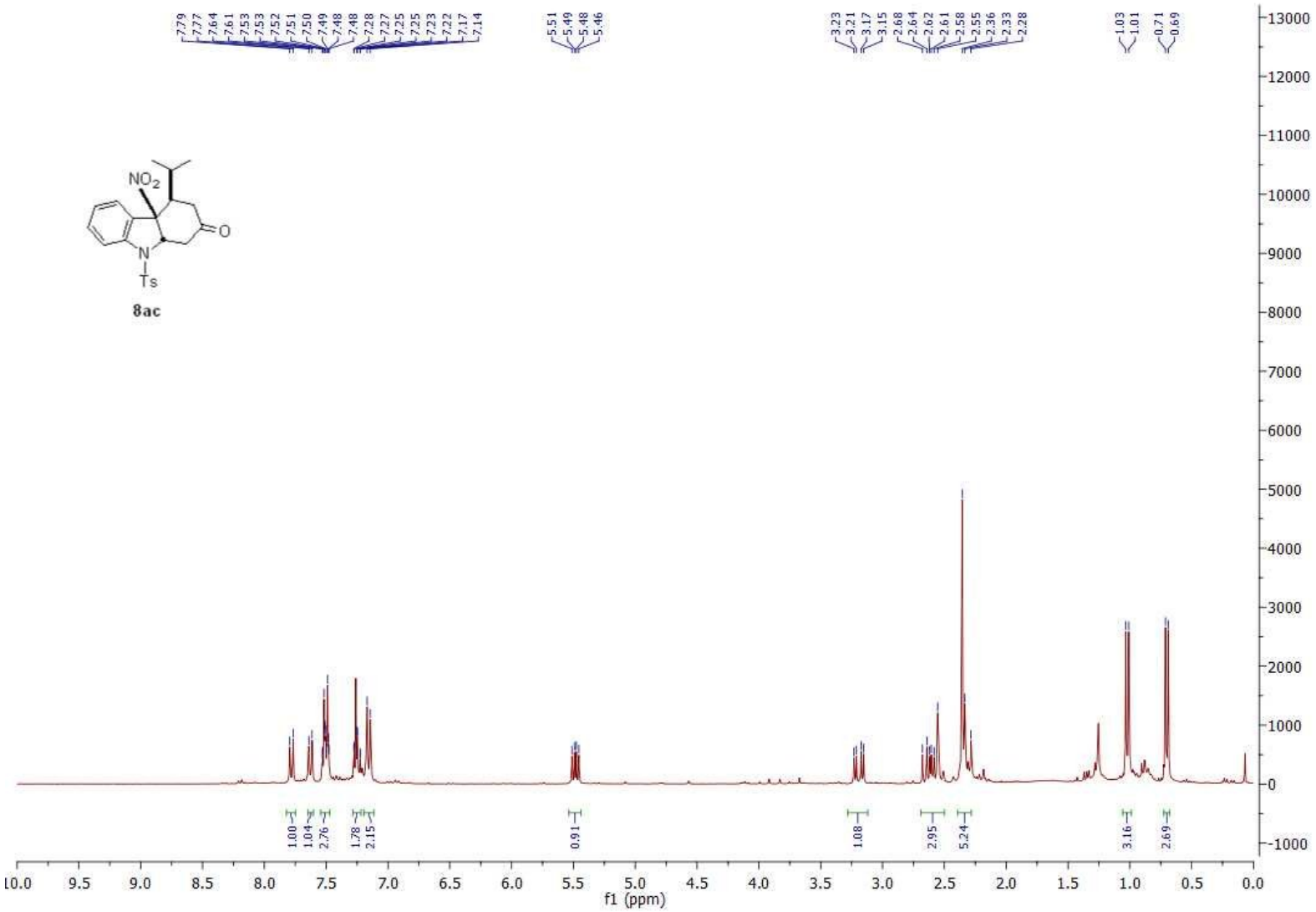

208.64
145.17
142.57
133.27
132.66
129.95
127.71
126.68
125.27
125.25
116.51
96.56
66.36
48.19
40.34
37.38
21.71
20.09
19.34
NO2
O
N
Ts
8ab (major diastereomer)
f1 (ppm)


7.85
7.85
7.82
7.82
7.68
7.66
7.48
7.47
7.45
7.45
7.26
7.22
7.20
7.17
7.17
7.15
7.15
5.33
5.33
5.32
5.32
3.32
3.31
3.30
3.23
3.22
3.21
3.20
2.35
NO2
O
N
Ts
8ab (minor diastereomer)
1.00
2.14
2.04
3.25
0.98
1.00
1.05
3.87
1.25
1.11
2.26
1.13
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5


209.39
145.26
143.33
133.13
132.59
130.00
127.68
127.10
125.41
125.07
116.24
96.69
77.16
63.50
48.51
41.26
36.70
21.65
15.29
NO2
O
N
Ts
8ab (minor diastereomer)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


7.78
7.76
7.75
7.70
7.67
7.46
7.46
7.44
7.43
7.42
7.41
7.23
7.21
7.12
7.12
7.10
7.10
7.07
7.07
6.93
6.91
6.88
6.86
6.08
6.08
6.03
6.02
5.51
5.50
5.28
5.27
5.27
5.26
5.24
5.24
5.23
5.23
3.67
3.66
3.61
3.60
3.10
3.07
3.04
3.01
2.55
2.53
2.53
2.51
2.50
2.49
2.48
2.46
2.46
2.42
1.09
1.09
1.07
1.07
NO2
O
N
Ts
7ac
1.00
2.05
2.04
2.14
1.07
1.02
1.00
0.96
1.05
1.00
1.00
1.13
3.04
3.04
3.10
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


197.90
156.25
145.07
142.54
133.53
132.39
129.93
127.62
127.23
126.62
124.78
124.57
116.26
89.04
62.05
44.19
31.46
21.75
21.29
19.21
NO2
O
N
Ts
7ac
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.77
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7.51
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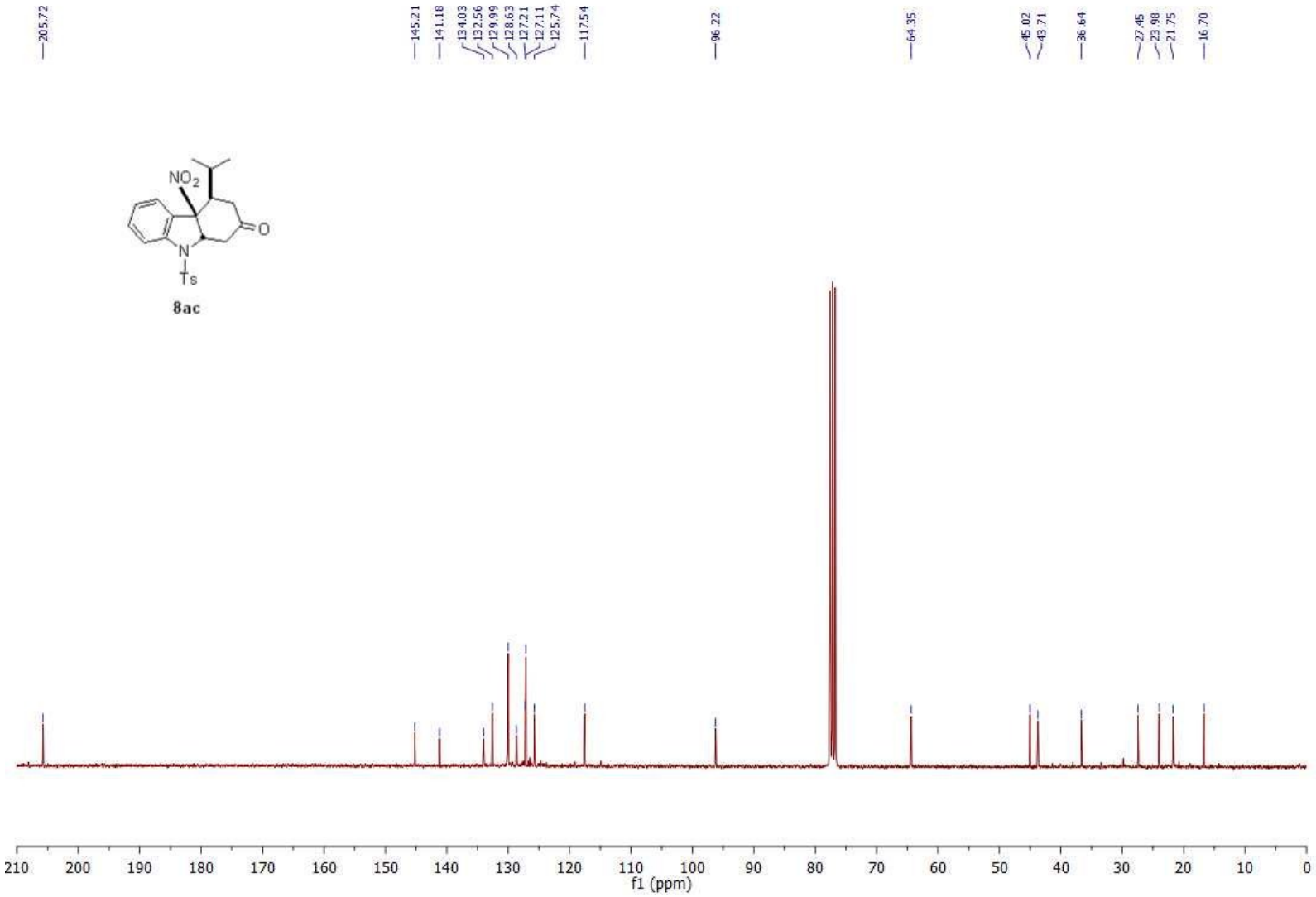
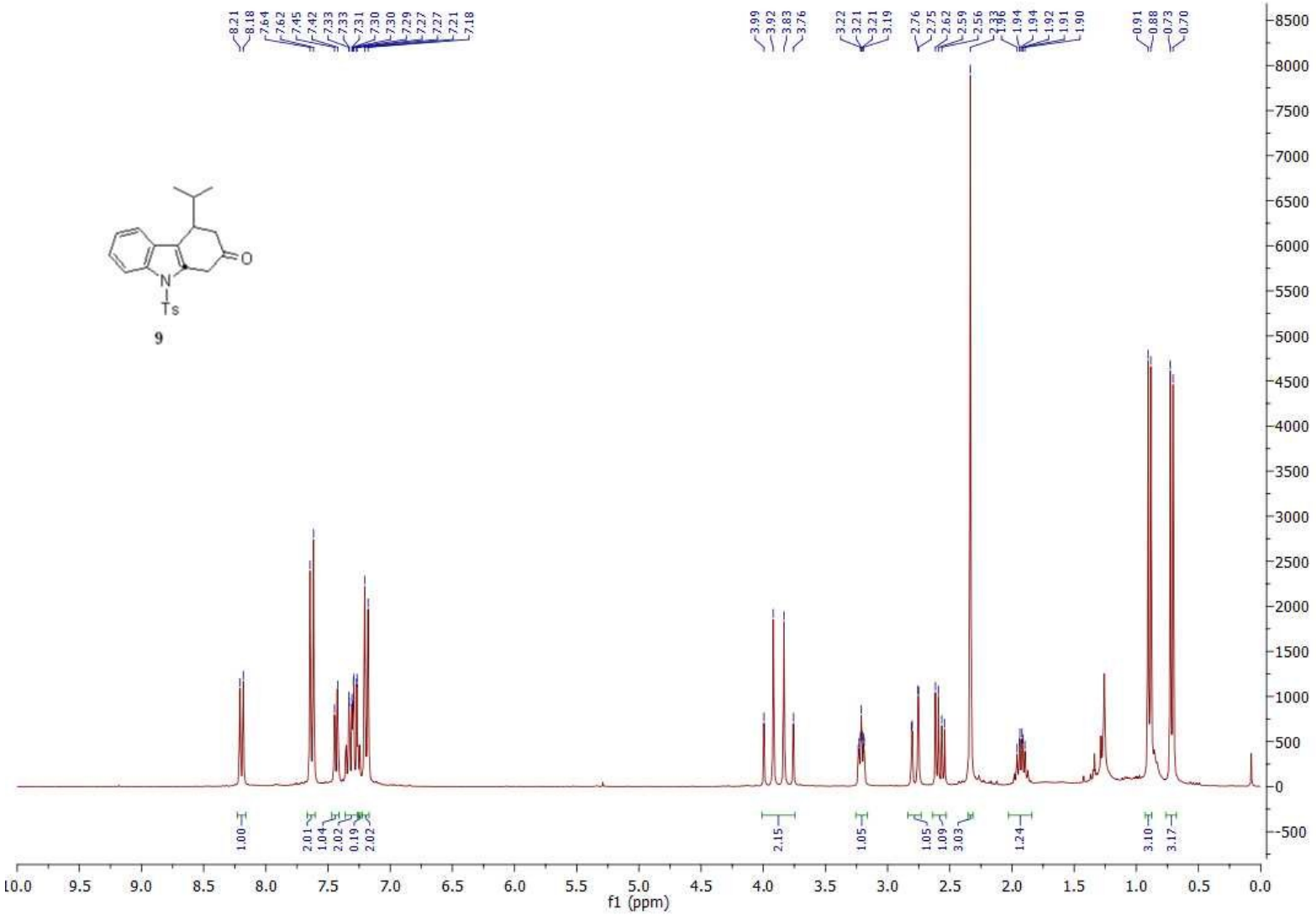
7.49
7.48
7.48
7.28
7.27
7.25
7.25
7.23
7.22
7.17
7.14
5.51
5.49
5.48
5.46
3.23
3.21
3.17
3.15
2.68
2.64
2.62
2.61
2.58
2.55
2.36
2.33
2.28
1.03
1.01
0.71
0.69
NO2
O
N
Ts
8ac
1.00
1.04
2.76
1.78
2.15
0.91
1.08
2.95
5.24
3.16
2.69
f1 (ppm)


205.72
145.21
141.18
134.03
132.56
129.99
128.63
127.21
127.11
125.74
117.54
96.22
64.35
45.02
43.71
36.64
27.45
23.98
21.75
16.70
NO2
O
N
Ts
8ac
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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8.18
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7.62
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7.42
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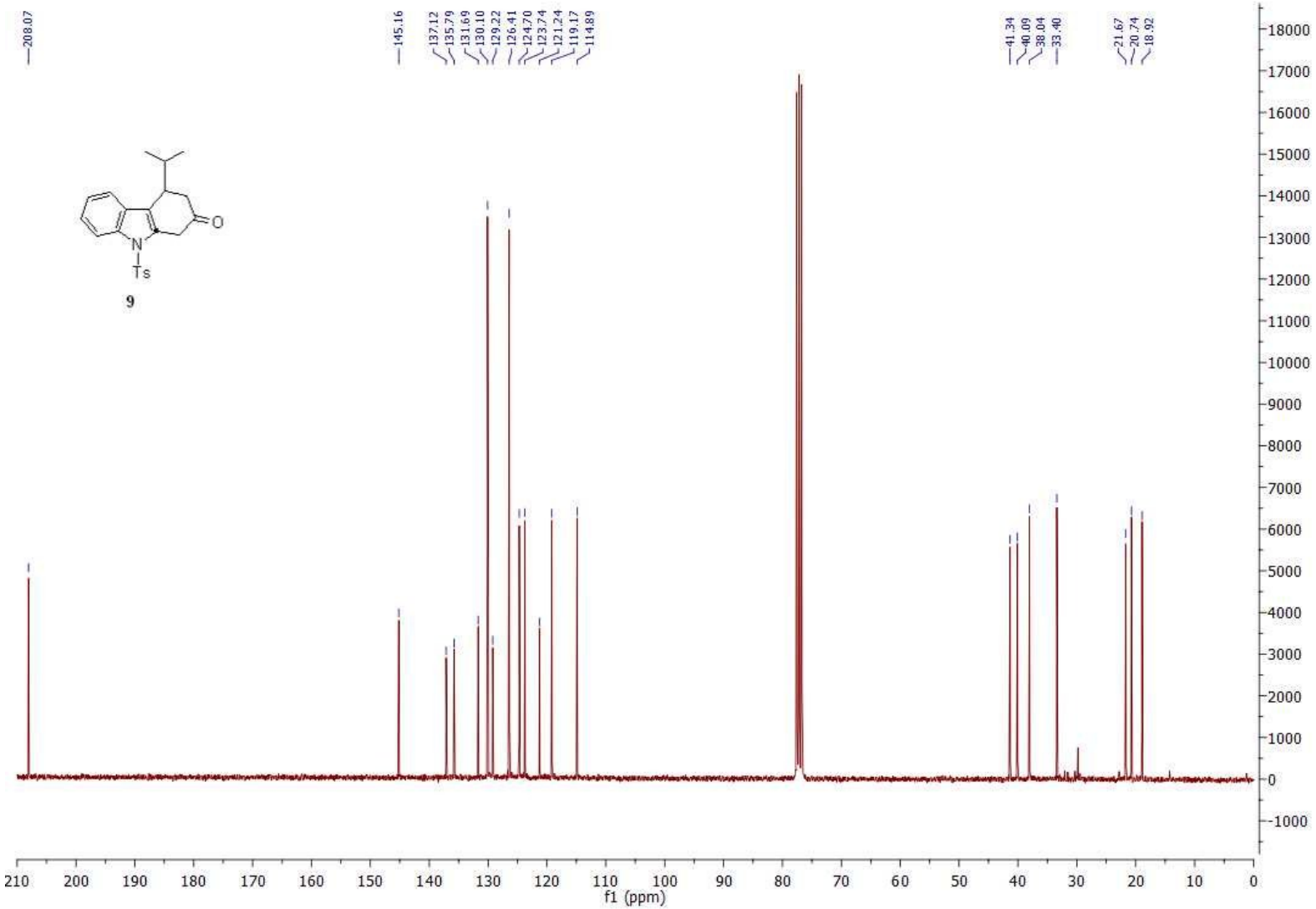
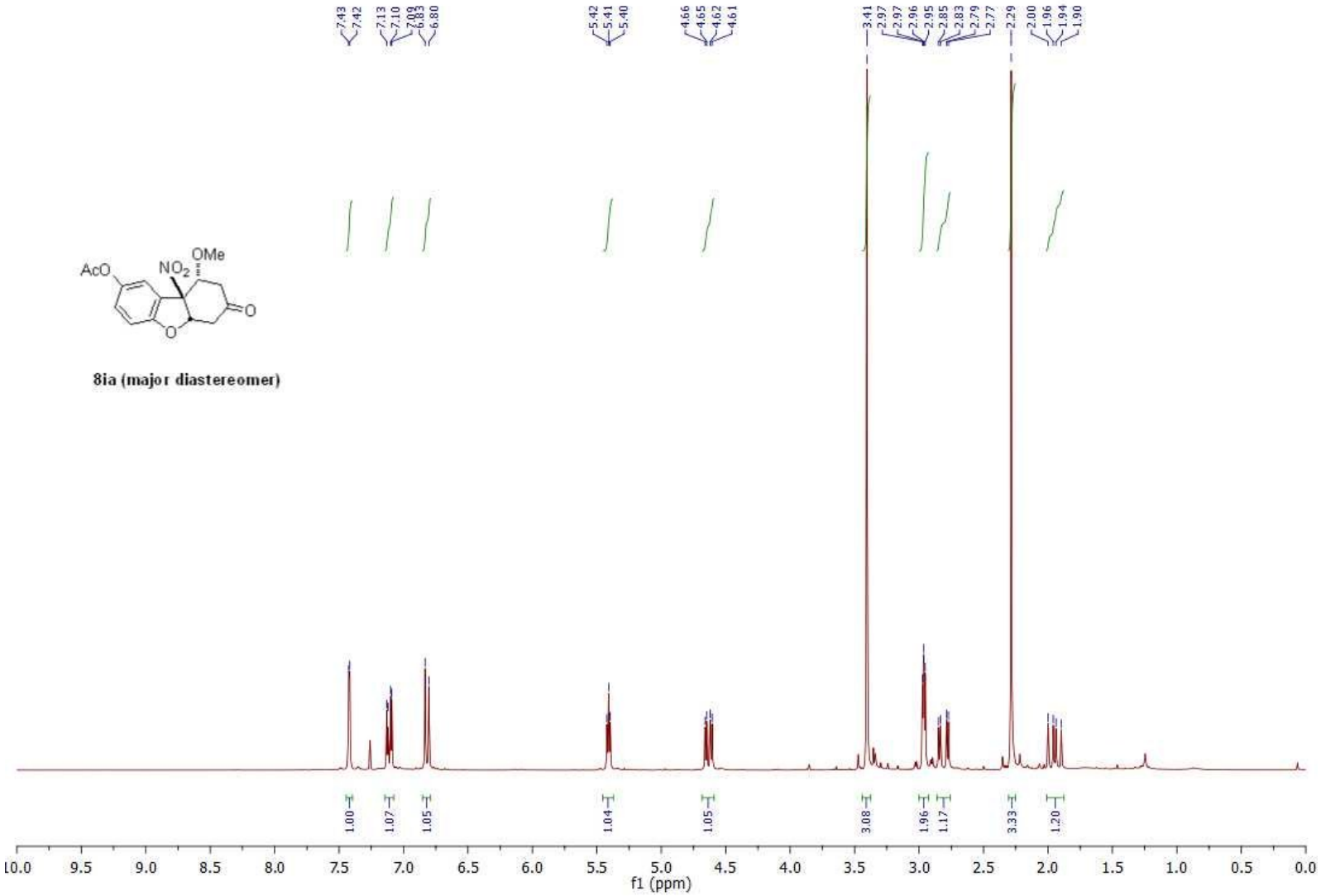
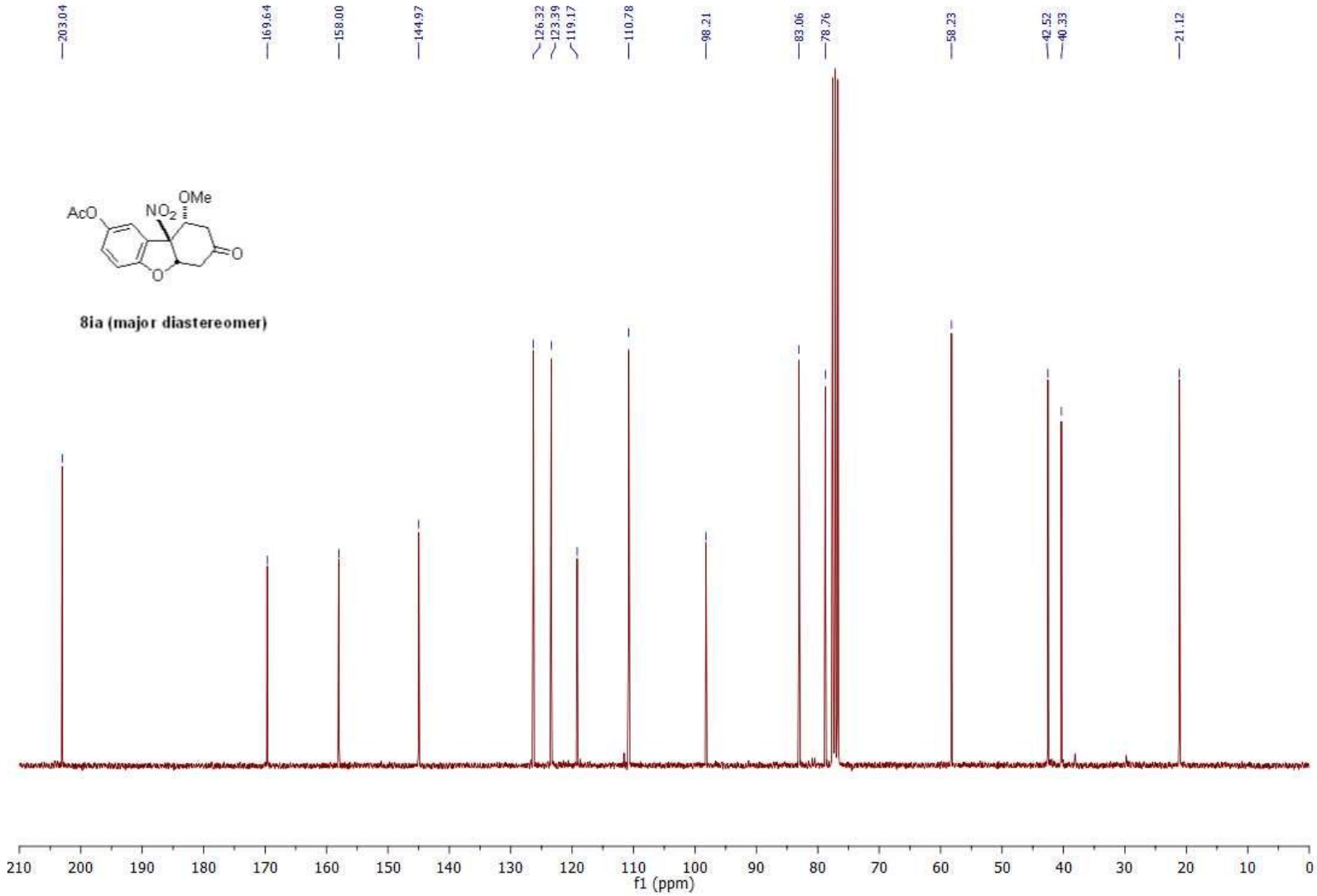
7.33
7.31
7.30
7.30
7.29
7.27
7.27
7.21
7.18
3.99
3.92
3.83
3.76
3.22
3.21
3.21
3.19
2.76
2.75
2.62
2.59
2.56
2.33
1.98
1.94
1.94
1.92
1.91
1.90
0.91
0.88
0.73
0.70
O
N
Ts
9
1.00
2.01
1.04
2.02
0.19
2.02
2.15
1.05
1.05
1.09
3.03
1.24
3.10
3.17
f1 (ppm)


208.07
145.16
137.12
135.79
131.69
130.10
129.22
126.41
124.70
123.74
121.24
119.17
114.89
41.34
40.09
38.04
33.40
21.67
20.74
18.92
O
N
Ts
9
f1 (ppm)



8ia (major diastereomer)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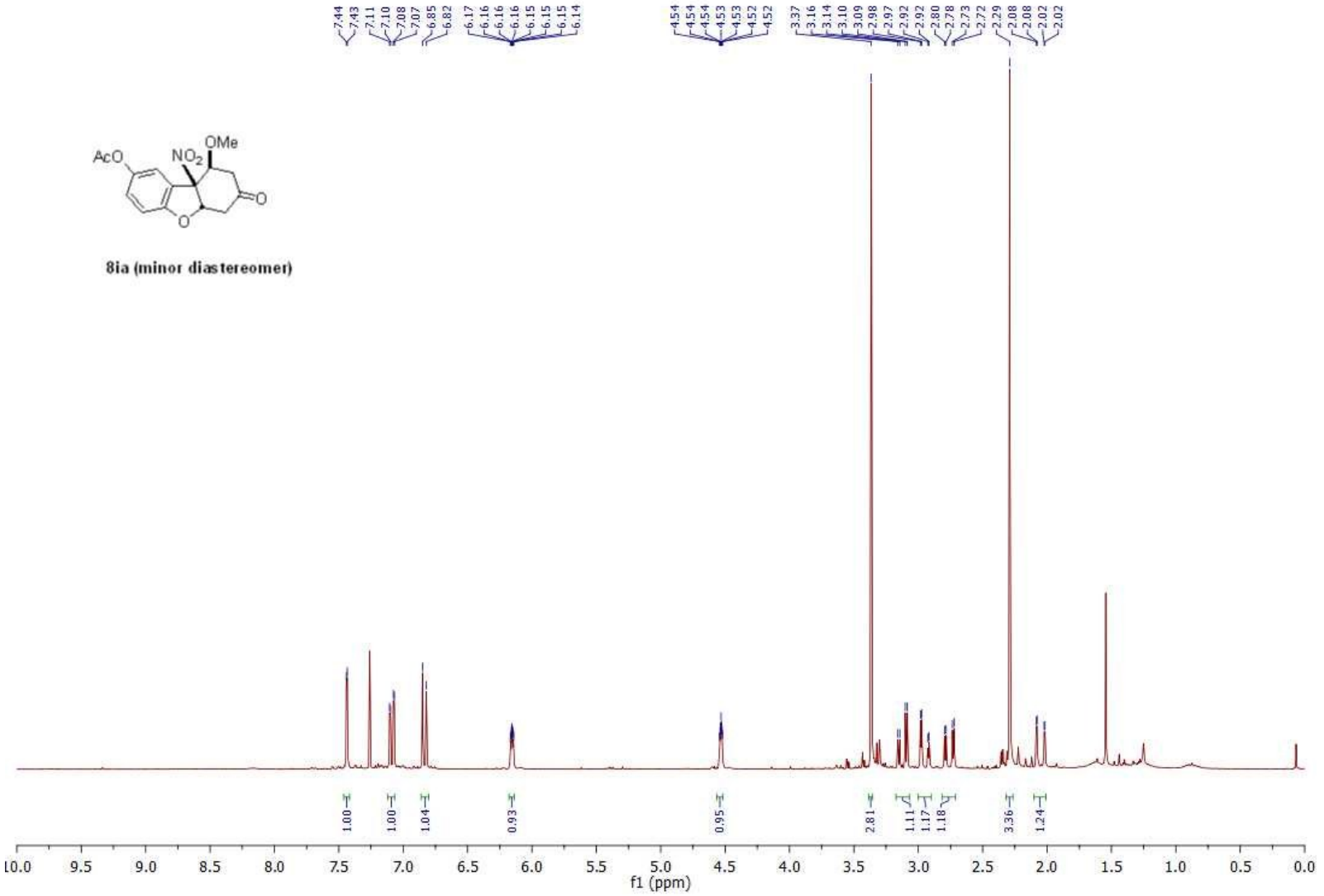
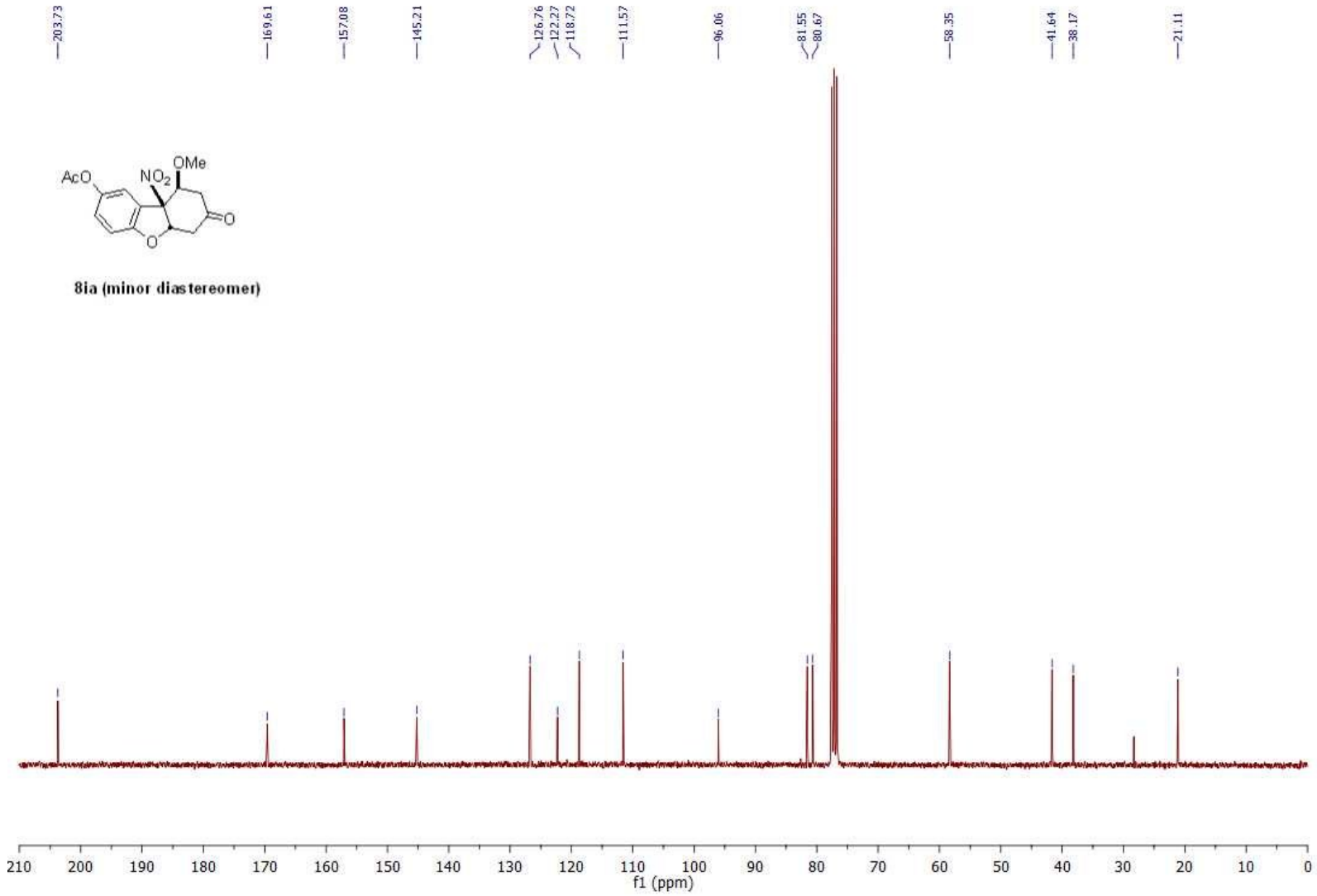
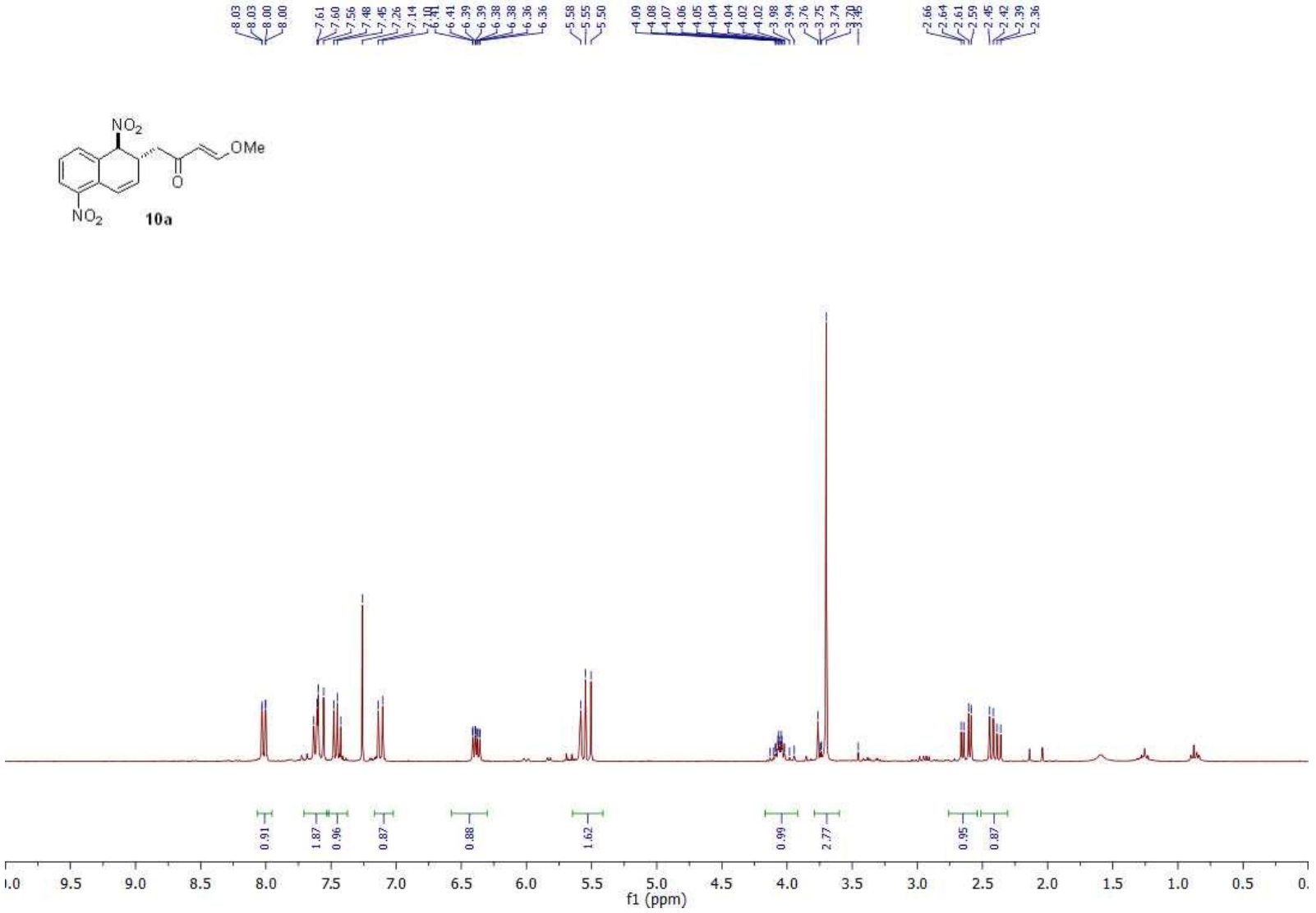
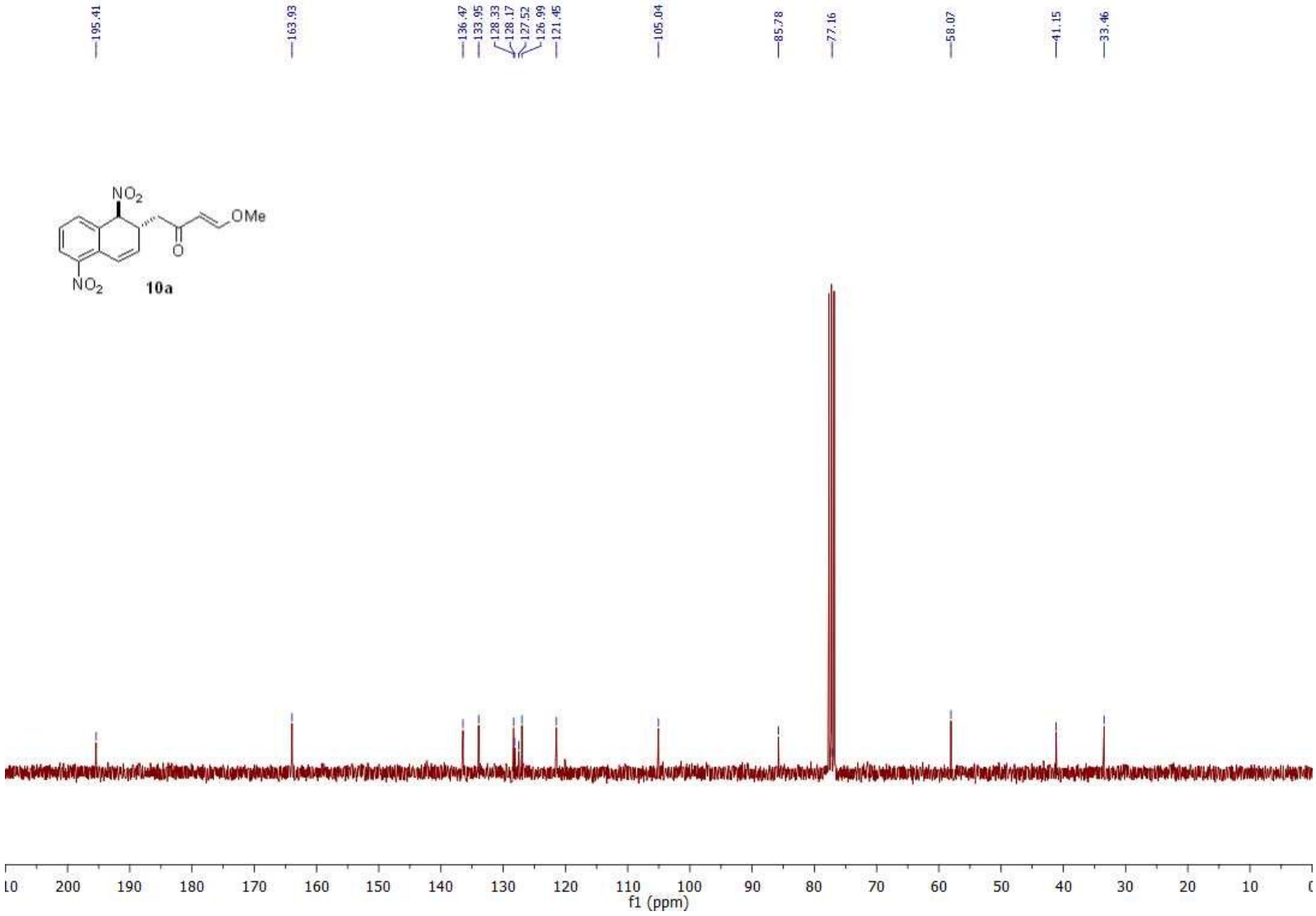
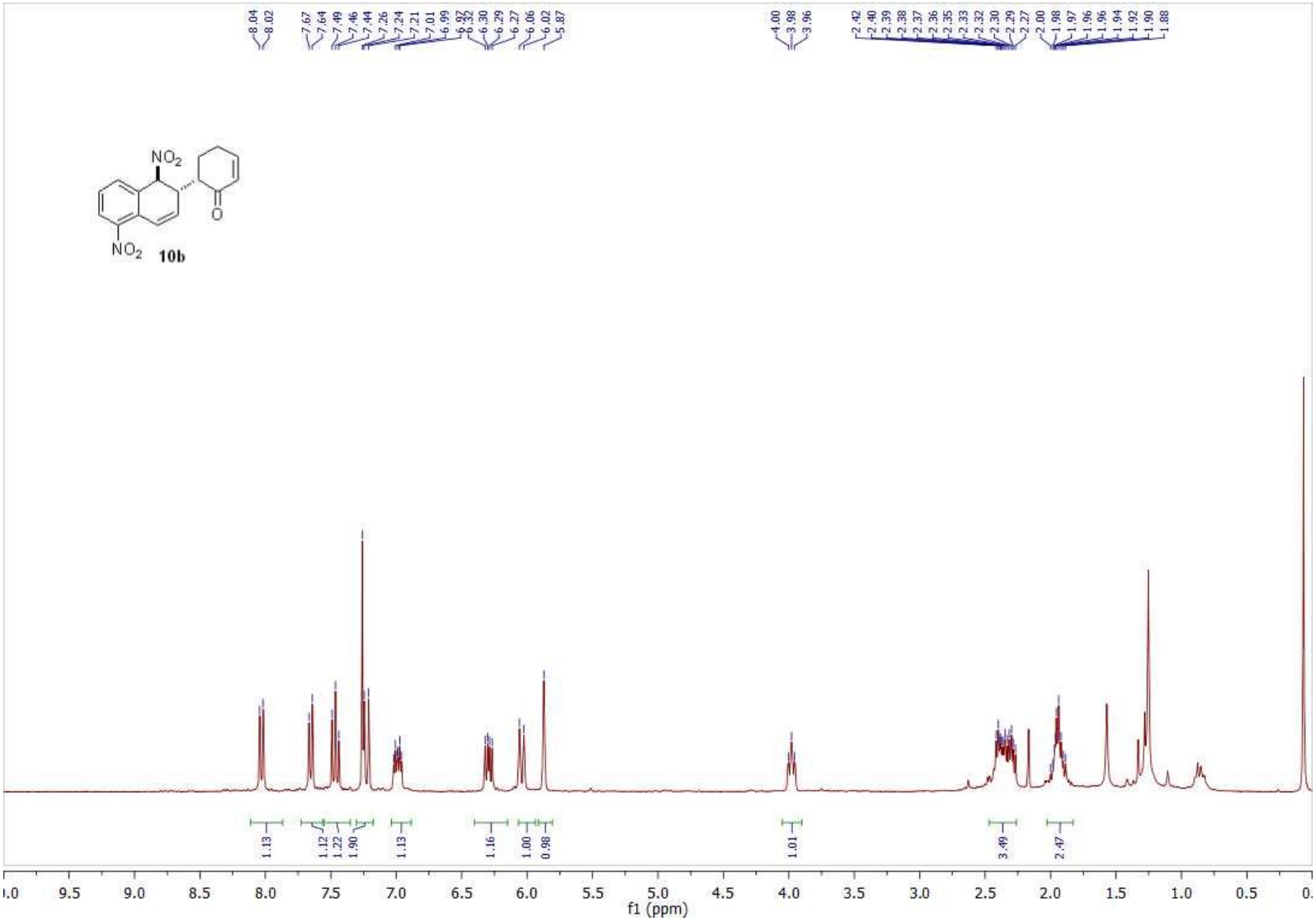
169.64
158.00
144.97
126.32
123.39
119.17
110.78
98.21
83.06
78.76
58.23
42.52
40.33
21.12
AcO
NO2
OMe
O
O
8ia (major diastereomer)
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

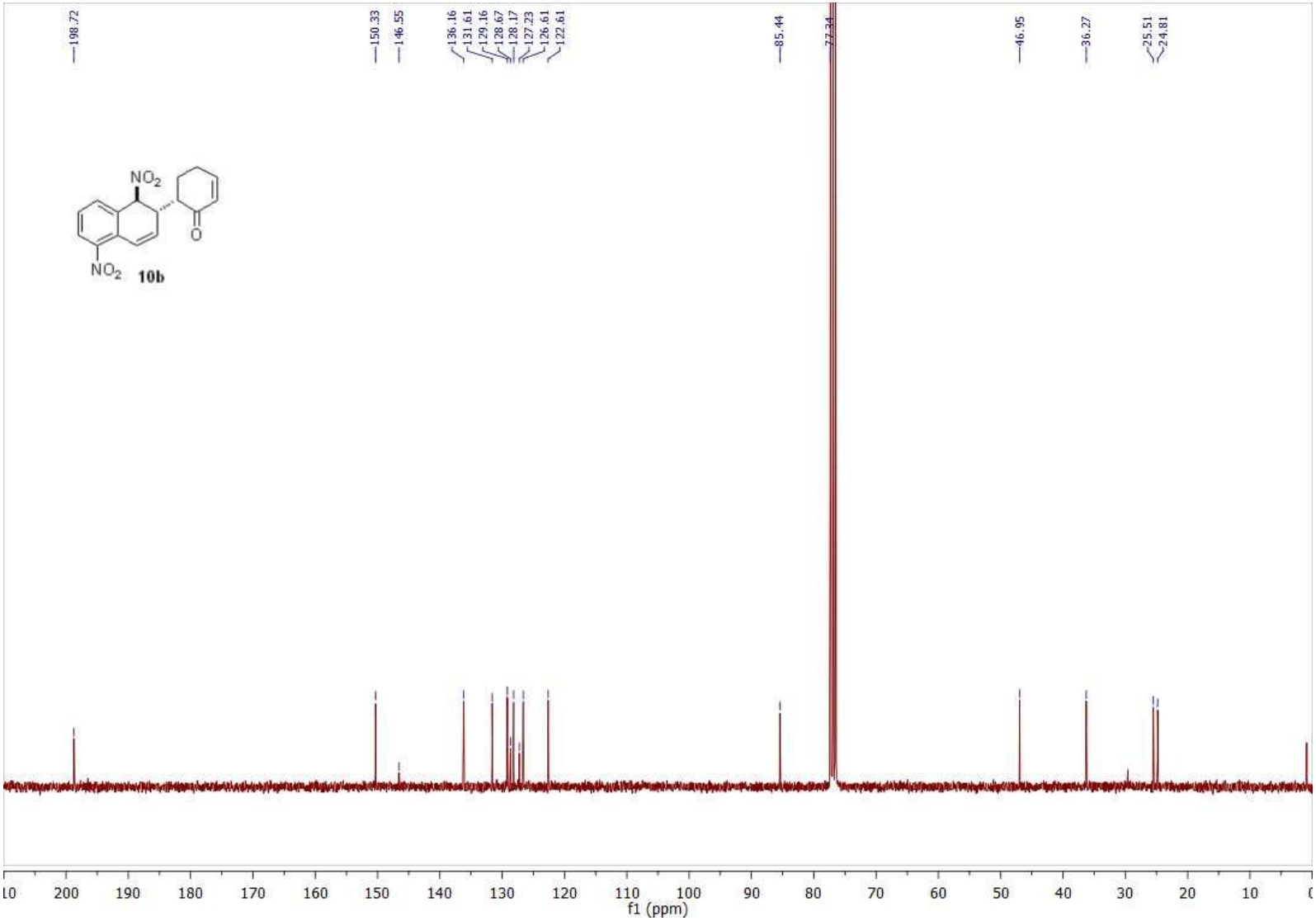

AcO
NO2
OMe
O
O
8ia (minor diastereomer)
7.44
7.43
7.11
7.10
7.08
7.07
6.85
6.82
6.17
6.16
6.16
6.16
6.15
6.15
6.15
6.14
4.54
4.54
4.54
4.53
4.53
4.52
4.52
3.37
3.16
3.14
3.10
3.09
2.98
2.97
2.92
2.92
2.92
2.80
2.78
2.73
2.72
2.29
2.08
2.08
2.02
2.02
1.00
1.00
1.04
0.93
0.95
2.81
1.11
1.17
1.18
3.36
1.24
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


203.73
169.61
157.08
145.21
126.76
122.27
118.72
111.57
96.06
81.55
80.67
58.35
41.64
38.17
21.11
AcO
NO2
OMe
O
O
8ia (minor diastereomer)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.03
8.03
8.00
8.00
7.61
7.60
7.56
7.48
7.45
7.26
7.14
6.41
6.39
6.39
6.38
6.38
6.36
6.36
5.58
5.55
5.50
4.09
4.08
4.07
4.06
4.05
4.04
4.04
4.02
4.02
3.98
3.94
3.76
3.75
3.74
2.66
2.64
2.61
2.59
2.45
2.42
2.39
2.36
NO2
OMe
O
NO2
10a
0.91
1.87
0.96
0.87
0.88
1.62
0.99
2.77
0.95
0.87
f1 (ppm)


195.41
163.93
136.47
133.95
128.33
128.17
127.52
126.99
121.45
105.04
85.78
77.16
58.07
41.15
33.46
NO2
OMe
O
NO2
10a
f1 (ppm)


8.04
8.02
7.67
7.64
7.49
7.46
7.44
7.26
7.24
7.21
7.01
6.99
6.32
6.30
6.29
6.27
6.06
6.02
5.87
4.00
3.98
3.96
2.42
2.40
2.39
2.38
2.37
2.36
2.35
2.33
2.32
2.30
2.29
2.27
2.00
1.98
1.97
1.96
1.96
1.94
1.92
1.90
1.88
NO2
NO2
O
10b
1.13
1.12
1.22
1.90
1.13
1.16
1.00
0.98
1.01
3.49
2.47
f1 (ppm)


198.72
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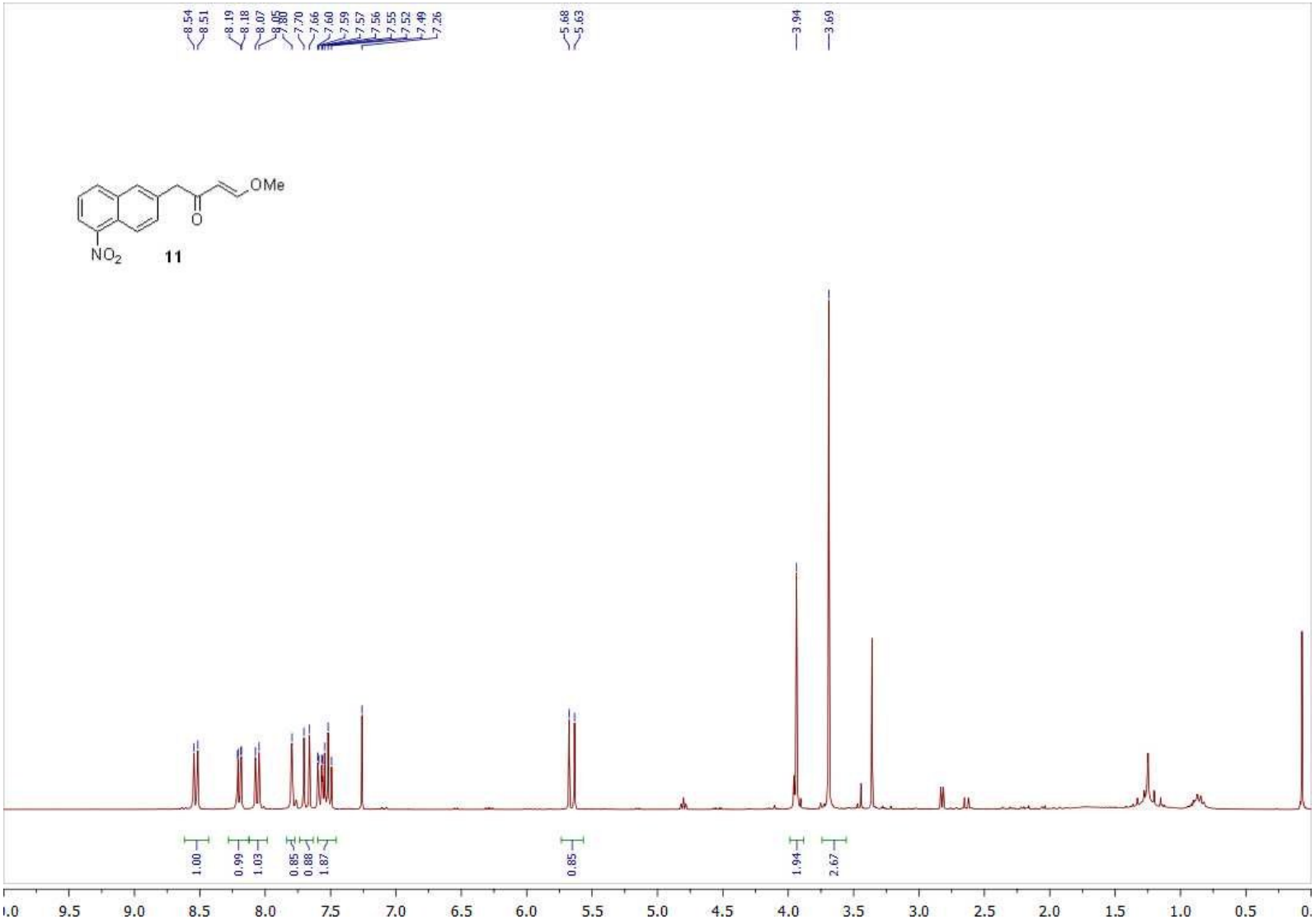
146.55
136.16
131.61
129.16
128.67
128.17
127.23
126.61
122.61
85.44
77.24
46.95
36.27
25.51
24.81
NO2
NO2
O
10b
f1 (ppm)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7.70
7.66
7.60
7.59
7.57
7.56
7.55
7.52
7.49
7.26
5.68
5.63
3.94
3.69
OMe
O
NO2
11
1.00
0.99
1.03
0.85
0.88
1.87
0.85
1.94
2.67
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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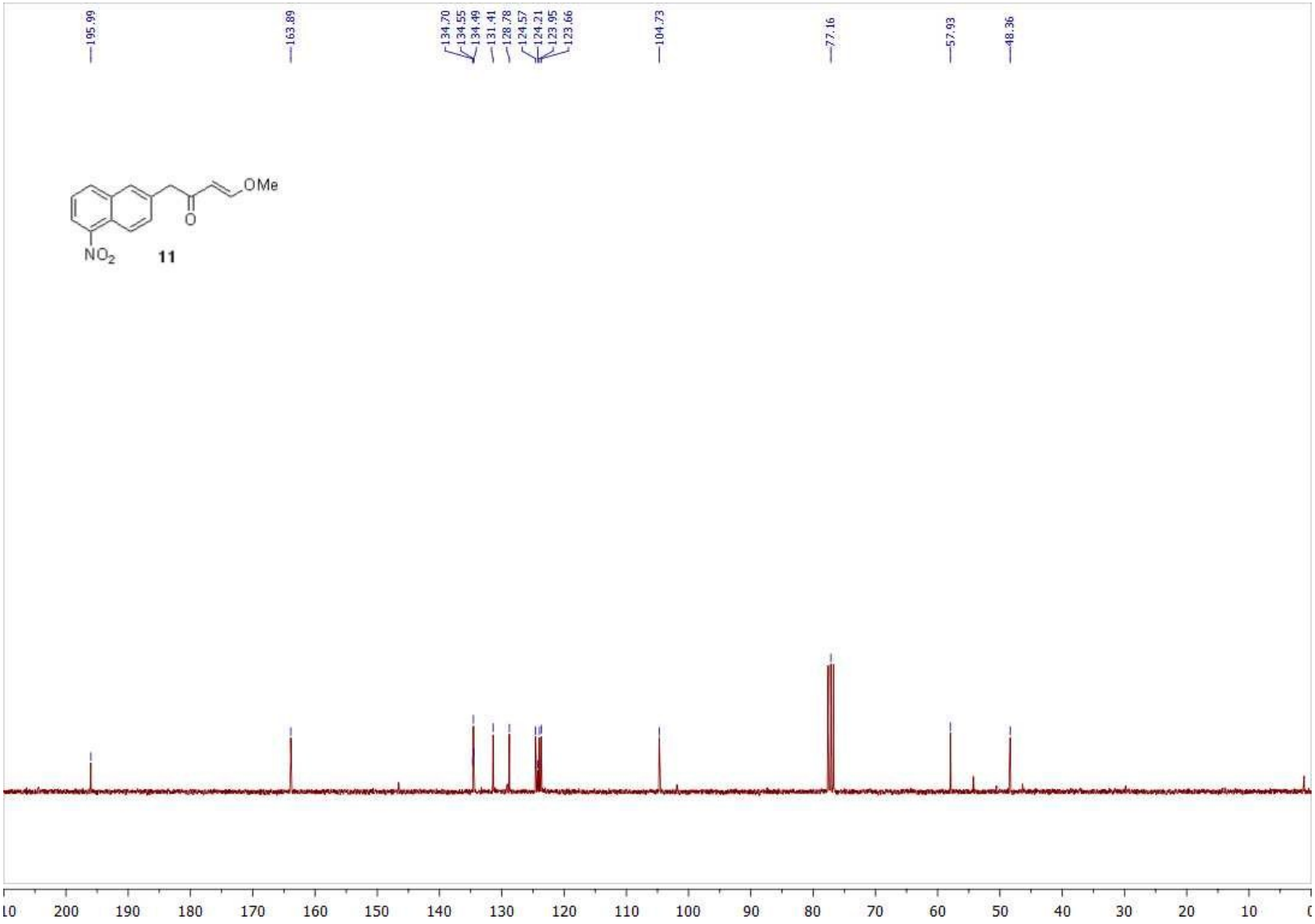
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5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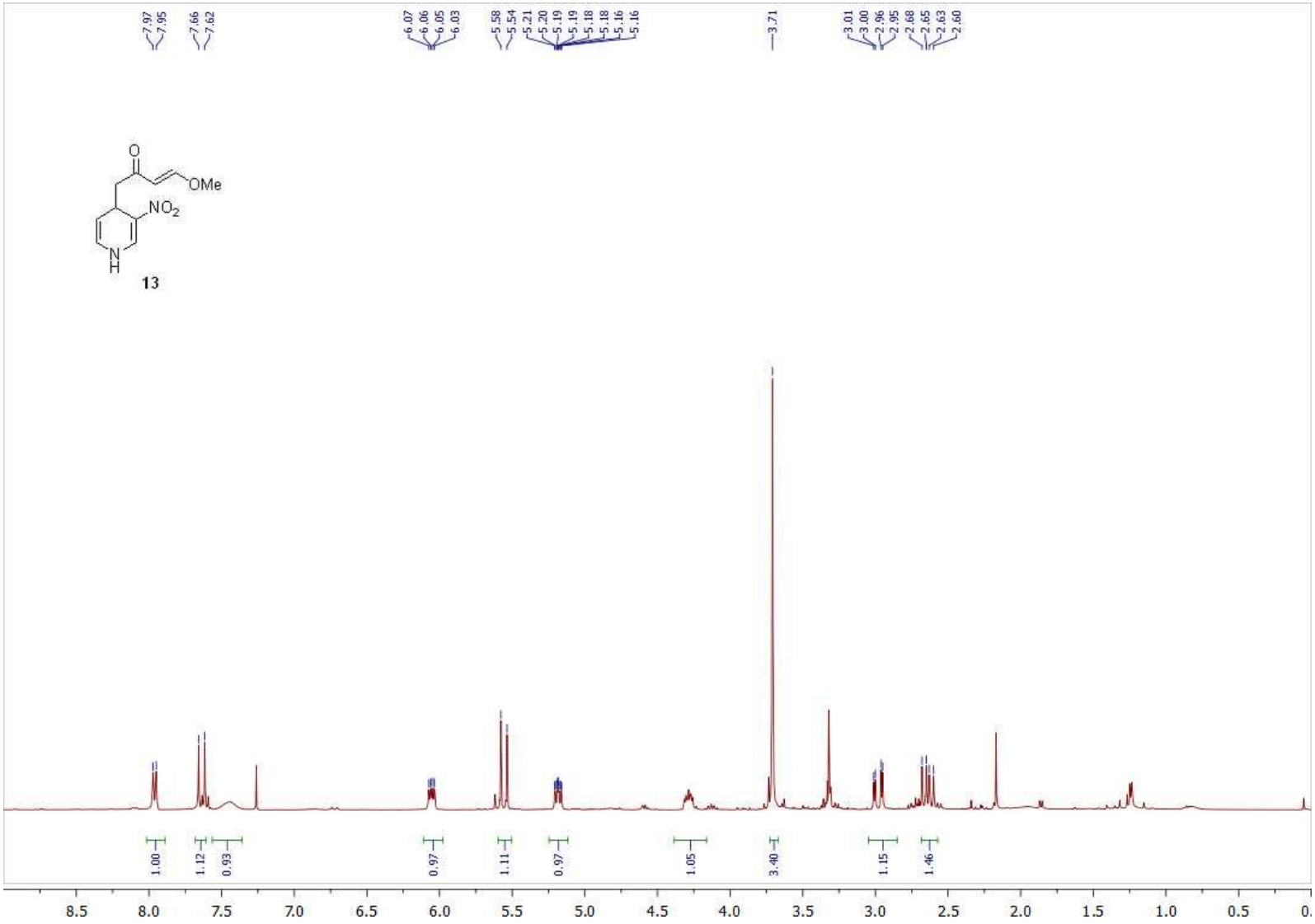
163.89
134.70
134.55
134.49
131.41
128.78
124.57
124.21
123.95
123.66
104.73
77.16
57.93
48.36
OMe
O
NO2
11
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10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7.95
7.66
7.62
6.07
6.06
6.05
6.03
5.58
5.54
5.21
5.20
5.19
5.19
5.18
5.18
5.16
5.16
3.71
3.01
3.00
2.96
2.95
2.68
2.65
2.63
2.60
O
OMe
NO2
N
H
13
1.00
1.12
0.93
0.97
1.11
0.97
1.05
3.40
1.15
1.46
8.5
8.0
7.5
7.0
6.5
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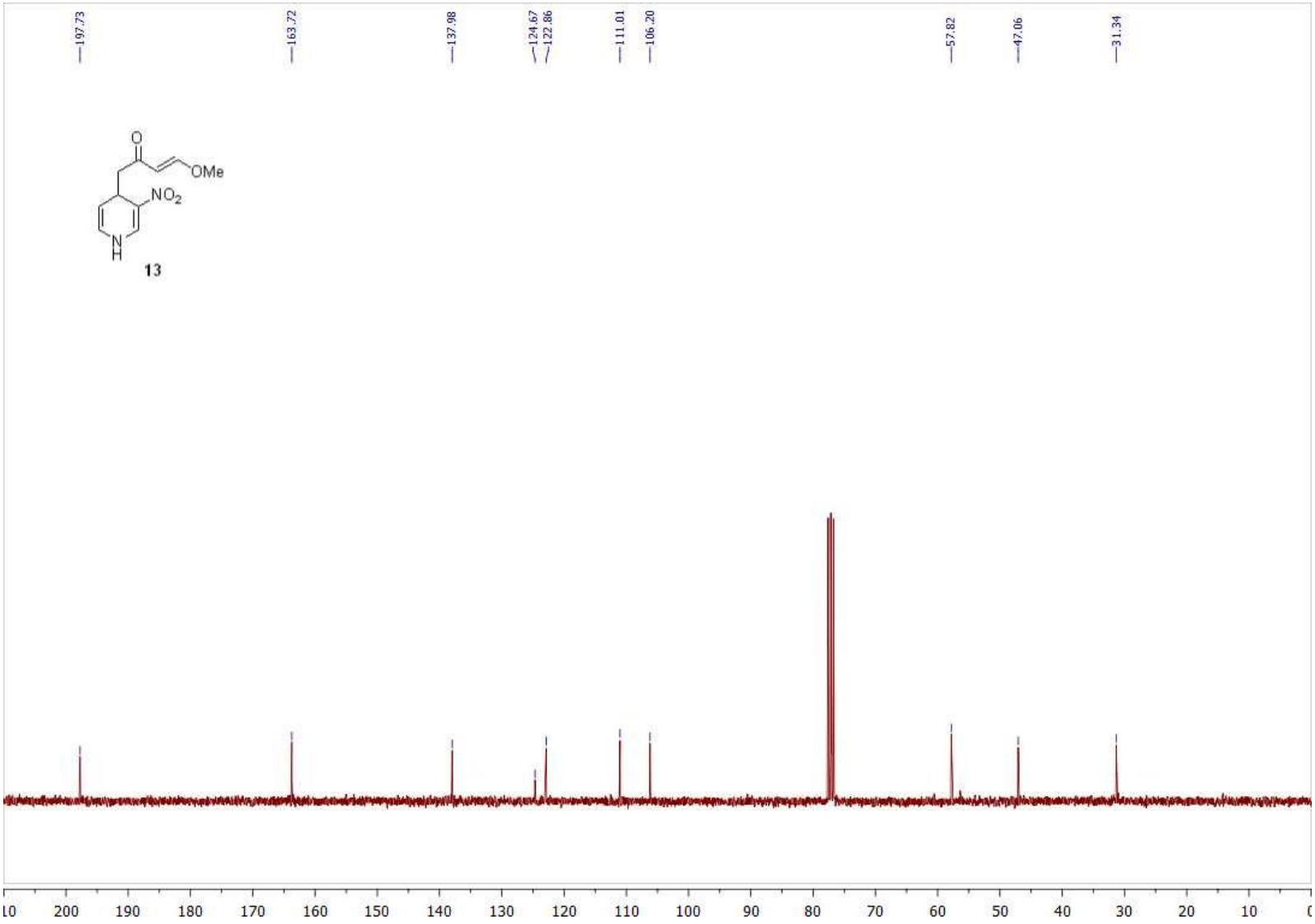
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5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111.01
106.20
57.82
47.06
31.34
O
OMe
NO2
N
H
13
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160
150
140
130
120
110
100
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80
70
60
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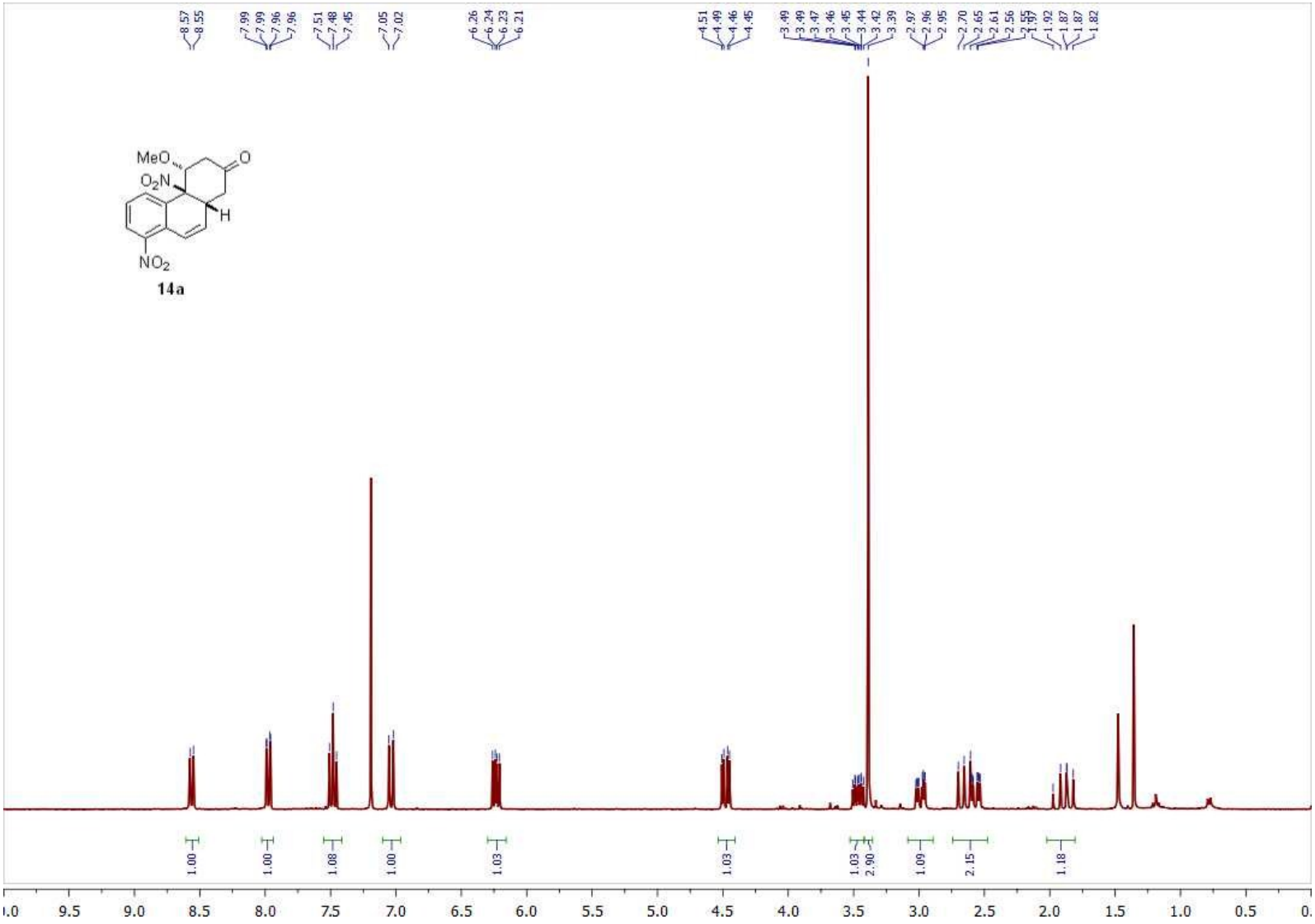
40
30
20
10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7.96
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7.48
7.45
7.05
7.02
6.26
6.24
6.23
6.21
4.51
4.49
4.46
4.45
3.49
3.49
3.47
3.46
3.45
3.44
3.42
3.39
2.97
2.96
2.95
2.70
2.65
2.61
2.56
1.92
1.87
1.87
1.82
MeO
O
O2N
H
NO2
14a
1.00
1.00
1.08
1.00
1.03
1.03
1.03
2.90
1.09
2.15
1.18
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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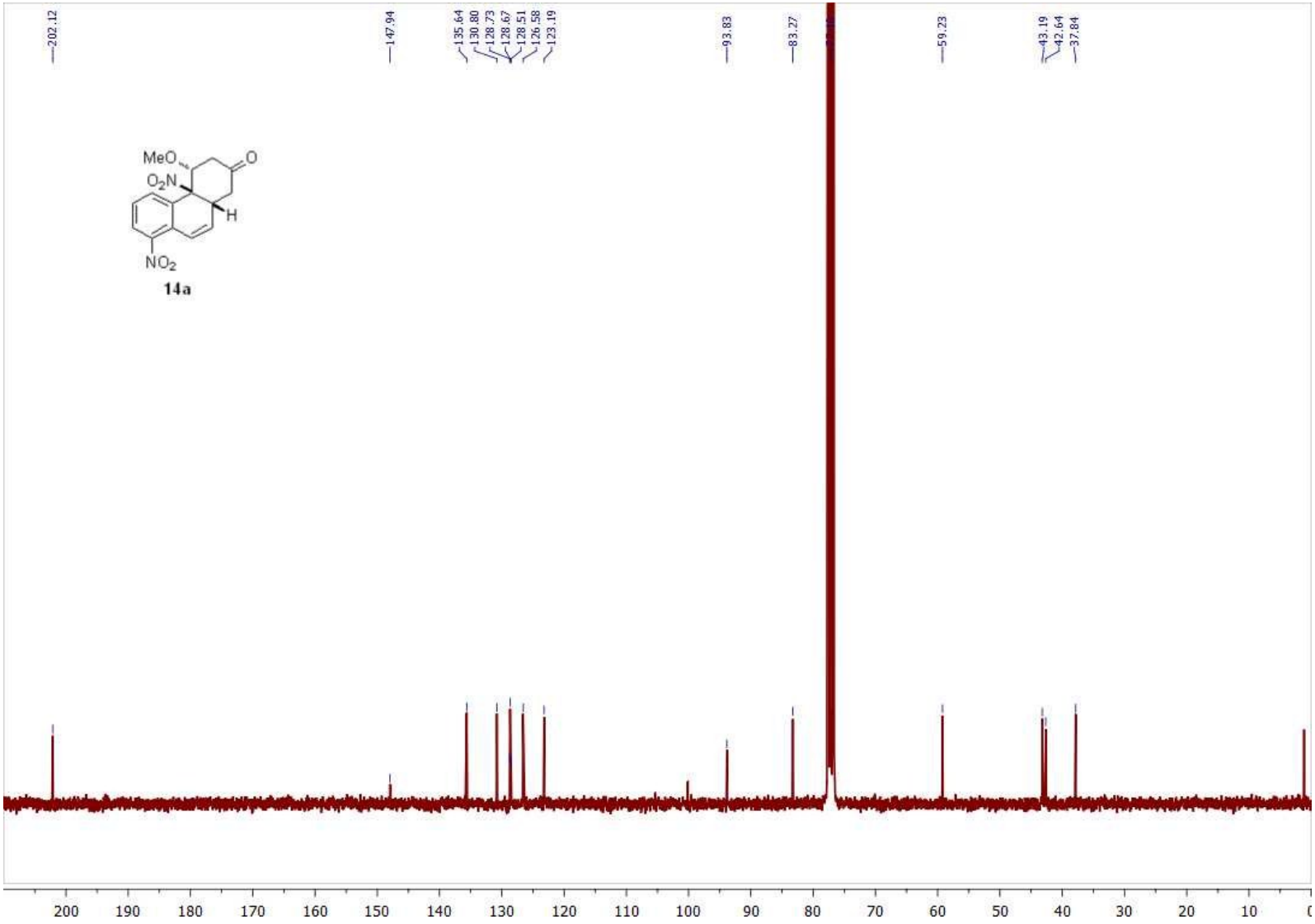
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5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130.80
128.73
128.67
128.51
126.58
123.19
93.83
83.27
59.23
43.19
42.64
37.84
MeO
O
O_2N
H
NO_2
14a
200
190
180
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160
150
140
130
120
110
100
90
80
70
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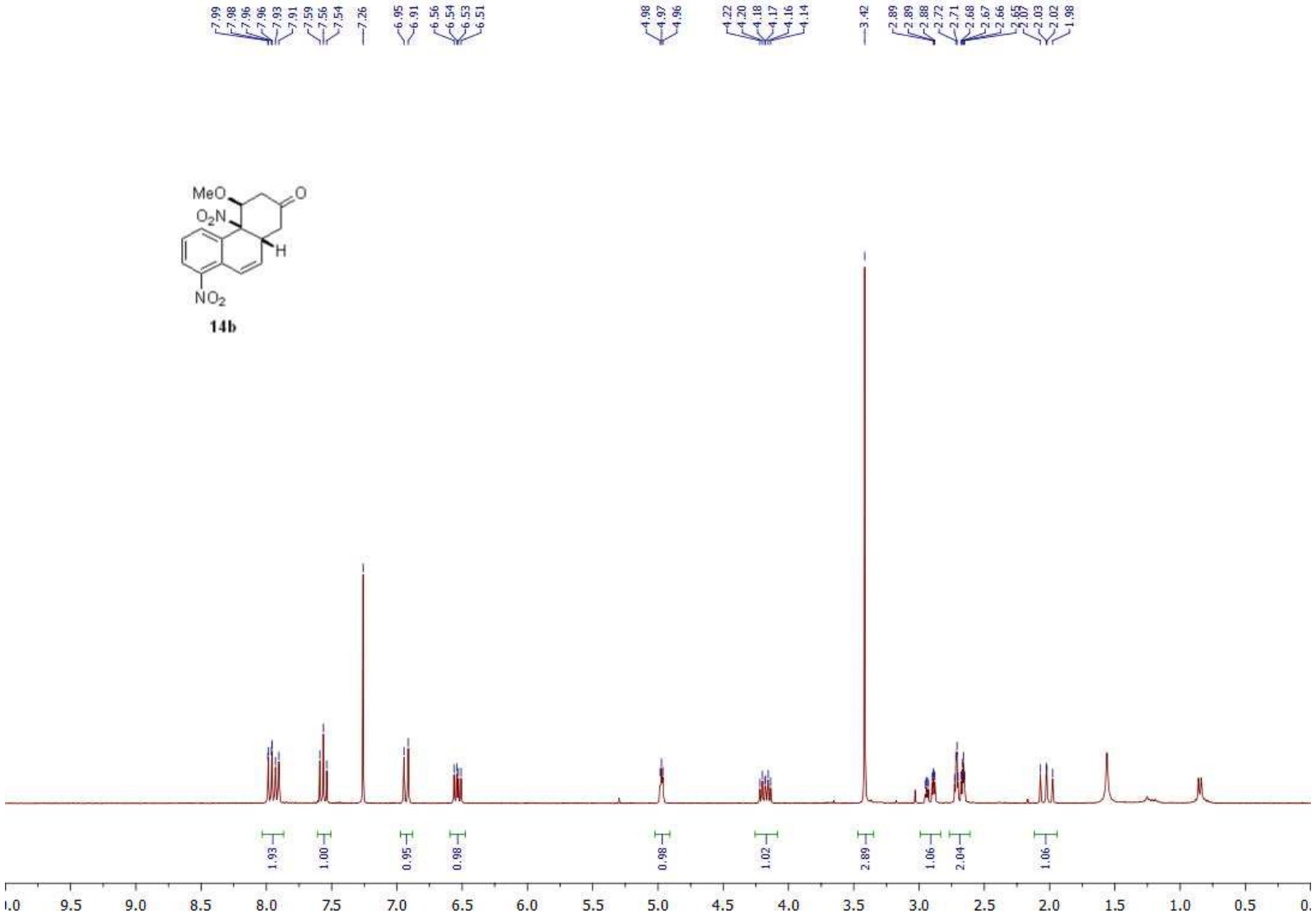
50
40
30
20
10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7.98
7.96
7.96
7.93
7.91
7.59
7.56
7.54
7.26
6.95
6.91
6.56
6.54
6.53
6.51
4.98
4.97
4.96
4.22
4.20
4.18
4.17
4.16
4.14
3.42
2.89
2.89
2.88
2.72
2.71
2.68
2.67
2.66
2.03
2.02
1.98
MeO
O2N
O
H
NO2
14b
1.93
1.00
0.95
0.98
0.98
1.02
2.89
1.06
2.04
1.06
9.5
9.0
8.5
8.0
7.5
7.0
6.5
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3.5
3.0
2.5
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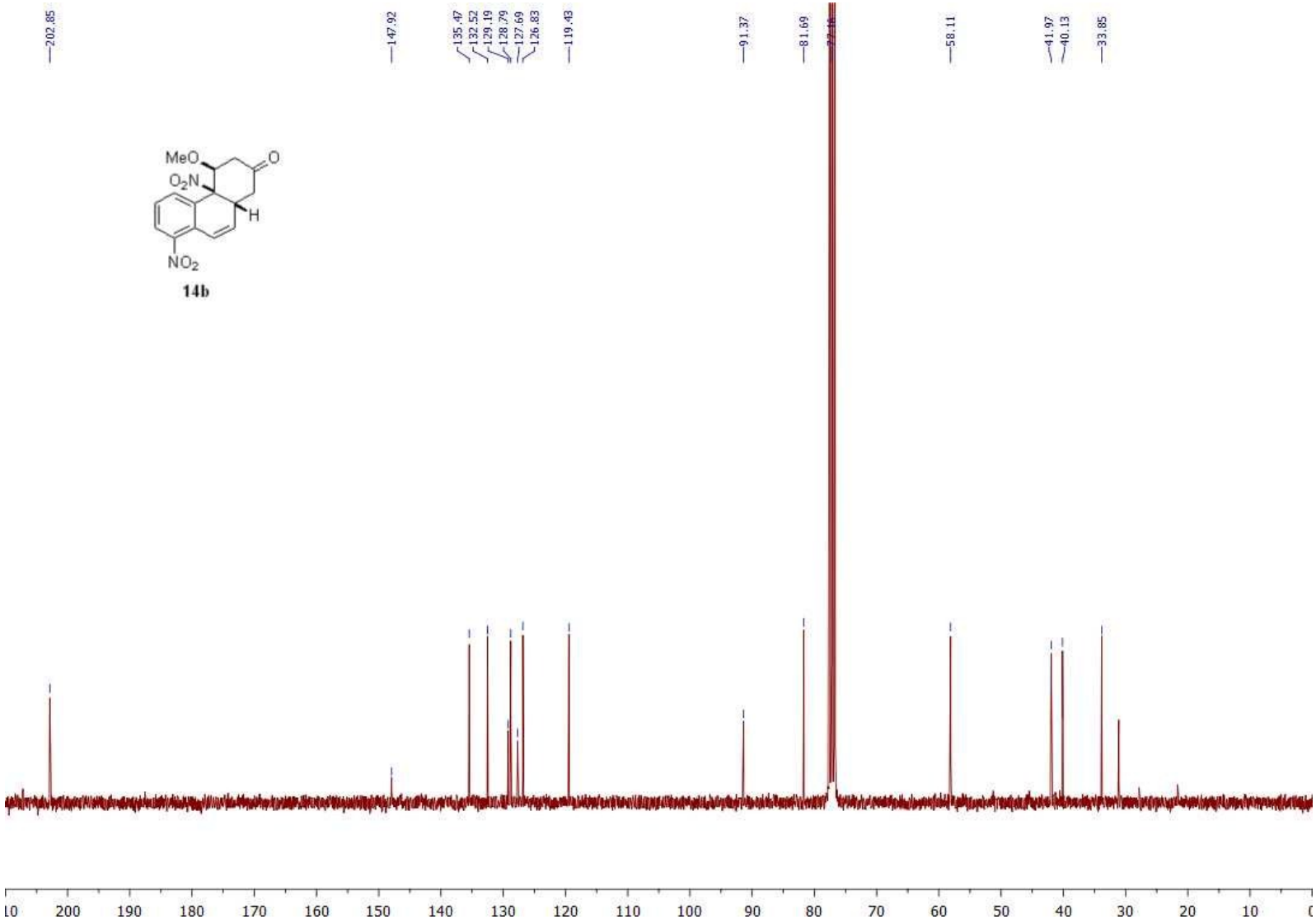
1.0
0.5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128.79
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126.83
119.43
91.37
81.69
77.16
58.11
41.97
40.13
33.85
MeO
O
O2N
H
NO2
14b
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10