Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.
This journal is © the Partner Organisations 2014

Cationic Gold(I)-Catalyzed Enantioselective Hydroalkylation of Unactivated Alkenes: Influence of the Chloride Scavenger on the Stereoselectivity

Weizhen Fang, Marc Presset, Amandine Guérinot, Christophe Bour, Sophie Bezzenine-Lafollée and Vincent Gandon

Supporting Information

Table of Contents

General information

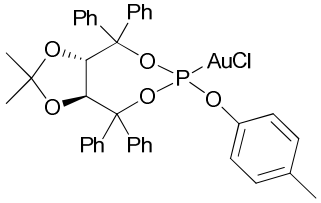
Unless otherwise stated, commercially available reagents were used as received without further purification. (*R*)-DTBM-SEGPHOS was purchased from Aldrich, $Cu(OTf)_2$ was purchased from Alfa Aesar. JohnPhosAuCl was either purchased from Strem Chemicals or prepared from Me_2S•AuCl (Aldrich) and JohnPhos (Aldrich).[1] Compounds **A1**,[2] **A1'**,[2] **A2**,[3] **B1**,[4] **B2**,[5] **C1**,[6] **C2**,[7] **D**,[8] **E**,[2,9] **G**,[10] **H**,[11] **I**,[12] and **K**[13] have been previously described. Complexes **F**[12,14] and **J**[15] are new but structurally close to other previously reported gold catalyst. Bis-oxazoline and Salen copper complexes were either generated in situ from $Cu(OTf)_2$ and **L1-L5**, or isolated prior to use in the catalytic reaction in the case of **L1**$Cu(SbF_6)_2$.[16] Toluene was distilled over calcium hydride. Tetrahydrofuran (THF) was distilled over sodium. Dioxane and $MeNO_2$ were used without purification. Products were purified by flash column chromatography on 40-63 μm silica gel. Analytical thin-layer chromatography (TLC) was performed on TLC silica gel plates (0.25 mm) precoated with a fluorescent indicator. Visualization was made with ultraviolet light and/or *p*-anisaldehyde stain.

NMR spectra were recorded on AM250, AV300, AV360, DRX400 MHz Bruker spectrometers. Chemical shifts are given in ppm. The spectra were calibrated to the residual ^1H and ^{13}C signals of the solvent. Data are represented as follows: chemical shift δ (ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet), coupling constant *J* (Hz) and integration. High-resolution mass spectra were obtained by electrospray ionization on a TOF instrument (MicrOTOFq Bruker spectrometer).

Compounds **1a**, **1b**, **2a**, **2a'**, and **2b** were already described.[17]

Preparation of the gold complex J

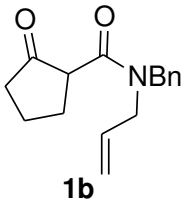
(3aS,8aS)-2,2-Dimethyl-4,4,8,8-tetraphenyl-6-(p-tolyloxy)tetrahydro-[1,3]dioxolo[4,5-e][1,3,2]dioxaphosphepine-(AuCl) (J)[15]



To a solution of Me_2S•AuCl (1 equiv) in CH_2Cl_2 (0.315 M) was added a solution of (–)TAD-P-cresol[18] in CH_2Cl_2 (0.0315 M). The mixture was stirred for 1.5 h at room temperature and then evaporated under reduced pressure to give the gold complex as a white solid, which was used without purification. **^{1}H NMR** (360 MHz / $CDCl_3$): δ 7.60–7.51 (m, 4H), 7.49–7.28 (m, 16H), 7.02 (d, *J*= 8.6 Hz, 2H), 6.65 (d, *J*= 8.6 Hz, 2H), 5.48 (d, *J*= 8.0 Hz, 1H), 5.42 (d, *J*= 8.0 Hz, 1H), 2.29 (s, 3H), 0.68 (s, 3H), 0.63 (s, 3H); **^{31}P NMR** (101 MHz / $CDCl_3$): 105.9; **^{13}C NMR** (90 MHz / $CDCl_3$): 147.4, 143.1, 142.7, 139.22, 139.16, 138.9, 138.8, 135.5, 130.3, 129.1, 128.9, 128.8, 128.6, 128.3, 128.0, 127.6, 127.5, 127.24, 127.20, 120.4, 120.3, 114.8, 92.6, 92.4, 89.3, 89.2, 80.51, 80.45, 79.21, 79.20, 29.7, 26.5, 26.4, 20.7.

Preparation of the substrates

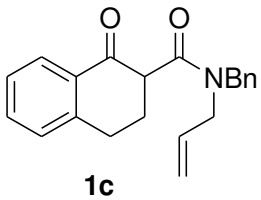
***N*-Benzyl-2-oxo-*N*-(prop-2-en-1-yl)cyclopentane-1-carboxamide (1b)**



1b

According a published procedure,[17] a solution of *N*-benzylprop-2-en-1-amine (2.9 g, 20.00 mmol, 1 equiv), ethyl 2-oxocyclopentane carboxylate (4.5 g, 28.80 mmol, 1.44 equiv) and DMAP (0.3 equiv) in toluene (15 mL) was refluxed for 22 h. The solvent was then removed under reduced pressure and the residue was purified by flash chromatography on silica gel (cyclohexane/EtOAc: 5/1) to give the desired product (3.5 g, 68%) and as mixture of tautomers and rotamers. **^{1}H NMR** (360 MHz / $CDCl_3$): δ 7.34–7.13 (m, 5H), 5.80–5.68 (m, 1H), 5.18–5.09 (m, 2H), 4.96 (t, *J*=20.4 Hz, 1H), 4.44–4.17 (m, 2H), 3.77–3.56 (m, 1H), 3.44–3.36 (m, 1H), 2.56–2.44 (m, 1H), 2.31–2.23 (m, 2H), 2.20–2.04 (m, 2H), 1.86–1.70 (m, 1H); **^{13}C NMR** (90 MHz / $CDCl_3$): 2 rotamers δ 214.6 (2 C), 169.5 (C), 169.3 (C), 137.1 (C), 136.8 (C), 133.0 (CH), 132.4 (CH), 128.9 (CH), 128.6 (2 CH), 127.7 (2 CH), 127.5 (CH), 127.2 (2 CH), 126.2 (2 CH), 117.1 (CH_2), 116.6 (CH_2), 52.1 (CH), 52.0 (CH), 50.2 (CH_2), 49.2 (CH_2), 48.6 (CH_2), 48.3 (CH_2), 38.6 (2 CH_2), 27.6 (CH_2), 27.5 (CH_2), 21.0 (2 CH_2); **HRMS (ESI)**: *m/z* calcd. for $C_{16}H_{19}NO_2Na$ $(M + Na)^+$ 280.1308, found 280.1296.

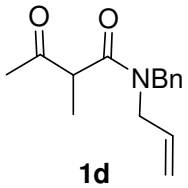
***N*-Allyl-*N*-benzyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxamide (1c)**



1c

According a published procedure,[17] the reaction was performed with methyl 1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (1.57 g, 7.69 mmol) to afford **1c** (1.54 g, 63%) as an orange oil and as mixture of tautomers and rotamers. **^{1}H NMR** (250 MHz / $CDCl_3$): δ 8.06–8.00 (m, 1H), 7.51–7.19 (m, 8H), 5.86–5.75 (m, 1H), 5.40–5.15 (m, 2H), 4.81–4.04 (m, 3H), 3.83–3.72 (m, 2H), 3.09–2.88 (m, 2H), 2.68–2.58 (m, 1H), 2.30–2.18 (m, 1H); **^{13}C NMR** (63 MHz / $CDCl_3$): 2 rotamers δ 194.6 (2 C), 170.7 (C), 170.5 (C), 144.1 (2 C), 137.2 (C), 136.9 (C), 133.8 (2 CH), 133.3 (2 CH), 132.4 (C), 132.0 (C), 128.9 (2 CH), 128.8 (2 CH), 128.6 (2 CH), 127.8 (2 CH), 127.5 (2 CH), 127.2 (2 CH), 126.7 (2 CH), 126.2 (2 CH), 117.2 (CH_2), 116.4 (CH_2), 51.8 (2 CH), 50.3 (CH_2), 49.2 (CH_2), 48.5 (CH_2), 48.2 (CH_2), 28.4 (CH_2), 28.2 (CH_2), 26.7 (CH_2), 26.6 (CH_2); **HRMS (ESI)**: *m/z* calcd. for $C_{21}H_{21}NO_2Na$ $(M + Na)^+$ 342.1465, found 342.1458.

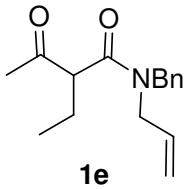
***N*-Allyl-*N*-benzyl-2-methyl-3-oxobutanamide (1d)**



1d

According a published procedure,[17] the reaction was performed with methyl 2-methyl-3-oxobutanoate (1.121 g, 8.62 mmol) to afford **1d** (813 mg, 38%) as a yellow oil and as mixture of tautomers and rotamers. **^{1}H NMR** (360 MHz / $CDCl_3$): 2 rotamers δ 7.37–7.15 (m, 10H), 5.79–5.69 (m, 2H), 5.19–5.14 (m, 4H), 4.76–4.43 (m, 2H), 4.47–4.43 (m, 2H), 4.19–3.57 (m, 6H), 2.16 (s, 3H), 2.12 (s, 3H), 1.38 (d, J = 7 Hz, 3H), 1.34 (d, J = 7 Hz, 3H); **^{13}C NMR** (90 MHz / $CDCl_3$): 2 rotamers δ 204.8 (C), 204.7 (C), 170.9 (C), 170.8 (C), 137.1 (C), 136.4 (C), 132.6 (CH), 132.3 (CH), 128.9 (2 CH), 128.5 (2 CH), 128.0 (2 CH), 127.7 (2 CH), 127.4 (CH), 126.2 (CH), 117.6 (CH_2), 117.0 (CH_2), 51.4 (CH), 51.3 (CH), 50.3 (CH_2), 49.2 (CH_2), 48.4 (CH_2), 48.3 (CH_2), 27.2 (2 CH_3), 13.9 (2 CH_3); **HRMS (ESI)**: *m/z* calcd. for $C_{15}H_{20}NO_2$ $(M + H)^+$ 246.1489, found 246.1492.

***N*-Allyl-*N*-benzyl-2-ethyl-3-oxobutanamide (1e)**

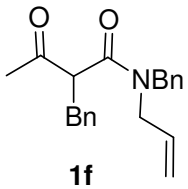


1e

To a solution of *N*-allyl-*N*-benzyl-3-oxobutanamide[17] (500 mg, 2.16 mmol, 1 equiv) in dry DMF (8 mL) at 0 °C was added K_2CO_3 (1.804 g, 13.05 mmol, 6 equiv). The mixture was stirred for 20 min and iodoethane (677 µL, 8.47 mmol, 3.9 equiv) was then added dropwise. The mixture was stirred at room temperature for 16 h. Water was then added at 0 °C and the mixture was extracted with EtOAc. The combined organic phases were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel (cyclohexane/EtOAc: 5/1) to give **1e** in 89% yield (500 mg) as an orange oil and as mixture of tautomers and rotamers. **^{1}H NMR** (360 MHz / $CDCl_3$): 2 rotamers δ 7.35–7.14 (m, 10H), 5.76–5.68 (m, 2H), 5.24–5.06 (m, 4H), 4.85–4.69 (m, 2H), 4.42–4.35 (m, 2H), 4.30–3.96 (m, 2H), 3.78–3.72 (m, 2H), 3.48–3.44 (m, 2H), 2.14 (d, J= 9.6 Hz, 6H), 2.20–1.97 (m, 2H), 1.94–1.86 (m, 2H), 0.90 (dt, J =21.8, 7.3 Hz, 6H); **^{13}C NMR** (90 MHz / $CDCl_3$): 2 rotamers δ 205.3 (2C), 169.6 (C), 169.4 (C), 137.4 (C), 136.6

(C), 132.7 (CH), 132.6 (CH), 129.0 (CH), 128.7 (2 CH), 128.2 (2 CH), 127.8 (CH), 127.6 (2 CH), 126.5 (2 CH), 117.8 (CH_2), 117.2 (CH_2), 60.1 (CH), 60.0 (CH), 50.2 (CH_2), 49.2 (CH_2), 48.8 (CH_2), 48.6 (CH_2), 27.0 (2 CH_3), 23.0 (2 CH_3), 12.3 (2 CH_3); **HRMS (ESI)**: *m*/*z* calcd. for $C_{16}H_{21}NO_2Na$ $(M + Na)^+$ 282.1465, found 282.1465

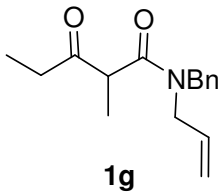
***N*-Allyl-*N*,2-dibenzyl-3-oxobutanamide (1f)**



1f

This compound was prepared according to the procedure described for **1e** with *N*-allyl-*N*-benzyl-3-oxobutanamide[17] (0.5 g, 2.16 mmol, 1 equiv) and benzylbromide (1.0 mL, 8.64 mmol, 4 equiv). The crude product was purified by flash chromatography on silica gel (cyclohexane/EtOAc: 5/1) to afford **1f** in 86% yield (600 mg) as a colorless oil and as mixture of tautomers and rotamers. **^{1}H NMR** (360 MHz / $CDCl_3$): 2 rotamers δ 7.36–6.83 (m, 20H), 5.75–5.42 (m, 2H), 5.15–4.87 (m, 4H), 4.69–4.06 (m, 5H), 3.89–3.69 (m, 4H), 3.53 (dd, *J*= 17.7, 4.9 Hz, 1H), 3.36–3.27 (m, 2H), 3.21–3.09 (m, 2H), 2.18 (d, *J*=20.7 Hz, 6H); **^{13}C NMR** (90 MHz / $CDCl_3$): 2 rotamers δ 204.0 (2C), 169.3 (C), 169.0 (C), 138.6 (C), 138.5 (C), 137.1 (C), 136.4 (C),132.4 (2 CH), 129.2 (4 CH), 129.0 (2 CH), 128.7 (6 CH), 128.3 (2 CH), 127.7 (CH), 127.6 (CH), 126.8 (2 CH), 126.5 (2 CH),118.0 (CH_2), 117.3 (CH_2), 60.0 (CH), 59.7 (CH), 50.2 (CH_2), 49.3 (CH_2), 48.9 (CH_2), 48.9 (CH_2), 35.6 (2 CH_2), 27.7 (CH_3), 27.6 (CH_3); **MS (CI)**: *m*/*z* calcd. for $C_{21}H_{24}NO_2$ $(M + H)^+$ 322.18, found 322.2.

***N*-Allyl-*N*-benzyl-2-methyl-3-oxopentanamide (1g)**



1g

This compound was prepared according to the procedure described for **1e** with *N*-allyl-*N*-benzyl-3-oxopentanamide (1.0 g, 4.08 mmol, 1 equiv) and iodomethane (1.0 mL, 16.31 mmol, 4 equiv). The crude product was purified by flash chromatography on silica gel (cyclohexane/EtOAc: 5/1) to afford **1g** in 94% yield (1.0 g) as a yellow oil and as mixture of tautomers and rotamers. **^{1}H NMR** (250 MHz / $CDCl_3$): δ 7.39–7.23 (m, 5H), 5.82–5.67 (m, 1H), 5.26–5.08 (m, 2H), 4.79–4.40 (m, 2H), 4.21–3.73 (m, 2H), 3.69–3.59 (m, 1H), 2.63–2.39 (m, 2H), 1.38 (dd, *J*=9.8, 6.9 Hz, 3H), 1.02 (dd, *J*=14.2, 7.3 Hz, 3H); **^{13}C NMR** (90 MHz / $CDCl_3$): 2 rotamers δ 207.6 (2C), 171.2 (C), 171.1 (C), 137.3 (C), 136.6 (C), 132.8 (CH), 132.6 (CH), 129.1 (CH), 128.7 (2 CH), 128.2 (2 CH), 127.9 (CH), 127.6 (2 CH), 126.4 (2 CH), 117.8 (CH_2), 117.2 (CH_2), 51.0 (CH_2), 50.9 (CH_2), 50.5 (CH), 49.4 (CH), 48.7 (CH_2), 48.5 (CH_2), 33.0 (2 CH_2), 14.1 (2 CH_3), 7.8 (2 CH_3); **HRMS (ESI)**: *m*/*z* calcd. for $C_{16}H_{21}NO_2Na$ $(M + Na)^+$ 282.1465, found 282.1463.

Procedures for enantioselective hydroalkylation of ene-β-ketoamides

*Enantioselective hydroalkylation of ene-β-ketoamide **1a** using an achiral gold complex and a chiral copper complex (Table S1)*

In air, a 10 mL oven-dried tube equipped with a Teflon-coated magnetic stir bar was charged with copper (II) triflate (3.6 mg, 0.010 mmol, 0.1 equiv), ligand **L1-L5** (0.010 mmol, 0.1 equiv) and toluene (0.5 mL) and the mixture was stirred at room temperature for 5 min. (JohnPhos)AuCl (10 mol% of gold) and substrate **1a** (27.3 mg, 0.10 mmol, 1 equiv) in toluene (0.5 mL) were added and the tube was sealed with a plastic stopper. The reaction tube was immersed and stirred in a preheated oil bath at 110 °C (external temperature) for 24 h. Then the reaction mixture was filtered through a pad of silica gel, rinsed with diethyl ether and evaporated to afford the crude product. Conversion and diasteroselectivity were determined by ^{1}H NMR analysis and enantioselectivity was analyzed by SFC.

*Solvent and gold catalyst screening in the enantioselective hydroalkylation of ene-β-ketoamide **1a** (Table 2).* A 10 mL oven-dried tube equipped with a Teflon-coated magnetic stir bar was charged with gold complex (10 mol% of gold), silver (I) triflate (2.6 mg, 0.010 mmol, 0.1 equiv) and solvent (0.5 mL) and the mixture was stirred at room temperature for 1 min. Substrate **1a** (27.3 mg, 0.10 mmol, 1 equiv) in solvent (0.5 mL) was added and the tube was sealed with a plastic stopper. The reaction tube was covered by aluminum foil, immersed and stirred in a preheated oil bath at indicated temperature for 24 h. Then, the reaction mixture was filtered through a short pad of silica gel, rinsed with diethyl ether, and evaporated to afford the crude product, which was analyzed by SFC.

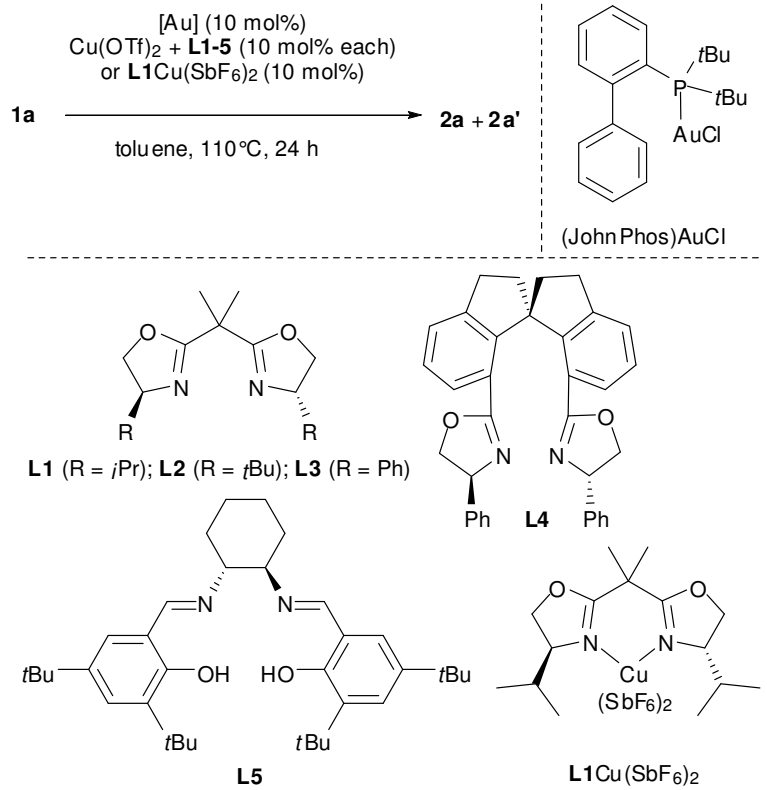
*Screening of activators in the enantioselective hydroalkylation of ene-β-ketoamide **1a** (Table 1, Table 2 entry 9, and Table 3).* A 10 mL oven-dried tube equipped with a Teflon-coated magnetic stir bar was charged with **C1** (8.2 mg, 0.0050 mmol, 0.05 equiv), Lewis acid (x mol%) and toluene (0.5 mL) and the mixture was stirred at room temperature for 1 min. Substrate **1a** (27.3 mg, 0.10 mmol, 1 equiv) in toluene (0.5 mL) was added and the tube was sealed with a plastic stopper. The reaction tube covered by aluminum foil, immersed and stirred in a preheated oil bath at indicated temperature. Then, the reaction mixture was filtered through a short pad of silica gel, rinsed with diethyl ether and evaporated to afford the crude product, which was analyzed by SFC.

Procedure for Table 4. The above procedure was used with AgOTf (2.6 mg, 0.010 mmol) and substrate **1b-g** (0.1 mmol).

Additional experiments not described in the manuscript

The unexpected activity of copper in the reaction of **1a** encouraged us to briefly examine the case of chiral ligands located at copper instead of gold (Table S1). With the inactive achiral monogold precatalyst (JohnPhos)AuCl, a preliminary control experiment showed that addition of $Cu(OTf)_2$ eventually provided the desired product in a 75/25 ratio (entry 1). Addition of bis-oxazoline or Salen ligands **L1-5** resulted in low enantioinductions (entries 2–6). Interestingly, the teamwork between gold and copper in this transformation was revealed when using Cu/**L2** without gold (entry 7), leading to **2a'** as major product instead of **2a** with Au/Cu/**L2** (entry 3). Besides, the enantioselectivity was greatly lowered in the absence of gold. Finally, in contrast with **L1**/$Cu(OTf)_2$, the use of **L1**$Cu(SbF_6)_2$ in the Au/Cu-catalyzed reaction led to a racemic mixture (entry 8), emphasizing a strong counterion effect in this chemistry.

Table S1 Enantioselective hydroalkylation of ene-β-ketoamide **1a** using an achiral gold complex and a chiral copper complex

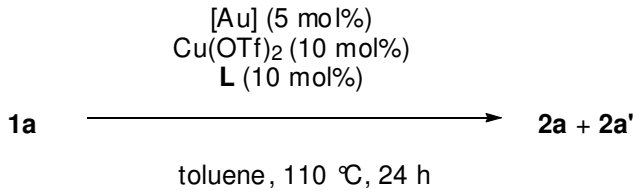


Entry	[Au]	L	Conv (%)[a]	*dr*[a]	*ee* (%)[a,b]
1	(JohnPhos)AuCl	none	100	75/25	-
2	(JohnPhos)AuCl	**L1**	100	68/32	15/3
3	(JohnPhos)AuCl	**L2**	100	66/34	38/5
4	(JohnPhos)AuCl	**L3**	89	67/33	24/2
5	(JohnPhos)AuCl	**L4**	100	41/59	5/7
6	(JohnPhos)AuCl	**L5**	100	50/50	0/8
7	none	**L2**	100	36/64	3/0
8	(JohnPhos)AuCl	**L1**$Cu(SbF_6)$	94	n.d.	0/0

[a] Estimated by chiral SFC; diastereomeric ratios shown are **2a/2a'**. [b] Corresponding to **2a/2a'**.

Having shown the existence of a partnership between gold and copper, we next checked whether a matched pair of chiral complexes could be formed (Table S2). This was not the case with **A** and **L1** (entries 1 and 2). On the other hand, **A1'** and **L1** formed a mismatched pair (entries 3 and 4).

Table S2 Enantioselective hydroalkylation of ene-β-ketoamide **1a** using a chiral gold and chiral copper complexes

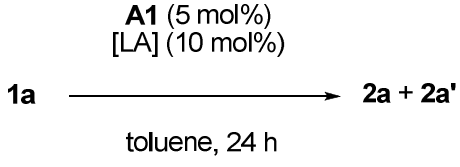


Entry	[Au]	L	Conv (%)[a]	*dr*[a]	*ee* (%)[a,b]
1	**A1**	none	100	68/32	59/35
2	**A1**	**L1**	100	60/40	59/44
3	**A1'**	none	100	65/35	–57/–39
4	**A1'**	**L1**	100	38/62	–22/–27

[a] Estimated by chiral SFC; diastereomeric ratios shown are **2a/2a'**. [b] Corresponding to **2a/2a'**.

The use of complex **A1** with various activators in summarized in Table S3 below. Again, the conversion reached with these activators in the absence of gold remained insignificant, except with $Zn(OTf_2)$ (entry 1) and $Ga(OTf)_3$ (entry 4). Looking at the diastereoselectivity, it is noteworthy that the nature of the major product varies as a function of the Lewis acid. Focusing on triflates, which allowed to reach high conversions, while In, Si, and Bi gave rise to **2a** as major diastereomer (entries 6, 10, and 12 respectively), Zn and Ga favored the formation of **2a'** (entries 2 and 4). 19 Although reasonable enantioselectivities were obtained with $In(OTf)_3$, $In(NTf_2)_3$, and $Bi(OTf)_3$ (entries 6–8, 11, and 12), the results were less satisfying than with AgOTf or $AgNTf_2$. Nevertheless, this study clearly shows that Lewis acids of different element series should be systematically tested during the optimization process of a stereoselective gold-catalyzed reaction.

Table S3 Screening of other activators in the enantioselective hydroalkylation of ene-β-ketoamide **1a**



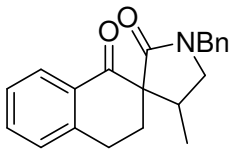
Entry	[LA]	T (°C)	Conv (%)[a,b]	*dr*[a]	*ee* (%)[a,c]
1[d]	$Yb(OTf)_3$	110	8	n.d.	n.d.
2[d]	$Zn(OTf)_2$	110	100 (27)	36/64	8/11
3[d]	$Al(OTf)_3$	110	30 (6)	40/60	50/39
4[d]	$Ga(OTf)_3$	110	100 (19)	36/64	65/21
5[d]	$GaCl_3$	110	trace	n.d.	n.d.

6	$In(OTf)_3$	50	100 (0)	61/39	63/29
7	$In(NTf_2)_3$	50	100 (0)	60/40	63/24
8	$In(OTf)_3$	110	100 (8)	57/43	65/30
9	$InCl_3$	110	trace	n.d.	n.d.
10[d]	Me_3SiOTf	110	100 (5)	71/29	58/51
11	$Bi(OTf)_3$	50	97 (0)	71/29	64/38
12	$Bi(OTf)_3$	110	100 (10)	53/47	63/45
13[d]	HOTf	110	10	n.d.	n.d.

[a] Estimated by chiral SFC; diastereomeric ratios shown are **2a/2a'**. [b] Conversion without gold is indicated in parentheses. [c] Corresponding to **2a/2a'**. [d] No conversion at 50 °C.

Characterization of the products

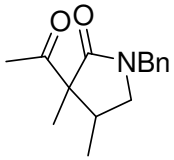
1'-Benzyl-4'-methyl-3,4-dihydro-1*H*-spiro[naphthalene-2,3'-pyrrolidine]-1,2'-dione (2c)



2c

The general procedure was followed using *N*-allyl-*N*-benzyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxamide (**1c**). The crude product was purified flash chromatography on silica gel (cyclohexane/EtOAc: 9/1) to afford **2c** (27 mg, 85%) as a yellow oil. The two diastereoisomers were separated by flash chromatography. **^{1}H NMR** (300 MHz / $CDCl_3$): Minor diastereoisomer δ 8.03 (d, *J* = 7.8 Hz, 1H), 7.51–7.46 (m, 1H), 7.39–7.24 (m, 7H), 4.63 (d, *J* = 14.9 Hz, 1H), 4.51 (d, *J* = 14.9 Hz, 1H), 3.31–3.22 (m, 2H), 3.16–3.07 (m, 2H), 2.89–2.79 (m, 1H), 2.58–2.45 (m, 1H), 2.10 (dt, *J* = 13.6, 4.9 Hz, 1H), 0.94 (d, *J* = 7.1 Hz, 3H); **^{13}C NMR** (63 MHz / $CDCl_3$): Minor diastereoisomer δ 196.1 (C), 173.1 (C), 144.4 (C), 136.6 (C), 133.8 (CH), 131.9 (C), 128.9 (3 CH), 128.4 (2 CH), 127.7 (2 CH), 126.8 (CH), 58.7 (C), 51.2 (CH_2), 47.0 (CH_2), 33.1 (CH), 25.7 (CH_2), 25.5 (CH_2), 14.7 (CH_3). **^{1}H NMR** (300 MHz / $CDCl_3$): Major diastereoisomer δ 8.04 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.46 (td, *J* = 7.7, 1.3 Hz, 1H), 7.39–7.24 (m, 7H), 4.55 (d, *J* = 14.9 Hz, 1H), 4.45 (d, *J* =14.9 Hz), 1H), 3.52–3.42 (m, 2H), 3.07 (dd, *J* = 13.6, 6.9 Hz, 1H); 2.97 (ddd, *J* = 16.9, 7.0, 5.1 Hz, 1H), 2.81 (dd, *J* = 9.5, 6.1 Hz, 1H), 2.40–2.33 (m, 1H), 2.23–2.14 (m, 1H), 1.03 (d, *J* = 7.0 Hz, 3H); **^{13}C NMR** (63 MHz / $CDCl_3$): Major diastereoisomer δ 196.5 (C), 174.6 (C), 143.8 (C), 136.5 (C), 133.9 (CH), 132.7 (C), 128.8 (3 CH), 128.2 (2 CH), 127.6 (2 CH), 127.0 (CH), 58.9 (C), 51.7 (CH_2), 47.0 (CH_2), 39.1 (CH), 32.0 (CH_2), 25.5 (CH_2), 14.7 (CH_3); **HRMS (ESI)**: *m/z* calcd. for $C_{21}H_{21}NO_2Na$ $(M + Na)^+$ 342.1465, found 342.1462.

3-Acetyl-1-benzyl-3,4-dimethylpyrrolidin-2-one (2d)

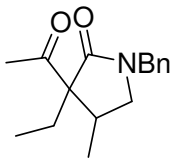


2d

The general procedure was followed with *N*-allyl-*N*-benzyl-2-methyl-3-oxobutanamide (**1d**). The crude product was purified flash chromatography on silica gel (cyclohexane/EtOAc: 9/1) to afford **2d** (15 mg, 60%) as a colorless oil. The two diastereoisomers were separated by flash chromatography. **^{1}H NMR** (360 MHz / $CDCl_3$): Minor diastereoisomer δ 7.33–7.26 (m, 3H), 7.21–7.18 (m, 2H), 4.43 (dd, *J* = 14.5, 6.4 Hz, 2H), 3.30 (dd, *J* = 6.8, 1.8 Hz, 1H), 2.83-2.71 (m, 2H), 2.31 (s, 3H), 1.24 (s, 3H), 0.91 (d, *J* = 7 Hz, 3H);

^{13}C NMR (90 MHz / $CDCl_3$): Minor diastereoismer δ 206.7 (C), 174.4 (C), 136.3 (C), 128.8 (2 CH), 128.1 (2 CH), 127.8 (CH), 60.7 (C), 50.9 (CH_2), 46.9 (CH_2), 32.8 (CH_3), 26.5 (CH), 14.0 (CH_3), 13.2 (CH_3); **^{1}H NMR** (360 MHz / $CDCl_3$): Major diastereoisomer δ 7.31–7.25 (m, 5H), 4.56 (d, *J* = 14.5 Hz, 1H), 4.42 (d, *J* = 14.5 Hz, 1H), 3.24 (t, *J* = 9.6 Hz, 1H), 2.98 (t, *J* = 9.6 Hz, 1H), 2.21−2.15 (m, 1H), 2.08 (s, 3H), 1.41 (s, 3H), 0.96 (d, *J* = 7 Hz, 3H); **^{13}C NMR** (90 MHz / $CDCl_3$): Major diastereoisomer δ 207.1 (C), 174.7 (C), 136.0 (C), 128.7 (2 CH), 128.3 (2 CH), 127.7 (CH), 60.9 (C), 51.4 (CH_2), 47.0 (CH_2), 39.5 (CH_3), 29.3 (CH), 19.7 (CH_3), 13.1 (CH_3); **HRMS (ESI)**: *m*/*z* calcd. for $C_{15}H_{19}NO_2Na$ $(M + Na)^+$ 268.1308, found 268.1311. The relative configuration of each diastereoisomer was determined by 1D selective NOE experiment (see pages S51 and S54).

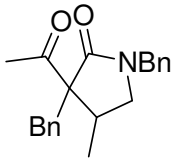
3-Acetyl-1-benzyl-3-ethyl-4-methylpyrrolidin-2-one (2e)



2e

The general procedure was followed with *N*-allyl-*N*-benzyl-2-ethyl-3-oxobutanamide **(1e)**. The crude product was purified flash chromatography on silica gel (cyclohexane/EtOAc: 9/1) to afford **2e** (16 mg, 60%) as a colorless oil and as a 78/22 mixture of diastereoisomers. **^{1}H NMR** (250 MHz / $CDCl_3$): Major diastereoisomer δ 7.35–7.24 (m, 5H), 4.52 (d, *J* = 4.7 Hz, 2H), 3.29 (dd, *J* = 9.5, 8.2 Hz, 1H), 2.94 (t, *J* = 9.1 Hz, 1H), 2.44–2.35 (m, 1H), 2.11 (s, 3H), 2.08−1.97 (m, 1H), 1.86−1.78 (m, 1H), 0.97−0.91 (m, 6H); **^{13}C NMR** (63 MHz / $CDCl_3$): Major diastereoisomer δ 207.6 (C), 173.9 (C), 136.3 (C), 128.9 (2 CH), 128.5 (2 CH), 127.9 (CH), 65.4 (C), 51.6 (CH_2), 47.1 (CH_2), 34.0 (CH_3), 30.0 (CH), 25.2 (CH_2), 14.0 (CH_3), 9.0 (CH_3); **HRMS (ESI)**: *m*/*z* calcd. for $C_{16}H_{21}NO_2Na$ $(M + Na)^+$ 282.1465, found 282.1459.

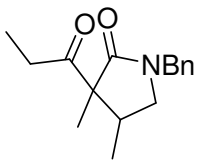
3-Acetyl-1,3-dibenzyl-4-methylpyrrolidin-2-one (2f)



2f

The general procedure was followed with *N*-allyl-*N*,2-dibenzyl-3-oxobutanamide (**1f**). The crude product was purified flash chromatography on silica gel (cyclohexane/EtOAc: 9/1) to afford **2f** (21 mg, 66%) as a colorless oil and as a 86/14 mixture of diastereoisomers. **^{1}H NMR** (250 MHz / $CDCl_3$): Mixture of two diastereoisomers δ 7.32–7.00 (m, 20H), 4.60−4.21 (m, 4H), 3.48−2.82 (m, 8H), 2.50−2.30 (m, 2H), 2.25 (s, 2H), 2.17 (s, 4H), 1.04 (d, *J*=7 Hz, 2H), 0.94 (d, *J*=7 Hz, 4H); **^{13}C NMR** (63 MHz / $CDCl_3$): Mixture of two diastereoisomers δ 206.4 (C), 205.8 (C), 173.4 (C), 172.2 (C), 136.9 (2 C), 136.1 (C), 135.8 (C), 130.9 (3 CH), 129.4 (CH), 128.8 (CH), 128.7 (3 CH), 128.4 (4 CH), 128.2 (CH), 128.1 (3 CH), 127.8 (CH), 127.7 (CH), 126.9 (CH), 126.7 (CH), 66.6 (C), 66.3 (C), 51.6 (CH_2), 51.4 (CH_2), 47.1 (CH_2), 46.8 (CH_2), 36.5 (CH_2), 34.7 (CH_2), 33.2 (CH_3), 32.2 (CH_3), 29.8 (CH), 27.0 (CH), 14.2 (CH_3), 13.3 (CH_3); **HRMS (ESI)**: *m*/*z* calcd. for $C_{21}H_{23}NO_2Na$ $(M + Na)^+$ 344.1621, found 344.1625.

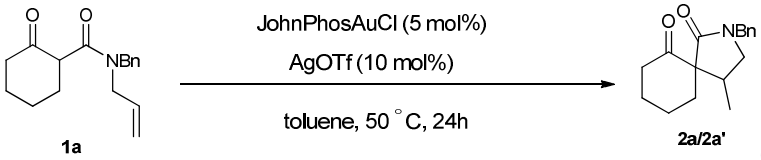
1-Benzyl-3,4-dimethyl-3-propionylpyrrolidin-2-one (2g)



2g

The general procedure was followed with *N*-allyl-*N*-benzyl-2-methyl-3-oxopentanamide (**1f**). The crude product was purified flash chromatography on silica gel eluting with cyclohexane/EtOAC (100/0 to 90/10) to afford **2g** (19 mg, 74%) as a colorless oil and as a 68/32 mixture of diastereoisomers. **^{1}H NMR** (250 MHz / $CDCl_3$): Mixture of two diastereoisomers δ 7.37–7.18 (m, 10H), 4.60−4.43 (m, 4H), 3.31−3.21 (m, 2H), 2.99 (t, *J*=9.5 Hz, 1H), 2.80−2.52 (m, 4H), 2.47−2.17 (m, 3H), 1.44 (s, 3H), 1.26 (s, 3H), 1.00 (dt, *J*=18.3, 7 Hz, 6H), 0.94−0.89 (m, 6H); **^{13}C NMR** (63 MHz / $CDCl_3$): Mixture of two diastereoisomers δ 209.6 (C), 209.4 (C), 175.1 (C), 174.6 (C), 136.3 (C), 136.2 (C), 128.9 (2 CH), 128.8 (2 CH), 128.4 (2 CH), 128.1 (2 CH), 127.8 (2 CH), 60.7 (C), 60.4 (C), 51.5 (CH_2), 51.0 (CH_2), 47.1 (CH_2), 46.9 (CH_2), 39.8 (CH), 34.7 (CH_2), 33.1 (CH), 31.7 (CH_2), 19.6 (CH_3), 14.0 (CH_3), 13.3 (CH_3), 13.2 (CH_3), 7.9 (CH_3), 7.1 (CH_3); **HRMS (ESI)**: *m*/*z* calcd. for $C_{16}H_{21}NO_2Na$ $(M + Na)^+$ 282.1465, found 282.1464.

Chiral SFC and HPLC Traces:



(Racemic reaction)

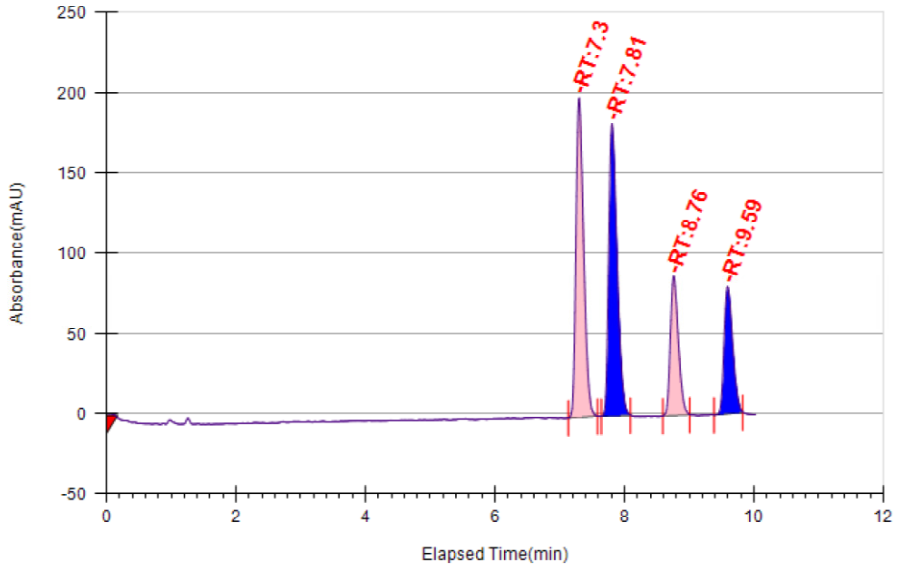
Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

Thar Investigator SFC Results

Sample	Column	Co-Solvent	Back Pressure	Col. Temp.
Fwz-456	IA 250*4.6	Methanol		35.1

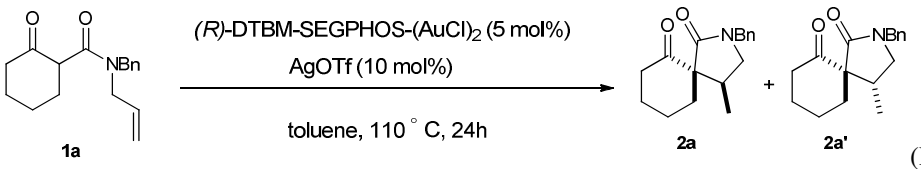
Instrument Method	Inj. Vol.	Total Flow	Pressure Drop
FWZ gradient method-35C	5	4	28

Single Absorbance (215nm) Plot



Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	34.47	1609.149	7.3 min	198.7184
2	Peak2	34.4167	1606.6623	7.81 min	181.8942
3	Peak3	15.6691	731.4723	8.76 min	86.5274
4	Peak4	15.4442	720.976	9.59 min	79.1261

FWZ gradient method-35C : Co-solvent from 3% to 10% during the first 10 min, then keep 10%



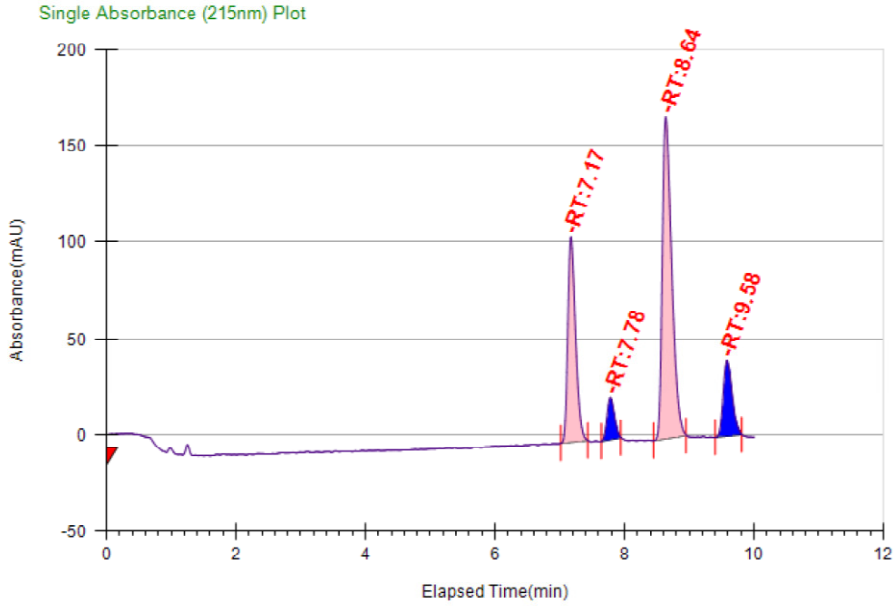
(Ref: Table 2, entry 1)

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

Thar Investigator SFC Results

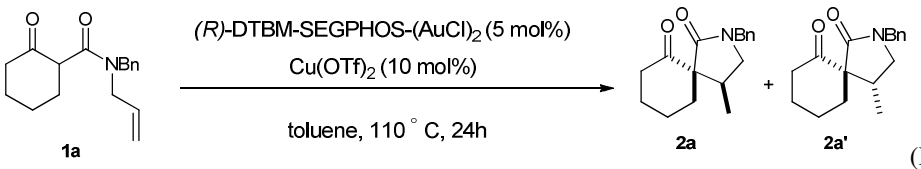
Sample	Column	Co-Solvent	Back Pressure	Col. Temp.
Fwz-461 D	IA 250*4.6	Methanol		30

Instrument Method	Inj. Vol.	Total Flow	Pressure Drop
FWZ gradient method	5	4	32



Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	28.1964	867.2895	7.17 min	106.5165
2	Peak2	5.5483	170.6587	7.78 min	21.7036
3	Peak3	54.1143	1664.4988	8.64 min	167.2622
4	Peak4	12.141	373.4451	9.58 min	39.8525

FWZ gradient method: Co-solvent from 3% to 10% during the first 10 min, then keep 10%



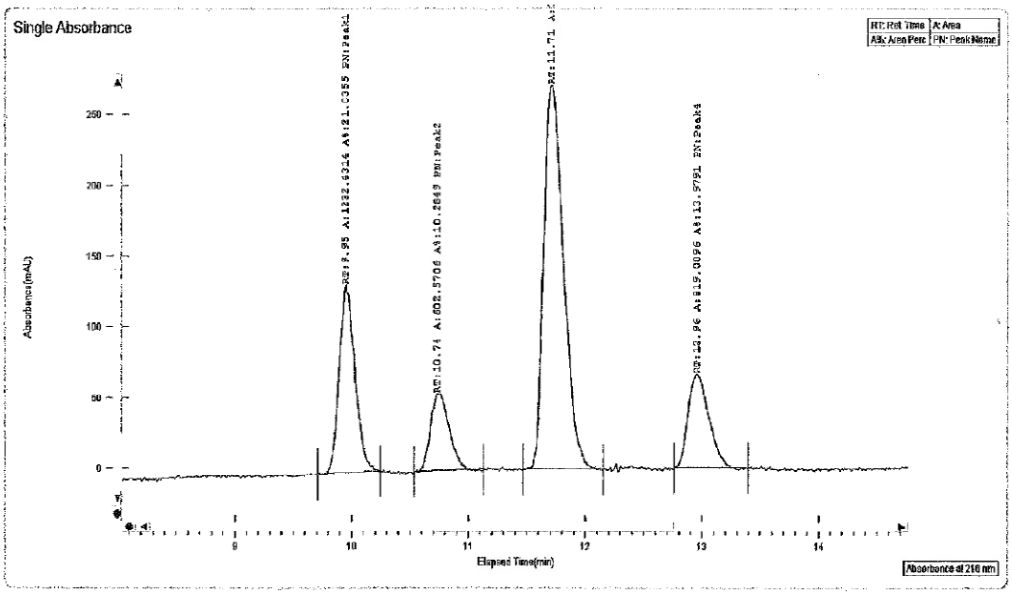
(Ref: Table 1, entry 1)

General Info		Notes
Log Author		
Log Date	12/17/2012 11:01:33 AM	
Report By	current_User	
Report Date	12/17/2012	
File Name	Fwz-269_12-17-2012_1.tta	
Method Name	FWZ gradient method.met	

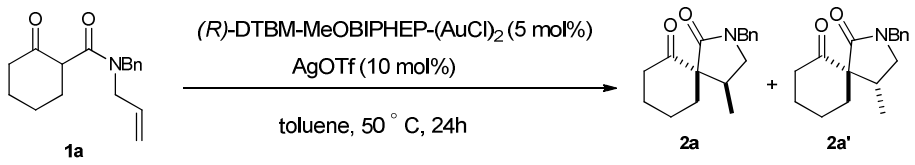
Injection Info	
Injection Date Time Stamp	12/17/2012 11:01:33 AM
Injection Volume	50
Co-Solvent	MeOH
Column	IA
Sample	Fwz-269
Column Temperature	30.2
Co-Solvent %	3
Total Flow	4
Pressure Drop	22
Back Pressure	147
Wavelength	0

Peak Info

Peak Name	Area %	Area	RT (min)
Peak1	21.0355	1232.4314	9.95
Peak2	10.2849	602.5706	10.74
Peak3	54.7005	3204.8032	11.71
Peak4	13.9791	819.0096	12.96



FWZ gradient method: Co-solvent from 3% to 10% during the first 10 min, then keep 10%



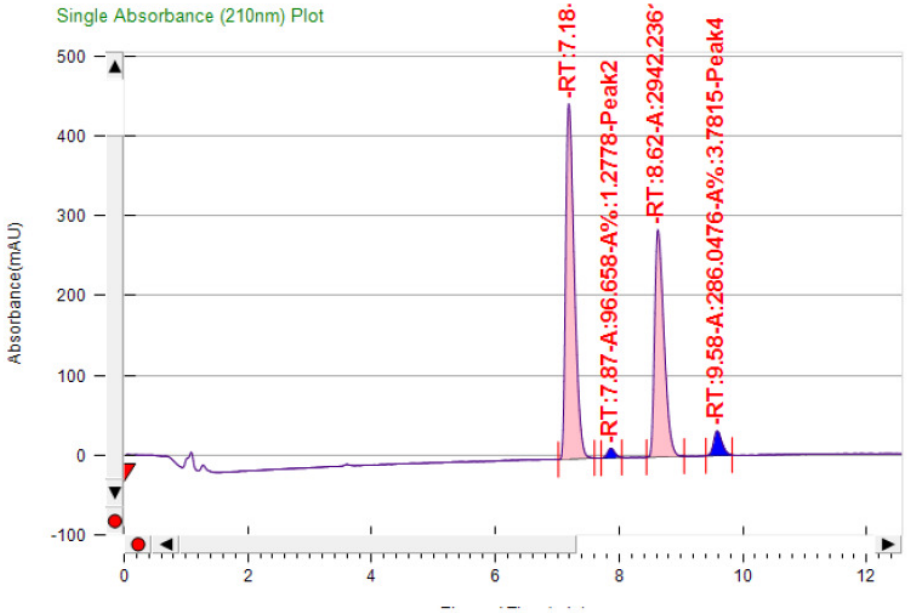
(Ref: Table 2, entry 9)

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

Thar Investigator SFC Results

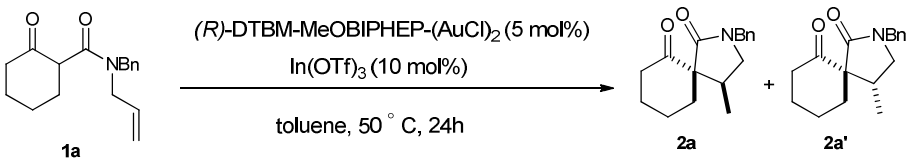
Sample	Column	Co-Solvent	Back Pressure	Col. Temp.
Fwz-661 B	IA 250*4.6	Methanol		31

Instrument Method	Inj. Vol.	Total Flow	Pressure Drop
FWZ gradient method	10	4	32



Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	56.0445	4239.3975	7.18 min	444.4769
2	Peak2	1.2778	96.658	7.87 min	11.987
3	Peak3	38.8961	2942.2361	8.62 min	284.2315
4	Peak4	3.7815	286.0476	9.58 min	30.6742

FWZ gradient method: Co-solvent from 3% to 10% during the first 10 min, then keep 10%



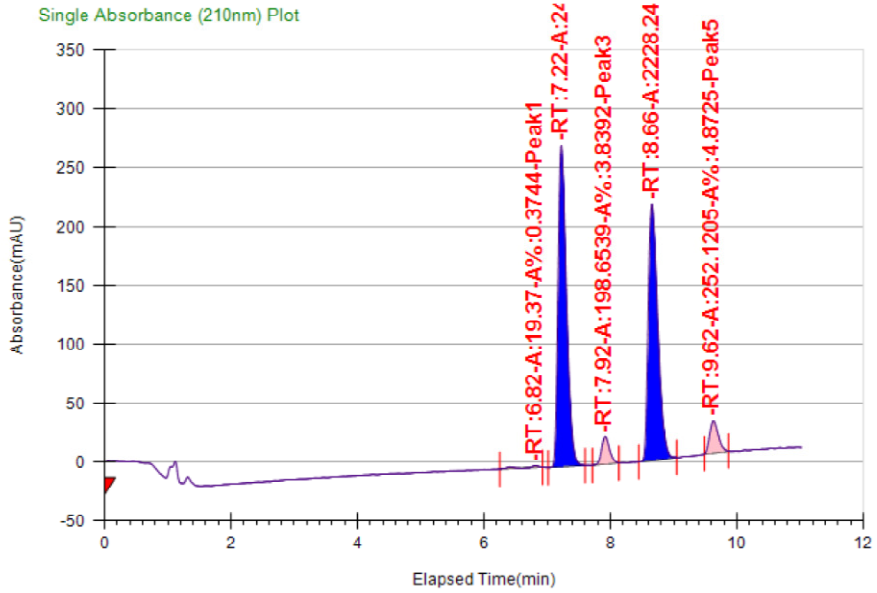
(Ref: Table 3, entry 7)

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

Thar Investigator SFC Results

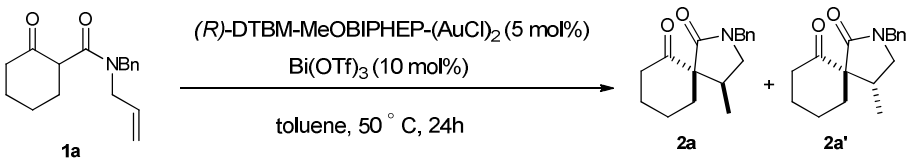
Sample	Column	Co-Solvent	Back Pressure	Col. Temp.
Fwz-671 B	IA 250*4.6	Methanol		30.4

Instrument Method	Inj. Vol.	Total Flow	Pressure Drop
FWZ gradient method	10	4	30



Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	0.3744	19.37	6.82 min	1.3446
2	Peak2	47.8503	2475.9193	7.22 min	273.8272
3	Peak3	3.8392	198.6539	7.92 min	23.2399
4	Peak4	43.0636	2228.2407	8.66 min	218.6184
5	Peak5	4.8725	252.1205	9.62 min	27.1627

FWZ gradient method: Co-solvent from 3% to 10% during the first 10 min, then keep 10%



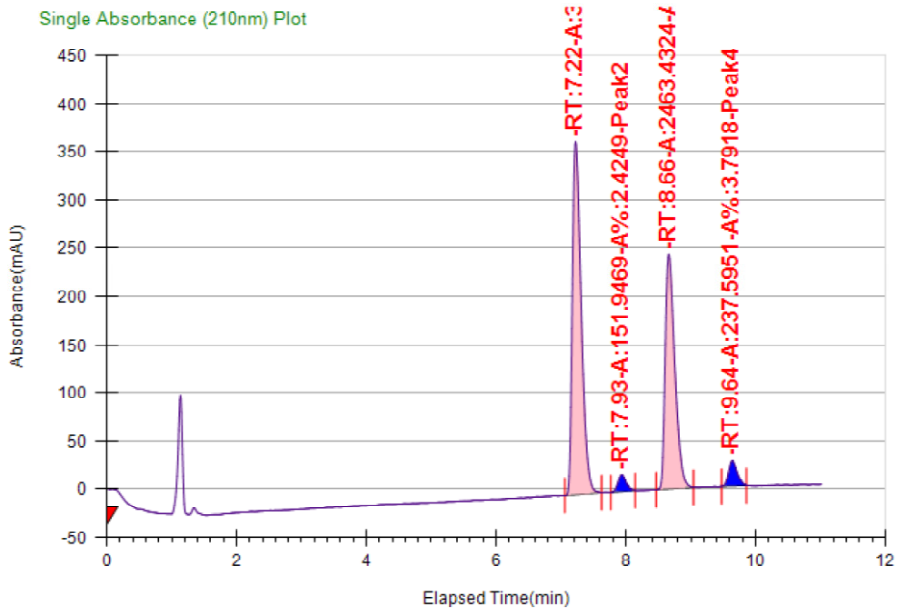
(Ref: Table 3, entry 8)

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

Thar Investigator SFC Results

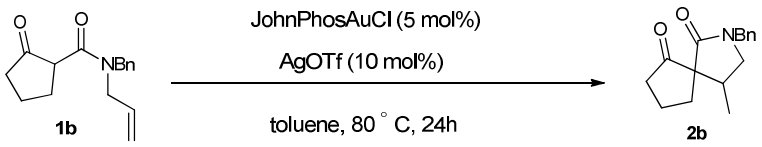
Sample	Column	Co-Solvent	Back Pressure	Col. Temp.
Fwz-671 C	IA 250*4.6	Methanol		30.1

Instrument Method	Inj. Vol.	Total Flow	Pressure Drop
FWZ gradient method	10	4	29



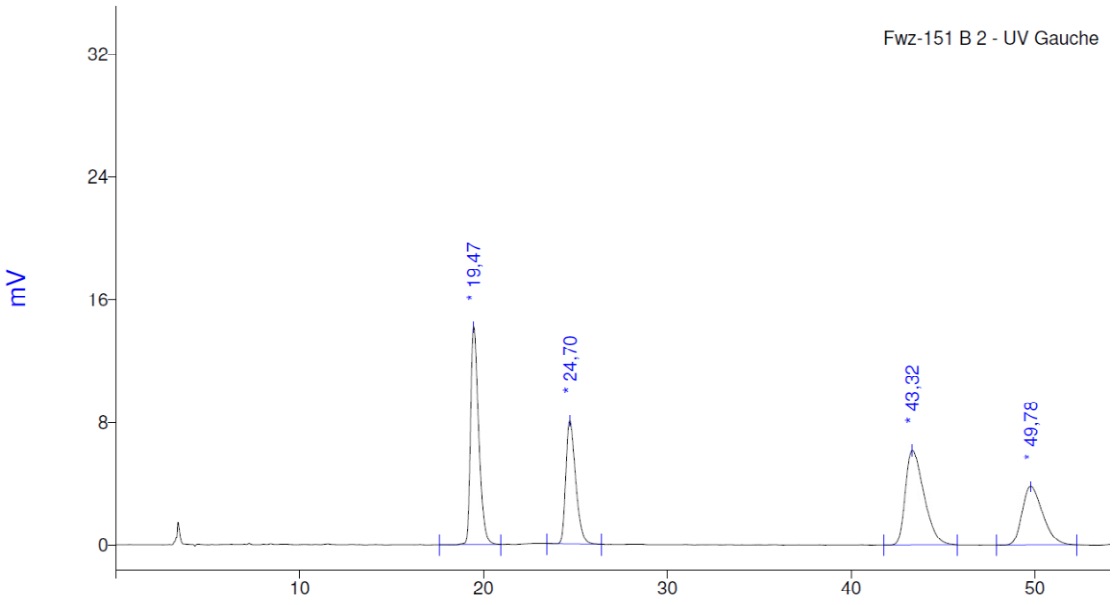
Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	54.4696	3413.1126	7.22 min	366.2136
2	Peak2	2.4249	151.9469	7.93 min	17.7955
3	Peak3	39.3137	2463.4324	8.66 min	243.6871
4	Peak4	3.7918	237.5951	9.64 min	26.1231

FWZ gradient method: Co-solvent from 3% to 10% during the first 10 min, then keep 10%



(Racemic reaction)

Analyse : Fwz-151 B 2 - UV Gauche



Résultats d'intégration

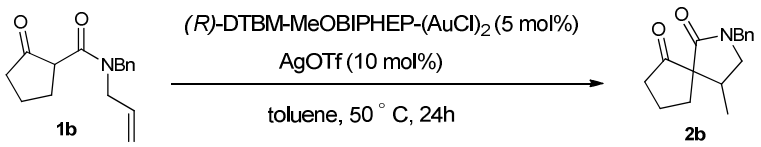
#	Nom du pic	Tr.	Aire	% Aire	Asymétrie (AIA)	Largeur (50%)	Plateaux (EP)
1		19,47	437,27	29,71	1,84	0,47	9602,60
2		24,70	299,68	20,36	1,64	0,57	10472,68
3		43,32	435,89	29,62	1,99	1,09	8797,36
4		49,78	298,78	20,30	1,58	1,21	9344,66
SOMME			**1471,62**	**100,00**			

Informations sur l'échantillon

Nom	Fwz-151 B	Type d'échantillon	Echantillon
N° Flacon	0		
Quantité	0,000000 mg	Volume d'injection	5,00 µl
Dilution	1	Diviseur	1

Informations :

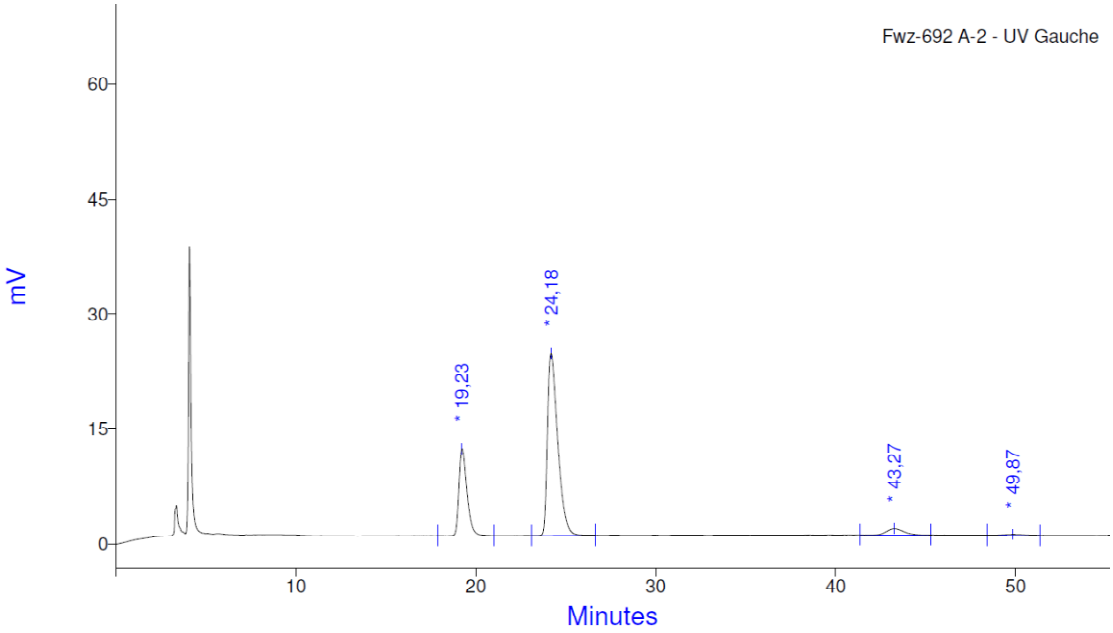
OJ-H Hex/EtOH 95/5; 1.0 ml/min, 210nm, 20°C



(Ref: Table 4, entry 1)

Analyse jeudi 3 avril 2014 11:04:54

Analyse : Fwz-692 A-2 - UV Gauche



Résultats d'intégration

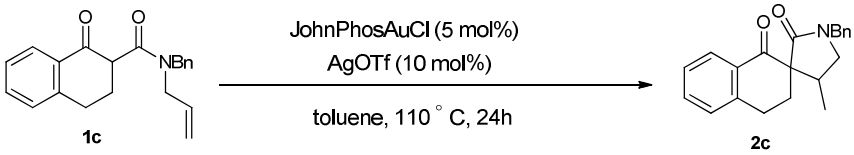
#	Nom du pic	Tr.	Aire	% Aire	Asymétrie (AIA)	Largeur (50%)	Plateaux (EP)
1		19,23	347,61	25,74	1,85	0,47	9472,71
2		24,18	936,61	69,34	2,27	0,60	8871,98
3		43,27	57,86	4,28	1,37	1,03	9695,07
4		49,87	8,61	0,64	1,10	1,21	9454,57
SOMME			**1350,69**	**100,00**			

Informations sur l'échantillon

Nom	Fwz-692 A-2	Type d'échantillon	Echantillon
N° Flacon	0		
Quantité	0,000000 mg	Volume d'injection	5,00 µl
Dilution	1	Diviseur	1

Informations :
O-JH hex/EtOH 95/5; 1.0 ml/min, 210nm, 10°C

Fwz-692 A-2 - UV Gauche Page 1/1



(Racemic reaction)

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

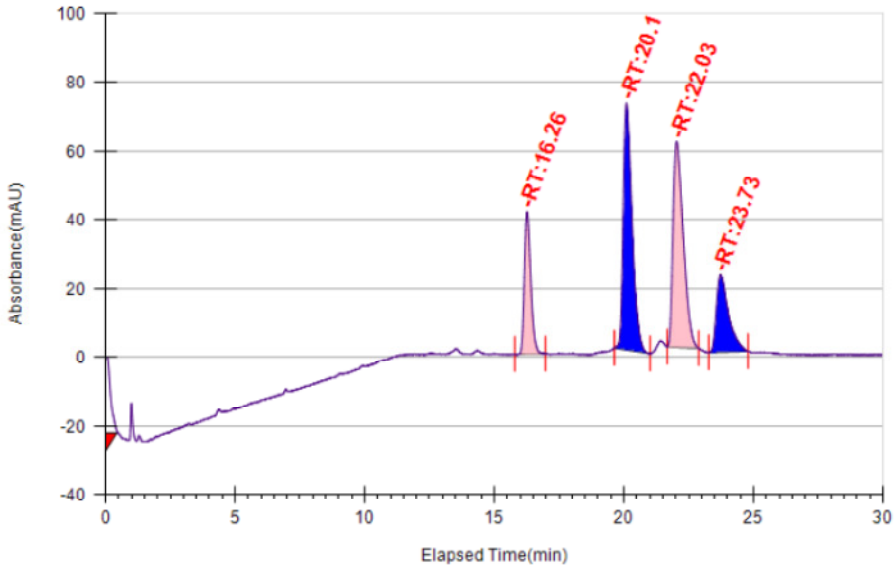
Thar Investigator SFC Results

ICMM

Sample	Column	Co-Solvent	Back Pressure	Col. Temp.
Fwz-578 B 5-6	IA 250*4.6	Methanol		34.2

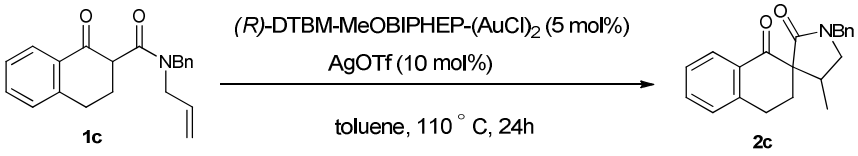
Instrument Method	Inj. Vol.	Total Flow	Pressure Drop
FWZ gradient method	10	4	27

Single Absorbance (215nm) Plot



Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	14.64	698.4441	16.26 min	41.4126
2	Peak2	35.7889	1707.4129	20.1 min	71.8401
3	Peak3	34.2307	1633.0762	22.03 min	59.8703
4	Peak4	15.3404	731.8609	23.73 min	22.5232

FWZ gradient method: Co-solvent from 3% to 10% during the first 10 min, then keep 10%



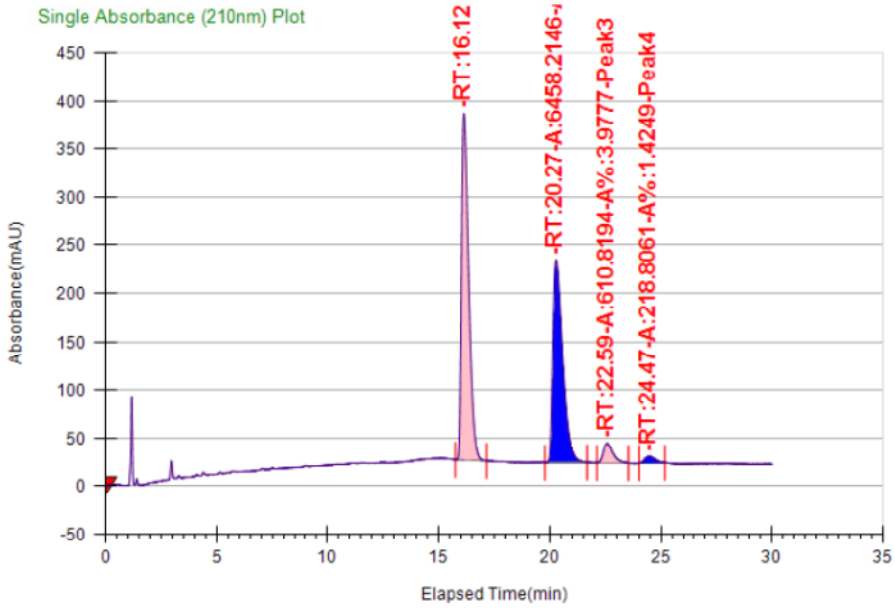
(Ref: Table 4, entry 3)

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

Thar Investigator SFC Results

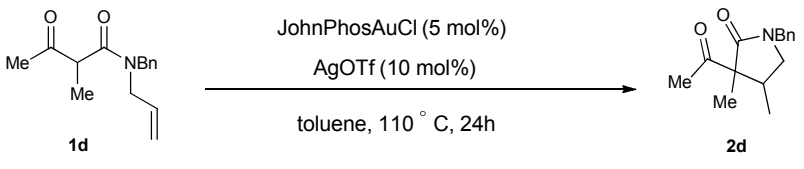
Sample	Column	Co-Solvent	Back Pressure	Col. Temp.
Fwz-691 B	IA 250*4.6	Methanol		30.3

Instrument Method	Inj. Vol.	Total Flow	Pressure Drop
FWZ gradient method	10	3.9995	26



Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	52.5415	8068.3958	16.12 min	359.8721
2	Peak2	42.056	6458.2146	20.27 min	209.8053
3	Peak3	3.9777	610.8194	22.59 min	20.5684
4	Peak4	1.4249	218.8061	24.47 min	7.1224

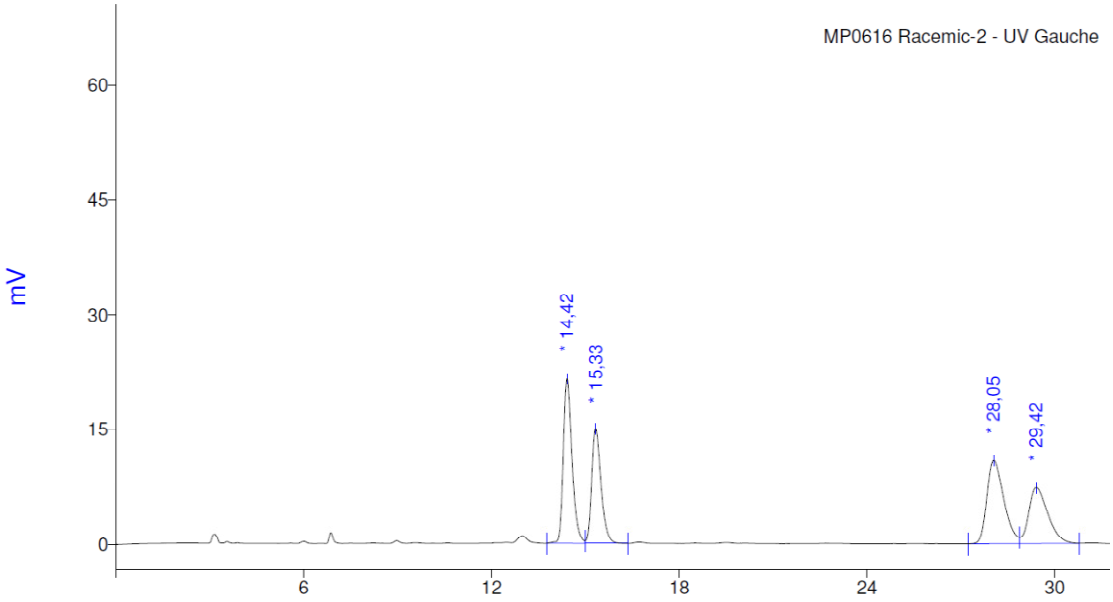
FWZ gradient method: Co-solvent from 3% to 10% during the first 10 min, then keep 10%



(Racemic reaction)

Analyse mercredi 9 avril 2014 17:19:49

Analyse : MP0616 Racemic-2 - UV Gauche



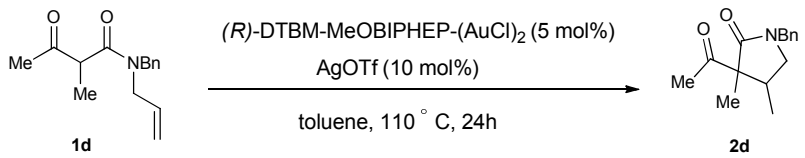
Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Asymétrie (AIA)	Largeur (50%)	Plateaux (EP)
1		14,42	417,97	28,89	1,55	0,29	13539,47
2		15,33	310,87	21,49	1,56	0,31	13176,01
3		28,05	408,20	28,21	1,78	0,58	12844,79
4		29,42	309,78	21,41	#	0,65	11320,41
SOMME			**1446,82**	**100,00**			

Informations sur l'échantillon

Nom	MP0616 Racemic-2	Type d'échantillon	Echantillon
N° Flacon	0		
Quantité	0,000000 mg	Volume d'injection	5,00 µl
Dilution	1	Diviseur	1

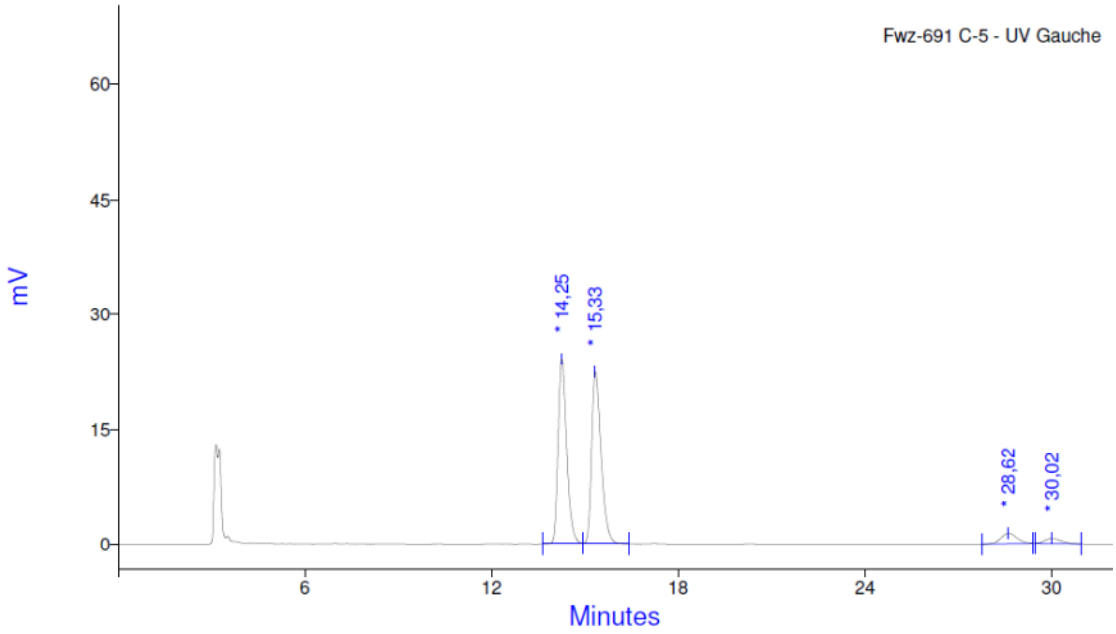
Informations :
AD-H Hex/EtOH 90/10; 1.0 ml/min, 210nm, 20°C



(Ref: Table 4, entry 5)

Analyse lundi 7 avril 2014 21:08:15

Analyse : Fwz-691 C-5 - UV Gauche



Résultats d'intégration

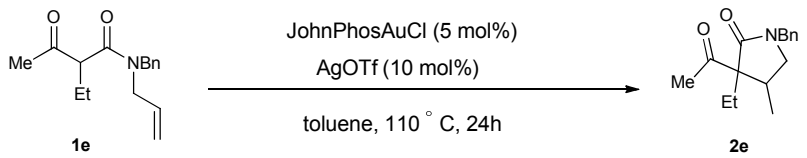
#	Nom du pic	Tr.	Aire	% Aire	Asymétrie (AIA)	Largeur (50%)	Plateaux (EP)
1		14,25	462,37	45,83	1,63	0,29	13439,78
2		15,33	474,27	47,01	1,82	0,32	12669,12
3		28,62	48,37	4,79	1,33	0,56	14536,23
4		30,02	23,79	2,36	1,21	0,56	15941,21
SOMME			**1008,80**	**100,00**			

Informations sur l'échantillon

Nom	Fwz-691 C-5	Type d'échantillon	Echantillon
N° Flacon	0		
Quantité	0,000000 mg	Volume d'injection	5,00 µl
Dilution	1	Diviseur	1

Informations :
AD-H hex/EtOH 90/10; 1.0 ml/min, 210nm, 20°C

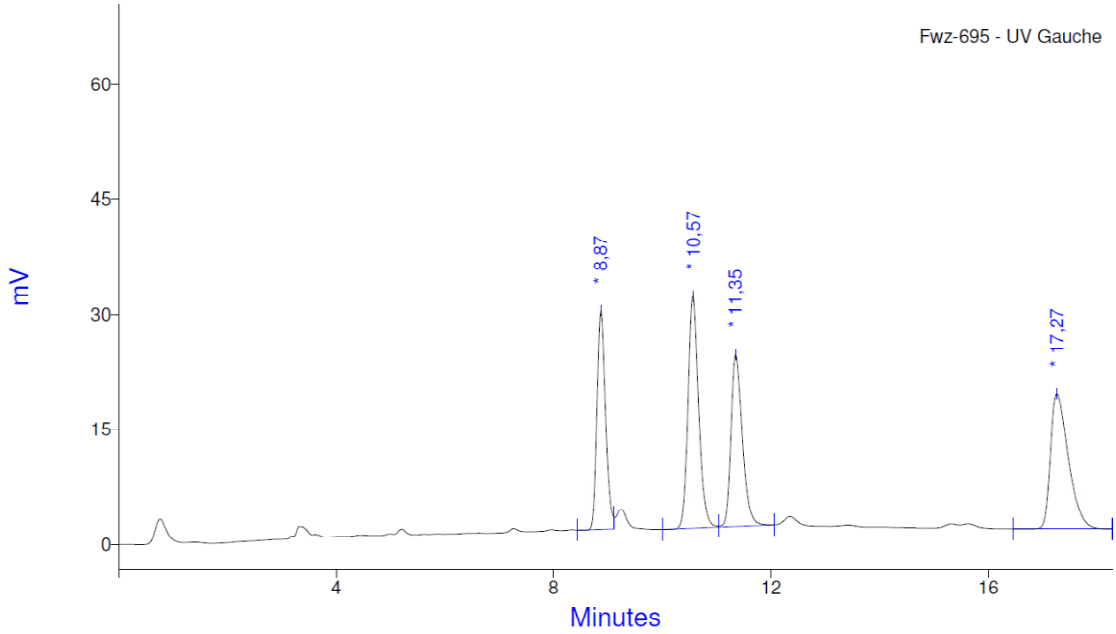
Fwz-691 C-5 - UV Gauche Page 1/1



(Racemic reaction)

Analyse jeudi 10 avril 2014 15:23:14

Analyse : Fwz-695 - UV Gauche



Résultats d'intégration

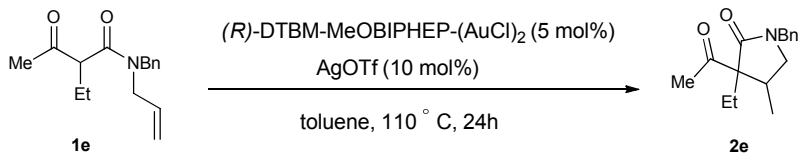
#	Nom du pic	Tr.	Aire	% Aire	Asymétrie (AIA)	Largeur (50%)	Plateaux (EP)
1		8,87	311,40	21,45	1,47	0,17	15585,57
2		10,57	412,84	28,44	1,29	0,21	14445,73
3		11,35	324,53	22,36	1,62	0,22	15003,91
4		17,27	402,71	27,74	2,05	0,35	13674,61
SOMME			**1451,49**	**100,00**			

Informations sur l'échantillon

Nom	Fwz-695	Type d'échantillon	Echantillon
N° Flacon	0		
Quantité	0,000000 mg	Volume d'injection	5,00 µl
Dilution	1	Diviseur	1

Informations :

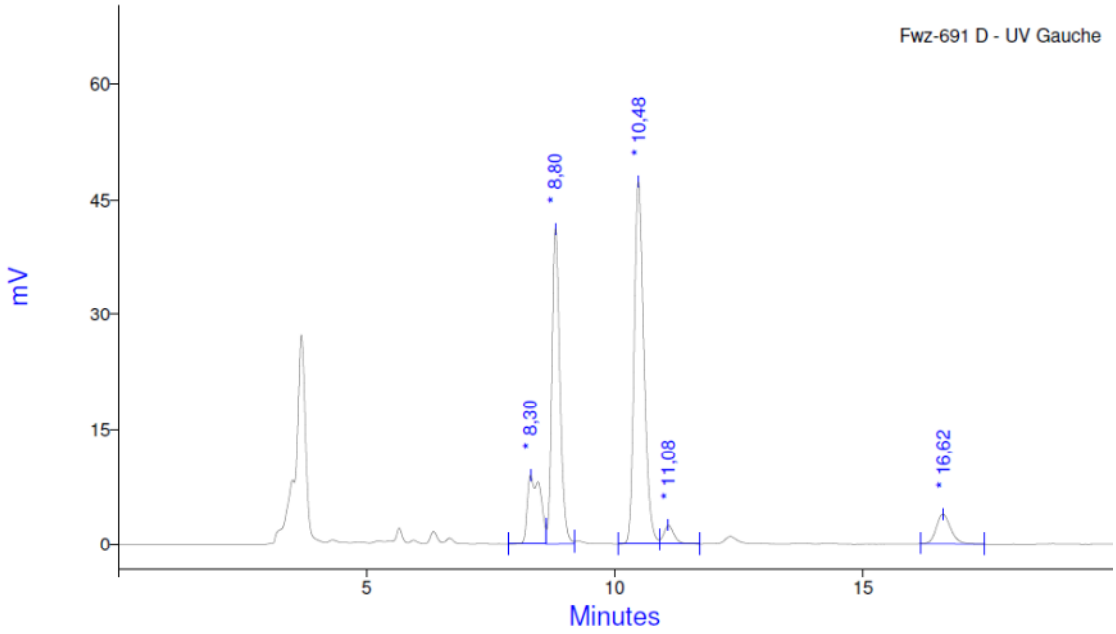
IA Hex/EtOH 90/10; 1.0 ml/min, 210nm, 20°C



(Ref: Table 4, entry 7)

Analyse lundi 31 mars 2014 13:54:33

Analyse : Fwz-691 D - UV Gauche



Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Asymétrie (AIA)	Largeur (50%)	Plateaux (EP)
1		8,30	162,14	11,74	#	0,32	3783,29
2		8,80	462,34	33,46	1,52	0,17	14917,87
3		10,48	645,26	46,70	1,38	0,21	14086,69
4		11,08	34,58	2,50	#	0,22	14228,74
5		16,62	77,29	5,59	1,24	0,31	16364,72
SOMME			**1381,61**	**100,00**			

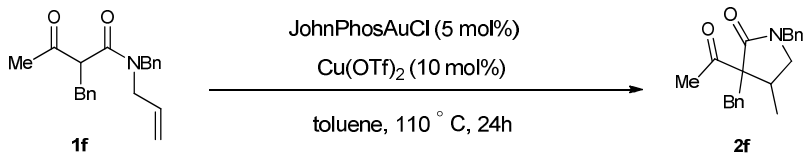
Informations sur l'échantillon

Nom	Fwz-691 D	Type d'échantillon	Echantillon
N° Flacon	0		
Quantité	0,000000 mg	Volume d'injection	5,00 µl
Dilution	1	Diviseur	1

Informations :

IA hex/EtOH 90/10; 1.0 ml/min, 210nm, 20°C

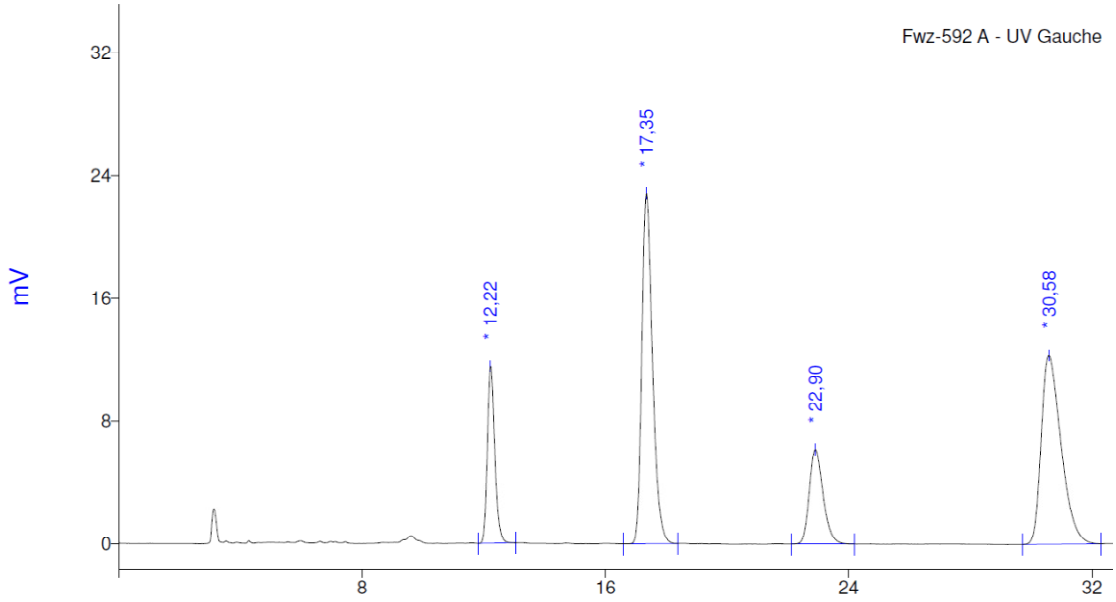
Fwz-691 D - UV Gauche Page 1/1



(Racemic reaction)

Analyse mercredi 9 avril 2014 17:57:16

Analyse : Fwz-592 A - UV Gauche



Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Asymétrie (AIA)	Largeur (50%)	Plateaux (EP)
1		12,22	195,69	12,97	1,46	0,26	12697,35
2		17,35	559,38	37,08	1,48	0,37	12053,59
3		22,90	195,17	12,94	1,44	0,48	12587,95
4		30,58	558,45	37,02	1,86	0,70	10699,59
SOMME			**1508,69**	**100,00**			

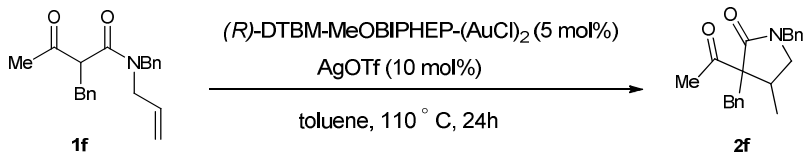
Informations sur l'échantillon

Nom	Fwz-592 A	Type d'échantillon	Echantillon
N° Flacon	0		
Quantité	0,000000 mg	Volume d'injection	5,00 µl
Dilution	1	Diviseur	1

Informations :

AD-H Hex/EtOH 90/10; 1.0 ml/min, 210nm, 20°C

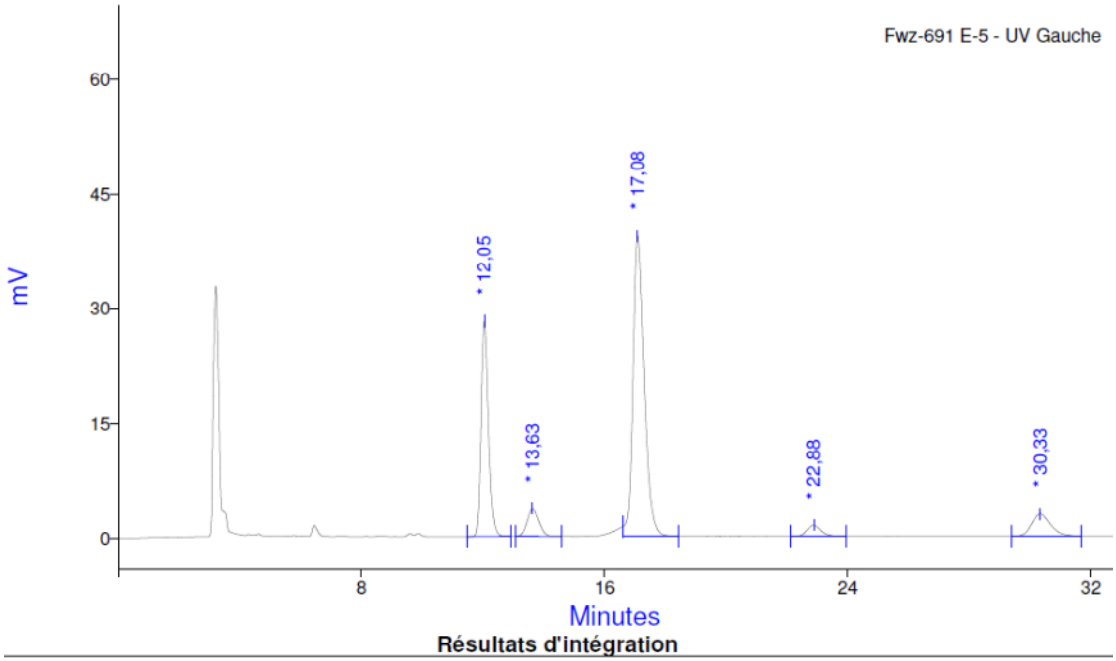
Fwz-592 A - UV Gauche Page 1/1



(Ref: Table 4, entry 9)

Analyse lundi 7 avril 2014 19:53:29

Analyse : Fwz-691 E-5 - UV Gauche



Résultats d'intégration

#	Nom du pic	Tr.	Aire	% Aire	Asymétrie (AIA)	Largeur (50%)	Plateaux (EP)
1		12,05	473,18	27,20	1,34	0,26	12325,70
2		13,63	94,65	5,44	1,18	0,42	5922,85
3		17,08	1005,68	57,81	1,62	0,38	11011,61
4		22,88	44,11	2,54	1,23	0,48	12793,39
5		30,33	122,11	7,02	1,37	0,65	12203,52
SOMME			**1739,72**	**100,00**			

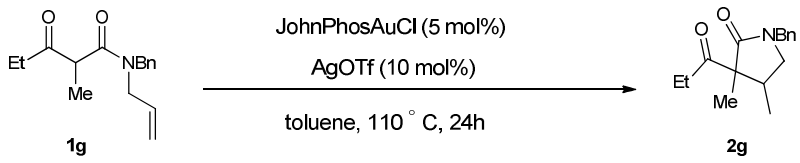
Informations sur l'échantillon

Nom	Fwz-691 E-5	Type d'échantillon	Echantillon
N° Flacon	0		
Quantité	0,000000 mg	Volume d'injection	5,00 µl
Dilution	1	Diviseur	1

Informations :

AD-H hex/EtOH 90/10; 1.0 ml/min, 210nm, 20°C

Fwz-691 E-5 - UV Gauche Page 1/1



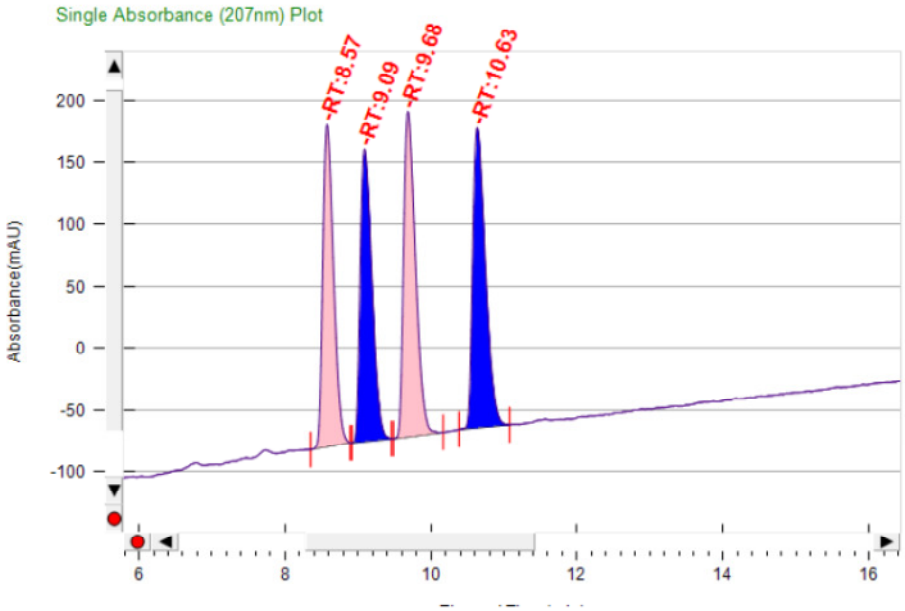
(Racemic reaction)

Waters
THE SCIENCE OF WHAT'S POSSIBLE.™

Thar Investigator SFC Results

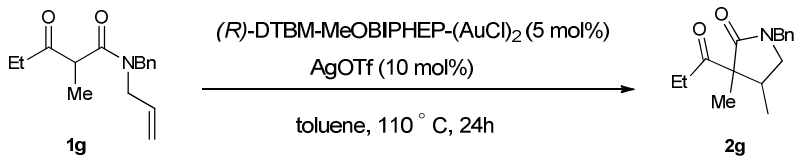
Sample	Column	Co-Solvent	Back Pressure	Col. Temp.
Fwz-611 A	IA 250*4.6	Methanol		30

Instrument Method	Inj. Vol.	Total Flow	Pressure Drop
Fwz gradient 1	10	4	26



Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	23.6756	2603.4471	8.57 min	259.694
2	Peak2	23.5372	2588.2277	9.09 min	235.8085
3	Peak3	26.4737	2911.1348	9.68 min	262.5573
4	Peak4	26.3134	2893.5054	10.63 min	241.8518

FWZ gradient method 1: Co-solvent from 1% to 10% during the first 20 min, then keep 10%



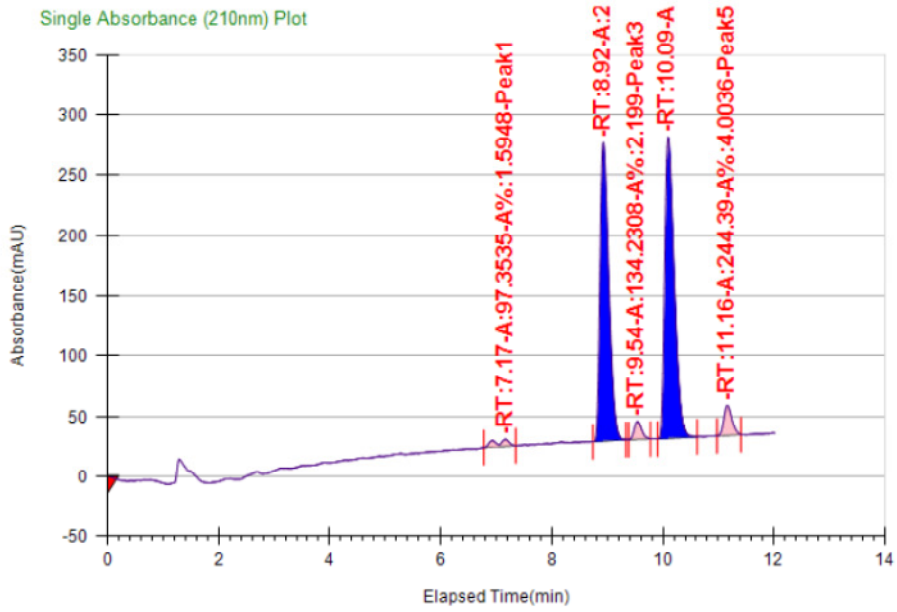
(Ref: Table 4, entry 11)

Waters
THE SCIENCE OF WHAT'S POSSIBLE.

Thar Investigator SFC Results

Sample	Column	Co-Solvent	Back Pressure	Col. Temp.
Fwz-691 F	IA 250*4.6	Methanol		30.3

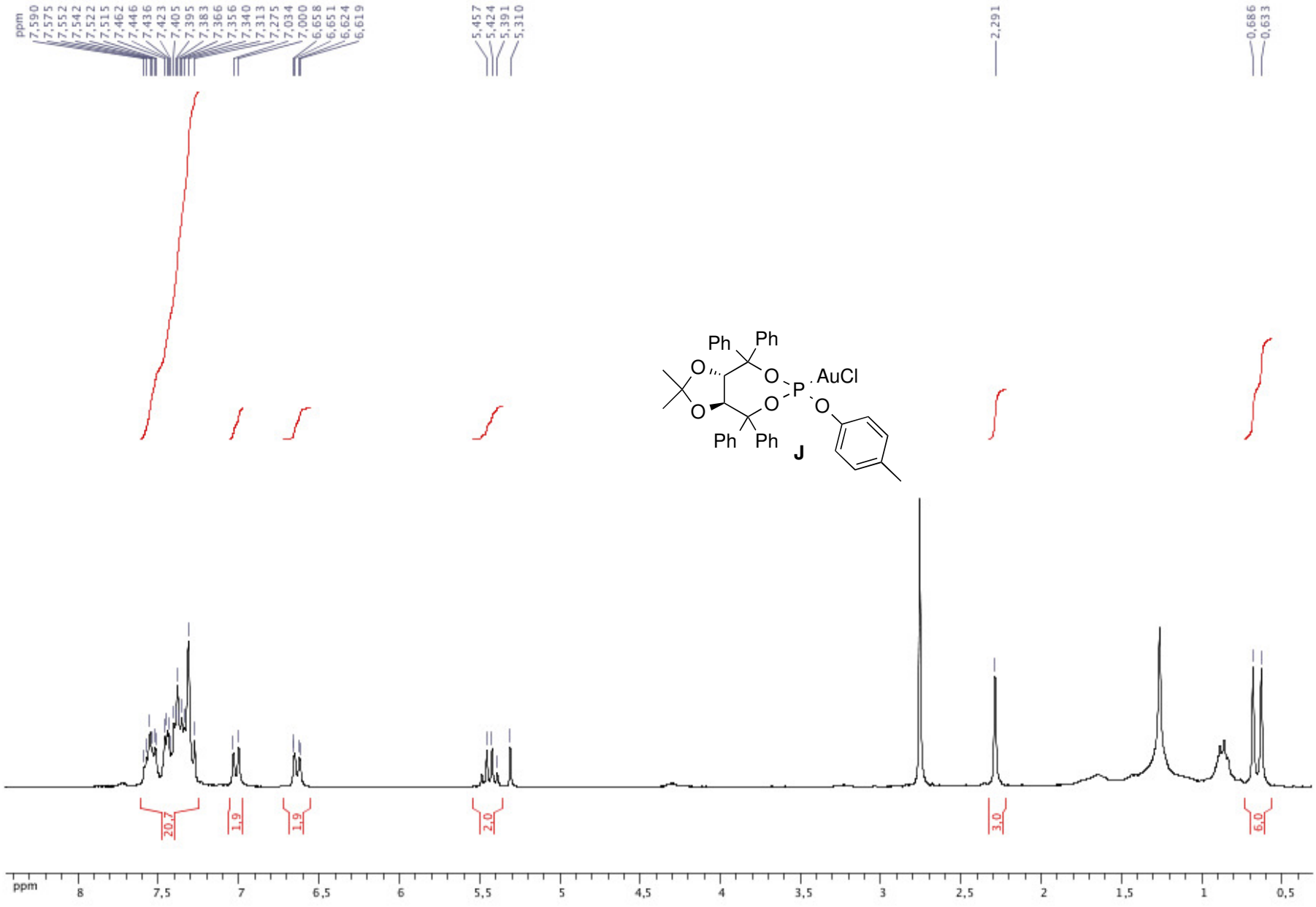
Instrument Method	Inj. Vol.	Total Flow	Pressure Drop
Fwz gradient 1	10	4	26

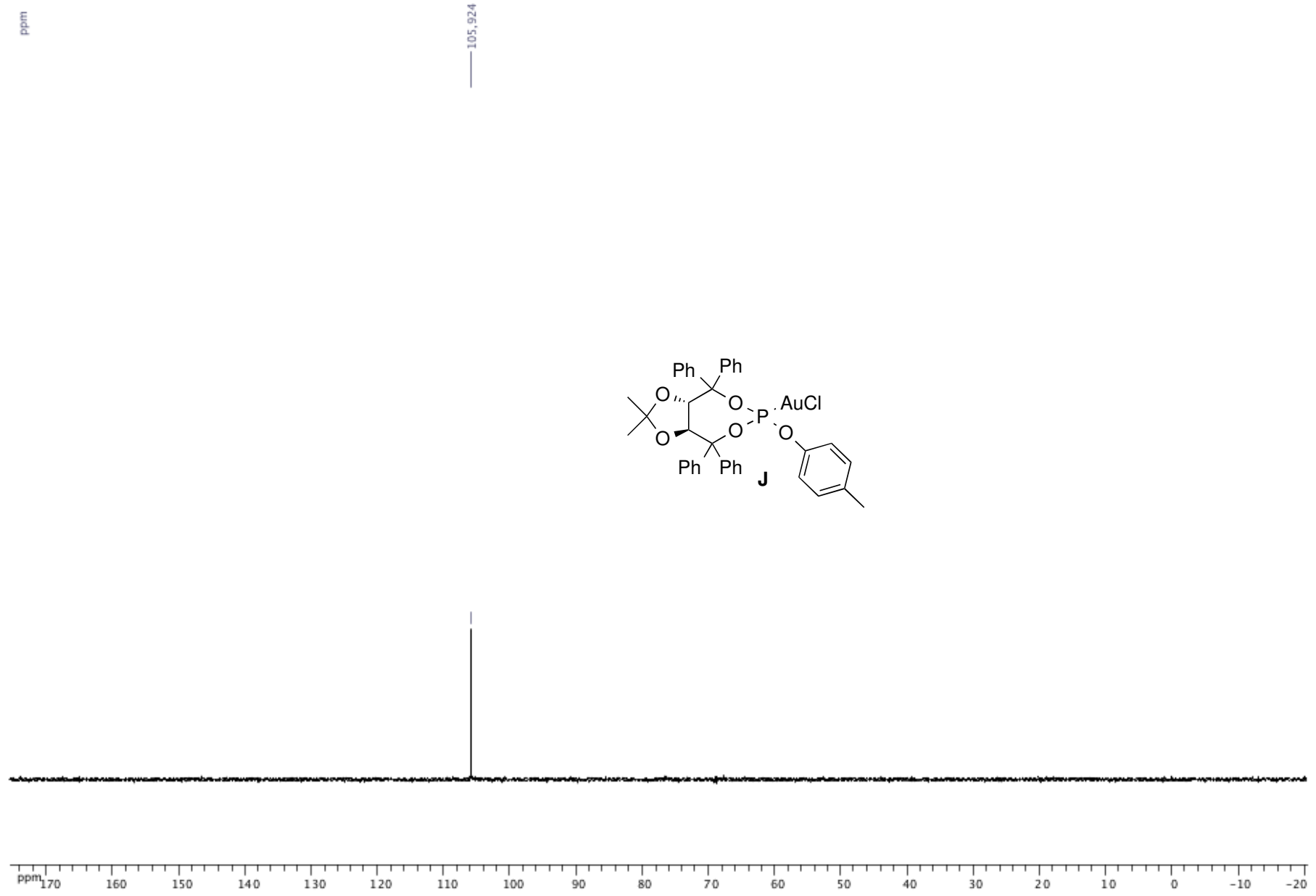


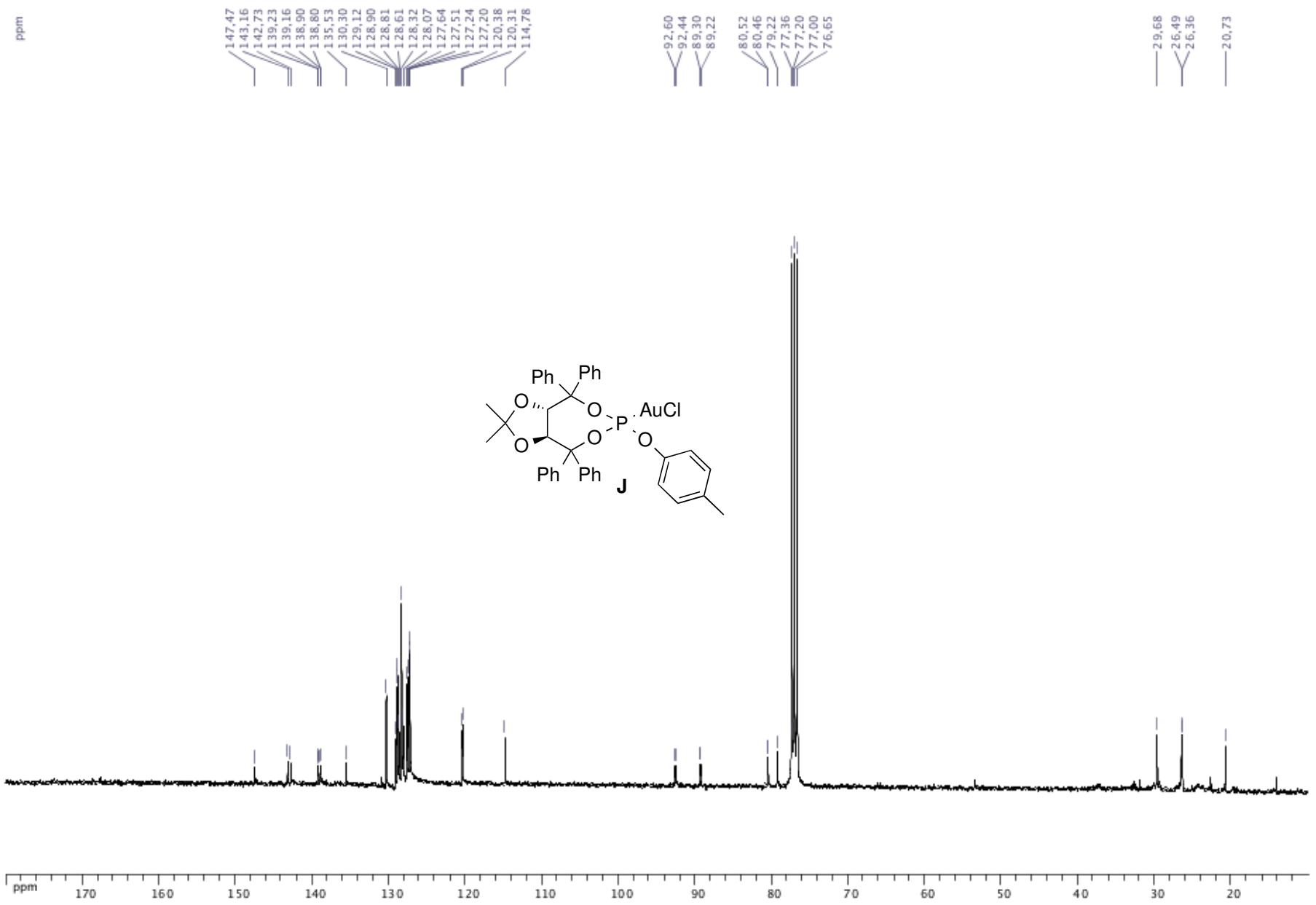
Peak #	Peak Name	Area %	Area	Ret. Time	Height
1	Peak1	1.5948	97.3535	7.17 min	5.7161
2	Peak2	44.0501	2688.9253	8.92 min	247.7833
3	Peak3	2.199	134.2308	9.54 min	14.9559
4	Peak4	48.1525	2939.3442	10.09 min	249.9144
5	Peak5	4.0036	244.39	11.16 min	24.8257

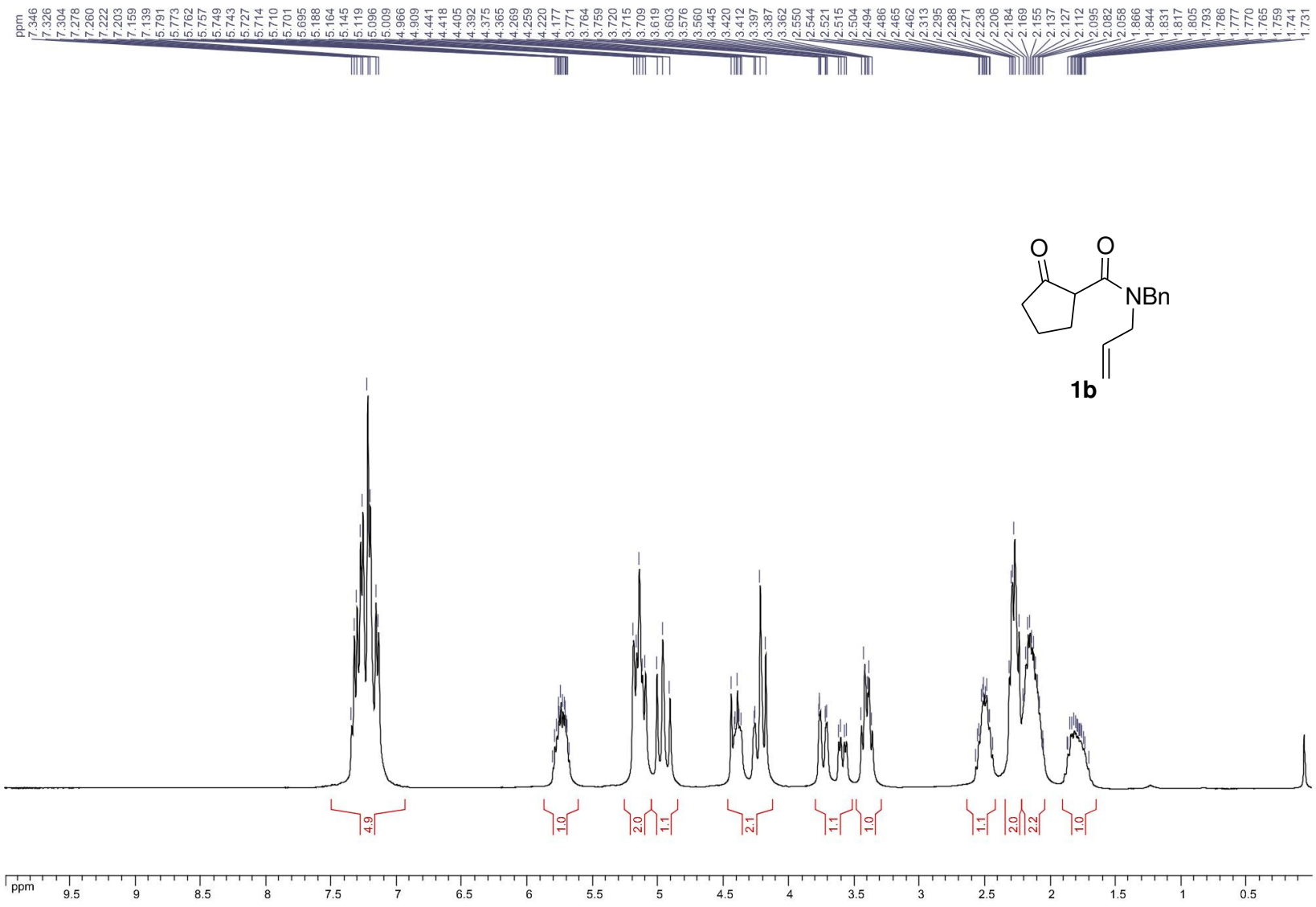
FWZ gradient method 1: Co-solvent from 1% to 10% during the first 20 min, then keep 10%

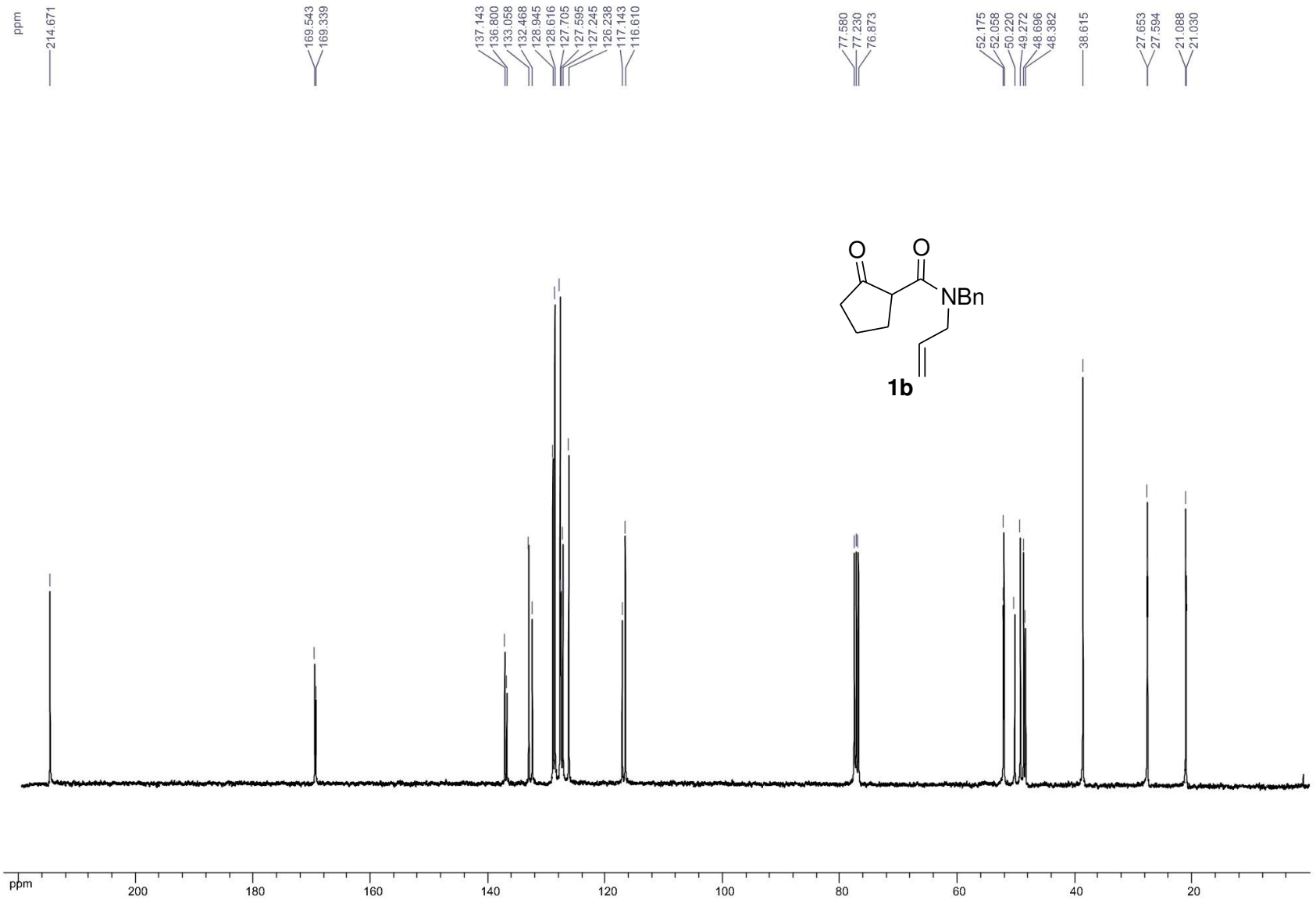
Spectra (^{1}H, ^{31}P, ^{13}C NMR)



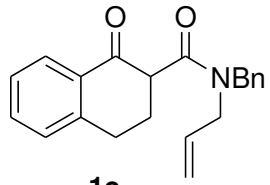

ppm
105,924
Ph
Ph
O
O
P
AuCl
O
O
Ph
Ph
J
ppm
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20


ppm
147,47
143,16
142,73
139,23
139,16
138,90
138,80
135,53
130,30
129,12
128,90
128,81
128,61
128,32
128,07
127,64
127,51
127,24
127,20
120,38
120,31
114,78
92,60
92,44
89,30
89,22
80,52
80,46
79,22
77,36
77,20
77,00
76,65
29,68
26,49
26,36
20,73
Ph
Ph
O
O
O
P
AuCl
O
O
Ph
Ph
J
ppm
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20

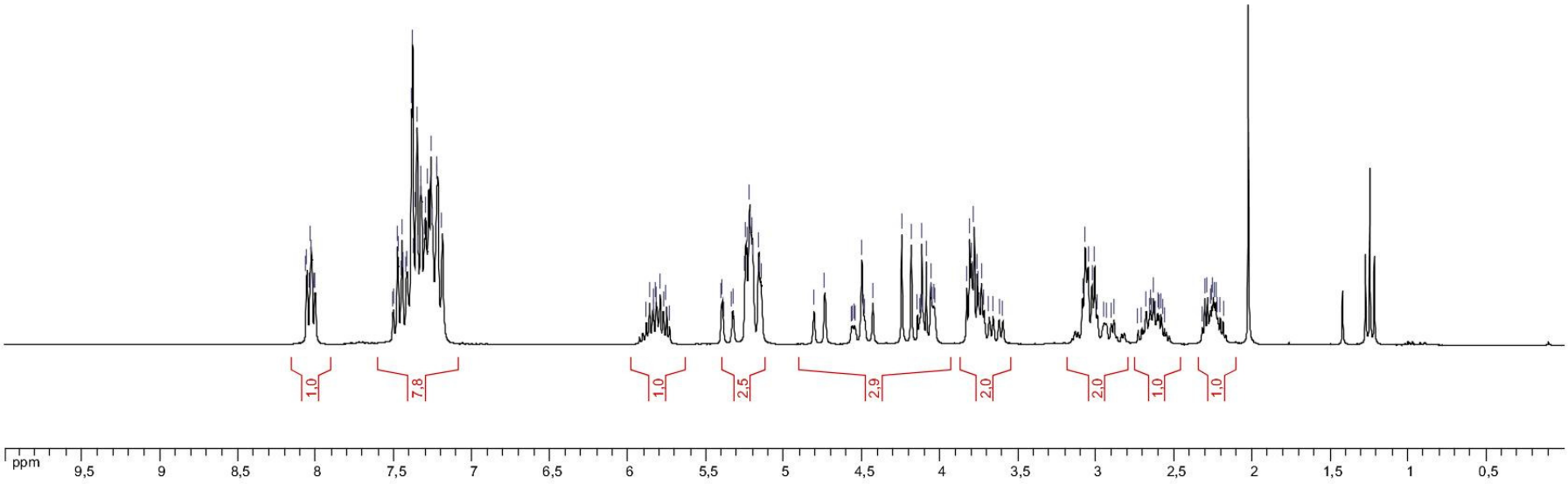

ppm
7.346
7.326
7.304
7.278
7.260
7.222
7.203
7.159
7.139
5.791
5.773
5.762
5.757
5.749
5.743
5.727
5.714
5.710
5.701
5.695
5.188
5.164
5.145
5.119
5.096
5.009
4.966
4.909
4.441
4.418
4.405
4.392
4.375
4.365
4.269
4.259
4.220
4.177
3.771
3.764
3.759
3.720
3.715
3.709
3.619
3.603
3.576
3.560
3.445
3.420
3.412
3.397
3.387
3.362
2.550
2.544
2.521
2.515
2.504
2.494
2.486
2.465
2.462
2.313
2.295
2.288
2.271
2.238
2.206
2.184
2.169
2.155
2.137
2.127
2.112
2.095
2.082
2.058
1.866
1.844
1.831
1.817
1.805
1.793
1.786
1.777
1.770
1.765
1.759
1.741
1.731
O
O
NBn
1b
4.9
1.0
2.0
1.1
2.1
1.1
1.0
1.1
2.0
2.2
1.0
ppm
9.5
9
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5

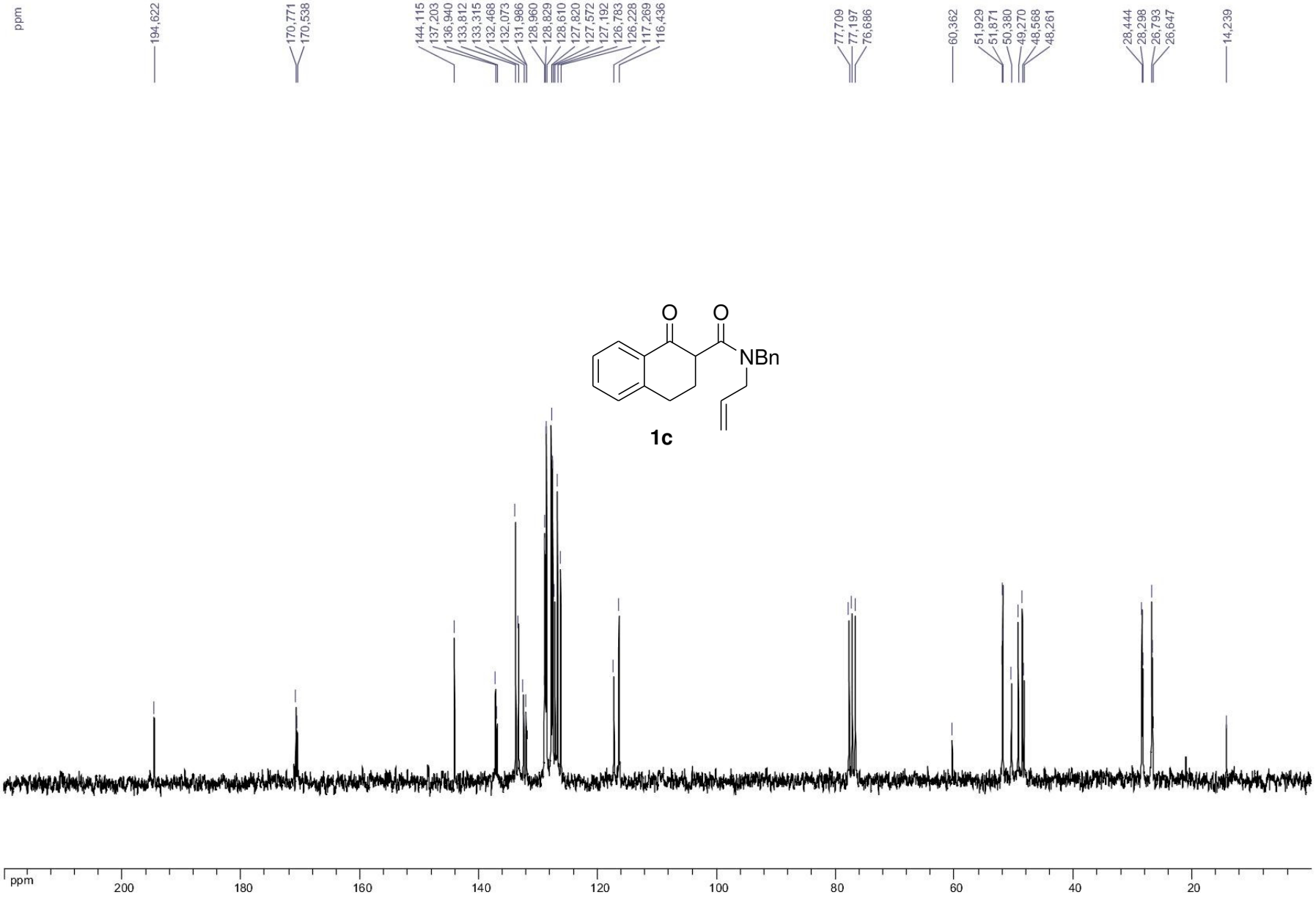

ppm
214.671
169.543
169.339
137.143
136.800
133.058
132.468
128.945
128.616
127.705
127.595
127.245
126.238
117.143
116.610
77.580
77.230
76.873
52.175
52.058
50.220
49.272
48.696
48.382
38.615
27.653
27.594
21.088
21.030
O
O
NBn
1b
ppm
200
180
160
140
120
100
80
60
40
20

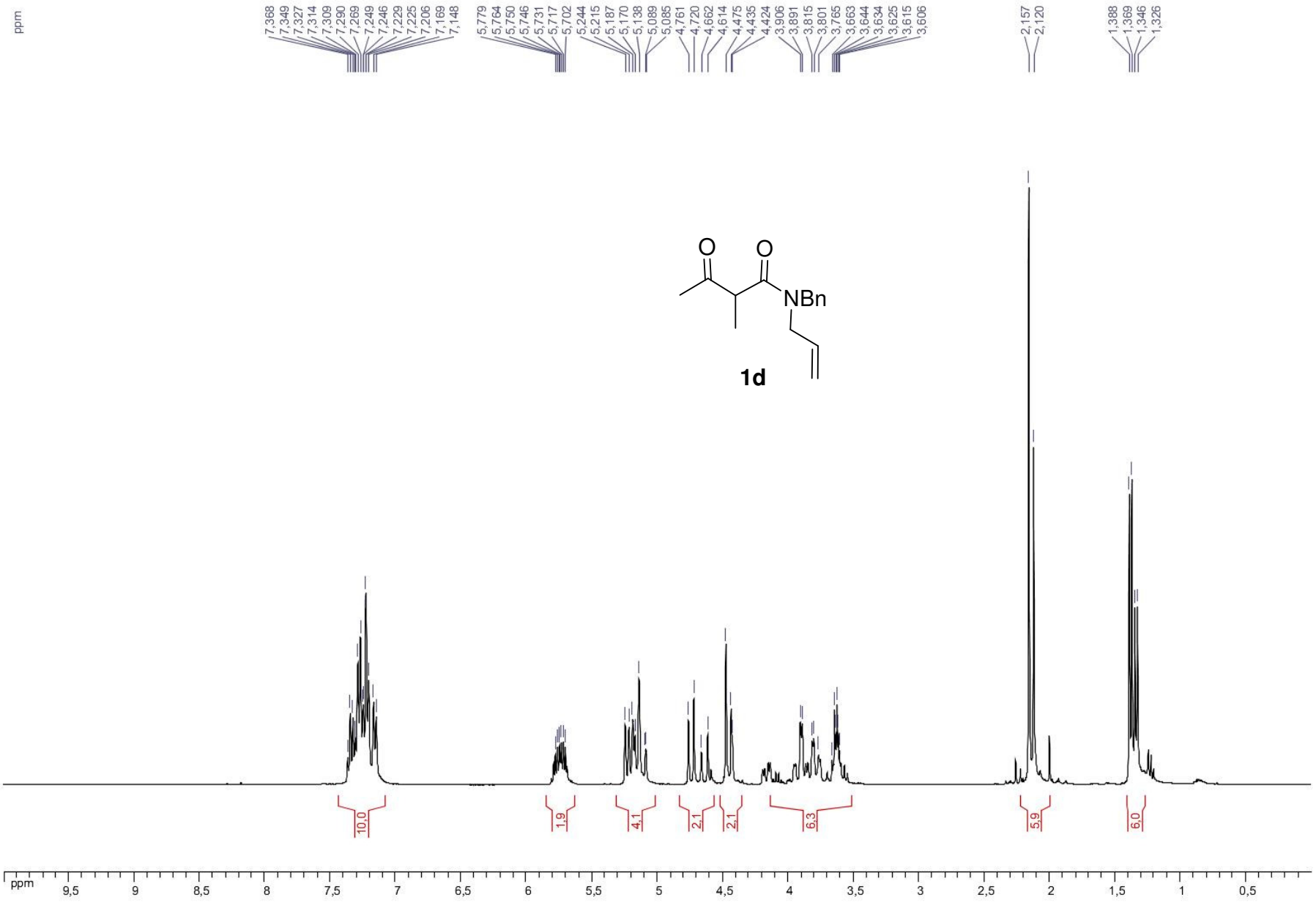

ppm
8,062
8,057
8,040
8,032
8,025
8,009
8,004
7,509
7,502
7,478
7,473
7,454
7,449
7,443
7,423
7,419
7,415
7,387
7,380
7,370
7,361
7,352
7,343
7,329
7,323
7,305
7,298
7,279
7,262
7,252
7,224
7,218
7,190
5,862
5,840
5,820
5,815
5,793
5,773
5,752
5,401
5,394
5,331
5,325
5,250
5,244
5,239
5,219
5,211
5,204
5,197
5,162
5,150
5,145
4,808
4,737
4,500
4,431
4,245
4,184
4,116
4,087
4,058
4,052
4,045
4,040
4,034
3,828
3,809
3,799
3,790
3,780
3,761
3,751
3,733
3,717
3,087
3,069
3,050
3,025
3,007
2,676
2,651
2,631
2,301
2,285
2,266
2,257
2,248
2,239
2,230

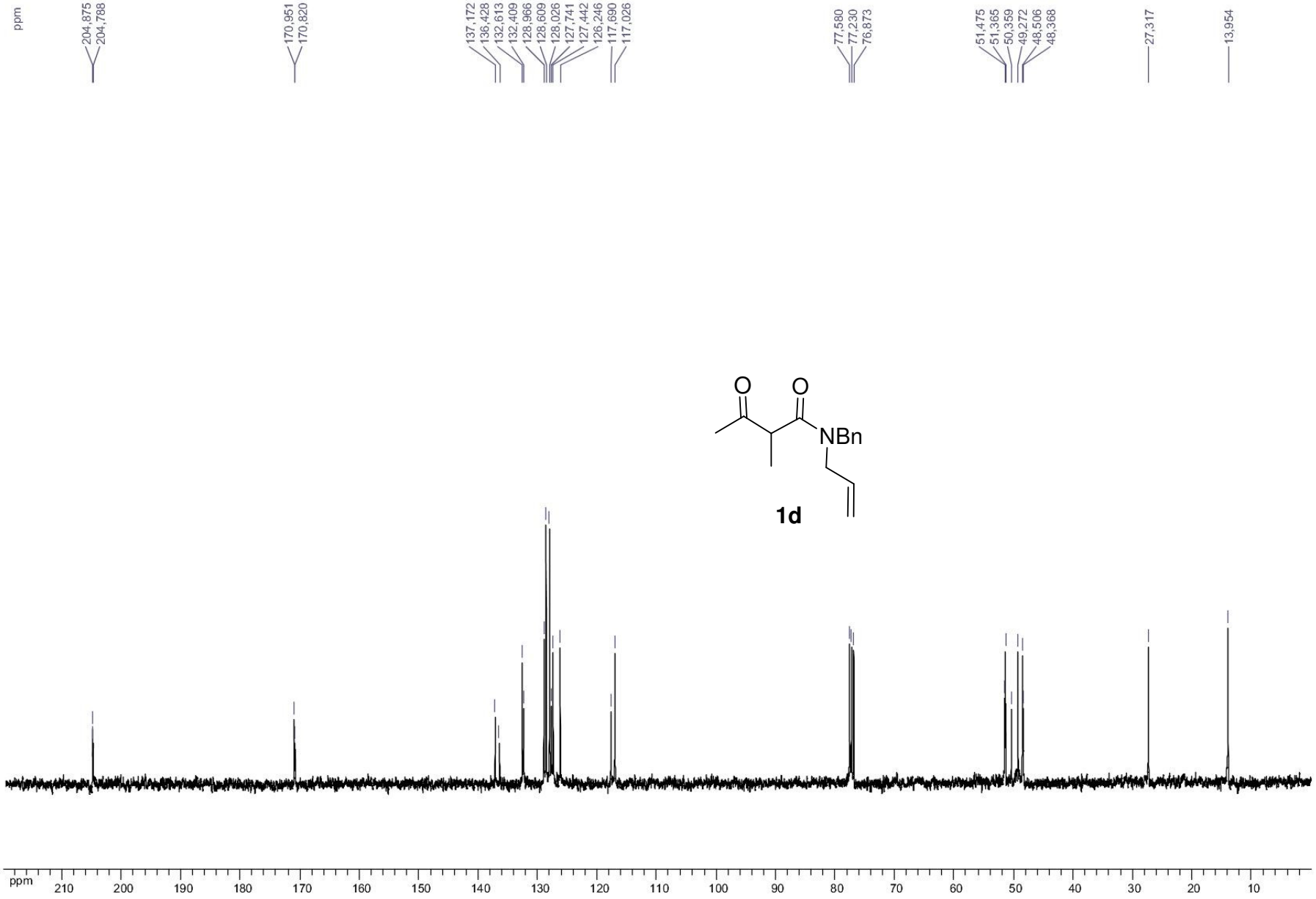

O
O
NBn

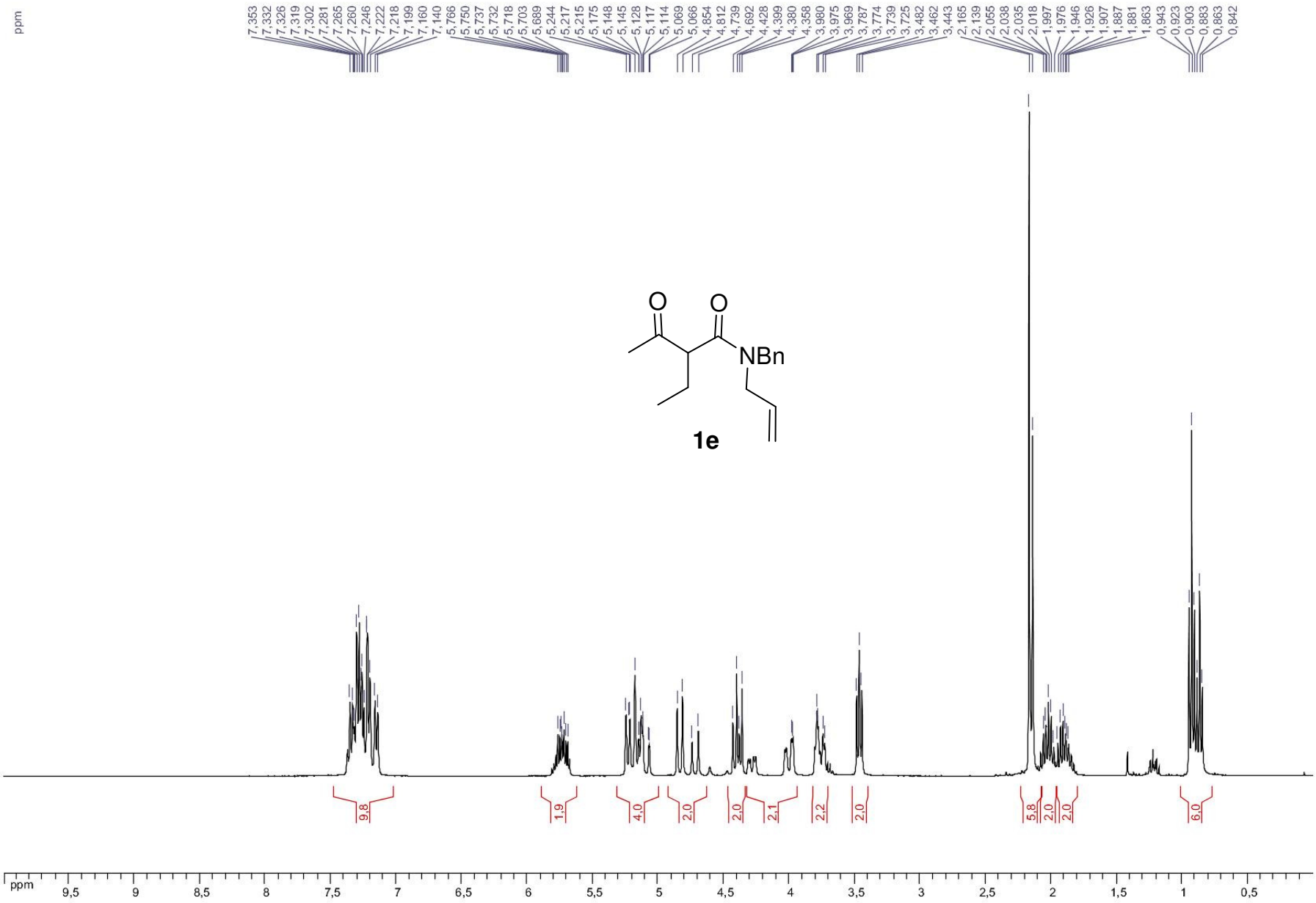
1c

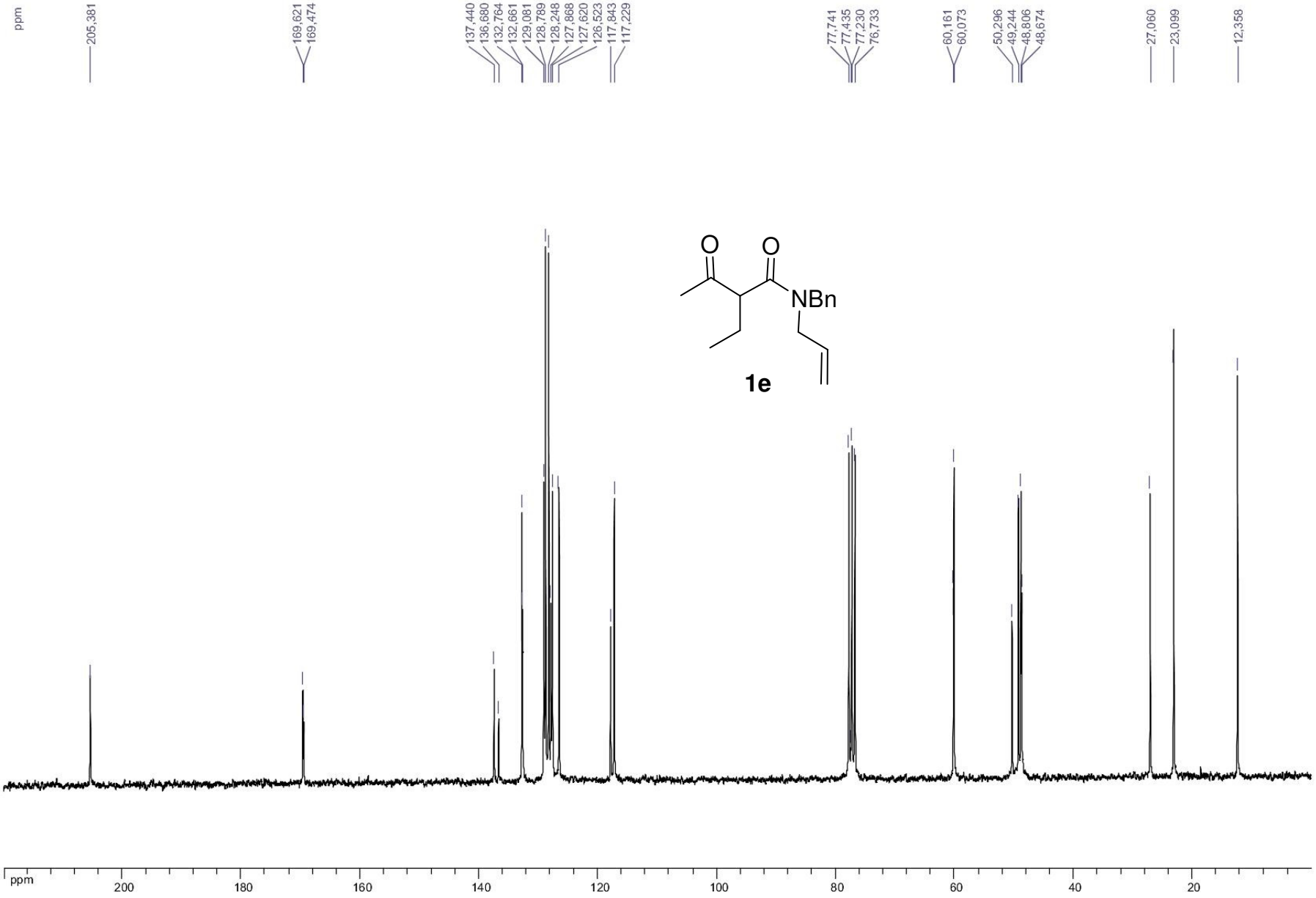

1,0
7,8
1,0
2,5
2,9
2,0
2,0
1,0
1,0
ppm
9,5
9
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5

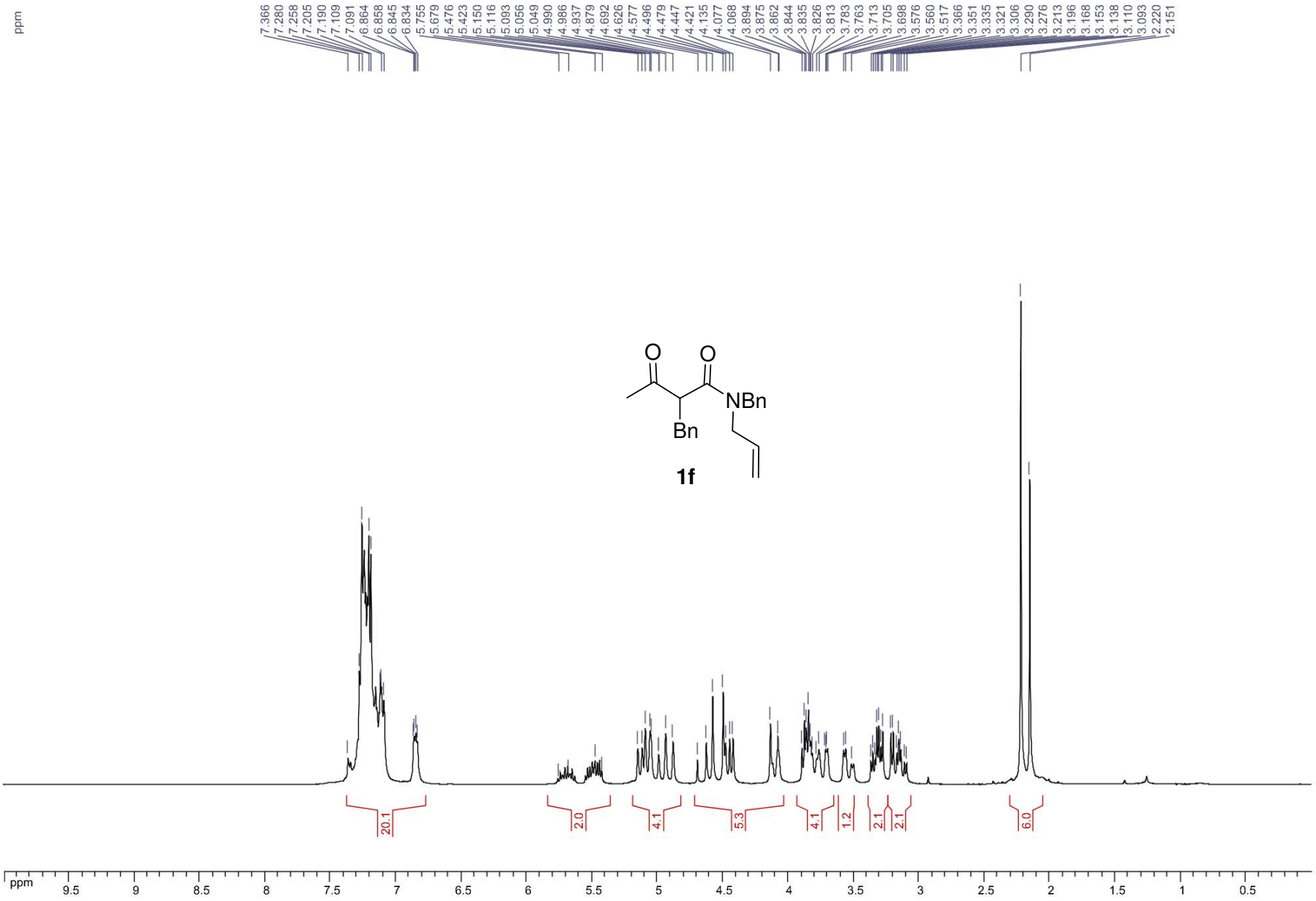

ppm
194,622
170,771
170,538
144,115
137,203
136,940
133,812
133,315
132,468
132,073
131,986
128,960
128,829
128,610
127,820
127,572
127,192
126,783
126,228
117,269
116,436
77,709
77,197
76,686
60,362
51,929
51,871
50,380
49,270
48,568
48,261
28,444
28,298
26,793
26,647
14,239
O
O
NBn
1c
ppm
200
180
160
140
120
100
80
60
40
20

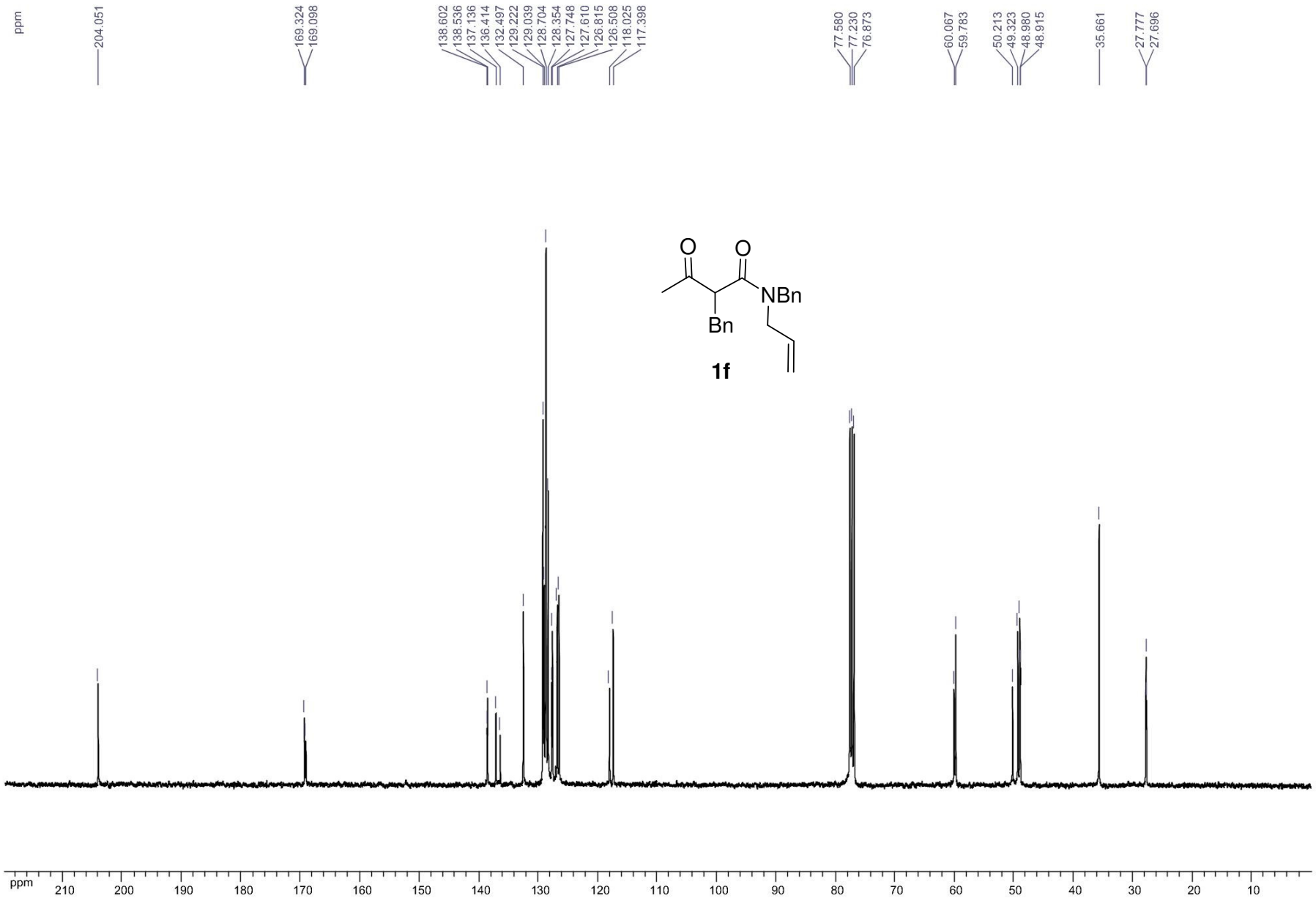

ppm
7,368
7,349
7,327
7,314
7,309
7,290
7,269
7,249
7,246
7,229
7,225
7,206
7,169
7,148
5,779
5,764
5,750
5,746
5,731
5,717
5,702
5,244
5,215
5,187
5,170
5,138
5,089
5,085
4,761
4,720
4,662
4,614
4,475
4,435
4,424
3,906
3,891
3,815
3,801
3,765
3,663
3,644
3,634
3,625
3,615
3,606
2,157
2,120
1,388
1,369
1,346
1,326
O
O
NBn
1d
10,0
1,9
4,1
2,1
2,1
6,3
5,9
6,0
ppm
9,5
9
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5

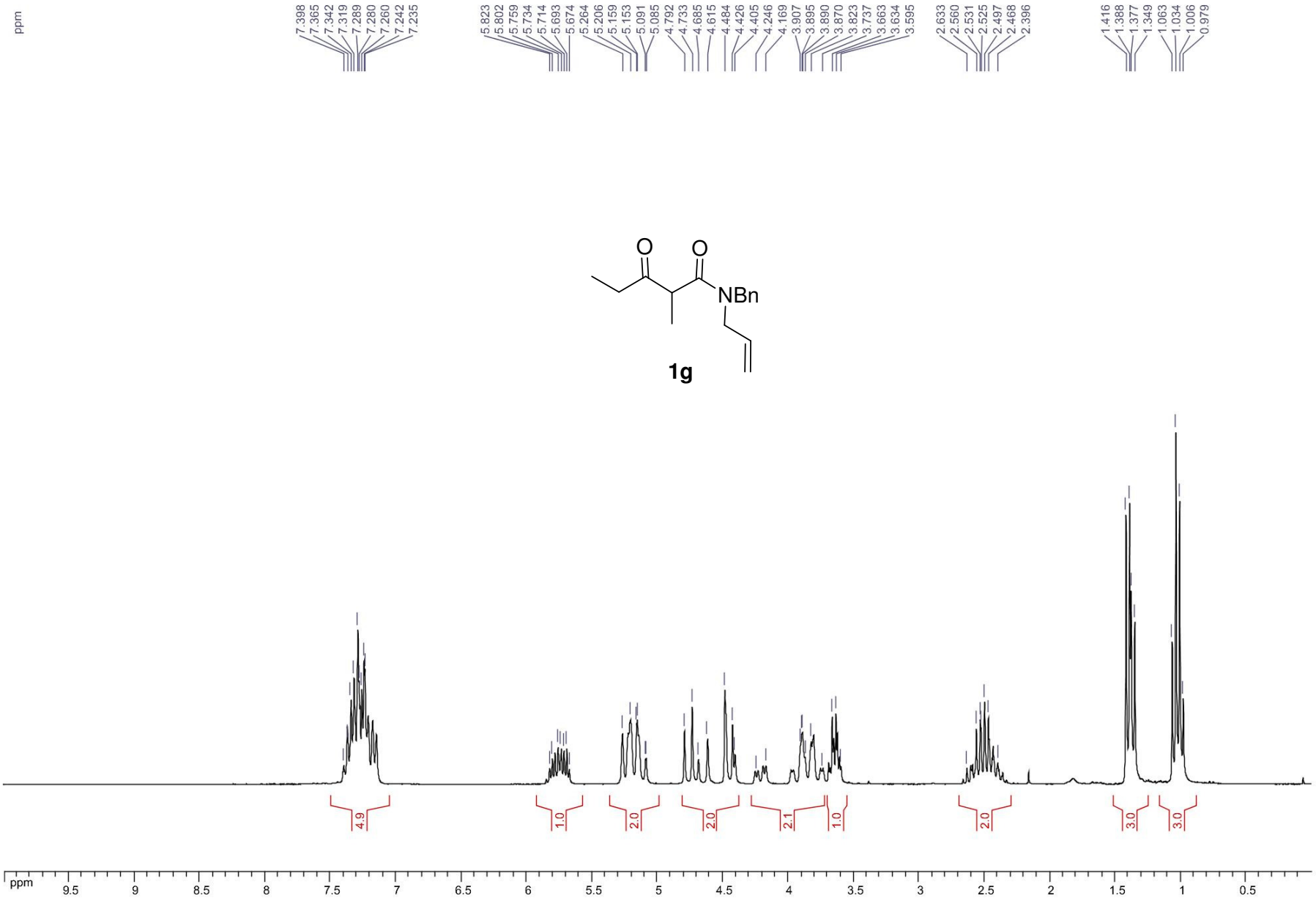

ppm
204,875
204,788
170,951
170,820
137,172
136,428
132,613
132,409
128,966
128,609
128,026
127,741
127,442
126,246
117,690
117,026
77,580
77,230
76,873
51,475
51,365
50,359
49,272
48,506
48,368
27,317
13,954
O
O
NBn
1d
ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

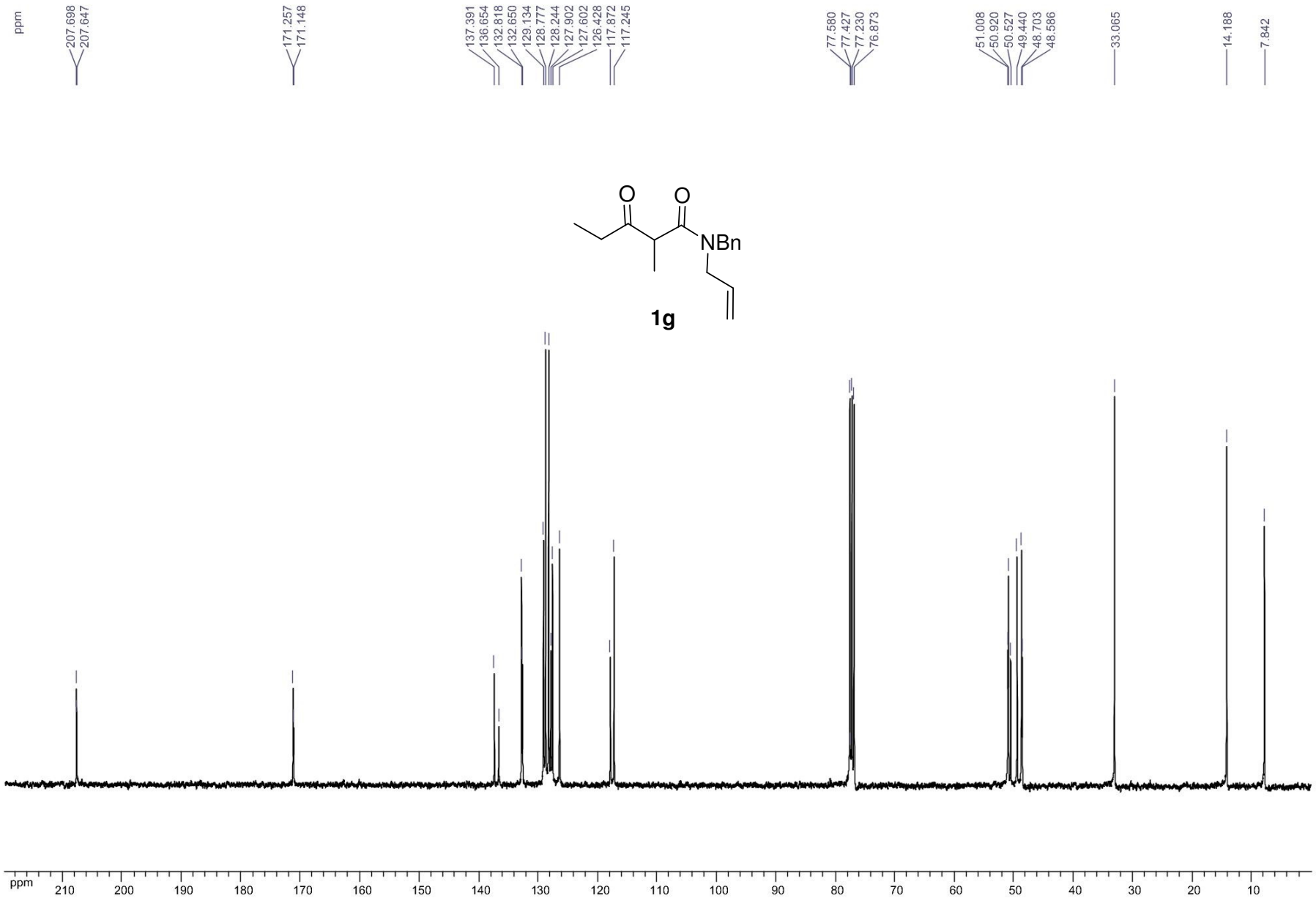

ppm
7,353
7,332
7,326
7,319
7,302
7,281
7,265
7,260
7,246
7,222
7,218
7,199
7,160
7,140
5,766
5,750
5,737
5,732
5,718
5,703
5,689
5,244
5,217
5,215
5,175
5,148
5,145
5,128
5,117
5,114
5,069
5,066
4,854
4,812
4,739
4,692
4,428
4,399
4,380
4,358
3,980
3,975
3,969
3,787
3,774
3,739
3,725
3,482
3,462
3,443
2,165
2,139
2,055
2,038
2,035
2,018
1,997
1,976
1,946
1,926
1,907
1,887
1,881
1,863
0,943
0,923
0,903
0,883
0,863
0,842
O
O
NBn
1e
9,8
1,9
4,0
2,0
2,0
2,1
2,2
2,0
5,8
2,0
2,0
6,0
ppm
9,5
9
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5

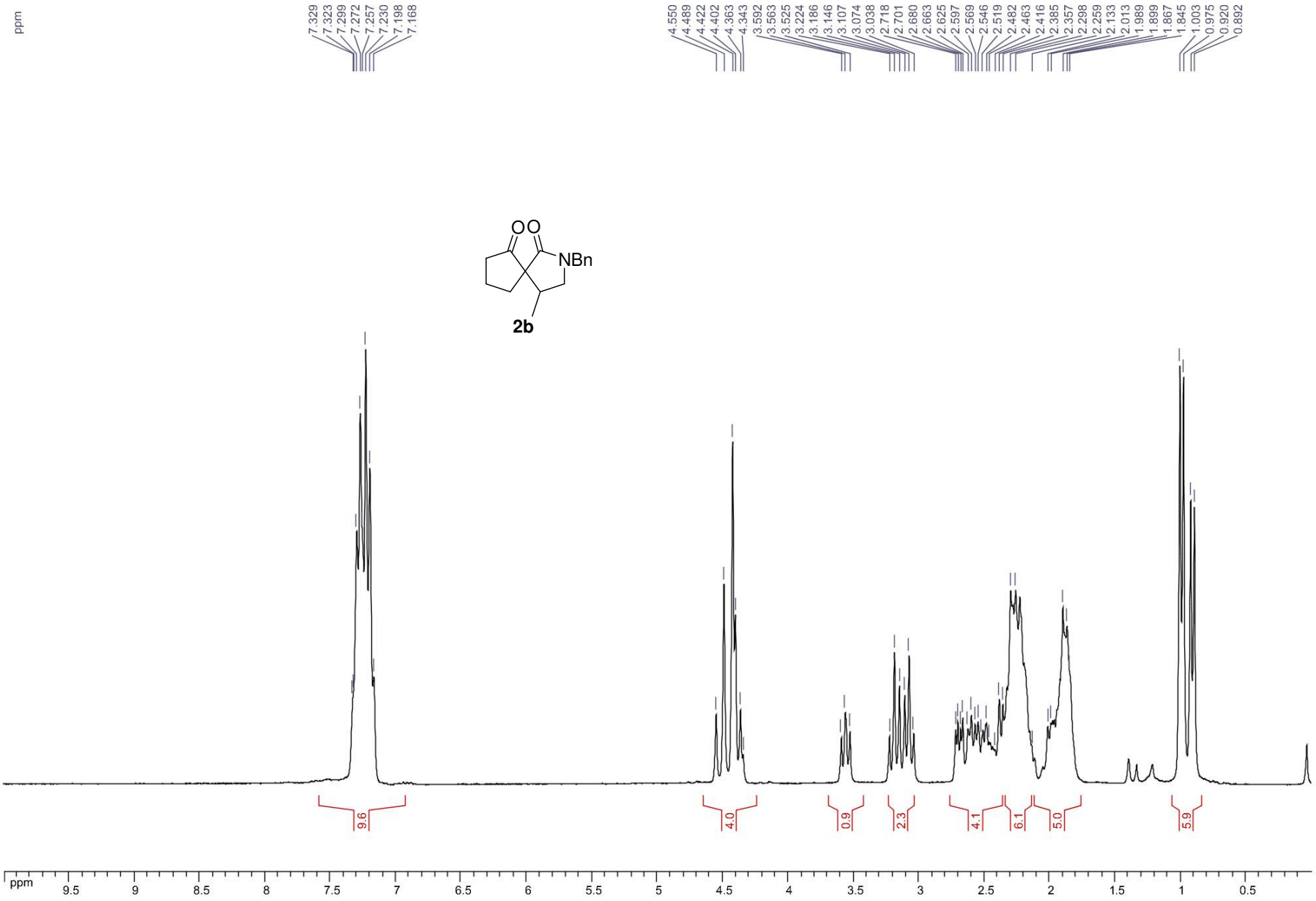

ppm
205,381
169,621
169,474
137,440
136,680
132,764
132,661
129,081
128,789
128,248
127,868
127,620
126,523
117,843
117,229
77,741
77,435
77,230
76,733
60,161
60,073
50,296
49,244
48,806
48,674
27,060
23,099
12,358
O
O
NBn
1e
ppm
200
180
160
140
120
100
80
60
40
20

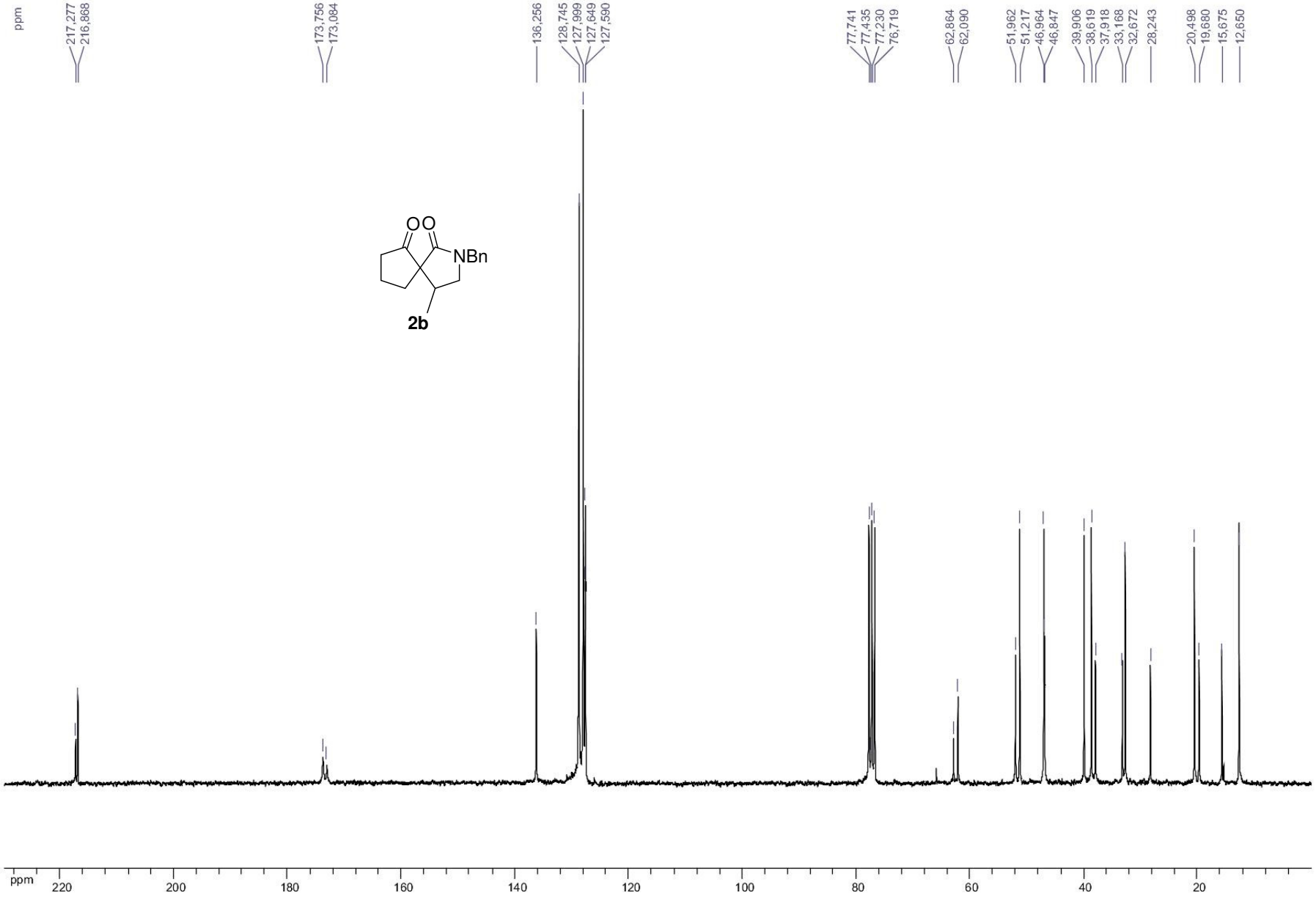

ppm
7.366
7.280
7.258
7.205
7.190
7.109
7.091
6.864
6.858
6.845
6.834
5.755
5.679
5.476
5.423
5.150
5.116
5.093
5.056
5.049
4.990
4.986
4.937
4.879
4.692
4.626
4.577
4.496
4.479
4.447
4.421
4.135
4.077
4.068
3.894
3.875
3.862
3.844
3.835
3.826
3.813
3.783
3.763
3.713
3.705
3.698
3.576
3.560
3.517
3.366
3.351
3.335
3.321
3.306
3.290
3.276
3.213
3.196
3.168
3.153
3.138
3.110
3.093
2.220
2.151
O
O
NBn
Bn
1f
20.1
2.0
4.1
5.3
4.1
1.2
2.1
2.1
6.0
ppm
9.5
9
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5

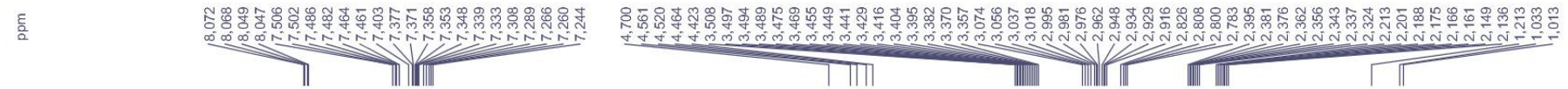

ppm
204.051
169.324
169.098
138.602
138.536
137.136
136.414
132.497
129.222
129.039
128.704
128.354
127.748
127.610
126.815
126.508
118.025
117.398
77.580
77.230
76.873
60.067
59.783
50.213
49.323
48.980
48.915
35.661
27.777
27.696
O
O
NBn
Bn
1f
ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

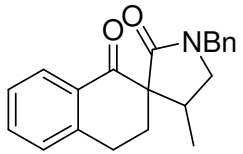

ppm
7.398
7.365
7.342
7.319
7.289
7.280
7.260
7.242
7.235
5.823
5.802
5.759
5.734
5.714
5.693
5.674
5.264
5.206
5.159
5.153
5.091
5.085
4.792
4.733
4.685
4.615
4.484
4.426
4.405
4.246
4.169
3.907
3.895
3.890
3.870
3.823
3.737
3.663
3.634
3.595
2.633
2.560
2.531
2.525
2.497
2.468
2.396
1.416
1.388
1.377
1.349
1.063
1.034
1.006
0.979
O
O
NBn
1g
4.9
1.0
2.0
2.0
2.1
1.0
2.0
3.0
3.0
ppm
9.5
9
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5


ppm
207.698
207.647
171.257
171.148
137.391
136.654
132.818
132.650
129.134
128.777
128.244
127.902
127.602
126.428
117.872
117.245
77.580
77.427
77.230
76.873
51.008
50.920
50.527
49.440
48.703
48.586
33.065
14.188
7.842
O
O
NBn
1g
ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10


ppm
7.329
7.323
7.299
7.272
7.257
7.230
7.198
7.168
4.550
4.489
4.422
4.402
4.363
4.343
3.592
3.563
3.525
3.224
3.186
3.146
3.107
3.074
3.038
2.718
2.701
2.680
2.663
2.625
2.597
2.569
2.546
2.519
2.482
2.463
2.416
2.385
2.357
2.298
2.259
2.133
2.013
1.989
1.899
1.867
1.845
1.003
0.975
0.920
0.892
O
O
NBn
2b
9.6
4.0
0.9
2.3
4.1
6.1
5.0
5.9
ppm
9.5
9
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5

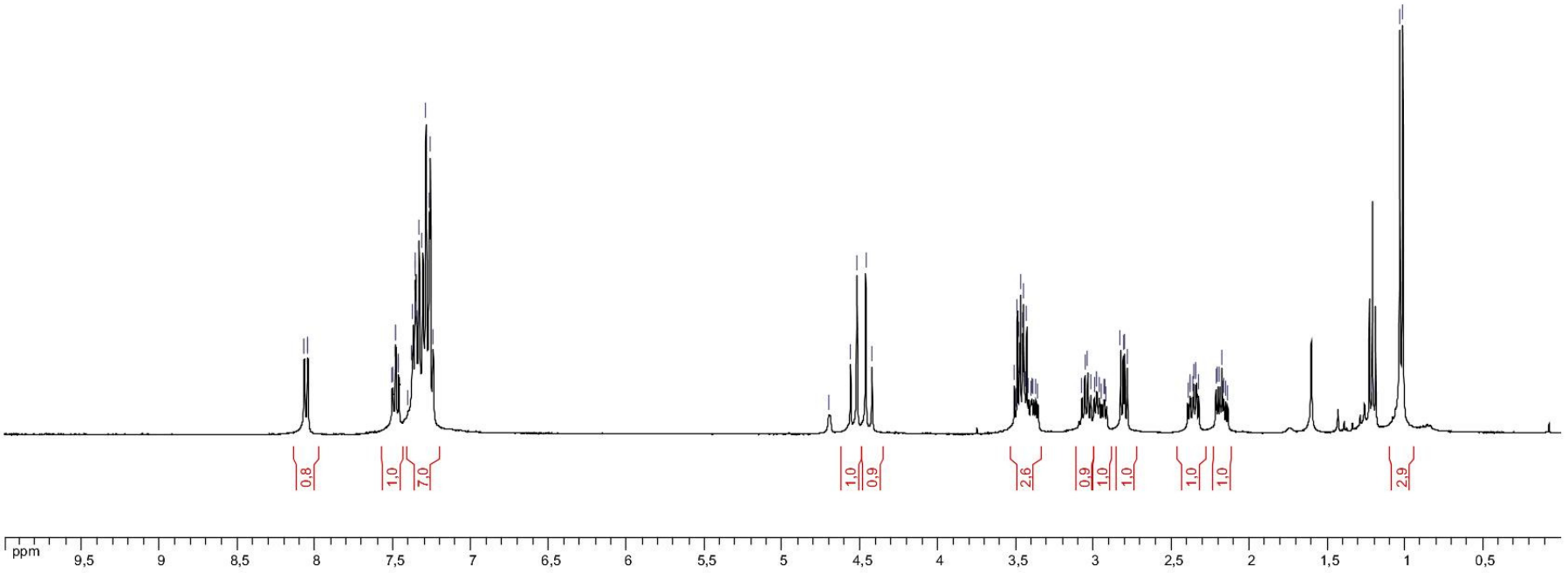

ppm
217,277
216,868
173,756
173,084
136,256
128,745
127,999
127,649
127,590
77,741
77,435
77,230
76,719
62,864
62,090
51,962
51,217
46,964
46,847
39,906
38,619
37,918
33,168
32,672
28,243
20,498
19,680
15,675
12,650
O
O
NBn
2b
ppm
220
200
180
160
140
120
100
80
60
40
20

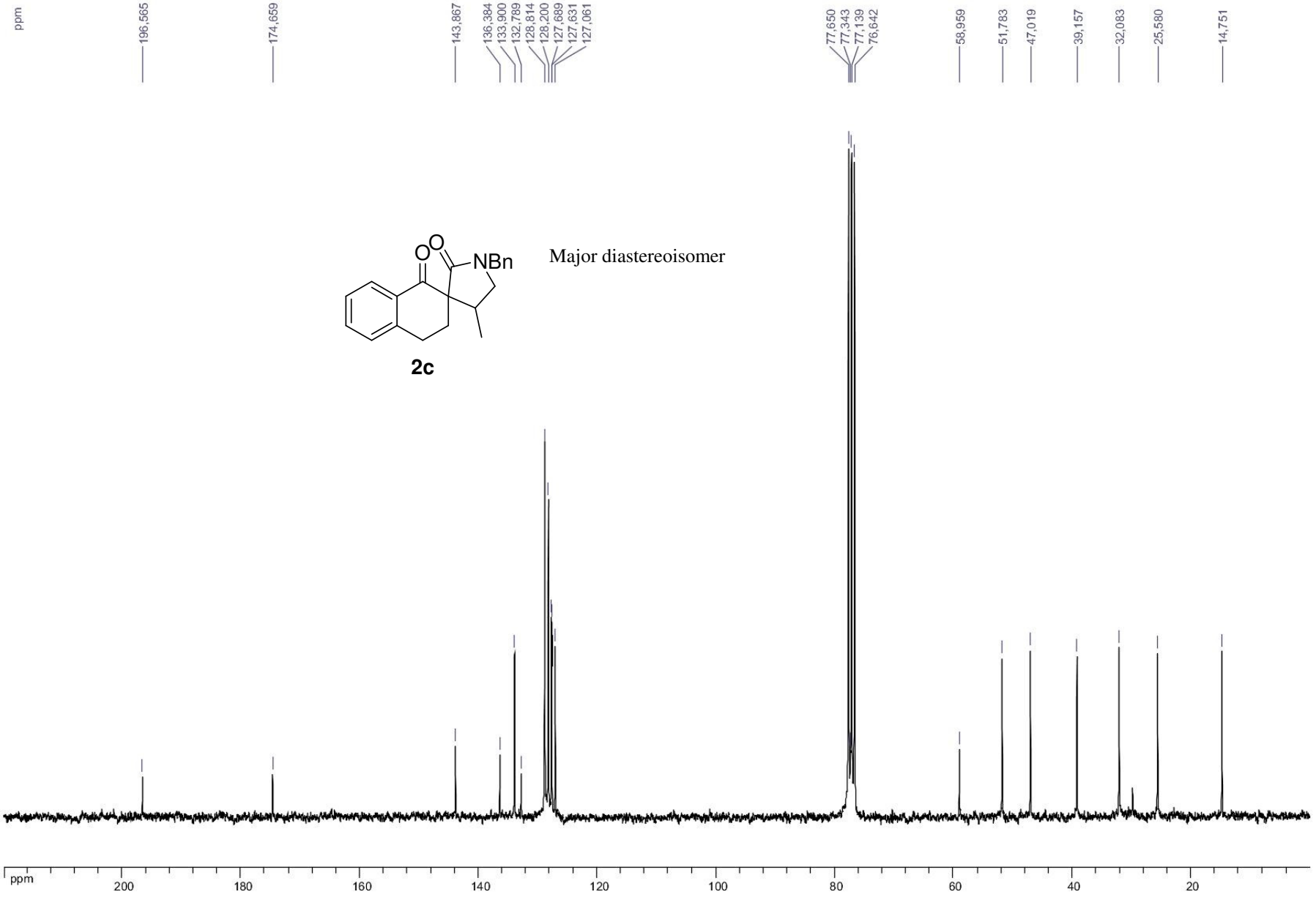


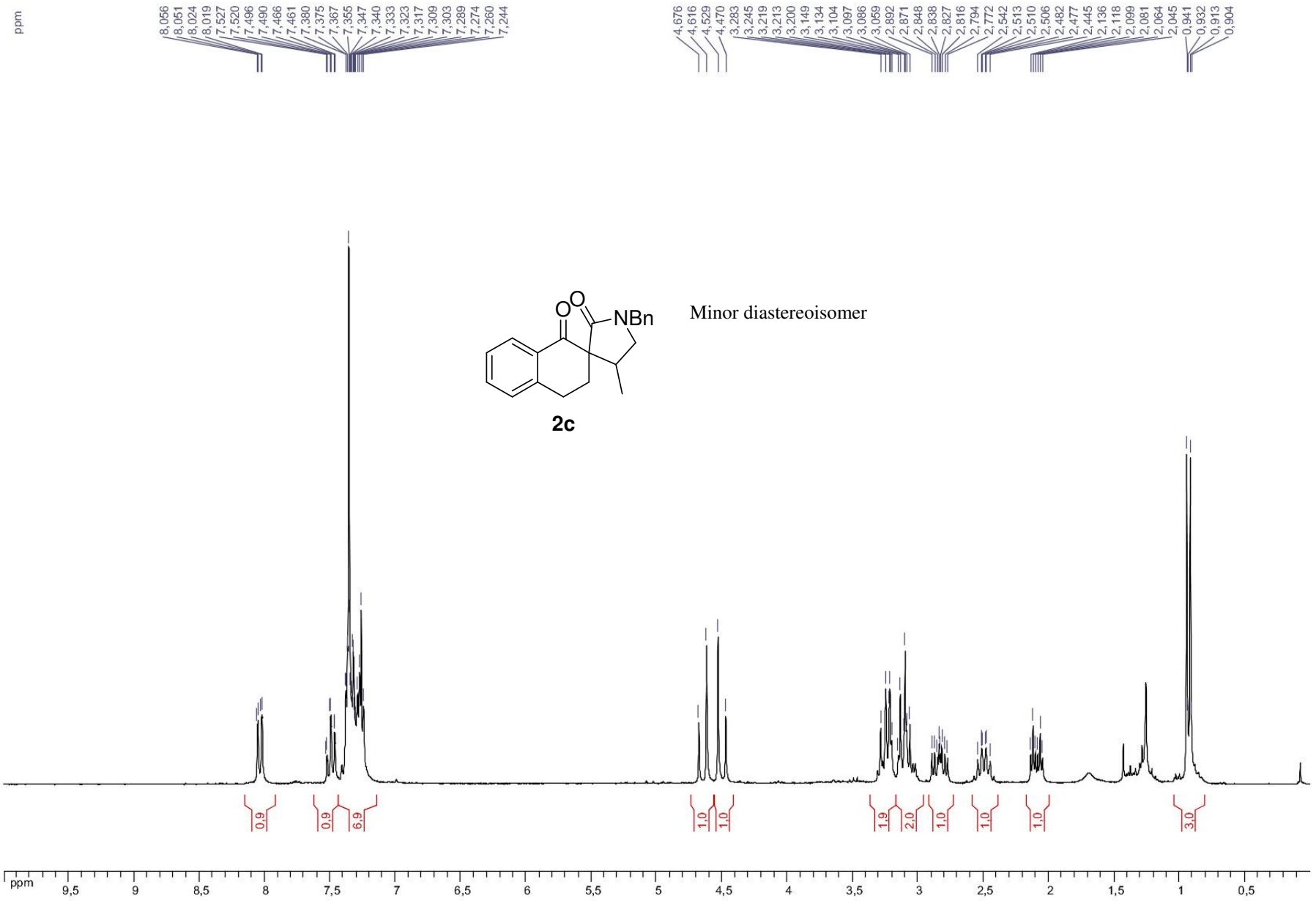


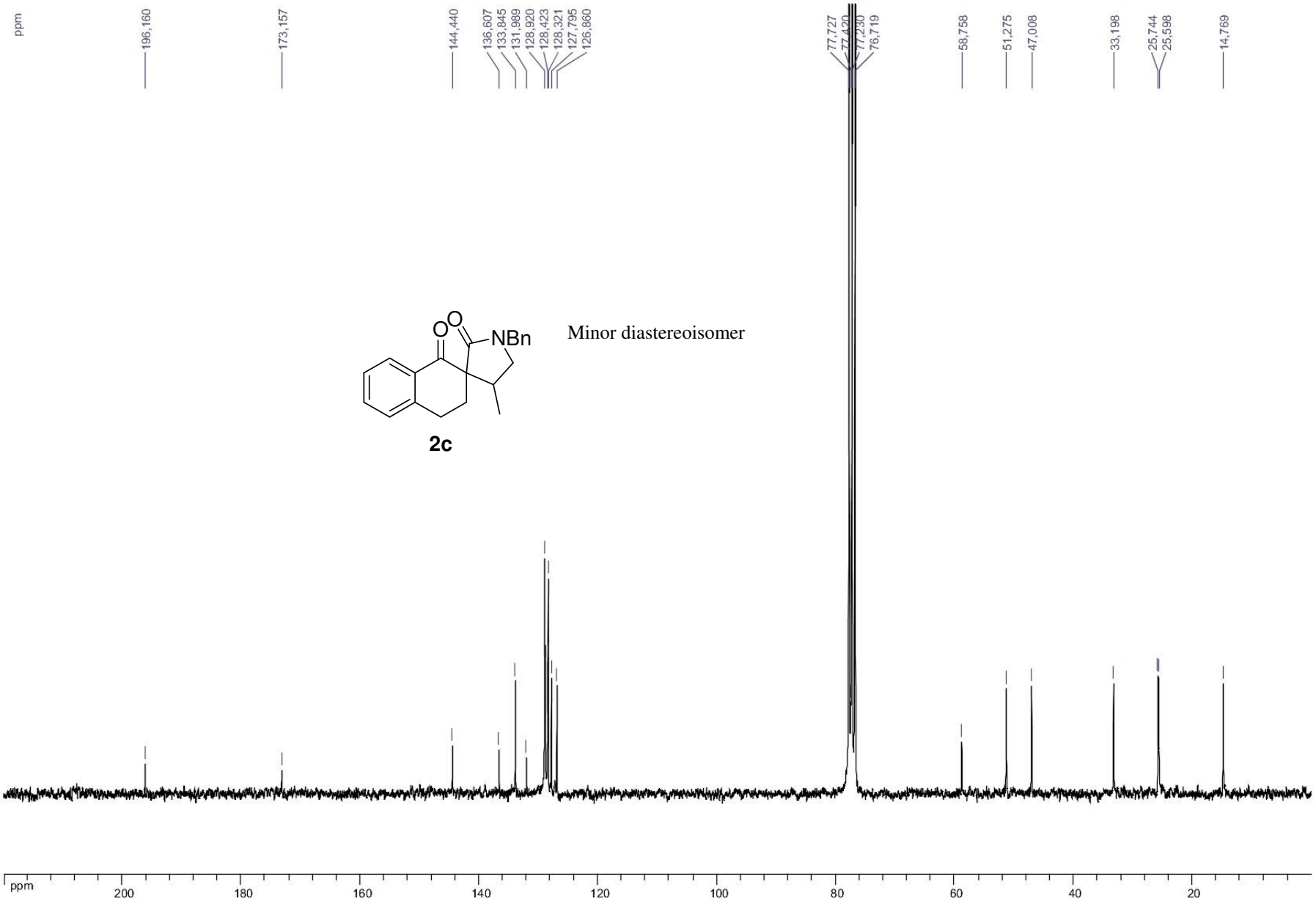
2c

Major diastereoisomer



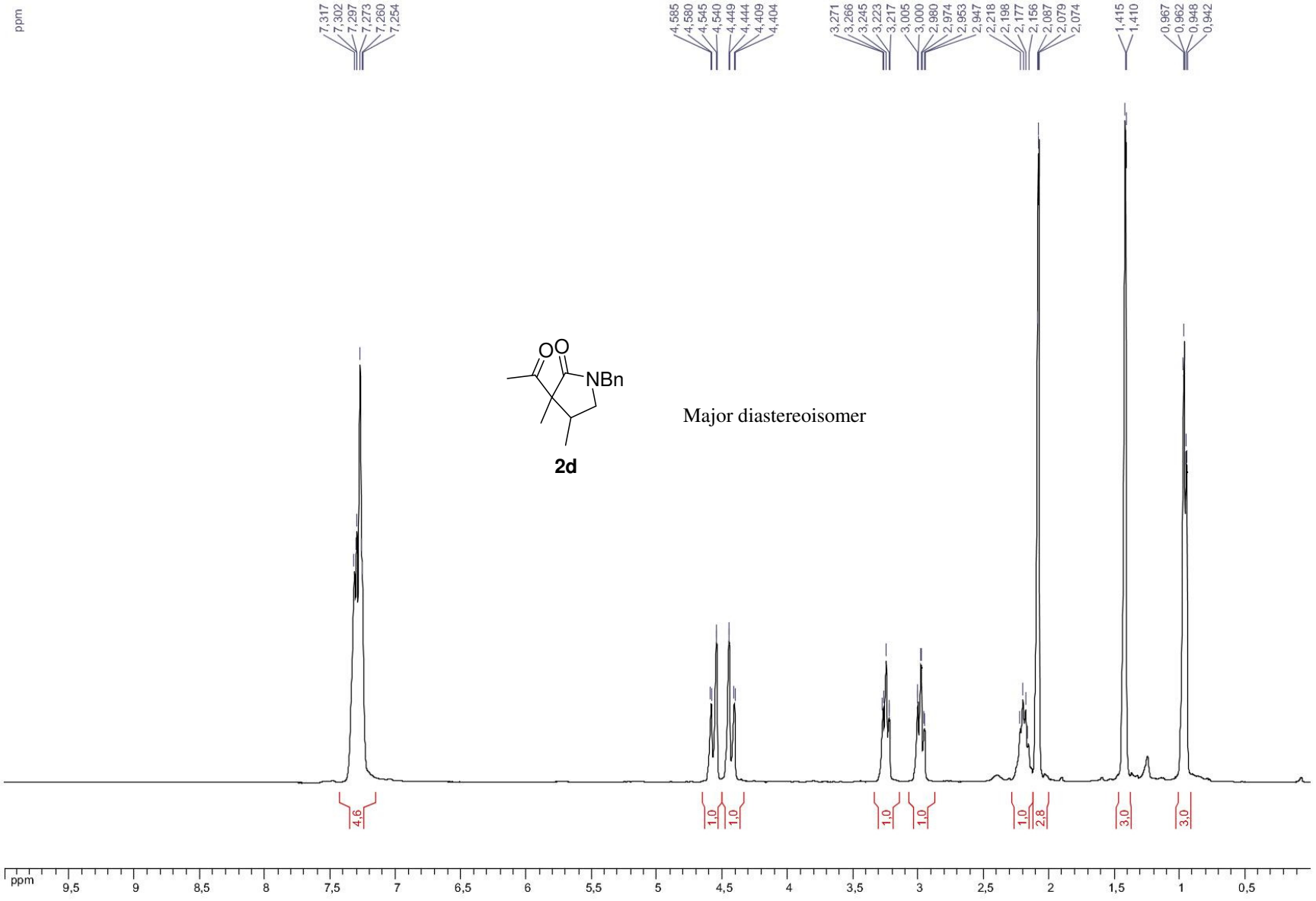

ppm
196,565
174,659
143,867
136,384
133,900
132,789
128,814
128,200
127,689
127,631
127,061
77,650
77,343
77,139
76,642
58,959
51,783
47,019
39,157
32,083
25,580
14,751
O
O
NBn
Major diastereoisomer
2c
ppm
200
180
160
140
120
100
80
60
40
20

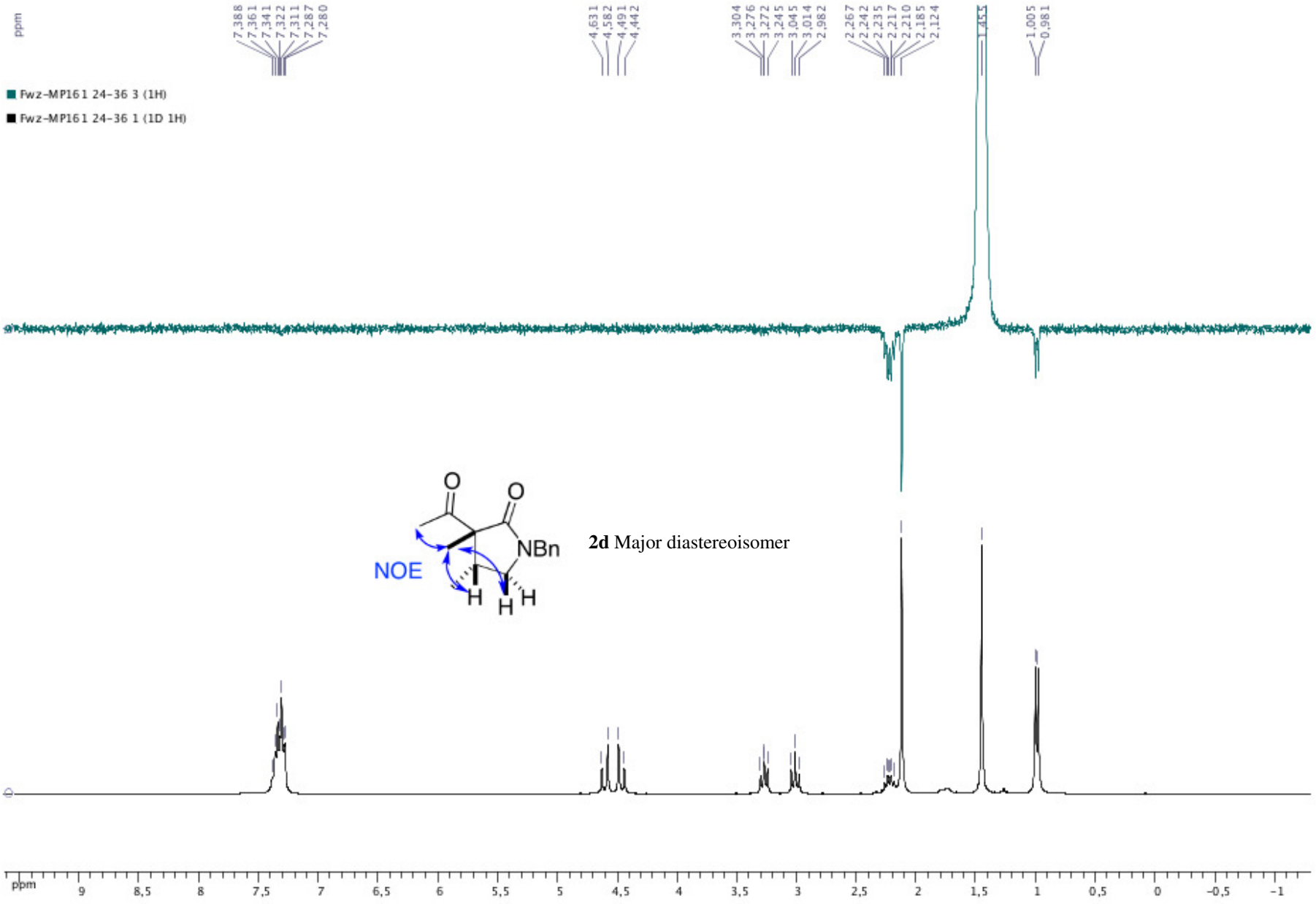

ppm
8,056
8,051
8,024
8,019
7,527
7,520
7,496
7,490
7,466
7,461
7,380
7,375
7,367
7,355
7,347
7,340
7,333
7,323
7,317
7,309
7,303
7,289
7,274
7,260
7,244
4,676
4,616
4,529
4,470
3,283
3,245
3,219
3,213
3,200
3,149
3,134
3,104
3,097
3,086
3,059
2,892
2,871
2,848
2,838
2,827
2,816
2,794
2,772
2,542
2,513
2,510
2,506
2,482
2,477
2,445
2,136
2,118
2,099
2,081
2,064
2,045
0,941
0,932
0,913
0,904
O
O
NBn
2c
Minor diastereoisomer
0,9
0,9
6,9
1,0
1,0
1,9
2,0
1,0
1,0
1,0
3,0
ppm
9,5
9
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5



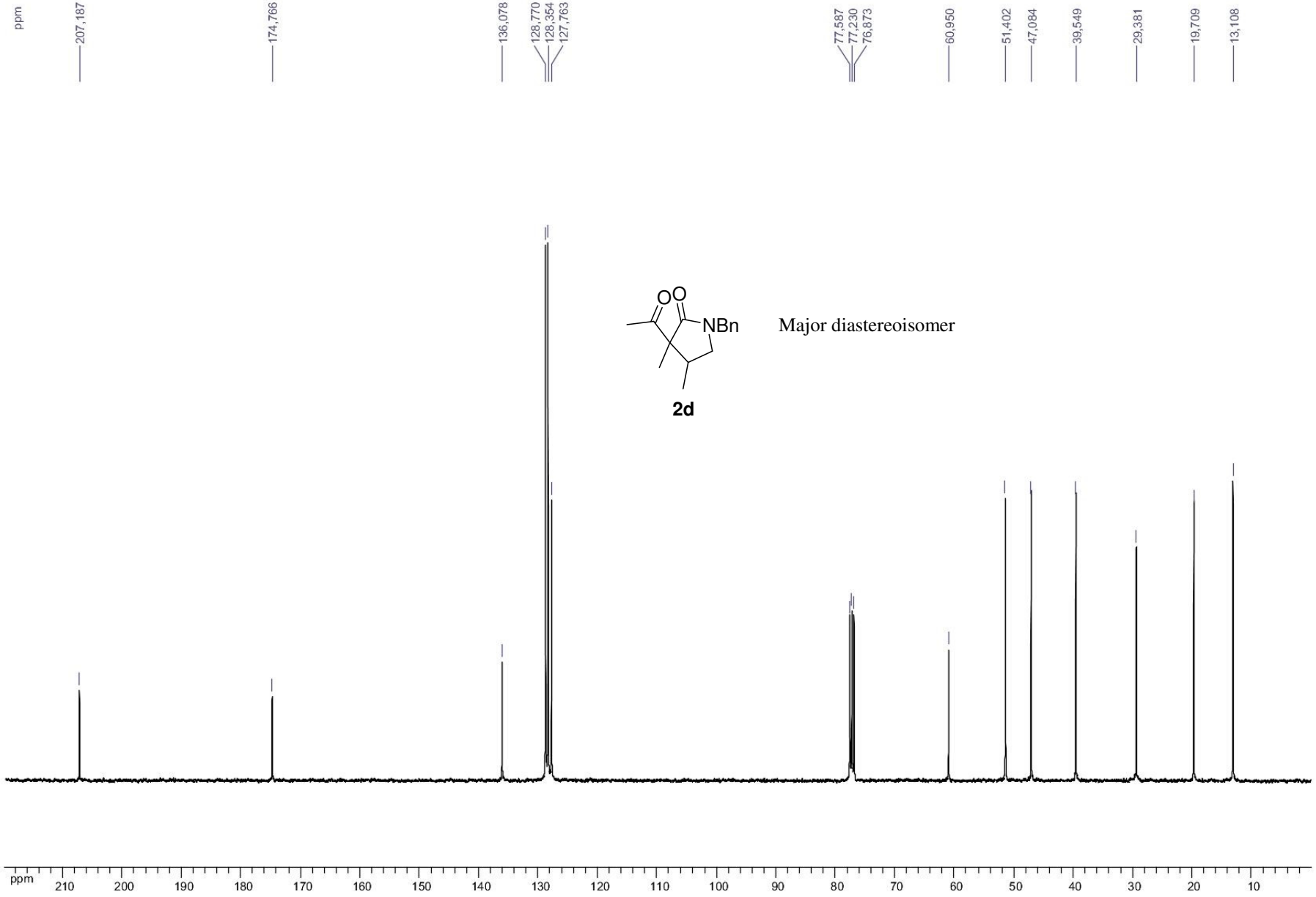
Minor diastereoisomer

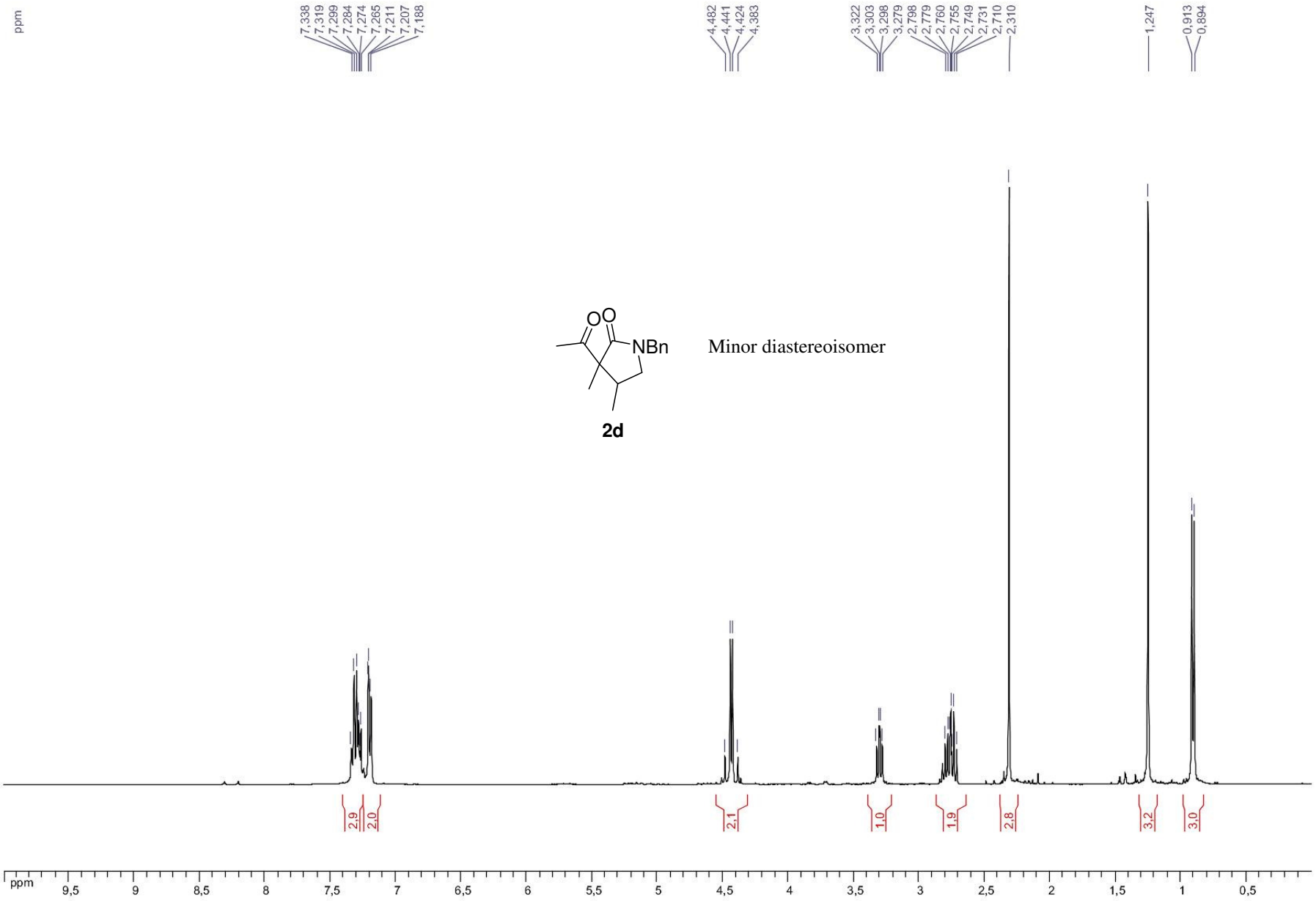
2c

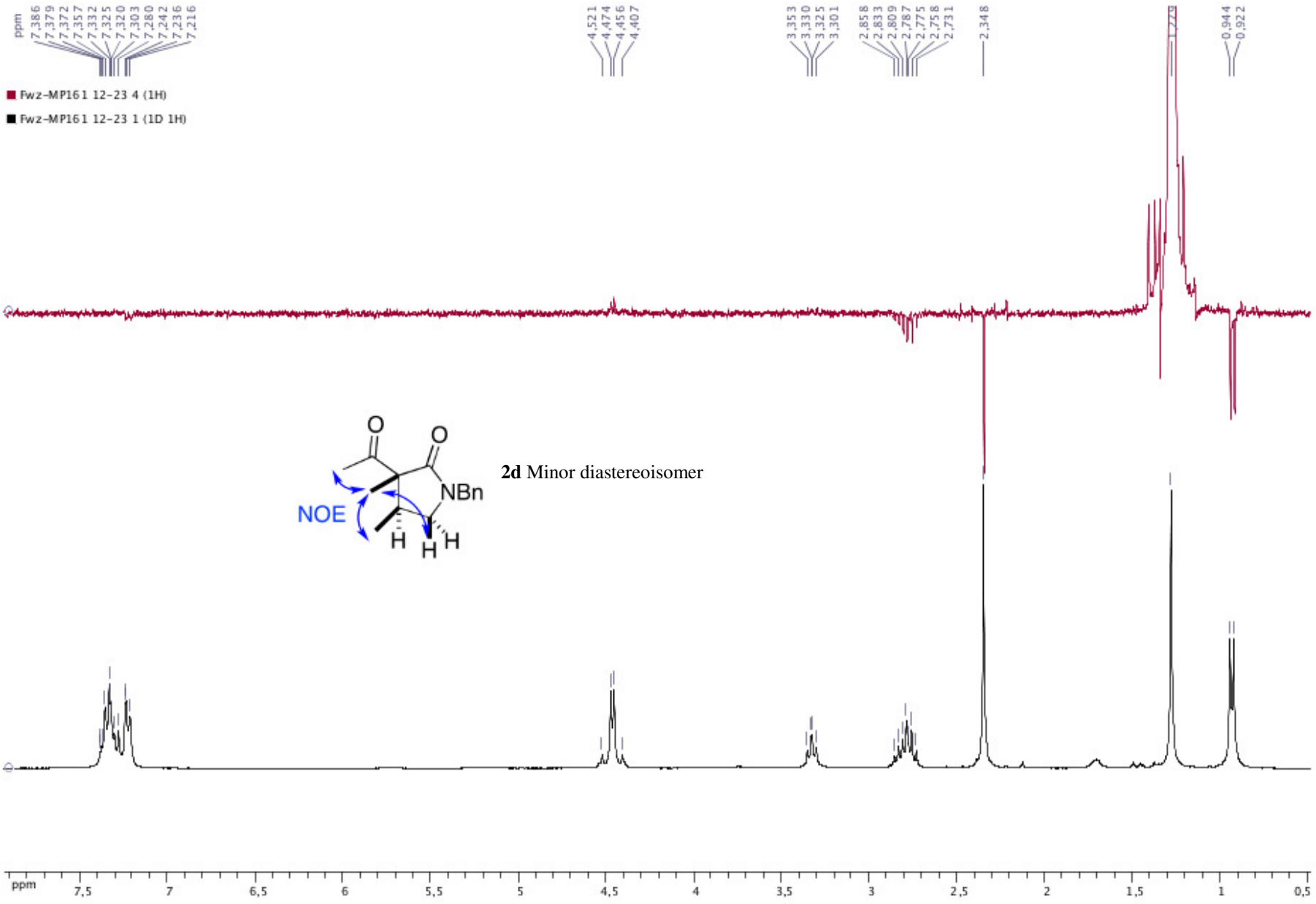

ppm
7,317
7,302
7,297
7,273
7,260
7,254
4,585
4,580
4,545
4,540
4,449
4,444
4,409
4,404
3,271
3,266
3,245
3,223
3,217
3,005
3,000
2,980
2,974
2,953
2,947
2,218
2,198
2,177
2,156
2,087
2,079
2,074
1,415
1,410
0,967
0,962
0,948
0,942
O
O
NBn
2d
Major diastereoisomer
4,6
1,0
1,0
1,0
1,0
1,0
2,8
3,0
3,0
ppm
9,5
9
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5



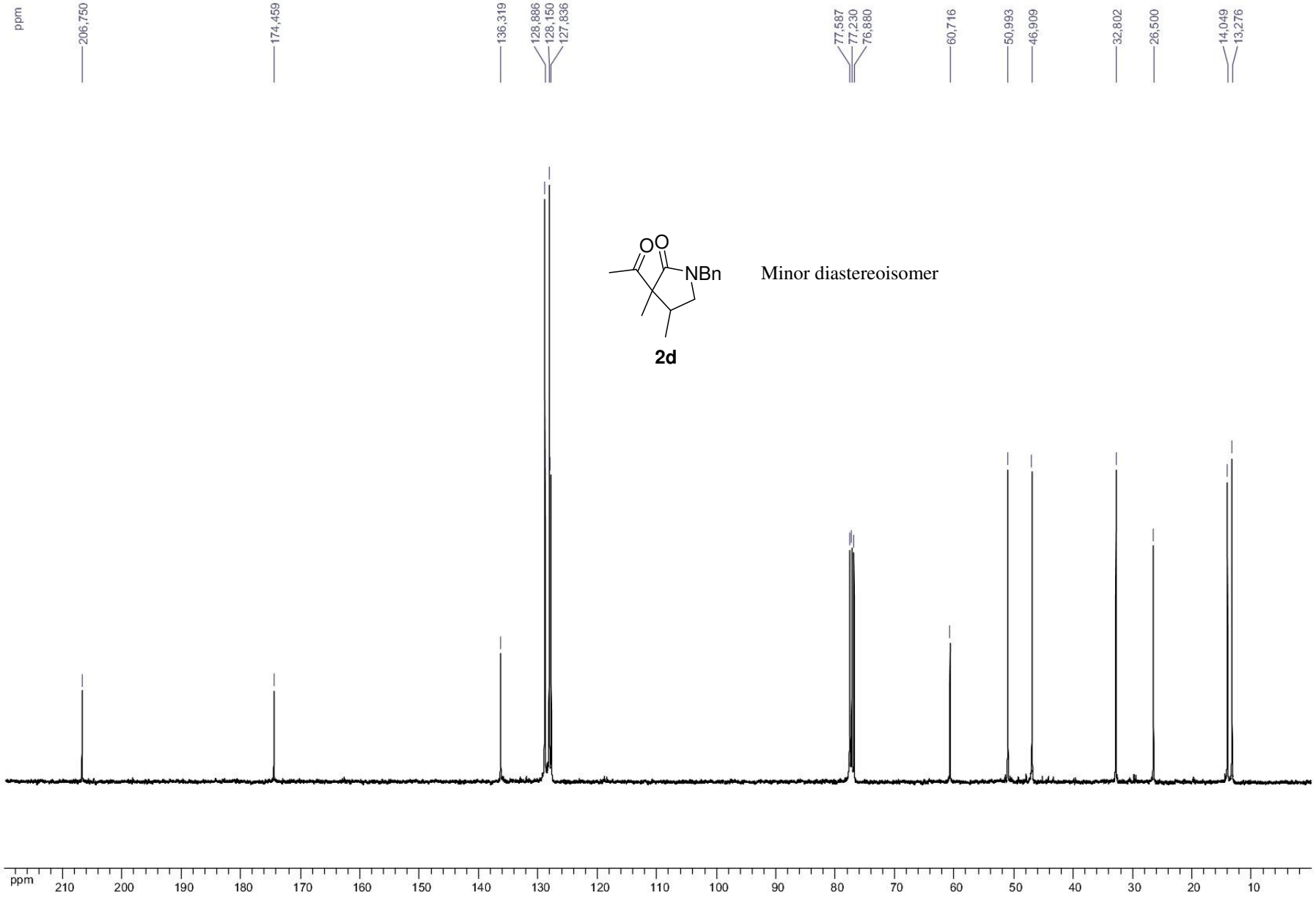
2d Major diastereoisomer

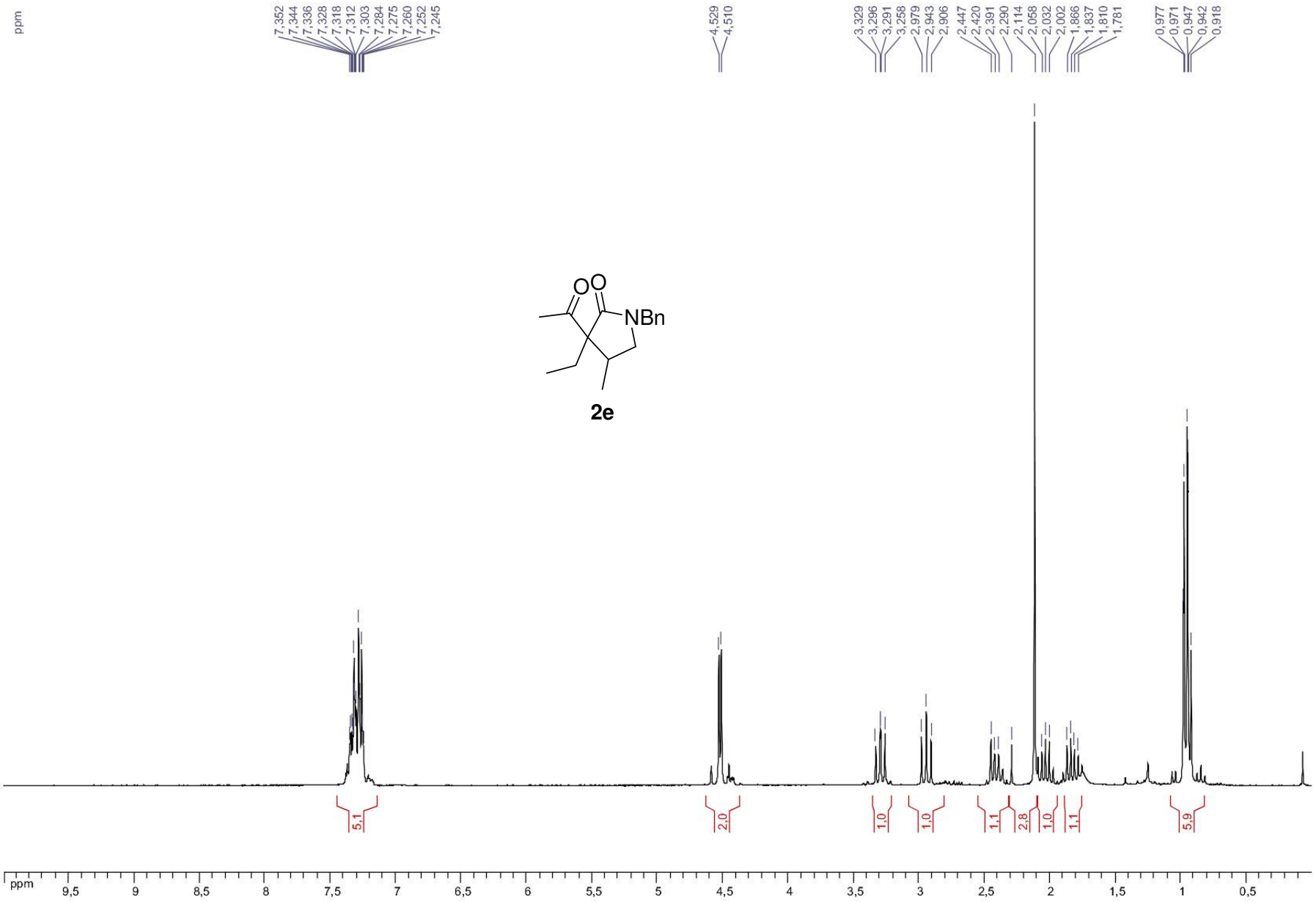

ppm
207,187
174,766
136,078
128,770
128,354
127,763
77,587
77,230
76,873
60,950
51,402
47,084
39,549
29,381
19,709
13,108
O
O
NBn
Major diastereoisomer
2d
ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

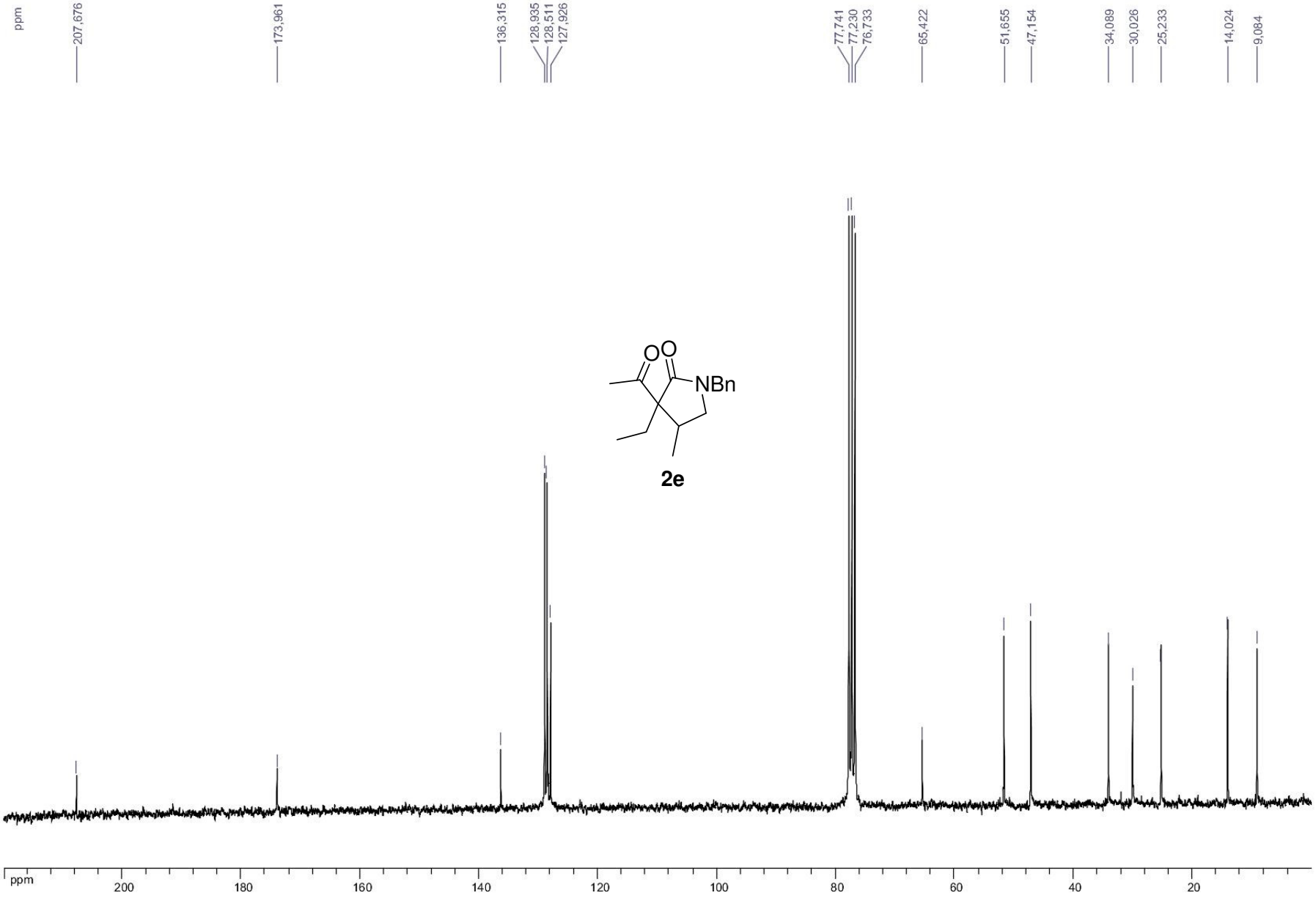

ppm
7,338
7,319
7,299
7,284
7,274
7,265
7,211
7,207
7,188
4,482
4,441
4,424
4,383
3,322
3,303
3,298
3,279
2,798
2,779
2,760
2,755
2,749
2,731
2,710
2,310
1,247
0,913
0,894
O
O
NBn
2d
Minor diastereoisomer
2,9
2,0
2,1
1,0
1,9
2,8
3,2
3,0
ppm
9,5
9
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5

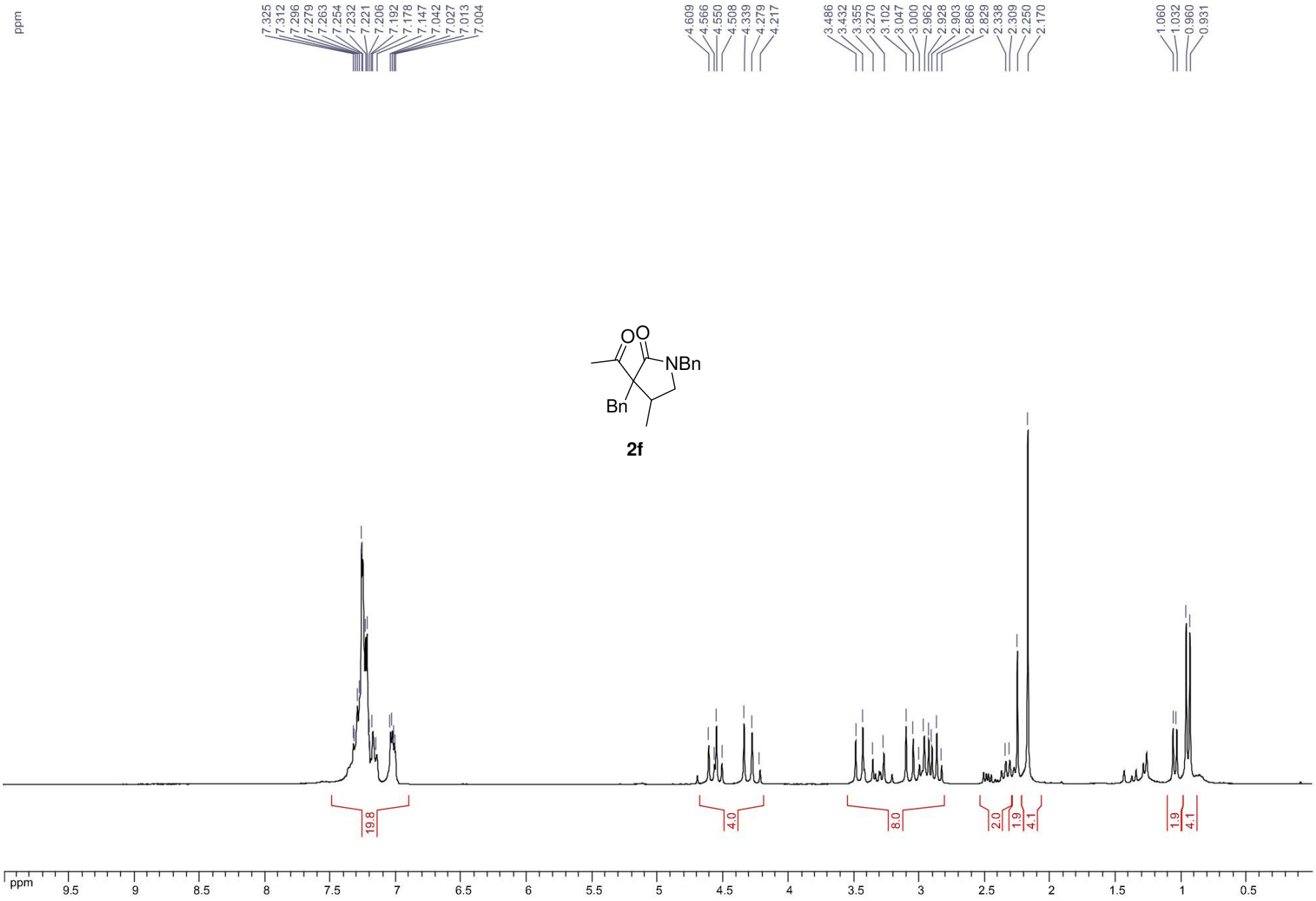


2d Minor diastereoisomer

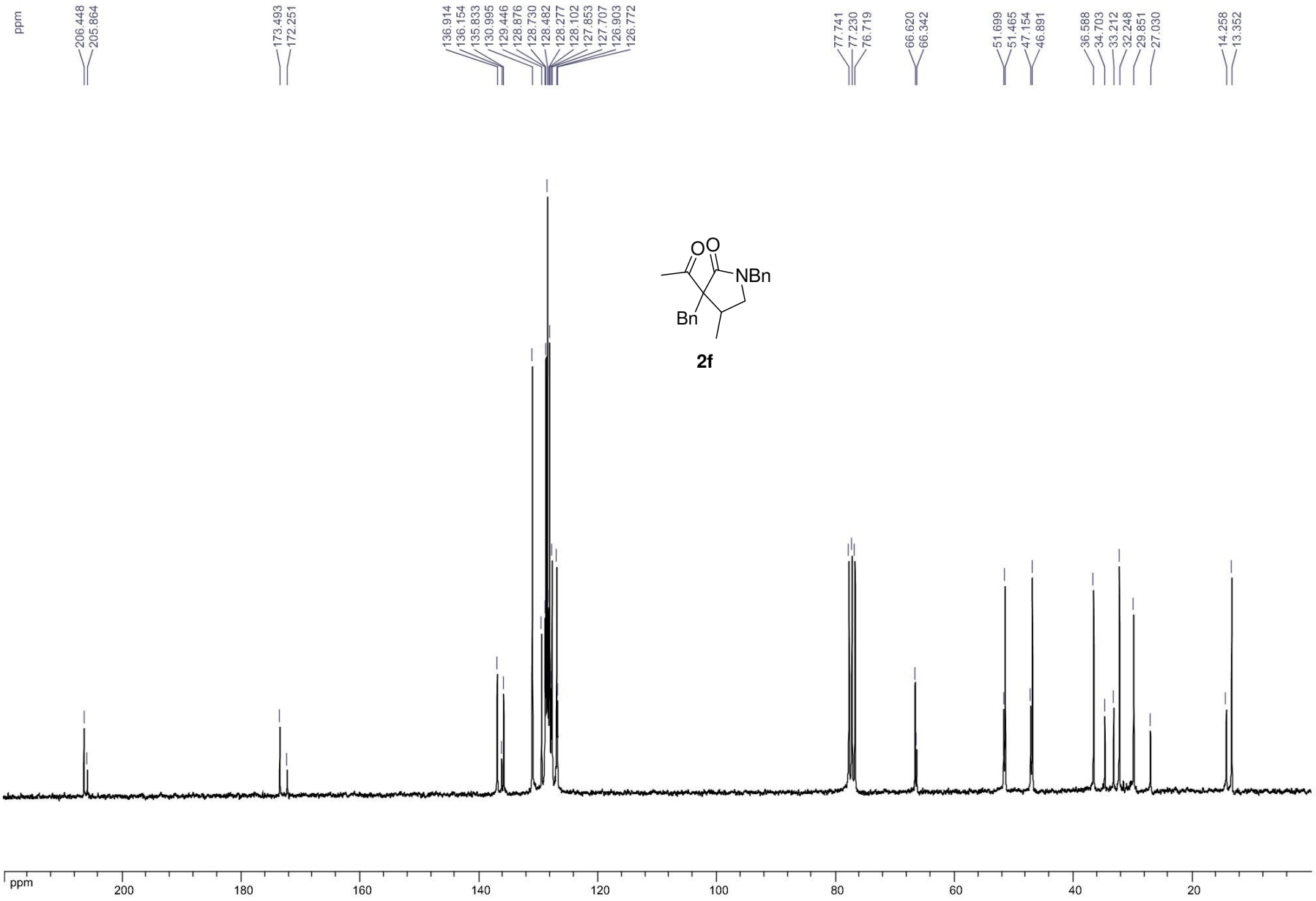

ppm
206,750
174,459
136,319
128,886
128,150
127,836
77,587
77,230
76,880
60,716
50,993
46,909
32,802
26,500
14,049
13,276
O
O
NBn
Minor diastereoisomer
2d
ppm
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10

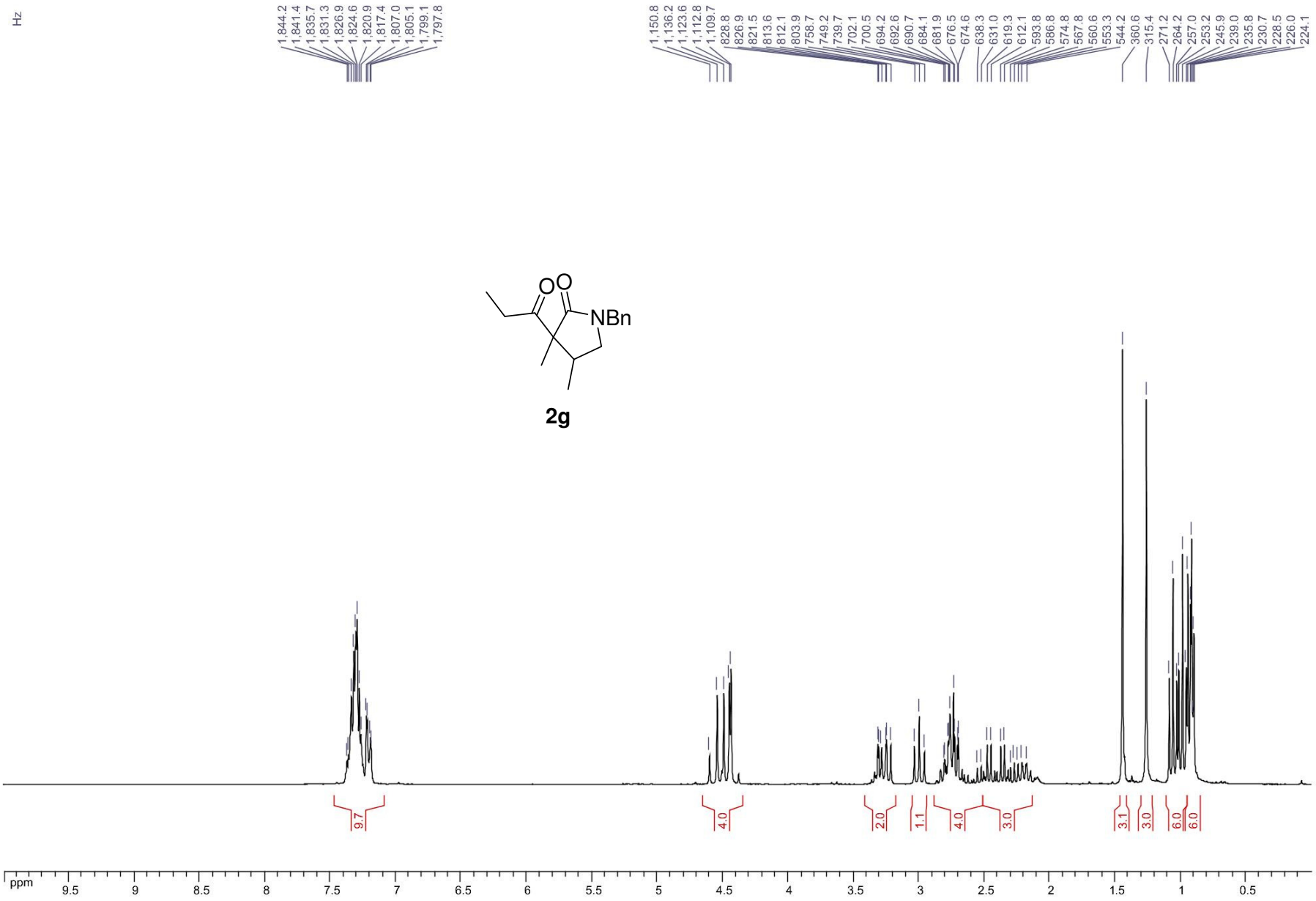

ppm
7,352
7,344
7,336
7,328
7,318
7,312
7,303
7,284
7,275
7,260
7,252
7,245
4,529
4,510
3,329
3,296
3,291
3,258
2,979
2,943
2,906
2,447
2,420
2,391
2,290
2,114
2,058
2,032
2,002
1,866
1,837
1,810
1,781
0,977
0,971
0,947
0,942
0,918
O
O
NBn
2e
5,1
2,0
1,0
1,0
1,1
2,8
1,0
1,1
5,9
ppm
9,5
9
8,5
8
7,5
7
6,5
6
5,5
5
4,5
4
3,5
3
2,5
2
1,5
1
0,5


ppm
207,676
173,961
136,315
128,935
128,511
127,926
77,741
77,230
76,733
65,422
51,655
47,154
34,089
30,026
25,233
14,024
9,084
O
O
NBn
2e
ppm
200
180
160
140
120
100
80
60
40
20

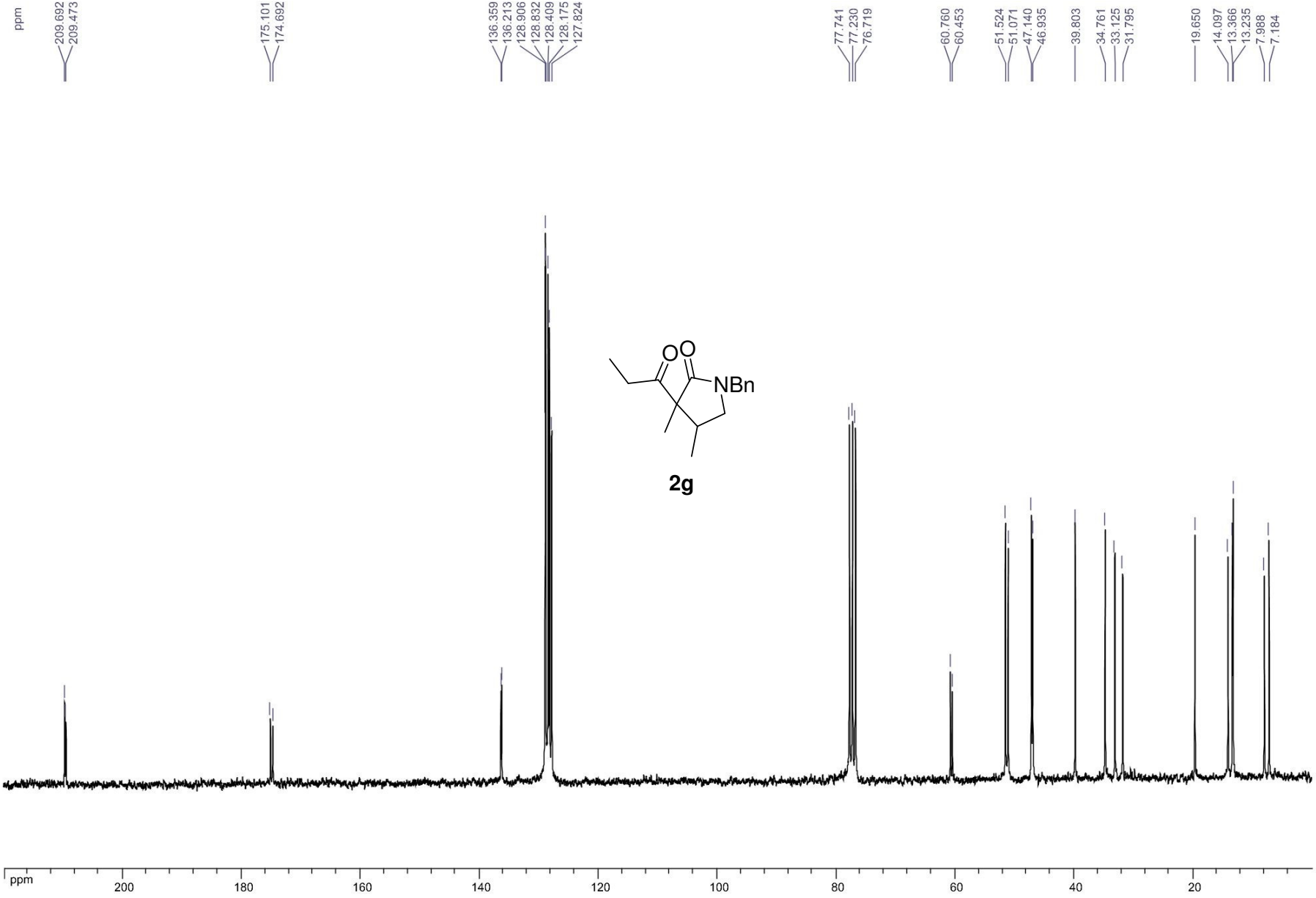

ppm
7.325
7.312
7.296
7.279
7.263
7.254
7.232
7.221
7.206
7.192
7.178
7.147
7.042
7.027
7.013
7.004
4.609
4.566
4.550
4.508
4.339
4.279
4.217
3.486
3.432
3.355
3.270
3.102
3.047
3.000
2.962
2.928
2.903
2.866
2.829
2.338
2.309
2.250
2.170
1.060
1.032
0.960
0.931
O
O
NBn
Bn
19.8
4.0
8.0
2.0
1.9
4.1
1.9
4.1
ppm
9.5
9
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5

2f


ppm
206.448
205.864
173.493
172.251
136.914
136.154
135.833
130.995
129.446
128.876
128.730
128.482
128.277
128.102
127.853
127.707
126.903
126.772
77.741
77.230
76.719
66.620
66.342
51.699
51.465
47.154
46.891
36.588
34.703
33.212
32.248
29.851
27.030
14.258
13.352
O
O
NBn
Bn
2f
ppm
200
180
160
140
120
100
80
60
40
20


Hz
1,844.2
1,841.4
1,835.7
1,831.3
1,826.9
1,824.6
1,820.9
1,817.4
1,807.0
1,805.1
1,799.1
1,797.8
1,150.8
1,136.2
1,123.6
1,112.8
1,109.7
828.8
826.9
821.5
813.6
812.1
803.9
758.7
749.2
739.7
702.1
700.5
694.2
692.6
690.7
684.1
681.9
676.5
674.6
638.3
631.0
619.3
612.1
593.8
586.8
574.8
567.8
560.6
553.3
544.2
360.6
315.4
271.2
264.2
257.0
253.2
245.9
239.0
235.8
230.7
228.5
226.0
224.1
O
O
NBn
9.7
4.0
2.0
1.1
4.0
3.0
3.1
3.0
6.0
6.0
ppm
9.5
9
8.5
8
7.5
7
6.5
6
5.5
5
4.5
4
3.5
3
2.5
2
1.5
1
0.5

2g


ppm
209.692
209.473
175.101
174.692
136.359
136.213
128.906
128.832
128.409
128.175
127.824
77.741
77.230
76.719
60.760
60.453
51.524
51.071
47.140
46.935
39.803
34.761
33.125
31.795
19.650
14.097
13.366
13.235
7.988
7.184
O
O
NBn
2g
ppm
200
180
160
140
120
100
80
60
40
20

References

[1] C. Nieto-Oberhuber, S. Lopez, A. M. Echavarren, *J. Am. Chem. Soc.*, 2005, **127**, 6178.
[2] M. J. Johansson, D. J. Gorin, S. T. Staben and F. D. Toste, *J. Am. Chem. Soc.*, 2005, **127**, 18002.
[3] D. Vasu, R. Liu, *Chem. Eur. J.* 2012, **18**, 13638.
[4] M. P. Muñoz, J. Adrio, J. C. Carretero and A. M. Echavarren, *Organometallics*, 2005, **24**, 1293.
[5] G. L. Lalonde, B. D. Sherry, E. J. Kang and F. D. Toste, *J. Am. Chem. Soc.* 2007, **129**, 2452.
[6] Z. Zhang, C. F. Bender, R. A. Widenhoefer, *J. Am. Chem. Soc.* 2007, **129**, 14148.
[7] P. García-García, A. Martínez, A. M. Sanjuán, M. A. Fernández-Rodríguez, R. Sanz, *Org. Lett.* 2012, **14**, 4970.
[8] a) A. Pradal, C.-M. Chao, M. R. Vitale, P. Y.Toullec and V. Michelet, *Tetrahedron*, 2011, **67**, 4371; b) C. Sarcher, A. Lühl, F. C. Falk, S. Lebedkin, M. Kühn, C. Wang, J. Paradies, M. M. Kappes, W. Klopper and P. W. Roesky, *Eur. J. Inorg. Chem.*, 2012, 5033.
[9] A. Arnanz, C. González-Arellano, A. Juan, G.Villaverde, A. Corma, M. Iglesias and F. Sánchez, *Chem. Commun.*, 2010, **46**, 3001.
[10] N. Delpont, I. Escofet, P. Pérez-Galán, D. Spiegl, M. Raducan, C. Bour, R. Sinisi and A. M. Echavarren, *Catal. Sci. Technol.*, 2013, **3**, 3007.
[11] A. Z. González and F. D. Toste, *Org. Lett.*, 2010, **12**, 200.
[12] A. Z. González, D. Benitez, E. Tkatchouk, W. A. Goddard III and F. D. Toste, *J. Am. Chem. Soc.*, 2011, **133**, 5500.
[13] B. W. Gung, L. N. Bailey, D. T. Craft, C. L. Barnes and K. Kirschbaum, *Organometallics*, 2010, **29**, 3450.
[14] I. Alonso, B. Trillo, F. López, S. Montserrat, G. Ujaque, L. Castedo, A. Lledós and J. L. Mascareñas, *J. Am. Chem. Soc.*, 2009, **131**, 13020.
[15] H. Teller, S. Flügge, R. Goddard and A. Fürstner, *Angew. Chem. Int. Ed.*, 2010, **49**, 1949.
[16] S. Ma, X. Han, S. Krishnan, S. C. Virgil and B. M. Stoltz, *Angew. Chem. Int. Ed.*, 2009, **48**, 8037.
[17] a) C.-Y. Zhou and C.-M. Che, *J. Am. Chem. Soc*., 2007, **129**, 5828; b) A. Guérinot, W. Fang, M. Sircoglou, C. Bour, S. Bezzenine-Lafollée and V. Gandon, *Angew. Chem. Int. Ed*., 2013, **52**, 5848; c) W. Fang, M. Presset, A. Guérinot, C. Bour, S. Bezzenine-Lafollée and V. Gandon, *Chem. Eur. J*., 2014, **20**, DOI: 10.1002/chem.201304831.
[18] S. M. Smith, G. L. Hoang, R. Pal, M. O. B. Khaled, L. S. W. Pelter, X. C. Zenga and J. M. Takacs, *Chem. Commun.*, 2012, **48**, 12180.
[19] For Au/Ga-catalyzed addition of 1,3-dicarbonyls to alkynes, see: Y. Xi, D. Wang, X. Ye, N. G. Akhmedov, J. L. Petersen and X. Shi, *Org. Lett.*, 2013, **16**, 306.