Supporting Information

for

Synthesis of *cis*-hydrindan-2,4-diones bearing an *all*-carbon quaternary center by a Danheiser annulation

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Experimental procedures and copies of ^{1}H and ^{13}C NMR spectra of all compounds.

Table of contents

General. All reactions were carried out under an argon atmosphere with dry, freshly distilled solvents under anhydrous conditions. All product mixtures were analyzed by thin-layer chromatography using TLC silica gel plates with a fluorescent indicator (λ = 254 nm). Analytical thin-layer chromatography was performed on SiO_2 (Merck silica gel 60 F_{254}), and the spots were located by UV light or/and a 1% $KMnO_4$ aqueous solution. Chromatography refers to flash chromatography and was carried out on SiO_2 (silica gel 60 ACC, 230–240 mesh). Drying of organic extracts during the reaction workup was performed over anhydrous Na_2SO_4. Chemical shifts of ^1H and ^{13}C NMR spectra are reported in ppm downfield (δ) from Me_4Si. All NMR data assignments are supported by gCOSY and gHSQC experiments.

5-Methyl-2-{3-[*N*-benzyl-*N*-(4-methylphenylsulfonyl)]aminopropyl} cyclohex-2-enone (4).

Method A: Decahydroquinoline **1** (5.0 g) was prepared from β-ketoester **2** in 79% yield on a 15 mmol scale, following our previously reported procedure.[1] Compound **1** (2.0 g, 4.75 mmol) was treated with TFA (3.3 mL) for 15 min at room temperature, the solvent was removed, and the last traces of TFA were removed by azeotroping with toluene (2 × 10 mL). The reaction flask was maintained on the rotatory evaporator in vacuo at 70 °C for 3 h. To a solution of the resulting ketone in THF (21 mL) were added successively LiOH (568 mg, 23.74 mmol, 5.0 equiv), KI (2.36 g, 14.24 mmol, 3.0 equiv) and benzyl bromide (1.7 mL, 14.24 mmol, 3.0 equiv), and the mixture was stirred at reflux temperature overnight. The mixture was allowed to reach room temperature, filtered through a pad of celite in vacuo and the filter cake was thoroughly washed with CH_2Cl_2. Volatiles were removed and the residue was purified by chromatography (2.5–10% EtOAc/hexane) to give cyclohexenone **4** (1.7 g, 86%, 68% overall yield from the starting material **2**); R_f = 0.42 (25% EtOAc/hexanes). ^1H NMR ($CDCl_3$, 400 MHz) δ 1.00 (d, J = 6.2 Hz, 3H, CH_3), 1.46 (quint, J = 7.7 Hz, 2H, H-2'), 1.90-2.06 (m, 4H, H-4, H-6, H-1'), 2.27-2.43

[1] Bradshaw, B.; Luque-Corredera, C.; Bonjoch, J. *Org. Lett.* **2013**, *15*, 326–329.

(m, 5H, H-4, H-6, $ArCH_3$), 3.03 (m, 2H, H-3'), 4.30 (CH_2Ph), 6.46 (m, 1H, H-3), 7.28 (m, 7H, *o*-Ts, Ph), 7.71 (d, *J* = 8.3 Hz, 2H, *m*-Ts); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.2 (CH_3), 21.6 ($ArCH_3$), 26.5 (C-5), 26.7 (C-2'), 30.6 (C-1'), 34.4 (C-4), 46.6 (C-6), 47.6 (C-3'), 51.9 (CH_2Ph), 127.3 (*o*-Ts), 127.8 (*p*-Bn), 128.6 (*o*-Bn), 129.8 (*m*-Ts), 136.6 (*ipso*-Bn), 137.0 (*p*-Ts), 138.2 (*ipso*-Ts), 143.3 (C-2), 145.1 (C-3), 199.5 (C-1). HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{24}H_{30}NO_3S$ 412.1941, found 412.1938.

Method B (one-pot procedure): To a cooled (0 °C) solution of keto ester **2** (1.05 g, 2.84 mmol, 1.0 equiv) in iPrOH (10 mL) and H_2O (0.5 mL, 28.4 mmol, 10 equiv) was added crotonaldehyde (0.26 mL, 3.13 mmol, 1.1 equiv) followed by $LiOH·H_2O$ (119 mg, 2.84 mmol, 1 equiv). The reaction mixture was allowed to reach room temperature and stirred for 24 h. To this flask was added the resin (PS) of *p*-toluenesulfonic acid (4.3 g, 30–60 mesh, Aldrich) and the mixture was stirred for 2 h. After filtration and concentration the crude toluenesulfonamide **3** was processed as in Method A to give **4** (674 mg, 56% from **2**).

(1*RS*,4*SR*,6*RS*)-1-[*N*-Benzyl-*N*-(4-methylphenylsulfonyl)-3-aminopropyl]-4,9-dimethyl-8 trimethylsilylbicyclo[4.3.0]non-8-en-2-one (5). To a cooled (−78 °C) solution of **4** (471 mg, 1.14 mmol) and 1-methyl-1-(trimethylsilyl)allene (0.32 mL, 1.94 mmol) in CH_2Cl_2 (6 mL), $TiCl_4$ (0.21 mL, 1.7 mmol) was added dropwise. The resulting dark red solution was stirred at that temperature for 1 h and then transferred to a mixture of water (25 mL) and diethyl ether (25 mL). The aqueous layer was extracted with diethyl ether (3 × 25 mL) and the combined organic layers were washed with brine (25 mL), dried, and concentrated. The crude product was purified by chromatography (2.5–10% EtOAc/hexane) to give **5** (385 mg, 63%), followed by **6** (78 mg, 15%), as an epimeric mixture.

Compund **5**: R_f = 0.54 (25% EtOAc/hexanes); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.09 (s, 9H, $(CH_3)_3Si$), 0.85 (d, *J* = 6.8 Hz, 3H, CH_3), 1.15-1.25 (m, 4H, H-5eq, H-1', 2H-2'), 1.39 (td, *J* = 12.4, 3.3 Hz, 1H, H-5ax), 1.44 (t, *J* = 2.1 Hz, 3H, 9-CH_3), 1.50 (dm, *J* = 13.6 Hz, 1H, H-1'), 1.77 (dd, *J* = 16.0, 8.5 Hz, 1H, H-3ax), 1.99-2.05 (m, 2H, H-4, H-7), 2.11 (dddd, *J* = 10, 5, 5, 5 Hz, 1H, H-6), 2.27 (ddd, *J* = 16.0, 5.6, 1.4 Hz, 1H, H-3eq), 2.43 (s, 3H, $ArCH_3$), 2.44 (ddq, *J* = 11.0, 5.5, 2.1

Hz, 1H, H-7), 3.06 (t, *J* = 7.4 Hz, 2H, H-3'), 4.30 (2d, *J* = 14.8 Hz, 2H, CH_2Ph), 7.30-7.35 (m, 7H, *o*-Ts, Ph), 7.73 (d, *J* = 8.3 Hz, 2H, *m*-Ts); ^{13}C NMR ($CDCl_3$, 100 MHz) δ -0.6 ($(CH_3)_3Si$), 14.0 (9-CH_3), 21.6 (CH_3), 21.6 ($ArCH_3$), 23.4 (C-2'), 26.9 (C-4), 31.0 (C-5), 37.0 (C-1'), 41.6 (C-6), 43.5 (C-7), 47.3 (C-3), 49.0 (C-3'), 52.4 (NCH_2Ar), 69.7 (C-1), 127.3 (*o*-Ts), 127.8 (Ph), 128.4 (Ph), 128.7 (Ph), 129.8 (*m*-Ts), 136.8 (*ipso*-Ph), 137.1 (*p*-Ts), 138.7 (*ipso*-Ts), 143.3 (C-8), 148.8 (C-9), 214.7 (C-2). HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{31}H_{44}NO_3SSi$ 538.2806, found 538.2798.

Data for 3-(2-butynyl)-5-methyl-2-[(*N*-benzyl-*N*-(4-methylphenylsulfonyl)-3-aminopropyl]cyclohexanone (**6**): R_f = 0.39 (25% EtOAc/hexanes); ^1H NMR ($CDCl_3$, 400 MHz, major isomer) δ 0.99 (d, *J* = 6.8 Hz, 5-CH_3), 1.14-1.54 (m, 4H, H-1' 2H-2', H-4), 1.63 (2dd, *J* = 11.0, 2.6 Hz, 1H, H-1'), 1.75 (t, *J* = 2.4 Hz, CH_3), 1.93 (m, 1H, H- 1''), 2.07 (m, 3H, H-1', H-4, H-5), 2.26 (m, 2H, H-3, H-6, H-2), 2.43 (s, $ArCH_3$), 3.06 (m, 2H, H-3'), 4.23 (s, 2H, CH_2Ph), 7.29 (m, 5H, Ph, *m*-Ts), 7.71 (d, *J* = 8.0 Hz, 2H *o*-Ts). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 3.6 (CH_3), 18.0 (C-1´´), 21.6 (CH_3Ts), 22.4 (5-CH_3), 23.2 (C-1´), 26.1 (C-2´), 29.8 (C-5), 38.7 (C-4), 40.2 (C-3), 47.6 (C-3´), 50.2 (C-6), 51.4 (NCH_2Ar), 52.6 (C-2), 76.5 (C-3´´), 77.8 (C-2´´), 127.3 (*o*-Ts), 127.8 (*p*-Bn), 128.5 (*m*-Bn), 128.6 (*o*-Bn), 129.8 (*m*-Ts), 136.6 (*ipso*-Bn), 136.7 (*p*-Ts), 137.1 (*ipso*-Ts), 143.3 (*p*-Ts), 211.8 (C-1). HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{28}H_{36}NO_3S$ 466.2410, found 466.2415.

(1*RS*,4S*R*,6*RS*,9*SR*)-1-[*N*-Benzyl-*N*-(4-methylphenylsulfonyl)-3-aminopropyl]-4,9-dimethylbicyclo[4.3.0]non-2,8-dione (8). To a solution of **5** (30 mg, 0.056 mmol) in CH_2Cl_2 (1 mL) was added $NaHCO_3$ (9 mg, 0.112 mmol) followed by *m*-CPBA (12 mg, 0.053 mmol) at 0 °C. After stirring for 1 h at 0 °C, 2-methyl-2-butene (0.12 mL) was added to quench the remaining traces of *m*-CPBA and the mixture was allowed to stir for 10 min at 0 °C. Filtration and concentration afforded a 3:1 mixture of diastereomeric epoxy silanes **7**, which was directly used in the following step without any further purification. An analytical sample of **7** was obtained by chromatography (5–25% EtOAc in hexanes): ^1H NMR ($CDCl_3$, 400 MHz) δ 0.08 (s, 9H, $(CH_3)_3Si$), 0.95 (d, *J* = 6.4 Hz, 3H, CH_3), 1.24 (m, 2H, H-1', H-5), 1.35 (s, 3H, 9-CH_3), 1.38-1.67 (m, 6H,

2H-2', 2H-7, H-5, H-1'), 1.84 (m, 2H, H-4, H-6), 1.95 (m, 2H, H-3), 3.06 (m, 2H, H-3'), 4.25 and 4.33 (2d, *J* = 14.8 Hz, 1H each, CH_2Ph), 7.32 (m, 7H, *o*-Ts, Ph), 7.73 (d, 2H, *J* = 8.0 Hz, *m*-Ts); ^{13}C NMR ($CDCl_3$, 100 MHz) δ −2.3 ($(CH_3)_3Si$), 16.2 (9-CH_3), 21.6 ($ArCH_3$), 22.4 (CH_3), 23.0 (C-2'), 28.0 (C-7), 31.4 (C-6), 31.6 (C-5), 33.3 (C-1'), 37.1 (C-4), 47.9 (C-3), 48.9 (C-3'), 52.4 (CH_2Ph), 59.5 (C-1), 61.4 (C-9), 69.3 (C-8), 127.3 (*o*-Ts), 127.9 (*p*-Bn), 128.7 (*m*-Bn), 128.8 (*o*-Bn), 129.9 (*m*-Ts), 136.5 (*ipso*-Bn), 137.0 (*p*-Ts), 143.4 (*ipso*-Ts), 214.7 (C-2), 217.8 (C-9). HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{31}H_{44}NO_4SSi$ 554.2755, found 554.2744.

A solution of the crude epoxide **7** in formic acid (1.0 mL) was heated at reflux for 1 h, cooled, concentrated, and purified by chromatography (2.5–10% EtOAc in hexanes) to afford diketone **8** as a 3.5:1 mixture of diastereomers (15 mg, 55% yield, over 2 steps). Data for the major diastereomer: R_f = 0.23 (50% EtOAc/hexanes); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.75 (d, *J* = 7.6 Hz, 3H, 9-CH_3), 0.97 (d, *J* = 6.4 Hz, 3H, 4-CH_3), 0.99 (m, 1H, H-2'), 1.04 (dd, *J* = 6.8, 4.0 Hz, 1H, H-2'), 1.36 (m, 2H, H-1'), 1.63-1.71 (m, 2H, H-5), 1.91-2.01 (m, 2H, H-7eq, H-3ax), 2.11 (m, 1H, H-4), 2.17 (m, 1H, H-7ax), 2.29 (dd, *J* = 13.6, 4.0 Hz, 2H, H-3eq), 2.45 (masked, 1H, H-6), 2.77 (q, *J* = 7.6 Hz, 1H, H-9), 2.97 (m, 1H, H-3'), 3.09 (q, *J* = 7.2 Hz, 1H, H-3'), 4.12-4.33 (2d, *J* = 14.8 Hz, 2H, CH_2Ph), 7.30-7.35 (m, 6H, *m*-Ts, Ph), 7.73 (d, *J* = 8.3 Hz, 2H, *o*-Ts); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 9.9 (9-CH_3), 21.1 (4-CH_3), 21.7 (CH_3Ar), 23.8 (C-2'), 28.0 (C-1'), 29.9 (C-4), 32.5 (C-5), 38.6 (C-6), 40.7 (C-7), 45.5 (C-3), 46.5 (C-9), 49.0 (C-3'), 53.0 (NCH_2Ar), 58.1 (C-1), 127.3 (*o*-Ts), 128.2 (Ph), 128.7 (Ph), 128.8 (Ph), 129.9 (*m*-Ts), 136.5 (*ipso*-Ph), 136.6 (*p*-Ts), 143.6 (*ipso*-Ts), 212.6 (C-8), 217.8 (C-2). HRMS (ESI-TOF) *m/z*: $[M + H]^+$ Calcd for $C_{28}H_{36}NO_4S$ 482.2360, found 482.2359.

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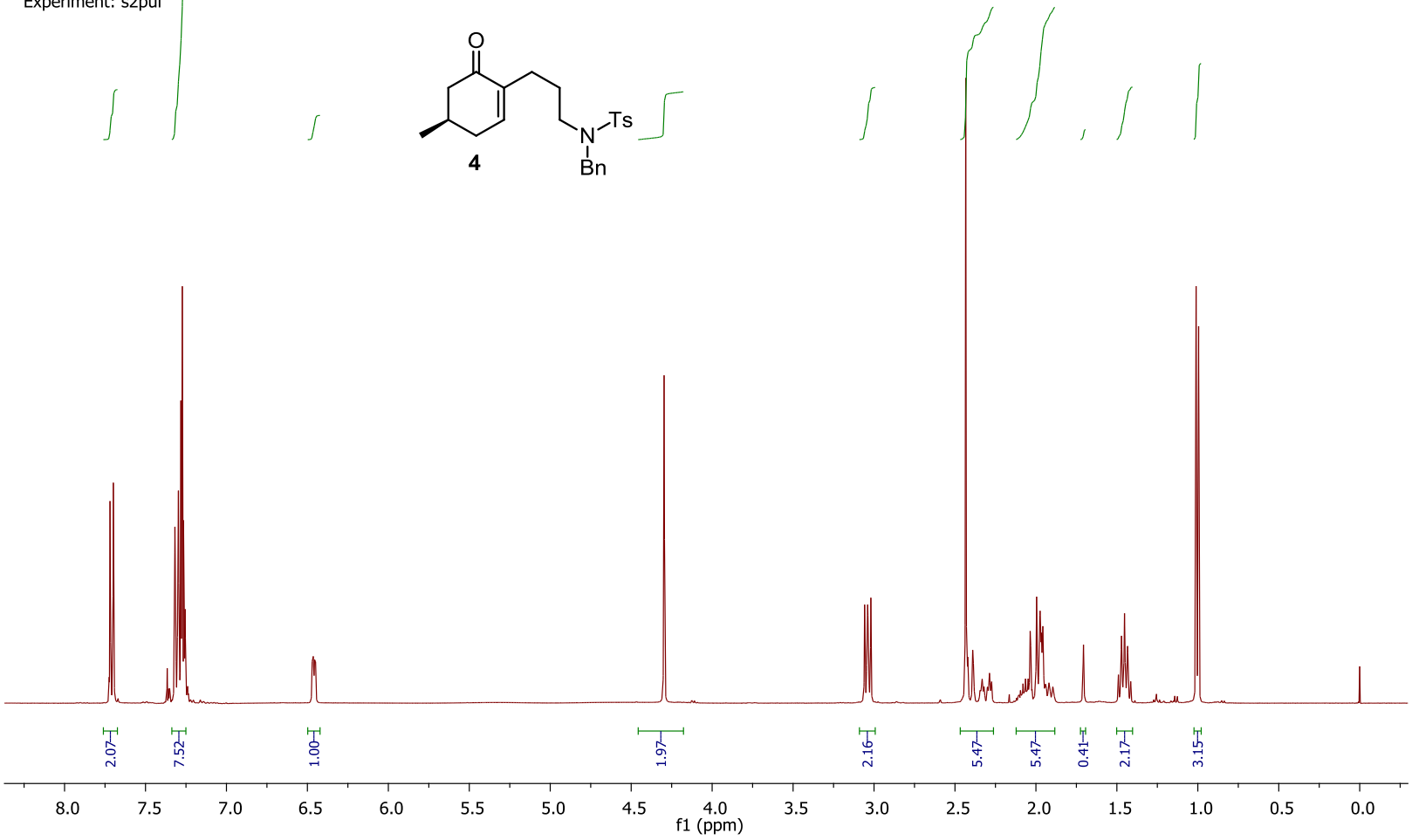

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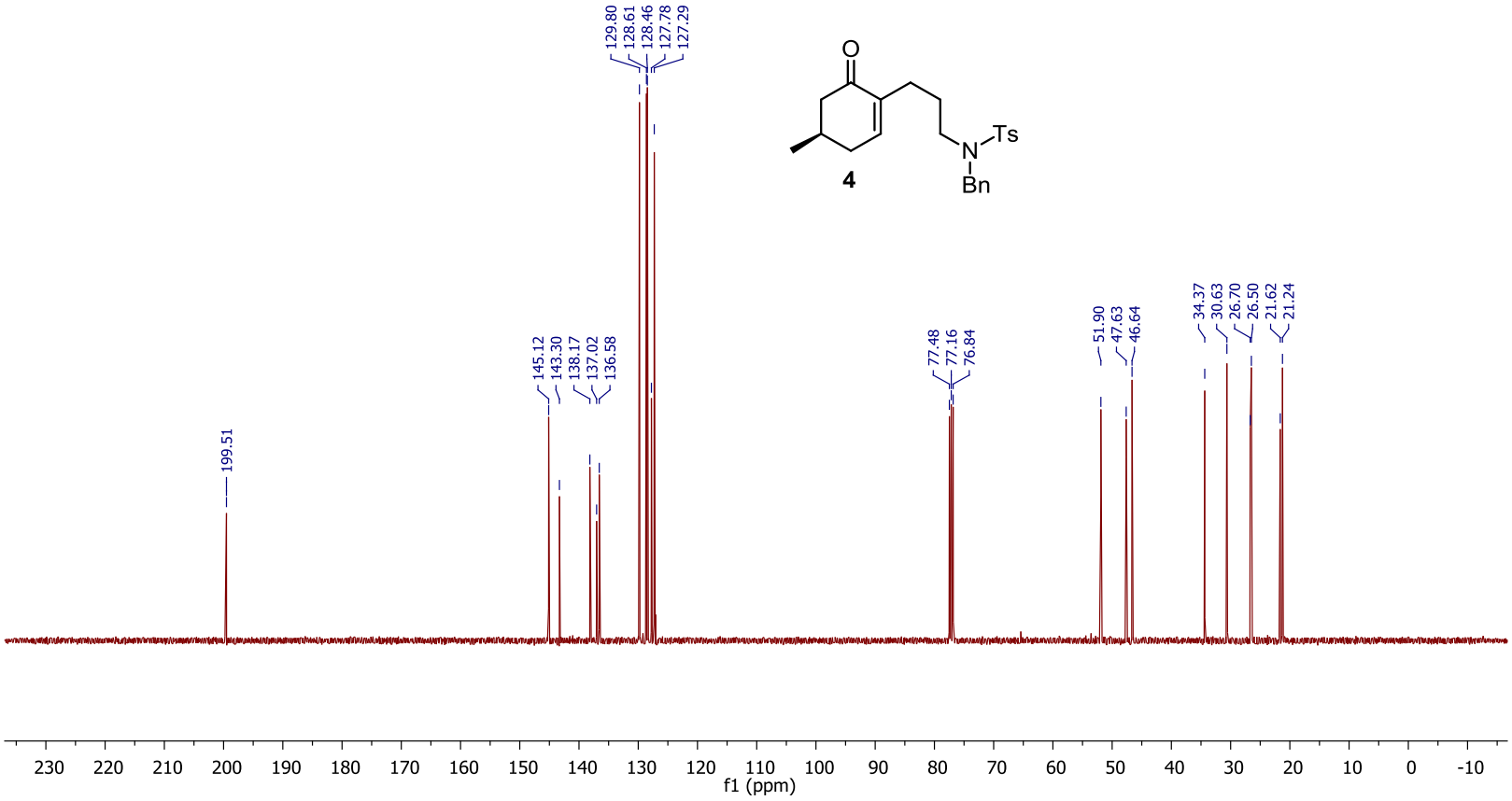
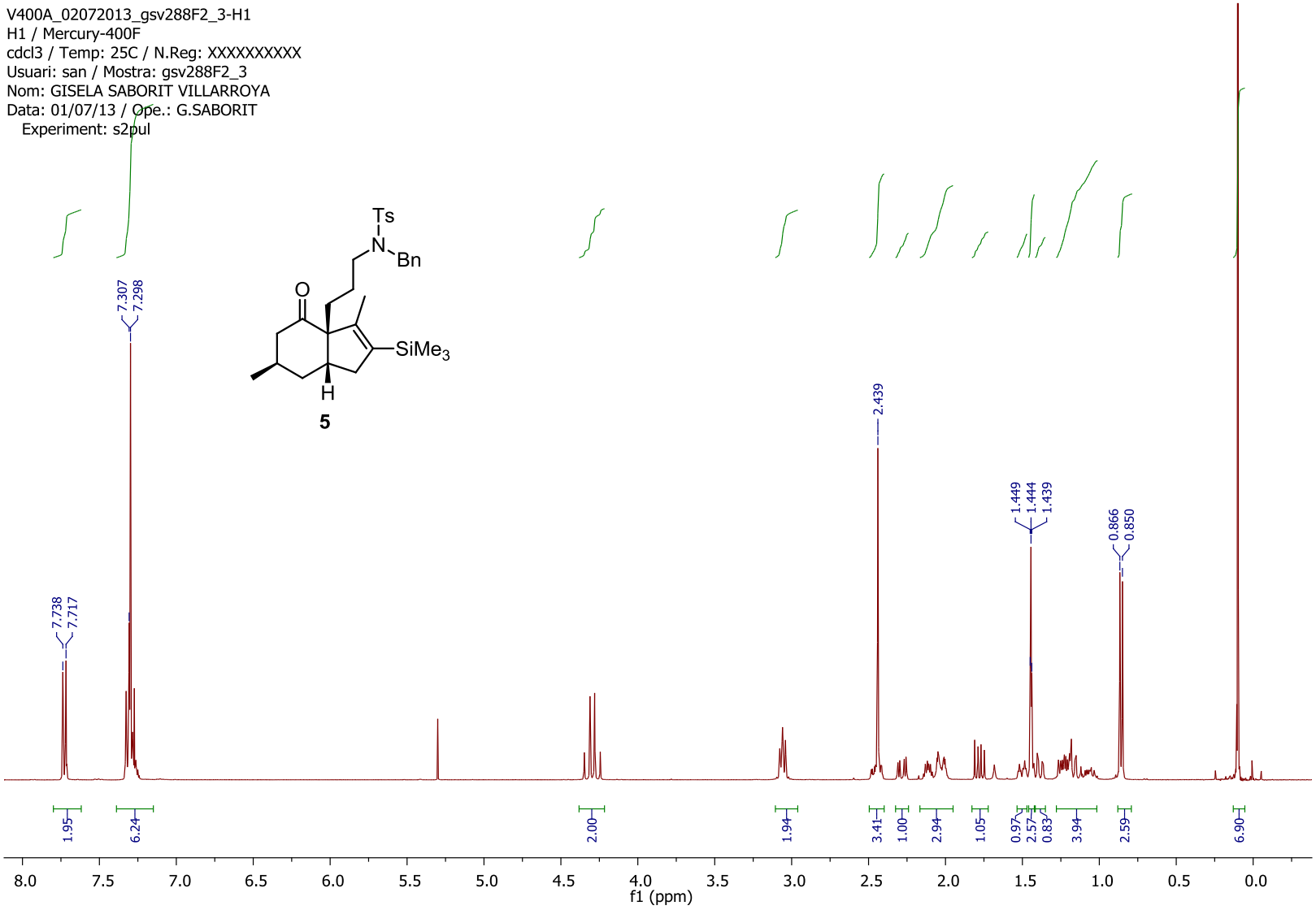
Experiment: s2pul

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Nom: GISELA SABORIT VILLARROYA
Data: 01/07/13 / Ope.: G.SABORIT
Experiment: s2pul
Ts
N
Bn
O
SiMe3
H
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7.717
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1.439
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6.24
2.00
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3.41
1.00
2.94
1.05
0.97
2.57
0.83
3.94
2.59
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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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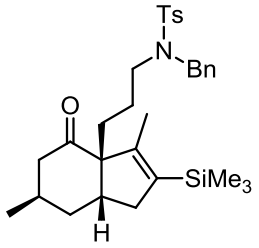
Data: 01/07/13 / Ope.: G.SABORIT
Experiment: s2pul



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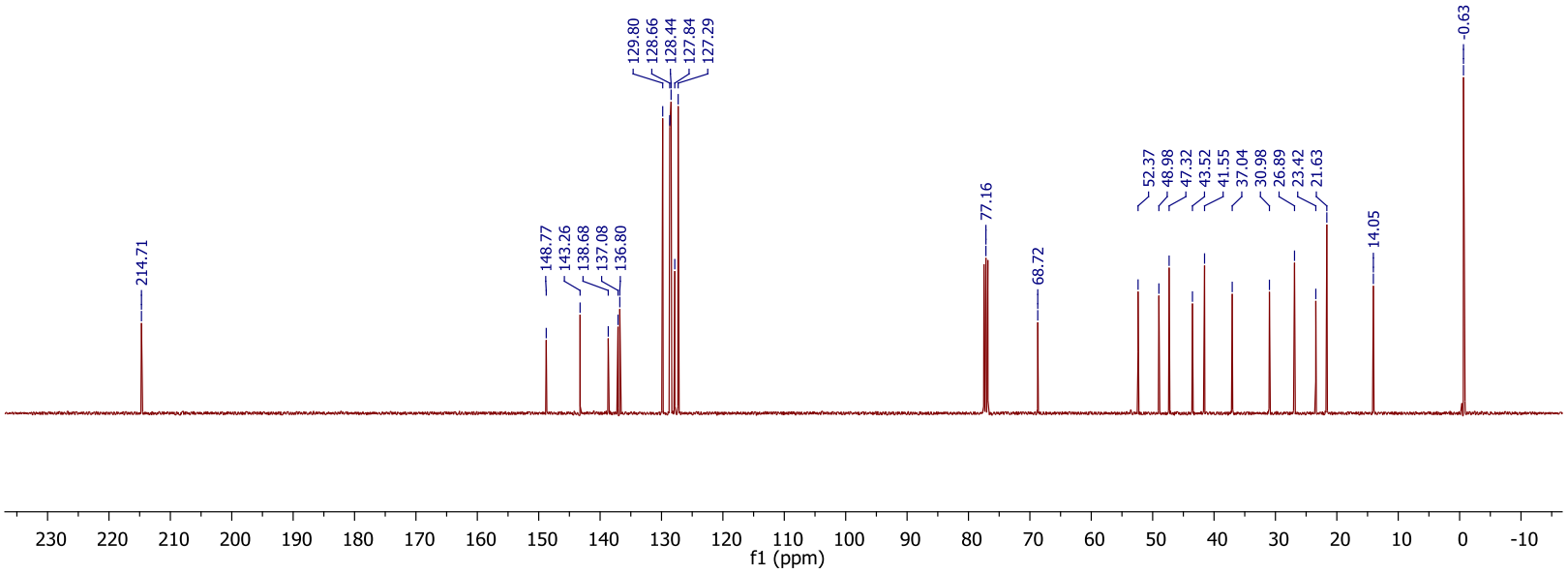

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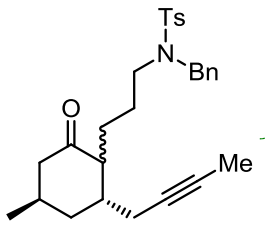
Data: 03/07/13 / Ope.: G.SABORIT
Experiment: s2pul



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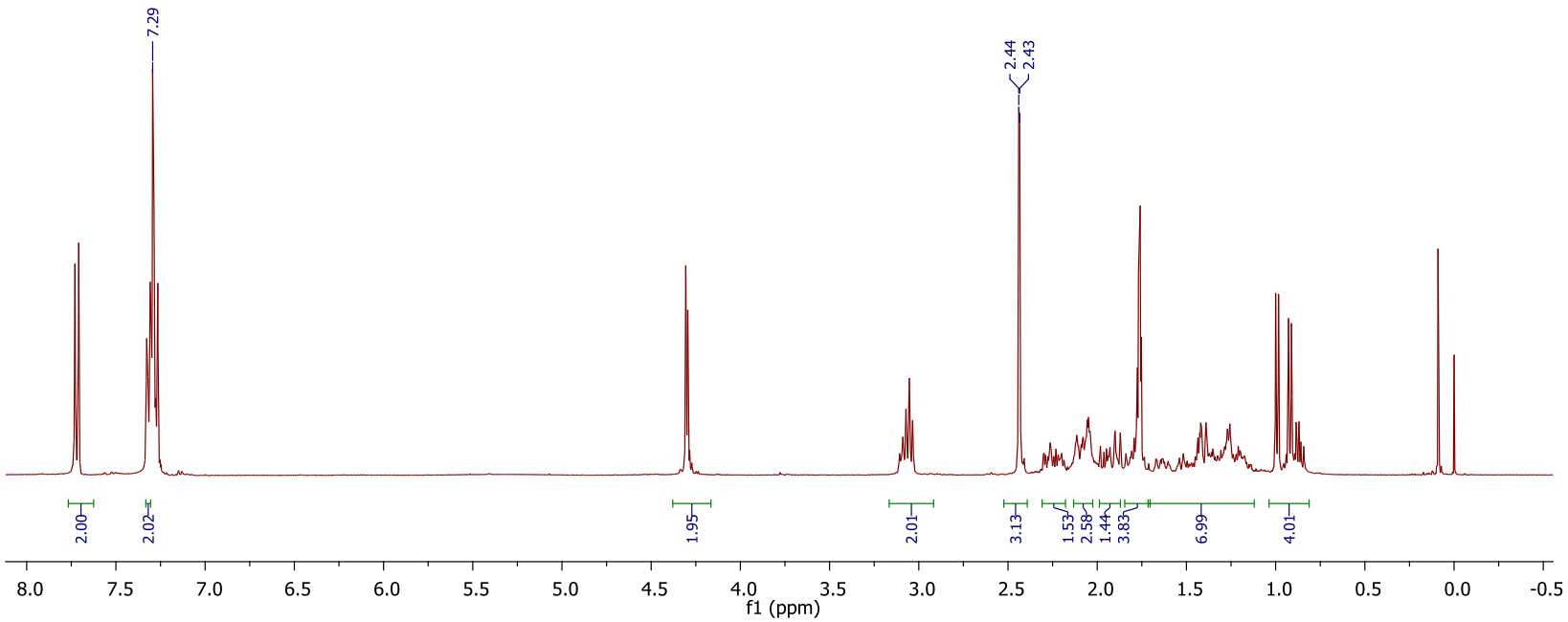

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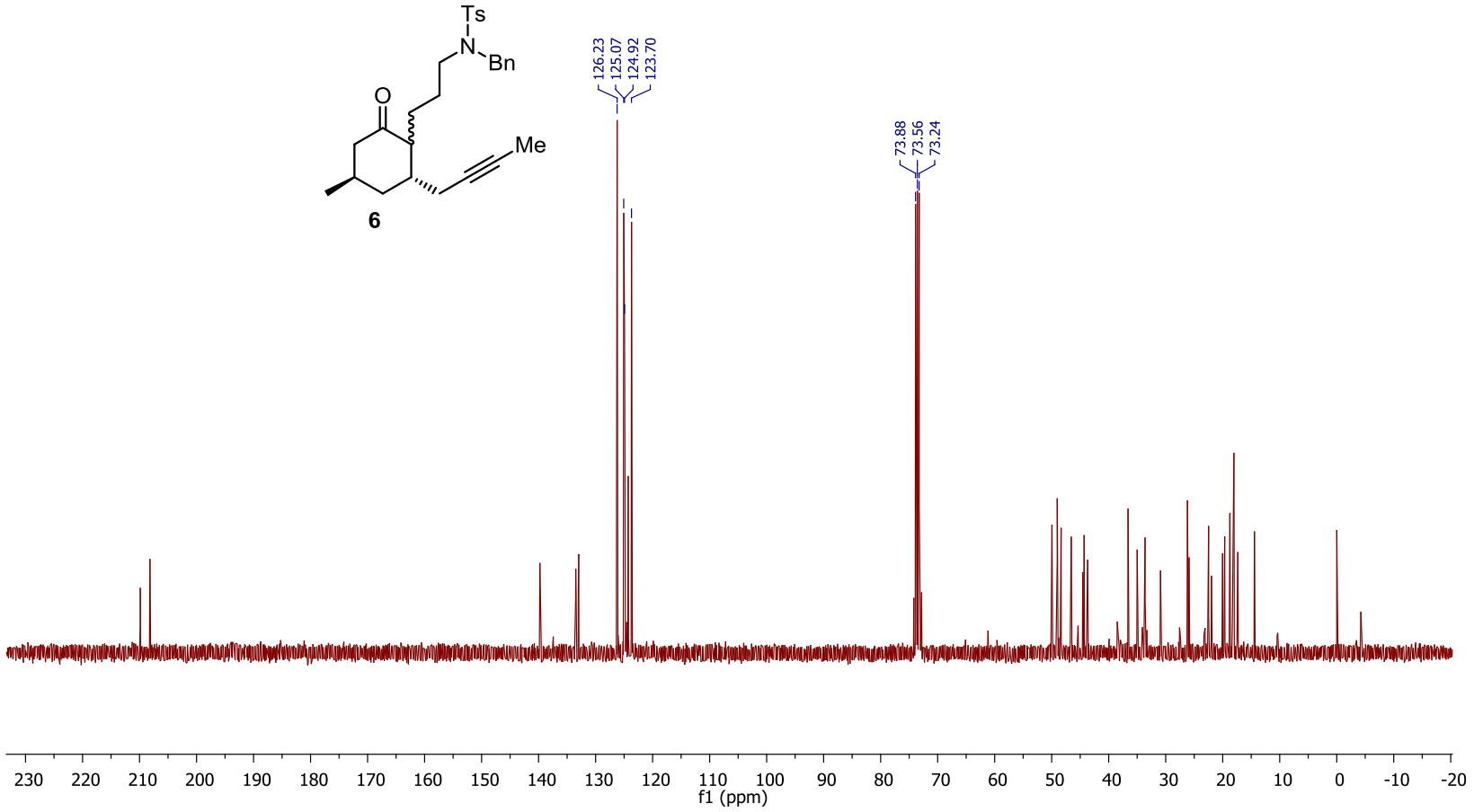
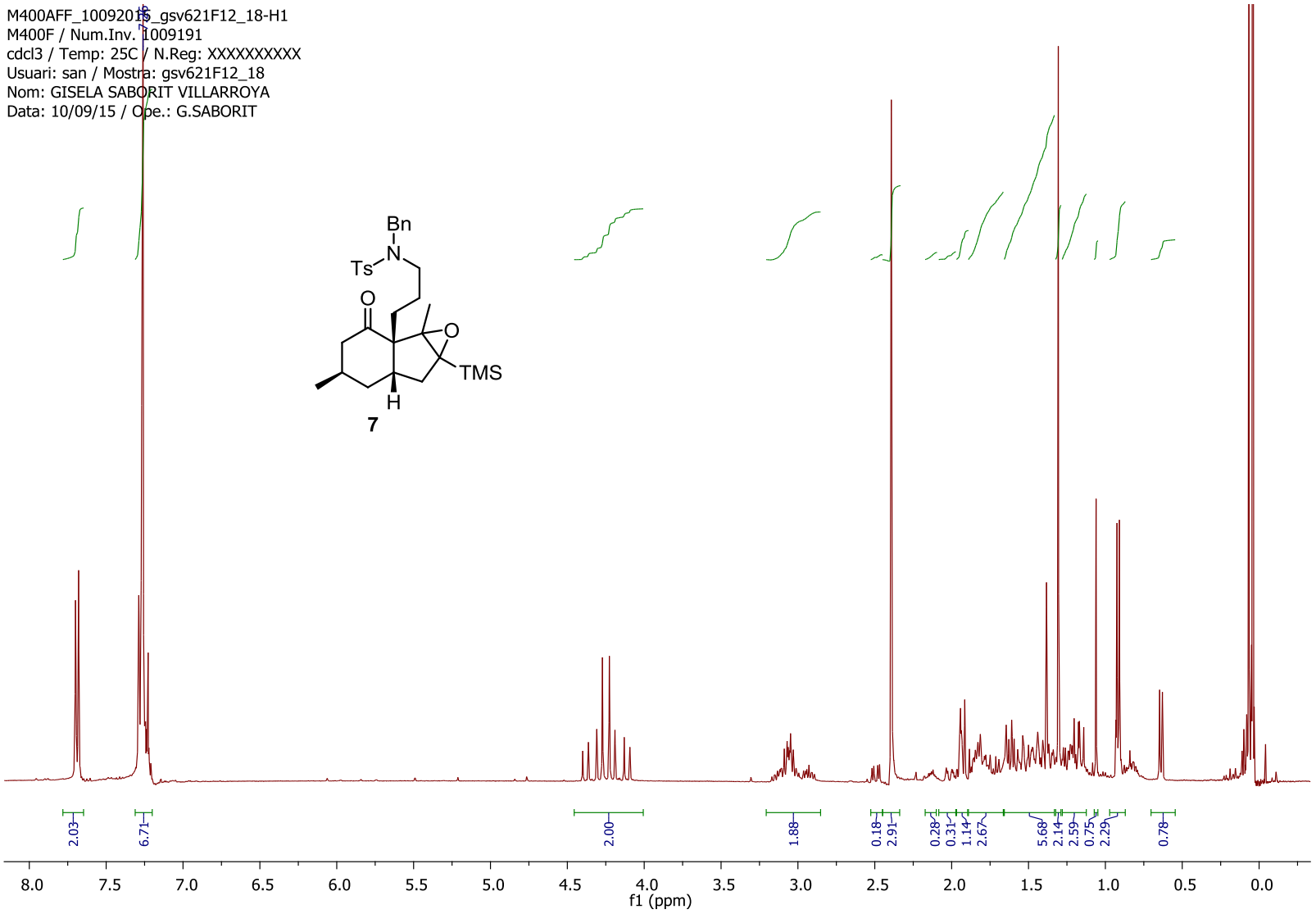
Data: 03/07/13 / Ope.: G.SABORIT
Experiment: s2pul

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Data: 10/09/15 / Ope.: G.SABORIT
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Ts
O
O
TMS
H
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0.28
0.31
1.14
2.67
5.68
2.14
2.59
0.75
2.29
0.78
8.0
7.5
7.0
6.5
6.0
5.5
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1.0
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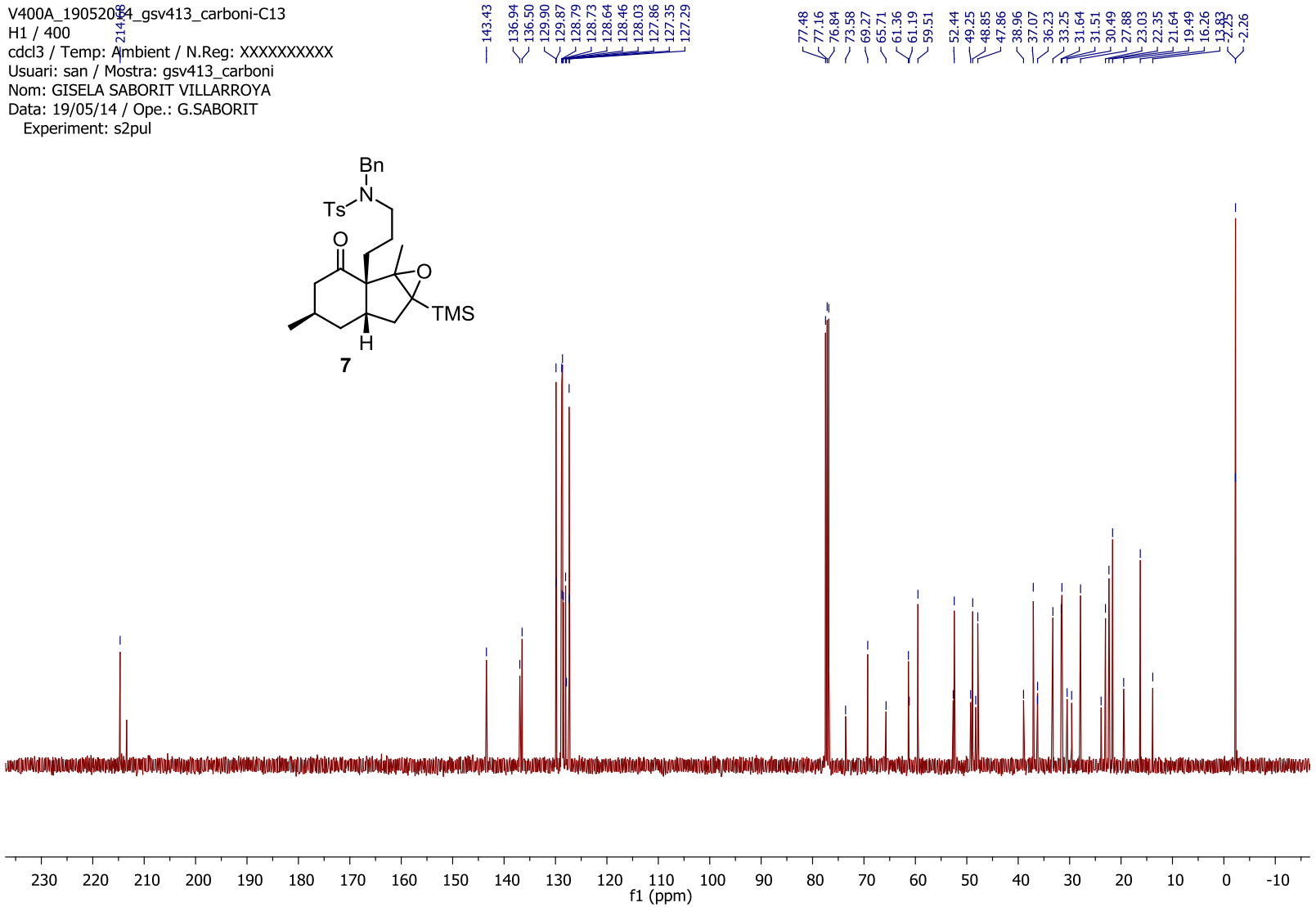
f1 (ppm)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Usuari: san / Mostra: gsv413_carboni
Nom: GISELA SABORIT VILLARROYA
Data: 19/05/14 / Ope.: G.SABORIT
Experiment: s2pul
214.08
143.43
136.94
136.50
129.90
129.87
128.79
128.73
128.64
128.46
128.03
127.86
127.35
127.29
77.48
77.16
76.84
73.58
69.27
65.71
61.36
61.19
59.51
52.44
49.25
48.85
47.86
38.96
37.07
36.23
33.25
31.64
31.51
30.49
27.88
23.03
22.35
21.64
19.49
16.26
13.83
-2.25
-2.26
Bn
N
Ts
O
O
TMS
H
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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)

M400AFF_22052014_gsv413_base-H1
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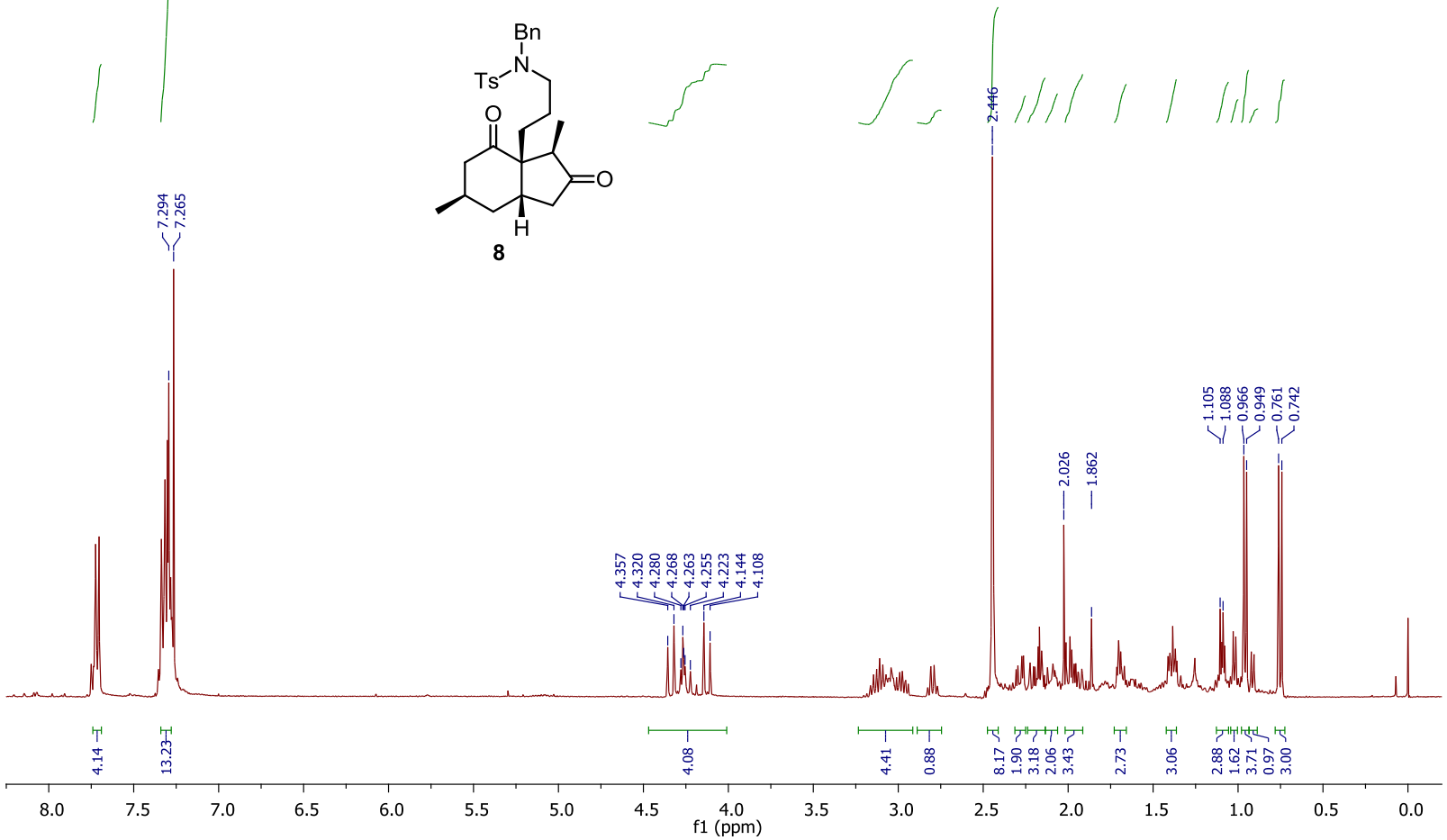
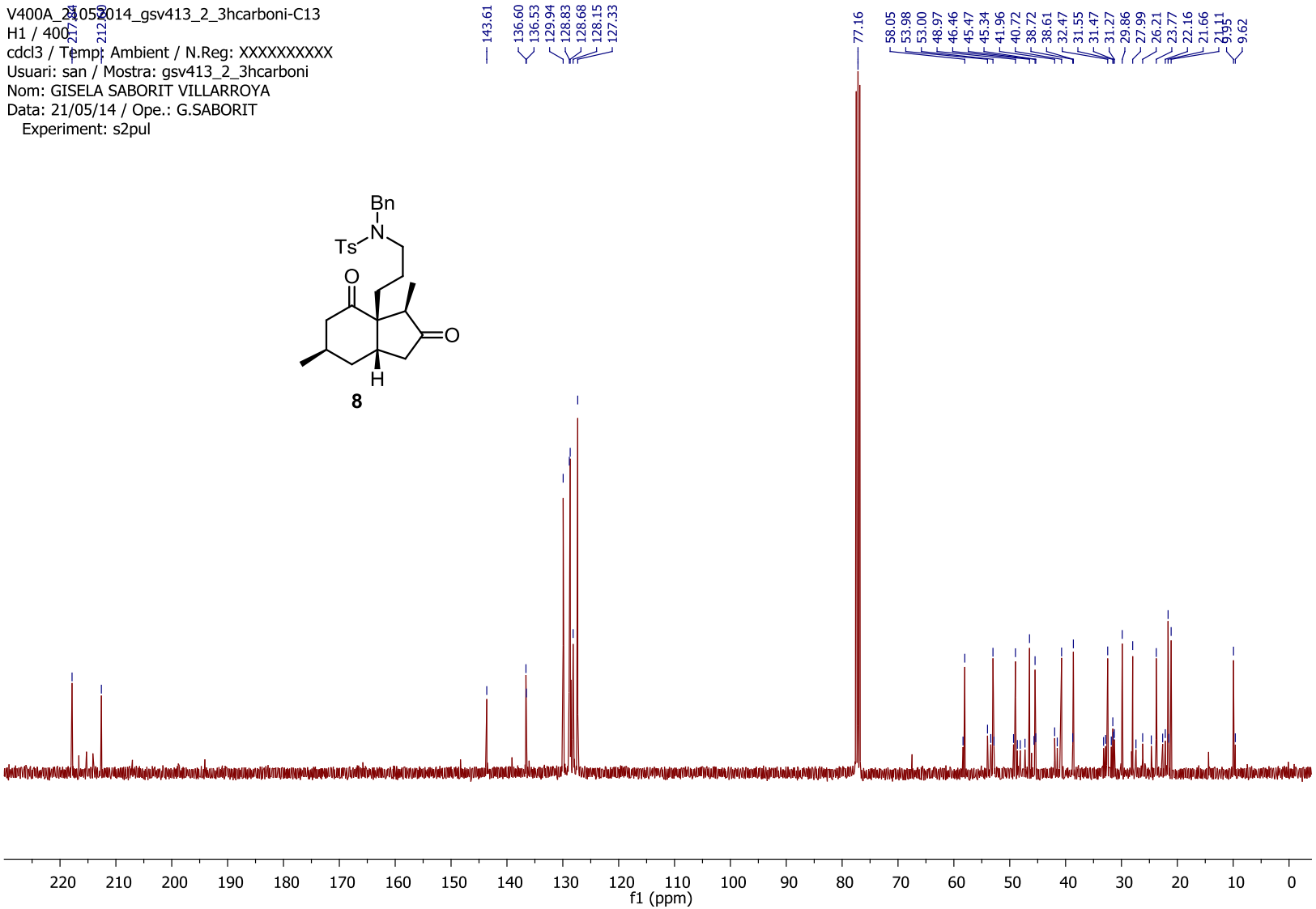
Data: 22/05/14 / Ope.: G.SABORIT

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Usuari: san / Mostra: gsv413_2_3hcarboni
Nom: GISELA SABORIT VILLARROYA
Data: 21/05/14 / Ope.: G.SABORIT
Experiment: s2pul
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136.60
136.53
129.94
128.83
128.68
128.15
127.33
77.16
58.05
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32.47
31.55
31.47
31.27
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27.99
26.21
23.77
22.16
21.66
21.11
9.95
9.62
Bn
N
Ts
O
O
H
8
f1 (ppm)