Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Supporting Information

Germanium(II)-Mediated Reductive Mannich-Type Reaction of α-Bromoketones to *N*-Alkylimines

Shin-ya Tanaka, Nobuo Tagashira, Kouji Chiba, Makoto Yasuda, and Akio Baba*

Department of Applied Chemistry, Center for Atomic and Molecular Technologies (CAMT), Graduate School of Engineering, Osaka University, 2-1 Yamadaoka, Suita, Osaka 565-0871, Japan and Science and Technology System Division, Ryoka Systems Inc.,1-28-38 Shinkawa, Chuo-ku, Tokyo 104-0033, Japan

Contents.

General. All reactions were carried out in flame-dried glassware under N_2 atmosphere and stirred via magnetic stir-plates. IR spectra were recorded as thin films or as solids in KBr pellets. ^1H (400 MHz) and ^{13}C NMR (100 MHz) spectra were obtained with TMS as internal standard. ^1H and ^{13}C NMR signals of compounds were assigned by using HMQC, HMBC, COSY, and ^{13}C off-resonance techniques. Column chromatography was performed on silica gel (Fuji Sylisia FL100DX). Yields were determined by ^1H NMR using internal standards.

Materials.

Dehydrated CH_2Cl_2 (stabilized with 2-methyl-2-butene) was used as obtained. $GeCl_2$-dioxane was prepared according to the literature method.[1] Zn, SmI_2 (0.1M solution in THF), and $SnCl_2$ were commercially available, and used as obtained. All catalysts in Table 1 were commercially available. Bromoketone **4c,** Imine **1a**-**b**, and **1f** were commercially available, and used as obtained. All other reagents and starting materials, unless otherwise noted, were commercially available and used as obtained.

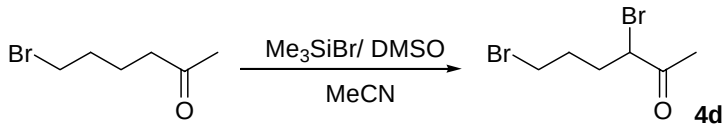
Preparation of imines. Imines **1c**-**e**, and **1g**-**i** were prepared according to the reported method[2] with slight modification. Imines **1j** and **1k** were prepared according to the literature method.[3]

***N*-Methylimines 1c-e; general procedure.**
Methylamine (100 mmol, commercially available as 2M MeOH solution) was slowly added for 60 min to a stirred suspension of the aldehyde (65 mmol) and MS 3Å (20 g) in CH_2Cl_2 (50 mL) at room temperature. After 12 h, the reaction mixture was filtered off, evaporated, and crude product was purified by distillation (**1d**-**1e**) or recrystallization in toluene/ hexane (**1c**).

***N*-Methylimines 1g-i; general procedure.**
The amine (105 mmol) in CH_2Cl_2 (15 mL) was slowly added for 30 min to a stirred suspension of the aldehyde (100 mmol) and $MgSO_4$ (30 g) in CH_2Cl_2 (75 mL) at room temperature. After 12 h, the reaction mixture was filtered off, evaporated, and crude product was purified by distillation.

Preparation of bromoketones. Bromoketones **4a-b** were prepared according to the literature method.[4]

3,6-Dibromo-2-hexanone (4d) [5]

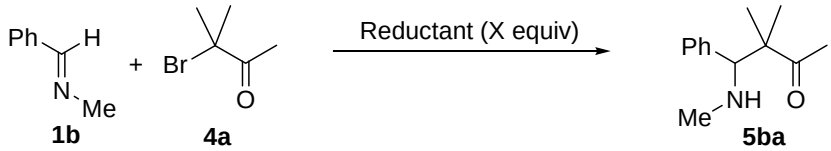


4d

Me_3SiBr (26 mmol) in MeCN (10 mL) was slowly added for 10 min to a stirred solution of 6-bromohexanone[6] (20 mmol) and DMSO (22 mmol) in MeCN (10 mL) at room temperature. After 4 h, the mixture was poured into Et_2O (50 mL) and brine (50 mL). The resulting mixture was extracted with Et_2O (30 mLx3) and the collected organic layer was dried over $MgSO_4$. The solvent was evaporated and the residue was purified by distillation to give the product as a slightly

yellowish liquid. (10.7 mmol, 54%)
Analytical data: bp: 57 ^{o}C /0.18 mmHg; ^{1}H NMR: (400 MHz, $CDCl_3$) 4.28 (dd, J = 8.3, 5.8 Hz, 1H, 3-H), 3.44 (t, J = 6.3 Hz, 1H, 6-H_2), 2.39 (s, 3H, 1-H_3), 2.26-2.02 (m, 3H, 4-H_2 and 5-H^A), 1.99-1.82 (m, 1H, 5-H^B); ^{13}C NMR: (100 MHz, $CDCl_3$) 201.3 (s, C-2), 53.0 (d, C-3), 32.4 (t, C-6), 31.7 (t, C-4), 30.1 (t, C-5), 26.5 (q, C-1); IR: (neat) 1720 (C=O); MS: (EI, 70 eV) 260 (M^+ + 4, 0.2), 258 (M^+ + 2, 0.5), 256 (M^+, 0.3), 179 (M^+ + 2 - Br, 15), 177 (M^+ - Br, 16), 43 (MeCO, 100); HRMS: (EI, 70 eV) Calculated ($C_6H_{10}Br_2O$) 255.9098 (M^+) Found: 255.9096

Various reductants (Zn, $SnCl_2$, and SmI_2) mediated reaction of 4a with 1b. (Table 1, entries 1-4)



1b **4a** **5ba**

Entry	Reductant	Solvent	X (equiv)	Condition	Catalyst	Yield [%]
1	Zn	THF	1.5	68 ^{o}C, 2 h	none	<1
2	$SnCl_2$	CH_2Cl_2	1.5	RT, 2 h	none	<1
3	SmI_2	THF	3.0	-78 ^{o}C, 2 h	none	14
4	SmI_2	THF	3.0	-78 ^{o}C to RT, 2 h	none	<1

Zn
3-Bromo-3-methyl-2-butanone **4a** (0.9 mmol) was added to a stirred suspension of Zn (0.9 mmol) and *N*-benzylidenemethylamine **1b** (0.6 mmol) in THF (2 mL) at room temperature. The reaction was stirred at 68 °C for 2 h, and then saturated aq. $NaHCO_3$ (10 mL) was added. The mixture was extracted with Et_2O (10 mLx3), dried ($MgSO_4$), and evaporated. No aminoketone **5ba** was observed by ^{1}H NMR.

$SnCl_2$
3-Bromo-3-methyl-2-butanone **4a** (0.9 mmol) was added to a stirred suspension of $SnCl_2$ (0.9 mmol) and *N*-benzylidenemethylamine **1b** (0.6 mmol) in CH_2Cl_2 (2 mL) at room temperature. The reaction was stirred at room temperature for 2 h, and then saturated aq. $NaHCO_3$ (10 mL) was added. The mixture was extracted with Et_2O (10 mLx3), dried ($MgSO_4$), and evaporated. No aminoketone **5ba** was observed by ^{1}H NMR.

SmI_2 (-78 ^{o}C, 2 h)
SmI_2 (1.8 mmol, 0.1M solution in THF) was slowly added to a stirred solution of 3-bromo-3-methyl-2-butanone **4a** (0.9 mmol) and *N*-benzylidenemethylamine **1b** (0.6 mmol) in THF (2 mL) at -78 ^{o}C. The reaction was stirred at -78 °C for 2 h, and then saturated aq. $NaHCO_3$ (10 mL) was added. The mixture was extracted with Et_2O (10 mLx3), dried ($MgSO_4$), and evaporated to yield the product **5ba** in 14%.

SmI_2 (-78 °C to room temperature, 2 h)

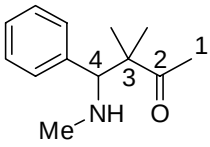
SmI_2 (1.8 mmol, 0.1M solution in THF) was slowly added to a stirred solution of 3-bromo-3-methyl-2-butanone **4a** (0.9 mmol) and *N*-benzylidenemethylamine **1b** (0.6 mmol) in THF (2 mL) at -78 °C. After 30 min, the addition was completed, and the reaction mixture was warmed to room temperature. The reaction was stirred at room temperature for 1.5 h, and then s saturated aq. $NaHCO_3$ (10 mL) was added. The mixture was extracted with Et_2O (10 mLx3), dried ($MgSO_4$), and evaporated. No aminoketone **5ba** was observed by ^1H NMR.

General procedure. (Table 2, entry 1)

3-Bromo-3-methyl-2-butanone **4a** (4.6 mmol) was added to a stirred suspension of *N*-benzylidenemethylamine **1b** (3.1 mmol), $Yb(OTf)_3$ (0.3 mmol), and $GeCl_2$-dioxane (4.5 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 2 h at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated. The crude product was purified by silica gel chromatography [solvent; hexane 100 mL, hexane/EtOAc = 90/10 (100 mL), 80/20 (100 mL), 70/30 (100 mL), and 60/40 (100 mL)] to afford the aminoketone **5ba** as a colorless solid (2.61 mmol, 84%).

Characterization of β-aminoketones

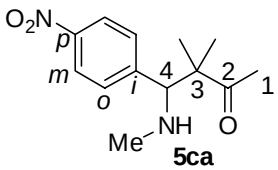
3,3-Dimethyl-4-(methylamino)-4-phenylbutan-2-one (5ba)



5ba

Analytical data: mp: 74-77 °C; ^1H NMR: (400 MHz, $CDCl_3$) 7.34 (t, J = 7.4 Hz, 2H, *m*-Ph), 7.28 (t, J = 7.4 Hz, 1H, *p*-Ph), 7.23 (d, J = 7.4 Hz, 2H, *o*-Ph), 3.81 (s, 1H, 4-H), 2.21 (s, 3H, 1-H_3), 2.18 (s, 3H, NMe), 1.50 (brs, 1H, NH), 1.02 (s, 3H, 3-Me^A), 0.96 (s, 3H, 3-Me^B); ^{13}C NMR: (100 MHz, $CDCl_3$) 213.3 (s, C-2), 138.5 (s, *i*-Ph), 128.8 (d, *o*-Ph), 127.7 (d, *m*-Ph), 127.1 (d, *p*-Ph), 70.2 (d, C-4), 52.0 (s, C-3), 34.6 (q, NMe), 25.5 (q, C-1), 23.9 (q, 3-Me^B), 17.8 (q, 3-Me^A); IR: (KBr) 3344 (NH), 1701 (C=O); MS: (CI, 200 eV) 206 (M^+ + 1, 33), 175 (M^+ - NHMe, 17), 120 (PhCHNHMe, 100); HRMS: (CI, 200 eV) Calculated ($C_{13}H_{20}NO$) 206.1545 (M^+ + 1); Found: 206.1543; Analysis: $C_{13}H_{19}NO$ Calcd: C, 76.06; H, 9.33; N, 6.82 Found: C, 75.99; H, 9.22; N, 6.80

3,3-Dimethyl-4-(methylamino)-4-(4-nitrophenyl)butan-2-one (5ca)

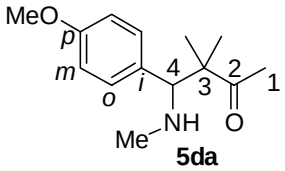


5ca

Bromoketone **4a** (2.76 mmol) was added to a stirred suspension of imine **1c** (1.81 mmol), $Yb(OTf)_3$ (0.18 mmol), and $GeCl_2$-dioxane (2.70 mmol) in CH_2Cl_2 (6 mL) at room temperature. The mixture was stirred for 15 min at room temperature, and then saturated aq. $NaHCO_3$ (50 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (86%). Purification by silica gel chromatography [solvent; hexane/EtOAc, 90/10 (200 mL) and then 50/50 (200 mL)] to afford the aminoketone **5ca** as a yellow solid (1.43 mmol, 79%).

Analytical data: mp: 118-121 ^{o}C; ^{1}H NMR: (400 MHz, $CDCl_3$) 8.21 (d, J = 9.1 Hz, 2H, *m*-Ph), 7.46 (d, J = 9.1 Hz, 2H, *o*-Ph), 3.95 (s, 1H, 4-H), 2.22 (s, 3H, 1-H_3), 2.18 (s, 3H, NMe), 1.54 (brs, 1H, NH), 1.05 (s, 3H, 3-Me^A), 0.98 (s, 3H, 3-Me^B); ^{13}C NMR: (100 MHz, $CDCl_3$) 212.6 (s, C-2), 147.2 (s), 147.1 (s), 129.8 (d, *o*-Ph) , 123.0 (d, *m*-Ph), 69.8 (d, C-4), 51.8 (s, C-3), 34.7 (q, NMe), 25.8 (q, C-1), 23.9 (q, 3-Me^B), 18.2 (q, 3-Me^A); IR: (KBr) 3344 (NH), 1701 (C=O); MS: (CI, 200 eV) 251 (M^+ + 1, 25), 165 (4-$NO_2C_6H_4CHNHMe$, 100), 87 (24); HRMS: (CI, 200 eV) Calculated ($C_{13}H_{19}N_2O_3$) 251.1396 (M^+ + 1); Found: 251.1388; Analysis: $C_{13}H_{18}N_2O_3$ Calcd: C, 62.38; H, 7.25; N, 11.19 Found: C, 62.42; H, 6.96; N, 11.14

4-(4-Methoxyphenyl)-3,3-dimethyl-4-(methylamino)butan-2-one (5da)

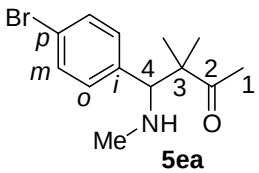


5da

Bromoketone **4a** (4.51 mmol) was added to a stirred suspension of imine **1d** (3.02 mmol), $Yb(OTf)_3$ (0.30 mmol), and $GeCl_2$-dioxane (4.49 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 2 h at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (97%). Purification by silica gel chromatography [solvent; hexane/EtOAc, 90/10 (200 mL) and then 50/50 (200 mL)] to afford the aminoketone **5da** as a colorless solid (2.52 mmol, 83%).

Analytical data: mp: 50-52 ^{o}C; ^{1}H NMR: (400 MHz, $CDCl_3$) 7.14 (d, J = 8.8 Hz, 2H, *o*-Ph), 6.88 (d, J = 8.8 Hz, 2H, *m*-Ph), 3.82 (s, 3H, OMe), 3.76 (s, 1H, 4-H) 2.19 (s, 3H, 1-H_3), 2.17 (s, 3H, NMe), 1.50 (brs, 1H, NH), 1.01 (s, 3H, 3-Me^A), 0.95 (s, 3H, 3-Me^B); ^{13}C NMR: (100 MHz, $CDCl_3$) 213.6 (s, C-2), 158.7 (s, *p*-Ph), 130.4 (s, *i*-Ph), 129.8 (d, *o*-Ph), 113.1 (d, *m*-Ph), 69.6 (d, C-4), 55.1 (q, OMe), 52.2 (s, C-3), 34.6 (q, NMe), 25.6 (q, C-1), 23.9 (q, 3-Me^B), 17.9 (q, 3-Me^A); IR: (KBr) 3348 (NH), 1701 (C=O); MS: (CI, 200 eV) 236 (M^+ + 1, 21), 205 (M^+ + 1 - OMe, 20), 150 (4-$MeOC_6H_4CHNHMe$, 100); HRMS: (CI, 200 eV) Calculated ($C_{14}H_{22}NO_2$) 236.1651 (M^+ + 1); Found: 236.1645; Analysis: $C_{14}H_{21}NO_2$ Calcd: C, 71.46; H, 8.99; N, 5.95 Found: C, 71.17; H, 9.28; N, 5.74

4-(4-Bromophenyl)-3,3-dimethyl-4-(methylamino)butan-2-one (5ea)



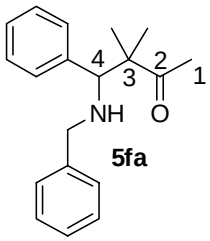
5ea

Bromoketone **4a** (4.46 mmol) was added to a stirred suspension of imine **1e** (2.96 mmol), $Yb(OTf)_3$ (0.30 mmol), and $GeCl_2$-dioxane (4.51 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 1 h at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (89%). Purification by silica gel chromatography [solvent; hexane (100 mL) and hexane/EtOAc, 90/10 (100 mL), 80/20 (100 mL) and then 70/30 (200 mL)] to afford the aminoketone **5ea** as a colorless solid (2.49 mmol, 84%).

Analytical data: mp: 93-95 ^{o}C; ^{1}H NMR: (400 MHz, $CDCl_3$) 7.47 (d, J = 8.3 Hz, 2H, *m*-Ph), 7.13 (d, J = 8.3 Hz, 2H, *o*-Ph), 3.77 (s, 1H, 4-H), 2.19 (s, 3H, 1-H_3), 2.16 (s, 3H, NMe), 1.49 (brs, 1H, NH), 1.01 (s, 3H, 3-Me^A), 0.95 (s, 3H, 3-Me^B); ^{13}C NMR: (100 MHz, $CDCl_3$) 213.0 (s, C-2), 137.7 (s, *i*-Ph), 130.8 (d, *o*-Ph), 130.5 (d, *m*-Ph), 120.9 (s, *p*-Ph), 69.6 (d, C-4), 51.8 (s, C-3), 34.5 (q, NMe), 25.6 (q, C-1), 23.8 (q, 3-Me^B), 17.8 (q, 3-Me^A); IR: (KBr) 3344 (NH), 1701 (C=O); MS: (CI, 200 eV) 286 (M^+ + 3, 38), 284 (M^+ + 1, 41), 200 (4-$BrC_6H_4CHNHMe$ + 2, 94), 198

(4-BrC_6H_4CHNHMe, 100), 87 (33); HRMS: (CI, 200 eV) Calculated ($C_{13}H_{19}BrNO$) 284.0650 (M^+ + 1); Found: 284.0648; Analysis: $C_{13}H_{18}BrNO$ Calcd: C, 54.94; H, 6.38; N, 4.93; Br, 28.12 Found: C, 54.94; H, 6.21; N, 4.80; Br, 27.96

4-(Benzylamino)-3,3-dimethyl-4-phenylbutan-2-one (5fa)

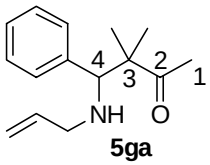


5fa

Bromoketone **4a** (4.49 mmol) was added to a stirred suspension of imine **1f** (2.97 mmol), $Yb(OTf)_3$ (0.30 mmol), and $GeCl_2$-dioxane (4.47 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 2 h at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (96%). Purification by silica gel chromatography [solvent; hexane (100 mL) and hexane/EtOAc, 90/10 (100 mL), 80/20 (100 mL) and then 70/30 (200 mL)] to afford the aminoketone **5fa** as a pale yellow liquid (2.46 mmol, 83%).

Analytical data: bp: 180 ^oC /0.3 mmHg; ^1H NMR: (400 MHz, $CDCl_3$) 7.36 (t, *J* = 7.3 Hz, 2H, 4-Ph(*m*)), 7.33-7.15 (m, 8H, 4-Ph(*o*, *p*) and NCH_2*Ph*), 3.90 (s, 1H, 4-H), 3.63 (d, *J* = 13.3 Hz, 1H, 4-NCH^A), 3.38 (d, *J* = 13.3 Hz, 1H, 4-NCH^B), 2.08 (s, 3H, 1-H_3), 1.82 (brs, 1H, NH, D_2O-exchangenable), 1.01 (s, 3H, 3-Me^A), 0.93 (s, 3H, 3-Me^B); ^{13}C NMR: (100 MHz, $CDCl_3$) 213.2 (s, C-2), 140.0 (s, NCH_2Ph(*i*)), 138.5 (s, 4-Ph(*i*)), 129.0 (d, NCH_2Ph(*o*)), 128.3 (d, 4-Ph(*o*)), 128.1 (d), 127.9 (d), 127.3 (d, 4-Ph(*p*)), 126.9 (d, NCH_2Ph(*p*)), 67.0 (d, C-4), 52.0 (s, C-3), 51.2 (t, NCH_2), 25.3 (q, C-1), 24.0 (q, 3-Me^B), 17.7 (q, 3-Me^A); IR: (neat) 3344 (NH), 1701 (C=O); MS: (CI, 200 eV) 282 (M^+ + 1, 27), 196 (PhCHNHCH_2Ph, 100), 87 (23); HRMS: (CI, 200 eV) Calculated ($C_{19}H_{24}NO$) 282.1858 (M^+ + 1); Found: 282.1863; Analysis: $C_{19}H_{23}NO$ Calcd: C, 81.10; H, 8.24; N, 4.98 Found: C, 80.88; H, 7.95; N, 5.05

4-(Allylamino)-3,3-dimethyl-4-phenylbutan-2-one (5ga)



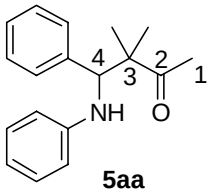
5ga

Bromoketone **4a** (4.55 mmol) was added to a stirred suspension of imine **1g** (3.01 mmol), $Yb(OTf)_3$ (0.30 mmol), and $GeCl_2$-dioxane (4.52 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 2 h at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (91%). Purification by silica gel chromatography [solvent; hexane (100 mL) and hexane/EtOAc, 90/10 (100 mL), 80/20 (100 mL) and then 70/30 (100 mL)] to afford the aminoketone **5ga** as a pale yellow liquid (2.47 mmol, 82%).

Analytical data: bp: 135 ^oC /0.4 mmHg; ^1H NMR: (400 MHz, $CDCl_3$) 7.34 (t, *J* = 6.8 Hz, 2H, *m*-Ph), 7.28 (t, *J* = 6.8 Hz, 1H, *p*-Ph), 7.22 (d, *J* = 6.8 Hz, 2H, *o*-Ph), 5.79 (dddd, *J* = 17.8, 9.7, 6.9, 5.4 Hz, 1H, NCH_2CH), 5.06-4.98 (m, 2H, NCH_2CHCH_2), 3.95 (s, 1H, 4-H), 3.09 (ddt, *J* = 14.2, 5.4, 1.6 Hz, 1H, 4-NCH^A), 2.86 (ddt, *J* = 14.2, 6.9, 1.2 Hz, 1H, 4-NCH^B), 2.21 (s, 3H, 1-H_3), 1.66 (brs, 1H, NH, D_2O-exchangenable), 1.02 (s, 3H, 3-Me^A), 0.96 (s, 3H, 3-Me^B); ^{13}C NMR: (100 MHz, $CDCl_3$) 213.0 (s, C-2), 138.6 (s, *i*-Ph), 136.5 (d, NCH_2CH), 128.7 (d, *o*-Ph), 127.7 (d, *m*-Ph), 127.1 (d, *p*-Ph), 115.8 (t, NCH_2CHCH_2), 66.9 (d, C-4), 51.9 (s, C-3), 49.8 (t, NCH_2), 25.4 (q, C-1), 23.9 (q, 3-Me^B), 17.8 (q, 3-Me^A); IR: (neat) 3344 (NH), 1701 (C=O); MS: (CI, 200 eV) 232 (M^+ + 1, 58), 146 (PhCHNHCH_2CHCH_2, 100); HRMS: (CI, 200 eV) Calculated ($C_{15}H_{22}NO$) 232.1701 (M^+ + 1); Found: 232.1712; Analysis: $C_{15}H_{21}NO$ Calcd: C, 77.88; H, 9.15; N, 6.05 Found: C,

77.60; H, 8.87; N, 6.10

3,3-Dimethyl-4-phenyl-4-(phenylamino)butan-2-one (5aa)

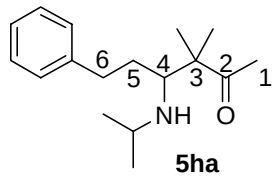


5aa

Bromoketone **4a** (2.72 mmol) was added to a stirred suspension of imine **1a** (1.80 mmol), $Yb(OTf)_3$ (0.18 mmol), and $GeCl_2$-dioxane (2.72 mmol) in CH_2Cl_2 (6 mL) at room temperature. The mixture was stirred for 2 h at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (93%). Purification by silica gel chromatography [solvent; hexane 100 mL, hexane/EtOAc = 90/10 (100 mL), 80/20 (100 mL) and 70/30 (100 mL)] to afford the aminoketone **5aa** as a colorless solid (1.45 mmol, 81%).

Analytical data: mp: 167-170 ^oC; ^1H NMR: (400 MHz, $CDCl_3$) 7.32-7.20 (m, 5H, 4-Ph), 7.04 (dd, *J* = 8.2, 7.5 Hz, 2H, NPh(*m*)), 6.60 (t, *J* = 7.5 Hz, 1H, NPh(*p*)), 6.46 (d, *J* = 8.2 Hz, 2H, NPh(*o*)), 4.55 (d, *J* = 7.1 Hz, 1H, 4-H), 4.46 (brd, *J* = 7.1 Hz, 1H, NH, D_2O-exchangenable), 2.13 (s, 3H, 1-H_3), 1.18 (s, 3H, 3-Me^A), 1.07 (s, 3H, 3-Me^B); ^{13}C NMR: (100 MHz, $CDCl_3$) 213.1 (s, C-2), 146.4 (s, NPh(*i*)), 138.6 (s, 1-Ph(*i*)), 129.0 (d, NPh(*m*)), 128.4 (d, 4-Ph(*o*)), 128.0 (d, 4-Ph(*m*)), 127.4 (d, 4-Ph(*p*)), 117.5 (d, NPh(*p*)), 113.3 (d, NPh(*o*)), 63.4 (d, C-4), 51.6 (s, C-3), 25.7 (q, C-1), 24.4 (q, 3-Me^A), 18.8 (q, 3-Me^B); IR: (KBr) 3406 (NH), 1693 (C=O); MS: (EI, 70 eV) 267 (M^+, 2), 182 (PhCHNHPh, 100); HRMS: (EI, 70 eV) Calculated ($C_{18}H_{21}NO$) 267.1623 (M^+); Found: 267.1625; Analysis: $C_{18}H_{21}NO$ Calcd: C, 80.86; H, 7.92; N, 5.24 Found: C, 80.63; H, 7.73; N, 4.96

4-(Isopropylamino)-3,3-dimethyl-6-phenylhexan-2-one (5ha)

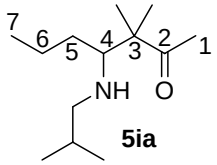


5ha

Bromoketone **4a** (4.51 mmol) was added to a stirred suspension of imine **1h** (3.01 mmol), $Yb(OTf)_3$ (0.30 mmol), and $GeCl_2$-dioxane (4.51 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 1 h at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (66%). Purification by silica gel chromatography [solvent; hexane (100 mL) and hexane/EtOAc, 90/10 (100 mL) and then 80/20 (200 mL)] to afford the aminoketone **5ha** as a pale yellow liquid (1.20 mmol, 40%).

Analytical data: bp: 155 ^oC /0.3 mmHg; ^1H NMR: (400 MHz, $CDCl_3$) 7.28 (t, *J* = 8.2 Hz, 2H, *m*-Ph), 7.22-7.15 (m, 3H, *o*, *p*-Ph), 2.90 (qq, *J* = 6.2, 6.2 Hz, 1H, 4-NCH), 2.87-2.78 (m, 2H, 4-H and 6-H^A), 2.60 (ddd, J = 13.8, 10.9, 6.0 Hz, 1H, 6-H^B), 2.11 (s, 3H, 1-H_3), 1.71 (dddd, *J* = 14.2, 11.1, 6.0, 3.1 Hz, 1H, 5-H^A), 1.46 (dddd, *J* = 14.2, 10.9, 8.7, 5.4 Hz, 1H, 5-H^B), 1.10 (s, 3H, 3-Me^A), 1.05 (s, 3H, 3-Me^B), 1.05 (d, *J* = 6.2 Hz, 3H, 4-NCHMe^A), 0.99 (d, *J* = 6.2 Hz, 3H, 4-NCHMe^B); ^{13}C NMR: (100 MHz, $CDCl_3$) 214.3 (s, C-2), 142.1 (s, *i*-Ph), 128.2 (d), 128.1 (d), 125.7 (d, *p*-Ph), 59.9 (d, C-4), 53.0 (s, C-3), 47.6 (d, 4-NCH), 35.7 (t, C-6), 34.3 (t, C-5), 26.2 (q, C-1), 24.1 (q), 23.2 (q), 21.3 (q), 20.7 (q); IR: (neat) 1701 (C=O); MS: (CI, 200 eV) 262 (M^+ + 1, 7), 218 (M^+ - $CHMe_2$, 13), 176 ($PhCH_2CH_2CHNHCHMe_2$, 100), 87 (35); HRMS: (CI, 200 eV) Calculated ($C_{17}H_{28}NO$) 262.2171 (M^+ + 1); Found: 262.2168; Analysis: $C_{17}H_{27}NO$ Calcd: C, 78.11; H, 10.41; N, 5.36 Found: C, 78.09; H, 10.13; N, 5.40

4-(Isobutylamino)-3,3-dimethylheptan-2-one (5ia)



5ia

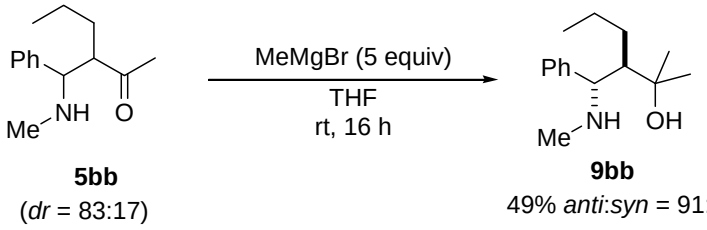
Bromoketone **4a** (4.55 mmol) was added to a stirred suspension of imine **1i** (3.01 mmol), $Yb(OTf)_3$ (0.16 mmol), and $GeCl_2$-dioxane (4.55 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 2 h at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (65%). Purification by silica gel chromatography [solvent; hexane (100 mL) and hexane/EtOAc, 90/10 (100 mL) and then 80/20 (200 mL)] to afford the aminoketone **5ia** as a pale yellow liquid (1.31 mmol, 44%).

Analytical data: bp: 110 ^{o}C /0.4 mmHg; ^{1}H NMR: (400 MHz, $CDCl_3$) 2.67-2.58 (m, 2H, 4-H and 4-NCH^{A}), 2.29 (dd, J = 11.0, 7.2 Hz, 1H, 4-NCH^{B}), 2.14 (s, 3H, 1-H_3), 1.64-1.45 (m, 2H, 4-NCH_2CH and 6-H^{A}), 1.42-1.26 (m, 2H, 5-H^{A} and 6-H^{B}), 1.23-1.11 (m, 1H, 5-H^{B}), 1.08 (s, 3H, 3-Me^{A}), 1.04 (s, 3H, 3-Me^{B}), 0.92 (t, J = 7.2 Hz, 3H, 7-H_3), 0.89 (d, J = 6.8 Hz, 3H, 4-NCH_2CHMe^{A}), 0.88 (d, J = 6.8 Hz, 3H, 4-NCH_2CHMe^{B}); ^{13}C NMR: (100 MHz, $CDCl_3$) 214.5 (s, C-2), 64.0 (d, C-4), 59.2 (t, 4-NCH_2), 53.1 (s, C-3), 35.3 (t, C-5), 29.4 (d, 4-NCH_2CH), 26.2 (q, C-1), 21.2, 21.1, 20.6, 20.6, 20.6, 14.3 (q, C-7); IR: (neat) 1701 (C=O); MS: (CI, 200 eV) 214 (M^+ + 1, 22), 128 ($CH_3CH_2CH_2CHNHCH_2CH(CH_3)_2$, 100), 87 (31); HRMS: (CI, 200 eV) Calculated ($C_{13}H_{28}NO$) 214.2171 (M^+ + 1); Found: 214.2160

Determination of the stereochemistry of 5bb, 5gd, and 5fd.

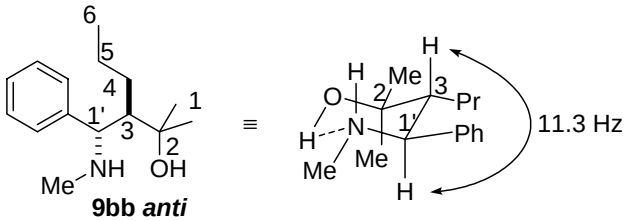
1. The stereoconfiguration of **5bb** was determined based on the coupling constant between hydrogens on chiral centers after a conversion to b-aminoalcohol **9bb**. The product exists as an intramolecularly hydrogen bonded six-membered ring. The ring has a chair conformation in which the substituents tend to locate in an equatrial position.[7]
2. The stereoconfiguration of **5gd** was assigned by analogy to **5bb**.
3. The stereoconfiguration of **5fd** was determined based on the coupling constant between hydrogens on chiral centers.

(3*R,1'*S**)-2-Methyl-3-[1-(methylamino)-1-phenylmethyl]hexan-2-ol (*anti*-9bb)**



5bb
(*dr* = 83:17)

9bb
49% *anti*:*syn* = 91:9



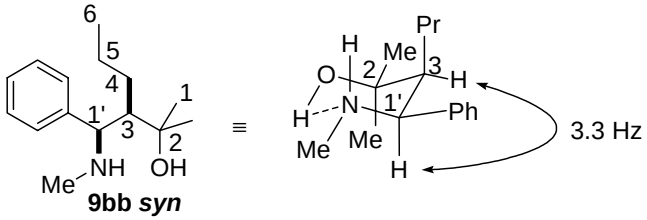
9bb *anti*

To a stirred solution of **5bb** (0.3 mmol, *dr* = 17:83) in THF (3 mL) was added MeMgBr (1.5 mmol) at room temperature. After the mixture was stirred for 16 h at this temperature, H_2O (30 mL) was added. The mixture was extracted with Et_2O (10 mLx3),

dried ($MgSO_4$), and evaporated to yield the product **9bb** in 49% (*anti*:*syn* = 91:9). The crude product was purified by silica gel chromatography [solvent; hexane (100 mL) and hexane/EtOAc, 90/10 (100 mL), 80/20 (100 mL), 70/30 (100 mL), 60/40 (100mL), and then 50/50 (100mL)] on silica gel to give the titled product.

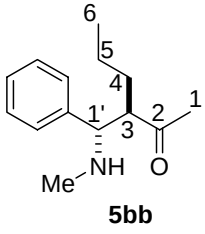
Analytical data: ^{1}H NMR: (400 MHz, $CDCl_3$) 7.35 (t, *J* = 7.3 Hz, 2H, *m*-Ph), 7.27 (t, *J* = 7.3 Hz, 1H, *p*-Ph), 7.22 (d, *J* = 7.2 Hz, 2H, *o*-Ph), 3.33 (d, *J* = 11.3 Hz, 1H, 1'-H), 2.18 (s, 3H, NMe), 1.70 (ddd, *J* = 11.3, 3.8, 3.8 Hz, 1H, 3-H), 1.26 (s, 3H, 1-H_3), 1.25 (s, 3H, 2-Me), 1.04-0.77 (m, 3H, 4-H_2 and 5-H^A), 0.73-0.58 (m, 1H, 5-H^B), 0.50 (t, *J* = 7.2 Hz, 3H, 6-H_3); ^{13}C NMR: (100 MHz, $CDCl_3$) 141.9 (s, *i*-Ph), 128.4 (d, *m*-Ph), 127.6 (d, *o*-Ph), 127.3 (d, *p*-Ph), 74.2 (s, C-2), 69.0 (d, C-1'), 52.6 (d, C-3), 33.5 (q, NMe), 32.5 (t, C-4), 29.7 (q, 2-Me), 24.8 (q, C-1), 23.0 (t, C-5), 14.4 (q, C-6); IR: (neat) 3267 (NH); MS: (CI, 200 eV) 236 (M^+ + 1, 100), 218 (M^+ - OH, 5), 120 (PhCHNHMe, 44); HRMS: (CI, 200 eV) Calculated ($C_{15}H_{26}NO$) 236.2014 (M^+ + 1) Found: 236.2010

(3*R,1'*R**)-2-Methyl-3-[1-(methylamino)-1-phenylmethyl]hexan-2-ol (*syn*-9bb)**



The compound was a minor product in the reaction of **5bb** with MeMgBr and was not purely isolated. Selected signals were shown below. ^{1}H NMR: (400 MHz, $CDCl_3$) 4.21 (d, *J* = 3.3 Hz, 1H, 1'-H), 2.35 (s, 3H, NMe), 1.47 (s, 3H, 1-H_3), 1.17 (s, 3H, 2-Me); ^{13}C NMR: (100 MHz, $CDCl_3$) 140.9 (*i*-Ph), 73.2 (C-2), 64.4 (C-1'), 52.9 (C-3), 33.7, 30.9, 28.3, 25.5, 24.6, 13.9 (C-6)

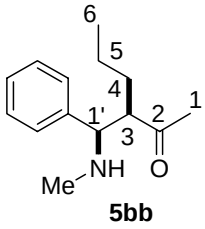
(3*R,1'*S**)-3-[1-(Methylamino)-1-phenylmethyl]hexan-2-one (*anti*-5bb)**



Bromoketone **4b** (4.44 mmol) was added to a stirred suspension of imine **1b** (3.04 mmol), $Yb(OTf)_3$ (0.30 mmol), and $GeCl_2$-dioxane (4.44 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 2 h at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (71%, *anti*:*syn* = 73:27). Purification by silica gel chromatography [solvent; hexane (100 mL) and hexane/EtOAc, 90/10 (100 mL), 80/20 (100 mL) and then 70/30 (100 mL)] to afford the aminoketone **5bb** as a pale yellow liquid (1.54 mmol, 51%, *anti*:*syn* = 82:18).

Analytical data: bp: 140 ^{o}C/ 0.3 mmHg; ^{1}H NMR: (400 MHz, $CDCl_3$) 7.36 (t, *J* = 7.2 Hz, 2H, *m*-Ph), 7.28 (t, *J* = 7.2 Hz, 1H, *p*-Ph), 7.22 (d, *J* = 7.2 Hz, 2H, *o*-Ph), 3.56 (d, *J* = 10.2 Hz, 1H, 1'-H), 2.70 (ddd, *J* = 10.2, 10.2, 3.5 Hz, 1H, 3-H), 2.19 (s, 3H, 1-H_3), 2.12 (s, 3H, NMe), 1.46-1.33 (m, 1H, 4-H^A), 1.22-1.00 (m, 3H, 4-H^B and 5-H_2), 0.75 (t, *J* = 7.2 Hz, 3H, 6-H_3); ^{13}C NMR: (100 MHz, $CDCl_3$) 212.5 (s, C-2), 141.2 (s, *i*-Ph), 128.4 (d, *m*-Ph), 127.4 (d, *o*-Ph), 127.3 (d, *p*-Ph), 67.1 (d, C-1'), 59.9 (d, C-3), 34.0 (q, NMe), 31.9 (t, C-4), 29.3 (q, C-1), 20.3 (t, C-5), 13.9 (q, C-6); IR: (neat) 3332 (NH), 1709 (C=O); MS: (CI, 200 eV) 220 (M^+ + 1, 76), 189 (M^+ - NHMe, 5), 120 (PhCHNHMe, 100), 101 (40); HRMS: (CI, 200 eV) Calculated ($C_{14}H_{22}NO$) 220.1701 (M^+ + 1) Found: 220.1698

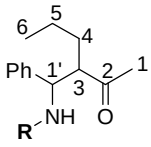
(3*R,1'*R**)-3-[1-(Methylamino)-1-phenylmethyl]hexan-2-one (*syn*-5bb)**



5bb

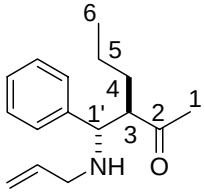
The compound was a minor product in the reaction of **1b** with **4b** and was not purely isolated. Selected signals were shown below. ^{1}H NMR: (400 MHz, $CDCl_3$) 3.60 (d, *J* = 7.7 Hz, 1H, 1'-H), 2.83 (ddd, *J* = 10.6, 7.7, 3.7 Hz, 1H, 3-H), 2.22 (s, 3H), 1.84 (s, 3H), 0.87 (t, *J* = 7.2 Hz, 3H, 6-H_3); ^{13}C NMR: (100 MHz, $CDCl_3$) 212.1 (C-2), 141.3 (*i*-Ph), 66.4 (C-1'), 59.6 (C-3), 34.4 (NMe), 31.7, 30.8, 21.0 (C-5), 14.2 (C-6)

^{1}H NMR data for the determination of stereochemistry of compound 5gb



			δ(^{1}H)/ ppm			
	R	*anti*/*syn*	1'-H	3-H	6-H_3	
5bb	Me	*anti*	3.56 (*J* = 10.2 Hz)	2.70 (*J* = 10.2, 10.2, 3.5 Hz)	0.75	
		syn	3.60 (*J* = 7.7 Hz)	2.83 (*J* = 10.6, 7.7, 3.7 Hz)	0.87	
		$\delta_{anti} - \delta_{syn}$	-0.04	-0.13	-0.12	
5gb	allyl	*major*	3.70 (*J* = 10.3 Hz)	2.69 (*J* = 10.5, 10.3, 3.5 Hz)	0.74	⇨ *anti*
		minor	3.77 (*J* = 8.0 Hz)	2.83 (*J* = 9.9, 8.0, 4.2 Hz)	0.88	⇨ *syn*
		$\delta_{maj} - \delta_{min}$	-0.07	-0.14	-0.14	

(3*R,1'*S**)-3-[1-(Allylamino)-1-phenylmethyl]hexan-2-one (*anti*-5gb)**

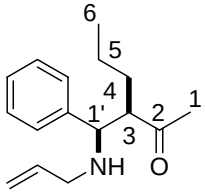


5gb *anti*

Bromoketone **4b** (4.50 mmol) was added to a stirred suspension of imine **1g** (3.01 mmol), $Yb(OTf)_3$ (0.30 mmol), and $GeCl_2$-dioxane (4.51 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 2 h at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (80%, *anti*:*syn* = 83:17). Purification by silica gel chromatography [solvent; hexane (100 mL) and hexane/EtOAc, 90/10 (100 mL), 80/20 (100 mL) and then 70/30 (100 mL)] to afford the aminoketone **5gb** as a pale yellow liquid (1.82 mmol, 60%, *anti*:*syn* = 92:8).

Analytical data: bp: 145 ^{o}C /0.4 mmHg; ^{1}H NMR: (400 MHz, $CDCl_3$) 7.36 (t, *J* = 7.2 Hz, 2H, *m*-Ph), 7.28 (t, *J* = 7.2 Hz, 1H, *p*-Ph), 7.21 (d, *J* = 7.2 Hz, 2H, *o*-Ph), 5.75 (dddd, *J* = 17.1, 10.5, 6.7, 5.5 Hz, 1H, NCH_2CH), 5.07-4.99 (m, 2H, NCH_2CHCH_2), 3.70 (d, *J* = 10.3 Hz, 1H, 1'-H), 3.01 (ddt, *J* = 14.2, 5.5, 1.6 Hz, 1H, 1'-$NHCH^{A}$), 2.84 (ddt, *J* = 14.2, 6.7, 1.2 Hz, 1H, 1'-$NHCH^{B}$), 2.69 (ddd, *J* = 10.5, 10.3, 3.5 Hz, 1H, 3-H), 2.20 (s, 3H, 1-H_3), 1.55 (brs, 1H, NH, D_2O-exchangenable), 1.45-1.33 (m, 1H, 4-H^{A}), 1.20-0.99 (m, 3H, 4-H^{B} and 5-H_2), 0.74 (t, *J* = 7.0 Hz, 3H, 6-H_3); ^{13}C NMR: (100 MHz, $CDCl_3$) 212.3 (s, C-2), 141.4 (s, *i*-Ph), 136.5 (d, NCH_2CH), 128.4 (d, *m*-Ph), 127.4 (d, *o*-Ph), 127.3 (d, *p*-Ph), 115.8 (t, NCH_2CHCH_2), 64.0 (d, C-1'), 60.0 (d, C-3), 49.3 (t, NCH_2), 31.8 (t, C-4), 29.0 (q, C-1), 20.3 (t, C-5), 13.8 (q, C-6); IR: (neat) 3325 (NH), 1709 (C=O); MS: (CI, 200 eV) 246 (M^{+} + 1, 86), 146 ($PhCHNHCH_2CHCH_2$, 100), 101 (35); HRMS: (CI, 200 eV) Calculated ($C_{16}H_{24}NO$) 246.1858 (M^{+} + 1) Found: 246.1852; Analysis: $C_{16}H_{23}NO$ Calcd: C, 78.32; H, 9.45; N, 5.71 Found: C, 78.11; H, 9.41; N, 5.52

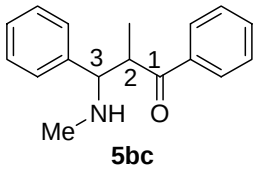
(3*R,1'*R**)-3-[1-(Allylamino)-1-phenylmethyl]hexan-2-one (*syn*-5gb)**



5gb *syn*

The compound was a minor product in the reaction of **1g** with **4b** and was not purely isolated. Selected signals were shown below. ^{1}H NMR: (400 MHz, $CDCl_3$) 5.82 (dddd, *J* = 17.3, 10.4, 6.8, 5.3 Hz, 1H, NCH_2CH), 3.77 (d, *J* = 8.0 Hz, 1H, 1'-H), 3.09 (ddt, *J* = 14.3, 5.3, 1.6 Hz, 1H, 1'-NHCH^A), 2.92 (ddt, *J* = 14.3, 6.8, 1.1 Hz, 1H, 1'-NHCH^B), 2.83 (ddd, *J* = 9.9, 8.0, 4.2 Hz, 1H, 3-H), 1.83 (s, 3H, 1-H_3), 0.88 (t, *J* = 7.0 Hz, 3H, 6-H_3); ^{13}C NMR: (100 MHz, $CDCl_3$) 212.0 (C-2), 141.6 (*i*-Ph), 136.6 (NCH_2CH), 115.9 (NCH_2CHCH_2), 63.3 (C-1'), 60.0 (C-3), 49.7 (NCH_2), 31.7, 30.7, 21.0 (C-5), 14.2 (C-6)

2-Methyl-3-(methylamino)-1,3-diphenylpropan-1-one (major isomer) (5bc)



5bc

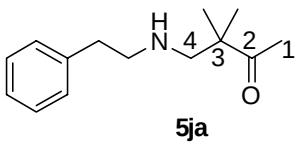
Bromoketone **4c** (4.55 mmol) was added to a stirred suspension of imine **1b** (2.96 mmol), $Yb(OTf)_3$ (0.30 mmol), and $GeCl_2$-dioxane (4.51 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 2 h at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (97%, *dr* = 55:45). Purification by silica gel chromatography [solvent; hexane (100 mL) and hexane/EtOAc, 90/10 (100 mL), 80/20 (100 mL) and then 70/30 (100 mL)] to afford the aminoketone **5bc** as a pale yellow liquid (2.87 mmol, 97%, *dr* = 55:45).

Analytical data: bp: 160 ^{o}C/ 0.35 mmHg; ^{1}H NMR: (400 MHz, $CDCl_3$) 8.02 (d, *J* = 7.2 Hz, 2H, 1-Ph(*o*)), 7.58 (t, *J* = 7.2 Hz, 1H, 1-Ph(*p*)), 7.48 (d, *J* = 7.2 Hz, 2H, 1-Ph(*m*)), 7.38-7.34 (m, 4H, 3-Ph(*o*, *m*)), 7.32-7.25 (m, 1H, 3-Ph(*p*)), 3.92 (d, *J* = 9.8 Hz, 1H, 3-H), 3.75 (dq, *J* = 9.8, 7.3 Hz, 1H, 2-H), 2.14 (s, 3H, NMe), 1.66 (brs, 1H, NH, D_2O-exchangenable), 0.92 (d, *J* = 7.3 Hz, 3H, 2-Me); ^{13}C NMR: (100 MHz, $CDCl_3$) 204.3 (s, C-1), 141.2 (s, 3-Ph(*i*)), 136.9 (s, 1-Ph(*i*)), 133.1 (d, 1-Ph(*p*)), 128.6 (d), 128.4 (d), 128.3 (d), 128.0 (d), 127.4 (d, 3-Ph(*p*)), 67.9 (d, C-3), 47.5 (d, C-2), 34.6 (q, NMe), 16.2 (q, 2-Me); IR: (neat) 3332 (NH), 1678 (C=O); MS: (CI, 200 eV) 254 (M^+ + 1, 33), 223 (M^+ - NHMe, 94), 135 (M^+ - PhCHNHMe, 85), 120 (PhCHNHMe, 100); HRMS: (CI, 200 eV) Calculated ($C_{17}H_{20}NO$) 254.1545 (M^+ + 1) Found: 254.1539

2-Methyl-3-(methylamino)-1,3-diphenylpropan-1-one (minor isomer) (5bc)

The compound was a minor product in the reaction of **1b** with **4c** and was not purely isolated. Selected signals were shown below. ^{1}H NMR: (400 MHz, $CDCl_3$) 7.85 (d, *J* = 8.1 Hz, 2H, 1-Ph(*o*)), 3.92 (d, *J* = 5.8 Hz, 1H, 3-H), 3.75 (qd, *J* = 6.8, 5.8 Hz, 1H, 2-H), 2.23 (s, 3H, NMe), 1.26 (d, *J* = 6.8 Hz, 3H, 2-Me); ^{13}C NMR: (100 MHz, $CDCl_3$) 203.7 (C-2), 141.9 (3-Ph(*i*)), 136.5 (1-Ph(*i*)), 132.9 (1-Ph(*p*)), 127.1 (3-Ph(*p*)), 66.0 (C-3), 47.3 (C-2), 34.7 (NMe), 12.6 (2-Me)

3,3-Dimethyl-4-(2-phenylethylamino)butan-2-one (5ja)

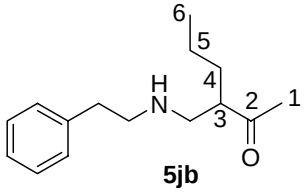


5ja

Bromoketone **4a** (4.51 mmol) was added to a stirred suspension of imine **1j** (3.01 mmol), $Bi(OTf)_3$ (0.30 mmol), and $GeCl_2$-dioxane (4.53 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 30 min at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3),

dried ($MgSO_4$), and evaporated to give the crude product (67%). Purification by silica gel chromatography [solvent; hexane (100 mL) and hexane/EtOAc, 80/20 (100 mL) and then 50/50 (200 mL)] to afford the aminoketone **5ja** as a pale yellow liquid (1.77 mmol, 58%).
Analytical data: bp: 140 ^oC /0.2 mmHg; ^1H NMR: (400 MHz, $CDCl_3$) 7.27 (t, J = 7.7 Hz, 2H, *m*-Ph), 7.22-7.15 (m, 3H, *o*, *p*-Ph), 2.83 (t, J = 7.1 Hz, 2H, NCH_2CH_2), 2.74 (t, J = 7.1 Hz, 2H, NCH_2CH_2), 2.69 (s, 2H, 4-H_2), 2.11 (s, 3H, 1-H_3), 1.10 (s, 6H, 3-Me_2); ^{13}C NMR: (100 MHz, $CDCl_3$) 213.7 (s, C-2), 140.0 (s, *i*-Ph), 128.6 (d, *o*-Ph), 128.3 (d, *m*-Ph), 126.0 (d, *p*-Ph), 58.3 (t, C-4), 51.9 (t, NCH_2CH_2), 48.5 (s, C-3), 36.2 (t, NCH_2CH_2), 25.2 (q, C-1), 23.0 (q, 3-Me_2); IR: (neat) 3332 (NH), 1705 (C=O); MS: (CI, 200 eV) 220 (M^+ + 1, 100), 134 ($PhCH_2CH_2NHCH_2$, 69), 128 ($CH_3COC(CH_3)_2CH_2NHCH_2$, 15); HRMS: (CI, 200 eV) Calculated ($C_{14}H_{22}NO$) 220.1701 (M^+ + 1); Found: 220.1696

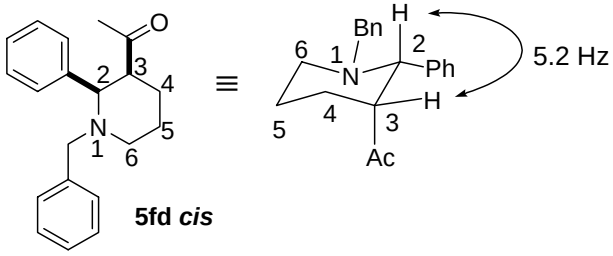
3-[(2-Phenylethylamino)methyl]hexan-2-one (5jb)



5jb

Bromoketone **4b** (4.49 mmol) was added to a stirred suspension of imine **1j** (3.01 mmol), $Bi(OTf)_3$ (0.30 mmol), and $GeCl_2$-dioxane (4.48 mmol) in CH_2Cl_2 (10 mL) at room temperature. The mixture was stirred for 30 min at room temperature, and then saturated aq. $NaHCO_3$ (100 mL) was added. The mixture was extracted with Et_2O (50 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (52%). Purification by silica gel chromatography [solvent; hexane (100 mL) and hexane/EtOAc, 80/20 (100 mL), 60/40 (100 mL) and then 50/50 (200 mL)] to afford the aminoketone **5ja** as a pale yellow liquid (1.32 mmol, 44%).
Analytical data: bp: 140 ^oC /0.15 mmHg; ^1H NMR: (400 MHz, $CDCl_3$) 7.29 (t, J = 7.6 Hz, 2H, *m*-Ph), 7.23-7.15 (m, 3H, *o*, *p*-Ph), 2.90-2.60 (m, 7H, 3-H, 3-CH_2N, NCH_2CH_2 and NCH_2CH_2), 2.13 (s, 3H, 1-H_3), 1.61-1.49 (m, 1H. 4-H^A), 1.42-1.20 (m, 3H, 4-H^B and 5-H_2), 0.90 (t, J = 7.3 Hz, 3H, 6-H_3); ^{13}C NMR: (100 MHz, $CDCl_3$) 212.3 (s, C-2), 139.9 (s, *i*-Ph), 128.6 (d), 128.3 (d), 126.0 (d, *p*-Ph), 53.1 (d, C-3), 51.3 (t), 50.8 (t), 36.2 (t, NCH_2CH_2), 32.0 (t, C-4), 29.2 (q, C-1), 20.5 (t, C-5), 14.1 (q, C-6); IR: (neat) 1709 (C=O); MS: (CI, 200 eV) 234 (M^+ + 1, 100), 134 ($PhCH_2CH_2NHCH_2$, 28); HRMS: (CI, 200 eV) Calculated ($C_{15}H_{24}NO$) 234.1858 (M^+ + 1); Found: 234.1854

(2*R,3*S**)-3-Acetyl-*N*-benzyl-2-phenylpiperidine (*cis*-5fd)**

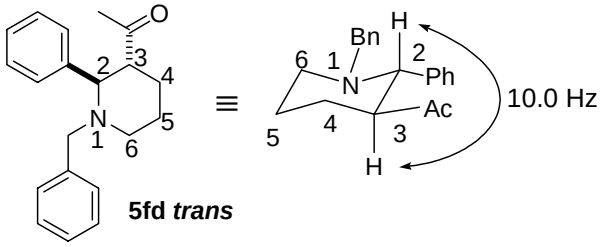


5fd *cis*

3,6-Dibromohexan-2-one **4d** (0.6 mmol) was added to a stirred suspension of $GeCl_2$-dioxane (0.6 mmol), *N*-benzylidenebenzylamine **1f** (0.284 mmol) and $Yb(OTf)_3$ (0.014 mmol) in CH_2Cl_2 (2 mL) at room temperature. After the mixture was stirred for 2 h at this temperature, saturated aq. $NaHCO_3$ (5 mL) was added. The mixture was stirred for 8 h at 50 ^oC, extracted with Et_2O (three times) and the organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure to give the product (83%, *cis*:*trans* = 84:16). Column chromatography [solvent; hexane (100 mL) and hexane/EtOAc, 90/10 (100 mL) and then 80/20 (100 mL)] was performed for the purification.

Analytical data: ^{1}H NMR: (400 MHz, $CDCl_3$) 7.38-7.20 (m, 10H, 2-Ph and NCH_2*Ph*), 3.85 (d, *J* = 5.2 Hz, 1H, 2-H), 3.70 (d, *J* = 14.1 Hz, 1H, NC*H*^{A}Ph), 3.20 (d, *J* = 14.1 Hz, 1H, NC*H*^{B}Ph), 3.07 (ddd, *J* = 6.4, 5.2, 5.2 Hz, 1H, 3-H), 2.94 (ddd, *J* = 11.9, 8.3, 3.7 Hz, 1H, 6-H^A), 2.23 (ddd, *J* = 11.9, 7.1, 3.7 Hz, 1H, 6-H^B), 2.13-1.95 (m, 2H, 4-H^A and 5-H^A), 1.79-1.68 (m, 1H, 4-H^B), 1.74 (s, 3H, COMe), 1.64-1.52 (m, 1H, 5-H^B); ^{13}C NMR: (100 MHz, $CDCl_3$) 210.3 (s, CO), 140.0 (s, 2-Ph(*i*)), 139.1 (s, NCH_2Ph(*i*)), 128.7 (d), 128.5 (d), 128.3 (d), 128.2 (d), 127.3 (d), 126.7 (d), 66.2 (d, C-2), 59.2 (t, N*C*H_2Ph), 53.0 (d, C-3), 49.8 (t, C-6), 31.0 (q, CO*Me*), 24.2 (t, C-4), 22.3 (t, C-5); IR: (neat) 1712 (C=O); MS: (EI, 70 eV) 293 (M^+, 8), 292 (M^+ - H, 11), 250 (M^+ - MeCO, 6), 222 (32), 216 (M^+ - Ph, 15), 202 (M^+ - $PhCH_2$, 100), 194 (31), 91 ($PhCH_2$, 89); HRMS: (EI, 70 eV) Calculated ($C_{20}H_{23}NO$) 293.178 (M^+) Found: 293.1777

(2*R,3*R**)-3-Acetyl-*N*-benzyl-2-phenylpiperidine (*trans*-5fd)**

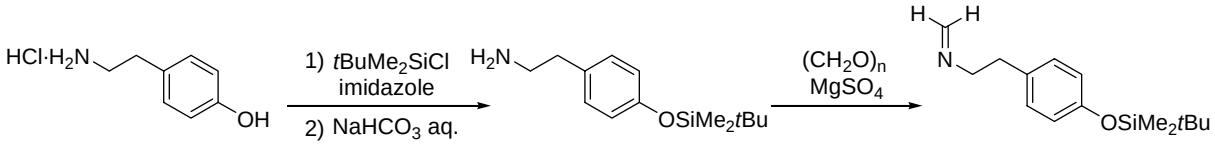


5fd *trans*

The compound was a minor product in the reaction of **1f** with **4d** and was not purely isolated. Selected signals were shown below. ^{1}H NMR: (400 MHz, $CDCl_3$) 3.70 (d, *J* = 13.8 Hz, 1H, NC*H*^{A}Ph), 3.32 (d, *J* = 10.0 Hz, 1H, 2-H), 2.80 (d, *J* = 13.8 Hz, 1H, NC*H*^{B}Ph), 1.62 (s, 3H, COMe); ^{13}C NMR: (100 MHz, $CDCl_3$) 211.5 (CO), 142.0, 139.4, 69.7 (C-2), 58.8, 58.4, 52.4, 31.1 (CO*Me*), 28.0, 24.7

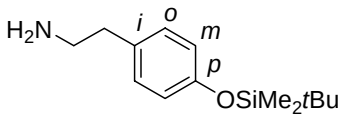
Be-2254 synthesis.

Methylidene-2-[4-(*tert*-butyldimethylsiloxy)]phenylethylamine (1k)



6 **7** **1k**

2-[4-(*tert*-butyldimethylsiloxy)]phenylethylamine (7)

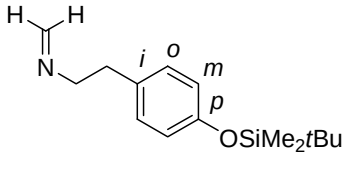


7

t$BuMe_2SiCl$ (15.0 mmol) was added to a stirred suspension of tyramine hydrogen chloride **6** (10.1 mmol) and imidazole (20.3 mmol) in CH_2Cl_2 (30 mL) at room temperature. After the mixture was stirred for 13 h at room temperature, it was slowly poured into saturated aq. $NaHCO_3$ (100 mL) at 0 ^{o}C. The mixture was extracted with CH_2Cl_2 (50 mLx3). This extract was washed with saturated aq. $NaHCO_3$ (30 mL) and brine (30 mL), dried ($MgSO_4$), and evaporated. The crude product was purified by silica gel chromatography [solvent; hexane 200 mL, hexane/EtOAc = 80/20 (200 mL), 50/50 (200 mL), EtOAc (200 mL), and MeOH (100 mL)] to afford the amine **7** (8.79 mmol, 87%). Further purification was performed by distillation to give pure **7** (8.55 mmol, 84%).
Analytical data: bp: 135 ^{o}C /0.4 mmHg; ^{1}H NMR: (400 MHz, $CDCl_3$) 7.05 (d, *J* = 8.7 Hz, 2H,

o-Ph), 6.77 (d, *J* = 8.7 Hz, 2H, *m*-Ph), 2.92 (t, *J* = 6.9 Hz, 2H, 1-H_2), 2.67 (t, *J* = 6.9 Hz, 2H, 2-H_2), 1.25 (brs, 2H, NH_2, D_2O-exchangenable), 0.98 (s, 9H, ^{t}Bu), 0.19 (s, 6H, $SiMe_2$); ^{13}C NMR: (100 MHz, $CDCl_3$) 153.9 (s, *p*-Ph), 132.4 (s, *i*-Ph), 129.6 (d, *o*-Ph), 120.0 (d, *m*-Ph), 43.7 (t, C-1), 39.3 (t, C-2), 25.7 (q, Si*C*Me_3), 18.2 (s, Si*C*Me_3), -4.5 (q, $SiMe_2$); IR: (neat) 3371 (NH); MS: (EI, 70 eV) 251 (M^+, 4), 222 (63), 221 (M^+ - NH_2CH_2, 38), 177 (24), 165 (100), 73 (45); HRMS: (EI, 70 eV) Calculated ($C_{14}H_{25}NOSi$) 251.1705 (M^+) Found: 251.1707; Analysis: $C_{14}H_{25}NOSi$ Calcd: C, 66.87; H, 10.02; N, 5.57 Found: C, 66.59; H, 9.91; N, 5.69

Methylidene-2-[4-(*tert*-butyldimethylsiloxy)]phenylethylamine (1k)

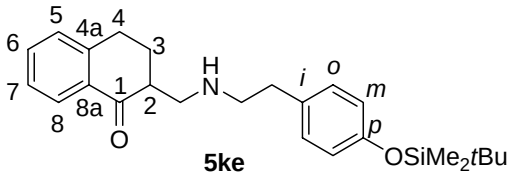


1k

Paraformaldehyde (45 mmol) was added to a stirred suspension of amine **7** (34.4 mmol) and $MgSO_4$ (10g) in CH_2Cl_2 (60 mL) at room temperature. After the mixture was stirred for 11 h at room temperature, it was filtered and rinsed with CH_2Cl_2. The resulting pale yellow solution was evaporated to yield the titled compound **1k** as a colorless solid (33.2 mmol, 96%).

Analytical data: bp: 170 ^{o}C /0.4 mmHg; mp: 70-73 ^{o}C; ^{1}H NMR: (400 MHz, $CDCl_3$) 7.04 (d, *J* = 8.5 Hz, 2H, *o*-Ph), 6.74 (d, *J* = 8.5 Hz, 2H, *m*-Ph), 3.41 (brs, 2H, N=CH_2), 2.73-2.61 (m, 4H, NCH_2CH_2), 0.97 (s, 9H, ^{t}Bu), 0.18 (s, 6H, $SiMe_2$); ^{13}C NMR: (100 MHz, $CDCl_3$) 153.7 (s, *p*-Ph), 132.9 (s, *i*-Ph), 129.5 (d, *o*-Ph), 119.8 (d, *m*-Ph), 74.5 (t, N=C), 54.7 (t, N*C*H_2CH_2), 33.7 (t, NCH_2*C*H_2), 25.6 (q, Si*C*Me_3), 18.1 (s, Si*C*Me_3), -4.5 (q, $SiMe_2$); IR: (neat) 1254 (O-Si); MS: (EI, 70 eV) 263 (M^+, 47), 221 (M^+ - CH_2NCH_2, 95), 206 (88), 177 (100), 73 (32); HRMS: (EI, 70 eV) Calculated ($C_{15}H_{25}NOSi$) 263.1705 (M^+) Found: 263.1700; Analysis: $C_{15}H_{25}NOSi$ Calcd: C, 68.38; H, 9.56; N, 5.32 Found: C, 68.43; H, 9.65; N, 5.38

2-{2-[4-(*tert*-Butyldimethylsiloxy)phenyl]ethylaminomethyl}-1-tetralone (5ke)



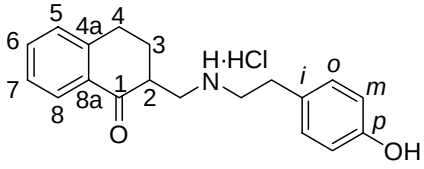
5ke

2-Bromo-1-tetralone **4e** (1.8 mmol) was added to a stirred suspension of imine **1k** (1.2 mmol), $Bi(OTf)_3$ (0.12 mmol), and $GeCl_2$-dioxane (1.8 mmol) in CH_2Cl_2 (4 mL) at room temperature. The mixture was stirred for 5 min at room temperature, and then saturated aq. $NaHCO_3$ (30 mL) was added. The mixture was extracted with Et_2O (20 mLx3), dried ($MgSO_4$), and evaporated to give the crude product (0.64 mmol, 53%). Purification by silica gel chromatography [solvent; hexane 100 mL, hexane/EtOAc = 90/10 (100 mL), 80/20 (100 mL), 70/30 (100 mL), and 60/40 (100 mL)] afforded the pure product **5ke** as a pale yellow liquid (0.36 mmol, 30%).

Analytical data: ^{1}H NMR: (400 MHz, $CDCl_3$) 8.00 (d, *J* = 7.8 Hz, 1H, 8-H), 7.45 (dd, *J* = 7.8, 7.8 Hz, 1H, 6-H), 7.29 (t, *J* = 7.8, 7.8 Hz, 1H, 7-H), 7.22 (d, *J* = 7.8 Hz, 1H, 5-H), 7.07 (d, *J* = 8.5 Hz, 2H, NCH_2CH_2Ph(*o*)), 6.77 (d, *J* = 8.5 Hz, 2H, NCH_2CH_2Ph(*m*)), 3.11 (dd, *J* = 11.9, 6.6 Hz, 1H, 2-CH^AN), 3.07-2.81 (m, 4H, 4-H_2 and N*C*H_2CH_2), 2.80-2.71 (m, 3H, 2-CH^BN and NCH_2*C*H_2), 2.71-2.62 (m, 1H, 2-H), 2.18 (dddd, *J* = 12.4, 4.4, 4.4, 4.4 Hz, 1H, 3-H^A), 1.93 (dddd, *J* = 12.4, 12.4, 12.4, 5.1 Hz, 1H, 3-H^B), 1.66 (brs, 1H, NH), 0.98 (s, 9H, *t*Bu), 0.19 (s, 6H, $SiMe_2$); ^{13}C NMR: (100 MHz, $CDCl_3$) 200.1 (s, C-1), 153.8 (s, NCH_2CH_2Ph(*p*)), 144.0 (s, C-4a), 133.3 (d, C-6), 132.7 (s), 132.5 (s), 129.5 (d, NCH_2CH_2Ph(*o*)), 128.6 (d, C-5), 127.2 (d, C-8),

126.5 (d, C-7), 119.9 (d, $NCH_2CH_2Ph(m)$), 51.8 (t, NCH_2CH_2), 50.2 (t, 2-CH_2N), 47.9 (d, C-2), 35.6 (t, NCH_2CH_2), 28.7 (t, C-4), 27.6 (t, C-3), 25.6 (q, $SiCMe_3$) , 18.1 (s, $SiCMe_3$), -4.5 (q, $SiMe_2$); IR: (neat) 3329 (NH), 1682 (C=O); MS: (CI, 200 eV) 410 (M^+ + 1, 7), 252 (66), 159 (M^+ - 4-(tBuMe$_2$SiO)$C_6H_4CH_2CH_2NH$, 100); HRMS: (CI, 200 eV) Calculated ($C_{25}H_{36}NO_2Si$) 410.2515 (M^+ + 1); Found: 410.2502

2-[2-(4-Hydroxyphenyl)ethylaminomethyl]-1-tetralone hydrochloride (Be-2254)



Be-2254 (**8ke**)

Aminoketone **5ke** (0.57 mmol) was suspended in 5M HCl (aqueous, 8 mL). After the reaction mixture was stirred at 100 ^oC for 18 h, cooled to room temperature, Et_2O (10 mL) was added. The phases separated, the organic phase was extracted with H_2O (10 mLx2). The combined aqueous layers were concentrated *in vacuo* to give the titled compound **8ke** (83%). Recrystallization from EtOH/hexane gave the pure product as a colorless solid (0.37 mmol, 64%). Analytical data: mp: 165-167 ^oC; ^1H NMR: (400 MHz, CD_3OD) 7.92 (d, J = 7.5 Hz, 1H, 8-H), 7.49 (dd, J = 7.5, 7.5 Hz, 1H, 6-H), 7.31-7.24 (m, 2H, 5-H and 7-H), 7.09 (d, J = 8.5 Hz, 2H, $NCH_2CH_2Ph(o)$), 6.74 (d, J = 8.5 Hz, 2H, $NCH_2CH_2Ph(m)$), 3.44 (dd, J = 12.6, 8.6 Hz, 1H, 2-CH^AN), 3.28-2.89 (m, 8H, 2-H, 4-H_2 2-CH^BN and NCH_2CH_2), 2.23 (dddd, J = 12.8, 3.6, 3.6, 3.6 Hz, 1H, 3-H^A), 1.85 (dddd, J = 12.8, 12.8, 12.8, 4.3 Hz, 1H, 3-H^B); ^{13}C NMR: (100 MHz, CD_3OD) 200.2 (s, C-1), 157.7 (s, $NCH_2CH_2Ph(p)$), 145.7 (s, C-4a), 135.4 (d, C-6), 132.7 (s, C-8a), 130.8 (d, $NCH_2CH_2Ph(o)$), 130.1 (d, C-5), 128.3 (s, $NCH_2CH_2Ph(i)$), 128.1 (d), 127.8 (d), 116.7 (d, $NCH_2CH_2Ph(m)$), 51.0 (t, NCH_2CH_2), 45.5 (d, C-2), 32.3 (t, NCH_2CH_2), 29.7 (t, C-4), 28.5 (t, C-3); IR: (KBr) 3437 (OH), 2800 (NH_2^+), 1674 (C=O); MS: (CI, 200 eV) 296 (M^+ + 1 - HCl, 3), 159 (M^+ - 4-(HO)$C_6H_4CH_2CH_2NH$, 100), 138 (46); Analysis: $C_{19}H_{22}ClNO_2$ Calcd: C, 68.77; H, 6.68; N, 4.22 Found: C, 68.59; H, 6.51; N, 4.46

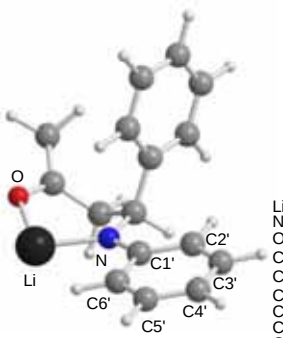
Computational method.

We applied the HF/DFT hybrid method referenced as B3PW91 three parameter hybrid functional.[8] All calculations were performed with Gaussian 03 revision C.02.[9] For basis sets, 6-31+G(d,p) was employed. Solvent effects were included via a PCM model with atomic radii of the United force field (referenced as UA0). All energies were calculated including the zero point energy correction.

Total energies for all of the calculated species (in hartree). All energies includes zero point vibration energy correction.

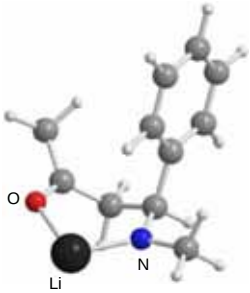
1a	-556.37849
1b	-364.748832
2a	-200.016252
2b	-275.20438
2c	-3647.973358
3a	-756.394236
3b	-564.743173

3c	-831.593859
3d	-639.942753
3e	-4204.390071
3f	-4012.759995



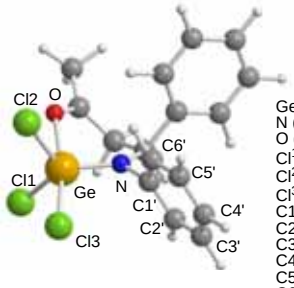
Li-N = 1.962 Å
N (-0.84498)
O (-0.6779)
C1' (0.16617)
C2' (-0.36276)
C3' (-0.25485)
C4' (-0.36252)
C5' (-0.26536)
C6' (-0.32048)

3a



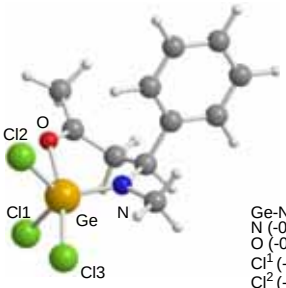
Li-N = 1.900 Å
N (-1.00322)
O (-0.67851)
Li (0.94035)

3b



Ge-N = 1.796 Å
N (-0.92023)
O (-0.61085)
Cl^1 (-0.3837)
Cl^2 (-0.37055)
Cl^3 (-0.44069)
C1' (0.13988)
C2' (-0.25453)
C3' (-0.25364)
C4' (-0.25886)
C5' (-0.25173)
C6' (-0.24769)

3e



Ge-N = 1.788 Å
N (-0.93238)
O (-0.61523)
Cl^1 (-0.38481)
Cl^2 (-0.37505)
Cl^3 (-0.45734)

3f

* Nunbers in parentheses are NBO charges.

Geometries (PDB)

1a

```
ATOM      1  C   UNK     1      -2.702   1.207  -0.454  1.00  0.00
ATOM      2  C   UNK     1      -1.845   0.160  -0.081  1.00  0.00
ATOM      3  C   UNK     1      -4.086   1.049  -0.384  1.00  0.00
ATOM      4  H   UNK     1      -2.278   2.150  -0.801  1.00  0.00
ATOM      5  C   UNK     1      -2.398  -1.053   0.366  1.00  0.00
ATOM      6  C   UNK     1      -4.626  -0.159   0.060  1.00  0.00
ATOM      7  H   UNK     1      -4.742   1.868  -0.675  1.00  0.00
ATOM      8  C   UNK     1      -3.778  -1.209   0.434  1.00  0.00
ATOM      9  H   UNK     1      -1.733  -1.864   0.656  1.00  0.00
ATOM     10  H   UNK     1      -5.707  -0.286   0.116  1.00  0.00
ATOM     11  H   UNK     1      -4.200  -2.151   0.780  1.00  0.00
ATOM     12  C   UNK     1      -0.397   0.371  -0.170  1.00  0.00
ATOM     13  H   UNK     1      -0.084   1.367  -0.524  1.00  0.00
ATOM     14  N   UNK     1       0.462  -0.535   0.122  1.00  0.00
ATOM     15  C   UNK     1       1.833  -0.232   0.069  1.00  0.00
ATOM     16  C   UNK     1       2.365   0.987   0.526  1.00  0.00
```

```
ATOM     17  C   UNK     1       2.708  -1.221  -0.410  1.00  0.00
ATOM     18  C   UNK     1       3.740   1.216   0.471  1.00  0.00
ATOM     19  H   UNK     1       1.705   1.740   0.953  1.00  0.00
ATOM     20  C   UNK     1       4.078  -0.979  -0.477  1.00  0.00
ATOM     21  H   UNK     1       2.292  -2.173  -0.738  1.00  0.00
ATOM     22  C   UNK     1       4.601   0.241  -0.037  1.00  0.00
ATOM     23  H   UNK     1       4.141   2.160   0.839  1.00  0.00
ATOM     24  H   UNK     1       4.742  -1.750  -0.866  1.00  0.00
ATOM     25  H   UNK     1       5.674   0.423  -0.076  1.00  0.00
CONECT    1    2    3    4
CONECT    2    1    5   12
CONECT    3    1    6    7
CONECT    4    1
CONECT    5    2    8    9
CONECT    6    3    8   10
CONECT    7    3
CONECT    8    5    6   11
CONECT    9    5
CONECT   10    6
CONECT   11    8
CONECT   12    2   13   14
CONECT   13   12
CONECT   14   12   15
CONECT   15   14   16   17
CONECT   16   15   18   19
CONECT   17   15   20   21
CONECT   18   16   22   23
CONECT   19   16
CONECT   20   17   22   24
CONECT   21   17
CONECT   22   18   20   25
CONECT   23   18
CONECT   24   20
CONECT   25   22
MASTER        0    0    0    0    0    0    0    0   25    0   25    0
END
```

1b

```
ATOM      1  C   UNK     1      -0.923   1.280   0.000  1.00  0.00
ATOM      2  C   UNK     1      -0.031   0.197   0.000  1.00  0.00
ATOM      3  C   UNK     1      -2.302   1.065   0.000  1.00  0.00
ATOM      4  H   UNK     1      -0.531   2.298   0.000  1.00  0.00
ATOM      5  C   UNK     1      -0.544  -1.110   0.000  1.00  0.00
ATOM      6  C   UNK     1      -2.802  -0.238   0.000  1.00  0.00
ATOM      7  H   UNK     1      -2.984   1.913   0.000  1.00  0.00
ATOM      8  C   UNK     1      -1.919  -1.324   0.000  1.00  0.00
ATOM      9  H   UNK     1       0.148  -1.950   0.000  1.00  0.00
ATOM     10  H   UNK     1      -3.878  -0.410   0.000  1.00  0.00
ATOM     11  H   UNK     1      -2.309  -2.341   0.000  1.00  0.00
ATOM     12  C   UNK     1       1.415   0.471   0.000  1.00  0.00
ATOM     13  H   UNK     1       1.692   1.541   0.000  1.00  0.00
ATOM     14  N   UNK     1       2.305  -0.443   0.000  1.00  0.00
ATOM     15  C   UNK     1       3.692  -0.028   0.000  1.00  0.00
ATOM     16  H   UNK     1       4.195  -0.446   0.880  1.00  0.00
```

```
ATOM     17  H   UNK     1       4.196  -0.447  -0.879  1.00  0.00
ATOM     18  H   UNK     1       3.826   1.065   0.000  1.00  0.00
CONECT    1    2    3    4
CONECT    2    1    5   12
CONECT    3    1    6    7
CONECT    4    1
CONECT    5    2    8    9
CONECT    6    3    8   10
CONECT    7    3
CONECT    8    5    6   11
CONECT    9    5
CONECT   10    6
CONECT   11    8
CONECT   12    2   13   14
CONECT   13   12
CONECT   14   12   15
CONECT   15   14   16   17   18
CONECT   16   15
CONECT   17   15
CONECT   18   15
MASTER        0    0    0    0    0    0    0    0   18    0   18    0
END
```

2a

```
ATOM      1  C   UNK     1       0.495   1.429   0.009  1.00  0.00
ATOM      2  H   UNK     1       1.535   1.741   0.045  1.00  0.00
ATOM      3  H   UNK     1      -0.269   2.204  -0.018  1.00  0.00
ATOM      4  C   UNK     1       0.154   0.107  -0.014  1.00  0.00
ATOM      5  C   UNK     1       1.241  -0.954   0.020  1.00  0.00
ATOM      6  H   UNK     1       1.154  -1.604  -0.859  1.00  0.00
ATOM      7  H   UNK     1       2.248  -0.528   0.045  1.00  0.00
ATOM      8  H   UNK     1       1.108  -1.594   0.902  1.00  0.00
ATOM      9  O   UNK     1      -1.068  -0.358  -0.065  1.00  0.00
ATOM     10 Li   UNK     1      -2.856  -0.282   0.105  1.00  0.00
CONECT    1    2    3    4
CONECT    2    1
CONECT    3    1
CONECT    4    1    5    9
CONECT    5    4    6    7    8
CONECT    6    5
CONECT    7    5
CONECT    8    5
CONECT    9    4
MASTER        0    0    0    0    0    0    0    0   10    0   10    0
END
```

2b

```
ATOM      1  C   UNK     1       0.177   1.640   0.003  1.00  0.00
ATOM      2  H   UNK     1      -0.843   2.000   0.005  1.00  0.00
ATOM      3  H   UNK     1       0.980   2.369   0.005  1.00  0.00
ATOM      4  C   UNK     1       0.509   0.318  -0.001  1.00  0.00
ATOM      5  O   UNK     1       1.672  -0.229  -0.004  1.00  0.00
ATOM      6 Li   UNK     1       1.312  -2.086   0.011  1.00  0.00
ATOM      7  O   UNK     1      -0.481  -0.687  -0.003  1.00  0.00
ATOM      8  C   UNK     1      -1.850  -0.309   0.000  1.00  0.00
```

```
ATOM      9  H   UNK     1      -2.097   0.280  -0.891  1.00  0.00
ATOM     10  H   UNK     1      -2.430  -1.234  -0.004  1.00  0.00
ATOM     11  H   UNK     1      -2.096   0.272   0.897  1.00  0.00
CONECT    1    2    3    4
CONECT    2    1
CONECT    3    1
CONECT    4    1    5    7
CONECT    5    4
CONECT    7    4    8
CONECT    8    7    9   10   11
CONECT    9    8
CONECT   10    8
CONECT   11    8
MASTER        0    0    0    0    0    0    0    0   11    0   11    0
END
```

2c

```
ATOM      1  C   UNK     1      -3.120  -1.266  -0.419  1.00  0.00
ATOM      2  H   UNK     1      -4.151  -1.083  -0.134  1.00  0.00
ATOM      3  H   UNK     1      -2.819  -2.279  -0.668  1.00  0.00
ATOM      4  C   UNK     1      -2.252  -0.254  -0.473  1.00  0.00
ATOM      5  C   UNK     1      -2.542   1.178  -0.157  1.00  0.00
ATOM      6  H   UNK     1      -2.343   1.815  -1.026  1.00  0.00
ATOM      7  H   UNK     1      -3.585   1.303   0.142  1.00  0.00
ATOM      8  H   UNK     1      -1.912   1.538   0.667  1.00  0.00
ATOM      9  O   UNK     1      -0.964  -0.517  -0.937  1.00  0.00
ATOM     10 Ge   UNK     1       0.478  -0.040  -0.028  1.00  0.00
ATOM     11 Cl   UNK     1       1.023   1.996  -0.400  1.00  0.00
ATOM     12 Cl   UNK     1       0.175  -0.311   2.073  1.00  0.00
ATOM     13 Cl   UNK     1       2.021  -1.321  -0.748  1.00  0.00
CONECT    1    2    3    4
CONECT    2    1
CONECT    3    1
CONECT    4    1    5    9
CONECT    5    4    6    7    8
CONECT    6    5
CONECT    7    5
CONECT    8    5
CONECT    9    4   10
CONECT   10    9   11   12   13
CONECT   11   10
CONECT   12   10
CONECT   13   10
MASTER        0    0    0    0    0    0    0    0   13    0   13    0
END
```

3a

```
HETATM    1  C   Grp     0      -2.458   1.632  -3.387                       C
HETATM    2  C   Grp     0      -2.346   0.378  -2.578                       C
HETATM    3  C   Grp     0      -1.096  -0.453  -2.709                       C
HETATM    4  N   Grp     0      -0.876  -1.097  -0.340                       N
HETATM    5  C   Grp     0       1.448  -2.516   2.918                       C
HETATM    6  C   Grp     0       0.063  -2.733   2.834                       C
HETATM    7  C   Grp     0       2.055  -1.793   1.889                       C
HETATM    8  C   Grp     0      -0.674  -2.250   1.763                       C
```

```
HETATM    9  C   Grp     0       1.324  -1.297   0.807                       C
HETATM   10  C   Grp     0      -0.084  -1.513   0.688                       C
HETATM   11  C   Grp     0      -0.200  -0.431  -1.428                       C
HETATM   12  C   Grp     0       0.056   3.109   0.053                       C
HETATM   13  C   Grp     0       1.027   3.692  -0.764                       C
HETATM   14  C   Grp     0      -0.326   1.781  -0.144                       C
HETATM   15  C   Grp     0       1.618   2.931  -1.778                       C
HETATM   16  C   Grp     0       0.250   1.012  -1.162                       C
HETATM   17  C   Grp     0       1.232   1.604  -1.969                       C
HETATM   18  H   Grp     0      -3.390   2.159  -3.174                       H
HETATM   19  H   Grp     0      -1.598   2.277  -3.167                       H
HETATM   20  H   Grp     0      -1.069   1.317   0.500                       H
HETATM   21  H   Grp     0       2.385   3.371  -2.414                       H
HETATM   22  H   Grp     0       1.706   1.015  -2.757                       H
HETATM   23  O   Grp     0      -3.253   0.038  -1.813                       O
HETATM   24 Li   Grp     0      -2.828  -1.279  -0.411                      LI
HETATM   25  H   Grp     0       1.329   4.727  -0.608                       H
HETATM   26  H   Grp     0      -0.400   3.691   0.853                       H
HETATM   27  H   Grp     0       0.705  -0.986  -1.740                       H
HETATM   28  H   Grp     0       1.849  -0.719   0.054                       H
HETATM   29  H   Grp     0      -1.748  -2.445   1.725                       H
HETATM   30  H   Grp     0       3.127  -1.597   1.927                       H
HETATM   31  H   Grp     0      -0.448  -3.291   3.619                       H
HETATM   32  H   Grp     0       2.027  -2.895   3.757                       H
HETATM   33  H   Grp     0      -1.392  -1.495  -2.886                       H
HETATM   34  H   Grp     0      -0.509  -0.108  -3.567                       H
HETATM   35  H   Grp     0      -2.400   1.388  -4.455                       H
TER
CONECT    1    2   19   35   18
CONECT    2    1    3   23
CONECT    3    2   11   33   34
CONECT    4   10   11   24
CONECT    5    7    6   32
CONECT    6    5    8   31
CONECT    7    5    9   30
CONECT    8    6   10   29
CONECT    9    7   10   28
CONECT   10    4    8    9
CONECT   11    3    4   16   27
CONECT   12   13   14   26
CONECT   13   12   15   25
CONECT   14   12   16   20
CONECT   15   13   17   21
CONECT   16   11   14   17
CONECT   17   15   16   22
CONECT   18    1
CONECT   19    1
CONECT   20   14
CONECT   21   15
CONECT   22   17
CONECT   23   24    2
CONECT   24   23    4
CONECT   25   13
```

```
CONECT   26   12
CONECT   27   11
CONECT   28    9
CONECT   29    8
CONECT   30    7
CONECT   31    6
CONECT   32    5
CONECT   33    3
CONECT   34    3
CONECT   35    1
END
```

3b

```
HETATM    1  C   Grp     0       1.793  -2.736   1.715                       C
HETATM    2  C   Grp     0      -1.849   0.347  -1.348                       C
HETATM    3  C   Grp     0      -1.428  -0.968  -0.763                       C
HETATM    4  C   Grp     0      -0.161  -1.602  -1.268                       C
HETATM    5  N   Grp     0       0.633  -2.482   0.896                       N
HETATM    6  C   Grp     0       0.985  -1.642  -0.206                       C
HETATM    7  C   Grp     0       1.255   1.764   1.575                       C
HETATM    8  C   Grp     0       2.085   2.482   0.710                       C
HETATM    9  C   Grp     0       0.917   0.440   1.287                       C
HETATM   10  C   Grp     0       2.580   1.860  -0.440                       C
HETATM   11  C   Grp     0       1.395  -0.192   0.133                       C
HETATM   12  C   Grp     0       2.240   0.534  -0.718                       C
HETATM   13 Li   Grp     0      -1.192  -2.860   1.268                       LI
HETATM   14  H   Grp     0       2.645  -3.177   1.148                       H
HETATM   15  H   Grp     0       1.546  -3.452   2.512                       H
HETATM   16  H   Grp     0       2.214  -1.839   2.220                       H
HETATM   17  H   Grp     0      -1.031   1.070  -1.231                       H
HETATM   18  H   Grp     0      -2.754   0.721  -0.868                       H
HETATM   19  H   Grp     0      -2.015   0.233  -2.426                       H
HETATM   20  H   Grp     0       0.185  -1.080  -2.166                       H
HETATM   21  H   Grp     0      -0.386  -2.645  -1.530                       H
HETATM   22  H   Grp     0       1.851  -2.053  -0.780                       H
HETATM   23  H   Grp     0       0.874   2.237   2.480                       H
HETATM   24  H   Grp     0       2.353   3.514   0.934                       H
HETATM   25  H   Grp     0       0.283  -0.139   1.958                       H
HETATM   26  H   Grp     0       3.236   2.406  -1.116                       H
HETATM   27  H   Grp     0       2.639   0.051  -1.612                       H
HETATM   28  O   Grp     0      -2.104  -1.508   0.117                       O
TER
CONECT    1    5   14   15   16
CONECT    2    3   17   18   19
CONECT    3    2    4   28
CONECT    4    3    6   20   21
CONECT    5    1    6   13
CONECT    6    4    5   11   22
CONECT    7    8    9   23
CONECT    8    7   10   24
CONECT    9    7   11   25
CONECT   10    8   12   26
CONECT   11    6    9   12
CONECT   12   10   11   27
```

```
CONECT   13   28    5
CONECT   14    1
CONECT   15    1
CONECT   16    1
CONECT   17    2
CONECT   18    2
CONECT   19    2
CONECT   20    4
CONECT   21    4
CONECT   22    6
CONECT   23    7
CONECT   24    8
CONECT   25    9
CONECT   26   10
CONECT   27   12
CONECT   28    3   13
END
```

3c

```
ATOM      1  C   UNK     1      -1.122   1.992  -1.119  1.00  0.00
ATOM      2  C   UNK     1      -0.582   0.970  -0.324  1.00  0.00
ATOM      3  C   UNK     1      -1.613   3.165  -0.546  1.00  0.00
ATOM      4  H   UNK     1      -1.150   1.870  -2.203  1.00  0.00
ATOM      5  C   UNK     1      -0.535   1.160   1.060  1.00  0.00
ATOM      6  C   UNK     1      -1.570   3.338   0.840  1.00  0.00
ATOM      7  H   UNK     1      -2.025   3.948  -1.182  1.00  0.00
ATOM      8  C   UNK     1      -1.026   2.332   1.640  1.00  0.00
ATOM      9  H   UNK     1      -0.091   0.382   1.678  1.00  0.00
ATOM     10  H   UNK     1      -1.949   4.255   1.290  1.00  0.00
ATOM     11  H   UNK     1      -0.977   2.462   2.721  1.00  0.00
ATOM     12  C   UNK     1      -0.086  -0.332  -0.971  1.00  0.00
ATOM     13  C   UNK     1       2.099  -0.689  -0.095  1.00  0.00
ATOM     14  C   UNK     1       2.612   0.516  -0.668  1.00  0.00
ATOM     15  C   UNK     1       3.061  -1.480   0.608  1.00  0.00
ATOM     16  C   UNK     1       3.959   0.866  -0.560  1.00  0.00
ATOM     17  H   UNK     1       1.945   1.196  -1.188  1.00  0.00
ATOM     18  C   UNK     1       4.396  -1.118   0.713  1.00  0.00
ATOM     19  H   UNK     1       2.725  -2.414   1.064  1.00  0.00
ATOM     20  C   UNK     1       4.875   0.064   0.126  1.00  0.00
ATOM     21  H   UNK     1       4.294   1.797  -1.019  1.00  0.00
ATOM     22  H   UNK     1       5.080  -1.769   1.258  1.00  0.00
ATOM     23  H   UNK     1       5.922   0.348   0.206  1.00  0.00
ATOM     24  N   UNK     1       0.812  -1.132  -0.172  1.00  0.00
ATOM     25 Li   UNK     1       0.063  -2.588   0.903  1.00  0.00
ATOM     26  C   UNK     1      -1.313  -1.175  -1.423  1.00  0.00
ATOM     27  H   UNK     1      -0.934  -2.088  -1.899  1.00  0.00
ATOM     28  H   UNK     1      -1.902  -0.621  -2.157  1.00  0.00
ATOM     29  C   UNK     1      -2.213  -1.597  -0.298  1.00  0.00
ATOM     30  O   UNK     1      -1.859  -2.277   0.664  1.00  0.00
ATOM     31  H   UNK     1       0.385  -0.040  -1.930  1.00  0.00
ATOM     32  O   UNK     1      -3.466  -1.174  -0.436  1.00  0.00
ATOM     33  C   UNK     1      -4.394  -1.540   0.602  1.00  0.00
ATOM     34  H   UNK     1      -4.070  -1.127   1.560  1.00  0.00
ATOM     35  H   UNK     1      -5.347  -1.108   0.301  1.00  0.00
```

```
ATOM     36  H   UNK     1      -4.469  -2.627   0.676  1.00  0.00
CONECT    1    2    3    4
CONECT    2    1    5   12
CONECT    3    1    6    7
CONECT    4    1
CONECT    5    2    8    9
CONECT    6    3    8   10
CONECT    7    3
CONECT    8    5    6   11
CONECT    9    5
CONECT   10    6
CONECT   11    8
CONECT   12    2   24   26   31
CONECT   13   14   15   24
CONECT   14   13   16   17
CONECT   15   13   18   19
CONECT   16   14   20   21
CONECT   17   14
CONECT   18   15   20   22
CONECT   19   15
CONECT   20   16   18   23
CONECT   21   16
CONECT   22   18
CONECT   23   20
CONECT   24   12   13   25
CONECT   25   24
CONECT   26   12   27   28   29
CONECT   27   26
CONECT   28   26
CONECT   29   26   30   32
CONECT   30   29
CONECT   31   12
CONECT   32   29   33
CONECT   33   32   34   35   36
CONECT   34   33
CONECT   35   33
CONECT   36   33
MASTER        0    0    0    0    0    0    0    0   36    0   36    0
END
```

3d

```
ATOM      1  C   UNK     1       1.895  -0.352   1.246  1.00  0.00
ATOM      2  C   UNK     1       1.054   0.271   0.315  1.00  0.00
ATOM      3  C   UNK     1       2.845  -1.294   0.845  1.00  0.00
ATOM      4  H   UNK     1       1.807  -0.093   2.303  1.00  0.00
ATOM      5  C   UNK     1       1.205  -0.057  -1.036  1.00  0.00
ATOM      6  C   UNK     1       2.976  -1.623  -0.507  1.00  0.00
ATOM      7  H   UNK     1       3.487  -1.768   1.587  1.00  0.00
ATOM      8  C   UNK     1       2.153  -0.997  -1.447  1.00  0.00
ATOM      9  H   UNK     1       0.571   0.455  -1.758  1.00  0.00
ATOM     10  H   UNK     1       3.720  -2.352  -0.825  1.00  0.00
ATOM     11  H   UNK     1       2.258  -1.236  -2.505  1.00  0.00
ATOM     12  C   UNK     1      -0.019   1.286   0.768  1.00  0.00
ATOM     13  N   UNK     1      -0.416   2.267  -0.192  1.00  0.00
```

```
ATOM     14 Li   UNK     1      -2.008   2.030  -1.205  1.00  0.00
ATOM     15  C   UNK     1      -1.248   0.502   1.321  1.00  0.00
ATOM     16  H   UNK     1      -1.954   1.246   1.712  1.00  0.00
ATOM     17  H   UNK     1      -0.948  -0.163   2.133  1.00  0.00
ATOM     18  C   UNK     1      -1.980  -0.294   0.282  1.00  0.00
ATOM     19  O   UNK     1      -2.539   0.182  -0.704  1.00  0.00
ATOM     20  H   UNK     1       0.410   1.758   1.686  1.00  0.00
ATOM     21  C   UNK     1       0.670   3.184  -0.434  1.00  0.00
ATOM     22  H   UNK     1       1.568   2.731  -0.909  1.00  0.00
ATOM     23  H   UNK     1       0.344   3.995  -1.102  1.00  0.00
ATOM     24  H   UNK     1       1.047   3.674   0.494  1.00  0.00
ATOM     25  O   UNK     1      -1.990  -1.604   0.528  1.00  0.00
ATOM     26  C   UNK     1      -2.663  -2.437  -0.432  1.00  0.00
ATOM     27  H   UNK     1      -2.192  -2.341  -1.413  1.00  0.00
ATOM     28  H   UNK     1      -2.558  -3.454  -0.055  1.00  0.00
ATOM     29  H   UNK     1      -3.717  -2.160  -0.502  1.00  0.00
CONECT    1    2    3    4
CONECT    2    1    5   12
CONECT    3    1    6    7
CONECT    4    1
CONECT    5    2    8    9
CONECT    6    3    8   10
CONECT    7    3
CONECT    8    5    6   11
CONECT    9    5
CONECT   10    6
CONECT   11    8
CONECT   12    2   13   15   20
CONECT   13   12   14   21
CONECT   14   13
CONECT   15   12   16   17   18
CONECT   16   15
CONECT   17   15
CONECT   18   15   19   25
CONECT   19   18
CONECT   20   12
CONECT   21   13   22   23   24
CONECT   22   21
CONECT   23   21
CONECT   24   21
CONECT   25   18   26
CONECT   26   25   27   28   29
CONECT   27   26
CONECT   28   26
CONECT   29   26
MASTER        0    0    0    0    0    0    0    0   29    0   29    0
END
```

3e

```
HETATM    1  C   UNK     1       1.819   0.521  -1.680                       C
HETATM    2  C   UNK     1       0.527   0.568  -1.149                       C
HETATM    3  C   UNK     1       2.688   1.604  -1.534                       C
HETATM    4  C   UNK     1       0.129   1.699  -0.428                       C
HETATM    5  C   UNK     1       2.277   2.738  -0.832                       C
```

```
HETATM    6  C   UNK     1       0.996   2.780  -0.275                       C
HETATM    7  C   UNK     1      -0.422  -0.595  -1.408                       C
HETATM    8  C   UNK     1      -0.293  -1.519   0.828                       C
HETATM    9  C   UNK     1      -0.204  -0.865   2.059                       C
HETATM   10  C   UNK     1       0.468  -2.672   0.606                       C
HETATM   11  C   UNK     1       0.609  -1.371   3.073                       C
HETATM   12  C   UNK     1       1.279  -3.179   1.619                       C
HETATM   13  C   UNK     1       1.349  -2.535   2.857                       C
HETATM   14  N   UNK     1      -1.144  -0.988  -0.192                       N
HETATM   15  C   UNK     1      -1.346  -0.309  -2.609                       C
HETATM   16  C   UNK     1      -2.416   0.689  -2.315                       C
HETATM   17  C   UNK     1      -2.628   1.864  -3.198                       C
HETATM   18  O   UNK     1      -3.148   0.516  -1.326                       O
HETATM   19  Ge  UNK     1      -2.920  -1.144   0.022                      GE
HETATM   20  Cl  UNK     1      -3.027  -2.888   1.461                      CL
HETATM   21  Cl  UNK     1      -4.171  -2.170  -1.497                      CL
HETATM   22  Cl  UNK     1      -3.981   0.226   1.372                      CL
HETATM   23  H   UNK     1       2.147  -0.367  -2.220                       H
HETATM   24  H   UNK     1       3.691   1.556  -1.957                       H
HETATM   25  H   UNK     1      -0.856   1.730   0.033                       H
HETATM   26  H   UNK     1       2.954   3.582  -0.709                       H
HETATM   27  H   UNK     1       0.674   3.655   0.289                       H
HETATM   28  H   UNK     1       0.191  -1.445  -1.739                       H
HETATM   29  H   UNK     1      -0.776   0.046   2.218                       H
HETATM   30  H   UNK     1       0.400  -3.194  -0.348                       H
HETATM   31  H   UNK     1       0.663  -0.855   4.030                       H
HETATM   32  H   UNK     1       1.850  -4.090   1.444                       H
HETATM   33  H   UNK     1       1.981  -2.937   3.648                       H
HETATM   34  H   UNK     1      -1.863  -1.237  -2.897                       H
HETATM   35  H   UNK     1      -0.736   0.005  -3.459                       H
HETATM   36  H   UNK     1      -2.771   1.521  -4.229                       H
HETATM   37  H   UNK     1      -3.483   2.457  -2.870                       H
HETATM   38  H   UNK     1      -1.718   2.477  -3.199                       H
CONECT    1    2    3   23
CONECT    2    1    4    7
CONECT    3    1    5   24
CONECT    4    2    6   25
CONECT    5    3    6   26
CONECT    6    4    5   27
CONECT    7    2   14   15   28
CONECT    8    9   10   14
CONECT    9    8   11   29
CONECT   10    8   12   30
CONECT   11    9   13   31
CONECT   12   10   13   32
CONECT   13   11   12   33
CONECT   14    7    8   19
CONECT   15    7   34   35   16
CONECT   16   15   17   18
CONECT   17   16   36   37   38
CONECT   18   16   19
CONECT   19   14   20   21   22   18
CONECT   20   19
```

```
CONECT   21   19
CONECT   22   19
CONECT   23    1
CONECT   24    3
CONECT   25    4
CONECT   26    5
CONECT   27    6
CONECT   28    7
CONECT   29    9
CONECT   30   10
CONECT   31   11
CONECT   32   12
CONECT   33   13
CONECT   34   15
CONECT   35   15
CONECT   36   17
CONECT   37   17
CONECT   38   17
END
```

3f

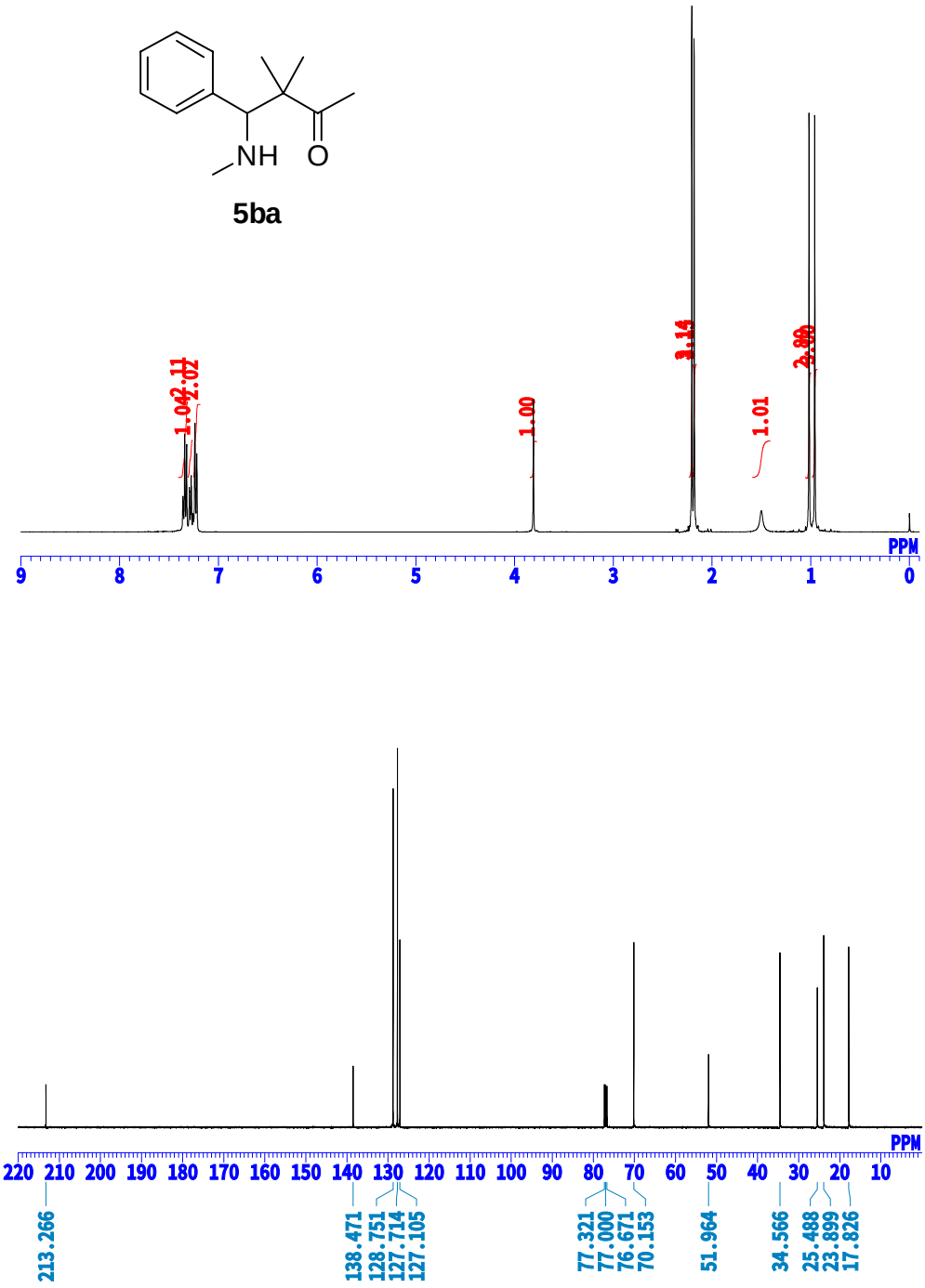
```
HETATM    1  C   UNK     1       2.998   0.111  -0.450                       C
HETATM    2  C   UNK     1       1.669  -0.058  -0.048                       C
HETATM    3  C   UNK     1       3.685   1.294  -0.170                       C
HETATM    4  C   UNK     1       1.052   0.955   0.696                       C
HETATM    5  C   UNK     1       3.057   2.305   0.559                       C
HETATM    6  C   UNK     1       1.742   2.129   0.999                       C
HETATM    7  C   UNK     1       0.929  -1.331  -0.445                       C
HETATM    8  N   UNK     1       0.243  -1.948   0.685                       N
HETATM    9  C   UNK     1       0.036  -1.101  -1.680                       C
HETATM   10  C   UNK     1      -1.191  -0.307  -1.390                       C
HETATM   11  C   UNK     1      -1.577   0.849  -2.239                       C
HETATM   12  O   UNK     1      -1.913  -0.635  -0.432                       O
HETATM   13  C   UNK     1       1.204  -2.442   1.670                       C
HETATM   14  Ge  UNK     1      -1.506  -2.292   0.830                      GE
HETATM   15  Cl  UNK     1      -2.720  -1.115   2.241                      CL
HETATM   16  Cl  UNK     1      -2.575  -3.394  -0.766                      CL
HETATM   17  Cl  UNK     1      -1.478  -4.114   2.201                      CL
HETATM   18  H   UNK     1       3.496  -0.684  -1.008                       H
HETATM   19  H   UNK     1       4.715   1.415  -0.500                       H
HETATM   20  H   UNK     1       0.037   0.819   1.062                       H
HETATM   21  H   UNK     1       3.593   3.224   0.794                       H
HETATM   22  H   UNK     1       1.253   2.906   1.584                       H
HETATM   23  H   UNK     1       1.694  -2.045  -0.794                       H
HETATM   24  H   UNK     1      -0.313  -2.073  -2.060                       H
HETATM   25  H   UNK     1       0.630  -0.635  -2.471                       H
HETATM   26  H   UNK     1      -1.617   0.528  -3.288                       H
HETATM   27  H   UNK     1      -2.537   1.264  -1.929                       H
HETATM   28  H   UNK     1      -0.792   1.613  -2.179                       H
HETATM   29  H   UNK     1       1.831  -1.614   2.023                       H
HETATM   30  H   UNK     1       0.701  -2.877   2.529                       H
HETATM   31  H   UNK     1       1.860  -3.206   1.226                       H
CONECT    1    2    3   18
CONECT    2    1    4    7
```

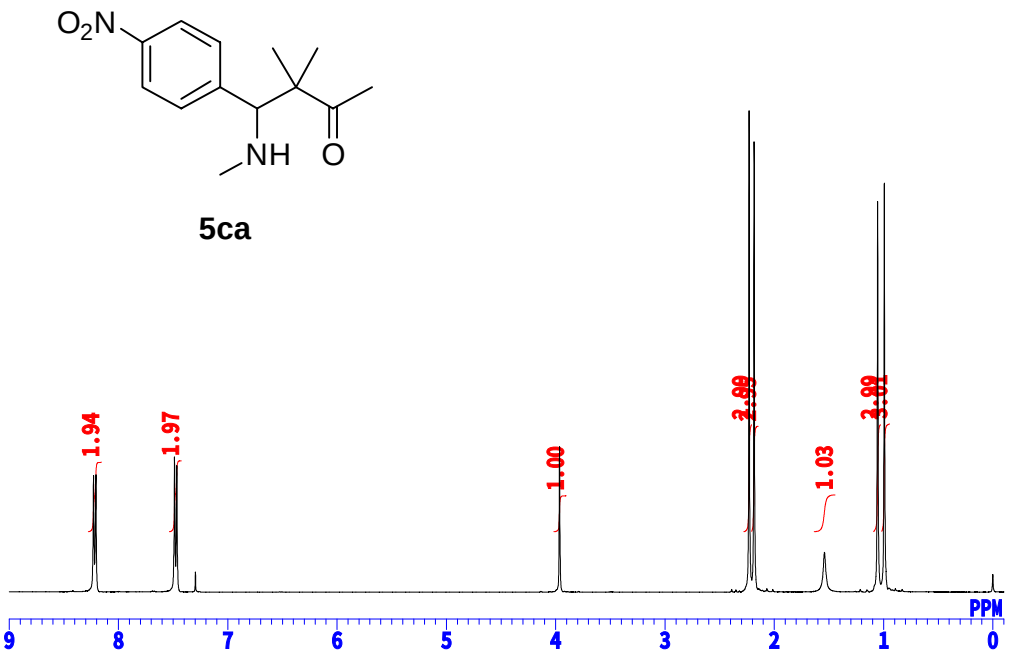
```
CONECT    3    1    5   19
CONECT    4    2    6   20
CONECT    5    3    6   21
CONECT    6   22    4    5
CONECT    7    2    8    9   23
CONECT    8    7   13   14
CONECT    9    7   24   25   10
CONECT   10   12    9   11
CONECT   11   26   27   10   28
CONECT   12   10   14
CONECT   13   31    8   29   30
CONECT   14    8   15   16   17   12
CONECT   15   14
CONECT   16   14
CONECT   17   14
CONECT   18    1
CONECT   19    3
CONECT   20    4
CONECT   21    5
CONECT   22    6
CONECT   23    7
CONECT   24    9
CONECT   25    9
CONECT   26   11
CONECT   27   11
CONECT   28   11
CONECT   29   13
CONECT   30   13
CONECT   31   13
END
```

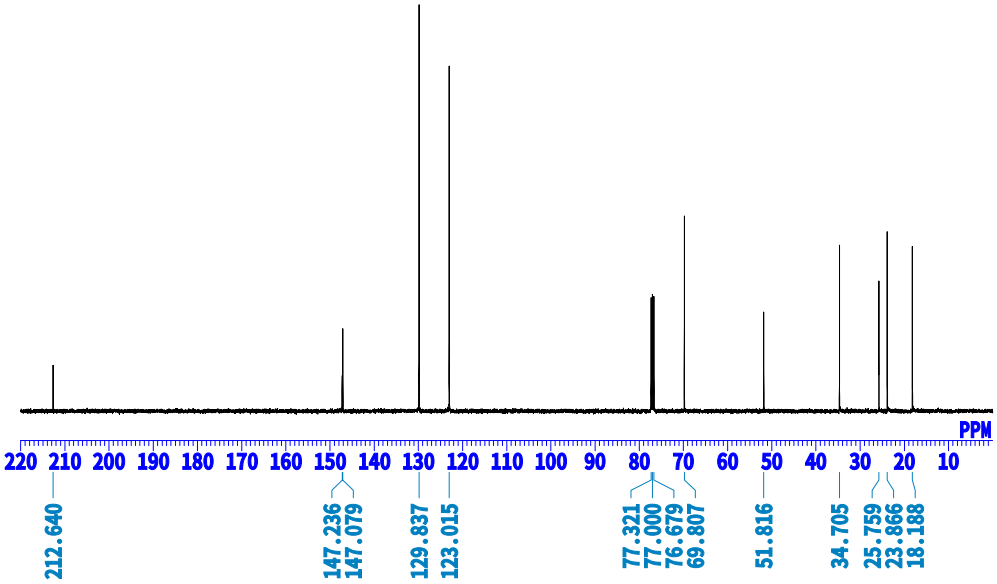
References

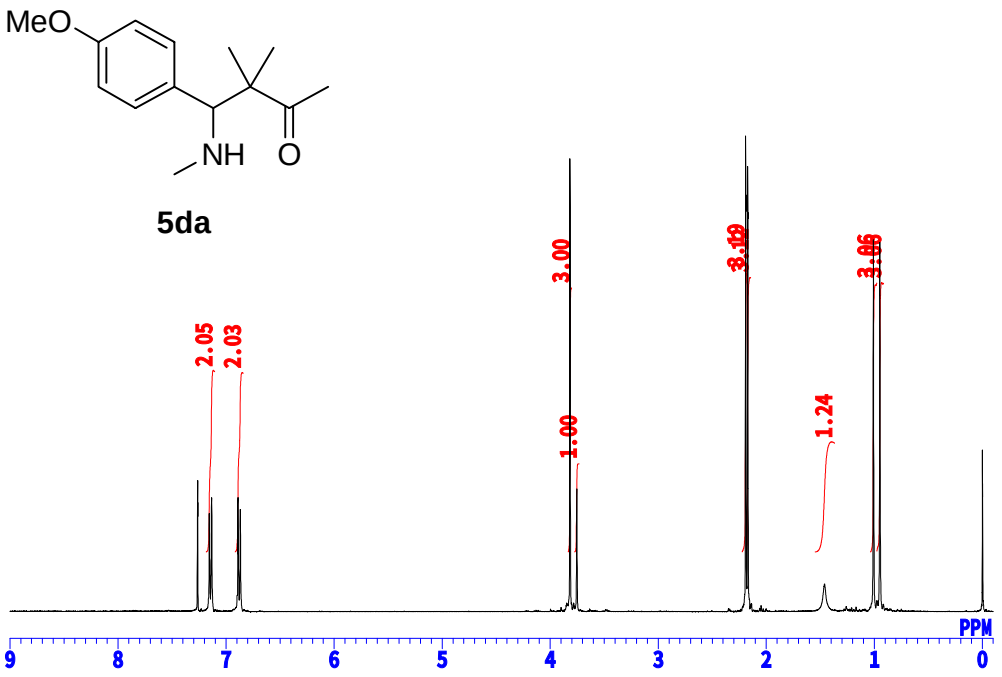
[1] V. Lemierre, A. Chrostowska, A. Dargelos, P. Baylère, W. J. Leigh, C. R. Harrington, *Appl. Organometal. Chem.* **2004**, *18*, 676-683.
[2] P. Mangeney, T. Tejero, A. Alexakis, F. Grosjean, J. Normant, *Synthesis* **1988**, 255-257.
[3] H. Sugimoto, S, Nakamura, T. Ohwada, *Adv. Synth. Catal.* **2007**, *349*, 669-679.
[4] C. F. Tormena, R. Rittner, R. J. Abraham, *J. Phys. Org. Chem.* **2002**, *15*, 211-217.
[5] F. Bellesia, F. Ghelfi, R. Grandi, U. M. Pagnoni, *J. Chem. Res. (S)* **1986**, 428-429.
[6] W.-C. Zhang, C.-J. Li, *J. Org. Chem.* **2000**, *65*, 5831-5833.
[7] H. O. House, D. S. Crumrine, A. Y. Teranishi, H. D. Olmstead, *J. Am. Chem. Soc.* **1973**, *95*, 3310-3324.
[8] a) B. Mennucci, J. Tomasi, *J. Chem. Phys.* **1997**, *106*, 5151-5158; b) E. Cancès, B. Mennucci, J. Tomasi, *J. Chem. Phys.* **1997**, *107*, 3032-3041; c) M. Cossi, V. Barone, B. Mennucci, J. Tomasi, *Chem. Phys. Lett.* **1998**, *286*, 253-260.
[9] Gaussian 03, Revision C.02. M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, Jr., T. Vreven, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, Gaussian, Inc., Wallingford CT, 2004.

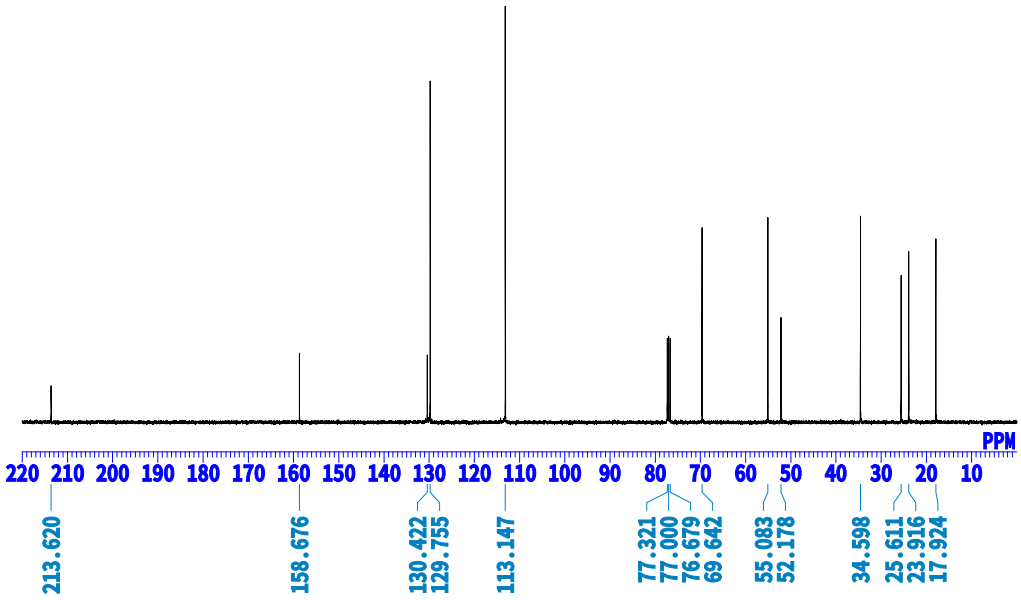
^{1}H and ^{13}C NMR spectra

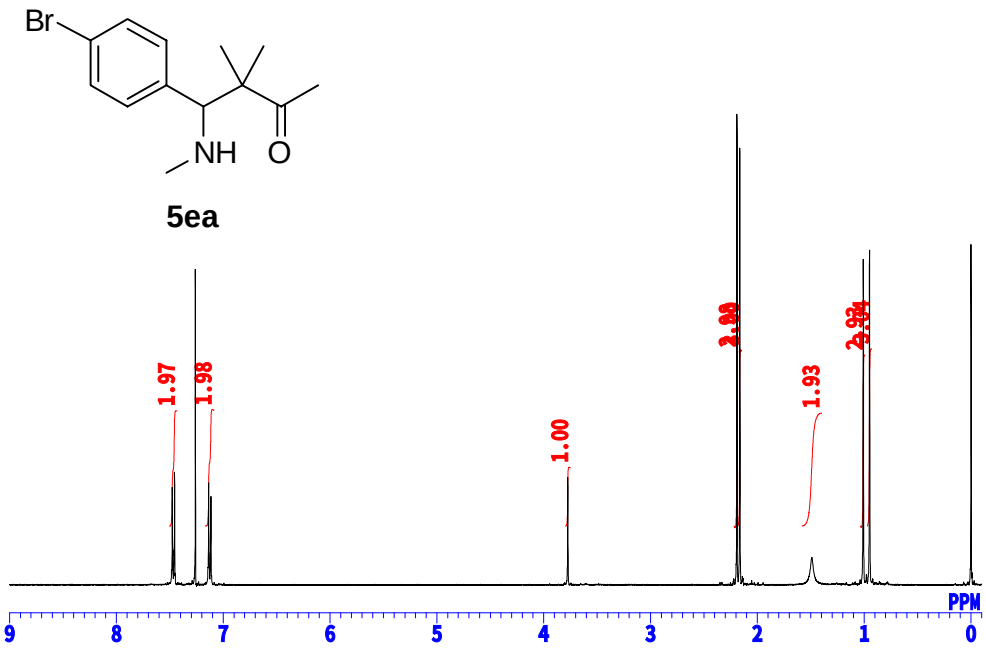


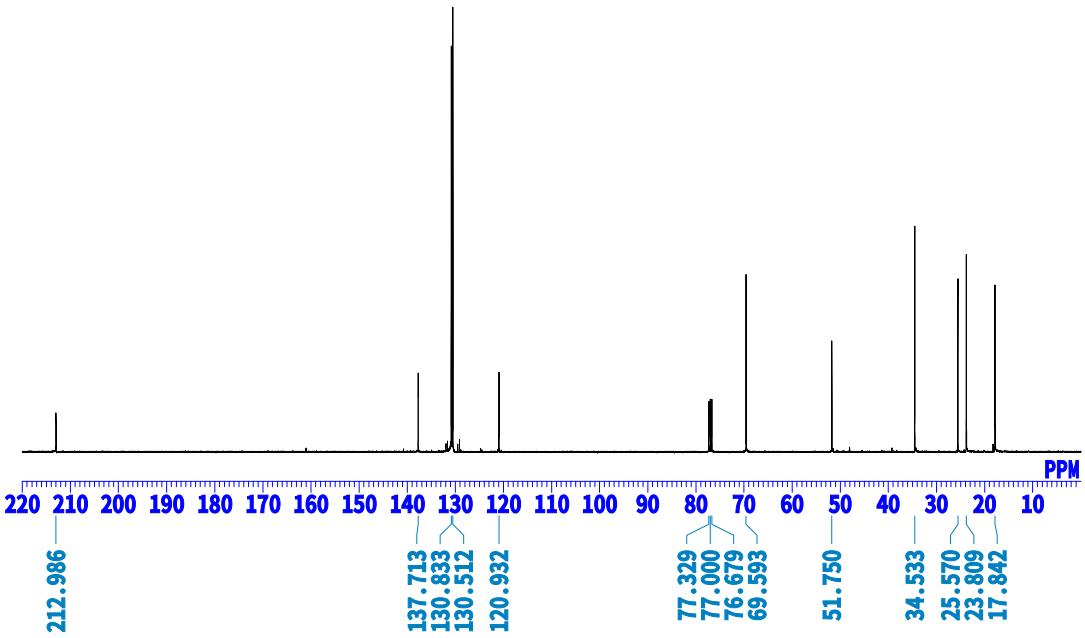

O2N
NH
O
5ca
1.94
1.97
1.00
2.09
1.03
2.99
3.01
PPM
9
8
7
6
5
4
3
2
1
0

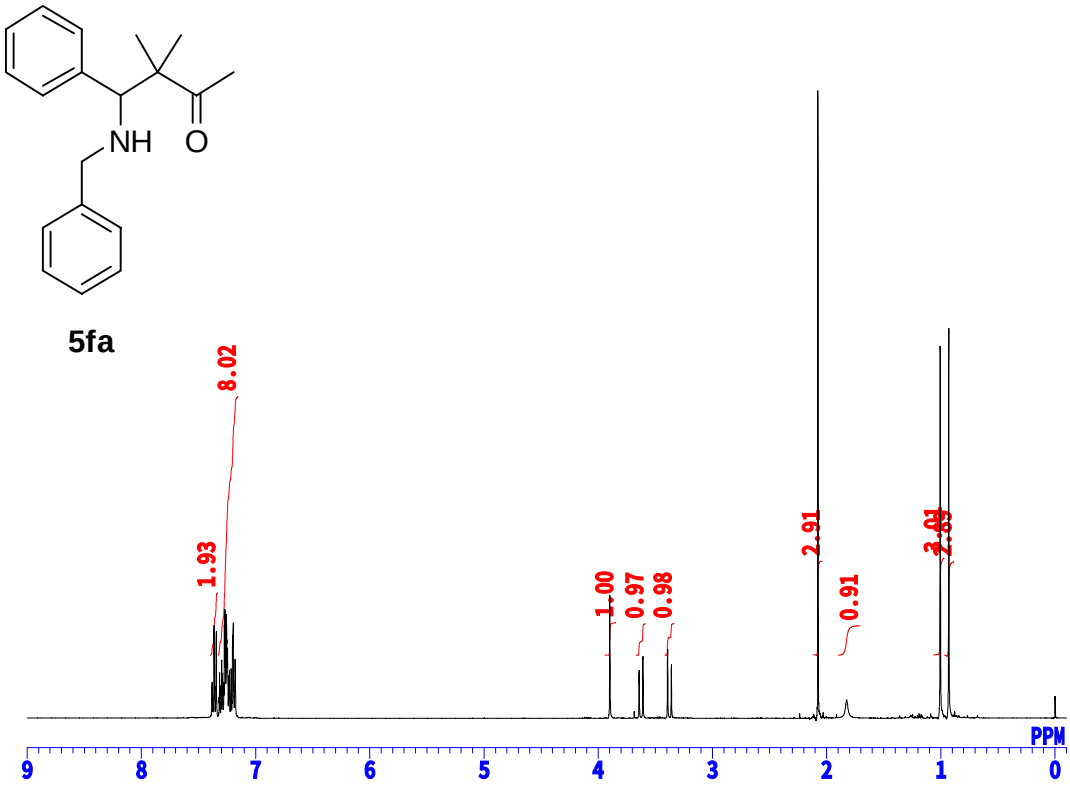

PPM
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
212.640
147.236
147.079
129.837
123.015
77.321
77.000
76.679
69.807
51.816
34.705
25.759
23.866
18.188

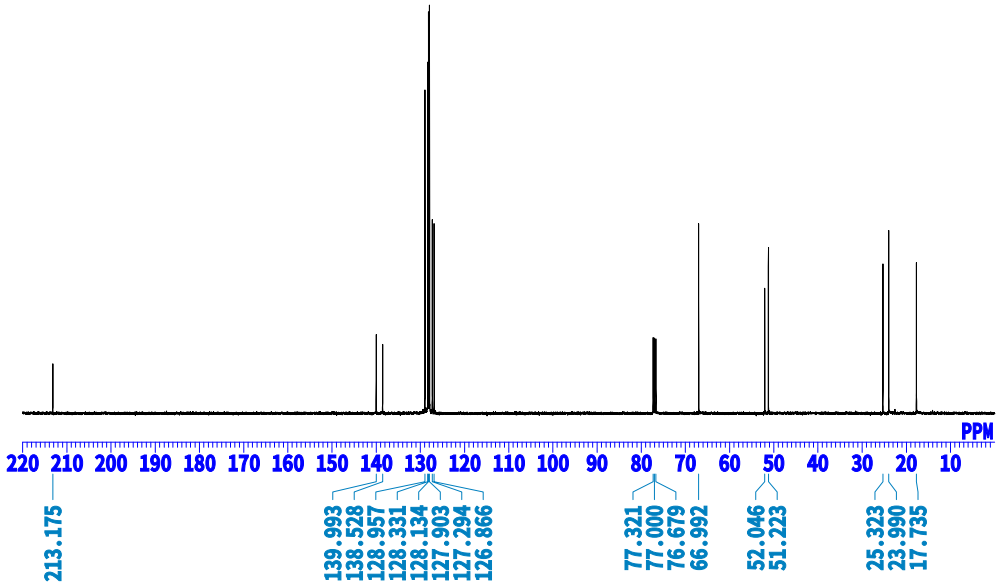

MeO
NH
O
5da
2.05
2.03
3.00
1.00
3.12
1.24
3.06
PPM
9
8
7
6
5
4
3
2
1
0

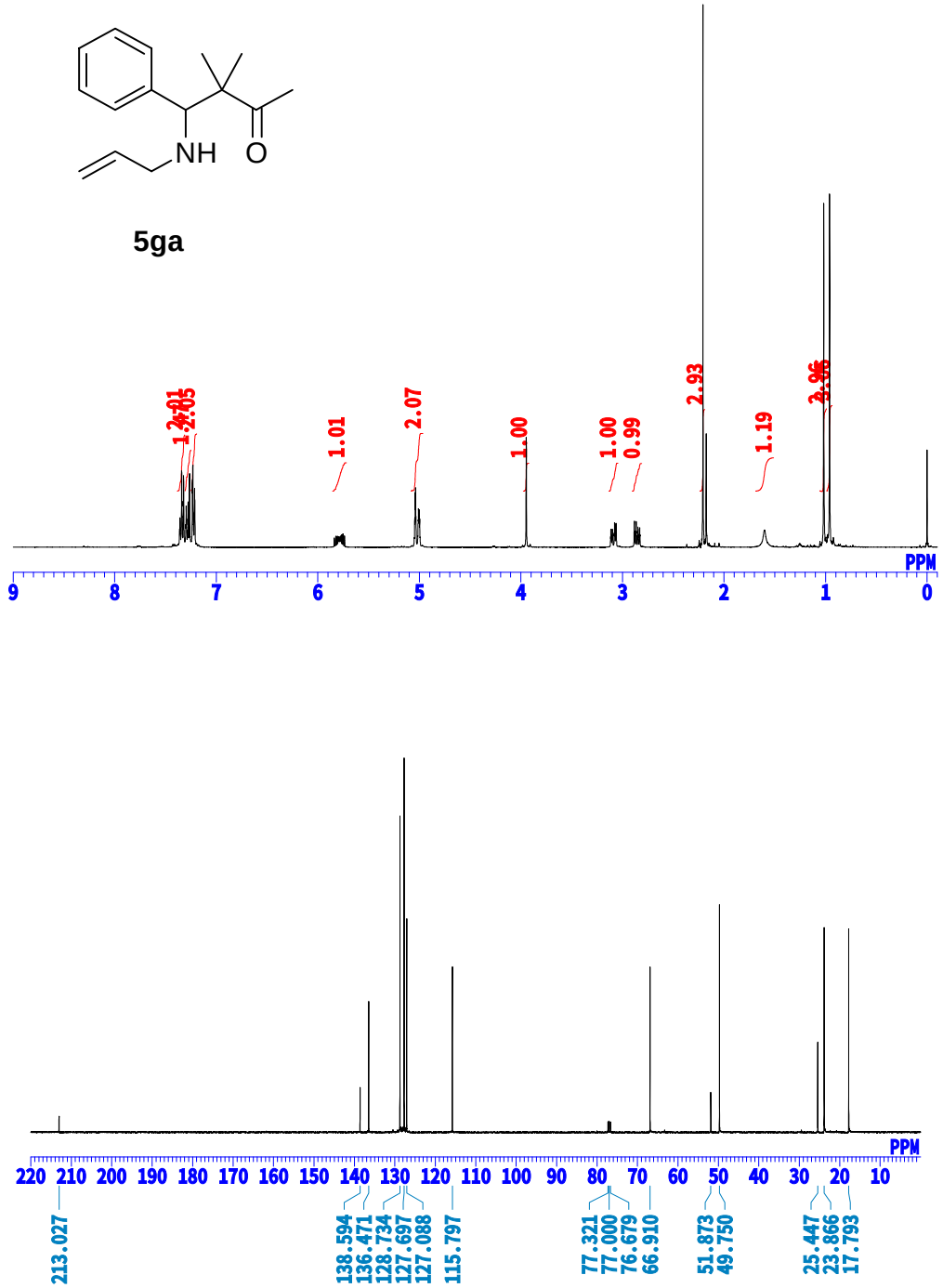

PPM
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
213.620
158.676
130.422
129.755
113.147
77.321
77.000
76.679
69.642
55.083
52.178
34.598
25.611
23.916
17.924

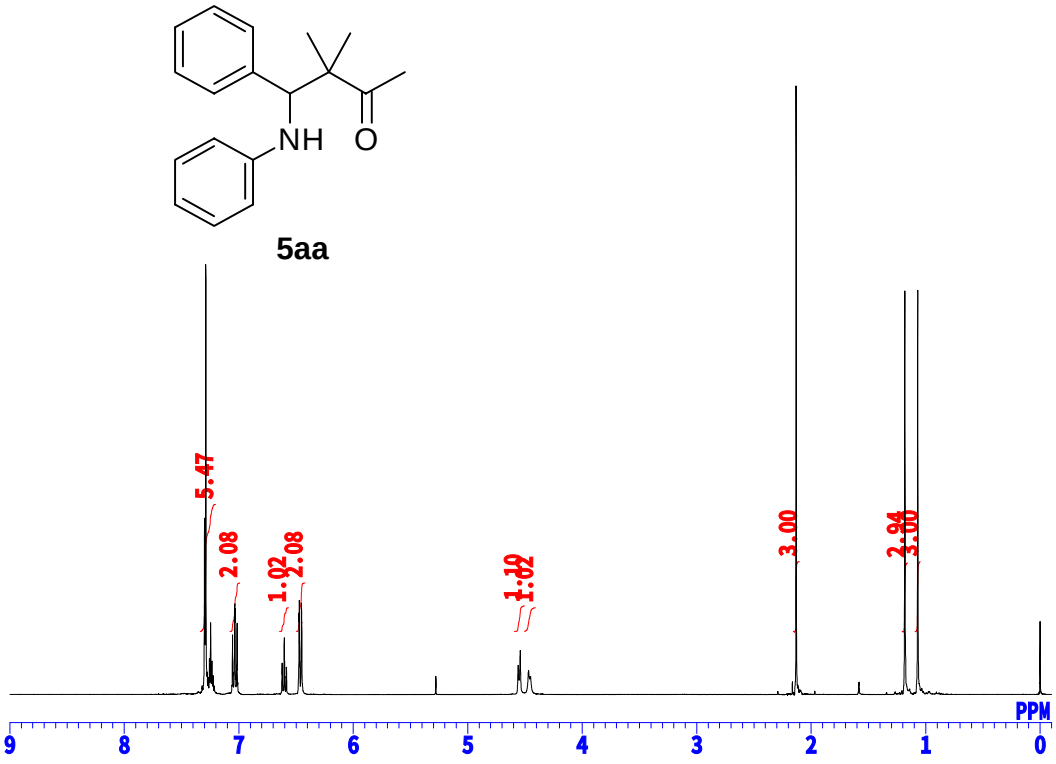

Br
NH
O
5ea
1.97
1.98
1.00
1.93
PPM
9
8
7
6
5
4
3
2
1
0

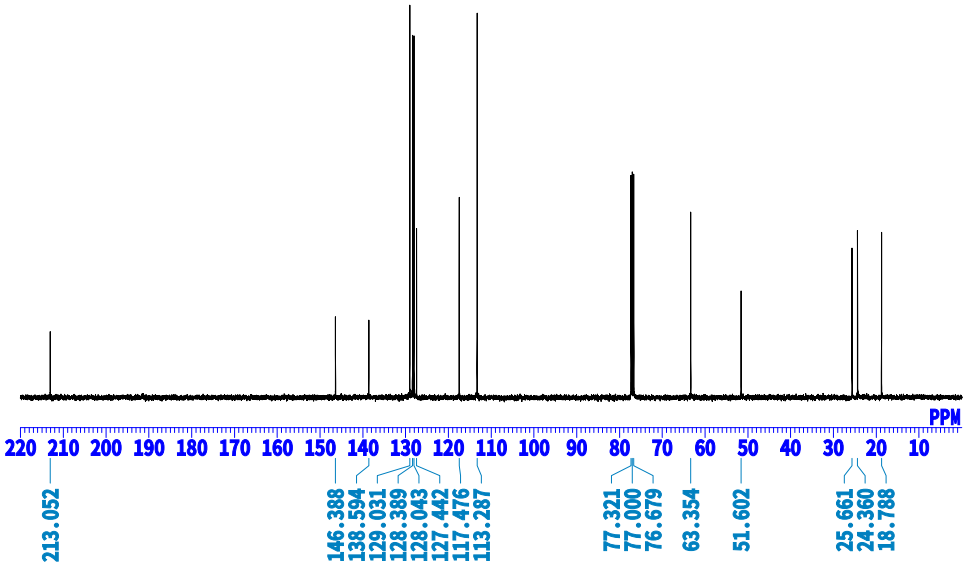

PPM
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
212.986
137.713
130.833
130.512
120.932
77.329
77.000
76.679
69.593
51.750
34.533
25.570
23.809
17.842

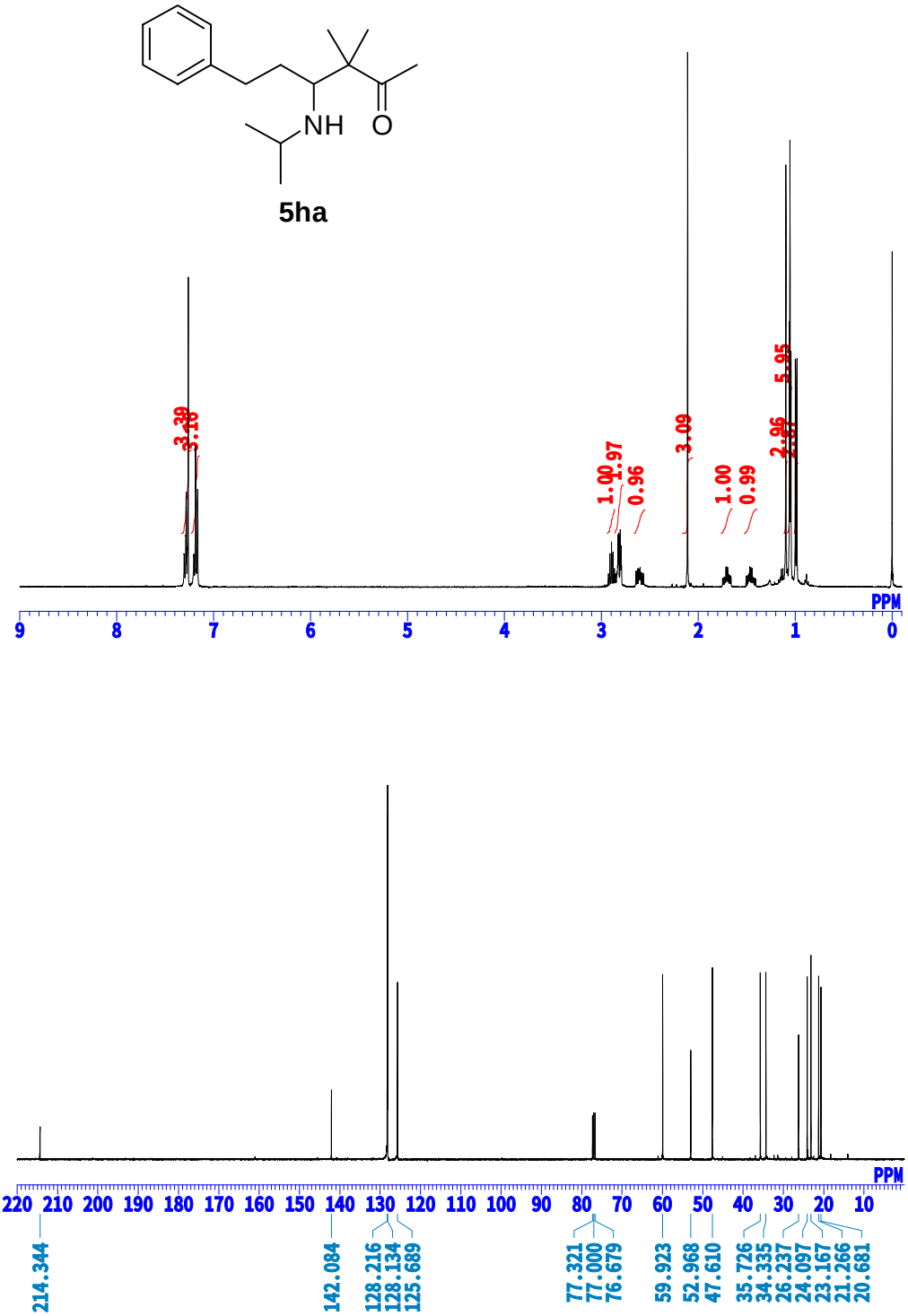

NH
O
5fa
8.02
1.93
1.00
0.97
0.98
2.91
0.91
2.03
2.01
PPM
9
8
7
6
5
4
3
2
1
0

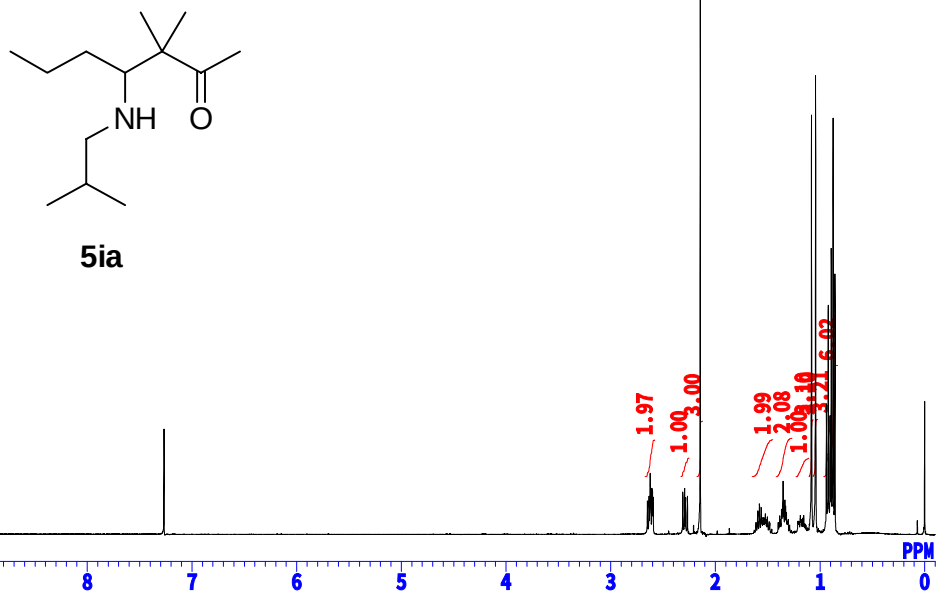

PPM
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
213.175
139.993
138.528
128.957
128.331
128.134
127.903
127.294
126.866
77.321
77.000
76.679
66.992
52.046
51.223
25.323
23.990
17.735


NH
O
5ga
1.01
2.07
1.00
1.00
0.99
2.93
1.19
PPM
9
8
7
6
5
4
3
2
1
0
PPM
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
213.027
138.594
136.471
128.734
127.697
127.088
115.797
77.321
77.000
76.679
66.910
51.873
49.750
25.447
23.866
17.793

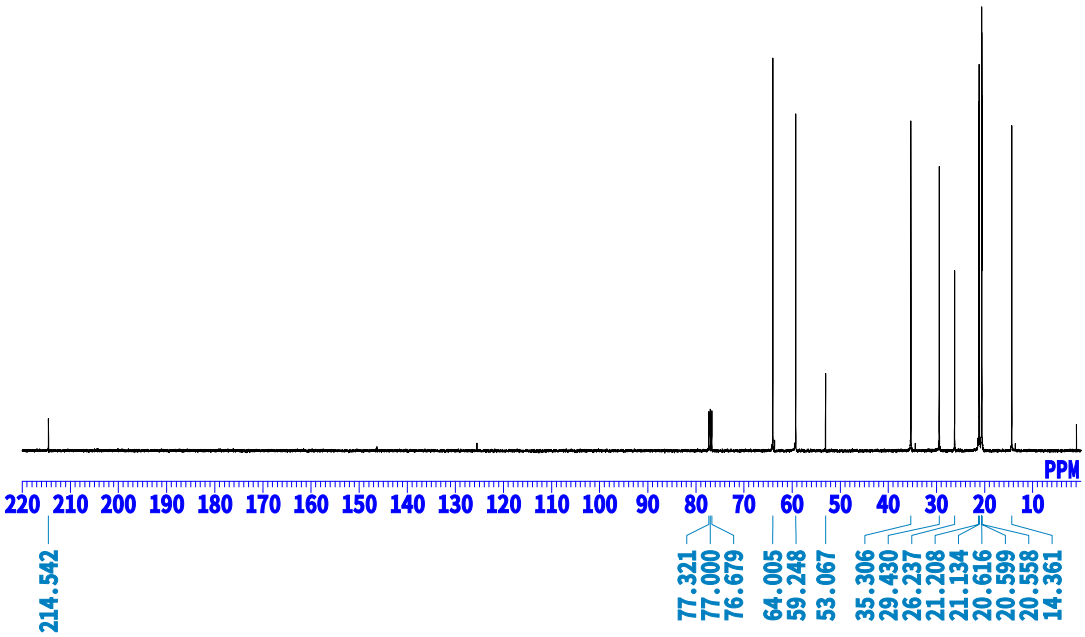

NH
O
5aa
5.47
2.08
1.02
2.08
1.10
1.02
3.00
2.94
3.00
PPM
9
8
7
6
5
4
3
2
1
0

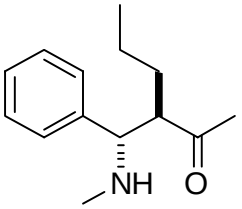

PPM
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
213.052
146.388
138.594
129.031
128.389
128.043
127.442
117.476
113.287
77.321
77.000
76.679
63.354
51.602
25.661
24.360
18.788


NH
O
5ha
3.39
3.10
1.00
1.97
0.96
3.09
1.00
0.99
5.95
2.96
PPM
9
8
7
6
5
4
3
2
1
0
PPM
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
214.344
142.084
128.216
128.134
125.689
77.321
77.000
76.679
59.923
52.968
47.610
35.726
34.335
26.237
24.097
23.167
21.266
20.681

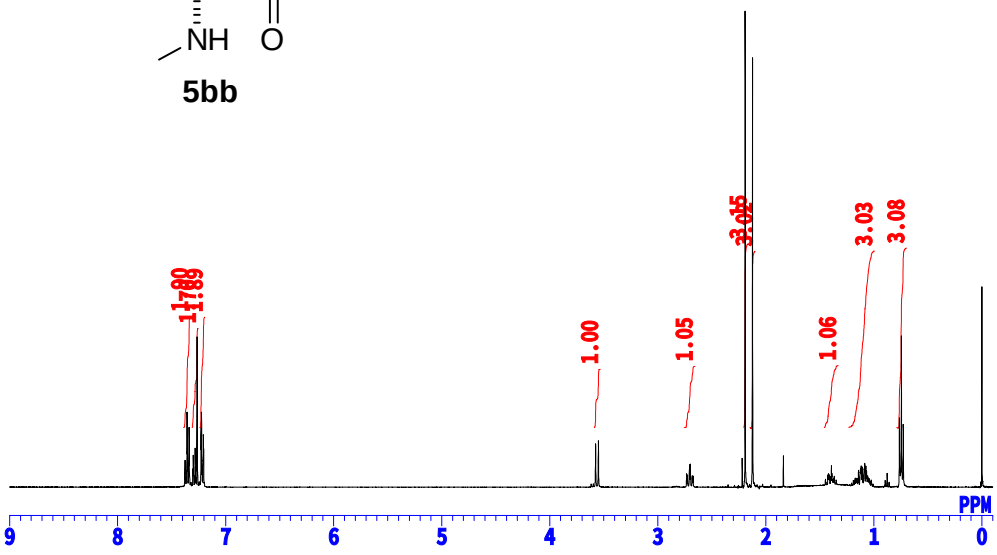

NH
O
1.97
1.00
3.00
1.99
2.08
1.00
1.10
3.21
6.02
PPM
9
8
7
6
5
4
3
2
1
0

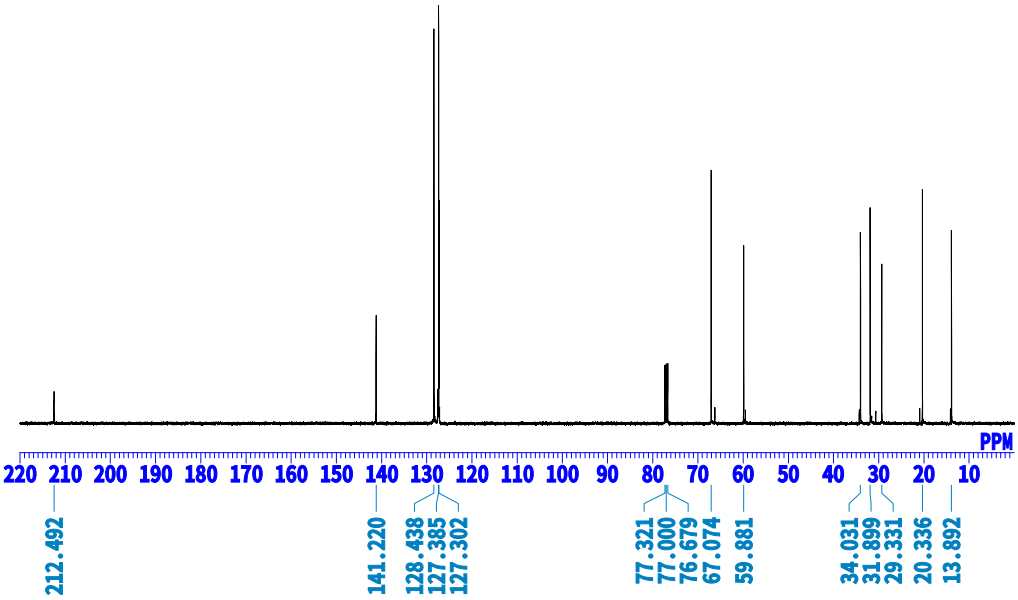
5ia

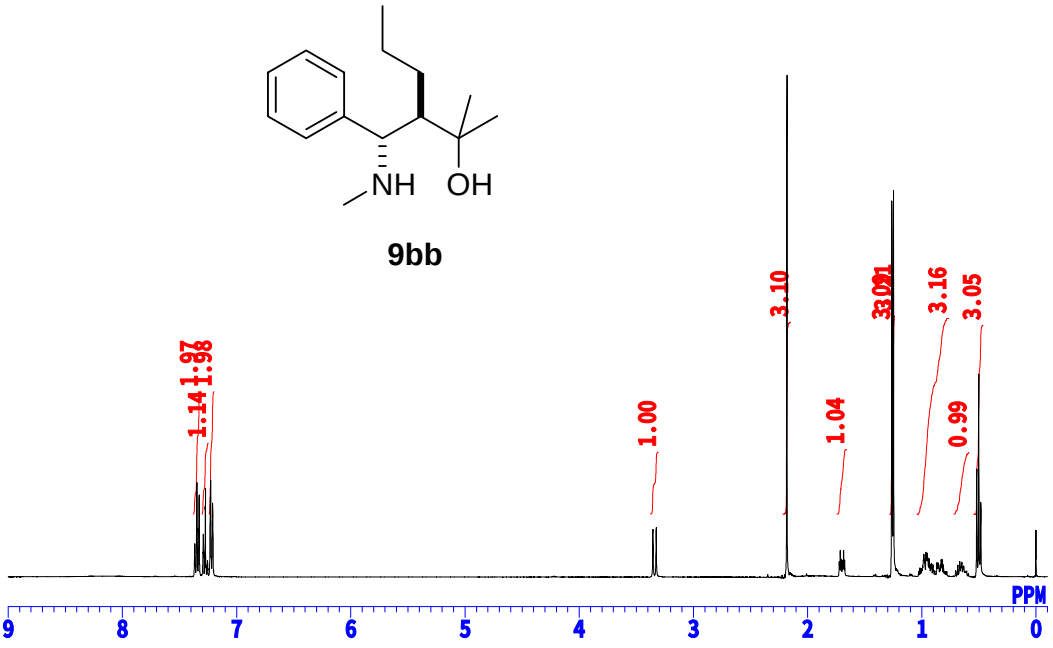

PPM
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
214.542
77.321
77.000
76.679
64.005
59.248
53.067
35.306
29.430
26.237
21.208
21.134
20.616
20.599
20.558
14.361

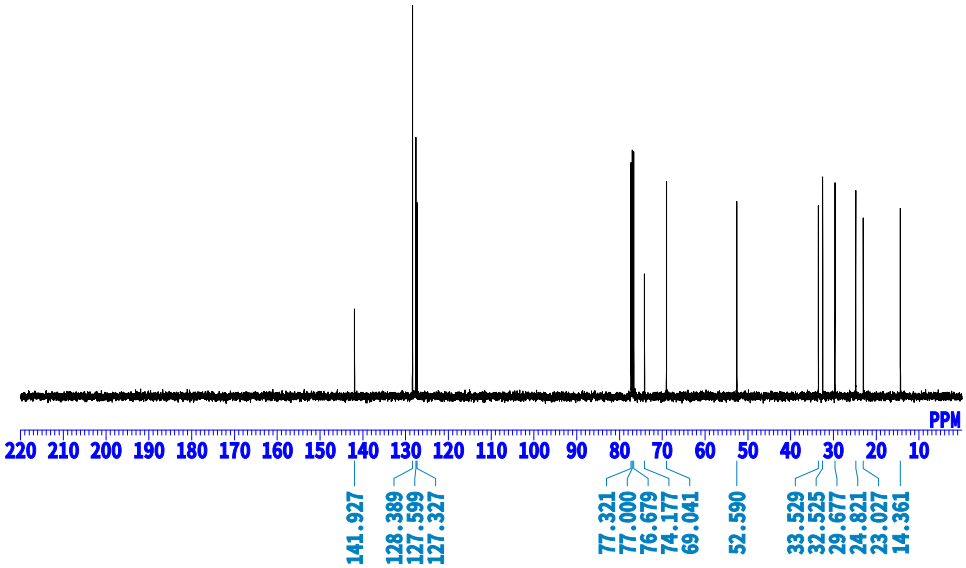

NH
O

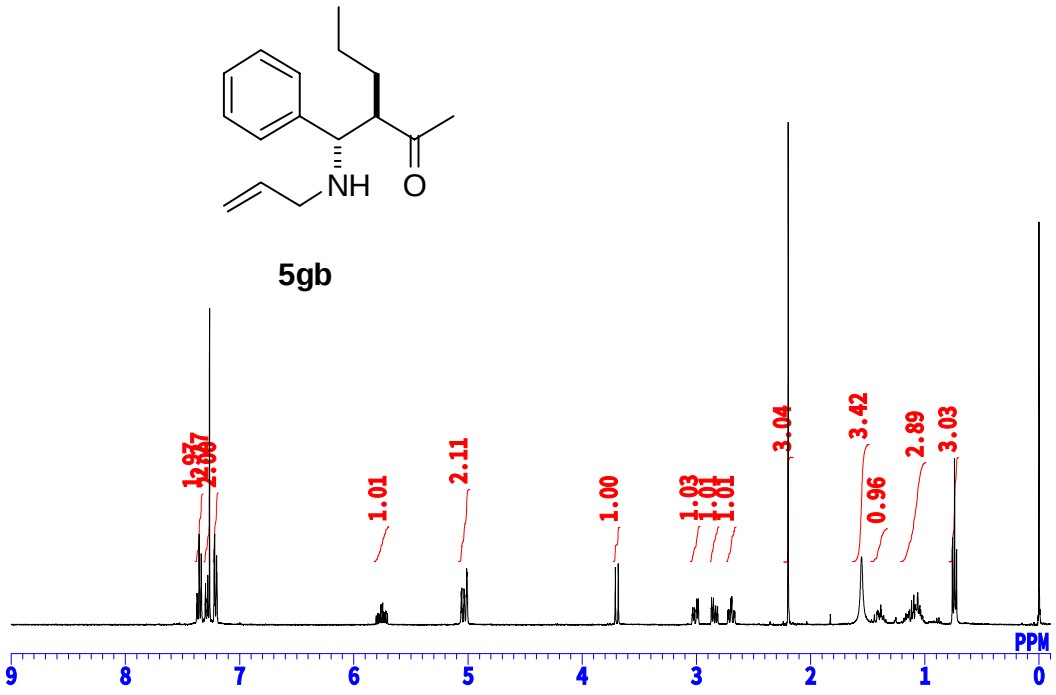
5bb

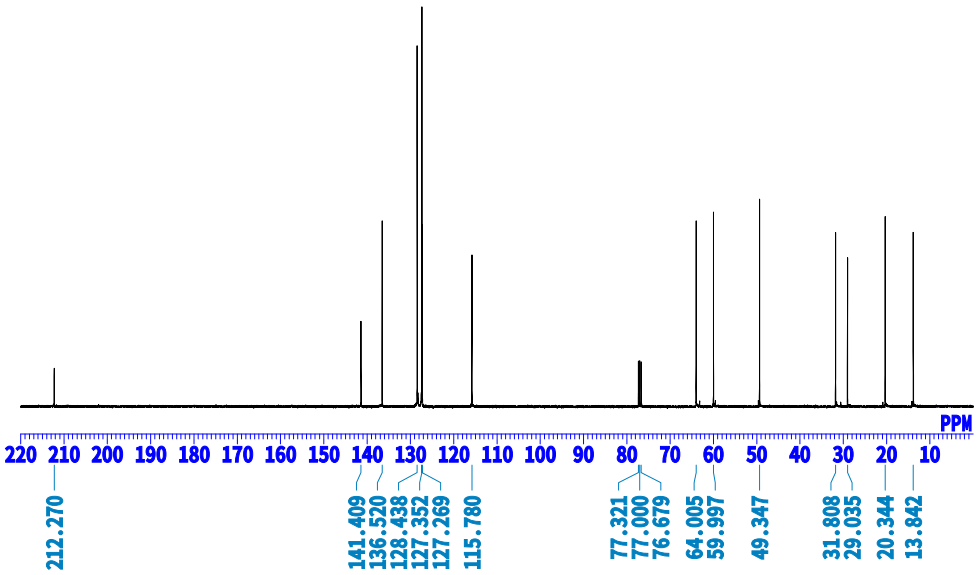

1.00
1.05
1.06
3.03
3.08
PPM
9
8
7
6
5
4
3
2
1
0

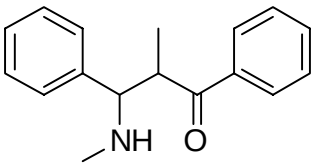

PPM
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
212.492
141.220
128.438
127.385
127.302
77.321
77.000
76.679
67.074
59.881
34.031
31.899
29.331
20.336
13.892


NH
OH
9bb
1.14
1.97
1.98
1.00
3.10
1.04
3.16
3.05
0.99
PPM
9
8
7
6
5
4
3
2
1
0

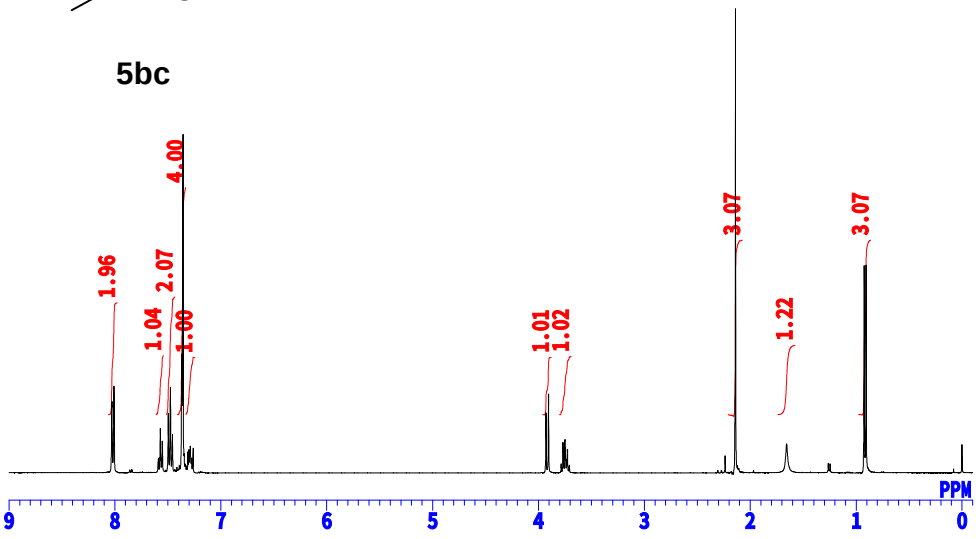

PPM
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
141.927
128.389
127.599
127.327
77.321
77.000
76.679
74.177
69.041
52.590
33.529
32.525
29.677
24.821
23.027
14.361

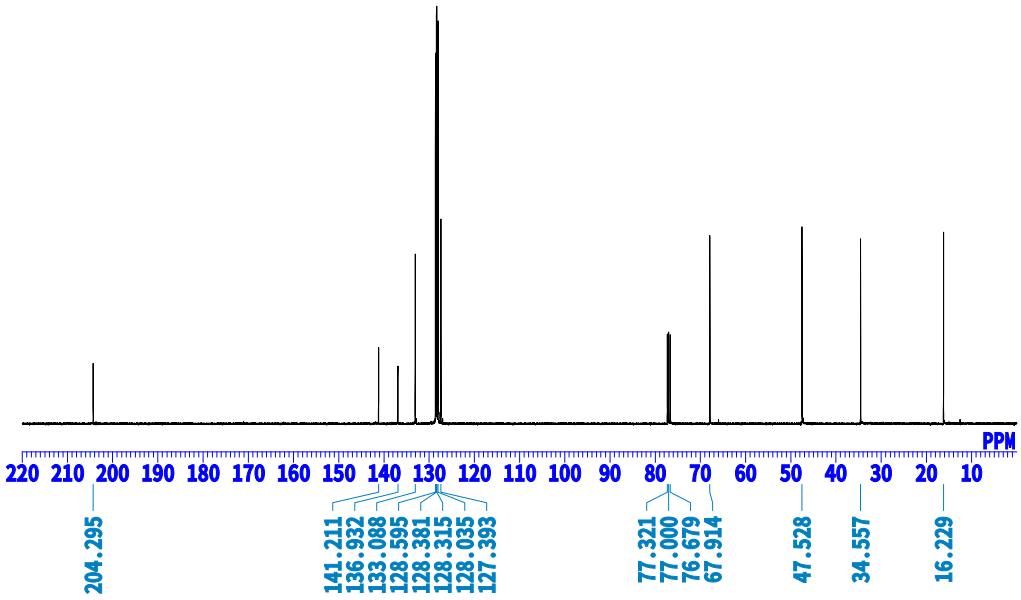

NH
O
5gb
1.01
2.11
1.00
1.03
1.01
1.01
3.04
3.42
0.96
2.89
3.03
PPM
9
8
7
6
5
4
3
2
1
0

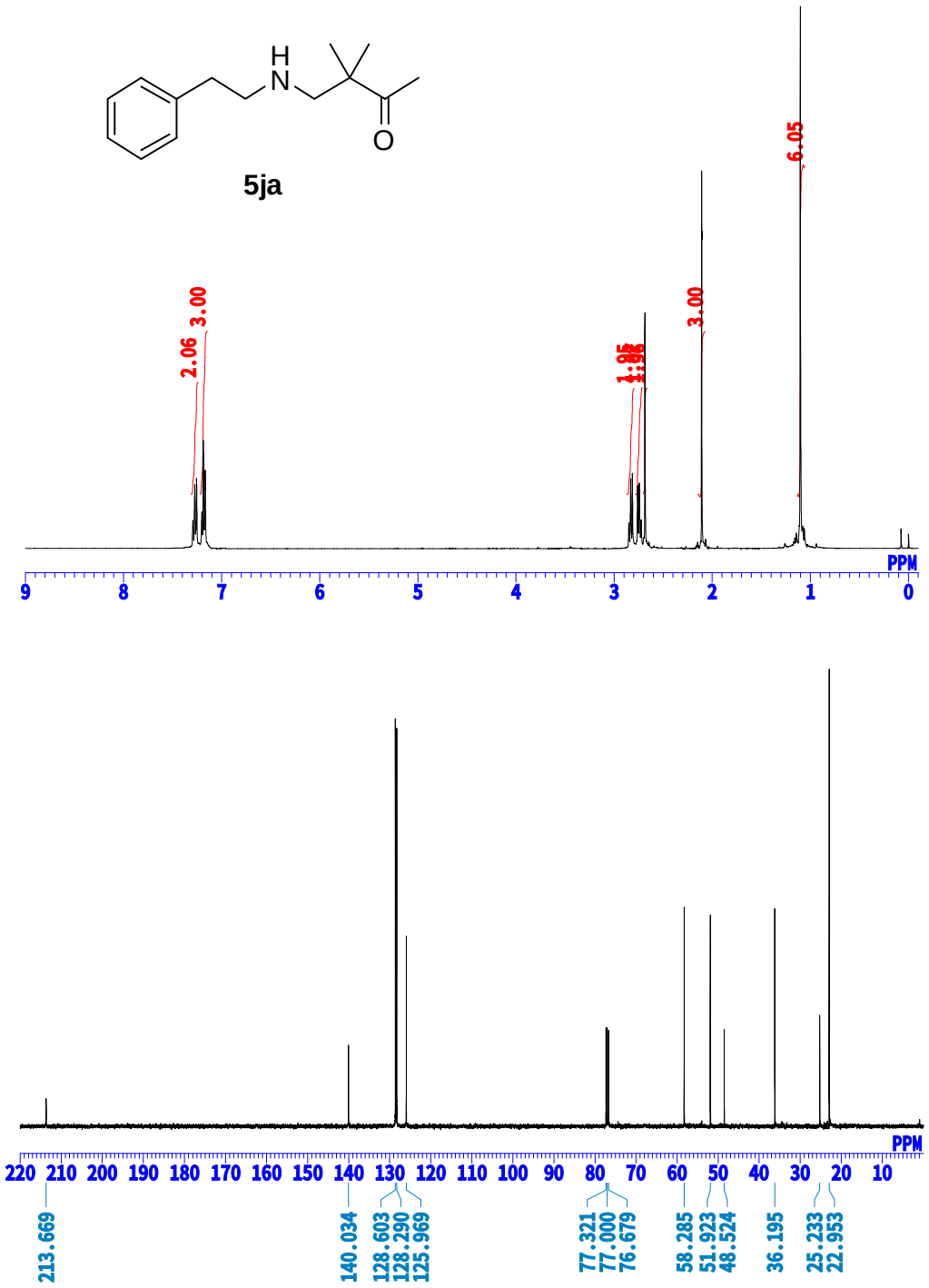

PPM
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
212.270
141.409
136.520
128.438
127.352
127.269
115.780
77.321
77.000
76.679
64.005
59.997
49.347
31.808
29.035
20.344
13.842

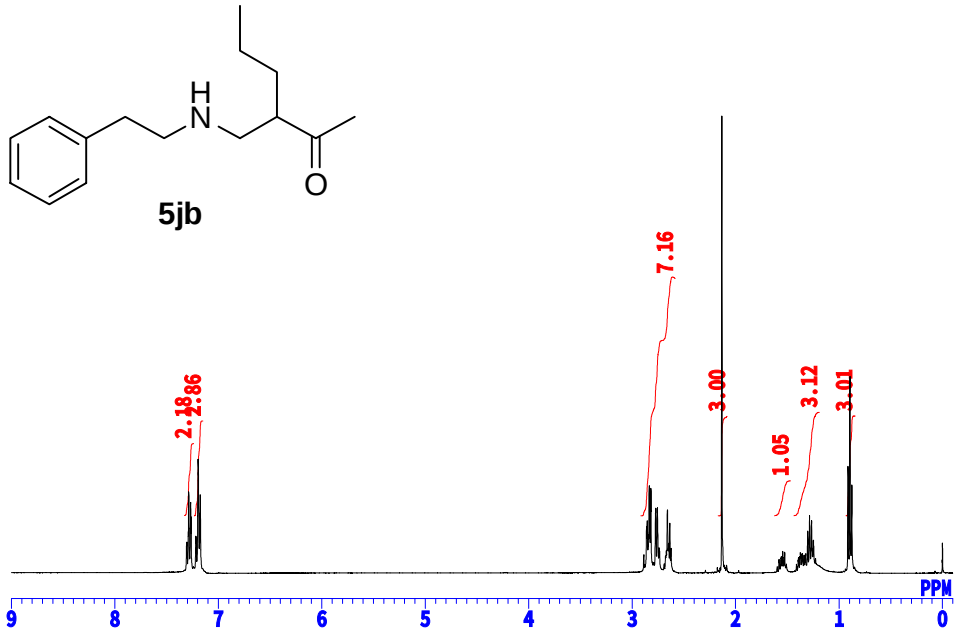

NH
O

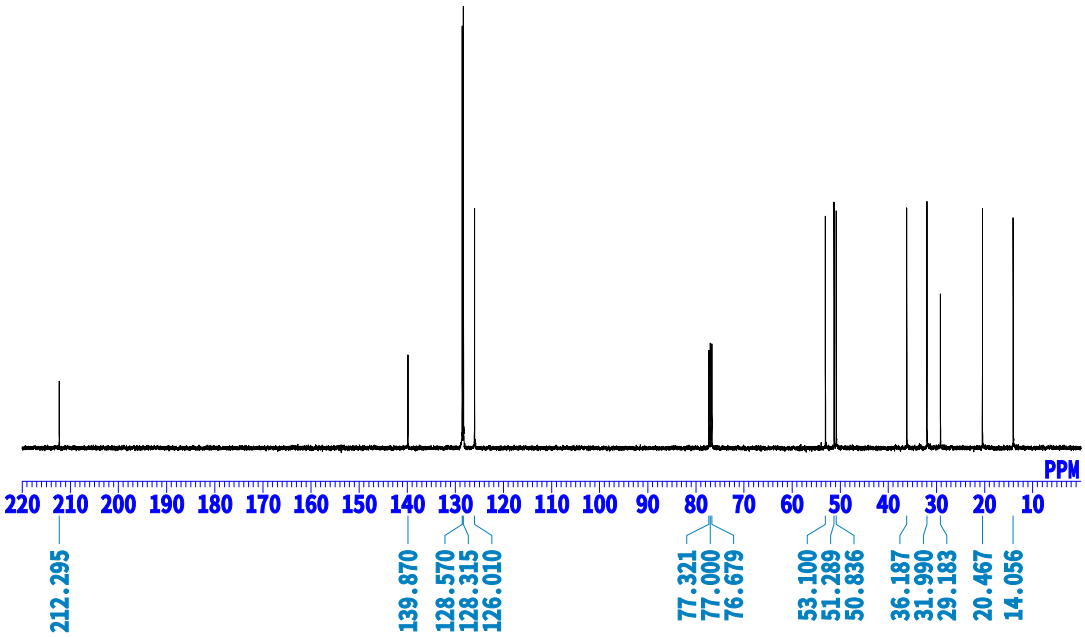
5bc

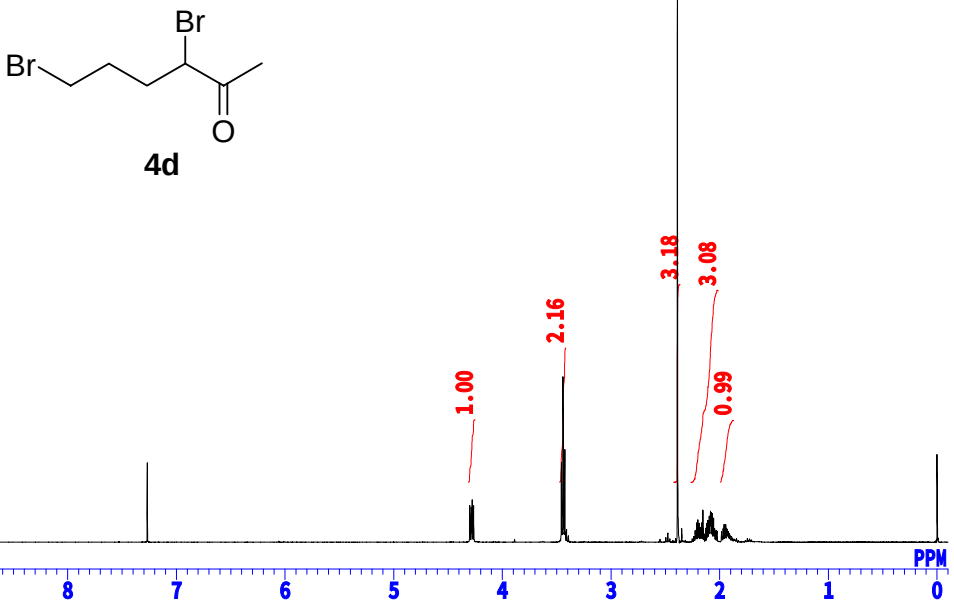

1.96
2.07
4.00
1.04
1.00
1.01
1.02
3.07
1.22
3.07
PPM
9
8
7
6
5
4
3
2
1
0

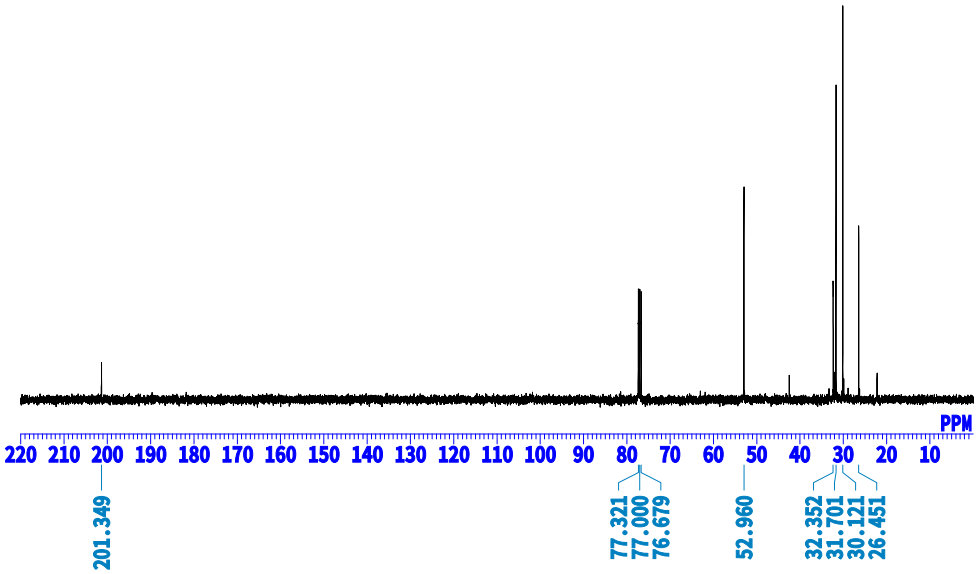

PPM
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
204.295
141.211
136.932
133.088
128.595
128.381
128.315
128.035
127.393
77.321
77.000
76.679
67.914
47.528
34.557
16.229

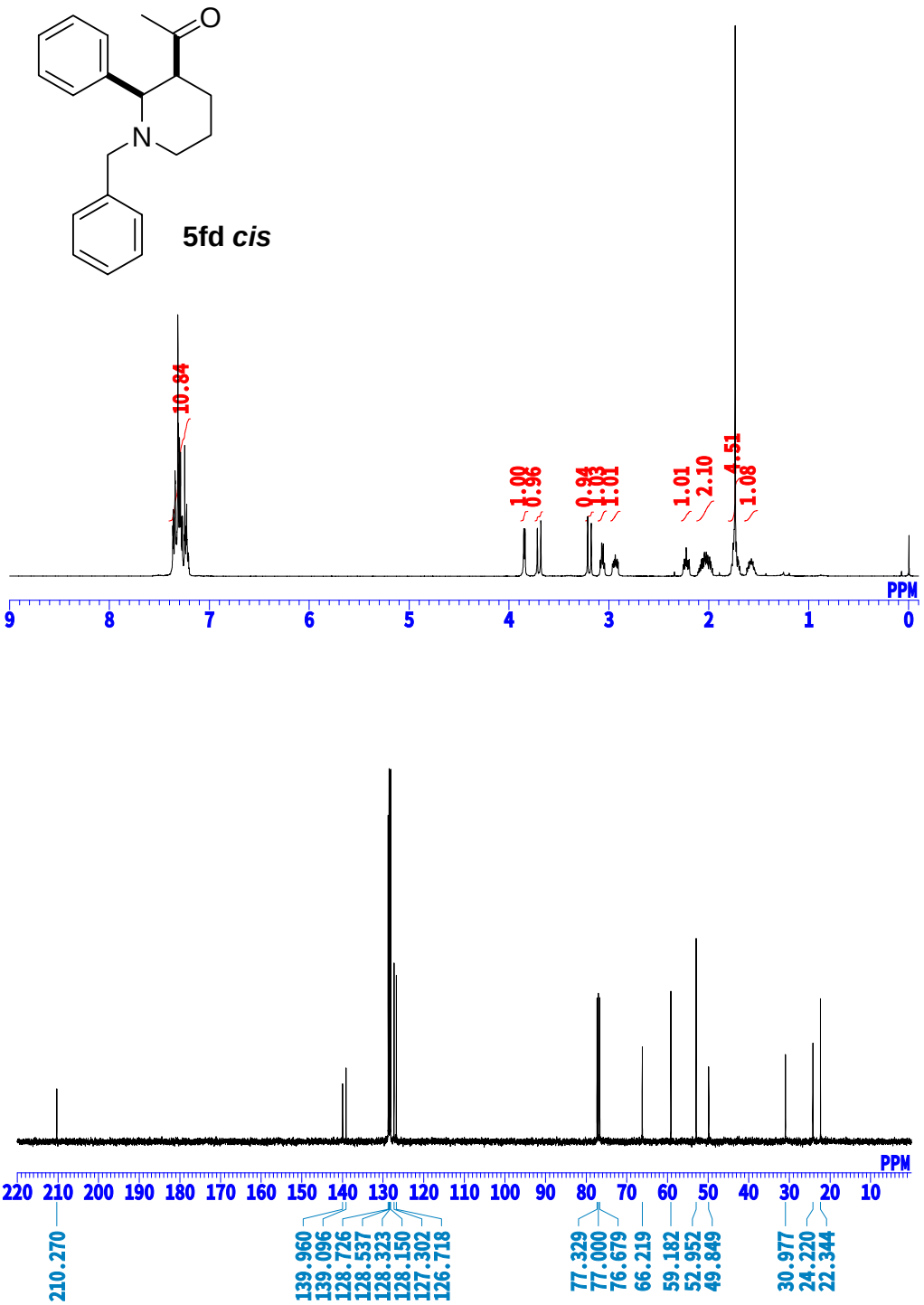

H
N
O
5ja
2.06
3.00
1.95
3.00
6.05
PPM
9 8 7 6 5 4 3 2 1 0
PPM
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
213.669
140.034
128.603
128.290
125.969
77.321
77.000
76.679
58.285
51.923
48.524
36.195
25.233
22.953

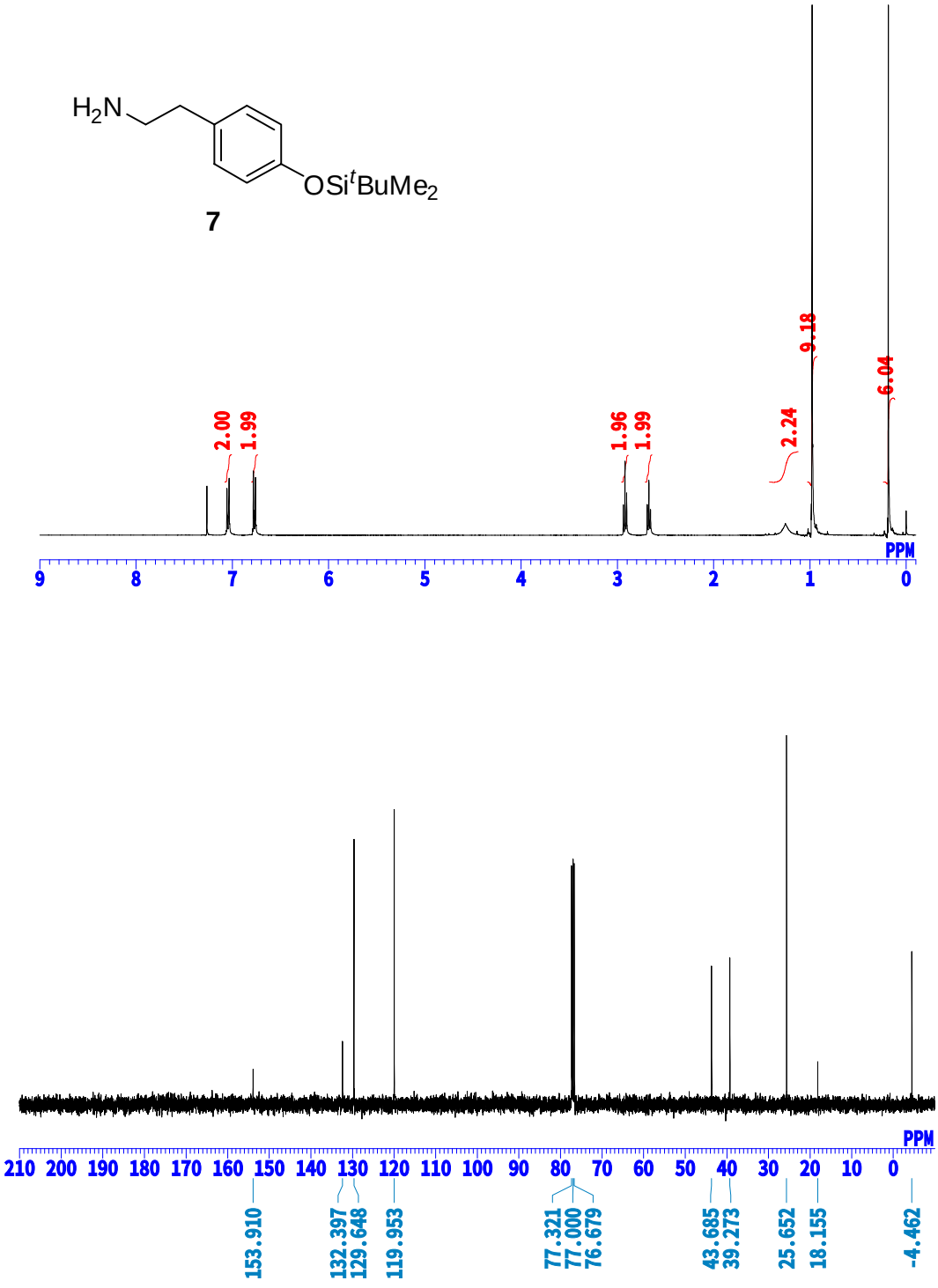

H
N
O
5jb
7.16
3.00
3.12
3.01
2.18
2.86
1.05
PPM
9
8
7
6
5
4
3
2
1
0

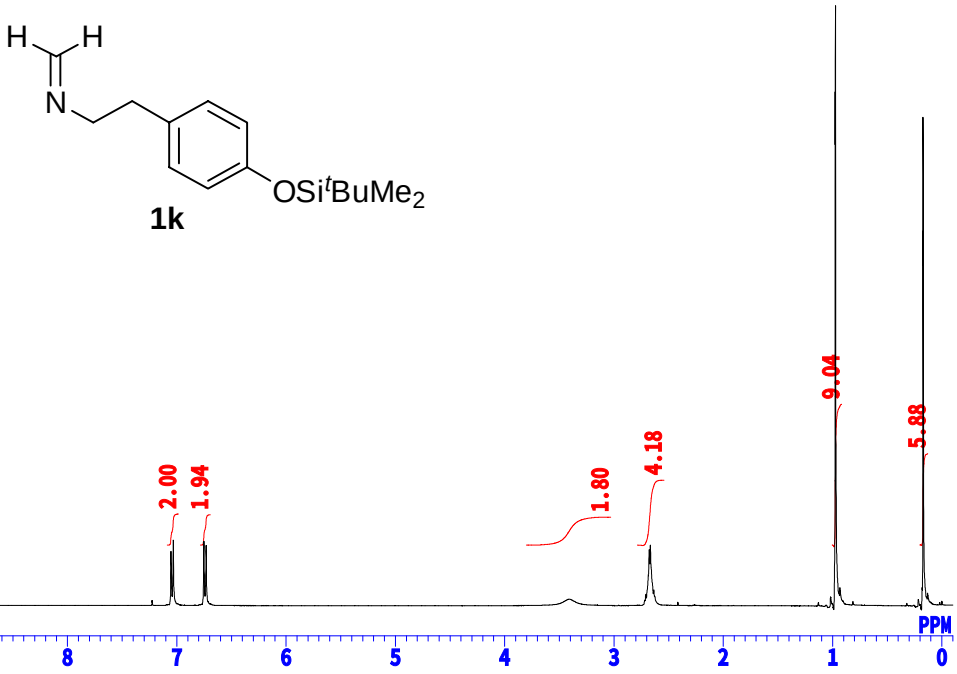

PPM
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
212.295
139.870
128.570
128.315
126.010
77.321
77.000
76.679
53.100
51.289
50.836
36.187
31.990
29.183
20.467
14.056

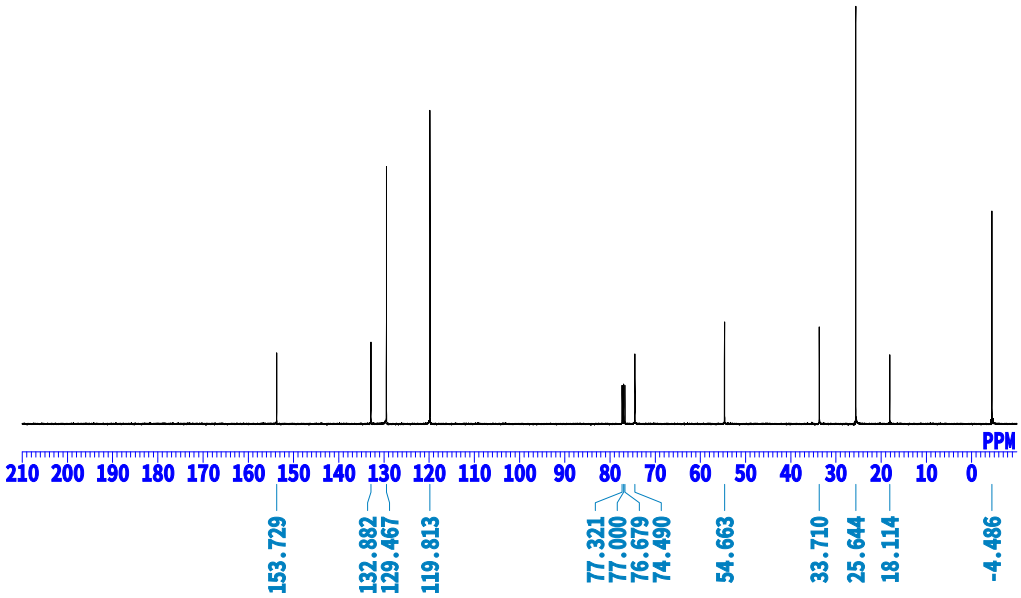

Br
Br
O
4d
1.00
2.16
3.18
3.08
0.99
PPM
9
8
7
6
5
4
3
2
1
0

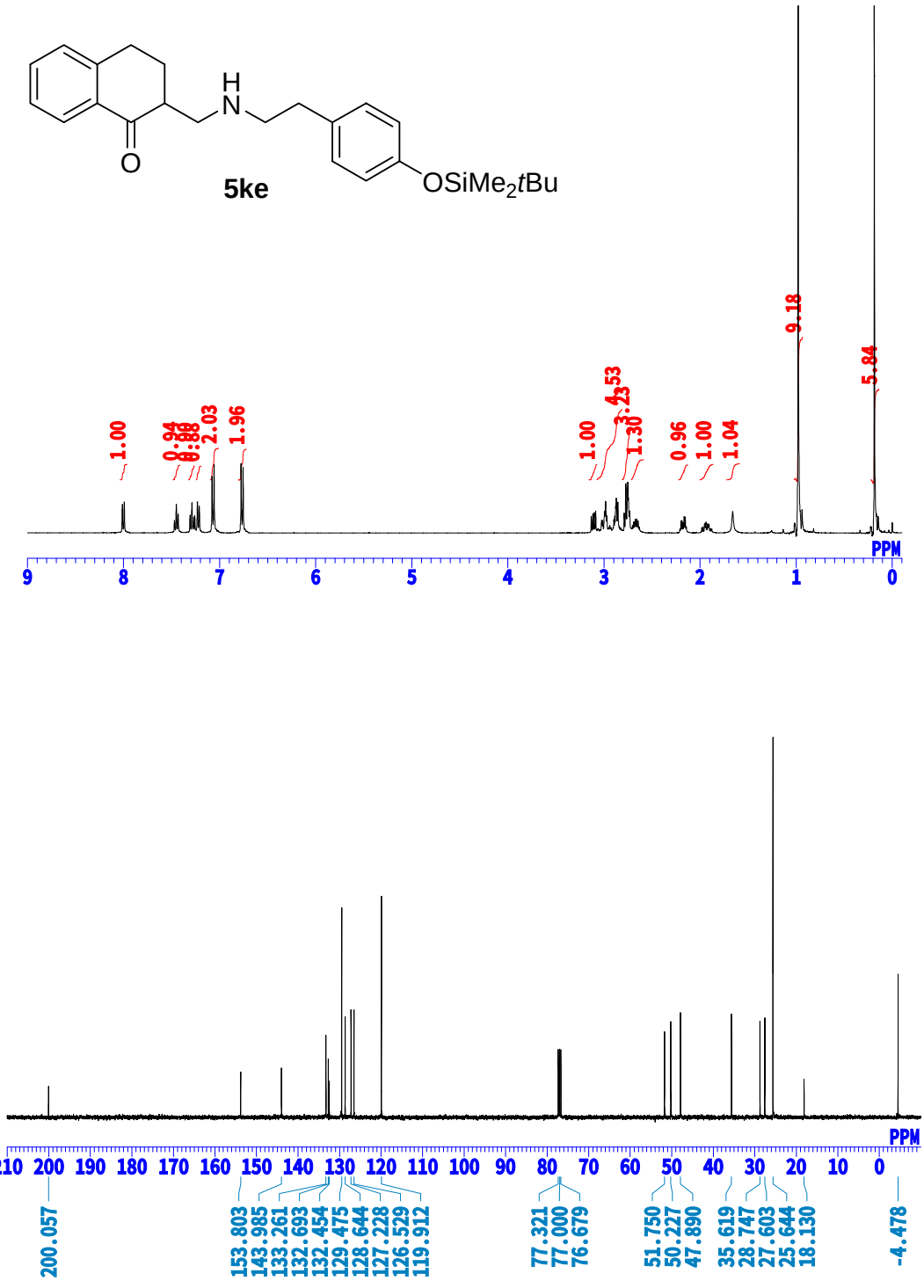

PPM
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
201.349
77.321
77.000
76.679
52.960
32.352
31.701
30.121
26.451

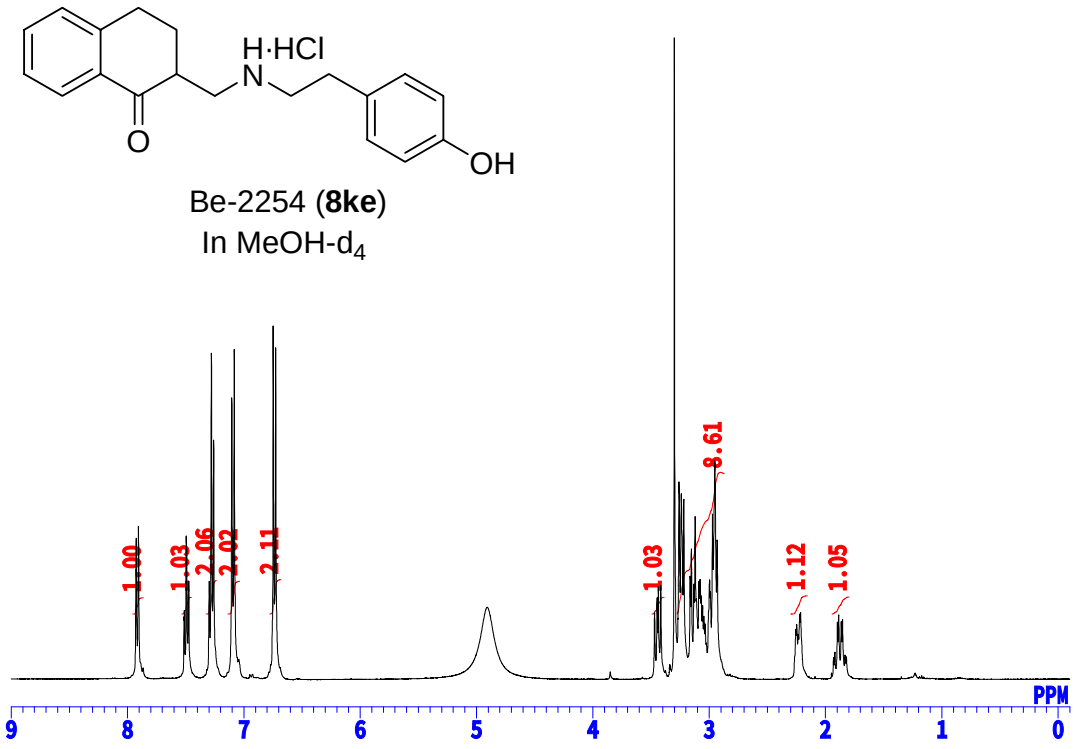

O
N
5fd *cis*
10.84
1.00
0.96
0.94
1.03
1.01
1.01
2.10
4.51
1.08
PPM
9 8 7 6 5 4 3 2 1 0
PPM
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
210.270
139.960
139.096
128.726
128.537
128.323
128.150
127.302
126.718
77.329
77.000
76.679
66.219
59.182
52.952
49.849
30.977
24.220
22.344

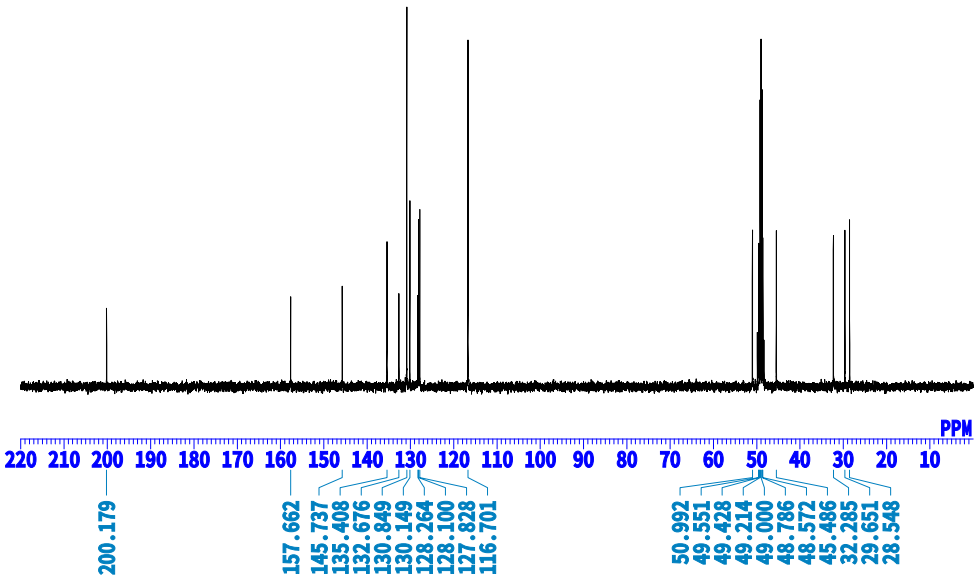

H2N
OSitBuMe2
7
2.00
1.99
1.96
1.99
2.24
9.18
6.04
PPM
9 8 7 6 5 4 3 2 1 0
PPM
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
153.910
132.397
129.648
119.953
77.321
77.000
76.679
43.685
39.273
25.652
18.155
-4.462


H
H
N
OSi^{t}BuMe$_2$
1k
2.00
1.94
1.80
4.18
9.04
5.88
PPM
9
8
7
6
5
4
3
2
1
0


PPM
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
153.729
132.882
129.467
119.813
77.321
77.000
76.679
74.490
54.663
33.710
25.644
18.114
-4.486


H
N
O
5ke
OSiMe2tBu
1.00
0.94
2.03
1.96
1.00
3.53
3.23
1.30
0.96
1.00
1.04
9.18
5.84
PPM
9 8 7 6 5 4 3 2 1 0
PPM
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
200.057
153.803
143.985
133.261
132.693
132.454
129.475
128.644
127.228
126.529
119.912
77.321
77.000
76.679
51.750
50.227
47.890
35.619
28.747
27.603
25.644
18.130
-4.478


H·HCl
N
O
OH
Be-2254 (8ke)
In MeOH-d4
1.00
1.03
2.06
2.02
2.11
1.03
8.61
1.12
1.05
PPM
9
8
7
6
5
4
3
2
1
0


PPM
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
200.179
157.662
145.737
135.408
132.676
130.849
130.149
128.264
128.100
127.828
116.701
50.992
49.551
49.428
49.214
49.000
48.786
48.572
45.486
32.285
29.651
28.548