*J. Braz. Chem. Soc.*, Vol. 24, No. 9, S1-S68, 2013.
Printed in Brazil - ©2013 Sociedade Brasileira de Química
0103 - 5053 $6.00+0.00

# Supplementary Information

## A Straightforward and Efficient Method for the Synthesis of Diversely Substituted β-Aminoketones and γ-Aminoalcohols from 3-(*N,N*-Dimethylamino)propiophenones as Starting Materials

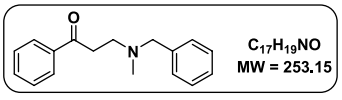
***Rodrigo Abonia,* Danny Arteaga, Juan Castillo, Braulio Insuasty, Jairo Quiroga and Alejandro Ortíz***

*Research Group of Heterocyclic Compounds, Department of Chemistry, Universidad del Valle, A. A. 25360, Cali, Colombia*

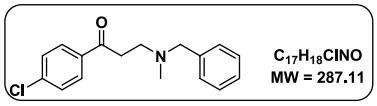
General procedure for the synthesis of Naftifine®

A solution of γ-aminoalcohol **11o** (200 mg) in 5 mol $L^{-1}$ HCl (5 mL) was stirred at reflux for 3 h until starting material was not detected by TLC (thin layer chromatoghaphy). Then the mixture was neutralized with 10 eq-g $L^{-1}$ NaOH until pH 7.0, the aqueous solution was extracted with ethyl acetate (2 × 5 mL) and the combined organic extracts were dried with anhydrous $Na_2SO_4$. After removal of the solvent, the residue was purified by column chromatography on silica gel, using a mixture of $CH_2Cl_2$/MeOH (20:1) as eluent.

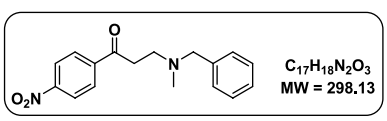
Characterization data for β-aminoketones **10**




3-(*N*-Benzyl-*N*-methylamino)-1-phenylpropan-1-one (**10a**): following the general procedure for the formation of β-aminoketones, the reaction of benzylmethylamine (300 mg, 2.48 mmol) and 3-(*N*,*N*-dimethylamino)-1-phenylpropan-1-one hydrochloride (531 mg, 2.49 mmol) in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10a** as a yellow oil. Yield: 88% (552 mg). Data: FTIR (film) ν/$cm^{-1}$ 2922, 2845, 1684 (C=O), 1598; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.28 (s, 3H, $NCH_3$), 2.91 (t, 2H, *J* 7.4 Hz, H-2), 3.21 (t, 2H, *J* 7.4 Hz, H-3), 3.58 (s, 2H, Bn-H), 7.23-7.31 (m, 5H, Ph-H), 7.46 (t, 2H, *J* 7.6 Hz, Ph-H), 7.56 (td, 1H, *J* 7.6, 1.2 Hz, Ph-H), 7.92-7.97 (m, 2H, Ph-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 36.8 ($CH_2$), 42.2 ($NCH_3$), 52.4 ($NCH_2$), 62.3 ($PhCH_2$), 127.0 (CH), 128.0 (CH), 128.2 (CH), 128.5 (CH), 129.0 (CH), 133.0 (CH), 136.9 (Cq), 138.6 (Cq), 199.4 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 162 $[M-91]^+$ (17), 134 (32), 91 (100) [$PhCH_2$], 77 (50); $C_{17}H_{19}NO$ (253.15): calcd. C 80.60, H 7.56, N, 5.53; found: C 80.31, H 7.23, N, 5.72.



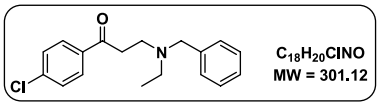

3-(*N*-Benzyl-*N*-methylamino)-1-(4-chlorophenyl)propan-1-one (**10b**): following the general procedure for the formation of β-aminoketones, the reaction of benzylmethylamine (291 mg, 2.40 mmol) and 1-(4-chlorophenyl)-3-(*N*,*N*-dimethylamino)propan-1-one hydrochloride (596 mg, 2.41 mmol) were dissolved in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10b** as a yellow oil. Yield: 78% (539 mg). Data: FTIR (film) ν/$cm^{-1}$ 2939, 2842, 1675 (C=O), 1600; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.28 (s, 3H, $NCH_3$), 2.88 (t, 2H, *J* 7.6 Hz, H-2), 3.16 (t, 2H, *J* 7.2 Hz, H-3), 3.56 (s, 2H, Bn-H), 7.25-7.49 (m, 7H, Ph-H, Ar-H), 7.88 (d, 2H, *J* 8.4 Hz, Ar-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 36.9 ($CH_2$), 42.2 ($NCH_3$), 52.3 ($NCH_2$), 62.4 ($PhCH_2$), 127.0 (CH), 128.2 (CH), 128.8 (CH), 128.9 (CH), 129.4 (CH), 135.2 (Cq), 138.7 (Cq), 139.4 (Cq), 198.2 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 289/287 $[M]^+$ (0.1 /0.3), 274/272 (0.1/0.3), 198/196 (3/10), 141/139 (5/16), 134 (40), 120 (14), 111 (65), 91 (100) [$PhCH_2$]; $C_{17}H_{18}ClNO$ (287.11): calcd. C 70.95, H 6.30, N 4.87; found: C 71.11, H 6.52, N 4.90.



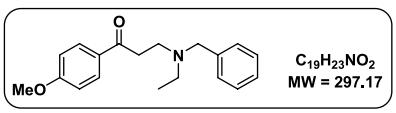

3-(*N*-Benzyl-*N*-methylamino)-1-(4-nitrophenyl)propan-1-one (**10c**): following the general procedure for the formation of β-aminoketones, the reaction of benzylmethylamine (288 mg, 2.38 mmol) and 3-(*N*,*N*-dimethylamino)-1-(4-nitrophenyl)propan-1-one hydrochloride (616 mg,

*e-mail: rodrigo.abonia@correounivalle.edu.co

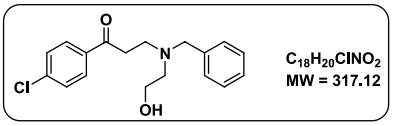
2.39 mmol) were dissolved in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10c** as a yellow oil. Yield: 62% (440 mg). Data: FTIR (film) ν/cm$^{-1}$ 2950, 2844, 1696 (C=O), 1603, 1529 ($NO_2$), 1348 ($NO_2$); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.29 (s, 3H, $NCH_3$), 2.89 (t, 2H, *J* 7.2 Hz, H-2), 3.21 (t, 2H, *J* 7.2 Hz, H-3), 3.56 (s, 2H, Bn-H), 7.24-7.30 (m, 5H, Ph-H), 8.06 (d, 2H, *J* 8.8 Hz, Ar-H), 8.30 (d, 2H, *J* 8.8 Hz, Ar-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 37.7 ($CH_2$), 42.3 ($NCH_3$), 52.1 ($NCH_2$), 62.5 ($PhCH_2$), 123.8 (CH), 127.1 (CH), 128.2 (CH), 128.9 (CH), 129.0 (CH), 138.6 (Cq), 141.3 (Cq), 150.2 (Cq), 197.9 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 120 [M-178]$^+$ (100), 106 (4), 91 (66) [$PhCH_2$], 65 (22); $C_{17}H_{18}N_2O_3$ (298.13): calcd. C 68.44, H 6.08, N 9.39; found: C 68.60, H 6.11, N 9.20.



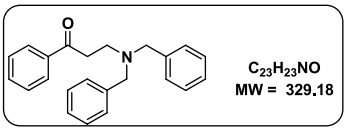

3-(*N*-Benzyl-*N*-ethylamino)-1-(4-chlorophenyl)propan-1-one (**10d**): following the general procedure for the formation of β-aminoketones, the reaction of benzylethylamine (302 mg, 2.24 mmol) and 1-(4-chlorophenyl)-3-(*N*,*N*-dimethylamino) propan-1-one hydrochloride (555 mg, 2.25 mmol) were dissolved in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10d** as a yellow oil. Yield: 74% (498 mg). Data: FTIR (film) ν/cm$^{-1}$ 2969, 2873, 1684 (C=O), 1608, 1589; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.07 (t, 3H, *J* 7.0 Hz, $CH_3$), 2.59 (q, 2H, *J* 7.0 Hz, $NCH_2$), 2.94 (t, 2H, *J* 7.3 Hz, H-2), 3.08 (t, 2H, *J* 7.3 Hz, H-3), 3.63 (s, 2H, Bn-H), 7.22-7.32 (m, 5H, Ph-H), 7.39 (d, 2H, *J* 8.5 Hz, Ar-H), 7.82 (d, 2H, *J* 8.5 Hz, Ar-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 11.7 ($CH_3$), 36.8 ($CH_2$), 47.5 ($NCH_2$), 48.5 ($NCH_2$), 58.2 ($PhCH_2$), 126.8 (CH), 128.1 (CH), 128.6 (CH), 128.7 (CH), 129.4 (CH), 135.2 (Cq), 139.2 (Cq), 139.4 (Cq), 198.4 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 304/302 [M+1]$^+$ (25/79), 274/272 (19/56), 212/210 (36/100), 168/166 (7/19), 141/139 (38/95), 113/111 (17/53), 91 (65) [$PhCH_2$]; $C_{18}H_{20}ClNO$ (301.12): calcd. C 71.63, H 6.68, N 4.64; found: C 71.87, H 6.55, N 4.80.




3-(*N*-Benzyl-*N*-ethylamino)-1-(4-methoxyphenyl)propan-1-one (**10e**): following the general procedure for the formation of β-aminoketones, the reaction of benzylethylamine (295 mg, 2.18 mmol) and 3-(*N*,*N*-dimethylamino)-1-(4-methoxyphenyl)propan-1-one hydrochloride (535 mg, 2.20 mmol) were dissolved in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10e** as a yellow oil. Yield: 90% (584 mg). Data: FTIR (film) ν/cm$^{-1}$ 2968, 2838, 1674 (C=O), 1601, 1170 and 1029 (C–O)**;** $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.07 (t, 3H, *J* 7.0 Hz, $CH_3$), 2.58 (q, 2H, *J* 7.0 Hz), 2.94 (t, 2H, *J* 7.8 Hz, H-2), 3.08 (t, 2H, *J* 8.0 Hz, H-3), 3.64 (s, 2H, Bn-H), 3.87 (s, 3H, $OCH_3$), 6.91 (d, 2H, *J* 8.8 Hz, Ar-H), 7.23 (td, 1H, *J* 7.0, 1.8 Hz, Ph-H), 7.27-7.35 (m, 4H, Ph-H), 7.89 (d, 2H, *J* 8.8 Hz, Ar-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 11.8 ($CH_3$), 36.4 ($CH_2$), 47.5 ($NCH_2$), 48.8 ($NCH_2$), 55.4 ($OCH_3$), 58.2 ($PhCH_2$), 113.6 (CH), 126.8 (CH), 128.1 (CH), 128.8 (CH), 130.1 (Cq), 130.3 (CH), 139.6 (Cq), 163.3 (Cq), 198.4 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 298 [M+1]$^+$ (100), 268 (20), 206 (18), 148 (29), 135 (11), 91 (11) [$PhCH_2$]; $C_{19}H_{23}NO_2$ (297.17): calcd. C 76.73, H 7.80, N 4.71; found: C 76.42, H 7.91, N 4.93.

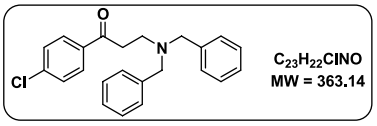



3-(*N*-Benzyl-*N*-(2-hydroxyethyl)amino)-1-(4-chlorophenyl) propan-1-one (**10f**): following the general procedure for the formation of β-aminoketones, the reaction of benzylethanolamine (301 mg, 1.99 mmol) and 1-(4-chlorophenyl)-3-(*N*,*N*-dimethylamino)propan-1-one hydrochloride (495 mg, 2.00 mmol) were dissolved in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10f** as a yellow oil. Yield: 65% (411 mg). Data: FTIR (film) ν/cm$^{-1}$ 3426 (O–H), 2955, 2811, 1683 (C=O), 1589; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.42 (bs, 1H, OH), 2.70 (t, 2H, *J* 5.2 Hz, $NCH_2$), 2.98 (t, 2H, *J* 6.6 Hz, H-2), 3.09 (t, 2H, *J* 6.6 Hz, H-3), 3.62 (t, 2H, *J* 5.2 Hz, $OCH_2$), 3.66 (s, 2H, Bn-H), 7.20-7.29 (m, 5H, Ph-H), 7.40 (d, 2H, *J* 8.8 Hz, Ar-H), 7.80 (d, 2H, *J* 8.8 Hz, Ar-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 36.6 ($CH_2$), 48.9 ($NCH_2$), 56.0 ($NCH_2$), 59.0 ($PhCH_2$ + $OCH_2$), 127.2 (CH), 128.4 (CH), 128.8 (CH), 128.9 (CH), 129.4 (CH), 135.0 (Cq), 138.6 (Cq), 139.6 (Cq), 198.3 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 141/139 [M-178]$^+$ (5/14), 120 (57), 113/111 (3/11), 91 (100) [$PhCH_2$]; $C_{18}H_{20}ClNO_2$ (317.12): calcd. C 68.03, H 6.34, N 4.41; found: C 68.10, H 6.52, N 4.51.

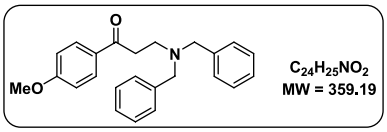



3-(Dibenzylamino)-1-phenylpropan-1-one (**10g**): following the general procedure for the formation of β-aminoketones, the reaction of dibenzylamine (321 mg, 1.63 mmol)

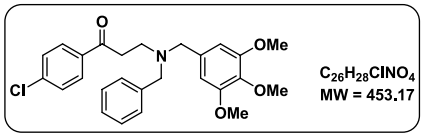
and 3-(*N*,*N*-dimethylamino)-1-phenylpropan-1-one hydrochloride (348 mg, 1.63 mmol) in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10g** as a colorless oil. Yield: 68% (365 mg). Data: FTIR (film) ν/cm$^{-1}$ 2927, 2849, 1682 (C=O), 1598; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.98 (t, 2H, *J* 7.3 Hz, H-2), 3.16 (t, 2H, *J* 7.3 Hz, H-3), 3.67 (s, 4H, Bn-H), 7.25 (t, 2H, *J* 7.3 Hz), 7.32 (t, 4H, *J* 7.3 Hz, Ph-H), 7.37 (d, 4H, *J* 7.0 Hz, Ph-H), 7.42 (t, 2H, *J* 7.6 Hz, Ph-H), 7.55 (t, 1H, *J* 7.3 Hz, Ph-H), 7.86 (d, 2H, *J* 7.3 Hz, Ph-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 36.9 ($CH_2$), 49.3 ($NCH_2$), 58.5 ($PhCH_2$), 126.9 (CH), 128.0 (CH), 128.2 (CH), 128.5 (CH), 128.7 (CH), 132.8 (CH), 136.8 (Cq), 139.4 (Cq), 199.6 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 238 [M-91]$^+$ (16), 210 (12), 118 (10), 105 (26), 91 (100) [$PhCH_2$]; $C_{23}H_{23}NO$ (329.18): calcd. C 83.85, H 7.04, N 4.25; found: C 83.93, H 7.11, N 4.19.



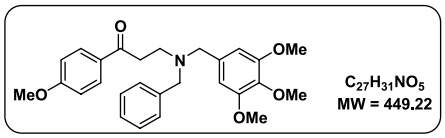

1-(4-Chlorophenyl)-3-(dibenzylamino)propan-1-one (**10h**): following the general procedure for the formation of β-aminoketones, the reaction of dibenzylamine (353 mg, 1.79 mmol) and 1-(4-chlorophenyl)-3-(*N*,*N*-dimethylamino) propan-1-one hydrochloride (445 mg, 1.80 mmol) were dissolved in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10h** as a yellow oil. Yield: 77% (501 mg). Data: FTIR (film) ν/cm$^{-1}$ 2939, 2851, 1683 (C=O), 1591; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 3.00 (t, 2H, *J* 7.3 Hz, H-2), 3.13 (t, 2H, *J* 7.3 Hz, H-3), 3.69 (s, 4H, Bn-H), 7.26-7.41 (m, 12H, Ph-H, Ar-H), 7.78 (d, 2H, *J* 8.5 Hz, Ar-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 36.9 ($CH_2$), 49.2 ($NCH_2$), 58.5 ($PhCH_2$), 126.8 (CH), 128.1 (CH), 128.6 (2 × CH), 129.3 (CH), 135.0 (Cq), 139.1 (Cq), 139.2 (Cq), 198.1 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 274/272 [M-91]$^+$ (10/30), 210 (26), 141/139 (10/33), 91 (100) [$PhCH_2$]; $C_{23}H_{22}ClNO$ (363.14): calcd. C 75.92, H 6.09, N 3.85; found: C 75.73, H 6.21, N 3.90.




3-(Dibenzylamino)-1-(4-methoxyphenyl)propan-1-one (**10i**): following the general procedure for the formation of β-aminoketones, the reaction of dibenzylamine (306 mg, 1.55 mmol) and 3-(*N*,*N*-dimethylamino)-1-(4-methoxyphenyl)propan-1-one hydrochloride (380 mg, 1.56 mmol) were dissolved in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10i** as a yellow oil. Yield: 69% (385 mg). Data: FTIR (film) ν/cm$^{-1}$ 2933, 2838, 1673 (C=O), 1600, 1171, 1112 and 1029 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.97 (t, 2H, *J* 7.3 Hz, H-2), 3.12 (t, 2H, *J* 7.2 Hz, H-3), 3.67 (s, 4H, Bn-H), 3.86 (s, 3H, $OCH_3$), 6.89 (d, 2H, *J* 8.8 Hz, Ar-H), 7.25 (t, 2H, *J* 7.0 Hz, Ph-H), 7.32 (t, 4H, *J* 7.0 Hz, Ph-H), 7.38 (d, 4H, *J* 7.0 Hz, Ph-H), 7.84 (d, 2H, *J* 8.8 Hz, Ar-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 36.5 ($CH_2$), 49.4 ($NCH_2$), 55.3 ($OCH_3$), 58.4 ($PhCH_2$), 113.6 (CH), 126.8 (CH), 128.1 (CH), 128.7 (CH), 129.9 (Cq), 130.2 (CH), 139.4 (Cq), 163.3 (Cq), 198.1 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 360 [M+1]$^+$ (8), 268 (100), 210 (23), 135 (6), 91 (11) [$PhCH_2$]; $C_{24}H_{25}NO_2$ (359.19): calcd. C 80.19, H 7.01, N 3.90; found: C 80.01, H 7.13, N 3.74.

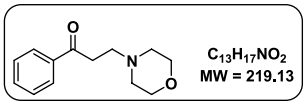



3-(*N*-(3,4,5-Trimethoxybenzyl)-*N*-benzylamino)-1-(4-chlorophenyl)propan-1-one (**10j**): following the general procedure for the formation of β-aminoketones, the reaction of *N*-(3,4,5-trimethoxybenzyl)(phenyl)methanamine (363 mg, 1.26 mmol) and 1-(4-chlorophenyl)-3-(*N*,*N*-dimethylamino) propan-1-one hydrochloride (315 mg, 1.28 mmol) were dissolved in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10j** as a yellow oil. Yield: 79% (453 mg). Data: FTIR (film) ν/cm$^{-1}$ 2937, 2835, 1671 (C=O), 1609, 1589, 1127 and 1093 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.95 (t, 2H, *J* 7.0 Hz, H-2), 3.08 (t, 2H, *J* 7.1 Hz, H-3), 3.57 (s, 2H, Bn-H), 3.60 (s, 2H, Bn-H), 3.81 (s, 3H, $OCH_3$), 3.83 (s, 6H, $OCH_3$ × 2), 6.57 (s, 2H, Ar-H), 7.21-7.30 (m, 5H, Ph-H), 7.36 (d, 2H, *J* 8.5 Hz, Ar-H), 7.74 (d, 2H, *J* 8.5 Hz, Ar-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 36.9 ($CH_2$), 49.5 ($NCH_2$), 56.0 ($OCH_3$ × 2), 58.6 ($PhCH_2$), 58.8 ($PhCH_2$), 60.8 ($OCH_3$), 105.4 (CH), 127.0 (CH), 128.2 (CH), 128.7 (CH), 128.8 (CH), 129.4 (CH), 135.1 (Cq), 135.2 (Cq), 136.9 (Cq), 139.2 (Cq), 139.4 (Cq), 153.1 (Cq), 198.3 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 456/454 [M+1]$^+$ (2/6), 364/362 (8/23), 181 (92), 139 (25), 91 (100) [$PhCH_2$]; $C_{26}H_{28}ClNO_4$ (453.17): calcd. C 68.79, H 6.22, N 3.09; found: C 68.75, H 6.11, N 3.21.

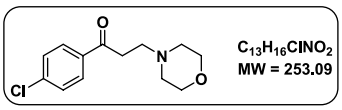



3-(*N*-(3,4,5-Trimethoxybenzyl)-*N*-benzylamino)-1-(4-methoxyphenyl)propan-1-one (**10k**): following the general procedure for the formation of β-aminoketones, the reaction of *N*-(3,4,5-trimethoxybenzyl)(phenyl)methanamine

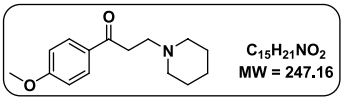
(321 mg, 1.12 mmol) and 3-(*N*,*N*-dimethylamino)-1-(4-methoxyphenyl)propan-1-one hydrochloride (275 mg, 1.13 mmol) were dissolved in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10k** as a yellow oil. Yield: 62% (312 mg). Data: FTIR (film) ν/cm$^{-1}$ 2928, 2842, 1681 (C=O), 1588, 1206, 1123 and 1093 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.98 (t, 2H, *J* 7.3 Hz, H-2), 3.09 (t, 2H, *J* 7.3 Hz, H-3), 3.59 (s, 2H, Bn-H), 3.64 (s, 2H, Bn-H), 3.83 (s, 3H, $OCH_3$), 3.84 (s, 6H, $OCH_3 \times 2$), 3.86 (s, 3H, $OCH_3$), 6.60 (s, 2H, Ar-H), 6.88 (d, 2H, *J* 8.8 Hz, Ar-H), 7.23 (td, 1H, *J* 7.0, 1.5 Hz, Ph-H), 7.28 (d, 2H, *J* 6.3 Hz, Ph-H), 7.33 (t, 2H, *J* 7.0 Hz, Ph-H), 7.83 (d, 2H, *J* 8.8 Hz, Ar-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 36.5 ($CH_2$), 49.8 ($NCH_2$), 55.4 ($OCH_3$), 56.0 ($OCH_3 \times 2$), 58.5 ($PhCH_2$), 58.7 ($PhCH_2$), 60.8 ($OCH_3$), 105.4 (CH), 113.6 (CH), 126.9 (CH), 128.2 (CH), 128.7 (CH), 130.0 (Cq), 130.3 (CH), 135.3 (Cq), 136.8 (Cq), 139.3 (Cq), 153.0 (Cq), 163.4 (Cq), 198.1 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 450 $[M+1]^+$ (4), 358 (41), 268 (55), 181 (100), 148 (13), 135 (50), 91 (55) $[PhCH_2]$; $C_{27}H_{31}NO_5$ (449.22): calcd. C 72.14, H 6.95, N 3.12; found: C 72.30, H 6.73, N 3.30.



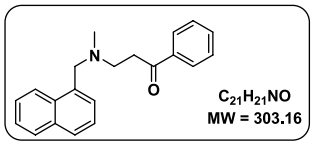

3-Morpholino-1-phenylpropan-1-one (**10l**): following the general procedure for the formation of b-aminoketones, the reaction of morpholine (309 mg, 3.55 mmol) and 3-(*N*,*N*-dimethylamino)-1-phenylpropan-1-one hydrochloride (755 mg, 3.54 mmol) in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10l** as a yellow oil. Yield: 63% (490 mg). Data: FTIR (film): ν = 2955, 2855, 1683 (C=O), 1217, 1116 and 1070 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.52 (t, 4H, *J* 4.5 Hz, $NCH_2$), 2.84 (t, 2H, *J* 7.3 Hz, H-2), 3.19 (t, 2H, *J* 7.3 Hz, H-3), 3.72 (t, 4H, *J* 4.6 Hz, $OCH_2$), 7.47 (t, 2H, *J* 7.5 Hz, Ph-H), 7.57 (t, 1H, *J* 7.3 Hz, Ph-H), 7.96 (d, 2H, *J* 7.3 Hz, Ph-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 36.0 ($CH_2$), 53.5 ($NCH_2$), 53.7 ($NCH_2$), 66.9 ($OCH_2$), 128.0 (CH), 128.6 (CH), 133.1 (CH), 136.9 (Cq), 198.9 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 132 $[M-87]^+$ (25), 105 (36), 100 (100); $C_{13}H_{17}NO_2$ (219.13): calcd. C 71.21, H 7.81, N 6.39; found: C 71.10, H 7.94, N 6.15.




1-(4-Chlorophenyl)-3-morpholinopropan-1-one (**10m**): following the general procedure for the formation of β-aminoketones, the reaction of morpholine (301 mg, 3.46 mmol) and 1-(4-chlorophenyl)-3-(*N*,*N*-dimethylamino) propan-1-one hydrochloride (854 mg, 3.46 mmol) were dissolved in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10m** as a yellow oil. Yield: 53% (464 mg). Data: FTIR (film) ν/cm$^{-1}$ 2958, 2834, 1682 (C=O), 1204, 1114 and 1013 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.50 (t, 4H, *J* 4.5 Hz, $NCH_2$), 2.81 (t, 2H, *J* 7.3 Hz, H-2), 3.14 (t, 2H, *J* 7.3 Hz, H-3), 3.70 (t, 4H, *J* 4.6 Hz, $OCH_2$), 7.44 (d, 2H, *J* 8.5 Hz, Ar-H), 7.89 (d, 2H, *J* 8.5 Hz, Ar-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 36.0 ($CH_2$), 53.4 ($NCH_2$), 53.7 ($NCH_2$), 66.9 ($OCH_2$), 128.9 (CH), 129.4 (CH), 135.1 (Cq), 139.5 (Cq), 197.7 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 168/166 $[M-87]^+$ (5/15), 141/139 (20/63), 100 (100), 75 (25); $C_{13}H_{16}ClNO_2$ (253.09): calcd. C 61.54, H 6.36, N 5.52; found: C 61.71, H 6.50, N 5.30.



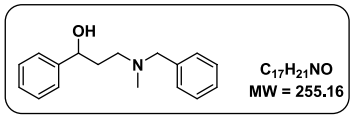

1-(4-methoxyphenyl)-3-(piperidin-1-yl)propan-1-one (**10n**): following the general procedure for the formation of β-aminoketones, the reaction of piperidine (298 mg, 3.51 mmol) and 3-(*N*,*N*-dimethylamino)-1-(4-methoxyphenyl)propan-1-one hydrochloride (852 mg, 3.51 mmol) were dissolved in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10n** as a yellow solid. Yield: 72% (624 mg). Mp 204-205 ºC. Data: FTIR (KBr): ν/cm$^{-1}$ 2953, 2842, 1669 (C=O), 1601, 1178 and 1026 (C–O); $^1$ H NMR (400 MHz, $CDCl_3$) $\delta$ 1.47-1.52 (m, 2H), 1.68-1.74 (m, 4H), 2.59-2.63 (m, 4H, $NCH_2$), 2.94 (t, 2H, *J* 7.4 Hz, H-2), 3.30 (t, 2H, *J* 7.3 Hz, H-3), 3.86 (s, 3H, $OCH_3$), 6.92 (d, 2H, *J* 8.8 Hz, Ar-H), 7.95 (d, 2H, *J* 8.8 Hz, Ar-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 23.6 ($CH_2$), 25.1 ($CH_2$), 35.2 ($CH_2$), 53.6 ($NCH_2$), 54.3 ($NCH_2$), 55.4 ($OCH_3$), 113.7 (CH), 129.6 (Cq), 130.4 (CH), 163.6 (Cq), 197.0 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 247 $[M]^+$ (2), 162 (29), 135 (100), 98 (39); $C_{15}H_{21}NO_2$ (247.16): calcd. C 72.84, H 8.56, N 5.66; found: C 72.93, H 8.62, N 5.51.



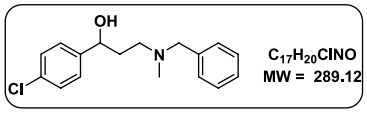

3-(*N*-Methyl-*N*-((naphthalen-5-yl)methyl)amino)-1-phenylpropan-1-one (**10o**): following the general procedure for the formation of β-aminoketones, the reaction of *N*-methyl(naphthalen-5-yl)methanamine (309 mg, 1.81 mmol) and 3-(*N*,*N*-dimethylamino)-1-phenylpropan-1-one hydrochloride (390 mg, 1.83 mmol) in a mixture of 1,4-dioxane (5 mL) and TEA (1 mL) afforded compound **10o** as a yellow solid. Yield: 89% (488 mg). Mp 85-86 ºC.

Data: FTIR (KBr) ν/cm$^{-1}$ 2946, 2844, 1683 (C=O), 1596; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 2.31 (s, 3H, $NCH_3$), 3.01 (t, 2H, *J* 7.3 Hz, H-2), 3.22 (t, 2H, *J* 7.3 Hz, H-3), 3.98 (s, 2H), 7.37-7.45 (m, 4H, Ph-H, Naph-H), 7.47-7.50 (m, 2H, Naph-H), 7.54 (t, 1H, *J* 7.3 Hz, Ph-H), 7.78 (d, 1H, *J* 7.5 Hz, Naph-H), 7.83-7.86 (m, 1H, Naph-H), 7.91 (d, 2H, *J* 7.3 Hz, Ph-H), 8.25-8.28 (m, 1H, Naph-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 36.8 ($CH_2$), 42.2 ($NCH_3$), 53.0 ($NCH_2$), 61.0 ($PhCH_2$), 124.6 (CH), 125.0 (CH), 125.5 (CH), 125.8 (CH), 127.3 (CH), 127.9 (CH), 128.0 (CH), 128.3 (CH), 128.5 (CH), 132.4 (Cq), 132.9 (CH), 133.8 (Cq), 134.6 (Cq), 136.9 (Cq), 199.5 (C=O) ppm; MS (70 eV, EI) *m/z* (%) 303 [M]$^+$ (2), 170 (21), 141 (100), 105 (34), 77 (27); $C_{21}H_{21}NO$ (303.16): calcd. C 83.13, H 6.98, N 4.62; found: C 83.21, H 6.89, N 4.50.

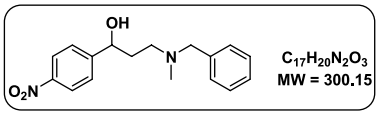
Characterization data for g-aminoalcohols **11** and Naftifine®



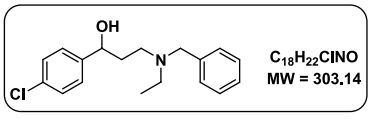

(±)-3-(*N*-Benzyl-*N*-methylamino)-1-phenylpropan-1-ol (**11a**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10a** (293 mg, 1.16 mmol) and sodium borohydride (78 mg, 2.06 mmol) in 5 mL of methanol afforded compound **11a** as a yellow oil. Yield: 82% (242 mg). Data: FTIR (film) ν/cm$^{-1}$ 3400 (O–H), 2923, 2849, 1066 and 1026 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.87-1.96 (m, 2H, H-2), 2.31 (s, 3H, $NCH_3$), 2.64 (ddd, 1H, *J* 12.6, 4.4, 4.4 Hz, H-3a), 2.86 (ddd, 1H, *J* 12.7, 9.1, 3.9 Hz, H-3b), 3.52 (d, 1H, *J* 12.8 Hz, Bn-H), 3.69 (d, 1H, *J* 12.8 Hz, Bn-H), 4.95 (dd, 1H, *J* 7.6, 4.0 Hz, CH–O), 7.27 (t, 1H, *J* 7.2 Hz, Ph-H), 7.32-7.42 (m, 9H, Ph-H) ppm, OH is absent; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 34.4 ($CH_2$), 41.7 ($NCH_3$), 56.4 ($NCH_2$), 62.7 ($PhCH_2$), 75.6 (CH–O), 125.5 (CH), 126.8 (CH), 127.3 (CH), 128.1 (CH), 128.4 (CH), 129.2 (CH), 137.7 (Cq), 144.9 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 255 [M]$^+$ (3), 134 (56), 121 (7), 91 (100) [$PhCH_2$]; $C_{17}H_{21}NO$ (255.16): calcd. C 79.96, H 8.29, N 5.49; found: C 79.73, H 8.18, N 5.60.




(±)-3-(*N*-Benzyl-*N*-methylamino)-1-(4-chlorophenyl)propan-1-ol (**11b**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10b** (299 mg, 1.04 mmol) and sodium borohydride (75 mg, 1.98 mmol) in 5 mL of methanol afforded compound **11b** as a colorless oil. Yield: 96% (289 mg). Data: FTIR (film) ν/cm$^{-1}$ 3402 (O–H), 2925, 2846, 1086 and 1014 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.82-1.87 (m, 2H, H-2), 2.28 (s, 3H, $NCH_3$), 2.60 (ddd, 1H, *J* 12.6, 4.4, 4.4 Hz, H-3a), 2.82 (ddd, 1H, *J* 13.1, 6.7, 6.7 Hz, H-3b), 3.49 (d, 1H, *J* 12.8 Hz, Bn-H), 3.65 (d, 1H, *J* 12.8 Hz, Bn-H), 4.88 (dd, 1H, *J* 5.8, 5.8 Hz, CH–O), 7.27-2.37 (m, 9H, Ph-H, Ar-H) ppm, OH is absent; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 34.4 ($CH_2$), 41.8 ($NCH_3$), 56.2 ($NCH_2$), 62.8 ($PhCH_2$), 75.1 (CH–O), 126.9 (CH), 127.5 (CH), 128.2 (CH), 128.5 (CH), 129.2 (CH), 132.4 (Cq), 137.6 (Cq), 143.5 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 291/289 [M]$^+$ (0.6/1.8), 134 (28), 120 (8), 105 (2), 91 (100) [$PhCH_2$]; $C_{17}H_{20}ClNO$ (289.12): calcd. C 70.46, H 6.96, N 4.83; found: C 70.31, H 6.79, N 4.79.

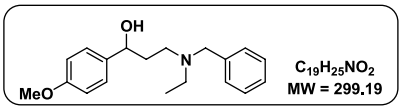



(±)-3-(*N*-Benzyl-*N*-methylamino)-1-(4-nitrophenyl)propan-1-ol (**11c**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10c** (287 mg, 0.96 mmol) and sodium borohydride (68 mg, 1.80 mmol) in 5 mL of methanol afforded compound **11c** as a yellow oil. Yield: 57% (165 mg). Data: FTIR (film) ν/cm$^{-1}$ 3382 (O–H), 2922, 2846, 1602, 1526 ($NO_2$), 1349 ($NO_2$), 1081 and 1043 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.79-1.94 (m, 2H, H-2), 2.31 (s, 3H, $NCH_3$), 2.61 (ddd, 1H, *J* 12.7, 5.5, 3.2 Hz, H-3a), 2.84 (ddd, 1H, *J* 12.8, 9.8, 3.1 Hz, H-3b), 3.51 (d, 1H, *J* 12.8 Hz, Bn-H), 3.64 (d, 1H, *J* 12.8 Hz, Bn-H), 5.00 (dd, 1H, *J* 8.2, 3.4 Hz, CH–O), 7.32-7.39 (m, 5H, Ph-H), 7.49 (d, 2H, *J* 8.8 Hz, Ar-H), 8.16 (d, 2H, *J* 8.8 Hz, Ar-H) ppm, OH is absent; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 34.0 ($CH_2$), 41.8 ($NCH_3$), 56.0 ($NCH_2$), 62.8 ($PhCH_2$), 75.0 (CH–O), 123.4 (CH), 126.2 (CH), 127.6 (CH), 128.6 (CH), 129.2 (CH), 137.3 (Cq), 146.8 (Cq), 152.4 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 300 [M]$^+$ (6), 134 (61), 91 (100) [$PhCH_2$], 65 (10); $C_{17}H_{20}N_2O_3$ (300.15): calcd. C 67.98, H 6.71, N 9.33; found: C 67.69, H 6.69, N 9.51.

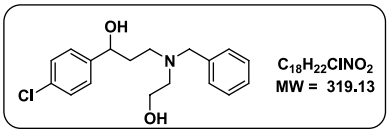



(±)-3-(*N*-Benzyl-*N*-ethylamino)-1-(4-chlorophenyl)propan-1-ol (**11d**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10d** (305 mg, 1.01 mmol) and sodium borohydride (74 mg, 1.96 mmol) in 5 mL of methanol afforded compound **11d** as a yellow oil. Yield: 83% (255 mg). Data: FTIR (film)

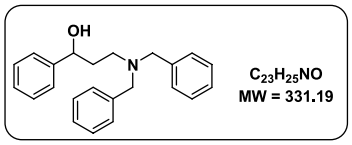
ν/cm$^{-1}$ 3218 (O–H), 2970, 2826, 1599, 1090, 1058 and 1014 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.15 (t, 3H, *J* 7.0 Hz, $CH_3$), 1.77-1.87 (m, 2H, H-2a, H-2b), 2.44-2.53 (m, 1H), 2.64 (ddd, 1H, *J* 12.9, 4.9, 3.5 Hz, H-3a), 2.68-2.77 (m, 1H), 2.85 (ddd, 1H, *J* 13.0, 9.4, 3.1 Hz, H-3b), 3.43 (d, 1H, *J* 13.3 Hz, Bn-H), 3.84 (d, 1H, *J* 13.3 Hz, Bn-H), 4.82 (dd, 1H, *J* 8.2, 3.6 Hz, CH–O), 7.22-7.42 (m, 9H, Ph-H, Ar-H) ppm, OH is absent; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 11.2 ($CH_3$), 34.4 ($CH_2$), 47.0 ($NCH_2$), 52.3 ($NCH_2$), 58.3 ($PhCH_2$), 75.0 (CH–O), 126.9 (CH), 127.4 (CH), 128.2 (CH), 128.5 (CH), 129.3 (CH), 132.3 (Cq), 137.8 (Cq), 143.5 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 306/304 $[M+1]^+$ (2/6), 148 (79), 134 (11), 91 (100) $[PhCH_2]$; $C_{18}H_{22}ClNO$ (303.14): calcd. C 71.16, H 7.30, N 4.61; found: C 71.01, H 7.15, N 4.60.



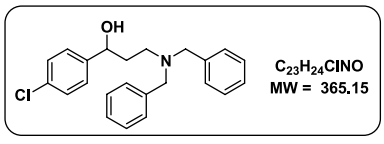

(±)-3-(*N*-Benzyl-*N*-ethylamino)-1-(4-methoxyphenyl) propan-1-ol (**11e**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10e** (289 mg, 0.97 mmol) and sodium borohydride (70 mg, 1.85 mmol) in 5 mL of methanol afforded compound **11e** as a yellow oil. Yield: 89% (259 mg). Data: FTIR (film) ν/cm$^{-1}$ 3223 (O–H), 2934, 2833, 1172, 1058 and 1036 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.14 (t, 3H, *J* 7.0 Hz, $CH_3$), 1.75-1.82 (m, 1H, H-2a), 1.86-1.96 (m, 1H, H-2b), 2.43-2.52 (m, 1H), 2.65 (ddd, 1H, *J* 12.9, 4.9, 3.5 Hz, H-3a), 2.69-2.78 (m, 1H), 2.85 (ddd, 1H, *J* 13.2, 10.2, 3.1 Hz, H-3b), 3.42 (d, 1H, *J* 13.3 Hz, Bn-H), 3.81 (s, 3H, $OCH_3$), 3.86 (d, 1H, *J* 13.1 Hz, Bn-H), 4.81 (dd, 1H, *J* 8.8, 2.8 Hz, CH–O), 5.42 (bs, 1H, OH), 6.87 (d, 2H, *J* 8.5 Hz, Ar-H), 7.27 (d, 2H, *J* 8.5 Hz, Ar-H), 7.30-7.38 (m, 5H, Ph-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 11.5 ($CH_3$), 34.6 ($CH_2$), 46.9 ($NCH_2$), 52.4 ($NCH_2$), 55.1 ($OCH_3$), 58.2 ($PhCH_2$), 75.1 (CH–O), 113.5 (CH), 126.6 (CH), 127.2 (CH), 128.4 (CH), 129.2 (CH), 137.2 (Cq), 137.9 (Cq), 158.4 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 299 $[M]^+$ (47), 148 (100), 134 (47), 120 (18), 109 (19), 91 (35) $[PhCH_2]$; $C_{19}H_{25}NO_2$ (299.19): calcd. C 76.22, H 8.42, N 4.68; found: C 76.30, H 8.21, N 4.76.




(±)-3-(*N*-Benzyl-*N*-(2-hydroxyethyl)amino)-1-(4-chlorophenyl) propan-1-ol (**11f**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10f** (296 mg, 0.93 mmol) and sodium borohydride (68 mg, 1.80 mmol) in 5 mL of methanol afforded compound **11f** as a colorless oil. Yield: 61% (182 mg). Data: FTIR (film) ν/cm$^{-1}$ 3409 (O–H), 2948, 2826, 1598, 1086 and 1014 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.89-1.91 (m, 2H, H-2), 2.67-2.85 (m, 4H, $NCH_2$, H-3a, H-3b), 3.13 (bs, 1H, OH), 3.64 (d, 1H, *J* 13.6 Hz, Bn-H), 3.68-3.71 (m, 2H, $OCH_2$), 3.78 (d, 1H, *J* 13.2 Hz, Bn-H), 4.81 (dd, 1H, *J* 6.8, 6.8 Hz, CH–O), 7.24-7.35 (m, 9H, Ph-H, Ar-H) ppm, OH is absent; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 36.0 ($CH_2$), 52.7 ($NCH_2$), 56.7 ($NCH_2$), 59.9 ($PhCH_2$), 60.2 ($OCH_2$), 73.7 (CH–O), 127.1 (CH), 127.5 (CH), 128.5 (CH), 128.6 (CH), 129.2 (CH), 133.1 (Cq), 138.5 (Cq), 143.6 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 290/288 $[M-31]^+$ (5/15), 164 (6), 134 (38), 91 (100) $[PhCH_2]$; $C_{18}H_{22}ClNO_2$ (319.13): calcd. C 67.60, H 6.93, N 4.38; found: C 67.79, H 6.70, N 4.51.

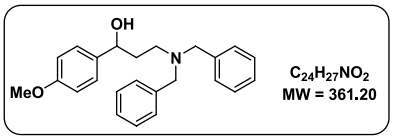



(±)-3-(Dibenzylamino)-1-phenylpropan-1-ol (**11g**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10g** (279 mg, 0.85 mmol) and sodium borohydride (63 mg, 1.66 mmol) in 5 mL of methanol afforded compound **11g** as a colorless oil. Yield: 85% (239 mg). Data: FTIR (film) ν/cm$^{-1}$ 3396 (O–H), 2943, 2827, 1603, 1129, 1059 and 1031 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.83-1.90 (m, 1H, H-2a), 1.94-2.04 (m, 1H, H-2b), 2.67 (ddd, 1H, *J* 13.0, 5.4, 3.4 Hz, H-3a), 2.88 (ddd, 1H, *J* 13.0, 10.0, 3.2 Hz, H-3b), 3.44 (d, 2H, *J* 13.1 Hz, Bn-H), 3.88 (d, 2H, *J* 13.1 Hz, Bn-H), 4.75 (dd, 1H, *J* 8.8, 2.8 Hz, CH–O), 6.32 (bs, 1H, OH), 7.23-7.41 (m, 15H, Ph-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 34.8 ($CH_2$), 52.3 ($NCH_2$), 58.5 ($PhCH_2$), 75.2 (CH–O), 125.5 (CH), 126.8 (CH), 127.4 (CH), 128.1 (CH), 128.5 (CH), 129.4 (CH), 137.8 (Cq), 144.7 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 331 $[M]^+$ (6), 240 (6), 210 (64), 181 (5), 120 (9), 91 (100) $[PhCH_2]$; $C_{23}H_{25}NO$ (331.19): calcd. C 83.34, H 7.60, N 4.23; found: C 83.20, H 7.72, N 4.19.

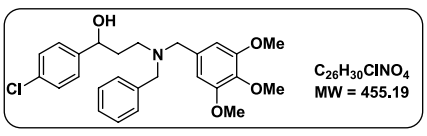



(±)-1-(4-Chlorophenyl)-3-(dibenzylamino)propan-1-ol (**11h**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10h** (311 mg, 0.86 mmol) and sodium borohydride (60 mg, 1.59 mmol) in 5 mL of methanol afforded compound **11h**

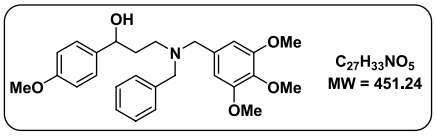
as a yellow oil. Yield: 92% (288 mg). Data: FTIR (film) ν/cm$^{-1}$ 3243 (O–H), 2934, 2825, 1599, 1089, 1074 and 1013 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.83-1.92 (m, 2H, H-2a, H-2b), 2.66 (ddd, 1H, *J* 12.9, 5.6, 3.5 Hz, H-3a), 2.84 (ddd, 1H, *J* 13.1, 9.1, 3.9 Hz, H-3b), 3.45 (d, 2H, *J* 13.1 Hz, Bn-H), 3.82 (d, 2H, *J* 13.1 Hz, Bn-H), 4.71 (dd, 1H, *J* 8.0, 3.5 Hz, CH–O), 6.46 (bs, 1H, OH), 7.15 (d, 2H, *J* 8.5 Hz, Ar-H), 7.24 (d, 2H, *J* 8.3 Hz, Ar-H), 7.30-7.42 (m, 10H, Ph-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 34.6 ($CH_2$), 52.0 ($NCH_2$), 58.6 ($PhCH_2$), 74.5 (CH–O), 126.9 (CH), 127.4 (CH), 128.2 (CH), 128.5 (CH), 129.4 (CH), 132.3 (Cq), 137.7 (Cq), 143.2 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 367/365 $[M]^+$ (8/23), 276/274 (10/32), 210 (100), 120 (49), 91 (48) $[PhCH_2]$; $C_{23}H_{24}ClNO$ (365.15): calcd. C 75.50, H 6.61, N 3.83; found: C 75.31, H 6.82, N 3.60.



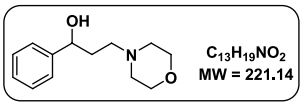

(±)-3-(Dibenzylamino)-1-(4-methoxyphenyl)propan-1-ol (**11i**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10i** (290 mg, 0.81 mmol) and sodium borohydride (59 mg, 1.56 mmol) in 5 mL of methanol afforded compound **11i** as a yellow oil. Yield: 93% (271 mg). Data: FTIR (film) ν/cm$^{-1}$ 3275 (O–H), 2942, 2832, 1611, 1176, 1075 and 1034 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.81-1.86 (m, 1H, H-2a), 1.95-2.03 (m, 1H, H-2b), 2.64-2.68 (m, 1H, H-3a), 2.87 (m, 1H, H-3b), 3.43 (d, 2H, *J* 13.1 Hz, Bn-H), 3.81 (s, 3H, $OCH_3$), 3.88 (d, 2H, *J* 13.1 Hz, Bn-H), 4.72 (dd, 1H, *J* 8.3, 2.7 Hz, CH–O), 6.06 (bs, 1H, OH), 6.85 (d, 2H, *J* 8.3 Hz, Ar-H), 7.20 (d, 2H, *J* 8.3 Hz, Ar-H), 7.33-7.43 (m, 10H, Ph-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 34.8 ($CH_2$), 52.2 ($NCH_2$), 55.1 ($OCH_3$), 58.5 ($PhCH_2$), 74.7 (CH–O), 113.4 (CH), 126.6 (CH), 127.3 (CH), 128.4 (CH), 129.3 (CH), 136.9 (Cq), 137.8 (Cq), 158.4 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 361 $[M^+]$ (78), 270 (11), 252 (26), 211 (23), 210 (100), 91 (24) $[PhCH_2]$; $C_{24}H_{27}NO_2$ (361.20): calcd. C 79.74, H 7.53, N 3.87; found: C 79.61, H 7.60, N 3.71.



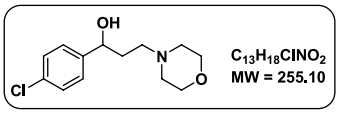

(±)-3-(*N*-(3,4,5-Trimethoxybenzyl)-*N*-benzylamino)-1-(4-chlorophenyl)propan-1-ol (**11j**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10J** (300 mg, 0.66 mmol) and sodium borohydride (48 mg, 1.27 mmol) in 5 mL of methanol afforded compound **11J** as a yellow oil. Yield: 91% (274 mg). Data: FTIR (film) ν/cm$^{-1}$ 3247 (O–H), 2929, 2837, 1591, 1126 and 1010 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.80-1.97 (m, 2H, H-2a, H-2b), 2.64 (ddd, 1H, *J* 13.1, 9.3, 3.3 Hz, H-3a), 2.86 (ddd, 1H, *J* 13.0, 9.8, 3.3 Hz, H-3b), 3.33 (d, 1H, *J* 13.3 Hz, Bn-H), 3.42 (d, 1H, *J* 13.3 Hz, Bn-H), 3.78 (d, 1H, *J* 13.1 Hz, Bn-H), 3.85-3.89 (m, 10H, $OCH_3 \times 3$, Bn-H), 4.73 (dd, 1H, *J* 8.6, 2.8 Hz, CH–O), 6.38 (bs, 1H, OH), 6.60 (s, 2H, Ar-H), 7.17 (d, 2H, *J* 8.5 Hz, Ar-H), 7.24 (d, 2H, *J* 8.5 Hz, Ar-H), 7.30-7.39 (m, 5H, Ph-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 34.8 ($CH_2$), 52.4 ($NCH_2$), 56.2 ($OCH_3 \times 2$), 58.8 ($PhCH_2$), 59.1 ($PhCH_2$), 60.9 ($OCH_3$), 74.8 (CH–O), 106.0 (CH), 126.9 (CH), 127.5 (CH), 128.3 (CH), 128.6 (CH), 129.4 (CH), 132.5 (Cq), 133.6 (Cq), 137.2 (Cq), 137.6 (Cq), 143.2 (Cq), 153.3 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 457/455 $[M]^+$ (2/6), 276/274 (3/10), 181 (100), 120 (24), 91 (24) $[PhCH_2]$; $C_{26}H_{30}ClNO_4$ (455.19): calcd. C 68.49, H 6.63, N 3.07; found: C 68.60, H 6.41, N 3.13.



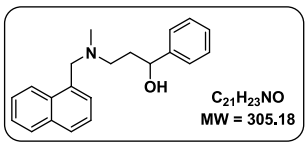

(±)-3-(*N*-(3,4,5-Trimethoxybenzyl)-*N*-benzylamino)-1-(4-methoxyphenyl)propan-1-ol (**11k**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10k** (291 mg, 0.65 mmol) and sodium borohydride (45 mg, 1.19 mmol) in 5 mL of methanol afforded compound **11k** as a yellow oil. Yield: 67% (196 mg). Data: FTIR (film) ν/cm$^{-1}$ 3259 (O–H), 2937, 2836, 1591, 1174, 1128, 1034 and 1009 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.73-1.83 (m, 1H, H-2a), 1.93-2.03 (m, 1H, H-2b), 2.62 (ddd, 1H, *J* 13.0, 4.8, 3.8 Hz, H-3a), 2.87 (ddd, 1H, *J* 13.1, 10.3, 3.1 Hz, H-3b), 3.29 (d, 1H, *J* 13.3 Hz, Bn-H), 3.40 (d, 1H, *J* 13.3 Hz, Bn-H), 3.79 (s, 3H, $OCH_3$), 3.82 (d, 1H, *J* 13.1 Hz, Bn-H), 3.86 (s, 3H, $OCH_3$), 3.88 (s, 6H, $OCH_3 \times 2$), 3.92 (d, 1H, *J* 13.1 Hz, Bn-H), 4.71 (dd, 1H, *J* 9.2, 2.8 Hz, CH–O), 6.22 (bs, 1H, OH), 6.61 (s, 2H, Ar-H), 6.83 (d, 2H, *J* 8.5 Hz, Ar-H), 7.19 (d, 2H, *J* 8.5 Hz, Ar-H), 7.28-7.40 (m, 5H, Ph-H) ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 35.0 ($CH_2$), 52.6 ($NCH_2$), 55.2 ($OCH_3$), 56.1 ($OCH_3 \times 2$), 58.7 ($PhCH_2$), 59.0 ($PhCH_2$), 60.8 ($OCH_3$), 75.0 (CH–O), 105.9 (CH), 113.6 (CH), 126.7 (CH), 127.4 (CH), 128.5 (CH), 129.4 (CH), 133.8 (Cq), 136.9 (Cq), 137.1 (Cq), 137.8 (Cq), 153.2 (Cq), 158.6 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 451 $[M]^+$ (16), 300 (10), 270 (20), 252 (14), 210 (40), 181 (100), 137 (39), 120 (56), 91 (72) $[PhCH_2]$; $C_{27}H_{33}NO_5$ (451.24): calcd. C 71.82, H 7.37, N 3.10; found: C 71.89, H 7.50, N 3.33.



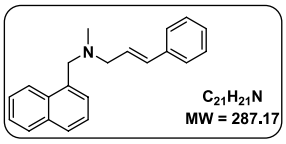

(±)-3-Morpholino-1-phenylpropan-1-ol (**11l**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10l** (279 mg, 1.27 mmol) and sodium borohydride (94 mg, 2.48 mmol) in 5 mL of methanol afforded compound **11l** as a colorless oil. Yield: 72% (203 mg). Data: FTIR (film) ν/cm$^{-1}$ 3413 (O–H), 2953, 2854, 1604, 1203, 1116, 1090 and 1029 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.88 (q, 2H, *J* 5.8 Hz, H-2), 2.48-2.70 (m, 6H, H-3, $NCH_2$), 3.75 (t, 4H, *J* 4.6 Hz, $OCH_2$), 4.94 (dd, 1H, *J* 5.8, 5.8 Hz, CH–O), 7.25 (td, 1H, *J* 6.9, 2.1 Hz, Ph-H), 7.32-7.39 (m, 4H, Ph-H) ppm, OH is absent; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 33.4 ($CH_2$), 53.6 ($NCH_2$), 57.4 ($NCH_2$), 66.9 ($OCH_2$), 75.4 (CH–O), 125.4 (CH), 126.9 (CH), 128.2 (CH), 144.6 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 221 $[M]^+$ (15), 104 (38), 100 (100); $C_{13}H_{19}NO_2$ (221.14): calcd. C 70.56, H 8.65, N 6.33; found: C 70.61, H 8.40, N 6.50.




(±)-1-(4-Chlorophenyl)-3-morpholinopropan-1-ol (**11m**): following the approach B for the formation of γ-aminoalcohols, the reaction of β-aminoketone **10m** (306 mg, 1.21 mmol) and sodium borohydride (89 mg, 2.35 mmol) in 5 mL of methanol afforded compound **11m** as a yellow oil. Yield: 89% (275 mg). Data: FTIR (film) ν/cm$^{-1}$ 3428 (O–H), 2957, 2818, 1597, 1119, 1086, 1030 and 1011 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.80-1.85 (m, 2H, H-2), 2.47-2.71 (m, 6H), 3.75 (t, 4H, *J* 4.5 Hz, $OCH_2$), 4.91 (dd, 1H, *J* 5.7, 5.7 Hz, CH–O), 7.26-7.33 (m, 4H, Ar-H) ppm, OH is absent; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 33.3 ($CH_2$), 53.6 ($NCH_2$), 57.5 ($NCH_2$), 66.8 ($OCH_2$), 74.9 (CH–O), 126.8 (CH), 128.3 (CH), 132.5 (Cq), 143.2 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 257/255 $[M]^+$ (2/8), 140/138 (4/13), 100 (100), 77 (19); $C_{13}H_{18}ClNO_2$ (255.10): calcd. C 61.05, H 7.09, N 5.48; found: C 61.16, H 7.21, N 5.59.




(±)-3-(*N*-Methyl-*N*-((naphthalen-5-yl)methyl)amino)-1-phenylpropan-1-ol (**11o**): following the approach B for the formation of γ–aminoalcohols, the reaction of β-aminoketone **10o** (336 mg, 1.11 mmol) and sodium borohydride (80 mg, 2.11 mmol) in 5 mL of methanol afforded compound **11o** as a yellow solid. Yield: 98% (332 mg), mp 76-77 ºC. Data: FTIR (KBr) ν/cm$^{-1}$ 3374 (O–H), 2949, 2843, 1598, 1129, 1047 and 1024 (C–O); $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 1.89-1.98 (m, 2H, H-2a, H-2b), 2.40 (s, 3H, $NCH_3$), 2.70 (ddd, 1H, *J* 12.5, 5.7, 4.0 Hz, H-3a), 2.85 (ddd, 1H, *J* 12.6, 8.4, 4.4 Hz, H-3b), 3.94 (d, 1H, *J* 13.1 Hz), 4.03 (d, 1H, *J* 13.1 Hz), 4.83 (dd, 1H, *J* 7.0, 4.3 Hz, CH–O), 7.18-7.28 (m, 5H, Ph-H, Naph-H), 7.45-7.47 (m, 2H, Ph-H, Naph-H), 7.55 (td, 1H, *J* 7.4, 1.0 Hz, Naph-H), 7.63 (td, 1H, *J* 7.6, 1.2 Hz, Naph-H), 7.85-7.88 (m, 1H, Naph-H), 7.92 (d, 1H, *J* 8.3 Hz, Naph-H), 8.24 (d, 1H, *J* 8.3 Hz, Naph-H) ppm, OH is absent; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 34.6 ($CH_2$), 42.1 ($NCH_3$), 56.2 ($NCH_2$), 61.1 ($NaphCH_2$), 75.2 (CH–O), 124.0 (CH), 125.1 (CH), 125.4 (CH), 125.8 (CH), 126.3 (CH), 126.7 (CH), 127.9 (CH), 128.0 (CH), 128.3 (CH), 128.6 (CH), 132.3 (Cq), 133.5 (Cq), 133.9 (Cq), 144.8 (Cq) ppm; MS (70 eV, EI) *m/z* (%) 287 $[M-18]^+$ (23), 196 (30), 141 (100), 115 (49), 91 (14) $[PhCH_2]$; $C_{21}H_{23}NO$ (305.18): calcd. C 82.58, H 7.59, N 4.59; found: C 82.45, H 7.38, N 4.67.




(E)-*N*-methyl-*N*-((naphthalen-5-yl)methyl)-3-phenylprop-2-en-1-amine: a solution of γ-aminoalcohol **11o** (200 mg) in 5 mol L$^{-1}$ HCl (5 mL) afforded Naftifine® as a yellow oil. Yield: 86% (162 mg). Data: FTIR (film) ν/cm$^{-1}$ 2943, 2835, 1596, 1589 cm$^{-1}$. The NMR signals corresponding to the Naftifine® obtained by Lipshutz *et al.*[1] are given in square brackets, which are compared with the signals assigned to the product obtained by us. $^1$H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H, $NCH_3$) [2.29 (s, 3H)], 3.34 (d, 2H, *J* 6.0 Hz, H-1) [3.29 (d, 2H, *J* 6.4 Hz)], 4.01 (s, 2H) [3.96 (s, 2H)], 6.43 (dt, 1H, *J* 15.6, 6.4 Hz, H-2) [6.38 (dt, 1H, *J* 16.0, 6.4 Hz)], 6.63 (d, 1H, *J* 15.6 Hz, H-3) [6.60 (d, 1H, *J* 16.0 Hz)], 7.25-7.62 (m, 9H, Ph-H, Naph-H) [7.23-7.57 (m, 9H)], 7.83 (d, 1H, *J* 8.0 Hz, Naph-H) [7.81 (d, 1H, *J* 8.0 Hz)], 7.90 (d, 1H, *J* 8.0 Hz, Naph-H) [7.88 (d, 1H, *J* 8.0 Hz)], 8.36 (d, 1H, *J* 8.4 Hz, Naph-H) [8.31 (d, 1H, *J* 8.2 Hz] ppm; $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 42.4 ($NCH_3$), 60.0 ($CH_2$), 60.3 ($CH_2$), 124.6 (CH), 125.1 (CH), 125.5 (CH), 125.8 (CH), 126.3 (CH), 127.3 (CH), 127.4 (CH), 127.9 (CH), 128.4 (CH), 132.5 (Cq), 132.6 (CH), 133.9 (Cq), 134.8 (Cq), 137.1 (Cq); MS (70 eV, EI) *m/z* (%) 287 $[M]^+$ (42), 196 (42), 141 (100), 115 (48), 91 (15) $[PhCH_2]$; $C_{21}H_{21}N$ (287.17): calcd. C 87.76, H 7.36, N 4.87; found: C 87.65, H 7.30, N 5.01.

## Reference

1. Nishikata, T.; Lipshutz, B. H.; *Org. Lett.* **2009**, *11*, 2377.

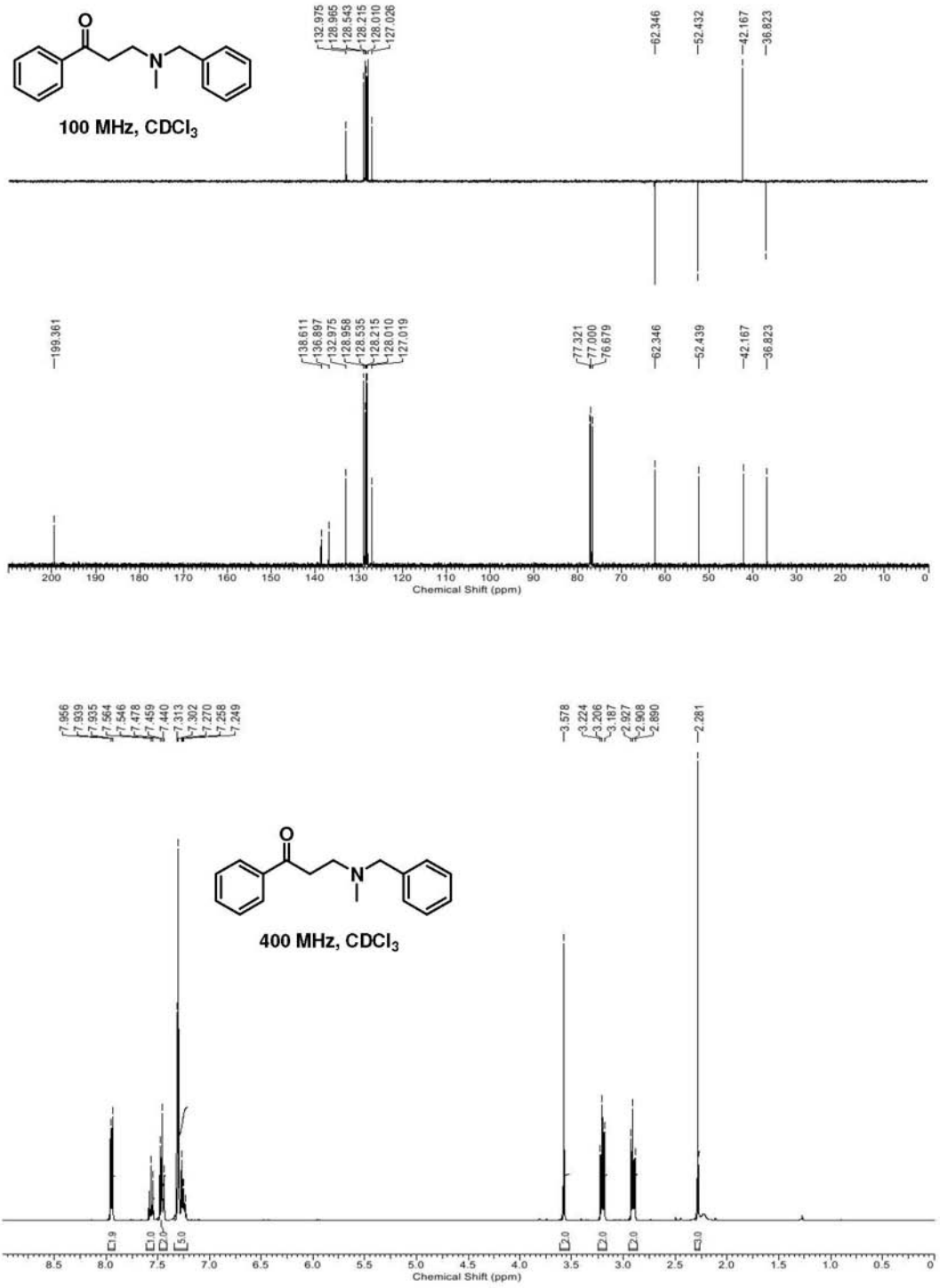
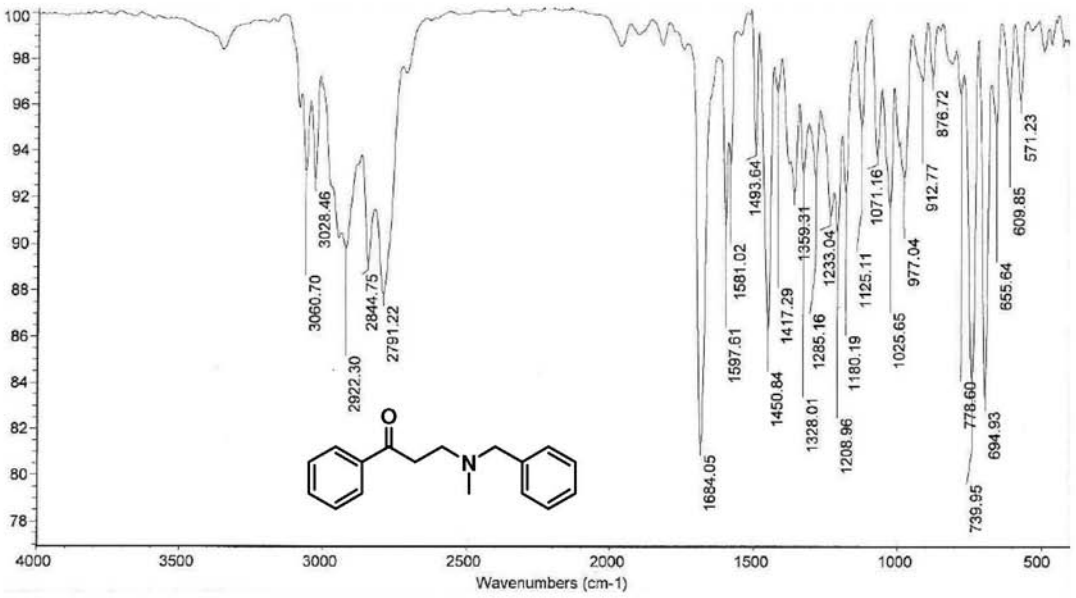



**Figure S1.** [1]H and [13]C spectra for compound **10a**.



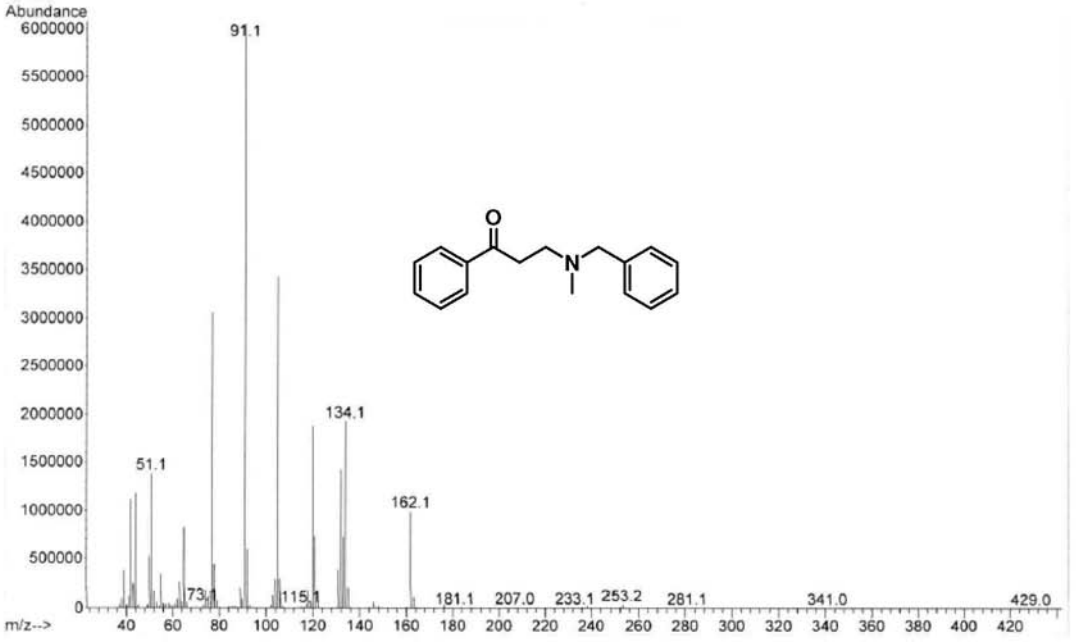




**Figure S2.** IR and MS spectra for compound **10a**.

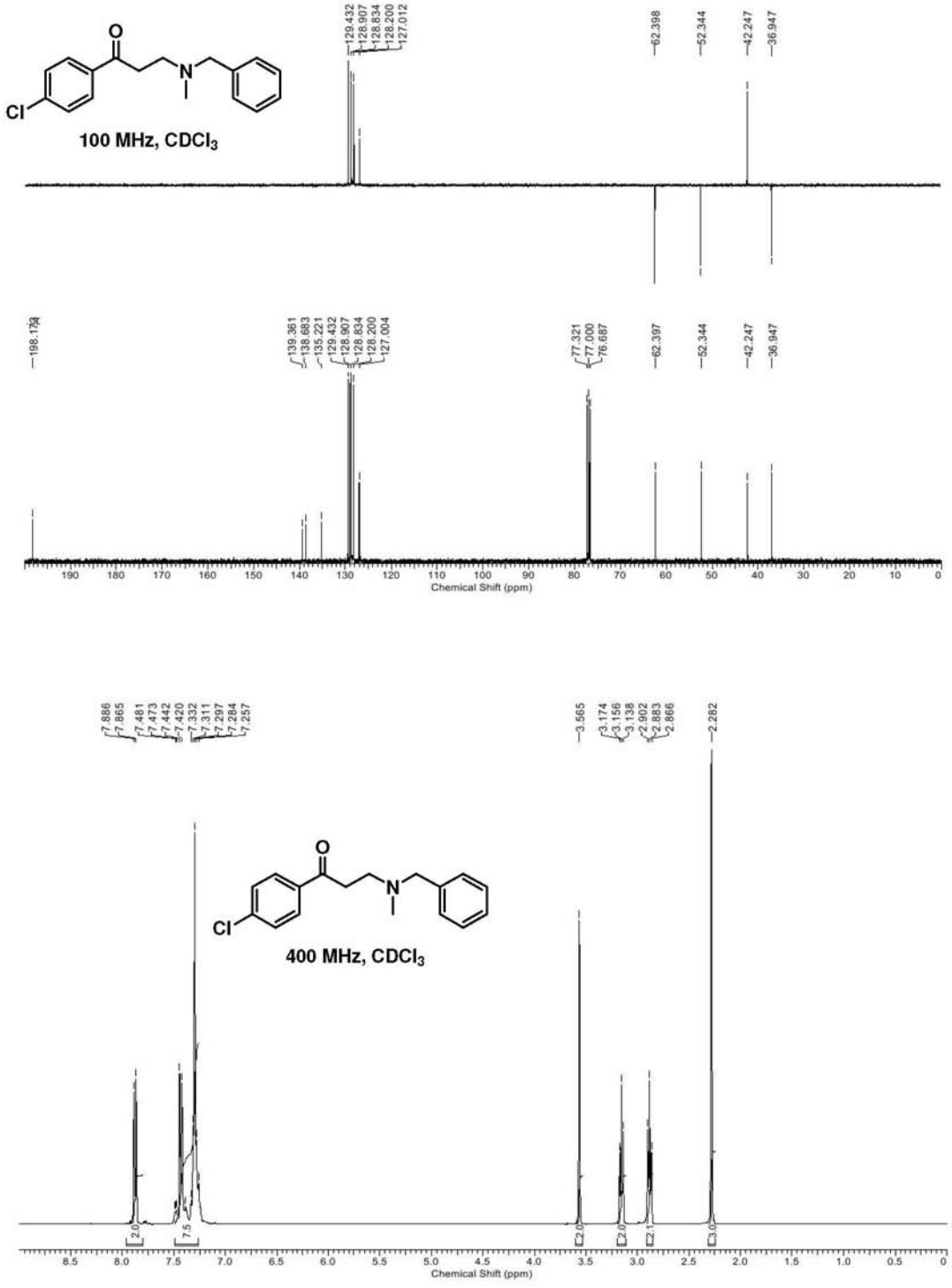
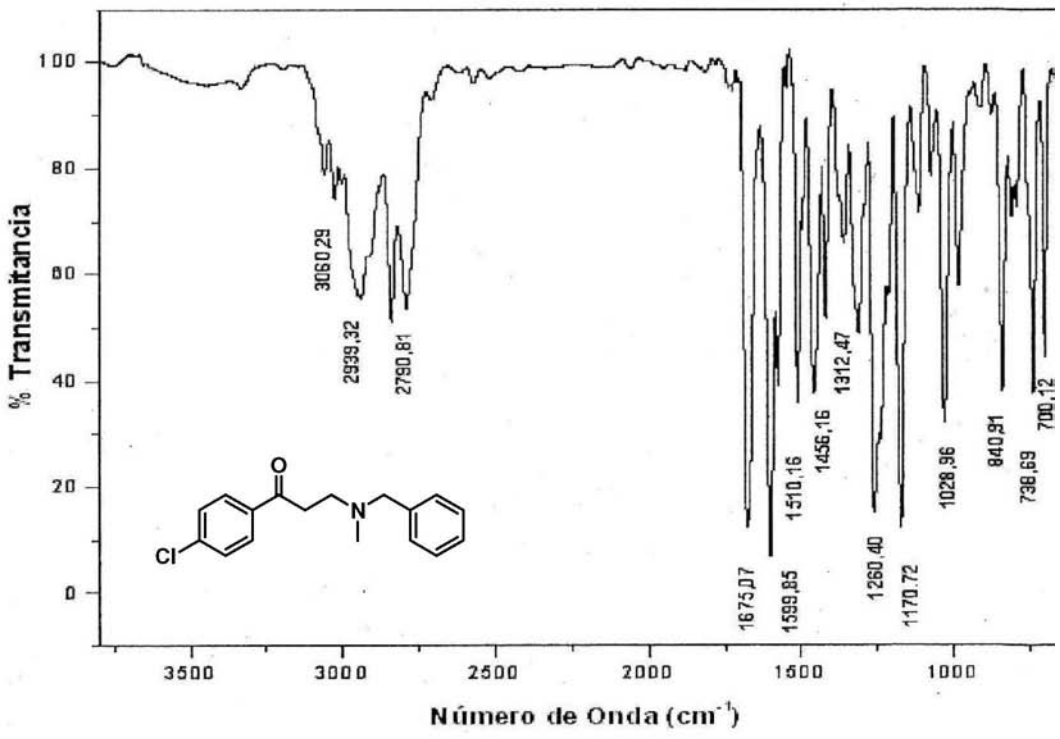



**Figure S3.** $^{1}H$ and $^{13}C$ spectra for compound **10b**.



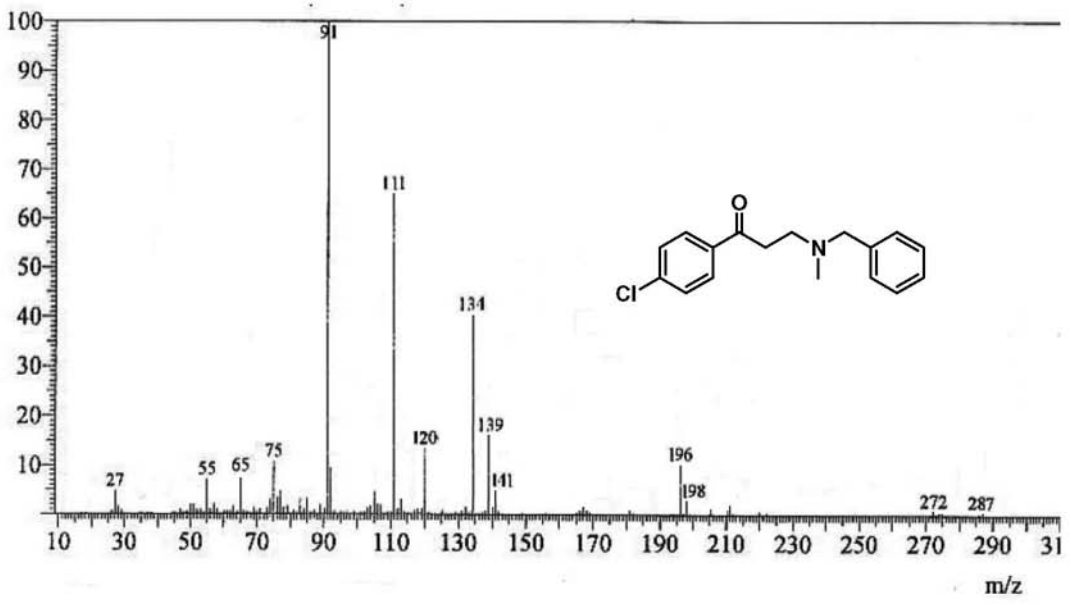




**Figure S4.** IR and MS spectra for compound **10b**.

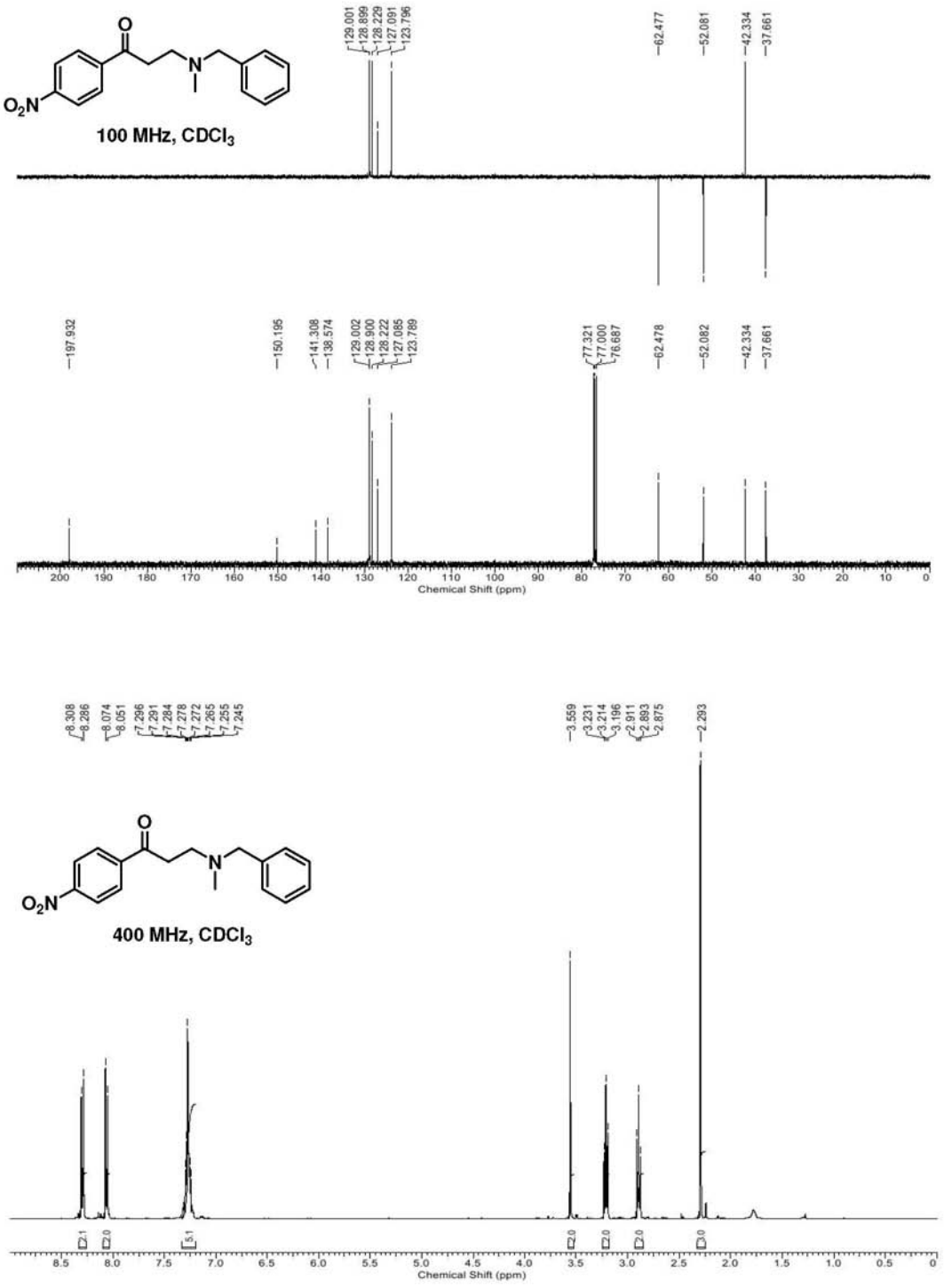
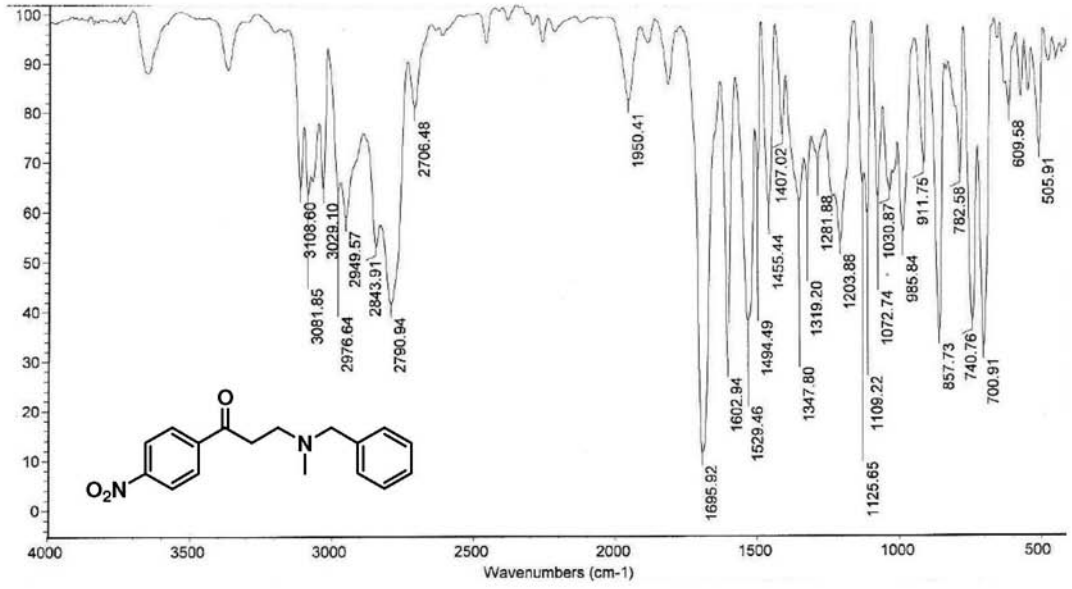



**Figure S5.** [1]H and [13]C spectra for compound **10c**.



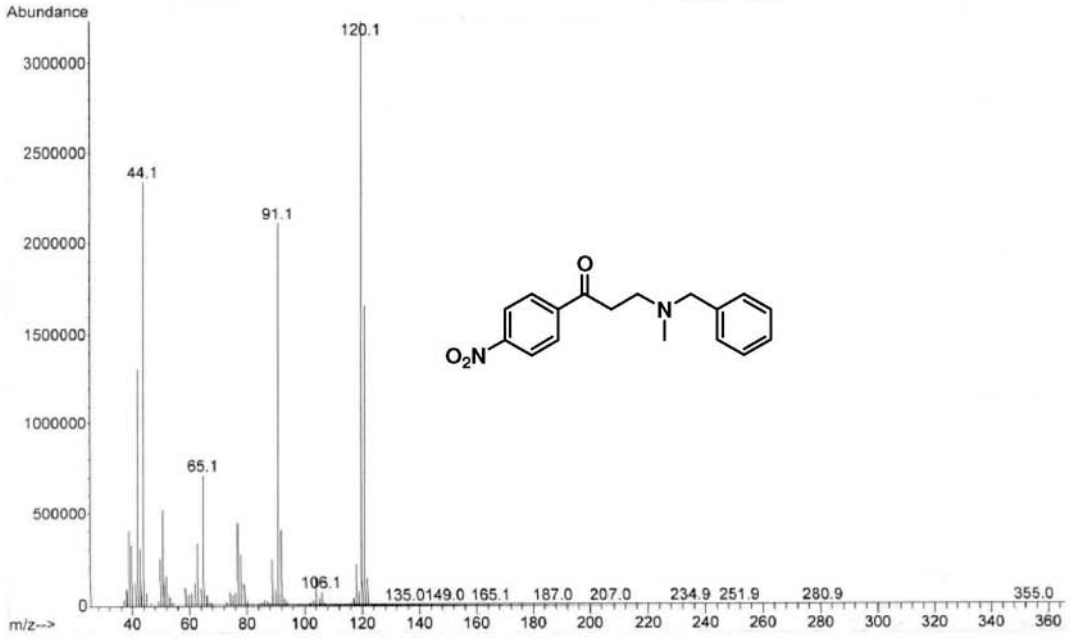




**Figure S6.** IR and MS spectra for compound **10c**.

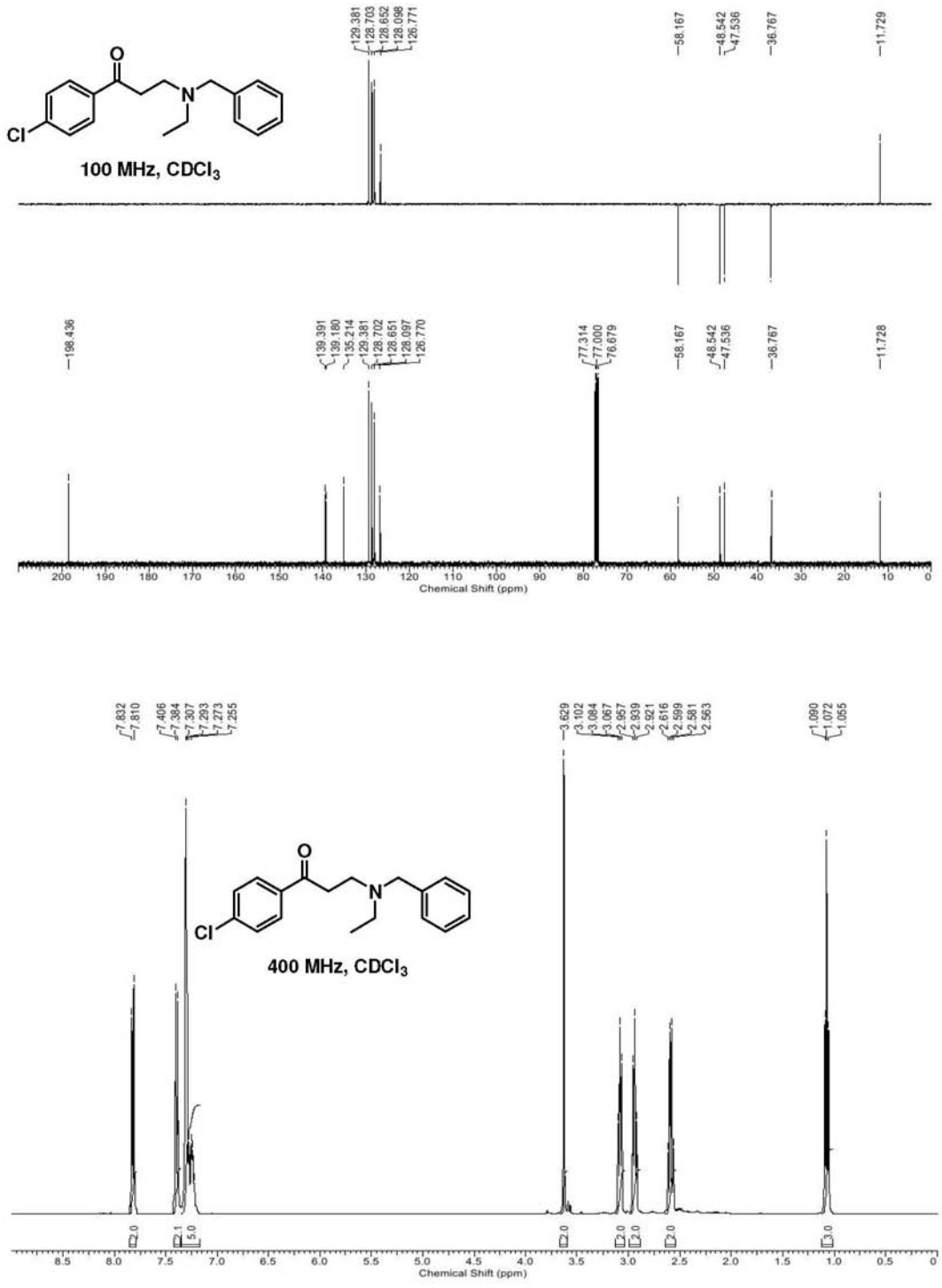



**Figure S7.** $^{1}H$ and $^{13}C$ spectra for compound **10d**.

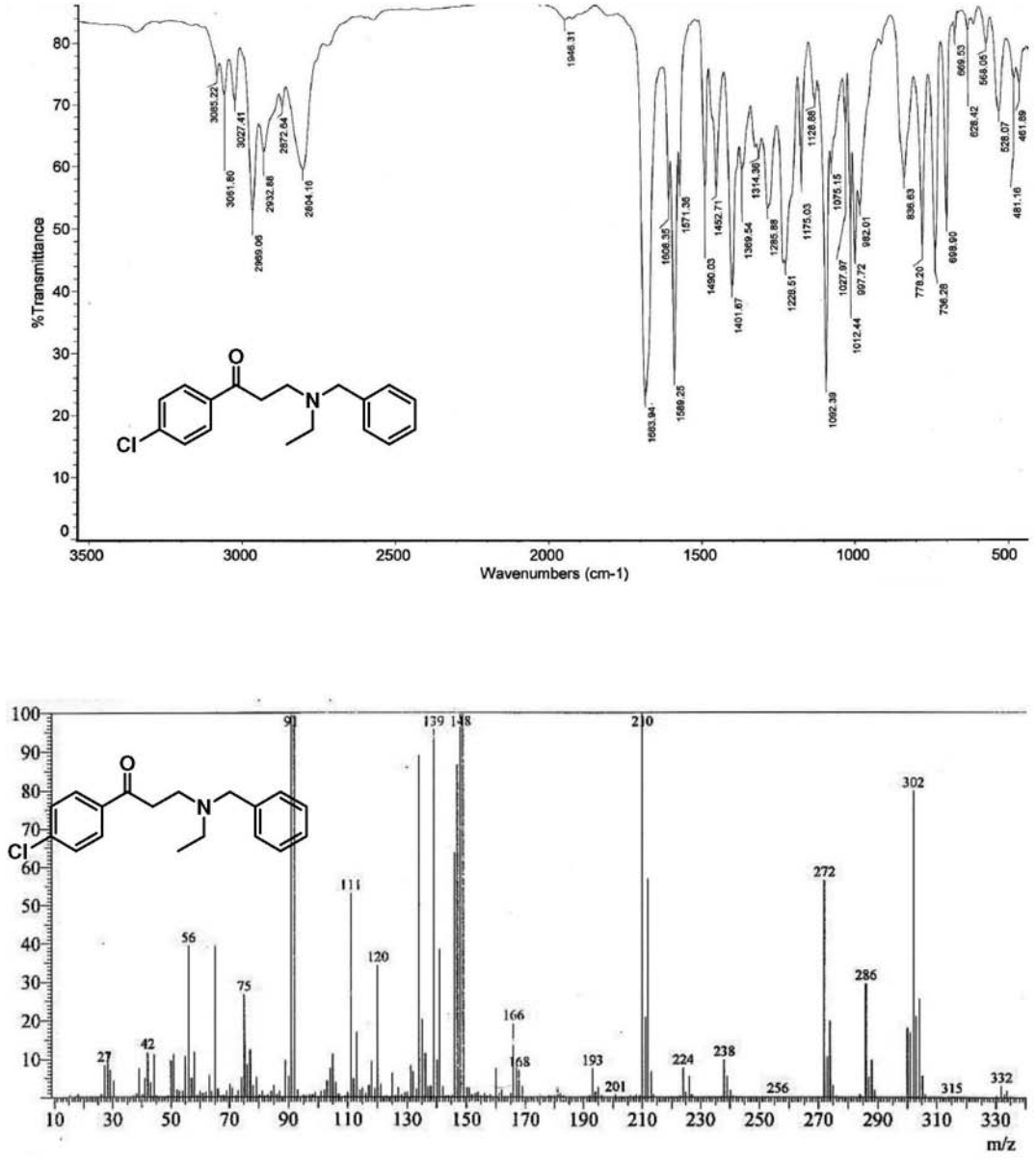



**Figure S8.** IR and MS spectra for compound **10d**.

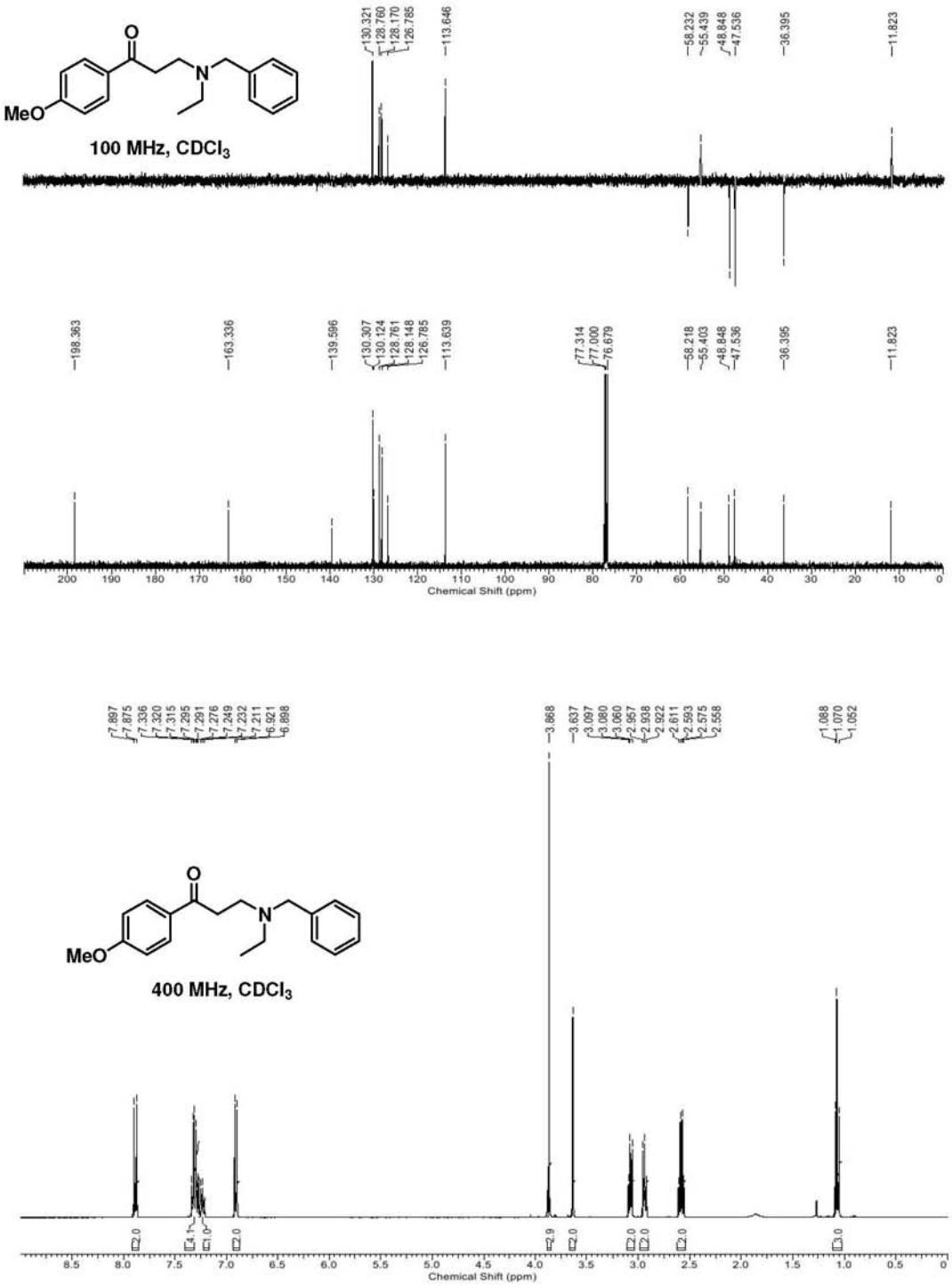
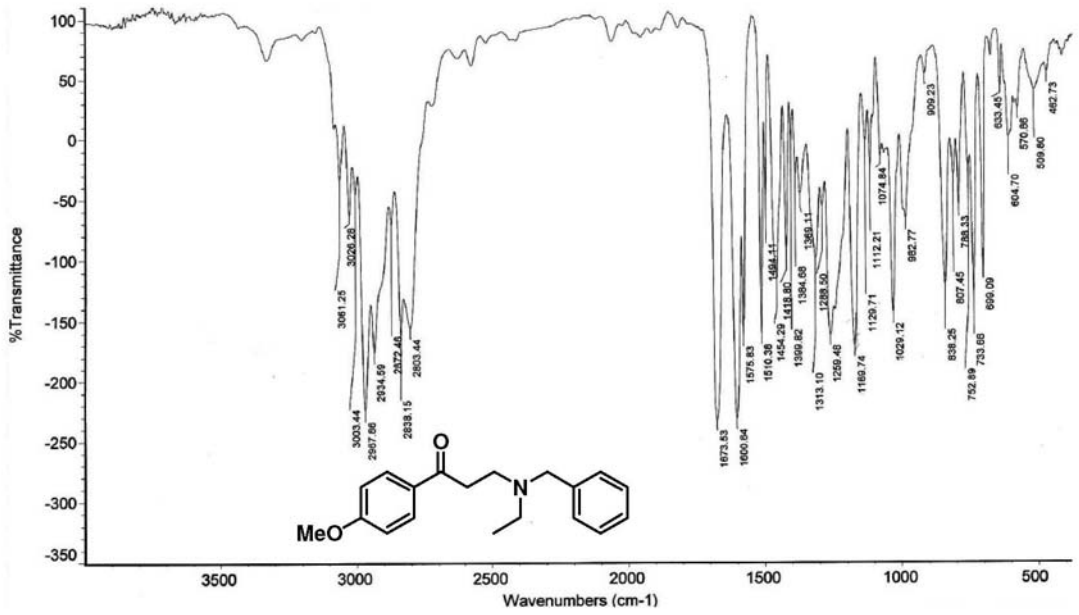



**Figure S9.** [1]H and [13]C spectra for compound **10e**.



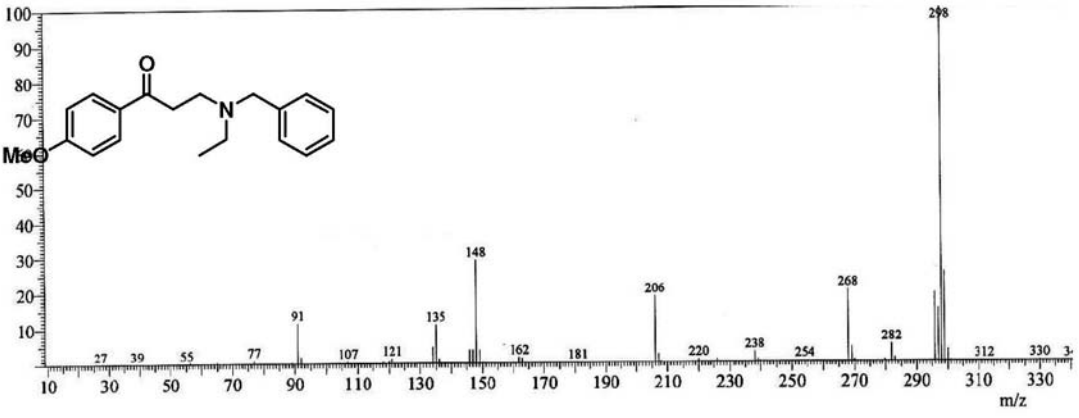




**Figure S10.** IR and MS spectra for compound **10e**.

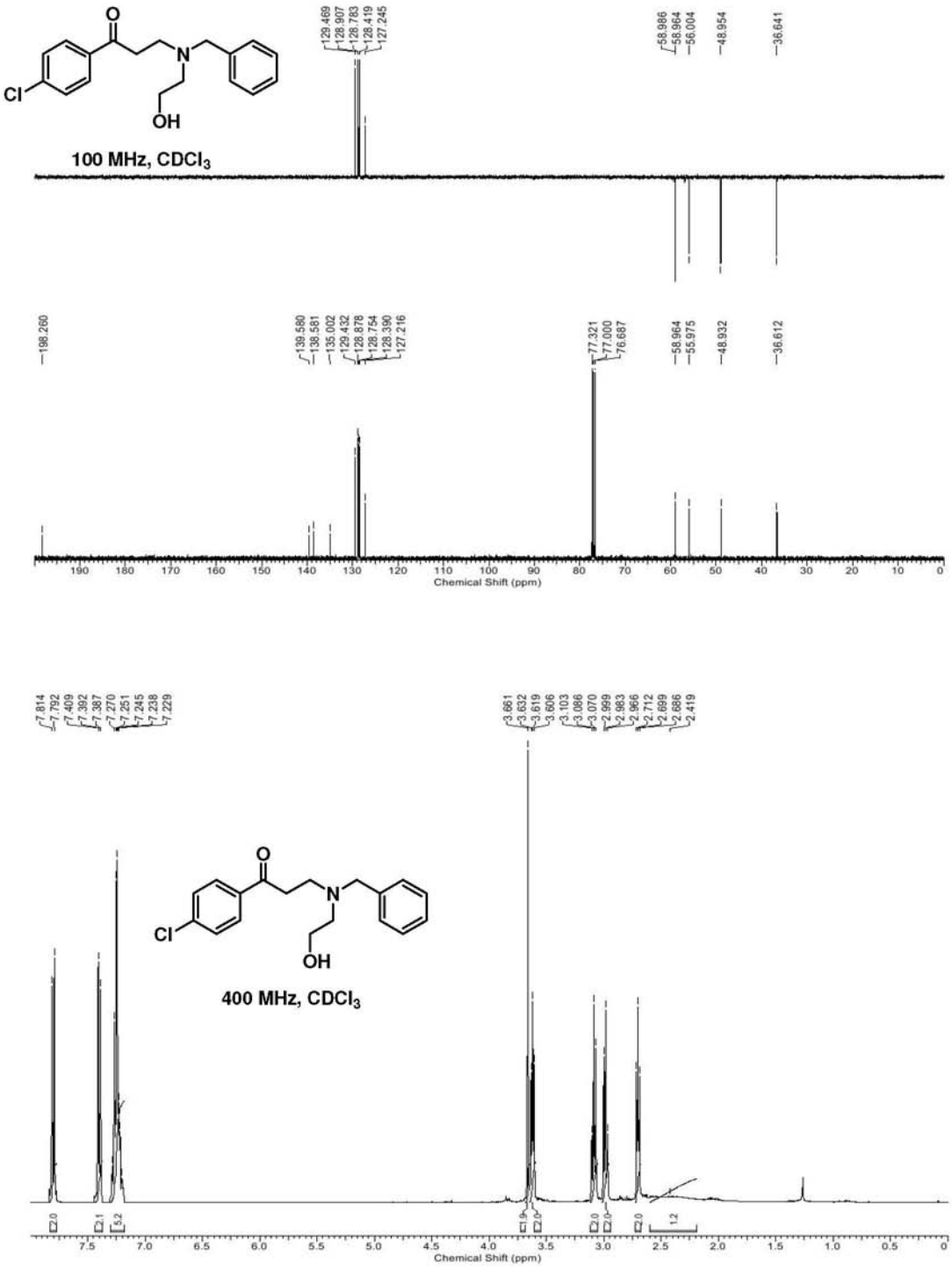
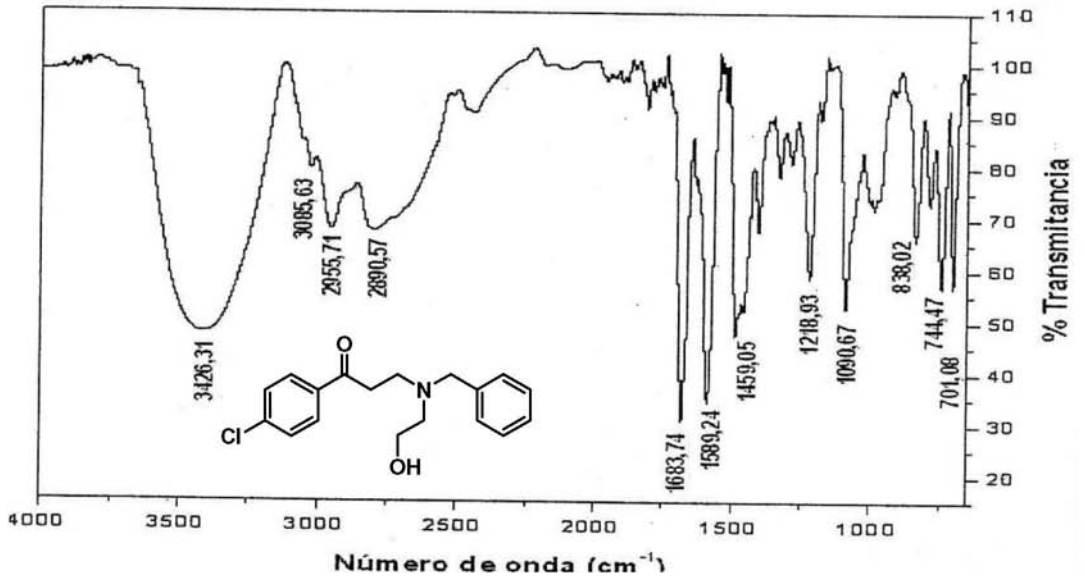



**Figure S11.** $^{1}H$ and $^{13}C$ spectra for compound **10f**.



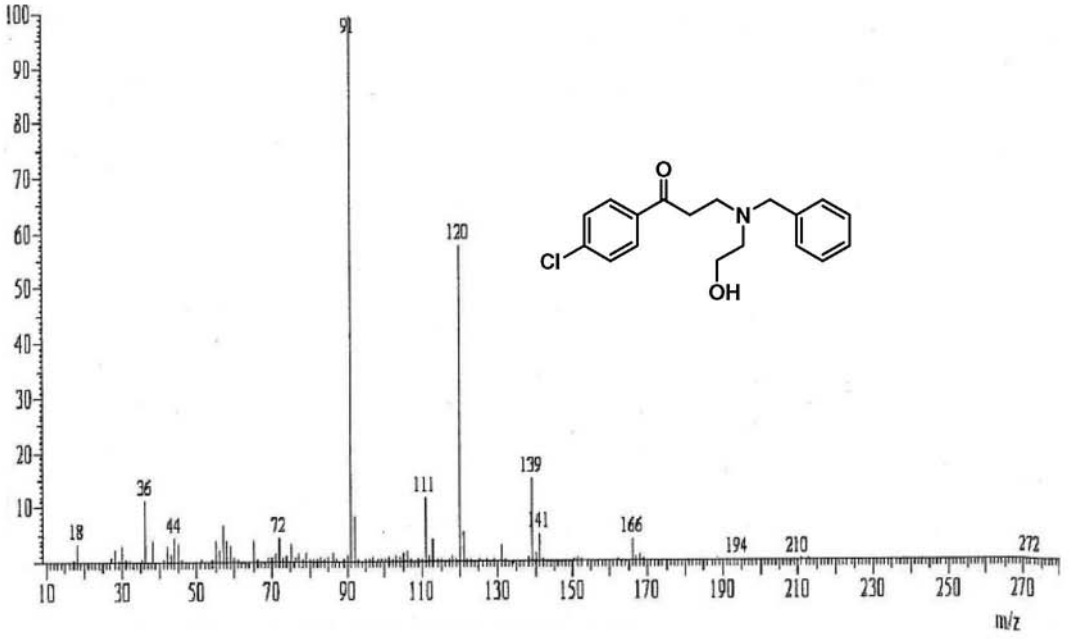




**Figure S12.** IR and MS spectra for compound **10f**.

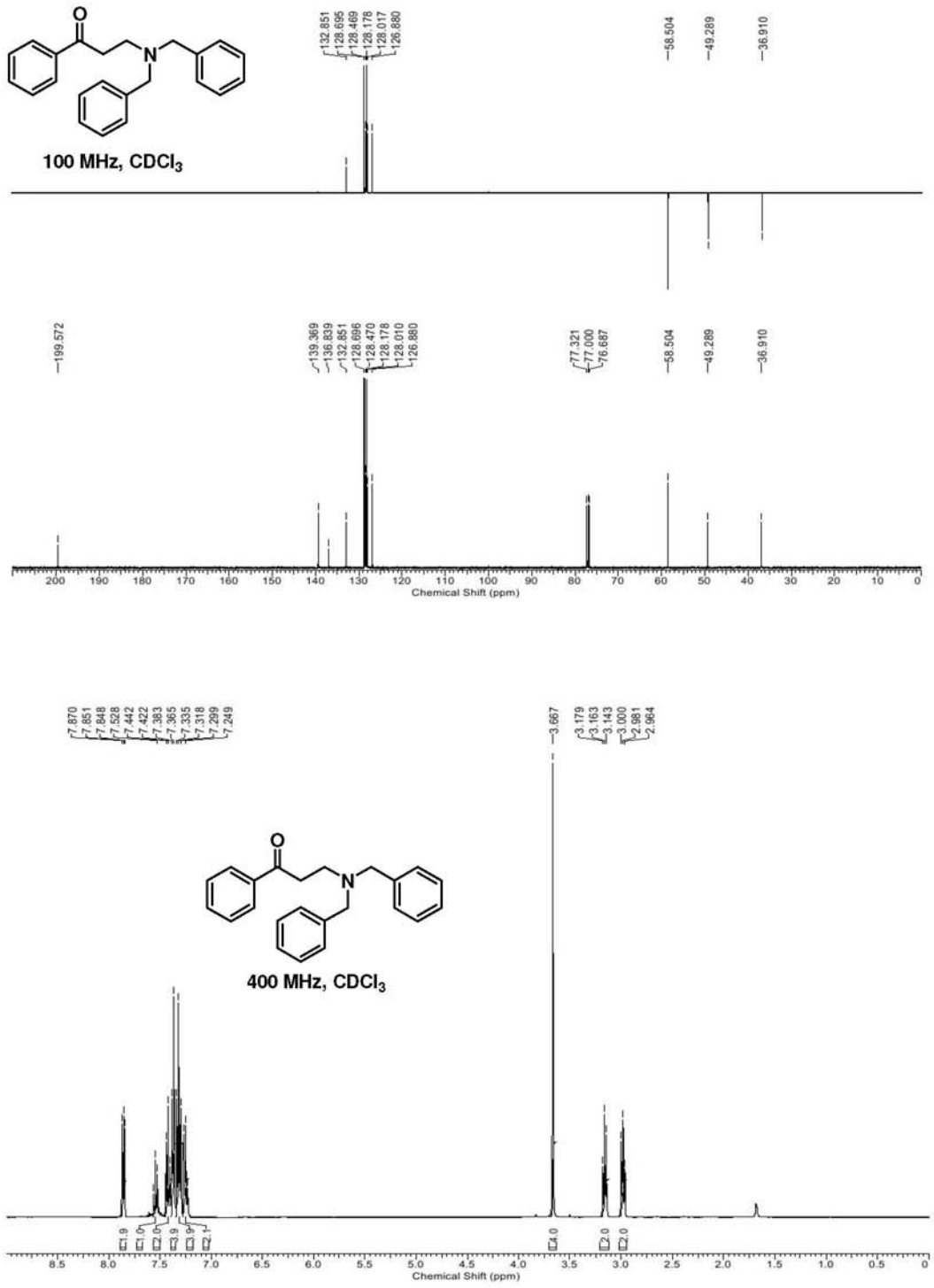
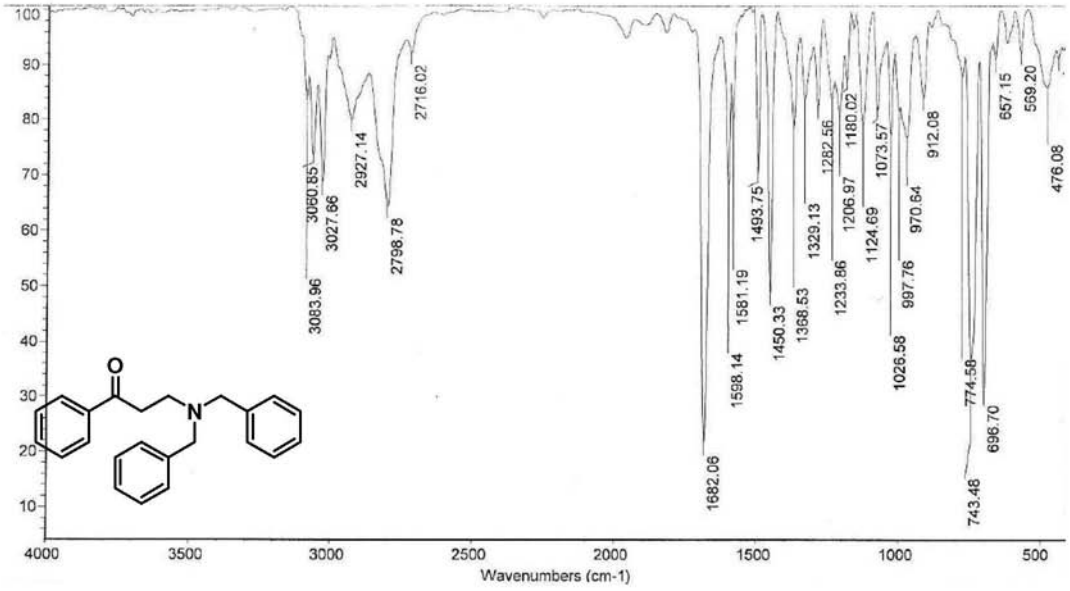



**Figure S13.** $^{1}H$ and $^{13}C$ spectra for compound **10g**.



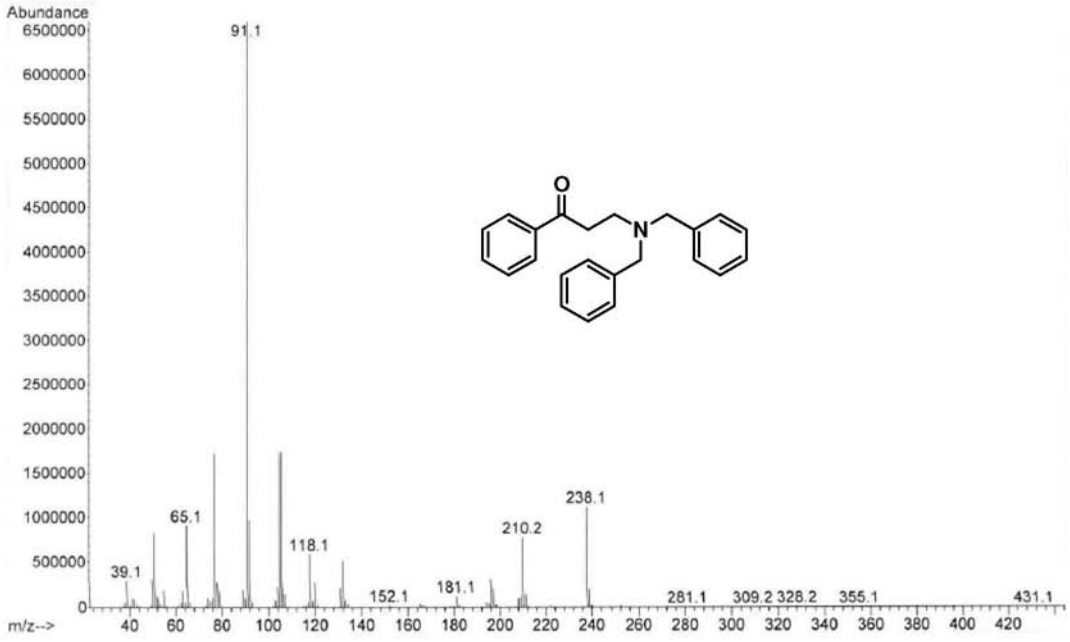




**Figure S14.** IR and MS spectra for compound **10g**.

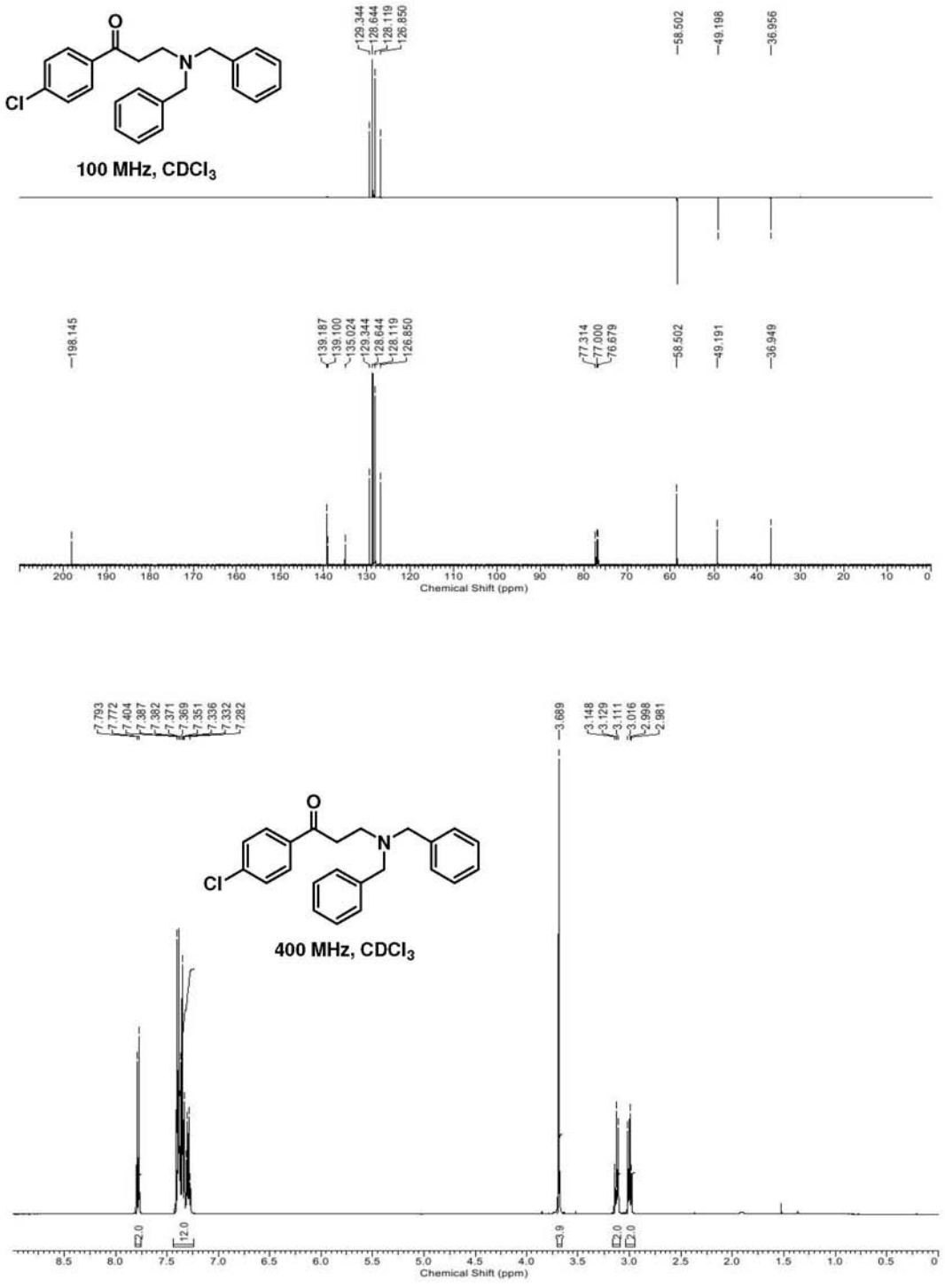



**Figure S15.** $^{1}H$ and $^{13}C$ spectra for compound **10h**.

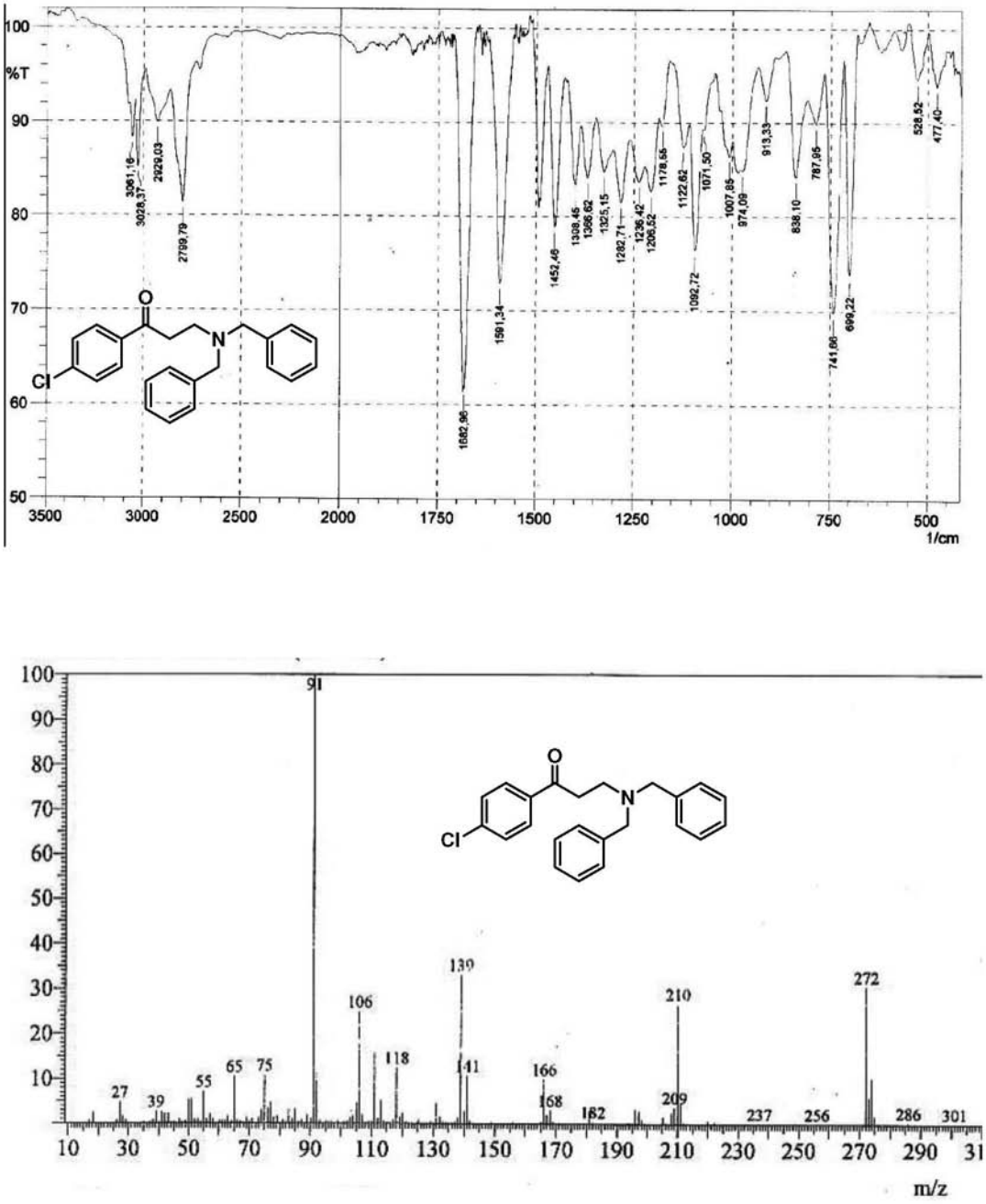



**Figure S16.** IR and MS spectra for compound **10h**.

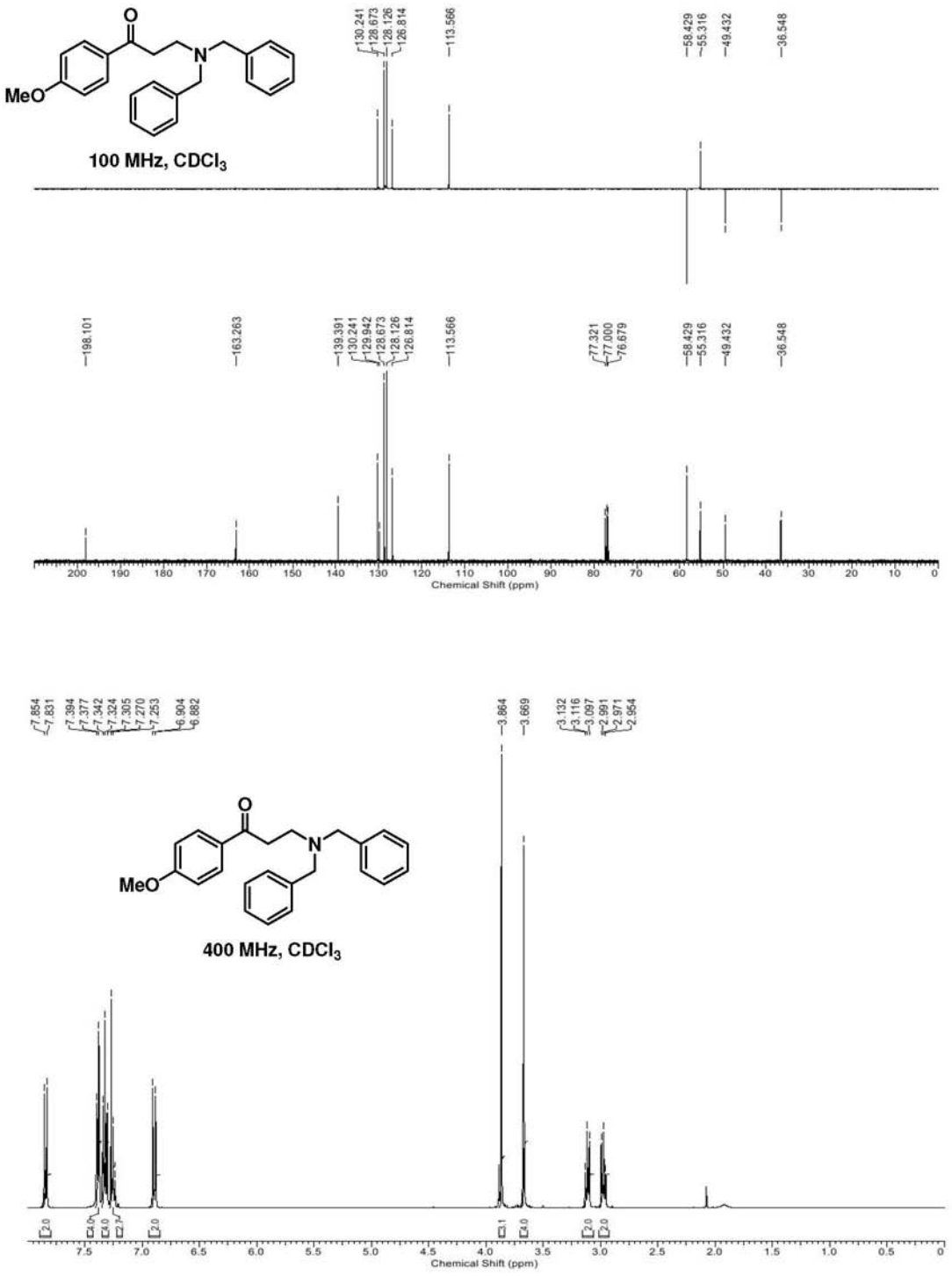



**Figure S17.** $^{1}H$ and $^{13}C$ spectra for compound **10i**.

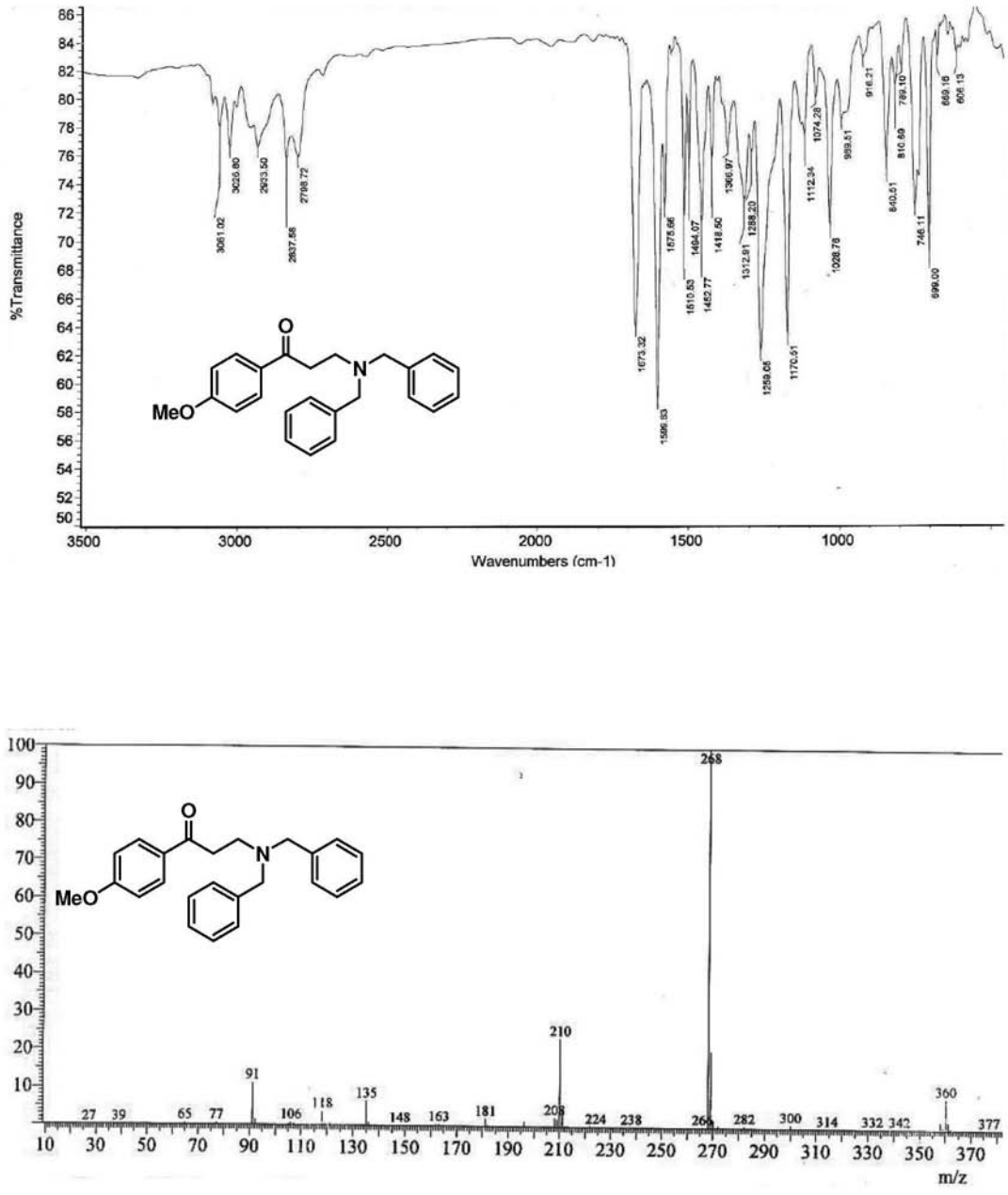



**Figure S18.** IR and MS spectra for compound **10i**.

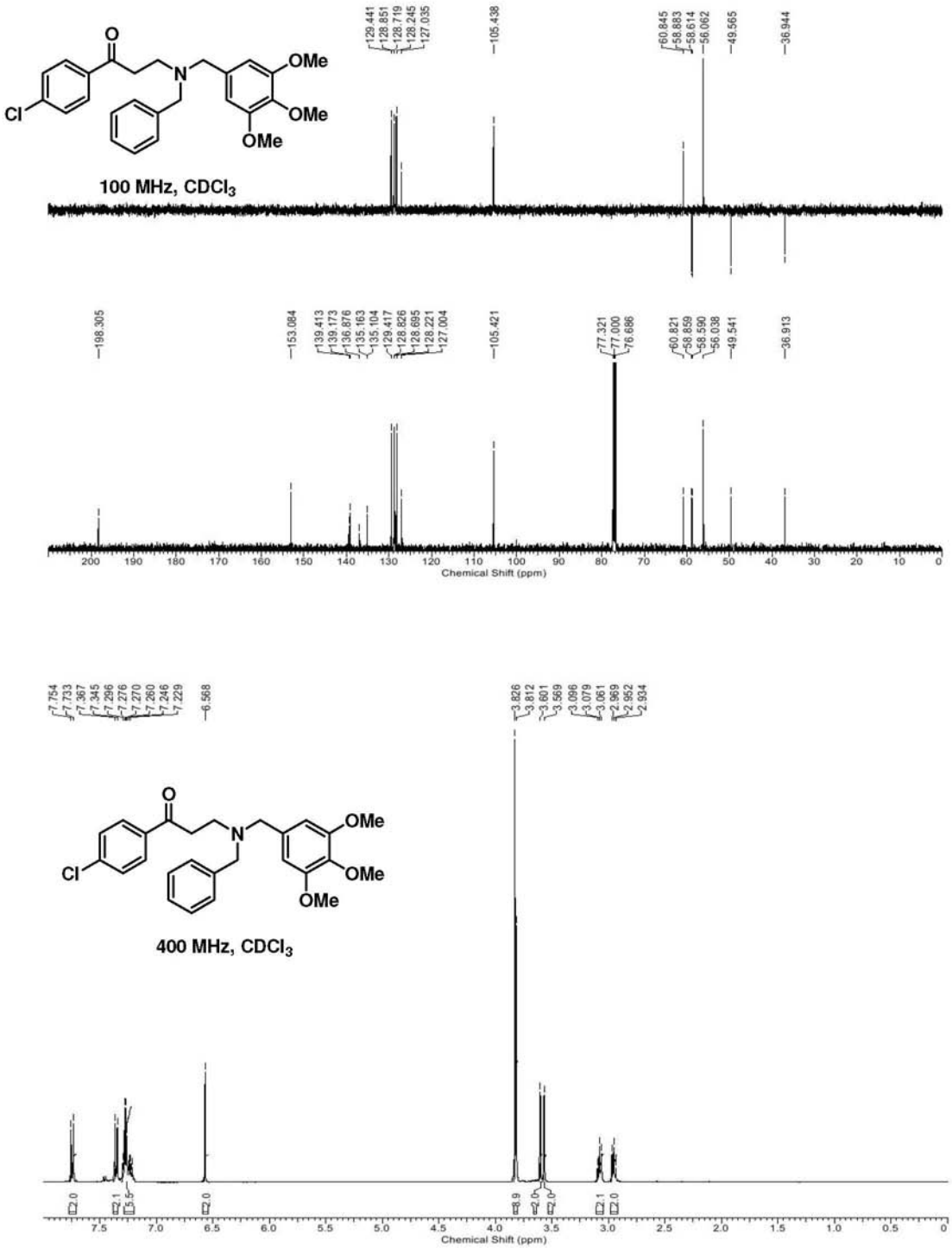
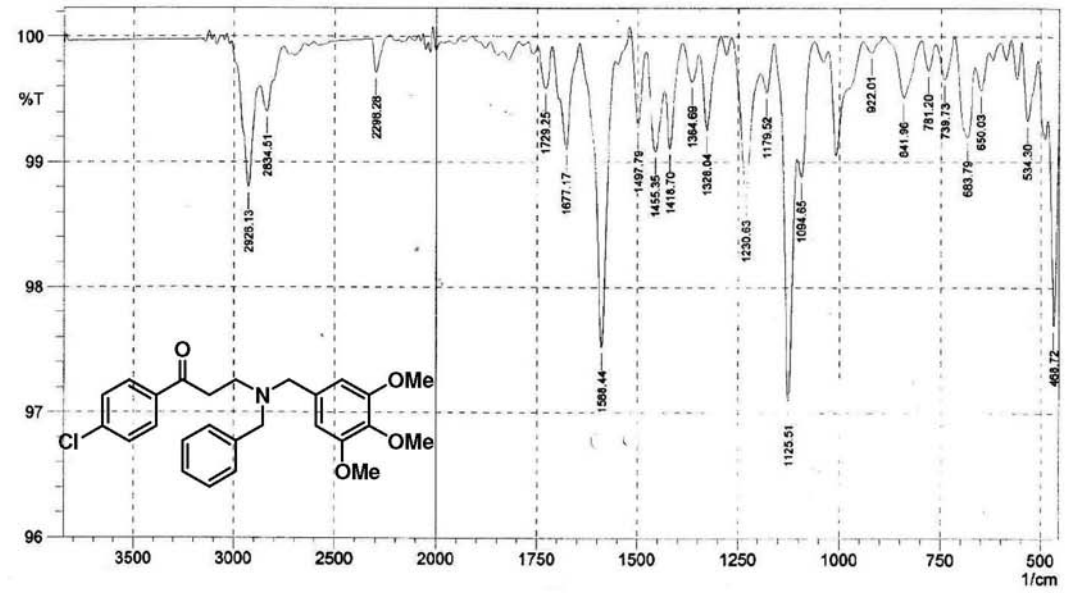



**Figure S19.** $^{1}H$ and $^{13}C$ spectra for compound **10j**.



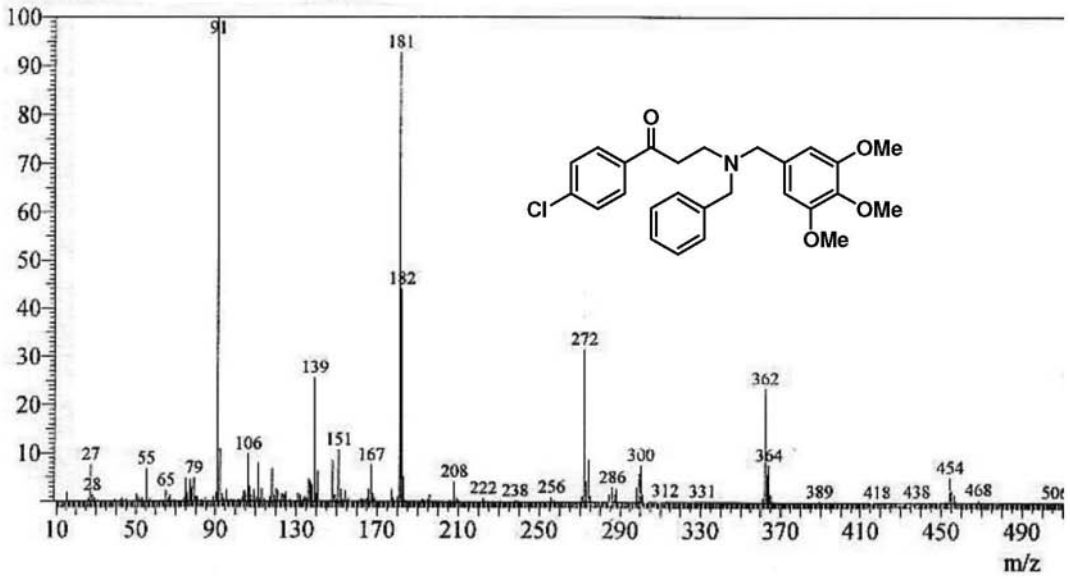




**Figure S20.** IR and MS spectra for compound **10j**.

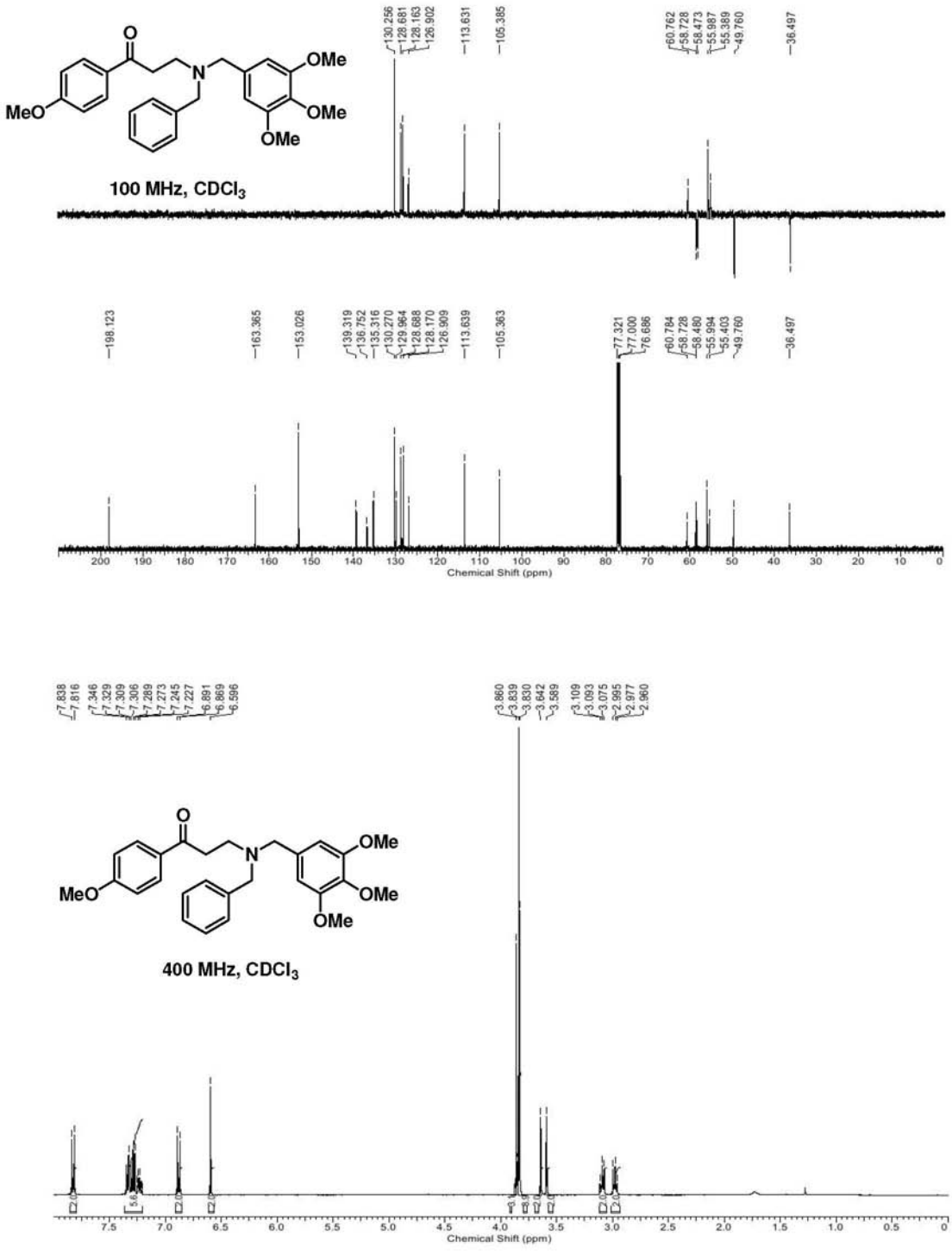



**Figure S21.** $^{1}H$ and $^{13}C$ spectra for compound **10k**.

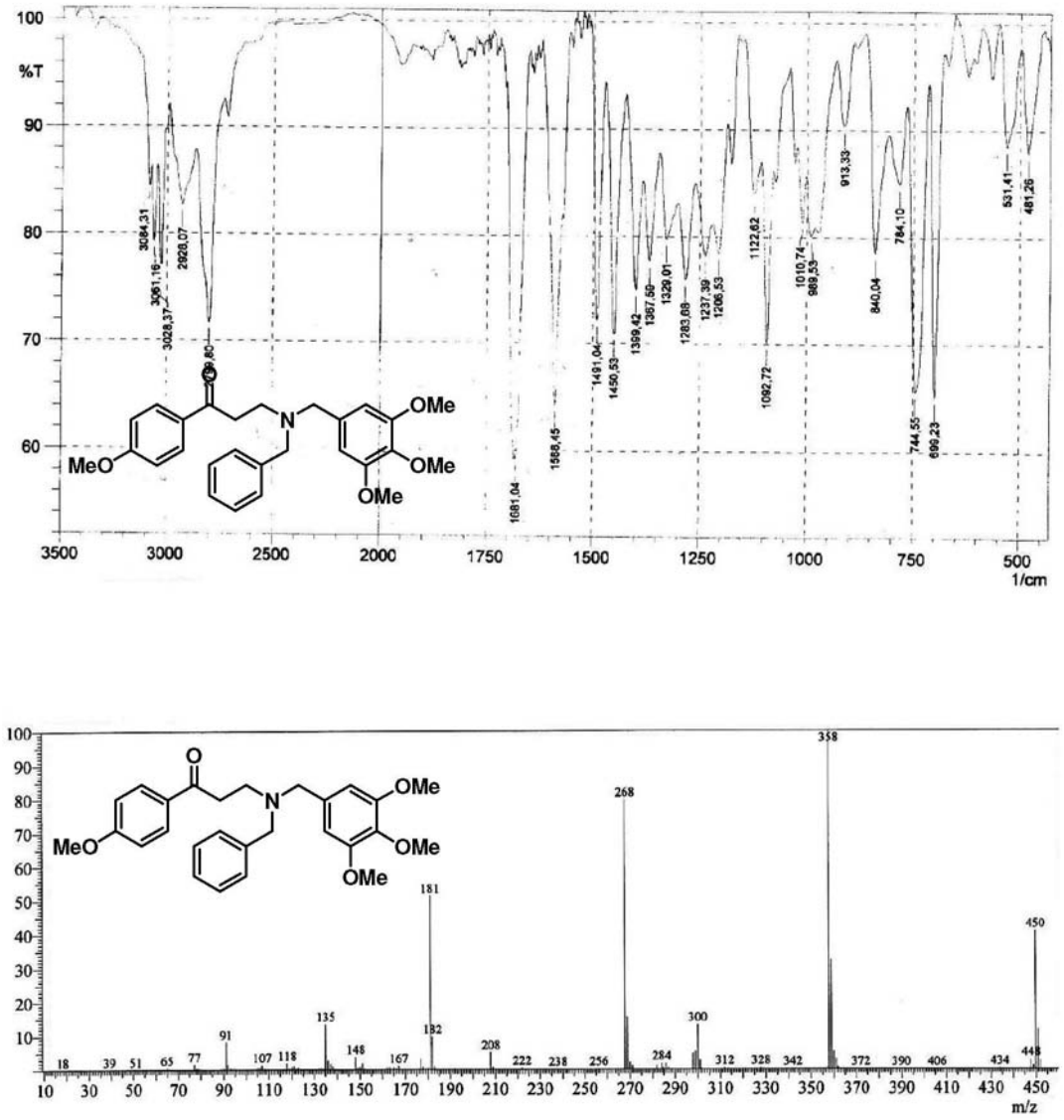






**Figure S22.** IR and MS spectra for compound **10k**.

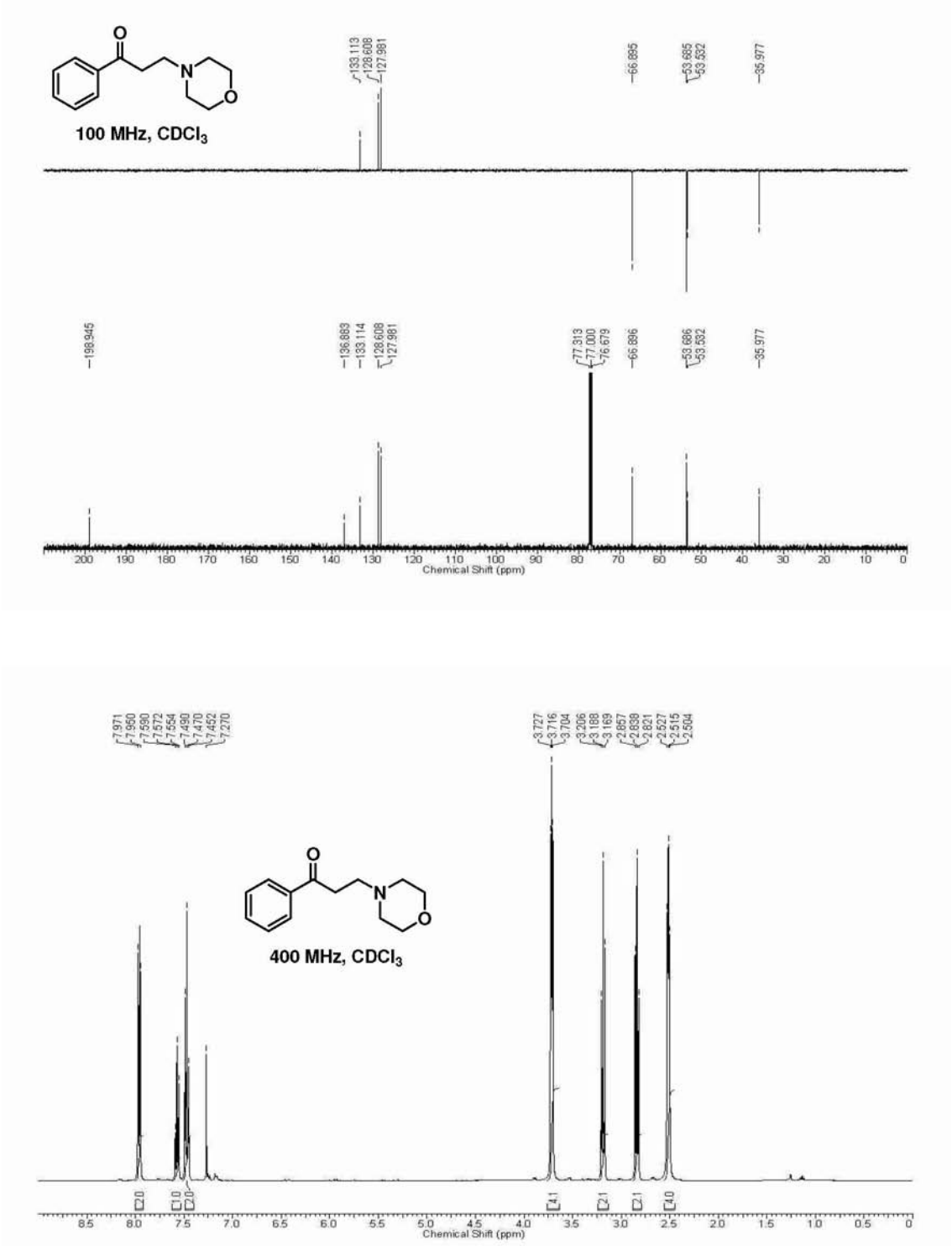
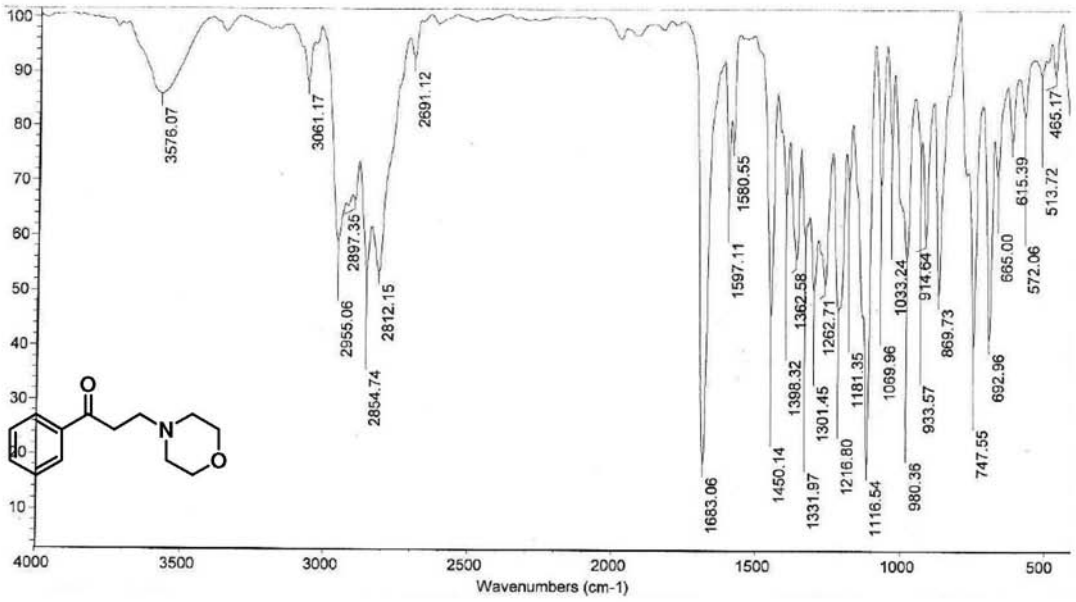



**Figure S23.** $^{1}H$ and $^{13}C$ spectra for compound **10l**.



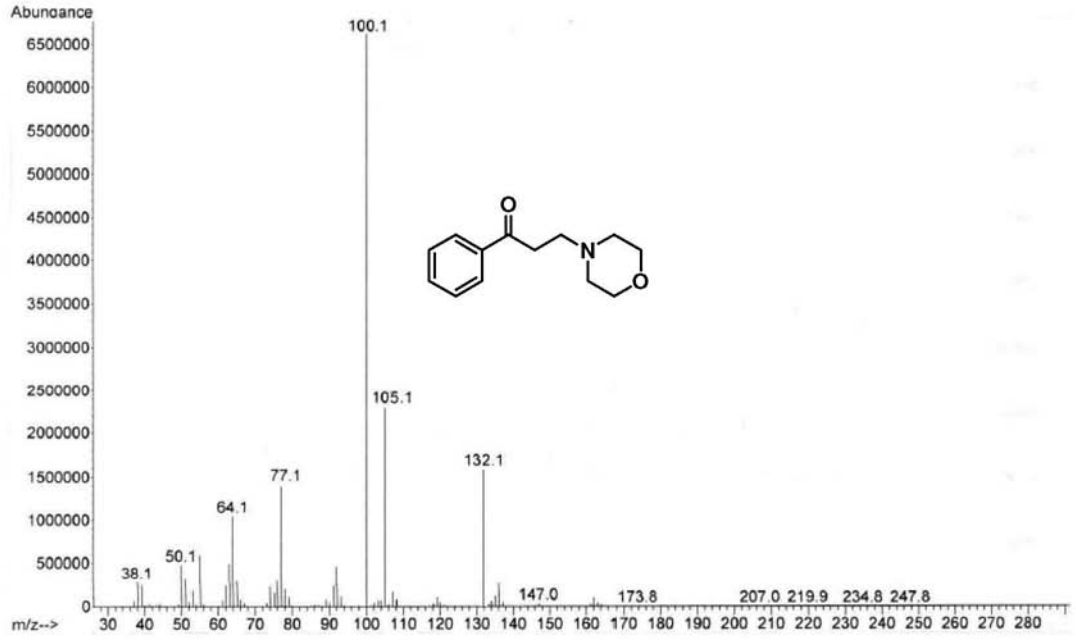




**Figure S24.** IR and MS spectra for compound **10l**.

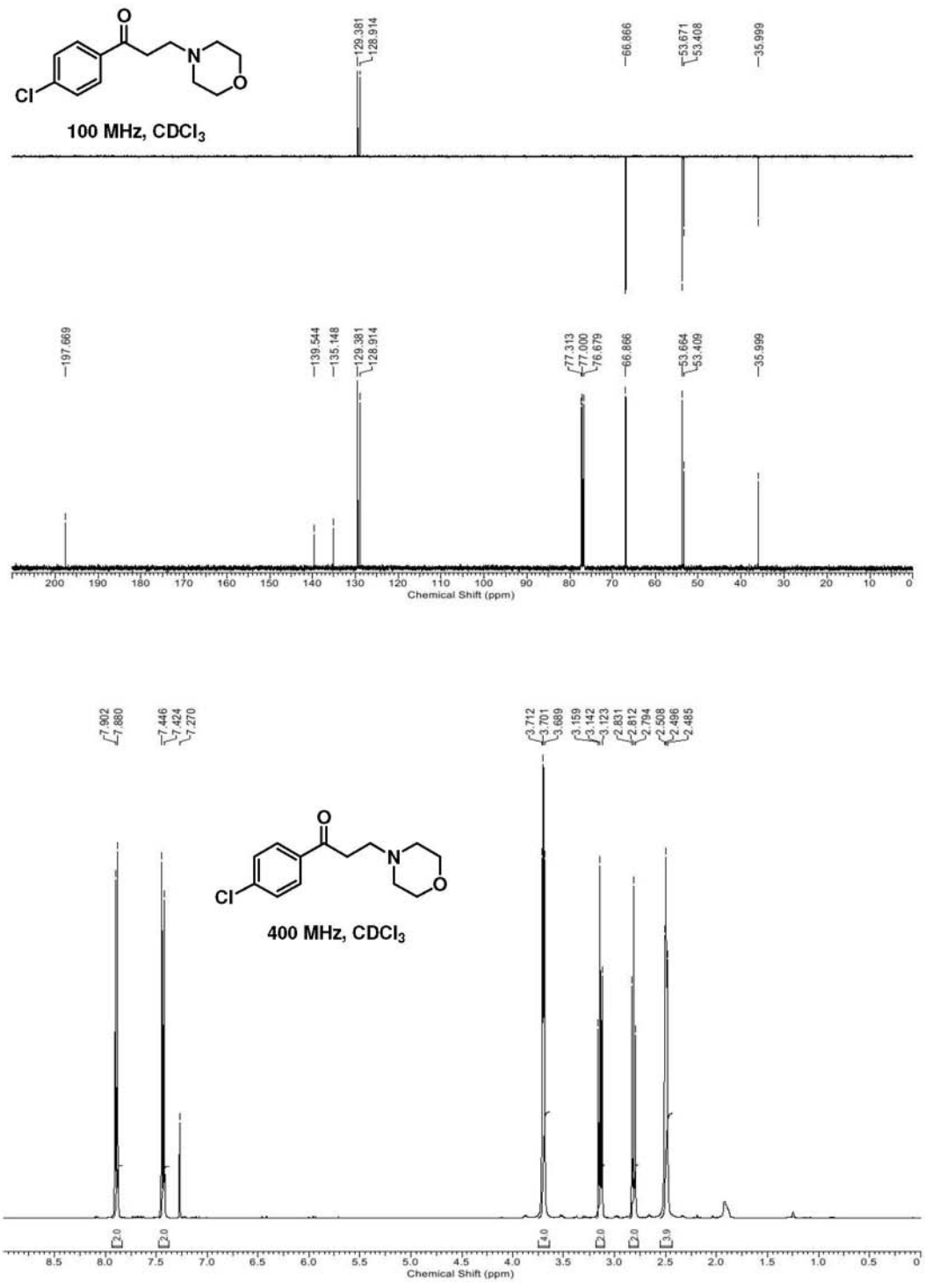
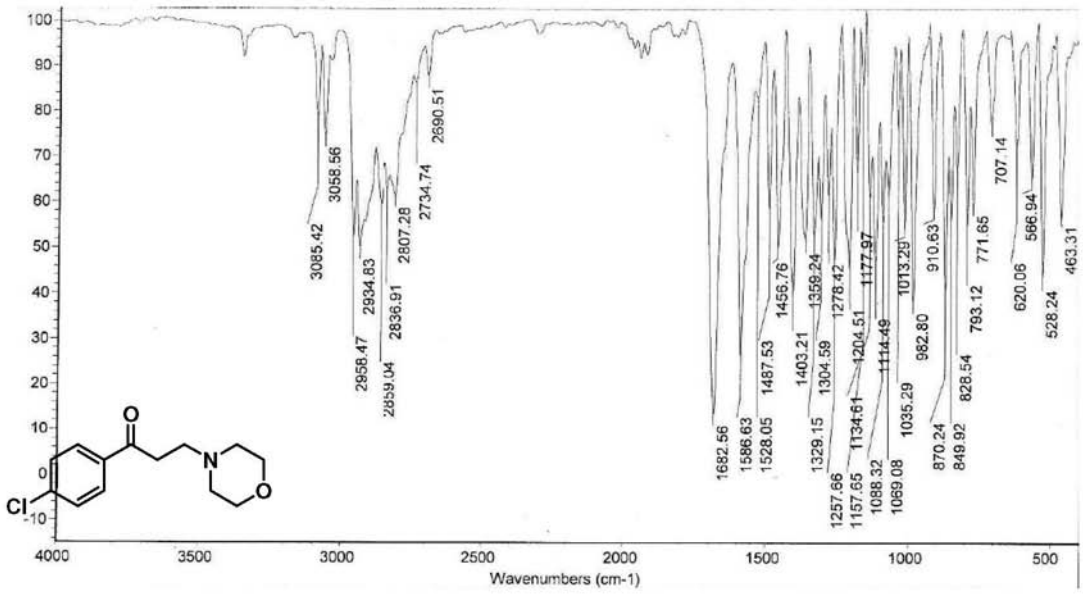



**Figure S25.** $^{1}H$ and $^{13}C$ spectra for compound **10m**.



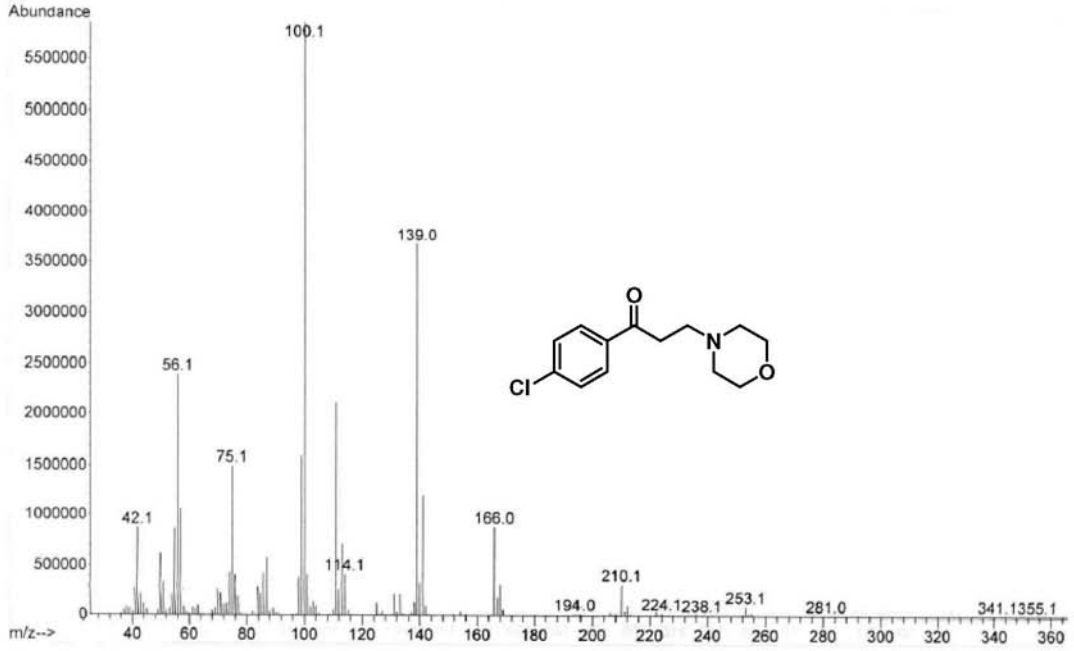




**Figure S26.** IR and MS spectra for compound **10m**.

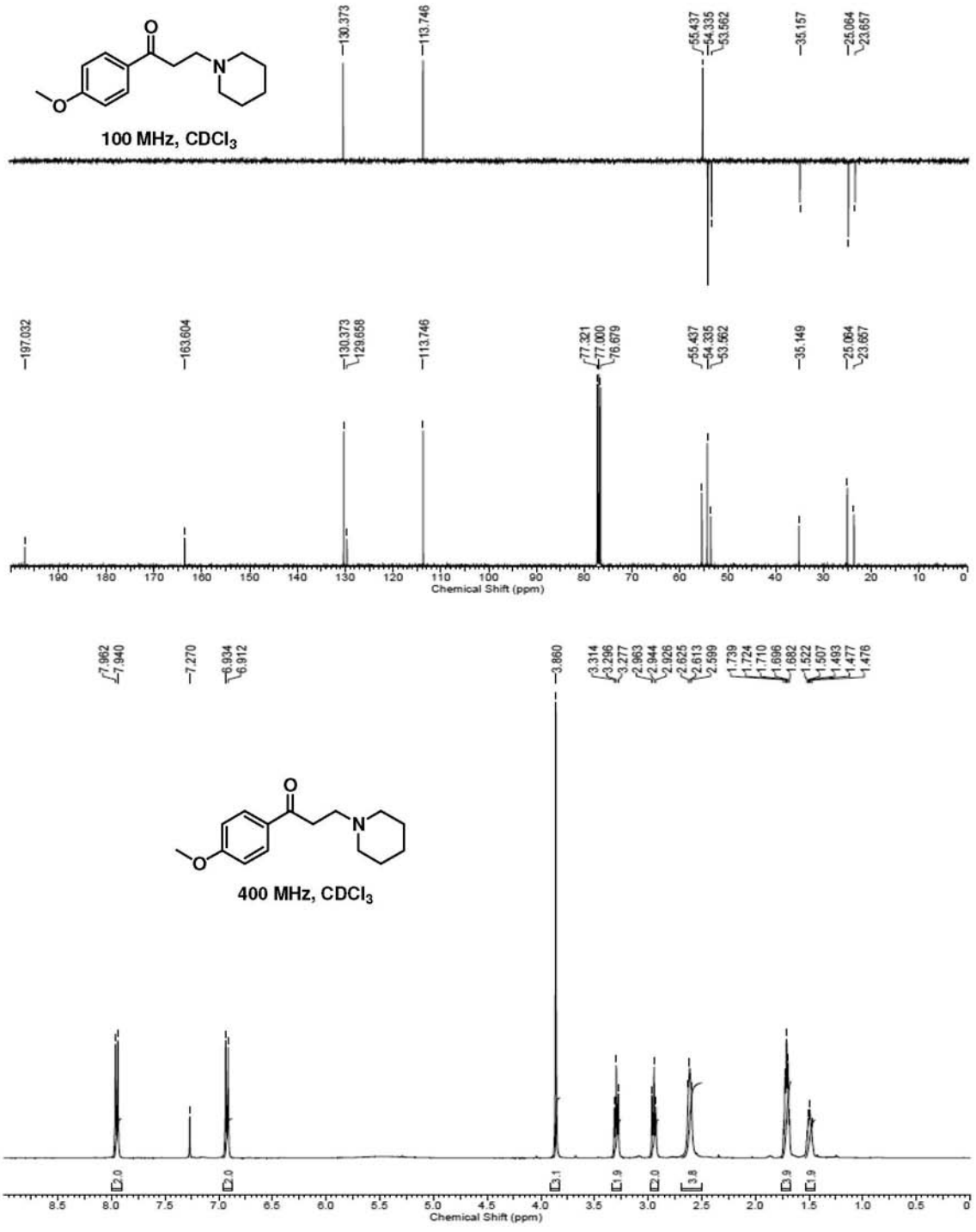
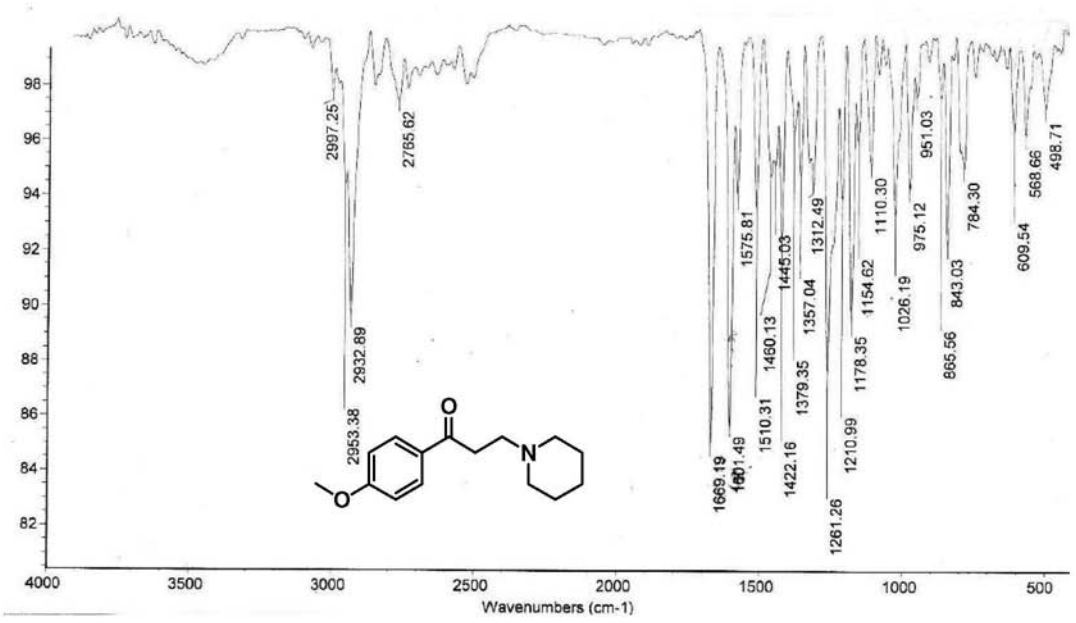



**Figure S27.** $^{1}H$ and $^{13}C$ spectra for compound **10n**.



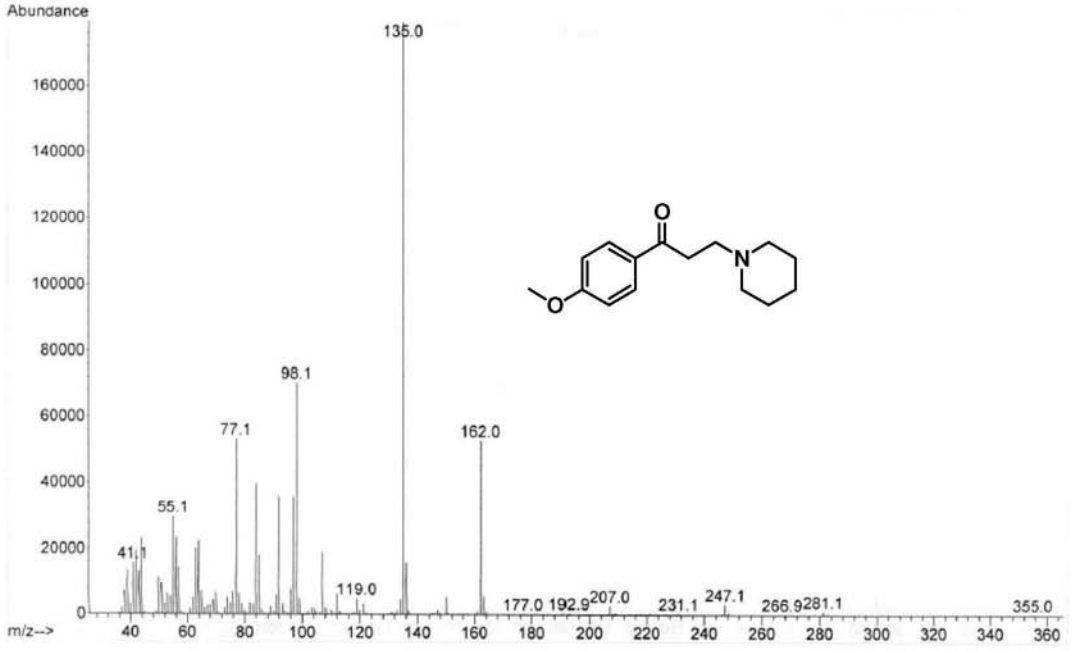




**Figure S28.** IR and MS spectra for compound **10n**.

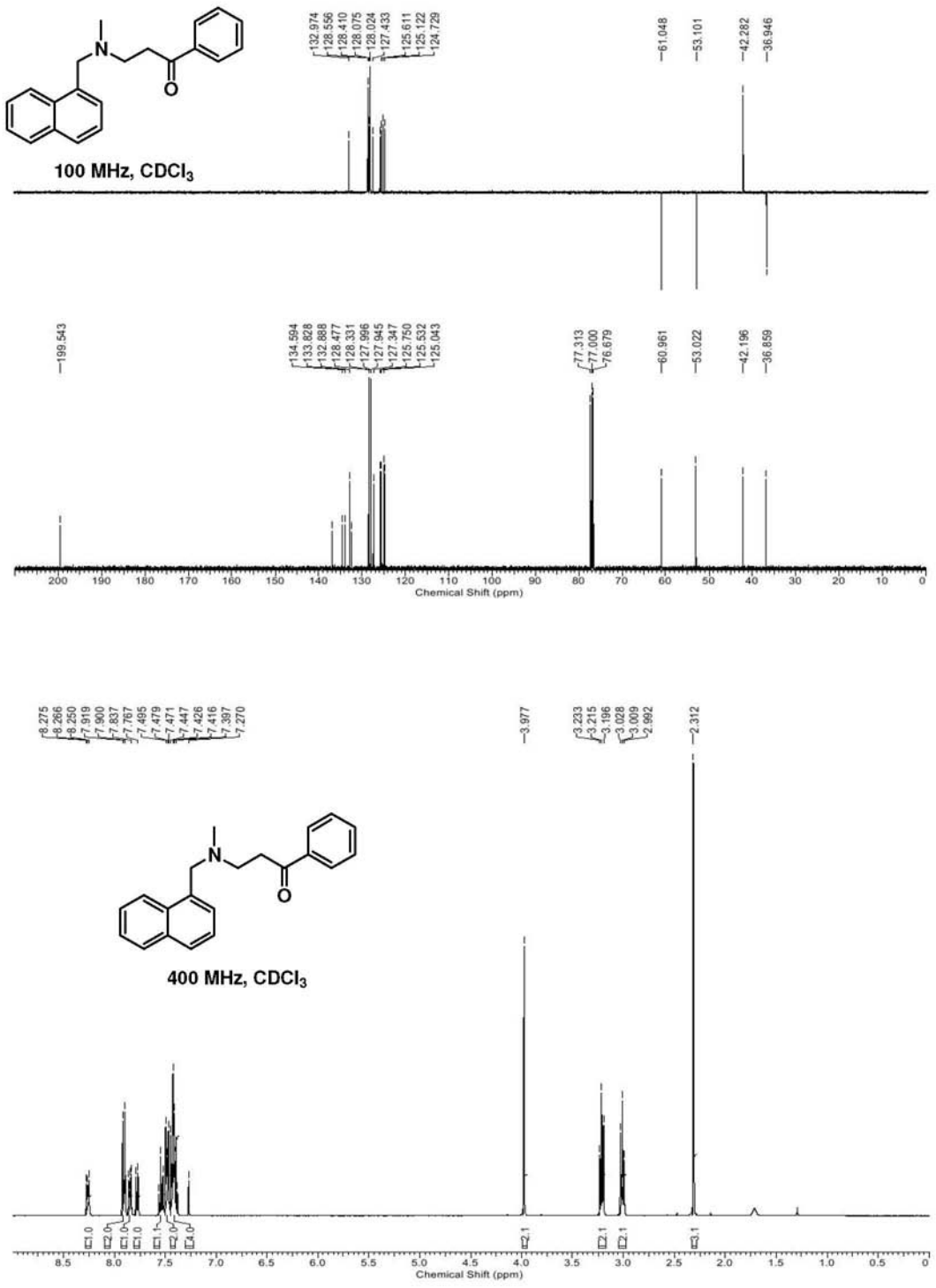
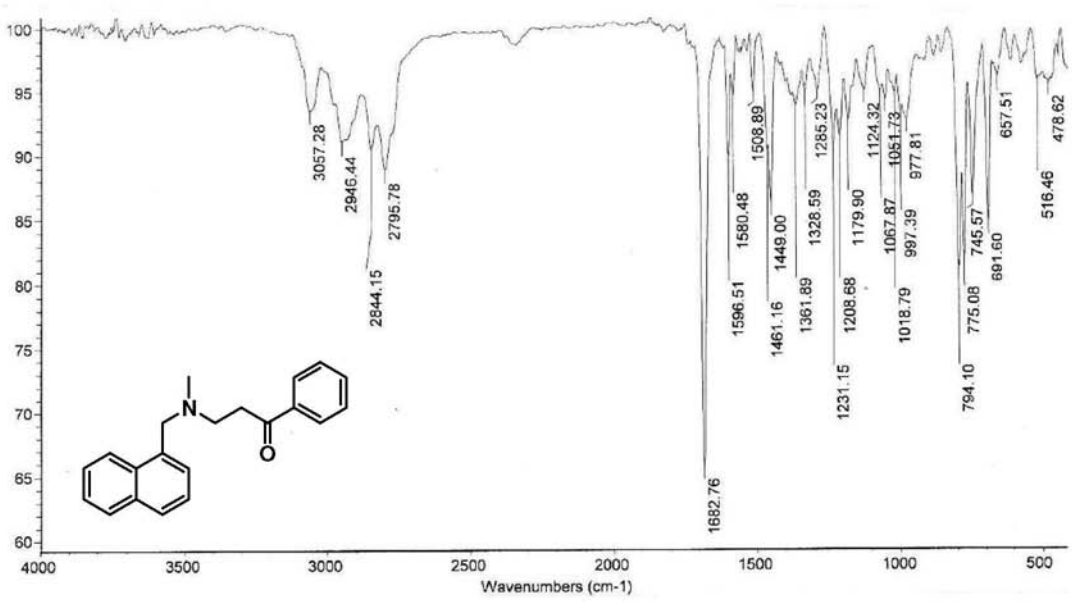



**Figure S29.** [1]H and [13]C spectra for compound **10o**.



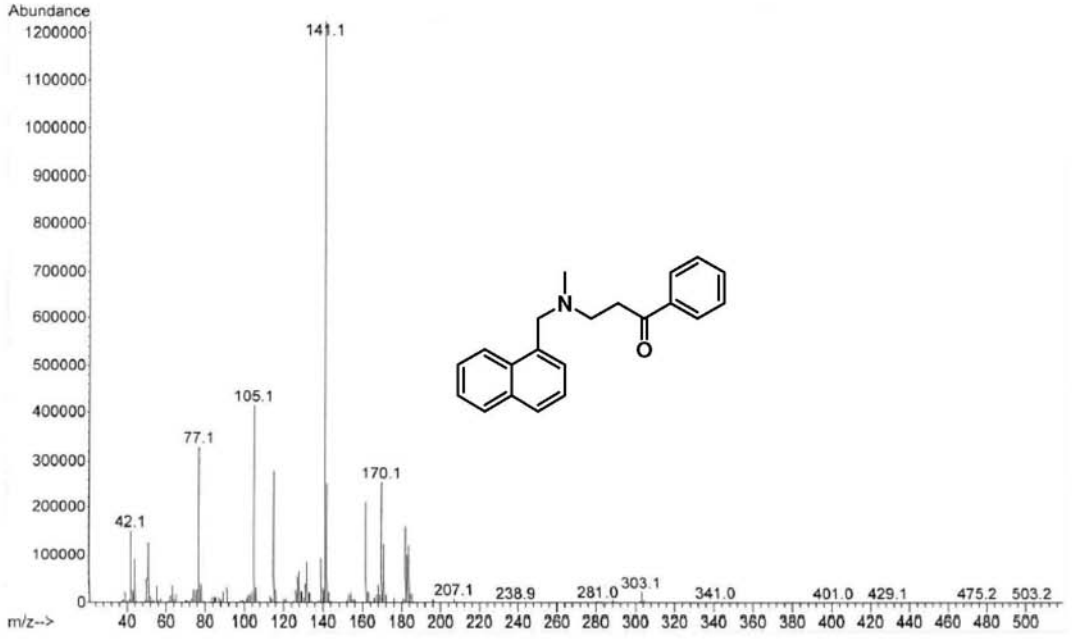




**Figure S30.** IR and MS spectra for compound **10o**.

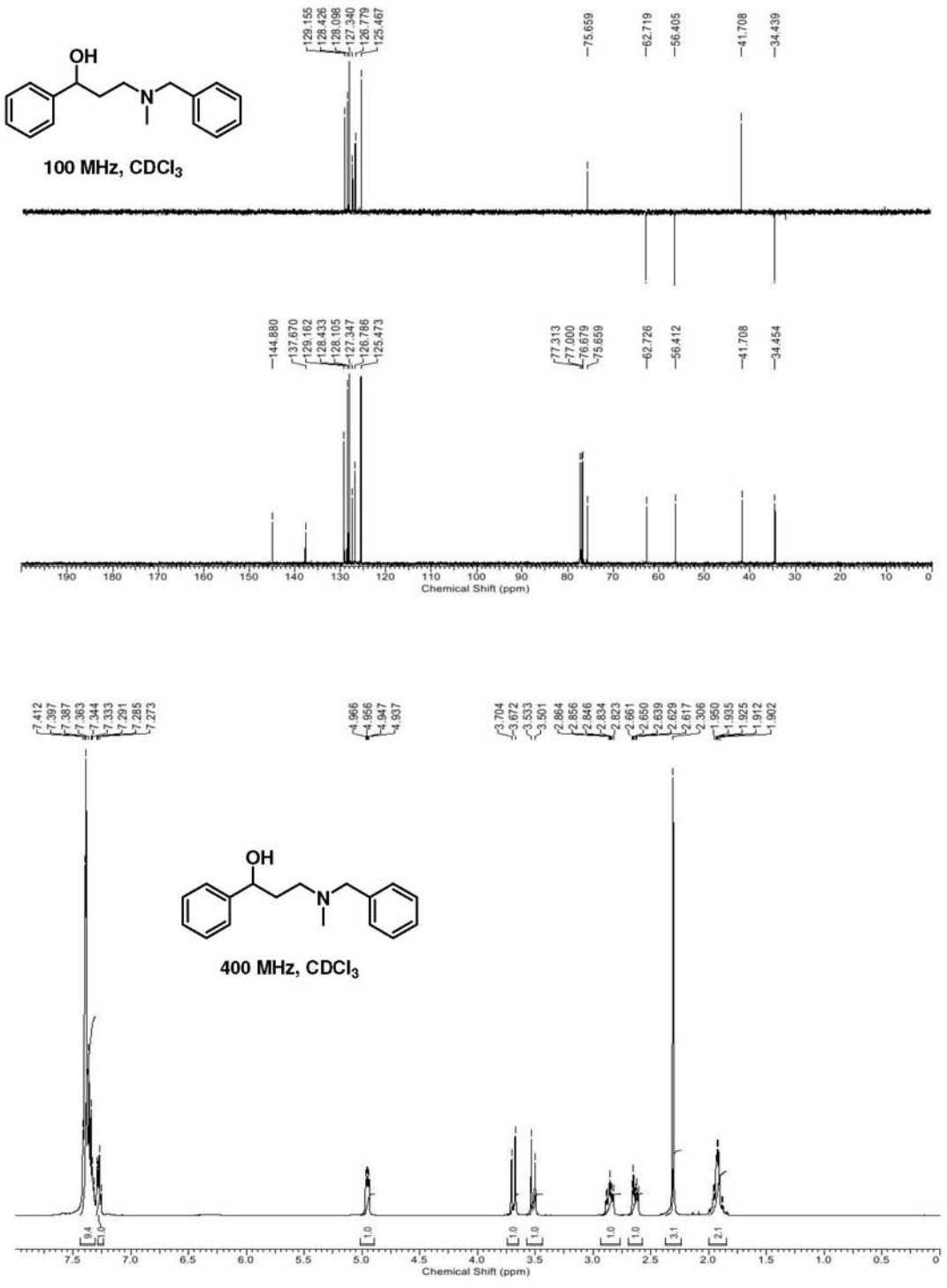
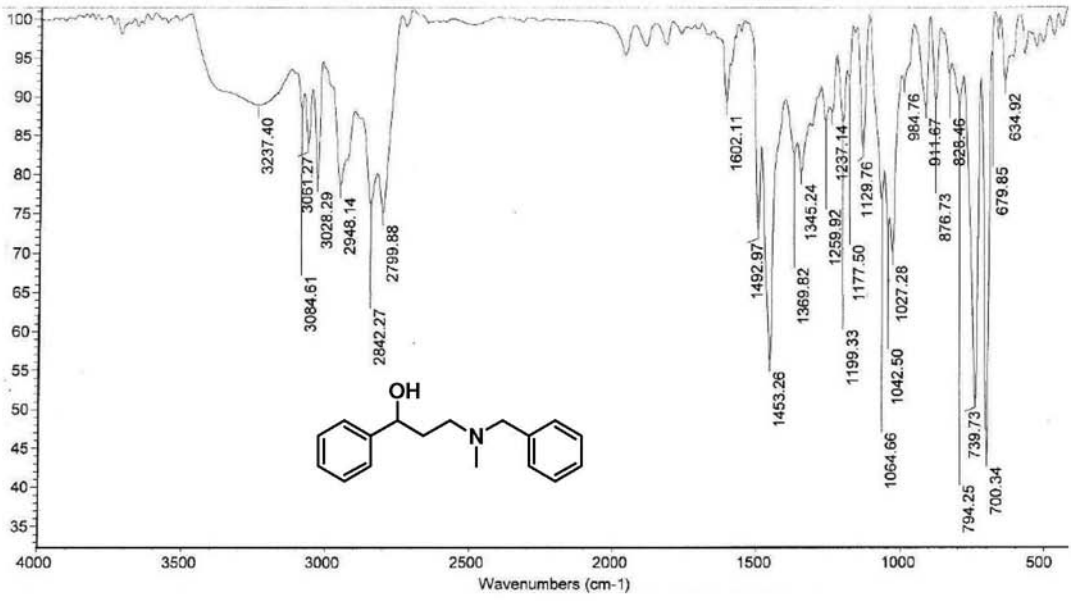



**Figure S31.** $^{1}H$ and $^{13}C$ spectra for compound **11a**.



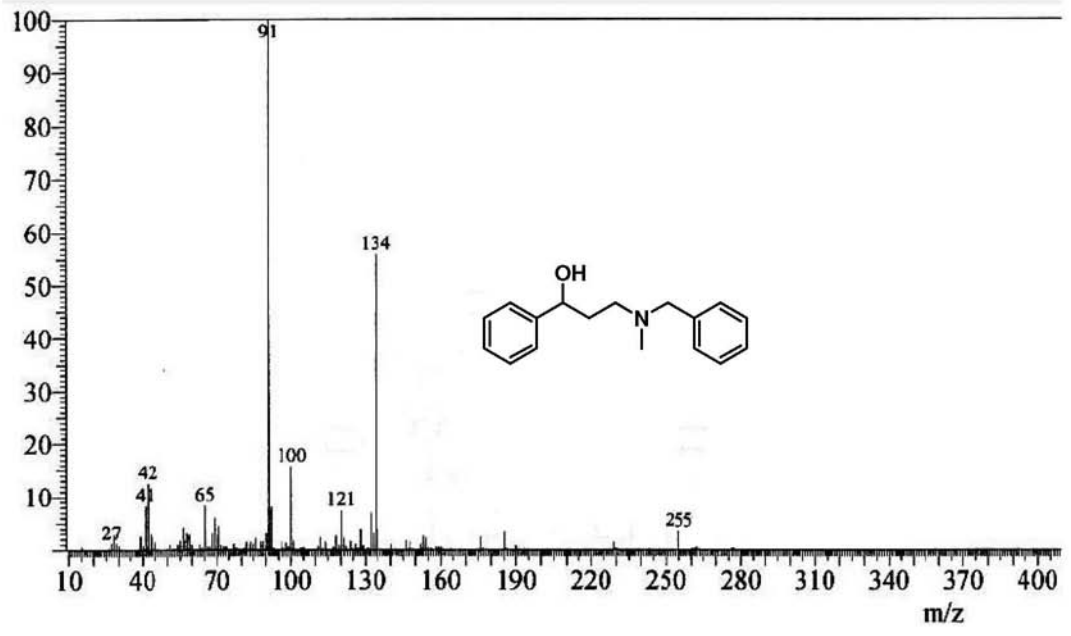




**Figure S32.** IR and MS spectra for compound **11a**.

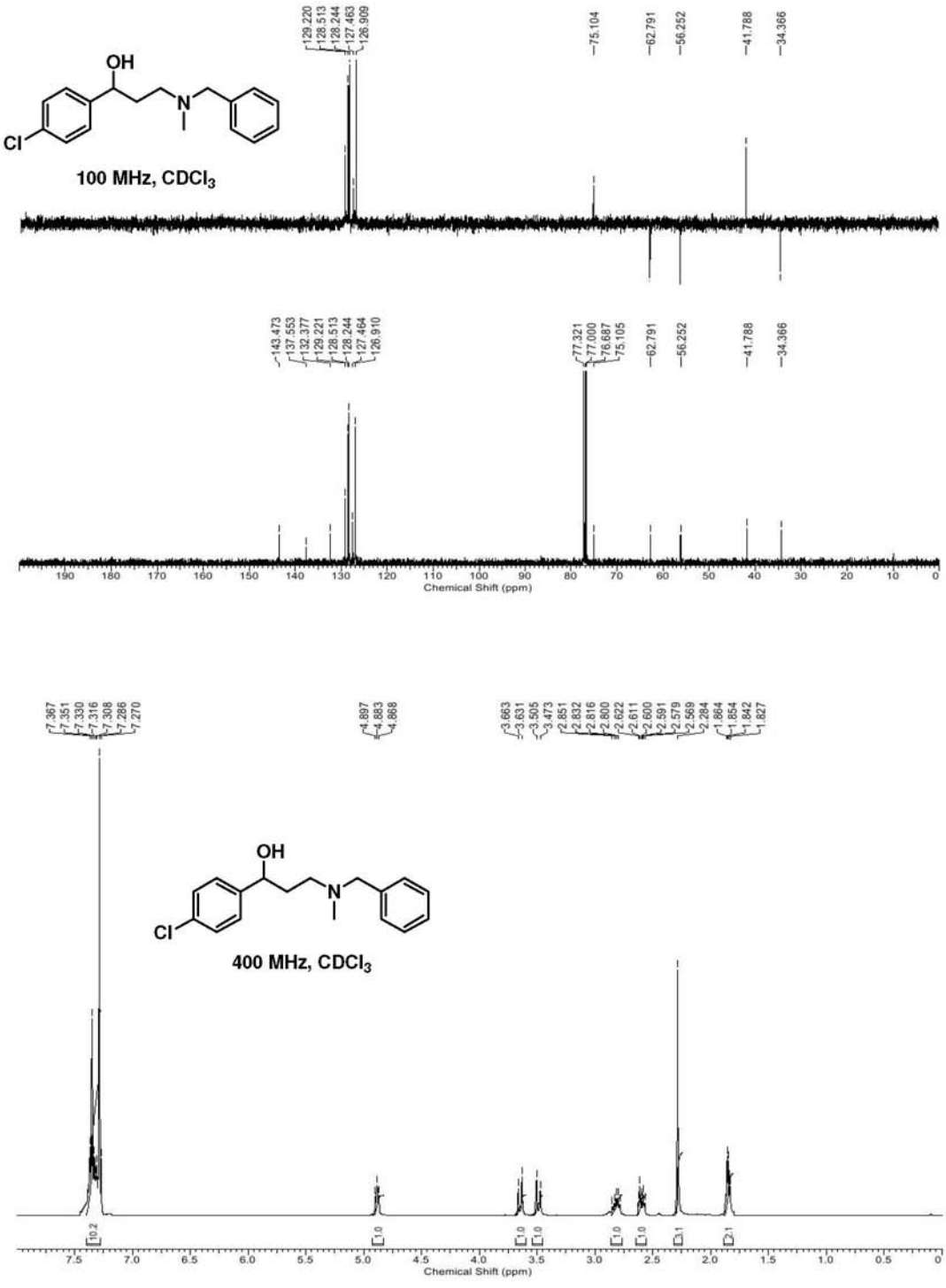
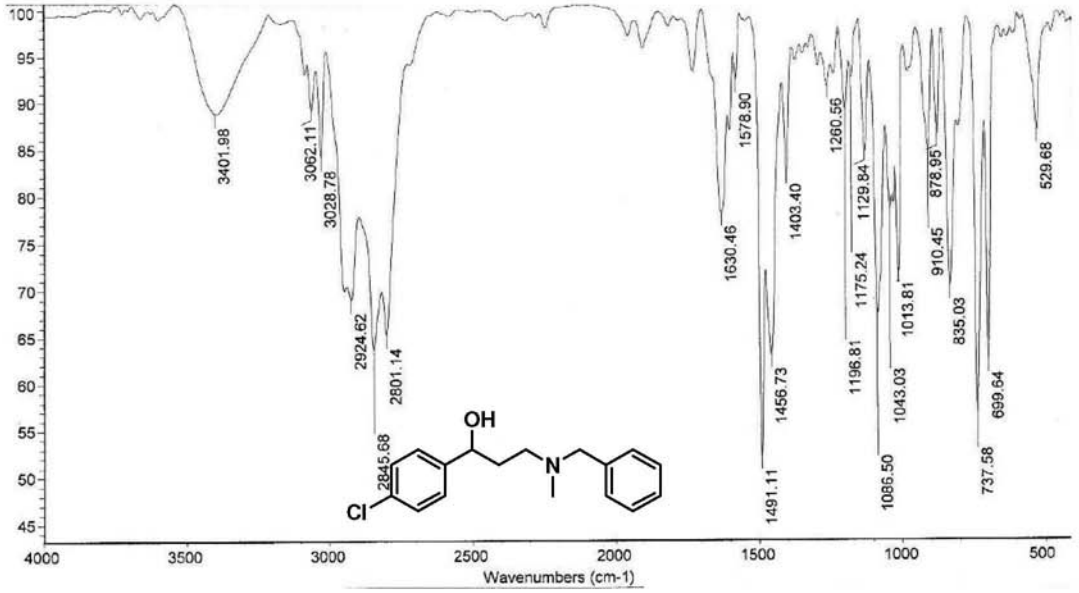



**Figure S33.** $^{1}H$ and $^{13}C$ spectra for compound **11b**.



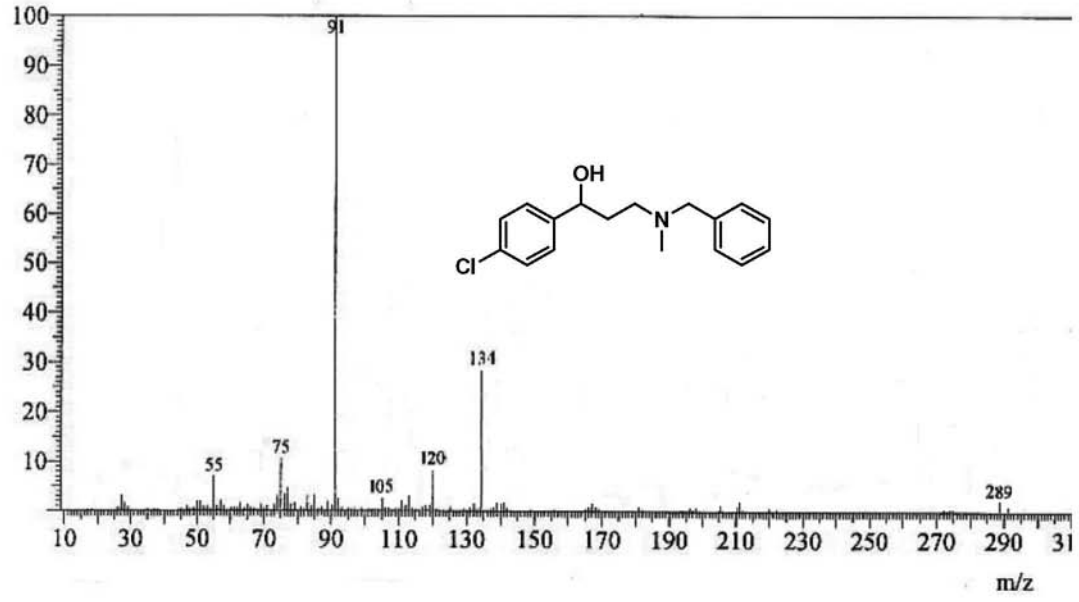




**Figure S34.** IR and MS spectra for compound **11b**.

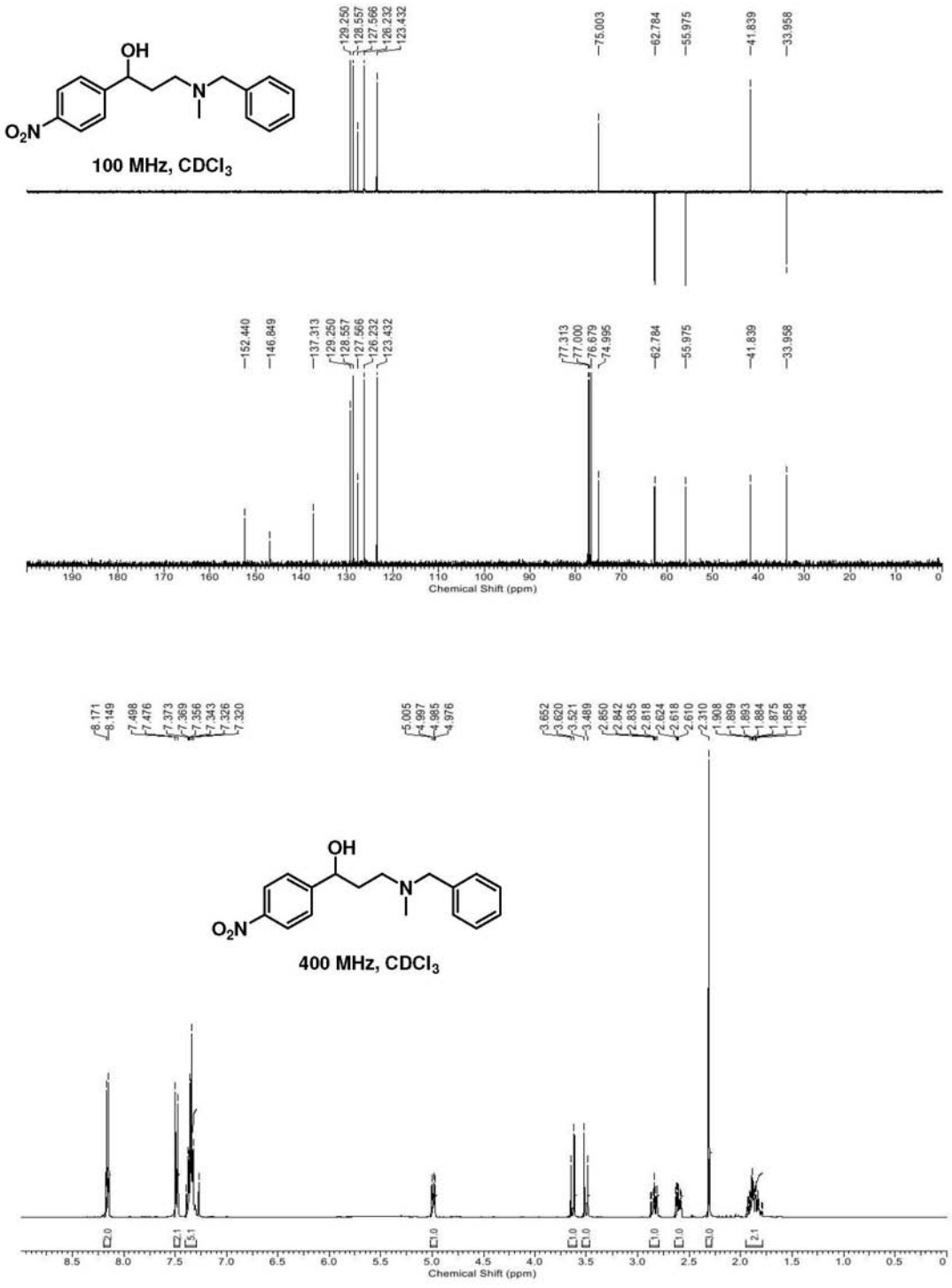
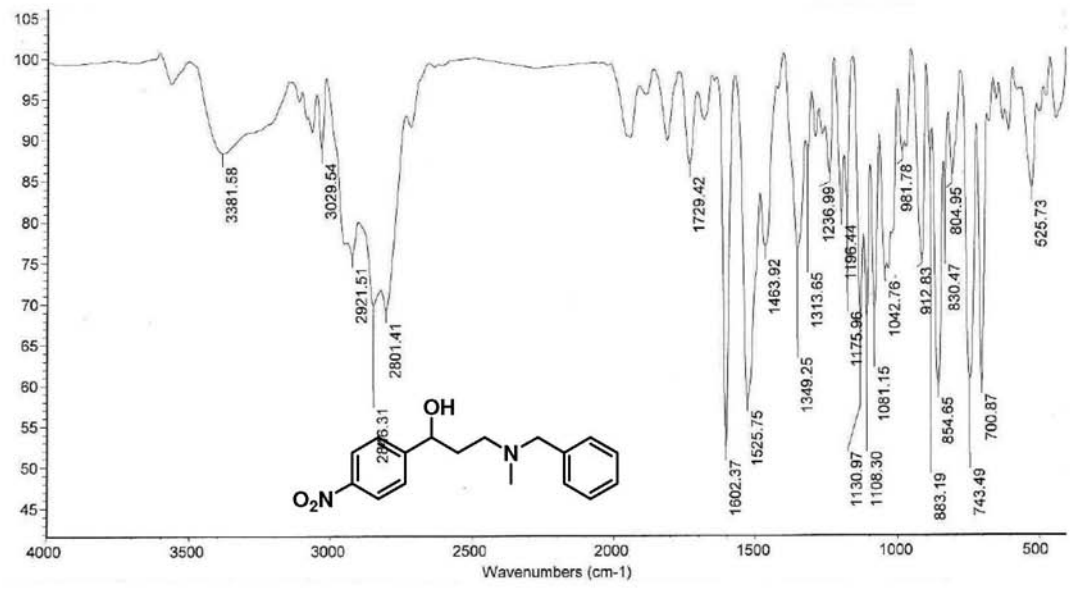



**Figure S35.** $^{1}H$ and $^{13}C$ spectra for compound **11c**.



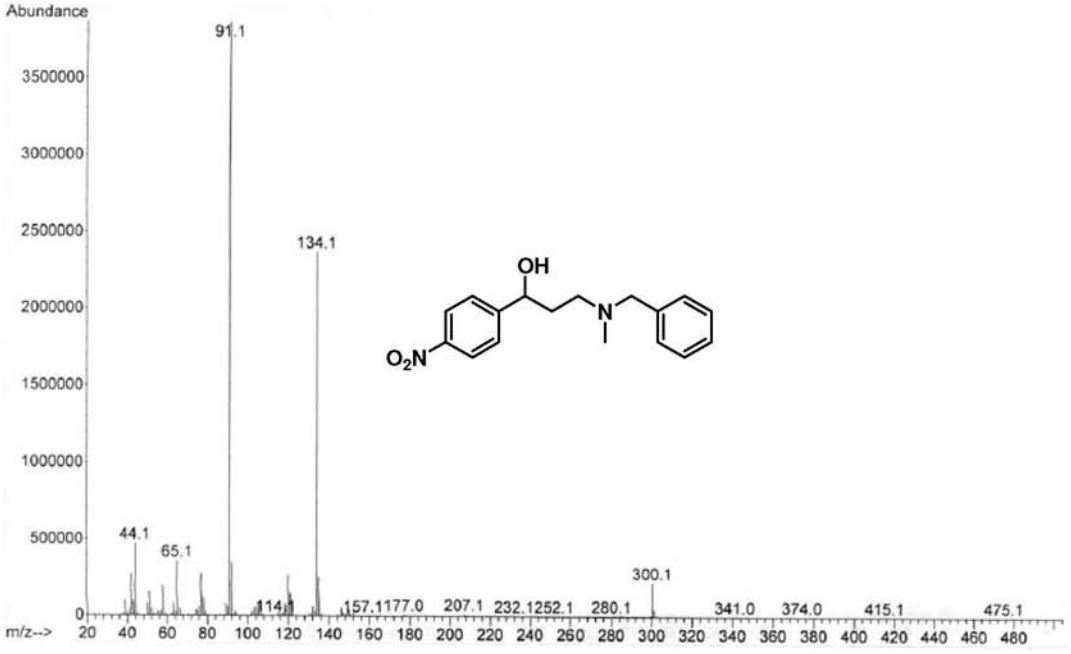




**Figure S36.** IR and MS spectra for compound **11c**.

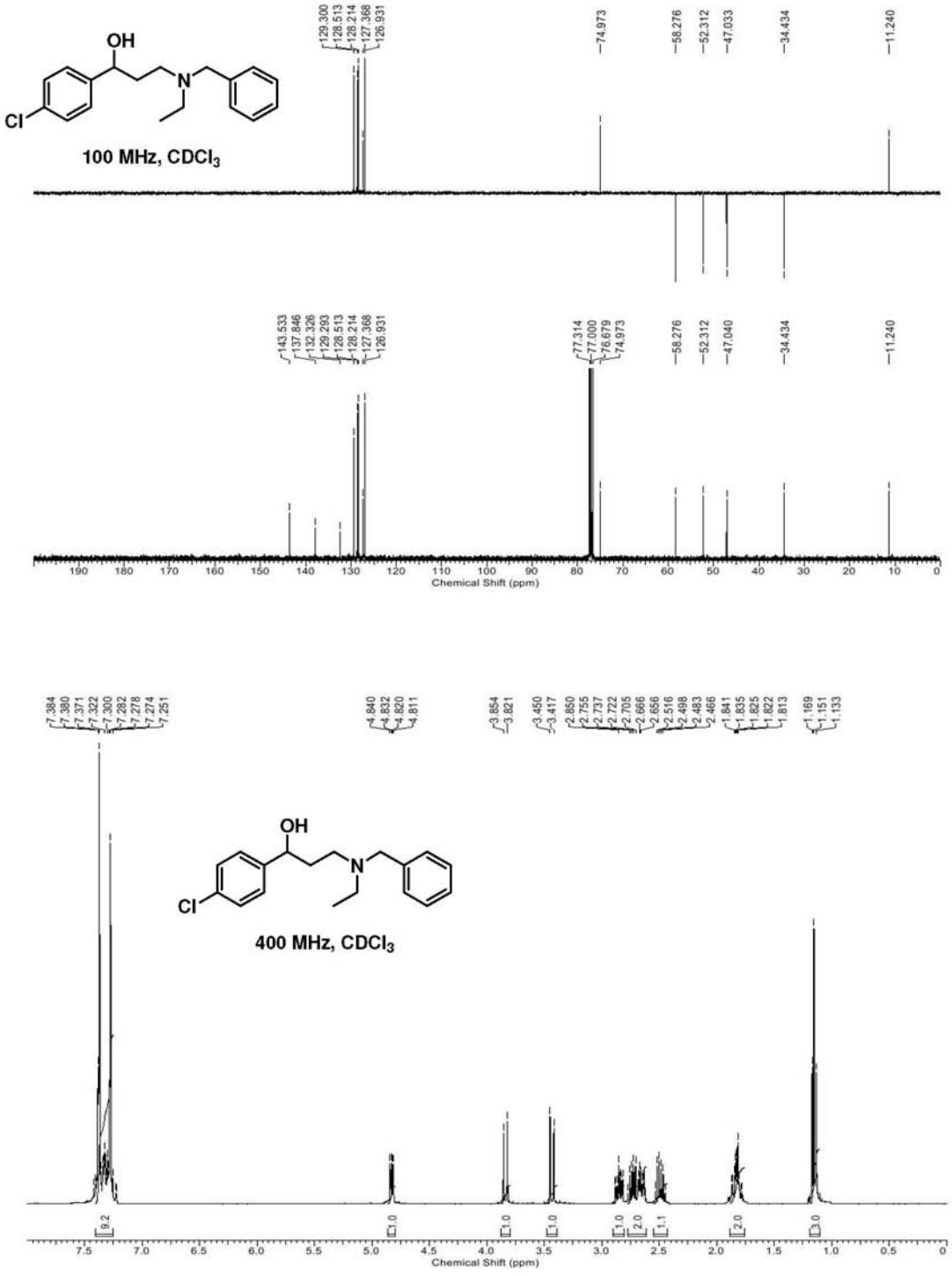
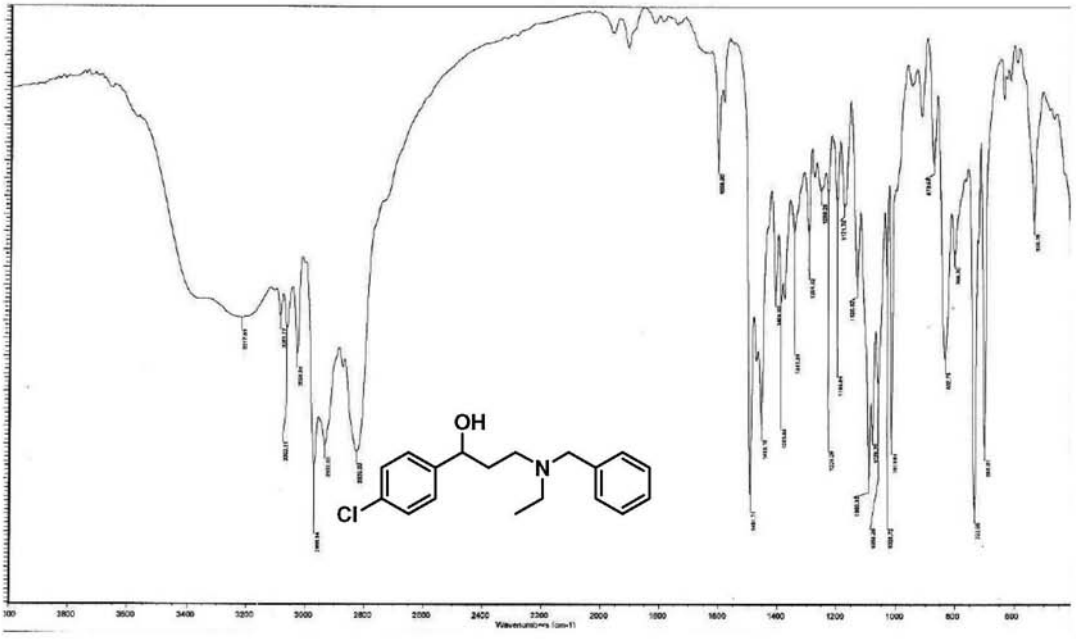



**Figure S37.** $^{1}H$ and $^{13}C$ spectra for compound **11d**.



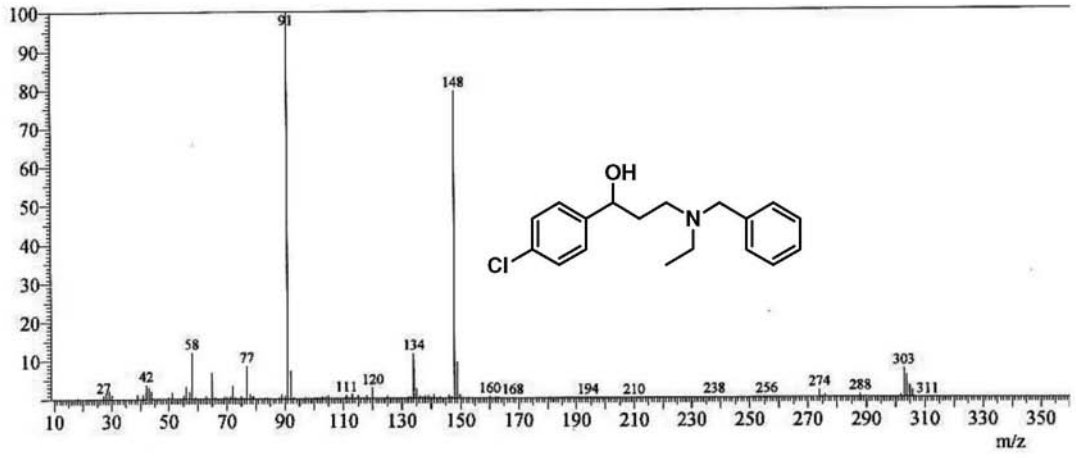




**Figure S38.** IR and MS spectra for compound **11d**.

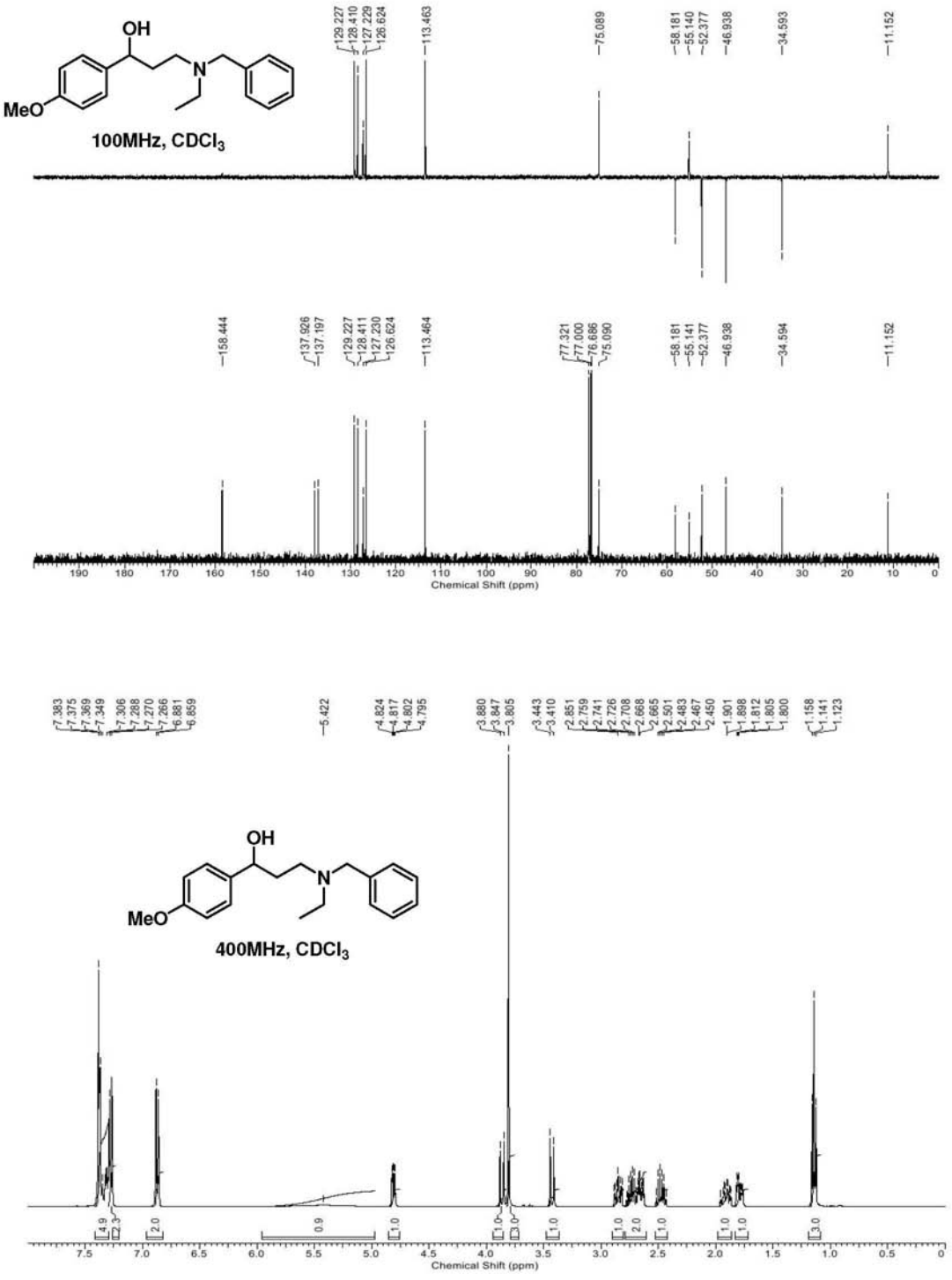
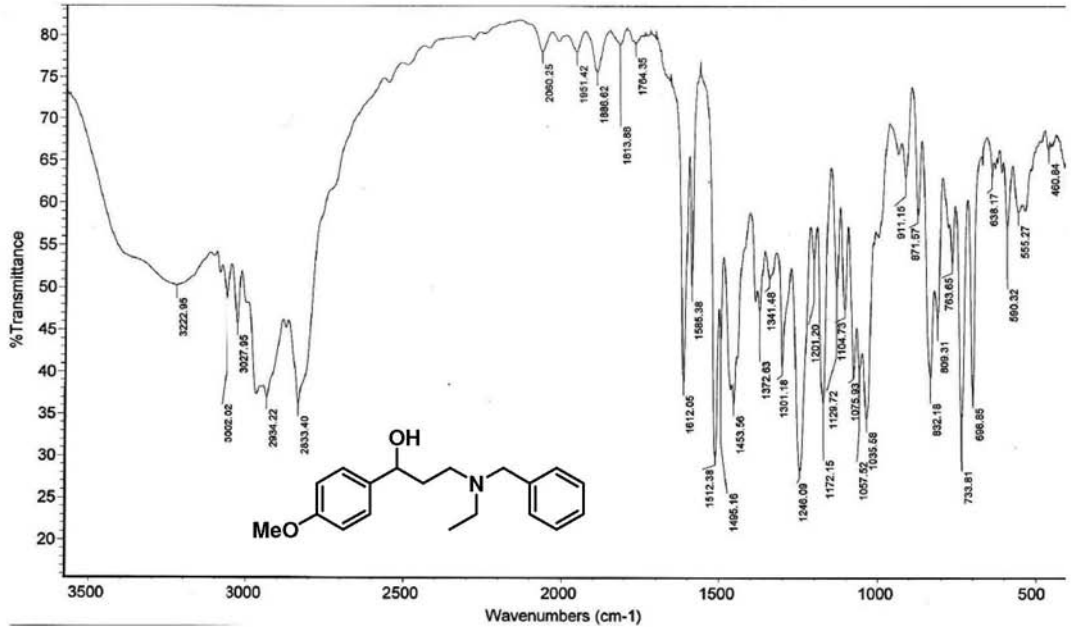



**Figure S39.** [1]H and [13]C spectra for compound **11e**.



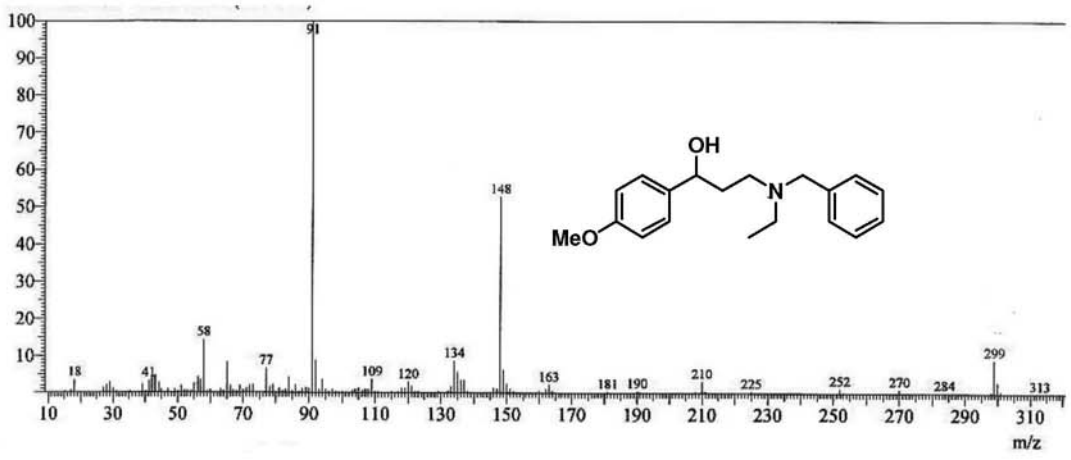




**Figure S40.** IR and MS spectra for compound **11e**.

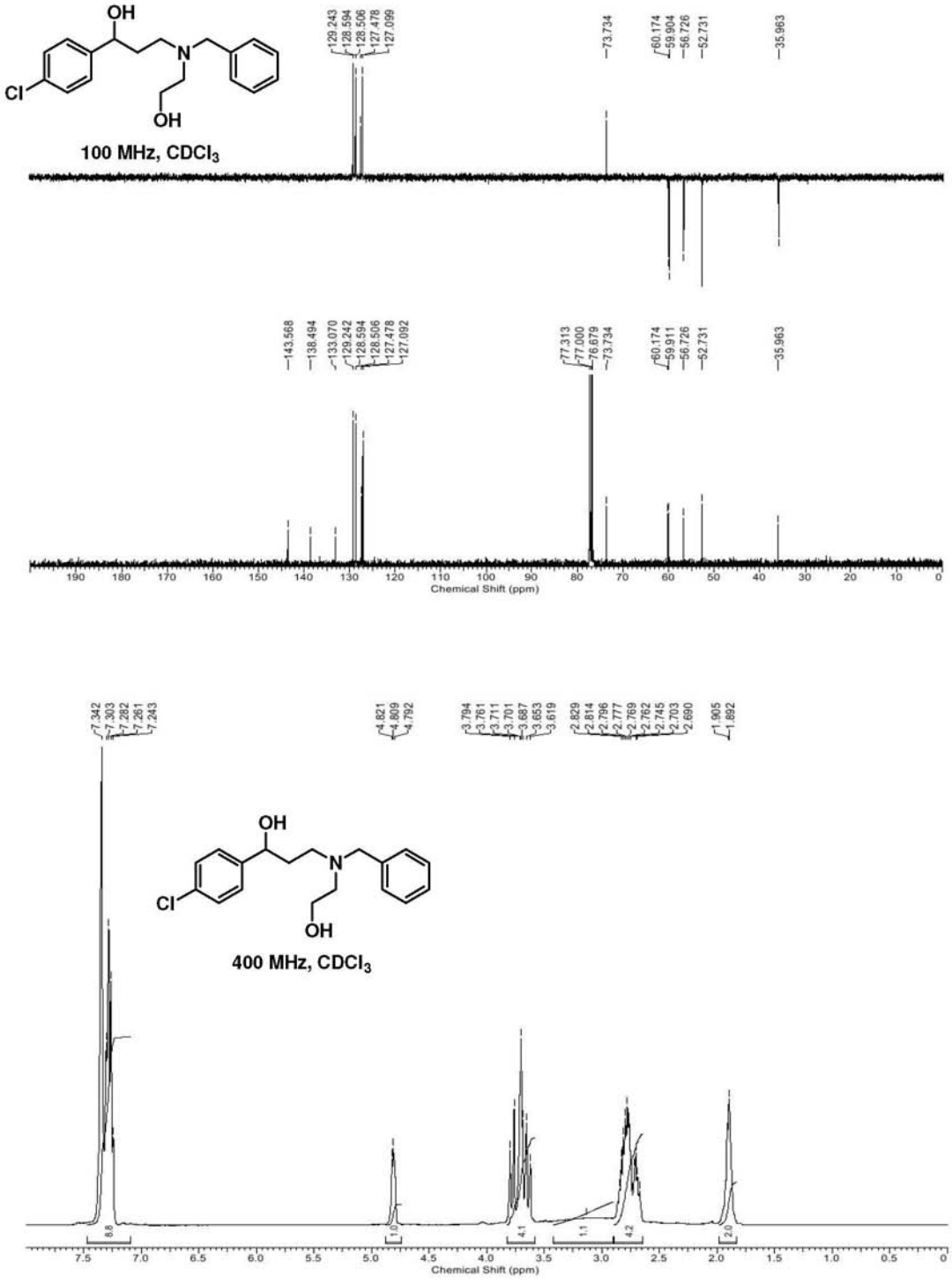
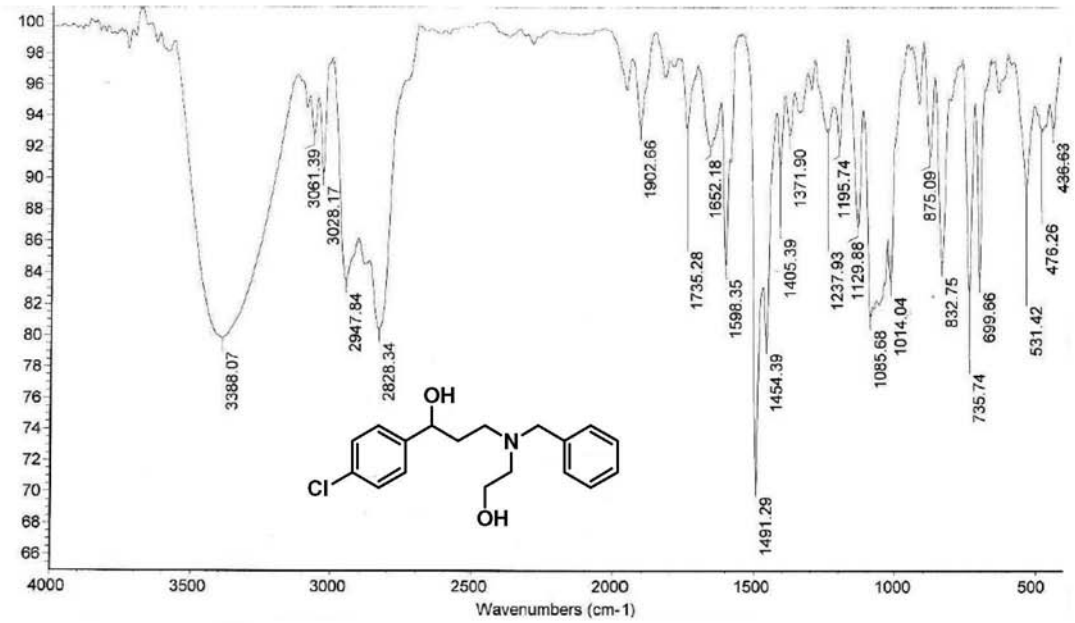



**Figure S41.** $^{1}H$ and $^{13}C$ spectra for compound **11f**.



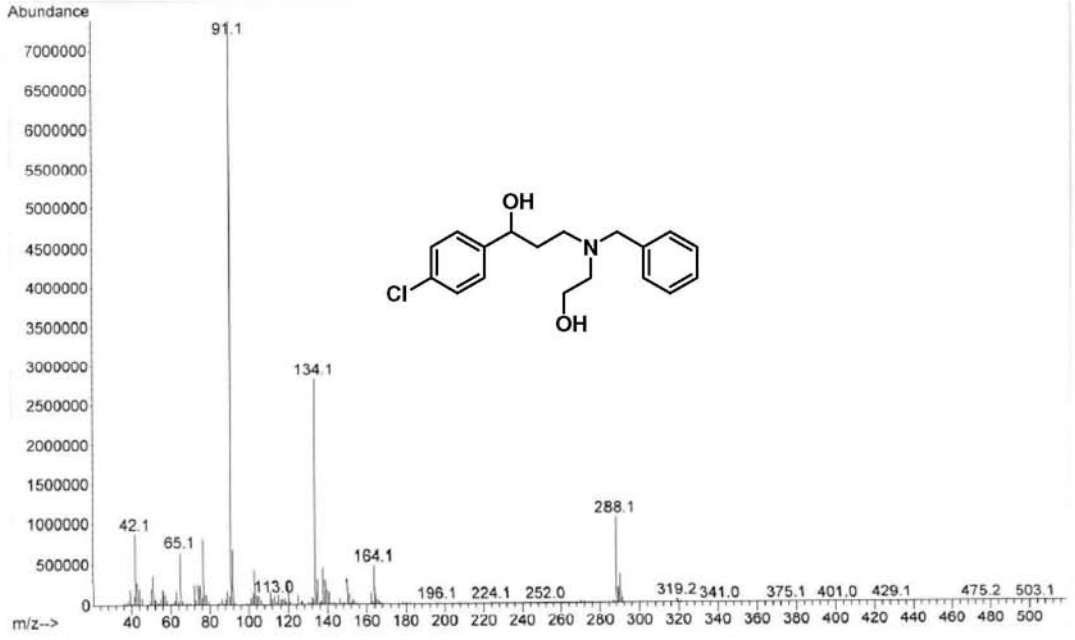




**Figure S42.** IR and MS spectra for compound **11f**.

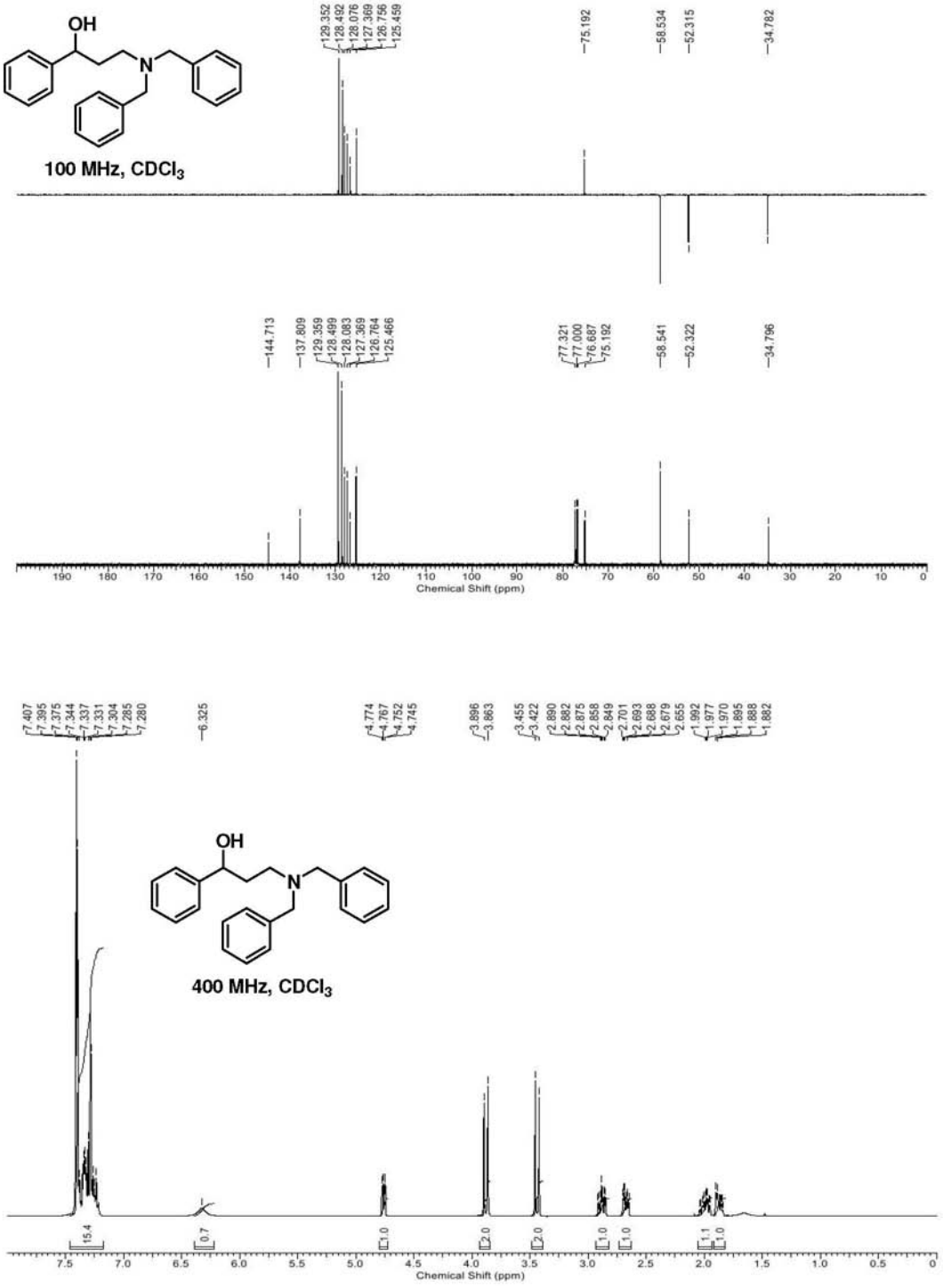
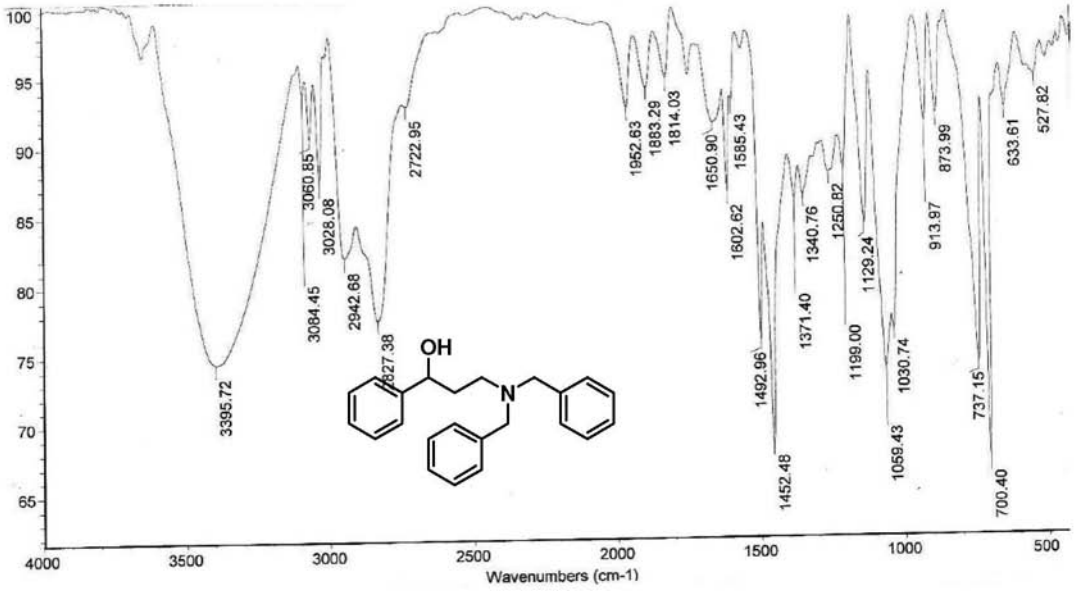



**Figure S43.** [1]H and [13]C spectra for compound **11g**.



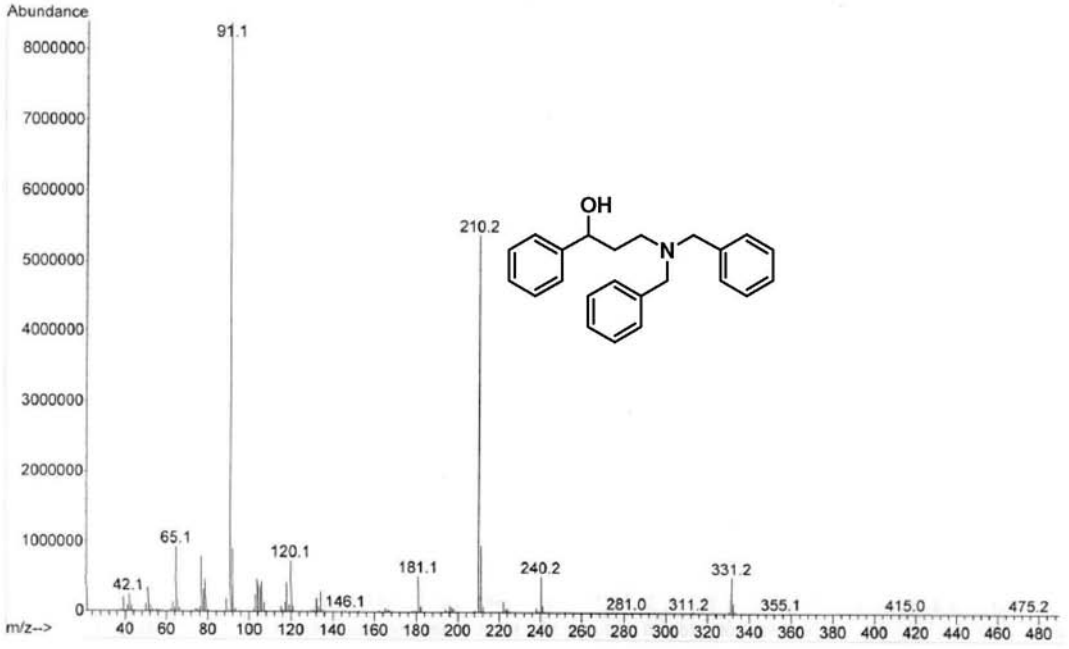




**Figure S44.** IR and MS spectra for compound **11g**.

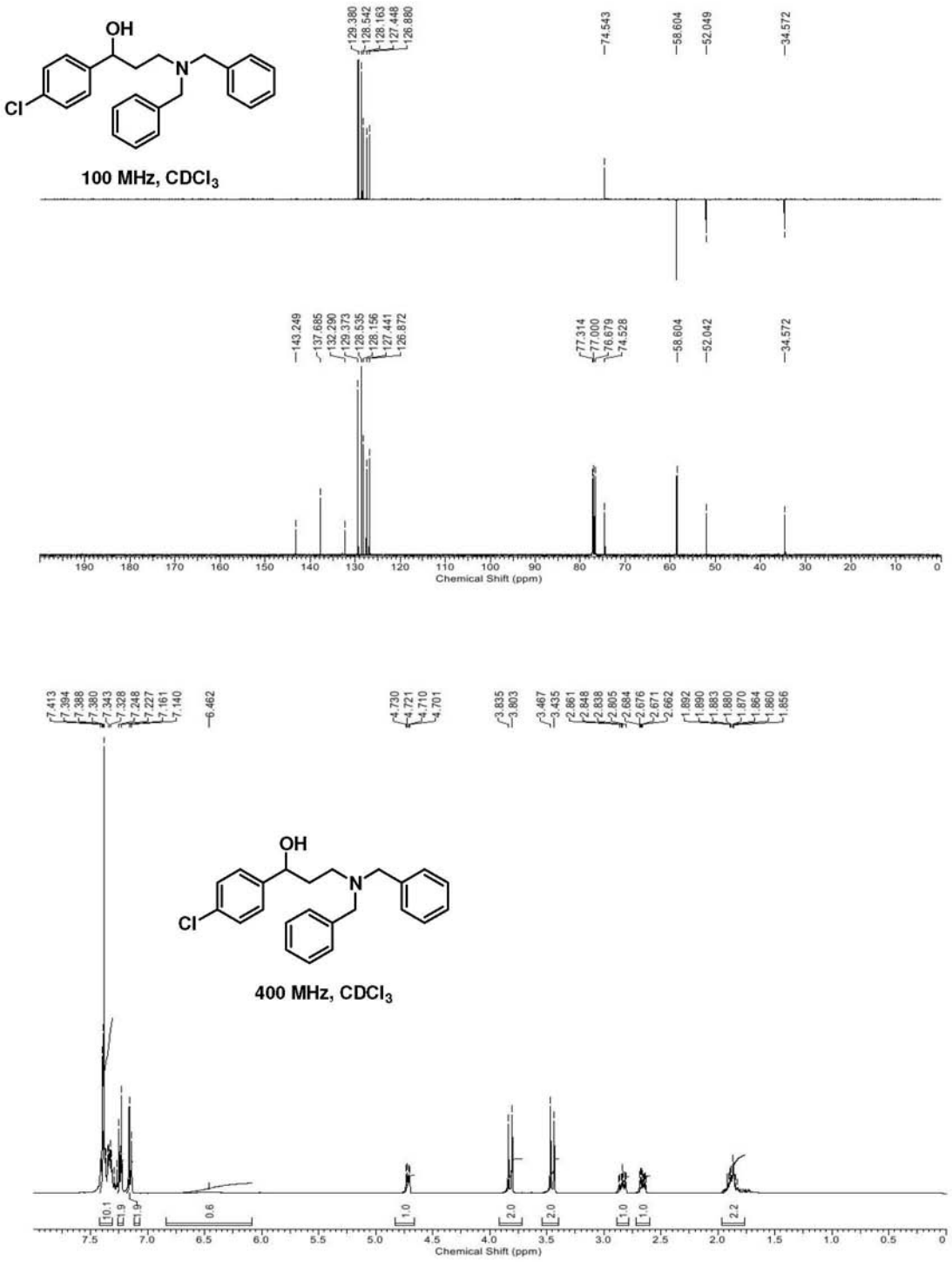
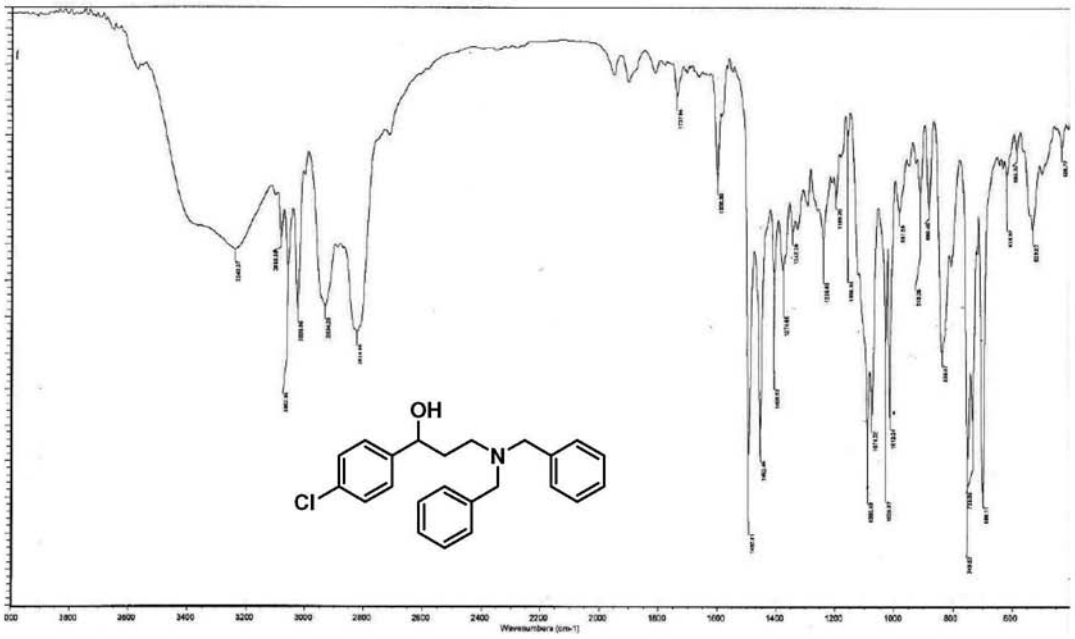



**Figure S45.** $^{1}H$ and $^{13}C$ spectra for compound **11h**.



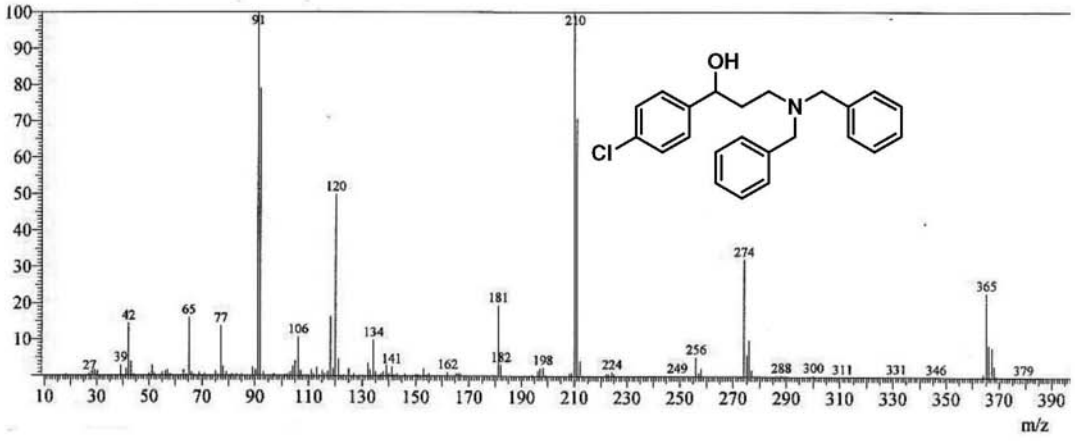




**Figure S46.** IR and MS spectra for compound **11h**.

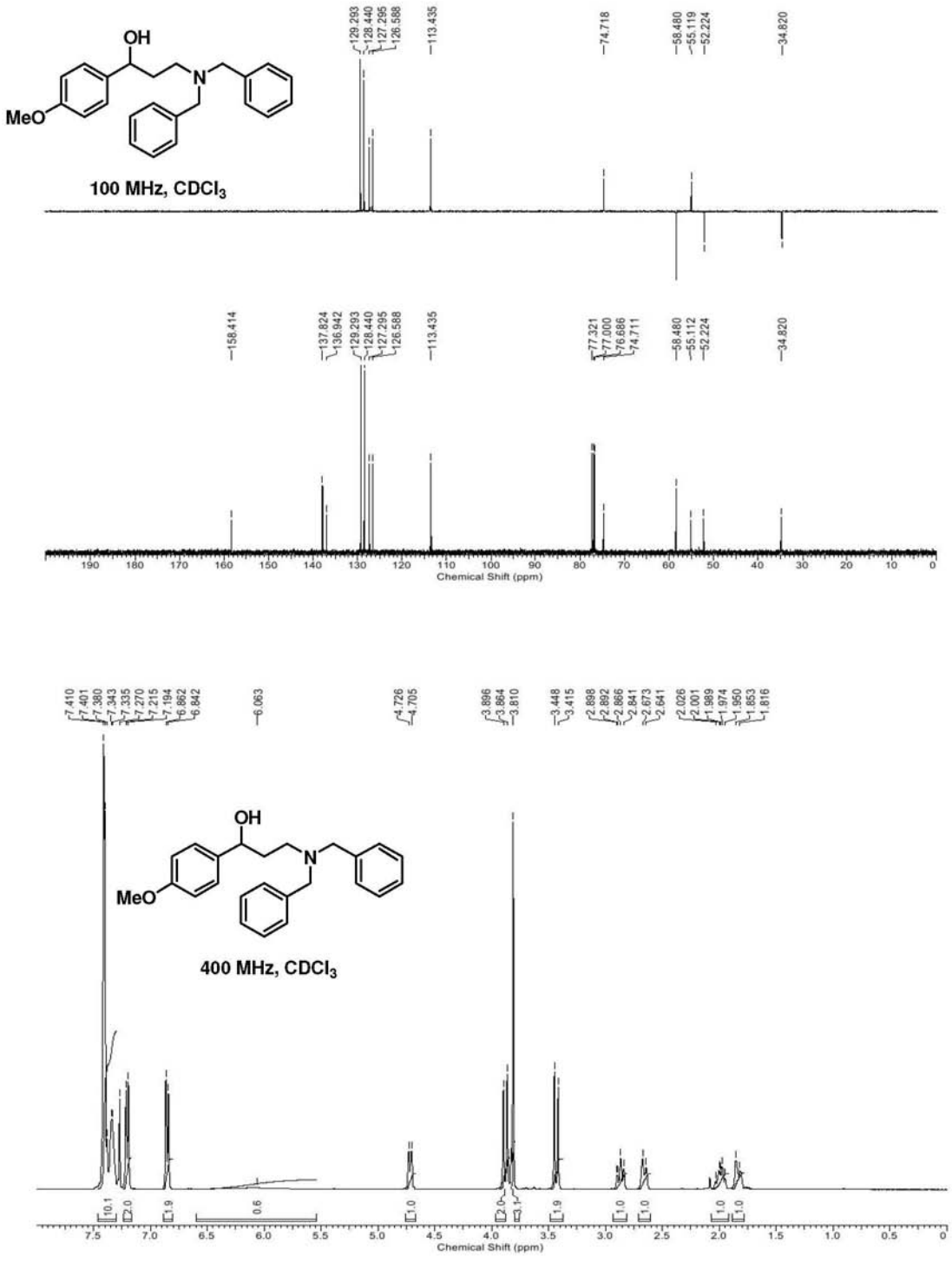



**Figure S47.** $^{1}H$ and $^{13}C$ spectra for compound **11i**.

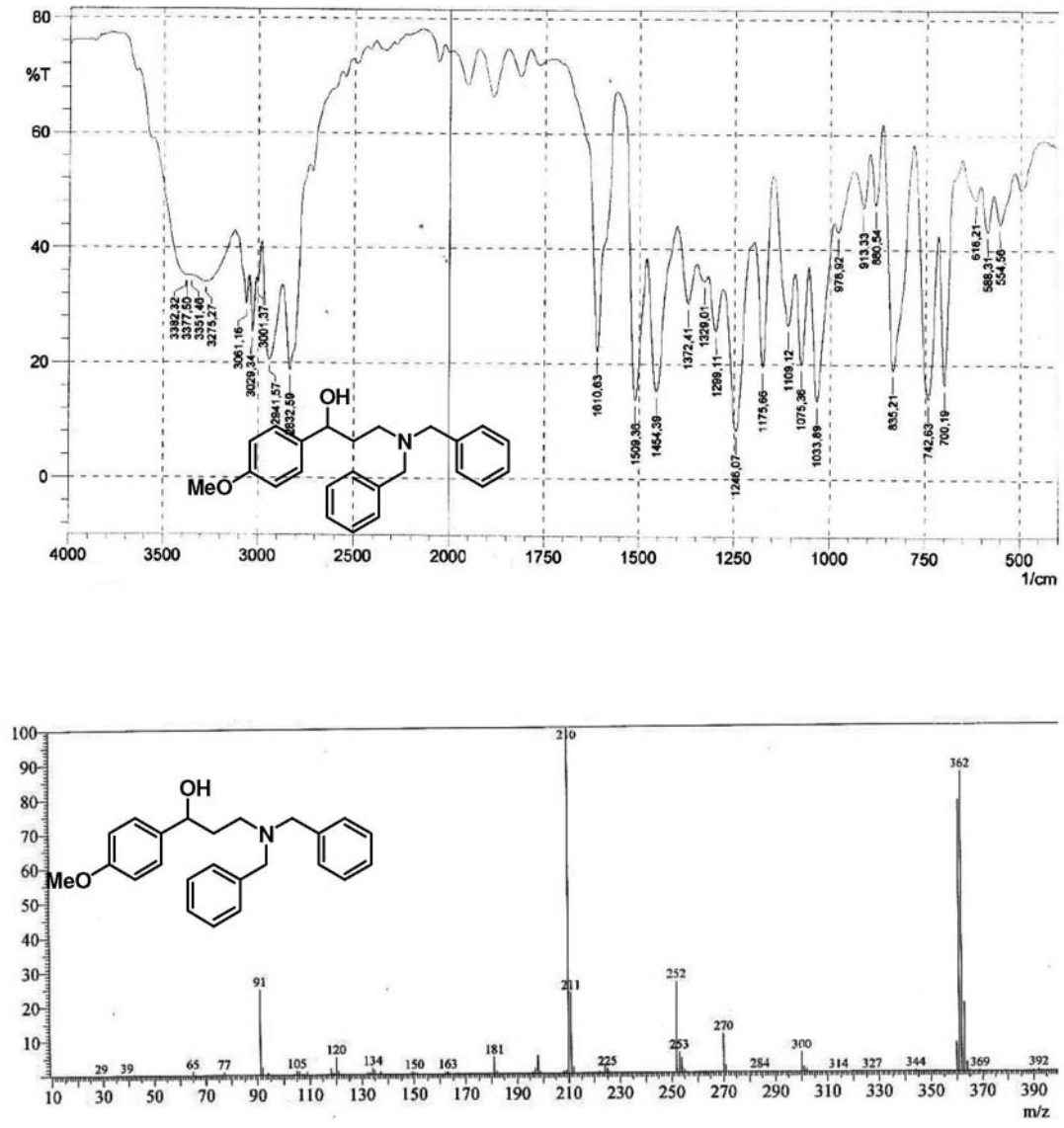



**Figure S48.** IR and MS spectra for compound **11i**.

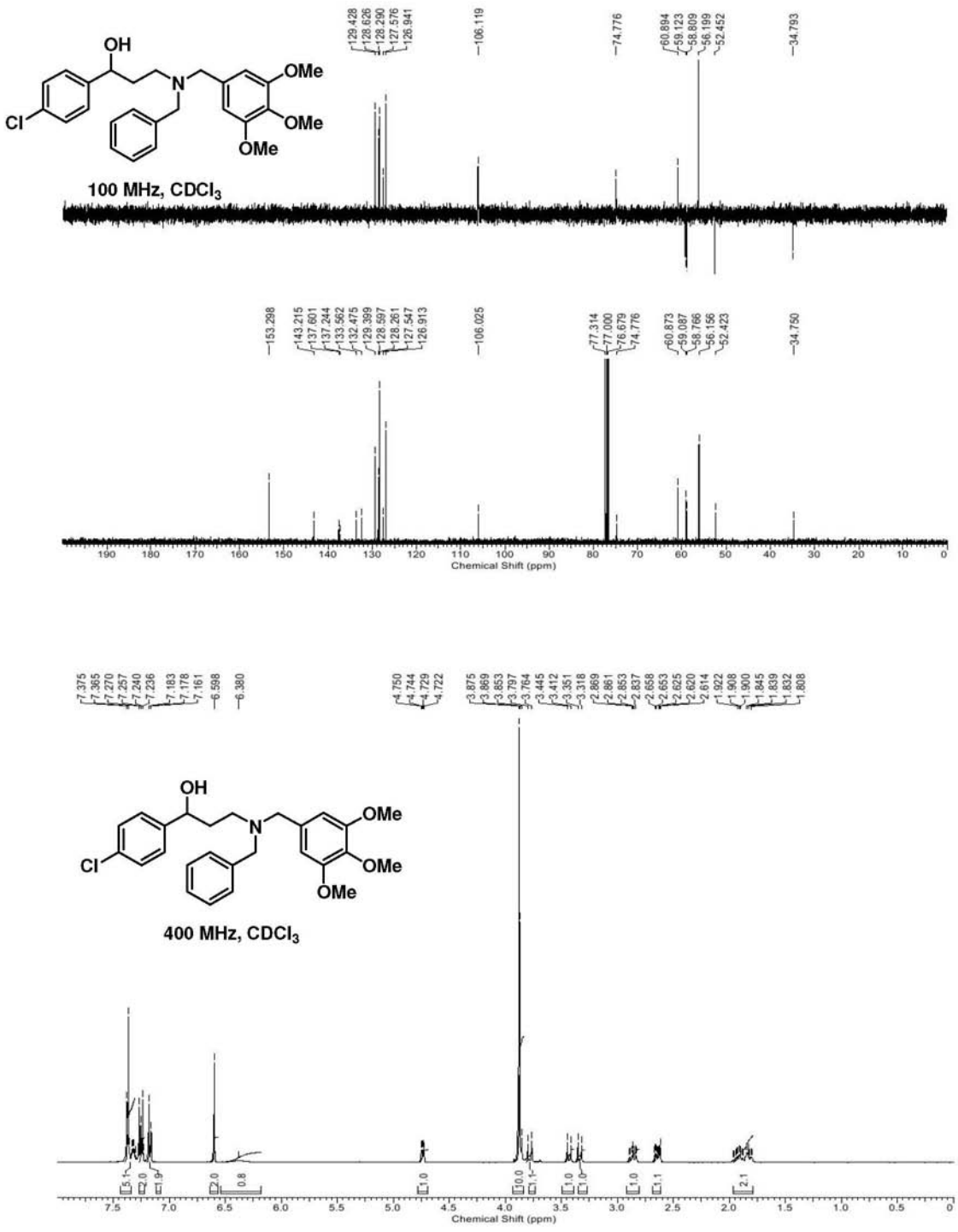



**Figure S49.** $^{1}H$ and $^{13}C$ spectra for compound **11j**.

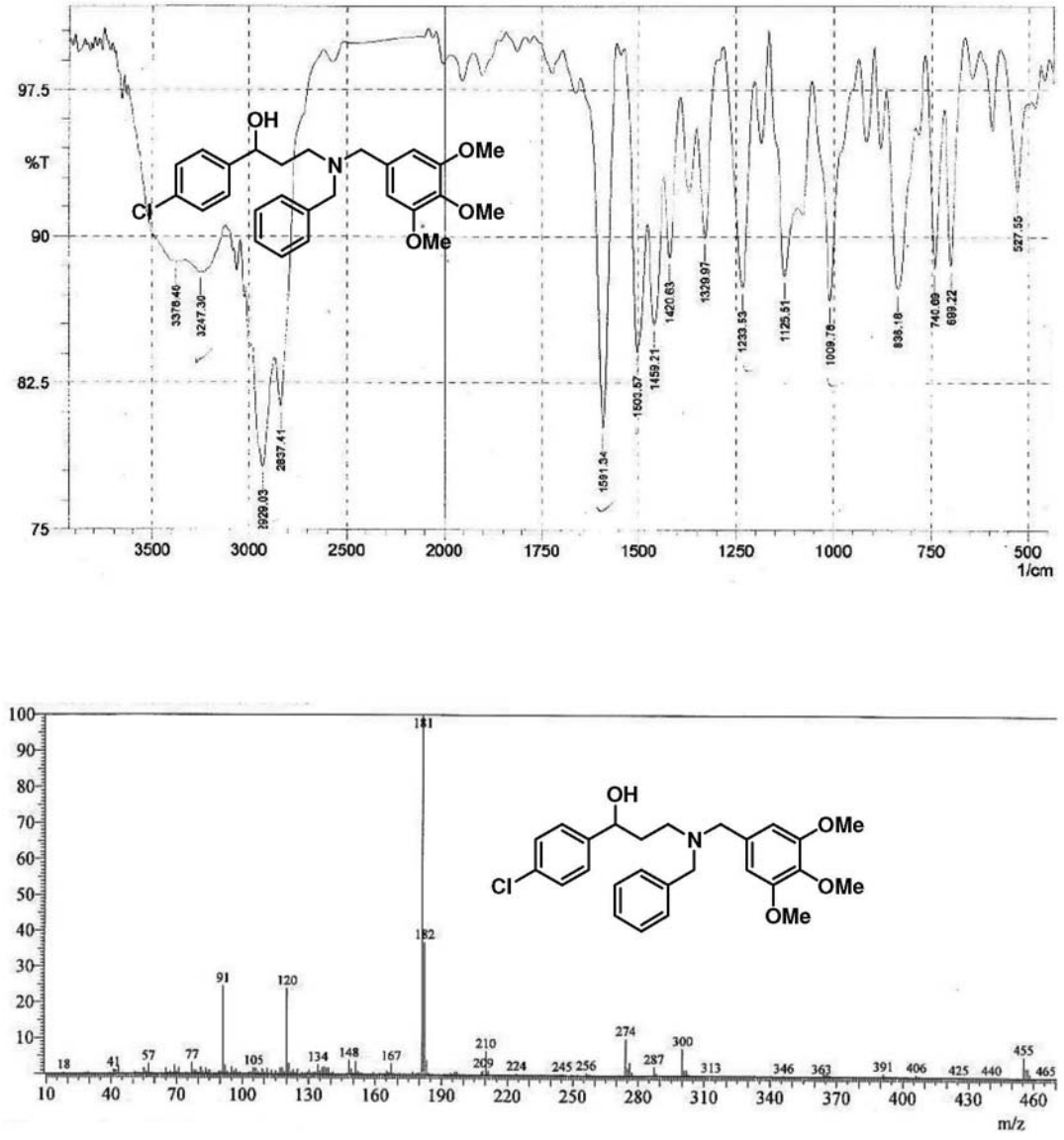



**Figure S50.** IR and MS spectra for compound **11j**.

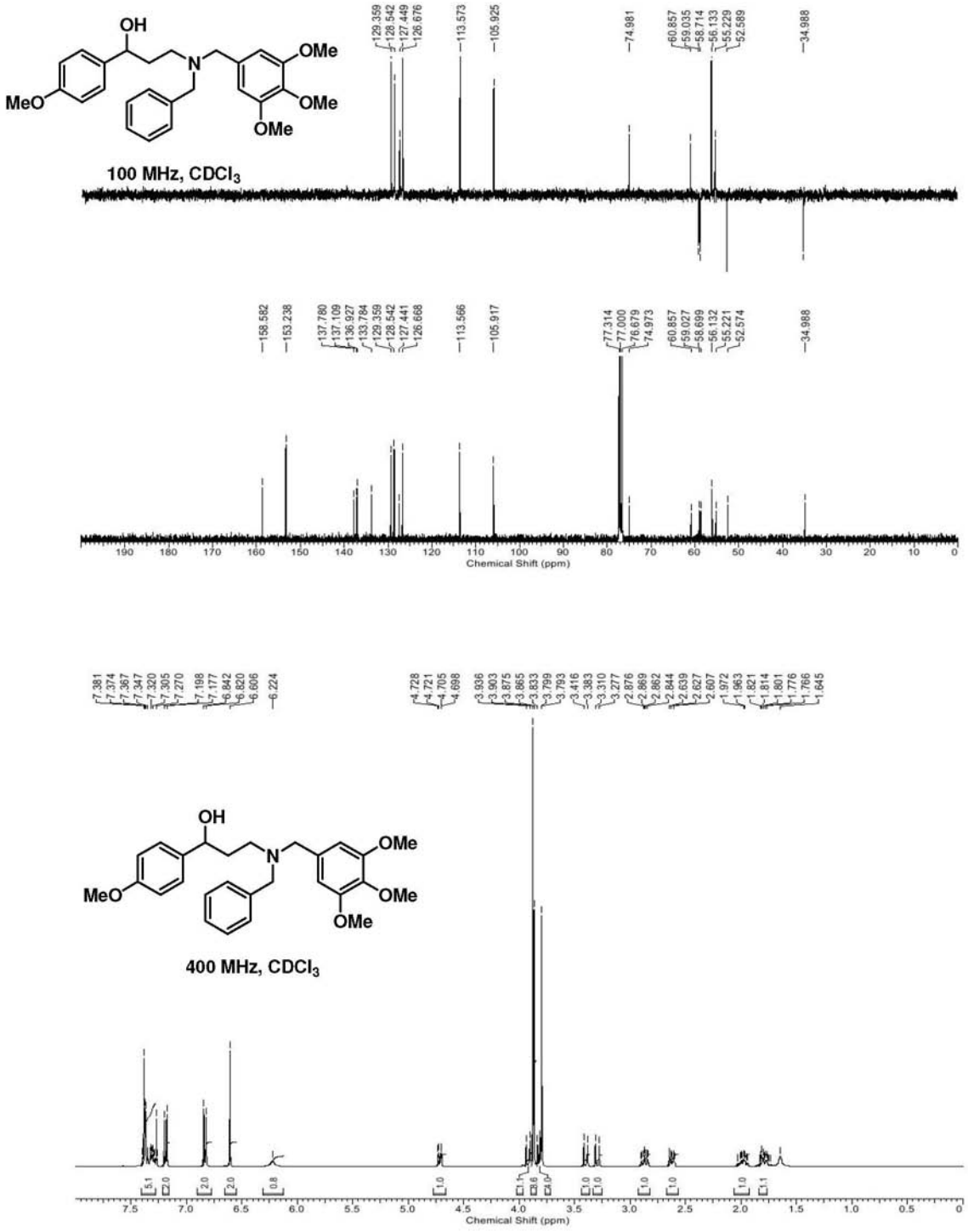



**Figure S51.** $^{1}H$ and $^{13}C$ spectra for compound **11k**.

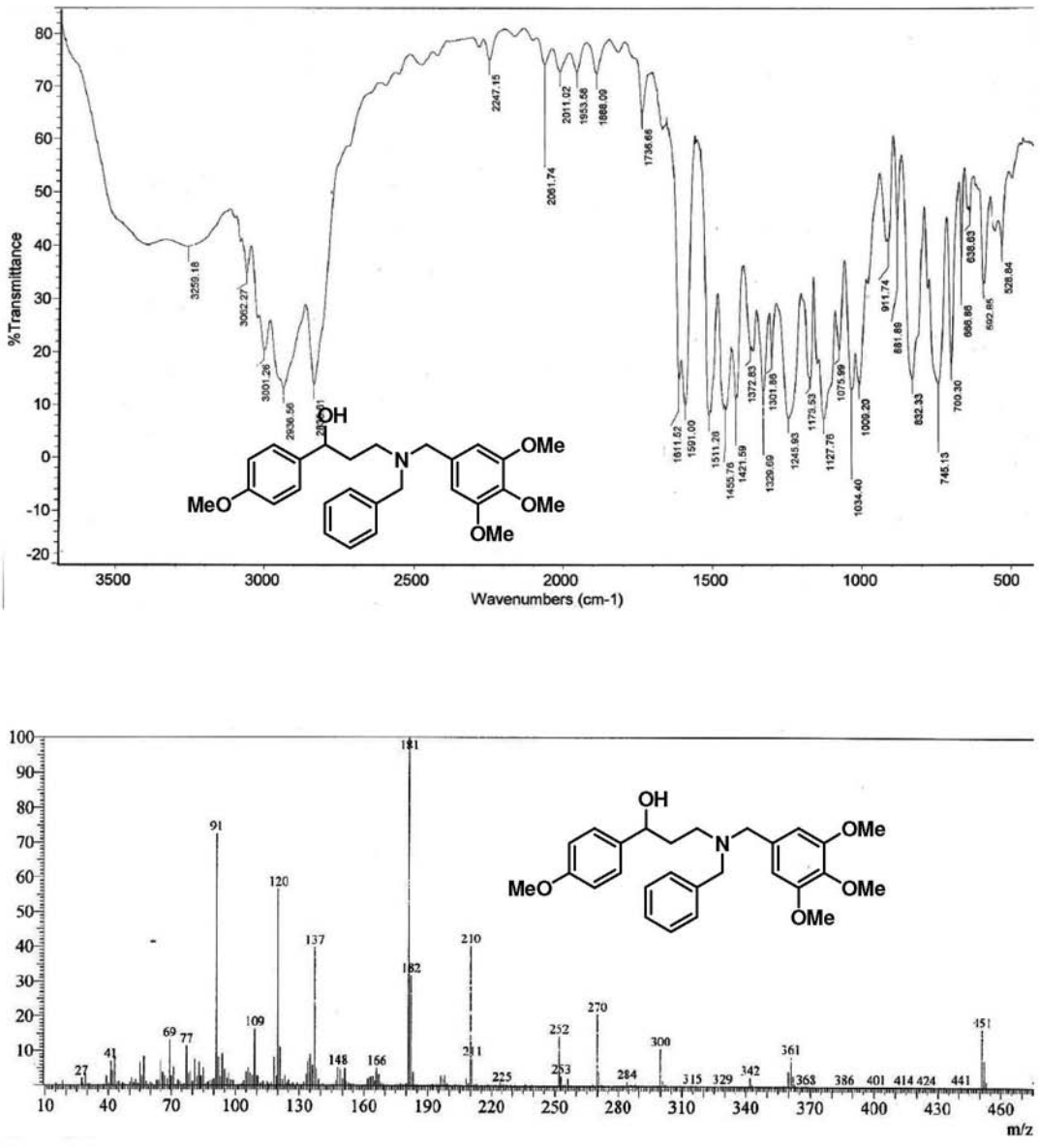



**Figure S52.** IR and MS spectra for compound **11k**.

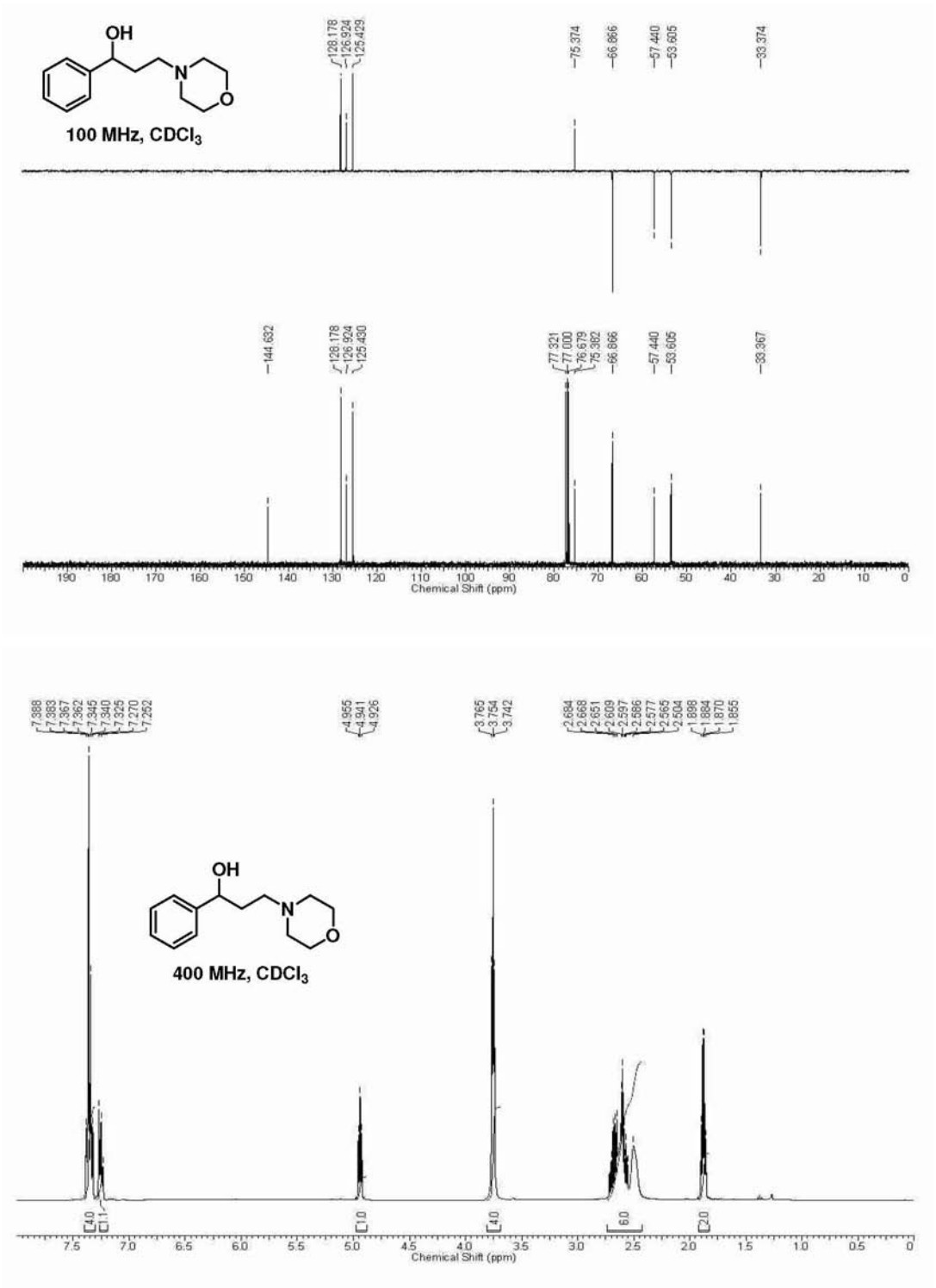
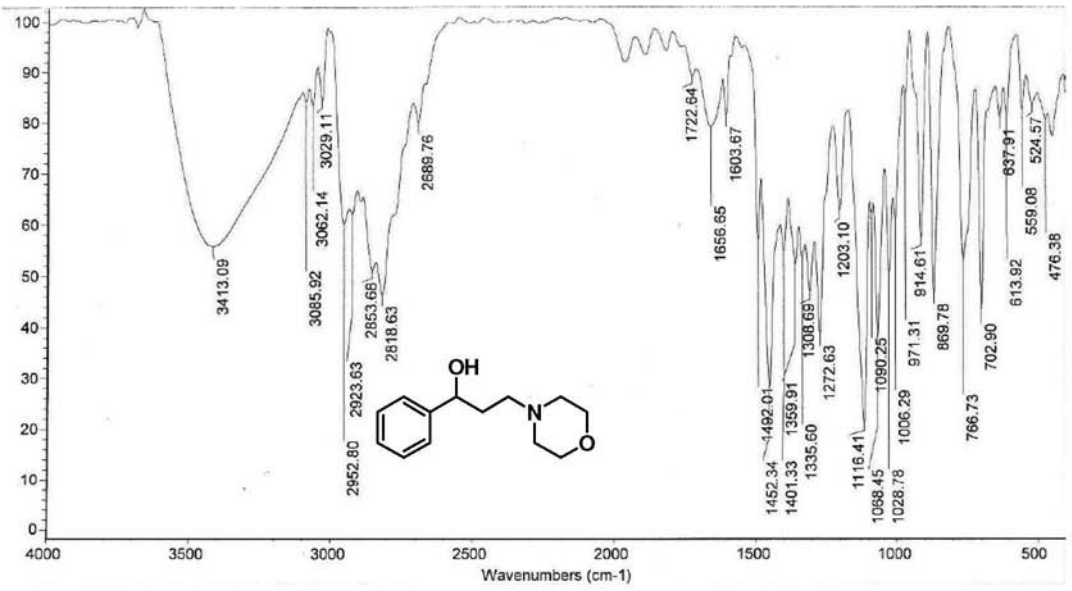



**Figure S53.** $^{1}H$ and $^{13}C$ spectra for compound **11l**.



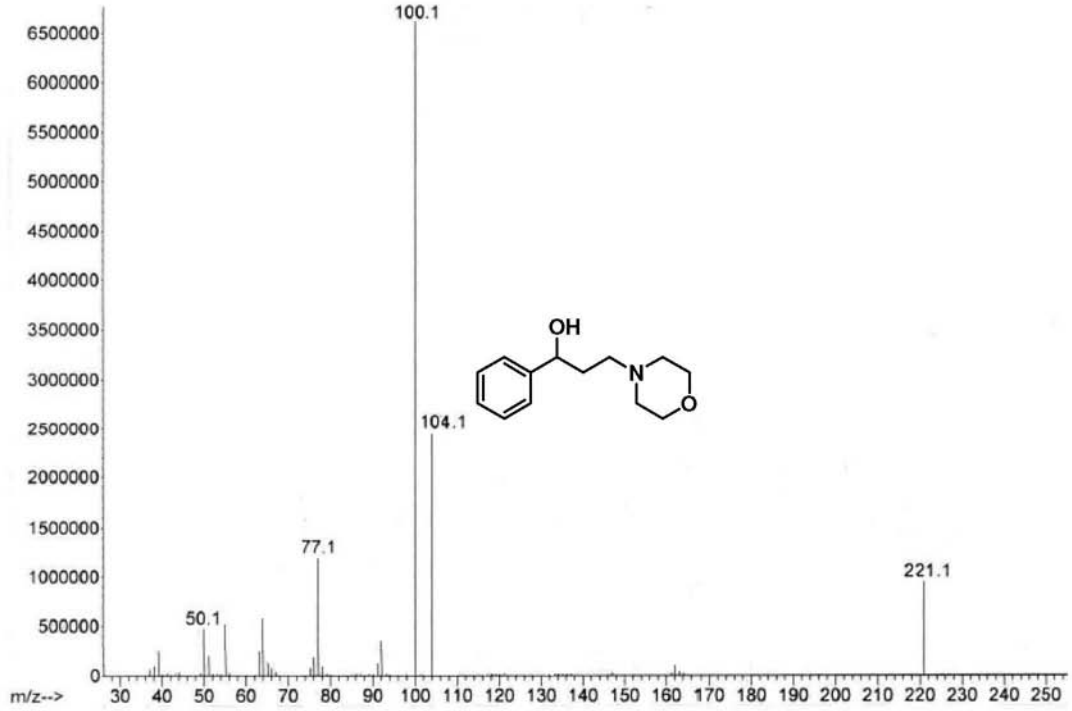




**Figure S54.** IR and MS spectra for compound **11l**.

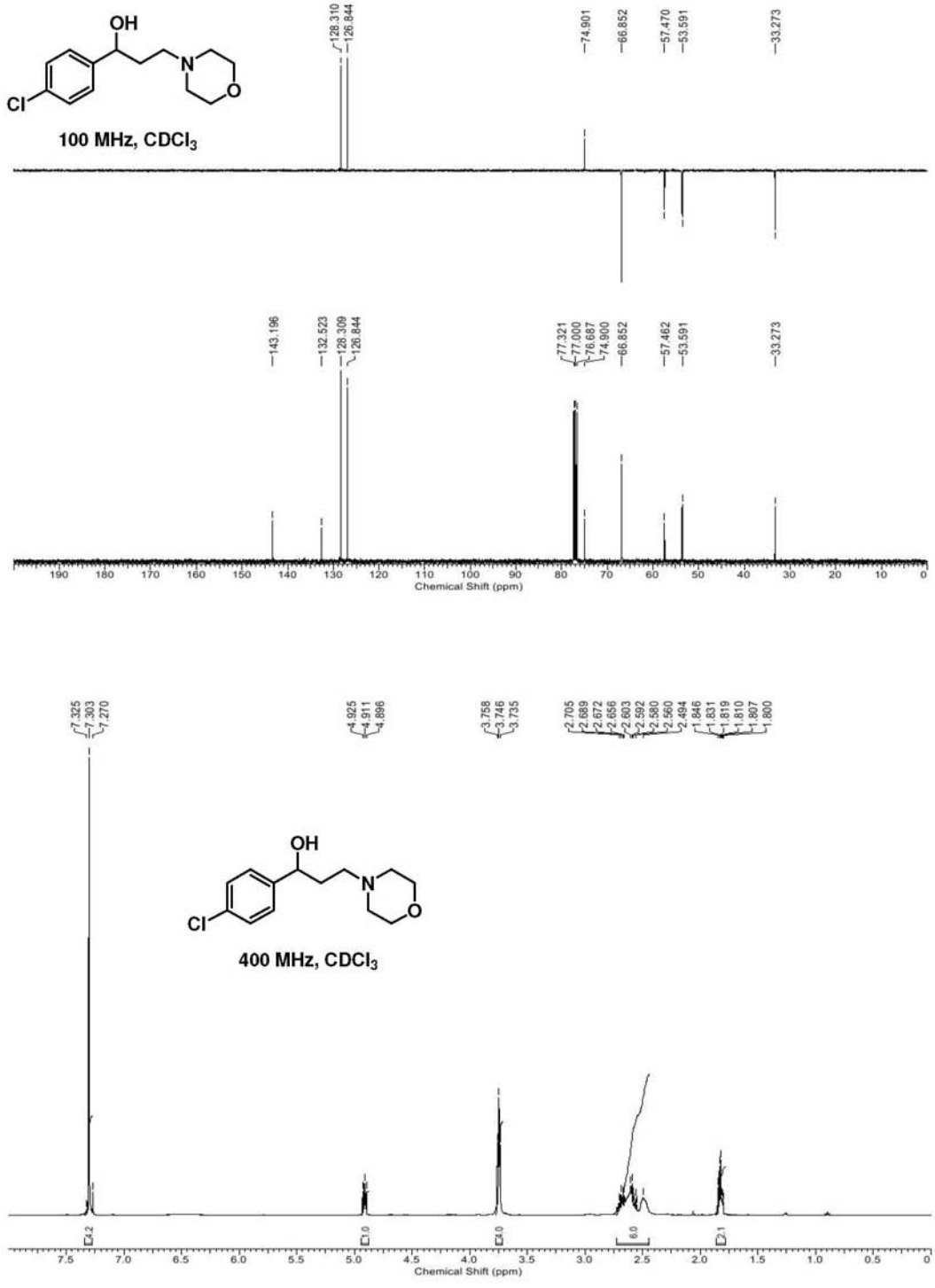
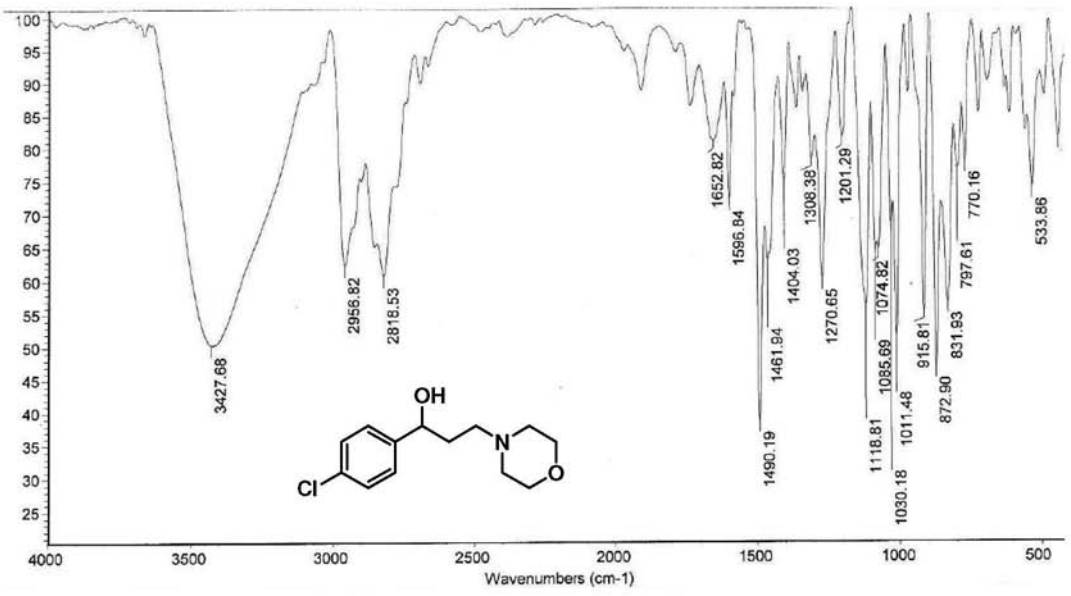



**Figure S55.** $^{1}H$ and $^{13}C$ spectra for compound **11m**.



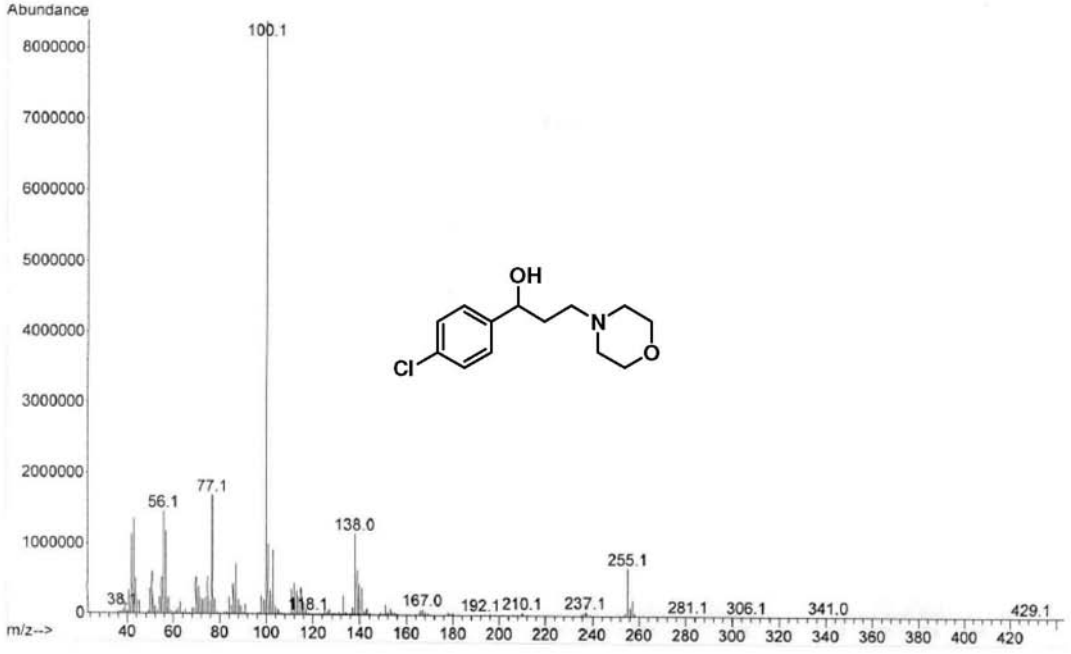




**Figure S56.** IR and MS spectra for compound **11m**.

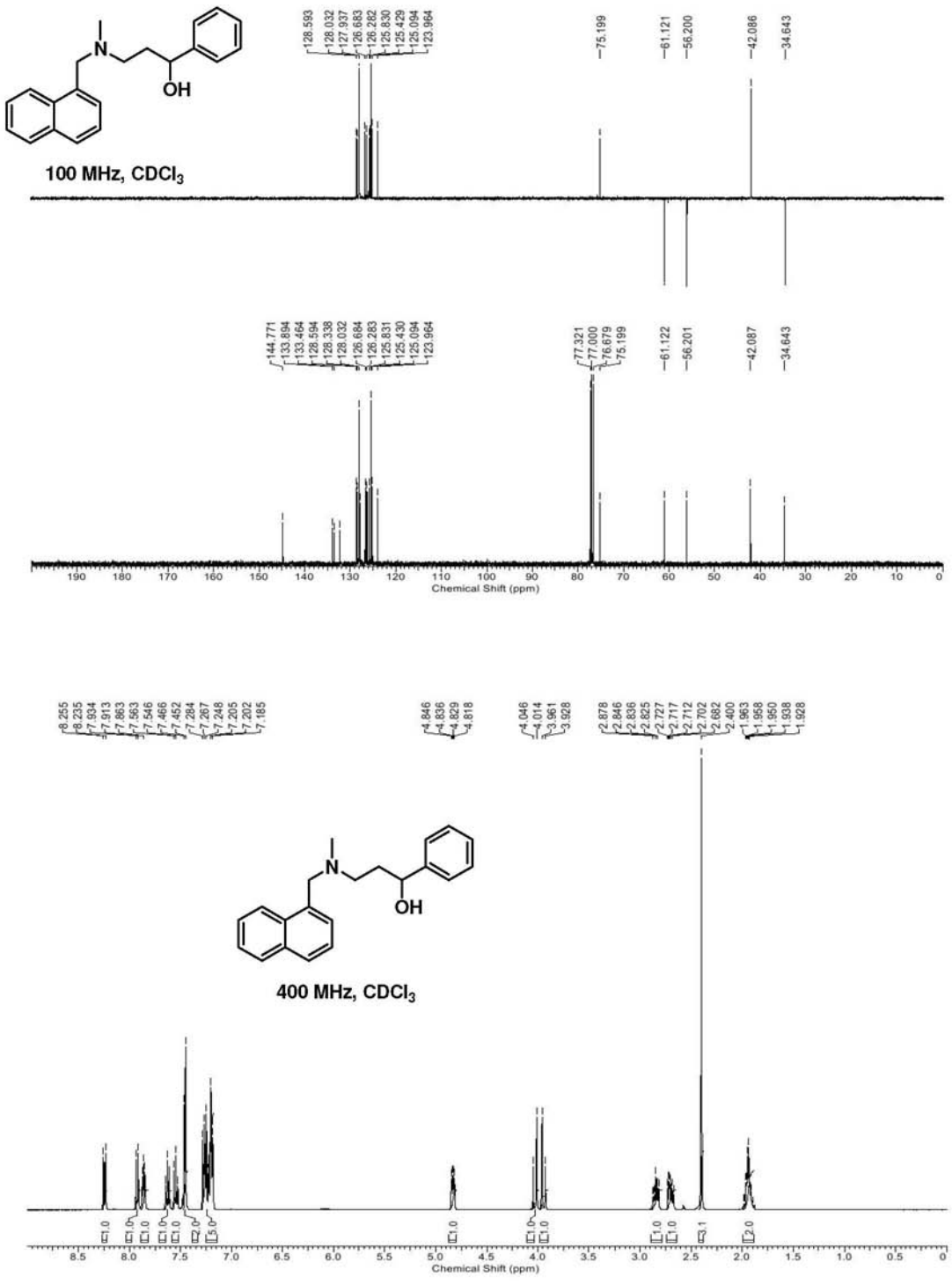
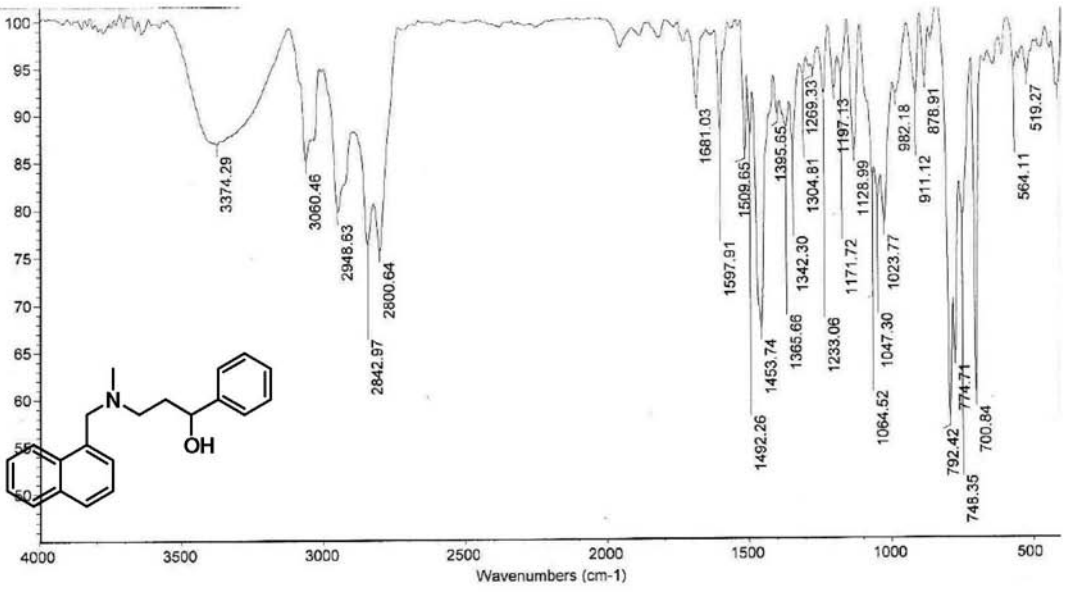



**Figure S57.** [1]H and [13]C spectra for compound **11o**.



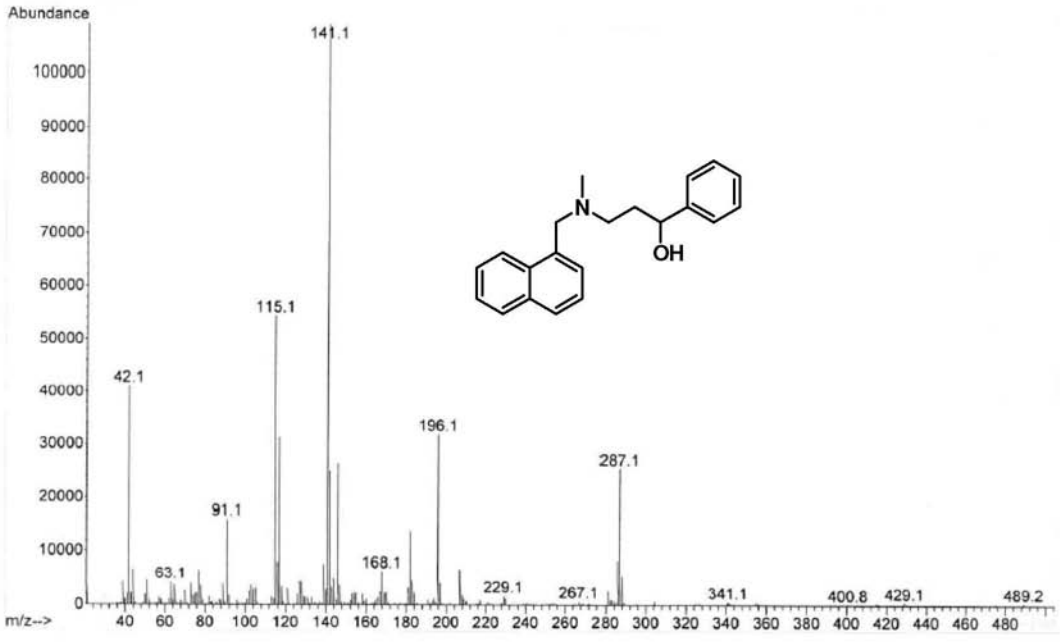




**Figure S58.** IR and MS spectra for compound **11o**.

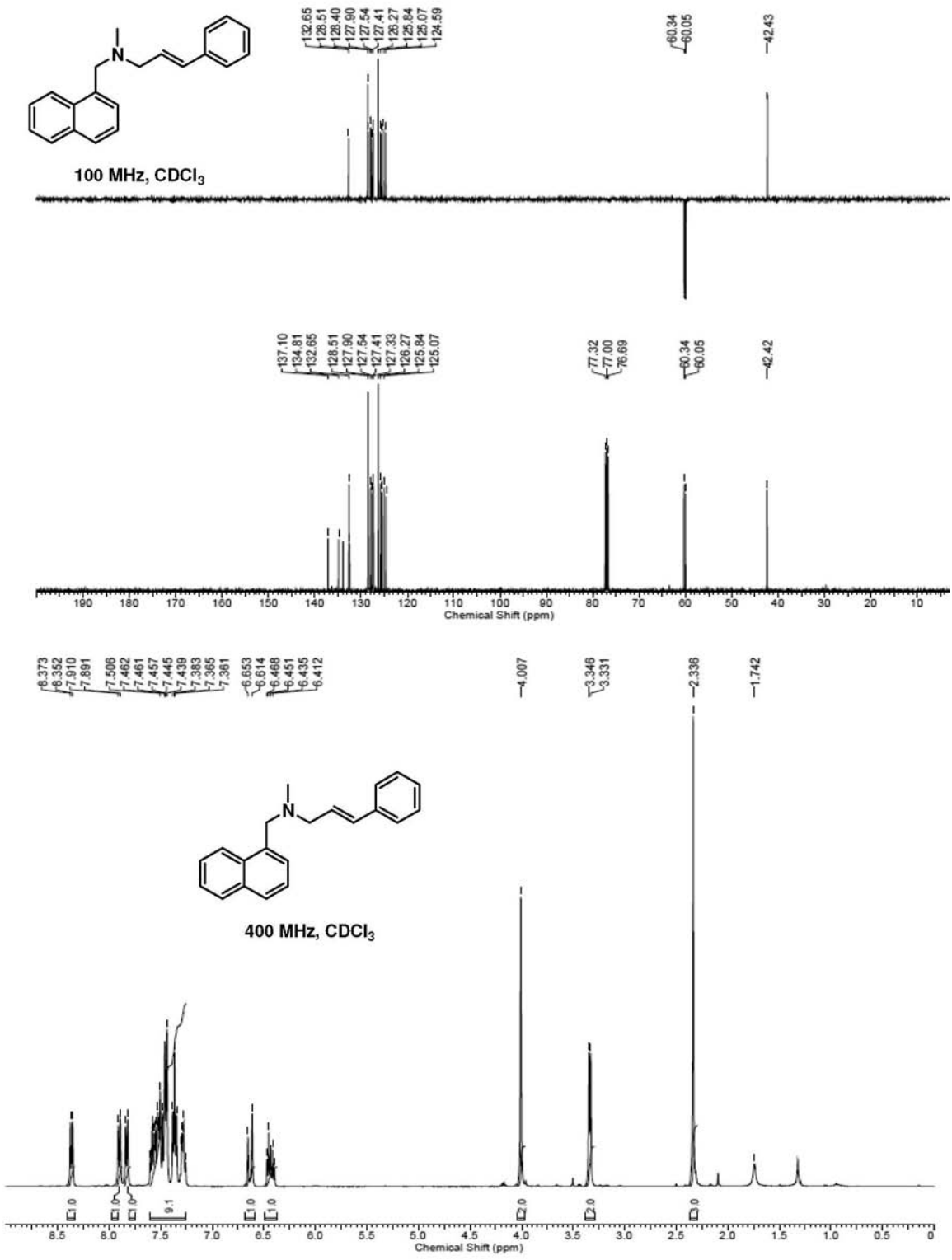
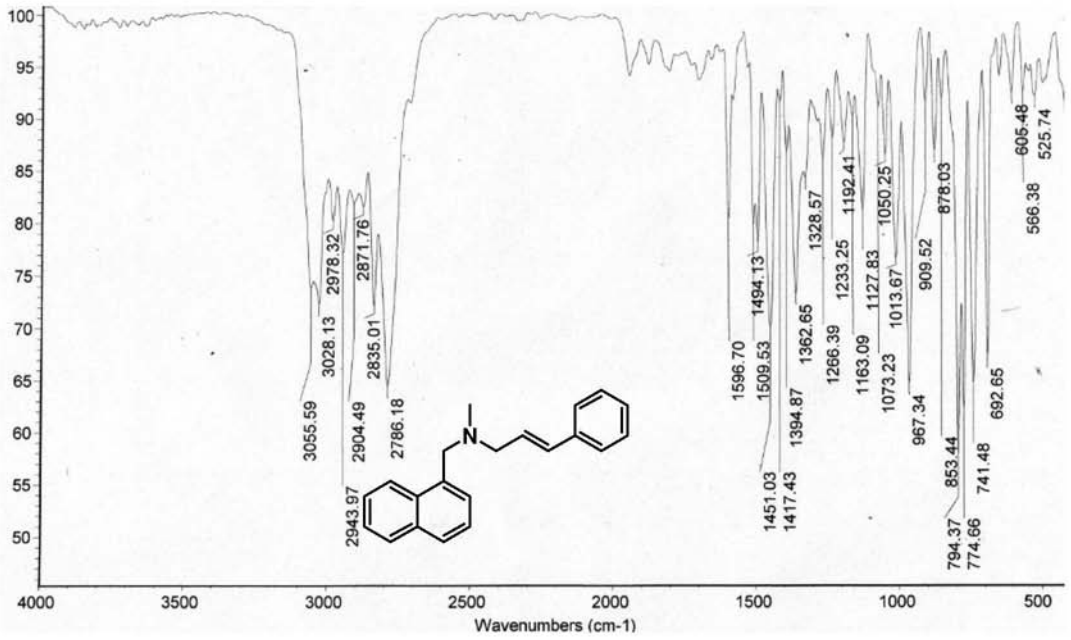



**Figure S59.** $^{1}H$ and $^{13}C$ spectra of Naftifine®.



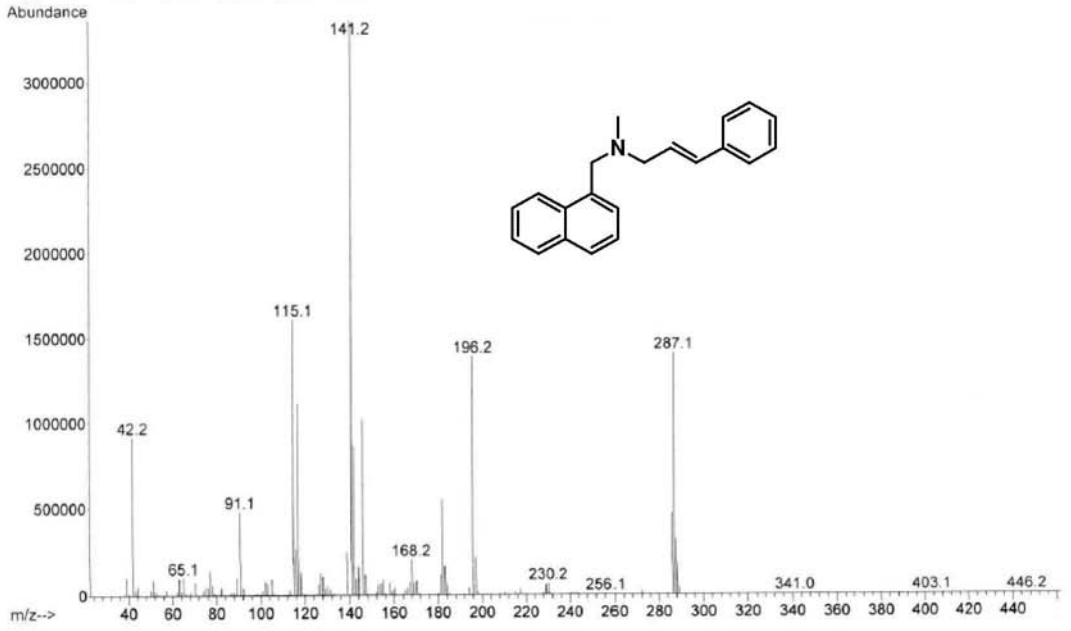




**Figure S60.** IR and MS spectra of Naftifine®.