

Experimental conditions for the preparation of compounds **8-11**, **15**, **17**, **20**, **23-26**:

Cyclopropyl-thiophen-2-yl-methanol (10). To a solution of cyclopropyl-2-thienylketone **5** (25 g, 0.16 mol) in MeOH (150 mL) was added portionwise an excess of sodium borohydride. After stirring at room temperature for 1.5 h, the solvent was evaporated under *vacuo* and the reaction mixture was poured into 5 N aqueous NaOH and extracted with CH₂Cl₂ (3 x 150 mL). The organic layer was dried over anhydrous MgSO₄ and concentrated under *vacuo* to give the alcohol **10** (25.33 g, quantitative yield) as a colorless oil : ¹H NMR (250 MHz, CDCl₃) δ 0.42-0.65 (m, 4H), 1.31 (m, 1H), 2.2 (s, 1H), 4.24 (dd, *J* = 5, 14Hz, 1H), 7.00 (dd, *J* = 2, 8Hz, 1H), 7.07 (dd, *J* = 2, 8Hz, 1H), 7.29 (dd, *J* = 2, 8Hz, 1H); ¹³C NMR (62.89 MHz, CDCl₃) δ 3.1, 3.7, 19.4, 74.5, 123.7, 124.6, 126.6, 148.0; IR (neat) 3369, 2872, 1430, 1027 cm⁻¹; MS (EI) *m/z* 154 (M⁺), 84 (C₄H₄S⁺).

tert-Butyl-(cyclopropyl-thiophen-2-yl-methoxy)-dimethyl-silane (11). To a solution of alcohol **10** (25.33 g, 0.16 mol) and imidazole (14.62 g, 0.21 mol) in DMF (50 mL) was added dropwise, at 0 °C, TBDMSCl (19.51 g, 0.16 mol) in DMF (15 mL) and the solution was stirred at room temperature overnight. The reaction mixture was poured into water (400 mL) and extracted with Et₂O (4 x 150 mL). The organic layer was dried over anhydrous MgSO₄ and concentrated under *vacuo* to give the silyl derivative **11** (23.13 g, 95% yield) as a colorless oil : ¹H NMR (250 MHz, CDCl₃) δ - 0.05 (s, 3H), 0.08 (s, 3H), 0.43-0.55 (m, 4H), 0.9 (s, 9H), 1.22 (m, 1H), 4.53 (d, *J* = 15Hz, 1H), 6.98 (m, 2H), 7.20 (dd, *J* = 2, 7Hz, 1H); ¹³C NMR (62.89 MHz, CDCl₃) δ - 4.6, - 4.5, 2.8, 3.2, 18.4, 20.4, 25.9, 73.6, 122.6, 123.8, 126.1, 150.3 ; IR (neat) 3435, 2957, 1472, 1252, 1058 cm⁻¹; MS (EI) *m/z* 268 (M⁺), 137 (C₈H₉S⁺).

3-(4-{5-[(tert-Butyl-dimethyl-silanyloxy)-cyclopropyl-methyl]-thiophen-2-yl}-but-3-enyl)-pyridine (15). To a vigorously stirred suspension of phosphonium salt **14** (33.55 g, 72.5 mmol) in THF (1 L) at 0 °C was added NaH (3.9 g, 0.16 mol) and the mixture was stirred at the same temperature for 30 min. After cooling to -78 °C, aldehyde **13** (14.32 g, 48.3 mmol) in THF (60 mL) was added dropwise and stirring was continued at room temperature overnight. The reaction mixture was poured into a saturated aqueous solution of NH₄Cl (300 mL) and extracted with AcOEt (4 x 250 mL). The organic layer was washed with water (100 mL), brine (100 mL), dried over anhydrous MgSO₄ and concentrated under *vacuo*.

The residue was purified by column chromatography (heptane/AcOEt : 90/10) on silica gel to furnish compound **15** (10.63 g, 55% yield) as a yellow oil : ^1H NMR (300 MHz, CDCl_3) δ 0.03 (s, 3H), 0.07 (s, 3H), 0.34-0.58 (m, 4H), 0.88 (s, 9H), 1.19 (m, 1H), 2.68-2.88 (m, 4H), 4.45 (d, J = 5Hz, 1H), 5.53 (dt, J = 5, 10Hz, 1H), 6.56 (d, J = 10Hz, 1H), 6.85 (d, J = 3Hz, 1H), 6.86 (d, J = 3Hz, 1H), 7.25 (dd, J = 4, 7Hz, 1H), 7.59 (dt, J = 7Hz, 1H), 8.54 (m, 2H) ; ^{13}C NMR (75.47 MHz, CDCl_3) δ - 4.6, - 4.5, 2.8, 3.3, 18.3, 20.2, 25.9, 30.5, 32.7, 73.7, 122.5, 123.4, 126.9, 127.2, 135.9, 136.9, 138.8, 147.5, 150.0, 150.3; IR (neat) 2955, 2929, 2856, 1472, 1057 cm^{-1} ; MS (IE) m/z 399 (M^+), 268 ($\text{C}_{17}\text{H}_{18}\text{NS}^+$), 93 ($\text{C}_6\text{H}_7\text{N}^+$); HRMS (EI) calcd for $\text{C}_{22}\text{H}_{33}\text{NOSSi}$ 399.2052, found 399.2034.

3-[9-(tert-Butyl-dimethyl-silanyloxy)-9-cyclopropyl-nonyl]-pyridine (17). To a solution of compound **15** (10.63 g, 26.6 mmol) in EtOH (300 mL) was added Na_2CO_3 (4 g) and a large excess of freshly prepared Raney nickel. After stirring under reflux for 2 h, another excess of Raney nickel was added and the mixture was stirred under reflux for 6 h. The resulting mixture was decanted, EtOH was collected and the catalyst was washed with petroleum ether (150 mL) CH_2Cl_2 (3 x 150 mL). The combined organic layers were washed with a saturated aqueous solution of NaHCO_3 , dried over anhydrous MgSO_4 , and concentrated under *vacuo*. Purification of the residue by column chromatography (heptane/AcOEt: 90/10) on silica gel afforded pyridine **17** (8.54 g, 85% yield) as a colorless oil : ^1H NMR (300 MHz, CDCl_3) δ 0.03 (s, 3H), 0.06 (s, 3H), 0.12-0.51 (m, 4H), 0.91 (s, 9H), 1.30 (m, 11H), 1.52 (m, 2H), 1.64 (m, 2H), 2.64 (t, J = 9Hz, 2H), 3.06 (dt, J = 9, 10Hz, 2H), 7.10 (dd, J = 6, 10Hz, 1H), 7.54 (d, J = 10Hz, 1H), 8.51 (m, 2H) ; ^{13}C NMR (62.89 MHz, CDCl_3) δ - 4.3, - 3.8, 2.3, 3.4, 17.5, 18.3, 25.5, 26.1, 29.3, 29.5, 29.7, 29.9, 31.2, 33.1, 38.4, 76.3, 123.3, 135.8, 137.2, 147.3, 150.1; IR (neat) 2928, 2855, 1463, 1253, 835, 774 cm^{-1} ; MS (IC) m/z 376 (MH^+), 244 ($\text{C}_{17}\text{H}_{26}\text{N}^+$).

1-Cyclopropyl-6-pyridin-3-yl-hexan-1-ol (20). To a solution of silyl derivative **16** (3.55 g, 10.6 mmol) in THF (35 mL) was added dropwise, at room temperature, Bu_4NF (1M solution in THF, 63.6 mmol, 63.6 mL). After stirring overnight, the reaction mixture was poured into H_2O (100 mL), extracted with AcOEt (4 x 100 mL), dried over anhydrous MgSO_4 and concentrated under *vacuo*. The residue was subjected to column chromatography (heptane /AcOEt : 1/1) on silica gel to furnish the alcohol **20** (2.22 g, 95% yield) as a deep yellow oil : ^1H NMR (250 MHz, CDCl_3) δ 0.23 (m, 2H), 0.49 (m, 2H), 0.89 (m, 1H), 1.32-1.73

(m, 8H), 2.12 (s, 1H), 2.63 (t, $J = 11$ Hz, 2H), 2.88 (dt, $J = 9, 12$ Hz, 1H), 7.24 (dd, $J = 6, 10$ Hz, 1H), 7.56 (dt, $J = 3, 10$ Hz, 1H), 8.51 (m, 2H); ^{13}C NMR (75.47 MHz, CDCl_3) δ 2.5, 2.8, 18.1, 25.6, 29.3, 31.5, 33.0, 37.2, 76.7, 123.3, 135.9, 137.9, 147.2, 149.9; IR (neat) 3369, 2931, 1577, 1081, 1026, 789 cm^{-1} ; MS (IC) m/z 220 (MH^+), 202 ($\text{C}_{14}\text{H}_{20}\text{N}^+$). HRMS (MALDI) calcd for $\text{C}_{14}\text{H}_{21}\text{NO}$ (MH^+) 220.17014, found 220.17059.

3-(12-Bromo-dodec-9-enyl)-pyridine (23). Treatment of alcohol **21** (2.16 g, 8.2 mmol) with ZnBr_2 (46 mg, 4.1 mmol) and Me_3SiBr (2.13 mL, 18.3 mmol) in the conditions used for the rearrangement of **20** gave bromide **23** (2.57 g, 96% yield) as a brown oil : ^1H NMR (300 MHz, CDCl_3) δ 1.09-1.37 (m, 10H), 1.52 (m, 2H), 1.93 (m, 2H), 2.45 (q, $J = 4$ Hz, 2H), 2.57 (t, $J = 4$ Hz, 2H), 3.29 (t, $J = 4$ Hz, 2H), 5.27-5.37 (dt, $J = 4, 14$ Hz, 1H), 5.43-5.53 (dt, $J = 4, 14$ Hz, 1H), 7.28 (dd, $J = 2, 4$ Hz, 1H), 7.58 (d, $J = 4$ Hz, 1H), 8.46 (dd, $J = 1, 4$ Hz, 1H), 8.50 (s, 1H); ^{13}C NMR (75.47MHz, CDCl_3) δ 28.7, 28.8, 28.9, 29.0, 30.9, 32.3, 32.7, 32.8, 35.9, 123.0, 126.2, 133.7, 135.5, 137.7, 146.9, 149.7; MS (IC) m/z 324 (MH^+), 244 ($\text{C}_{17}\text{H}_{26}\text{N}^+$).

3-(9-azido-non-6-enyl)-pyridine (24). The crude bromide **25** (3.28 g, 11.7 mmol) was immediately added to a suspension of finely powdered NaN_3 (3.8g, 58.5 mmol) in dry DMF (40 mL). After stirring overnight at 60 $^\circ\text{C}$, the mixture was poured into H_2O (50 mL) and extracted with Et_2O (3 x 150 mL). The combined organic layers were washed with water (100 mL), brine (100 mL), dried over anhydrous Na_2SO_4 and concentrated under *vacuo*. The residue was purified by column chromatography (heptane/AcOEt : 80/20) on silica gel to yield pure azide **24** (1.89 g, 66% yield) as a pale yellow oil : ^1H NMR (200 MHz, CDCl_3) δ 1.38 (m, 4H), 1.62 (q, $J = 4$ Hz, 2H), 2.02 (m, 2H), 2.29 (m, 2H), 2.63 (t, $J = 7$ Hz, 2H), 3.27 (t, $J = 7$ Hz, 2H), 5.40 (dt, $J = 6, 15$ Hz, 1H), 5.58 (dt, $J = 6, 15$ Hz, 1H), 7.24 (dd, $J = 4, 8$ Hz, 1H), 7.54 (dt, $J = 2, 8$ Hz, 1H), 8.49 (m, 2H); ^{13}C NMR (62.89 MHz, CDCl_3) δ 28.6, 29.0, 31.0, 32.5, 33.0, 51.2, 123.3, 125.8, 133.7, 135.82, 137.90, 147.25, 150.01; IR (neat) 2930, 2856, 2097, 1422, 1262 cm^{-1} ; MS (IE) m/z 244 (M^+), 202 ($\text{C}_{14}\text{H}_{20}\text{N}^+$), 188 ($\text{C}_{13}\text{H}_{18}\text{N}^+$), 92 ($\text{C}_6\text{H}_6\text{N}^+$). HRMS (MALDI) calcd for $\text{C}_{14}\text{H}_{20}\text{N}_4$ (MH^+) 245.17662, found 245.17769.

3-(12-Azido-dodec-9-enyl)-pyridine (25). The crude bromide **23** (2.57 g, 8 mmol) was treated in the conditions used for preparation of azide **24** to give azide **25** (2.18 g, 95% yield) as a pale yellow oil: ^1H

NMR (250 MHz, CDCl₃) δ 1.27 (m, 10H), 1.58 (m, 2H), 1.93 (q, J = 7Hz, 2H), 2.23 (q, J = 7Hz, 2H), 2.56 (t, J = 7Hz, 2H), 3.20 (t, J = 7Hz, 2H), 5.30 (dt, J = 7, 16Hz, 1H), 5.49 (dt, J = 7, 16Hz, 1H), 7.10 (dd, J = 5, 7Hz, 1H), 7.39 (dt, J = 2, 7Hz, 1H), 8.32 (m, 2H); ¹³C NMR (69.82 MHz, CDCl₃) δ 28.8, 29.0, 29.1, 30.9, 32.0, 32.3, 32.7, 50.8, 122.9, 125.2, 133.6, 135.4, 137.6, 146.9, 149.7; IR (neat) 2927, 2855, 2097, 1422, 1261, 1026, 714 cm⁻¹; MS (IC) m/z 287 (MH⁺), 259 (C₁₇H₂₆N₂⁺), 244 (C₁₇H₂₆N⁺), 230 (C₁₆H₂₄N⁺).

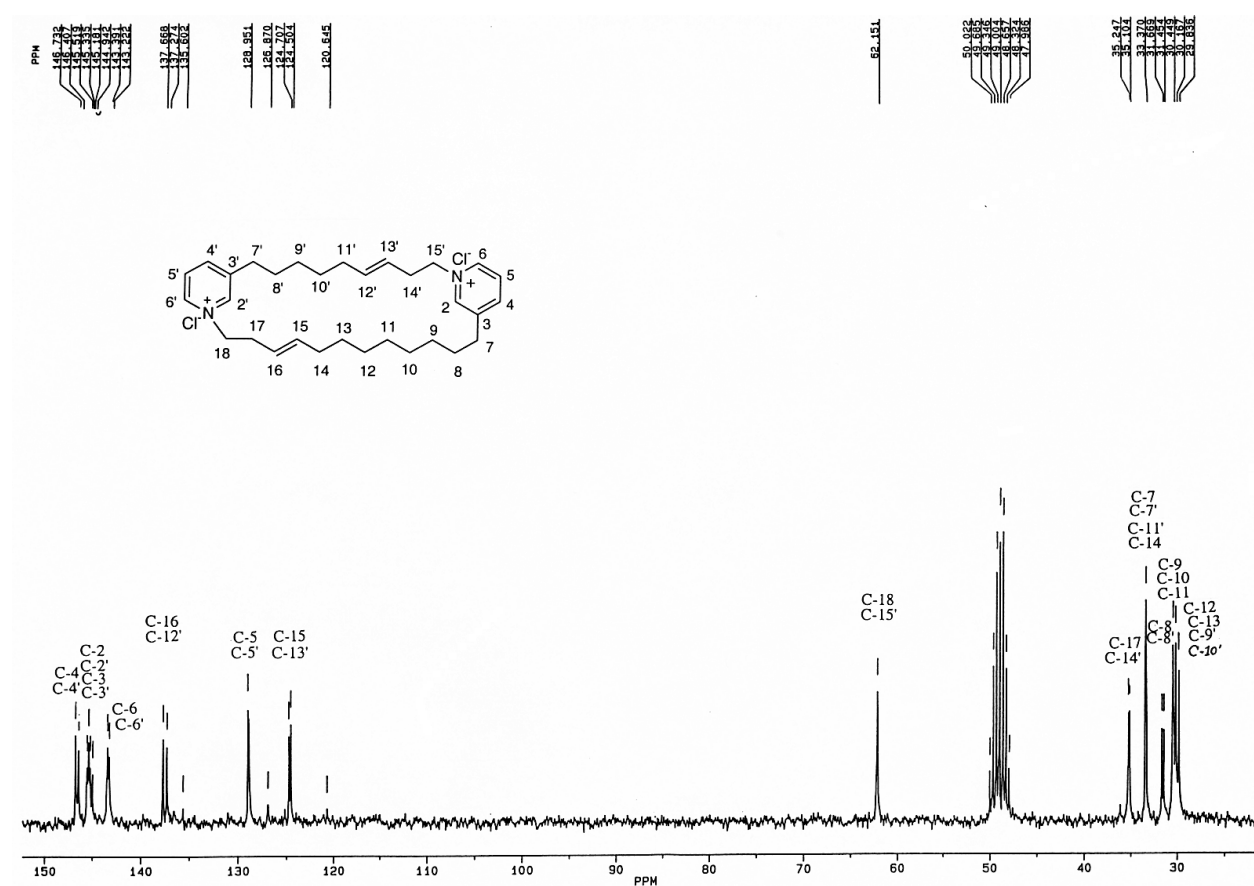
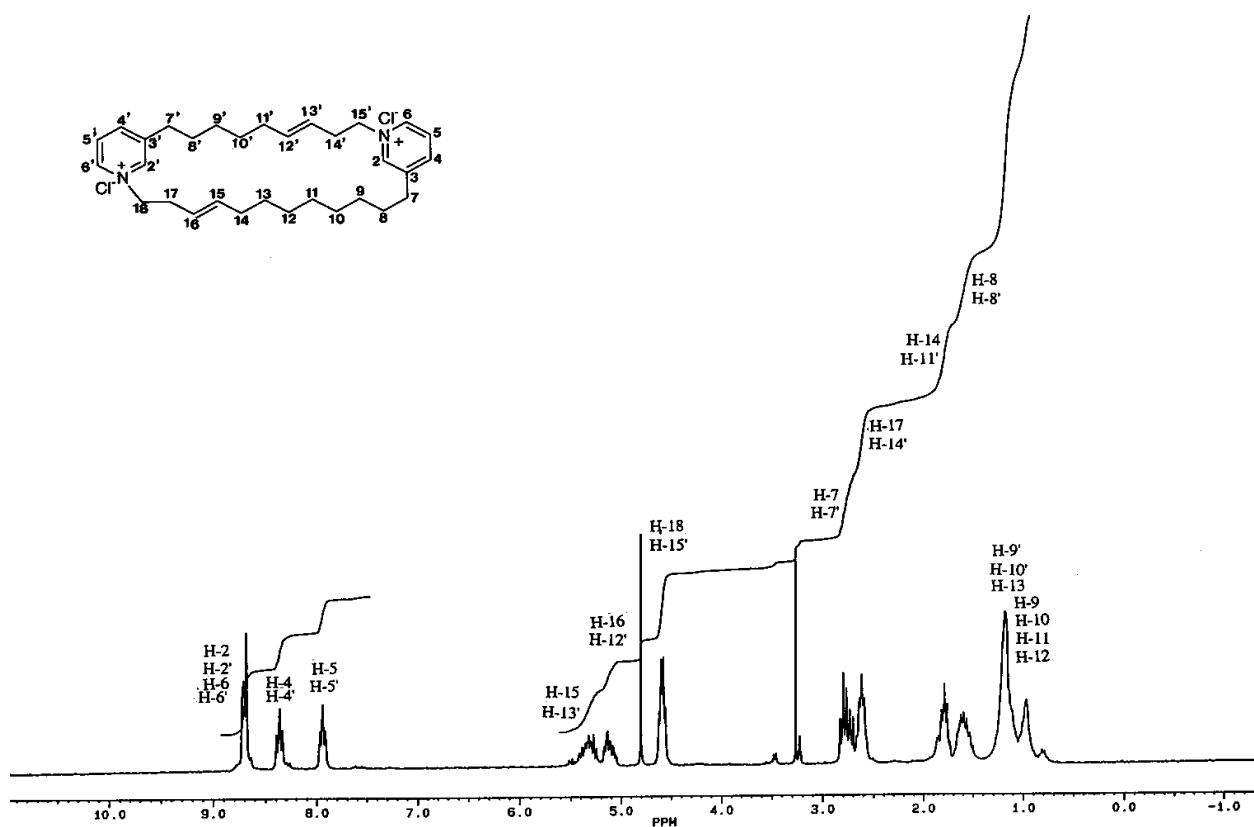
9-Pyridin-3-yl-6-non-enylamine (8). Triphenylphosphine (892 mg, 3.4 mmol) was added to a solution of the azide **24** (488 mg, 2 mmol) in pyridine (2 mL) at 0 °C. The reaction was allowed to reach room temperature and stirred overnight. After cooling to 0 °C, concentrated aqueous ammonia (1 mL) was added and stirring was continued at room temperature overnight. After removal of pyridine under reduced pressure, 2N HCl (20 mL) was added and the mixture was extracted with Et₂O (4 x 50 mL). The acidic phase was basified by portionwise addition of solid anhydrous Na₂CO₃, diluted with water and extracted with CH₂Cl₂ (3 x 50 mL). Drying over anhydrous Na₂SO₄ and concentration *in vacuo* afforded the amine **8** (403 mg, 92% yield) as a pale yellow oil: ¹H NMR (250 MHz, CDCl₃) δ 1.27-1.45 (m, 4H), 1.59 (m, 2H), 1.71 (s, 2H), 2.00 (m, 2H), 2.12 (m, 2H), 2.57 (t, J = 12Hz, 2H), 2.69 (t, J = 12Hz, 2H), 5.2-5.64 (m, 2H), 7.15 (dd, J = 6, 12Hz, 1H), 7.46 (dt, J = 2, 12Hz, 1H), 8.37 (m, 2H); ¹³C NMR (62.89 MHz, CDCl₃) δ 28.1, 28.8, 30.5, 32.0, 32.5, 36.2, 41.2, 122.8, 127.0, 132.2, 135.3, 137.4, 146.7, 149.5; IR (neat) 3233, 2927, 2854, 1436, 1027, 970, 713 cm⁻¹; MS (IC) m/z 219 (MH⁺). HRMS (MALDI) calcd for C₁₄H₂₂N₂ (MH⁺) 219.18612, found 219.18536.

12-Pyridin-3-yl-dodec-3-enylamine (9). Triphenylphosphine (892 mg, 3.4 mmol) was added to a solution of the azide **25** (572 mg, 2 mmol) in pyridine (2 mL) at 0 °C. The reaction was allowed to reach room temperature and stirred overnight. After cooling to 0 °C, concentrated aqueous ammonia (1 mL) was added and stirring was continued at room temperature overnight. After removal of pyridine under reduced pressure, 2N HCl (25 mL) was added and the mixture was extracted with Et₂O (4 x 50 mL). The acidic phase was basified by portionwise addition of solid anhydrous Na₂CO₃, diluted with H₂O and extracted with CH₂Cl₂ (3x50 mL). Drying over anhydrous Na₂SO₄ and concentration under *vacuo* afforded the amine **9** (479 mg, 92% yield) as a pale yellow oil : ¹H NMR (250 MHz, CDCl₃) δ 1.27 (m, 10H), 1.59 (m, 2H), 1.96 (m, 2H), 2.34 (m, 2H), 2.56 (t, J = 5Hz, 2H), 2.91 (t, J = 5Hz, 2H), 5.27 (dt, J = 5, 13Hz, 1H),

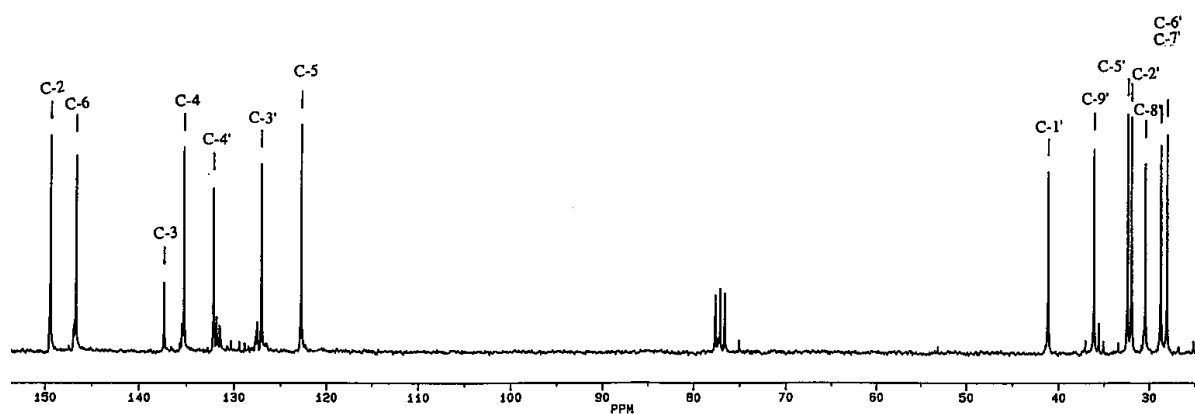
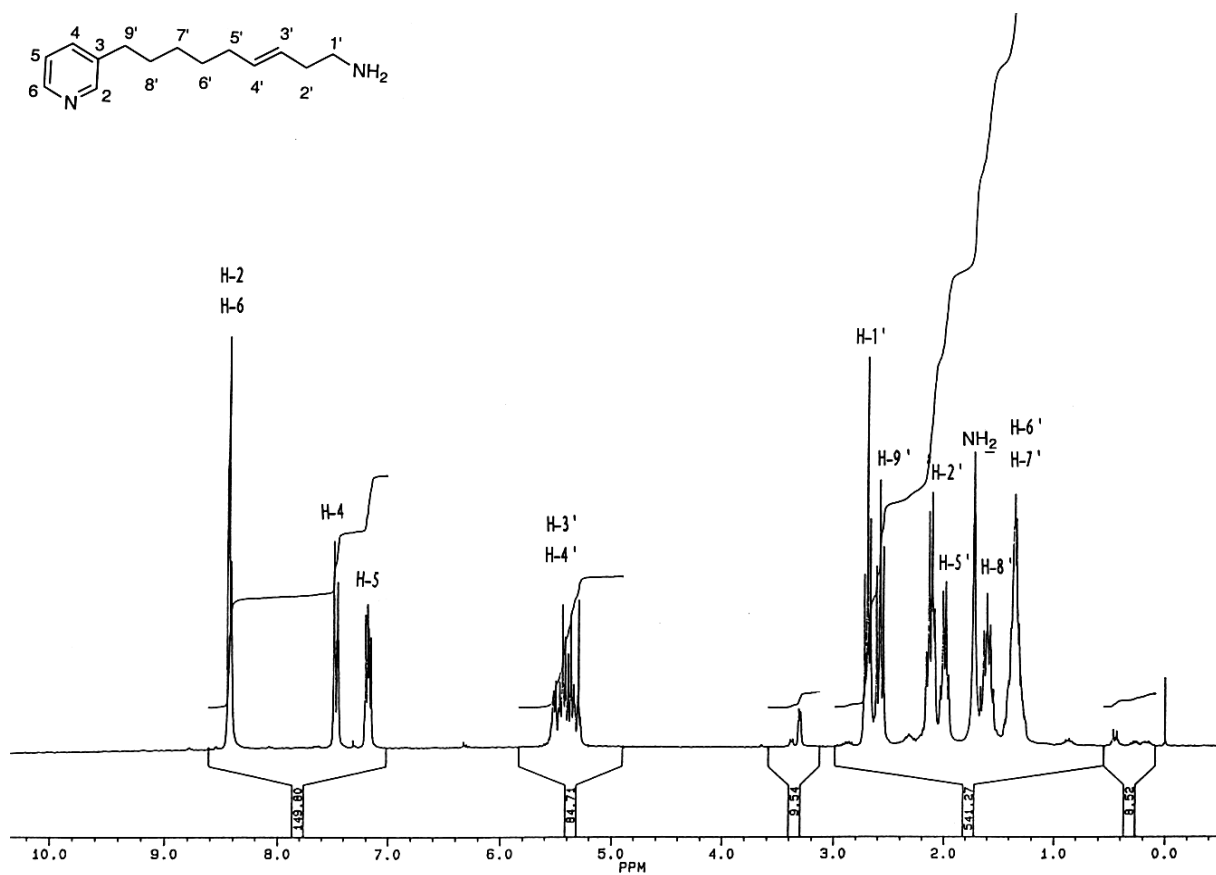
5.54 (dt, $J = 5$, 13Hz, 1H), 6.08 (s, 2H), 7.18 (dd, $J = 3$, 7Hz, 1H), 7.42 (d, $J = 7$ Hz, 1H), 8.35 (m, 2H) ; ^{13}C NMR (69.82 MHz, CDCl_3) δ 29.1, 29.3, 29.3, 31.1, 32.3, 32.6, 33.0, 40.3, 123.4, 124.6, 134.8, 136.0, 138.1, 147.1, 149.9 ; IR (neat) 3367, 2926, 2853, 1422, 1026, 714 cm^{-1} ; MS (ESI) m/z 261 (MH^+) ; HRMS (IC) calcd for $\text{C}_{17}\text{H}_{29}\text{N}_2$ (MH^+) 261.2331, found 261.2343.

(12-Pyridin-3-yl-dodec-3-enyl)-carbamic acid *tert*-butylester (26). To the amine **9** (416 mg, 1.6 mmol) in CH_2Cl_2 (10 mL) was added dropwise, at 0 °C, a solution of di-*tert*-butyldicarbonate (419 mg, 1.92 mmol) in CH_2Cl_2 (2 mL). After stirring at room temperature overnight, a mixture of $\text{H}_2\text{O}/\text{NaHCO}_3$ (7 : 1) was added and the product was extracted with CH_2Cl_2 (3 x 50 mL). The organic layer was dried over anhydrous Na_2SO_4 and concentrated *in vacuo*. Purification of the residue by column chromatography (heptane/AcOEt : 80/20) on silica gel afforded the protected amine **27** (537 mg, 93% yield) as a yellow oil : ^1H NMR (300 MHz, CDCl_3) δ 1.23 (m, 10H), 1.36 (s, 9H), 1.54 (m, 2H), 1.88 (m, 2H), 2.05 (m, 2H), 2.50 (t, $J = 5$ Hz, 2H), 3.05 (m, 2H), 4.75 (s, 1H), 5.24 (dt, $J = 4$, 17Hz, 1H), 5.39 (dt, $J = 4$, 17Hz, 1H), 7.11 (dd, $J = 3$, 5Hz, 1H), 7.42 (d, $J = 5$ Hz, 1H), 8.38 (m, 2H); ^{13}C NMR (75.47 MHz, CDCl_3) δ 27.2, 28.3, 29.0, 31.0, 32.5, 32.9, 33.0, 40.2, 53.3, 78.8, 123.1, 126.5, 133.1, 135.6, 137.8, 147.1, 149.8, 155.9; IR (neat) 3351, 2928, 1710, 1523, 1365, 1174, 968 cm^{-1} ; MS (IC) m/z 361 (MH^+).

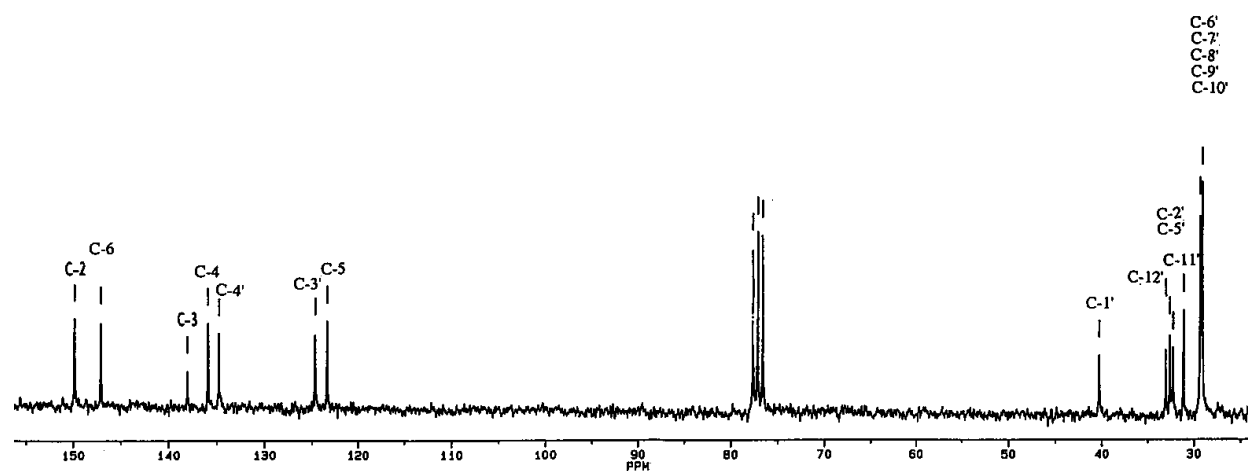
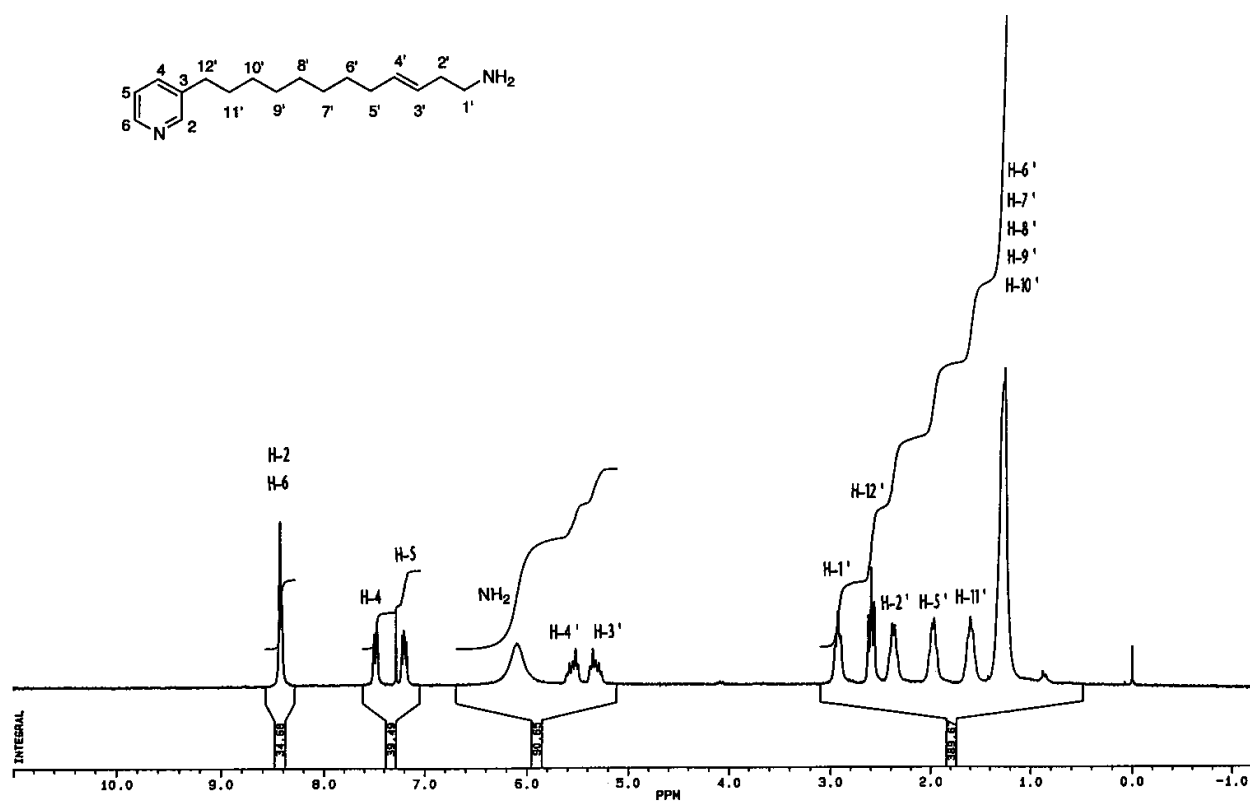
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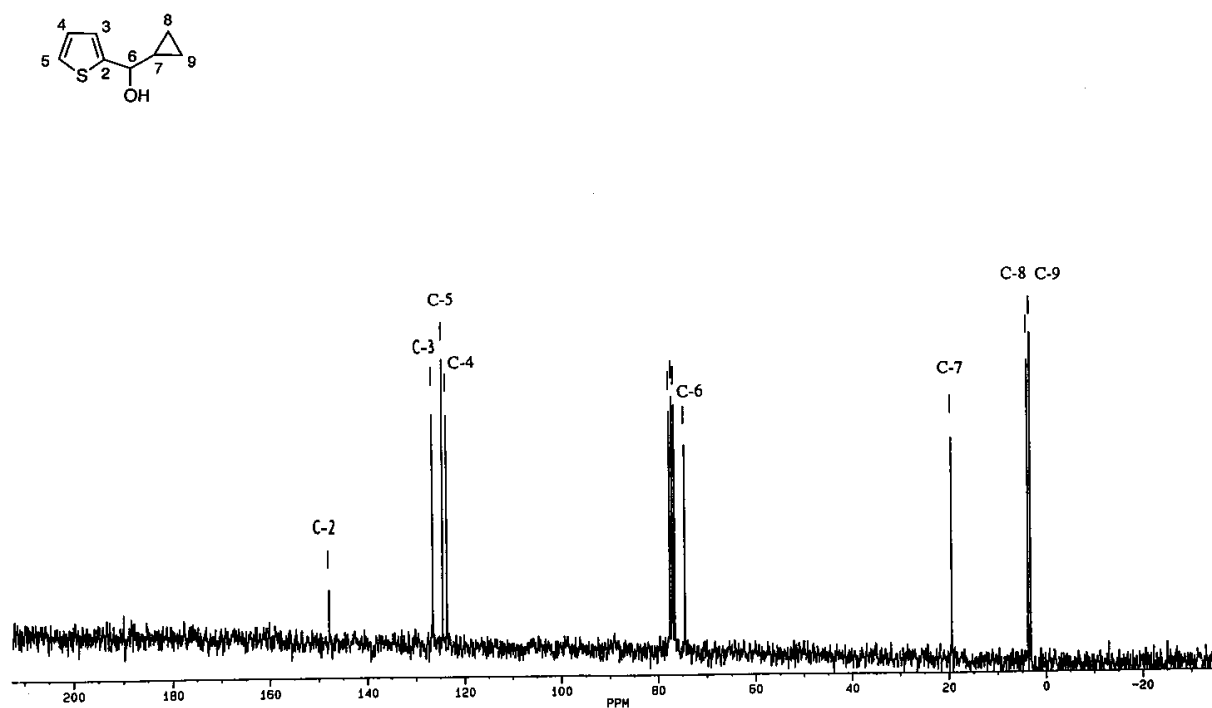
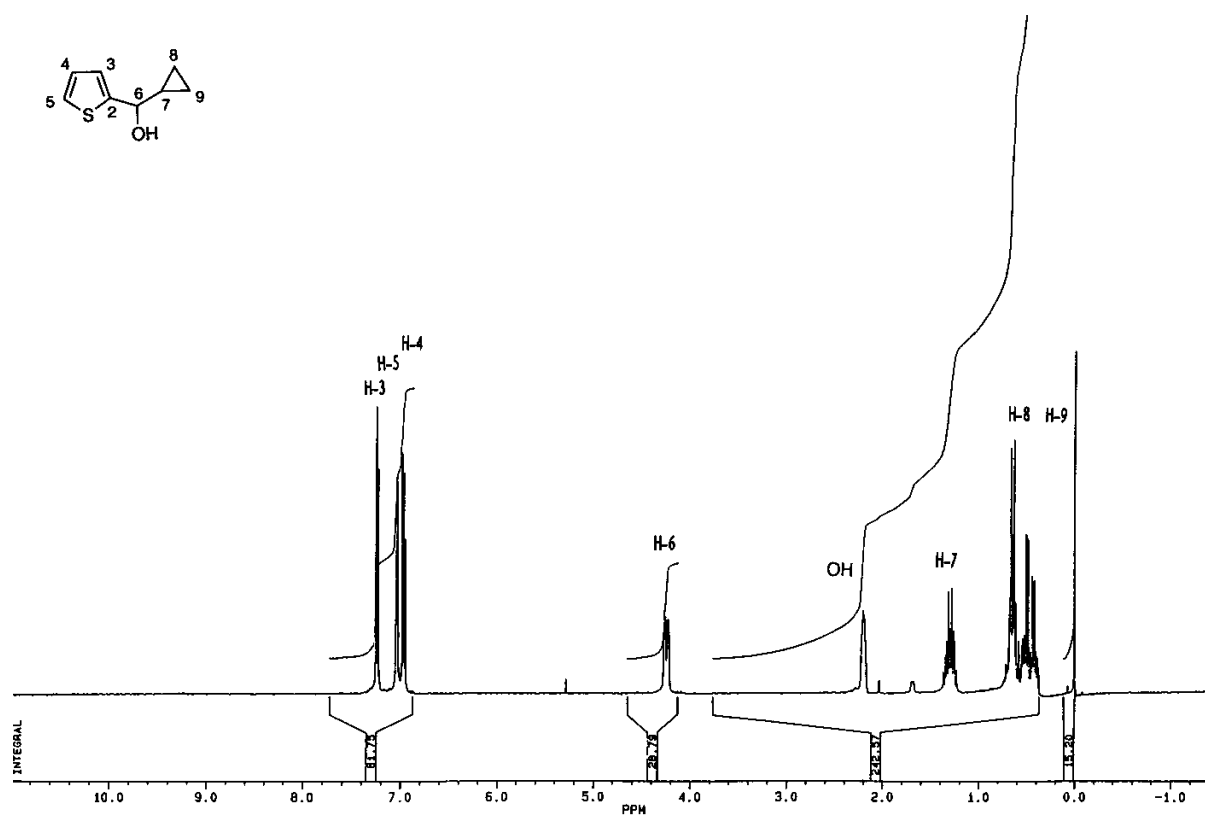
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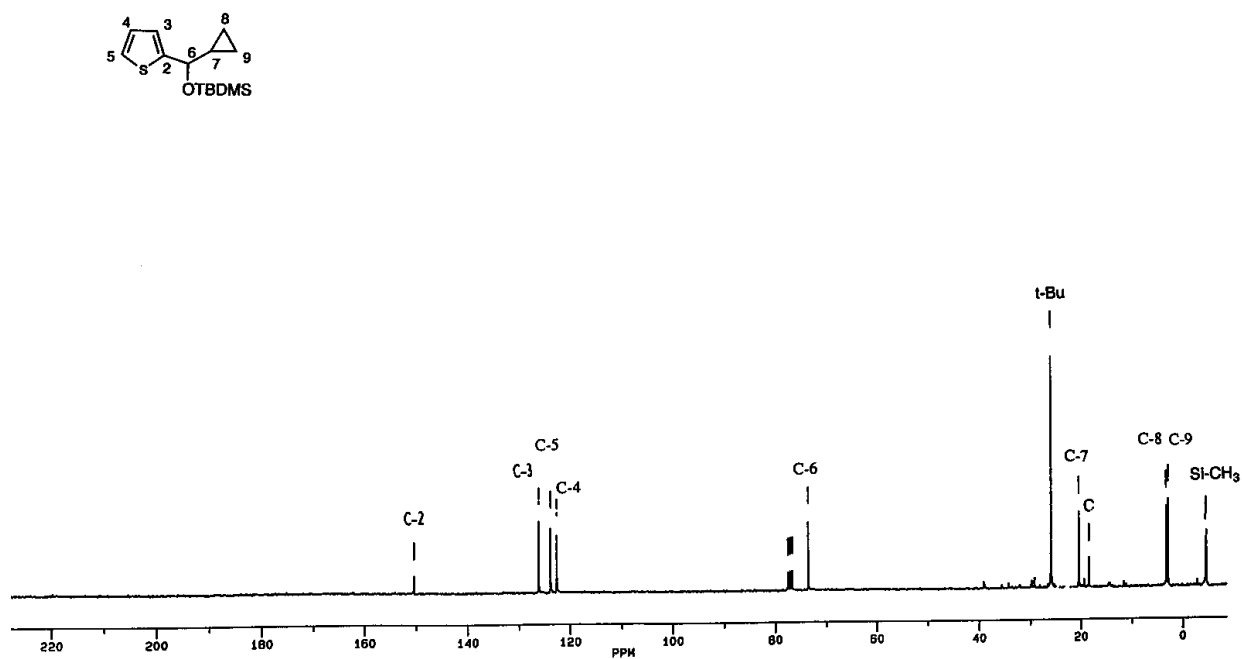
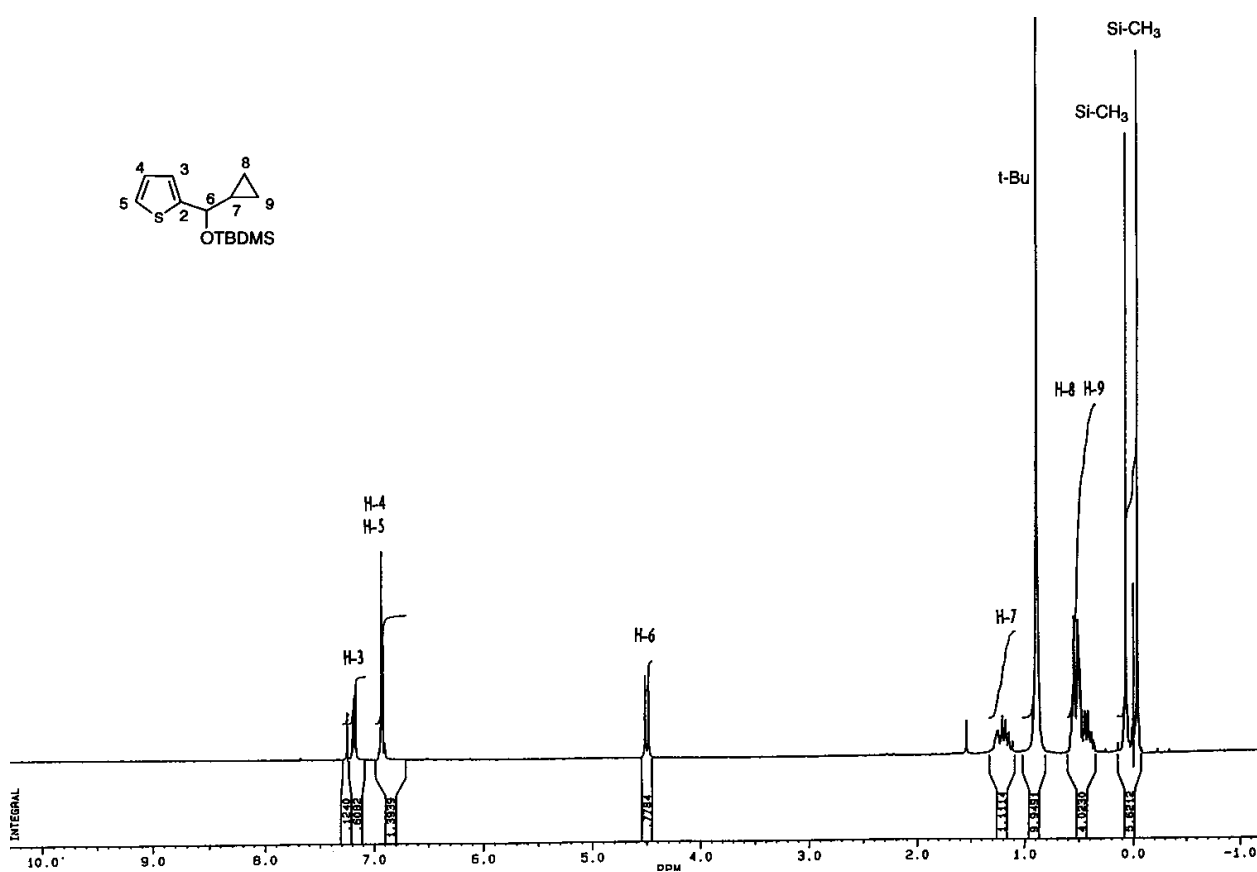
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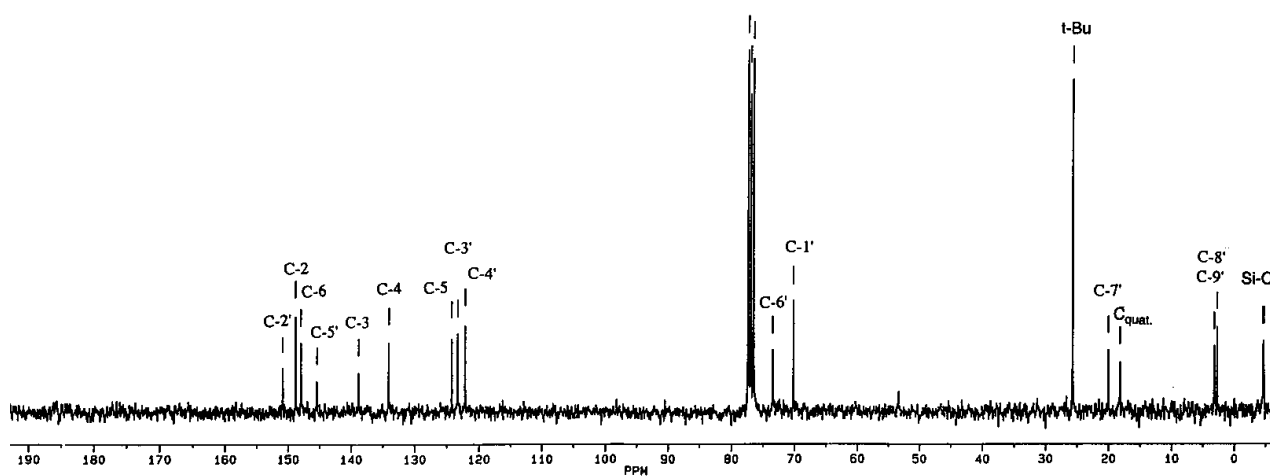
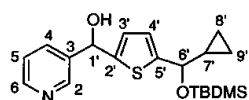
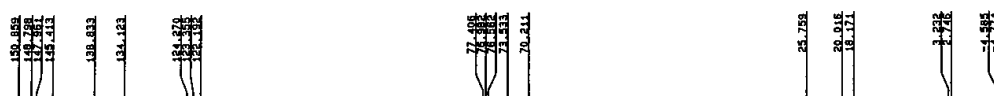
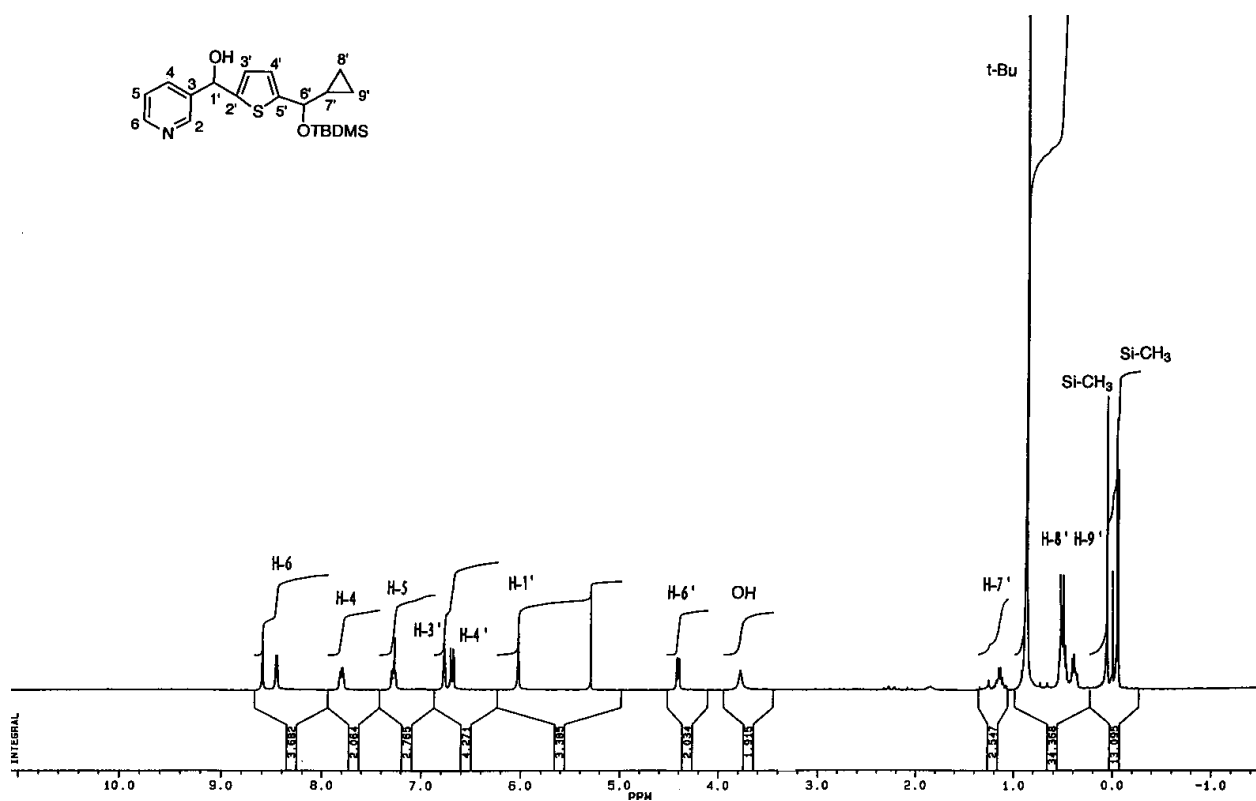
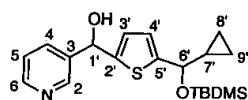
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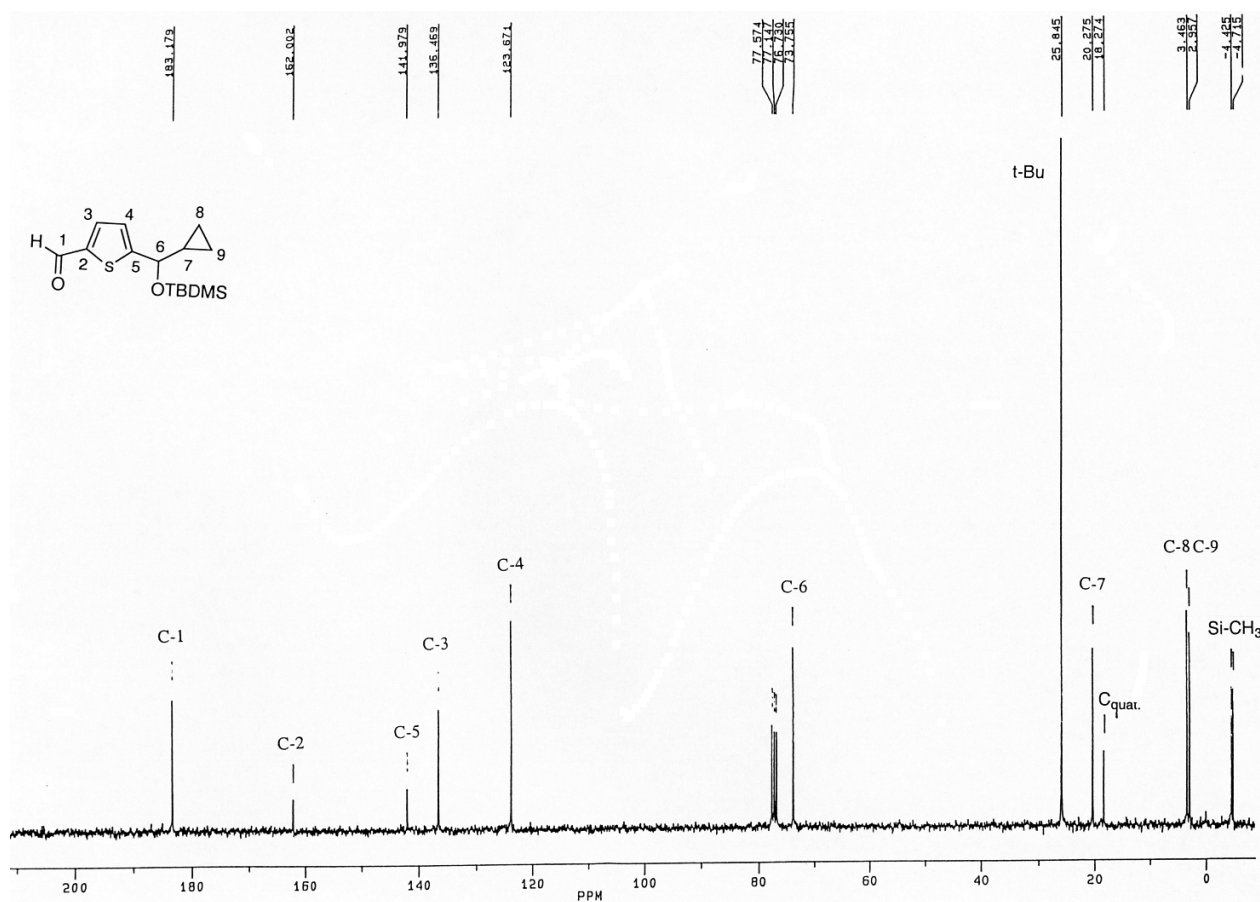
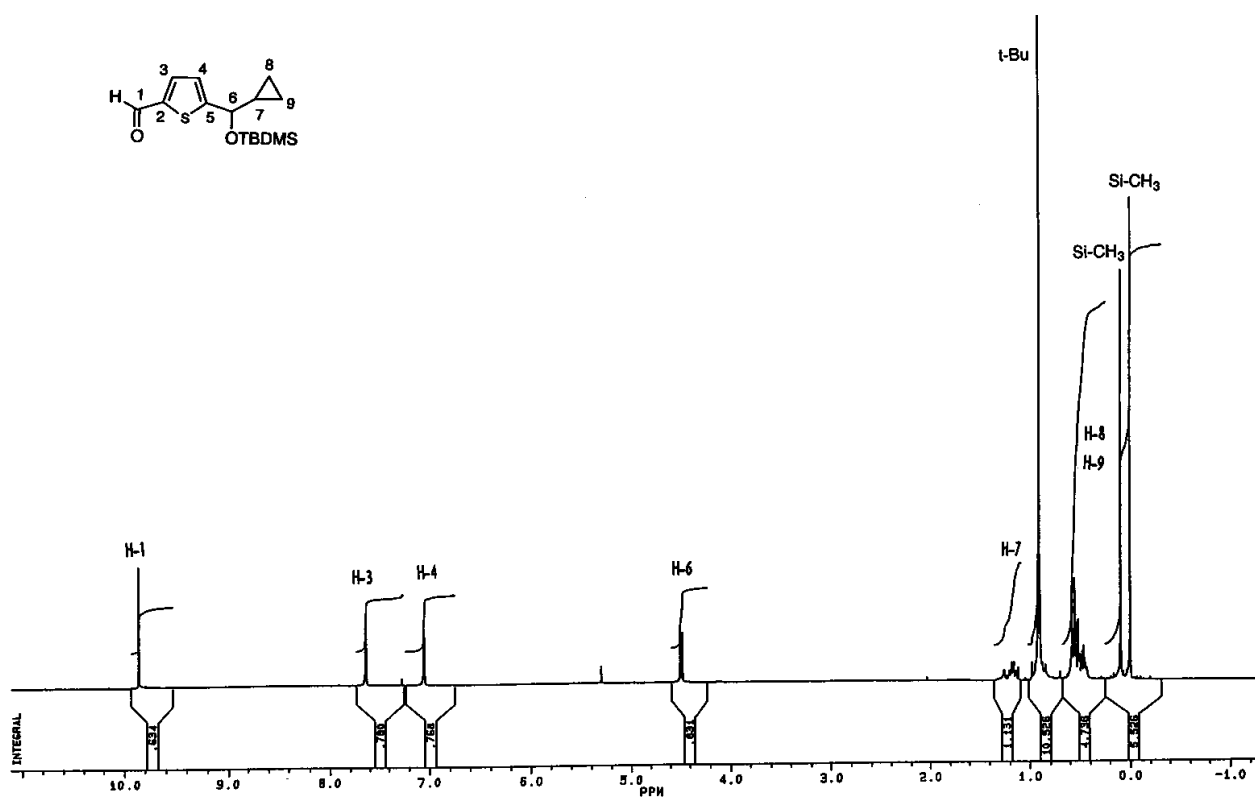
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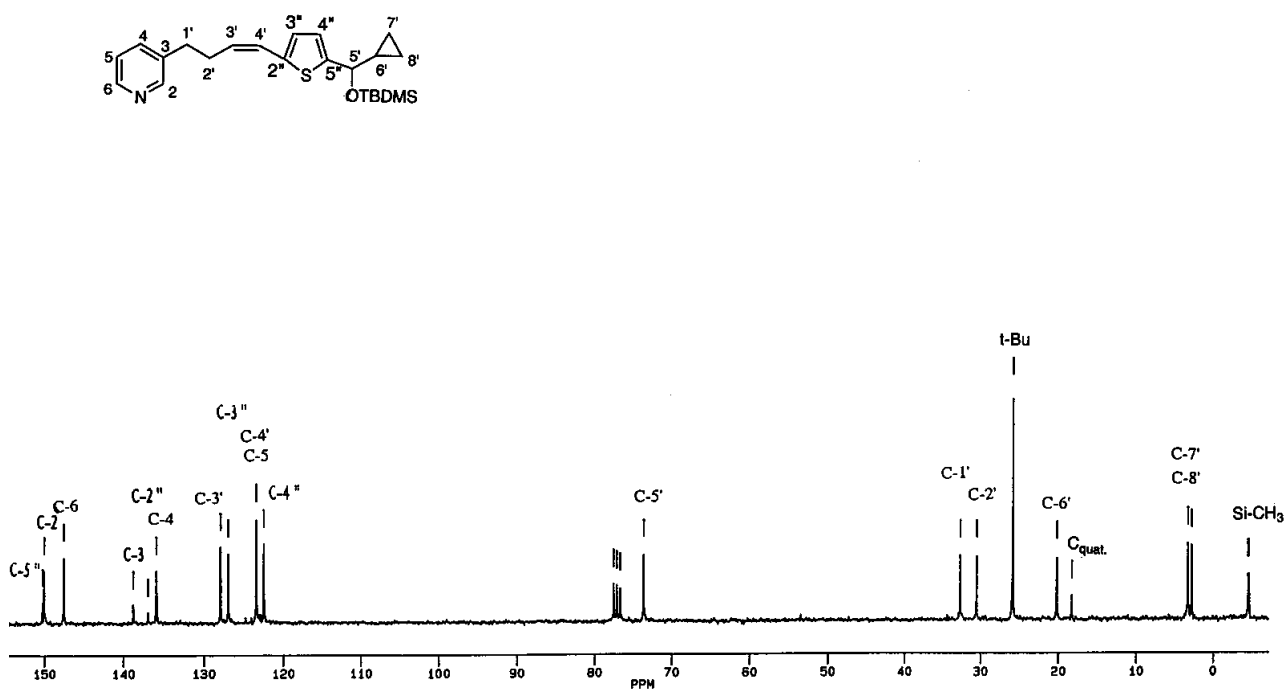
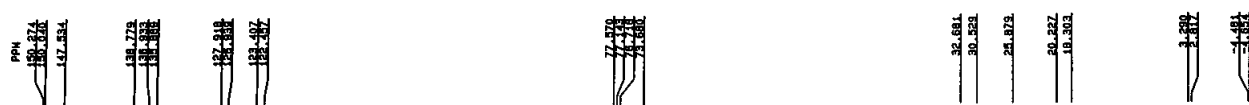
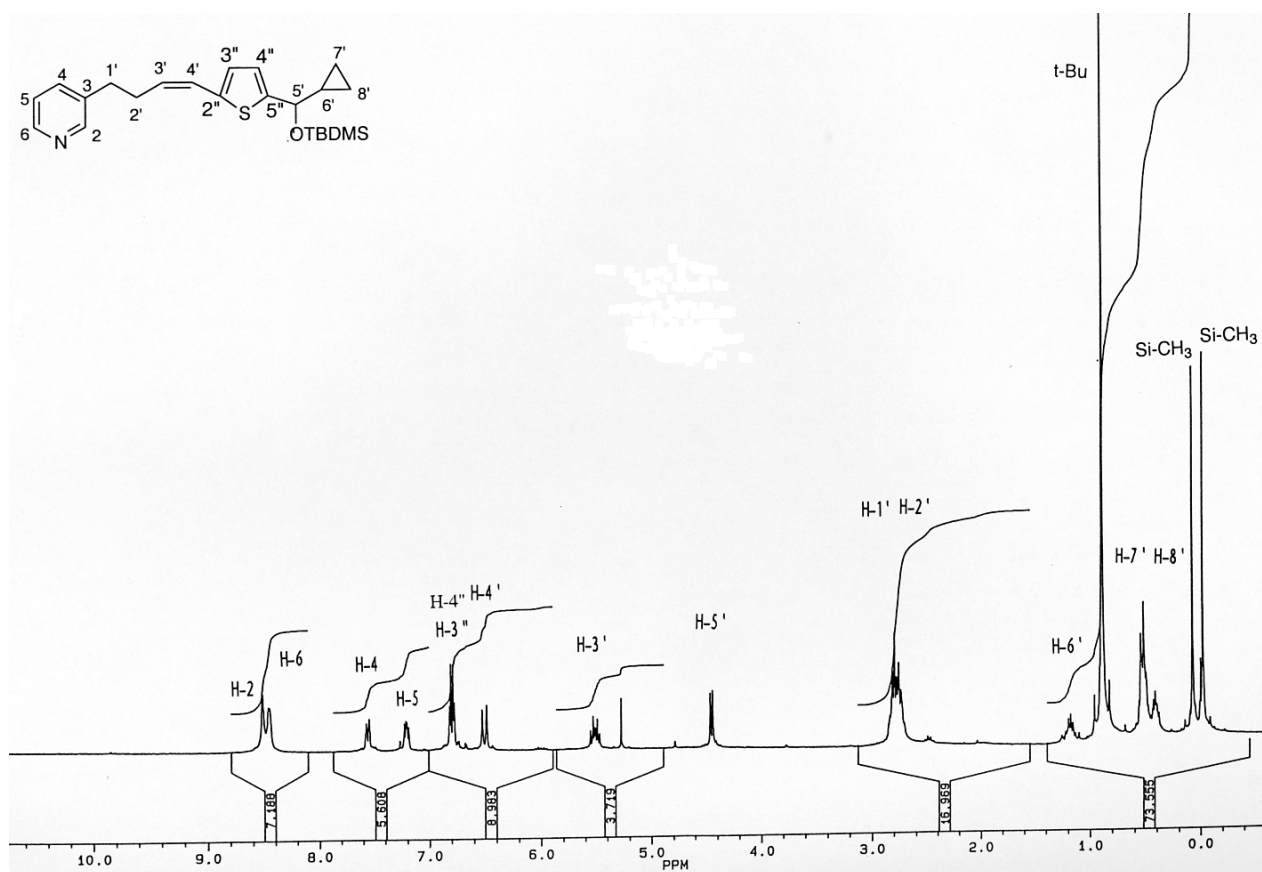
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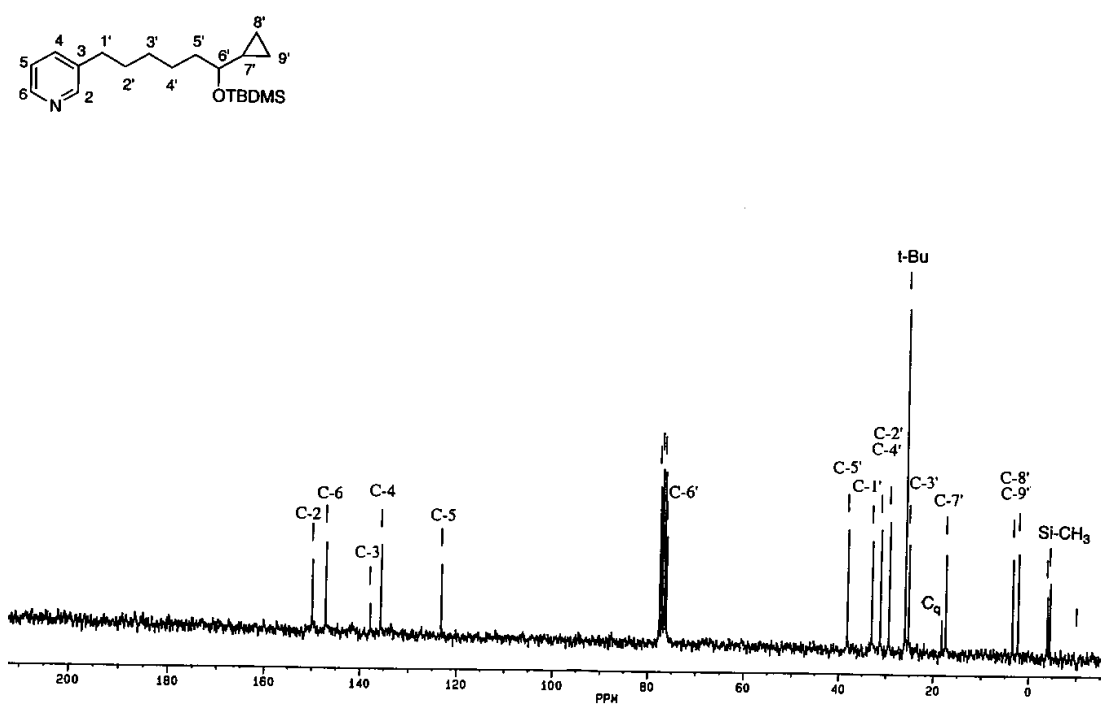
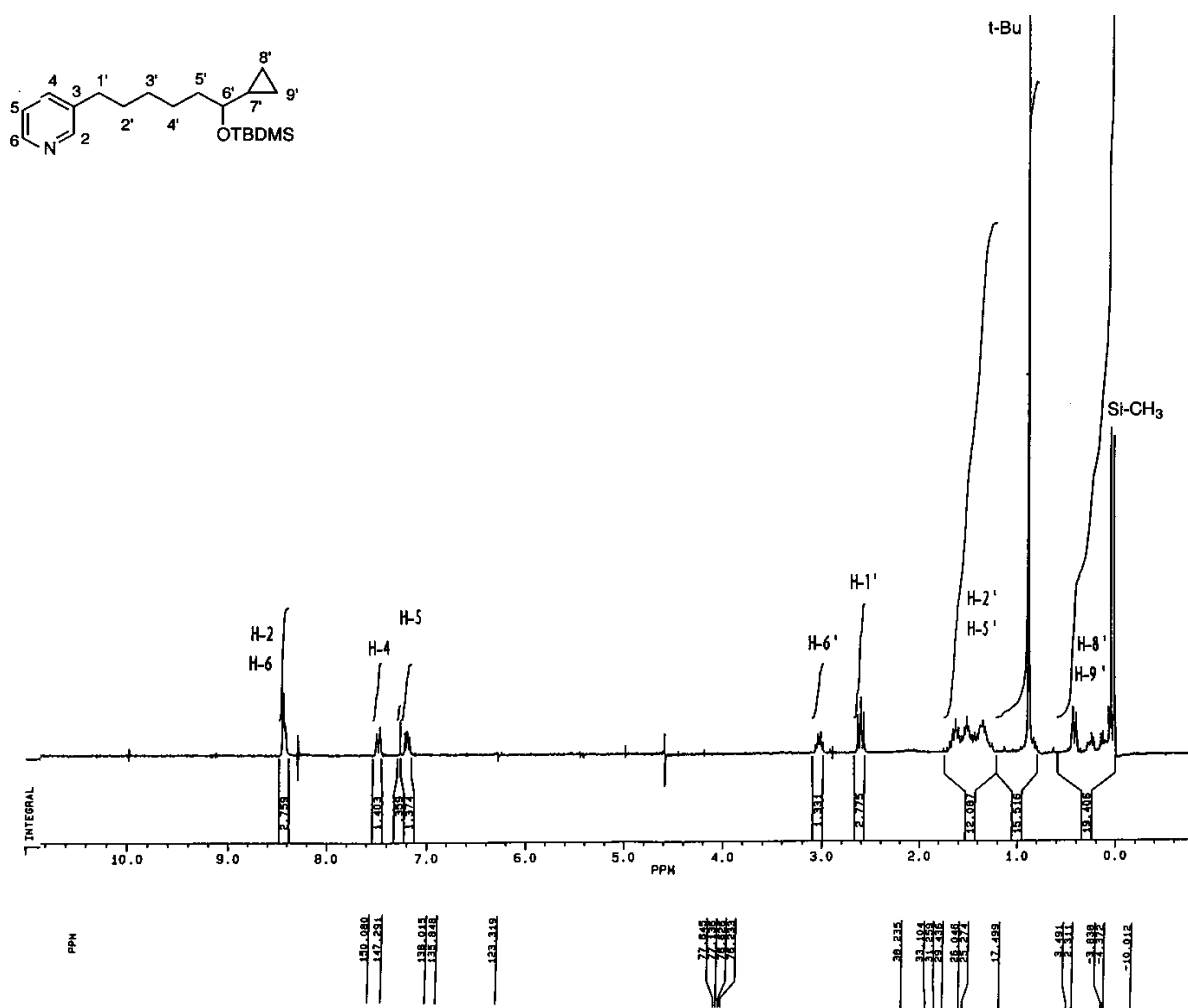
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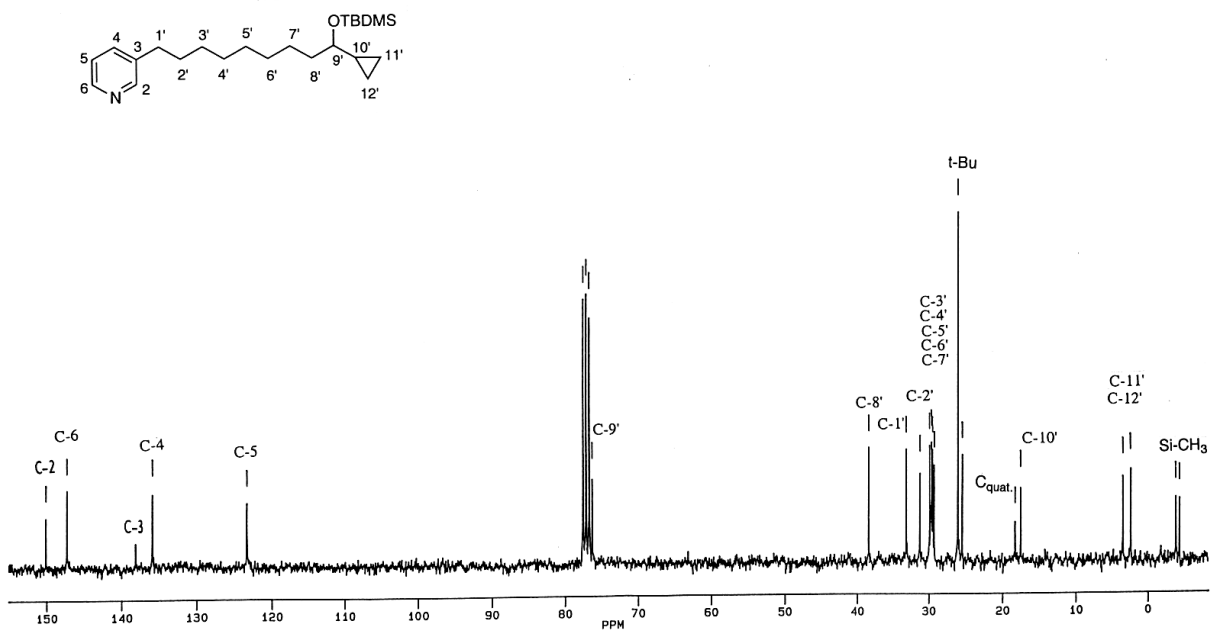
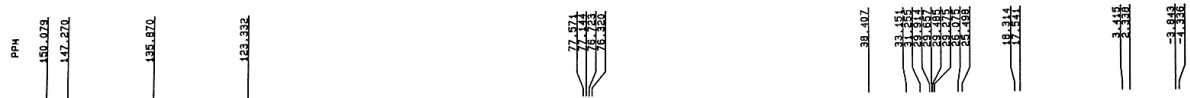
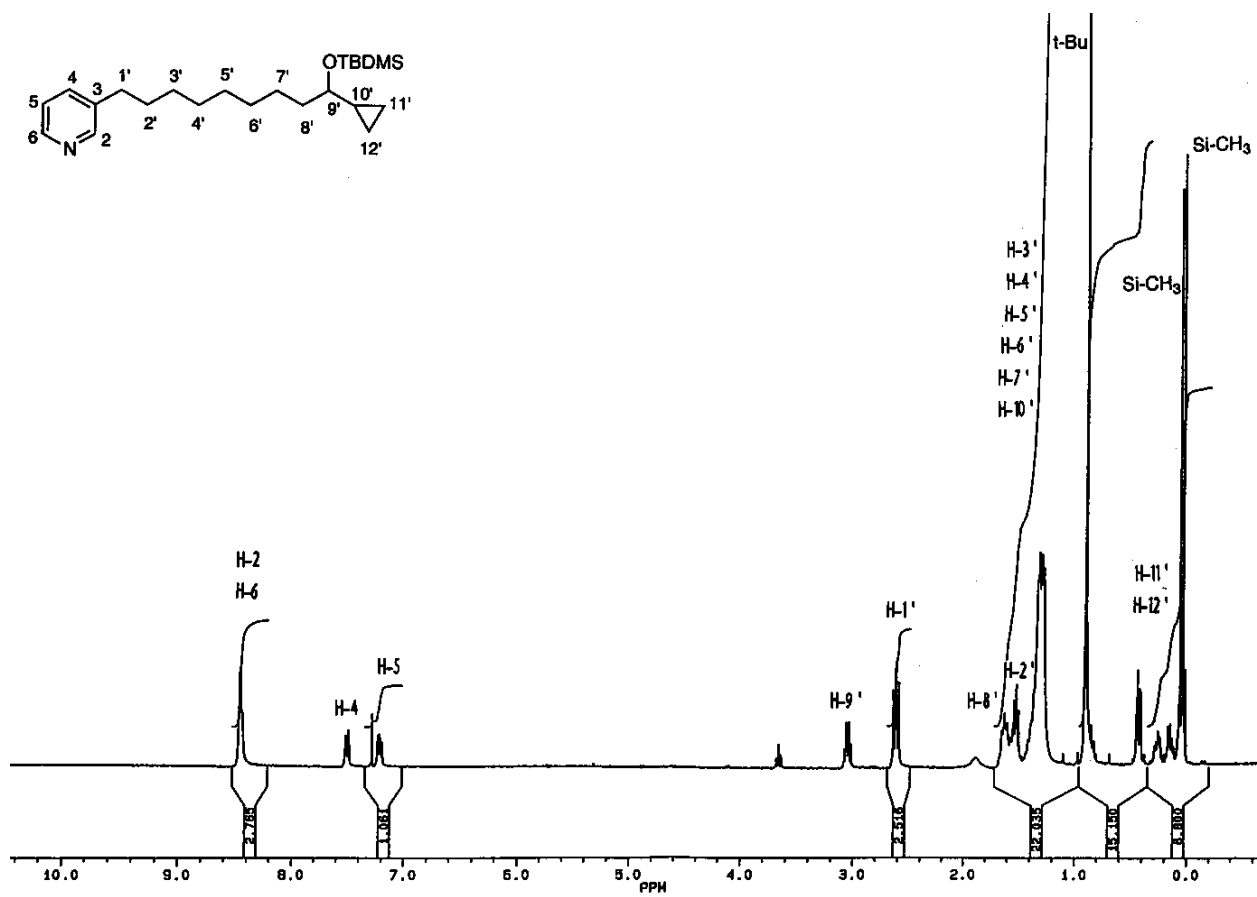
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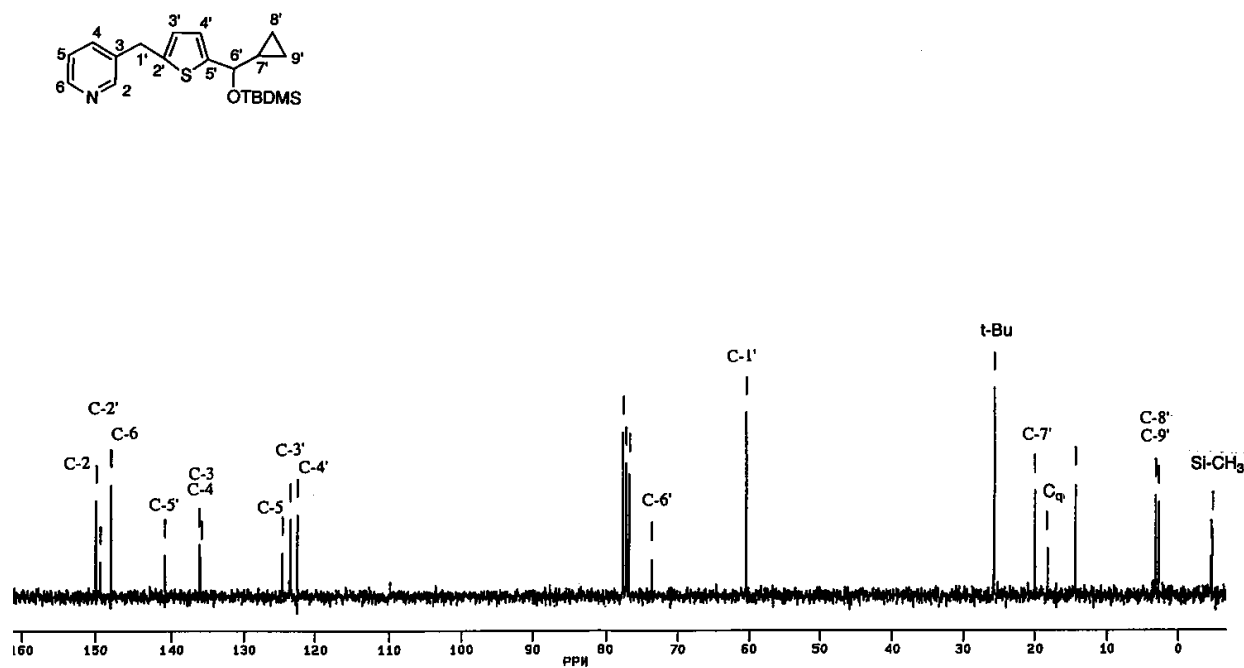
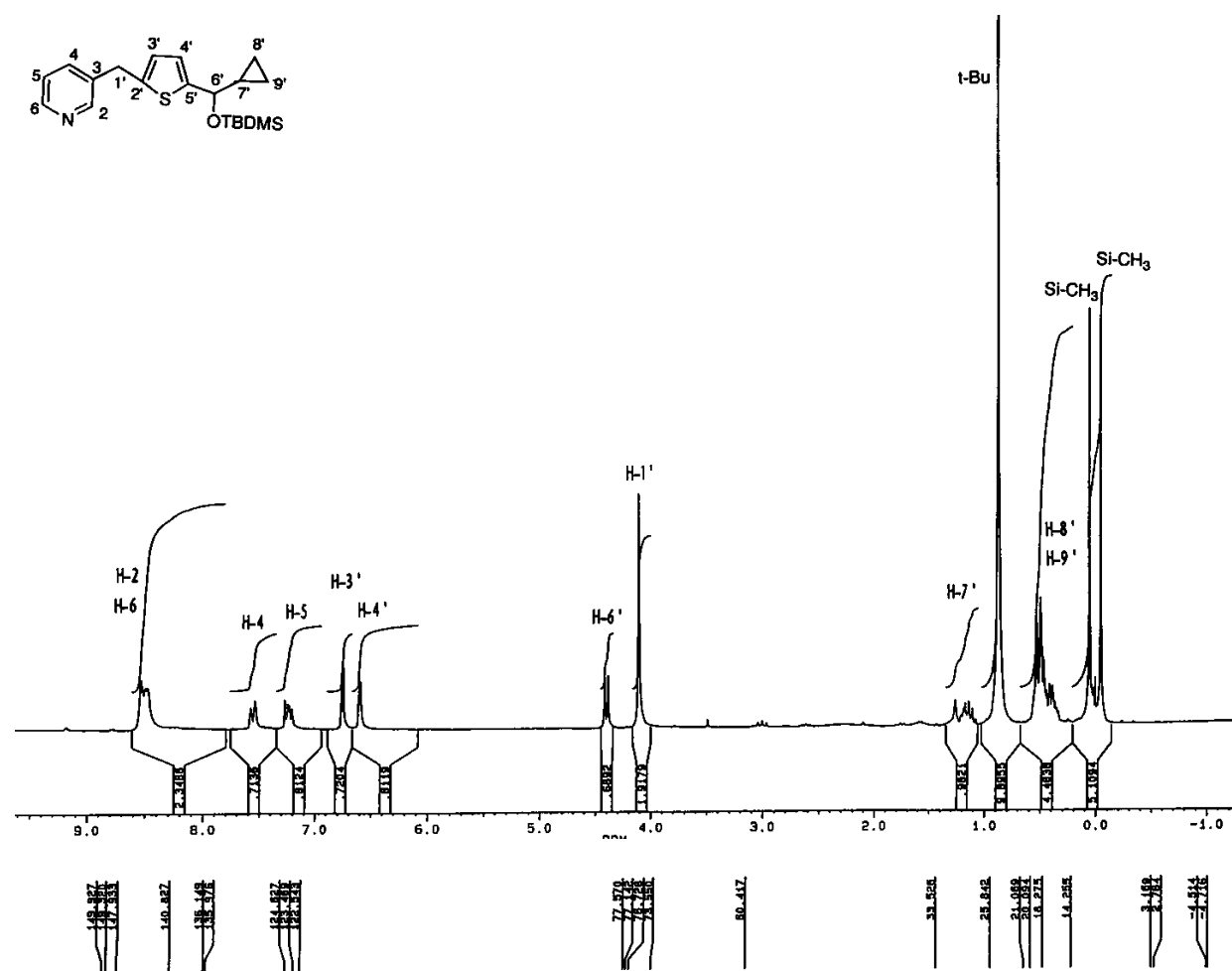
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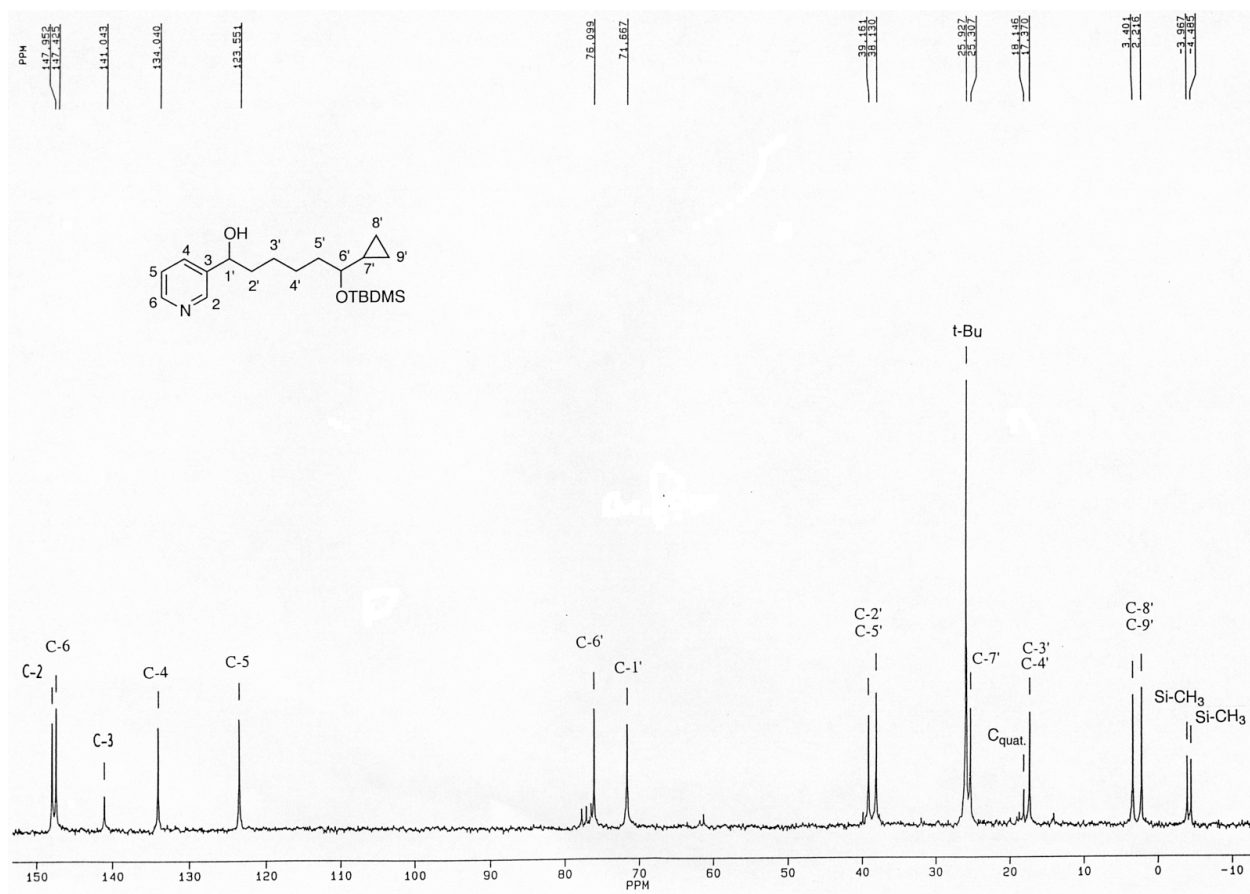
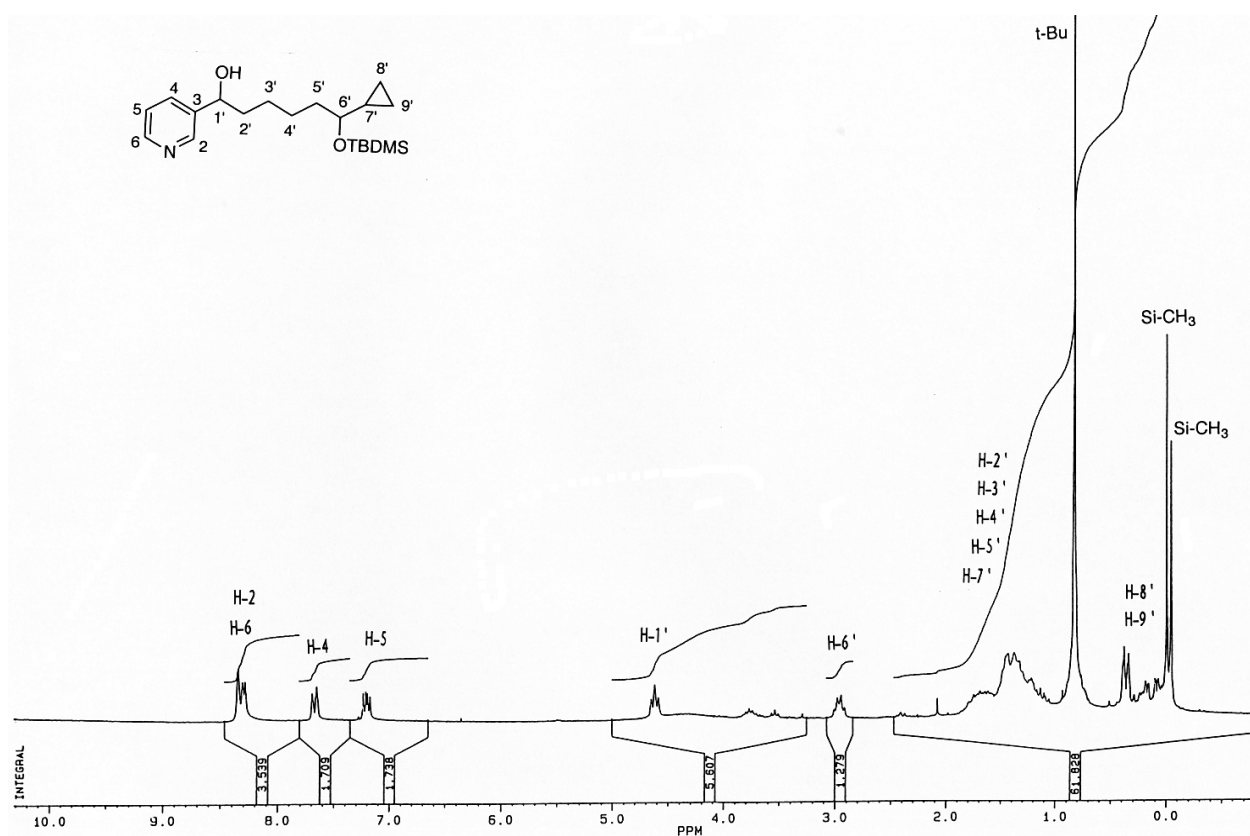
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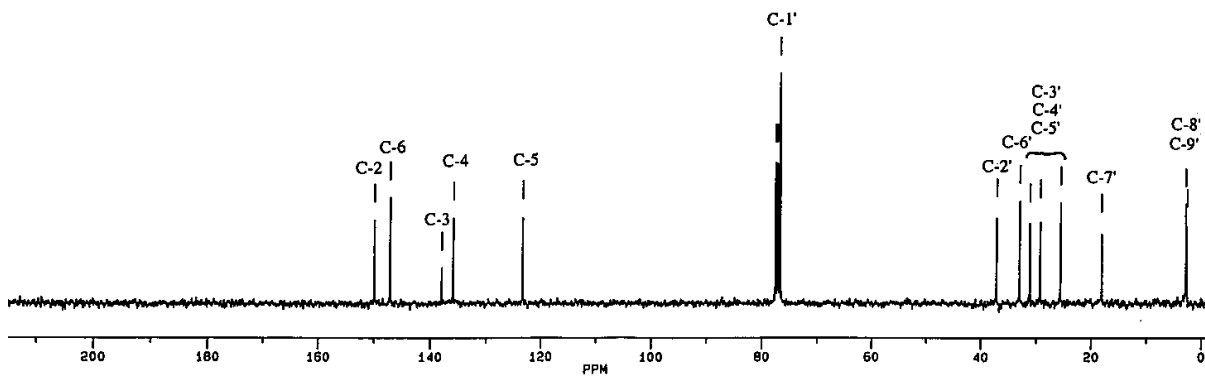
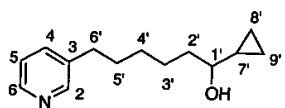
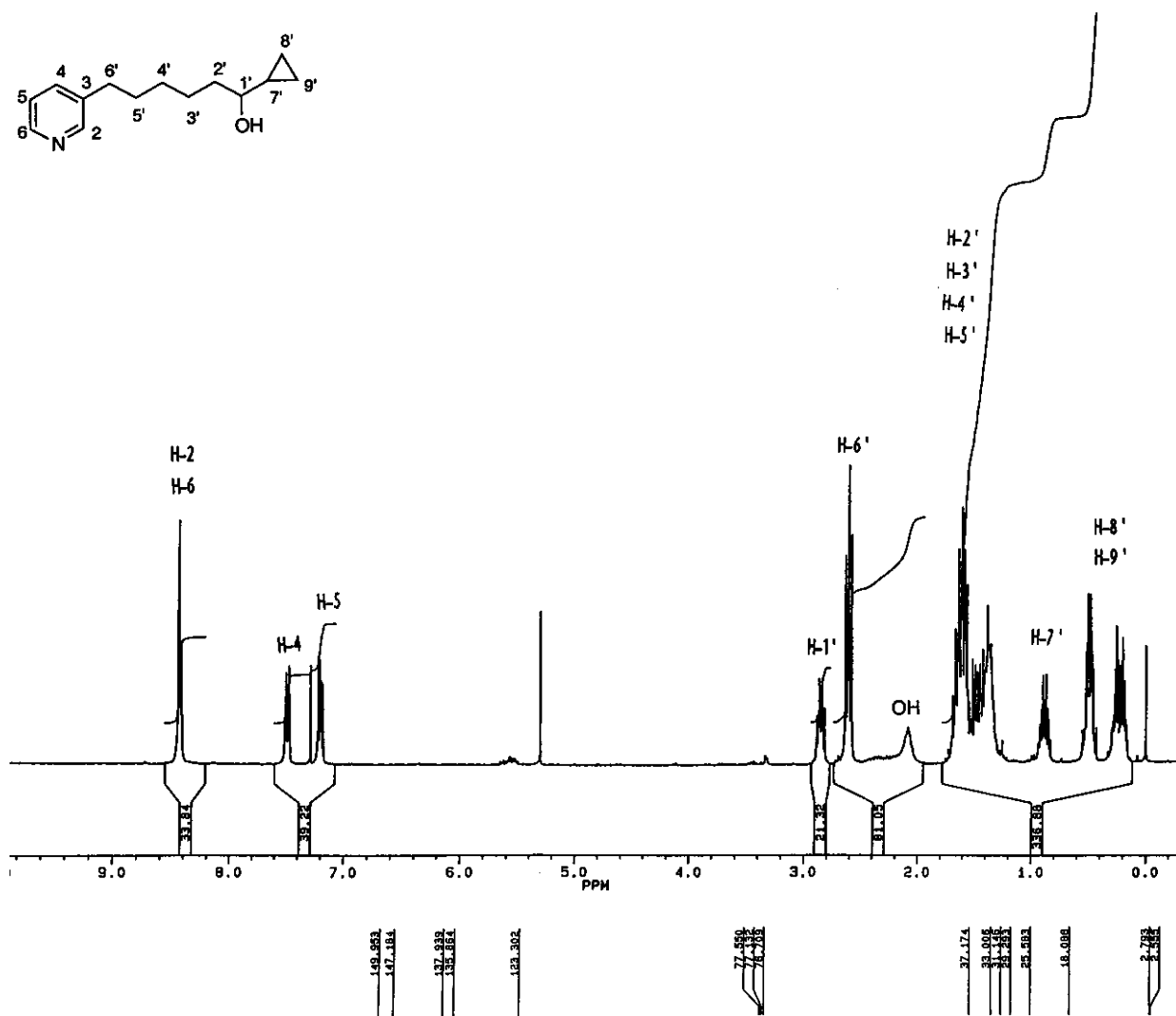
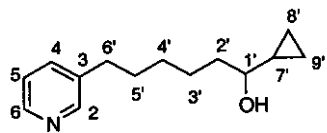
Compound 18



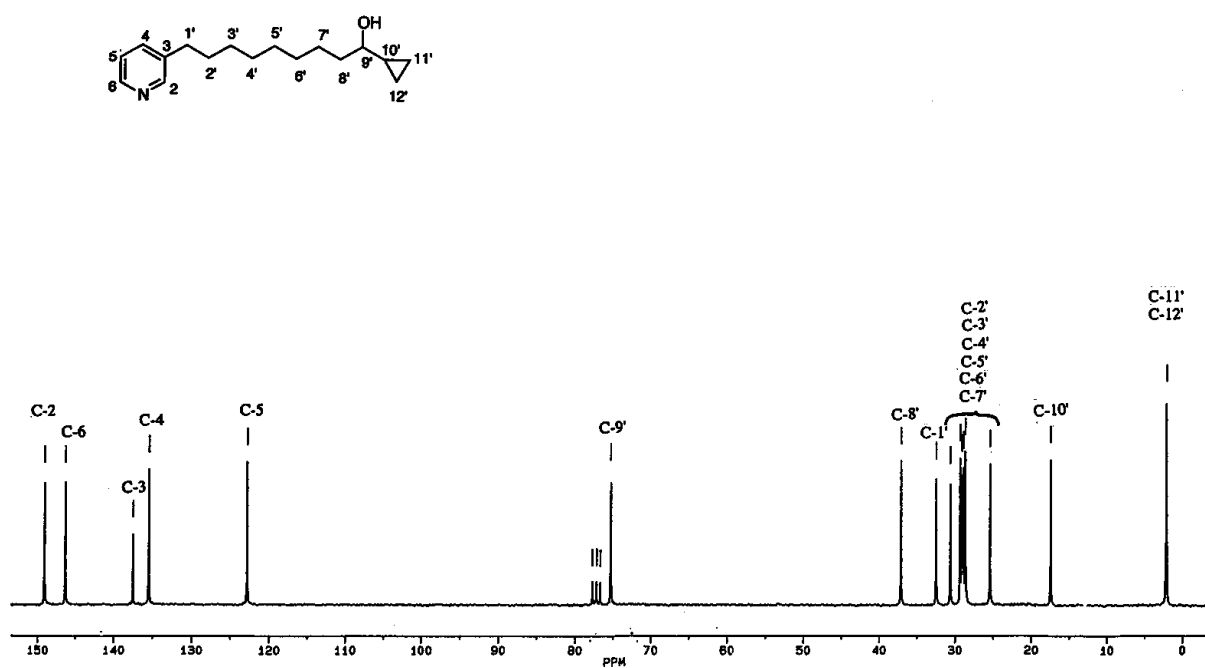
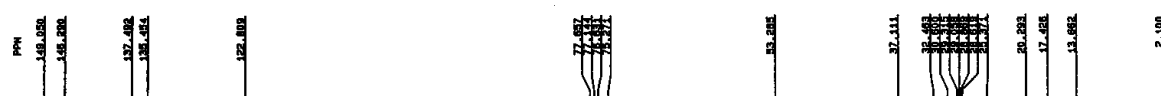
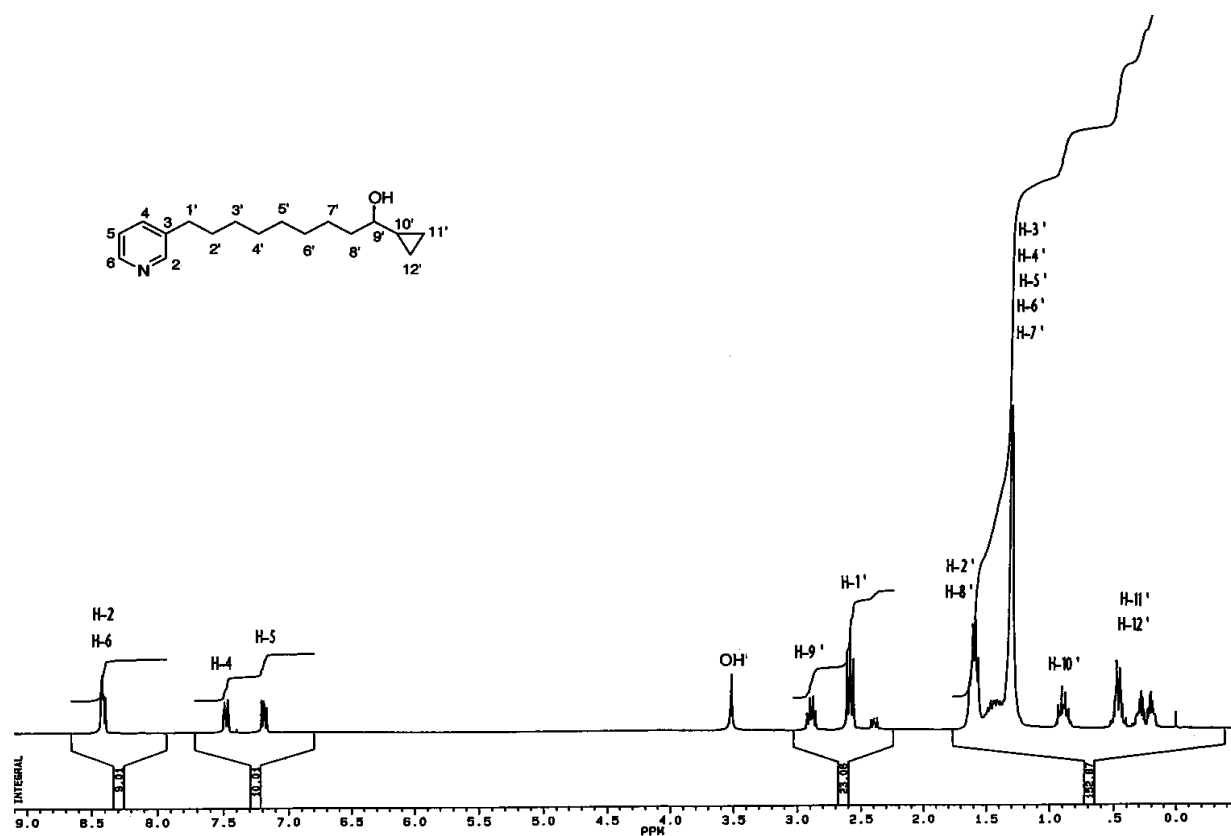
Compound 19



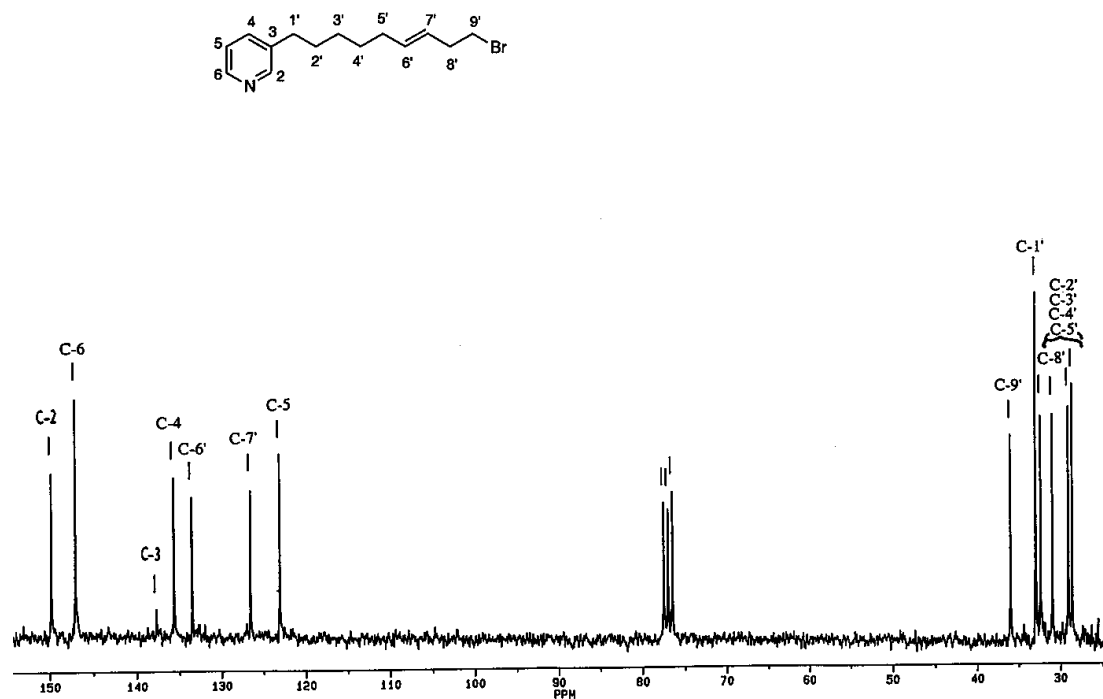
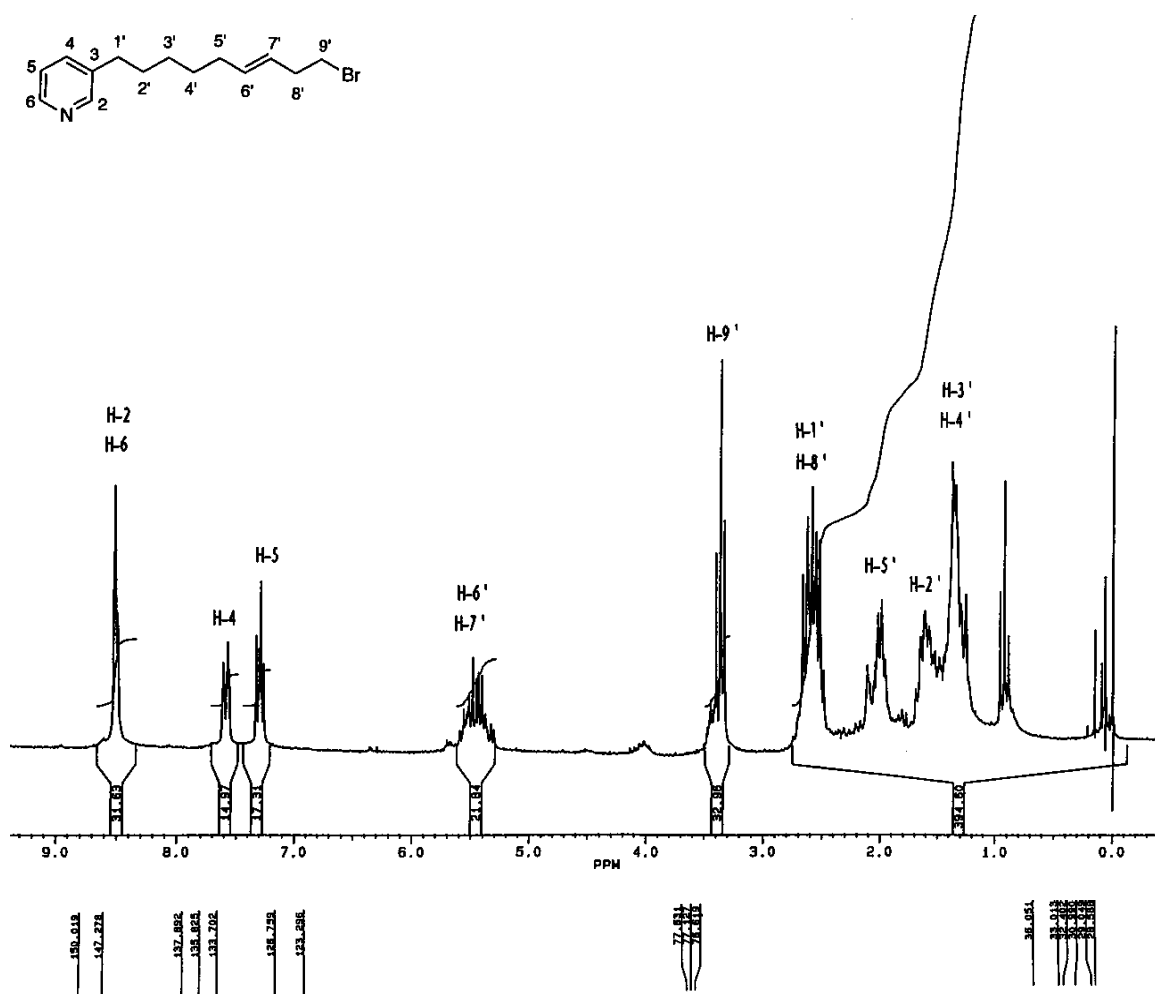
Compound 20



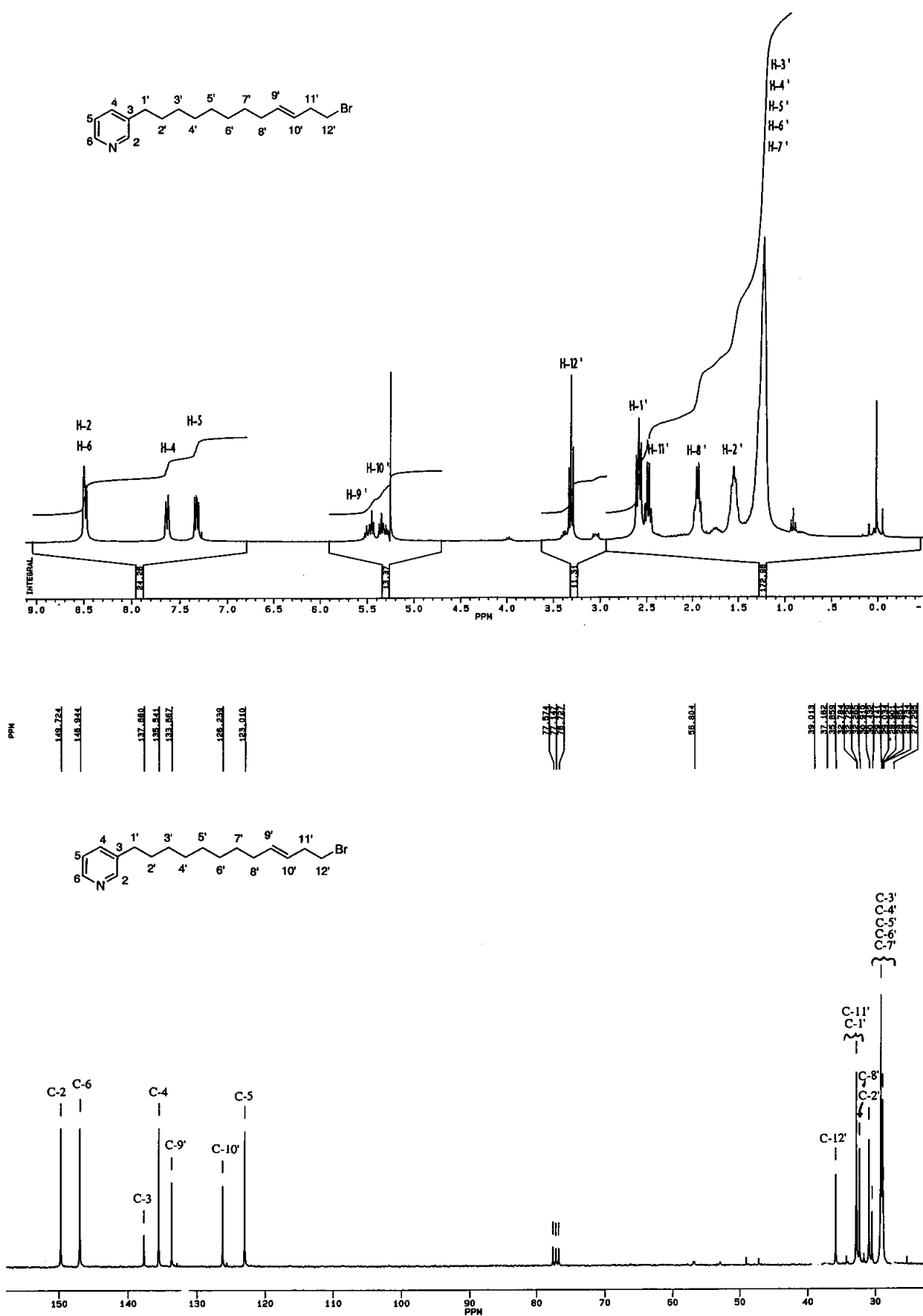
Compound 21



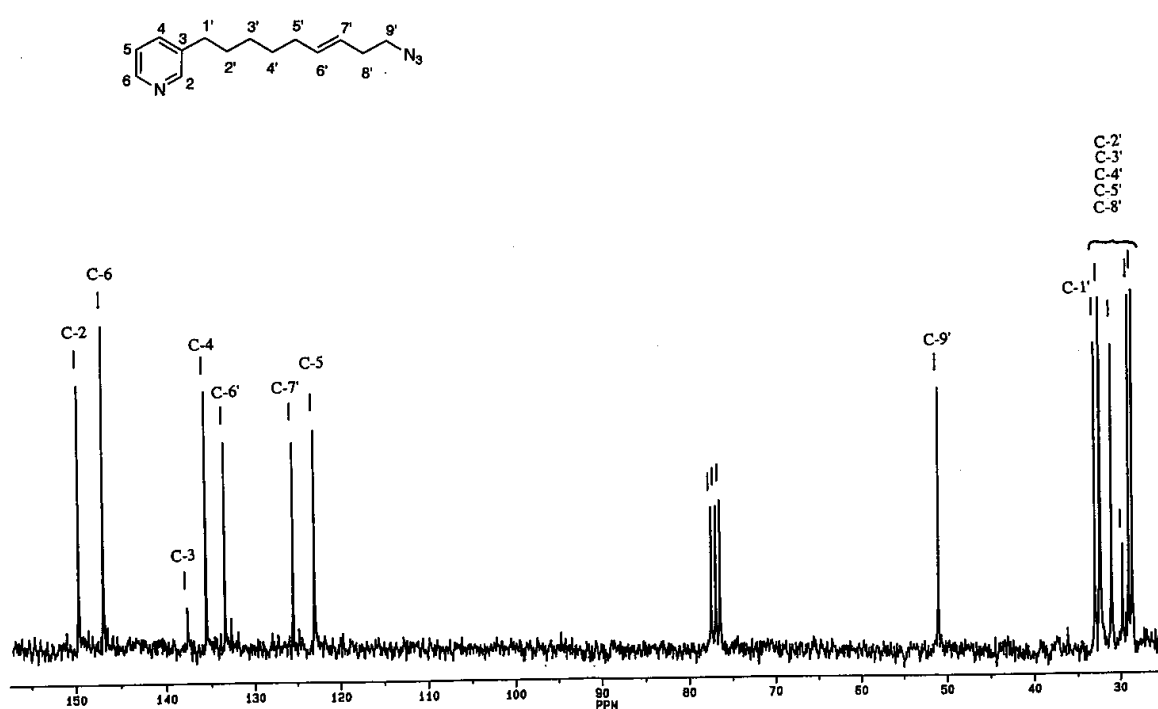
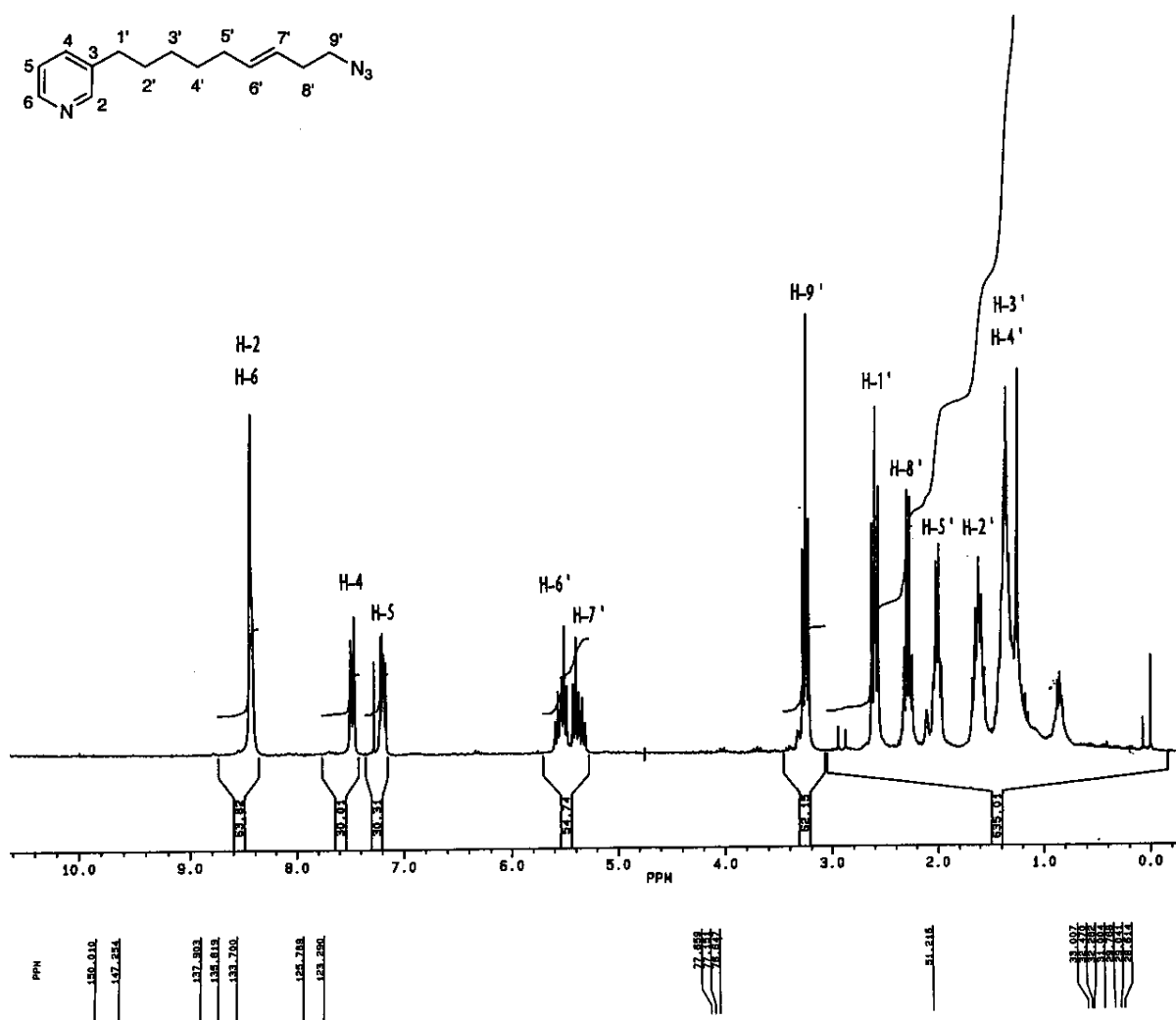
Compound 22



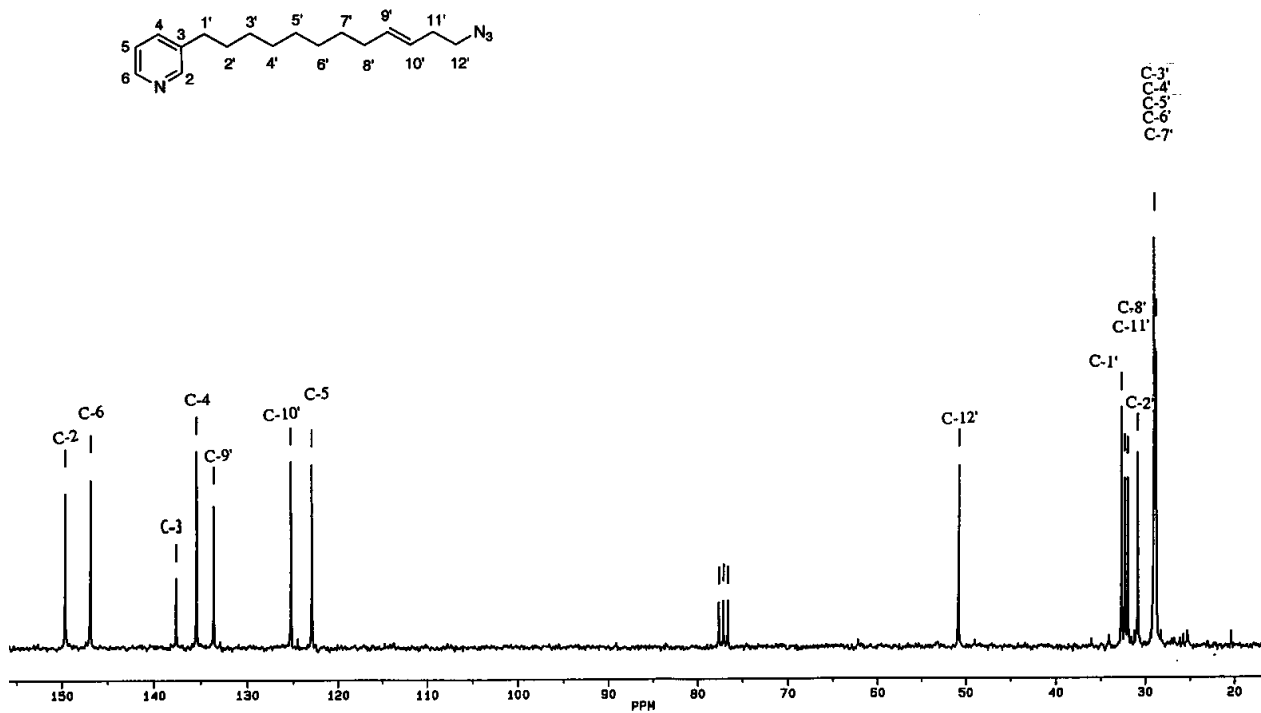
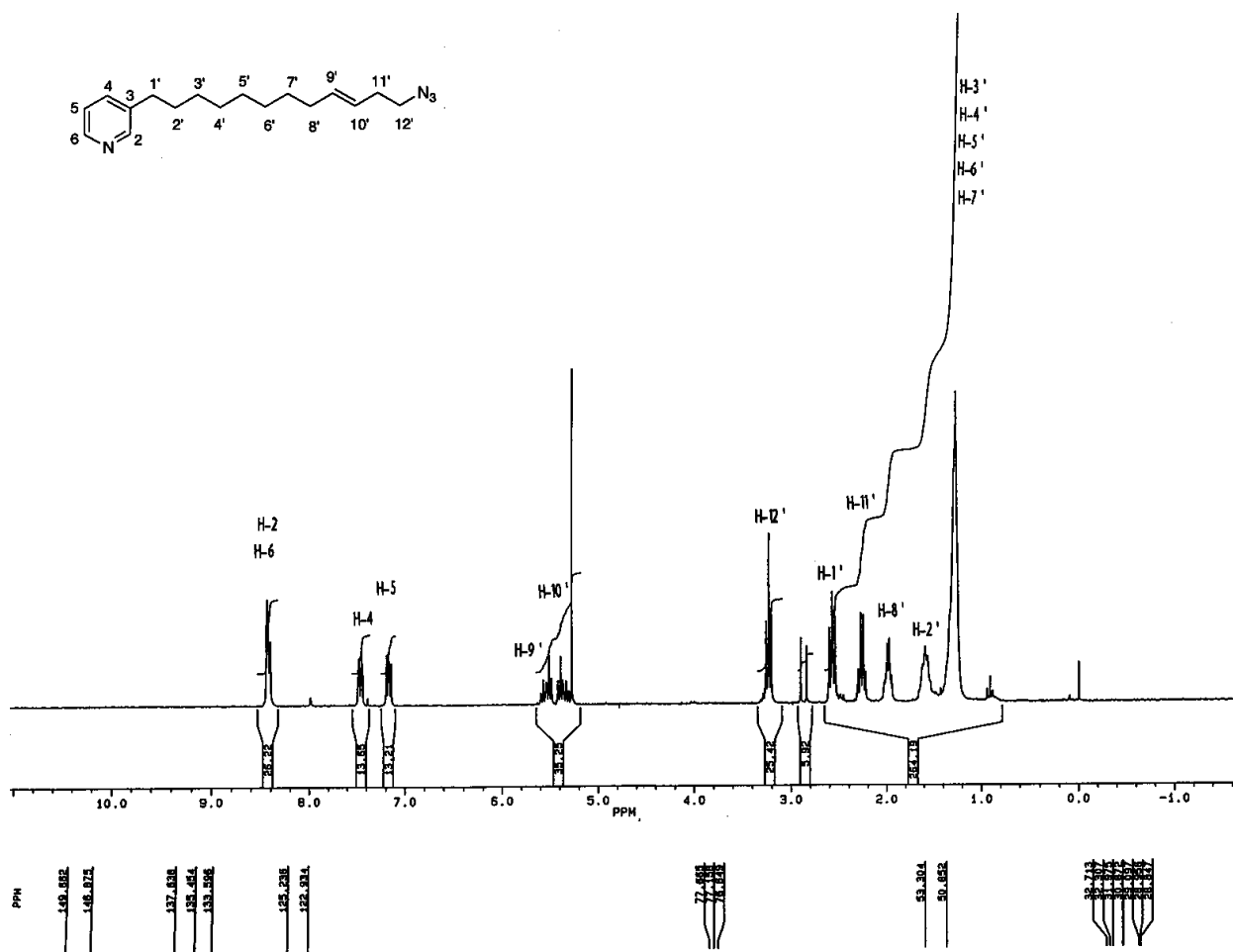
Compound 23



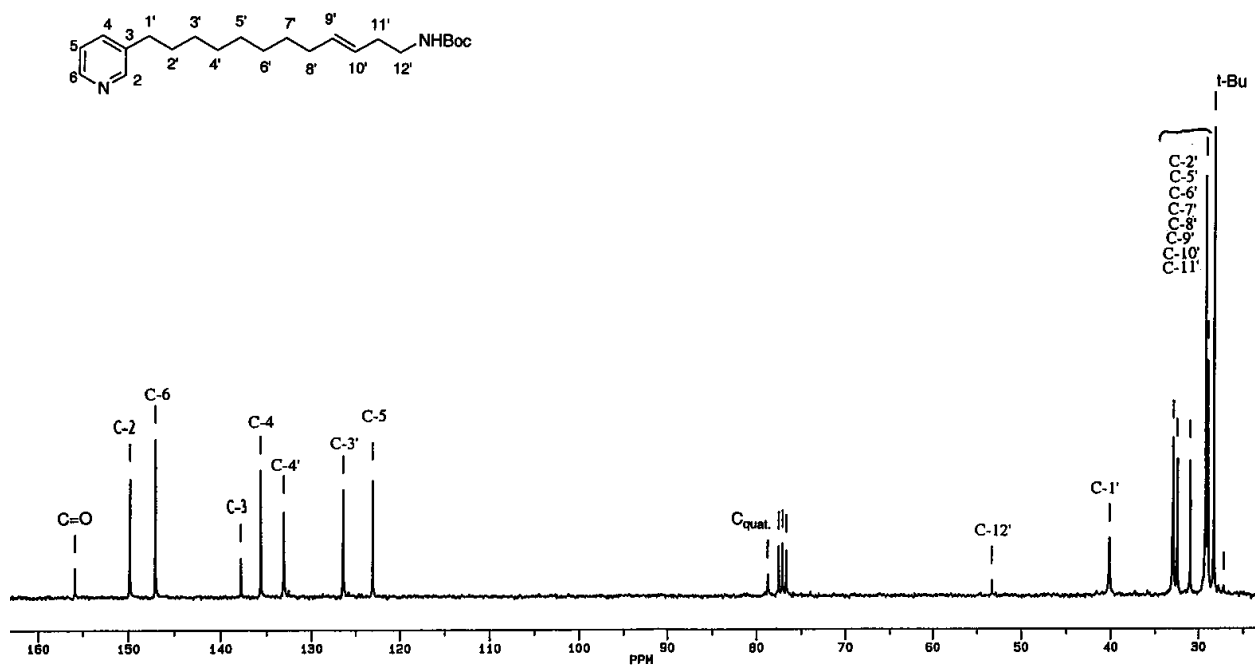
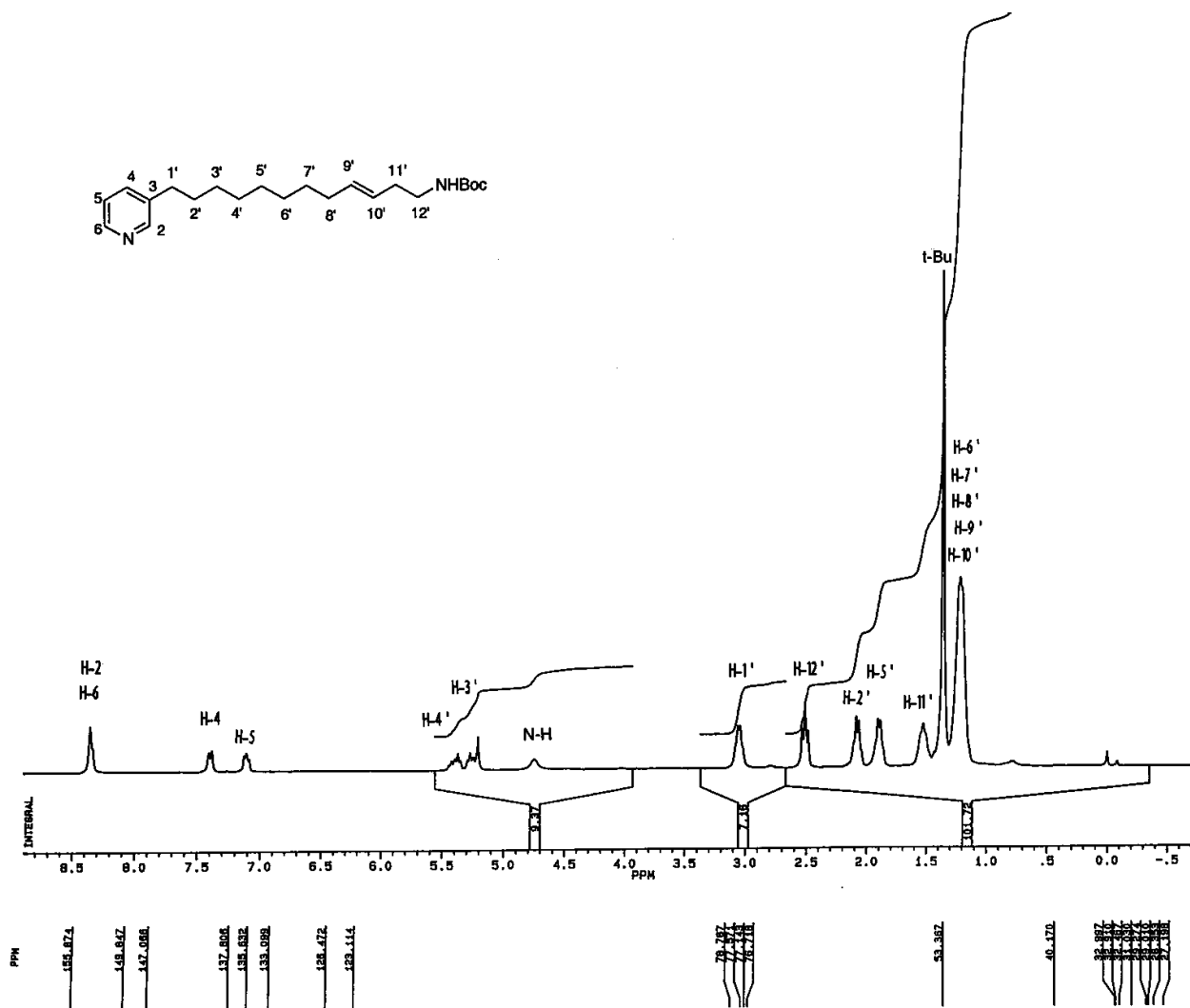
Compound 24



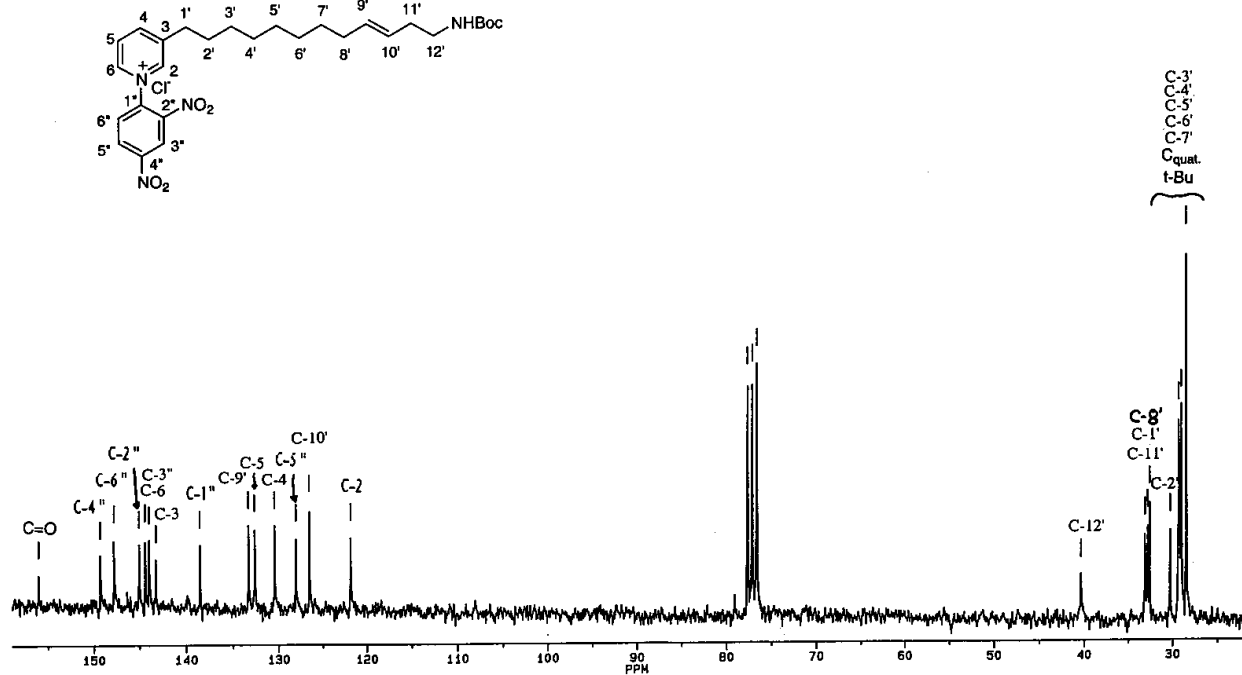
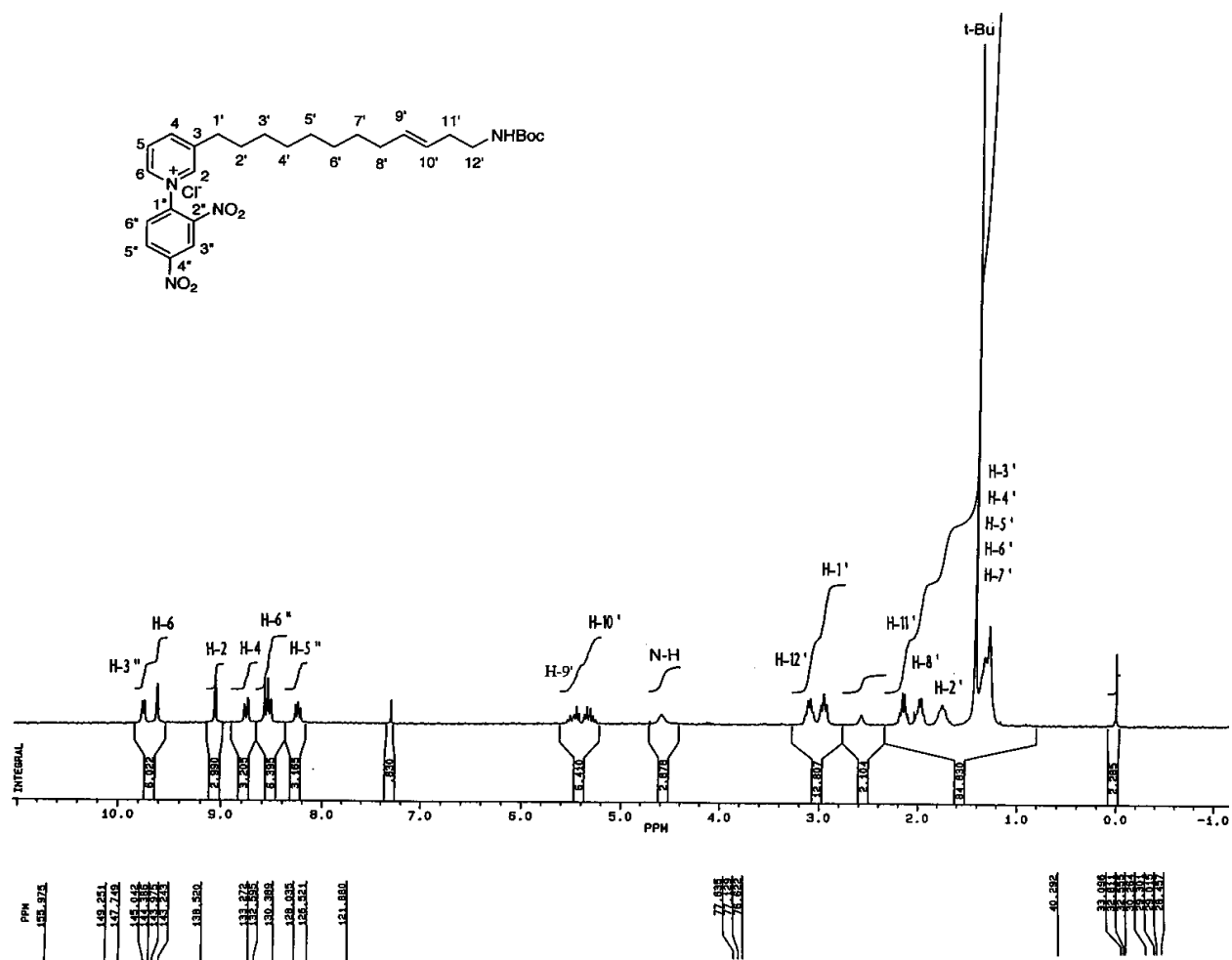
Compound 25



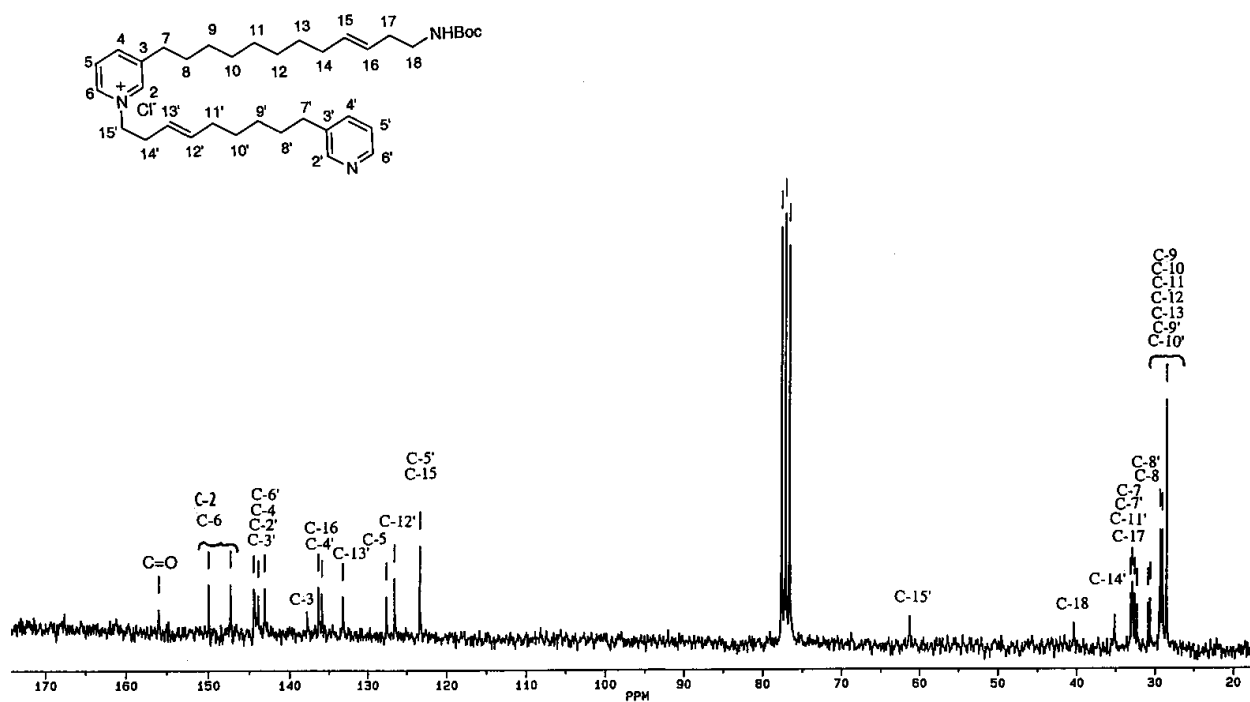
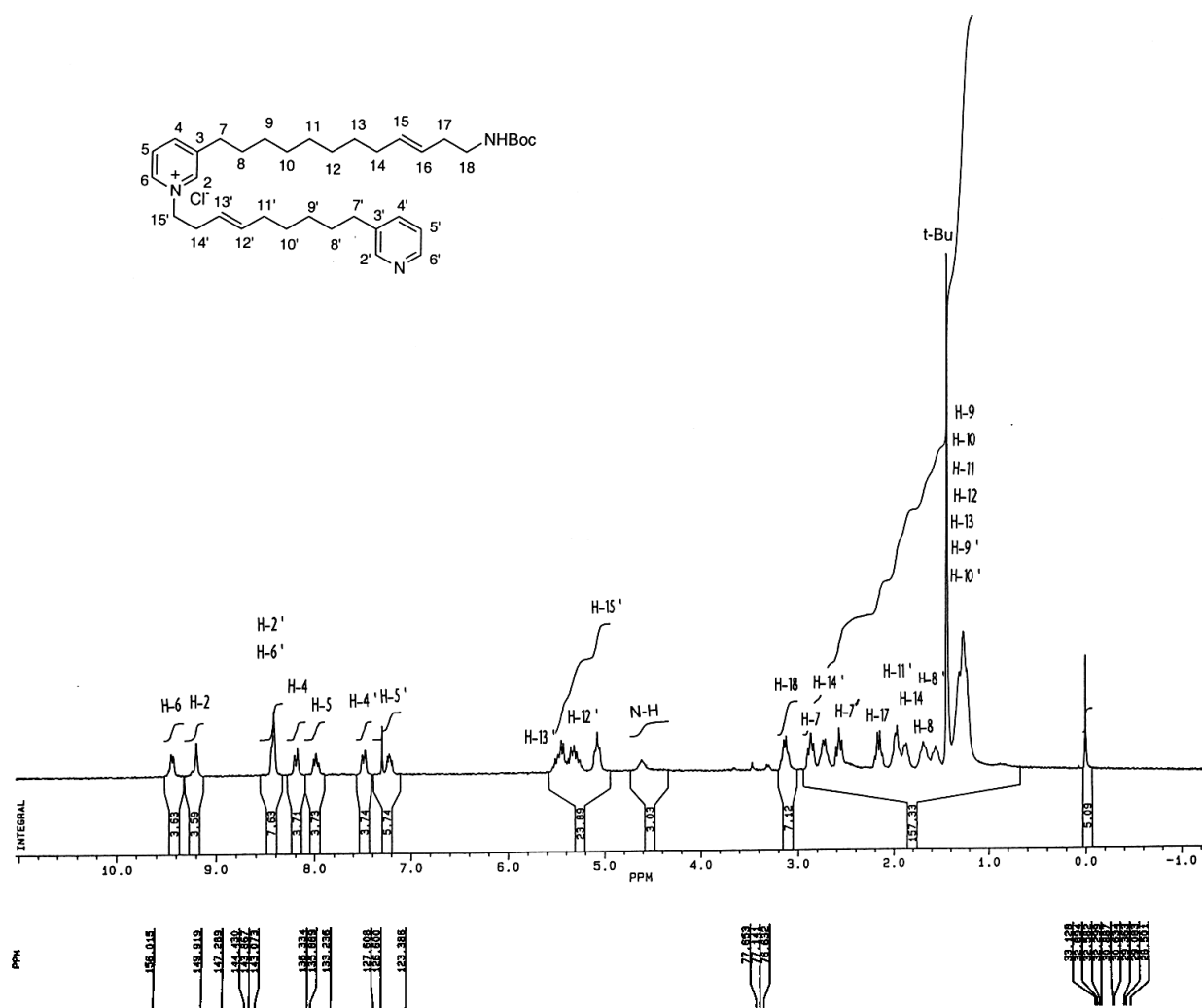
Compound 26



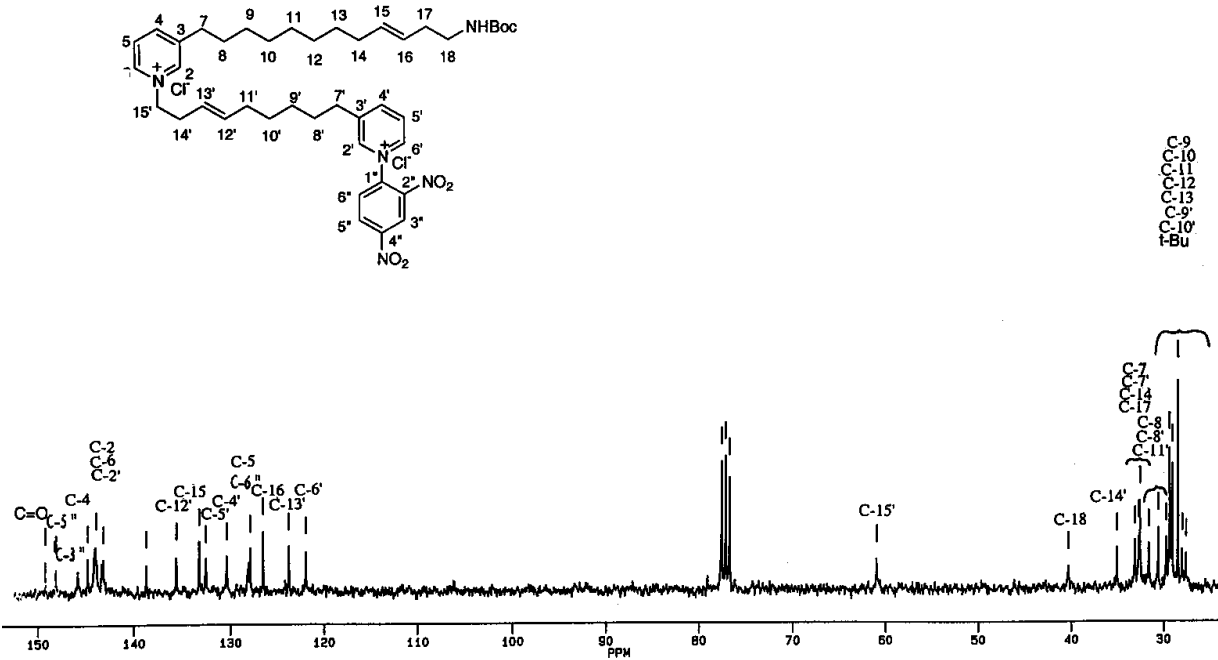
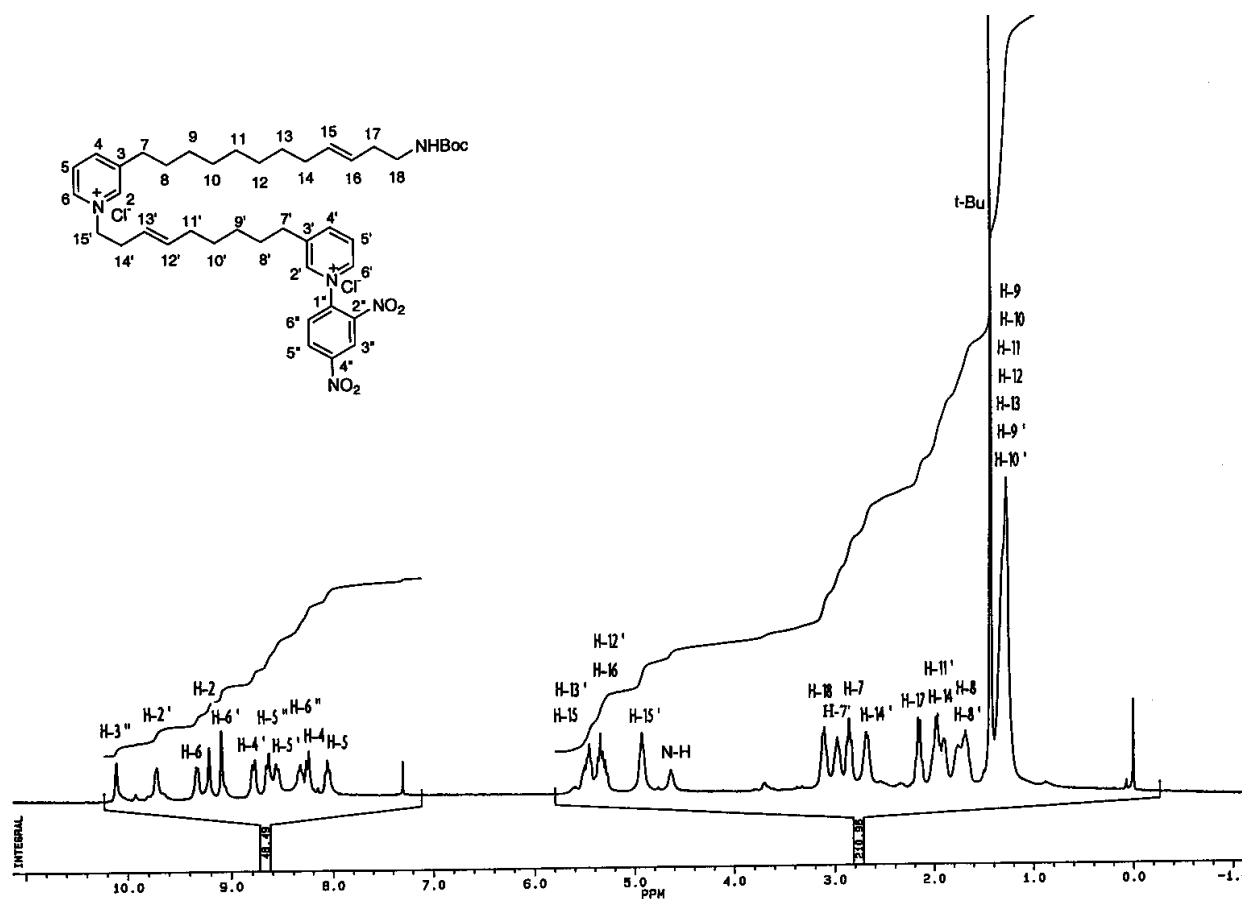
Compound 27



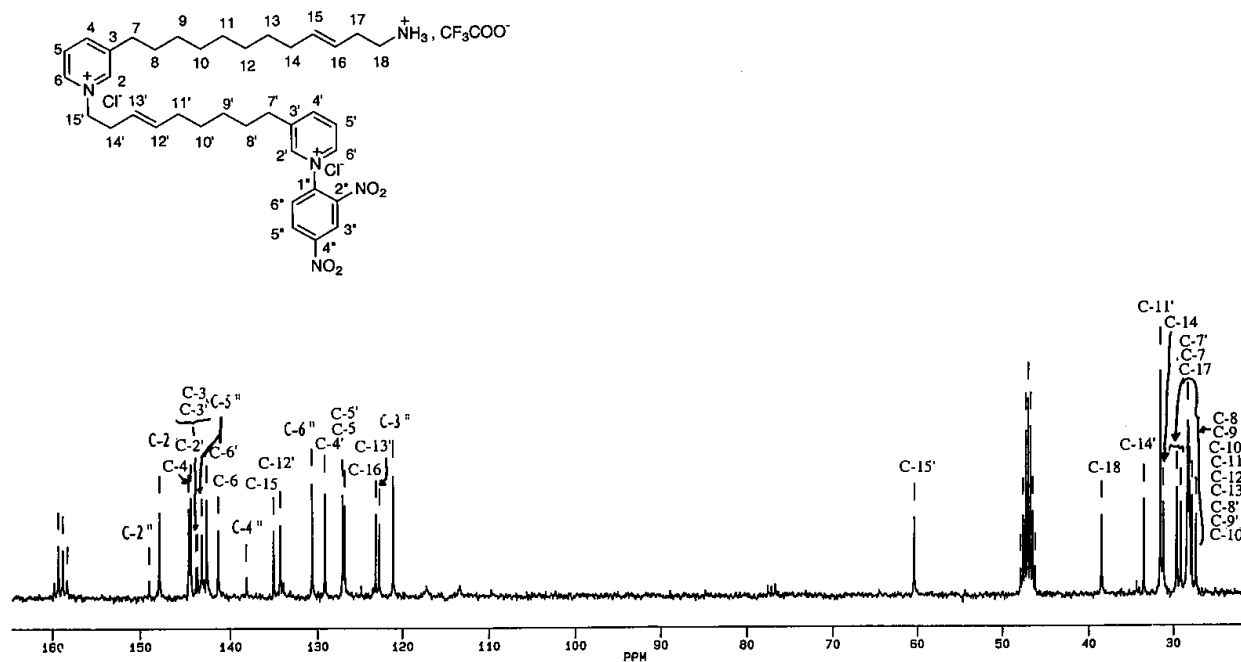
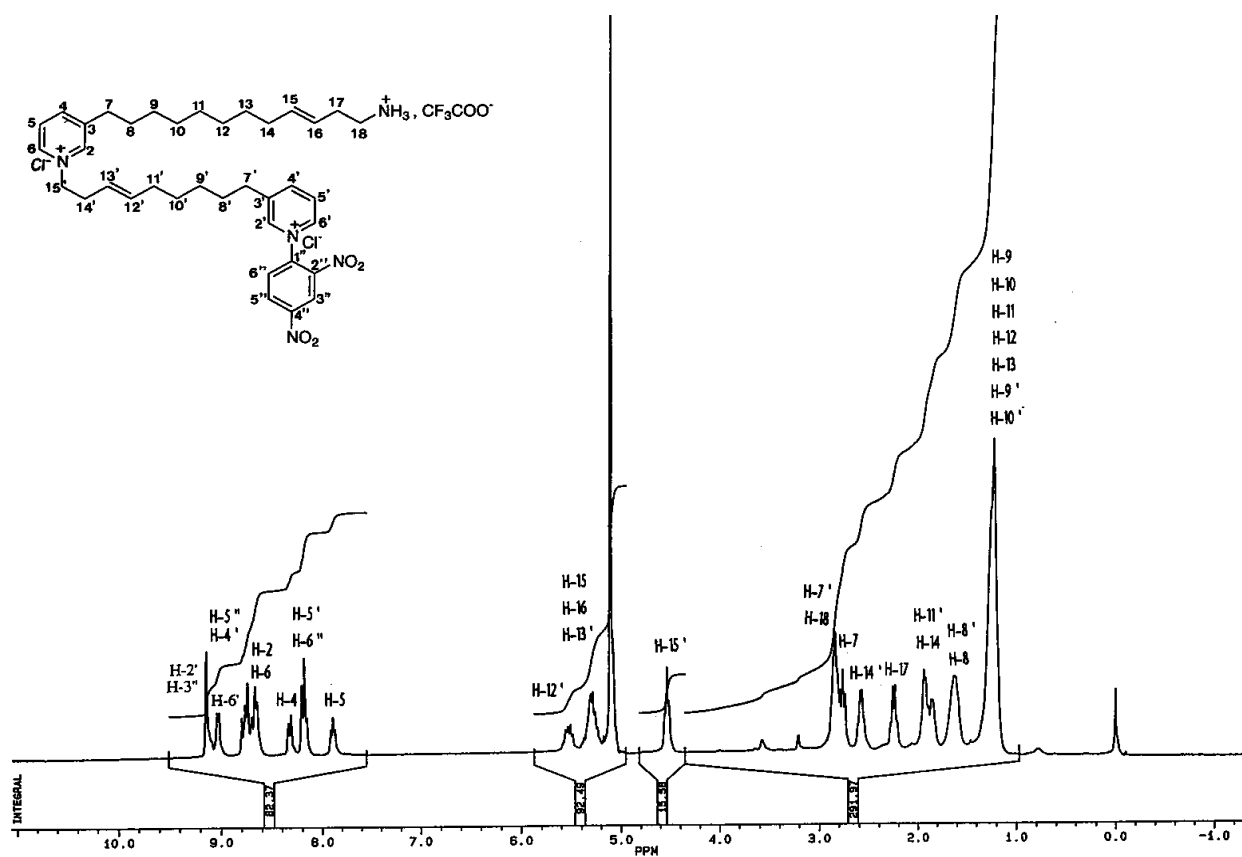
Compound 28



Compound 29



Compound 30



Haliclamine A

