Supplementary Material

for the manuscript entitled

A mild, catalyst-free synthesis of 2-aminopyridines

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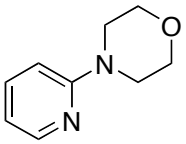
Department of Chemistry, University of California, Davis, CA

submitted to *Tetrahedron*

Spectral data for **3a-k** (prepared using Method A unless otherwise indicated)

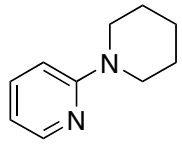
Spectral Data for Compounds 3a-k



4-Pyridin-2-yl-morpholine (3a)

^{1}H NMR, 400 MHz (DMSO-d^6) δ 8.19 (d, J = 4.8 Hz, 1H), 7.51-7.46 (m, 1H), 6.66-6.62 (m, 2H), 3.81 (t, J = 8.0 Hz, 4H), 3.49 (t, J = 8.0 Hz, 4H)

Lit.: Grasa, G. A.; Viciu, M. S.; Huang, J.; Nolan, S. P. *J. Org. Chem.* **2001**, *66*, 7729.

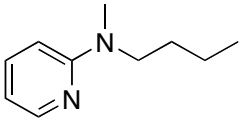


***N*-Pyridin-2-yl-piperidine (3b)**

^{1}H NMR, 500 MHz ($CDCl_3$) δ 8.11 (d, J = 6.0 Hz, 1H), 7.36 (t, J = 7.0 Hz, 1H), 6.57 (d, J = 8.5 Hz, 1H), 6.48 (t, J = 6.5 Hz, 1H), 3.46 (m, 4H), 1.58 (m, 6H).

^{13}C NMR ($CDCl_3$) δ 159.7, 147.9, 137.2, 112.4, 107.1, 46.3, 25.5, 24.7

Lit.: Pasumansky, L.; Hernandez, A. R.; Gamsey, S.; Goralski, C. T.; Singaram, B. *Tetrahedron Lett*. **2004**, *45*, 6417.

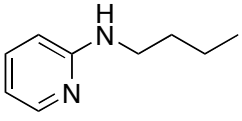


***N*-Butyl-*N*-methyl-pyridin-2-yl-amine (3c)**

^{1}H NMR, 400 MHz ($CDCl_3$) δ 8.02 (d, J = 4.8 Hz, 1H), 7.41 (t, J = 9.6 Hz, 1H), 6.53 (d, J = 8.8 Hz, 1H), 6.46 (t, J = 6.4 Hz, 1H), 3.44 (t, J = 8.8 Hz, 2H), 2.92 (s, 3H), 1.45 (m, 2H), 2.24 (m, 2H), 0.87 (t, J = 7.2 Hz, 3H)

^{13}C NMR ($CDCl_3$) δ 159.0, 148.2, 137.2, 111.2, 105.8, 50.2, 36.5, 29.6, 20.5, 14.3

Lit.: Strekowski, L.; Dworniczak, M; Kowalewski, A. *Polish J. Chem.* **1980**, *54,*1557.

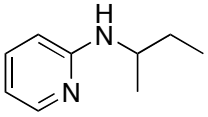


***N*-Butyl-pyridin-2-yl-amine (3d)**

^{1}H NMR, 400 MHz ($CDCl_3$) δ 8.07 (d, J = 4.8 Hz, 1H), 7.43-7.27 (m, 1H), 6.54 (t, J = 5.2 Hz, 1H), 6.36 (d, J = 8.4 Hz, 1H), 4.50 (br s, 1H), 3.27-3.22 (m, 2H), 1.64-1.56 (m, 2H), 1.48-1.38 (m, 2H), 0.95 (t, J = 7.2 Hz, 3H)

^{13}C NMR ($CDCl_3$) δ 148.4, 137.6, 112.8, 106.5, 94.6, 42.2, 31.9,20.4, 14.1

Lit.: Okano, K.; Tokuyama, H.; Fukuyama, T. *Organic Lett.,* **2003,** *5,* 4987.

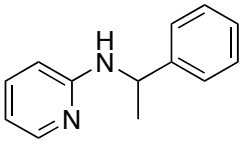


***N*-(*s*-Butyl)-pyridin-2-yl-amine (3e)**

^{1}H NMR, 400 MHz ($CDCl_3$) δ 8.06 (d, J = 5.2 Hz, 1H), 7.39 (t, J = 6.8 Hz, 1H), 6.52 (t, J = 6.0 Hz, 1H), 6.34 (d, J = 8.4 Hz, 1H), 4.39 (br s, 1H), 3.67 (m, 1H), 1.57 (m, 2H), 1.19 (d, J = 6.4 Hz, 3H), 0.96 (t, 7.6 Hz, 3H)

^{13}C NMR ($CDCl_3$) δ 158.6, 148.5, 137.6, 112.5, 106.8, 48.7, 30.0, 20.6, 10.6

Lit.: Abarghaz, M.; Kerbal, A.; Bourguignon, J-J. *Tetrahedron Lett*. **1995**, *36*, 6463.

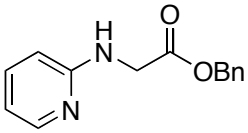


***N*-(1-Phenyl-ethyl)-pyridin-2-yl-amine (3f)**

^{1}H NMR, 400 MHz (DMSO d_6) δ 8.07-8.05 (m, 1H), 7.38-7.20 (m, 6H), 6.53-6.50 (m, 1H), 6.18 (dd, J = 0.8, 7.6 Hz, 1H), 5.18 (br s, 1H), 4.71 (m, 1H), 1.53 (d, J = 6.8 Hz, 3H)

^{13}C NMR (DMSO d_6) δ 158.4, 148.4, 145.0, 137.7, 128.9, 127.2, 126.1, 113.2, 106.9, 52.2, 24.7

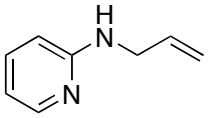
Lit.: Pasumansky, L.; Hernandez, A. R.; Gamsey, S.; Goralski, C. T.; Singaram, B. *Tetrahedron Lett*. **2004**, *45*, 6417.



***N*-(2-Pyridyl)-glycine benzyl ester (3g)**

^{1}H NMR, 500 MHz ($CDCl_3$) δ 8.08 (d, J = 4.5 Hz, 1H), 7.42-7.25 (m, 6H), 6.61 (m, 1H), 6.45 (d, J = 8.5 Hz, 1H), 5.20 (s, 2H), 5.01 (br. s, NH), 4.19 (d, J = 5.0 Hz, 2H)

^{13}C NMR ($CDCl_3$) δ 171.4, 157.7, 147.9, 137.7, 135.7, 128.8, 128.6, 128.4, 113.9, 108.7, 67.1, 44.0

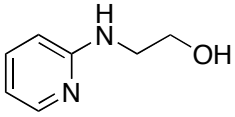


Allyl-pyridin-2-yl-amine (3h)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03-8.04 (m, 1H), 7.36 (t, J = 8 Hz, 1H), 6.50-6.54 (m, 1H), 6.34 (d, J = 8 Hz, 1H), 5.80-6.0 (m, 1H), 5.22 (d, J = 17 Hz, 1H), 5.10 (d, J = 10.5 Hz, 1H), 4.82 (br s, 1H), 3.88 (s, 2H)

^{13}C NMR (125 MHz, $CDCl_3$) δ 158.6, 148.0, 137.3, 135.0, 115.8, 112.8, 106.6, 44.5

Lit.: Blomberg, D.; Brickmann, K.; Kihlberg, J. *Tetrahedron* **2006**, *62*, 10937.

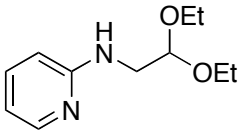


2-(Pyridin-2-ylamino)ethanol (3i)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.92 (br s, 1H), 7.25-7.36 (m ,1H), 6.47 (d, J = 4 Hz, 1H), 6.33-6.37 (m, 1H), 5.25 (br, 1H), 5.06 (br s, 1H), 3.69-3.72 (m, 2H), 3.37 (br s, 1H)

^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 147.1, 137.5, 112.8, 108.2, 62.8, 45.1

Lit.: Blomberg, D.; Brickmann, K.; Kihlberg, J. *Tetrahedron* **2006**, *62*, 10937.

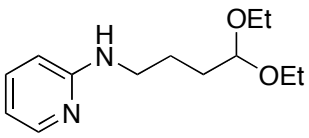


***N*-(2-Pyridyl)aminoacetaldehyde diethyl acetal (3j)**

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (br s, 1H), 7.38-7.30 (m, 1H), 6.53-6.50 (m, 1H), 6.36 (d, J = 8.5 Hz, 1H), 4.68 (br s, 1H), 4.62-4.58 (m, 1H), 3.70-3.65 (m, 2H), 3.54-3.50 (m, 2H), 3.43-3.40 (m, 2H), 1.19-1.15 (m, 6H)

^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 147.9, 137.1, 112.8, 107.3, 101.0, 62.4, 44.3, 15.2

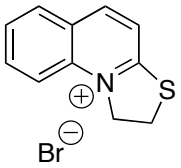
Lit.: Ziegler, R.; Ho, B.; Castagnoli, N. *J. Med. Chem*. **1981**, *24*, 1133.



4-*N*-(2-Pyridyl)amino-butyraldehyde diethyl acetal (3k)

^{1}H NMR (500 MHz, $CDCl_3$) δ 8.0-7.98 (m, 1H), 7.31 (t, J = 8 Hz, 1H), 6.46 (t, J = 6 Hz, 1H), 6.29 (d, J = 8.5 Hz, 1H), 4.70 (br s, 1H), 4.45-4.43 (m, 1H), 3.60-3.50 (m, 2H), 3.45-3.40 (m, 2H), 3.24-3.21 (m, 2H), 1.65-1.64 (m, 4H), 1.15-1.10 (m, 6H)

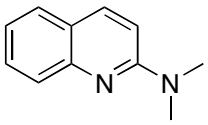
^{13}C NMR (125 MHz, $CDCl_3$) δ 158.7, 147.9, 137.2, 112.4, 106.4, 102.5, 61.0, 41.8, 31.0, 24.6, 15.2



1,2-Dihydrothiazolo[3,2-a]quinolinium bromide (7)

^{1}H NMR (500 MHz, DMSO-d_6) δ 8.97-8.85 (m, 1H), 8.38-8.28 (m, 1H), 8.25-8.05 (m, 3H), 7.92-7.80 (m, 1H), 5.41-5.30 (m, 2H), 4.05-3.90 (m, 2H)

^{13}C NMR (125 MHz, DMSO-d_6) δ 165.3, 144.3, 137.6, 134.7, 130.0, 128.0, 126.0, 118.5, 56.8, 29.2

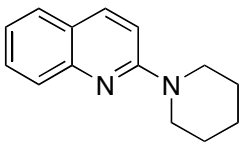


2-Dimethylaminoquinoline (8a)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 (d, J = 9 Hz, 1H), 7.73 (d, J = 8 Hz, 1H), 7.58 (d, J = 8 Hz, 1H), 7.53 (t, J = 7.7 Hz, 1H), 7.19 (t, J = 7.5 Hz, 1H), 6.88 (d, J = 9 Hz, 1H), 3.23 (s, 6H)

^{13}C NMR (500 MHz, $CDCl_3$) δ 157.5, 148.0, 137.1, 129.4, 127.2, 126.2, 122.3, 121.6, 109.0, 38.0

Lit.: Gupton, J. T.; Idoux, J. P.; Baker, G.; Colon, C.; Crews, D.; Jurss, C. D.; Rampi, R. C. *J. Org. Chem*. **1983**, *48*, 2933.



2-Piperidinylquinoline (8b)

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, J = 9 Hz, 1H), 7.73 (d, J = 8.5 Hz, 1H), 7.58 (d, J = 8 Hz, 1H), 7.54 (t, J = 7.7 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 6.98 (d, J = 9 Hz, 1H), 3.80-3.70 (m, 4H), 1.69 (s, 6H)

^{13}C NMR (125 MHz, $CDCl_3$) δ 157.5, 148.0, 137.1, 129.2, 127.0, 126.4, 122.7, 121.8, 109.7, 46.1, 25.7, 24.8

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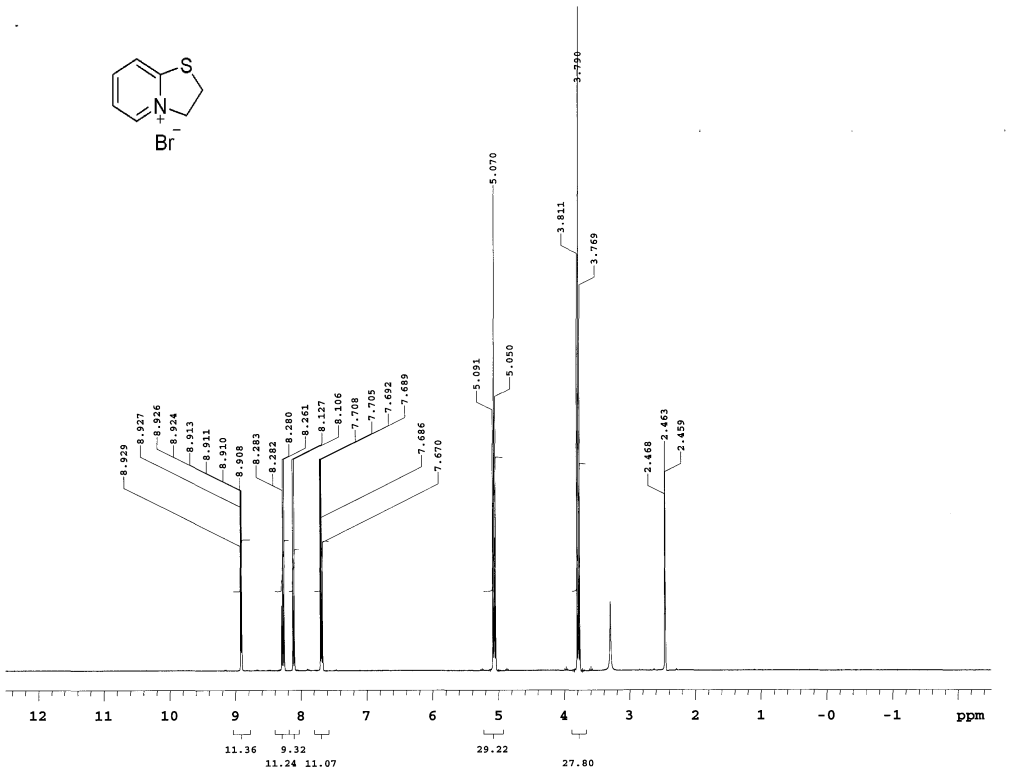
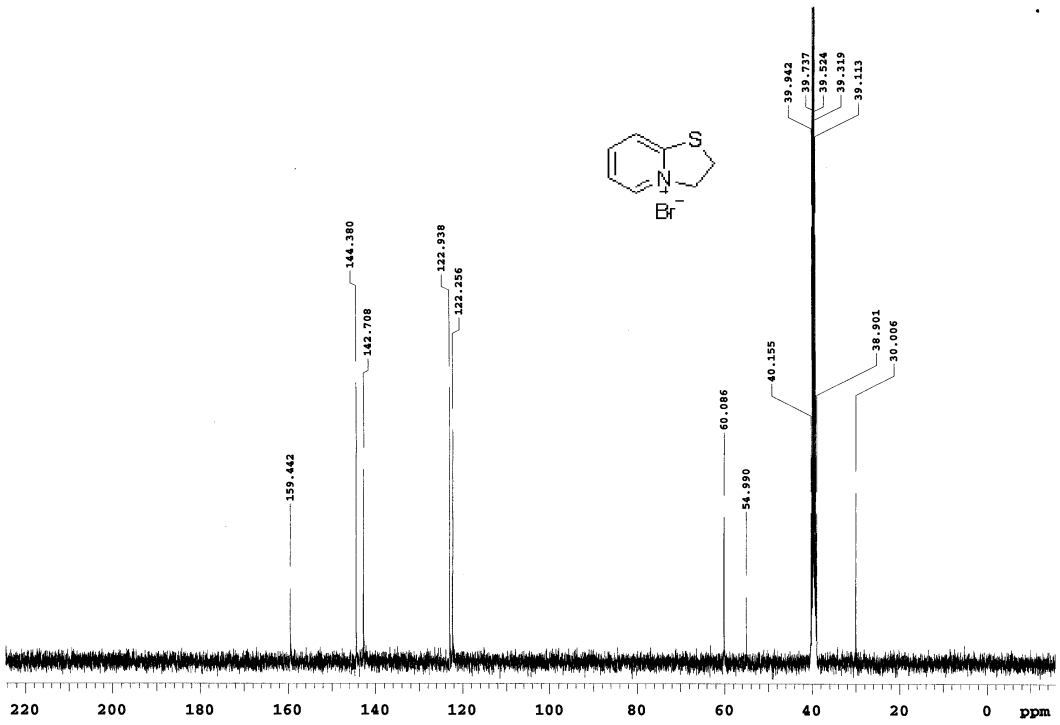
^{1}H and ^{13}C NMR Spectra of Dihydrothiazolopyridinium Bromide 2

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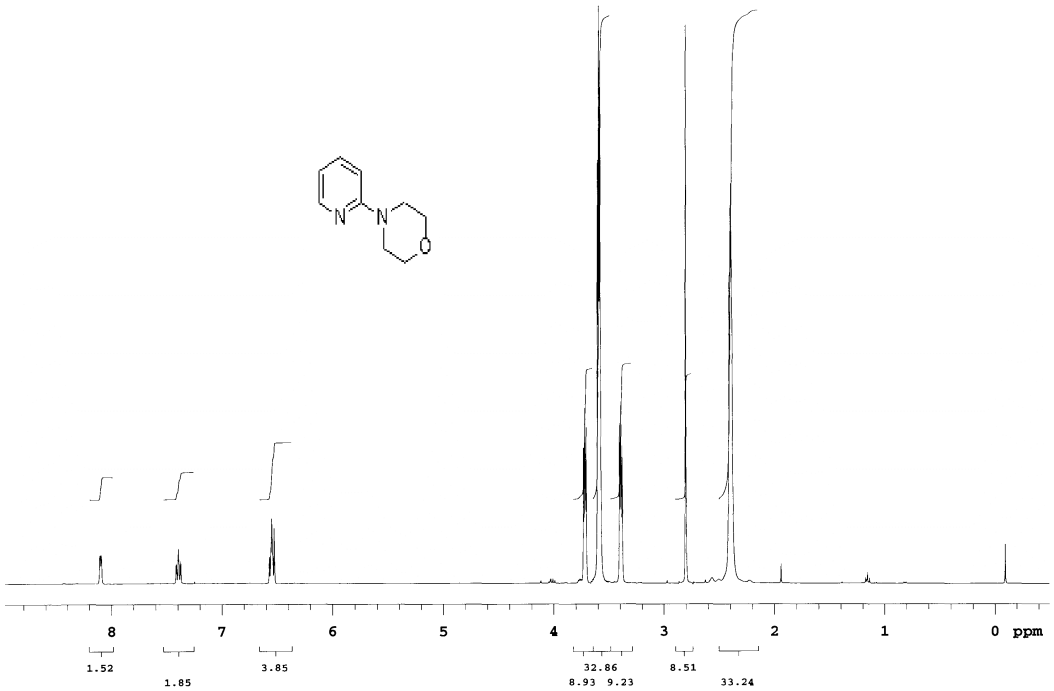
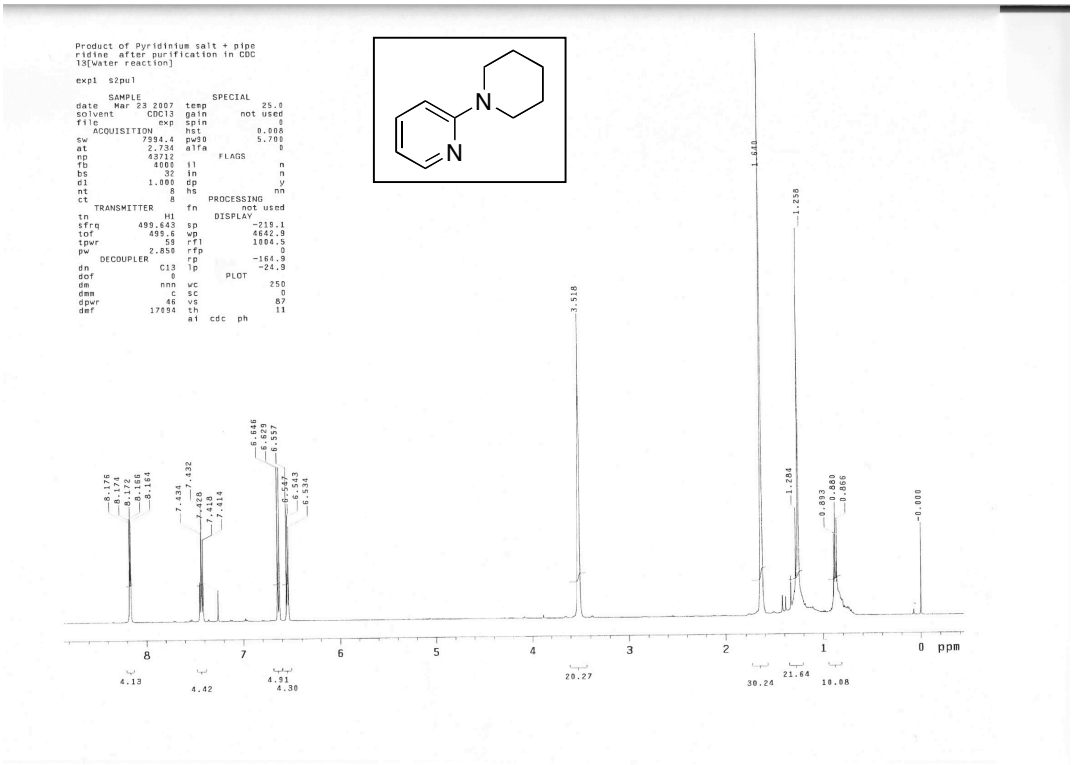
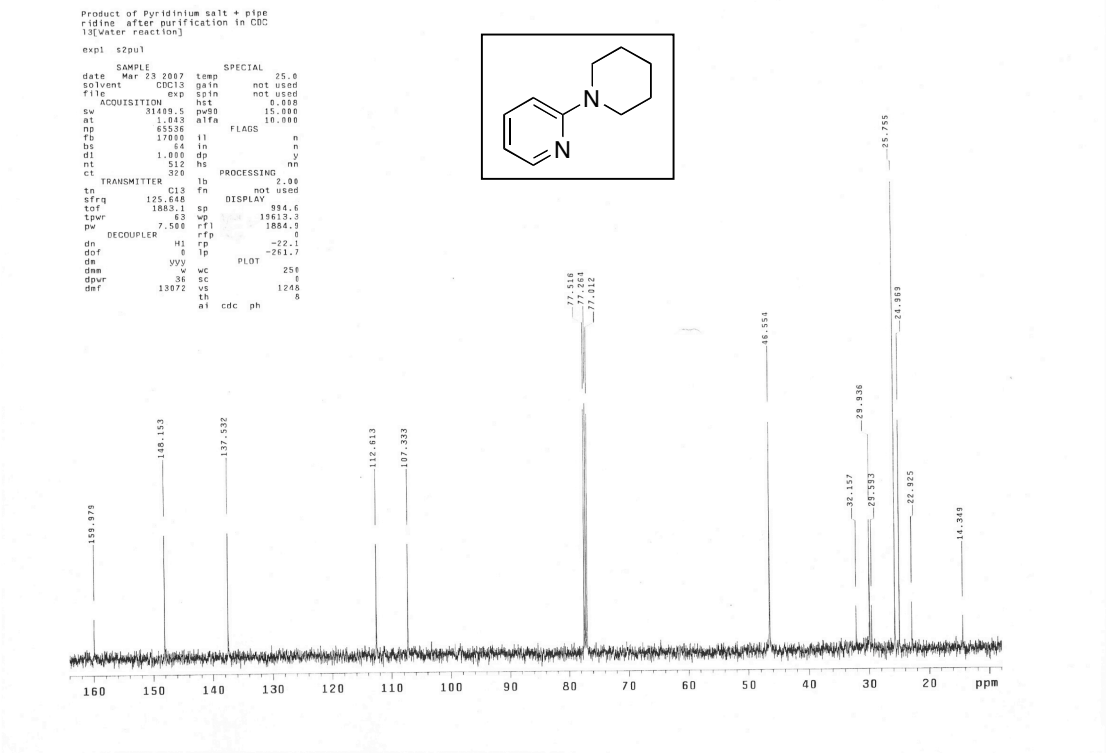
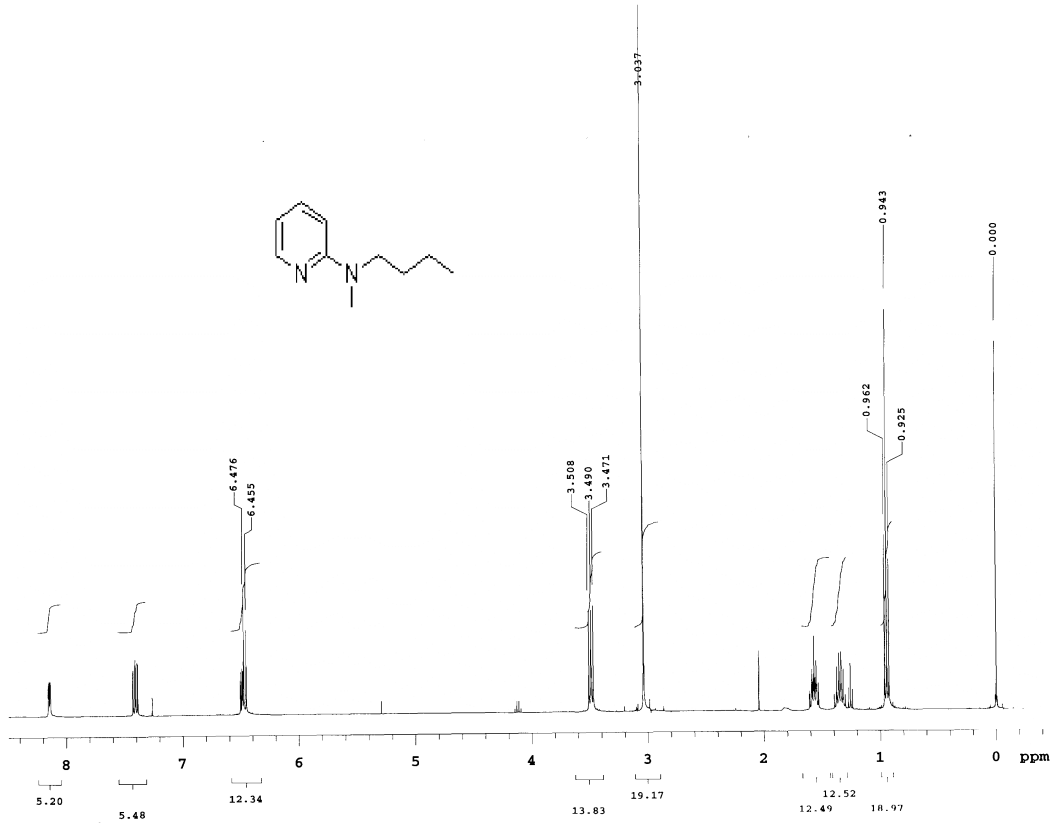


^{1}H NMR spectrum of 4-pyridin-2-yl-morpholine (**3a**)

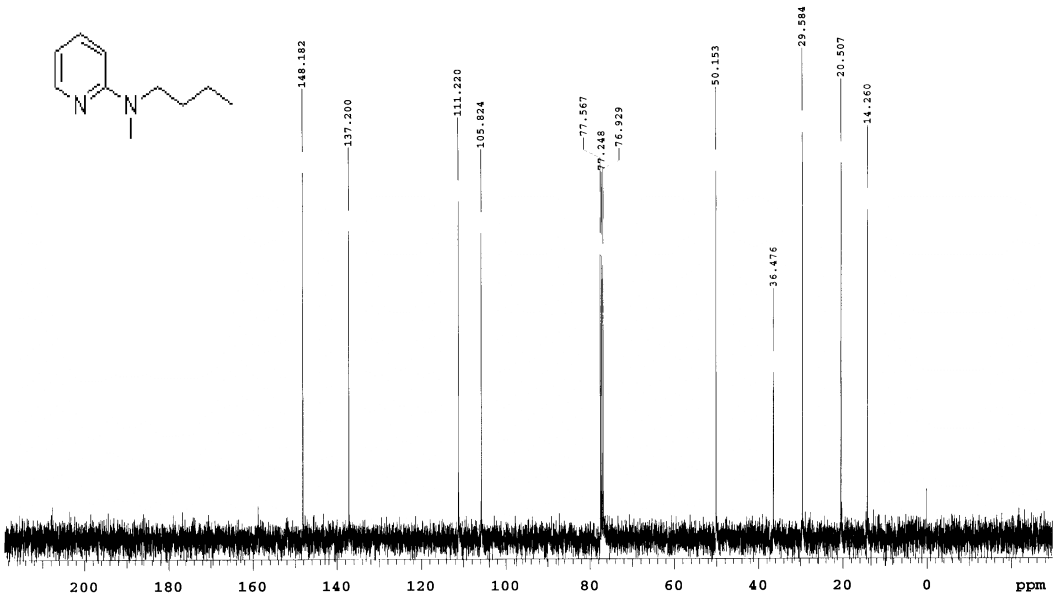
^{1}H and ^{13}C nmr spectra of 3b prepared in H_2O



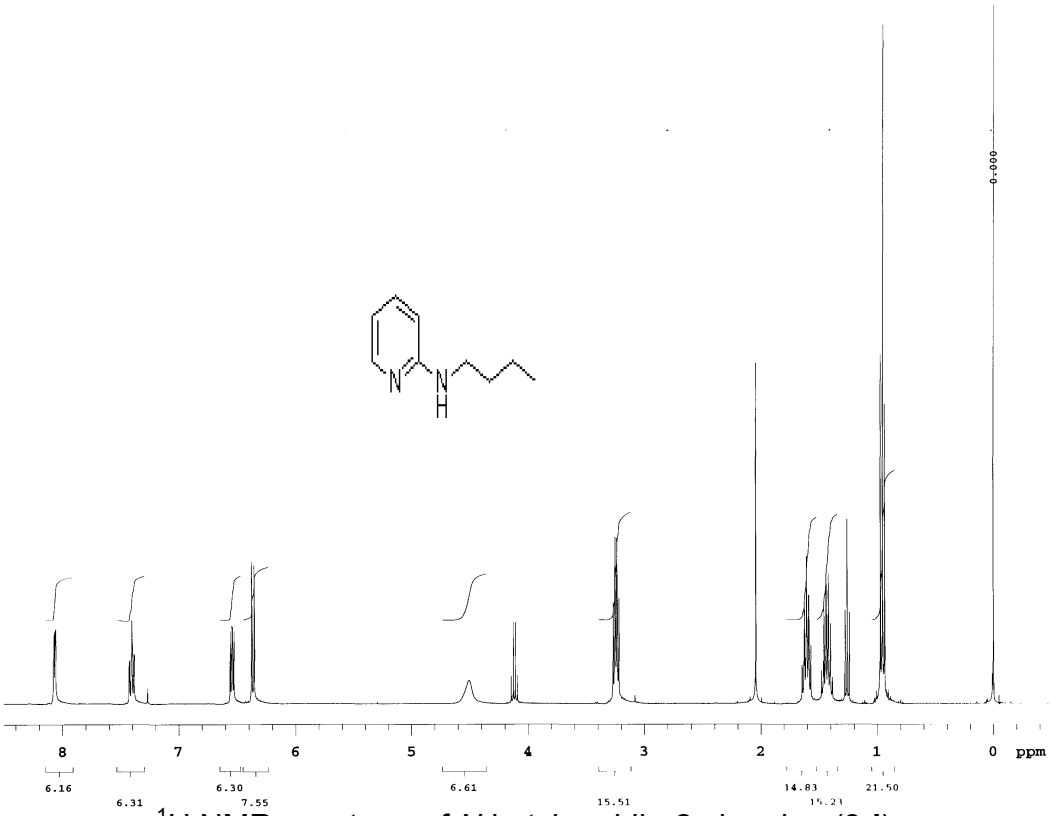




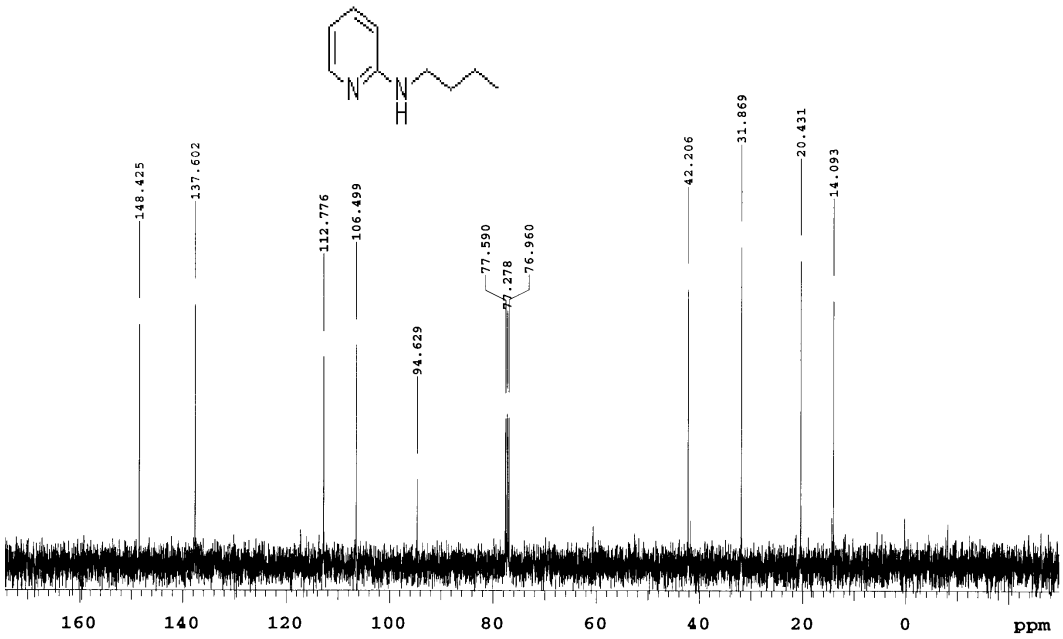
^{1}H NMR spectrum of *N*-butyl-*N*-methyl-pyridin-2-yl-amine (**3c**)



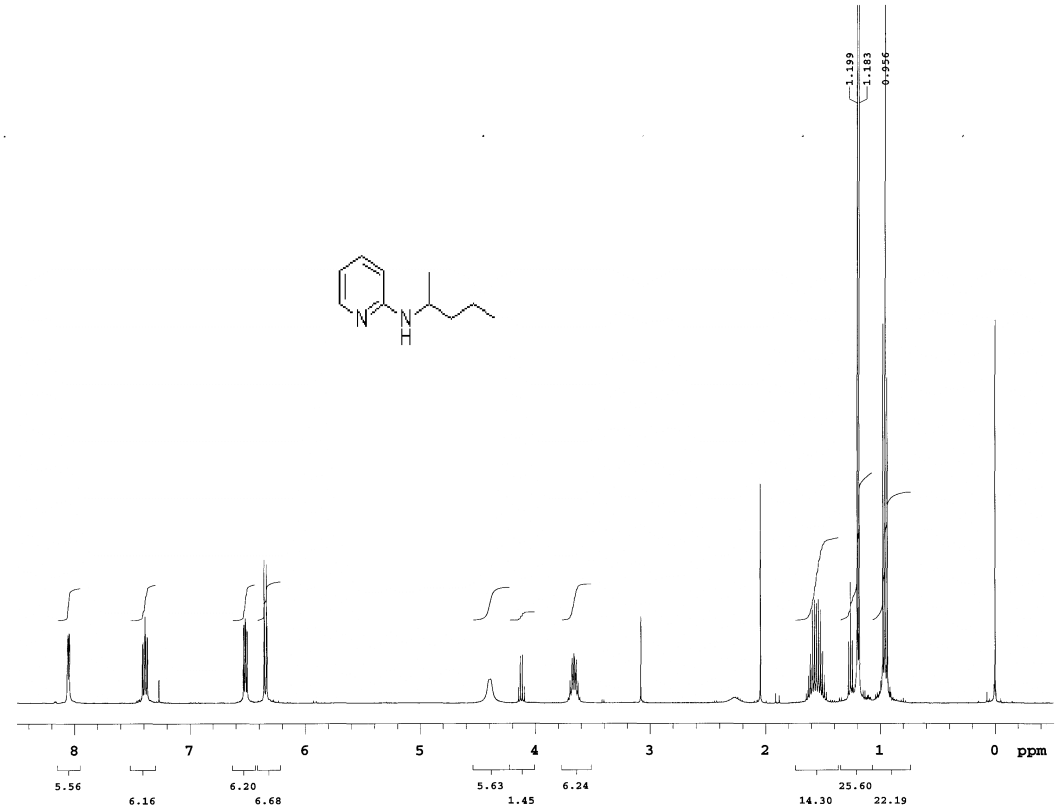
^{13}C NMR spectrum of *N*-butyl-*N*-methyl-pyridin-2-yl-amine (**3c**)



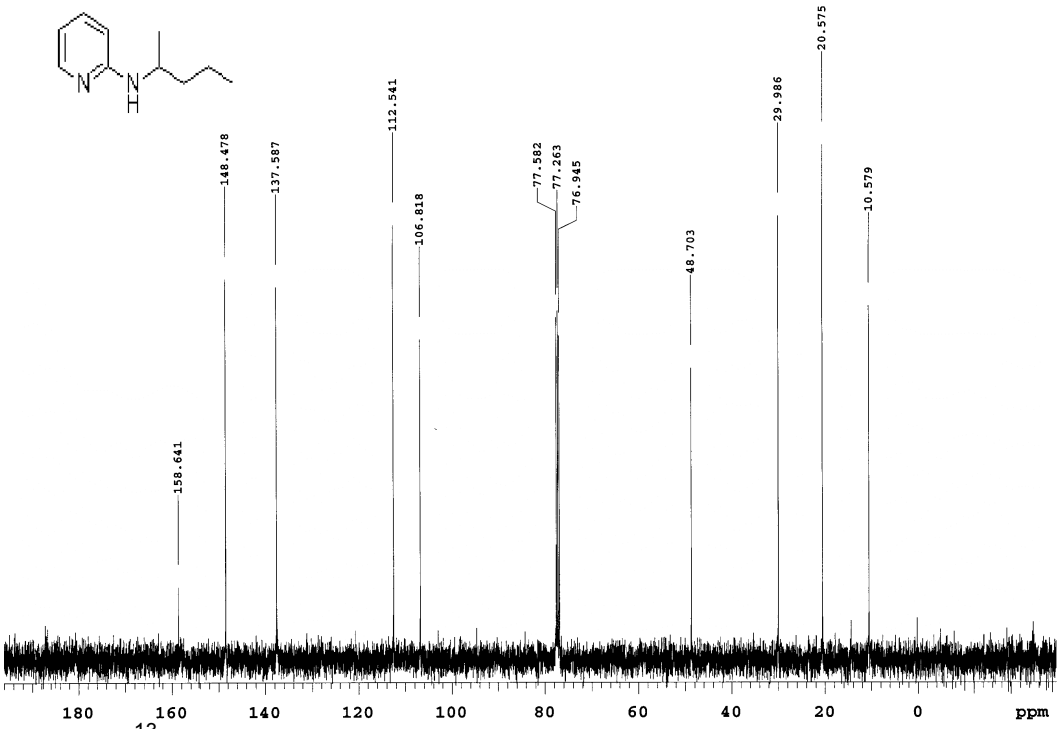
^{1}H NMR spectrum of *N*-butyl-pyridin-2-yl-amine (**3d**)



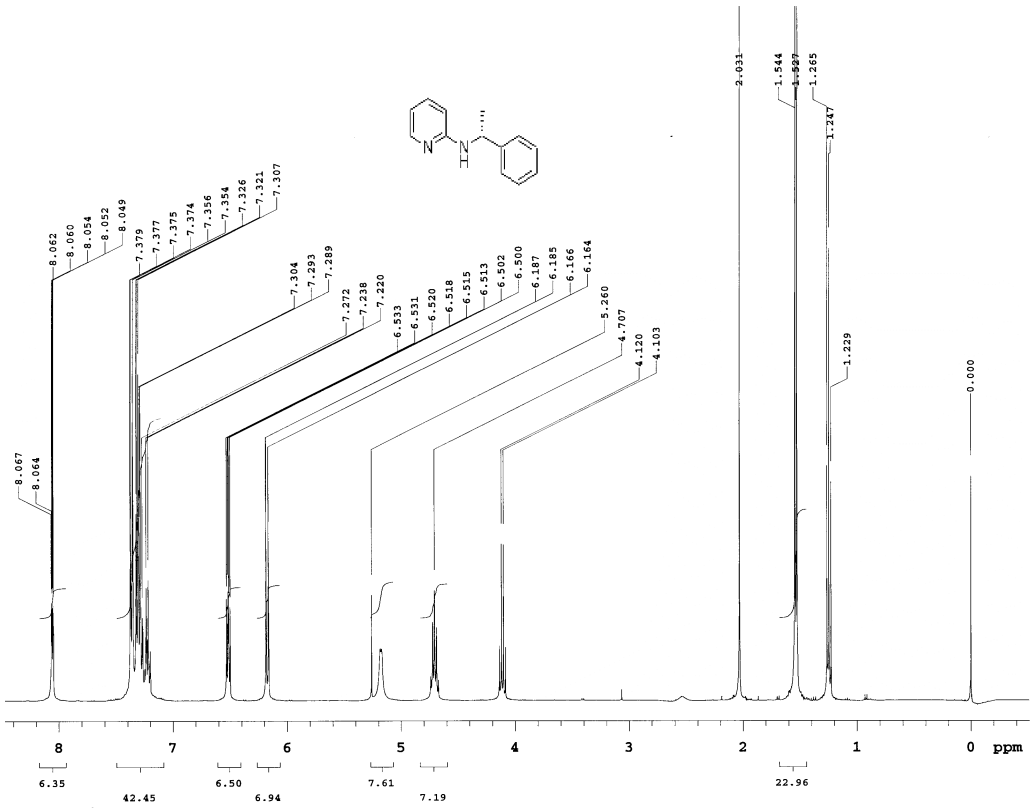
^{13}C NMR spectrum of *N*-butyl-pyridin-2-yl-amine (**3d**)



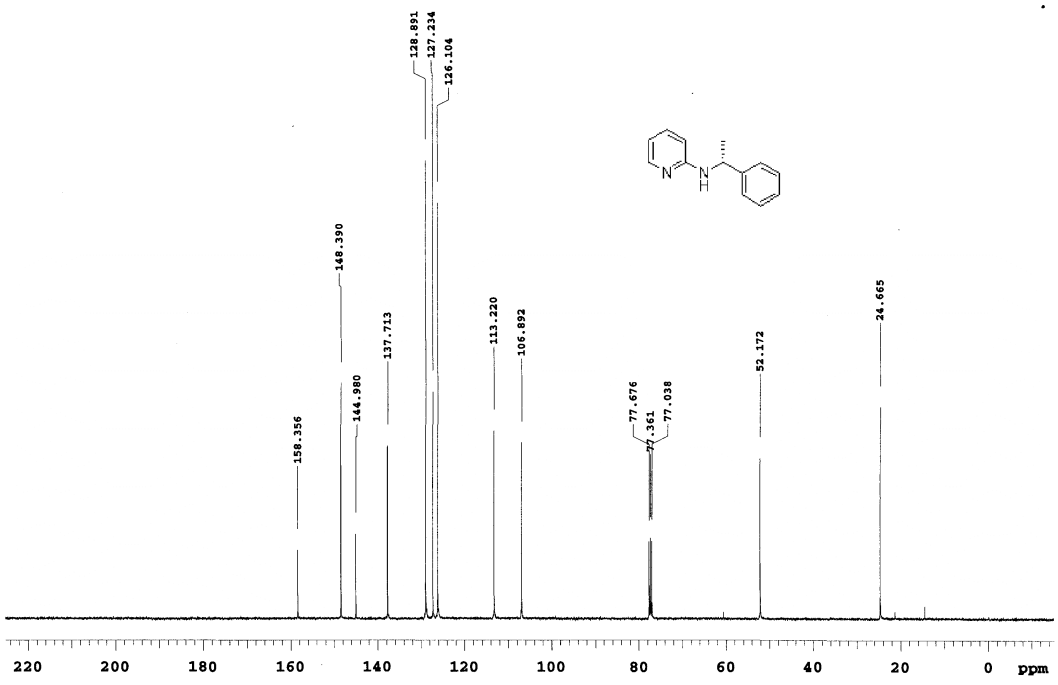
^{1}H NMR spectrum of *N*-(*s*-butyl)-pyridin-2-yl-amine (**3e**)



^{13}C NMR spectrum of *N*-(*s*-butyl)-pyridin-2-yl-amine (**3e**)

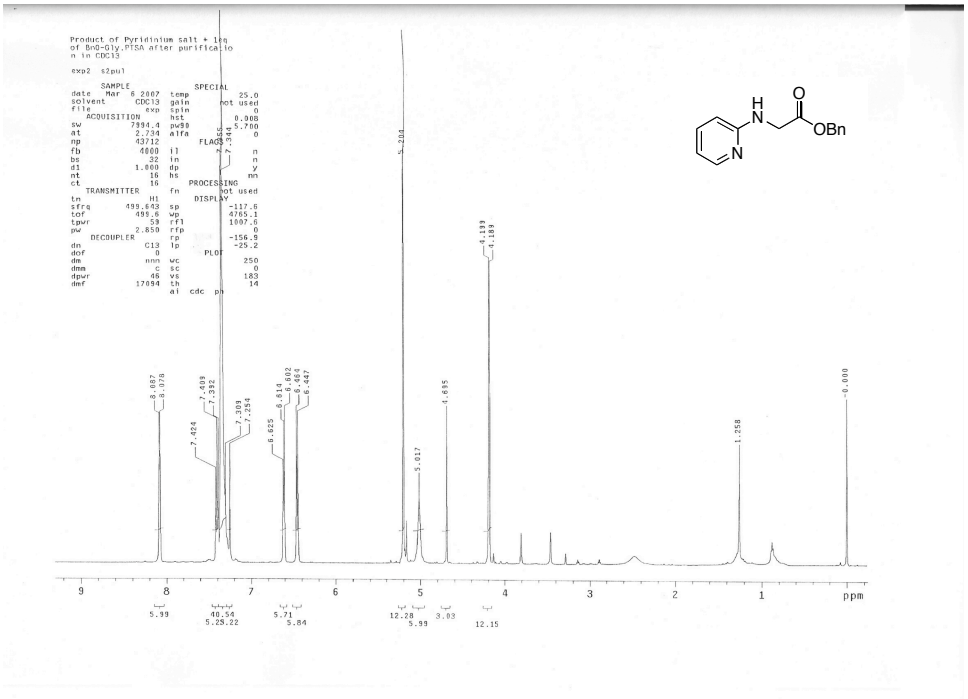


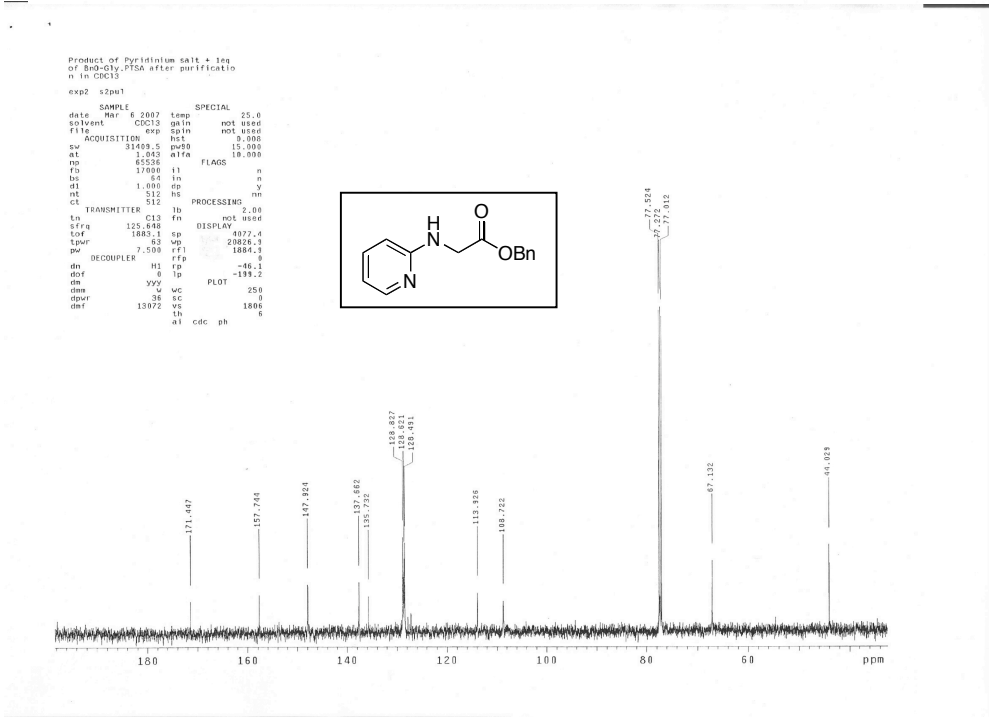
^{1}H NMR spectrum of *N*-(1-phenylethyl)-pyridin-2-yl-amine (**3f**)



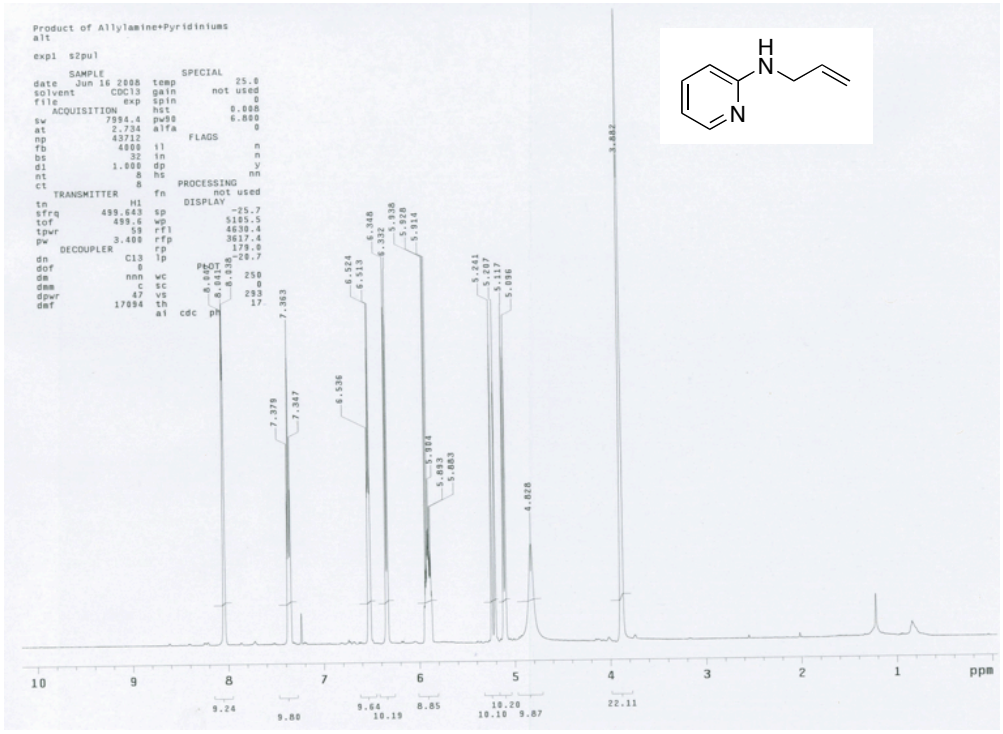
^{13}C NMR spectrum of *N*-(1-phenylethyl)-pyridin-2-yl-amine (**3f**)

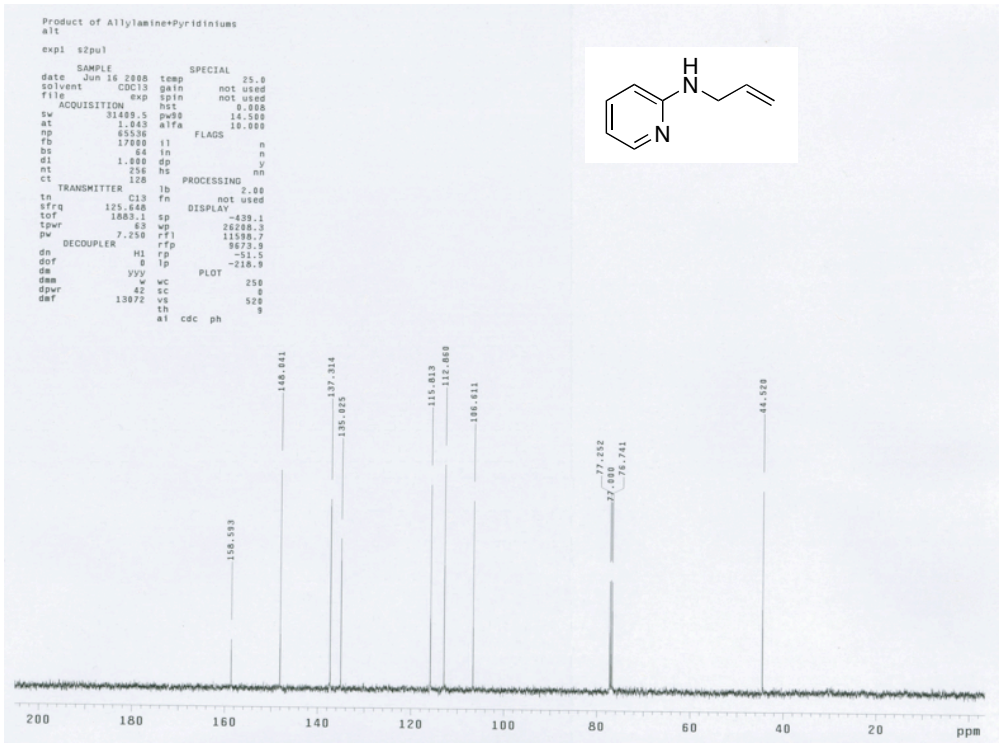
^{1}H and ^{13}C nmr spectra of **3g**



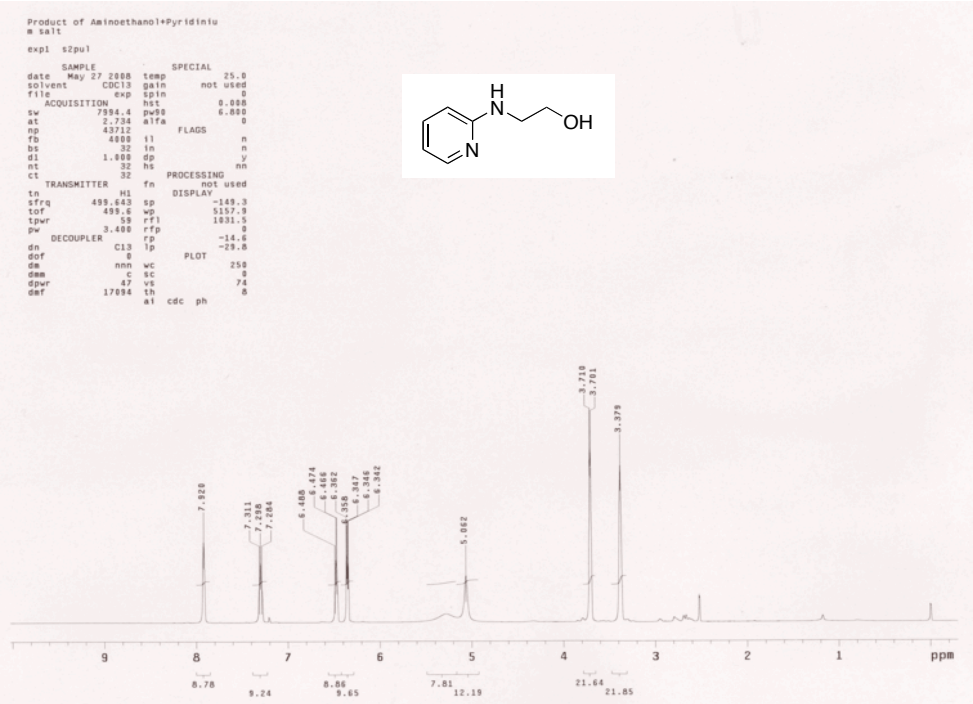


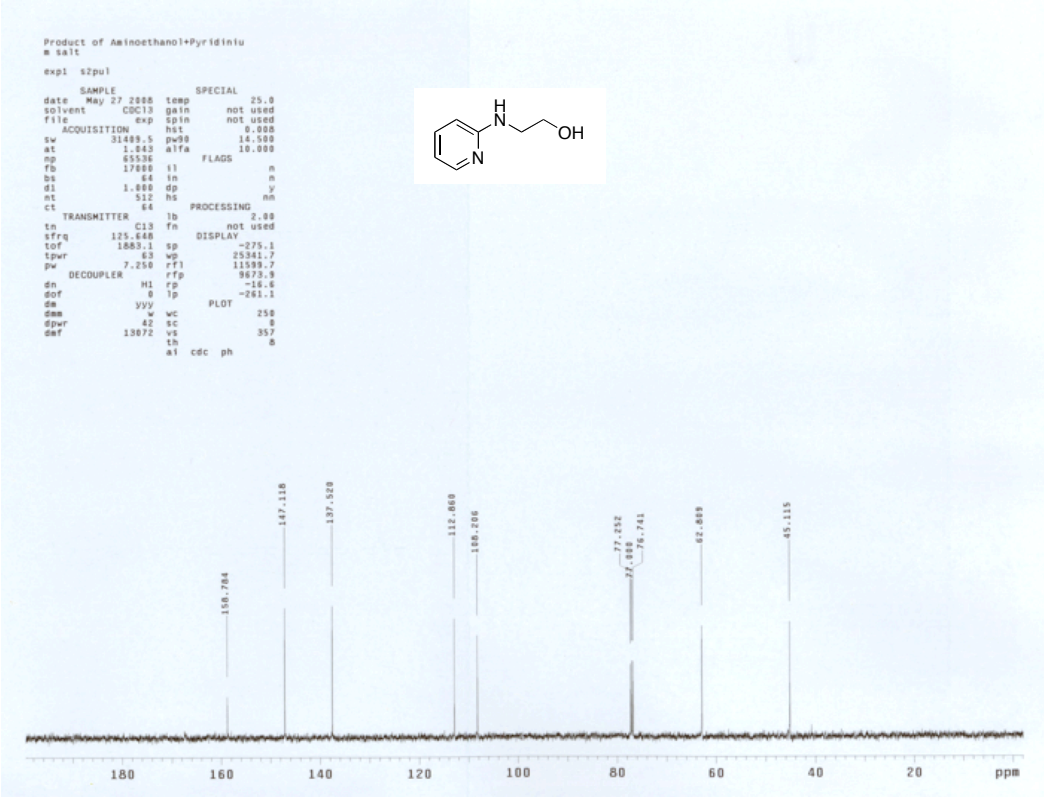
^{1}H and ^{13}C nmr spectra of **3h**



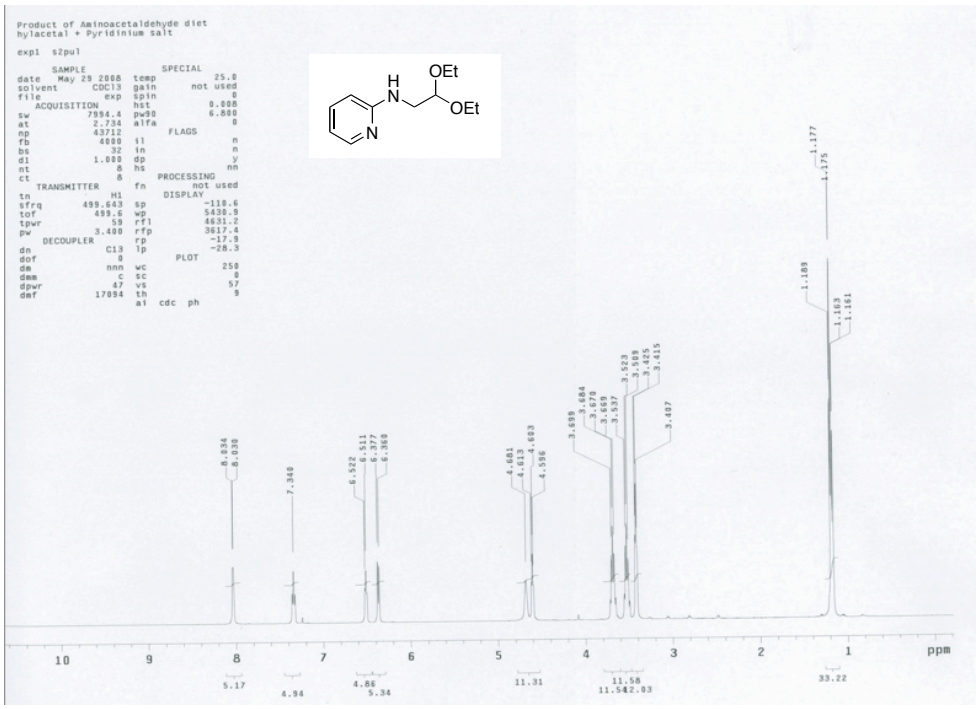


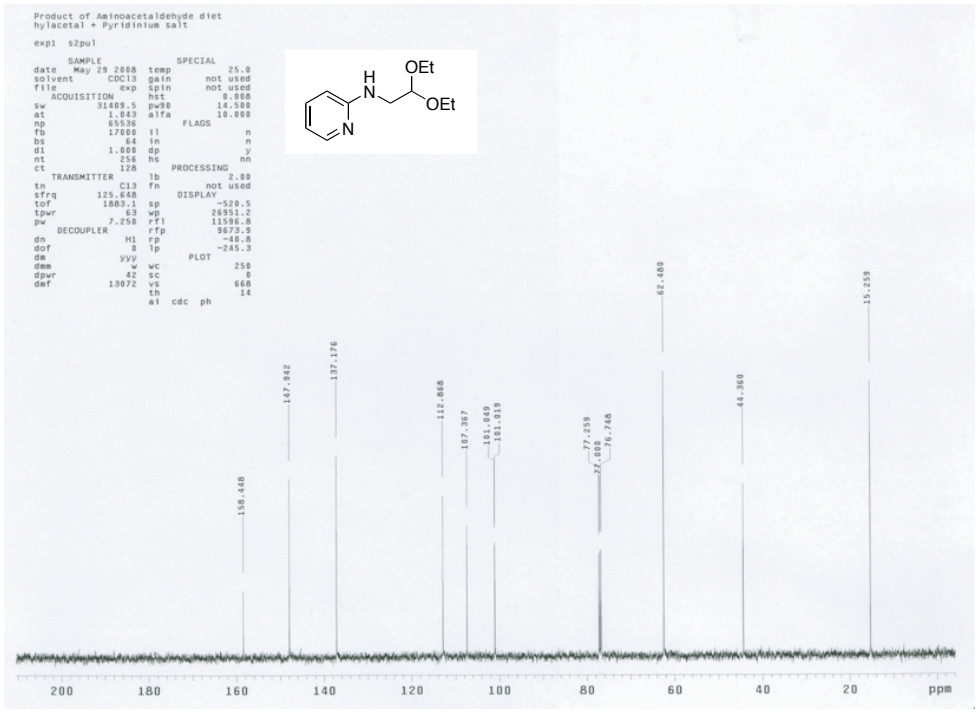
^{1}H and ^{13}C nmr spectra of **3i**



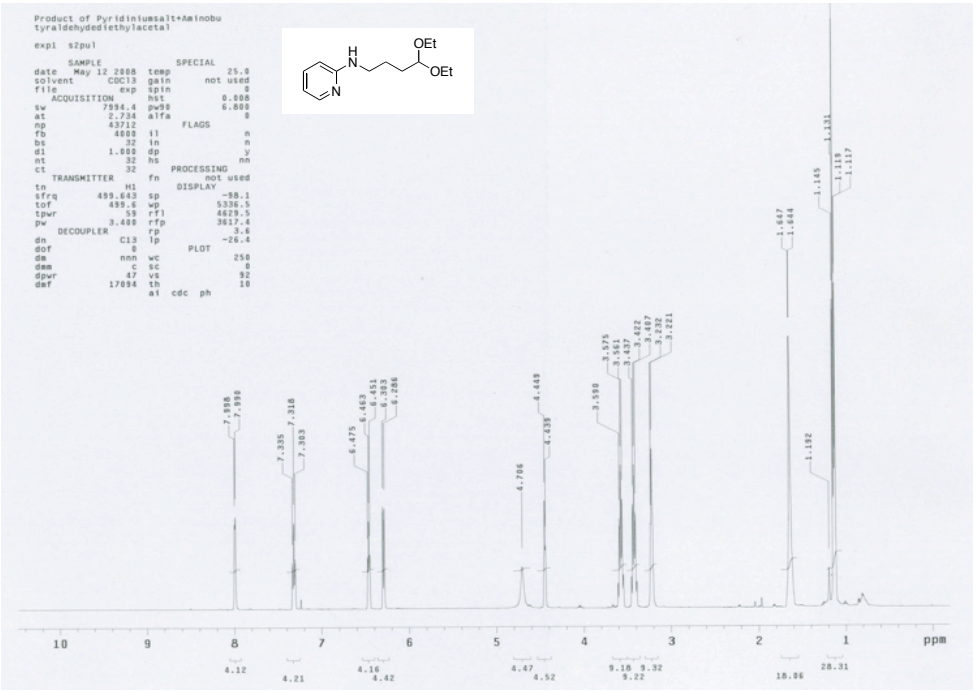


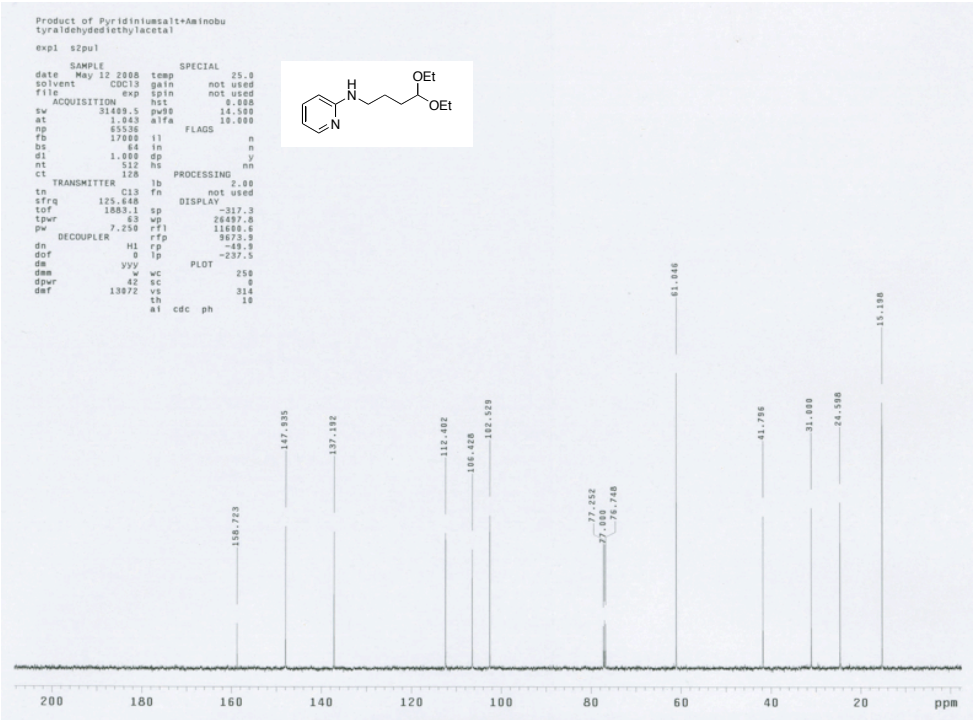
^{1}H and ^{13}C nmr spectra of **3j**



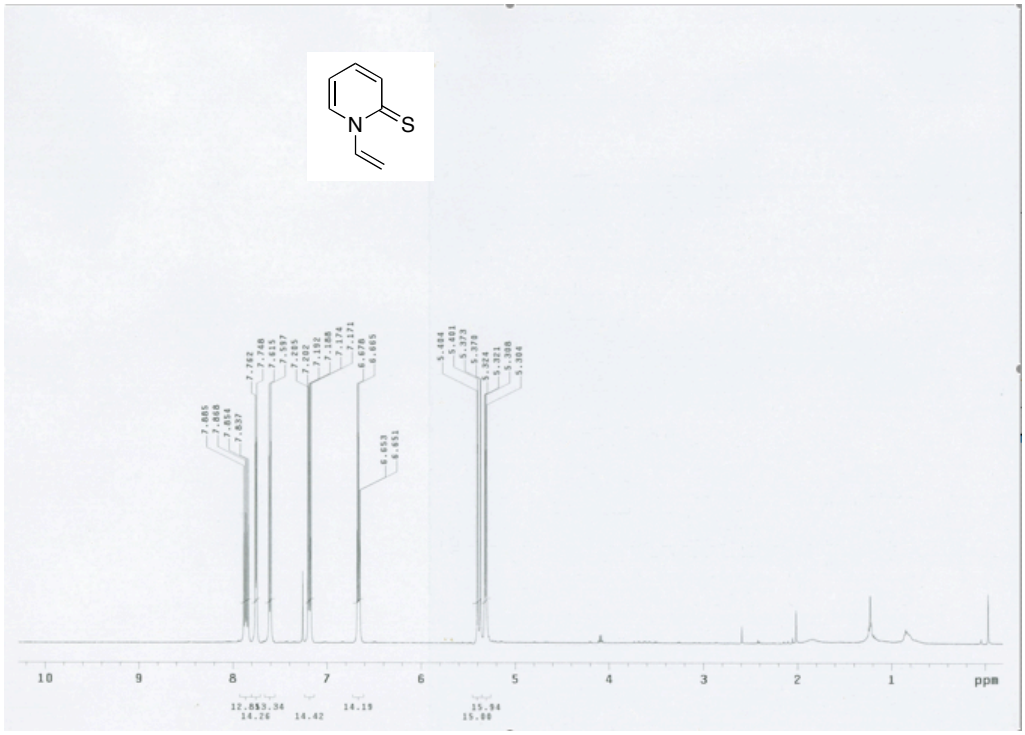


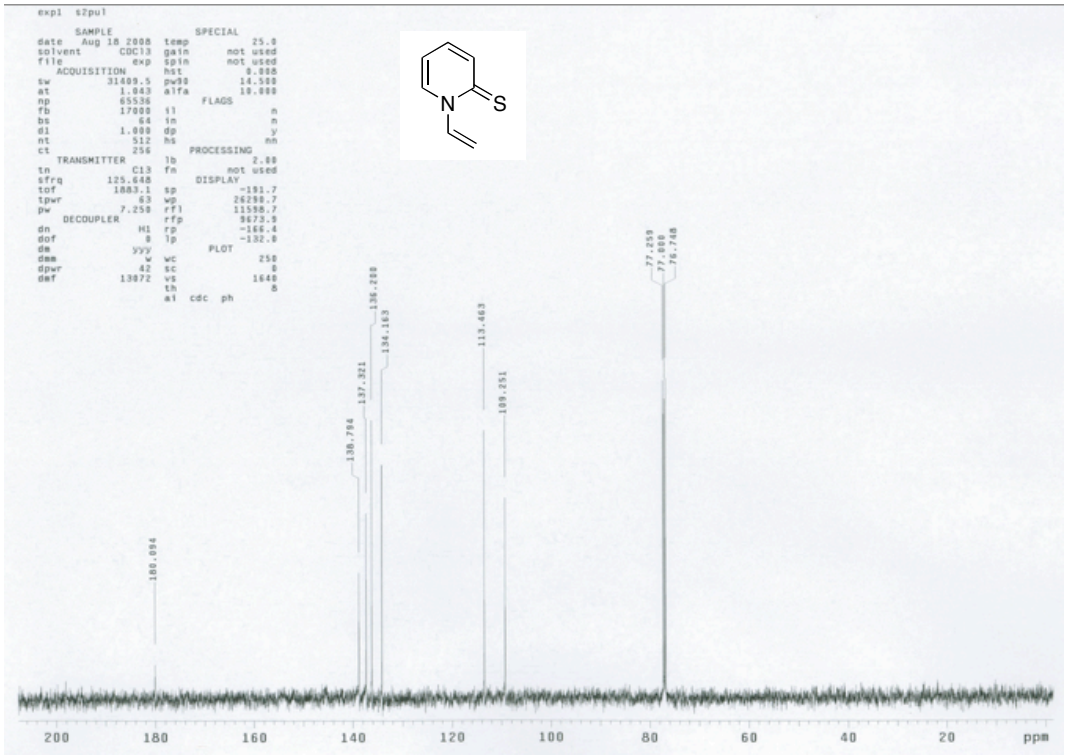
^{1}H and ^{13}C nmr spectra of **3k**



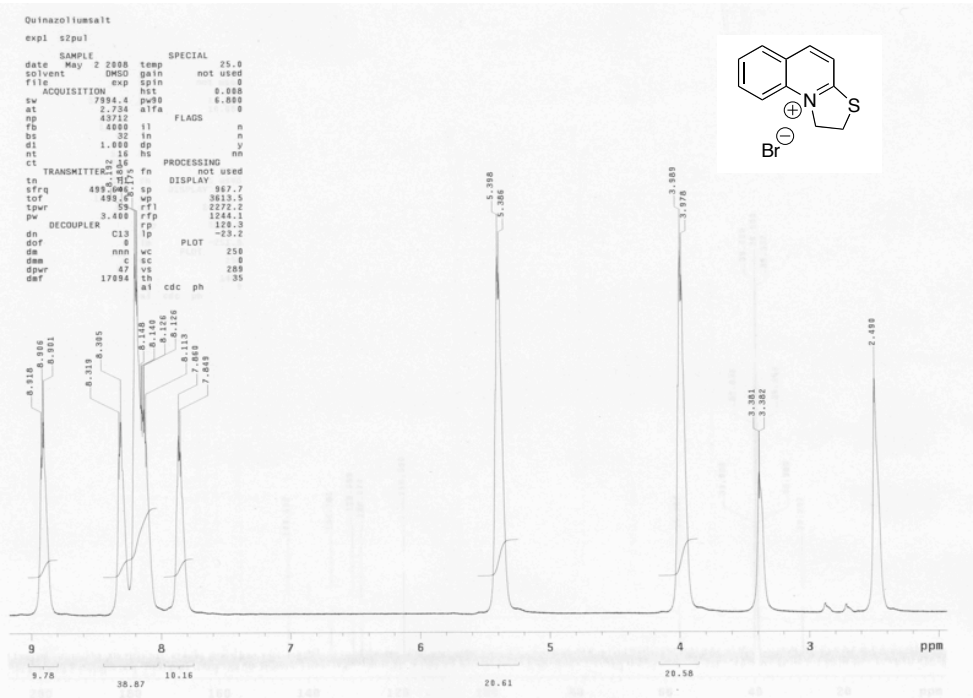


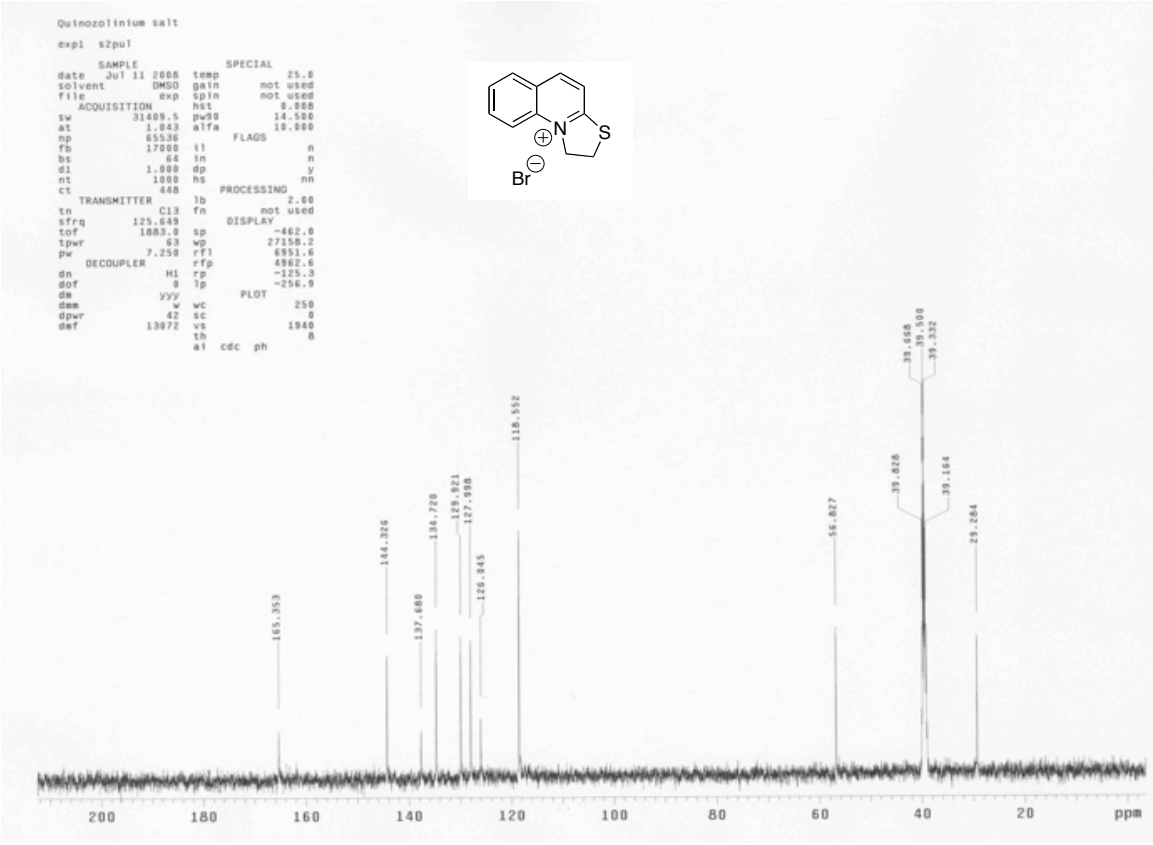
^{1}H and ^{13}C nmr spectra of **5**



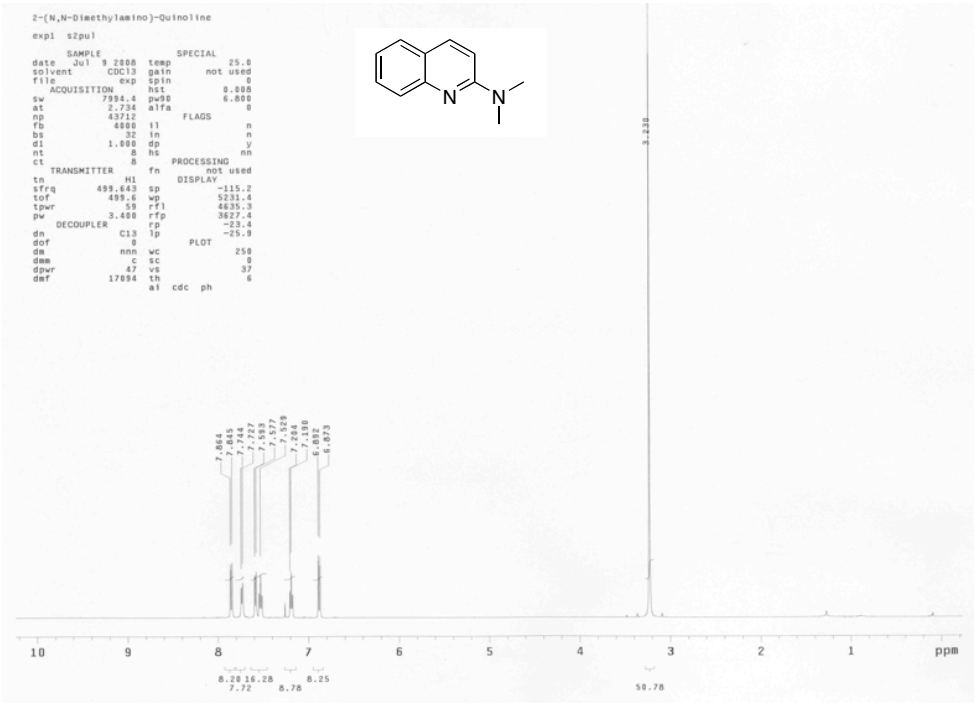


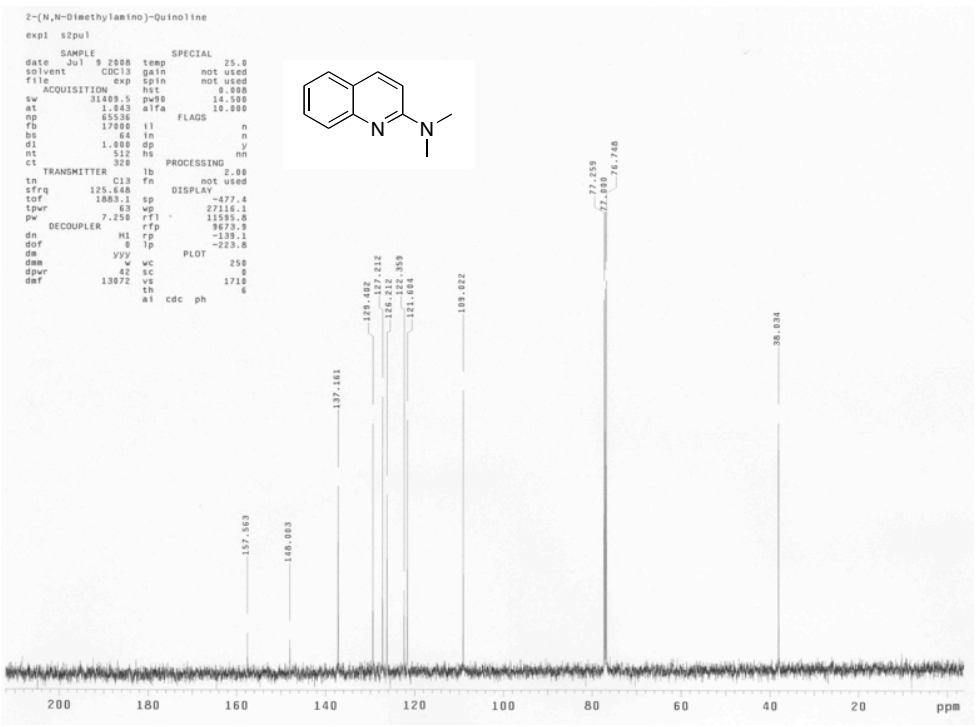
^{1}H and ^{13}C nmr spectra of **7**



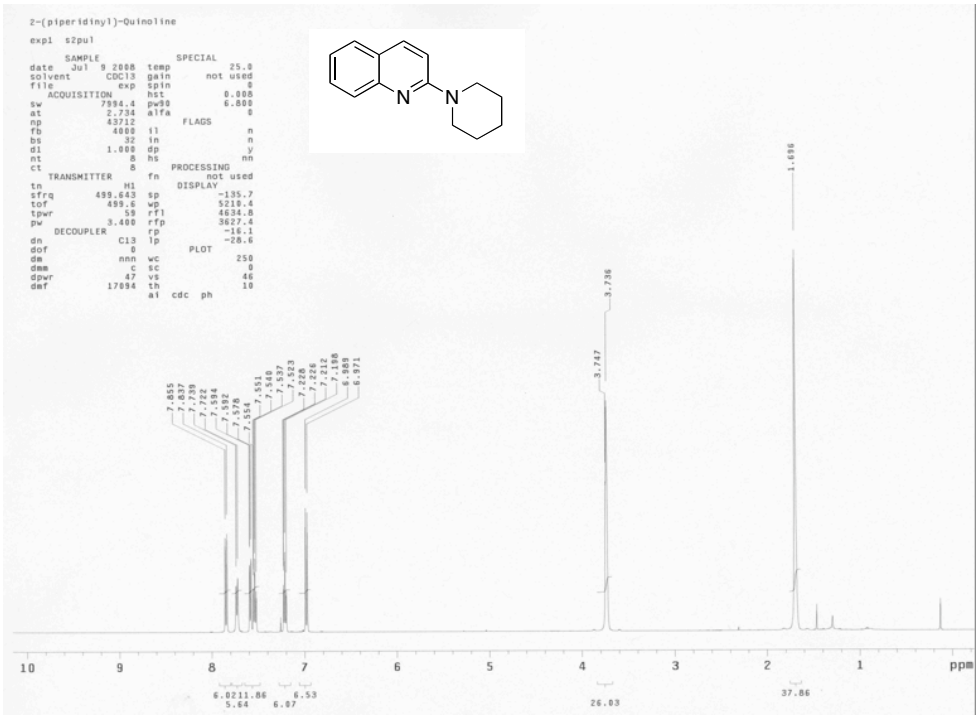


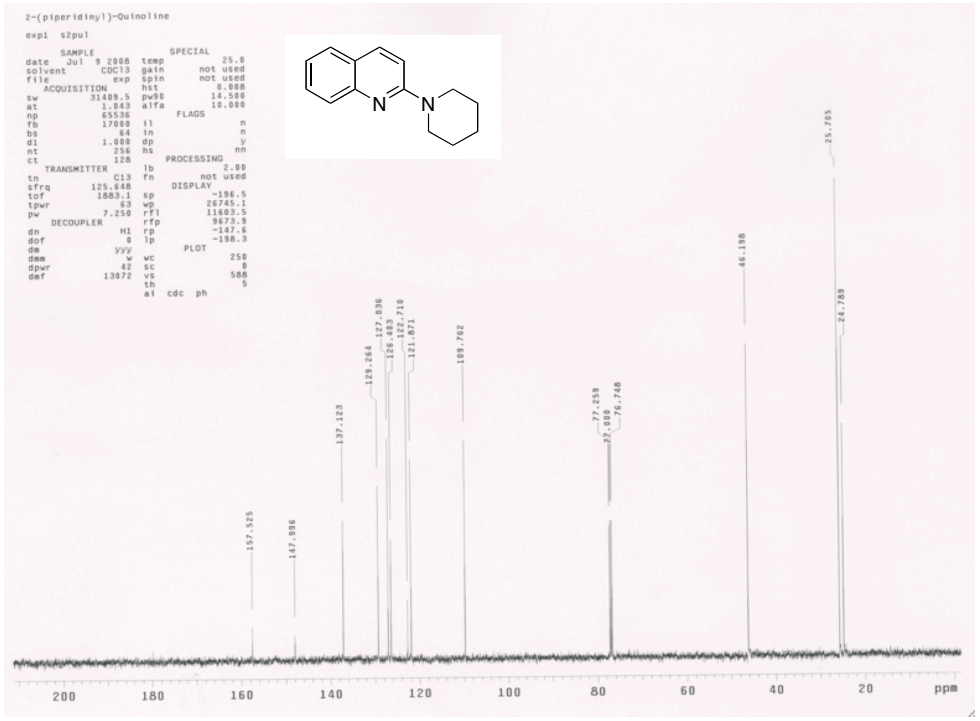
^{1}H and ^{13}C nmr spectra of **8a**



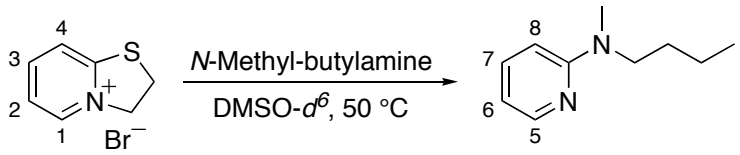


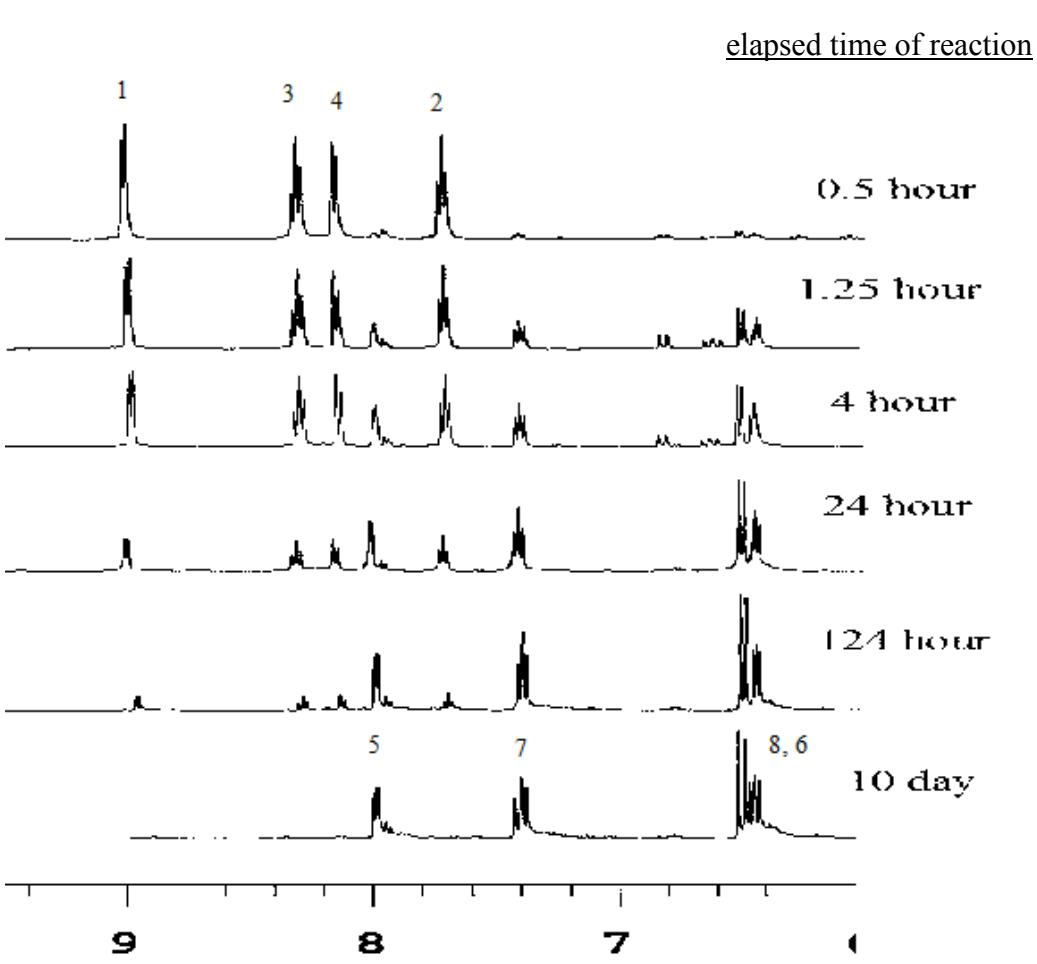
^{1}H and ^{13}C nmr spectra of **8b**



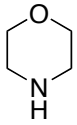
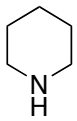
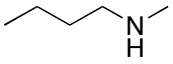
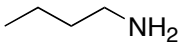
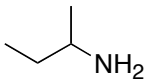
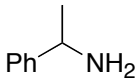
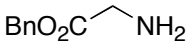
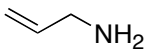


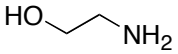
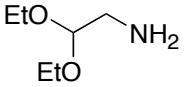
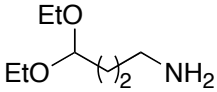
Monitoring the Formation of 3c by ^{1}H NMR





Comparison of Present Method with Previous Syntheses

Entry	Amine	Conditions[a]	Yield 3[b]	Prior Syntheses
a		A B C	75 78 94	fr. 2-fluoro-pyridine + Li-amide, rt (85%)[4] fr. 2-chloro-pyridine + Pd cat., 100 °C (99%)[5a]
b		A	94	fr. 2-fluoro-pyridine + Li-amide, rt (82%)[4] fr. 2-chloro-pyridine + Pd cat., rt (98)[11d]
c		A B C	78 77 75	fr. 2-bromo-pyridine 160 °C, 40h (76%)[6a]
d		A B C	56 63 65	fr. 2-iodo-pyridine + CuI, CsOAc, 90 °C, (80%)[7] fr. 2-amino-pyridine (80%)[3f]
e		A B C	65 57 79	fr. 2-amino-pyridine (21%)[3b]
f		A B C	75 59 61	fr. 2-fluoro-pyridine + Li-amide, rt (64%)[4] fr. 2-bromo-pyridine + Pd cat., 90 °C (70%)[6b]
g		A -	36 48[c]	not previously prepared
h		A	73	fr. 2-fluoropyridine + MW irradiation, 190 °C (64%)[17]

i		A	71	fr. 2-fluoropyridine + MW irradiation 210 °C (74%)[17]
j		A	86	fr. 2-aminopyridine + $NaNH_2$, 150 °C (47%)[18]
k		A	78	not previously prepared

[a] Reactions analyzed after 48h; A: 4.0 eq. amine, DMSO, 50 °C; B: neat amine (*ca*. 0.4 – 0.5M), rt; C: neat amine (*ca*. 0.4–0.5M), 50 °C. [b] percent, after chromatography. [c] 4.0 eq. amine, DMSO, rt.