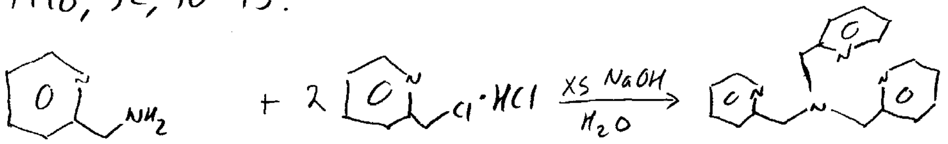
Title: Synthesis of Tris[(2-pyridyl)methyl]amine June 10, 2003
J. M. McCormick

Statement of Purpose: Tris[(2-pyridyl)methyl]amine, TPA, will be synthesized in order to explore ~~ist~~ its 6/10/03 coordination chemistry with Pb^{2+}.

Background:
Reference: Canary, J. W.; Wang, Y.; Roy, Jr., R. "Tris[(2-pyridyl)methyl]amine (TPA) and (+)-bis[(2-pyridyl)-methyl-1-(2-pyridyl)ethylamine (α-MeTPA)" Inorg. Synth. 1998, 32, 70-75.



2-(aminomethyl)pyridine   2-picolylchloride hydrochloride   tris[(2-pyridyl)methyl]amine TPA

Physical Properties:

Compound	Formula	Molar Mass (g/mole)	Melting Point (°C)	Density (g/cm³)	Hazards
2-(aminomethyl)pyridine	$C_6H_8N_2$	108.14		1.049	corrosive
2-picolylchloride hydrochloride	$C_6H_7Cl_2N$	164.03	125-129		irritant, hydroscopic
TPA	$C_{18}H_{18}N_4$	290.36	73-77		
water	H_2O	18.02			
sodium hydroxide	$NaOH$	40.00			corrosive, toxic
methylene chloride	CH_2Cl_2	84.93			toxic, irritant
hexane	C_6H_{14}	86.18			flammable, irritant
sodium sulfate (anhydrous)	Na_2SO_4	142.04			irritant, hygroscopic
deuterochloroform	$CDCl_3$	120.39			highly toxic, carcinogen

J. M. McCormick June 10, 2003

Synthesis of Tris[(2-pyridyl)methyl]amine

June 10, 2003

Procedural Outline:

• In a 200-mL round bottom flask place 25.6g (160 mmol) 2-picolylchloride hydrochloride in 40mL distilled water	• Change to 10g in 20mL H_2O
• Add 8mL (80mmol) 2-(aminomethyl)pyridine	• Change to 3 mL
• Slowly add 31.0mL of a 10 M NaOH solution (aqueous) dropwise over 2 hr.	• Change to 5.03g NaOH in 12 mL H_2O
• Heat flask at 70°C for 30 min	• Change to 20 min.
• Cool red reaction mixture and extract 3 x 150-mL $CHCl_3$	• Substitute CH_2Cl_2 for $CHCl_3$ and change to 4 x 50 mL
• Combine extracts and dry over Na_2SO_4	
• Remove $CHCl_3$ by rotary evaporation	
• Vacuum distill (200°C, 0.01mm Hg) to obtain product (yield: 11.3g, 50%)	• Dissolve residue in minimal amount of hot hexane. • Filter hot solution and let stand (crystals should form). • Recover crystals by vacuum filtration • Recrystallize from hexane

June 10, 2003
J. M. McCormick

Synthesis of Tris[(2-pyridyl)methyl]amine June 13, 2003

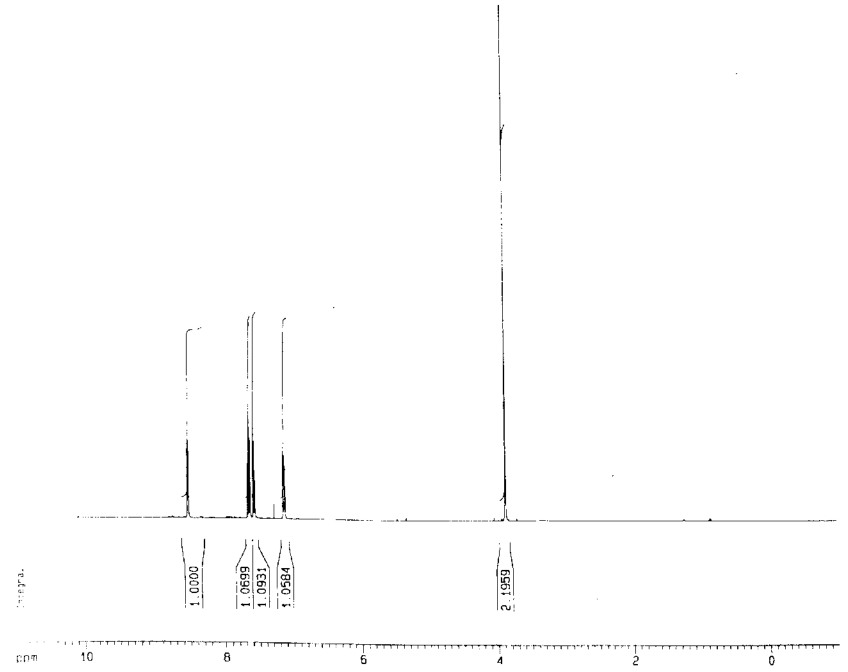
Results:

To a solution of 10.11g 2-picolylchloride hydrochloride (Acros, Lot # A016040301) in 20 mL distilled H_2O was added 3.20 mL 2-(aminomethyl)pyridine (Acros, Lot # A013625401) with stirring. To this mixture was added a solution of 5.03g NaOH (Fisher, Lot # ~~995321~~ 995312 wrong lot # 6/13/03) in 12 mL H_2O in a slow, dropwise manner using an addition funnel. The addition was regulated so that it took approximately 1.5 hr to add all of the NaOH solution. During the addition the initially yellow reaction mixture turned deep red and droplets of an oily (red?) substance separated. After all of the NaOH solution had been added, the reaction mixture was heated to 70°C and held there for 20 min. The cooled reaction mixture was extracted four times with 50 mL CH_2Cl_2 (Fisher, Lot # 010927). The combined extracts were dried over Na_2SO_4 (Aldrich, Lot # 04218 KZ) and gravity filtered to remove the Na_2SO_4. The CH_2Cl_2 was removed by rotary evaporation to give a red oil that solidified upon standing. The red solid was dissolved in the minimal amount of hot hexane. The yellow solution was decanted from a small amount of a red oil that did not dissolve, and filtered hot. Some oil was accidently poured into the filter paper, but it adhered to the paper and did not pass through. No solids were observed on the filter paper. Upon cooling light-yellow crystals formed from the red-orange solution. These were collected by vacuum filtration and dried briefly in air. Crude product was recrystallized

J. M. McCormick June 13, 2003

Synthesis of Tris[(2-pyridyl)methyl]amine June 13, 2003

from hot hexane and allowed to air dry over the weekend. Final yield was 2.08g (24%) of light-yellow crystals. The melting point of the product was determined to be 85°C, sharp (uncorrected) using a Mel-Temp (no serial number evident). NMR spectra of the product were recorded using a Brüker Avance 400 MHz spectrometer (serial # BH040699). All manipulations of the spectra were performed using Brüker's XWINNMR version 3.1 running on a Silicon Graphics O2 workstation.



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PROCNO                   1

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HZCM             240.07800 Hz/cm
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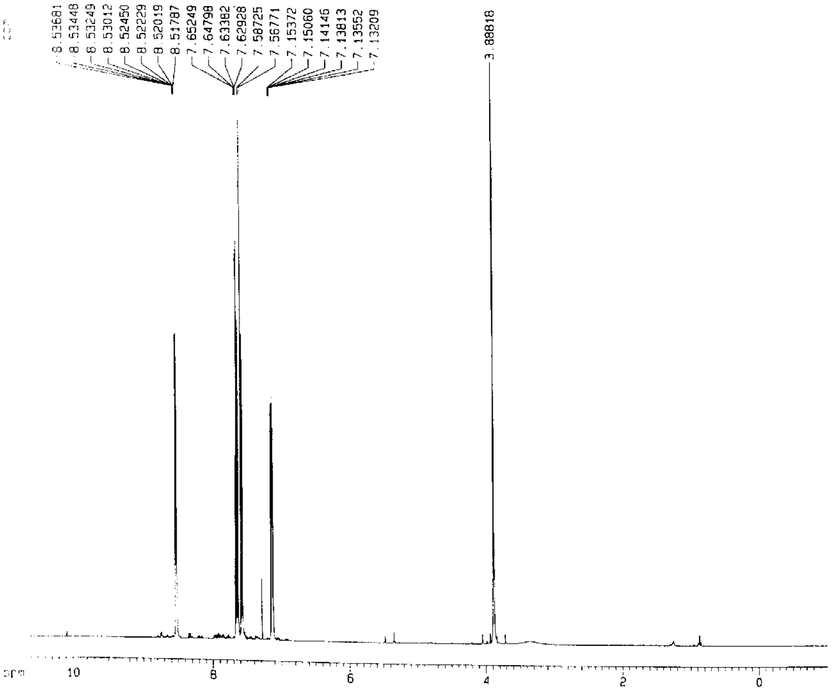
^{1}H NMR of TPA (Jun16-2003, expt. 40, $CDCl_3$ solvent)

J.M. McCormick June 16, 2003

Synthesis of Tris[(2-pyridyl)methyl]amine

June 16, 2003



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======== CHANNEL f1 ========
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1D NMR plot parameters
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F2P                  -1.000 ppm
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HZCM              240.07800 Hz/cm
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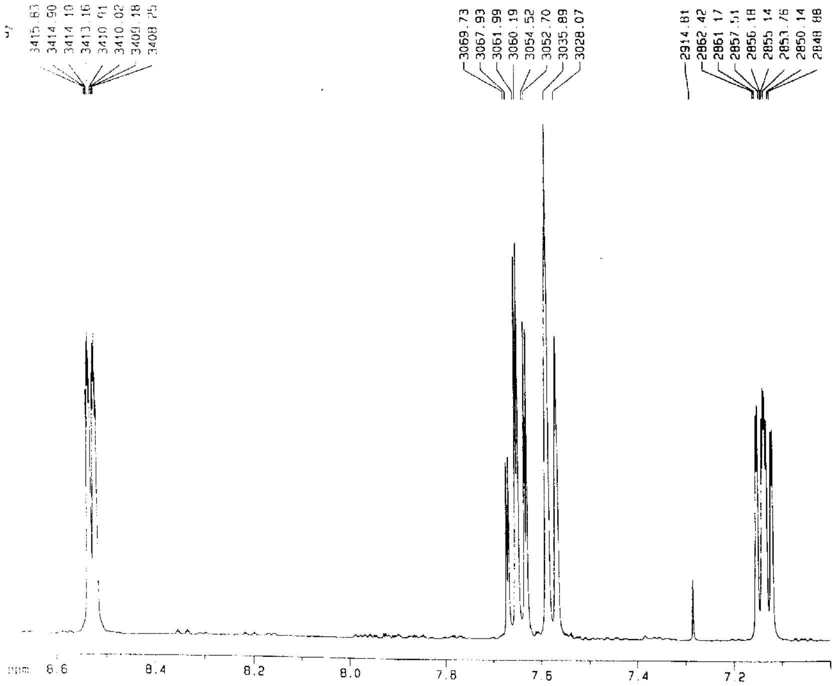
^{1}H NMR of TPA showing peak positions in ppm



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TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH                8250.825 Hz
FIDRES             0.125898 Hz
AQ                3.9715922 sec
RG                     80.6
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DE                     6.00 usec
TE                    300.0 K
D1               1.00000000 sec

======== CHANNEL f1 ========
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F2 - Processing parameters
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WDW                      EM
SSB                       0
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PC                     1.00

1D NMR plot parameters
CX                    20.00 cm
CY                    50.00 cm
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F1                  3481.13 Hz
F2P                   7.000 ppm
F2                  2800.91 Hz
PPMCM               0.08500 ppm/cm
HZCM               34.01105 Hz/cm
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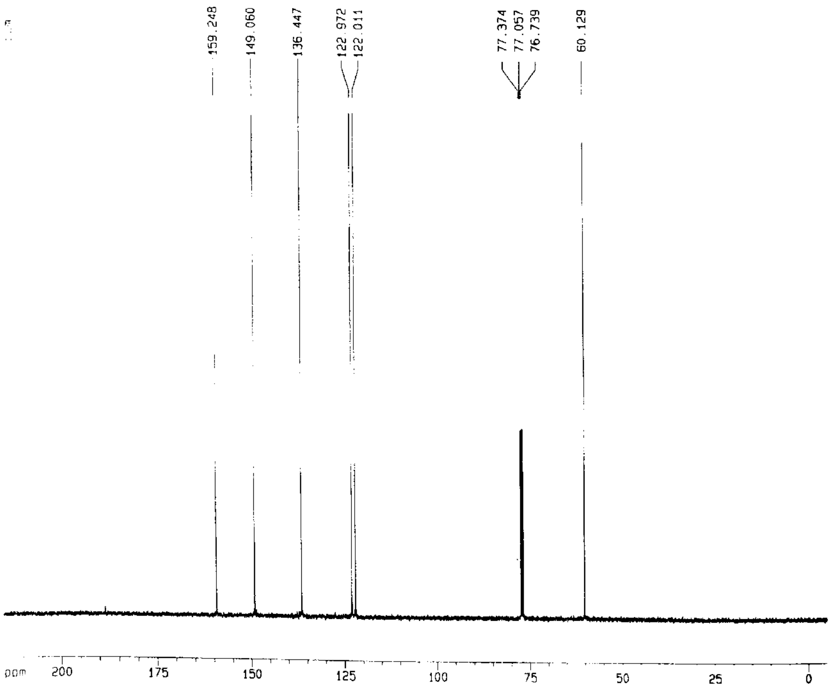
^{1}H NMR of TPA showing peak positions in Hz

J. McComick
June 16, 2003

Synthesis of Tris[(2-pyridyl)methyl]amine

June 16, 2003



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PL2                -3.00 dB
PL12               17.00 dB
PL13               17.00 dB
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F2 - Processing parameters
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WDW                   EM
SSB                    0
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GB                     0
PC                  1.40

1D NMR plot parameters
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F1              21631.75 Hz
F2P               -5.000 ppm
F2               -503.06 Hz
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HZCM          1106.74048 Hz/cm
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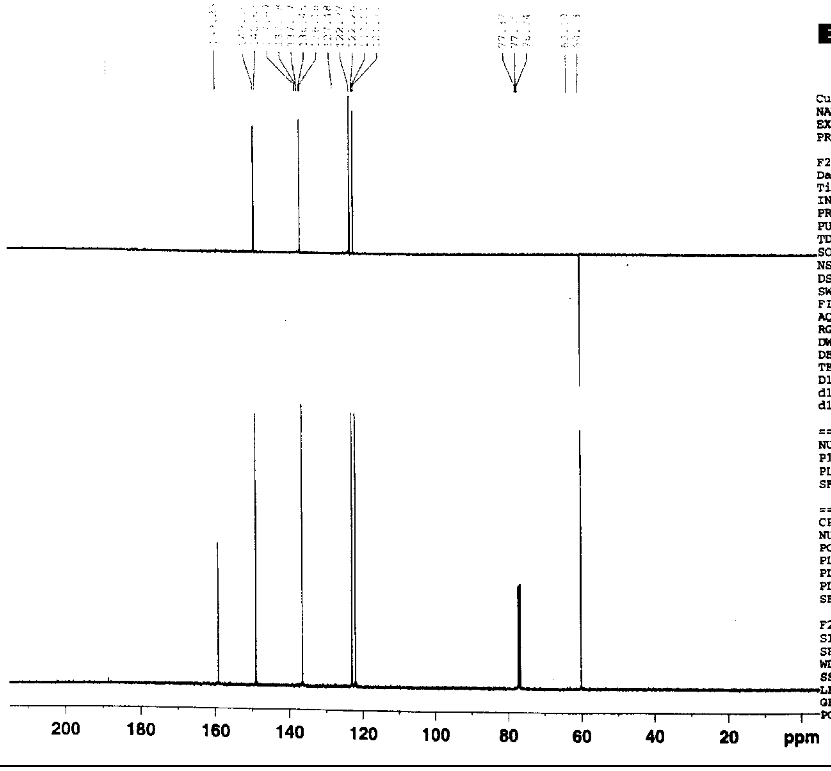
^{13}C NMR of TPA ↑ DEPT-135 spectrum of TPA →



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SOLVENT            CDC13
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DS                     2
SWH            24038.461 Hz
FIDRES          0.366798 Hz
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RG                  3251
DW                20.800 usec
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======== CHANNEL f1 ========
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P1                  7.75 usec
PL1                -5.00 dB
SFO1         100.6228298 MHz

======== CHANNEL f2 ========
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NUC2                  1H
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F2 - Processing parameters
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WDW                   EM
SSB                    0
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PC                  1.40
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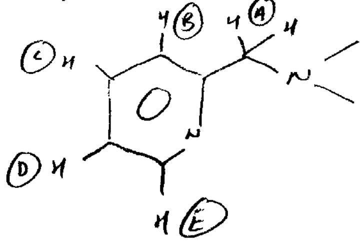
J.M. McCormick
June 16, 2003

Synthesis of Tris[(2-pyridyl)methyl]amine June 16, 2003

δ (ppm)	Multiplicity	# ^1H	J (Hz)	Assignment
3.89	singlet	2	—	Ⓐ
7.14	triplet of doublets	1	1.3, 6.1	Ⓓ
7.58	doublet	1	7.8	Ⓑ
7.63	triplet of doublets	1	1.8, 7.6	Ⓒ
8.15	doublet of quartets	1	0.9, 4.9	Ⓔ

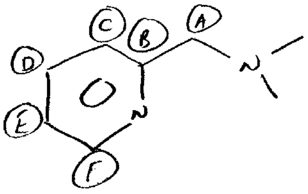


Peak at 3.89 ppm clearly does not couple to any other ^1H, and so must be Ⓐ, as confirmed by integration. Peak at 8.15 ppm is the most different of the peaks in the aromatic region, so it is most likely Ⓔ. The value of J for this resonance and the one at 7.14 ppm suggests ~~tha~~ the ^1H are adjacent to each other. Thus, the 7.14 ppm resonance is assigned as ^1H Ⓓ. The peak at 7.58 ppm is assigned as Ⓑ as it shows the cleanest splitting (only one strong coupling to Ⓒ is expected). The peak at 7.63 ppm is coupled to Ⓓ ($J \approx 1.5$ Hz) and Ⓑ ($J \approx 7.7$ Hz), which is consistent with it being ^1H Ⓒ. There appears to be higher order effects present, and perhaps coupling to ^{15}N in ^1H Ⓔ.

J.M. McCormick June 16, 2003

Synthesis of Tris[(2-pyridyl)methyl]amine June 16, 2003

δ(ppm)	Assignment
60.13	Ⓐ
122.01	Ⓓ or Ⓔ
122.97	Ⓔ or Ⓓ
136.06	Ⓕ
159.25	Ⓑ

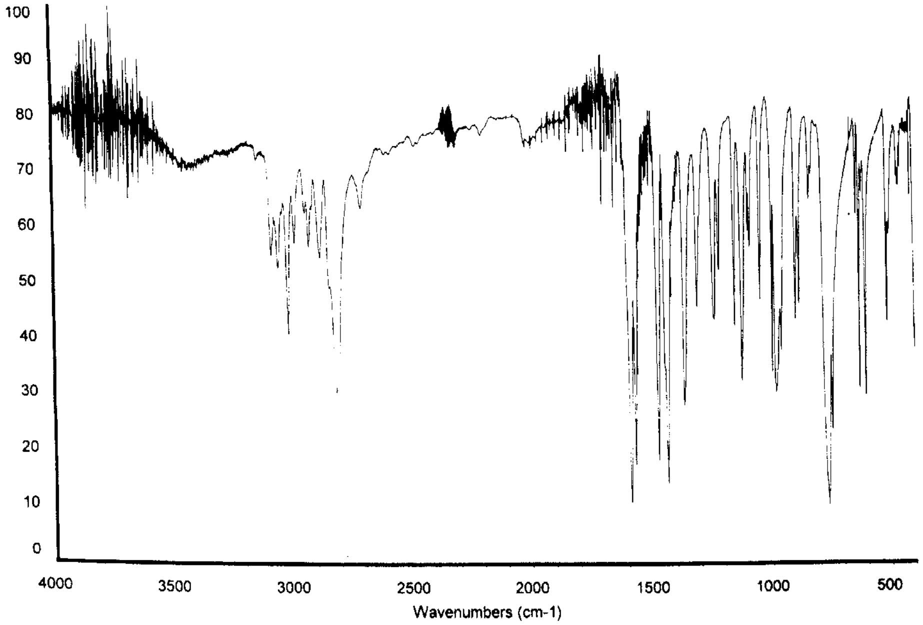


From DEPT-135, peak at 60.13 ppm is negative and must be carbon Ⓐ. The peak at 159.25 ppm does not appear in the DEPT, and so is carbon Ⓑ. The remaining peaks are the other pyridine carbons. The peaks at ~122 ppm can be accounted for by carbons Ⓓ and Ⓔ, as the are expected to be very similar. This leaves the 136.06 ppm peak as arising from carbon Ⓕ.

J.M.McCormick June 16, 2003

Synthesis of Tris[(2-pyridyl)methyl]amine

June 16, 2003



Date: Tue Jul 01 13:00:08 2003

** 2895, Tue Jul 01 12:57:16 2003

Scans: 32

Resolution: 1.000

IR Spectrum of TPA (32 scans, 1cm^{-1} resolution, background collected before scan, automatic baseline correction and scaling).

The IR spectrum was obtained on a Nicolet 210 FTIR Spectrometer (serial number AAC9100467). Peaks to left of 3000 cm^{-1} indicate aromatic C-H, and peaks to right of 3000cm^{-1} are consistent with aliphatic C-H. Peaks in 1500-1700 cm^{-1} region could be aromatic C-C. Broad peak at ~3600 cm^{-1} could be either N-H (unlikely) or an artifact of the background correction (from H_2O).

J.M. McCormick June 16, 2003

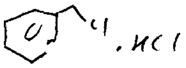
Synthesis of Tris[(2-pyridyl)methyl]amine — June 16, 2003

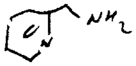
Calculations:

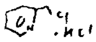
Volume	3.20 mL	—	—
Density	1.049 g/mL	—	—
Mass	3.36 g	10.11 g	
Molar Mass	108.14 g/mole	164.03 g/mole	290.36 g/mole
Moles	0.0310 moles	0.0612 mole	0.0306 mole

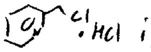
$3.20\,mL\left(\frac{1.049\,g}{mL}\right) = 3.36\,g$

$3.36\,g\left(\frac{1\,mole}{108.14\,g}\right) = 0.0310\,mole$ 

$10.11\,g\left(\frac{1\,mole}{164.03\,g}\right) = 0.0612\,mole$ 

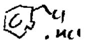
$0.0612\,mole\left(\frac{1\,mole}{2\,mole}\right) = 0.0306\,mole$ 





is the limiting reagent

$0.0612\,mole\left(\frac{1\,mole\ TPA}{2\,mole}\right)\left(\frac{290.36\,g}{1\,mole\ TPA}\right) = 8.89\,g$



$\%\,yield = \frac{2.08\,g}{8.89\,g} \times 100 = 24\%$

J.M. McCormick June 16, 2003

Synthesis of Tris[(2-pyridyl)methyl]amine June 16, 2003

Discussion of Conclusions and Error Analysis:

The reported melting point is lower and has broader range (73-77°C) than what was found (85°C, sharp) using the modified procedure. This indicates higher product purity was obtained with new method. The reported ^1H NMR consists of peaks at 3.9 ppm (singlet) and between 7.1 and 8.5 ppm (multiplets), which matches what was found here (singlet at 3.89 ppm, multiplets at 7.14, 7.58, 7.63 and 8.15 ppm). The ^{13}C NMR has not been reported, but the peaks at 60.13 ppm ($-\underline{C}H_2-$), 122.01 (pyridine $\underline{C}$-H), 122.97 (pyridine $\underline{C}$-H) 136.06 ppm (pyridine $\underline{C}$-H) and 159.25 (pyridine $\underline{C}-CH_2-$) are consistent with the structure of TPA. The IR spectrum of TPA was not reported, but the presence of aromatic and aliphatic C-H is consistent with TPA. The 1500-1700 cm^{-1} is similar to that of pyridine (Dolphin, D. and Wick, A. "Tabulation of Infrared Spectral Data" Wiley-Interscience; New York, 1977, p. 537). Taken together it appears that the target molecule was synthesized with high purity.

The 24% yield was disappointing, given the reported yield was 51%, albeit for a material of lower purity. The yield could be increased, perhaps, by minimizing the side reaction that leads to the red oil. Whether this a light-induced reaction or a redox reaction with the atmosphere deserves further investigation.

J.M. McCormick June 16, 2003

Synthesis of Tris[(2-pyridyl)methyl] amine June 16, 2003

The synthetic procedure apparently gives the desired product in high purity, but low yield is a problem. Further investigations on optimizing the reaction conditions is necessary, but for the desired purpose of this synthesis, probably unnecessary.

Summary of Results:

Properties of TPA

Melting Point: 85°C, sharp (uncorrected)

Physical appearance: light yellow crystals

NMR ($CDCl_3$), all values in ppm

^1H: 3.89 (1), 2H; 7.14 (m), 1H; 7.58 (m), 1H; 7.63 (m), 1H; 8.15 (m), 1H

^{13}C: 60.13, 122.01, 122.97, 136.06, 159.25

Yield: 24%

J.M. McCormick June 16, 2003