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Heterocyclic Amines. II. 3-Methylaminothiophene and a 3-Thienyl Diamine

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3-Methylaminothiophene (II) has been prepared by the reduction of methyl N-(3-thienyl)carbamate (I) with lithium aluminum hydride and the free base has been isolated by preparative gas chromatography. We believe this to be the first isolation of a thienyl secondary amine that does not contain additional stabilizing groups attached to the thiophene ring. The preparation of similar simple 3-thienyl tertiary amines by two different routes has recently been reported (1, 2).

A 3-thienyl-diamine has been prepared by a route analogous to that previously reported (1) for the synthesis of 3-dimethylaminothiophene. Methyl N-(3-thienyl)carbamate (I) was alkylated with sodium hydride and N,N-diethyl- α -chloroacetamide to methyl N-(N', N'-diethylcarbamylmethyl) - N-(3-thienyl)carbamate (III), which was reduced with lithium aluminum hydride to N-(3-thienyl) - N-methyl-N', N'-diethylethylenediamine (IV). This diamine was isolated as its dimethiodide salt (V).

The n.m.r. spectra were determined for both the secondary amine (II) and the diamine (IV).

EXPERIMENTAL

3-Methylaminothiophene (II).

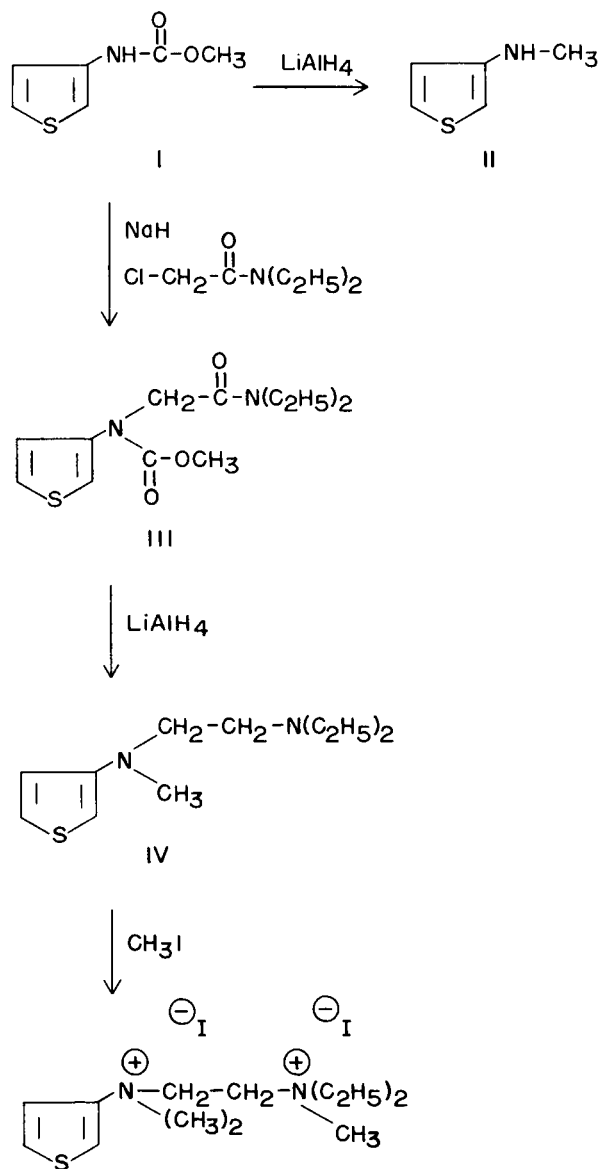
To a boiling solution of 1.5 g. (0.04 mole) of lithium aluminum hydride in 50 ml. of anhydrous tetrahydrofuran under nitrogen, there was added a solution of 3.0 g. (0.02 mole) of methyl N-(3-thienyl)carbamate (I) in 50 ml. of anhydrous tetrahydrofuran, at such a rate that refluxing was maintained without additional heating. After the addition was complete, the mixture was refluxed for an additional 18 hours. The reduction complex was decomposed with water, this mixture was filtered under nitrogen, the residue was washed with ether, and the solvent was partly removed under reduced pressure. The amine was purified by gas chromatography in a Beckman GC-2 instrument at 100° through a 5 foot QF-1 (fluorocarbon silicone) column with an emission time of 7 minutes under 30 p.s.i. of helium. The free base is stable in inert atmosphere, but rapidly polymerizes in contact with air.

The n.m.r. spectrum (3) in tetrachloroethylene was $\delta = 2.78$ (d, CH₃, 3H), 3.34 (broad band, NH, 1H), 5.80 (q, 2-CH, 1H), 6.40 (q, 4-CH, 1H), 6.99 (q, 5-CH, 1H) p.p.m.; $J_{24} = 1.6$, $J_{25} = 3.0$, and $J_{45} = 5.1$ (all ± 0.2) c.p.s. The splitting of the methyl group appears to be due to coupling with the proton on the nitrogen, $J = 1.2$ c.p.s.

Anal. Calcd. for C₆H₇NS: C, 53.06; H, 6.24; N, 12.38; S, 28.32. Found: C, 52.99; H, 6.40; N, 12.25; S, 28.08 (4).

N-(3-Thienyl)-N-methyl-N', N'-diethylethylenediamine (IV).

A solution of 5.0 g. (0.03 mole) of methyl N-(3-thienyl)carbamate (I) in 150 ml. of anhydrous xylene was added to a stirred suspension of 6.0 g. (0.125 mole) of 50% sodium hydride dispersion in 50 ml. of xylene. After adding 30 g. (0.2 mole) of N,N-diethyl- α -chloroacetamide, the mixture was refluxed with stirring under nitrogen for 8 hours.



The mixture was filtered and the solvent was evaporated under reduced pressure. Upon vacuum distillation of the oily residue, the unreacted excess chloro- compound distilled first, followed by 6 g. of alkylated urethan at 174-186° at 1.3 mm. This product showed slight contamination with mineral oil from the sodium hydride dispersion, but its infrared spectrum showed the expected two carbonyl absorption peaks at 1710 cm⁻¹ corresponding to the urethan carbonyl and at 1650 cm⁻¹ corresponding to the amide carbonyl.

This product, in 100 ml. of anhydrous tetrahydrofuran, was reduced

with 6 g. (0.16 mole) of lithium aluminum hydride in 100 ml. of anhydrous tetrahydrofuran by refluxing for 24 hours. The reduction complex was decomposed with water, this mixture was filtered under nitrogen, the residue was washed with ether, and the solvent was partly removed in a rotary evaporator.

From a portion of this solution, the amine was isolated by gas chromatography in a Beckman GC-2 instrument at 185° through a 5 foot carbowax column with an emission time of 35 minutes under 30 p.s.i. of helium. The identity of this amine was confirmed by its n.m.r. spectrum in CCl_4 : $\delta = 0.96$ (t, C- CH_3 , 6H), 2.49 (superimposed t+q, N-(CH_2 -C) $_3$, 6H), 2.84 (s, N- CH_3 , 3H), 3.26 (t, Thi-N- CH_2 -C, 2H), 5.76 (q, 2-CH, 1H), 6.66 (q, 4-CH, 1H), 7.08 (q, 5-CH, 1H) p.p.m.; $J_{\text{CH}_2-\text{CH}_3} = 6.9$, $J_{\text{CH}_2-\text{CH}_2} = 7.1$, $J_{24} = 1.9$, $J_{25} = 2.9$, $J_{45} = 5.3$ (all ± 0.4) c.p.s.

N-(3-Thienyl)-N-methyl-N',N'-diethylethylenediamine Dimethiodide (V).

Methyl iodide (1.2 ml.) was added to a one-eighth portion of the solution of the diamine from the above preparation. Within two minutes, a yellow-brown solid separated. This was decolorized with carbon and recrystallized several times from anhydrous ethanol as white crystals, m.p. 143-144° dec.

Anal. Calcd. for $\text{C}_{13}\text{H}_{26}\frac{1}{2}\text{N}_2\text{S}$: C, 31.47; H, 5.28; I, 51.15; N, 5.65; S, 6.46. Found: C, 31.54; H, 5.55; I, 51.18; N, 5.56; S, 6.25.

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- (3) N.m.r. spectra were determined by Mr. B. J. Nist of the Department of Chemistry, University of Washington. These spectra were measured at 60 mc., and the chemical shifts are reported as delta values (ppm) from internal tetramethylsilane. The multiplicity is shown by s = singlet, d = doublet, t = triplet, q = quadruplet. Assignments are shown in parentheses.
- (4) Elemental analyses by A. Bernhardt, Mülheim (Ruhr), Germany.

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