

Heterocyclic Amines. VI (1). Isolation and Characterization of 3-Aminothiophene

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Aminothiophenes have long been noted for their instability (3,4). 3-Aminothiophene has hitherto eluded isolation, although the also unstable isomeric 2-aminothiophene was isolated by Steinkopf (5,6) over sixty years ago. 3-Aminothiophene was first reported in 1933 by Steinkopf (7) who reduced the nitro compound with tin and hydrochloric acid; the formation of the amine was demonstrated by the preparation of acetyl and benzoyl derivatives, but attempts at isolation of the free base were unsuccessful. Campaigne (8) used the Hofmann rearrangement to convert 3-thenamide to 3-aminothiophene; again the formation of the amine was demonstrated by preparation of acyl and sulfonyl derivatives but attempts at isolation of the free base were also unsuccessful. Hoffman and Gronowitz (9) used the same Hofmann rearrangement, extracted the 3-aminothiophene into cyclohexane, evaporated most of the solvent under nitrogen, and determined the nmr spectrum of 3-aminothiophene in this concentrated solution. Reinecke (10) has formed 3-aminothiophene from 2-bromothiophene by rearrangement with potassium amide in liquid ammonia; the presence of the amine was demonstrated by isolation of the acetyl derivative.

Following the isolation of 3-dimethylaminothiophene (11) and 3-methylaminothiophene (12) in this laboratory by preparative gas chromatography, it was felt that the corresponding primary amine should also be amenable to isolation by this method. We now report that 3-aminothiophene has been isolated as a colorless oil which is stable under helium at dry ice temperature for several days, but it resinifies rapidly on warming to room temperature and exposure to air.

Both the infrared spectrum of the neat base and the nmr spectrum of its solution in carbon tetrachloride indicate that 3-aminothiophene exists principally as the amine rather than the imine tautomer. This is in agreement with the study by Hoffman and Gronowitz (9) of the nmr spectrum of 3-aminothiophene in cyclohexane.

EXPERIMENTAL

3-Aminothiophene.

A sodium hypobromite solution was prepared by dropping

3.7 ml. of bromine with stirring into a solution of 11.22 g. of sodium hydroxide in 92 ml. of ice cold water. To the cold yellow solution under nitrogen was added 6.56 g. of 3-thenamide. The mixture was stirred for one hour, and then was warmed to 70-80° for about 45 minutes. The solution became dark red in color. The cold reaction mixture was extracted with *p*-xylene. The extract was dried over Drierite and subjected to gas chromatography with an Aerograph Autoprep model A-700 fitted with a three-eighths inch by ten foot column packed with 20% Carbowax 20M on Chromosorb W 60/8. On-column injection was used with temperature programmed from 140 to 185° in about five minutes. Under these conditions, at a flow rate of 200 mls. per minute of helium, the emission time was approximately eleven minutes. The product peak effluent from the column was collected in a flask immersed in a refrigerated (dry ice) bath, $n_D^{20} = 1.6152$, nmr (carbon tetrachloride): $\tau = 6.71$ (s, 2H, NH₂), 4.07 (q, 1H, 2-position), 3.55 (q, 1H, 4-position), 3.04 (q, 1H, 5-position), $J_{24} = 1.5$ Hz, $J_{25} = 3.0$ Hz, $J_{45} = 5.0$ Hz; $\nu_{\max}$ (liquid film): 3440 and 3350 (asymmetric and symmetric NH₂ stretching) (13), 3235 (hydrogen bonded amine), 3115 (CH stretching) 1617 (NH₂ scissors), 1550 (thiophene ring), 1410 (thiophene ring), 1260 (CN stretching of aromatic primary amine), 1180, 1075, 945, 860, 833, and 757 cm⁻¹.

N-(3-Thienyl)-*N'*-phenylthiourea.

Liquid 3-aminothiophene was mixed with an equal volume of phenyl isothiocyanate (14). The solid product was washed with a small amount of ligroin, then washed with 50% aqueous ethanol, decolorized with acid-washed decolorizing carbon and recrystallized from dilute alcohol to give white plates, m.p. 138-139°.

Anal. Calcd. for C₁₁H₁₀N₂S₂: C, 56.37; H, 4.30; N, 11.95; S, 27.36. Found: C, 56.63; H, 4.04; N, 12.20; S, 27.50.

N-(3-Thienyl)-*N'*-methylthiourea.

Prepared similarly from 3-aminothiophene and methyl isothiocyanate and recrystallized from alcohol to give white plates, m.p. 148-149°.

Anal. Calcd. for C₆H₈N₂S₂: C, 41.82; H, 4.68; N, 16.26; S, 37.22. Found: C, 42.00; H, 4.56; N, 16.17; S, 37.28.

N-(3-Thienyl)-*N'*-(*t*-butyl)thiourea.

Prepared similarly from 3-aminothiophene and *t*-butyl isothiocyanate and recrystallized from alcohol, m.p. 161-161.5°.

Anal. Calcd. for C₉H₁₄N₂S₂: C, 50.43; H, 6.58; N, 13.07; S, 29.92. Found: C, 50.47; H, 6.58; N, 12.96; S, 30.01.

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