Synthesis of Selenobispyridines

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2,3'-Selenobispyridine, 2,4'-selenobispyridine, 3,3'-selenobispyridine and 3,4'-selenobispyridine have been synthesised.

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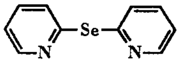
Only 2,2'-selenobispyridine (**1**) and 4,4'-selenobispyridine (**2**) [1] of the six possible selenobispyridines have so far been reported. As part of our continuing study of the chemistry of oxybispyridines [1-3], thiobispyridines [1] and selenobispyridines [1] we now report the synthesis of the four remaining selenobispyridines, namely, 2,4'-selenobispyridine (**3**), 2,3'-selenobispyridine (**4**), 3,3'-selenobispyridine (**5**) and 3,4'-selenobispyridine (**6**).



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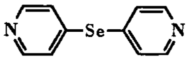

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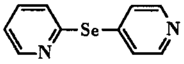

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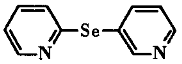

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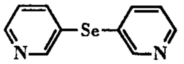

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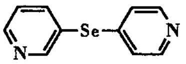

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2,4'-Selenobispyridine (**3**) was obtained in 80% yield by reaction of 4-bromopyridine (**7**) with pyridine-2-selenol (**8**) in 2-ethoxyethanol. The pyridine-2-selenol was generated *in situ* from 2-bromopyridine and sodium hydrogen selenide, the latter being obtained from reduction of selenium with sodium borohydride in 2-ethoxyethanol by adaptation of the method reported by Klayman and Griffin [4].

The preparation of 2,3'-selenobispyridine (**4**) required the generation of the hitherto unknown pyridine-3-selenol (*cf* ref [5]). To accomplish its synthesis the route chosen involved the preparation of the new 3-selenocyanatopyridine (**9**) which was readily obtained by diazotization of 3-aminopyridine followed by reaction of the pyridine-3-diazonium salt with potassium selenocyanate. 3-Selenocyanatopyridine (**9**) was then reduced to pyridine-3-selenol (**10**) with sodium borohydride in a mixture of 2-ethoxyethanol and ethanol. Without isolation the pyridine-3-selenol was reacted with 2-bromopyridine (**11**) to afford 2,3'-selenobispyridine (**4**) in good yield.

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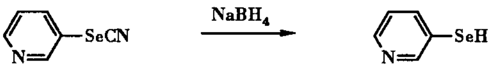

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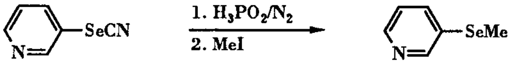
Other reactions investigated with 3-selenocyanatopyridine (**9**) included its conversion to 3-methylselenylpyridine (**12**) by reduction with hypophosphorous acid in an inert atmosphere followed by reaction with methyl iodide and its reaction with hypophosphorous acid in air to form 3,3'-diselenobispyridine (**13**).



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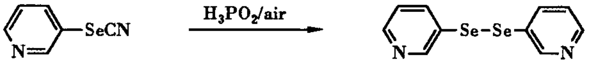

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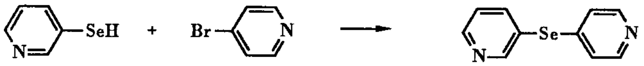
3,4'-Selenobispyridine (**6**) was obtained in high yield by an analogous route to the synthesis of 2,3'-selenobispyridine (**4**) from 3-selenocyanatopyridine (**9**) and 4-bromopyridine (**7**) without isolating the intermediate pyridine-3-selenol (**10**).

The remaining selenobispyridine, namely 3,3'-selenobispyridine (**5**) was obtained from 3-bromopyridine (**14**) and pyridine-3-selenol (**10**) by heating them together to 180° in



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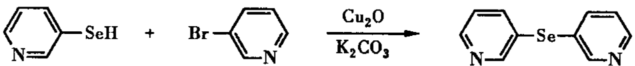

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a sealed tube in the presence of potassium carbonate and cuprous oxide in an analogous way to the reported synthesis of 3,3′-oxybispyridine [6] and 3,3′-thiobispyridine [7].

All the compounds gave satisfactory elemental analyses and nmr spectra. In the electron impact mass spectra the molecular ion was not the base peak with any of the four selenobispyridines. The molecular ion at mass 236 gave a peak of 40-80% of the intensity of the base peak. The base peak was due to the $C_5H_4N^+$ ion at mass 78 with 2,3′- and 2,4′-selenobispyridines. This recalls that the base peak in the mass spectrum of 2,2′-selenobispyridine was also at mass 78 [8]. With 3,3′- and 3,4′-selenobispyridines the base peak was at mass 51 due to the $C_4H_3^+$ ion. One of the major fragmentation routes from the molecular ion in all four cases involved loss of selenium from the molecular ion or the M-1 ion to afford bipyridine species.

EXPERIMENTAL

The nmr spectra refer to ^{1}H spectra (90 MHz) with tetramethylsilane as internal standard. Ultraviolet absorption spectra were taken in ethanol solution. Electron impact mass spectra were performed at Flinders University of South Australia by Dr. M. J. Thompson and the microanalyses at Australian National University.

2,4′-Selenobispyridine (**3**).

Selenium powder (6 g) and sodium borohydride (5 g) were mixed in the dry state under nitrogen. With vigorous agitation 2-ethoxyethanol (100 ml) was added dropwise to initiate reduction of the selenium. The solution was then heated to reflux to complete the reduction and generate a colorless solution of sodium hydrogen selenide. 2-Bromopyridine (8.4 g) in 2-ethoxyethanol (25 ml) was added slowly and the solution boiled for 18 hours. The bright yellow solution was cooled and 4-bromopyridine (8.4 g) in 2-ethoxyethanol (25 ml) was added. The mixture was stirred at ambient temperature for 1 hour and then refluxed for 3 hours. After cooling, the solvent was removed *in vacuo*. The residue was dissolved in aqueous potassium carbonate (1*M*, 100 ml) and the solution extracted thrice with benzene (150 ml). After drying over magnesium sulfate, the benzene was evaporated off yielding a dark yellow oil. The oil was chromatographed on an alumina column using benzene as eluant. The major product from the column was distilled twice at reduced pressure to afford 2,4′-selenobispyridine as a yellow oil, bp 143°/0.4 mm (yield 9.97 g). The ^{1}H nmr spectrum (deuteriochloroform) consisted of a multiplet at δ 7.11-7.67 (5H, 3, 4, 5, 3′, 5′ protons) and a multiplet at 8.44-8.55 ppm (3H, 6, 2′, 6′ protons). The uv spectrum (ethanol) showed λ max 232 sh, 260, 268 and 295 nm (log ϵ 3.77, 3.88, 3.88 and 3.83). The mass spectrum showed peaks above 10% intensity of base peak at 237 (13%), 236 ($M^{+\cdot}$, 44), 235 (M-1, 48), 234 (18), 233 (32), 232 (15), 231 (13), 172 (12), 159 (17), 157 (15), 156 (65), 155 (27), 129 (11), 79 (23), 78 (100), 59 (14), 52 (24), 51 (95).

Anal. Calcd. for $C_{10}H_8N_2Se$: C, 51.1; H, 3.4; N, 11.9. Found: C, 51.3; H, 3.7; N, 12.2.

3-Selenocyanatopyridine (**9**).

3-Aminopyridine (15 g) was dissolved in a solution of concentrated sulfuric acid (17 g) and water (100 ml) and cooled to 0-5°. Sodium nitrite (11.4 g) in water (20 ml) was added slowly and the mixture stirred for 30 minutes. Ice (500 g) was added to the solution and an aqueous solution of potassium selenocyanate (22.9 g) added over 15 minutes. A brown precipitate formed at once. The mixture was stirred at 0° for 1 hour and allowed to warm to room temperature. The precipitate was crystallized three times from petroleum (bp 40-70°) to afford the product as colorless prisms, mp 84° (yield 20.9 g). The ^{1}H nmr spectrum (deuteriochloroform) consisted of a multiplet at δ 7.29-7.43 (1H, 5 proton), a doublet at 7.95-8.07 (1H, 4 proton), a doublet at 8.62-8.67 (1H, 6 proton) and a singlet at 8.80 ppm (1H, 2 proton). The uv spectrum (ethanol) showed λ max 237 and 260 nm (log ϵ 3.63 and 3.46). The ir spectrum showed a strong peak at 2140 cm^{-1} (SeCN).

Anal. Calcd. for $C_6H_4N_2Se$: C, 39.4; H, 2.2; N, 15.3. Found: C, 39.6; H, 2.15; N, 15.35.

2,3′-Selenobispyridine (**4**).

3-Selenocyanatopyridine (10 g) was dissolved in 2-ethoxyethanol (70 ml). A slurry of sodium borohydride (5 g) in ethanol (30 ml) was then added slowly over 20 minutes under nitrogen. To the resultant yellow-orange solution, 2-bromopyridine (8.7 g) was added dropwise and the solution heated under reflux for 20 hours. The mixture was cooled and filtered and the solvent removed under vacuum. The residue was dissolved in aqueous potassium carbonate (1*M*, 70 ml) and the solution extracted with chloroform (500 ml). The chloroform extract was dried over magnesium sulfate and the solvent removed to yield to brown oil. The oil was extracted with hot benzene (250 ml) and the solvent then evaporated. The yellow-orange oil was distilled to afford 2,3′-selenobispyridine, bp 126-130°/0.3 mm (yield 10.63 g). The ^{1}H nmr spectrum (deuteriochloroform) consisted of a multiplet at δ 7.03-7.12 (2H, 5,5′ protons), a multiplet at 7.24-7.53 (2H, 3,4 protons), a doublet at 7.96-8.05 (1H, 4′ proton) a doublet at 8.36-8.44 (1H, 6 proton), a doublet at 8.59-8.64 (1H, 6′ proton) and a singlet at 8.84 ppm (1H, 2′ proton). The uv spectrum (ethanol) showed λ max 250 and 290 nm (log ϵ 3.88 and 3.75). The mass spectrum showed peaks above 10% intensity of base peak at 237 (18), 236 ($M^{+\cdot}$, 31), 235 (M-1, 91), 234 (16), 233 (46), 232 (22), 231 (18), 173 (27), 171 (14), 158 (14), 156 (17), 155 (10), 131 (10), 95 (21), 79 (22), 78 (100), 67 (16), 52 (30), 51 (84).

Anal. Calcd. for $C_{10}H_8N_2Se$: C, 51.1; H, 3.4; N, 11.9. Found: C, 51.4; H, 3.3; N, 11.7.

3-Methylselenylpyridine (**12**).

3-Selenocyanatopyridine (10 g) was dissolved in aqueous hydrochloric acid (6*M*, 50 ml) in an atmosphere of nitrogen. Hypophosphorous acid (50%, 30 ml) was added dropwise over 20 minutes and the mixture stirred at ambient temperature for 3 hours. The *p*H of the solution was adjusted to ~12 with concentrated sodium hydroxide. After cooling, methyl iodide (7.8 g) was added dropwise and after five minutes a dark liquid phase separated. Stirring was continued for 2 hours and the mixture allowed to stand overnight. It was then extracted with chloroform (500 ml). The chloroform extract was dried over magnesium sulfate and the solvent removed. The brown liquid residue was distilled to afford a light yellow liquid of unpleasant odor, bp 64°/0.46 mm (yield 7.89 g). 3-Methylselenylpyridine has been reported [5] but no bp was given. The ^{1}H nmr spectrum (deuteriochloroform) consisted of a singlet at δ 2.31 (3H, methyl protons), a multiplet at 7.10-7.23 (1H, 5 proton), a multiplet at 7.65-7.76 (1H, 4 proton), a doublet at 8.38-8.42 (1H, 6 proton) and a singlet at 8.61 ppm (1H, 2 proton). The uv spectrum (ethanol) showed λ max 251, 267 and 295 nm (log ε 3.65, 3.65, 3.42).

Anal. Calcd. for C_6H_7NSe: C, 41.9; H, 4.1; N, 8.1. Found: C, 42.3; H, 4.15; N, 8.2.

3,3'-Diselenobispyridine (**13**).

3-Selenocyanatopyridine (5 g) and hypophosphorous acid (50%, 60 ml) were warmed on a water bath for 5 hours. The *p*H of the solution was adjusted to ~8 using concentrated aqueous sodium hydroxide and then extracted with chloroform (3 x 100 ml). The extract was dried with magnesium sulfate and the solvent evaporated off to yield an orange oil. The oil was chromatographed on an alumina column using hexane as eluant. The resultant oil was distilled to afford 3,3'-diselenobispyridine as an orange oil, bp 148°/0.33 mm (yield 3.76 g). The ^{1}H nmr spectrum (deuteriochloroform) consisted of a multiplet at δ 7.12-7.28 (2H, 5,5' protons), a multiplet at 7.81-7.95 (2H, 4,4' protons), a multiplet at 8.46-8.53 (2H, 6,6' protons) and a singlet at 8.74 ppm (2H, 2,2' protons). The uv spectrum (ethanol) showed λ max 240 and 275 nm (log ε 4.17 and 3.74).

Anal. Calcd. for $C_{10}H_8N_2Se_2$: C, 38.2; H, 2.6; N, 8.9. Found: C, 37.9; H, 2.5; N, 8.5.

3,4'-Selenobispyridine (**6**).

3-Selenocyanatopyridine (10 g) was dissolved in 2-ethoxyethanol (70 ml). A slurry of sodium borohydride (5 g) in ethanol (30 ml) was added to the solution in an atmosphere of nitrogen over a period of 20 minutes. To the resultant yellow-orange solution 4-bromopyridine (8.7 g) was added dropwise and the solution refluxed for 20 hours. The mixture was then worked up by the method used for 2,3'-selenobispyridine. 3,4'-Selenobispyridine distilled as an orange-yellow oil, bp 122-124°/0.23 mm (yield 11.99 g). The ^{1}H nmr spectrum (deuteriochloroform) consisted of a multiplet at δ 7.03-7.15 (2H, 3',5' protons), a multiplet at 7.27-7.42 (1H, 5 proton), a multiplet at 7.87-8.01 (1H, 4 proton), a multiplet at 8.27-8.40 (2H, 2',6' protons) and a multiplet at 8.64-8.84 ppm (2H, 2,6 protons). The uv spectrum (ethanol) showed λ max 235, 264 and 292 nm (log ε 3.63, 3.97 and 3.63). The mass spectrum showed peaks above 10% intensity of base peak at 238 (16), 237 (14), 236 ($M^{+\cdot}$, 82), 235 (M-1, 29), 234 (45), 233 (27), 232 (21), 156 (34), 155 (22), 79 (11), 78 (68), 52 (15), 51 (100), 50 (24).

Anal. Calcd. for $C_{10}H_8N_2Se$: C, 51.1; H, 3.4; N, 11.9. Found: C, 51.2; H, 3.7; N, 12.0.

3,3'-Selenobispyridine (**5**).

3-Selenocyanatopyridine (25 g) was dissolved in aqueous hydrochloric acid (6*M*, 110 ml) under nitrogen. With stirring hypophosphorous acid (50%, 135 ml) was added dropwise over 15 minutes. The orange solution was stirred at ambient temperature for 30 minutes and then heated to 70° for 30 minutes. After cooling, the *p*H was adjusted to ~5.5 with concentrated sodium hydroxide solution. The solution was quickly extracted with chloroform (2 litres). The extract was dried over calcium chloride and the solvent evaporated off under reduced pressure to yield a dark yellow oil of pyridine-3-selenol. Without purification the yellow oil (15 g), 3-bromopyridine (15 g), potassium carbonate (12.1 g) and cuprous oxide (1.43 g) were heated in a sealed vessel at 180° for six hours. The black solid was extracted with hot benzene (6 x 50 ml). The extract was dried over magnesium sulfate and the solvent evaporated. The liquid residue was added to the top of a chromatographic column packed with potassium carbonate. On elution with benzene the first yellow fraction was collected, the solvent removed and the residue distilled to afford 3,3'-selenobispyridine as a pale yellow liquid, bp 139°/0.35 mm (yield 9.37 g). The ^{1}H nmr spectrum (deuteriochloroform) consisted of a multiplet at δ 7.14-7.28 (2H, 5,5' protons), a multiplet at 7.71-7.84 (2H, 4,4' protons), a doublet at 8.51-8.56 (2H, 2,2' protons). The uv spectrum (ethanol) showed λ max 256 and 289 nm (log ε 3.82 and 3.62). The mass spectrum showed peaks above 10% intensity of base peak at 238 (14), 237 (12), 236 ($M^{+\cdot}$, 69), 235 (M-1, 21), 234 (44), 233 (21), 232 (20), 156 (61), 155 (31), 131 (11), 79 (31), 78 (80), 69 (10), 52 (37), 51 (100), 50 (37).

Anal. Calcd. for $C_{10}H_8N_2Se$: C, 51.1; H, 3.4; N, 11.9. Found: C, 50.8; H, 3.5; N, 11.9.

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