(1-Adamantanethio)pyridines and Tetrahydropyridines from the Reaction of 1-Adamantanethiol with Pyridine 1-Oxide in Acetic Anhydride (1)

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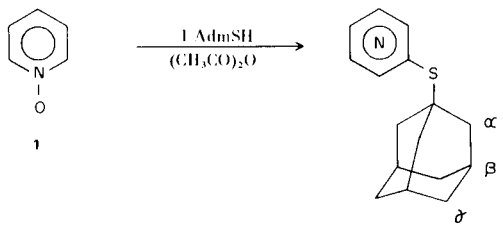
The reaction of pyridine 1-oxide with 1-adamantanethiol in acetic anhydride produced a mixture of 2- and 3-(1-adamantanethio)pyridines, 1-acetyl-2-(1-adamantanethio)-3-hydroxy-4-acetoxy-1,2,3,4-tetrahydropyridine and the corresponding 3-acetoxyderivative. Pure substances were separated by means of column chromatography on alumina. The tetrahydropyridines were identified by means of their proton magnetic and mass spectra. 4-(1-Adamantanethio)pyridine was synthesized from 4-chloropyridine and 1-adamantanethiol. The three isomeric (1-adamantanethio)-pyridines were, each, cleaved by concentrated hydrochloric acid to give 1-chloroadamantane and the corresponding pyridinethiol.

As part of our continuing program to investigate the deoxydative substitution of pyridine *N*-oxides by mercaptans (2), a study was carried out on the reaction of pyridine 1-oxide, **1**, with 1-adamantanethiol, (1-AdmSH), in the presence of acetic anhydride. It was anticipated that this reaction would yield not only pyridyl adamantyl sulfides but some interesting tetrahydropyridines (2). The isomeric 1-adamantyl pyridyl sulfides were also desired in order to study their behavior towards cleavage by concentrated hydrochloric acid (3).

Synthesis of 1-Adamantyl Pyridyl Sulfides.

The deoxydative substitution reaction of pyridine *N*-oxides by mercaptans in acetic anhydride has in general produced 2- and 3-pyridyl sulfides (2). Therefore, it was not surprising to find that pyridine 1-oxide, **1**, reacted with 1-AdmSH to provide a combined yield of 44% of a mixture of **2** and **3** in the ratio of about 15:7. As expected from previous experiments (2), the addition of triethylamine to a similar reaction mixture diminished the yield of **3** in relation to **2** to give a product ratio of **2** and **3** of about 4:1, with a combined yield of 35%. In order to prevent possible pyrolysis of any tetrahydropyridine byproducts, the sulfides, **2** and **3**, were not isolated as described for previous experiments. Instead of distillation, **2** and **3** were separated from the crude reaction mixture by means of extensive column chromatography, as described in the Experimental Section.

The synthesis of the third required isomer, *viz.*, **4** was undertaken independently. The reaction of 4-chloropyridine with 1-AdmSH in *N,N*-dimethylformamide furnished **4**, in a reasonable yield.



1

2 2-Pyridyl Sulfide
3 3-Pyridyl Sulfide
4 4-Pyridyl Sulfide

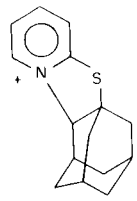
Spectral Characterization of **2-4**.

Proton magnetic resonance (pmr) spectra confirmed the structure of these sulfides. The pattern for the resonance signals for the aromatic protons was as expected for monosubstituted pyridines (4).

The fragmentation patterns of **2-4** upon electron-bombardment were relatively simple and for the most part

quite similar. The mass spectrum of each sulfide exhibited the expected molecular ion, m/e 245, and the ion m/e 135 was found to be the base peak. In view of our studies on the fragmentation of 1-adamantyl sulfides (5), the appearance of the intense peak at m/e 135 due to the 1-adamantyl cation was expected. The ions below m/e 107 in the mass spectrum of each sulfide were characteristic of those found for 1-adamantane derivatives. Several ions which were not common to the fragmentation pattern for each sulfide, are commented on.

The mass spectrum of **2** exhibited a considerable ion, m/e 244, which represents the loss of H from the molecular ion, but was absent to any significant degree in the fragmentation pattern of either **3** or **4**. Such an (M-H) ion was quite prominent in the mass spectra of 2-methyl and 2-ethylthiopyridines (6). It is conceivable that expulsion of H$^{\bullet}$ from the molecular ion of **2** would lead to an ion, structure **2a**. Its formation is governed by the proximity of the ring nitrogen atom to the adamantane ring and this type of fragmentation would be expected to be absent for **3** and **4**. Fragmentation of **2** also produced an ion, m/e 212,



2a

which represents the loss of HS$^{\bullet}$ from the molecular ion of **2**. The loss of HS$^{\bullet}$ from the series was only observed for the fragmentation of **2** but no possible structure for the resultant ion is advanced. Plausible mechanisms for this loss have been discussed previously (6). Although an ion, m/e 111 was observed in the mass spectrum of **2**, it is absent for that **3** and **4**. The m/e 111 ion was frequently observed in pyridyl alkyl sulfides, and was the base peak in the fragmentation of 2-*t*-butylthiopyridine and represents the 2-pyridthione ion (6).

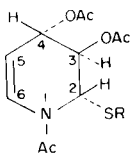
Acid Cleavage of **2-4**.

It had been reported previously (3) that sulfides, of type 1-AdmSR, were cleaved by concentrated hydrochloric acid to give 1-AdmCl and RSH. One of the structural requirements necessary for this cleavage to take place was determined to be that the side chain, R, contain a basic function such as an amino or amidino group. It was therefore interesting to study the behavior of **2-4** under similar reaction conditions.

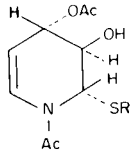
Treatment of isomers **2**, **3** and **4** with boiling hydrochloric acid in each case furnished 1-chloroadamantane in good yield. Attack of chloride ion on any incipient 1-adamantyl cation would lead to the observed 1-AdmCl and the corresponding pyridinethiol (or thione). Conversely, had displacement occured on the pyridine ring the observed products would have been 1-AdmSH and a chloropyridine. Additionally, it has been demonstrated that 1-AdmSH could not be converted to 1-AdmCl by concentrated hydrochloric acid (3). Therefore, the major cleavage of these sulfides must involve a nucleophilic displacement on the adamantane bridgehead carbon and not on the pyridine ring. Furthermore, the corresponding 2- and 3-pyridinethiols were isolated, although in low yield, mainly due to the inherent difficulty in handling these compounds on a small scale. The presence of 4-pyridinethione was demonstrated by examining the pmr spectrum of this product in aqueous acidic solution. A symmetrical AA′XX′ pmr pattern was observed. The reaction of these new 1-adamantyl sulfides do not shed any further light on the detailed mechanism for the C-S cleavage. However, **2-4** do possess the structure requirement essential for cleavage in the aliphatic series of 1-adamantyl sulfides (3) *viz.*, that the chain attached to sulfur contain a basic group. Here, that group is the weakly basic pyridine ring.

Tetrahydropyridines.

In addition to sulfides **2** and **3**, this reaction yielded two tetrahydropyridines which were isolated after extensive column chromatography. Their mass and pmr spectra indicated that these compounds were related to the series of 1-acetyl-1,2,3,4-tetrahydropyridines having acetoxy and sulfide groups (3). It became evident that one of these compounds contained one adamantane thioether and two acetoxy groups and can be represented by structure **5a** (CH_3CO = Ac). The other tetrahydropyridine was shown to contain an acetoxy group, a sulfide and an alcoholic group and was eventually proved to possess structure **6**. When **6** was reacted with acetic anhydride, the alcoholic group was acetylated to produce **5a**. This conversion proved that the stereo-chemistry of the substituents on the ring of **5a** and **6** was identical.



5a, R = 1-Adm
5b, R = *t*-C_4H_9
5c, R = *n*-C_4H_9



6, R = 1-Adm

The structure proof for **5a** rested primarily on the analysis of its pmr spectrum. The pmr spectral parameters closely resembled those published for the analogs, **5b** and **5c** (Table I). From the close match of the chemical shifts of the ring protons and the size of the coupling constants, **5a** was assigned to the structure of the new tetrahydropyridine isolated here. The close values of the coupling

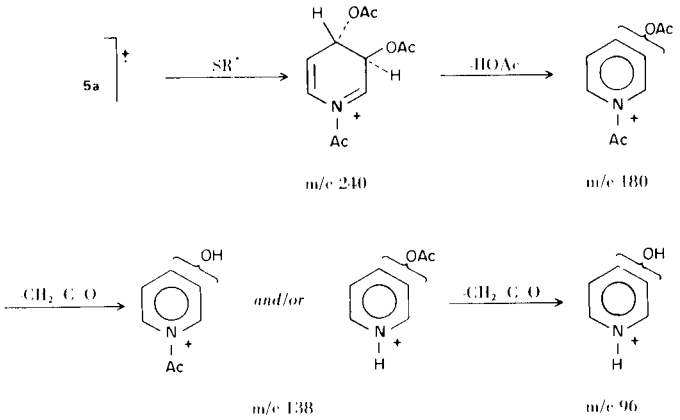
Table I

Pmr Parameters of **5** and **6** in Perdeuteriopyridine

Compounds	Chemical Shifts (a), δ, from Internal $(CH_3)_4Si$						Coupling Constants, J.								
	H-2	H-3	H-4	H-5	H-6	OH	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	$J_{2,4}$	$J_{3,5}$	$J_{4,6}$	$J_{2,6}$	J
5a	6.50	5.67	5.30	5.40	7.12	--	2.8	1.5	4.2	7.5	~1	~1	1.8	~1	--
5b	6.31	5.51	5.15	5.30	7.04	--	3.0	1.4	4.4	8.2	1.2	1.2	1.8	1.2	--
5c	6.39	5.65	5.25	5.36	7.08	--	2.5	1.4	4.5	7.5	1.2	~1	1.8	1.2	--
6	6.47	4.86	5.58	5.45	7.14	7.83	2.6	1.2	4.5	8.0	1.2	~1	1.8	~1	4.5

(a) Footnote: Chemical shift range for NAc and OAc, sharp singlets δ 2.00-2.33; *t*-Butyl, 1.33; 1-Adm, two broad singlets δ 1.6-2.2.

Chart I



constants for **5a-5c** also support the *trans*-diaxial stereochemistry of the substituents at C-2 and C-3, and of those at C-3 and C-4 as had been established for **5b** and **5c** (2,7). The assignment of the chemical shifts in Table I for **5a** were checked by as many decoupling experiments as the system permitted.

The mass spectrum of **5a** also supported this structure and is summarized in Chart I. Loss of the 1-adamantanethio radical from the molecular ion yields an intense ion, m/e 240. Subsequent fragmentations of note from m/e 240 involve the loss of acetic acid to give rise to an ion, m/e 180, which then eliminates ketene to give the base peak m/e 138. Some ambiguity exists on the structure of that ion since ketene can be eliminated from the ester or amide function. However, further loss of ketene produces an hydroxypridininium ion, m/e 96.

There remained the problem of determining whether the hydroxyl group in **6** was at C-3 or C-4. It would be expected that the loss of one of the ring proton signals to move upfield. The pmr spectrum of **6**, displayed a set of signals around δ 4.86. This observation was significant since the pmr spectrum of **5a** had all signals below δ 5.30. The signal at δ 4.86 in the pmr spectrum of **6** represents the resonance of the proton on the carbon to which the OH was attached, since exchange of the hydroxyl proton with deuterium oxide caused simplification of that multiplet.

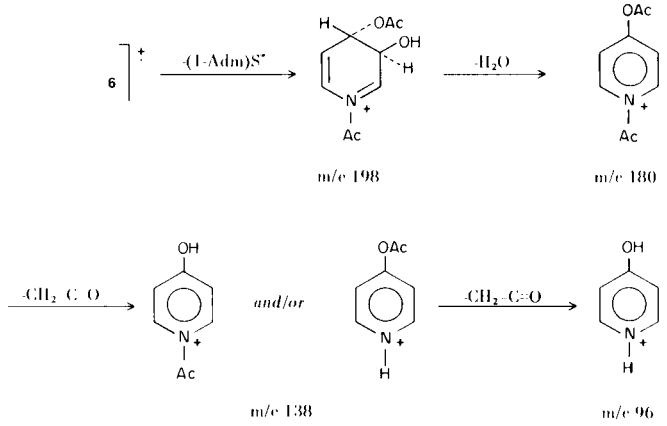
Table II

$Eu(FOD)_3$ LIS Values (a) (Δ Eu) (b)

	2	**3**	**4**
H-2	--	310.0 (c)	368.0
H-3	98.5	--	119.0
H-4	37.5	112.0	--
H-5	-9.5	100.5	119.0
H-6	-153.5	320.0 (c)	368.0
α-CH_2	122.0	56.0	50.5
β-CH	29.5	18.0	18.0
γ-eqCH	33.0	17.0	18.0
γ-axCH	21.0	17.0	14.0

(a) Negative sign indicates upfield shift. (b) P. V. Demarco, T. K. Elzey, R. B. Lewis and E. Wenkert, *J. Am. Chem. Soc.*, 92, 5734 (1970). (c) Extremely broad resonance makes accurate chemical shift determinations possible only after one addition of $Eu(FOD)_3$.

Chart II



A number of decoupling experiments were carried out to substantiate the proton chemical shift assignments in **6**. One important experiment, consisting of the irradiation of the signal at δ 6.47 (H-2), caused simplification of the δ 4.86 multiplet thereby confirming that H-3 resonated at δ 4.86 and that the OH group is attached to C-3.

The mass spectrum of **6** has several noteworthy points (Chart II). The molecular ion losses again 1-AdmS·, and

then water, to furnish an ion, m/e 180. Significant ions are observed due to successive losses of ketene from m/e 180, resulting in the base peak, m/e 96.

Conclusions.

Although no mechanisms can be advanced for the preferential formation of **5a** and **6** from **1** in the presence or absence of triethylamine, the isolation of these tetrahydropyridines add to the array of different tetrahydropyridines formed during the deoxydative substitution of pyridine *N*-oxide (2).

EXPERIMENTAL

Melting points were determined on a Mel-Temp apparatus and are uncorrected. Infrared spectra were determined on a Perkin-Elmer Model 337 spectrophotometer. Pmr spectra were recorded on either a Varian A-60 or HA-100 spectrometer. Chemical shifts are in parts per million (δ) downfield from TMS and were assigned on integral information, an analysis of spin-spin patterns, and whenever possible on decoupling experiments. Mass spectra were determined at 70 eV by Mr. Richard Dvorak using a Hitachi Perkin-Elmer RMU-6D single focusing mass spectrometer. Usually, ions with 5% of base peak intensity were recorded above m/e 30. Microanalyses for nitrogen were determined in this Department with a Coleman D29 analyzer, those for carbon and hydrogen were determined by Micro-Tech Laboratories, Skokie, Illinois.

Atarting Materials.

Generous gifts of the following chemicals are most gratefully acknowledged: *n*-butyl mercaptan from Pennsalt Chemical Co. and Phillips Petroleum Co.; pyridine 1-oxide from Reilly Tar and Chemical Co.; 1-Bromoadamantane was purchased from Aldrich Chemical Co.

Chromatographic Separations.

Column chromatography was carried out on alumina (Alcoa, grade F-20; 20 to 30 times the weight of alumina was used to that of crude materials, to be separated. Solvents for elution were reagent grade; petroleum ether used was the fraction b.p. 30-60°; benzene was thiophene-free. Eluents were monitored using thin layer chromatography on Eastman Chromagram silica gel sheets with fluorescent indicator (no. 6060, on strips, 5″ long) with the following developing solvents: *A*:pentane, *B*:pentane-ether in a ratio of 7:3, C:ether.

4-(1-Adamantanethio)pyridine.

1-Adamantanethiol (8.40 g., 0.05 mole) was added to a stirred ice-cold suspension of sodium hydride (2.35 g.) in DMF (50 ml.). 4-Chloropyridine hydrochloride (3.75 g., 0.025 mole) was then added in small portions. After the addition, the mixture was heated at 95° for 1 hour. Solvents were removed *in vacuo* and the residue diluted with water (50 ml.). Extraction with ether-benzene (1:1) produced 8.85 g. of impure **4**, which was chromatographed on alumina (200 g.). Elution with methylene chloride (375 ml.) provided **4** (2.76 g., 45%) which was recrystallized from petroleum ether, m.p. 58-60°; mass spectrum m/e (rel intensity): 246 (4), 245 (22), 136 (12), 135 (100), 107 (9), 93 (19), 91 (8), 81 (6), 79 (21), 77 (8), 67 (9), 55 (5), 41 (9).

Anal. Calcd. for $C_{15}H_{19}NS$: N, 5.71. Found: N, 5.45.

Reaction of 1-Adamantanethiol with Pyridine 1-Oxide in Acetic Anhydride.

A solution of redistilled pyridine 1-oxide (20.4 g., 0.214 mole) and 1-adamantanethiol (3) (33.0 g., 0.20 mole) in acetic anhydride (150 ml.) was heated over a steam bath for three hours. Solvents were removed, *in vacuo* and the oily residue stirred with 50% aqueous potassium carbonate (200 ml.) for one hour at 25°. The benzene extract was washed with saturated salt solution, dried (potassium carbonate), and solvents were stripped off.

The residue (60 g.) was dissolved in benzene (50 ml.) and placed on a column of alumina (450 g.). Benzene (525 ml.) eluted a mixture (32.5 g., fraction *A*) which contained 1-adamantanethiol (Rf = 0.86, solvent *A*), S-(1-adamantanethiol) acetate (5) (Rf = 0.45, Solvent *A*), 2-(1-adamantanethio)pyridine, **2**, (Rf = 0.72, Solvent *B*), 3-(1-adamantanethio)pyridine, **3**, (Rf = 0.39, Solvent *B*), and 1-acetyl-2-(1-adamantanethio)-3,4-diacetoxy-1,2,3,4-tetrahydropyridine, **5a**, (Rf = 0.29, Solvent *B*). The next one liter of benzene (fraction *B*) contained **2** and **3**. Evaporation of the solvent and addition of petroleum ether (20 ml.) to the residue yielded crude **5a** (500 mg.). Interestingly enough, although fractions *A* and *B* originally contained the bis-acetate, it was absent after subsequent chromatography of these fractions (see below). Recrystallization from benzene-petroleum ether afforded pure **5a**, (300 mg.), m.p. 151-152°; ir (potassium bromide): 1740, 1685 (ester C=O), 1645 cm^{-1} (amide C=O); mass spectrum m/e (rel intensity): 407 (2), 288 (8), 246 (6), 240 (8), 198 (6), 180 (39), 138 (69), 135 (42), 107 (9), 96 (42), 95 (13), 93 (16), 91 (81), 81 (7), 80 (10), 79 (24), 78 (6), 77 (7), 67 (12), 60 (38), 57 (9), 56 (7), 55 (9), 52 (8), 51 (8), 45 (58), 43 (100), 42 (16), 41 (20), 39 (19), 32 (20).

Anal. Calcd. for $C_{21}H_{29}NO_5S$: C, 61.90; H, 7.17; N, 3.44. Found: C, 61.93; H, 7.27; N, 3.36.

Further elution with methylene chloride (5.5 l.) produced a negligible quantity of an intractable oil. Elution with chloroform (500 ml. fraction *C*) afforded a residue which, when triturated with petroleum ether yielded crude 1-acetyl-2-(1-adamantanethio)-3-hydroxy-4-acetoxy-1,2,3,4-tetrahydropyridine, **6** (1.0 g. Rf = 0.30, Solvent *C*). The next chloroform fraction (6 l., fraction *D*) upon similar work up gave additional crude **6**, (2.4 g.); A final elution with methanol (1 l., fraction *E*) gave additional impure **6** (800 mg.). Fractions *C* and *E* combined and recrystallized from benzene to give pure **6** (100 mg.) m.p. 194-195°. Recrystallization of fraction *D* gave additional pure **6** (1.2 g.), m.p. 194-195°.

Fraction *A* and the filtrate of *B* (after the removal of 300 mg. of **5a**) were combined in petroleum ether (50 ml.) and rechromatographed on alumina (1 kg.).

Fraction *F* (10.5 l. of petroleum ether) contained 1-AdmSH and 1-AdmSAc. Fraction *G* (10.5 l. of 20-50% benzene in petroleum ether) afforded pure 2-(1-adamantanethio)pyridine (14.5 g.), m.p. 82°, unchanged after recrystallization from petroleum ether; gc (8) showed Rt = 12.0 minutes; mass spectrum, m/e (rel. intensity): 246 (7), 245 (30), 244 (44), 212 (12), 136 (12), 135 (100), 112 (9), 111 (10), 107 (13), 93 (28), 91 (13), 81 (9), 79 (32), 78 (11), 77 (12), 67 (17), 55 (8), 53 (5), 41 (14).

Anal. Calcd. for $C_{15}H_{19}NS$: N, 5.71. Found: N, 5.60.

Further elution with benzene (10.5 l., fraction *G*) yielded nearly pure 3-(1-adamantanethio)pyridine (6.7 g.), m.p. 82-87° [gc (8) showed Rt = 13.5 minutes with 3% of the 2-isomer as an impurity], recrystallized from petroleum ether, m.p. 87-90°; mass spectrum m/e (rel. intensity): 246 (4), 245 (20), 136 (12), 135 (100), 107 (14), 93 (24), 91 (9), 81 (7), 79 (24), 77 (9), 67 (11), 55 (7), 41 (11), 39 (10), 32 (13).

Anal. Calcd. for $C_{15}H_{19}NS$: N, 5.71. Found: N, 5.43.

Further elution with methanol (3 l., fraction *H*) yielded after trituration of the residue with petroleum ether, 1-acetyl-2-(1-

adamantanethio)-3-hydroxy-4-acetoxy-1,2,3,4-tetrahydropyridine, **6** (2 g.), m.p. 194-195°, after crystallization from benzene; ir (potassium bromide): 3540 (OH), 1740 (ester C=O), 1630 cm^{-1} (amide (C=O); mass spectrum, m/e (rel. intensity): 365 (9), 198 (15), 197 (9), 180 (25), 156 (22), 138 (34), 135 (50), 106 (9), 97 (8), 96 (100), 95 (6), 93 (16), 91 (7), 79 (19), 77 (7), 68 (7), 67 (9), 55 (7), 43 (31), 41 (11).

Anal. Calcd. for $C_{19}H_{27}NO_4S$: N, 3.84. Found: N, 3.93.

The following estimates are provided for the yield of 2-(1-adamantanethio)pyridine, 30%; 3-(1-adamantanethio)pyridine, 14%; 1-acetyl-(2-1-adamantanethio)-3,4-diacetoxy-1,2,3,4-tetrahydropyridine, 0.4%; and 1-acetyl-2-(1-adamantanethio)-3-hydroxy-4-acetoxy-1,2,3,4-tetrahydropyridine, combined, 4.5%.

When the reaction was similarly conducted in the presence of distilled triethylamine (56 ml., 0.40 mole) and worked up, the 2- and 3-sulfides were obtained in 28 and 7%, **5a** 0.5%, and **6** in 2.9% yields.

Reaction of **6** with Acetic Anhydride.

A mixture of **6** (0.27 g.), pyridine (1 ml.) and acetic anhydride (5 ml.) was heated at the reflux for 2 hours. Solvents were evaporated *in vacuo* and the residue washed with petroleum ether to provide **5a** (0.30 g., 99.7%) m.p. 144-146°, and identical with the sample isolated above.

Cleavage of (1-Adamantanethio)pyridines by Concentrated Hydrochloric Acid.

A solution of **2** (2.0 g., 0.0081 mole) in concentrated hydrochloric acid (40 ml.) was refluxed for three hours. To prevent the sublimation of 1-chloroadamantane on to the condenser, toluene (5 ml.) was added to the reaction mixture after solution of **2** had been affected. After reflux, the mixture was cooled and extracted with benzene (two 35 ml. portions). The extract was dried (potassium carbonate) and the solvent removed to give 1-chloroadamantane (0.80 g.), m.p. 157-160°, [lit. (9) m.p. 165° sublimes].

The acid phase was evaporated to dryness *in vacuo*, the residue dissolved in water (10 ml.), and the *p*H adjusted to ten, with 5*N* sodium hydroxide solution. Extraction with benzene (four 25 ml. portions) gave a mixture consisting of **2** and 2-pyridthione. The mixture was washed with hot pentane (2 ten ml. portions) to afford pure 2-pyridthione (0.05 g.) m.p. 125-127° [lit. (10) m.p. 128°]. Evaporation of the pentane extract yielded pure starting material **2** (0.0 g., 25%).

The basic aqueous phase was neutralized with dilute aqueous hydrochloric acid and extracted several times with benzene (200 ml. in all). The benzene extracts yielded an additional quantity of 2-pyridthione (0.2 g.). Based on recovered **2**, the yield of 1-chloroadamantane was 77%, and that of 2-pyridthione, 37%.

In a similar fashion, **3** (2.0 g., 0.0081 mole) was cleaved by reflux in a mixture of concentrated hydrochloric acid (40 ml.) and toluene (5 ml.). From the benzene extract of the acidic media was obtained 950 mg. (86% based on recovered **3**) of 1-chloroadamantane. From the basic solution (*p*H = 14) there was precipitated 400 mg. of **3**. Chloroform extraction of the reacidified solution (*p*H = 4.5) yielded 250 mg. (34% based on recovered **3**) of 3-pyridinethiol, m.p. 74-77° (lit. (11) m.p. 75-77); pmr (deuteriochloroform): δ 4.20 (bd s, SH); d of t, δ 7.15 (H-5); d of t; δ 7.60 (H-4); d of d, δ, 8.40 (H-6); d, δ 8.55 (H-2); ir (chloroform): 2000 (Ar-H), 2500 cm^{-1} (SH).

After a mixture of **4** (0.7 g.) and concentrated hydrochloric acid (13 ml.) was refluxed for 3 hours, cooled, and extracted with ether, there was isolated 1-chloroadamantane (0.44 g., 92%).

LIS Studies of 1-Adamantyl Pyridyl Sulfides.

The three 1-adamantyl pyridyl sulfides (**2-4**) proved to be interesting substrates for lanthanide induced shift (LIS) studies with tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octadione)europeum III, $EU(FOD)_3$. The 3- and 4-pyridyl sulfides (**3** and **4**) showed similar results with the expected downfield shifts of both aromatic and adamantyl protons. The magnitude of the shifts (Table II) are in agreement with published values for similar heteroaromatic (13-15) and adamantyl systems (15,16).

The 1-adamantyl 2-pyridyl sulfide (**2**) LIS experiment was unique and revealed *upfield* induced shifts for H-5 and H-6 (Table II). The shifts of H-3 and H-4 were downfield but reduced in magnitude. This unusual observation can be attributed to the very bulky substituent at C-2 which forces the lanthanide to move laterally toward C-6 away from the C_2 axis of the pyridine ring. This change in geometry of the complex, because of the angular dependence of LIS shifts, (17) causes upfield shifts of H-5 and H-6. Anomalous shifts observed in other 2-substituted pyridines might be explained by a similar mechanism (18).

Acknowledgements.

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