Carbon-13 Spectra of Some Tetrahydropyridines. The Structure of the Tetrahydropyridines from 3,5-Lutidine 1-Oxide and Mercaptans in Acetic Anhydride (1,2)

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The reaction of 3,5-lutidine 1-oxide (**1**) with *t*-butyl mercaptan in acetic anhydride, with or without triethylamine, was reinvestigated. There was obtained 2-*t*-butylthio-3,5-lutidine as the major product, a small quantity of 3-(*t*-butylthio)methyl-5-picoline, 1-acetyl-2,3-diacetoxy-3,5-dimethyl-6-*t*-butylthio-1,2,3,6-tetrahydropyridine (which represents a structure revision) and 1-acetyl-2,6-dihydroxy-3-*t*-butylthio-3,5-dimethyl-1,2,3,6-tetrahydropyridine. A similar reaction of **1** with 1-adamantyl mercaptan furnished 2-(1-adamantylthio)-3,5-lutidine and 1-acetyl-2,3-diacetoxy-3,5-dimethyl-6-(1-adamantylthio)-1,2,3,6-tetrahydropyridine. The structures of these new tetrahydropyridines were established primarily by carbon-13 nmr spectra.

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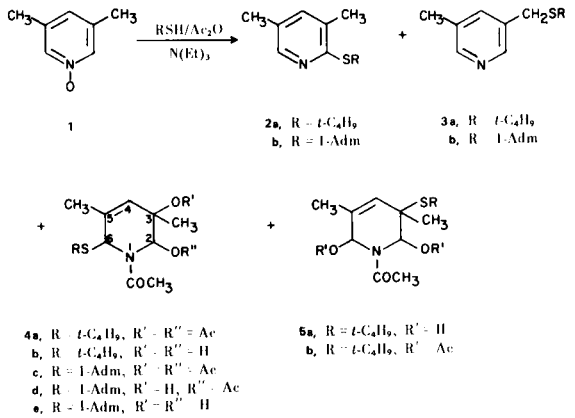
In our continuing study of the reaction of pyridine *N*-oxides with thiols in acid anhydrides (2-5), the reaction of 3,5-lutidine 1-oxide (**1**) with *t*-butyl and 1-adamantyl mercaptan (1-Adm-SH) in acetic anhydride was investigated.

In an earlier report, the reaction of **1** with *t*-butyl mercaptan in acetic anhydride afforded the expected pyridyl sulfide, namely, 2-(*t*-butylthio)-3,5-lutidine (**2a**) and a heavily substituted tetrahydropyridine (3). Additional products have now been isolated from the reaction of **1** with mercaptans in acetic anhydride, with or without triethylamine, as expressed by the following equation:

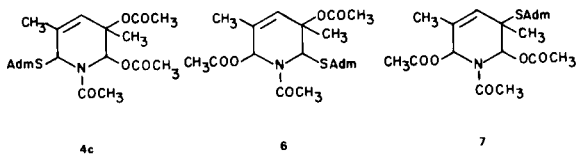


From mass spectral and ^{1}H nmr data, the previously isolated tetrahydropiperidyl monosulfide *bis*-ester was assigned structure **5b** (3), which is now revised to be **4a**. Using ^{13}C nmr spectra of related tetrahydropyridines as models (**9-20** in Table II) (2,4,5), it was possible to arrive at structures **4** and **5** in this work (Table I).

The Reaction of 3,5-Lutidine 1-Oxide with 1-Adamantyl Mercaptan in Acetic Anhydride.

The various products obtained from this reaction were separated entirely by chromatography on alumina. The major product was of course 2-(1-adamantylthio)-3,5-lutidine (**2b**) whose structure was confirmed by its characteristic ^{1}H nmr spectrum. The pyridine ring proton resonances at 7.26 and 8.23 ppm (deuteriochloroform) were relatively broad signals showing small long-range coupling of the ring protons with the *vicinal* methyl protons. Irradiation of the methyl signals collapsed these broad signals to two doublets with a coupling constant of 2.0 Hz, indicative of 1,3-arene proton coupling. This pattern is typical of a 2- rather than a 4-substituted 3,5-lutidine.

As the chromatographic separation continued, the *bis*-acetoxy sulfide, **4c**, was eluted, followed by the hydroxy acetoxy sulfide **4d**. Both **4c** and **4d** were hydrolyzed independently to the diol sulfide **4e**. The availability of these three related tetrahydropyridines permitted their structure elucidation. The uv absorption at 204 nm (ϵ = 7,410) suggested that the double bond of **4e** was not part of an enamine and was either at the 3,4 or 4,5 position of the tetrahydropyridine. Barring deep-seated rearrangements, the methyl groups on the ring of **4c-e** were at 3 and 5. Furthermore, their ^{1}H nmr spectra did not show a mixture of rotamers and exhibited signal attributable to the substituent suggested for **4c-e**. However, these spectra could not distinguish between isomers **4c** and **6** or **7**, because of the proximity of the ring proton chemical shifts (between 5.90 and 6.25 ppm) and the lack of



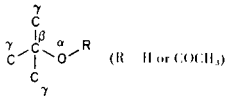
large spin-spin coupling constants.

Therefore, ^{13}C spectra were utilized to locate the ring substituents of **4c-e**. Single frequence off-resonance decoupling (SFORD) established that the resonances at 79.6, 51.4 and 122.6 ppm in **4c** became doublets and those at 77.9 and 137.9 ppm remained singlets. This established the ^{13}C chemical shifts for C-4 (122.6 ppm) and C-5 (137.9 ppm).

In identical structural environments, carbons bearing sulfides are considerably more shielded than those carrying oxy substituents (6,7). If one examines the ^{13}C chemical shifts of ring carbons bearing sulfide groups at either C-2 or C-6 in the series listed in Table II, irrespective of which rotamer might be involved, one concludes that the 51.4 ppm signal is due to a CHSR resonance. Since the SFORD experiment showed that the sulfide had to be on a secondary carbon, structure **7** was eliminated. Then the 79.6 ppm signal arises from the CHOAc carbon either at C-2 of **4c**, or at C-6 in **6**.

This point was settled with the help of ^{13}C spectral data from the hydroxy acetate **4d** and diol **4e**. A SFORD experiment established that the resonances at 51.4 and 82.3 ppm in **4d** became doublets and the one at 68.4 ppm remained a singlet. This is interpreted that the 68.4 ppm signal is from the tertiary carbinol carbon at C-3 and is as expected considerably more shielded than the corresponding acetoxymethine carbon.

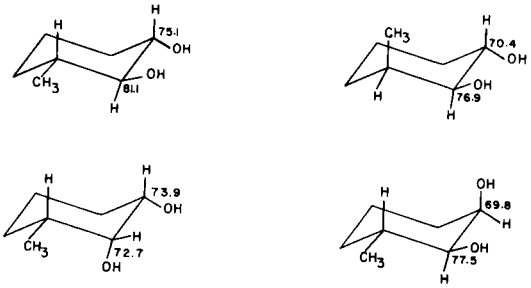
Acetylation of an alcohol not only effects the chemical shifts of the β but also that of the neighboring γ-carbons (see partial structures for the convention of labelling the carbons).



(R = H or $COCH_3$)

Diagnostically, acylation of an alcohol usually deshields the β-carbon (which is the carbinol carbon) and shields the γ-carbons (those next to the carbinol carbon), all other matters being equal. Therefore, if one considers "acetylation" of the OH group on C-3 in **4d**, equivalent to **4d** → **4c**, the carbinol (β) carbon experiences a downfield shift (68.4 → 77.9 ppm) and the γ-carbons, upfield shifts (for C-2, 82.3 → 79.6; for C-4, 126.1 → 122.6; for CH_3 on C-3, 23.7 → 21.8 ppm). Equally important is the observation that the 51.4 ppm signal in **4c** and **4d**, which represents the methine bearing the sulfide group, is unaffected. Hence, the alcohol and acetoxy groups are *vicinal* and the structure of the hydroxy acetate and *bis*-acetate are **4d** and **4c**, respectively.

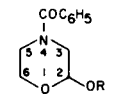
Hydrolysis of either **4c** or **4d** provided the diol **4e**. Unfortunately, no model *vicinal* tetrahydropyridinediols related to **4** have been isolated so far. Since no *vicinal* proton coupling constants are available in **4e**, one cannot postulate on the stereochemistry of **4e**. Model cyclohexanediols cannot be used, really. There is considerable



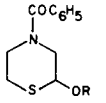
latitude in carbon chemical shifts with changes in the configurations of the carbinyl carbons, judging from the reported shifts for the four isomers in deuteriochloroform (8).

^{13}C shifts are quite sensitive not only to configurational changes, but also to hydrogen-bondings and 1,3-diaxial steric interactions. In a systematic study of known *vicinal* steroidal diols, some unpredicted carbon shifts were noted (9). In *vicinal* cyclohexene or piperideine diols, changes in hydrogen bonding could flip substituents from a ψ-axial to a ψ-equatorial position, and such conformational changes could very much effect ^{13}C shifts.

An analysis of the chemical shifts of the ring carbons of **4e** and **4d**, which is equivalent to the monoacetylation of the 2 OH in **4e**, showed that 51.6 ppm signal in **4e** moved to 51.4 in **4d**, showing little electronic or steric change in the vicinity of the methine bearing the sulfide group. As expected, the γ-shift in **4e** → **4d** was upfield, 70.2 → 68.4 ppm. However, the β-effect was unexpectedly also upfield, *viz.*, 85.3 → 82.3 ppm. There are a number of recently reported examples of smaller than expected downfield, and even upfield β-effects when a secondary alcohol was acetylated. Monoacetylation of the *vicinal* diol 5α-cholestane-3α,4β-diol to give the 4β-acetate, produced chemical shift changes as expected, for C-3 (70.3 → 67.0) and for C-4 (76.1 → 77.0) (9); similar changes for 3β-acetoxycholestane-5α,6β-diol going to the 6β-acetate were for C-5 (75.7 → 74.8) and C-6 (76.2 → 76.4) (10). However, quite an unexpected upfield β-effect was noted when 4-benzoyl-2-hydroxy-1-oxa- and 1-thia-4-azacyclohexanes **8a** and **8b**, respectively, were acetylated. The ^{13}C resonances moved slightly upfield, for **8a** → **8c** (91.0 → 89.6 ppm) and **8b** → **8d** (69.4 → 69.3) at 57° (in deuteriochloroform) (15).



8a, R = H
c, R = $COCH_3$

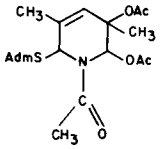
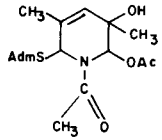
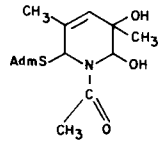
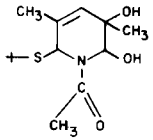
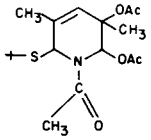
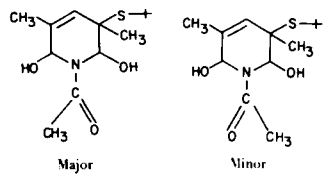


8b, R = H
d, R = $COCH_3$

Unexpected upfield β shifts were recorded for the acetylation of certain hydroxyl groups in some macrolide antibiotics and these anomalies were attributed to conformational changes (11). When erythronolide B was converted to 3,5-diacetylerythronolide B, the carbinyl

Table I

Ring ^{13}C and ^{1}H Nmr Chemical Shifts in Deuteriochloroform (ppm from TMS) of 3,5-Lutidine Derivatives (a)

Compound Number	Structure	C-2	C-3	C-4	C-5	C-6	H-2	H-4	H-6	CH_3 at C-3	CH_3 at C-5	OH	$J_{2,4}$	$J_{4,6}$	Other
4c		79.6	77.9	122.6	137.9	51.4	6.23	5.91	6.01	1.60	2.05	---	1.4	1.6	$J_{CH_3,4} = 0.7$ $J_{CH_3,6} = 0.5$
4d		82.3	68.4	126.1	136.4	51.4	6.01	5.46	5.89	1.31	1.95	4.15	1.4	1.6	$J_{CH_3,4} \simeq 0.7$ $J_{CH_3,6} \simeq 0.5$
4e		85.3	70.2	127.3	134.9	51.6	5.23	5.50	6.10	1.37	2.00	2.60 (3) 4.07 (2)	1.2	1.8	$J_{2,OH} = 6.0$
4b		85.5	70.3	127.6	134.4	53.7	5.28	5.51	6.10	1.40	1.80	2.80 (3) 4.23 (2)	1.2	1.8	$J_{2,OH} = 7.0$
4a		79.6	77.9	122.8	137.6	53.8	6.25	5.93	6.03	1.62	1.95	---	1.0	1.2	
5a (Ratio of Rotamers is 1:1)	 Major Minor	83.0 77.1 (b)	52.3 51.2	126.5 126.5	132.1 131.5	73.2 75.8 (b)	6.23 5.31	5.39 5.46	5.31 5.15	1.68 1.70	1.90 1.88	(c) (c)	1.5 1.0	1.2 1.2	

(a) Only ring carbon and proton nmr data are provided. Chemical shifts due to other ring substituents are similar to those reported for related tetrahydropyridines (References 2-5); +— stands for *t*-butyl and Adm for 1-adamantyl. (b) These resonances can be interchanged. (c) OH Proton signals were observed but could not be assigned with any degree of certainty.

Table II

Comparison of ^{13}C Nmr Chemical Shifts in Deuteriochloroform (ppm from TMS) (a)

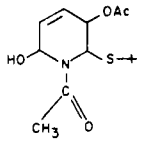
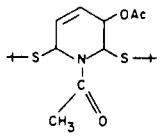
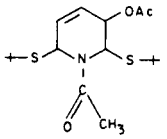
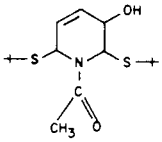
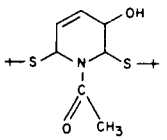
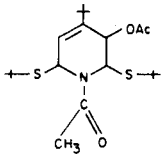
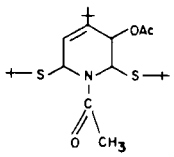
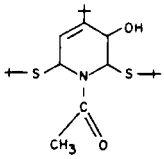
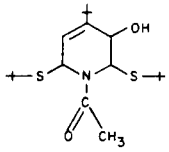
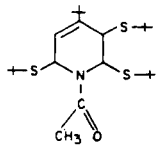
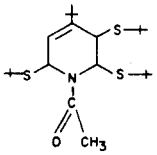
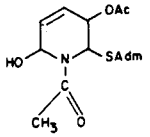
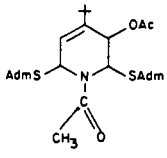
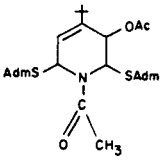
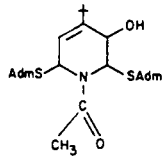
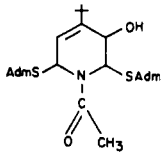
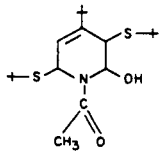
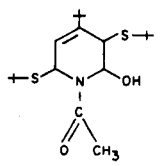
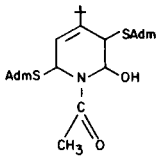
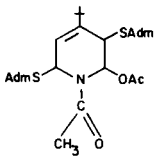
Compound Number	Structure Major	Structure Minor		C-2	C-3	C-4	C-5	C-6
9				51.2	67.4	124.3	133.8	75.1
10			Major Minor	57.7 51.8	69.9 68.9	118.1 120.0	136.9 135.3	51.4 55.3
11			Major Minor	61.4 55.0	68.5 67.4	122.8 123.8	134.0 132.8	51.4 55.3
12			Major Minor	55.9 52.1	68.0 69.3	137.6 137.4	126.7 121.3	52.1 57.6
13			Major Minor	61.6 55.4 (b)	68.1 66.8	143.2 144.1	124.9 123.6	52.3 55.9 (b)
14			Major Minor	56.0 (b) 52.3	44.2 45.4	142.6 140.1	124.0 126.2	55.1 (b) 62.0
15				48.8	67.6	124.3	133.8	75.2
16			Major Minor	55.1 49.7	68.3 69.8	139.4 137.0	127.5 128.6	49.8 53.7
17			Major Minor	58.7 52.9	68.5 67.4	142.6 143.8	125.8 124.6	49.7 53.7
18			Major Minor	82.1 74.5	43.0 41.8	139.6 (c)	122.4 121.8	51.0 54.9

Table II (Continued)

Compound Number	Structure Major	Minor	C-2	C-3	C-4	C-5	C-6
19			82.6	40.6	139.0	123.5	47.5
20			81.3	38.2	137.5	124.3	49.2

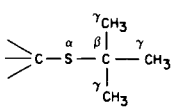
(a) Only ring ^{13}C resonances are reported. Carbon resonances for substituents resembled those reported earlier (References 2-5); ⊣⊢ stands for *t*-butyl and Adm for 1-adamantyl. (b) Resonances can be interchanged. (c) Weak signal lost in the noise.

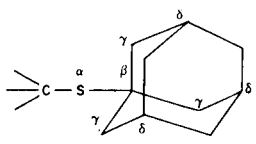
carbons resonances moved upfield, for C-3 (79.4 → 76.9), for C-5 (81.3 → 79.1) and downfield (as expected) for C-11 (70.2 → 72.9).

To conclude this section, the structure of **4c**, **4d** and **4e** is based on the 2,3-dioxy-6-alkylthio-3,5-dimethyl-1,2,3,6-tetrahydropyridine system. This substitution pattern is a departure from the types of tetrahydropyridines isolated so far as reflected by the examples listed in Table II. Furthermore, type **4** did not show up as a mixture of rotamers in their nmr spectra.

The Reaction of **1** with *t*-Butyl Mercaptan in Acetic Anhydride.

The *bis*-acetoxy monosulfide isolated from this reaction is now postulated to be **4a** since the ^{1}H and ^{13}C chemical shifts of the ring atoms were virtually identical to those of **4d** (Table I). The largest discrepancy was in the C-6 carbon resonance, differing by 2.4 ppm downfield in the *t*-butyl derivative to the comparable resonance in the 1-adamantyl thioether. Although relatively little has been published on ^{13}C spectra of the thioethers (6), this shift difference is explained in terms of the number of β, γ and δ-substituents for the two substituents, as shown by partial structures. Since the 1-adamantyl group has more δ-substituents with reference to sulfur, this group exerts a larger shielding effect than *t*-butyl.





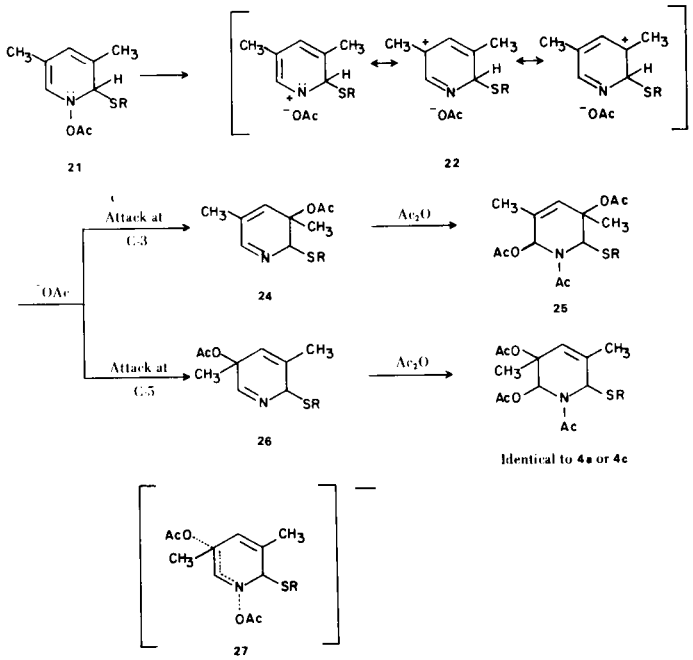
Although no hydroxy acetate corresponding to **4a** was isolated from **4a**, the requisite diol was obtained, whose ^{13}C nmr data corresponded to that of **4e** and the diol was assigned structure **4b**. When this reaction was repeated, it yielded, besides 2-*t*-butylthio-3,5-lutidine (**2a**) (3), an isomeric sulfide, 3-(*t*-butylthiomethyl)-5-picoline (**3a**). This isomer was characterized by its ^{1}H nmr spectrum which presented one more ring proton signal than **2a**, and only one CH_3 proton resonance signal along with the CH_2SR pmr signal.

A reaction of **1** with *t*-butyl mercaptan in acetic anhydride in the presence of triethylamine yielded some **4a**, but the major tetrahydropyridine was the isomeric *bis*-hydroxy mono-sulfide **5a**. The latter existed as a mixture of rotamers since on heating, the chloroform solution broadened the ^{1}H nmr signals due to H-2 and and H-6 and sharpened those due to H-4. The ^{13}C ring resonances of **5a** are in agreement with the proposed structure. SFORD Experiments showed that the 51.2 and 52.3 ppm ^{13}C signals remained singlets and, therefore, hence represented the carbons (C-3) bearing the sulfide group.

Suggested Pathways for the Formation of **3**, **4** and **5**.

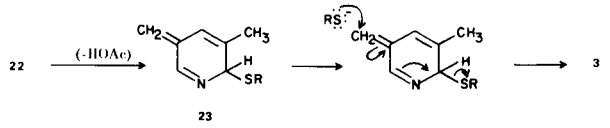
The formation of 2,3-dioxy-3,5-dimethyl-1,2,3,6-tetrahydropyridines reported now can be rationalized in terms of the general pathways suggested for the synthesis of the differently substituted tetrahydropyridines, like those listed in Table II (5). Quaternization of **1** by acetic anhydride results in the 1-acetoxy-3,5-lutidinium ion, which is attacked by the thiol on C-2 to produce the 1,2-dihydropyridine **21**. Whether **21** dissociates into a resonance-stabilized nitrenium-carbonium ion-pair in a solvent cage, **22**, which is attacked at either C-3 or C-5 by acetate ion to create **24** or **26**, or whether acetate ion attacks the same ring positions in a concerted type of displacement (*e.g.*, **27** for C-5 attack), remains a mute point. It would appear that the formation of **4** can be explained if acetate attacks C-5 rather than C-3. It could

just be that C-5 is less hindered at this point than C-3. However, this pathway is a departure since prior tetrahydropyridine formation was accounted for by nucleophilic attack at the carbon at C-3 (5). Either of the tetrahydropyridines, **24** or **26**, can add acetic anhydride to the Schiff's base to form either **25** or **4**.



Similar arguments can be advanced on how **21** can be converted to **5** and plausible pathways are presented in a previous paper (5).

The formation of **3** can also be rationalized also *via* **22**. The loss of acetic acid from **22** can give rise to the dihydropyridine **23**, which can undergo the addition and loss of a molecule of mercaptan, as shown, to produce **3**.



EXPERIMENTAL

Melting points were determined on a Mel-Temp apparatus and are uncorrected. Uv spectra were obtained on a Perkin Elmer 202 spectrophotometer. ^{1}H Nmr spectra were recorded on Varian T60A and HA-100 spectrometers and ^{13}C nmr spectra (at 25.2 MHz) on a Varian Fourier Transform XL-100 Spectrometer. Chemical shifts are reported downfield from internal tetramethylsilane. Proton chemical shifts were checked by decoupling experiments, and carbon-13 chemical shifts by single frequency decoupling experiments. Mass spectra were obtained by 70 eV by Mr. Richard Dvorak using a Hitachi-Perkin Elmer RMU-6D single focusing spectrometer. Only the more intense ions are reported, unless essential to a structure proof. Microanalyses were carried out by Micro-Tech Laboratories, Skokie, Illinois. Thin layer chromatograms (tlc) were obtained on 8 x 4 cm. strips of Eastman Chromagram silica gel sheets (No. 13181) mixed with a fluorescent indicator (No. 6060). Developing solvents were petroleum ether-ether, 7:3 (solvent A) and ether (solvent B). The products were identified either by uv light and/or iodine vapor stains. For column chromatography (5), silica gel was Mallinckrodt's neutral SilicAR CC-7, 200-325 mesh and alumina was Alcoa's F-20.

The Reaction of **1** with *t*-Butyl Mercaptan.

t-Butyl mercaptan (96 ml., 0.9 mole) (12) was added to a solution of **1** (36.9 g., 0.3 mole) (13) in acetic anhydride (300 ml.). The temperature rose to 110° and when the initial reaction subsided, the mixture was heated on the steam bath for 3 hours. Solvents and most of the sulfide, **2a**, were distilled *in vacuo*, first at 20 Torr and then at 1 Torr, keeping the external heating bath at 85° or lower (3). The remaining oil was dissolved in a little benzene and was placed on alumina (750 g.). The initial benzene fractions contained primarily **2a**, and these were not examined further. Later benzene fractions eluted some **4a**. Ether was used to elute **4a** completely (total 2.3 g., 2%), m.p. 125-127°, which was identical to the reported m.p. (3); tlc, Rf = 0.44, 0.78 (solvents A, B).

The final eluate with ether-methanol (4:1) yielded another fraction (6.0 g.) which was rechromatographed on alumina. Elution from the second column with ether-chloroform (4:1) furnished **3a**, which was recrystallized from petroleum ether (1.3 g., 4%), m.p. 29-30°; Rf = 0.29 (solvent A); ^{1}H nmr (deuteriochloroform): δ 8.49 (br s, H-2, H-6), 7.60 (br s, H-4), 3.80 (s, CH_2S), 2.39 (CH_3), 1.40 (*t*-C_4H_9).

Anal. Calcd. for $C_{11}H_{17}NS$: N, 7.19. Found: N, 6.98.

Reaction of **1** with *t*-Butyl Mercaptan in the Presence of Triethylamine.

t-Butyl mercaptan (40 ml., 0.35 mole) was added last and rapidly (through the condenser) to a solution of **1** (40 g., 0.35 mole) in acetic anhydride (300 ml.) and triethylamine (100 ml.). The internal temperature of the reaction mixture rose to 118° and commenced to drop after 10 minutes. The mixture was heated on the steam bath for an additional 80 minutes. Solvents and volatile sulfides were removed at 0.01 Torr (bath temperature < 60°) and the resultant oil (57.4 g.) placed on a column of silica gel (600 g.) in benzene. The initial benzene eluates contained **2a**, and the latter ones, **4a** (2.4 g., 2.2%). Benzene mixed with various proportions of ether eluted mixtures which were not separated further. However, ether eluted **5a**, which was recrystallized from ether (at -30°) to produce the pure diol (4.5 g., 4.7%), m.p. 130-131°; tlc, Rf = 0.33 (solvent B). Its mass spectrum (70 eV) showed the following major ions (relative intensities), m/e 273 (molecular ion, 5) and a large number of fragment ions, the most prominent being ones at m/e 255 (5), 183 (15), 166 (15), 142 (40), 129 (50), 124 (100).

Anal. Calcd. for $C_{13}H_{23}NO_3S$: C, 57.13; H, 8.48; N, 5.12. Found: C, 57.04; H, 8.35; N, 5.00.

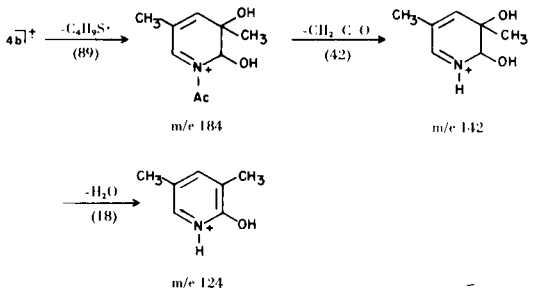
Acetylation of **5a** (0.2 g., 0.00073 mole) with acetic anhydride (1 ml.) in pyridine (1 ml.) for 24 hours at 25° afforded, after addition of water, **5b** (0.16 g., 61%), m.p. 118-120°; tlc, Rf = 0.26, 0.68 (solvents A, B). Its nmr spectra were too complicated to interpret since there was a chance that **5b** consisted of mixtures of rotamers and epimers.

Its mass spectrum showed a small molecular ion, m/e 357 (2%), and the only other major ions were m/e 267 (30), m/e 124 (100), all other ions being 20% or less of the base peak.

Anal. Calcd. for $C_{17}H_{27}NO_5S$: C, 57.13; H, 7.61; N, 3.92. Found: C, 57.22; H, 7.53; N, 3.91.

Hydolysis of **4a** to give **4e**.

A solution of **4a** (0.36 g., 0.001 mole) in methanolic sodium hydroxide (0.02 g., 0.0005 mole; 5.0 ml.) was warmed for 5 minutes (tlc indicated disappearance of starting ester). The product was isolated by the addition of ice to the reaction mixture saturating with salt, followed by chloroform extraction. Evaporation of the solvents yielded **4b** (0.27 g., 100%), which crystallized from petroleum ether, m.p. 135-137°; tlc, Rf = 0.24 (solvent B), uv (ethanol), 211 nm (ϵ = 7,010). A similar hydrolysis with boiling methanol containing potassium bicarbonate (4) proceeded slower and produced **4b** in poorer yield. Its mass spectrum showed besides a small molecular ion, m/e 273 (3), prominent ions at m/e 184 (60), 142 (100), 124 (25) attributable to the following structures:



Anal. Calcd. for $C_{13}H_{23}NO_3S$: C, 57.13; H, 8.48; N, 5.12. Found: C, 57.27; H, 8.56; N, 5.08.

The Reaction of **1** with 1-Adamantyl Mercaptan.

A solution of **1** (24.6 g., 0.2 mole) and 1-adamantyl mercaptan (34.6 g., 0.21 mole) (4,14) in acetic anhydride (200 ml.) were warmed to 70° when a spontaneous reaction ensued and the temperature rose to 100°. After the temperature commenced to drop, the solution was heated on the steam bath for 3 hours. Acetic anhydride was removed using a flash evaporator (20 Torr, bath temperature $<85°$) and the residue was dissolved in chloroform and washed with ice-cold 50% potassium carbonate solution. After drying the chloroform solution, solvents were evaporated *in vacuo* and the residue (60 g.) placed on a column of alumina (1200 g.) in petroleum ether. Petroleum ether eluates brought forth the starting thiol. Petroleum ether-benzene mixtures (from 9:1 to 1:1) eluted 2-(1-adamantylthio)-3,5-lutidine (**2b**) (27.8 g., 50%), m.p. 58-59°; tlc, Rf = 0.58 (solvent B); ^{1}H nmr (deuteriochloroform): δ 8.22 (br s, H-6), 7.19 (br s, H-4), 2.27, 2.20 (ring CH_3's), 2.20-1.60 (adamantane protons).

Anal. Calcd. for $C_{17}H_{23}NS$: N, 5.12. Found: N, 5.08.

Subsequent elution with benzene-chloroform (9:1, 4:1, 7:3, 3:2 and 1:1) yielded **4c** (5.1 g., 6.0%) which crystallized from petroleum ether, m.p. 154-155°; tlc, Rf = 0.31 (solvent A).

Anal. Calcd. for $C_{23}H_{33}NO_5S$: N, 3.22. Found: N, 3.13.

Further elution with chloroform and chloroform-methanol (4:1) produced a fraction from which, after crystallization from petroleum ether, there was obtained **4d** (0.3 g., 0.4%), m.p. 177-179°; tlc, Rf = 0.48 (solvent B). A reproducible mass spectrum was difficult to obtain. At an inlet temperature of 110°, no molecular ion were observed and the two major ions above m/e 100 were m/e 135 (Adm.$^+$, 40) and m/e 124 (100). At 150°, the molecular ion m/e 393 was observed ($<1\%$) and m/e 135 ion became the base peak with m/e 124 (25) and 123 (30).

Anal. Calcd. for $C_{21}H_{31}NO_4S$: N, 3.56. Found: N, 3.70.

Hydrolysis of **4c** and **4d** and **4e**.

The *bis*-acetate **4c** (0.87 g., 0.002 mole) was refluxed in methanol (15 ml.) containing potassium bicarbonate (0.1 g., 0.001 mole) for 90 minutes. The solution was evaporated to dryness *in vacuo*. The residue was triturated with ether, filtered and the ether solution evaporated. The residue was crystallized from petroleum ether to give **4e** (0.3 g., 43%), m.p. 164-166°; tlc, Rf = 0.26 (solvent B); uv (ethanol): 204 nm (ϵ = 7,410). Its mass spectrum showed the following significant ions, m/e 351 (molecular ion 5), 184 (82), 142 (100), 135 (5), 134 (45) and 124 (25). This fragmentation is quite compatible to that proposed above for the decomposition of the molecular ion of **5b**. No structure is proposed for the relatively strong m/e 134 ion. It is interesting that the adamantyl ion m/e 135 is not the predominent decomposition ion, frequently observed to be so in 1-adamantyl compounds.

Anal. Calcd. for $C_{19}H_{29}NO_3S$: C, 64.93; H, 8.32; N, 3.99. Found: C, 64.82; H, 8.43; N, 3.91.

The hydroxy acetate **4d** (0.1 g.) was warmed in 5 ml. of methanol containing 0.005 g. of sodium hydroxide for 5 minutes. The solution was poured onto ice. The solid (0.062 g.) was recrystallized and proved to be identical to **4e**.

REFERENCES AND NOTES

(1) Support for this work by a Research Grant CA-13964 from the National Cancer Institute, NIH, US Public Health Service is most gratefully acknowledged.

(2) Part XVI. The deoxydative substitution of pyridine *N*-oxides. For Part XV, see J. M. Kokosa, I. Chu, L. Bauer and R. S. Egan, *J. Heterocyclic Chem.*, **13**, 861 (1976).

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(12) We thank the Phillips Petroleum Co. and Penn-Salt Chemical Co. for their generous gift of this mercaptan. Caution in handling this chemical must be observed (Reference 3a).

(13) We thank the Reilly Tar and Chemical Co., Indianapolis, Indiana for their generous gift of 3,5-lutidine. The *N*-oxide was prepared as stated in Reference 3a.

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