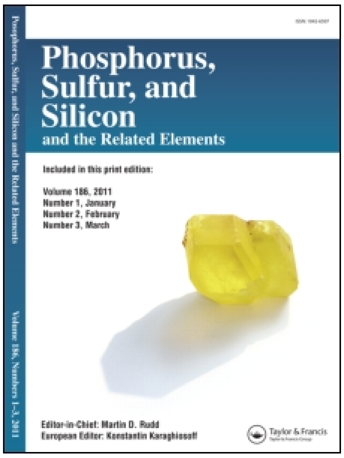


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

STUDIES ON THE CONFORMATIONS OF 4-*N,N*-DIMETHYLAMINOTHIANES AND THE CORRESPONDING METHIODIDES. EVIDENCE FROM A SINGLE CRYSTAL X-RAY DIFFRACTION ANALYSIS THAT A TWIST-BOAT CONFORMER EXISTS IN THE SOLID STATE FOR TRIMETHYL-[2,2-DIMETHYL-*trans*-6-PHENYLTHIAN-*r*-4-YL]-AMMONIUM IODIDE

Pullachipatti K. Subramanian[a][b]; Kondareddiar Ramalingam[a]; Nantelle S. Pantaleo[c]; Dick Van Der Helm[d]; Nagichettiar Satyamurthy[e]; K. Darrell Berlin[e]
[a] Department of Chemistry, PSG College of Arts & Sciences, Coimbatore, India [b] University of Madras, India [c] Department of Chemistry, University of Tulsa, Tulsa, Oklahoma [d] Department of Chemistry, University of Oklahoma, Norman, Oklahoma [e] Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma

To cite this Article Subramanian, Pullachipatti K. , Ramalingam, Kondareddiar , Pantaleo, Nantelle S. , Van Der Helm, Dick , Satyamurthy, Nagichettiar and Berlin, K. Darrell(1983) 'STUDIES ON THE CONFORMATIONS OF 4-*N,N*-DIMETHYLAMINOTHIANES AND THE CORRESPONDING METHIODIDES. EVIDENCE FROM A SINGLE CRYSTAL X-RAY DIFFRACTION ANALYSIS THAT A TWIST-BOAT CONFORMER EXISTS IN THE SOLID STATE FOR TRIMETHYL-[2,2-DIMETHYL-*trans*-6-PHENYLTHIAN-*r*-4-YL]-AMMONIUM IODIDE', Phosphorus, Sulfur, and Silicon and the Related Elements, 17: 3, 343 — 365

To link to this Article: DOI: 10.1080/03086648308077555

URL: http://dx.doi.org/10.1080/03086648308077555

Phosphorus and Sulfur, 1983, Vol. 17, pp. 343–365
0308-664X/83/1703-0343/$18.50/0

STUDIES ON THE CONFORMATIONS OF 4-*N*,*N*-DIMETHYLAMINOTHIANES AND THE CORRESPONDING METHIODIDES. EVIDENCE FROM A SINGLE CRYSTAL X-RAY DIFFRACTION ANALYSIS THAT A TWIST-BOAT CONFORMER EXISTS IN THE SOLID STATE FOR TRIMETHYL-[2,2-DIMETHYL-*trans*-6-PHENYLTHIAN-*r*-4-YL]-AMMONIUM IODIDE

PULLACHIPATTI K. SUBRAMANIAN[1]
and KONDAREDDIAR RAMALINGAM*

*Department of Chemistry, PSG College of Arts & Sciences,
Coimbatore-641 014, India*

NANTELLE S. PANTALEO*

Department of Chemistry, University of Tulsa, Tulsa, Oklahoma 74014

DICK VAN DER HELM*

Department of Chemistry, University of Oklahoma, Norman, Oklahoma 73019

NAGICHETTIAR SATYAMURTHY and K. DARRELL BERLIN*

*Department of Chemistry, Oklahoma State University, Stillwater, Oklahoma
74078*

(*Received July 14, 1983; in final form August 2, 1983*)

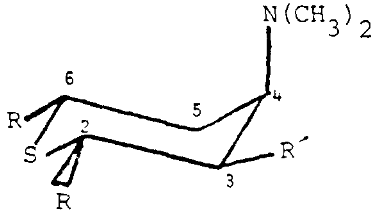
A number of 4-*N*,*N*-dimethylaminothianes have been prepared by a reaction of 4-aminothianes with formaldehyde and formic acid. ^{1}H and ^{13}C NMR spectral analysis suggest twist conformations for 2,2-dimethyl-*trans*-6-phenyl-*r*-4-*N*,*N*-dimethylaminothiane and 2,2-dimethyl-*trans*-6-(4-chlorophenyl)-*r*-4-*N*,*N*-dimethylaminothiane. Reaction of the tertiary amines with methyl iodide gave the quaternary ammonium iodides. The ^{1}H NMR (270 MHz) spectra of the methiodides in DMSO-d_6 indicated twist conformations for the compounds with axial C—N bonds. The spectra also suggested a possible boat conformation for the methiodides of 2,2-dimethyl-*trans*-6-phenyl-*r*-4-*N*,*N*-dimethylaminothiane and 2,2-dimethyl-*trans*-6-(4-chlorophenyl)-*r*-4-*N*,*N*-dimethylaminothiane in equilibrium with the twist conformation. Kinetics of quaternization of six epimeric pairs of *N*,*N*-dimethylaminothianes with methyl iodide in acetonitrile at 10 ± 0.05°C have been carried out and the causes for the rate differences are discussed in terms of steric effects and nonchair conformers. A single crystal X-ray diffraction analysis of trimethyl[2,2-dimethyl-*trans*-6-phenyl-thian-*r*-4-yl]ammonium iodide [a = 20.581(14), b = 20.260(9), c = 8.615(3) Å; space group Pbca] was completed to confirm a twist-boat conformation of the thiane ring in the solid state. The S—C(2) bond is much longer [1.851(6) Å] than the S—C(6) bond [1.809(6) Å] which probably reflects the strain in the system. This situation is also manifested in the endocyclic bond angles at C(3), C(4), C(5) and C(6) which are larger than the normal tetrahedral value. In an ideal boat, the torsion angles at C(6) S(1) C(2) C(3) and C(3) C(4) C(5) C(6) should be 0° but in the title compound the angles are 14.8° and 20.9°, respectively. Other angles show large differences and thus confirm the molecule is a twist-boat form.

INTRODUCTION

The synthesis and conformational analysis of several thiane derivatives have been reported from our laboratory.[2] Stereochemical data on 4-*N*,*N*-dimethylaminothianes is essentially nonexistent. We now report the first synthesis of several substituted 4-*N*,*N*-dimethylaminothianes and the corresponding methiodides. The conformations of these compounds were diagnosed from ^1H and ^{13}C NMR spectral data. As a corroborative evidence to the spectral studies, the kinetics of quaternization of *N*,*N*-dimethylaminothianes with methyl iodide were also examined.

RESULTS AND DISCUSSION

N,*N*-Dimethylaminothianes **1a–d**, **2a–d**, **3a**, **3b**, **4a**, **4b**, **5** and **6** were synthesized by methylating the corresponding 4-aminothianes[2e] with formaldehyde and formic acid.[3] Additional details are given in the experimental section and properties are found in Table I.



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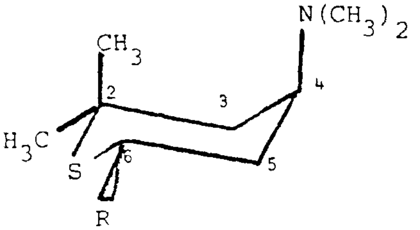
	R	R′
a	C_6H_5	H
b	p-ClC_6H_4	H
c	C_6H_5	CH_3
d	C_6H_5	C_2H_5



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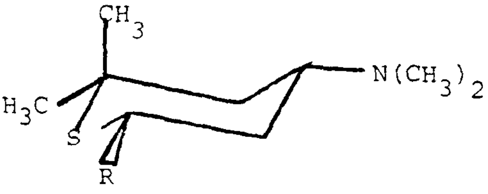

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TABLE I

Physical constants of substituted 4-*N*,*N*-dimethylaminothianes

				Analysis					
				Found			Calculated		
Compd.	Yield	mp/bp °C	Formula	C	H	N	C	H	N
1a	75	78–79[a]	$C_{19}H_{23}NS$	76.92	7.82	4.69	76.72	7.79	4.71
1b	46	160–161[a]	$C_{19}H_{21}NSCl_2$	62.14	5.80	3.81	62.29	5.78	3.82
1c	84	86–87[a]	$C_{20}H_{25}NS$	77.29	8.12	4.48	77.12	8.09	4.50
1d	76	77–78[a]	$C_{21}H_{27}NS$	77.38	8.39	4.29	77.48	8.36	4.30
2a	77	108–109[a]	$C_{19}H_{23}NS$	76.58	7.78	4.72	76.72	7.79	4.71
2b	49	69–70[a]	$C_{19}H_{21}NSCl_2$	62.22	5.79	3.82	62.29	5.78	3.82
2c	80	92–93[a]	$C_{20}H_{25}NS$	77.00	8.07	4.51	77.12	8.09	4.50
2d	79	101–102[a]	$C_{21}H_{27}NS$	77.62	8.38	4.31	77.48	8.36	4.30
3a	56	120–122/1.6 mm	$C_{15}H_{23}NS$	72.36	9.27	5.64	72.23	9.30	5.62
3b	65	61–62[b]	$C_{15}H_{22}NSCl$	63.38	7.83	4.93	63.47	7.81	4.94
4a	68	93–94[a]	$C_{15}H_{23}NS$	72.05	9.32	5.61	72.23	9.30	5.62
4b	72	63–64[b]	$C_{15}H_{22}NSCl$	63.60	7.82	4.95	63.47	7.81	4.94
5	66	53–54[b]	$C_{11}H_{23}NS$	65.45	11.50	6.98	65.61	11.51	6.96
6	54	76–78/1.9 mm	$C_7H_{15}NS$	58.02	10.39	9.65	57.88	10.41	9.64

[a] Recrystallized from petroleum ether (60–80°C).
[b] Recrystallized from petroleum ether (40–60°C).

TABLE II

^{1}H NMR (100 MHz) data for substituted 4-*N*,*N*-dimethylaminothianes (in $DCCl_3$)

Compd.	H(2)	H(3)	H(4)	H(5)	H(6)	Others
1a	4.56 (dd) $J = 3.0$ Hz $J = 12.0$ Hz [2 H, H(2), H(6)]	1.90–2.62 (m) [5 H, H(3), H(4), H(5)]	Overlapped with H(3)			2.26 [s, 6 H, $N(C\underline{H}_3)_2$] 7.13–7.46 (m, 10 H, Ar—H)
1b	4.55 (dd) $J = 3.0$ Hz $J = 12.0$ Hz [2 H, H(2), H(6)]	1.80–2.40 (m) [4 H, H(3), H(5)]	2.46^a $w_{1/2} = 9.0$ Hz			2.25 [s, 6 H, $N(C\underline{H}_3)_2$] 7.07–7.48 (m, 8 H, Ar—H)
1c	4.38 (d) $J = 11.0$ Hz	1.98–2.54 (m) [3 H, H(3), H(5)]	2.58^a $w_{1/2} = 9.0$ Hz		4.64 (dd) $J = 3.0$ Hz $J = 12.0$ Hz	0.93 (d, 3 H, $C\underline{H}_3$, $J = 7.0$ Hz) 2.38 [s, 6 H, $N(C\underline{H}_3)_2$] 7.12–7.60 (m, 10 H, Ar—$\underline{H}$)
1d	4.46 (d) $J = 11.0$ Hz	1.95–2.76 (m) [3 H, H(3), H(5)]	2.84^a $w_{1/2} = 9.5$ Hz		4.62 (dd) $J = 3.0$ Hz $J = 12.0$ Hz	0.75 (t, 3 H, $CH_2C\underline{H}_3$, $J = 7.0$ Hz) 1.34^a (m, 2 H, $C\underline{H}_2CH_3$) 2.42 [s, 6 H, $N(C\underline{H}_3)_2$] 7.12–7.50 (m, 10 H, Ar—$\underline{H}$)
2a	4.08 (dd) $J = 3.0$ Hz $J = 12.0$ Hz [2 H, H(2), H(6)]	1.70–2.46 (m) [4 H, H(3), H(5)]	2.63 (tt) $J = 3.0$ Hz $J = 11.5$ Hz $w_{1/2} = 26.0$ Hz			2.32 [s, 6 H, $N(C\underline{H}_3)_2$] 7.16–7.46 (m, 10 H, Ar—$\underline{H}$)
2b	4.06 (dd) $J = 3.0$ Hz $J = 12.0$ Hz [2 H, H(2), H(6)]	1.60–2.68 (m) [5 H, H(3), H(4), H(5)]	Overlapped with H(3)			2.32 [s, 6 H, $N(C\underline{H}_3)_2$] 7.10–7.36 (m, 8 H, Ar—$\underline{H}$)
2c	3.74 (d) $J = 10.0$ Hz	1.76–2.50 (m) [4 H, H(3), H(4), H(5)]	Overlapped with H(3)		4.00 (dd) $J = 2.0$ Hz $J = 11.0$ Hz	0.87 (d, 3 H, $C\underline{H}_3$, $J = 6.0$ Hz) 2.26 [s, 6 H, $N(C\underline{H}_3)_2$] 7.02–7.50 (m, 10 H, Ar—$\underline{H}$)
2d	4.02 (d) $j = 10.0$ Hz	1.48–2.40 (m) [5 H, H(3), H(5), $C\underline{H}_2CH_3$]	2.55^a $w_{1/2} = 25.5$ Hz		3.98 (dd) $J = 2.0$ Hz $J = 11.0$ Hz	0.70 (t, 3 H, $CH_2C\underline{H}_3$, $J = 8.0$ Hz) 2.28 [s, 6 H, $N(C\underline{H}_3)_2$] 7.14–7.48 (m, 10 H, Ar—$\underline{H}$)
3a		1.70–2.42 (m) [4 H, H(3), H(5)]	2.64 (m) $w_{1/2} = 16.0$ Hz		4.28 (t) $J = 6.0$ Hz	1.18 (s, 3 H, CH_{3a}), 1.55 (s, 3 H, CH_{3e}) 2.28 (d, 6 H, $N(C\underline{H}_3)_2$, $J = 3.0$ Hz) CH_{3e} 7.03–7.60 (m, 5 H, Ar—$\underline{H}$)

3b		1.62–2.38 (m) [4 H, H(3), H(5)]	2.59 (m) $w_{1/2} = 16.0$ Hz		4.24 (t) $J = 6.0$ Hz	1.16 (s, 3 H, $C\underline{H}_{3a}$) 1.53 (s, 3 H, $C\underline{H}_{3e}$) 2.26 [s, 6 H, $N(C\underline{H}_3)_2$] 7.18–7.46 (m, 4 H, Ar—$\underline{H}$)
3a[b]		1.73 (dd) $J = 3.13$ Hz $J = 13.79$ Hz (1 H, H_a) 2.27[a] [2 H, $H_e(3,5)$]	2.68[c] $J = 3.68$ Hz $w_{1/2} = 15.75$ Hz	1.96 (dd) $J = 7.91$ Hz $J = 13.79$ Hz (1 H, H_a)	4.29[d] $J = 4.04$ Hz	1.17 (s, 3 H, $C\underline{H}_{3a}$) 1.54 (s, 3 H, $C\underline{H}_{3e}$) 2.29 [s, 6 H, $N(C\underline{H}_3)_2$] 7.17–7.50 (m, 5 H, Ar—$\underline{H}$)
3b[b]		1.72 (dd) $J = 3.13$ Hz $J = 13.79$ Hz (1 H, H_a) 2.28[a] [2 H, $H_e(3,5)$]	2.66[c] $J = 3.68$ Hz $w_{1/2} = 15.75$ Hz	1.94 (dd) $J = 7.91$ Hz $J = 13.79$ Hz (1 H, H_a)	4.25[d] $J = 4.04$ Hz	1.15 (s, 3 H, $C\underline{H}_{3a}$) 1.52 (s, 3 H, $C\underline{H}_{3e}$) 2.29 [s, 6 H, $N(C\underline{H}_3)_2$] 7.25–7.45 (m, 4 H, Ar—$\underline{H}$)
4a		1.60–2.26 (m) [4 H, H(3), H(5)]	2.74 (tt) $J = 3.0$ Hz $J = 12.0$ Hz $w_{1/2} = 26.0$ Hz		4.00 (dd) $J = 3.0$ Hz $J = 12.0$ Hz	1.32 (s, 3 H, $C\underline{H}_{3a}$) 1.46 (s, 3 H, $C\underline{H}_{3e}$) 2.28 [s, 6 H, $N(C\underline{H}_3)_2$] 7.14–7.46 (m, 5 H, Ar—$\underline{H}$)
4b		1.53–2.38 (m) [4 H, H(3), H(5)]	2.72 (tt) $J = 3.0$ Hz $J = 12.0$ Hz $w_{1/2} = 27.0$ Hz		3.96 (dd) $J = 3.0$ Hz $J = 12.0$ Hz	1.31 (s, 3 H, $C\underline{H}_{3a}$) 1.44 (s, 3 H, $C\underline{H}_{3e}$) 2.28 [s, 6 H, $N(C\underline{H}_3)_2$] 7.10–7.36 (m, 4 H, Ar—$\underline{H}$)
5		1.12–2.1 (m) [4 H, H(3), H(5)]	2.81 (tt) $J = 12.0$ Hz $J = 3.0$ Hz $w_{1/2} = 25$ Hz			1.24 (s, 6 H, $C\underline{H}_{3a}$) 1.44 (s, 6 H, $C\underline{H}_{3e}$) 2.27 [s, 6 H, $N(C\underline{H}_3)_2$]
6	2.58–2.72 (m) [4 H, H(2,6)]	1.40–1.85 (m) [4 H, H(3,5)]	1.98–2.18 (m) [1 H, H(4)]	1.40–1.85 (m) [4 H, H(3,5)]	2.58–2.72 (m) [4 H, H(2,6)]	2.25 (s, 6 H, $(H_3C)_2N$)

Abbreviations used: s, singlet; d, doublet; dd, doublet of doublet; t, triplet; tt, triplet of triplet; m, multiplet.

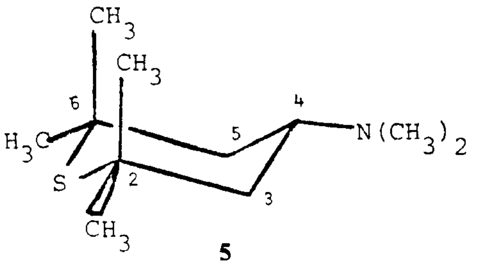
[a] Center of multiplet.

[b] Recorded at 270 MHz.

[c] Septet.

[d] Equally spaced doublet of doublet.

	R
a	C_6H_5
b	p-ClC_6H_4



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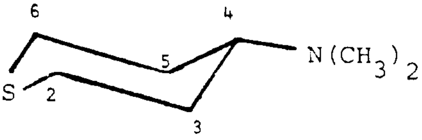

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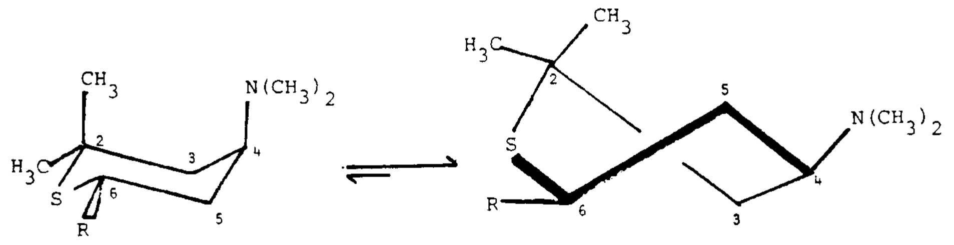
The ^1H NMR data of these amines are summarized in Table II. In general, the signal for the equatorial proton H(4) in the axial tertiary amine occurs at a lower field than the axial proton H(4) in the epimer. It was observed that an axial dimethylamino group was found to *deshield* the H(2) and H(6) axial protons by 0.4–0.6 ppm. For example, the H(2,6) protons of the axial amine **1a** appeared downfield (δ 4.56) relative to the counterparts in the equatorial tertiary amine **2a** (δ 4.08). The half-band width of H(4) signal was valuable in the assignment of the stereochemistry at C(4). To illustrate, with **1d** the H(4) resonance had a half-band width ($w_{1/2}$) of 9.5 Hz while the corresponding width in the epimer **2d** was found to be 25.5 Hz. Similar differences have been observed in the case of 4-thianols and 4-aminothianes.[2a,e]

Examination of the data in Table II indicate that the introduction of a 3-alkyl substituent leads to a small decrease in $J_{2a,3a}$ in **1c**, **1d**, **2c** and **2d**. This may be attributed to substituent electronegativity effect.[4–7] The influence of a methyl group on the vicinal proton coupling constants in carbon systems have been studied by Booth and co-workers.[7]

In the ^1H NMR (100 MHz) spectrum of **4a**, the H(4) resonance was a triplet of triplets ($w_{1/2}$ = 26.0 Hz) at δ 2.74. As expected from conformation **4b**, the H(4) resonance appeared at δ 2.72 as a triplet of triplets ($w_{1/2}$ = 27.0 Hz). The H(6) signals in **4a** and **4b** occurred at δ 4.00 and 3.96, respectively, as a doublet of doublets ($J_{6a,5a}$ = 12.0 Hz and $J_{6a,5e}$ = 3.0 Hz) and indicated that these compounds exist in chair conformations. Interestingly, the H(6) signals in the amines **3a** and **3b** appeared at δ 4.28 and 4.24, respectively, as 1 : 2 : 1 triplets (J = 6.0 Hz). The approximate equal coupling with axial and equatorial H(5) protons and the significant decrease in coupling constant ($J_{6a,5a}$ = 6.0 Hz) are the consequences of bond angle changes resulting from the steric interactions of the axial dimethylamino group with the axial methyl and axial hydrogen H(6). Moreover, the width at the half-height ($w_{1/2}$) of the H(4) signals in **3a** and **3b** was found to be 16.0 Hz. This value of $w_{1/2}$ is unusually large for an axial tertiary amine in comparison with the values found for other axial tertiary amines **1b**–**1d** ($w_{1/2}$ = 9.0–9.5 Hz). These data suggest that compounds **3a** and **3b** exist mostly in twist conformations such as **3a′** and **3b′**, rather than in chair conformations. Also in the twist conformations **3′**, the 1,3-diaxial interaction between the bulky *N,N*-dimethylamino group and the methyl group and the other 1,3-interactions would be largely relieved. The ^{13}C NMR analysis of these compounds (given later in the discussion) also support this.



3 a. R = C_6H_5

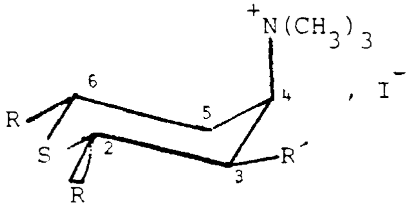
b. R = p-ClC_6H_4

3′ a. R = C_6H_5

b. R = p-ClC_6H_4

The effect of an axial methyl group was investigated in terms of causing ring deformation of the thiane system, as reflected in the values of vicinal proton coupling constants derived from ^1H NMR spectra taken at 270 MHz. In the ^1H NMR spectra of **3a**, the signal for H(4) appeared at δ 2.68 as a septet (J = 3.68; $w_{1/2}$ = 15.75 Hz) and that for H(6) at δ 4.29 as an equally spaced doublet of doublets. From the ^1H NMR spectrum of **3b** recorded at 270 MHz, the signal for H(4) and H(6) were located at δ 2.66 and δ 4.25, respectively. The signal for H(4) appeared as a well resolved septet (J = 3.68 Hz) and that for H(6) appeared as a doublet of doublets ($J_{6a,5a} = J_{6a,5e}$ = 4.0 Hz). For comparison, the coupling constants $J_{6a,5a}$ and $J_{6a,5e}$ obtained from the conformationally biased **4a** are 12.0 Hz and 3.0 Hz, respectively, (Table II).

The stereoisomeric tertiary amines were further characterized by the preparation of their methiodides. Relevant properties for these compounds are given in Table III.



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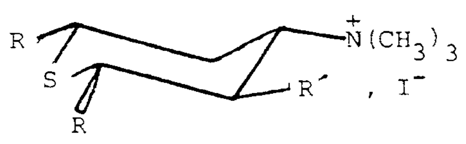

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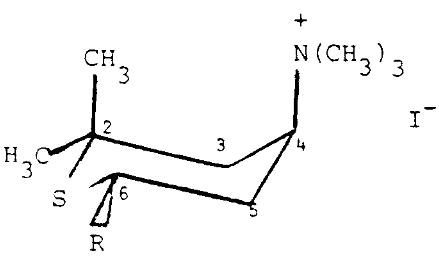
	R	R′
a	C_6H_5	H
b	p-ClC_6H_4	H
c	C_6H_5	CH_3
d	C_6H_5	C_2H_5

TABLE III

Physical constants of methiodides of substituted 4-*N*,*N*-dimethylaminothianes

				Analysis					
				Found			Calculated		
Compd.	Yield	mp°C	Formula	C	H	N	C	H	N
7a	63	225–226[a]	$C_{20}H_{26}NSI$	54.82	5.94	3.20	54.67	5.96	3.19
7b	62	275–277[b]	$C_{20}H_{24}NSCl_2I$	47.16	4.78	2.75	47.26	4.76	2.76
7c	66	205–207[c]	$C_{21}H_{28}NSI$	55.80	6.20	3.10	55.63	6.22	3.09
7d	64	213–215[a]	$C_{22}H_{30}NSI$	56.63	6.45	3.01	56.53	6.47	3.00
8a	74	246–247[b]	$C_{20}H_{26}NSI$	54.54	5.97	3.18	54.67	5.96	3.19
8b	72	187–189[b]	$C_{20}H_{24}NSCl_2I$	47.34	4.77	2.77	47.26	4.76	2.76
8c	64	197–199[a]	$C_{21}H_{28}NSI$	55.48	6.23	3.10	55.63	6.22	3.09
8d	60	127–128[a]	$C_{22}H_{30}NSI$	56.44	6.48	3.00	56.53	6.47	3.00
9a	70	251–252[b]	$C_{16}H_{26}NSI$	49.02	6.72	3.59	49.10	6.70	3.58
9b	68	245–247[b]	$C_{16}H_{25}NSClI$	45.01	5.94	3.30	45.13	5.92	3.29
10a	76	278–280[c]	$C_{16}H_{26}NSI$	49.24	6.68	3.57	49.10	6.70	3.58
10b	75	307–309[b]	$C_{16}H_{25}NSClI$	45.26	5.90	3.30	45.13	5.92	3.29
11	78	292–294[b]	$C_{12}H_{26}NSI$	41.89	7.65	4.07	41.98	7.63	4.08

[a] Recrystallized from methanol/ether.
[b] Recrystallized from ethanol.
[c] Recrystallized from ethanol/ether.



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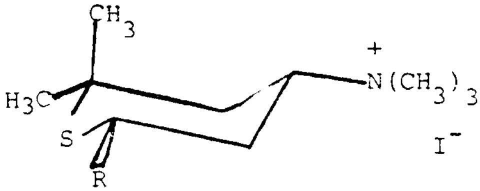

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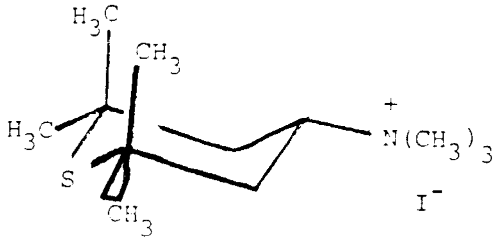
	R
a	C_6H_5
b	p-ClC_6H_4



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The ^1H spectra of the quaternary ammonium iodides **7a**, **7d**, **8a**, **8d**, **9a**, **9b**, **10a** and **10b** were recorded at 270 MHz in DMSO-d_6. Chemical shifts and coupling constants for the methiodides are summarized in Table IV.

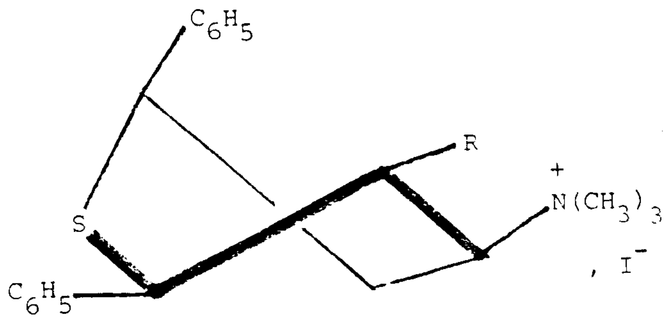
Quaternization causes characteristic downfield shifts of the signal for H(4) so that the range is δ 3.67–4.40. The resonance for ^1H in $(\underline{H}_3C)_3N^+$ appears as sharp singlet in each case. Two aspects of the spectra that are of vital importance are the coupling constants of H(2,6) and the half-band width of the H(4) signal. The wide range of values for $J_{2a,3a}$, $J_{6a,5a}$ and $J_{6a,5e}$ are especially noteworthy. The spectrum of **8a** in DMSO-d_6 indicates that the compound is conformationally homogeneous and the value of 10.29 Hz for $J_{2a,3a}$ shows that both the phenyl groups are in equatorial orientations. The H(4) signal of **8a** at δ 3.74 was a triplet (J = 11.25 Hz) which is characteristic of an axial H(4) proton. In **7a**, the H(2,6) diaxial protons appear as a triplet at δ 4.73 (J = 6.80 Hz). The H(4) proton signal in **7a** appears as a broad unresolved hump ($w_{1/2}$ = 20.0 Hz). The bulky $(\underline{H}_3C)_3N^+$ group is sterically equivalent (isosteric) to a tertiary butyl group and is likely to cause distortion of the thiane ring. The $J_{2a,3a}$ value for H(2,6) decreases from 10.29 Hz in **8a** to 6.80 Hz in **7a** and this appears only compatible with a twist conformation. The large half intensity width ($w_{1/2}$ = 20.0 Hz) further supports the argument that the ammonium iodide **7a** probably exists predominately as twist conformer **7a′**.

TABLE IV

^{1}H NMR (270 MHz) data for methiodides of 4-*N*,*N*-dimethylaminothianes (in DMSO-d_6)

Compd.	H(2)	H(3)	H(4)	H(5)	H(6)	Others
7a	4.73 (t) J = 6.8 Hz [2 H, H(2), H(6)]	2.38–3.48 (m) [4 H, H(3), H(5)]	4.12^a $w_{1/2}$ = 20.0 Hz			3.07 [s, 9 H, $\overset{+}{N}(C\underline{H}_3)_3$] 7.28–7.55 (m, 10 H, Ar—$\underline{H}$)
7d	4.56 (s)	2.40–3.58 (m) [3 H, H(3), H(5)]	4.40^a $w_{1/2}$ = 22.5 Hz		4.74 (t) J = 8.3 Hz	1.06 (t, 3 H, $CH_2C\underline{H}_3$, J = 7.0 Hz) 1.85^a (m, 2 H, $C\underline{H}_2CH_3$) 3.15 [s, 9 H, $\overset{+}{N}(C\underline{H}_3)_3$] 7.26–7.68 (m, 10 H, Ar—H)
8a	4.28 (d) J = 10.29 Hz [2 H, H(2), H(6)]	2.20 (qt) J = 11.77 Hz [2 H, H_a(3,5)] 2.71 (d) J = 12.50 Hz [2 H, H_e(3,5)]	3.74 (t) J = 11.25 Hz $w_{1/2}$ = 27.0 Hz			3.12 [s, 9 H, $\overset{+}{N}(C\underline{H}_3)_3$] 7.26–7.52 (m, 10 H, Ar—$\underline{H}$)
8d	4.12 (d) J = 10.03 Hz	2.20–3.50 (m) [3 H, H(3), H(5)]	3.67^a $w_{1/2}$ = 26.0 Hz		4.46 (d) J = 3.30 Hz	1.16 (t, 3 H, $CH_2C\underline{H}_3$), 2.04^a (m, 2 H, $C\underline{H}_2CH_3$) 2.83 [s, 9 H, $\overset{+}{N}(C\underline{H}_3)_3$] 7.20–7.62 (m, 10 H, Ar—$\underline{H}$)
9a		1.96 (t) J = 12.87 Hz (1 H, H_a) 2.46^a [2 H, H_e(3,5)]	3.80^b J = 6.75 Hz $w_{1/2}$ = 25.0 Hz	2.20 (d) J = 13.24 Hz (1 H, H_a)	4.49 (dd) J = 9.93 Hz J = 5.88 Hz	1.29 (s, 3 H, $C\underline{H}_{3a}$) 1.48 (s, 3 H, $C\underline{H}_{3e}$) 3.08 [s, 9 H, $\overset{+}{N}(C\underline{H}_3)_3$] 7.24–7.46 (m, 5 H, Ar—$\underline{H}$)
9b		1.95 (t) J = 12.38 Hz (1 H, H_a) 2.48^a [2 H, H_e(3,5)]	3.80^b J = 6.75 Hz $w_{1/2}$ = 25.0 Hz	2.22 (d) J = 12.87 Hz (1 H, H_a)	4.54 (dd) J = 9.10 Hz J = 5.90 Hz	1.27 (s, 3 H, $C\underline{H}_{3a}$) 1.47 (s, 3 H, $C\underline{H}_{3e}$) 3.09 [s, 9 H, $\overset{+}{N}(C\underline{H}_3)_3$] 7.38–7.56 (s, 4 H, Ar—H)
10a		1.77 (t) J = 12.50 Hz (1 H, H_a) 2.38 (d) J = 12.13 Hz (1 H, H_e)	3.82 (t) J = 11.70 Hz $w_{1/2}$ = 26.0 Hz	2.00 (qt) J = 11.77 Hz (1 H, H_a) 2.61 (d) J = 11.40 Hz (1 H, H_e)	4.23 (dd) J = 9.6 Hz J = 1.8 Hz	1.36 (s, 3 H, $C\underline{H}_{3a}$) 1.49 (s, 3 H, $C\underline{H}_{3e}$) 3.08 [s, 9 H, $\overset{+}{N}(C\underline{H}_3)_3$] 7.27–7.48 (m, 5 H, Ar—H)
10b		1.77 (t) J = 12.50 Hz (1 H, H_a) 2.38 (d) J = 12.13 Hz (1 H, H_e)	3.80 (t) J = 11.40 Hz $w_{1/2}$ = 26.0 Hz	2.00 (qt) J = 11.77 Hz (1 H, H_a) 2.60 (d) J = 11.03 Hz (1 H, H_e)	4.26 (d) J = 10.30 Hz	1.36 (s, 3 H, $C\underline{H}_{3a}$) 1.49 (s, 3 H, $C\underline{H}_{3e}$) 3.08 [s, 9 H, $\overset{+}{N}(C\underline{H}_3)_3$] 7.40–7.52 (s, 4 H, Ar—H)

Abbreviations used: s, singlet; d, doublet; dd, doublet of doublet; t, triplet; qt, quartet; m, multiplet; a, center of multiplet; b, poorly resolved quintet.



7a′ R = H

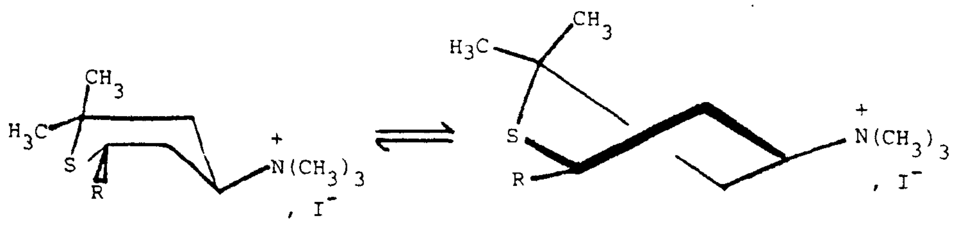
7d′ R = C_2H_5

Methiodide of **2d** is expected to exist in a chair conformation **8d**. In the spectrum of **8d**, the H(2) and H(6) protons appear as doublets at δ 4.12 (J = 10.03 Hz) and δ 4.46 (J = 3.30 Hz) due to coupling with H(3) and H(5), respectively. The signal for H(4) appeared at δ 3.67 as a multiplet ($w_{1/2}$ = 26.0 Hz). In the spectrum of **7d**, the H(6) resonance appeared at δ 4.74 as a triplet (J = 8.30 Hz) while the H(2) signal appeared at δ 4.56 as a sharp singlet rather than an expected doublet. The H(2) signal in the corresponding tertiary amine **1d** appears as a doublet at δ 4.46 (J = 11.0 Hz). The half-band width ($w_{1/2}$ = 22.5 Hz) found for the equatorial H(4) resonance in **7d** is very close to the half-band width ($w_{1/2}$ = 26.0 Hz) found for the axial H(4) resonance in **8d**. The small coupling observed at δ 4.46 hints at ring distortion in **8d**.

In the chair conformation **7d**, the axial $(\underline{H}_3C)_3N^+$ group is not only exposed to the normal 1,3-hydrogen interactions but also to an additional gauche interaction due to the presence of an ethyl group. The accidental magnetic equivalence of protons H(5) [as illustrated by 1 : 2 : 1 triplets exhibited by the H(6) proton] suggests that methiodide **7d** spends most of its time in a rapidly interconverting twist conformation **7d′** to avoid intolerable steric interactions.

In the case of **10a**, the H(6) resonance is a doublet of doublets ($J_{6a,5a}$ = 9.6 Hz and $J_{6a,5a}$ = 1.8 Hz) at δ 4.23. The spectrum of **10b** shows the resonance of axial proton H(6) at δ 4.26 as a doublet (J = 10.3 Hz). In **10a** and **10b**, the values of axial–axial coupling constants are slightly affected by the presence of the axial methyl group and the values correspond to a slightly deformed chair conformation.

The spectrum of methiodide **9a** at 270 MHz shows the following: (i) H(4) at δ 3.80 as poorly resolved quintet ($w_{1/2}$ = 25.0 Hz); and (ii) H(6) at δ 4.49 as a doublet of doublets. Surprisingly, the half-band width for H(4) in **9a** and **10a** are quite similar. Methiodide **9a** in the regular chair conformation has one 1,3-interaction between $H_3C—\overset{+}{N}(CH_3)_3$, one $H_3C—H$ interaction and one $H—\overset{+}{N}(CH_3)_3$ interaction. Consequently, **9a** should be severely distorted and the methiodide could exist as an equilibrium mixture of boat and twist conformations (**9a′** ⇌ **9a″**). This is substantiated for **9a″** which is a twist boat in the solid state as shown by X-ray analysis later described in the paper.

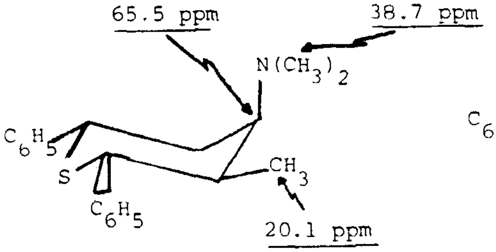


9a′ R = C_6H_5 **9a″** R = C_6H_5

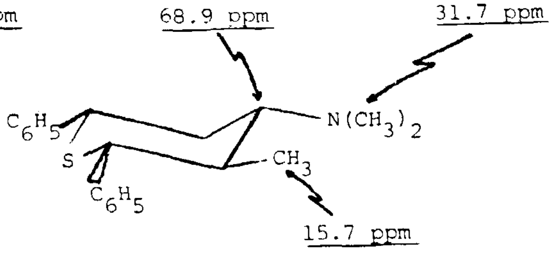
9b′ R = p-$C\ell C_6H_4$ **9b″** R = p-$C\ell C_6H_4$

Quaternary ammonium salt **9b** is another compound which is expected to avoid adopting a chair conformation. Interestingly, the H(4) signal at δ 3.80 in the NMR spectrum was a poorly resolved quintet and its broadness ($w_{1/2}$ = 25.0 Hz) greatly reduces the possibility of a major contribution from a regular chair conformation in which $\overset{+}{N}(CH_3)_3$ is axial. We therefore conclude that methiodide **9b** also exists as a mixture of rapidly interconverting boat and twist conformations (**9b′** ⇌ **9b″**).

The ^{13}C NMR chemical shifts of epimeric tertiary amines **1a–d**, **2a–d**, **3a**, **3b**, **4a** and **4b** and related compounds are recorded in Table V. Shielding of C(4) appears to depend upon the orientation of the dimethylamino group as expected; an axial dimethylamino group tends to shield C(4) by about 3 ppm. The equatorial methyl carbon had a resonance in **2c** which was shifted upfield by 4.38 ppm compared to the corresponding signal for the equatorial methyl carbon in **1c**. In the epimers **1c** and **2c**, the dimethylamino group and the methyl group are gauche and the upfield shift of 4.38 ppm in **2c** found for the equatorial methyl carbon, relative to its shielding in the tertiary amine **1c**, may be attributed to the γ-antiperiplanar effect of the nitrogen.[8]



1c



2c

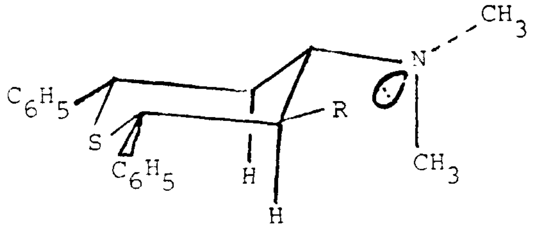
TABLE V

^{13}C Chemical shifts (δ) for substituted 4-*N*,*N*-dimethylaminothianes[a]

Compd.	C(2)	C(3)	C(4)	C(5)	C(6)	Others
1a	43.45	41.41	61.13			$N(\underline{C}H_3)_2$, 37.23; Ar, 141.78, 128.28, 127.58, 127.31, 127.05
1b	43.36	40.77	60.76			$N(\underline{C}H_3)_2$, 37.12; Ar, 140.12, 132.74, 128.66, 128.45
1c	48.38	43.40	65.57	42.67	45.41	$\underline{C}H_3$, 20.11; $N(\underline{C}H_3)_2$, 38.78; Ar, 141.65, 140.42, 128.25, 128.17, 127.35, 127.03
1d	50.39	48.47	60.34	42.86	44.91	$CH_2\underline{C}H_3$, 13.28; $\underline{C}H_2CH_3$, 24.71, $N(\underline{C}H_3)_2$, 37.73; Ar, 141.82, 140.85, 128.28, 128.19, 127.38, 127.08
2a	48.42	40.77	64.09			$N(\underline{C}H_3)_2$, 36.76; Ar, 141.26, 128.37, 127.20
2b	47.68	40.65	63.76			$N(\underline{C}H_3)_2$, 36.51; Ar, 139.51, 132.92, 128.51
2c	55.13	41.56	68.93	40.01	48.07	$\underline{C}H_3$, 15.73; $N(\underline{C}H_3)_2$, 31.75, Ar, 141.53, 140.54, 128.29, 127.93, 127.15
2d	51.38	45.67	64.32	40.12	48.09	$CH_2\underline{C}H_3$, 8.20; $\underline{C}H_2CH_3$, 20.17; $N(\underline{C}H_3)_2$, 31.86, Ar, 141.47, 140.24, 128.31, 127.95, 127.17, 127.09
3a	42.52	42.78	58.83	41.67	40.30	$\underline{C}H_{3a}$, 31.61; $\underline{C}H_{3e}$, 31.69; $N(\underline{C}H_3)_2$, 34.99; Ar, 142.14, 128.25, 128.05; 127.29, 126.48
3b	42.48	43.01	58.62	41.64	39.80	$\underline{C}H_{3a}$, 31.63; $\underline{C}H_{3e}$, 31.69; $N(\underline{C}H_3)_2$, 35.02; Ar, 140.83, 132.19, 128.75, 128.19
4a	43.02	44.53	59.62	43.57	40.54	$\underline{C}H_{3a}$, 28.22; $\underline{C}H_{3e}$, 31.87; $N(\underline{C}H_3)_2$, 36.23; Ar, 141.42, 128.28, 127.29, 127.06
4b	43.13	43.83	59.44	43.33	40.53	$\underline{C}H_{3a}$, 28.16; $\underline{C}H_{3e}$, 31.81, $N(\underline{C}H_3)_2$, 36.33; Ar, 140.01, 132.57, 128.66, 128.34
5	40.33	43.04	56.17			$\underline{C}H_{3a}$, 30.96; $\underline{C}H_{3e}$, 33.62; $N(\underline{C}H_3)_2$, 42.
6	30.03	40.76	62.51			$N(\underline{C}H_3)_2$, 28.45

[a] All data are given in ppm downfield from Me_4Si; solutions used were 0.3 M in $DCCl_3$.
r-2,*cis*-6-Diphenylthiane (**12**^{2e}); 49.07 [C(2,6)], 34.17 [C(3,5)], 27.51 [C(4)], 141.87, 128.21, 127.17, 126.99 (C—Ar).

In general, the *N*-methyl carbons of the equatorial dimethylamino groups are shielded compared to the corresponding signal found for the axial dimethylamino carbons. The striking feature of the ^{13}C NMR chemical shift data, however, is the marked *increase* in the upfield shift of the dimethylamino carbons in **2c** and **2d**. Examination of the Dreiding stereo model indicates that in the tertiary amines **2c** and **2d** the dimethylamino group may preferentially exist in a rotamer **2c′** and **2d′** (related by C–N rotation) in which the nitrogen lone pair points towards the equatorial alkyl group.

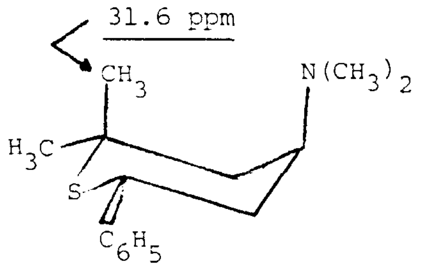


2′ c. R = CH_3

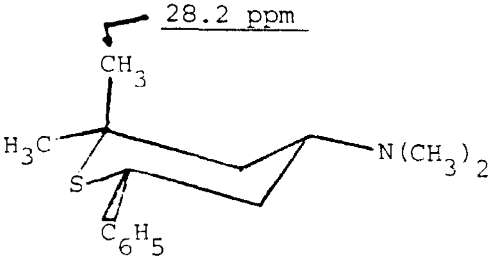
d. R = C_2H_5

In such rotameric conformations as **2c′** and **2d′**, one of the dimethylamino methyl groups and the axial H(3a) and H(5a) are in close proximity and the resulting non-bonded interactions tend to increase the shielding. For the same reason C(3,5) in **2c** are also slightly shielded compared to the corresponding carbons in **1c**.

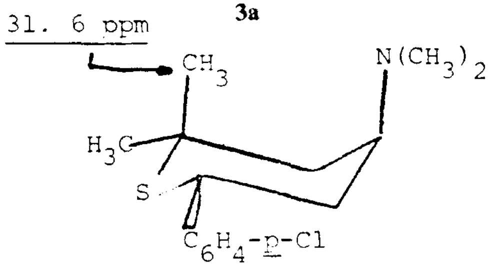
A ^{13}C NMR spatial interaction effect of a dimethylamino group on delta methyl carbon resonance has also been noted. For example, signals for the methyl groups in



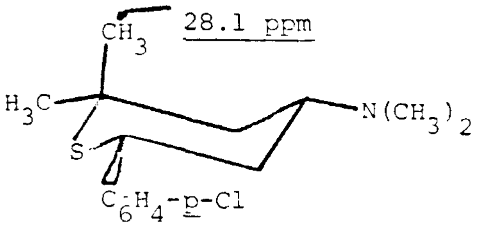
3a



4a



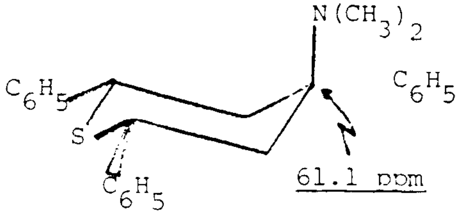
3b



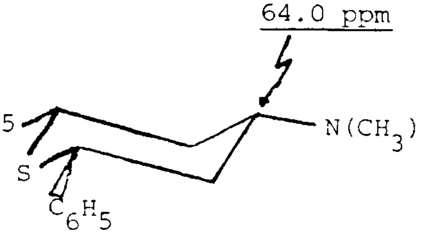
4b

3a and **3b**, which are syn to the dimethylamino group, are deshielded (by about 3.4 ppm) and occur downfield from their position in **4a** and **4b**, respectively. Assignments for the resonances for the axial methyl group(s) at C(2) in **3a**, **3b**, **4a**, and **4b** was done on the basis of the more shielded methyl carbon should be axial. Also, we note the significant difference in shieldings for the axial methyl groups in **4a** and **4b** compared to those in **3a** and **3b**. In contrast, the signals for the equatorial carbons in all four molecules is essentially unchanged. We suspect some ring distortion in structures **3a** and **3b** which may account for the increased deshielding of the methyl carbons attached to C(2) in **3a** and **3b** as compared to the counterparts in **4a** and **4b**.

The chemical shifts of C(4) in **3a**, **3b**, **4a** and **4b** are almost similar. The chemical shift (58.83 ppm) of C(4) in the axial isomer **3a** is not very much less than the chemical shift (59.62 ppm) for C(4) in the equatorial epimer **4a**. Similarly, the chemical shift (58.62 ppm) for C(4) in the axial isomer **3b** also does not differ much from the chemical shift (59.44 ppm) for C(4) in the equatorial tertiary amine **4b**. We therefore conclude that tertiary amines **3a** and **3b** exist in an equilibrium mixture of chair and twist conformations (**3a** $\rightleftharpoons$ **3a′**) and (**3b** $\rightleftharpoons$ **3b′**) in which the dimethylamino group will be bonded to C(4) in a pseudo equatorial fashion. ^{1}H NMR spectral studies also led to similar conclusions. In order to assess the substituent effect of the $N(CH_3)_2$ group on the ring carbon shieldings in epimeric 4-*N*,*N*-dimethylaminothianes **1a** and **2a**, the observed values for the specific carbons may be compared with those for the corresponding carbons in *r*-2,*cis*-6-diphenylthiane (**12**).[2e] For example, C(4) in **12** absorbs at 27.51 ppm, while C(4) in **2a** appears at 64.09 ppm. The difference $\delta_{C(4)}^{(RNMe_2)} - \delta_{C(4)}^{(RH)}$ of +36.58 ppm can be taken as the $N(CH_3)_2$ substituent effect at C(4) in the tertiary amine **2a**. Likewise, the $N(CH_3)_2$ substituent effects at C(3) and C(2) have been calculated as +6.6 ppm and −0.65 ppm, respectively. The corresponding values of axial $N(CH_3)_2$ group are +33.62 ppm, +7.24 ppm and −5.62 ppm.



1a



2a

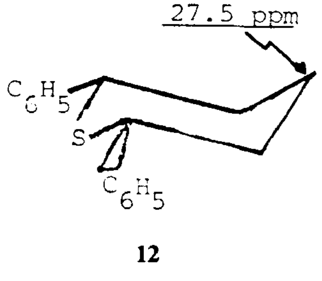


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TABLE VI

Pseudo first order rate constants for the reaction of substituted 4-*N*,*N*-dimethylaminothianes with methyl iodide in acetonitrile at 10 ± 0.05°C[a]

Compd.	$k_1 \times 10^4$ sec^{-1}	k_e/k_a
1a	0.074 ± 0.001	480.2
1b	0.054 ± 0.001	515.9
1c	0.18 ± 0.001	0.24
1d	0.091 ± 0.001	
2a	35.52 ± 0.23	
2b	28.06 ± 0.17	
2c	0.043 ± 0.001	
2d	Too slow to follow	
3a	16.29 ±0.1	2.4
3b	14.85 ±0.1	2.4
4a	39.56 ±0.21	
4b	35.78 ±0.18	
5	46.16 ±0.12	

[a] The rate of quaternization of **6** was too fast to measure at 10°C.

The rates of quaternization of six epimeric pairs of substituted 4-*N*,*N*-dimethylaminothianes and related compounds with methyl iodide in acetonitrile were determined conductometrically[9] at 10 ± 0.05°C. The kinetic data obtained with *N*,*N*-dimethylaminothianes are shown in Table VI. The reaction of *N*,*N*-dimethylaminothianes with methyl iodide is of course, a nucleophilic, bimolecular substitution reaction. Steric crowding of groups around nitrogen should increase the energy of the activated state and lower the rate constant. In *N*,*N*-dimethylaminothiane **6**, the $N(CH_3)_2$ group can occupy either the axial or equatorial position. The 1,3-diaxial interaction of the axial dimethylamino group at C(4) with axial H(2,6) can be expected to lower the rate constants for the axial tertiary amine compared with the equatorial isomer. Comparing the specific rate constants of **1a** and **2a**, one might expect **2a** with an equatorial dimethylamino group to react more rapidly than **1a** with an axial dimethylamino group. Our results show that this is indeed so. For the epimeric 2,6-diaryl-*N*,*N*-dimethylaminothianes, the all equatorial systems **2a** and **2b** react much more quickly than the epimers **1a** and **1b**. The order of reactivity is reversed for **1c**, **1d**, **2c**, and **2d**, the axial isomers **1c** and **1d** reacting much more rapidly than the equatorial isomers **2c** and **2d**.

cis-2,6-Diphenyl-*r*-4-*N*,*N*-dimethylaminothiane (**2a**) is about 480 times as reactive as *trans*-2,6-diphenyl-*r*-4-*N*,*N*-dimethylaminothiane (**1a**). The large difference in rate as well as the large size of the phenyl groups strongly suggest that these two compounds are conformationally homogeneous. Tertiary amine **2b** is slightly less reactive that the "parent" compound **2a**, indicating the operation of an inductive effect by the chlorine atom. Likewise **1b** is less reactive than **1a**.

The behaviour of **3a**, **3b**, **4a** and **4b** is of particular interest. The specific rate constant for methylation of **4a** ($k_1 = 39.56 \times 10^{-4}$) is higher than the [$k_1 = (35.52 \times 10^{-4})$] of **2a**. It is reasonable to expect that an axial substituent at C(2) will not have a polar effect or steric effect on the equatorial dimethylamino group provided the thiane ring is not distorted. The expectation has *not* been borne out by the present studies and leads to the conclusion that even a single axial methyl group distorts the chair conformation. The trend that the presence of an axial methyl group at C(2) increases the rate of quaternization of an equatorial dimethylamino function can also be seen in **4b**. The effect could be steric in origin and the presence of an axial methyl group may cause a slight distortion of the chair in order to relieve the syn-axial 1,3-interactions. The very high rate of quaternization for **5** supports this hypothesis.

The rate constants for **3a** and **3b** are much higher than those for **1a** and **1b**. This is probably because of the severe 1,3-diaxial interactions present in the compounds **3a** and **3b** which make the thiane ring highly strained. Hence these amines probably occur in twist conformations **3a′** and **3b′** in which the dimethylamino group is again bonded via a pseudo equatorial bond. As already discussed, the ^1H and ^{13}C NMR analysis of **3a** and **3b** also support a twist conformations **3a′** and **3b′** as being present in high populations.

The behaviour of **1c**, **1d**, **2c** and **2d** is also worthy of consideration. The rate data in Table VI indicate that the tertiary amine **1c** [with an equatorial methyl group alpha to the axial dimethylamino group] reacts at a faster rate than the "parent" tertiary amine **1a**. However, introduction of an equatorial methyl group at C(3) greatly lowers the rate of quaternization of tertiary amine **2c**. The 3-ethyl derivatives **1d** and **2d** react significantly slower than 3-methyl substituted tertiary amines **1c** and **2c**. In fact, the trend in the pK_a values of the tertiary amines[10] is the same as that of methylation rates, with the latter values showing much larger difference between epimers. The rate of quaternization depends upon the availability of the nitrogen lone pair to participate in a nucleophilic substitution reaction. As discussed earlier, amines **2c** and **2d** may prefer the rotational conformers such as **2c′** and **2d′**, in which the lone pair is pointing towards the alkyl group. In such rotational conformations, the line pair of electrons is sterically shielded by the alkyl group and hence tertiary amines **2c** and **2d** react at a slower rate in acetonitrile than the axial isomers **1c** and **1d**. Such a reversal in order of reactivity for 2-alkylcyclohexyldimethylamines has been reported.[11,12]

SINGLE CRYSTAL ANALYSIS

As shown in the ORTEP[13] drawing, Figure 1, the thiane **9a** exists in a twist-boat conformation in the solid state. The conformation of the molecule with C(3) and C(6) in the prow and stern positions of the boat allows most of the substituent groups of the ring to be in pseudo-equatorial positions. Only carbon C(8) occupies a pseudo-axial position.

The bond distances and bond angles for the molecule are shown in Figures 2 and 3. Sutton gives a value of 1.817(5) Å for the mean distance for paraffinic carbon-sulfur bonds.[14] One of the C—S bonds in this compound is slightly shorter than this while the other is longer by over 0.03 Å. In comparison with other sulfur-containing, six-membered ring systems examined previously, the shorter bond of 1.809 Å lies at the short end of the range (1.802–1.840 Å)[2a,2c,15,16] while the longer bond is 0.01 Å greater than previously studied C—S bonds. This difference in C—S distances is probably due to the strain in the system, which is also clearly visible in the

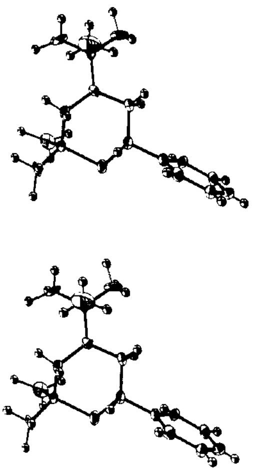


FIGURE 1 ORTEP drawing of trimethyl[2,2-dimethyl-*trans*-6-phenylthian-*r*-4-yl]ammonium iodide (**9a**).

endocyclic bond angles, which at C(3) C(4) C(5) C(6) are significantly larger than the tetrahedral value. The C(12)—N(9) and C(4)—N(9) distances are normal for a C—N$^+$ bond, while the C(10)—N(9) and C(11)—N(9) bond lengths are shortened due to the thermal motion of C(10) and C(11). The average carbon–carbon bond distance within the sulfur-containing ring is 1.534(12) Å which compares well with the normal C-C bond distance of 1.537 Å.

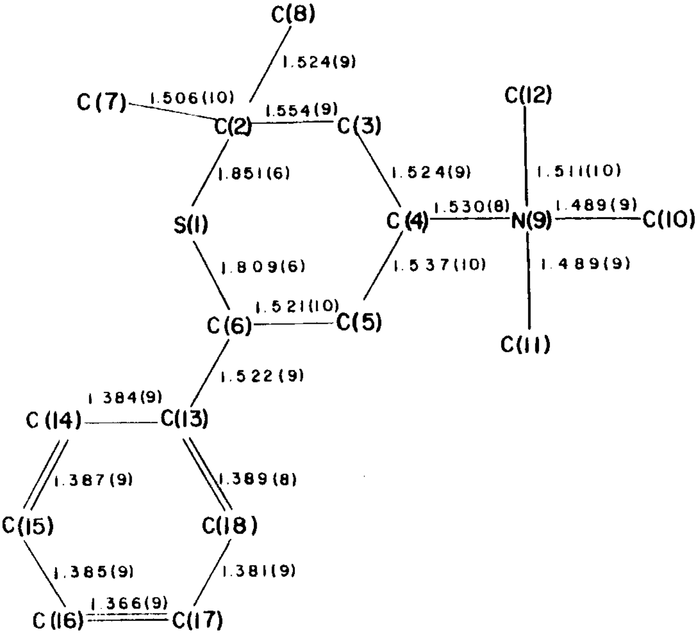
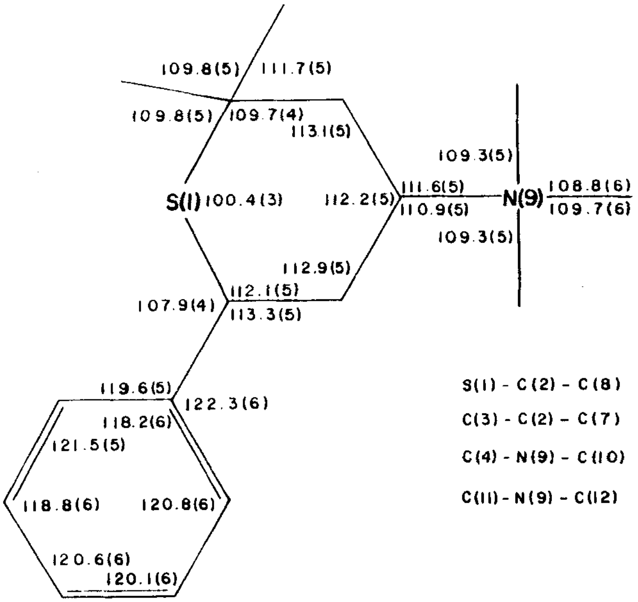


FIGURE 2 Schematic diagram of the molecule showing the numbering scheme used for the atoms and bond distances in angstroms. Estimated standard deviations are shown in parentheses.



S(1) - C(2) - C(8)	107.3(4)
C(3) - C(2) - C(7)	108.4(5)
C(4) - N(9) - C(10)	113.3(5)
C(11) - N(9) - C(12)	106.3(5)

FIGURE 3 Bond angles in degrees. Estimated standard deviations are shown in parentheses.

TABLE VII

Dihedral angles in **9a**

S(1) C(2) C(3) C(4)	46.0°
C(2) C(3) C(4) C(5)	−72.8
C(3) C(4) C(5) C(6)	20.9
C(4) C(5) C(6) S(1)	45.2
C(5) C(6) S(1) C(2)	−61.5
C(6) S(1) C(2) C(3)	14.8
S(1) C(6) C(13) C(14)	−117.1
C(5) C(6) C(24) C(18)	−63.4
C(2) S(1) C(6) C(13)	173.1
C(4) C(5) C(6) C(13)	167.7
C(2) C(3) C(4) N(9)	162.0
C(6) C(5) C(4) N(9)	146.5

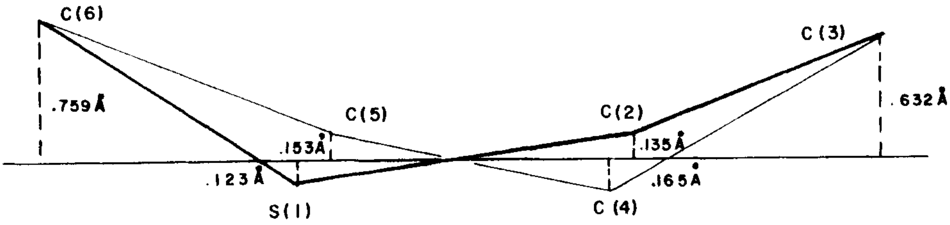


FIGURE 4 Perpendicular distances in angstroms between the atoms and the indicated plane.

The twist in the boat conformation can be seen in Figure 1, Table VII, which gives the dihedral angles and Figure 4 which gives distances of atoms from the best least squares plane formed by S(1), C(2), C(4), and C(5). In an ideal boat, two torsion angles would be 0° while in this molecule these angles are 14 and 20°. The remaining torsion angles should be equal in absolute value. As can be seen in Table VII, these angles show large differences. The distances shown in Figure 4 also clearly indicate the non-ideality of the conformation of this ring system. The four atoms used to calculate the plane average 0.144 Å from the plane. The prow and stern carbon atoms average 0.696 Å from the plane. The water molecule, which shows high thermal motion, has only one weak interaction with I^- at 3.426 Å, while the closest $I^- \cdots$ N(9) distance is 4.527 Å.

EXPERIMENTAL

General data. Melting points were taken on a BOETIUS microheating table and are uncorrected. Proton magnetic resonance spectra for tertiary amines were obtained on a Varian XL-100(15) high resolution NMR spectrometer (with a time averaging computer accessory, C-1024) operating at 100.0 MHz and are expressed in δ values relative to internal standard Me_4Si. ^1H NMR spectra for methiodides were recorded at 270 MHz on a Bruker WH 270 NMR spectrometer (with Bruker data system model B-Nc 12, Nicolet NIC-model 294 disc memory coupler and Type 602 display unit) and are expressed in δ values relative to internal standard Me_4Si in DMSO-d_6. Proton-noise decoupled ^{13}C NMR spectra were recorded at 25.2 MHz on a Varian XL-100(15) NMR spectrometer equipped with a Nicolet TT-100 Fourier Transform accessory. Chemical shift data encompassing a 5000 Hz spectral region were collected into 8K data points. Single frequency, off resonance spectra were obtained by irradiating with a single frequency at about δ-5 compared to Me_4Si in the proton spectrum. The samples were run as 0.3 M solution in $DCCl_3$ containing Me_4Si as an internal reference. The spectra of all samples were recorded at 37°C. Assignments have been made on the basis of signal multiplicity found in the off-resonance decoupled spectra and from the magnitude of the $^1J_{^{13}C-H}$ couplings.

Preparation of substituted 4-N,N-dimethylaminothianes. A 4-aminothiane (0.2 mol) was added slowly with cooling to a mixture of formic acid (85%, 1.0 mol) and aqueous formaldehyde (37%, 0.6 mol). The mixture was heated in an oil bath at 90–100°C. A vigorous evolution of carbon dioxide began after 5 minutes, and the flask was removed from the oil bath and left to stand until the gas evolution subsided (20–30 min). Then it was returned to the bath and heating was continued for 6–8 h. The mixture was concentrated under reduced pressure; acetic anhydride (1 mol) was added and the solution was heated over a steam bath for 4–6 h. The resulting mixture was then poured into ice-cold water, acidified with 1 : 1 HCl and extracted with ether (3 × 50 mL). The aqueous layer was basified with 1 : 1 ammonia. An oil separated and solidified upon standing. It was filtered, washed with water, dried and recrystallized from a suitable solvent. If an oil separated and did not solidify upon standing, it was taken up in ether, and the ethereal solution was dried (Na_2SO_4). After evaporating the solvent, the residual liquid was distilled under reduced pressure. The relevant data are furnished in Table I.

Preparation of methiodides of substituted-4-N,N-dimethylaminothianes. Addition of excess methyl iodide to an ethereal solution of a tertiary amine (0.003 mol) and allowing the solution to stand afforded the methiodide. This was crystallized from a suitable solvent. The details are given in Table III.

Kinetic procedure. Acetonitrile was purified as reported in the literature.[17] Methyl iodide was successively washed with an aqueous solution of sodium thiosulfate, water and an aqueous solution of sodium carbonate; it was then dried over $CaCl_2$ and distilled.[18] The liquid distilling at 42.7°C was collected and stored over mercury in an amber colored bottle.

The kinetics of alkyl iodide formation was followed conductometrically[9] by measuring the conductance of the reaction mixture as a measure of the amount of salt formed. The apparatus consisted of a conductivity cell with black platinized electrodes connected to a conductivity bridge to measure the conductance of the solution in the cell.

A solution of the tertiary amine in acetonitrile, [approximately 10^{-3} molar (10 mg in 10 mL of acetonitrile)] was introduced into the cell kept at 10 ± 0.05°C. Nitrogen was bubbled through the system. The solution of methyl iodide in acetonitrile was then added in approximately a one hundred fold excess

TABLE VIII

Summary of crystallographic data for trimethyl[2,2-dimethyl-*trans*-6-phenylthian-*r*-4-yl]ammonium iodide (**9a**)

Molecule Formula	$C_{16}H_{26}NSI \cdot H_2O$	
Molecular Weight	409.4 g/mole	
Linear Absorption Coefficient	18.89 cm^{-1} (MoKα)	
Density (Calculated)	1.489 g/cm^3	
Space Group	Pbca	
Cell Dimensions	298°K	128°K
a	20.629(13) Å	20.581(14) Å
b	20.384(5)	20.260(9)
c	8.684(2)	8.615(3)
$\alpha = \beta = \gamma$	90.0°	90.0°
V	3652 Å^3	3592 Å^3
Z	8	8
Crystal Size	0.15 × .06 × 0.34 mm	
Number of Reflections	Measured 3214	
	Observed (1 > 2.5(I)) 2086	
Final R	0.0422 (observed)	
Rw	0.0383 (observed)	

and at the same time a timer was started. Conductance readings were taken at appropriate intervals until the reaction had reached completion, at which time the conductance remained constant. The alkyl iodide was used in large excess so that the second order reaction would follow a pseudo first order kinetic law. The pseudo first order rate constant k_1 is given by the equation,

$$k_1 = \frac{2.303}{t} \log \frac{C_\alpha}{C_\alpha - C_t}$$

where, C_α is the conductance at the end of the reaction and C_t is the conductance at time 't'.

Crystallographic experimental data. The compound was recrystallized from aqueous/ethanol solution in a thermal gradient. The crystallization apparatus was similar to one described by Watkin.[19] The crystals were relatively thin needles belonging to the orthorhombic space group Pbca. The unit cell dimensions and intensity data were obtained with an Enraf-Nonius CAD-4 diffractometer fitted with a low temperature apparatus. The cell parameters (Table VIII) were obtained by a least-squares fit to the $+2\theta$ and -2θ values of 50 reflections at 138 ± 2K using MoKα_1 ($\lambda = 0.70926$ Å) radiation. The intensity data for all reflections with $1° \leqslant 2\theta \leqslant 53°$ were measured using MoK$_\alpha$ radiation ($\lambda = 0.71069$ Å) and the $\theta - 2\theta$ scan technique. The angular scan width was variable and taken to be $(0.80 + 0.20 \tan\theta)°$. A receiving aperture with a variable width of $(3.0 + 0.86 \tan\theta)$mm and a constant height of 6 mm was located at a distance of 173 mm from the crystal. The maximum scan time for a reflection was 90 seconds. For each reflection 2/3 of the scan time was spent scanning the peak and 1/6 was spent scanning each of the two backgrounds. During the intensity measurements, the intensities of three standard reflections were monitored after every 5000 seconds of X-ray exposure time and indicated no appreciable decomposition of the crystal. A total of 3214 unique reflections were measured of which 1128 were considered to be unobserved having intensities less than 2.5 $\sigma(I)$. All intensity date were corrected for Lorentz and polarization factors and numerical absorption corrections were applied ($\mu_{MoK\alpha} = 18.9$ cm^{-1}).

The structure was solved by first locating the iodine atom by means of a Patterson map calculated using the program SHELX.[20] The remaining non-hydrogen atoms were located by difference maps. Following isotropic and anisotropic refinement of the non-hydrogen atoms, the hydrogen atoms were located in difference maps and then refined isotropically. One relatively large peak in the difference maps was too far from the other non-hydrogen atoms to be part of the molecular structure. This peak was identified as the oxygen atom of a water of hydration and refined as such. The difference maps did not clearly reveal the hydrogen atoms associated with this water molecule so they were not included in the final refinement.

TABLE IX

Fractional coordinates ($\times 10^4$) for non-hydrogen atoms in trimethyl-[2,2-dimethyl]-*trans*-6-phenylthian-*r*-4-yl]ammonium iodide (**9a**)

S(1)	3951.9(8)	3025.9(9)	4126(2)
C(2)	4651(3)	3489(3)	4928(8)
C(3)	4405(3)	4024(3)	6077(8)
C(4)	3896(3)	3766(3)	7210(7)
C(5)	3237(3)	3645(4)	6423(9)
C(6)	3290(3)	3566(3)	4673(8)
C(7)	5013(3)	3828(4)	3633(9)
C(8)	5094(3)	2991(3)	5725(9)
N(9)	3822(2)	4221(2)	8616(6)
C(10)	3640(5)	4909(4)	8193(10)
C(11)	3326(4)	3940(4)	9689(8)
C(12)	4453(4)	4236(5)	9511(10)
C(13)	2672(3)	3303(3)	3926(8)
C(14)	2347(3)	3686(3)	2846(8)
C(15)	1796(3)	3456(3)	2093(9)
C(16)	1572(3)	2828(3)	2432(8)
C(17)	1885(3)	2443(3)	3500(8)
C(18)	2427(3)	2681(3)	4260(8)
I	1450.7(2)	408.0(2)	3019.0(6)
O(w)	5783(4)	3557(4)	9691(10)

Standard deviations for last digit in parentheses.

The least squares refinements were carried out by a blocked full matrix method using the computer program SHELX. The scattering factors were taken from the International Tables, Vol. 4, pages 99 and 149. The weighting scheme and variance calculation have been described in a previous publication.[16] After the final cycle of refinement the value of K in the weighting factor was 1.558. The analysis of the variance in terms of the parity of the reflection indices, $\sin\theta$, and $[F_0/F_{max}]^{1/2}$ showed no significant variation for various ranges of the functions tested. The refinement was terminated when all parameter shifts for the non-hydrogen atoms were less than 0.4 times their corresponding standard deviations (Table IX). The final value of R was 0.042 and for R_w was 0.038.

ACKNOWLEDGMENTS

The authors (PKS and KR) would like to thank Professor D. K. P. Varadarajan, Principal P.S.G. College of Arts and Sciences, Coimbatore, India and Mr. G. Varadaraj, Managing Trustee, P.S.G. Institutions, Coimbatore, India, for constant encouragement and financial support. P.K.S. would like to thank C.S.I.R., New Dehli, India, for the award of a Junior Research Fellowship. One (DvdH) gratefully acknowledges partial support by a grant from the USPHS, National Cancer Institute grant CA 17562. One (K.D.B.) of us gratefully acknowledges the partial support by the College of Arts and Sciences Office of Research in the form of salary. The Oklahoma State University is grateful for partial funding from the National Science Foundation in the form of Department grants to purchase the XL-100(15) NMR spectrometer (GP 17641) and the TT-100 PFT accessory (CHE-7605571).

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