Studies on 1,2,4-Thiadiazolidine Derivatives. I. The Synthesis and Structural Determination of 2,4-Disubstituted 3,5-Disubstituted Imino-1,2,4-thiadiazolidines

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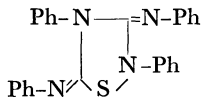
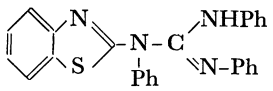
The reaction of symmetrical thiourea derivatives, RNHCSNHR, with benzoyl peroxide (BPO) gave only one isomer of 2,4-disubstituted 3,5-disubstituted imino-1,2,4-thiadiazolidines, and that of nonsymmetrical thiourea derivatives, RNHCSNHR′, with BPO yielded a mixture of some of the possible isomeric derivatives. The structures of these compounds were determined by means of NMR, mass spectra, and X-ray analyses. The steric effects of peripheral groups around the thiadiazolidine ring and some reaction mechanism are discussed.

In the past years, we have studied the oxidation reactions of thiourea derivatives with benzoyl peroxide (BPO). As reported in a preliminary paper, the oxidation of 1,3-dimethylthiourea with BPO was found to afford 2,4-dimethyl-3,5-bis(methylimino)-1,2,4-thiadiazolidine (**1a**). This reaction was initially discovered in a mass spectrometer, wherein both reagents were made to react in a sample tube and we called this a mass spectrometry reaction.[1] Later on, substance **1a** was synthesized on a laboratory scale in a good yield. In 1890 Hector[2] reported the oxidation of 1,3-diphenylthiourea by use of hydrogen peroxide and assigned, without sufficient evidence, the structure **1k** (mp 136 °C) to the product of the reaction. However, IR ane UV spectral data[3] have shown that the assignment is erroneous and the structure represented by **2** is correct. This assignment has also been confirmed by an independent synthesis from 2-anilinobenzothiazole with diphenylcarbodiimide.[4]



1k



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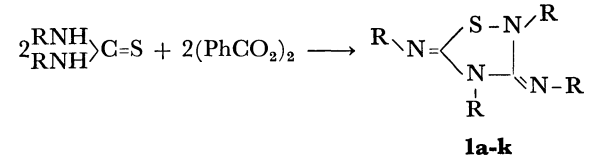
However, under our experimental conditions, the oxidation of 1,3-diphenylthiourea afforded 2,4-diphenyl-3,5-bis(phenylimino)-1,2,4-thiadiazolidine (**1k**, mp 51—52 °C) along with 1-benzoyl-1,3-diphenylurea. Many homologous derivatives could be synthesized under similar reaction conditions. The present paper describes these oxidation reactions and structural evidences for the related products.

Results and Discussion

Various types of thiourea derivatives have been examined as substrates for the BPO oxidation. The overall reaction may be represented in the following scheme, wherein the major by-products were benzoic acid and sulfur. The same reaction conditions were employed throughout this work, *i.e.*, the reactions were carried out by stirring the dichloromethane solution of thiourea derivatives with 1.15 equivalents of BPO for one hour at 5—10 °C. Most of the structures of the reaction products have been established by means of NMR, IR, and mass spectra and the final structural assignments of some isomers required X-ray analyses.



1a-k

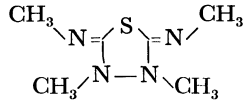
$+ 4PhCO_2H + 1/8\ S_8$

The first choice as the substrate for the reaction was symmetrical thiourea derivatives, RNHCSNHR, which gave 1,2,4-thiadiazolidines, **1a—k**. The fundamental reaction product of **1a** ($C_6H_{12}N_4S$, *m/e* 172) was obtained from 1,3-dimethylthiourea. The NMR spectrum showed four singlet peaks at 2.49, 3.00, 3.11, and 3.28 (δ, ppm, C_6D_6). The IR absorption at 1650 cm^{-1} and the UV spectrum, λ_{max} 229 nm (EtOH), indicate that none of the C=N bonds in this molecule are conjugated. The data including the major mass fragment ions of *m/e* 102 ($M^+ - CH_3NCNCH_3$), 73 (CH_3NCS), 70 (CH_3NCNCH_3), and 61 (CH_3NS), strongly suggest that the product **1a** should be 2,4-dimethyl-3,5-bis-(methylimino)-1,2,4-thiadiazolidine.* The formation of such a thiadiazolidine ring system has also been established by an independent X-ray analysis of an other derivative as described in a later section.

Other 1,2,4-thiadiazolidine derivatives were synthesized by similar reactions (Table 1). Boiling points of some products (**1e—i**) were difficult to measure since they easily decomposed even under reduced pressure (*ca.* 2 mmHg). The yields of **1a—k** were determined by weighing the product directly after isolation by column chromatography. The mass spectrum of one of these derivatives, **1k**, is shown Fig. 1.

Four structural isomers are possible in this series of compounds as shown in Fig. 2, but in fact only one isomer could be isolated. The three isomers, **1a′**, **1a″**, and **1a‴** might be unstable, since their molecular models are considerably sterically hindered; the methyl group at the 4-position in each structure can be but-

* There is another possibility of producing the mirror symmetrical derivative, *i.e.*,



but in the NMR spectrum of **1a**, the chemical shifts of the four methyl groups have quite different values indicating that they are each situated in a different intramolecular environment. This homologue can therefore be excluded.

Table 1. Physical properties and analytical data of 1,2,4-thiadiazolidines (**1**)

Compd	R	Yield (%)	Bp °C/mmHg (Mp °C)	GLC[a] Time	GLC[a] Temp	IR[b] (cm^{-1}) C=N	Molecular[c] formula	Found (Calcd) C%	H%	N%	S%
1a	CH_3	40	88—90/2	1.42	150	1650	$C_6H_{12}N_4S$	41.78	7.06	32.45	18.68
								(41.84	7.02	32.53	18.61)
1b	CH_3CH_2	65	104—106/2.5	1.83	150	1640	$C_{10}H_{20}N_4S$	52.51	8.74	24.63	14.38
								(52.60	8.83	24.53	14.04)
1c	$CH_3CH_2CH_2$	68	126—128/2	1.83	180	1640	$C_{14}H_{28}N_4S$	59.63	9.76	19.48	11.11
								(59.11	9.92	19.70	11.27)
1d	$CH_3(CH_2)_3$	65	144—146/1.5	6.17	180	1640	$C_{18}H_{36}N_4S$	63.27	10.55	16.49	9.65
								(63.48	10.65	16.45	9.41)
1e	$CH_3(CH_2)_4$	63	oil[d]	2.33	230	1640	$C_{22}H_{44}N_4S$	66.53	11.24	14.03	8.35
								(66.61	11.18	14.12	8.08)
1f	$CH_3(CH_2)_5$	67	oil[d]	6.50	230	1640	$C_{26}H_{52}N_4S$	68.82	11.55	12.58	7.32
								(68.97	11.58	12.37	7.08)
1g	$CH_3(CH_2)_6$	72	oil[d]	3.17	270	1640	$C_{30}H_{60}N_4S$	70.66	12.00	10.94	6.40
								(70.81	11.88	11.01	6.30)
1h	$CH_3(CH_2)_7$	70	oil[d]	7.92	270	1640	$C_{34}H_{68}N_4S$	72.10	12.09	9.97	5.80
								(72.28	12.13	9.92	5.67)
1i	$EtOCH_2CH_2$	67	oil[d]	3.75	230	1640	$C_{18}H_{36}N_4O_4S$	53.58	9.01	13.75	8.02
								(53.44	8.97	13.85	7.92)
1j	$C_6H_5CH_2$	57	(81.5)	—	—	1630	$C_{30}H_{28}N_4S$	75.54	5.98	11.61	6.92
								(75.60	5.92	11.75	6.73)
1k	C_6H_5	13	(51—52)	—	—	1625	$C_{26}H_{20}N_4S$	74.31	4.75	13.28	7.69
								(74.26	4.79	13.32	7.62)

a) 2% Silicone OV-17 on Gas Chrom Q (80—100 mesh), 1 m×2 mm i. d. glass column, flow rate: 30 ml/min He, retention time in min. b) Measured in liq. film (**1a—i**) and Nujol mulls (**1j—k**). c) Molecular formula were determined by high resolution mass spectrometry. d) Decomposed at 170—200 °C (bath temp)/2—3 mmHg.

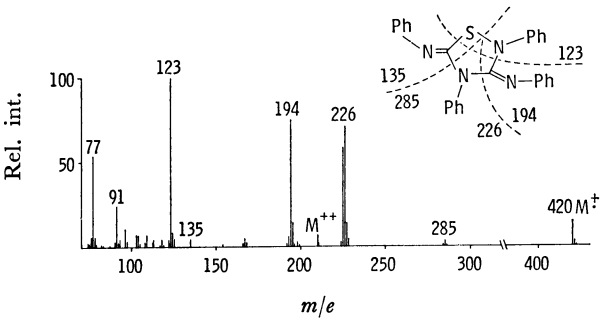


Fig. 1. Mass spectrum of **1k**.

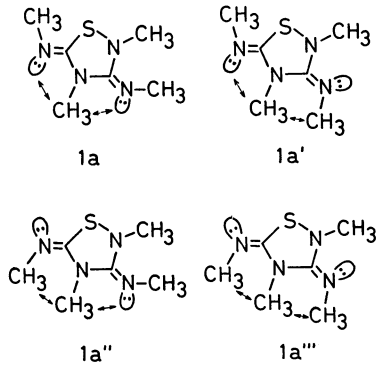
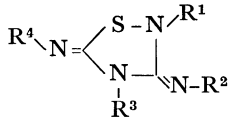


Fig. 2. Geometrical isomers of 2,4-dimethyl-3,5-bis-(methylimino)-1,2,4-thiadiazolidine.

tressed either by one or two adjacent methyl groups.[5] The lone pair electrons on the imino nitrogen atoms attached to the 3- and 5-positions might affect neighbouring substituents to a smaller extent than methyl groups. The hindrances are shown by the double headed arrows in Fig. 2.

Structurally interesting molecules could be synthesized from the nonsymmetrical thiourea derivatives ($R^1NHCSNHR^2$; R^1=aryl, R^2=alkyl). There are sixteen possible different isomeric 1,2,4-thiadiazolidine derivatives through these reactions. Even if we neglect the three labile isomers such as **1a'**, **1a''**, and **1a'''**, and the four possible isomers of each (Fig. 2), there are still four isomers, **A**, **B**, **C**, and **D** left:

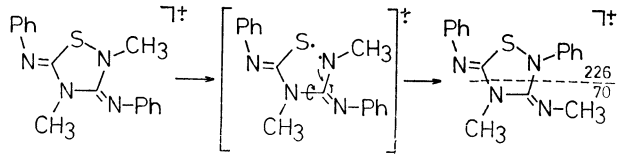


A; $R^1=R^3$=alkyl, $R^2=R^4$=aryl
B; $R^1=R^4$=aryl, $R^2=R^3$=alkyl
C; $R^1=R^4$=alkyl, $R^2=R^3$=aryl
D; $R^1=R^3$=aryl, $R^2=R^4$=alkyl

Three of these isomers could be obtained from the derivatives of 1-alkyl-3-arylthiourea. They were isolated by means of column chromatography or solubility differences in ethanol. The molecular structure of **3a** (**A**-type) was determined by X-ray analysis. The NMR spectrum of **3a** gave upfield (δ, 2.68) and down field (δ, 3.44) absorptions which were assigned to the N2 and N4 methyl groups, respectively. The assignments could be made by considering the shielding effects exerted by the diamagnetic anisotropy of the phenyl groups.

The mass spectrum of **3a** (Fig. 3) shows an ion at

m/e 226 ($C_{13}H_{10}N_2S$, MW. obsd=226.057, MW. calcd=226.056) which corresponds to the ($M^+-C_3H_6N_2$) ion. This should arise from the transannular cleavage of **3a-B** ion. Thus, the results of the mass spectrum and X-ray analysis for **3a** are apparently inconsistent. Such conflicting evidence can be explained by an intramolecular rearrangement induced by electron bombardment when the mass spectral measurement is taken.[6] Such a reaction is shown in the following scheme:

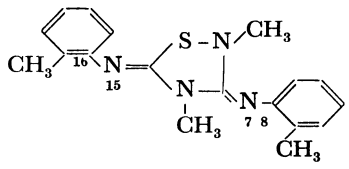


3a 3a-B

The analytical data of some **A**-type isomers are summarized in Tables 2 and 3. Their structures were established by comparison of the chemical shifts in the NMR spectra and the mass fragmentation patterns with those of **3a**.

The same reactions for thiourea derivatives containing more bulky groups at the *ortho* position in the phenyl group, such as 1-methyl-3-*o*-tolylthiourea or 1-methyl-3-(2,6-xylyl)thiourea, were carried out. These thiourea derivatives reacted with BPO to give the corresponding 1,2,4-thiadiazolidine derivatives which are sterically more hindered around the 1,2,4-thiadiazolidine ring system.

These structures were also assigned to **5** and **6** by the same procedure.



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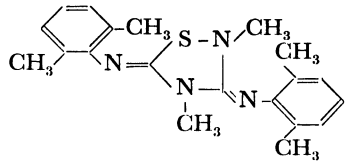

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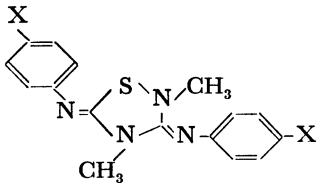
Table 4 shows the chemical shifts of the N2 and N4 methyl groups of **3a**, **5**, and **6**, in which the diamagnetic shift of the N2-methyl protons induced by virture of the benzene rings increases in the order of **6>5>3a**. Thus, the rotational angles about N7–C8 and N15–C16 bonds seem to parallel the increasing degree of steric hindrance.

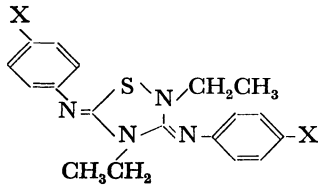
On the other hand, it is noteworthy that 1-*t*-butyl-3-methylthiourea is oxidized to the corresponding urea and benzoic anhydride but not to a 1,2,4-thiadiazolidine derivative. In view of these results we propose the reaction mechanism as shown in Scheme 1.

TABLE 2. PHYSICAL PROPERTIES AND ANALYTICAL DATA OF 1,2,4-THIADIAZOLIDINES (**3**)



Compd	X	Yield (%)	Mp °C	NMR (δ)[a] N(2)CH_3	NMR (δ)[a] N(4)CH_3	IR[b] (cm^{-1}) C=N	Molecular[c] formula	Found (Calcd) C%	H%	N%	S%
3a	H	58	137.5	2.67	3.43	1622	$C_{16}H_{16}N_4S$	64.69	5.68	19.19	10.88
								(64.84	5.44	18.90	10.82)
3b	Me	59	136	2.67	3.41	1620	$C_{18}H_{20}N_4S$	66.71	6.23	17.08	9.91
								(66.64	6.21	17.27	9.88)
3c	OMe	64	118	2.69	3.41	1630	$C_{18}H_{20}N_4O_2S$	60.32	5.70	15.81	9.08
								(60.65	5.66	15.72	8.99)
3d	F	67	76.5	2.70	3.41	1612	$C_{16}H_{14}F_2N_4S$	57.74	4.29	16.92	9.80
								(57.82	4.25	16.86	9.65)
3e	Cl	71	126.5	2.72	3.41	1612	$C_{16}H_{14}Cl_2N_4S$	52.55	3.74	15.45	8.88
								(52.61	3.86	15.34	8.78)
3f	Br	62	128.5	2.73	3.42	1618	$C_{16}H_{14}Br_2N_4S$	42.71	3.27	12.20	7.16
								(42.31	3.11	12.34	7.06)
3g	I	53	186	2.72	3.40	1620	$C_{16}H_{14}I_2N_4S$	34.84	2.54	10.23	5.99
								(35.06	2.57	10.22	5.85)
3h	Ac	38	120.5	2.74	3.46	1612	$C_{20}H_{20}N_4O_2S$	63.18	5.23	14.77	8.44
								(63.14	5.30	14.73	8.43)
3i	NO_2	13	199.5	(2.82)	(3.50)	1616	$C_{16}H_{14}N_6O_4S$	49.94	3.75	21.71	8.43
								(49.74	3.65	21.75	8.30)

TABLE 3. PHYSICAL PROPERTIES AND ANALYTICAL DATA OF 1,2,4-THIADIAZOLIDINES (**4**)

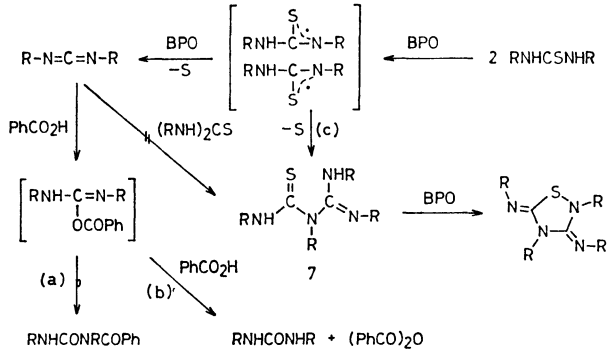


Compd	X	Yield (%)	Mp °C	NMR (δ)[a] N(2)CH_2	NMR (δ)[a] N(4)CH_2	IR[b] (cm^{-1}) C=N	Molecular[c] formula	Found (Calcd) C%	H%	N%	S%
4a	H	27	77.5	2.99	4.09	1625	$C_{18}H_{20}N_4S$	66.47	6.18	17.16	10.01
								(66.64	6.21	17.27	9.88)
4b	Me	30	93	2.98	4.06	1625	$C_{20}H_{24}N_4S$	68.48	6.76	15.63	9.11
								(68.15	6.86	15.89	9.10)
4c	OMe	31	80.5	2.98	4.05	1613	$C_{20}H_{24}N_4O_2S$	62.97	6.26	14.81	8.41
								(62.48	6.29	14.57	8.34)
4d	F	34	99	3.01	4.06	1625	$C_{18}H_{18}F_2N_4S$	59.90	4.98	15.71	8.98
								(59.98	5.03	15.54	8.90)
4e	Cl	26	117	3.03	4.06	1610	$C_{18}H_{18}Cl_2N_4S$	55.15	4.59	14.20	8.33
								(54.97	4.61	14.24	8.15)
4f	Br	49	161	3.04	4.06	1615	$C_{18}H_{18}Br_2N_4S$	45.00	3.83	11.70	6.88
								(44.83	3.76	11.62	6.65)
4g	I	49	198.5	(3.02)	(4.04)	1610	$C_{18}H_{18}I_2N_4S$	37.75	3.30	9.79	5.58
								(37.52	3.15	9.72	5.56)

a) Observed in CCl_4($CDCl_3$). b) Measured in Nujol mulls. c) Determined by high resolution mass spectrometry.

TABLE 4. PROTON CHEMICAL SHIFTS OF **3a**, **5**, AND **6** (δ, ppm)

Compd	N(2)-CH_3 CCl_4	N(2)-CH_3 C_6D_6	$\Delta^{CCl_4}_{C_6D_6}$	N(4)-CH_3 CCl_4	N(4)-CH_3 C_6D_6	$\Delta^{CCl_4}_{C_6D_6}$
3a	2.67	2.16	+0.51	3.43	3.30	+0.13
5	2.60	2.13	+0.47	3.48	3.38	+0.10
6	2.48	2.08	+0.40	3.47	3.46	+0.01



Scheme 1.

Zetzsche and his collaborators studied the reactions of carbodiimides with carboxylic acids,[7] wherein two reaction paths were reported: (a) the formation of *N*-acylureas and (b) the formation of acid anhydrides and ureas. As a general rule, aromatic carbodiimides react through route (a), but aliphatic carbodiimides give mainly acid anhydrides through route (b).[8]

Free rotation about the N–C(phenyl) bond in such a thiourea derivative as 1-methyl-3-(2,6-xylyl)thiourea may act to minimize steric hindrance when the reactants are brought closely together. However, 1-*t*-butyl-3-methylthiourea which has an even more bulky substituent may resist passing through route (c). Consequently, the latter reacts to produce a carbodiimide as a transient intermediate through route (b).

There are other reasons to support the mechanism of the formation of 1,2,4-thiadiazolidines through route (c) in Scheme 1.

1) No additional product was obtained when the mixture of 1,3-dimethylthiourea and 1,3-diisopropylcarbodiimide was brought to react in CH_2Cl_2 at room temperature for a long period. Thus the corresponding carbodiimide is not an intermediate for the formation of 1,2,4-thiadiazolidines.

2) Using a smaller amount of BPO with 1,3-diethylthiourea, the intermediate **7a** (R=Et in Scheme 1) could be isolated. Further reaction of **7a** with BPO yielded 2,4-diethyl-3,5-bis(ethylimino)-1,2,4-thiadiazolidine (**1b**). The structures of **7a** and **1b** were confirmed by their mass spectra as shown in Figs. 4 and 5,

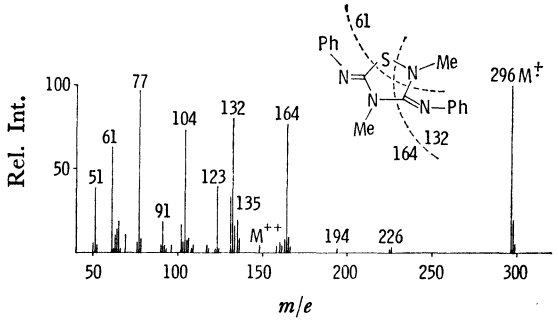


Fig. 3. Mass spectrum of **3a**.

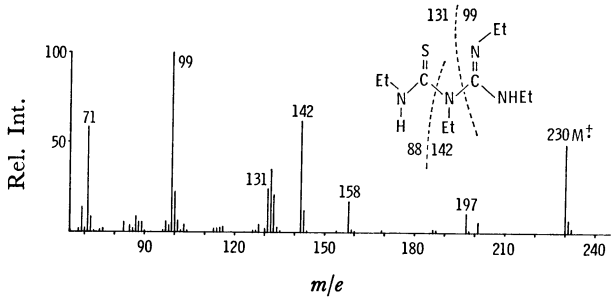


Fig. 4. Mass spectrum of **7a**.

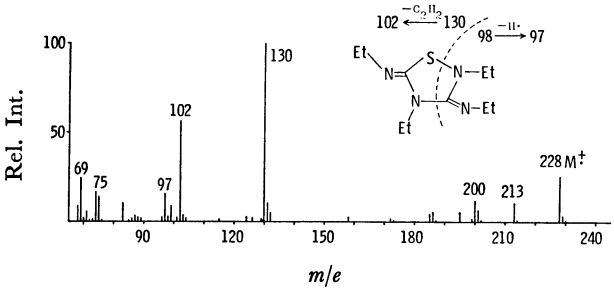
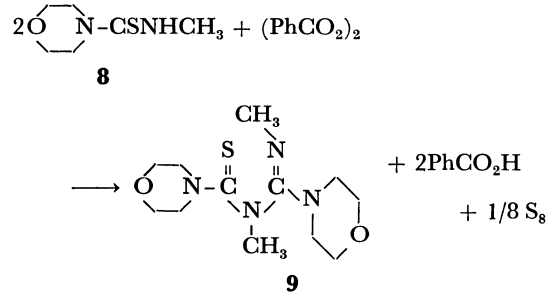


Fig. 5. Mass spectrum of **1b**.

respectively.

3) Treatment of *N*-methyl-4-morpholinethiocarboxamide(**8**) with BPO gave N^1,N^2-dimethyl-N^1-morpholinothiocarbonyl-4-morpholinecarboxamidine(**9**) which is an analog of the intermediate **7** *via* route (c). The molecular structure of **9** was determined by X-ray analysis.



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The investigation of the **B**, **C**, and **D** isomers of 1,2,4-thiadiazolidine derivatives is currently under progress.[9]

Experimental

All the melting points were measured on a Mitamura Riken micromelting point apparatus and are uncorrected. The IR spectra were obtained on a JASCO IRA-2 spectrophotometer and the UV spectra on a Cary 14 spectrophotometer. The NMR spectra were taken on a Varian A-60D spectrometer, using tetramethylsilane as an internal standard, and the mass spectra on a JEOL JMS-O1SG mass spectrometer, using a direct inlet and an ionization energy of 75 eV. The GLC analyses were carried out on a JEOL JGC-20KFP gas chromatograph equipped with a flame-ionization detector.

Materials. Commercial methyl, ethyl, *p*-nitrophenyl, phenyl isothiocyanates, benzoyl peroxide, and amines of the purest grade were used. Thiourea derivatives were prepared according to methods in literatures.[10-12]

Reaction of Symmetric Thioureas with BPO. To a solution of 1,3-dimethylthiourea (10.4 g, 0.1 mol) in dichloromethane (200 ml) was added dropwise a solution of BPO (27.8 g, 0.115 mol) in dichloromethane (200 ml) at 5—10 °C. After addition was over, the resulting slurry was stirred at the same temperature for one hour. The solution was then washed with an aqueous solution of sodium hydroxide (10 g, 0.25 mol) to remove benzoic acid.

The solvent was removed under reduced pressure and the resulting residue was chromatographed with petroleum ether-AcOEt (6 : 1) on a silica gel column to give **1a** (3.44 g). The physical properties and analytical data of **1a** are summarized in Table 1 along with the other derivatives (**1b-k**).

Reaction of Nonsymmetric Thioureas with BPO. From a dropping funnel, a solution of BPO (14 g, 0.058 mol) in CH_2Cl_2 (200 ml) was added to a solution of 1-methyl-3-phenylthiourea (8.3 g, 0.05 mol) in CH_2Cl_2 (200 ml) at 5—10 °C, and the reaction mixture was stirred at the same temperature for 1 h. Benzoic acid was removed with an aqueous solution of NaOH, and the solvent was removed under reduced pressure. The resulting residue was dissolved in cold acetone and filtered to remove the insoluble sulfur. After evaporation of the solvent, the residue was triturated with a small amount of cold ethanol and filtered to give **3a** (2.8 g). The filtrate was separated on a silica gel column using petroleum ether-AcOET (6 : 1) as an eluent to give **3a** (1.5 g). The physical properties and analytical data for the thiadiazolidine (**3a-i**, and **4a-g**) are summarized in Tables 2 and 3. Compounds **5** and **6** were obtained in a similar manner: **5** (in a 62% yield) oil. GLC: Retention Time 3.0 min, 2% Silicone OV-17 on Gas Chrom Q (80—100 mesh), 1 m×2 mm i. d. glass column, He flow rate 30 ml/min. Found: C, 66.69; H, 6.24; N, 17.22; S, 9.94%. Calcd for $C_{18}H_{20}N_4S$: C, 66.64; H, 6.21; N, 17.27; S, 9.88%. IR (Nujol): 1628 cm^{-1} (ν C=N). NMR (CCl_4): δ 2.19 (s, 3H), 2.23 (s, 3H), 2.60 (s, 3H), 3.48 (s, 3H), and 6.7—7.3 (m, 8H). **6** (in a 32% yield): mp 133.5 °C (from ethanol). Found: C, 68.23; H, 6.85; N, 15.68; S, 9.13%. Calcd for $C_{20}H_{24}N_4S$: C, 68.15; H, 6.86; N, 15.89; S, 9.10%. IR(Nujol): 1630 cm^{-1} (ν C=N). NMR (CCl_4): δ 2.12 (s, 6H), 2.48 (s, 3H), 3.47 (s, 3H), and 6.7—7.0 (m, 6H).

Reaction of 1-t-Butyl-3-methylthiourea with BPO. To a solution of 1-*t*-butyl-3-methylthiourea (0.05 mol) in CH_2Cl_2 was added a solution of BPO (0.06 mol) in CH_2Cl_2 with stirring under ice-cooling. The reaction is exothermic and started at once. After stirring for 1 h, the solvent was removed under reduced pressure and the residue was chromatographed over silica gel to give 1-*t*-butyl-3-methylurea, 1-*t*-butyl-3-benzoyl-3-methylurea and other by-products. None of 1,2,4-thiadiazolidine derivatives could be isolated under these conditions.

Isolation of the Intermediary Compound 7a. A solution of BPO (12.1 g, 0.05 mol) in CH_2Cl_2 was added dropwise to a solution of 1,3-diethylthiourea (13.2 g, 0.1 mol) in CH_2Cl_2 (200 ml) during 10 min with stirring under ice-cooling. The reaction mixture was kept at 5—10 °C for 30 min, and then washed with a solution of NaOH to remove the benzoic acid. After removal of CH_2Cl_2, the residue was separated on a silica gel column using ether as an eluent, and **7a** was isolated in a 2% yield (230 mg) along with the main product **1b**. Upon recrystallization from ether **7a** was obtained as colorless needles, mp 76.5 °C. Found: C, 52.23; H, 9.65; N, 24.28; S, 13.97%. Calcd for $C_{10}H_{22}N_4S$: C, 52.14; H, 9.63; N, 24.32; S, 13.92%. IR (Nujol): 3200, 1650, and 1560 cm^{-1}. NMR (CCl_4): δ 1.13 (t, 6H, J=7 Hz), 1.16 (t, 3H, J=7 Hz), 1.18 (t, 3H, J=7 Hz), 3.10 (q, 4H, J=7 Hz), 3.55 (q, 2H, J=7 Hz), and 3.88 (q, 2H, J=7 Hz).

Reaction of N-Methyl-4-morpholinethiocarboxamide 8 with BPO.

According to the usual procedure for the synthesis of thioureas, **8** was prepared from morpholine and methyl isothiocyanate. To a solution of **8** (3.2 g, 0.02 mol) in CH_2Cl_2 (200 ml) was added BPO (2.76 g, 0.0115 mol) portionwise at 5 °C. Separation was carried out in the same way as in the case of symmetric thioureas to give N^1,N^2-dimethyl-N^1-morpholinothiocarbonyl-4-morpholinecarboxamidine **9** (2.4 g, 84%), mp 151.5 °C (from benzene). Found: C, 50.37; H, 7.72; N, 19.50; S, 11.22%. Calcd for $C_{12}H_{22}N_4O_2S$: C, 50.32; H, 7.74; N, 19.50; S, 11.19%. IR (Nujol): 1645, 1470, 1300, and 1115 cm^{-1}. NMR (CCl_4): δ 2.94 (s, 3H), 3.22 (s, 3H), and 3.0—4.2 (m, 16H). Mass: *m/e* (rel. intensity) 286 (13, M^+), 271 (7, $M^+ - CH_3$), 253 (6, $M^+ - HS$), 200 (17, $M^+ - C_4H_8NO$), 127 (100, $M^+ - C_6H_{11}N_2OS$), 86 (12), and 83 (26).

Structure Determination by Means of X-Ray Analysis

Compounds **3a** and **9** were recrystallized from ethanol and from benzene, respectively. Intensity data of **3a** were obtained on a Rigaku four-circle automatic diffractometer with $\omega/2\theta$ scan technique up to $2\theta \leq 55°$ using Mo$K\alpha$ radiation, and those of **9** were collected from the equi-inclination Weissenberg photographs (*hk*0—*hk*6) with Cu$K\alpha$ radiation. They were corrected as regards Lorentz and polarization factors. No absorption correction was applied. Reflections of 1478 and 2439 were used for **3a** and **9**, respectively. The crystal data are given in Table 5.

3a: The structure of **3a** was solved by the symbolic addition technique. Nine atoms involving the thiadiazolidine ring system were revealed on the first E-map. Subsequent Fourier synthesis gave the position of all non-hydrogen atoms. Refinement of this structure was carried out by the block diagonal least-squares method to give the final *R*-factor of 0.082 including hydrogen atoms which are obtained from the difference map.

9: The structure of **9** was determined by the Patterson method. Several cycles of a block-diagonal least-squares refinement for all the atoms except hydrogen atoms gave the final *R*-factor of 0.133.

The fractional coordinates and anisotropic thermal parameters for **3a** and **9** are given in Tables 6 and 7, respectively, together with their standard deviations.

Table 5. Crystal data of **3a** and **9**

	3a	**9**
Formula	$C_{16}H_{16}N_4S$	$C_{12}H_{22}N_4O_2S$
M. W.	297.4	286.4
a (Å)	23.69	11.13
b	15.42	9.51
c	8.09	7.61
α (°)	90	100.8
β	90	86.1
γ	90	116.2
V (Å^3)	2955	710
Space group	Pccn	$P\bar{1}$
Z	8	2
D_{obsd} (g cm^{-3})	1.30	1.32
D_{calcd}	1.31	1.34

Lists of observed and calculated structure factors are preserved by the Chemical Society of Japan. (Document No. 7631)

Results and Discussion

3a:[13] The bond lengths and angles are given in Fig. 6. The estimated standard deviations in the bond lengths range from 0.009 to 0.016 Å; those for the bond angles range from 0.5 to 0.9°. A stereoscopic view of the molecule projected along the b-axis is shown in Fig. 7. The deviations from various least-squares planes are given in Table 8.

The S(1)–N(2) and S(1)–C(5) bond lengths of 1.731 and 1.750 Å are comparable with those found in the S(II)–Nsp^3 and S(II)–Csp^2 single bonds. The mean

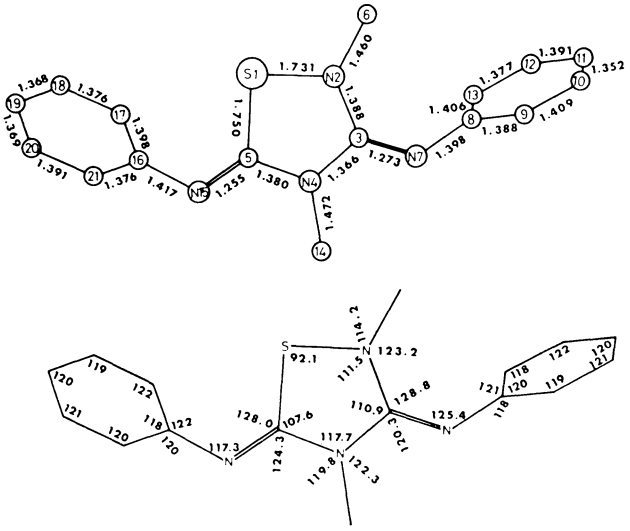

Fig. 6. Bond lengths (Å) and angles (°) of **3a**.
The mean estimated standard deviation of bond lengths is 0.011 Å, and that of bond angles is 0.7°.

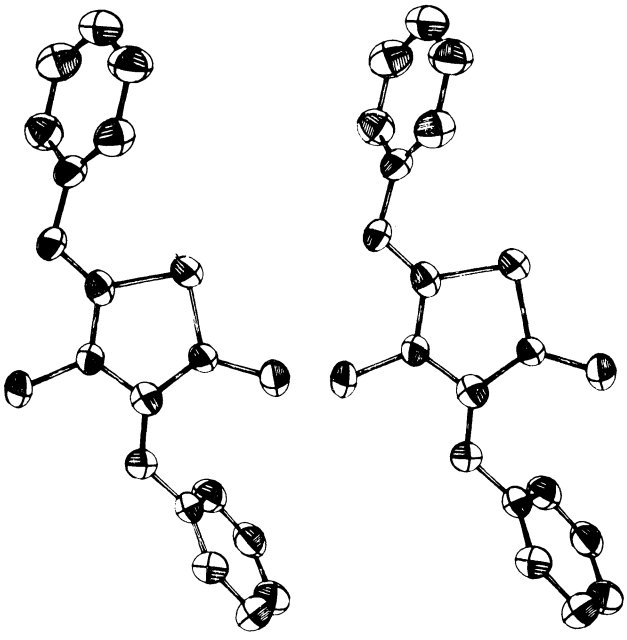

Fig. 7. Stereoscopic view down the b axis of **3a**.

TABLE 6a. FRACTIONAL COORDINATES AND ANISOTROPIC THERMAL PARAMETERS ($\times 10^4$) OF **3a**
Estimated standard deviations are given in parentheses. The anisotropic thermal parameters are in the form: $\exp[-(b_{11}h^2+b_{22}k^2+b_{33}l^2+b_{12}hk+b_{13}hl+b_{23}kl)]$.

	x	y	z	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
S (1)	4716(1)	1151(2)	3057(3)	12(1)	73(1)	131(3)	−2(1)	4(1)	21(2)
N (2)	5349(2)	1027(4)	4098(7)	11(1)	51(4)	108(9)	1(2)	3(3)	17(5)
C (3)	5806(3)	1218(5)	3089(10)	14(1)	45(4)	129(13)	1(2)	5(4)	−6(7)
N (4)	5634(2)	1373(4)	1505(7)	13(1)	43(4)	89(9)	−4(2)	2(3)	−8(5)
C (5)	5061(3)	1388(5)	1199(9)	15(1)	28(4)	114(12)	−2(2)	9(3)	−18(6)
C (6)	5325(3)	1262(6)	5845(10)	17(2)	68(5)	110(11)	7(3)	7(4)	3(7)
N (7)	6328(2)	1255(5)	3463(8)	12(1)	57(4)	119(11)	−1(2)	−2(3)	10(6)
C (8)	6565(3)	962(5)	4943(9)	12(1)	47(4)	109(12)	2(2)	4(3)	−12(6)
C (9)	6938(3)	1507(6)	5761(11)	14(1)	61(5)	151(14)	−3(2)	−1(4)	−10(8)
C (10)	7216(3)	1202(6)	7187(11)	18(2)	71(6)	146(15)	−1(3)	−8(4)	−21(9)
C (11)	7130(3)	385(6)	7740(11)	13(2)	80(6)	169(17)	10(3)	0(4)	4(9)
C (12)	6759(3)	−157(6)	6900(11)	16(2)	62(5)	168(16)	5(2)	12(5)	14(9)
C (13)	6479(3)	108(6)	5497(11)	15(2)	53(5)	168(15)	2(2)	4(4)	12(8)
C (14)	6035(3)	1454(6)	124(9)	17(2)	64(5)	97(12)	2(3)	5(4)	31(7)
N (15)	4846(2)	1503(4)	−202(7)	15(1)	47(4)	95(10)	−1(2)	−4(3)	23(5)
C (16)	4250(3)	1512(6)	−302(9)	15(1)	49(5)	118(13)	−1(2)	−6(4)	19(7)
C (17)	3923(3)	2154(5)	459(11)	19(2)	38(4)	162(15)	0(2)	−8(4)	−20(7)
C (18)	3346(3)	2177(6)	282(12)	17(2)	57(5)	212(19)	6(2)	−6(5)	−4(8)
C (19)	3085(4)	1563(7)	−669(12)	16(2)	72(6)	209(18)	4(3)	−8(5)	−5(9)
C (20)	3394(4)	928(6)	−1429(12)	21(2)	59(6)	213(19)	−4(3)	−15(5)	−6(9)
C (21)	3978(4)	900(6)	−1249(11)	18(2)	45(5)	176(16)	−2(2)	0(4)	−3(7)

TABLE 6b. FRACTIONAL COORDINATES ($\times 10^3$) AND ISOTROPIC THERMAL PARAMETERS OF **3a**
Estimated standard deviations are given in parentheses.

	x	y	z	Bi
H(C6a)	497(4)	60(6)	628(12)	6.0(2.7)
H(C6b)	518(4)	187(6)	604(11)	5.3(2.5)
H(C6c)	569(4)	122(6)	650(11)	5.1(2.5)
H(C9)	701(3)	219(5)	524(11)	3.7(2.2)
H(C10)	749(4)	165(5)	773(11)	4.6(2.2)
H(C11)	735(3)	19(5)	883(10)	3.1(2.1)
H(C12)	670(3)	−80(5)	742(10)	3.2(2.2)
H(C13)	739(4)	53(7)	879(13)	7.3(2.9)
H(C14a)	601(4)	216(5)	−47(11)	4.2(2.2)
H(C14b)	596(4)	99(6)	−64(11)	4.3(2.3)
H(C14c)	645(4)	137(6)	51(12)	5.3(2.3)
H(C17)	410(4)	261(7)	119(13)	5.4(2.5)
H(C18)	311(3)	266(6)	91(11)	3.9(2.9)
H(C19)	264(4)	157(5)	−70(11)	4.7(2.3)
H(C20)	321(4)	45(5)	−226(11)	4.3(2.4)
H(C21)	422(3)	43(5)	−179(11)	3.2(2.1)

value of C–N bond lengths in the thiadiazolidine ring is 1.378 Å which is compatible with those found in conjugated C–N bonds.[14] The sums of bond angles around the nitrogen atoms, N(2) and N(4), are 348.9 and 359.8° and the deviations of N(2) and N(4) from the plane consisting of the three adjacent atoms are 0.292 and 0.034 Å, respectively. The values suggest that the atomic configuration of N(4) is sp^2 hybridized, whereas the N(2) atom is sp^3 hybridized. Furthermore, there is no double bond in the thiadiazolidine ring system, only a small ring current may be expected. However, this ring system is almost planar and the maximum deviation from the mean plane is 0.035 Å. The two phenyl groups are *trans* with respect to C(3)–N(4) and the C(5)–N(4) bonds, respectively. The intramolecular non-bonded distances for N(2) ... C(8) and S(1) ... C(16) are 2.963 and 2.985 Å. The dihedral angles between the thiadiazolidine ring and these phenyl groups are 118.2 and 67.7° for planes B and C, respectively, and that between the two phenyl groups is 69.7°. The C(3)–N(7)–C(8) bond angle is 125.4° which is much greater than C(5)–N(15)–C(16) of 117.3°. This may be due to the steric hindrance between the phenyl group attached to N(7) and the

TABLE 7. FRACTIONAL COORDINATES AND ANISOTROPIC THERMAL PARAMETERS ($\times 10^4$) OF **9**

Estimated standard deviations are given in parentheses. The anisotropic thermal parameters are in the form: $\exp[-(b_{11}h^2+b_{22}k^2+b_{33}l^2+b_{12}hk+b_{13}hl+b_{23}kl)]$.

	x	y	z	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
S (1)	1363(2)	−1170(2)	−152(3)	82(2)	66(2)	83(4)	30(2)	−47(2)	−18(2)
C (2)	1979(6)	−729(7)	1909(9)	40(6)	30(7)	75(15)	11(5)	−7(6)	−6(7)
N (3)	2334(5)	761(6)	2939(8)	50(5)	24(6)	111(13)	27(5)	−14(6)	−5(6)
C (4)	3483(6)	1535(7)	4116(9)	52(6)	38(7)	66(15)	30(6)	−7(7)	−17(7)
N (5)	4624(6)	1569(7)	3793(9)	44(6)	83(9)	136(15)	26(6)	−1(7)	−35(9)
N (6)	2198(6)	−1769(6)	2671(8)	95(7)	18(6)	103(14)	37(6)	−19(7)	−16(7)
C (7)	2498(8)	−1613(9)	4559(11)	89(9)	41(8)	134(19)	19(7)	−23(9)	−4(9)
C (8)	1619(10)	−3138(8)	5218(13)	150(13)	32(9)	179(22)	43(9)	25(12)	5(10)
C (9)	1730(6)	−4477(6)	4134(8)	130(8)	29(6)	192(15)	43(6)	−20(8)	5(7)
C (10)	1364(10)	−4623(8)	2334(12)	150(12)	22(8)	148(21)	35(8)	−18(12)	−12(9)
C (11)	2254(9)	−3190(8)	1543(12)	120(10)	32(8)	156(20)	52(8)	−4(10)	−23(9)
C (12)	1904(8)	1827(8)	2305(12)	105(9)	60(9)	178(20)	69(8)	−43(10)	−11(10)
N (13)	3271(5)	2402(6)	5640(8)	50(5)	56(7)	84(13)	23(5)	1(6)	−30(7)
C (14)	4423(8)	3397(9)	6865(11)	69(8)	100(11)	116(19)	22(8)	−22(9)	−72(11)
C (15)	4208(10)	4811(9)	7797(13)	124(12)	58(10)	143(22)	1(9)	28(12)	−42(11)
C (16)	3011(7)	4318(6)	8784(8)	135(8)	75(8)	144(15)	42(7)	44(12)	−31(8)
C (17)	1886(10)	3386(10)	7530(14)	110(11)	100(12)	248(26)	72(10)	57(13)	−12(13)
C (18)	2005(7)	1907(8)	6573(11)	69(8)	56(9)	138(19)	30(7)	34(9)	5(9)
C (19)	4946(8)	959(11)	1999(13)	65(8)	150(15)	181(23)	44(9)	16(10)	−63(14)

TABLE 8. DEVIATIONS (Å) OF THE ATOMS FROM SEVERAL LEAST-SQUARES PLANES OF **3a**

Atom	Plane A	Atom	Plane B	Atom	Plane C
S (1)	−0.012	C (8)	0.010	C (16)	0.000
N (2)	0.029	C (9)	−0.006	C (17)	−0.002
C (3)	−0.035	C (10)	0.001	C (18)	0.003
N (4)	0.014	C (11)	0.000	C (19)	−0.002
C (5)	0.006	C (12)	0.003	C (20)	0.000
C (6)	−0.650[a]	C (13)	−0.008	C (21)	0.000
N (7)	−0.120[a]	C (3)	0.641[a]	C (5)	0.893[a]
C (14)	0.180[a]	N (7)	−0.101[a]	N (15)	−0.071[a]
N (15)	0.076[a]				

a) Not included in the calculations of the planes.

TABLE 9. INTERMOLECULAR CONTACTS WITHIN 3.7 Å OF **3a**

S (1)···C (13) (I)	3.629	C (3)···C (21) (II)	3.625
N (4)···C (21) (II)	3.629	C (5)···C (6) (III)	3.670
C (6)···N (15) (IV)	3.413	N (7)···C (10) (V)	3.601
C (8)···C (10) (V)	3.666	C (8)···C (11) (V)	3.677
C (9)···C (10) (V)	3.549	C (10)···C (14) (IV)	3.692
C (11)···C (14) (IV)	3.628	C (13)···C (20) (II)	3.671

(I)	1−x,	−y,	1−z
(II)	1−x,	−y,	−z
(III)	x,	1/2−y,	−1/2+z
(IV)	x,	y,	1+z
(V)	3/2−y,	y,	−1/2+z

C(6) atom. The intermolecular atomic distances within 3.7 Å are given in Table 9, wherein no special short interatomic distances are observed.

9: The molecular structure of **9** is shown in Fig. 8 with the bond lengths and angles. A stereoscopic drawning of the molecule is given in Fig. 9. The

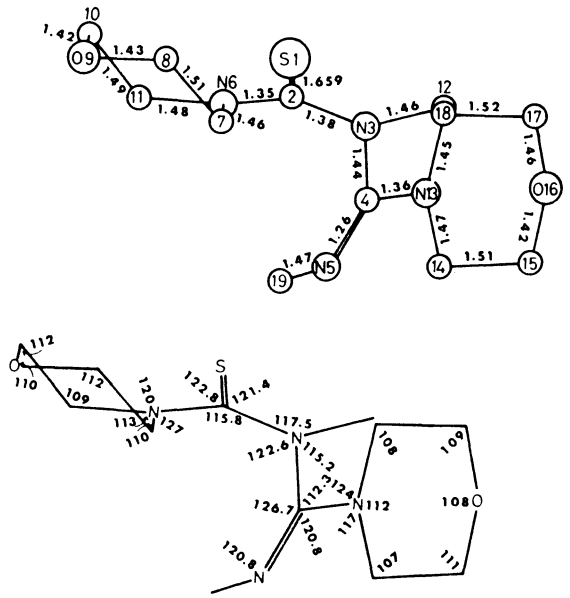

Fig. 8. Bond lengths (Å) and angles (°) of **9**.
The mean estimated standard deviation of bond lengths is 0.012 Å, and that of bond angles is 0.7°.

deviations from several least-squares planes are given in Table 10 and selected torsional angles are given in Table 11.

The sulfur atom is not bonded to N(5) and the intramolecular interatomic distance is 4.38 Å. The S=C bond length of 1.659 Å is slightly larger than the proposed value for a pure S=C bond of 1.608 Å.[15] Generally, the C–N bond distance in which the nitrogen atom is adjacent to C=X, (X=C, N, O, and S) is shorter than the usual C–Nsp^3 bond distance.[14] The values are in the range of 1.34—1.40 Å.[14] In such cases, the atomic configuration of the nitrogen atom is usually

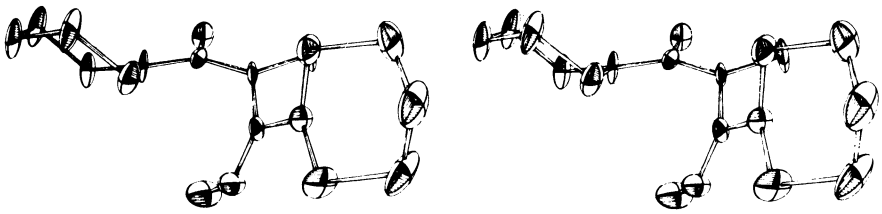

Fig. 9. Stereoscopic view down the c axis of **9**.

TABLE 10. DEVIATIONS (Å) OF THE ATOMS FROM SEVERAL LEAST-SQUARES PLANES OF **9**

Atom	Plane A	Atom	Plane B
C (14)	−0.002	C (7)	0.009
C (15)	0.002	C (8)	−0.009
C (17)	−0.002	C (10)	0.009
C (18)	0.002	C (11)	−0.009
N (13)	0.658[a)]	N (6)	0.616[a)]
O (16)	−0.707[a)]	O (9)	−0.656[a)]

a) Not included in the calculations of the planes.

TABLE 11. SELECTED TORSIONAL ANGLES (°) OF **9**

S(1)-C(2)-N(3)-C(12)	12.1	S(1)-C(2)-N(6)-C(11)	17.0
N(6)-C(2)-N(3)-C(4)	36.1	C(7)-C(2)-N(6)-N(3)	13.8
C(2)-N(3)-C(4)-N(5)	41.6	N(3)-C(4)-N(13)-C(18)	37.4
C(12)-N(3)-C(4)-N(13)	60.8	N(5)-C(4)-N(13)-C(14)	1.2

TABLE 12. INTERMOLECULAR CONTACTS WITHIN 3.7 Å OF **9**

N (5) ··· C (7) (I)	3.50	N (5) ··· C (17) (II)	3.52
C (8) ··· O (9) (III)	3.46	C (8) ··· C (10) (III)	3.66
O (9) ··· C (12) (IV)	3.61	O (9) ··· C (15) (IV)	3.63
C (10) ··· C (12) (IV)	3.68	C (10) ··· O (16) (V)	3.41
C (11) ··· O (16) (V)	3.22	C (19) ··· C (19) (VI)	3.27

(I)	1−x,	−y,	1−z
(II)	1−x,	1−y,	1−z
(III)	−x,	−1−y,	1−z
(IV)	x,	−1+y,	z
(V)	x,	−1+y,	−1+z
(VI)	1−x,	−y,	−z

in the sp^2 hybridized form due to participation with π-electrons from the neighboring double bond. In this molecule, there are three such bonds, C(2)–N(3), C(2)–N(6), and C(4)–N(13), wherein the distances are reasonable except the N(3)–C(4) distance of 1.44 Å. Lengthening of the N(3)–C(4) bond may be due to the reduction of π-bond character at this bond by twisting. The torsional angles, C(2)–N(3)–C(4)–N(5) and C(12)–N(3)–C(4)–N(13) are 41.6 and 60.8°. The dihedral angle between the mean planes consisting of C(2)–N(3)–C(12)–C(4) and N(3)–C(4)–N(13)–N(5) is 127.6°. The sums of the bond angles around nitrogen atom are 355.3, 359.9, and 353.3° for N(3), N(6), and N(13) respectively, indicating that the N(6) atom has more sp^2 character, and the other two nitrogen atoms have sp^3 character owing to the intramolecular atomic repulsion between C(12) and C(18) The interatomic distance between these atoms is 3.24 Å. A noticeably short intermolecular atomic contact is at C(19) related by a center of symmetry with a value of 3.27 Å (Table 12).

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References

1) T. Kinoshita and C. Tamura, *Tetrahedron Lett.*, **1969**, 4963.
2) D. S. Hector, *Ber.*, **23**, 357 (1890).
3) K. S. Suresh and C. N. R. Rao, *J. Indian Chem. Soc.*, **37**, 581 (1960).
4) V. K. Verma and K. M. Sarkar, *J. Sci. Ind. Res. (India)*, **21B**, 236 (1962).
5) M. Rieger and F. H. Westheimer, *J. Am. Chem. Soc.*, **72**, 19 (1950).
6) T. Kinoshita, S. Sato, and C. Tamura, "Abstracts of Third International Congress of Heterocyclic Chemistry," (1971), p. 531.
7) F. Zetzsche, E. Lüscher, and H. E. Meyer, *Ber.*, **71**, 1088 (1938).
8) H. G. Khorana and A. R. Todd, *J. Chem. Soc.*, **1953**, 2257.
9) T. Kinoshita, S. Sato, Y. Furukawa, and C. Tamura, *Heterocycles*, **3**, 83 (1975).
10) H. Salkowski, *Ber.*, **24**, 2724 (1891).
11) A. Skita and H. Rolfes, *Ber.*, **53**, 1247 (1920).
12) E. C. Horning, *Org. Synth.*, Coll. Vol. III, 617 (1955).
13) S. Sato, T. Kinoshita, T. Hata, and C. Tamura, *Acta Crystallogr., Sect. A*, **28**, S25 (1972); Independent analysis of this compound has appeared in C. Christophersen, T. Øttersen, K. Seff, and S. Treppendahl, *J. Am. Chem. Soc.*, **97**, 5237 (1975).
14) J. Karle and I. L. Karle, *J. Am. Chem. Soc.*, **89**, 804 (1967).
15) S. C. Abrahams, *Quart. Rev.*, **10**, 407 (1956).