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1,3-Oxazines and Related Compounds. VII.[1] Unusual Dimerization of 2-Alkyl-4*H*-1,3-thiazin-4-one Derivatives and the Structures of the Dimers[2]

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2-Alkyl-4*H*-1,3-thiazin-4-one derivatives (**1**) were readily dimerized on being allowed to stand at room temperature, leading to linearly combined dimers. In addition, the 1,3-thiazines (**1**) were found to be converted into another type of dimer, having a novel spiro structure, by the action of an acid such as CF_3CO_2H, $ClSO_3H$, or FSO_3H. The structures of the dimers were elucidated.

Keywords——1,3-thiazin-4-one; dimerization; spiro compound; 2-pyridone; X-ray analysis

In the preceding paper,[1] 1,3-thiazin-4-ones bearing a variety of substituents at the 2- and 6-positions of the 1,3-thiazine ring were synthesized through 1,3-oxazinium and 1,3-thiazinium salts. Among them, the 1,3-thiazin-4-ones possessing an unbranched alkyl group (such as methyl, ethyl, and *n*-propyl) at the 2-position were found to have special properties of dimerization. This paper describes the dimerization and the structures of the dimers.

Dimerization proceeded in two modes; one led to linearly combined dimers **2** when 2-alkyl-6-methyl-4*H*-1,3-thiazin-4-ones (**1**) were allowed to stand at room temperature (dimerization A), and the other resulted in the formation of novel spiro compounds **3** on treatment of **1** with acid (**4**) (dimerization B).

2,6-Dimethyl-4*H*-1,3-thiazin-4-one (**1a**), which was isolated as a liquid,[1] spontaneously dimerized on being allowed to stand at room temperature overnight to give rise to a crystalline compound **2a**, mp 169—170°C. The structural determination of **2a** was carried out on the basis of analytical and spectroscopic data such as infrared (IR), field desorption mass spectra (FD-MS), and ^1H- and ^{13}C-nuclear magnetic resonance (NMR) spectra. The results of ^1H- and ^{13}C-NMR are shown in Table IV. Compound **2a** showed signals due to three methyl groups and one methylene group. The chemical shifts of the two olefinic protons at the 5- and 5′-positions were also significant for assignment of the ring system, because they have strong structure dependence (**1**, **5**, and **6** in Fig. 1) as reported in the preceding paper.[1]

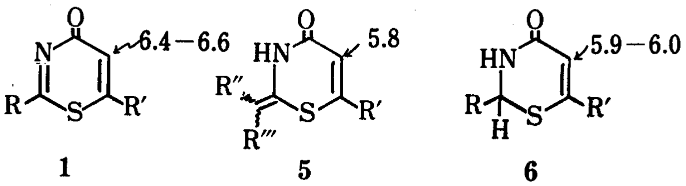

Fig. 1. Chemical Shift of 5-H on the 1,3-Thiazine Ring

1,3-Thiazin-4-ones (**1b**, **c**) were likewise transformed into the corresponding dimers **2b**, **c**, respectively (Table I). In contrast, the 1,3-thiazin-4-ones (**1d**—**f**), having an alkyl group other than methyl at the 6-position, remained unchanged, although the reason for this is obscure.

TABLE I. Dimerization into **2a—c**

Compd.	R^1	R^2	R^3	Yield (%)	mp (°C) (Solvent)	IR (KBr) cm^{-1}	Formula	Analysis (%) Calcd (Found) C	H	N
2a	H	H	H	60	169—170 (dec.) (C_6H_6)	1640	$C_{12}H_{14}N_2O_2S_2$	51.04 (51.19	5.00 4.88	9.92 9.62)
2b	Me	H	H	64	163—164 (dec.) (Acetone)	1640	$C_{14}H_{18}N_2O_2S_2$	54.17 (54.43	5.84 5.87	9.02 8.91)
2c	Et	H	H	73	179—180 (dec.) (Acetone)	1650	$C_{16}H_{22}N_2O_2S_2$	56.77 (57.00	6.55 6.54	8.28 7.99)

On the other hand, treatment of **1a** with an acid (**4**) such as trifluoroacetic acid (CF_3CO_2H), chlorosulfonic acid ($ClSO_3H$), or fluorosulfonic acid (FSO_3H) gave rise to another type of dimer (**3a**). The elemental analysis data and electron impact mass (EI-MS) spectrum of **3a** dafforde the same formula, $C_{12}H_{14}N_2O_2S_2$, as that of **2a**. The ^1H- and ^{13}C-NMR spectra of **3a** provided useful information about the structure; thus, characteristic signals due to *exo*-methylene ($>C=CH_2$), methylene ($-CH_2-$), and methine ($>CH$) groups, along with those due to two methyl groups, were distinguished.

Desulfurization of **3a** was accomplished to furnish further evidence for the structure of **3a**: that is, heating a solution of **3a** in ethanol in the presence of excess Raney nickel (Raney-Ni) for 60 h under reflux yielded the 2-pyridone derivative **7a** (Chart 1). These results suggested that the dimer **3a** has the spiro structure as formulated in Chart 1.

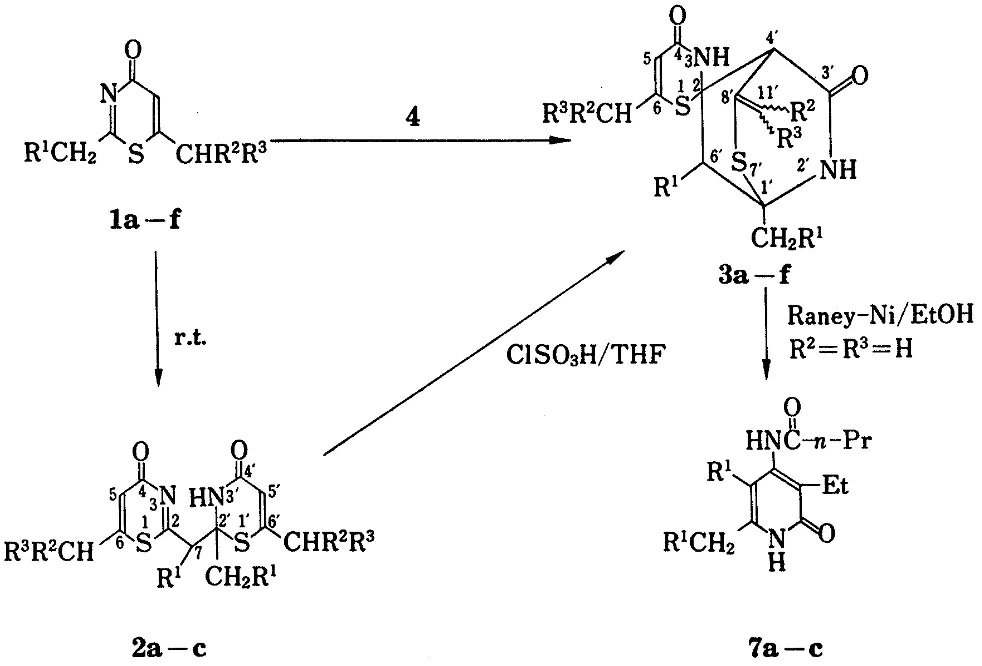

Chart 1

Similar treatment of **1b—f** with **4** afforded the corresponding dimers **3b—f**, respectively. The results are given in Table II.

Furthermore, the dimer **3a** was also obtained in an excellent yield on heating a solution of the dimer **2a** in the presence of a catalytic amount of $ClSO_3H$ in tetrahydrofuran (THF) under reflux for 6 h. Similar treatment of **1a** resulted in the quantitative recovery of **1a**.

Table II. Dimerization into **3a**—**f**

Compd.	R^1	R^2	R^3	Yield (%)	mp (°C) (Solvent)	IR (KBr) cm^{-1}	Formula	Analysis (%) Calcd (Found) C	H	N
3a	H	H	H	74	249—252 (dec.) (EtOH)	1680 1640	$C_{12}H_{14}N_2O_2S_2$	51.04 (50.85	5.00 5.09	9.92 9.98)
3b	Me	H	H	72	251—255 (dec.) (EtOH)	1685 1640	$C_{14}H_{18}N_2O_2S_2$	54.17 (53.89	5.84 5.79	9.02 8.93)
3c	Et	H	H	80	248—250 (dec.) (EtOH)	1685 1640	$C_{16}H_{22}N_2O_2S_2$	56.77 (56.96	6.55 6.71	8.28 8.00)
3d	H	Me	H	78	262—268 (dec.) (MeOH)	1690 1640	$C_{14}H_{18}N_2O_2S_2$	54.17 (54.41	5.84 5.62	9.02 8.81)
3e	H	Me	Me	80	249—253 (dec.) (MeOH)	1690 1640	$C_{16}H_{22}N_2O_2S_2$	56.77 (56.71	6.55 6.58	8.28 8.25)
3f	H	Ph	H	74	258—260 (dec.) (AcOH)	1690 1640	$C_{24}H_{22}N_2O_2S_2$	66.33 (66.10	5.10 5.03	6.45 6.31)

Hence, dimer **2** appears to be an intermediate in the dimerization of **1** into **3**, and a likely pathway of the dimerizations A and B is illustrated in Chart 2.

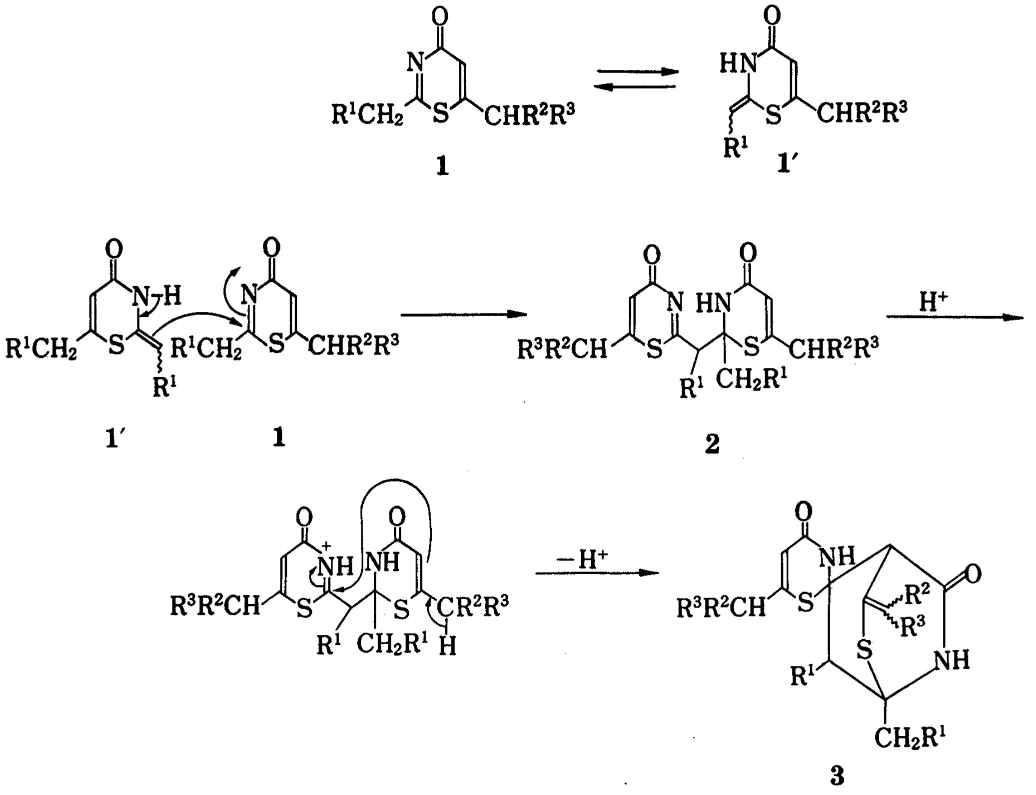

Chart 2

The complete molecular structure of **3a** was determined by X-ray crystallographic analysis. As shown in Fig. 2, the two 1,3-thiazine rings are linked to each other through the C_6 carbon atom, and are bonded between the carbon atom (C_2) at the 2-position in the 1,3-thiazine ring and a carbon ($C_{4'}$) in the other ring to form the spiro structure. The bond lengths and angles of **3a** are shown in Fig. 3. The dihedral angles between the least-squares planes were obtained as listed in Table III.

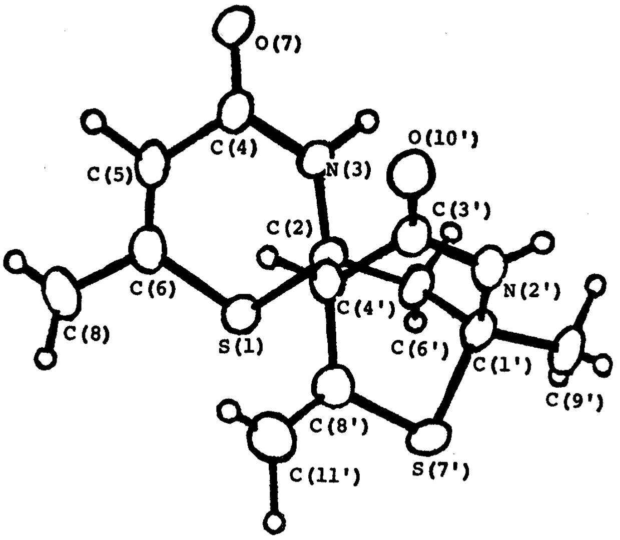

Fig. 2. Molecular Structure of 3a

TABLE III. The Least-Squares Planes and Dihedral Angles of **3a**

A—Ring: S (1), C (2), N (3), C (4), C (5), C (6)
B—Ring: C (1′), N (2′), C (3′), C (4′)
C—Ring: C (1′), N (7′), C (8′), C (4′)
D—Ring: C (1′), C (6′), C (2′), C (4′)
A-Ring—D-Ring: 93.1°
B-Ring—C-Ring: 120.5°
B-Ring—D-Ring: 121.2°
C-Ring—D-Ring: 118.3°

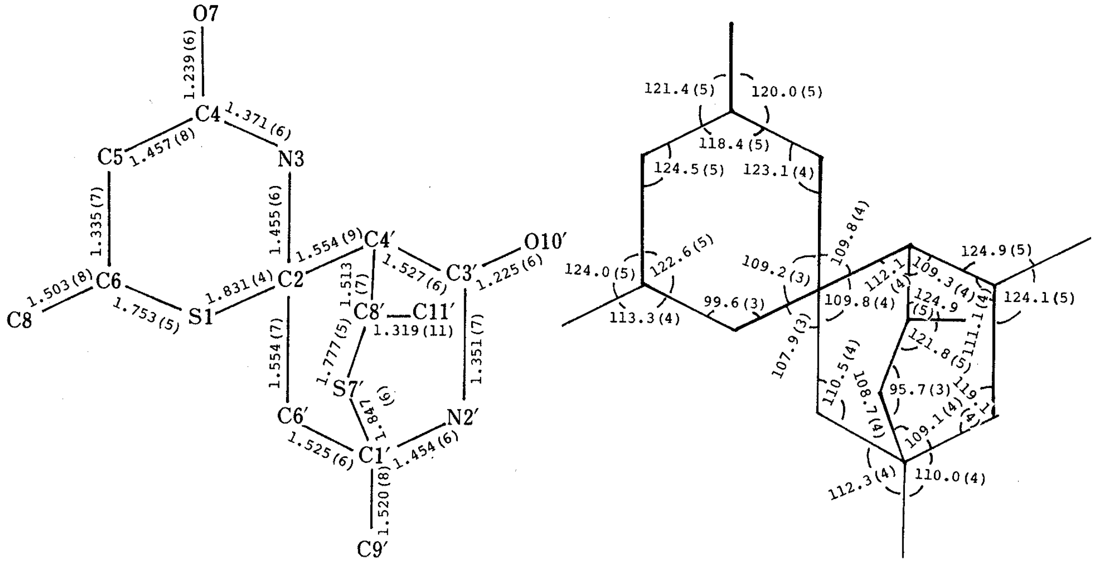

Fig. 3. Bond Lengths (Å) and Angles(°) of **3a**

Experimental

Melting points were obtained in a Mel-Temp melting point apparatus with an open capillary tube, and are uncorrected. IR spectra were taken on a Shimadzu IR-400 or IR-430 spectrometer. ^{13}C-NMR spectra were obtained on a JEOL JNM-FX 100 spectrometer. ^{1}H-NMR spectra were measured on a JEOL JNM-PMX 60 instrument. Chemical shifts are reported in δ values downfield relative to internal tetramethylsilane. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, and br=broad. EI-MS were taken on a Hitachi RMU-6MG spectrometer. FD-MS were measured on a JEOL D-300 spectrometer or on a JMS-01SG2 double-focus mass spectrometer.

Dimerization of 1 into 2——General Procedure for **2a**—**c**: 2,6-Dimethyl-4*H*-1,3-thiazin-4-one (**1a**) was allowed to stand without a solvent at room temperature for about 10 h; it changed into a crystalline material. Washing of the product with hexane, followed by recrystallization from the solvent indicated in Table I, afforded the dimer **2a**. ^{1}H- and ^{13}C-NMR data for **2** are summarized in Table IV.

Dimerization into 3 with Acid (4)——a) A typical procedure for **3a**—**f** in Table II is as follows. 1,3-Thiazine **1a** (1.4 g, 10 mmol) was dissolved in CF_3CO_2H (10 ml). The resulting solution was concentrated under an aspirator-generated vacuum. The residue was washed with ether and purified by recrystallization from the solvent indicated in Table II.

TABLE IV. ^{1}H- and ^{13}C-NMR Spectral Data for **2a**—**c** and **3a**—**f**[a]

Position[b] No.	**2a**		**2b**		**2c**	
	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR
2	165.3 (s)		165.2 (s)		165.3 (s)	
4	169.1 (s)		168.7 (s)		169.1 (s)	
5	117.7 (d)	6.50 (s)	118.1 (d)	6.47 (s)	118.0 (d)	6.50 (s)
6	151.2 (s)[d]		150.8 (s)[d]		151.0 (s)[d]	
7	52.3 (t)	3.33 (dd, J=14.20 Hz)	53.7 (d)	1.9—2.4 (m)	61.2 (d)	2.9—3.3 (m)
1′						
2′	62.8 (s)		71.1 (s)		70.3 (s)	
3′		7.16 (br)[c]		7.33 (br)[c]		6.90 (br)[c]
4′	173.1 (s)		179.2 (s)		178.9 (s)	
5′	115.9 (d)	5.93 (s)	115.3 (d)	5.83 (s)	115.4 (d)	5.83 (s)
6′	149.9 (s)[d]		148.8 (s)[d]		149.1 (s)[d]	
R^{1}CH$_2$	27.0 (q)	1.83 (3H, s)	9.2 (q) 53.7 (t)	1.03 (3H, t, J=7 Hz) 3.37 (2H, q, J=7 Hz)	12.4 (q) 18.4 (t) 38.4 (t)	0.7—1.1 (3H, m) 1.3—2.0 (4H, m)
R^{2}R^{3}CH	22.6 (q)[e]	2.30 (3H, s)	22.5 (q)[e]	2.30 (3H, s)	22.9 (q)[e]	2.30 (3H, s)
R$^{2\prime}$R$^{3\prime}$CH	23.0 (q)[e]	2.07 (3H, s)	23.0 (q)[e]	2.08 (3H, s)	23.1 (q)[e]	2.07 (3H, s)
R^1			15.7 (q)	1.47 (3H, d, J=7 Hz)	14.0 (q) 22.5 (t)	0.7—1.1 (3H, m) 1.3—2.0 (2H, m)

Position[b] No.	**3a**		**3b**		**3c**	**3d**	**3e**	**3f**
	^{13}C-NMR	^{1}H-NMR	^{13}C-NMR	^{1}H-NMR	^{1}H-NMR	^{1}H-NMR	^{1}H-NMR	^{1}H-NMR
2	62.3 (s)[d]		69.8 (s)[d]					
3		8.26 (br)[c]		8.10 (br)[c]	8.50 (br)[c]		8.87 (br)[c]	
4	168.2 (s)[e]		168.1 (s)[e]					
5	116.2 (s)	6.00 (s)	116.9 (d)	5.97 (s)	6.00 (s)	6.15 (s)	6.07 (s)	6.13 (s)
6	147.5 (s)		147.4 (s)					
1′	63.3 (s)[d]		70.6 (s)[d]					
2′		9.13 (br)[c]		9.07 (br)[c]	9.90 (br)[c]		10.10 (br)[c]	
3′	163.6 (s)[e]		163.3 (s)[e]					
4′	59.2 (d)	3.87 (s)	59.4 (d)	3.86 (s)	3.95 (s)	4.22 (s)	4.36 (s)	4.23 (s)
6′	53.3 (d)	3.33 (s)	48.6 (d)	2.6—3.3 (m)	2.6—3.4 (m)	2.53 (s)	2.47 (s)	2.56 (s)
8′	139.3 (s)		139.9 (s)					
11′	110.4 (t)	5.08 (2H, d, J=14 Hz)	109.6 (t)	5.00 (d, J=9 Hz) 5.10 (d, J=9 Hz)	4.93 (d, J=12 Hz) 5.00 (d, J=12 Hz)	5.65 (q, J=7 Hz)		6.36 (s)
R^{1}CH$_2$	22.3 (q)[f]	1.60 (3H, s)	7.4 (q) 26.5 (t)	0.98 (3H, t, J=7 Hz) 1.85 (2H, q, J=7 Hz)	0.9—2.5 (7H, m)	1.73 (3H, s)	1.67 (3H, s)	1.76 (3H, s)
R^{2}R^{3}CH	22.5 (q)[f]	2.10 (3H, s)	22.5 (q)	2.07 (3H, s)	2.10 (3H, s)	1.18 (3H, t, J=7 Hz) 2.43 (2H, q, J=7 Hz)	1.25 (6H, d, J=7 Hz) 2.3—2.8 (1H, m)	7.1—7.3 (5H, m) 3.86 (2H, s)
R^1			12.6 (q)	1.18 (3H, d, J=6 Hz)	0.9—2.5 (5H, m)			
R^2 (R^3)						1.60 (3H, d, J=7 Hz)	1.73 (6H, d, J=2 Hz)	7.1—7.3 (5H, m)

[a] CDCl$_3$ was used as a solvent for **2a**—**c**, DMSO-d_6 for **3a**—**c**,**e**, and CD$_3$COOD for **3d**,**f**.
[b] Position numbering is shown in Chart 1.
[c] Exchangeable with deuterium oxide.
[d—f] Assingments may be interchanged.

b) A solution of **2a** (0.28 g, 1 mmol) in THF (50 ml) in the presence of a catalytic amount of $ClSO_3H$ was heated for 6 h under reflux. The reaction solution was concentrated under an aspirator-generated vacuum. The residue was recrystallized from ethanol to give **3a**. Yield: 89%. Table IV summarized ^1H- and ^{13}C-NMR data for **3**.

Desulfurization of 3 with Raney-Ni——A typical procedure for **3a—c** is as follows. A mixture of **3a** (1.41 g, 5 mmol) and Raney-Ni (10 g) in 95% ethanol (100 ml) was heated for 60 h under reflux. Insoluble materials were removed by filtration and washed with 95% ethanol. The filtrate and washings were combined and concentrated under an aspirator-generated vacuum. The residue was recrystallized from acetone to give the 6-methyl-2-pyridone derivative (**7a**, 0.6 g, 54%). The results obtained are summarized in Table V.

TABLE V. Desulfurization of **3**

Compd.	R^1	Yield (%)	mp (°C) (Solvent)	IR (KBr) cm^{-1}	^1H-NMR ($CDCl_3$—CF_3COOH) δ:	Formula	Analysis (%) Calcd (Found) C	H	N
7a	H	54	241—242 (Acetone)	1650	1.0—1.3 (6H, m), 1.6—2.0 (2H, m), 2.4—2.8 (4H, m), 2.53 (3H, s), 7.70 (1H, br), 7.97 (1H, s)	$C_{12}H_{18}N_2O_2$	64.84 (65.09	8.16 8.30	12.60 12.52)
7b	Me	51.5	315—320 (MeOH)	1640	0.9—1.5 (9H, m), 1.6—2.2 (2H, m), 2.15 (3H, s), 2.4—3.1 (6H, m) 8.00 (1H, br)	$C_{14}H_{22}N_2O_2$	67.17 (66.90	8.86 8.79	11.19 11.10)
7c	Et	62.5	293—295 (MeOH)	1640	0.8—1.3 (12H, m), 1.4—2.2 (4H, m), 2.2—3.3 (8H, m), 7.80 (1H, br)	$C_{16}H_{26}N_2O_2$	69.03 (69.02	9.41 9.16	10.06 10.02)

X-Ray Analysis of 3a——Crystals were grown in acetonitrile as colorless prisms. A computer-controlled Philips PW 1100 four-circle X-ray auto diffractometer was used for all measurements. The unit cell dimensions and orientation matrix were derived from a least-squares fit of the angular values of 25 reflections. The crystal data for **3a** are listed in Table VI.

The intensity data were collected by the θ—2θ scan technique with a 2θ scan speed of 6°/min. The total number of reflections is given in Table VI.

TABLE VI. Crystal Data for **3a**

Molecular formula		$C_{12}H_{14}N_2O_2S_2$
Molecular weight		282.37
Crystal system		Triclinic
Lattice constants	a	9.7967 (3) Å
	b	9.3638 (2) Å
	c	8.6754 (3) Å
	α	115.191 (4) °
	β	69.548 (3) °
	γ	109.989 (3) °
	v	657.01Å^3
Systematic absences		none
Space group		$P\bar{1}$
Number of molecules in a unit cell	z	2
Calculated density		1.428 g/cm^3
Observed density		1.419 g/cm^3
Radiation used		Cu$K\alpha$
Theta range		$3<\theta<78°$
No. of obsd. reflections		2521

The structure of **3a** was solved by the direct method using MULTAN[3] and refined by the block-diagonal least-squares procedure. A difference Fourier synthesis was used to locate the hydrogen atoms. *R* was reduced to 6.56% after several cycles of least-squares calculation assuming anisotropic thermal parameters for the non-hydrogen atoms and isotropic ones for the hydrogen atoms. The final positional and thermal parameters are given in Table VII. The atomic scattering factors for carbon and oxygen were taken from the International Tables for X-ray Crystallography,[4] and that for hydrogen, from Stewart *et al.*[5]

TABLE VII. Positional Parameters ($\times 10^4$) and Thermal Parameters of **3a**

	X	Y	Z	$\beta 11$	$\beta 22$	$\beta 33$	$\beta 12$	$\beta 13$	$\beta 23$
S (1)	5829 (1)	8064 (2)	9170 (2)	81 (2)	94 (2)	93 (2)	20 (1)	−9 (1)	24 (1)
C (2)	7365 (5)	8436 (5)	7339 (6)	89 (6)	69 (6)	82 (7)	23 (5)	−24 (5)	14 (5)
N (3)	7876 (5)	10173 (4)	7689 (5)	105 (6)	65 (5)	78 (6)	15 (4)	−30 (5)	10 (5)
C (4)	8279 (6)	11262 (6)	9209 (6)	104 (7)	89 (7)	79 (7)	28 (6)	−22 (6)	5 (6)
C (5)	7712 (6)	10791 (6)	10758 (6)	119 (8)	106 (8)	77 (8)	33 (6)	−27 (6)	14 (6)
C (6)	6583 (6)	9530 (6)	10931 (6)	106 (8)	125 (8)	78 (8)	52 (6)	−14 (6)	24 (6)
O (7)	9025 (5)	12646 (4)	9277 (4)	148 (6)	81 (5)	94 (6)	0 (5)	−26 (5)	4 (5)
C (8)	5780 (7)	9267 (8)	12649 (7)	143 (9)	181 (11)	96 (9)	50 (8)	−0 (7)	62 (8)
C (1′)	7631 (5)	6375 (6)	4260 (6)	87 (6)	81 (7)	85 (7)	20 (5)	−28 (6)	8 (6)
N (2′)	9209 (5)	7181 (5)	4004 (5)	84 (5)	97 (6)	78 (6)	12 (5)	−22 (5)	20 (5)
C (3′)	9824 (5)	7946 (6)	5403 (6)	85 (6)	84 (7)	91 (8)	28 (5)	−21 (6)	19 (6)
C (4′)	8687 (5)	7725 (6)	7062 (6)	82 (6)	90 (7)	81 (7)	29 (5)	−21 (5)	23 (6)
C (6′)	6751 (5)	7618 (6)	5662 (6)	76 (6)	91 (7)	92 (8)	24 (5)	−34 (6)	5 (6)
S (7′)	7312 (2)	4724 (1)	5065 (2)	118 (2)	68 (2)	138 (2)	10 (1)	−42 (2)	24 (2)
C (8′)	8195 (6)	5942 (6)	6829 (6)	90 (7)	98 (7)	107 (8)	35)6)	−11 (6)	31 (6)
C (9′)	7171 (6)	5664 (7)	2532 (7)	120 (8)	125 (9)	90 (8)	26 (7)	−47 (7)	−6 (7)
O (10′)	11120 (4)	8728 (4)	5340 (5)	81 (5)	119 (6)	120 (6)	−1 (4)	−31 (4)	40 (5)
C (11′)	8388 (7)	5313 (7)	7819 (8)	153 (10)	143 (10)	163 (11)	62 (8)	−30 (8)	71 (9)
H (N3)	7954 (80)	10640 (87)	6778 (94)						
H (C5)	8297 (75)	11651 (81)	11796 (87)						
H1 (C8)	5986 (82)	8127 (89)	12717 (95)						
H2 (C8)	6071 (92)	10001 (**)	13517 (**)						
H3 (C8)	4599 (79)	9429 (85)	12947 (91)						
H (N2′)	9708 (80)	7288 (87)	3011 (94)						
H (C4′)	9160 (59)	8311 (64)	8104 (69)						
H1 (C6′)	5778 (54)	7143 (58)	5760 (63)						
H2 (C6′)	6748 (57)	8453 (62)	5094 (67)						
H1 (C9′)	7310 (61)	6699 (66)	2055 (71)						
H2 (C9′)	7633 (71)	5175 (77)	1794 (83)						
H3 (C9′)	5970 (77)	5398 (83)	2745 (89)						
H1 (C11′)	8996 (72)	5868 (78)	8514 (84)						
H2 (C11′)	8113 (79)	3903 (86)	7646 (92)						

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