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Effects of C(O)−N Bond Rotation on the ^{13}C, ^{15}N, and ^{17}O NMR Chemical Shifts, and Infrared Carbonyl Absorption in a Series of Twisted Amides

Shinji Yamada[†]

Department of Materials Science, Faculty of Science, Kanagawa University,
Hiratsuka, Kanagawa 259-12, Japan

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A series of the C(O)−N twisted amides, 3-acyl-4-alkyl-1,3-thiazolidine-2-thiones **1a**−**e**, was synthesized, and the structures were elucidated by X-ray crystallographic analysis. The relationship between the C(O)−N twist angles τ, the ^{13}C, ^{15}N, and ^{17}O NMR chemical shifts, and the infrared absorption of carbonyl groups were investigated in order to provide insight into the changes in charge distribution dependence on the C(O)−N twist angle. Furthermore, the relationship of the $\nu_{C=O}$ and the ^{15}N chemical shift was also investigated. Because the spectral data reflect considerable substituent effects, the ^{13}C and ^{17}O chemical shifts and $\nu_{C=O}$ were compared with those of corresponding *N*,*N*-dimethylamides **2a**−**c**, and the ^{15}N chemical shifts were compared with those of corresponding *N*-methyl-1,3-thiazolidine-2-thiones **3a**−**c**. As the twist angle increased, the $\Delta\delta^{13}$C and $\Delta\delta^{17}$O increased, whereas, the $\Delta\delta^{15}$N decreased. Furthermore, the $\Delta\nu_{C=O}$ increased with increasing τ and decreased with increasing $\Delta\delta^{15}$N. The relationship of the results to the classical amide resonance model and recently proposed model is also discussed.

Introduction

The structure and spectroscopic properties of twisted amides have recently received considerable attention not only in organic chemistry[1−3] but also in biochemistry.[4] The influence of the rotation about the C(O)−N bond on IR,[5] UV,[6] and ^{1}H,[7] ^{13}C,[8] , ^{15}N[9] NMR and ESCA[10] spectroscopic data has been studied, and large differences between those in planar and twisted amides have been observed. The differences are attributable to the reducing of amide resonance[11] throughout the C(O)−N bond rotation. However, the quantitative and systematic relationships between the twist angles and the spectroscopic data have not always been explored. In particular, there has been no investigation of the ^{17}O NMR chemical shift dependence of the C(O)−N twist angles, although it has been recognized that the ^{17}O NMR chemical shift is more sensitive to structural variation than the shifts of ^{13}C and ^{15}N.[12,13]

The resonance model in amides[11] has been generally accepted to interpret their chemical and physical properties; however, it was challenged[14] on the basis of comparison of the calculated C, N, O electron populations between planar **I** and twisted **IV** amides calculated with Bader's method.[15] In the calculation, the electron population of N in planar form **I** is larger than that in twisted form **IV**, whereas the electron population of C in **I** is less than that in **IV** and that of O in **I** is a little larger than that in **IV**.[16] These results do not fit the classical resonance model (eq 1); therefore, Wiberg and Rablen proposed a new resonance model (eq 2)[17] instead of the classical one. The new model describes that the dominant canonical contributor is highly polarized **III**, and consequently the nitrogen lone pair can donate electrons to the carbon without needing to further displace much charge density from the carbon to the oxygen. In connection with the calculation and the new model, a number of theoretical studies have been extensively undertaken;[18−26] however, there have been only a few experimental approaches.[10b,25]

[†] Present address: Department of Chemistry, Faculty of Science, Ochanomizu University, Bunkyo-ku, Tokyo 112, Japan.

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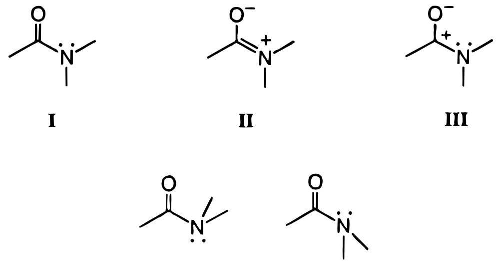


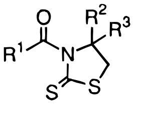
I **II** **III**

IV

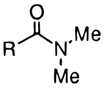
$$\mathbf{I} \longleftrightarrow \mathbf{II} \qquad (1)$$

$$\mathbf{I} \longleftrightarrow \mathbf{III} \longleftrightarrow \mathbf{II} \qquad (2)$$

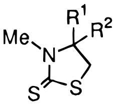
We have previously reported[3] that the C(O)−N bond of 3-pivaloyl-1,3-thiazolidine-2-thione (**1c**) is highly twisted, whereas that of 3-acetyl-1,3-thiazolidine-2-thione (**1a**) is almost planar; both results were confirmed by X-ray crystallographic analysis. We describe here the relationships between C(O)−N twist angles and the ^{13}C, ^{15}N, and ^{17}O NMR chemical shifts and the infrared carbonyl absorption of a series of 3-acyl-1,3-thiazolidine-2-thione derivatives **1a**−**e** in order to provide insight into the changes in charge distribution dependence on the C(O)−N bond rotation. Furthermore, the relationship to the proposed and classical resonance models will also be described.



1a R^1 = Me; R^2, R^3 = H
1b R^1, R^2, R^3 = Me
1c R^1 = *t*-Bu; R^2, R^3 = H
1d R^1 = *t*-Bu; R^2 = *i*-Bu; R^3 = H
1e R^1 = CH_2Ph; R^2, R^3 = H



2a R = Me
2b R = *t*-Bu
2c R = CH_2Ph



3a R^1, R^2 = H
3b R^1, R^2 = Me
3c R^1 = *i*-Bu, R^2 = H

Results and Discussion

Synthesis of a Series of Twisted Amides. A series of twisted amides **1a**−**e** having a variety of twist angles between 0−90°, and *N*-methyl-1,3-thiazolidine-2-thiones **3a**−**c**, which are partial structures of **1a**−**e**, were synthesized. The amides **1a**,[27] **1c**, and **1e**[28] were prepared by the acylation of commercially available 1,3-thiazolidine-2-thione with acetyl, pivaloyl, and phenylacetyl chloride, respectively. Similarly, acetylation of 4, 4-dimethyl-1,3-thiazolidine-2-thione[29] and pivaloylation of 4-isobutyl-1,3-thiazolidine-2-thione gave **1b** and **1d**. *N*-Methyl-1,3-thiazolidine-2-thiones **3a**−**c** were prepared from the corresponding *N*-methylamino alcohols with carbon disufide in alkaline solution.

Table 1. Selected Structural Parameters for 1a−e

compd	χ_C (deg)	χ_N (deg)	τ (deg)	r(C(O)−N) (Å)	r(C(S)−N) (Å)	r(C=O) (Å)
1a[a]	4.3	11.9	20.1	1.413(9)	1.380(8)	1.21(1)
1b[b]	5.8	11.6	36.5	1.432(3)	1.363(3)	1.210(3)
1c[a]	8.3	29.5	74.3	1.448(4)	1.351(4)	1.196(4)
1d[b]	8.3	31.4	65.5	1.466(5)	1.340(5)	1.195(5)
1e[b]	0.6	13.4	10.2	1.415(6)	1.372(6)	1.203(7)

[a] Reference 3. [b] Reference 36.

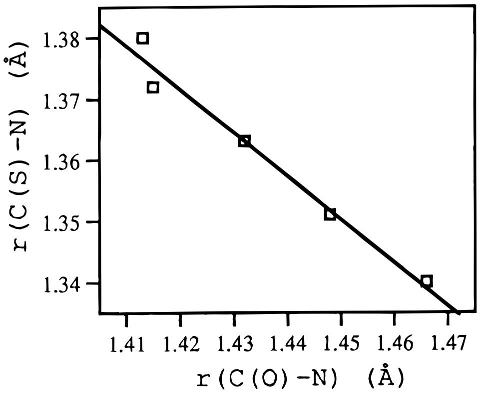


Figure 1. Plot of r(C(S)−N) vs r(C(O)−N).

X-ray Crystallographic Analysis. Table 1 shows the Dunitz parameters τ, χ_N, and χ_C,[30] which symbolize the C(O)−N twist angle, N-pyramidalization, and C-pyramidalization, respectively, and the structural parameters r(C(O)−N), r(C(S)−N) and r(C=O) of **1a**−**e**.

The value of the twist angles τ lies in the range of 10° to 75°. The carbonyl group and the thiazolidine-2-thione ring of **1a** and **1e** are almost coplanar, whereas those of **1c** and **1d** are nearly orthogonal because of their steric repulsion between the bulky *t*-Bu and C=S groups. In amide **1b**, the *gem*-dimethyl group at the C-4 twists the C(O)−N bond to produce a twist angle of 36.5°, which is almost half the value of those of **1c** and **1d**. Although **1c** and **1d** have large twist angles, their χ_N values are much smaller than those of reported distorted amides.[31] χ_C values are scarcely influenced by τ. The r(C(O)−N) of **1a**−**e** are longer than the general C(O)−N bond length,[32] in particular, that of **1d** is 1.466(5) Å, which may be the longest value ever reported for C(sp^2)−N bonds.[31] On the other hand, their r(C(S)−N) are shorter than that of thiazol-2(3*H*)-thiones[33] of which framework structures are similar to those of **1a**−**e**. An increase in the twist angle causes lengthening of the C(O)−N bond and shortening of the C(S)−N bond. Figure 1 shows the relationship between r(C(O)−N) and r(C(S)−N). As the r(C(O)−N) becomes shortened, the r(C(S)−N) lengthens linearly. These observations can explain that the lone pair of the N atom partly distributes to the C=S bond.[34] In contrast to the r(C(O)−N), r(C=O) remains virtually unchanged during the C−N bond rotation. Such inde-

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Table 2. ^{13}C, ^{15}N, and ^{17}O NMR Chemical Shifts (δ, ppm) for **1a**−**e**, ^{13}C, and ^{17}O Chemical Shifts (δ, ppm) for **2a**−**c**, and ^{15}N Chemical Shifts (δ, ppm) for **3a**−**c**

compd	$\delta\,^{13}C^a$	$\delta\,^{15}N^b$	$\delta\,^{17}O^c$	compd	$\delta\,^{13}C^a$	$\delta\,^{17}O^c$	compd	$\delta\,^{15}N^b$	$\Delta\delta\,^{13}C$	$\Delta\delta\,^{15}N$	$\Delta\delta\,^{17}O$
1a	171.3	−184.8	438	**2a**	170.6	338	**3a**	−234.0	0.7	49.2	100
1b	174.3	−168.3	476	**2a**	170.6	338	**3b**	−215.4	3.7	47.1	138
1c	187.8	−195.2	506	**2b**	177.5	340	**3a**	−234.0	10.3	38.8	166
1d	189.0	−182.5	513	**2b**	177.5	340	**3c**	−223.6	11.5	41.0	173
1e	172.8	−185.7	436	**2c**	171.0	335	**3a**	−234.0	1.8	48.3	101

[a] Recorded at 100.4 MHz in $CDCl_3$. Chemical shifts are referred to internal TMS. [b] Recorded at 40.4 MHz in C_6D_6. Chemical shifts are referred to internal CH_3NO_2. [c] Recorded at 54.1 MHz in CD_3CN. Chemical shifts are referred to external H_2O. Linewidths at half heights: see reference 36.

pendence of C=O bond lengths on twist angles has also been observed in bicyclic distorted amides.[35]

It has been reported that rotation of the C(O)−N bond is generally accompanied by N-pyramidalization, because the hybridization of amide nitrogen changes from sp^2 to sp^3 during the rotation.[31] Therefore, it is generally difficult to avoid such an intrinsic property in the synthesis of twisted amides. It is noteworthy that the changes in χ_N values of the present model compounds with τ are relatively very small compared to the reported distorted amides.[1,35] Therefore, they will be suitable models to investigate the net effect of rotation about the C(O)−N bond on spectroscopic data.

^{13}C, ^{15}N, and ^{17}O NMR Chemical Shift.[36] The relationships of ^{13}C, ^{15}N, and ^{17}O NMR chemical shifts with twist angles were explored. Table 2 shows the ^{13}C, ^{15}N, and ^{17}O NMR chemical shifts for **1a**−**e** and those for **2a**−**c** and **3a**−**c** which are partial structures of **1a**−**e**. In order to compensate for the substituent effects around the carbonyl groups, the $\Delta\delta^{13}$C and $\Delta\delta^{17}$O values are given as the differences in the ^{13}C and ^{17}O chemical shifts between **1a**−**e** and the corresponding *N*,*N*-dimethylamides **2a**−**c**. Similarly, the $\Delta\delta^{15}$N values represent the difference in the ^{15}N chemical shifts between **1a**−**e** and the corresponding *N*-methyl-1,3-thiazolidine-2-thione derivatives **3a**[37] −**c**. The reason for employing the *N*-methyl derivatives is to eliminate the aggregation effect on the chemical shifts.[38]

Figure 2, parts a−c, show the plots of τ with the $\Delta\delta^{13}$C, $\Delta\delta^{15}$N, and $\Delta\delta^{17}$O, respectively. As shown in Figure 2a, the $\Delta\delta^{13}$C values lie in the range of 1−12 ppm and $\Delta\delta^{13}$C increases with increasing τ. It has been suggested that substituent groups that contribute to resonance at a carbonyl carbon decrease the electron deficiency and cause an upfield shift of the carbon.[39] The present relation suggests that the N atom in the planar amides serves as an electron donor.

The $\Delta\delta^{15}$N values lie in the range of 39−49 ppm. As shown in Figure 2b, $\Delta\delta^{15}$N decreases with increasing τ value. The slope in Figure 2b is opposite to that in Figure 2a. In the ^{15}N chemical shift, the paramagnetic term in the Ramsey equation is considered to be dominant, and this term is influenced by a complex mixture of inductive, steric, and conjugation effects.[40] Because the present compounds have a similar framework structure and their χ_N values are close together, the term seems to be largely affected by the charge density of the N atom. Therefore,

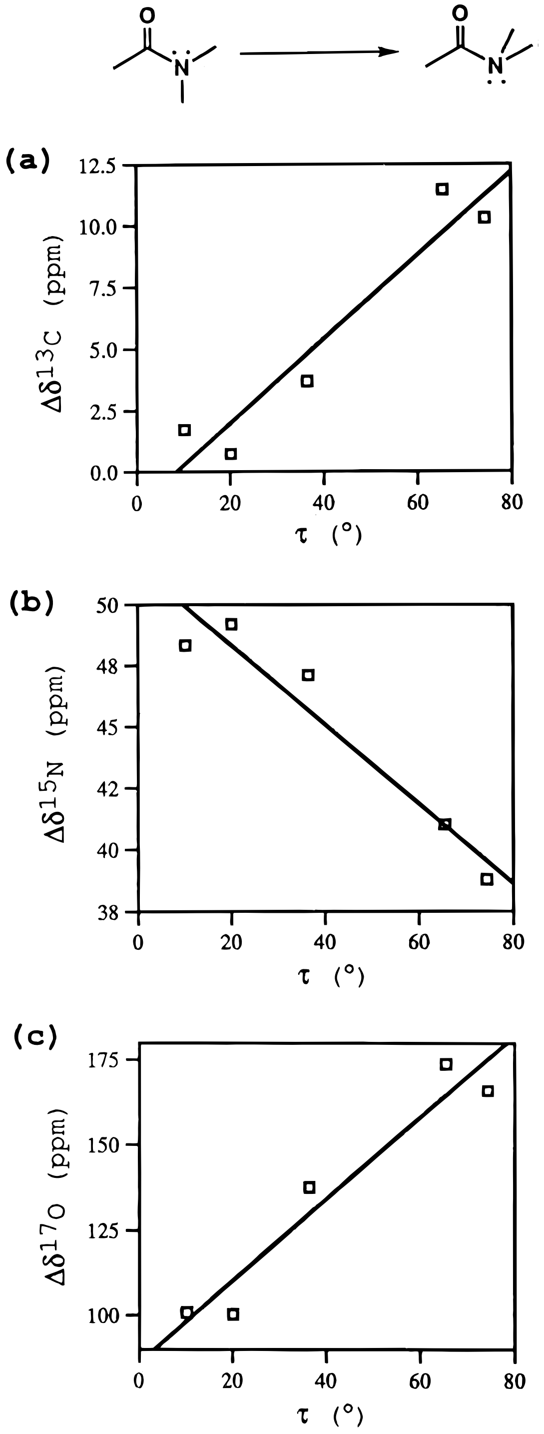

Figure 2. Plots of (a) $\Delta\delta\,^{13}$C vs τ; (b) $\Delta\delta\,^{15}$N vs τ; (c) $\Delta\delta\,^{17}$O vs τ.

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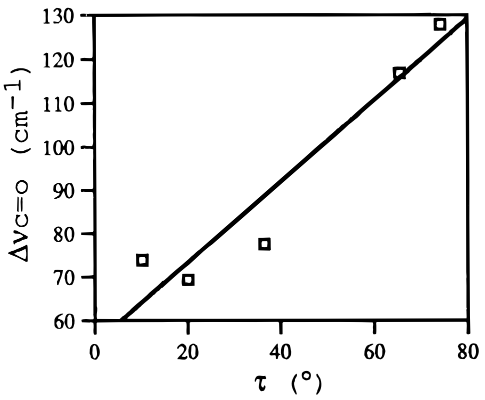

Figure 3. Plot of $\Delta\nu_{C=O}$ vs τ.

Table 3. IR C=O Frequencies (cm^{-1}) for 1a–e and 2a–c in CHCl$_3$

compd	$\nu_{C=O}$	compd	$\nu_{C=O}$	$\Delta\nu_{C=O}$
1a	1704.0	**2a**	1634.6	69.4
1b	1712.2	**2a**	1634.6	77.6
1c	1738.4	**2b**	1610.6	127.8
1d	1727.4	**2b**	1610.6	116.8
1e	1711.5	**2c**	1637.6	73.9

the result also suggests that the N atom acts as an electron donor in the planar form.

The range of the $\Delta\delta^{17}$O (100–173 ppm) is much larger than those of the $\Delta\delta^{13}$C and $\Delta\delta^{15}$N. A plot of $\Delta\delta^{17}$O vs τ is given in Figure 2c. An almost linear relationship was observed between them; increasing the twist angle causes a increase in the $\Delta\delta^{17}$O value. The slope was similar to that in Figure 2a but opposite to that in Figure 2b. It has been known that the structural variation generally causes serious effects on the chemical shifts.[13] Because these amides have similar structures, the influence on the chemical shift arising from the structural differences among them should be negligible. Moreover, the influence of the NC(S)S ring on the chemical shift of the carbonyl groups seems to be very small because the NC(S)S and carbonyl groups are not very close together. In general, ^{17}O NMR chemical shifts are thought to be essentially dependent upon the paramagnetic term which is proportional to the charge density.[13] Therefore, the changes in $\Delta\delta^{17}$O are largely ascribed to those in the charge density of the O atom during C(O)–N bond rotation.

These results suggest that the rotation of C(O)–N bond causes increasing in the positive charge densities of C and O and decreasing in that of N.

IR (C=O) Frequency. Table 3 shows the carbonyl stretching frequencies of **1a**–**e** and the standard *N*,*N*-dimethylamides **2a**–**c** in CHCl$_3$ and $\Delta\nu_{C=O}$, which represents the difference between **1** and **2**. Because the substituents at the carbonyl groups affect the carbonyl stretching frequencies, the net effect in the rotation about the C(O)–N bond is represented by $\Delta\nu_{C=O}$. The values for **1a** and **1e** are 69.4 and 73.9 cm^{-1}, whereas those of highly twisted amides **1c** and **1d** containing a bulky *t*-Bu group are 127.8 and 116.8 cm^{-1}. The value of the amide **1b** is 77.6 cm^{-1}. Figure 3 shows a plot of the $\Delta\nu_{C=O}$ vs τ. As the twist angle increases, the $\Delta\nu_{C=O}$ also increases. The tendency is similar to those in the relationships of τ with the $\Delta\delta^{13}$C or $\Delta\delta^{17}$O. In the plot of the $\Delta\nu_{C=O}$ vs $\Delta\delta^{15}$N, good correlation was observed as shown in Figure 4. It has been known that the $\nu_{C=O}$ decreases with increasing electron-donating ability of the substituent; therefore, these results also indicate that the N atom donates the lone pair electron to the carbonyl group in the planar form, and the effect decreases with increasing twist angle. In the reported relationship between the $\Delta\delta^{15}$N and $\nu_{C=O}$ of toluamides,[26] general correlation was not observed. This seems to be ascribed to the structural diversity among a variety of the amides used.

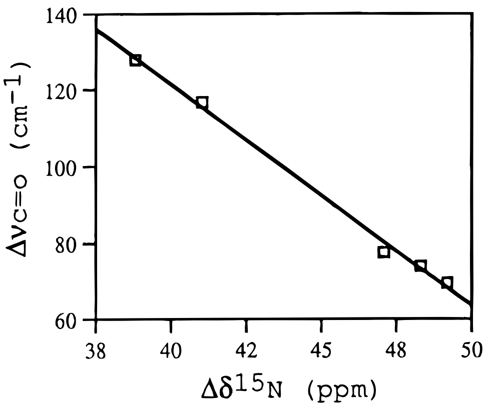

Figure 4. Plot of $\Delta\nu_{C=O}$ vs $\Delta\delta$ ^{15}N.

Conclusions

Present studies elucidated the relationships between the degree of twisting of C(O)–N bond and the ^{13}C, ^{15}N, and ^{17}O NMR chemical shifts and the $\nu_{C=O}$. As the twist angle increases, the $\Delta\delta^{13}$C, $\Delta\delta^{17}$O, and $\Delta\nu_{C=O}$ increase, whereas the $\Delta\delta^{15}$N decreases. Although the NMR chemical shifts are influenced by various effects, the ^{13}C, ^{15}N, and ^{17}O NMR chemical shifts are thought to be mainly attributed to their charge densities within the series of structurally related compounds. Therefore, these results can be explained in terms of the classical amide resonance model (eq 1). Thus, an increase in the twist angle interrupts the contribution of the canonical form **II**; as a result, it leads to a decrease in the charge density of the C, O atoms and an increase in that of the N atom. The relationship of $\Delta\nu_{C=O}$ to τ also supports the classical model. Thus, an increase in $\Delta\nu_{C=O}$ with increasing τ indicates that the N atom acts as an electron donor to the carbonyl group in the planar form. Furthermore, the correlation of the $\Delta\nu_{C=O}$ with $\Delta\delta^{15}$N in Figure 4 strongly suggests the role of the N atom as an electron donor. According to the calculations of planar (**I**) and twisted (**IV**) amides by Wiberg and Leidig,[14,16] the charge densities of C and N are opposite of what would be expected on the basis of a classical resonance model, and the charge density of O in **I** is a little larger than that in **IV**. However, the present results are not in agreement with the calculations.

The proposed model[17] (eq 2), where the contribution of the C$^+$–O$^-$ canonical structure **III** is predominant, indicates that there is no correlation in the charge densities between N and O atoms during the C(O)–N bond rotation and that the charge density on the O atom is little affected by the twist angle. However, the observations that the $\Delta\delta^{17}$O and $\Delta\nu_{C=O}$ increase with increasing τ and decrease with increasing $\Delta\delta^{15}$N are not in agreement with the model.

Although insight into the existence of amide resonance was obtained with spectroscopic studies of the series of twisted amides, the relative independence of the C=O bond length on the twist angle compared to the C(O)−N still remains to be explained.

Experimental Section

Melting points are uncorrected. Silica gel chromatography was carried out using Wakogel C-200 or Florisil (100−200 mesh). Infrared spectra were obtained as a $CHCl_3$ solution using NaCl chamber. ^1H NMR spectra were obtained at 400 MHz as dilute solutions in $CDCl_3$, and the chemical shifts were reported relative to internal TMS. ^{13}C NMR spectra were obtained at 100.4 MHz as a 0.5 M solution in $CDCl_3$, and chemical shifts were reported relative to internal TMS. ^{15}N NMR spectra were acquired at natural abundance on 2 M solution in benzene-d_6 at 40.4 MHz. The chemical shifts were referenced to internal CH_3NO_2. Each spectrum was obtained using a repetition rate of 8.0 s, an acquisition time of 0.41 s, and a total accumulation of 2×10^3 to 6×10^3. ^{17}O NMR spectra were acquired at natural abundance on 2−3 M solution in CD_3CN at 54.1 MHz. Each spectrum was obtained using an acquisition delay of 0.2 s, an acquisition time of 0.33 s and a total accumulation of 10^4 to 2×10^5. The chemical shifts were referenced to external H_2O. High and low-resolution mass spectra were recorded at an ionizing voltage of 70 eV by electron impact. Elemental analyses were performed at Faculty of Pharmaceutical Science, Hokkaido University, and were within 0.3% of the theoretical values.

3-Acetyl-4,4-dimethyl-1,3-thiazolidine-2-thione (1b). To a solution of 4,4-dimethyl-1,3-thiazolidine-2-thione (1.0 g, 6.8 mmol) and triethylamine (1.36 g,13.6 mmol) in dichloromethane (30 mL) was added dropwise acetyl chloride (0.65 g, 8.16 mmol) at 0 °C. The solution was stirred for 8 h at rt. The reaction mixture was washed with water and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a crude **1b** which was subjected to column chromatography (40 g of Florisil) with a 2:1 mixture of $CHCl_3$ and hexane to give a pure specimen (1.10 g, 85.6%). A sample for analysis was obtained by recrystallization from hexane−ether: mp 74.5−75.5 °C; IR (KBr) 1709, 1311, 1256, 1220, 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.65 (6H, s), 2.66 (3H, s), 3.19 (2H, s); ^{13}C NMR ($CDCl_3$) δ 25.27, 28.49, 44.40, 74.41, 174.29, 201.83; MS m/z 189 (M^+, 100), 147 (22), 132 (14), 100 (38), 88 (32). Anal. Calcd for $C_7H_{11}NOS_2$: C, 44.42; H, 5.86; N, 7.40. Found: C, 44.48; H, 5.98; N, 7.43.

4-Isobutyl-1,3-thiazolidine-2-thione. Leucinol (5.0 g, 42.7 mmol) and potassium hydroxide (5.0 g, 90.9 mmol) were dissolved in a 5:1 mixed solvent of EtOH and H_2O (60 mL). Then CS_2 (6.0 g, 78.9 mmol) was added dropwise to the solution and refluxed for 18 h. The solution was neutralized with 2 N HCl and then extracted with three 30 mL portions of $CHCl_3$. The combined organic layer was dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a crude product, which was recrystallized from hexane−ether to give a pure specimen (4.3 g, 58%): mp 52−54 °C; IR (KBr) 3145, 2958, 1508, 1468, 1307, 1034, 1016 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.96 and 0.97 (each 3H, d, J = 6.34 Hz), 1.49−1.54 (1H, m) 1.66−1.77 (2H, m), 3.22 (1H, d, J = 10.74, 7.81 Hz), 3.59 (1H, dd, J = 10.74, 7.32 Hz), 4.33 (1H, m), 8.05 (1H, br s); ^{13}C NMR δ 22.3, 22.68, 25.29, 38.92, 42.98, 62.71, 200.56; MS m/z 175 (M^+, 10), 118 (9), 86 (54), 55 (100).

4-Isobutyl-3-pivaloyl-1,3-thiazolidine-2-thione (1d). To a solution of 4-isobutyl-1,3-thiazolidine-2-thione (2.0 g, 11.4 mmol) and triethylamine (2.29 g, 22.9 mmol) in dry dichloromethane (50 mL) was added dropwise pivaloyl chloride (1.65 g, 13.7 mmol) at 0 °C. The solution was stirred for 8 h at rt. The reaction mixture was washed with water and dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a crude **1d** which was recrystallized from ether to give pure crystals (2.4 g, 81%): mp 88.5−91.5 °C; IR (KBr) 2970, 1720, 1365, 1342, 1296, 1275, 1244, 1183; ^1H NMR ($CDCl_3$) δ 0.92 and 0.97 (each 3H, d, J = 6.34 Hz), 1.40 (9H, s), 1.58−1.69 (2H, m), 3.26 (1H, dd, J = 11.23, 9.77 Hz), 3.52 (1H, dd, J = 11.23, 6.84 Hz), 4.59 (1H, m); ^{13}C NMR δ 20.92, 23.90, 25.04, 27.85, 37.09, 41.53, 44.29, 68.38, 118.95, 200.07; MS m/z 259 (M^+, 21), 202 (3), 174 (7), 142 (8), 118 (15), 85 (19), 55 (100). Anal. Calcd for $C_{12}H_{21}NOS_2$: C, 55.56; H, 8.16; N, 5.40. Found: C, 55.50; H, 8.31; N, 5.44.

4,4-Dimethyl-3-methyl-1,3-thiazolidine-2-thione (3b). 2-Methyl-2-(N-methylamino)propyl hydrogen sulfate (3.0 g, 16.3 mmol) and potassium ethyl xanthate (4.0 g, 25 mmol) were dissolved in 10 mL of 2 N NaOH. The solution was stirred at 80 °C for 20 h. The reaction mixture was neutralized with 2 N HCl and extracted with three 30 mL portions of $CHCl_3$. The combined organic layer was dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a crude **3b**. This was purified with silica gel column chromatography using a 2:1 mixture of chloroform and hexane as an eluent solvent to give crystals (1.6 g, 61%): mp 43−44 °C; IR (KBr) 2965, 1482, 1383, 1240, 1109, 1071, 989 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.42 (6H, s), 3.16 (3H, s); ^{13}C NMR δ 24.71, 31.46, 41.26, 70.76, 195.17; MS m/z 161 (M^+, 100), 146 (28), 105 (59). Anal. Calcd for $C_6H_{11}NS_2$: C, 44.68; H, 6.87; N, 8.68. Found: C, 44.74; H, 7.05; N, 8.77.

4-Isobutyl-3-methyl-1,3-thiazolidine-2-thione (3c). 4-Methyl-2-(N-methylamino)pentyl hydrogen sulfate (3.0 g, 14.2 mmol) and potassium ethyl xanthate (3.5 g, 21.9 mmol) were dissolved in 15 mL of 2 N NaOH. The solution was stirred at 80 °C for 10 h. The reaction mixture was neutralized with 2 N HCl and extracted with three 30 mL portions of $CHCl_3$. The combined organic layer was dried over anhydrous $MgSO_4$. Evaporation of the solvent gave a crude **3c**. This was purified with silica gel column chromatography using a 1:1 mixture of chloroform and hexane as an eluent solvent to give crystals (1.8 g, 67%): mp 66.5−67 °C; IR (KBr) 2952, 1490, 1396, 1303, 1220, 1113 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.97 and 1.01 (each 3H, d, J = 6.35 Hz), 1.56 (1H, m), 1.72 (2H, m), 2.97 (1H, dd, J = 11.23, 4.39 Hz), 3.50 (1H, dd, J = 11.23, 8.30 Hz), 4.19 (1H, m); ^{13}C NMR δ 21.45, 23.72, 24.95, 32.50, 35.30, 39.83, 68.84, 195.74. Anal. Calcd for $C_8H_{15}NS_2$: C, 50.75; H, 7.99; N, 7.40. Found: C, 50.78; H, 8.03; N, 7.37.

X-ray Crystallographic Analysis of 1b.[41] A colorless crystal with dimensions $0.3 \times 0.35 \times 0.4$ mm of **1b** was used for data collection. The lattice parameters and intensity data were measured at 23 °C on a Rigaku AFC5S diffractometer with graphite-monochromated Mo Kα radiation (l = 0.71069 Å). Crystal data for **1b** at 296K: $C_7H_{11}NOS_2$, M = 189.29, monoclinic, space group $P2_1/c$, a = 7.521(1), b = 13.735(2), c = 9.051(2) Å, β = 93.56(2)°, V = 933.1(3) $Å^3$, Z = 4, r_{calcd} = 1.347 g cm^{-3}. The structure was solved by direct methods, and the non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 1166 observed reflections to give R = 0.038 and Rw = 0.043. All calculations were performed using TEXANE crystallographic software package developed by Molecular Structure Corp. (1985).

X-ray Crystallographic Analysis of 1d.[41] A colorless crystal with dimensions $0.3 \times 0.4 \times 0.4$ mm of **1d** was used for data collection. The lattice parameters and intensity data were measured at 23 °C on a Rigaku AFC5S diffractometer with graphite-monochromated Cu Kα radiation (l = 1.54178 Å). Crystal data for **1d** at 296 K: $C_{12}H_{21}NOS_2$, M = 259.42, monoclinic, space group $P2_1$, a = 5.9956(8), b = 12.692(1), c = 9.7791(6) Å, β = 98.813(8)°, V = 735.4(1) $Å^3$, Z = 4, r_{calcd} = 2.343 g cm^{-3}. The structure was solved by direct methods, and the non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 1057 observed reflections to give R = 0.038 and Rw = 0.046. All calculations were performed using TEXANE crystallographic software package developed by Molecular Structure Corp.

X-ray Crystallographic Analysis of 1e.[41] A colorless crystal with dimensions $0.35 \times 0.35 \times 0.4$ mm of **1e** was used for data collection. The lattice parameters and intensity data were measured at 23 °C on a Rigaku AFC5S diffractometer with graphite-monochromated Cu Kα radiation (l = 1.54178

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(41) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

Å). Crystal data for **1e** at 296 K: $C_{11}H_{11}NOS_2$, $M = 237.33$, monoclinic, space group $P2_1/c$, $a = 11.518(1)$, $b = 7.7755(6)$, $c = 12.6752(6)$ Å, $\beta = 90.519(6)°$, $V = 1135.1(2)$ Å^3, $Z = 4$, $r_{\mathrm{calcd}} = 1.389$ g cm^{-3}. The structure was solved by direct methods, and the non-hydrogen atoms were refined anisotropically. The final cycle of full-matrix least-squares refinement was based on 1408 observed reflections to give $R = 0.068$ and $Rw = 0.091$. All calculations were performed using TEXANE crystallographic software package developed by Molecular Structure Corp.

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