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Mass Spectrometry of 2-Alkylthio-2-methylpropanoic Acids and Their Esters and Amides.[1a] Structural and Steric Effects on the McLafferty Rearrangement

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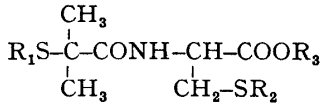
The electron ionization mass spectra (MS) of *S*-methylated derivatives of *N*-(2-mercapto-2-methylpropanoyl)-L-cysteine and 2-alkylthio-2-methylpropanoic acids, as well as their esters and amides, were examined. Use of the deuterium labeling technique and accurate mass measurement supported the proposed fragmentation pathways.

Extensive loss of CH_2S from a molecular ion by the McLafferty rearrangement of a primary hydrogen is important in the MS of *S*-methyl compounds of amide derivatives. It was demonstrated that the intensity of the rearrangement ion decreases in the order of amide, ester, and acid, and in the case of amides the rearrangement is suppressed by the nonbonded interaction between methyl groups on the α carbon and the amide nitrogen.

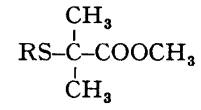
Keywords——*N*-(2-mercapto-2-methylpropanoyl)-L-cysteine; 2-alkylthio-2-methylpropanoic acid and methyl ester; 2-alkylthio-2-methylpropanamide; electron impact mass spectrometry; McLafferty rearrangement; steric interaction

In connection with the synthetic study of a series of mercaptoacyl amino acids with inhibitory activity against angiotensin I-converting enzyme,[1b] we have examined the mass spectra of the metabolites of *N*-(2-mercapto-2-methylpropanoyl)-L-cysteine (**1**) and have encountered intense McLafferty rearrangement ions in the electron ionization mass spectra (MS) of *S*-methyl compounds of **1**; a hydrogen of the *S*-methyl group of the 2-propanoyl moiety transfers to the carbonyl oxygen, resulting in the loss of CH_2S from the molecular ions.[2]

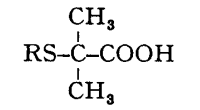
In the so-called McLafferty rearrangement,[3] it has generally been accepted that transfer of a primary hydrogen occurs only in low abundance and a secondary hydrogen is abstracted more readily than a primary one.[4] Therefore, the abundant loss of CH_2S from the molecular



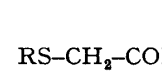
1: $R_1=R_2=R_3=H$
2: $R_1=H$, $R_2=R_3=CH_3$
3: $R_1=R_3=CH_3$, $R_2=H$
4: $R_1=R_2=R_3=CH_3$
5: $R_1=CD_3$, $R_2=R_3=CH_3$



6: $R=CH_3$
7: $R=C_2H_5$
8: $R=n\text{-}C_3H_7$
9: $R=\text{iso-}C_3H_7$
10: $R=CH_2C_6H_5$

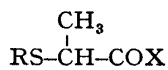


11: $R=CH_3$
12: $R=C_2H_5$
13: $R=n\text{-}C_3H_7$
14: $R=\text{iso-}C_3H_7$
15: $R=CH_2C_6H_5$



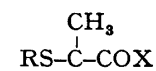
26a—i

a: $R=CH_3$, $X=NH_2$
b: $R=CH_3$, $X=NHCH_3$
c: $R=CH_3$, $X=N(CH_3)_2$



27a—i

d: $R=n\text{-}C_3H_7$, $X=NH_2$
e: $R=n\text{-}C_3H_7$, $X=NHCH_3$
f: $R=n\text{-}C_3H_7$, $X=N(CH_3)_2$



28a—i

g: $R=CH_2C_6H_5$, $X=NH_2$
h: $R=CH_2C_6H_5$, $X=NHCH_3$
i: $R=CH_2C_6H_5$, $X=N(CH_3)_2$

Chart 1

ion observed here is unusual. This observation prompted us to study in detail the structural factors affecting the rearrangement. For this purpose, we examined the MS of 2-alkylthio-2-methylpropanoic acids (**11**—**15**) and their esters (**6**—**10**) and amides (**26a**—**i**), (**27a**—**i**), and (**28a**—**i**).

Results and Discussion

MS of *N*-(2-Mercapto-2-methylpropanoyl)-L-cysteine Derivatives

Fig. 1 shows the MS of methyl esters of the *S*-methyl derivatives, (**2**—**4**) which were synthesized as authentic samples of the metabolites of **1**. The base peaks in these spectra are the peak at *m/z* 75 for **2** and that at *m/z* 89 for **3** and **4**, corresponding to 2-mercaptopropyl and 2-methylthiopropyl cations, respectively, generated by α-cleavage at the sulfur atom. Molecular ion peaks were observed in 15—30% relative intensities. Prominent ions were observed at *m/z* 205 for **3** and *m/z* 219 for **4**, and these can be explained in terms of the loss of

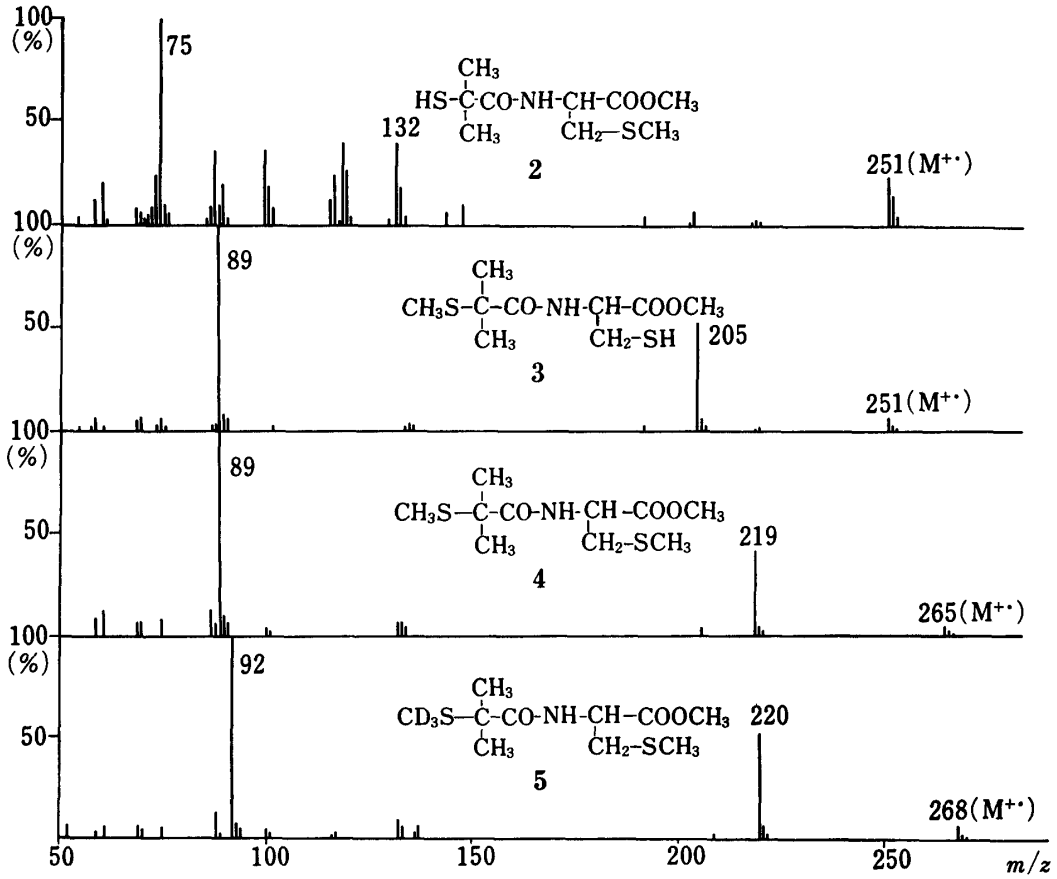


Fig. 1. EIMS of the *S*-Methylated Derivatives of *N*-(2-Mercapto-2-methylpropanoyl)-L-cysteine (**1**)

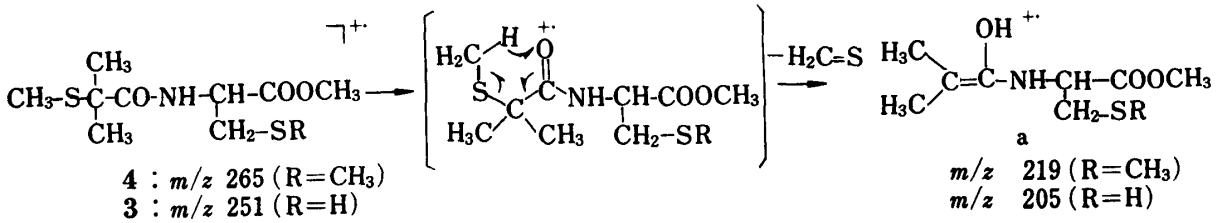


Chart 2

CH_2S from the molecular ions. The absence of the corresponding $[M-CH_2S]^{+\cdot}$ ion in the spectrum of **2** leads to the conclusion that a methyl group on the sulfur atom in the mercaptoacyl group is essential for this fragmentation. Therefore, the intense ion $[M-CH_2S]^{+\cdot}$ must be formed by the McLafferty rearrangement, which yields the ion a *via* the six-membered transition depicted in Chart 2.

A striking feature of these spectra is the abundance of the ion a, 54% for **3** and 43% for **4**. This is unusual, since it is known with some certainty that the McLafferty rearrangement of a primary hydrogen occurs only to a very slight extent and is less than 10% of that of a secondary one. Formation of the prominent ion a by a primary hydrogen transfer was confirmed by the following experiments: i) the mass spectrum of the trideuteriomethyl compound (**5**) (Fig. 1) shows the ion a corresponding to $[M-CD_2S]^{+\cdot}$ at *m/z* 220 as well as the three mass unit-shifted molecular ion at *m/z* 268, and ii) the high resolution mass measurement of the ion at *m/z* 219 of **4** and that at *m/z* 220 of **5** (see "Experimental"). From the evidence stated above, the occurrence of primary hydrogen transfer to a large extent was unambiguously demonstrated.

MS of 2-Alkylthio- and 2-Alkoxy-2-methylpropanoic Acids and Their Esters

Although the mass spectra of *S*-alkyl thioglycolic acids, the simplest 2-alkylthio-acid system, have been examined,[5] the McLafferty rearrangement of an *S*-methyl compound has not been studied previously. In order to study in more detail the unusual behavior of the rearrangement involved in the loss of CH_2S from the molecular ion, 2-alkylthio-2-methylpropanoic acid derivatives (**6**—**10**) were prepared and their mass spectra were examined.

Fig. 2 shows the MS of compounds (**6** and **8**). Loss of CH_2S from the *S*-methyl compound (**6**) takes place to form an ion of *m/z* 102 in 15% relative intensity. The intensity is not great as compared with that of compound (**3**), whereas other *S*-alkyl compounds (**7**—**10**) containing secondary hydrogens gave an abundant ion of *m/z* 102, as expected. The results are summarized in Table I. A hydrogen transfer from the C-1 position of the *S*-alkyl group to the carbonyl oxygen was confirmed by the shifting technique using (1-deuterioalkylthio)-esters of (**6**—**10**). In all cases, the rearrangement ion peak appeared at *m/z* 103 (Table IV). Accurate mass measurement of methyl 2-(1-dideuteriopropylthio)-2-methylpropanoate showed that the composition of the ion at *m/z* 103 is $C_5H_9DO_2$ (Calcd: 103.0744; Found: 103.0797), exhibiting incorporation of one deuterium from the dideuterated propyl group.

Next, the MS of five 2-alkylthio-2-methylpropanoic acids (**11**—**15**) were examined and those of compounds (**11** and **13**) are shown in Fig. 3. All exhibited behavior similar to that observed for the methyl esters; only small differences can be found. The peak formed by

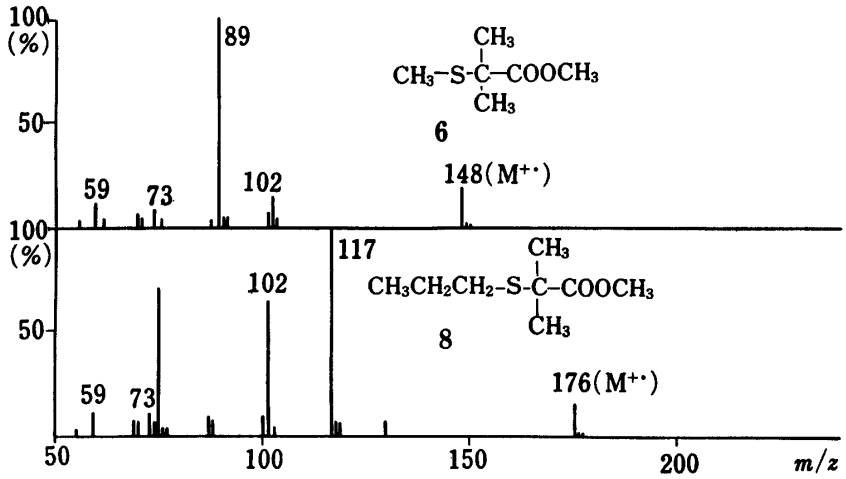


Fig. 2. EIMS of Methyl 2-Methylthio- and 2-(*n*-Propyl)thio-2-methylpropanoates (**6**) and (**8**)

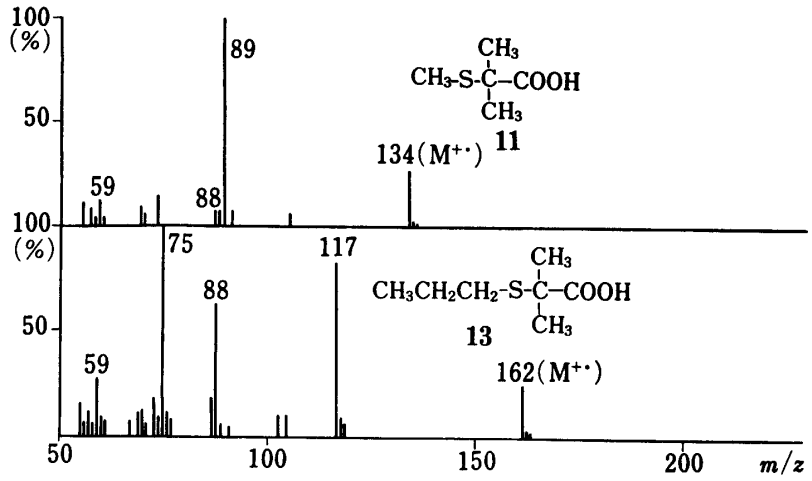


Fig. 3. EIMS of 2-Methylthio- and 2-(*n*-Propyl)thio-2-methylpropanoic Acids (**11** and **13**)

TABLE I. Intensity of the McLafferty Rearrangement Ions of 2-Alkylthio-2-methylpropanoic Acids and Methyl Esters

$R-S-C(CH_3)_2COOCH_3$	R	**6** CH_3	**7** C_2H_5	**8** n-C_3H_7	**9** iso-C_3H_7	**10** $CH_2C_6H_5$
$CH_3C(OH^{+\cdot})=C(CH_3)OCH_3$ b *m/z* 102	R. I.[a] (%)	15	43	63	50	31
	% Σ_{40}	7	15	18	18	12
$R-S-C(CH_3)_2COOH$	R	**11** CH_3	**12** C_2H_5	**13** n-C_3H_7	**14** iso-C_3H_7	**15** $CH_2C_6H_5$
$CH_3C(OH^{+\cdot})=C(CH_3)OH$ c *m/z* 88	R. I.[a] (%)	8	50	63	22	5
	% Σ_{40}	3.5	11	13	6	3

a) R. I. = relative intensity (%).

TABLE II. Intensity of the McLafferty Rearrangement Ions of 2-Alkoxy-2-methylpropanoic Acids and the Methyl Esters

$R-O-C(CH_3)_2COOCH_3$	R	**16** CH_3	**17** C_2H_5	**18** n-C_3H_7	**19** iso-C_3H_7	**20** $CH_2C_6H_5$
b *m/z* 102	R. I.[a] (%)	0	1.3	6.6	5.5	42.2
$R-O-C(CH_3)_2COOH$	R	**21** CH_3	**22** C_2H_5	**23** n-C_3H_7	**24** iso-C_3H_7	**25** $CH_2C_6H_5$
c *m/z* 88	R. I.[a] (%)	4	6	7	2	8

a) R. I. = relative intensity (%).

the McLafferty rearrangement appeared at *m/z* 88. In the case of 2-(1-deuterioalkylthio)-acids of (**11**—**15**) the corresponding peak is shifted to *m/z* 89, a monodeuterated ion (Table V). The rearrangement peak of the *S*-methyl acid (**11**) has lower intensity than that of the *S*-methyl ester (**6**), and then there appears to be a slight preference for hydrogen transfer to ester carbonyl as compared to acid carbonyl (Table I).

We have also studied the mass spectra of 2-alkoxy-2-methylpropanoic acid derivatives (**16**—**25**) where the sulfur atom of the alkylthio group is replaced by oxygen, in order to

compare the mass spectral behavior, especially the McLafferty rearrangement, with that of 2-alkylthio-2-methylpropanoic acid derivatives. The intensities of the rearrangement ions shown in Table II are very weak. Considering that the McLafferty rearrangement is a stepwise reaction,[4] the cation radical geminal to oxygen, formed by abstraction of a hydrogen, would not as stable as that geminal to sulfur which has a vacant 3*d*-orbital that could stabilize the radical formed. Therefore, the hydrogen abstraction might be suppressed in the case of 2-alkoxy acid derivatives.

Some other major fragmentation pathways of 2-alkylthio- and 2-alkoxy-2-methylpropanoic acids and their methyl esters are summarized in Chart 3. In both esters and acids, the most favorable pathway is path B. The presence of a metastable ion peak at *m/z* 54.6 in the spectra of the *S*-ethyl compounds (**7** and **12**) substantiates the view that the ion e at *m/z* 75 was formed from the ion d by a four-membered transition mechanism.

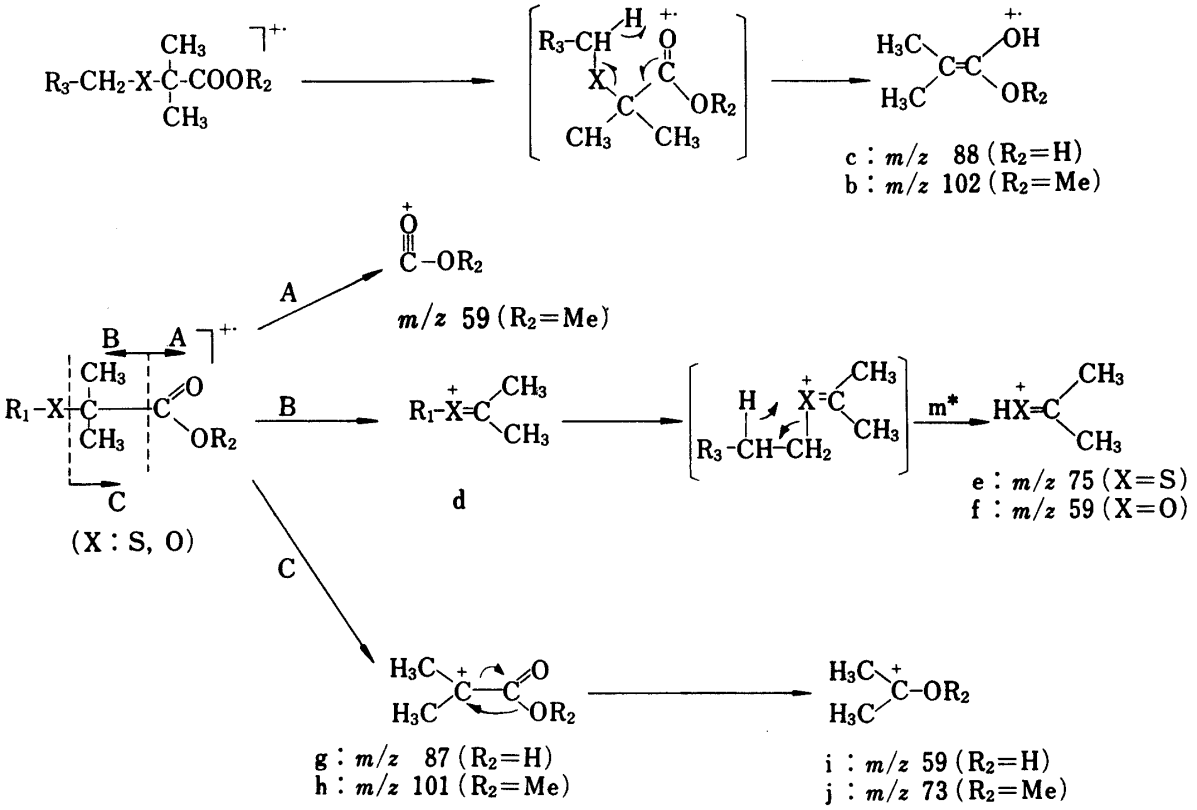


Chart 3

It should be noted that the peak at *m/z* 73 of the esters (**6**—**10**) is probably formed by elimination of the alkylthio group followed by skeletal rearrangement of the methoxy group with expulsion of carbon monoxide (path C in Chart 3). In the case of the trideuteriomethyl ester of **6**, the corresponding peak was also observed at *m/z* 76, showing the inclusion of all the deuterium atoms. The high resolution MS of methyl 2-(1-dideuteriopropylthio)-2-methylpropanoate showed the skeletal rearrangement peak at *m/z* 73 with the composition of C_4H_9O (Calcd: 73.0653; Found: 73.0646). These experimental results suggest that process C operates, giving the ion formed by the skeletal rearrangement. The rearrangement initiated by cleavage of the alkylthio or alkoxy function has not been found previously, although such a type of rearrangement has been discussed with α-bromophenylacetic acid and diethyl phenylethylmalonate.[6] Another type of skeletal rearrangement observed in the mass spectra of 3-alkylthiopropanoic acids[5] could not be found in our cases.

MS of 2-Alkylthioglycolamides, 2-Alkylthiopropanamides, and 2-Alkylthio-2-methylpropanamides

By the use of the isotopically labeled compound (**5**) it has been shown unambigously that a hydrogen of the *S*-methyl group is transferred to the amide carbonyl group in the mass spectra of compounds (**3** and **4**), but in the case of the model compounds, 2-methylthio-2-methylpropanoic acid (**6**) and the methyl ester (**11**), the rearrangement peaks were observed only to a small extent in the spectra. This difference was considered to be based on the nature of the carbonyl group (amide, ester or acid). Thus, we carried out mass spectrometry of 2-alkylthioglycolamides (**26a—i**), 2-alkylthiopropanamides (**27a—i**), and 2-alkylthio-2-methylpropanamides (**28a—i**).

Fig. 4 shows the MS of the *S*-methylamide derivatives(**28a—c**). The MS of twenty-seven amides examined are similar in many respects to the spectra of 2-alkylthio-2-methylpropanoic acids and the esters. The major fragmentation pathways, except for the McLafferty rearrangement, of the amides (**28a—i**) are shown in Chart 4.

The outstanding feature of the spectra of the amides (**26a—i**), (**27a—i**), and (**28a—i**) is that the McLafferty rearrangement takes place prominently with the formation of the ions m, n, and o, respectively, in the intensities summarized in Table III. In most cases the rearrangement ions appeared as base peaks. Even in the *S*-methyl compounds the ion peak considered was observed in greater than 42% relative intensity, except for compound (**28c**), in which the rearrangement is markedly suppressed (14.7%). This result suggests that the amide carbonyl group participates strongly in the hydrogen transfer of the *S*-methyl compounds and substantiates the extensive loss of CH_2S from the molecular ions of **3** and **4**.

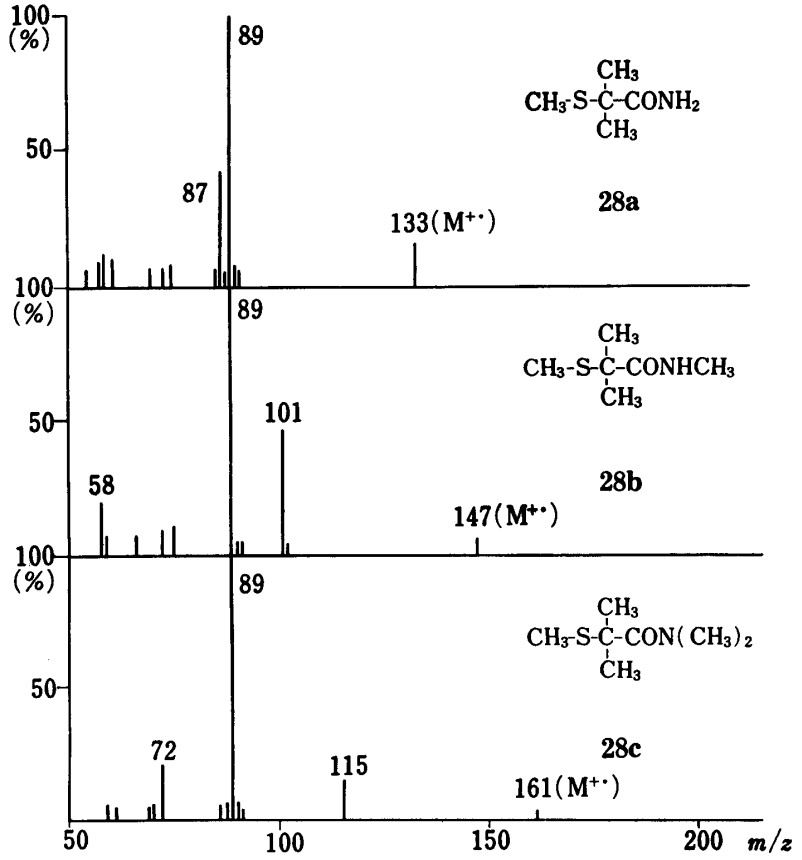


Fig. 4. EIMS of 2-Methylthio-2-methylpropanamides (**28a—c**).

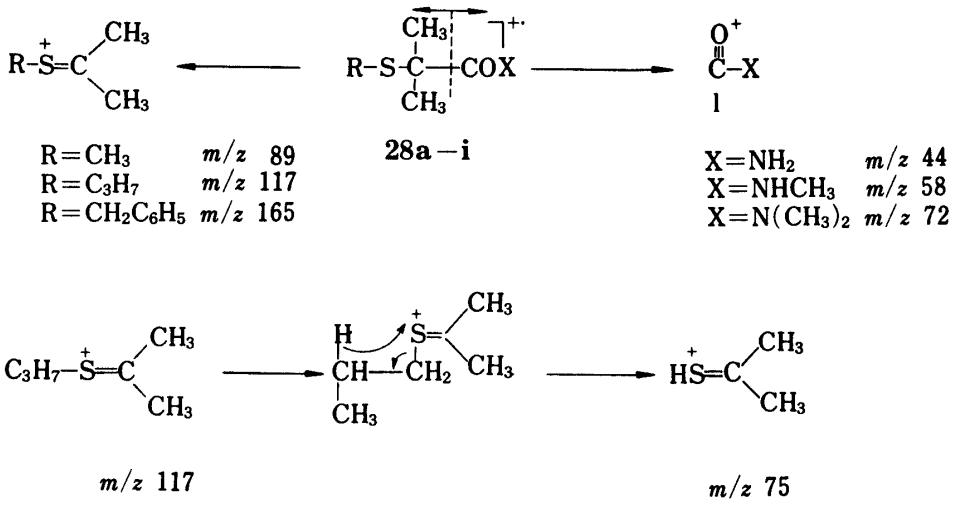
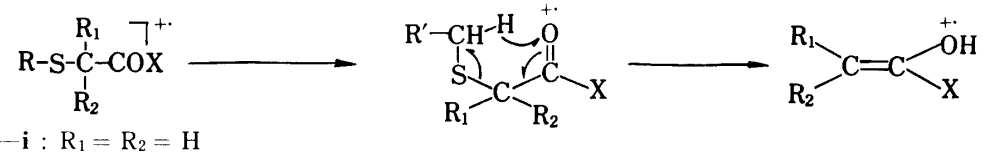


Chart 4

Another obvious aspect of the results is the large difference in the extent of the rearrangement depending on the type of carbonyl (amide, ester, or acid). The tendency for hydrogen transfer is in the following order: amide>ester>acid (Tables I and II). This tendency presumably reflects the electronic factor of the carbonyls affecting the hydrogen transfer, and is in good accordance with the results of the previous studies on the McLafferty rearrangement of carbonyl compounds by Nakata *et al.*[7] and the molecular orbital calculations of the rearrangement by Konishi *et al.*[8]

TABLE III. Intensity of the McLafferty Rearrangement Ions of 2-Alkylthio-amide Derivatives (**26a—i**), (**27a—i**), and (**28a—i**)



26a—i : $R_1 = R_2 = H$
27a—i : $R_1 = CH_3$ $R_2 = H$
28a—i : $R_1 = R_2 = CH_3$

	26 R	X = NH_2 (*m/z* 59) % Σ_{40} (R. I.)[a]	X = $NHCH_3$ (*m/z* 73) % Σ_{40} (R. I.)	X = $N(CH_3)_2$ (*m/z* 87) % Σ_{40} (R. I.)
m	CH_3	22.1 (100)	18.6 (100)	16.0 (50.4)
	$CH_3CH_2CH_2$	31.4 (100)	29.1 (100)	21.6 (100)
	$C_6H_5CH_2$	17.8 (71.0)	26.2 (100)	25.5 (100)
	27 R	X = NH_2 (*m/z* 73) % Σ_{40} (R. I.)	X = $NHCH_3$ (*m/z* 87) % Σ_{40} (R. I.)	X = $N(CH_3)_2$ (*m/z* 101) % Σ_{40} (R. I.)
n	CH_3	12.2 (72.5)	19.7 (93.8)	16.1 (85.3)
	$CH_3CH_2CH_2$	26.0 (100)	28.3 (100)	21.4 (100)
	$C_6H_5CH_2$	33.6 (100)	38.4 (100)	34.1 (100)
	28 R	X = NH_2 (*m/z* 87) % Σ_{40} (R. I.)	X = $NHCH_3$ (*m/z* 101) % Σ_{40} (R. I.)	X = $N(CH_3)_2$ (*m/z* 115) % Σ_{40} (R. I.)
o	CH_3	10.2 (42.4)	14.0 (45.0)	5.1 (14.7)
	$CH_3CH_2CH_2$	17.9 (100)	16.2 (100)	10.1 (42.9)
	$C_6H_5CH_2$	32.0 (95.8)	30.3 (100)	17.5 (51.4)

a) R. I. = relative intensity (%).

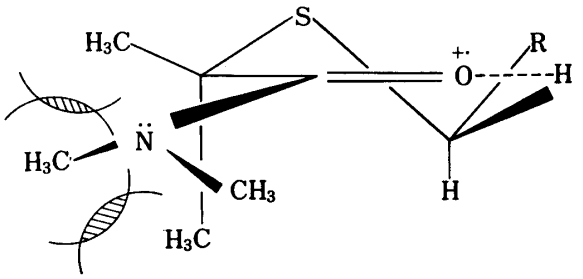


Fig. 5

Moreover, as can been seen from Table III, the abundance of the rearrangement ion was markedly influenced by the methyl groups of the α carbon and the nitrogen of amides. The rearrangement is more suppressed when a molecule contains more methyl groups, and is drastically reduced in the case of compound (**28c**) which has geminal dimethyls at the α carbon and *N*,*N*-dimethyls.

We propose nonbonded interaction as the reason for the low intensity of the rearrangement peak in the amide (**28c**). Fig. 5 shows the six-membered transition state of the McLafferty rearrangement, where the highly directional orbital of the unpaired electrons on nitrogen overlaps with the π-orbital of the carbonyl to form an energetically favorable intermediate. In that conformer there would be severe nonbonded interaction between the methyl groups on the α carbon and the nitrogen, which would prevent the formation of a favorable transition state. Therefore, the McLafferty rearrangement would be more suppressed in the MS of *N*, *N*-dimethyl-2-alkylthio-2-methylpropanamides (**28**: R=alkyl, X=$N(CH_3)_2$) than in those of other amide derivatives.

Although there are some studies of the influence of steric hindrance on the rearrangement,[4,9] no systematic study has been carried out. In this study, have found a clear-cut example of the effect of nonbonded interaction on the McLafferty rearrangement.

Experimental

All melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Hitachi 215 spectrometer in $CHCl_3$. Unless otherwise specified, nuclear magnetic resonance (NMR) spectra were measured on a Hitachi R-24 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. The abbreviations s, d, t, q, and m signify singlet, doublet, triplet, quartet, and multiplet in the NMR spectra, and the coupling constant (J) is given in Hz. Electron impact MS (EIMS) were recorded on a Hitachi RMU-6E mass spectrometer under the following conditions: ionization voltage, 70 eV; ion accelerating voltage, 1.8 kV; ion source temperature, 200—250°C. Samples were introduced through a heated inlet system at 150°C. High resolution electron impact mass spectra (HREIMS) were taken on a Hitachi RMU-7L double focusing mass spectrometer. Operating conditions: ion source temperature, 100°C; ionization voltage, 70 eV; accelerating voltage, 3.2 kV.

Column chromatographies were performed on silica gel (Merck Kieselgel 70—230 mesh). Silica gel 60 GF_{254} (Merck) was used for thin layer chromatography (TLC) and Silica gel 60 PF_{254} (Merck) for preparative TLC. Oily substances were purified by evaporative bulb-to-bulb distillation using a Büchi Kugelrohr distillation apparatus at the oven temperature and pressure indicated. Unless otherwise specified, the extracts were dried over anhydrous magnesium sulfate.

***N*-(2-Mercapto-2-methylpropanoyl)-*S*-methyl-L-cysteine Methyl Ester** (**2**)——*S*-Methyl-L-cysteine (4.7 g, 0.035 mol) was dissolved in 0.5 N sodium hydroxide (67.5 ml) and then 2-benzylthio-2-methylpropanoyl chloride (7.9 g, 0.035 mol) was added at 0°C with stirring. The reaction mixture was stirred for 1 h at room temperature and then acidified with 6 N hydrochloric acid. The separated oil was extracted with ethyl acetate. The extract was washed with water, dried, and concentrated to dryness *in vacuo* to give 7.5 g of *N*-(2-benzylthio-2-methylpropanoyl)-*S*-methyl-L-cysteine. The benzylthio compound (909 mg, 2.78 mmol) was dissolved in liquid ammonia (50 ml) and metallic sodium (140 mg, 6.09 mg atom) was added in small portions with stirring to the solution. After completion of the reaction, ammonium chloride was added to the mixture and ammonia was removed by evaporation. The residual solid was dissolved ice-water and washed with ether. The aqueous layer was acidified with dil. hydrochloric acid and extracted with ethyl acetate. The extract was washed with water, dried, and concentrated to dryness to give 583 mg (88.4%) of *N*-(2-mercapto-2-methylpropanoyl)-*S*-methyl-L-cysteine as an amorphous powder, mp 77—79°C. $[\alpha]_D^{23}$ −15.9° (c=0.9, MeOH). IR ν_{max} cm^{-1}: 3360 (NH), 1730 (COOH), 1620 (CONH). NMR δ: 1.61 (6H, s, gem-CH_3×2), 2.14 (3H, s, S–CH_3), 2.31 (1H, s, SH), 3.02 (2H, d, J=5.4 Hz, CH_2), 4.51—4.93 (1H, m, CH), 7.69 (1H, d, J=8 Hz, NH), 9.49 (1H, s, COOH). EIMS m/z: 237 ($M^{+\cdot}$).

Treatment of the compound obtained with an ethereal diazomethane solution for 1 min gave the oily methyl ester (**2**). IR ν_{max} cm^{-1}: 3370 (NH), 1735 (COO), 1660 (CONH). NMR δ: 1.60 (6H, s, gem-CH_3×2), 2.12 (3H, s, S–CH_3), 2.28 (1H, s, SH), 2.98 (2H, d, J=5 Hz, CH_2), 3.78 (3H, s, OCH_3), 4.75 (1H, m, CH),

7.6 (1H, br, NH). EIMS *m/z*: 251 ($M^{+\cdot}$).

***N*-[2-Methyl-2-(methylthio)propanoyl]-L-cysteine Methyl Ester (3)**——2-Methyl-2-(methylthio)propanoyl chloride was added dropwise to a solution of L-cysteine (7.1 g, 0.059 mol) in 2 M potassium carbonate (88 ml) with stirring under a nitrogen atmosphere at 0°C. The mixture was stirred overnight at room temperature and acidified with hydrochloric acid. The precipitated crystals were recrystallized from ethyl acetate to give 10.4 g (89.8%) of *N*-[2-methyl-2-(mercapto)propanoyl]-L-cysteine. mp 110.5—112°C. $[\alpha]_D^8$ +7.4° (c=1.1, MeOH). IR ν_{max} cm^{-1}: 3350 (NH), 1730 (COOH), 1622 (CONH). NMR δ: 1.46 (1H, t, J=9 Hz, CH_2SH), 1.53 (6H, s, gem-$CH_3\times2$), 2.10 (3H, s, S-CH_3), 2.93—3.20 (2H, d, J=9.4 Hz, CH_2), 4.66—4.95 (1H, m), 7.93 (1H, d, J=8 Hz, NH), 10.40 (1H, s, COOH). *Anal.* Calcd for $C_{18}H_{15}NO_3S_2$: C, 40.49; H, 6.37; N, 5.90; S, 27.02. Found: C, 40.55; H, 6.36; N, 5.84; S, 27.05.

Treatment of the compound obtained with an ethereal diazome hane solution for 1 min gave the methyl ester (3). Colorless oil. IR ν_{max} cm^{-1}: 3350 (NH), 1735 (COO), 1660 (CONH). NMR δ: 1.37 (1H, t, J= 9 Hz), 1.52 (6H, s, gem-$CH_3\times2$), 2.10 (3H, s, S-CH_3), 3.02 (2H, d, J=9.4 Hz, CH_2), 3.80 (3H, s, OCH_3), 4.80 (1H, m, CH), 7.80 (1H, br, NH). E MS *m/z*: 251 ($M^{+\cdot}$).

***S*-Methyl-*N*-[2-methyl-2-(methylthio)propanoyl]-L-cysteine Methyl Ester(4)**——*N*-(2-Mercapto-2-methylpropanoyl)-L-cysteine[1] (11.2 g, 0.05 mol) was dissolved in 2 N potassium carbonate (75 ml), and methyl iodide (17 g, 0.12 mol) was added to the solution with stirring. The mixture was stirred for 1 h at room temperature and then acidified with hydrochloric acid. The precipitates were collected and recrystallized from ethanol–hexane to give 9.44 g (75%) of the *S*-methyl compound. mp 120.5—121°C. $[\alpha]_D^{19}$ −19.3° (c=0.7, MeOH). IR ν_{max} cm^{-1}: 3350 (NH), 1726 (COOH), 1620 (CONH). NMR δ: 1.53 (6H, s, gem-$CH_3\times2$), 2.10 (3H, s, SCH_3), 2.15 (3H, s, SCH_3), 3.02 (2H, d, J=6 Hz, CH_2), 4.55—4.90 (1H, m, CH), 7.87 (1H, d, J=8 Hz, NH), 11.15 (1H, s, COOH). *Anal.* Calcd for $C_9H_{17}NO_3S_2$: C, 43.01; H, 6.82; N, 5.57; S, 25.51. Found C, 43.07; H, 6.80; N, 5.54; S, 25.36.

Treatment of the *S*-methyl compound with an ethereal diazomethane solution gave the methyl ester (4). Colorless oil. IR ν_{max} cm^{-1}: 3360 (NH),1740 (COO), 1660 (CONH). NMR δ: 1.52 (6H, s, gem-$CH_3\times2$), 2.13 (6H, s, $SCH_3\times2$), 2.98 (2H, d, J=6 Hz, CH_2), 3.78 (3H, s, OCH_3), 4.77 (1H, dt, J=8 and 6 Hz), 7.80 (1H, br, NH). HREIMS *m/z*: 265.0760 ($M^{+\cdot}$, Calcd for $C_{10}H_{19}NO_3S_2$: 265.0716), 219.0934 (Calcd for $C_9H_{17}NO_3S$: 219.0929).

***S*-Methyl-*N*-[2-methyl-2-(trideuteriomethylthio)propanoyl]-L-cysteine Methyl Ester (5)**——A solution of the ester (2) (10 mg) in 0.5 ml of dry tetrahydrofuran (THF) was added to a stirred suspension of sodium

TABLE IV. Characterization of Methyl 2-Alkylthio-2-methylpropanoates (**6**—**10**)

Compd.	R	bp (°C) (mmHg)[a]	IR (cm^{-1})	R-S-C(CH_3)$_2$COOCH_3 NMR (δ)	EIMS *m/z* (%)[b]
6	CH_3	130—135(760)	1720	1.51 (6H, s), 2.12 (3H, s), 3.74 (3H, s)	148 ($M^{+\cdot}$, 18), 103 (14), 102 (15), 89 (100), 73 (9), 59 (12)
	CD_3	130—135(760)	1715	1.51 (6H, s), 3.73 (3H, s)	151 ($M^{+\cdot}$, 19), 103, (6), 92 (100), 73 (9), 59 (13)
7	CH_3CH_2	130—135(760)	1715	1.21 (3H, t, J=7 Hz), 1.52 (6H, s), 2.63 (2H, q, J=7 Hz), 3.72 (3H, s)	162 ($M^{+\cdot}$, 17), 103 (100), 102 (43), 75 (28), 73 (9), 59 (20)
	CH_3CD_2	140(760)	1720	1.18 (3H, s), 1.49 (6H, s), 3.70 (3H, s)	164 ($M^{+\cdot}$, 17), 105,(100), 103 (38), 75 (29), 59 (22)
8	$CH_3CH_2CH_2$	125(760)	1715	0.95 (3H, t, J=7 Hz), 1.49 (6H, s), 1.57 (2H, m), 2.56 (2H, t, J=7 Hz)	176 ($M^{+\cdot}$, 15), 117 (100), 102 (63), 75 (70), 73 (10), 59 (11)
	$CH_3CH_2CD_2$	135—140(760)	1715	0.98 (3H, t, J=7 Hz), 1.52 (6H, s), 1.60 (2H, q, J=7 Hz), 3.73 (3H, s)	178 ($M^{+\cdot}$, 15), 119 (100), 103 (41), 75 (45), 59 (17)
9	$CH_3\overset{\vert}{C}HCH_3$	125(760)	1720	1.26 (6H, d, J=7 Hz), 1.52 (6H, s), 2.91 (1H, m), 3.72 (3H, s)	176 ($M^{+\cdot}$, 10), 117 (43), 102 (50), 75 (100), 74 (11), 73 (6), 59 (11)
	$CH_3\overset{\vert}{C}DCH_3$	125(760)	1720	1.23 (6H, s), 1.50 (6H, s), 3.71 (3H, s)	177 ($M^{+\cdot}$, 8), 118 (38), 103 (86), 75 (100), 59 (24)
10	$C_6H_5CH_2$	130(6)	1720	1.53 (6H, s), 3.62 (3H, s), 3.82 (2H, s), 7.29 (5H, s)	224 ($M^{+\cdot}$, 2), 165 (6), 123 (31), 102 (31), 91 (100), 73 (10), 59 (12)
	$C_6H_5CD_2$	130(6)	1720	1.51 (6H, s), 3.61 (3H, s), 7.26 (5H)	226 ($M^{+\cdot}$, 2), 167 (6), 125 (29), 103 (42), 93 (100), 59 (19)

a) Oven temperature of Kugelrohr distillation apparatus.

b) (%)=Relative intensity.

TABLE V. Characterization of 2-Alkylthio-2-methylpropanoic Acids (**11**—**15**)

Compd.	R	mp or bp (°C) (mmHg)[a]	IR (cm^{-1})	R-S-C(CH_3)$_2$COOH NMR (δ)	EIMS *m/z* (%)[b]
11	CH_3	92—95(7.5)	1695	1.51 (6H, s), 2.17 (3H, s), 9.59 (1H, br[c])	134(M^+, 26), 105 (8), 89 (100), 88 (8), 87 (9), 73 (13), 58 (14)
	CD_3	94(7)	1690	1.54 (6H, s), 8.05 (1H, br)	137 (M^+, 20), 92 (100), 89 (9), 59 (25)
12	CH_3CH_2	94—96(6.5)	1690	1.24 (3H, t, J=7 Hz), 1.54 (6H, s), 2.70 (2H, q, J=7 Hz), 9.70 (1H, br)	148(M^+, 30), 103 (100), 88 (50), 75 (47), 73 (16), 61 (19), 59 (33)
	CH_3CD_2	105(6)	1692	1.23 (3H, s), 1.53 (6H, s), 10.05 (1H, br)	150 (M^+, 23), 105 (100), 89 (38), 75 (40), 59 (21)
13	$CH_3CH_2CH_2$	96(7)	1690	0.97 (3H, t, J=7 Hz), 1.52 (6H, s), 1.58 (2H, m), 2.64 (2H, t, J=7 Hz), 7.85 (1H, b)	162(M^+, 24), 117(83), 105(11), 103 (10), 88 (63), 75 (100), 73 (18), 59 (27)
	$CH_3CH_2CD_2$	105(6)	1695	0.97 (3H, t, J=7 Hz), 1.15 (6H, s), 1.52 (2H, superimposed), 9.50 (1H, br)	164(M^+, 27),119 (100),105 (6), 89 (62), 75 (75), 59 (19)
14	$CH_3\overset{\vert}{C}HCH_3$	86—90(7)	1695	1.28 (6H, d, J=7 Hz), 1.55 (6H, s), 3.18 (1H, m), 8.35 (1H, br)	162 (M^+, 16), 117 (36), 88 (22), 75 (100), 59 (12)
	$CH_3\overset{\vert}{C}DCH_3$	85—90(6)	1695	1.27 (6H, s), 1.52 (6H, s), 8.1 (1H, br)	163 (M^+, 10), 118 (28), 88 (9), 89 (9), 75 (100), 59 (21)
15	$C_6H_5CH_2$	95—96	1690	1.53 (6H, s), 3.89 (2H, s) 7.27 (5H), 9.25 (1H, br)	210 (M^+, 1), 165 (1), 123 (41). 91 (100), 88 (5), 77 (8), 65 (22), 59 (12), 51 (13)
	$C_6H_5CD_2$	96—98	1690	1.54 (6H, s), 7.29 (5H), 9.15 (1H, br)	212 (M^+, 2), 167 (2), 125 (25), 93 (100), 89 (5)

a) Oven temperature of Kugelrohr distillation apparatus.
b) (%)=Relative intensity.
c) br=broad.

TABLE VI. Characterization of 2-Alkoxy-2-methylpropanoic Acids (**21**—**25**)and the Methyl Esters (**16**—**20**)

Compd.	R_1	R_2	bp(°C) (mmHg)[a]	IR (cm^{-1})	R_1-O-C(CH_3)$_2$COOR_2 NMR (δ)	CIMS *m/z* (MH^+)	EIMS *m/z* (%)[b]
16	CH_3	CH_3	125 (760)	1725	1.43 (6H, s), 3.30 (3H, s), 3.80 (3H, s)	133	73 (100), 59 (27)
17	CH_3CH_2	CH_3	133—135 (760)	1725	1.20 (3H, t, J=6.5 Hz), 1.40 (6H, s), 3.42 (2H, q, J=6.5 Hz), 3.70 (3H, s)	147	102(1), 87(41), 73(4), 59 (100)
18	$CH_3CH_2CH_2$	CH_3	128—130 (760)	1725	0.90 (3H, t, J=6.5 Hz), 1.42 (6H, s), 1.60 (2H, m), 3.32 (2H, t, J=6.5 Hz), 3.73 (3H, s)	161	102 (7), 101 (28), 73 (6), 59 (100)
19	$CH_3\overset{\vert}{C}HCH_3$	CH_3	90—93 (760)	1725	1.16 (6H, d, J=6.5 Hz), 1.50 (6H, s), 3.68 (1H, m), 3.85 (3H, s)	161	102 (6), 101 (74), 73 (22), 59 (100)
20	$C_6H_5CH_2$	CH_3	100—102 (20)	1725	1.50 (6H, m), 3.75 (3H, s), 4.50 (2H, s), 7.36 (5H)	208	149 (15), 102 (42), 91 (100), 77 (12), 73 (7), 65 (26), 59 (12)
21	CH_3	H	108—110 (16)	1770 1705	1.43 (6H, s), 3.30 (3H, s), 6.10 (1H, br[c])	119	88 (4), 87 (3), 86 (10), 73 (100), 59 (16)
22	CH_3CH_2	H	113—115 (15)	1770 1710	1.21 (3H, t, J=6.5 Hz), 1.47 (6H, s), 3.51 (2H, q, J=6.5 Hz), 6.05 (1H, br)	133	88 (6), 87 (44); 59 (100)
23	$CH_3CH_2CH_2$	H	78—80 (5)	1730 1700	0.91 (3H, t, J=6.5 Hz), 1.43 (6H, s) 1.50 (2H, m), 3.40 (2H, J=6.5 Hz) 5.0 (1H, br)	147	101(25), 88(7), 87(8), 59 (100)
24	$CH_3\overset{\vert}{C}HCH_3$	H	98—100 (20)	1770 1707	0.98 (6H, d, J=7 Hz), 1.43 (6H, s) 3.87 (1H, m), 7.95 (1H, br)	147	101(26), 88(2), 77(18), 69 (10), 59 (100)
25	$C_6H_5CH_2$	H	133—135 (3)	1770 1710	1.57 (6H, s), 4.57 (2H, s), 7.40 (5H), 7.50 (1H, br)	195	149 (4), 109 (16), 108, (19), 91 (100), 88 (8), 79 (28), 77 (20), 59 (54)

a) Oven temperature of Kugelrohr distillation apparatus.
b) Molecular ion peaks were not detected by EIMS. (%)=Relative intensity.
c) br=broad.

TABLE VII. Characterization of the 2-Alkylthio-amide Derivatives (**26—28**)

Compd.	R	X	mp or bp (°C) (mmHg)[a]	IR (cm^{-1})	NMR (δ)	EIMS *m/z* (%)[b]
26a	CH_3	NH_2	102—104	3500 3380 1680	2.16 (3H, s), 3.17 (2H, s), 5.00—6.80 (2H, br[c])	105 (M^+, 44), 62 (19), 61 (69), 59 (100)
26b	CH_3	$NHCH_3$	120(6)	3300 1640	2.12 (3H, s), 2.85 (3H, d, J=6 Hz), 3.18 (2H, s), 6.00—7.50 (1H, br)	119 (M^+, 42), 73 (100), 62 (34), 61 (72), 58 (88)
26c	CH_3	$N(CH_3)_2$	100(6)	1630	2.21 (3H, s), 2.98 (3H, s), 3.09 (3H, s), 3.30 (2H, s)	133 (M^+, 23), 87 (50), 72 (100), 61 (22), 58 (8)
26d	$CH_3CH_2CH_2$	NH_2	51—53	3500 3380 1670	0.98 (3H, t, J=7 Hz), 1.63 (2H, m), 2.56 (2H, t, J=7 Hz), 3.19 (2H, s), 5.30—7.05 (2H, br)	133 (M^+, 9), 91 (9), 89 (8), 61 (19), 59 (100)
26e	$CH_3CH_2CH_2$	$NHCH_3$	127(9)	3300 1640	0.97 (3H, t, J=7 Hz), 1.61 (2H, m), 2.51 (2H, t, J=7 Hz), 2.84 (3H, d, J=5 Hz), 3.20 (2H, s), 6.00—7.20 (1H, br)	147 (M^+, 8), 73 (100), 61 (16), 58 (42)
26f	$CH_3CH_2CH_2$	$N(CH_3)_2$	110(5)	1640	0.96 (3H, t, J=7 Hz), 1.64 (2H, m), 2.63 (2H, t, J=7 Hz), 2.94 (3H, s), 3.06 (3H, s), 3.27 (2H, s)	161 (M^+, 10), 89 (8), 87 (100), 72 (89), 61 (17), 58 (18)
26g	$C_6H_5CH_2$	NH_2	94—95	3500 3380 1670	3.10 (2H, s), 3.74 (2H, s), 7.28 (5H, s), 5.00—7.00 (2H, br)	181 (M^+, 17), 123 (38), 91 (100), 65 (26), 59 (71)
26h	$C_6H_5CH_2$	$NHCH_3$	69—71	3380 1660	2.72 (3H, d, J=6 Hz), 3.13 (2H, s), 3.70 (2H, s), 6.20—6.90 (1H, br), 7.27 (5H, s)	195 (M^+, 12), 123 (11), 91 (84), 73 (100), 65 (25), 59 (21), 58 (20)
26i	$C_6H_5CH_2$	$N(CH_3)_2$	171(4)	1630	2.94 (3H, s), 2.97 (3H, s), 3.18 (2H, s), 3.82 (2H, s), 7.30 (5H, s)	209 (M^+, 8), 91 (49), 87 (100), 72 (51), 65 (16)
27a	CH_3	NH_2	94—96	3500 3380 1680	1.45 (3H, d, J=7 Hz), 2.10 (3H, s), 3.31 (1H, q, J=7 Hz), 5.50—7.00 (2H, br)	119 (M^+, 28), 75 (100), 73 (73)
27b	CH_3	$NHCH_3$	102(3)	3380 1660	1.44 (3H, d, J=7 Hz), 2.06 (3H, s), 2.82 (3H, d, J=6 Hz), 3.31 (1H, q, J=7 Hz), 6.10—7.20 (1H, br)	133 (M^+, 17), 87 (94), 75 (100), 58 (44)
27c	CH_3	$N(CH_3)_2$	85(5)	1640	1.44 (3H, d, J=7 Hz), 2.03 (3H, s), 2.95 (3H, s), 3.08 (3H, s), 3.56 (1H, q, J=7 Hz)	147 (M^+, 11), 101 (85), 75 (100), 72 (98)
27d	$CH_3CH_2CH_2$	NH_2	56—58	3500 3400 1680	0.96 (3H, t, J=7 Hz), 1.45 (3H, d, J=7 Hz), 1.64 (2H, m), 2.55 (2H, t, J=7 Hz), 3.36 (1H, q, J=7 Hz), 5.50—7.00 (2H, br)	147 (M^+, 12), 103 (34), 73 (100), 61 (69)
27e	$CH_3CH_2CH_2$	$NHCH_3$	103(4)	3300 1650	0.96 (3H, t, J=7 Hz), 1.45 (3H, d, J=7 Hz), 1.60 (2H, m), 2.51 (2H, t, J=8 Hz), 2.83 (3H, d, J=5 Hz), 3.37 (1H, q, J=7 Hz), 6.40—7.20 (1H, br)	161 (M^+, 2), 103 (34), 87 (100), 61 (58), 58 (33)
27f	$CH_3CH_2CH_2$	$N(CH_3)_2$	117(5)	1640	0.97 (3H, t, J=7 Hz), 1.48 (3H, d, J=7 Hz), 1.59 (2H, m), 2.56 (2H, t, J=7 Hz), 2.98 (3H, s), 3.12 (3H, s), 3.61 (3H, q, J=7 Hz)	175 (M^+, 2), 103 (51), 101 (100), 72 (62), 61 (47)
27g	$C_6H_5CH_2$	NH_2	85—86	3500 3370 1680	1.44 (3H, d, J=7 Hz), 3.28 (1H, q, J=7 Hz), 3.76 (2H, s), 5.50—6.70 (2H, br), 7.28 (5H, s)	195 (M^+, 4), 123 (8), 91 (81), 73 (100)
27h	$C_6H_5CH_2$	$NHCH_3$	152(3)	3300 1640	1.42 (3H, d, J=7 Hz), 2.71 (3H, d, J=5 Hz), 3.31 (1H, q, J=7 Hz), 3.71 (2H, s), 6.30—6.80 (1H, br), 7.27 (5H, s)	209 (M^+, 1), 91 (64), 87 (100), 58 (10)
27i	$C_6H_5CH_2$	$N(CH_3)_2$	161(4)	1640	1.48 (3H, d, J=7 Hz), 2.87 (6H, s), 3.53 (1H, q, J=7 Hz), 3.77 (2H, s), 7.28 (5H, s)	223 (M^+, <1), 151 (1), 101 (100), 91 (64), 72 (38)
28a	CH_3	NH_2	112—114	3500 3400 1680	1.50 (6H, s), 2.10 (3H, s), 5.30—6.60 (2H, br)	133 (M^+, 15), 89 (100), 87 (42)
28b	CH_3	$NHCH_3$	106(5)	3400 1660	1.50 (6H, s), 2.02 (3H, s), 2.82 (3H, d, J=6 Hz), 6.30—7.50 (1H, br)	147 (M^+, 5), 101 (45), 89 (100), 75 (10), 58 (19)
28c	CH_3	$N(CH_3)_2$	115(10)	1600	1.53 (6H, s), 2.00 (3H, s), 3.17 (6H, s)	161 (M^+, 3), 115 (15), 89 (100), 72 (21)
28d	$CH_3CH_2CH_2$	NH_2	94—95	3500 3380 1670	0.98 (3H, t, J=7 Hz), 1.50 (6H, s), 1.60 (2H, m), 2.54 (2H, t, J=7 Hz), 5.40—7.10 (2H, br)	161 (M^+, 6), 117 (76), 87 (100), 75 (95)
28e	$CH_3CH_2CH_2$	$NHCH_3$	110(5)	3350 1650	0.96 (3H, t, J=7 Hz), 1.50 (6H, s), 1.57 (2H, m), 2.47 (2H, t, J=7 Hz), 2.81 (3H, d, J=6 Hz), 6.70—7.30 (1H, br)	175 (M^+, 4), 117 (77), 101 (100), 75 (92), 58 (23)

(continued)

Compd.	R	X	mp or bp (°C) (mmHg)[a]	IR (cm^{-1})	NMR (δ)	EIMS m/z (%)[b]
28f	$CH_3CH_2CH_2$	$N(CH_3)_2$	80(3)	1620	0.93 (3H, t, J=6 Hz), 1.51 (2H, m), 1.53 (6H, s), 2.48 (2H, t, J=7 Hz), 3.16 (6H, s)	189 (M^+, <1), 117 (100), 115 (43), 75 (70), 72 (26)
28g	$C_6H_5CH_2$	NH_2	100—101	3500 3380 1670	1.54 (6H, s), 3.77 (2H, s), 5.50—7.00 (2H, br), 7.26 (5H, s)	209 (M^+, 2), 165 (3), 91 (100), 87 (96), 65 (16)
28h	$C_6H_5CH_2$	$NHCH_3$	143(3)	3350 1650	1.52 (6H, s), 2.65 (3H, d, J=6 Hz), 3.70 (2H, s), 6.10—6.88 (1H, br), 7.24 (5H, s)	223 (M^+, <1), 165 (5), 101 (100), 91 (94), 65 (12), 58 (12)
28i	$C_6H_5CH_2$	$N(CH_3)_2$	142(4)	1620	1.57 (6H, s), 3.00 (6H, s), 3.68 (2H, s), 7.22 (5H, s)	237 (M^+, <1), 165 (12), 115 (51), 91 (100), 72 (20)

a) Oven temperatire of Kugelrohr distillation apparatus.
b) (%)=Relative intensity.
c) br=broad.

hydride (10 mg, 50% mineral oil suspension) in 2 ml of dry THF under argon, and the mixture was stirred at room temperature for 1 h. To this mixture was added 0.2 ml of trideuteriomethyl iodide at the same temperature. After 15 h, the reaction mixture was quenched with water and extracted with ether. Concen tration of the combined ether extracts to dryness gave an oily residue. Purification by preparative TLC (benzene: acetone=9 : 1) gave the ester (**5**) (7.3 mg) as a colorless oil. IR ν_{max} cm^{-1}: 3360 (NH), 1720 (COO), 1660 (CONH). NMR δ: 1.52 (6H, s, gem-C$\underline{H}_3\times 2$), 2.12 (3H, s, SC$\underline{H}_3$), 2.98 (2H, d, J=5.4 Hz, C$\underline{H}_2$), 3.78 (3H, s, OC$\underline{H}_3$), 4.75 (1H, m, C$\underline{H}$), 7.76 (1H, br, N$\underline{H}$). HREIMS m/z: 268.1054 ($M^{+\cdot}$, Calcd for $C_{10}H_{16}D_3NO_3S_2$: 268.1088), 220.0974 (Calcd for $C_9H_{16}DNO_3S$: 220.0992).

General Procedure for Preparation of the 2-Alkylthio-2-methylpropanoic Acids (11—15) and the Methyl Esters (6—10)——A solution of methyl 2-mercapto-2-methylpropanoate (1 mmol) [prepared by the treatment of 2-mercapto-2-methylpropanoic acid with an ethereal diazomethane solution for 1 min] in dry THF (1 ml) was added to a stirred slurry of sodium hydride (1.5 mmol) in dry THF (3 ml) under argon. After being stirred for 1 h at room temperature, the mixture was treated with alkyl halide (0.2 ml) and then stirred overnight. The reaction mixture was quenched with water and extracted with ether. The extract was dried, and concentrated to dryness. The oily residue was purified by Kugelrohr distillation to yield the desired methyl 2-alkylthio-2-methylpropanoate (Table IV).

Hydrolysis [1N NaOH–MeOH (1 : 5), 5 h] of the methyl ester obtained above at room temperature followed by bulb-to-bulb distillation gave the pure 2-alkylthio-2-methylpropanoic acid (Table V).

General Procedure for Preparation of the 2-Alkoxy-2-methylpropanoic Acids (21—25) and the Methyl Esters (16—20)——2-Methoxy-, 2-ethoxy-, and 2-*n*-propoxy-2-methylpropanoic acids and the methyl esters were prepared in the same manner as described for the 2-alkylthio-2-methylpropanoic acid derivatives.

Preparation of 2-isopropoxy-and 2-benzyloxy-2-methylpropanoic acids and the methyl esters from methyl 2-isopropoxy- and 2-benzyloxyacetate, respectively, was carried out by use of the procedure of Schlessinger *et al.*[10] The spectral data are summarized in Table VI.

General Procedure for Preparation of the 2-Alkylthio-amides (26a—i), (27a—i), and (28a—i)——i) *S*-Alkylation of 2-Mercapto-acids: *S*-Methylation of thioglycolic acid, 2-mercaptopropanoic acid, and 2-mercapto-2-methylpropanoic acid was carried out as follows. The mercapto-acid (1.0 g) was dissolved in 2.75 N sodium hydroxide (10 ml), and dimethyl sulfate (1.0 ml) was added to the solution at 0°C. After being heated at 40—50°C for 1 h, the reaction mixture was acidified (pH 1.0) and worked up in the usual manner. Bulb-to-bulb distillation of the residue gave the desired *S*-methyl compound (47—84%).

Treatment of a 2-mercapto-acid (1.3 g) in 2N K_2CO_3(10 ml)–MeOH (2 ml) with *n*-propyl bromide (benzyl bromide) (1.8 ml) with stirring for 48 h at room temperature followed by work-up and distillation gave the *S*-propyl (*S*-benzyl) compound (66—84%).

ii) Conversion of the *S*-Alkyl-acids to the Amides: *S*-Alkyl-acid (1 mmol) in dry benzene (20 ml) was treated with thionyl chloride (0.3 ml) and the reaction mixture was refluxed for 3 h, then cooled. Benzene and excess thionyl chloride were removed under reduced pressure. The residue was dissolved in dry benzene (10 ml) and amine gas (ammonia, monomethylamine, or dimethylamine) was bubbled into the solution for 5 min. Extractive work-up gave a residue. Recrystallization or bulb-to-bulb distillation afforded the pure amide. (Table VI1).

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References and Notes

1) *a*) This paper constitutes Part VII of the series entitled "Thiol Compounds." Thiol Compounds. VI:

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