

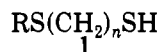
# NMR and Mass Spectroscopic Studies on *n*-(Alkylthio)-1-alkanethiols

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Results on mass and  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectral data of *n*-(alkylthio)-1-alkanethiols ( $\text{RS}(\text{CH}_2)_n\text{SH}$ ) are presented. These compounds, which have been identified as flavors in natural products, show characteristic behavior in NMR and mass spectroscopy depending on the number of methylene groups (*n*) between the sulfur atoms. 2-(Alkylthio)-1-ethanethiols (*n* = 2) can easily be identified by their typical  $^1\text{H}$  NMR spectra; they show an additional coupling for the SH protons with the  $\text{RSCH}_2$  protons. Generally, fragmentation of molecular ions of the title compounds occurs mainly by  $\alpha$ - and  $\beta$ -cleavage, leading to intense peaks of *m/e* 61 and 47. For 3-(alkylthio)-1-propanethiols (*n* = 3), characteristic peaks with *m/e* 107 and 106 corresponding to  $[\text{M} - (\text{R})]^{*+}$  and  $[\text{M} - (\text{R} - (\text{H}))]^{*+}$ , respectively. Such fragments are not generated from molecular ions of all other *n*-(alkylthio)-1-alkanethiols.

*n*-(Alkylthio)-1-alkanethiols **1** have been identified as flavors in natural compounds and foodstuffs (Brinkman et al., 1972; Golovnya et al., 1983; Mikhailova et al., 1975; Schutte and Koenders, 1972) and have been proposed as warning agents for gaseous hydrocarbon fuels (Crouch and Williams, 1974). It has been shown that they are generated by thermal treatment of industrial broths (Mikhailova et al., 1975); e.g., they have been detected in the headspace of simmering beef broth (Brinkman et al., 1972a; Schutte et al., 1972). They have also been found in the aroma of synthetic meat flavors obtained by baker's yeast autolysate in Maillard reactions (Golovnya et al., 1983), and it has been discovered that such compounds strengthen the meat flavor in foods (Brinkmann et al., 1972b). 2-(Methylthio)-1-ethanethiol smells like fresh onions (Brinkman and van der Heyden, 1971), whereas the organoleptic characteristic of 3-(methylthio)-1-propanethiol is watermelon-like (Mikhailova et al., 1975). The title compounds have been mostly identified by GC/MS analysis; only very few such compounds have been synthesized and characterized by NMR.



We now report results on synthesis, mass spectra, and  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of a series of *n*-(alkylthio)-1-alkanethiols **1**.

## EXPERIMENTAL SECTION

**Synthesis.** All compounds were synthesized by reaction of *n*-(alkylthio)-1-haloalkanes with thiourea as described in the literature for **1a** (Yarv et al., 1976), **1f** (Furukawa et al., 1984) and **1g** (van Noort et al., 1983). The precursor *n*-(alkylthio)-1-haloalkanes were purchased from Aldrich [1-chloro-2-(methylthio)ethane] or Fairfield [1-chloro-2-(ethylthio)ethane, 1-chloro-2-(isopropylthio)ethane, 1-chloro-2-(butylthio)ethane] or were synthesized according to the literature (Anklam, 1987). Yields were in the range of 52–68%.

**NMR Studies.** The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker WM 400 or Bruker WM 270 spectrometer of  $10^{-3}$  M solutions of **1** in  $\text{CDCl}_3$ . Chemical shifts ( $\delta$ ) are given vs TMS as internal standard; coupling constants are given in hertz.

**Mass Spectroscopy.** The mass spectra were obtained on a Varian MAT 44 mass spectrometer. The spectra were run at 70 eV with an emission current of 100  $\mu\text{A}$ .

## RESULTS AND DISCUSSION

Most of the investigated *n*-(alkylthio)-1-alkanethiols **1** were newly synthesized. 2-(Alkylthio)-1-ethanethiols can

be obtained by several methods as reaction of 1,3-dithiolane derivatives with  $\text{Ca}/\text{NH}_3$  (Newman and Eliel, 1970) or of thiirane with alkyl mercaptans (Fokin et al., 1975; Meade and Woodward, 1948; Oswald, 1971, 1979) or reaction of 2-(alkylthio)-1-haloethanes with thiourea (Yarv et al., 1976). The latter reaction of *n*-(alkylthio)-1-haloalkanes (Anklam, 1987; Palmer and Taylor, 1986) with thiourea is most useful for syntheses of all compounds with *n* > 2. The chemical shifts of  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra and mass spectral data of compounds **1** are listed in Table I.

The molecular ions of **1** are intense, as observed for other organic sulfides (van de Sande, 1981) and thiols (Levy and Stahl, 1961; Lifshitz and Zaretski, 1974). Similar to the mass spectral behavior of 1,*n*-bis(alkylthio)alkanes **2** ( $\text{RS}(\text{CH}_2)_n\text{SR}$ ) (Anklam, 1989b; Shuttleworth, 1964), fragmentation occurs mainly by  $\alpha$ - and  $\beta$ -cleavage to one sulfur atom. For 2-(alkylthio)-1-ethanethiols (**1a–e**) the ratio of fragments derived by  $\alpha$ - and  $\beta$ -cleavage is about 1:1. Either base or strong peaks of *m/e* 61 corresponding to  $[\text{C}_2\text{H}_5\text{S}]^+$  and *m/e* 47 corresponding to  $[\text{CH}_2\text{SH}]^+$  are observed. Fragmentation of  $[\text{C}_2\text{H}_5\text{S}]^+$  (de Broer and Weringa, 1978; van de Graaf et al., 1975) and generation of  $[\text{CH}_2\text{SH}]^+$  from thiols (Levy and Stahl, 1961; Lifshitz and Zaretski, 1974) are well described in the literature.

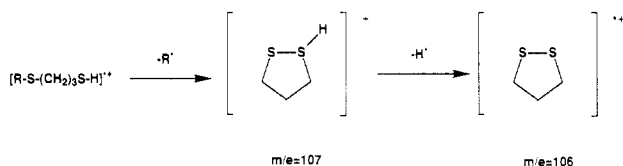
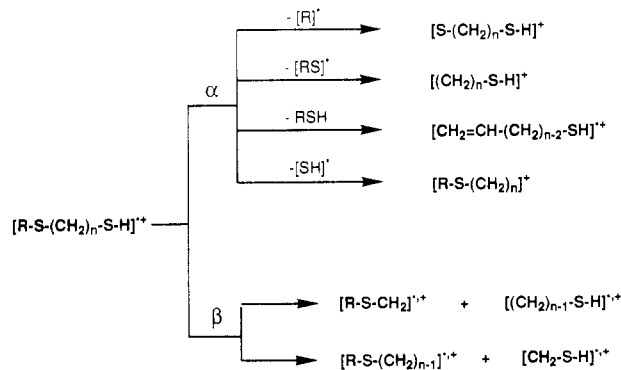
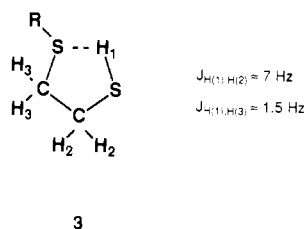
Fragmentation of 3-(alkylthio)-1-propanethiols occurs mainly by  $\beta$ -cleavage whereby the stable ions with *m/e* 61 and 47 are generated. This is in contrast to the fragmentation pattern of 1,3-bis(alkylthio)propanes where  $\alpha$ -cleavage is found to be predominant (Anklam, 1989b). For 1,3-bis(alkylthio)propanes strong peaks corresponding to  $[\text{M} - (\text{R})]^{*+}$  and  $[\text{M} - (\text{R} - (\text{H}))]^{*+}$  were detected; they were assigned to five-membered cyclic ions (Anklam, 1989b; Budzikiewicz et al., 1967; Musker et al., 1978). Also similar to these compounds, strong peaks with *m/e* 107 derived from  $\alpha$ -cleavage are observed for compounds **1f–i**, which correspond to  $[\text{M} - (\text{R})]^{*+}$ . In addition, peaks with *m/e* 106 related to  $[\text{M} - (\text{R} - (\text{H}))]^{*+}$  are generated in relatively high intensities. The occurrence of the intense peaks *m/e* 107 and 106 can be explained by the assumption that these fragments undergo stabilization by cyclization to form five-membered rings (Scheme I).

By comparing the relative intensities of the fragments with *m/e* 107, it can be seen that the loss of a methyl radical is preferred relative to that of other alkyl radicals (ethyl, propyl, isopropyl). Similar results for neu-

**Table I. Chemical Yields and Mass and <sup>1</sup>H and <sup>13</sup>C NMR Data of Compounds 1**

compd	n	R	MS, m/e (%)	<sup>1</sup> H NMR, δ	<sup>13</sup> C NMR, δ
1a	2	CH <sub>3</sub>	108 (16), 61 (100), 60 (28), 59 (22), 47 (75)	1.70 (m, 1 H), 2.09 (s, 3 H), 2.69–2.73 (m, 4 H) <sup>c</sup>	15.3, 24.1, 38.1 <sup>c</sup>
1b	2	C <sub>2</sub> H <sub>5</sub>	122 (21), 75 (15), 61 (42), 60 (31), 59 (22), 47 (100)	1.25 (t, 3 H), 1.73 (7, 1 H), 2.45 (t, 2 H), 2.50–2.55 (m, 4 H) <sup>d</sup>	14.8, 24.6, 25.7, 35.6 <sup>d</sup>
1c	2	C <sub>3</sub> H <sub>7</sub>	136 (24), 89 (21), 61 (100), 60 (34), 59 (25), 47 (90)	0.98 (t, 3 H), 1.61 (m, 2 H), 1.73 (m, 1 H), 2.50 (t, 2 H), 2.70–2.75 (m, 4 H) <sup>d</sup>	14.0, 22.9, 24.7, 34.0, 36.0 <sup>d</sup>
1d	2	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	136 (25), 89 (11), 61 (52), 60 (29), 59 (29), 55 (36), 47 (100)	1.23 (d, 6 H), 1.69 (m, 1 H), 2.65–2.75 (m, 4 H), 2.91 (m, 1 H) <sup>c</sup>	23.4 (2), 24.9, 34.6, 34.9 <sup>c</sup>
1e	2	C <sub>4</sub> H <sub>9</sub>	150 (13), 61 (100), 60 (18), 57 (12), 56 (18), 5 (20), 47 (32)	0.92 (t, 3 H), 1.41 (m, 2 H), 1.56 (m, 2 H), 1.74 (m, 1 H), 2.52 (t, 2 H), 2.69–2.75 (m, 4 H) <sup>d</sup>	13.6, 21.9, 22.0, 24.7, 31.6, 31.7, 31.8, 36.1 <sup>d</sup>
1f <sup>a,b</sup>	3	CH <sub>3</sub>	122 (27), 107 (69), 106 (20), 88 (17), 75 (17), 74 (72), 73 (40), 61 (100), 47 (63)	1.36 (t, 1 H), 1.86 (m, 2 H), 2.07 (s, 3 H), 2.53–2.63 (m, 4 H) <sup>c</sup>	15.4, 23.3, 32.5, 32.8 <sup>c</sup>
1g	3	C <sub>2</sub> H <sub>5</sub>	136 (28), 107 (40), 106 (13), 75 (55), 61 (80), 47 (100)	1.26 (t, 3 H), 1.37 (t, 1 H), 1.87 (m, 2 H), 2.53 (q, 2 H), 2.60–2.66 (m, 4 H) <sup>d</sup>	14.7, 23.4, 25.8, 29.8, 33.3 <sup>d</sup>
1h	3	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	150 (18), 107 (15), 106 (9), 75 (6), 61 (21), 47 (100)	1.23 (d, 6 H), 1.34 (t, 1 H), 1.85 (m, 2 H), 2.59–2.65 (m, 4 H), 2.89 (m, 1 H) <sup>c</sup>	23.4, 23.6, 28.8, 33.5, 34.8 <sup>c</sup>
1i	3	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	164 (20), 107 (21), 106 (4), 57 (100), 47 (55)	1.29 (s, 9 H), 1.33 (t, 1 H), 1.85 (m, 2 H), 2.53–2.63 (m, 4 H) <sup>c</sup>	23.7, 26.6, 31.0 (3), 33.7 <sup>c</sup>
1j <sup>c</sup>	4	CH <sub>3</sub>	136 (31), 103 (36), 61 (100), 60 (28), 47 (32)	1.36 (t, 1 H), 1.72 (m, 4 H), 2.10 (s, 3 H), 2.49–2.57 (m, 4 H) <sup>d</sup>	15.4, 24.2, 27.2, 32.9, 33.6 <sup>d</sup>
1k	4	C <sub>2</sub> H <sub>5</sub>	150 (15), 75 (53), 61 (42), 47 (100)	1.24 (t, 3 H), 1.36 (t, 1 H), 1.72 (m, 4 H), 2.48 (t, 2 H), 2.50–2.55 (m, 4 H) <sup>c</sup>	15.3, 23.2, 25.7, 27.5, 29.6, 33.1 <sup>c</sup>
1l	5	CH <sub>3</sub>	150 (30), 117 (55), 69 (52), 68 (22), 61 (100), 47 (33)	1.36 (t, 1 H), 1.52 (m, 2 H), 1.57–1.68 (m, 4 H), 2.10 (s, 3 H), 2.48–2.55 (m, 4 H) <sup>d</sup>	15.5, 24.5, 27.4, 28.4, 33.6, 34.1 <sup>d</sup>
1m	5	C <sub>2</sub> H <sub>5</sub>	164 (27), 131 (80), 101 (15), 87 (17), 75 (100), 69 (92), 61 (30), 47 (55)	1.25 (t, 3 H), 1.35 (t, 1 H), 1.52 (m, 2 H), 1.56–1.67 (m, 4 H), 2.48–2.58 (m, 6 H) <sup>d</sup>	14.8, 24.5, 25.9, 28.1, 28.8, 31.4, 33.6 <sup>d</sup>

<sup>a</sup> Bannister et al. (1978). <sup>b</sup> Furukawa et al. (1984). <sup>c</sup> 400-MHz NMR. <sup>d</sup> 270-MHz NMR.

**Scheme I****Scheme II****Chart I**

3

No occurrence of fragments corresponding to  $[M - (R)]^{+}$  is observed for the 4-(alkylthio)-1-butanethiols. It has been shown that such fragments have only low intensities for the corresponding 1,4-bis(alkylthio)butanes (Anklam, 1989b). One may expect that the six-membered rings are less stabilized than their five-membered analogues. Fragmentation of molecular ions of 4-(alkylthio)-1-butanethiols 1j,k leads to peaks corresponding to  $[M - (HS)]^{+}$  which are not observed in compounds 1 with  $n = 2$  and 3.

Such fragments have very high intensities in compounds 1l,m with  $n = 5$ ; the further fragmentation by loss of RSH leads to strong peaks of  $m/e$  69.

An overview of these different fragmentation patterns from molecular ions of 1 is summarized in Scheme II.

As seen from Table I the <sup>13</sup>C NMR data for all compounds 1 are very similar. While the chemical shifts and coupling constants of the <sup>1</sup>H NMR spectra of compounds with  $n = 3$ –5 are almost comparative (CH<sub>2</sub>SH; CH<sub>2</sub>SR:  $\delta \approx 2.6$ ,  $J \approx 7$  Hz), those of the 2-(alkylthio)-1-ethanethiols show remarkable differences. It can be seen in the spectra of 1a–e that there is an additional coupling ( $\approx 1.5$  Hz) for the SH protons with the RSCH<sub>2</sub> protons. In addition the SH protons are shifted to lower field ( $\delta \approx 1.7$  Hz) compared to those of compounds with  $n = 3$ –5 ( $\delta \approx 1.3$ ). This may be explained by formation of 3 via interaction of the SH proton with the second sulfur atom as shown in Chart I.

The present results demonstrate that 2-(alkylthio)-1-ethanethiols can easily be identified by their typical <sup>1</sup>H NMR spectra. Fragmentation of molecular ions of compounds 1 occurs by  $\alpha$ - and  $\beta$ -cleavage leading to intense peaks on  $m/e$  61 and 47. Typical peaks with  $m/e$  107 and 106 are observed for compounds with  $n = 3$ ; such fragments are not observed for all other  $n$ -(alkylthio)-1-alkanethiols investigated with  $n = 2$  and  $n > 3$ . These fragments are characteristic for compounds 1 with  $n = 3$ , and their occurrence supports the assumption of cyclization to form the five-membered ions as already discussed for 1,3-bis(alkylthio)propanes. The present data may be helpful in the characterization of  $n$ -(alkylthio)-1-alkanethiols in aroma compounds, foodstuffs, and natural products.

tral excited parent molecules have been found in photochemical studies of 1, $n$ -bis(alkylthio)alkanes 2 (Anklam, 1989a).

**Registry No.** 1a, 22322-43-6; 1b, 26750-44-7; 1c, 26733-37-9; 1d, 20157-77-1; 1e, 25543-40-2; 1f, 26718-09-2; 1g, 36044-02-7; 1h, 120462-80-8; 1i, 120462-82-0; 1j, 66890-94-6; 1k, 36044-03-8; 1l, 123674-86-2; 1m, 36044-04-9.

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