Mass Spectra of Some Alkylthiazoles

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The mass spectra of 24 alkylthiazoles have been measured and the major peaks tabulated. The compounds were synthesized by general methods and purified by gas chromatography. The synthesis of 16 of the alkylthiazoles had not previously been reported.

Workers analyzing the volatile aroma constituents of foods by the direct combination of capillary gas–liquid chromatography (glc) and mass spectrometry frequently obtain large numbers of mass spectra which they can not interpret because of the lack of published spectra of the types of compounds commonly found in foods. The publication of mass spectra of families of food compounds, such as that of terpenoids by Ryhage and von Sydow (1963) and alkylpyrazines by Bondarovich *et al.* (1967), has allowed many other workers to identify such compounds in various food products. In our own studies in recent years, in order to interpret some unknown mass spectra, we synthesized and obtained mass spectra of a number of alkylthiazoles. As there are limited published spectra of these compounds available (Clarke *et al.*, 1966; Webster and Rix, 1971) we report their spectra here in the hope that they may be of use to other workers. Alkylthiazoles have been found in several foods, including roasted filberts (Kinlin *et al.*, 1972), roasted peanuts (Walradt *et al.*, 1971), and roasted coffee (Stoll *et al.*, 1967). Related thiazolines (4,5-dihydrothiazoles) have been found in beef broth (Tonsbeek *et al.*, 1971). Benzothiazole has been reported in a large number of foods varying from beer (Buttery *et al.*, 1967) to chocolate (Flament *et al.*, 1967).

Pittet and Hruza (1972) recently discussed the synthesis and odor properties of some food-related alkyl-, acyl-, and alkoxythiazoles. Their manuscript, which will also include some additional mass spectral data, will be published in the near future (Forss, 1973).

MATERIALS AND METHODS

Synthesis of Bromoketones. These were generally synthesized by the method described by Catch *et al.* (1948), which involves essentially direct bromination of the appropriate ketone. With unsymmetrical ketones, two bromoketones are formed. In some cases it was possible to separate these by fractional distillation with a spinning band (Teflon) column. In most cases, the mixture of the two bromides was taken through the thiazole synthesis and the two thiazoles were separated by glc.

Synthesis of 2-Bromoaldehydes. These were synthesized by the method of Bedoukian (1944), which involves conversion of the corresponding saturated aldehyde to its enol acetate followed by addition of bromine, and then conversion to the dimethyl acetal and hydrolysis to the bromoaldehyde.

Synthesis of Alkylthiazoles. These were synthesized by the method of Kurkjy and Brown (1952) by addition of the bromoaldehyde of bromoketone to the preformed thioamide. Yields were all generally quite satisfactory at about 50%. The steam distilled products were purified by glc using a 5 ft × ¼ in. aluminum column packed with 80–100 mesh Chromosorb P coated with 15% Amine 220. In some cases where a mixture of two bromoketones was used, the two thiazoles were separated by glc. Proton magnetic resonance (pmr) spectra was used to confirm the structure, in addition to the fairly clear mass spectral differentiation.

Mass Spectra. These were all measured on glc purified samples using a modified Consolidated 21-620 cycloidal type mass spectrometer with batchwise introduction. Ionization voltage was 70 V. The inlet system was constructed of stainless steel and was held at 100°.

Proton Magnetic Resonance Spectra. These were measured in $CDCl_3$ at 100 MHz using a Varian HA-100.

RESULTS AND DISCUSSION

Figure 1 shows the structures of the alkylthiazoles studied. Table I lists the mass spectra of the alkylthiazoles using the method of presentation of Herz *et al.* (1971), which involves dividing the spectrum up into consecutive regions of 14 mass units starting, in our case, at m/e 34, and listing the two most intense ions in each region. Intensities relative to the most intense ion whose intensity is taken as 100 are shown in parentheses immediately following the m/e value.

The mechanism of mass spectral fragmentation of some alkyl- and arylthiazoles has been previously discussed by Clarke *et al.* (1966) and Webster and Rix (1971). The authors are not experts in the mechanism of fragmentation and do not intend to cover this aspect except to mention a few empirical observations. The spectra are presented

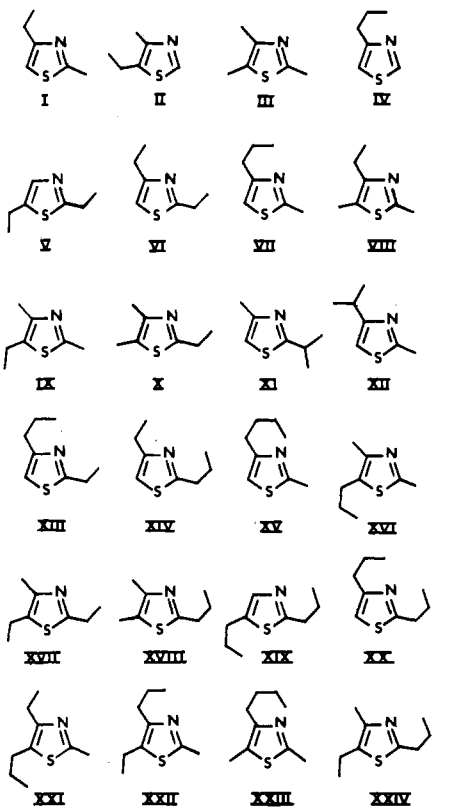

Figure 1. Structures of alkylthiazoles.

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mostly for their fingerprint nature. There are two main types of fragmentation which are very characteristic of alkylthiazoles. One is of the well known McLafferty rearrangement type. Alkylthiazoles with alkyl side chains (R) three carbons long or longer in the 2 or 4 positions show intense ions at M − (R − 15). On the other hand, alkylthiazoles with alkyl side chains (R) three carbons long or longer in the 5 position show intense ions at M − (R − 14). Thus, the mass spectrum of 4-propylthiazole has its most intense ion at m/e 99 (M − 28). Similarly, the mass spectrum of 2-propyl-4,5-dimethylthiazole has its most intense ion at m/e 127 (M − 28). In contrast, 2,4-dimethyl-5-propylthiazole has its most intense ion at m/e 126 (M − 29).

At least eight of the compounds shown in Figure 1 had been previously synthesized. These are II by Lindberg *et al.* (1970), III by Takahashi and Hayami (1961), V by Chouteau *et al.* (1962), VIII by Metzger and Berand (1956), X by Pyl *et al.* (1964), XI by Vincent *et al.* (1966), and XIII and XVIII by Asinger *et al.* (1964). As far as the authors can determine, the other compounds in Figure 1 had not previously been reported.

In several cases in the syntheses of the compounds in Figure 1, a mixture of two bromoketones was used in the synthesis, which resulted in two thiazoles. These were readily separable by glc. They were fairly easily differentiated from their mass spectral fragmentation patterns but this was also confirmed by pmr spectra in the following way. XVI was differentiated from XV, as were IX from VII, XVII from XIII, and XXIV from XX by the presence of an absorption maximum characteristic of the 5 position ring proton at *ca.* δ 6.7 (s) in the disubstituted member of the pairs mentioned and by the absence of this absorption in the trisubstituted compounds. In a similar way II was differentiated from IV by the absence of the 5 position proton absorption in the spectrum of II. XXIII

Table I. Mass Spectra of Alkylthiazoles[a]

Compound	Mass spectra
2-Methyl-4-ethylthiazole (I), C_6H_9NS	42 (16), 45 (24); 53 (13), 59 (30); 71 (98), 72 (15); 85 (35), 86 (91); 94 (0.6), 99 (0.7); 112 (2), 113 (0.2); 126 (6), *127* (100)
4-Methyl-5-ethylthiazole (II), C_6H_9NS	39 (16), 45 (36); 58 (5), 59 (9); 67 (7), 71 (9); 85 (33), 86 (3); 99 (5), 100 (5); 112 (100), 113 (9); 126 (4), *127* (60)
2,4,5-Trimethylthiazole (III), C_6H_9NS	39 (21), 45 (48); 53 (11), 59 (10); 69 (6), 71 (68); 85 (45), 86 (29); 99 (9), 100 (2); 112 (24), 113 (3); 126 (64), *127* (100)
4-Propylthiazole (IV), C_6H_9NS	39 (17), 45 (50); 58 (6), 59 (3); 71 (36), 72 (14); 85 (11), 86 (6); 98 (48), 99 (100); 112 (31), 113 (6); 126 (17), *127* (25)
2,5-Diethylthiazole (V), $C_7H_{11}NS$	40 (67), 45 (45); 53 (14), 57 (11); 71 (55), 73 (8); 85 (35), 86 (43); 93 (3), 99 (4); 112 (4), 113 (2); 126 (63), 127 (4); 140 (45), *141* (100)
2,4-Diethylthiazole (VI), $C_7H_{11}NS$	39 (14), 45 (24); 53 (14), 59 (21); 71 (65), 73 (7); 85 (21), 86 (69); 96 (0.4), 99 (0.8); 113 (5), 114 (2); 126 (28), 127 (3); 140 (49), *141* (100)
2-Methyl-4-propylthiazole (VII), $C_7H_{11}NS$	42 (16), 45 (47); 58 (7), 59 (9); 71 (60), 72 (13); 84 (1), 85 (9); 97 (2), 99 (7); 112 (25), 113 (100); 126 (20), 127 (1); 140 (13), 141 (24)
2,5-Dimethyl-4-ethylthiazole (VIII), $C_7H_{11}NS$	39 (20), 45 (22); 58 (11), 59 (45); 67 (10), 71 (5); 85 (86), 86 (7); 99 (15), 100 (23); 113 (5), 114 (0.9); 126 (48), 127 (5); 140 (39), *141* (100)
2,4-Dimethyl-5-ethylthiazole (IX), $C_7H_{11}NS$	39 (20), 45 (33); 58 (8), 59 (29); 67 (13), 71 (14); 85 (59), 86 (12); 99 (12), 100 (23); 112 (2), 113 (4); 126 (100), 127 (13); *141* (71), 142 (5)
2-Ethyl-4,5-dimethylthiazole (X), $C_7H_{11}NS$	39 (20), 45 (54); 53 (13), 56 (11); 71 (58), 73 (7); 85 (41), 86 (37); 96 (4), 99 (1); 112 (1), 113 (10); 125 (1), 126 (2); 140 (94), *141* (100)
2-Isopropyl-4-methylthiazole (XI), $C_7H_{11}NS$	39 (24), 45 (38); 54 (5), 55 (60); 71 (42), 72 (39); 85 (0.8), 87 (0.4); 96 (8), 99 (12); 112 (0.7), 113 (2); 126 (100), 127 (10); 140 (17), *141* (49)
2-Methyl-4-isopropylthiazole (XII), $C_7H_{11}NS$	39 (17), 45 (38); 58 (7), 59 (9); 63 (6), 67 (4); 85 (33), 86 (7); 99 (10), 100 (4); 108 (1); 113 (4); 126 (100), 127 (11); 140 (14), *141* (51)
2-Ethyl-4-propylthiazole (XIII), $C_8H_{13}NS$	39 (15), 45 (40); 56 (10), 58 (4); 71 (44), 72 (8); 84 (0.7), 85 (7); 97 (2), 99 (4); 112 (2), 113 (4); 126 (20), 127 (100); 140 (21), 141 (0.7); 154 (17), *155* (25)
2-Propyl-4-ethylthiazole (XIV), $C_8H_{13}NS$	41 (12), 45 (19); 53 (10), 59 (16); 70 (4), 71 (33); 85 (14), 86 (28); 96 (1), 99 (0.6); 112 (1), 114 (0.6); 126 (33), 127 (100); 140 (18); 154 (8), *155* (21)
2-Methyl-4-butylthiazole (XV), $C_8H_{13}NS$	43 (13), 45 (35); 58 (4), 59 (6); 71 (30), 72 (17); 85 (6), 86 (3); 97 (1), 99 (3); 112 (17), 113 (100); 141 (9), 142 (3); 154 (3), *155* (10)
2,4-Dimethyl-5-propylthiazole (XVI), $C_8H_{13}NS$	41 (9), 45 (16); 58 (4), 59 (11); 69 (3), 71 (5); 85 (18), 86 (3); 97 (0.9), 99 (2); 113 (4), 114 (0.9); 126 (100), 127 (4); 140 (0.4), 141 (0.2); *155* (30), 156 (8)
2,5-Diethyl-4-methylthiazole (XVII), $C_8H_{13}NS$	39 (17), 45 (27); 58 (5), 59 (15); 67 (8), 71 (10); 82 (6), 85 (32); 99 (12), 100 (26) 107 (2), 113 (1); 126 (3), 127 (5); 140 (100), 141 (5); 154 (22), *155* (81)
2-Propyl-4,5-dimethylthiazole (XVIII), $C_8H_{13}NS$	39 (15), 45 (38); 53 (9), 58 (5); 70 (4), 71 (29); 85 (21), 86 (13); 99 (4); 112 (4), 113 (2); 126 (11), 127 (100); 140 (23); 154 (17), *155* (20)
2,5-Dipropylthiazole (XIX), $C_9H_{15}NS$	39 (17), 45 (23); 58 (7), 59 (6); 67 (5), 71 (18); 79 (2), 85 (7); 98 (16), 99 (9); 112 (15), 113 (4); 124 (1), 125 (2); 140 (26), 141 (100); 154 (18), 155 (0.6); 168 (9), *169* (15)
2,4-Dipropylthiazole (XX), $C_9H_{15}NS$	41 (13), 45 (30); 55 (3), 58 (4); 70 (6), 71 (33); 85 (6), 87 (2); 99 (3), 100 (3); 112 (7), 113 (5); 125 (2), 127 (1); 141 (100), 142 (10); 154 (22), 155 (3); 168 (11), *169* (19)
2-Methyl-4-ethyl-5-propylthiazole (XXI), $C_9H_{15}NS$	39 (12), 45 (15); 58 (5), 59 (20); 65 (8), 71 (6); 79 (2), 85 (5); 97 (3), 99 (15); 112 (2), 113 (3); 126 (3), 127 (2); 140 (100), 141 (18); 154 (15), 155 (2); 168 (3), *169* (33)
2-Methyl-4-propyl-5-ethylthiazole (XXII), $C_9H_{15}NS$	39 (10), 45 (25); 58 (7), 59 (26); 65 (11), 71 (10); 79 (3), 85 (5); 97 (5), 99 (31); 112 (2), 113 (3); 126 (12), 127 (3); 140 (66), 141 (100); 154 (27), 155 (11); 168 (10), *169* (52)
2,5-Dimethyl-4-butylthiazole (XXIII), $C_9H_{15}NS$	41 (12), 45 (16); 58 (5), 59 (28); 65 (3), 71 (5); 85 (30), 86 (10); 97 (1), 99 (3); 111 (1), 112 (3); 126 (21), 127 (100); 140 (23), 141 (4); 154 (11), 155 (2), *169* (18), 170 (3)
2-Propyl-4-methyl-5-ethylthiazole (XXIV), $C_9H_{15}NS$	41 (22), 45 (28); 53 (6), 59 (20); 65 (9), 71 (12); 85 (24), 87 (2); 99 (14), 100 (12); 112 (6), 113 (2); 126 (16), 127 (2); 140 (15), 141 (100); 154 (31), 155 (1); 168 (7), *169* (22)

[a] Method of presentation is that of Herz *et al.* (1971). Molecular ions are italicized.

was differentiated from XXI by the presence of two ring methyl absorption maxima at δ 2.3 (s) and 2.6 (s) in XXIII and the absence of the δ 2.3 (s) absorption in the spectrum of XXI. In all cases other features of the spectra also confirmed these assignments.

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Ethylene-Accelerated Limonoid Metabolism in Citrus Fruits: A Process for Reducing Juice Bitterness

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A 3-hr treatment of citrus fruits (navel oranges, lemons, grapefruit) with 20 ppm of ethylene induces accelerated limonoate A-ring lactone metabolism. Accelerated metabolism continues after ethylene exposure ceases and results in substantial loss of limonoate A-ring lactone in several days. Juice from treated fruit has a lower limonin content, is less bitter, and is more preferred by judges than juice from untreated fruit. Longer exposure to ethylene has no greater effect on limonoate A-ring lactone metabolism than the 3-hr treatment, but it can be detrimental to juice quality. The ethylene treatment has no effect on the naringin content of grapefruit juice nor on ascorbic acid content. Spraying fruit with 2-chloroethylphosphonic acid in wax is another way of achieving the ethylene effect.

The problem of delayed bitterness in citrus products is becoming more acute with the yearly increases in citrus production. As production increases, a higher percentage of the crop goes to citrus products rather than to the fresh fruit market. Citrus products from navel oranges, as well as some lemons and grapefruit, are bitter if their limonin content is over 6–9 ppm (Kefford and Chandler, 1970). Early investigators observed that juice from late-season oranges was less bitter than that from early-season fruit. Unfortunately, the low bitterness level is reached only late in the harvest season, after much of the crop has been harvested. Other investigators attempted to simulate this on-the-tree debittering by storing early-season navel oranges in warm, moist rooms (Rockland *et al.*, 1957). Although this approach had a number of serious drawbacks that prevented its commercialization, some debittering was achieved during prolonged storage.

Maier and Beverly (1968) found that delayed bitterness is caused by the conversion of the nonbitter limonoid limonoate A-ring lactone to bitter limonin by the juice acids during juice extraction. In later work, Maier and Margileth (1969) found that the metabolic debittering system of the late-season fruit acts to prevent bitterness by destroying the nonbitter precursor substance, limonoate A-ring lactone. It was reasoned that a logical approach to solving the limonin bitterness problem would be to find a way to accelerate the natural slow metabolism of limonoate A-ring lactone in the fruit.

Since limonin content had been observed to be inversely related to fruit maturity, the ripening hormone ethylene and the ethylene-generating compound 2-chloroethylphosphonic acid (CEPA) were considered likely agents to promote accelerated limonoid metabolism. Study of ethylene was also of interest because earlier investigators, working without benefit of an analytical method for limonin, found either no acceleration effect of ethylene on debittering (Samish and Ganz, 1950) or an increase in other off-flavors (Emerson, 1949). Our preliminary studies demonstrated that ethylene does, in fact, accelerate limonoid metabolism in citrus fruits (Maier and Brewster, 1971; Maier *et al.*, 1971). This paper reports the effects of ethylene and CEPA concentration, time of exposure, temperature, and length of holding time on limonin content and flavor of the juice.

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