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New Volatile Sulfur-Containing Constituents in a Simultaneous Distillation−Extraction Extract of Red Bell Peppers (*Capsicum annuum*)

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An extract of red bell peppers (*Capsicum annuum*) was prepared by simultaneous distillation−extraction (SDE, Likens−Nickerson). In addition to the already known (3*E*)-3-hepten-2-one (**1**), the unsaturated C9-ketones 1-nonen-4-one (**2**), (2*E*)-2-nonen-4-one (**3**), and (2*E*,5*E*)-2,5-nonadien-4-one (**4**), 2-methoxy-3-isobutylpyrazine (**5**), and heptane-2-thiol (**6**), we identified 19 new thiols (the aliphatic saturated and unsaturated thiols **14**–**16**, and **22**–**27**, the mercapto-ketones **12** and **13**, the mercapto-alcohols **17**, **18**, and **30**, the dithiols **19** and **28**, the methylthio-thiols **20** and **21**, and the thiophene-thiol **31**) and the two new dithiolanes **10** and **29**. All of them are structurally related to the unsaturated C7- and C9-ketones **1**−**4**. The free thiols were enriched using Affi-Gel 501 (*p*-aminophenyl-mercuric acetate grafted on an agarose gel). The new compounds were confirmed by syntheses and were organoleptically evaluated.

KEYWORDS: Bell peppers; *Capsicum annuum*; sulfur compounds; thiols; dithiolanes; identification; GC-MS; syntheses; odor-description

INTRODUCTION

The species *Capsicum annuum* (Solanaceae) includes a large number of cultivars, among them sweet peppers and chilli peppers, mostly consumed as fresh fruits, as well as mild and hot varieties converted to ground Cayenne pepper or paprika, both used as spices. Sweet peppers, so-called bell peppers, are large, crisp and thick-walled fruits, green in the unripe and red in the ripe state and usually bell-shaped. They have a pleasant sweet taste with a slight pungency. Their outstanding, peculiar flavor is reflected in the very particular composition of the volatile constituents. Numerous publications describe the volatile constituents of bell peppers (*1*−*4*). Buttery et al. first recognized the special composition of a steam-distillate, identifying (3*E*)-3-hepten-2-one (**1**), the unsaturated C9-ketones 1-nonen-4-one (**2**), (2*E*)-2-nonen-4-one (**3**), and (2*E*,5*E*)-2,5-nonadien-4-one (**4**) as well as 2-methoxy-3-isobutylpyrazine (**5**) (*1*). An overview of various papers is given by Mazida et al., who investigated the various maturity stages of peppers by solid phase microextraction (SPME) (*5*). A recent publication by Simian et al. (*6*) summarizes analytical investigations of the bell pepper flavor but focuses on the identification and synthesis of heptane-2-thiol (**6**), to which the typical sensory properties of bell pepper was attributed. The abundance of various unsaturated C7- and C9-compounds in bell pepper extracts aroused our curiosity as to the possibility that other potent sulfur compounds would contribute to their flavor, either by the addition of a sulfur atom to the C=C double bonds or by replacement of oxygen by sulfur. Because cooked red bell peppers are known to contain the highest amounts of **6** (*6*), and are thus favorably disposed for the discovery of further sulfur-containing compounds, the starting material for our analytical investigation was an extract of red bell peppers prepared by the simultaneous distillation extraction (SDE) method following Likens and Nickerson (*7*). The free thiols were concentrated on an agarose gel grafted with mercury that is selective for mercaptans (*8*–*10*). Indeed, the GC-MS-analysis of this thiol fraction revealed a multitude of compounds present in very low concentrations, which had unknown mass spectra (MS) showing fragments consistent with the presence of sulfur atoms. In this work we discuss 21 new sulfur containing compounds that were, as supposed, related to the unsaturated ketones **1**–**4**. They have interesting organoleptic properties useful for red pepper flavors as well as for savory flavors in general. All of them were synthesized for structural confirmation and for organoleptic evaluation.

EXPERIMENTAL PROCEDURES

Preparation of the Bell Pepper Extracts. Red bell peppers from Spain, bought from the local market, without seeds, and cut into small cubes (597 g) in water (demineralised, 1000 mL), were submitted to SDE in a classical Likens−Nickerson apparatus for 90 min with pentane (150 mL). The organic phase was dried with $MgSO_4$ and concentrated using a Vigreux column. This procedure was repeated six times; 190 mg of extract were obtained from 3.55 kg of bell peppers.

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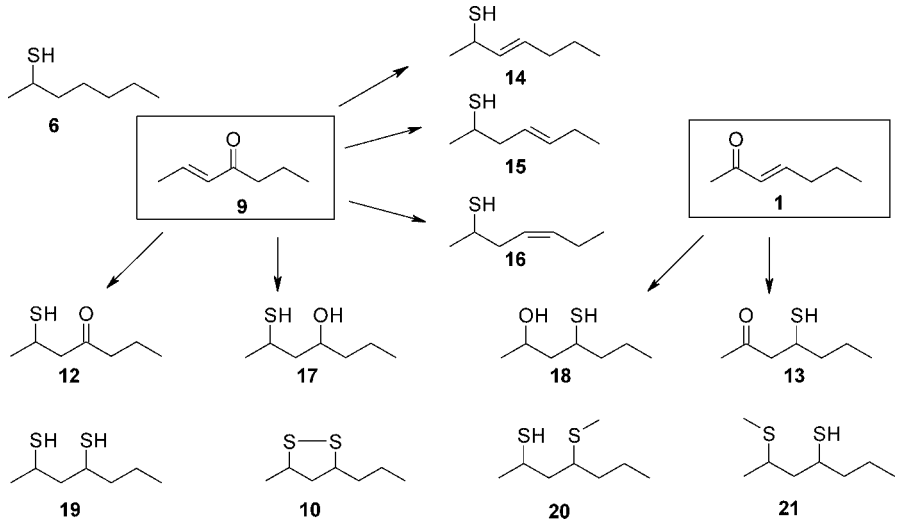

Figure 1. New sulfur-containing heptane derivatives in bell peppers.

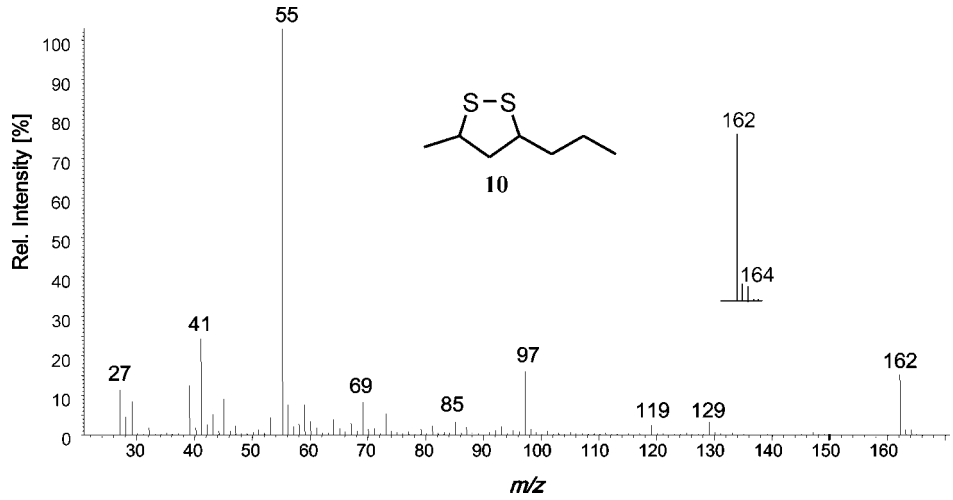

Figure 2. Mass spectrum of dithiolane **10**.

Isolation of the Thiols. In analogy to refs *8 and 9*, a Pasteur pipet, equipped with a small cotton plug, was charged with Affi-Gel 501 (*9*, 3 mL), which was conditioned with isopropanol (5 mL) and CH_2Cl_2 (5 mL). The red bell pepper extract (50 mg) dissolved in CH_2Cl_2 (1 mL) was slowly applied. The gel was washed with CH_2Cl_2 (10 mL) prior to the desorption of the thiols with a 10 mM solution of dithiothreitol (5 mL). The extract was concentrated to about 0.1 mL using a Vigreux column.

Preparation of the "Blank". To exclude artifacts created by the extraction procedure, a blank extract was prepared following the same procedure under strictly identical conditions, with the only exception being that no bell peppers were added to the Likens−Nickerson extraction.

GC-MS Analysis. GC-MS was performed on a GC 6890 (Agilent, Palo Alto, CA, USA) equipped with a 30 m × 0.25 mm i.d. fused silica Supelcowax polar capillary column (SPWax), with a film thickness of 0.25 μm, held at 50 °C for 5 min, then increased at 5°/min to 240 °C, coupled to a MS 5972 (Agilent) or on a GC 6890 N equipped with a 30 m × 0.25 mm i.d. fused silica SPB-1 apolar capillary column, with a film thickness of 1 μm, held at 60 °C for 5 min, then increased at 5°/min to 250 °C, coupled to a MS 5973 Inert (Agilent). The carrier gas was He (63 kPa) for both systems. The mass spectra in the electron impact mode (EI) were measured at 70 eV in a scan range from *m/z* 30 to 300. The relative percentages were calculated by integration of the total ion stream.

Nuclear Magnetic Resonance Spectra. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker DPX 400 instrument with tetramethylsilane as internal standard, $\delta = 0.00$ ppm (coupling constants *J* in Hz); pulse sequence: power-gated decoupled ^{13}C experiments with 30 °C excitation pulse (decoupling scheme WALTZ16); multiplicity was obtained from DEPT90 and DEPT135 experiments; recycle delay: 1 s; sweep width: 26000 Hz; data-points: 32768; line-broadening: 1.5 Hz. COSY, ^{13}C, ^{1}H-HSQC and ^{13}C, ^{1}H-HMBC experiments were performed on a Bruker AVANCE 500 MHz instrument (Karlsruhe, Germany) at 25 °C under standard conditions with coherence selection by gradients and 256 increments. Because of the extent of the synthetic work, the coupling constants (*J*) are only determined for double bonds in order to corroborate their (*E*) or (*Z*) geometry. For the other compounds, only the multiplicity is given, because *J* is not crucial for the confirmation of structures with alkyl chains. For complex intermediates (tosylates and ethanethioates) only the characteristic signals are given.

HPLC. An Agilent 1100 series system equipped with an analytical fraction collector, G 1364A, and an Uptisphere column 5 ODB, 250 × 10 mm i.d. (Interchrom) was used. Isocratic elution was performed with water/acetonitril (30/70) at 40 °C, with a flow rate of 4 mL/min and UV detection at 260 nm.

Linear Retention Indices (RI). RI values were determined after injection of a series of *n*-alkanes under the same conditions.

Syntheses. *General Methods.* Method A: transformation of alcohols to tosylates (*6*). Method B: transformation of tosylates to thioacetates (*6*). Method C: transformation of thioacetates to thiols (*6*). Chromatographic purification on Silica gel (35–70 μm, SDS, France) with eluent mixtures in volume-%.

*(±)-Nonane-2-thiol (***22***).* See **Figure 5**. Under nitrogen, 2-bromononane (**32**, 10.04 g, 48.5 mmol, Lancaster), thiourea (4.46 g, 58.2 mmol), and ethylene glycol (25 mL) were heated at 80 °C for 17.5 h. When the reaction mixture was cooled to about 40 °C, NaOH (2.9 g,

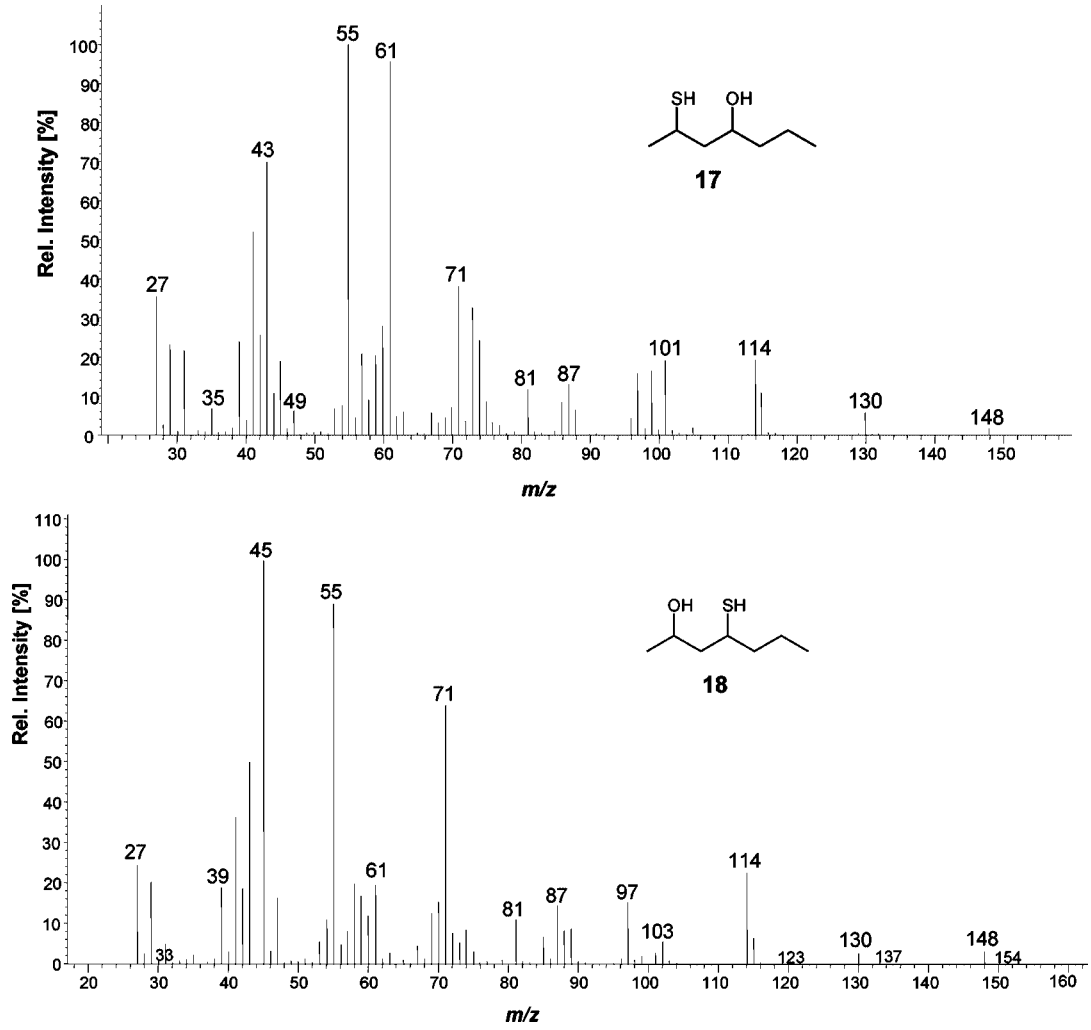

Figure 3. MS of compounds **17** and **18**.

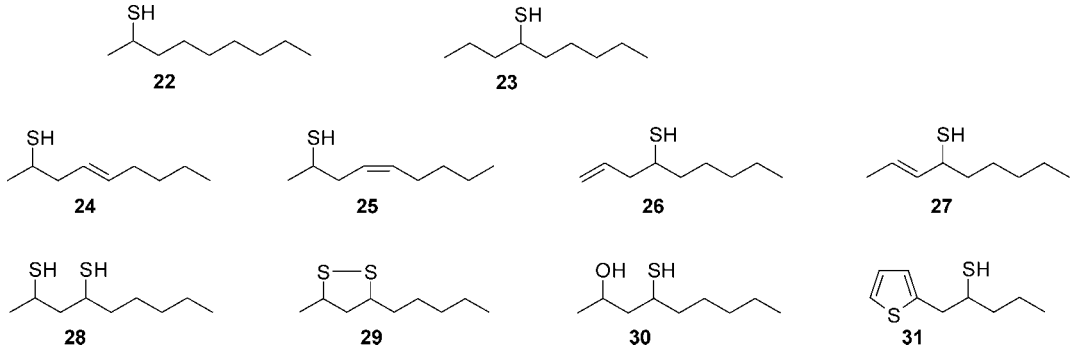

Figure 4. New sulfur-containing nonane derivatives in red bell peppers.

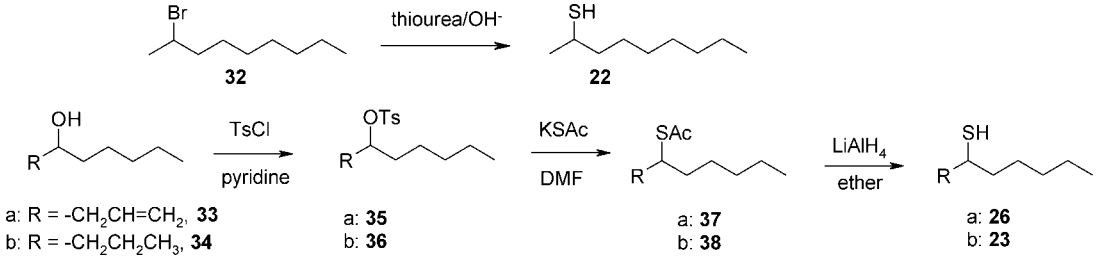

Figure 5. Synthesis of compounds **23** and **26**.

72.5 mmol) in H_2O (29 mL) was added dropwise over 10 min. Then, the reaction mixture was heated at 80 °C for 2 h. Then, at 20 °C, HCl (10%) was added until the pH was acidic (formation of CO_2). After addition of NaCl, the mixture was extracted with pentane (3×), washed with brine until neutral (4×), and dried over $MgSO_4$; the solvent was removed. The residue was distilled using a Vigreux-column (81–82°/12 Torr) to give 5.13 g of pure **22** (yield: 66%). For spectral data, see ref *13*.

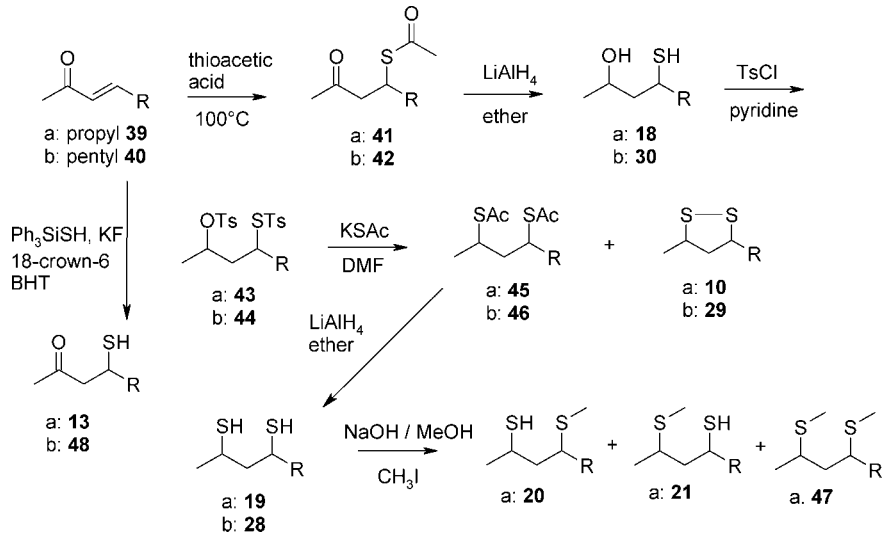

Figure 6. Syntheses of compounds **18**, **30**, **10**, **29**, **13**, **19**, **28**, **20** and **21**.

*(±)-1-Nonene-4-thiol (***26***) and (±)-nonane-4-thiol (***23***).* See **Figure 5**. Tosylates **35** and **36** were prepared following Method A. 1-Nonen-4-ol (**33**) was purchased from ABCR, and 4-nonanol (**34**) was from Alfa Aesar. (±)-1-Pentyl-3-butenyl-4-methylbenzenesulfonate (**35**), yield: 78%. ^{1}H NMR: 0.82 (t, 3H); 1.10–1.30 (m, 6H); 1.55 (m, 2H); 2.36 (m, 2H); 2.43 (s, 3H); 4.57 (m, 1H); 5.03 (br. d, 2H); 5.62 (m, 1H); 7.32 (d, 2H); 7.79 (d, 2H). ^{13}C NMR: 144.5 (s); 134.6 (s); 132.4 (d); 129.7 (2d); 127.8 (2d); 118.6 (t); 83.1 (d); 38.8 (t); 33.6 (t); 31.4 (t); 24.4 (t); 22.4 (t); 21.6 (q); 13.9 (q). (±)-1-Propylhexyl 4-methylbenzenesulfonate (**36**), yield: 78%. ^{1}H NMR: 0.82 (t, 6H); 1.10–1.40 (m, 8H); 1.45–1.60 (m, 4H); 2.45 (s, 3H); 4.57 (m, 1H); 7.32 (d, 2H); 7.79 (d, 2H). ^{13}C NMR: 144.3 (s); 134.8 (s); 129.6 (2d); 127.7 (2d); 84.4 (d); 36.3 (t); 34.1 (t); 31.5 (t); 24.4 (t); 22.4 (t); 21.6 (q); 18.0 (t); 13.9 (q); 13.8 (q).

Thioacetates **37** *and* **38** were prepared following Method B. (±)-*S*-[(1-pentyl-3-butenyl)] ethanethioate (**37**), yield: 63%, purity: 97% (GC/MS). MS: *m/z* 200 ($M^{+\cdot}$, 3), 159 (8), 157 (10), 124 (15), 117 (97), 97 (6), 83 (29), 67 (14), 60 (5), 55 (30), 43 (100), 29 (8). ^{1}H NMR: 0.88 (t, 3H); 1.20–1.70 (m, 8H); 2.30 (s, 3H); 2.35 (m, 2H); 3.57 (m, 1H); 5.07 (m, 2H); 5.77 (m, 1H). ^{13}C NMR: 195.8 (s); 135.1 (d); 117.4 (t); 43.9 (d); 39.3 (t); 33.9 (t); 31.6 (t); 30.8 (q); 26.5 (t); 22.5 (t); 14.0 (q). (±)-*S*-[(1-Propylhexyl)] ethanethioate (**38**), yield: 63%, purity: 98% (GC/MS). MS: *m/z* 202 ($M^{+\cdot}$, 3), 159 (17), 131 (10), 126 (80), 117 (12), 100 (13), 97 (22), 89 (12), 83 (21), 71 (31), 55 (38), 43 (100), 29 (10); ^{1}H NMR: 0.89 (2t, 6H); 1.20–1.70 (m, 12H); 2.30 (s, 3H); 3.52 (m, 1H). ^{13}C NMR: 196.1 (s); 44.5 (d); 37.1 (t); 34.8 (t); 31.7 (t); 30.8 (q); 26.5 (t); 22.6 (t); 20.0 (t); 14.0 (q); 13.9 (q).

Thiols **26** *and* **23** were prepared following Method C. (±)-1-Nonene-4-thiol (**26**), b.p.: 75°/12 Torr, yield: 76%. MS: *m/z* 158 ($M^{+\cdot}$, 2), 129 (8), 117 (60), 87 (22), 83 (100), 67 (16), 60 (18), 55 (100), 47 (13), 41 (43), 29 (12). ^{1}H NMR: 0.89 (t, 3H); 1.20–1.70 (m, 8H); 1.50 (d, 1H); 2.25–2.45 (m, 2H); 2.87 (m, 1H); 5.10 (m, 2H); 5.80 (m, 1H). ^{13}C NMR: 135.5 (d); 117.4 (t); 43.3 (t); 40.4 (d); 38.1 (t); 31.6 (t); 26.8 (t); 22.6 (t); 14.0 (q). (±)-Nonane-4-thiol (**23**), b.p.: 79°/12 Torr, yield: 76%. MS: *m/z* 160 ($M^{+\cdot}$, 38), 126 (30), 117 (10), 97 (27), 89 (21), 83 (36), 71 (52), 60 (12), 55 (100), 47 (18), 43 (52), 29 (17). ^{1}H NMR: 0.90 (2t, 6H); 1.25–1.70 (m, 12H); 1.38 (d, 1H); 2.80 (m, 1H). ^{13}C NMR: 41.2 (t); 40.9 (d); 39.0 (t); 31.6 (t); 26.8 (t); 22.6 (t); 20.3(t); 14.1 (q); 13.8 (q).

For 4-mercapto-2-heptanol (**18**), 4-mercapto-2-nonanol (**30**), 3-methyl-5-propyl-1,2-dithiolane (**10**), 3-methyl-5-pentyl-1,2-dithiolane (**29**), 4-mercapto-2-heptanone (**13**), heptane-2,4-dithiol (**19**), nonane-2,4-dithiol (**28**), 4-(methylthio)-2-heptane-2-thiol (**20**) and 2-(methylthio)-heptane-4-thiol (**21**), see **Figure 6**.

Thioacetates **41** *and* **42**. The corresponding ketone (100 mmol, (3*E*)-3-hepten-2-one (**39**) from Alfa Aesar and (3*E*)-3-nonen-2-one (**40**) from Aldrich) and thioacetic acid (11.4 g, 150 mmol) were heated at 100 °C for 4 h. Then, the condenser was replaced by a Vigreux-column, and the product was directly distilled. (±)-*S*-[(3-Oxo-1-propylbutyl)] ethanethioate (**41**), b.p.: 115°/12 Torr, yield: 85%, purity: 95% (GC/MS). MS: *m/z* 188 ($M^{+\cdot}$, 0.5), 145 (14), 128 (2), 113 (59), 103 (7), 97 (9), 87 (4), 69 (9), 55 (13), 43 (100), 27 (3). ^{1}H NMR: 0.89 (t, 3H); 1.25–1.45 (m, 2H); 1.55–1.65 (m, 2H); 2.17 (s, 3H); 2.31 (s, 3H); 2.75 (dd, 2H); 3.85 (m, 1H). ^{13}C NMR: 206.0 (s); 195.6 (s); 48.6 (t); 39.5 (d); 36.3 (t); 30.7 (q); 30.1 (q); 20.2 (t); 13.7 (q). (±)-*S*-[(3-Oxo-1-propylhexyl)] ethanethioate (**42**), b.p.: 133–138°/12 Torr, yield: 64%, purity: 98% (GC/MS). MS: *m/z* 216 ($M^{+\cdot}$, 0), 141 (47), 125 (22), 115 (8), 97 (20), 82 (11), 71 (20), 55 (54), 43 (100), 29 (7). ^{1}H NMR: 0.88 (t, 3H); 1.20–1.45 (m, 6H); 1.55–1.70 (m, 2H); 2.14 (s, 3H); 2.30 (s, 3H); 2.75 (dd, 2H); 3.84 (m, 1H). ^{13}C NMR: 206.0 (s); 195.6 (s); 48.6 (t); 39.8 (d); 34.1 (t); 31.4 (t); 30.7 (q); 30.1 (q); 26.7 (t); 22.5 (t); 14.0 (q).

Hydroxymercaptans **18** *and* **30** were prepared following Method C. (±)-4-Mercapto-2-heptanol (**18**), two diastereoisomers (55:45), b.p.: 94–95°/12 Torr, yield: 65%, purity: 99% (GC/MS). MS (both isomers identical): *m/z* 148 ($M^{+\cdot}$, 8), 130 (10), 114 (52), 97 (33), 87 (25), 81 (20), 74 (13), 71 (87), 61 (23), 58 (21), 55 (100), 47 (13), 45 (79), 43 (43), 27 (13). ^{1}H NMR: 0.92 (t, 3H); 1.20 and 1.22 (d, 3H); 1.38–1.80 (m, 6H); 2.88 and 3.05 (m, 1H); 4.01 and 4.15 (m, 1H). ^{13}C NMR: major isomer: 65.4 (d); 47.8 (t); 42.0 (t); 38.6 (d); 23.6 (q); 20.1 (t); 13.8 (q); minor isomer: 67.0 (d); 48.3 (t); 41.7 (t); 37.5 (d); 24.0 (q); 20.0 (t); 12.8 (q). (±)-4-Mercapto-2-nonanol (**30**), two diastereoisomers (1:1), b.p.: 119–121°/12 Torr, yield: 72%, purity: 99% (GC/MS). MS (both isomers identical): *m/z* 176 ($M^{+\cdot}$, 6), 142 (51), 125 (7), 115 (20), 102 (28), 95 (19), 87 (25), 83 (38), 71 (100), 61 (37), 58 (32), 55 (78), 45 (95), 41 (54), 29 (27). ^{1}H NMR: 0.90 (t, 3H); 1.20 and 1.22 (d, 3H); 1.25–1.35 (m, 10H); 1.39 and 1.48 (d, 1H); 2.85 and 3.02 (m, 1H); 4.00 and 4.12 (m, 1H). ^{13}C NMR: 67.0 and 65.4 (d); 48.3 and 47.8 (t); 39.9 and 39.6 (t); 38.9 and 37.8 (d); 31.5 and 31.6 (t); 26.7 and 26.5 (t); 24.1 and 23.6 (q); 22.6 (t); 14.0 (q).

Tosylates **43** *and* **44** were prepared following Method A; both compounds were directly used in the next step. (±)-*S*-[(1-Propyl-3-tosyloxybutyl)] *p*-toluenethiosulfonate (**43**), yield: 28%. (±)-*S*-[1-(Tosyloxypropyl)hexyl] *p*-toluenethiosulfonate (**44**), yield: 35%. *Dithioacetates* **45** and **46** and *dithiolanes* **10** and **29** were prepared following Method B. The residue was purified by chromatography on silica gel using a gradient from 3% ether in pentane to 10% ether in pentane. Respectively, **45** and **10**, as well as **46** and **29,** were isolated as pure compounds. (±)-*S*,*S*′-Heptane-2,4-diyl diethanethioate (**45**), two diastereoisomers (3:2). MS (both isomers identical): *m/z* 248 ($M^{+\cdot}$, 2), 205 (72), 163 (100), 129 (35), 97 (20), 87 (10), 69 (5), 55 (27), 43 (75), 29 (7). (±)-*S*,*S*′-Nonane-2,4-diyl diethanethioate (**46**), two diastereoisomers (4:3). MS (both isomers identical): *m/z* 276 ($M^{+\cdot}$, 1), 233 (46), 191 (100), 157 (23), 125 (22), 115 (4), 87 (5), 83 (9), 69 (15), 55 (10), 43 (39). ^{1}H NMR (characteristic signals): 0.88 (t, 3H); 1.29 (d, 3H); 2.31 (s, 3H); 2.34 (s, 3H); 3.64 (d, 1H); 3.60 (d, 1H). ^{13}C NMR (main isomer): 195.7 (s); 195.6 (s); 42.3 (d); 41.4 (t); 37.1 (d); 34.9 (t); 31.6 (t); 30.8 (q); 30.7 (q); 26.2 (t); 22.5 (t); 20.9 (q); 14.0 (q). (±)-3-Methyl-

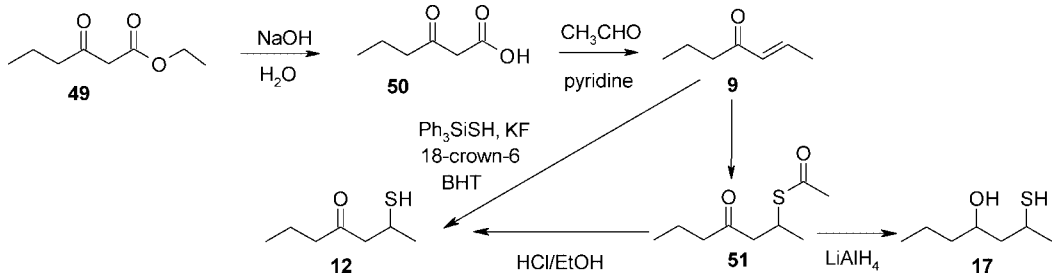

Figure 7. Syntheses of compounds **9, 12**, and **17**.

5-propyl-1,2-dithiolane (**10**), two diastereoisomers (1:2), yield: 67%, purity: 98% (GC/MS). MS (both isomers identical): *m/z* 162 ($M^{+\cdot}$, 56), 129 (10), 119 (59), 97 (32), 85 (5), 69 (10), 64 (6), 59 (11), 55 (100), 45 (12), 41 (15). ^{1}H NMR: 0.94 (t, 3H); 1.40 and 1.43 (d, 3H); 1.41 (m, 2H); 1.65 and 1.70 (m, 2H); 2.09 (m, 2H); 2.67 (m, 1H); 3.60–3.77 (m, 2H).^{13}C NMR (major isomer): 55.5 (d); 49.7 (d); 48.4 (t); 37.3 (t); 22.3 (t); 20.4 (q); 13.9 (q). ^{13}C NMR (minor isomer): 56.9 (d); 51.3 (d); 49.3 (t); 37.8 (t); 22.5 (t); 20.0 (q); 13.9 (q). (±)-3-Methyl-5-pentyl-1,2-dithiolane (**29**), two diastereoisomers (1:1), yield: 67% (based on 100% dithiolane), purity: 99% (GC/MS). MS (isomers identical): *m/z* 190 ($M^{+\cdot}$, 62), 157 (16), 119 (7), 101 (6), 83 (49), 69 (100), 59 (10), 55 (65), 41 (32). ^{1}H NMR (major isomer, attributed by HSQC): 0.89 (t, 6H); 1.43 (d, 6H); 1.30–1.71 (m, 9H); 2.67 (m, 1H); 3.58 (m, 1H). ^{13}C NMR: 57.2 (d); 51.3 (d); 49.3 (t); 35.2 (t); 31.6 (t); 28.8 (t); 22.5 (t); 20.0 (q); 14.0 (q).

Dithiols **19** *and* **28** were prepared from **45** and **46**, respectively, following Method C and were purified by bulb-to-bulb distillation. (±)-Heptane-2,4-dithiol (**19**), two diastereoisomers (2:1), b.p.: 140°/12 Torr, yield: 77%, purity: 99% (GC/MS). MS (both isomers identical): *m/z* 164 (25), 130 (8), 115 (6), 102 (8), 97 (30), 87 (32), 74 (44), 61 (60), 55 (100), 47 (26), 41 (43), 27 (6). ^{1}H NMR (mixture of isomers): 0.93 (t, 3H); 1.33 and 1.38 (d, 3H); 1.40–1.80 (m, 6H); 2.78 and 3.03 (br. m, 1H); 3.17 and 3.25 (m, 1H). ^{13}C NMR (major isomer): 50.4 (t); 40.9 (t); 38.6 (d); 32.8 (d); 24.8 (q); 20.0 (t); 13.7 (q). ^{13}C NMR (minor isomer): 49.7 (t); 41.8 (t); 39.2 (d); 33.8 (d); 26.5 (q); 20.1 (t); 13.7 (q). (±)-Nonane-2-4-dithiol (**28**), two diastereoisomers 3:2, b.p.: 160°/12 Torr, yield: 78%, purity: 98% (GC/MS). MS (both isomers identical, SPWax): *m/z* 192 ($M^{+\cdot}$, 40), 126 (15), 115 (13), 102 (27), 87 (43), 83 (34), 74 (100), 69 (68), 61 (85), 55 (95), 47 (22), 41 (85), 29 (40). ^{1}H NMR (both isomers): 0.92 (t, 3H); 1.32 and 1.38 (d, 3H); 1.30–3.20 (m); 2.88 and 3.02 (m, 1H); 3.18 and 3.24 (m, 1H). ^{13}C NMR (major isomer): 49.7 (t); 39.7 (t); 39.5 (d); 33.9 (d); 31.5 (7); 26.6 (t); 26.5 (q); 22.6 (t); 14.0 (q).

*4-(Methylthio)-2-thiol (***20***) and 2-(methylthio)-4-thiol (***21***).* Dithiol **19** (1.3 g, 7.9 mmol) was added to a solution of NaOH (0.27 g, 7.1 mmol) dissolved in water (0.53 mL) and methanol (6.84 mL) at 0 °C. Then, methyl iodide (1.0 g, 7.1 mmol) was introduced dropwise. After reflux for 2 h, the mixture was extracted with ether (3×), which was washed with brine and dried over $MgSO_4$. The solvent was removed, and the mixture containing **20**, **21**, and **47** was purified by chromatography on silica gel with pentane. A small sample of pure **21** could be obtained for spectral characterization. (±)-2-(Methylthio)-heptane-4-thiol (**21**), one pure diastereoisomer. MS: *m/z* 178 ($M^{+\cdot}$, 87), 163 (4), 145 (7), 130 (29), 115 (11), 102 (35), 97 (68), 87 (50), 75 (80), 61 (21), 55 (100), 47 (26), 41 (43), 27 (11). ^{1}H NMR: 0.92 (t, 3H); 1.32 (t, 3H); 1.43–1.60 (m, 5H); 1.78 (m, 1H); 2.06 (s, 3H); 2.98 (m, 1H); 3.08 (m, 1H). ^{13}C NMR: 45.6 (t); 41.5 (t); 39.1 (d); 38.7 (d); 21.8 (q); 20.2 (t); 13.8 (q); 12.4 (q).(±)-4-(Methylthio)-heptane-2-thiol (**20**). MS of one pure isomer: 178 ($M^{+\cdot}$, 93), 129 (10), 103 (20), 97 (72), 87 (35), 74 (70), 61 (100), 55 (83), 47 (12), 41 (35), 27 (12). NMR of mixtures too complex.

Keto-mercaptanes **13** *and* **48**. (3*E*)-3-Hepten-2-one (**39**) was purchased from Alfa Aesar, and (3*E*)-3-nonen-2-one (**40**) was from Aldrich. To the ketone (10 mmol), BHT (1.0 g, 4.5 mmol) and THF (25 mL) under argon, the following were successively introduced: triphenylsilanethiol (5.86 g, 20 mmol, Fluka), 18-crown-6-ether (2.64 g, 10 mmol, Fluka), and potassium fluoride (1.16 g, 20 mmol). The reaction mixture was stirred overnight at room temperature. To the mixture, H_2SO_4 10% (10 mL) was added. After filtration, the mixture was extracted with pentane (2×). The organic phase was washed with H_2O and dried with $MgSO_4$. The solvent was removed using a Vigreux-column. The product was purified by chromatography on silica gel using 10% ether in pentane. (±)-4-Mercapto-2-heptanone (**13**), yield: 14%, purity: 99% (GC/MS). MS: *m/z* 146 ($M^{+\cdot}$, 6), 128 (8), 113 (27), 97 (38), 88 (5), 69 (23), 55 (57), 43 (100), 27 (7). ^{1}H NMR: 0.92 (t, 3H); 1.35–1.65 (m, 4H); 1.70 (d, 1H); 2.17 (s, 3H); 2.75 (m, 2H); 3.25 (m, 1H). ^{13}C NMR: 206.6 (s); 52.9 (t); 40.2 (t); 34.9 (d); 30.7 (q); 20.2 (t); 13.6 (q). (±)-4-Mercapto-2-nonanone (**48**), yield: 21%, purity 99% (GC/MS). MS: *m/z* 174 ($M^{+\cdot}$, 0.5), 156 (4), 141 (49), 125 (30), 111 (6), 97 (30), 82 (18), 71 (34), 55 (80), 43 (100), 29 (10). ^{1}H NMR: 0.90 (t, 3H); 1.25–1.65 (m, 8H); 1.70 (d, 1H); 2.18 (s, 3H); 2.74 (m, 2H); 3.24 (m, 1H). ^{13}C NMR: 206.6 (s); 52.9 (t); 38.1 (t); 35.2 (d); 31.4 (t); 30.6 (q); 26.7 (t); 22.5 (t); 14.0 (q). This compound could not be identified in the bell pepper extract.

*(±)-2-Mercapto-4-heptanone (***12***) and (±)-2-mercapto-4-heptanol (***17***).* See **Figure 7**. 3-Oxo-hexanoic acid (**50**). In a round-bottomed flask, NaOH (10.08 g, 252 mmol) and H_2O (240 mL) were introduced. Then, under cooling with a water bath at max, 20 °C ethyl butyrylacetate (**49**, 37.92 g, 240 mmol, Aldrich) was added dropwise (mixture became yellow). The reaction was stirred at room temperature overnight. Saturated $(NH_4)_2SO_4$ aq. (500 mL) was added, then the mixture was cooled down with a water/ice bath, and a solution of H_2SO_4 (8 mL) in water (100 mL) was added dropwise (pH 3). The mixture was extracted with ether (2 × 300 mL), washed with brine (1x) to pH 5, and dried over $MgSO_4$. The solvent was removed at 30 °C (max) under vacuum. The solid residue (28.41 g, yield: 91%) was immediately used in the next step.

*(2E)-2-Hepten-4-one (***9***).* In a round-bottomed flask, flame-dried under argon, acetaldehyde (10.70 g, 243 mmol) and pyridine (25 mL) were introduced. The reaction mixture was cooled down with a water/ice bath prior to the addition of a suspension of **50** (28.41 g, 219 mmol) in a few milliliters of pentane using a pipet. The flask was rinsed with pyridine (5–10 mL). After 30 min, the water/ice bath was removed, and the mixture was stirred at room temperature overnight. The reaction was heated at 90 °C for 15 min, cooled down to room temperature, and then water was added. Then, the mixture was extracted with ether (2 × 300 mL), washed with H_2SO_4 2N (5×), an aq. solution of saturated $NaHCO_3$, and brine (1×) to pH 7, dried over $MgSO_4$, and concentrated. The residue was distilled using a Vigreux column, 68–73°/50 mbar to give the desired ketone **9** (6.69 g, purity: 87%, yield: 27%). MS: *m/z* 112 ($M^{+\cdot}$, 0.5), 97 (30), 84 (10), 69 (100), 55 (3), 41 (28), 27 (4). ^{1}H NMR: 0.92 (t, 3H); 1.65 (m, 2H); 1.90 (d, J = 7.4, 3H); 2.50 (t, 2H); 6.12 (d, J = 17.4, 1H); 6.84 (dq, J = 17.6, 7.4, 1H). ^{13}C NMR: 200.5 (s); 142.2 (d); 132.0 (d); 41.9 (t); 18.2 (q); 17.7 (t); 13.8 (q).

*(±)-2-Mercapto-4-heptanone (***12***).* Same procedure as described for **13** and **48**, yield: 14%. MS: *m/z* 146 ($M^{+\cdot}$, 32), 128 (22), 113 (36), 103 (17), 97 (25), 84 (8), 75 (50), 71 (100), 61 (39), 58 (25), 43 (83), 27 (14). ^{1}H NMR: 0.92 (t, 3H); 1.32 (d, 3H); 1.62 (sext., 2H); 1.82 (d, 1H); 2.38 (t, 2H); 2.70 (m, 2H); 3.43 (m, 1H). ^{13}C NMR: 208.7 (s); 53.5 (t); 45.4 (t); 30.0 (d); 24.8 (q); 17.1 (t); 13.7 (q).

*(±)-S-[(1-Methyl-3-oxohexyl)] ethanethioate (***51***).* Same procedure as described for **41**, yield: 78%, purity: 97%. MS: *m/z* 188 ($M^{+\cdot}$, 0.5), 145 (10), 113 (95), 103 (10), 97 (23), 84 (7), 75 (16), 71 (83), 61 (5), 43 (100), 27 (7). ^{1}H NMR: 0.92 (t, 3H); 1.32 (d, 3H); 1.60 (dd, 2H); 2.28 (s, 3H); 2.62 (dd, 1H); 2.78 (dd, 1H). ^{13}C NMR: 208.1 (s); 195.5 (s); 48.8 (t); 34.7 (d); 30.6 (q); 20.6 (q); 17.1 (t); 13.7 (q).

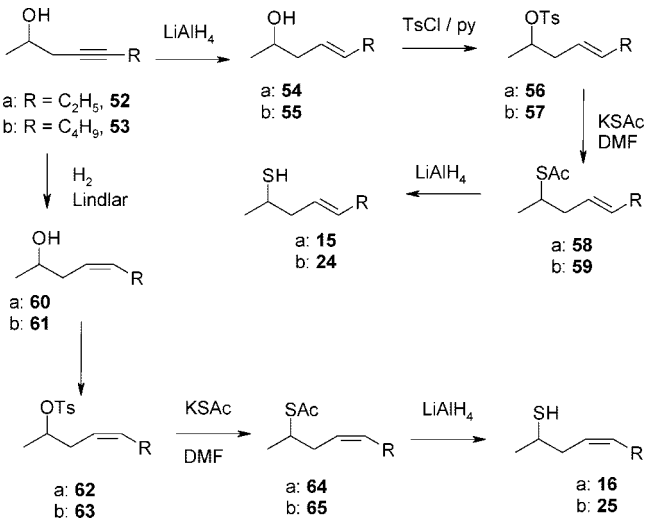

Figure 8. Syntheses of compounds **15**, **24**, **16**, and **25**.

*(±)-2-Mercapto-4-heptanol (***17***)* was prepared following Method C from **51**. Two diastereoisomers (1:1), yield: 40%, purity: 99%. MS (both isomers identical): *m/z* 148 ($M^{+\bullet}$, 4), 130 (17), 114 (42), 99 (32), 87 (23), 81 (21), 73 (45), 71 (64), 61 (94), 55 (100), 43 (58), 31 (8). ^{1}H NMR (both isomers): 0.94 (t, 3H); 1.35–1.60 (m, 4H); 1.39 and 1.40 (d, 3H); 1.62 and 1.70 (d, 1H); 2.05 (br. s, 1H); 3.09 and 3.20 (m, 1H); 3.72 and 3.88 (m, 1H). ^{13}C NMR (one isomer established by HMBC): 70.2 (d); 48.4 (t); 40.1 (t); 32.9 (d); 25.8 (q); 18.6 (t); 14.1 (q).

*(±)-(4E)-4-Heptene-2-thiol (***15***) and (±)-(4E)-4-nonene-2-thiol (***24***)*. See **Figure 8**. (±)-4-Heptyn-2-ol (**52**) was prepared following the procedures described by Jones and Knight (*21*). Yield: 46%, purity: 95%. MS: *m/z* 112 ($M^{+\bullet}$, 0), 97 (12), 68 (86), 67 (100), 53 (38), 45 (59), 41 (24), 27 (8). ^{1}H NMR: 1.12 (t, 3H); 1.24 (d, 3H); 2.1–2.4 (m, 4H); 3.90 (sext., 1H). ^{13}C NMR: 84.6 (s); 75.5 (s); 66.6 (d); 29.4 (t); 22.2 (q); 14.2 (q); 12.4 (t).

*(±)-(4E)-4-Hepten-2-ol (***54***)*. Same procedure as described for **55**, but using **52** as starting material. The product was purified using a Vigreux-column. b.p.: 60°/15 Torr. Yield: 33%, purity: 90%. MS: *m/z* 114 ($M^{+\bullet}$, 1), 96 (6), 81 (10), 70 (90), 55 (84), 45 (100), 42 (32), 27 (11). ^{1}H NMR: 0.98 (t, 3H); 1.20 (d, 3H); 2.0–2.3 (m, 4H); 3.78 (sext., 1H); 5.40 (ddd, J = 15.7, 7.6, 7.6, 1H); 5.59 (ddd, J = 15.7, 6.2, 6.2, 1H). ^{13}C NMR: 136.2 (d); 124.8 (d); 67.2 (d); 42.5 (t); 25.7 (t); 22.6 (q); 13.8 (q).

*(±)-(3E)-1-Methyl-3-hexenyl 4-methylbenzenesulfonate (***56***)*, Method A, yield 73%. ^{1}H NMR: 0.90 (t, 3H); 1.25 (d, 3H); 1.92 (m, 2H); 2.15–2.35 (m, 2H); 2.44 (s, 3H); 4.57 (sext., 1H); 5.16 (ddd, J = 15.7, 7.1, 7.1, 1H); 5.45 (ddd, J = 15.7, 5.8, 5.8, 1H); 7.32 (d, 2H); 7.79 (d, 2H). ^{13}C NMR: 144.4 (s); 136.4 (d); 134.6 (s); 129.7 (2s); 127.8 (2s); 80.1 (d); 39.6 (t); 25.5 (t); 21.6 (q); 20.4 (t); 20.4 (q); 13.5 (q).

*(±)-S-[(3E)-1-Methyl-3-hexenyl] ethanethioate (***58***)* was prepared following Method B, yield: 39%, purity: 95% (GC/MS). MS: *m/z* 172 ($M^{+\bullet}$, 0), 129 (2), 103 (12), 96 (57), 81 (38), 61 (16), 55 (22), 43 (100), 27 (8). ^{1}H NMR: 0.97 (t, 3H); 1.27 (d, 3H); 2.02 (m, 2H); 2.25 (m, 2H); 2.30 (s, 3H); 3.57 (sext., 1H); 5.36 (ddd, J = 15.7, 6.2, 6.2, 1H); 5.52 (ddd, J = 15.7, 7.6, 7.6, 1H). ^{13}C NMR: 195.9 (s); 135.4 (d); 125.1 (d); 39.5 (d); 39.5 (t); 30.8 (q); 25.6 (t); 20.4 (q); 13.8 (q).

*(±)-(4E)-4-Heptene-2-thiol (***15***)* was prepared following Method C, yield: 71%, purity: 95%. MS: *m/z* 130 ($M^{+\bullet}$, 1), 115 (2), 101 (24), 96 (9), 81 (11), 69 (12), 61 (100), 55 (37), 45 (5), 41 (43), 27 (16). ^{1}H NMR: 0.98 (t, 3H); 1.30 (d, 3H); 1.62 (d, 1H); 2.03 (m, 2H); 2.21 (m, 2H); 2.96 (m, 1H); 5.39 (ddd, J = 15.2, 6.2, 6.2, 1H); 5.55 (ddd, J = 15.2, 6.6, 6.6, 1H). ^{13}C NMR: 135.4 (d); 125.8 (d); 44.0 (t); 35.5 (d); 25.6 (t); 24.5 (q); 13.8 (q).

*(±)-4-Nonyn-2-ol (***53***)* was prepared following the procedures described by Jones and Knight (*21*). Pure compound **53** was obtained (6.51 g) by chromatography on silica gel using 30% ether in pentane., yield: 35%, purity: 99%. MS: *m/z* 140 ($M^{+\bullet}$, 0), 125 (3), 96 (11), 81 (52), 67 (33), 54 (100), 45 (50), 43 (23), 27 (12). ^{1}H NMR: 0.91 (t, 3H); 1.23 (d, 2H); 1.35–1.55 (m, 4H); 2.17–2.40 (m, 4H); 3.89 (sext., 1H). ^{13}C NMR: 83.2 (s); 76.1 (s); 66.5 (d); 31.1 (t); 29.4 (t); 22.1 (q); 22.0 (t); 18.4 (t); 13.6 (q).

*(±)-(4E)-4-Nonen-2-ol (***55***)*. In a flask, flame-dried under argon, **53** (5.32 g, 38 mmol) in toluene/THF 1:1 (50 mL) was added to $LiAlH_4$ (4.64 g) in toluene/THF 1:1 (50 mL), the mixture was stirred at 90 °C for 22 h. After cooling with an ice bath, NH_4Cl was slowly added, followed by HCl (10%). NaCl was added, and the mixture was extracted with ether (2×) and dried over $MgSO_4$, and the solvent was removed. A 500 mg portion was bulb-to-bulb distilled to give **55,** which was used in the next step. b.p.: 140°/12 Torr. MS: *m/z* 142 ($M^{+\bullet}$, 3), 124 (4), 109 (3), 98 (53), 83 (10), 69 (46), 56 (83), 45 (100), 41 (38), 27 (15). ^{1}H NMR: 0.90 (t, 3H); 1.18 (d, 3H); 1.25–1.40 (m, 4H); 2.00–2.25 (m, 4H); 3.78 (sext., 1H); 5.40 (ddd, J = 15.2, 7.0, 6.8, 1H); 1.52 (ddd, J = 15.2, 7.0, 7.0, 1H). ^{13}C NMR: 134.7 (d); 125.8 (d); 67.2 (d); 42.6 (t); 32.4 (t); 31.6 (t); 22.6 (q); 22.2 (t); 13.9 (q).

*(±)-(3E)-1-Methyl-3-octenyl 4-methylbenzenesulfonate (***57***)* was prepared from **55** following Method A, yield: 53%. ^{1}H NMR (characteristic signals): 2.45 (s, 3H); 4.58 (sext., 1H); 5.64 (ddd, J = 15.1, 7.0, 7.0, 1H); 5.41 (ddd, J = 15.1, 7.0, 7.0, 1H). ^{13}C NMR: 144.4 (s); 135.0 (d); 134.6 (s); 129.7 (2s); 127.7 (2s); 123.4 (d); 80.1 (d); 39.7 (t); 32.2 (t); 31.4 (t); 22.2 (t); 21.6 (q); 20.3 (q); 13.9 (q).

*(±)-S-[(3E)-1-Methyl-3-octenyl] ethanethioate (***59***)* was prepared following Method B, using **57** as starting material. Yield: 63%, purity: 95% (GC/MS). MS: *m/z* 200 ($M^{+\bullet}$, 0.5), 157 (7), 124 (93), 103 (21), 95 (20), 81 (35), 68 (48), 61 (16), 55 (27), 43 (100), 27 (9). ^{1}H NMR: 0.88 (t, 3H); 1.27 (d, 3H); 1.25–1.40 (m, 4H); 2.00 (m, 2H); 2.22 (m, 2H); 2.29 (s, 3H); 3.58 (sext., 1H); 5.35 (ddd, J = 15.3, 6.8, 6.8, 1H); 5.48 (ddd, J = 15.3, 6.6, 6.6, 1H). ^{13}C NMR: 195.9 (s); 133.9 (d); 126.1 (d); 39.6 (t); 39.5 (d); 32.2 (t); 31.6 (t); 30.8 (q); 22.2 (t); 20.5 (q); 13.9 (q).

*(±)-(4E)-4-Nonene-2-thiol (***24***)* was prepared following Method C, using **59** as starting material. Yield: 33%, purity: 93%. MS: *m/z* 158 ($M^{+\bullet}$, 4), 143 (2), 124 (7), 115 (6), 101 (43), 81 (12), 69 (20), 61 (100), 55 (46), 41 (28), 27 (10). ^{1}H NMR: 0.90 (t, 3H); 1.30 (d, 3H); 1.25–1.40 (m, 4H); 1.62 (d, 1H); 2.02 (m, 2H); 2.22 (m, 2H); 2.97 (sext., 1H); 5.38 (ddd, J = 15.4, 7.0, 7.0, 1H); 5.51 (ddd, J = 15.4, 7.0, 7.0, 1H). ^{13}C NMR: 133.9 (d); 126.7 (d); 44.0 (t); 35.5 (d); 32.3 (t); 31.6 (t); 24.5 (q); 22.2 (t); 13.9 (q).

*(±)-(4Z)-4-Heptene-2-thiol (***16***) and (±)-(4Z)-4-nonene-2-thiol (***25***)*. See **Figure 8**.

*(±)-(4Z)-4-Hepten-2-ol (***60***)*. A solution of **52** (4.03 g, 36 mmol) in hexane (400 mL) was hydrogenated at room temperature in the presence of Pd 5% on $BaSO_4$ (40 mg). After filtration and concentration, the pure **60** (3.41 g, yield: 83%) was used in the next step.

*(±)-(3Z)-1-Methyl-3-hexenyl 4-methylbenzenesulfonate (***62***)* was prepared following Method A, using **60** as starting material. Yield: 7%. ^{1}H NMR: 0.90 (t, 3H); 1.26 (d, 3H); 1.93 (m, 2H); 2.2–2.4 (m, 2H); 2.43 (s, 3H); 4.58 (sext., 1H); 5.16 (ddd, J = 12.5, 1H); 5.43 (ddd, J = 12.5, 1H); 7.32 (d, 2H); 7.79 (d, 2H). ^{13}C NMR: 144.4 (s); 135.3 (d); 134.5 (s); 129.7 (2s); 127.8 (2s); 79.9(d); 34.1 (t); 21.6 (q); 20.6 (t); 20.3(q); 14.0 (q).

*(±)-S-[(3Z)-1-Methyl-3-hexenyl] ethanethioate (***64***)* was prepared following Method B, using **62** as starting material. Purification was by chromatography on silica gel using 5% ether in pentane. Yield: 74%, purity by GC/MS: ca. 80%. MS: *m/z* 172 ($M^{+\bullet}$, 1), 129 (7), 103 (18), 96 (92), 81 (50), 61 (20), 55 (22), 43 (100), 27 (6). ^{1}H NMR: 0.97 (t, 3H); 1.28 (d, 3H); 2.05 (m, 2H); 2.30 (s, 3H); 2.31 (m, 2H); 3.58 (sext., 1H); 5.3–5.6 (m, 2H). ^{13}C NMR: 196.0 (s); 134.4 (d); 125.0 (d); 39.5 (d); 33.8 (t); 30.8 (q); 20.7 (t); 20.5 (q); 14.1 (q). The compound decomposed before NMR measurements could be taken.

*(±)-(4Z)-4-Heptene-2-thiol (***16***)* was prepared following Method C, using **64** as starting material. Purification was by chromatography on silica gel with pentane. Yield: 90%, purity by GC/MS: 85%. MS: *m/z* 130 ($M^{+\bullet}$, 2), 115 (3), 101 (37), 96 (13), 81 (20), 61 (100), 55 (38), 45 (7), 41 (38), 27 (17).

*(±)-(4Z)-4-Nonen-2-ol (***61***)*. A solution of **53** (11.9 g, 85 mmol) in ethanol (100 mL) was hydrogenated at room temperature in the presence of 5% Pd on $CaCO_3$ (Strem Chemicals, 500 mg). After filtration and concentration, the product was purified by chromatography on silica gel using pentane with 20% ether. A 7.87 g portion of compound **61**

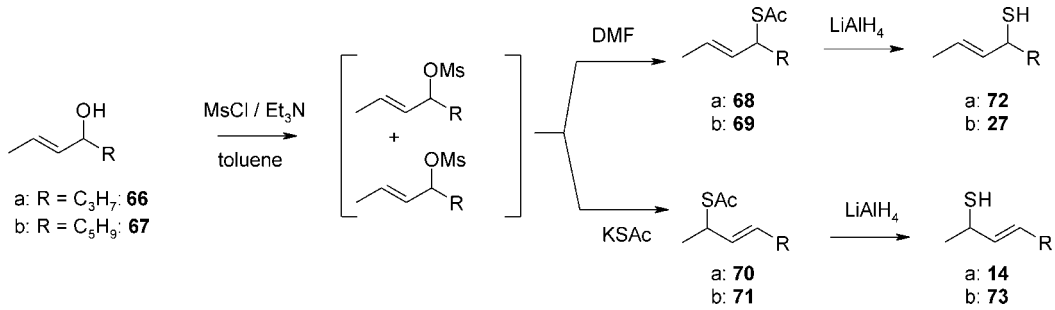

Figure 9. Syntheses of compounds **72**, **27**, **14**, and **73**.

that contained 7% of isomer **55** was obtained. Yield: 65%, purity: 91%. MS: *m/z* 142 ($M^{+\cdot}$, 4), 124 (6), 109 (4), 98 (56), 83 (11), 69 (52), 56 (91), 45 (100), 41 (33), 27 (10). ^{1}H NMR: 0.90 (t, 3H); 1.20 (d, 3H); 1.30–1.40 (m, 4H); 2.05 (m, 2H); 2.21 (m, 2H); 3.92 (sext., 1H); 5.2–5.6 (m, 2H). ^{13}C NMR: 133.4 (d); 125.1 (d); 67.7 (d); 37.2 (t); 31.9 (t); 27.1 (t); 22.8 (q); 22.4 (t); 14.0 (q).

*(±)-(3Z)-1-Methyl-3-octenyl 4-methylbenzenesulfonate (***63***)* was prepared following Method A, using **61** as starting material. Yield: 74%. ^{1}H NMR (characteristic signals): 4.59 (sext., 1 H); 5.17 (ddd, J = 11.0, 7.5, 7.0, 1H); 5.43 (ddd, J = 11.0, 7.5, 7.5, 1H); 7.32 (d, 2H); 7.78 (d, 2H). ^{13}C NMR: 144.4 (s); 134.5 (s); 133.7 (d); 129.7 (2d); 127.8 (2d); 122.7 (d); 79.9 (d); 34.2 (t); 31.6 (t); 27.0 (t); 22.3 (t); 21.6 (q); 20.4 (q); 13.9 (q).

*(±)-S-[(3Z)-1-Methyl-3-octenyl] ethanethioate (***65***)* was prepared following Method B, using **63** as starting material. Yield: 64%, purity by GC/MS: 93% + 5% isomer (*E*). MS: *m/z* 200 ($M^{+\cdot}$, 0), 157 (6), 124 (100), 103 (26), 95 (24), 81 (36), 68 (53), 61 (19), 55 (27), 43 (100). ^{1}H NMR: 0.90 (t, 3H); 1.29 (d, 3H); 1.25–1.35 (m, 4H); 2.05 (m, 2H); 2.30 (s, 3H); 2.32 (m, 2H); 3.49 (sext., 1H); 5.35 (ddd, J = 11.1, 7.2, 7.0, 1H); 5.49 (ddd, J = 11.1, 7.7, 7.2, 1H). ^{13}C NMR: 195.9 (s); 132.7 (d); 126.1 (d); 39.6 (d); 33.9 (t); 31.8 (t); 30.8 (q); 27.1 (t); 22.4 (t); 20.5 (q); 14.0 (q).

*(±)-(4Z)-4-Nonene-2-thiol (***25***)* was prepared following Method C, using **65** as starting material. Yield: 52%, purity by GC/MS: 84% + 11% isomer (*E*). MS: *m/z* 158 ($M^{+\cdot}$, 2), 124 (5), 115 (5), 101 (32), 81 (10), 69 (26), 61 (100), 55 (45), 41 (29), 27 (9). ^{1}H NMR: 0.90 (t, 3H); 1.20–1.40 (m, 4H); 1.32 (d, 3H); 1.61 (d, 1H); 2.04 (m, 2H); 2.30 (m, 2H); 2.97 (m, 1H); 5.38 (ddd, J = 10.7, 7.1, 7.1, 1H); 5.51 (ddd, J = 10.7, 7.1, 7.1, 1H). ^{13}C NMR: 132.7 (d); 126.2 (d); 38.5 (t); 35.5 (d); 31.8 (t); 27.2 (t); 24.7 (q); 22.4 (t); 14.0 (q).

*(±)-(3E)-3-Heptene-2-thiol (***14***) and (±)-(2E)-2-nonene-4-thiol (***27***).* See **Figure 9**.

*(±)-S-[(2E)-1-Propyl-2-butenyl] ethanethioate (***68***), (±)-S-[(2E)-1-methyl-2-hexenyl] ethanethioate (***70***), (±)-S-[(2E)-1-pentyl-2-butenyl] ethanethioate (***69***), and (±)-S-[(2E)-1-methyl-2-octenyl] ethanethioate (***71***).* In a 2 L flask, flame-dried under argon, (2*E*)-2-hepten-4-ol (**66**, 51.0 g, 447 mmol, Alfa Aesar) in toluene (750 mL) was introduced. The solution was cooled to −35 °C using an ethanol/dry ice bath. Triethylamine (195 mL, 1386 mmol) and then methanesulfonyl chloride (52 mL, 668 mmol) were added. The ethanol/dry ice bath was removed after 15 min (temperature kept below 5 °C) and replaced by an ice-bath for 2.5 h, and then the mixture was kept at room temperature overnight before the addition of DMF (450 mL). This suspension was added dropwise to a mixture of KSAc (129.71 g, 1148 mmol) in DMF (380 mL). After stirring at room temperature overnight, the reaction mixture was poured into water, extracted with ether (3×), washed with brine (2×), dried over $MgSO_4$, and concentrated. The residue was distilled using a Fischer-column (79.0–82.4°/6.3 mbar) to give 6.28 g of a 1:2 mixture of **68** and **70**. After separation by preparatory HPLC of an aliquot, both isomers were characterized. Compound **68**: purity: 87%. MS: *m/z* 172 ($M^{+\cdot}$, 5), 130 (20), 87 (17), 81 (7), 67 (7), 55 (100), 43 (32), 27 (6). ^{1}H NMR: 0.90 (t, 3H); 1.37 (sext., 2H); 1.55–1.65 (m, 2H); 1.67 (dd, 3H); 2.30 (s, 3H); 4.02 (q, 1H); 5.38 (dd, J = 15.4, 8.7, 1H); 5.66 (qd, J = 15.4, 6.6, 1H). ^{13}C NMR: 195.2 (s); 130.7 (d); 127.3 (d); 46.0 (d); 36.9 (t); 30.8 (q); 20.3 (t); 17.8 (q); 13.7 (q). Compound **70**: purity: 93%. MS: *m/z* 172 ($M^{+\cdot}$, 3), 130 (16), 97 (37), 81 (7), 67 (8), 55 (100), 43 (30), 29 (6). ^{1}H NMR: 0.88 (t, 3H); 1.38 (d, 3H); 1.38 (m, 2H); 1.98 (q, 2H); 4.13 (m, 1H); 5.45 (dd, J = 15.3, 7.5, 1H); 5.65 (dd, J = 15.3, 6.9, 6.6, 1H). ^{13}C NMR: 195.4 (s); 131.7 (d); 130.4 (s); 40.8 (d); 34.3 (t); 30.6 (q); 22.3 (t); 20.6 (q); 13.6 (q).

Compounds **69** *and* **71** were prepared from (2*E*)-2-nonen-4-ol (**67**), which was prepared by Grignard reaction of (*E*)-2-butenal and 1-bromopentane (yield: 72%, purity: 97.7%) and purified by HPLC in analogy to **68** and **70**. Compound **69**: purity: 85%. MS: *m/z* 200 ($M^{+\cdot}$, 2), 125 (24), 102 (5), 87 (23), 83 (42), 69 (100), 55 (85), 43 (52), 29 (15). ^{1}H NMR: 0.88 (t, 3H); 1.20–1.65 (m, 8H); 1.68 (d, 3H); 2.30 (s, 3H); 4.01 (m, 1H); 5.37 (dq, J = 15.2, 8.6, 1H); 5.67 (dd, J = 15.2, 6.4, 1H). ^{13}C NMR: 195.3 (s); 130.8 (d); 127.3 (d); 46.2 (d); 34.7 (t); 31.5 (t); 30.8 (q); 26.8 (t); 22.5 (t); 17.8 (q); 14.0 (q). Compound **71**: purity: 98%. MS: *m/z* 200 ($M^{+\cdot}$, 3), 158 (21), 125 (28), 95 (4), 83 (46), 69 (100), 55 (74), 43 (37), 29 (8). ^{1}H NMR: 0.88 (t, 3H); 1.20–1.35 (m, 6H); 1.38 (d, 3H); 1.99 (m, 2H); 2.29 (s, 3H); 5.44 (ddd, J = 15.5, 7.6, 6.6, 1H); 5.64 (dd, J = 15.5, 7.0, 1H). ^{13}C NMR: 195.5 (s); 132.0 (d); 130.2 (d); 40.8 (d); 32.2 (t); 31.3 (t); 30.6 (q); 28.8 (t); 22.5 (t); 20.6 (q); 14.0 (q).

*(±)-(3E)-3-Heptene-2-thiol (***14***), (±)-(2E)-2-heptene-4-thiol (***72***), (±)-(3E)-3-nonene-2-thiol (***73***) and (±)-(2E)-2-nonene-4-thiol (***27***).* Method C was used. Compound **72**, Yield: 66%, purity: 90%. MS: *m/z* 130 ($M^{+\cdot}$, 8), 97 (39), 87 (20), 81 (7), 67 (8), 55 (100), 45 (10), 41 (18), 27 (10). ^{1}H NMR: 0.90 (t, 3H); 1.20–1.60 (m, 4H); 1.58 (d, 1H); 1.68 (d, 3H); 3.42 (m, 1H); 5.41 (dd, J = 15.0, 8.6, 1H); 5.53 (dq, J = 15.0, 6.3, 1H). ^{13}C NMR: 135.0 (d); 124.9 (d); 42.2 (d); 40.6 (t); 17.5 (q); 13.6 (q). This compound could not be identified in the bell pepper extract. Compound **14**, Yield: 75%, purity: 90%. MS: *m/z* 130 ($M^{+\cdot}$, 2), 97 (29), 96 (26), 81 (5), 67 (10), 61 (4), 59 (8), 55 (100), 41 (15), 27 (8). ^{1}H NMR: 0.89 (t, 3H); 1.38 (d, 3H); 1.65 (m, 1H); 1.95 (m, 3H); 3.62 (m, 1H); 5.50 (m, 2H). ^{13}C NMR: 135.0 (d); 129.1(d); 37.0 (d); 34.1 (t); 24.8 (q); 22.4 (t); 13.6 (q). Compound **73** Yield: 86%, purity: 98%. MS: *m/z* 158 ($M^{+\cdot}$, 1), 125 (24), 124 (32), 87 (8), 83 (40), 69 (95), 59 (12), 55 (100), 41 (45), 29 (15). ^{1}H NMR: 0.88 (t, 3H); 1.2–1.4 (m, 5H); 1.38 (d, 3H); 1.65 (d, 1H); 1.98 (m, 2H); 3.60 (m, 1H); 5.50 (m, 2H). ^{13}C NMR: 134.8 (d); 129.4 (d); 37.0 (d); 32.0 (t); 31.4 (t); 28.9 (t); 24.8(q), 22.5 (t); 14.0 (q). This compound could not be identified in the bell pepper extract. Compound **27**, Yield: 92%, purity: 85%. MS: *m/z* 158 ($M^{+\cdot}$, 5), 125 (47), 87 (43), 83 (42), 69 (100), 55 (98), 47 (5), 41 (48), 29 (18). ^{1}H NMR: 0.88 (t, 3H); 1.2–1.4 (m, 5H); 1.55–1.60 (m, 3H); 1.68 (d, 3H); 3.40 (m, 1H); 5.41 (dd, J = 15.2, 8.6, 1H); 5.53 (dq, J = 15.2, 6.9, 1H). ^{13}C NMR: 135.0 (d); 124.9 (d); 42.5 (d); 38.5 (t); 31.4 (t); 27.2 (t); 22.5 (t); 17.5 (q); 14.0 (q).

*(±)-1-(2-Thienyl)-2-pentanethiol (***31***).* See **Figure 10**. *1-(2-Thienyl)-1,2-epoxyethane(***75***)* was prepared following the procedure described by Borredon et al. (*22*). The crude product was directly used in the next step.

*2-Thienylacetaldehyde (***76***)* was prepared following the method of Lemini et al. (*22*). MS: *m/z* 126 ($M^{+\cdot}$, 26), 97 (100), 69 (5), 53 (11), 45 (13). ^{1}H NMR: 3.39 (d, 2H); 6.92 (m, 1H); 7.03 (m, 1H); 7.28 (m, 1H); 9.70 (t, 1H). ^{13}C NMR: 197.6 (d); 132.8 (s); 127.5 (d); 127.2 (d); 125.6 (d); 44.0 (t).

*(±)-1-(2-Thienyl)-2-pentanol (***77***).* In an apparatus, flame-dried under argon, a solution of 1-bromopropane (17.0 g, 140 mmol) in ether (100 mL) was added dropwise to a suspension of magnesium (3.6 g) in ether (10 mL) containing a trace of iodomethane at reflux. After an additional hour, the mixture was cooled to 0 °C, and a solution of crude **76** (17.58

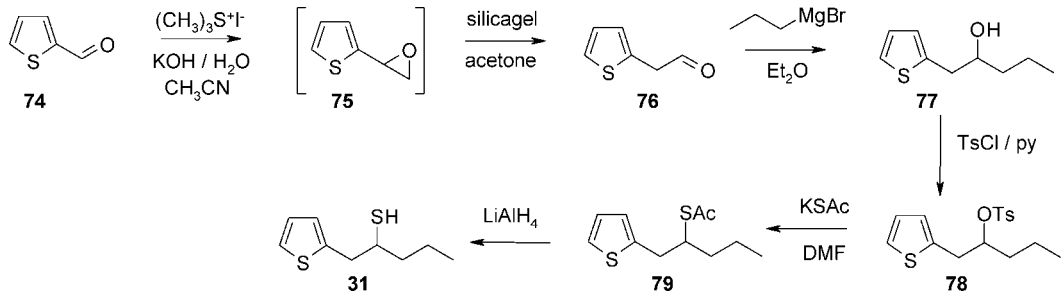

Figure 10. Synthesis of compound **31**.

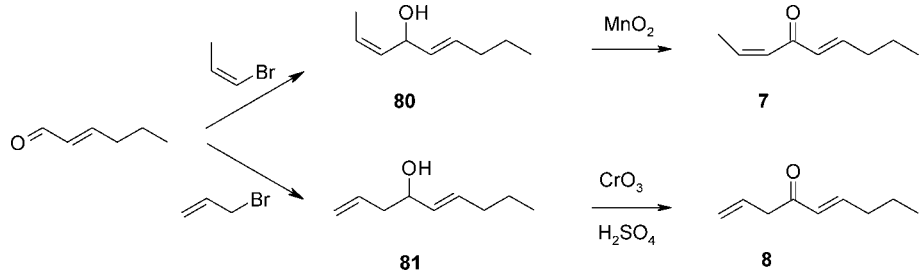

Figure 11. Synthesis of compound **7** and **8**.

g, 140 mmol) in ether (100 mL) was added dropwise over 1 h while maintaining the reaction temperature at 10 °C. Then, the reaction mixture was stirred for another hour at room temperature. The cooled reaction mixture was poured into cold aq. NH_4Cl, saturated with NaCl, extracted with ether (3×), washed with brine (2×), dried over $MgSO_4$, and concentrated. The residue was purified by chromatography on silicagel using 20% ether in pentane. Pure compound **77** was obtained. Yield: 12%, purity: 99%. MS: *m/z* 170 ($M^{+\cdot}$, 5), 152 (2), 123 (4), 98 (100), 97 (90), 55 (25), 45 (11). ^{1}H NMR: 0.95 (t, 3H); 1.35–1.55 (m, 4H); 2.88 (dd, 1H); 3.01 (dd, 1H); 3.80 (br.s, 1H); 6.75 (m, 1H); 6.93 (m, 1H); 7.17 (m, 1H). ^{13}C NMR: 140.7 (s); 127.0 (d); 126.0 (d); 124.2 (d); 72.1 (d); 38.7 (t); 38.0 (t); 18.9 (t); 14.0 (q).

*(±)-1-(2-Thienylmethyl)butyl 4-methylbenzenesulfonate (***78***)*. Method A was used. Yield: 79%, purity: 99%. ^{1}H NMR: 0.98 (t, 3H); 1.22 (m, 1H); 1.34 (m, 1H); 1.5–1.65 (m, 2H); 2.43 (s, 3H); 3.10 (d, 2H); 4.70 (m, 1H); 6.75 (m, 1H); 6.87 (m, 1H); 7.12 (m, 1H); 7.29 (d, 2H); 7.74 (d, 2H). ^{13}C NMR: 144.5 (s); 137.8 (s); 134.2 (s); 129.7 (2d); 127.7 (2d); 126.9 (d); 126.7 (d); 124.4 (d); 83.1 (d); 35.5 (t); 34.7 (t); 21.6 (q); 18.0 (t); 13.6 (q).

*(±)-S-[1-(2-Thienylmethyl)butyl] ethanethioate (***79***)*. Method B was used. Yield: 72%, purity: 90%. MS: *m/z* 152 ($M^{+\cdot}$, 100), 123 (58), 110 (12), 97 (60), 89 (16), 43 (47). ^{1}H NMR (characteristic signals): 2.30 (s, 3H); 3.05–3.15 (m, 2H); 3.76 (m, 1H); 6.84, 6.93, 7.15 (3d, 3H). ^{13}C NMR: 195.6 (s); 140.9 (s); 126.7 (d); 126.1 (s); 124.0 (d); 45.4 (d); 35.5 (t); 35.3 (t); 30.8 (q); 20.1 (t); 13.8 (q).

*(±)-1-(2-Thienyl)-2-pentanethiol (***31***)*. Method C was used. Yield: 36%, purity: 95%. MS: *m/z* 186 ($M^{+\cdot}$, 16), 152 (4), 123 (13), 110 (8), 98 (100), 97 (97), 89 (18), 55 (33), 47 (25), 45 (24). ^{1}H NMR: 0.90 (t, 3H); 1.55 (d, 1H); 1.40–1.75 (m, 4H); 2.95–3.20 (m, 3H); 6.85, 6.94, 7.16 (3m, 3H). ^{13}C NMR: 141.5 (s); 126.7 (d); 126.1 (d); 124.0 (d); 42.2 (d); 39.8 (t); 39.6 (t); 20.3 (t); 13.7 (q).

*(2Z,5E)-2,5-Nonadien-4-one (***7***)*. See **Figure 11**.

*(2Z,5E)-2,5-Nonadien-4-ol (***80***)*. In a flame-dried apparatus under argon, a solution of (2*E*)-2-hexenal (9.8 g, 0.1.mol) and 1-bromo-1-propene (mainly *Z*, 14.5 g, 0.12 mol) in THF (100 mL) was added dropwise to Mg (2.88 g, 0.12 m), 1 crystal of I_2, and some drops of 1-bromo-1-propene in THF (50 mL). After 3 h the mixture was poured on ice and extracted with ether, which was washed with a 20% aq. NH_4Cl (300 mL) and brine (2×), dried over $MgSO_4$, and concentrated. The residue was purified by bulb-to-bulb distillation (159 °C, 10 Torr) to obtain **80** (10.73 g), yield 77%, purity 90%, *Z*/*E* = 8/2. MS (*Z*-isomer): *m/z* 140 (1), 124 (15), 111 (13), 97 (100), 59 (28), 69 (83), 55 (59), 41 (63), 27 (32). ^{1}H NMR (*Z*-isomer): 0.90 (t, 3H); 1.41 (m, 2H); 1.69 (d, 3H); 2.02 (m, 2H); 4.93 (dd, *J* = 7.0, 6.5, 1H); 5.45 (dd, *J* = 10.9, 7.0, 1H); 5.53 (dd, *J* = 15.4, 6.5, 1H); 5.58 (dq, *J* = 10.9, 6.1, 1H); 5.68 (dt, *J* = 15.4, 6.6, 1H). ^{13}C NMR (*Z*-isomer): 132.2 (d); 131.8 (d); 131.5 (d); 126.0 (d); 68.5 (d); 34.3 (t); 22.3 (t); 13.6 (q); 13.2 (q).

*(2Z,5E)-2,5-Nonadien-4-one (***7***)*. Alcohol **80** (2.8 g, 0.02 mol) and MnO_2 (22 g, 0.25 mol, Fluka) in pentane (100 mL) were stirred overnight at room temperature. The mixture was filtered over Celite, washed, dried, and concentrated. Ketone **7** (0.8 g) was obtained after purification by chromatography on silica gel using cyclohexane/ether 95/5 at a purity of 98.6%. MS: *m/z* 138 ($M^{+\cdot}$, 2), 123 (2), 109 (8), 95 (100), 81 (15), 69 (28), 55 (32), 41 (36), 27 (14). ^{1}H NMR: 0.94 (t, 3H); 1.51 (m, 2H); 2.10 (d, 3 H); 2.20 (m, 2H); 6.15 (d, *J* = 15.8, 1H); 6.25 (dq, *J* = 11.5, 6.9, 1H); 6.34 (d, *J* = 11.5, 1H); 6.84 (dt, *J* = 15.8, 6.9, 1H). ^{13}C NMR: 191.6 (s); 147.5 (d); 142.7 (d); 131.9 (d); 126.7 (d); 34.6 (t); 21.5 (t); 16.0 (q); 13.7 (q). RI_{SPWax} = 1512, RI_{SPB-1} = 1110.

*(5E)-1,5-Nonadien-4-one (***8***)*. See **Figure 11**.

*(5E)-1,5-nonadien-4-ol (***81***)*. In a flame-dried apparatus under argon, a solution of 2-propene bromide (0.33 mol) in ether (120 mL) was added dropwise to a suspension of magnesium (8.8 g, 0.36 mol) in ether (30 mL) containing a trace of iodomethane at reflux. After an hour of refluxing, the mixture was cooled to 0 °C, and a solution of (2*E*)-2-hexenal (32.34 g, 0.33 mol) in ether (70 mL) was added dropwise over 1 h while maintaining the reaction temperature at 10 °C. When the introduction finished, the reaction mixture was stirred for another hour at room temperature. The cooled reaction mixture was poured into cold 20% aq. NH_4Cl (300 mL), then saturated with NaCl, extracted with ether (3×), washed with brine (2×), dried over $MgSO_4$, and concentrated. The residue was distilled. Compound **81** was purified by chromatography on silica gel using 20% ether in pentane, yield 7%, purity 90%. MS: *m/z* 140 ($M^{+\cdot}$, 0), 122 (1), 99 (32), 81 (6), 69 (4), 57 (100), 41 (24), 29 (10). ^{1}H NMR: 0.90 (t, 3H); 1.40 (m, 2H); 2.01 (m, 2H); 2.30 (dd, 2H); 4.12 (m, 1H); 5.15 (d, *J* = 10.0, 1H); 5.18 (d, *J* = 17.2, 1H); 5.48 (dd, *J* = 15.4, 6.7, 1H); 5.66 (dt, *J* = 15.4, 6.6, 1H); 5.81 (m, 1H). ^{13}C NMR: 134.6 (d); 132.0 (d); 117.8 (t); 71.8 (d); 42.0 (t); 34.3 (t); 22.3 (t); 13.7 (q). RI_{SPWax} = 1550, RI_{SPB-1} = 1050.

*(5E)-1,5-Nonadien-4-one (***8***)*. Compound **81** (4 g, 28 mmol) and acetone (50 mL) were introduced to the flask and cooled down with an ice bath. Jones' reagent (CrO_3/H_2SO_4) was added until the brown color persisted. The reaction mixture was stirred for 1 h at room temperature. After the addition of water, the mixture was extracted with pentane (3×), washed with brine (2×), and dried over $MgSO_4$. The residue was purified by chromatography on silica gel using 10% ether in pentane to give pure **8** (yield: 66%, purity: 90%). MS: *m/z* 138 ($M^{+\cdot}$, 2), 123 (3), 97 (100), 69 (14), 55 (94), 41 (30), 27 (6). ^{1}H NMR: 0.95 (t, 3H); 1.50 (m, 2H); 2.20 (m, 2H); 3.32 (m, 2H); 5.15 (d, *J* = 10.2,

Table 1. Sulfur-containing Compounds Identified in Red Bell Peppers

compound	RI (SPWax)	RI (SPB-1)	flavor description[a]
2-heptanethiol (**6**) *6*	1160	956	*6*
(*E*)-3-heptene-2-thiol (**14**)	1183	943	sesame, green, bell peppers, citrus, fresh (0.1 ppm)
(*Z*)-4-heptene-2-thiol (**16**)	1186	946	seanut, sesame, green coffee beans (10 ppm)
(*E*)-4-heptene-2-thiol (**15**)	1204	952	seanuts sesame, coffee, bitterness of peppers (2 ppm)
4-nonanethiol (**23**)	1327	1145	sulfury, fruity, sweaty, fatty (0.3 ppm)
2-nonanethiol (**22**)	1356	1160	roasted, roasted chicken, sesame, lettuce (0.5 ppm)
1-nonene-4-thiol (**26**)	1372	1132	berry, green, fruity, tropical fruit (0.2 ppm)
(*E*)-2-nonene-4-thiol (**27**)	1387	1142	green, vegetal, weak (50 ppm)
(*E*)-4-nonene-2-thiol (**24**)	1372	1148	green, mushroom, rubbery (1 ppm)
(*Z*)-4-nonene-2-thiol (**25**)	1399	1152	fruity, green, vegetal, mushroom (2 ppm)
2,4-heptane-dithiol (isomer 1) (**19**)	1548	1172	spring onion, green, alliaceous (50 ppm)
2-mercapto-4-heptanone (**12**)	1547	1076	grapefruit, sesame, earthy, rocket (0.5 ppm)
2,4-heptane-dithiol (isomer 2) (**19**)	1587	1187	[b]
4-mercapto-2-heptanone (**13**)	1585	1080	green, peely, vegetable (0.5 ppm)
4-methylthio-2-heptanethiol (isomer 1) (**20**)	1605	[c]	[d]fruity, minty, green, rhubarb, tropical fruit, alliaceous (1 ppm)
2-methylthio-4-heptanethiol (isomer 1) (**21**)	1623	1272	[d]
4-methylthio-2-heptanethiol (isomer 2) (**20**)	1640	[c]	[d]
3-methyl-5-propyl-1,2-dithiolane (isomer 1) (**10**)	1662	1252	[b]very green, plastic, mustard, watercress, alliaceous (2 ppm)
3-methyl-5-propyl-1,2-dithiolane (isomer 2) (**10**)	1670	1257	[b]
2-methylthio-4-heptanethiol (isomer 2) (**21**)	1672	[c]	[d]
2-mercapto-4-heptanol (isomer 1) (**17**)	1722	1108	[b]fruity, tropical, guava, watercress, vegetal (0.5 ppm)
2-mercapto-4-heptanol (isomer 2) (**17**)	1745	1119	[b]
4-mercapto-2-heptanol (isomer 1) (**18**)	1746	1112	[b]onion, liver, meaty, sweaty, resinous (50 ppm)
4-mercapto-2-heptanol (isomer 2) (**18**)	1763	1121	[b]
2,4-nonane-dithiol (**28**)	1793	1390	rotten, melon, chemical (0.5 ppm)
3-methyl-5-pentyl-1,2-dithiolane (**29**)	1886	1470	rubbery, sulfury, green, rotten (2 ppm)
1-(2-thienyl)-2-pentanethiol (**31**)	1992	1389	tropical, passion fruit, common, weak (1 ppm)
4-mercapto-2-nonanol (isomer 1) (**30**)	1939	1315	synthetic, rubbery, unpleasant (50 ppm)

[a] Tasted in NaCl (0.3%) and sugar (0.5%) solutions. [b] Evaluation of the diastereomeric mixture. [c] Mixture on apolar column not determined, RI = 1272, 1275, and 1289. [d] Evaluation of the mixture of **20** and **21**.

1H); 5.18 (d, J = 16.9, 1H); 5.95 (ddd, J = 16.9, 10.2, 6.8, 1H); 6.11 (d, J = 15.9, 1H); 6.88 (dt, J = 15.9, 6.9, 1H). ^{13}C NMR: 198.1 (s); 148.1 (d); 131.1 (d); 129.8 (d); 118.6 (t); 45.1 (t); 34.5 (t); 21.4 (t); 13.7 (q). RI_{SPWax} = 1504, RI_{SPB-1} = 1083.

RESULTS AND DISCUSSION

Red Bell Pepper Extract. The composition of the volatile constituents of the bell pepper extract prepared by SDE is unique. As already discovered by Buttery et al. (*1*), (3*E*)-3-hepten-2-one (**1**, 5.3%), 1-nonen-4-one (**2**, 10.2%), (2*E*)-2-nonen-4-one (**3**, 2.8%), (2*E*,5*E*)-2,5-nonadien-4-one (**4**, 7.9%), and 2-methoxy-3-isobutylpyrazine (**5**, ca. 3.5%) are the main compounds.

In addition, we have newly identified (2*Z*,5*E*)-2,5-nonadien-4-one (**7**, 1.6%), (5*E*)-1,5-nonadien-4-one (**8**, 1.8%), and (2*E*)-2-hepten-4-one (**9**, 0.35%); all three exhibit green, leafy, herbaceous, and hay-like notes. As indicated by the typical asymmetric shape of the peak, compound **7** readily isomerizes to compound **4**.

Linalool (4.8%) and β-damascenone (1.3%), compounds with an important aroma impact, contribute to the fruity aspect of the bell pepper flavor. In the total extract, three sulfur compounds could be detected: the already known heptane-2-thiol (**6**, 0.2%) (*6*), the new diastereoisomers of 3-methyl-5-propyl-1,2-dithiolane (**10**, 0.9% and 0.7%) structurally related to the heptenones **1** and **9**, and 1-(2-thienyl)-pentan-1-one (**11**, trace), already identified in yeast (*11*), which may be derived from the nonadienones.

Detection of New Sulfur-containing Compounds. Because of their low detection threshold sulfur-containing compounds, even at very low concentrations, contribute to the organoleptic profile of flavors and essential oils. The lowest thresholds are observed for free thiols (*p*-1-menthene-8-thiol (*12*), Sclarymol (*10*)). They can be selectively enriched on Affi-Gel 501, which forms reversible covalent bonds with thiols (*8, 10*). The nonthiol compounds are removed with an organic solvent, and then the thiols are liberated by elution with an excess of dithiothreitol (1,4-dimercapto-2,3-butanediol). The concentrated thiol fraction was analyzed by GC-MS. The bulk of the fraction consisted of artifacts of the agarose gel and of the dithiothreitol used for the desorption of the thiols. Therefore, a blank experiment was performed under identical conditions without the addition of bell peppers to distinguish authentic constituents of the bell peppers from these artifacts. We could detect a multitude of small peaks with MS not existing in the commercial as well as in our in-house data libraries, but their fragmentation patterns had similarities with aliphatic sulfur-containing compounds. The comprehension of fragmentation mechanisms of known sulfur compounds combined with information given by the new MS allowed us to deduct the structures of 19 new thiols and 2 new 1,2-dithiolanes. The results are summarized in **Table 1**. Compounds **6**, **18**, and **22** have been cited before; all other structures are, to the best of our knowledge, described here for the first time.

Sulfur-containing Heptane Derivatives. Racemic **6** was synthesized and organoleptically evaluated by Sakoda (*13*). Simian et al. identified it for the first time in nature (*6*) and determined the threshold of the synthetic racemate and of the two synthetic enantiomers (10 μg/l, orthonasal measurements in water). Their organoleptic properties were both described as "bell pepper, fruity, vegetable" in low concentrations (about 100 μg/L) and "sulfury, onion and mushroom" in higher concentrations (1 mg/L).

Figure 1 gives a schematic presentation of the structural relationship of the heptane derivatives. Mercapto-ketones **12** and **13** are formed by the formal addition of H_2S, most probably introduced by cysteine, to ketones **1** and **9**. For the formation of the unsaturated thiols **14**, **15**, and **16** as well as the mercapto-alcohols **17** and **18**, the dithiol **19**, and the methylthio-thiols **20** and **21**, an additional reduction step is involved. 2,4-Dithiol **19**

is probably oxidized during cooking to the two diastereoisomers of dithiolane **10** that were identified in the total extract in an abundance comparable to compound **6** (0.9 and 0.7%). This disulfide is not extracted by Affi-Gel 501 and, therefore, its presence in trace amounts in the thiol fraction confirms the easy oxidation of **19**. The MS of **10** (**Figure 2**) shows the presence of two sulfur atoms ($164 = M^+ + 2$ is about 9% of M^+). The fragment *m*/*z* 64 is S_2, characteristic for disulfides. The two sulfur atoms are cleaved off in two steps: *m*/*z* 129 is $M^+ - 33$ (SH) and then a loss of 32 (S) results in the heptene fragment *m*/*z* 97. Dithiolanes are extremely rare flavor compounds, as the only other examples were found by Tressl et al. in coffee (3,3-dimethyl-1,2-dithiolane (*14*)) and in asparagus (1,2-dithiolane-4-carboxylic acid (*15*)).

Three compounds between $RI_{polar} = 1180$ and 1205 showed distinct MS with $M^{+\cdot} = 130$, two mass units less than compound **6**. Two of them had a base peak of *m*/*z* = 61, suggesting a secondary thiol. This structural element combined with an allylic double bond was consistent with the structures of **15** and **16**. For compound **14**, no allylic cleavage is possible, but the loss of HS and H_2S to *m*/*z* = 97 and 96 was observed. In **Figure 3** typical MS patterns for bifunctional mercapto-alcohols are demonstrated. Compound **17** is characterized by the fragment *m*/*z* 61 for the secondary thiol, whereas **18** shows *m*/*z* 45 for the secondary alcohol. Furthermore, both compounds lose water (*m*/*z* 130) and H_2S (*m*/*z* 114); *m*/*z* 73 in **17** is the butanol fragment, and *m*/*z* 101 is M − 18 – 29 by loss of C_2H_5 via allylic fragmentation.

Both diastereoisomers of compounds **10**, **17**, **18**, **19**, **20**, and **21**, showing strictly identical MS, were detected in the bell pepper extract, a fact that increased the complexity of the GC-MS-profile. The heptane derivatives **12**, **13**, **17**, and **18** fall under the claim of a recent patent application, which describes the use of sulfur compounds for enhancing coffee flavors (*16*) without being mentioned explicitely. The synthetic study by Ozeki et al. (*17*) reports the detailed NMR spectra of (2*S*,4*S*)-4-mercapto-2-heptanol (**18**, *anti*).

Sulfur-containing Nonane Derivatives. Because the conditions in bell peppers are prosperous for the formation of sulfur-containing compounds starting from unsaturated ketones, we expected to identify similar derivatives of the abundant unsaturated C9-ketones **2**, **3**, **4**, **7**, and **8**. And indeed, a series of such compounds was detected in trace amounts as summarized in **Figure 4**.

The MS were deduced by analogy with the compounds of the heptane series. Compound **22** has been described by Sakoda et al. (*13*), and **30** was synthesized by Vermeulen et al. by combinatorial synthesis and described to have an odor of rhubarb, sweat, and mushrooms (at the sniffing port) (*18*). All of the other substances are described here for the first time. A new structural element is the substitution at position 4 in compounds **23**, **26**, and **27**. The structure of (4*E*)-4-nonene-2-thiol (**24**) as well as the homologous (4*E*)-4-heptene-2-thiol (**15**) were established because of their MS fragmentations, which imply cyclization of the thiol to a 2-alkyl-5-methyl-thiolane, alkyl being butyl for **24** and ethyl for **15**, followed by the loss of *m*/*z* = 15−115 in **15** or 143 in **24** or the loss of *m*/*z* 29 in **15** or 57 in **24** to give *m*/*z* 101. Without the formulation of this cyclization, the fragment *m*/*z* = 101 cannot be understood. The fragment *m*/*z* = 61 (100%), the result of allylic fragmentation, is nearly absent in the 3-alkenyl-2-thiol **14** (4%).

Compounds **28**, **29**, and **30** are homologous of **19**, **10**, and **18**. But because of their extremely low concentrations, only the presence of one diastereoisomer in each diastereoisomeric pair could be detected in the natural extract. The thiophene **31** is structurally related to ketones **4**, **7**, or **8**. Under MS conditions it falls into two parts and gives the fragments *m*/*z* 97/98, characteristic for methyl-thiophene radicals, as well as *m*/*z* 89, for the butanethiol moiety.

These new sulfur compounds cover a whole palette of organoleptic properties (see **Table 1**). Only three of them, compounds **28, 29**, and **30**, have the unpleasant rubbery, rotten notes notorious of sulfur compounds. Compounds **17**, **20/21**, **23**, **25**, **26**, and **31** exhibit fruity flavors reminiscent of berries and tropical fruits. The flavor of compounds **10**, **24**, **25**, and **27** is very green and vegetable-like. Meaty, alliaceous, and onion-like notes characterize compounds **10**, **18**, and **19**, whereas compounds **12**, **14**, **15**, and **16** can be used for sesame-, peanut-, coffee-like, and roasted flavors, respectively. Characteristic bell pepper notes could be attributed to compounds **14** and **15**.

SYNTHESIS

All of the syntheses performed to corroborate the new compounds gave racemates. Nonane-2-thiol (**22**, **Figure 5**) was obtained by treatment of 2-bromononane (**32**) with thiourea (*19*). Simian et al. (*6*) prepared 2-heptanethiol (**6**) starting from 2-heptanol that was converted to the tosylate and the thioacetate, followed by reduction with $LiAlH_4$ in ether. We used this pathway to prepare compounds **23** and **26** (**Figure 5**).

1,4-Addition of thioacetic acid to the unsaturated ketones **39** and **40** gave the corresponding thioacetates **41** and **42**, which were reduced into the mercapto-alcohols **18** and **30** (**Figure 6**).

Treatment with tosyl chloride of **18** and **30** led to the mixed tosylates **43** and **44**, a class of compounds never described before. These compounds were not characterized and were immediately transformed into the dithioacetates **45** and **46**, which were reduced with $LiAlH_4$ at room temperature to the dithiols **19** and **28**. Compounds **45** and **46** underwent partially spontaneous oxidation to the 1,2-dithiolanes **10** or **29**, probably due to the reaction temperature (80 °C). Methylation of **19** gave a mixture of the monomethylthio thiols **20** and **21** and the bis(methylthio) derivative **47.** Triphenylsilanethiol, a solid hydrogen sulfide equivalent, and potassium fluoride under phase transfer conditions (18-crown-6) were efficient for the transformation of the unsaturated ketones **39** and **40** into of the mercapto-ketones **13** and **48** (*20*). Ketone **9**, prepared in two steps from ethyl 3-oxohexanoate, was the starting material for the synthesis of **12** and **17**, as depicted in **Figure 7**. Saponification using HCl/EtOH can be used as an alternative to deprotect the thioacetate **51** in the presence of the ketone function.

The homoallylic alcohols **54** and **55**, obtained by the addition of the corresponding alkyne to propylene oxide as described by Jones et al. (*21*) to give the acetylenic alcohols **52** and **53**, followed by selective reduction with $LiAlH_4$, were the starting materials for thiols **15** and **24** with a (*E*)-double-bond. Replacing $LiAlH_4$ by the H_2/Lindlar reagent led to the (4*Z*)-alkene-thiols **16** and **25** (**Figure 8**).

Treatment of **66** and **67** with methanesulfonyl chloride gave the corresponding mesylates, which were not isolated but were directly converted to the *S*-thioacetates **68**, **70** and **69**, **71**. The isomers were separated by preparative HPLC and then reduced individually to compounds **72**, **27**, **14**, and **73** with $LiAlH_4$ (**Figure 9**).

The synthesis of **31** started from 2-thiophene-carbaldehyde (**74**) which was transformed into **75** with trimethylsulfonium iodide, with the addition of water being essential (*22, 23*). Compound **75** was not isolated and was immediately treated with silica gel in acetone to give aldehyde **76**. A Grignard

addition with propyl magnesiumbromide led to alcohol **77**, which was converted to its tosylate **78** and to the thioacetate **79**, which, by treatment with $LiAlH_4$, gave thiol **31** (**Figure 10**). Ketones **7** and **8**, new compounds related to the known ketones **2**, **3**, and **4**, were prepared by Grignard addition of propene units to (2*E*)-2-hexenal to give to alcohols **80** and **81**, followed by specific oxidation (**Figure 11**).

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