Supporting Information

A Practical Approach to α - or γ -Heterosubstituted Enoic Acids

Julia L. Shamshina and Timothy S. Snowden*

Department of Chemistry, the University of Alabama, Tuscaloosa, Alabama, 35487, USA

snowden@bama.ua.edu

General Experimental Section	S2
Preparation of Alkenyl Trichloromethyl Carbinols	S2
Preparation of α- or γ-Alkoxy-substituted Enoic Acids	S4
Preparation of α- or γ-Hydroxy-substituted Enoic Acids	S4
Preparation of α- or γ-Benzylmercaptosubstituted Enoic Acids	S4
References	S10
$^1\text{H}/^{13}\text{C}$ Spectra of Reported Major Products	S11

General Information.

The ^1H and ^{13}C NMR spectra were recorded at 360 or 500 MHz and 90 or 125 MHz respectively. All melting points are uncorrected. High-resolution mass spectra for the trichloromethyl carbinols were recorded on an AutoSpec-UltimaTM NT mass spectrometer using electron ionization (EI) at 70 eV. High resolution mass spectra for the carboxylic acids were recorded on a Micromass Q-ToF Ultima instrument with an electrospray probe and a Z-spray source. All reagents were used directly as obtained from commercial sources unless otherwise noted.

Synthesis of Alkenyl Trichloromethyl Carbinols.

Compounds **13**, **18**, **23**, **28a-b**, **35**, and **39** were prepared by the method of Corey and Link¹ from the respective enals. Yields and reaction times are unoptimized. The following serves as a general procedure: To a solution of aldehyde (1 mmol) in 1.35 mL of anhydrous DMF was added trichloroacetic acid (1.5 mmol) and sodium trichloroacetate (1.5 mmol) with stirring at room temperature. Initially rapid evolution of CO_2 was observed. After 3-6 hours the mixture was diluted with 5 mL of diethyl ether and washed with saturated aqueous sodium bicarbonate. Precipitated solids were filtered and washed three times with diethyl ether. The filtrate was washed two more times with sodium bicarbonate solution and once with brine. The organic phase was dried with sodium sulfate and the diethyl ether was evaporated under reduced pressure. The resulting residue was eluted through a plug of silica gel with 95:5 hexane/ethyl acetate to afford the corresponding trichloromethyl carbinol.

The spectral properties of **28b** were in accordance with those previously reported.¹ The enals used to afford **35** and **39** were synthesized from 3-phenylpropanal (86% yield) and *n*-octenal (74%) following the published procedure of Hon et al.²

The enal used to afford **23** was prepared from nerol by manganese dioxide oxidation:

3,7-Dimethylocta-2,6-dienal.

Nerol (1 mmol) was dissolved in dichloromethane (10 mL) and activated manganese dioxide (heated at 160 °C for > 24 h) (10 mmols) was then added to the solution. The mixture was stirred at room temperature for 4 hours, while being monitored by TLC for the loss of starting alcohol (95:5 hexane/EtOAc). After the starting alcohol was consumed, the reaction mixture was filtered through Celite, and the salts were washed with dichloromethane. The filtrate was evaporated under reduced pressure leaving the indicated aldehyde as a yellow oil in 85% crude yield of *E* and *Z* isomers. The material was sufficiently pure to be used directly for the preparation of **23** as described in the general procedure above.

1,1,1-Trichloro-3-methylhex-3-en-2-ol (13)

The crude material was purified by silica gel flash chromatography using 95:5 hexane/EtOAc as eluent. The indicated compound was obtained as a colorless oil in 76% yield. ^1H NMR (CDCl_3 , 500 MHz) δ 5.74 (t, 1H, $J=7.0$ Hz), 4.55 (d, 1H, $J=2.7$ Hz), 2.89 (d, 1H, $J=4.1$ Hz), 2.12 (p, 2H, $J=7.6$ Hz), 1.82 (s, 3H), 1.01 (t, 3H, $J=7.6$ Hz); ^{13}C NMR (CDCl_3 , 90 MHz) δ 137.7, 129.1, 87.7, 21.2, 13.4, 13.0; HRMS m/z calcd for $\text{C}_7\text{H}_{11}\text{Cl}_3\text{O}$, 215.9875; found 214.9803 which corresponds to $[\text{M}-1]^+$.

1,1,1-Trichloro-4-methylpent-3-en-2-ol (18)

The crude material was purified by silica gel flash chromatography using 95:5 hexane/EtOAc as eluent. The indicated compound was obtained as a white solid in 72% yield; m.p. 84-86 °C. ¹H NMR (CDCl₃, 360 MHz) δ 5.35 (d, 1H, J=1.08 Hz), 4.79 (t, 1H), 2.59 (d, 1H, J=5.76 Hz), 1.83 (s, 6H); ¹³C NMR (CDCl₃, 90 MHz) δ 142.5, 119.5, 103.6, 79.5, 26.1, 19.2; HRMS *m/z* calcd for C₅H₉Cl₃O, 201.9719; found 85.0652 which corresponds to [M-CCl₃]⁺.

1,1,1-Trichloro-4,8-dimethylnona-3,7-dien-2-ol (23)

The crude material was purified by silica gel flash chromatography using 95:5 hexane/EtOAc as eluent. The indicated compound was obtained as slightly yellow crystals as a 1:5 mixture of *E/Z* diastereomers in 78% yield; m.p. 41-42 °C.

Z: ¹H NMR (CDCl₃, 360 MHz) δ 5.36 (dd, 1H), 5.09 (m, 1H), 4.65 (dt, 1H), 2.48 (s, 1H), 2.25 (m, 4H), 1.81 (d, 3H, J=1.4 Hz), 1.68 (s, 3H), 1.60 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 146.1, 132.7, 123.4, 120.0, 103.3, 79.0, 33.1, 26.2, 25.7, 23.7, 17.7; HRMS *m/z* calcd for C₁₁H₁₇Cl₃O, 270.0345; found 270.0332.

E: ¹H NMR (CDCl₃, 360 MHz) δ 5.40 (dd, 1H, J=1.3 Hz, J=8.5 Hz), 5.14 (m, 1H), 4.79 (d, 1H, J=7.9 Hz), 2.59 (s, 1H), 2.15 (m, 4H), 1.83 (d, 3H, J=1.4 Hz), 1.70 (s, 3H), 1.62 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 146.1, 132.7, 123.4, 120.0, 103.3, 79.0, 33.1, 26.2, 25.7, 23.7, 17.7; HRMS *m/z* calcd for C₁₁H₁₇Cl₃O, 270.0345; found 270.0332.

1,1,1-Trichloronon-3-en-2-ol (28a)

The crude material was purified by silica gel flash chromatography using 95:5 hexane/EtOAc as eluent. The indicated compound was obtained as a yellow oil in 75% yield. ¹H NMR (CDCl₃, 500 MHz) δ 6.02 (m, 1H), 5.65 (tdd, 1H, J=1.4 Hz, J=6.5 Hz, J=15.4 Hz), 4.53 (t, 1H, J=6.1 Hz), 2.74 (d, 1H, J=5.9 Hz), 2.13 (q, 2H, J=7.8 Hz), 1.43 (td, 2H, J=7.3 Hz, J=14.5 Hz), 1.31 (m, 4H), 0.89 (t, 3H, J=7.0 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 139.6, 123.7, 103.1, 83.5, 32.4, 31.2, 28.3, 22.4, 14.0; HRMS *m/z* calcd for C₉H₁₅Cl₃O, 244.0188; found 127.1122 which corresponds to [M-CCl₃]⁺.

3-Benzyl-1,1,1-trichlorobut-3-en-2-ol (35)

The crude material was purified by silica gel flash chromatography using 95:5 hexane/EtOAc as eluent. The indicated compound was obtained as a slightly yellow oil in 85% yield. ¹H NMR (CDCl₃, 360 MHz) δ 7.32 (m, 5H), 5.61 (s, 1H), 5.22 (s, 1H), 4.66 (s, 1H), 3.73 (dd, 2H, J=16.1 Hz, J=42.0 Hz), 3.12 (s, 1H); ¹³C NMR (CDCl₃, 90 MHz) δ 143.7, 138.5, 129.3, 128.5, 126.5, 120.8, 102.5, 83.7, 40.6; HRMS *m/z* calcd for C₁₁H₁₁Cl₃O, 263.9875; found 263.9880.

1,1,1-Trichloro-3-methylenenonan-2-ol (39)

The crude material was purified by silica gel flash chromatography using 95:5 hexane/EtOAc as eluent. The indicated compound was obtained as a slightly yellow oil in 74% yield. ¹H NMR (CDCl₃, 360 MHz) δ 5.44 (s, 1H), 5.27 (dd, 1H, J=1.0 Hz, J=1.4 Hz), 4.61 (s, 1H), 3.07 (s, 1H), 2.29 (dq, 2H, J=7.1 Hz, J=15.8 Hz), 1.51 (m, 2H), 1.31 (m, 6H), 0.88 (t, 3H, J=6.8 Hz); ¹³C NMR (CDCl₃, 90 MHz) δ 144.7, 117.8, 102.6, 84.9, 33.5, 31.7, 29.0, 28.2, 22.6, 14.0; HRMS *m/z* calcd for C₁₀H₁₇Cl₃O, 258.0345; found 258.0333.

General Procedure for the Synthesis of α - or γ -Alkoxy-substituted Enoic Acids.

The trichloromethyl carbinol (1.0 mmol) in the appropriate alcohol (3.0 mL) was placed in a 4-dram vial, and then powdered NaOH (6.0 mmol) was added. The reaction mixture was stirred at room temperature for 5 min. and then at 55 °C for 12 h. The mixture was cooled to room temperature, and then the alcohol was evaporated under reduced pressure. The resulting residue was acidified to pH=1 with 2N HCl, extracted with EtOAc, dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent.

General Procedure for the Synthesis of α - or γ -Hydroxy-substituted Enoic Acids.

The trichloromethyl carbinol (1.0 mmol) in DME/water (4/3 mL) was placed in a 4-dram vial, and then powdered NaOH (6.0 mmol) was added. The reaction mixture was stirred at room temperature for 5 min. and then at 55 °C for 12 h. The mixture was cooled to room temperature, and then the DME was evaporated under reduced pressure. The remaining aqueous phase was acidified to pH=1 with 2N HCl, extracted with EtOAc, dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent.

General Procedure for the Synthesis of α -Benzylmercaptosubstituted Enoic Acids. The trichloromethyl carbinol (1.0 mmol) in methanol (3 mL) was placed in a 4-dram vial, and then benzylmercaptan (3 mmol) and powdered NaOH (6.0 mmol) were added. The reaction mixture was stirred at room temperature for 5 min. and then at 55 °C for 12 h. The mixture was cooled to room temperature, and then the methanol was evaporated under reduced pressure. The residue was acidified to pH=1 with 2N HCl, extracted with EtOAc, dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography using 9:1 then 8:2 hexane/EtOAc as eluent (if necessary).

2-Benzylsulfanyl-3-methylhex-3-enoic acid (14)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a slightly yellow oil in 85% yield. ¹H NMR (CDCl₃, 500 MHz) δ 9.29 (br s, 1H), 7.22 (m, 5H), 5.38 (t, 1H, J=7.0 Hz), 3.84 (s, 1H), 3.64 (dd, 2H, J=13.5 Hz, J=38.6 Hz), 2.02 (qd, 2H, J=7.3 Hz, J=14.5 Hz), 1.69 (s, 3H), 0.94 (t, 3H, J=7.5 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 176.6, 137.2, 133.7, 129.0, 128.4, 127.9, 127.1, 55.6, 35.5, 21.4, 13.8, 13.4; HRMS *m/z* calcd for C₁₄H₁₈O₂NaS, 273.0925; found 273.0917.

4-Methoxy-3-methylhex-2-enoic acid (15)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a colorless oil in 76% yield. ¹H NMR (CDCl₃, 500 MHz) δ 11.13 (br s, 1H), 5.87 (s, 1H), 3.47 (t, 1H, J=6.4 Hz), 3.25 (s, 3H), 2.08 (d, 3H, J=1.2 Hz), 1.59 (m, 2H), 0.89 (t, 3H, J=7.4 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 170.6, 161.2, 116.1, 87.9, 56.9, 26.6, 14.2, 9.9; HRMS *m/z* calcd for C₈H₁₄O₃Na, 181.0841; found 181.0839.

4-Allyloxy-3-methylhex-2-enoic acid (16)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a colorless oil in 63% yield. ¹H NMR (360 MHz) δ 10.73 (br s, 1H), 5.89 (m, 2H), 5.25 (ddd, 1H, J=1.6 Hz, J=3.3 Hz, J=17.2 Hz), 5.16 (ddd, 1H, J=1.3 Hz, J=2.8 Hz, J=10.4 Hz), 3.94 (tdd, 1H, J=1.5 Hz, J=5.1 Hz, J=12.7 Hz), 3.75 (tdd, 1H, J=1.3 Hz, J=6.1 Hz, J=12.7 Hz), 3.64 (t, 1H, J=6.4 Hz), 2.08 (d, 3H, J=1.3 Hz), 1.61 (qd, 2H, J=7.1 Hz, J=14.4 Hz), 0.89 (t, 3H, J=7.4 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 171.9, 161.3, 134.5, 117.0, 116.5, 85.3, 69.8, 26.6, 14.4, 9.9; HRMS *m/z* calcd for C₁₀H₁₆O₃, 184.1099; found 184.1094.

4-Hydroxy-3-methylhex-2-enoic acid (17)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a slightly yellow oil in 75% yield. ¹H NMR (CDCl₃, 500 MHz) δ 10.10 (br s, 1H), 5.95 (s, 1H), 4.06 (m, 1H), 2.11 (s, 3H), 1.63 (m, 2H), 1.31 (dd, 1H, J=1.7 Hz, J=7.3 Hz), 0.93 (t, 3H, J=7.4 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 171.5, 162.7, 114.6, 77.7, 27.8, 15.1, 9.6; HRMS *m/z* calcd for C₇H₁₂O₃Na, 167.0684; found 167.0696.

2-Benzylsulfanyl-4-methylpent-3-enoic acid (19)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a yellow oil in 75% yield. ¹H NMR (CDCl₃, 500 MHz) δ 11.61 (br s, 1H), 7.36 (m, 5H), 5.40 (m, 1H), 4.05 (d, 1H, J=9.7 Hz), 3.90 (dd, 2H, J=13.5 Hz, J=39.2 Hz), 1.77 (s, 3H), 1.49 (s, 3H); ¹³C NMR (CDCl₃, 90 MHz) δ 178.1, 138.6, 137.3, 129.1, 128.4, 127.1, 117.2, 43.7, 36.0, 25.7, 17.9; HRMS *m/z* calcd for C₁₃H₁₆O₂NaS, 259.0769; found 259.0758.

4-Methoxy-4-methylpent-2-enoic acid (20)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent, m.p. 79-80 °C. The indicated compound was obtained as white crystals in 80% yield. ¹H NMR (CDCl₃, 360 MHz) δ 11.22 (br s, 1H), 7.01 (d, 1H, J=16.0 Hz), 5.94 (d, 1H, J=16.0 Hz), 3.21 (s, 3H), 1.33 (s, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.4, 155.6, 119.4, 74.8, 50.9, 25.2; HRMS *m/z* calcd for C₇H₁₂O₃Na, 167.0684; found 167.0692.

4-Allyloxy-4-methylpent-2-enoic acid (21)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a slightly yellow oil in 72% yield. ¹H NMR (CDCl₃, 500 MHz) δ 10.17 (br s, 1H), 7.03 (d, 1H, J=15.9 Hz), 5.94 (d, 1H, J=15.9 Hz), 5.90 (m, 1H), 5.31 (ddd, 1H, J=1.5 Hz, J=3.2 Hz, J=17.2 Hz), 5.15 (ddd, 1H, J=1.5 Hz, J=10.4 Hz), 3.88 (td, 2H, J=1.4 Hz, J=5.3 Hz), 1.36 (s, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.8, 155.8, 135.2, 119.3, 116.2, 75.0, 64.5, 25.8; HRMS *m/z* calcd for C₉H₁₄O₃Na, 193.0841; found 193.0833.

4-Hydroxy-4-methylpent-2-enoic acid (22)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent, m.p. 93-94 °C. The indicated compound was obtained as white crystals in 89% yield. ¹H NMR (CDCl₃, 360 MHz) δ 10.18 (br s, 1H), 7.11 (d, 1H, J=15.7 Hz), 6.04 (d, 1H, J=15.6 Hz), 2.10 (s, 1H), 1.39 (s, 6H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.6, 157.1, 117.3, 70.9, 29.2, 20.7; HRMS *m/z* calcd for C₆H₁₀O₃Na, 153.0528; found 153.0525.

2-Benzylsulfanyl-4,8-dimethylnona-3,7-dienoic acid (24)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a yellow oil in 83% yield. ¹H NMR (CDCl₃, 500 MHz) δ 11.30 (br s, 1H), 7.35 (m, 5H), 5.41 (d, 1H, J=9.9 Hz), 4.99 (t, 1H, J=6.5 Hz), 4.08 (d, 1H, J=9.8 Hz), 3.89 (dd, 2H, J=13.4 Hz, J=55.1 Hz), 2.02 (td, 2H, J=6.9 Hz, J=13.8 Hz), 1.86 (t, 2H, J=7.0 Hz), 1.77 (s, 3H), 1.71 (s, 3H), 1.59 (s, 3H); ¹³C NMR (CDCl₃, 90 MHz) δ 178.0, 142.2, 137.3, 132.0, 129.1, 128.4, 127.2, 123.5, 117.6, 43.4, 36.1, 32.2, 26.2, 25.6, 23.5, 17.6; HRMS *m/z* calcd for C₁₈H₂₄O₂NaS, 327.1395; found 327.1391.

4-Methoxy-4,8-dimethylnona-2,7-dienoic acid (25)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a yellow oil in 85% yield. ¹H NMR (CDCl₃, 500 MHz) δ 10.57 (br s, 1H), 6.97 (d, 1H, J=15.9 Hz), 5.95 (d, 1H, J=15.9 Hz), 5.06 (m, 1H), 3.20 (s, 3H), 1.96 (td, 2H, J=7.0 Hz, J=17.4 Hz), 1.67 (s, 3H), 1.59 (s, 3H), 1.58 (m, 2H), 1.30 (s, 3H); ¹³C NMR (CDCl₃, 90 MHz) δ 171.3, 155.2, 132.0, 123.8, 119.7, 76.6, 50.4, 38.7, 25.7, 22.1, 17.7; HRMS *m/z* calcd for C₁₂H₂₀O₃Na 235.1310. found 235.1309.

4-Allyloxy-4,8-dimethylnona-2,7-dienoic acid (26)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a yellow oil in 70% yield. ¹H NMR (CDCl₃, 500 MHz) δ 10.00 (br s, 1H), 7.02 (d, 1H, J= 15.9 Hz), 5.98 (d, 1H, J=15.9 Hz), 5.94 (m, 1H), 5.44 (d, 2H), 5.35 (dq, 1H), 5.17 (dq, 1H), 5.09 (tt, 1H), 3.89 (tt, 1H), 2.25 (m, 2H), 2.01 (m, 2H), 1.69 (s, 3H), 1.51 (s, 3H), 1.35 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.8, 155.4, 135.2, 132.0, 123.8, 119.7, 115.9, 63.8, 39.3, 31.6, 26.5, 25.7, 22.9, 22.2, 17.7; HRMS *m/z* calcd for C₁₄H₂₂O₃, 238.1659; found 238.1667.

4-Hydroxy-4,8-dimethylnona-2,7-dienoic acid (27)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a slightly yellow oil in 84% yield. ¹H NMR (CDCl₃, 360 MHz) δ 9.92 (br s, 1H), 7.06 (d, 1H, J=15.6 Hz), 6.05 (d, 1H, J=15.6 Hz), 5.10 (m, 1H), 2.04 (m, 2H), 1.67 (s, 3H), 1.64 (m, 2H), 1.59 (s, 3H), 1.34 (s, 3H); ¹³C NMR (CDCl₃, 90 MHz) δ 171.8, 156.6, 132.8, 123.6, 118.1, 73.6, 41.5, 27.8, 25.7, 22.7, 17.8, HRMS *m/z* calcd for C₁₁H₁₈O₃Na, 221.1154; found 221.1151.

4-Oxo-4-phenylbutyric acid (34)

The trichloromethyl carbinol **28b** (1.0 mmol) in DME/water (4/3 mL/mL) was placed in a 10mL vial, and then powdered NaOH (6.0 mmol) was added. The reaction was stirred at 55 °C for 12 h. The mixture was then cooled to room temperature, and the DME was evaporated under reduced pressure. The remaining aqueous phase was acidified to pH=1 with 2N HCl, extracted with EtOAc, dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The crude material was purified by silica gel flash chromatography using 9:1 hexane/EtOAc as eluent. The indicated compound was obtained as a colorless oil in 97% yield.

¹H NMR (CDCl₃, 500 MHz) δ 10.81 (br s, 1H), 7.98 (m, 2H), 7.57 (m, 1H), 7.47 (m, 2H), 3.32 (t, 2H, J=6.6 Hz), 2.82 (t, 2H, J=6.6 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 197.8, 178.8,

136.4, 133.4, 128.7, 128.1, 33.2, 28.1; HRMS m/z calcd for $C_{10}H_{10}O_3$, 178.0630; found 178.0638.

2-Benzylsulfanyl-3-methyl-4-phenylbut-3-enoic acid (36)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a dark yellow oil in 78% yield. 1H NMR ($CDCl_3$, 360 MHz) δ 11.16 (br s, 1H), 7.31 (m, 5H), 6.48 (s, 1H), 4.07 (s, 1H), 3.78 (dd, 2H, $J=13.7$ Hz, $J=26.8$ Hz), 2.00 (d, 3H, $J=1.1$ Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.3, 137.0, 136.8, 131.5, 130.9, 129.1, 129.0, 128.6, 128.2, 127.3, 127.0, 56.3, 35.8, 15.4; HRMS m/z calcd for $C_{18}H_{18}O_2NaS$, 321.0925; found 321.0924.

3-Benzyl-2-methoxybut-3-enoic acid (37)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a colorless oil in 76% yield. 1H NMR ($CDCl_3$, 360 MHz) δ 8.99 (br s, 1H), 7.29 (m, 5H), 5.36 (m, 1H), 5.08 (s, 1H), 4.25 (s, 1H), 3.49 (q, 2H, $J=15.9$ Hz), 3.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 173.7, 142.7, 137.9, 129.4, 128.4, 126.5, 117.4, 82.4, 57.0, 38.5; HRMS m/z calcd for $C_{12}H_{14}O_3$, 206.0943; found 206.0951.

2-Allyloxy-3-benzylbut-3-enoic acid (38)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a colorless oil in 79% yield. 1H NMR ($CDCl_3$, 360 MHz) δ 10.51 (br s, 1H), 7.32 (m, 5H), 5.90 (ddd, 1H, $J=5.9$ Hz, $J=11.5$ Hz, $J=16.5$ Hz), 5.39 (s, 1H), 5.26 (d, 1H, $J=5.3$ Hz), 5.22 (s, 1H), 5.11 (s, 1H), 4.44 (s, 1H), 4.02 (ddd, 2H, $J=5.9$ Hz, $J=12.5$ Hz, $J=31.1$ Hz), 3.53 (q, 2H, $J=15.7$ Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.9, 143.0, 137.9, 133.1, 129.3, 128.2, 126.3, 118.4, 117.1, 79.3, 70.0, 38.6; HRMS m/z calcd for $C_{14}H_{16}O_3$, 232.1099; found 232.1091.

2-Benzylsulfanyl-3-methylnon-3-enoic acid (40)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a colorless oil in 92% yield of 1:1 mixture with 2-(benzylthio)-3-methylenenonanoic acid. 1H NMR ($CDCl_3$, 500 MHz) δ 1H 10.00 (br s, 1H), 7.24 (m, 5H), 5.48 (t, 1H, $J=7.1$ Hz), 3.94 (s, 1H), 3.73 (dd, 2H, $J=13.5$ Hz, $J=39.8$ Hz), 1.78 (s, 3H), 1.42 (td, 2H, $J=7.2$ Hz, $J=14.7$ Hz), 1.32 (m, 6H), 0.94 (t, 3H, $J=6.9$ Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 176.3, 137.3, 132.4, 129.1, 128.5, 128.4, 127.2, 55.7, 35.6, 31.5, 29.0, 28.2, 22.5, 14.0, 13.6; HRMS m/z calcd for $C_{12}H_{24}O_2S$, 292.1497; found 292.1496.

2-Methoxy-3-methylenenonanoic acid (41)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a colorless oil in 72% yield. 1H NMR ($CDCl_3$, 500 MHz) δ 8.58 (br s, 1H), 5.19 (d, 2H, $J=29.5$ Hz), 4.22 (s, 1H), 3.38 (s, 3H), 2.06 (dd, 2H, $J=9.1$ Hz, $J=16.5$ Hz), 1.48 (m, 2H), 1.29 (m, 6H), 0.87 (t, 3H, $J=6.2$ Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 174.1, 143.2, 115.8, 83.7, 56.9, 31.6, 31.1, 29.0, 27.2, 22.6, 14.0; HRMS m/z calcd for $C_{11}H_{20}O_3$, 200.1417; found 200.1418.

2-Allyloxy-3-methylenenonanoic acid (42)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a colorless oil in 76% yield. ¹H NMR (CDCl₃, 500 MHz) δ 9.02 (br s, 1H), 5.92 (ddd, 1H, J=5.8 Hz, J=11.0 Hz, J=23.2 Hz), 5.30 (ddd, 1H, J=1.4 Hz, J=13.9 Hz, J=11.7 Hz), 5.21 (d, 1H, J=40.5 Hz), 4.41 (s, 1H), 4.06 (ddd, 1H, J=5.8 Hz, J=12.6 Hz, J=18.8 Hz), 2.11 (dt, 1H, J=7.7 Hz, J=15.7 Hz), 1.49 (m, 1H), 1.32 (m, 1H), 0.90 (t, 1H, J=6.8 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 174.4, 43.5, 133.3, 118.5, 115.6, 80.8, 77.4, 70.0, 31.7, 31.6, 31.3, 29.0, 28.9, 27.2, 22.5, 14.0; HRMS *m/z* calcd for C₁₃H₂₂O₃, 226.1569; found 226.1569.

2-Methoxynon-3-enoic acid (29, entries 1 and 2 Table2)

The indicated compounds were initially obtained as a mixture of α- and γ-addition products. 2-Methoxynon-3-enoic acid was afforded as the major product using both methanol as a solvent (55% isolated yield) and with a DME/MeOH mixture (81% isolated yield). The isolated yields are given after purification by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent.

¹H NMR (CDCl₃, 500 MHz) δ 10.56 (br s, 1H), 5.92 (m, 1H), 5.44 (tdd, 1H, J=1.3 Hz, J=7.3 Hz, J=15.4 Hz), 4.21 (d, 1H, J=7.3 Hz), 3.39 (s, 3H), 2.07 (q, 2H, J=7.0 Hz), 1.39 (td, 2H, J=7.3 Hz, J=14.5 Hz), 1.28 (m, 6H), 0.86 (t, 3H, J=6.9 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 174.8, 138.4, 123.2, 80.9, 56.9, 32.2, 31.3, 28.4, 22.4, 14.0; HRMS *m/z* calcd for C₁₀H₁₈O₃Na, 209.1154; found 209.1151.

4-Hydroxynon-2-enoic acid (30, entry 3 Table2)

The indicated compound was initially obtained as a mixture of α- and γ-addition products. 4-Hydroxynon-2-enoic acid was isolated as the major product as a slightly yellow oil in 64% yield after purification by silica gel flash chromatography with 8:2 hexane/EtOAc as eluent.

¹H NMR for major product: (CDCl₃, 500 MHz) δ 9.87 (br s, 1H), 7.06 (dd, 1H, J=4.7 Hz, J=15.6 Hz), 6.06 (dd, 1H, J=1.2 Hz, J=15.6 Hz), 4.35 (dt, 1H, J=1.4 Hz, J=6.7 Hz), 1.61 (m, 2H), 1.42 (m, 2H), 1.32 (m, 4H), 0.89 (t, 3H, J=6.8 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 171.2, 152.8, 119.2, 71.1, 36.5, 31.6, 24.8, 22.5, 14.0, HRMS *m/z* calcd for C₉H₁₆O₃Na, 195.0997; found 195.1003.

2-Allyloxynon-3-enoic acid (29, entry 4 Table2)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a yellow oil in 93% yield. ¹H NMR (CDCl₃, 500 MHz) δ 10.82 (br s, 1H), 5.90 (m, 1H), 5.47 (dd, 1H, J=7.2 Hz, J=15.4 Hz), 5.24 (ddd, 1H, J=1.2 Hz, J=13.8 Hz, J=11.4 Hz), 4.38 (d, 1H, J=7.2 Hz), 4.05 (d, 2H, J=5.8 Hz), 2.06 (dd, 2H, J=6.7 Hz, J=13.8 Hz), 1.39 (m, 2H), 1.28 (dp, 4H, J=3.8 Hz, J=7.3 Hz), 0.86 (t, 3H, J=6.9 Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 176.0, 137.9, 133.5, 123.5, 118.2, 78.2, 70.1, 32.2, 31.3, 28.3, 22.4, 13.9; HRMS *m/z* calcd for C₁₂H₂₀O₃Na, 235.1310; found 235.1307.

2-Benzylsulfanylnon-2-enoic acid (29, entry 5 Table 2)

The crude material was purified by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. The indicated compound was obtained as a yellow oil in 64% yield. ¹H NMR (CDCl₃, 500 MHz) δ 10.65 (br s, 1H), 7.33 (m, 1H), 3.96 (s, 2H), 2.24 (d, 2H, J=6.6 Hz), 1.29 (dd, 2H, J=6.6 Hz, J=13.2 Hz), 1.22 (m, 6H, J=20.7 Hz), 0.90 (t, 3H, J=7.1 Hz); ¹³C NMR

(CDCl₃, 125 MHz) δ 170.7, 157.1, 137.9, 129.0, 128.5, 128.4, 127.1, 38.4, 31.5, 31.0, 28.94, 28.0, 22.5, 14.0; HRMS m/z calcd for C₁₆H₂₂O₂S, 278.1341, found 278.1338.

2-Methoxy-4-phenylbut-3-enoic acid (29, entries 6 and 7 Table 2)

The indicated compounds were initially obtained as a mixture of α - and γ -addition products. 2-Methoxy-4-phenylbut-3-enoic acid was afforded as the major product using both methanol as a solvent (37 % isolated yield) and mixture DME/MeOH (47% isolated yield). The isolated yields are given after purification by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent.

¹H NMR (CDCl₃, 500 MHz) δ 10.17 (br s, 1H), 7.37 (ddd, 1H, J=7.2 Hz, J=21.3 Hz, J=35.7 Hz), 6.41 (t, 1H), 5.94 (d, 1H, J=8.1 Hz), 5.92 (d, 1H, J=10.1 Hz), 3.35 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 171.0, 151.1, 139.8, 128.6, 128.1, 126.9, 119.2, 78.13, 56.45; HRMS m/z calcd for C₁₁H₁₂O₃Na, 215.0684; found 215.0681.

2-Benzylsulfanyl-4-phenylbut-3-enoic acid (29, entry 9 Table 2)

The indicated compounds were initially obtained as a mixture of α - and γ -addition products. 2-Benzylsulfanyl-4-phenylbut-3-enoic acid was afforded as the major product (52 % isolated yield). The isolated yield is given after purification by silica gel flash chromatography using 8:2 hexane/EtOAc as eluent. ¹H NMR (CDCl₃, 500 MHz) δ 9.61 (br s, 1H), 7.37 (m, 5H), 6.53 (d, 1H, J=15.8 Hz), 6.27 (dd, 1H, J=9.0 Hz, J=15.8 Hz), 4.03 (d, 1H, J=9.0 Hz), 3.87 (q, 2H, J=13.4Hz); ¹³C NMR (CDCl₃, 125 MHz) δ 176.1, 137.0, 135.9, 134.3, 129.1, 128.6, 128.2, 127.3, 126.9, 126.6, 122.5, 48.8, 35.8; HRMS m/z calcd for C₁₇H₂₂O₂NaS, 307.0769; found 307.0778.

References.

1. Corey, E.J.; Link, J.O., Shao, Y. *Tetrahedron Lett.* **1992**, 33, 3435-3438.
2. Hon, Y.-S.; Chang, F.-J.; Lu, L.; Lin, W.-C. *Tetrahedron* **1998**, 54, 5233-5246.

18

23

37

Table 2
Entries 1 and 2

Table 2 Entry 3

Table 2 Entry 4

Table 2
Entries 6 and 7

Table 2
Entries 6 and 7

Table 2 Entry 9