Advanced
Synthesis &
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Supporting Information

Supporting information

(16 pages)

Practical Synthesis of (*E*)-a,ß-Unsaturated Carboxylic Acids Using a One-pot Hydroformylation/Decarboxylative Knoevenagel Reaction Sequence

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I General remarks

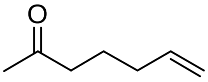
All reactions were carried out under argon 5.0 (Südwest-Gas) atmosphere in dried glassware. Air and moisture sensitive liquids and solutions were transferred *via* syringe. All solvents were dried and distilled by standard procedures. Solutions were concentrated under reduced pressure by rotary evaporation. Chromatographic purification of products was accomplished on Merck silica gel Si 60® (200-400 mesh).

Nuclear magnetic resonance spectra were acquired on a Varian Mercury spectrometer (300 MHz and 75 MHz for ^{1}H and ^{13}C respectively), on a Bruker AMX 400 (400 MHz and 101 MHz for ^{1}H and ^{13}C respectively) and were referenced according to internal TMS standard. Data for ^{1}H-NMR are reported as follows: chemical shift (*d* in ppm), multiplicity (s, singlet; bs, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constant (Hz), integration. Data for ^{13}C-NMR are reported in terms of chemical shift (*d* in ppm), multiplicity and coupling constant (Hz).

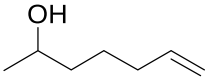
High-resolution mass spectra were obtained on a Finnigan MAT 8200 instrument. Elementary analysis was performed on an Elementar vario (Fa. Elementar Analysensysteme GmbH).

The following reagents were prepared according to literature reported procedures:

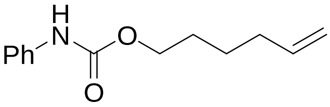
Hept-6-en-2-one[1]



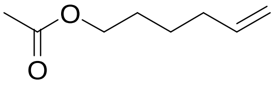
Hept-6-en-2-ol [2]



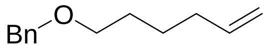
Phenylcarbamic acid hex-5-enyl ester [3]



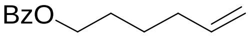
Acetic acid hex-5-enyl ester [4]



Hex-5-enyloxymethylbenzene [5]

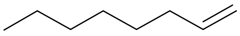


Benzoic acid hex-5-enyl-ester [6]

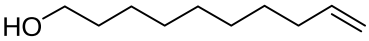


The following reagents were obtained commercially:

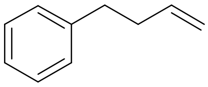
Oct-1-ene



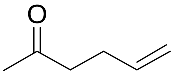
Dec-9-en-1-ol



But-3-enylbenzene



Hex-5-en-2-one



The following substrates were prepared as described below:

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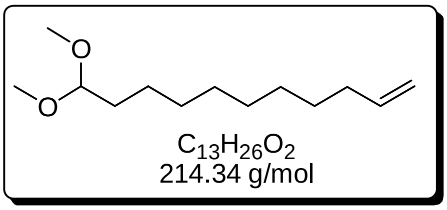
[1] D. J . Dixon, S. V. Ley, E. W. Tate, *J. Chem. Soc., Perkin Trans 1* **2000**, 15, 2385-2395.
[2] D. V. Gribkov, K. C. Hultzsch, F. Hampel, *J. Am. Chem. Soc.* **2006**, *128*, 3748-3759.
[3] B. Breit, W. Seiche, *J. Am. Chem. Soc.* **2003**, *125*, 6608-6611.
[4] H. C. Brown, G. C. Lynch, *J. Org. Chem.* **1981**, *46*, 531-538.
[5] P. Srihari, E. V. Bhasker, S. J. Harshavardhan, J. S. Yadav, *Synthesis* **2006**, *23*, 4041-4046.
[6] K. D. Schleicher, T. F. Jamison, *Org. Lett.* **2007,** *9*, 875-878.

II Synthesis of alkenic-starting materials

11,11-Dimethoxy-undec-1-ene



$C_{13}H_{26}O_2$
214.34 g/mol

To a solution of 2.00 g undec-8-enal (11.9 mmol, 1 eq) in MeOH (30 ml) 120 mg pyridinium-para-oluolsulfonate (0.48 mmol, 0.04 eq) was added. After 20 h stirring at room temperature the reaction mixture was diluted with CH_2Cl_2 (50 ml) and saturated aqueous Na_2CO_3-solution (2 × 50 ml) was added. The product was extracted two times with CH_2Cl_2 (50 ml) and dried over Na_2SO_4. The solvent was removed in vacuo to give 2.04 g (80%) of the acetal as a colourless liquid.

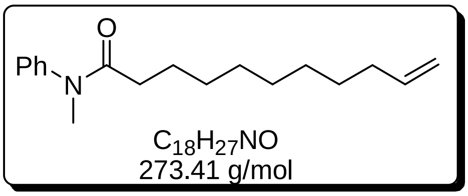
^{1}H-NMR (400.132 MHz, $CDCl_3$):

d = 1.25-1.38 (m, 12H), 1.56-1.61 (m, 2H), 2.00-2.06 (m, 2H), 3.30 (s, 6H), 4.35 (t, *J* = 5.7 Hz, 1H),4.91-5.01 (m, 2H), 5.75-5.85 (m, 1H).

^{13}C{^{1}H}-NMR (100.612 MHz, $CDCl_3$):

d = 24.7, 29.0, 29.2, 29.5, 29.5, 29.6, 32.6, 33.9, 52.7, 106.7, 114.2, 139.3.

Undec-10-enoic acid methylphenylamide



$C_{18}H_{27}NO$
273.41 g/mol

To a solution of 2.19 ml *N*-methylaniline (20.0 mmol, 1.0 eq), 4.05 ml undecyl-11-en-acid (20.0 mmol, 1 eq) and 1.69 g DMAP (22.0 mmol, 1.1 eq) in CH_2Cl_2 (20 ml) under argon 4.0 g DCC (20.0 mmol, 1.0 eq) was added at 0 °C. The reaction mixture was stirred for 24 h at room tempearture and then filtrated and washed with CH_2Cl_2. The solvent was removed in vacuo and the product was purified by chromatography (SiO_2, CH:EE = 6:1) to give 3.71 g (80%) of the amide as a light-yellow oil.

^{1}H-NMR (400.132 MHz, $CDCl_3$):

d = 1.17-1.21 (m, 8H), 1.29-1.34 (m, 2H), 1.53-1.57 (m, 2H), 1.97-2.04 (m, 4H), 3.52 (s, 3H), 4.89-4.99 (m. 2H), 5.73-5.84 (m, 1H), 7.60-7.17 (m, 2H), 7.31-7.34 (m, 1H), 7.38-7.42 (m, 2H).

^{13}C{^{1}H}-NMR (100.612 MHz, $CDCl_3$):

d = 25.6, 29.0, 29.1, 29.3, 29.3, 33.8, 34.1, 37.4, 77.3, 114.2, 127.4, 127.7, 129.8, 139.3, 144.4, 173.5.

MS ($C_{13}H_{26}O_2$, M = 273.2 g/mol)

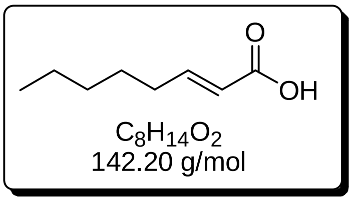
(EI, 70 eV)

273.2 (M^+, 10), 149.1 ($C_9H_{11}NO^+$, 29), 134.1 ($C_8H_8NO^+$, 4), 106.1 ($C_7H_8N^+$, 22), 77.0 ($C_6H_5^+$, 7), 55.0 ($C_4H_7^+$, 10).

III General procedure for the decarboxylative Knoevenagel reaction (base screening)

Malonic acid (1.0 eq), base 1 (2.0 eq) and base 2 (1 mol %) were added to olefin (1.0 eq) at 0 °C. Trimethoxybenzol was added as NMR-standard. The reaction mixture was warmed to room temperature and stirred for 24 h. Conversion and yield was determined by H-NMR-spectroscopy.

IV Synthesis of (*E*)-Oct-2-enoic acid by decarboxylative Knoevenagel reaction



5.2 g malonic acid (50.0 mmol, 1 eq) was dissolved in a mixture of 8.09 ml pyridine (100 mmol, 2 eq) and 41.4 µl pyrrolidine (0.5 mmol, 1 mol%). Then 7.11 g aldehyde (50.0 mmol, 1 eq) was added at 0°C under argon. The reaction mixture was stirred for 24 h at rt. At 0°C H_3PO_4 (20%, 60 ml) was added and the mixture was extracted with ethylacetate (3 × 50 ml) and dried over Na_2SO_4. The solvent was removed in vacuo and the product was purified by bulb-to-bulb distillation to give 6.3 g (89%) of the acid as a colorless liquid yield.

^{1}H-NMR (400.132 MHz, $CDCl_3$):

d = 0.87-0.91 (m, 3H), 1.28-1.35 (m, 4H), 1.43-1.51 (m, 2H), 2.19-2.25 (m, 2H), 5.80-5.84 (m, 1H),7.05-7.12 (m, 1H).

^{13}C{^{1}H}-NMR (100.612 MHz, $CDCl_3$):

d = 14.0, 22.5, 27.6, 31.4, 32.4, 120.7, 152.6, 172.5.

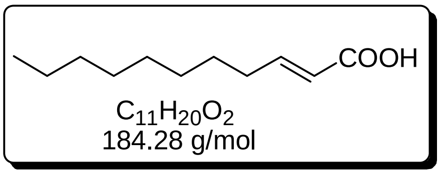
The spectroscopical data match with those reported in literature.[7]

V General procedure for the one-pot hydroformylation/ decarboxylative Knoevenagel reaction

Under an atmosphere of argon the olefin (5.00 mmol, 150 equiv.) was added to a solution of 6-DPPon (167 µmol, 5 equiv.) and [Rh(CO)$_2$acac] (33.0 µmol, 1 equiv.) in THF (5 ml, 1 M according to the olefin) at room temperature. The argon atmosphere was replaced by synthesis gas (balloon). The reaction mixture was stirred at room temperature and ambient pressure for 20 h.[8] Subsequently, synthesis gas was removed over 20 minutes by bubbling argon through the solution. The solution was cooled to 0 °C and malonic acid (5.00 mmol, 150 equiv.), pyridine (10.0 mmol, 300 equiv.) and pyrrolidine (24.0 µmol, 1.5 equiv.) were added. The reaction mixture was warmed to 10 °C and stirred for 20 h at this temperature, and additional 4 h at room temperature. The reaction was finished by the addition of aqueous H_3PO_4 (20%, 10 ml). After phase separation, the aqueous phase was extracted three times with ethylacetate and the combined organic phases were dried over $MgSO_4$. The solvent was removed in vacuum. The product was purified by chromatography (SiO_2, petroleum ether : diethyl ether : acetic acid = 100:25:1 to 100:100:2).

VI One-pot hydroformylation/Knoevenagel reaction to a,ß-unsaturated acids according to general procedure V

(*E*)-Undec-2-enoic acid



Purification via flash chromatography (SiO_2, petroleum ether:diethylether:acetic acid =100:20:1) furnished 710 mg (77%) of the acid as a colourless oil.

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[7] J. L. Brevet, K. Mori, *Synthesis* **1992**, 1007-1013.

[8] (a) W. Seiche, A. Schuschkowski, B. Breit, *Adv. Synth. Catal.* **2005**, *347*, 1488-1494; (b) W. Seiche, B. Breit, *J. Am. Chem. Soc.* **2003**, *125*, 6608-6611.

^{1}H-NMR (400.132 MHz, $CDCl_3$):

d = 0.88 (t, *J* = 7.0 Hz, 3H), 1.20-1.36 (m, 10H), 1.43-1.50 (m, 2H), 2.23 (tdd, *J* = 7.2, 7.2, 1.6 Hz, 2H), 5.82 (dt, *J* = 15.6, 1.6 Hz, 1H), 7.09 (dt, *J* = 15.6, 7.0 Hz, 1H), 11.9 (bs, 1H).

^{13}C{^{1}H}-NMR (100.626 MHz, $CDCl_3$):

d = 14.1, 22.7, 27.9, 29.2, 29.2, 29.4, 31.9, 32.3, 120.6, 152.5, 172.3.

MS ($C_{11}H_{20}O_2$, M = 184.15 g/mol)

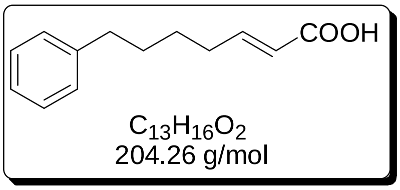
(CI, NH_4Cl, 130 eV)

202.1 ($(M+NH_4)^+$, 100).

CHN (%): calcd.: C: 71.20 H: 10.94

found: C: 71.53 H: 10.98

(*E*)-Phenylhept-2-enoic acid



Purification via flash chromatography (SiO_2, petroleum ether:diethylether:acetic acid =100:25:1) furnished 797 mg (78%) of the acid as a white crystalline solid.

^{1}H-NMR (400.132 MHz, $CDCl_3$):

d = 1.47-1.55 (m, 2H), 1.62-1.69 (m, 2H), 2.25 (tdd, *J* = 7.2, 7.2, 1.5 Hz, 2H), 2.62 (t, *J* = 7.6 Hz, 2H), 5.81 (dt, *J* = 15.7, 1.6 Hz, 1H), 7.07 (dt, *J* = 15.6, 7.0 Hz, 1H), 7.14-7.30 (m, 5H), 11.7 (bs, 1H).

^{13}C{^{1}H}-NMR (100.626 MHz, $CDCl_3$):

d = 27.5, 30.9, 32.2, 35.7, 120.8, 125.8, 128.3, 128.4, 142.1, 152.1, 172.2.

MS ($C_{13}H_{16}O_2$, M = 204.12 g/mol)

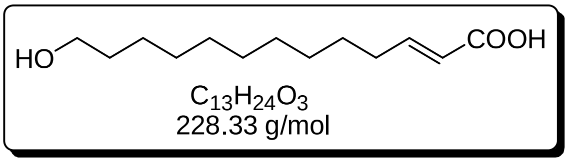
(CI, NH_4Cl, 130 eV)

222.1 ($(M+NH_4)^+$, 100).

CHN (%): calcd.: C: 76.44 H: 7.90

found: C: 76.40 H: 8.00

(*E*)-13-Hydroxy-tridec-2-enoic acid



Purification via flash chromatography (SiO_2, petroleum ether:diethylether:acetic acid =100:20:1) furnished 710 mg (77%) of the acid as a colourless oil.

^{1}H-NMR (400.132 MHz, $CDCl_3$):

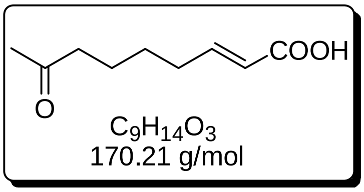
d = 1.23-1.39 (m, 12H), 1.41-1.51 (m, 2H), 1.52-1.61 (m, 2H), 2.22 (tdd, *J* = 7.2, 7.2, 1.5 Hz, 2H), 3.64 (t, *J* = 6.7 Hz, 2H), 5.82 (dt, *J* = 15.6, 1.5 Hz, 1H), 7.07 (dt, *J* =5.6, 7.0 Hz, 1H), 7.05 (bs, 2H).

^{13}C{^{1}H}-NMR (100.626 MHz, $CDCl_3$):

d = 25.7, 27.9, 29.1, 29.3, 29.4, 29.4, 29.5, 32.3, 32.6, 63.0, 120.7, 152.2, 171.6.

The spectroscopical data match with those reported in literature.[9]

(*E*)-8-Oxonon-2-enoic acid



Purifucation via flash chromatography (SiO_2, petroleum ether:diethylether:acetic acid =100:100:2) furnished 570 mg (67%) of the acid as a white crystalline solid.

^{1}H NMR (400.132 MHz, $CDCl_3$):

d = 1.43-1.53 (m, 2H), 1.56-1.67 (m, 2H), 2.15 (s, 3H), 2.22-2.28 (m, 2H), 2.46 (t, *J* = 7.4 Hz, 2H), 5.83 (dt, *J* = 15.6, 1.6 Hz, 1H), 7.06 (dt, *J* = 15.6, 6.9 Hz, 1H), 11.5 (bs, 1H).

^{13}C{^{1}H}-NMR (100.626 MHz, $CDCl_3$):

d = 23.2, 27.4, 30.0, 32.1, 43.3, 121.1, 151.6, 171.9, 208.8.

MS ($C_9H_{14}O_3$, M = 170.09 g/mol)

(CI, NH_4Cl, 130 eV)

171.1 ($(M+H)^+$,100), 188.1 ($(M+NH_4)^+$, 100).

CHN (%): calcd.: C: 63.51 H: 8.29

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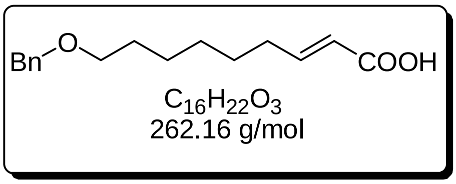
[9] M. Nagarajan, V. Satish Kumar , B. Venkateswara Rao, *Tetrahedron* **1999**, *55*, 12349-12360.

found: C: 63.17 H: 8.30

(*E*)-9-Benzyloxynon-2-enoic acid



Purification via flash chromatography (SiO_2, petroleum ether:diethylether:acetic acid =100:50:1) furnished 981 mg (75%) of the acid as a white crystalline solid.

^{1}H-NMR (400.132 MHz, $CDCl_3$):

d = 1.28-1.71 (m, 8 H), 2.20-2.26 (tdd, *J* = 7.1, 7.1, 1.5 Hz, 2H), 3.47 (t, *J* = 6.4 Hz, 2H), 5.51 (s, 2H, $PhCH_2$), 5.80-5.86 (dt, *J* = 15.6, 1.6 Hz, 1H), 7.04-7.11 (dt, *J* = 15.4, 7.1 Hz, 1H), 7.26-7.39 (m, 5H).

^{13}C{^{1}H}-NMR (100.612 MHz, $CDCl_3$):

d = 26.0, 27.9, 29.0, 29.7, 32.3, 70.4, 73.0, 120.7, 127.6, 127.7, 128.4, 138.7, 152.3, 171.8 (C-1).

MS ($C_{16}H_{22}O_3$, M = 262.16 g/mol)

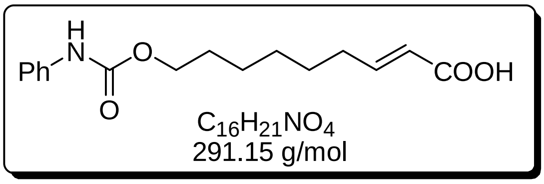
(EI, 70 eV)

262.2 (M^+, 7), 107.1 ($BnOH^+$, 30), 99.0 ($C_5H_7O_2^+$, 6), 91.1 (Bn^+100), 77.1 (Ph^+, 10), 55.1 (CH_7^+, 6).

CHN (%): calcd.: C 73.25 H 8.45

found: C 73.25 H 8.45

(*E*)-9-Phenylcarbamoyloxy-non-2-enoic acid



Purification via flash chromatography (SiO_2, petroleum ether:diethylether:acetic acid =100:100:2) furnished 911 mg (68%) of the acid as a white crystalline solid.

^{1}H-NMR (400.132 MHz, $CDCl_3$):

d = 1.36-1.71 (m, 8H), 2.22-2.27 (tdd, *J* = 7.1, 7.1, 1.4 Hz, 2H), 4.17 (t, *J* = 6.7 Hz, 2H), 5.81-5.86 (dt, *J* = 15.7, 1.5, Hz, 1H), 6.72 (bs, 1H), 7.04-7.11 (m, 2H), 7.28-7.39 (m, 4H).

^{13}C{^{1}H}-NMR (100.612 MHz, $CDCl_3$):

d = 25.7, 27.8, 28.8, 28.9, 32.2, 65.4, 118.8, 118.9, 120.8, 123.5, 129.1, 138.0, 152.2, 171.5.

MS ($C_{16}H_{21}NO_4$, M = 291.34 g/mol)

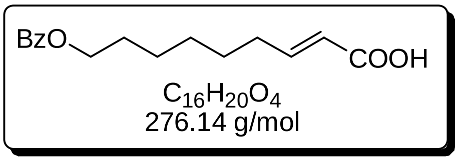
(EI, 130 eV)

291.3 (M^+, 49), 137.1 ($C_7H_7NO_2^+$, 30), 119.1 ($C_7H_5NO^+$, 78), 93.1 ($C_6H_7N^+$, 100).

CHN (%): calcd.: C 65.96 H 7.42 N 4.70

found: C 65.92 H 7.27 N 4.81

Benzoic acid (*E*)-8-carboxy-oct-7-enyl ester



Purification via flash chromatography (SiO_2, petroleum ether:diethylether:acetic acid =100:100:2) furnished 953 mg (69%) of the acid as a white crystalline solid.

^{1}H-NMR (400.132 MHz, $CDCl_3$):

d = 1.37-1.55 (m, 6 H), 1.74-1.81 (m, 2 H) 2.22-2.27 (tdd, *J* = 7.1, 7.1, 1.4 Hz, 2H), 4.31 (t, *J* = 5.7 Hz, 2H), 5.80-5.85 (dt, *J* = 15.7, 1.5, Hz, 1H), 7.04-7.11 (td, *J* = 15.4, 7.1 Hz, 1H), 7.42-7.46 (m, 2H), 7.53-7.57 (m, 1H), 8.02-8.06 (m, 1H).

^{13}C{^{1}H}-NMR (100.612 MHz, $CDCl_3$):

d = 25.9, 27.6, 28.7, 28.9, 32.3, 65.0, 120.7, 128.4, 129.6, 130.5, 132.9, 152.1, 166.8, 171.4.

MS ($C_{16}H_{20}O_4$, M = 276.33 g/mol)

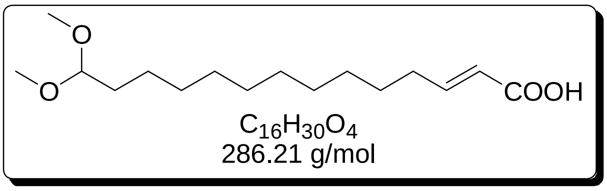
(CI, NH_4Cl, 130 eV)

294.2 ($(M + NH_4)^+$, 100), 277.2 ($(M\text{-}OH, +NH_4)^+$, 85), 276.2 (M^+, 33), 105 (Bz^+, 15).

CHN (%): calcd.: C 69.54 H 7.30

found: C 69.54 H 7.56

(*E*)-14,14-Dimethoxy-tetradec-2-enoic acid



Purification via flash chromatography (SiO_2, petroleum ether:diethylether:acetic acid =100:50:1) furnished 1.03 g (72%) of the acid as a white crystalline solid.

^{1}**H-NMR** (400.132 MHz, $CDCl_3$):

d = 1.25-1.36 (m, 14 H), 1.42-1.48 (m, 2H), 1.56-1.62 (m, 2H), 2.19-2.25 (tdd, *J* = 7.1, 7.1, 1.4 Hz, 2H), 3.31 (s, 6H), 4.36 (t, *J* = 5.7 Hz, 1H), 5.80-5.84 (dt, *J* = 15.7, 1.5, Hz, 1H), 7.04-7.11 (td, *J* = 15.4, 7.1 Hz, 1H).

^{13}**C{^{1}H}-NMR** (100.612 MHz, $CDCl_3$):

d = 20.8, 24.7, 27.9, 29.2, 29.4, 29.4, 29.5, 29.5, 29.5, 29.6, 29.6, 32.4, 32.6, 52.6, 77.3, 104.7, 120.6, 152.5, 171.6.

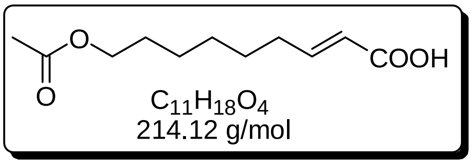
MS ($C_{16}H_{30}O_4$, M = 286.41 g/mol)

(CI, NH_4Cl, 130 eV)

304.3 ($(M + NH_4)^+$, 3), 240.2 ($C_4H_{24}O_3^+$, 100), 71.0 ($C_3H_3O_2^+$, 3), 75.0 ($C_2H_5NO_2^+$, 48).

CHN (%): calcd.: C 67.10 H 10.56
found: C 67.32 H 10.69

(*E*)-9-Acetoxy-non-2-enoic acid



Purification via flash chromatography (SiO_2, petroleum ether:diethylether:acetic acid =100:50:1) furnished 578 mg (71%) of the acid as a colourless oil.

^{1}**H-NMR** (400.132 MHz, $CDCl_3$):

d = 1.34-1.37 (m, 4 H), 1.42-1.52 (m, 2 H), 1.59-1.66 (m, 2 H), 2.21-2.26 (tdd, *J* = 7.1, 7.1, 1.4 Hz, 2H), 2.84 (s, 3H), 4.05 (t, *J* = 6.7 Hz, 2H), 5.80-5.85 (dt, *J* = 15.7, 1.5 Hz, 1H), 7.03-7.10 (td, *J* = 15.4, 7.1 Hz, 1H).

^{13}**C{^{1}H}-NMR** (100.612 MHz, $CDCl_3$):

d = 21.1, 25.8, 27.8, 28.6, 28.8, 32.3, 64.6, 120.8, 152.1, 171.4, 171.5.

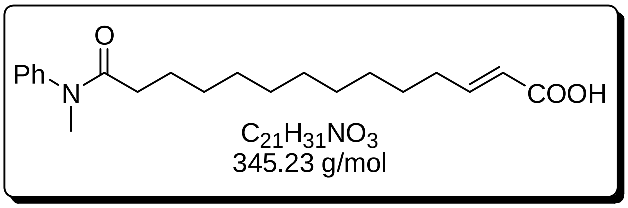
MS ($C_{11}H_{18}O_4$, M = 212.12 g/mol)

(CI, NH_4Cl, 130 eV)

232.2 ($(M + NH_4)^+$, 100), 214.2 (M^+, 47).

HR-MS: calcd.: 196.110005 ($M-H_2O$)
found: 196.109945 ($M- H_2O$)

(*E*)-13-(Methylphenylcarbamoyl)-tridec-2-enoic acid



Purification via flash chromatography (SiO_2, petroleum ether:diethylether:acetic acid =100:100:2) furnished 1.34 g (77%) of the acid as a light yellow oil.

^{1}H-NMR (400.132 MHz, $CDCl_3$):

d = 1.15-1.37 (m, 4H), 1.41-1.48 (m, 2H), 1.52-1.54 (m, 2H), 2.04-2.10 (m, 2H), 2.18-2.26 (m, 2H), 3.26 (s, 3H), 5.79-5.83 (dt, *J* = 15.7, 1.5 Hz, 1H), 7.03-7.10 (td, *J* = 15.4, 7.1 Hz, 1H). 7.15- 7.18 (m, 2H), 7.31-7.43 (m, 3H).

^{13}C{^{1}H}-NMR (100.612 MHz, $CDCl_3$):

d = 25.7, 27.9, 29.1, 29.3, 29.3, 29.4, 29.4, 32.4, 34.1, 37.6, 39.9, 120.6, 127.3, 127.9, 129.8, 144.2, 152.5, 171.6, 174.0.

MS ($C_{21}H_{31}NO_3$, M = 345.23 g/mol)

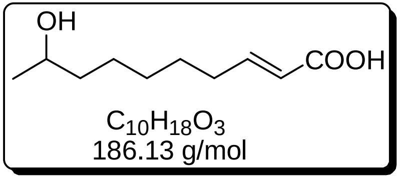
(CI, NH_4Cl, 130 eV)

346.3 ($(M + H)^+$, 100), 345.3 (M^+, 6), 149 ($(C_9H_{10}NO)^+$, 7), 107 ($(PhNMe)^+$, 8).

HR-MS: calcd.: 345.230197 (M)
found: 345.230394 (M)

VII Synthesis of pheromones 9-HDA und 9-ODA

(*E*)-9-hydroxydecenoic acid (9-HDA)



The scale of general method **V** was halved. Purification via flash chromatography (SiO_2, petroleum ether:diethylether:acetic acid =100:100:2) furnished 335 mg (72%) of the acid as a colourless oil.

^{1}H-NMR (400.132 MHz, $CDCl_3$):

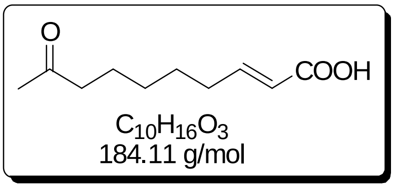
d = 1.19 (d, *J* = 6.1 Hz, 3H), 1.31-1.52 (m, 8H), 2.20-2.26 (tdd, J = 7.0, 7.0, 1.7 Hz, 2H), 3.77-3.84 (m, 1H), 5.80-5.85 (dt, *J* = 15.7, 1.6 Hz, 1H), 7.03-7.10 (td, *J* = 15.7, 6.9 Hz, 1H).

^{13}C{^{1}H}-NMR (100.612 MHz, $CDCl_3$):

d = 23.6, 25.6, 27.9, 29.2, 32.3, 39.1, 68.3, 120.7, 152.3, 171.1.

The spectroscopical data match with those reported in literature.[10]

(2*E*)-9-oxodecenoic acid (9-ODA)



The scale of general method **V** was halved. Purification via flash chromatography (SiO_2, petroleum ether:diethylether:acetic acid =100:100:2) furnished 331 mg (72%) of the acid as a white crystalline solidl.

^{1}H-NMR (400.132 MHz, $CDCl_3$):

d = 1.28-1.62 (m, 6H), 2.13 (s, 3H), 2.26-2.29 (tdd, *J* = 7.1, 7.1, 1.6 Hz, 2H), 2.43 (t, *J* = 7.3Hz, 2H), 5.80-5.84 (dt, *J* = 15.7, 1.6 Hz, 1H), 7.02-7.09 (td, *J* = 15.7, 6.9 Hz, 1H).

^{13}C{^{1}H}-NMR (100.612 MHz, $CDCl_3$):

d = 23.5, 27.7, 28.7, 30.0, 32.2, 43.6, 120.8, 152.1, 171.7, 209.2.

The spectroscopical data match with those reported in literature.[11]

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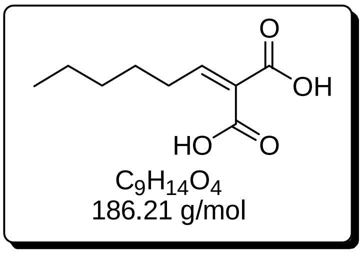
[10] A. S. Pawar, S. S. Chattopadhyay, S. Chattopadhyay , *Tetrahedron* **1995**, *6*, 2219-2226.

[11] R. Y. Kharisov, O. V. Botsman, L. P. Botsman, N. M. Ishmuratova, G. Y. Ishmuratov, G. A. Tolstikov, *Chemistry of Natural Compounds* **2002**, *38*, 145-148.

VIII Procedure for step-by-step Knoevenagel-Doebner reaction to Hexylidene-malonic acid and (*E*)-Undec-2-enoic acid. Kinetic Study

VIIIa Procedure for step-by-step Knoevenagel-Doebner reaction to Hexylidene-malonic acid and (*E*)-Undec-2-enoic acid

Hexylidenemalonic acid



1.04 g malonic acid (10.0 mmol, 1.0 eq) and 8 µl pyrrolidine (0.10 mmol, 1 mol %) were added to 1.22 ml capronaldehyde (10.0 mmol, 1.0 eq) in 10 ml THF at 0 °C. The reaction mixture was warmed to 10 °C and stirred for 20 h at this temperature, and additional 4 h at room temperature. The solvent was removed in vacuo and Et_2O (10 ml) and H_2O (10 ml) were added. After extraction with Et_2O (3 × 10 ml) and drying over Na_2SO_4 the solvent was removed in vacuo (the solvent could not totally be removed in vacuo) to give 1.60 g (86%) of the diacid as a white crystalline solid.

^{1}H-NMR (400.132 MHz, $CDCl_3$):

d = 0.83-0.94 (m, 3H), 1.29-1.39 (m, 4H), 1.53-1.59 (m, 2H), 2.82 (dd, *J* = 15.0, 7.5 Hz, 2H), 7.87 (t, J = 7.5 Hz, 1H), 8.69 (bs, 2H, OH).

^{13}C{^{1}H}-NMR (100.612 MHz, $CDCl_3$):

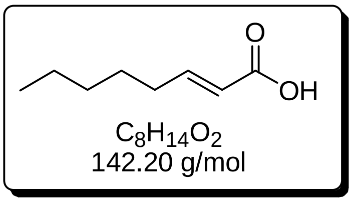
d = 14.9, 22.4, 28.1, 31.3, 31.6, 100.2, 121.1, 166.8, 196.4.

MS ($C_9H_{14}O_4$, M = 186.21 g/mol)

(CI, NH_4Cl, 130 eV)

187.2 ($(M+H)^+$,10), 186.1 (M^+,100), 158.1($(M+NH_3\text{-}COOH)^+$, 25).

(*E*)-Oct-2-enoic acid



150 µl pyridine (1.84 mmol, 2.0 eq) were added to 171 mg hexylidenemalonic acid (0,92 mmol, 1.0 eq) at 0 °C. The reaction mixture was warmed to room temperature and stirred for further 24 h. The reaction was finished by the addition of aqueous H_3PO_4 (20%, 10 ml). After phase separation, the organic phase was washed three times with ethylacetate and dried ($MgSO_4$). The solvent was removed in vacuo and the crude product was purified by kugelrohr distillation to give 112 mg (79%) of the acid as a colourless oil..

^{1}H-NMR (400.132 MHz, $CDCl_3$):

d = 0.87-0.91 (m, 3H), 1.28-1.35 (m, 4H), 1.43-1.51 (m, 2H), 2.19-2.25 (m, 2H), 5.80-5.84 (m, 1H),7.05-7.12 (m, 1H).

^{13}C{^{1}H}-NMR (100.612 MHz, $CDCl_3$):

d = 14.0, 22.5, 27.6, 31.4, 32.4, 120.7, 152.6, 172.5.

The spectroscopical data match with those reported in literature.[12]

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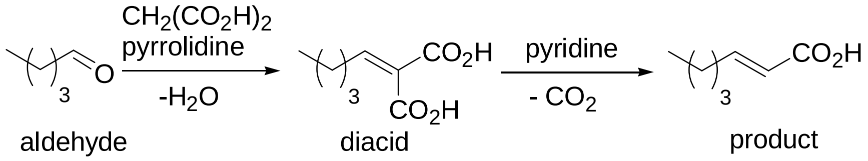
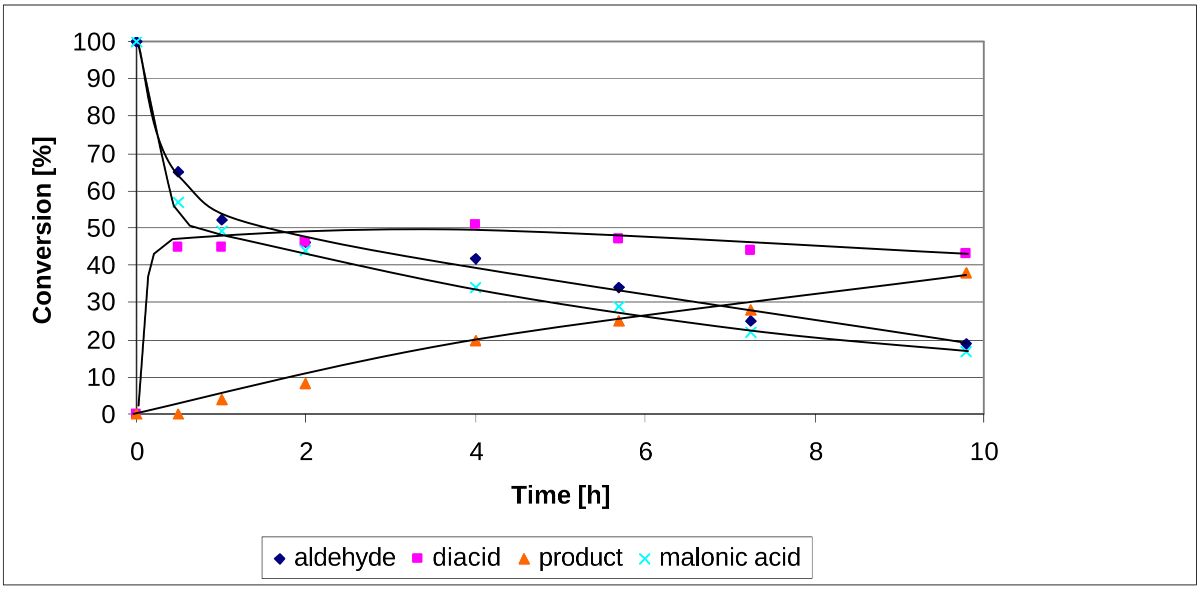
[12] J. L. Brevet, K. Mori, *Synthesis* **1992**, 1007-1013.

VIIIb Kinetic Study





The general method **V** was used at 10 °C. Trimethoxybenzene (1.66 mmol, 0.33 eq) was added as NMR standard and the conversion was determined by ^{1}H-NMR.