

Ruthenium-alkylidene Catalysed Cross-Metathesis of Fatty Acid Derivatives with Acrylonitrile and Methyl Acrylate: a Key Step Toward Long-Chain Bifunctional and Aminoacid Compounds

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Supplementary informations

General remarks : All the reactions were conducted under an inert atmosphere of argon using standard Schlenck tube techniques. Solvent were dried by distillation prior to use. CH_2Cl_2 , was dried over CaH_2 , toluene over Na. Methyl 10-undecenoate **1** was provided by Arkema and distilled prior to use. Dimethyl octadec-9-en-1,18-dioate **5** was prepared by standard $\text{MeOH}/\text{H}_2\text{SO}_4$ esterification of the diacid furnished by Arkema. Methyl ricinoleate **9** was prepared from castor oil (Alfa Aesar) according to a reported procedure. Acrylonitrile, purchased from Acros Organics, was distilled, stored over 4Å molecular sieves and degassed by Argon bubbling. Methyl acrylate was purchased from Acros Organics and directly stored (without distillation to avoid rapid polymerisation) over 4Å molecular sieves and degassed by argon bubbling. Catalysts **A**, **B** and **C** were purchased from Sigma-Aldrich and stored under argon. Catalysts **D-H** were purchased from Umicore company. The reactions were monitored using a Shimadzu 2014 gas chromatograph fitted with an Equity-1 capillary column (0.25µm x 30m). NMR spectra were recorded on a Bruker Avance 200 MHz spectrometer and a Bruker Avance 300 MHz spectrometer.

Data for prepared dimethyl octadec-9-en-1,18-dioate **5**

^1H NMR (200 MHz, CDCl_3) δ ppm:

1.31 (broad s, 16H, CH_2); 1.56-1.70 (broad t, 4H, CH_2); 2.00 (broad d, 4H, CH_2); 2.32 (t, 4 H, 2 $\text{CH}_2\text{CO}_2\text{CH}_3$); 3.68 (s, 6H, CO_2CH_3); 5.3-5.38 (m, 2H, $\text{CH}=\text{CH}$).

^{13}C NMR (75.5 MHz, CDCl_3) δ ppm:

24.9, 27.2, 29.1, 29.1, 29.1, 29.7, 34.1, 51.4 (OCH_3), 129.8 (CH), 174.3 (CO).

Elemental Analysis: $\text{C}_{20}\text{H}_{36}\text{O}_4$ th.: C 70.55, H 10.66, measured: C 70.57, H 10.68.

HRMS: $[\text{M}+\text{Na}]^+$ ($\text{C}_{20}\text{H}_{36}\text{O}_4\text{Na}$) m/z th.: 363.25113, measured: 363.2509

Data for the prepared methyl ricinoleate **9**

¹H NMR (200.12 MHz, CDCl₃) δ ppm:

0.87-0.94 (broad t, 3H, CH₂CH₃); 1.32-1.68 (m, 20H, CH₂); 2.00-2.36 (m, 6H, CH₂CHOH + COCH₂ + CH₂CH=CH); 3.60-3.69 (m, 4H, CHOH + OCH₃); 5.36-5.65 (m, 2H, CH=CH).

¹³C NMR (75.5 MHz, CDCl₃) δ ppm:

14.1, 22.6, 24.9, 25.7, 27.4, 29.1, 29.1, 29.4, 29.6, 31.8, 34.1, 35.4, 36.9, 51.4 (OCH₃), 71.5 (CHOH), 125.2 (CH), 133.3 (CH), 174.3 (CO).

HRMS: [M+Na]⁺ (C₁₉H₃₆O₃Na) m/z Calculated: 335.25622, found: 335.2555

General procedure for the single dose addition.

Synthesis of **2**

In a Schlenk tube under argon, 99 mg (0.5 mmol) of **1** and 53 mg of acrylonitrile (1 mmol, 2 equiv.) were dissolved in 10 mL of distilled toluene, Hoveyda II catalyst **A** (0.005 mmol, 3.1 mg, 1 mol%) and dodecane (10 μl) were then added and the reaction mixture was stirred at 80 °C for 2 h. Purification by column chromatography on silica gel (1.5 cm x 12 cm) using a mixture of petroleum ether/diethyl ether (8/2) as eluent furnished 102.5 mg of **2** obtained as a colorless oil (92% isolated yield). The key reactions leading to the highest TONs were double checked and resulted in high repeatability (± 3%). The best result is provided.

General procedure for the syringe-pump Addition of Catalyst (0.05 mol%): In a Schlenk tube under argon, 99 mg (0.5 mmol) of **1** and 53 mg of acrylonitrile (1 mmol, 2 equiv.) were dissolved in 8 mL of distilled toluene (with 10 μl of dodecane as internal standard). In another Schlenk tube under argon, Hoveyda II catalyst **A** (0.0025 mmol, 1.57 mg) was dissolved in 20 mL of distilled toluene. 2 mL of this catalyst solution was taken in a degassed syringe and slowly added through a new rubber septum over a period of 2h40 into the Schlenk tube containing **1** and acrylonitrile stirred at 100 °C (see picture below). After completion of the addition of catalyst, the reaction mixture was left stirring for another 2 h 20 min. Purification by column chromatography on silica gel (1.5 cm x 12 cm) using a mixture of petroleum ether/diethyl ether (8/2) as eluent furnished 100.2 mg of **2** obtained as a colorless oil (90% isolated yield).



Syringe pump addition setup

Characterisation data for methyl 11-cyanoundec-10-enoate **2**

¹H NMR (300.13 MHz, CDCl₃) δ ppm:

1.30-1.64 (m, 12H, CH₂); 2.17-2.45 (m, 4H, COCH₂ + CH=CHCH₂); 3.66 (s, 3H, OCH₃); 5.29-5.35 (m, 1H, CH=CHCN, *Z* + *E*); 6.48 (dt, 0.78H, ³*J* = 10.9 Hz, ³*J* = 7.7, CH=CHCN, *Z*); 6.71 (dt, 0.22H, ³*J* = 16.3 Hz, ³*J* = 7.0 Hz, CH=CHCN, *E*).

¹³C NMR (75.5 MHz, CDCl₃) δ ppm:

24.9, 27.6, 28.2, 28.8, 28.9, 29.0, 29.0, 31.8, 33.2, 34.0, 51.4 (OCH₃), 99.5 (CH, *Z*), 99.7 (CH, *E*), 116.0 (CN, *Z*), 116.4 (CN, *E*), 155.2 (CH, *Z*), 156.1 (CH, *E*), 174.2 (CO).

Elemental Analysis: C₁₃H₂₁NO₂, th: C 69.92, H 9.48, N 6.27, measured C: 69.55 H: 9.48; N 6.20

HRMS: [M+Na]⁺ (C₁₃H₂₁NO₂Na) *m/z* th: 246.1470, measured 246.1471

Characterisation data for dimethyl dodec-2-enedioate **4 (*E* isomer)**

¹H NMR (200.12 MHz, CDCl₃) δ ppm:

1.31-1.50 (m, 10H, 5 CH₂); 1.57-1.68 (m, 2H, COCH₂CH₂); 2.16-2.36 (m, 4H, COCH₂CH₂ + CH=CHCH₂); 3.69 (s, 3H, OCH₃); 3.75 (s, 3H, OCH₃); 5.83 (d, 1 H, ³*J*_{HH} = 15.6 Hz, CH=CHCH₂); 6.91-7.06 (dt, 1H, ³*J*_{HH} = 15.6 Hz, ³*J*_{HH} = 6.9 Hz, CH=CHCH₂).

¹³C NMR (50.3 MHz, CDCl₃) δ ppm:

25.3, 28.4, 29.5, 29.5, 29.8, 29.6, 32.6, 34.5, 51.9 (OCH₃), 52.0 (OCH₃), 121.2 (CH), 150.3 (CH), 167.7 (CO), 174.8 (CO).

Elemental Analysis: C₁₄H₂₄O₄ th: C 65.60, H 9.44, measured C 65.63, H: 9.54.

Characterisation data for dimethyl dodec-2-enedioate 4 (*Z* isomer)

¹H NMR (200.12 MHz, CDCl₃) δ ppm:

1.25-1.70 (m, 12H, CH₂); 2.28-2.36 (t, 2H, ³J_{HH} = 7.4 Hz, COCH₂CH₂); 2.60-2.72 (m, 2H, CH=CHCH₂); 3.68 (s, 3 H, OCH₃); 3.73 (s, 3 H, OCH₃); 5.78 (d, 1 H, ³J_{HH} = 11.5 Hz, CH=CHCH₂); 6.17-6.31 (m, 1H, ³J_{HH} = 11.5 Hz, CH=CHCH₂).

Elemental Analysis: C₁₄H₂₄O₄ th: C 65.60, H 9.44, measured: C 65.89, H 9.65.

Characterisation data for methyl 10-cyanoundec-10-enoate 6

¹H NMR (300.13 MHz, CDCl₃) δ ppm:

1.26-1.57 (m, 10H, CH₂); 2.12-2.38 (m, 4H, COCH₂ + CH=CHCH₂); 3.59 (s, 3H, OCH₃); 5.24-5.30 (m, 1H, CH=CHCN, *Z* + *E*); 6.43 (dt, 0.8H, ³J_{HH} = 10.9 Hz, ³J_{HH} = 7.7 Hz, CH=CHCN, *Z*); 6.65 (dt, 0.2H, ³J_{HH} = 16.4 Hz, ³J_{HH} = 7.0 Hz, CH=CHCN, *E*).

¹³C NMR (75.5 MHz, CDCl₃) δ ppm:

24.7, 27.4, 28.0, 28.7, 28.7, 28.8, 28.8, 31.7, 33.2, 33.9, 51.3 (OCH₃), 99.5 (CH, *Z*), 99.6 (CH, *E*), 116.0 (CN, *Z*), 117.5 (CN, *E*), 155.0 (CH, *Z*), 156.0 (CH, *E*), 174.0 (CO).

HRMS: [M+Na]⁺ (C₁₂H₁₉NO₂Na) m/z th: 232.1314, measured: 232.1313

Characterisation data for dimethyl undec-2-enedioate 7 (*E* isomer)

¹H NMR (200.12 MHz, CDCl₃) δ ppm:

1.27-1.50 (m, 8H, CH₂); 1.60-1.70 (m, 2H, COCH₂CH₂); 2.15-2.36 (m, 4H, COCH₂CH₂ + CH=CHCH₂); 3.68 (s, 3H, OCH₃); 3.74 (s, 3H, OCH₃); 5.78-5.88 (dt, 1 H, ³J_{HH} = 15.6 Hz, ³J_{HH} = 1.6, CH=CHCH₂); 6.90-7.05 (dt, 1H, ³J_{HH} = 15.6 Hz, ³J_{HH} = 7.0 Hz, CH=CHCH₂).

¹³C NMR (50.3 MHz, CDCl₃) δ ppm:

25.3, 28.3, 29.3, 29.4, 32.6, 34.5, 51.8 (OCH₃), 51.9 (OCH₃), 121.3 (CH), 150.1 (CH), 167.6 (CO), 174.7 (CO).

Elemental Analysis: C₁₃H₂₂O₄ th: C 64.44, H 9.15, measured: C 64.67, H 9.26.

Characterisation data for 5-hydroxyundec-2-enenitrile 10

¹H NMR (300.13 MHz, CDCl₃) δ ppm:

0.87 (broad t, 3H, CH₃); 1.27-1.47 (m, 10H, CH₂); 2.18 (s, 1H, OH); 2.25-2.66 (m, 2H, CH₂CH=CHCN); 3.73-3.77 (m, 1 H, CHOH); 5.41 (d, 1H, ³J_{HH} = 11.1 Hz, CH=CHCN); 6.64 (dt, 0.78 H, ³J_{HH} = 11.0 Hz, ³J_{HH} = 7.6 Hz, CH=CHCN, *Z*); 6.78 (dt, 0.22H, ³J_{HH} = 16.4 Hz, ³J_{HH} = 7.4 Hz, CH=CHCN, *E*).

^{13}C NMR (75.5 MHz, CDCl_3) δ ppm:

14.0, 22.5, 25.5, 29.1, 31.7, 37.2, 37.2, 39.5, 41.0, 70.1 (CHOH, *E*), 70.5 (CHOH, *Z*), 101.1 (CH, *Z*), 101.7 (CH, *E*), 116.1 (CN, *Z*), 117.3 (CN, *E*), 152.0 (CH, *Z*), 152.9 (CH, *E*).

HRMS: $[\text{M}+\text{Na}]^+$ ($\text{C}_{11}\text{H}_{19}\text{NONa}$) m/z th: 204.1364, measured: 204.1366

Characterisation data for methyl 5-hydroxyundec-2-enoate 11 (*E* isomer)

^1H NMR (200.12 MHz, CDCl_3) δ ppm:

0.86 (broad t, 3H, CH_3); 1.26-1.46 (m, 10H, CH_2); 2.19 (s, 1H, OH); 2.30-2.39 (m, 2 H, $\text{CH}_2\text{CH}=\text{CH}$); 3.71 (s, 4H, OCH_3 + CHOH); 5.89 (d, 1H, $^3J_{\text{HH}} = 15.6$ Hz, $\text{CH}_2\text{CH}=\text{CH}$); 6.91-7.06 (m, 1H, $\text{CH}_2\text{CH}=\text{CH}$).

^{13}C NMR (50.3 MHz, CDCl_3) δ ppm:

14.4, 23.0, 25.9, 29.6, 32.2, 37.5, 40.6, 51.9 (OCH_3), 70.9 (CHOH), 123.6 (CH), 146.3 (CH), 167.3 (CO).

HRMS: $[\text{M}+\text{Na}]^+$ ($\text{C}_{11}\text{H}_{22}\text{O}_3\text{Na}$) m/z th: 237.1466, measured: 237.1468