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Supplementary Materials for

Schrock Molybdenum Alkylidene Catalyst Enables Selective Formation of Macrocyclic Unsaturated Lactones by Ring-Closing Metathesis at High-Concentration

Adrian Sytniczuk, Mariusz Milewski, Michał Dąbrowski, Karol Grela,* and Anna Kajetanowicz*

prof.grela@gmail.com, a.kajetanowicz@uw.edu.pl

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Materials and Methods

General

All glassware was dried overnight in oven (135 °C). Joints were greased with Apiezon L, except for a Hickman adapter and flask containing reaction mixture, where Apiezon H was used. During the reaction, the Hickman adapter was cooled using dry ice. For High-Concentration Ring-Closing Metathesis reactions (**HC-RCM**) the following vacuum pumps were used (as noted in descriptions of reaction procedures):

- Rotary Vane Pump (**RVP**): Vacuumbrand RZ 6 (maximum nominal vacuum of 1×10^{-3} mBar)
- Oil Diffusion Pump (**ODP**): Vacuumbrand High-Vacuum Pumping Unit HP 40 B2/RZ 6 (maximum *nominal* vacuum of 1×10^{-6} mBar)

Analytical thin-layer chromatography (**TLC**) was performed using silica gel 60 F254 precoated plates (0.25 mm thickness, Merck) with a fluorescent indicator. Visualization of TLC plates was performed by $KMnO_4$ aqueous solution and anisaldehyde/H_2SO_4 stain. Flash column chromatography was performed using Merck silica gel 60 (230–400 mesh) with *n*-hexane/ethyl acetate eluent system, unless stated otherwise.

GC analyses were performed by means of PerkinElmer Clarus 580 chromatograph with FID detector and GL Sciences InertCap 5MS/Sil Capillary Column (Inner Diameter 0.25 mm, Length 30 m, df 0.50 μm). **GC-MS** analyses were performed by means of PerkinElmer Clarus 680 chromatograph with Mass Spectrometer Clarus SQ 8C detector and GL Sciences InertCap 5MS/Sil Capillary Column (Inner Diameter 0.25 mm, Length 30 m, df 0.50 μm). **NMR** spectra were recorded on an Agilent 400-MR DD2 400 MHz spectrometer. NMR chemical shifts are reported in ppm with $CDCl_3$ residual peak as a reference: 7.26 for ^1H and 77.16 ppm for ^{13}C. The following abbreviations are used in reporting NMR data: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet). ^1H NMR signals are given followed by multiplicity, coupling constants *J* in Hertz, and integration in parentheses. Deuterated $CDCl_3$ was purchased from Sigma-Aldrich, stored over molecular sieves, and used without further purification. Infrared (**IR**) spectra were recorded on a Perkin-Elmer Spectrum One FTIR spectrometer with diamond ATR accessory, wave numbers are in cm^{-1}. Elemental Analyses (**EA**) were provided by the EA analytical laboratory at the Institute of Organic Chemistry, Polish Academy of Sciences (PAS). High Resolution Mass Spectra (**HR-MS**) were provided by the Faculty of Chemistry University of Warsaw or analytical laboratory at the Institute of Organic Chemistry, PAS. Matrix-assisted laser desorption/ionization (**MALDI**) was provided by the Centre of Molecular and Macromolecular Studies, PAS.

Solvents and diluents

Toluene (**PhMe**) was purified using mBraun's SPS (solvent purification system), the water content was measured with the Karl-Fisher apparatus (Titroline® 7500 KF trace) and did not exceed 2 ppm in both cases. Pyridine (anhydrous) was purchased from Sigma-Aldrich and used as received. *N*-Hexane and ethyl acetate (**EtOAc**) for column chromatography were purchased from Avantor Performance Materials Poland S.A. and distilled prior to use. PAO 6 (Synfluid® PAO 6 cSt) was purchased from Chevron Phillips Chemical Company LP and purified by heating under vacuum at 160 °C overnight followed by filtration through activated neutral alumina and stored under an argon atmosphere.

Reagents

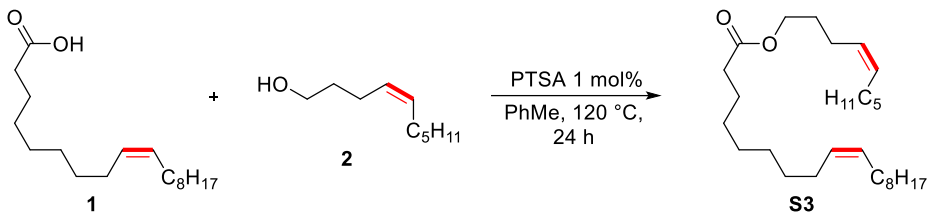
Unless otherwise noted, all common laboratory reagents (Na_2SO_4, $NaHCO_3$) were purchased from Avantor Performance Materials Poland S.A. and used as received. Aluminium oxide (Neutral, Brockmann grade I) was purchased from Sigma Aldrich and activated by heating for at least 3 days at 200 °C prior to use.
Oleic acid, *(Z)*-5-octen-1-ol, *(Z)*-3-hexen-1-ol, *(Z)*-4-decen-1-ol were purchased from Sigma Aldrich and used as received. Hept-6-en-1-ol was purchased from TCI Chemicals and used as received.
The following dienes were synthesized according to literature procedures and stored over activated, neutral Al_2O_3 prior use: *(Z)*-non-6-en-1-yl oleate (**S1a**),[1] *(Z)*-non-6-en-1-yl dec-9-enoate (**S1b**),[1] hept-6-en-1-yl dec-9-enoate (**S1c**),[1] octacosa-6,22-diene (**S2**),[1] hex-5-en-1-yl dec-10-enoate (**S4b**),[2] hex-5-en-1-yl undec-10-enoate (**S5**),[3] tridec-12-en-2-yl pent-4-enoate (**S6**),[4, 5] hept–6–en–1–yl undec–10–enoate (**S7**),[1] oleyl oleate (**S9**),[6] oct-7-en-1-yl oleate (**S11**).[1]
Schrock's molybdenum catalyst (in paraffin pills or as a powder) was purchased from XiMo and used as received.

Preparation of substrates

General procedure for synthesis of esters - Method A

In a round bottom flask equipped with magnetic stirring element oleic acid (1.20 equiv.), alcohol (1.00 equiv.), and *p*-toluenesulfonic acid (PTSA) (0.01 equiv.) were dissolved in toluene (0.85 M). After assembling the Dean-Stark apparatus, the reaction mixture was carried out at reflux for 24 h. TLC was used to control the progress of the reaction (10% EtOAc in *n*-hexane). The flask was cooled to room temperature (RT) and the reaction mixture was transferred to a separation funnel, washed with $NaHCO_3$ (2×10 mL), brine (10 mL), and finally dried over Na_2SO_4. The solids were filtered off, and the solvent was evaporated in *vacuo*. The resulting oily residue was purified by flash column chromatography (1% EtOAc in *n*-hexane) to obtain the final product as a colourless liquid.

Synthesis of *(Z)*-dec-4-en-1-yl oleate (S3)

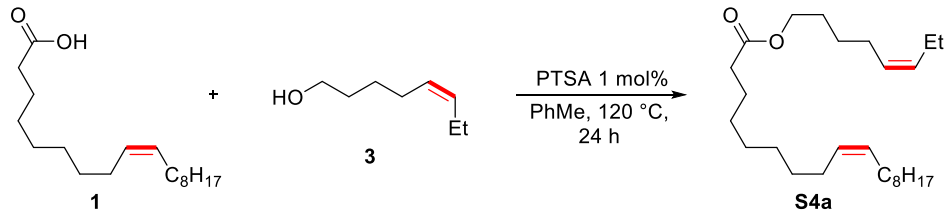


Scheme 1. Synthesis of *(Z)*-dec-4-en-1-yl oleate (**S3**).

Ester **S3** was prepared according to the ***method A***: oleic acid (**1**) (4.4 g, 5.0 mL, 14.1 mmol), *(Z)*-dec-4-en-1-ol (**2**) (2.7 g, 3.2 mL, 16.9 mmol), and PTSA (24 mg 0.14 mmol, 1 mol%) were used to afford diene **S3** as a colourless oil (5.5 g, 13.1 mmol, yield 83%).

^{1}H NMR (400 MHz, Chloroform–*d*): δ 5.48 – 5.28 (m, 4H), 4.06 (t, *J* = 6.6 Hz, 2H), 2.29 (t, *J* = 7.6 Hz, 2H), 2.14 – 1.93 (m, 7H), 1.72 – 1.57 (m, 4H), 1.39 – 1.20 (m, 25H), 0.93 – 0.82 (m, 6H); **^{13}C NMR (101 MHz, Chloroform–*d*)**: δ 174.1, 131.3, 130.1, 129.9, 128.3, 63.9, 34.5, 32.1, 31.7, 29.9, 29.8, 29.7, 29.5, 29.5, 29.3, 29.3, 29.3, 28.8, 27.4, 27.3, 27.3, 25.2, 23.7, 22.8, 22.7, 14.3, 14.2; **IR (film)**: 3006, 2925, 2855, 1739, 1655, 1464, 1378, 1359, 1243, 1172, 1087, 1036, 723; **HRMS ([M+Na]$^+$)**: calculated for: 441.3709, found 441.3700; **Elemental analysis**: calculated for $C_{28}H_{52}O_2$: C 79.74, H 12.39; found: C 79.97, H 12.40.

Synthesis of *(Z)*–oct–5–en–1–yl oleate (S4a)

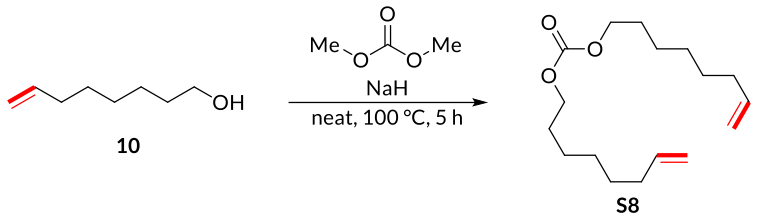


Scheme 2. Synthesis of *(Z)*–oct–5–en–1–yl oleate (**S4a**).

Ester **S4a** was prepared according to the ***method A***: oleic acid (**1**) (12.0 g, 13.5 mL, 42.0 mmol), *(Z)*-oct-5-en-1-ol (**3**) (4.6 g, 5.4 mL, 35.0 mmol), and PTSA (60 mg 0.35 mmol, 1 mol%) were used to afford diene **S4a** as a colourless oil (12.0 g, 30.6 mmol, yield 87%).

^{1}H NMR (400 MHz, Chloroform–*d*): δ 5.45 – 5.25 (m, 2H), 4.06 (t, *J* = 6.7 Hz, 2H), 2.33 – 2.24 (m, 2H), 2.10 – 1.96 (m, 8H), 1.68 – 1.56 (m, 4H), 1.46 – 1.21 (m, 24H), 0.95 (t, *J* = 7.5 Hz, 3H), 0.92 – 0.84 (m, 3H); **^{13}C NMR (101 MHz, Chloroform–*d*)**: δ 174.1, 132.3, 130.1, 129.9, 128.6, 64.4, 34.5, 32.1, 29.9, 29.8, 29.7, 29.5, 29.3, 29.3, 29.3, 28.4, 27.4, 27.3, 26.8, 26.2, 25.2, 22.8, 20.7, 14.5, 14.3; **IR (film)**: 3454, 3005, 2925, 2854, 1739, 1655, 1462, 1354, 1304, 1242, 1172, 1119, 1089, 968, 722; **HRMS ([M+Na]$^+$)**: calculated for: 415.3552, found 415.3554; **Elemental analysis**: calculated for $C_{26}H_{48}O_2$: C 79.53, H 12.32; found: C 79.77, H 12.35.

Synthesis of di(oct-7-en-1-yl) carbonate (S8)

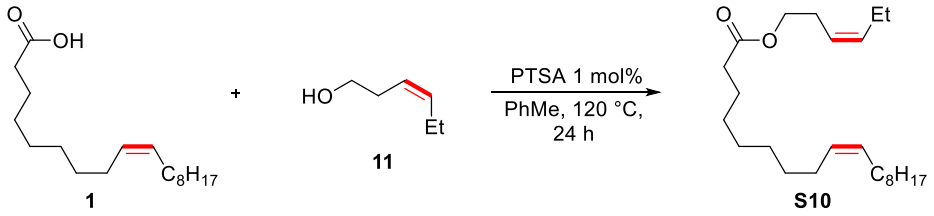


Scheme 3. Synthesis of di(oct-7-en-1-yl) carbonate (**S8**).

Under protective atmosphere of argon in a 100 mL round bottom flask equipped with magnetic stirring element 60% NaH (0.1 g, 2.5 mmol, 0.05 equiv.) was added and washed with dry *n*-hexane (2×5 mL). The remaining solvent was removed in *vacuo* and degassed DMC (4.6 g, 4.3 mL, 50.0 mmol, 1.00 equiv.) was added dropwise, followed by addition of 7-octen-1-ol (**10**) (14.0 g, 16.6 mL, 105.0 mmol, 2.1 equiv.). Reaction mixture was heated for 2 h with simultaneous distillation of methanol under reduced pressure. Crude product was purified by distillation (main fraction was collected at 110-115 °C, 1×10^{-3} mbar). Finally diene was distilled on Kugelrohr over CaH_2 to afford colourless liquid (10.7 g, 38.0 mmol, 76%).

^{1}H NMR (400 MHz, Chloroform–*d*): δ 5.80 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 2H), 5.02 – 4.91 (m, 4H), 4.12 (t, *J* = 6.7 Hz, 4H), 2.08 – 2.00 (m, 4H), 1.71 – 1.62 (m, 4H), 1.45 – 1.27 (m, 12H); **^{13}C NMR (101 MHz, Chloroform–*d*): δ** 155.5, 139.0, 114.5, 68.1, 33.8, 28.8, 28.8, 28.7, 25.7, 25.7. The spectra correspond to those described in the literature.[7]

Synthesis of *(Z)*–hex–3–en–1–yl oleate (S10)



Scheme 4. Synthesis of *(Z)*–hex–3–en–1–yl oleate (**S10**).

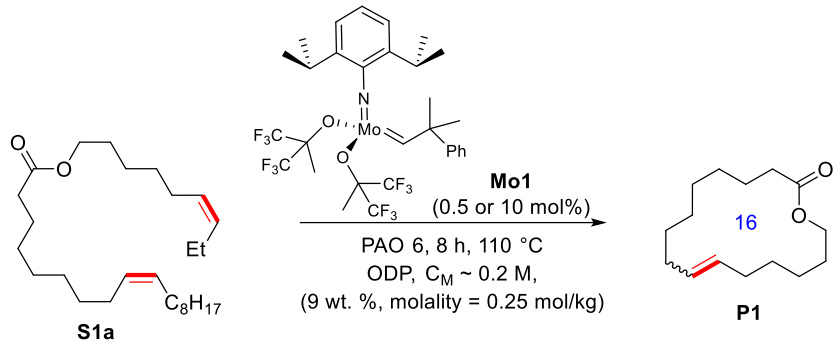
Ester **S10** was prepared according to the ***method A***: oleic acid (**1**) (12.0 g, 13.5 mL, 42.0 mmol), *(Z)*-hex-3-en-1-ol (**11**) (3.5 g, 4.1 mL, 35.0 mmol), and PTSA (60 mg 0.35 mmol, 1 mol%) were used to afford diene **S10** as a colourless oil (12.5 g, 34.3 mmol, yield 98%).

^{1}H NMR (400 MHz, Chloroform–*d*): δ 5.50 (dtt, *J* = 10.4, 7.3, 1.6 Hz, 1H), 5.41 – 5.25 (m, 3H), 4.06 (t, *J* = 6.9 Hz, 2H), 2.42 – 2.32 (m, 2H), 2.33 – 2.24 (m, 2H), 2.11 – 1.96 (m, 7H), 1.66 – 1.56 (m, 2H), 1.38 – 1.19 (m, 22H), 0.97 (t, *J* = 7.5 Hz, 3H), 0.92 – 0.84 (m, 3H); **^{13}C NMR (101 MHz, Chloroform–*d*)**: δ 174.1, 134.6, 130.1, 129.9, 123.9, 63.9, 34.5, 32.0, 29.9, 29.8, 29.7, 29.5, 29.3, 29.3, 29.2, 27.4, 27.3, 26.9, 25.1, 22.8, 20.7, 14.4, 14.3; **IR (film)**: 3453, 3007, 2952, 2854, 1739, 1656, 1463, 1384, 1353, 1305, 1242, 1172, 1119, 1091,

1012, 903, 723; **HRMS ([M+Na]⁺)**: calculated for: 387.3239; found; 387.3243 **Elemental analysis**: calculated for $C_{24}H_{44}O_2$: C 79.06, H 12.16; found: C 79.00, H 12.21.

HC-RCM macrocyclization using oil diffusion pump - Preliminary studies

Schrock catalyst Mo1 used as a powder



Scheme 5. HC-RCM macrocyclization using oil diffusion pump with **Mo1** (powder).

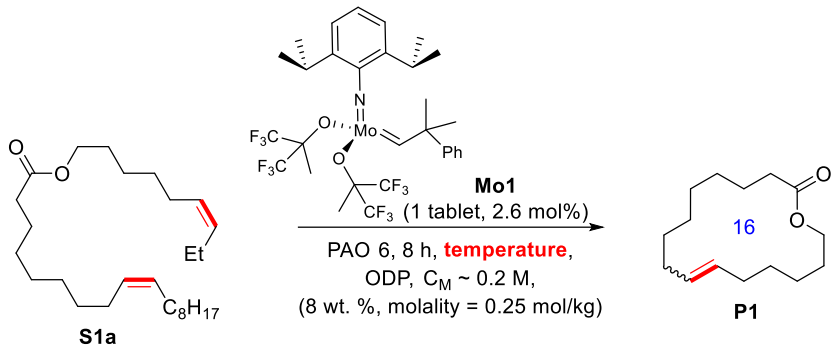
Table 1. Results for reaction on oil diffusion pump with **Mo1** (powder).

Entry	Loading [mol%]	Temperature [°C]	Yield [%]	Selectivity [%]	*(E)/(Z)*
1	0.5	110	0	–	–
2	0.5	40⟶110	0	–	–
3	10	110	84	96	4.7

General procedure for preparation reactions with Mo1 in powder

In a glovebox under protective atmosphere of argon in a 10 mL round bottom flask equipped with magnetic stirring element *(Z)*–non–6–en–1–yl oleate (**S1a**) (0.2 g, 0.5 mmol, molality = 0.25 mol/kg) was diluted in the PAO 6 (2.0 g) followed by addition of the solid catalyst (0.5 or 10 mol%). The flask was sealed with a septa and withdrew from glovebox. The flask was quickly assembled with the Hickman adapter (previously purged with argon) connected with the diffusion pump (giving nominal pressure of 10^{-6} mBar measured at the pump inlet) through two freezers/cold–fingers immersed in liquid nitrogen filled Dewars. The valve to the pump was opened and the flask was immersed into preheated oil bath (110 °C) or (40 °C⟶ heated to 110 °C), and the reaction mixture was stirred for 8 hours under vacuum. After disassembling the apparatus the crude product was washed out from the Hickman adapter receiver with *n*-hexane. The crude product was deposited on silica gel and purified by short flash chromatography (*n*-hexane was used to elute nonpolar fractions, then the macrocycle was eluted with ethyl acetate). Product obtained as a colourless oil was analysed by GC. According to the general procedure complex **Mo1** (1.9 mg, 2.5 µmol, 0.5 mol%) was used in entry 1. According to the general procedure complex **Mo1** (1.9 mg, 2.5 µmol, 0.5 mol%) was used in entry 2. According to the general procedure complex **Mo1** (38 mg, 50 µmol, 10 mol%) was used in entry 3.

Temperature studies



Scheme 6. HC-RCM macrocyclization using oil diffusion pump - temperature screening.

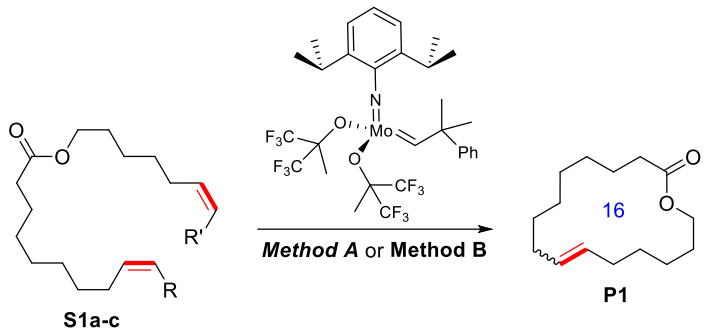
Table 2. Studies on influence of temperature on model RCM reaction of **S1a**

Entry	Temperature [°C]	Yield [%]	Selectivity [%]	*(E)/(Z)*
1	80	46	98	4.7
2	90	76	98	4.6
3	100	89	96	4.3
4	110	92	94	4.7
5	120	80	95	4.4

General procedure for preparation reactions with Mo1 – temperature screening

In a glovebox under protective atmosphere of argon in a 10 mL round bottom flask equipped with magnetic stirring element *(Z)*–non–6–en–1–yl oleate (**S1a**) (0.2 g, 0.5 mmol, molality = 0.25 mol/kg) was diluted in the PAO 6 (2.0 g). The flask was sealed with septa and withdrew from glovebox. Next, the catalyst **Mo1** (2.6 mol%, 1 tablet) was added on air. The flask was assembled with the Hickman adapter equipped with small basked filled with dry ice connected with the diffusion pump (giving nominal pressure of 10^{-6} mBar measured at the pump inlet) through two freezers/cold–fingers immersed in liquid nitrogen filled dewars. The valve to the pump was opened and the flask was left on vacuum for 5 min, then it was immersed into preheated oil bath (**see table 2**), and the reaction mixture was stirred for 8 hours under vacuum. After disassembling the apparatus the crude product was washed out from the Hickman adapter receiver with *n*–hexane. The crude product was deposited on silica gel and purified by short flash chromatography (*n*–hexane was used to elute nonpolar fractions, then the macrocycle was eluted with ethyl acetate). Product obtained as a colourless oil was analysed by GC.

Optimization of alkyl substituent



Scheme 7. HC-RCM macrocyclization using oil diffusion pump - alkyl substituent study.

Table 3. Alkyl substituent study.

Entry	Diene	R	R'	Method	Yield (%)	Selectivity (%)	*(E)/(Z)*
1	***S1a***	C_8H_{17}	Et	A	92	94	4.7
2	***S1b***	H	Et	B	67	95	4.6
3	***S1c***	H	H	B	57	94	4.4

General procedure for preparation reactions with Mo1 – double bond substituents optimization

In a glovebox under protective atmosphere of argon in a 10 mL round bottom flask equipped with magnetic stirring element **S1a**, **S1b** or **S1c** (0.5 mmol, molality = 0.25 mol/kg) was diluted in the PAO 6 (2.0 g). The flask was sealed with septa and withdrew from glovebox. Next, the catalyst **Mo1** (2.6 mol%, 1 tablet – ***Method A*** or 7.8 mol%, 3 tables – ***Method B***) was added on air. The flask was assembled with the Hickman adapter equipped with small basked filled with dry ice connected with the diffusion pump (giving nominal pressure of 10^{-6} mBar measured at the pump inlet) through two freezers/cold–fingers immersed in liquid nitrogen filled Dewars. The valve to the pump was opened and the flask was left on vacuum for 5 min, then it was immersed into preheated oil bath (110 °C – ***Method A***) or (40 °C⟶ heated to 110 °C ***Method B***), and the reaction mixture was stirred for 8 hours under vacuum. After disassembling the apparatus the crude product was washed out from the Hickman adapter receiver with *n*–hexane. The crude product was deposited on silica gel and purified by short flash chromatography (*n*–hexane was used to elute nonpolar fractions, then the macrocycle was eluted with ethyl acetate). Product obtained as a colourless oil was analysed by GC and ^{1}H and ^{13}C NMR.

Analysis of polymer – MALDI

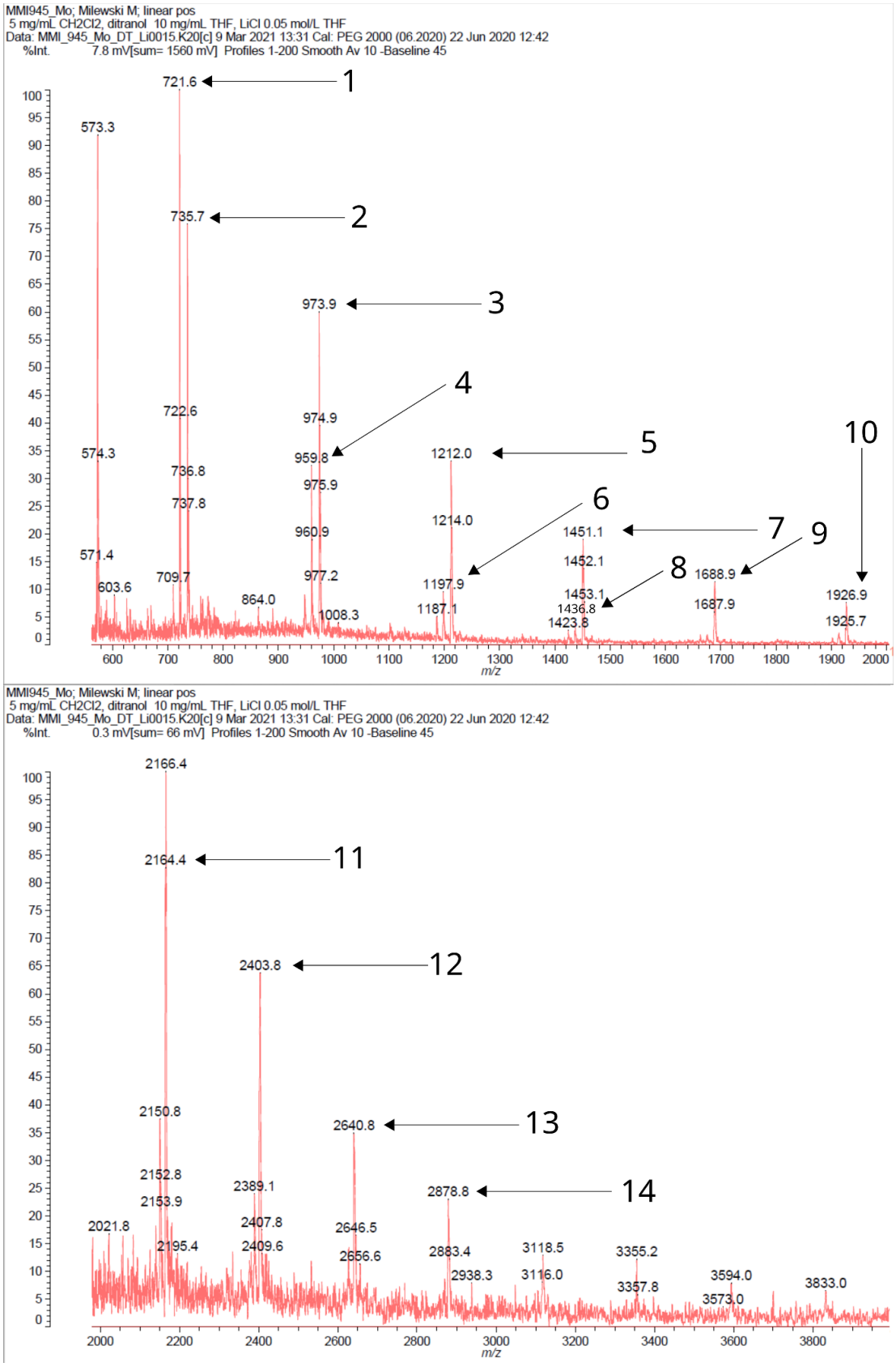
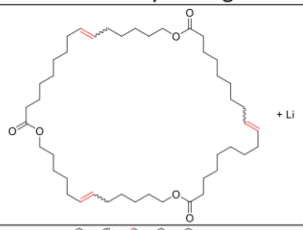
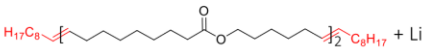
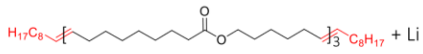
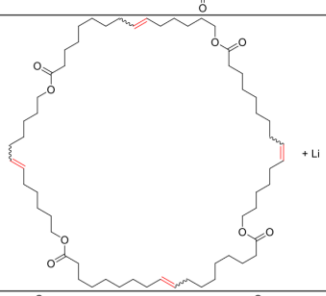
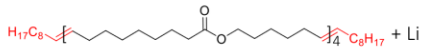
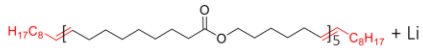
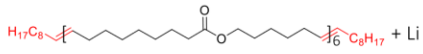
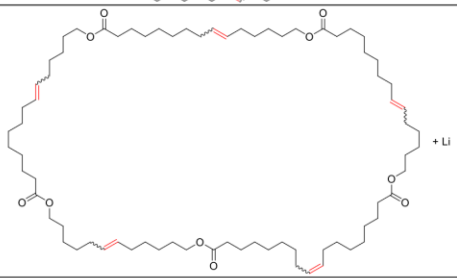
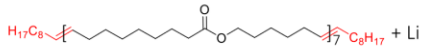
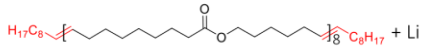
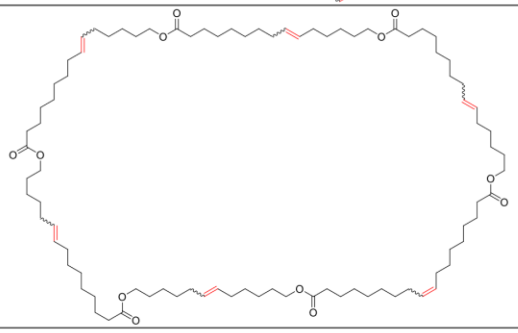
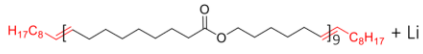
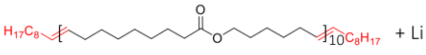
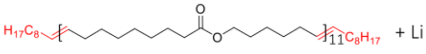
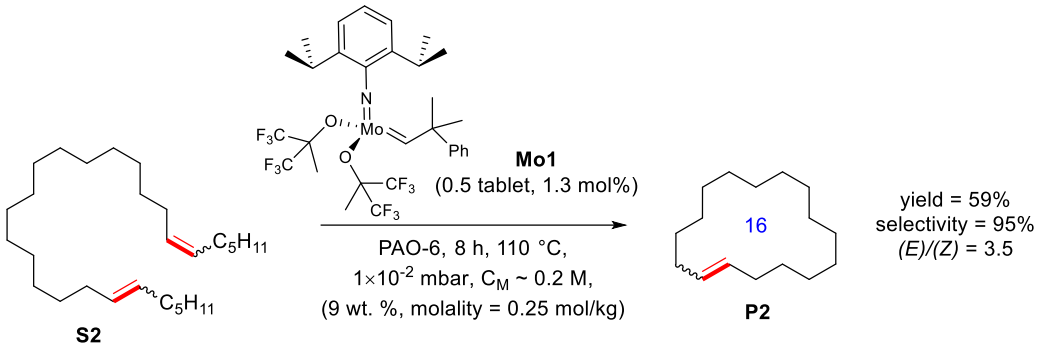


Figure 1. MALDI spectrum of polymerized reaction mixture of **S1a**.

Table 4. Observed linear and cyclic oligomers on MALDI spectrum

No.	Structure of cyclic oligomer	mass	No.	Structure of linear oligomer	mass
1		721.60	2		735.68
			3		973.88
4		959.79	5		1212.07
			7		1450.26
			9		1688.46
6		1197.98	10		1926.65
			11		2164.84
8		1436.18	12		2403.04
			13		2641.23
			14		2879.42

Synthesis of cyclohexadecene (P2)



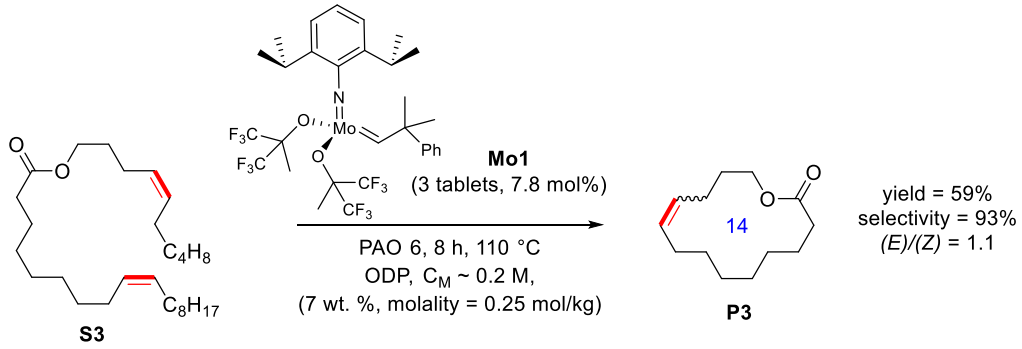
Scheme 8. HC-RCM macrocyclisation of octacosa-6,22-diene (**S2**).

In a 10 mL round bottom flask octacosa-6,22–diene (**S2**) (0.2 g, 0.5 mmol, molality = 0.25 mol/kg) was diluted in the PAO 6 (2.0 g), followed by addition of **Mo1** (1.3 mol%, 0.5 tablet). The flask was assembled with the Hickman adapter connected with the RVP pump (giving nominal pressure of 10^{-3} mBar measured at the pump inlet). The valve to the pump was opened and the flask was left on vacuum for minimum 5 min. and then it was immersed into preheated oil bath (**110 °C**), and the reaction mixture was stirred for 8 hours under vacuum. After disassembling the apparatus the crude product was washed out from the Hickman adapter receiver with *n*–hexane. The crude product was deposited on silica gel and purified by short flash chromatography (*n*–pentane was used to elute product fraction). Product obtained as a colourless oil was analysed by GC.

Scope and limitations

Synthesis of macrocycles on ODP

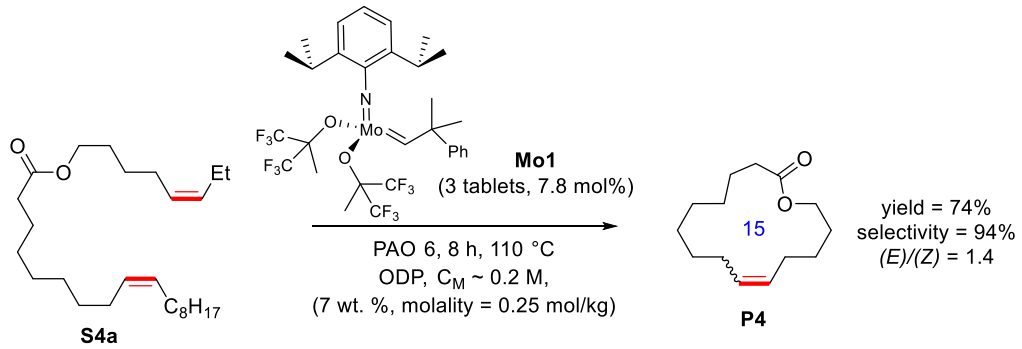
Synthesis of *(E/Z)*-oxacyclotetradec-10-en-2-one (P3)



Scheme 9. HC-RCM macrocyclisation of (*Z*)-dec-4-en-1-yl oleate (**S3**).

According to the general procedure: *(Z)*-dec-4-en-1-yl oleate (**S3**) (0.21 g, 0.5 mmol), catalyst **Mo1** (30 mg, 39 µmol, 7.8 mol%), and PAO 6 (2.00 g) were used to afford as a final product colourless oil with musk scent (63 mg, 0.29 mmol, yield 59%).

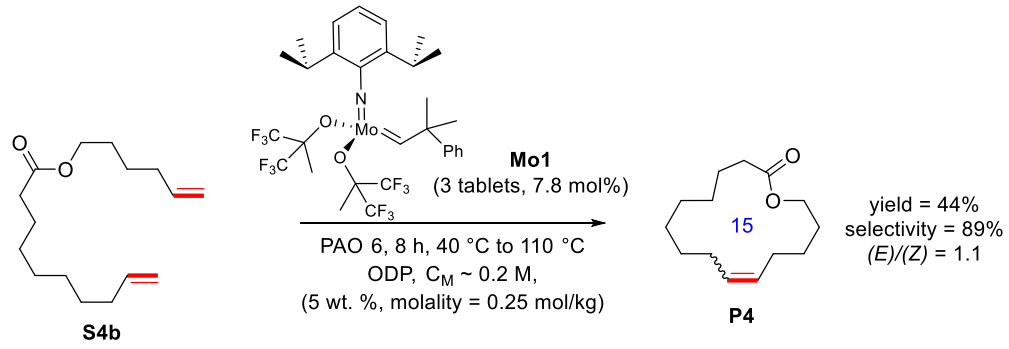
Synthesis of *(E/Z)*-oxacyclopentadec-10-en-2-one (P4) from S4a



Scheme 10. HC-RCM macrocyclisation of *(Z)*-oct-5-en-1-yl oleate (**S4a**).

According to the general procedure: *(Z)*-oct-5-en-1-yl oleate (**S4a**) (0.20 g, 0.5 mmol), catalyst **Mo1** (30 mg, 39 µmol, 7.8 mol%), and PAO 6 (2.00 g) were used to afford as a final product colourless oil with musk scent (83 mg, 0.37 mmol, yield 74%).

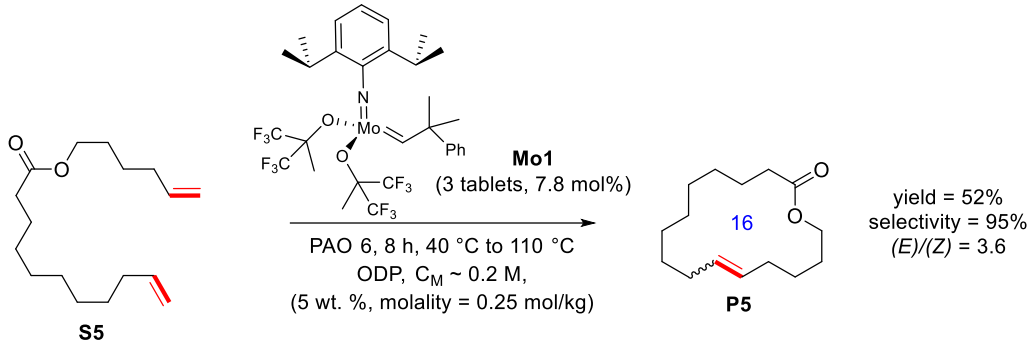
Synthesis of *(E/Z)*-oxacyclopentadec-10-en-2-one (P4) from S4b



Scheme 11. HC-RCM macrocyclisation of hex-5-en-1-yl dec-9-enoate (**S4b**).

According to the general procedure: hex-5-en-1-yl dec-9-enoate (**S4b**) (0.13 g, 0.5 mmol), catalyst **Mo1** (30 mg, 39 µmol, 7.8 mol%), and PAO 6 (2.00 g) were used to afford as a final product colourless oil with musk scent (49 mg, 0.22 mmol, yield 44%).

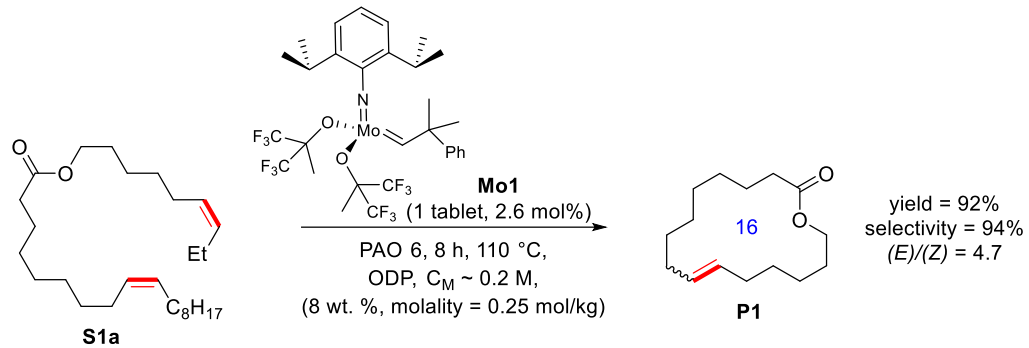
Synthesis of *(E/Z)*-oxacyclohexadec-11-en-2-one (P5)



Scheme 12. HC-RCM macrocyclisation of hex-5-en-1-yl undec-10-enoate (**S5**).

According to the general procedure: hex-5-en-1-yl undec-10-enoate (**S5**) (0.13 g, 0.5 mmol), catalyst **Mo1** (30 mg, 39 µmol, 7.8 mol%) and PAO 6 (2.00 g) were used to afford as a final product colourless oil with musk scent (62 mg, 0.26 mmol, yield 52%).

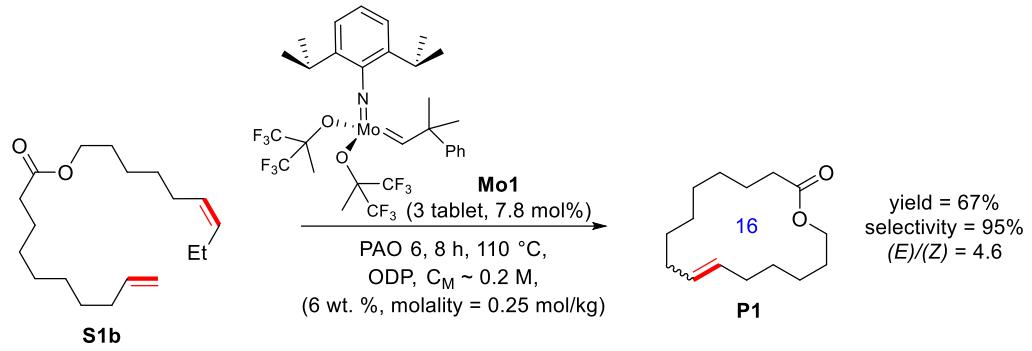
Synthesis of *(E/Z)*-oxacyclohexadec-10-en-2-one (P1) from S1a



Scheme 13. HC-RCM macrocyclisation of (*Z*)-non-6-en-1-yl oleate (**S1**a).

According to the general procedure: *(Z)*-non-6-en-1-yl oleate (**S1a**) (0.20 g, 0.5 mmol), catalyst **Mo1** (10 mg, 13 µmol, 2.6 mol%), and PAO 6 (2.00 g) were used to afford as a final product colourless oil with musk scent (110 mg, 0.46 mmol, yield 92%).

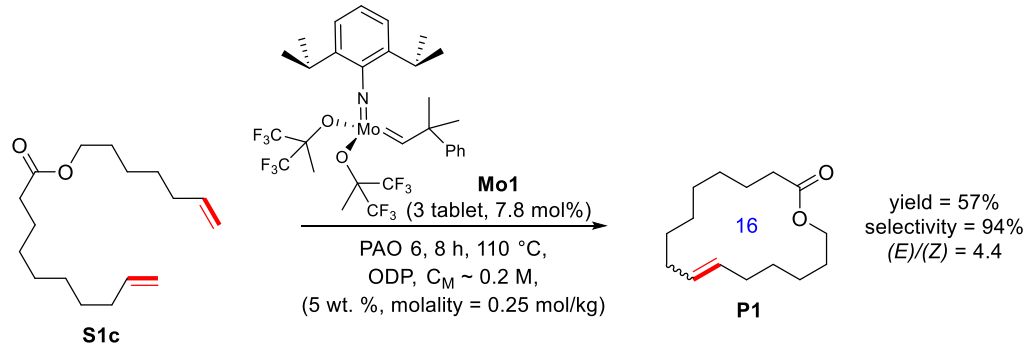
Synthesis of *(E/Z)*-oxacyclohexadec-10-en-2-one (P1) from S1b



Scheme 14. HC-RCM macrocyclisation of (*Z*)-non-6-en-1-yl dec-9-enoate (**S1b**).

According to the general procedure: *(Z)*-non-6-en-1-yl dec-9-enoate (**S1b**) (0.15 g, 0.5 mmol), catalyst **Mo1** (30 mg, 39 µmol, 7.8 mol%), and PAO 6 (2.00 g) were used to afford as a final product colourless oil with musk scent (80 mg, 0.34 mmol, yield 67%).

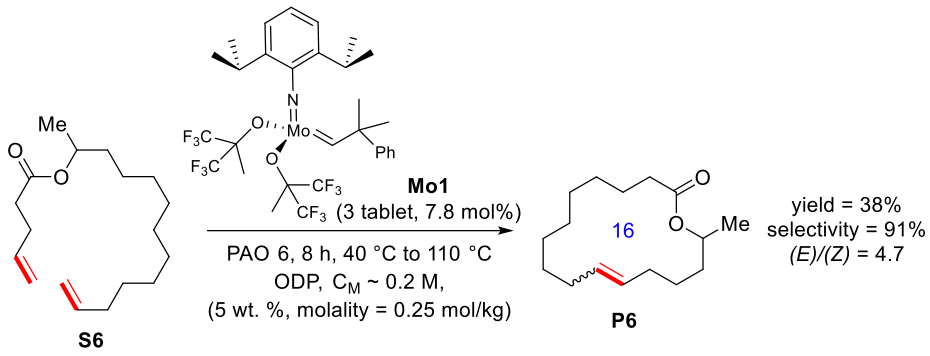
Synthesis of *(E/Z)*-oxacyclohexadec-10-en-2-one (P1) from S1c



Scheme 15. HC-RCM macrocyclisation of hept-6-en-1-yl dec-9-enoate (**S1c**).

According to the general procedure: hept-6-en-1-yl dec-9-enoate (**S1c**) (0.13 g, 0.5 mmol), catalyst **Mo1** (30 mg, 39 µmol, 7.8 mol%), and PAO 6 (2.00 g) were used to afford as a final product colourless oil with musk scent (68 mg, 0.28 mmol, yield 57%).

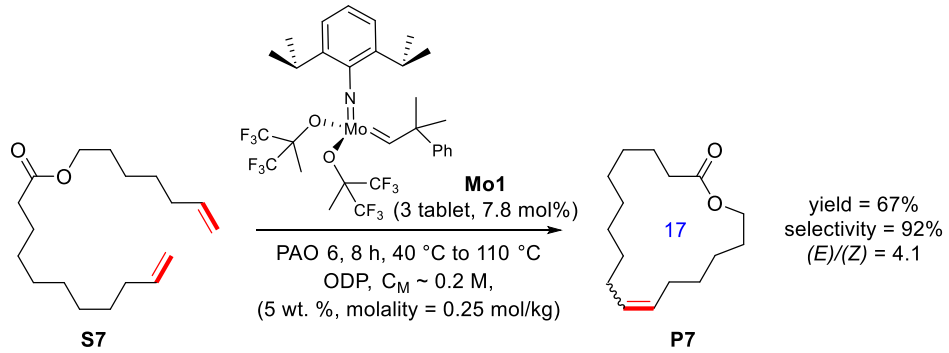
Synthesis of *(E/Z)*-16-methyloxacyclohexadec-11-en-2-one (P6)



Scheme 16. HC-RCM macrocyclisation of tridec-12-en-2-yl pent-4-enoate (**S6**).

According to the general procedure: tridec-12-en-2-yl pent-4-enoate (**S6**) (0.15 g, 0.54 mmol), catalyst **Mo1** (30 mg, 39 μmol, 7.8 mol%), and PAO 6 (2.00 g) were used to afford as a final product colourless oil with musk scent (52 mg, 0.21 mmol, yield 38%).

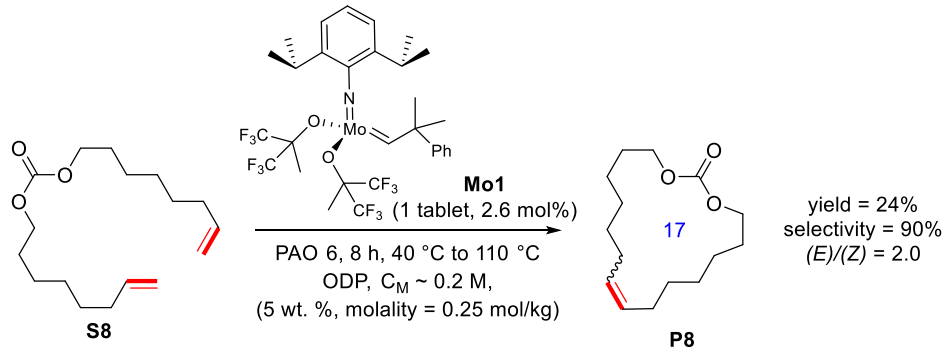
Synthesis of *(E/Z)*-oxacycloheptadec-11-en-2-one (P7)



Scheme 17. HC-RCM macrocyclisation of hept-6-en-1-yl undec-10-enoate (**S7**).

According to the general procedure: hept-6-en-1-yl undec-10-enoate (**S7**) (0.14 g, 0.5 mmol), catalyst **Mo1** (30 mg, 39 μmol, 7.8 mol%), and PAO 6 (2.00 g) were used to afford as a final product colourless oil with musk scent (84 mg, 0.33 mmol, yield 67%).

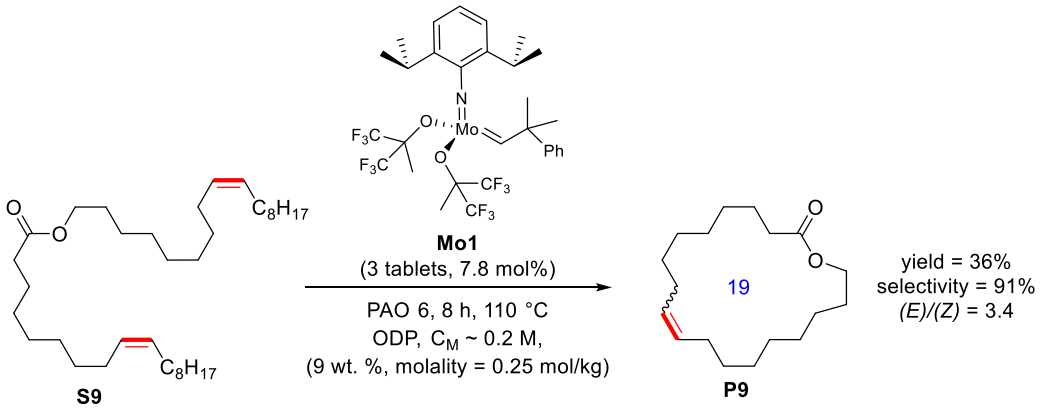
Synthesis of *(E/Z)*-1,3-dioxacycloheptadec-10-en-2-one (P8)



Scheme 18. HC-RCM macrocyclisation of di(oct-7-en-1-yl) carbon **S8**ate ().

According to the general procedure: di(oct-7-en-1-yl) carbonate (**S8**) (0.14 g, 0.5 mmol), catalyst **Mo1** (10 mg, 13 µmol, 2.6 mol%), and PAO 6 (2.00 g) were used to afford as a final product colourless oil with musk scent (30 mg, 0.12 mmol, yield 24%).

Synthesis of *(E/Z)*-oxacyclononadec-10-en-2-one (P9)



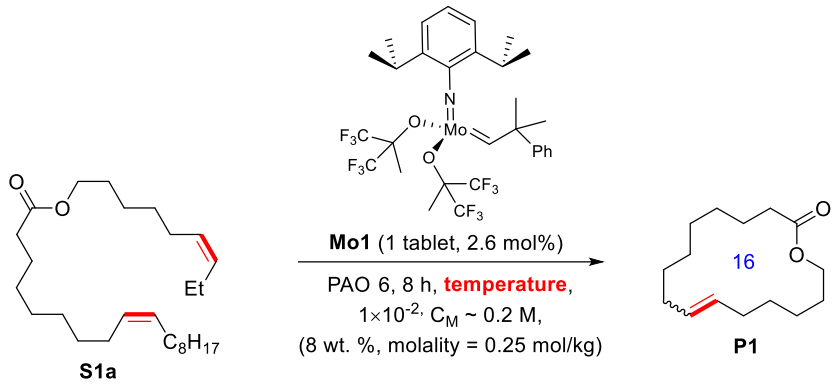
Scheme 19. HC-RCM macrocyclisation of (*Z*)-octadec-9-en-1-yl oleate (**S9**).

According to the general procedure: (*Z*)-octadec-9-en-1-yl oleate (**S9**) (0.27 g, 0.5 mmol), catalyst **Mo1** (30 mg, 39 µmol, 7.8 mol%), and PAO 6 (2.00 g) were used to afford as a final product colourless oil with musk scent (50 mg, 0.18 mmol, yield 36%).

Scope and limitations

Synthesis of macrocycles on RVP

General procedure for preparation reactions with Mo1



Scheme 20. HC-RCM macrocyclization using RVP - temperature screening.

Table 5. Results for temperature studies for Schrock catalyst on RVP.

Entry	Temperature [°C]	Yield [%]	Selectivity [%]	*(E)*/*(Z)*
1	100	54	97	4.4
2	110	84	96	4.4
3	115	59	97	4.2
4	120	62	95	4.3

In a glovebox under protective atmosphere of argon in a 10 mL round bottom flask equipped with magnetic stirring element *(Z)*–non–6–en–1–yl oleate (**S1a**) (0.1 g, 0.25 mmol, molality = 0.25 mol/kg) was diluted in the PAO 6 (1.0 g). The flask was sealed with septa and withdrew from glovebox. Next, the catalyst **Mo1** (2.6 mol%, 0.5 tablet) was added on air. The flask was assembled with the Hickman adapter equipped with small basked filled with dry ice connected with the diffusion pump (giving nominal pressure of 10^{-6} mBar measured at the pump inlet) through two freezers/cold–fingers immersed in liquid nitrogen filled Dewars. The valve to the pump was opened and the flask was left on vacuum for 5 min, then it was immersed into preheated oil bath (**see table 5**), and the reaction mixture was stirred for 8 hours under vacuum. After disassembling the apparatus the crude product was washed out from the Hickman adapter receiver with *n*–hexane. The crude product was deposited on silica gel and purified by short flash chromatography (*n*-hexane was used to elute non–polar fractions, then the macrocycle was eluted with ethyl acetate). Product obtained as a colourless oil was analysed by GC.

Calculation of reaction parameters

Environmental (E) factor

The calculation of **E** is defined by the ratio of the mass of waste per mass of product.[7] E = total waste / product by incorporating yield, stoichiometry and solvent usage the E-factor is an excellent metric.

$$E = \frac{\Sigma m(rawmaterials) + \Sigma m(solvent) - \Sigma m(products)}{\Sigma m(products)}$$

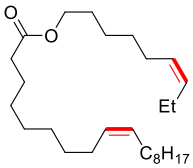
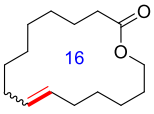
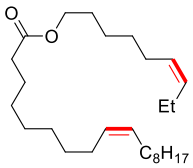
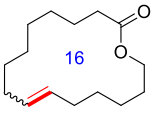
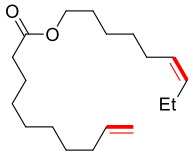
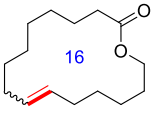
$$E(1-14) = \frac{\Sigma m(rawmaterials) + \Sigma m(solvent) - \Sigma m(products)}{\Sigma m(products)} =$$

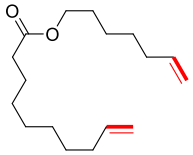
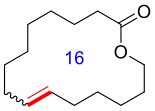
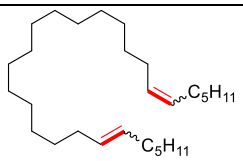
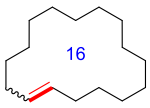
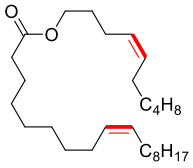
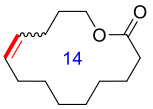
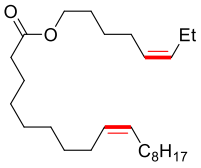
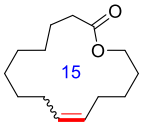
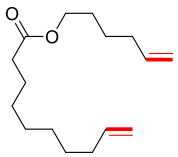
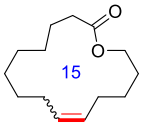
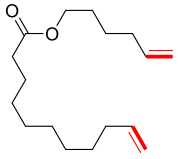
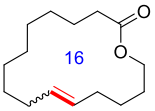
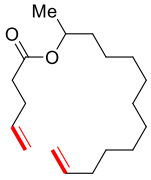
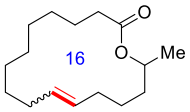
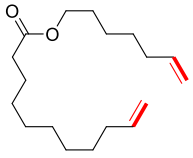
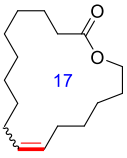
$$\frac{\Sigma m(diene + Mo \in tablets + PAO6) + \Sigma m(EtOAc + nhexane) - m(macrocycle)}{m(macrocycle)}$$

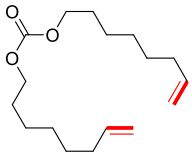
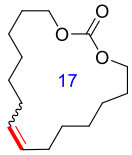
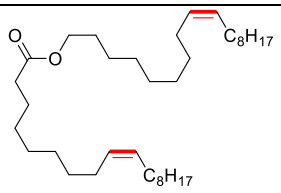
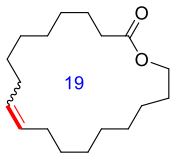
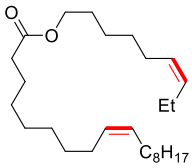
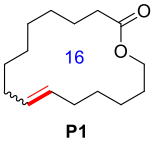
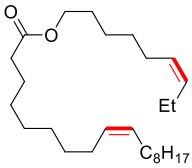
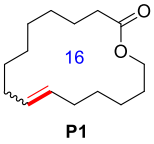
$$E(15) = \frac{\Sigma m(rawmaterials) + \Sigma m(solvent) - \Sigma m(products)}{\Sigma m(products)} =$$

$$\frac{\Sigma m(diene + Ru + TFBQ) + \Sigma m(EtOAc + chexane + PhMe) - m(macrocycle)}{m(macrocycle)}$$

Table 6. Values for E factor for reactions in various conditions (Entry 1-14: HC-RCM; entry 15 classical RCM in solution).

No.	Diene	Macrocycle	Conditions	E-factor
1	 **S1a**	 **P1**	2.6 mol% **Mo**, 80 – 120 °C, 8 hours, PAO 6, oil diffusion pump (**Mo** in tablets)	E(**80 °C**) = ((203 mg + 2000 mg +100 mg + 9020 mg + 6550 mg) – 55 mg) ÷ 55 mg = **324** E(**90 °C**) = ((203 mg + 2000 mg +100 mg + 9020 mg + 6550 mg) – 91 mg) ÷ 91 mg = **195** E(**100 °C**) = ((203 mg + 2000 mg +100 mg + 9020 mg + 6550 mg) – 55 mg) ÷ 106 mg = **168** E(**110 °C**) = ((203 mg + 2000 mg +100 mg + 9020 mg + 6550 mg) – 110 mg) ÷ 110 mg = **161** E(**120 °C**) = ((203 mg + 2000 mg +100 mg + 9020 mg + 6550 mg) – 96 mg) ÷ 96 mg = **185**
2	 **S1a**	 **P1**	10 mol% **Mo**, 110 °C, 8 hours, PAO 6, oil diffusion pump (**Mo** in powder)	E = ((203 mg + 2000 mg +10 mg + 9020 mg + 6550 mg) – 100 mg) ÷ 100 mg = **177**
3	 **S1b**	 **P1**	7.2 mol% **Mo**, 110 °C, 8 hours, PAO 6, oil diffusion pump (**Mo** in tablets)	E = ((147 mg + 2000 mg +300 mg + 9020 mg + 6550 mg) – 80 mg) ÷ 80 mg = **224**

No.	Diene	Macrocycle	Conditions	E-factor
4	 **S1c**	 **P1**	7.2 mol% **Mo**, 110 °C, 8 hours, PAO 6, oil diffusion pump (**Mo** in tablets)	E = ((133 mg + 2000 mg +300 mg + 9020 mg + 6550 mg) − 68 mg) ÷ 68 mg = **264**
5[a]	 **S2**	 **P2**	1.3 mol% **Mo**, 110 °C, 8 hours, PAO 6, RVP - 1×10^{-2} (**Mo** in tablets)	E = ((195 mg + 2000 mg +50 mg) − 65 mg) ÷ 65 mg = **34**
6	 **S3**	 **P3**	7.2 mol% **Mo**, 110 °C, 8 hours, PAO 6, oil diffusion pump (**Mo** in tablets)	E = ((210 mg + 2000 mg +300 mg + 9020 mg + 6550 mg) − 63 mg) ÷ 63 mg = **286**
7	 **S4a**	 **P4**	7.2 mol% **Mo**, 110 °C, 8 hours, PAO 6, oil diffusion pump (**Mo** in tablets)	E = ((196 mg + 2000 mg +300 mg + 9020 mg + 6550 mg) − 83 mg) ÷ 83 mg = **217**
8	 **S4b**	 **P4**	7.2 mol% **Mo**, 110 °C, 8 hours, PAO 6, oil diffusion pump (**Mo** in tablets)	E = ((126 mg + 2000 mg +300 mg + 9020 mg + 6550 mg) − 49 mg) ÷ 49 mg = **366**
9	 **S5**	 **P5**	7.2 mol% **Mo**, 110 °C, 8 hours, PAO 6, oil diffusion pump (**Mo** in tablets)	E = ((133 mg + 2000 mg +300 mg + 9020 mg + 6550 mg) − 62 mg) ÷ 62 mg = **389**
10	 **S6**	 **P6**	7.2 mol% **Mo**, 110 °C, 8 hours, PAO 6, oil diffusion pump (**Mo** in tablets)	E = ((150 mg + 2000 mg +300 mg + 9020 mg + 6550 mg) − 52 mg) ÷ 52 mg = **346**
11	 **S7**	 **P7**	7.2 mol% **Mo**, 110 °C, 8 hours, PAO 6, oil diffusion pump (**Mo** in tablets)	E = ((140 mg + 2000 mg +300 mg + 9020 mg + 6550 mg) − 84 mg) ÷ 84 mg = **213**

No.	Diene	Macrocycle	Conditions	E-factor
12	 **S8**	 **P8**	2.6 mol% **Mo**, 110 °C, 8 hours, PAO 6, oil diffusion pump (**Mo** in tablets)	E = ((141 mg + 2000 mg +100 mg + 9020 mg + 6550 mg) − 30 mg) ÷ 30 mg = **593**
13	 **S9**	 **P9**	7.2 mol% **Mo**, 110 °C, 8 hours, PAO 6, oil diffusion pump (**Mo** in tablets)	E = ((266 mg + 2000 mg +300 mg + 9020 mg + 6550 mg) − 50 mg) ÷ 50 mg = **362**
14	 **S1a**	 **P1**	2.6 mol% **Mo**, 100 − 120 °C, 8 hours, PAO 6, RVP - 1×10^{-2} (**Mo** in tablets)	E(**100 °C**) = ((102 mg + 1000 mg +50 mg + 4510 mg + 3275 mg) − 32 mg) ÷ 32 mg = **278** E(**110 °C**) = ((102 mg + 1000 mg +50 mg + 4510 mg + 3275 mg) − 50 mg) ÷ 50 mg = **178** E(**115 °C**) = ((102 mg + 1000 mg +50 mg + 4510 mg + 3275 mg) − 35 mg) ÷ 35 mg = **254** E(**120 °C**) = ((102 mg + 1000 mg +50 mg + 4510 mg + 3275 mg) − 37 mg) ÷ 37 mg = **240**
15[2]	 **S1a**	 **P1**	0.5 - 2 mol% **Ru**, 1 - 4 mol% **TFBQ** 77 °C, 5 − 24 hours, EtOAc, c= 1.5 − 29 mM	E(**c=1.5 mM**) = ((150 mg + 222.49 g + 4.97 mg + 2.66 mg 747.84 g + 208.08 g) − 81 mg) ÷ 81 mg = **14 549** E(**c=5 mM**) = ((150 mg + 66.75 g + 4.97 mg + 2.66 mg 747.84 g + 208.08 g) − 79 mg) ÷ 79 mg = **12 946** E(**c=10 mM**) = ((150 mg + 33.37 g + 4.97 mg + 2.66 mg 747.84 g + 208.08 g) − 71 mg) ÷ 71 mg = **13 934** E (**c=29 mM**) = ((60 mg + 4.67 g + 4.97 mg + 2.66 mg 186.96 g + 52.02 g) − 81 mg) ÷ 81 mg = **14 549**

[a] GC Yield

Calculation of EcoScale score

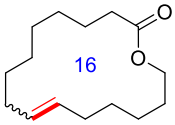
The EcoScale[8] allows the evaluation of the effectiveness of a synthetic reaction. It gives a score from 0 to 100, but also takes into account cost, safety, technical set-up, energy and purification aspects. It is obtained by assigning a value of 100 to an ideal reaction and then subtracting penalty points for non-ideal conditions. These penalty points taken into account both the advantages and disadvantages of specific reagents, set-ups and technologies. According to Van Aken "The EcoScale tool uses a scale from 0 to 100 with 0 representing a totally failed reaction (0% yield) and 100 representing the ideal reaction which is defined as follows: Compound A (substrate) undergoes a reaction with (or in the presence of) inexpensive compound(s) B to give the desired compound C in 100% yield at room temperature with a minimal risk for the operator and a minimal impact on the environment. Six general parameters which influence the quality of reaction conditions are analysed. Within each of these parameters, individual penalty points of various relative weights are assigned that take into account all possible situations when setting up an organic chemistry experiment. The penalty points are cumulative for all components of the preparation. In order to simplify the EcoScale design, the usual differentiation between solvents, reagents, auxiliary or coreagents and catalysts is not made. EcoScale can be summarizing by this simple equation: EcoScale = 100 - sum of individual penalties." Usually Ranking of reaction conditions is defined as follow: On a scale from 0 to 100 using the following scores: > 75 is excellent; > 50 is acceptable and < 50 is inadequate.

Table 7. EcoScale for RCM and HC-RCM of **S1a**

Parameter	**Classical RCM (5 mM)[2]**	**HC-RCM (0.2 M)**
Yield	**4** (91%)	**4** (92%)
Price for compounds	**5** (Ru (258.38 $) + TFBQ (9.52) + Diene (11.21 $) + PhMe 2.24 L (158.60 $) = in total 437.71 $)	**5** (Mo (180$) + Diene (11.42$) + PAO 6 0.13 L (0.45$) = in total 191.87 $)
Safety	**10** (PhMe (T + F))	-
Technical setup	-	**3** (pressure equipment)
Temperature/Time	**3** (50°C for 5 h)	**3** (110°C for 8 h)
Workup and purification	**10** (column chromatography or any other method of purification—the same in both methods) Penalty for evaporation of 2,4 L of PhMe not added.	**10** (column chromatography or any other method of purification—the same in both methods)
Summary of penalty points	**32**	**25**
Total Score	**68**	**75**

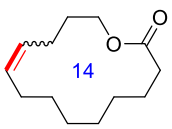
Analytical data for synthesized macrocycles

(E/Z)-oxacyclohexadec-10-en-2-one (P1)



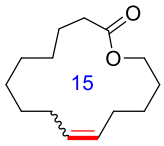
^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.39 – 5.23 (m, 2H), 4.12 – 4.02 (m, 2H), 2.38 – 2.27 (m, 2H), 2.13 – 1.97 (m, 4H), 1.69 – 1.55 (m, 4H), 1.46 – 1.20 (m, 12H); **^{13}C NMR (101 MHz, Chloroform-*d*):** δ 174.1, 174.1, 131.4, 130.9, 130.4, 130.1, 64.7, 64.6, 35.5, 34.9, 32.4, 31.6, 29.3, 29.2, 29.1, 28.8, 28.6, 28.4, 28.3, 28.2, 27.8, 27.8, 27.6, 27.4, 27.1, 26.5, 26.4, 25.6, 25.1, 24.7. The spectra correspond to those described in the literature.[1]

(E/Z)-oxacyclotetradec-10-en-2-one (P3)



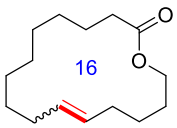
^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.57 – 5.24 (m, 2H), 4.17 – 4.07 (m, 2H), 2.44 – 2.37 (m, 1H), 2.37 – 2.31 (m, 1H), 2.28 – 2.18 (m, 2H), 2.11 – 1.97 (m, 2H), 1.81 – 1.62 (m, 4H), 1.44 – 1.25 (m, 8H); **^{13}C NMR (101 MHz, Chloroform-*d*):** δ 174.3, 173.9, 131.2, 130.7, 130.5, 128.5, 64.9, 62.8, 33.6, 33.1, 31.5, 31.0, 29.1, 28.3, 27.2, 27.0, 26.8, 26.8, 26.7, 26.0, 25.2, 25.1, 25.1, 24.6, 24.2, 23.7. The spectra correspond to those described in the literature.[9]

(E/Z)-oxacyclopentadec-10-en-2-one (P4)



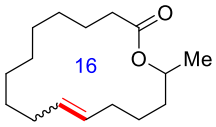
^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.53 – 5.26 (m, 2H), 4.17 – 4.07 (m, 2H), 2.39 – 2.26 (m, 2H), 2.07 – 1.96 (m, 4H), 1.73 – 1.56 (m, 4H), 1.54 – 1.21 (m, 10H); **^{13}C NMR (101 MHz, Chloroform-*d*):** δ 174.2, 174.1, 131.6, 130.8, 130.8, 129.3, 64.0, 63.9, 34.7, 34.5, 31.8, 31.4, 28.6, 28.4, 28.1, 27.9, 27.9, 27.8, 27.6, 27.4, 27.3, 27.2, 27.1, 26.4, 25.6, 25.2, 25.0. The spectra correspond to those described in the literature.[2]

(E/Z)-oxacyclohexadec-11-en-2-one (P5)



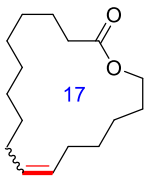
^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.44 – 5.23 (m, 2H), 4.18 – 4.08 (m, 2H), 2.37 – 2.27 (m, 2H), 2.09 – 1.97 (m, 4H), 1.69 – 1.54 (m, 4H), 1.45 – 1.16 (m, 12H); **^{13}C NMR (101 MHz, Chloroform-*d*):** δ 174.1, 174.1, 132.0, 130.5, 130.2, 129.7, 64.2, 64.1, 34.9, 34.0, 32.2, 32.1, 29.3, 28.5, 28.5, 28.4, 28.3, 28.3, 28.1, 28.1, 27.7, 27.3, 27.3, 27.2, 26.7, 26.7, 26.6, 25.6, 25.4, 25.3. The spectra correspond to those described in the literature.[1]

(E/Z)-16-methyloxacyclohexadec-11-en-2-one (P6)



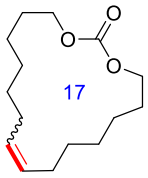
^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.48 – 5.36 (m, 2H), 5.04 – 4.90 (m, 1H), 2.51 – 2.26 (m, 3H), 2.25 – 2.14 (m, 1H), 2.11 – 1.91 (m, 2H), 1.64 – 1.23 (m, 16H), 1.20 (d, J = 6.3 Hz, 3H); **^{13}C NMR (101 MHz, Chloroform-*d*):** δ 173.1, 172.9, 131.7, 131.4, 128.9, 128.0, 71.1, 70.2, 35.8, 35.3, 35.2, 34.8, 31.1, 27.8, 27.7, 27.5, 27.4, 27.3, 27.3, 26.8, 26.7, 26.6, 26.5, 26.2, 26.2, 25.8, 23.9, 23.8, 23.3, 20.3**; IR (film)**: 2974.18, 2964.54, 2925.48, 2877.75, 2854.61, 2763.49, 1731.28, 1580.38, 1458.89, 1397.17, 1370.18, 1353.30, 1338.84, 1316.18, 1250.61, 1237.59, 1202.40, 1185.04, 1173.47, 1160.94, 1149.85, 1140.21, 1121.89, 1065.00, 1037.03, 1007.14, 967.13, 768.49, 712.57, 548.17, ; **HRMS ([M+Na]$^+$)**: calculated for: 253.2168, found 253.2166; **Elemental analysis**: calculated for $C_{16}H_{28}O_2$: C 76.14, H 11.18; found: C 76.24, H 11.24.

(E/Z)-oxacycloheptadec-11-en-2-one (P7)



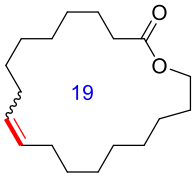
^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.33 – 5.27 (m, 2H), 4.11 – 4.06 (m, 2H), 2.34 – 2.29 (m, 2H), 2.11 – 1.98 (m, 4H), 1.67 – 1.57 (m, 4H), 1.43 – 1.21 (m, 14H); **^{13}C NMR (101 MHz, Chloroform-*d*):** δ 174.6, 174.1, 131.0, 130.9, 130.4, 130.3, 65.1, 64.7, 34.8, 34.4, 32.8, 31.9, 29.4, 29.4, 29.3, 28.9, 28.9, 28.8, 28.8, 28.7, 28.6, 28.3, 28.2, 28.1, 27.7, 27.3, 27.1, 26.6, 26.2, 26.1, 25.6, 25.5. The spectra correspond to those described in the literature.[10]

(E/Z)-1,3-dioxacycloheptadec-10-en-2-one (P8)



^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.38 – 5.29 (m, 2H), 4.26 – 4.15 (m, 4H), 2.08 – 1.99 (m, 4H), 1.73 – 1.62 (m, 4H), 1.48 – 1.30 (m, 12H); **^{13}C NMR (101 MHz, Chloroform-*d*):** δ 155.5, 155.4, 130.7, 130.2, 68.7, 68.1, 31.9, 29.0, 28.9, 28.7, 28.3, 27.8, 27.7, 26.9, 26.1, 25.3. The spectra correspond to those described in the literature.[11]

(E/Z)-oxacyclononadec-10-en-2-one (P9)

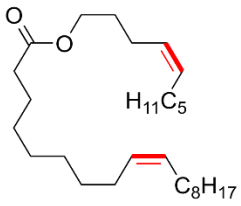


^{1}H NMR (400 MHz, Chloroform-*d*): δ 5.34 – 5.26 (m, 2H), 4.14 – 4.06 (m, 2H), 2.30 (t, J = 6.9 Hz, 2H), 2.09 – 1.95 (m, 4H), 1.67 – 1.56 (m, 4H), 1.42 – 1.20 (m, 18H); **^{13}C NMR (101 MHz, Chloroform-*d*)** δ 174.3, 174.3, 131.0, 130.9, 130.4, 130.3, 64.7, 64.4, 35.1, 35.1, 32.3, 32.3, 29.8, 29.7, 29.5, 29.5, 29.4, 29.4, 29.3, 29.3, 29.3, 29.2, 29.1, 29.0, 29.0, 28.9, 28.2, 28.0, 27.9, 27.3, 26.5, 26.5, 26.3, 25.5, 25.5. The spectra correspond to those described in the literature.[12]

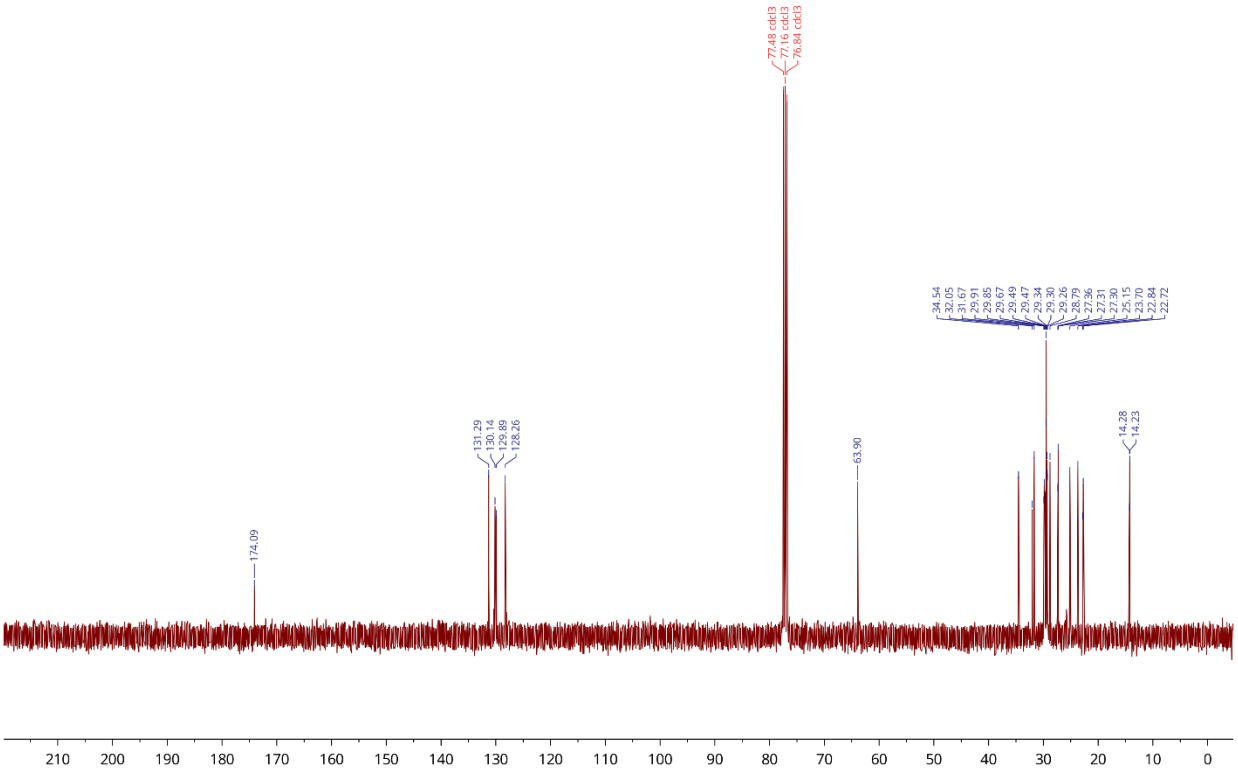
^{1}H & ^{13}C NMR spectra

(*Z*)-dec-4-en-1-yl oleate (S3)

Nucleus: 1H, Solvent: cdcl3
Scans: 32, Relaxation: 2.0000
Spectrometer Frequency: 399.71

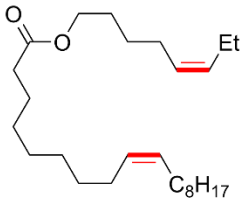


Nucleus: 13C, Solvent: cdcl3
Scans: 512, Relaxation: 1.0000
Spectrometer Frequency: 100.52

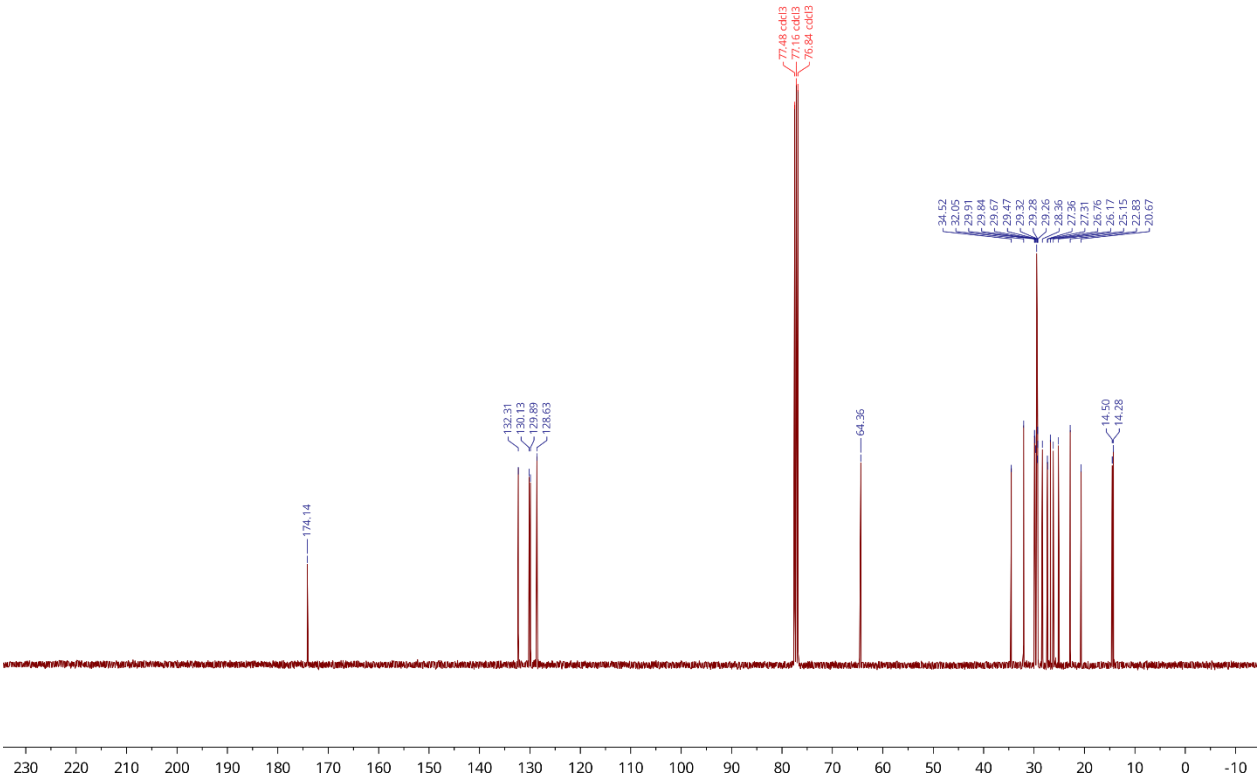


(*Z*)-oct-5-en-1-yl oleate (S4a)

Nucleus: 1H, Solvent: cdcl3
Scans: 16, Relaxation: 5.0000
Spectrometer Frequency: 399.71

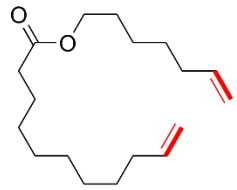


Nucleus: 13C, Solvent: cdcl3
Scans: 1000, Relaxation: 3.0000
Spectrometer Frequency: 100.52

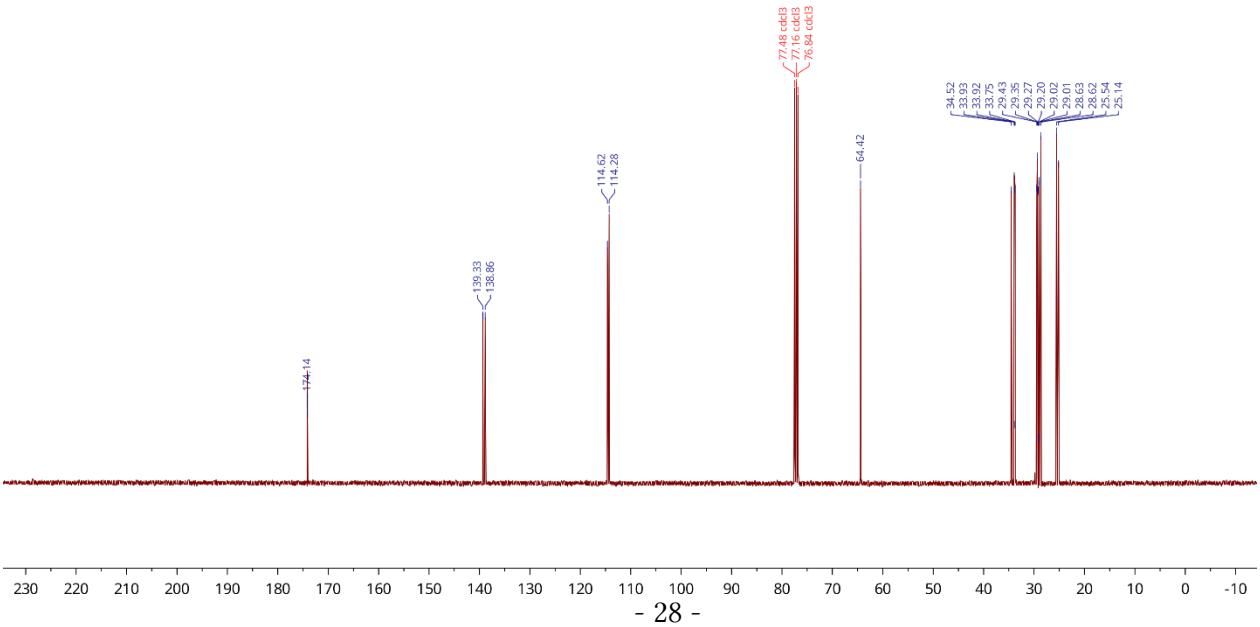


Hept-6-en-1-yl undec-10-enoate (S7)

Nucleus: 1H, Solvent: cdcl3
Scans: 32, Relaxation: 5.0000
Spectrometer Frequency: 399.72

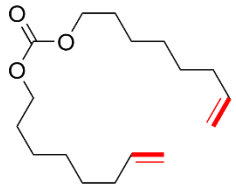


Nucleus: 13C, Solvent: cdcl3
Scans: 2000, Relaxation: 2.0000
Spectrometer Frequency: 100.52

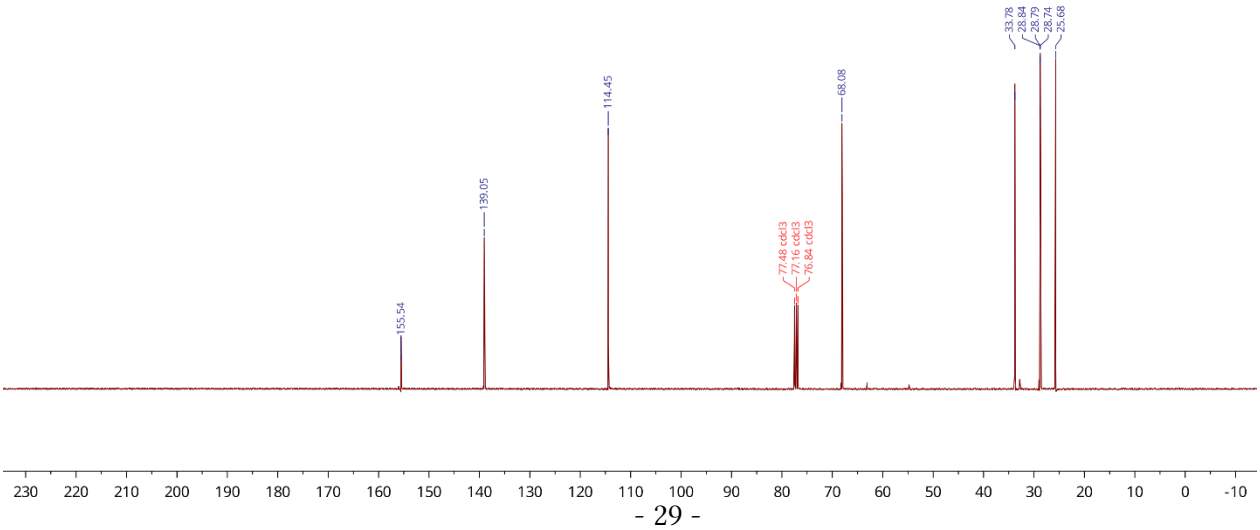


Di(oct-7-en-1-yl) carbonate (S8)

Nucleus: 1H, Solvent: cdcl3
Scans: 32, Relaxation: 2.0000
Spectrometer Frequency: 399.71

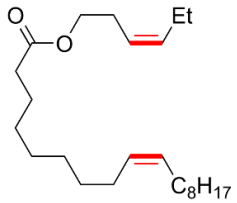


Nucleus: 13C, Solvent: cdcl3
Scans: 2000, Relaxation: 1.0000
Spectrometer Frequency: 100.52

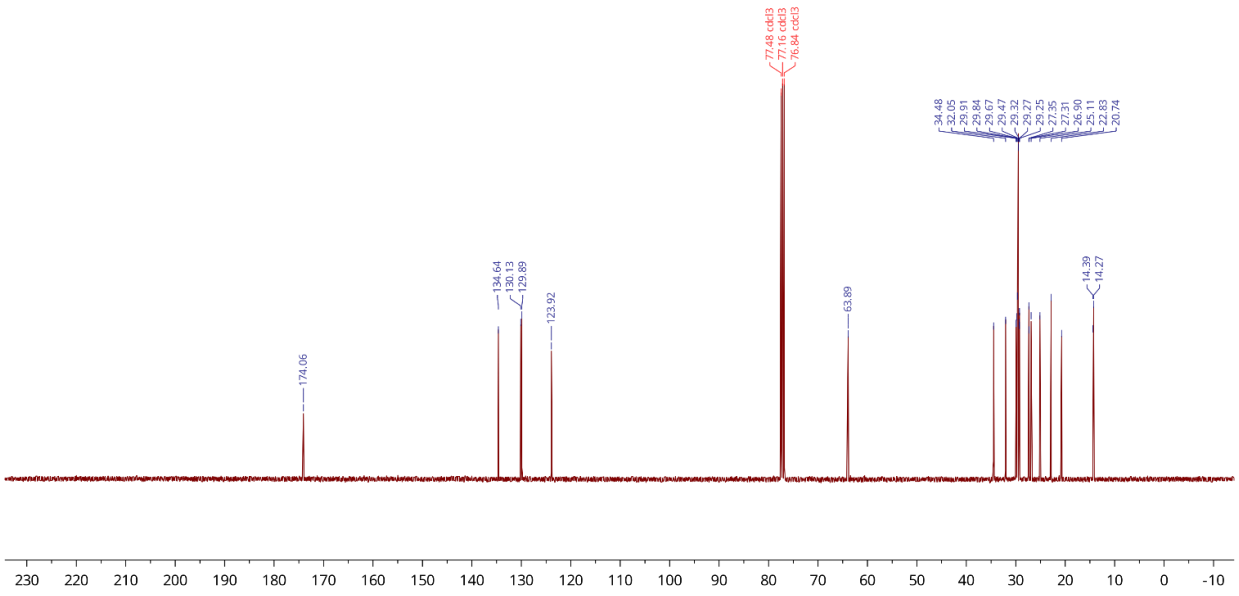


(*Z*)-hex-3-en-1-yl oleate (S10)

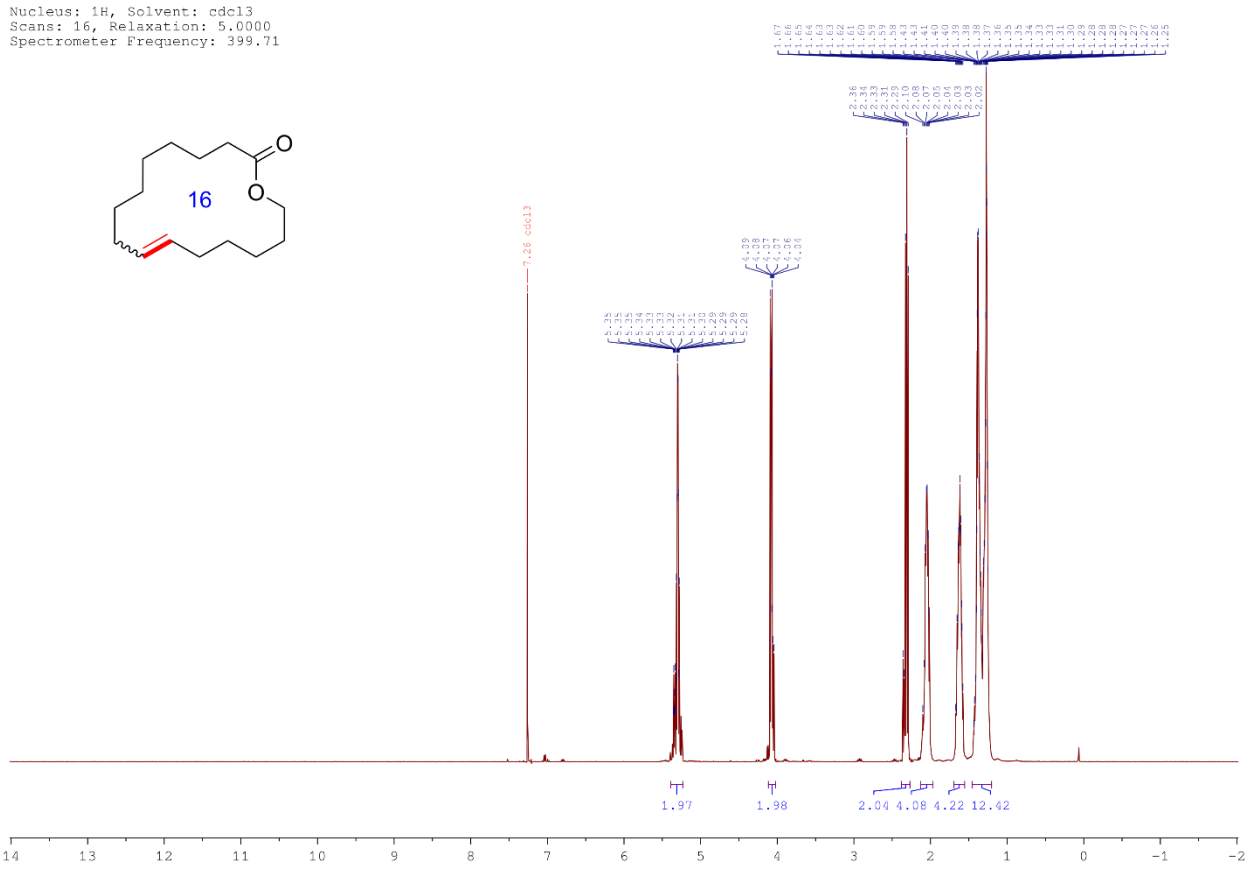
Nucleus: 1H, Solvent: cdcl3
Scans: 16, Relaxation: 5.0000
Spectrometer Frequency: 399.71

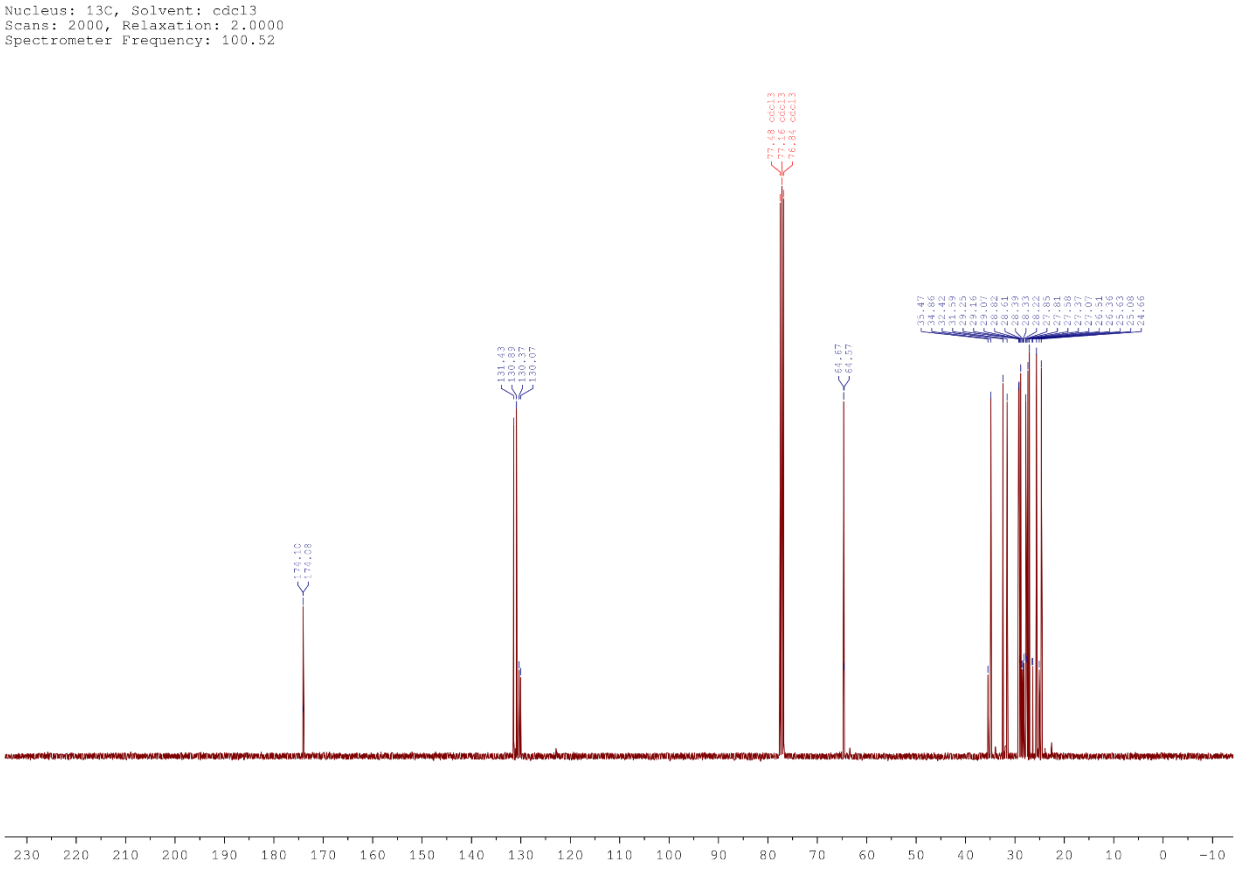


Nucleus: 13C, Solvent: cdcl3
Scans: 1000, Relaxation: 3.0000
Spectrometer Frequency: 100.52

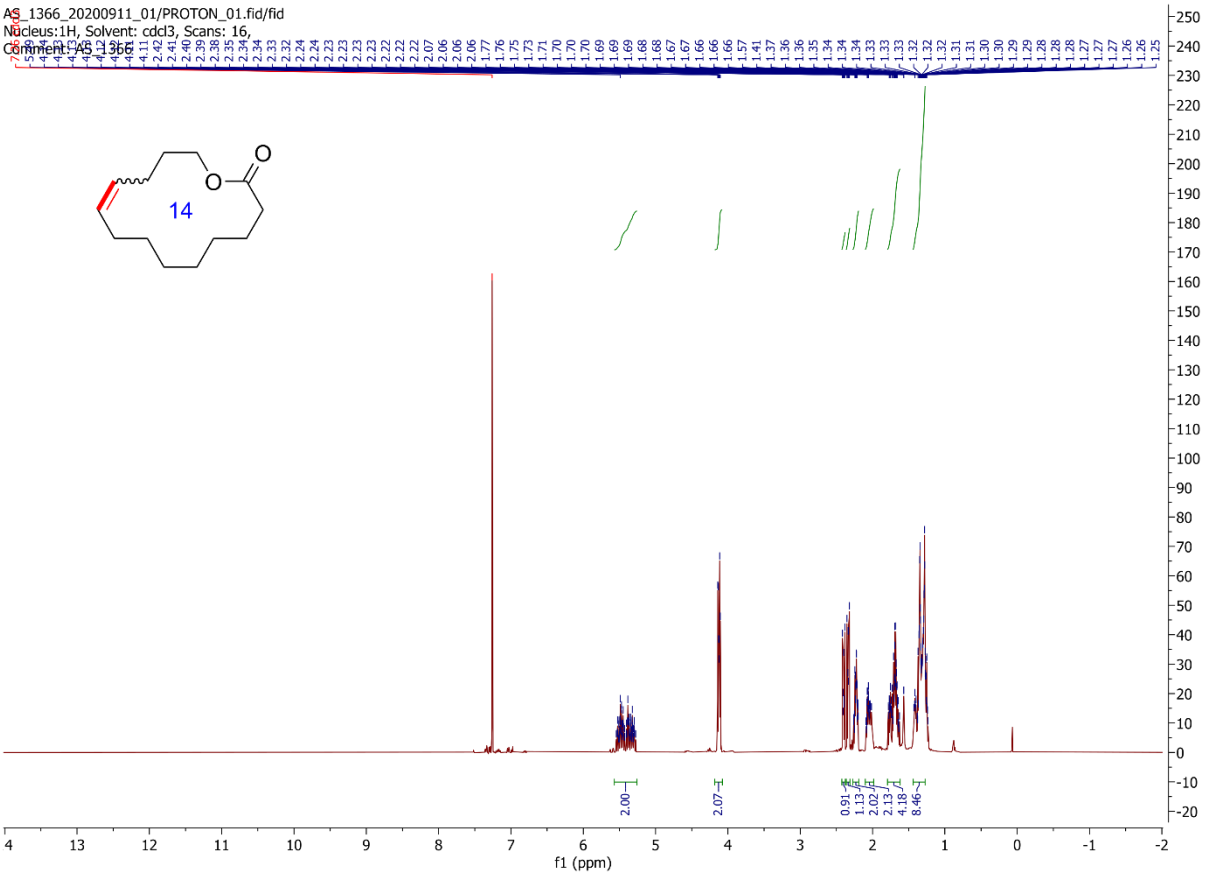


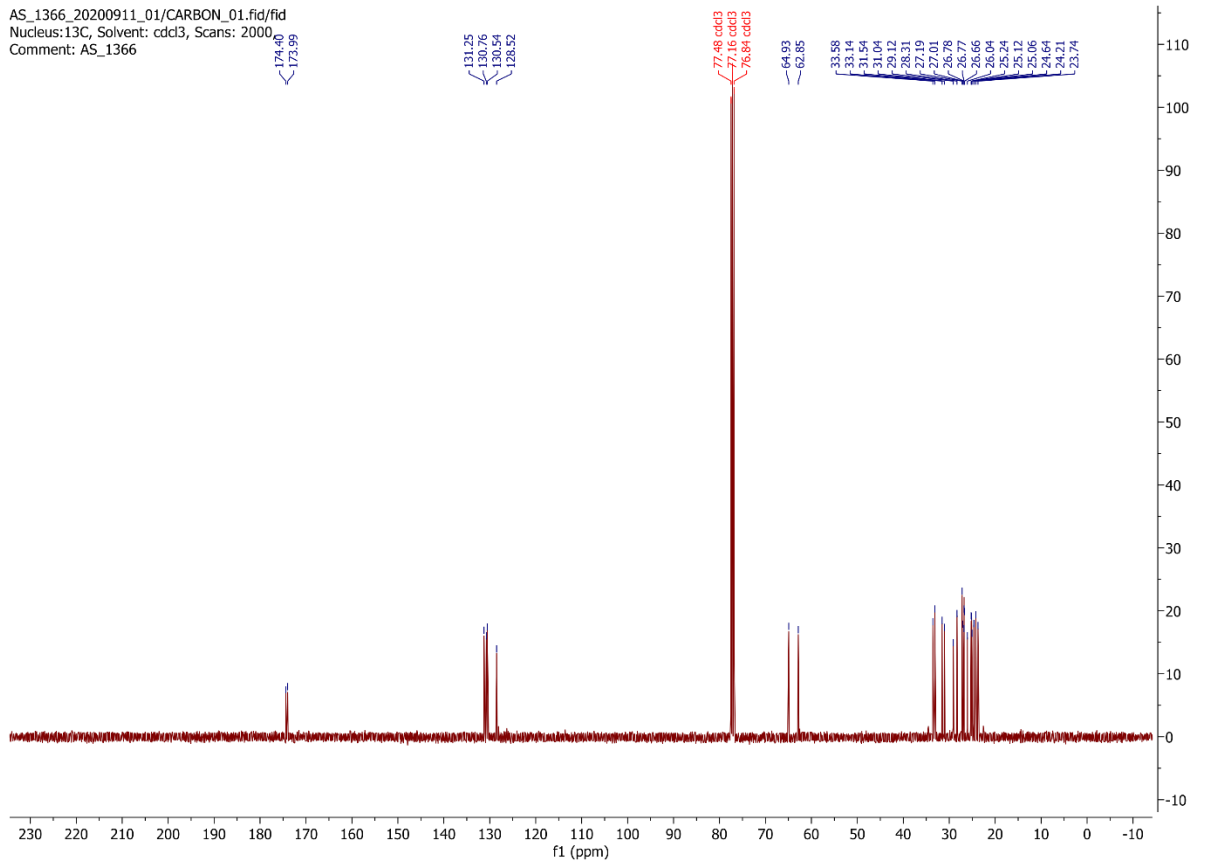
(E/Z)-oxacyclohexadec-10-en-2-one (P1)





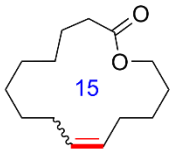
(E/Z)-oxacyclotetradec-10-en-2-one (P3)



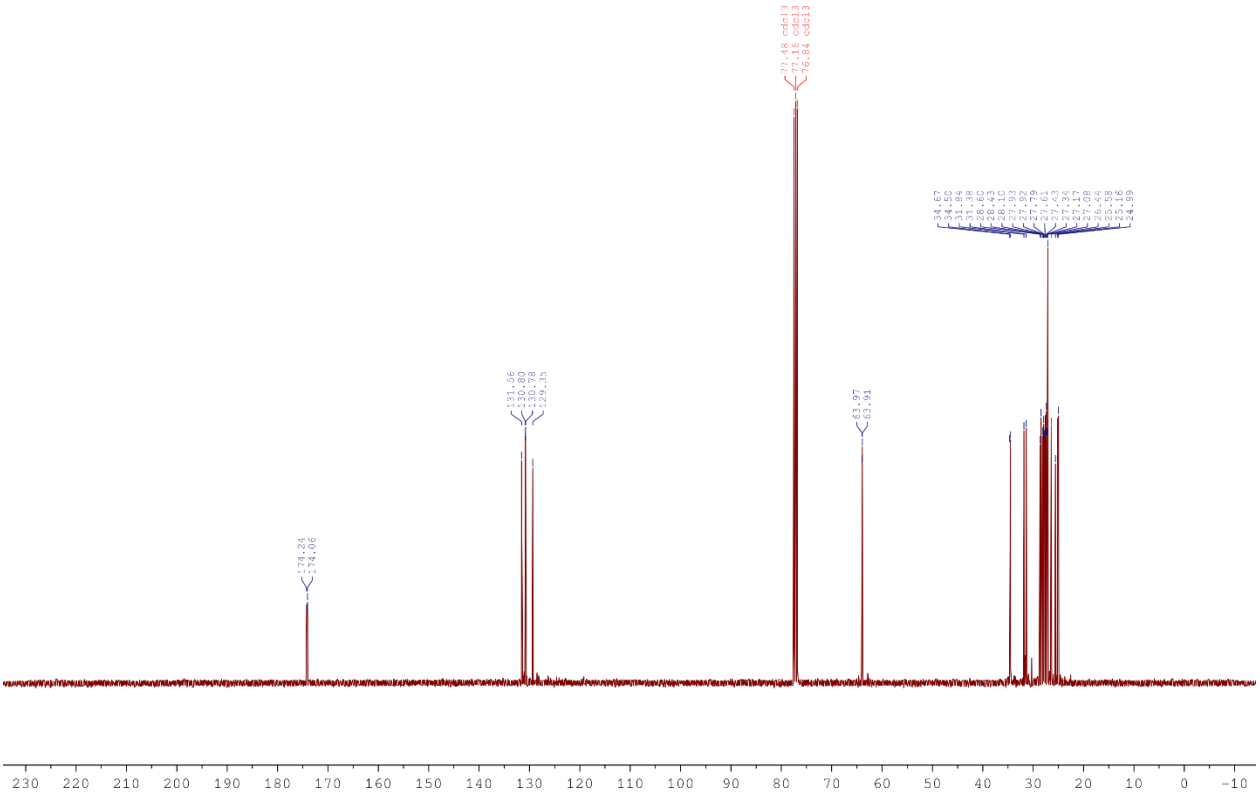


(E/Z)-oxacyclopentadec-10-en-2-one (P4)

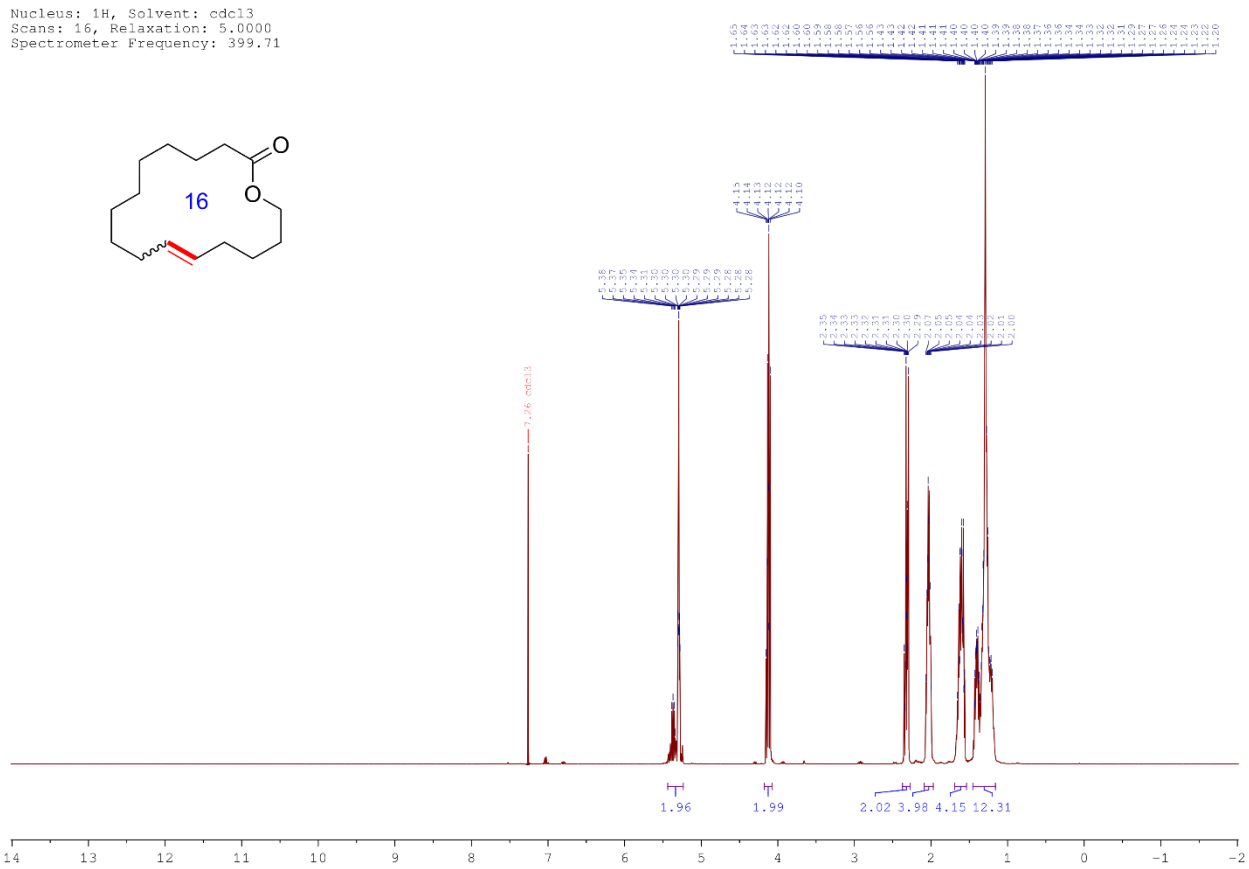
Nucleus: 1H, Solvent: cdcl3
Scans: 16, Relaxation: 5.0000
Spectrometer Frequency: 399.71

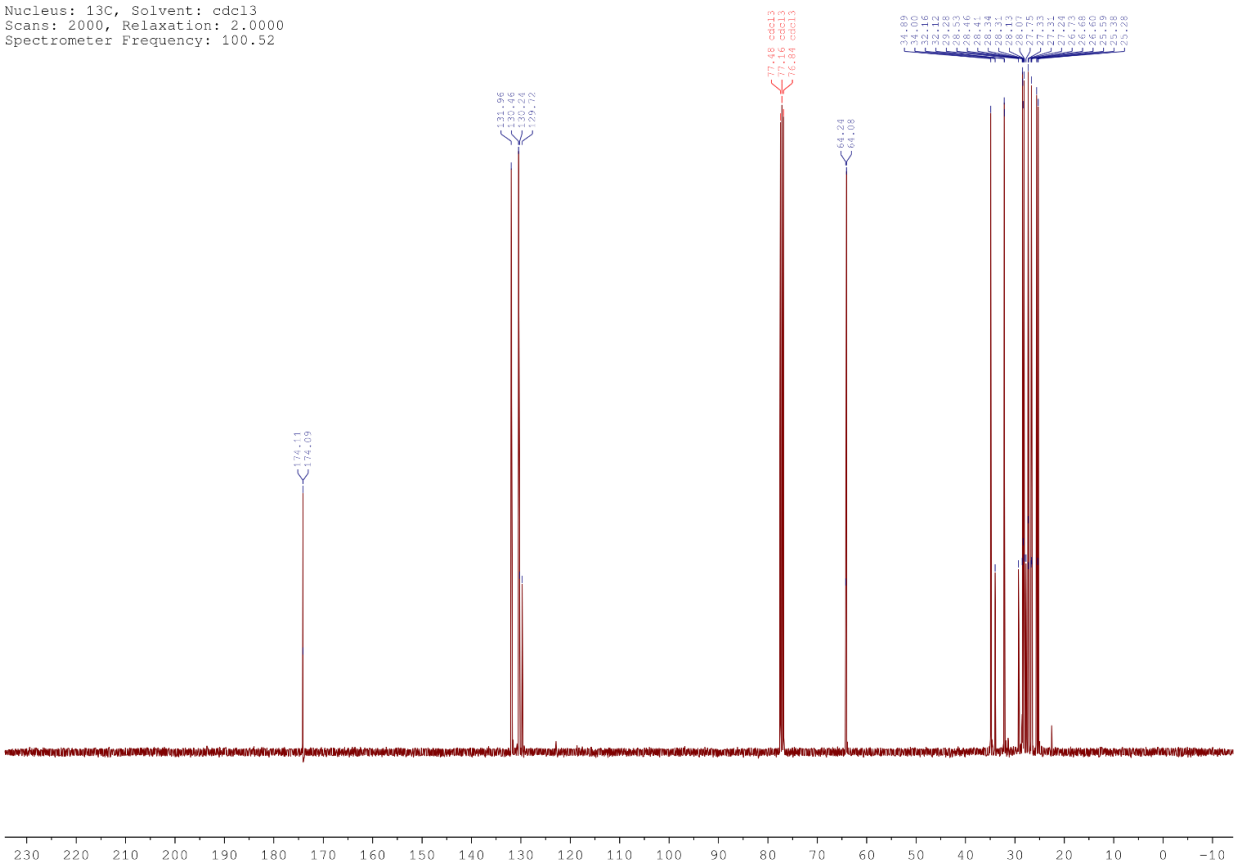


Nucleus: 13C, Solvent: cdcl3
Scans: 2000, Relaxation: 2.0000
Spectrometer Frequency: 100.52

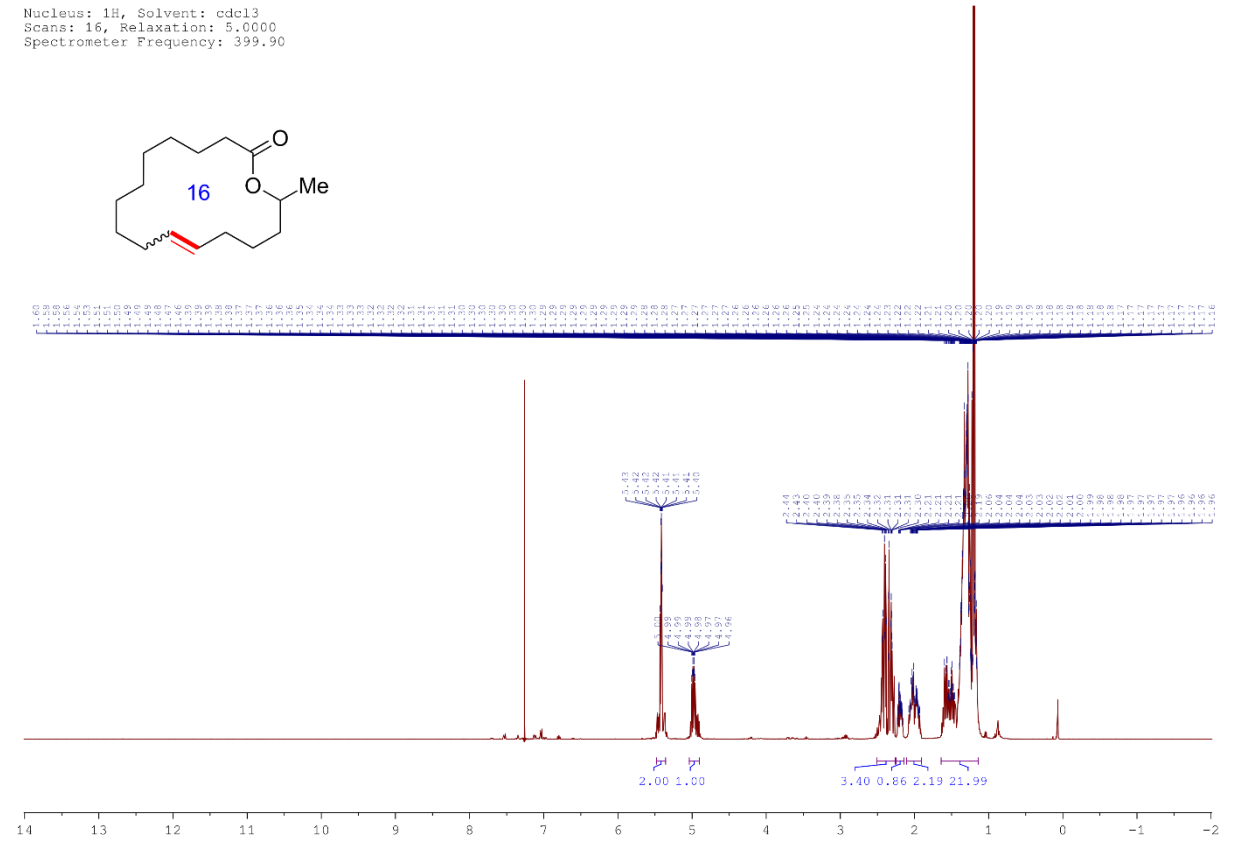


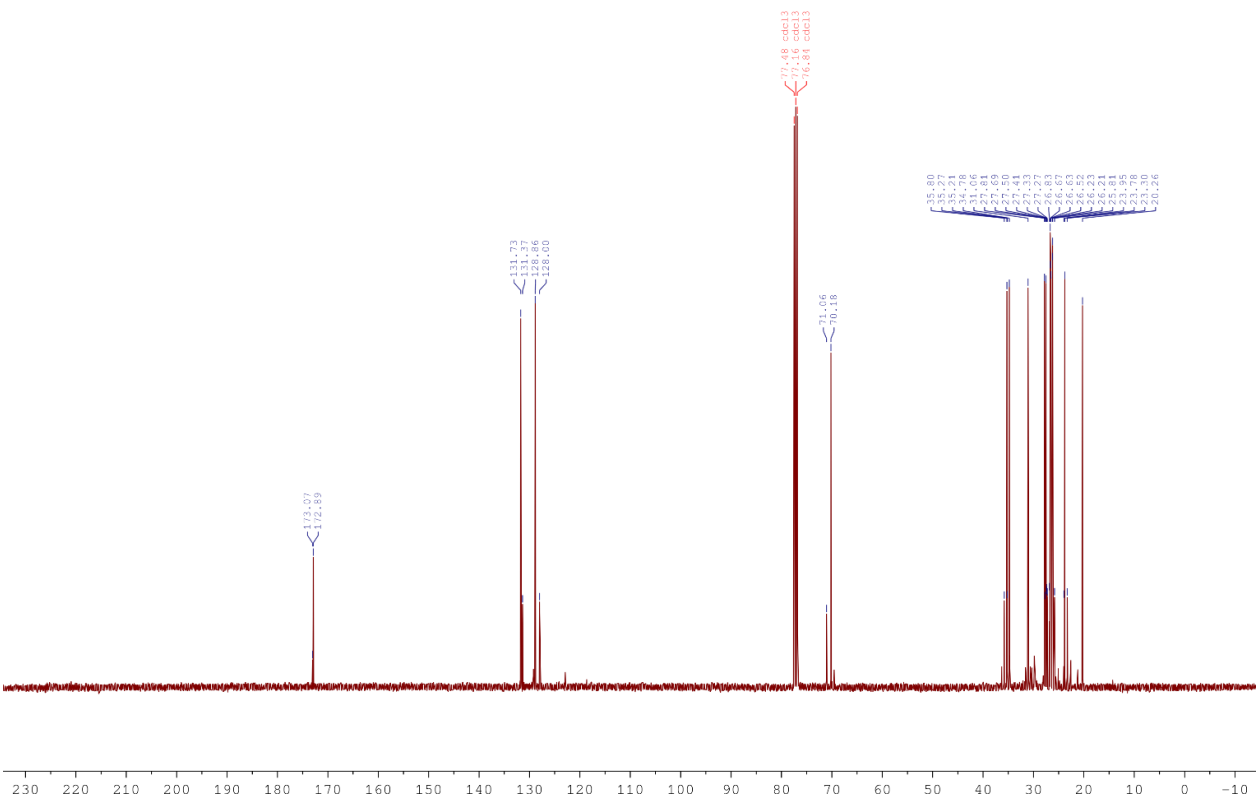
(E/Z)-oxacyclohexadec-11-en-2-one (P5)



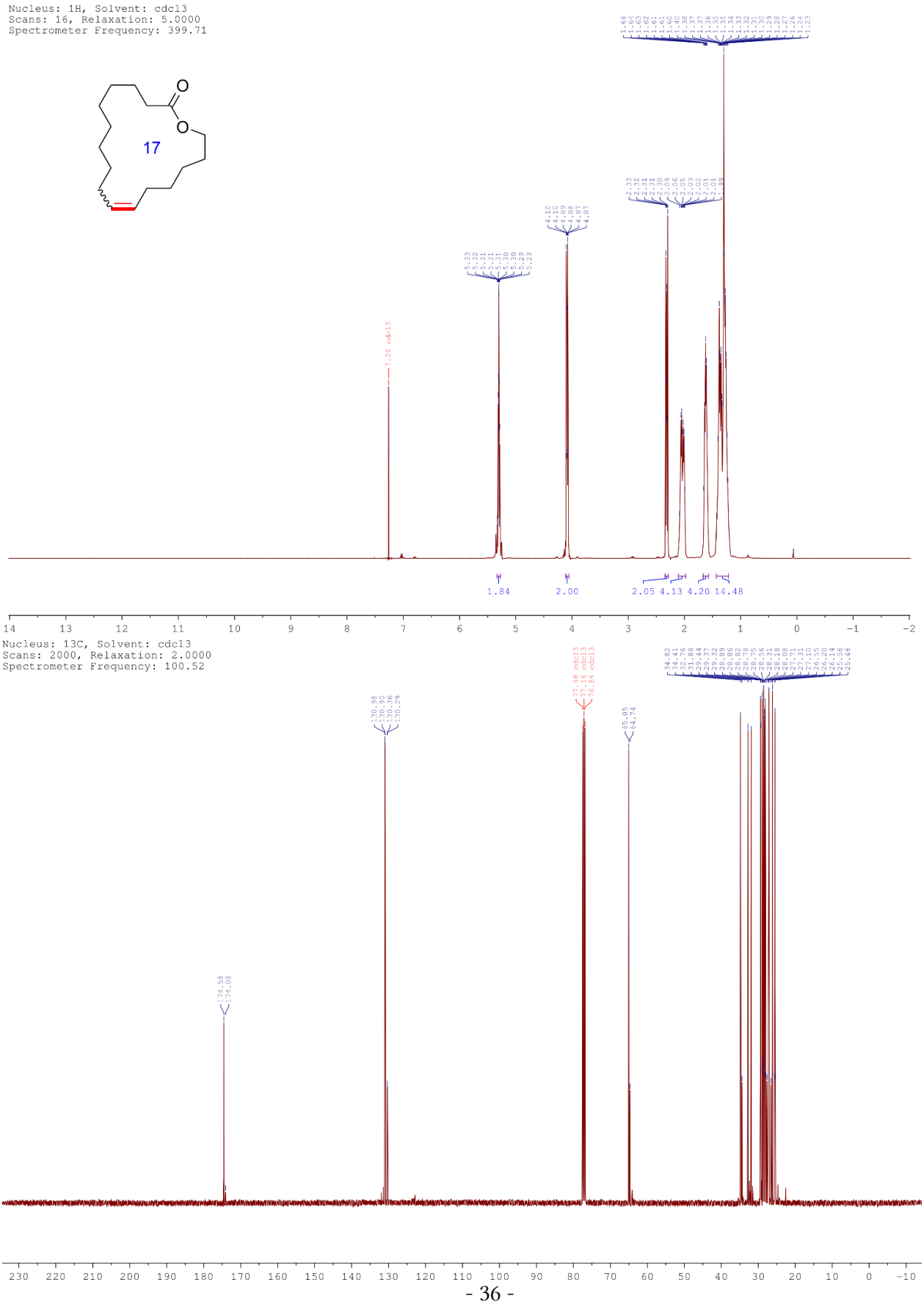


(E/Z)-16-methyloxacyclohexadec-11-en-2-one (P6)

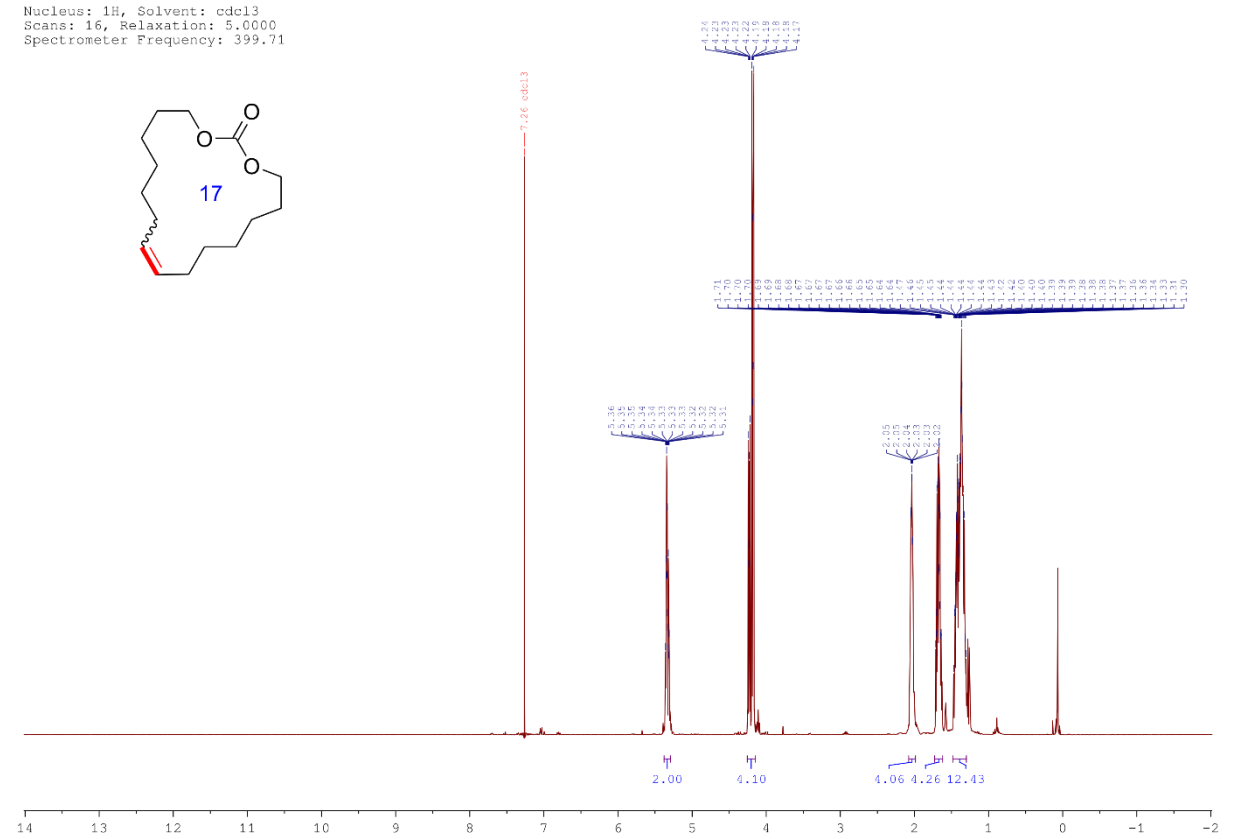


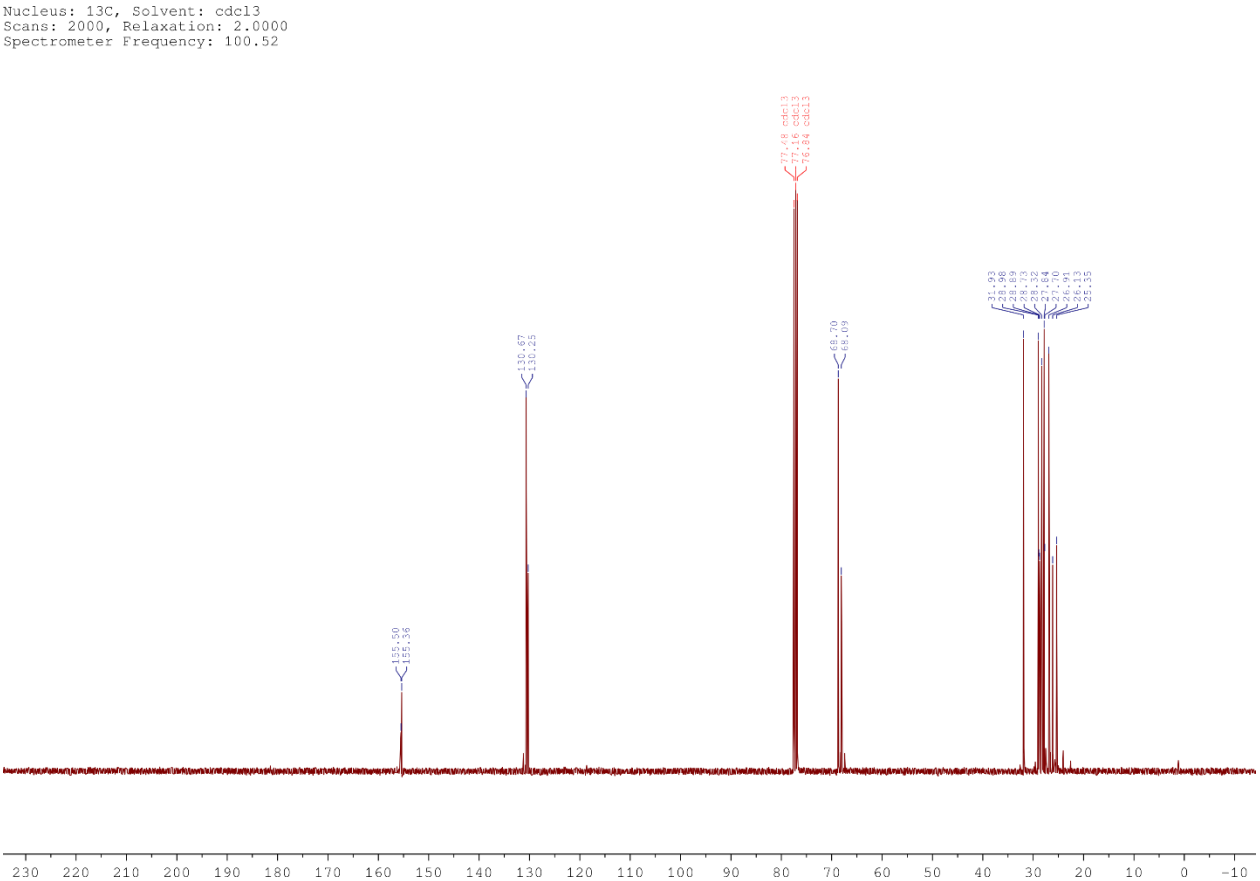


(E/Z)-oxacycloheptadec-11-en-2-one (P7)



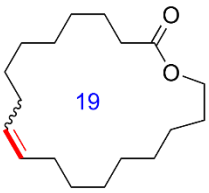
(E/Z)-1,3-dioxacycloheptadec-10-en-2-one (P8)



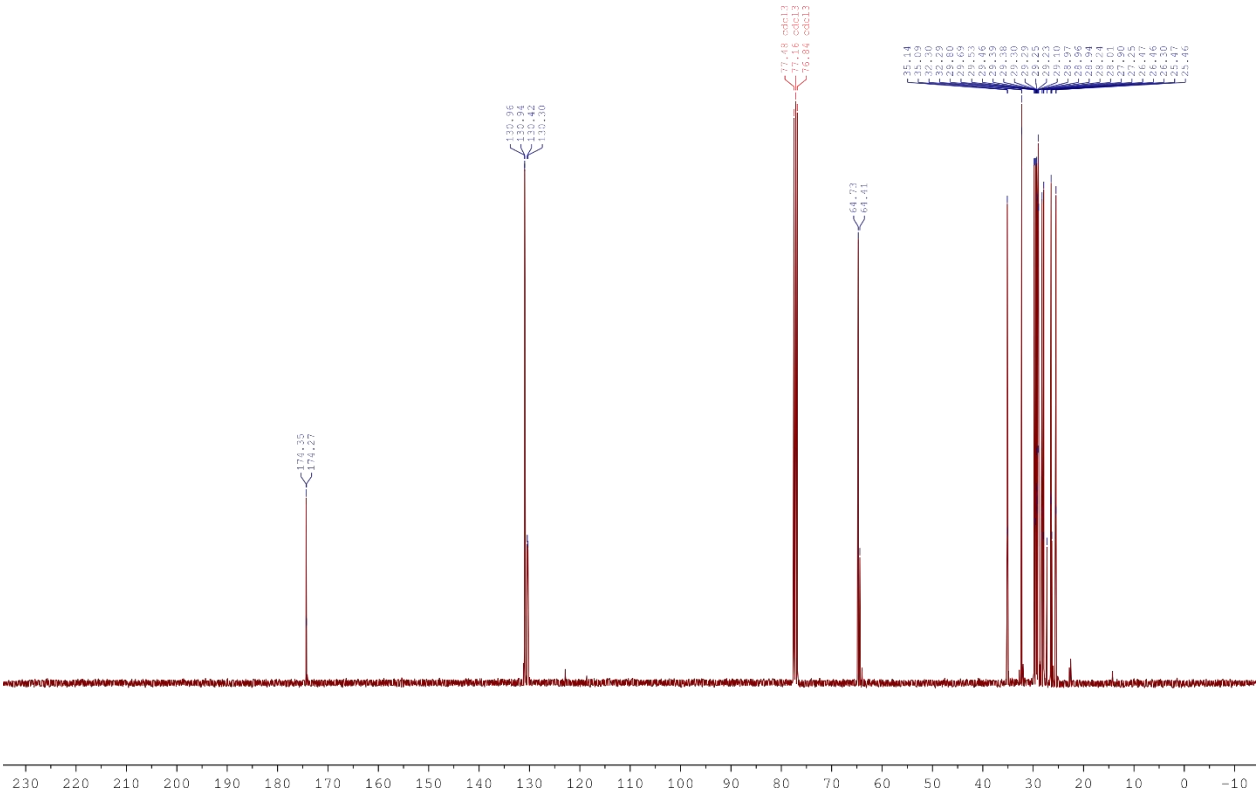


(E/Z)-oxacyclononadec-10-en-2-one (P9)

Nucleus: 1H, Solvent: cdcl3
Scans: 16, Relaxation: 5.0000
Spectrometer Frequency: 399.71



Nucleus: 13C, Solvent: cdcl3
Scans: 2000, Relaxation: 2.0000
Spectrometer Frequency: 100.52



References

1. Sytniczuk, A.; Dąbrowski, M.; Banach, Ł.; Urban, M.; Czarnocka-Śniadała, S.; Milewski, M.; Kajetanowicz, A.; Grela, K., At Long Last: Olefin Metathesis Macrocyclization at High Concentration. *J. Am. Chem. Soc.* **2018,** *140* (28), 8895-8901.
2. Sytniczuk, A.; Leszczyńska, A.; Kajetanowicz, A.; Grela, K., Preparation of Musk-Smelling Macrocyclic Lactones from Biomass: Looking for the Optimal Substrate Combination. *ChemSusChem* **2018,** *11* (18), 3157-3166.
3. Kadyrov, R., Low Catalyst Loading in Ring-Closing Metathesis Reactions. *Chem. Eur. J.* **2013,** *19* (3), 1002-1012.
4. Patrzałek, M.; Zasada, A.; Kajetanowicz, A.; Grela, K., Tandem Olefin Metathesis/α-Ketohydroxylation Revisited. *Catalysts* **2021,** *11* (6), 719.
5. Zasada, A., *MCs Thesis* **2018**.
6. Tsuji, J.; Hashiguchi, S., Metathesis reactions of unsaturated esters catalyzed by homogenous tungsten complexes. Syntheses of civetone and macrolides. *J. Organomet. Chem.* **1981,** *218* (1), 69-80.
7. Roschangar, F.; Sheldon, R. A.; Senanayake, C. H., Overcoming barriers to green chemistry in the pharmaceutical industry – the Green Aspiration Level™ concept. *Green Chem.* **2015,** *17* (2), 752-768.
8. Van Aken, K.; Strekowski, L.; Patiny, L., EcoScale, a semi-quantitative tool to select an organic preparation based on economical and ecological parameters. *Beilstein J. Org. Chem.* **2006,** *2*, 3.
9. Hagiwara, H.; Nakamura, T.; Okunaka, N.; Hoshi, T.; Suzuki, T., Catalytic Performance of Ruthenium-Supported Ionic-Liquid Catalysts in Sustainable Synthesis of Macrocyclic Lactones. *Helv. Chim. Acta* **2010,** *93* (1), 175-182.
10. Ahmed, T. S.; Grubbs, R. H., A Highly Efficient Synthesis of Z-Macrocycles Using Stereoretentive, Ruthenium-Based Metathesis Catalysts. *Angew. Chem. Int. Ed.* **2017,** *56* (37), 11213-11216.
11. Michrowska, A.; Wawrzyniak, P.; Grela, K., Synthesis of Macrocyclic Carbonates with Musk Odor by Ring-Closing Olefin Metathesis. *Eur. J. Org. Chem.* **2004,** *2004* (9), 2053-2056.
12. Ouadi, A.; Habold, C.; Keller, M.; Bekaert, V.; Brasse, D., Synthesis of new 123I-labeled free fatty acids analogues and first evaluation as potential tracers for SPECT imaging to elucidate fatty acid flux in mouse. *RSC Adv.* **2013,** *3* (41), 19040-19050.