Cyclic Alternating ROMP (CAROMP). Rapid Access to Functionalized Cyclic Polymers

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Materials and General Procedures. Coupling agents used were purchased from Advanced Chem Tech. (Louisville, KY) or PerSeptive Biosystems (Framingham, MA). Solvents, chemical reagents, cyclohexene **2**, and catalysts were obtained from Fisher Scientific, Inc. (Springfield, NJ) or Sigma-Aldrich (Milwaukee, WI). Cyclohexene-D_{10}, **2-D_{10}**, was purchased from CDN Isotope Inc. (Cat #: D0173). (H_2IMes)(3-Brpyr)$_2Cl_2$Ru=CHPh **3**[1] 1-cyclobutenecarboxylic acid and **1a**[2,3] were prepared according to the literature. CH_2Cl_2, benzene, Et_2O, THF and CH_3OH were dried in a GlassContour solvent pushstill system; pentane was used without further purification. All reactions were carried out under an Ar atmosphere in oven-dried glassware unless otherwise specified. Analytical thin layer chromatography (TLC) was performed on precoated silica gel plates (60F254), flash chromatography on silica gel-60 (230–400 mesh) and Combi-Flash chromatography on RediSep normal phase silica columns (Teledyne Isco, silica gel-60, 230–400 mesh). TLC spots were detected by UV light and by staining with phosphomolybdic acid (PMA). Inova400, Inova500 and Inova600 MHz NMR Instruments were used to perform NMR analysis. ^{1}H-NMR spectra are reported as chemical shift in parts per million (multiplicity, coupling constant in Hz, integration) and were acquired in $CDCl_3$ unless otherwise noted. ^{1}H-NMR data are assumed to be first order. High resolution mass spectra were obtained on Thermo Fisher Scientific LTQ Orbitrap XL ETD. For PDI (Polydispersity Index) determination, polymers (before flash column chromatography purification) were dissolved in THF (0.5 mg/mL). An aliquot (100 μL) of the polymer solution was injected and analyzed by gel permeation chromatography using a Phenogel column (300 x 7.80 mm, 5 μm, linear mixed bed, 0-40k MW range). Elution was performed at 0.7 mL/min with THF and detection at 220 nm and 254 nm at 30 °C. Narrowly dispersed polystyrene standards from Aldrich were used as molecular weight calibrants. The number average and weighted average molecular weights were calculated from the chromatogram.

1-Cyclobutenecarboxylic acid chloride. 1-Cyclobutenecarboxylic acid (1.02 mmol, 100 mg) was dissolved in 1.5 mL dry CH_2Cl_2. The solution was cooled to 0 ºC and oxalyl dichloride (4.08 mmol, 345 µL) was added. The temperature of the solution was raised to rt, and the mixture was allowed to react for 1 h. The solvent was evaporated to generate 1-cyclobutenecarboxylic acid chloride as a viscous oil that was used immediately without further purification.

Cyclobutene ester, 1b. 4-Chlorobutanol (1.36 mmol, 148 mg) and triethylamine (2.72 mmol, 379 µL) were dissolved in 1.0 mL dry CH_2Cl_2, and the solution was stirred at 0 ºC for 45 min before being added to a vial containing 1-cyclobutenecarboxylic acid chloride (1.02 mmol). The reaction mixture was stirred for 16 h at rt. The reaction mixture was diluted with CH_2Cl_2, washed three times with 5% $NaHCO_3$, followed by three washes with 1 N HCl and the CH_2Cl_2 dried over Na_2SO_4. The CH_2Cl_2 solution was concentrated by rotary evaporation, and then purified by flash column chromatography (60% CH_2Cl_2/pentane) to yield **1b** as a colorless oil (98 mg, 38%). ^{1}H-NMR (500 MHz) δ 6.73 (s, 1H), 4.11 (t, J=6.0 Hz, 2H), 3.54 (t, J=6.0 Hz, 2H), 2.68 (t, J=6.0 Hz, 2H), 2.43 (m, 2H), 1.81 (m, 4H). ^{13}C NMR (100 MHz) δ 162.27, 146.69, 138.71, 63.31, 44.58, 29.31, 29.20, 27.20, 26.20. HRMS (ESI) calcd for $C_9H_{14}ClO_2$ $[M+H]^+$ 189.0677; found 189.0674.

General Procedure for NMR AROMP Reactions. An NMR tube was evacuated under high vacuum for 15 min, and then was purged with Ar for another 15 min. Under an Ar atmosphere, a solution of monomer **A** (1-cyclobutenecarboxylate ester) in CD_2Cl_2 (300 µL) was added to the NMR tube. Then a solution of ruthenium precatalyst in CD_2Cl_2 (300 µL) was added to the NMR tube. After complete mixing of the solution, the NMR tube was spun for 4-30 min at 25 °C in the NMR spectrometer (400, 500 or 600 MHz) until the precatalyst had reacted. Then monomer **B** (cyclohexene derivatives) in CD_2Cl_2 (300 µL) was added to the NMR tube. After all of monomer **A** was converted, the reaction was quenched with ethylvinyl ether (50 µL) and was stirred for 1 h.

Cyclic (1a-2-D_{10})$_n$ + cyclic (1a-2-D_{10})$_n$1a. Cyclobutene **1a** (0.12 mmol), cyclohexene **2-D_{10}** (0.24 mmol) and **4** (0.006 mmol) were allowed to react for 9 h to reach 89% completion. The solvent was evaporated and the residue was purified by flash column chromatography (acetone:CH_2Cl_2/3:97) to provide polymer **cyclic *(1a-2-D_{10})$_n$ + cyclic (1a-2-D_{10})$_n$1a*** (11 mg, 44%). ^{1}H-NMR (500 MHz, CD_2Cl_2) δ 6.79 (m, 2H), 5.40 (s, 18H), 3.71 (s, 60H), 2.34-2.07 (m, 80H).

Cyclic (1b-2)$_n$ + cyclic (1b-2)$_n$1b. Cyclobutene **1b** (0.15 mmol), cyclohexene **2** (0.30 mmol) and **4** (0.006 mmol) were allowed to react for 5 h at rt to reach 90% completion. The solvent was evaporated, and the residue was purified by flash column chromatography (acetone:CH_2Cl_2/5:95) to provide **cyclic (1b-2)$_n$ + cyclic (1b-2)$_n$1b** (16 mg, 39%). ^{1}H NMR (600 MHz) δ 6.75 (b, 25H), 5.39 (b, 30H), 4.16 (b, 50H), 3.57 (b, 50H), 2.48-1.98 (164H), 1.85 (b, 100H), 1.49-1.37 (b, 64H). *M_n (PSS):* 1327. *PDI:* 2.1.

Cyclic (1NMe$_3$-2)$_n$ + cyclic (1NMe$_3$-2)$_n$1NMe$_3$. **Cyclic (1b-2)$_n$ + cyclic (1b-2)$_n$1b** and aqueous trimethylamine (45% wt, 1 mL) were mixed in acetonitrile (2 mL). The solution was heated to 70 °C for 4 h. The solvent was evaporated to provide **cyclic (1NMe$_3$-2)$_n$ + cyclic (1NMe$_3$-2)$_n$1NMe$_3$** as a brown powder. ^{1}H NMR (600 MHz, D_2O) δ 6.89 (b, 25H), 5.42 (b, 30H), 4.28 (s, 50H), 3.42 (s, 50H), 3.19 (b, 225H), 2.42-1.26 (m, 328H).

References

(1) Love, J. A.; Morgan, J. P.; Trnka, T. M.; Grubbs, R. H., A practical and highly active ruthenium-based catalyst that effects the cross metathesis of acrylonitrile. *Angew. Chem. Int. Ed.* **2002,** 41, 4035-4037.

(2) Lee, J. C.; Parker, K. A.; Sampson, N. S., Amino acid-bearing ROMP polymers with a stereoregular backbone. *J. Am. Chem. Soc.* **2006,** 128, 4578-4579.

(3) Campbell, A.; Rydon, H. N., The synthesis of caryophyllenic acid. *J. Chem. Soc.* **1953**, 3002-3008.

Table S1. CAROMP of 1-substituted cyclobutene esters with cyclohexenes using Hoveyda-Grubbs II catalyst, 4.[a]

A	B	[Ru] (M)	[A]:[B]:[Ru]	Rxn time (h)	Prod.	% conv[b]
1a	**2-D_{10}**	0.01	20:40:1	9	**cyclic (1a-2-D_{10})$_n$ +**	89[c]
1b	**2**	0.01	25:50:1	4	**cyclic (1a-2-D_{10})$_n$1a cyclic (1b-2)$_n$ + cyclic (1b-2)$_n$1b**	92[d]

[a]Both AROMP reactions were monitored by ^{1}H-NMR spectroscopy. [b]Percent conversion determined by integration of ^{1}H-NMR spectra. [c]Reaction was performed in CD_2Cl_2 at rt. [d]Reaction was performed in $CDCl_3$ at 50 ºC.

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4	Owner	
5	Solvent	CD2Cl2
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8	Modification Date	
9	Temperature	25.0
10	Number of Scans	56
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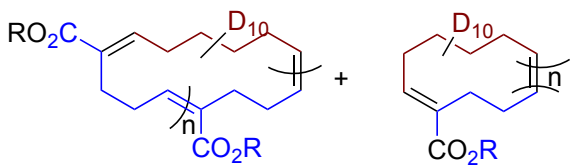
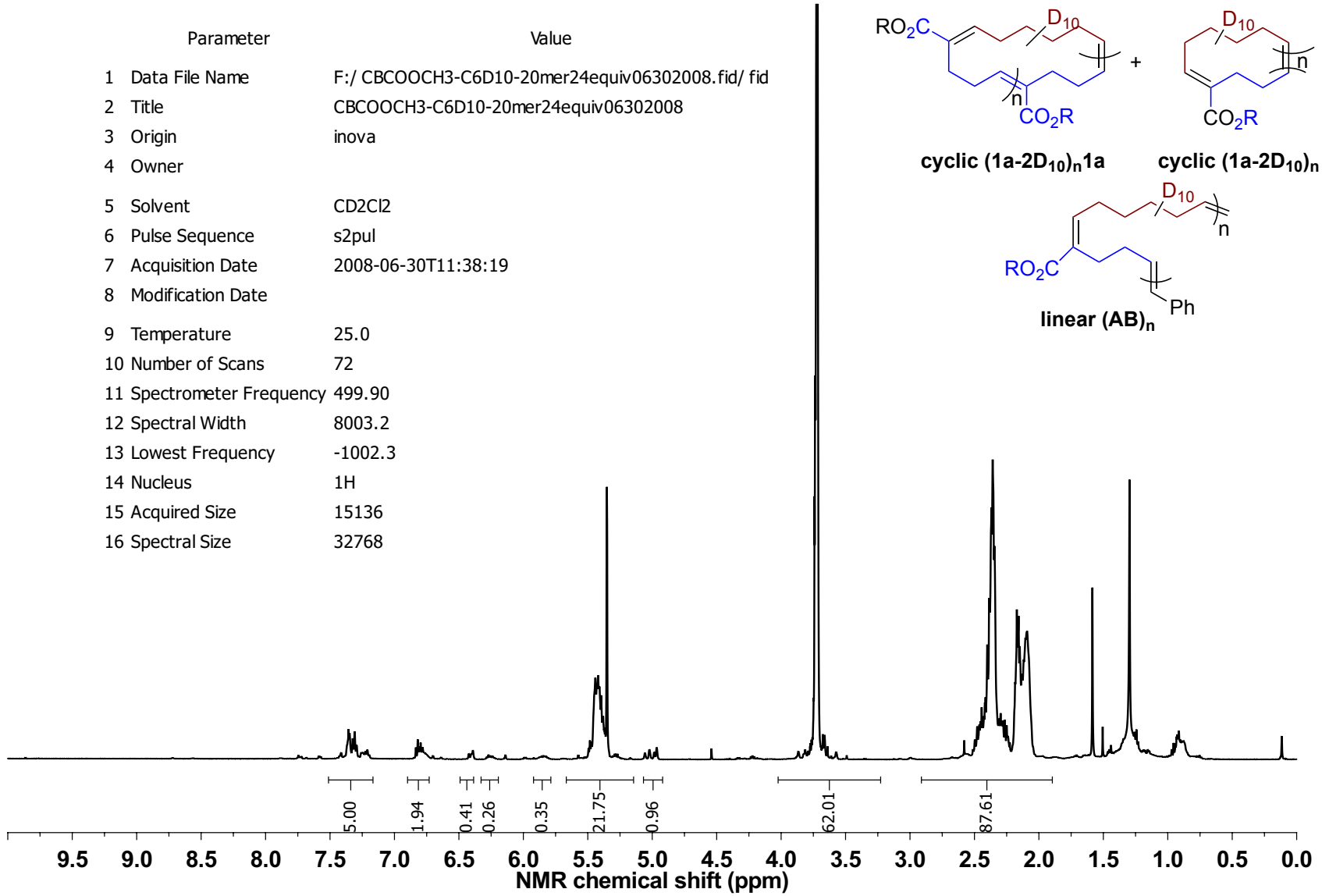
12	Spectral Width	8000.0
13	Lowest Frequency	-1001.2
14	Nucleus	1H
15	Acquired Size	15136
16	Spectral Size	32768

Figure S1: ^{1}H-NMR spectrum of **cyclic (1a-2-D10)$_n$1a** + **(1a-2-D10)$_n$** prepared from Hoveyda-Grubbs II catalysis



cyclic (1a-2D$_{10}$)$_n$1a **cyclic (1a-2D$_{10}$)$_n$**

Figure S2: ^{1}H-NMR spectrum of **linear/cyclic (1a-2-D10)$_n$1a + (1a-2-D10)$_n$** prepared from Grubbs III catalysis



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5	Author	
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8	Pulse Sequence	s2pul
9	Number of Scans	96
10	Receiver Gain	44
11	Relaxation Delay	1.0000
12	Pulse Width	0.0000
13	Acquisition Time	1.8920
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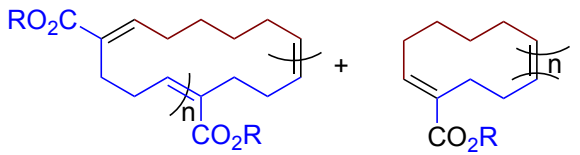
15	Modification Date	2010-02-22T10:25:48
16	Spectrometer Frequency	599.72
17	Lowest Frequency	-1001.2
18	Nucleus	1H

Figure S3: ^{1}H-NMR spectrum of **cyclic (1b-2)$_n$1b + (1b-2)$_n$**



cyclic (1b-2)$_n$1b, R = $CH_2CH_2CH_2CH_2Cl$

cyclic (1b-2)$_n$ R = $CH_2CH_2CH_2CH_2Cl$

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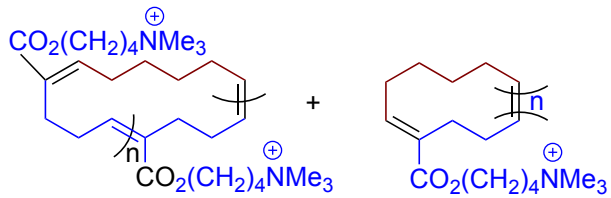
15	Modification Date	2010-02-24T07:09:04
16	Spectrometer Frequency	599.72
17	Lowest Frequency	-908.5
18	Nucleus	1H

Figure S4: ^{1}H-NMR spectrum of **cyclic (1NMe$_3$-2)$_n$1NMe$_3$ + (1NMe$_3$-2)$_n$**



cyclic (1NMe$_3$-2)$_n$1NMe$_3$** **cyclic (1NMe$_3$-2)$_n$

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8	Modification Date	
9	Temperature	25.0
10	Number of Scans	16
11	Spectrometer Frequency	599.72
12	Spectral Width	8000.0
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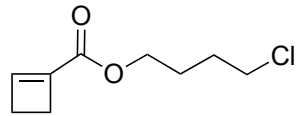
14	Nucleus	1H
15	Acquired Size	15136
	Spectral Size	32768

^{1}H-NMR spectrum of **1b**



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12	Spectral Width	25000.0
13	Lowest Frequency	-2991.4
14	Nucleus	13C
15	Acquired Size	29984
16	Spectral Size	65536

^{13}C-NMR spectrum of **1b**