Tandem Development of Aqueous Indium Chemistry and Ring-Closing Metathesis as a General Route to Fused-Ring α-Methylene-γ-butyrolactones

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Abstract: A program directed toward a general synthesis of α-methylenelactones *cis*- or *trans*-fused to larger rings is reported. The protocol originates with two ω-unsaturated aldehydes of the same or different chain length. One of these is initially transformed by way of the Baylis–Hillman reaction into a functionalized allylic bromide. Merger of the two building blocks is subsequently accomplished in aqueous solution with powdered indium metal serving as the initiator. Once the lactone ring is crafted, the end products are generated by application of ring-closing metathesis. The central issues surrounding this final step are the effects of the stereochemical disposition of the side chains, the consequences of ring strain, and the locus of the double bonds on cyclization efficiency.

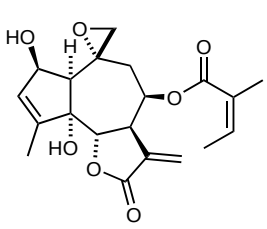
Keywords: alkenes; cyclization; indium; lactones; metathesis

Introduction

The field of synthetic organic chemistry undergoes refinement, gains momentum, and matures as a direct consequence of the discovery of new reagents capable of performing specific chemical transformations efficiently. Organoindium chemistry is an area that has elicited considerable interest in the recent past because of the recognition that selected carbon-carbon bond-forming processes can be implemented in high yield with water as the reaction medium.[1] These discoveries have had a significant impact on the area of green chemistry and more specifically on the quest for alternative synthetic pathways that result in pollution prevention. Similarly, the development of new reagents capable of accomplishing ring-closing metathesis under notably mild conditions has provided the organic chemist with a powerful tool for molecular constructions.[2]

While both methodologies have *individually* been responsible for numerous advances in synthetic chemistry during the past decade,[3,4] there has to our knowledge appeared no report of their use in a tandem manner. In this context, we saw an opportunity to merge these rapidly expanding technologies so as to achieve a direct, highly convergent route to α-methylene-γ-lactones fused to medium and large rings.[5] Compounds of this general class occur widely in nature.[6] The ability of the unsaturated lactone functionality to act as a highly reactive Michael acceptor has brought forth the realization of its crucial role as a physiologically important building block.[7] Often this functionality is found fused to six- to fourteen-membered carbocyclic rings. Included among the many complex structures are euparotin (**1**),[8] elephantopin (**2**),[9] heliangine (**3**),[10] and kericembranolide A (**4**).[11]

Understandably, many methods have been developed for proper installation of an α-methylene structural unit onto a γ-lactone ring.[12] Other more direct approaches



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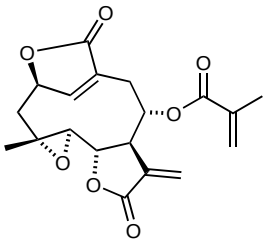

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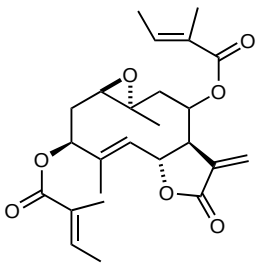

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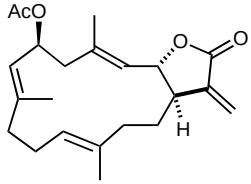

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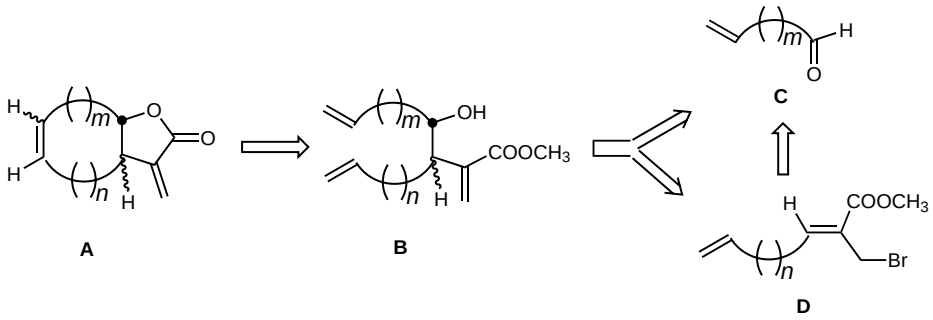
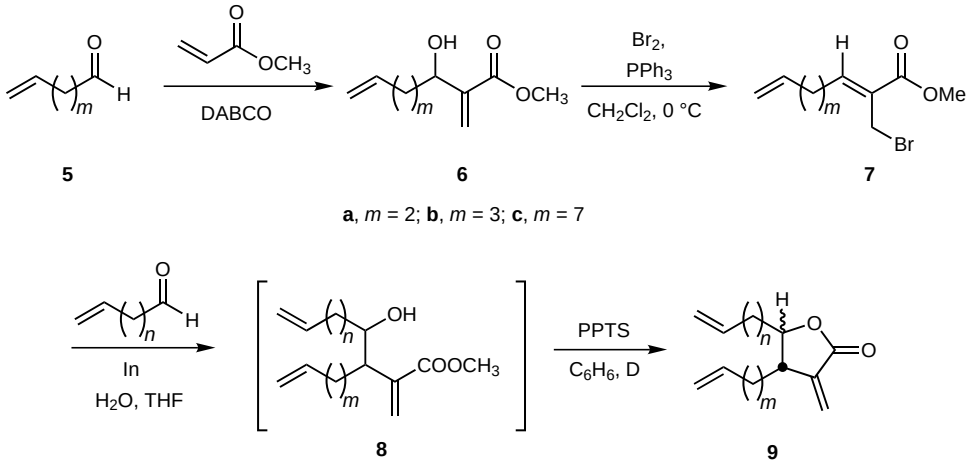


Scheme 1.

have also been devised.[13] Nevertheless, a simpler tactic would clearly be desirable. The new strategy is founded on the interrelationship of the structural elements resident in **A** to those present in **B** (Scheme 1). For this tactic to be workable, **B** must be capable of efficient two-fold cyclization, and the interconnective carbon-carbon bond between the upper and lower segments of this hydroxy ester conveniently installed. A notable and important aspect of this retrosynthetic plan is its convergency. Thus, our intent was to craft both building blocks from the same aldehyde **C**.

Results and Discussion

The route starts by Baylis–Hillman coupling[14] of aldehydes **5** to methyl acrylate in the presence of DABCO (Scheme 2) and progresses forward by conversion of **6** to bromide **7**, a transformation that invariably operates with allylic rearrangement[15] and gives rise only to the thermodynamically favored *Z*-isomer.[16] The condensation of **5** with **7**, under conditions where either $m = n$ or $m \neq n$, is most efficiently carried out with powdered indium metal in 50%



compound	*m*	*n*	*cis/trans* ratio	two-step yield [%]
9a	2	2	3:2	74
9b	3	3	3:2	67
9c	2	7	3:2	40
9d	3	7	3:2	72
9e	7	2	3:2	60
9f	7	3	3:2	70
9g	7	4	3:2	69
9h	7	5	3:2	64

Scheme 2.

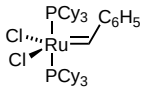


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Figure 1.

aqueous tetrahydrofuran. Good to excellent yields were realized when vigorous stirring was maintained at room temperature for one hour. At high (1 M) bromide concentration, the 1,2-addition leading to **8** proved to be totally γ-regioselective, but not diastereoselective.[17] In fact, the *cis/trans* ratio in all eight examples was invariably 3:2. In order to facilitate matters, the pairs of hydroxy esters **8** were directly subjected to the action of pyridinium *p*-toluenesulfonate in refluxing benzene in order to effect cyclization to the chromatographically separable *cis*- and *trans*-lactones **9**. The distinction between the two isomers was accomplished on the basis of NOE studies. In line with expectation, the effect for *cis*-disposed ring protons was significantly larger than that observed for the more distal *trans* arrangement.

The standardized protocol utilized for all ring-closing metatheses involved 6 mM solutions of **9** in CH_2Cl_2. After the introduction of 30 mol percent of ruthenium catalyst **10** (Figure 1) under N_2, each reaction mixture was heated at 50 °C for 24 h. Under these conditions neither isomer of **9b**, **9c**, or **9e** underwent cyclization, whereas *cis*-**9a** was transformed into **11** in only 11% yield at 60% conversion. All of the other substrates examined were smoothly and efficiently converted into cyclized products (Table 1). A mixture of *E*- and *Z*-isomers was generated in all of the successful case studies, except for the cyclooctene examples **11** and **12**. In no instance was there any indication of possible involvement of the conjugated double bond in the metathesis process despite its favorable logistical position in several instances.

For the metathesis products **13** – **20**, it was conveniently possible to distinguish the *E*-isomers on the basis of the narrow chemical shift difference exhibited by their two olefinic protons, usually a narrow multiplet near $\delta = 5.5$ in $CDCl_3$. In contrast, the *Z*-isomers are characterized by two more widely spaced multiplets ($\Delta\delta \approx 0.2$ ppm).[18]

Table 1. Catalytic ring-closing metathesis results.

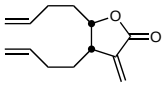
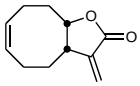
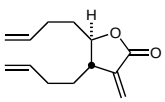
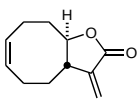
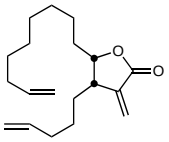
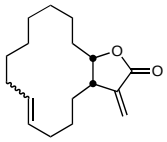
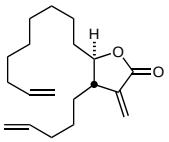
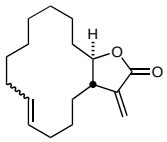
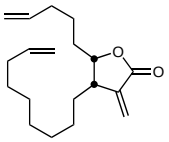
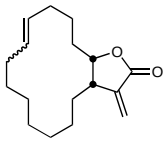
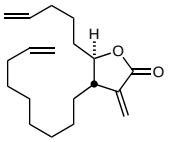
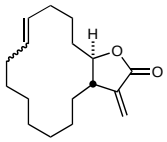
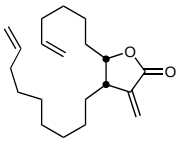
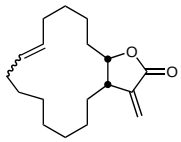
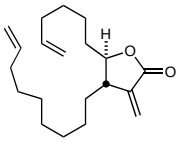
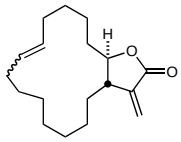
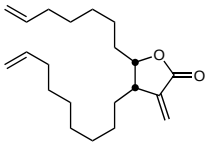
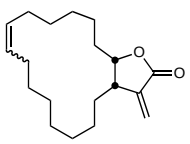
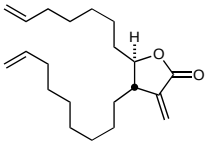
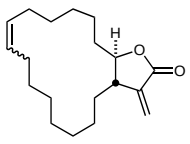
substrate	product	*E/Z* ratio	yield [%]
 *cis*-**9a**	 **11**	0:100	11[a]
 *trans*-**9a**	 **12**	0:100	65[b]

Table 1. Continued.

substrate	product	*E/Z* ratio	yield [%]
 *cis*-**9d**	 **13**	10:1	68
 *trans*-**9d**	 **14**	4:1	72
 *cis*-**9f**	 **15**	13:1	72
 *trans*-**9f**	 **16**	7:1	67
 *cis*-**9g**	 **17**	6:1	71
 *trans*-**9g**	 **18**	3:1	70
 *cis*-**9h**	 **19**	3:1	72
 *trans*-**9h**	 **20**	3:1	71

[a] Under the reaction conditions employed, unreacted *cis*-**9a** was recovered to the extent of 39%.

[b] N. Bensel, H. Marschall, P. Weyerstahl, *Chem. Ber.* **1975**, *108*, 2697.

In line with general precedent,[19] the ring-closing metathesis protocol is not well suited to the formation of *cis*-fused cyclooctenes. Although *cis*-**9a** does not react well, its *trans*-isomer behaves normally and delivers **12** with the usual efficiency. Therefore, the small increase in ring strain associated with the formation of **11** translates into an unfavorable K_{eq} value for the closure of *cis*-**9a**. Medium-sized rings are often more demanding both in terms of catalysts employed and the reaction conditions necessary to achieve good yields. The experimental conditions adopted in this study reflect a good compromise position.

Ring strain contributions do have an effect on the ease of ring closure of bifunctional chain molecules and deserves full consideration in the evaluation of the present results. Galli and Mandolini have examined this matter extensively in general terms and have found that the role of ring strain on the ease of ring closure calls for the strain energies of the transition states to be compared to the strain energies of the ring products.[20] The maximum effects are made evident when the ring size is between 8 and 11.[21,22] Thus, the failure of either isomer of **9b**, **9c**, and **9e** to undergo cyclization is not unexpected in light of the added stereochemical demands brought on by the lactone ring fusion and the increased eclipsing interactions operational in the targeted bicyclic molecules.

A notable feature of those cyclizations that provide 14-membered rings is the more elevated *E/Z* ratio observed when a *cis*-lactone (e.g., **13** and **15**) is involved. The locus of the double bond in the carbocyclic ring also holds importance. This heightened stereoselectivity is construed to be a reflection of the more elevated barrier to ring closure in the *cis* series due to ring strain. In line with these expectations, the more pronounced medium-ring strain effect operational as the ring size is reduced precludes metathesis at the 13-membered ring level independent of *cis/trans* side chain stereochemistry and the relative positioning of the double bonds (as in **9c** and **9e**). At the 15-membered ring level, more equitable *E/Z* distributions approaching 3:1 are the norm (as in **17 – 20**), indicating that the stereochemistry of the lactone precursor is no longer sterically discriminating.

Conclusion

In summary, a general procedure for the synthesis of α-methylene lactones *cis*- or *trans*-fused to larger rings is described and the existence of certain limitations has been made clear. The convenient approach originates with two ω-unsaturated aldehydes of the same or different chain length. These penultimate intermediates are formed by the application of organoindium chemistry in water. Subsequent to the completion of this investigation, water-soluble metathesis catalysts have been developed[23] and efficient means for implementing the Baylis–Hillman reaction in aqueous media have been reported.[24] Consequently, the prospects for carrying out all three steps in an aqueous environment looms on the horizon.

Experimental Section

General Methods

The column chromatographic separations were performed with Woelm silica gel (230 – 400 mesh). Solvents were reagent grade and in most cases dried prior to use. The purity of all compounds was shown to be $>95\%$ by TLC and high field ^{1}H (300 MHz) and ^{13}C NMR (75 MHz). The high-resolution mass spectra were obtained at The Ohio State University Campus Chemical Instrumentation Center. Elemental analyses were performed at Atlantic Microlab, Inc., Norcross, GA.

Prototypical Baylis–Hillman Coupling: 3-Hydroxy-2-methylenehept-6-enoic Acid Methyl Ester (6a)

A mixture of 4-pentenal (1.91 g, 22.7 mmol), methyl acrylate (3.07 mL, 34.1 mmol) and DABCO (637 mg, 5.68 mmol) was vigorously stirred for 21 days at room temperature. After the removal of excess methyl acrylate under reduced pressure, the residue was chromatographed on silica gel (elution with 20% ethyl acetate in petroleum ether) to furnish **6a** as a colorless oil; yield: 2.37 g (61%). IR (neat): $\nu = 3462$, 1718, 1640 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.22$ (s, 1H), 5.89 – 5.75 (m, 1H), 5.80 (s, 1H), 5.03 (d, $J = 15.6$ Hz, 1H), 4.96 (d, $J = 10.2$ Hz, 1H), 4.40 (dd, $J = 12.8$, 7.0 Hz, 1H), 3.76 (s, 3H), 2.52 (br s, 1H), 2.27 – 2.06 (m, 2H), 1.82 – 1.64 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 166.9$, 142.4, 138.0, 125.0, 115.0, 71.0, 51.8, 35.3, 29.9; HRMS: *m/z* ($M^+ - H$) calcd. 169.0865, obsd. 169.0894.

3-Hydroxy-2-methyleneoct-7-enoic Acid Methyl Ester (6b): Silica gel (elution with 10% ether in petroleum ether); yield: 71%; colorless oil; IR (neat): $\nu = 3456$, 1715, 1640 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.18$ (d, $J = 0.8$ Hz, 1 H), 5.82 – 5.67 (m, 1H), 5.77 (d, $J = 0.8$ Hz, 1H), 4.96 (d, $J =$ 17.3 Hz, 1H), 4.91 (d, $J = 10.2$ Hz, 1H), 4.36 (dd, $J = 7.0$, 5.3 Hz, 1H), 3.73 (s, 3H), 2.69 (br s, 1H), 2.04 (dd, $J = 14.4$, 7.7 Hz, 2H), 1.69 – 1.34 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 166.9$, 142.5, 138.4, 124.8, 114.5, 71.2, 51.7, 35.6, 33.3, 24.9; HRMS: *m/z* ($M^+ + H$) calcd. 185.1178, obsd. 185.1138; Anal. calcd. for $C_{10}H_{16}O_3$: C 65.19, H 8.75; found: C 65.32, H 8.70.

3-Hydroxy-2-methylenedodec-11-enoic Acid Methyl Ester (6c): Silica gel (elution with 10% ether in petroleum ether); yield: 86%; colorless oil; IR (neat): $\nu = 3462$, 1720, 1640 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 6.20$ (d, $J = 1.0$ Hz, 1H), 5.82 – 5.67 (m, 1H), 5.78 (t, $J = 1.0$ Hz, 1H), 5.01 – 4.88 (m, 2H), 4.40 – 4.35 (m, 1H), 3.76 (s, 3H), 2.57 (br s, 1H), 2.02 (dd, $J = 14.1$, 6.8 Hz, 2H), 1.69 – 1.54 (m, 2H), 1.49 – 1.28 (series of m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 167.0$, 142.5, 139.1, 124.8, 114.0, 71.7, 51.8, 36.2, 33.7, 29.3, 29.0, 28.0, 25.8; HRMS: *m/z* (M^+) calcd. 240.1725, obsd. 240.1728. Anal. calcd. for $C_{14}H_{24}O_3$: C 69.96, H 10.07; found: C 70.15, H 10.22.

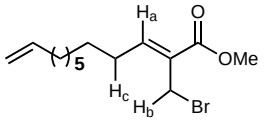
General Bromination Protocol: (*Z*)-2-Bromomethylhepta-2,6-dienoic Acid Methyl Ester (7a)

To a solution of triphenylphosphine (1.57 g, 5.97 mmol) in dry CH_2Cl_2 (20 mL) was added bromine (310 μL, 5.97 mmol) dropwise at –20 °C. After 15 min, a solution of **6a** (1.00 g, 5.43 mmol) in CH_2Cl_2 (5 mL) was introduced dropwise over 5 min. Following the addition, the cold bath was removed and the reaction mixture was quenched with methanol 30 min later. The solvent was evaporated under reduced pressure and the residue was chromatographed on silica gel (elution with 5% ether in petroleum ether) to afford **7a** as a colorless oil; yield: 1.19 g (68%); IR (neat): ν = 1719, 1640, 1440 cm^{-1}; ^1H NMR (300 MHz, C_6D_6): δ = 6.95 (t, *J* = 7.4 Hz, 1H), 5.87 – 5.73 (m, 1H), 5.10 – 5.00 (m, 2H), 4.21 (s, 2H), 3.78 (s, 3H), 2.39 (dd, *J* = 14.4, 7.0 Hz, 2H), 2.25 (dd, *J* = 13.9, 7.0 Hz, 2H); ^{13}C NMR (75 MHz, C_6D_6): δ = 165.9, 147.3, 136.7, 129.6, 115.9, 52.1, 31.9, 28.1, 24.1; HRMS: *m/z* (M^+) calcd. 232.0100, obsd. 232.0091.

(*Z*)-2-Bromomethylocta-2,7-dienoic Acid Methyl Ester (7b): Silica gel (elution with 5% ether in petroleum ether); yield: 70%; colorless oil; IR (neat): ν = 1722, 1641, 1438 cm^{-1}; ^1H NMR (300 MHz, C_6D_6): δ = 6.91 (t, *J* = 7.7 Hz, 1H), 5.77 – 5.64 (m, 1H), 5.05 – 4.99 (m, 2H), 4.11 (s, 2H), 3.51 (s, 3H), 1.99 (q, *J* = 7.5 Hz, 2H), 1.91 (q, *J* = 7.5 Hz, 2H), 1.33 (quintet, *J* = 7.5 Hz, 2H); ^{13}C NMR (75 MHz, C_6D_6): δ = 165.6, 147.6, 138.0, 130.0, 115.3, 51.7, 33.4, 28.2, 27.4, 24.5; HRMS: *m/z* (M^+) calcd. 246.0255, obsd. 246.0251.

(*Z*)-2-Bromomethyldodeca-2,11-dienoic Acid Methyl Ester (7c): Silica gel (elution with 5% ether in petroleum ether); yield: 92%; colorless oil; IR (neat): ν = 1722, 1641, 1435 cm^{-1}; ^1H NMR (300 MHz, C_6D_6): δ = 6.93 (t, *J* = 7.6 Hz, 1H), 5.90 – 5.76 (m, 1H), 5.12 – 5.00 (m, 2H), 4.07 (s, 2H), 3.43 (s, 3H), 2.05 – 1.99 (ddd, *J* = 7.6, 6.8, 6.8 Hz, 2H), 1.93 (q, *J* = 7.3 Hz, 2H), 1.38 – 1.28 (m, 2H), 1.26 – 1.14 (series of m, 8H); ^{13}C NMR (75 MHz, C_6D_6): δ = 165.7, 148.0, 139.1, 130.1, 114.6, 51.6, 34.1, 29.5 (2C), 29.2 (2C), 28.8, 28.3, 24.5; HRMS: *m/z* (M^+) calcd. 302.0881, obsd. 302.0903.

NOE difference data for **7c**:



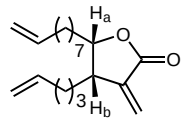
irradiated	δ, ppm	observed	NOE, %
H_a	6.93	H_b	0
H_b	4.07	H_c, H_a	6.4, 0
Me	3.43	H_a, H_c	1.0, 0

Indium-Promoted Coupling of 5 with 7; Direct Conversion to α-Methylene-γ-lactones 9

Bromide **7c** (485 mg, 2.02 mmol) and 5-hexenal (191 mg, 2.22 mmol) were stirred in 2.0 mL of 50% THF/H_2O for 5 min. Powdered indium metal (253 mg, 2.22 mmol) was introduced and the mixture was vigorously agitated for 1 h. Subsequently, chloroform (40 mL), water (10 mL) and 10% Na_2SO_4 solution (2 mL) were added and the mixture was stirred for 15 min. The separated aqueous layer was extracted with chloroform (2 × 25 mL) and the combined organic extracts were dried, filtered, and concentrated under reduced pressure. The resulting oil was dissolved in 25 mL of benzene, treated with pyridinium *p*-toluenesulfonate (100 mg, 0.404 mmol), refluxed for 30 min, and freed of the solvent under reduced pressure. The residue was chromatographed on silica gel with 15% ether in ligroin as eluent to furnish a 3:2 *cis*/*trans* mixture of lactones **9d**; yield: 423 mg (72%). The isomeric lactones were easily separated on silica gel upon elution with 0 – 5% ether in ligroin.

***cis*-3-Methylene-5-(non-8-enyl)-4-(pent-4-enyl)-dihydrofuran-2-one** (*cis*-**9d**): Yield: 43%; colorless oil; IR (neat): ν = 1765, 1640, 1459 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 6.20 (d, *J* = 2.4 Hz, 1H), 5.87 – 5.72 (m, 2H), 5.50 (d, *J* = 2.2 Hz, 1H), 5.06 – 4.91 (m, 4H), 4.52 – 4.45 (m, 1H), 2.98 – 2.92 (m, 1H), 2.13 – 2.00 (m, 4H), 1.63 – 1.30 (series of m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.6, 139.6, 139.1, 137.8, 120.9, 115.2, 114.2, 81.1, 43.1, 33.7, 33.5, 30.2, 29.3, 29.2, 28.9, 28.8, 26.7, 25.9, 25.6; HRMS: *m/z* (M^+ – H) calcd. 289.2168, obsd. 289.2164. Anal. calcd. for $C_{19}H_{30}O_2$: C 78.57, H 10.41; found: C 78.67, H 10.52.

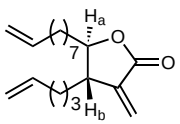
NOE difference data for *cis*-**9d**:



irradiated	δ, ppm	observed	NOE, %
H_a	4.52-4.45	H_b	10.9
H_b	2.98-2.92	H_a	11.4

***trans*-3-Methylene-5-(non-8-enyl)-4-(pent-4-enyl)-dihydrofuran-2-one** (*trans*-**9d**): Yield: 29%; colorless oil; IR (neat): ν = 1766, 1640, 1459 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 6.25 (d, *J* = 2.6 Hz, 1H), 5.87 – 5.71 (m, 2H), 5.57 (d, *J* = 2.2 Hz, 1H), 5.05 – 4.91 (m, 4H), 4.16 (dd, *J* = 10.5, 6.1 Hz, 1H), 2.66 – 2.60 (m, 1H), 2.12 – 2.00 (m, 4H), 1.64 – 1.30 (series of m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3, 139.4, 139.1, 137.8, 122.1, 115.2, 114.2, 83.3, 44.4, 36.2, 33.7, 33.5 (2C), 29.3 (2C), 28.9, 28.8, 25.6, 25.1; HRMS: *m/z* (M^+ – H) calcd. 289.2168, obsd. 289.2176. Anal. calcd. for $C_{19}H_{30}O_2$: C 78.57, H 10.41; found: C 78.75, H 10.48.

NOE difference data for *trans*-**9d**:



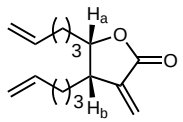
irradiated	δ, ppm	observed	NOE, %
H_a	4.16	H_b	1.9
H_b	2.66-2.60	H_a	1.7

4,5-Di(butenyl)dihydro-3-methylene-2(3*H*)-furanone (9a): Silica gel (elution with 5 – 10% ether in petroleum ether);

yield: 74%; colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.25 (d, *J* = 2.6 Hz, 0.42H), 6.20 (d, *J* = 2.5 Hz, 0.58H), 5.84 – 5.70 (m, 2H), 5.59 (d, *J* = 2.6 Hz, 0.42H), 5.52 (d, *J* = 2.5 Hz, 0.58H), 5.10 – 4.98 (m, 2H), 4.50 (q, *J* = 6.9 Hz, 0.58H), 4.20 (dt, *J* = 10.6, 6.4 Hz, 0.42H), 3.03 – 2.95 (m, 0.58H), 2.69 – 2.63 (m, 0.42H), 2.36 – 2.01 (series of m, 4H), 1.78 – 1.54 (series of m, 4 H). For *cis*-**9a**: ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3, 139.2, 137.1, 137.0, 121.1, 115.8, 115.7, 80.0, 42.2, 30.4, 29.6, 29.5, 26.4. For *trans*-**9a**: ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.1, 139.0, 137.0, 136.9, 122.4, 115.7, 115.6, 82.4, 43.7, 35.2, 33.2, 30.3, 29.3.

***cis*-3-Methylene-4,5-di(pent-4-enyl)-dihydrofuran-2-one** (*cis*-**9b**): Silica gel (elution with 5% ether in petroleum ether); yield: 42%; colorless oil; IR (neat): ν = 1765, 1640, 1406 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.18 (d, *J* = 2.4 Hz, 1H), 5.83 – 5.70 (m, 2H), 5.49 (d, *J* = 2.4 Hz, 1H), 5.04 – 4.94 (m, 4H), 4.52 – 4.45 (m, 1H), 2.96 – 2.93 (m, 1H), 2.11 – 2.05 (m, 4H), 1.68 – 1.37 (series of m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4, 139.4, 138.0, 137.8, 120.9, 115.2, 115.1, 80.9, 43.1, 33.5, 33.3, 29.5, 26.7, 25.8, 24.8; HRMS: *m/z* (M^+) calcd. 234.1620, obsd. 234.1618. Anal. calcd. for $C_{15}H_{22}O_2$: C 75.88, H 9.46; found: C 77.07, H, 9.35.

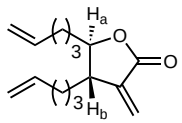
NOE difference data for *cis*-**9b**:



irradiated	δ, ppm	observed	NOE, %
H_a	4.52-4.45	H_b	8.8
H_b	2.96-2.93	H_a	9.5

***trans*-3-Methylene-4,5-di(pent-4-enyl)-dihydrofuran-2-one** (*trans*-**9b**): Silica gel (elution with 5% ether in petroleum ether); yield: 25%; colorless oil; IR (neat): ν = 1766, 1637, 1401 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.20 (d, *J* = 2.6 Hz, 1H), 5.80 – 5.66 (m, 2H), 5.54 (d, *J* = 2.6 Hz, 1H), 5.00 – 4.91 (m, 4H), 4.15 – 4.09 (m, 1H), 2.61 – 2.58 (m, 1H), 2.08 – 2.01 (m, 4H), 1.62 – 1.38 (series of m, 8H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.2, 139.3, 137.9, 137.8, 122.0, 115.2, 115.1, 83.1, 44.4, 35.4, 33.4 (2C), 33.2, 25.5, 24.3; HRMS: *m/z* (M^+) calcd. 234.1620, obsd. 234.1633.

NOE difference data for *trans*-**9b**:



irradiated	δ, ppm	observed	NOE, %
H_a	4.15-4.09	H_b	1.6
H_b	2.61-2.58	H_a	1.7

***cis*-4-(But-3-enyl)-3-methylene-5-(non-8-enyl)-dihydrofuran-2-one** (*cis*-**9c**): MPLC on silica gel (elution with 6% ether in petroleum ether); yield: 24%; colorless oil; IR (neat): ν = 1766, 1640, 1455 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.21 (d, *J* = 2.4 Hz, 1H), 5.87 – 5.72 (m, 2H), 5.52 (d, *J* = 2.4 Hz, 1H), 5.09 – 4.90 (m, 4H), 4.52 – 4.45 (m, 1H), 3.03 – 2.94 (m, 1H), 2.21 – 2.00 (m, 4H), 1.69 – 1.30 (series of m, 14H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.5, 139.4, 139.1, 137.2, 121.1, 115.8, 114.2, 81.0, 42.4, 33.7, 30.5, 30.3, 29.3 (2C), 28.9, 28.8, 26.5, 25.6; HRMS: *m/z* (M^+) calcd. 276.2089, obsd. 276.2063. Anal. calcd. for $C_{18}H_{28}O_2$: C 78.21, H 10.21; found: C 78.35, H 10.09.

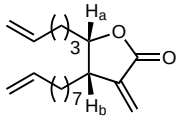
***trans*-4-(But-3-enyl)-3-methylene-5-(non-8-enyl)-dihydrofuran-2-one** (*trans*-**9c**): MPLC on silica gel (elution with 6% ether in petroleum ether); yield: 16%; colorless oil; IR (neat): ν = 1765, 1640, 1453 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.26 (d, *J* = 2.5 Hz, 1H), 5.86 – 5.71 (m, 2H), 5.59 (d, *J* = 2.5 Hz, 1H), 5.08 – 4.90 (m, 4H), 4.18 (dd, *J* = 10.3, 6.1 Hz, 1H), 2.70 – 2.63 (m, 1H), 2.13 (dd, *J* = 14.5, 7.4 Hz, 2H), 1.71 – 1.57 (series of m, 4H), 1.55 – 1.25 (series of m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.2, 139.2, 139.1, 137.1, 122.3, 115.8, 114.2, 83.3, 43.7, 36.1, 33.7, 33.4, 30.3, 29.2 (2C), 28.9, 28.8, 25.04; HRMS: *m/z* (M^+) calcd. 276.2089, obsd. 276.2079. Anal. calcd. for $C_{18}H_{28}O_2$: C 78.21, H 10.21; found: C 78.46, H 9.98.

***cis*-5-(But-3-enyl)-3-methylene-4-(non-8-enyl)-dihydrofuran-2-one** (*cis*-**9e**): Silica gel (elution with 5 – 10% ether in petroleum ether); yield: 34%; colorless oil; IR (neat): ν = 1765, 1660, 1640 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.15 (d, *J* = 2.4 Hz, 1H), 5.83 – 5.69 (m, 2H), 5.47 (d, *J* = 2.4 Hz, 1H), 5.05 – 4.90 (m, 4H), 4.52 – 4.44 (m, 1H), 2.96 – 2.89 (m, 1H), 2.34 – 2.21 (m, 1H), 2.19 – 2.06 (m, 1H), 1.66 – 1.29 (series of m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.3, 139.3, 138.8, 137.0, 120.7, 115.6, 114.1, 80.1, 43.0, 33.6, 29.6, 29.4, 29.3, 29.1, 28.8, 28.7, 27.2, 26.4.

***trans*-5-(But-3-enyl)-3-methylene-4-(non-8-enyl)-dihydrofuran-2-one** (*trans*-**9e**): Silica gel (elution with 5 – 10% ether in petroleum ether); yield: 26%; colorless oil; IR (neat): ν = 1763, 1665, 1639 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.23 (d, *J* = 2.6 Hz, 1H), 5.85 – 5.71 (m, 2H), 5.56 (d, *J* = 2.6 Hz, 1H), 5.08 – 4.89 (m, 4H), 4.20 – 4.14 (m, 1H), 2.65 – 2.58 (m, 1H), 2.29 – 2.12 (m, 2H), 2.02 (q, *J* = 6.9 Hz, 2 H), 1.69 (dd, *J* = 14.0, 6.6 Hz, 2H), 1.58 – 1.52 (m, 2H), 1.47-1.29 (series of m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.2, 139.3, 138.9, 137.0, 122.1, 115.6, 114.2, 82.5, 44.4, 35.3, 34.0, 33.6, 29.4, 29.3, 29.2, 28.9, 28.7, 26.3.

***cis*-3-Methylene-4-(non-8-enyl)-5-(pent-4-enyl)-dihydrofuran-2-one** (*cis*-**9f**): Silica gel (elution with 5 – 10% ether in petroleum ether); yield: 42%; colorless oil; IR (neat): ν = 1767, 1664, 1640, 1459 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.16 (d, *J* = 2.5 Hz, 1H), 5.82 – 5.71 (m, 2H), 5.47 (d, *J* = 2.5 Hz, 1H), 5.02 – 4.88 (m, 4H), 4.48 – 4.45 (m, 1H), 2.94 – 2.91 (m, 1H), 2.09 – 1.98 (m, 4H), 1.66 – 1.29 (series of m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.4, 139.4, 139.0, 137.9, 120.7, 114.9, 114.1, 83.8, 43.1, 33.6, 33.2, 33.6, 29.4, 29.1, 28.8, 28.7, 27.2, 26.5, 24.7; HRMS: *m/z* (M^+) calcd. 290.2246, obsd. 290.2237. Anal. calcd. for $C_{19}H_{30}O_2$: C 78.57, H 10.41; found: C 78.50, H 10.31.

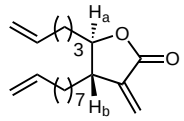
NOE difference data for *cis*-**9f**:



irradiated	δ, ppm	observed	NOE, %
H_a	4.48-4.45	H_b	10.5
H_b	2.94-2.91	H_a	12.4

***trans*-3-Methylene-4-(non-8-enyl)-5-(pent-4-enyl)-dihydrofuran-2-one** (*trans*-**9f**): Silica gel (elution with 5 – 10% ether in petroleum ether); yield: 28%; colorless oil; IR (neat): $\nu = 1766$, 1661, 1637, 1460 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.23$ (d, $J = 2.5$ Hz, 1H), 5.86 – 5.70 (m, 2H), 5.56 (d, $J = 2.5$ Hz, 1H), 5.04 – 4.89 (m, 4H), 4.18 – 4.12 (m, 1H), 2.64 – 2.57 (m, 1H), 2.12 – 1.99 (m, 4H), 1.66 – 1.29 (series of m, 16H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.3$, 139.4, 139.0, 138.0, 121.9, 115.1, 114.2, 83.2, 44.5, 35.5, 34.1, 33.6, 33.2, 29.4, 29.2, 28.9. 28.8, 26.3, 24.3; HRMS: *m/z* (M^+) calcd. 290.2246, obsd. 290.2234. Anal. calcd. for $C_{19}H_{30}O_2$: C 78.57, H 10.41; found: C 78.71, H 10.33.

NOE difference data for *trans*-**9f**:



irradiated	δ, ppm	observed	NOE, %
H_a	4.18-4.12	H_b	2.1
H_b	2.64-2.57	H_a	1.9

***cis*-5-(Hex-5-enyl)-3-methylene-4-(non-8-enyl)-dihydrofuran-2-one** (*cis*-**9g**): Silica gel (elution with 5% ether in petroleum ether); yield: 41%; colorless oil; IR (neat): $\nu = 1767$, 1640, 1268 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.16$ (d, $J = 2.3$ Hz, 1H), 5.84 – 5.70 (m, 2H), 5.48 (d, $J = 2.3$ Hz, 1H), 5.01 – 4.88 (m, 4H), 4.50 – 4.43 (m, 1H), 2.96 – 2.88 (m, 1H), 2.14 – 2.01 (m, 4H), 1.69 – 1.27 (series of m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 170.4, 139.5, 138.9, 138.4, 120.7, 114.5, 114.1, 81.0, 43.1, 33.6, 33.4, 30.0, 29.4, 29.2, 28.9, 28.7, 28.5, 27.2, 26.5, 25.1; HRMS: *m/z* (M^+) calcd. 304.2402, obsd. 304.2414. Anal. calcd. for $C_{19}H_{30}O_2$: C 78.90, H 10.59; found: C 78.66, H 10.57.

***trans*-5-(Hex-5-enyl)-3-methylene-4-(non-8-enyl)-dihydrofuran-2-one** (*trans*-**9g**): Silica gel (elution with 5% ether in petroleum ether); yield: 28%; colorless oil; IR (neat): $\nu = 1766$, 1640, 1268 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.23$ (d, $J =$ 2.4 Hz, 1H), 5.85 – 5.70 (m, 2H), 5.55 (d, $J = 2.4$ Hz, 1H), 5.01 – 4.89 (m, 4H), 4.17 – 4.11 (m, 1H), 2.64 – 2.57 (m, 1H), 2.06 – 1.99 (m, 4H), 1.63 – 1.29 (series of m, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.3$, 139.5, 139.0, 138.4, 121.9, 114.6, 114.2, 83.3, 40.5, 36.0, 34.2, 33.7, 33.5, 29.5, 29.2, 28.9, 28.8, 28.5, 26.3, 24.6; HRMS: *m/z* (M^+) calcd. 304.2402, obsd. 304.2401. Anal. calcd. for $C_{19}H_{30}O_2$: C 78.90, H 10.59; found: C 78.67, H 10.70.

***cis*-5-(Hept-6-enyl)-3-methylene-4-(non-8-enyl)-dihydrofuran-2-one** (*cis*-**9h**): Silica gel (elution with 5% ether in petroleum ether); yield: 38%; colorless oil; IR (neat): $\nu = 1766$, 1640, 1464 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.18$ (d, $J =$ 2.3 Hz, 1H), 5.86 – 5.71 (m, 2H), 5.49 (d, $J = 2.3$ Hz, 1H), 5.01 – 4.91 (m, 4H), 4.51 – 4.44 (m, 1H), 2.97 – 2.89 (m, 1H), 2.04 – 1.97 (m, 4H), 1.83 – 1.24 (series of m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.6$, 139.6, 139.0, 138.8, 120.7, 114.3, 114.2, 81.1, 43.2, 33.7, 33.6, 30.2, 29.5, 29.2, 29.0 (2C), 28.8, 28.7, 26.6, 25.5; HRMS: *m/z* (M^+) calcd. 318.2559, obsd. 318.2581. Anal. calcd. for $C_{21}H_{34}O_2$: C 79.19, H 10.76; found: C 79.02, H 10.67.

***trans*-5-(Hept-6-enyl)-3-methylene-4-(non-8-enyl)-dihydrofuran-2-one** (*trans*-**9h**): Silica gel (elution with 5% ether in petroleum ether); yield: 26%; colorless oil; IR (neat): $\nu = 1766$, 1640, 1463 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.24$ (d, $J =$ 2.5 Hz, 1H), 5.87 – 5.56 (m, 2H), 5.02 (d, $J = 2.5$ Hz, 1H), 4.96 – 4.91 (m, 4H), 4.16 – 4.12 (m, 1H), 2.65 – 2.57 (m, 1H), 2.07 – 2.00 (m, 4H), 1.63 – 0.82 (series of m, 20H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.4$, 139.5, 139.0, 138.8, 122.0, 114.4, 114.2, 83.4, 44.5, 36.1, 34.2, 33.7, 33.6, 29.5, 29.2, 29.0, 28.8 (2C), 28.7, 26.3, 25.0; HRMS: *m/z* (M^+) calcd. 318.2559, obsd. 318.2539. Anal. calcd. for $C_{21}H_{34}O_2$: C 79.19, H 10.76; found: C 79.04, H 10.68.

General Procedure for Catalytic Ring-Closing Metathesis

A 0.43 mmol sample of the appropriate **9** derivative was placed in a 200-mL round-bottomed flask, sealed with a rubber septum, and flushed with dry N_2. Dichloromethane (42 mL) and 106 mg (0.129 mmol, 30 mol %) of Grubbs catalyst dissolved in dichloromethane (30 mL) were introduced via cannula under N_2. After the transfer, the flask was further sealed by placing a second septum (up-side down above the first) and securing it with copper wire. The system was allowed to stir for 24 h at 50 °C, the solvent was evaporated under reduced pressure, and the residue was chromatographed on silica gel using 5% ether/ligroin as the eluent to give the cyclized product. The yields and *E/Z* composition are specified in Table 1.

***trans*-3-Methylene-3a,4,5,8,9,9a-hexahydro-3*H*-cycloocta[*b*]furan-2-one (12):** Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 6.20$ (d, $J = 2.5$ Hz, 1H), 5.76 – 5.62 (m, 2H), 5.50 (d, $J = 2.5$ Hz, 1H); 4.35 – 4.28 (m, 1H), 2.92 – 2.84 (m, 1H), 2.44 – 2.12 (series of m, 4H), 2.10 – 1.94 (m, 2H), 1.56 – 1.43 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 170.0$, 140.5, 129.7, 129.6, 120.7, 83.8, 43.3, 33.2, 30.8, 23.8, 21.5.

***cis*-3-Methylene-3a,4,5,6,7,8,9,10,13,14,15,15a-dodecahydro-3*H*-1-oxacyclopentacyclotetradecen-2-one (13):** Colorless oil; IR (neat): $\nu = 1766$, 1664, 1443 cm^{-1}; ^1H NMR (300 MHz, C_6D_6): $\delta = 6.22$ (d, $J = 2.7$ Hz, 0.8H), 6.19 (d, $J = 2.4$ Hz, 0.8H), 5.38 – 5.28 (m, 0.4H), 5.22 – 5.14 (m, 0.8H), 5.10 – 5.01 (m, 0.8H), 5.05 (d, $J = 2.7$ Hz, 0.8H), 5.00 (d, $J = 2.4$ Hz, 0.2H), 3.84 – 3.79 (m, 0.2H), 3.73 – 3.68 (m, 0.8H), 2.24 – 2.18 (m, 1H), 2.06 – 1.66 (series of m, 4H), 1.53 – 1.46 (m, 1H), 1.41 – 0.92 (series of m, 15H); ^{13}C NMR (75 MHz, C_6D_6) (for major isomer): $\delta =$ 169.5, 140.2, 132.3, 130.7, 120.6, 81.6, 42.9, 33.5, 31.8, 30.8, 30.0, 27.8, 26.6, 25.9, 25.5, 24.7, 22.7; HRMS: *m/z* (M^+) calcd. 262.1933, obsd. 262.1954.

***trans*-3-Methylene-3a,4,5,6,7,8,9,10,13,14,15,15a-dodecahydro-3*H*-1-oxacyclopentacyclotetradecen-2-one (14):** Colorless oil; IR (neat): $\nu = 1766$, 1664, 1442 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): $\delta = 6.22$ (d, $J = 2.7$ Hz, 0.8H), 6.19 (d, $J = 2.4$ Hz, 0.2H), 5.38 – 5.28 (m, 0.4H), 5.22 – 5.14 (m, 0.8H), 5.10 – 5.01 (m, 0.8H), 5.05 (d, $J = 2.7$ Hz, 0.8H), 5.00 (d, $J = 2.4$ Hz, 0.2H), 3.84 – 3.79 (m, 0.2H), 3.73 – 3.68 (m, 0.8H), 2.24 – 2.18 (m, 1H), 2.06 – 1.66 (series of m, 4H), 1.53 – 1.46 (m, 1H), 1.41 – 0.92 (series of m, 15H); ^{13}C NMR (75 MHz, C_6D_6) (for major isomer): $\delta =$ 169.5, 140.2, 132.3, 130.7, 120.6, 81.6, 42.9, 33.5, 31.8, 30.8, 30.0, 27.8, 26.6, 25.9, 25.5, 24.7, 22.7; HRMS: *m/z* (M^+) calcd. 262.1933, obsd. 262.1954. Anal. calcd for $C_{17}H_{26}O_2$: C 77.82, H 9.99; found: C 77.91, H 9.91.

***cis*-3-Methylene-3a,4,5,6,9,10,11,12,13,14,15,15a-dodecahydro-3*H*-1-oxacyclopentacyclotetradecen-2-one (15):** Colorless oil; IR (neat) $\nu = 1759$, 1668, 1442 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): $\delta = 6.16$ (d, $J = 3.0$ Hz, 1H), 5.27 – 5.20 (m, 0.14H), 5.05 – 4.98 (m, 1.86H), 4.94 (d, $J = 3.0$ Hz, 1H), 3.94 – 3.90 (m, 0.07H), 2.41 – 2.35 (m, 0.93H), 2.29 – 2.27 (m, 0.07H), 2.01 – 1.65 (series of m, 4H), 1.47 – 0.83 (series of m, 16H); ^{13}C NMR (75 MHz, C_6D_6) (for major isomer): $\delta = 169.8$, 140.3, 132.3, 131.5, 118.6,

80.1, 43.2, 31.9, 31.7, 28.7, 27.7, 27.5, 25.9, 25.3, 24.7, 24.3, 23.5; HRMS: *m/z* (M^+) calcd. 262.1933, obsd. 262.1921.

***trans*-3-Methylene-3a,4,5,6,9,10,11,12,13,14,15,15a-dodecahydro-3*H*-1-oxacyclopentacyclotetradecen-2-one (16):** Colorless oil; IR (neat): $\nu = 1766$, 1661, 1442 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): $\delta = 6.03$ (d, $J = 3.1$ Hz, 1H), 5.22 – 5.17 (m, 0.14H), 5.06 – 5.03 (m, 0.14H), 5.01 – 4.95 (m, 0.86H), 4.90 – 4.79 (m, 0.86H), 4.82 (d, $J = 3.1$ Hz, 1H), 3.67 – 3.64 (m, 0.14H), 3.59 – 3.55 (m, 0.86H), 2.01 – 1.50 (series of m, 5H), 1.37 – 1.23 (series of m, 4H), 1.18 – 0.65 (series of m, 14H); ^{13}C NMR (75 MHz, C_6D_6) (for major isomer): $\delta = 196.5$, 141.0, 132.6, 130.8, 119.8, 81.7, 44.1, 33.9, 32.0, 31.8, 30.6, 27.4, 26.4, 25.9, 24.7, 24.3, 23.9; HRMS: *m/z* (M^+) calcd. 262.1933, obsd. 262.1938.

***cis*-3-Methylene-3a,5,6,7,8,9,10,13,14,15,16,16a-dodecahydro-3*H*,4*H*-1-oxacyclopentacyclopentadecen-2-one (17):** Colorless oil; IR (neat): $\nu = 1766$, 1665, 1444 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): $\delta = 6.13$ (d, $J = 1.8$ Hz, 1H), 5.34 – 5.29 (m, 0.17H), 5.23 – 5.11 (m, 1.83H), 4.97 (d, $J = 1.8$ Hz, 0.83H), 4.94 (d, $J = 2.6$ Hz, 0.17H), 4.02 – 3.98 (m, 0.17H), 3.94 – 3.89 (m, 0.83H), 2.36 – 2.32 (m, 0.17H), 2.27 – 2.23 (m, 0.83H), 2.01 – 1.91 (m, 2H), 1.79 – 1.73 (m, 1H), 1.45 – 0.82 (series of m, 19H); ^{13}C NMR (75 MHz, C_6D_6) (for major isomer): $\delta = 169.6$, 140.8, 131.5, 131.0, 119.6, 80.3, 42.9, 31.9, 31.4, 30.3, 28.6, 28.2, 26.9, 26.7, 26.5, 25.1, 24.4, 23.6; HRMS: *m/z* (M^+) calcd. 276.2089, obsd. 276.2089. Anal. calcd. for $C_{18}H_{28}O_2$: C 78.21, H 10.21; found: C 77.95, H 10.19.

***trans*-3-Methylene-3a,5,6,7,8,9,10,13,14,15,16,16a-dodecahydro-3*H*,4*H*-1-oxacyclopentacyclopentadecen-2-one (18)**: Colorless oil; IR (neat): $\nu = 1766$, 1660, 1460 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): $\delta = 6.21$ (d, $J = 2.4$ Hz, 1H), 5.38 – 5.31 (m, 0.25H), 5.26 – 5.21 (m, 0.25H), 5.19 – 4.99 (m, 1.50H), 5.07 (d, $J = 2.4$ Hz, 1H), 3.75 – 3.68 (m, 1H), 2.18 – 2.15 (m, 1H), 2.01 – 1.70 (series of m, 4H), 1.56 – 1.46 (m, 1H), 1.40 – 0.81 (series of m, 17H); ^{13}C NMR (75 MHz, C_6D_6) (for major isomer): $\delta =$ 169.3, 140.9, 131.7, 130.5, 120.9, 82.7, 43.9, 36.0, 33.8, 32.7, 32.2, 28.4, 28.3, 27.6 (2C), 26.7, 25.1, 23.9; HRMS: *m/z* (M^+) calcd. 276.2089, obsd. 276.2094. Anal. calcd. for $C_{18}H_{28}O_2$: C 78.21, H 10.21; found: C 78.17, H 10.27.

***cis*-3-Methylene-3a,4,5,6,7,8,9,10,13,14,15,16,17,17a-tetradecahydro-3*H*-1-oxacyclopentacyclohexadecen-2-one (19):** Colorless oil; IR (neat): $\nu = 1759$, 1668, 1442 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): $\delta = 6.14$ (d, $J = 3.0$ Hz, 1H), 5.39 – 5.37 (m, 0.50H), 5.24 – 5.15 (m, 1.50H), 4.93 (d, $J = 3.0$ Hz, 1H), 4.15 – 4.06 (m, 1H), 2.46 – 2.41 (m, 1H), 2.05 – 1.76 (series of m, 4H), 1.40 – 0.83 (series of m, 20H); ^{13}C NMR (75 MHz, C_6D_6) (for major isomer): $\delta = 170.8$, 139.5, 131.5, 130.8, 119.8, 80.4, 43.0, 32.3, 31.2, 30.2, 29.1, 28.9, 28.1, 27.8, 27.2, 27.1, 27.0, 24.7, 23.5; HRMS: *m/z* (M^+) calcd. 290.2249, obsd. 290.2242. Anal. calcd. for $C_{19}H_{30}O_2$: C 78.57, H 10.41; found: C 78.30, H 10.29.

***trans*-3-Methylene-3a,4,5,6,7,8,9,10,13,14,15,16,17,17a-tetradecahydro-3*H*-1-oxacyclopentacyclohexadecen-2-one (20)**: Colorless oil; IR (neat): $\nu = 1766$, 1660, 1461 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): $\delta = 6.21$ (d, $J = 2.6$ Hz, 1H), 5.39 – 5.36 (m, 0.50H), 5.27 – 5.18 (m, 1.50H), 5.00 (d, $J = 2.6$ Hz, 1H), 3.89 – 3.86 (m, 0.75H), 3.81 – 3.78 (m, 0.25H), 2.11 – 1.83 (series of m, 4H), 1.50 – 0.83 (series of m, 20H); ^{13}C NMR (75 MHz, C_6D_6) (for major isomer): $\delta = 169.4$, 140.8, 131.3 (2C), 120.6, 81.2, 44.0, 36.4, 34.1, 32.8, 32.3, 29.2, 28.7, 28.3, 27.8, 27.7, 26.4, 25.1, 24.8; HRMS: *m/z* (M^+) calcd. 290.2249, obsd. 290.2230. Anal. calcd. for $C_{19}H_{30}O_2$: C 78.57, H 10.41; found: C 78.34, H 10.41.

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