Intercalation of Multiple Carbon Atoms between the Carbonyls of α-Diketones

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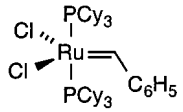
The reaction of open-chain or cyclic α-diketones with specific *ω*-alkenyl organometallics leads readily under the proper conditions to 1,2-diols bonded to terminal olefinic chains. With 1-phenyl-1,2-propanedione, biacetyl, and cyclohexane-1,2-dione, allylindation in aqueous THF proceeds readily at both adjacent carbonyls. For cyclododecane-1,2-dione, recourse must be made to allylmagnesium bromide for completing the second-stage condensation. Grignard reagents have also served well as reactants for biacetyl monoadducts. In contrast, monoallylated camphorquinone is reluctant to couple to Grignard reagents and reacts only when Barbier-type alkyllithium reactions are applied. The ring closing metatheses of these products have been examined. Where six-membered ring formation operates, cyclization can be performed directly on diols. When larger rings are involved, the diols will react only if structural preorganization capable of facilitating mutual approach of the two double bonds is at play. For this purpose, the prior conversion to a cyclic carbonate holds considerable utility. In the latter setting, saponification must precede the diol cleavage step which has been performed with lead tetraacetate. The latter reagent also exhibits the very beneficial effect of facilitating removal of ruthenium and phosphorus byproducts generated during the metathesis step. This chemistry conveniently lends itself to the controlled intercalation of multiple methylene groups between the carbonyl carbons of readily available α-diketones to deliver linear or cyclic products.

The carbonyl functionality has played a pivotal role in the evolution of synthetic organic chemistry. The fact that some attention has been paid to the development of methods for the controlled placement of two such groups at differing distances is therefore not surprising. Indeed, the numerous routes to 1,4- and 1,5-diketones, both symmetrical and unsymmetrical, are generally convenient and often adaptable to new structural settings.[1] In contrast, 1,6-diketones are recognized to be accessed less readiy,[2] and pathways leading to higher homologues are sparse,[3−5] despite notable advances in chain-extension methodology.[6] In recent years, the coupling of aldehydes and ketones to allylic indium reagents generated in water as the reaction medium,[7] and ring-closing metatheses promoted by ruthenium-based catalysts such as **1**[8] have emerged as useful new preparative tools. These remarkably versatile reactions have been successfully applied to the acquisition of various targets of interest. We have presently examined the merging of these two processes in both cyclic and acyclic contexts, with 1,2-dicarbonyl compounds serving as the starting materials.[9] In addition to the convergency associated with this protocol and the range of possibilities that it offers for the controlled insertion of carbon chains or loops of different length, the reaction sequences are short and practical. Limitations have surfaced only when entropic, ring strain, and steric effects kinetically deter the ease of large-ring formation.[10]



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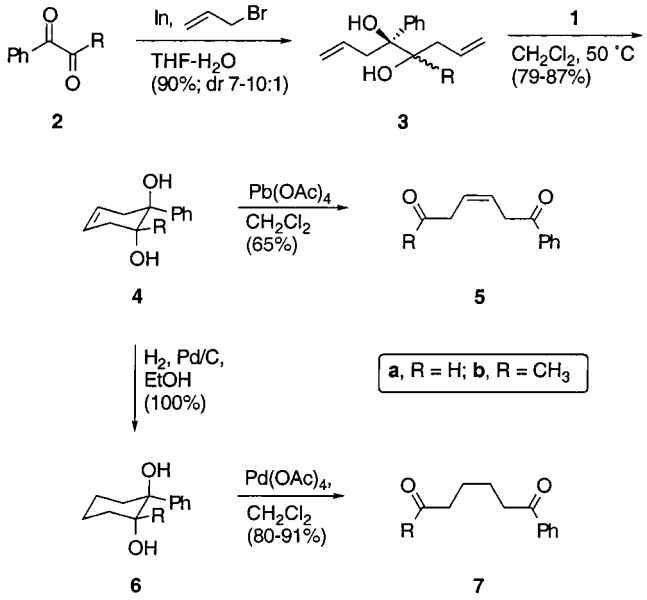
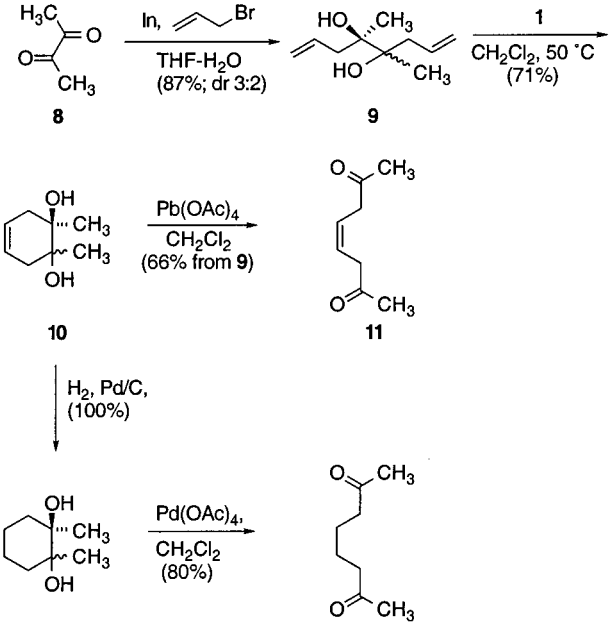
Scheme 1



Scheme 2



Results

Phenylglyoxal and 1-Phenyl-1,2-propanedione. When commercially available **2a** was stirred vigorously with an excess of powdered indium metal and allyl bromide in 4:1 THF/H_2O, the reaction mixture gradually took on a milky white appearance during 3 h and afforded the bisallylated diols **3a**[11] efficiently and in a diastereomeric ratio of 10:1 (Scheme 1). We attribute this kinetic bias to the likely intervention of a chelated transition state as the intermediate α-ketol is brought into the second carbon−carbon bond-forming step.[12] Heating **3a** with **1** in CH_2Cl_2 at 50 °C for 3 h led readily to **4a** (87%). Despite the recognized preference of neighboring trans-related C−O alkyl bonds on cyclohexane rings for adoption of a diequatorial arrangement,[13] we regard the low energy conformation of **4a** to be as illustrated based on decoupling experiments.[14] Following the catalytic hydrogenation of **4a** to generate **6a**,[15] the stage was set for diol cleavage with lead tetraacetate. While both **5a** and **7a**[16] were conveniently obtained, the ready polymerizability of the unsaturated keto aldehyde precluded its complete spectral characterization.[17]

The allylindation of **2b** likewise proceeded smoothly and gave **3b**.[11a] On this occasion, a kinetic imbalance with regard to diastereomer formation was again recognized, although the level of π-facial discrimination had dropped somewhat to 7:1 as a consequence of the steric bulk of the added methyl group. After the ring closure of **3b** under the influence of **1**, lead tetraacetate (1.1 equiv) was added directly to the reaction mixture. After overnight stirring, cleavage to give **5b** was encountered. We were also pleased to see that the darkly colored ruthenium and phosphine impurities could now be removed simply by filtration through a pad of silica gel rather than by laborious chromatographic methods. These observations were the bases of our convenient methodology for the improved workup of such ring closures.[18] Its effectiveness was early recognized and used throughout this investigation. The catalytic hydrogenation of **4b** to **6b**[19] made possible the analogous conversion to **7b**.[20]

Biacetyl. Our attempt to effect comparable four-carbon homologation of biacetyl (**8**) again proceeded efficiently (Scheme 2). This α-diketone proved to be extraordinarily electrophilic, giving rise to **9** in 87% yield and a diastereomeric ratio of 3:2.[11a,21] The ring-closing metathesis of **9** to produce the previously unknown diol **10** was followed by hydrogenation to the widely described saturated congener **12**.[22] Cleavage of both **10** and **12** as before led with consistently good efficiency to **11**[23a] and **13**,[23b] respectively. The latter 1,4-diketone has often been utilized in synthesis.

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(16) (a) Yamaguchi, M.; Takata, T.; Endo, T. *J. Org. Chem.* **1990**, *55*, 1490. (b) Kabalka, G. W.; Yu, S.; Li, N.-S. *Can. J. Chem.* **1998**, *76*, 800.

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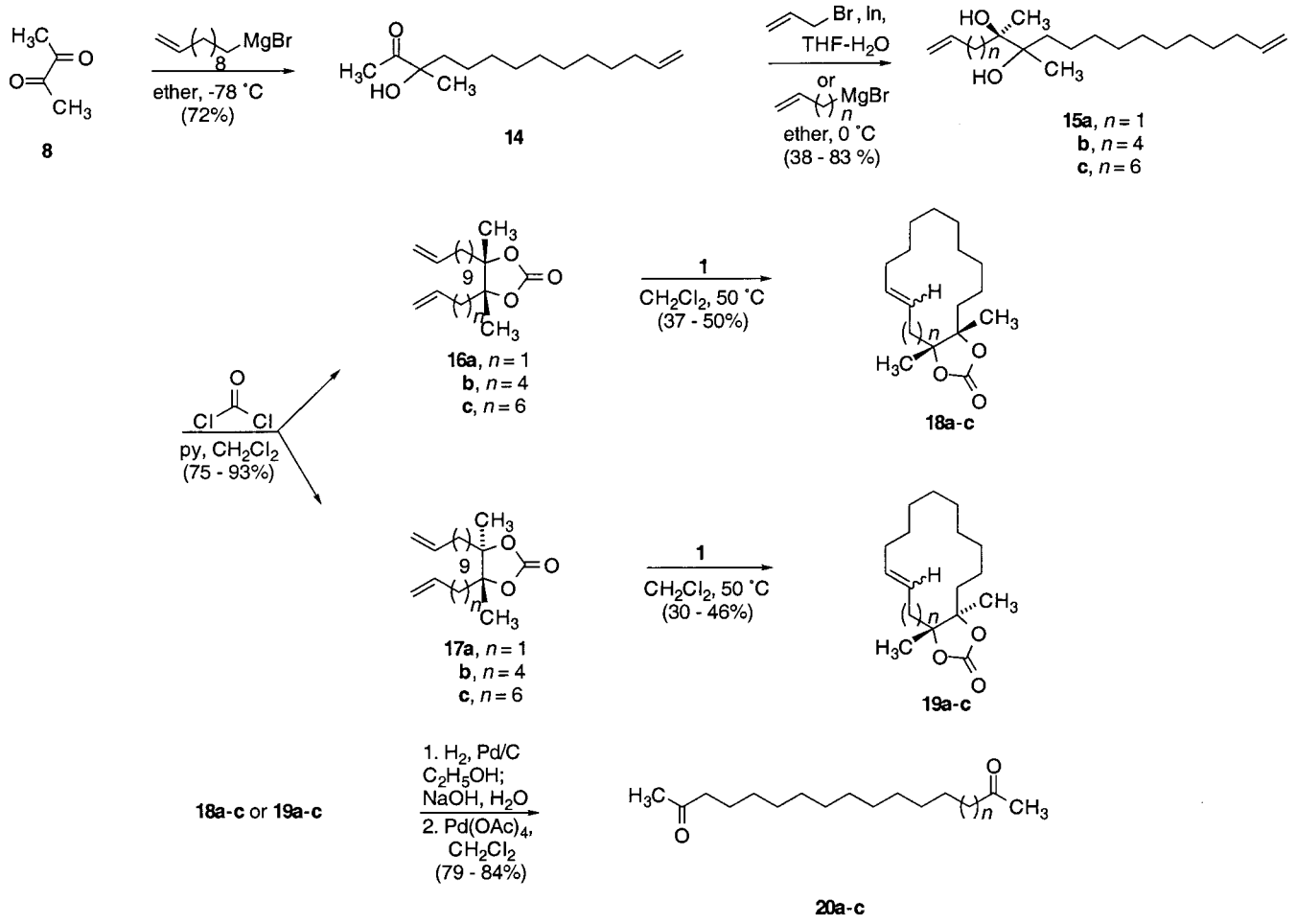
Scheme 3



The successful application of this methodology to four-carbon intercalation prompted attempts to introduce larger numbers of methylene units in systematic fashion. The most direct approach consisted of the controlled stepwise addition of ω-unsaturated Grignard reagents of differing chain lengths to **8** (Scheme 3). The commercial availability of 11-bromo-1-undecene was sufficient cause for its generic use in the formation of **14** from which **15a**−**c** was subsequently produced. The adoption of this route would ultimately provide the opportunity to investigate the ring-closing metathesis of large-ring systems with unprotected diol functionality and cyclic carbonate derivatives thereof. Such systems are largely absent in the literature.

The feasibility and practicality of monoallylating **14** with allyl bromide and indium powder in aqueous THF soon became apparent as a utilitarian route to **15a**. Since the halogen atom in 6-bromo-1-hexene and 8-bromo-1-octene is not comparably activated, their incorporation into **14** rests on their reactivity as Grignard reagents. Competitive enolization proved not to be a problem, and diols **15b** and **15c** were obtained in 38% and 40% yield, respectively.

All attempts to engage **15a**−**c** to undergo productive ring-closing metathesis in the presence of **1** at the reflux temperature of CH_2Cl_2 were to no avail. In some runs, unreacted diol was largely recovered. On occasion, partial conversion to polymerization products was noted. When the more reactive 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene-substituted ruthenium complex[24] was utilized in benzene at the higher reflux temperature, the results were closely comparable. These observations hold interest in that they appear to contraindicate hypotheses formulated in the context of previous findings involving unfunctionalized dienes.[25,26] Coordination to some type of functionality is generally believed to be required in order to realize efficient ring closure.[27]

The failure to obtain cyclized products from **15a**−**c**, which contain hydroxyl groups capable of coordination to the ruthenium center, could be suggestive that entropic factors arising from the nonrigid nature of these substrates may play an important role. Metathesis reactions are driven by an increase in entropy (e.g., the evolution of ethylene). Molecules such as the diols in question, which enjoy high levels of entropy prior to cyclization, would consequently incur a smaller gain in entropy during ring formation, the level of which may be too small to drive the reaction to completion. At this point, it was

(23) (a) The reported trans isomer exhibits a very different ^{1}H NMR spectrum: Yasuda, H.; Okamoto, T.; Mashima, K.; Nakamura, A. *J. Organomet. Chem.* **1989**, *363*, 61. (b) Jiang, J.-L.; Shi, Z. *Synth. Commun.* **1998**, *28*, 4137.

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(26) See also: (a) Paquette, L. A.; Méndez-Andino, J. *Tetrahedron Lett.* **2001**, *42*, 967. (b) Paquette, L. A.; Fabris, F.; Tae, J.; Gallucci, J. C.; Hofferberth, J. E. *J. Am. Chem. Soc.* **2000**, *122*, 3391.

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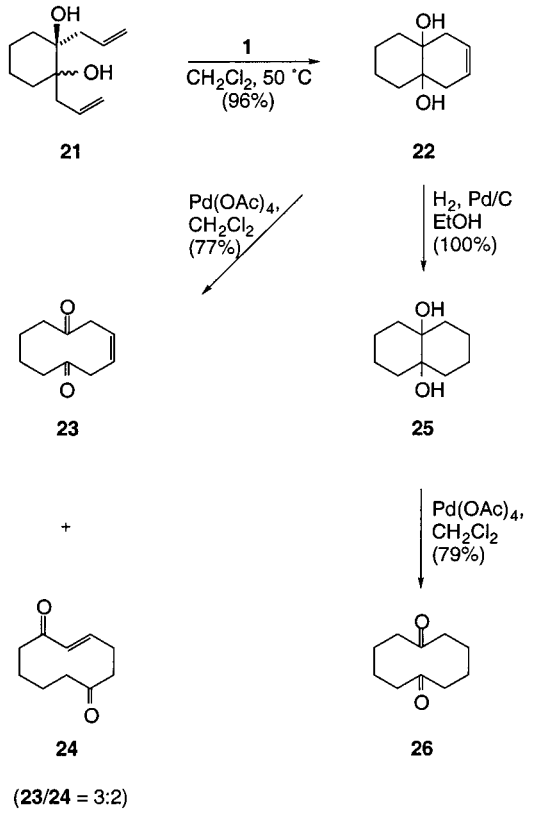
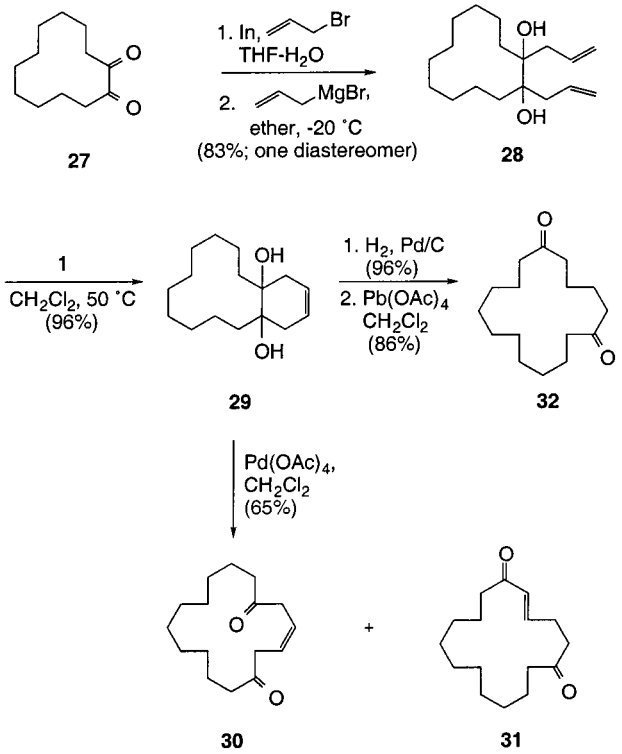
Scheme 4



(**23**/**24** = 3:2)

Scheme 5



clear that the availability of cyclic carbonates **16** and **17** could shed added light on this relevant issue. Formation of the heterocyclic ring greatly limits the degrees of freedom available to diols **15**.

When the diols were reacted with phosgene in the presence of pyridine, the resulting diastereomercic products could be separated chromatographically. No effort was made to distinguish the stereochemical features of the carbonates. The less polar isomers were arbitrarily labeled cis as **16a**−**c**; the more polar diastereomers carry the trans designation **17a**−**c**. The ring closing metathesis of these cyclic carbonates were carried out at high dilution (≤5 mM) with a catalyst loading of 20% for a total reaction time of 40 h in CH_2Cl_2 at 40−50 °C. Every run returned starting material (total accounting of materials approximately 80%), with the series when $n = 1$ advancing to the lowest extent. The formation of small amounts of more polar, unidentified materials (polymers?) was also noted. The cis and trans isomers were found to react equally well. The process therefore shows little, if any, stereochemical dependency. Our observations of limited reactivity in the *a* series suggests that it is probably best to have both double bonds as distal as possible from the quaternary centers. This is particularly true if the ring double bond is destined to be saturated as in the present instance.

In the hydrogenations of **18** and **19** ultimately to generate **20**, the reaction mixtures were not freed of catalysts, but treated directly with aqueous NaOH to liberate the diols. Exposure of these intermediates to lead tetraacetate as before furnished the extended diketones. In examples where sensitivity to base may surface, cleavage of the carbonate by hydride reduction remains an attractive alternative.

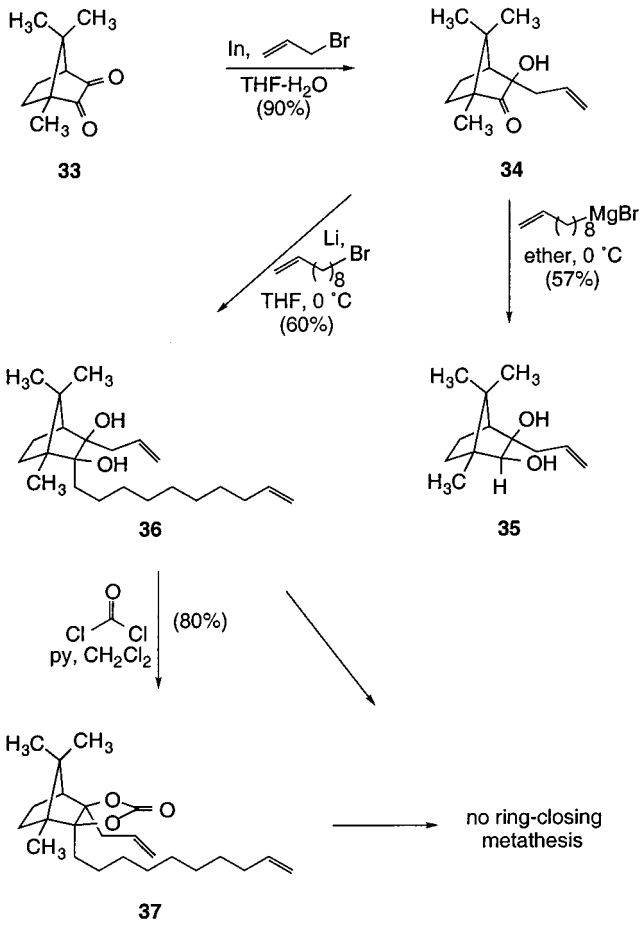
Cyclohexane-1,2-dione. When the allylindation of cyclohexane-1,2-dione was performed at the 0.08 M level with excess reagent under the predescribed aqueous conditions, rapid reaction ensued to deliver **21**[11a,21b,28] in 92% yield (Scheme 4). The subsequent metathesis step, performed with **1** in the usual manner gave rise to **22**[29] as a 3:1 diastereomeric mixture in near-quantitative yield. Once again, the introduction of lead tetraacetate immediately following the ring closure gave optimal results. Sequential catalytic hydrogenation of **22** provided **25**[30] from which 1,6-cyclodecanedione (**26**)[31] was derived. Entirely comparable application of this chemistry directly onto **22** gave a separable 3:2 mixture of **23** and **24**. In **23** where no double bond migration occurs, the olefinic linkage must necessarily be cis. When conjugation does materialize as in **24**, the favored double bond geometry is trans ($J_{2,3} = 11.9$ Hz).

Cyclododecane-1,2-dione. If one examines a broad range of α-diketones in terms of their behavior under the conditions of exhaustive allylindation, one feature is made immediately obvious. Successful introduction of the second allyl group is strongly dependent on steric factors. In the case of the large-ring example **27**,[32] nonbonded transannular interactions are sufficient to impede formation of the second carbon−carbon bond. This is not problematic in this instance since the more reactive allyl Grignard reagent transforms the monoadduct cleanly into **28** (Scheme 5). In fact, a single diol diastereomer is formed (83%).

With **28** in hand, the discovery was soon made that the conversion to **29** via ring-closing metathesis was

(28) Marvell, E. N.; Cheng, J. C.-P. *J. Org. Chem.* **1980**, *45*, 4511.
(29) The trans isomer of **22** has been reported: Hückel, W.; Wörffel, U. *Chem. Ber.* **1956**, *89*, 2098.
(30) (a) Dev, S. *J. Ind. Chem. Soc.* **1954**, *31*, 1. (b) Betzemeier, B.; Lhermitte, F.; Knochel, P. *Synlett* **1999**, 489.
(31) House, H. O.; Lee, J. H. C.; VanDerveer, D.; Wissinger, J. E. *J. Org. Chem.* **1983**, *48*, 5285.
(32) Kawada, K.; Gross, R. S.; Watt, D. S. *Synth. Commun.* **1989**, *19*, 777.

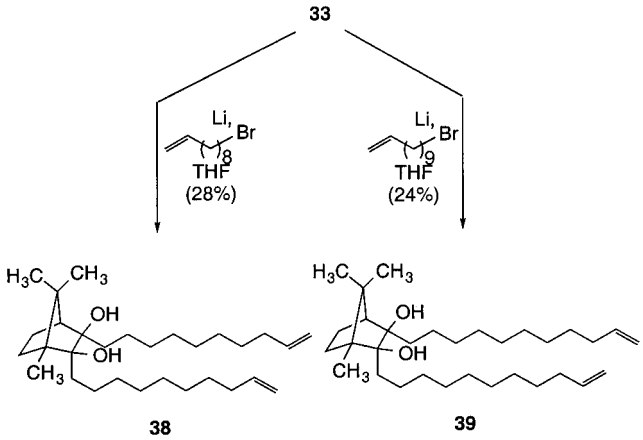
Scheme 6



again notably efficient. Obviously, there is no problem associated with activation of the double bonds in this example. As well, minimal difficulty was associated with the ensuing production of **32**[33] on one hand, and an easily separable mixture of **30** and **31** on the other.

(1*R*)-(−)-Camphorquinone. As expected from earlier developments,[34] Barbier allylation of **33** was met with exclusive monoallylation at its less sterically congested carbonyl from the endo π-surface (Scheme 6). When attempts were subsequently made to add Grignard reagents to **34**, the substantive steric shielding about the resident ketone carbonyl was made apparent. For example, the exposure of **34** to 10-decenyl-1-magnesium bromide resulted in reduction to diol **35**. This problematic behavior was reflected as well in the attempted coupling of **34** to 10-decenyl-1-lithium. Only unreacted starting material was returned. This complication was resolved and second-stage addition successfully achieved when **34** was subjected to Barbier-type alkyllithium reactions. The Barbier approach differs from a typical alkyllithium reaction in that the lithium reagent is not preformed.[35] Rather, the ketone, halide, and lithium metal are introduced simultaneously to the reaction vessel. The consensus view is that a mechanistic crossover also materializes. In short, the evidence suggests that an alkyllithium intermediate is not involved and that reaction occurs

Scheme 7



instead on the surface of the metal.[36] Semiempirical MO calculations[37] are likewise consistent with initial single electron transfer from elemental lithium to the halide with formation of the transient radical anion.[38] The presence of the latter species may account for the increased reactivity and heightened efficiency observed under these circumstances.[35]

This tactic provided a useful route from **34** to **36** (60% isolated). However, a careful study of the ability of this diol and its cyclic carbonate **37** to enter into ring-closing metathesis clearly denoted their inertness to these conditions. The Weiler group had previously disclosed that a structurally unrelated substrate was equally reluctant to form a 14-membered ring.[39] Several factors were considered to be potentially contributive to inhibition of the desired cyclization. Of these, the sterically shielded nature of the allylic double bond featured prominently. As a consequence, the further use of monoallylated α-ketols was abandoned.

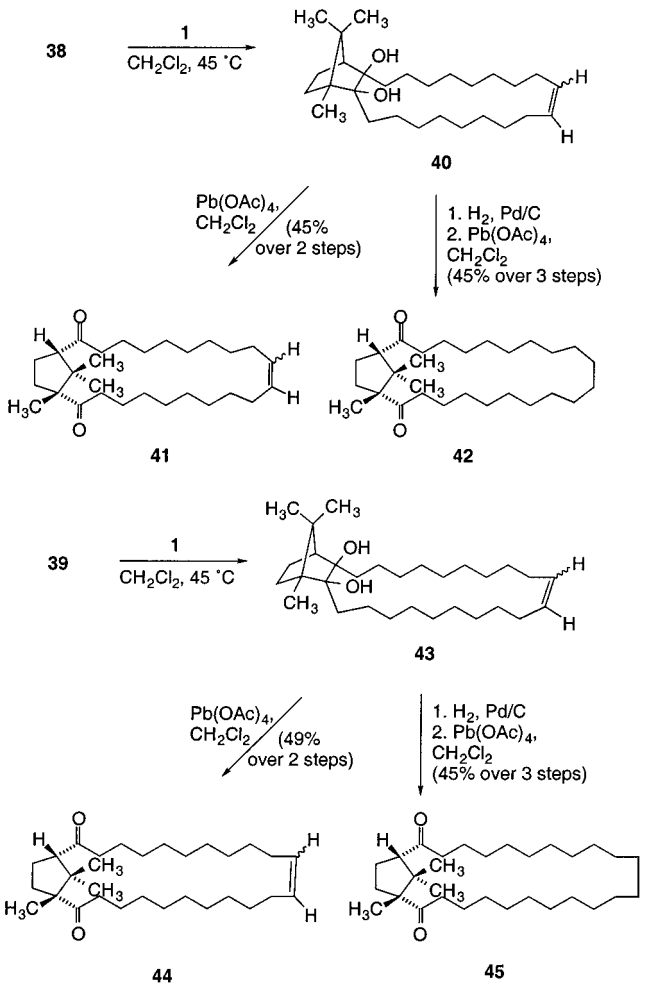
As outlined in Schemes 7 and 8, a variant of the Barbier alkyllithium reaction found application in producing two useful metathesis substrates. In the new approach, two identical ω-alkenyl groups were added concurrently to both carbonyl of camphorquinone to provide **38** and **39**, respectively. Once again, only single diastereomeric products were generated and these are formulated as the exo,exo-diols because of sterically enforced endo attack at both carbonyl reaction sites.

The Grubbs catalyst **1** was found to be effective for transforming **38** and **39** into the 20- and 22-membered cyclic diols **40** and **43**, respectively. These large-ring systems were expectedly generated as E/Z mixtures; these were not differentiated. Instead, cleavage with lead tetraacetate was subsequently carried out with and without prior hydrogenation of the intracyclic double bond to provide the saturated (**42** and **45**) and unsaturated intercalation products (**41** and **44**). In all four examples, the overall yield of these two- or three-step conversions was in the 45−50% range. The straightforward nature of all the transformations delineated in Scheme 8 is noteworthy.

A direct comparison of the reactivity differences noted for the biacetyl and camphorquinone adducts is difficult

(33) Leriverend, P.; Conia, J. M. *Bull. Soc. Chim. Fr.* **1970**, 1040.
(34) Ancillary studies have made clear that 1,2-cyclooctanedione, 5-cyclooctene-1,2-dione, and dimethyl squarate also share in this reluctance to enter into 2-fold allylation in an aqueous environment.
(35) Pearce, P. J.; Richards, D. H.; Scilly, N. F. *J. Chem. Soc., Perkin Trans. 1* **1972**, 1655.
(36) Molle, G.; Bauer, P. *J. Am. Chem. Soc.* **1982**, *104*, 3481.
(37) Moyano, A.; Pericàs, M. A.; Riera, A.; Luche, J.-L. *Tetrahedron Lett.* **1990**, *31*, 7619.
(38) When aromatic aldehydes and ketones are involved, ketyl radical anions may form competitively.
(39) Goldring, W. P. D.; Hodder, A. S.; Weiler, L. *Tetrahedron Lett.* **1998**, *39*, 4955.

Scheme 8



and may be unwarranted. The structural features and applicable conformational criteria vary significantly. When entropic factors are weighed, the camphor-derived diols **38** and **39** can reliably be regarded as topologically more restricted than **15a**−**c**. The bicyclo[2.2.1]heptane part structure resident in **38** and **39** probably serves to ensure that the terminal double bonds of both long chains are constrained to a more or less proximal relationship than otherwise.

Experimental Section

General Considerations. Melting points are uncorrected. The column chromatographic separations were performed on silica gel (230−400 or 200−325 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 NMR spectroscopy. The high-resolution mass spectra were recorded at The Ohio State University Campus Chemical Instrumentation Center. Elemental analyses were performed at Atlantic Microlab, Inc., Norcross, GA.

General Procedure for Indium-Promoted Allylation. Phenyl glyoxal monohydrate (670 mg, 5.0 mmol) dissolved in 65 mL of 4:1 THF/H_2O was vigorously stirred while indium powder (1.53 g, 2.7 equiv) and then allyl bromide (1.73 mL, 4.0 equiv) were introduced. The reaction mixture was stirred for 3 h during which time a milky appearance developed and the metal separated as pellets. At this point, 5 mL of 2 N potassium hydrogen sulfate solution and 75 mL of $CHCl_3$ were introduced. The separated aqueous phase was extracted with $CHCl_3$ (2 × 75 mL), and the combined organic layers were dried and concentrated to leave a residue that was chromatographed on silica gel (elution with 25% ether in petroleum ether) to give 977 mg (90%) of **3a** as a white solid, mp 42−46 °C, consisting of a 10:1 mixture of diastereomers.[11] For the major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41−7.32 (m, 4 H), 7.30−7.22 (m, 1 H), 5.88−5.69 (m, 1 H), 5.59−5.46 (m, 1 H), 5.20−4.99 (m, 4 H), 3.80 (dd, J = 9.7, 3.1 Hz, 1 H), 2.86 (dd, J = 14.0, 8.5 Hz, 1 H), 2.77 (dd, J = 14.0, 6.0 Hz, 1 H), 2.22 (br s, 2 H), 2.09−1.93 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.8, 135.5, 133.4, 128.2 (2C), 126.8, 125.5 (2C), 119.3, 117.7, 77.6, 76.1, 43.9, 36.1.

4-Methyl-5-phenyl-1,7-octadiene-4,5-diol (3b).[11a] Colorless oil; 90% yield; 7:1 mixture of diastereomers. For the major diastereomer: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 7.1 Hz, 2 H), 7.38−7.23 (m, 3 H), 5.90−5.76 (m, 1 H), 5.54−5.40 (m, 1 H), 5.20−4.93 (series of m, 4 H), 3.07 (dd, J = 13.9, 5.2 Hz, 1 H), 2.78 (dd, J = 13.9, 9.3 Hz, 1 H), 2.61 (br s, 1 H), 2.47 (dd, J = 14.0, 6.8 Hz, 1 H), 2.38 (br s, 1 H), 1.73 (dd, J = 14.0, 7.8 Hz, 1 H), 1.21 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.1, 134.5, 134.0, 127.7 (2C), 127.1 (2C), 126.8, 119.9, 118.1, 79.7, 76.1, 41.2, 39.8, 21.0. For minor diastereomer: ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.2, 134.1, 132.1, 127.6 (2C), 127.3 (2C), 125.8, 119.8, 119.4, 76.2, 76.0, 41.4, 40.7, 21.9.

General Ring Closing Metathesis Procedure. Diene diol **3a** (500 mg, 2.29 mmol) was placed in a septum-capped recovery flask under argon and diluted with CH_2Cl_2 (30 mL). A solution of **1** in CH_2Cl_2 (55 mg/30 mL) was transferred via cannula into the reaction mixture. A second septum was placed atop the existing one and secured with Parafilm. The reaction mixture was stirred at 50 °C for 3 h, allowed to cool, and opened to the atmosphere for 2 h. After solvent evaporation, the residue was chromatographed on silica gel (elution with 40% ethyl acetate in petroleum ether) to furnish **4a** as a white solid, mp 108−109 °C (380 mg, 87%); IR ($CHCl_3$, cm^{-1}) 3588, 3440, 1654, 1602; ^{1}H NMR (300 MHz, C_6D_6) δ 7.55−7.51 (m, 1 H), 7.22−7.11 (m, 4 H), 5.52−5.46 (m, 1 H), 5.44−5.38 (m, 1 H), 3.80−3.74 (m, 1 H), 2.75−2.67 (m, 1 H), 2.34−2.26 (m, 1 H), 2.18−2.10 (m, 1 H), 1.86 (s, 1 H), 1.76−1.67 (m, 1 H), 1.32 (d, J = 5.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.9, 128.4 (2C), 127.5, 126.1 (2C), 74.5, 73.2, 31.4, 28.4, 21.0, 19.2; EI MS m/z (M^+) calcd 190.0944, obsd 190.1005. Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C 75.56; H, 7.60.

2-Methyl-1-phenyl-4-cyclohexene-1,2-diol (4b). White crystals, mp 104−106 °C (79% yield); IR ($CHCl_3$, cm^{-1}) 3591, 1654, 1601; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, J = 7.0 Hz, 2 H), 7.38−7.27 (m, 3 H), 5.83−5.74 (m, 2 H), 3.12−3.04 (m, 1 H), 2.53−2.46 (m, 1 H), 2.33 (br s, 1 H), 2.24−2.03 (series of m, 2 H), 1.78 (br s, 1 H), 1.05 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.4, 127.6 (2C), 126.9, 126.5 (2C), 125.4, 125.1, 76.0, 72.9, 38.5, 38.1, 23.6; EI MS m/z (M^+) calcd 204.1150, obsd 204.1147. Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.59; H, 7.97.

General Procedure for Catalytic Hydrogenation. A mixture of **4a** (200 mg, 1.05 mmol) and 10% palladium on charcoal (10 mg) in absolute ethanol (2 mL) was stirred overnight under 1 atm of hydrogen. The reaction mixture was filtered through a pad of silica gel, and the pad was rinsed with ether. The solvent was removed under reduced pressure to yield 205 mg (quant) of **6a**; white solid, mp 98−99 °C;[41] ^{1}H NMR (300 MHz, C_6D_6) δ 7.45 (d, J = 7.2 Hz, 2 H), 7.19−7.05 (series of m, 3 H), 3.59 (m, 1 H), 2.32 (td, J = 12.6, 4.2 Hz, 1 H), 1.81−1.57 (series of m, 4 H), 1.54−1.33 (series of m, 4 H), 1.07 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.9, 128.5 (2C), 127.6, 126.1 (2C), 74.6, 73.3, 31.5, 28.5, 21.1, 19.2.

2-Methyl-1-phenyl cyclohexane-1,2-diol (6b).[19] Quantitative yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (dt, J = 7.1, 1.5 Hz, 2 H), 7.38−7.24 (series of m, 3 H), 2.62 (td, J = 12.4, 4.6 Hz, 1 H), 1.99−1.89 (m, 1 H), 1.84−1.33 (series of m, 8 H), 0.97 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.6, 127.6 (2C), 126.9, 126.8 (2C), 77.1, 72.5, 35.3, 34.5, 25.4, 21.0, 20.8.

General Procedure for One-Pot Ring-Closing Metathesis/Oxidative Cleavage. The first stage of the process was carried out exactly as described above. The cooled reaction mixture was treated portionwise with lead tetraacetate (892 mg, 2.0 mmol), stirred for 20 min at room temperature, and concentrated in vacuo. The residue was taken up in ether (50

mL) and the solids were removed by filtration through a short pad of silica gel. The pad was rinsed with ether (20 mL) and the filtrate was washed with dilute $NaHCO_3$ solution and water, dried, and concentrated. The residue was chromatographed on silica gel (elution with 40% ethyl acetate in petroleum ether).

For **(*Z*)-1-Phenyl-3-heptene-1,6-dione (5b)**: 65% yield; colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (dd, J = 7.2, 1.5 Hz, 2 H), 7.57−7.52 (m, 1 H), 7.44 (t, J = 7.2 Hz, 2 H), 5.97−5.76 (series of m, 2 H), 3.71 (d, J = 6.8 Hz, 2 H), 3.22 (d, J = 6.9 Hz, 2 H), 2.15 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.7, 197.1, 136.4, 133.1, 128.5 (2C), 128.1 (2C), 125.1, 124.5, 42.5, 37.4, 29.5.

6-Oxo-6-phenylhexanal (7a).[16] White solid, mp 32−33 °C;[15a] (91% yield); IR (neat, cm^{-1}) 1720, 1688; ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.78 (t, J = 1.6 Hz, 1 H), 7.94 (d, J = 7.1 Hz, 2 H), 7.58−7.52 (m, 1 H), 7.48−7.42 (m, 2 H), 2.99 (t, J = 6.9 Hz, 2 H), 2.49 (td, J = 7.1, 1.6 Hz, 2 H), 1.84−1.67 (m, 4 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 202.1, 199.6, 136.8, 132.9, 128.5 (2C), 127.9 (2C), 43.6, 38.0, 23.5, 21.6.

1-Phenylheptane-1,6-dione (7b).[20] White solid, mp 42−43 °C;[20] (80% yield); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (dd, J = 7.1, 1.2 Hz, 2 H), 7.54−7.48 (m, 1 H), 7.44−7.39 (m, 2 H), 2.95 (t, J = 7.1 Hz, 2 H), 2.45 (t, J = 7.1 Hz, 2 H), 2.10 (s, 3 H), 1.75−1.57 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.5, 199.7, 136.8, 132.8, 128.5 (2C), 127.9 (2C), 43.4, 38.1, 29.7, 23.5, 23.3.

4,5-Dimethyl-1,7-octadiene-4,5-diol (9).[11a,21] Colorless oil (87% yield, dr 3:2); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.04−5.89 (m, 2 H), 5.19−5.09 (m, 4 H), 2.54−2.42 (m, 2 H), 2.24−2.17 (m, 2 H), 2.06 (br s, 2 H), 1.19 (s, 0.40 × 6 H), 1.16 (s, 0.60 × 6 H). For the major diastereomer: ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.5 (2C), 118.7 (2C), 76.1 (2C), 41.1 (2C), 21.5 (2C). For the minor diastereomer: ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.4 (2C), 118.5 (2C), 76.2 (2C), 40.9 (2C), 21.8 (2C).

1,2-Dimethyl-4-cyclohexene-1,2-diol (10). Colorless oil (71%); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.58 (s, 2 H), 2.32−2.26 (m, 2 H), 2.19−2.10 (m, 2 H), 1.93 (br s, 2 H), 1.24 (s, 0.76 × 6 H), 1.21 (s, 0.24 × 6 H). For the major diastereomer: ^{13}C NMR (125 MHz, $CDCl_3$) δ 125.6 (2C), 73.6 (2C), 39.2 (2C), 22.8 (2C). For the minor diastereomer: ^{13}C NMR (75 MHz, $CDCl_3$) δ 125.2 (2C), 73.8 (2C), 39.3 (2C), 23.1 (2C).

(*Z*)-4-Octene-2,7-dione (11).[23a] Colorless oil (66% from **9**); IR (neat, cm^{-1}) 1714; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.77 (t, J = 5.5 Hz, 2 H), 3.15 (d, J = 5.5 Hz, 4 H), 2.13 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.4 (2C), 124.3 (2C), 42.0 (2C), 29.3 (2C); EI MS m/z (M^+) calcd 140.0837, found 140.0836.

1,2-Dimethylcyclohexane-1,2-diol (12).[22] Colorless oil (quant yield); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.06 (br s, 2 H), 1.70−1.25 (series of m, 8 H), 1.22 (s, 0.8 × 6 H), 1.15 (s, 0.2 × 6 H); For the major diastereomer: ^{13}C NMR (75 MHz, $CDCl_3$) δ 74.3 (2C), 36.4 (2C), 23.2 (2C), 22.1 (2C). For the minor diastereomer: ^{13}C NMR (75 MHz, $CDCl_3$) δ 73.9 (2C), 36.6 (2C), 23.4 (2C), 22.2 (2C).

Octane-2,8-dione (13). White solid, mp 42−44 °C;[23b] (80% yield); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45−2.40 (m, 4 H), 2.11 (s, 6 H), 1.57−1.52 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.6 (2C), 43.4 (2C), 29.9 (2C), 23.1 (2C).

α-Ketol 14: Magnesium metal (4.63 g, 190.6 mmol) was ground and added to 10 mL of anhydrous ether. To this mixture was added dropwise a solution of 8.00 g (34.3 mmol) of 11-bromo-1-undecene with vigorous stirring at 0 °C under argon. After the addition was complete, the mixture was warmed to room temperature and stirred for an additional 3 h. The resulting Grignard reagent was added to a solution of 3.30 g (38.1 mmol) of 2,3-butanedione during 12 h at room temperature under argon. The reaction mixture was stirred for 10 h, quenched with 10% HCl solution, and extracted with 3 × 200 mL of ether. The combined organic phases were washed with brine, dried, and evaporated. Chromatography of the residue on silica gel (elution with hexanes:ethyl acetate: 6:1) gave 6.58 g (72%) of **14** as a colorless oil; IR (neat, cm^{-1}) 3474, 1711, 1641; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.86−5.72 (m, 1 H), 5.01−4.89 (m, 2 H), 2.19 (s, 3 H), 2.06−1.97 (m, 2 H), 1.72−1.62 (m, 2 H), 1.49−1.17 (series of m, 15 H), 1.34 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 212.3, 139.1, 114.1, 78.7, 39.4, 33.7, 29.7 (2C), 29.4 (2C), 29.0, 28.8, 25.4, 23.6, 23.3, ES MS m/z $(M + Na)^+$ calcd 263.1987, obsd 263.1985.

Diol 15a. Colorless oil (83% yield); IR (neat, cm^{-1}) 3451; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.03−5.89 (m, 1 H), 5.88−5.74 (m, 1 H), 5.20−5.08 (m, 2 H), 5.02−4.89 (m, 2 H), 2.45 (dd, J = 13.7, 7.3 Hz, 1 H), 2.25−2.15 (m, 1 H), 2.10−2.00 (m, 2 H), 1.96 (br s, 2 H), 1.67−1.20 (series of m, 16 H), 1.15 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2, 134.65, 134.58, 118.9, 118.8, 114.1, 76.7, 76.4, 41.1, 40.8, 36.2, 36.0, 33.8, 30.4, 29.7, 29.6, 29.5, 29.1, 28.9, 23.7, 23.6, 22.0, 21.6, 21.0, 20.7; ES MS m/z $(M + Na)^+$ 305.2457, obsd 305.2451. Anal. Calcd for $C_{18}H_{34}O_2$: C, 76.54; H, 12.13. Found: C, 76.18; H, 11.86.

Diol 15b. Magnesium metal (0.608 g, 25.0 mmol) was ground and added to 3 mL of anhydrous ether. To this mixture was added dropwise a solution of 6-bromo-1-hexene (2.04 g, 12.5 mmol) with vigorous stirring at 0 °C under argon. After the addition was complete, the mixture was warmed to room temperature and stirred for the additional 3 h. The resulting Grignard reagent was added to the solution of 600.0 mg (2.50 mmol) of **14** during a period of 1 h at 0 °C under argon. The mixture was warmed to room temperature, stirred for an additional 24 h, quenched with 10% HCl solution, and extracted with 3 × 50 mL of ether. The combined organic phases were washed with brine, dried, and evaporated. The residue was chromatographed on silica gel (elution with hexanes:ethyl acetate 4:1) to give 0.312 g (38%) of **15b** as well as unreacted **14**; colorless oil; IR (neat, cm^{-1}) 3446; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88−5.73 (m, 2 H), 5.03−4.91 (m, 4 H), 2.12−1.97 (m, 4 H), 1.80 (br s, 2 H), 1.60−1.20 (series of m, 22 H), 1.14 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2, 138.9, 114.3, 114.1, 77.1, 36.3, 36.1, 36.0, 35.7, 33.8, 31.4, 29.7, 29.64, 29.59, 29.53, 29.48, 29.4, 29.1, 28.9, 23.8, 23.5, 23.3, 21.2, 20.9 (2C); ES MS m/z $(M + Na)^+$ calcd 347.2926, obsd 347.2919.

Diol 15c. Colorless oil (40% yield); IR (neat, cm^{-1}) 3418; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.90−5.73 (m, 2 H), 5.04−4.90 (m, 4 H), 2.10−2.00 (m, 4 H), 1.79 (br s, 2 H), 1.63−1.19 (series of m, 26 H), 1.15 (s, 3 H), 1.14 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2, 139.1, 114.15, 114.07, 77.1, 36.3, 35.9, 33.8, 33.7, 30.4, 30.3, 29.7, 29.6, 29.5, 29.2, 29.1, 28.9, 23.74, 23.71, 21.1, 20.7 (3C not observed); ES MS m/z $(M + Na)^+$ calcd 375.3239, obsd 375.3255. Anal. Calcd for $C_{23}H_{44}O_2$: C, 78.35; H, 12.58. Found: C, 78.13; H, 12.56.

General Procedure for Cyclic Carbonate Formation. A solution of the diol (0.60 mmol) in dry CH_2Cl_2 (20 mL) was cooled to 0 °C, treated with pyridine (290 μL) and then a 1.9 M solution of phosgene in toluene (0.60 mmol), and allowed to warm to 20 °C over 1 h. The volatiles were evaporated, and the residue was chromatographed on silica gel (elution with 5% ether in petroleum ether) to achieve separation of the less polar from the more polar isomer.

For **16a** and **17a**: (combined 87% yield; 4:1 ratio); less polar isomer: colorless oil; IR (neat, cm^{-1}) 1801, 1641; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.84−5.69 (m, 2 H), 5.22−5.09 (m, 2 H), 4.99−4.85 (m, 2 H), 2.58 (dd, J = 14.2, 5.9 Hz, 1 H), 2.27 (dd, J = 14.2, 8.8 Hz, 1 H), 2.06−1.93 (m, 2 H), 1.85−1.15 (series of m, 16 H), 1.36 (s, 3 H), 1.32 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.7, 139.0, 131.2, 120.0, 114.0, 88.2, 87.4, 39.7, 35.0, 33.6, 29.8, 29.3 (2C), 29.2, 28.9, 28.8, 23.7, 19.1, 18.6; ES MS m/z $(M + Na)^+$ calcd 331.2249, obsd 331.2231. Anal. Calcd for $C_{19}H_{32}O_3$: C, 73.98; H, 10.46. Found: C, 74.16; H, 10.28.

More polar isomer: colorless oil; IR (neat, cm^{-1}) 1800, 1641; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87−5.74 (m, 2 H), 5.24−5.14 (m, 2 H), 5.04−4.90 (m, 2 H), 2.62 (dd, J = 14.6, 5.9 Hz, 1 H), 2.29 (dd, J = 14.6, 8.9 Hz, 1 H), 2.09−2.00 (m, 2 H), 1.87−1.22 (series of m, 16 H), 1.35 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.8, 139.1, 131.3, 120.2, 114.1, 88.3, 87.5, 39.3, 34.3, 33.7, 29.9, 29.40, 29.36, 29.3, 29.0, 28.9, 23.7, 19.7, 19.5; ES MS m/z $(M + Na)^+$ calcd 331.2249, obsd 331.2234.

For **16b** and **17b**: (combined 93% yield; 3:1 ratio); less polar isomer: colorless oil; IR (neat, cm^{-1}) 1799, 1640; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87−5.72 (m, 2 H), 5.05−4.91 (m, 4 H), 2.15−2.00 (m, 4 H), 1.85−1.28 (series of m, 22 H), 1.35 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 139.2, 138.3, 114.8, 114.1, 88.5, 88.4, 35.0, 34.8, 33.8, 33.4, 29.9, 29.43 (2C), 29.39 (2C), 29.1,

28.9, 23.9, 23.3, 18.9 (2C); ES MS *m/z* $(M + Na)^+$ calcd 373.2719, obsd 373.2723.

More polar isomer: colorless oil; IR (neat, cm^{-1}) 1799, 1640; ^1H NMR (300 MHz, $CDCl_3$) δ 5.86−5.72 (m, 2 H), 5.05−4.90 (m, 4 H), 2.13−2.01 (m, 4 H), 1.85−1.29 (series of m, 22 H), 1.36 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 139.2, 138.3, 114.8, 114.1, 88.4, 88.3, 34.4, 34.2, 33.8, 33.4, 30.0, 29.44 (2C), 29.40 (2C), 29.1, 28.9, 23.7, 23.1, 19.42, 19.39; EI MS *m/z* $(M + H)^+$ calcd 351.2899, obsd 351.2904.

For **16c** and **17c**: (combined 75% yield; 3:1 ratio); less polar isomer: colorless oil; IR (neat, cm^{-1}) 1802, 1640; ^1H NMR (300 MHz, $CDCl_3$) δ 5.88−5.73 (m, 2 H), 5.03−4.91 (m, 4 H), 2.07−2.00 (m, 4 H), 1.81−1.73 (m, 2 H), 1.63−1.20 (series of m, 24 H), 1.35 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 139.2, 138.9, 114.3, 114.1, 88.4 (2C), 35.0, 33.8, 33.6, 29.9, 29.8, 29.43 (2C), 29.39 (2C), 29.1, 28.9, 28.8, 28.7, 23.90, 23.87, 18.9 (2C); ES MS *m/z* $(M + Na)^+$ calcd 401.3032, obsd 401.3034. Anal. Calcd for $C_{24}H_{42}O_3$: C, 76.14, H, 11.18. Found: C, 76.32; H, 11.33.

More polar isomer: colorless oil; IR (neat, cm^{-1}) 1799, 1641; ^1H NMR (300 MHz, $CDCl_3$) δ 5.88−5.73 (m, 2 H), 5.02−4.91 (m, 4 H), 2.07−2.01 (m, 4 H), 1.80−1.70 (m, 2 H), 1.59−1.28 (series of m, 24 H), 1.35 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2, 139.2, 138.9, 114.3, 114.1, 88.5, 88.4, 34.4, 33.8, 33.7, 29.9, 29.8, 29.42 (2C), 29.40 (2C), 29.1, 28.9 (2C), 28.7, 23.72, 23.68, 19.4 (2C); ES MS *m/z* $(M + Na)^+$ calcd 401.3032, obsd 401.3036.

Ring Closing Metathesis of Cyclic Carbonates. To a solution of **16** or **17** (0.10 mmol) in CH_2Cl_2 (25 mL) was added 17 mg (0.02 mmol) of Grubbs's catalyst at 20 °C under argon. The reaction mixture was stirred at 40 °C for 36 h, cooled, treated with 15 mg of lead tetraacetate, and stirred overnight. Following solvent evaporation under reduced pressure, the residue was taken up in hexanes and filtered through a short pad of silica gel. The filtrate was evaporated and final purification was achieved by flash chromatography on silica gel (elution with hexanes to 3% ethyl acetate in hexanes). Unreacted **16** or **17** was invariably recovered (25−40%).

Compounds 18a and 19a. Ring closing metathesis of **16a** (less polar) gave rise to **18a** in 37% yield; colorless oil; IR (neat, cm^{-1}) 1800; ^1H NMR (300 MHz, $CDCl_3$) δ 5.41−5.19 (m, 2 H), 2.42−2.32 (m, 2 H), 2.27−1.08 (m, 18 H), 1.39 (s, 3 H), 1.36 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9, 130.8, 129.9, 126.4, 125.6, 88.7, 87.9, 40.3, 39.3, 34.4, 34.2, 33.5, 33.2, 29.9, 29.7, 29.43, 29.37, 29.2, 29.0, 27.3, 23.2, 23.0, 20.5, 20.4, 19.7, 19.5; ES MS *m/z* $(M + Na)^+$ calcd 303.1931, obsd 303.1941. Anal. Calcd for $C_{17}H_{28}O_3$: C, 72.82; H, 10.06. Found: C, 72.60; H, 10.14.

Ring closure of **17a** (more polar) afforded **19a** (30%) as a colorless oil; IR (neat, cm^{-1}) 1801; ^1H NMR (300 MHz, $CDCl_3$) δ 5.30−5.18 (m, 2 H), 2.43−2.30 (m, 2 H), 2.25−1.07 (m, 18 H), 1.38 (s, 3 H), 1.36 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 130.7, 129.7, 126.2, 125.7, 88.6, 87.7, 41.2, 39.2, 34.2, 34.1, 33.4, 33.2, 29.8, 29.6, 29.2, 29.1, 29.0, 28.9, 23.2, 22.9, 20.6, 20.4, 19.8, 19.7; ES MS *m/z* $(M + Na)^+$ calcd 303.1931, obsd 303.1904.

Compounds 18b and 19b. Ring closing metathesis of **16b** (less polar) furnished **18b** in 47% yield as a colorless oil; IR (neat, cm^{-1}) 1799; ^1H NMR (300 MHz, $CDCl_3$) δ 5.46−5.17 (m, 2 H), 2.26−1.07 (series of m, 26 H), 1.39 (s, 3 H), 1.38 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 131.8, 131.1, 129.8, 129.6, 88.7, 88.3, 35.4, 34.0, 33.9, 32.6, 32.0, 29.4, 29.01, 28.96, 28.9, 28.04, 27.97, 27.62, 27.57, 27.42, 27.36, 26.6, 26.3, 25.6, 25.3, 23.1, 23.0, 21.9, 21.5, 20.5, 20.4, 19.4; ES MS *m/z* $(M + Na)^+$ calcd 345.2400, obsd 345.2398.

Comparable treatment of **17b** (more polar) gave rise to **19b** (45%) as a colorless oil; IR (neat, cm^{-1}) 1798; ^1H NMR (300 MHz, $CDCl_3$) δ 5.39−5.29 (m, 2 H), 2.12−1.95 (m, 4 H), 1.87−1.66 (m, 4 H), 1.61−1.22 (series of m, 18 H), 1.40 (s, 3 H), 1.36 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.1, 131.2, 130.3, 130.1, 129.4, 88.6, 88.2, 36.3, 34.54, 34.49, 33.1, 31.8, 31.6, 30.4, 29.9, 28.4, 28.0, 27.9, 27.72, 27.69, 27.5, 27.4, 26.8, 26.6, 26.5, 26.2, 25.9, 22.9, 22.8, 22.1, 21.8, 21.1, 20.6, 20.3, 19.7; ES MS *m/z* calcd 345.2400, obsd 345.2411.

Compounds 18c and 19c. Ring closing metathesis of **16c** (less polar) afforded **18c** in 50% yield as a colorless oil; IR (neat, cm^{-1}) 1800; ^1H NMR (300 MHz, $CDCl_3$) δ 5.35−5.29 (m, 2 H), 2.05−1.95 (m, 4 H), 1.76−1.59 (m, 4 H), 1.53−1.17 (series of m, 22 H), 1.39 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.0, 130.9, 130.5, 130.3, 129.7, 88.63, 88.57, 34.9, 34.3, 32.6, 32.1, 29.5, 29.0, 28.8, 28.72, 28.67, 28.4, 28.3, 28.0, 27.8, 27.7, 27.6, 27.1, 24.2, 22.9, 22.8, 20.1, 19.9; ES MS *m/z* (M^+) calcd 373.2719, obsd 373.2723. Anal. Calcd for $C_{22}H_{38}O_3$: C, 75.38; H, 10.93. Found: C, 75.26; H, 11.04.

Comparable treatment of **17c** (more polar) furnished **19c** in 46% yield as a colorless oil; IR (neat, cm^{-1}) 1799, 1641; ^1H NMR (300 MHz, $CDCl_3$) δ 5.39−5.27 (m, 2 H), 2.09−2.00 (m, 4 H), 1.80−1.63 (m, 4 H), 1.58−1.24 (series of m, 22 H), 1.36 (s, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.2, 130.7, 130.6, 130.3, 130.0, 88.5, 88.3, 35.0, 34.8, 34.3, 33.5, 32.1, 32.0, 29.7, 29.3, 28.9, 28.83, 28.76, 28.7, 28.5, 27.7, 27.4, 26.8, 26.6, 23.6, 23.4, 22.9, 22.5, 20.3, 20.2, 20.1, 20.0; ES MS *m/z* $(M + Na)^+$ calcd 373.2719, obsd 373.2714.

General Procedure for the Generation of Ketones 20. A solution of **19b** (22 mg, 0.068 mmol) in absolute ethanol (3 mL) containing 4 mg of 10% palladium on charcoal was vigorously stirred overnight under 1 atm of H_2, treated with 2 mL of 2 M sodium hydroxide solution, and stirred for an additional 2 h. The mixture was filtered through a small pad of Celite, and the filtrate was partitioned between water (100 mL) and CH_2Cl_2 (100 mL). The separated aqueous layer was extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were dried and evaporated. The residue was taken up in CH_2Cl_2 (5 mL), treated with lead tetraacetate (60 mg, 0.14 mmol), stirred for 30 min, and freed of solvent. The diketone was purified by flash chromatography on silica gel.

2,15-Hexadecanedione (20a).[40] Obtained from **19a** in 79% overall yield; white solid, mp 82−83 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 2.40 (t, J = 7.0 Hz, 4 H), 2.12 (s, 6 H), 1.59−1.53 (m, 4 H), 1.27−1.24 (m, 16 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.1 (2C), 43.6 (2C), 29.8 (2C), 29.6 (2C), 29.5 (2C), 29.4 (2C), 29.2 (2C), 23.8 (2C).

2,18-Nonadecanedione (20b).[41a] Obtained from **19b** in 84% overall yield; white solid, mp 89.5−90.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 2.40 (t, J = 7.4 Hz, 4 H), 2.12 (s, 6 H), 1.58−1.53 (m, 4 H), 1.26−1.24 (m, 22 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 209.3 (2C), 43.8 (2C), 29.8 (2C), 29.59 (3C), 29.56 (2C), 29.43 (2C), 29.36 (2C), 29.2 (2C), 23.9 (2C).

2,20-Heneicosanedione (20c).[41b] Obtained from **19c** in 80% overall yield; colorless solid, mp 91−92 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 2.41 (t, J = 7.4 Hz, 4 H), 2.13 (s, 6 H), 1.61−1.52 (m, 4 H), 1.27−1.25 (m, 26 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 205.7 (2C), 43.8 (2C), 29.8 (2C), 29.7 (3C), 29.65 (2C), 29.61 (2C), 29.5 (2C), 29.4 (2C), 29.2 (2C), 23.9 (2C).

1,2-Diallylcyclohexane-1,2-diol (21).[11a,21b,28] Isolated as a colorless oil in 92% yield; ^1H NMR (500 MHz, $CDCl_3$) δ 5.95−5.87 (m, 2 H), 5.14−5.08 (m, 4 H), 2.47−2.20 (m, 4 H), 2.15 (s, 2 H), 1.70−1.65 (m, 2 H), 1.58−1.47 (series of m, 4 H), 1.37−1.30 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 134.0 (2C), 118.4 (2C), 75.2 (2C), 39.1 (2C), 32.9 (2C), 21.5 (2C).

1,2,3,4,5,8-Hexahydronaphthalene-4a,8a-diol (22).[29] Colorless oil; 96% yield; ^1H NMR (500 MHz, $CDCl_3$) δ 5.75−5.72 (m, 0.18 × 2 H), 5.57−5.52 (m, 0.82 × 2 H), 2.31−2.05 (series of m, 6 H), 1.83−1.56 (series of m, 4 H), 1.53−1.21 (series of m, 4 H); For the major diastereomer ^{13}C NMR (75 MHz, $CDCl_3$) δ 124.2 (2C), 72.0 (2C), 37.1 (2C), 34.5 (2C), 22.4 (2C). For the

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minor diastereomer ^{13}C NMR (75 MHz, $CDCl_3$) δ 133.3 (2C), 71.7 (2C), 36.1 (2C), 31.7 (2C), 24.4 (2C).

(*Z*)-3-Cyclodecene-1,4-dione (23). White solid, mp 78−79 °C; 46% yield; IR (neat, cm^{-1}) 1705; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.81 (t, J = 4.9 Hz, 2 H), 3.12 (d, J = 6.1 Hz, 4 H), 2.43−2.40 (m, 4 H), 1.84−1.79 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.2 (2C), 126.1 (2C), 41.7 (2C), 40.4 (2C), 23.3 (2C); EI MS m/*z* (M^+) calcd 166.0944, obsd 166.0993. Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.42; H, 8.68.

(*E*)-2-Cyclodecene-1,6-dione (24). White solid, mp 85−87 °C; 23% yield; IR (neat, cm^{-1}) 1709, 1634, 1460; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.14 (d, J = 11.9 Hz, 1 H), 5.80 (dt, J = 11.9, 8.4 Hz, 1 H), 2.82−2.75 (m, 2 H), 2.45−2.34 (m, 6 H), 1.84−1.72 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.0, 208.2, 136.8, 132.0, 44.0, 42.0, 36.0, 23.7, 23.2, 23.0; EI MS *m*/*z* (M^+) calcd 166.0944, obsd 166.0984. Anal. Calcd $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.31; H, 8.61.

Octahydronaphthalene-4a,8a-diol (25).[30] Colorless oil obtained in quantitative yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.03 (br s, 2 H), 1.79−1.56 (m, 8 H), 1.54−1.19 (m, 8 H); ^{13}C NMR (75 MH, $CDCl_3$) δ 73.0 (2C), 36.7 (4C), 33.2 (4C), 23.4 (4C), 20.9 (4C).

Cyclodecane-1,6-dione (26).[31] White solid, mp 99−100 °C;[32] 79% yield; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.45−2.33 (m, 8 H), 1.86−1.79 (m, 8 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.1 (2C), 42.2 (4C), 23.4 (4C).

2-Allyl-2-hydroxycyclododecanone. This α-ketol was prepared in the manner described above in 95% yield: colorless solid; mp 55−56 °C; IR ($CHCl_3$, cm^{-1}) 3478, 1704, 1640; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.79−5.65 (m, 1 H), 5.10−5.04 (m, 2 H), 3.97 (m, 1 H), 3.08−2.97 (m, 1 H), 2.49−2.39 (m, 2 H), 2.20−2.07 (m, 2 H), 1.89−1.66 (series of m, 2 H), 1.55−1.17 (series of m, 14 H), 0.83−0.71 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 213.9, 132.5, 118.3, 82.2, 43.2, 36.5, 32.7, 26.4, 26.2, 23.9, 22.7, 22.5, 22.4, 21.6, 19.6; EI MS *m*/*z* (M^+) calcd 238.1933, obsd 238.1939. Anal. Calcd for $C_{15}H_{26}O_2$: C, 75.58; H, 10.99. Found: C, 75.29; H, 11.01.

1,2-Diallylcyclododecane-1,2-diol (28). The preceding α-ketol (500 mg, 3.1 mmol) was dissolved in anhydrous ether (30 mL) and treated with 1 M allylmagnesium bromide in ether (9.0 mL, 9.0 mmol) at −20 °C. After 30 min, the reaction mixture was poured into saturated NH_4Cl solution, the layers were separated, and the aqueous layer was extracted with ether (2 × 35 mL). The combined organic fractions were dried, filtered, and concentrated under reduced pressure. The residue was chromatographed on silica gel (elution with 10% ether in ligroin) to give 755 mg (87%) of **28** as a single diastereomer: colorless oil; IR ($CHCl_3$, cm^{-1}) 3540, 1637; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.04−5.89 (m, 2 H), 5.14−5.08 (m, 4 H), 2.43−2.25 (m, 4 H), 2.36 (br s, 2 H), 1.83−1.24 (series of m, 20 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 134.9 (2C), 118.3 (2C), 78.5 (2C), 40.9 (2C), 34.6 (2C), 26.7 (2C), 24.7 (2C), 23.2 (2C), 21.5 (2C); EI MS *m*/*z* (M^+) 280.2402, obsd 280.2403. Anal. Calcd for $C_{18}H_{32}O_2$: C, 77.09; H, 11.50. Found: C, 77.13; H, 11.51.

1,4,5,6,7,8,9,10,11,12,13,14-Dodecahydrobenzocyclododecene-4a,14a-diol (29). White solid, mp 73−75 °C; 96% yield; IR ($CHCl_3$, cm^{-1}) 3567, 1470; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.51 (s, 2 H), 2.23−2.09 (series of m, 6 H), 1.75−1.59 (series of m, 4 H), 1.53−1.25 (series of m, 16 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 124.3 (2C), 75.5 (2C), 37.4 (2C), 33.2 (2C), 26.0 (2C), 24.1 (2C), 22.8 (2C), 20.8 (2C); EI MS *m*/*z* (M^+) calcd 252.2089, obsd 252.2084. Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 76.24; H, 11.24.

(Z)-3-Cyclohexadecene-1,6-dione (30). White solid, mp 92−93 °C; 42% yield; IR (neat, cm^{-1}) 1703, 1438; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.77 (t, J = 4.8 Hz, 2 H), 3.18 (d, J = 5.9 Hz, 4 H), 2.43 (t, J = 6.8 Hz, 4 H), 1.68−1.42 (m, 4 H), 1.26−1.15 (m, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 208.4 (2C), 124.1 (2C), 42.1 (2C), 41.3 (2C), 27.1 (2C), 26.3 (2C), 26.1 (2C), 22.7 (2C); EI MS *m*/*z* (M^+) calcd 250.1933, obsd 250.1936. Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.75; H, 10.39.

(*E*)-2-Cyclohexadecene-1,6-dione (31). Colorless oil; 23% yield; IR (neat, cm^{-1}) 1710, 1640, 1463; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.21−6.10 (m, 2 H), 2.92−2.85 (m, 2 H), 2.56 (t, J = 6.7 Hz, 2 H), 2.44 (t, J = 6.3 Hz, 2 H), 2.37 (t, J = 7.1 Hz, 2 H), 1.77−1.24 (series of m, 16 H); ^{13}C NMR (75 MHZ, $CDCl_3$) δ 211.2, 202.5, 145.7, 128.0, 43.3, 42.5, 41.0, 27.5, 27.4, 26.9, 26.8, 26.5, 26.2, 24.4, 23.4, 22.7; EI MS *m*/*z* (M^+) calcd 250.1933, obsd 250.1933.

Cyclohexadecane-1,6-dione (32).[33] White solid, mp 83−84 °C; 86% yield; IR ($CHCl_3$, cm^{-1}) 1706; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.36 (t, J = 6.7 Hz, 8 H), 1.61−1.54 (m, 8 H), 1.33−1.16 (m, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.8 (2C), 42.2 (2C), 41.4 (2C), 27.4 (2C), 26.9 (2C), 26.6 (2C), 23.6 (2C), 23.0 (2C); HRMS *m*/*z* (M^+) calcd 252.2089, obsd 252.2083. Anal. Calcd for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found C, 76.96; H, 11.23.

3-Allyl-3-hydroxy-1,7,7-trimethylbicyclo[2.2.1]heptan-2-one (34). Colorless oil; 90% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.91−5.80 (m, 1 H), 5.14−5.08 (m, 2 H), 2.69 (br s, 1 H), 2.27 (dd, J = 14.8, 6.6 Hz, 1 H), 2.18 (dd, J = 14.8, 7.7 Hz, 1 H), 1.92 (d, J = 4.2 Hz, 1 H), 1.85−1.75 (m, 1 H), 1.64−1.48 (m, 2 H), 1.42−1.35 (m, 1 H), 0.98 (s, 3 H), 0.91 (s, 3 H), 0.85 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 220.4, 132.3, 119.3, 77.6, 58.2, 51.4, 46.1, 40.7, 29.7, 22.3, 22.1, 20.3, 9.4.

Compound 36. Colorless oil; 60% yield; IR (neat, cm^{-1}) 3440, 1640; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.99−5.82 (m, 1 H), 5.80−5.74 (m, 1 H), 5.19−5.12 (m, 2 H), 5.02−4.90 (m, 2 H), 2.82 (br s, 2 H), 2.70 (dd, J = 14.0, 6.7 Hz, 1 H), 2.22, (dd, J = 14.0, 7.7 Hz, 1 H), 2.03 (m, 2 H), 1.75−1.17 (series of m, 22 H), 0.91 (s, 3 H), 0.83 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.0, 135.0, 118.1, 114.0, 83.1, 82.2, 53.8, 53.4, 48.4, 40.8, 35.4, 33.7, 30.8, 29.7, 29.5, 29.4, 29.0, 28.8, 24.8, 23.2, 23.1, 22.5, 11.6; ES MS *m*/*z* (M + Na)$^+$ calcd 371.2926, obsd 371.2935; $[\alpha]^{22}_D$ +4.7 (*c* 1.0, $CHCl_3$).

Compound 37. Colorless oil; 80% yield; IR (neat, cm^{-1}) 1789, 1641; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.90−5.71 (m, 2 H), 5.17−5.12 (m, 2 H), 4.99−4.87 (m, 2 H), 2.65 (dd, J = 14.6, 8.6 Hz, 1 H), 2.46 (dd, J = 14.6, 5.5 Hz, 1 H), 2.05−1.97 (m, 3 H), 1.93−1.83 (m, 1 H), 1.73−1.58 (m, 2 H), 1.53−1.20 (series of m, 15 H), 1.13 (s, 3 H), 0.98 (s, 3 H), 0.92 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 154.8, 139.0, 131.9, 118.9, 114.1, 94.6, 94.2, 53.2, 50.3, 47.3, 37.7, 33.7, 31.9, 30.2, 29.3 (2C), 29.0, 28.9, 28.7, 24.4, 24.3, 21.7, 20.5, 10.7; ES MS *m*/*z* (M + Na)$^+$ calcd 397.2719, obsd 397.2725; $[\alpha]^{22}_D$ −11.5 (*c* 0.98, $CHCl_3$). Anal. Calcd for $C_{24}H_{38}O_3$: C, 76.96; H, 10.23. Found: C, 76.97; H, 10.36.

General Procedure for Twofold Alkyllithium Addition. (1*R*)-(−)-Camphorquinone (100 mg, 0.60 mmol) was dissolved in dry THF (2 mL), treated with lithium wire (74 mg, 10.6 mmol), placed under argon, and cooled to 0 °C. A solution of 10-bromo-1-decene (1.05 g, 4.8 mmol) in dry THF (3 mL) was introduced dropwise into the stirred reaction mixture, which was allowed to warm to room temperature after the addition was complete. After 12 h, the solvent was evaporated, and the residue was taken up in ether (10 mL) and added to a separatory funnel containing water (10 mL) and 1 M NH_4Cl solution (1 mL). Extraction of the aqueous layer with ether (3 × 10 mL) following by drying, concentration, and flash chromatographic purification (silica gel, elution with 9:1 petroleum ether/ether) afforded diol **38** as a colorless oil (75 mg, 28%); IR (neat, cm^{-1}) 3440, 1462; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.88−5.74 (m, 2 H), 5.02−4.91 (m, 4 H), 2.07−2.00 (m, 4 H), 1.70−1.15 (series of m, 35 H), 1.25 (s, 3 H), 0.90 (s, 3 H), 0.83 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2 (2C), 114.1 (2C), 83.6, 83.5, 53.3, 48.4, 36.5, 35.1, 33.8 (2C), 30.8, 30.4, 29.9, 29.7, 29.64, 29.57, 29.5 (2C), 29.1 (2C), 28.9 (2C), 24.9, 24.6, 23.32, 23.27, 22.8, 11.7; ES MS (M + Na)$^+$ calcd 469.4022, obsd 469.4038; $[\alpha]^{22}_D$ +0.7 (*c* 2.4, $CHCl_3$). Anal. Calcd for $C_{30}H_{54}O_2$: C, 80.65; H, 12.18. Found: C, 80.32; H. 12.16.

Compound 39. Colorless oil; 24% yield; IR (neat, cm^{-1}) 3442, 1463; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87−5.73 (m, 2 H), 5.01−4.90 (m, 4 H), 2.58 (br s, 2 H), 2.06−2.00 (m, 4 H), 1.81−1.03 (m, 40 H), 0.89 (s, 3 H), 0.83 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2 (2C), 114.1, (2C), 83.6, 83.5, 53.4, 53.3, 48.3, 36.5, 35.1, 33.8 (2C), 30.8, 30.4, 29.8, 29.7, 29.60, 29.58 (2C), 29.5 (2C), 29.1 (2C), 28.9 (2C), 24.9, 24.6, 23.30, 23.25, 22.8, 11.6; ES MS *m*/*z* (M + Na)$^+$ calcd 497.4335, obsd 497.4318; $[\alpha]^{22}_D$ +2.7 (*c* 1.73, $CHCl_3$). Anal. Calcd for $C_{32}H_{58}O_2$: C, 80.95; H, 12.31. Found: C, 80.88; H. 12.46.

Compound 41. Submission of **38** (70 mg, 0.16 mmol) to one-pot ring-closing metathesis/oxidative cleavage according to the general protocol furnished 29.4 mg (45% overall) of diketone **41** as a colorless oil; IR (neat, cm^{-1}) 1696; ^1H NMR (300 MHz, $CDCl_3$) δ 5.33−5.32 (m, 2 H), 2.93 (dd, J = 9.6, 8.4 Hz, 1 H), 2.66−2.35 (m, 5 H), 2.27−2.15 (m, 1 H), 1.93−1.89 (m, 4 H), 1.78−1.37 (m, 6 H), 1.33−1.14 (m, 23 H), 1.16 (s, 3 H), 0.70 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.2, 214.0, 212.2, 212.0, 130.3, 130.2, 129.8, 61.4, 61.3, 60.0, 59.8, 47.6, 47.3, 43.3, 39.3, 32.8, 32.5, 32.4, 29.6, 29.2, 29.0, 28.9, 28.72, 28.67, 28.6, 28.5, 28.3, 28.2, 28.13, 28.06, 27.9, 27.8, 27.7, 27.5, 27.2, 27.1, 24.7, 24.4, 22.9, 22.7, 22.2, 21.9, 21.6, 21.2, 21.0; EI MS m/z (M^+) calcd 416.3654, obsd 416.3649; $[\alpha]^{22}_D$ +30.9 (c 0.22, $CHCl_3$). Anal. Calcd for $C_{28}H_{48}O_2$: C, 80.71; H, 11.61. Found: C, 80.72; H, 11.65.

Compound 42. Sequential ring closing metathesis/hydrogenation/oxidative cleavage of **37** (47 mg, 0.11 mmol) gave 19.5 mg (45% over three steps) of **42** as a colorless oil; IR (neat, cm^{-1}) 1727; ^1H NMR (300 MHz, $CDCl_3$) δ 2.95 (dd, J = 8.2, 9.7 Hz, 1 H), 2.65−2.30 (m, 5 H), 2.26−2.16 (m, 1 H), 1.78−1.16 (series of m, 37 H), 1.16 (s, 3 H), 0.70 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.2, 212.1, 61.4, 59.8, 47.4, 43.6, 39.5, 32.5, 29.1 (2C), 29.0 (2C), 28.8, 28.7, 28.44, 28.36, 28.2, 28.1, 27.8 (2C), 27.6 (2C), 24.4, 22.8, 22.2 (2C), 21.6, 21.2; EI MS m/z (M^+) calcd 418.3811, obsd 418.3790; $[\alpha]^{20}_D$ +46.3 (c 0.45, $CHCl_3$).

Compound 44. Colorless oil; 49% yield over two steps; IR (neat, cm^{-1}) 1704, 1462; ^1H NMR (300 MHz, $CDCl_3$) δ 5.36−5.33 (m, 2 H), 2.95−2.89 (m, 1 H), 2.57−2.36 (m, 5 H), 2.19 (m, 1 H), 1.98−1.94 (m, 4 H), 1.75−1.40 (m, 6 H), 1.33 (s, 3 H), 1.33−1.14 (m, 24 H), 1.14 (s, 3 H), 0.69 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.3, 214.0, 212.3, 212.1, 130.4, 130.3, 129.82, 129.77, 61.3, 61.2, 59.9, 59.8, 47.5, 47.4, 43.7, 43.5, 39.8, 39.6, 32.7, 32.6, 32.3, 29.8, 29.4, 29.33, 29.26, 29.2, 29.1, 28.9, 28.8, 28.7, 28.6, 28.54, 28.51, 28.4, 28.3, 28.25, 28.20, 28.15, 28.1, 28.06, 27.9, 27.13, 27.10, 24.6, 24.5, 22.9, 22.8, 22.54, 22.47, 22.3, 21.6, 21.2, 21.1; EI MS m/z (M^+) calcd 444.3967, obsd 444.4017; $[\alpha]^{22}_D$ +42.4 (c 0.50, $CHCl_3$).

Compound 45. Colorless oil; 45% yield over three steps; IR (neat, cm^{-1}) 1701; ^1H NMR (300 MHz, $CDCl_3$) δ 2.95 (dd, J = 8.3, 9.6 Hz, 1 H), 2.61−2.32 (m, 5 H), 2.30−2.14 (m, 1 H), 1.78−1.41 (m, 6 H), 1.33 (s, 3 H), 1.33−1.15 (m, 32 H), 1.15 (s, 3 H), 0.70 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 214.2, 212.2, 61.2, 59.7, 47.3, 43.8, 39.8, 32.5, 29.25, 29.15, 29.0 (2C), 28.8, 28.7, 28.42, 28.38, 28.33, 28.26, 28.2, 28.1, 28.0 (2C), 27.9 (2C), 24.3, 22.73, 22.65, 22.5, 21.4, 21.3; ES MS m/z $(M + Na)^+$ calcd 469.4022, obsd 469.4059; $[\alpha]^{22}_D$ +51.3 (c 2.71, $CHCl_3$).

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