Pergamon

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Tetrahedron 59 (2003) 8919–8930

TETRAHEDRON

Development of novel Lewis acid catalyzed cycloisomerizations: synthesis of bicyclo[3.1.0]hexenes and cyclopentenones

Aubry K. Miller, Matthew R. Banghart, Christopher M. Beaudry, Judy M. Suh and Dirk Trauner*

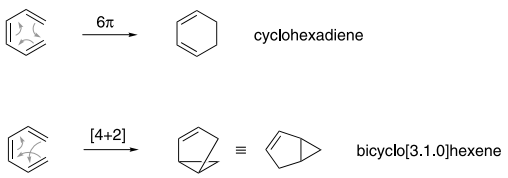
Department of Chemistry, Center for New Directions in Organic Synthesis, University of California, 419 Latimer Hall, Berkeley, CA 94720, USA

Received 10 February 2003; accepted 4 April 2003

Abstract—The Lewis acid catalyzed cyclization of hexatrienes and pentadienals to bicyclo[3.1.0]hexenes and cyclopentenones, respectively, was investigated. The application of the former reaction to the total synthesis of photodeoxytridachione, a molluscan polypropionate, is described.

1. Introduction

Thermal and photochemical 6π electrocyclizations are ubiquitous within the chemical literature (Scheme 1).[1] Their development as a powerful synthetic tool has been greatly aided by advances in theory, culminating in the Woodward–Hoffmann principle of conservation of orbital symmetry.[2] The discovery of these reactions in many biosynthetic pathways, has further added to their importance.[3]

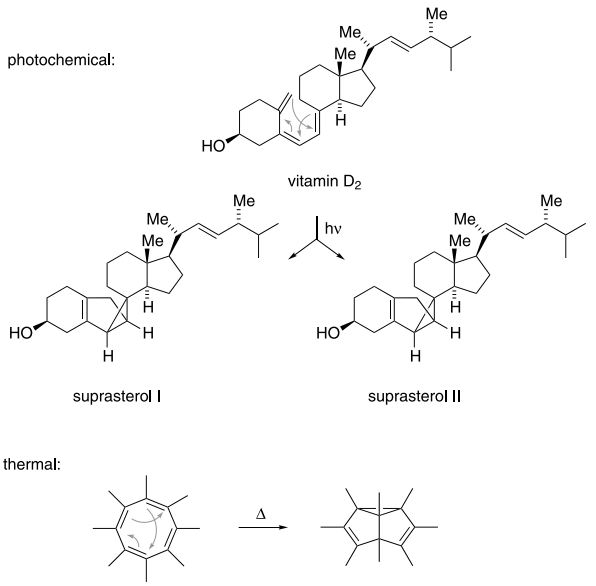


Scheme 1.

In comparison, the isomerization of hexatrienes to bicyclo[3.1.0]hexenes has received relatively little attention (Scheme 1). Nevertheless, photochemical versions of the reaction are well known.[4] One example, the photolysis of vitamin D_2 to afford a mixture of suprasterol I and II, is shown in Scheme 2.[5]

In a sense, these isomerizations can be seen as intramolecular [4+2] cycloadditions with a tether consisting of a single bond. Hence, they have been dubbed the 'photochemical Diels–Alder reaction'.[2] In accordance with the Woodward–Hoffmann rules, they proceed as $[_\pi4_a+_\pi2_s]$ or $[_\pi4_a+_\pi2_s]$ cycloadditions—antarafacial with respect to one component and suprafacial with respect to the other.

Very few thermal isomerizations of this type, which, if concerted, necessarily proceed as $[_\pi4_a+_\pi2_a]$ cycloadditions, have been reported. Most of these involve cyclooctatetraenes as substrates (Scheme 2).[6] To the best of our knowledge, no intermolecular $[_\pi4_a+_\pi2_a]$ cycloadditions have been reported. Steric constraints usually favor the $[_\pi4_s+_\pi2_s]$ pathway found in a 'regular' Diels–Alder reaction and preclude the diene and dienophile from approaching each other in such a fashion as to allow concerted twofold antarafacial bond formation.



Scheme 2. [4+2] cycloadditions affording bicyclo[3.1.0]hexenes.

Keywords: Lewis acid; cycloisomerization; molluscan polypropionate.
* Corresponding author. Tel.: +1-510-643-5507; fax: +1-510-643-9480; e-mail: trauner@cchem.berkeley.edu

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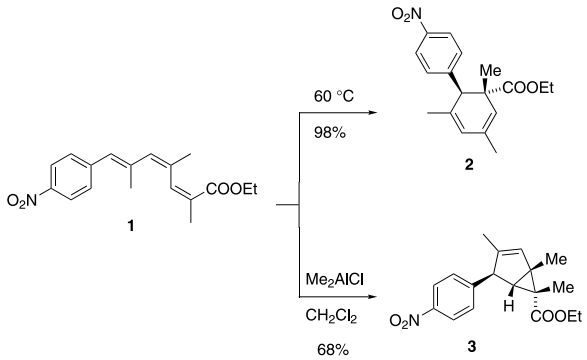
doi:10.1016/j.tet.2003.04.006



Scheme 3.

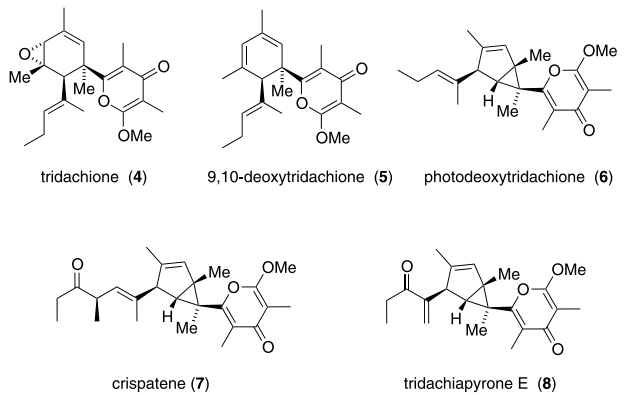


Figure 2. Polypropionates from sacoglossan molluscs.

We now report the discovery of a Lewis acid catalyzed cycloisomerization of substituted hexatrienes that resembles such a thermal [$_{\pi}4_{a}+_{\pi}2_{a}$] cycloaddition. Following its initial serendipitous discovery, the reaction was systematically studied and applied to the total synthesis of natural products featuring a bicyclo[3.1.0]hexene skeleton.[7] A full account of this work, as well as a preliminary report on the extension of the methodology to the cyclization to pentadienals, is given herein.

2. Discovery and application

During our investigations directed at the SNF4435 class of immunosupressants,[3b] it was found that trienoate **1** readily underwent disrotatory electrocyclization to afford cyclohexadiene **2** (Scheme 3). The X-ray crystal structure of this product is shown in Figure 1. The relatively slow rate of the reaction at room temperature offered an opportunity to investigate whether it could be catalyzed. Being quite aware that substituted trienes of type **1** may not be ideal substrates, we wondered what influence, if any, a Lewis acid would have. To the best of our knowledge, electrocyclizations have not yet succumbed to asymmetric catalysis in stark contrast to other pericyclic reactions such as cycloadditions or sigmatropic rearrangements.[8]

To our surprise, treatment of **1** with various Lewis acids did not result in the formation of **2** but rather gave bicyclo[3.1.0]hexene **3** in modest to good yields. No other diastereomers were found. Under optimized conditions, i.e. in the presence of 20% dimethylaluminum chloride, 68% of the bicyclic product was obtained.

It was soon discovered that the trimethyl bicyclo[3.1.0]hexene core of compound **3** occurs in several natural products produced by sacoglossan molluscs.[9] These unusual animals lack a protective shell and rely on chemical defenses against predators. In addition, they harvest functional chloroplasts from algae and use these organelles to live autotrophically through photosynthesis. This fact has provoked investigations to determine if photochemical steps play a role in the biosynthesis of natural products isolated from their tissues.

Most of these metabolites fall into two general classes: cyclohexadiene derivatives and bicyclo[3.1.0]hexenes (Fig. 2). Tridachione (**4**) was isolated from *Tridachiella diomedea*.[10a] The isomers 9,10-deoxytridachione (**5**) and photodeoxytridachione (**6**) were both found in the Pacific mollusc *Placobranchus ocellatus*[10b] and later identified in the Mediterranean *Elysia timida*.[10c] Photodeoxytridachione has shown activity in an ichthyotoxicity assay at 5 ppm.

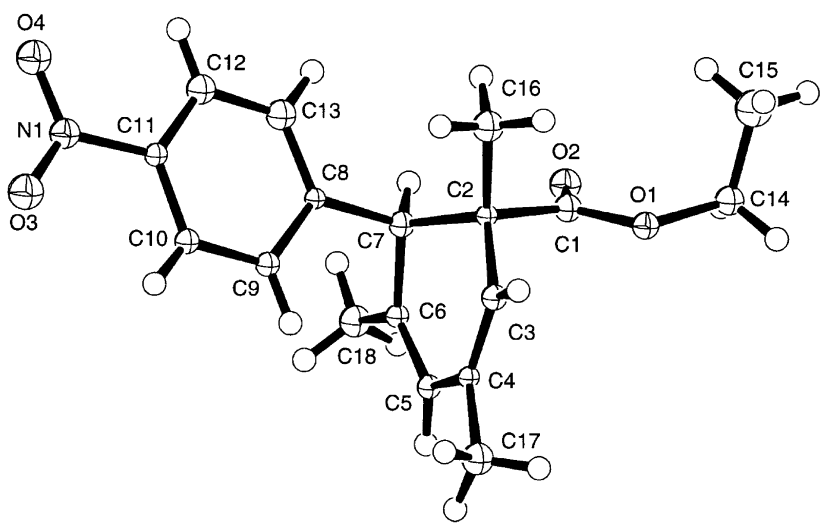


Figure 1. X-Ray structure of compound **2**.

Crispatene (**7**) and tridachiapyrone E (**8**) were isolated from *Elysia crispata*.[10d,e] Crispatene was moderately active in a lymphocytic leukemia assay (ED_{50}=3.7 μg/mL).[10e]

The isomers 9,10-deoxytridachione and photodeoxytridachione have received considerable attention due to their interesting biogenetic relationship. In important studies, Ireland, Faulkner and Scheuer demonstrated that 9,10-deoxytridachione can be photochemically converted in vivo and in vitro into photodeoxytridachione.[10b,d] Thus it appears that the bicyclo[3.1.0]hexene class is biosynthetically derived from the cyclohexadiene class.

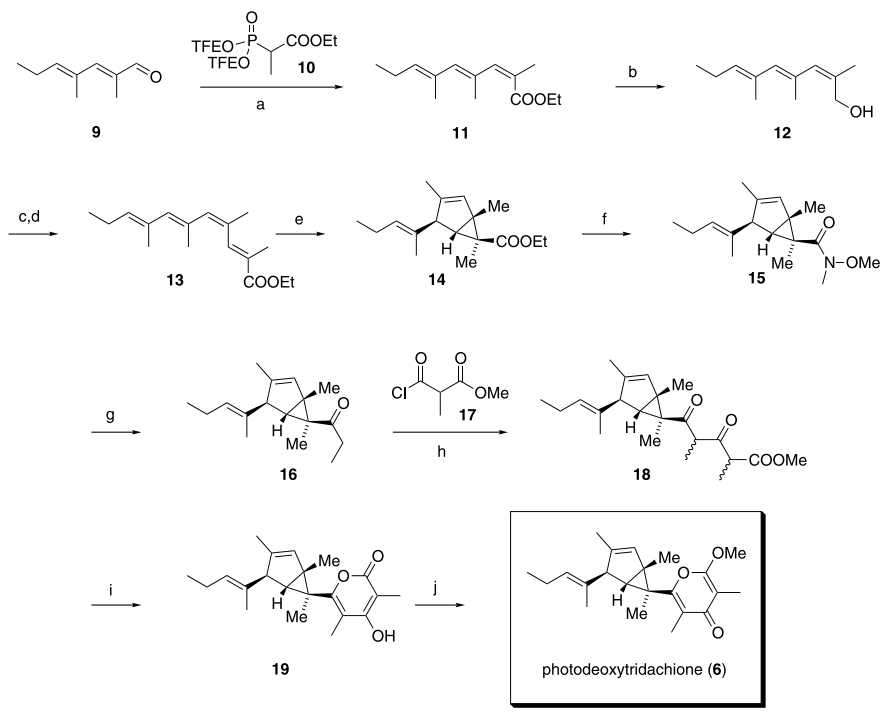
Interestingly, despite their unusual and attractive chemical structures, none of the natural products shown in Figure 2 have been previously prepared by total synthesis. With rapid synthetic access to the bicyclo[3.1.0]hexene core of photodeoxytridachione (**6**), crispatene (**7**) and tridachiapyrone E (**8**) at hand, we decided to launch a program aimed at their total synthesis, starting with the simplest member of the family, **6**.

At the outset of our studies, one important issue remained unresolved: the stereochemistry at one of the quaternary centers in **3** does not correspond to the natural products. We reasoned that this could be potentially overcome by performing the reaction with a geometric isomer of the starting material—a prediction that ultimately proved correct (vide infra).

Our synthesis of photodeoxytridachione started with the conversion of known unsaturated aldehyde **9**[11] into tetraene **13** (Scheme 4). Still–Gennari condensation[12] of **9** with trifluoroethylphosphonate **10** yielded the (*Z*,*E*,*E*)-configured ester **11** with high diastereoselectivity (>20:1). This material was subsequently reduced to allylic alcohol **12**. Oxidation gave a very sensitive aldehyde, which was subjected to a Horner–Wadsworth–Emmons condensation to afford cyclization precursor **13**.

The stage was now set for the application of the newly discovered reaction toward the synthesis of photodeoxytridachione. In the event, treatment of **13** with catalytic amounts of dimethylaluminum chloride effected the cyclization to afford compound **14**, featuring the bicyclic core of photodeoxytridachione, in good yield. Scandium triflate also promoted the cycloisomerization, albeit in lower yields. Again, the bicyclo[3.1.0]hexene product was formed as a single diastereomer. Note that all four stereocenters of the target molecule were set correctly in a relative sense. Clearly, the use of a chiral Lewis acid might provide a way to control the absolute stereochemistry of the reaction as well. We are currently pursuing this possibility. Complicating this task somewhat, the absolute stereochemistry of the natural product remains unknown.

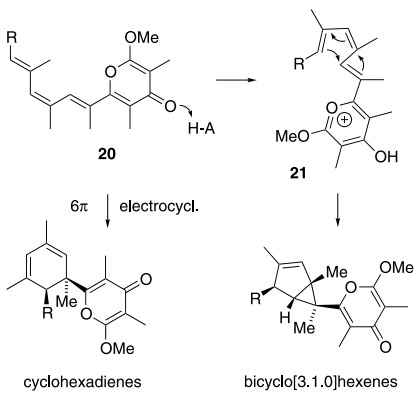
The completion of the synthesis required elaboration of the α-methoxy-γ-pyrone moiety from an ethyl ester—a seemingly straightforward task. However, due to the sterically hindered nature of this neopentylic ester, this transformation proved to be more difficult than anticipated. For instance, **14** could not be converted to the desired tricarbonyl compound **18** by cross Claisen condensation with the corresponding dianion. Therefore, an indirect strategy was chosen. The Weinreb amide **15** was obtained in good yield under carefully controlled conditions.[13] Exposure of **15** to ethyl magnesium bromide then afforded ethyl ketone **16**. Deprotonation of **16** with excess base and



Scheme 4. Total synthesis of (±)-photodeoxytridachione. *Reagents and conditions*: (a) **9**, KHMDS, 18-C-6, THF, −78°C, 79%; (b) DIBAH, CH_2Cl_2, 0°C, 93%; (c) TPAP, NMO, 4 Å mol sieves, CH_2Cl_2; (d) $(EtO)_2P(O)CH(Me)COOEt$, LiCl, DBU, MeCN, 43% from **12**; (e) Me_2AlCl (0.2 equiv.), CH_2Cl_2, 73%; (f) MeHNOMe·HCl, *i*-PrMgCl, THF, 0°C, 63%; (g) EtMgBr, THF, 87%; (h) LiHMDS (3 equiv.), **17**, THF, hexanes, −78°C, 59% (95% borsm); (i) DBU, PhH, rflx., 78%; (j) FSO_2OMe, CH_2Cl_2, 77%.

addition of malonyl chloride **17** gave **18** as an inconsequential mixture of diastereomers in very good yield based on recovered starting material.[14] This reaction presumably proceeds via an acyl ketene intermediate. Cyclization of **18** under basic conditions resulted in formation of the desired pyrone **19**.[15] Finally, regioselective methylation under the conditions described by Beak[16] afforded photodeoxytridachione in good yield. Although a sample of the natural product was not available to us, comparison of the ^{1}H-, ^{13}C-, IR- and MS spectra with the published data confirmed the identity of our synthetic material with the natural product.[7,10c]

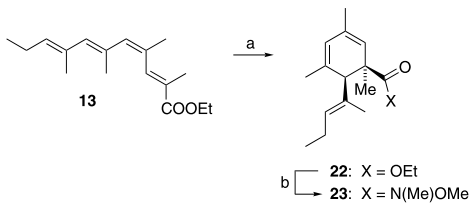
It is interesting to speculate to which extent our synthesis is biomimetic. As mentioned above, Ireland, Faulkner, and Scheuer's work points to a photochemical origin of photodeoxytridachione (**6**) from 9,10-deoxytridachione (**5**), at least in *P. ocellatus*.[10b,d] However, according to Gavagnin and Cimino, the relative amount of **5** and **6** in *E. timida* is independent on the level of exposure to light and the collection season.[9a,10c] Very recently, Baldwin suggested that the bicyclo[3.1.0]hexene core of crispatene is biosynthetically formed from a linear all-*trans* polyene through a series of double bond isomerizations followed by $[_{\pi}4_{s}+_{\pi}2_{a}]$ cycloaddition.[17] The ease of our Lewis acid catalyzed cyclization at low temperatures raises the question whether a similar reaction could occur in nature—perhaps proceeding through pyrylium ion **21** (Scheme 5). Note that thermal 6π-electrocyclization of the putative polyene precursor **20** leads to the cyclohexadiene class of molluscan polypropionates.



Scheme 5.

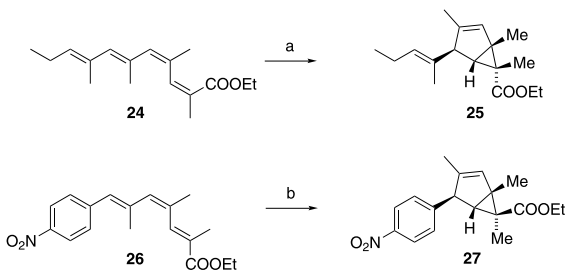
3. Scope and mechanism

Several experiments were performed to gain more insight into the scope and mechanism of the cycloisomerization. First, it is important to note that in the absence of a Lewis acid tetraene **13** undergoes disrotatory 6π electrocyclization to afford cyclohexadiene **22** (Scheme 6). This material may serve as an intermediate in the total syntheses of 9,10-deoxytridachione (**5**) and tridachione (**4**), both of which are currently underway in our laboratories. Conversion to the Weinreb amide **23** sets the stage for the installment of the pyrone moiety analogous to the synthesis of photodeoxytridachione.



Scheme 6. *Reagents and conditions*: (a) PhH, rflx., 98% (b) MeHNOMe·HCl, *i*-PrMgCl, THF, 0°C, 28% (91% borsm).

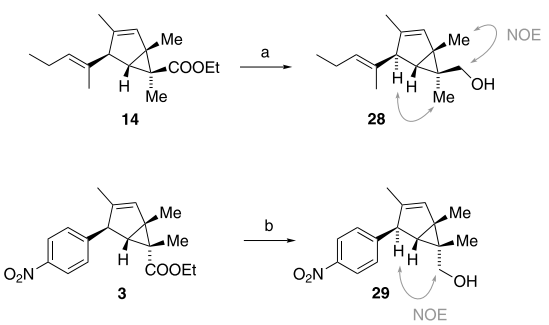
Next, the stereospecificity of the reaction was probed (Scheme 7). The (*Z*,*Z*,*E*,*E*)-configured ester **24** and the (*E*,*Z*,*E*)-configured ester **26** were prepared using stereoselective olefination methods as before (see Section 5). Each underwent stereospecific cyclization to afford **25** and **27**, respectively, as single diastereomers. Hence, the stereochemistry of the α,β-unsaturated ester moiety is reflected in the cyclization product.



Scheme 7. *Reagents and conditions*: (a) Me_2AlCl (0.2 equiv.), CH_2Cl_2, 61%. (b) Me_2AlCl (0.8 equiv.), CH_2Cl_2, 84%.

Ester **24** was never fully purified due to rapid 6π-electrocyclization at room temperature affording an epimer of **22**. Generally, we observed that compounds **1** and **24** underwent both the electrocyclizations and Lewis acid catalyzed cycloisomerizations noticeably faster than their stereoisomers **26** and **13**.

The stereochemistry of the bicyclo[3.1.0]hexenes **14** and **3** was elucidated by reduction to the corresponding primary alcohols **28** and **29**, respectively, and extensive NOE measurements. Selected NOE signals are shown in Scheme 8.



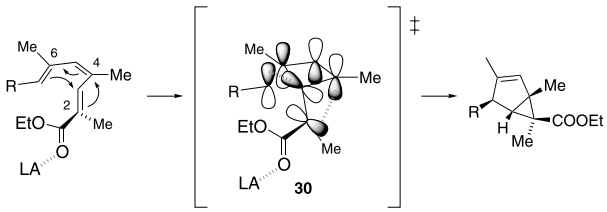
Scheme 8. *Reagents and conditions*: (a) DIBAH, CH_2Cl_2, −78°C, 76%. (b) DIBAH, CH_2Cl_2, −78°C, 42%.

With respect to the mechanism of the cyclization, two scenarios are conceivable. The reaction could either proceed in a concerted fashion, involving only one transition state, or in a stepwise fashion through zwitterionic intermediates.

Formally, the isomerization has the hallmarks of a concerted

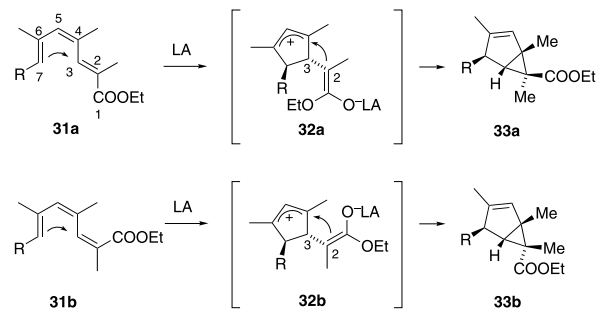
[4+2] cycloaddition: two σ-bonds are formed at the expense of two π-bonds, which accounts for its thermodynamic driving force despite the formation of a strained bicyclic framework. Four new stereocenters, two of them quaternary, are created from an acyclic precursor. In analogy to an intramolecular Diels–Alder reaction, two rings are created in a single step.

In a traditional Diels–Alder reaction, i.e. a $[_\pi4_s+_\pi2_s]$ cycloaddition, the reaction of diene and dienophile proceeds through a transition state wherein both components are aligned parallel to each other. Catalysis is achieved by lowering the energy of the LUMO and closing the HOMO–LUMO gap. By contrast, in the case of trienes of type **1**, this approach is geometrically impossible since the 'tether' connecting the diene and dienophile consists of a single bond. Nevertheless, cycloaddition could occur, provided the reaction proceeds through a transition state **30** wherein the diene and dienophile are oriented more or less perpendicular to each other (Scheme 9). The conformational constraints of the methyl substituted triene system work in favor of such a transition state (**30**). Due to severe A[1,3]-strain between the methyl groups at C2 and C4, the triene is effectively dissected into a diene and a dienophile moiety. The C6 methyl group assures that the diene can assume an *s-cis* conformation without paying too high an energy cost. Concerted bond formation then occurs in a $[_\pi4_a+_\pi2_a]$ fashion to afford a bicyclo[3.1.0]hexene. The LUMO-lowering effect of a Lewis acid accounts for the rate acceleration, allowing this reaction to effectively compete with a 6π electrocyclization. Note that the stereospecificity of the reaction is nicely explained by this concerted mechanism.



Scheme 9. The $[_\pi4_a+_\pi2_a]$ mechanism.

Alternatively, a stepwise mechanism could operate (Scheme 10). Coordination of the Lewis acid to the carbonyl group of trienoic ester **31a** or its isomer **31b** triggers a conrotatory cyclization, placing the two substituents on the five-membered ring *anti* with respect to each other. The resulting zwitterionic intermediates **32a**,**b** stabilize themselves by C,C-bond formation to yield **33a** or **33b**. Provided this last step is considerably faster than rotation around the C2–C3 bond, the reactions could proceed with complete stereocontrol. In this mechanism, the methyl substituents not only conformationally preorganize the substrate but also stabilize the intermediary allyl cation **32a**,**b**.

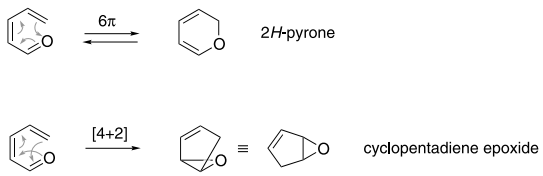


Scheme 10. Stepwise mechanism of the cyclization.

Although the Lewis acid catalyzed cycloisomerization of trienes to bicyclo[3.1.0]hexenes has been presented in the context of pericyclic reactions, it is by no means implied that we believe it proceeds in a concerted fashion. Based on the available experimental data, we are unable to determine which mechanism applies. The concerted pathway is currently being probed by computational studies.

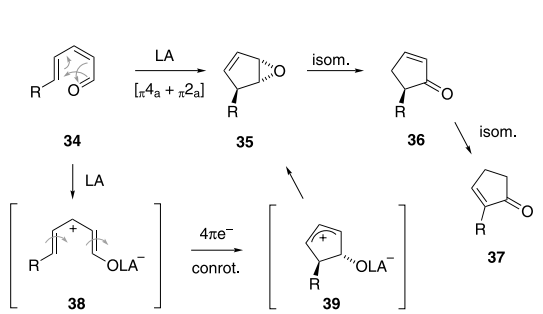
4. Extension to pentadienals: towards an 'iso-Nazarov cyclization'

With the above mechanisms in mind, we wondered whether the reaction could be extended to pentadienals by replacing the electrophilic double bond with a carbonyl group (Scheme 11). In principle, such a substitution should lead to cyclopentadiene epoxides that would possibly undergo further isomerizations in the presence of a Lewis acid. In the absence of a Lewis acid, pentadienals with appropriate double bond geometry are well known to undergo reversible 6π electrocyclizations to afford 2*H*-pyrones.[1]



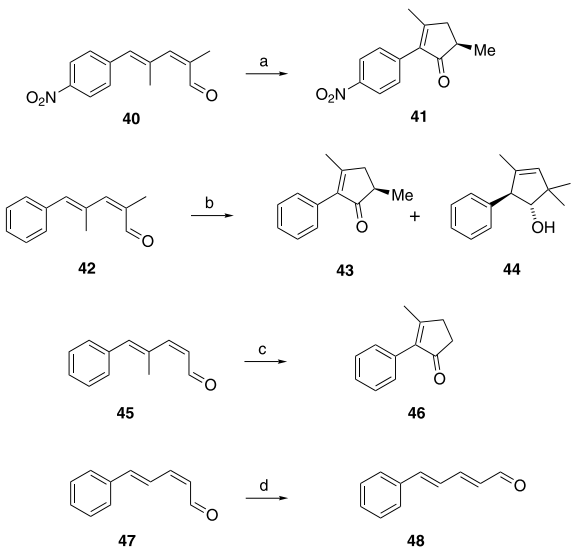
Scheme 11.

Again, a stepwise or a concerted mechanism could be formulated (Scheme 12). In the latter scenario, hetero $[_\pi4_a+_\pi2_a]$ cycloaddition directly leads to cyclopentadiene epoxide **35**. Under the Lewis acidic reaction conditions, this intermediate is likely to undergo further isomerizations to cyclopentenones **36** and ultimately **37**. Alternatively, a Nazarov-like mechanism involving the conrotatory cyclization of an oxy-pentadienyl cation **38** could be operating. The resulting zwitterion **39** reacts further to afford cyclopentadiene epoxides or cyclopentenones. Note that compounds of type **34** are isomers of the divinylketones used in the classical Nazarov cyclization.[18] Remarkably, the isomerization of pentadienals to cyclopentenones appears to be largely unknown.[19]



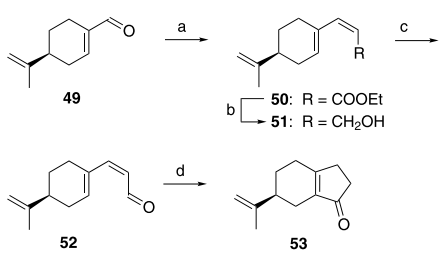
Scheme 12. Extension to pentadienals.

Treatment of pentadienal **40** with dimethylaluminum chloride indeed afforded the known cyclopentenone **41**,[19a] in moderate yield (not optimized). Apparently, the double bond isomerizes into the thermodynamically most stable position under the reaction conditions. Similarly, **42** gave cyclopentenone **43**. In this case, the secondary alcohol **44** bearing an extra methyl group was isolated as a byproduct. This compound presumably stems from nucleophilic opening of the vinyl epoxide intermediate **35** with a dimethylaluminate or from interception of the allylic cation corresponding to **39**. Pentadienal **45** afforded the known cyclopentenone **46**.[20] Compound **47**, however, only underwent *E*,*Z*-isomerization to the all-*trans* aldehyde **48**, indicating a potential limitation of the method (Scheme 13).



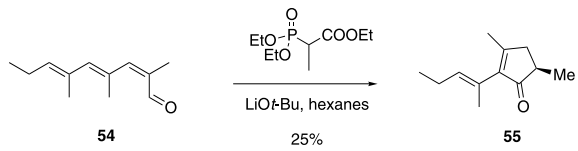
Scheme 13. *Reagents and conditions*: Me_2AlCl (0.2 equiv.), CH_2Cl_2, 0°C; (a) 47%; (b) **43**: 25%, **44**: 17%; (c) 28%; (d) 80%.

The pentadienals **40**, **42**, **45** and **47** were synthesized using a combination of stereoselective olefinations, reductions and oxidation steps. This synthetic strategy is further illustrated in the synthesis of hexahydroindanone **53** (Scheme 14). Still–Gennari olefination of (−)-perillaldehyde (**49**) afforded unsaturated ester **50**. Reduction of this material with diisobutylaluminum hydride, followed by allylic oxidation then gave pentadienal **52**. Exposure of this material to dimethylaluminum chloride or borontrifluoride etherate resulted in a complex mixture of products from which cyclopentenone **53** could be isolated in low yields. Interestingly, the relative amount of **53** appeared to increase over time, suggesting that the complex mixture consisted mainly of isomeric vinyl epoxides and cyclopentenones analogous to **35** and **36**.



Scheme 14. *Reagents and conditions*: (a) KHMDS, $(CF_3CH_2O)_2P(O)CH_2$-COOEt, 18-C-6, THF, −78°C, 85%; (b) DIBAH, CH_2Cl_2, 0°C, 88%; (c) MnO_2, CH_2Cl_2, 56%. (d) Me_2AlCl (0.2 equiv.), CH_2Cl_2, 0°C, 22%.

A rather curious result was obtained with the sensitive aldehyde **54**, an intermediate in our synthesis of photodeoxytridachione. Attempted olefination of this material with triethyl phosphonopropionate using the conditions described by Petroski[21] gave very little of the intended product **13**. Instead, a considerable amount of cyclopentenone **55** was isolated. Presumably, the Lewis acidic properties of the lithium phosphate formed as a by-product of the Horner–Wadsworth–Emmons reaction account for its formation. A base-mediated alternative mechanism is difficult to imagine and was excluded by control experiments. Interestingly, attempts to isomerize **54** to **55** using dimethylaluminum chloride as a catalyst failed (Scheme 15).



Scheme 15.

These preliminary results suggest that dimethylaluminum chloride may not be the optimal Lewis acid for this type of reaction and that a thorough survey might yield a better catalyst. Further investigations will also show whether the corresponding ketones and silyl ketones will undergo the isomerization perhaps leading to more stable vinyl epoxides and silyl enol ethers. The Lewis acid catalyzed isomerization of 2*H*-pyrones, whose electrocyclic ring opening affords pentadienals, to cyclopentenones is also under investigation.

In summary, we have demonstrated how the serendipitous discovery of a reaction can form the basis of a wide-ranging synthetic program. Total syntheses of all the molluscan polypropionates shown in Figure 2 are currently pursued in our laboratories. In this context, the asymmetric control of 6π electrocyclizations and the newly discovered cycloisomerization will receive special attention. Furthermore, the extension of the cyclization to other substrate classes will be explored.

5. Experimental

5.1. General

Unless otherwise noted, all reagents were purchased from commercial suppliers and used without further purification. Melting points were measured on a Büchi melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker DRX 500, a Bruker AM 400 or a Bruker AMX 300. Optical rotations were measured on a Perkin–Elmer 241 polarimeter. Mass spectra were recorded on a VG ProSpec. Silica gel chromatography was carried out using ICN SiliTech 32–63 D 60 Å. Thin layer chromatography (TLC) was performed with Merck Silica Gel 60 plates. Elemental analysis was performed by the

Microanalytical Laboratory operated by the UCB College of Chemistry. X-Ray analysis was performed on a Bruker SMART CCD area-detector diffractometer. All reactions were carried out under an atmosphere of Ar or N_2 in oven-dried glassware. External bath temperatures were used to record all reaction mixture temperatures. Tetrahydrofuran (THF), methylene chloride (CH_2Cl_2), and toluene were dried by passing through activated alumina columns. Benzene, hexanes and DBU were distilled from calcium hydride. *n*-Butyl lithium was titrated using diphenylacetic acid in THF.

5.2. Compounds

5.2.1. 2,4,6-Trimethyl-7-(4-nitro-phenyl)-hepta-(*Z*)-2,(*Z*)-4,(*E*)-6-trienoic acid ethyl ester (1). To a mixture of 18-crown-6 (2.09 g, 7.91 mmol) and **10** (770 mg, 2.22 mmol) in 5.0 mL of THF was added a solution of potassium bis(trimethylsilyl)amide (4.40 mL, 2.20 mmol, 0.5 M in toluene) at −78°C under nitrogen. After 5 min, a solution of **40** (462 mg, 2.01 mmol) in 5.0 mL of THF was added. After 2.5 h, the reaction mixture was quenched with 20 mL of a 1:1 mixture of saturated NH_4Cl and H_2O, and diluted with 10 mL of EtOAc. The two layers were separated and the aqueous layer was extracted with EtOAc (2×10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (10% EtOAc in hexanes) to afford 570 mg (90%) of **1** as a yellow oil: R_f=0.35 (silica, 20% EtOAc in hexanes); IR (thin film) ν_{max}=2926, 1711, 1516, 1342 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.16 (d, *J*=8.8 Hz, 2H), 7.83 (d, *J*=8.8 Hz, 2H), 6.51 (s, 1H), 6.40 (s, 1H), 5.96 (s, 1H), 4.18 (q, *J*=7.2 Hz, 2H), 1.98 (d, *J*=1.2 Hz, 3H), 1.97 (d, *J*=1.2 Hz, 3H), 1.94 (s, 3H), 1.27 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 146.0, 145.0, 139.6, 136.8, 135.9, 133.0, 129.8, 129.6, 128.9, 123.6, 60.8, 24.0, 21.1, 19.2, 14.2; HRMS (EI): calcd for $C_{18}H_{21}NO_4$: 315.1470; found: 315.1466; Anal. calcd for $C_{18}H_{21}NO_4$: C 68.55, H 6.71, N 4.44; found: C 68.41, H 6.80, N 4.47.

5.2.2. (1*R, 6*R**) 1,3,5-Trimethyl-6-(4-nitro-phenyl)-cyclohexa-2,4-dienecarboxylic acid ethyl ester (2).** A solution of **1** (100 mg, 0.317 mmol) in 3.0 mL of toluene was heated at 60°C under nitrogen for 16 h. The solution was concentrated in vacuo and the product was purified by column chromatography (10% EtOAc in hexanes) to afford 98.0 mg (98%) of **2** as a yellow solid: R_f=0.37 (silica, 20% EtOAc in hexanes); mp 105–106°C; IR (KBr pellet) ν_{max}=2979, 1715, 1521, 1348 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, *J*=8.4 Hz, 2H), 7.33 (d, *J*=8.4 Hz, 2H), 5.72 (s, 1H), 5.07 (s, 1H), 4.18 (dq, *J*=10.4, 7.2 Hz, 1H), 4.10 (dq, *J*=10.4, 7.2 Hz, 1H), 3.83 (s, 1H), 1.85 (d, *J*=1.2 Hz, 3H), 1.66 (s, 3H), 1.23 (t, *J*=7.2 Hz, 3H), 0.95 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 176.7, 147.4, 145.8, 139.4, 133.5, 130.7, 123.6, 123.5, 121.9, 61.2, 51.0, 47.5, 23.2, 22.2, 21.2, 14.3; HRMS (EI): calcd for $C_{18}H_{21}NO_4$: 315.1470; found: 315.1463; Anal. calcd for $C_{18}H_{21}NO_4$: C 68.55, H 6.71, N 4.44; found: C 68.69, H 6.78, N 4.30.

5.2.3. (1*S,4*S**,5*R**,6*R**) 1,3,6-Trimethyl-4-(4-nitro-phenyl)-bicyclo[3.1.0]hex-2-ene-6-carboxylic acid ethyl ester (3).** To a solution of **1** (103 mg, 0.33 mmol) in 3.0 mL of CH_2Cl_2 was added a solution of dimethylaluminum chloride (65 μL, 0.065 mmol, 1.0 M in hexanes) at 0°C under a blanket of nitrogen. After 30 min, the reaction mixture was allowed to warm to 23°C and after 3 h was quenched with 3.0 mL of H_2O. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2×2 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (5% EtOAc in hexanes) to yield 70 mg (68%) of **3** as a yellow oil: R_f=0.25 (silica, 10% Et_2O in hexanes); IR (thin film) ν_{max}=2978, 2934, 1725, 1520, 1346 cm^{-1}; ^1H NMR (400 MHz, C_6D_6): δ 7.85 (d, *J*=8.8 Hz, 2H), 6.77 (d, *J*=8.8 Hz, 2H), 5.32 (d, *J*=0.8 Hz, 1H), 4.05 (s, 1H), 4.05 (dq, *J*=10.4, 7.2 Hz, 1H), 3.90 (dq, *J*=10.4, 7.2 Hz, 1H), 1.33 (s, 3H), 1.18 (s, 3H), 1.16 (s, 3H), 0.99 (t, *J*=7.2 Hz, 3H), 0.87 (s, 1H); ^{13}C NMR (125 MHz, C_6D_6): δ 171.9, 151.3, 147.6, 141.8, 132.3, 129.0, 124.2, 60.4, 55.8, 41.3, 40.3, 37.1, 18.1, 14.8, 14.3, 14.1; HRMS (EI): calcd for $C_{18}H_{21}NO_4$: 315.1470; found: 315.1471; Anal. calcd for $C_{18}H_{21}NO_4$: C 68.55, H 6.71, N 4.44; found: C 68.55, H 6.76, N 4.30.

5.2.4. 2,4,6-Trimethyl-nona-(*Z*)-2,(*E*)-4,(*E*)-6-trienoic acid ethyl ester (11). To a mixture of 18-crown-6 (12.60 g, 47.67 mmol) and **10** (6.06 g, 17.5 mmol) in 160 mL of THF was added a solution of potassium bis(trimethylsilyl)amide (35.0 mL, 17.5 mmol, 0.5 M in toluene) at −78°C under a blanket of argon. After 5 min, a solution of **9** (2.19 g, 15.8 mmol) in 25 mL of THF was added dropwise. After 45 min, the reaction mixture was allowed to warm to 0°C. Upon reaching 0°C, the mixture was quenched with 200 mL of a 3:1 mixture of H_2O and saturated NH_4Cl and diluted with 100 mL of Et_2O. The two layers were separated and the aqueous layer was extracted with Et_2O (2×100 mL). The combined organic layers were washed with 100 mL of brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (5–10% Et_2O in hexanes) to afford 2.78 g (78.9%) of **11** as a colorless oil: R_f=0.56 (silica, 10% Et_2O in hexanes); IR (thin film) ν_{max}=2965, 2933, 2873, 1723 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.12 (s, 1H), 5.85 (s, 1H), 5.36 (t, *J*=7.2 Hz, 1H), 4.18 (q, *J*=7.2 Hz, 2H), 2.10 (quint, *J*=7.2 Hz, 2H), 1.97 (d, *J*=1.6 Hz, 3H), 1.85 (s, 3H), 1.73 (s, 3H), 1.28 (t, *J*=7.2 Hz, 3H), 0.98 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 138.6, 136.3, 134.2, 131.9, 131.6, 127.2, 60.6, 21.8, 21.7, 16.9, 16.8, 14.3, 14.2; HRMS (EI): calcd for $C_{14}H_{22}O_2$: 222.1619; found: 222.1615; Anal. calcd for $C_{14}H_{22}O_2$: C 75.63, H 9.97; found: C 75.60, H 10.13.

5.2.5. 2,4,6-Trimethyl-nona-(*Z*)-2,(*E*)-4,(*E*)-6-trien-1-ol (12). To a solution of **11** (2.78 g, 12.5 mmol) in 120 mL of CH_2Cl_2 was added a solution of DIBAH (30.0 mL, 30.0 mmol, 1.0 M in toluene) at 0°C under a blanket of argon. After the addition was complete, the reaction mixture was allowed to warm to 23°C. After 1 h, the reaction mixture was cooled to 0°C and quenched with 150 mL of a 4:1 mixture of H_2O and saturated Rochelle's salt and stirred vigorously for 2 h. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2×100 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (20% Et_2O in hexanes) to afford 2.09 g

(92.8%) of **12** as a colorless oil: R_f=0.30 (silica, 15% EtOAc in hexanes); IR (thin film) ν_{max}=3324 (br) 2963, 2933, 2872, 1447 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.82 (s, 1H), 5.64 (s, 1H), 5.32 (t, J=7.2 Hz, 1H), 4.26 (s, 2H), 2.10 (quint, J=7.2 Hz, 2H), 1.86 (d, J=1.6 Hz, 3H), 1.84 (s, 3H), 1.73 (s, 3H), 0.99 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 135.2, 133.4, 133.3, 133.0, 131.9, 131.6, 62.7, 22.8, 21.7, 19.0, 17.0, 14.3; HRMS (EI): calcd for $C_{12}H_{20}O$: 180.1514; found: 180.1517.

5.2.6. 2,4,6,8-Tetramethyl-undeca-(*E*)-2,(*Z*)-4,(*E*)-6,(*E*)-8-tetraenoic acid ethyl ester (13). To a mixture of **12** (1.39 g, 7.71 mmol), NMO (1.40 g, 12.0 mmol), and 3.50 g of 4 Å molecular sieves in 30 mL of CH_2Cl_2 was added TPAP (84.0 mg, 0.239 mmol) at 0°C under a blanket of argon. Immediately after the addition, the reaction flask was wrapped in aluminum foil and allowed to warm to 23°C. After 4 h, the reaction mixture was filtered through a thin pad of silica and washed with CH_2Cl_2 (3×30 mL). The combined filtrate was concentrated in vacuo to give 995 mg of crude aldehyde **54** as a yellow oil that was used in the next step without further purification. To a mixture of LiCl (338 mg, 7.97 mmol), DBU (0.90 mL, 6.02 mmol), and triethyl phosphonopropionate (4.16 g, 17.5 mmol) in 25 mL of CH_3CN was added a solution of crude aldehyde (995 mg, 5.58 mmol) in 35 mL of CH_3CN at 23°C under a blanket of argon. After 5 h, the mixture was concentrated in vacuo and diluted with 200 mL of H_2O and 100 mL of Et_2O. The two layers were separated and the aqueous layer was extracted with Et_2O (2×50 mL). The combined organic layers were washed with 50 mL of brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (1–5% Et_2O in hexanes) to afford 860 mg (42.5% from **12**) of **13** as a colorless oil: R_f=0.45 (silica, 5% Et_2O in hexanes); IR (thin film) ν_{max}=2954, 2932, 2873, 1709 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.45 (s, 1H), 6.01 (s, 1H), 5.78 (s, 1H), 5.34 (t, J=7.2 Hz, 1H), 4.20 (q, J=7.2 Hz, 2H), 2.10 (quint, J=7.2 Hz, 2H), 1.95 (s, 3H), 1.89 (d, J=1.2 Hz, 3H), 1.83 (s, 3H), 1.73 (s, 3H), 1.29 (t, J=7.2 Hz, 3H), 0.98 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.9, 140.6, 137.5, 136.4, 133.4, 132.3, 132.1, 131.1, 127.2, 60.7, 31.8, 24.2, 21.8, 18.4, 17.0, 14.4, 14.2; HRMS (EI): calcd for $C_{17}H_{26}O_2$: 262.1932; found: 262.1930.

5.2.7. (1*S,δ4*S**,5*R**,6*S**) 1,3,6-Trimethyl-4-(1-methyl-but-1-enyl)-bicyclo[3.1.0]hex-2-ene-6-carboxylic acid ethyl ester (14).** To a solution of **13** (425 mg, 1.62 mmol) in 16 mL of CH_2Cl_2 was added a solution of dimethyl-aluminum chloride (0.35 mL, 0.35 mmol, 1.0 M in hexanes) at 0°C under a blanket of argon. The reaction mixture was allowed to warm to 23°C and was wrapped in aluminum foil. After 8 h, the reaction mixture was quenched with 15 mL of H_2O. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2×15 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (5% Et_2O in hexanes) to afford 312 mg (73.4%) of **14** as a colorless oil: R_f=0.34 (silica, 5% Et_2O in hexanes); IR (thin film) ν_{max}=2961, 2930, 2872, 1717 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.25 (m, 2H), 4.13 (q, J=7.2 Hz, 2H), 2.60 (s, 1H), 2.02 (quint, J=7.6 Hz, 2H), 1.92 (s, 1H), 1.53 (s, 3H), 1.47 (s, 3H), 1.30 (s, 3H), 1.26 (t, J=7.2 Hz, 3H), 1.05 (s, 3H), 0.96 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.2, 144.1, 134.1, 129.3, 128.9, 60.5, 59.1, 43.1, 37.9, 33.7, 21.4, 14.6, 14.5, 14.5, 13.8, 12.5, 10.1; HRMS (EI): calcd for $C_{17}H_{26}O_2$: 262.1932; found: 262.1936; Anal. calcd for $C_{17}H_{26}O_2$: C 77.82, H 9.99; found: C 78.16, H 10.20.

5.2.8. (1*S,4*S**,5*R**,6*S**) 1,3,6-Trimethyl-4-(1-methyl-but-1-enyl)-bicyclo[3.1.0]hex-2-ene-6-carboxylic acid methoxy-methyl-amide (15).** To a slurry of **14** (120 mg, 0.457 mmol) and *N*,*O*-dimethylhydroxylamine hydrochloride (226 mg, 2.32 mmol) in 2.0 mL of THF was added a solution of isopropyl magnesium chloride (2.1 mL, 4.2 mmol, 2.0 M in Et_2O) at −10°C under a blanket of argon. The reaction mixture was allowed to warm to 23°C and, after 1 h, was quenched with 20 mL of a 1:1 mixture of saturated NH_4Cl and H_2O and diluted with 20 mL of Et_2O. The two layers were separated and the aqueous layer was extracted with Et_2O (2×20 mL). The combined organic layers were washed with 20 mL of brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (25% Et_2O in hexanes) to yield 80.0 mg (63.1%) of **15** as a colorless oil: R_f=0.13 (silica, 25% Et_2O in hexanes); IR (thin film) ν_{max}=2963, 2931, 2870, 1658 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.25 (t, J=7.5 Hz, 1H), 5.23 (s, 1H), 3.71 (s, 3H), 3.23 (s, 3H), 2.62 (s, 1H), 2.01 (quint, J=7.5 Hz, 2H), 1.69 (s, 1H), 1.53 (s, 3H), 1.45 (s, 3H), 1.22 (s, 3H), 1.03 (s, 3H), 0.95 (t, J=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 210.0, 144.3, 134.1, 128.8, 128.0, 60.6, 58.8, 40.3, 34.9, 34.6, 34.3, 21.4, 16.2, 14.5, 13.8, 12.6, 11.0; HRMS (EI): calcd for $C_{17}H_{27}NO_2$: 277.2041; found: 277.2044; Anal. calcd for $C_{17}H_{27}NO_2$: C 73.61, H 9.81, N 5.05; found: C 73.72, H 9.98, N 4.90.

5.2.9. (1*S,4*S**,5*R**,6*S**) 1-[1,3,6-Trimethyl-4-(1-methyl-but-1-enyl)-bicyclo[3.1.0]hex-2-en-6-yl]-propan-1-one (16).** To a solution of **15** (16.9 mg, 0.061 mmol) in 0.8 mL of THF was added a solution of ethyl magnesium bromide (0.20 mL, 0.60 mmol, 3.0 M in Et_2O) at 0°C under a blanket of argon. After 3 h, the reaction mixture was quenched with 2.0 mL of a 1:1 mixture of saturated NH_4Cl and H_2O and diluted with 2.0 mL of Et_2O. The two layers were separated and the aqueous layer was extracted with Et_2O (2×2 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (5% Et_2O in hexanes) to yield 13.0 mg (86.6%) of **16** as a colorless oil: R_f=0.71 (silica, 25% Et_2O in hexanes); IR (thin film) ν_{max}=2963, 2932, 2872, 1689 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.25 (s, 1H), 5.23 (t, J=7.2 Hz, 1H), 2.65 (dq, J=17.6, 7.2 Hz, 1H), 2.55 (s, 1H), 2.49 (dq, J=17.6, 7.2 Hz, 1H), 2.07 (s, 1H), 2.01 (quint, J=7.2 Hz, 2H), 1.55 (s, 3H), 1.45 (s, 3H), 1.13 (s, 3H), 1.11 (s, 3H), 1.04 (t, J=7.2 Hz, 3H), 0.94 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.0, 144.8, 134.2, 129.2, 128.8, 59.1, 45.2, 40.6, 37.1, 34.6, 21.4, 14.5, 14.0, 13.9, 12.6, 10.6, 8.3; HRMS (EI): calcd for $C_{17}H_{26}O$: 246.1985; found: 246.1983.

5.2.10. (1*S,4*S**,5*R**,6*S**) 2,4-Dimethyl-3,5-dioxo-5-[1,3,6-trimethyl-4-(1-methyl-but-1-enyl)-bicyclo[3.1.0]-hex-2-en-6-yl]-pentanoic acid methyl ester (18).** To a solution of **16** (75.0 mg, 0.304 mmol) in 5.0 mL of THF was added a solution of lithium bis(trimethylsilyl)amide

(1.30 mL, 1.30 mmol, 1.0 M in hexanes) at −78°C under a blanket of argon. After addition, the mixture was allowed to warm to 23°C for 5 min before being cooled to −78°C and diluted with 5.0 mL of hexanes. To this mixture was added a solution of malonyl chloride **17** (63.2 mg, 0.420 mmol) in 5.0 mL of hexanes over 20 min. The reaction mixture was stirred at −78°C for 45 min and then allowed to warm to 23°C. After 2 h, the reaction mixture was quenched with 10 mL of a 1:1 mixture of H_2O and saturated NH_4Cl and diluted with 10 mL of Et_2O. The two layers were separated and the aqueous layer was extracted with Et_2O (2×10 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (10–30% Et_2O in hexanes) to afford 64.8 mg (59.1%, 95% based on recovered starting material) of **18** as a mixture of diastereomers as a colorless oil: R_f=0.19 (silica, 10% Et_2O in hexanes); HRMS (EI): calcd for $C_{22}H_{32}H_4$: 360.2301; found: 360.2302.

5.2.11. (1*S,4*S**,5*R**,6*S**) 4-Hydroxy-3,5-dimethyl-6-[1,3,6-trimethyl-4-(1-methyl-but-1-enyl)-bicyclo[3.1.0]-hex-2-en-6-yl]-pyran-2-one (19).** A mixture of **18** (100 mg, 0.277 mmol) and DBU (50 μL, 0.334 mmol) in 3.0 mL of benzene was heated to reflux under argon. After 3 h, the reaction mixture was concentrated in vacuo and the product was purified by column chromatography (CH_2Cl_2/MeOH/AcOH=97.5:2.5:0.125) to yield 71.0 mg (77.9%) of **19** as a white foam: R_f=0.38 (silica, 5% MeOH in CH_2Cl_2); IR ($CDCl_3$) ν_{max}=3136 (br), 3032, 2962, 2928, 2870, 1665 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.82 (bs, 1H), 5.28 (m, 2H), 2.69 (s, 1H), 2.03 (quint, *J*=7.5 Hz, 2H), 2.01 (s, 3H), 1.99 (s, 3H), 1.55 (s, 1H), 1.54 (s, 3H), 1.45 (s, 3H), 1.16 (s, 3H), 1.07 (s, 3H), 0.96 (t, *J*=7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.2, 166.2, 161.3, 144.3, 134.1, 129.0, 128.6, 109.4, 98.9, 58.7, 40.9, 31.9, 29.9, 21.4, 17.0, 14.5, 13.8, 13.3, 12.7, 10.7, 8.8; HRMS (EI): calcd for $C_{21}H_{28}O_3$: 328.2038; found: 328.2035.

5.2.12. (±)-Photodeoxytridachione (6). To a solution of **19** (12.5 mg, 0.038 mmol) in 0.3 mL of CH_2Cl_2 was added methyl fluorosulfonate (30 μL, 0.38 mmol) at 23°C under a blanket of argon. After 3 h, the reaction mixture was concentrated in vacuo, dissolved in 2 mL of CH_2Cl_2 and concentrated. The crude material was taken up in 2 mL of CH_2Cl_2 and 2 mL of 1N NaOH. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2×2 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was further purified by column chromatography (2% MeOH in CH_2Cl_2) to yield 10.0 mg (76.7%) of **6** as a white solid: R_f=0.50 (silica, 5% MeOH in CH_2Cl_2); IR (thin film) ν_{max}=1661 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.33 (s, 1H), 5.30 (t, *J*=7.2 Hz, 1H), 3.96 (s, 3H), 2.73 (bs, 1H), 2.04 (dq, *J*=7.6, 7.2 Hz, 2H), 1.97 (s, 3H), 1.84 (s, 3H), 1.57 (s, 3H), 1.48 (s, 3H), 1.42 (bs, 1H), 1.19 (s, 3H), 1.10 (s, 3H), 0.97 (t, *J*=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 181.8, 162.5, 160.7, 144.2, 134.2, 129.0, 128.8, 120.6, 99.7, 58.6, 55.5, 40.9, 37.0, 32.0, 21.4, 17.3, 14.5, 13.9, 12.9, 11.0, 7.1; HRMS (EI): calcd for $C_{21}H_{30}O_3$: 343.2228; found: 343.2248.

5.2.13. (1*S,6*R**) 1,3,5-Trimethyl-6-(1-methyl-but-1-enyl)-cyclohexa-2,4-dienecarboxylic acid ethyl ester (22).** A solution of **13** (100.0 mg, 0.381 mmol) in 38 mL of benzene was heated at 60°C under argon. After 2 d, the reaction mixture was concentrated in vacuo to yield 98.3 mg (98.3%) of **22** as a colorless oil: R_f=0.71 (silica, 15% EtOAc in hexanes); IR (thin film) ν_{max}=2963, 2933, 2874, 1719 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.39 (s, 1H), 5.00 (s, 1H), 4.07 (m, 2H), 2.93 (t, *J*=7.5 Hz, 1H), 2.34 (s, 1H), 1.65 (d, *J*=1.2 Hz, 3H), 1.63 (s, 3H), 1.40 (m, 2H), 1.38 (s, 3H), 1.21 (t, *J*=7.2 Hz, 3H), 1.05 (s, 3H), 0.84 (t, *J*=7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 176.1, 131.9, 127.2, 126.6, 123.2, 60.5, 55.0, 54.1, 51.6, 36.3, 23.9, 22.4, 22.0, 21.7, 19.6, 14.4, 13.5; HRMS (EI): calcd for $C_{17}H_{26}O_2$: 262.1933; found: 262.1935.

5.2.14. (1*S,6*R**) 1,3,5-Trimethyl-6-(1-methyl-but-1-enyl)-cyclohexa-2,4-dienecarboxylic acid methoxy-methyl-amide (23).** To a solution of **22** (55.0 mg, 0.210 mmol) in 4.0 mL of THF was added *N*,*O*-dimethyl hydroxylamine hydrochloride (204 mg, 2.09 mmol). To this mixture was added isopropyl magnesium chloride (1.78 mL, 3.56 mmol, 2.0 M in Et_2O) at 0°C under a blanket of argon. After 4 h, the reaction mixture was quenched with 4.4 mL of a 1:1 mixture of saturated NH_4Cl and H_2O and diluted with 2.2 mL of Et_2O. The two layers were separated and the aqueous layer was extracted with Et_2O (2×4.4 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (20% EtOAc in hexanes) to yield 16.7 mg (28.8%, 91% based on recovered starting material) of **23** as a colorless oil: R_f=0.29 (silica, 15% EtOAc in hexanes); IR (thin film) ν_{max}=2961, 2933, 2873, 1668 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 5.42 (s, 1H), 4.97 (s, 1H), 3.63 (s, 3H), 3.08 (s, 3H), 2.66 (dd, *J*=6.0, 4.8 Hz, 1H), 2.36 (s, 1H), 1.79 (s, 3H), 1.65 (d, *J*=1.2 Hz, 3H), 1.51 (m, 2H), 1.39 (s, 3H), 1.04 (s, 3H), 0.89 (t, *J*=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 178.4, 133.5, 127.4, 127.0, 122.4, 60.2, 56.1, 54.5, 52.9, 36.4, 34.0, 23.8, 23.5, 22.2, 21.9, 19.5, 13.8; HRMS (EI): calcd for $C_{17}H_{27}NO_2$: 277.2042; found: 277.2041.

5.2.15. 2,4,6,8-Tetramethyl-undeca-(*E*)-2,(*Z*)-4,(*E*)-6,(*Z*)-8-tetraenoic acid ethyl ester (24). To a mixture of **10** (343 mg, 0.991 mmol) and 18-crown-6 (700 mg, 2.65 mmol) in 10 mL of THF was added a solution of potassium bis(trimethylsilyl)amide (2.0 mL, 1.0 mmol, 0.5 M in toluene) at −78°C under argon. After 5 min, a solution of **54** (150 mg, 0.84 mmol) in 2.0 mL of THF was added. After 2 h, the reaction mixture was quenched with 10 mL of a 4:1 mixture of H_2O: saturated NH_4Cl. The two layers were separated and the aqueous layer was extracted with 10 mL of Et_2O. The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (5–10% Et_2O in hexanes) to yield 180 mg of a 3:1 mixture of **24** and the product of 6π electrocyclization (51%). Compound **24** was used immediately in the next step without further purification.

5.2.16. (1*S,4*S**,5*R**,6*R**) 1,3,6-Trimethyl-4-(1-methyl-but-1-enyl)-bicyclo[3.1.0]hex-2-ene-6-carboxylic acid ethyl ester (25).** To a solution of **24** (21.0 mg, 0.083 mmol) in 1.0 mL of CH_2Cl_2 was added a solution of dimethylaluminum chloride (30 μL, 0.030 mmol, 1.0 M in

hexanes) at 0°C under a blanket of argon. The reaction mixture was warmed to 23°C over 2 h at which time it was quenched with 5 mL of H_2O and diluted with 4 mL of CH_2Cl_2. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2×2 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (50% benzene in hexanes) to yield 13.0 mg (61%) of **25** as a colorless oil: R_f=0.34 (silica, 5% Et_2O in hexanes); IR (thin film) ν_{max}=2961, 2928, 2872, 1729 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.30 (t, J=7.2 Hz, 1H), 5.28 (s, 1H), 4.08 (dq, J=10.8, 7.2 Hz, 1H), 3.99 (dq, J=10.8, 7.2 Hz, 1H), 3.24 (s, 1H), 2.01 (dq, J=7.6, 7.2 Hz, 2H), 1.43 (bs, 6H), 1.30 (s, 3H), 1.28 (s, 3H), 1.18 (t, J=7.2 Hz, 3H), 0.97 (s, 1H), 0.95 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.0, 140.5, 134.9, 131.2, 128.7, 60.1, 59.3, 39.4, 39.1, 36.1, 29.9, 21.4, 18.2, 14.6, 14.0, 13.9, 12.2; HRMS (EI): calcd for $C_{17}H_{26}O_2$: 262.1932; found: 262.1928.

5.2.17. 2,4,6-Trimethyl-7-(4-nitro-phenyl)-hepta-(*E*)-2,(*Z*)-4,(*E*)-6-trienoic acid ethyl ester (26). To a suspension of sodium hydride (72 mg, 1.80 mmol, 60% in oil) in 3.0 mL of THF was added a solution of triethyl phosphonopropionate (423 mg, 1.78 mmol) in 5.0 mL of THF at 23°C under a blanket of argon. After 2 h, a solution of **40** (1.72 mmol) in 9.0 mL of THF was added. After 3 h, the reaction mixture was quenched with 25 mL of H_2O and diluted with 20 mL of Et_2O. The two layers were separated and the aqueous layer was extracted with Et_2O (2×25 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (10–20% Et_2O in hexanes) to afford 89 mg (16%) of **26** as a yellow oil which slowly solidified in the freezer: R_f=0.48 (silica, 25% Et_2O in hexanes); IR (thin film) ν_{max}=2980, 2932, 1707, 1591, 1515 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (d, J=8.8 Hz, 2H), 7.45 (s, 1H), 7.39 (d, J=8.8 Hz, 2H), 6.42 (s, 1H), 6.13 (s, 1H), 4.20 (q, J=7.2 Hz, 2H), 2.02 (s, 3H), 1.98 (s, 3H), 1.92 (s, 3H), 1.27 (t, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.8, 168.4, 144.7, 139.7, 139.3, 135.4, 134.7, 129.7, 129.4, 128.5, 123.6, 60.9, 24.4, 18.6, 14.4, 14.2; HRMS (EI): calcd for $C_{18}H_{21}NO_4$: 315.1471; found: 315.1469.

5.2.18. (1*S,4*S**,5*R**,6*S**) 1,3,6-Trimethyl-4-(4-nitro-phenyl)-bicyclo[3.1.0]hex-2-ene-6-carboxylic acid ethyl ester (27).** To a solution of **26** (75 mg, 0.24 mmol) in 2.4 mL of CH_2Cl_2 was added a solution of dimethylaluminum chloride (0.10 mL, 0.10 mmol, 1.0 M in hexanes) at 0°C under a blanket of argon. The reaction mixture was allowed to warm to 23°C, and after 8 h additional dimethylaluminum chloride (0.10 mL, 0.10 mmol) was added. After 16 h, the reaction mixture was quenched with 4 mL of a 1:1 mixture of H_2O and saturated Rochelle's salt and diluted with 3 mL of CH_2Cl_2. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2×2 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (5–10% Et_2O in hexanes) to yield 63 mg (84%) of **27** as a yellow oil: R_f=0.38 (silica, 10% EtOAc in hexanes); IR (thin film) ν_{max}=2975, 2932, 2873, 1712, 1604, 1520 cm^{-1}; ^1H NMR (500 MHz, C_6D_6): δ 7.82 (d, J=7.0 Hz, 2H), 6.71 (d, J=7.0 Hz, 2H), 5.13 (s, 1H), 4.02 (m, 2H), 2.89 (s, 1H), 2.27 (s, 1H), 1.44 (s, 3H), 1.25 (s, 3H), 1.21 (s, 3H), 1.00 (t, J=7.0 Hz, 3H); ^{13}C NMR (100 MHz, C_6D_6): δ 173.1, 150.0, 147.6, 144.4, 131.0, 129.0, 124.3, 61.0, 55.5, 43.7, 40.6, 35.3, 14.8, 14.8, 13.9, 10.6; HRMS (EI): calcd for $C_{18}H_{21}NO_4$: 315.1471; found: 315.1468.

5.2.19. (1*S,4*S**,5*R**,6*S**) [1,3,6-Trimethyl-4-(1-methyl-but-1-enyl)-bicyclo[3.1.0]hex-2-en-6-yl]-methanol (28).** To a solution of **14** (25 mg, 0.095 mmol) in 1.0 mL of CH_2Cl_2 was added a solution of DIBAH (0.25 mL, 0.25 mmol, 1.0 M in toluene) at −78°C under a blanket of argon. After 5 min, the reaction mixture was quenched with 4 mL of a 1:1 mixture of saturated Rochelle's salt and H_2O and diluted with 4 mL of hexanes. The layers were separated and the aqueous layer was extracted with Et_2O (2×5 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (25% Et_2O in hexanes) to afford 16 mg (76%) of **28** as a colorless oil: R_f=0.20 (silica, 25% Et_2O in hexanes); IR (thin film) ν_{max}=3350 (br), 2961, 2929, 2871, 1449, 1376 cm^{-1}; ^1H NMR (400 MHz, C_6D_6): δ 5.32 (t, J=6.8 Hz, 1H), 5.19 (s, 1H), 3.49 (d, J=11.2 Hz, 1H), 3.20 (d, J=11.2 Hz, 1H), 2.68 (s, 1H), 2.03 (quint, 2H), 1.51 (s, 6H), 1.28 (s, 3H), 1.05 (s, 3H), 0.97 (t, J=7.2 Hz, 3H), 0.81 (s, 1H), 0.76 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 141.8, 135.1, 130.8, 128.3, 69.3, 58.4, 38.8, 36.4, 31.7, 21.4, 15.5, 14.6, 13.8, 12.5, 11.1; HRMS (EI): calcd for $C_{15}H_{24}O$: 220.1827; found: 220.1830.

5.2.20. (1*S,4*S**,5*R**,6*R**) (1,3,6-Trimethyl-4-phenyl-bicyclo[3.1.0]hex-2-en-6-yl)-methanol (29).** To a solution of **3** (41.3 mg, 0.13 mmol) in 1.5 mL of CH_2Cl_2 was added a solution of DIBAH (0.35 mL, 0.35 mmol, 1.0 M in toluene) at −78°C under a blanket of argon. After 5 min, the reaction mixture was quenched with 4 mL of a 3:1 mixture of H_2O and saturated Rochelle's salt and diluted with 5 mL of CH_2Cl_2. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2×5 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (30% EtOAc in hexanes) to yield 15 mg (42%) of **29** as a yellow oil: R_f=0.47 (silica, 33% EtOAc in hexanes); IR (thin film) ν_{max}=3401 (br), 2931, 2872, 1603, 1517 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 8.16 (d, J=8.5 Hz, 2H), 7.30 (d, J=6.8 Hz, 2H), 5.47 (s, 1H), 3.56 (d, J=11.5 Hz, 1H), 3.53 (d, J=11.5 Hz, 1H), 3.34 (s, 1H), 1.47 (s, 3H), 1.41 (s, 3H), 1.22 (s, 3H), 1.04 (s, 1H); ^{13}C (125 MHz, $CDCl_3$): δ 151.7, 146.9, 142.1, 131.2, 128.9, 124.0, 63.7, 55.2, 42.1, 40.1, 32.8, 18.7, 15.4, 14.0; HRMS (EI): calcd for $C_{16}H_{19}NO_3$: 273.1365; found: 273.1370.

5.2.21. 2,4-Dimethyl-5-(4-nitro-phenyl)-penta-(*Z*)-2,(*E*)-4-dienal (40). To 2,4-Dimethyl-5-(4-nitro-phenyl)-penta-2,4-dien-1-ol[3b] (468 mg, 2.01 mmol) in 20 mL of CH_2Cl_2 was added Dess–Martin periodinane (1.07 g, 2.52 mmol) at 23°C. After 30 min, the reaction mixture was quenched with 30 mL of a 1:1:1 mixture of saturated $NaHCO_3$, saturated $Na_2S_2O_3$, and H_2O, and diluted with 20 mL of Et_2O. The two layers were separated and the aqueous layer was extracted with 20 mL of Et_2O. The combined organic layers

were washed with 30 mL of brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude product was used without further purification in the next step.

5.2.22. 3,5-Dimethyl-2-(4-nitro-phenyl)-cyclopent-2-enone (41).[19a] To a solution of **40** (53 mg, 0.23 mmol) in 2.3 mL of CH_2Cl_2 was added a solution of dimethylaluminum chloride (0.07 mL, 0.07 mmol, 1.0 M in hexanes) at −10°C under a blanket of argon. After 1 h, the reaction mixture was quenched with 5 mL of a 1:1 mixture of H_2O and saturated Rochelle's salt and diluted with 5 mL of CH_2Cl_2. The two layers were separated and the aqueous layer was extracted with CH_2Cl_2 (2×5 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (25% Et_2O in hexanes) to yield 25 mg (47%) of **41** as a yellow solid: R_f=0.16 (silica, 20% EtOAc in hexanes); IR ($CDCl_3$) ν_{max}=2967, 2931, 1702, 1637, 1598, 1518 cm^{-1}; 1H (400 MHz, $CDCl_3$): δ 8.24 (d, J=9.2 Hz, 2H), 7.48 (d, J=9.2 Hz, 2H), 2.97 (dd, J=18.8, 6.8 Hz, 1H), 2.52–2.63 (m, 1H), 2.32 (d, J=18.8 Hz, 1H), 2.21 (s, 3H), 1.26 (d, J=7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.8, 172.5, 145.1, 139.1, 137.5, 130.2, 123.6, 41.4, 40.4, 18.6, 16.7; HRMS (EI): calcd for $C_{13}H_{13}NO_3$: 231.0895; found: 231.0899.

5.2.23. 3,5-Dimethyl-2-phenyl-cyclopent-2-enone (43) and 2,2,4-Trimethyl-5-phenyl-cyclopent-3-enol (44). To a solution of **42** (230 mg, 1.24 mmol) in CH_2Cl_2 (10 mL) was added a solution of Me_2AlCl (0.37 mL, 0.37 mmol, 1.0 M in hexanes) at −78°C under a blanket of nitrogen. The mixture was warmed to 23°C. After 16 h, the reaction mixture was quenched with saturated $NaHCO_3$ and was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated in vacuo. The product was purified by column chromatography (silica, hexanes/EtOAc=15:1) to yield 58 mg (25%) of **43** as colorless oil. Further elution gave 43 mg (17%) of **44** as a colorless oil.

Data for **43**: IR (thin film) ν_{max}=2927, 1700, 1494, 1379 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.28–7.43 (m, 5H), 2.88–2.95 (m, 1H), 2.51–2.59 (m, 1H), 2.23–2.30 (m, 1H), 2.17 (s, 3H), 1.26 (d, J=7.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 209.9, 169.8, 139.0, 131.9, 129.1, 128.2, 127.5, 40.9, 40.0, 18.2, 16.7; HRMS (EI): calcd for $C_{13}H_{14}O$: 186.1045; found: 186.1048.

Data for **44**: IR (thin film) ν_{max}=3399, 2957, 1453 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.16–7.43 (m, 5H), 5.38 (m, 1H), 3.84 (d, J=7.9 Hz, 1H), 3.54 (d, J=7.9 Hz, 1H), 1.46 (m, 3H), 1.13 (s, 3H), 1.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 141.9, 136.6, 135.9, 128.5, 128.4, 126.5, 89.6, 61.1, 45.2, 27.1, 20.5, 15.4; HRMS (EI): calcd for $C_{14}H_{18}O$: 202.1358; found: 202.1363.

5.2.24. 2-Phenyl-3-methyl-cyclopent-2-ene-1-one (46).[20] To a solution of **45** (65 mg, 0.38 mmol) in CH_2Cl_2 (3 mL) was added a solution of Me_2AlCl (0.076 mL, 0.076 mmol, 1.0 M in hexanes) at −40°C under a blanket of nitrogen. The solution was warmed to 23°C. After 16 h, the reaction mixture was quenched with saturated $NaHCO_3$ and extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated in vacuo. Purification by column chromatography (silica, hexanes/EtOAc=6:1) afforded 18 mg (28%) of **46** as a colorless oil. IR, ^1H NMR, ^{13}C NMR and MS data are consistent with the literature.[20]

5.2.25. (4*S*)-3-(4-Isopropenyl-cyclohex-1-enyl)-acrylic acid ethyl ester (50). To a solution of [bis-(2,2,2-trifluoroethoxy)phosphoryl]acetic acid ethyl ester (3.22 g, 8.70 mmol) and 18-crown-6 (4.95 g, 18.72 mmol) in THF (60 mL), was added a solution of potassium bis(trimethylsilyl)amide (19.08 mL, 9.54 mmol, 0.5 M in toluene) at −78°C under a blanket of nitrogen. After 5 min, a solution of **49** (1.0 g, 6.1 mmol) in THF (4 mL) was added. After 1 h, the reaction mixture was quenched with saturated NH_4Cl. The mixture was diluted with H_2O and extracted with Et_2O. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated in vacuo. Purification by column chromatography (silica, hexanes/Et_2O=40:1) afforded 1.15 g (85%) of **50** as a yellow oil. $[\alpha]_D$=−141° (c=0.33); IR (thin film) ν_{max}=2934, 1723, 1625, 1434, 1177 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 6.19 (d, J=12.5 Hz, 1H), 5.88 (s br, 1H), 5.46 (d, J=12.5 Hz, 1H), 4.60 (s, 1H), 4.59 (s, 1H), 3.98–4.06 (m, 2H), 2.28–2.38 (m, 1H), 2.11–2.20 (m, 2H), 1.91–2.09 (m, 2H), 1.69–1.76 (m, 1H), 1.60 (s, 3H), 1.31 (dq, J=11.5, 5.2 Hz, 1H), 1.14 (t, J=7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 166.4, 148.9, 143.7, 134.9, 134.7, 116.3, 108.7, 59.8, 40.2, 31.5, 27.4, 27.2, 20.5, 14.0; HRMS (EI): calcd for $C_{14}H_{20}O_2$: 220.1463; found: 220.1465.

5.2.26. (4*S*)-3-(4-Isopropenyl-cyclohex-1-enyl)-prop-2-enol (51). To a solution of **50** (500 mg, 2.3 mmol) in CH_2Cl_2 (20 mL) was added a solution of DIBAH (4.60 mL, 4.60 mmol, 1.0 M in hexanes) at −78°C under a blanket of nitrogen. After 20 min, the reaction mixture was quenched with aqueous saturated Rochelle's salt and extracted with EtOAc. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated in vacuo. Purification by column chromatography (silica, hexanes/EtOAc=10:1) to afford 360 mg (88%) of **51** as a yellow oil. $[\alpha]_D$=−102° (c=0.51); IR (thin film) ν_{max}=3325, 2919, 1644, 1435, 1029 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 5.89 (d, J=11.9 Hz, 1H), 5.59 (s br, 1H), 5.45 (dt, J=12.5, 6.5 Hz, 1H), 4.70 (s, 1H), 4.68 (s, 1H), 3.98–4.06 (m, 2H), 2.12–2.28 (m, 4H), 1.91–2.09 (m, 1H), 1.82–1.88 (m, 1H), 1.74 (s, 3H), 1.44–1.53 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 149.5, 134.4, 132.6, 128.5, 128.0, 108.7, 59.6, 40.5, 31.0, 29.1, 27.6, 20.7; HRMS (EI): calcd for $C_{12}H_{18}O$: 178.1358; found: 178.1358.

5.2.27. (4*S*)-3-(4-Isopropenyl-cyclohex-1-enyl)-prop-2-enal (52). To a suspension of activated MnO_2 (3.30 g, 37.9 mmol) in CH_2Cl_2 (25 mL), was added a solution of **51** (340 mg, 1.90 mmol) in CH_2Cl_2 (3 mL) at 0°C under a blanket of argon. After stirring for 2 h, the reaction mixture was filtered and the solution was concentrated in vacuo. Purification by column chromatography (silica, hexanes/EtOAc=12:1) provided 180 mg (56%) of **52** as a yellow oil. Due to its sensitivity, the aldehyde was immediately used in the next step. $[\alpha]_D$=−41° (c=0.95); IR (thin film) ν_{max}=2925, 1663, 1436 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 10.05 (d, J=8.2 Hz, 1H), 6.88 (d, J=11.8 Hz, 1H), 6.10 (s

br, 1H), 5.84 (dd, J=11.8, 8.2 Hz, 1H), 4.69–4.79 (m, 2H), 2.28–2.42 (m, 3H), 2.05–2.27 (m, 2H), 1.88–1.97 (m, 1H), 1.75 (s, 3H), 1.49–1.60 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 192.0, 150.5, 148.5, 137.7, 134.8, 128.3, 109.2, 39.9, 31.6, 29.2, 27.2, 20.7.

5.2.28. (6*S*)-6-Isopropenyl-2,3,4,5,6,7-hexahydro-inden-1-one (53). To a solution of **52** (100 mg, 0.57 mmol) in CH_2Cl_2 (25 mL), was added a solution of Me_2AlCl (0.11 mL, 0.11 mmol, 1.0 M in hexanes) at −78°C under a blanket of nitrogen. The solution was warmed to 23°C. After 16 h, the reaction mixture was quenched with saturated $NaHCO_3$ then extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried ($MgSO_4$), filtered and concentrated in vacuo. Purification by column chromatography (silica, Hex/EtOAc=15:1) afforded 22 mg (22%) of **53**. $[\alpha]_D$=−94° (c=0.30); IR (thin film) ν_{max}=2921, 1696, 1650, 1439 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.74 (s, 1H), 4.71 (s, 1H), 2.31–2.57 (m, 6H), 2.08–2.19 (m, 1H), 1.86–1.99 (m, 2H), 1.76 (s, 3H), 1.49–1.65 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 208.9, 173.3, 148.5, 138.6, 109.4, 40.6, 35.0, 29.8, 28.8, 27.2, 25.4, 21.0; HRMS (EI): calcd for $C_{12}H_{16}O$: 176.1201; found: 176.1202.

5.2.29. 3,5-Dimethyl-2-(1-methyl-but-2-enyl)-cyclopent-2-enone (55). To a solution of triethyl phosphonopropionate (2.98 g, 12.5 mmol) in hexanes (25 mL) was added a solution of lithium *t*-butoxide (13.0 mL, 13.0 mmol, 1.0 M in hexanes) at 23°C under a blanket of argon. After 4 h, a solution of crude **54** (1.78 g, 10.0 mmol) in 10 mL of hexanes was added. After 30 min, the reaction mixture was quenched with 50 mL of H_2O and the two layers were separated. The organic layer was washed with 25 mL of brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The product was purified by column chromatography (5–20% Et_2O in hexanes) to yield 500 mg (28%) of **55** as a colorless oil: R_f=0.55 (silica, 20% EtOAc in hexanes); IR (thin film) ν_{max}=2963, 1703, 1629 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.23 (tq, J=7.2, 1.6 Hz, 1H), 2.76 (dd, J=18.4, 6.8 Hz, 1H), 2.37 (m, 1H), 2.20–2.08 (m, 3H), 2.04 (s, 3H), 1.77 (s, 3H), 1.66 (d, J=7.2 Hz, 3H), 1.01 (t, J=7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 211.1, 168.0, 143.2, 133.6, 127.0, 40.8, 39.9, 21.4, 18.0, 16.7, 15.7, 14.1; HRMS (EI): calcd for $C_{12}H_{18}O$: 178.1358; found: 178.1358.

Acknowledgements

We thank Professor Rick L. Danheiser (MIT) for stimulating discussions. Financial support by Merck and Co. and the ACS Petroleum Research Fund (PRF#37520-AC1) is gratefully acknowledged. The center of New Directions in Organic synthesis is supported by Bristol-Myers Squibb as a sponsoring and Novartis as a supporting member. We thank Dr Frederick J. Hollander and Dr Allen G. Oliver for the crystal structure determination of compound **2**.

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