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Studies toward the Total Syntheses of Cucurbitacins B and D

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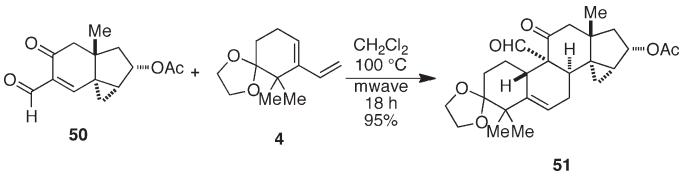

Synthetic efforts toward the convergent construction of the tetracyclic triterpenoids cucurbitacins B and D are described. The results of a Diels−Alder study examining the effects of steric and electronic variations of 2-methyl-2-cyclohexenone on the *endo*/*exo*-diastereoselectivity of the reaction are presented. The diastereomer of the core of the cucurbitacins, epimeric at C8, C9, and C10, **51**, was synthesized via a highly regio- and stereoselective Diels−Alder reaction of the diene **4** and the novel dienophile **50**.

Introduction

The cucurbitacins, first isolated from the bitter principles of Cucurbitaceae plants in 1957, are a group of triterpenoids characterized by the tetracyclic cucurbitane nuclear skeleton 19-(10→9β)-abeo-10α-lanost-5-ene.[1] Two notably pharmacologically potent members of this family are cucurbitacins B and D, **1** and **2**, respectively (Figure 1).[2] Cucurbitacin B has exhibited significant anti-inflammatory activity[3] and preventive and curative effects against hepatotoxicity[4] and has shown potency as an antagonist of CD 18-mediated cell adhesion.[5] In addition, recent *in vitro* studies have demonstrated that **1** exhibits antiproliferative activity against various leukemia and lymphoma cell lines[6] as well as human breast cancer cells.[7] *In vivo* studies suggest that **1** may be an effective treatment for ER-, Her2/neu-amplified and p53 mutant breast cancers. Cucurbitacin D has displayed cytotoxic activity against a variety of human cancer cell lines, including lung, human colon, human oral epidermoid carcinoma, hormone-dependent prostate, breast, and central nervous system cancer cell lines.[2]

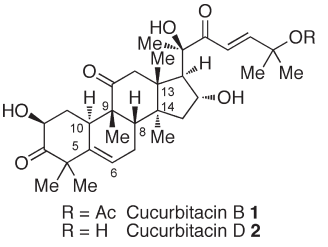

FIGURE 1. Cucurbitacins B and D.

In addition to the potent biological activity exhibited by **1** and **2**, the core structure of the cucurbitacins possesses several interesting features, which render it an attractive synthetic target. The 5,6-double bond as well as the C9 β-methyl group and the C14 α-methyl group are unique to this group of steroids. To date, no total syntheses have been reported on any members of the cucurbitacin family. Herein, we report our progress toward a convergent synthesis of the core of the cucurbitacins via a Diels−Alder reaction.

Results and Discussion

Retrosynthesis of the Cucurbitacin Core. The cyclohexene moiety of the B ring of the cucurbitacins indicated that a Diels−Alder reaction could be employed to efficiently construct the core of this steroid (Scheme 1). The stereochemical

(1) Rehm, S.; Enslin, P. R.; Meeuse, D. J; Wessels, J. M. *J. Sci. Food Agric.* **1957**, *8*, 679.
(2) Chen, J. C.; Chiu, M. H.; Nie, R. L.; Cordell, G. A.; Qiu, S. X. *Nat. Prod. Rep.* **2005**, *22*, 386.
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(6) Haritunians, T.; Gueller, S.; Zhang, L.; Badr, R.; Yin, D.; Xing, H.; Fung, M.-C.; Koeffler, H. P. *Leuk. Res.* **2008**, *32*, 1366.
(7) Wakimoto, N.; Yin, D.; O'Kelly, J.; Haritunians, T.; Karlan, B.; Said, J.; Xing, H.; Koeffler, H. P. *Cancer Sci.* **2008**, *99*, 1793.

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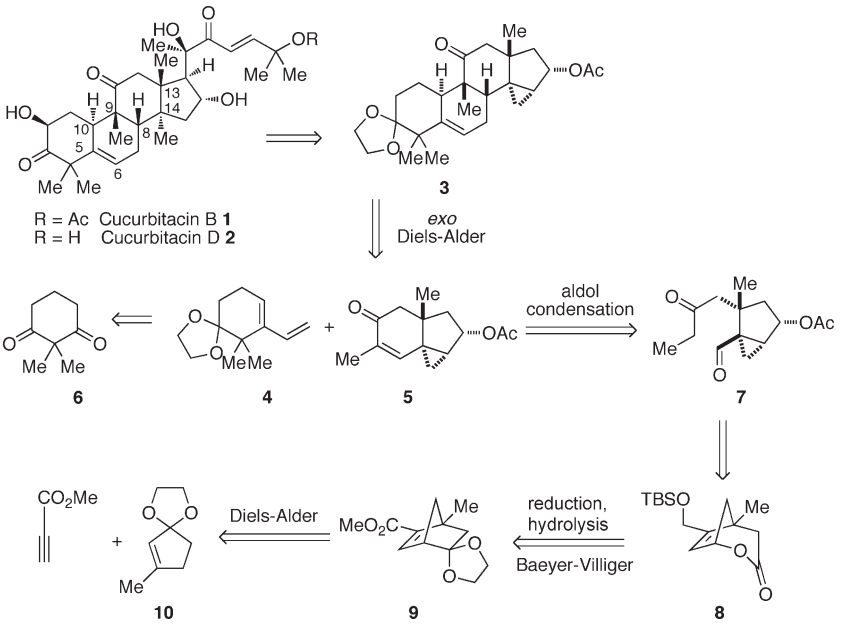
SCHEME 1. Retrosynthetic Analysis



relationship between C10 and C8/C9 requires that the Diels–Alder reaction occur in an *exo*-selective fashion. In addition, it was apparent that the cycloaddition must also be facially selective, whereby the diene **4** would approach the dienophile **5** *anti* to the C13 angular methyl substituent. Since it was likely that a C14α-methyl group would both retard the cycloaddition and most likely give the opposite facial selectivity,[8] we chose to mask this methyl group as a cyclopropyl group with the intention of decreasing the steric hindrance on the α-face of the enone **5**, thereby increasing the accessibility for approach of the diene **4** to that face. Eventual conversion of the acetate to the ketone (via hydrolysis and oxidation) and reductive opening of the cyclopropyl ketone would afford the desired C14 methyl group. The diene **4** could be derived in four steps from the known 2,2-dimethylcyclohexane-1,5-dione, **6**.[9] The more complex dienophile **5** could be generated via an intramolecular aldol condensation of the dicarbonyl compound **7**. Given that the ethyl ketone and the secondary alcohol are on the same face of the cyclopentene **7**, it was envisioned that the two functional groups could be obtained through a methoxide-mediated ring-opening of the lactone **8**, which could in turn be synthesized via a Baeyer–Villiger reaction on the corresponding ketone prepared from the norbornenone ketal **9**. Finally, the norbornenone ketal **9** could be accessed through a Diels–Alder reaction between the ketal **10** and methyl propiolate.

***exo*-Selective Diels–Alder Reactions.** In general, it has been observed that most intermolecular Diels–Alder reactions proceed to form *endo* cycloadducts. The "*endo* rule" of selectivity was first rationalized by Alder and Stein as a result of the principle of "maximum accumulation of unsaturation" in the transition state of the reaction.[10] Woodward and Katz elaborated further by attributing the favorability of the *endo* transition state to the stabilizing effect of the second-order orbital interactions.[11] Other theories have considered inductive or charge transfer interactions and the geometrical overlap relationships of the π-orbitals at the primary centers.[12] The few reported examples of intermolecular Diels–Alder reactions that deviate from the *endo* rule have been mainly attributed to steric factors.[13]

Danishefsky has reported a total synthesis of (±)-mamanuthaquinone, which features an exclusively *exo*-selective intermolecular Diels–Alder reaction as the key step of the synthesis (Scheme 2).[14] It was suggested that the *exo*-selectivity of this reaction arose from the destabilization of the *endo* transition state due to steric repulsion between the *gem*-dimethyl groups of the diene **11** and the aroyl group of the dienophile **12**. We hypothesized that the Diels–Alder reaction between the diene **4** and the dienophile **5**, possessing similar *gem*-dimethyl functionality, might exhibit the same repulsive effect to yield the desired *exo* cycloadduct **3**. Although a less sterically encumbering methylene unit is present in the dienophile **5** at the position analogous to the aroyl group of the dienophile **12**, it was conceivable that the steric bulk at the adjacent centers of the dienophile **5** could serve to disfavor the *endo* transition state and yield the desired *exo*-diastereomer.

(8) Engler, T. A.; Sampath, U. S.; Vander Velde, D.; Takusagawa, F. *Tetrahedron* **1992**, *48*, 9399.

(9) Jacobson, B. M.; Soterpoulos, P.; Bahadori, S. *J. Org. Chem.* **1988**, *53*, 3247.

(10) Alder, K.; Stein, G. *Angew. Chem.* **1937**, *50*, 510.

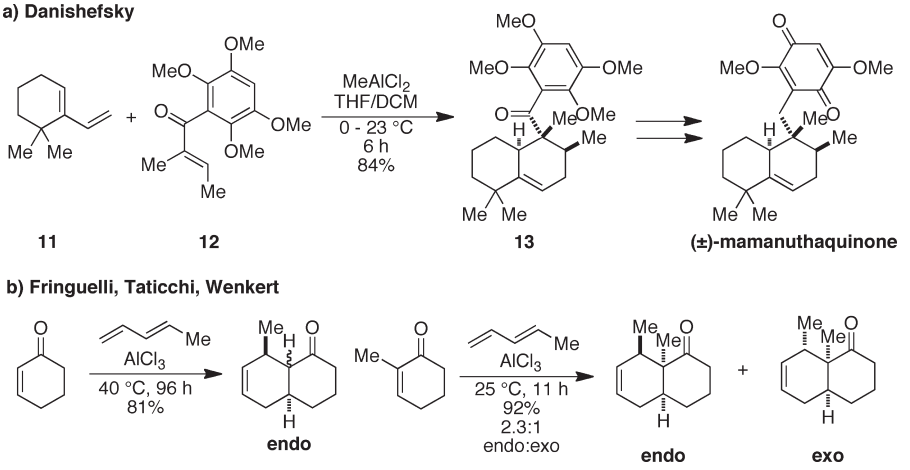
(11) (a) Woodward, R. B.; Katz, T. J. *Tetrahedron* **1959**, *5*, 70. (b) Hoffmann, R.; Woodward, R. B. *J. Am. Chem. Soc.* **1965**, *87*, 4388. (c) Hoffmann, R.; Woodward, R. B. *Acc. Chem. Res.* **1968**, *1*, 17. (d) Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779. (e) Houk, K. N. *J. Am. Chem. Soc.* **1973**, *95*, 4094.

(12) (a) Wassermann, A. *J. Chem. Soc.* **1935**, 825. (b) Wassermann, A. *J. Chem. Soc.* **1935**, 1511. (c) Wassermann, A. *J. Chem. Soc.* **1936**, 432. (d) Woodward, R. B.; Baer, H. *J. Am. Chem. Soc.* **1944**, *66*, 645. (e) Herndon, W. C.; Hall, L. H. *Tetrahedron Lett.* **1967**, 3095.

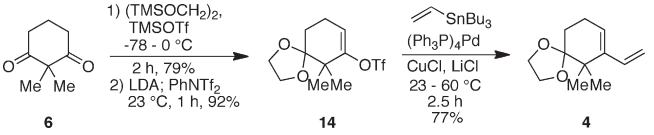
(13) (a) Lam, Y.; Cheong, P. H.; Blasco Mata, J. M.; Stanway, S. J.; Gouverneur, V.; Houk, K. N. *J. Am. Chem. Soc.* **2009**, *131*, 1947. (b) Powers, T. S.; Jiang., W.; Su, J.; Wulff, W. D.; Waltermire, B. E.; Rheingold, A. L. *J. Am. Chem. Soc.* **1997**, *119*, 6438. (c) Maruoka, K.; Imoto, H.; Yamamoto, H. *J. Am. Chem. Soc.* **1993**, *115*, 8517. (d) Kano, T.; Tanaka, Y.; Maruoka, K. *Chem.–Asian J.* **2007**, *2*, 1161. (e) Zeng, Y.; Aube, J. *J. Am. Chem. Soc.* **2005**, *127*, 15712. (f) Ge, M.; Stoltz, B. M.; Corey, E. J. *Org. Lett.* **2000**, *2*, 1927.

(14) Yoon, T.; Danishefsky, S. J.; de Gala, S. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 853.

SCHEME 2. Relevant *exo*-Selective Diels–Alder Reactions



SCHEME 3. Synthesis of the Diene 4



In addition, it has been demonstrated by Fringuelli, Taticchi, and Wenkert that the presence of a methyl group at the olefinic α-carbon of a dienophile can increase the *exo*-selectivity of the cycloaddition.[15] They reported that the reaction between (*E*)-piperylene and 2-methyl-2-cyclohexenone gave a 2.3:1 mixture of *endo:exo* Diels–Alder adducts, whereas the reaction with 2-cyclohexenone produced the *endo* product exclusively, with epimerization at the α-center (Scheme 2). Encouraged by these results, we sought to study the *endo*/*exo*-selectivity of our Diels–Alder system through several model reactions between the diene **4** and various analogues of 2-methyl-2-cyclohexenone.

Synthesis of the Diene 4. The synthesis of the diene **4** was achieved in three steps starting from the known 2,2-dimethylcyclohexene-1,3-dione **6** (Scheme 3). Ketalization of the dione **6** using Noyori's conditions followed by treatment with LDA and *N*-phenyl triflimide gave the enol triflate **14**. Stille coupling between the triflate **14** and tributylvinyltin produced the diene **4** in an overall yield of 56%.

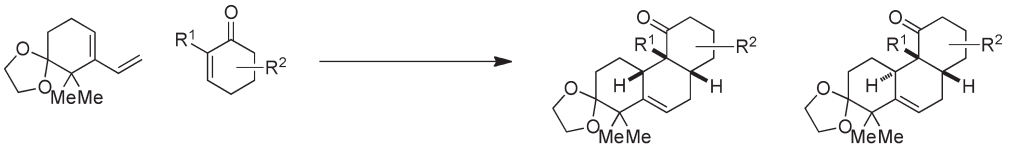
***endo*/*exo*-Diastereoselectivity Studies.** The *endo*/*exo*-diastereoselectivity of the Diels–Alder reactions between the diene **4** and six dienophiles was examined. The investigation began with a $MeAlCl_2$-mediated cycloaddition between the diene **4** and 2-methyl-2-cyclohexenone **15** (Table 1, entry 1). The Diels–Alder adduct was obtained in excellent yield in a 2.5:1 ratio of *endo*:*exo* isomers **21n** and **21x**, similar to the reported ratio of the reaction between the dienophile **15** and (*E*)-piperylene.[14] Next, we chose to study the reaction of the diene **4** with the dienophiles **16** and **17** (entries 2 and 3), which possessed *gem*-dimethyl substitution at the positions analogous to the quaternary centers on the dienophile **5**. It was thought that substitution at C4 and C5 would greatly increase the *exo*-selectivity since the substituents at C4 and C5 of the dienophile **5** would be in close proximity to the *gem*-dimethyl group of the diene **4** in the *endo* transition state. Unfortunately, both dienophiles produced almost exclusively the *endo* cycloadducts, **22n** and **23n**. In addition, the presence of the *gem*-dimethyl substituents at C4 and C5 appeared to impede the reaction, as higher temperatures or longer reaction times were required to carry out the reaction. The dienophile **18** (entry 4), containing the *gem*-dimethyl substitution at C6, corresponding to the position of the aroyl group in the dienophile **12**, was the only substituted dienophile tested that increased the *exo*-selectivity, resulting in an unassigned 2:1 diastereomeric ratio of the cycloadducts **24n** and **24x**. The results obtained from the dienophiles **16**, **17**, and **18** indicate that the C6 position is the most important in influencing *exo*-selectivity. It is interesting to note that the dienophile **15**, lacking *gem*-dimethyl substitution at any position, produced the *exo* adduct in a ratio similar to that from the dienophile **18**. This anomaly was also observed in a similar study with the same dienophiles and (*E*)-piperylene.[14]

On the basis of the model systems, it seemed that the substituents on the dienophile **5** might not be sufficiently sterically encumbering to generate the *exo* adduct **3** with high selectivity. Thus, we decided to manipulate the electronic nature of the dienophile by replacing the methyl group at the olefinic α-carbon with an electron-withdrawing group (entries 5 and 6). We speculated that an aldehyde or an ester group might become the directing group on the dienophile, thereby delivering the desired keto-*exo* cycloadduct. If successful, the aldehyde or ester of the keto-*exo* cycloadduct would have to be reduced following established protocols in similar systems to provide the desired methyl group.[16] The Diels–Alder reaction of the β-keto ester dienophile **19** with the diene **4** gave a 1.3:1 mixture of the keto-*endo*:keto-*exo* products **25n** and **25x**. To our delight the dienophile **20**, with an α-formyl group, provided the keto-*exo* adduct **26x** exclusively, albeit in only 20% yield. The low yield most likely resulted from the decomposition of the dienophile due to the highly acidic conditions. Since the dienophile **20** is more reactive than the dienophiles **15**–**18** because of the additional

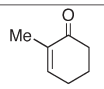
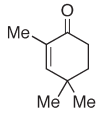
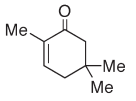
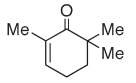
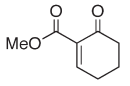
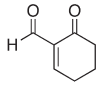
(15) (a) Fringuelli, F.; Pizzo, F.; Taticchi, A.; Halls, T. D. J.; Wenkert, E. *J. Org. Chem.* **1982**, *47*, 5056. (b) Angell, E. C.; Fringuelli, F.; Minuti, L.; Pizzo, F.; Porter, B.; Taticchi, A.; Wenkert, E. *J. Org. Chem.* **1986**, *51*, 2649.

(16) Ramachandran, S. A.; Kharul, R. K.; Marque, S.; Soucy, P.; Jacques, F.; Chenevert, R.; Deslongchamps, P. *J. Org. Chem.* **2006**, *71*, 6149.

TABLE 1. Model Studies of *endo*/*exo*-Diastereoselectivity



4 **dienophile** **n (endo)** **x (exo)**

Entry	Dienophile	Temp	Time	Product	Isolated Yield	Keto-*Endo*: Keto-*Exo*
1	 **15**	0 °C – 23 °C	6 h	**21n, 21x**	98%	2.5:1
2	 **16**	0 °C – 40 °C	3 d	**22n**	56%	>99:1
3	 **17**	0 °C – 23 °C	2 d	**23n, 23x**	92%	10:1
4	 **18**	0 °C – 23 °C	7 h	**24n, 24x**	92%	2:1[a]
5	 **19**	–78 °C – –20 °C	14 h	**25n, 25x**	76%	1.3:1
6	 **20**	23 °C	14 h	**26n, 26x**	86%	1:4

[a]The ratio of diastereomers was not assigned.

activating group, milder conditions were employed. The reaction of the dienophile **20** and the diene **4** at room temperature without Lewis acid produced in high yield the desired keto-*exo* cycloadduct **26x** as the major isomer.

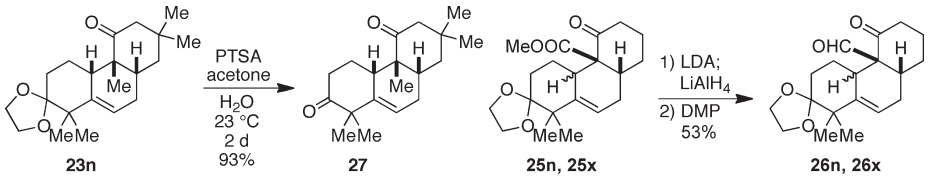
The structures of the major diastereomers of the cycloadducts **21**, **22**, and **26** were unambiguously determined by X-ray crystallography. The minor diastereomers of the adducts **21** and **26** were assumed to be the other *endo*/*exo* diastereomer as opposed to the possible regioisomers. Examples in the literature have shown that 1,2-disubstituted dienes with substituents of similar reactivity yield the *ortho* Diels–Alder adduct as the only regioisomer.[17] Attempts at growing crystals of the major diastereomers of **23** and **24** proved to be unsuccessful. The ketal of the cycloadduct **23n** was cleaved under acidic conditions to produce the diketone **27**, which provided a crystal for analysis. Similar derivatization on the major isomer of the cycloadduct **24** was carried out but failed to provide adequate crystals, and 2D homo- and heteronuclear NMR data were inconclusive. Consequently, the diastereomers remain unassigned. Unfortunately, the cycloadducts **25n** and **25x** proved to be inseparable, and therefore X-ray crystallographic analysis could not be used for structure assignment. Instead, the cycloadducts **25n** and **25x** were derivatized by subjecting the mixture to LDA, LAH reduction conditions[18] followed by oxidation with Dess-Martin periodinane (DMP) to provide the corresponding keto-aldehyde adducts **26n** and **26x**. Comparison of the ^{1}H NMR and ^{13}C NMR of the derivatized products with those of the keto-aldehyde adducts established that the cycloadducts **25n** and **25x** were obtained in a 1.3:1 ratio (Scheme 4).

Although the model systems indicated that the presence of the aldehyde moiety at the olefinic α-carbon was necessary to obtain the desired keto-*exo* cycloadduct, we nonetheless proceeded with the synthesis and testing of the dienophile **5**, as we were interested in determining if the reaction would

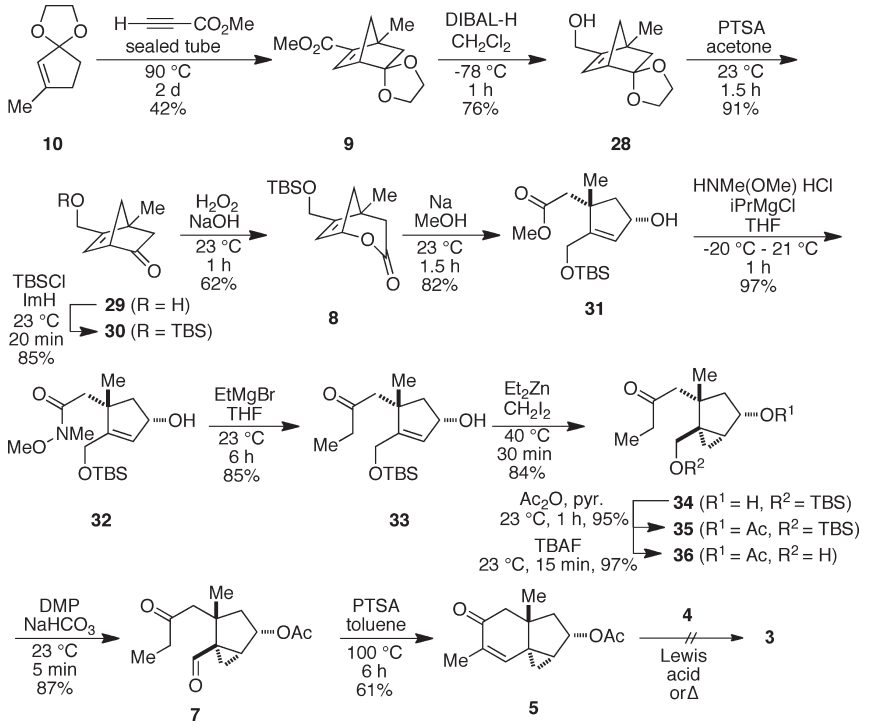
(17) (a) Grieco, P. A.; Nunes, J. J.; Gaul, M. D. *J. Am. Chem. Soc.* **1990**, *112*, 4595. (b) Handy, S.; Greico, P.; Mineur, C.; Ghosez, L. *Synlett* **1995**, 565. (c) Pai, C.-C.; Liu, R.-S. *Org. Lett.* **2001**, *3*, 1295. (d) Minuti, L.; Taticchi, A.; Marrocchi, A.; Broggi, A.; Gacs-Baitz, E. *Tetrahedron: Asymmetry* **2004**, *15*, 1187.

(18) Kraus, G. A.; Frazier, K. *J. Org. Chem.* **1980**, *45*, 4262.

SCHEME 4. Transformations of the Cycloadducts



SCHEME 5. Synthesis of the Dienophile 5



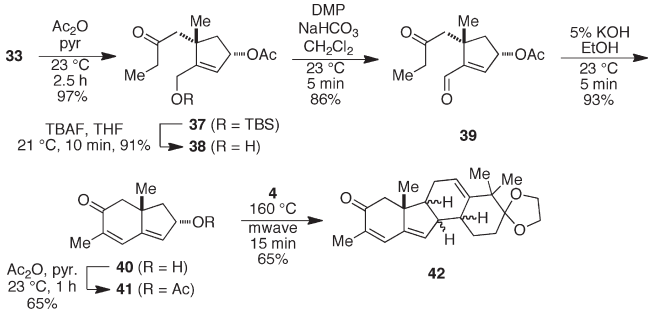
deviate from the predictions set forth by the models. In addition, utilizing the dienophile **5** as opposed to the aldehyde analogue would afford a more expedient synthetic route to the core, provided the Diels–Alder reaction was successful.

Synthesis of the Dienophile 5. The synthesis of the dienophile **5** commenced with the construction of the norbornenone ethylene ketal **9** via a Diels–Alder reaction between methyl propiolate and the ethylene ketal of 3-methylcyclopent-2-enone **10** (Scheme 5). It has been demonstrated that under mild conditions, 2-cyclopenten-1-one ethylene ketals can interconvert with the ring-opened 2-(2-hydroxyethoxy)-cyclopenta-1,3-diene form, the latter of which can undergo cycloaddition and then intramolecular reacetalization with a variety of doubly activated dienophiles to generate the 2-norbornenone ethylene ketals in good to excellent yields.[19] We found that using a monoactivated dienophile such as methyl propiolate required harsher conditions and produced the cycloadduct in moderate yield. The norbornenone ethylene ketal **9** was converted into the norbornenone **30** in three steps involving DIBAL–H reduction of the ester to the corresponding primary alcohol, followed by deprotection of the ketal and silyl protection of the primary alcohol. Nucleophilic Baeyer–Villiger conditions were employed to generate the bicyclic lactone **8** while avoiding epoxidation of the alkene. Treatment of the lactone **8** with sodium in methanol furnished the corresponding ester, which was in turn converted to the Weinreb amide **32** using isopropylmagnesium chloride and *N,O*-dimethylhydroxylamine hydrochloride in 79% over two steps. Alternatively, the Weinreb amide **32** could be generated directly from the lactone **8** in a slightly lower yield of 66%. Addition of the ethyl Grignard reagent to the amide **32** provided the ethyl ketone **33** in 85% yield. Hydroxyl-directed cyclopropanation was followed using the Furukawa modified Simmons–Smith conditions to generate the *syn* cyclopropane **34** in 84% yield. With all the carbons of the dienophile present, the synthesis of **5** was completed in four high-yielding steps involving protection of the secondary alcohol, deprotection and oxidation of the primary alcohol, and acid-catalyzed intramolecular aldol condensation.

We began our attempts at effecting the Diels–Alder reaction between the diene **4** and the dienophile **5** to give the tetracyclic core **3** by utilizing the $MeAlCl_2$ conditions employed in the model systems. No reaction was observed in dichloromethane, even under refluxing conditions. Changing the solvent to benzene and heating to 80 °C led to decomposition of the dienophile **5**. A variety of other Lewis acids such as Me_2AlCl, $SnCl_4$, $BF_3 \cdot Et_2O$, $ZnBr_2$, and $Sc(OTf)_3$

(19) Ohkita, M.; Nishizawa, O.; Tsuji, T.; Nishida, S. *J. Org. Chem.* **1993**, *58*, 5200.

SCHEME 6. Synthesis of the Dienophile 41



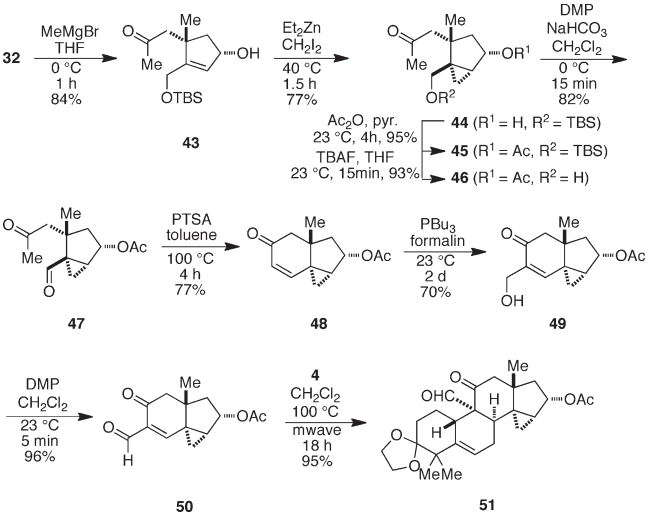
were screened but resulted in either recovery of starting material or the decomposition of the diene **4**.

As stated previously, the presence of the *gem*-dimethyl substituents at the C4 and C5 positions of 2-methylcyclohexenone required elevated temperatures or longer reaction times to facilitate the Diels−Alder reaction, so it was not surprising that the reaction between the diene **4** and the dienophile **5** would be recalcitrant. We hypothesized that if we replaced the cyclopropyl group with a less encumbering alkene moiety, we could reduce the steric hindrance of the dienophile, which would have a beneficial effect on the reactivity. In addition, the less sterically hindering alkene would further increase the steric bias between the faces of the dienophile and thereby further favor the desired facial selectivity. The cyclopropyl group, which is a protected form of the requisite C14 methyl, could be installed after the Diels−Alder adduct was obtained. Thus, we set out to synthesize the dienophile **41**.

Synthesis of the Dienophile 41. The synthesis of the dienophile **41** followed a similar strategy to that of the dienophile **5** (Scheme 6). Starting from the ethyl ketone **33**, rather than cyclopropanation of the double bond, the secondary alcohol was protected to provide the acetate **37**. The primary alcohol was then deprotected and oxidized to furnish the keto-aldehyde **39**. Due to the acid-sensitive allylic alcohol moiety, base-catalyzed aldol condensation conditions were used to generate the enone **40**, with simultaneous cleavage of the acetate group. Subsequently, the alcohol was reprotected to give the dienophile **41**. Acid-mediated reaction between the diene **4** and the dienophile **41** using $MeAlCl_2$, was unsuccessful, leading only to racemization of the dienophile **41**. Attempts at effecting the cycloaddition under microwave irradiation led to the thermal elimination of the acetate, generating the corresponding trienone, which underwent a [4+2] cycloaddition with the diene **4** at the least hindered double bond to give the cycloadduct **42**. Faced with this result, we decided to pursue the synthesis of the dienophile **50**. On the basis of model systems, we were confident that the aldehyde at the olefinic α-carbon would direct the *endo*/*exo*-diastereoselectivity of the reaction to generate the desired keto-*exo* adduct preferentially. In addition, we reasoned that the cycloaddition would be more facile with the dienophile **50** than with the dienophiles **5** and **41** due to the enhanced activation provided by the additional aldehyde functionality.

Synthesis of the Dienophile 50. In developing an approach to the dienophile **50**, we planned to intercept an intermediate along the route to the dienophile **5**. The formyl group could be introduced at various points along the synthetic route, but it was decided that late stage installation via a Baylis−Hillman

SCHEME 7. Synthesis of the Dienophile 50 and [4+2] Cycloaddition to Provide the Cycloadduct 51



reaction followed by oxidation of the resultant alcohol on the demethylated analogue of the dienophile **5** would be the most efficient. Addition of the methyl Grignard reagent to the Weinreb amide **32** provided the methyl ketone **43** in 84% yield (Scheme 7). The ketone **43** underwent hydroxyl-directed cylcopropanation to provide the cyclopropane **44**, which was then subjected to secondary alcohol protection and cleavage of the silyl ether to provide the primary alcohol **46**. Oxidation of **46** to the aldehyde followed by acid-catalyzed intramolecular aldol condensation produced the enone **48**. Treatment of the enone **48** with tributylphosphine and formaldehyde effected the Baylis−Hillman reaction to provide the alcohol **49**, which was subsequently oxidized using Dess−Martin periodinane to give the desired doubly activated dienophile **50**.

Following the Diels−Alder protocol previously applied to the dienophile **20**, the thermal reaction of the diene **4** and the dienophile **50** was conducted. The reaction was carried out under microwave conditions at 100 °C for 18 h and yielded a single diastereomer of the cycloadduct in 95% yield. X-ray crystallographic analysis was employed to unambiguously assign the structure of the cycloadduct **51**. It was shown that the desired keto-*exo*-diastereoselectivity was achieved (the relative stereochemistry between C8/C9 and C10 was correct). Unfortunately, the relative stereochemistry between C8/C9 and C13/C14 indicated that the reaction had occurred with the undesired facial selectivity to provide us with the diastereomer of the cucurbitacins epimeric at C8, C9, and C10. Contrary to our initial proposal, the angular C13 methyl group was too far from the Diels−Alder reaction site to overcome the steric bias imposed by the proximal cyclopropane.

Conclusion

In summary, after investigating the *endo*/*exo*-diastereoselectivity imparted by substitution at various positions of 2-methyl-2-cyclohexenone, we have found that the *exo*-selectivity of the reaction can be increased by the addition of an alternate directing group, e.g., an ester or an aldehyde, as in the case of the dienophiles **19**, **20**, and **50**, or by increasing the steric bulk at the C6 position as in the case of the dienophile **18**. In addition, we have synthesized the diastereomer

of the cucurbitacin core epimeric at C8, C9, and C10. Studies are currently underway to reverse the facial selectivity of the [4+2] cycloaddition and obtain the correct diastereomer by further increasing the steric bias between the faces of the dienophile.

Experimental Section

6,6-Dimethyl-7-ethenyl-1,4-dioxaspiro[4.5]dec-7-ene (4). To a solution of the triflate **14** (2.37 g, 7.5 mmol, 1 equiv) in 46 mL of DMSO was added $Pd(PPh_3)_4$ (0.86 g, 0.75 mmol, 0.1 equiv) followed by LiCl (1.90 g, 45 mmol, 6 equiv), CuCl (3.70 g, 37 mmol, 5 equiv), and tributylvinyltin (4.4 mL, 15 mmol, 2 equiv). The mixture was subjected to three cycles of freeze−thaw degassing, and stirred at room temperature for 1 h, and then heated at 60 °C for 2 h. The reaction was quenched with a solution of NH_4Cl-NH_3 (pH = 8). The aqueous layer was extracted with diethyl ether (3 × 20 mL). The combined extracts were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 10:1) yielded 1.12 g of the diene **4** (5.8 mmol, 77%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.28 (dd, 1H, J = 17.0, 10.8 Hz), 5.75 (t, 1H, J = 4.0 Hz), 5.31 (dd, 1H, J = 17.5, 2.0 Hz), 4.95 (dd, 1H, J = 10.8, 2.0 Hz), 3.96−4.00 (m, 4H), 2.21−2.25 (m, 2H), 1.76 (t, 2H, J = 6.5 Hz), 1.11 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 144.1, 136.0, 120.9, 114.0, 111.9, 64.9, 41.9, 26.3, 23.9, 22.7. FTIR (thin film): 2970, 2950, 2876, 1471, 1381, 1348, 1201, 1144, 1099, 1042, 997, 915, 841 cm^{-1}. HRMS-CI (m/z): $[M + H]^+$ calculated for $C_{12}H_{18}O_2H$ 195.1385, found 195.1385.

(±)-(1*R*,2*S*,3a*S*,7a*S*)-3a,6-Dimethyl-5-oxo-1a,2,3,3a,4,5-hexahydro-1*H*-cyclopropa[*c*]inden-2-yl Acetate (5). To a solution of the aldehyde **7** (100 mg, 0.4 mmol, 1 equiv) in 8 mL of toluene was added *p*-toluenesulfonic acid (4 mg, 0.02 mmol, 0.05 equiv). The flask was equipped with a Dean−Stark trap and a reflux condenser, and the reaction was refluxed for 2.5 h. The solution was cooled to ambient temperature and quenched with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with ether (3 × 5 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (hexanes−ethyl acetate, 10:1) to afford 57 mg of the enone **5** (0.24 mmol, 61%) as a white solid: mp 73−76 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.43 (s, 1H), 5.41 (ddd, 1H, J = 8.0, 8.0, 4.0 Hz), 2.52 (s, 2H), 2.26 (ddd, 1H, J = 4.0, 4.0, 4.0 Hz), 2.05 (s, 3H), 1.82 (dd, 1H, J = 12.8, 7.5 Hz), 1.78 (s, 3H), 1.40 (dd, 1H, J = 5.3, 3.0 Hz), 1.31 (dd, 1H, J = 12.8, 8.5 Hz), 1.12 (s, 3H), 0.52 (dd, 1H, J = 7.5, 6.0 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 199.5, 171.0, 145.0, 135.1, 75.2, 49.1, 40.8, 37.1, 36.4, 26.0, 25.0, 21.0, 15.9, 11.5. FTIR (thin film): 2966, 1735, 1665, 1380, 1245, 1021 cm^{-1}. HRMS-ESI (m/z): $[M+Na]^+$ calculated for $C_{14}H_{18}O_3Na$ 257.1154, found 257.1159.

(±)-(1*R*,2*S*,4*S*,5*R*)-5-Formyl-4-methyl-4-(2-oxobutyl)bicyclo[3.1.0]hexan-2-yl Acetate (7). To a cooled solution of the alcohol **36** (767 mg, 3.0 mmol, 1 equiv) in 20 mL of dichloromethane at 0 °C was added sodium bicarbonate (1.01 g, 12 mmol, 4 equiv) followed by Dess-Martin periodinane (2.56 g, 6.0 mmol, 2 equiv). The reaction was stirred at 22 °C for 5 min and quenched with a 1:1 solution of saturated Na_2SO_3−saturated $NaHCO_3$. The aqueous layer was extracted with ethyl acetate (3 × 15 mL). The combined organic extracts were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 4:1) yielded 662 mg of the aldehyde **7** (2.6 mmol, 87%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.06 (s, 1H), 5.34 (ddd, 1H, J = 8.5, 8.5, 4.5 Hz), 2.83 (d, 1H, J = 16.0 Hz), 2.52 (d, 1H, J = 16.0 Hz), 2.42 (q, 2H, J = 7.5 Hz), 2.34 (ddd, 1H, J = 8.5, 4.5, 4.5 Hz), 2.12 (dd, 1H, J = 7.5 Hz), 2.04 (s, 3H), 1.38 (s, 3H), 1.39−1.42 (m, 1H), 1.35 (dd, 1H, J = 6.0, 5.0 Hz), 1.27 (dd, 1H, J = 8.5, 6.0 Hz), 1.02 (t, 3H, J = 7.3 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 210.1, 197.9, 170.9, 72.7, 49.5, 46.5, 39.7, 39.4, 37.4, 28.8, 23.7, 20.9, 12.7, 7.5. FTIR (thin film): 2970, 2938, 2917, 2843, 1732, 1699, 1458, 1377, 1238, 1033 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{14}H_{20}O_4Na$ 275.1259, found 275.1253.

(±)-(1*S*,5*S*)-6-([(1,1-Dimethylethyl)dimethylsilyloxy]methyl)-5-methyl-2-oxabicyclo[3.2.1]oct-6-en-3-one (8). To a cooled solution of the norbornenone **30** (41 mg, 0.15 mmol, 1 equiv) in 1.5 mL of methanol at 0 °C was added sodium hydroxide (6 mg, 0.15 mmol, 1 equiv) followed by a 30% aqueous solution of hydrogen peroxide (0.02 mL, 0.15 mmol, 1 equiv). After stirring at 0 °C for 1.5 h, the reaction was quenched by the addition of water and ethyl acetate. The organic layer was washed with a saturated solution of $NaHCO_3$ and once with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 10:1) to afford 0.027 g of the lactone **8** (0.1 mmol, 62%) as a white solid: mp 48−51 °C . ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.09 (d, 1H, J = 1.5 Hz), 5.05 (s, 1H), 4.28 (d, 1H, J = 15.0 Hz), 4.21 (dd, 1H, J = 15.3, 1.5 Hz), 2.77 (d, 1H, J = 18.0 Hz), 2.55 (d, 1H, J = 18.0 Hz), 1.91−1.97 (m, 2H), 1.22 (s, 3H), 0.90 (s, 9H), 0.06 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 170.3, 158.0, 126.2, 80.5, 59.1, 47.9, 45.4, 43.6, 25.7, 20.0, 18.1, −5.6. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{15}H_{26}O_3SiNa$ 305.1549, found 305.1542.

(±)-(1*S*,4*S*)-Methyl 4-Methylspiro[bicyclo[2.2.1]hept[5]ene-2,2′-[1,3]dioxolane]-5-carboxylate (9). To a sealed tube containing the ketal **10** (4.15 g, 29 mmol, 1 equiv) was added methyl propiolate (5.3 mL, 59 mmol, 2 equiv). The mixture was purged with argon for 15 min and then heated at 90 °C for 20 h. The residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 7:1) to afford 2.65 g of the norbornenone ketal ester **9** (11.8 mmol, 42%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.91 (d, 1H, J = 3.5 Hz), 3.85−3.96 (m, 4H), 3.69 (s, 3H), 2.74−2.75 (m, 1H), 1.75 (d, 1H, J = 12.5 Hz), 1.64−1.70 (m, 3H), 1.44 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 165.0, 145.3, 144.8, 119.7, 64.8, 64.2, 54.2, 51.0, 50.4, 49.5, 46.0, 17.7. FTIR (thin film): 2978, 2950, 2876, 1712, 1589, 1434, 1344, 1307, 1279, 1242, 1156, 1091, 1042, 1013 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{12}H_{16}O_4Na$ 247.0946, found 247.0945.

6,6-Dimethyl-1,4-dioxaspiro[4.5]dec-7-en-7-yl Trifluoromethanesulfonate (14). To a solution of the diketone **6** (1.0 g, 7.1 mmol, 1 equiv) in 17 mL of dichloromethane at −78 °C was added 1,2-bis(trimethylsilyloxy)ethane (1.7 mL, 7.1 mmol, 1 equiv) followed by trimethylsilyl trifluoromethanesulfonate (0.13 mL, 0.7 mmol, 0.1 equiv). The reaction was stirred at −78 °C for 1 h and then warmed to 0 °C and stirred for an additional hour. The mixture was quenched with a solution of saturated $NaHCO_3$. The aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 10:1) afforded 1.04 g (5.7 mmol, 79%) of the monoketal as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 3.93 (s, 4H), 2.40 (t, 2H, J = 7.0 Hz), 1.88 (t, 2H, J = 6.5 Hz), 1.75 (tt, 2H, J = 7.0, 6.5 Hz), 1.12 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 212.8, 113.2, 65.3, 55.1, 36.3, 29.6, 19.9, 19.1. FTIR (thin film): 2978, 2953, 2876, 1712, 1462, 1381, 1315, 1262, 1185, 1140, 1074 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{10}H_{16}O_3Na$ 207.0997, found 207.1000.

A 1.6 M solution of *n*-butyllithium (7.1 mL, 11.3 mmol, 1.4 equiv) was added dropwise to a solution of diisopropylamine (1.5 mL, 10.5 mmol, 1.3 equiv) in 24 mL of THF at 0 °C, and the mixture was stirred for 20 min. The reaction was cooled to −78 °C, and a solution of the monoketal (1.5 g, 8.1 mmol, 1 equiv) in 12 mL of THF was added. After 2 h, *N*-phenyltriflimide (5.9 g, 16.2 mmol, 2 equiv) was added, and the solution was warmed to

23 °C and stirred for 1 h. The reaction was quenched with water, and the aqueous layer was extracted with diethyl ether (3 × 15 mL). The organic layers were combined, washed with brine, dried with $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 20:1) to yield 2.37 g of the triflate **14** (7.5 mmol, 92%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.69 (t, 1H, J = 4.0 Hz), 4.00 (s, 4H), 2.24 (td, 2H, J = 6.5, 4.0 Hz), 1.77 (t, 2H, J = 6.5 Hz), 1.18 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 152.7, 118.3 (q, J = 317 Hz), 114.9, 110.8, 65.2, 44.3, 26.4, 20.9, 20.7. FTIR (thin film): 2987, 2958, 2946, 2884, 1675, 1417, 1246, 1209, 1144, 1029, 988 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calculated for $C_{11}H_{15}O_5F_3SNa$ 339.0490, found 339.0490.

(±)-(4a′*S*,4b′*R*,8a′*R*)-1′,1′,4b′-Trimethyl-4′,4a′,4b′,6′,7′,8′,8a′,9′-octahydro-1′*H*-spiro[[1,3]dioxolane-2,2′-phenanthren]-5′(3′*H*)-one (21n) and (±)-(4a′*R*,4b′*R*,8a′*R*)-1′,1′,4b′-Trimethyl-4′,4a′,4b′,6′,7′,8′,8a′,9′-octahydro-1′*H*-spiro[[1,3]dioxolane-2,2′-phenanthren]-5′(3′*H*)-one (21x). A cooled solution of the dienophile **15** (50 mg, 0.45 mmol, 1 equiv) in 3.5 mL of DCM at 0 °C was treated with a 1.0 M solution of $MeAlCl_2$ (0.68 mL, 0.68 mmol, 1.5 equiv) followed by a solution of the diene **4** (132 mg, 0.68 mmol, 1.5 equiv) in 1 mL of DCM. The reaction was warmed to 23 °C, stirred for 6 h, and then quenched with a saturated solution of NH_4Cl. The aqueous layer was extracted with diethyl ether (3 × 2 mL). The organic layers were combined, washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 10:1) afforded 96 mg of **21n** (0.32 mmol, 70%) and 39 mg of **21x** (0.13 mmol, 28%) as white solids. **21n**: mp 126−129 °C . ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.48−5.49 (m, 1H), 3.88−3.95 (m, 4H), 2.55 (dt, 1H, J = 11.0, 6.0 Hz), 2.25−2.36 (m, 2H), 2.02−2.09 (m, 2H), 1.89−1.93 (m, 1H), 1.63−1.86 (m, 6H), 1.55−1.58 (m, 1H), 1.46−1.49 (m, 1H), 1.16 (s, 3H), 1.11 (s, 3H), 1.05 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 216.4, 141.1, 115.1, 112.6, 65.1, 50.2, 45.6, 40.5, 40.2, 39.0, 31.5, 29.2, 28.5, 27.5, 24.9, 24.3, 22.8, 19.8 (one high-field carbon not observed). FTIR (thin film): 2962, 2925, 2876, 1687, 1450, 1352, 1197, 1144, 1082 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calculated for $C_{19}H_{28}O_3Na$ 327.1935, found 327.1938. **21x**: mp 143−146 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.57−5.58 (m, 1H), 3.91−3.98 (m, 4H), 2.63−2.73 (m, 2H), 2.38 (brd, 1H, J = 18.5 Hz), 2.29, (brd, 1H, J = 14.5 Hz), 2.02−2.05 (m, 1H), 1.62−1.84 (m, 6H), 1.40−1.49 (m, 2H), 1.25−1.28 (m, 1H), 1.19 (s, 3H), 1.08 (s, 3H), 1.03 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 214.9, 141.5, 116.1, 112.3, 65.1, 64.9, 51.2, 45.1, 43.0, 37.3, 34.6, 29.8, 28.3, 26.7, 26.5, 25.8, 23.1, 19.6, 16.8. FTIR (thin film): 2971, 2931, 2876, 1696, 1465, 1449, 1434, 1378, 1136, 1064 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calculated for $C_{19}H_{28}O_3Na$ 327.1936, found 327.1939.

(±)-(4a′*S*,4b′*R*,8a′*S*)-1′,1′,4b′,8′,8′-Pentamethyl-4′,4a′,4b′,6′,7′,8′,8a′,9′-octahydro-1′*H*-spiro[[1,3]-dioxolane-2,2′-phenanthren]-5′(3′*H*)-one (22n). To a cooled solution of the dienophile **16** (50 mg, 0.36 mmol, 1 equiv) in 2.5 mL of DCM at 0 °C was added a 1.0 M solution of $MeAlCl_2$ (0.54 mL, 0.54 mmol, 1.5 equiv) followed by a solution of the diene **4** (105 mg, 0.49 mmol, 1.5 equiv) in 1 mL of DCM. The reaction was heated to 40 °C, stirred for 3 days, and then quenched with a saturated solution of NH_4Cl. The aqueous layer was extracted with diethyl ether (3 × 2 mL). The organic layers were combined and washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 10:1) afforded 68 mg of **22n** (0.20 mmol, 56%) as a white solid. **22n**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.48−5.49 (m, 1H), 3.84−3.95 (m, 4H), 2.45 (ddd, 1H, J = 15.5, 11.3, 4.8 Hz), 2.17−2.26 (m, 4H), 1.76−1.82 (m, 1H), 1.55−1.69 (m, 5H), 1.41−1.44 (m, 1H), 1.19 (s, 3H), 1.12 (s, 3H), 1.02 (s, 3H), 1.01 (s, 3H), 0.98 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 218.6, 140.8, 116.3, 112.7, 65.1, 65.0, 48.7, 45.6, 44.9, 39.5, 37.4, 35.4, 32.5, 31.9, 31.4, 29.3, 26.4, 24.9, 24.4, 22.7, 19.7. FTIR (thin film): 2958, 2876, 2357, 1712, 1466, 1135, 1086 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calculated for $C_{21}H_{32}O_3Na$ 355.2249, found 355.2253.

(±)-(4a′*S*,4b′*R*,8a′*S*)-1′,1′,4b′,7′,7′-Pentamethyl-4′,4a′,4b′,6′,7′,8′,8a′,9′-octahydro-1′*H*-spiro[[1,3]-dioxolane-2,2′-phenanthren]-5′(3′*H*)-one (23n). To a cooled solution of the dienophile **17** (50 mg, 0.36 mmol, 1 equiv) in 2.5 mL of DCM at 0 °C was added a 1.0 M solution of $MeAlCl_2$ (0.54 mL, 0.54 mmol, 1.5 equiv) followed by a solution of the diene **4** (105 mg, 0.49 mmol, 1.5 equiv) in 1 mL of DCM. The reaction was warmed to 23 °C, stirred for 2 days, and then quenched with a saturated solution of NH_4Cl. The aqueous layer was extracted with diethyl ether (3 × 2 mL). The organic layers were combined, washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 10:1) afforded 114 mg of a mixture of **23n** and **23x** (0.34 mmol, 92%, 10:1 ratio) as a colorless oil. **23n**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.52 (m, 1H), 3.89−3.96 (m, 4H), 2.40−2.46 (m, 1H), 2.31 (dd, 1H, J = 16.5, 2.0 Hz), 2.22 (d, 1H, J = 16.5 Hz), 1.93−2.03 (m, 3H), 1.88 (dd, 1H, J = 13.5, 13.5 Hz), 1.71 (ddd, 1H, J = 13.3, 13.3, 4.5 Hz), 1.55−1.61 (m, 2H), 1.44−1.48 (m, 1H), 1.23 (brd, 1H, J = 13.5 Hz), 1.14 (s, 3H), 1.11 (s, 3H), 1.05 (s, 3H), 1.00 (s, 3H), 0.95 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 216.3, 140.7, 115.2, 112.4, 65.15, 65.10, 55.3, 49.2, 45.7, 42.6, 39.8, 34.2, 32.6, 32.2, 31.7, 30.6, 28.5, 27.8, 24.8, 24.5, 19.8. FTIR (thin film): 2954, 2925, 2876, 1691, 1467, 1377, 1189, 1136, 1074, 943 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calculated for $C_{21}H_{32}O_3Na$ 355.2249, found 355.2249.

(±)-(4a′*S*,4b′*R*,8a′*R*)-1′,1′,4b′,6′,6′-Pentamethyl-4′,4a′,4b′,6′,7′,8′,8a′,9′-octahydro-1′*H*-spiro[[1,3]-dioxolane-2,2′-phenanthren]-5′(3′*H*)-one (24n) and (±)-(4a′*R*,4b′*R*,8a′*R*)-1′,1′,4b′-Trimethyl-4′,4a′,4b′,6′,7′,8′,8a′,9′-octahydro-1′*H*-spiro[[1,3]dioxolane-2,2′-phenanthren]-5′(3′*H*)-one (24x). To a cooled solution of the dienophile **18** (50 mg, 0.36 mmol, 1 equiv) in 2.5 mL of DCM at 0 °C was added a 1.0 M solution of $MeAlCl_2$ (0.54 mL, 0.54 mmol, 1.5 equiv) followed by a solution of the diene **4** (105 mg, 0.49 mmol, 1.5 equiv) in 1 mL of DCM. The reaction was warmed to 23 °C, stirred for 7 h, and then quenched with a saturated solution of NH_4Cl. The aqueous layer was extracted with diethyl ether (3 × 2 mL). The organic layers were combined, washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 10:1) afforded 111 mg of a mixture of **24n** and **24x** (0.33 mmol, 92%, 1:0.5 ratio diastereomers, unassigned) as a colorless oil. **24** major: ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.55−5.56 (m, 1H), 3.89−3.97 (m, 4H), 2.60 (brd, 1H, J = 12.0 Hz), 2.40 (brd, 1H, J = 16.0 Hz), 1.76−1.89 (m, 4H), 1.70 (ddd, 1H, J = 13.5, 13.5, 4.0 Hz), 1.61−1.69 (m, 2H), 1.42−1.49 (m, 1H), 1.34−1.40 (m, 2H), 1.23 (s, 3H), 1.16 (s, 3H), 1.09 (s, 3H), 1.07 (s, 3H), 1.05 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 217.5, 142.2, 115.8, 112.4, 65.1, 64.9, 50.2, 45.2, 43.2, 41.3, 38.6, 33.1, 30.0, 29.0, 28.9, 28.7, 26.4, 23.7, 22.7, 19.6, 18.1. FTIR (thin film): 2973, 2935, 2881, 1693, 1470, 1377, 1137, 1089 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calculated for $C_{21}H_{32}O_3Na$ 355.2249, found 355.2247. **24** minor: ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.40−5.41 (m, 1H), 3.86−3.98 (m, 4H), 2.31−2.38 (m, 1H), 2.16−2.28 (m, 2H), 1.94 (dd, 1H, J = 18.0, 5.5 Hz), 1.35−1.88 (m, 8H), 1.19 (s, 3H), 1.16 (s, 3H), 1.14 (s, 3H), 1.04 (s, 3H), 1.01 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 222.7, 141.7, 114.2, 112.8, 65.1, 64.9, 48.6, 45.7, 42.8, 41.4, 32.9, 32.4, 32.0, 28.6, 28.5, 27.0, 26.1, 24.6, 23.8, 19.7 (one high-field carbon not observed).

(±)-(4a′*S*,4b′*S*,8a′*R*)-Methyl 1′,1′-dimethyl-5′-oxo-3′,4′,4a′,4b′,5′,6′,7′,8′,8a′,9′-decahydro-1′*H*-spiro[[1,3]dioxolane-2,2′-phenanthrene]-4b′-carboxylate (25n) and (±)-(4a′*R*,4b′*S*,8a′*R*)-Methyl 1′,1′-dimethyl-5′-oxo-3′,4′,4a′,4b′,5′,6′,7′,8′,8a′,9′-decahydro-1′*H*-spiro[[1,3]dioxolane-2,2′-phenanthrene]-4b′-carboxylate (25x). To a cooled solution of the dienophile **19** (120 mg, 2.3 mmol, 3 equiv) in 2 mL of DCM at −78 °C was added a 1.0 M solution of $MeAlCl_2$ (0.77 mL, 2.3 mmol, 3 equiv) followed by a solution of the diene **4** (50 mg, 0.26 mmol, 1 equiv) in 1 mL of DCM. The reaction was

stirred at −78 °C for 1 h, then warmed to −20 °C, and stirred for 14 h. A saturated solution of NH_4Cl was added, and the aqueous layer was extracted with diethyl ether (3 × 2 mL). The organic layers were combined, washed with brine, dried with $MgSO_4$, filtered, and concentrated in *vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 10:1) afforded 68 mg of a mixture of **25n** and **25x** (0.20 mmol, 76%, 1.3:1 ratio) as a white solid. **25n**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.39−5.40 (m, 1H), 3.88−3.96 (m, 4H), 3.73 (s, 3H), 3.09 (d, 1H, J = 12.5 Hz), 2.65−2.71 (m, 2H), 1.33−2.39 (m, 11H), 1.32 (s, 3H), 1.07 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 205.7, 173.6, 142.1, 115.4, 112.3, 65.2, 65.1, 63.9, 52.3, 45.4, 40.2, 37.6, 34.1, 31.2, 27.1, 26.2, 25.7, 24.1, 22.7, 19.9. **25x**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.47−5.48 (m, 1H), 3.88−3.96 (m, 4H), 3.74 (s, 3H), 2.94 (d, 1H, J = 13.0 Hz), 2.65−2.71 (m, 1H), 1.33−2.39 (m, 12H), 1.19 (s, 3H), 1.01 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 208.2, 171.4, 141.0, 115.7, 112.5, 65.1, 65.0, 63.8, 51.9, 45.6, 40.0, 37.2, 33.2, 30.6, 27.0, 25.9, 25.5, 24.1, 22.6, 19.6. **25n**+**25x**: mp 170−173 °C. FTIR (thin film): 2950, 2881, 1716, 1437, 1245, 1220, 1139, 1089 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{20}H_{28}O_5Na$ 371.1834, found 371.1832.

(±)-(4a′*S*,4b′*R*,8a′*R*)-1′,1′-Dimethyl-5′-oxo-3′,4′,4a′,4b′,5′,6′,7′,8′,8a′,9′-decahydro-1′*H*-spiro[[1,3]-dioxolane-2,2′-phenanthrene]-4b′-carbaldehyde (26n) and (±)-(4a′*R*,4b′*R*,8a′*R*)-1′,1′-Dimethyl-5′-oxo-3′,4′,4a′,4b′,5′,6′,7′,8′,8a′,9′-decahydro-1′*H*-spiro[[1,3]dioxolane-2,2′-phenanthrene]-4b′-carboxaldehyde (26x). To a solution of the dienophile **20** (290 mg, 2.3 mmol, 9 equiv) in 2 mL of DCM was added a solution of the diene **4** (50 mg, 0.26 mmol, 1 equiv) in 1 mL of DCM. The reaction was stirred at 23 °C for 14 h and then concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 10:1) afforded 70 mg of a mixture of **26n** and **26x** (0.22 mmol, 86%, 1:4 ratio) as a white solid. **26x**: mp 94−97 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.73 (s, 1H), 5.50 (brs, 1H), 3.92−3.99 (m, 4H), 3.11 (d, 1H, J = 12.5 Hz), 2.60−2.65 (m, 1H), 2.42−2.47 (m, 1H), 2.33−2.37 (m, 1 H), 2.17 (brd, 1H, J = 18.3 Hz) 1.82−2.04 (m, 5H), 1.62−1.72 (m, 3H), 1.51−1.54 (m, 1H), 1.25 (s, 3H), 1.04 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 208.3, 203.5, 141.7, 116.6, 112.2, 66.0, 65.18, 65.17, 45.6, 39.0, 33.7, 33.6, 30.6, 26.5, 25.9, 25.0, 24.6, 23.3, 19.6. FTIR (thin film): 2939, 2881, 1728, 1705, 1451, 1380, 1234, 1194, 1163, 1140, 1070, 1043 cm^{-1}. HRMS-ESI (m/z): $[M+Na]^+$ calculated for $C_{19}H_{26}O_4Na$ 341.1729, found 341.1729. **26n**: ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.45 (s, 1H), 5.47 (brs, 1H), 3.89−3.97 (m, 4H), 2.96 (d, 1H, J = 10.3 Hz), 2.59−2.66 (m, 1H), 2.42−2.48 (m, 1H), 2.32−2.38 (m, 1H), 1.61−2.08 (m, 9H), 1.44−1.46 (m, 1H), 1.22 (s, 3H), 1.05 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 210.9, 200.1, 140.9, 116.0, 112.2, 66.3, 65.2, 65.1, 45.7, 40.8, 34.1, 33.1, 31.1, 27.6, 27.3, 26.5, 25.1, 23.2. 19.7.

To a cooled solution of the diisopropylamine (0.03 mL, 0.19 mmol, 1.3 equiv) in 2 mL of THF at −78 °C was added dropwise a 1.6 M solution of *n*-butyllithium in hexanes (0.13 mL, 0.20 mmol, 1.4 equiv). The mixture was warmed to 0 °C and stirred for 20 min. The reaction was cooled to −78 °C, and a solution of **25n** and **25x** (1.3:1 ratio) in 1 mL of THF was added and stirred for 20 min. Lithium aluminum hydride was added (11 mg, 0.29 mmol, 1.4 equiv), and the mixture was stirred for 5 min at −40 °C. The reaction was quenched by the addition of 0.5 mL of 0.5 M HCl. The aqueous layer was extracted with ether, and the combined organic extracts were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Half of the crude material was carried forward in the subsequent oxidation step. To a solution of the crude material in 0.5 mL of dichloromethane was added Dess-Martin periodinane (61 mg, 0.14 mmol, 2 equiv). After 5 min of stirring, the contents were filtered through a plug of silica gel (pentanes−ethyl acetate, 2:1) and the filtrate was concentrated *in vacuo* to yield 0.012 g of the aldehydes **26n** and **26x** (0.04 mmol, 53%) in a 1.3:1 ratio of diastereomers.

(±)-(4a*S*,4b*R*,8a*S*)-1,1,4b,7,7-Pentamethyl-4,4a,4b,6,7,8,8a,9-octahydrophenanthrene-2,5(1*H*,3*H*)-dione (27). To the ketal **23n** (5 mg, 0.02 mmol, 1 equiv) in 0.5 mL of acetone were added *p*-toluenesulfonic acid (0.2 mg, 0.001 mmol, 0.05 equiv) and one drop of water. The reaction was stirred at 23 °C for 2 days and then quenched by the addition of saturated $NaHCO_3$. The aqueous layer was extracted with ethyl acetate, and the organic layers were combined, washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 10:1) afforded 0.004 mg of the diketone **27** (0.02 mmol, 93%) as a white solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.58−5.59 (m, 1H), 2.56 (ddd, 1H, J = 15.0, 12.7, 6.5 Hz), 2.49 (brdd, 1H, J = 18.5, 8.0 Hz), 2.34−2.40, (m, 3H), 2.17 (d, 1H, J = 16.5 Hz), 1.95−2.04 (m, 3H), 1.82−1.85 (m, 1H), 1.69−1.78 (m, 2H), 1.25 (s, 3H), 1.24 (s, 3H), 1.22 (s, 3H), 0.99 (s, 3H), 0.97 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 215.7, 213.1, 140.0, 116.8, 55.0, 52.2, 49.1, 42.8, 40.2, 38.3, 34.0, 32.4, 32.2, 31.9, 28.6, 28.0, 27.4, 24.8, 21.5. FTIR (thin film): 2947, 2885, 1704, 1683 cm^{-1}.

(±)-(1*S*,4*S*)-4-Methylspiro[bicyclo[2.2.1]hept[5]ene-2,2′-[1,3]dioxolan]-5-yl)methanol (28). To a cooled solution of the norbornenone ketal ester **9** (1.25 g, 6.7 mmol, 1 equiv) in 58 mL of dichloromethane at −78 °C was added dropwise a 1.0 M solution of diisobutylaluminum hydride in dichloromethane (16 mL, 16 mmol, 2.4 equiv). After 15 min, the solution was quenched with Na/K-tartrate. The biphasic solution was stirred at 23 °C for 2 h. The layers were separated, and the aqueous layer was extracted with ethyl acetate (3 × 40 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 2:1) yielded 0.81 g of the alcohol **28** (4.1 mmol, 74%) as a white solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.91 (s, 1H), 4.24 (d, 1H, J = 14.5 Hz), 4.16 (d, 1H, J = 14.5 Hz), 3.86−3.97 (m, 4H), 2.62 (brs, 1H), 1.88 (brs, 1H), 1.70 (d, 1H, J = 12.5 Hz), 1.68 (d, 1H, J = 10.5 Hz), 1.58−1.60 (m, 1H), 1.55 (dd, 1H, J = 12.0, 3.5 Hz), 1.26 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 153.5, 127.1, 120.1, 64.5, 64.1, 59.7, 54.5, 49.4, 49.2, 46.8, 16.9. FTIR (thin film): 3428, 2954, 2929, 2868, 1454, 1319, 1238, 1152, 1074, 1013 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{11}H_{16}O_3Na$ 219.0997, found 219.0996.

(±)-(1*S*,4*S*)-5-(Hydroxymethyl)-4-methylbicyclo[2.2.1]hept-5-en-2-one (29). To a solution of the alcohol **28** (2.69 g, 13.7 mmol, 1equiv) in 60 mL of acetone was added *p*-toluenesulfonic acid (0.21 g, 1.1 mmol, 0.08 equiv) and 0.1 mL of water. The reaction was stirred at 23 °C for 1.5 h and then quenched with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 3:1) to provide 1.88 g of the norbornenone **29** (12.5 mmol, 91%) as a yellow oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.89 (s, 1H), 4.34 (dd, 1H, J = 15.5, 3.5 Hz), 4.18 (dd, 1H, J = 15.0, 3.0 Hz), 3.04 (brs, 1H), 2.05 (dd, 1H, J = 8.8, 4.5 Hz), 1.91 (dd, 1H, J = 16.5, 4.5 Hz), 1.84 (d, 1H, J = 9.0 Hz), 1.83 (d, 1H, J = 16.0 Hz), 1.62−1.65 (m, 1H), 1.36 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 214.7, 157.0, 123.6, 59.8, 56.3, 55.7, 48.4, 43.4, 16.9. FTIR (thin film): 3420, 2954, 2925, 2872, 1736, 1450, 1409, 1377, 1311, 1234, 1192, 1021 cm^{-1}. HRMS-ESI (m/z): $[M+Na]^+$ calculated for $C_9H_{12}O_2Na$ 175.0735, found 175.0739.

(±)-(1*S*,4*S*)-5-([(1,1-Dimethylethyl)dimethylsilyloxy]methyl)-4-methylbicyclo[2.2.1]hept-5-en-2-one (30). To a solution of the norbornenone **29** (1.88 g, 12.5 mmol, 1 equiv) and imidazole (2.52 g, 37.5 mmol, 3 equiv) in 60 mL of DMF was added *tert*-butyldimethylsilyl chloride (2.83 g, 18.8 mmol, 1.5 equiv). The reaction was stirred at 23 °C for 20 min and then quenched with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with ethyl acetate (3 × 45 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the

residue on silica gel (hexanes−ethyl acetate, 10:1) afforded 3.17 g of the silyl ether **30** (11.9 mmol, 96%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.83 (s, 1H), 4.32 (dd, 1H, J = 15.0, 1.5 Hz), 4.15 (dd, 1H, J = 15.0, 1.5 Hz), 3.01 (brs, 1H), 2.03 (dd, 1H, J = 9.0, 4.5 Hz), 1.91 (dd, 1H, J = 16.0, 4.5 Hz), 1.81 (d, 1H, J = 9.0 Hz), 1.80 (d, 1H, J = 15.5 Hz), 1.33 (s, 3H), 0.90 (s, 9H), 0.05 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 214.8, 156.8, 123.2, 60.1, 56.3, 55.6, 48.3, 43.5, 25.7, 18.2, 16.9, −5.6. FTIR (thin film): 2954, 2929, 2851, 1748, 1475, 1458, 1258, 1131, 1099, 1070, 1038, 841 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calculated for $C_{15}H_{26}O_2SiNa$ 289.1600, found 289.1597.

(±)-(1*S*,4*S*)-Methyl 2-([(1,1-Dimethylethyl)dimethylsilyloxy]-methyl)-4-hydroxy-1-methylcyclopent-2-en-1-yl)acetate (31). To a solution of the lactone **8** (111 mg, 0.40 mmol, 1 equiv) in 13 mL of methanol was added sodium (108 mg, 4.7 mmol, 12 equiv). The reaction was stirred for 1.5 h and quenched with water. The aqueous layer was extracted with chloroform (3 × 10 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 5:1) afforded 95 mg of the methyl ester **31** (0.30 mmol, 82%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.73 (s, 1H), 4.68 (brt, 1H, J = 8.5 Hz), 4.20 (s, 2H), 3.63 (s, 3H), 2.71 (d, 1H, J = 9.5 Hz), 2.60 (d, 1H, J = 15.5 Hz), 2.45 (d, 1H, J = 15.0 Hz), 2.24 (dd, 1H, J = 14.5, 8.0 Hz), 2.05 (dd, 1H, J = 14.5, 3.0 Hz), 1.15 (s, 3H), 0.91 (s, 9H), 0.06 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 173.0, 151.3, 128.3, 74.4, 59.6, 51.4, 48.5, 46.4, 44.2, 28.0, 25.8, 18.2, −5.6. FTIR (thin film): 3420, 2954, 2929, 2852, 1732, 1479, 1454, 1434, 1254, 1209, 1111 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calculated for $C_{16}H_{30}O_4SiNa$ 337.1811, found 337.1817.

(±)-(1*S*,4*S*)-2-([(1,1-Dimethylethyl)dimethylsilyloxy]methyl)-4-hydroxy-1-methylcyclopent-2-en-1-yl)-*N*-methoxy-*N*-methylacetamide (32). To a solution of dried *N*,*O*-dimethylhydroxylamine hydrochloride (2.34 g, 24 mmol, 3 equiv) in 13 mL of THF was added a solution of the methyl ester **31** (2.51 g, 8 mmol, 1 equiv) dissolved in 13 mL of THF. The reaction was cooled to −20 °C, and a 2.0 M solution of isopropylmagnesium chloride (20 mL, 40 mmol, 5 equiv) was added dropwise. After 45 min, the reaction was quenched with a saturated solution of NH_4Cl. The aqueous layer was extracted with ethyl acetate (3 × 15 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel to provide 2.66 g of the Weinreb amide **32** (7.8 mmol, 97%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.73 (s, 1H), 4.63 (brt, 1H, J = 7.5 Hz), 4.21 (s, 2H), 3.67 (s, 3H), 3.61 (d, 1H, J = 10.0 Hz), 3.14 (s, 3H), 2.80 (brd, 1H, J = 16.0 Hz), 2.47 (d, 1H, J = 16.0 Hz), 2.22 (dd, 1H, J = 14.5, 7.5 Hz), 2.10 (dd, 1H, J = 14.5, 1.5 Hz), 1.18 (s, 3H), 0.90 (s, 9H), 0.05 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 172.8, 151.1, 128.2, 74.3, 61.0, 59.6, 48.7, 46.4, 40.0, 31.7, 29.1, 25.8, 18.3, −5.5, −5.6. FTIR (thin film): 3432, 2950, 2929, 2852, 1650, 1458, 1380, 1254, 1189, 1119, 1054, 1005, 837 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calculated for $C_{17}H_{33}O_4NSiNa$ 366.2077, found 366.2076.

(±)-(1*S*,4*S*)-2-([(1,1-Dimethylethyl)dimethylsilyloxy]methyl)-4-hydroxy-1-methylcyclopent-2-en-1-yl)butan-2-one (33). To a cooled solution of the Weinreb amide **32** (100 mg, 0.29 mmol, 1 equiv) in 2 mL of THF at 0 °C was added a 3.0 M solution of ethylmagnesium bromide (0.39 mL, 1.16 mmol). The reaction was warmed to 23 °C and stirred for 6 h. A saturated solution of NH_4Cl was added to quench the reaction. The aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the mixture on silica gel (hexanes−ethyl acetate, 5:1) provided 77 mg of the ethyl ketone **33** (0.25 mmol, 85%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.70 (s, 1H), 4.65−4.69 (m, 1H), 4.18 (d, 1H, J = 14.0 Hz), 4.13 (d, 1H, J = 14.5 Hz), 3.09−3.17 (m, 1H), 2.78 (d, 1H, J = 17.5 Hz), 2.56 (d, 1H, J = 17.5 Hz), 2.37 (q, 2H, J = 7.5 Hz), 2.22 (dd, 1H, J = 14.3, 7.5 Hz), 1.93 (dd, 1H, J = 14.0, 2.5 Hz), 1.11 (s, 3H), 0.99 (t, 3H, J = 7.5 Hz), 0.9 (s, 9H), 0.06 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 211.2, 151.3, 128.3, 74.6, 59.8, 51.2, 48.8, 45.9, 37.3, 28.3, 25.8, 18.3, 7.4, −5.5, −5.6. FTIR (thin film): 3412, 2954, 2929, 2856, 1716, 1462, 1356, 1254, 1193, 1111, 1062, 1005, 837, 772 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calculated for $C_{17}H_{32}O_3SiNa$ 335.2018, found 335.2009.

(±)-(1*R*,2*S*,4*S*,5*R*)-1-([(1,1-Dimethylethyl)dimethylsilyloxy]-methyl)-4-hydroxy-2-methylbicyclo[3.1.0]hexan-2-yl)butan-2-one (34). To a cooled solution of the ethyl ketone **33** (1.22 g, 3.9 mmol, 1 equiv) in 24 mL of dichloromethane at 0 °C was added dropwise a 1.0 M solution of diethyl zinc (7.8 mL, 7.8 mmol, 2 equiv). The solution was stirred at 0 °C for 30 min. Diiodomethane was added dropwise, and the reaction was heated at 40 °C for 30 min. The reaction was removed from heat and quenched with a saturated solution of NH_4Cl. The aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 10:1) to afford 1.07 g of the cyclopropane **34** (3.3 mmol, 88%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 4.51−4.57 (m, 1H), 4.02 (dd, 1H, J = 10.8, 1.5 Hz), 3.18 (d, 1H, J = 11.0 Hz), 2.81 (d, 1H, J = 16.0 Hz), 2.51 (d, 1H, J = 16.0 Hz), 2.47 (dq, 1H, J = 18.0, 7.5 Hz), 2.36 (dq, 1H, J = 18.0, 7.5 Hz), 2.03 (dd, 1H, J = 13.5, 7.5 Hz), 1.38 (ddd, 1H, J = 4.0, 4.0, 4.0 Hz), 1.31 (brs, 1H), 1.19 (dd, 1H, J = 13.5, 9.0 Hz), 1.16 (s, 3H), 1.01 (t, 3H, J = 7.5 Hz), 0.90 (s, 9H), 0.81 (t, 1H, J = 4.5 Hz), 0.53 (dd, 1H, J = 7.8, 5.0 Hz), 0.03 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 211.5, 71.9, 64.3, 51.1, 43.3, 41.7, 37.64, 37.59, 26.6, 25.8, 23.9, 18.1, 9.8, 7.6, −5.5, −5.6. FTIR (thin film): 3387, 2954, 2925, 2884, 2856, 1716, 1463, 1356, 1258, 1074, 829 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calculated for $C_{18}H_{34}O_3SiNa$ 349.2175, found 349.2174.

(±)-(1*R*,2*S*,4*S*,5*R*)-5-([(1,1-Dimethylethyl)dimethylsilyloxy]-methyl)-4-methyl-4-(2-oxobutyl)bicyclo[3.1.0]hexan-2-yl Acetate (35). Acetic anhydride (1.9 mL, 20 mmol, 6 equiv) was added to a solution of the cyclopropane alcohol **34** (1.07 g, 3.3 mmol, 1 equiv) and pyridine (2.6 mL, 33 mmol, 10 equiv). The reaction was stirred at 23 °C for 1 h and quenched with water. The aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel provided 1.14 g of the acetate **35** (3.1 mmol, 95%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.31 (ddd, 1H, J = 8.5, 8.5, 4.5 Hz), 4.04 (dd, 1H, J = 10.5, 1.5 Hz), 3.17 (d, 1H, J = 10.5 Hz), 2.82 (d, 1H, J = 15.5 Hz), 2.51 (d, 1H, J = 15.5 Hz), 2.49 (dq, 1H, J = 17.5, 7.0 Hz), 2.36 (dq, 1H, J = 17.5, 7.0 Hz), 2.08 (dd, 1H, J = 13.5, 8.0 Hz), 2.01 (s, 3H), 1.51 (ddd, 1H, J = 4.0, 4.0, 4.0 Hz), 1.34 (dd, 1H, J = 13.5, 9.0 Hz), 1.19 (s, 3H), 1.01 (t, 1H, J = 7.5 Hz), 0.90 (s, 9H), 0.81 (brt, 1H, J = 4.0 Hz), 0.59 (dd, 1H, J = 7.5, 5.5 Hz), 0.03 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 211.3, 171.2, 74.9, 64.2, 51.0, 41.2, 39.5, 37.6, 25.8, 24.0, 23.7, 21.2, 18.1, 10.8, 7.6, −5.6 (one high-field carbon not observed). FTIR (thin film): 2953, 2929, 2888, 2856, 1732, 1462, 1360, 1250, 1074, 1029 cm^{-1}. HRMS-ESI (m/z): [M + Na]$^+$ calculated for $C_{20}H_{36}O_4SiNa$ 391.2281, found 391.2281.

(±)-(1*R*,2*S*,4*S*,5*R*)-5-(Hydroxymethyl)-4-methyl-4-(2-oxobutyl)-bicyclo[3.1.0]hexan-2-yl Acetate (36). To a solution of the acetate **35** (1.14 g, 3.1 mmol, 1 equiv) in 31 mL of THF was added dropwise a 1.0 M solution of tetrabutylammonium fluoride (6.2 mL, 6.2 mmol, 2 equiv) in THF. The reaction was stirred at 23 °C for 15 min. The volatiles were evaporated *in vacuo*, and the residue was purified by flash column chromatography on silica gel

(hexanes−ethyl acetate, 3:1) to produce 0.77 g of the alcohol **36** (3.0 mmol, 97%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.30 (ddd, 1H, J = 8.3, 8.3, 4.5 Hz), 4.13 (dd, 1H, J = 11.5, 5.0 Hz), 3.13 (dd, 1H, J = 11.5, 4.5 Hz), 2.78 (d, 1H, J = 15.5 Hz), 2.55 (d, 1H, J = 16.0 Hz), 2.45 (q, 2H, J = 7.5 Hz), 2.15−2.17 (bt, 1H, J = 5.5 Hz), 2.04 (dd, 1H, J = 8.0, 4.0 Hz), 2.02 (s, 3H), 1.58 (dd, 1H, J = 4.0, 4.0 Hz), 1.31 (dd, 1H, J = 13.5, 9.0 Hz), 1.24 (s, 3H), 1.03 (t, 3H, J = 7.5 Hz), 0.86 (brt, 1H, J = 4.0 Hz), 0.65 (dd, 1H, J = 8.0, 5.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 212.0, 171.2, 74.3, 64.4, 50.8, 41.1, 40.1, 38.1, 37.9, 25.1, 24.4, 21.1, 10.9, 7.6. FTIR (thin film): 3444, 2977, 2939, 2877, 1734, 1711, 1456, 1372, 1244, 1032 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{14}H_{22}O_4Na$ 277.1416, found 277.1422.

(±)-(1*S*,4*S*)-3-([(1,1-Dimethylethyl)dimethylsilyloxy]methyl)-4-methyl-4-(2-oxobutyl)cyclopent-2-en-1-yl Acetate (37). To the ethyl ketone **33** (200 mg, 0.64 mmol, 1 equiv) was added pyridine (2.6 mL, 3.2 mmol, 5 equiv) followed by acetic anhydride (0.19 mL, 2.0 mmol, 3 equiv). After stirring at 23 °C for 2 h, the reaction was quenched with water. The aqueous layer was extracted with ethyl acetate (3 × 2 mL). The combined organic extracts were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 10:1) afforded 221 mg of the acetate **37** (0.62 mmol, 97%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.67−5.69 (m, 1H), 5.58−5.60 (m, 1H), 4.19−4.26 (m, 2H), 2.69 (d, 1H, J = 16.0 Hz), 2.55 (d, 1H, J = 16.0 Hz), 2.34−2.43 (m, 2H), 2.25 (dd, 1H, J = 14.0, 7.5 Hz), 2.06 (dd, 1H, J = 14.0, 3.5 Hz), 2.01 (s, 3H), 1.18 (s, 3H), 1.02 (t, 3H, J = 7.5 Hz), 0.91 (s, 9H), 0.07 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 209.9, 170.8, 156.5, 123.0, 77.5, 59.7, 51.3, 46.3, 44.9, 37.5, 25.8, 25.5, 21.2, 18.2, 7.5, −5.5, −5.6. FTIR (thin film): 2955, 2927, 2856, 1736, 1461, 1378, 1247, 1116, 1060, 1012 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{19}H_{34}O_4SiNa$ 377.2124, found 377.2121.

(±)-(1*S*,4*S*)-3-(Hydroxymethyl)-4-methyl-4-(2-oxobutyl)cyclopent-2-en-1-yl Acetate (38). To a solution of the acetate **37** (162 mg, 0.46 mmol, 1 equiv) in 4 mL of THF was added dropwise a 1.0 M solution of tetrabutylammonium fluoride (0.92 mL, 0.92 mmol, 2 equiv) in THF. After stirring for 10 min, the volatiles were evaporate *in vacuo* and the residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 3:1) to afford 100 mg of the alcohol **38** (0.42 mmol, 91%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.71 (brs, 1H), 5.57−5.59 (m, 1H), 4.27 (d, 1H, J = 14.0 Hz), 4.19 (d, 1H, J = 14.5 Hz), 2.72 (d, 1H, J = 15.5 Hz), 2.64 (d, 1H, J = 15.0 Hz), 2.46 (q, 2H, J = 7.5 Hz), 2.28 (dd, 1H, J = 14.5, 7.5 Hz), 2.01 (s, 3H), 1.97 (dd, 1H, J = 14.3, 3.5 Hz), 1.20 (s, 3H), 1.03 (t, 3H, J = 7.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 211.2, 170.8, 155.9, 124.6, 59.2, 51.3, 46.7, 44.9, 38.1, 26.6, 21.2, 7.4, 7.3. FTIR (thin film): 3440, 2972, 2936, 2872, 1711, 1457, 1373, 1244, 1107, 1087, 1022, 978 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{13}H_{20}O_4Na$ 263.1259, found 263.1259.

(±)-(1*S*,4*S*)-3-Formyl-4-methyl-4-(2-oxobutyl)cyclopent-2-en-1-yl Acetate (39). To a solution of the alcohol **38** (100 mg, 0.42 mmol, 1 equiv) in 2.6 mL of dichloromethane was added sodium bicarbonate (140 mg, 1.7 mmol, 4 equiv) followed by Dess-Martin periodinane (353 mg, 0.83 mmol, 2 equiv). After stirring for 5 min, the mixture was filtered through a plug of silica gel. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 4:1) yielded 85 mg of the aldehyde **39** (0.36 mmol, 86%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.77 (s, 1H), 6.67 (s, 1H), 5.80−5.84 (m, 1H), 2.92 (d, 1H, J = 17.5 Hz), 2.88 (d, 1H, J = 17.5 Hz), 2.34−2.39 (m, 3H), 2.15 (dd, 1H, J = 13.5, 6.5 Hz), 2.07 (s, 3H), 1.24 (s, 3H), 1.00 (t, 3H, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 209.8, 190.0, 170.6, 153.9, 147.1, 76.7, 49.3, 44.8, 44.7, 36.9, 26.0, 21.0, 7.4. FTIR (thin film): 2974, 2933, 1740, 1716, 1683, 1458, 1368, 1238, 1115, 1091, 1029 cm^{-1}. HRMS-ESI (m/z): $[M+Na]^+$ calculated for $C_{13}H_{18}O_4Na$ 261.1103, found 261.1107.

(±)-(2*S*,7a*S*)-2-Hydroxy-5,7a-dimethyl-7,7a-dihydro-1*H*-inden-6(2*H*)-one (40). A solution of 5% ethanolic potassium hydroxide (0.09 mL, 0.080 mmol, 1.1 equiv) was added to the aldehyde **39** (18 mg, 0.076 mmol, 1 equiv). After stirring for 5 min, the reaction was quenched by adding a few drops of 1 N HCl. The aqueous layer was extracted with diethyl ether (3 × 0.5 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 3:1) to afford 12.5 mg of the enone **40** (0.070 mmol, 93%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.95 (s, 1H), 5.79 (s, 1H), 5.09 (brt, 1H, J = 6.5 Hz), 2.58 (d, 1H, J = 15.5 Hz), 2.55 (d, 1H, 15.5 Hz), 2.39 (dd, 1H, J = 12.5, 6.5 Hz), 1.87 (s, 3H), 1.61 (dd, 1H, J = 12.3, 8.0 Hz), 1.12 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 199.5, 146.8, 136.0, 134.7, 131.1, 76.3, 52.1, 50.4, 47.3, 25.8, 15.9. FTIR (thin film): 3399, 2950, 2917, 2864, 1671, 1450, 1221, 1050 cm^{-1}. HRMS-CI (m/z): $[M + H]^+$ calculated for $C_{11}H_{14}O_2H$ 179.1072, found 179.1079.

(±)-(2*S*,7a*S*)-5,7a-Dimethyl-6-oxo-2,6,7,7a-tetrahydro-1*H*-inden-2-yl Acetate (41). To the enone **40** (30 mg, 0.17 mmol, 1 equiv) was added pyridine (0.14 mL, 1.7 mmol, 10 equiv) followed by acetic anhydride (0.1 mL, 1.0 mmol, 6 equiv). The mixture was stirred at 23 °C for 1 h and was subsequently quenched with water. The aqueous layer was extracted with diethyl ether (3 × 0.1 mL). The organic layers were combined, washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 10:1) provided 25 mg of the dienophile **41** (0.11 mmol, 65%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.96 (s, 1H), 5.87 (brt, 1H, J = 7.5 Hz), 5.76 (s, 1H), 2.61 (d, 1H, J = 15.5 Hz), 2.55 (d, 1H, J = 16.0 Hz), 2.42 (dd, 1H, J = 12.8, 7.0 Hz), 2.07 (s, 3H), 1.87 (s, 3H), 1.76 (dd, 1H, J = 12.8, 7.5 Hz), 1.15 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 199.1, 170.8, 148.2, 136.4, 134.2, 126.5, 79.2, 51.9, 47.1, 46.3, 26.1, 21.1, 16.0. FTIR (thin film): 2958, 1736.2, 1679, 1442, 1377, 1352, 1234, 1021 cm^{-1}.

4,4,6b,9-Tetramethyl-1,4,6,6a,6b,7,11a,11b-octahydrospiro-[benzo[*a*]fluorene-3,2′-[1,3]dioxolan]-8(2*H*)-one (42). To a microwave vial containing a solution of the dienophile **41** (2.3 mg, 0.01 mmol, 1 equiv) in 0.5 mL of dichloromethane was added the diene **4** (4.0 mg, 0.02 mmol, 2 equiv). The reaction was subjected to 300 W microwave irradiation at 160 °C for 15 min. The volatiles were evaporated *in vacuo*, and the residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 20:1) to afford 2.4 mg of the cycloadduct **42** (0.007 mmol, 65%) as a white solid. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.86 (s, 1H), 5.92 (s, 1H), 5.57 (brd, 1H, J = 6.5 Hz), 3.91−4.00 (m, 4H), 3.42 (m, 1H), 2.75 (d, 1H, J = 15.5 Hz), 2.72 (m, 1H), 2.23 (d, 1H, J = 15.5 Hz), 2.01−2.08 (m, 1H), 1.84 (s, 3H), 1.78−1.95 (m, 3H), 1.71−1.75 (m, 1H), 1.51−1.55 (m, 1H), 1.25−1.27 (m, 1H), 1.16 (s, 3H), 1.11 (s, 3H), 1.04 (s, 3H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 200.8, 144.4, 142.8, 136.0, 133.5, 131.3, 117.5, 112.8, 65.2, 65.1, 49.0, 46.4, 45.4, 45.0, 44.8, 32.6, 30.6, 29.2, 25.7, 23.7, 21.1, 19.7, 16.0. FTIR (thin film): 2950, 2921, 2876, 1659, 1146, 1377, 1149, 1091, 1062 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{23}H_{30}O_3Na$ 377.2093, found 377.2100.

(±)-(1*S*,4*S*)-2-([(1,1-Dimethylethyl)dimethylsilyloxy]methyl))-4-hydroxy-1-methylcyclopent-2-en-1-yl)propan-2-one (43). To a cooled solution of the Weinreb amide **32** (649 mg, 1.9 mmol, 1 equiv) in 18 mL of THF at 0 °C was added a 3.0 M solution of methylmagnesium bromide (1.57 mL, 4.7 mmol, 2.5 equiv) in THF. The reaction was warmed to 23 °C and stirred for 1 h. A saturated solution of NH_4Cl was added to quench the reaction. The aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 3:1) to provide 470 mg of the methyl ketone **43** (1.6 mmol, 84%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz)

δ: 5.71 (s, 1H), 4.65−4.71 (m, 1H), 4.19 (d, 1H, J = 14.0 Hz), 4.14 (d, 1H, J = 14.5 Hz), 3.03 (d, 1H, J = 9.5 Hz), 2.84 (d, 1H, J = 17.5 Hz), 2.59 (d, 1H, J = 18.0 Hz), 2.23 (dd, 1H, J = 14.3, 8.0 Hz), 2.10 (s, 3H), 1.94 (dd, 1H, J = 14.0, 2.5 Hz), 1.12 (s, 3H), 0.91 (s, 9H), 0.07 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 208.6, 151.3, 128.4, 74.6, 59.8, 52.4, 48.7, 45.8, 31.5, 28.1, 25.8, 18.3, −5.5. FTIR (thin film): 3407, 2958, 2925, 2852, 1712, 1471, 1360, 1250, 1111, 1066 cm^{-1}. HRMS-ESI (m/z): $[M+Na]^+$ calculated for $C_{16}H_{30}O_3SiNa$ 321.1862, found 321.1858.

(±)-(1*R*,2*S*,4*S*,5*R*)-1-([(1,1-Dimethylethyl)dimethylsilyloxy]-methyl)-4-hydroxy-2-methylbicyclo[3.1.0]hexan-2-yl)propan-2-one (44). To a cooled solution of the methyl ketone **43** (2.5 g, 8.3 mmol, 1 equiv) in 46 mL of dichloromethane at 0 °C was added dropwise a 1.0 M solution of diethylzinc (16.8 mL, 16.8 mmol, 2 equiv). After stirring for 30 min, diiodomethane (1.2 mL, 14.2 mmol, 1.7 equiv) was added and the reaction was heated at 40 °C for 1 h. The mixture was cooled to ambient temperature and quenched with a cold saturated solution of NH_4Cl. The aqueous layer was extracted with dichloromethane (3 × 30 mL). The combined organic extracts were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 3:1) to provide 2.02 g of the cyclopropane **44** (6.5 mmol, 77%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 4.54 (brdd, 1H, J = 12.5, 8.0 Hz), 4.01 (d, 1H, J = 11.0 Hz), 3.18 (d, 1H, J = 11.0 Hz), 2.83 (d, 1H, J = 16.0 Hz), 2.54 (d, 1H, J = 16.0 Hz), 2.12 (s, 3H), 2.02 (dd, 1H, J = 13.8, 7.5 Hz), 1.37−1.40 (m, 1H), 1.17 (s, 3H), 1.15−1.19 (m, 1H), 0.90 (s, 9H), 0.81−0.83 (m, 1H), 0.53 (dd, 1H, J = 7.5, 5.5 Hz), 0.03 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 208.9, 71.9, 64.2, 52.4, 43.2, 41.6, 37.7, 31.8, 26.6, 25.8, 23.8, 18.1, 9.9, −5.5, −5.6. FTIR (thin film): 3383, 2954, 2933, 2856, 1720, 1475, 1356, 1254, 1070, 841 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{17}H_{32}O_3SiNa$ 335.2018, found 335.2026.

(±)-(1*R*,2*S*,4*S*,5*R*)-5-([(1,1-Dimethylethyl)dimethylsilyloxy]-methyl)-4-methyl-4-(2-oxopropyl)bicyclo[3.1.0]hexan-2-yl Acetate (45). Acetic anhydride (3.7 mL, 39 mmol, 6 equiv) was added to a mixture of the cyclopropane **44** (2.02 g, 6.4 mmol, 1 equiv) and pyridine (5.2 mL, 64 mmol, 10 equiv). After stirring at 23 °C for 4 h, the reaction was quenched with water. The aqueous layer was extracted with diethyl ether (3 × 10 mL). The organic layers were combined and washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography on silica gel (hexanes−ethyl acetate, 10:1) furnished 2.14 g of the acetate **45** (6.0 mmol, 93%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.31 (ddd, 1H, J = 8.5, 8.5, 4.5 Hz), 4.04 (d, 1H, J = 11.0 Hz), 3.17 (d, 1H, J = 11.0 Hz), 2.85 (d, 1H, J = 16.0 Hz), 2.54 (d, 1H, J = 16.0 Hz), 2.13 (s, 1H), 2.09 (dd, 1H, J = 13.8, 8.0 Hz), 2.01 (s, 3H), 1.51 (ddd, 1H, J = 4.0, 4.0, 4.0 Hz), 1.32 (dd, 1H, J = 13.5, 9.0 Hz), 0.89 (s, 9H), 0.82 (brdd, 1H, J = 4.5, 4.5 Hz), 0.59 (dd, 1H, J = 8.0, 5.5 Hz), 0.03 (s, 6H). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 208.7, 171.2, 74.9, 64.1, 52.3, 41.1, 39.4, 37.6, 31.8, 25.8, 23.9, 23.7, 21.1, 18.1, 10.9, −5.6. FTIR (thin film): 2955, 2927, 2852, 1732, 1469, 1358, 1251, 1080, 1032 cm^{-1}. HRMS-ESI (m/z): $[M + Na]^+$ calculated for $C_{19}H_{34}O_4SiNa$ 377.2124, found 377.2121.

(±)-(1*R*,2*S*,4*S*,5*R*)-5-(Hydroxymethyl)-4-methyl-4-(2-oxopropyl)-bicyclo[3.1.0]hexan-2-yl Acetate (46). To a solution of the acetoxy silyl ether **45** (2.14 g, 6.0 mmol, 1 equiv) in 54 mL of THF was added dropwise a 1.0 M solution of tetrabutylammonium fluoride (12.0 mmol, 12.0 mmol, 2 equiv) in THF. After stirring for 15 min, the volatiles were removed *in vacuo* and the residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 1:1) to afford 1.35 g of the alcohol **46** (5.6 mmol, 93%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 5.30 (ddd, 1H, J = 8.5, 8.5, 4.5 Hz), 4.12 (dd, 1H, J = 11.8, 5.5 Hz), 3.14 (dd, 1H, J = 11.8, 4.5 Hz), 2.83 (d, 1H, J = 16.0 Hz), 2.57 (d, 1H, J = 16.0 Hz), 2.16 (s, 3H), 2.06 (dd, 1H, J = 13.5, 8.0 Hz), 2.02 (s, 3H), 1.99 (dd, 1H, J = 5.5, 5.5 Hz), 1.57−1.60 (m, 1H), 1.30 (dd, 1H, J = 13.5, 9.0 Hz), 0.87−0.89 (m, 1H), 0.65 (dd, 1H, J = 7.8, 5.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 209.2, 171.1, 74.3, 64.5, 52.1, 41.0, 39.9, 38.1, 32.1, 25.0, 24.3, 21.1, 10.9. FTIR (thin film): 3431, 2959, 2927, 2880, 1732, 1362, 1247, 1024 cm^{-1}. HRMS-ESI (m/z): $[M+Na]^+$ calculated for $C_{13}H_{20}O_4Na$ 263.1259, found 263.1256.

(±)-(1*R*,2*S*,4*S*,5*R*)-5-Formyl-4-methyl-4-(2-oxopropyl)bicyclo-[3.1.0]hexan-2-yl Acetate (47). To a solution of the alcohol **46** (1.35 g, 5.6 mmol, 1 equiv) in 35 mL of dichloromethane was added sodium bicarbonate (1.89 g, 22.5 mmol, 4 equiv) followed by Dess-Martin periodinane (3.58 g, 8.4 mmol, 1.5 equiv). The reaction was stirred at 23 °C for 15 min and then filtered through a plug of silica gel. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 4:1) provided 1.10 g of the aldehyde **47** (4.6 mmol, 82%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.05 (s, 1H), 5.33 (ddd, 1H, J = 8.5, 8.5, 4.7 Hz), 2.88 (d, 1H, J = 16.5 Hz), 2.53 (d, 1H, J = 16.5 Hz), 2.34 (ddd, 1H, J = 8.5, 4.5, 4.5 Hz), 2.14 (s, 3H), 2.11−2.16 (m, 1H), 2.04 (s, 3H), 1.39 (s, 3H), 1.34−1.37 (m, 2H), 1.27 (dd, 1H, J = 8.0, 6.0 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 207.4, 197.9, 170.9, 72.8, 50.8, 46.6, 39.6, 39.3, 31.6, 28.8, 23.5, 21.0, 12.7. FTIR (thin film): 2967, 2880, 1732, 1704, 1434, 1358, 1239, 1167, 1032 cm^{-1}. HRMS-ESI (m/z): $[M+Na]^+$ calculated for $C_{13}H_{18}O_4Na$ 261.1103, found 261.1099.

(±)-(1*R*,2*S*,3a*S*,7a*R*)-3a-Methyl-5-oxo-1a,2,3,3a,4,5-hexahydro-1*H*-cyclopropa[*c*]inden-2-yl Acetate (48). To a solution of the aldehyde **47** (1.10 g, 4.6 mmol, 1 equiv) in 90 mL of toluene was added *p*-toluenesulfonic acid (44 mg, 0.23 mmol, 0.05 equiv). The flask was equipped with a Dean−Stark trap and a reflux condenser, and the reaction was refluxed for 4 h. The solution was cooled and quenched with a saturated solution of $NaHCO_3$. The aqueous layer was extracted with ethyl acetate (3 × 50 mL). The combined organic extracts were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 3:1) to yield 786 mg of the enone **48** (3.6 mmol, 77%) as a white solid: mp 84−87 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.68 (d, 1H, J = 9.5 Hz), 5.98 (d, 1H, J = 9.5 Hz), 5.43 (ddd, 1H, J = 8.0, 8.0, 4.0 Hz), 2.53 (d, 1H, J = 16.5 Hz), 2.49 (d, 1H, J = 16.5 Hz), 2.33 (ddd, 1H, J = 4.0, 4.0, 4.0 Hz), 2.06 (s, 3H), 1.84 (dd, 1H, J = 12.8, 7.5 Hz), 1.46 (dd, 1H, J = 5.5, 3.5 Hz), 1.32 (dd, 1H, J = 12.8, 8.5 Hz), 1.16 (s, 3H), 0.61 (dd, 1H, J = 7.5, 5.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 199.5, 171.0, 150.2, 128.9, 75.0, 49.1, 40.4, 37.0, 36.6, 26.3, 24.9, 21.0, 12.1. FTIR (thin film): 2971, 1732, 1660, 1596, 1370, 1239, 1032 cm^{-1}. HRMS-CI (m/z): $[M + Na]^+$ calculated for $C_{13}H_{16}O_3H$ 221.1178, found 221.1182.

(±)-(1*R*,2*S*,3a*S*,7a*R*)-6-(Hydroxymethyl)-3a-methyl-5-oxo-1a,2,3,3a,4,5-hexahydro-1*H*-cyclopropa[*c*]inden-2-yl Acetate (49). To a solution of the enone **48** (25 mg, 0.11 mmol, 1 equiv) in 0.2 mL of THF was added tributylphosphine (0.024 mL, 0.09 mmol, 0.85 equiv) followed by a 37% aqueous solution of formaldehyde (0.024 mL, 0.29 mmol, 2.6 equiv). The reaction was stirred for 24 h, and additional tributylphosphine (0.024 mL, 0.09 mmol, 0.85 equiv) was added. After 24 h, the reaction was quenched with water and the aqueous layer was extracted with ethyl acetate (3 × 0.5 mL). The combined organic extracts were washed with brine, dried with $MgSO_4$, filtered, and concentrated *in vacuo*. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetate, 1:1) furnished 20 mg of alcohol **49** (0.08 mmol, 70%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 6.64 (s, 1H), 5.42 (ddd, 1H, J = 8.5, 8.5, 4.0 Hz), 4.27 (d, 1H, J = 13.0 Hz), 4.22 (d, 1H, J = 13.0 Hz), 2.53 (s, 2H), 2.46 (brs, 1H), 2.34 (ddd, 1H, J = 4.0, 4.0, 3.6 Hz), 2.05 (s, 3H), 1.84 (dd, 1H, J = 12.5, 7.0 Hz), 1.46 (dd, 1H, J = 5.5, 3.5 Hz), 1.32 (dd, 1H, J = 12.5, 9.0 Hz), 1.14 (s, 3H), 0.62 (dd, 1H, J = 7.5, 5.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 200.3, 171.0, 146.6, 137.5,

74.9, 61.8, 49.1, 40.4, 36.9, 36.3, 26.4, 24.9, 21.0, 12.1. FTIR (thin film): 3440, 2970, 2929, 2876, 1736, 1654, 1376, 1250, 1025 cm^{-1}. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calculated for $C_{14}H_{18}O_4Na$ 273.1103, found 273.1104.

(±)-(1*R*,2*S*,3a*S*,7a*R*)-6-Formyl-3a-methyl-5-oxo-1a,2,3,3a,4,5-hexahydro-1*H*-cyclopropa[*c*]inden-2-yl Acetate (50). Dess-Martin periodinane (508 mg, 1.2 mmol, 1.5 equiv) was added to a solution of the alcohol **49** (200 mg, 0.80 mmol, 1 equiv) in 8 mL of dichloromethane. After the reaction stirred for 5 min, the contents were filtered through a plug of silica gel. Flash column chromatography of the residue on silica gel (hexanes−ethyl acetat, 4:1) yielded 190 mg of the aldehyde **50** (0.77 mmol, 96%) as a white solid: mp 145−147 °C . ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 10.0 (s, 1H), 7.58 (s, 1H), 5.46 (ddd, 1H, J = 7.8, 7.8, 4.0 Hz), 2.56−2.63 (m, 3H), 2.07 (s, 3H), 1.92 (dd, 1H, J = 12.8, 7.5 Hz), 1.64 (dd, 1H, J = 5.3, 4.0 Hz), 1.36 (dd, 1H, J = 12.8, 9.0 Hz), 1.14 (s, 3H), 0.92 (dd, 1H, J = 8.0, 6.0 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 197.3, 188.5, 170.9, 158.3, 133.8, 74.2, 49.0, 39.6, 38.5, 36.6, 28.5, 24.9, 21.0, 15.0. FTIR (thin film): 2966, 2864, 1732, 1671, 1577, 1373, 1230, 1029 cm^{-1}. HRMS-ESI (*m*/*z*): $[M + Na]^+$ calculated for $C_{14}H_{16}O_4Na$ 271.0946, found 271.0946.

(±)-(2*S*,3*R*,3a*R*,3b*R*,9a*S*,9b*R*,11a*S*)-9b-Formyl-6,6,11a-trimethyl-10-oxo-1,2,2a,3,3b,4,6,8,9,9a,9b,10,11,11a-tetradecahydrospiro[cyclopropa[1,5]cyclopenta[1,2-*a*]phenanthrene-7,2′-[1,3]dioxolan]-2-yl Acetate (51). The diene **4** (31 mg, 0.16 mmol, 2 equiv) was added to a microwave vial containing a solution of the dienophile **50** (20 mg, 0.081 mmol, 1 equiv) in 1 mL of dichloromethane. The reaction was subjected to 250 W microwave irradiation at 100 °C for 18 h. The volatiles were evaporated in *vacuo*, and the residue was purified by flash column chromatography on silica gel (hexanes−ethyl acetate, 2:1) to afford 34 mg of the cycloadduct **51** (0.077 mmol, 95%) as a white solid: mp 164−167 °C. ^{1}H NMR ($CDCl_3$, 500 MHz) δ: 9.66 (s, 1H), 5.39−5.43 (m, 2H), 3.90−3.97 (m, 4H), 3.48 (brd, 1H, J = 12.0 Hz), 2.66 (d, 1H, J = 12.5 Hz), 2.56 (dd, 1H, J = 9.0, 9.0 Hz), 2.44−2.53 (m, 1H), 2.38 (d, 1H, J = 13.0 Hz), 2.33−2.39 (m, 1H), 2.07−2.10 (m, 1H), 2.04 (s, 3H), 1.89 (ddd, 1H, J = 13.5, 13.5, 4.5 Hz), 1.68 (brd, 1H, J = 10.5 Hz), 1.54−1.58 (m, 2H), 1.42 (dddd, 1H, J = 12.0, 12.0, 12.0, 4.0 Hz), 1.31 (s, 3H), 1.20−1.27 (m, 1H), 1.11 (s, 3H), 1.05−1.07 (m, 1H), 1.02 (s, 3H), 0.40 (dd, 1H, J = 7.8, 5.5 Hz). ^{13}C NMR ($CDCl_3$, 125 MHz) δ: 206.1, 204.3, 171.2, 142.3, 115.7, 112.4, 75.4, 66.5, 65.3, 65.1, 51.3, 46.3, 43.1, 39.4, 39.0, 35.0, 33.9, 31.5, 29.2, 26.2, 25.8, 23.9, 23.0, 21.1, 19.7, 14.1. FTIR (thin film): 2978, 2880, 1728, 1474, 1442, 1380, 1242, 1140, 1066, 1033, 915, 735 cm^{-1}. HRMS-ESI (*m*/*z*): $[M+Na]^+$ calculated for $C_{26}H_{34}O_6Na$ 465.2253, found 465.2253.

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Supporting Information Available: Proton and carbon NMR data for all compounds and X-ray crystallographic data (ORTEP and cif files) for compounds **21n**, **22n**, **26x**, **27**, and **51**. This material is available free of charge via the Internet at http://pubs.acs.org.