Regio- and stereoselective ring openings of unsymmetrical oxatricyclo adducts

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Abstract: S_N2' ring-opening reactions of a number of substituted 11-oxatricyclo[6.2.1.$0^{1,6}$]undec-9-en-5-ones prepared via the intramolecular Diels–Alder reaction employing a furan diene (IMDAF) are reported. Primary, secondary, and tertiary organolithium reagents were capable of effecting the ring-opening reaction, while methyllithium required activation before any ring opening was observed. Hydride reagents, organocuprates, and Grignard reagents were generally ineffective. The ring-opening reaction was highly regio- and stereoselective for attack at C_9 *syn* to the bridging oxygen atom provided that C_8 was not substituted. A highly stereoselective nucleophilic addition to the carbonyl group *anti* to the bridging oxygen was also observed. The high selectivity appears to be due to a combination of steric and electronic effects.

Key words: S_N2' reactions, oxatricyclo adducts, Diels–Alder reaction, ring opening.

Résumé : On a effectué des réactions d'ouverture de cycles S_N2' sur un certain nombre de 11-oxatricyclo[6.2.1.$0^{1,6}$]undéc-9-én-5-ones substituées préparées par une réaction de Diels–Alder intramoléculaire à l'aide d'une furane diène («IMDAF»). Les réactifs organolithiens primaires, secondaires et tertiaires permettent d'effectuer la réaction d'ouverture de cycle; toutefois, avec le méthyllithium, il est nécessaire de procéder à une activation avant de pouvoir observer une ouverture. Les hydrures, les organocuprates et les réactifs de Grignard sont généralement inefficaces. Lorsque le carbone en C-8 n'est pas substitué, la réaction d'ouverture de cycle est extrêmement régio- et stéréosélective par rapport aux attaques en C-9 *syn* relatives à l'atome d'oxygène format le pont. On a aussi observé une réaction d'addition extrêmement stéréosélective sur le groupe carbonyle en *anti* par rapport à l'atome d'oxygène formant le pont. La sélectivité élevée semble être due à une combinaison d'effets stériques et électroniques.

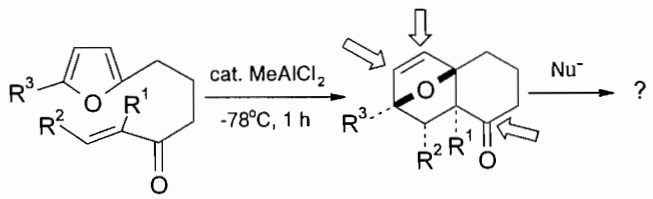
Mots clés : réactions S_N2', adduits oxatricyclo, réaction de Diels–Alder, ouverture de cycle.

[Traduit par la rédaction]

Introduction

The intramolecular Diels–Alder reaction with a furan diene (IMDAF) is capable of forming oxatricyclo adducts (Scheme 1) with a great deal of stereocontrol, producing only *exo* products with the sidearm oriented *syn* relative to the bridging oxygen atom (1). Preliminary experiments with DIBAL-H in 1986 had suggested that these cycloadducts may be amenable to ring openings; however, at that time, the methodology for preparing the cycloadducts had not been fully developed. By 1990, the oxatricyclo adducts were readily accessible using methodology developed in our laboratory (1), and the S_N2' ring-opening studies were initiated. At that time, ring openings on oxatricyclo adducts had not been attempted (2). In addition, when these studies were first started in 1990, little was known about the factors affecting the regioselectivity of the S_N2' ring openings of unsymmetrical oxabicyclo systems, as only the group of Arjona and Plumet (3) had observed a large degree of regioselectivity at that time. Lautens et al. had also reported a regioselective opening of some oxabicyclo adducts but the regioselectivity was reported to be marginal (60:40) (4). More recently, however, many groups have reported on several advances in the S_N2' ring-opening reactions of oxa-*n*-cyclic compounds and a review on this topic has recently been published (2).

Scheme 1.



A number of questions about the reactivity of the IMDAF cycloadducts with regard to the S_N2' ring-opening reactions therefore remained unanswered in 1990. These questions included:

1. What conditions were required to effect an S_N2' ring opening of the IMDAF cycloadducts?
2. What was the chemoselectivity with respect to nucleophilic addition to the ketone carbonyl group versus the S_N2' ring opening (arrows in Scheme 1)?
3. What degree of regioselectivity would be observed in the ring opening-reactions of the unsymmetrical IMDAF cycloadducts?

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This paper is dedicated to Professor William A. Ayer on the occasion of his 65th birthday.

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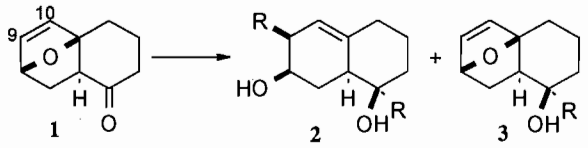
Table 1. Reaction of **1** with various organometallic reagents.



R	Reagent/conditions	Product	% Yield
1 *n*-Bu	3 eq. *n*-BuLi, Et_2O, −78°C → r.t., 16 h	**2***a*	66
2 i-Pr	3 eq. i-PrLi, Et_2O, −78°C → r.t., 16 h	**2***b*	68
3 *t*-Bu	3 eq. *t*-BuLi, Et_2O, −78°C → 0°C, 2 h	**2***c*	90
4 Vinyl	3 eq. vinyl MgBr, Et_2O, −78°C → r.t., 20 h	**3***d*	73
5 Me	2 eq. $Me_2CuLi{\cdot}LiCN$, THF, 0°C → r.t., 25 h	**3***e*	95
6 Me	2 eq. $Me_2CuLi{\cdot}LiI$, THF, 0°C → r.t., 19 h	**3***e*	100
7 Ph	3 eq. PhLi, Et_2O, −78°C → r.t., 18 h	**3***f*	87
8 Me	2 eq. MeLi, Et_2O, −78°C → r.t., 22 h	**3***e*	64
9 Me	8 eq. MeLi, Et_2O, reflux, 22 h	**2***e*:**3***e*	27:59
10 Me	3 eq. MeLi, 1:1 TMEDA:Et_2O, 0°C → r.t., 48 h	**2***e*:**3***e*	30:33[a]
11 Me	40 eq. MeLi, DME, −20°C → r.t., 22 h	**2***e*	73
12 H	1.5 eq. LiAl(*t*-Bu)(i-Bu)$_2$H, THF, 0°C, 1 h	**3***g*	83

[a]Other unidentified side-products produced as well.

4. What degree of stereoselectivity would be observed with both the nucleophilic addition to the carbonyl group and the ring opening, and from which face would nucleophilic attack predominantly occur?
5. What effect would the presence of other substituents on the IMDAF cycloadducts have on these variables, if any?

With these questions answered, an assessment of the applicability of an IMDAF ring-opening reaction sequence for the synthesis of natural products would be possible. As a result, a study of the scope and limitations of the S_N2' ring-opening reactions of the IMDAF cycloadducts was undertaken and our initial results communicated (5, 1*c*). Recently, an application illustrating the usefulness of the IMDAF ring-opening sequence towards the C_{15}–C_{23} fragment of venturicidin A was described (6). In this paper, a full account of the S_N2' ring openings of the IMDAF oxatricyclo adducts is reported.

Results

Oxatricyclo adducts **1**, **14**, **29**, and **35** with methyl substituents at various positions were prepared as previously described (1*d*, 1*e*) and subjected to a number of reaction conditions to investigate the scope and limitations of the ring-opening reaction.

The simplest of these systems, **1**, was chosen for initial study to determine the conditions required for the S_N2' ring openings. Compound **1** was treated with a variety of organometallic reagents, and the results are summarized in Table 1. Primary (*n*-butyllithium), secondary (isopropyllithium (7)), and tertiary (*tert*-butyllithium) organolithium reagents were capable of effecting a highly regio- and stereoselective ring opening of **1** and a highly stereoselective nucleophilic addition to the ketone carbonyl group, so that only one diastereomer **2** was produced in good to excellent yields (Table 1, entries 1–3). *sec*-Butyllithium reacted similarly, but a mixture of diastereomers was formed due to the presence of an additional stereogenic centre in the nucleophile.

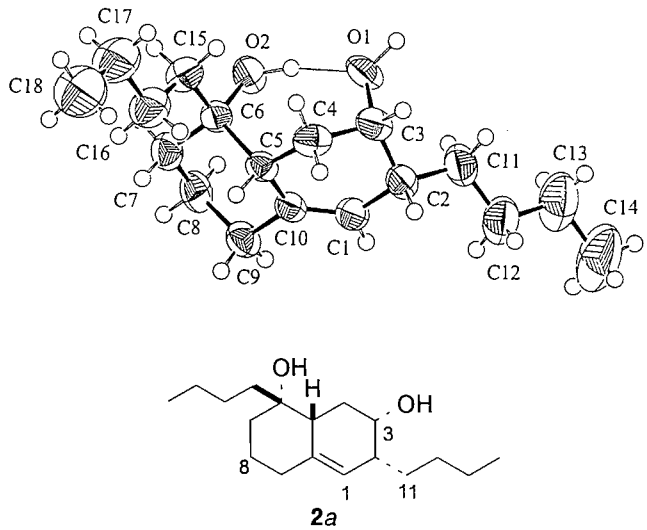
The direction of regioselectivity was evident from the integration of the ^{1}H NMR spectrum, since the broadened signal at 5.3–5.5 ppm, assigned to the alkene proton of **2**, integrated to one proton instead of the two alkene protons required for the regioisomer. The stereochemistry of the resulting products was not easily determined by ^{1}H NMR, so a suitable crystal of **2***a*, produced by recrystallization from hexane, was subjected to X-ray crystallographic analysis.[2] The ORTEP plot (Fig. 1) clearly shows that *n*-butyllithium attacked the ketone carbonyl from the α-face, and had effected a ring-opening reaction by attacking C_9 from the β-face.[3]

The crystal structure of **2***a* also aided in the explanation of the appearance of the alkene proton as a broadened signal in the ^{1}H NMR spectrum rather than a doublet with additional coupling. The solution structure should also show the intramolecular hydrogen bonding in an aprotic solvent such as deuteriochloroform, and should therefore resemble the crystal structure. Examination of molecular models shows that, in this conformation, the dihedral angle between H_7 and H_8 is close to

[2] Details of the X-ray crystal analysis, including tables of atomic coordinates, bond lengths and angles, anisotropic displacement parameters, torsion angles, and nonbonded contacts, have been deposited as supplementary material and can be purchased from: The Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, Canada K1A 0S2. Except for the tables of anisotropic displacement parameters, torsion angles, and nonbonded contacts, this material has also been deposited with the Cambridge Crystallographic Data Centre, and can be obtained on request from The Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, 12 Union Road, Cambridge, CB2 1EZ, U.K.

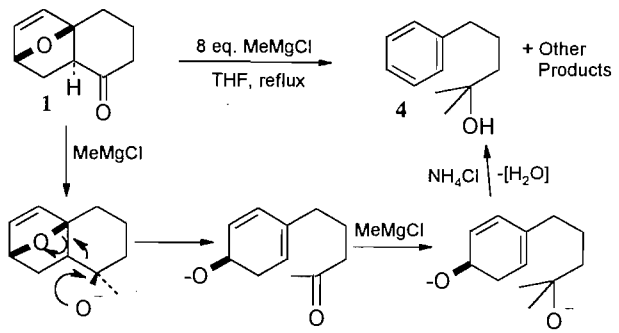
[3] The numbering of atoms in the compounds will reflect the numbering required to name the compound by IUPAC rules. As a result, the number of a particular atom may be different in the reactants versus the products.

Fig. 1. X-ray crystal structure of compound **2***a*.



2*a*

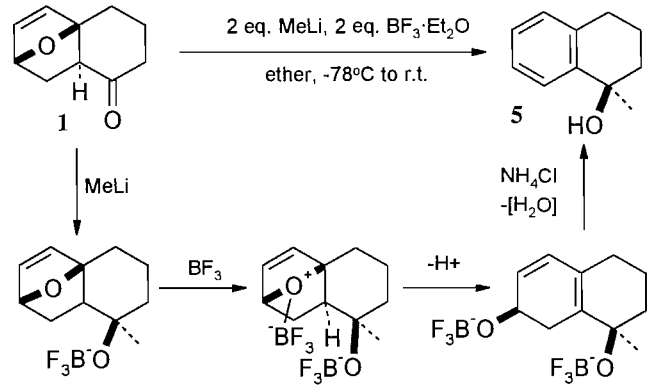
Scheme 2.



90° so that the vicinal coupling between these protons should be small. When this small coupling is combined with the several small allylic couplings between H_8 and the protons on C_1 and C_5, the net result is expected to be a broadened signal. Since the ^{1}H NMR signals for the alkene protons of **2***b* and **2***c* were similar to that of **2***a* in appearance, the same analysis holds and the stereochemistry of all three products should be the same.

Other less reactive organometallic reagents did not cause any ring opening, but did react stereoselectivity with the ketone carbonyl group to generate **3**, indicating that nucleophilic addition to the ketone carbonyl was more facile than the ring opening. Reagents in this category included Grignard reagents, organocuprate reagents ($Me_2CuLi{\cdot}LiCN$ (8) and $Me_2CuLi{\cdot}LiI$ (9)), and the less reactive organolithium reagents phenyllithium and methyllithium (Table 1, entries 4–8). Although some ring opening was observed with methyllithium when the reaction was carried out in refluxing diethyl ether (Table 1, entry 9), the reaction was slow. Increasing the reaction temperature further was not an option, since the reaction of **1** with methylmagnesium chloride in refluxing THF had produced some of the fragmentation product **4** (Scheme 2). This product likely resulted from a Grob-type fragmentation (10) of the intermediate alkoxide. Addition of a second equivalent of methylmagnesium chloride to the resulting alkoxyketone, followed by aromatization by dehydration on work-up, would generate **4**. The inability to easily cause an S_N2' ring opening with methyllithium was disappointing so methods for assisting the ring opening or enhancing the reactivity of the methyllithium were therefore investigated.

Scheme 3.



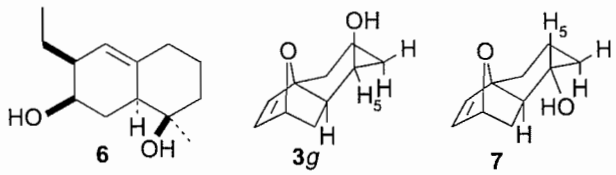
The use of lithium salts for increasing the rate of nucleophilic addition of methyllithium to ketones has been reported (11). This effect has been attributed to the complexation of the lithium salt with the ketone carbonyl group, allowing the lithium salt to act as a Lewis acid catalyst. A similar assistance in the S_N2' ring openings could result from the complexation of a lithium salt to the bridging oxygen atom. The addition of excess lithium iodide or lithium perchlorate to a mixture of **1** and methyllithium, however, produced less than 10% of the ring-opened product based on integration of the ^{1}H NMR spectrum of the crude reaction mixture. Boron trifluoride etherate has also been employed in the reaction of organolithium reagents with epoxides and oxetanes (12). Only **3***e* was produced when **1** was treated with methyllithium and boron trifluoride etherate at −78°C. Slowly increasing the reaction temperature to 25°C produced **5** (Scheme 3). This product presumably arose from cleavage of the oxygen bridge via a Lewis acid assisted β-elimination followed by aromatization on work-up. The addition of the methyl moiety to the carbonyl group could either precede, as drawn, or succeed the elimination step.

Since the attempts to facilitate the ring opening were unsuccessful, altering the reactivity of the methyllithium was tried next. Electron-donating solvents or additives such as HMPA and TMEDA have been reported to increase the nucleophilicity of organolithium reagents (13). This higher reactivity has traditionally been attributed to the formation of more reactive lower aggregates of the organolithium in the presence of electron donors, but this explanation was questioned recently by Collum (14). He argued that the lability of the organolithium–ligand complex may be more important, or that the stabilization of transition states by the additive may be the source of increased reactivity. Regardless of the reason for the effect, the increase in reactivity could allow for the S_N2' ring opening of **1** to be accomplished at room temperature. Although the addition of HMPA to the reaction mixture still resulted in the production of only **3***e*, a substantial amount of **2***e* was observed in addition to **3***e* (Table 1, entry 10) when TMEDA was employed as a cosolvent with diethyl ether. The ^{1}H NMR

spectrum of the crude reaction mixture, however, showed the presence of a significant amount of unidentified side products as well.

DME has been reported to be a slightly weaker activator than TMEDA (see ref. 13, p. 7). The use of DME as the electron-donating reaction solvent provided the best results since **2***e* was formed in good yield and fewer side products were observed (Table 1, entry 11). Unfortunately, since organolithium reagents react with DME (15) at the higher reaction temperatures required for the ring-opening reaction, a large excess of methyllithium was required to ensure enough reagent was present to drive the reaction to completion. The use of less methyllithium resulted in the production of a mixture of **2***e* and **3***e*. DME that was freshly distilled from benzophenone ketyl was essential for the success of the reaction, since the use of Aldrich Sure-Seal® DME gave only **3***e*. The only observed side product was tentatively identified as **6**. This structural assignment was based on the ^{13}C NMR spectrum, which was very similar to the ^{13}C NMR spectrum **2***e* but contained an additional signal at 24.3 ppm resulting from a methylene carbon based on DEPT experiments. A similar product resulting from the reaction of methyllithium with another oxatricyclo adduct in DME has also been characterized by X-ray crystallography. This X-ray crystal structure and a possible mechanism for the formation of these side products will be discussed later.

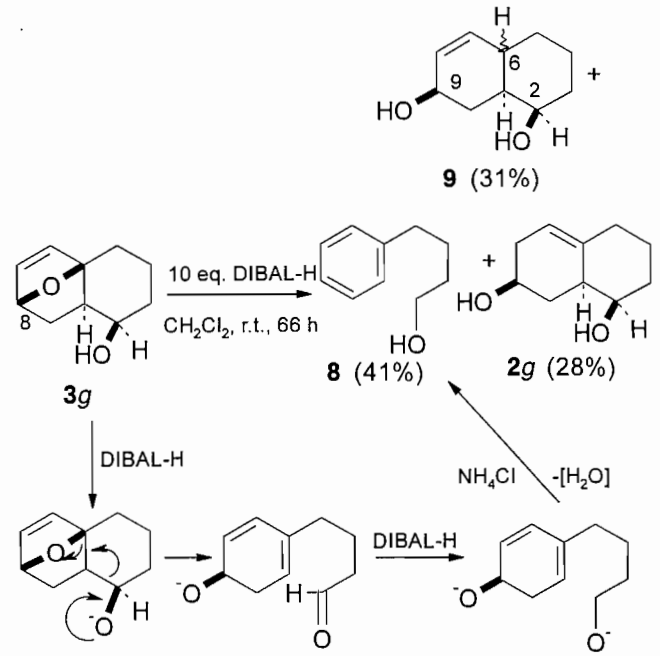
The treatment of **1** with DIBAL-H (16), in an attempt to effect a reductive ring opening, produced a complex mixture of products. The isolation of both **3***g* and the epimeric alcohol **7** from the reaction mixture indicated that the complexity of the mixture was due, in part, to the fact that the reduction of the ketone carbonyl group was not stereoselective.



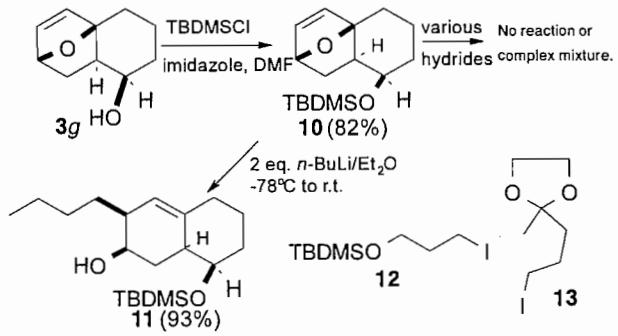
This problem of a non-stereoselective ketone reduction was circumvented by reducing the ketone in a separate step with a bulkier hydride reagent, lithium *tert*-butyldiisobutylaluminohydride (17), to form the axial alcohol **3***g* exclusively (Table 1, entry 12). When **3***g* was treated with DIBAL-H, a mixture of three products was formed (Scheme 4). The ring-opened product **2***g* was accompanied by a considerable amount of 4-phenyl-1-butanol (**8**). This product was possibly formed via a Grob-type fragmentation (10) of the initially formed alkoxide, and reduction of the resulting alkoxyaldehyde to produce a dialkoxide, followed by aromatization upon work-up with saturated ammonium chloride as illustrated in Scheme 4. The third product, which could not be completely separated from **2***g*, was tentatively identified as **9** with unknown stereochemistry at C_6. This product may have been formed from a direct reduction of the oxygen bridge. If the reduction had occurred via an S_N2-like process, attack should have occurred at the less hindered carbon atom, C_8, of **3***g*. Due to the Lewis acidic nature of DIBAL-H, however, the reduction may be more S_N1-like so that **9** was produced.

In an attempt to suppress the fragmentation reaction, compound **3***g* was converted to its *tert*-butyldimethylsilyl ether **10**

Scheme 4.



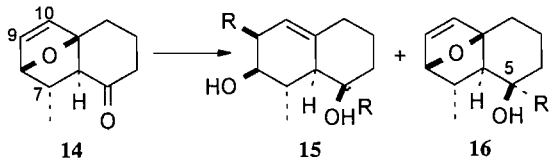
Scheme 5.



under standard conditions (18) (Scheme 5). When the protected compound was treated with DIBAL-H, however, no reaction was observed. A number of other reducing agents, including 9-BBN (19), sodium amalgam (16), lithium di-*tert*-butylbiphenyl (LiDBB) radical anion (20), and Super-Hydride® (21), also returned only unreacted starting material. Both lithium aluminum hydride (22) and DIBAL-H in hexanes produced a complex mixture of products in which the unprotected alcohol **3***g* was the major component. Although the reducing agents were unable to effect an S_N2' ring opening of compound **10**, *n*-butyllithium reacted in a highly regio- and stereoselective manner to produce **11** in high yield. This reaction illustrated that a free alkoxide was not required for the regiochemical control and that two different groups could be introduced due to the difference in the rates of the ring-opening reaction and nucleophilic attack at the ketone carbonyl. Unfortunately, attempts to extend this reaction to the functionalized nucleophiles derived from lithium–halogen exchange of the iodides **12** and **13** were unsuccessful, and only unreacted starting material was isolated.

The initial studies with **1** provided some idea of the condi-

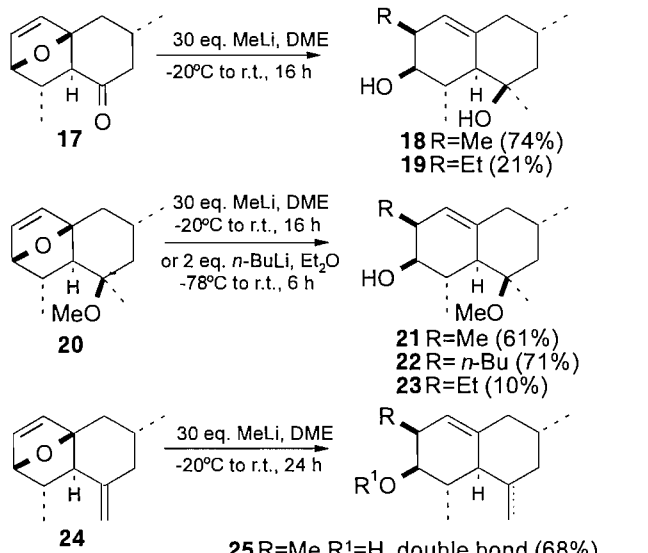
Table 2. Reaction of **14** with various organometallic reagents.



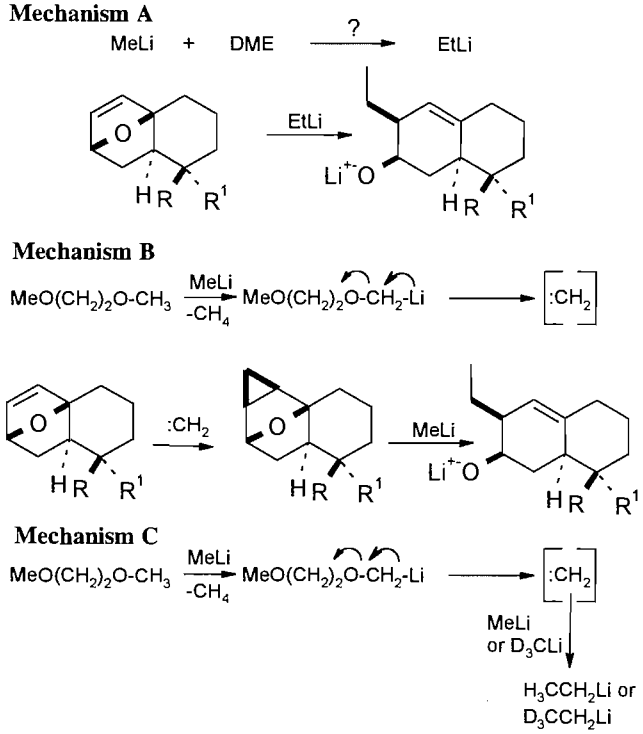
14 **15** **16**

R	Reagent/conditions	Product	% Yield
n-Bu	3 eq. *n*-BuLi, Et_2O, –78°C → r.t., 16 h	**15***a*	72
Me	3 eq. MeLi, 1:1 TMEDA:Et_2O, 0°C → r.t., 312 h	**16***b*	95
H	1.5 eq. LiAl(*t*-Bu)(i-Bu)$_2$H, THF, 0°C, 1 h	**16***c*	100

Scheme 6.



Scheme 7.

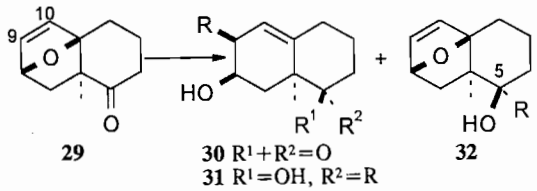


tions required to induce the S_N2' ring openings of the IMDAF cycloadducts. The effect of methyl substituents was examined next. Compound **14**, with a methyl group at C_7, was subjected to some of the reaction conditions that were successful with **1**. The results of these experiments are presented in Table 2.

n-Butyllithium smoothly reacted with **14** to generate **15***a* exclusively, showing that a C_7 methyl group had no effect on the regioselectivity of the ring-opening reaction. Surprisingly, however, the methyllithium–TMEDA system did not successfully cleave the bridging ether linkage. While the methyllithium–DME reagent was not tried with **14**, it was successful with the related compounds **17**, **20**, and **24**, giving **18**, **21**, and **25**, respectively (Scheme 6). Compounds **17**, **20**, and **24** were prepared as previously described (1). In each of these reactions, varying amounts of the ethyl derivatives **19**, **23**, and **26** were formed as side products. All three compounds were detected by GC–MS, and the *p*-nitrobenzoate ester **27**, prepared from the hydrogenation product of **26**, was characterized by X-ray crystallography. While the X-ray diffraction data were not good enough to allow for complete refinement of the crystal structure (R = 0.108), the identity and relative stereochemistry of the compound was still clearly established. Compound **20** also reacted cleanly with *n*-butyllithium, providing **22** in good yield. The reactions of **20** and **24** provided additional proof that the regioselectivity was not dependent on the presence of a free alkoxide.

Since the formation of the ethyl derivatives was both unexpected and intriguing, possible mechanisms for their formation were investigated further. The fact that the reaction was observed with **20** and **24** in addition to **17** suggested that a free alkoxide at C_5 was not involved in the reaction mechanism. Several possible mechanisms are illustrated in Scheme 7. The first possibility, mechanism A, requires the presence of ethyllithium as an impurity in the methyllithium or the formation, in some way, of ethyllithium under the reaction conditions. The homologation of secondary and tertiary organolithium reagents, usually by two carbon atoms, due to reaction with diethyl ether at room temperature is known (23). An S_N2' ring-opening reaction by the ethyllithium would then produce the

Table 3. Reaction of **29** with various organometallic reagents.



29 **30** $R^1+R^2=O$ **31** $R^1=OH$, $R^2=R$ **32**

R	Reagent/conditions	Product(s)	% Yield
n-Bu	3 eq. *n*-BuLi, Et_2O, −78°C → r.t., 16 h	**30***a*:**31***a*	62:8
Me	3 eq. MeLi, 1:1 TMEDA:Et_2O, 0°C → r.t., 312 h	**32***b*	61
H	1.5 eq. LiAl(*t*-Bu)(i-Bu)$_2$H, THF, 0°C, 1 h	**32***c*	100

observed products. A second potential mechanism, mechanism B, involves an α-elimination from the DME-derived primary anion to produce a carbene or carbenoid. The decomposition of α-haloorganolithium (see ref. 13, pp. 169–172) and α-phenoxyorganolithium (24) reagents to carbenes or carbenoids has been reported and, while an alkoxide is a poorer leaving group than either a halide or a phenoxide, the proposed α-elimination is still reasonable. The carbene or carbenoid could then react with the strained double bond of the IMDAF cycloadducts to introduce a cyclopropane ring. Attack of methyllithium to cleave the cyclopropane ring and effect the ring opening would then furnish the observed product. The chemical reactivity of cyclopropanes is similar to that of alkenes (25), and this type of reaction leading to the cleavage of the cyclopropane ring in 1-cyclopropyl-1-bromoalkanes by organocuprates (26) or piperidine (27) is known. Several experiments were performed on both the cycloadducts and on model compounds in an attempt to find support for these mechanisms.

One of the first experiments involved treatment of acetophenone with methyllithium, but no product of ethyl addition to acetophenone was detected. In addition, only 2-phenyl-2-propanol was formed when acetophenone was treated with an aliquot of a mixture of methyllithium and DME that had been stirred at room temperature for 1.5, 8.5, or 25 h. There was a possibility that any other organolithium reagents formed were simply behaving as bases with acetophenone and causing enolate formation rather than reacting with the carbonyl group. This possibility was addressed by carrying out the same experiment with benzaldehyde since benzaldehyde cannot enolize. Once again, however, only 1-phenylethanol, resulting from the addition of methyllithium to benzaldehyde, was observed. These experiments appeared to refute mechanism A since products resulting from the addition of the ethyl anion required for this mechanism should have occurred.

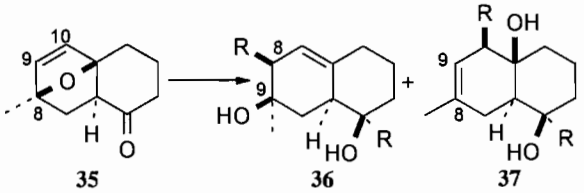
The treatment of **1** with trideuteriomethyllithium in DME provided **28** (Scheme 6). The mass spectrum of the reaction mixture showed that three deuterium atoms had been incorporated into **28** (M^- = 223). This result provided support for mechanism B (Scheme 7) since, in this mechanism, the methylene and methyl groups of the ethyl moiety originate from the DME and MeLi, respectively. An attempt to provide additional support for mechanism B involved performing a Simmons–Smith cyclopropanation (28) on compound **1** to introduce a cyclopropane ring on the strained double bond. Treatment of this compound with methyllithium in DME, however, returned only the cyclopropanated product, suggesting that mechanism B was not operating.

A potential explanation using a combination of mechanisms A and B is shown in mechanism C (Scheme 7). This involves the formation of ethyllithium from methyllithium and a carbene or carbenoid species generated from DME. The ethyllithium formed could then react with the oxatricyclo compound (mechanism A). In the absence of the oxatricyclo compound to immediately trap the ethyllithium formed, however, the ethyllithium could decompose the DME by the more conventional route of deprotonation of one of the methylene groups followed by β-elimination. As a result, none of the products resulting from the addition of ethyllithium to acetophenone or benzaldehyde was observed in the quenching experiments. This last explanation is purely speculative, and the possibility of a different mechanism has not been refuted.

Compound **14** reacted with lithium *tert*-butyldiisobutylaluminohydride to produce the axial alcohol **16***c* exclusively in excellent yield (Table 2). The proton on C_5 appeared as a broadened multiplet at 3.99 ppm, establishing the stereochemistry of the hydroxyl group. This result also confirmed that the ketone carbonyl group of **14** was still biased towards attack from the α-face. When **16***c* was treated with DIBAL-H, a complex mixture of compounds was produced. As the production of the complex mixture meant that the reaction would not be synthetically useful, no attempt was made to characterize any of the compounds in the mixture.

The effect of a methyl group adjacent to the carbonyl group in the IMDAF cycloadducts was probed with **29** and the results are shown in Table 3. *n*-Butyllithium once again caused a regioselective S_N2' ring opening; however, the major product isolated was **30***a*, in which nucleophilic addition to the carbonyl group had *not* occurred. A small amount of the "normal" product **31***a* was also isolated. The methyl group adjacent to the carbonyl group was apparently hindering nucleophilic attack at the carbonyl group from the α-face so that the ring-opening reaction became comparatively more facile. However, slightly less bulky alkyl groups, such as methyllithium, could still attack the carbonyl group. In fact, the methyllithium–TMEDA mixture attacked the carbonyl group, producing only **32***b*, and did not produce any ring-opened products. The production of the axial alcohol **32***c* exclusively upon treatment of **29** with lithium *tert*-butyldiisobutylaluminohydride illustrated that reaction at the carbo-

Table 4. Reaction of **35** with various organometallic reagents.

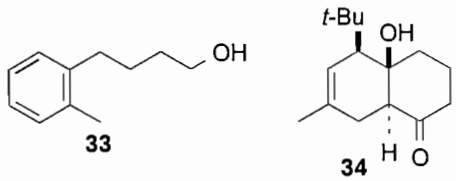


35 **36** **37**

R	Reagent/conditions	Ratio of **36**:**37**	Combined yield (%)
n-Bu	3 eq. *n*-BuLi, Et_2O, −78°C → r.t., 16 h	1.7:1	80
i-Pr	3 eq. i-PrLi/Et_2O, −78°C → r.t., 16 h	1.5:1	95
t-Bu	3 eq. *t*-BuLi, Et_2O, −78°C → 0°C, 3 h	2.2:1	55

nyl group was still biased towards attack from the α-face. Treatment of **32***c* with DIBAL-H produced predominantly the fragmentation product **33**. The formation of **33** could occur via the same mechanism for the formation of **8** from **3***g* (Scheme 4) under the same conditions.

Finally, compound **35** was used to investigate the effect of a methyl group on the bridgehead position of the IMDAF cycloadducts. The results of these experiments are summarized in Table 4. Although the ring-opening reaction could be effected with organolithium reagents, the presence of the bridgehead methyl group caused a dramatic decrease in the regioselectivity so that both **36** and **37** were formed in ratios varying from 1.5:1 to 2.2:1. In the case of the reaction with *tert*-butyllithium, a small amount (12%) of **34** was isolated as



33 **34**

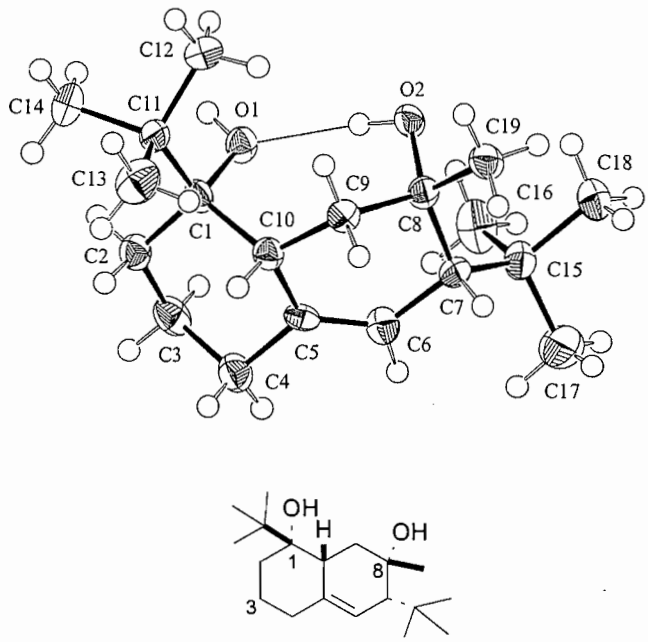
well. Because the two regioisomers were not easily separated by column chromatography and only the regioisomer that eluted first could be cleanly isolated, the ratios of products were determined by integration of the alkene protons. The major isomer from the reaction with *t*-BuLi was confirmed by an X-ray crystal structure (Fig. 2) and assigned structure **36***c*.[2] The X-ray crystal structure also established the facial selectivity of both the ring-opening reaction and the nucleophilic addition to the carbonyl group.

None of the normal S_N2' ring-opened products was observed when **35** was treated with the methyllithium–TMEDA reagent. Instead, a mixture of the non-ring-opened product **38** and the diene **39** was isolated (Scheme 8). Compound **39** was presumably formed via a β-elimination reaction as shown in Scheme 8. A similar reaction has been reported by Arjona et al. (29). This compound was somewhat unstable, and decomposed overnight upon storage in deuteriochloroform.

Discussion

Three items regarding the selectivity of the reaction of the organolithium reagents with the IMDAF cycloadducts need to be addressed. These items are the regioselectivity of the ring-opening reactions, the stereoselectivity of the ring-opening reactions, and the stereoselectivity of the nucleophilic addition to the ketone carbonyl group.

Fig. 2. X-ray crystal structure of compound **36***c*.



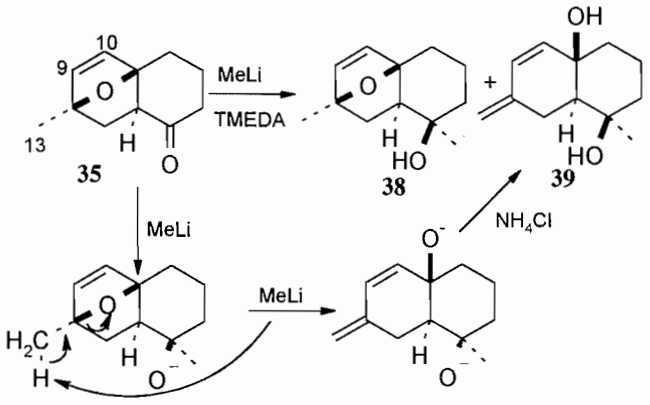
36*c*

Since the nucleophile would be donating electrons into the lowest unoccupied molecular orbital (LUMO) of the IMDAF cycloadducts, a difference in the lobe sizes at C_9 and C_{10} of the LUMO could be used to explain the regioselectivity. The LUMOs of several IMDAF cycloadducts, calculated at the AM1 semiemperical level using the SPARTAN molecular modelling program,[4] did not show a noticeable variation in the C_9 and C_{10} lobe sizes. Other explanations were therefore investigated.

The regioselectivity could be rationalized by electronic effects. Because the organolithium reagents also behave as Lewis acids, coordination of the lithium to the bridging oxygen atom likely occurs first. The developing positive charge

[4] SPARTAN 3.0, Wavefunction, Inc., Irvine, Calif.

Scheme 8.



Scheme 9.

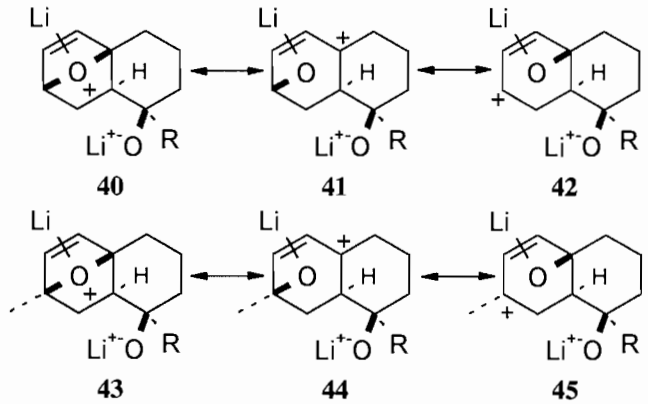


Table 5. Carbon–oxygen bond lengths of 3-21G(*) optimized structures of intermediates **40** and **43**.

Bond lengths for **40** (Å)		Bond lengths for **43** (Å)	
C_1–oxygen	1.5430	C_1–oxygen	1.5366
C_8–oxygen	1.5144	C_8–oxygen	1.5230
Difference	0.0286	Difference	0.0136

on the oxygen atom could be stabilized by resonance structures **41** or **42** for the intermediate **40** or structures **44** or **45** for the intermediate **43** (Scheme 9). For **40**, the resonance structure **41** should make a greater contribution to the resonance hybrid since the positive charge resides on a tertiary allylic carbon atom as opposed to a secondary allylic carbon atom in **42**. As a consequence, the C_1—O bond should be longer and weaker than the C_8—O bond, so that attack of a nucleophile at C_9 of **40** in an S_N2' fashion should be more facile than attack at C_{10}. On the other hand, the positive charge resides on a tertiary allylic carbon atom in both resonance structures **44** and **45**, so that these two structures should contribute equally to the resonance hybrid. As a result, the carbon–oxygen bond lengths should be more similar, and attack at C_9 or C_{10} of **43** should have more similar energy barriers. This argument was supported by the calculated structures of the intermediates **40** and **43** at the 3-21G(*) level using the SPARTAN molecular modelling program[3] (Table 5). The C_1—O bond length is longer than the C_8—O bond length in **40** and **43**; however, the difference is smaller in **43**. The slightly longer C_1_O bond length in **43** could also account for the slight preference for attack at C_9 in **35**. A similar argument has been used to rationalize the regioselectivity of acid-catalyzed ring openings of epoxides (30).

Steric arguments could also be used to rationalized the observed regioselectivity. The space-filling model of the 3-12G(*) optimized structure of **1** indicated that one of the hydrogen atoms on C_2 hinders attack at C_{10}, while attack at C_9 is less encumbered. The space-filling model of **35** indicated the same hindrance at C_{10}, but attack at C_9 is also obstructed by the hydrogen atoms (H_{13}) of the methyl group on C_8. As a result, the steric environments are more similar, leading to a corresponding decrease in the regioselectivity. A combination of steric and electronic effects is likely responsible for the observed regioselectivity.

The stereoselectivity of the S_N2' ring opening may be the result of the approach of the nucleophile from the less sterically hindered *exo* face of the oxatricyclic system (31). Coordination of the organolithium to the bridging oxygen atom or stereoelectronic effects favouring a *syn* S_N2' attack (32) are other possible contributing factors.

Steric effects are likely responsible for the stereoselective nucleophilic addition to the ketone carbonyl group. A steric argument is the classical explanation for the preference for equatorial attack at the carbonyl group of cyclohexanone when larger nucleophiles are employed (33). A different view of the space-filling model of **1** (optimized at the 3-21G(*) level) illustrated that the face of the carbonyl group opposite the bridging oxygen atom is more accessible to an attacking nucleophile.

Conclusions

The IMDAF cycloadducts are amenable to S_N2' ring openings by organolithium reagents. The minimum reactivity of the organolithium reagent required to effect the ring-opening reaction appeared to lie somewhere between that of *n*-butyllithium and methyllithium, since the former reagent and more reactive secondary and tertiary organolithium reagents were able to cause the ring opening, while methyllithium required activation by DME before any ring opening was observed. Less reactive organometallic reagents provided no ring-opened products. The reaction showed high facial selectivity for attack *syn* to the bridging oxygen atom, and was highly regioselective for attack at C_9 providing that the bridgehead position (C_8) of the IMDAF cycloadducted was not substituted. A combination of steric and electronic effects may be responsible for the high degree of selectivity. Substituents at other positions (C_3, C_6, and C_7) of the IMDAF cycloadducts were tolerated, and had no effect on the regioselectivity or stereoselectivity of the reaction.

Nucleophilic addition to the ketone carbonyl group of the IMDAF cycloadducts was generally more facile than the S_N2' ring-opening reaction unless the carbon atom adjacent to the carbonyl group bore a substituent. This addition was also highly stereoselective, providing products resulting from nucleophilic attack at the carbonyl group from the face opposite to the bridging oxygen atom. The IMDAF–S_N2' ring-opening reaction sequence provided products with up to five contiguous asymmetric centres of known relative stereochemistry in good to excellent yields.

All of the questions posed at the beginning of this article were answered by this study. With the viability of the S_N2' ring-openings established, we are continuing to apply this methodology to the enantioselective synthesis of natural products (6).

Experimental section

General experimental

Melting points were determined on solids purified by column chromatography using an Electrothermal® melting point apparatus and are uncorrected. Boiling points are uncorrected and refer to air-bath temperatures using a Kugelrohr short-path distillation apparatus. Optical rotations were measured with a Rudolph Research Autopol® III polarimeter using a 1 cm path length cell. Infrared spectra were recorded using a Mattson Galaxy Series 4030 FT-IR spectrophotometer. Solid samples were handled as pressed KBr discs, while liquid samples were placed neat between NaCl plates. Nuclear magnetic resonance spectra were obtained on either a Bruker ACE-200 (^{1}H 200 MHz, ^{13}C 50 MHz) or Bruker AM-400 (^{1}H 400 MHz, ^{13}C 100 MHz) spectrometer using deuteriochloroform as solvent. ^{13}C NMR spectra were referenced to the ^{13}C resonance of deuteriochloroform (δ 77.0), while ^{1}H NMR spectra were referenced to the ^{1}H resonance of residual chloroform (δ 7.27). Low-resolution mass spectra were either obtained using a Hewlett Packard 5890 Series II gas chromatograph interfaced to a Hewlett Packard 5971A mass selective detector or acquired by Mrs. Q. Wu (University of Calgary) using a VG-7070 spectrometer. High-resolution mass spectra were obtained by Mrs. D. Fox (University of Calgary) on a Kratos MS-80 spectrometer. Elemental analyses were also performed by Mrs. D. Fox using a Control Equipment Corporation 440 elemental analyzer. Chiral phase gas–liquid chromatography was performed on a Shimadzu GC-9A gas chromatograph equipped with a flame ionization detector using a 25 m × 0.33 mm (i.d.) × 0.25 μm (film thickness) Cydex-B (Scientific Glass Engineering) fused silica column. Analytical gas–liquid chromatography was performed on the same instrument using a 25 m × 0.53 mm (i.d.) × 3 μm (film thickness) 007 Series Methyl Silicone (Quadrex Corporation) fused silica column. Helium was used as the carrier gas in both cases. Flash column chromatography was accomplished with silica gel 60 (E. Merck, 0.04–0.063 mm, 230–400 mesh). Radial plate chromatography was performed with a Chromatotron (Harrison Research, model 7924T) with plates bearing 1, 2, or 4 mm thicknesses of silica gel (EM Science silica gel 60 PF_{254} with gypsum binder). Solvent systems refer to mixtures, by volume, of hexanes and ethyl acetate unless otherwise specified.

General procedure 1 for the S_N2' ring openings

A N_2-purged three-neck round-bottom flask equipped with an addition funnel containing a solution of the oxatricyclo compound (0.32 mmol) in anhydrous Et_2O (6 mL) was cooled with a −78°C bath. The flask was charged with anhydrous Et_2O (4 mL) and the organometallic reagent (1.0 mmol), and the solution of the oxatricyclo compound was added dropwise from the addition funnel. The mixture was warmed to 0°C and, if the reaction was not complete within 2 h, was then warmed to room temperature and stirred overnight. Wet Et_2O (10 mL) and saturated aqueous NH_4Cl (10 mL) were added sequentially, and the aqueous layer was extracted with Et_2O (4 × 10 mL). After the combined organic layers had been dried over anhydrous Na_2SO_4 and filtered, the solvent was removed in vacuo to provide the crude product. Purification was effected by flash column chromatography.

General procedure 2 for the S_N2' ring openings with methyllithium

A solution of the oxatricyclo compound (1.1 mmol) in anhydrous DME (29 mL) in a N_2-purged three-neck round-bottom flask was cooled with a −23°C bath. Methyllithium (33 mmol, 1.4 M in Et_2O) was added to the cooled reaction mixture, which was then warmed to 0°C and allowed to slowly reach room temperature overnight. The reaction was cooled back down to −23°C, and wet Et_2O (30 mL) and saturated aqueous NH_4Cl (30 mL) were cautiously added sequentially. The aqueous layer was extracted with Et_2O (4 × 30 mL), and the combined organic layers were dried over anhydrous Na_2SO_4. The dried solution was filtered, and the solvent was removed in vacuo to provide the crude product. Purification was effected by flash column chromatography.

(1*RS*,2*SR*,8*RS*,9*SR*)-2,8-Dibutylbicyclo[4.4.0]dec-6-en-2,9-diol (2*a*)

General procedure 1 was used to prepare compound **2***a*. Cycloadduct **1** (52.7 mg, 0.321 mmol) was treated with *n*-butyllithium (0.40 mL of 2.5 M in hexanes, 1.00 mmol) for 16 h to give diol **2***a* (59.4 mg, 0.212 mmol) as a white solid in 66% yield following purification by flash column chromatography (5:1); mp 104–105°C; IR (KBr): 3192 cm^{-1}; ^{1}H NMR (400 MHz): 0.92 and 0.93 (overlapping t, 6H, J = 7.0 Hz), 1.23–1.42 (m, 10H), 1.48–1.70 (m, 7H), 1.79 (ddd, 1H, J = 3.1 Hz, J = 8.8 Hz, J = 14.4 Hz), 1.96–2.05 (m, 2H), 2.13 (ddd, 1H, J = 3.4 Hz, J = 6.0 Hz, J = 14.4 Hz), 2.20–2.25 (m, 2H), 2.86 (br s, 1H), 3.88 (m, 1H), 5.36 (br s, 1H); ^{13}C NMR (50 MHz): 2 × 14.1, 22.5, 23.0, 23.3, 26.3, 28.1, 29.4, 31.0, 35.4, 36.6, 40.1, 40.3, 42.6, 66.4, 74.2, 124.5, 136.3; MS: 280 (8, M^+), 113 (100). Anal. calcd. for $C_{18}H_{32}O_2$: C 77.09, H 11.50; found: C 77.43, H 11.12.

X-ray crystal data for compound 2*a*

A sample of **2***a* was recrystallized from hexane to give colorless needles that were submitted for X-ray crystallographic analysis. See Fig. 1 for the X-ray crystal structure. Crystal data: empirical formula $C_{18}H_{32}O_2$; space group $P2_1/n$; a = 12.566(2) Å; b = 8.617(3) Å; c = 16.227(2) Å; β = 90.50(1)°; V = 1757.0 Å^3; Z = 4; d = 1.06 g/cm^3; Mo-Kα radiation (22°C); total of 3564 reflections in the range 2° < θ < 25°, of which 2247 were used ($I > 3\sigma(I)$) in the structure solution; R = 0.0516 and Rw = 0.0575.

(1*RS*,2*RS*,8*RS*,9*SR*)-2,8-Di(1-methylethyl)bicyclo[4.4.0]dec-6-en-2,9-diol (2*b*)

A solution of isopropyllithium was prepared using the method of Gilman et al. (7). An argon-purged three-neck round-bottom flask equipped with a glass-coated stirring bar and a dropping funnel containing a solution of freshly distilled 2-chloropropane (1.60 g, 2.04 mmol) in dry pentane (7 mL) was charged with dry penatane (13 mL). Freshly cut pieces of high-sodium (1%) lithium wire (0.2 g, 28.8 mmol) were added to the three-neck flask and the 2-chloropropane solution was

added dropwise to the reaction mixture. The addition funnel was replaced with a condenser and the solution was heated at reflux overnight. The resulting purple suspension was allowed to settle, and the supernatant was withdrawn and used. Standardization against 2,5-dimethoxybenzyl alcohol (34) indicated that the supernatant was 0.33 M in isopropyllithium.

General procedure 1 was used to prepare compound **2***b*. Cycloadduct **1** (48.2 mg, 0.294 mmol) was treated with the prepared solution of isopropyllithium (3.1 mL of 0.33 M in pentane, 1.02 mmol) for 16 h to give diol **2***b* (50.3 mg, 0.199 mmol) as a white solid in 68% yield following purification by flash column chromatography (5:1); mp 140–141.5°C; IR (KBr): 3250, 3117, 1385, 1363 cm^{-1}; ^1H NMR (200 MHz): 0.89 (d, 3H, J = 7.0 Hz), 0.95 (d, 3H, J = 6.8 Hz), 1.02 (d, 6H, J = 6.0 Hz), 1.35–1.83 (m, 7H), 1.98–2.37 (m, 5H), 2.97 (br s, 2H), 4.01 (m, 1H), 5.48 (br t, 1H, J = 1.6 Hz); ^{13}C NMR (50 MHz): 16.6, 17.6, 20.8, 20.8, 22.4, 28.3, 28.6, 29.5, 34.1, 34.1, 40.8, 47.1, 64.3, 76.3, 121.7, 137.1; MS: 252 (11, $M^{+\cdot}$), 131 (100). Exact Mass calcd. for $C_{16}H_{28}O_2$: 252.2089; found: 252.2084.

(1*RS*,2*SR*,8*SR*,9*SR*)-2,8-Di(1,1-dimethylethyl)bicyclo[4.4.0]dec-6-en-2,9-diol (2*c*)

General procedure 1 was used to prepare compound **2***c*. Cycloadduct **1** (49.8 mg, 0.303 mmol) was treated with *tert*-butyllithium (0.40 mL of 1.7 M in hexanes, 0.68 mmol) for 2 h at 0°C to give diol **2***c* (76.8 mg, 0.274 mmol) as a white solid in 90% yield following purification by flash column chromatography (9:1; mp 144–145.5°C; IR (KBr): 3231, 1395, 1365 cm^{-1}; ^1H NMR (400 MHz): 1.04 and 1.09 (two s, 9H each), 1.59–1.87 (m, 6H), 1.95–2.06 (m, 1H), 2.22–2.27 (m, 1H), 2.44 (br d, 1H, J = 7.1 Hz), 2.69 (dd, 1H, J = 4.2 Hz, J = 15.1 Hz), 2.82 (br s, 1H), 3.96 (br s, 1H), 4.16 (m, 1H), 5.49 (br t, 1H, J = 1.7 Hz); ^{13}C NMR (50 MHz): 23.8, 27.8, 28.2, 32.3, 32.7, 34.3, 36.9, 38.6, 42.5, 49.7, 65.4, 78.4, 121.7, 137.9; MS: 280 (4, $M^{+\cdot}$), 57 (100). Exact Mass calcd. for $C_{18}H_{32}O_2$: 280.2402; found: 280.2412.

(1*RS*,5*SR*,6*RS*,8*RS*)-5-Ethenyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-ol (3*d*)

General procedure 1 was used to prepare compound **3***d*. Cycloadduct **1** (45.6 mg, 0.278 mmol) was treated with vinylmagnesium bromide (0.83 mL of 1.0 M in THF, 0.83 mmol) for 20 h to give alcohol **3***d* (39.2 mg, 0.204 mmol) as a slightly yellow oil in 73% yield following purification by flash column chromatography (3:1); bp 40–45°C/0.06 Torr (1 Torr = 133.3 Pa); IR (neat): 3478, 1630 cm^{-1}; ^1H NMR (200 MHz): 1.26 (dd, 1H, J = 8.0 Hz, J = 11.8 Hz), 1.42–1.67 (m, 3H), 1.72–2.32 (m, 5H), 3.52 (br s, 1H), 4.88 (dd, 1H, J = 1.7 Hz, J = 4.9 Hz), 5.00 (dd, 1H, J = 1.9 Hz, J = 10.6 Hz), 5.26 (dd, 1H, J = 1.9 Hz, J = 17.2 Hz), 5.75 (dd, 1H, J = 10.6 Hz, J = 17.2 Hz), 5.93 (d, 1H, J = 5.7 Hz), 6.47 (dd, 1H, J = 1.7 Hz, J = 5.7 Hz); ^{13}C NMR (50 MHz): 16.4, 27.6, 28.4, 36.9, 41.1, 71.9, 78.4, 87.7, 112.0, 137.2, 139.1, 144.0; MS: 192 (1, $M^{+\cdot}$), 94 (100). Exact Mass calcd. for $C_{12}H_{16}O_2$: 192.1150; found: 192.1138.

(1*RS*,5*RS*,6*RS*,8*RS*)-5-Methyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-ol (3*e*)

General procedure 1 was used to prepare compound **3***e*. Cycloadduct **1** (48.6 mg, 0.296 mmol) was treated with methyllithium (0.46 mL of 1.4 M in Et_2O, 0.64 mmol) for 22 h to give alcohol **3***e* (34.1 mg, 0.189 mmol) as a colorless oil in 64% yield following purification by flash column chromatography (20:1 benzene:acetone); bp 50–60°C/0.07 Torr; IR (neat): 3497 cm^{-1}; ^1H NMR (200 MHz): 1.12 (s, 3H), 1.25–1.63 (m, 4H), 1.67–2.01 (m, 3H), 2.17–2.30 (m, 2H), 3.36 (br s, 1H), 4.89 (dd, 1H, J = 1.7 Hz, J = 4.9 Hz), 5.93 (d, 1H, J = 5.7 Hz), 6.47 (dd, 1H, J = 1.7 Hz, J = 5.7 Hz); ^{13}C NMR (50 MHz): 16.7, 27.8, 28.5, 28.9, 38.6, 42.7, 69.5, 78.5, 88.0, 137.5, 138.8; MS: 180 (weak, $M^{+\cdot}$), 94 (100). Exact Mass calcd. for $C_{11}H_{16}O_2$: 180.1150; found: 180.1154.

(1*RS*,5*RS*,6*SR*,8*RS*)-5-Phenyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-ol (3*f*)

General procedure 1 was used to prepare compound **3***f*. Cycloadduct **1** (47.3 mg, 0.288 mmol) was treated with phenyllithium (0.45 mL of 2.0 M in cyclohexane–Et_2O, 0.90 mmol) for 18 h to give alcohol **3***f* (60.6 mg, 0.250 mmol) as a yellow solid in 87% yield following purification by flash column chromatography (5:1); mp 114–115°C; IR (KBr): 3459, 1491, 1451 cm^{-1}; ^1H NMR (200 MHz): 1.11 (dd, 1H, J = 7.8 Hz, J = 11.7 Hz), 1.67–1.76 (m, 1H), 1.87–2.13 (m, 6H), 2.36–2.42 (m, 1H), 4.13 (s, 1H), 4.91 (dd, 1H, J = 1.7 Hz, J = 4.7 Hz), 6.00 (d, 1H, J = 5.7 Hz), 6.48 (dd, 1H, J = 1.7 Hz, J = 5.7 Hz), 7.19–7.52 (m, 5H); ^{13}C NMR (50 MHz): 17.2, 27.6, 28.5, 39.1, 43.4, 73.3, 78.5, 88.2, 124.8, 126.2, 127.9, 137.2, 139.1, 147.7; MS: 242 (1, $M^{+\cdot}$), 94 (100). Exact Mass calcd. for $C_{16}H_{18}O_2$: 242.1307; found: 242.1305.

(1*RS*,2*SR*,8*RS*,9*SR*)-2,8-Dimethylbicyclo[4.4.0]dec-6-en-2,9-diol (2*e*) and (1*RS*,2*SR*,8*RS*,9*SR*)-8-ethyl-2-methylbicyclo[4.4.0]dec-6-en-2,9-diol (6)

(a) Using methyllithium–TMEDA

Anhydrous Et_2O (2 mL) was placed in a N_2-purged three-neck round-bottom flask equipped with an addition funnel containing a solution of cycloadduct **1** (48.0 mg, 0.292 mmol) in anhydrous Et_2O (5 mL). The flask was cooled with an ice bath, and methyllithium (0.80 mL of 1.4 M in Et_2O, 1.12 mmol) and dry TMEDA (7.8 mL) was added. The solution of **1** was added dropwise from the addition funnel, and the reaction was warmed to room temperature and stirred for 48 h. Wet Et_2O (10 mL) and saturated aqueous NH_4Cl (10 mL) were then added sequentially, and the aqueous layer was extracted with Et_2O (4 × 10 mL). The combined organic layers were washed with 10% aqueous $CuSO_4$ (2 × 30 mL), dried over anhydrous Na_2SO_4, and filtered. The solvent was removed from the filtrate in vacuo. The crude product contained a mixture of **2***e*:**3***e* in a ratio of approximately 1:1. Flash column chromatography (3:1) provided **3***e* (17.5 mg, 0.0971 mmol) and **2***e* (16.9 mg, 0.0861 mmol) in yields of 33 and 30%, respectively.

(b) Using methyllithium–DME

Cycloadduct **1** (36.0 mg, 0.219 mmol) was treated with methyllithium (6.30 mL of 1.4 M in Et_2O, 8.82 mmol) for 22 h according to general procedure 2. Flash column chromatography (3:1) provided diol **2***e* (31.6 mg, 0.161 mmol) and a compound tentatively identified as **6** (12.0 mg, 0.0570 mmol) in yields of 74 and 26%, respectively. Compound **2***e* was characterized as a white solid, mp 124–125°C; IR (KBr): 3244 cm^{-1}; ^1H NMR (200 MHz): 1.05 (d, 3H, J = 7.2 Hz), 1.26 (s, 3H), 1.44–2.35 (m, 10H), 2.89 (br s, 2H), 3.84 (m, 1H), 5.33 (br s,

1H); ^{13}C NMR (50 MHz): 16.0, 22.6, 27.7, 28.1, 35.0, 35.1, 40.3, 45.2, 67.9, 72.0, 126.1, 136.0; MS: 196 (6, $M^{+\cdot}$), 120 (100). Anal. calcd. for $C_{12}H_{20}O_2$: C 73.41, H 10.29; found: C 73.27, H 10.10.

The second compound (**6**) was also a white solid, but was contaminated. ^{1}H NMR (200 MHz): 1.00 (t, 3H, J = 7.3 Hz), 1.27 (s, 3H), 1.32–2.33 (m, 18H, high due to contaminant), 3.00 (br s, 2H), 3.91 (br m, 1H), 5.34 (br s, 1H); ^{13}C NMR (50 MHz): 12.0, 22.7, 24.3, 28.0, 28.7, 35.4, 40.4, 42.1, 44.9, 66.0, 72.2, 124.0, 136.2; MS: No $M^{+\cdot}$, 192 (27, $M^{+\cdot} - H_2O$).

(1*RS*,5*RS*,6*RS*,8*RS*)-11-Oxatricyclo[6.2.1.0^{1,6}[undec-9-en-5-ol (3*g*) and (1*RS*,5*SR*,6*RS*,8*RS*)-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-ol (7)

(a) Using DIBAL-H

Cycloadduct **1** (77.3 mg, 0.471 mmol) was placed in a N_2-purged three-neck round-bottom flask and dissolved in CH_2Cl_2 (10 mL). The solution was cooled using a −78°C cold bath, and DIBAL-H (1.10 mL of 1.0 M in THF, 1.10 mmol) was added by syringe. The reaction was warmed to 0°C, and then slowly warmed to room temperature and stirred for 22 h. Wet Et_2O (10 mL) and saturated aqueous NH_4Cl (10 mL) were then added to quench the reaction, and the mixture was filtered through Celite.® The Celite® was washed well with several portions of Et_2O. The aqueous layer was extracted with Et_2O (4 × 10 mL) and the combined organic layers were dried with anhydrous Na_2SO_4. The drying agent was removed by filtration, and the solvent was removed in vacuo to provide a crude reaction product. Flash column chromatography (3:1, then 1:1) provided **3***g* (13.2 mg, 0.0794 mmol) and **7** (29.0 mg, 0.174 mmol) in yields of 17 and 37%, respectively. A mixture of uncharacterized compounds (29.9 mg) was also isolated.

(b) Using lithium tert-butyldiisobutylaluminohydride

Cycloadduct **1** (71.0 mg, 0.432 mmol) was placed in a N_2-purged three-neck round-bottom flask and dissolved in THF (6 mL). The solution was cooled using a −78°C cold bath, and lithium *tert*-butyldiisobutylaluminohydride (0.65 mL of 1.0 M in THF, 0.65 mmol) was added by syringe. The mixture was stirred at −78°C until analysis by TLC indicated that the starting material had been consumed (15 min). Solid $Na_2SO_4 \cdot 10H_2O$ (274 mg, 0.850 mmol) was added, and the reaction was poured into a mixture of 0.5 M aqueous $KHSO_4$ (8 mL) and $CHCl_3$ (6 mL) and stirred for 15 min. The aqueous layer was extracted with $CHCl_3$ (4 × 10 mL). After the combined organic layers had been dried with anhydrous Na_2SO_4 and filtered, the solvent was removed in vacuo to give **3***g* (59.9 mg, 0.360 mmol) exclusively in 83% yield after purification by flash column chromatography (3:1). Compound **3***g* was characterized as a colorless oil, bp 44–50°C/0.08 Torr; IR (neat): 3493 cm^{-1}; ^{1}H NMR (200 MHz): 1.38 (dd, 1H, J = 8.1 Hz, J = 11.5 Hz), 1.43–2.08 (m, 6H), 2.17–2.33 (m, 2H), 3.08 (d, 1H, J = 8.2 Hz), 3.82–3.99 (br m, 1H), 4.90 (dd, 1H, J = 1.7 Hz, J = 4.9 Hz), 5.91 (d, 1H, J = 5.7 Hz), 6.47 (dd, 1H, J = 1.7 Hz, J = 5.7 Hz); ^{13}C NMR (50 MHz): 14.7, 27.9, 29.5, 32.0, 37.5, 67.2, 78.1, 87.6, 137.2, 138.8; MS: 166 (1, $M^{+\cdot}$), 94 (100). Exact Mass calcd. for $C_{10}H_{14}O_2$: 166.0994; found: 166.0980.

Compound **7** was characterized as a colorless oil, bp 40–50°C/0.08 Torr; IR (neat): 3392 cm^{-1}; ^{1}H NMR (200 MHz): 1.29–1.98 (m, 9H), 2.16–2.26 (m, 1H), 3.39 (ddd, 1H, J = 3.8 Hz, J = 9.2 Hz, J = 11.2 Hz), 4.95 (dd, 1H, J = 1.7 Hz, J = 4.5 Hz), 5.99 (d, 1H, J = 5.7 Hz), 6.38 (dd, 1H, J = 1.7 Hz, J = 5.7 Hz); ^{13}C NMR (50 MHz): 20.5, 28.2, 33.8, 34.8, 44.0, 76.0, 78.9, 88.3, 137.5, 137.8; MS: 166 (1, $M^{+\cdot}$), 94 (100). Exact Mass calcd. for $C_{10}H_{14}O_2$: 166.0994; found: 166.0996.

(1*RS*,2*SR*,9*RS*)-Bicyclo[4.4.0]dec-6-en-2,9-diol (2*g*) and (1*RS*,2*SR*,6*SR*,9*SR*)- or (1*RS*,2*SR*,6*RS*,9*SR*)-bicyclo[4.4.0]dec-7-en-2,9-diol (9)

Compound **3***g* (51.8 mg, 0.312 mmol) was placed in a N_2-purged three-neck round-bottom flask and dissolved in CH_2Cl_2 (10 mL). The solution was cooled using a −78°C cold bath, and DIBAL-H (3.20 mL of 1.0 M in THF, 3.20 mmol) was added by syringe. The reaction was warmed to 0°C, and then slowly warmed to room temperature and stirred for 66.5 h. Wet Et_2O (10 mL) and saturated aqueous NH_4Cl (10 mL) were then added to quench the reaction, and the mixture was filtered through Celite.® The Celite® was washed well with several portions of Et_2O. The aqueous layer was extracted with Et_2O (4 × 10 mL) and the combined organic layers were dried with anhydrous Na_2SO_4. The drying agent was removed by filtration, and the solvent was removed in vacuo to provide a crude reaction product. Flash column chromatography (1:5) provided 4-phenyl-1-butanol **8** (19.1 mg, 0.127 mmol), **2***g* (14.8 mg, 0.0880 mmol), and a third compound tentatively identified as **9** (16.2 mg, 0.0963 mmol, contaminated by **2***g*) in yields of 41, 28, and 31%, respectively. Compound **2***g* was characterized as a white solid. IR (KBr): 3395 cm^{-1}; ^{1}H NMR (200 MHz): 1.53–2.40 (m, 11H), 2.74 (br s, 2H), 3.89 (br s, 1H), 4.03 (m, 1H), 5.45 (br s, 1H); ^{13}C NMR (50 MHz): 20.9, 33.2, 2 × 33.8, 34.9, 40.8, 64.5, 71.3, 118.5, 136.0; MS: 168 (23, $M^{+\cdot}$), 55 (100). Exact Mass calcd. for $C_{10}H_{16}O_2$: 168.1150; found: 168.1148.

The impure sample of **9** was partially characterized. ^{13}C NMR (50 MHz) following elimination of signals due to **2***g*: 20.6, 32.2, 33.4, 34.5, 36.9, 44.1, 69.1, 70.3, 130.0, 134.7. 4-Phenyl-1-butanol **8** exhibited ^{1}H NMR (200 MHz): 1.30 (br s, 1H) 1.40–1.85 (m, 4H), 2.63 (t, 2H, J = 7 Hz), 3.69 (t, 2H, J = 7 Hz), 7.11–7.36 (m, 5H).

(1*RS*,5*RS*,6*RS*,8*RS*)-5-(*tert*-Butyldimethylsiloxy)-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-ene (10)

Compound **3***g* (0.112 g, 0.676 mmol) was dissolved in dry DMF (2 mL) in a N_2-purged three-neck round-bottom flask. Freshly distilled TBDMSCl (0.369 g, 2.45 mmol) and imidazole (0.349 g, 5.13 mmol) were added, and the reaction was stirred at room temperature for 16 h. When analysis by TLC indicated that the reaction was complete, Et_2O (10 mL) and saturated aqueous NaCl (3 mL) was added. The organic layer was separated and washed with additional saturated aqueous NaCl (3 × 3 mL). After the organic phase had been dried with anhydrous Na_2SO_4 and filtered, the solvent was removed in vacuo. Purification by flash column chromatography (20:1) provided **10** (0.156 g, 0.554 mmol) as a colorless liquid in 82% yield; bp 50–60°C/0.06 Torr; IR (neat): 2900 cm^{-1}; ^{1}H NMR (200 MHz): 0.04 (s, 6H), 0.91 (s, 9H), 1.23 (dd, 1H, J = 8.3 Hz, J = 10.7 Hz), 1.35–1.57 (m, 3H), 1.80–2.12 (m, 4H), 2.22–2.28 (m, 1H), 4.03 (br m, 1H), 4.83 (dd, 1H, J = 1.6 Hz, J = 4.7 Hz), 5.96 (d, 1H, J = 5.6 Hz), 6.33 (dd, 1H, J = 1.6 Hz, J = 5.6 Hz); ^{13}C NMR (50 MHz): −5.2, −4.3, 15.1, 18.1, 25.8,

28.4, 28.5, 32.8, 39.8, 66.9, 77.9, 85.8, 137.7, 139.4; MS: 280 (0.4, $M^{+\cdot}$), 75 (100). Exact Mass calcd. for $C_{16}H_{28}O_2Si$: 280.1859; found: 280.1850.

(1*RS*,3*SR*,4*RS*,10*SR*)-4-Butyl-10-(*tert*-butyldimethylsiloxy)bicyclo[4.4.0]dec-5-en-3-ol (11)

Compound **10** (58.2 mg, 0.207 mmol) was treated with *n*-butyllithium (0.17 mL of 2.5 M in hexanes, 0.425 mmol) for 18 h according to general procedure 1 to give compound **11** (65.0 mg, 0.192 mmol) as a white solid in 93% yield following purification by flash column chromatography (9:1); mp 44–46°C; IR (KBr): 3345 cm^{-1}; ^1H NMR (200 MHz): 0.09, 0.13 (two s, 3H each), 0.91 (overlapping t and s, 12h), 1.21–2.05 (m, 15H), 2.18–2.35 (m, 2H), 3.81 (m, 1H), 3.89 (br s, 1H), 5.29 (br s, 1H); ^{13}C NMR (50 MHz): −4.6, −4.2, 14.1, 18.3, 20.5, 23.0, 26.0, 29.6, 31.0, 32.6, 33.7, 34.9, 40.7, 41.3, 67.1, 72.5, 85.8, 124.1, 135.4; MS: 338 (0.1, $M^{+\cdot}$), 189 (100). Exact Mass calcd. for $C_{16}H_{29}O_2Si$ $M^{+\cdot}$ − *t*-Bu): 281.1936; found: 281.1911.

(1*RS*,2*SR*,8*RS*,9*RS*,10*RS*)-2,8-Dibutyl-10-methylbicyclo[4.4.0]dec-6-en-2,9-diol (15*a*)

General procedure 1 was used to prepare compound **15***a*. Cycloadduct **14** (30.3 mg, 0.170 mmol) was treated with *n*-butyllithium (0.20 mL of 2.5 M in hexanes, 0.50 mmol) for 16 h to give diol **15***a* (36.1 mg, 0.123 mmol) as a white solid in 72% yield following purification by flash column chromatography (5:1); mp 122–123°C; IR (KBr): 3198 cm^{-1}; ^1H NMR (200 MHz): 0.93–0.97 (d and two overlapping t, 9H, J = 7.3 Hz (for d)), 1.22–2.18 (m, 19H), 2.21–2.28 (m, 1H), 2.37 (dq, 1H, J = 2.7 Hz, J = 7.3 Hz), 3.55 (2 overlapping br s, 3H), 5.23 (br s, 1H); ^{13}C NMR (50 MHz): 14.1, 14.1, 20.5, 22.9, 23.0, 23.4, 26.5, 29.3, 31.1, 32.7, 35.6, 36.3, 37.2, 40.8, 50.1, 70.7, 74.7, 122.3, 135.0; MS: 294 (1, $M^{+\cdot}$), 174 (100). Exact Mass calcd. for $C_{19}H_{34}O_2$: 294.2559; found: 294.2566.

(1*RS*,5*RS*,6*RS*,7*SR*,8*SR*)-5,7-Dimethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-ol (16*b*)

Anhydrous Et_2O (2 mL) was placed in a N_2-purged three-neck round-bottom flask equipped with an addition funnel containing a solution of cycloadduct **14** (56.7 mg, 0.318 mmol) in anhydrous Et_2O (5 mL). The flask was cooled with an ice bath, and methyllithium (0.70 mL of 1.4 M in Et_2O, 0.98 mmol) and dry TMEDA (7.7 mL) were added. The solution of **14** was added dropwise from the addition funnel, and the reaction was warmed to room temperature and stirred for 312 h. Wet Et_2O (10 mL) and saturated aqueous NH_4Cl (10 mL) were added sequentially, and the aqueous layer was extracted with Et_2O (4 × 10 mL). The combined organic layers were washed with 10% aqueous $CuSO_4$ (2 × 30 mL), dried over anhydrous Na_2SO_4, and filtered. The solvent was removed from the filtrate in vacuo. Flash column chromatography (20:1 benzene:acetone) provided **16***b* (58.5 mg, 0.301 mmol) as a white solid in 95% yield; mp 41–42°C; IR (KBr): 3492 cm^{-1}; ^1H NMR (200 MHz): 0.92 (d, 3H, J = 7.1 Hz), 1.03 (d, 1H, J = 3.0 Hz), 1.18 (s, 3H), 1.30–1.97 (m, 5H), 2.10–2.24 (m, 1H), 2.71 (m, 1H), 3.33 (s, 1H), 4.72 (dd, 1H, J = 1.7 Hz, J = 4.9 Hz), 6.05 (d, 1H, J = 5.8 Hz), 6.43 (dd, 1H, J = 1.7 Hz, J = 5.8 Hz); ^{13}C NMR (50 MHz): 16.6, 18.1, 28.1, 29.0, 35.3, 38.5, 51.6, 69.7, 81.9, 88.9, 136.4, 138.7; MS: 194 (weak, $M^{+\cdot}$), 94 (100). Exact Mass calcd. for $C_{12}H_{18}O_2$: 194.1307; found: 194.1312.

(1*RS*,5*RS*,6*RS*,7*SR*,8*SR*)-7-Methyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-ol (16*c*)

Cycloadduct **14** (51.0 mg, 0.286 mmol) was placed in a N_2-purged three-neck round-bottom flask and dissolved in THF (4 mL). The solution was cooled using a −78°C cold bath, and lithium *tert*-butyldiisobutylaluminohydride (0.43 mL of 1.0 M in THF, 0.43 mmol) was added by syringe. The mixture was stirred at −78°C until analysis by TLC indicated that the starting material had been consumed (50 min). Solid $Na_2SO_4 \cdot 10H_2O$ (150 mg, 0.466 mmol) was added, and the reaction was poured into a mixture of 0.5 M aqueous $KHSO_4$ (10 mL) and $CHCl_3$ (5 mL) and stirred for 30 min. The aqueous layer was extracted with $CHCl_3$ (4 × 10 mL). After the combined organic layers had been dried with anhydrous Na_2SO_4 and filtered, the solvent was removed in vacuo to give **16***c* (51.5 mg, 0.286 mmol) exclusively in 100% yield after purification by flash column chromatography (5:1). Compound **16***c* was characterized as a colorless oil, bp 45–50°C/0.05 Torr; IR (neat): 3501 cm^{-1}; ^1H NMR (200 MHz): 0.86 (d, 3H, J = 7.0 Hz), 1.14 (t, 1H, J = 3.6 Hz), 1.20–1.52 (m, 2H), 1.69–2.01 (m, 3H), 2.17–2.24 (m, 1H), 2.64–2.90 (overlapping m and br s, 2H), 3.99 (br t, 1H), 4.71 (dd, 1H, J = 0.9 Hz, J = 4.6 Hz), 6.01 (d, 1H, J = 5.8 Hz), 6.41 (dd, 1H, J = 0.9 Hz, J = 5.8 Hz); ^{13}C NMR (50 MHz): 14.5, 16.6, 28.2, 31.8, 35.7, 46.7, 66.1, 81.7, 88.3, 136.2, 138.5; MS: 180 (1, $M^{+\cdot}$), 94 (100). Exact Mass calcd. for $C_{11}H_{16}O_2$: 180.1150; found: 180.1151.

(1*S*,2*R*,4*S*,8*S*,9*S*,10*S*)-2,4,8,10-Tetramethylbicyclo[4.4.0]dec-6-en-2,9-diol ((+)-18)

Cycloadduct (−)-**17** (prepared according to ref. 1*c*) (123.8 mg, 0.644 mmol) was treated with methyllithium (14.0 mL of 1.4 M in Et_2O, 20 mmol) for 16 h according to general procedure 2. Integration of the alkene signals of the ^1H NMR spectrum of the crude reaction mixture showed the presence of (+)-**18** and a compound tentatively identified as the ethyl derivative **19** in a 3.5:1 ratio. Flash column chromatography (3:1) provided diol (+)-**18** (106.6 mg, 0.4751 mmol) as a white solid in 74% yield; mp 139.5–141°C; $[\alpha]_D^{23}$ +40.7 (*c* 3.08, $CHCl_3$); IR (KBr): 3253 cm^{-1}; ^1H NMR (200 MHz): 0.89, 0.98, and 1.07 (d, 3H each, J = 6.4 Hz, J = 7.3 Hz, J = 7.3 Hz), 1.22 (dd, 1H, J = 12.1 Hz, J = 13.5 Hz), 1.28 (s, 3H), 1.55–1.78 (m, 3H), 1.80–1.97 (m, 1H), 2.17–2.30 (m, 2H), 2.39 (dq, 1H, J = 3.2 Hz, J = 7.3 Hz), 3.47 (br m, 1H), 3.72 (br s, 2H), 5.14 (br s, 1H); ^{13}C NMR (50 MHz): 16.8, 20.7, 21.9, 28.3, 29.2, 30.3, 33.2, 44.7, 49.7, 51.7, 72.3, 72.5, 123.3, 134.8; MS: 224 (5, $M^{+\cdot}$), 107 (100). Exact Mass calcd. for $C_{14}H_{24}O_2$: 224.1776; found: 224.1774.

Compound **19** was detected by GC–MS. MS: 238 (3, $M^{+\cdot}$), 220 (15, $M^{+\cdot}$ − H_2O), 180 (31, retro Diels–Alder), 133 (100).

(1*RS*,2*RS*,3*RS*,4*RS*,8*RS*,10*SR*)-10-Methoxy-2,4,8,10-tetramethylbicyclo[4.4.0]-dec-5-en-3-ol (21)

Cycloadduct **20** (174.7 mg, 0.786 mmol) was treated with methyllithium (17.0 mL of 1.4 M in Et_2O, 24 mmol) for 16 h according to general procedure 2. Integration of the alkene signals of the ^1H NMR spectrum of the crude reaction mixture showed the presence of **21** and a compound tentatively identified as the ethyl derivative **23** in a 6.25:1 ratio. Flash column chromatography (3:1) provided **21** (114.5 mg, 0.480 mmol) as a viscous colorless oil in 61% yield. Since this compound was

prone to decomposition, it was not fully characterized; bp 70–80°C/0.05 Torr; ^{1}H NMR (200 MHz): 0.89, 0.98, and 1.08 (three d, 3H each, J = 6.1 Hz, J = 7.4 Hz, J = 7.3 Hz), 1.03 (overlapping with doublets, 1H), 1.24 (s, 3H), 1.58–1.74 (m, 3H), 1.95–2.04 (m, 1H), 2.16–2.27 (m, 2H), 2.39 (dq, 1H, J = 3.2 Hz, J = 7.4 Hz), 3.15 (s, 3H), 3.35 (br s, 1H), 4.83 (br s, 1H), 5.11 (br m, 1H); ^{13}C NMR (50 MHz): 17.2, 21.4, 21.8, 22.1, 28.4, 30.5, 33.6, 42.9, 44.6, 48.6, 52.5, 71.9, 77.2, 124.1, 133.8; MS: 238 (3, $M^{+\cdot}$), 99 (100).

Compound **23** was detected by GC–MS. MS: 252 (1, $M^{+\cdot}$), 237 (weak, $M^{+\cdot} - CH_3$), 220 (4, $M^{+\cdot}$ − MeOH), 202 (2, $M^{+\cdot}$ − MeOH − H_2O), 191 (6, $M^{+\cdot} - CH_3OH - CH_2CH_3$), 163 (7, $M^{+\cdot} - CH_3O$ retro Diels–Alder), 99 (100).

(1*RS*,2*RS*,3*RS*,4*RS*,8*RS*,10*SR*)-4-Butyl-10-methoxy-2,8,10-trimethylbicyclo[4.4.0]dec-5-en-3-ol (22)

Cycloadduct **20** (39.3 mg, 0.177 mmol) was treated with *n*-butyllithium (0.15 mL of 2.5 M in Et_2O, 0.38 mmol) for 6 h according to general procedure 1. Flash column chromatography (3:1) provided **22** (35.2 mg, 0.125 mmol) as a viscous colorless oil in 71% yield; bp 85–95°C/0.08 Torr; IR (neat): 3368 cm^{-1}; ^{1}H NMR (200 MHz): 0.89, 0.92, and 0.97 (overlapping d, t, and d, 9H, coupling for doublets J = 6.0 Hz, J = 7.4 Hz), 1.03 (dd, 1H, J = 11.6 Hz, J = 14.2 Hz), 1.24 (s, 3H), 1.29–1.74 (m, 9H), 1.96–2.05 (m, 2H), 2.21–2.27 (m, 1H), 2.36 (dq, 1H, J = 2.9 Hz, J = 7.4 Hz), 3.15 (s, 3H), 3.45 (dm, 1H, J = 9.2 Hz), 4.91 (d, 1H, J = 9.2 Hz), 5.18 (br s, 1H); ^{13}C NMR (50 MHz): 14.1, 21.4, 21.8, 22.1, 23.0, 28.4, 29.4, 31.4, 33.5, 35.8, 42.8, 44.7, 48.6, 52.8, 70.2, 77.2, 122.9, 133.8; MS: 280 (1, $M^{+\cdot}$), 99 (100). Exact Mass calcd. for $C_{18}H_{32}O_2$: 280.2402; found: 280.2410.

(1*RS*,2*SR*,3*SR*,4*SR*,8*SR*)-2,4,8-Trimethyl-10-methylidenebicyclo[4.4.0]dec-5-en-3-ol (25) and (1*RS*,2*SR*,3*SR*,4*SR*,8*SR*)-4-ethyl-2,8-dimethyl-10-methylidenebicyclo-[4.4.0]dec-5-en-3-ol (26)

Compound **24** (6) (1.027 g, 5.40 mmol) was treated with methyllithium (116 mL of 1.4 M in Et_2O, 162 mmol) for 24 h according to general procedure 2. Flash column chromatography (9:1) provided **25** (0.755 g, 3.66 mmol) and **26** (0.136 g, 0.615 mmol) in yields of 68 and 11%, respectively. Both compounds were relatively unstable and were therefore not fully characterized. Compound **25** was a viscous colorless oil that sometimes crystallized upon storage in the refrigerator; mp 61–62.5°C; ^{1}H NMR (200 MHz): 0.94, 0.98, and 1.08 (d, 3H each, J = 6.2 Hz, J = 7.0 Hz, J = 6.3 Hz), 1.36–1.61 (m, 2H), 1.75 (apparent br t composed of 2 overlapping br d at 1.72 and 1.78, 2H, J = 12.6 Hz, J = 12.2 Hz), 2.12–2.42 (m, 5H), 3.60 (dd, 1H, J = 4.8 Hz, J = 8.8 Hz), 4.76–4.79 (m, 2H), 5.28 (m, 1H); ^{13}C NMR (50 MHz): 14.9, 17.7, 22.1, 31.3, 33.8, 35.7, 44.1, 45.9, 50.1, 74.8, 106.1, 123.2, 137.6, 149.4; MS: 206 (2, $M^{+\cdot}$), 188 (27, $M^{+\cdot} - H_2O$), 173 (35, $M^{+\cdot} - H_2O - CH_3$), 148 (100, retro Diels–Alder).

Compound **26** was a viscous colorless oil. ^{1}H NMR (200 MHz): 0.98 and 1.05 (overlapping d and t, d, 9H, J = 6.2 Hz, J = 6.2 Hz, J = 6.3 Hz), 1.12–1.32 (m, 1H), 1.33–1.89 (m, 5H), 1.97–2.15 (br s, 1H), 2.20–2.48 (m, 4H), 3.65 (br s, 1H), 4.80 (br s, 2H), 5.33 (m, 1H); ^{13}C NMR (50 MHz): 11.9, 18.1, 22.1, 23.3, 31.9, 35.8, 40.1, 44.4, 46.0, 49.6, 73.9, 106.2, 121.2, 137.7, 149.7; MS: 220 (2, $M^{+\cdot}$), 202 (27, $M^{+\cdot} - H_2O$), 162 (100, retro Diels–Alder).

(1*RS*,2*RS*,3*RS*,4*RS*,8*SR*,10*SR*)-4-Ethyl-2,8,10-trimethylbicyclo[4.4.0]dec-5-en-3-ol from hydrogenation of 26

Compound **26** (51.8 mg, 0.235 mmol) was dissolved in a mixture of EtOH (10 mL) and benzene (1 mL) in a round-bottom flask. Platinum oxide hydrate (10 mg) was added, and the reaction vessel was evacuated with a water aspirator and back-purged with hydrogen three times. After the reaction had been stirred under a balloon atmosphere of hydrogen for 50 min at room temperature, the catalyst was removed by filtration and the reaction flask and catalyst were washed well with additional ethanol. The solvent was removed from the combined organic phases in vacuo to give the hydrogenated compound (52.2 mg, 0.235 mmol) as a white solid in 100% yield following purification by flash column chromatography (5:1). Sublimation point 64–70°C/0.05 Torr; IR (KBr): 3393 cm^{-1}; ^{1}H NMR (200 MHz): 0.80, 0.86, and 1.01 (d, 3H each, J = 7.0 Hz, J = 6.0 Hz, J = 6.2 Hz), 0.98 (t, 3H, J = 6.9 Hz), 1.05–1.27 (m, 2H), 1.42–1.82 (m, 7H), 2.03–2.22 (m, 3H), 3.50 (dd, 1H, J = 5.3 Hz, J = 10.7 Hz), 5.57 (dt, 1H, J = 1.7 Hz, J = 6.2 Hz); ^{13}C NMR (50 MHz): 12.2, 14.4, 15.9, 22.5, 22.8, 26.9, 30.3, 32.5, 42.4, 42.8, 44.0, 49.2, 75.5, 123.7, 136.9; MS: 222 (23, $M^{+\cdot}$), 204 (9, $M^{+\cdot} - H_2O$) 135 (100, $M^{+\cdot} - CH_2CH_3$ retro Diels–Alder). Exact Mass calcd. for $C_{15}H_{26}O$: 222.1984; found: 222.1975.

(1*RS*,2*RS*,3*RS*,4*RS*,8*SR*,10*SR*)-4-Ethyl-2,8,10-trimethylbicyclo-[4.4.0]dec-5-en-3-yl *p*-nitrobenzoate (27)

The hydrogenated compound produced above (33.3 mg, 0.150 mmol) was sublimed under reduced pressure (0.05 Torr) and dissolved in dry CH_2Cl_2 (5 mL) in a N_2-purged round-bottom flask. DMAP (27.9 mg, 0.228 mmol) and *para*-nitrobenzoyl chloride (41.7 mg, 0.225 mmol) were added to the flask and the reaction mixture was stirred at room temperature for 19 h. Et_2O (20 mL) and H_2O (5 mL) were added to the reaction, and the organic layer was washed with 1% aqueous HCl (3 mL) and 5% aqueous $NaHCO_3$ (5 mL). After the organic layer had been dried with anhydrous Na_2SO_4 and filtered, the solvent was removed in vacuo to provide ester **27** (55.5 mg, 0.149 mmol) as a slightly yellow solid in 99% yield after purification by flash column chromatography (9:1); mp 141–142°C; ^{1}H NMR (200 MHz): 0.85 and 0.87 (overlapping d and t, 6H, J = 6.8 Hz, J = 7.0 Hz), 0.97 (d, 6H, J = 6.6 Hz), 1.18–1.37 (m, 2H), 1.57–1.74 (m, 4H), 1.89–2.30 (m, 2H), 2.30–2.49 (m, 1H), 5.03 (dd, 1H, J = 5.4 Hz, J = 11.3 Hz), 5.59 (br d, 1H, J = 6.3 Hz), 8.21–8.34 (AA′BB′ m, 4H); ^{13}C NMR (50 MHz): 12.0, 14.4, 15.8, 22.5, 23.7, 26.8, 30.1, 30.4, 39.4, 42.6, 43.7, 48.9, 79.9, 122.8, 123.6, 130.6, 136.2, 137.1, 150.5, 164.2.

X-ray crystal structure data for compound 27

A sample of **27** was recrystallized from pentane to give slightly yellow plates, which were submitted for X-ray crystallographic analysis. Crystal data: empirical formula $C_{22}H_{29}NO_4$; space group $C2/c$ (no. 15); a = 10.678(7) Å, b = 9.076(8) Å; c = 42.37(2) Å; β = 93.24(5)°; V = 4099(4) Å^3; Z = 8; d = 1.204 g/cm^3; Mo-Kα radiation (−73°C); total of 3046 reflections in the range $0 < 2\theta < 50.1°$, of which 517 were used ($I > 3\sigma(I)$) in the structure solution; R = 0.108 and Rw = 0.119.

(1*RS*,8*RS*,9*SR*)-8-Butyl-9-hydroxy-1-methylbicyclo[4.4.0]dec-6-en-2-one (30*a*) and (1*RS*,2*SR*,8*RS*,9*SR*)-2,8-dibutyl-1-methylbicyclo[4.4.0]dec-6-en-2,9-diol (31*a*)

General procedure 1 was used to prepare compounds **30*a*** and **31*a***. Cycloadduct **29** (55.3 mg, 0.310 mmol) was treated with *n*-butyllithium (0.37 mL of 2.5 M in hexanes, 0.93 mmol) for 89 h to give ketone **30*a*** (45.1 mg, 0.191 mmol) and diol **31*a*** (7.6 mg, 0.026 mmol) in yields of 6 and 8%, respectively, following purification by flash column chromatography (3:1). Compound **30*a*** was a white solid, mp 55–57°C; IR (KBr): 3445, 1707, 1659 cm^{-1}; ^1H NMR (200 MHz): 0.88 (br m, 3H), 1.10–1.40 (m, 5H), 1.33 (s, 3H), 1.46 (dd, 1H, J = 2.6 Hz, J = 14.1 Hz), 1.50–1.80 (m, 2H), 1.78 (br s, 1H), 1.98–2.15 (m, 2H), 2.16–2.41 (m, 2H), 2.44–2.74 (overlapping m, 3H), 3.95–4.02 (m, 1H), 5.36 (poorly resolved dd, 1H, J = 1.4 Hz, J = 3.0 Hz); ^{13}C NMR (50 MHz): 14.0, 22.9, 26.0, 26.5, 29.4, 30.0, 30.5, 36.4, 37.7, 40.3, 51.0, 66.7, 125.6, 139.0, 214.5; MS: 236 (17, $M^{+\cdot}$), 192 (28, retro Diels–Alder), 137 (100). Exact Mass calcd. for $C_{15}H_{24}O_2$: 236.1776; found: 236.1768.

Compound **31*a*** was characterized as a white solid, mp 104–106°C; IR (KBr): 3348 cm^{-1}; ^1H NMR (200 MHz): 0.91 and 0.92 (two overlapping br t, 6H), 1.15 (s, 3H), 1.22–1.74 (m, 18H), 1.90–2.38 (m, 4H), 2.33 (dd, 1H, J = 8.0 Hz, J = 13.9), 3.89 (m, 1H), 5.41 (poorly resolved dd, 1H, J = 1.7 Hz, J = 3.8 Hz); ^{13}C NMR (50 MHz): 14.1, 14.2, 22.3, 23.0, 23.6, 25.4, 25.5, 29.6, 30.4, 31.3, 31.4, 34.6, 36.7, 40.4, 44.6, 67.3, 76.2, 125.5, 141.9; MS: 294 (1, $M^{+\cdot}$), 276 (8, $M^{+\cdot} - H_2O$), 41 (100). Exact Mass calcd. for $C_{19}H_{34}O_2$: 294.2559; found: 294.2534.

(1*RS*,5*RS*,6*RS*,8*RS*)-5,6-Dimethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-ol (32*b*)

Anhydrous Et_2O (2 mL) was placed in a N_2-purged three-neck round-bottom flask equipped with an addition funnel containing a solution of cycloadduct **29** (67.7 mg, 0.380 mmol) in anhydrous Et_2O (5 mL). The flask was cooled with an ice bath, and methyllithium (0.80 mL of 1.4 M in Et_2O, 1.1 mmol) and dry TMEDA (7.8 mL) were added. The solution of **29** was added dropwise from the addition funnel, and the reaction was warmed to room temperature and stirred for 312 h. Wet Et_2O (10 mL) and saturated aqueous NH_4Cl (10 mL), were then added sequentially, and the aqueous layer was extracted with Et_2O (4 × 10 mL). The combined organic layers were washed with 10% aqueous $CuSO_4$ (2 × 30 mL), dried over anhydrous Na_2SO_4, and filtered. The solvent was removed from the filtrate in vacuo. Flash column chromatography (20:1 benzene:acetone) provided **32*b*** (44.9 mg, 0.231 mmol) as a colorless oil in 61% yield; bp 40–50°C /0.07 Torr; IR (neat): 3457 cm^{-1}; ^1H NMR (200 MHz): 0.91 (d, 1H, J = 11.5 Hz), 0.96 (s, 3H), 1.10 (d, 3H, J = 1.1 Hz), 1.51–2.25 (m, 6H), 2.66 (dd, 1H, J = 5.2 Hz, J = 11.5 Hz), 4.42 (d, 1H, J = 1.1 Hz), 4.84 (dd, 1H, J = 1.7 Hz, J = 5.2 Hz), 6.04 (d, 1H, J = 5.8 Hz), 6.48 (dd, 1H, J = 1.7 Hz, J = 5.8 Hz); ^{13}C NMR (50 MHz): 16.7, 21.3, 25.5, 26.7, 34.7, 35.7, 44.3, 73.1, 78.6, 91.6, 137.6, 138.0; MS: 194 (weak, $M^{+\cdot}$), 176 (4, $M^{+\cdot} - H_2O$), 94 (100). Exact Mass calcd. for $C_{12}H_{18}O_2$: 194.1307; found: 194.1294.

(1*RS*,5*RS*,6*RS*,8*RS*)-6-Methyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-ol (32*c*)

Cycloadduct **29** (56.4 mg, 0.316 mmol) was placed in a N_2-purged three-neck round-bottom flask and dissolved in THF (4 mL). The solution was cooled using a −78°C cold bath, and lithium *tert*-butyldiisobutylaluminohydride (0.48 mL of 1.0 M in THF, 0.48 mmol) was added by syringe. The mixture was stirred at −78°C until analysis by TLC indicated that the starting material had been consumed (30 min). Solid $Na_2SO_4 \cdot 10H_2O$ (150 mg, 0.466 mmol) was added, and the reaction was poured into a mixture of 0.5 M aqueous $KHSO_4$ (10 mL) and $CHCl_3$ (5 mL) and stirred for 30 min. The aqueous layer was extracted with $CHCl_3$ (4 × 10 mL). After the combined organic layers had been dried with anhydrous Na_2SO_4 and filtered, the solvent was removed in vacuo to give **32*c*** (57.0 mg, 0.316 mmol) exclusively in 100% yield after purification by flash column chromatography (5:1). Compound **32*c*** was characterized as a colorless oil, bp 45–50°C/0.05 Torr; IR (neat): 3488 cm^{-1}; ^1H NMR (200 MHz): 0.95 (overlapping s and d, 4 H, J = 11.4 Hz for d), 1.46–1.52 (m, 1H), 1.72–2.19 (m, 5H), 2.66 (dd, 1H, J = 5.2 Hz, J = 11.4 Hz), 3.27 (br s, 1H), 3.58 (br s, 1H), 4.82 (dd, 1H, J = 1.6 Hz, J = 5.2 Hz), 5.98 (d, 1H, J = 5.8 Hz), 6.50 (dd, 1H, J = 1.6 Hz, J = 5.8 Hz); ^{13}C NMR (50 MHz): 15.0, 22.4, 25.5, 28.5, 37.5, 40.5, 73.4, 78.2, 90.5, 136.6, 138.7; MS: 180 (1, $M^{+\cdot}$), 162 (3, $M^{+\cdot} - H_2O$), 94 (100). Exact Mass calcd. for $C_{11}H_{16}O_2$: 180.1150; found: 180.1154.

(1*RS*,2*SR*,8*RS*,9*SR*)-2,8-Dibutyl-9-methylbicyclo[4.4.0]dec-6-en-2,9-diol (36*a*) and (1*RS*,5*RS*,6*RS*,10*RS*)-5,10-dibutyl-8-methylbicyclo[4.4.0]dec-8-en-1,5-diol (37*a*)

General procedure 1 was used to prepare a mixture of compounds **36*a*** and **37*a***. Cycloadduct **35** (69.5 mg, 0.390 mmol) was treated with *n*-butyllithium (0.47 mL of 2.5 M in hexanes, 1.2 mmol) for 16 h to give compounds **36*a*** and **37*a*** in a 1.7:1 ratio based on the integration of the alkene signals at 5.50 and 5.23 ppm, respectively, in the crude ^1H NMR spectrum. These two compounds could not be separated by column chromatography. Fortunately, compound **36*a*** was slightly less soluble in a mixture of 1:1 petroleum ether:Et_2O so that washing the mixture of compounds with this solvent system provided a pure sample of **36*a*** (25.6 mg, 0.0869 mmol) along with a mixture of both compounds (66.0 mg, 0.224 mmol) in a combined yield of 80%. Attempts to secure a pure sample of **37*a*** through recrystallization were not successful.

Compound **36*a*** was characterized as a white solid, mp 132–133°C; IR (KBr): 3230 cm^{-1}; ^1H NMR (200 MHz): 0.92 and 0.93 (overlapping t, 6H, J = 7.0 Hz), 1.22 (s, 3H), 1.11–1.78 (m, 18H), 1.79–2.04 (overlapping m and dd, 3H, J = 4.7 Hz, J = 13.9 Hz for dd), 2.11–2.28 (m, 2H), 2.63 (br s, 1H), 5.50 (br s, 1H); ^{13}C NMR (50 MHz): 14.1, 14.1, 22.5, 23.0, 23.3, 26.2, 28.3, 29.9, 30.1, 30.1, 34.4, 35.0, 36.5, 43.5, 45.2, 69.7, 74.3, 125.2, 135.3; MS: 294 (3, $M^{+\cdot}$), 276 (49, $M^{+\cdot} - H_2O$), 174 (100). Exact Mass calcd. for $C_{19}H_{34}O_2$: 294.2559; found: 294.2559.

Since compound **37*a*** could not be purified, it was not characterized. The ^1H NMR spectrum showed signals at 1.75 (br s, 3H) and 5.23 (br s, 1H). The compound was detected by GC–MS. MS: 294 (100, $M^{+\cdot}$), 276 (78, $M^{+\cdot} - H_2O$), 258 (13, $M^{+\cdot} - 2H_2O$), 237 (17, $M^{+\cdot} - n$-Bu), 219 (41, $M^{+\cdot} - H_2O - n$-Bu), 201 (39, $M^{+\cdot} - 2H_2O - n$-Bu).

(1*RS*,2*RS*,8*RS*,9*SR*)-9-Methyl-2,8-di-(1-methylethyl)bicyclo[4.4.0]dec-6-en-2,9-diol (36*b*) and

(1*RS*,5*SR*,6*RS*,10*RS*)-8-methyl-5,10-di-(1-methylethyl)bicyclo[4.4.0]dec-8-en-1,5-diol (37*b*)

A solution of isopropyllithium was prepared using the method of Gilman et al. (7) as described for compound **2*b***. Standardization against 2,5-dimethoxybenzyl alcohol (34) indicated that the supernatant was 0.22 M in isopropyllithium.

General procedure 1 was used to prepare a mixture of compounds **36*b*** and **37*b***. Cycloadduct **35** (51.2 mg, 0.287 mmol) was treated with the prepared solution of isopropyllithium (5.6 mL of 0.22 M in pentane, 1.2 mmol) for 16 h to give compounds **36*b*** and **37*b*** in a 1.5:1 ratio based on the integration of the alkene signals at 5.43 and 5.23 ppm, respectively, in the crude ^{1}H NMR spectrum. Flash column chromatography (5:1) provided a pure sample of **37*b*** (18.6 mg, 0.0698 mmol) and a mixture of **36*b*** and **37*b*** (54.2 mg, 0.203 mmol) in a combined yield of 95%.

An impure mixture of **36*b*** containing approximately 15% of **37*b*** was partially characterized. ^{1}H NMR (200 MHz, not including signals due to **37*b***): 0.88 (d, 3H, J = 7.1 Hz), 0.93 (d, 6H, J = 6.7 Hz), 1.01 (d, 3H, J = 7.0 Hz), 1.22 (s, 3H), 1.24–2.50 (m, 13H), 2.82 (br s, 1H), 5.43 (br s, 1H); ^{13}C NMR (50 MHz, not including signals due to **37*b***): 16.4, 17.4, 19.3, 22.4, 23.9, 26.8, 29.2, 29.5, 33.6, 34.9, 35.3, 42.4, 50.2, 70.1, 76.4, 121.9, 136.6; MS: 266 (1, $M^{+\cdot}$), 248 (7, $M^{+\cdot} - H_2O$), 230 (0.3, $M^{+\cdot} - 2H_2O$), 223 (1, $M^{+\cdot} - (CH_3)_2CH$), 43 (100).

Compound **37*b*** was characterized as a white solid, mp 109–111°C; IR (KBr): 3430, 3373 cm^{-1}; ^{1}H NMR (200 MHz): 0.80, (d, 3H, J = 7.0 Hz), 0.88 (d, 3H, J = 6.6 Hz), 0.91 (d, 3H, J = 6.6 Hz), 0.96 (d, 3H, J = 7.0 Hz), 1.05–1.30 (m, 3H), 1.51–2.02 (m, 7H), 1.77 (br s, 3H), 2.02–2.41 (m, 3H), 3.95 (br s, 1H), 5.23 (br s, 1H); ^{13}C NMR (50 MHz): 15.7, 16.4, 17.4, 18.0, 23.4, 23.7, 25.3, 26.2, 29.0, 33.3, 35.0, 42.7, 51.8, 74.2, 75.8, 118.1, 135.1; MS: 266 (8, $M^{+\cdot}$), 248 (1, $M^{+\cdot} - H_2O$), 230 (0.3, $M^{+\cdot} - 2H_2O$), 223 (1, $M^{+\cdot} - (CH_3)_2CH$), 113 (100). Exact Mass calcd. for $C_{17}H_{30}O_2$: 266.2246; found: 266.2243.

(1*RS*,2*SR*,8*SR*,9*SR*)-2,8-Di(1,1-dimethylethyl)-9-methylbicyclo[4.4.0]dec-6-en-2,9-diol (36*c*), (1*RS*,5*RS*,6*SR*,10*SR*)-5,10-di-(1,1-dimethylethyl)-8-methylbicyclo[4.4.0]dec-8-en-1,5-diol (37*c*), and (1*RS*,6*SR*,7*RS*)-7-(1,1-dimethylethyl)-6-hydroxy-9-methylbicyclo[4.4.0]dec-8-en-2-one (34)

General procedure 1 was used to prepare a mixture of compounds **36*c***, **37*c***, and **34**. Cycloadduct **35** (56.4 mg, 0.316 mmol) was treated with *tert*-butyllithium (0.56 mL of 1.7 M in hexanes, 0.95 mmol) for 3 h at 0°C to give compounds **36*c***, **37*c***, and **34**. The ratio of **36*c***:(**37*c*** and **34**) was 2.2:1 based on the integration of the alkene signals at 5.54 and 5.35 ppm, respectively, in the crude ^{1}H NMR spectrum. Flash column chromatography (9:1) provided a pure sample of **36*c*** (31.7 mg, 0.108 mmol) and a mixture of **36*c*** and **37*c*** (19.1 mg, 0.0648 mmol) in a combined yield of 55%. Compound **34** (8.8 mg, 0.037 mmol) was also isolated in 12% yield.

Compound **36*c*** was characterized as a white solid, mp 128–129°C; IR (KBr): 3439, 3362 cm^{-1}; ^{1}H NMR (200 MHz): 1.07 and 1.11 (two s, 9H each), 1.30 (s, 3H), 1.26–1.73 (m, 6H), 1.80–2.05 (m, 3H), 2.13–2.41 (m, 3H), 5.54 (m, 1H); ^{13}C NMR (50 MHz): 23.4, 27.7, 30.3, 32.6, 33.7, 35.2, 36.1, 38.6, 39.6, 44.2, 53.7, 72.8, 78.1, 125.5, 136.8; MS: no $M^{+\cdot}$, 276 (8, $M^{+\cdot} - H_2O$), 261 (0.5, $M^{+\cdot} - H_2O - CH_3$), 237 (0.5, $M^{+\cdot} - t$-Bu), 57 (100). Anal. calcd. for $C_{19}H_{34}O_2$: C 77.48, H 11.66; found: C 77.39, H 11.21.

X-ray crystal structure data for compound 36*c*

A sample of **36*c*** was recrystallized from pentane to give colorless prisms that were submitted for X-ray crystallographic analysis. See Fig. 2 for the X-ray crystal structure. Crystal data: empirical formula $C_{19}H_{34}O_2$; space group $P2_1/c$ (no. 14); a = 8.715(3) Å; b = 20.215(4) Å; c = 9.866(3) Å; β = 94.01(2)°; V = 1733.9(8) Å^3; Z = 4; d = 1.128 g/cm^3; Mo-Kα radiation (−123°C); total of 3396 reflections in the range $0 < 2\theta < 50.1°$, of which 1941 were used ($I > 3\sigma(I)$) in the structure solution; R = 0.066 and Rw = 0.091.

Since compound **37*c*** could not be purified, it was not characterized. The ^{1}H NMR spectrum showed signals at 1.02 and 1.08 (two s, 9H each), 1.78 (br s, 3H), and 5.35(br s, 1H).

Compound **34** was characterized as a white solid, mp 80–82.5°C; IR (KBr): 3501, 1703 cm^{-1}; ^{1}H NMR (200 MHz): 1.10 (s, 9H), 1.51–1.80 (m, 2H), 1.77 (br s, 3H), 1.88–2.56 (m, 8H), 2.67–2.81 (dm, 1H, J = 13.7 Hz), 5.35 (br s, 1H); ^{13}C NMR (50 MHz): 21.8, 23.8, 25.3, 30.6, 35.4, 37.7, 41.4, 54.8, 55.9, 78.6, 122.2, 133.0, 211.0; MS: 236 (2, $M^{+\cdot}$), 221 (1, $M^{+\cdot} - CH_3$), 218 (1, $M^{+\cdot} - H_2O$), 180 (15, $M^{+\cdot} - C_4H_8$), 109 (100). Exact Mass calcd. for $C_{15}H_{24}O_2$: 236.1776; found: 236.1774.

(1*RS*,5*RS*,6*RS*,8*RS*)-5,8-Dimethyl-11-oxatricyclo[6.2.1.0^{1,6}]undec-9-en-5-ol(38) and (1*RS*,5*RS*,6*RS*)-5-methyl-8-methylidenebicyclo[4.4.0]dec-9-en-1,5-diol (39)

Anhydrous Et_2O (2 mL) was placed in a N_2-purged three-neck round-bottom flask equipped with an addition funnel containing a solution of cycloadduct **35** (59.9 mg, 0.366 mmol) in anhydrous Et_2O (5 mL). The flask was cooled with an ice bath, and methyllithium (0.70 mL of 1.4 M in Et_2O, 0.98 mmol) and dry TMEDA (7.8 mL) were added. The solution of **35** was added dropwise from the addition funnel, and the reaction was warmed to room temperature and stirred for 53 h. Wet Et_2O (10 mL) and saturated aqueous NH_4Cl (10 mL) were then added sequentially, and the aqueous layer was extracted with Et_2O (4 × 10 mL). The combined organic layers were washed with 10% aqueous $CuSO_4$ (2 × 30 mL), dried over anhydrous Na_2SO_4, and filtered. The solvent was removed from the filtrate in vacuo. Flash column chromatography (5:1) provided **38** (22.1 mg, 0.114 mmol) and **39** (25.8 mg, 0.133 mmol) in yields of 31 and 36%, respectively.

Compound **38** was characterized as a colorless oil, bp 40–50°C/0.07 Torr; IR (neat): 3485 cm^{-1}; ^{1}H NMR (200 mHz): 1.12 (s, 3H), 1.15–1.62 (m, 4H), 1.63–1.98 (m, 3H), 1.61 (s, 3H), 2.21–2.34 (m, 2H), 3.46 (br s, 1H), 5.95 (d, 1H, J = 5.6 Hz), 6.30 (d, 1H, J = 5.6 Hz); ^{13}C NMR (50 MHz): 16.7, 28.2, 35.1, 38.6, 18.7, 28.9, 46.2, 69.4, 86.5, 88.2, 138.2, 141.8; MS: 194 (1, $M^{+\cdot}$), 176 (1, $M^{+\cdot} - H_2O$), 161 (1, $M^{+\cdot} - H_2O - CH_3$), 108 (100). Exact Mass calcd. for $C_{12}H_{18}O_2$: 194.1307; found: 194.1293.

Compound **39** was characterized as a light tan solid, mp 129–135°C (dec.); IR (KBr): 3456, 1634, 1597 cm^{-1}; ^{1}H NMR (200 MHz): 1.20 (s, 3H), 1.31–1.59 (m, 4H), 1.71–2.11 (m, 3H), 2.20–3.10 (overlapping m and br s, 4H), 4.96–4.99 (m, 2H), 5.64 and 6.16 (d, 1H each, J = 9.5 Hz); ^{13}C NMR (50 MHz): 17.1, 25.3, 38.2, 40.6, 27.6, 47.2, 69.8, 71.9, 114.2, 131.4, 134.2, 142.9; MS: 194 (4, $M^{+\cdot}$), 176 (17, $M^{+\cdot} - H_2O$),

118 (100). Exact Mass calcd. for $C_{12}H_{18}O_2$: 194.1307; found: 194.1318.

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