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Facial Selectivity in the Nucleophilic Additions of Vinylmagnesium Bromide to Bicyclo[2.2.2]oct-5-en-2-one Derivatives†

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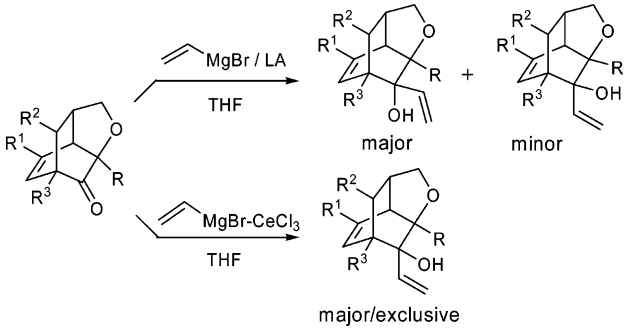

The levels of diastereoselection attainable by addition of vinylmagnesium bromide to a selection of bicyclo-[2.2.2]octenone derivatives **1**−**6** in the presence of various Lewis acids such as LiBr, $CeCl_3$, $TiCl_4$, $ZnBr_2$, $MgBr_2$, and Et_2AlCl have been determined. The 1,2-addition of ketone **1** with vinylmagnesium bromide in THF provided a mixture of *anti*- and *syn*-isomers. The reactions of **2** with vinylmagnesium bromide at room temperature afforded *anti*- and *syn*-isomers with preference to *anti*-isomers in most cases. These reactions in the presence of Lewis acids afforded *anti*-isomers as the major product with an excellent stereoselectivity or as single isomers in some cases. The ketones **3** gave surprisingly different results providing *anti*-isomers predominantly even in the presence of Lewis acids. The bicyclic ketones **4** and **5** and all-carbon tricyclic ketone **6** furnished the *syn*-isomer as the main product. There is no significant effect of Lewis acid catalysis in the nucleophilic addition reactions of **1**, **4**, **5**, and **6**. The use of a preformed vinylmagnesium bromide−$CeCl_3$ reagent for the addition reactions of **2d**−**f** and **3d**−**f** provided almost exclusively *syn*-isomers. The substituents and reaction conditions can influence facial selectivity in the nucleophilic additions to the bicyclo[2.2.2]oct-5-en-2-one derivatives.

Introduction

Bicyclo[2.2.2]octenones and their derivatives are useful synthons that are convertible into polysubstituted cyclohexenes,[1] bicyclo[3.2.1]octenones,[2] bicyclo[4.2.0]octenones,[3,4] tricyclo-[3.3.0.0^{2,8}]octanones,[3] variously fused triquinanes,[5] *cis*-decalins,[6] and bicyclo[4.2.2]decenones[3a] and their intermediates. Organometallic reagents were used in 1,2-addition of bicyclo[2.2.2]-octenone derivatives for the synthesis of natural products such as forskolin,[7] (+)-pallescensin A,[8] and (−)-9-epi-ambrox[9] in

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† This paper is dedicated to the memory of Prof. Yoshihiko Ito.

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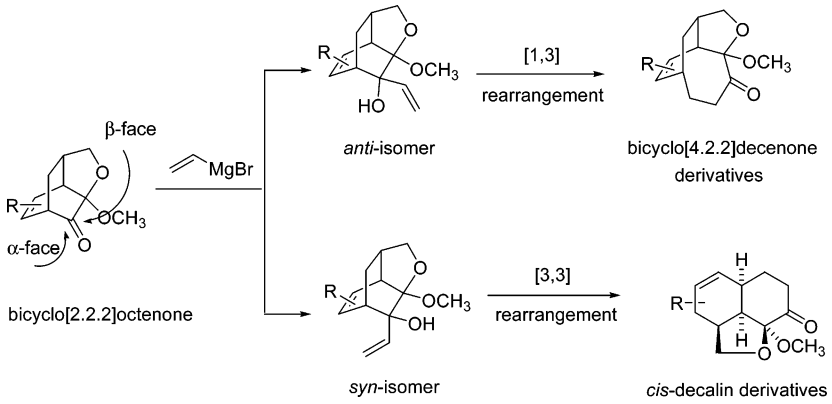
SCHEME 1



which facial selectivity played an important role. Recent reports[10−14] of the stereochemistry of these reactions have stressed applications to the syntheses of natural products. Addition of the Grignard reagent to bicyclo[2.2.2]octenone derivatives followed by anionic oxy-Cope rearrangement is considered as one of the important methodologies for the synthesis of natural products. Stereoselective addition of vinylmagnesium bromide to bicyclo[2.2.2]octenone derivatives is used in the synthesis of pallescensin B[11] and enantiopure *cis*-decalins.[12] An interesting selectivity was observed in the addition of vinylmagnesium bromide to tricyclic hydroxyketone, which is a bicyclo[2.2.2]octanone derivative in the synthesis of vinigrol.[13] Here the addition occurred from the sterically more hindered α-face, which was explained as the presumable influence of chelation versus steric factors.

The addition of vinylmagnesium bromide to bicyclo[2.2.2]-octenone derivatives provides two diastereomers, the *syn*-isomer formed by attack of the nucleophile on the α-face and the *anti*-isomer formed by attack of the nucleophile on the *β*-face of the molecule, respectively. The *anti*-isomer undergoes [1,3]-sigmatropic rearrangement to afford ring expansion products, whereas *syn*-isomer undergoes [3,3]-sigmatropic rearrangement to furnish highly substituted *cis*-decalins (Scheme 1). Both these classes of products are very useful intermediates in the total synthesis of natural products.[10−14] Therefore, knowing how to gain access to each of these isomers in a stereoselective manner is vital to their inclusion in such synthetic strategies being truly effective. In view of the wide applications of vinylbicyclo[2.2.2]-octenol derivatives, we focused on the facial selectivity in the 1,2-addition reaction of vinylmagnesium bromide to bicyclo-[2.2.2]oct-5-en-2-one derivatives.[6a] Herein we describe the details of our studies.

Results

Preparation of Bicyclo[2.2.2]octenone Derivatives 1−6. Bicyclo[2.2.2]octenones **1**−**6** were used as substrates in this study to examine the facial selective outcome upon the addition of vinylmagnesium bromide to their carbonyl function (Figure 1). Bicyclo[2.2.2]octenone **1** was synthesized according to a

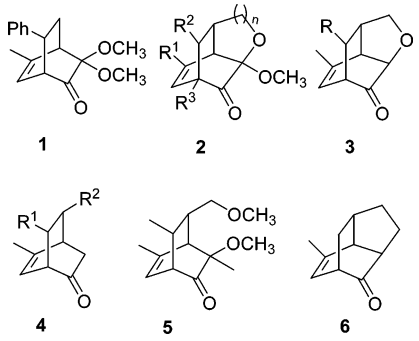


FIGURE 1. Bicyclo[2.2.2]octenone derivatives **1**−**6**.

reported procedure from our laboratory.[15] The tricyclic adducts **2a**−***l*** were synthesized via the intramolecular Diels−Alder reactions of masked *o*-benzoquinones generated in situ from the corresponding 2-methoxyphenols in the presence of substituted alkenols in moderate to good yields.[16] The oxatricyclic enones **3d**−**f** were obtained from **2d**−**f** in a three-step process, namely sequential SmI_2-mediated acetal cleavage,[17a,b] bromination, and cyclization (Scheme 2). Thus, when the compounds **2d**−**f** were treated with 4 equiv of SmI_2 in THF at room temperature, the acetal function was cleaved to provide the alcohols **7d**−**f**. The bromination of **7e** was studied extensively under various conditions with use of $PhNMe_3Br_3$ and NBS in the presence of different bases.[17c] The best results were obtained when the reaction was performed at −78 to 0 °C in THF with $PhNMe_3Br_3$/LDA in the presence of TMSCl as a promoter[17c] (Table 1). These conditions were extended to **7d**,**f** to afford the corresponding products **8d**,**f** in about 76% yield. The cyclization of **8d**−**f** was achieved with NaH/TBAI to give **3d**−**f** in excellent yields.

TABLE 1. Bromination of 7e under Various Reaction Conditions

				yield (%)	
entry	brominating agent	base	promoter	**8e**	**9e**
1	NBS	LDA	TMSCl	53	0
2	$PhNMe_3Br_3$	LDA	TMSCl	76	0
3	$PhNMe_3Br_3$	Et_3N	TMSCl	34	27
4	NBS	Et_3N	TMSCl	33	24
5	NBS	NaH		3	20
6	NBS	Et_3N		0	23
7	NBS	LHMDS		0	44
8	$PhNMe_3Br_3$	LHMDS		0	53

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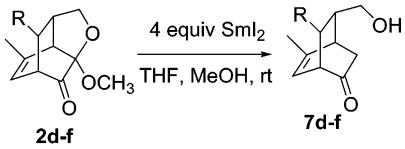
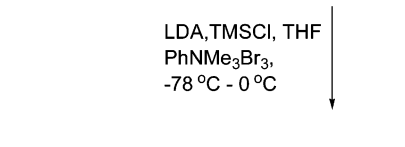
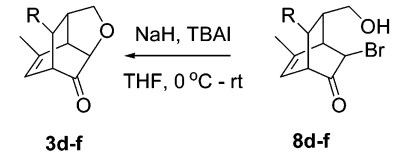
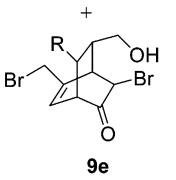
SCHEME 2



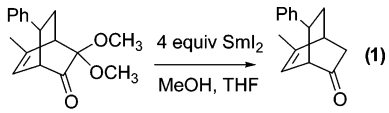


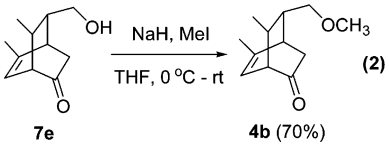


	d	e	f
R	H	CH_3	Ph
7	80%	89%	98%
8	76%	75%	75%
3	93%	95%	96%



The cleavage of the dimethoxyacetal moiety of bicyclo[2.2.2]-octenone **1**[15] with 4 equiv of SmI_2 proceeded smoothly to produce **4a** in high yield (eq 1). The methyl ether **4b** was obtained from the methylation of **7e** (eq 2). Treatment of **2b**



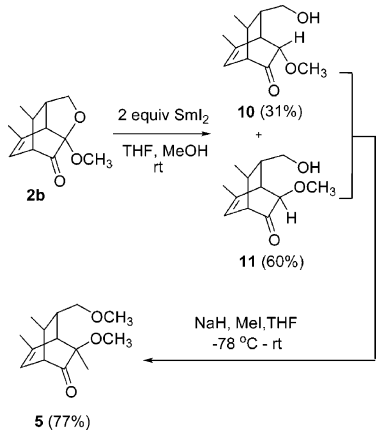


with 2 equiv of SmI_2 resulted in the formation of isomeric alcohols **10** and **11** in 1:2 ratio by cleaving the labile cyclic ether moiety (Scheme 3); the latter compounds were methylated with methyl iodide to obtain **5** in 77% yield.

The all-carbon tricyclic enone **6** was synthesized from the known cycloadduct **2g**.[16] Treatment of **2g** with 4 equiv of SmI_2 provided alcohol **12**, which was then transformed into the mesylate **13**. Cyclization of **13** occurred in the presence of KHMDS to afford **6** in good yield (Scheme 4).

Addition of Vinylmagnesium Bromide under Various Reaction Conditions. The reaction of compound **1** with vinylmagnesium bromide did not proceed at −78 °C; however, **1** afforded the *anti*-**14** and *syn*-**15** isomers in 1.0:0.67 ratio at

SCHEME 3



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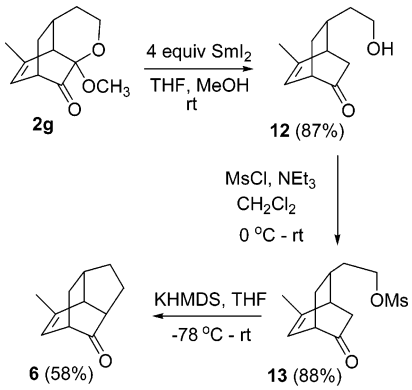

55 °C (eq 3, Table 2). The nucleophilic addition provided similar results when the reaction was carried out in the presence of LiBr. The use of Lewis acids such as $CeCl_3$, $ZnBr_2$, $MgBr_2$, and Et_2AlCl in the reaction enhanced the formation of *syn*-product providing a considerable change in the selectivity of the reaction.[18−20] The reaction did not take place when **1** was

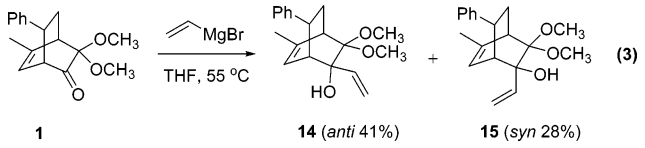

TABLE 2. Product Ratios of Diastereomers in Nucleophilic Addition of Vinylmagnesium Bromide to Ketone 1[a]

entry	reagent[b]	Lewis acid	temp (°C)	products[c] **14**:**15**	yield (%)[d] **14** + **15**
1	RMgBr−$CeCl_3$		−78		0[e]
2	RMgBr		−78 to 5		0[e]
3	RMgBr	$MgBr_2/ZnBr_2$	25		0[e]
4	RMgBr		55	1.0:0.67	69
5	RMgBr	LiBr	55	1.0:0.77	71
6	RMgBr	$CeCl_3$	55	1.0:2.0	76
7	RMgBr	$ZnBr_2$	55	1.0:1.2	71
8	RMgBr	$MgBr_2$	55	1.0:2.0	73
9	RMgBr	Et_2AlCl	55	1.0:1.1	63

[a] All reactions were carried out in THF. [b] R = vinyl. [c] Diastereomeric ratio was based on ^1H NMR integration of the crude reaction mixture. [d] Isolated yields of the diastereomeric mixture. [e] Recovery of **1**.

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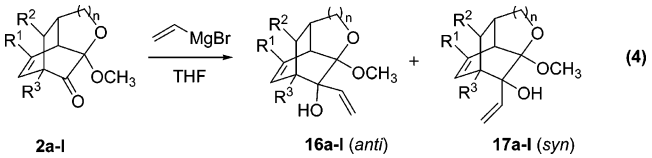

(4)

TABLE 3. Product Ratios in Nucleophilic Addition of Vinylmagnesium Bromide to Ketones 2a−*l*[a]

entry	compd	R^1	R^2	R^3	*n*	products[b] **16**:**17**	yield (%)[c] **16** + **17**
1	**2a**	H	H	H	1	1.0:0.77	82
2	**2b**	H	CH_3	H	1	1.0:0.67	58
3	**2c**	H	Ph	H	1	1.0:1.67	84
4	**2d**	CH_3	H	H	1	1.0:0.63	75
5	**2e**	CH_3	CH_3	H	1	1.0:0.59	81
6	**2f**	CH_3	Ph	H	1	1.0:0.63	73
7	**2g**	CH_3	H	H	2	1.0:2.0	75
8	**2h**	CH_3	H	OCH_3	2	1.0:5.0	86
9	**2i**	CH_3	H	OCH_3	1	1.0:0.43	89
10	**2j**	CH_3	Ph	OCH_3	1	1.0:0.37	86
11	**2k**	CO_2CH_3	H	H	1	1.0:2.0	65
12	**2*l***	CO_2CH_3	CH_3	H	1	1.0:3.3	70

[a] All reactions were carried out in THF at rt. [b] Diastereomeric ratio was based on ^{1}H NMR integration of the crude reaction mixture. [c] Mixture of diastereomers/combined yields of pure and isolated isomers.

treated with a preformed vinylmagnesium bromide−cerium(III) chloride reagent[21] at −78 °C and the starting material **1** was recovered after workup. Addition of Lewis acids, which are expected to increase the carbonyl reactivity and facial selectivity, led only up to a 1.0:2.0 *anti*/*syn* ratio (entries 6 and 8, Table 2), which is unsatisfactory from the synthetic application standpoint.

As the selectivity obtained in the above case was not encouraging, we turned our attention to bicyclo[2.2.2]octenone derivatives **2a**−***l***, anticipating that these compounds bearing a fused oxygen ring system with more rigid structure and various possible chelation sites might lead to increased facial differentiation and provide better selectivities. Consequently, bicyclo[2.2.2]octenone derivatives **2a**−***l*** were subjected to nucleophilic addition reactions with vinylmagnesium bromide in THF at room temperature to afford a mixture of *anti*-**16a**−***l*** and *syn*-**17a**−***l*** vinylbicyclo[2.2.2]octenol derivatives (eq 4, Table 3).[6a] These results are interesting and contrast to those obtained with bicyclo[2.2.2]octenone **1**. The *anti*-isomers **16** were isolated as the major products for the reactions of **2a**,**b**,**d**−**f**,**i**,**j** and the *syn*-isomers **17** were isolated as the major products for the reactions of **2c**,**g**,**h**,**k**,***l*** (eq 4, Table 3). From Table 3 it is essential to note that even in the absence of any chelating agents for the facial differentiation, good selectivities were observed. This suggests that in fact the introduction of a fused ring system in the bicyclo[2.2.2]octenone moiety provided greater effect on the facial differentiation due to the rigid molecular structure.

The selectivity with **2d** was dramatically improved to 1.0:0.2 with preference for the *anti*-isomer when the reaction was performed at −78 °C to rt (Table 4, entry 3). Though the diastereoselectivities from the above studies were impressive, we anticipated enhanced selectivities by the addition of Lewis acid catalysts. Accordingly, the alkoxyketone is tied up with a Lewis acid capable of bis-ligation and the intermediate chelate is then reacted with vinyl Grignard. In the Lewis acid-mediated addition reactions of **2d**−**f**, *anti*-isomers were preferentially formed. Again, $MgBr_2$ showed more promise by providing a single diastereomer in all the cases studied, while $ZnBr_2$ and Et_2AlCl were also effective to furnish such high selectivities as shown in entries 7, 14, and 23 of Table 4. The addition with a preformed vinylmagnesium bromide−cerium(III) chloride reagent at −78 °C offered surprising results with the formation of the highly selective *syn*-isomer in the ratio of 1:15 **(**entries 24−26, Table 4). This kind of reversal in diastereofacial selectivity was also observed previously during the study of organometallic additions to carbonyl compounds.[21c,d,i]

The difference in the facial selectivity between the two series of compounds **1** and **2** prompted us to examine the tricyclic ketones **3d**−**f**, lacking a methoxy group at the cyclic ether

TABLE 4. Product Ratios in Nucleophilic Addition of Vinylmagnesium Bromide to Ketones 2d−f with and without Lewis Acids[a]

entry	compd	Lewis acid/ reagent[b]	products[c] **16**:**17**	yield (%)[d] **16** + **17**
1[e]	**2d**		1.0:0.63	75
2[f]	**2d**		1.0:0.5	78
3	**2d**		1.0:0.2	78
4	**2d**	LiBr	1.0:0.27	65
5	**2d**	$CeCl_3$	1.0:0.25	70
6	**2d**	$TiCl_4$	1.0:0.17	60
7[g]	**2d**	$ZnBr_2$	1.0:<0.01	74
8[g]	**2d**	$MgBr_2$	1.0:<0.01	85
9[g]	**2d**	Et_2AlCl	1.0:<0.01	83
10	**2e**		1.0:0.59	81
11	**2e**	LiBr	1.0:0.63	73
12	**2e**	$CeCl_3$	1.0:0.2	78
13	**2e**	$TiCl_4$	1.0:0.1	67
14[g]	**2e**	$ZnBr_2$	1.0:<0.01	75
15[g]	**2e**	$MgBr_2$	1.0:<0.01	83
16	**2e**	Et_2AlCl	1.0:0.2	69
17	**2f**		1.0:0.33	70
18	**2f**	LiBr	1.0:0.5	72
19	**2f**	$CeCl_3$	1.0:0.25	73
20	**2f**	$TiCl_4$	1.0:0.14	69
21	**2f**	$ZnBr_2$	1.0:0.1	75
22[g]	**2f**	$MgBr_2$	1.0:<0.01	83
23[g]	**2f**	Et_2AlCl	1.0:<0.01	80
24[h]	**2d**	RMgBr−$CeCl_3$	1.0:15	89
25[h]	**2e**	RMgBr−$CeCl_3$	1.0:15	94
26[h]	**2f**	RMgBr−$CeCl_3$	1.0:17	92

[a] All reactions were carried out in THF at − 78 °C to rt unless otherwise mentioned. [b] R = vinyl. [c] Diastereomeric ratio was based on ^{1}H NMR integration of the crude reaction mixture. [d] Isolated yields of diastereomeric mixture. [e] At rt. [f] At 0 °C to rt. [g] *Syn*-isomer was not observed from the ^{1}H NMR of the crude reaction mixture. [h] At − 78 °C.

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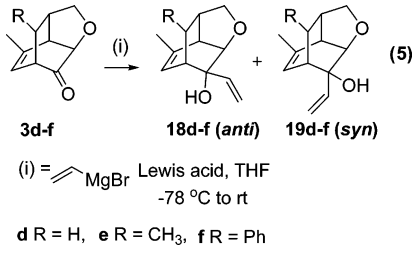


TABLE 5. Product Ratios in Nucleophilic Addition of Vinylmagnesium Bromide to Ketones 3d−f with and without Lewis Acids[a]

entry	compd	Lewis acid/ reagent[b]	products[c] **18**:**19**	yield (%)[d] **18** + **19**
1	**3d**		1.0:0.33	70
2	**3d**	LiBr	1.0:0.5	72
3	**3d**	$CeCl_3$	1.0:0.25	73
4	**3d**	$TiCl_4$	1.0:0.14	69
5	**3d**	$ZnBr_2$	1.0:0.1	75
6[e]	**3d**	$MgBr_2$	1.0:<0.01	83
7[e]	**3d**	Et_2AlCl	1.0:<0.01	80
8	**3e**		1.0:1.0	64
9	**3e**	LiBr	1.0:1.0	61
10	**3e**	$CeCl_3$	1.0:0.33	69
11	**3e**	$TiCl_4$	1.0:0.1	67
12	**3e**	$ZnBr_2$	1.0:0.07	65
13[e]	**3e**	$MgBr_2$	1.0:<0.01	80
14	**3e**	Et_2AlCl	1.0:0.14	75
15	**3f**		1.0:0.5	73
16	**3f**	LiBr	1.0:0.5	69
17	**3f**	$CeCl_3$	1.0:0.2	78
18	**3f**	$TiCl_4$	1.0:0.33	67
19	**3f**	$ZnBr_2$	1.0:0.1	75
20[e]	**3f**	$MgBr_2$	1.0:<0.01	81
21	**3f**	Et_2AlCl	1.0:0.08	79
22[f]	**3d**	RMgBr−$CeCl_3$	1:>99	86
23[f]	**3e**	RMgBr−$CeCl_3$	1:>99	83
24[f]	**3f**	RMgBr−$CeCl_3$	1:>99	91

[a] All reactions were carried out in THF at − 78 °C to rt unless otherwise mentioned. [b] R = vinyl. [c] Diastereomeric ratio was based on ^{1}H NMR integration of the crude reaction mixture. [d] Isolated yields of diastereomeric mixture. [e] *Syn*-isomer was not observed from the ^{1}H NMR of crude reaction mixture. [f] At − 78 °C.

linkage. The nucleophilic addition of vinyl Grignard on to these compounds in the presence of Lewis acids provided *anti*-isomers as major adducts (eq 5, Table 5). But it is important to note that the addition with a preformed vinylmagnesium bromide−cerium(III) chloride reagent provided highly selective *syn*-isomers almost exclusively (entries 22−24, Table 5). From Table 5, it is apparent that the cyclic ether moiety still plays a vital role in dictating the facial selectivity in the nucleophilic addition to carbonyl of bicyclooctenones **3d**−**f**.

To evaluate the effect of the cyclic ether ring in the diastereochemical outcome, we next studied the nucleophilic addition reactions of bicyclo[2.2.2]octenones **4a**,**b** which lack a cyclic ether moiety. The compounds **4a** and **4b**, with no substitutions at C3, reacted with vinylmagnesium bromide at −78 °C to room temperature and afforded a mixture of *anti*-**20a**,**b** and *syn*-**21a**,**b** isomers, the latter compound being the predominant isomeric product. The observed diastereoselectivity reversal in the nucleophilic addition reaction of **4a** in comparison to that of **1**−**3** indicates the profound effect of the dimethoxy group in **1** at the α-position to the reacting carbonyl moiety and fused cyclic ether in **2**, **3**. The reactions of **4a** were studied in detail in the presence of several Lewis acids and no significant difference in the facial selectivity was observed (eq 6, Table 6).

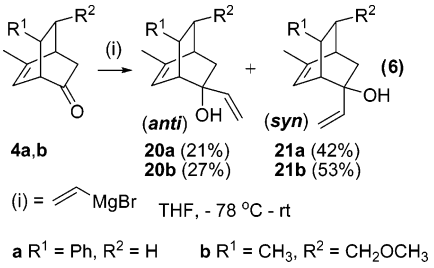


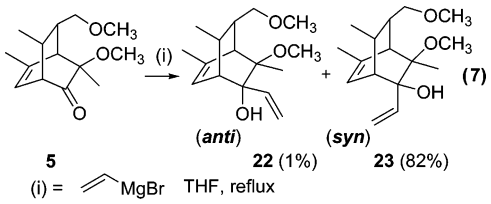
TABLE 6. Product Ratios of Diastereomers in Nucleophilic Addition of Vinylmagnesium Bromide to Ketone 4a[a]

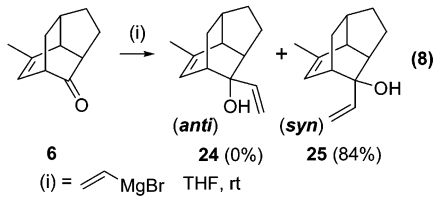
entry	reagent[b]	Lewis acid	temp (°C)	products[c] **20a**:**21a**	yield (%)[d] **20a** + **21a**
1	RMgBr−$CeCl_3$		−78		−[e]
2	RMgBr		−78 to rt	1.0:2.0	63
3	RMgBr	LiBr	−78 to rt	1.0:2.0	61
4	RMgBr	$CeCl_3$	−78 to rt	1.0:3.0	69
5	RMgBr	$TiCl_4$	−78 to rt	1.0:3.0	67
6	RMgBr	$ZnBr_2$	−78 to rt	1.0:2.5	65
7	RMgBr	$MgBr_2$	−78 to rt	1.0:3.0	80
8	RMgBr	Et_2AlCl	−78 to rt	1.0:2.0	75

[a] All reactions were carried out in THF. [b] R = vinyl. [c] Diastereomeric ratio was based on ^{1}H NMR integration of the crude reaction mixture. [d] Isolated yields of diastereomeric mixture. [e] Recovery of **4a**.

Compounds **4a** and **4b** behaved similar to parent bicyclooctenone **26**, further indicating the effect of α-substituents in the observed selectivities in other bicyclooctenone systems studied. As in the case of **1**, bicyclo[2.2.2]octenones **4a**,**b** did not react with the vinylmagnesium bromide−cerium(III) chloride system at −78 °C and the starting materials were recovered after workup.

The bicyclo[2.2.2]octenone **5** with 3α-methyl and 3*β*-methoxy groups was then subjected to nucleophilic addition with vinylmagnesium bromide. *syn*-Isomer was formed almost exclusively (eq 7). With an intension to know the part played by oxygen of the cyclic ether present in the 5-membered rigid moiety, compound **6** having no oxygen atom was synthesized. A single diastereomer *syn*-**25** was obtained in excellent yield upon vinylmagnesium bromide addition (eq 8).





A chemical correlation was performed to prove the stereochemistry of isomers **16** and **17**. Thus, when a set of selected *syn*-isomers were subjected to anionic oxy-Cope rearrangement conditions, *cis*-decalins were furnished in excellent yields, whereas under similar conditions, the *anti*-isomers afforded

bicyclo[4.2.2]octenone systems by a 1,3-sigmatropic rearrangement.[6a] This variation in the rearrangement reaction can be accounted for in terms of the geometrical orientation of the vinyl moieties in the isomers; *syn*-isomers with proximate double bonds easily underwent anionic oxy-Cope rearrangement but not the *anti*-isomers.

Interesting correlation can also be inferred from diagnostic chemical shifts of the vinyl moiety of the *anti*-**16** and *syn*-**17** isomers (Figure 2). In the ^{1}H NMR, the vinyl protons at the terminus of the allylic alcohol moiety of *anti*-isomer (δ_{12a} and δ_{12b} in **16**, Figure 2) are more separated (0.26−0.31 ppm) than the corresponding protons of the *syn*-isomer (δ_{12a} and δ_{12b} in **17**). The stereochemical assignment of these products is supported by the observation that the vinyl protons at the terminus of the allylic alcohol moiety of *syn*-adducts **17** (α-face approach) appear at higher field than the corresponding protons of **16**. In the *anti*-adducts **16** (*β*-face approach), the methine proton H-11 of the vinyl group appears more downfield than the methine proton of the *syn*-adducts **17**. The variation in the vinyl protons of *anti*-**16** and *syn*-**17** isomers is presumably a consequence of the anisotropic effect of the C_8-C_9 double bond,[13a−c] and the deshielding effect of the neighboring ketal group on them. This trend could be observed in all the *anti*/*syn*-isomers **16a**−***l*** and **17a**−***l***. The structures of all the *anti*/*syn*-isomers were determined by analogy of their coupling patterns and the chemical shift values (see the Supporting Information).

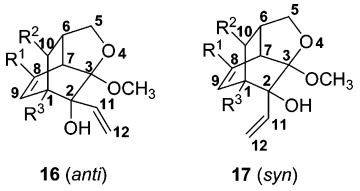


FIGURE 2. Structural determination of compounds **16** (*anti*-isomer) and **17** (*syn*-isomer).

Discussion

Recently, the facial selectivity in nucleophilic additions to the bicyclo[2.2.2]octan-2-one derivatives was studied in detail.[13,23,24] The 1,2-addition of alkenyl anions to *β*,*γ*-unsaturated ketones operates under kinetic control and the outcome of the facial selectivity is most often governed by steric and electronic factors.[18−20,22] In the nucleophilic additions on the parent bicyclo[2.2.2]octenone system **26**,[25]the α-face is electronically rich and hence the hydride nucleophile (which is smaller in size) comes from the *β*-face and provides the *anti*-isomer **29** as the major adduct. But when a nucleophile such as vinyl Grignard is used, steric effects come into play. Thus, compared to C(sp^2)-H, the C(sp^3)-H is more crowded and hence bulky vinyl Grignard (compared to hydride) attacks from the α-face to provide *syn*-isomer **28** as the major adduct (Figure 3).[25]

In the present study, bicyclo[2.2.2]octenone derivatives **4a** and **4b** with no α-substitutions have shown similar selectivities

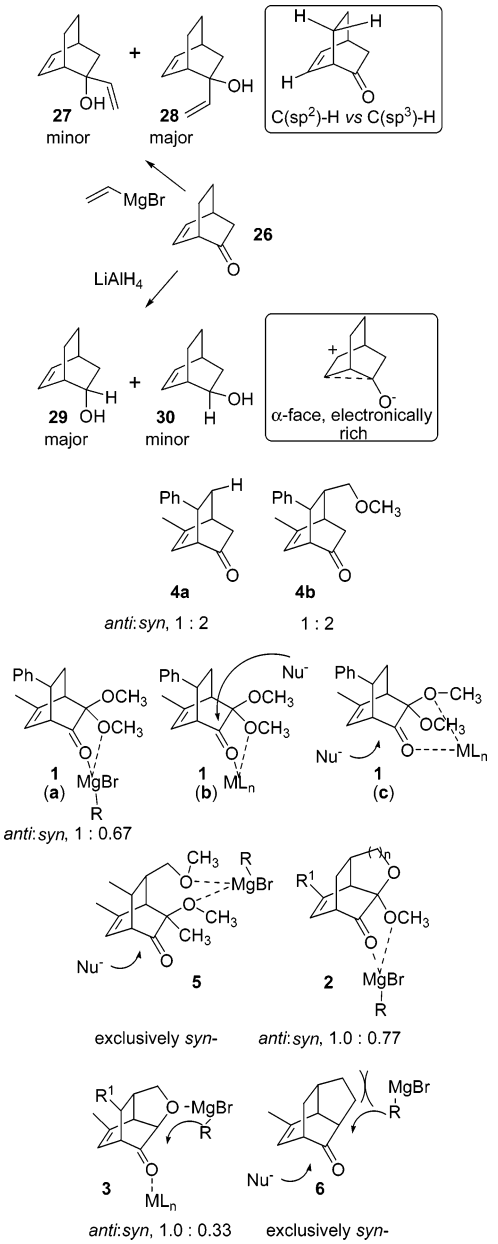


FIGURE 3. Transition state models for the nucleophilic addition to bicyclo[2.2.2]octenone systems.

in the vinyl Grignard addition as in parent bicyclo[2.2.2]-octenone **26** and provided a 1:2 ratio of *anti*/*syn* adducts with steric effects dominating electronic effects. It may be noted that the bicyclo[2.2.2]octenone derivative **4a** preferentially forms *syn*-isomer upon treatment with vinylmagnesium bromide in the presence or absence of appropriate Lewis acid, and does not react with vinylmagnesium bromide−cerium(III) chloride reagent at −78 °C. In compound **4a**, there is no effect of the phenyl group on selectivity as it falls on the same side as the double bond and *syn*-**21a** was isolated as the major product.

But when substrates with α-substitutions to the carbonyl group are used, the steric differentiation of the α- and *β*-faces is clearly observed and the outcome is different from that of the parent bicyclo[2.2.2]octenone system **26**. The addition of vinylmagnesium bromide to bicyclo[2.2.2]oct-5-en-2-one **1** takes place from the *β*-face of the carbonyl group leading to the major product (*anti*-isomer **14**, Table 2).[18] Thus, it can be understood

(22) Pudzianowski, A. T.; Barrish, J. C.; Spergel, S. H. *Tetrahedron Lett.* **1992**, *33*, 293.
(23) (a) Mehta, G.; Khan, F. A.; Ganguly, B.; Chandrasekhar, J. *J. Chem. Soc., Chem. Commun.* **1992**, 1711. (b) Mehta, G.; Khan, F. A. *J. Am. Chem. Soc.* **1990**, *112*, 6140.
(24) Deva Priyakumar, U. D.; Shastri, G. N.; Mehta, G. *Tetrahedron* **2004**, *60*, 3465.
(25) Berson, J. A.; Jones, M., Jr. *J. Am. Chem. Soc.* **1964**, *86*, 5019.

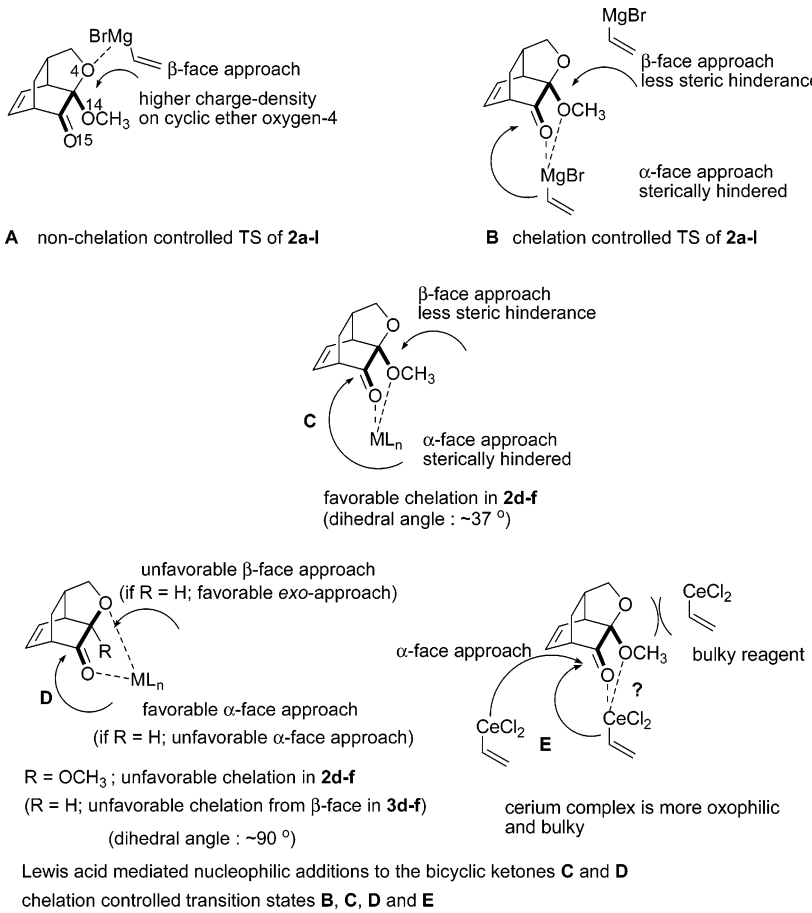


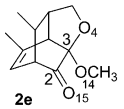
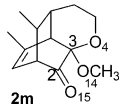
FIGURE 4. Transition state models for the nucleophilic addition to bicyclo[2.2.2]octenone systems **2a**−***l***.

that the *β*-face of **1** is less hindered compared to the α-face and is sterically different from that of the parent bicyclo[2.2.2]-octenone (Figure 3, **1**). The marked preference of Grignard reagents for chelation to α-substitutions to the carbonyl group is a well-known phenomena.[26] In the absence of a Lewis acid, the Grignard reagent itself can chelate with the carbonyl group and the 2-methoxy group making the α-face sterically hindered and the nucleophilic Grignard addition takes place from the *β*-face providing the *anti*-isomer as the major product or if the chelated Grignard itself undergoes carbonyl addition furnishes the *syn*-isomer. However, in the case of Lewis acid mediated Grignard addition to compound **1**, intermediates as in Figure 3 might undergo the addition process. Both the methoxy groups with the dihedral angle of 63.9° and 62.5° (obtained from the STO 3-21 G* method with the SPARTAN program) with the carbonyl functionality have a chance to chelate with the added Lewis acid or the Grignard reagent itself.

The steric factors are playing a major role in directing the facial selectivity for the nucleophilic attack to compound **5**. As can be seen from the structure, the *β*-face in compound **5** is more crowded, which prevents the attack of nucleophile from the upper side and hence one may expect the addition from the α-face. The other explanation for such a result is that the two methoxy oxygen atoms of compound **5** are first chelated and then the addition takes place from the less hindered α-face providing the observed result.

(26) Still, W. C.; Schneider, J. A. *Tetrahedron Lett.* **1980**, *21*, 1035.

TABLE 7. Electrostatic Charges on O4 and O14 and Dihedral Angles of 2e and 2m from Semiemperical Calculations

compound	Method	Dihedral angle O_4-C_3-C_2-O_{15}	Dihedral angle O_{14}-C_3-C_2-O_{15}	Electrostatic Charge O_4	Electrostatic Charge O_{14}
 **2e**	AM1	79.6	40.9		
	PM3	78.6	43.0	-0.276	-0.246
	X-ray[16]	82.0	36.5		
 **2m**	AM1	55.2	67.6	-0.276	-0.276
	PM3	58.2	67.6		

In the case of compounds **2a**,**b**,**d**−**f**,**i**,**j** with five-membered cyclic ether, the *β*-face approach is favorable (entries 1, 2, 4−6, 9, and 10, Table 3), whereas for the compounds **2g**,**h** with six-membered cyclic ether, the α-face approach of the nucleophile is predominant (entries 9 and 10). We attempted to give a qualitative reasoning, by performing a semiempirical calculation at the PM3 level to get the electrostatic charges on O_4 and O_{14} of **2e** and a model molecule **2m**, which was not synthesized (Table 7).

The results suggest that the electrostatic charge on O_4 is greater than that on O_{14} in **2e** bearing a 5-membered cyclic ether; consequently the electron-deficient magnesium bromide species approaches O_4 from the *β*-face and the nucleophilic attack occurs

from the same face (Figure 4, **A**). On the contrary, the electrostatic charges on O_4 and O_{14} are the same in **2m** bearing a 6-membered cyclic ether; here, we can expect that the nucleophile approaches preferentially from the less sterically hindered α-face to form the *syn*-product. The observed selectivity for **2e** and **2m** by semiempirical calculation was seen in the cases of **2e** and **2g** (Table 3). In the addition of nucleophile to **2k** and **2*l***, the *syn*-isomers (**17k**,***l***) were isolated as the major products due to the presence of the deactivating $COOCH_3$ group at C5.[23a] This result can be explained by invoking the hyperconjugation from the more electron rich C(6)−C(10) σ bond with the reactive carbonyl functionality making the β-face electron rich and favors the α-face approach of the nucleophile. Due to the presence of methoxy and phenyl groups in **2j**, there is a repulsion that leads to distortion of the molecule, consequently steric hindrance becomes more significant at the lower face and nucleophile attacks from the less hindered β-face preferentially to form *anti*-isomer. Also, we cannot discount the possibility that the magnesium ion of the Grignard reagent can form a complex simultaneously with the ketone oxygen and the free methoxy oxygen present on the less hindered α-face; this leads to the rigid structure that can easily be accessed by the Grignard reagent virtually from the other side (Figure 4, **B**). As shown in Table 3, the substituents have a significant effect on the facial-selectivity in nucleophilic additions to **2a**−***l***.

It is well-known that the diastereoselectivity of nucleophilic 1,2-addition mainly depends on the chelating ability of Lewis acid with the carbonyl group.[18−22] In all the Lewis acid-mediated addition reactions of **2d**−**f** and *anti*-isomers **16d**−**f** were preferentially formed (Table 4). Except for LiBr, other Lewis acids such as $CeCl_3$, $TiCl_4$, $ZnBr_2$, $MgBr_2$, and Et_2AlCl improve the selectivity because more than one ligand can be coordinated to the metal ions of these Lewis acids to form chelation.[20] The reaction of bicyclo[2.2.2]octenones **2d**−**f** with vinylmagnesium bromide in the presence of $CeCl_3$ gave rise to **16d**−**f** (*anti*) and **17d**−**f** (*syn*) in the ratio of 4:1 to 8:1 (entries 5, 12, and 19, Table 4), respectively, indicating that $CeCl_3$ improves selectivity. The reactions mediated by $ZnBr_2$, $MgBr_2$, $TiCl_4$, and Et_2AlCl provided the *anti*-isomers **16d**−**f** in very high yields (entries 6−9, 13−16, and 20−23, Table 4). In some cases there is no *syn*-product as indicated by the ^{1}H NMR spectrum of the crude reaction mixture. Selectivity with these Lewis acids was improved more than that obtained with $CeCl_3$.

As can be seen from Table 7, for the substrates **2** containing a five-membered cyclic ether moiety, the dihedral angle between two C−O ($O_4-C_3-C_2-O_{15}$) is nearly 90°; this increases the distance between −O− in the cyclic ether and −O− in the carbonyl group (Figure 4, **D**). Therefore, the Lewis acid can coordinate favorably with O_{15} and O_{14} to form a complex from the lower side of the carbonyl group, increasing steric hindrance which can prevent the attack of the vinyl group fromthe α-face (Figure 4, **C**). Consequently, the vinyl group can have easy access for attack from the β-face to form *anti*-product **16**, preferentially. For the substrates **2** containing the six-membered cyclic ether moiety, the two dihedral angles corresponding to $O_4-C_3-C_2-O_{15}$ and $O_{14}-C_3-C_2-O_{15}$ are almost the same, in the range of 55−60°. Thus, in the absence of Lewis acid the addition of Grignard reagent to carbonyl group from the less hindered α-face will be preferred to form *syn*-product **17g**,**h**.

The reaction of **2d**−**f** with a preformed vinylmagnesium bromide−cerium(III) chloride reagent at −78 °C proceeded with completely reversed diastereoselectivity affording a mixture of *anti*-**16d**−**f** and *syn*-**17d**−**f** isomers with high yield and high selectivity (1:15 ratio) (entries 24−26, Table 4), which is in sharp contrast to the nucleophilic addition of vinylmagnesium bromide in the presence of cerium(III) chloride where it acts as a Lewis acid (entries 5, 12, and 19, Table 4). The Grignard reagent with cerium(III) chloride at −78 °C in THF exhibits enhanced oxophilicity and reacts readily with ketones. Imamoto[21d−f] reported that the outcome of diastereoselectivity in cerium(III) chloride-promoted reactions is in sharp contrast to that of Grignard reagent alone. The reversal selectivity with high yield was achieved by Luche reduction,[21a] using $NaBH_4-CeCl_3$ in the synthesis of taxane derivatives.[21l,j] Although reported examples with Grignard reagent−$CeCl_3$ systems with different carbonyl compounds are many, the mechanisms underlying these reactions remain unclear. In the vinylmagnesium bromide−cerium(III) chloride system, the combined use of vinylmagnesium bromide and $CeCl_3$ in THF, which was stirred vigorously in advance at −78 °C, undergoes transmetallation to generate a more negative species, vinylcerium(II) chloride, $CH_2{=}CHCeCl_2$, by the loss of MgBrCl.[21d−f] The organocerium species $CH_2{=}CHCeCl_2$, which is one of the active species in the vinylmagnesium bromide−$CeCl_3$ system, attacks from the less hindered α-face of the carbonyl group to deliver the vinyl group from the same face to form *syn*-**17** as the major product. This reversal stereoselectivity is also caused due to the steric effect of RMgX−$CeCl_3$ in which coordination bias is overridden by the increased steric bulk of the organocerium reagent (Figure 4, **E**). Thus, the incoming nucleophile might directly attack from the α-face or can attack by initial chelation as shown in Figure 4, **E**.

Treatment of **3d**−**f** with vinylmagnesium bromide at −78 °C to room temperature afforded a mixture of isomers **18d**−**f** and **19d**−**f** in 1:1 to 1:0.33 ratio with a similar diastereofacial selectivity (eq 5, Table 5) in comparison with the reactions of ketones **2d**−**f** bearing a methoxy group at C3. When the above reactions were performed with the Lewis acids $ZnBr_2$, $TiCl_4$, and Et_2AlCl, selectivity increases excellently and *anti*-**18d**−**f** become the major products (1:0.33 to 1:0) and with $MgBr_2$ only *anti*-isomers (**18d**−**f)** were formed in each case.

A remarkable inversion of diastereoselectivity was observed when **3d**−**f** reacted with a preformed vinylmagnesium bromide−cerium(III) chloride reagent at −78 °C; the reactions afforded *syn*-isomer **19d**−**f** in 83−91% yield as the only discernible product. In this system, vinylcerium(II) chloride will be generated by transmetallation and the increased steric crowding of the reagent can be invoked to explain this reversal of stereoselectivity.[21] As the organocerium chloride is unstable at 0 °C,[21b] these reactions were carried out at −78 °C in THF. It is worth noting here that the reagent forms *syn*-isomers as major products in **2d**−**f** (entries 24−26, Table 4) but as an exclusive diastereomeric product in **3d**−**f** (entries 22−24, Table 5). It may be due to the absence of the $-OCH_3$ group at C3, which causes little steric hindrance at the α-face in **2d**−**f** compared to negligible steric hindrance in **3d**−**f**. It is pertinent to mention that among all the Lewis acids exploited, $ZnBr_2$ and $MgBr_2$ exhibited excellent selectivity in the formation of the *anti*-isomer with the ketones **2d**−**f** and **3d**−**f**, containing cyclic ether moieties (Tables 4 and 5). We envisioned that the addition sequence of the cerium(III) chloride-mediated reactions has a profound effect on the face-selective outcome. When vinylmagnesium bromide was added to a mixture of appropriate

ketones **2d**−**f** and **3d**−**f** and $CeCl_3$ in THF, the *anti*-isomers were obtained as the major products whereas the addition of ketones to a preformed Grignard reagent−$CeCl_3$ in THF resulted in the almost exclusive formation of *syn*-isomers.

In the case of compound **6** the β-face is more sterically hindered due to the presence of the carbocyclic ring and provides *syn*-isomer **25** as the only discernible product in its nucleophilic addition reactions. For unknown reasons, the reaction with preformed vinylmagnesium bromide−cerium(III) chloride reagent in THF at −78 °C is not proceeding in the cases of **1**, **4a**, **5**, and **6**. The substituents such as methoxy, fused carbocyclic, and cyclic ether can also influence the facial selectivity in the nucleophilic addition to the bicyclo[2.2.2]oct-5-en-2-one derivatives.

In conclusion, these nucleophilic additions provide an easy access to highly diastereoselective bicyclic and tricyclic vinylcarbinols that are potential synthetic intermediates. The diastereoselectivities in additions to bicyclo[2.2.2]octenones can be altered by the substituents and reaction conditions. The *syn*- and *anti*-isomeric carbinols are easily separable by column chromatography. We are successful in achieving a high degree of facial selectivity using a particular Lewis acid such as $CeCl_3$, $ZnBr_2$, $MgBr_2$, or vinylmagnesium bromide−cerium(III) chloride system in several cases. The reversal of diastereoselectivities was observed in the reactions of **2d**−**f** and **3d**−**f** by using a cerium(III) chloride and vinylmagnesium bromide−cerium(III) chloride system. The present Lewis acid-mediated nucleophilic addition reactions were employed as the key steps in our laboratory for the synthesis of natural products such as *cis*-clerodane diterpenic acid[11a,b] and pallescensin B,[11c] refuted (±)-bilosespenes A and B.[11d]

Experimental Section

The general procedure for the preparation and the spectral analysis of compounds **1** and **2a**−***l*** were reported earlier.[15,16]

(1*S,4*R**,8*R**)-8-Hydroxymethyl-5-methylbicyclo[2.2.2]oct-5-en-2-one (7d).** To a solution of **2d** (1.001 g, 5.20 mmol) in dry methanol (5 mL) and dry THF (50 mL) was added SmI_2 (229 mL, 0.1 M in THF, 22.9 mmol) dropwise at rt and the reaction mixture was stirred for 15 min. The reaction was quenched with 0.1 N HCl. The resulting mixture was diluted with ethyl acetate, washed with brine solution followed by aqueous sodium thiosulphate wash, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel with a 1:1 mixture of hexanes and ethyl acetate as an eluent to obtain a colorless liquid **7d** (0.69 g, 80%). IR (neat) 3392, 3032, 2920, 2861, 1713, 1231, 1202, 1047, 886, 813 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.26 (ddd, J = 13.2, 5.8, 1.6 Hz, 1H), 1.88 (d, J = 1.2 Hz, 3H), 1.78−2.02 (m, 3H), 2.24 (dd, J = 19.0, 2.2 Hz, 1H), 2.76−2.80 (m, 1H), 2.98−3.01 (m, lH), 3.53 (dd, J = 10.6, 8.8 Hz, 1H), 3.75 (dd, J = 10.6, 2.0 Hz, lH), 5.78 (dq, J = 6.4, 1.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 27.0, 34.3, 37.4, 38.6, 48.4, 64.3, 120.3, 148.2, 213.0; MS (EI, 70 eV) *m*/*z* (rel intensity) 166 (M^+, 18), 124 (63), 105 (8), 93 (100), 92 (47), 91 (53), 77 (40), 65 (12), 39 (28), 27 (23); HRMS (EI) calcd for $C_{10}H_{14}O_2$ 166.0994, found 166.0993.

(1*S,4*R**,7*R**,8*R**)-8-Hydroxymethyl-5,7-dimethylbicyclo[2.2.2]oct-5-en-2-one (7e).** Compound **7e** was prepared from **2e** following the procedure described for the preparation of **7d**. Colorless liquid; yield 89%; IR (neat) 3428, 3030, 2959, 1717, 1443, 1175, 1075, 1042, 1007, 903 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.98 (d, J = 7 Hz, 3H), 1.37−1.43 (m, 1H), 1.52−1.58 (m, 1H), 1.74 (br s, 1H), 1.89 (d, J = 1.7 Hz, 3H), 1.90−1.96 (m, 1H), 2.18 (dd, J = 18.7, 1.9 Hz, 1H), 2.71−2.73 (m, 1H), 2.80 (dd, J = 6.2, 1.6 HZ, 1H), 3.51 (dd, J = 10.6, 10.0 Hz, 1H), 3.77 (dd, J = 10.6, 5.9 Hz, 1H), 5.69 (apparent d, J = 6.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.7, 20.3, 33.3, 33.6, 38.7, 46.7, 55.6, 63.3, 118.2, 147.9, 213.2; MS (EI, 70 eV) *m*/*z* (rel intensity) 181 (M^+ + 1, 4), 180 (M^+, 10), 162 (1), 138 (24), 107 (100), 91 (28), 77 (10), 41 (13); HRMS (EI) calcd for $C_{11}H_{16}O_2$ (M^+) 180.1151, found 180.1167.

(1*S,4*R**,7*R**,8*R*)-8-Hydroxymethyl-5-methyl-7-phenylbicyclo[2.2.2]oct-5-en-2-one (7f).** Compound **7f** was prepared from **2f** following the procedure described for the preparation of **7d**. Colorless liquid; yield 98%; IR (neat) 3416, 3017, 2918, 2856, 1719, 1660, 1561, 1216, 755, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.34−1.37 (m, 1H), 2.01 (d, J = 1.6 Hz, 3H), 2.06−2.13 (m, 2H), 2.38 (dd, J = 18.6, 1.8 Hz, 1H), 2.61 (d, J = 8.0 Hz, 1H), 2.92−2.95 (m, 1H), 3.07 (dd, J = 6.4, 1.6 Hz, 1H), 3.61 (ddd, J = 10.2, 9.8, 5.2 Hz, 1H), 3.80−3.86 (m, 1H), 5.79 (dq, J = 6.4, 1.6 Hz, 1H), 7.18−7.29 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 33.2, 39.1, 44.2, 47.5, 56.1, 63.1, 118.4, 126.9, 127.5, 128.5, 143.3, 148.5, 211.1; MS (EI, 70 eV) *m*/*z* (rel intensity) 242 (M^+, 8), 200 (17), 182 (8), 169 (100), 154 (23), 134 (46), 108 (18), 92 (30), 91 (26), 77 (12); HRMS (El) calcd for $C_{16}H_{18}O_2$ 242.1307, found 242.1305.

(1*S,3*R**,4*R**,8*R**)-3-Bromo-8-hydroxymethyl-5-methylbicyclo[2.2.2]oct-5-en-2-one (8d).** A solution of **7d** (461.5 mg, 2.78 mmol) in dry THF (8 mL) was added dropwise at −78 °C with stirring to an excess of LDA prepared from diisopropylamine (2.0 mL, 13.9 mmol) in dry THF (4 mL) and *n*-BuLi (4.6 mL, 2.4 M in hexane, 11.12 mmol) at 0 °C in a period of 10 min. After the solution was stirred for 30 min, TMSCl (1.0 mL, 8.34 mmol) was added to the reaction mixture and the resulting mixture was stirred for 1 h. *n*-Hexane was added and the mixture was filtered off the solid and concentrated, and then THF (10 mL) and $PhNMe_3Br_3$ (1.03 g, 2.78 mmol) in THF (18 mL) were added dropwise at 0 °C. The resulting mixture was stirred for 1 h at 0 °C, quenched with 10% HCl, diluted with ethyl acetate, washed with saturated $NaHCO_3$ solution followed by saturated NaCl solution, dried over Na_2SO_4, and concentrated. The residue was chromatographed over silica gel with hexanes and ethyl acetate (1:1) as an eluent to obtain colorless liquid **8d** (0.515 g, 76%). IR (neat) 3440, 3051, 2962, 2394, 2869, 1736, 1442, 1377, 1241, 1044 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.39 (ddd, J = 13.6, 6.4, 1.6 Hz, 1H), 1.82 (ddd, J = 13.6, 11.2, 4.0 Hz, 1H), 1.91 (d, J = 1.6 Hz, 3H), 2.02−2.11 (m, 1H), 3.10 (dd, J = 4.8, 2.4 Hz, 1H), 3.15 (ddd, J = 6.4, 4.0, 2.0 Hz, 1H), 3.60 (dd, J = 10.8, 8.8 Hz, 1H), 3.79 (dd, J = 10.8, 5.6 Hz, 1H), 4.39 (d, J = 2.4 Hz, 1H), 5.80 (dq, J = 6.4, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 25.2, 38.3, 42.7, 47.5, 47.5, 63.6, 119.7, 147.3, 206.5; MS (EI, 70 eV) *m*/*z* (rel intensity) 246 (M^+ + 2, 7), 244 (M^+, 7), 165 (8), 124 (32), 119 (24), 105 (24), 105 (24), 93 (100), 91 (39), 77 (26); HRMS (EI) calcd for $C_{10}H_{13}O_2{}^{79}Br$ 244.0099, found 244.0098; HRMS (EI) calcd for $C_{10}H_{13}O_2{}^{81}Br$ 246.0078, found 246.0067.

(1*S,3*R**,4*R**,7*R**,8*R**)-3-Bromo-8-hydroxymethyl-5,7-dimethylbicyclo[2.2.2]oct-5-en-2-one (8e).** Compound **8e** was obtained as a colorless solid (75%) from **7e** following the procedure described for the preparation of **8d**. Mp 95.7−95.9 °C (from ethyl acetate−hexanes); IR (neat) 3439, 3044, 2961, 2928, 2907, 2871, 1731, 1650, 1060, 1042 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.98 (d, J = 6.8 Hz, 3H), 1.50 (m, 1H), 1.71 (dq, J = 6.8, 6.4 Hz, 1H), 1.93 (d, J = 1.6 Hz, 3H), 2.96 (dd, J = 6.2, 1.6 Hz, 1H), 3.04 (dt, J = 2.4, 2.0 Hz, 1H), 3.61 (m, 1H), 3.81 (m, 1H), 4.37 (d, J = 3.2 Hz, 1H), 5.73 (dq, J = 6.4, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 21.5, 31.5, 42.5, 47.3, 47.6, 54.5, 62.4, 117.5, 146.9, 206.6; MS (EI, 70 eV) *m*/*z* (rel intensity) 258 (M^+, 10), 260 (M^+ + 2, 10), 149 (19), 148 (12), 117 (6), 107 (100), 106 (26), 105 (42), 91 (54), 77 (32); HRMS (EI) calcd for $C_{11}H_{15}O_2{}^{79}Br$ (M^+) 258.0256, found 258.0249; HRMS (EI) calcd for $C_{11}H_{15}O_2{}^{81}Br$ 260.0235, found 260.0211. Anal. Calcd for $C_{11}H_{15}O_2Br$: C, 50.98; H, 5.83. Found: C, 50.77; H, 5.85.

(1*S,3*R**,4*R**,7*R**,8*R**)-3-Bromo-8-hydroxymethyl-5-methyl-7-phenylbicyclo[2.2.2]oct-5-en-2-one (8f).** Compound **8f** was obtained as a colorless solid (75%) from **7f** following the procedure described for the preparation of **8d**. Mp 182.5−183.0 °C (from hexanes−ethyl acetate); IR (neat) 3430, 2964, 2934, 2876, 1735, 1642, 1442, 1377, 1043, 981 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.06 (d, J = 1.6 Hz, 3H), 2.19 (dddd, J = 8.0, 7.6, 4.4, 2.0 Hz, 1H), 2.83 (d, J = 8.0 Hz, 1H), 3.24 (dd, J = 6.4, 1.4 Hz, 1H). 3.27 (dd, J = 4.4, 2.4 Hz, lH), 3.70 (dd, J = 10.6, 8.0 Hz, 1H), 3.86 (dd, J = 10.6. 4.4 Hz, 1H), 4.63 (d, J = 2.8 Hz, 1H), 5.85 (dq, J = 6.4, 1.6 Hz, 1H), 7.16−7.30 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.7, 41.9, 42.5, 48.1, 48.5, 55.0, 62.4, 117.6, 127.2, 127.4, 128.6, 142.4, 147.6, 204.7; MS (EI, 70 eV) *m*/*z* (rel intensity) 322 (M^+ + 2, 5), 320 (M^+, 5), 169 (24), 134 (100), 133 (31), 115 (18), 108 (13), 105 (21), 92 (68), 91 (34); HRMS (EI) calcd for $C_{16}H_{17}O_2{}^{79}Br$ 320.0412, found 320.0415; HRMS (EI) calcd for $C_{16}H_{17}O_2{}^{81}Br$ 322.0391, found 322.0407. Anal. Calcd for $C_{16}H_{17}O_2Br$: C, 59.83; H, 5.33. Found: C, 59.60; H, 5.42.

(1*S,3*R**,6*R**,7*R**)-8-Methyl-4-oxatricyclo[4.3.1.0^{3,7}]dec-8-en-2-one (3d).** Compound **8d** (709.9 mg, 2.90 mmol) in THF (10 mL) and TBAI (55.4 mg, 0.15 mmol) in THF (10 mL) were mixed in a round-bottomed flask. To this mixture was added a solution of NaH (173.9 mg, 4.35 mmol, w/w in oil) in THF (10 mL) at 0 °C. The reaction mixture was brought to rt and stirred for 3 h. Then water and 10% HCl were added sequentially to quench the reaction, and the resulting mixture was extracted with ethyl acetate. The separated organic layer was washed with saturated NaCl solution, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel with ethyl acetate and hexanes (1:3) as an eluent to afford **3d** (0.45 g, 93%) as a colorless liquid. IR (neat) 2944, 2877, 1736, 1443, 1202, 1054, 1032, 917, 888, 822 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.72−1.77 (m, 2H), 1.89 (d, J = 1.6 Hz, 3H), 2.44−2.49 (m, 1H), 2.95−2.99 (m, 1H), 3.05 (ddd, J = 5.4, 4.4, 2.2 Hz, 1H), 3.66 (d, J = 5.6 Hz, 1H), 3.83 (d, J = 8.0 Hz, 1H), 3.97 (dd, J = 8.0, 3.6 Hz, 1H), 5.92 (dq, J = 6.4, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 32.0, 33.7, 44.4, 47.9, 74.4, 76.4, 123.4, 138.4, 205.5; MS (EI, 70 eV) *m*/*z* (rel intensity) 164 (M^+, 3), 163 (1), 136 (47), 121 (13), 106 (29), 91 (100), 77 (28), 65 (16), 51 (15), 29 (45); HRMS (El) calcd for $C_{10}H_{12}O_2$ 164.0837, found 164.0842.

(1*S,3*R**,6*R**,7*R**,10*R**)-8,10-Dimethyl-4-oxatricyclo[4.3.1.0^{3,7}]-dec-8-en-2-one (3e).** Compound **3e** was obtained as colorless liquid (95%) from **8e** following the procedure described for the preparation of **3d**. IR (neat) 2962, 2873, 1737, 1446, 1057, 996, 925, 882, 803, 732 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (d, J = 6.4 Hz, 3H), 1.89 (d, J = 1.6 Hz, 3H), 1.91 (m, 1H), 1.99 (ddq, J = 6.4, 2.8, 1.6 Hz, lH), 2.82 (dd, J = 6.4, 2.8 Hz, 1H), 2.99 (ddd, J = 4.4, 4.8, 4.4, 2.0 Hz, 1H), 3.60 (d, J = 4.8 Hz, 1H), 3.81 (d, J = 8.0 Hz, 1H), 3.91 (dd, J = 8.0, 3.6 Hz, 1H), 5.76 (dq, J = 6.8, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 18.4, 20.9, 37.2, 42.7, 47.8, 51.3, 73.1, 76.2, 120.2, 137.7, 205.7; MS (EI, 70 eV) *m*/*z* (rel intensity) 178 (M^+, 4), 150 (70), 135 (24), 120 (45), 105 (100), 91 (51), 77 (30), 65 (11), 39 (18), 29 (16); HRMS (EI) calcd for $C_{11}H_{14}O_2$ 178.0994, found 178.1006.

(1*S,3*R**,6*R**,7*R**,10*R**)-8-Methyl-10-phenyl-4-oxatricyclo-[4.3.1.0^{3,7}]dec-8-en-2-one (3f).** Compound **3f** was obtained as a colorless solid (96%) from **8f** following the procedure described for the preparation of **3d**. Mp 182.5−183 °C (from CH_2Cl_2−hexanes); IR (neat) 3070, 3051, 2965, 2920, 2889, 1947, 1725, 1451, 1047, 766 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.01 (d, J = 1.4 Hz, 3H), 2.75−2.78 (m, 1H), 3.11 (dd, J = 6.6, 3.0 Hz, 1H), 3.19−3.21 (m, 1H), 3.23 (ddd, J = 5.2, 4.4, 2.0 Hz, 1H), 3.75 (d, J = 5.6 Hz, 1H), 3.99 (d, J = 8.0 Hz, 1H), 4.06 (dd, J = 8.0, 3.6 Hz, 1H), 5.61 (dq, J = 6.8, 1.4 Hz, 1H), 7.05−7.29 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.1, 42.9, 47.7, 48.5, 52.3, 73.7, 76.7, 120.3, 126.6, 128.0, 128.2, 138.8, 142.1, 204.4; MS (EI, 70 eV) *m*/*z* (rel intensity) 240 (M^+, 7), 212 (M − CO, 100), 183 (49), 182 (45), 167 (72), 165 (33), 115 (36), 91 (34), 77 (21); HRMS (EI) calcd for $C_{16}H_{16}O_2$ 240.1150, found 240.1147. Anal. Calcd for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.63; H, 6.67.

(1*S,4*R**,7*R**)-5-Methyl-7-phenylbicyclo[2.2.2]oct-5-en-2-one (4a).** Compound **4a** was obtained as a colorless liquid (91%) from **1** following the procedure described for the preparation of **7d**. IR (neat) 3032, 2938, 2906, 1732, 1602, 1493, 1407, 1286, 740, 700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.69−1.76 (m, 1H), 1.97 (d, J = 1.2 Hz, 3H), 2.13 (dd, J = 6.0, 2.8 Hz, 2H), 2.28 (ddd, J = 13.2, 9.2, 2.8 Hz, 1H), 2.85 (ddd, J = 4.4, 4.0, 1.2 Hz, 1H), 3.14 (dd, J = 6.6, 1.4 Hz, 1H), 3.31 (dd, J = 8.8, 6.4 Hz, 1H), 5.71 (dq, J = 5.6, 1.2 Hz, lH), 7.13−7.28 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.1, 33.9, 38.4, 38.5, 40.3, 55.7, 117.9, 126.5, 127.6, 118.4, 144.3, 147.5, 211.9; MS (EI, 70 eV) *m*/*z* (rel intensity) 212 (M^+, 39), 182 (1), 170 (34), 155 (46), 141 (12), 128 (17), 115 (21), 104 (100), 91 (40), 80 (37); HRMS (El) calcd for $C_{15}H_{16}O$ 212.1201, found 212.1209.

(1*S,4*R**,7*R**,8*R**)-8-Methoxymethyl-5,7-dimethylbicyclo-[2.2.2]oct-5-en-2-one (4b).** To a mixture of NaH (288 mg, 7.20 mmol, 60% w/w) in dry THF (5 mL) at 0 °C was added **7e** (1.08 g, 6.00 mmol) in THF (6 mL) with stirring. Then methyl iodide (808 mg, 5.70 mmol) was added to the contents and the resulting solution was stirred for 20 min, brought to rt, and stirred for a further 30 min, then a saturated NH_4Cl solution was added and extracted with ethyl acetate. The combined organic layer was dried ($MgSO_4$), filtered, and concentrated. The residue was purified by column chromatography (hexanes/EtOAc 6:1) on silica gel to obtain **4b** (812 mg, 70%) as a colorless liquid. IR (neat) 3035, 2911, 1726, 1651, 1449, 1197,1163, 1115, 1065, 960 cm^{-1} ; ^1H NMR (400 MHz, $CDCl_3$) δ 0.97 (d, J = 6.7 Hz, 3H), 1.42−1.48 (m, 1H), 1.54 (apparent q, J = 6.7 Hz, 1H), 1.87 (d, J = 1.6 Hz, 3H), 1.88−1.94 (m, 1H), 2.17 (dd, J = 18.7, 1.8 Hz, 1H), 2.66 (m, 1H), 2.79 (dd, J = 6.6, 1.6 Hz, 1H), 3.25 (t, J = 9.4 Hz, 1H), 3.35 (s, 3H), 3.43 (dd, J = 9.4, 5.2 Hz, 1H), 5.67 (apparent d, J = 6.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 20.3, 33.3, 33.8, 39.2, 44.3, 55.7, 58.9, 73.7, 118.2, 147.9, 212.7; MS (70 eV) *m*/*z* (rel intensity) 194 (M^+, 21), 119 (27), 117 (25), 106 (100), 104 (51), 87 (21), 86 (28), 75 (15), 74 (13); HRMS calcd for $C_{12}H_{18}O_2$ 194.1306, found 194.1321.

(1*S,3*S**,4*R**,7*R**,8*R**)-8-Hydroxymethyl-3-methoxy-5,7-dimethylbicyclo[2.2.2]oct-5-en-2-one (10) and (1*S**,3*R**,4*R**,7*R**,8*R**)-8-Hydroxymethyl-3-methoxy-5,7-dimethylbicyclo[2.2.2]-oct-5-en-2-one (11).** To a solution of **2b** (2.02 g, 9.69 mmol) in dry THF (60 mL) and dry methanol (6 mL) was added SmI_2 (194 mL, 0.1 M in THF, 19.4 mmol) dropwise at −78 °C and the reaction mixture was stirred for 30 min at rt. HCl (0.1 N) was added to quench the reaction. The resulting mixture was diluted with CH_2Cl_2, washed with brine solution and $Na_2S_2O_3$ solution, dried (Na_2SO_4), filtered, and concentrated. The residue was purified by column chromatography on silica gel with a 1:1 mixture of hexanes and ethyl acetate as eluent to obtain colorless liquids **10** (630 mg, 31%) and **11** (1220 mg, 60%). **10**: IR (neat) 3416, 3043, 2911, 1725, 1447, 1376, 1177, 1088, 1019, 891 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.97 (d, J = 6.8 Hz, 3H), 1.37−1.44 (m, 1H), 1.47−1.53 (br s, 1H), 1.59−1.67 (m, 1H), 1.90 (d, J = 2.0 Hz, 3H), 2.81 (dd, J = 6.6, 1.6 Hz, 1H), 2.88 (dd, J = 4.4, 2.2 Hz, 1H), 3.49 (d, J = 2.2 Hz, 1H), 3.51 (s, 3H), 3.57−3.63 (m, 1H), 3.77−3.82 (m, 1H), 5.69 (apparent d, J = 6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.5, 21.0, 32.0, 43.2, 46.3, 54.7, 58.9, 62.9, 75.2, 116.7, 146.7, 208.7; MS (EI, 70 eV) *m*/*z* (rel intensity) 210 (M^+, 5), 182 (21), 120 (100), 119 (72), 107 (26), 106 (10), 105 (26), 91 (8), 77 (1); HRMS (El) calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1256. **11**: IR (neat) 3420, 3042, 2915, 1728, 1446, 1376, 1183, 1103, 1011, 942 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.96 (d, J = 6.8 Hz, 3H), 1.33−1.39 (m, 1H), 1.88 (d, J = 1.6 Hz, 3H), 2.10−2.18 (m, 1H), 2.80−2.83 (m, 2H), 3.00 (br s, 1H), 3.30 (dd, J = 2.8, 1.2 Hz, 1H), 3.60 (s, 3H), 3.68−3.78 (m, 2H), 5.66 (dq, J = 6.1, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 20.2, 33.3, 46.1, 46.2, 54.1, 59.2, 62.9, 77.9, 119.3, 144.8, 208.5; MS (EI, 70 eV) *m*/*z* (rel intensity) 210 (M^+, 2), 182 (11), 120 (69), 119 (54), 107

(26), 105 (25), 91 (11), 77 (2), 45 (100); HRMS (El) calcd for $C_{12}H_{18}O_3$ 210.1256, found 210.1253.

(1*S,3*R**,4*R**,7*R**,8*R**)-3-Methoxy-8-methoxymethy1−3,5,7-trimethylbicyclo[2.2.2]oct-5-en-2-one (5).** Compound **5** was obtained as a colorless liquid (77%) from **10** + **11** when the reaction was performed at −78 °C as described for the preparation of **4b**. IR (neat) 3037, 2921, 1729, 1646, 1452, 1371, 1196, 1111, 1053, 846 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.99 (d, J = 6.8 Hz, 3H), 1.23 (s, 3H), 1.38−1.43 (m, 1H), 1.79−1.85 (m, 1H), 1.87 (d, J = 1.7 Hz, 3H), 2.77 (d, J = 1.7 Hz, 1H), 2.81 (dd, J = 6.0, 1.5 Hz, 1H), 3.35 (s, 3H), 3.29 (s, 3H), 3.54 (dd, J = 9.0, 6.3 Hz, 1H), 3.71 (dd, J = 9.0, 8.7 Hz, 1H), 5.60 (apparent d, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.6, 20.6, 21.1, 33.9, 45.8, 48.8, 50.3, 54.4, 58.6, 75.3, 76.1, 118.1, 147.8, 208.4; MS (EI, 70 eV) *m*/*z* (rel intensity) 238 (M^+, 1), 209 (92), 206 (100), 176 (15), 162 (11), 145 (29), 132 (69), 144 (23), 102 (26), 87 (21); HRMS (El) calcd for $C_{14}H_{22}O_3$ 238.1569, found 238.1570.

(1*S,4*R**,8*S**)-8-(2-Hydroxyethyl)-5-methylbicyclo[2.2.2]oct-5-en-2-one (12).** To a solution of **2g** (527 mg, 2.53 mmol) in dry THF (15 mL) and dry methanol (1.5 mL) was added SmI_2 (101 mL, 0.1 M in THF, 10.1 mmol) dropwise and the mixture was stirred for 10 min at rt. The reaction was quenched with 0.1 N HCl. The resulting mixture was diluted with CH_2Cl_2, washed with brine solution followed by aqueous $Na_2S_2O_3$, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel with a 1:1 mixture of hexanes and ethyl acetate as an eluent to obtain **12** (396 mg, 87%) as a colorless liquid. IR (neat) 3405, 3042, 2918, 1715, 1440, 1410, 1211, 1060, 938, 881 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.30 (ddd, J = 12.8, 5.2, 1.2 Hz, 1H), 1.60−1.65 (m, 3H), 1.68 (s, OH), 1.83 (d, J = 1.6 Hz, 3H), 1.88 (dd, J = 12.8, 4.0 Hz, 1H), 1.95 (ddd, J = 19.0, 3.6, 1.6 Hz, 1H), 2.20 (dd, J = 19.0, 1.9 Hz, 1H), 2.46 (dd, J = 5.4, 1.8 Hz, 1H), 2.95 (ddd, J = 6.0, 3.6, 1.9 Hz, 1H), 3.62−3.75 (m, 2H), 5.70 (dq, J = 6.0, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 30.5, 31.4, 34.4, 37.3, 42.3, 48.7, 61.2, 119.6, 148.5, 213.2; MS (EI, 70 eV) *m*/*z* (rel intensity) 181 (60), 180 (M^+, 13), 138 (49), 120 (23), 105 (95), 94 (84), 91 (100), 77 (36), 65 (17), 51 (15); HRMS (El) calcd for $C_{11}H_{16}O_2$ 180.1150, found 180.1148.

(1*S,4*R**,8*S**)-8-(2-Methanesulfonyloxyethyl)-5-methylbicyclo[2.2.2]oct-5-en-2-one (13).** To a solution of **12** (400 mg, 2.22 mmol) in CH_2Cl_2 (22 mL) at 0 °C was added triethylamine (1.23 g, 11.1 mmol) over 10 min followed by MsCl (506 mg, 4.44 mmol) and the resulting content was stirred for an additional 10 min at 0 °C and at rt for a further 30 min. The reaction mixture was quenched with 0.1 N HCl. The residue was diluted with ethyl acetate, washed with brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by column chromatography on silica gel with a 4:5 mixture of hexanes and ethyl acetate as an eluent to obtain a colorless liquid **13** (504 mg, 88%). IR (neat) 3050, 2937, 1721, 1413, 1347, 1173, 1076, 967, 933 cm^{-1} ; ^1H NMR (400 MHz, $CDCl_3$) δ 1.31 (dd, J = 12.4, 3.6 Hz, 1H), 1.77−1.85 (m, 3H), 1.85 (d, J = 1.6 Hz, 3H), 1.90−1.97 (m, 1H), 1.98 (dd, J = 18.7, 3.6 Hz, 1H), 2.17 (dd, J = 18.7, 1.8 Hz, 1H), 2.48 (d, J = 3.0 Hz, 1H), 2.97 (ddd, J = 5.9, 3.6, 1.8 Hz, 1H), 3.00 (s, 3H), 4.20−4.32 (m, 2H), 5.72 (dq, J = 5.9, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.0, 30.1, 31.2, 33.7, 34.2, 37.4, 41.9, 48.5, 68.2, 119.8, 148.1, 212.0; MS (EI, 70 eV) *m*/*z* (rel intensity) 258 (M^+, 1), 216 (22), 163 (3), 145 (7), 135 (10), 120 (68), 105 (100), 91 (29), 65 (5); HRMS (El) calcd for $C_{12}H_{18}O_4S$ 258.0926, found 258.0915.

(1*S,3*R**,6*R**,7*S**)-8-Methyltricyclo[4.3.1.0^{3,7}]dec-8-en-2-one (6).** To a solution of KHMDS (0.33 mL, 0.5 M in THF) in dry THF (0.7 mL) was added **13** (22 mg, 0.085 mmol) in dry THF (1 mL) at −78 °C then the solution was stirred for 30 min. The reaction mixture was brought to rt and the content was stirred for a further 2 h. Then saturated NH_4Cl solution was added and extracted with ethyl acetate. The organic layer was dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by column chromatography (EtOAc/hexanes 1:7) on silica gel to obtain **6** (8 mg, 58%) as a colorless liquid. IR (neat) 3030, 2943, 2872, 1724, 1444, 1138, 1044, 986, 915, 821 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.29 (ddd, J = 13.0, 3.2, 1.2 Hz, 1H), 1.56−1.62 (m, 3H), 1.66 (dd, J = 13.0, 2.0 Hz, 1H), 1.83 (d, J = 1.6 Hz, 3H), 1.96 (dd, J = 18.0, 2.2 Hz, 1H), 2.15−2.21 (m, 2H), 2.56 (ddd, J = 4.4, 4.2, 2.0 Hz, 1H), 2.91 (ddd, J = 7.2, 2.8, 2.2 Hz, 1H), 5.80 (dq, J = 7.2, 1.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 26.4, 32.3, 33.2, 33.8, 47.3, 47.4, 49.8, 121.5, 142.3, 216.4; MS (EI, 70 eV) *m*/*z* (rel intensity) 163 (M + 1, 52), 162 (M^+, 78), 145 (4), 134 (27), 118 (57), 105 (92), 91 (100), 77 (16), 65 (13), 51 (12); HRMS (El) calcd for $C_{11}H_{14}O$ 162.1045, found 162.1037.

(1*R,2*S**,4*S**,7*S**)-3,3-Dimethoxy-5-methyl-7-phenyl-2-vinylbicyclo[2.2.2]oct-5-en-2-ol (14) and (1*R**,2*R**,4*S**,7*S**)-3,3-Dimethoxy-5-methyl-7-phenyl-2-vinylbicyclo[2.2.2]oct-5-en-2-ol (15).** To a solution of **1** (434 mg, 1.60 mmol) in THF (5 mL) was added dropwise vinylmagnesium bromide (8.0 mL, 1.0 M in THF, 8.0 mmol) at rt then the solution was heated to 55 °C for 10 min. The reaction mixture was cooled to rt, diluted with ethyl acetate, washed with saturated NH_4Cl solution followed by saturated NaCl solution, dried (anhydrous Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel with a 2:3 mixture of hexanes and dichloromethane to yield **14** (197 mg, 41%) and **15** (134 mg, 28%) as colorless liquids. **14:** IR (neat) 3536, 3030, 2943, 1727, 1601, 1494, 1447, 1319, 1080, 924 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.30 (ddd, J = 12.9, 6.3, 2.6 Hz, 1H), 1.97 (apparent s, 3H), 2.27 (ddd, J = 12.9, 9.7, 3.1 Hz, 1H), 2.56 (dd, J = 6.0, 1.6 Hz, 1H), 2.64 (s, 1H), 2.72−2.73 (m, 1H), 3.28−3.36 (m, 1H), 3.30 (s, 3H), 3.32 (s, 3H), 5.23 (dd, J = 11.1, 1.9 Hz, 1H), 5.54 (dd, J = 17.2, 1.9 Hz, 1H), 5.80 (apparent d, J = 6.3 Hz, 1H), 6.57 (dd, J = 17.2, 11.1 Hz, 1H), 7.09−7.25 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 30.4, 37.6, 44.7, 50.1, 51.9, 52.9, 78.3, 105.5, 113.3, 122.8, 125.8, 127.7, 128.1, 139.0, 142.3, 146.5; MS (EI, 70 eV) *m*/*z* (rel intensity) 244 (32), 229 (19), 215 (6), 201 (100), 187 (13), 173 (10), 159 (12), 145 (5), 136 (10), 119 (3), 109 (2); HRMS (El) calcd for $C_{19}H_{24}O_3$ 300.1725, found 300.1730. **15**: IR (neat) 3440, 2740, 1727, 1658, 1601, 1494, 1448, 1327, 1082, 916 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.34 (ddd, J = 13.5, 6.8, 2.6 Hz, 1H), 1.94 (d, J = 2.4 Hz, 3H), 2.19 (ddd, J = 13.5, 9.1, 3.2 Hz, 1H), 2.30 (dd, J = 6.1, 1.7 Hz, 1H), 2.70−2.71 (m, 1H), 3.12 (s, 3H), 3.41 (s, 3H), 3.48−3.52 (m, 1H), 3.97 (s, 1H), 5.00 (dd, J = 10.6, 2.5 Hz, 1H), 5.46 (dd, J = 17.2, 2.5 Hz, 1H), 5.70−5.72 (m, 1H), 6.07 (dd, J = 17.2, 10.6 Hz, 1H), 7.11−7.25 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 30.6, 35.7, 44.5, 50.4, 51.0, 53.6, 78.8, 102.5, 111.7, 123.1, 125.7, 128.0, 140.3, 143.0, 146.8; MS (EI, 70 eV) *m*/*z* (rel intensity) 268 (M^+ − MeOH, 8), 237 (2), 209 (2), 196 (2), 156 (4), 130 (100), 121 (12), 115 (25), 108 (3), 100 (5), 87 (5); HRMS (El) calcd for $C_{19}H_{24}O_3$ 300.1725, found 300.1733.

(1*S,2*S**,3*R**,6*R**,7*R**)-3-Methoxy-2-vinyl-4-oxatricyclo-[4.3.1.0^{3,7}]dec-8-en-2-ol (16a) and (1*S**,2*R**,3*R**,6*R**,7*R**)-3-Methoxy-2-vinyl-4-oxatricyclo[4.3.1.0^{3,7}]dec-8-en-2-ol (17a).** To a solution of **2a** (646 mg, 3.59 mmol) in THF (15 mL) was added dropwise vinylmagnesium bromide (4.3 mL, 1.0 M in THF, 4.3 mmol) at rt. The contents were stirred for 10 min, then saturated NH_4Cl solution was added to quench the reaction. The reaction mixture was extracted with ethyl acetate and the organic layer was washed with saturated NaCl solution, dried (anhydrous Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel with hexanes and ethyl acetate (8:1) as an eluent to afford colorless liquids **16a** (350 mg, 47%) and **17a** (261 mg, 35%). **16a**: IR (neat) 3537, 3055, 2952, 1632, 1542, 1409, 1317, 1251, 1171, 1079 cm^{-1}; ^1H (400 MHz, $CDCl_3$) δ 1.51−1.63 (m, 2H), 2.12−2.17 (m, 1H), 2.59 (ddd, J = 6.7, 4.1, 2.6 Hz, 1H), 2.62 (s, 1H), 2.98−3.01 (m, 1H), 3.35 (s, 3H), 3.62 (d, J = 7.7 Hz, 1H), 3.97 (dd, J = 7.7, 3.8 Hz, 1H), 5.16 (dd, J = 10.8, 2.1 Hz, 1H), 5.46 (dd, J = 17.2, 2.1 Hz, 1H), 6.04 (ddd, J = 8.0, 6.7, 1.5 Hz, 1H), 6.26 (dd, J = 17.2, 10.8 Hz, 1H), 6.36 (ddd, J = 8.0, 4.1, 0.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 30.4, 35.3, 41.4, 41.9, 51.0, 72.3, 79.2, 109.7, 113.6, 124.7, 136.0, 138.2; MS (EI, 70 eV) *m*/*z* (rel intensity) 209 (M^+ + 1, 25), 208 (M^+, 14), 191

(100), 177 (34), 176 (27), 148 (21), 131 (54), 121 (21), 93 (84), 91 (51); HRMS (El) calcd for $C_{12}H_{16}O_3$ 208.1099, found 208.1101. **17a**: IR (neat) 3475, 3053, 2931, 1630, 1454, 1406, 1255, 1005 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.41 (ddd, J = 13.2, 10.6, 2.4 Hz, 1H), 1.77 (apparent d, 1H), 2.15−2.18 (m, 1H), 2.32−2.35 (m, 1H), 3.04−3.10 (m, 1H), 3.28 (s, 3H), 3.71 (d, J = 7.7 Hz, 1H), 4.01 (dd, J = 7.7, 3.6 Hz, 1H), 4.99 (dd, J = 10.7, 2.2 Hz, lH), 5.41 (dd, J = 17.2, 2.2 Hz, 1H), 5.94 (dd, J = 17.2, 10.7 Hz, 1H), 5.95 (ddd, J = 7.6, 5.1, 1.6 Hz, 1H), 6.31 (ddd, J = 7.6, 7.2, 0.8 Hz, lH); ^{13}C NMR (100 MHz, $CDCl_3$) δ 29.6, 36.4, 41.9, 44.3, 50.9, 73.2, 80.1, 108.7, 112.3, 125.2, 136.2, 140.1; MS (EI, 70 eV) *m*/*z* (rel intensity) 208 (M^+, 7), 191 (32), 176 (37), 148 (43), 131 (6), 91 (54), 77 (100), 55 (44); HRMS (El) calcd for $C_{12}H_{16}O_3$ 208.1099, found 208.1105.

(1*S,2*R**,3*R**,6*R**,7*R**,10*R**)-8,10-Dimethyl-2-vinyl-4-oxatricyclo[4.3.1.0^{3,7}]dec-8-en-2-ol (18e) and (1*S**,2*S**,3*R**,6*R**,7*R**,10*R**)-8,10-Dimethyl-2-vinyl-4-oxatricyclo[4.3.1.0^{3,7}]dec-8-en-2-ol (19e).** The addition of vinylmagnesium bromide to **3e** was carried out following the procedure described for the addition reaction of **3d** to provide **18e** (32%) and **19e** (32%) as colorless liquids. **18e**: IR (neat) 3436, 2957, 2930, 2870, 1638, 1450, 1372, 1307, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.85 (d, J = 6.4 Hz, 3H), 1.59 (1H, −OH), 1.62−1.64 (m, 1H), 1.74 (d, J = 1.2 Hz, 1H), 1.93 (d, J = 1.6 Hz, 3H), 2.30−2.36 (m, 1H), 2.80−2.84 (m, 1H), 3.57 (d, J = 5.2 Hz, lH), 3.66 (d, J = 7.8 Hz, 1H), 3.80 (dd, J = 7.8, 3.6 Hz, 1H), 5.23 (dd, J = 11.2, 2.0 Hz, 1H), 5.47 (dd, J = 17.0, 2.0 Hz, 1H), 5.85 (dq, J = 6.4, 1.6 Hz, 1H), 6.26 (dd, J = 17.0, 11.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.7, 20.8, 37.1, 43.0, 47.8, 48.0, 74.7, 77.5, 83.2, 113.9, 123.1, 137.2, 138.1; MS (EI, 70 eV) *m*/*z* (rel intensity) 206 (M^+, 2), 121 (100), 105 (38), 93 (52), 91 (48), 77 (30), 55 (23), 41 (19), 39 (18), 27 (21); HRMS (El) calcd for $C_{13}H_{18}O_2$ 206.1307, found 206.1315. **19e**: IR (neat) 3459, 2957, 2933, 2871, 1639, 1449, 1406, 1046, 1000, 921 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.82 (d, J = 7.2 Hz, 3H), 1.66 (dd, J = 3.6, 2.4 Hz, 1H), 1.83 (d, J = 2.4 Hz, 3H), 1.98 (ddq, J = 7.2, 2.8, 2.0 Hz, 1H), 2.18 (dd, J = 6.8, 2.8 Hz, 1H), 2.77−2.80 (m, 1H), 3.56 (d, J = 5.2 Hz, 1H), 3.77 (d, J = 7.6 Hz, 1H), 3.84 (1H, −OH), 3.85 (dd, J = 7.6, 3.6 Hz, lH), 5.00 (dd, J = 10.8, 2.0 Hz, lH), 5.27 (dd, J = 17.4, 2.0 Hz, lH), 5.78 (dd, J = 17.4, 10.8 Hz, lH), 5.91 (dq, J = 6.4, 2.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.3, 20.7, 36.3, 43.7, 47.7, 47.9, 75.5, 75.6, 77.7, 112.7, 126.0, 133.0, 143.2; MS (EI, 70 eV) *m*/*z* (rel intensity) 206 (M^+, 1), 121 (34), 105 (7), 93 (14), 91 (6), 77 (4), 43 (11), 28 (72), 18 (100); HRMS (El) calcd for $C_{13}H_{18}O_2$ 206.1307, found 206.1308.

(1*S,2*R**,3*R**,6*R**,7*R**,10*R**)-8-Methyl-10-phenyl-2-vinyl-4-oxatricyclo[4.3.1.0^{3,7}]dec-8-en-2-ol (18f) and (1*S**,2*S**,3*R**,6*R**,7*R**,10*R**)-8-Methyl-10-phenyl-2-vinyl-4-oxatricyclo[4.3.1.0^{3,7}]-dec-8-en-2-ol (19f).** The addition of vinylmagnesium bromide to **3f** was carried out following the procedure described for the addition reaction of **3d** to provide **18f** (49%) and **19f** (24%) as colorless liquids. **18f**: IR (neat) 3433, 3085, 3056, 3028, 2934, 2871, 1951, 1869, 1654, 1599 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.78 (1H, −OH), 2.03 (d, J = 1.6 Hz, 3H), 2.50 (dddd, J = 3.8, 3.6, 2.6, 1.0 Hz, 1H), 2.65 (ddd, J = 6.4, 2.4, 1.6 Hz, 1H), 2.89 (dd, J = 2.6, 2.4 Hz, 1H), 3.01 (dd, J = 5.0, 3.8, 1.6 Hz, 1H), 3.69 (dd, J = 5.0, 1.0 Hz, 1H), 3.79 (d, J = 8.0 Hz, 1H), 3.91 (dd, J = 8.0, 3.6 Hz, 1H), 5.34 (dd, J = 10.8, 1.6 Hz, 1H), 5.56 (dd, J = 17.2, 1.6 Hz, 1H), 5.71 (dq, J = 6.4, 1.6 Hz, 1H), 6.43 (dd, J = 17.2, 10.8 Hz, 1H), 7.01−7.27 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.9, 43.2, 47.9, 48.1, 48.7, 75.2, 77.2, 83.4, 114.7, 123.1, 126.1, 128.1, 128.1, 137.6, 138.1, 144.6; MS (70EI, eV) *m*/*z* (rel intensity) 268 (M^+, 1), 250 (2), 183 (19), 167 (31), 165 (30), 117 (50), 115 (68), 91 (100), 77 (30), 55 (46); HRMS (El) calcd for $C_{18}H_{20}O_2$ 268.1463, found 268.1463. **19f**: IR (neat) 3455, 3022, 2919, 2850, 1660, 1601, 1455, 1216, 1149, 757 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.95 (d, J = 1.6 Hz, 3H), 2.46 (ddd, J = 6.8, 2.8, 0.8 Hz, 1H), 2.53−2.56 (m, 1H), 2.98 (ddd, J = 5.2, 4.0, 2.0 Hz, 1H), 3.19 (t, J = 2.4 Hz, 1H), 3.67 (d, J = 5.2 Hz, 1H), 3.89 (d, J = 7.8 Hz, lH), 3.96 (dd, J = 7.8, 3.8 Hz, 1H), 4.00 (1H, −OH), 5.02 (dd, J = 10.8, 1.8 Hz, 1H), 5.31 (dd, J = 17.2, 1.8 Hz, 1H), 5.63 (dq, J = 6.8, 1.6 Hz, 1H), 5.78 (dd, J = 17.2, 10.8 Hz, 1H),7.03−7.27 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 43.6, 47.1, 48.1, 48.9, 75.4, 75.8, 77.9, 113.1, 125.9, 125.9, 127.9, 128.2, 134.1, 142.6, 144.9; MS (EI, 70 eV) *m*/*z* (rel intensity) 268 (M^+, 2), 250 (2), 183 (27), 167 (25), 165 (22), 115 (45), 105 (19), 91 (100), 77 (29), 55 (41); HRMS (El) calcd for $C_{18}H_{20}O_2$ 268.1463, found 268.1460. Anal. Calcd for $C_{18}H_{20}O_2$: C, 80.56; H, 7.51. Found: C, 80.55; H, 7.55.

(1*S,2*R**,4*R**,7*R**)-5-Methyl-7-phenyl-2-vinylbicyclo[2.2.2]-oct-5-en-2-ol (20a) and (1*S**,2*S**,4*R**,7*R**)-5-Methyl-7-phenyl-2-vinylbicyclo[2.2.2]oct-5-en-2-ol (21a).** The addition of vinylmagnesium bromide to **4a** was carried out following the procedure described for the addition reaction of **3d** to provide **20a** (21%) and **21a** (42%) as colorless liquids. **20a**: IR (neat) 3431, 3027, 2932, 2865, 1642, 1491, 1459, 1444, 1414, 1376 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.41−1.49 (m, 2H), 1.94−2.02 (m, 3H), 1.97 (d, J = 1.6 Hz, 3H), 2.58−2.60 (m, 2H), 3.14 (dd, J = 9.2, 6.0 Hz, 1H), 5.26 (dd, J = 10.4, 1.6 Hz, 1H), 5.44 (dd, J = 17.2, 1.6 Hz, 1H), 5.79 (dq, J = 6.0, 1.6 Hz, 1H), 6.15 (dd, J = 17.2, 10.4 Hz, 1H), 7.07−7.24 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.2, 34.3, 37.3, 38.8, 41.0, 50.2, 76.6, 114.2, 121.3, 125.8, 127.8, 128.1, 142.8, 146.6, 146.6; MS (70 EI, eV) *m*/*z* (rel intensity) 240 (M^+, 3), 170 (100), 155 (81), 141 (14), 128 (21), 115 (28), 91 (45), 77 (26), 70 (31), 55 (28); HRMS (El) calcd for $C_{17}H_{20}O$ 240.1514, found 240.1512. **21a**: IR (neat) 3429, 3027, 2930, 2865, 1640, 1492, 1445, 1408, 1376, 1244 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.58−1.60 (m, 3H), 1.71 (ddd, J = 13.6, 3.2, 2.8 Hz, 1H), 1.87 (d, J = 1.6 Hz, 3H), 2.20 (ddd, J = 12.4, 10.4, 2.8 Hz, 1H), 2.39 (dd, J = 6.4, 2.0 Hz, 1H), 2.47−2.51 (m, 1H), 3.80 (ddd, J = 9.8, 5.2, 2.0 Hz, 1H), 4.94 (dd, J = 10.8, 1.2 Hz, 1H), 5.13 (dd, J = 17.8, 1.2 Hz, 1H), 5.64 (dq, J = 6.8, 1.6 Hz, lH), 5.95 (dd, J = 17.8, 10.8 Hz, 1H), 7.13−7.26 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.9, 34.2, 36.8, 37.3, 40.1, 50.0, 77.2, 110.0, 122.8, 125.6, 127.9, 128.2, 143.3, 146.9, 147.4; MS (EI, 70 eV) *m*/*z* 240 (M^+, 4), 212 (2), 170 (100), 155 (67), 154 (8), 115 (10), 104 (9), 91 (29), 77 (8), 55 (4); HRMS (EI) calcd for $C_{17}H_{20}O$ 240.1514, found 240.1507.

(1*S,2*R**,4*R**,7*R**,8*R**)-8-Methoxymethyl-5,7-dimethyl-2-vinylbicyclo[2.2.2]oct-5-en-2-ol (20b) and (1*S**,2*S**,4*R**,7*R**,8*R**)-8-Methoxymethyl-5,7-dimethyl-2-vinylbicyclo[2.2.2]oct-5-en-2-ol (21b).** The addition of vinylmagnesium bromide to **4b** was carried out following the procedure described for the addition reaction of **2a** to provide **20b** (27%) and **21b** (53%) as colorless liquids. **20b**: IR (neat) 3419, 3035, 2916, 1643, 1449, 1378, 1195, 1107, 1001, 921 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.84 (d, J = 6.8 Hz, 3H), 1.14−1.18 (m, 1H), 1.23 (ddd, J = 14.7, 3.3, 1.3 Hz, 1H), 1.29−133 (m, 1H), 1.89 (d, J = 1.6 Hz, 3H), 1.94 (br s, −OH), 2.03 (dd, J = 14.7, 1.9 Hz, 1H), 2.22 (dd, J = 6.1, 1.4 Hz, 1H), 2.41 (apparent d, J = 3.3 Hz, 1H), 3.22 (dd, J = 9.6, 9.3 Hz, 1H), 3.35 (s, 3H), 3.36 (dd, J = 9.3, 4.8 Hz, 1H), 5.16 (dd, J = 10.6, 1.6 Hz, 1H), 5.36 (dd, J = 17.2, 10.6 Hz, 1H), 5.79 (apparent d, J = 5.8 Hz, 1H), 6.02 (dd, J = 17.2, 10.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.8, 21.5, 31.5, 34.7, 38.1, 44.7, 50.7, 58.8, 73.7, 76.4, 113.8, 121.7, 142.6, 147.3; MS (EI) *m*/*z* (rel intensity) 222 (M^+, 0.4), 204 (9), 189 (9), 172 (26), 151 (10), 130 (7), 119 (33), 106 (100), 105 (62), 87 (22); HRMS calcd for $C_{14}H_{22}O_2$ 222.1619, found 222.1632. **21b**: IR (neat) 3491, 3031, 2922, 1645, 1149, 1255, 1196, 1101, 1001, 948 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.84 (d, J = 6.8 Hz, 3H), 1.18−1.22 (m, 1H), 1.43−1.48 (m, 1H), 1.70 (dd, J = 13.9, 2.4 Hz, 1H), 1.78 (d, J = 1.6 Hz, 3H), 2.07−2.10 (m, 2H), 2.23 (br s, −OH), 2.29−2.31 (m, 1H), 3.38 (s, 3H), 3.49−3.56 (m, 2H), 4.91 (dd, J = 11.1, 1.6 Hz, 1H), 5.12 (dd, J = 17.2, 1.6 Hz, 1H), 5.66−5.68 (m, 1H), 5.89 (dd, J = 17.2, 11.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 19.5, 21.6, 29.0, 34.8, 39.4, 44.3, 50.0, 58.8, 74.2, 76.4, 109.5, 123.1, 143.9, 147.3; MS (70 eV) *m*/*z* (rel intensity) 222 (M^+, 1), 204 (100), 189(13), 172 (89), 128 (13), 126 (12), 115 (26), 114 (34), 102 (51), 101 (40); HRMS (EI) calcd for $C_{14}H_{22}O_2$ 222.1619, found 222.1620.

(1*S,2*R**,3*R**,4*R**,7*R*,8*R**)-3-Methoxy-8-methoxymethy1-3,5,7-trimethyl-2-vinylbicyclo[2.2.2]oct-5-en-2-ol (22) and (1*S**,2*S**,3*R**,4*R**,7*R**,8*R**)-3-Methoxy-8-methoxymethyl-3,5,7-trimethyl-2-vinylbicyclo[2.2.2]oct-5-en-2-ol (23).** To a solution of **5** (1.81 g, 7.60 mmol) in THF (76 mL) was added dropwise vinylmagnesium bromide (22.8 mL, 1 M in THF, 22.8 mmol) at rt and the solution was refluxed for 10 min. A workup procedure the same as that described for the addition of vinylmagnesium bromide to **2a** was followed to obtain **22** (20 mg, 1%) and **23** (1.66 g, 82%) as colorless liquids. **22**: IR (neat) 3491, 3050, 2906, 1638, 1453, 1373, 1115, 920, 880, 822 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.92 (d, J = 6.8 Hz, 3H), 1.01 (s, 3H), 1.20−1.40 (m, 2H), 1.60 (d, J = 1.4 Hz, 3H), 1.87−1.96 (m, 1H), 2.12 (dd, J = 5.9, 1.4 Hz, 1H), 2.48 (s, 1H), 3.03 (s, 3H), 3.21 (s, 3H), 3.59 (dd, J = 8.9, 7.0 Hz, 1H), 3.68 (dd, J = 8.9, 8.1 Hz, 1H), 5.22 (dd, J = 10.8, 2.4 Hz, 1H), 5.43 (apparent d, J = 5.9 Hz, 1H), 5.73 (dd, J = 17.2, 2.4 Hz, 1H), 6.73 (dd, J = 17.2, 10.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 21.3, 21.4, 23.0, 33.6, 47.6, 50.7, 51.0, 55.3, 59.1, 77.3, 79.8, 85.2, 113.0, 123.0, 142.5, 146.3; MS (EI, 70 eV) *m*/*z* (rel intensity) 234 (M^+ − MeOH, 5), 216 (67), 184 (30), 158 (21), 144 (20), 130 (18), 113 (100), 110 (82), 92 (47), 55 (48); HRMS (El) calcd for $C_{16}H_{26}O_3$ 266.1882, found 266.1877. **23**: IR (neat) 3489, 3027, 2930, 1646, 1454, 1373, 1191, 1116, 1061, 1004 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.84 (d, J = 6.8 Hz, 3H), 1.00 (s, 3H), 1.18−1.25 (m, 1H), 1.81 (d, J = 1.3 Hz, 3H), 2.02−2.05 (m, 1H), 2.14 (dd, J = 6.6, 1.5 Hz, 1H), 2.60 (d, J = 1.4 Hz, 1H), 3.31 (s, 3H), 3.36 (s, 3H), 3.48 (dd, J = 9.3, 6.0 Hz, 1H), 3.62 (dd, J = 9.4, 9.3 Hz, 1H), 4.28 (s, 1H), 4.99 (dd, J = 10.6, 2.3 Hz, 1H), 5.39 (dd, J = 17.1, 2.3 Hz, 1H), 5.69 (apparent d, J = 6.6 Hz, 1H), 5.76 (dd, J = 17.1, 10.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 21.5, 23.1, 28.4, 45.1, 46.2, 49.9, 50.5, 58.4, 75.0, 76.1, 77.8, 111.7, 123.3, 143.1, 144.0; MS (EI, 70 eV) *m*/*z* (rel intensity) 234 (M^+ − MeOH, 1), 216 (14), 184 (8), 158 (8), 132 (7), 113 (100), 110 (17), 90 (10), 76 (12), 54 (20); HRMS (El) calcd for $C_{16}H_{26}O_3$ 266.1882, found 266.1879.

(1*S,2*S**,3*R**,6*R**,7*S**)-8-Methyl-2-vinyltricyclo[4.3.1.0^{3,7}]dec-8-en-2-ol (25).** The addition of vinylmagnesium bromide to **6** was carried out following the procedure described for the addition reaction of **2a** to provide **25** (84%). **25**: IR (neat) 3451, 2934, 2867, 1635, 1444, 1377, 1140, 994, 915, 885 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.33−1.39 (m, 2H), 1.45−1.57 (m, 3H), 1.79 (d, J = 1.6 Hz, 3H), 1.81−2.00 (m, 4H), 2.11 (td, J = 6.4, 2.8 Hz, 1H), 2.27 (dt, J = 4.0, 1.6 Hz, 1H), 4.89 (dd, J = 10.8, 0.8 Hz, 1H), 5.07 (dd, J = 17.5, 0.8 Hz, 1H), 5.86 (dq, J = 6.6, 1.6 Hz, 1H), 5.91 (dd, J = 17.5, 10.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 20.8, 23.7, 32.6, 33.8, 34.1, 42.4, 44.7, 49.8, 77.8, 109.2, 126.1, 138.5, 147.8; MS (EI, 70 eV) *m*/*z* (rel intensity) 190 (M^+, 5), 118 (100), 105 (13), 93 (23), 91 (21), 77 (17), 65 (9), 55 (31); HRMS (El) calcd for $C_{13}H_{18}O$ 190.1359, found 190.1355.

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Supporting Information Available: Copies of ^1H and ^{13}C NMR and DEPT spectra for all new compounds, general procedures and spectral data for compounds **16b** and **17b** to **16*l*** and **17*l***, **18d**, and **19d**, and tables containing diagnostic ^1H NMR peaks for *syn*/*anti* isomers. This material is available free of charge via the Internet at http://pubs.acs.org.

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