Reductive Cleavage Reaction of γ-Functionalized α,β-Unsaturated Esters and Halomethyls Mediated with Magnesium in Methanol

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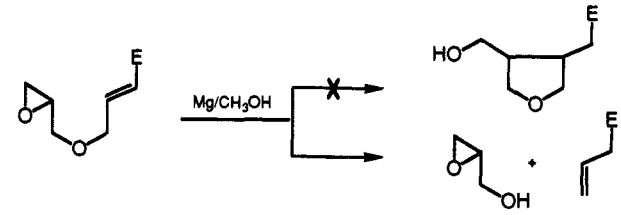
Reductive cleavage of various types of C–O and C–N bonds tethered to α,β-unsaturated esters and halomethyls was mediated with magnesium in methanol, which provided a facile method for the synthesis of δ-hydroxy or δ-amino β,γ-unsaturated esters and allylic alcohols. Regardless of the geometry (*E* or *Z*) of the α,β-unsaturated esters, **1a–b**, **5a–c**, **11**, **13**, and **23**, the cleavage product obtained was exclusively the *E* isomer of the corresponding deconjugated hydroxy and amino esters. The steric bias and ring strain of **15**, **17**, and **21** gave rise to a product mixture of *E* and *Z* isomers.

Introduction

The ability of magnesium in methanol (Mg/CH_3OH) to reduce conjugated ketones[1] was discovered many years ago, but its use has been limited to the reduction of double and triple bonds conjugated to diverse functional groups such as esters,[2,5b] nitriles,[3] amides,[4] and aromatics[5] to the corresponding saturated analogs and to the dehalogenation[6] of alkyl halides. A particular advantage of this method over numerous other reduction methods is the regioselective reduction of a conjugated double bond in the presence of a nonconjugated double bond. Even though the reactivity and mechanism of magnesium in aprotic solvents has been investigated quite thoroughly,[7] its behavior in protic solvents has not yet been well studied. However, Birch-type radical anion formation followed by an additional electron transfer and protonation[2f] and a transient radical anion which undergoes a coupling reaction[8] have been suggested. In order to examine the possibility of radical cyclization an epoxy ether tethered to an α,β-unsaturated ester was subjected to Mg/CH_3OH as follows:



However, the reductive cleavage products, rather than cyclized product, were observed. In light of this result, we set forth to exploit the potential application of Mg/CH_3OH to reductive cleavages of synthetic utility. We report herein the unprecedented reductive cleavage of α,β-unsaturated esters and halomethyls by Mg/CH_3OH, as well as our efforts to expand its synthetic utility and to determine its usefulness as an electron-transferring agent in protic solvents. In the past, other reagents have been employed to accomplish reductive cleavage of the C–O bond tethered to the γ-position of α,β-unsaturated esters and halomethyls. Until now, Zn(Hg)/HCl[9], SmI_2,[10] and $Na[PhSeB(OEt)_3]$[11] were the reagents of choice for γ-functionalized α,β-unsaturated esters, while, depending on the type of substrates, Zn(Cu) couple,[12] Zn/Ag graphite,[13] C_8K,[13d] Zn/alcohol,[14] and Zn/acetic acid[15] were used

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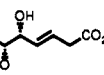
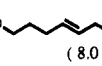
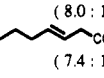
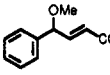
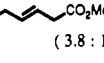
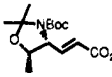
(1) Zechmeister, L.; Rom. P. *Liebigs Ann. Chem.* **1929**, *468*, 117.
(2) (a) de Laszlo, S. E.; Ley, S. V.; Porter, R. A. *J. Chem. Soc., Chem. Commun.* **1986**, 344. (b) Youn, I. K.; Yon, G. H.; Pak, C. S. *Tetrahedron Lett.* **1986**, *21*, 2409. (c) Boyle, E. A.; Mangan, F. R.; Markwell, R. E.; Smith, S. A.; Thomson, M. M.; Ward, R. W.; Wyman, P. A. *J. Med. Chem.* **1986**, *29*, 894. (d) Youn, I. K.; Pak, C. S. *Bull. Korean Chem. Soc.* **1987**, *8*, 434. (e) Hudlicky, T.; Siani-Zingde, G.; Natchus, M. G. *Tetrahedron Lett* **1987**, *44*, 5287. (f) Hudlicky, T.; Natchus, M. G.; Sinai-Zingde, G. *J. Org. Chem.* **1987**, *52*, 4641. (g) Choi, E. B.; Youn, J. K.; Pak, C. S. *Synthesis* **1988**, 792. (h) Walkup, R. D.; Park, G. S. *Tetrahedron Lett.* **1988**, *29*, 5505. (i) Walkup, R. D.; Park, G. S. *J. Am. Chem. Soc.* **1990**, *112*, 1597.
(3) (a) Corey, E. J.; Watt, D. S. *J. Am. Chem. Soc.* **1973**, *95*, 2303. (b) Profitt, J. A.; Watt, D. S.; Corey, E. J. *J. Org. Chem.* **1975**, *40*, 127. (c) Camps, P.; Ortuno, R. M.; Serratosa, F. *Tetrahedron* **1976**, *32*, 2583. (d) Freerksen, R. W.; Pabst, W. E.; Raggio, M. L.; Sherman, S. A.; Wroble, R. R.; Watt, D. S. *J. Am. Chem. Soc.* **1977**, *99*, 1536. (e) Profitt, J. A.; Ong, H. H. *J. Am. Chem. Soc.* **1979**, *44*, 3972. (f) Heissler, D.; Riehl, J.-J. *Tetrahedron Lett.* **1979**, 3957. (g) Geze, M.; Blanchard, P.; Fourrey, J. L.; Roberto-Gero, M. *J. Am. Chem. Soc.* **1983**, *105*, 7638. (h) Maity, S. K.; Mukherjee, D. *Tetrahedron* **1984**, *40*, 757. (i) Braish, T. F.; Fuchs, P. L. *Synth. Commun.* **1985**, *15*, 549. (j) Garratt, P. J.; Doeche, C. W.; Weber, J. C.; Paquette, L. A. *J. Org. Chem.* **1986**, *51*, 449. (k) Molander, G. A.; La Belle, B. E.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 5259. (l) Lansbury, P. T.; Glbo, J. P., Springer, J. P. *Tetrahedron Lett.* **1988**, *29*, 147. (m) Paquette, L. A.; Okazaki, M. E.; Caille, J.-C. *J. Org. Chem.* **1988**, *53*, 477.
(4) (a) Brettle, R.; Shibib, S. M. *Tetrahedron Lett.* **1980**, *21*, 2915. (b) Brettle, R.; Shibib, S. M. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2912. (c) Palmisano, G.; Danieli, B.; Lesma, G.; Riva, R.; Riva, S.; Demartin, F.; Masciocchi, N. *J. Org. Chem.* **1984**, *49*, 4138. (d) Ainscow, R. B.; Brettle, R.; Shibib, S. M. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1781.
(5) (a) Profitt, J. A.; Ong, H. H. *J. Am. Chem. Soc.* **1979**, *44*, 3972. (b) Hutchins, R. O.; Suchismita *Tetrahedron Lett.* **1989**, *30*, 55.
(6) Hutchins, R. O.; Suchismita *Synth. Commun.* **1989**, *19*, 1519.
(7) Walborsky, H. M.; Topolski, M. *J. Am. Chem. Soc.* **1992**, *114*, 3455 and references cited therein.
(8) Osborn, M. E.; Pegues, J. F.; Paquette, L. A. *J. Org. Chem.* **1980**, *45*, 167.
(9) Corey, E. J.; Clark, D. A.; Goto, G.; Marfat, A.; Moiskowski, C.; Samuelsson, B.; Hammarstrom, S. *J. Am. Chem. Soc.* **1980**, *102*, 1436.
(10) (a) Molander, G. A., La Belle, B. E.; Hahn, G. *J. Org. Chem.* **1986**, *51*, 5259. (b) Otsubo, K.; Inanaga, J.; Yamaguchi, M. *Tetrahedron Lett.* **1987**, 4437. (c) Molander, G. A. *Chem. Rev.* **1992**, *92*, 29.
(11) Sasaki, N.; Ohfune, Y. *J. Am. Chem. Soc.* **1992**, *114*, 998.
(12) Sarandases, L. A.; Mourino, A.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1991**, *12*, 818.
(13) (a) Fürstner, A.; Weidmann, H. *J. Org. Chem.* **1989**, *54*, 2307. (b) Fürstner, A.; Weidmann, H. *J. Org. Chem.* **1990**, *55*, 1363. (c) Weidmann, H.; Koglbauer, U.; Fürstner, A. *J. Carbohydr. Chem.* **1990**, *9*, 561. (d) Fürstner, A.; Jumbam, D.; Teslic, J.; Weidmann, H. *J. Org. Chem.* **1991**, *56*, 2213.
(14) (a) Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1979**, *62*, 2400. (b) Bernet, B.; Vasella, A. *Helv. Chim. Acta* **1979**, *62*, 2411. (c) Ferrier, R. J.; Prasit, P. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1645. (d) Beau, J.-M.; Aburaki, S.; Pougny, J.-R.; Siany, P. *J. Am. Chem. Soc.* **1983**, *105*, 621. (e) Ferrier, R. J.; Schmidt, P.; Tyler, P. C. *J. Chem. Soc., Perkin Trans. 1*, **1985**, 301. (f) Bernotas, R. C.; Ganem, B. *Tetrahedron Lett.* **1985**, 1123. (g) Villalobos, A.; Danishefsky, S. J. *J. Org. Chem.* **1989**, *54*, 12. (h) Coleman, R. S.; Dong, Y.; Carpenter, A. J. *J. Org. Chem.* **1992**, *57*, 3732.

0022-3263/93/1958-1523$04.00/0

Table I. Reductive Cleavage Reaction of α,β-Unsaturated Esters and Halomethyls with Mg/MeOH[a]

substrate (E/Z)	product (E/Z)	isolated yield (%)
		
1a : R_1 = CH_2OBn, R_2 = H, X = CH=$CHCO_2Me$ (Z or E)	2 : Y = CH_2CO_2Me	98
1b : R_1 = H, R_2 = CH_2OBn, X = CH=$CHCO_2Me$ (Z or E)	2	98
1c : R_1 = H, R_2 = CH_2OBn, X = CH_2Cl		no reaction
1d : R_1 = H, R_2 = CH_2OBn, X = CH_2Br	3 : Y = H	98
1e : R_1 = H, R_2 = CH_2OBn, X = I	3	98
1f : R_1 = H, R_2 = Ph, X = CH_2Br	4 : Y = H	100
		
5a : R_1 = CH_2OBn, R_2 = H, X = CH=$CHCO_2Me$ (Z or E)	(R)-2	99
5b : R_1 = H, R_2 = CH_2OBn, X = CH=$CHCO_2Me$ (Z or E)	(R)-2	99
5c : R_1 = H, R_2 = H, X = CH=$CHCO_2Me$ (0.7 : 1)	6 : Y = CH_2CO_2Me	98
5d : R_1 = CH_2OBn, R_2 = H, X = CH_2Cl		no reaction
5e : R_1 = CH_2OBn, R_2 = H, X = CH_2Br	(R)-3	99
5f : R_1 = CH_2OBn, R_2 = H, X = CH_2I	(R)-3	99
		
7a : X = CO_2Me (1 : 1.6)	8a : X = CO_2Me	98 (68)[b]
7b : X = CN (1 : 1.6)	8b : X = CN	98 (71)[b]
9 	10 	98 (85)[b]
11  (7.3 : 1)	12 	98
13  (2.5 : 1)	14 	97
15  (3.9 : 1)	16  (8.0 : 1)	97
17  (0.4 : 1)	18  (7.4 : 1)	46[c]
19  (5.4 : 1)	20 	98
21  (3.4 : 1)	22  (3.8 : 1)	96
23  (6.3 : 1)	24 	95
25 	26 	99[d]

[a] E/Z isomer ratio are in parentheses; otherwise assume 100% E isomer. [b] Numbers in parentheses are reported yields by SmI_2.[10a] [c] Saturated product 18a was obtained in 51%. [d] Cleavage product was not observed.

for halomethyls. However, on the basis of our results Mg/CH_3OH, which has never been used for reductive cleavage, seems to be the preferred reagent due to its economy, ease of use, and high product yields.

Results and Discussion

Reductive Cleavage Reactions. Various substrates containing C–O or C–N bonds tethered to the γ-position of α,β-unsaturated esters or to halomethyls were subjected to reductive cleavage reaction conditions to give the corresponding alcohols, alkenes, and amines in almost quantitative yields as shown in Table I. All substrates containing the α,β-unsaturated ester moiety were prepared either from the corresponding alcohols via Swern oxidation followed by Wittig reaction in one pot or from the corresponding aldehydes and ketones via the Horner–Emmons reaction. Halomethyls were prepared from the corresponding alcohols by halogenation with Ph_3P/CCl_4 and Ph_3P/CBr_4 for chloride and bromide and by a modified Mitsunobe reaction[16] and halide-exchange reaction for iodide (see Experimental Section). Epoxy esters **1a–b** and **7a** afforded the corresponding allylic alcohols **2** and **8a** as *E* isomers, exclusively. In the cases where lactone formation is favorable, the product was isolated as a pure lactone instead of the allylic alcohol (**10** from **9**). Until now, SmI_2 was the only reagent available for this particular transformation.[10] In order to investigate the effects of substrate stereochemistry on product formation, the *E* and *Z* stereoisomers of each of the cis and trans (R_1 vs X) epoxy esters were prepared separately and subjected to the reaction conditions. Regardless of substrate stereochemistry, all four isomers of **1a** and **1b** provided the identical *E* isomer, **2**, as noted previously with SmI_2.[10a] The *E* isomer configuration was assigned on the basis of the ^1H NMR (500 MHz) coupling constant ($J_{3,4}$ = 15.5 Hz) of the vinyl protons. Although the results are quite similar to those obtained with SmI_2, the isolated yields are significantly higher using Mg/CH_3OH (see Table I). In the case of epoxy halomethyls **1d–f**, cleavage of the epoxides was facile for the bromide and iodide to give **3** and **4**, but chlorides **1c** and **5d** were inert and did not yield a terminal allylic alcohol. The preferential reactivity of the halides (I > Br > Cl) toward Mg/CH_3OH has been reported previously.[6] Very recently, other workers have reported similar reductive cleavage of epoxy halomethyls to allylic alcohols by the use of Zn(Cu) couple under sonochemical conditions.[12] Our results indicate that the reaction mechanism closely resembles the one suggested for the Zn(Cu) coupld reduction, wherein the carbanion, generated in a stepwise single electron transfer from the metal to the substrate via a carbon-centered radical, opens selectivity to the alkoxide.[17] Similarly, dioxolanyl esters **5a–c**, **11**, and **13** all afforded the *E* isomer of (*R*)-**2**, **2**, **6**, **12**, and **14** respectively, as the sole product, regardless of the original substrate stereochemistry (Figure 1). Steric hindrance exerted by the epoxy or dioxolanyl group on the conformation of the radical anion must play a major

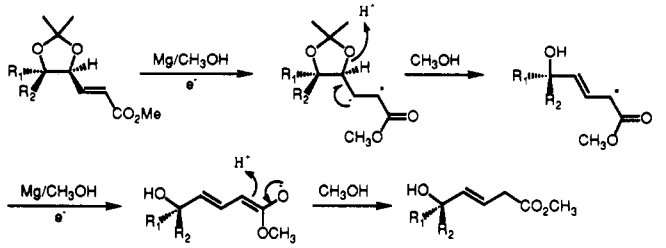
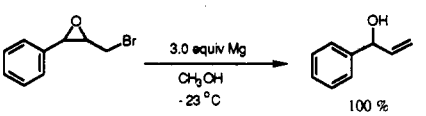


Figure 1.

(15) Ferrier, R. J.; Furneaux, R. H.; Prasit, P.; Tyler, P. C.; Brown, K. L.; Gainsford, G. J.; Diehl, J. W. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1621.

(16) Manna, S.; Falck, J. R.; Mioskowski, C. *Synth. Commun.* **1985**, *15*, 663.

(17) Since the possibility of a radical intermediate was suggested in the reduction of an α,β-unsaturated nitrile with Mg/CH_3OH (see ref 8), it was necessary to investigate the nature of the Mg/CH_3OH system by carrying out a diagnostic reaction to differentiate between radical and anion intermediates as follows (see: Dikinson, J. M.; Murphy, J. A.; Patterson, C. W.; Wooster, N. J. *J. Chem. Soc., Perkin Trans 1* **1990**, 1179). Exclusive formation of allylic alcohol instead of vinyl ether stemming from radical cleavage of the C–C bond of the epoxide strongly suggests that Mg/CH_3OH produces carbanions which then undergo a cleavage reaction.



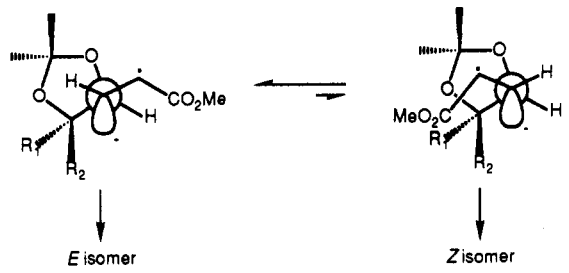


Figure 2.

role during the formation of the new olefinic bond, and thus controls the stereochemistry of the product (Figure 2). The results also indicate that steric effects from R_2 on the conformational equilibrium are negligible, since **5c** (R_2 = H), as a mixture of *E*/*Z* isomers, provided a single *E* isomer. Reductive cleavage of dioxolanyl esters has not been previously reported in the literature,[18] however, there is a report of the cleavage of dioxolanyl halomethyls incorported in carbohydrates by reaction with Zn/Ag graphite or C_8K[13d] in varying yields.

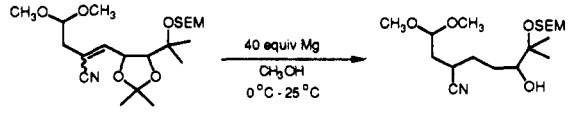
The reductive cleavage of cyclic ether linkages in halofuranose and halopyranose derivatives was previously achieved using Zn/Ag graphite, Zn/alcohol, or Zn/AcOH. Extensive studies by Weidmann et al. on the zinc-induced ring-opening of 6-deoxy-6-halofuranose and 6-deoxy-6-halopyranose revealed that Zn/Ag graphite was the reagent of choice for the reductive cleavage of the cyclic ether linkage, albeit in varying yields,[13] and so far, only the zinc-induced reaction has been used to cleave a cyclic ether linkage in a reductive manner. Turning now to our efforts to use the α,β-unsaturated ester group as an electron acceptor, we found that substrate **15** undergoes a cleavage reaction to give the corresponding alcohol **16** in almost quantitative yield, contrasting sharply with the low (46%) yield of cleavage product **18** from substrate **17**. The remaining product was identified as simple reduction product **18a** without ring opening. These results indicate that the ring strain of the tetrahydrofuranyl moiety in **15** plays a major role during the cleavage of the C–O bond. In contrast to the foregoing examples, the stereoselectivity seems to have been lost. However, by comparing the cyclic moiety in **15** with that in **5c**, we believe that the methyl group of **5c**, which is syn to the α,β-unsaturated ester moiety, must have forced the equilibrium to shift to the more favorable conformer (*E* isomer). Thus, the absence of the methyl group in the tetrahydrofuranyl moiety of **15** has led to a significant loss of stereoselectivity, resulting in the formation of a significant amount of *Z* isomer (11%) in sharp contrast to the foregoing examples. The same loss of stereoselectivity was observed when the pure *E* isomer of **15** was substituted for the original 3.9:1 *E*/*Z* mixture. It is plausible that a conformational equilibrium was reached before the formation of double bond (Figure 2). In the same manner, strict stereocontrol was observed for **19**, but was lost for acetate **21**. Thus, pure *E* isomer of methyl ether **19** gave alkene **20** as a single isomer, but acetate **21**, as a mixture of isomers (*E*/*Z* = 3.4/1) gave **22** as a mixture of isomers (*E*/*Z* = 3.8/1). In the case of optically active substrates **5a,b,e,f**, **9**, **11**, **13**, and **25**, chirality, as expected from our other work, was preserved in the corresponding product. In further efforts to expand the reaction scope, the ability to cleave C–N bonds was studied by employing aziridinyl ester **23** and oxazolidinyl ester **25**. While aziridinyl ester **23**, as a mixture of isomers (*E*/*Z* = 6.3/1), gave exclusively the *E* isomer of allyl amine **24**, the corresponding *E* isomer of **25** afforded only the saturated analog **26**. The driving force for the cleavage reaction must be coming from the ring strain of aziridine, as well as the antiperiplanar conformation of the generated anionic lobe. For oxazolidine, however, not only the relief of ring strain compared with aziridine but also deformation of the antiperiplanar conformation due to steric repulsion between the *t*-Boc group and the ester appendage might have played a critical role in giving the reduction product, exclusively.[19] It is very important to note that isomerization of all the products to conjugated form can be completely prevented by using the specified reaction conditions. However, when the reaction conditions are changed, e.g., higher temperature, prolonged reaction time, or an excess amount of Mg, the formation of saturated products was observed as a result of over-reduction via conjugation by $Mg(OCH_3)_2$.[18] Ester exchange can also take place in an uncontrolled reaction.[20]

Synthetic Applications. Substrate **11** was chosen specifically to demonstrate the explicit synthetic applications of Mg/CH_3OH. Corey and Goto had prepared **12a**, the saturated analog of **12**, as an intermediate in their synthesis of 6-epileukotriene.[21] Their transformation scheme from the bisacetonide of (+)-D-mannose was rather tedious, requiring a total of 11 reactions and resulting in a 67% overall yield. We were able to obtain the same hydroxy ester **12a** in three steps from the same bisacetonide of (+)-D-mannose in a greatly improved 94% overall yield by applying the reductive cleavage reaction (Figure 3). The bisacetonide of (+)-D-mannose was transformed into α,β-unsaturated ester **11** by reaction with 1.2 equiv of methyl (triphenylphosphoranylidene)acetate in dry dimethoxyethane containing a trace of benzoic acid at 70 °C for 6 h, followed by tetrahydropyranylation (2.0 equiv of dihydropyran and pyridinium *p*-toludnesulfonate in methylene chloride at room temperature for 15 h) in 94% yield. Reductive cleavage of **11** with 10 equiv of Mg/CH_3OH at −23 °C warmed to 0 °C provided the hydroxy ester **12a** in quantitative yield. Reduction could be halted at the deconjugated ester **12** stage in 98% yield by using 3 equiv of Mg/CH_3OH maintained at −23 °C. Using catalytic hydrogenation (10% Pd/C) unsaturated ester **12** could also be converted to **12a** in 91% yield. It is clear that reductive cleavage followed by conjugation in the presence of excess amounts of $Mg(OCH_3)_2$ at higher temperatures results in complete reduction.

Conclusion

The Mg/CH_3OH system is an extremely efficient, economical and convenient reducing agent for the reduc-

(18) Kandil, A. A.; Slessor, K. N. *J. Org. Chem.* **1985**, *50*, 5649. Unexpected reductive cleavage of the dioxolanyl group was reported in an attempt to reduce the olefinic double bond of an α,β-unsaturated nitrile.



(19) Research on the detailed conformational features is underway and will be published in due course.

(20) Complete exchange reaction of ethyl ester of **5c** was observed at 0 °C. See ref 2b,d, and f for other examples.

(21) Corey, E. J.; Goto, G *Tetrahedron Lett.* **1980**, *21*, 3463.

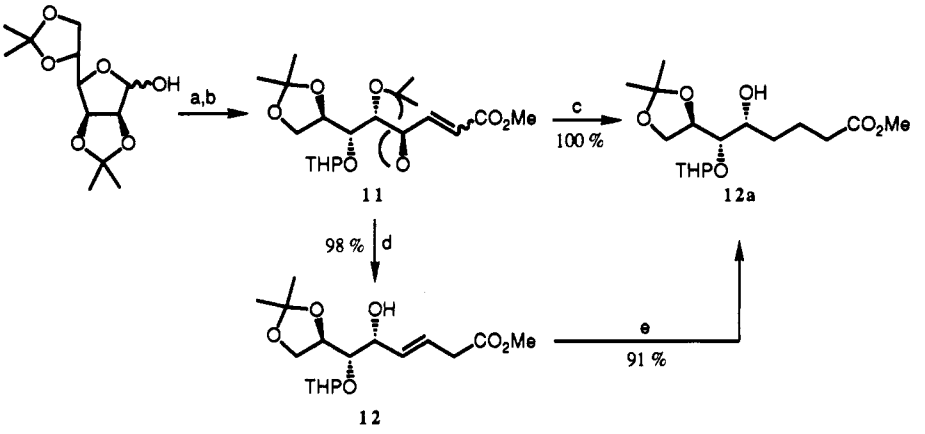


Figure 3. Key: (a,b) ref 20; (c) 10 equiv of Mg/MeOH, −23 to 0 °C; (d) 3 equiv of Mg/MeOH, −23 °C, (e) H_2 (1 atm), 10% Pd/C, MeOH, rt.

tive cleavage of various γ-functionalized α,β-unsaturated esters and halomethyls. Although stereoselectivity was partially lost in a few products due to the steric environment of the substrates, kinetic protonation was found to provide the single geometric *E* isomer in nearly all cases regardless of the substrate stereochemistry, and under the specified reaction conditions, isomerization to the conjugated ester was completely prohibited. Further studies on the carbanion-based synthetic applications of Mg/CH_3OH are underway.

Experimental Section

General. The ^{1}H and ^{13}C NMR spectra were recorded on Brucker AM-300 and AMX-500 spectrometers, unless otherwise specified, in $CDCl_3$ solution using tetramethylsilane as internal standard. Optical rotations were measured at the 589-nm sodium D line. GC analyses were performed on a Schimadzu GC-8A flame ionization detector gas chromatograph fitted with a 1-m × 1/8-in. column (5% Dexil 300 on Gas Chrom W, 100–120 mesh) working in the range of 50–230 °C (5–20 deg min^{-1}), with nitrogen as carrier gas, and with the injector and detector temperatures both at 230 °C. Flash column chromatography was performed with Merck Kieselgel 60 (230–400 mesh ASTM) silica. Analytical thin-layer chromatography was performed on precoated silica gel plates (0.25-mm 60 F-254 E. Merck). All the reagent-grade chemicals, purchased from Aldrich, Fluka, Merck, and TCI chemical companies, were used without further purification. All the organic solvents were obtained from Tedia, Oriental, Duksan and Jin Chemical companies. Triethylamine, methylene chloride, and dimethyl sulfoxide were distilled from calcium hydride.

General Procedure for the Preparation of 1a–b, 5a–b, 13, 15, 19, 23, and 25. The above α,β-unsaturated esters were prepared from the corresponding alcohols via Swern oxidation followed by Wittig reaction in one pot. A representative example is given below.

Methyl *trans*-4,5-Epoxy-6-(benzyloxy)-2-hexenoate (1a). To a stirred solution of oxalyl chloride (2.79 g, 22.0 mmol) in dry CH_2Cl_2 (50 mL) was added dropwise a solution of DMSO (3.4 mL, 44.0 mmol) in dry CH_2Cl_2 (10 mL) at −78 °C over a period of 5 min. After 5 min, a solution of *trans*-2,3-epoxy-4-(benzyloxy)-1-butanol (3.88 g, 20.0 mmol) in dry CH_2Cl_2 (10 mL) was added over a period of 5 min, and stirring was continued for an additional 15 min. To the reaction mixture was added triethyl amine (14.0 mL, 100.0 mmol). Stirring was continued for 5 min and then allowed to warm to room temperature. After 5 min, methyl (triphenylphosphoranylidene)acetate (10.03 g, 30 mmol) was added, and the reaction mixture was refluxed for 30 min. The reaction mixture was cooled and concentrated in vacuo to give a viscous residue which was diluted with ether (50 mL). The insoluble white solid was filtered, and the filtrate was concentrated in vacuo to give a pale brown oil as a mixture of *Z* and *E* isomers, which was separated by flash column chromatography (SiO_2, hexane/ether (3:1)) to afford *Z* (0.36 g, 7%) and *E* (4.17 g, 84%) isomers as colorless oils.

***Z* isomer:** R_f 0.38 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.22–7.42 (m, 5 H, aromatic), 6.01 (dd, *J* = 11.6, 0.9 Hz, 1 H, H-2), 5.81 (dd, *J* = 11.6, 8.2 Hz, 1 H, H-3), 4.60 and 4.57 (ABq, *J* = 11.1 Hz, 2 H, $PhCH_2O$), 4.48 (ddd, *J* = 8.2, 2.2, 0.9 Hz, 1 H, H-4), 3.86 (dd, *J* = 11.6, 3.0 Hz, 1 H, H-6), 3.74 (s, 3 H, OCH_3), 3.52 (dd, *J* = 11.6, 5.9 Hz, 1 H, H-6′), 3.17 (ddd, *J* = 5.9, 3.0, 2.2 Hz, 1 H, H-5); ^{13}C NMR (75.4 MHz) δ 166.13, 145.91, 137.69, 128.34 (2), 127.80, 127.71 (2), 123.62, 73.19, 69.86, 58.23, 51.59, 51.50; IR (neat) 3001, 2835, 1708, 1636, 1433, 1343, 1193, 1091, 990, 870, 819, 736, 694 cm^{-1}; MS *m/e* (intensity) 250 (M^+ + 2, 16.5), 249 (M^+ + 1, 100.0), 248 (M^+, 48.0), 231 (74.2), 181 (21.3), 140 (12.7), 127 (37.6), 111 (24.7), 98 (70.3), 91 (67.3), 82 (12.3).

***E* isomer:** R_f 0.24 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.22–7.40 (m, 5 H, aromatic), 6.68 (dd, *J* = 15.7, 7.2 Hz, 1 H, H-3), 6.16 (dd, *J* = 15.7, 0.7 Hz, 1 H, H-2), 4.59 and 4.57 (ABq, *J* = 11.8 Hz, 2 H, $PhCH_2O$), 3.77 (dd, *J* = 11.8, 3.1 Hz, 1 H, H-6), 3.75 (s, 3 H, OCH_3), 3.58 (dd, *J* = 11.8, 5.0 Hz, 1 H, H-6′), 3.43 (ddd, *J* = 7.2, 2.1, 0.7 Hz, 1 H, H-4), 3.15 (ddd, *J* = 5.0, 4.5, 3.1 Hz, 1 H, H-5); ^{13}C NMR (75.4 MHz) δ 165.90, 144.03, 137.53, 128.43 (2), 127.83, 127.73 (2), 123.82, 73.42, 69.03, 59.45, 53.60, 51.73; IR (neat) 3003, 2835, 1706, 1650, 1427, 1251, 1190, 1136, 1091, 1024, 972, 849, 736, 695 cm^{-1}; MS *m/e* (intensity) 249 (M^+ + 1, 18.8), 248 (M^+, 9.7), 247 (25.8), 231 (20.5), 219 (18.6), 201 (16.2), 181 (23.3), 171 (13.8), 157 (18.1), 142 (65.4), 129 (10.4), 111 (31.0), 104 (15.2), 99 (40.0), 91 (100.0), 71 (11.1).

Methyl *cis*-4,5-Epoxy-6-(benzyloxy)-2-hexanoate (1b). *Z* isomer: yield 8%; R_f 0.32 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.20–7.50 (m, 5 H, aromatic), 5.95–6.10 (m, 2 H, H-2, H-3), 4.61 and 4.44 (ABq, *J* = 11.9 Hz, 2 H, $PhCH_2O$), 4.45–4.60 (m, 1 H, H-6), 3.74 (s, 3 H, OCH_3), 3.62–3.80 (m, 1 H, H-6′), 3.40–3.60 (m, 2 H, H-4, H-5); ^{13}C NMR (75.4 MHz) δ 165.99, 143.78, 137.56, 128.34 (2), 127.72, 127.68 (2), 123.99, 73.10, 68.26, 57.70, 52.46, 51.52; IR (neat) 3005, 2881, 1708, 1634, 1433, 1349, 1198, 1088, 906, 818, 736, 695 cm^{-1}; MS *m/e* (intensity) 250 (M^+ + 2, 1.3), 249 (M^+ + 1, 8.6), 248 (M^+, 4.2), 231 (15.0), 185 (25.0), 127 (62.9), 113 (14.3), 107 (12.2), 98 (45.5), 91 (100.0), 83 (12.2).

***E* isomer:** yield 88%; R_f 0.24 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.25–7.40 (m, 5 H, aromatic), 6.78 (dd, *J* = 15.7, 6.6 Hz, 1 H, H-3), 6.16 (dd, *J* = 15.7, 0.7 Hz, 1 H, H-2), 4.61 and 4.38 (ABq, *J* = 11.9 Hz, 2 H, $PhCH_2O$), 3.75 (s, 3 H, OCH_3), 3.54–3.70 (m, 3 H, H-6, H-4), 3.45 (m, 1 H, H-5); ^{13}C NMR (75.4 MHz) δ 165.71, 141.24, 137.49, 128.42 (2), 127.82, 127.75 (2), 125.14, 73.30, 67.33, 57.48, 54.18, 51.74; IR (neat) 3002, 2836, 1706, 1650, 1427, 1300, 1253, 1190, 1151, 1089, 1024, 973, 903, 837, 779, 736, 695 cm^{-1}; MS *m/e* (intensity) 249 (M^+ + 1, 9.1), 248 (M^+, 8.4), 247 (21.7), 231 (15.3), 201 (12.7), 181 (40.4), 180 (15.0), 171 (14.1), 157 (18.2), 142 (40.9), 129 (13.1), 111 (24.8), 99 (39.3), 91 (100.0).

Methyl *trans*-4,5-(Isopropylidenedioxy)-6-(benzyloxy)-2-hexenoate (5a). *Z* isomer: yield 24%; R_f 0.38 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.20–7.40 (m, 5 H, aromatic), 6.21 (dd, *J* = 11.6, 8.5 Hz, 1 H, H-3), 5.94 (dd, *J* = 11.6, 1.6 Hz, 1 H, H-2), 5.39 (td, *J* = 8.5, 1.6 Hz, 1 H, H-4), 4.63 and 4.56 (ABq, *J* = 12.1 Hz, 2 H, $PhCH_2O$), 3.98 (ddd, *J* = 9.8, 8.5, 3.8 Hz, 1 H, H-5), 3.60–3.75 (m, 2 H, H-6), 3.67 (s, 3 H, OCH_3), 1.46 (s, 6 H, 2 CH_3); ^{13}C NMR (75.4 MHz) δ 165.73, 145.82, 137.98, 128.20 (2), 127.61 (2), 127.45, 122.40, 110.26, 80.29, 73.61, 73.40, 70.40, 51.42,

27.05, 26.98; IR (intensity) 3303, 2295, 2842, 1714, 1650, 1430, 1365, 1195, 1070, 1030, 990, 854, 818, 735, 694 cm^{-1}; MS *m/e* (intensity) 307 (M^+ + 1, 18.7), 306 (M^+, 10.6), 291 (10.0), 249 (37.0), 231 (45.1), 185 (13.4), 181 (12.3), 170 (17.0), 156 (24.3), 142 (52.6), 127 (100.0), 111 (12.1), 98 (72.0), 91 (57.5), 73 (18.5).

***E* isomer**: yield 74%; R_f 0.29 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.25–7.50 (m, 5 H, aromatic), 6.92 (dd, *J* = 15.5, 5.4 Hz, 1 H, H-3), 6.11 (dd, *J* = 15.5, 1.6 Hz, 1 H, H-2), 4.60 (s, 2 H, $PhCH_2O$), 4.43 (ddd, *J* = 8.4, 5.4, 1.6 Hz, 1 H, H-4), 3.96 (dt, *J* = 4.7, 3.4 Hz, 1 H, H-5), 3.75 (s, 3 H, OCH_3), 3.61 (d, *J* = 4.7 Hz, 2 H, H-6), 1.46 and 1.43 (two singlets, 6 H, 2 CH_3); ^{13}C NMR (75.4 MHz) δ 166.38, 144.39, 137.65, 128.40 (2), 127.75, 127.67 (2), 121.95, 110.19, 79.49, 73.60, 69.22, 51.68, 26.91, 26.63; IR (neat) 3301, 2840, 1716, 1653, 1427, 1363, 1230, 1159, 1087, 1022, 975, 845, 734, 694 cm^{-1}; MS *m/e* (intensity) 307 (M^+ + 1, 25.8), 306 (M^+, 16.2), 291 (45.0), 249 (38.8), 230 (28.4), 185 (28.4), 156 (36.4), 142 (38.3), 98 (100.0), 91 (35.4), 73 (27.9).

Methyl *cis*-4,5-(Isopropylidenedioxy)-6-(benzyloxy)-2-hexenoate (5b). *Z* isomer: yield 22%; R_f 0.38 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.20–7.40 (m, 5 H, aromatic), 6.30 (dd, *J* = 11.7, 7.3 Hz, 1 H, H-3), 5.86 (dd, *J* = 11.7, 1.6 Hz, 1 H, H-2), 5.66 (td, *J* = 7.3, 1.6 Hz, 1 H, H-4), 4.73 (ddd, *J* = 7.3, 6.4, 3.6 Hz, 1 H, H-5), 4.52 (s, 2 H, $PhCH_2O$), 3.68 (s, 3 H, OCH_3), 3.47 (dd, *J* = 10.4, 3.6 Hz, 1 H, H-6), 3.35 (dd, *J* = 10.4, 6.4 Hz, 1 H, H-6′), 1.53 and 1.40 (two singlets, 6 H, 2 CH_3); ^{13}C NMR (75.4 MHz) δ 165.96, 146.61, 137.98, 128.21 (2), 127.51 (2), 127.44, 120.69, 109.18, 77.33, 74.13, 73.19, 69.16, 51.45, 27.48, 24.98; IR (neat) 2958, 2845, 1711, 1658, 1429, 1365, 1212, 1068, 851, 816, 735, 694 cm^{-1}; MS *m/e* (intensity) 307 (M^+ + 1, 43.2), 306 (M^+, 27.9), 291 (11.3), 249 (97.9), 231 (69.5), 185 (12.6), 156 (20.0), 142 (34.2), 127 (100.0), 98 (53.8), 73 (15.0).

***E* isomer**: yield 74%; R_f 0.29 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.25–7.40 (m, 5 H, aromatic), 6.93 (dd, *J* = 15.6, 5.3 Hz, 1 H, H-3), 6.14 (dd, *J* = 15.6, 1.6 Hz, 1 H, H-2), 4.80 (ddd, *J* = 6.9, 5.3, 1.6 Hz, 1 H, H-4), 4.56 and 4.50 (ABq, *J* = 11.8 Hz, 2 H, $PhCH_2O$), 4.46 (ddd, *J* = 6.9, 6.5, 6.0 Hz, 1 H, H-5), 3.75 (s, 3 H, OCH_3), 3.48 (dd, *J* = 9.6, 6.5 Hz, 1 H, H-6), 3.38 (dd, *J* = 9.6, 6.5 Hz, 1 H, H-6′), 1.50 and 1.39 (two singlets, 6 H, 2 CH_3); ^{13}C NMR (75.4 MHz) δ 166.35, 142.99, 137.56, 128.37 (2), 127.84 (2), 127.75, 122.09, 109.48, 76.16, 73.49, 68.91, 51.62, 27.59, 25.18; IR (neat) 3002, 2996, 2841, 1714, 1653, 1427, 1365, 1246, 1209, 1158, 1086, 977, 870, 735, 694 cm^{-1}; MS *m/e* (intensity) 307 (M^+ + 1, 38.4), 306 (M^+, 10.9), 291 (45.0), 249 (50.4), 230 (37.4), 185 (28.2), 175 (43.6), 156 (35.0), 142 (32.6), 127 (22.7), 98 (100.0), 91 (27.2), 73 (25.1).

Methyl *trans*-4,5-(Isopropylidenedioxy)-2-hexenoate (13). *Z* isomer: yield 21%; R_f 0.44 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 6.12 (dd, *J* = 11.7, 8.3 Hz, 1 H, H-3), 5.97 (dd, *J* = 11.7, 1.1 Hz, 1 H, H-2), 5.23 (td, *J* = 8.3, 1.1 Hz, 1 H, H-4), 3.80–3.90 (m, 1 H, H-5), 3.73 (s, 3 H, OCH_3), 1.36 (d, *J* = 7.5 Hz, 3 H, H-6), 1.36 and 1.33 (two singlets, 6 H, 2 CH_3); ^{13}C NMR (75.4 MHz) δ 165.68, 145.61, 122.44, 108.99, 77.53, 76.73, 51.33, 27.26, 26.87, 16.97; IR (neat) 2956, 1717, 1650, 1428, 1365, 1241, 1165, 1099, 1031, 975, 856 cm^{-1}; MS *m/e* (intensity) 201 (M^+ + 1, 3.6), 185 (18.6), 143 (16.6), 125 (31.8), 111 (22.2), 98 (58.5), 83 (26.4), 73 (20.1), 59 (13.6), 55 (16.0), 43 (100.0), 41 (16.4).

***E* isomer**: yield 71%; R_f 0.38 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 6.88 (dd, *J* = 15.7, 5.8 Hz, 1 H, H-3), 6.14 (dd, *J* = 15.7, 1.3 Hz, 1 H, H-2), 4.09 (m, 1 H, H-4), 3.80–3.90 (m, 1 H, H-5), 3.76 (s, 3 H, OCH_3), 1.45 and 1.42 (two singlets, 6 H, 2 CH_3), 1.42 (d, *J* = 7.5 Hz, 3 H, H-6); ^{13}C NMR (75.4 MHz) δ 166.22, 143.69, 122.17, 81.48, 76.35, 51.57, 27.16, 26.49, 16.53; IR (neat) 2995, 1719, 1653, 1426, 1364, 1241, 1164, 1095, 1022, 976, 845 cm^{-1}; MS *m/e* (intensity) 201 (M^+ + 1, 3.2), 185 (28.6), 143 (14.6), 125 (51.8), 111 (23.8), 98 (68.1), 83 (26.0), 73 (21.9), 59 (12.1), 55 (12.9), 43 (100.0), 41 (18.8).

Methyl 3-(2-Tetrahydrofuranyl)propenoate (15). *Z* isomer: yield 20%; R_f 0.52 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 6.33 (dd, *J* = 11.7, 7.3 Hz, 1 H, H-3), 5.79 (dd, *J* = 11.7, 1.6 Hz, 1 H, H-2), 5.29 (m, 1 H, OCH), 3.80–4.00 (m, 2 H, OCH_2), 3.72 (s, 3 H, OCH_3), 1.50–2.50 (m, 4 H, CH_2CH_2); ^{13}C NMR (75.4 MHz) δ 166.11, 151.53, 118.62, 75.80, 68.27, 51.20, 32.04, 25.99.

***E* isomer**: yield 79%; R_f 0.43 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 6.93 (dd, *J* = 15.7, 4.8 Hz, 1 H, H-3), 6.03 (dd, *J* = 15.7, 1.6 Hz, 1 H, H-2), 4.52 (m, 1 H, OCH), 3.80–4.00 (m, 2 H, OCH_2), 3.74 (s, 3 H, OCH_3), 1.50–2.30 (m, 4 H, CH_2CH_2); ^{13}C NMR (75.4 MHz) δ 166.88, 148.67, 119.57, 77.36, 68.42, 51.46, 31.49, 25.42.

Methyl 4-Methoxy-4-phenyl-2-butenoate (19). *Z* isomer: yield 13%; R_f 0.55 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.25–7.50 (m, 5 H, aromatic), 6.31 (dd, *J* = 11.5, 8.8 Hz, 1 H, H-3), 5.98 (dd, *J* = 8.8, 1.1 Hz, 1 H, H-4), 5.84 (dd, *J* = 11.5, 1.1 Hz, 1 H, H-2), 3.73 (s, 3 H, CO_2CH_3), 3.33 (s, 3 H, OCH_3); ^{13}C NMR (75.4 MHz) δ 166.22, 149.10, 141.30, 128.45 (2), 127.86, 126.79 (2), 119.38, 79.99, 56.30, 51.30; IR (neat) 3004, 2801, 1713, 1638, 1428, 1392, 1196, 1087, 962, 890, 845, 815, 756, 696 cm^{-1}; MS *m/e* (intensity) 207 (M^+ + 1, 4.6), 206 (M^+, 15.2), 191 (22.8), 175 (18.5), 159 (72.0), 145 (48.5), 131 (46.7), 121 (30.4), 115 (100.0), 105 (36.3), 91 (30.1), 77 (67.2), 63 (18.7), 55 (12.9), 51 (37.6), 43 (33.7).

***E* isomer**: yield 70%; R_f 0.45 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.25–7.40 (m, 5 H, aromatic), 6.95 (dd, *J* = 15.7, 5.5 Hz, 1 H, H-3), 6.10 (dd, *J* = 15.7, 1.6 Hz, 1 H, H-2), 4.78 (dd, *J* = 5.5, 1.6 Hz, 1 H, H-4), 3.71 (s, 3 H, CO_2CH_3), 3.32 (s, 3 H, OCH_3); ^{13}C NMR (75.4 MHz) δ 166.61, 147.47, 138.73, 128.63 (2), 128.20, 126.99 (2), 120.33, 82.34, 56.62, 51.48; IR (neat) 3001, 2805, 1715, 1653, 1427, 1261, 1185, 1161, 1106, 1040, 977, 762, 696 cm^{-1}; MS *m/e* (intensity) 206 (M^+ 0.9), 191 (3.0), 175 (13.9), 159 (11.0), 147 (100.0), 131 (13.6), 121 (31.0), 115 (74.3), 105 (32.0), 91 (20.8), 77 (37.4), 63 (7.9), 55 (5.3), 51 (19.6), 43 (33.8).

Methyl 6-(benzyloxy)-*trans*-4,5-[*N*-(*tert*-butoxycarbonyl)epimino]-2-hexenoate (23): yield 96%: ratio of *E*/*Z* 6.3/1; R_f 0.46 (hexane/EtOAc, 3/1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.20–7.50 (m, 5 H, aromatic), 7.10 (m, 1 H), 6.85 (m, 1 H), 6.10 (dd, *J* = 15.4, 3.4 Hz, 1 H, H-2), 4.47 (s, 2 H, $PhCH_2O$), 3.80-4.15 (m, 1 H), 3.65 (s, 3 H, OCH_3), 3.35–3.80 (m, 2 H), 1.35 (s, 9 H, *t*-BuO); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 165.45, 165.35, 155.33, 143.58, 138.03, 128.18, 127.50, 127.45, 123.54, 122.52, 78.25, 72.14, 68.88, 68.73, 64.90, 61.07, 59.53, 54.41, 51.55, 28.03, 27.65, 15.13; IR (neat) 2946, 1706, 1487, 1359, 1239, 1159, 1099, 1037, 971, 736, 694 cm^{-1}; MS *m/e* (intensity) 330 (M^+ − 15, 1.9), 284 (20.6), 150 (22.4), 91 (100.0), 59 (21.3), 57 (89.2), 41 (22.9).

Methyl (2*E*,4*R*,5*R*)-4-[(*tert*-butoxycarbonyl)amino]-5-hydroxy-2-hexenoate acetonide (25): yield 93%; R_f 0.54 (hexane/EtOAc, 3/1); ^{1}H NMR (300 MHz, DMSO-d_6) δ 6.71 (dd, *J* = 15.6, 8.0 Hz, 1 H, H-3), 5.99 (d, *J* = 15.6 Hz, 1 H, H-2), 3.90 (m, 2 H, H-4, H-5), 3.69 (s, 3 H, OCH_3), 1.51 and 1.48 (two singlets, 6 H, 2 CH_3), 1.26–1.46 (br s, 9 H, *t*-BuO), 1.20 (d, *J* = 5.8 Hz, 3 H, H-6); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 165.62, 150.92, 147.19, 121.65, 93.57, 79.29, 73.88, 64.46, 51.32, 27.78, 26.06, 24.92 (3), 16.83; IR (neat) 2950, 1719, 1690, 1654, 1428, 1360, 1239, 1165, 1126, 1078, 976, 853 cm^{-1}; MS *m/e* (intensity) 301 (M^+ − 18, 2.8), 300 (7.1), 284 (11.1), 244 (25.1), 200 (25.0), 184 (100.0), 168 (12.2), 155 (12.7), 142 (20.3), 110 (15.1), 94 (10.7), 57 (86.5), 41 (36.3).

General Procedure for Synthesis of 1c–d and 5d–e. X = Cl. A stirred mixture of the corresponding alcohol (25.0 mmol), triphenylphosphine (30.0 mmol), and carbon tetrachloride (20 mL) in dry methylene chloride (30 mL) was refluxed for 2 h. The reaction mixture was concentrated in vacuo to give a viscous residue, which was purified by flash column chromatography (SiO_2) to afford the corresponding chloride as a colorless oil.

X = Br. To a stirred solution of the corresponding alcohol (10.0 mmol) and carbon tetrabromide (11.0 mmol) in dry methylene chloride (20 mL) was added dropwise a solution of triphenylphosphine (12.0 mmol) in dry methylene chloride (10 mL) over 5 min at 0 °C. After 1 h, the reaction mixture was concentrated in vacuo to give a viscous residue, which was purified by flash column chromatography (SiO_2) to afford the corresponding bromide as a colorless oil.

***cis*-2,3-Epoxy-4-(benzyloxy)butyl chloride (1c):** yield 85%; R_f 0.32 (hexane/ether, 5/1); ^{1}H NMR (300 MHz) δ 7.25–7.45 (m, 5 H, aromatic), 4.61 and 4.54 (ABq, *J* = 11.9 Hz, 2 H, $PhCH_2O$), 3.73 (dd, *J* = 11.4, 4.2 Hz, 1 H, H-4), 3.64 (dd, *J* = 11.5, 6.9 Hz, 1 H, H-1), 3.59 (dd, *J* = 6.0, 4.2 Hz, 1 H, H-4′), 3.51 (dd, *J* = 6.9, 5.9 Hz, 1 H, H-1′), 3.25–3.35 (m, 2 H, H-2, H-3); ^{13}C NMR (75.4 MHz) δ 137.44, 128.42 (2), 127.83, 127.71 (2), 73.32, 67.27, 56.04, 54.98, 41.65; IR (neat) 3001, 2836, 1442, 1253, 1089, 733, 694 cm^{-1}; MS *m/e* (intensity) 214 (M^+ + 1, 0.7), 212 (M^+ − 1, 1.8), 107 (42.0), 105 (22.8), 91 (100.0), 79 (18.3), 65 (16.7), 51 (9.8), 43 (13.2).

***cis*-2,3-Epoxy-4-(benzyloxy)butyl bromide (1d):** yield 93%; R_f 0.32 (hexane/ether, 5/1); ^{1}H NMR (300 MHz) δ 7.23–7.45 (m, 5 H, aromatic), 4.61 and 4.55 (ABq, *J* = 11.9 Hz, 2 H, $PhCH_2O$),

3.75 (dd, J = 11.3, 6.0 Hz, 1 H, H-4), 3.58 (dd, J = 11.3, 4.0 Hz, 1 H, H-4'), 3.36 (dd, J = 6.5, 3.9 Hz, 1 H, H-1), 3.22–3.38 (m, 3 H, H-1', H-2, H-3); ^{13}C NMR (75.4 MHz) δ 137.44, 128.40 (2), 127.81, 127.70 (2), 73.32, 67.14, 56.99, 54.89, 28.80; IR (neat) 3004, 2836, 1443, 1257, 1214, 1090, 737, 708, 654 cm^{-1}; MS m/e (intensity) 239 (M$^+$ – 18, 0.4), 181 (4.7), 129 (8.3), 107 (48.2), 105 (24.5), 91 (100.0), 77 (17.0), 71 (6.5), 65 (24.1), 51 (13.9), 43 (15.4).

***trans*-2,3-(Isopropylidenedioxy)-4-(benzyloxy)butyl chloride (5d)**: yield 85%; R_f 0.42 (hexane/ether, 5/1); ^{1}H NMR (300 MHz) δ 7.25–7.40 (m, 5 H, aromatic), 4.58 (s, 2 H, PhCH$_2$O), 4.09 (m, 2 H, H-2, H-3), 3.60–3.72 (m, 4 H, H-1, H-4), 1.44 and 1.43 (two singlets, 6 H, 2 CH$_3$); ^{13}C NMR (75.4 MHz) δ 137.69, 128.34 (2), 127.67, 127.56 (2), 109.95, 78.03, 77.82, 73.50, 70.38, 44.42, 27.03, 26.92; IR (neat) 3005, 2842, 1440, 1365, 1239, 1210, 1076, 738, 694 cm^{-1}; MS m/e (intensity) 271 (M$^+$ + 1, 0.3), 270 (M$^+$, 0.3), 269 (M$^+$ – 1, 0.4), 255 (4.0), 177 (9.0), 107 (7.4), 91 (100.0), 85 (9.0), 79 (10.9), 65 (13.9), 59 (29.4), 43 (86.9).

***trans*-2,3-(Isopropylidenedioxy)-4-(benzyloxy)butyl bromide (5e)**: yield 96%; R_f 0.47 (hexane/ether, 5/1); ^{1}H NMR (300 MHz) δ 7.20–7.40 (m, 5 H, aromatic), 4.59 (s, 2 H, PhCH$_2$O), 4.08 (m, 2 H, H-2, H-3), 3.60–3.70 (m, 2 H, H-4), 3.40–3.55 (m, 2 H, H-1), 1.45 and 1.43 (two singlets, 6 H, 2 CH$_3$); ^{13}C NMR (75.4 MHz) δ 137.69, 128.36 (2), 127.75, 127.70 (2), 109.94, 78.73, 73.52, 70.41, 32.56, 30.84, 27.05; IR (neat) 3005, 2840, 1444, 1252, 1220, 1085, 1022, 751, 707, 601 cm^{-1}; MS m/e (intensity) 300 (M$^+$ – CH$_3$, 0.9), 209 (2.6), 181 (3.2), 177 (4.1), 133 (3.2), 105 (31.0), 91 (100.0), 77 (13.8), 65 (10.0), 43 (26.9).

***cis*-2,3-Epoxy-4-(benzyloxy)butyl Iodide (1e)**. From the corresponding alcohol, P(C$_6$H$_5$)$_3$, DEAD, and LiI in anhydrous THF at 0 °C to room temperature:[16] yield 61%; R_f 0.42 (hexane/ether, 5/1); ^{1}H NMR (300 MHz) δ 7.25–7.45 (m, 5 H, aromatic), 4.61 and 4.55 (ABq, J = 11.8 Hz, 2 H, PhCH$_2$O), 3.76 (dd, J = 11.3, 6.1 Hz, 1 H, H-4), 3.55 (dd, J = 11.3, 4.0 Hz, 1 H, H-4'), 3.20–3.30 (m, 3 H, H-1, H-2, H-3), 3.03 (dd, J = 10.0, 7.4 Hz, 1 H, H-1'); ^{13}C NMR (75.4 MHz) δ 137.44, 128.56 (2), 127.76, 127.69 (2), 73.31, 66.93, 58.01, 55.93, 0.74; MS m/e (intensity) 305 (M$^+$ + 1, 0.8), 3.04 (M$^+$, 1.1), 254 (9.0), 127 (7.0), 107 (9.1), 91 (100.0), 65 (12.5), 57 (6.9), 41 (7.5).

***trans*-2,3-(Isopropylidenedioxy)-4-(benzyloxy)butyl Iodide (5f)**. From the corresponding chloride and sodium iodide in dimethyl sulfoxide at 120 °C for 4 h: yield 74%; R_f 0.45 (hexane/ether, 5/1); ^{1}H NMR (300 MHz) δ 7.20–7.40 (m, 5 H, aromatic), 4.58 (s, 2 H, PhCH$_2$O), ^{13}C NMR (75.4 MHz) δ 137.64, 128.29 (2), 127.61, 127.52 (2), 109.63, 79.91, 73.42, 70.31, 30.78, 27.22, 27.14, 6.31; IR (neat) 3036, 2839, 1444, 1363, 1231, 1205, 1160, 1086, 878, 733, 693 cm^{-1}; MS m/e (intensity) 363 (M$^+$ + 1, 6.5), 347 (63.7), 303 (10.2), 241 (26.4), 182 (46.2), 177 (99.9), 129 (11.7), 107 (10.9), 91 (100.0), 85 (15.0), 43 (14.9).

***trans*-2,3-Epoxy-3-phenylpropyl Bromide (1f)**. From cinnamyl bromide and m-CPBA in CH$_2$Cl$_2$ at room temperature: yield 84%; R_f 0.43 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.15–7.40 (m, 5 H, aromatic), 3.76 (d, J = 1.8 Hz, 1 H, H-3), 3.45 (dd, J = 10.7, 5.2 Hz, 1 H, H-1), 3.43 (dd, J = 10.7, 6.3 Hz, 1 H, H-1'); 3.26 (ddd, J = 6.3, 5.2, 1.8 Hz, 1 H, H-2); ^{13}C NMR (75.4 MHz) δ 135.76, 128.33 (3), 125.43 (2), 60.72, 59.96, 31.96; MS m/e (intensity) 215 (M$^+$ + 2, 1.9), 213 (M$^+$, 2.1), 133 (100.0), 105 (97.2), 89 (26.8), 79 (50.9), 63 (15.7), 51 (27.8).

General Procedure for the Preparation of 7a–b and 9. The above α,β-unsaturated esters were prepared from the corresponding ketones via Horner–Emmons reaction.

Methyl (7-oxabicyclo[4.1.0]hept-2-ylidene)ethanoate (7a): yield 99%; R_f 0.34 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 6.02 (m, 1 H), 5.96 (m, 1 H), 4.69 (d, J = 3.9 Hz, 1 H, H-1), 3.74 (s, 3 H, OCH$_3$), 3.71 (s, 3 H, OCH$_3$), 3.40–3.52 (m, 2 H), 3.35 (d, J = 3.9 Hz, 1 H, H-1), 2.93 (m, 1 H), 2.34–2.64 (m, 2 H), 1.40–2.20 (m, 9 H); ^{13}C NMR (75.4 MHz) δ 166.27, 165.85, 154.88, 154.68, 120.70, 120.35, 55.54, 55.18, 54.49, 51.20, 51.02, 49.72, 30.80, 25.01, 23.59, 23.47, 19.96, 17.28; IR (neat) 2916, 1708, 1632, 1426, 1377, 1248, 1226, 1191, 1150, 866, 825 cm^{-1}; MS m/e (intensity) 169 (M$^+$ + 1, 3.1), 168 (M$^+$, 1.6), 151 (4.7), 137 (14.6), 112 (100.0), 81 (20.1), 65 (9.2), 53 (18.7), 41 (23.7).

General Procedure for the Preparation of 5c, 17, and 21. The above α,β-unsaturated esters were prepared from the corresponding aldehydes via Wittig reaction in methanol.

Methyl (3*R*)-4,5-(Isopropylidenedioxy)-2-pentenoate (5c). *Z* isomer: yield 57%; R_f 0.37 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 6.38 (dd, J = 10.7, 6.7 Hz, 1 H, H-3), 5.87 (dd, J = 10.7, 1.7 Hz, 1 H, H-2), 5.50 (qd, J = 6.8, 1.7 Hz, 1 H, H-4), 4.39 (dd, J = 8.2, 6.8 Hz, 1 H, H-5), 3.73 (s, 3 H, OCH$_3$), 3.56 (dd, J = 8.2, 6.7 Hz, 1 H, H-5'), 1.45 (s, 6 H, 2 CH$_3$); ^{13}C NMR (75.4 MHz) δ 166.02, 149.48, 120.27, 109.69, 73.46, 69.29, 51.44, 26.50, 25.34.

***E* isomer**: yield 39%; R_f (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 6.90 (dd, J = 15.6, 5.6 Hz, 1 H, H-3), 6.12 (dd, J = 15.6, 1.5 Hz, 1 H, H-2), 4.68 (m, 1 H, H-4), 4.19 (dd, J = 8.2, 6.9 Hz, 1 H, H-5), 3.76 (s, 3 H, OCH$_3$), 3.68 (dd, J = 8.2, 7.0 Hz, 1 H, H-5'), 1.41 and 1.40 (two singlets, 6 H, 2 CH$_3$); ^{13} C NMR (75.4 MHz) δ 166.41, 144.99, 121.87, 110.16, 74.85, 68.72, 51.65, 26.37, 25.66.

Methyl 3-(2-Tetrahydropyranyl)propenoate (17). *Z* isomer: yield 69%; R_f 0.55 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 6.16 (dd, J = 11.8, 7.4 Hz, 1 H, H-3), 5.70 (dd, J = 11.8, 1.5 Hz, 1 H, H-2), 4.84 (m, 1 H, OCH), 3.90-4.00 (m, 1 H, OCH$_2$), 3.66 (s, 3 H, OCH$_3$), 1.20–1.90 (m, 6 H, CH$_2$CH$_2$CH$_2$); ^{13}C NMR (75.4 MHz) δ 166.07, 150.65, 117.98, 75.12, 67.79, 51.20, 30.53, 25.55, 23.14; IR (neat) 2909, 1714, 1641, 1428, 1193, 1167, 1082, 1034, 967, 887, 815 cm^{-1}; MS m/e (intensity) 171 (M$^+$ + 1, 2.9), 170 (M$^+$, 11.7), 155 (29.1), 138 (33.4), 111 (53.4), 99 (72.8), 83 (40.0), 67 (17.4), 55 (100.0), 41 (19.4).

***E* isomer**: yield 29%; R_f 0.45 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 6.84 (dd, J = 15.8, 4.2 Hz, 1 H, H-3), 5.97 (dd, J = 15.8, 1.8 Hz, 1 H, H-2), 3.95–4.05 (m, 1 H, OCH), 3.67 (s, 3 H, OCH$_3$), 3.46 (m, 2 H OCH$_2$), 1.20–1.90 (m, 6 H, CH$_2$CH$_2$CH$_2$); ^{13} C NMR (75.4 MHz) δ 167.08, 148.40, 119.26, 76.02, 68.23, 51.46, 31.33, 25.55, 23.31; IR (neat) 2908, 1715, 1644, 1426, 1192, 1164, 1081, 1033, 884, 813 cm^{-1}; MS m/e (intensity) 171 (M$^+$ + 1, 9.2), 170 (M$^+$, 15.6), 155 (20.1), 138 (41.8), 111 (65.1), 99 (52.8), 83 (43.7), 67 (7.5), 55 (100.0), 41 (29.1).

Methyl 4-(Acetyloxy)-5-phenyl-2-pentenoate (21): yield of Z and E mixture 95%; ratio of E/Z 3.4/1; IR (neat) 3035, 2924, 1715, 1654, 1487, 1426, 1362, 1303, 1223, 1165, 1079, 1037, 978, 748, 696 cm^{-1}; MS m/e (intensity) 189 (M$^+$ – OAc, 26.9), 188 (55.0), 175 (18.8), 157 (24.7), 129 (95.4), 115 (36.8), 91 (20.9), 43 (100.0).

***Z* isomer**: R_f 0.49 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.15–7.35 (m, 5 H, aromatic), 6.40 (m, 1 H, H-4), 6.10 (dd, J = 11.7, 7.6 Hz, 1 H, H-3), 5.86 (dd, J = 11.7, 1.4 Hz, 1 H, H-2), 3.74 (s, 3 H, OCH$_3$), 3.00 (m, 2 H, H-5), 1.96 (s, 3 H, COCH$_3$); ^{13}C NMR (75.4 MHz) δ 170.10, 165.69, 147.31, 136.77, 129.61 (2), 128.16 (2), 126.54, 120.19, 72.34, 51.48, 39.93, 20.92.

***E* isomer**: R_f 0.49 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 7.15–7.35 (m, 5 H, aromatic), 6.88 (dd, J = 15.8, 5.2 Hz, 1 H, H-3), 5.91 (dd, J = 15.8, 1.6 Hz, 1 H, H-2), 5.62 (m, 1 H, H-4), 3.73 (s, 3 H, OCH$_3$), 3.96 (m, 2 H, H-5), 2.30 (s, 3 H, COCH$_3$); ^{13}C NMR (75.4 MHz) δ 169.76, 166.25, 144.71, 135.85, 129.38 (2), 128.45 (2), 126.88, 121.46, 72.90, 51.66, 40.28, 20.84.

General Procedure for Reductive Cleavage Reaction. The substrate in dry methanol (0.2 M solution) was cooled in a dry ice bath (–23 °C) before 3.0 equiv of magnesium powder fresh from the bottle (50 mesh, Aldrich) was added. The reaction mixture was stirred for 2 h under nitrogen atmosphere. To the gray solution was added an equal volume of diethyl ether, the whole mixture was filtered through a silica gel pad and concentrated in vacuo, and then the crude product was purified by flash chromatography (SiO$_2$). Analytical data are given below.

Methyl (5*R*,3*E*)-6-(benzyloxy)-5-hydroxy-3-hexenoate (2): yield 98%; R_f 0.42 (hexane/EtOAc, 1/1); $[\alpha]^{25}_D$ –8.5° (c 1.0 in CHCl$_3$); ^{1}H NMR (300 MHz) δ 7.22–7.41 (m, 5 H, aromatic), 5.89 (dtd, J = 15.5, 7.1, 1.3 Hz, 1 H, H-3), 5.59 (ddt, J = 15.5, 6.2, 1.4 Hz, 1 H, H-4), 4.55 (s, 2 H, PhCH$_2$O), 4.35 (m, 1 H, H-5), 3.68 (s, 3 H, OCH$_3$), 3.53 (dd, J = 9.6, 3.5 Hz, 1 H, H-6), 3.37 (dd, J = 9.6, 7.6 Hz, 1 H, H-6'), 3.09 (d, J = 7.1 Hz, 2 H, H-2), 2.46 (br s, 1 H, OH); ^{13}C NMR (75.4 MHz) δ 171.80, 137.71, 132.29, 128.40 (2), 127.76, 127.72 (2), 124.56, 73.87, 73.28, 70.76, 51.61, 37.48; IR (neat) 3407, 3001, 2835, 1724, 1155, 1091, 967, 735, 695 cm^{-1}; MS m/e (intensity) 251 (M$^+$ + 1, 6.7), 250 (M$^+$, 2.9), 249 (3.1), 233 (47.6), 201 (14.3), 183 (12.8), 176 (15.7), 159 (16.5), 155 (12.2), 143 (17.8), 129 (16.8), 97 (57.9), 91 (100.0). Anal. Calcd for C$_{14}$H$_{18}$O$_4$: C, 67.18; H, 7.25. Found: C, 67.32; H, 7.21.

(2*R*)-1-(Benzyloxy)-3-buten-2-ol (3): yield 98%; R_f 0.60 (hexane/EtOAc, 1/1); $[\alpha]^{25}_D$ +2.9° (c 1.0 in CHCl$_3$); ^{1}H NMR (300 MHz) δ 7.22–7.40 (m, 5 H, aromatic), 5.84 (ddd, J = 17.4, 10.5, 5.6 Hz, 1 H, H-3), 5.36 (ddd, J = 17.4, 1.6, 1.4 Hz, 1 H, H-4), 5.19 (ddd, J = 10.5, 1.6, 1.4 Hz, 1 H, H-4'), 4.57 (s, 2 H, PhCH$_2$O),

4.35 (m, 1 H, H-2), 3.54 (dd, J = 9.6, 3.6 Hz, 1 H, H-1), 3.48 (dd, J = 9.6, 7.9 Hz, 1 H, H-1'), 2.67 (br s, 1 H, OH); ^{13}C NMR (75.4 MHz) δ 137.72, 136.52, 128.36 (2), 127.69 (2), 116.30, 73.92, 73.24, 71.38, 30.81; IR (neat) 3300, 3041, 2836, 1097, 986, 921, 734, 694 cm^{-1}; MS m/e (intensity) 178 (M$^+$, 0.5), 107 (17.5), 91 (100.0), 71 (5.0), 57 (27.6). Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 74.10; H, 7.99.

1-Phenyl-2-propen-1-ol (4): yield 100%; R_f 0.68 (hexane/EtOAc, 1/1); ^{1}H NMR (300 MHz) δ 7.18–7.42 (m, 5 H, aromatic), 5.99 (ddd, J = 15.8, 10.3, 6.1 Hz, 1 H, H-2), 5.28 (dt, J = 15.8, ~1.4 Hz, 1 H, H-3), 5.14 (dt, J = 10.3, ~1.4 Hz, 1 H, H-3'), 5.10 (dt, J = 6.1, ~1.4 Hz, 1 H, H-1), 2.56 (br s, 1 H, OH); ^{13}C NMR (75.4 MHz) δ 142.51, 140.14, 128.40 (2), 127.57, 126.26 (2), 114.95, 75.12; IR (neat) 3314, 3041, 2839, 1018, 984, 922, 756, 695 cm^{-1}; MS m/e (intensity) 134 (M$^+$, 41.3), 133 (100.0), 115 (35.7), 105 (69.6), 92 (67.1), 77 (95.4), 63 (19.3), 55 (66.1), 51 (82.6), 43 (31.8). Anal. Calcd for $C_9H_{10}O$: C, 80.56; H, 7.51. Found: C, 80.63; H, 7.59.

3-(Carbomethoxymethyl)-2-cyclohexen-1-ol (8a): yield 98%; R_f 0.37 (hexane/EtOAc, 1/1); ^{1}H NMR (300 MHz) δ 5.65 (m, 1 H, H-2), 4.21 (m, 1 H, H-1), 3.69 (s, 3 H, OCH_3), 3.01 (s, 2 H, CH_2CO_2), 2.69 (br s, 1 H, OH), 2.20 (m, 2 H, H-4), 1.72–1.90 (m, 2 H), 1.50-1.68 (m, 2 H); ^{13}C NMR (75.4 MHz) δ 171.91, 134.42, 128.55, 65.35, 51.72, 42.67, 31.15, 28.27, 18.88; IR (neat) 3315, 2845, 1714, 1420, 1246, 1149, 1021, 943, 907 cm^{-1}; MS m/e (intensity) 170 (M$^+$, 1.2), 169 (2.4), 153 (52.0), 110 (22.1), 97 (100.0), 92 (16.5), 82 (17.3), 79 (11.3), 74 (25.1), 67 (11.4), 55 (10.8), 43 (11.5). Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.65; H, 8.25.

Methyl (*E*)-5-hydroxy-3-pentenoate (6): yield 98%; R_f 0.31 (hexane/EtOAc, 1/1); ^{1}H NMR (500 MHz) δ 5.81 (dt, J = 15.5, 6.0 Hz, 1 H, H-3), 5.77 (dt, J = 15.5, 4.6 Hz, 1 H, H-4), 4.14 (d, J = 4.6 Hz, 2 H, H-5), 3.69 (s, 3 H, OCH_3), 3.11 (d, J = 6.0 Hz, 2 H, H-2), 2.0 (br s, 1 H, OH); ^{13}C NMR (125.7 MHz) δ 172.19, 133.30, 123.10, 62.63, 51.73, 37.20; IR (neat) 3335, 2975, 2842, 1716, 1426, 1248, 1198, 1155, 1082, 968 cm^{-1}; MS m/e (intensity) 131 (M$^+$ + 1, 8.0), 130 (M$^+$, 2.1), 113 (100.0), 98 (27.2), 74 (12.8), 71 (56.6), 60 (23.2), 45 (34.7). Anal. Calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.41; H, 7.70.

Methyl (5*S*,6*S*,7*R*,3*E*)-7,8-(Isopropylidenedioxy)-5-hydroxy-6-(1-tetrahydropyranyloxy)-3-octenoate (12): yield 98%; R_f 0.43 (hexane/EtOAc, 1/1); $[\alpha]^{25}_D$ +32.6° (c 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz) δ 5.82–5.97 (m, 1 H, H-3), 5.73 (dd, J = 15.6, 4.9 Hz, 0.5 H, H-4), 5.63 (dd, J = 15.5, 6.9 Hz, 0.5 H, H-4), 4.60 (m, 1 H), 4.35 (m, 0.5 H), 3.70–4.40 (m, 6 H), 3.69 (s, 3 H, OCH_3), 3.50 (m, 1 H), 3.12 (m, 2 H), 2.86 (d, J = 8.9 Hz, 0.5 H), 1.40–1.95 (m, 6 H), 1.43 and 1.40 (two singlets, 3 H, 2 CH_3), 1.35 (s, 3 H, 2 CH_3); ^{13}C NMR (75.4 MHz) δ 171.72, 171.51, 133.62, 132.35, 125.32, 123.05, 109.30, 108.54, 102.40, 99.66, 81.96, 79.07, 75.65, 74.75, 72.53, 71.03, 67.43, 65.12, 64.07, 63.73, 51.73, 51.70, 37.48, 37.42, 31.00, 30.63, 26.62, 26.27, 25.46, 25.08, 25.01, 24.88, 21.09, 20.19; IR (neat) 3427, 2916, 1732, 1428, 1365, 1244, 1199, 1153, 1126, 1058, 1026, 970, 932, 851, 806 cm^{-1}; MS m/e (intensity) 345 (M$^+$ + 1, 0.2), 261 (1.2), 203 (2.7), 101 (9.1), 97 (4.3), 85 (100.0), 67 (9.5), 57 (11.6), 43 (23.8). Anal. Calcd for $C_{17}H_{28}O_7$: C, 59.29; H, 8.19. Found: C, 59.21; H, 8.23.

Methyl (5*S*,6*S*,7*R*)-7,8-(isopropylidenedioxy)-5-hydroxy-6-(1-tetrahydropyranyloxy)octanoate (12a): yield 100%; R_f 0.45 (hexane/EtOAc, 1/1); $[\alpha]^{25}_D$ +24.8° (c 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz) δ 4.58 (m, 2 H), 4.04–4.26 (m, 4 H), 3.85–4.02 (m, 4 H), 3.56–3.78 (m, 2 H), 3.68 (s, 3 H, OCH_3), 3.67 (s, 3 H, OCH_3), 3.40–3.56 (m, 4 H), 2.52 (d, J = 9.3 Hz, 1 H, OH), 2.38 (m, 4 H, H-2), 1.68–2.00 (m, 8 H), 1.44–1.68 (m, 12 H), 1.42 (s, 3 H, CH_3), 1.40 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.35 (s, 3 H, CH_3); ^{13}C NMR (75.4 MHz) δ 173.91, 173.88, 109.25, 108.56, 102.10, 100.20, 81.45, 79.69, 76.00, 75.09, 71.09, 71.04, 67.79, 64.93, 63.91, 51.36, 33.72, 33.67, 32.47, 32.29, 31.09, 31.02, 26.58, 26.33, 25.44, 25.07, 25.02, 24.93, 21.50, 21.06, 20.81, 20.38; IR (neat) 3434, 2916, 1731, 1429, 1364, 1203, 1153, 1126, 1068, 1026, 978, 928, 850, 808 cm^{-1}; MS m/e (intensity) 347 (M$^+$ + 1, 15.0), 263 (62.1), 205 (18.8), 137 (9.2), 101 (11.8), 85 (100.0), 67 (7.4), 49 (18.9), 47 (19.0). Anal. Calcd for $C_{17}H_{30}O_7$: C, 58.94; H, 8.73. Found: C, 58.99; H, 8.70.

Methyl (5*R*,3*E*)-5-hydroxy-3-hexenoate (14): yield 97%; R_f 0.37 (hexane/EtOAc, 1/1); $[\alpha]^{25}_D$ −3.9° (c 1.0 in $CHCl_3$); ^{1}H NMR (500 MHz) δ 5.75 (dtd, J = 15.4, 6.8, 0.9 Hz, 1 H, H-3), 5.66 (ddt, J = 15.4, 6.0, 1.1 Hz, 1 H, H-4), 4.31 (q, J = 6.3 Hz, 1 H, H-5), 3.69 (s, 3 H, OCH_3), 3.08 (d, J = 6.3 Hz, 2 H, H-2), 2.43 (br s, 1 H, OH), 1.26 (d, J = 6.3 Hz, 3 H, H-6); ^{13}C NMR (75.4 MHz) δ 172.19, 138.29, 121.57, 68.07, 51.77, 37.19, 22.95; IR (neat) 3362, 2937, 1721, 1427, 1250, 1199, 1158, 1057, 167 cm^{-1}; MS m/e (intensity) 145 (M$^+$ + 1, 1.2), 144 (M$^+$, 1.2), 127 (100.0), 112 (24.3), 97 (14.2), 84 (26.9), 43 (12.4). Anal. Calcd for $C_7H_{12}O_3$: C, 58.32; H, 8.39. Found: C, 58.31; H, 8.35.

Methyl 7-hydroxy-3-heptenoate (16): yield of E and Z mixture 46%; ratio of E/Z 8.0/1; R_f 0.43 (hexane/EtOAc, 1/1); IR (neat) 3333, 2905, 1722, 1427, 1245, 1188, 1157, 1050, 1011, 965 cm^{-1}; MS m/e (intensity) 159 (M$^+$ + 1, 18.7), 158 (M$^+$, 10.8), 127 (44.0), 111 (11.1), 98 (25.8), 85 (18.1), 81 (100.0), 74 (27.0), 68 (27.4), 59 (13.7), 55 (14.2), 41 (13.0). Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.69; H, 8.90.

***E* isomer**: ^{1}H NMR (500 MHz) δ 5.55 (dt, J = 15.2, 5.2 Hz, 1 H, H-3), 5.52 (dt, J = 15.2, 5.5 Hz, 1 H, H-4), 3.64 (s, 3 H, OCH_3), 3.60 (t, J = 6.5 Hz, 2 H, H-7), 2.99 (d, J = 5.2 Hz, 2 H, H-2), 2.1 (m, 2 H, H-5), 1.81 (br s, 1 H, OH), 1.60 (m, 2 H, H-6); ^{13}C NMR (75.4 MHz) δ 172.57, 134.11, 121.86, 61.92, 51.66, 37.63, 31.77, 28.70.

***Z* isomer**: ^{1}H NMR (500 MHz) δ 5.50–5.56 (m, 2 H, H-3, H-4), 3.65 (s, 3 H, OCH_3), 3.59 (t, J = 6.3 Hz, 2 H, H-7), 3.07 (d, J = 6.0 Hz, 2 H, H-2), 2.10 (m, 2 H, H-5), 1.81 (br s, 1 H, OH), 1.60 (m, 2 H, H-6); ^{13}C NMR (75.4 MHz) δ 172.57, 132.82, 121.17, 61.51, 51.79, 32.59, 31.77, 23.44.

Methyl 8-hydroxy-3-octenoate (18): yield of E and Z mixture 97%; ratio of E/Z 7.4/1; R_f 0.43 (hexane/EtOAc, 1/1); ^{13}C NMR (75.4 MHz) δ 172.65, 172.46, 134.46, 133.16, 121.78, 120.99, 62.58, 51.74, 37.81, 32.74, 32.08, 27.01, 25.40, 25.17; IR (neat) 3340, 2902, 1729, 1427, 1245, 1189, 1161, 1052, 965 cm^{-1}; MS m/e (intensity) 173 (M$^+$ + 1, 26.5), 172 (M$^+$, 15.7), 141 (65.0), 123 (20.5), 110 (40.4), 95 (99.8), 84 (100.0), 79 (68.2), 71 (50.9), 67 (68.8), 59 (32.7), 55 (25.9), 43 (24.0). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.75; H, 9.37.

***E* isomer**: ^{1}H NMR (500 MHz) δ 5.52 (dt, J = 15.2, 5.3 Hz, 1 H, H-3), 5.49 (dt, J = 15.2, 5.4 Hz, 1 H, H-4), 3.64 (s, 3 H, OCH_3), 3.59 (t, J = 6.5 Hz, 2 H, H-8), 2.99 (d, J = 5.3 Hz, 2 H, H-2), 2.03 (m, 2 H, H-5), 1.65 (br s, 1 H, OH), 1.52 (m, 2 H), 1.41 (m, 2 H).

***Z* isomer**: ^{1}H NMR (500 MHz) δ 5.50–5.57 (m, 2 H, H-3, H-4), 3.65 (s, 3 H, OCH_3), 3.60 (t, J = 6.4 Hz, 2 H, H-8), 3.05 (d, J = 5.3 Hz, 2 H, H-2), 2.03 (m, 2 H, H-5), 1.65 (br s, 1 H, OH), 1.52 (m, 2 H), 1.41 (m, 2 H).

Methyl 3-(2-tetrahydropyranyl)propanoate (18a): yield 51%; R_f 0.54 (hexane/ether, 3/1); ^{1}H NMR (300 MHz) δ 3.95 (m, 1 H, OCH), 3.66 (s, 3 H, OCH_3), 3.20–3.43 (m, 2 H, OCH_2), 2.35–2.49 (m, 2 H, CH_2CO_2), 1.70–1.84 (m, 3 H), 1.45–1.70 (m, 4 H), 1.20–1.45 (m, 1 H); ^{13}C NMR (75.4 MHz) δ 174.10, 76.57, 68.31, 51.34, 31.68, 31.35, 29.99, 25.95, 23.31; IR (neat) 2896, 1725, 1427, 1342, 1161, 1082, 1043, 985, 878 cm^{-1}; MS m/e (intensity) 174 (M$^+$ + 2, 41.3), 173 (M$^+$ + 1, 44.4), 172 (M$^+$, 7.2), 141 (87.2), 123 (20.7), 111 (18.3), 98 (46.3), 85 (100.0), 67 (19.0), 57 (31.0), 41 (89.3). Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.85; H, 9.41.

Methyl (*E*)-4-phenyl-3-butenoate (20): yield 98%; R_f 0.41 (hexane/ether, 5/1); ^{1}H NMR (300 MHz) δ 7.15–7.45 (m, 5 H, aromatic), 6.48 (dt, J = 15.9, 1.3 Hz, 1 H, H-4), 6.29 (dt, J = 15.9, 7.0 Hz, 1 H, H-3), 3.70 (s, 3 H, OCH_3), 3.24 (dd, J = 7.0, 1.3 Hz, 2 H, H-2); ^{13}C NMR (75.4 MHz) δ 171.88, 136.72, 133.38, 128.44-(2), 127.47, 126.19 (2), 121.56, 51.80, 38.10; IR (neat) 3001, 2892, 1726, 1427, 1245, 1193, 1154, 957, 742, 689 cm^{-1}; MS m/e (intensity) 177 (M$^+$ + 1, 32.9), 176 (M$^+$, 87.1), 134 (11.6), 117 (100.0), 115 (11.1). Anal. Calcd for $C_{12}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.91; H, 6.90.

Methyl 5-phenyl-3-pentenoate (22): yield of E and Z mixture 96%; ratio of E/Z 3.8/1; R_f 0.41 (hexane/ether, 5/1); ^{13}C NMR (75.4 MHz) δ 172.32, 172.19, 140.02, 133.21, 131.64, 128.47, 128.39, 128.29, 126.06, 123.03, 121.77, 51.74, 51.64, 38.85, 37.70, 33.54, 32.75; IR (neat) 3000, 2881, 1730, 1487, 1426, 1242, 1188, 1154, 965, 740, 695 cm^{-1}; MS m/e (intensity) 191 (M$^+$ + 1, 8.6), 190 (M$^+$, 34.7), 130 (100.0), 117 (36.6), 91.0 (9.2). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.77; H, 7.40.

***E* isomer**: ^{1}H NMR (500 MHz) δ 5.71 (dt, J = 15.3, 6.7 Hz, 1 H, H-4), 5.63 (dt, J = 15.3, 6.9 Hz, 1 H, H-3), 3.67 (s, 3 H, OCH_3), 3.37 (d, J = 6.7 Hz, 2 H, H-5), 3.07 (d, J = 6.9 Hz, 2 H, H-2).

Z isomer: ^{1}H NMR (500 MHz) δ 5.67–5.80 (m, 2 H, H-3, H-4), 3.69 (s, 3 H, OCH_3), 3.40 (d, J = 7.0 Hz, 2 H, H-5), 3.20 (d, J = 7.0 Hz, 2 H, H-2).

Methyl (*E*)-6-(benzyloxy)-5-[(*tert*-butoxycarbonyl)amino]-3-hexenoate (24): yield 95%; R_f 0.31 (hexane/EtOAc, 3/1); ^{1}H NMR (500 MHz) δ 7.25–7.37 (m, 5 H, aromatic), 5.78 (dtd, J = 15.5, 7.0, 1.5 Hz, 1 H, H-3), 5.62 (ddt, J = 15.5, 5.8, 1.1 Hz, 1 H, H-4), 4.89 (m, 1 H, H-5), 4.54 and 4.51 (ABq, J = 12.0 Hz, 2 H, $PhCH_2O$), 4.32 (br s, 1 H, NH), 3.68 (s, 3 H, OCH_3), 3.54 (dd, J = 9.5, 4.6 Hz, 1 H, H-6), 3.49 (dd, J = 9.5, 4.6 Hz, 1 H, H-6′), 3.09 (dd, J = 7.0, 1.1 Hz, 2 H, H-2), 1.43 (s, 9 H, t-BuO); ^{13}C NMR (125.7 MHz) δ 171.86, 155.30, 137.92, 132.18, 128.36 (2), 127.68 (2), 127.59, 123.42, 79.44, 73.15, 72.10, 51.75, 37.54, 37.49, 28.34 (3); IR (neat) 3319, 2944, 1729, 1702, 1486, 1359, 1241, 1160, 1092, 1013, 735, 694 cm^{-1}; MS m/e (intensity) 351 (M^+ + 2, 11.1), 350 (M^+ + 1, 16.0), 294 (15.8), 250 (39.8), 232 (38.4), 172 (67.0), 142 (10.7), 128 (100.0), 96 (20.7), 91 (33.9), 57 (49.2). Anal. Calcd for $C_{19}H_{27}NO_5$: C, 65.31; H, 7.79; N, 4.01. Found: C, 65.40; H, 7.82; N, 4.03.

Methyl (2*R*,3*R*)-4-[(*tert*-butoxycarbonyl)amino]-5-hydroxyhexanoate acetonide (26): yield 99%; R_f 0.54 (hexane/EtOAc, 3/1); $[\alpha]^{25}_D$ −28.6° (c 1.0 in $CHCl_3$); ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.94 (m, 1 H, H-5), 3.60 (s, 3 H, OCH_3), 3.38 (m, 1 H, H-4), 2.24–2.40 (m, 2 H, H-2), 1.94 (m, 2 H, H-3), 1.50 and 1.39 (two singlets, 6 H, 2 CH_3), 1.42 (s, 9 H, t-BuO), 1.21 (d, J = 6.2 Hz, 3 H, H-6); ^{13}C NMR (75.4 MHz, DMSO-d_6) δ 172.81, 151.19, 92.95, 78.98, 74.07, 62.08, 51.22, 29.08, 27.88 (3), 26.0–27.5 (3) 19.79; IR (neat) 2948, 1733, 1686, 1360, 1244, 1165, 1080 cm^{-1}; MS m/e (intensity) 303 (M^+ −38, 0.3), 302 (0.4), 200 (8.4), 186 (57.3), 145 (9.3), 112 (24.1), 96 (8.7), 84 (19.2), 57 (100.0), 43 (44.0), 41 (58.5). Anal. Calcd for $C_{15}H_{27}NO_5$: C, 59.78; H, 9.03; N, 4.65. Found: C, 59.75; H, 8.97; N, 4.66.

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