Tetrahedron Vol 42, No. 11, pp. 2993 to 3001, 1986
Printed in Great Britain.

0040–4020/86 $3.00 + .00
Pergamon Journals Ltd.

ASYMMETRIC INDUCTION IN THE ENE REACTION OF GLYOXYLATE ESTERS OF 8-PHENYLMENTHOL

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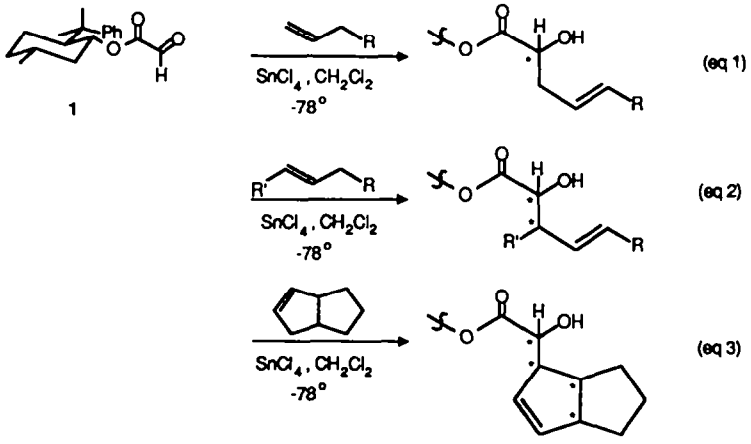
(*Received in U.S.A.* 1 *July* 1985)

Abstract—We recently communicated (J. K. Whitesell, A. Bhattacharya, D. A. Aguilar and K. Henke, *J. Chem. Soc. Chem. Commun.* 989 (1982)) a highly efficient and effective method for the control of absolute stereochemistry through asymmetric induction in the ene reaction the chiral glyoxylate **1** with alkenes. We now have accumulated sufficient information on this process in terms of both its mechanistic details as well as its scope and applicability to a variety of situations that warrants a more complete presentation of these reactions.

The potential for asymmetric induction in a variety of reactions of chiral glyoxylates and, as well, substituted glyoxylates has been the subject of extensive research efforts for a number of years.[2] Nonetheless, none of these studies resulted in levels of stereochemical control that by any means would be considered to represent practical tools for the construction of complex, chiral molecules. Our recent application of the chiral auxiliary 8-phenylmenthol to this area has dramatically changed this perspective and indeed we now feel that these reactions represent extraordinarily valuable tools for the synthetic chemist interested in controlling not only absolute stereochemistry but relative stereochemistry as well. The ene reactions of such species with alkenes are perhaps the most versatile of all of these reactions as the homoallylic alcohols generated in these processes represent not only the functional equivalent of aldols but also are suitably arranged for elaboration to a great range of other functionalities.

We have divided these reactions into three distinct classes, distinguished by the number of stereochemical centers formed within the products. Thus, the reaction with monosubstituted or 2,2-disubstituted alkenes provides for the introduction of but one stereochemical center (Eq. 1). On the other hand, use of 1,2-disubstituted as well as trisubstituted alkenes leads to the formation of chirality at two new centers (Eq. 2). Finally, reaction with alkenes which themselves are chiral provides the opportunity to create new chiral centers while at the same time effecting a kinetic resolution of the racemic form of the starting material (Eq. 3). Our studies in this last class are as yet only preliminary and will be the subject of a separate communication.



Attachment of the substrate to the chiral auxiliary

Direct esterification of substituted glyoxylic acids with 8-phenylmenthol (**2**) leads to the corresponding esters in quite acceptable yields. Unfortunately, the same is not true for the preparation of the parent aldehyde. We have developed two practical syntheses[3] of the glyoxylate ester as outlined in Fig. 1. While the sequence that involves oxidative cleavage of the acrylate ester is superior overall, both sequences produce glyoxylate in acceptable yield and purity. Interestingly, the methylene protons of the acetate moiety in both the bromide **5** and the nitrate ester **6** show enhanced diastereotopicity as compared with similar substances lacking the phenyl moiety of the chiral auxiliary, as evidenced by the difference in chemical shifts in the ^{1}H-NMR. Additionally, the aldehyde proton of the glyoxylate **1** is shifted upfield due to the anisotropic influence of the aromatic ring of the chiral auxiliary by 0.5 δ relative to that in other glyoxylates lacking the aromatic nucleus.† The hydrate **4** is obtained as the product from both sequences and can be dehydrated thermally or used directly in the ene

† The significance of these observations as they pertain to the level of asymmetric induction will be reported elsewhere.

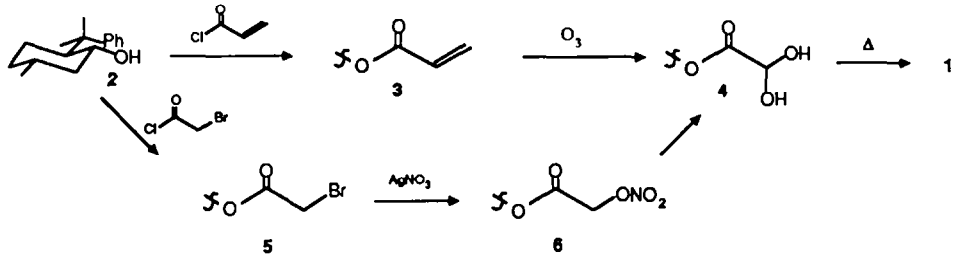


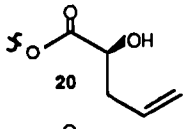
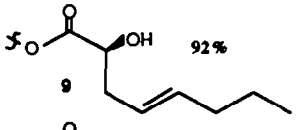
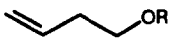
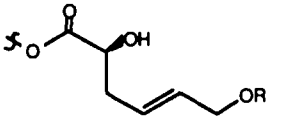
Fig. 1.

reactions, although a second equivalent of $SnCl_4$ is then required.

Reaction with mono- and 2,2-substituted alkenes

The reaction of glyoxylate **1** with simple, monosubstituted alkenes such as propene and 1-hexene (Table 1) proceeds quite rapidly at −78° in methylene chloride with one equivalent of $SnCl_4$. The reactions are generally complete within a matter of minutes and the products obtained by simple isolation techniques are usually quite pure and satisfactory for continued synthetic operations without further purification. It should also be noted that while the product is itself an alkene and potentially a substrate for ene reaction, we have as yet obtained no evidence for the formation of any bis-adducts. While this could be attributed in the majority of instances to the use of an excess of the alkene, there are cases in which the alkene was used in a stoichiometric fashion and even then there was no bis-adduct formation. The reluctance of the products from this reaction to undergo further transformation may well indeed be due to their formation as a complex between the Lewis acid and the alcohol functionality created in the reaction. Approximately 6% of the *cis*-alkene is formed when there is the possibility of geometric isomers involving the newly formed double bond.

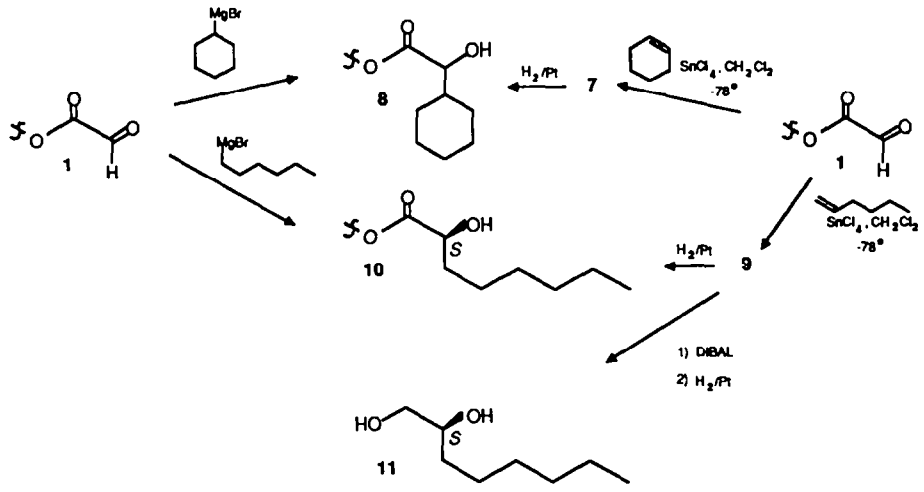
Table 1. Reaction of monosubstituted alkenes with phenmenthyl glyoxylate

Alkene	Product
	 **20** 99%
	 **9** 92%
	
	21 R = H 100% **22** Ac 59 **23** CH_2Ph 99 **24** TBS 89

A minimum level of asymmetric induction obtained in these reactions could, in many cases, be directly assessed from a chromatographic analysis of the diastereomers formed. The retention volumes of both diastereomers could be determined by analysis of the thermal ene reaction products where little selectivity is obtained. However, direct isolation of the minor diastereomers from the catalyzed reactions is impractical since they are formed in such small quantities and we have no hard evidence that the minor diastereomer is formed at all in these reactions. Indeed, while we had originally reported a diastereomeric ratio 98.8:1.2 for the ene reaction with 1-hexene, a more recent examination showed that the minor diastereomer appeared as a shoulder of the 1.2% peak and represented no more than 0.1% of the products. While the difference between a diastereomeric excess of 97.6 and 99.8% is both practically and energetically significant, we have not expended the relatively large effort that would be required to analyze the ene reactions of each of the substrate alkenes with this degree of care. In cases where *trans* and *cis* geometric isomers of the product were formed in the ene reaction, the analysis was carried out after removal of the double bond by catalytic reduction.

The absolute sense of the stereochemistry formed in the ene reactions was determined to be the same as that obtained in reactions involving nucleophilic addition[4] by comparison of the ene adducts from 1-hexene and from cyclohexene, after reduction of the double bonds (**7** to **8** and **9** to **10**), with the products formed by addition of the corresponding Grignard reagents to the glyoxylate. In addition, the ene adduct **9** was chemically correlated with *S*-1,2-dihydroxyoctane[5] (**11**) through reduction of the ester and alkene functionalities.

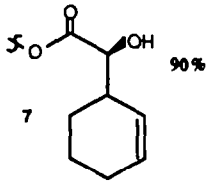
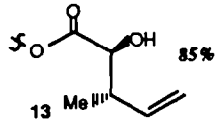
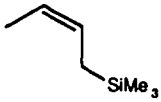
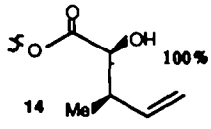
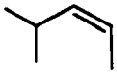
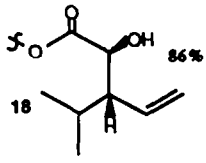
While the ene adducts from simple monosubstituted alkenes are suitably functionalized at the α-hydroxy ester for elaboration to more complex arrays, the tail added in ene reaction by the alkene unit itself is relatively simple. In order to establish what functionality might be tolerated in this process, we explored several protected forms of 3-buten-1-ol (Table 1). The t-butyldimethylsilyl and the benzyl ether protecting groups both survived completely intact after the normal reaction period of 10 min at −78°. However, the t-butyldimethylsilyl ether was cleaved when the reaction was effected at 0° over a period of several hours, although the product was still only the *trans* geometric isomer (see below). In the majority of cases this treatment represents rather unnecessarily drastic reaction conditions for the ene reaction. We were also pleased to observe that the acetate protected hydroxyl group survived the reaction conditions and



by implication, it would appear that an ester would be a suitable protecting group and not partake in the reaction under the mild conditions which are required by most substrates.

Interestingly, when the 3-butene-1-ol was used directly without protection of the hydroxyl group, an approximately 2:1 mixture of the *cis*- and *trans*-alkene geometric isomers was produced. We believe that the *cis*-alkene **12** results mainly from a competing reaction pathway that involves simultaneous complexation of the Lewis acid to both the glyoxylate carbonyls and the free hydroxyl group. In an attempt to make this pathway dominant, the Lewis acid and the free alcohol were combined prior to addition to the glyoxylate. In this process no ene adduct resulted. This result is consistent with our argument above that the alkenes produced are inhibited from undergoing the initial stages of this reaction so long as the hydroxyl group is complexed with the Lewis acid. This complexation inhibits reactivity not only in the ene adducts but also apparently for 3-buten-1-ol as well.

Table 2. Reaction of 1,2-disubstituted alkenes with phenmenthyl glyoxylate

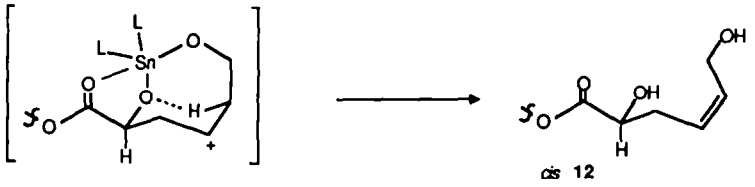
Alkene	Product
	 90% 7
	 85% 13 (15:1 erythro/threo)
	" (8:1 erythro/threo)
	 100% 14 (1:15 erythro/threo)
	 86% 18

The ene reaction with 2,2-disubstituted alkenes can provide adducts with a single stereocenter, at carbon 2, or in very special cases, two chiral centers. These possibilities are illustrated by the reaction of *exo*-methylenecyclohexane and 4-t-butyl-*exo*-methylenecyclohexane, respectively. In the first case, only a single diastereomer was observed by both ^{13}C-NMR and LC analysis while two diastereomers were formed in the second case.

With the 2,2-disubstituted alkenes (e.g. **30**, Table 3) where the two substituents are structurally different there is the possibility of producing regioisomerically distinct products. Indeed, both geometric isomers of the trisubstituted alkene product as well as the adduct with a disubstituted double bond were formed in the reaction with **29** (R = OAc, Table 3). Interestingly, the free alcohol **29** (R = H) afforded dominantly the adduct with the disubstituted alkene.

Reactions with 1,2-disubstituted alkenes

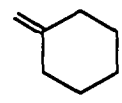
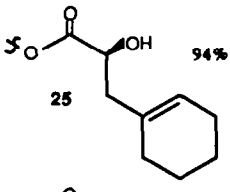
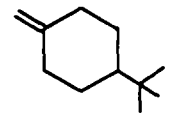
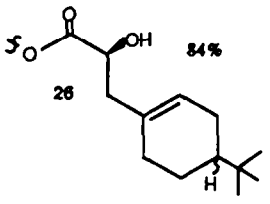
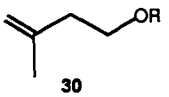
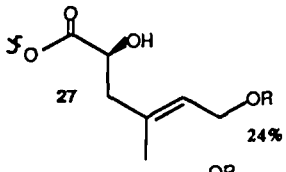
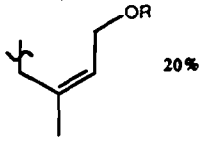
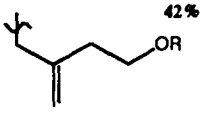
The ene reaction with a disubstituted alkene such as *trans*-butene will afford two stereochemical centers in the adduct. The ene reaction with this alkene provided the 2*S*,3*S* isomer (**13**) as the major diastereomer in a 15:1 ratio with the alternate 2*S*,3*R* stereoisomer (**14**). The assignment of relative configuration was made by hydrolysis of **13** and **14** to the known acids **15** and **16** which show distinct ^{13}C-NMR adsorptions.[6] It is important to note that the hydrolysis of both esters to the corresponding acids could be effected without a detectable change in the diastereomeric ratio, thus



cis **12**

indicating that no significant epimerization had occurred. Additional evidence for the stereochemical assignments was obtained by the conversion of **14** to the known lactone **17**.[7] The diastereomers **13** and **14** (as well as **15** and **16**) would be referred to respectively as *threo* and *erythro* according to the Heathcock nomenclature system, which although it involves very significant ambiguities is perhaps best used here since it speaks directly to the applicability of the major ene adduct for the construction of certain classes of natural products. The homoallylic functionality present would appear to be an ideally protected form of an aldol, having neither the propensity to undergo retroaldol or loss of water and thereby the stereochemistry built into this material by the ene reaction can be preserved through a large variety of reactions until that point when the aldol functionality itself is desired. Indeed, the *threo* stereoisomer which is the dominant product of our ene reaction is just that which is not yet available from directed aldol chemistry with a high level of control of both relative and absolute stereochemistry. Nonetheless, we wished to have a procedure which, at choice, could provide either the *threo* or the *erythro* relative relationship and to this end we examined the reaction with *cis*-butene. This simple expedient was not effective in reversing the stereochemical selection as the dominant stereoisomer was still the *threo* although the ratio was not as high as obtained with the *trans*-alkene. This outcome could be most simply explained by isomerization between the *cis* and *trans* isomers during the course of the reaction. However, when *cis*-butene was subjected to the catalyst at $-78°$ as well as to the catalyst plus isopropyl alcohol under these same reaction conditions, no isomerization to *trans*-butene was observed. The presence of the glyoxylate would thus appear to be required for isomerization. These observations are consistent with a reaction pathway as outlined in Fig. 2.

Table 3. Reaction of 2,2-disubstituted alkenes with phenmenthyl glyoxylate

Alkene	Product
	 94% **25**
	 84% **26**
 **30**	 **27** 24%
R = OAc	 20% **28**
	 42% **29**

An intermediate carbocation is formed rapidly and reversibly and reversal of this cation to starting materials is faster than progression onto product ($K_{-1} > K_2$). Such a scenario requires that the second step, the loss of a proton, be not only the rate limiting but also the product-determining step. Based on the relatively high level of selectivity observed for formation of the *threo* isomer, we feel that this loss of a proton must represent an intramolecular process and indeed such a hypothesis explains the predominance of the *threo* isomer through competition between transition states **A** and **B** in Fig. 2. Product control through such a cyclic proton transfer transition state also explains the preference for formation of the *trans*-alkene (cf. transition states **C** and **D**, Fig. 3).

While the stereochemistry observed in these reactions is consistent with a two-step reaction pathway where the proton transfer controls the ultimate stereochemistry, a concerted cycloaddition type reaction could also be used to rationalize the result. Our only firm evidence that points to the two-step pathway is the requirement for the glyoxylate to be present for *cis–trans* isomerization, and this process may be occurring via the cation while the ene reaction is the result of a separate, concerted process.

The ene reaction of glyoxylate **1** and 4-methyl-*cis*-2-pentene (presumably through isomerization to the *trans* isomer) afforded a single diastereomer as well as only one regioisomer (**18**) resulting from C—C bond formation at carbon 3.

As above, this outcome can be rationalized as the result of the stereochemical and regiochemical control at the stage of proton transfer from an intermediate carbocation as well as by assuming that the processes were concerted. In comparing transition states **E–H** in Fig. 4, those leading to product from attack at carbon 2 must necessarily have at least one methyl group axial in the transition state.

The difference between the transition states **E** and **F** leading to the *threo* and *erythro* stereoisomers, re-

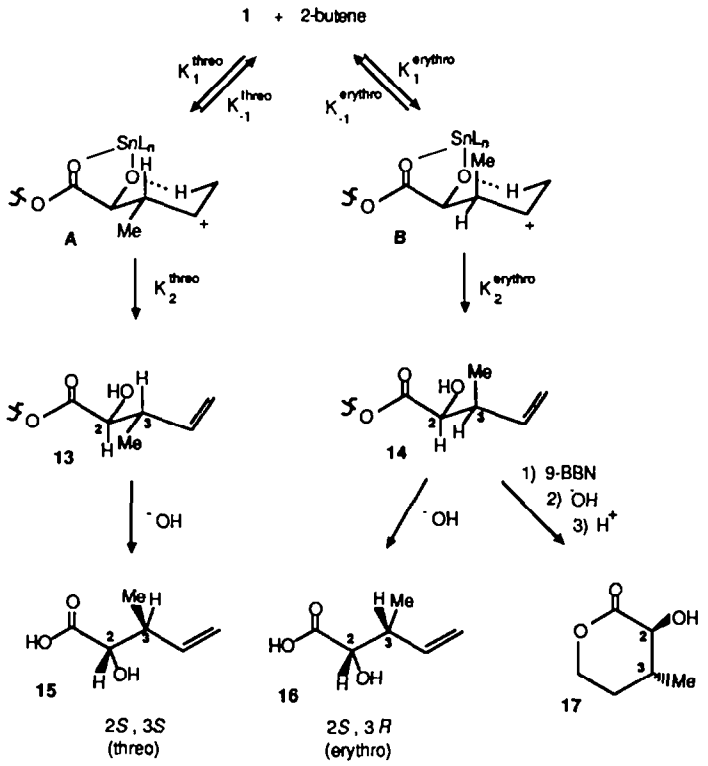


Fig. 2.

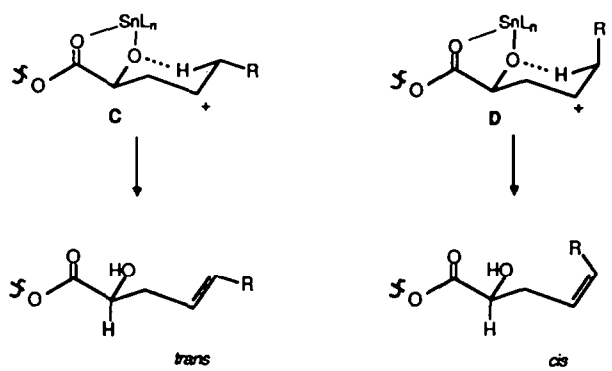


Fig. 3.

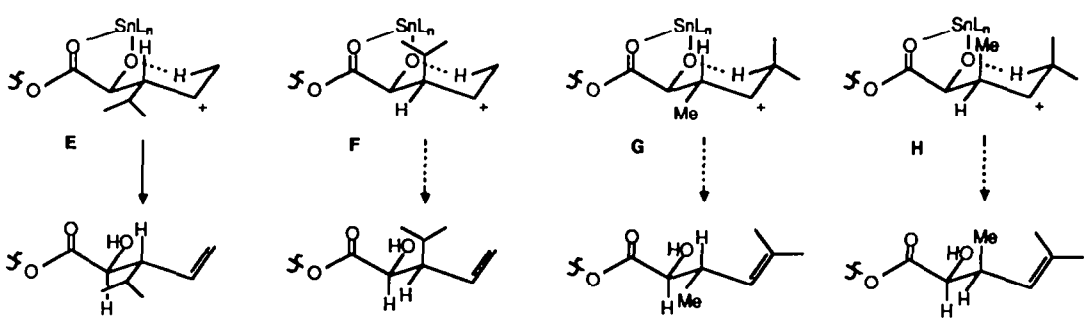


Fig. 4.

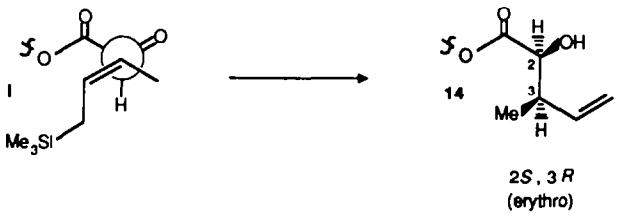


Fig. 5.

spectively, would be expected to be greater than in the case of the butene reactions since now the difference is between an isopropyl group either equatorial or axial in the transition state. Note that this outcome represents a significant advantage in the use of these ene adducts as aldol equivalents since the more complex substituent on the original alkene would be retained after oxidative cleavage.

The geometric constraints imposed upon such a proton transfer transition state by placing the alkene moiety within a medium ring dictate that only the 2*S*,3*S* stereochemistry would be anticipated, and indeed only a single diastereomer was observed in the ene reaction with cyclohexene. We were able to establish that the absolute stereochemistry at carbon 2 in **7** was the same as that obtained by the addition of cyclohexyl Grignard to aldehyde **1** through a reduction of the double bond in the ene adduct (**7** to **8**).

Based on our analysis of the course of this reaction we felt it might be possible to obtain the *erythro* relationship through the use of 1-trimethylsilyl-*cis*-2-butene,[8] since the additional stabilization of the intermediate carbocation afforded by a silicon substituent might reverse the relative ease with which the intermediate reverted to starting material and proceeded on to product. Indeed, this analysis appears to be correct as the *cis*-allyl silane does not undergo geometric isomerization under the reaction conditions and the product is dominantly of the 2*S*,3*R* configuration (**14**) at the level of 15:1. This outcome is best rationalized by assuming stereochemical control in the addition stage through a transition state **I**, represented as a Newman projection in Fig. 5. This arrangement has previously been invoked to explain the stereochemical outcome of similar reactions.[9]

Trisubstituted alkenes afford ene adducts with two chiral centers while progressing through an intermediate, tertiary carbocation, which might be anticipated to affect the rates K_{-1} and K_2 (Fig. 2). Indeed, the reaction of **1** with 2-methyl-2-butene afforded a 2:1 mixture of diastereomers (**20**), presumably differing at C-3 (Fig. 6).

We have examined a wide range of Lewis acids for use in promoting the ene reactions of **1**, including Et_2AlCl, $EtAlCl_2$, BF_3, $ZnCl_2$, $FeCl_3$, $MgBr_2$, and $TiCl_4$. All of these were significantly less effective in terms of chemical yields of ene adducts when compared with $SnCl_4$ and in many cases no ene adduct was observed. It is interesting to contrast these results with those reported by Snider and van Straten[10] for the ene reaction of methyl glyoxylate where ferric chloride was found to be superior to other Lewis acids and *erythro/threo* stereochemical control was no better than 2:1.

As should be clear, the ene reaction of 8-phenylmenthyl glyoxylate presents a powerful tool for the development of absolute stereochemistry in acyclic systems. In all cases examined, the control of absolute stereochemistry at carbon 2 in the adducts is at the level of at least 95:5, as evidenced by the absence of diastereomeric contamination in the ^{13}C-NMR spectra. In several cases examined, the level of induction could be directly assessed by LC analysis and was consistently in excess of 99.8% d.e. The method can also be used to control absolute and therefore of course relative stereochemistry at carbon 3 in the adducts and relatively simple modification of the alkene substrate affords the opportunity to produce either stereochemistry at this center at will. We have demonstrated that the adducts can be removed from the chiral auxiliary without significant degradation of the stereochemical integrity of carbon 2. We believe that this method will find wide application in the construction of a variety of more complex chemical arrays in which the control of absolute stereochemistry is essential.

EXPERIMENTAL

Materials. Ether and THF were distilled prior to use from a deep-blue soln resulting from benzophenone and Na. Skelly-B (hexane) was stirred with H_2SO_4 and solid Na_2CO_3 and distilled before use. All other solvents and reagents were used as obtained from commercial sources.

Procedures. Reactions were routinely run under dry N_2 with magnetic stirring. Organic solns of products were dried with molecular sieves prior to concentration *in vacuo*. Crude products were routinely passed through short columns of silica gel with an appropriate mixture of hexane and EtOAc. Reference to purification by HPLC refers to the use of a Waters Prep-500 system with two silica gel cartridges.

Spectra. ^{1}H-NMR were obtained using either a Varian EM-390 or a Nicolet 200 MHz instrument. ^{13}C-NMR data were

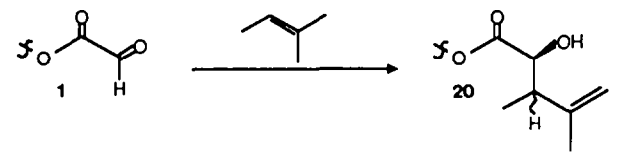


Fig. 6.

obtained using either a Brucker WD-90 or a Varian FT-80A instrument. Both ^{1}H- and ^{13}C-NMR were obtained with $CDCl_3$ as solvent and values are reported in ppm downfield from TMS as internal standard, except as noted. The absorptions in the carbon spectra for the 8-phenylmenthol subunit are listed after those for the substrate subunit and assignments are provided only for the latter except in the case of the glyoxylate **1** and the bromoacetate ester **5** since the adsorptions for the chiral auxiliary unit are relatively unaffected by the nature of the other. IR spectra were obtained on dilute, CH_2Cl_2 solns using a Perkin–Elmer 237B instrument. High-resolution mass spectra were recorded with a Dupont 21-110B instrument.

(1*R*,2*S*,5*R*) - 2 - (1 - *Methyl* - 1 - *phenylethyl*) - 5 - *methylcyclohexyl glyoxylate* (**1**)

Method A. To 43.4 g (130 mmol) of 8-phenylmenthyl nitrooxyacetate dissolved in 100 ml of DMSO was added a suspension of 17.7 g (130 mmol) of sodium acetate trihydrate in 250 ml of DMSO. The mixture was stirred at room temp under N_2 for 70 min before pouring it into 1400 ml of ice–water. After saturating with NaCl, the soln was extracted thoroughly with ether, which was washed with sat $NaHCO_3$ and water. Concentration *in vacuo* gave 61.0 g of an orange oil which was distilled under reduced pressure using a short path distillation head. The glyoxylate distilled as a pale yellow viscous oil at 135–142°/0.1 mm Hg to give 34.6 g (92%) of the title product.

Method B. O_3 in oxygen was bubbled into a soln of 47.3 g (167 mmol) of 8-phenylmenthyl acrylate in 250 ml of MeOH and 400 ml of CH_2Cl_2 at −78° until a blue color persisted. The mixture was flushed with dry N_2 to remove excess O_3 and 63.5 g (1.02 mol) of Me_2S added before warming to −25° for 13.5 h. The soln was concentrated and the resulting oil was taken up in ether and washed with two 200 ml portions of sat $NaHCO_3$ and 200 ml of water. The aqueous layers were extracted with two 200 ml portions of ether. The solvent was removed and the aldehyde dehydrated by heating to 90°/0.1 mm Hg for 4.5 h. This yielded 42.6 g (89%) of glyoxylate which was used in ene reactions without further purification. ^{13}C-NMR: 186.6 (d, C1), 157.9 (nd, C2), 151.2 (s, C11'), 128.0 (d, C13'), 125.4 (d, C12' & C14'), 76.4 (d, C1'), 50.5 (d, C2'), 41.3 (t, C6'), 39.5 (s, C7'), 34.4 (t, C4'), 31.3 (d, C5'), 29.6 (q, C9' or C10'), 26.2 (t, C3'), 22.8 (q, C9' or C10'), 21.7 (q, C8'). ^{1}H-NMR: 8.38 (s, 1H), 7.34–7.05 (m, 5H), 5.0 (dt, J = 4.2, 10.5 Hz, 1H), 1.32 (s, 3H), 1.24 (s, 3H), 0.9 (d, J = 6.3 Hz, 3H), 2.25–0.8 (m, 8H). IR: 3020, 2980, 2300, 1740, 1720, 1420, 1260 cm^{-1}.

(1*R*,2*S*,5*R*) - 2 - (1 - *Methyl* - 1 - *phenylethyl*) - 5 - *methylcyclohexanol* (**2**)

(−)-8-Phenylmenthol was prepared by the procedure detailed by Corey and Ensley.[11] ^{13}C-NMR: 151.2 (s, C11), 128.3 (d, C13), 125.8 (d, C12), 125.6 (d, C14), 72.8 (d, C1), 54.2 (d, C2), 45.7 (t, C6), 39.9 (s, C7), 35.0 (t, C4), 31.6 (d, C5), 28.0 (q, C9), 26.7 (t, C3), 25.3 (q, C10), 22.0 (q, C8).

(1*R*,2*S*,5*R*) - 2 - (1 - *Methyl* - 1 - *phenylethyl*) - 5 - *methylcyclohexyl acrylate* (**3**)

To a soln of 44.7 g (192 mmol) of 8-phenylmenthol, 3.29 g (26.9 mmol) of 4-dimethylaminopyridine, and 38.9 g (385 mmol) of Et_3N in 200 ml of CH_2Cl_2 at 0° was slowly added 34.8 g (384 mmol) of acryloyl chloride. The mixture was stirred at 0° for 2.2 h before adding 100 ml of water. The aq layer was extracted with five 50 ml portions of CH_2Cl_2 and the combined organic layers were concentrated. The orange residue was partitioned between water and ether, and the aq layer was extracted with three 100 ml portions of ether. The combined organic layers were concentrated and then passed through a short column of silica gel with EtOAc. Concentration *in vacuo* yielded 47.3 g (87%) of an orange oil. ^{13}C-NMR: 165.1 (s, Cl), 129.6 (t, C3), 129.0 (d, C2); 151.4 (s), 128.0 (d), 125.4 (d), 125.0 (d), 74.4 (d), 50.6 (d), 41.7 (t), 39.7 (s), 34.6 (t), 31.3 (d), 27.6 (q), 26.7 (d), 25.4 (q), 21.8 (q); ^{1}H-NMR: 7.34–7.0 (m, 5H), 6.1–5.5 (m, 3H), 4.88 (dt, J = 4.2, 10.5 Hz, 1H), 1.32 (s, 3H), 1.2 (s, 3H), 0.85 (d, J = 6.3 Hz, 3H), 2.14–0.7 (m, 8H).

(1*R*,2*S*,5*R*) - 2 - (1 - *Methyl* - 1 - *phenylethyl*) - 5 - *methylcyclohexyl bromoacetate* (**5**)

A mixture of 41.8 g (180 mmol) of 8-phenylmenthol, 62.5 g (450 mmol) of bromoacetic acid, and 4.11 g (21.6 mmol) of *p*-toluenesulfonic acid monohydrate in 500 ml of benzene was refluxed for 11 h with removal of water via a Dean–Stark trap. After cooling, the reaction was quenched by adding 500 ml of 2 N Na_2CO_3. The aq layer was extracted thoroughly with ether. Concentration yielded 60.1 g (95%) of bromoacetate as reddish crystals. ^{13}C-NMR: 166.1 (C1), 29.4 (C2); 151.6, 127.9, 125.3, 125.1, 75.7, 50.3, 41.2, 39.4, 34.4, 31.3, 29.4, 26.2, 23.1, 21.7; ^{1}H-NMR: 7–7.4 (m, 5H), 4.82 (dt, J = 4, 10.2 Hz, 1H), 2.94 (s, 2H), 1.30 (s, 3H), 1.19 (s, 3H), 0.91 (d, J = 6 Hz, 3H); HRMS: calc for $C_{18}H_{25}BrO_2$: 352.1038; found: 352.1026.

(1*R*,2*S*,5*R*) - 2 - (1 - *Methyl* - 1 - *phenylethyl*) - 5 - *methylcyclohexyl nitrooxyacetate* (**6**)

To 60.0 g (170 mmol) of 8-phenylmenthyl bromoacetate dissolved in 137 ml of acetonitrile was added a soln of 54.9 g (323 mmol) of $AgNO_3$ in 200 ml of acetonitrile. The mixture was stirred at room temp under N_2 for 94 h and then filtered and the solvent removed *in vacuo*. The oil was taken up in ether and washed with water. Removal of the ether gave 43.4 g (81%) of the nitrate ester. ^{13}C-NMR: 165.0 (C1), 151.8, 128.1, 125.4, 76.0, 66.9, 50.2, 41.6, 39.5, 34.5, 31.4, 29.9, 26.3, 22.6, 21.7; ^{1}H-NMR: 7.03–7.33 (m, 5H), 4.9 (dt, J = 4, 10.2 Hz, 1H), 4.23 (d, J = 19.5 Hz, 1H), 3.8 (d, J = 19.5 Hz, 1H), 1.3 (s, 3H), 1.17 (s, 3H), 0.86 (d, J = 6 Hz, 3H).

(−)-8-*Phenylmenthyl* (2*S*,3*S*) - 2 - *hydroxy* - 3 - *methyl* - 4 - *pentenoate* (**13**)

A soln of 40.1 g (139 mmol) of 8-phenylmenthyl glyoxylate in 1100 ml of CH_2Cl_2 was cooled to −78°. Excess *trans*-2-butene which had been precooled to −78° was added followed by 54.3 g (209 mmol) of $SnCl_4$ which was added over a 10 min period. The reaction was stirred at −78° for 3.2 h before quenching with 450 ml of ether. The mixture was allowed to warm to room temp before it was poured into 500 ml of sat $NaHCO_3$. The organic layer was washed with 250 ml of sat $NaHCO_3$. The organics were concentrated and passed through a short column of silica (1 : 1 hexane–EtOAc). Concentration *in vacuo* yielded 40.6 g (118 mmol, 85%) of an orange oil. ^{13}C-NMR analysis showed that the ratio of the *threo* and *erythro* isomers was 15 : 1. If the butene is added directly to the reaction mixture without precooling the ratio of diastereomers was 8 : 1.

Major (*threo*): ^{13}C-NMR: 173.5 (s, C1), 137.8 (d, C4), 115.6 (t, C5), 73.4 (d, C2), 16.4 (q, C6), 41.4 (d, C3), 125.2 (d), 151.7 (s), 128.0 (d), 75.6 (d), 50.4 (d), 41.7 (d), 39.4 (s), 34.6 (t), 31.3 (t), 29.4 (q), 26.3 (t), 23.2 (q), 21.8 (q); ^{1}H-NMR: 7.34–7.23 (m, 5H), 5.56 (ddd, J = 8.2, 10.5, 18.9 Hz, 1H), 5.0–4.77 (m, 3H), 3.09 (d, J = 3 Hz, 1H), 2.58 (bs, 1H), 1.28 (s, 3H), 1.18 (s, 3H), 0.96 (d, J = 6.5 Hz, 3H), 0.87 (d, J = 6.5 Hz, 3H). HRMS: calc for $C_{22}H_{32}O_3$: 344.2351; found: 344.2346.

(−)-8-*Phenylmenthyl* (2*S*,3*R*) - 2 - *hydroxy* - 3 - *methyl* - 4 - *pentenoate* (**14**)

Using the standard procedure, 0.57 g (2.0 mmol) of **1** and 0.37 g (2.9 mmol) of 1-trimethylsilyl-(*Z*)-2-butene[7] gave 0.69 g (100% crude) of the ene adduct with a 15 : 1 ratio of *erythro* to *threo* diastereomers.

For the major, *erythro* isomer: ^{13}C-NMR: 173.7 (s, C1), 139.6 (d, C4), 115.0 (t, C5), 73.0 (d, C2), 41.0 (d, C3), 13.1 (q, C6), 151.7 (s), 128.0 (d), 125.2 (d), 76.0 (d), 50.4 (d), 41.6 (t), 39.5 (s), 34.6 (t), 31.3 (d), 29.5 (q), 26.4 (t), 23.2 (q), 21.8 (q); ^{1}H-NMR (200 MHz): 7.07–7.35 (m, 5H), 5.57–5.74 (ddd, J = 6.9, 10.9, 17.1 Hz, 1H), 4.92–5.04 (d with fine splitting, J = 2, 17.1 Hz, 1H), 4.97–5.04 (d with fine splitting, J = 2.0, 10.9 Hz, 1H), 4.78–4.93 (td, J = 7.9, 10.6 Hz, 1H), 3.13–3.21 (br t, [d, J = 3.2 Hz in D_2O], 1H), 2.59–2.67 (br d, J = 4.8 Hz, 1H), 2.09–2.22 (m, 2H), 1.79–1.94 (m, 2H), 1.64–1.78 (m, 1H), 1.40–1.59 (m, 1H), 1.29 (s, 3H), 1.19 (s, 4H), 0.75–1.10 (complex, with: 0.88 (d, J = 6.9 Hz,

3H), 0.78 (d, J = 7.2 Hz, 3H), 8H total); HRMS: calc for $C_{22}H_{32}O_3$: 344.2351; found: 344.2356. The minor isomer was identical to **13**, described above.

(2S,3S)-2-Hydroxy-3-methyl-4-pentenoic acid (**15**)

The general procedure for the hydrolysis of ene adducts is given below. To a soln of 2.22 g (6.44 mmol) of ene adduct **13** in 20 ml of THF was added 20 ml (20 mmol) of 1 N NaOH and 40 ml of MeOH. The soln was heated at reflux for 12 h, then cooled to room temp and extracted with three 40 ml portions of Skelly B to remove (−)-8-phenylmenthol. The aq mixture was saturated with NaCl, acidified with 2 N HCl, and extracted with four 40 ml portions of EtOAc. The combined EtOAc extracts were concentrated to afford 0.66 g (79%) of **15** as a brown oil with spectral data identical with literature values.[5] ^{13}C-NMR: 177.6 (C1), 137.4 (C4), 116.9 (C5), 74.2 (C2), 41.7 (C3), 16.4 (C6).

(2S,3R)-2-Hydroxy-3-methyl-4-pentenoic acid (**16**)

According to the general procedure, 0.35 g (1.0 mmol) of crude ene adduct **14** afforded 0.14 g (100%) of hydroxy acids as a 15:1 mixture with the *erythro* diastereomer as the major isomer. ^{13}C-NMR: 177.7 (C1), 139.1 (C4), 116.0 (C5), 73.8 (C2), 41.6 (C3), 13.5 (C6).

(2S,3R)-2-Hydroxy-3-methylvalerolactone (**17**)

To a 0.5 M soln of 9-BBN (10.0 ml, 5 mmol) in THF was added 0.30 g (0.87 mmol) of ene adduct **14** in 2 ml of THF. The soln was heated at 65° for 3 h. The reaction was cooled to room temp and then 3 ml of EtOH, 1 ml of 6 N NaOH, and 2 ml of 30% H_2O_2 were added. The reaction was heated at 50° for 8 h. The cooled soln was saturated with K_2CO_3 and the layers were separated. The aq layer was acidified with 6 N HCl and then stirred overnight. The soln was saturated with NaCl and extracted with three 5 ml portions of EtOAc and three 5 ml portions of acetone. The combined organic layers concentrated. Preparative HPLC afforded 21 mg (17%, low due to mechanical losses) of **17**. Sublimation afforded pure lactone, m.p. 103–104°. ^{1}H-NMR: 4.24–4.45 (m, 2H), 3.80–3.89 (d, J = 10.7 Hz, 1H), 3.26 (br s, 1H), 1.90–2.17 (m, 2H), 1.60–1.79 (m, 1H), 1.22–1.29 (d, J = 6.3 Hz, 3H). Specific rotation: $[\alpha]_D$ −12.4° (*c* = 0.42, $CHCl_3$), (lit.[12] −11 ± 2°, *c* = 0.33, $CHCl_3$).

(−)-8-*Phenylmenthyl* (*2S*)-2-*hydroxy*-2-(2-*cyclohexenyl*)*acetate* (**7**)

Glyoxylate **1** (1.96 g, 6.80 mmol), 1.77 g (6.79 mmol) of $SnCl_4$, and 1.12 g (13.6 mmol) of cyclohexene were reacted under the standard conditions to afford 2.27 g (90%) of **7**. ^{13}C-NMR: 173.9 (C1), 130.3 (C4), 125.6 (C5), 73.0 (C2), 39.5 (C3), 25.5 (C8), 24.9 (C6), 21.8 (C7); 151.8, 128.0, 125.3, 125.1, 75.7, 50.4, 41.5, 39.4, 34.6, 31.3, 29.4, 26.3, 23.2, 21.8; ^{1}H-NMR: 7.36–7.0 (m, 5H), 5.73 (dd, J = 3.3, 9.6 Hz, 1H), 5.13 (br d, J = 10.2 Hz, 1H), 4.84 (dt, J = 4.2, 10.4 Hz, 1H), 3.1 (dd, J = 3.6, 6 Hz, 1H), 2.52 (br d, J = 6 Hz, 1H, exchangeable with D_2O), 1.27 (s, 3H), 1.1 (s, 3H), 0.85 (d, J = 6 Hz, 3H).

(−)-8-*Phenylmenthyl* (*2S*)-2-*hydroxy*-2-*cyclohexylacetate* (**8**)

A soln of 0.67 g (1.8 mmol) of ene adduct **7** in 20 ml of MeOH with 0.12 g of 5% Pd/C was exposed to an atmosphere of H_2 with stirring for 6 h. The catalyst was removed by filtration. Concentration afforded 0.67 g (100%) of spectroscopically pure **8**. ^{13}C-NMR: 174.3 (C1), 74.0 (C2), 41.4 (C3), 29.0 (C4), 26.4 (C6), 26.1 (C5), 151.7, 128.0, 125.2, 125.2, 75.8, 50.4, 41.4, 39.5, 34.6, 31.3, 29.2, 26.3, 23.5, 21.8; ^{1}H-NMR: 7.4–7.1 (m, 4H), 4.87 (dt, J = 4.5, 10.8 Hz, 1H), 3.07 (br s, 1H), 2.53 (br s, 1H), 1.3 (s, 3H), 1.2 (s, 3H), 0.9 (d, J = 3 Hz, 3H).

(−)-8-*Phenylmenthyl* (*2S,4E*)-2-*hydroxy*-4-*octenoate* (**9**)

Using the standard procedure, 2.06 g (7.15 mmol) of glyoxylate **1**, 1.86 g (7.14 mmol) of $SnCl_4$, and 1.2 g (14.3 mmol) of 1-hexene were converted to 2.45 g (92%) of ene adduct **9**: ^{13}C-NMR: 173.9 (s, C1), 134.1 (d, C5), 123.9 (d, C4), 69.7 (d, C2), 37.2 (t, C3), 34.6 (t, C6), 22.4 (t, C7), 13.6 (q, C8), 151.6, 127.9, 125.2, 75.5, 50.4, 41.8, 39.4, 34.6, 31.2, 29.0, 26.4, 23.6, 21.8; ^{1}H-NMR: 7.35–7.21 (m, 4H), 7.1 (m, 1H), 5.5–5.14 (m, 2H), 4.85 (dt, J = 4.2, 10.4 Hz, 1H), 3.28 (m, 1H), 2.78 (br d, J = 5.2 Hz, 1H, D_2O exchangeable), 1.28 (s, 3H), 1.18 (s, 3H); HMRS: calc for $C_{24}H_{36}O_3$: 372.2821; found: 372.2818.

(−)-8-*Phenylmenthyl* (*2S*)-2-*hydroxyoctanoate* (**10**)

Ene adduct **9** (0.96 g, 2.58 mmol) was reduced as described above for **8** to afford 0.96 g (100%) of spectroscopically pure **10**. ^{13}C-NMR: 174.8 (C1), 69.9 (C2), 34.0 (C3), 31.6 (C4), 28.9 (C5), 24.6 (C4), 22.5 (C7), 14.0 (C8), 151.7, 128.0, 125.3, 75.6, 50.4, 41.6, 39.5, 34.6, 31.3, 29.2, 26.4, 23.5, 21.8; ^{1}H-NMR: 7.04–7.33 (m, 6H), 4.84 (dt, J = 4.5, 10.8 Hz, 1H), 3.2 (m, 1H), 2.53 (br s, 1H, D_2O exchangeable), 1.28 (s, 3H), 1.19 (s, 3H), 0.9 (t, J = 3 Hz, 3H); HMRS: calc for $C_{24}H_{38}O_3$: 374.2821; found: 374.2816.

(2S,4E)-4-Octene-1,2-diol (**11**)

To a −78° soln of 0.914 g (2.46 mmol) of **10** in 25 ml of THF was slowly added 9.8 ml of a 1.0 M (9.8 mmol) hexane soln of diisobutylaluminum hydride. The mixture was allowed to slowly warm up to room temp over a period of 16 h. After 15 ml of MeOH and 15 ml of water were added, the mixture was filtered through a pad of Celite. The filtrate was concentrated and extracted with three 50 ml portions of ether. Concentration of the organic layers gave 2.20 g of crude product. The *S*-diol was purified by HPLC (1:1 hexanes–EtOAc) to yield 0.42 g (42%) of **11**. ^{13}C-NMR: 134.4 (d, C5), 125.4 (d, C4), 71.9 (d, C2), 66.3 (t, C1), 36.8 (t, C3), 34.8 (t, C6), 22.6 (t, C7), 13.7 (q, C8); ^{1}H-NMR (200 MHz): 0.9 (t, J = 6.9 Hz, 3H, CH_3), 1.28–1.50 (m, 2H, CH_2), 2.0 (q, J = 7.4 Hz, 2H, CH_2), 2.18 (t, J = 6.3 Hz, 2H, CH_2), 3.18 (br s, 2H, OH), 3.37–3.55 (m, 1H, CH—O—), 3.58–3.80 (m, 2H, CH_2—O—), 5.30–5.64 (m, 2H, CH=CH); specific rotation: $[\alpha]_D$ = +11.1° (EtOH).

(−)-8-*Phenylmenthyl* (*2S,3S*)-2-*hydroxy*-3-*isopropyl*-4-*pentenoate* (**18**)

Using the standard procedure, 0.32 g (1.12 mmol) of glyoxylate **1** and 0.189 g (2.25 mmol) of (*Z*)-4-methyl-2-pentene afforded 0.47 g of crude product. Purification of 0.14 g of this material by HPLC (2.9 column volumes with 15:1 SKB–EtOAc) afforded 0.11 g (86% yield). ^{13}C-NMR: 174.6 (C1), 135.7 (C4), 117.9 (C5), 70.5 (C2), 54.5 (C3), 28.0 (C6), 21.1 (C7), 20.6 (C8), 151.8, 128.0, 125.3, 75.4, 50.3, 41.9, 39.4, 34.6, 31.3, 29.8, 26.3, 22.8, 21.8; ^{1}H-NMR (200 MHz): 7.07–7.36 (m, 5H), 5.42–5.63 (dt, J = 10.5, 17.0 Hz, 1H), 4.95–5.04 (dd with fine coupling, J = 3, 10.5 Hz, 1H), 4.77–4.95 (complex, with: td (J = 3, 17.0 Hz) at 5.33, 2H), 3.22 (broad s, 1H), 2.54 (broad s, 1H), 2.03–2.19 (td, J = 4.6, 12.0 Hz, 1H), 1.43–1.96 (complex, with td (J = 2.9, 9.7 Hz) at 1.49, 6H), 1.29 (s, 3H), 1.17 (s, 4H), 0.74–1.05 (complex, with: 0.88 d (J = 6.5 Hz, 3H), 0.83 (d, J = 6.5 Hz, 3H), 0.78 (d, J = 6.1 Hz, 3H), 11H total); HMRS: calc for $C_{24}H_{36}O_3$: 372.2664; found: 372.2673.

(2S,3S)-2-Hydroxy-3-isopropyl-4-pentenoic acid

Using the general procedure, 0.86 g (2.3 mmol) of ene adduct **18** afforded 0.35 g (96%) of hydroxy acid. ^{13}C-NMR: 179.7 (C1), 135.4 (C4), 118.6 (C5), 71.8 (C2), 54.8 (C3), 28.2 (C6), 21.0 (C7), 20.5 (C8).

(−)-8-*Phenylmenthyl* (*2S,3S*)-*and* (*2S,3R*)-2-*hydroxy*-3,4-*dimethyl*-4-*pentenoate* (**19**)

According to the standard procedure, 1.00 g (3.46 mmol) of **1** and 0.55 ml (5.2 mmol) of 2-methyl-2-butene afforded 89 mg (72% yield) of adducts in a diastereomeric ratio of 2:1.

Major diastereomer (*threo,2S,3S*). ^{13}C-NMR: 173.8 (C1), 145.7 (C4), 112.4 (C5), 73.1 (C2), 44.4 (C3), 20.7 (C7), 15.9 (C6), 151.8, 128.0, 125.3, 125.1, 75.9, 50.5, 41.8, 39.5, 34.6, 31.4, 29.4, 26.4, 23.4, 21.8.

Minor diastereomer (*erythro, 2S,3R*). ^{13}C-NMR: 174.1 (C1), 146.1 (C4), 111.6 (C5), 71.7 (C2), 43.6 (C3), 21.3 (C7), 12.2 (C6), 151.7, 128.0, 125.3, 75.7, 50.5, 41.6, 39.5, 34.6, 31.4, 29.4, 26.4, 23.2, 21.8.

(−)-8-*Phenylmenthyl* (2*S*)-2-*hydroxy*-4-*pentenoate* (**20**)

Using the standard procedure, 5.08 g (17.6 mmol) of glyoxylate **1** and 9 ml (111 mmol) of propene were converted to 5.8 g (99%) of crude ene adduct that was pure by ^{13}C-NMR analysis except for two impurity peaks, approximately 5% each, at 52.9 (CH_2Cl_2) and 125.7. ^{13}C-NMR: 173.7 (s, C1), 132.7 (d, C4), 118.0 (t, C5), 69.2 (d, C2), 38.2 (t, C3), 151.6, 127.9, 125.2, 75.6, 50.3, 41.6, 39.4, 34.5, 31.2, 29.3, 26.3, 23.3, 21.7.

(−)-8-*Phenylmenthyl* (2*S*)-2,6-*dihydroxy*-4-*hexenoate* (**21**)

From 0.53 g (1.7 mmol) of **1** and 0.12 g (1.7 mmol) 3-buten-1-ol was obtained by the standard procedure at 0° 0.64 g (100%) of a 1:1 *E*/*Z* mixture of ene adducts. A 2.5:1 ratio resulted when the reaction was conducted at −78°. The geometric isomers were separated by preparative HPLC (1:2 SKB–EtOAc).

E-Isomer (oil). ^{13}C-NMR: 173.8 (C1), 133.1 (C5), 126.2 (C4), 69.4 (C2), 63.2 (C6), 36.7 (C3), 151.8, 128.0, 125.3, 75.9, 50.4, 41.7, 39.5, 34.5, 31.3, 29.4, 26.4, 23.3, 21.8.

Z-Isomer (oil). ^{13}C-NMR: 173.5 (C1), 132.4 (C5), 126.7 (C4), 68.8 (C2), 57.9 (C6), 31.5 (C3), 151.9, 128.0, 125.3, 76.2, 50.4, 41.6, 39.4, 34.5, 31.3, 29.7, 26.3, 22.9, 21.8.

(−)-8-*Phenylmenthyl* (2*S*,4*E*)-2-*hydroxy*-6-*acetoxy*-4-*hexenoate* (**22**)

Using the standard procedure, 0.53 g (1.7 mmol) of **1** and 0.19 g (1.7 mmol) of 4-acetoxy-1-butene (**30**) afforded 0.40 g (59%) of ene adduct after purification by HPLC (4.8:1 SKB–EtOAc). ^{13}C-NMR: 173.6 (C1), 170.6 (C7), 129.5 (C5), 127.5 (C4), 69.2 (C2), 64.7 (C6), 36.6 (C3), 20.9 (C8), 151.7, 128.0, 125.2, 75.9, 50.3, 41.6, 39.4, 34.5, 31.2, 29.4, 26.3, 23.0, 21.8.

(−)-8-*Phenylmenthyl* (2*S*,4*E*)-2-*hydroxy*-6-*benzyloxy*-4-*hexenoate* (**23**)

Using the standard procedure (at 0°) 3.02 g (10.5 mmol) of glyoxylate **1**, 1 equiv of $SnCl_4$, and 1.7 g (10.5 mmol) of 4-benzyloxy-1-butene were converted to 4.66 g (99%) of adduct after purification by flash column chromatography (silica, 1:1 SKB–EtOAc). ^{13}C-NMR: 173.7 (C1), 138.3 (C8), 130.1 (C5), 128.3 (C10), 127.9 (C4), 127.7 (C9), 127.5 (C11), 71.8 (C7), 70.4 (C6), 69.4 (C2), 36.8 (C3), 151.7, 127.9, 125.2, 75.8, 50.3, 41.6, 39.4, 34.5, 31.2, 29.2, 26.3, 23.3, 21.7.

8-*Phenylmenthyl* (2*S*,4*E*)-2-*hydroxy*-6-(t-*butyldimethyl*-*siloxy*)-4-*hexenoate* (**24**)

Using the standard procedure, 5.7 g (20 mmol) of glyoxylate **1**, 5.1 g (20 mmol) of $SnCl_4$ and 3.68 g (20 mmol) of 4-(t-butyldimethylsiloxy)-1-butene gave 8.34 g (89%) of adduct. Further purification of product by HPLC (10:1 hexane–EtOAc) provided 4.34 g (46%) of **24**. ^{13}C-NMR: 173.7 (C1), 151.5 (C5), 124.5 (C4), 69.4 (C2), 63.5 (C6), 36.7 (C3), 26.0 (C9), 18.3 (C8), −5.2 (C7), 132.9, 127.9, 125.1, 75.5, 50.4, 41.7, 39.4, 34.5, 31.2, 29.2, 26.3, 23.4, 21.8.

(−)-8-*Phenylmenthyl* (2*S*)-2-*hydroxy*-3-(1-*cyclohexenyl*)*propionate* (**25**)

Using the standard procedure, 0.71 g (2.5 mmol) of glyoxylate **1**, 0.59 g (2.3 mmol) of tin tetrachloride, and 0.24 g (2.5 mmol) of methylenecyclohexane afforded 0.90 g (94%) of the ene adduct as a yellow oil as a single diastereomer by ^{13}C-NMR analysis. ^{13}C-NMR: 175.9 (C1), 134.8 (C4), 126.0 (C5), 44.5 (C3), 29.8 (C9), 26.7 (C6), 24.3 (C8), 23.7 (C7), 153.2, 129.4, 126.7, 77.0, 70.1, 51.9, 43.2, 40.9, 36.0, 32.7, 30.7, 27.9, 24.9, 23.3.

(−)-8-*Phenylmenthyl* (2*S*)-2-*hydroxy*-3-(4-t-*butyl*-1-*cyclohexenyl*)*propionate* (**26**)

Using the standard procedure, 0.24 g (0.84 mmol) of glyoxylate **1**, 0.23 g (0.86 mmol, 0.1 ml) of anhyd tin tetrachloride, and 0.23 g (1.5 mmol) of 4-t-butylmethylenecyclohexane were converted to 0.31 g (84%) of ene adduct as a yellow oil. Two compounds were obtained in a 4:1 ratio according to HPLC analysis, while analysis by ^{13}C-NMR indicated two compounds in a 2.5:1 ratio, probably diastereomeric at the chiral center bearing the t-butyl group. ^{13}C-NMR (distinct adsorptions of the minor component are shown in parentheses): 174.3 (s, C1), 133.0 (s, C4), 124.8 (124.7), (d, C5), 68.7 (d, C2), 43.8 (44.0), (d, C7), 42.5 (42.4), (t, C3), 29.7 (t, C9), 27.2 (q, C11), 26.8 (t, C6), 151.6, 127.9, 125.2, 75.5, 50.4, 41.8 (41.7), 39.4, 34.5, 32.1, 31.2, 29.1, 26.3, 24.1, 23.5, 21.7.

(−)-8-*Phenylmenthyl* (2*S*)-2-*hydroxy*-4-*methyl*-6-*acetoxy*-4-*hexenoate* (**27**/**28**) *and* (−)-8-*phenylmenthyl* (2*S*)-2-*hydroxy*-4-(2-*acetoxyethyl*)-4-*pentenoate* (**29**)

From 0.25 g (0.85 mmol) of **1** and 0.11 g (0.85 mmol) of **30** was obtained 0.30 g (85%) of a mixture of three components (1.2:1.0:2.1, **27**:**28**:**29**). Separation on a 7.8 mm Microporasil HPLC column (5:1 SKB–EtOAc) provided analytically pure samples.

Compound **27**. ^{13}C-NMR (rel. external D_2O): 173.3 (C1), 169.8 (C8), 136.6 (C4), 121.3 (C5), 68.0 (C2), 60.4 (C6), 43.3 (C3), 20.0 (C9), 15.8 (C7), 151.1, 127.4, 124.6, 74.7, 49.8, 41.0, 38.7, 33.9, 30.6, 28.6, 25.7, 22.6, 21.1.

Compound **28**. ^{13}C-NMR (rel. external D_2O): 173.3 (C1), 169.8 (C8), 136.5 (C4), 121.7 (C5), 67.7 (C2), 60.4 (C6), 36.0 (C3), 22.3 (C7), 20.0 (C9), 151.0, 127.3, 124.5, 74.7, 49.6, 40.8, 38.6, 33.8, 30.5, 28.7, 25.6, 22.8, 21.0.

Compound **29**. ^{13}C-NMR (rel. external D_2O): 173.2 (C1), 169.8 (C8), 140.7 (C4), 113.7 (C7), 68.1 (C2), 61.9 (C6), 39.9 (C3), 34.1 (C5), 20.0 (C9), 151.1, 127.3, 124.5, 74.7, 49.6, 40.9, 38.6, 33.9, 30.5, 28.7, 25.6, 22.4, 21.1.

Acknowledgement—Financial support for this research has come mainly from the National Institutes of Health (GM-31750) and the Robert A. Welch Foundation (F-626).

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