mixtures were incubated at 37 °C for 16 h and were periodically analyzed by LVE followed by ninhydrin visualization of the unreacted amino acid. See Table III for specific results.

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Supplementary Material Available: Table IV, positional and thermal parameters, Table V, bond distances, and Table VI, bond angles (4 pages). Ordering information is given on any current masthead page.

Alkylation of Allylic Derivatives. 10.[1] Relative Rates of Reactions of Allylic Carboxylates with Lithium Dimethylcuprate

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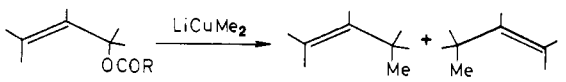
Relative rates of reaction of 19 allylic esters with $LiCuMe_2$ in ether have been determined by a competitive reaction technique. The reactivity range for the series is $>3 \times 10^5$. The relationship between structure and reactivity is compatible with a rate-limiting S_N2' oxidative addition to give a σ-allyl copper(III) complex.

In connection with our mechanistic studies of alkylation of allylic carboxylates with organocopper reagents[1] we have examined the relationship between structure and reactivity for alkylation of allylic esters with $LiCuMe_2$ in ether (eq 1). In this study a competitive reaction technique[3] was



(1)

used to determine rate-constant ratios for pairs of allylic carboxylates. This method was chosen instead of attempting absolute rate measurements because of anticipated difficulties with reproducing reaction conditions—reactions are rapid (typically complete in <10 min at 0 °C)[4] and decomposition of the cuprate accompanies the reaction. Absolute rate measurements have been reported for reaction of $LiCuMe_2$ with enones,[5] alkyl tosylates,[6] and iodides.[7] However, the special techniques involved did not appear applicable for the present study.

The competitive method,[3] in which pairs of allylic carboxylates compete for a limited amount of cuprate, is foolproof with regard to comparison of two substrates under identical conditions. The ratio of the rate constant for substrate A (k_A) to that for substrate B (k_B) is given by eq 2 in which A_0 and B_0 are initial amounts and A and

$$\frac{k_A}{k_B} = \frac{\ln (A/A_0)}{\ln (B/B_0)} \qquad (2)$$

B are final amounts.[3] This equation is based on the assumption that the reaction is first order with respect to the allylic substrate. This has been shown to be the case in other work.[8] The order with respect to $LiCuMe_2$ need not be known because any functional dependence on this reagent cancels in the ratio.

The A/A_0 and B/B_0 ratios are fractions of the original amounts of competing esters that remain when the reaction terminates. An important feature of this function is that except for $k_A/k_B = 1$, the $(A/A_0)/(B/B_0)$ ratio tends toward zero ($k_A > k_B$) or infinity ($k_A < k_B$) as A and B approach zero.[3a] Thus accurate rate-constant ratios will only be obtained if an appreciable amount of the more reactive partner remains unreacted. At the same time, the less reactive partner must undergo enough reaction so that the difference between initial and final concentrations is large relative to experimental error. This means that reliable rate-constant ratios are obtained only when comparing substrates of similar reactivity, for example, when the difference in rate constants is <50-fold. In this work a ladder technique was used to span a reactivity range of $>3 \times 10^5$ which corresponds to a difference in free energy of activation ($\Delta\Delta G^{\ddagger}$) of ~7 kcal/mol.

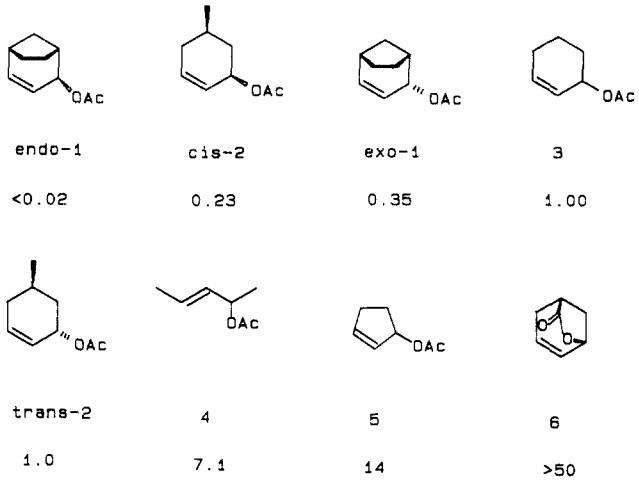
The $LiCuMe_2$ used in these experiments was either prepared directly from cuprous iodide and 2 equiv of methyllithium–lithium bromide complex or by treating well washed methyl copper with 1 equiv of methyllithium–lithium bromide complex. Thus the $LiCuMe_2$ solution contained either 1 or 3 equiv of lithium bromide. The presence of lithium halide salts increases the rate of reaction of $LiCuMe_2$ with alkyl iodides[7] and decreases the rate with enones;[5] however, these salts do not appreciably change the magnitude of rate differences.[5] In this work we observed that $LiCuMe_2$ prepared by the two methods gave similar results.

In the competitive experiments, ethereal $LiCuMe_2$ was added rapidly to an excess of an equimolar mixture of a pair of allylic carboxylates (substrates A and B) and an internal standard in ether at 0 °C. The reaction mixture

(1) Previous paper in this series: Goering, H. L.; Tseng, C. C. *J. Org. Chem.* **1985**, *50*, 1597.
(2) National Science Foundation Fellow, 1977–1980.
(3) (a) Gilliom, R. D. "Introduction to Physical Organic Chemistry"; Addison-Wesley: Reading, MA, 1970; pp 96–99. Melander, L. "Isotope Effects on Reaction Rates"; Ronald Press: New York, 1960; Chapter 3. (b) Walling, C.; Helmreich, W. *J. Am. Chem. Soc.* **1959**, *81*, 1144.
(4) Goering, H. L.; Seitz, E. P., Jr.; Tseng, C. C. *J. Org. Chem.* **1981**, *46*, 5304.
(5) Krause, S. R.; Smith, S. G. *J. Am. Chem. Soc.* **1981**, *103*, 141.
(6) Johnson, C. R.; Dutra, G. A. *J. Am. Chem. Soc.* **1973**, *95*, 7783.
(7) Pearson, R. G.; Gregory, C. D. *J. Am. Chem. Soc.* **1976**, *98*, 4098.
(8) Paisley, S. D., unpublished work in these laboratories.

0022-3263/85/1950-5495$01.50/0

Chart I



was stirred 10 min at 0 °C, then quenched with water, concentrated, and analyzed by one of three methods.

Capillary GC analysis is applicable for the low molecular weight thermally stable allylic esters. In this case relative GC peak areas for an appropriate internal standard, and the allylic esters (A and B) were determined for initial and final mixtures. As has been noted,[3b] the competitive method does not require accurate weighings or determination of response factors and ratios of peak areas for esters and internal standard can be substituted directly into eq 2. This method was used for the allylic esters in Chart I which were reacted competitively with 2-cyclohexenyl acetate (**3**) using cyclohexyl acetate as an internal standard. Rate-constant ratios are shown under the structures.

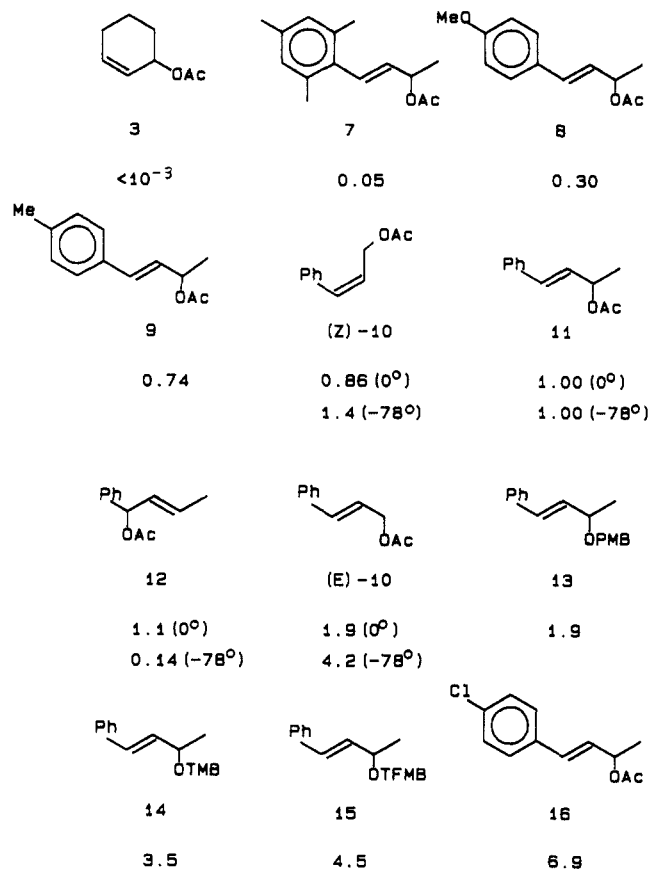
Allylic esters with an α- or γ-aromatic substituent are thermally labile and cannot be analyzed by capillary GC.[4] With these esters, reaction mixtures were analyzed by either a proton NMR or deuterium NMR method.

The proton NMR method involved determination of relative areas of resolved peaks for the competing pair of esters and that of an appropriate internal standard. This method was used for competitive experiments of *trans*-γ-methyl-α-phenylallyl acetate (**12**) and *trans*-α-methyl-γ-phenylallyl *p*-toluate (**13**), mesitoate (**14**), and *p*-(trifluoromethyl)benzoate (**15**) with *trans*-α-methyl-γ-phenylallyl acetate (**11**). Either 1-methylnaphthalene or mesitylene was used as an internal standard.

The deuterium NMR method involved using deuterium-labeled substrates and internal standards. Judicious choice of the location of the deuterium label gave cleanly resolved ^{2}H NMR signals. This method was used for *trans*-γ-(2,4,6-trimethylphenyl)-α-methylallyl acetate (**7**), (*E*)- and (*Z*)-cinnamyl acetate (**10**), *trans*-γ-(*p*-methoxyphenyl)-α-methylallyl acetate (**8**), *trans*-γ-(*p*-methylphenyl)-α-methylallyl acetate (**9**), and *trans*-γ-(*p*-chlorophenyl)-α-methylallyl acetate (**16**). In each case, the α-D-ester was reacted competitively with γ-D-**11** using 1-D-cyclohexyl acetate or 4-D-anisole as an internal standard. Calculation of rate-constant ratios from ^{2}H and ^{1}H NMR measurements is the same as from capillary GC data. The results of these competitive experiments are shown under the structures in Chart II.

A ladder technique was used to span the reactivity gap between **3** and **11**. This connects the reactivities of the less reactive (Chart I) and more reactive esters (Chart II). The thousandfold difference in reactivity for **3** and **11** was determined from the **11**/**7** and **7**/**3** ratios. The former is 20 and the latter was found to be ~50 by the competitive reaction of γ-D-**3** and α-D-**7**. As indicated for selected

Chart II



substrates in Chart II, the rate-constant ratios are rather insensitive to change in temperature. The reaction time was extended to 2 h for the experiments at −78 °C. Control experiments showed that in all cases the original structure of the allylic carboxylate is preserved under the conditions of the reaction and analysis, i.e., isomeric allylic or $E \rightleftarrows Z$ isomerizations are not involved.

Probably the most remarkable findings in the present work are the low reactivity of the *endo*-bicyclo[3.2.1]oct-3-en-2-yl system (*endo*-**1**) relative to the exo isomer (*exo*-**1**) and the substantial rate acceleration by an α- or γ-phenyl substituent. The similar reactivity for primary (**10**) and secondary esters (**11**) is also noteworthy.

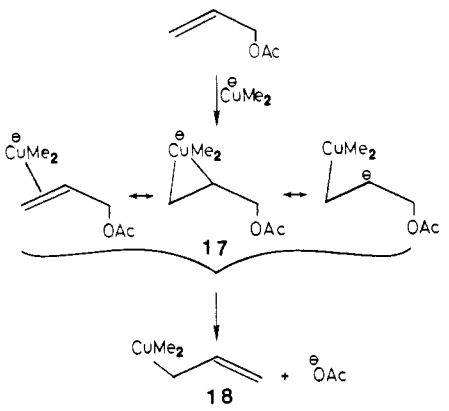
Earlier[9-11] we presented evidence that this reaction (eq 1) involves oxidative addition to give the S_N2' σ-allyl copper(III) complex **18** followed by reductive elimination to give alkylation product. The σ-allyl complex with two alkyl ligands on copper undergoes rapid isomeric allylic rearrangement by a $\sigma \rightleftarrows \pi$ mechanism.[9-11] Presumably oxidative addition is the rate limiting step.

Anti stereochemistry is favored for alkylation, and thus for oxidative addition, in both cyclic[11,12] and acyclic systems.[13] For example in **2**, the anti product predominates by at least a factor of 50:1.[11,12] This corresponds to a free energy of activation difference of about 2 kcal/mol for syn and anti oxidative addition.

As shown in Chart I, *endo*-**1**, in which the anti (exo) surface of the molecule is relatively unhindered, is substantially less reactive than *exo*-**1** in which the anti (endo) side is sterically hindered. In the latter case the stereo-

(9) Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1983**, *48*, 721.
(10) Goering, H. L.; Singleton, V. D., Jr. *J. Org. Chem.* **1983**, *48*, 1531.
(11) Goering, H. L.; Kantner, S. S. *J. Org. Chem.* **1984**, *49*, 422.
(12) Goering, H. L.; Singleton, V. D., Jr. *J. Am. Chem. Soc.* **1976**, *98*, 7854.
(13) Goering, H. L.; Tseng, C. C. *J. Org. Chem.* **1983**, *48*, 3986.

Scheme I



chemistry is reversed and syn alkylation is observed.[11] It is interesting that in spite of the forced syn stereochemistry, *exo*-**1** is only three times less reactive than *trans*-**2** or **3**. Evidently destabilization of the syn transition state by steric crowding is offset somewhat by the fact that in this rigid structure the allyl system is held in a transition-state-like geometry for cleavage of the axial allyl bond.[14]

There are two plausible reasons for the low reactivity of *endo*-**1**. One is that the leaving group is locked in a pseudoequatorial position and overlap of the C–O bond with the π system is poor.[14] The other is that steric hindrance interfers with any type of complexation with the leaving group that may facilitate reaction.[15]

Presumably oxidative addition is a two-step process and involves initial complexation of the cuprate with the olefin followed by conversion of complex **17** to the σ-allyl copper(III) complex **18** as illustrated in Scheme I.[9,11] As noted earlier,[9] it is instructive to represent the initial complex **17** as a hybrid of copper(I) and copper(III) resonance structures because the latter are useful for visualizing plausible mechanistic details for the **17** → **18** transformation. A qualitative molecular orbital interpretation of the anti S_N2' oxidative addition was recently presented.[16] It seems that the earlier resonance description of **17**[9] (Scheme I) provides a more straightforward explanation for formation of the S_N2' σ-allyl complex **18** instead of a π-allyl complex. Also, the generally favored anti stereochemistry ($\Delta\Delta G^{\ddagger} \approx 2$ kcal/mol) can be accounted for in terms of steric factors in the transition state for the **17** → **18** transformation.[9,11]

The accelerating effect of an α- or γ-phenyl substituent suggests that the **17** → **18** transformation is rate determining. Comparison of **11** and **12** with **3** (Chart II) and **3** with **4** (Chart I) shows that replacement of either an α- or γ-methyl group by a phenyl group results in an over hundredfold increase in rate. This is similar to the effect of an α-phenyl substituent in an S_N2 reaction.[17] Presumably in each case, conjugation of the reaction center with an aromatic ring stabilizes the transition state about 3 kcal/mol.

Comparison of **11** with (*E*)- and (*Z*)-**10** shows that an α-methyl substituent has a negligible effect. The similar rates for primary and secondary systems is compatible with a rate-limitng S_N2' oxidative addition but not with an S_N2 process[18] or rate-limiting ion-pair formation.[19]

The relative reactivities of the para-substituted α-methyl-γ-phenylallyl acetates **8**, **9**, and **16** are correlated by the Hammett equation. Attempts to extend the correlation to include the *p*-nitro substituent were unsuccessful. Reactions of $LiCuMe_2$ with substrates containing aryl nitro groups have been reported.[20] However, it is our experience that this group in either the allyl or carboxylate part of the ester interferes with the reaction and there is little, if any, alkylation. Meaningful data could not be obtained for esters with this substituent. The Hammett plot for **8**, **9**, **11**, and **16** has a slope (ρ) of 2.0 which shows that negative charge is transferred from copper to the allyl system in the transition state for the **17** → **18** transformation.

It is interesting that in **7** the accelerating effect on the aromatic substituent is attenuated but not eliminated. Two factors, both resulting from the ortho methyl groups, could account for the 20-fold decrease in rate. In systems of this type the aromatic ring is twisted about 60° out of the plane of the double bond.[21] Thus the **17** → **18** transition state could be destabilized by reduction of conjugation or by steric interactions with the ortho methyl groups that flank the γ-carbon.

The difference in reactivity for *cis*- and *trans*-5-methyl-2-cyclohexenyl acetate (**2**) is in the expected direction but too small for sound interpretation ($\Delta\Delta G^{\ddagger} < 1$ kcal/mol). In cyclohexenyl systems, presumably the conformation with the leaving group in the pseudoaxial position is related to the best transition state.[12,22] Thus, in *cis*-**2** steric crowding results from a 1,3-diaxial interaction between the carboxylate group and the C-5 methyl group. This destabilizing interaction is absent in *trans*-**2** in which case the C-5 methyl is in an equatorial position. The observed similar reactivities for *trans*-**2** and 2-cyclohexenyl acetate (**3**) is expected because replacement of an equatorial C-5 proton in **3** by a methyl group does not change the immediate environment of the allylic system.

Three factors may contribute to the enhanced reactivity of 7-oxabicyclo[3.2.1]oct-2-en-6-one (**6**) relative to **2** and **3**. The cyclohexenyl ring is locked in the reative conformation with the leaving group in the axial position and the C-5 carbon held on the same side of the allyl system as the leaving group.[12] Also, in the bicyclic system there is less steric hindrance for anti (exo) approach to the double bond than in monocyclic cyclohexenyl systems. Finally, the reaction results in relief of strain present in the bicyclic structure.

Comparison of α-methyl-γ-phenylallyl acetate (**11**) with the *p*-toluate **13**, mesitoate **14**, and *p*-(trifluoromethyl)-benzoate **15** shows the reaction is remarkably insensitive to changing the leaving group. The change from acetate **11** to *p*-(trifluoromethyl)benzoate **15**, which represnts a two pK_a unit change in the strength of the corresponding acids, results in only a 4.5-fold increase in reactivity. For reasons mentioned above, nitrobenzoate esters could not be included in this investigation. It may be important for the leaving group to be complexed with a Lewis acid in the transition stage[15] as well as to tolerate negative charge. These two change in opposite directions with change in

(14) In this system the exo (axial) isomer is >100 times more reactive than the endo (equatorial) isomer for heterolytic cleavage of the allyl bond. Goering, H. L.; Vlazny, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 1801.

(15) Some type of complexation with the carboxylate leaving group during and subsequent to bond cleavage (e.g., with lithium or an organometallic species) would be expected because of the lack of hydrogen-bond donor properties of the solvent.

(16) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1984**, *25*, 3063.

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leaving group, and this may be the reason for the small overall effect.

Experimental Section

General Methods. NMR spectra were determined with a Brucker WH-270 instrument. Proton-decoupled ^2H NMR spectra were obtained with a JEOLCO FX-200 (30.6-MHz) spectrometer. Peak areas for capillary GC analysis were determined with an electronic integrator. Purification of ethyl ether and cuprous iodide and standardization of methyllithium has been previously described.[4] Boiling points and melting points are uncorrected. Satisfactory spectral data were obtained for all compounds.

Materials. *exo*- and *endo*-Bicyclo[3.2.1]oct-3-en-2-yl acetate (*exo*-1 and *endo*-1),[11] *cis*- and *trans*-5-methyl-2-cyclohexenyl acetate (*cis*-2 and *trans*-2),[11] 7-oxabicyclo-[3.2.1]oct-2-en-6-one (6),[23] *trans*-α-methyl-γ-phenylallyl acetate (11),[4] and *trans*-γ-methyl-α-phenylallyl acetate (12)[4] were prepared by methods reported earlier.

***trans*-α,γ-Dimethylallyl acetate (4)**, bp 120–122 °C (lit.[24a] 50 °C, 23 mm), was prepared from the corresponding alcohol.[24b]

2-Cyclopentenyl acetate (5), bp 65 °C (37 mm) (lit.[25] 69–72 °C (40 mm)), was prepared[4] from 2-cyclopentenol which was obtained by cesium chloride catalyzed sodium borohydride reduction[26] of 2-cyclopentenone.[27]

2-Cyclohexenyl acetate (3), bp 63–64 °C (9.5 mm) (lit.[28] 68–71 °C (12 mm)), was prepared[4] from 2-cyclohexenol[29] and γ-D-3 was prepared from γ-D-2-cyclohexenol.[29] The ^2H NMR spectrum of γ-D-3 has a single signal at δ 5.96.

α-D-*trans*-γ-(2,4,6-Trimethylphenyl)-α-methylallyl acetate (α-D-7) was prepared[4] from the corresponding deuterated alchol which was obtained by cesium chloride catalyzed sodium borodeuteride reduction[26] of (*E*)-1-(2,4,6-trimethylphenyl)-1-buten-3-one.[30] The ^2H NMR spectrum has a single signal at δ 5.26. Properties of unlabeled 7 were reported earlier.[11]

γ-D-*trans*-α-Methyl-γ-phenylallyl acetate (γ-D-11) was prepared[4] from the corresponding alcohol which was obtained as follows. Reduction of methyl benzoate with lithium aluminum deuteride followed by oxidation of the resulting dideuterated benzyl alcohol with pyridinium chlorochromate[31] gave 1-D-benzaldehyde. Condensation of the latter with acetone[32] gave (*E*)-1-D-1-phenyl-1-buten-3-one which was converted to the alcohol related to γ-D-11 by cesium chloride catalyzed sodium borohydride reduction.[26] The ^2H NMR spectrum of γ-D-11 has a single signal at δ 6.66.

***trans*-α-Methyl-γ-phenylallyl *p*-toluate (13)** was prepared from the corresponding alcohol[4] and *p*-toluyl chloride. After purification by chromatography (Woelm III neutral alumina, hexane–ether eluent) 13 had: mp 60.7–62.7 °C; IR (neat) 3060 (w), 3030 (w), 2980 (m), 2920 (w), 1715 (s), 1615 (m), 1275 (s), 970 (m), 840 (m), 750 (m), 690 (m) cm^{-1}; NMR (CCl_4) δ 7.88 (d, 2 H, J = 8 Hz), 7.4–7.0 (m, 7 H), 6.60 (d, 1 H, J = 16 Hz), 6.18 (dd, 1 H, J = 16, 7 Hz), 5.7 (m, 1 H), 2.18 (s, 3 H), 1.46 (d, 3 H, J = 7 Hz); high resolution mass spectrum, calcd for $C_{18}H_{18}O_2$ m/e 266.1307, found m/e 266.1300.

***trans*-α-Methyl-γ-phenylallyl mesitoate (14)** was prepared from the alcohol[4] and mesitoyl chloride.[33] After purification by the method described for 13, 14 had: IR (CCl_4) 3030 (w), 2980 (m), 2930 (w), 2860 (w), 2720 (s), 1615 (m), 1260 (s), 1080 (s), 1040 (s), 970 (m), 850 (m) cm^{-1}; NMR (CCl_4) δ 7.4–7.1 (m, 5 H), 6.83 (s, 2 H), 6.6 (m, 1 H), 6.18 (dd, 1 H, J = 16, 6 Hz), 5.7 (m, 1 H), 2.4–2.0 (m, 9 H), 1.46 (d, 3 H, J = 6 Hz); high resolution mass spectrum, calcd for $C_{20}H_{22}O_2$ m/e 294.1621, found m/e 294.1616.

***trans*-α-Methyl-γ-phenylallyl *p*-(trifluoromethyl)-benzoate (15)** was prepared from the alcohol[4] and *p*-(trifluoromethyl)benzoyl chloride. After purification as for 13 and 14, 15 had: IR (neat) 3020 (w), 2990 (m), 2930 (w), 1720 (s), 1130 (s), 960 (m), 855 (m), 770 (m), 745 (m), 705 (m), 690 (m) cm^{-1}; NMR (CCl_4) δ 7.86 (m, 4 H), 7.5–6.9 (m, 5 H), 6.66 (d, 1 H, J = 16 Hz), 6.25 (dd, 1 H, J = 16, 7 Hz), 5.7 (m, 1 H), 1.52 (d, 3 H, J = 7 Hz); high resolution mass spectrum, calcd for $C_{20}H_{22}O_2$ m/e 320.1025, found m/e 320.1020.

***trans*-Cinnamyl acetate-d_3 ((*E*)-10-d_3)**, bp 137–139 °C (10 mm), was prepared from freshly distilled *trans*-cinnamyl alcohol and acetyl chloride-d_3.[34] Signals for the cis isomer could not be detected in the 270-MHz NMR spectrum. The ^2H NMR spectrum had a single signal at δ 1.98.

***cis*-Cinnamyl acetate-d_3 ((*Z*)-10-d_3)**, bp 116 °C (6.5 mm), was prepared from the corresponding alchol which was obtained as follows. A solution of 1-phenyl-1-propyn-3-ol[35] in dry pyridine was hydrogenated over 5% $Pd/BaSO_4$ at atmospheric pressure. The reaction mixture was filtered and diluted with chloroform, and the resulting organic layer was washed with aqueous 10% $NaHSO_4$ (4×), aqueous $NaHCO_3$, and brine and dried over Na_2SO_4. After removal of solvent the residual *cis*-cinnamyl alcohol, bp 103 °C (3 mm), was purified by distillation. The NMR spectrum of (*Z*)-10-d_3 showed no evidence for the presence of the trans isomer. The ^2H NMR spectrum showed a single signal at δ 1.92.

α-D-*trans*-α-Methyl-γ-(*p*-methoxyphenyl)allyl acetate (α-D-8) was prepared[4] from the corresponding alcohol which was obtained by cesium chloride catalyzed sodium borodeuteride reduction[26] of (*E*)-1-*p*-methoxyphenyl-1-buten-3-one.[32] After purification by distillation, α-D-8 had: bp 120–124 °C (0.45 mm); IR (neat) 3020 (w), 2960 (m), 2920 (m), 2820 (w), 1730 (s), 1655 (w), 1605 (m), 1510 (s), 1250 (s), 965 (m), 825 (m) cm^{-1}; NMR ($CDCl_3$) δ 7.32 (d, 2 H, J = 8.5 Hz), 6.84 (d, 2 H, J = 8.52 Hz), 6.54 (d, 1 H, J = 16.5 Hz), 6.03 (br d, 1 H, J = 16.5 Hz), 3.77 (s, 3 H), 2.06 (s, 3 H), 1.36 (br s, 3 H). The ^2H NMR spectrum has a signal at δ 5.50.

α-D-*trans*-α-Methyl-γ-(*p*-methylphenyl)allyl acetate (α-D-9) was prepared from the corresponding alcohol which in turn was obtained by sodium borodeuteride reduction[26] of (*E*)-1-*p*-methylphenyl-1-buten-3-one.[36] After distillation, α-D-9 had: bp 97–100 °C (0.5 mm); IR (neat) 3010 (w), 2960 (m), 2910 (w), 2850 (w), 1725 (s), 1650 (w), 1605 (w), 1365 (m), 1245 (s), 1095 (m), 964 (m), 805 (m), 790 (m) cm^{-1}; NMR ($CDCl_3$) δ 7.26 (d, 2 H, J = 8 Hz), 7.09 (d, 2 H, J = 8 Hz), 6.55 (d, 1 H, J = 16 Hz), 6.09 (br d, 1 H, J = 16 Hz), 2.34 (s, 3 H), 2.06 (s, 3 H), 1.37 (br s, 3 H). The ^2H NMR shows a single signal at δ 5.50.

α-D-*trans*-α-Methyl-γ-(*p*-chlorophenyl)allyl acetate (α-D-13) was prepared from (*E*)-1-*p*-chlorophenyl-1-buten-3-one[37] as described for 8 and 9. After distillation α-D-13 had: bp 118–122 °C (0.5 mm); NMR ($CDCl_3$) δ 7.32 (s, 4 H), 6.56 (d, 1 H, J = 16 Hz), 6.16 (br d, 1 H, J =]6 Hz), 2.04 (s, 3 H), 1.40 (br s, 3 H). The ^2H NMR spectrum has a single signal at δ 5.46.

Competitive Rate Studies. A. Capillary GC Analysis. In a typical experiment a mixture of 130.4 mg (0.85 mmol) of *cis*-2, 71.7 mg (0.51 mmol) of 3 and 78.2 mg (0.55 mmol) of cyclohexyl acetate was placed in a small nitrogen-purged vial that was capped with a septum. The mixture was dissolved in 2 mL of dry ether. The resulting solution was thoroughly mixed, chilled to 0 °C, and all but ~10% was transferred rapidly to a stirred chilled (0 °C) solution of 0.5 mmol of $LiCuMe_2$ in 5 mL of ether. After being stirred 10 min at 0 °C, the reaction mixture was quenched by addition of 0.5 mL of saturated aqueous NH_4Cl. The resulting mixture was centrifuged, and the ether layer was removed with

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a pipet and concentrated by fractional distillation. Capillary GC analysis (61-ft column, LAC-2R-446) of the reaction product and the reserved starting mixture gave peak areas of reactants (*cis*-**2** and **3**) and the internal standard (cyclohexyl acetate). From these values the rate-constant ratio for *cis*-**2** and **3** can be calculated with eq 2. This particular experiment gave a value of 0.31 for the rate of *cis*-**2** relative to **3**. Another experiment gave a value of 0.15. Thus the averaged rate for *cis*-**2** relative to **3** is 0.23 ± 0.11 as indicated in Chart I. The other values in Chart I are similarly averages of two or more independent experiments.

B. Proton NMR Analysis. In a typical experiment an ether solution of 163.4 mg (0.61 mmol) of **13**, 183.6 mg (0.97 mmol) of **11**, and 90.9 mg (0.64 mmol) of 1-methylnaphthalene was prepared as described above. This solution was cooled to 0 °C and added to a solution of 0.5 mmol of $LiCuMe_2$ in 5 mL ether at 0 °C. After being stirred 10 min, the reaction mixture was quenched with 0.5 mL of H_2O and centrifuged. The ether layer was dried (K_2CO_3), concentrated, and taken up in CCl_4 for NMR analysis. The peak areas for the acetyl methyl of **11**, the aromatic methyl of **13**, and the aromatic methyl of the internal standard (1-methylnaphthalene) for the reaction product and reserved starting mixture were determined with a planimeter. In this experiment a value of 1.51 was obtained for the **13**/**11** rate-constant ratio. Another experiment gave a value of 2.53. Thus the average rate of **13** relative to **11** is 1.9 ● 0.7 as indicated in Chart II. The other values in Chart II that were determined by this method are also average values of two or more independent experiments.

C. Deuterium NMR Analysis. In a typical experiment a mixture of 127.7 mg (0.97 mmol) of (*Z*)-**10**-d_3, 170.7 mg (1.20 mmol) of γ-D-**11**, and 78.9 mg (0.74 mmol) of cyclohexyl acetate-*1*-*d* in 3 mL of dry ether was prepared as described above. After thorough mixing, two-thirds of the solution was transferred to a small flask and the stirred solution was cooled to 0 °C. A prechilled solution of 0.1 M $LiCuMe_2$ (5 mL) was added rapidly to the stirred solution. After being stirred 10 min at 0 °C, the reaction was quenched with 0.5 mL of saturated aqueous NH_4Cl and the ether layer separated and concentrated by fractional distillation. Deuterium NMR analysis of the concentrated reaction product and the reserved starting mixture gave values for the areas (determined with a planimeter) of the reactants ((*Z*)-**10**-*d* and γ-D-**11**) relative to the internal standard (cyclohexyl acetate-*1*-*d*). From these values the rate-constant ratio of 0.86 for (*Z*)-**10** and **11** was obtained with eq 2.

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Photophysical Probes of Intramolecular Interactions Responsible for Asymmetric Induction

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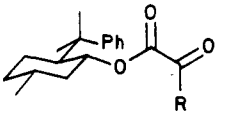
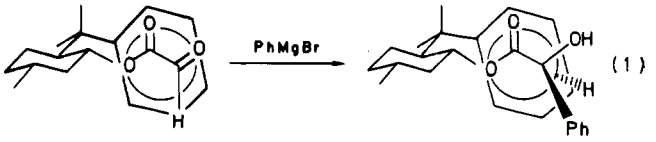
The study of fluorescence quantum yields and excited-state lifetimes for a family of α-carbonyl esters of 8-phenylmenthol reveals significant intramolecular quenching. The efficiency of the intramolecular quenching is conformationally dependent. Shifts in emission bands upon the addition of Lewis acid are consistent with excited-state charge-transfer interactions and with substantial HOMO–LUMO interactions. The observed unidirectional intramolecular quenching can be rationalized by a mechanism involving either electron or energy transfer from the excited arene to the proximate α-carbonyl ester.

α-Carbonyl esters **1** and **2** of 8-phenylmenthol exhibit excellent degrees (90–99.4%) of asymmetric induction in ene reactions,[1] reductions,[2] and nucleophilic additions with Grignard reagents.[3] For example, addition of phenyl-



1, R = H
2, R = Me

magnesium bromide to **1** gives the corresponding α-hydroxy ester in 90% chemical yield with 99.1% diastereomeric excess.[3] Such high levels of induction require both



(1)

diastereoface selectivity and a fixed orientation of the carbonyl groups in the transition state. The configuration of the chiral centers generated in these reactions is consistent with addition from the front face of the glyoxylate ester as drawn in eq 1. The carbonyls are cis to one another, and the phenyl ring is positioned to block one face of the dicarbonyl, rendering the opposite face accessible to incoming reagents. This fixed orientation requires a stabilizing interaction between the phenyl and glyoxylate moieties as steric requirements would not favor close approach between the two groups. Such interaction could conceivably result from stabilizing overlap of the frontier molecular orbitals of the two functionalities. Through-space π–π overlap has also been invoked by Oppolzer[4] as an explanation for the asymmetric induction seen in Diels–Alder reactions of cyclopentadiene with 8-phenylmenthol acrylates and in Corey's observation of face selective reduction of α,β-unsaturated ketones in the prostaglandin series.[5]

Molecular models reveal that the two carbonyls and the phenyl ring are quite well situated to facilitate HOMO–LUMO interaction. The frontier orbitals of the 1,2-dicarbonyl may be approximated as a butadiene system, and the frontier orbitals of the phenyl substituent may be

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