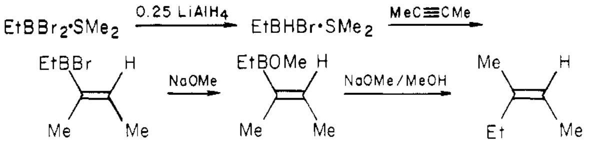
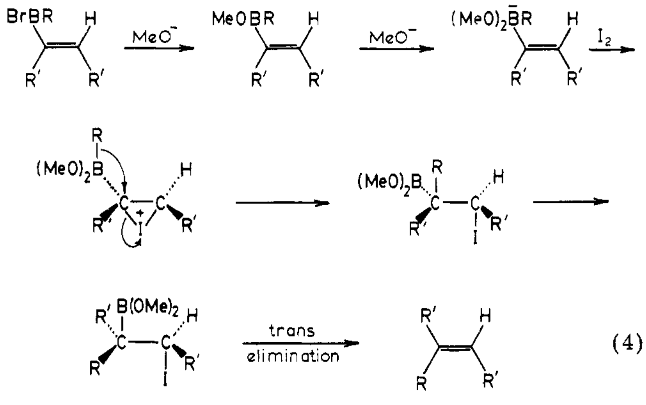


(3)

separate nicely on a 12 ft × 0.25 in. column packed with 20% tricresyl phosphate on firebrick (60–80 mesh). The alkene, obtained via the reaction in eq 3, proved identical with the *Z* isomer, with no detectable amount of the *E* isomer.

The ^{13}C NMR spectra of (*E*)- and (*Z*)-3-methyl-2-pentenes are distinctly different. We found that the higher alkenes, obtained via the reaction sequence in eq 2, did not indicate the presence of more than one isomer in the ^{13}C NMR spectrum or on the tricresyl phosphate column. Consequently, we conclude that these higher alkenes should have the same stereochemistry as that of (2*Z*)-3-methyl-2-pentene. These results also clearly show that a mechanism similar to that involved in the formation of *Z*-disubstituted alkenes is operative. The migration of the alkyl group proceeds with inversion at the migration terminus and deiodoboronation occurs in a trans manner, thus resulting in the trans stereochemistry of the two alkyl groups from the internal alkyne (eq 4).



(4)

1

The following procedure for the synthesis of (6*Z*)-7-*n*-pentyl-6-tridecene (**1d**) is representative. To 30 mmol of *n*-hexyldibromoborane–dimethyl sulfide,[10] prepared from 1-hexene and dibromoborane–dimethyl sulfide, were added at 0 °C 3 mL of SMe_2 and 25 mL of Et_2O, followed by a slow addition of $LiAlH_4$ in Et_2O (7.5 mmol) with stirring under nitrogen. The reaction was allowed to proceed 3 h at 0 °C and 1 h at room temperature. The resulting alkylbromoborane was slowly transferred to a solution of 6-dodecyne (4.99 g, 30 mmol) in Et_2O at 0 °C and the reaction mixture was stirred 0.5 h at 0 °C and 1.5 h at room temperature. Then the resulting vinylborane was added slowly to a solution of NaOMe (150 mmol) in MeOH at 0 °C. After 0.5 h at room temperature, the solvent ether was removed under vacuum and 30 mL of MeOH was added. Iodine (7.60 g, 30 mmol) was added to this vinylborane solution in MeOH at 0 °C and the mixture was stirred at room temperature for 3 h. Aqueous $Na_2S_2O_3$ solution was added and the reaction mixture was extracted with pentane and the extract dried over anhydrous $MgSO_4$. Solvent was removed under reduced pressure and distillation afforded 5.6 g (74%) of (6*Z*)-7-*n*-pentyl-6-tridecene (**1d**): bp 120–122 °C (0.5 mm); $n^{20}{}_D$ 1.4479. GC analysis showed 99% chemical purity; ^1H NMR ($CDCl_3$, Me_4Si) δ 0.70–1.66 (m, 29 H), 1.73–2.26 (m, 6 H), 5.00 (t, $J = 6$ Hz, 1 H); ^{13}C NMR ($CDCl_3$, Me_4Si) δ 13.60, 22.41, 27.46, 27.78, 28.25, 29.25, 29.69, 31.46, 31.68, 39.69 (alkyl C), 124.61, 138.73 (C=C). For the assignment of stereochemistry (2*Z*)-3-methyl-2-pentene (**1a**) was prepared from $EtBBr_2·SMe_2$[11] and 2-butyne following this procedure.

This procedure circumvents the significant problem associated with the earlier procedure,[4] thus providing a general one-pot and stereospecific synthesis of trisubstituted alkenes under mild conditions. However, it needs to be pointed out that this procedure has a significant limitation. This method is mainly applicable to symmetrical alkynes as the hydroboration of unsymmetrical alkynes is not completely regioselective. We are now exploring the possibilities of surmounting this limitation to provide a general and stereospecific synthesis of trisubstituted alkenes with all three groups different.

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[10] Brown, H. C.; Ravindran, N.; Kulkarni, S. U. *J. Org. Chem.* **1980**, *45*, 384.

[11] $EtBBr_2$ was prepared via redistribution of Et_3B and BBr_3 catalyzed by $BH_3·SMe_2$ (7–10%) in pentane at room temperature [$EtBBr_2·SMe_2$, bp 112–114 °C (15 mm)]: Brown, H. C.; Basavaiah, D.; Bhat, N. G., manuscript in preparation.

[12] Postdoctoral research associate on Grant GM 10937-19 from the National Institutes of Health.

Observations on the Mechanism of the Lewis Acid Catalyzed Ene Reaction

Summary: The product resulting from the $SnCl_4$-catalyzed reaction of allylbenzene and diethyl mesoxalate is shown to be an oxetane, contrary to the tetrahydrofuran structure assigned by previous authors.[4] This evidence, taken together with the evidence of a β-secondary deuterium isotope effect in the $SnCl_4$-catalyzed reaction, supports a mechanism of rate-limiting complex formation, in contrast to the corresponding purely thermal superene[2,3] reaction where the rate-determining step has been previously shown to involve pseudopericyclic H transfer in a rapidly formed (2 + 2) charge-transfer intermediate.

Sir: Through measurements of the temperature dependence of the kinetic isotope effect (TDKIE)[1] in the ene reactions of certain heteroatom multiple bonds,[2] which could be classified as superenophiles,[3] it has been shown that H transfer effected by purely thermal means takes place angularly, i.e., in a bent transition state (TS). Studies of the secondary D-isotope effects at the ene centers,[2b] as well as the regio- and stereoselectivity[2,3] associated with the ene reaction mechanism, have enforced the conclusion that in such cases a rapidly reversible (2 + 2) charge-transfer (CT) complex is formed between the ene and

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[1] (a) Kwart, H.; Nickle, J. H. *J. Am. Chem. Soc.* **1973**, *95*, 3394; **1976**, *98*, 2881. (b) Janssen, J. W. A. M.; Kwart, H. *J. Org. Chem.* **1977**, *42*, 1530. (c) Kwart, H.; George, T. J.; Louw, R.; Ultee, W. *J. Am. Chem. Soc.* **1978**, *100*, 3927. (d) Kwart, H.; Benko, D. A.; Bromberg, M. E. *Ibid.* **1978**, *100*, 7093. (e) Kwart, L. D.; Kwart, H.; Horgan, A. G. *Ibid.* **1981**, *103*, 1232. (f) Kwart, H.; Brechbiel, M. *Ibid.* **1981**, *103*, 4050.

[2] (a) Münsterer, H.; Kresze, G.; Kwart, H.; Brechbiel, M. *J. Org. Chem.* **1982**, *47*, in press. (b) Kwart, H.; Brechbiel, M. *Ibid.* **1982**, *47*, 3353.

[3] (a) Schönberger, N.; Kresze, G. *Justus Liebigs Ann. Chem.* **1975**, 1725. (b) Bussas, R.; Kresze, G. *Ibid.* **1980**, 629; **1982**, 545. (c) Kresze, G.; Bussas, R. *Ibid.* **1980**, 843.

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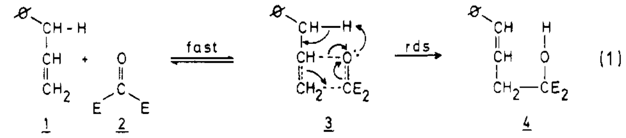
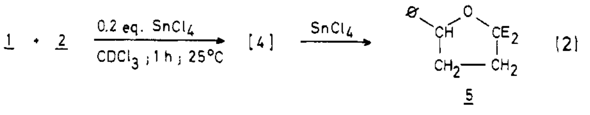
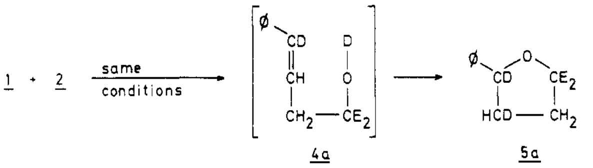
superenophile in a preliminary step preceding the rate-determining H transfer to the unshared pair of the appropriately situated heteroatom. A model of this TS (**3**) is illustrated for the superene reaction of mesoxalic esters with allylbenzene in eq 1. The mechanistic change entailed in the corresponding reaction catalyzed by strong Lewis acids such as $SnCl_4$ has been the subject of a recent communication in this Journal,[4] wherein measurements of both the inter- and intramolecular KIE yielded values of $k_H/k_D \approx 1.1$, which are considerably less than that observed for the purely thermal reaction where $k_H/k_D \approx 3.3$. The data reported in this paper[4] have now been examined and reevaluated and somewhat different conclusions concerning the mechanistic course of the Lewis acid catalyzed ene reaction have been reached.



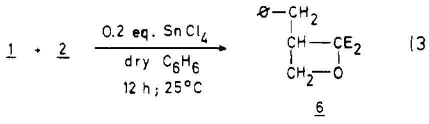
where E = COOEt

Salomon and co-workers[5] have verified that $SnCl_4$-catalyzed reaction of diethyl mesoxalate with various unconjugated dienes leads to ene reaction products (homoallylic alcohols) corresponding to very different regioselectivity than the products of the thermal reaction. In the case of **1**, Stephenson and Orfanopoulos[4] report that the expected homoallylic alcohol product **4** (see eq 1) cannot be isolated but appears to undergo cyclization to the tetrahydrofuran **5**. This would presume the reaction course that is outlined in eq 2.





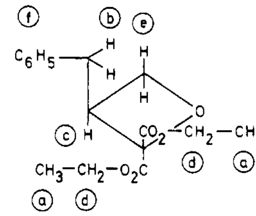
Under similar reaction conditions, however, entirely different results were realized here. Instead of **5**, the product obtained proved to be the cycloadduct, the oxetane **6**, presumably in accordance with the reaction expressed by eq 3. The oxetane structure assigned to **6** is



fully in keeping with both ^1H and ^{13}C NMR data listed in Tables I and II and not consistent with the tetrahydrofuran structure **5** reported previously[4] to be formed at even shorter reaction times (1 h compared to 12 h) of exposure to the $SnCl_4$ catalyst in solution.

Other lines of evidence that indicate that an ene reaction product was not formed as a precursor to the formation of the observed oxetane (**6**) are based on ^2H NMR data.

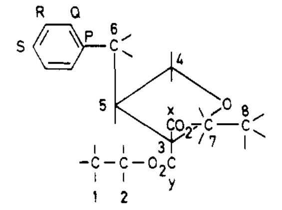
Table I. 60-MHz Proton NMR Resonances Identifying the Oxetane Product of the $SnCl_4$-Catalyzed Reaction of Allylbenzene (1) and Diethyl Mesoxalate (2)



a	δ 1.25 (t, 6)
b	δ 2.70 (d, 2)
c[a]	δ 3.20 (m, 1)
d	δ 4.25 (q, 4)
e[b]	δ 4.80 (d, 2)
f	δ 7.20 (s, 5)

[a] The somewhat low field position of this proton is suggested to originate from the same factors that give rise to the low field position of the carbon to which it is attached; see footnote *a*, Table II. [b] The equivalence of these resonances is regarded as a reflection of the rapid ring pseudorotation, i.e., the folding of the ring along the two (perpendicular) planes that would bisect a square oxetane.

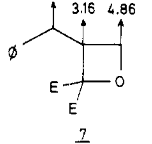
Table II. ^{13}C NMR Resonances Identifying the Oxetane Product of the $SnCl_4$-Catalyzed Reaction of Allylbenzene (1) and Diethyl Mesoxalate (2)



1	δ 13.92		
2	δ 63.50	X	δ 169.97
3	δ 78.38	Y	δ 169.75
4	δ 62.51	P	δ 128.43
5[a]	δ 63.41	Q	δ 128.71
6	δ 39.41	R	δ 129.34
7	δ 63.50	S	δ 127.11
8	δ 13.23		

[a] The somewhat unusual resonance of this carbon (labeled 5) can be explained by inspection of a model. Therein it is seen that a COOEt group will always tend to lie close to the single hydrogen substituted on this carbon due to steric factors and repulsive interactions with the lone pairs on the ring oxygen. This field effect of COOEt reinforces that arising from the transannular oxygen exerting a strong electronegative (coulombic) effect across the low dielectric cavity of the ring; it is suggested to account for the low field position of the only ring carbon that is not directly bonded to the oxygen.

Calibrating experiments demonstrate the distinctive differences in the deuterium (^2H) resonances outlined in **7**.



7

Thus, when 3-phenylpropene-*3-d* was subjected to the $SnCl_4$-catalyzed reaction with **2**, the product showed only one peak at δ 2.64, without a trace of any other peak that could indicate migration of the ^2H label in accordance with the formation of **5** in eq 2. When 3-phenylpropene-*2-d* was the substrate, the product again showed only a single peak

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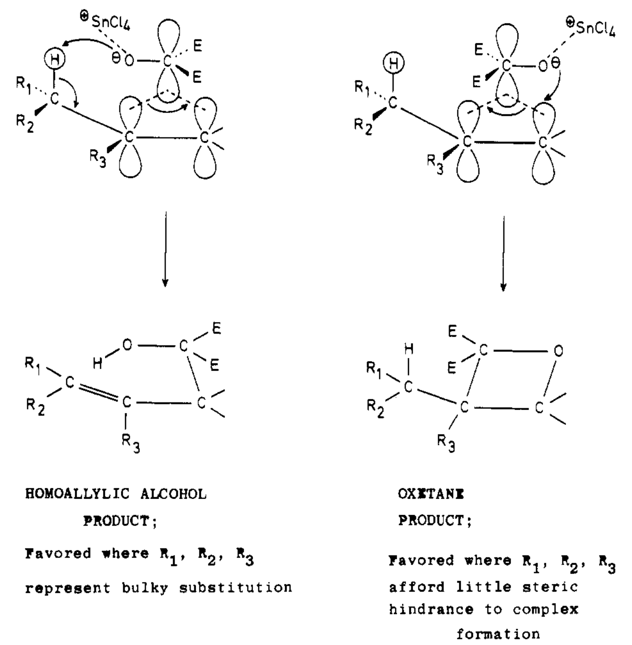
[4] Stephenson, L. M.; Orfanopoulos, M. *J. Org. Chem.* **1981**, *46*, 2201.

[5] Salomon, M. F.; Pardo, S. N.; Salomon, R. G. *J. Am. Chem. Soc.* **1980**, *102*, 2473.

Scheme I



in the ^2H NMR, at δ 3.16. Finally, when 3-phenylpropene-*1,1*-d_2, **1a**, was run, the reaction product exhibited a peak at δ 4.86 in a ^2H NMR spectrum devoid of any signs of a second deuterated component like **4a** or **5a**; cf. eq 2a. These results are completely consistent with the formulation of the reaction course expressed by eq 3.

Apparently, however, $SnCl_4$ catalysis does afford a normal course of reaction of superenophiles with some ene substrates (see for example Salomon[5] and Stephenson[4]). While the formation of an oxetane byproduct has not been previously noted in the mesoxalic ester reactions,[6] (2 + 2) cycloadducts have often been observed in the purely thermal reactions of other superenophiles; e.g., the >S=N- enophiles pioneered by the Kresze school.[3,7] In fact, these observations constitute one of the lines of evidence for the requirement of a preliminary complex of the reactants as a step that organizes the subsequent rate-determining, pseudopericyclic, angular H abstraction by the nonbonding pair at the heteroatom center.

From such considerations we have arrived at the understanding that in the Lewis acid catalyzed reaction of mesoxalates (and probably, also, with other superenophiles subject to such catalysis), the rate-determining step has been shifted to the *formation* of a three-membered complex. This case is clearly identified by the low value of $k_H/k_D \approx 1.1$ observed,[4] where the normal ene reaction product (homoallyl alcohol) results from $SnCl_4$ catalysis, i.e., where R_1 and R_3 are the bulky groups phenyl and methyl, respectively. In these terms, it is a β-secondary deuterium isotope effect attributable to the recognized[8] hyperconjugative influence on the activity of the double bond in the electrophilic addition producing a three-membered intermediate complex in the rate-determining step (see Scheme I).

In summary, in the purely thermal superene reaction the TS arises from a rapidly formed, unstable (2 + 2) CT complex in which an unshielded *n* electron pair is positioned for angular abstraction of an allylic H in a concerted, pseudopericyclic process. By contrast, in the Lewis acid catalyzed mechanism the rate-determining step becomes the formation of a three-membered complex. Therein, the ease of its formation as well as its structural orientation and therefore the nature of the product-forming step are sharply affected by the substitutents on the double bond, i.e., (a) through the above-mentioned hyperconjugative influence on double bond activity in complex formation, and (b) through steric constraints stemming from repulsive interactions between the ene and enophile substituents. Scheme I depicts the alternative orbital interactions involved and the structural orientations of the complexes that can form as a result of rate-determining attack on the ene double bond by the carbonyl carbon (of the enophile) made strongly electrophilic by preliminary reaction with the $SnCl_4$ catalyst.

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[7] See also, Hori, T.; Singer, S. P.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 1956.

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A Stereoselective Approach to Steroid Trans C/D Ring Synthons

Summary: A stereoselective approach to the vitamin D skeleton that controls the stereochemistry at C_{13}, C_{14}, C_{17}, and C_{20} is described.

Sir: The discovery of highly active metabolites of vitamin D[1] has spurred renewed interest in synthetic studies that attack the two classic problems in steroid synthesis: (1) preparation of the C/D *trans*-hydrindan ring system[2,3] and (2) the stereospecific construction of side chain stereochemistry (at C_{20}). In particular, several papers have recently appeared[3-6] that apply the intramolecular Diels-Alder to the synthesis of angularly methylated hydrindan systems. With two exceptions, most examples give >50% cis ring fusion.[4] For several years we have been interested

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[1] (a) Holick, M. F.; DeLuca, H. F. *Ann. Rev. Med.* **1974**, *25*, 349. (b) Bell, P. A. In "Vitamin D"; Lawson, D. E. M., Ed.; Academic Press: New York, 1978; pp 1-50. (c) DeLuca, H. F.; Paaren, H. E.; Schnoes, H. K. *Top. Curr. Chem.* **1979**, *83*, 3-65. (d) DeLuca, H. F. *Monogr. Endocrinol.* **1979**, 13. (e) Uskokovic, M. R.; Partridge, J. J.; Narwid, T. A.; Baggiolini, E. G. In "Vitamin D: Molecular Biology and Clinical Nutrition"; Norman, A. W., Ed.; Marcel Dekker: New York, 1980; pp 1-57.

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