The present data, besides supporting the mechanism (see Scheme I) we suggested in order to rationalize the acid-catalyzed reactions of 1-arylcyclohexene oxides, seem to confirm the hypothesis that conformationally mobile epoxides **1** react preferentially through conformation **1''** corresponding to **3** rather than through the alternative one (**1'**).

In conclusion the reactions of both the rigid epoxides **2** and **3** occur to give definite amounts of syn adduct **12** and **13**, respectively, which both depend, as shown by the Hammett-type treatment, in a similar, although not identical, manner on the substituents on the aryl.

It appears that in the 1-arylcyclohexene oxide system, according to the mechanism we proposed[4,9-12] (see Scheme I), the conformation in which the epoxide reacts can be of some importance, but it cannot be decisive for the product distribution.

It appears very likely that the mechanism through which 2-aryloxiranes react under acidic conditions should be practically independent of the nature of the epoxide and that therefore the rationalization of the product distribution in the reactions both of epoxides of type **1** and **14** and in general of other 2-aryloxiranes should follow the same scheme. On the basis of the results obtained, it appeared to be a logical consequence that our mechanism would be able to rationalize the product distribution in acid solvolysis of benzo-epoxides of type **14**. However, attempts were unsuccessful to rationalize the product distribution of the acid hydrolysis of the rigid benzo-epoxides **15** and **16**[30] through a mechanism analogous to the one proposed for 1-arylcyclohexene oxides[4,9-12] (see Scheme I) in terms of the hypothesis that one of the determining factors in these reactions is the preferential "axial cleavage" of the epoxide ring. Maybe factors other than "axial cleavage" are important in determining the reactivity of such systems. The different conformational rigidity of the aryl in the two systems (1-arylcyclohexene oxides and benzo-epoxides of type **14**) could also be of some importance. Studies are in progress in order to clear up this point.

Experimental Section

Melting points are uncorrected. IR spectra for the determination of OH-stretching bands were taken with a Perkin-Elmer Model 257 double beam grating spectrophotometer in dried (P_2O_5) CCl_4 with use of the indene band at 3110 cm^{-1} as a calibration standard; a quartz cell of 2-cm optical length was employed, and the concentration of the solution was 5×10^{-3} M or lower to prevent intramolecular association. ^1H NMR spectra were determined on ca. 10% $CDCl_3$ solution with a Varian EM 360 with Me_4Si as an internal standard. GLC analyses were performed in the following way: hydroxy ethers **26-29b,c**, **31b,c**, and **32-33b,c**, a Perkin-Elmer Mod. SIGMA 3B (column packed with 10% neopentyl glycol succinate on 80-100 mesh silanized Chromosorb W, 2.0 m × 2.5 mm); **26-29b**, column 200 °C, nitrogen flow 60 mL/min; **26-39c**, column 210 °C, nitrogen flow 60 mL/min; **32-33b,c**, column 190 °C, nitrogen flow 50 mL/min. Diols **35-38a-c** were analyzed on a Carlo Erba Fractovap Model 2300 (column packed with 3% neopentyl glycol succinate on 80-100 mesh silanized Chromosorb W, 1.5 m × 2.5 mm): **35-38a**, column 190 °C, nitrogen flow 40 mL/min; **35-38b,c**, column 205 °C, nitrogen flow 40 mL/min. In every case evaporator and detector were at 270 °C.

Reactions of Epoxides 1-3 in Dioxane-Water and in Methanol in the Presence of Acid. A solution of the epoxide (0.020 g) in a thermostated (25 °C) 1:1 dioxane-aqueous 0.2 N H_2SO_4 (20 mL) or 0.2 N H_2SO_4 in anhydrous methanol (2 mL) was stirred at 25 °C during the time reported in Table I, quenched with solid $NaHCO_3$ and saturated aqueous $NaHCO_3$, and extracted with ether. Evaporation of the washed (water) and dried ether extracts yielded mixtures consisting of hydroxy ethers **26** and **27** from **2**, **28** and **29** from **3**, **32** and **33** from **1** (reaction in methanol), and diols **35** and **36** from **2**, **37** and **38** from **3**, and **40** and **41** from **1** (reaction in dioxane-water) which were analyzed by GLC (see Table I). The solvolysis addition products from each epoxide were completely stable under the exact reaction conditions used. The values given in Table I were the average of at least three measurements done on at least two different runs for each point.

Acknowledgment. We gratefully thank Professor Giancarlo Berti for his constant interest in this work and his advice. This work was supported in part by Consiglio Nazionale delle Ricerche (CNR) (Roma) and Ministero della Pubblica Istruzione (Roma).

Registry No. 1a, 4829-01-0; **1b**, 7583-80-4; **1c**, 54637-84-2; **2a**, 17851-86-4; **2b**, 106267-70-3; **2c**, 106267-71-4; **3a**, 4341-22-4; **3b**, 106356-38-1; **3c**, 106356-39-2; **21b**, 106267-72-5; **21c**, 106267-73-6; **22c**, 106267-74-7; **23b**, 106267-75-8; **26b**, 106267-76-9; **26c**, 106267-77-0; **27b**, 106267-78-1; **27c**, 106267-79-2; **28b**, 106267-80-5; **28c**, 106267-81-6; **29b**, 106267-82-7; **29c**, 106267-83-8; **31b**, 106295-68-5; **31c**, 106267-84-9; **32b**, 106267-85-0; **32c**, 106267-86-1; **33b**, 106267-87-2; **33c**, 106267-88-3; **35b**, 106295-69-6; **35c**, 106267-89-4; **36b**, 106267-90-7; **36c**, 106267-91-8; **37b**, 106267-92-9; **37c**, 106267-93-0; **38b**, 106267-94-1; **38c**, 106267-95-2.

Supplementary Material Available: All the experimental details for the preparation of products shown in Schemes III-V and listed in Table III (13 pages). Ordering information is given on any current masthead page.

Chemoselectivity and Stereocontrol in Molybdenum-Catalyzed Allylic Alkylations

Barry M. Trost* and Mark Lautens

Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. *Received August 11, 1986*

Abstract: Molybdenum-catalyzed allylic alkylations exhibit excellent chemoselectivity. Carbonyl functional groups like esters and ketones need not be protected. The order of reactivity of a normal alkylating agent like an alkyl bromide and an allyl acetate is inverted compared to the uncatalyzed reaction—an observation that means that an alkyl bromide is compatible. In contrast to palladium-mediated reactions, silicon substituents at the allylic or vinylic position of the allylic acetate do not protodesilylate. Control of olefin geometry is exercised. The metal template favors formation of an (*E*)-olefin exocyclic to a ring. Both *E* and *Z* disubstituted allyl acetates give (*E*)-olefinic products. The stereochemistry of substitution with a cyclic allylic acetate depends upon the base and nucleophile. With BSA as base, clean net retention of configuration is observed. On the other hand, both diastereomers of 1-vinyl-1-acetoxycyclohexane give the same product arising from equatorial attack. Mechanistic and synthetic implications are discussed.

Controlling reactivity by the use of metal templates has the promise of enhancing our ability to perform selective transformations and to modify traditional reactivity patterns. For example, metal-catalyzed asymmetric hydrogenation[1] and epoxidations[2]

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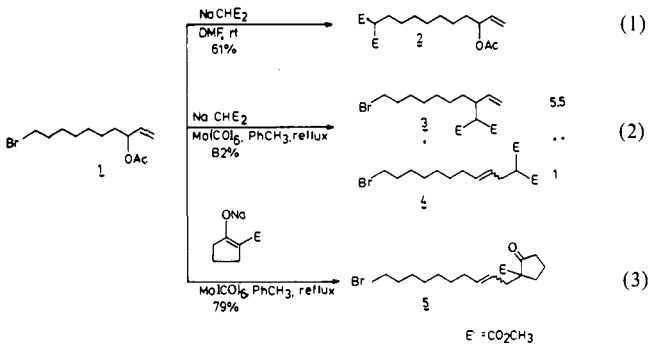
have enabled us to begin to address the difficult problem of enantioselectivity. In allylic alkylations, palladium-catalyzed reactions have activated normally unreactive leaving groups and have permitted substitutions to proceed with net retention of configuration—a stereocomplement to normal displacements.[3] The success of the palladium-based methodology led us to explore alternative catalysts to expand the range of structural control in such reactions. The success of the molybdenum-based reactions in providing a regiochemical alternative[4] led us to explore the chemo- and stereoselectivity of this process.[5]

Chemoselectivity

Minimization of the use of protecting or activating groups requires the development of reactions which are increasingly chemoselective. In substitution reactions, one of the severest tests is competing the metal-catalyzed alkylation of allyl acetates with noncatalyzed displacements of alkyl halides. Bromoacetate **1** provides such a challenge.[6]

The normal reactivity pattern of bromoacetate **1** was established by reaction under standard displacement conditions in a dipolar aprotic solvent utilizing dimethyl sodiomalonate (eq 1). A single



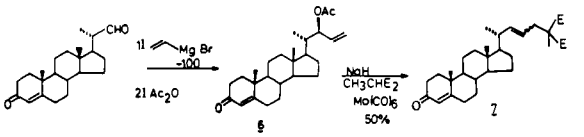
(1)

(2)

(3)

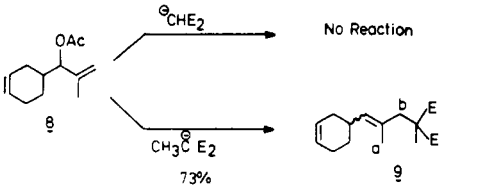
product emerged; spectral data easily allow assignment as the bromide displacement product **2**. A heterogeneous reaction with the same nucleophile in toluene in the presence of molybdenum hexacarbonyl ($Mo(CO)_6$) proceeded exclusively by acetate (*not bromide*) substitution to give **3** and **4**—a structural assignment easily verified by spectroscopic analysis. The typical pattern of a monosubstituted double bond (^1H NMR δ 5.70 (dt, J = 17, 10 Hz), 5.08 (d, J = 17 Hz), 5.00 (d, J = 10 Hz); ^{13}C NMR δ 138.0 and 117.2) confirmed the major regioisomer as the now expected internal alkylation product **3**. The minor terminal alkylation product was assigned as an approximately 4:1 E:Z mixture on the basis of the ^{13}C NMR signals (E, δ 133.7 and 124.9; Z, δ 132.9 and 124.3). Use of *O,N*-bis(trimethylsilyl)acetamide (BSA) as base in this alkylation gave virtually identical regioselectivity. Use of the sterically more demanding nucleophile derived from 2-carbomethoxycyclopentanone in the molybdenum-catalyzed reaction also gave excellent chemoselective displacement of acetate only. The now established regioselectivity pattern of terminal attack for this nucleophile was confirmed with the keto ester **5** being formed as a 5:1 (E)-olefin:(Z)-olefin mixture. The E stereochemistry of the major isomer was established by the 15.5-Hz coupling and the typical ^{13}C NMR signals for the E (δ 135.0 and 124.0) and Z (δ 133.5 and 123.2) isomers.

The importance of carbonyl groups makes compatability with such functionality important. In the earlier alkylations, the tolerance of esters in the allylating agent was established. We, therefore, sought to test the compatibility with a ketone. Chemoselective addition of vinylmagnesium bromide to bisnorcholenaldehyde and acetylation generated the substrate **6**. Alkylation with malonate anion generated by utilizing either sodium hydride or BSA as base failed to give any reaction! On the other hand, the anion of dimethyl methylmalonate reacts with the allyl acetate to give the expected alkylation product **7** as an E,Z isomeric pair (eq 4).



(4)

While the successful alkylation of **6** with dimethyl methylmalonate suggested the enone was not responsible for the lack of any reaction with dimethyl malonate, we sought to pursue this question further. To assess local steric factors, we examined the allyl acetate **8** in its reactions with the two nucleophiles. A



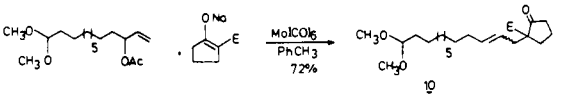
(5)

(6)

completely parallel result was obtained—alkylation of dimethyl malonate led to no reaction, whereas dimethyl methylmalonate produced the expected alkylation product **9** as a 4.5:1 mixture of olefin isomers. The assignment of the major isomer as the (E)-olefin rests upon ^{13}C NMR analysis. By use of the ERNST experiment[7] with $\tau = 3/4J$, the vinyl methyl (C_a) and allylic methylene (C_b) were assigned at δ 19.7 and 44.9 in the major isomer and δ 23.7 and 36.8, respectively, in the minor isomer. The known steric compression effect[8] on ^{13}C NMR shifts establishes the vinyl methyl group as cis to cyclohexenyl and the allylic methylene group as trans in the major isomer, i.e., the (E)-olefin.

The identical behavior of **6** and **8** toward the two nucleophiles reveals that the presence of the enone in **6** is *not* responsible for the alkylation behavior. Two observations suggest that the absence of alkylation with dimethyl malonate may arise from the formation of a different catalyst. First, in both cases, starting material is recovered in excellent yield. If ionization by molybdenum was occurring, at least elimination products should have resulted[9]—not recovered starting material. Second, addition of malonate anion to a reaction mixture of allyl acetate **8** and methylmalonate anion completely inhibited the latter reaction. While it is appropriate to postpone commentary on these observations to the Discussion section, suffice it to say at this time that the presence of the enone in **6** does not interfere in the molybdenum-catalyzed reaction.

The fact that $Mo(CO)_6$ is a Lewis acid[10,11] led us to consider an acid-sensitive group such as an acetal in these reactions. As eq 7 illustrates, no difficulties arising from possible Lewis acid properties of $Mo(CO)_6$ arose during alkylation reactions. NMR spectroscopy revealed the product **10** to be an approximately 3:1 mixture of the (E)- and (Z)-olefins.



(7)

The fact that allylsilanes showed a propensity to undergo protodesilylation under alkylation conditions with palladium

(1) For a recent review, see: Kagan, H. B. *Compr. Org. Chem.* **1982**, *8*, 463.

(2) For a recent review, see: Sharpless, K. B.; Behrens, C. H.; Katsuki, T.; Lee, A. W. M.; Martin, V. S.; Takatani, M.; Walker, F. J.; Woodward, S. S. *Pure Appl. Chem.* **1983**, *55*, 589.

(3) For reviews, see: Trost, B. M.; Verhoeven, T. R. *Compr. Org. Chem.* **1982**, *8*, 799. Tsuji, J. *Organic Synthesis with Palladium Compounds*; Springer-Verlag: Berlin, 1980.

(4) Trost, B. M.; Lautens, M., unpublished results.

(5) For preliminary reports of portions of this work, see: Trost, B. M.; Lautens, M. *Organometallics* **1983**, *2*, 1687. Trost, B. M.; Lautens, M. *J. Am. Chem. Soc.* **1983**, *105*, 3343.

(6) The symbol E denotes CO_2CH_3 throughout this paper.

(7) Bohlman, F.; Zeisberg, R.; Klein, E. *Org. Magn. Reson.* **1975**, *7*, 426.

(8) Trost, B. M.; Lautens, M.; Peterson, B. *Tetrahedron Lett.* **1983**, *24*, 4525.

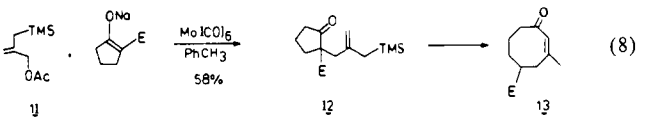
(9) Morris, G. A.; Freeman, R. *J. Am. Chem. Soc.* **1979**, *101*, 760. Doddrell, D. M.; Pegg, D. T.; Brooks, W.; Bendall, M. R. *J. Am. Chem. Soc.* **1981**, *103*, 727 and references therein.

(10) Farona, M. F.; White, J. F. *J. Organomet. Chem.* **1973**, *63*, 329. Farona, M. F.; White, J. F. *J. Am. Chem. Soc.* **1971**, *93*, 2826.

(11) Trost, B. M.; Ghadiri, M. R. *J. Am. Chem. Soc.* **1984**, *106*, 7260.

catalysts led us to examine the effect of molybdenum catalysts on this reaction. The bifunctional conjuctive reagent **11** is particularly prone to protodesilylation with palladium catalysts.

On the other hand, alkylation to **12** occurred without any protodesilylation with $Mo(CO)_6$ as catalyst. In fact, attempts

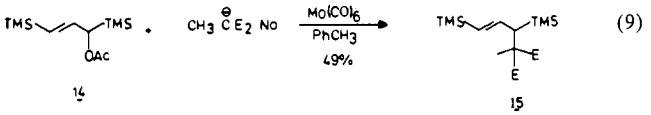


(8)

11 **12** **13**

to promote desilylation failed as did all attempts to effect cycloadditions analogous to the palladium-catalyzed reactions.[12a,13] We have previously shown that the products like **12** are very useful in three carbon intercalations[15] as in the conversion of **12** to **13**.

Palladium-catalyzed alkylations of disilylallyl acetate **14** with the anion of dimethyl methylmalonate gave an approximately equimolar mixture of alkylated and protodesilylated alkylated products.[12b,14] The molybdenum reaction proceeded smoothly to give only the simple displacement product **15**.

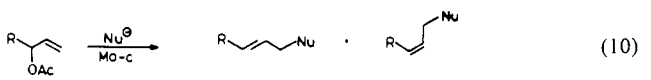


(9)

14 **15**

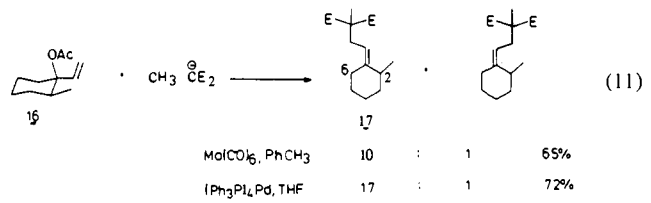
Geometric Selectivity

The geometry of the olefin in the alkylation products may be created in the alkylation step as in eq 10. As several of the



(10)

examples already reported demonstrate, a selectivity for the (*E*)-olefin of around 4–5:1 exists in most cases. A particularly intriguing question is what the stereoselectivity would be for an olefin exocyclic to a ring. For this purpose, we chose allyl acetate **16** since its reactions with lithium dimethylcuprate led to a 1:1



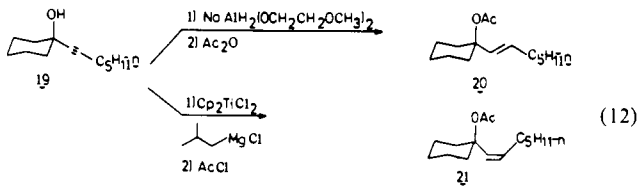
(11)

16 **17**

mixture of the two olefin isomers.[16] In contrast to the organocuprate reaction, the molybdenum-catalyzed reaction led to good control of olefin geometry. Somewhat higher geometric selectivity was obtained by using a palladium catalyst. The latter may arise because of the somewhat lower temperature of reaction with palladium compared to that with molybdenum.

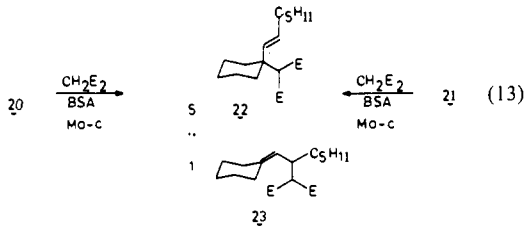
The assignment of the olefin geometry was based upon ^{13}C NMR shifts. Crabbe determined that the shifts of C(2) and C(6) in a related series were δ 38.4 (*E*) vs. 28.2 (*Z*) and δ 28.2 (*E*) vs. 32.5 (*Z*), respectively. The closeness of the values for our major isomer, δ 38.7 and 25.1 for C(2) and C(6), respectively, to those of the *E* isomer of Crabbe leads us to assign the geometry as *E* as depicted.

An alternative question relates to retention of olefin geometry during the course of alkylation. The sluggishness of alkylation with geranyl acetate, a substrate bearing a trisubstituted double bond, led us to explore this question with disubstituted olefin pair **20** and **21**, both derived from the acetylene **19**.[17,18] NMR



(12)

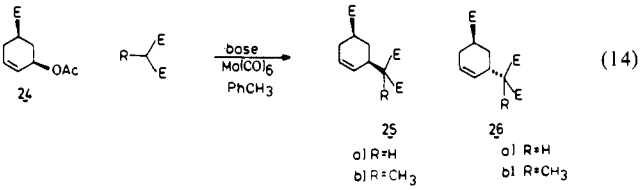
spectroscopy established the isomeric purity of each to be >10:1. Alkylation of both with malonate anion proceeds smoothly under our standard conditions to give the same 5:1 mixture of tertiary vs. secondary attack. Most importantly, the major regioisomer in both is identical, i.e., an (*E*)-olefin as revealed by the 15-Hz coupling of the vinyl protons. Clearly, equilibration of geometry is faster than alkylation.



(13)

Diastereoselectivity

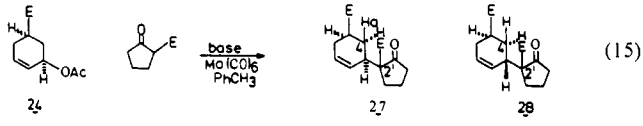
The complementary stereochemistry of the palladium-based substitution compared to normal noncatalyzed displacement represents an important advantage of the palladium reaction. To explore this question in the molybdenum-catalyzed reaction, we employed the cyclohexenyl acetate **24**.[19] The stereochemical



(14)

outcome was critically dependent upon both the base and nucleophile. Performing the alkylation with malonate anion generated by using sodium hydride as base led to a 2:1 mixture of **25** and **26** at 40% reaction and a 1:1 mixture at 90% reaction. Equilibration of **25** and **26** establishes the equilibrium to be 3:1. This latter fact suggested that if the changing ratio under the conditions of alkylation were due to equilibration, the ratio of 2:1 should have increased to 3:1 and not decreased to 1:1. To establish unambiguously that equilibration was not occurring, independent control experiments demonstrate that both the starting material and the products are indeed unchanged. In contrast to the above experiment, using BSA as base led only to **25** in 75% yield, i.e., complete retention of configuration, in good agreement with the palladium-catalyzed reaction.

The reactions of 2-carbomethoxycyclopentanone paralleled those of dimethyl malonate. Analysis of the reaction may be conveniently accomplished by vapor-phase chromatography, which easily resolves the cis and trans alkylation products **27** and **28** but not the diastereomers epimeric at the cyclopentanone asymmetric center. The reaction using BSA as base gave only the cis-alkylated



(15)

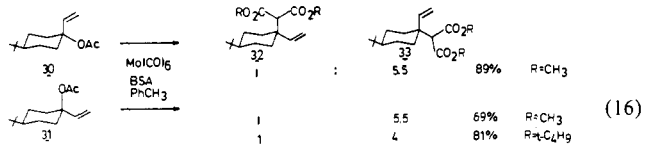
product **27** as determined by both vapor-phase chromatography

(12) (a) Trost, B. M.; Chan, D. M. T. *J. Am. Chem. Soc.* **1983**, *105*, 2315, 2326. (b) Trosi, B. M.; Self, C. R. *J. Am. Chem. Soc.* **1983**, *105*, 5942.
(13) Trosi, B. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1.
(14) Trosi, B. M.; Brandi, A. *J. Org. Chem.* **1984**, *49*, 4811.
(15) Trosi, B. M.; Vincent, J. E. *J. Am. Chem. Soc.* **1980**, *102*, 5680.
(16) Crabbe, P.; Dollat, J. M.; Gallina, J.; Luche, J. L.; Valarde E.; Maddox, M. L.; Tokes, L. *J. Chem. Soc., Perkin Trans. 1* **1978**, 730.
(17) For Red-Al reduction of propargyl alcohols, see: Jones, T. K.; Denmark, S. E. *Org. Synth.* **1985**, *64*, 182.
(18) Semihydrogenation of **19** failed. For the titanium method, see: Saio, F.; Ishikawa, H.; Watanabe, H.; Miyake, T.; Saio, M. *J. Chem. Soc., Chem. Commun.* **1981**, 718.
(19) Trosi, B. M.; Verhoeven, T. R. *J. Am. Chem. Soc.* **1980**, *102*, 4730.

and NMR spectral analysis. On the other hand, alkylation using sodium hydride as base gave a 1:1 mixture of cis and trans alkylation products **27** and **28**. The diastereomeric ratio in each series was most easily revealed by the methyl ester signals as well as by ^{13}C NMR spectroscopy. The protons on C(4) are diagnostic of the stereochemistry of alkylation with H(a) being a quartet with a large coupling constant due to the coincidence of the geminal and two trans diaxial coupling constants.[19] The cis isomer **27** shows this characteristic absorption at δ 1.37 and 1.30, J = 12 Hz, for the major and minor cis diastereomers. For the Z alkylation product **27**, the C(2′) epimers show ^1H NMR absorptions for the methyl esters at δ 3.64 and 3.70 vs. δ 3.66 and 3.71 and ^{13}C absorptions for the olefinic carbons at δ 127.7 and 127.2 vs. δ 128.3 and 126.7. On this basis, the Z alkylation product derived from the BSA experiment was predominantly (>6:1) a single diastereomer showing signals at δ 3.64 and 3.70 in the ^1H spectrum and δ 127.7 and 127.2 in the ^{13}C spectrum, whereas that derived from the sodium hydride experiment was a 1.9:1 mixture of epimers at C(2′) with the major epimer in both alkylations being the same. For the E alkylation product **28**, the C(2′) epimers show ^1H absorptions for the methyl esters at δ 3.66 and 3.68 vs. δ 3.65 and 3.71, with the former signals corresponding to the major diastereomer (1.5:1).

Alkylation with dimethyl methylmalonate (**29**) gave a significantly different result from the above. Whereas the alkylations of dimethyl malonate and 2-carbomethoxycyclopentanone gave mixtures of E and Z products with sodium hydride, such was not the case with **29**. The Z product **25b** formed predominantly (8:1) when sodium hydride was employed under conditions identical with those that produced 1:1 mixtures with the other two nucleophiles. Thus, it is clear that these alkylations can proceed with very high diastereofacial selectivity with respect to the nucleophile.

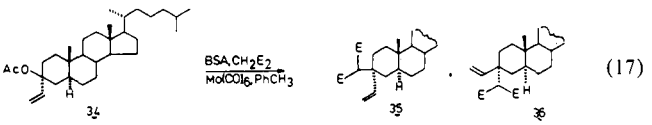
To contrast a cyclic π-allyl-type system to an acyclic one, we explored the epimeric pair of allyl acetates **30** and **31**. Sur-



(16)

prisingly, both gave the same major product. ^{13}C NMR data and correlation with closely related literature compounds[20] permitted assignment of stereochemistry. In particular, the α-carbon of the axial vinyl group should appear at a higher field than the equatorial one.[21] The major isomer shows an absorption for this carbon at δ 142.7 and at δ 146.7 for the minor isomer—consistent with the major product being **33**. Use of the anion derived from di-*tert*-butyl malonate as the nucleophile caused a slight decrease in the diasteroselectivity.

The trend appears to be general. The allylic acetate **34**, prepared in straightforward fashion from the corresponding ketone, gave a 4:1 mixture of the two alkylated products, with the major isomer again being assigned by ^{13}C NMR analysis as **35**. It appears that alkylation of acyclic systems is stereoselective and not stereospecific.

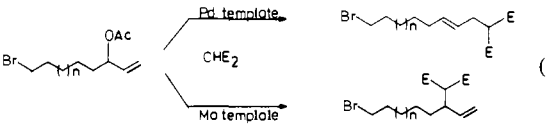


(17)

Discussion

The molybdenum-catalyzed reactions enjoy a chemoselectivity comparable to that of the palladium-catalyzed reactions in spite of the higher reaction temperatures required. It should be noted that these reactions do not have as high a turnover number since 10–15 mol % of catalyst appears to be required for most molybdenum reactions (in a few cases such as linalyl acetate 5 mol % may be used), whereas 1–5 mol % suffices for the corresponding scale of reaction in palladium-catalyzed reactions. While we have established that substantial increases in scale in the palladium-catalyzed reaction may be accompanied by substantial decreases in the amount of catalyst, we have not established this point for the corresponding molybdenum reactions although the trend appears similar. The much lower cost of the molybdenum catalyst, however, compensates for its lower turnover numbers.

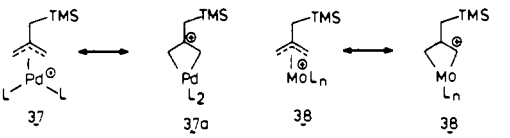
Several aspects of the chemoselectivity are particularly noteworthy. The inversion of reactivity of an allyl acetate and an alkyl bromide toward displacements is complete. In the specific case of malonate anion, complete control of chemo- and regiochemistry is now possible, as summarized in eq 18. The compatibility with



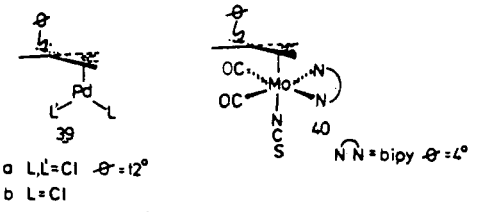
(18)

ketones, esters, sulfones, acetals, olefins, and allyl- and vinylsilanes has also been established and bodes well for good chemoselectivity with other funtionality not yet tested.

The difference between the palladium and molybdenum catalysts with respect to the bifunctional conjunctive reagent **11** is striking. The propensity for desilylation in the palladium-catalyzed reaction compared to the total lack of desilylation in the molybdenum reaction presumably reflects the ability of **37** vs. that of **38** to activate the cleavage of the C–Si bond. If one attributes



the activation of the C–Si bond toward cleavage with the net electron-withdrawing nature of the (π-allyl)metal fragment, we can conclude that the palladium fragments are more electrophilic than the molybdenum fragments. Since the catalytically active species in the latter case remains unknown, it is not possible to comment further on this point. An additional consideration invokes the amount of leakage of electron deficiency to the central carbon as depicted in the resonance forms **37a** and **38a**. The C–Si bond would be activated toward cleavage the greater the extent that **37a** contributes to the structure of the (π-allyl)palladium complex compared to **38a** contributing to the (π-allyl)molybdenum complex. X-ray structural data may shed light on this notion. When the X-ray structures of several palladium[23] and molybdenum[24] complexes are examined, it is very interesting to note that the methyl group at C(2) is bent 12–19° out of the plane of the π-allyl unit *toward* the metal in **39** but only 4° in **40**. Ligands clearly



have an effect on the magnitude of the deformation, with acceptor ligands more effective than donor ligands. The change in the energy levels of the metal upon changing ligands and their ability to mix with the π-allyl orbitals appear to be responsible for the deformations.[25] An alternative way to view these deformations

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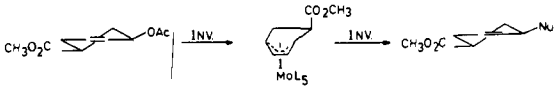
invokes a valence bond notion of a metallocyclobutane contributing to the ground state. The larger deformation denotes a larger contribution of the metallocyclobutane and consequently more leakage of positive charge to the central carbon of the allyl fragment.

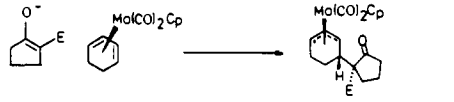
The stereochemical dependence on nucleophile, base, and allyl substrate reveals the complexity of this alkylation reaction. With BSA as base, the generalization that the alkylation proceeds with net retention of configuration independent of nucleophile in cyclic substrates would appear valid. Such a net retention can arise either by an inversion in the activation step and an inversion in the alkylation step as depicted in eq 19 or by a double retention.



(19)

Analogy to the palladium-catalyzed reaction suggests a double-inversion mechanism—a conclusion also supported by the limited data on the stereochemistry of attack on some (π-allyl)molybdenum complexes.[27-29] However, since such stereochemical features may depend on the nature of the ligands, which remains undefined at present in the catalytically active species, a double-retention mechanism cannot be ruled out. The loss of stereocontrol due to the use of sodium hydride with some but not all nucleophiles will be discussed later.

The high facial selectivity with respect to the nucleophile of **24** with 2-carbomethoxycyclopentanone when BSA was the base is similar to that seen by Pearson[30] in a stoichiometric alkylation of a cationic diene–molybdenum complex. Approach of the nucleophile on the face *opposite* molybdenum occurred so as to minimize steric interactions and led to a single product (eq 20). We assume that a similar approach takes place in the π-allyl intermediate to yield the relative stereochemistry shown in **41** (eq 21). Kochi has also reported high diastereoselectivity with this nucleophile in the case of a stoichiometric (π-allyl)molybdenum reaction, but he has not established the stereochemistry.[29]



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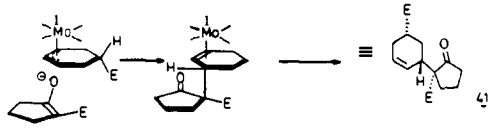
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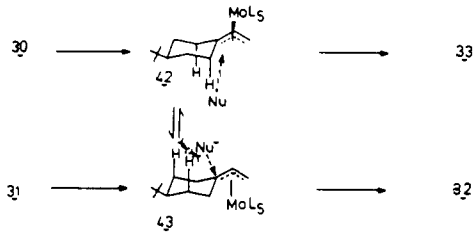
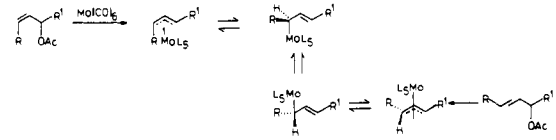
In the acyclic case, however, stereochemistry is lost. Kinetically, allylic acetate **30** should generate **42** and **31** should generate **43** (eq 22). The fact that both give identical product mixtures in



(22)

which **33** dominates suggests that interconversion between **42** and **43** must be rapid relative to the rate of alkylation. Two mechanisms may be envisioned for the migration of molybdenum. A rationale well documented in transition-metal chemistry invokes formation of a σ-complex, rotation around a single bond to place the metal on the opposite face, and reformation of a π-complex (vide infra). Alternatively, a bimolecular molybdenum exchange could invert the faces. The latter mechanism can operate in both cyclic and acyclic systems. The fact that in our cyclic substrate we see no loss of stereochemistry under conditions identical with those that give complete scrambling in the acylic case mitigates against the bimolecular molybdenum exchange. Synthetically, since the stereochemistry of carbonyl additions may not be so easily controlled, the fact that both diastereomers give the same product derived from equatorial attack in molybdenum-catalyzed allylic alkylations demonstrates the ability of the metal to impose diastereo- as well as regiocontrol. The preferential equatorial attack as in **42** presumably reflects less steric hindrance in the transition state for alkylation compared to axial attack as in **43**. The three axial H interactions with the nucleophile are presumably more important than the two axial H interactions to account for this result. An attempt to increase the effective steric bulk of the nucleophile by using di-*tert*-butyl malonate caused little change in the diastereoselectivity.

Support for rapid interconversion of (π-allyl)molybdenum complexes via π-bond formation and rotation arises in the determination of the selectivity associated with olefin geometry. Both the (*E*)- and (*Z*)-olefins **20** and **21** gave the same product which possessed the *E* geometry. Since neither starting material nor product equilibrates, this loss of geometry must occur in the intermediate (π-allyl)molybdenum complex. A reasonable explanation invoking π-complexes is outlined in eq 23. The combination of this result with the stereochemical studies (which is explainable on a similar basis) lends credence to this mechanism being operative here.



(23)

While the geometry of a *Z* disubstituted olefin is not retained, the high selectivity for the *E* geometry in the product may be an advantage. For example, mixtures of (*E*)- and (*Z*)-olefinic starting materials will stereoconverge to the (*E*)-olefinic product. In the case of a trisubstituted double bond, formation of a molybdenum–carbon σ-bond at a tertiary center will be hindered, and thus, the equilibration will be slowed. Thus, it is likely that olefin geometry will be preserved in such cases. The low reactivity of trisubstituted olefinic starting materials in molybdenum-catalyzed reactions has so far precluded our testing of this prediction.

This method appears to have promise in controlling olefin geometry exocyclic to a ring. Thus, high selectivity for the (*E*)-olefin **17** (eq 11) is observed for both a molybdenum and a palladium catalyst. This result is in contrast to the organocopper chemistry of the same substrate which produced a 1:1 mixture of *E* and *Z* products.[16] The existence of the palladium and molybdenum intermediates as π-allyl structures combined with the steric bulk of these templates accounts for the good control of olefin geometry. The likelihood that organocopper intermediates are σ-structures accounts for the lower selectivity seen in its reactions.[31] Carbonyl olefination normally produces the *Z* product or mixtures of *E* and *Z* products.[32] The ability to effect an equivalent process by addition of vinyl Grignard reagent to a cyclic ketone followed by metal-catalyzed alkylation then complements, in a geometrical sense, olefination methods.

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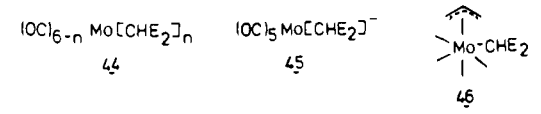
Two issues that remain to be addressed are (1) the effect of base on the stereochemistry of reaction with some of the nucleophiles and (2) the divergent reactivity of the anions of dimethyl malonate and a dimethyl alkylmalonate with some allylic acetates. Stereocontrol is lost in the reaction of dimethyl malonate when sodium hydride is used as base but not BSA, whereas high stereocontrol is retained regardless of base in the reaction of dimethyl methylmalonate. Furthermore, in the former reaction, the stereochemistry varies as a function of time. Following the reaction by vapor-phase chromatography reveals that there is no isomerization of starting allylic acetate under the reaction conditions in contrast to palladium-catalyzed reactions. Subjecting the products to the reaction conditions establishes their stability. Furthermore, as already pointed out, the ratio of the two isomeric products is moving away from the thermodynamic ratio. A possible explanation is a change in catalyst as a function of time. Dimethyl malonate may react with molybdenum hexacarbonyl to generate new molybdenum species such as **44** or **45**.[33] This



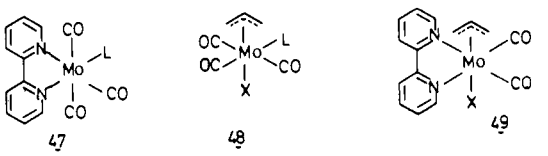
44 45 46

new species may function as an alternative catalyst which gives rise to an intermediate such as **46**. Intramolecular migration of malonate from the metal to carbon then accounts for the product of net inversion, i.e., **26a** (eq 14). Since the concentration of this new catalytic species increases with time, the ratio of reaction proceeding with net retention and inversion varies with reaction time, with the process giving net inversion increasing with time. Addition of BSA either inhibits this migration, presumably because it also is complexed with molybdenum, or displaces malonate from molybdenum. Placing an alkyl group on the malonate sterically precludes attack on $Mo(CO)_6$ and thereby prevents formation of analogues of **44** or **45**. Thus, alkylations with substituted malonates show no dependence of stereochemistry on base. Decreasing the electrophilicity of the molybdenum catalyst should decrease its propensity to be attacked by malonate anion and thereby inhibit the net inversion process. Indeed, by using the bipyridylmolybdenum complex **47** (X = CO)[34] as a catalyst in the alkylation of **24** with dimethyl malonate using sodium hydride as base decreases the net inversion product from 55% with $Mo(CO)_6$ to only 15% with **47**.

In an ancillary study, we compared the relative reactivity of dimethyl malonate and dimethyl methylmalonate in molybdenum-catalyzed reactions. Using BSA as base, a competitive reaction of 1 equiv of dimethyl malonate, 1 equiv of dimethyl methylmalonate, and 1 equiv of allylic acetate **31** led to preferential alkylation of dimethyl malonate, with the ratio of the two alkylation products being 82:13. A reverse selectivity was observed with sodium hydride as base—the alkylation product derived from dimethyl methylmalonate predominated to the extent of 85:15. We attribute the rate difference in the BSA experiment to the higher kinetic acidity of dimethyl malonate compared to dimethyl methylmalonate, whereas in the sodium hydride experiment where the anions are fully generated, the higher reactivity of the anion of dimethyl methylmalonate leads to its preferential reaction. It has been previously noted in enolate alkylations that the more substituted enolate is kinetically more reactive in alkylations.[35]

This explanation nicely accommodates the differential reactivity of the dimethyl malonate and dimethyl alkylmalonate with some allylic acetates such as **8** (eq 5 and 6). With the former nucleophile, the excellent recovery of starting allylic acetate indicates the initial ionization is inhibited. If formation of a modified molybdenum complex such as **44** or **45** occurs, its lower electrophilicity should diminish its ability to coordinate with a sterically more congested electron-rich double bond. Consequently, with a substrate such as **8**, it is incapable of initiating the ionization of the allyl acetate. The latter nucleophile, which apparently fails to react with $Mo(CO)_6$, proceeds normally. That dimethyl malonate indeed serves as a catalyst modifier is demonstrated by addition of this nucleophile to a reaction of dimethyl methylmalonate with **8**. Under these conditions, all reactions cease.

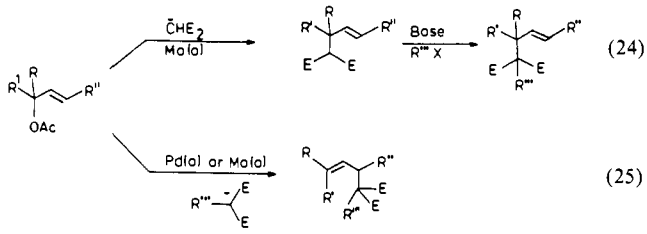
We must yet define the nature of the catalytically active species. Spectroscopic analysis of the reaction mixtures has so far been unrevealing. Attempts to examine molybdenum by NMR spectroscopy failed due to loss of all signals—perhaps the result of the generation of a paramagnetic species. An alternative approach to generate the presumed intermediate **47**, which would be neutral



47 48 49

if X is an anionic ligand but positively charged if X is a neutral ligand, has also not succeeded.[36] At present, only circumstantial evidence supports structures like **48** for non-malonate reactions. Thus, analogues of **48** containing solvent in place of carbon monoxide can be isolated in reactions with allylic acetates[37] or trifluoroacetates.[38] Furthermore, complexes like **47** serve as catalysts, albeit somewhat poorer than $Mo(CO)_6$, and the related stoichiometrically generated complex **49** does react with these nucleophiles. While much more work is obviously required to elucidate the exact nature of the catalysts, at present the results clearly indicate that there are more than one molybdenum catalyst and that both BSA and methyl malonate modify $Mo(CO)_6$.

Synthetically, the molybdenum catalyst complements the palladium-catalyzed reaction. It provides better chemoselectivity in that vinyl and allylsilyl substrates react without accompanying desilylation. Excellent stereocontrol exists. Cyclic allylic carboxylates react with complete stereospecificity, i.e., with complete net retention of configuration, but acyclic allylic carboxylates react with high stereoselectivity; i.e., both diastereomers of starting material produce mainly one diastereomeric product. The generality of this latter observation, however, remains yet to be established. Palladium catalysts in acyclic systems have afforded both high retention of configuration and stereoconvergence. The startling difference is clearly the regioselectivity. Molybdenum catalysts now permit chemo-, regio-, and diastereoselective introduction of nucleophiles at the more hindered terminus of an allyl unit. While such regioselectivity is limited to malonate anions and some β-keto esters, the ability to subsequently alkylate the initial product permits expansion of the application of this process (see eq 24). Either regioisomer is now available since direct alkylation with Pd(0) templates or Mo(0) templates and alkylmalonates gives rise to attack at the less substituted terminus (see eq 25). Of special interest is the ease with which quaternary centers are created with stereocontrol.[39]



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There are some drawbacks to Mo(0) reactions vs. Pd(0) reactions. Lewis basic sites poison the Mo(0) reactions such that

(33) Dunne, T. G.; Cotton, F. A. *Inorg. Chem.* **1963**, *2*, 2633. Darensbourg, M. Y.; Conder, H. L.; Darensbourg, D. J.; Hasday, C. *J. Am. Chem. Soc.* **1973**, *95*, 5919. For pioneering work in this general field, see: Fischer, E. O.; Kiener, V. *J. Organomet. Chem.* **1970**, *23*, 215.

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ethereal solvents are not satisfactory. Toluene has been preferred, but solubility problems can slow reactions. The turnover numbers for molybdenum appear lower than for palladium—a fact that is negated, in part, by the much lower cost of molybdenum. On the other hand, the air stability of the molybdenum catalyst greatly facilitates its handling compared to the air-sensitive palladium catalysts.

Tungsten,[40] nickel,[41] and rhodium[42] catalysts have been recently introduced for allylic alkylations. Of these, only tungsten has shown regioselectivity comparable or better to that of molybdenum. However, its generality and general utility have not yet been established. A rhodium catalyst appears to initiate mainly direct displacement although the regioselectivity is not high. A non-catalyzed reaction involving Claisen rearrangement has provided a regioselective route to substituted malonates.[43] Such a method which always proceeds with allyl inversion does not permit the same substrate to be diverted to either product just by changing reaction conditions. While much remains to be learned, each of these methods will undoubtedly have a role to play in complex synthesis. At the forefront for future efforts will undoubtedly be the quest for enantioselectivity.

Experimental Section

General. Unless otherwise noted all reactions were run under a positive pressure of dry nitrogen in flasks which were flame dried and allowed to cool under a stream of nitrogen. ^{1}H NMR spectra were recorded in $CDCl_3$ or C_6D_6 which was dried over 4-Å molecular sieves. As noted within each procedure they were recorded on a IBM WP200 at 200 MHz or on a Bruker WH270 at 270 MHz with the chemical shifts reported in δ, parts per million (ppm) downfield from tetramethylsilane. Splitting patterns are designed as s, singlet; d, doublet; t, triplet, q, quartet; m, multiplet; and br, broad. Coupling constants are reported in hertz, Hz. ^{13}C NMR spectra were recorded in $CDCl_3$ at 50.19 MHz on a JEOL-CO-FX-200 spectrometer and are reported in ppm relative to the center line of a triplet at 77.0 ppm which is attributed to the solvent. Infrared spectra were recorded on a Beckmann Acculab 7 or a Perkin-Elmer 1420 as neat oils on sodium chloride plates or as deuteriochloroform solutions in 0.1-mm path length sodium chloride cells run against deuteriochloroform in the reference beam and are reported in cm^{-1}. Mass spectra were recorded on an AE1-MS902 or Kratos MS80 at 30- or 70-eV ionizing current. Melting points were obtained on a Thomas-Hoover apparatus in open capillary tubes and are uncorrected. Microanalyses were performed by Spang Microanalytical Laboratories, Eagle Harbor, MI, or Galbraith Microanalytical Laboratories, Knoxville, TN. Vapor-phase chromatography analyses were performed on a Varian Model 3700 with a flow rate of 30 mL/min measured at the initial temperature for those systems studied with a temperature program. Integrations were carried out on a Hewlett-Packard 3390A connected to the gas chromatograph.

For reactions requiring dry solvents, tetrahydrofuran (THF), 1,2-dimethoxyethane (DME), ethyl ether, toluene, and benzene were distilled from sodium and benzophenone. Pyridine, methylene chloride, acetonitrile, benzene-d_6 (C_6D_6), and dimethylformamide (DMF) were distilled from calcium hydride. Sodium hydride was employed as a 60% dispersion in mineral oil, and weights are recorded for the dispersion. All palladium(0) catalysts were transferred to flame-dried vials in a glovebag, dissolved in freshly distilled THF, and transferred to the reaction mixture via syringe techniques.

Flash chromatography following the method of Still[44] employed Merck EM silica gel 60 (230–400 mesh) with the elution solvent described above giving a R_f of 0.25 for the fastest eluting compound.

Molybdenum hexacarbonyl, $Mo(CO)_6$, was used as received from Aldrich. All other reagents were distilled before use, and their purity was checked by 100-MHz NMR spectroscopy. Evaporation in vacuo refers to removal of solvent with a Buchi Brinkman rotary evaporator using a water aspirator.

Preparation of 3-Acetoxy-10-bromodec-1-ene (1). PCC[45] (7.0 g, 32 mmol) was added in one portion to a solution of 1-bromo-8-octanol[46] (3.14 g, 15 mmol) in methylene chloride (75 mL) at 0 °C. After 15 min at 0 °C and warming to room temperature, the reaction mixture was stirred for an additional 2 h. Ether (150 mL) was added to the suspension, and then the mixture was filtered through a Celite–silica gel pad. Evaporation under reduced pressure yielded a pale-green liquid which was used directly in the next reaction.

The crude bromoaldehyde in 20 mL of THF was added dropwise to a solution of vinylmagnesium bromide (60 mL of 0.5 M, 30 mmol) in THF (30 mL) at −78 °C. Fifteen minutes after addition was complete, acetic anhydride (3.4 g, 30 mmol) was added and the mixture warmed to room temperature. After stirring for 1 h, the mixture was concentrated to remove THF and then poured into ether–water. The organic layers were washed with water (1×) and aqueous sodium bicarbonate (1×) and then dried over magnesium sulfate. Evaporation of volatiles followed by flash chromatography (9:1 hexane:ether) yielded 2.2 g (57%) of allyl acetate **1**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.79 (1 H, ddd, J = 17, 11, 6 Hz), 5.26 (1 H, d, J = 17 Hz), 5.20 (1 H, d, J = 6 Hz), 5.17 (1 H, d, J = 11 Hz), 3.38 (2 H, t, J = 6 Hz), 2.08 (3 H, s), 1.85 (2 H, m), 1.60 (2, m), 1.35 (10 H, br); IR (neat) 1744 cm^{-1}. Anal. Calcd for $C_{12}H_{21}BrO_2$: C, 52.19; H, 7.30. Found: C, 52.25; H, 7.46.

Preparation of Methyl 10-Acetoxy-2-carbomethoxydodec-11-enoate (2). Dimethyl malonate (185 mg, 1.4 mmol) was added to a suspension of sodium hydride (50 mg, 1.25 mmol) in DMF (2 mL) at room temperature. A solution of bromoacetate **1** (280 mg, 1.0 mmol) in DMF (1 mL) was added to the above solution, and the resulting solution was stirred at room temperature for 18 h. The mixture was then heated at 50 °C for 3 h, cooled, and poured into a separatory funnel containing ether–water. After extraction of the organic phase with water (3×) and 10% aqueous sodium hydroxide, the ether was dried over magnesium sulfate. Evaporation of the volatiles in vacuo was followed by flash chromatography (ether:hexane 2:1) to provide **2** (200 mg, 61%) as a clear oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.78 (1 H, m), 5.20 (3 H, m), 3.73 (6 H, s), 3.35 (1 H, t, J = 7 Hz), 2.08 (3 H, s), 1.90 (H, br m), 1.60 (2 H, br s), 1.27 (10 H, m); ^{13}C NMR ($CDCl_3$) δ 169.7, 169.5, 136.5, 115.9, 74.4, 51.9, 33.9, 28.8, 28.5, 26.9, 24.6, 20.8; IR (neat) 1757, 1741 cm^{-1}; exact mass calcd for $C_{17}H_{28}O_6$ 328.1938, found 328.1887.

Preparation of Methyl 10-Bromo-3-ethenyl-2-carbomethoxydecanoate (3). Bromoallylic acetate **2** (280 mg, 1.0 mmol), dimethyl malonate (264 mg, 2.0 mmol), BSA (365 mg, 1.8 mmol), and $Mo(CO)_6$ (26 mg, 10 mol %) in toluene (3 mL) were combined and heated at reflux for 9 h following general procedure B.[4] After workup, bulb-to-bulb distillation (160 °C at 0.004 mmHg) afforded 250 mg (70%) of the bromo diester **3** as a clear oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.70 (1 H, dt, J = 17, 10 Hz), 5.08 (1 H, d, J = 17 Hz), 5.00 (1 H, dd, J = 10, 2 Hz), 3.48 (1 H, d, J = 9.0 Hz), 3.30 (6 H, s), 2.95 (2 H, t, J = 7 Hz), 1.50 (4 H, m), 1.10 (8 H, m); ^{13}C NMR ($CDCl_3$) δ 168.6, 168.4, 138.0, 117.2, 56.2, 52.0, 44.0, 33.7, 32.7, 32.1, 28.9, 28.5, 27.9, 26.7; IR (neat) 1750, 1740, 1643 cm^{-1}; exact mass calcd for $C_{11}H_{25}BrO_4$ 348.0929, found 238.0937.

Preparation of 2-Carbomethoxy-2-(10′-bromodec-2′-enyl)cyclopentanone (5). Following general procedure A,[4] bromoallylic acetate **1** (280 mg, 1.0 mmol), toluene (6 mL), 2-carbomethoxycyclopentanone (292 mg, 2.0 mmol), sodium hydride (72 mg, 1.8 mmol), and $Mo(CO)_6$ (26 mg, 1.0 mol %) were combined and heated at reflux for 6 h. After standard workup, the crude oil was bulb-to-bulb distilled (150 °C at 0.002 mmHg) to yield 250 mg (70%) of **5** as a clear oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.50 (1 H, m), 5.28 (1 H, m), 3.71 (3 H, s), 3.40 (2 H, t, J = 7 Hz), 2.63 (1 H, dd, J = 15, 7 Hz), 2.35 (5 H, m), 1.95 (2 H, m), 1.90 (2 H, m), 1.20 (10 H, m); ^{13}C NMR ($CDCl_3$) δ 213.9, 171.1, 135.0, 133.5, 123.2, 60.0, 59.8, 52.0, 37.8, 36.5, 33.5, 33.4, 32.1, 31.7, 28.9, 28.3, 27.8, 19.2; IR (neat) 1749, 1718 cm^{-1}. Anal. Calcd for $C_{20}H_{33}BrO_3$: C, 56.83; H, 7.57. Found: C, 56.89; H, 7.65.

Preparation of 20-(1′-Acetoxy-2′-propen-1′-yl)-3-oxopregn-4-ene (6). To a suspension of vinylmagnesium bromide (3.0 mL, 1.50 mmol) in THF at −100 °C (ether–liquid nitrogen bath) was added a solution of bisnorcholenaldehyde (250 mg, 0.76 mmol) in THF (2 mL) slowly over 5 min. After stirring for 15 min at −100 °C, the mixture was poured into saturated sodium carbonate. The combined organic layers were washed 2 times with water and then dried over magnesium sulfate. Evaporation of the solution under reduced pressure yielded a yellow oil which was flash chromatographed (40% ethyl acetate–hexane) to yield a white solid (121 mg, 45%): mp 174–175 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.85 (1 H, ddd, J = 18, 11, 7 Hz), 5.73 (1 H, s), 5.22 (1 H, d, J = 18 Hz), 5.15 (1 H, d, J = 11 Hz), 4.25 (1 H, br s), 2.35 (4 H, m), 2.35–0.9 (17 H, m), 1.15 (3 H, s), 0.88 (3 H, d, J = 7 Hz), 0.74 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 199.3, 171.3, 141.1, 123.6, 113.5, 55.7, 53.7, 52.3, 42.2, 40.9, 29.5, 38.5, 35.6, 33.8, 32.8, 31.9, 27.6, 24.1, 20.9, 17.3, 11.8; IR (neat) 3450, 1672, 1623 cm^{-1}; exact mass calcd for $C_{24}H_{36}O_2$ 356.2706, found 356.2714.

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To a solution of the alcohol prepared above (430 mg, 1.25 mmol) in methylene chloride (5 mL) was added pyridine (0.200 mL), followed by DMAP (20 mg). After the mixture cooled to 0 °C, acetyl chloride (0.470 mL) was added dropwise over 5 min. The white slurry was stirred for 4 h at 0 °C and then poured into ethyl acetate saturated aqueous sodium bicarbonate. The organic layer was washed once with saturated aqueous sodium hydrogen sulfate and once with saturated aqueous sodium bicarbonate and then dried over magnesium sulfate. Evaporation of solvent under reduced pressure followed by chromatography (1:1 hexane:ether) yielded 370 mg (77%) of the acetate as a white solid: mp 124.5–126.0 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.75 (1 H, m), 5.72 (1 H, s), 5.40 (1 H, bs), 5.15 (1 H, d, J = 9 Hz), 5.07 (1 H, d, J = 17 Hz), 2.35 (4 H, m), 0.85–2.10 (17 H, m), 2.08 (3 H, s), 1.20 (3, s), 0.95 (3 H, d, J = 7 Hz), 0.72 (3 H, s); IR (neat) 1742, 1682, 1625 cm^{-1}; exact mass calcd for $C_{26}H_{38}O_3$ 398.2811, found 398.2820.

Alkylation of 6 with Dimethyl Methylmalonate. Following the procedure outlined in general procedure A,[4] allylic acetate **6** (100 mg, 0.25 mmol), toluene (1.2 mL), sodium hydride (22 mg, 0.55 mmol), dimethyl methylmalonate (68 mg, 0.52 mmol), and $Mo(CO)_6$ (13 mg, 20 mol %) were combined and heated at reflux for 20 h. Standard workup followed by flash chromatography (1:1 hexane:ether) yielded 60 mg (50%) of a clear viscous oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.79 (1 H, s), 5.25 (2 H, m), 3.75 (4.2 H, s), 3.72 (0.9 H, s), 3.70 (0.9 H, s), 2.95 (0.5 H, d, J = 8 Hz), 2.58 (1.5 H, d, J = 7 Hz), 2.38 (4 H, m), 0.9–2.1 (17 H, m), 1.50 (3 H, s), 1.42 (3 H, s), 1.20 (3 H, s), 1.05 (0.9 H, d, J = 7 Hz), 0.78 (2.1 H, d, J = 7 Hz); IR (neat) 1739, 1669, 1621 cm^{-1}; mass spectrum, m/e (relative intensity) 427 (0.3), 357 (0.7), 341 (3.3), 253 (0.6), 213 (1.5), 175 (1.7), 161 (2.1), 153 (3.1), 145 (5.3), 123 (3.3), 107 (6.1), 95 (12.1), 86 (28.4), 83 (100), 67 (11.3), 47 (45.9).

Preparation of (*E*,*Z*)-Methyl 5-(Cyclohex-3′-en-1′-yl)-2,4-dimethyl-2-carbomethoxypent-4-enoate (9). Following general procedure A,[4] allylic acetate **8** (196 mg, 1.0 mmol), sodium hydride (72 mg, 1.8 mmol), and dimethyl methylmalonate (292 mg, 2.0 mmol) in toluene (3 mL) containing $Mo(CO)_6$ (72 mg, 27 mol %) were combined and heated at reflux for 36 h. After workup, flash chromatography (7:1 hexane:ether) yielded 297 mg (73.4%) of **9** as a clear oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.68 (2 H, s), 5.20 (0.2 H, d, J = 10 Hz), 5.10 (0.8 H, d, J = 10 Hz), 3.75 (1.2 H, s), 0.72 (4.8 H, s), 2.80 (0.4 H, s), 2.65 (1.6 H, s), 2.50 (1 H, m), 2.05 (4 H, m), 1.70 (2 H, m), 1.59 (3 H, d, J = 1.5 Hz), 1.38 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 172.5, 135.8, 128.6, 126.7, 125.9, 53.5, 52.6, 44.9, 32.6, 31.3, 28.5, 24.5, 19.8, 16.9; IR (neat) 1745, 1450 cm^{-1}; exact mass calcd for $C_{16}H_{24}O_4$ 280.1668, found 280.1675. Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63. Found: C, 68.68; H, 8.79.

Preparation of 11-Acetoxy-1,1-dimethoxy-12-tridecene. To a solution of 1,1-dimethoxyundec-10-ene (1.75 g, 8.00 mmol) in hexane (4 mL) at 0 °C was added BH_3·SMe_2 (0.290 mL, 2.9 mmol) over 3 min. The ice bath was removed and the mixture stirred for 1 h. Ethanol (4 mL) was added followed by an aqueous solution of sodium hydroxide (2 mL of 3 M solution). After the mixture cooled to 0 °C, hydrogen peroxide (2 mL of 30%) was added over 5 min. This mixture was refluxed for 1 h, and then the resulting suspension was poured into ether–ice water. The organic layer was washed with water and then dried over magnesium sulfate. Evaporation of solvent yielded 1.62 g (86%) of 1,1-dimethoxy-11-hydroxyundecane as a clear oil judged pure by NMR spectroscopy: ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.38 (1 H, t, J = 5 Hz), 3.62 (2 H, t, J = 6 Hz), 3.30 (6 H, s), 1.80 (1 H, br s), 1.55 (4 H, br s), 1.30 (14 H, s); ^{13}C NMR ($CDCl_3$) δ 104.5, 62.6, 52.4, 32.7, 32.3, 29.4, 25.5, 24.4; IR (neat) 3400, 1460, 1390 cm^{-1}; exact mass calcd for $C_{13}H_{28}O_3$ 232.2031, found 232.2038.

Sodium acetate (174 mg) followed by PCC[45] (1.4 g, 6.4 mmol) was added to a solution of the above alcohol (750 mg, 3.2 mmol) in methylene chloride (10 mL) at 0 °C. After stirring 10 min at 0 °C, the reaction mixture was warmed to room temperature and stirred for a further 45 min. Ether (23 mL) was added followed by filtration of the brown suspension through Celite–silica gel. Evaporation yielded a pale-yellow oil which was used directly in the next step: ^{1}H NMR (200 MHz, $CDCl_3$) δ 9.78 (1 H, s), 4.35 (1 H, t, J = 5 Hz), 3.30 (6 H, s), 2.42 (2 H, t, J = 8 Hz), 1.60 (4 H, br s), 1.30 (14 H, s); ^{13}C NMR ($CDCl_3$) δ 202.1, 104.4, 52.2, 43.5, 32.2, 29.1, 29.0, 28.9, 24.3, 21.8; IR (neat) 2755, 1730 cm^{-1}; exact mass calcd for $C_{13}C_{26}O_3$ 230.1875, found 230.1883.

The crude aldehyde prepared above (13.4 mmol) in THF (20 mL) was added to a solution of vinylmagnesium bromide (20 mL of 1.25 M, 25 mmol) at 0 °C. After 15 min at 0 °C, acetic anhydride (3 mL) was added and the mixture warmed to ambient temperature where it was allowed to stir a further hour. Evaporation of 50% of the THF yielded a yellow solution which was poured into saturated aqueous sodium bicarbonate–ether. The organic layer was washed with water, 10% aqueous potassium hydroxide, and saturated aqueous sodium bicarbonate and was then dried over magnesium sulfate. Evaporation of the solvent under reduced pressure yielded a pale-yellow oil which was purified by flash chromatography (10:1 hexane:ether) to yield a clear oil: 3.2 g (80%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.78 (1 H, m), 5.20 (1 H, d, J = 17.5 Hz), 5.18 (1 H, m), 5.12 (1 H, d, J = 10 Hz), 4.35 (1 H, t, J = 5 Hz), 3.30 (6 H, s), 2.08 (3 H, s), 1.60 (4 H, m), 1.30 (14 H, b); ^{13}C NMR ($CDCl_3$) δ 169.5, 136.5, 115.9, 104.2, 74.3, 52.0, 33.9, 32.2, 29.1, 24.7, 24.2, 20.6; IR (neat) 1747, 1650 cm^{-1}. Anal. Calcd for $C_{17}H_{32}O_4$: C, 67.96; H, 10.73. Found: C, 67.94; H, 10.74.

Preparation of 2-Carbomethoxy-2-(12′,12′-dimethoxydodec-2-enyl)cyclopentanone (10). Following general procedure A,[4] 11-acetoxy-1,1-dimethoxy-12-tridecene (286 mg, 1.0 mmol), 2-carbomethoxycyclopentanone (292 mg, 2.0 mmol), sodium hydride (72 mg, 1.8 mmol), $Mo(CO)_6$ (25 mg, 10 mol %), and toluene (4 mL) were combined and heated to reflux for 9 h. Workup followed by flash chromatography (3:1 hexane:ether) produced a clear oil: 264 mg (71.5%); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.50 (1 H, m), 5.28 (1 H, m), 4.38 (1 H, t, J = 7 Hz), 3.75 (3 H, s), 3.31 (6 H, s), 2.60 (1 H, dd, J = 15, 7 Hz), 2.35 (4 H, m), 1.97 (5 H, br s), 1.60 (2 H, br s), 1.28 (14 H, b); ^{13}C NMR ($CDCl_3$) δ 213.6, 170.9, 135.1, 133.5, 123.8, 123.1, 104.3, 59.9, 52.9, 52.1, 37.6, 36.4, 32.2, 31.6, 29.1, 28.7, 24.2, 19.1; IR (neat) 1759, 1740 cm^{-1}. Anal. Calcd for $C_{22}H_{38}O_5$: C, 69.08; H, 10.10. Found: C, 69.08; H, 9.95.

Preparation of 2-Carbomethoxy-2-(2′-(trimethylsilyl)methallyl)cyclopentanone (12). Following general procedure A,[4] 2-(trimethylsilyl)-methallyl acetate[12a] (90 mg, 0.5 mmol), 2-carbomethoxycyclopentanone (146 mg, 1.9 mmol), sodium hydride (36 mg, 0.9 mmol), and $Mo(CO)_6$ (12 mg, 8 mol %) in toluene (2 mL) were heated at reflux for 24 h. Further portions of $Mo(CO)_6$ (12 mg, 8 mol %) were added at 24 and 48 h by cooling the mixture to room temperature and then, after addition of the catalyst, returning it to a temperature to initiate reflux. Standard workup (avoiding an acid wash) and flash chromatography (4:1 hexane:ether) provided **12** as a clear oil: 70 mg (58%); ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.60 (1 H, s), 4.54 (1 H, s), 3.68 (3 H, s), 2.73 (1 H, d, J = 15 Hz), 2.4–2.6 (2 H, m), 2.30 (1 H, d, J = 15 Hz), 1.43 (2 H, s), –0.2 (9 H, s); IR (neat) 1755, 1729, 1641, 1632 cm^{-1}; exact mass calcd for $C_{14}H_{24}O_3Si$ 268.1511, found 268.1495.

Preparation of Methyl 3,5-Bis(trimethylsilyl)-2-carbomethoxy-2-methylpent-4(*E*)-enoate (15). A solution of dimethyl methylmalonate (120 mg, 0.82 mmol) and BSA (162 mg, 0.80 mmol) in toluene (1 mL) was heated at reflux for 40 min, and then 1,3-bis(trimethylsilyl)allyl acetate (**14**)[14] (80 mg, 0.33 mmol) was added followed by $Mo(CO)_6$ (27 mg, 25 mol %). This mixture was heated at reflux for 1 h, and then the crude mixture was diluted with hexane and the organic layer washed twice with water. After the organic layer was dried over sodium sulfate, the solvent was removed under reduced pressure and the crude oil flash chromatographed (8:2 hexane:ether) to yield 53 mg (49%) of **15** as a clear oil: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.80 (1 H, dd, J = 19, 9 Hz), 5.55 (1 H, d, J = 19 Hz), 3.82 (3 H, s), 3.75 (3 H, s), 2.41 (1 H, d, J = 9 Hz), 1.48 (3 H, s), 0.03 (9 H, s); IR (neat) 1740, 1605 cm^{-1}; exact mass calcd for $C_{15}H_{30}O_4Si_2$ 330.1674, found 330.1683.

Preparation of Methyl 2-Carbomethoxy-2-methyl-3(*E*)-(2′-methylcyclohexylidene)propanoate (17). Molybdenum Catalyst. Following general procedure A,[4] dimethyl methylmalonate (440 mg, 3.0 mmol), sodium hydride (112 mg, 2.8 mmol), *cis*-1-methyl-2-vinyl-2-acetoxycyclohexane[16] (**16**) (280 mg, 1.54 mmol), and $Mo(CO)_6$ (80 mg, 15 mol %) in toluene (8.0 mL) were combined and heated at reflux for 1.5 h. Standard workup and flash chromatography (10:1 hexane:ethyl acetate) provided a clear oil, 262 mg (65%). Capillary vapor-phase chromatography (5% SE-30, 12 m × 0.32 mm, 120 °C for 2 min, 10 deg/min to 180 °C) showed the ratio of the two peaks (T_1 = 6.2, T_2 = 6.8 min) to be 10:1. The major isomer (*E*) was assigned on the basis of the carbon shift of the methine carbon (38.7 ppm) by comparison with the *E* and *Z* isomers of 1-(2′-methylcyclohexylidene)propane (38.4 vs. 33.3 ppm). Below are reported the ^{1}H NMR spectral data for the major isomer: ^{1}H NMR (270 MHz, $CDCl_3$) δ 4.93 (1 H, t, J = 7.5 Hz), 3.72 (6 H, s), 2.65 (1 H, d, J = 7.5 Hz), 2.45 (1 H, m), 2.11 (1 H, m), 1.85–1.00 (7 H, m), 1.41 (3 H, s), 1.00 (3 H, d, J = 6.4 Hz); ^{13}C NMR ($CDCl_3$) δ 172.6, 147.6, 112.2, 53.5, 52.3, 38.7, 36.5, 33.2, 27.9, 25.1, 19.7, 13.6; IR (neat) 1740, 1465 cm^{-1}; exact mass calcd for $C_{15}H_{24}O_4$ 268.1675, found 268.1677.

Palladium Catalyst. Dimethyl methylmalonate (59 mg, 0.41 mmol) was added dropwise to a suspension of sodium hydride (15 mg, 0.38 mmol) in THF (0.300 mL). Tetrakis(triphenylphosphine)palladium(0) (8 mg, 2 mol %) in THF (0.300 mL), triphenylphosphine (2 mg, 2 mol %), and *cis*-2-acetoxy-1-methyl-2-vinylcyclohexane[16] (**16**) (50 mg, 0.27 mmol) were added to the above mixture. The reaction mixture was heated at reflux for 5.5 h. The crude reaction mixture was added to a flash chromatography column, and the title compound eluted (10:1 hexane:ethyl acetate) as a clear oil, 36 mg (72%). Capillary GC analysis as in the molybdenum-catalyzed alkylation provided a ratio of *E* to *Z* isomers of 17:1.

Preparation of 1-Acetoxy-1-(1′(*E*)-heptenyl)cyclohexane (20). A solution of alcohol **19** (388 mg, 2.0 mmol) in ether (2 mL) was added to a mixture of sodium bis(methoxyethoxy)aluminum dihydride (Red-Al, 0.940 mL, 3.2 mmol) in ether at 0 °C. The reaction mixture was warmed to room temperature and then heated at reflux for 16 h, followed by being cooled and quenched with 1 N sulfuric acid (2 mL). Dilution with ether was followed by washing the organic phase twice with water and once with saturated aqueous sodium chloride followed by drying over magnesium sulfate. Evaporation of solvent under reduced pressure followed by flash chromatography (3:1 hexane:ether) yielded the allyl alcohol as a clear oil: 267 mg, 70%; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.62 (1 H, dt, J = 16, 7 Hz), 5.53 (1 H, d, J = 16 Hz), 2.02 (2 H, m), 1.58 (10 H, m), 1.32 (9 H, m), 0.89 (3 H, t, J = 7 Hz); IR (neat) 3380 cm^{-1}; exact mass calcd for $C_{13}H_{24}O$ 196.1831, found 196.1828.

Pyridine (0.700 mL, 6.3 mmol) and DMAP (12 mg, 0.1 mmol) were added dropwise, and after the mixture was warmed to room temperature, stirring was continued for 16 h. A further aliquot each of acetic anhydride (0.120 mL) and DMAP (10 mg) was added, and the reaction mixture was stirred for 24 h. The crude reaction mixture was poured into ether, and the organic phase was washed twice with 10% aqueous hydrochloric acid, once with water, and once with saturated aqueous sodium chloride. After this phase was dried over magnesium sulfate and the solvent evaporated, flash chromatography yielded a clear oil: 46 mg, 50.5%, ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.75 (1 H, d, J = 16 Hz), 5.60 (1 H, dt, J = 16, 6.4 Hz), 2.15 (2 H, m), 2.05 (2 H, m), 2.00 (3 H, s), 1.55 (9 H, m), 1.25 (9 H, m), 0.90 (3 H, t, J = 6.4 Hz); ^{13}C NMR ($CDCl_3$) δ 169.5, 133.4, 130.4, 81.7, 35.4, 32.3, 31.3, 28.8, 25.4, 22.4, 22.1, 13.9; IR (neat) 1739 cm^{-1}; exact mass calcd for $C_{15}H_{26}O_2$ 238.1926, found 238.1933.

Preparation of 1-Acetoxy-1-(1′(*Z*)-heptenyl)cyclohexane (21). Dicyclopentadienyltitanium dichloride (25 mg, 0.1 mmol) was added to a 0 °C solution of *sec*-butylmagnesium bromide (1.25 mL, 2.5 mmol) in 1.25 mL of ether. The color of the mixture turned from red to green. After the mixture stirred for 5 min, the alkynyl alcohol **19** (196 mg, 1.0 mmol) was added dropwise, and the reaction mixture was allowed to stir for 30 min at 0 °C and then for 2.5 h at room temperature. The reaction was quenched by careful addition of water (1 mL) and then 10% aqueous hydrochloric acid (5 mL). This mixture was poured into a separatory funnel containing ether–10% aqueous hydrochloric acid. The organic phase was washed sequentially with saturated aqueous sodium bicarbonate and saturated aqueous sodium chloride and then dried over magnesium sulfate. After evaporation of the solvent in vacuo, the resultant oil was purified by flash chromatography (2:1 hexane:ether) to yield the known compound[47] as a clear oil: 91 mg, 46%; ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.46 (1 H, d, J = 10 Hz), 5.35 (1 H, dt, J = 10, 6.5 Hz), 2.35 (2 H, m), 1.70 (11 H, m), 1.50–1.20 (5, m), 0.92 (3 H, m); IR (neat) 3400, 2938, 2862, 1469, 1271, 981 cm^{-1}.

DMAP (93 mg, 0.76 mmol) and pyridine (0.600 mL, 7.4 mmol) were added to a solution of the above allylic alcohol (150 mg, 0.76 mmol) in methylene chloride (4 mL) at 0 °C. Acetyl chloride (596 mg, 7.6 mmol) was added dropwise over 5 min, the mixture was warmed to room temperature, and the slurry was stirred for a total of 20 h. Workup of the reaction consisted of pouring the slurry into ether-saturated sodium bicarbonate and washing the organic layer 2 times with saturated aqueous sodium bicarbonate, 3 times with saturated aqueous copper sulfate, and once with saturated aqueous sodium chloride. Following drying of the organic phase with magnesium sulfate and evaporation of the solvent under reduced pressure, the yellow oil was purified by flash chromatography (20:1 hexane:ether) to yield a clear oil: 148 mg, 83%; ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.55 (1 H, d, J = 10 Hz), 5.38 (1 H, d, t, J = 10, 6.4 Hz), 2.10 (4 H, m), 2.05 (3 H, s), 1.72 (2 H, m), 1.50 (6 H, m), 1.32 (9 H, br s), 0.90 (3 H, t, J = 7 Hz); IR (neat) 1741, 1655 cm^{-1}; exact mass calcd for $C_{15}H_{26}O_2$ 238.1926, found 238.1921.

$Mo(CO)_6$-Catalyzed Alkylation of 20 with Dimethyl Malonate. A solution of dimethyl malonate (0.070 mL, 0.60 mmol) and BSA (0.150 mL, 0.60 mmol) in toluene (0.750 mL) was heated at 100 °C for 1 h. After the mixture cooled to 0 °C acetate **20** (90 mg, 0.38 mmol) and $Mo(CO)_6$ (20 mg, 20 mol %) were added, and the mixture was heated at reflux for 2.5 h. The crude reaction mixture was added to a flash chromatography column and eluted (5:1 hexane:ether) a clear oil, 87 mg, 74%. Integration of signals in the ^{1}H NMR spectrum at 5.71 and 4.92 ppm provides a ratio of 4.9:1 for **22** vs. **23**: ^{1}H NMR (270 MHz, C_6D_6) δ 5.73 (1 H, d, J = 15 Hz), 5.46 (1 H, dt, J = 15, 7 Hz), 3.57 (1 H, s), 3.31 (6 H, s), 2.05 (4 H, m), 1.78 (2 H, m), 1.50–1.10 (12 H, m), 0.89 (3 H, m); IR (neat) 1732 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 168.2, 133.3, 131.5, 61.7, 51.7, 41.6, 33.9, 32.8, 31.3, 29.2, 26.8, 22.5, 22.0, 13.9; exact mass calcd for $C_{18}H_{30}O_4$ 310.2136, found 310.2080.

$Mo(CO)_6$-Catalyzed Alkylation of 21 with Dimethyl Malonate. Dimethyl malonate (0.065 mL, 0.55 mmol) was added to a flask containing toluene (0.750 mL) and BSA (0.135 mL, 0.55 mmol), and the mixture was heated at reflux for 45 min. After the mixture cooled to room temperature, allylic acetate **21** (75 mg, 0.32 mmol) and $Mo(CO)_6$ (16 mg, 20 mol %) were added, and the mixture was heated at reflux for 1 h. Workup and purification consisted of addition of the crude reaction mixture to a flash chromatography column and elution (5:1 hexane:ether) to provide a clear oil (70 mg, 75%). Comparison of ^{1}H NMR spectra of the products from alkylation of the *E* allylic acetate **20** with dimethyl malonate showed them to be identical in all respects.

Alkylations of *cis*-3-Acetoxy-1-carbomethoxycyclohex-4-ene (24). Dimethyl Malonate with Sodium Hydride as Base. Following general procedure A,[4] allylic acetate **24** (100 mg, 0.5 mmol), dimethyl malonate (132 mg, 1.0 mmol), sodium hydride (32 mg, 0.8 mmol), and $Mo(CO)_6$ (30 mg, 20 mol %) in toluene (3 mL) were heated at reflux for 24 h. As thin-layer chromatography (TLC) indicated that starting material remained, a further portion of $Mo(CO)_6$ (30 mg, 20 mol %) was added, and the suspension was heated at reflux a further 24 h. Standard workup and chromatography (2:1 hexane:ether) provided 30 mg (30%) of recovered starting material and 75 mg (50%) of alkylated products as clear oils. ^{1}H NMR spectroscopic analysis of the alkylation products reveals a 1:1 cis:trans ratio of products by comparison with authentic samples.

With BSA as Base. Following general procedure B,[4] allylic acetate **24** (100 mg, 0.5 mmol), BSA (230 mg, 1.0 mmol), dimethyl malonate (132 mg, 1.0 mmol), and $Mo(CO)_6$ (30 mg, 20 mol %) in toluene (2 mL) were heated at reflux for 24 h. Standard workup and flash chromatography (2:1 hexane:ether) provides 220 mg (75%) of a clear oil identified by ^{1}H NMR spectroscopy (as above) to be a single stereoisomer (cis).

With Sodium Hydride and $Mo(CO)_4$bpy. Following general procedure A,[4] allylic acetate **24** (100 mg, 0.5 mmol), sodium hydride (32 mg, 0.8 mmol), dimethyl malonate (132 mg, 1.0 mmol), and Mobpy (72 mg, 20 mol %) in toluene (3 mL) were heated at reflux for 48 h. Standard workup and flash chromatography provided the alkylation products as a clear oil, 50 mg (36%). ^{1}H NMR analysis (as above) revealed an 85:15 mixture of cis and trans alkylation products.

2-Carbomethoxycyclopentanone with Sodium Hydride and $Mo(CO)_6$. Following general procedure A,[4] allylic acetate **24** (200 mg, 1.0 mmol), sodium hydride (64 mg, 1.6 mmol), 2-carbomethoxycyclopentanone (262 mg, 1.8 mmol), and $Mo(CO)_6$ (26 mg, 10 mol %) in toluene (4 mL) were combined and heated at reflux for 24 h. As TLC indicated starting material remained, the reaction mixture was cooled to room temperature, a second portion of $Mo(CO)_6$ (26 mg, 10 mol %) was added, and the mixture was heated at reflux for a further 24 h. Standard workup and flash chromatography (3:2 hexane:ether) provide 50 mg (25%) of recovered starting material as well as 120 mg (57%) of a clear oil judged by ^{1}H NMR and vapor-phase chromatography to be a mixture of four compounds, a mixture of the cis and trans alkylated cyclohexane derivatives each as a mixture of diastereomers.

Alkylation with BSA and $Mo(CO)_6$. Following general procedure B,[4] allylic acetate **24** (200 mg, 1.0 mmol), BSA (325 mg, 1.6 mmol), 2-carbomethoxycyclopentanone (262 mg, 1.8 mmol), and $Mo(CO)_6$ (26 mg, 10 mol %) in toluene (3 mL) were heated at reflux for 24 h. As TLC indicated that starting material remained, the reaction mixture was cooled to room temperature, a further portion of $Mo(CO)_6$ (26 mg, 10 mol %) was added, and the mixture was heated at reflux for a further 24 h. Standard workup and flash chromatography (3:2 hexane:ether) provide 25 mg (12.5%) of recovered starting material and a clear oil (105 mg, 50%) judged by ^{1}H and ^{13}C NMR spectroscopies to be a 6:1 ratio of diastereomers derived from the cis alkylation product.

Vapor-phase chromatography analysis provided a convenient means of determining the cis:trans ratio (5% SE-30 on Chrom W, 80/100 mesh, 7 ft × $^1/_8$ in., T = 180 °C): the two peaks observed from the alkylation with sodium hydride had retention times T_1 = 4.4, T_2 = 5.0 min. As was found for the cis and trans isomers derived from the alkylation with dimethyl malonate, the trans isomer eluted more rapidly than the cis isomer. The alkylation of **24** with BSA as base showed a single peak in the vapor-phase chromatography spectrum with retention time T = 5.0 min. ^{1}H NMR spectroscopy offered an opportunity to confirm the above-mentioned vapor-phase chromatography trend and also to identify the diastereomeric nature of the products. In particular, the cis isomers have a quartet at δ 1.37 with J = 12 Hz that is a doublet of triplets in the trans isomers. The ratio of diastereomers was measured by comparing the integration of a broad doublet at δ 5.47 vs. that of a broad doublet at δ 5.15 in the cis products. In the trans alkylation products, doublets at δ 5.54 and 5.24 were assigned as the diastereomeric cyclopentanones (ratio 1.5:1): ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.80 (1 H, m), 5.47 (1 H, d, J = 11 Hz), 3.75 (3 H, s), 3.68 (3 H, s), 3.20 (1 H, m), 1.80–2.80 (10 H, m), 1.37 (1 H, q, J = 12 Hz); IR (neat) 1751, 1747,

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1731 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 213.6, 175.4, 170.6, 127.7, 127.2, 52.5, 51.5, 39.8, 39.3, 38.8, 28.8, 28.0, 27.7, 26.7, 19.6; exact mass calcd for $C_{15}H_{20}O_5$ 280.1305, found 280.1309.

Dimethyl Methylmalonate with Sodium Hydride as Base. Dimethyl methylmalonate (0.146 g, 1.0 mmol) was added dropwise to a suspension of sodium hydride (0.0432 g, 0.9 mmol) (washed with 1 mL of hexane) in toluene (4 mL). The solution was warmed to 100 °C and stirred for 15 min. Then *cis*-3-acetoxy-1-carbomethoxycyclohex-4-ene (0.100 g, 0.5 mmol) and molybdenum hexacarbonyl (0.013 g, 0.05 mmol) were added, and the solution was heated at reflux for 24 h. As TLC indicated remaining starting material, a second portion of molybdenum hexacarbonyl (0.013 g, 0.05 mmol) was added, and reflux was continued another 12 h. The mixture was added to ether (30 mL) and washed with 10% aqueous potassium hydroxide solution (2 × 20 mL) and saturated aqueous sodium chloride solution (20 mL). The ether solution was dried ($MgSO_4$) and chromatographed (80:20 hexane:ethyl acetate) to yield 0.112 g (79%) of the product as a colorless oil. Gas chromatography (12 m × 0.32 mm, SE-30, 100–200 °C via 10 deg/min intervals) showed a 89:11 cis:trans ratio of alkylated products: IR ($CHCl_3$) 1730 cm^{-1}; ^{1}H NMR (270 MHz, $CDCl_3$) δ 5.85–5.75 (1 H, m), 5.57–5.48 (1 H, m), 3.73 (6 H, s), 3.69 (3 H, s), 3.20–3.10 (1 H, m), 2.73–2.58 (1 H, m), 2.36–2.10 (2 H, m), 1.97–1.88 (1 H, m), 1.43 (1 H, q, J = 12.3 Hz), 1.35 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.4, 171.5, 171.3, 127.3, 127.1, 56.6, 52.3 (2), 51.5, 40.3, 39.5, 27.6, 26.8, 16.0; exact mass calcd for $C_{14}H_{20}O_6$ 284.1260 found 284.1253.

Preparation of Dimethyl (4-*tert*-Butyl-1-vinylcyclohex-1-yl)malonate (33). Alkylation of Allylic Acetate 30 with Dimethyl Malonate. Following general procedure B,[4] allylic acetate **30** (330 mg, 1.47 mmol), dimethyl malonate (306 mg, 2.5 mmol), BSA (445 mg, 2.2 mmol), and $Mo(CO)_6$ (40 mg, 10 mol %) in toluene (4 mL) were heated at reflux for 1.75 h. Standard workup and bulb-to-bulb distillation (100 °C at 0.01 mmHg) provided a clear oil, 388 mg (89%). The product exhibited identical spectral characteristics with those derived from alkylation of allylic acetate **31** (see below). Furthermore, the ratio of stereoisomers was also identical as determined by integration of signals at δ 6.38 and 5.80 (i.e., 1:5).

Alkylation of Allylic Acetate 31 with Dimethyl Malonate. Following general procedure B,[4] allylic acetate **31** (330 mg, 1.47 mmol), dimethyl malonate (306 mg, 2.5 mmol), BSA (4.45 mg, 2.2 mmol), and $Mo(CO)_6$ (40 mg, 10 mol %) in toluene (4 mL) were heated at reflux for 2.5 h. Purification via bulb-to-bulb distillation (100 °C at 0.01 mmHg) provided a clear oil, 301 mg (69%). Integration of signals in the ^{1}H NMR spectrum at δ 6.38 and 5.80 provides the ratio of isomers (1:5): ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.38 (0.13 H, dd, J = 19, 11 Hz), 5.80 (0.87 H, dd, J = 18, 11 Hz), 5.28 (0.87 H, d, J = 11 Hz), 5.08 (0.87 H, d, J = 18 Hz), 3.92 (0.13 H, s), 3.70 (5.2 H, s), 3.32 (0.87 H, s), 2.10 (0.87 H, br d, 11 Hz), 1.8–1.0 (8 H, m), 0.89 (1.18 H, s), 0.80 (7.83 H, s); ^{13}C NMR ($CDCl_3$) δ 168.2, 167.6, 144.5 (minor), 141.6, 116.0, 112.5 (minor), 62.7, 51.5, 47.6, 41.9, 33.5, 32.0, 27.2, 22.8; IR (neat) 1755, 1735, 1635 cm^{-1}. Anal. Calcd for $C_{17}H_{28}O_4$: C, 68.89; H, 9.52. Found: C, 68.71; H, 9.40.

Alkylation of Allyl Acetate 31 with Di-*tert*-butyl Malonate. Following general procedure B,[4] allylic acetate **31** (228 mg, 1.0 mmol), toluene (3 mL), BSA (375 mg, 1.8 mmol), di-*tert*-butyl malonate (432 mg, 2.0 mmol), and $Mo(CO)_6$ (25 mg, 10 mol %) were heated at reflux for 1.5 h. Flash chromatography (10:1 hexane:ether) yielded 311 mg (81.4%) of a clear viscous oil. A 1:4 ratio of isomers was observed in the alkylation reaction, which was measured by integration of signals in the ^{1}H NMR spectrum at δ 6.40 and 5.82: ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.40 (0.2 H, dd, J = 18, 12 Hz), 5.82 (0.8 H, dd, J = 18, 10 Hz), 5.25 (0.8 H, d, J = 10 Hz), 5.05 (0.8 H, d, J = 18 Hz), 3.64 (0.2 H, s), 3.08 (0.8 H, s), 2.10 (1.6 H, br d, J = 12 Hz), 1.6–1.0 (9 H, m), 1.45 (1.8 H, s), 0.86 (1.8 H, s), 0.82 (5.6 H, s); ^{13}C NMR ($CDCl_3$) δ 167.2, 166.8, 144.2 (minor), 141.5, 115.5 (minor), 112.0, 80.5, 77.1, 64.5, 47.7, 41.6, 33.4, 31.9, 27.7, 22.7; IR (neat) 1755, 1730, 1648 cm^{-1}. Anal. Calcd for $C_{23}H_{40}O_4$: C, 72.59; H, 10.59. Found: C, 72.77; H, 10.68.

Preparation of 3β-Acetoxy-3α-ethenyl-5α-cholestane (34). To a solution of the allylic alcohol[21] derived from addition of vinylmagnesium bromide to cholestanone (1.33 mg, 3.22 mmol) in methylene chloride (15 mL) was added DMAP (65 mg, 0.53 mmol) and pyridine (550 mL, 6.8 mmol). The reaction mixture was cooled to 0 °C, and then acetyl chloride (1.2 mL, 16.9 mmol) was added dropwise. The reaction mixture was stirred for 1 h at 0 °C, warmed to room temperature, and stirred for 24 h. The crude reaction mixture was then poured into ether and washed with saturated aqueous sodium bicarbonate. After the mixture was dried over magnesium sulfate, the solvent was removed under reduced pressure to yield a solid which was recrystallized from acetone: 1.1 g, 71%; mp 75.5–77.0 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.10 (1 H, dd, J = 17, 11 Hz), 5.12 (1 H, d, J = 17 Hz), 5.06 (1 H, d, J = 11 Hz), 2.20 (1 H, d, J = 15 Hz), 1.02 (3 H, s), 1.00–2.00 (29 H, m), 0.91 (3 H, d, J = 7 Hz), 0.88 (6 H, d, J = 6 Hz), 0.81 (3 H, s), 0.68 (3 H, s); IR ($CDCl_3$) 1738, 1550 cm^{-1}; exact mass calcd for $C_{31}H_{52}O_2$ 456.3959, found 456.3969.

Preparation of 3β-Ethenyl-3α-(bis(carbomethoxy)methyl)-5α-cholestane (35). Following general procedure B,[4] allylic acetate **34** (228 mg, 0.5 mmol), toluene (1 mL), BSA (190 mg, 0.95 mmol), dimethyl malonate (132 mg, 1.0 mmol), and $Mo(CO)_6$ (13 mg, 10 mol %) were combined and heated at reflux for 3 h. Standard workup procedures followed by flash chromatography (5:1 hexane:ether) afforded 183 mg (69%) of a clear viscous oil which slowly solidified to a waxy solid. The ratio of stereoisomers was determined by measuring the signals in the ^{1}H NMR spectrum at δ 6.32 and 5.80 (ratio found = 1:4): ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.32 (0.20 H, dd, J = 17, 11 Hz), 5.80 (0.80 H, dd, J = 18, 11.5 Hz), 5.25 (1 H, d, J = 11.5 Hz), 5.05 (1 H, d, J = 18 Hz), 3.70 (6 H, s), 3.34 (91 H, s), 1.00–1.80 (3 H, m), 0.89 (3 H, s), 0.84 (6 H, d), 0.80 (3 H, s), 0.68 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 167.9, 142.1, 115.8, 62.8, 56.5, 56.3, 54.3, 51.8, 42.6, 41.7, 39.9, 39.5, 36.2, 35.9, 35.8, 35.5, 34.4, 31.9, 28.7, 28.2, 27.9, 24.1, 23.9, 22.7, 22.5, 20.9, 18.7, 12.9; IR (neat) 1762, 1742 cm^{-1}; exact mass calcd for $C_{34}H_{56}O_4$ 628.4164, found 528.4176.

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Chemistry of Singlet Oxygen. 49. Photooxidation of Thiiranes

Frank Jensen and Christopher S. Foote*

Contribution from the Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90024. *Received September 26, 1986*

Abstract: The reaction between thiiranes and singlet oxygen has been investigated. Diphenylthiirane is unreactive, but simple alkyl thiiranes react readily, even at low temperature. The products depend on solvent and substrate concentration. In nonnucleophilic solvents, the primary product is the thiirane oxide. In methanol, the primary products are sulfinic esters at low substrate concentration and thiirane oxide at high concentration. It is suggested that the reaction proceeds via an intermediate, for which we assign a peroxythiirane oxide structure. The structures of potential intermediates have been calculated at the ab initio level using a 3-21 G(*) basis set. The reaction mechanism is discussed on the basis of Frontier Molecular Orbital theory and ab initio calculations.

The reaction between organic sulfur compounds and singlet oxygen continues to yield intriguing results.[1-6] The reactions of simple organic sulfides have been extensively studied by Foote et al.[2,5b,6b,14a,b] Recently Ando et al.[3] have reported an interesting

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