Lewis Acid Catalyzed Reactions of Acetylenic Esters with Alkenes. Stereochemistry and Regiochemistry

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The Lewis acid catalyzed reaction of methyl chloropropiolate or dimethyl acetylenedicarboxylate with alkenes leads to ene reactions and/or stereospecific [2 + 2] cycloaddition. Ethylaluminum dichloride was found to be a very effective catalyst since it is a strong Lewis acid and an HCl scavenger. With trisubstituted alkenes the ene reaction is regiospecific. A hydrogen is transferred from the alkyl group trans to the alkenyl hydrogen. The regio- and stereoselectivity of the ene reactions of methyl chloropropiolate, methyl propiolate, and dimethyl acetylenedicarboxylate are described. From cyclohexenes, pseudoaxial hydrogens are transferred exclusively. The relative reactivity of alkenes was found to be 1,1-disubstituted > trisubstituted ≫ monosubstituted and 1,2-disubstituted. The ene adducts and cyclobutenecarboxylates derived from methyl chloropropiolate undergo substitution reactions with organocuprates and can be hydrolyzed to β-keto esters and substituted dimethyl glutarates, respectively.

We have found that methyl propiolate (1) undergoes Lewis acid catalyzed reactions with alkenes.[2] With alkenes containing at least one disubstitued carbon, ene adducts are the exclusive product (Figure 1, X = H). With 1,2-disubstituted alkenes, stereospecific [2 + 2] cycloaddition, leading to cyclobutenecarboxylates, is the exclusive reaction mode (Figure 2, X = H). Monosubstituted alkenes give mixtures of ene adducts and both possible cyclobutenes. This Lewis acid catalyzed reaction can be used with alkenes containing a wide variety of functional groups, including ester, ether, nitrile, nitro, and trifluoroacetamide groups. These results contrast with the thermal reactions of methyl propiolate with alkenes which proceed in low yield at 200–300 °C and give only ene adducts as mixtures of regioisomers.[3]

Our original studies used aluminum chloride as the catalyst.[2b] More recently we have found that ethylaluminum dichloride ($EtAlCl_2$), used as a solution in heptane, is a more efficacious catalyst.[2a] Although $EtAlCl_2$ is a strong Lewis acid, it can act as a proton scavenger, reacting with hydrogen chloride to give ethane and aluminum chloride. The use of $EtAlCl_2$ as catalyst minimizes the isomerization of acid-senstive alkenes and the deleterious effects of traces of water.

Since the α,β-unsaturated esters resulting from the reaction are much more basic than methyl propiolate, opitmal yields are usually obtained with close to 1 equiv of catalyst (plus an additional equivalent for each basic functional group in the alkene.) More than 1 equiv of catalyst often leads to extensive decomposition.

The extension of this reaction to methyl chloropropiolate (Figures 1 and 2, X = Cl) reported here provides a stereospecific route to methyl (*Z*)-3-chloro-2,5-alkadienoates and an efficient route to methyl 2-chlorocyclobutenecarboxylates which are versatile synthetic intermediates.[2c] Since our earlier work,[2b] McCulloch and McInnes have extended these reactions to dimethyl acetylenedicarboxylate.[4] (Figures 1 and 2, X = CO_2Me). In this paper we present our results describing the selectivity, regiochemistry, and stereochemistry of the reactions of methyl propiolate, methyl chloropropiolate, and dimethyl acetylenedicarboxylate and the differences between the reactions of these three acetylenic esters.

Results and Discussion

Methyl Chloropropiolate. Addition of methyl chloroformate to lithium chloroacetylide[5] gives a 65% yield of methyl chloropropiolate (2). Methyl bromopropiolate is prepared by the procedure of Chodkiewicz by treatment of methyl propiolate with sodium hypobromite.[6]

Methyl chloropropiolate–Lewis acid complexes, which are somewhat more reactive than the corresponding propiolate complexes, give good yields of ene adducts and cyclobutenes with a variety of alkenes (see Table I). Optimal conditions are 0.9 equiv of $EtAlCl_2$ in CH_2Cl_2. The yields of reactions not run under these conditions can usually be improved significantly. Monosubstituted and 1,2-disubstituted alkenes give exclusively 2-chloro-1-cyclobutenecarboxylates resulting from stereospecific cis [2 + 2] cycloaddition (runs 1, 2, 4, and 6). More highly substituted alkenes give mixtures of ene adducts and cyclobutenes (runs 8, 9, 10, and 11).

The most significant effect of the chlorine is observed in the reactions of 2,3-dimethyl-2-butene which gives exclusively ene adduct with methyl propiolate (1)[2] and greater than 95% cyclobutene 17 with methyl chloropropiolate (2) (run 12). The effect of the chlorine is easily understood by examining the transition states of the two competing concerted reactions—an ene reaction[3] and a [$_\pi 2_s$ + $_\pi 2_a$] cycloaddition.[7] An examination of the transition state required for an ene reaction (Figure 1) indicates that for R = CH_3 and X = Cl severe steric hindrance retards the reaction. For methyl propiolate (X = H), the steric hindrance is apparently not severe.

Runs 16 and 19 with (*E*)- and (*Z*)-3-methyl-2-pentene, were carried out to test this hypothesis. If the mechanism shown in Figure 1 is correct, the hydrogen on the carbon trans to the alkenyl hydrogen should be transfered preferentially in ene reactions of 2. The major ene adduct in both runs (90% in run 16, and 77% in run 19) is the one obtained via the less hindered transition state (Figure 1, R = H, R′ = CH_3). With aluminum chloride as catalyst, the starting alkene is slowly isomerized. No alkene isomerization occurs with $EtAlCl_2$, but the same isomer mixture is obtained. Reaction of 2 with the 3-methyl-3-hexenes

(1) Fellow of the Alfred P. Sloan Foundation, 1979–1981.
(2) (a) Snider, B. B.; Rodini, D. J.; Conn, R. S. E.; Sealfon, S. *J. Am. Chem. Soc.* **1979**, *101*, 5283. (b) Snider, B. B. *J. Org. Chem.* **1976**, *41*, 3061. (c) Some of these results were published in preliminary form: Snider, B. B.; Roush, D. M. *J. Am. Chem. Soc.* **1979**, *101*, 1906.
(3) Hoffman, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 556. Alder, K.; von Brachel, H. *Justus Liebigs Ann. Chem.* **1962**, *651*. 141.
(4) McCulloch, A. W.; McInnes, A. G. *Tetrahedron Lett.* **1979**, 1963.
(5) Viehe, H. G. *Chem. Ber.* **1959**, *92*, 1950.
(6) Chodkiewicz, W. *Ann. Chim. (Paris)* **1957**, [13] 2, 819.
(7) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781. It has been proposed that Woodward–Hoffmann rules need not apply to polar [2 + 2] cycloadditions: Epiotis, N. D. "Theory of Organic Reactions"; Springer-Verlag: West Berlin and Heidelberg, 1978.

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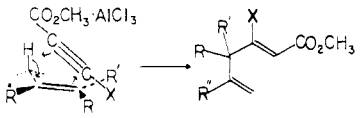


Figure 1. Transition state for concerted ene reaction.

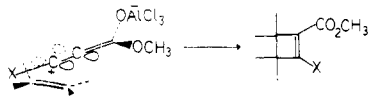


Figure 2. Possible transition state for $[_\pi2_s + _\pi2_a]$ cycloaddition with the vinyl cation resonance structure of the ester–Lewis acid complex.

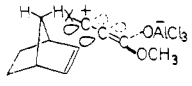


Figure 3. Possible transition state for $[_\pi2_s + _\pi2_a]$ cycloaddition of norbornene and acetylenic esters.

(Figure 1, R = H, R′ = Et) gives identical selectivity for the hydrogen on the carbon trans to the alkene hydrogen. As predicted, 1:1 mixtures of regioisomeric ene adducts are obtained from either 3-methyl-2-pentene or **1**.[2a] Similar interactions are responsible for the formation of primarily or exclusively the endocyclic ene adducts in runs 11, 22, and 26.

We believe that the cycloaddition reaction is a concerted $[_\pi2_s + _\pi2_a]$ cycloaddition.[7] Reaction of *trans*- or *cis*-2-butene with **2** (runs 2 and 4) is stereospecific. Propene gives two cyclobutenes (run 1). A polar two-step sequence for the formation of the minor isomer **4** from propene requires that a primary carbenium ion intermediate be formed almost as easily as a secondary carbenium ion. A $[_\pi2_s + _\pi2_a]$ cycloaddition is consistent with the formation of two isomers, since dichloroketene, which is believed to add to alkenes by a $[_\pi2_s + _\pi2_a]$ process,[7] gives mixtures of regioisomers with 1-methylcyclohexene.[8]

Norbornene cannot undergo an ene reaction and is hindered toward $[_\pi2_s + _\pi2_a]$ cycloaddition (Figure 3), as exemplified by its poor reaction with ketenes.[9] Since the norbornyl cation is very stable, norbornene reacts with acetylenic esters, at least partially, by a stepwise mechanism.[10] Methyl propiolate gives a product mixture which contains 70% of the cyclobutene corresponding to **19** and 30% of rearranged products corresponding to **20** and **21**.[2a] Methyl chloropropiolate (run 13), which gives rise to a more hindered transition state for a $[_\pi2_s + _\pi2_a]$ cycloaddition (Figure 3, X = Cl), gives a mixture containing only 5% of the cyclobutene **19** and 95% of **20** and **21**.[11] Similar hindrance of the transition state of a $[_\pi2_s + _\pi2_a]$ cycloaddition by the ring may be responsible for the smaller proportion of cyclobutene formed from **2** and 1-methylcyclohexene or 1,2-dimethylcyclohexene (runs 11 and 23) as compared to the acyclic analogues 2-methyl-2-butene or 2,3-dimethyl-2-butene (runs 10 and 12).

The reaction of **1** or **2** with 0.2 equiv of $AlCl_3$ and 2-methyl-2-butene was followed by NMR spectroscopy (see Figure 4). The rates of these reactions decrease too rapidly to fit the expected rate equation,[12] $d[\mathbf{1(2)}]/dt = -k$-

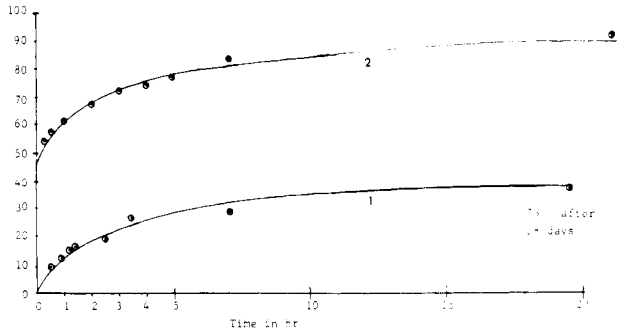


Figure 4. Rate of reaction of **1** and **2** with 2-methyl-2-butene and 0.2 equiv of $AlCl_3$ in benzene.

[**1(2)**][2-methyl-2-butene], unless catalyst is being consumed. This could occur by preferential complexation of the $AlCl_3$ to the product alkenyl ester if it is more basic than **1** or **2**. Since alkynyl groups are more electron withdrawing than alkenyl groups, alkynyl ester **1** or **2** should be less basic than the product ester.[13] For this reason best results are obtained with close to 1 equiv of catalyst.

A similar analysis explains the relative reactivity of **1** and **2**. Chlorine, an electron-withdrawing group,[14] makes **2** less basic than **1**, giving a **2**·$AlCl_3$ complex that is 3–4 times as reactive as the **1**·$AlCl_3$ complex.

Methyl bromopropiolate reacts analogously to **2** to give with 2-methyl-2-butene in the presence of $AlCl_3$ a mixture of ene adduct and cyclobutene. This may be of value in some cases due to the greater reactivity of the resulting β-bromo, α,β-unsaturated ester and the fact that preparation of methyl bromopropiolate does not involve an explosive intermediate.

Dimethyl Acetylenedicarboxylate. McCulloch and McInnes recently reported that aluminum chloride catalyzes the reaction of dimethyl acetylenedicarboxylate (DMAD) with alkenes.[4] We have briefly studied these reactions in an attempt to correlate their behavior with the reactions of **1** and **2**. Since the DMAD·$AlCl_3$ complex is insoluble in benzene, CH_2Cl_2 must be used as solvent. Under these conditions some rearrangement of double bonds occurs (runs 18 and 21). This can be avoided by the use of $EtAlCl_2$ as catalyst (runs 17 and 20). A key feature of DMAD reactions is the preference for the formation of ene adducts rather than cyclobutenes. Cyclobutenes (as mixtures with ene adducts) are formed only from monosubstituted and 1,2-disubstituted alkenes.

The ene reactions of DMAD with trisubstitued alkenes are even more regiospecific than those of **2**, since the carbomethoxy group is larger than chlorine (Figure 1, X = CO_2Me). The product resulting from hydrogen transfer from the carbon trans to the alkenyl hydrogen accounts for at least 95% of the ene adduct mixture. With 1-methyl-1-cyclohexenes, the endocyclic isomer is formed exclusively (runs 26 and 28). With $EtAlCl_2$ as catalyst, (*E*)-3-methyl-2-pentene gives exclusively **25b** (run 17), while the *Z* isomer gives ~95% of **26b** (run 20). Under McCulloch and McInnes' conditions, with aluminum chloride as catalyst, partial isomerization of starting material occurs, giving mixtures containing more of the minor isomers (runs 18, 21).

(8) Bak, D. A.; Brady, W. T. *J. Org. Chem.* **1979**, *44*, 107.
(9) Dichloroketene reacts poorly with norbornene: Ghosez, L.; Montaigne, R.; Roussel, A.; Vanlierde, H.; Mollet, P. *Tetrahedron* **1971**, *27*, 615.
(10) For a similar polar ene reaction in which norbornene is a special case, see: Hoffmann, H. M. R.; Tsushima, T. *J. Am. Chem. Soc.* **1977**, *99*, 6008.
(11) For similar uncatalyzed reactions of chloropropiolonitrile, see: Sasaki, T.; Eguchi, S.; Ogawa, T. *J. Am. Chem. Soc.* **1975**, *97*, 4413; Sasaki, T.; Eguchi, S.; Sugimoto, M.; Hibi, F. *J. Org. Chem.* **1972**, *37*, 2317.
(12) Aluminum chloride catalyzed Diels–Alder reactions of methyl acrylate are second order: Inukai, T.; Kojima, T. *J. Org. Chem.* **1967**, *32*, 872.
(13) Puchkova, V. V.; Gur'yanova, E. N.; Laba, V. I.; Prilezhaeva, E. N. *Bull Acad. Sci. USSR, Div. Chem. Sci. (Eng. Transl.)* **1973**, 1117.
(14) The σ_p^+ for Cl^- is 0.035: Swain, C. G.; Lupton, E. C. *J. Am. Chem. Soc.* **1968**, *90*, 4328.

Due to DMAD's propensity to undergo ene reactions, cis and trans 1,2-disubstituted alkenes react differently with DMAD.[15] DMAD·$EtAlCl_2$ reacts stereospecifically with *trans*-2-butene (run 3) to give exclusively cyclobutene **5b** and dimethyl (*Z,Z*)-2,4-hexadiene-3,4-dicarboxylate derived from conrotatory ring opening of **5b**. On the other hand, *cis*-2-butene or cyclohexene reacts with DMAD·$EtAlCl_2$ (runs 5 and 7) to give a mixture of ene adduct and cyclobutene. These differences are not surprising since with *trans*-2-butene the transition state of the ene reaction is sterically hindered [see Figure 1 (R = CH_3, R′ and R″ = H)].

Comparison of Acetylenic Esters. In addition to steric inhibition of the ene reaction (Figure 1) and steric inhibition of the cycloaddition reaction (Figure 3), electronic factors also control the competition between the ene and cycloaddition reactions. Apparently the ene reaction is more polar than the cycloaddition. The buildup of considerable positive charge on the central carbon of the alkene in the transition state explains the preference of alkenes which contain two substituents on one carbon to give primarily (or exclusively) ene adducts. The formation of some ene adduct from monosubstituted alkenes may be due to the steric accessibility of the terminal methylene.

Methyl chloropropiolate gives a higher percentage of cyclobutene and DMAD a lower percentage of cyclobutene than methyl propiolate. On the other hand, DMAD and methyl chloropropiolate are both more reactive than methyl propiolate. The reactivity order is explained by the fact that electron-withdrawing groups (Cl, CO_2Me) decrease the basicity of the ester carbonyl group, thereby increasing the reactivity of the Lewis acid complex. A [$_\pi2_s + {}_\pi2_a$] cycloaddition of the vinyl cation form of the acetylenic ester–Lewis acid complex (Figure 2) explains the varying percentage of cyclobutene formed. Chlorine, which stabilizes an adjacent positive charge by resonance, gives more cyclobutene, while a carbomethoxy group, which destabilizes an adjacent positive charge, gives less cyclobutene.

Stereo- and Regiochemistry. In order for these ene and cycloaddition reactions to be synthetically useful, the stereo and regiochemistry with unsymmetrical alkenes must be determined. 1,6-Dimethylcyclohexene (run 22) reacts with **2** to give a 35% yield of a 4:1 mixture of cyclobutenes **28** and **29** and a 54% yield of a 12:1 mixture of ene adducts **30** and **31**. The structure **29** is assigned to the minor isomer since the methyl group is expected to hinder the approach of **2** from the same side of the molecule. Formation of a small amount of exocyclic ene adduct **31** probably occurs because the endocyclic hydrogen is somewhat hindered. 5-Cholestene (run 30) reacts with **1** to give a single ene adduct, resulting from the expected axial approach with abstraction of an axial hydrogen.

1,3-Dimethylcyclohexene reacts with DMAD (run 28) to give an inseparable 3:2 mixture of **43** and **44**, which are easily distinguished by the NMR signal of the doubly allylic proton. In **43** the proton is shielded by the methyl group and therefore absorbs 0.4 ppm upfield of the analogous proton of **44**. Since abstraction of the pseudoaxial hydrogen is required (vide supra), **43** arises from the conformer with a pseudoaxial methyl group while **44** results from the conformer with a pseudoequatorial methyl group. Allinger's calculation indicates that the conformer leading to **44** is more stable by 0.84 kcal/mol.[16] Since the

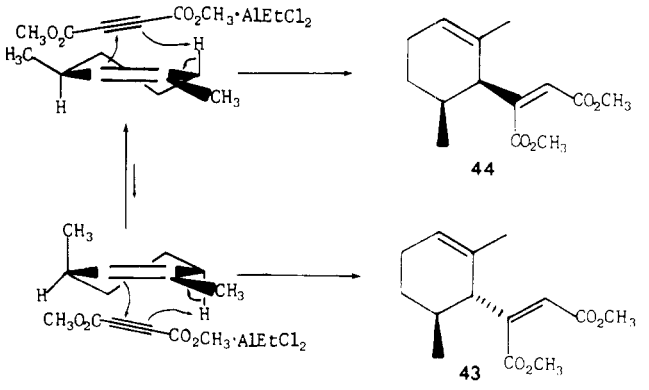


Figure 5. Transition states for the reaction of 1,3-dimethylcyclohexene with DMAD leading to **43** and **44**.

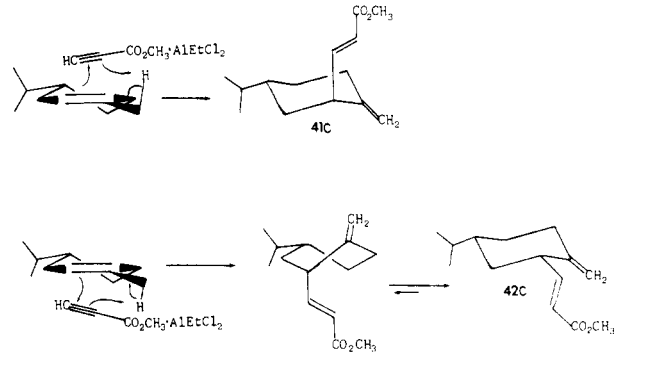


Figure 6. Transition states for the reaction of menthene with methyl propiolate leading to **41c** and **42c**.

major conformer with the pseudoequatorial methyl group leads to the minor isomer, the methyl group must hinder the approach of DMAD from the same side of the ring (see Figure 5).

Menthene was investigated with all three acetylenic esters. With **1** (run 27), menthene gives 32% of **41c**, 22% of **40c**, and 6% of **42c**. The 3:2 ratio of exocyclic/endocyclic adducts is consistent with earlier results with 1-methylcyclohexene.[2] Cyclohexene **40c** is formed exclusively by axial approach and abstraction of a pseudoaxial hydrogen. Both methylenecyclohexanes are formed. The major isomer, **41c**, is formed by approach from the side opposite the isopropyl group, initially giving a chair cyclohexane. The minor isomer, **42c**, is formed by approach from the same side as the isopropyl, leading to a cyclohexane in a twist-boat conformation (Figure 6). As with alkylation of cyclohexanones, the axial product which does not require a twist-boat conformation is favored. It should be noted that similar results are obtained from 3-methyl-2-cholestene and singlet oxygen.[17] With **2** (run 25), menthene gives a 16% yield of a 3:2 mixture of cyclobutenes and a 50% yield of a 95:5 mixture of **40a** and **41a**. The isopropyl group exerts a slight steric effect on the cycloaddition. With DMAD (run 26) menthene gives exclusively the expected ene adduct **40b** resulting from pseudoaxial hydrogen transfer from the sterically unhindered transition state (see Figure 1).

The [2 + 2] cycloaddition is stereospecifically cis in all cases. Trisubstituted alkenes (runs 10 and 11) or 1,1-disubstituted alkenes (runs 8 and 9) react with **2** to give only

(15) Photolysis of DMAD and 2-butene gives exclusively 2:1 adducts: Majeti, S.; Majeti, V. A.; Foote, C. S. *Tetrahedron Lett.* **1975**, 1177. Photolysis of DMAD and norbornene gives **19b**: Hara, M.; Odaira, Y.; Tsutsumi, S. *Tetrahedron* **1966**, *22*, 95.

(16) Allinger, N. L.; Hirsch, J. A.; Miller, M. A.; Tyminski, I. J. *J. Am. Chem. Soc.* **1968**, *90*, 5773.

(17) Nickon, A.; Chuang, V. T.; Daniels, P. J. L.; Denny, R. W.; DiGiorgio, J. B.; Tsunetsugu, J.; Vilhuber, H. G.; Werstiuk, E. *J. Am. Chem. Soc.* **1972**, *94*, 5517.

Table I. Lewis Acid Catalyzed Reactions of Alkenes with Acetylenic Esters

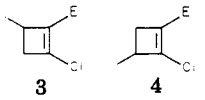
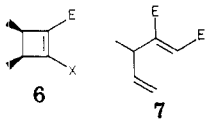
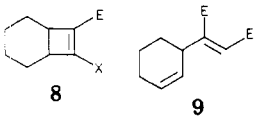
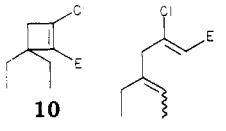
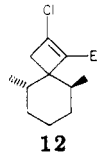
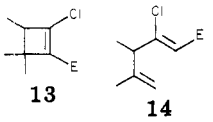
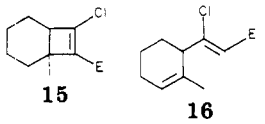
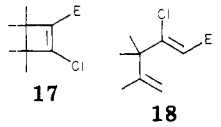
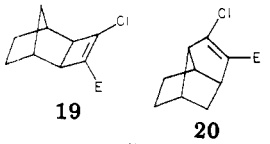
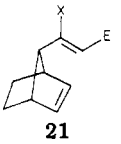
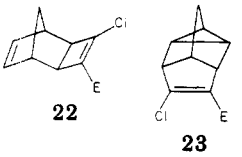
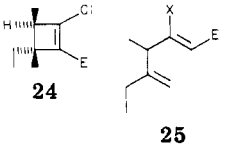
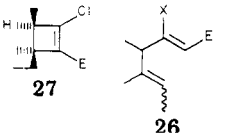
alkene	products (E = CO_2CH_3)	run	acetylenic ester (conditions,[a] mol % catalyst)	yield, % (product)[g]
	 3 4	1	2 (A, 32)	16 (3), 8 (4)
	 5	2 3	2 (A, 50) DMAD (B, 90)	64 (5a) 16[b] (5b)
	 6 7	4 5	2 (A, 50) DMAD (B, 90)	74 (6a) 10 (6b), 10 (7)
	 8 9	6 7	2 (A, 76) DMAD (B, 90)	51 (8a) 14 (8b), 38 (9)
	 10 11	8	2 (A, 50)	21 (10), 33 (11)
	 12	9	2 (A, 47)	52 (12)
	 13 14	10	2 (A, 45)	41 (13), 24 (14)
	 15 16	11	2 (A, 22)	18 (15), 58 (16)
	 17 18	12	2 (A, 42)	76 (17), 4 (18)
	 19 20  21	13 14	2 (A, 70) DMAD (B, 90)	3 (19), 8 (20), 72[c] (21a) 10[d] (21b)
	 22 23	15	2 (A, 40)	33 (22), 20 (23)
	 24 25	16 17 18	2 (A, 66) DMAD (B, 90) DMAD (C, 95)	47 (24), 28 (25a), 4 (26a) 78 (25b) 7 (25), 63 (26b)
	 27 26	19 20 21	2 (A, 66) DMAD (B, 90) DMAD (C, 95)	53 (27), 9 (25a), 29 (26a) 5 (25b), 74 (26b) 21 (25b), 49 (26b)

Table I (*Continued*)

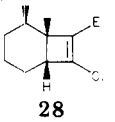
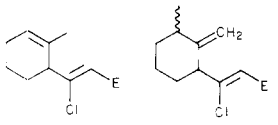
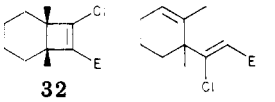
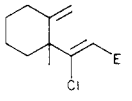
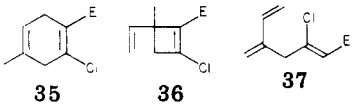
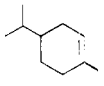
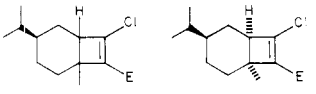
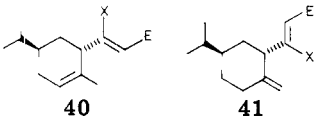
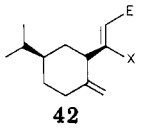
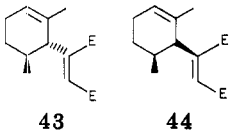
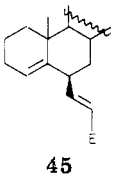
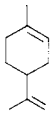
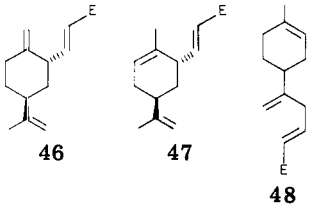
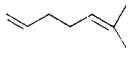
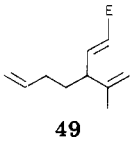
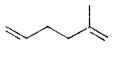
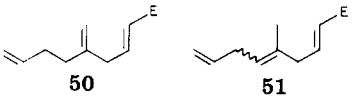
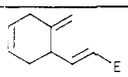
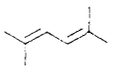
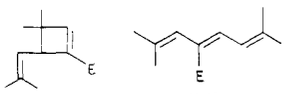
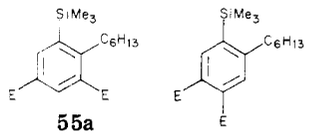
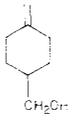
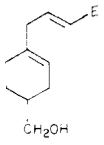
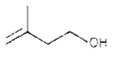
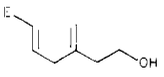
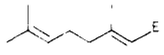
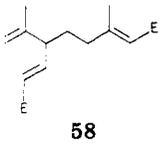
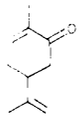
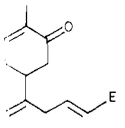
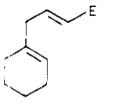
alkene	products (E = CO_2CH_3)	run	acetylenic ester (conditions,[a] mol % catalyst)	yield, % (product)[g]
	 **28** **29**  **31**	22	2 (B, 90)	28 (**28**), 7 (**29**), 50 (**30**), 4 (**31**)
	 **32** **33**  **34**	23	2 (B, 90)	45 (**32**), 28 (**33**), 8 (**34**)
	 **35** **36** **37**	24	2 (B, 90)	36 (**35**), 10 (**36**), 20 (**37**)
	 **38** **39**	25	2 (B, 90)	10 (**38**), 6 (**39**), 48 (**40a**), 3 (**41a**)
		26	DMAD (B, 90)	63 (**40b**)
	 **40** **41**  **42**	27	1 (B, 90)	22 (**40c**), 32 (**41c**), 6 (**42c**)
	 **43** **44**	28	DMAD (B, 90)	31 (**43**), 20 (**44**)
2-cholestene		29	1 (B, 90)	*e*
5-cholestene	 **45**	30	1 (B, 90)	17 (**45**)
	 **46** **47** **48**	31	1 (B, 90)	12 (**46**), 8 (**47**), 39 (**48**)
	 **49**	32	1 (B, 90)	75 (**49**)
	 **50** **51**	33	1 (B, 90)	30 (**50**), 25 (**51**)

Table I (*Continued*)

alkene	products (E = CO_2CH_3)	run	acetylenic ester (conditions,[a] mol % catalyst)	yield, % (product)[g]
	 **52** **53**	34	1 (B, 90)	66 (**52**), 13 (**53**)
	 **54a** **54b**	35	1 (B, 90)	45 (**54b**)
$C_6H_{13}C{\equiv}CSiMe_3$	 **55a** **55**	36	1 (B, 90)	7 (**55a**), 5 (**55b**)
	 **56**	37	1 (B, 200)	74 (**56**)
	 **57**	38	1 (B, 200)	37 (**57**)
	 **58**	39	1 (B, 200)	47 (**58**)
	 **59**	40	1 (B, 200)	22 (**59**)[f]
	 **60**	41	1 (A, 50, and 12% di-*tert*-butylpyridine)	65 (**60**)

[a] A = $AlCl_3$ in benzene, B = $EtAlCl_2$ in CH_2Cl_2, C = $AlCl_3$ in CH_2Cl_2. [b] Yield of an inseparable 7:3 mixture with the ring-opened diene. [c] Contains ca. 10% of an impurity which is probably the anti isomer. [d] Estimated from the crude reaction mixture. [e] Gives a complex mixture of ene adducts and cyclobutenes. [f] A 67% yield based on recovered carvone. [g] a, X = Cl; b, X = CO_2CH_3; c, X = H.

a single cyclobutene. Minor amounts of the other regioisomer may be formed but could not be detected. The regiochemistry of the cycloaddition was determined by hydrolysis of **13** (vide infra) to dimethyl 2,3,3-trimethylglutarate (**70a**). The regioisomer of **13** would have given dimethyl 2,2,3-trimethylglutarate, which is easily distinguished from **70a** by ^1H NMR spectroscopy. The orientation of **13** is expected since polarity considerations indicate that bond formation between C_3 of **2** and the less substituted carbon of the alkene should be favored. The regiochemistry of other unsymmetrical cyclobutenes is assigned by analogy.

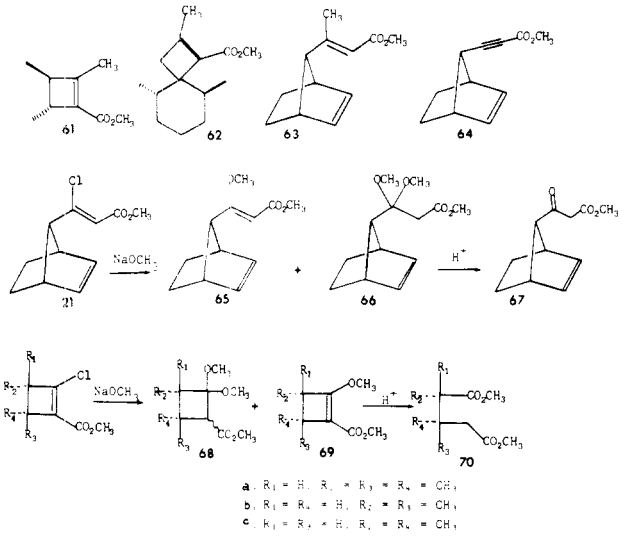
With monosubstituted or 1,2-disubstituted alkenes the cycloaddition is not regioselective.[2a] This is most notable in reactions with propene (run 1) which gives both cyclobutenes and with 2-cholestene (run 29) which gives a complex mixture of ene adducts and cycloadducts. It should be noted that 2-cholestene gives a single adduct with dichloroketene.[18]

Selectivity. Reactions with dienes and **1** were investigated to determine the relative reactivities of variously substituted double bonds. Reaction of **1** with limonene (run 31) indicates that a 1,1-disubstituted double bond is ca. 2 times as reactive as a trisubstituted double bond. Runs 32 and 33 indicate that a 1,1-disubstituted or a trisubstituted double bond is much more reactive than a monosubstituted double bond. Run 34 indicates that a trisubstituted alkene is much more reactive than a 1,2-disubstituted alkene. In this run the expected endocyclic ene adduct probably reacts with **1**·$AlEtCl_2$ to give a Diels–Alder adduct which then undergoes a Lewis acid catalyzed retro-Diels–Alder reaction leading to **53** and methyl 2,4-pentadienoate.

Reactions with conjugated dienes provide several novel results. 2,5-Dimethyl-2,4-hexadiene reacts with **1** (run 35) to give exclusively triene **54b** resulting from ring opening of the cyclobutene **54a**. Electronic effects cause formation of the cyclobutene in which the hydrogen-bearing carbon is attached to the quaternary carbon. With this diene, dichloroketene gives both regioisomers.[8] Reaction of **2** with isoprene (run 24) gives a 55:15:30 mixture of Diels–Alder

(18) Cragg, G. M. L. *J. Chem. Soc. C* **1970**, 1829.

Scheme I



adduct **35**, cyclobutene **36**, and ene adduct **37** in 68% yield. Even at −78 °C, selectivity for Diels–Alder adduct formation is not observed. The presence of significant amounts of ene adduct as a byproduct in the Lewis acid catalyzed Diels–Alder reaction of chloral and isoprene has been previously observed.[19] Anthracene and **2** react in the presence of aluminum chloride (CH_2Cl_2, 4 days, 25 °C) to give a 66% yield of Diels–Alder adduct. Since the resulting β-chloro enoate can be hydrolyzed to a β-keto ester, **2** can function as a (carbomethoxy)ketene equivalent in the Diels–Alder reaction, giving ketones whose regiochemistry with unsymmetrical dienes is opposite to that obtained from other ketene equivalents.[20]

Functionalized Alkenes. Since our detailed study of functional-group tolerances in Lewis acid catalyzed methyl propiolate ene reactions was reported,[2a] several new types of alkenes have been examined. Free alcohols (runs 37 and 38) are suitable substrates if 2 equiv of $EtAlCl_2$ is used. The second equivalent reacts with the alcohol to give ethane and alkoxyaluminum dichloride.[21] Unsaturated esters and ketones can be present in alkenes (runs 39 and 40) if a second equivalent of $EtAlCl_2$ is used to complex with them. Use of a 4:1 mixture of $AlCl_3$–2,6-di-*tert*-butylpyridine with **1** and methylenecyclohexane (run 41) gives a 63% yield of **60**, uncontaminated with ene adduct derived from 1-methylcyclohexene. Thus use of $AlCl_3$, with 2,6-di-*tert*-butylpyridene present as an HCl scavenger, is an alternative to the use of $EtAlCl_2$.

The reaction of **1** with 1-octynyltrimethylsilane gives a 7% yield of **55a** and a 5% yield of **55b**. This novel acetylene trimerization reaction may be of value in some cases.

Reactions of Adducts. The chemistry of the chloropropiolate adducts was briefly investigated. Treatment of **5a**, **12**, or **21** with lithium dimethylcuprate results in replacement of the chlorine with a methyl group, giving **61**, **62**, and **63** in high yield (see Scheme I). In the case of **63** the stereochemistry appears to be preserved.[22] Dehydrochlorination of **21** with tetraethylammonium fluoride and potassium carbonate in acetonitrile gives an 84% yield of acetylenic ester **64**.[23] Treatment of **21** with 2 equiv of sodium methoxide in refluxing methanol gives a mixture of **65** and **66** which is hydrolyzed with HCl in wet methanol to give β-keto ester **67** in 47% yield based on **21**.[24] Treatment of **13** with 2 equiv of sodium methoxide in methanol at reflux gives a 1:1 mixture of dimethyl ketal **68a** and enol ether **69a** which is hydrolyzed to give a 56% yield of **70a** based on **13**. Treatment of **5a** and **6a** under similar conditions gives **70b**[25] and **70c**[25] in 55 and 42% yields, respectively, without epimerization at the α-carbon. Ring openings of cyclobutenes thus provide a method for stereocontrolled synthesis of acyclic systems.

The Lewis acid induced reactions of acetylenic esters with alkenes provide a versatile method for formation of new carbon–carbon double bonds with a great deal of stereo- and regiocontrol.

Experimental Section

Materials and Methods. Infrared spectra were obtained from thin films on sodium chloride plates on a Perkin-Elmer 237 or 283 spectrometer. NMR spectra were determined on a Varian A-60, Varian Xl-100, Perkin-Elmer R32, or JEOL FX90Q spectrometer in $CDCl_3$, CCl_4, or benzene-d_6 with Me_4Si as an internal standard. Mass spectra were obtained on an AEI MS9 mass spectrometer. Gas chromatographic separations were accomplished on a 5% DEGS, 10% SE-30, or 10% XF-1150 on Chromosorb W column. Benzene was dried by distillation from sodium benzophenone ketyl. Methylene chloride was dried by distillation from calcium hydride. Methyl propiolate was used as purchased from Farchan Co. Alkenes were purchased from Aldrich or Chemical Samples Co. and used without further purification. Aluminum chloride was sublimed before use and stored in vacuo. Ethylaluminum dichloride was purchased as a 25% solution in heptane from Texas Alkyls.

General Procedure. To anhydrous powdered aluminum chloride under nitrogen in a 50-mL flask were added benzene and the acetylenic ester. The mixture was stirred until most of the aluminum chloride had dissolved (15–45 min) and a homogeneous yellow solution had formed. The alkene was added, and the solution was stirred 2–7 days, giving an orange to brown solution containing some precipitate. With reactive alkenes the initial reaction was exothermic, and the vessel was cooled in an ice bath before the alkene was added.

Workup was accomplished by pouring the solution into a saturated sodium dihydrogen phosphate solution. After the mixture was stirred for 10 min, 10% hydrochloric acid was added dropwise until the precipitated alumina had dissolved. The aqueous layer was washed with three portions of ether, the combined organic layers were washed with brine and dried over magnesium sulfate, and the solvent was removed in vacuo.

For acid-sensitive products, the reaction was quenched in saturated sodium bicarbonate solution, followed by suction filtration through Celite to remove the precipitated alumina. Extraction with ether was then carried out as described above.

For the ethylaluminum dichloride catalyzed reactions, 25% ethylaluminum dichloride in heptane was added to the solvent under nitrogen. The aceteylenic ester and then the alkene were added, and the reaction was stirred at room temperature and worked up as described above.

Synthesis of Methyl Chloropropiolate (2). To a solution of 12.6 g (0.13 mol) of distilled *trans*-1,2-dichloroethene in 100 mL of anhydrous Et_2O at 0 °C was slowly added 100 mL of 1.8 M (0.18 mol) low-halide methyllithium in Et_2O. The resulting solution was stirred for 15 min and cooled to -78 °C, and 12 g (0.13 mol) of methyl chloroformate (distilled from K_2CO_3) was added rapidly. This was stirred at −78 °C for 30 min and at 25 °C for 15 min. The reaction mixture was quenched with 100 mL of 10%

(19) Klimova, E. I.; Treshchova, E. G.; Arbuzov, Y. A. *Dokl. Akad. Nauk SSSR* **1968**, *180*, 865; *Dokl. Chem. (Engl. Transl.)* **1968**, *180*, 504.

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HCl. The organic phase was separated, washed with brine, and dried (Na_2SO_4). The Et_2O was removed in vacuo (≥100 torr) at room temperature. Distillation yielded 6.8 g (64%) of pure methyl chloropropiolate (**2**): bp 40–45 °C (15 torr); IR (neat) 2220, 1720, 1435, 1360, 1034, cm^{-1}; NMR (CCl_4) δ 3.73 (s).

Due to the explosive nature of the lithium chloroacetylide and the fact that methyl chloropropiolate is a very potent lachrymator, all reactions and distillations were carried out in a hood behind a safety shield. In one instance, when methyl chloroformate was added slowly, an explosion occurred, possibly due to the formation of tris(chloroethynyl)carbinol.

Reaction of Propene with Methyl Chloropropiolate (Run 1). To a slurry of 0.31 g (2.3 mmol) of $AlCl_3$ in 10 mL of benzene was added 0.822 g (7.19 mmol) of methyl chloropropiolate dissolved in 5 mL of benzene. After the $AlCl_3$ dissolved, the reaction mixture was cooled to −78 °C, and 2–3 mL of propene was condensed into the reaction vessel. This was warmed to 25 °C, at which point the internal pressure was 80 psi. The solution was stirred for 3 days and worked up in the usual manner to yield 0.59 g (51%) of crude product. Purification of 100 mg of product by column chromatography (10 g of silica gel, eluting with 95:5 petroleum ether–Et_2O) gave 32 mg (16%) of **3** followed by 16 mg (8%) of **4**. The spectral data for **3** are as follows: IR (neat) 1720, 1639 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 3.78 (s, 3), 2.90 (dd, 1, J = 4.5, 15 Hz), 2.8–3.2 (m, 1), 2.26 (dd, 1, J = 2, 15 Hz), 1.31 (d, 3, J = 7.5 Hz); mass spectrum, m/e 160 (M^+), 145, 129. The spectral data for **4** are as follows: IR (neat) 1720, 1630 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 3.78 (s, 3), 2.96 (ddq, 1, J = 1.2, 4.5, 7 Hz), 2.83 (dd, 1, J = 4.5, 11 Hz), 2.20 (dd, 1, J = 1.2, 11 Hz), 1.23 (d, 3, J = 7 Hz); mass spectrum, m/e 160 (M^+), 145, 129, 125, 101.

Structures **3** and **4** are assigned by chromatographic and spectral comparison to dechloro analogues in which coupling to the alkenyl hydrogen allows unambiguous structure assignment.[2a]

Reaction of *trans*-2-Butene with Methyl Chloropropiolate (Run 2). To a mixture of 0.31 g (2.3 mmol) of $AlCl_3$ and 5 mL of benzene was added 0.552 g (4.55 mmol) of methyl chloropropiolate dissolved in 5 mL of benzene. After the $AlCl_3$ dissolved, an excess (2–3 mL) of *trans*-2-butene was condensed into the reaction vessel. After 2 days, normal workup yielded 0.90 g of crude product which consisted of 88% **5a** and 6% of ring-opened diene. Chromatography of 0.800 g of product on 10 g of silica gel (eluting with 9:1 petroleum ether–Et_2O) gave 0.460 g (64%) of pure cyclobutene **5a**: IR (neat) 1720, 1630 cm^{-1}; NMR (CCl_4) δ 3.72 (s, 3), 2.2–2.7 (m, 2), 1.25 (d, 3, J = 7 Hz), 1.22 (d, 3, J = 7 Hz).

Reaction of *trans*-2-Butene with Dimethyl Acetylenedicarboxylate (Run 3). Dimethyl acetylenedicarboxylate (1.53 g, 10.8 mmol), $EtAlCl_2$ (5.0 mL of a 1.57 M solution, 7.8 mmol), and *trans*-2-butene (0.60 g, 10.8 mmol) were stirred for 1 day in 20 mL of CH_2Cl_2. Normal workup gave 1.553 g of product, a portion of which (0.250 g) was purified by chromatography on 20 g of silica gel with 9:1 petroleum ether–Et_2O as eluent to give 0.165 g (16%) of an inseparable 7:3 mixture of cyclobutene **5b** and dimethyl (*Z*,*Z*)-2,4-hexadiene-3,4-dicarboxylate and 0.168 g of recovered DMAD. The spectral data for **5b** are as follows: IR (neat) 1725, 1643 cm^{-1}; NMR ($CDCl_3$) δ 3.82 (s, 6), 2.50 (q, 2, J = 6.5 Hz), 1.28 (d, 6, J = 6.5 Hz). The spectral data for the diene are as follows: NMR ($CDCl_3$) δ 6.30 (q, 2, J = 7 Hz), 3.73 (s, 6), 2.08 (d, 6, J = 7 Hz).

Reaction of *cis*-2-Butene with Methyl Chloropropiolate (Run 4). To a slurry of 0.33 g (2.5 mmol) of $AlCl_3$ in 10 mL of benzene was added 0.408 g (3.44 mmol) of methyl chloropropiolate dissolved in 10 mL of benzene. An excess (~2 mL) of *cis*-butene was condensed in after all the $AlCl_3$ dissolved. The reaction was stirred for 2 days and worked up in the usual manner to yield 0.530 g (88%) of crude cyclobutene **6a**. The product was purified further on 10 g of silica gel with 95:5 petroleum ether–Et_2O as eluent to yield 0.446 g (74%) of pure cyclobutene **6a**: IR (neat) 1720, 1635 cm^{-1}; NMr (CCl_4) δ 3.68 (s, 3), 2.7–3.2 (m, 2), 1.14 (d, 3, J = 7 Hz), 1.10 (d, 3, J = 7 Hz); mass spectrum, m/e 174 (M^+), 139.

Reaction of *cis*-2-Butene with Dimethyl Acetylenedicarboxylate (Run 5). Dimethyl acetylenedicarboxylate (1.59 g, 11 mmol), $EtAlCl_2$ (6.35 mL of a 1.57 M solution, 10 mmol), and *cis*-2-butene (0.62 g, 11 mmol) were stirred in 10 mL of CH_2Cl_2 in a pressure bottle at 9–12 psi for 4 days. Normal workup gave 1.58 g of product. A portion (0.300 g) was purified by chromatography on 30 g of silica gel with 9:1 petroleum ether–Et_2O as eluent to give 0.078 g (19%) of an inseparable 1:1 mixture of **6b** and **7** as well as 0.027 g (9%) of recovered DMAD. The spectral data for **6b** are as follows: IR (neat) 1730, 1640 cm^{-1}; NMR ($CDCl_3$) δ 3.81 (s, 6), 3.10 (q, 2, J = 6 Hz), 1.18 (d, 6, J = 6 Hz). The spectral data for **7** are as follows: IR (neat) 1730, 1640, 1008, 915 cm^{-1}; NMR ($CDCl_3$) δ 5.85 (d, 1, J = 1 Hz), 5.83 (ddd, 1, J = 16, 10, 7.5 Hz), 5.3–5.0 (m, 2), 3.85 (s, 3), 3.76 (s, 3), 3.4–3.0 (m, 1), 1.19 (d, 3, J = 7 Hz).

Reaction of Cyclohexene with Methyl Chloropropiolate (Run 6). To a slurry of 0.33 g (2.5 mmol) of $AlCl_3$ in 10 mL of benzene was added 0.383 g (3.23 mmol) of methyl chloropropiolate dissolved in 5 mL of benzene. After the $AlCl_3$ dissolved, 0.29 g (3.6 mmol) of cyclohexene was added. The reaction was stirred at 25 °C for 3 days. Workup in the usual manner yielded 0.38 g (60%) of crude cyclobutene **8a**. The product was purified by chromatography on 10 g of silica gel with 9:1 petroleum ether–Et_2O as eluent to yield 0.333 g (51%) of pure cyclobutene **8a**: IR (neat) 1735, 1635 cm^{-1}; NMR (CCl_4) δ 3.70 (s, 3), 3.00 (m, 2), 1.2–2.2 (m, 8); mass spectrum, m/e 200 (M^+), 165. Anal. Calcd for $C_{10}H_{13}ClO_2$: C, 59.86; H, 6.53; Cl, 17.67. Found: C, 59.47; H, 6.32; Cl, 17.69.

Reaction of Cyclohexene with Dimethyl Acetylenedicarboxylate (Run 7). Dimethyl acetylenedicarboxylate (0.717 g, 5.0 mmol), $EtAlCl_2$ (2.87 mL, 1.57 M, 4.5 mmol), and cyclohexene (0.45 g, 5.5 mmol) were stirred for 6 days in 10 mL of CH_2Cl_2. Normal workup gave 1.014 g (90%) crude product. Column chromatography on silica gel using 8:2 petroleum ether–Et_2O as eluent gave 0.159 g (14%) of cyclobutene **8b** followed by 0.425 g (38%) of ene adduct **9**. The spectral data for **8b** are as follows: IR (neat) 1725, 1638 cm^{-1}; NMR (CCl_4) δ 3.74 (s, 6), 3.14–2.80 (m, 2), 1.84–0.90 (m, 8). The spectral data for **9** are as follows: IR (neat) 1726, 1642 cm^{-1}; NMR (CCl_4) δ 5.73 (d, 1, J = 1 Hz), 6.05–5.52 (m, 2), 3.75 (s, 3), 3.68 (s, 3), 3.25–2.98 (m, 1), 2.17–1.54 (m, 6).

Reaction of 2-Ethyl-1-butene with Methyl Chloropropiolate (Run 8). To a slurry of 0.28 g (2.1 mmol) of $AlCl_3$ in 10 mL of benzene was added 0.50 g (4.2 mmol) of methyl chloropropiolate dissolved in 5 mL of benzene. After most of the $AlCl_3$ dissolved, 0.41 g (4.9 mmol) of 2-ethyl-1-butene was added. The reaction was stirred for 2 days at 25 °C. Normal workup gave 0.800 g of crude product. Purification of 0.510 g of this product by chromatography on silica gel with 9:1 petroleum ether–Et_2O as eluent gave 0.111 g (21%) of cyclobutene **10** and 0.183 g (33%) of ene adduct **11** as a 1:1 mixture of isomers. The spectral data for **10** are as follows: IR (neat) 1720, 1630 cm^{-1}; NMR (CCl_4) δ 3.72 (s, 3), 2.38 (s, 2), 1.69 (q, 4, J = 7 Hz), 0.88 (t, 6, J = 7 Hz); mass spectrum, m/e 202 (M^+), 167. The spectral data for **11** are as follows: IR (neat) 1735, 1635 cm^{-1}; NMR (CCl_4) δ 5.93 (br s, 1), 5.35, 5.47 (2 br q, 1, J = 7 Hz), 3.67 (s, 3), 3.17, 3.07 (2 br s, 2), 2.07 (br q, 2, J = 7 Hz), 1.64 (br d, 3, J = 7 Hz), 0.97, 1.00 (2 t, 3, J = 7 Hz); mass spectrum, m/e 202 (M^+), 167.

Reaction of *trans*-2,6-Dimethylmethylenecyclohexane with Methyl Chloropropiolate (Run 9). To a slurry of 0.35 g (2.6 mmol) of $AlCl_3$ in 5 mL of benzene was added 0.647 g (5.46 mmol) of methyl chloropropiolate dissolved in 5 mL of benzene. After the $AlCl_3$ dissolved, the reaction mixture was cooled to 4 °C, and 0.754 g (6 mmol) of alkene was added. This was stirred at 4 °C for 5 days and at 25 °C for 1 day. Normal workup yielded 0.80 g (61%) of crude product. Purification of 0.36 g of this product on 10 g of silica gel yielded 0.30 g (52%) of pure **12**: IR (neat) 1730, 1630 cm^{-1}; NMR (CCl_4) δ 3.70 (s, 3), 2.31 (d, 1, J = 15 Hz), 2.21 (d, 1, J = 15 Hz), 1.8–1.2 (m, 8), 1.04 (d, 3, J = 7 Hz), 0.81 (d, 3, J = 7 Hz). Anal. Calcd for $C_{13}H_{19}ClO_2$: C, 64.32; H, 7.89; Cl, 14.84. Found: C, 64.55; H, 7.99; Cl, 14.84.

Reaction of 2-Methyl-2-butene with Methyl Chloropropiolate (Run 10). To a slurry of 0.51 g (3.8 mmol) of $AlCl_3$ in 10 mL of benzene was added 1.003 g (8.46 mmol) of methyl chloropropiolate dissolved in 3 mL of benzene. After the $AlCl_3$ dissolved, the reaction mixture was cooled to 4 °C, 0.73 g (10 mmol) of 2-methyl-2-butene was added, and the reaction was stirred at 4 °C for 3 days and at 25 °C for 1 day. Normal workup gave 1.33 g (64%) of crude product. Purification on 100 g of silica gel (eluting with 9:1 petroleum ether–ether) yielded 0.651 g (41%) of cyclobutene **13** and 0.379 g (24%) of ene adduct **14**. The

spectral data for **13** are as follows: IR (neat) 1720, 1640 cm^{-1}; NMR ($CDCl_3$) δ 3.74 (s, 3), 2.62 (q, 1, J = 7 Hz), 1.28 (s, 3), 1.15 (s, 3), 1.09 (d, 3, J = 7 Hz); mass spectrum, m/e 188 (M^+), 173, 153. Anal. Calcd for $C_9H_{13}ClO_2$: C, 57.30; H, 6.94. Found: C. 56.75; H, 7.20. The spectral data for **14** are as follows: IR (neat) 1735, 1630 cm^{-1}; NMR ($CDCl_3$) δ 6.13 (s, 1), 4.9 (m, 2), 3.75 (s, 3), 3.18 (br q, 1, J = 7 Hz), 1.75 (br t, 3, J = 1 Hz), 1.32 (d, 3, J = 7 Hz); mass spectrum, m/e 188 (M^+), 173, 157, 153, 152.

A similar reaction was run to monitor the reaction rate. In an NMR tube was placed 39.5 mg (0.30 mmol) of $AlCl_3$. To this was added 189 mg (1.59 mmol) of methyl chloropropiolate dissolved in 0.5 mL of benzene-d_6. After most of the $AlCl_3$ dissolved, the reaction mixture was frozen in dry ice–acetone. To the frozen mixture was added 0.2 mL (1.19 mmol) of 2-methyl-2-butene dissolved in 0.3 mL of benzene-d_6. The NMR tube was evacuated and sealed. The reaction was monitored by NMR. The time in hours and the percent reaction are as follows: 0.25, 55; 0.5, 58; 1, 62; 2, 68; 3, 73; 4, 75; 5, 78; 7, 84; 21, 93.

Kinetics of the Reaction of 1-Methylcyclohexene with Methyl Chloropropiolate (Run 11). In an NMR tube was placed 56.7 mg (0.42 mmol) of $AlCl_3$ and 234 mg (1.97 mmol) of methyl chloropropiolate in 0.8 mL of benzene-d_6. When most of the $AlCl_3$ had dissolved, the reaction mixture was frozen in dry ice–acetone and the NMR tube evacuated. To the frozen mixture was added 0.21 g (2.1 mmol) of 1-methylcyclohexene. The tube was sealed in vacuo and the reaction followed by NMR. The time in hours and the percent reaction are as follows: 0.25, 10; 0.5, 13; 1, 15; 3.5, 20; 7, 25; 21, 35; 24, 35; 48, 45; 72, 51; 192, 68; 240, 70; 480, 83; 576, 86.

Normal workup gave 385 mg (91%) of crude product. Purification on 10 g of silica gel with 95:5 petroleum ether–Et_2O as eluent yielded 76 mg (18%) of cyclobutene **15** and 245 mg (58%) of ene adduct **16**. The spectral data for cyclobutene **15** are as follows: IR (neat) 1720, 1635 cm^{-1}; NMR ($CDCl_3$) δ 3.76 (s, 3), 2.56 (t, 1, J = 4.5 Hz), 1.4–2.0 (m, 8), 1.17 (s, 3). The spectral data for **16** are as follows: IR (neat) 1735, 1630 cm^{-1}; NMR ($CDCl_3$) δ 6.05 (s, 1), 5.6–5.9 (m, 1), 3.77 (s, 3), 2.8–3.1 (m, 1), 1.5–2.2 (m, 8); mass spectrum, m/e 214 (M^+), 199, 183, 179, 178. Anal. Calcd for $C_{11}H_{15}ClO_2$: C, 61.54; H, 7.04; Cl, 16.51. Found: C, 61.56; H, 6.99; Cl, 16.44.

Reaction of 2,3-Dimethyl-2-butene with Methyl Chloropropiolate (Run 12). To 0.41 g (3.0 mmol) of $AlCl_3$ in 10 mL of benzene was added 0.841 g (7.1 mmol) of methyl chloropropiolate dissolved in 5 mL of benzene. The reaction mixture was stirred until the $AlCl_3$ dissolved and then cooled to 4 °C. An excess (0.78 g, 9.3 mmol) of 2,3-dimethyl-2-butene was added. The reaction was stirred for 3 days at 4 °C and for 4 days at 25 °C. Normal workup yielded 1.27 g (88%) of fairly pure material. A portion (200 mg) of the product was purified by column chromatography on silica gel with 95:5 petroleum ether–Et_2O as eluent, yielding 172 mg (76%) of cyclobutene **17** and 8 mg (4%) of ene adduct **18**. The spectral data for **17** are as follows: IR (neat) 1720, 1635 cm^{-1}; NMR (CCl_4) 3.67 (s, 3), 1.18 (s, 6), 1.08 (s, 6). Anal. Calcd for $C_{10}H_{15}ClO_2$: C, 59.26; H, 7.46; Cl, 17.49. Found: C, 59.08; H, 7.30; Cl, 17.48. The spectral data for **18** are as follows: IR (neat) 1735, 1630 cm^{-1}; NMR ($CDCl_3$) δ 6.12 (s, 1), 4.90 (m, 2), 3.73 (s, 3), 1.70 (br s, 3), 1.37 (s, 6).

Reaction of Norbornene with Methyl Chloropropiolate (Run 13). To a solution of 0.80 g (6.0 mmol) of $AlCl_3$ and 1.025 g (8.65 mmol) of methyl chloropropiolate in 15 mL of benzene was added 0.99 g (10.5 mmol) of norbornene dissolved in 5 mL of benzene. The reaction was stirred at 25 °C overnight. Normal workup yielded 1.54 g (84%) of crude product. Analysis by gas chromatography (6 ft × $^1/_4$ in. column, 5% DEGS, 170 °C) showed that the three isomers **19**, **20**, and **21a** with retention times of 7, 9, and 13 min were present in the ratio of 4:10:86. Chromatography on 100 g of silica gel with 95:5 petroleum ether-Et_2O as eluent gave 0.085 g (5%) of a mixture of **19** and **20** followed by 1.325 g (72%) of **21a**. The spectral data for **19** and **20** are as follows: IR (neat) 1720, 1625 cm^{-1}; NMR (CCl_4) δ 3.68 (s, 3), 2.62 (br s, 2), 2.1–2.4 (m, 2), 0.9–1.9 (m, 6). The spectral data for **21a** are as follows: IR (neat) 1735, 1640 cm^{-1}; NMR (CCl_4) δ 5.92 (dd, 2, J = 2, 2 Hz), 5.68 (d, 1, J = 1.5 Hz), 3.63 (s, 3), 2.9–3.2 (m, 2), 2.4–2.6 (m, 1), 1.6–2.0 (m, 2), 1.02 (dd, 2, J = 4, 10 Hz). Anal. Calcd for $C_{11}H_{13}ClO_2$: C, 62.12; H, 6.16; Cl, 16.67. Found: C, 61.96; H, 6.23; Cl, 16.81.

The NMR spectrum of chromatographically pure **21a** also showed a signal at δ 3.68 (s, 3, OMe) which was ca. 10% of the area of the peak at δ 3.63 and may be due to the anti isomer of **21a**.

Reaction of Norbornene with Dimethyl Acetylenedicarboxylate (Run 14). Dimethyl acetylenedicarboxylate (0.77 g, 5.0 mmol), $EtAlCl_2$ (2.5 mL of a 1.57 M solution, 4.0 mmol), and norbornene (0.471 g, 5.0 mmol) were stirred for 1 day in 10 mL of CH_2Cl_2. Normal workup gave 0.85 g of crude product. The NMR spectrum showed mainly oligomer and ~10% of **21b** as determined by the signals at δ 5.95 (dd, 2, J = 2, 2 Hz) and 5.68 (d, 1, J = 1.4 Hz).

Reaction of Norbornadiene with Methyl Chloropropiolate (Run 15). To a mixture of 0.20 g (1.5 mmol) of $AlCl_3$ and 5 mL of benzene was added 0.461 g (3.89 mmol) of methyl chloropropiolate dissolved in 5 mL of benzene. After all of the $AlCl_3$ dissolved, the reaction mixture was cooled to 4 °C, and 0.5 mL (4.7 mmol) of norbornadiene was added. The solution was stirred for 5 days at 4 °C and for 2 days at 25 °C. Workup in the usual manner yielded 0.62 g (76%) of crude product. The isomers were separated by chromatography on silica gel with 97:3 hexane–ethyl acetate as eluent to yield 271 mg (33%) of cyclobutene **22** and 162 mg (20%) of homo-Diels–Alder adduct **23**. The spectral data for **22** are as follows: IR (neat) 1720, 1630 cm^{-1}; NMR (CCl_4) δ 6.1 (m, 2), 3.72 (s, 3), 2.5–2.8 (m, 4), 1.4 (m, 2). Anal. Calcd for $C_{11}H_{11}ClO_2$: C, 62.72; H, 5.26; Cl, 16.83. Found: C, 62.84; H, 5.28; Cl, 17.05. The spectral data for **23** are as follows: IR (neat) 1715, 1595 cm^{-1}; NMR (CCl_4) δ 3.70 (s, 3), 3.1 (br, 1), 2.7 (br, 1), 2.15 (br, 1), 1.7–2.0 (m, 1), 1.6 (m, 4).

Reaction of (*E*)-3-Methyl-2-pentene with Methyl Chloropropiolate (Run 16). To a slurry of 0.28 g (2.1 mmol) of $AlCl_3$ in 10 mL of benzene was added 0.376 g (3.17 mmol) of methyl chloropropiolate in 5 mL of benzene. After the $AlCl_3$ dissolved, the reaction mixture was cooled to 4 °C, and 0.44 mL (3.6 mmol) of (*E*)-3-methyl-2-pentene was added. The mixture was stirred at 4 °C for 3 days and at 25 °C for 1 day. Normal workup gave 0.578 g (90%) of crude product. Purification by chromatography on silica gel with 97:3 hexane–ethyl acetate as eluent gave 0.301 g (47%) of cyclobutene **24** and 0.202 g (31%) of an 88:12 mixture of **25a** and **26a**. The spectral data for **24** are as follows: IR (neat) 1720, 1635 cm^{-1}; NMR (CCl_4) δ 3.70 (s, 3), 2.62 (q, 1, J = 7 Hz), 1.3–1.9 (m, 2), 1.15 (s, 3), 1.08 (d, 3, J = 7 Hz), 0.88 (t, 3, J = 7 Hz). The spectral data for **25a** are as follows: IR (neat) 1730, 1630 cm^{-1}; NMR (CCl_4) δ 5.97 (d, 1, J = 0.6 Hz), 4.93 (m, 2), 3.67 (s, 3), 3.13 (br q, 1, J = 7 Hz), 2.03 (br q, 2, J = 7 Hz), 1.31 (d, 3, J = 7 Hz), 1.05 (t, 3, J = 7 Hz).

Reaction of (*E*)-3-Methyl-2-Pentene with Dimethyl Acetylenedicarboxylate (Run 17). Dimethyl acetylenedicarboxylate (0.717 g, 5.0 mmol), $EtAlCl_2$ (2.87 mL of a 1.57 M solution, 4.5 mmol), and (*E*)-3-methyl-2-pentene (0.46 g, 4.5 mmol) were stirred 5 days in 10 mL of CH_2Cl_2. Normal workup gave 0.932 g (82%) of crude product. Column chromatography on silica gel using 9:1 petroleum ether–Et_2O as eluent gave 0.884 g (78.1%) of ene adduct **25b**: IR (neat) 1730, 1640 cm^{-1}; NMR (CCl_4) δ 5.75 (d, 1, J = 1 Hz), 4.99 (m, 2), 3.68 (s, 3), 3.64 (s, 3), 3.20 (br q, 1, J = 6 Hz), 2.03 (br q, 2, J = 7 Hz), 1.22 (d, 3, J = 7 Hz), 1.01 (t, 3, J = 6 Hz). The NMR spectrum showed that <5% of **26b** was present.

Run 18 was conducted by adding 0.52 g (3.7 mmol) of dimethyl acetylenedicarboxylate to 0.49 g (3.7 mmol) of $AlCl_3$ in 10 mL of CH_2Cl_2 followed by addition of 0.34 g (4.1 mmol) of (*E*)-3-methyl-2-pentene. After the mixture was stirred for 1 h, the reaction was worked up, giving 0.713 g (85%) of crude product which consisted of an 80% pure 9:1 mixture of **25b** and **26b**.

Reaction of (*Z*)-3-Methyl-2-pentene with Methyl Chloropropiolate (Run 19). To a slurry of 0.27 g (2.02 mmol) of $AlCl_3$ in 10 mL of benzene was added 0.353 g (2.99 mmol) of methyl chloropropiolate. After the $AlCl_3$ dissolved, the reaction mixture was cooled to 4 °C, and 0.41 mL (3.4 mmol) of (*Z*)-3-methyl-2-pentene was added. The mixture was stirred 3 days at 4 °C and 1 day at 25 °C. Normal workup gave 0.590 g (97%) of crude product. Purification as described for run 16 gave 0.312 g (53%) of cyclobutene **27** and 0.224 g (37%) of a 78:22 mixture of **26a** and **25a**. The spectral data for **27** are as follows: IR (neat) 1720, 1635 cm^{-1}; NMR (CCl_4) δ 3.67 (s, 3), 2.55 (q, 1, J = 7 Hz), 1.3–1.8 (m, 2), 1.25 (3, s), 1.11 (d, 3, J = 7 Hz), 0.92 (t, 3, J = 7 Hz). The

spectral data for **26a** are as follows: IR (neat) 1735, 1630 cm^{-1}; NMR (CCl_4) δ 5.92 (d, 1, J = 0.8 Hz), 5.1–5.7 (m, 1), 3.65 (s, 3), 3.05 (br q, 1, J = 7 Hz), 1.81 (d, 3, J = 7 Hz), 1.57 (br s, 3), 1.26 (d, 3, J = 7 Hz).

Isomerization of (*Z*)-3-methyl-2-pentene was followed by GC monitoring of a reaction mixture prepared as described above. Aliquots (0.5 mL) were quenched in 10% hydrochloric acid and analyzed by GC on a 6 ft × $^1/_4$ in., 10% SE-30 column at 40 °C. The *Z* alkene elutes in 4.8 min and the *E* alkene in 5.2 min. The time in hours and the percent isomerization are as follows: 0.5, 8; 1.5, 15; 3, 15; 21, 18. After 21 h, 8% 2-ethyl-1-butene was present. The same 78:22 mixture of **26a** and **25a** was isolated.

Addition of 3.5 mmol of barium oxide to the reaction mixture had no effect.

Use of 0.9 equiv of $EtAlCl_2$ as a catalyst gave the same 76:24 mixture of **26a** and **25a**. However GC showed that no isomerization of starting material occurred.

Reaction of (*Z*)-3-Methyl-2-Pentene with Dimethyl Acetylenedicarboxylate (Run 20). Dimethyl acetylenedicarboxylate (0.717 g, 5.0 mmol), $EtAlCl_2$ (2.87 mL of a 1.57 M solution, 4.5 mmol), and (*Z*)-3-methyl-2-pentene (0.46 g, 5.5 mmol) were stirred 5 days in 10 mL of CH_2Cl_2. Normal workup gave 1.075 g (95%) of crude product. Column chromatography on silica using 8:2 petroleum ether–Et_2O as eluent gave ene adduct (0.89 g, 79%) which was shown by NMR to be a 6:94 mixture of **25b** and **26b**, which were not separated. The spectral data for **26b** are as follows: IR (neat) 1730, 1640 cm^{-1}; NMR (CCl_4) δ 5.68 (d, 1, J = 1.5 Hz), 5.44–5.27 (m, 1), 3.67 (s, 3), 3.65 (s, 3), 3.15 (br q, 1, J = 7 Hz), 1.57 (d, 3, J = 8 Hz), 1.53 (s, 3), 1.18 (d, 3, J = 7 Hz).

Run 21 was carried out by addition of 0.58 g (4.1 mmol) of dimethyl acetylenedicarboxylate to 0.52 g (3.9 mmol) of $AlCl_3$ in 10 mL of CH_2Cl_2 followed by addition of 0.36 g (4.5 mmol) of (*Z*)-3-methyl-2-pentene. After the mixture was stirred 1 h, the reaction was worked up to give 0.936 g (90%) of a 70% pure 7:3 mixture of **26b** and **25b**.

Reaction of 1,6-Dimethylcyclohexene with Methyl Chloropropiolate (Run 22). To 0.384 g (3.24 mmol) of methyl chloropropiolate in 10 mL of CH_2Cl_2 were added 1.8 mL of 1.57 M $EtAlCl_2$ (2.8 mmol) and 0.4 g (3.6 mmol) of 1,6-dimethylcyclohexene. The reaction was stirred 2 days and worked up in the normal manner to give 0.81 g of crude product which was shown by NMR to be a 60:40 mixture of ene adduct–cyclobutenes. A portion (0.318 g) was purified on 10 g of silica gel with 95:5 petroleum ether–Et_2O as eluent. The early fractions (0.053 g, 18%) were an 80:20 mixture of cyclobutenes **28** and **29**. The middle fractions contained 0.113 g (38%) of a 4:1:5 mixture of **28**, **29**, and **30**. The final fractions (0.112 g, 38%) contain only ene adducts **30** and **31** in a 9:1 ratio.

The spectral data for **28** are as follows: IR (neat) 1720, 1625 cm^{-1}; NMR (CCl_4) δ 3.75 (s, 3), 2.52 (dd, 1, J = 3, 3 Hz), 1.3–1.9 (m, 7), 1.35 (s, 3), 0.99 (d, 3, J = 7 Hz). The spectral data for **29** are as follows: NMR (CCl_4) δ 1.20 (s, 3), 1.04 (d, 3, J = 7 Hz). The spectral data for **30** are as follows: IR (neat) 1735, 1630 cm^{-1}; NMR (CCl_4) δ 5.92 (s, 1), 3.68 (s, 3), 3.0 (m, 1), 1.52–2.1 (m, 6), 1.67 (m, 6). The spectral data for **31** are as follows: NMR (CCl_4) δ 6.07 (s, 1), 4.9 (m, 2), 1.15 (d, 3, J = 7 Hz).

Reaction of 1,2-Dimethylcyclohexene with Methyl Chloropropiolate (Run 23). To 0.332 g (2.80 mmol) of methyl chloropropiolate in 10 mL of CH_2Cl_2 were added 1.6 mL of 1.57 M $EtAlCl_2$ (25 mmol) and 0.4 g (3.6 mmol) of 1,2-dimethylcyclohexene. After 2 days, workup gave 0.69 g of crude product. A portion (0.410 g) was purified by chromatography on silica gel, eluting with 9:1 hexane–ethyl acetate. The early fractions contained 0.170 g (45%) of cyclobutene **32**. The second fraction contained 0.140 g (36%) of ene adducts as a 4:1 mixture of **33** and **34**. The spectral data for cyclobutene **32** are as follows: IR (neat) 1720, 1635 cm^{-1}; NMR (CCl_4) δ 3.76 (s, 3), 1.6 (m, 8), 1.20 (s, 3), 1.09 (s, 3). The spectral data for **33** are as follows: IR (neat) 1735, 1630 cm^{-1}; NMR (CCl_4) δ 5.96 (s, 1), 5.62 (m, 1), 3.71 (s, 3), 1.9–2.4 (m, 4), 1.7 (br s, 3), 1.4–1.7 (m, 2), 1.33 (s, 3). The spectral data for **34** are as follows: NMR (CCl_4) δ 6.00 (s, 1), 5.0 (m, 2).

Reaction of Isoprene with Methyl Chloropropiolate (Run 24). To a solution of 0.204 g (1.72 mmol) of methyl chloropropiolate and 0.1 mL of 1.57 M $EtAlCl_2$ in 10 mL of benzene was added 0.14 g (2.0 mmol) of isoprene. The reaction mixture was stirred for 2–3 h at 25 °C. Workup yielded 92 mg of a 55:15:30 mixture of **35**, **36**, and **37**.

In a similar manner, 0.277 g (2.34 mmol) of methyl chloropropiolate, 2.0 mmol of $EtAlCl_2$, and 0.17 g (2.5 mmol) of isoprene in 10 mL of CH_2Cl_2 were stirred for 6 h at −78 °C. The reaction mixture was slowly warmed to 25 °C. Normal workup yielded 0.324 g (74%) of crude product. Chromatography on silica gel with 98:2 pentane–Et_2O as eluent gave 0.042 g (10%) of cyclobutene **36**, 0.158 g (36%) of Diels–Alder adduct **35**, and 0.018 g (20%) of ene adduct **37**. The spectral data for **36** are as follows: NMR (CCl_4) δ 4.9–6.2 (m, 3), 3.62 (s, 3), 2.52 (AB d, 2, J = 14 Hz), 1.38 (s, 3). The spectral data for **35** are as follows: NMR (CCl_4) δ 5.4 (s, 1), 3.68 (s, 3), 2.89 (br s, 4), 1.65 (br s, 3). The spectral data for **37** are as follows: NMR (CCl_4) 6.25 (dd, 1, J = 16, 11 Hz). 5.83 (d, 1, J = 1.5 Hz), 4.8–5.3 (m, 4), 3.68 (s, 3), 3.25 (br s, 2).

Reaction of 4-Isopropyl-1-methylcyclohexene with Methyl Chloropropiolate (Run 25). To a solution of 0.570 g (4.80 mmol) of methyl chloropropiolate in 15 mL of CH_2Cl_2 were added 2.7 mL of a 1.57 M solution (4.2 mmol) of $EtAlCl_2$ and then 0.82 g (5.3 mmol) of 4-isopropyl-1-methylcyclohexene. The reaction mixture was stirred 24 h at 25 °C and worked up to give 1.08 g (88%) of a 4:1 mixture of ene adduct cyclobutenes. A portion (0.89 g) was purified by chromatography on silica gel, eluting with 9:1 hexane–ethyl acetate. The early fractions (0.060 g, 6%) were a 2:1 mixture of cyclobutenes **38** and **39**. The middle fractions (0.489 g, 49%) were a 12:2:1 mixture of **40a**, **38**, and **39**. The later fractions (0.12 g, 12%) were a 3:1 mixture of **40a** and **41a**. The spectral data for **38** are as follows: IR (neat) 1720, 1630 cm^{-1}; NMR (CCl_4) δ 3.74 (s, 3), 2.5 (m, 1), 1.30 (s, 3), 1.0–2.0 (m, 8), 0.93 (d, 6, J = 6 Hz). The spectral data for **39** are as follows: NMR (CCl_4) δ 3.76 (s, 3), 1.25 (s, 3). The spectral data for **40a** are as follows: IR (neat) 1735, 1630 cm^{-1}; NMR (CCl_4) δ 5.82 (s, 1), 5.62 (m, 1), 3.71 (s, 3), 2.91 (m, 1, $W_{1/2}$ = 8 Hz), 1.69 (s, 3), 1.2–2.2 (m, 6), 0.91 (br d, 6, J = 6 Hz). Anal. Calcd for $C_{14}H_{21}ClO_2$: C, 65.49; H, 8.25; Cl, 13.81. Found: C, 65.75; H, 8.22; Cl, 13.97. The spectral data for **41a** are as follows: NMR (CCl_4) δ 6.01 (s, 1), 4.6–5.0 (m, 2), 3.73 (s, 3).

Reaction of 4-Isopropyl-1-methylcyclohexene with Dimethyl Acetylenedicarboxylate (Run 26). Dimethyl acetylenedicarboxylate (0.717 g, 5.0 mmol), $EtAlCl_2$ (2.87 mL of a 1.57 M solution, 4.5 mmol), and (+)-4-isopropyl-1-methylcyclohexene (0.869 g, 5.7 mmol) were stirred for 8 days in 10 mL of CH_2Cl_2. Normal workup gave 1.271 g (91%) of crude product. Column chromatography of 0.50 g of this product on silica gel with 9:1 hexane–ethyl acetate as eluent gave ene adduct **40b**: 0.438 g (80%); IR (neat) 1726, 1640 cm^{-1}; NMR (CCl_4) δ 5.8–5.5 (m, 1), 5.55 (d, 1, J = 1 Hz), 3.72 (s, 3), 3.64 (s, 3), 3.12–2.85 (m, 1), 2.15–1.07 (m, 5), 1.64 (br s, 3), 0.88 (d, 6, J = 6 Hz).

Reaction of 4-Isopropyl-1-methylcyclohexene with Methyl Propiolate (Run 27). A solution of methyl propiolate (0.420 g, 5 mmol), 4-isopropyl-1-methylcyclohexene (0.690 g, 4 mmol), and $EtAlCl_2$ (2.9 mL of a 1.67 M solution, 4.5 mmol) in 15 mL of CH_2Cl_2 was stirred for 7 days. Normal workup gave 0.890 g of crude product which was purified by chromatography on silica gel with 5:1 hexane–ethyl acetate as eluent, giving 0.665 g (60%) of a mixture of ene adducts. GC analysis (10-ft 10% XF-1150 column, 150 °C) showed two peaks in a 9:1 ratio at t_R = 21 and 27 min, respectively. NMR analysis showed that a 54:36:10 mixture of **41c**, **40c**, and **42c** was present.

The spectral data for **41c** are as follows: NMR ($CDCl_3$) δ 7.00 (dd, 1, J = 16, 8 Hz), 5.76 (dd, 1, J = 16, 1.5 Hz), 4.74 (s, 1), 4.68 (s, 1), 3.73 (s, 3), 3.20 (m, 1), 0.89 (br d, 6, J = 7 Hz), 0.73–2.36 (m, 8). The spectral data for **40c** are as follows: NMR ($CDCl_3$) δ 6.87 (dd, 1, J = 16, 8 Hz), 5.69 (dd, 1, J = 16, 1.5 Hz), 5.51 (br, 1), 3.73 (s, 3), 2.8 (m, 1), 1.64 (br s, 3), 0.89 (br d, 6, J = 7 Hz), 0.13–2.36 (m, 6). The spectra data for **42c** are as follows: NMR ($CDCl_3$) δ 7.00 (dd, 1, J = 16, 8 Hz), 5.77 (dd, 1, J = 16, 1.5 Hz), 4.76 (s, 1), 4.47 (s, 1), 3.73 (s, 3), 3.44 (br s, 1), 0.73–2.36 (m, 8), 0.89 (d, 6, J = 7 Hz).

The IR (neat) of the mixture shows absorptions at 1732, 1675, and 872 cm^{-1}. Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.98. Found: C, 75.48; H, 9.77.

Reaction of 1,3-Dimethylcyclohexene with Dimethyl Acetylenedicarboxylate (Run 28). Dimethyl acetylenedicarboxylate (0.717 g, 5.0 mmol), $EtAlCl_2$ (2.87 mL of a 1.57 M

solution, 4.5 mmol), and 1,3-dimethylcyclohexene (0.625 g, 5.5 mmol) were stirred 6 days in 10 mL of CH_2Cl_2. Normal workup gave 1.182 g (95%) of crude product. Column chromatography on silica gel with 8:2 petroleum ether–Et_2O as eluent gave 0.636 g (51.3%) of product which was shown by NMR to be a 3:2 mixture of **43** and **44**, which were not separated: IR (neat) 1725, 1638 cm^{-1}; NMR for **43** δ 5.76 (s, 1), 5.5–5.9 (m, 1), 3.80 (s, 3), 3.74 (s, 3), 2.5 (m, 1), 2.2–1.5 (m, 5), 1.72 (s, 3), 1.00 (d, 3, J = 6 Hz); NMR for **44** δ 5.81 (s, 1), 5.5–5.9 (m, 1), 3.90 (s, 3), 3.77 (s, 3), 3.0 (m, 1), 2.2–1.5 (m, 5), 1.72 (s, 3), 0.91 (d, 3, J = 6 Hz).

Reaction of 2-Cholestene with Methyl Propiolate (Run 29). A solution of methyl propiolate (0.50 g, 0.6 mmol), 2-cholestene (0.200 g, 0.54 mmol), and $EtAlCl_2$ (0.52 mL of a 1.57 M solution, 0.81 mmol) in 5 mL of CH_2Cl_2 was stirred for 7 days. Normal workup gave 0.163 g of product which was shown by NMR to be a mixture of all four possible cyclobutenes and some ene adduct.

Reaction of 5-Cholestene with Methyl Propiolate (Run 30). A solution of methyl propiolate (0.023 g, 0.27 mmol), 5-cholestene (0.1 g, 0.27 mmol, 1.0 equiv), and $EtAlCl_2$ (0.153 mL of a 1.57 M solution, 0.24 mmol) in 5 mL of CH_2Cl_2 was stirred for 7 days. Normal workup gave 0.081 g of product. Purification by preparative TLC gave 0.023 g of recovered 5-cholestene and 0.022 g (17%) of ene adduct **45**: IR ($CHCl_3$) 1730, 1650 cm^{-1}; NMR ($CDCl_3$) δ 7.12 (dd, 1, J = 16, 6 Hz), 5.79 (dd, 1, J = 16, 1.7 Hz), 5.41 (dd, 1, J = 4, 4 Hz), 3.73 (s, 3), 3.07 (br, 1), 0.955 (s, 3), 0.905 (d, 3, J = 6 Hz), 0.866 (d, 6, J = 6 Hz), 0.686 (s, 3), 0.6–2.3 (m, 28). The signal at δ 3.07 is 11 Hz wide at half-height. Decoupling from the signal at δ 7.12 gives a peak at δ 3.07 with width at half-height of 5 Hz. Therefore, the proton at C-6 is equatorial (α).

Use of more than 1 equiv of $EtAlCl_2$ or use of $AlCl_3$ as the catalyst leads to more than one ene adduct, because of rearrangement of the acid-sensitive steroid either before or after ene reaction.

Reaction of Methyl Propiolate with Limonene (Run 31). A solution of methyl propiolate (0.382 g, 4.5 mmol), limonene (0.681 g, 5 mmol), and $EtAlCl_2$ (1.45 mL of a 1.57 M solution, 2.28 mmol) in 15 mL of CH_2Cl_2 was stirred for 7 days. Normal workup gave 0.646 g (65%) of crude product. GC analysis (6-ft, 10% XF-1150 column, 160 °C) showed that two peaks in a 1:2 ratio at 18.8 and 27.6 min accounted for 90% of the product mixture. These fractions were isolated by preparative GC.

NMR analysis showed fraction 1 (~30% of mixture) to consist of a 3:2 mixture of **46** and **47**. The spectral data for **46** are as follows: NMR ($CDCl_3$) δ 7.00 (dd, 1, J = 16, 7 Hz), 5.82 (dd, 1, J = 16, 1.7 Hz), 4.78 (br s, 1), 4.73 (br s, 1), 4.72 (br s, 2), 3.67 (s, 3), 3.02 (m, 1), 1.48–2.53 (m, 10). The spectral data for **47** are as follows: NMR ($CDCl_3$) δ 6.82 (dd, 1, J = 16, 7 Hz), 5.79 (dd, 1, J = 16, 1.5 Hz), 5.56 (m, 1), 4.68 (br s, 2), 3.69 (s, 3), 3.23 (m, 1), 1.74 (br s, 6), 1.61–2.41 (m, 5). NMR analysis showed fraction 2 (60% of mixture) to be **48**: NMR ($CDCl_3$) δ 7.15 (dt, 1, J = 16, 7 Hz), 5.87 (dt, 1, J = 16, 1.5 Hz), 5.37 (m, 1), 4.87 (s, 1), 4.79 (s, 1), 3.67 (s, 3), 2.93 (d, 2, J = 7 Hz), 1.48–2.53 (m, 10).

Reaction of Methyl Propiolate with 6-Methyl-1,5-heptadiene (Run 32). Methyl propiolate (0.378 g, 4.5 mmol), 6-methyl-1,5-heptadiene (0.54 g, 5.0 mmol), and $EtAlCl_2$ (2.6 mL of a 1.57 M solution, 3.7 mmol) were stirred for 6 days in 15 mL of CH_2Cl_2. Normal workup followed by evaporative distillation (70 °C, 0.25 torr) gave 0.648 g (75%) of ene adduct **49**: IR ($CDCl_3$) 1730, 1640, 1000, 910, 900 cm^{-1}; NMR (CCl_4) δ 6.78 (dd, 1, J = 6, 15 Hz), 5.43–6.02 (m, 1), 5.72 (dd, 1, J = 1.2, 15 Hz), 5.05 (m, 2), 4.83 (br s, 2), 3.67 (s, 3), 2.90 (dt, 1, J = 6, 7 Hz), 1.42–2.32 (m, 4), 1.73 (s, 3).

Reaction of 2-Methyl-1,5-hexadiene with Methyl Propiolate (Run 33). Methyl propiolate (0.378 g, 4.55 mmol), 2-methyl-1,5-hexadiene (0.48 g, 5 mmol), and $EtAlCl_2$ (1.45 mL of a 1.57 M solution, 2.26 mmol) were stirred 7 days in 12 mL of CH_2Cl_2. Normal workup followed by evaporative distillation (75 °C, 0.25 torr) gave 0.450 g (55%) of a mixture of ene adducts. GC (6-ft, 10% XF-1150 column, 125 °C) showed two peaks in a 5:4 ratio at 25.8 and 27.3 min. The NMR spectrum indicated that a 5:4 mixture of **50** and **51** was present: IR (neat) 1725, 1653, 1645 cm^{-1}; NMR for **50** ($CDCl_3$) δ 6.85 (td, 1, J = 7, 17 Hz), 5.77 (td, 1, J = 1.7, 17 Hz), 5.4–5.8 (m, 1), 5.05 (br, 2), 4.83 (br s, 2), 3.66 (s, 3), 2.89 (br d, 2, J = 7 Hz), 2.1–2.4 (m, 4); NMR for **51** ($CDCl_3$) δ 6.85 (td, 1, J = 7, 17 Hz), 5.77 (td, J = 1.7, 17 Hz), 5.3–5.8 (m, 2), 5.05 (br, 2), 3.66 (s, 3), 2.89 (br d, 2, J = 7 Hz), 2.1–2.4 (m, 2), 1.75, 1.67 (2 br s, 3).

Reaction of Methyl Propiolate with 1-Methyl-1,4-cyclohexadiene (Run 34). Methyl propiolate (0.378 g, 4.55 mmol), 1-methyl-1,4-cyclohexadiene (0.475 g, 5.0 mmol), and $EtAlCl_2$ (6.2 mL of a 1.57 M solution, 8.8 mmol) were stirred for 4 days in 12 mL of CH_2Cl_2. Normal workup gave 0.656 g (79%) of a 5:1 mixture of **52** and **53**, which were purified by preparative GC. The data for **52** are as follows: GC t_R = 14.5 min (6-ft, 10% XF-1150 column, 125 °C); IR (neat) 1730, 1660 cm^{-1}; NMR (CCl_4) δ 6.96 (dd, 1, J = 7.5, 17 Hz), 5.78 (dd, 1, J = 1.5, 17 Hz), 5.63 (s, 2), 4.86 (s, 1), 4.71 (s, 1), 3.68 (s, 3), 3.12 (m, 2), 2.80 (m, 2) 1.96–2.53 (m, 1). The data for **53** are as follows: GC t_R = 7 min (6-ft, 10% XF-1150 column, 125 °C); IR (neat) 1730, 1600, 1570 cm^{-1}; NMR (CCl_4) δ 7.86 (d, 1, J = 9 Hz), 6.99–7.41 (m, 3), 3.85 (s, 3), 2.59 (s, 3).

Reaction of 2,5-Dimethyl-2,4-hexadiene with Methyl Propiolate (Run 35). A solution of methyl propiolate (0.42 g, 5 mmol), 2,5-dimethyl-2,4-hexadiene (0.550 g, 5 mmol), and $EtAlCl_2$ (2.9 mL of a 1.57 M solution, 4.5 mmol) in 15 mL of CH_2Cl_2 was stirred for 3 days. Normal workup gave 0.882 g of crude product. Purification of 0.707 g of this product by chromatography on silica gel with 5:1 hexane–ethyl acetate as eluent gave 0.354 g (45%) of triene **54b**: IR (neat) 1718, 1628, 1582 cm^{-1}; NMR ($CDCl_3$) δ 6.56 (AB q, 2, J = 12 Hz), 5.87 (br s, 1), 3.70 (s, 3), 1.87 (s, 3), 1.82 (s, 6), 1.71 (s, 3). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.18; H, 9.34. Found: C, 74.11; H, 9.36.

Reaction of Methyl Propiolate with 1-Octyn-1-yltrimethylsilane (Run 36). Octynyltrimethylsilane (0.46 g, 2.5 mmol), methyl propiolate (0.42 g, 3.0 mmol), and $EtAlCl_2$ (2.89 mL of a 1.57 M solution, 4.5 mmol) in 8 mL of CH_2Cl_2 were stirred for 8 days. Normal workup gave 0.689 g of crude product. The NMR spectrum shows about 20% of **55a** and **55b**. Evaporative distillation at 200 °C (0.05 torr) gave 0.14 g of a mixture of **55a** and **55b**. Chromatography on silica gel with 5:1 hexane–ethyl acetate as eluent gave 0.061 g (7%) of **55a** and 0.044 g (5%) of **55b**.

The spectral data for **55a** are as follows: IR (neat) 1732, 1598 cm^{-1}; NMR ($CDCl_3$) δ 8.02 (d, 1, J = 1.7 Hz), 7.92 (d, 1, J = 1.7 Hz), 3.92 (s, 3), 3.87 (s, 3), 2.7–3.0 (m, 2), 0.67–1.77 (m, 11), 0.27 (s, 9); ^{13}C NMR ($CDCl_3$) δ 168.5, 168.3, 152.6, 142.3, 135.0, 133.1, 128.4, 127.8, 52.4, 52.3, 36.2, 32.0, 31.7, 29.5, 22.6, 13.9, 0.2; mass spectrum, m/e (relative intensity) 350 (M^+, 19), 335 (50), 319 (45), 303 (21), 280 (100), 245 (23), 207 (14), 203 (16), 201 (27), 189 (40), 176 (100).

The spectral data for **55b** are as follows: IR (neat) 1730, 1600 cm^{-1}; NMR ($CDCl_3$) δ 7.81 (s, 1), 7.50 (s, 1), 3.89 (s, 6), 2.73 (t, 2, J = 7 Hz), 0.73–1.78 (m, 11), 0.31 (s, 9); ^{13}C NMR ($CDCl_3$) δ 166.4, 150.8, 140.3, 131.7, 131.6, 130.0, 126.5, 52.2, 52.0, 36.7, 32.4, 31.7, 29.3, 22.5, 13.9, 2.0; mass spectrum, m/e (relative intensity) 350 (M^+, 12), 335 (100), 319 (12), 280 (24).

Reaction of 4-Methylenecyclohexylmethanol with Methyl Propiolate (Run 37). A solution of (4-methylenecyclohexyl)-methanol (0.63 g, 5 mmol), methyl propiolate (0.382 g, 4.5 mmol), and $EtAlCl_2$ (6.37 mL of a 1.57 M solution, 10 mmol) in 15 mL of CH_2Cl_2 was stirred for 7 days. Normal workup followed by evaporative distillation (95 °C, 0.05 torr) gave 0.774 g (74%) of **56**: IR (neat) 3640, 1722, 1650 cm^{-1}; NMR ($CDCl_3$) δ 6.96 (td, 1, J = 8, 16 Hz), 5.80 (td, 1, J = 1.5, 16 Hz), 5.46 (m, 1), 3.76 (s, 3), 3.51 (d, 2, J = 7 Hz), 2.83 (d, 2, J = 7 Hz), 1.11–2.37 (m, 7). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63. Found: C, 68.61; H, 8.71.

Reaction of 3-Methyl-3-buten-1-ol with Methyl Propiolate (Run 38). A solution of 3-methyl-3-buten-1-ol (0.430 g, 5 mmol), methyl propiolate (0.42 g, 5 mmol) and $EtAlCl_2$ (6.4 mL of a 1.57 M solution, 10 mmol) in 15 mL of CH_2Cl_2 was stirred for 7 days. Normal workup gave 0.778 g of crude product. Purification of 0.594 g of this product by chromatography on silica gel with 1:1 hexane–ethyl acetate as eluent gave 0.238 g (37%) of **57**: IR (neat) 3440, 1725, 1658, 1645, 900 cm^{-1}; NMR ($CDCl_3$) δ 6.97 (dt, 1, J = 16, 8 Hz), 5.85 (dt, 1, J = 16, 1.5 Hz), 4.7 (br s, 2), 3.76 (s, 3), 3.73 (t, 2, J = 7 Hz), 2.98 (d, 2, J = 8 Hz), 2.77 (br s, 1, OH), 2.33 (t, 2, J = 7 Hz). Anal. Calcd for $C_9H_{14}O_3$: C, 63.51; H, 8.09. Found: C, 63.57; H, 8.03.

Reaction of Methyl Geranoate with Methyl Propiolate (Run 39). A solution of methyl geranoate (0.469 g, 2.5 mmol),

methyl propiolate (0.21 g, 2.5 mmol), and $EtAlCl_2$ (3.18 mL of a 1.57 M solution, 5 mmol) in 8 mL of CH_2Cl_2 was stirred for 3 days. Normal workup gave 0.610 g of crude product. Evaporative distillation (70 °C, 0.05 torr) gave 0.311 g (47% yield) of ene adduct **58**: IR (neat) 1722, 1649 cm^{-1}; NMR (CCl_4) δ 6.81 (dd, 1, J = 8, 16 Hz), 5.82 (dd, 1, J = 1.5, 16 Hz), 5.63 (m, 1), 4.75 (m, 2), 3.73 (s, 3), 3.67 (s, 3), 2.94 (t, 1, J = 6 Hz), 2.18 (br s, 3), 1.75 (br s, 3), 1.53–2.11 (m, 4). Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.71; H, 8.39.

Reaction of *l*-Carvone with Methyl Propiolate (Run 40). A solution of *l*-carvone (0.750 g, 5 mmol), methyl propiolate (0.429 g, 5 mmol), and $EtAlCl_2$ (6.37 mL of a 1.57 M solution, 10 mmol) in 15 mL of CH_2Cl_2 was stirred for 7 days. Normal workup gave 0.904 g of crude product. Purification on silica gel with 1:1 petroleum ether–Et_2O as eluent gave 0.498 g (66%) of recovered carvone and 0.262 g (22%) of ene adduct **59**: IR (neat) 1725, 1678 cm^{-1}; NMR (CCl_4) δ 6.84 (dt, 1, J = 15, 7 Hz), 6.45 (br, 1), 5.80 (dt, 1, J = 15, 1.5 Hz), 4.95 (br s, 1), 4.89 (br s, 1), 3.69 (s, 3), 2.97 (br d, 2, J = 7 Hz), 2.0–2.9 (m, 5), 1.73 (s, 3). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.58; H, 7.93.

Reaction of Methylenecyclohexane with Methyl Propiolate in the Presence of 2,6-Di-*tert*-butylpyridine (Run 41). A solution of methyl propiolate (0.339 g, 4.05 mmol), methylenecyclohexane (0.427 g, 4.44 mmol), $AlCl_3$ (0.270 g, 2.02 mmol), and 2,6-di-*tert*-butylpyridine (0.106 g, 0.56 mmol) in 7 mL of benzene was stirred for 7 days. Normal workup gave 0.496 g (68%) of crude ene adduct. The NMR spectrum showed that the product was >90% **60**, uncontaminated with ene adduct derived from 1-methylcyclohexene.

Reaction of Methyl Bromopropiolate with 2-Methyl-2-Butene. $AlCl_3$ (31 mg, 0.23 mmol) was placed in an NMR tube. Methyl bromopropiolate[6] (0.290 g, 1.78 mmol) dissolved in 0.4 mL of benzene-d_6 was added. After most of the $AlCl_3$ had dissolved, the solution was cooled to 0 °C, and 0.2 mL of alkene in 0.5 mL of benzene-d_6 was added. The tube was kept at 25 °C and the reaction followed by NMR spectroscopy. After 1 day all the methyl bromopropiolate had reacted. Normal workup gave 0.386 g (93%) of an ~75% pure 5:4 mixture of cyclobutene and ene adduct as determined by NMR.

Reaction of Anthracene with Methyl Chloropropiolate. Anthracene (0.169 g, 0.95 mmol), methyl chloropropiolate (0.102 g, 0.86 mmol), and $AlCl_3$ (0.104 g, 0.78 mmol) were stirred for 98 h at 25 °C in 3 mL of CH_2Cl_2. Normal workup gave 0.232 g (93%) of crude product. Chromatography on silica gel with 9:1 petroleum ether–Et_2O as eluent gave 0.165 g (66%) of pure Diels–Alder adduct methyl 12-chloro-9,10-dihydro-9,10-ethenoanthracene-11-carboxylate: NMR ($CDCl_3$) δ 7.08 (m, 8), 5.62 (s, 1), 5.02 (s, 1), 3.77 (s, 3).

Methyl *trans*-2,3,4-Trimethyl-1-cyclobutenecarboxylate (61). To a slurry of 0.20 g (1.05 mmol) of cuprous iodide, 0.20 mL (2.6 mmol) of dimethyl sulfide, and 5 mL of Et_2O was added 1.1 mL (2.0 mmol) of 1.8 M methyllithium in Et_2O. The solution was stirred at 0 °C for 30 min, and 0.129 g (0.734 mmol) of **5a** dissolved in 5 mL of Et_2O was added. After the mixture was stirred at room temperature for 4 h, the reaction was quenched with aqueous NH_4Cl and 1–2 mL of concentrated NH_3. The Et_2O layer was separated and the aqueous layer washed twice with Et_2O. The organic layers were combined, washed with brine, and dried ($MgSO_4$). Removal of the solvents in vacuo yielded 0.106 g (93%) of ~70% pure **61**. Chromatography on silica gel with CH_2Cl_2 as eluent gave 65 mg (56%) of **61**: IR (neat), 1715, 1665 cm^{-1}; NMR (CCl_4) δ 3.64 (s, 3), 2.0–2.7 (m, 2), 1.95 (br s, 3), 1.18 (d, 3, J = 6.5 Hz), 1.12 (d, 3, J = 6.5 Hz).

Methyl 2-*trans*-5,9-Trimethylspiro[3.5]nonene-1-carboxylate (62). To a slurry of 0.20 g (1.05 mmol) of cuprous iodide, 0.20 mL (2.6 mmol) of dimethyl sulfide, and 5 mL of anhydrous ether at 0 °C was added 1.1 mL (2.0 mmol) of 1.8 M methyllithium in Et_2O. The reaction mixture was stirred for 30 min at 0 °C, and 0.169 g (0.697 mmol) of **12** dissolved in 5 mL of Et_2O was added. The reaction was stirred at 25 °C for 2 h. Workup as described above gave 0.126 g (18%) of crude **62**. Purification by preparative thick-layer chromatography with 1:1 petroleum ether–Et_2O as eluent gave 89 mg (57%) of **62**: IR (neat) 1715, 1662 cm^{-1}; NMR (CCl_4) δ 3.65 (s, 3), 2.5–1.2 (m, 10), 1.98 (br s, 3), 1.01 (d, 3, J = 7 Hz), 0.91 (d, 3, J = 7 Hz). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.98. Found: C, 75.40; H, 9.65.

Methyl (*E*)-3-(*syn*-Bicyclo[2.2.1]hept-2-en-7-yl)but-2-enoate (63). To a cold slurry (0 °C) of 0.310 g (1.63 mmol) of cuprous iodide and 10 mL of Et_2O was added 1.7 mL (3.2 mmol) of 1.9 M methyllithium in Et_2O. The reaction mixture was stirred 30 min at 0 °C, and 0.120 g (0.56 mmol) of **21** (ca. 90% pure) dissolved in 5 mL of Et_2O was added. After the mixture was stirred for 4 h, workup as described above yielded 0.107 g (99%) of **63**: IR (neat) 1720, 1650 cm^{-1}; NMR (CCl_4) δ 5.82 (dd, 2, J = 2 Hz), 5.35 (br, 1), 3.58 (s, 3), 2.92 (m, 2), 2.45 (m, 1), 2.02 (br s, 3), 1.5–1.9 (m, 2), 0.8–1.5 (m, 2). An impurity present to the extent of 10% which may be the anti isomer of **63** was detected by NMR signals at δ 3.63 (s, 3) and 2.05 (s, 3). A similar impurity was present in **21**.

Methyl 3-(*syn*-Bicyclo[2.2.1]hept-2-en-7-yl)propiolate (64). To 0.42 g (2.7 mmol) of potassium carbonate, 0.5 g (27 mmol) of tetraethylammonium fluoride dihydrate, and 5 mL of acetonitrile was added 58.5 mg (0.275 mmol) of **21** (~90% pure). After being stirred for 5 min, the reaction mixture was poured into 25 mL of water and extracted with 75 mL of Et_2O. The Et_2O layer was washed with brine and dried ($MgSO_4$), and the solvent was removed to yield 40.8 mg (84%) of product which the NMR showed to be ≥90% pure: IR (neat) 2215, 1710, 1600 cm^{-1}; NMR (CCl_4) δ 5.98 (dd, 2, J = 2, 2 Hz), 3.63 (s, 3), 2.90 (m, 2), 2.33 (m, 1), 1.0–2.0 (m, 4). An impurity (~10%) which may be the anti isomer was detected by an NMR signal at δ 3.68 (s, 3). A similar impurity was present in **21**.

Methyl 3-(*syn*-Bicyclo[2.2.1]hept-2-en-7-yl)-3-oxopropionate (67). To a solution of 0.129 g (0.61 mmol) of **21** in 5 mL of MeOH was added 0.44 mL of 1.5 M NaOMe in MeOH. The reaction was heated at reflux overnight, and an additional 0.44 mL of NaOMe was added. After being heated at reflux overnight, the reaction mixture was poured into 25 mL of 10% HCl and extracted (2 × 50 mL) with Et_2O. The Et_2O layer was washed with brine and dried (K_2CO_3), and the solvent was removed in vacuo. The crude reaction product was dissolved in 2 mL of MeOH, and 2 drops of concentrated HCl and 10 drops of water were added. The solution was stirred for 2 days. Normal workup gave 77 mg (65%) of crude **67**. Purification on silica gel with 4:1 petroleum ether–Et_2O as eluent gave 56 mg (47%) of pure **67** as a 3:1 mixture of the keto and enol forms: IR (neat) 1750, 1710, 1650, 1630 cm^{-1}; NMR (CCl_4) δ 10.9 (s, 1, enol OH), 5.8 (dd, 2, J = 2, 2 Hz), 4.68 (s, 1, enol HC=C), 3.57 (s, 3), 3.17 (s, 2, ketone), 3.12 (m, 2), 2.37 (m, 1), 1.8–2.0 (m, 2), 0.9–1.2 (m, 2). Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26. Found: C, 67.81; H, 7.48.

Dimethyl 2,3,3-Trimethylpentanedioate (70a). To 135.1 mg (0.716 mmol) of **13** were added 1.5 mL of 1.6 M NaOMe in MeOH and 10 mL of MeOH. This was refluxed for 10 h, poured into saturated aqueous NH_4Cl, and extracted with Et_2O. The organic phase was washed with brine, dried (K_2CO_3), and evaporated, giving 112 mg of a 1:1 mixture of di- and monoadducts **68a** and **69a**: NMR (CCl_4) δ 4.07 (s, 3, **69**), 3.55 and 3.60 (2 s, 3, **68** and **69**), 3.18 (s, 3, **68**), 3.08 (s, 3, **68**), 2.58 (br s, 1, **68**), 2.0–2.5 (m, 1), 1.20, 1.17, 1.07, and 1.03 (4 s, 6, **68** and **69**), 0.95 and 0.88 (2 d, 3, J = 7 Hz, **68** and **69**). The crude reaction product was dissolved in 10 mL of MeOH, excess hydrochloric acid was added, and the solution was stirred overnight and worked up as described above, giving 81 mg (56%) of **70a**: NMR (CCl_4) δ 3.62 (s, 3), 2.52 (q, 1, J = 7 Hz), 2.28 (AB d, 2), 1.11 (d, 3, J = 7.5 Hz), 1.03 (s, 6).

Dimethyl *threo*-2,3-Dimethylpentanedioate (70b). To a solution of 68 mg (0.39 mmol) of **5a** in 5 mL of MeOH was added 0.3 mL of 1.5 M NaOMe in MeOH. The reaction was stirred at 25 °C for 2 days. Workup yielded 51 mg (77%) of a 3:1 mixture of **69b** and **68b**. The spectral data for **69b** are as follows: NMR (CCl_4) δ 4.10 (s, 3), 3.60 (s, 3), 1.8–2.3 (m, 2), 1.15 (d, 3, J = 7 Hz), 1.12 (d, 3, J = 7 Hz). The spectral data for **68b** are as follows: NMR (CCl_4) δ 3.70 (s, 3), 3.17 (s, 3), 3.13 (s, 3), 1.8–2.3 (m, 2), 1.22 (d, 3, J = 7 Hz), 1.18 (d, 3, J = 7 Hz). The crude reaction mixture was dissolved in 25 mL of MeOH, and 10 drops of concentrated HCl was added. After the solution had been stirred overnight, K_2CO_3 was added to it and the solvent removed. Et_2O and 10% HCl was added. The organic phase was separated, washed with brine, dried (K_2CO_3), and evaporated, yielding 30.5 mg (42%) of **70b** which was chromatographically pure: NMR (CCl_4) δ 3.63 (s, 6), 2.0–2.4 (m, 3), 1.09 (d, 3, J = 6.5 Hz), 0.92 (m, 3); GC t_R = 18.1 min (5-ft, 20% DEGS column, 120 °C). The NMR absorption at δ 0.92 is a multiplet since the 3-methyl group

is virtually coupled to the 4-methylene group.[26]

Dimethyl *erythro*-2,3-Dimethylpentanedioate (70c). To 108 mg (0.62 mmol) of **6a** were added 0.5 mL (0.7 mmol) of 1.5 M NaOMe in MeOH and 0.5 mL of MeOH. This was stirred at 25 °C for 2 days, hydrogen chloride was bubbled in, and 0.25 mL of water was added. The solution was stirred overnight and poured into 30 mL of water, and the mixture was extracted with Et_2O (3 × 25 mL). The Et_2O layer was washed with water and brine, dried ($MgSO_4$), and evaporated, giving 64 mg (55%) of pure **70c**: NMR (CCl_4) δ 3.63 (s, 6), 2.0–2.4 (m, 3), 1.10 (d, 3, J = 6 Hz), 0.90 (m, 3); GC t_R 17.2 min (5-ft, 20% DEGS column, 120 °C). The NMR absorption at δ 0.90 is a multiplet since the 3-methyl group is virtually coupled to the 4-methylene group.[26]

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Asymmetric Addition of Organometallics to Chiral Ketooxazolines. Preparation of Enantiomerically Enriched α-Hydroxy Acids

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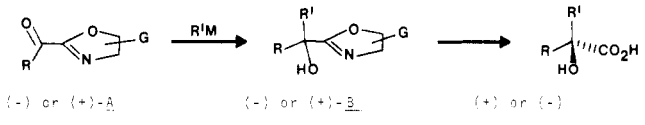
Addition of Grignard and organolithium reagents to chiral α-ketooxazolines results in α-substituted α-hydroxyoxazoline derivatives which on hydrolytic removal of the chiral auxiliary groups give rise to α-substituted α-hydroxy acids in 30–87% enantiomeric excess (ee). Studies on the various parameters (solvents, temperature, substituents) were undertaken to reach optimum asymmetric induction.

In 1904, McKenzie[1] applied the newly discovered Grignard reaction to the first asymmetric addition to chiral α-keto esters, forming the basis for extensive studies later performed by Prelog.[2] The results of these studies by Prelog and others are now well-known as the "Prelog rule"[3] and are widely used for the correlation of absolute configuration of chiral alcohols and acids. Furthermore, Grignard addition to chiral α-keto esters has been employed as a route to chiral α-hydroxy acids. However, in spite of the many studies[4] in this area, all but the single example by Berson and Greenbaum[5] have generally met with disappointing results. The enantiomeric purity of various α-hydroxy acids derived from chiral α-keto esters ranged from 0 to 30% except in the Berson report which utilized a chiral biaryl system to achieve atrolactic acid in 93% ee. Recently, several studies have appeared using novel variations of the above method which have shown greater potential in reaching chiral α-hydroxy acids in greater enantioselectivity (50–99%).[6]

This report is concerned with the further use of chiral oxazolines as auxiliary groups in asymmetric synthesis[7] and their application to chiral α-substituted α-hydroxy acids. By addition of organolithium or Grignard reagents to various optically active α-ketooxazolines ((+)-A), excellent



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