Acyclic Stereoselection. 44. Diastereoselectivity in the Ortho Ester Claisen Rearrangement of Chiral Propargylic Alcohols. Use of β-Allenic Esters as Chiral Methylmalonaldehyde Synthons[1]

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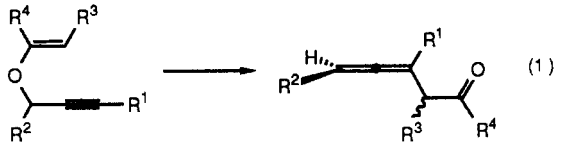
Received February 2, 1988

The diastereoselectivity of the ortho ester Claisen rearrangement of chiral propargylic alcohols has been investigated for alcohols **6–12** (eq 3). The results of this study, summarized in Table II, show that aryl-substituted propargyl alcohols **11** and **12** react stereorandomly. However, alkyl-substituted propargyl alcohols **6–10** show a preference for formation of the 2*S**,4*S** diastereomer, with stereoselectivity increasing with increasing steric bulk of R. In the most favorable case (compound **10**), a 95:5 mixture of diastereomeric products is produced. The diastereoselectivity of the process was established by the use of scalemic alcohols (*R*)-(+)-**8**, (*S*)-(−)-**10**, and (*R*)-(+)-**10**, which were obtained by resolution of the racemates (Schemes II and III). As shown in Scheme IV, (*R*)-(+)-**8** and (*S*)-(−)-**10** were each converted into the known acid (*S*)-(+)-**28**. Given the known relationship between the stereogenicity of a chiral propargylic alcohol and the chiral allene resulting from Claisen rearrangement, it may be deduced that (*S*)-**8** and (*R*)-**10** react via the derived *E* ketene acetals to give, preferentially, the 2*S*,4*S* β-allenic esters. For the alkyl series, the results are explained by a mechanism (Scheme I) wherein the *E* and *Z* ketene acetals are in rapid equilibrium, with the *E* isomer reacting significantly more rapidly than the *Z* isomer. The observed effect of size of R on the stereoselectivity of the reaction is explained in terms of 1,3-interactions in the two alternative reacting conformations of the ketene acetal (Scheme I, E vs E′). For propargyl alcohols **11** and **12**, it is postulated that Claisen rearrangement is sufficiently accelerated by the aryl substituent that ketene acetal formation becomes the rate-limiting step; the observed 1:1 product ratios in these cases are believed to be a reflection of the ratio of double-bond isomers in the initial ketene acetal. It has been demonstrated that the ester and allenic functions may be manipulated independently, so that the chiral β-allenic esters may be used as "chiral methylmalonaldehyde" synthons.

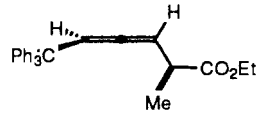
Introduction

The propargylic Claisen rearrangement involving a β-substituted vinyl participant is a potentially powerful reaction because diastereomeric products may be generated, one asymmetric center positioned at the central atom of the allene, the other flanked by the allene and the newly formed carbonyl functionality (eq 1). Remarkably, there



(1)

are apparently only three such reactions reported in the literature,[3-5] and only one of these[5] addresses stereochemistry. In this paper, we report a study of this question. It will be shown that, in suitable cases, the reaction proceeds with high diastereoselectivity. In these cases, use of a secondary propargylic alcohol in which the carbinol position is stereogenic leads to products (e.g., **1**, **2**) that are "chiral methylmalonaldehyde" equivalents.



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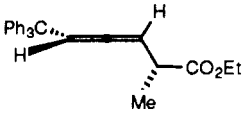

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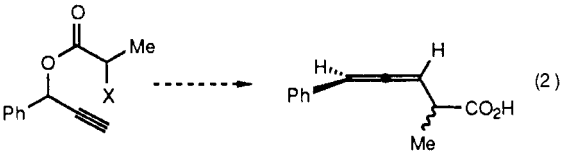
Table I. Synthesis of Ynols 6–12

aldehyde	product	yield (%)	scale
isobutyraldehyde	**7**	73	73 mmol
pivalaldehyde	**8**	86	200 mmol
cyclohexanecarboxaldehyde	**9**	76	50 mmol
triphenylethanal	**10**	83	83 mmol
benzaldehyde	**11**	50	240 mmol
mesitaldehyde	**12**	67	36 mmol

Results and Discussion

In our first approach to the problem, we sought to employ the Ireland modification of the Claisen rearrangement[6] with propionate **3** (eq 2), since the scalemic[7] sec-



(2)

3: X = H
4: X = Br

5

ondary alcohol is available in high enantiomeric purity.[8] Examination of this reaction using racemic ynol demonstrated the problems encountered with this reaction scheme. All attempts to perform the Ireland–Claisen rearrangement on ester **3** met with failure. The key problem with this reaction was competitive removal of the ace-

(1) For part 43, see: Hoagland, S.; Morita, Y.; Bai, D. L.; Märki, H.-P.; Kees, K.; Heathcock, C. H. *J. Org. Chem.*, previous paper in this issue.
(2) Present address: Syntex Research, Mailstop R6-201, 3401 Hillview Avenue, Palo Alto, CA 94304.
(3) Saucy, G.; Marbet, R. *Helv. Chim. Acta* **1967**, *50*, 1158.
(4) Saucy, G.; Cohen, N.; Banner, B. L.; Trullinger, D. P. *J. Org. Chem.* **1980**, *45*, 2080.
(5) Fujisawa, T.; Maehata, E.; Kohama, H.; Sato, T. *Chem. Lett.* **1985**, 1457.
(6) Ireland, R. E.; Mueller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1979**, *101*, 6693.
(7) The term *scalemic* has been suggested by Professor James Brewster, of Purdue University, to describe an unequal mixture of enantiomers (personal communication). According to Brewster's suggestion, scalemic and racemic are the macroscopic analogues of chiral and achiral, adjectives that are best reserved for single objects, such as molecules.
(8) Midland, M. M.; Tramontano, A.; Kazubski, A.; Graham, R. S.; Tsai, D. J. S.; Cardin, D. B. *Tetrahedron* **1984**, *40*, 1371.

0022-3263/88/1953-4736$01.50/0

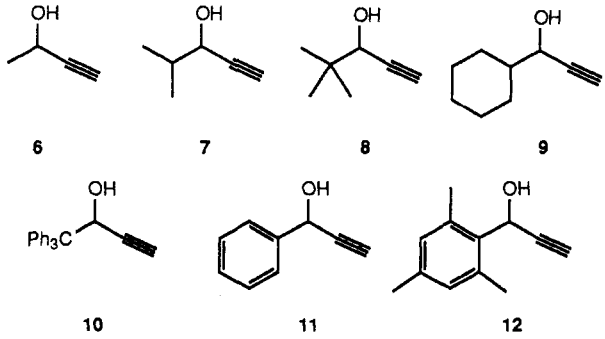
Table II. Ortho Ester Claisen Rearrangement of Ynols 6–12 (eq 3) (Conditions: 100 °C, 2.5 h, cat. C_2H_5COOH)

ynol	product	yield (%)	diastereomer ratio (a:b)
6	13	63	65:35[a]
7	14	47	86.7:13.3[b]
8	15	62	89.6:10.4[b]
9	16	76	81.1:18.9[b]
10	17	39	92:8[a]
11	18	56	50:50[a]
12	19	63	50:50[a]

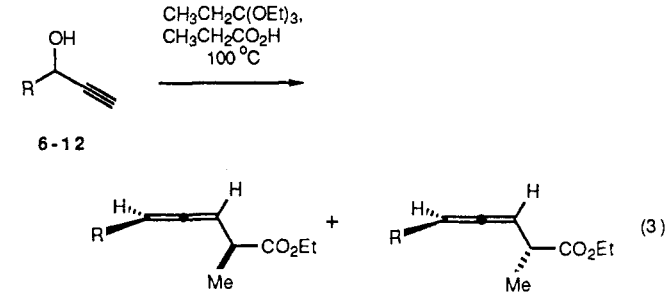
[a] Measured by ^1H NMR and ^{13}C NMR spectroscopy. [b] Determined by capillary gas–liquid chromatography.

tylenic proton; only a complex mixture of decomposition products could be isolated. Use of the Reformatsky–Claisen[9] variation, using bromo ester **4**, led mainly to debrominated ester **3**; only a trace of what appeared to be allene was identified by ^1H NMR spectroscopy.

More success was encountered with the ortho ester Claisen rearrangement, a well-known process for the preparation of β-allenic esters.[5,10] The reagents required for this study were readily accessible. Triethyl orthopropionate and but-1-yn-3-ol (**6**) were used as supplied by commercial sources. The remaining ynols (**7–12**) were synthesized by the addition of the corresponding aldehydes to a solution of lithium acetylide. A variation of a procedure by Midland,[11] acetylene was bubbled into THF at −78 °C until an excess was assured. Slow addition of *n*-butyllithium in hexanes at this low temperature allows formation of lithium acetylide while suppressing the dimer formed by disproportionation. Addition of aldehydes to the lithium acetylide solution at −78 °C followed by warming to room temperature led to good to excellent yields of ynols (Table I).



Ynols **6–12** served as probes of the stereochemical course of the ortho ester Claisen rearrangement of propargylic alcohols with triethyl orthopropionate. Each ynol was subjected to identical reaction conditions. A stirring solution of 2.0 mmol of ynol, 3.3 mmol of ortho ester, and 1 drop of propanoic acid was heated in an oil bath maintained at 100 °C for 2.5 h. These reactions resulted in the formation of allene ester diastereomers **13a–19a** and **13b–19b** (eq 3). No attempts to maximize the yields of these reactions were made for this particular study. The crude reaction mixtures were analyzed by capillary gas–liquid-phase chromatography and NMR spectroscopy. The results of these reactions are enumerated in Table II.



13a: R = Me
14a: R = i-Pr
15a: R = t-Bu
16a: R = cyclohexyl
17a: R = Ph_3C
18a: R = Ph
19a: R = mesityl

13b: R = Me
14b: R = i-Pr
15b: R = t-Bu
16b: R = cyclohexyl
17b: R = Ph_3C
18b: R = Ph
19b: R = mesityl

In the series of aliphatic ynols **6–8**, a clear correlation of diastereoselectivity and steric bulk is observed. These findings prompted the inclusion of cyclohexyl ynol **9** and triphenylmethyl ynol **10** in the study. The cyclohexyl ring apparently presents a smaller steric target than a *tert*-butyl group, or even an isopropyl group. The triphenylmethyl group, as expected, provided the highest diastereoselectivity, confirming the unquestionable influence of steric bulk on the stereochemical course of these reactions. In contrast, however, both of the aromatic substrates (**11** and **12**) display identical results of no diastereoselectivity despite their considerably different sizes.[12]

The stereochemistry of the ortho ester Claisen rearrangement may be discussed in light of Scheme I (in which the *S* enantiomer of the secondary propargyl alcohol is used for illustration). Structures E and E′ represent the two possible reacting conformations of the *E* ketene acetal and structures Z and Z′ are the corresponding reacting conformations of the *Z* stereoisomer. It will be seen from the scheme that conformations E′ and Z lead to the *RS* diastereomer of the β-allenic ester, whereas E and Z′ deliver the *SS* diastereomer. Our hypothesis is as follows:

(1) The ketene acetals are initially formed as a mixture of *E* and *Z* double-bond isomers; each ketene acetal may undergo the Claisen rearrangement through two conformations, or it may convert to the other isomer.

(2) For the aliphatic ynols **6–10** the rate of double-bond isomerization is greater than the rate of Claisen rearrangement; the *E* and *Z* ketene acetals are, therefore, in equilibrium. Either one stereoisomeric form is significantly more stable than the other, or one reacts faster than the other.

(3) The results in Table II show that in the aliphatic series (**6–10**) diastereoselectivity increases as the size of R increases. Conformations E′ and Z′ bring R and OEt into closer proximity than do conformations E and Z. Thus, increasing the size of R should favor E over E′ and Z over Z′. Note, however, that we cannot say *which* stereoisomeric ketene acetal is involved from the data in hand at this point.

(4) For the aromatic ynols **11** and **12**, we believe that the rate of Claisen rearrangement is greater than the rate of double-bond isomerization; the 50:50 mixture seen in these cases probably reflects the composition of the initially formed ketene acetal mixture. Precedent exists for such an acceleration by an aryl substituent.[13]

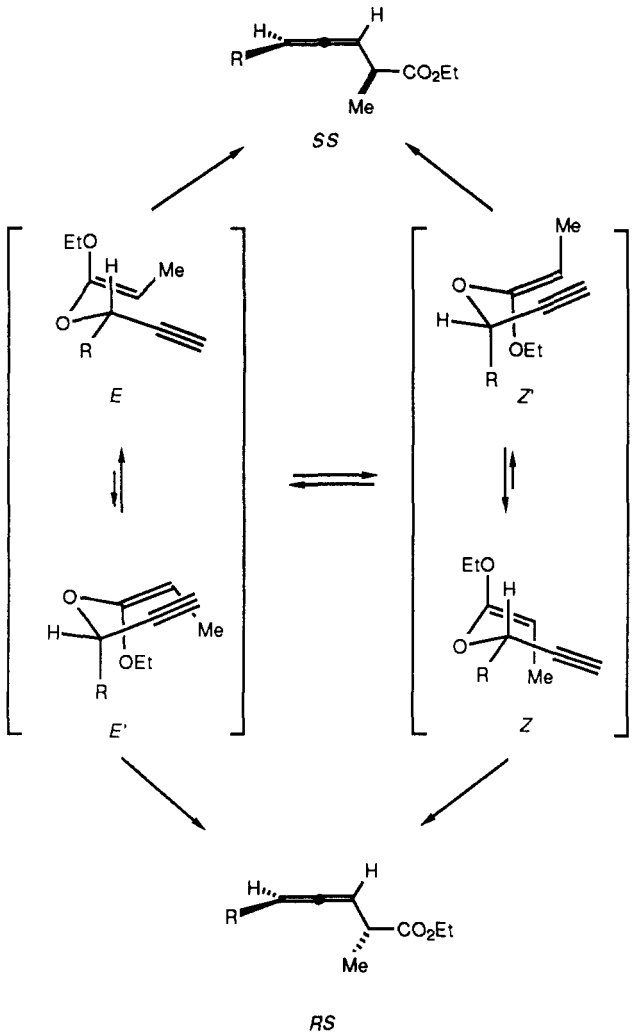
(9) Baldwin, J. E.; Walker, J. A. *J. Chem. Soc., Chem. Commun.* **1973**, 117.

(10) (a) Crandall, J. K.; Tindell, G. L. *J. Chem. Soc. D* **1970**, 1411. (b) Henrick, C. A.; Willy, W. E.; McKean, D. R.; Baggioline, E.; Siccall, J. B. *J. Org. Chem.* **1975**, *40*, 8. (c) Kocienski, P. J.; Cernigliaro, G.; Feldstein, G. *J. Org. Chem.* **1977**, *42*, 353. (d) Mori, K.; Nukada, T.; Ebata, T. *Tetrahedron* **1981**, *37*, 1343. (e) Saucy, G.; Cohen, N.; Banner, B. L.; Trullinger, D. P. *J. Org. Chem.* **1980**, *45*, 2080.

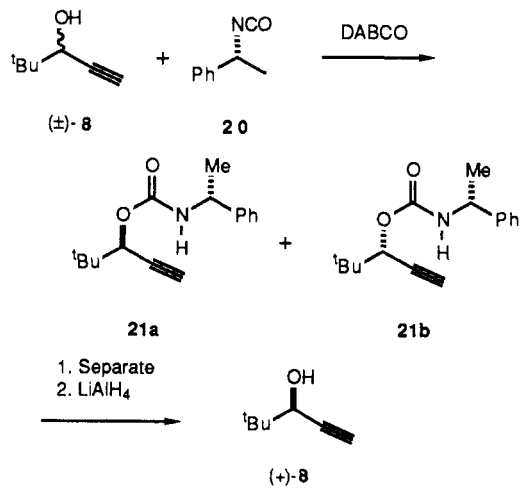
(11) Midland, M. M. *J. Org. Chem.* **1975**, *40*, 2250.

(12) The term "aromatic ynol" refers to **11** and **12**, which have an aromatic substituent directly bonded to the carbinol carbon. Triphenylmethyl ynol **10** possesses aliphatic character at the carbinol carbon and, consequently, should be considered an aliphatic ynol.

Scheme I

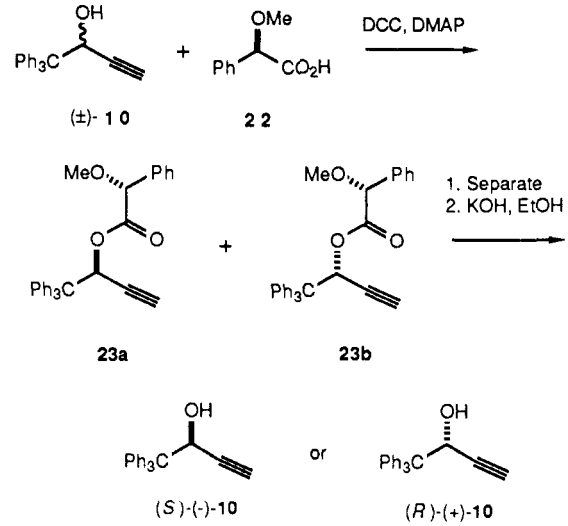


Scheme II



To determine which ketene acetal is involved in the aliphatic ynol series, we prepared the optically active ynols (*R*)-(+)-**8**, (*R*)-(+)-**10**, and (*S*)-(−)-**10**. As shown in Scheme II, racemic ynol **8** was heated at 60 °C with (*R*)-(−)-1-phenylethyl isocyanate (**20**) and a catalytic amount of triethylenediamine, producing the diastereomeric carbamates **21a** and **21b**.[14] Preparative high performance liquid chromatography (HPLC), followed by recrystallization, gave both diastereomers in pure form. Conventional efforts to release the desired ynols from these carbamates were unsuccessful. Treatment of **21a** with trichlorosilane–triethylamine complex[15] produced only modest yields, with starting carbamate present in the reaction mixture after more than 3 days at ambient temperature. Reduction of **21a** with a large excess of $LiAlH_4$ in refluxing ether–THF produced (*R*)-(+)-**8** (98% ee) in good yield. The absolute configuration and optical purity of this material were established by comparison of optical rotation measurements with literature values.[16]

Scheme III



As shown in Scheme III, racemic **10** was converted into diastereomeric esters **23a** and **23b** by using (*R*)-(−)-*O*-methylmandelic acid (**22**)[17] and dicyclohexylcarbodiimide (DCC).[18] Chromatography and recrystallization of these esters, followed by gentle hydrolysis with KOH/methanol, provided (*R*)-(+)-**10** and (*S*)-(−)-**10**. The absolute configurations of (*R*)-(+)-**10** and (*S*)-(−)-**10** were assigned by the ^1H NMR chemical shift method of Dale and Mosher.[19] This assignment is confirmed by the reactivity of (*S*)-(−)-**10**, which gives a β-allenic ester of the same configuration as does (*R*)-(+)-**8** (vide infra).[34]

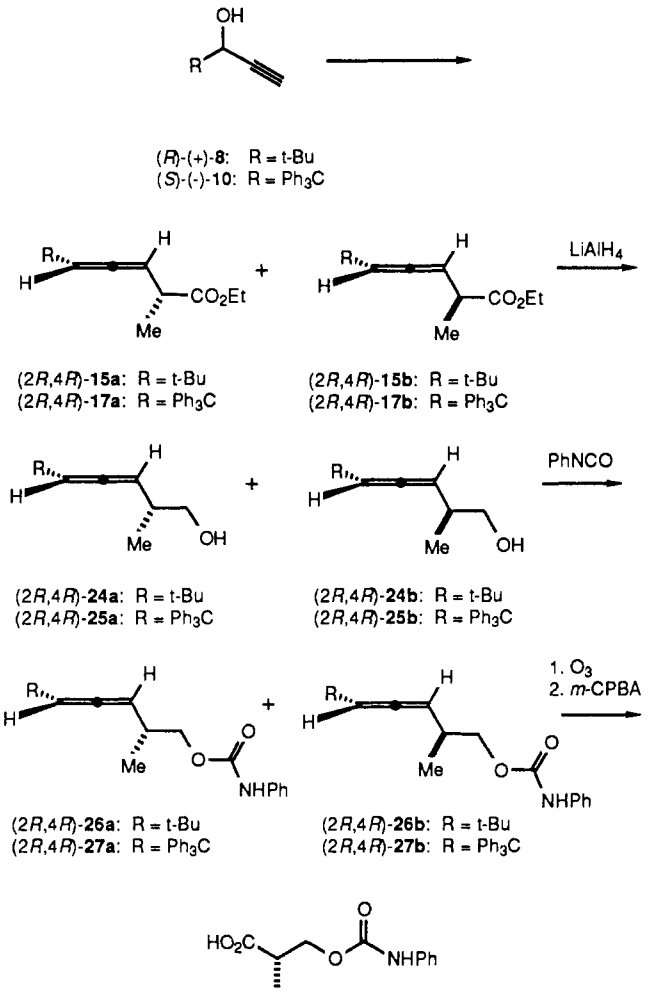
The relative diastereoselectivity of the ortho ester Claisen rearrangement of propargylic alcohols with triethyl orthopropionate was determined as follows. It has previously been shown that, in the Claisen rearrangement of the propargyl vinyl ethers, the absolute configuration of the carbinol is directly correlated with that of the allene.[10d,20] Consequently, (*R*)-(+)-**8** and (*S*)-(−)-**10** should give 4*R* allenes **15** and **17**, respectively. Given this fact, the relative diastereoselectivity of these reactions may be ascertained simply by determining the absolute configuration of C-2 in the β-allenic ester products.

As shown in Scheme IV the ortho ester Claisen rearrangement of (*R*)-(+)-**8** gives a 9:1 mixture of (2*R*,4*R*)-**15a** and (2*S*,4*R*)-**15b**. Reduction of this mixture of diastereomers with $LiAlH_4$ at 0 °C in ether provides allenols (2*R*,4*R*)-**24a** and (2*S*,4*R*)-**24b** in excellent yields. Reaction of **24a** and **24b** with phenyl isocyanate at 60 °C leads to

(13) Gajewski, J. J.; Emrani, J. *J. Am. Chem. Soc.* **1984**, *106*, 5733.

(14) Pirkle, W. H.; Hoekstra, M. S. *J. Org. Chem.* **1974**, *39*, 3904.
(15) Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1977**, *42*, 2781.
(16) Vigneron, J.-P.; Bloy, V. *Tetrahedron Lett.* **1979**, 2683.
(17) Neilson, D. G.; Peters, D. A. V. *J. Chem. Soc.* **1962**, 1519.
(18) Hassner, A.; Alexania, V. *Tetrahedron Lett.* **1978**, 4475.
(19) Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.
(20) Jones, E. R. H.; Loder, J. D.; Whiting, M. C. *Proc. Chem. Soc.* **1960**, 180.

Scheme IV



a 9:1 mixture of carbamates (2*R*,4*R*)-**26a** and (2*S*,4*R*)-**26b**. Unfortunately, none of these diastereomers may be conveniently separated, either by chromatography or recrystallization. Ozonolysis of the 9:1 mixture of **26a** and **26b** followed by oxidation of the product aldehyde with *m*-chloroperoxybenzoic acid (MCPBA) gave known carboxylic acid **28**.[21] The optical rotation of this product corresponded to an optical purity of 68% ee for (*S*)-(+)-**28**. This 84:16 mixture of enantiomers is in good agreement with the expected value, given the diastereomeric ratio of **15a** and **15b** and the optical purity of (*R*)-(+)-**8**. Reaction with (*S*)-(−)-**10** and (*R*)-(+)-**10** proceeded in an analogous manner, (*S*)-(−)-**10** leading to (*S*)-(+)-**28** via allenols (2*R*,4*R*)-**25a** and (2*S*,4*R*)-**25b**, and carbamates (2*R*,4*R*)-**27a** and (2*S*,4*R*)-**27b**, while (*R*)-(+)-**10** provided (*R*)-(−)-**28** by way of allenols (2*S*,4*S*)-**25a** and (2*R*,4*S*)-**25b**, which were in turn converted to carbamates (2*S*,4*S*)-**27a** and (2*R*,4*S*)-**27b**.

These results lead to the conclusion that the major diastereomer of the products of the ortho ester Claisen rearrangement of ynols **6–10** results from rearrangement of the intermediate possessing the *E* configuration of the ketene acetal double bond. However, it is still not clear why this should be so. There are two possibilities: (a) Claisen rearrangement is rate-limiting, the *E* and *Z* ketene acetals are in rapid equilibrium, and the *E* isomer undergoes the Claisen rearrangement much faster than the *Z* isomer or, (b) the Claisen rearrangement is rate-limiting, the *E* and *Z* ketene acetals are in rapid equilibrium, and the *E* isomer is significantly more stable than the *Z* isomer. We favor the former explanation because there is, in fact, literature precedent that *E* crotyl-type systems undergo the Claisen rearrangement faster than their *Z* counterparts.[22,23]

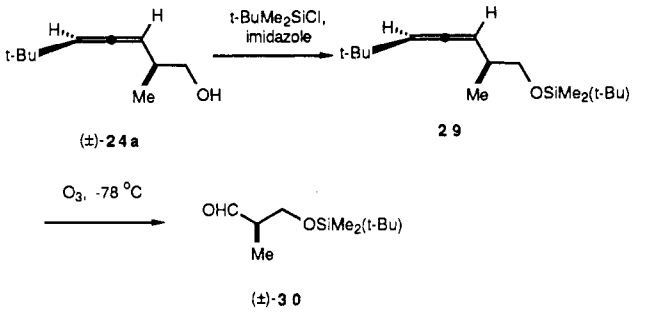
(21) Sprecher, M.; Sprinson, D. B. *J. Biol. Chem.* **1966**, *241*, 868.

Table III. Preparative Ortho Ester Claisen Rearrangements of Ynols 8 and 10

ynol	mmol ynol	mmol ortho ester	acid[a]	conditions[b]	yield, %	diastmr ratio
8	2.0	3.3	1 drop	A	58	91:9
8	6.0	10	2 drops	B	76	91:9
8	10.0	40	0.13 mmol	C	92	90:10
10	2.0	10	0.20 mmol	D	89	95:5
10	3.8	19	0.40 mmol	E	82	93:7
10	10.0	50	1.00 mmol	F	81	95:5

[a] Propanoic acid. [b] See Experimental Section for reaction conditions.

Scheme V



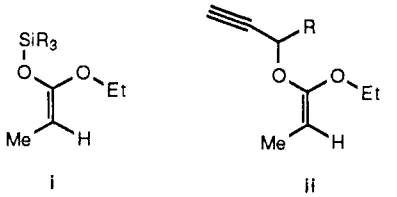
Synthetic Utility. The original purpose of this study was the development of a chiral methylmalonaldehyde equivalent. Steps were therefore taken to optimize the stereoselectivity of the process on a preparative scale and demonstrate that β-allenic esters are viable methylmalonaldehyde synthons.

As expected, reduction of the reaction temperature increases the diastereoselectivity of the rearrangement (Table III). Ynols **8** and **10** both show marked increases in selectivity when the reaction is performed initially at 80 °C, with final heating to 100 °C to drive the reaction to completion. Allenic ester **15** may be produced in high yields with consistent 10:1 diastereoselectivity. Ynol **10** leads to excellent yields of **17** with a diastereoselectivity of 95:5.

In general, the aliphatic β-allenic ester products of the Claisen rearrangement are stable and may be stored at

(22) (a) Vittorelli, P.; Winkler, T.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta* **1968**, *51*, 1457. (b) Hansen, H.-J.; Schmid, H. *Tetrahedron* **1974**, *30*, 1959. (c) Cresson, P.; Lecour, L. *C. R. Acad. Sci., Ser. C* **1966**, *262*, 1157. (d) Cresson, P.; Bancel, S. *Ibid.* **1968**, *266*, 409. (e) Wilcox, C. S.; Babston, R. E. *J. Am. Chem. Soc.* **1986**, *108*, 6636.

(23) It is true that silyl alkyl ketene acetals exhibit a thermodynamic preference for the *Z* stereoisomer; Wilcox, C. S.; Babston, R. E. *J. Org. Chem.* **1984**, *49*, 1451. The rationale for this behavior is that the ketene acetal adopts a "pinwheel" conformation (i). However, the presumably more stable Wilcox–Babston conformation of the intermediate ketene acetals of ynols 6–10 (structure ii) cannot undergo the Claisen rearrangement.



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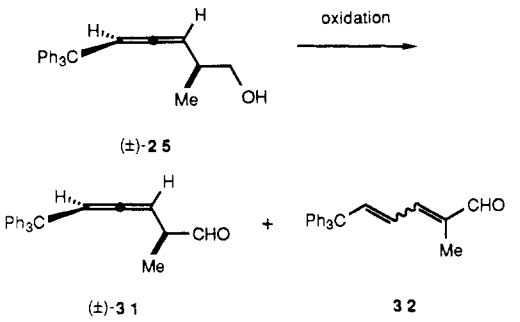
Scheme VI



room temperature under a normal atmosphere for long periods. The aromatic products **18** and **19**, however, appear to be oxygen-sensitive; benchtop storage of **18** for less than 1 day led to the distinct odor of benzaldehyde. As the aromatic allenes cannot be made in synthetically useful diastereomeric ratios, this problem is of little concern.

Utilization of β-allenic esters as synthons for the methylmalonaldehyde unit requires manipulation of both the ester and allene groups. As noted previously (Scheme IV) reduction of **15** or **17** with $LiAlH_4$ at 0 °C leads to β-allenic alcohols **24** and **25**, respectively.[24] Of particular importance, the diastereomers of **25** are crystalline compounds. Recrystallization of the 95:5 mixture of **25** from hexanes allows the isolation of the major diastereomer. Both **24** and **25** have been successfully derivatized to their phenylcarbamates (**26** and **27**), and **24** may be protected with *N*-(*tert*-butyldimethylsilyl)imidazole[25] to give silyl ether **29** (Scheme V). Ozonolysis[26] of **29** leads directly to aldehyde **30** with no workup of reactive intermediates required.

Formation of β-allenic aldehyde **31** is much more difficult. Although the aliphatic β-allenic esters **13**–**19** all appear to be stable to mildly basic conditions, aldehydes, such as **31**, readily isomerize to the conjugated dienal in the presence of base. Oxidation of β-allenic alcohol **25** with CrO_3–pyridine complex by the Ratcliff–Rodehorst procedure[27] leads to rearranged dienal **32** as a mixture of stereoisomers. Swern oxidation[28] also produced only conjugated dienal, as did oxidation using pyridinium dichromate.[29] The desired aldehyde **31** may be synthesized in crude form through the use of the acidic oxidizing reagent, pyridinium chlorochromate (PCC) (Scheme VI).[30] Oxidation of **25** by PCC at room temperature in CH_2Cl_2, followed by workup with dilute aqueous acid to remove free pyridine, leads to a mixture of **31** and **32** in a ratio of >90:10. Attempted purification of this material by column chromatography on silica gel, however, promotes rearrangement. Consequently, the recommended use of this compound as a synthon calls for the direct use of the crude oxidation product.

In summary, the practical synthesis of a "chiral methylmalonaldehyde" equivalent has been demonstrated. The ortho ester Claisen rearrangement of optically active ynol **10** produces β-allenic esters **17** with high diastereoselectivity. The synthesis of optically active **10** is somewhat cumbersome at present; a more effective route to these enantiomers would be welcome.[31] Nevertheless, the demonstrated ability of this reaction to selectively produce either absolute configuration for an asymmetric carbon center between two carbonyl equivalents should make this new method a useful synthetic tool.

Experimental Section

General. Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Ether and tetrahydrofuran (THF) were distilled from sodium/benzophenone immediately before use. Acetylene was scrubbed by sequential passage through concentrated H_2SO_4 and KOH pellets. All reactions involving organometallic reagents were conducted under a nitrogen atmosphere. Boiling points and melting points (Pyrex capillary) are uncorrected. IR spectra were determined as solutions in chloroform unless otherwise noted. All NMR spectra were measured by using $CDCl_3$ solutions, unless otherwise noted. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane. Significant ^1H NMR data are tabulated in order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), number of protons, coupling constant(s) in hertz. High performance liquid chromatography (HPLC) was done with a Waters Model ALC/GPC-244 liquid chromatograph equipped with a Hewlett-Packard Model 3390A reporting integrater (analytical) or a Waters PrepLC/system 500 (preparative). μ-Porasil columns were used unless otherwise indicated. Capillary gas–liquid-phase (GLP) chromatographic analyses were performed on a Hewlett-Packard Model 5890A gas chromatograph equipped with a Hewlett-Packard Model 3392A integrator. Elemental analyses were performed by the Microanalytical Laboratory, operated by the College of Chemistry, University of California, Berkeley, CA 94720.

General Procedure for the Synthesis of Ynols 6–12. A dry three-necked, round-bottomed flask equipped with a magnetic stirring bar, septum, and a sintered glass gas bubbling tube was purged with nitrogen, charged with THF, and cooled in a dry ice–acetone bath. Scrubbed acetylene was introduced until an excess volume was present. A 1.5 M solution of *n*-butyllithium in hexanes was slowly added to the acetylene solution to form an approximate 0.5 M solution of lithium acetylide. After a few minutes, the corresponding aldehyde was introduced at −78 °C. The reaction mixtures were allowed to warm to room temperature and were worked up by one of two methods. **Method A.** The reaction was quenched with 40 mL of water, and anhydrous K_2CO_3 was added until the aqueous layer had the consistency of paste. The organic portion was decanted, and the paste was washed with 4 × 50 mL of ether. The combined organic portions were dried ($MgSO_4$), filtered, and concentrated. **Method B.** The reaction mixture was quenched with water and diluted with ether, and the organic layer was washed with water to remove the THF. The organic portion was dried ($MgSO_4$), filtered, and concentrated.

4-Methylpent-1-yn-3-ol (7). Following the general procedure, a 300-mL flask was charged with 110 mL of THF and at least 4 mL of acetylene. Over 15 min, 50.0 mL (80 mmol) of *n*-butyllithium in hexanes was added. After 10 min, 5.2 g (6.6 mL, 73 mmol) of isobutyraldehyde was added by syringe over 2 min. The mixture was stirred for 20 min, the cooling bath was removed, and the solution warmed to room temperature over 2 h. Workup (method A) followed by distillation of the residue at atmospheric pressure afforded 5.23 g (73%) of **7**, bp 130–135 °C (lit.[32] bp 131–132 °C). IR (neat): 3380 (br), 3320, 2120, 1475, 1040 cm^{-1}. ^1H NMR: δ 1.01 (d, 3, J = 6.8), 1.02 (d, 3, J = 6.8), 1.8–2.0 (m, 2), 2.46 (d, 1, J = 2.1), 4.18 (ddd, 1, J = 2.1, 5.7, 5.7). ^{13}C NMR: δ 17.17, 17.90, 34.12, 67.47, 73.42, 83.59.

(24) Attempted reduction of **15** with diisobutylaluminum hydride led to a conjugated aldehyde.

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(31) It is possible that scalemic **8** and **10** could be obtained by the method of Mukaiyama and co-workers, reaction of 1-lithio-2-(trimethylsilyl)acetylene with the appropriate aldehydes in the presence of the chiral auxiliary (2*S*,2′*S*)-2-(hydroxymethyl)-1-[(1-methylpyrrolidin-2-yl)methyl]pyrrolidine; Mukaiyama, T.; Suzuki, K.; Soai, K.; Sato, T. *Chem. Lett.* **1979**, 447.

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4,4-Dimethylpent-1-yn-3-ol (8). Following the general procedure, a 300-mL flask was charged with 150 mL of THF and at least 5 mL of condensed acetylene. Over 20 min, 73 mL (0.11 mol) of *n*-butyllithium in hexanes was added, the solution was stirred for 5 min, and 8.6 g (10.8 mL, 0.10 mol) of pivalaldehyde was added. The reaction mixture was stirred for 1 h and warmed to room temperature over 2 h. Workup (method B) followed by Kugelrohr distillation provided 9.77 g (87%) of **8**. IR (neat): 3420 (br), 3325, 2130, 1375, 1070, 1020 cm^{-1}. ^1H NMR: δ 1.01 (s, 9), 1.76 (d, 1, J = 6.2), 2.45 (d, 1, J = 2.2), 4.02 (dd, 1, J = 2.2, 6.2). ^{13}C NMR: δ 25.04, 35.46, 70.91, 73.56, 83.61.

(1-Hydroxyprop-2-ynyl)cyclohexane (9). Following the general procedure, a 300-mL flask was charged with 70 mL of THF and at least 2 mL of condensed acetylene. Over 30 min, 33.4 mL (50.1 mmol) of *n*-butyllithium in hexanes was added, the solution was stirred for 5 min, and 5.61 g (6.06 mL, 50.0 mmol) of freshly distilled cyclohexanecarboxaldehyde was added at once. The reaction mixture was stirred for 30 min and warmed to room temperature over 1.5 h. Workup (method B) followed by Kugelrohr distillation produced 5.22 g (76%) of **9**. IR (neat): 3380 (br), 3310, 2935, 2860, 1505, 1030 cm^{-1}. ^1H NMR: δ 1.0–1.2 (m, 5), 1.24–1.9 (m, 7), 2.47 (d, 1, J = 2.2), 4.16 (ddd, 1, J = 2.2, 5.9, 5.9). ^{13}C NMR: δ 25.75, 25.78, 26.27, 27.88, 28.36, 43.79, 66.88, 73.54, 83.91. Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.01; H, 10.14.

4,4,4-Triphenylbut-1-yn-3-ol (10). Following the general procedure, a 300-mL flask was charged with 70 mL of THF and at least 3 mL of condensed acetylene. Over 30 min, 32 mL (48.0 mmol) of *n*-butyllithium in hexanes was added, the mixture was stirred for 5 min, and a solution of 12.3 g (45.0 mmol) of 2,2,2-triphenylethanal[33] and 20 mL of THF was added with a syringe. The mixture was allowed to warm to room temperature over 1 h. Workup (method B) provided crystalline **10**, mp 80–82 °C, which required no further purification. IR: 3560, 3310, 1595, 1495, 1450, 1100 cm^{-1}. ^1H NMR: δ 1.96 (d, 1, J = 9.0), 2.41 (d, 1, J = 2.2), 5.84 (dd, 1, J = 2.2, 9.0), 7.22–7.37 (m, 15). ^{13}C NMR: δ 62.26, 68.13, 76.49, 83.63, 126.76, 127.89, 129.95, 143.84. Anal. Calcd for $C_{22}H_{18}O$: C, 88.56; H, 6.08. Found: C, 88.64; H, 6.05.

1-Phenylprop-2-yn-1-ol (11). Following the general procedure, a 300-mL flask was charged with 100 mL of THF and an excess of condensed acetylene. Over 30 min, 225 mL (0.34 mol) of *n*-butyllithium in hexanes was added and the mixture was stirred for 20 min. A solution of 25.5 g (24.4 mL, 0.24 mol) of benzaldehyde and 25 mL of THF was added and the mixture was warmed to room temperature over 2 h. Workup (method B) followed by vacuum distillation led to 15.8 g (50%) of **11**, bp 63–65 °C (0.10 Torr). IR: 3595, 3400 (br), 3310, 2120, 1495, 1455, 1030, 945, 700, 655 cm^{-1}. ^1H NMR: δ 2.24 (d, 1, J = 6.3), 2.68 (d, 1, J = 2.2), 5.47 (dd, 1, J = 2.2, 6.3), 7.39 (m, 3), 7.56 (m, 2). ^{13}C NMR: δ 64.1, 74.7, 83.4, 126.5, 128.3, 128.5, 139.9.

1-(2,4,6-Trimethylphenyl)prop-2-yn-1-ol (12). Following the general procedure, a 300-mL flask was charged with 50 mL of THF and at least 2 mL of condensed acetylene. Over 20 min, 25 mL (39.8 mmol) of *n*-butyllithium in hexanes was added. Mesitaldehyde (5.34 g, 5.36 mL, 36 mmol) was added by syringe over 5 min, the reaction mixture was stirred for 2 h, and the system was allowed to warm to room temperature over 1 h. Workup (method A) followed by vacuum distillation of the residue gave 4.17 g (67%) of **12** which crystallized on standing, bp 92–94 °C (0.05 Torr), mp 65–66.5 °C. IR: 3600, 3430 (br), 3315, 2125, 1615, 1215 cm^{-1}. ^1H NMR: δ 2.0–2.2 (br s, 1), 2.26 (s, 3), 2.49 (s, 6), 2.56 (d, 1, J = 2.4), 6.89 (br d, 1, J = 2.1), 6.85 (s, 2). ^{13}C NMR: δ 20.2, 20.8, 60.1, 73.9, 83.2, 130.0, 133.0, 136.4, 137.9. Anal. Calcd for $C_{12}H_{14}O$: C, 82.72; H, 8.10. Found: C, 82.83; H, 8.08.

2,2,2-Triphenylethanal. A dry 1-L, round-bottomed flask equipped with a magnetic stirring bar and nitrogen atmosphere was charged with 500 mL of dry ether and 27.2 g (0.10 mol) of 1,1,2-triphenyloxirane. The stirring solution was treated with 71 g (61.5 mL, 0.50 mol) of freshly distilled boron trifluoride etherate and stirred at room temperature for 10 min, after which no starting material was apparent by TLC. After 20 min, water was carefully added, the organic layer was washed with water and dried ($MgSO_4$). Filtration and removal of the solvent with a rotary evaporator provided a light brown solid which was triturated with ether–hexanes to produce 22.65 g (83%) of 2,2,2-triphenylethanal, mp 101–102 °C (lit.[31] mp 104 °C). IR: 2840, 2735, 1725, 1495, 1450, 1090 cm^{-1}. ^1H NMR: δ 7.05–7.09 (m, 6), 7.31–7.36 (m, 9), 10.29 (s, 1). ^{13}C NMR: δ 69.91, 127.38, 128.35, 130.38, 140.44, 198.16.

General Procedure for Ortho Ester Claisen Rearrangements of Ynols 6–12 with Triethyl Orthopropionate. A dry round-bottomed flask equipped with a magnetic stirring bar, a nitrogen atmosphere, and a condenser was charged with 0.59 g (3.3 mmol) of commercially available triethyl orthopropionate, 2.0 mmol of ynol, and 1 drop of propionic acid. The reaction mixture was heated for 2.5 h in an oil bath maintained at 100 °C using an Omega Model 6100 temperature controller. Allene diastereomer ratios were determined by using crude products. After the ethanol produced in the reaction was removed with a rotary evaporator, the excess ortho ester was removed under high vacuum. Allenes **13** and **14** are too volatile for this method and were chromatographed directly. The allene products were isolated by column chromatography on silica gel using 2.5% ether–hexanes as eluent.

2-Methylhexa-3,4-dienoic Acid, Ethyl Ester (13). Following the general procedure, a mixture of triethyl orthopropionate, acid, and 0.14 g (2.0 mmol) of ynol **6** was heated. Chromatography yielded 0.19 g (63%) of allene diastereomers **13a** and **13b**. The ratio of diastereomers was ca. 35:65, as determined by ^1H NMR spectroscopy (peak heights of the allenic protons). IR: 3000, 1970, 1730, 1460, 1190 cm^{-1}. ^1H NMR: δ 1.25 (d, 3, J = 7.1), 1.27 (t, 3, J = 7.1), 5.17–5.28 (m, 2). ^{13}C NMR major (minor): δ 14.1, 14.2, (16.3), 16.5, (39.2), 39.3, 60.5, 88.0, (90.7), 90.8, 174.5, 204.2, (204.3). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.94; H, 9.33.

2,6-Dimethylhepta-3,4-dienoic Acid, Ethyl Ester (14). Following the general procedure, a mixture of triethyl orthopropionate, acid, and 0.20 g (2.0 mmol) of ynol **7** was heated. Capillary GLP chromatography of the crude product showed a 83.7:16.3 ratio of allene diastereomers which were not separable by ^1H NMR spectroscopy. Column chromatography led to 0.18 g (49%) of **14a** and **14b**. IR: 2980, 1960, 1730, 1185 cm^{-1}. ^1H NMR: δ 1.005 (d, 3, J = 6.8), 1.007 (d, 3, J = 6.9), 1.25 (d, 3, J = 7.1), 1.26 (t, 3, J = 7.2), 2.30 (m, 1), 3.08 (m, 1), 4.15 (q, 2, J = 7.2), 5.25–5.39 (m, 2). ^{13}C NMR: δ 14.08, 16.42, 22.18, 22.28, 27.69, 39.34, 60.52, 92.52, 174.53, 201.85. Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.64; H, 10.04.

2,6,6-Trimethylhepta-3,4-dienoic Acid, Ethyl Ester (15). Following the general procedure, a mixture of triethyl orthopropionate, acid, and 0.22 g (2.0 mmol) of ynol **8** was heated. Analysis of the crude product by capillary GLP chromatography showed a 89.55:10.45 ratio of allene diastereomers. Purification by column chromatography provided 0.24 g (62%) of **15a** and **15b**. IR (neat): 2980, 1960, 1740, 1185 cm^{-1}. ^1H NMR (major diastereomer only): δ 1.04 (s, 9), 1.25 (d, 3, J = 7.2), 1.26 (t, 3, J = 7.4), 3.08 (m, 1), 4.15 (q, 2, J = 7.1), 5.26 (dd, 1, J = 2.9, 6.3), 5.37 (dd, 1, J = 6.3, 6.3). ^{13}C NMR: δ 14.15, 16.40, 30.01, 31.75, 39.42, 60.53, 93.03, 105.48, 174.52, 200.78. Anal. Calcd for $C_{12}H_{20}O_2$: C, 73.43; H, 10.27. Found: C, 73.17; H, 10.32.

5-Cyclohexyl-2-methylpenta-3,4-dienoic Acid, Ethyl Ester (16). Following the general procedure, a mixture of triethyl orthopropionate, acid, and 0.28 g (2.0 mmol) of ynol **9** was heated. Analysis of the crude product using capillary GLP chromatography showed an allene diastereomer ratio of 80.1:19.9. Purification by column chromatography yielded 0.33 g (76%) of **16a** and **16b**. IR (neat): 2940, 1950, 1740, 1455, 1185 cm^{-1}. ^1H NMR: δ 1.0–1.2 (m, 5), 1.25 (d, 3, J = 7.2), 1.26 (t, 3, J = 7.6), 1.6–1.85 (m, 5), 1.97 (m, 1), 3.08 (m, 1), 4.15 (q, 2, J = 7.1), 5.24 (m, 1), 5.33 (m, 1). ^{13}C NMR: δ 14.10, (16.26 minor), 16.45 major, 25.95, 26.05, 32.86, 36.99, 39.35, 60.47, 92.21, (99.46 minor), 99.54 major, 174.47, 202.27 major, (202.33 minor). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.46; H, 9.97.

2-Methyl-6,6,6-triphenylhexa-3,4-dienoic Acid, Ethyl Ester (17). Following the general procedure, a mixture of triethyl orthopropionate, acid, and 0.60 g (2.0 mmol) of ynol **10** was heated. Analysis by ^1H NMR spectroscopy showed the reaction to be ca. 50% complete. The ratio of allene diastereomers was 92:8.

(33) Cope, A. C.; Trumbull, P. A.; Trumbull, E. R. *J. Am. Chem. Soc.* **1958**, *80*, 2844.

(34) Note that, because of the sequence rules, (*R*)-**8** and (*S*)-**10** have the same absolute configuration.

(Capillary GLP chromatography was not successful with this compound.) Column chromatography provided 0.30 g (39%) of pure **17a** and **17b**. IR: 3065, 1965, 1730, 1600, 1495, 1450, 1185 cm^{-1}. ^1H NMR: δ 0.91 (d, 3, J = 7.1), 1.19 (t, 3, J = 7.2), 2.98 (m, 1), 4.05 (dq, 2, J = 1.9, 7.2), 5.22 (dd, 1, J = 6.2, 8.1), 6.34 (dd, 1, J = 2.1, 6.2), 7.08–7.17 (m, 6), 7.18–7.33 (m, 9). ^{13}C NMR: δ 14.11, 16.83, 39.75, 59.07, 60.54, 94.60, 102.97, 126.28, 127.50, 129.76, 145.93, 173.91, 203.33. Anal. Calcd for $C_{27}H_{26}O_2$: C, 84.78; H, 6.85. Found: C, 84.55; H, 6.65.

2-Methyl-5-phenylpenta-3,4-dienoic Acid, Ethyl Ester (18). Following the general procedure, a mixture of triethyl orthopropionate, acid, and 0.26 g (2.0 mmol) of ynol **11** was heated. Analysis of the crude mixture using ^1H NMR showed an allene diastereomer ratio of ca. 50:50. Column chromatography led to 0.24 g (56%) of **18a** and **18b**. IR: 2990, 1955, 1730, 1190 cm^{-1}. ^1H NMR: δ 1.27 and 1.28 (2 t's, 3, J = 7.2, 7.2), 1.33 and 1.34 (2 d's, 3, J = 7.1, 7.1), 3.18–3.33 (m, 1), 4.17 and 4.18 (dq and q, 2, J = 0.5, 7.2; 7.1), 5.77 (dd, 1, J = 6.6, 14.3), 6.27, (m, 1), 7.18–7.36 (m, 5). ^{13}C NMR: δ 14.0, 16.2, 16.5, 39.3, 39.4, 60.7, 95.3, 95.4, 96.7, 96.8, 126.6, 126.9, 128.4, 133.9, 173.8, 173.9, 204.9. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 78.04; H, 7.50.

2-Methyl-5-(2,4,6-trimethylphenyl)penta-3,4-dienoic Acid, Ethyl Ester (19). Following the general procedure, a mixture of triethyl orthopropionate, acid, and 0.35 g (2.0 mmol) of ynol **12** was heated. Analysis of the crude allenes by ^1H NMR spectroscopy indicated a ca. 50:50 ratio of diastereomers. Purification by column chomatography produced 0.33 g (63%) of **19a** and **19b**. IR (neat): 3300, 3000, 1960, 1745, 1620, 1185, 865 cm^{-1}. ^1H NMR: δ 1.13 and 1.25 (2 t's, 3, J = 7.6, 7.1), 1.30 and 1.32 (2 d's, 3, J = 7.1, 7.0), 2.26 and 2.33 (2 s's, 6), 2.52 (s, 3), 3.20 (m, 1), 4.15 (q, 2, J = 7.1), 5.48 (dd, 1, J = 7.2, 15.2), 6.39 (m, 1), 6.85 (m, 2). ^{13}C NMR: δ 14.04, 16.44, 16.68, 20.74, 21.09, 21.14, 39.58, 39.69, 60.56, 91.82, 91.91, 127.95, 128.95, 129.73, 136.31, 174.07, 174.14, 205.80. Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 79.17; H, 8.51.

(3*R*,1′*R*)-4,4-Dimethylpent-1-yn-3-ol, (1′-Phenylethyl)carbamate (21a) and (3*S*,1′*R*)-4,4-Dimethylpent-1-yn-3-ol, (1′-Phenylethyl)carbamate (21b). A dry 100-mL, round-bottomed flask equipped with a condenser, magnetic stirring bar, and nitrogen atmosphere was charged with 11.2 g (0.10 mol) of racemic ynol **8**, 14.7 g (0.10 mol) of (*R*)-(+)-1-phenylethyl isocyanate, and 1.12 g (0.010 mol of triethylenediamine. This mixture was heated with stirring in an 80 °C oil bath for 5 h, at which time no isocyanate was detected by TLC. The resultant viscous oil was triturated with ether, the suspension was filtered through a medium scintered glass frit, and the filtrate was concentrated with a rotary evaporator. This mixture was subjected, in three batches, to preparative HPLC using 15% ether–hexanes as eluent, providing 10.24 g (79%) of carbamate **21a**, corresponding to (*R*)-(+)-**8**, and 10.16 g (78%) of **21b**, corresponding to (*S*)-(−)-**8**.

Isomer 21a: mp 66.5–67 °C; $[\alpha]^{23}_D$ +121.5° (*c* 0.039, CH_3OH). IR: 3440, 3310, 1725, 1505, 1070 cm^{-1}. ^1H NMR: δ 0.99 (s, 9), 1.50 (d, 3, J = 6.9), 2.44 (br s, 1), 4.87 (br m, 1), 5.05 (br s, 2), 7.32 (m, 5). ^{13}C NMR: δ 22.42, 25.37, 34.99, 50.70, 72.16, 73.86, 80.43, 125.81, 127.25, 128.56, 143.39, 154.75. Anal. Calcd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 74.28; H, 8.00; N, 5.52.

Isomer 21b: mp 52–55 °C; $[\alpha]^{23}_D$ +33.8° (*c* 0.151, CH_3OH). IR (neat): 3310, 2125, 1715, 1385, 1060 cm^{-1}. ^1H NMR: δ 1.02 (s, 9), 1.50 (d, 3, J = 6.3), 2.40 (s, 1), 4.7–5.1 (m, 2), 5.07 (s, 1), 7.32 (s, 5). ^{13}C NMR: δ 22.24, 25.34, 35.02, 50.62, 72.09, 73.85, 80.36, 125.89, 127.18, 128.45, 143.20, 154.74. Anal. Calcd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40. Found: C, 73.95; H, 8.17; N, 5.35.

(*R*)-(+)-4,4-Dimethylpent-1-yn-3-ol ((*R*)-(+)-8). A dry 200-mL, three-necked round-bottomed flask equipped with a condenser, nitrogen atmosphere, and magnetic stirring bar was charged with 50 mL of ether, 40 mL of THF, and 9.08 g (35.0 mmol) of **21a**. To the stirring solution was added 1.90 g (50.0 mmol) of $LiAlH_4$. This mixture was heated at reflux for 1 h, 20 mL of THF and 0.75 g (20.0 mmol) of $LiAlH_4$ were added, and the heating was resumed for 2.5 h. The mixture was cooled in an ice bath and the reaction was carefully quenched with 5% aqueous HCl. The layers were separated, and the aqueous layer was treated with Na_2SO_4 and extracted with ether. The combined organic portions were washed with 4 × 50 mL of water and dried ($MgSO_4$). Filtration followed by concentration with a rotary evaporator and Kugelrohr distillation of the residue provided 3.46 g (88%) of (*R*)-(+)-**8**, $[\alpha]^{20}_D$ +17.95° (neat). The spectra of this material were identical in all respects with those of the racemic mixture.

Resolution of Racemic Ynol 10. A dry 300-mL, round-bottomed flask equipped with a magnetic stirring bar and nitrogen atmosphere was charged with 120 mL of ether, 5.83 g (35.1 mmol) of (*R*)-(−)-**22** (98% ee), 10.4 g (35.0 mmol) of **10**, 7.29 g (35.4 mmol) of dicyclohexylcarbodimide, and 0.39 g (3.5 mmol) of 4-(dimethylamino)pyridine. This suspension was stirred at room temperature for 18 h, the precipitated urea was filtered, and the ether solution was washed with 5% aqueous HCl and water and dried ($MgSO_4$). Filtration and removal of the solvent with a rotary evaporator produced a residue which was subjected to rotary chromatography on silica gel with 20% ether–hexanes as eluent. Concentration of the resulting fractions produced 4.21 g (72%) of **23a** and **23b** and 2.6 g (25%) of recovered **10**. The diastereomers **23a** and **23b** were partially resolved by rotary chromatography, and each was recrystallized twice from ethyl acetate–hexanes to provide 1.61 g (21%) of **23a** and 1.56 g (20%) of **23b**.

(2*R*,2′*S*)-(+)-2-Methoxy-2-phenylethanoic acid, 1′,1′,1′-triphenylbut-3′-yn-2′-yl ester (23a): mp 115–116 °C. $[\alpha]^{21}_D$ +16.2° (*c* 0.0623, CH_3OH). IR: 3320, 2140, 1760, 1605, 1500, 1455, 1120 cm^{-1}. ^1H NMR: δ 2.29 (d, 1, J = 2.2), 3.28 (s, 3), 4.49 (s, 1), 6.69 (d, 1, J = 2.2), 7.11 (m, 2), 7.23 (m, 18). ^{13}C NMR: δ 57.54, 60.91, 69.51, 77.63, 79.38, 82.51, 126.67, 127.66, 128.41, 129.75, 129.93, 135.37, 143.35, 169.35. Anal. Calcd for $C_{31}H_{26}O_3$: C, 83.38; H, 5.87. Found: C, 83.39; H, 5.79.

(2*R*,2′*R*)-(−)-2-Methoxy-2-phenylethanoic acid, 1′,1′,1′-triphenylbut-3′-yn-2′-yl ester (23b): mp 108–109 °C. $[\alpha]^{21}_D$ −50.4° (*c* = 0.0825, CH_3OH). IR: 3320, 1760, 1505, 1180, 1140 cm^{-1}. ^1H NMR: δ 2.37 (d, 1, J = 2.2), 3.23 (s, 3), 4.59 (s, 1), 6.84 (d, 1, J = 2.2), 6.99–7.34 (m, 20). ^{13}C NMR: δ 57.22, 60.76, 68.83, 77.49, 79.68, 82.56, 126.52, 127.27, 127.52, 127.81, 128.40, 129.54, 135.24, 143.19, 169.14. Anal. Calcd for $C_{31}H_{26}O_3$: C, 83.38; H, 5.87. Found: C, 83.07; H, 5.70.

(*S*)-(−)-1,1,1-Triphenylbut-3-yn-2-ol ((*S*)-(−)-10). A 100-mL, round bottomed flask was charged with 1.50 g (3.36 mmol) of **23a** and 20 mL of a 1 M solution of KOH in ethanol. This solution was allowed to sit, with occasional stirring, at ambient temperature for 2 h. The ethanol was removed with a rotary evaporator, the residue was dissolved in ether and washed with 5% aqueous $NaHCO_3$, and the organic layer was dried ($MgSO_4$). The solution was filtered and concentrated with a rotary evaporator to provide 0.99 g (99%) of (*S*)-(−)-**10**, mp 92–93 °C, $[\alpha]^{22}_D$ −9.81° (*c* 0.031, $CHCl_3$). The spectral properties of this compound are identical with those of the racemic mixture.

(*R*)-(+)-1,1,1-Triphenylbut-3-yn-2-ol ((*R*)-(+)-10). A 50-mL, round-bottomed flask was charged with 1.50 g (3.36 mmol) of **23b** and 20 mL of a 1 M solution of KOH in ethanol. This solution was allowed to sit, with occasional stirring, at ambient temperature for 1 h. Identical workup as given above provided 0.99 g (99%) of (*R*)-(+)-**10**, mp 90–91 °C, $[\alpha]^{22}_D$ +8.00° (*c* 0.035, $CHCl_3$). The spectral properties of this compound are identical with those of the racemic mixture.

Structure Proof of Claisen Rearrangement Product 15. Step 1. Ortho Ester Claisen Rearrangement of (*R*)-(+)-8. A dry 50-mL, round-bottomed flask equipped with a condenser, magnetic stirring bar, and nitrogen atmosphere was charged with 1.12 g (10.0 mmol) of (*R*)-(+)-**8**, 7.20 g (40.0 mmol) of triethyl orthopropionate, and 0.01 g (0.13 mmol) of propanoic acid. The mixture was heated in an 80 °C oil bath for 1.5 h. The ethanol produced was removed with a rotary evaporator, 1 drop of acid was added, and the mixture was stirred at 80 °C for 1.5 h. This process was repeated for a total heating time of 5.5 h, and the mixture was finally heated at 100 °C for 1.5 h. The ethanol was removed, and the crude mixture was filtered through a short column of silica gel with 5% ether–hexanes as eluent. Rotary chromatography on silica gel with 2.5% ether–hexanes as eluent provided 1.70 g (92%) of a 89.9:10.1 mixture of (2*R*,4*R*)-**15a** and (2*S*,4*R*)-**15b**. These diastereomers could not be separated. The spectral properties of this material are identical with those of the racemic mixture.

Step 2. Reduction of 15. The foregoing mixture of (2*R*,4*R*)-**15a** and (2*S*,4*R*)-**15b** (1.60 g, 8.15 mmol) was dissolved in 15 mL of ether in a dry 50-mL, round-bottomed flask and was cooled in an ice bath. While stirring, 0.31 g (8.15 mmol) of $LiAlH_4$ was added. After 30 min, the mixture was carefully quenched with 10% aqueous HCl, the layers were separated, the aqueous portion was extracted with ether, and the combined organic portions were dried ($MgSO_4$). Filtration and concentration of this solution gave 1.21 g (96%) of product. Rotary chromatography on silica gel with 5% ether–hexanes as eluent gave 1.08 g (86%) of (2*R*,4*R*)-**24a** and (2*S*,4*R*)-**24b** as a 89.9:10.1 mixture. These diastereomers could not be separated. The spectral properties of this material are identical with those of the racemic mixture.

Step 3. Reaction of 24 with Phenyl Isocyanate. The foregoing mixture of (2*R*,4*R*)-**24a** and (2*S*,4*R*)-**24b** (1.00 g, 6.5 mmol) was placed in a dry 5-mL round-bottomed flask equipped with a magnetic stirring bar and nitrogen atmosphere and was treated with 0.83 g (0.77 mL, 7.0 mmol) of phenyl isocyanate. This mixture was stirred at room temperature for 1 h and heated at 60 °C for 2 h. Column chromatography of the crude product on silica gel with 20% ether–hexanes as eluent gave 1.45 g (86%) of a 90:10 mixture of (2*R*,4*R*)-**26a** and (2*S*,4*R*)-**26b**, mp 49–50.5 °C. These diastereomers could not be separated. IR: 3440, 1960, 1730, 1600, 1530, 1445, 1210 cm^{-1}. ^1H NMR: δ 1.04 (s, 9), 1.07 (d, 3, *J* = 6.9), 2.54 (m, 1), 4.07 (m, 2), 5.20 (m, 2), 6.57 (br s, 1), 7.06 (m, 1), 7.31 (m, 4). ^{13}C NMR: δ 16.69, 30.12, 31.60, 33.06, 69.58, 94.66, 104.75, 118.63, 123.32, 128.97, 137.83, 153.52, 200.64. Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48; N, 5.12. Found: C, 74.73; H, 8.51; N, 5.09.

Step 4. Ozonolysis of 26. The foregoing 90:10 mixture of (2*R*,4*R*)-**26a** and (2*S*,4*R*)-**26b** (0.50 g, 1.8 mmol) was dissolved in 10 mL of CH_2Cl_2 and placed in a dry three-necked, round-bottomed flask equipped with a gas inlet tube and an oil trap outlet. The system was purged with nitrogen and cooled in a dry ice–acetone bath. Ozone (generated with a Wellsbach ozonator) was introduced until the solution maintained a blue color. The solution was purged with nitrogen, and 0.34 g (2.0 mmol) of *m*-chloroperoxybenzoic acid (*m*-CPBA) was added. The mixture warmed to room temperature over 2 h. Concentration of the mixture followed by recrystallization of the residue from water–ethanol gave *m*-chlorobenzoic acid. The filtrate was concentrated and the residue was recrystallized to provide 0.35 g (85%) of (*S*)-(+)-**28**,[20] mp 103–105 °C, $[\alpha]^{21}_D$ +11.8° (*c* 0.101, CH_3OH) (68% ee). IR: 3600–2400 (br), 3440, 1740, 1605, 1530, 1445 cm^{-1}. ^1H NMR: δ 1.28 (d, 3, *J* = 7.2), 2.90 (m, 1), 4.33 (d, 2, *J* = 6.3), 6.78 (br s, 1), 7.06 (t, 1, *J* = 7.0), 7.32 (m, 5). ^{13}C NMR: δ 13.51, 39.27, 66.01, 118.78, 123.60, 128.96, 133.71, 137.48, 179.85.

Structure Proof of Claisen Rearrangement Product 17. Step 1a. Ortho Ester Claisen Rearrangement of (*R*)-(+)-10. A dry 10-mL, round-bottomed flask equipped with a short-path distillation head, magnetic stirring bar, and nitrogen atmosphere was charged with 2.30 g (13.1 mmol) of triethyl orthopropionate, 0.015 g (0.2 mmol) of propanoic acid, and 0.78 g (2.6 mmol) of (*R*)-(+)-**10**. The mixture was heated in an 80 °C oil bath for 1 h. The ethanol produced was removed with a rotary evaporator, 0.10 g of triethyl orthopropionate and 0.015 g of acid were added, and the heating continued for 1.5 h. The ethanol removal and additions were repeated, and a sequence of heating at 90 °C for 1.5 h and reagent additions was performed 2 times. After the last addition, the mixture was heated at 105 °C for 1 h. The excess reagents were removed under high vacuum, and the crude product was subjected to rotary chromatography on silica gel with 2% ether–hexanes as eluent, providing 0.74 g (74%) of (2*S*,4*S*)-**17a** and (2*R*,4*S*)-**17b** as a 95:5 mixture. $[\alpha]^{22}_D$ +72.2° (*c* 0.009, $CHCl_3$). The spectral data of this product are identical with those of the racemic mixture. Anal. Calcd for $C_{27}H_{26}O_2$: C, 84.78; H, 6.85. Found: C, 84.53; H, 6.95.

Similar rearrangement of (*S*)-(−)-**10** gave a 95:5 mixture of (2*R*,4*R*)-**17a** and (2*S*,4*R*)-**17b**, $[\alpha]^{21}_D$ −79.3° (*c* 0.009, $CHCl_3$). Anal. Calcd for $C_{27}H_{26}O_2$: C, 84.78; H, 6.85. Found: C, 84.51; H, 6.82. The spectra of this mixture are identical with those of the foregoing mixture and the racemic mixture.

Step 2. Reduction of 17. A dry 100-mL, pear-shaped flask equipped with a magnetic stirring bar and nitrogen atmosphere was charged with 10 mL of ether and 0.65 g (1.7 mmol) of the foregoing 95:5 mixture of (2*S*,4*S*)-(+)-**17a** and (2*R*,4*S*)-(+)-**17b**. The flask was cooled in an ice bath, and 0.065 g (1.7 mmol) of $LiAlH_4$ was carefully added. After 1 h, the mixture was quenched with 10% HCl, diluted with ether, and washed with water, and the organic layer was dried ($MgSO_4$). Filtration and concentration with a rotary evaporator gave 0.56 g (97%) of a 95:5 mixture of (2*S*,4*S*)-**25a** and (2*R*,4*S*)-**25b**, $[\alpha]^{20}_D$ +67.95° (*c* 0.011, $CHCl_3$). The spectral data of this product are identical with those of the racemic mixture. Anal. Calcd for $C_{25}H_{24}O$: C, 88.20; H, 7.11. Found: C, 88.30; H, 7.15.

Similar reduction of (*R*)-(−)-**17** gave 0.58 g (98%) of a 95:5 mixture of **25a** and **25b**, $[\alpha]^{22}_D$ −82.3° (*c* 0.015, $CHCl_3$). Anal. Calcd for $C_{25}H_{24}O$: C, 88.20; H, 7.11. Found: C, 88.22; H, 7.16.

Step 3. Reaction of 25 with Phenyl Isocyanate. A dry 10-mL, pear-shaped flask equipped with a magnetic stirring bar and nitrogen atmosphere was charged with 0.50 g (1.5 mmol) of the foregoing mixture of (2*S*,4*S*)-**25a** and (2*R*,4*S*)-**25b** and 0.19 g (0.20 mL, 1.6 mmol) of phenyl isocyanate. The mixture was heated in a 60 °C oil bath for 1 h, was dissolved in 50% ether–hexanes, and was washed through a short silica gel column. Rotary chromatography of the crude concentrate on silica gel with 5% ether–hexanes as eluent gave 0.59 g (85%) of (2*S*,4*S*)-**27a** and (2*R*,4*S*)-**27b** as a 95:5 mixture, $[\alpha]^{22}_D$ +56.7° (*c* 0.021, $CHCl_3$). IR: 3450, 3000, 1740, 1520, 1535, 1455, 1395, 1120 cm^{-1}. ^1H NMR: δ 0.83 (d, 3, *J* = 6.8), 2.43 (m, 1), 3.79 (d, 2, *J* = 6.8), 5.10 (dd, 1, *J* = 6.5, 6.5), 6.31 (dd, 1, *J* = 2.6, 6.2), 6.46 (s, 1), 7.0–7.4 (m, 20). ^{13}C NMR: δ 16.37, 33.29, 59.11, 69.13, 96.49, 102.56, 118.60, 123.34, 126.32, 127.53, 128.99, 129.86, 137.79, 146.14, 153.33, 203.53. Anal. Calcd for $C_{32}H_{29}NO_2$: C, 83.63; H, 6.36; N, 3.05. Found: C, 83.67; H, 6.34; N, 3.07. The isomers could not be separated.

Similar treatment of (−)-**25** provided 0.61 g (88%) of a 95:5 mixture of **27a** and **27b**, $[\alpha]^{21}_D$ −61.8° (*c* 0.011, $CHCl_3$). Anal. Calcd for $C_{32}H_{29}NO_2$: C, 83.63; H, 6.36; N, 3.05. Found: C, 83.27; H, 6.47; N, 3.15.

Step 4. Ozonolysis of (4*S*)-(+)-27. A 95:5 mixture of (2*S*,4*S*)-**27a** and (2*R*,4*S*)-**27b** (0.46 g, 1.0 mmol) was dissolved in 10 mL of CH_2Cl_2 and placed in a three-necked, round-bottomed flask equipped with a gas inlet tube and an oil trap outlet. Ozone (generated with a Wellsbach ozonator) was introduced until the solution maintained a blue color. The solution was purged with nitrogen, and 0.20 g (1.0 mmol) of *m*-CPBA was added. The mixture was warmed to room temperature and stirred for 12 h, then concentrated and the solid recrystallized from water–ethanol to remove the *m*-chlorobenzoic acid. Recrystallization of the residue provided 0.054 g (25%) of (*R*)-(−)-**28**,[20] mp 103–104 °C, $[\alpha]^{21}_D$ −12.0° (*c* 0.015, CH_3OH) (67% ee). The spectral data for this product are identical with those of (*S*)-(+)-**28** (vide supra).

Similar ozonolysis of (4*R*)-(−)-**27** provided 0.16 g (73%) of (*S*)-(+)-**28**, mp 101–102 °C, $[\alpha]^{21}_D$ +13.1° (*c* 0.013, CH_3OH) (73% ee).

Ortho Ester Claisen Rearrangements of Ynols 8 and 10 under Conditions of Optimal Diastereoselectivity. General. All reactions were performed in a round-bottomed flask equipped with a short-path distillation head, magnetic stirring bar, and nitrogen atmosphere. Propanoic acid served as the reaction catalyst. The reaction mixtures were heated in an oil bath maintained at the given temperature. Ethanol produced during the reaction was periodically removed with a rotary evaporator. Excess reagents were typically removed under high vacuum before chromatography of the crude product. All diastereomer ratios given are for the crude reaction product.

Method A. A mixture of 0.59 g (3.3 mmol) of triethyl orthopropionate, 1 drop of acid, and 0.22 g (2.0 mmol) of **8** was heated at 80 °C for 3 h. Capillary GLP chromatographic analysis showed a 58:42 ratio of **15** to **8**. The ratio of diastereomers **15a**:**15b** was 90.9:9.1.

Method B. A mixture of 1.76 g (10.0 mmol) of triethyl orthopropionate, 2 drops of acid, and 0.67 g (6.0 mmol) of **8** was heated at 80 °C for 2.5 h. Ethanol was removed, 0.18 g (1.0 mmol) of triethyl orthopropionate and 1 drop of acid were added, and heating continued for 2.5 h. After another removal/addition sequence, heating resumed at 80 °C for 3.5 h, and at 100 °C for 1 h. Column chromatography of the crude product on silica gel with 2.5% ether–hexanes as eluent gave 0.89 g (76%) of a 90.9:9.1 mixture of **15a** and **15b**.

Method C. A mixture of 7.20 g (40.0 mmol) of triethyl orthopropionate, 0.01 g (0.13 mmol) of acid, and 1.12 g (10.0 mmol)

of **8** was heated at 80 °C for 1.5 h. Ethanol was removed, 0.10 mmol of acid was added, and heating continued for 1.5 h. After another removal/addition sequence, the mixture was heated for 2.5 h at 80 °C, and at 100 °C for 1 h. The crude product was filtered through a short silica gel column and the concentrated filtrate was subjected to rotary chromatography on silica gel with 2.5% ether–hexanes as eluent to provide 1.80 g (92%) of a 89.9:10.1 mixture of **15a** and **15b**.

Method D. A mixture of 1.76 g (10.0 mmol) of triethyl orthopropionate, 0.015 g (0.20 mmol) of acid, and 0.60 g (2.0 mmol) of **10** was heated at 80 °C for 1 h. Ethanol was removed, 0.2 mmol of acid was added, and heating resumed for 2 h. Ethanol removal/acid addition was repeated, followed by heating at 90 °C for 1.5 h. A final removal/addition sequence was followed by heating at 90 °C for 1 h, and at 100 °C for 1 h. Rotary chromatography of the crude product on silica gel with 2.5% ether–hexanes as eluent gave 0.69 g (89%) of a 95:5 mixture of **17a** and **17b**.

Method E. A mixture of 3.40 g (19.3 mmol) of triethyl orthopropionate, 0.03 g (0.40 mmol) of acid, and 1.15 g (3.85 mmol) of **10** was heated at 75 °C for 2 h. Ethanol removal and addition of 1 drop of acid was followed by heating for 2 h. The removal/addition sequence was repeated, and heating was resumed at 85 °C for 2 h. The removal/addition sequence was repeated, the mixture was heated at 85 °C for 2 h, and heating increased to 100 °C for 2 h. The crude product was filtered through a short silica gel column and the concentrated product was subjected to rotary chromatography on silica gel with 2.5% ether–hexanes as eluent, providing 1.21 g (82%) of a 93:7 mixture of **17a** and **17b**.

Method F. A mixture of 8.81 g (50 mmol) of triethyl orthopropionate, 0.074 g (1.0 mmol) of acid, and 2.98 g (10.0 mmol) of **10** was heated at 80 °C for 1 h. Ethanol removal and addition of 0.074 g of acid was followed by heating for 2 h. The removal/addition sequence was repeated, the mixture was heated at 90 °C for 1.5 h, and another removal/addition sequence was performed. The mixture was heated at 90 °C for 1 h, and at 100 °C for 1 h. The crude product was filtered through a short silica gel column, concentrated, and subjected to rotary chromatography on silica gel with 2.5% ether–hexanes as eluent, isolating 3.10 g (81%) of **17a** and **17b** as a 95:5 mixture, and 0.24 g (8%) of recovered **10**.

2,6,6-Trimethylhepta-3,4-dien-1-ol ((±)-24). A dry 100 mL, three-necked round-bottomed flask equipped with a magnetic stirring bar and nitrogen atmosphere was charged with 40 mL of ether and 2.0 g (10.2 mmol) of a 90.9:9.1 mixture of allene esters **15a** and **15b**. The system was cooled in an ice bath, and 0.39 g (10.2 mmol) of $LiAlH_4$ was carefully added. After 1 h, the reaction mixture was carefully quenched with 10% aqueous HCl and diluted with ether, and the layers were separated. The ether layer was washed with water and dried ($MgSO_4$). Filtration and removal of the solvent with a rotary evaporator produced 1.60 g (99%) of a 90.9:9.1 mixture of (±)-**24a** and (±)-**24b** as a clean oil. IR (neat): 3360 (br), 1960, 1465, 1365, 1040 cm^{-1}. ^1H NMR: δ 1.03 (d, 3, J = 6.4), 1.04 (s, 9), 1.51 (br m, 1), 2.36 (m, 1), 3.53 (m, 2), 5.12–5.22 (m, 2). ^{13}C NMR: δ 16.4, 30.1, 31.6, 36.3, 67.7, 95.1, 104.3, 200.8. Anal. Calcd for $C_{10}H_{18}O$: C, 77.87; H, 11.76. Found: C, 77.64; H, 11.81.

(2*R,4*R**)-2-Methyl-6,6,6-triphenylhexa-3,4-dien-1-ol ((±)-25a).** A dry-100 mL, round-bottomed flask equipped with a magnetic stirring bar and a nitrogen atmosphere was charged with 30 mL of ether and 3.10 g (8.1 mmol) of a 95:5 mixture of allene esters **17a** and **17b**. The system was cooled in an ice bath and the solution was carefully treated with 0.31 g (8.1 mmol) of $LiAlH_4$. After being stirred for 30 min, the reaction mixture was carefully quenched with 10% aqueous HCl. The mixture was diluted with ether and washed with water, and the organic layer was dried ($MgSO_4$). Filtration and removal of the solvent with a rotary evaporator gave a crude product as a 95:5 mixture of diastereomers, which was purified by rotary chromatography on silica gel with 20% ether–hexanes as eluent. The material crystallized on sitting and was recrystallized from hexanes to provide 2.33 g (84%) of (±)-**25a** as a single diastereomer, mp 67–69 °C. IR: 3620, 3560, 3070, 1965, 1600, 1495, 1455, 1040 cm^{-1}. ^1H NMR: δ 0.81 (t, 1, J = 6.7), 0.84 (d, 3, J = 6.9), 2.24 (m, 1), 3.18–3.32 (m, 2), 5.11 (dd, 1, J = 6.4, 6.5), 6.33 (dd, 1, J = 2.6, 6.3), 7.15 (m, 6), 7.25 (m, 9). ^{13}C NMR: δ 15.96, 36.15, 59.09, 67.12, 97.02, 102.49, 126.41, 127.57, 129.86, 145.99, 203.67. Anal. Calcd for $C_{25}H_{24}O$: C, 88.20; H, 7.11. Found: C, 88.05; H, 6.88.

1-[[Dimethyl(1,1-dimethylethyl)silyl]oxy]-2,6,6-trimethylhepta-3,4-diene ((±)-29). A dry 25-mL, round-bottomed flask equipped with a magnetic stirring bar was purged with nitrogen and charged with 1.54 g (10.0 mmol) of allene alcohol **24** (the foregoing 90:10 mixture of diastereomers) and 5.0 mL of freshly distilled dimethylformamide (DMF). Imidazole (1.70 g, 25.0 mmol) was added, followed by 1.81 g (12.0 mmol) of *tert*-butyldimethylsilyl chloride. The mixture was stirred at room temperature for 3 h, after which no starting material appeared by TLC. Water was added, the mixture was diluted with ether, and the organic portion was washed with 4 × 50 mL of water and dried ($MgSO_4$). Filtration and concentration with a rotary evaporator gave a crude product which was subjected to flash chromatography on silica gel using 2.5% ether–hexanes as eluent, producing 2.57 g (96%) of **29**. IR (neat): 2980, 1965, 1470, 1265, 1100, 850 cm^{-1}. ^1H NMR: δ 0.47 (s, 6), 0.90 (s, 9), 0.98 (d, 3, J = 6.7), 1.02 (s, 9), 2.29 (m, 1), 3.40 (dd, 1, J = 7.2, 9.7), 3.53 (dd, 1, J = 6.2, 9.7), 5.14 (dd, 1, J = 3.2, 6.3), 5.22 (dd, 1, J = 5.9, 6.1). ^{13}C NMR: δ −5.3, 16.3, 18.4, 26.0, 30.2, 31.5, 36.0, 68.5, 95.5, 104.0, 200.5. Anal. Calcd for $C_{16}H_{32}OSi$: C, 71.57; H, 12.01. Found: C, 71.64; H, 12.12.

3-[[Dimethyl(1,1-dimethylethyl)silyl]oxy]-2-methylpropanal ((±)-30). A dry 50-mL, three-necked round-bottomed flask equipped with an oil-filled gas bubbler, magnetic stirring bar, stopper, and sintered-glass gas-bubbling tube was charged with 15 mL of CH_2Cl_2 and 0.81 g (3.0 mmol) of silyl ether **29** to give a 0.2 M solution. The system was cooled in a dry ice–acetone bath, and ozone (generated with a Wellsbach ozonator) was introduced until the solution turned blue. (Prior to the color change, the solution foams due to the evolution of CO.) The solution was purged with nitrogen and transferred to a pear-shaped flask, and the solvent was removed with a rotary evaporator. Column chromatography of the residue on silica gel with 5% ether–hexanes as eluent afforded 0.38 g (62%) of **30**. IR (neat): 2720, 1745, 1265, 1110, 850, 790 cm^{-1}. ^1H NMR: δ 0.05 (s, 6), 0.88 (s, 9), 1.09 (d, 3, J = 7.0), 2.53 (m, 1), 3.83 (m, 2), 9.74 (d, 1, J = 1.6). ^{13}C NMR: δ −5.6, 10.2, 18.2, 25.6, 48.7, 63.4, 204.5. Anal. Calcd for $C_{10}H_{22}O_2Si$: C, 59.35; H, 10.96. Found: C, 59.09; H, 11.02.

2-Methyl-6,6,6-triphenylhexa-3,4-dienal ((±)-31). A dry 25-mL, round-bottomed flask equipped with a magnetic stirring bar and nitrogen atmosphere was charged with 0.22 g (1.0 mmol) of pyridinium chlorochromate (PCC) and 10 mL of dry CH_2Cl_2. A solution of 0.17 g (0.50 mmol) of (±)-**25a** in 5 mL of CH_2Cl_2 was added and the suspension was stirred at room temperature for 1.5 h. Another 0.22 g (1.0 mmol) of PCC was added to the stirring mixture, and the reaction continued for 30 min. The mixture was treated with 10% aqueous HCl and diluted with ether. The separated ether layered was washed with water and dried ($MgSO_4$). The solution was filtered through a short column of Florisil and the solvent was removed with a rotary evaporator to provide 0.14 g (82%) of crude product containing (analysis by ^1H NMR spectroscopy) a ca. 10:90 mixture of dienes **32** and **31**. All attempts to isolate **31** by chromatography on silica gel resulted in isomerization to **32**. Crude ^1H NMR: δ 0.96 (d, 3, J = 7.0), 2.7–2.9 (m, 1), 5.12 (dd, 1, J = 6.3, 6.3), 6.42 (dd, 1, J = 2.5, 6.3), 7.13 (m, 6), 7.24 (m, 9), 9.10 (d, 1, J = 2.0).

Acknowledgment. This research was supported by a research grant from the United States Public Health Service (AI 15027).

Registry No. **6**, 65337-13-5; **7**, 73262-61-0; **8**, 61348-37-6; (*R*)-(+)-**8**, 61317-72-4; **9**, 97563-45-6; **10**, 115533-97-6; (*S*)-(−)-**10**, 115648-30-1; (*R*)-(+)-**10**, 115648-31-2; **11**, 64937-86-6; **12**, 115533-98-7; **13a**, 115533-99-8; **13b**, 115534-11-7; **14a**, 115534-00-4; **14b**, 115534-12-8; **15a**, 115534-01-5; (2*R*,4*R*)-**15a**, 115648-32-3; **15b**, 115534-06-0; (2*S*,4*R*)-**15b**, 115648-33-4; **16a**, 115534-02-6; **16b**, 115534-07-1; **17a**, 115534-03-7; (2*S*,4*S*)-**17a**, 115648-34-5; (2*R*,4*R*)-**17a**, 115648-36-7; **17b**, 115534-08-2; (2*R*,4*S*)-**17b**, 115648-35-6; (2*S*,4*R*)-**17b**, 115648-37-8; **18a**, 115534-04-8; **18b**, 115534-09-3; **19a**, 115534-05-9; **19b**, 115534-10-6; **20**, 33375-06-3; **21a**, 115534-13-9; **21b**, 115534-14-0; (*R*)-(−)-**22**, 3966-32-3; **23a**, 115534-15-1; **23b**, 115534-16-2; (±)-**24a**, 115648-38-9; (2*R*,4*R*)-**24a**, 115534-17-3; (±)-**24b**, 115648-39-0; (2*S*,4*R*)-**24b**, 115534-18-4; (±)-**25a**, 115648-40-3; (2*S*,4*S*)-**25a**, 115534-21-9; (2*R*,4*R*)-**25a**,

115534-23-1; (2*R*,4*S*)-**25b**, 115534-22-0; (2*S*,4*R*)-**25b**, 115534-24-2; (2*R*,4*R*)-**26a**, 115534-19-5; (2*S*,4*R*)-**26b**, 115534-20-8; (2*S*,4*S*)-**27a**, 115534-25-3; (2*R*,4*R*)-**27a**, 115534-27-5; (2*R*,4*S*)-**27b**, 115534-26-4; (2*S*,4*R*)-**27b**, 115534-28-6; (*S*)-(+)-**28**, 59965-08-1; (*R*)-(−)-**28**, 6154-33-2; (±)-**29**, 115534-29-7; (±)-**30**, 115648-41-4; (±)-**31**, 115534-30-0; **32**, 115534-31-1; $CH_3CH_2C(OEt)_3$, 115-80-0; $CH_3C-H_2CO_2H$, 79-09-4; $_tBuMe_2SiCl$, 18162-48-6; methylmalonaldehyde, 16002-19-0; acetylene, 74-86-2; isobutyraldehyde, 78-84-2; pivaldehyde, 630-19-3; cyclohexanecarboxaldehyde, 2043-61-0; 2,2,2-triphenylethanal, 42365-04-8; benzaldehyde, 100-52-7; mesitaldehyde, 487-68-3; 1,1,2-triphenyloxirane, 4479-98-5; phenyl isocyanate, 103-71-9.

Bisannelated Derivatives of 2,2′-Bipyridine

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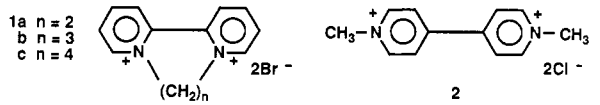
Received October 22, 1987

A series of 3,3′-polymethylene 2,2′-bipyridines has been treated with 1,*n*-dibromoalkanes (n = 2–4) to afford a corresponding series of bisannelated bipyridinium dibromides. The conformational properties of this series of salts were examined by high-field NMR. As the molecule becomes less planar, the UV absorption maxima shift toward shorter wavelength, and the reduction potentials become more negative. For the least planar system, both electron-transfer steps are found to be irreversible.

Diquaternary derivatives of 2,2′-bipyridine and 4,4′-bipyridine are important electron-transfer agents in biological and other photocatalytic systems. Both 1,1′-dimethylene-2,2′-bipyridinium dibromide (**1a**, diquat) and 1,1′-dimethyl-4,4′-bipyridinium dichloride (**2**, paraquat) function as effective herbicides by viture of their ability to reversibly accept one electron to form a radical cation and thus interfere with the electron-transfer step in photosynthesis.[1] Paraquat, also known as methyl viologen, has been extensively utilized to transfer an electron from the photoexcited state of $Ru(bpy)_3^{2+}$ to an appropriate catalyst, which can then reduce water to evolve hydrogen gas.[2]

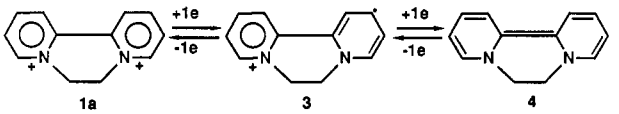


Variously substituted viologens have been examined as quenchers, electron relays, and herbicides. As expected, electron-withdrawing groups tend to destabilize the radical cation intermediate and shift the first reduction to more negative potential while electron-releasing substituents have the opposite effect.[3] Steric effects also can play an important role in determining the redox[4] and spectroscopic[5] properties of these diquaternary salts. The radical cation **3**, formed after one-electron reduction of diquat, is stabilized by resonance delocalization of the odd electron throughout both pyridine rings. Although of less importance from an electrocatalytic point of view, the fully reduced species **4** is of interest because the aromaticity of both pyridine rings has been destroyed and a formal double bond now exists between them. Both steps are favored by coplanarity of the pyridine rings, and thus one finds that lengthening the 1,1′-bridge to a trimethylene or tetramethylene unit accordingly increases both reduction potentials (see Table I). Electron-transfer quenching of photoexcited $Ru(bpy)_3^{2+}$ is similarly diminished as the 2,2′-bipyridinium unit becomes less planar.[4b,6] Nevertheless, Okura and co-workers have reported that **1b** and **1c** are more effective than **2** for photoinduced hydrogen evolution where zinc tetraphenylporphyrin trisulfonate is the photosensitizer.[7]

Table I. Ultraviolet Absorption Data and Reduction Potentials for *N*,*N*′-Bridged Bipyridinium Dibromides

compound	λ_{max} ($\epsilon \times 10^{-4}$)[a]	$E_{1/2}$, V (vs SCE)[b] redn 1	redn 2
1a	308 (2.03)	−0.35 (80)	−0.82 (80)
1b	289 (1.54)	−0.52 (80)	−0.83 (80)
1c	273 (1.13)	−0.64 (80)	irrev
6d	350 (1.32), 335 (1.42)	−0.39 (80)	−0.89 (80)
6e	330 (1.51)	−0.39 (80)	−0.85 (80)
6f	325 (1.6)	−0.40 (70)	−0.82 (80)
6g	317 (1.28)	−0.48 (90)	−0.93 (90)
6h	299 (1.29)	−0.60 (90)	−1.03 (90)
6i	296 (1.31)	−0.65 (100)	−1.01 (100)
6j	314 (1.19)	−0.56 (80)	−0.92 (80)
6k	294 (1.2)	−0.72 (40)	irrev
6m	286 (1.26)	irrev	irrev

[a] Absorption maxima reported in nanometers for 10^{-4} M solutions in H_2O at 25 °C. [b] Potentials are in volts vs SCE for saturated CH_3CN solutions, 0.1 M in TBAP recorded at 25 ± 1 °C at a scan rate of 200 mV/s. The difference between cathodic and anodic peak potentials (mV) is given in parentheses.



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