Asymmetric Induction in Intramolecular [2 + 2]-Photocycloadditions of 1,3-Disubstituted Allenes with Enones and Enoates

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*Received January 3, 1994**

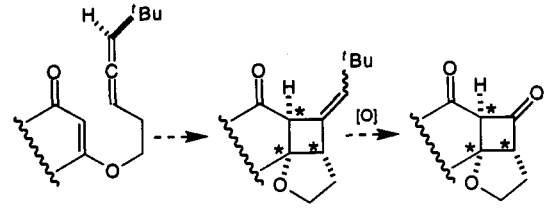
Abstract: Irradiation of optically active allenes (89–92% ee) appended to enones and enoates affords alkylidenecyclobutane photoadducts with high levels of asymmetric induction (83–100%) derived exclusively from the allene fragment. The substrates studied include allenes tethered to enones such as 1,3-cyclohexanedione and 1,3-cyclopentanedione, as well as allenes tethered to functionalized coumarins. The enantiomer ratios of the photoadducts were quantified by derivatization of the products as the corresponding Mosher MTPA esters and analysis by ^{1}H NMR spectroscopy. The *exo*-methylenecyclobutanes obtained upon irradiation of allene–coumarins are isolated as single olefin diastereomers. Irradiation of a coumarin tethered at C(5) with an optically active allene affords an alkynyl-substituted oxepane with complete asymmetric induction.

Introduction

The intramolecular photocycloaddition of monosubstituted allenes with chiral enones and enoates is a powerful tool for the construction of carbon–carbon bonds in polycyclic structures.[1,2] The conformational, steric, and stereoelectronic constraints accompanying ring formation in these photochemical processes allow control over reaction diastereoselection. In principle, the corresponding [2 + 2]-photocycloaddition of chiral, 1,3-disubstituted allenes with enones provides an enantioselective route to optically active polycyclic systems (Scheme 1). The alkylidenecyclobutane adducts along with the corresponding derived cyclobutanones[3] provide access to a large family of structures that are otherwise not readily available by asymmetric synthesis. Oxidative cleavage to the cyclobutanone would afford the synthetic equivalent of a chiral ketene–enone photocycloaddition (Scheme 1).

In early investigations of alkene–enone photocycloadditions, Corey noted that the rate of ring closure by the putative 1,4-biradical intermediate formed can exceed the rate of reversion to starting olefin and enone.[4] More recently, Becker has reported similar observations in intramolecular alkene–enone photocycloadditions.[5] These studies suggest that the stereochemistry established in the initial C–C bond-forming step leading to the 1,4-biradical can be kinetically controlled and transferred to the photoadducts. In principle, the presence of similar kinetic preferences in allene–enone cycloadditions makes enantioselective stereocontrol in photocycloadditions with optically active allenes

Scheme 1



possible. In a separate study,[6] Becker prepared two optically active allenes tethered to an enone through an all-carbon tether in an effort to investigate asymmetric induction in allene–enone [2 + 2]-photocycloadditions. On the basis of circular dichroic spectra, it was determined that the photoadducts possessed some optical activity; however, the extent of asymmetric induction in the photocyclization reactions was not quantified. Moreover, neither the enantiomeric purity nor the absolute configuration of the two allenes employed was established.

We wish to describe our observations of asymmetric induction in intramolecular photoadditions of optically active 1,3-disubstituted allenes with enones and enoates. The substrates studied include allenes appended to enones such as 1,3-cyclohexanedione and 1,3-cyclopentanedione, as well as allenes tethered to functionalized coumarins. Uniformly high levels of absolute asymmetric induction were observed (83–100%). In addition, the coumarin substrates afford photoadducts as single olefin diastereomers in all cases. The use of tethered, optically active 1,3-disubstituted allenes in the [2 + 2]-photocyclization reaction provides access to intermediates for enantioselective synthesis of members of the ellagitannin class of natural products such as chebulic acid I (Scheme 2).[7]

Results

Preparation of Optically Active Substrates. In order to access optically active 1,3-disubstituted allenes, we have used the methodology developed by Myers for the preparation of eneyne

* Abstract published in *Advance ACS Abstracts,* June 15, 1994.

(1) For comprehensive reviews on [2 + 2]-cycloadditions in synthesis, see: (a) Crimmins, M. T. *Chem. Rev.* **1988**, *88*, 1453. (b) Crimmins, M. T.; Reinhold, T. L. *Organic Reactions*; Wiley: New York, 1993; Vol. 44, p 297. See also: (c) Schreiber, S. L. *Science* **1985**, *227*, 857.

(2) (a) Becker, D.; Harel, Z.; Birnbaum, D. *J. Chem. Soc., Chem. Commun.* **1975**, 377. (b) Becker, D.; Harel, Z.; Nagler, M.; Gillon, A. *J. Org. Chem.* **1982**, *47*, 3297. (c) Baker, W. R.; Senter, P. D.; Coates, R. M. *J. Chem. Soc., Chem. Commun.* **1980**, 1011. (d) Dauben, W. G.; Shapiro, G. *Tetrahedron Lett.* **1985**, *35*, 989. (e) Dauben, W. G.; Shapiro, G.; Luders, L. *Tetrahedron Lett.* **1985**, *26*, 1429.

(3) Bellus, D.; Ernst, B. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 797.

(4) Corey, E. J.; Bass, J. D.; LeMahieu, R.; Mitra, R. B. A. *J. Am. Chem. Soc.* **1964**, *86*, 5570.

(5) Becker, D.; Nagler, M.; Sahali, Y.; Haddad, N. *J. Org. Chem.* **1991**, *56*, 4537.

(6) (a) Becker, D.; Nagler, M.; Harel, Z.; Gillon, A. *J. Org. Chem.* **1983**, *48*, 2584. (b) For a leading reference involving thermal cycloadditions of optically active dialkylallenes, see: Pasto, D. J.; Brophy, J. *J. Phys. Org. Chem.* **1993**, *6*, 95.

(7) Yoshida, T.; Okuda, T.; Koga, T.; Toh, N. *Chem. Pharm. Bull.* **1982**, *30*, 2655.

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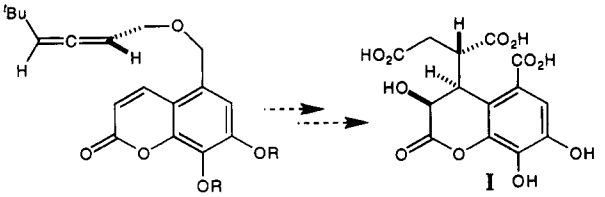
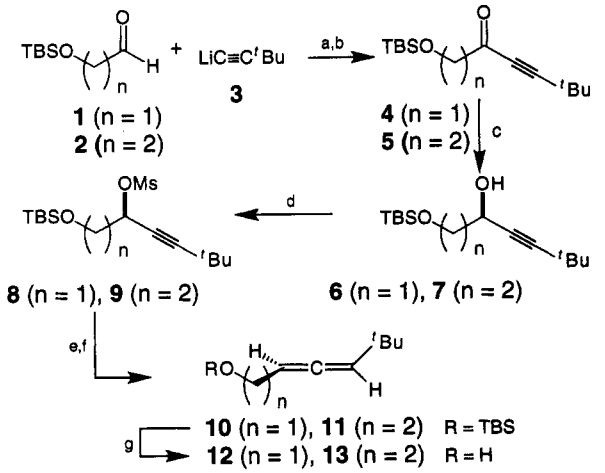
Scheme 2



Chebulic Acid

Scheme 3[a]

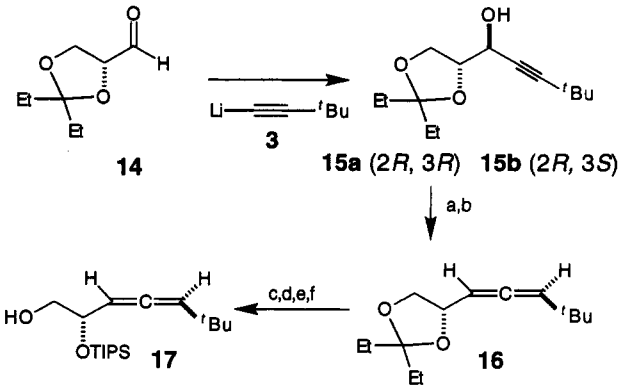


[a] (a) Et_2O, −78 °C (77%, 72%); (b) Dess–Martin periodinane, CH_2Cl_2, 23 °C, (95%, 90%); (c) (*S*)-Alpine Borane; 23 °C (78%, 93%); (d) MsCl, Et_3N, CH_2Cl_2, 0 °C; (e) NH_2NH_2, MeOH, 0 °C; (f) 4-Ph-1,2,4-triazolone-3,5-dione, 1:1 Et_2O/CH_2Cl_2, 0 °C, (70%, 71%); (g) Bu_4NF, THF, 23 °C, (80%, 89%).

allenes.[8] We wished to employ a synthesis strategy that provided ready access to a range of substrates for the enantioselective [2 + 2]-photocycloaddition reaction. The selection of allenic alcohols **12** and **13** (Scheme 3) allowed the optically active allenes to be appended to cyclic β-dicarbonyls and to substituted hydroxycoumarins using the Mitsunobu condensation and the Williamson ether coupling reactions. The preparation of optically active allenes **12** and **13** is illustrated in Scheme 3. Treatment of **4** and **5** with (*S*)-Alpine-Borane[9] (Aldrich) affords carbinols **6** and **7** in 85–88% yields and 89–92% ee. The enantiomeric purity of the allenic alcohols **12** and **13** was determined by conversion of each to the derived Mosher (*S*)-MTPA ester and analysis by ^1H NMR spectroscopy.[10] It has been demonstrated that the synthetic steps which convert propargyl methanesulfonates analogous to **8** and **9** into allenes **10** and **11** are completely stereospecific.[8] Thus, the enantiomeric purity of the allenes is established exclusively in the reduction of ynones **4** (92% ee) and **5** (89% ee).[11]

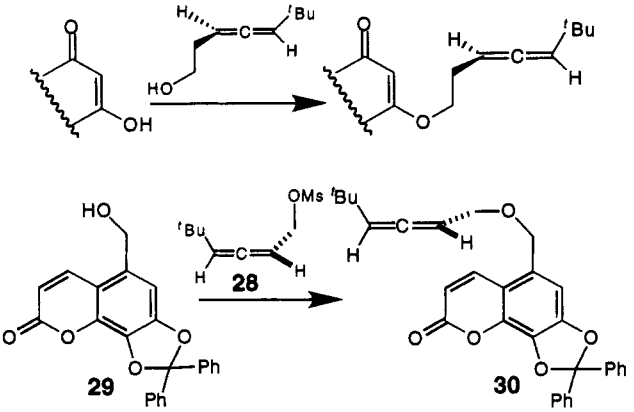
In order to establish the absolute sense of induction in these photocycloadditions, the diastereoselective cycloaddition of a coumarin appended to allene **17**, which incorporates a stereogenic center on the tether, was investigated. Addition of **3** (Scheme 4) to glyceraldehyde diethyl ketal (**14**) provided a mixture of propargyl alcohols **15a** and **15b** which were separated by

Scheme 4[a]



[a] (a) MsCl, Et_3N, CH_2Cl_2, 0 °C; (b) NH_2NH_2, MeOH, 23 °C; then 4-Ph-1,2,4-triazoline-3,5-dione, 1:1 Et_2O/CH_2Cl_2, 0 °C (64%); (c) $(CO_2H)_2$, MeOH, 23 °C (65%); (d) TBSCl, DMAP, CH_2Cl_2, 23 °C (54%); (e) TlPSOTf, Et_3N, CH_2Cl_2, 23 °C (97%); (f) HF·Py, 23 °C (79%).

Scheme 5

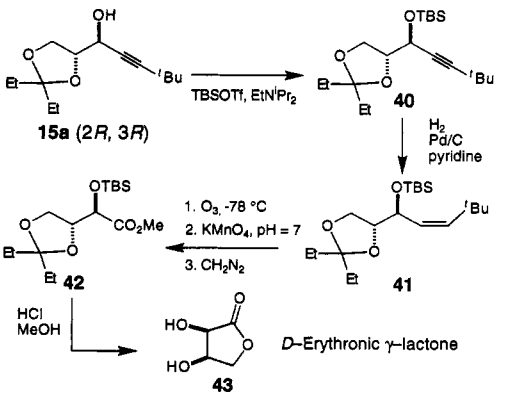


chromatography on silica gel.[12] The conversion of **15a** to **17** proceeded in a manner similar to that described for the conversion of **6** and **7** to **10** and **11**, respectively.

The allene–enoate cycloaddition substrates for study were assembled (Scheme 5) by condensation of allenic alcohol **13** with 1,3-cyclohexanedione, 1,3-cyclopentanedione, and 4-hydroxycoumarin (Ph_3P, $EtO_2CN{=}NCO_2Et$, THF, 23 °C) affording **18** (eq 1), **21** (eq 2), and **24** (eq 3), respectively, in 56–71% yields. Allene–enoate **30** (Scheme 5) was prepared by treatment of allenic mesylate **28** (**12**, MsCl, Et_3N, CH_2Cl_2, 0 °C) with the sodium alkoxide derived from **29** (Scheme 5).[13]

Enantioselective [2 + 2]-Photocycloadditions. All photocycloaddition reactions were performed in cyclohexane or dichlo-

(12) The relative stereochemistry of propargyl alcohol **15a** was established by conversion to the known, commercially available lactone **43** as follows:



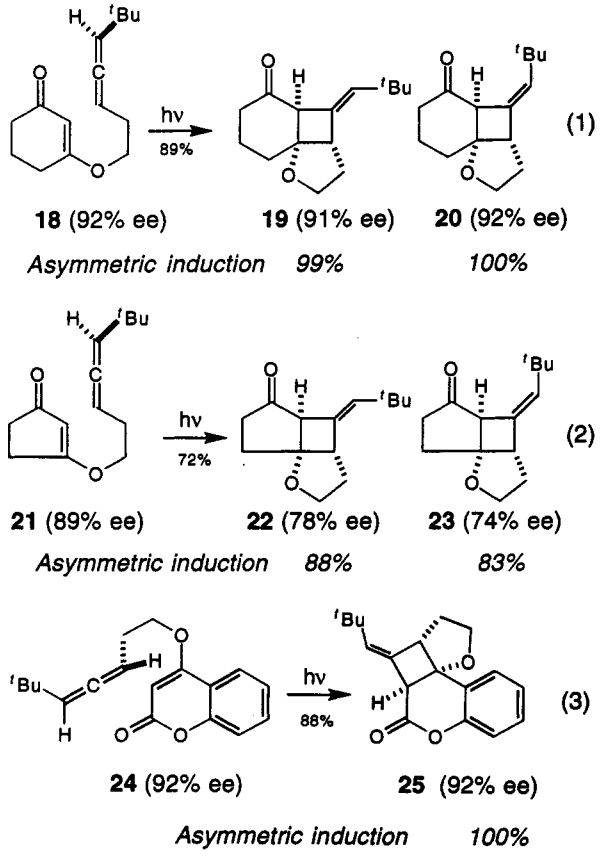
(13) The preparation of **30** will be described in full as part of studies directed toward the enantioselective synthesis of chebulic acid.

(8) Myers, A. G.; Finney, N. S.; Kuo, E. Y. *Tetrahedron Lett.* **1989**, *30*, 5747.

(9) Midland, M. M.; Tramontano, A.; Zderic, S. A. *J. Am. Chem. Soc.* **1977**, *99*, 5211.

(10) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(11) For the aims of this investigation, the allenes employed need not be 100% optically pure. The use of newer enantioselective reductants should provide propargyl alcohols of high optical purity. For example, see: (a) Singh, V. K. *Synthesis* **1992**, 605. (b) Brown, H. C.; Ramachandran, P. V. *Acc. Chem. Res.* **1992**, *25*, 16.



romethane at 23 °C with a Hanovia 450-W Hg medium-pressure UV lamp in a water-cooled quartz immersion apparatus through a Pyrex filter ($\lambda > 293$ nm). Irradiation of **18** (eq 1) and **21** (eq 2) afforded alkylidenecyclobutanes (**18** → **19** + **20**; **21** → **22** + **23**) as 1.2:1 mixtures of olefin diastereomers which were readily separated by chromatography on silica gel. In each case, the relative stereochemistry of the photoadducts was established by ^{1}H NMR NOE difference experiments (Figure 1). In addition, treatment of **19** and **20** at −78 °C in MeOH with a dilute stream of O_3 gave the same methyl ester resulting from retro-Claisen fragmentation of the intermediate β-diketone. Similarly, the methyl esters derived from ozonolysis of **22** and **23** were shown to be identical. The enantiomeric purity of each photoadduct (**19**, **20**, **22**, **23**) was assayed by ^{1}H NMR spectroscopy employing 1.0 equiv of Ag(fod) and 2.0 equiv of (+)-Eu(hfc)$_3$. The enantiomeric purities of **19** (91% ee) and **20** (92% ee) were shown to equal, within experimental error, that of **18** (92% ee). In contrast, the photoadducts derived from **21** (89% ee) (eq 2) displayed diminished levels of stereochemical transfer (**22**, 78% ee; **23**, 74% ee). Thus, **21** displays only 83% and 88% asymmetric induction in the formation of **22** and **23**, respectively. Experiments aimed at elucidating the nature of the diminished levels of induction with **21** revealed that the enantiomeric purity of **22** changed during the course of the reaction. Thus, when the irradiation of **21** (89% ee) is interrupted at 14% conversion, **22** is isolated in 88% ee, while at 38% conversion **22** is isolated in 82% ee.[14] In a separate experiment, **22** and **23** were shown to be stable upon irradiation under otherwise identical conditions.

Irradiation of coumarin **24** (eq 3) afforded **25** as a crystalline solid with excellent diastereoselection (10:1 of olefin diastereomers by ^{1}H NMR spectroscopy). In a separate experiment aimed at elucidating the nature of the excited state undergoing photoaddition, irradiation of **24** in benzene in the presence of benzophenone

(14) A decrease in the optical activity of **23** was observed as well. However, the enantiomeric purity of **23** was more difficult to quantify at low conversion as a result of a minor side product from the photocycloaddition reaction which possessed ^{1}H NMR signals that overlapped with those of **23**.

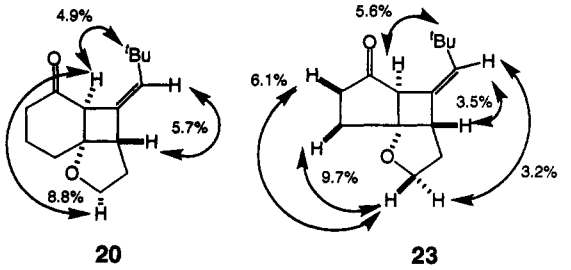


Figure 1. Representative ^{1}H NMR NOE data for photoadducts **20** and **23**.

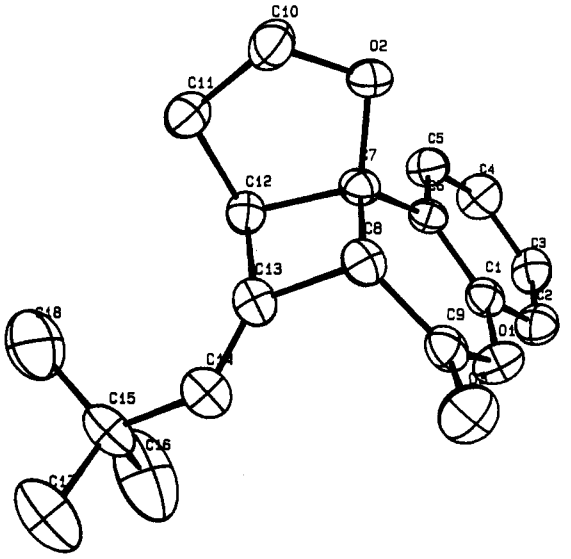
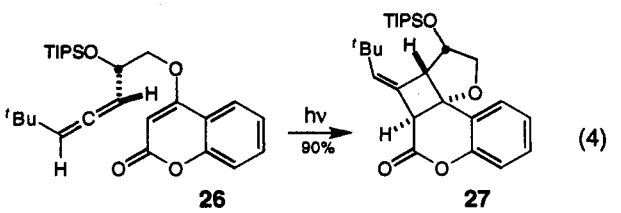


Figure 2. X-ray crystal structure of the photoadduct **25**.

gave identical results, affording **25** as a 10:1 mixture of olefin diastereomers.[15] The enantiomeric purity of **25** was assayed by reduction of **25** with $LiBH_4$ (0 °C, THF, 30 min) and derivatization of the resulting 1° alcohol phenol as the bis-Mosher ester with (*S*)-MTPA-Cl.[10] Analysis of the diastereomeric ^{1}H NMR resonances revealed that **25** had been produced in 92% ee. The stereochemical assignments obtained by ^{1}H NMR NOE difference experiments for **25** were subsequently confirmed by single crystal X-ray crystallography (Figure 2).

Irradiation of **26** afforded **27** (90%) as a single diastereomer by ^{1}H NMR spectroscopy (eq 4).[16] The stereochemical assignment



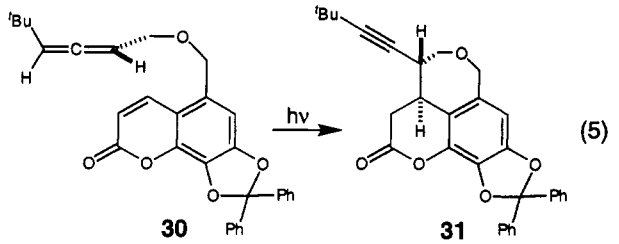
of **27** was secured by analysis of vicinal coupling constants and by NOE difference experiments. The structural determination of **27** was facilitated by comparison to **25**, for which ^{1}H NMR and X-ray crystallographic data had been obtained (*vide supra*). The optical activity of the *exo*-methylenecyclobutane adduct **27** was assayed by conversion of **27** corresponding to the 1° alcohol

(15) The conditions used in the photosensitization experiments are similar to those used by Morrison in a study of the photocycloaddition of coumarin to tetramethylethylene: Wells, P. P.; Morrison, H. *J. Am. Chem. Soc.* **1975**, *97*, 154. See also: Hammond, G. S.; Stout, C. A.; Lamola, A. A. *J. Am. Chem. Soc.* **1964**, *86*, 3103.

(16) Photocyclizations employing the diastereomeric allenic silyl ether indicated that asymmetric induction for a coumarin with an existing stereocenter in the tether is controlled exclusively by the allene and not by the carbinol stereocenter.

phenol and preparation of the bis-(*S*)-MTPA ester.[10] Analysis by ^{1}H NMR spectroscopy revealed that **27** had been formed with 100% asymmetric induction.

In addition to studying the enantioselective [2 + 2]-photocyclizations of simple tethered allenic ethers, we investigated whether high levels of asymmetric induction could be observed in functionalized substrates which would be useful synthetic intermediates. Our interest in developing an enantioselective synthesis of chebulic acid **I** (Scheme 2) compelled us to prepare **30** and examine it as a substrate for enantioselective photochemistry. Irradiation of **30** through a Pyrex filter (0 °C, CH_2Cl_2, 4 h) provided alkyne **31** as a single diastereomer, as determined by ^{1}H NMR spectroscopy, in 60% yield (eq 5). Analysis of the



(5)

Single Diastereomer
100% Asymmetric Induction

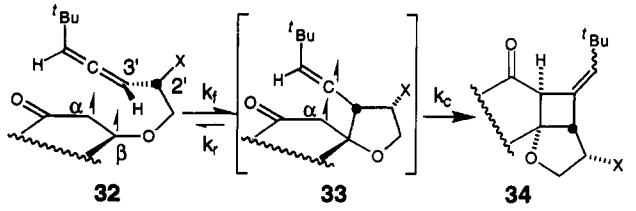
^{1}H NMR vicinal coupling constants along with ^{1}H NMR NOE difference experiments allowed the relative stereochemistry of the substituted oxepane to be established. In order to assay for the level of asymmetric induction in this unusual photoaddition reaction, **31** was reduced ($LiBH_4$, THF, 0 °C) and the resulting 1° alcohol phenol esterified with (*S*)-MTPA-Cl.[10] Analysis of the ^{1}H NMR spectrum revealed that **31** had been formed in 92% ee with 100% asymmetric induction derived from the allene fragment.

Discussion

Since the first report of allene–enone photocycloadditions by Eaton,[17] this photochemical cycloaddition reaction has been employed as a powerful means of efficiently synthesizing polycyclic systems.[1,2] The intermolecular photoaddition reactions of allenes and enones typically require large excesses of allenes. The photochemical steps (addition, cyclization) are inefficient and do not compete with the photophysical processes that reduce the lifetime of the reactive excited states.[18,19] Consequently, the intermolecular [2 + 2]-cycloaddition has been limited to inexpensive, readily available allenes such as propadiene.[20]

The intramolecular variant is a much more efficient process.[2] Wiesner was the first to demonstrate the utility of intramolecular diastereoselective allene–enone [2 + 2]-cycloadditions in natural products synthesis.[21] Dauben has reported a synthesis of the diterpene trihydroxydecipiadiene *via* an intramolecular allene–enone photocyclization.[22] More recently, Pirrung has employed the intramolecular allene–enone cycloaddition in an elegant

Scheme 6

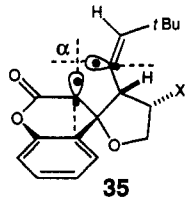


32 **33** **34**

synthesis of pentalenolactone G.[23] In contrast to the [2 + 2]-photochemistry of monosubstituted allenes, the photoreactions of di-, tri-, and tetra-substituted allenes have not received much attention. This is primarily due to the synthetic limitations associated with the preparation of these 1,2-dienes. Moreover, since photochemical additions to enones are believed to proceed through the intermediacy of a 1,4-biradical species which may revert to the starting allene and enone with loss of allene optical activity, it was not clear whether the absolute stereochemistry of the allene would be effectively transferred to the photoadducts.[24] Becker's studies as well as the seminal contributions by Corey in related alkene–enone cycloadditions provide a starting point from which to investigate asymmetric induction with optically active 1,3-disubstituted allenes.

The high levels of asymmetric induction presented herein are accommodated by the accepted model for intramolecular allene–enone photocycloadditions described by Becker.[2,5] For the cases studied, the triplet enone C(β) adds to the less hindered end of the allene C(3′), opposite the *tert*-butyl substituent, to give a 1,4-biradical intermediate **33** which undergoes spin inversion and collapses to a diastereomeric mixture of *exo*-methylenecyclobutanes **34** (Scheme 6).[25] The regiochemistry of the initial bond formation uniformly follows Hammond's and Srinivasan's "rule of five".[26] The observation of high enone face selectivity is accommodated by *exo*-approach of the allene onto the enone such that H(3′) and not C(2′)H_2 resides over the ring. The high levels of asymmetric induction in the photoadducts are consistent with the observations that the configuration of the newly formed vicinal stereocenters is established kinetically upon formation of the C(β)–C(3′) bond and that for **18**, **24**, **26**, and **30** reversion does not occur competitively with ring closure ($k_c \gg k_r$) (Scheme 6).[27,28] However, subtle conformational effects can affect the relative rates of closure, k_c, and reversion, k_r (Scheme 6).[29] Thus, the fact that the optical activity of **22** (eq 2) is observed to diminish during the course of the reaction is consistent with a mechanism

(17) Eaton, P. E. *Tetrahedron Lett.* **1964**, 3695.
(18) For an excellent discussion of competing photophysical and chemical processes in the photochemistry of cyclooctenones, see: Pirrung, M. C.; Webster, N. J. G. *J. Org. Chem.* **1987**, *52*, 3603.
(19) This inefficiency is particularly true in photoadditions involving coumarin substrates: Lewis, F. D.; Barancyk, S. V. *J. Am. Chem. Soc.* **1989**, *111*, 8653.
(20) (a) Guthrie, R. W.; Valenta, Z.; Wiesner, K. *Tetrahedron Lett.* **1966**, 4645. (b) Wiesner, K.; Uyeo, S.; Philipp, A.; Valenta, Z. *Tetrahedron Lett.* **1968**, 6279. (c) Wiesner, K.; Poon, L.; Jirkovsky, I.; Fishman, M. *Can. J. Chem.* **1969**, *47*, 433. (d) Kelly, R. B.; Zamecnik, J.; Beckett, B. A. *Can. J. Chem.* **1972**, *50*, 3455. (e) Kelly, R. B.; Eber, J.; Hung, H. K. *Can. J. Chem.* **1973**, *51*, 2534. (f) Wiesner, K. *Pure Appl. Chem.* **1975**, *41*, 93. (g) Duc, D. K. M.; Fetizon, M.; Lazare, S. A. *J. Chem. Soc., Chem. Commun.* **1975**, 282. (h) McKay, W. R.; Ounsworth, J.; Sum, P.; Weiler, L. *Can. J. Chem.* **1982**, *60*, 872.
(21) Wiesner, K.; Musil, V.; Wiesner, K. J. *Tetrahedron Lett.* **1968**, 5643.
(22) Dauben, W. G.; Shapiro, G. *J. Org. Chem.* **1984**, *49*, 4252.
(23) Pirrung, M. C.; Thomson, S. A. *J. Org. Chem.* **1988**, *53*, 227.
(24) (a) de Mayo, P.; Nicholson, A. A.; Tchir, M. F. *Can. J. Chem.* **1969**, *47*, 711. (b) For a recent, thorough compilation on the mechanism of photocycloaddition reactions, see: Schuster, D. I.; Lem, G.; Kaprinidis, N. *Chem. Rev.* **1993**, *93*, 3.
(25) Experiments in which the triplet 1,4-biradical intermediate has been trapped with H_2Se have been recently described. For a discussion of the regioselectivity in the photocycloaddition reaction of 2-cyclopentenone with allene and its correlation with kinetic selectivity of biradical formation, see: Maradyn, D. J.; Sydnes, L. K.; Weedon, A. C. *Tetrahedron Lett.* **1993**, *34*, 2413.
(26) (a) Liu, R. S. H.; Hammond, G. S. *J. Am. Chem. Soc.* **1967**, *89*, 4936. (b) Srinivasan, R.; Carlough, K. H. *J. Am. Chem. Soc.* **1967**, *89*, 4932.
(27) The geometry of the enone triplet illustrated in Scheme 6 is not intended to represent a detailed structure of the excited state. Wiesner has suggested that diastereoselection in alkene/allene–enone photoadditions is explained by considering the C(β) to be pyramidalized at the transition state: (a) Wiesner, K. *Tetrahedron* **1975**, 1655. (b) Blount, J. F.; Gray, G. D.; Atwal, K. S.; Tsai, T. Y. R.; Weisner, K. *Tetrahedron Lett.* **1980**, *21*, 4413. However, it has been suggested that sterics determine the enone face selectivity: (c) Loufty, R. O.; de Mayo, P. *J. Am. Chem. Soc.* **1977**, *99*, 3559. A study of high-resolution polarized singlet–triplet spectra of unsaturated ketones suggests that C_β may be planar: (d) Jones, C. R.; Kearns, D. R. *J. Am. Chem. Soc.* **1977**, *99*, 344.
(28) Ziegler has documented a [2 + 2]-photocycloaddition that is consistent with the hypothesis proposed by Wiesner: Ziegler, F. E.; Kloek, J. A. *Tetrahedron Lett.* **1974**, 315.
(29) For a discussion of the dynamic properties of triplet excited states of cyclic enones, see: (a) Bonneau, R. *J. Am. Chem. Soc.* **1980**, *102*, 3816. (b) Schuster, D. I.; Dunn, D. A.; Heibel, G. E.; Brown, P. B.; Rao, J. M.; Woning, J.; Bonneau, R. *J. Am. Chem. Soc.* **1991**, *113*, 6245.



35

Figure 3. Proposed transition-state for the formation of **25** and **27** illustrating the optimal geometry for the manifestation of conformational memory effects.

in which reversion of the corresponding biradical intermediate formed from **21** (eq 2) competes with ring formation ($k_c \cong k_r$) (Scheme 6).

In addition to proceeding with high levels of enantioselectivity, the [2 + 2]-cycloadditions of coumarins **24** and **26** afford in each case a single olefin diastereomer. The formation of a single alkene may result from conformational memory effects in the 1,4-biradical intermediate as it undergoes intersystem crossing and ring closure (Figure 3).[30-32] Griesbeck has investigated these "memory effects" in the Paterno–Buchi cycloaddition reaction. Griesbeck's results suggest that for a 1,4-biradical with a short singlet lifetime, the spatial arrangement of substituents in the optimal conformation for intersystem crossing may result in diastereoselective product formation. The optimal spatial disposition for a 1,4-biradical to undergo intersystem crossing through a mechanism involving spin–orbit coupling is defined by the Salem–Roland rules.[33] The efficiency of spin–orbit coupling between the singlet and triplet states (1) increases with decreasing distance between the two centers, (2) is maximized when the orbitals are orthogonal, and (3) is proportional to the ionic character of the radicals. For the cases we have investigated, the putative 1,4-biradical formed upon addition of the coumarin to the allene (**35**, Figure 3) is likely an ideal candidate for rapid intersystem crossing (according to the Salem–Roland rules) and ring closure.[34] The spiro–fused ring system, buttressed by the adjacent, fused aromatic ring, is limited in the conformations it has available. Moreover, models suggest that in the coumarin-derived 1,4-biradicals (**35**, Figure 3), the orbitals are disposed in an arrangement with an interorbital angle α close to 90°. Thus, the formation of a single olefin diastereomer from **24** and **26** is a consequence of two rapid, successive processes, intersystem crossing and ring closure, which allow the initial orientation of the *tert*-butyl substituent on the allene to be reflected in the stereochemistry of product.

The transition-state model that accounts for the asymmetric induction in the photocycloaddition reaction of **30** is depicted in Scheme 7. The regiochemical outcome can be understood as a preference for forming an oxepane over an 8- or 9-membered heterocyclic ring. The enone face selectivity results from approach by the allene tether *exo* to the coumarin, placing the 2′-vinylic C–H over the fused rings, favoring structure **36** over **37** (Scheme 7). It is interesting to note that most allene–enone photocycloadditions that have been reported typically form five- and six-membered rings, yet irradiation of **30** affords a 7-membered ring in good yield with complete asymmetric induction.

The formation of alkyne **31** (Scheme 7) is accommodated by a mechanism in which the intermediate 1,4-biradical **38** undergoes a 1,5 H-shift at a faster rate than it closes to form an *exo*-methylenecyclobutane ($k_{1,5\text{-shift}} \gg k_{\text{closure}}$).[35] It is likely that the 5-6-6-7 tetracyclic ring system in **38** disposes the 1,4-biradical at a distance which precludes ring closure to form **39**. The isolation of alkyne **31** highlights the fact that alternate reaction processes (other than ring closure) may be accessed by the 1,4-biradical intermediate formed in the intramolecular allene–enone photoaddition, and these can yield products with excellent asymmetric induction. Alkynyloxepane **31** is a synthetically useful intermediate (Scheme 8) for the synthesis of chebulic acid **I**.[36] The photocycloaddition reaction **30** → **31** installs two of the three requisite stereogenic centers present in chebulic acid **I** with the oxepane serving as a masked dicarboxylic acid equivalent (Scheme 8).

Conclusion. The photocycloadditions described herein quantify asymmetric induction derived from the intramolecular cycloaddition reaction of optically active, 1,3-disubstituted allenes with enones and enoates. In all of the cases studied, high levels of enantioinduction are observed in the photoadducts. In addition, the intramolecular [2 + 2]-cycloadditions of allenes appended to 4-hydroxycoumarin at C(4) afforded *exo*-methylenecyclobutanes as a single olefin diastereomer. The enantioselective [2 + 2]-photocyclization reaction can provide access to optically active fused polycyclic structures that are otherwise not readily synthesized using current enantioselective methods.

Experimental Section

General Procedures. All nonaqueous reactions were performed using oven-dried glassware under an atmosphere of dry nitrogen. Photoreactions were performed in Pyrex flasks ($\lambda > 293$ nm) using a Hanovia 450-W Hg medium-pressure UV lamp in a water-cooled quartz immersion apparatus as the light source. Diethyl ether and tetrahydrofuran (THF) were distilled from sodium benzophenone ketyl prior to use. *N,N*-Diisopropylethylamine, dichloromethane, pyridine, and triethylamine were distilled from calcium hydride prior to use. Methanol was distilled from magnesium methoxide prior to use. Spectroscopy grade cyclohexane was used in photoreactions. Chromatographic purification of products was accomplished using forced flow chromatography on Baker 7024-R silica gel according to the method of Still.[37] NMR spectra were recorded on a Bruker AM-500 operating at 500 and 126 MHz for ^{1}H and ^{13}C, respectively, a JEOL GSX-400 operating at 400 and 100 MHz for ^{1}H and ^{13}C, respectively, or a General Electric QE Plus operating at 300 and 75 MHz for ^{1}H and ^{13}C, respectively, and were referenced to internal solvent signals. Data for ^{1}H are reported as follows: chemical shift (δ in ppm), integration, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; qn, quintet; m, multiplet), and coupling constant (J in Hz). NOE difference spectra were recorded on degassed samples and were quantitated by integrating the difference spectra. The phase-sensitive NOESY spectra were recorded at 300 MHz using the TPPI technique with a mixing time of 0.5 s, a recycle delay of 2.0 s, F2 and F1 spectral widths of 2717, and an initial matrix size of 256 × 1024 points, which was transformed into a 512 × 512 matrix after symmetrization. IR spectra were recorded on a Perkin-Elmer 1600 Series spectrometer. Optical rotations were determined on a JASCO DIP-181 polarimeter operating at the sodium D line and are reported as follows: $[\alpha]^{23}_D$, concentration (g/100 mL), and solvent. High-resolution mass spectrometry was performed by the Midwest Center for Mass Spectrometry at the University of Nebraska, with partial support by the National Science Foundation, Biology Division (Grant No. DIR9017262).

A. General Procedure for the Preparation of Enantioenriched Allenyl Alcohols. (i) *rac*-6, *rac*-7. To a solution of 2.45 mL (19.9 mmol, 1.5 equiv) of *tert*-butylacetylene in 100 mL of Et_2O at −78 °C was added dropwise 10.2 mL (17.3 mmol, 1.3 equiv) of a 1.7 M solution of ^{t}BuLi in pentane. The resulting mixture was stirred for 2 h, and a solution of 13.3 mmol (1 equiv) of aldehyde **1** or **2** in 10 mL of Et_2O was added

(30) (a) Griesbeck, A. G.; Stadtmuller, *J. Am. Chem. Soc.* **1990**, *112*, 1281. (b) Griesbeck, A. G.; Stadtmuller, S. *J. Am. Chem. Soc.* **1991**, *113*, 6923. (c) For a general review, see: Griesbeck, A. G.; Mauder, H.; Stadtmuller, S. *Acc. Chem. Res.* **1994**, *27*, 70.

(31) The possibility that [2 + 2]-photocycloadditions proceed in one step has been discussed: (a) Shaik, S.; Epiotis, N. D. *J. Am. Chem. Soc.* **1978**, *100*, 18. (b) Shaik, S. *J. Am. Chem. Soc.* **1979**, *101*, 3184.

(32) It has been suggested that intersystem crossing ($T_1 \rightarrow S_1$) by the putative 1,4-biradical may be the rate-determining step, see: Engel, P. S. *Chem. Rev.* **1980**, *80*, 318.

(33) Salem, L.; Rowland, C. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 92.

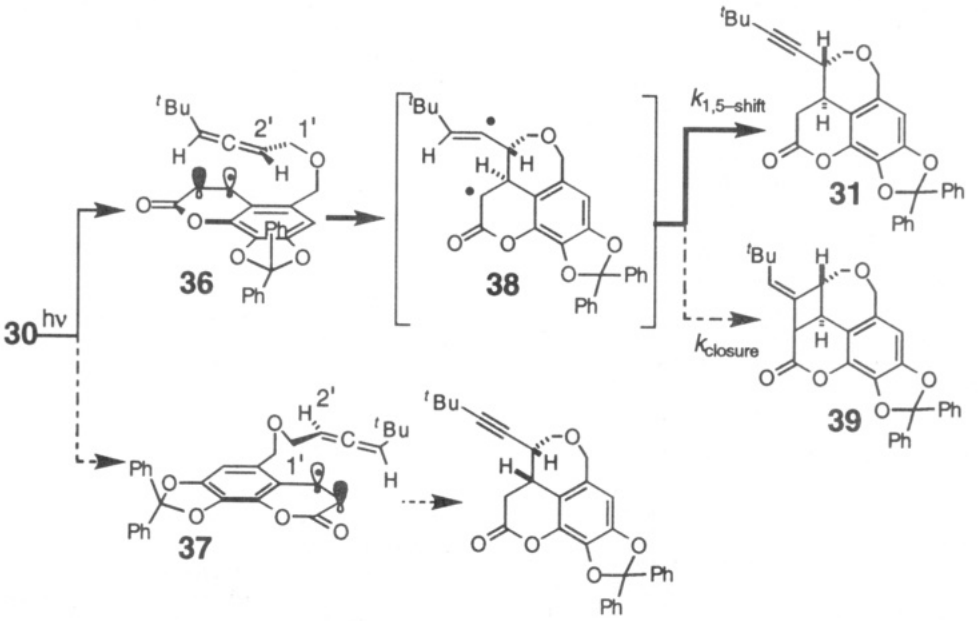
(34) For an elegant example of stereospecific ring closure of a 1,4-biradical intermediate proceeding through a singlet state, see: Bartlett, P. D.; Porter, N. A. *J. Am. Chem. Soc.* **1968**, *90*, 5317.

(35) The putative 1,4-biradicals formed in [2 + 2]-photoadditions have been reported to undergo 1,5-hydrogen shifts with concomitant fragmentation reactions. See, for example: (a) Berettoni, M.; Cocchi, R.; Bettolo, R. M.; Montagnini, L.; Romeo, S. *Tetrahedron Lett.* **1993**, *34*, 715. (b) Reference 27b.

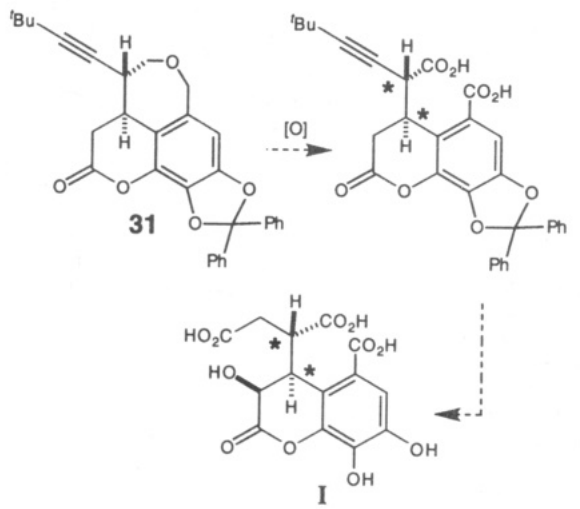
(36) The conversion of **31** to chebulic acid is part of ongoing studies in our laboratories and will be reported in due course.

(37) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

Scheme 7



Scheme 8



dropwise. The reaction mixture was stirred at −78 °C for 1 h and allowed to warm to 23 °C thereafter. When warming was complete, the reaction mixture was poured into 100 mL of 1.0 M aqueous KH_2PO_4 solution (pH 4.5). The aqueous layer was extracted with an additional 100 mL of Et_2O, and the combined organic layers were washed with saturated aqueous NaCl solution, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*.

Data for *rac*-6. Purification of the residue by chromatography on silica gel (40 × 100 mm, 8:1 hexanes:EtOAc, R_f 0.31) afforded 2.63 g (77%) of ***rac*-6** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.38 (1H, dt, J = 7.6, 3.8), 3.72 (1H, dd, J = 13.9, 3.9), 3.58 (1H, dd, J = 13.7, 7.7), 2.54 (1H, d, J = 3.7), 1.22 (9H, s), 0.91 (9H, s), 0.09 (3H, s), 0.08 (3H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 94.3, 76.3, 67.3, 63.2, 30.9, 30.7, 25.8, 18.3, −5.3; IR (thin film) ν 3422, 2956, 2929, 2858, 2244, 1473, 1462, 1389, 1362, 1319, 1256, 1204, 1123, 1063, 837, 778.

Data for *rac*-7. Purification of the residue by chromatography on silica gel (30 × 150 mm, 10:1 hexanes:EtOAc, R_f 0.29) afforded 2.59 g (72%) of ***rac*-7** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.59 (1H, td, J = 6.2, 4.3), 4.02 (1H, ddd, J = 10.7, 7.7, 4.1), 3.81 (1H, ddd, J = 10.9, 7.5, 5.8), 3.19 (1H, d, J = 6.0), 1.98–1.92 (1H, m), 1.86–1.80 (1H, m), 1.22 (9H, s), 0.91 (9H, s), 0.09 (3H, s), 0.08 (3H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 93.7, 79.1, 62.0, 61.2, 39.2, 31.0, 27.3, 25.9, 18.2, −5.52, −5.54; IR (thin film) ν 3407, 2956, 2930, 2859, 2235, 1470, 1390, 1326, 1257, 1204, 1097, 1021, 943, 834, 777, 733, 664.

(ii) 6, 7. To a solution of 19.6 mmol (1.0 equiv) of ***rac*-6** or ***rac*-7** in 100 mL of CH_2Cl_2 was added 12.7 g (29.9 mmol, 1.5 equiv) of the Dess–Martin periodinane, prepared according to the procedure of Ireland.[38] The reaction mixture was stirred for 15 min at 23 °C, and 300 mL of Et_2O was added. The precipitates were removed by filtration through Celite, and the filtrate was concentrated *in vacuo*.

Data for 4. Purification of the residue by chromatography on silica gel (20 × 80 mm, 8:1 hexanes:EtOAc, R_f 0.45) afforded 4.82 g (95%) of **4** as a clear, colorless oil.

Data for 5. Purification of the residue by chromatography on silica gel (30 × 100 mm, 10:1 hexanes:EtOAc, R_f 0.32) afforded 4.75 g (90%) of **5** as a clear, colorless oil.

The alkynones **4** and **5** were used immediately. To 1.68 g (6.49 mmol, 2 equiv) of neat (+)-β-isopinocampheyl-9-borabicyclo[3.3.1]nonane was added 3.24 mmol (1 equiv) of neat **4** or **5**, and the resulting yellow solution was stirred at 23 °C for 7 h. To the reaction mixture was added 100 mL of Et_2O followed by 100 mL of 6 M NaOH aqueous solution. The layers were separated and the aqueous layer extracted with 2 × 50 mL Et_2O. The combined organic layers were washed with 50 mL 1.0 M aqueous KH_2PO_4 solution (pH 4.5) and 50 mL saturated aqueous NaCl solution, dried over anhydrous Na_2SO_4 and concentrated *in vacuo*.

Data for 6. Purification of the residue by chromatography on silica gel (20 × 100 mm, 8:1 hexanes:EtOAc, R_f 0.31) afforded 648 mg (78%) of **6**, spectroscopically and chromatographically identical to ***rac*-6**. A small portion was treated with DMAP (5.0 equiv) and (*S*)-MTPACl (2.0 equiv) in CH_2Cl_2. Integration of the ^{1}H NMR (300 MHz, $CDCl_3$) resonances at δ 1.21 (major) and δ 1.18 (minor) ppm indicated a diastereomer ratio of 11.9:1.00 (84% ee).[39]

Data for 7. Purification of the residue by chromatography on silica gel (30 × 150 mL, 10:1 hexanes:EtOAc, R_f 0.29) afforded 0.860 g (93%) of **7**, spectroscopically and chromatographically identical to ***rac*-7** except for optical rotation, $[\alpha]^{23}_D$ −17.6° (c = 1.87, CH_2Cl_2). A small portion was treated with DMAP (5 equiv) and (*S*)-MTPA-Cl (2 equiv) in CH_2Cl_2. Integration of the ^{1}H NMR (500 MHz, $CDCl_3$) resonances at δ 1.22 (major) and δ 1.18 (minor) ppm indicated a diastereomer ratio of 18.8:1.00 (90% ee).

(iii) 10, 11. To a solution of 2.77 mmol) (1.0 equiv) of **6** or **7** and 577 μL (4.16 mmol, 1.5 equiv) Et_3N in 20 mL CH_2Cl_2 at 0 °C was added dropwise 258 μL (3.33 mmol, 1.2 equiv) MsCl at such a rate that the internal temperature was maintained below 5 °C. After stirring for 0.5 h the reaction mixture was transferred *via* cannula into a solution of 6.5 mL MeOH and 6.5 mL anhydrous H_2NNH_2. The reaction mixture was stirred at 23 °C for 36 h and poured into 120 mL water. The aqueous layer was extracted with 2 × 100 mL 95:5 CH_2Cl_2:MeOH. The organic layers were combined, washed with 50 mL saturated aqueous NaCl solution, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The residue was redissolved in 66 mL 1:1 Et_2O:CH_2Cl_2 and cooled to 0 °C. 986 mg (5.63 mmol, 2.0 equiv) 4-phenyl-1,2,4-triazoline-3,5-dione

(38) Ireland, R. E.; Liu, L. *J. Org. Chem.* **1993**, *58*, 2899.

(39) The enantiomeric excesses varied from batch to batch but were reproducibly 84–92% ee.

(PTAD) were added in one portion. When gas evolution was complete 65 mL *n*-pentane were added and the reaction mixture filtered through a pad (2 × 5 cm) of silica gel. The pad was washed with 100 mL 4:1 *n*-pentane:CH_2Cl_2 and the filtrate concentrated *in vacuo*.

Data for 10. Purification of the residue by chromatography on silica gel (20 × 80 mm; 4:1 *n*-pentane:CH_2Cl_2, R_f 0.48) afforded 466 mg (70%) **10** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.27 (1H, q, J = 6.3), 5.20 (1H, dt, J = 6.3, 2.6), 4.21–4.13 (2H, m), 1.04 (9H, s), 0.90 (9H, s), 0.08 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.7, 104.3, 93.5, 62.2, 31.8, 30.2, 25.9, 18.4, –5.1; IR (thin film) ν 2960, 2931, 2901, 2857, 1962, 1473, 1411, 1389, 1362, 1255, 1205, 1190, 1143, 1086, 1048, 1006, 938, 925, 887, 837, 814, 776, 717, 678, 664.

Data for 11. Purification of the residue by chromatography on silica gel (20 × 80 mm, *n*-pentane, R_f 0.33) afforded 503 mg (71%) **11** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.14 (1H, q, J = 6.6), 5.11–5.05 (1H, m), 3.67 (2H, t, J = 7.0), 2.21 (2H, dq, J = 7.0, 3.9), 1.02 (9H, s), 0.90 (9H, s), 0.06 (s, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.7, 102.9, 89.1, 63.1, 32.9, 31.6, 30.2, 26.0, 18.4, –5.3; IR (thin film) ν 2960, 2901, 2859, 2738, 2710, 1962, 1472, 1462, 1408, 1387, 1361, 1327, 1254, 1206, 1191, 1103, 1006, 937, 873, 836, 811, 776, 736, 663; $[\alpha]^{23}_D$ +21.8° (c = 4.59, CH_2Cl_2).

(iv) 12, 13: To a solution of 1.95 mmol (1.0 equiv) of **10** or **11** in 8 mL of THF was added 2.34 mL (2.34 mmol, 1.2 equiv) of a 1.0 M solution of TBAF in THF. The reaction mixture was stirred for 30 min at 23 °C and poured into 35 mL of 1.0 M aqueous KH_2PO_4 (pH 4.5) solution. The aqueous layer was extracted with 50 mL of Et_2O. The combined organic layers were washed with 20 mL of 1.0 M aqueous KH_2PO_4 solution, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*.

Data for 12. Purification of the residue by chromatography on silica gel (10 × 60 mm, 4:1 hexanes:EtOAc, R_f 0.27) afforded 219 mg (89%) of **12** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.40 (1H, q, J = 5.9), 5.32 (1H, dt, J = 6.2, 2.9), 4.12–4.10 (2H, m), 2.04 (1H, br s), 1.05 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.3, 106.1, 93.6, 60.9, 31.8, 30.1; IR (thin film) ν 3332, 2960, 2903, 2866, 1961, 1742, 1727, 1475, 1462, 1412, 1389, 1363, 1253, 1206, 1190, 1119, 1049, 1013, 941, 870, 740, 692.

Data for 13. Purification of the residue by chromatography on silica gel (20 × 80 mm, 2:1 *n*-pentane:Et_2O, R_f 0.48) afforded 221 mg (80%) of **13** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.20–5.16 (2H, m), 3.72 (1H, dt, J = 7.9, 6.0, 1.7), 2.29–2.23 (2H, m), 1.53 (1H, t, J = 6.0), 1.04 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.9, 103.7, 89.0, 62.1, 32.5, 31.7, 30.1; IR (thin film) ν 3419, 2959, 2901, 2866, 1961, 1638, 1474, 1460, 1362, 1253, 1191, 1049, 874; $[\alpha]^{23}_D$ +74.1° (c = 1.43, CH_2Cl_2); HRMS (EI) calcd for $C_9H_{16}O$ 140.1201, found 140.1205.

B. Preparation of Photosubstrates by Mitsunobu Condensation. 18, 21, 24. To a solution of 108 mg (0.770 mmol, 1.0 equiv) of **13** in 8 mL of THF were added 0.942 mmol (1.2 equiv) of 1,3-dione, 246 mg (1.15 mmol, 1.5 equiv) of Ph_3P, and 182 μL (1.15 mmol, 1.5 equiv) of DEAD, and the resulting orange solution was stirred for 15 min at 23 °C. The reaction mixture was concentrated *in vacuo*.

Data for 18. Purification of the residue by chromatography on silica gel (20 × 100 mm, 3:1 hexanes:EtOAc, R_f 0.25) afforded 101 mg (56%) of **18** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.34 (1H, s), 5.18–5.14 (2H, m), 3.91–3.87 (2H, m), 2.46–2.36 (4H, m), 2.33 (2H, t, J = 6.4), 1.97 (2H, q, J = 6.4), 1.01 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.7, 199.7, 177.8, 104.2, 102.8, 88.2, 67.6, 36.8, 31.6, 30.1, 29.0, 28.2, 21.2; IR (thin film) ν 2956, 2900, 2867, 1961, 1653, 1604, 1460, 1428, 1395, 1365, 1327, 1219, 1181, 1135, 1058, 1009, 962, 928, 876, 826, 757; $[\alpha]^{23}_D$ +33.9° (c = 0.414, CH_2Cl_2); HRMS (EI) calcd for $C_{15}H_{22}O_2$ 234.1620, found 234.1630.

Data for 21. Purification of the residue by chromatography on silica gel (20 × 80 mm, 5:2 hexanes:EtOAc, R_f 0.25) afforded 121 mg (71%) of **21** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.28 (1H, t, J = 1.1), 5.19–5.15 (2H, m), 4.02 (2H, m), 2.62–2.59 (2H, m), 2.49–2.40 (4H, m), 0.86 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 205.8, 202.1, 190.1, 104.9, 104.6, 88.3, 71.1, 34.2, 31.9, 30.1, 28.6, 28.4; IR (thin film) ν 3093, 2958, 2865, 2358, 1962, 1705, 1680, 1592, 1462, 1439, 1413, 1389, 1288, 1248, 1222, 1180, 1008, 930, 879, 830; $[\alpha]^{23}_D$ +42.6° (c = 4.07, CH_2Cl_2); HRMS (EI) calcd for $C_{14}H_{20}O_2$ 220.1463, found 220.1466.

Data for 24. Purification of the residue by chromatography on silica gel (20 × 100 mm, 5:1 hexanes:EtOAc, R_f 0.21) afforded 123 mg (57%) of **24** as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 (1H, dd, J = 7.9, 1.6), 7.51 (1H, dd, J = 8.6, 7.0, 1.6), 7.27 (1H, dd, J = 8.5, 0.7), 7.23 (1H, ddd, J = 8.5, 7.1, 1.1), 5.64 (1H, s, C^3*H*), 5.25 (1H, q, J = 6.4), 5.18–5.15 (1H, m), 4.17 (2H, t, J = 6.6), 2.61–2.54 (2H, m), 0.99 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 201.8, 165.5, 162.8, 153.3, 132.2, 123.7, 123.0, 116.6, 115.6, 104.4, 90.4, 87.8, 68.4, 31.6, 30.0, 28.1; IR (thin film) ν 3093, 3044, 2957, 2864, 1963, 1826, 1743, 1610, 1567, 1495, 1473, 1459, 1415, 1369, 1328, 1279, 1239, 1205, 1184, 1158, 1147, 1107, 1081, 1033, 997, 933, 912, 894, 874, 827, 769, 750, 734, 684, 646; $[\alpha]^{23}_D$ +45.0° (c = 4.00, CH_2Cl_2); HRMS (EI) calcd for $C_{18}H_{20}O_3$ 284.1412, calcd for $C_{18}H_{19}O_3$ (M^+ – H) 283.1334, found 283.1338.

C. Irradiation of Allene–Enones. A 200-mL Pyrex flask was charged with a solution of 0.556 mmol of photosubstrate in 120 mL of cyclohexane. The solution was degassed by argon sparge for 10 min and irradiated at 23 °C for 4 h. The solvent was removed *in vacuo*.

(i) Irradiation of 18. Purification of the residue by chromatography on silica gel (20 × 100 mm, 4:1 hexanes:EtOAc, R_f 0.42 (**20**), 0.33 (**19**)) afforded 41 mg (32%) of **19** and 74 mg (57%) of **20** as clear, colorless oils. Data for **19**: ^{1}H NMR (500 MHz, C_6D_6) δ 5.52 (1H, t, J = 2.4), 3.83 (1H, ddd, J = 9.3, 7.8, 1.7), 3.65 (1H, ddd, J = 10.4, 9.3, 5.6), 3.50 (1H, t, J = 2.8), 3.02 (1H, dt, J = 7.2, 2.6), 2.29 (1H, dt, J = 18.3, 3.7), 1.91–1.40 (7H, m), 0.93 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 208.2, 136.4, 127.6, 84.0, 67.4, 59.5, 50.5, 38.7, 33.8, 33.1, 31.1, 30.2, 19.1; IR (thin film) ν 2950, 2861, 1700, 1603, 1461, 1360, 1280, 1220, 1171, 1144, 1076, 995, 955, 918, 869, 835; $[\alpha]^{23}_D$ –106.7° (c = 0.150, CH_2Cl_2). Integration of the ^{1}H NMR (500 MHz, $CDCl_3$) resonances at δ 1.31 (major) and 1.26 (minor) in the presence of 1.0 equiv of Ag(fod) and 2.0 equiv of (+)-Eu(hfc)$_3$ indicated an enantiomer ratio of 22.1:1.00 (91% ee). Data for **20**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.40 (1H, t, J = 2.4), 4.11 (1H, dd J = 8.9, 0.2), 3.98 (1H, ddd, J = 11.2, 8.9, 5.3), 3.64 (1H, t, J = 2.8), 3.30 (1H, dt, J = 7.5, 2.6), 2.55 (1H, ddd, J = 16.6, 6.3, 3.2), 2.28 (1H, ddd, J = 16.8, 9.8, 7.6), 2.08–1.78 (6H, m), 1.04 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 209.4, 138.9, 130.0, 87.1, 67.8, 60.6, 51.0, 38.8, 33.4, 32.8, 30.8, 29.8, 19.7; IR (thin film) ν 2947, 2866, 1704, 1465, 1358, 1310, 1275, 1218, 1142, 1068, 992, 955, 905, 854; $[\alpha]^{23}_D$ +53.3° (c = 0.357, CH_2Cl_2). Integration of the ^{1}H NMR (500 MHz, $CDCl_3$) resonances at δ 1.25 (major) and 1.23 (minor) in the presence of 1.0 equiv of Ag(fod) and 2.0 equiv of (+)-Eu(hfc)$_3$ indicated an enantiomer ratio of 23.0:1.00 (92% ee).

(ii) Irradiation of 21. Purification of the residue by chromatography on silica gel (20 × 100 mm, 5:1 hexanes:EtOAc, R_f 0.33 (**23**), 0.27 (**22**, and an unidentified side product)) afforded 48 mg (37%) of **23** as a clear, colorless oil and 46 mg (35%) of an inseparable mixture of two products, one of which was assigned as **22** on the basis of the ^{1}H NMR spectrum, as a clear, colorless oil. Data for **23**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.33 (1H, t, J = 1.8), 4.18 (1H, t, J = 8.1, 7.9, 0.2), 3.92 (1H, ddd, J = 12.8, 7.7, 3.9), 3.36 (1H, d, J = 1.9), 3.37–3.31 (1H, m), 2.66 (1H, ddd, J = 19.8, 9.4, 8.2), 2.53–2.45 (1H, m), 2.21–2.11 (2H, m), 2.04–1.98 (1H, m), 1.82 (1H, ddd, J = 12.2, 5.2, 0.2), 1.06 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 212.7, 138.6, 118.2, 88.4, 68.9, 57.1, 38.5, 33.7, 33.4, 30.6, 29.9; IR (thin film) ν 2950, 2864, 1737, 1469, 1413, 1360, 1314, 1264, 1199, 1138, 1068, 983, 912, 854; $[\alpha]^{23}_D$ +21.6° (c = 0.247, CH_2Cl_2). Integration of the ^{1}H NMR (500 MHz, $CDCl_3$) resonances at δ 1.37 (major) and 1.34 (minor) in the presence of 1.0 equiv of Ag(fod) and 2.0 equiv of (+)-Eu(hfc)$_3$ indicated an enantiomer ratio of 6.68:1.00 (74% ee). Data for **22**: integration of the ^{1}H NMR (500 MHz, $CDCl_3$) resonances at δ 1.19 (major) and 1.18 (minor) in the presence of 1.0 equiv of Ag(fod) and 2.0 equiv of (+)-Eu(hfc)$_3$ indicated an enantiomer ratio of 7.94:1.00 (78% ee).

(iii) Irradiation of 24. Purification of the residue by chromatography on silica gel (20 × 100 mm, 5:1 hexanes:EtOAc, R_f 0.34) afforded 139 mg (88%) of **25** as a white solid: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (1H, ddd, J = 8.1, 1.1, 0.3); 7.35 (1H, ddd, J = 8.3, 7.4, 1.7), 7.22 (1H, td, J = 7.4, 1.1), 7.10 (1H, ddd, J = 7.4, 1.7, 0.2), 5.78 (1H, t, J = 2.4), 4.45 (1H, ddd, J = 8.7, 1.7, 1.6), 4.18 (1H, ddd, J = 10.9, 9.3, 5.8), 4.01 (1H, t, J = 3.0), 3.70–3.67 (1H, m), 2.40–2.32 (1H, m), 2.18–2.14 (1H, m), 1.09 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.1, 150.4, 138.9, 130.0, 126.7, 126.0, 125.1, 121.7, 117.3, 79.7, 68.6, 57.9, 49.8, 34.0, 33.7, 30.1; IR (thin film) ν 2956, 2867, 1761, 1616, 1588, 1490, 1474, 1455, 1363, 1328, 1260, 1203, 1186, 1167, 1115, 1087, 1069, 1034, 999, 955, 927, 758; $[\alpha]^{23}_D$ +162° (c = 0.363, CH_2Cl_2). A solution of 11 mg (37 μmol, 1 equiv) of **15** in 1 mL of THF at 0 °C was treated with 40 μL (80 μM, 2.2 equiv) of a 2.0 M solution of $LiBH_4$ in THF. The reaction mixture was stirred at 0 °C for 30 min, poured into 2 mL of 1.0 M aqueous KH_2PO_4 solution, and extracted with 3 mL of Et_2O. Concentration *in vacuo* and chromatography on silica gel (4 × 20 mm, 2:1 hexanes:EtOAc, R_f 0.36) afforded 4 mg (80%) of a diol which was treated with DMAP (10 equiv) and (*S*)-MTPA-Cl (4 equiv) in CH_2Cl_2. Integration

of the ^{1}H NMR (500 MHz, $CDCl_3$) resonances at δ 1.04 (minor) and 1.02 (major) indicated a diastereomer ratio of 22.9:1.00 (92% ee).

(iv) Irradiation of 21 to Partial Conversion. A solution of 40 mg of **21** of 89% ee in 36 mL of cyclohexane was degassed and irradiated according to the procedure above. The reaction was stopped at various intervals and the solvent removed *in vacuo*. The extent of conversion of **21** to **22**, **23**, and an unidentified side product was determined by integration of the ^{1}H NMR (500 MHz, $CDCl_3$) resonances at δ 5.56–5.54 (unidentified side product), 5.39–5.39 (**22**), 5.34–5.33 (**23**), and 5.30–5.29 (**21**). The crude reaction mixture was purified by chromatography on silica gel (10 × 80 mm, 5:1 hexanes:EtOAc, R_f 0.33) to isolate **23**. The enantiomeric excess of the product was determined by integration of the ^{1}H NMR (500 MHz, $CDCl_3$) resonances at δ 1.37 (major) and 1.34 (minor) in the presence of 1 equiv of Ag(fod) and 2 equiv of (+)-Eu(hfc)$_3$. When the reaction was stopped at 14% (20 min) and 38% (2 h) conversion, the enantiomeric excess of **23** was 88% and 82% respectively.

(v) Triplet-Sensitized Irradiation of 24. A solution of 31 mg of **24** and 286 mg of benzophenone in 1 mL of benzene was irradiated through a uranium glass filter for 2 h. The volatiles were removed *in vacuo*. Analysis of the residue by ^{1}H NMR (500 MHz, $CDCl_3$) indicated that only **25** was formed during the reaction.

28. To a solution of 361 mg (2.86 mmol, 1.0 equiv) of **13** in 6 mL of 1:1 hexanes:CH_2Cl_2 was added 600 μL (4.32 mmol, 1.5 equiv) of TEA. The reaction mixture was cooled to 0 °C, and 265 μL (3.42 mmol, 1.2 equiv) of MsCl was added dropwise *via* syringe. The reaction mixture was stirred at 0 °C for 15 min, filtered, and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (20 × 30 mm, 1:1 hexanes:Et_2O with 2% v/v TEA) to afford 453 mg (78%) of **28**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.40–5.35 (2H, m), 4.72–4.70 (2H, m), 3.03 (3H, s), 1.06 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.9, 105.5, 87.5, 69.0, 38.3, 30.0, 12.1; IR (thin film) ν 2955, 1960, 1461, 1349, 1255, 1173, 920, 820, 714.

30. A 25-mL round-bottom flask was charged with 76 mg (2.5 mmol, 1.2 equiv) of an 80% dispersion of NaH in mineral oil. The dispersion was washed three times with anhydrous hexanes and dried briefly under high vacuum. A nitrogen atmosphere was reestablished, and 5 mL of DMF was added. The solution was cooled to 0 °C, and 782 mg (2.1 mmol, 1.0 equiv) of **29** was added as a solution in 5 mL of DMF *via* cannula. Fifteen minutes after gas evolution ceased, 450 mg (2.2 mmol, 1.1 equiv) of **28** was added, and the mixture was stirred at 23 °C for 2 h. The reaction mixture was diluted with 20 mL of H_2O, and extracted with 3 × 10 mL of Et_2O. The organic layers were combined, washed with 10 mL of saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. Purification of the residue by chromatography on silica gel (60 × 250 mm, 1.8:1 hexanes:Et_2O, R_f 0.23) afforded 807 mg (80%) of **30** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58–7.53 (4H, m), 7.48 (1H, d), 7.42–7.36 (6H, m), 6.70 (1H, s), 6.22 (1H, d, J = 12.3), 5.40 (1H, q, J = 6.5), 5.17 (1H, dt, J = 6.2, 2.2), 4.91–4.82 (4H, m), 0.92 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 203.0, 168.2, 150.1, 140.1, 139.3, 137.1, 135.7, 131.2, 129.5, 128.4, 126.3, 123.1, 119.8, 118.5, 104.8, 103.7, 89.3, 70.9, 68.5, 31.7, 29.9; IR (thin film) ν 3062, 2959, 2926, 2862, 1963, 1713, 1622, 1614, 1592, 1488, 1453, 1383, 1304, 123.8, 1209, 1116, 1086, 1045, 1021, 949, 818, 762, 699.

31. A 250-mL Schlenk flask charged with a solution of 250 mg of **30** in 167 mL of CH_2Cl_2. The solution was degassed by three cycles of freeze–pump–thaw and irradiated for 4 h at 0 °C. The volatiles were removed *in vacuo*, and the residue was purified by chromatography on silica gel (20 × 100 mm, 3:1 hexanes:EtOAc, R_f 0.33) to afford 151 mg (60%) of **31** as a white solid: ^{1}H NMR (500 MHz, C_6D_6) δ 7.70–7.61 (4H, m), 7.08–6.97 (6H, m), 6.07 (1H, s), 4.52 (1H, d, J = 14.0), 4.43 (1H, d, J = 14.0), 3.69 (1H, dd, J = 10.6, 5.5), 3.65 (1H, dd, J = 10.6, 3.4) 2.84 (1H, dd, J = 15.4, 12.3), 2.76 (1H, dd, J = 15.5, 4.0), 2.71 (1H, dt, J = 12.2, 4.0), 2.30–2.27 (1H, m), 0.97 (9H, s); ^{13}C NMR (126 MHz, C_6D_6) δ 171.3, 147.2, 140.8, 140.7, 139.1, 135.3, 129.3, 129.2, 128.5, 128.4, 126.7, 118.2, 117.7, 102.3, 94.3, 74.4, 68.8, 67.7, 38.3, 33.2, 31.3, 30.9, 27.4; IR (thin film) ν 3063, 3032, 2967, 2927, 2900, 2866, 2280, 2268, 1746, 1732, 1716, 1637, 1496, 1471, 1450, 1392, 1372, 1337, 1315, 1286, 1262, 1240, 1209, 1181, 1128, 1113, 1095, 1083, 1045, 1020, 1002, 949, 921, 906, 834, 812, 778, 764, 700, 676, 660, 642, 629, 616. A solution of 6.0 mg of **31** in 1.5 mL of THF was cooled to 0 °C. To the solution was added 13.2 μL (26.4 μM, 2.1 equiv) of a 2.0 M solution of $LiBH_4$ in THF. The reaction mixture was stirred at 0 °C for 30 min, poured into 2 mL of 1.0 M aqueous KH_2PO_4 solution, and extracted with 5 mL of Et_2O. Concentration *in vacuo* and chromatography on silica gel (4 × 20 mm, 1:1 hexanes:EtOAc, R_f 0.19) afforded 4 mg (80%) of a diol which was treated with DMAP (10 equiv) and (*S*)-MTPA-Cl (4.0 equiv) in CH_2Cl_2. Integration of the ^{1}H NMR (500 MHz, $CDCl_3$) resonances at δ 5.17 (major) and 5.12 (minor) indicated a diastereomer ratio of 23.5:1.00 (92% ee).

15. To a solution of 693 μL (5.68 mmol, 1.6 equiv) of *tert*-butylacetylene in 5 mL of THF at –78 °C was added dropwise 3.32 mL (5.31 mmol, 1.5 equiv) of a 1.6 M solution of ^{t}BuLi in pentane. The resulting mixture was stirred for 30 min at –78 °C, and a solution of 550 mg (3.48 mmol, 1.0 equiv) of D-glyceraldehyde diethyl ketal, prepared according to the procedure of Schmid,[40] in 5 mL of THF was added dropwise. The transfer was quantitated with an additional 2 mL of THF. The reaction mixture was warmed to 23 °C. When warming was complete, the reaction mixture was poured into 20 mL of 1.0 M aqueous KH_2PO_4 solution (pH 4.5) and 25 mL of Et_2O. The aqueous layer was extracted with an additional 3 × 20 mL of Et_2O, and the combined organic layers were washed with saturated aqueous NaCl solution, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (20 × 350 mm, 4:1 hexanes:Et_2O, R_f 0.25) to afford 210 mg (25%) of **15** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.57–4.53 (1H, m), 4.21 (1H, td, J = 7.1, 3.5), 4.06 (1H, dd, J = 8.2, 6.7), 3.98 (1H, t, J = 8.1), 2.23–2.20 (1H, br s), 1.76–1.62 (4H, m), 1.21 (9H, s), 0.94 (3H, t, J = 7.3), 0.90 (3H, t, J = 7.5); ^{13}C NMR (126 MHz, $CDCl_3$) δ 113.8, 95.4, 78.2, 75.2, 65.3, 62.1, 30.8, 29.8, 28.9, 27.4, 8.1; IR (thin film) ν 3444, 2969, 2240, 1836, 1463, 1378, 1362, 1263, 1202, 1173, 1124, 1082, 1060, 1040, 978, 941, 919, 870, 831, 767, 709, 676; $[\alpha]^{23}_D$ +47.1° (c = 0.170, CH_2Cl_2).

16. To a solution of 581 mg (2.42 mmol, 1.0 equiv) of **15** and 503 μL (3.63 mmol, 1.5 equiv) of Et_3N in 5 mL of CH_2Cl_2 at 0 °C was added dropwise 225 μL (2.90 mmol, 1.2 equiv) of MsCl at such a rate that the internal temperature was maintained below 5 °C. After being stirred for 0.5 h, the reaction mixture was transferred *via* cannula into a solution of 10 mL of MeOH and 10 mL of anhydrous H_2NNH_2. The reaction mixture was stirred at 23 °C for 144 h and poured into 100 mL of water. The aqueous layer was extracted with 2 × 40 mL of 95:5 CH_2Cl_2:MeOH. The organic layers were combined, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was redissolved in 20 mL of 1:1 Et_2O:CH_2Cl_2 and cooled to 0 °C. An 848-mg portion (4.84 mmol, 2.0 equiv) of PTAD was added at once. When gas evolution was complete, 20 mL of *n*-pentane was added, and the reaction mixture was filtered through a pad (1 × 2 cm) of silica gel. The pad was washed with 20 mL of 4:1 *n*-pentane:CH_2Cl_2, and the filtrate was concentrated *in vacuo*. The residue was purified by chromatography on silica gel (20 × 80 mm, 1:1 *n*-pentane:CH_2Cl_2, R_f 0.19) to afford 348 mg (64%) of **16** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.30 (1H, dd, J = 6.2, 1.5), 5.24 (1H, dd, J = 7.3, 6.3), 4.53 (1H, dddd, J = 7.9, 7.4, 6.1, 1.5), 4.08 (1H, dd, J = 8.0, 6.1), 3.66 (1H, t, J = 7.9), 1.69–1.62 (4H, m), 1.03 (9H, s), 0.93–0.89 (6H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.0, 113.3, 105.1, 92.3, 75.3, 69.9, 31.6, 30.1, 30.0, 29.8, 8.1, 8.0; IR (thin film) ν 2964, 2881, 1964, 1463, 1390, 1362, 1336, 1310, 1272, 1250, 1232, 1198, 1173, 1132, 1078, 1038, 961, 918, 875, 748; $[\alpha]^{23}_D$ –25.1° (c = 2.47, CH_2Cl_2).

44. To a solution of 300 mg (1.34 mmol, 1.0 equiv) of **16** in 13 mL of MeOH was added 20 mg (0.222 mmol, 0.17 equiv of oxalic acid. The solution was stirred for 48 h at 23 °C and concentrated *in vacuo*, and the residue was purified by chromatography on silica gel (20 × 100 mm, 1.5:1 hexanes:EtOAc, R_f 0.23) to afford 136 mg (65%) of a diol, **44**, as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.35 (1H, dd, J = 6.3, 2.4), 5.28 (1H, t, J = 6.2), 4.26–4.22 (1H, m), 3.68 (1H, dd, J = 11.2, 3.5), 3.54 (1H, dd, J = 11.3, 7.2), 2.32–2.06 (2H, br s), 1.04 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.3, 106.5, 93.5, 70.4, 66.7, 31.8, 30.1; IR (thin film) ν 3358, 2959, 2865, 1964, 1647, 1472, 1458, 1395, 1362, 1317, 1253, 1205, 1190, 1123, 1080, 871; $[\alpha]^{23}_D$ –62.6° (c = 0.303, CH_2Cl_2).

45. To a solution of 136 mg (0.871 mmol, 1.0 equiv) of **44** in 15 mL of CH_2Cl_2 were added sequentially 181 μL (1.31 mmol, 1.5 equiv) of Et_3N, 131 mg (0.871 mmol, 1.0 equiv) of TBSCl, and 11 mg (0.087 mmol, 0.1 equiv) of DMAP. The solution was stirred for 16 h at 23 °C, poured into 20 mL of 1.0 M aqueous KH_2PO_4 solution (pH 4.5), and extracted with 2 × 20 mL of Et_2O. The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*, and the residue was purified by chromatography on silica gel (20 × 60 mm, 1:1 hexanes:CH_2Cl_2, R_f 0.26) to afford 120 mg (54%) of primary silyl ether **45** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.29 (1H, dd, J = 6.3, 2.2), 5.24 (1H, t, J = 6.3), 4.20–4.14 (1H, m), 3.66 (1H, dd, J =

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10.0, 3.9), 3.52 (1H, dd, J = 10.0, 7.4), 2.48 (1H, d, J = 2.0), 1.04 (9H, s), 0.91 (9H, s), 0.81 (6H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.6, 105.4, 93.2, 70.6, 67.4, 31.7, 30.1, 25.9, 18.3, -5.4; IR (thin film) ν 3566, 3441, 2958, 2929, 2902, 2859, 1964, 1732, 1473, 1463, 1390, 1362, 1318, 1254, 1218, 1190, 1109, 1073, 1006, 938, 837, 815, 728, 668; $[\alpha]^{23}_D$ +4.0° (c = 3.02, CH_2Cl_2).

46. To a solution of 100 mg (0.370 mmol, 1.0 equiv) of **45** in 12 mL of CH_2Cl_2 were added successively 103 μL (0.739 mmol, 2.0 equiv) of Et_3N and 129 μL (0.4812 mmol, 1.3 equiv) of TIPSOTf. The reaction was stirred at 23 °C for 2 h, poured into 20 mL of 1.0 M aqueous KH_2PO_4 solution (pH 4.5), and extracted with 2 × 15 mL of Et_2O. The organic layers were dried over anhydrous Na_2SO_4 and concentrated *in vacuo*, and the residue was purified by chromatography on silica gel (20 × 80 mm, hexanes, R_f 0.19) to afford 154 mg (97%) of disilyl ether **46** as a clear, colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.16–5.14 (2H, m), 4.28–4.22 (1H, m), 3.64 (1H, dd, J = 9.9, 6.2), 3.54 (1H, dd, J = 10.0, 5.5), 1.26–0.98 (30H, m), 0.88 (9H, s), 0.05 (6H, s); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.9, 103.9, 95.3, 73.5, 68.8, 31.6, 30.2, 36.1, 22.7, 18.1, 18.0, 12.4, -5.3; IR (thin film) ν 2958, 2866, 2714, 1963, 1463, 1408, 1388, 1362, 1255, 1195, 1126, 1070, 998, 967, 939, 919, 883, 836, 777, 740, 680; $[\alpha]^{23}_D$ -27.3° (c = 3.96, CH_2Cl_2).

17. A solution of 152 mg of **46** and HF·pyridine in pyridine:THF, prepared according to the procedure of Trost,[41] was stirred at 23 °C for 6 h, poured into 20 mL of 1.0 M aqueous KH_2PO_4 solution (pH 4.5), and extracted with 20 mL of Et_2O. The organic layer was washed with 2 × 10 mL of saturated aqueous $CuSO_4$ solution, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*, and the residue was purified by chromatography on silica gel (20 × 80 mm, 2:1 hexanes:CH_2Cl_2, R_f 0.20) to afford 89 mg (79%) of **17** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.22 (1H, dd, J = 6.3, 1.4), 5.19 (1H, t, J = 6.4), 4.33–4.30 (1H, m), 3.60 (1H, dd, J = 10.9, 4.4), 3.54 (1H, dd, J = 10.9, 6.6), 2.14–1.90 (1H, br s), 1.13–1.05 (21H, m), 1.03 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.8, 104.4, 94.1, 73.0, 67.7, 31.6, 30.1, 18.0, 17.9, 12.3; IR (thin film) ν 3584, 3453, 2960, 2866, 1963, 1463, 1387, 1363, 1325, 1253, 1205, 1188, 1099, 1062, 1015, 997, 946, 920, 882, 825, 747, 680; $[\alpha]^{23}_D$ -25.6° (c = 2.97, CH_2Cl_2).

26. To a solution of 88 mg (0.282 mmol, 1.0 equiv) of **17** in 6.5 mL of THF were added 126 mg (0.479 mmol, 1.7 equiv) of Ph_3P, 68 mg (0.4222 mmol, 1.5 equiv) of 4-hydroxycoumarin, and 66 μL (0.422 mmol, 1.5 equiv) of DEAD, and the resulting orange solution was stirred for 30 min at 23 °C. The reaction mixture was concentrated *in vacuo*, and the residue was purified by chromatography on silica gel (20 × 80 mm, 6:1 hexanes:Et_2O, R_f 0.19) to afford 73 mg (57%) of **26** as a clear, colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (1H, dd, J = 7.9, 1.2), 7.56 (1H, ddd, J = 10.4, 7.8, 1.2), 7.32 (1H, d, J = 10.4), 7.26 (1H, t, J = 7.8), 5.72 (1H, s), 5.34–5.30 (2H, m), 4.77–4.74 (1H, m), 4.18 (1H, dd, J = 9.8, 6.5), 4.12 (1H, dd, J = 9.8, 4.5), 1.22–1.06 (30H, m); ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.9, 165.6, 162.8, 153.3, 132.3, 123.7, 123.1, 116.7, 115.6, 105.2, 93.9, 90.7, 73.8, 70.2, 31.7, 30.0, 18.0, 17.9, 12.3; IR (thin film) ν 3089, 2947, 2867, 1963, 1732, 1715, 1622, 1568, 1494, 1453, 1410, 1372, 1326, 1274, 1239, 1184, 1159, 1141, 1106, 1068, 1030, 998, 970, 928, 883, 820, 764, 752, 682, 594; $[\alpha]^{23}_D$ +8.3° (c = 2.04, CH_2Cl_2).

27. Irradiation of **26** according to the general procedure for allene–enones and purification of the residue by chromatography on silica gel (20 × 80 mm, 5:1 hexanes:Et_2O, R_f 0.31) afforded 61 mg (90%) of **27** as a clear, colorless oil which solidified on standing: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.36–7.30 (2H, m), 7.18 (1H, td, J = 7.6, 1.2), 7.04 (1H, dd, J = 8.2, 1.1), 5.70 (1H, t, J = 2.4), 4.84 (1H, dt, J = 7.6, 5.1), 4.36 (1H, dd, J = 9.6, 4.9), 4.18 (1H, t, J = 2.8), 4.05 (1H, dd, J = 9.5, 5.4), 3.75 (1H, dt, J = 7.5, 2.5), 1.16–1.04 (21H, m), 1.02 (9H, s); ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.6, 150.5, 139.1, 130.3, 127.0, 125.1, 121.8, 119.6, 117.5, 80.0, 76.3, 74.6, 62.7, 51.6, 34.1, 29.9, 18.3, 18.1, 12.9; IR (thin film) ν 2952, 2866, 1760, 1588, 1491, 1451, 1392, 1364, 1341, 1304, 1201, 1117, 1066, 1040, 1015, 998, 950, 909, 883, 836, 763; $[\alpha]^{23}_D$ -6.7° (c = 0.300, CH_2Cl_2).

41. To a solution of 222 mg (0.916 mmol, 1.0 equiv) of **15** in 10 mL of CH_2Cl_2 was added 320 μL (1.83 mmol, 2.0 equiv) of *N,N*-diisopropylethylamine. The solution was cooled to -78 °C, and 315 μL (1.37 mmol, 1.5 equiv) of TBSOTf was added dropwise. The solution was allowed to warm to 0 °C and stirred for 1 h at 0 °C. The reaction mixture was poured into 10 mL of 1.0 M aqueous KH_2PO_4 solution (pH 4.5) and extracted with 3 × 20 mL of Et_2O. The combined organic layers were washed with saturated aqueous NaCl solution, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was redissolved in 10 mL of pyridine, to which was added 100 mg of 5% palladium on carbon. The resulting slurry was stirred under 1 atm of H_2 for 8 h and filtered through a plug of Celite. The plug was washed with *n*-heptane and the filtrate concentrated *in vacuo*. The residue was purified by chromatography on silica gel (20 × 150, 20:1 hexanes:Et_2O) to afford 244 mg (75%) of **41**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.37 (1H, d, J = 12.5), 5.04 (1H, dd, J = 12.5, 9.2), 4.86 (1H, dd, J = 9.2, 5.1), 4.03 (1H, t, J = 7.1), 3.94 (1H, dd, J = 7.1, 5.1), 3.85 (1H, t, J = 7.1), 1.69–1.61 (4H, m), 1.15 (9H, s), 0.89–0.86 (15H, m), 0.09 (3H, s), 0.08 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.9, 128.3, 113.1, 79.8, 69.1, 66.6, 34.5, 31.1, 29.9, 29.8, 29.8, 18.1, 8.5, 8.2, -3.9, -4.4; IR (thin film) ν 2931, 2872, 1467, 1360, 1249, 1196, 1173, 1126, 1085, 1002, 920, 838, 773, 679.

42. A solution of 214 mg (0.600 mmol, 1.0 equiv) of **41** in 10 mL of CH_2Cl_2 was cooled to -78 °C and then was treated with a dilute stream of ozone in oxygen for 7.5 min (0.8 mmol/min, 6.00 mmol, 10 equiv). Nitrogen was bubbled through the reaction mixture to remove excess ozone, and 2 mL of Me_2S was added. The solution was allowed to slowly warm to 23 °C and was stirred at 23 °C for 2 h. The volatiles were removed *in vacuo*, and the residue was redissolved in 5 mL of ^{t}BuOH. To this solution was added 5 mL of 1.25 M pH 7 aqueous phosphate buffer. The solution was cooled to 0 °C, and 2 mL of 0.4 M aqueous $KMnO_4$ solution was added. The reaction mixture was stirred for 6 h at 23 °C. Saturated aqueous Na_2SO_3 was added until the purple color discharged. The reaction mixture was filtered through Celite. The aqueous layers were treated with 10 mL of 1.0 M aqueous KH_2PO_4 solution (pH 4.5) and extracted with 3 × 10 mL of EtOAc. The combined organic layers were washed with saturated aqueous NaCl solution, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was redissolved in 5 mL of Et_2O and treated with an ethereal solution in diazomethane until a yellow color persisted. Excess diazomethane was quenched by addition of a few drops of AcOH. The reaction mixture was washed with 5 mL of saturated aqueous NaCl solution, dried over anhydrous Na_2SO_4, and concentrated *in vacuo*. The residue was purified by chromatography on silica gel (20 × 100, 2:1 hexanes:EtOAc, R_f 0.30) to afford 77 mg (39%) of **42**: ^{1}H NMR (300 MHz, C_6D_6) δ 4.43–4.33 (2H, m), 4.04 (1H, dd, J = 8.4, 5.8), 3.90 (1H, dd, J = 8.4, 6.2), 3.31 (3H, s), 1.77–1.69 (2H, m), 1.55 (2H, q, J = 7.5), 1.02–0.87 (15H, m), 0.08 (3H, s), 0.04 (3H, s); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 113.6, 77.1, 72.9, 66.2, 66.0, 29.7, 28.7, 25.6, 18.1, 8.1, -5.3; IR (thin film) ν 2930, 2884, 2858, 2711, 1752, 1459, 1438, 1389, 1361, 1255, 1198, 1160, 1086, 1059, 1005, 916, 870, 855, 838, 780, 675; $[\alpha]^{23}_D$ +18.8° (c = 2.57, CH_2Cl_2).

43. To a solution of 10 mg (0.030 mmol, 1.0 equiv) of **42** in 2 mL of MeOH was added 100 μL of concentrated aqueous HCl. The solution was stirred at 23 °C for 30 min and concentrated to afford 3.4 mg (97%) of **43**, spectroscopically identical with an authentically prepared sample.[42]

Acknowledgment. C.A.H. thanks W. R. Grace and Co. for a summer fellowship award. M.S.S. is grateful to the Office of Naval Research for a graduate fellowship. We are grateful to Professor K. I. Hardcastle (California State University, Northridge) for obtaining an X-ray crystal structure of (±)-**25**. This research has been supported by a Beckman Young Investigator Award, the National Science Foundation (CHE-9221945), and a Camille and Henry Dreyfus New Faculty Award (NF-92-46).

Supplementary Material Available: Crystallographic data for (±)-**25** (7 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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