effects of the nitrosamino group.[6,7] In a hope to gain some understanding on the geometric arrangement of the ground-state complex X_S, molecular-mechanics computations based on the force field MM2 method[36] was applied to the interaction of 1-NpOH and NND. These computations certainly confirmed the parallel orientation of the molecular planes of 1-NpOH and NND but also yielded widely fluctuating minimal energies with small rotations of substrate orientations. While the intuitive geometry (Figure 5) is one of relatively low energy species, it is not the geometry possessing lowest relative energy (see supplementary material, Figure 7).

The structure of the exciplex $^*X_D$ is suggested to have NND oriented in the direction so ESPT can occur. Among all conceivable geometrical arrangements for the encounter complex formation from random collisions of *1-NpOH and NND, only those arrangements with the probability of ESPT can develop into the exciplex $^*X_D$ within which proton transfer and energy migration can occur in the correct sequence to give a successful reaction. The encounter complexes of other geometrical arrangements decay to the ground state by energy transfer to NND as discussed above. Owing to such stringent geometric requirements, it is consistent that the self-photonitrosation of 1-NpOH with NND gives low quantum yields in spite of the efficient quenching process by NND. While there are other unknown factors involved, the more facile self-photonitrosation of 1,5-dihydroxynaphthalene may be interpreted as increased availability of ESPT and supports the proposed geometry of exciplex $^*X_D$ in Figure 5.

Experimental Section

The instrumentation, chemicals and general conditions of experiments followed those described in the previous paper.[3] Fluorescence lifetime determinations used, as the excitation source, a synchronously pumped, cavity dumped, and mode locked dye laser system operating at 600 nm with 4 MHz repetition rate and a 10-ps pulse width at 300 nm after frequency doubling. A fast photomultiplier tube operating in single-photon counting mode was used as the signal detector. A detailed description of the apparatus is given in a previous publication[37] and in the thesis submitted by one of us.[38]

Transient fluorescence spectra of 1-NpOH (0.0006 M) in dioxane or THF ranging from 320 to 520 nm were recorded at room temperature at several time windows (0–1, 1–3, 3–8, 8–14, 14–20 and 20–40 ns) after pulsing with the 300-nm laser source. Similar transient fluorescence spectra of 1-NpOH in the presence of NND were recorded. The logarithmic decays of fluorescence intensity vs time at three different wavelengths were measured and plotted, and τ_0 and τ were obtained from the slopes. Lifetime measurements involving 1-NpOD used either a vacuum transfer method or drybox operation to prepare solutions: glasswares were flame-dried and materials were freshly prepared and dried.

Acknowledgment. We thank the Natural Science and Engineering Research Council of Canada for generous support of the research project. We also thank Professor S. Nagakura for his stimulating discussion. Z.Z.W. gratefully acknowledge Simon Fraser University for the award of a Simon Fraser University Open Scholarship.

Registry No. 1, 4965-30-4; 1-NpOH, 90-15-3; $(CH_3)_2NNO$, 62-75-9.

Supplementary Material Available: Plot of $1/\Delta\delta$ against $1/[NND]$ for C-3 to C-7 protons of 1-N_pOH (Figure 6) and the energy-minimized geometry of the ground-state complex X_s obtained by the force field MM-2 computation (Figure 7) (3 pages). Ordering information is given on any current masthead page.

(36) (a) Allinger, N. L. *J. Am. Chem. Soc.* **1977**, *99*, 8127. (b) Allinger, N. L. *Adv. Phys. Org. Chem.* **1976**, *13*, 1.

(37) Bruce, D.; Biggins, J.; Steiner, T. W.; Thewalt, M. L. W. *Biochim. Biophys. Acta* **1985**, *806*, 237.

(38) Steiner, T. W.; Ph.D. Thesis Dissertation, Simon Fraser University, 1986.

Intramolecular 2 + 2 Photocycloadditions of 4-(3′-Alkenyl)- and 4-(3′-Pentynyl)-2,5-cyclohexadien-1-ones

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Contribution from the Department of Chemistry, Rensselaer Polytechnic Institute, Troy, New York 12180-3590, and Sterling-Winthrop Research Institute, Rensselaer, New York 12144. *Received December 24, 1987*

Abstract: The first examples of the intramolecular 2 + 2 photocycloaddition of 4-(3′-alkenyl)-2,5-cyclohexadien-1-ones are described. 2,5-Cyclohexadienones **11a–f**, **24a–b**, and **26a–e** undergo photocyclization to tricyclo[4.3.1.^{1,5}0^{7,10}]dec-2-en-4-ones **12a–h**, **25a–b**, and **27a–e**, respectively, in excellent yields without competition from the type A photorearrangement. Tricyclodecenones **12g** and **12h** undergo slower but efficient secondary photorearrangements to oxetanols **16a** and **16b**, presumably by γ-hydrogen atom transfer from the C(5)-methoxy substituent to the photoexcited enone carbonyl group to give the intermediate biradicals **15a** and **15b**. Stereochemical studies with the enantiomerically pure 4-(3′-butenyl)-2,5-cyclohexadienone **22** demonstrated that 2 + 2 photocycloaddition to give **23** occurs without racemization. Irradiation of the (*cis*-3′-pentenyl)-2,5-cyclohexadienone **26a** and the *trans*-3′-pentenyl isomer **26b** revealed that the cycloaddition is nonstereospecific and probably involves biradicals of type **28**. Preliminary characterization of the excited state responsible for cyclobutane formation also is presented. The C(4)-substituted 3′-pentynyl derivative **30** gave the unstable cyclobutene **31** in high yield. The conversion of **31** to oxidation and reduction products **32**, **33**, and **27b** demonstrates potential synthetic utility of the intramolecular acetylene to 2,5-cyclohexadienone cycloaddition.

Intramolecular cycloadditions of oxyallyl zwitterions **2** generated from consecutive photorearrangements of 4-substituted 2,5-cyclohexadien-1-ones **1** have been shown to be useful for the construction of carbocyclic and heterocyclic ring systems. The zwitterionophile (X) tethered at C(4) of **1** can be an azide 1,3-dipole,[1,2] a diene,[2,3] or an alkene.[4]

† Rensselaer Polytechnic Institute.
‡ Sterling-Winthrop Research Institute.

(1) Schultz, A. G.; Myong, S. O.; Puig, S. *Tetrahedron Lett.* **1984**, *25*, 1011.

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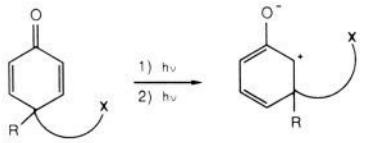
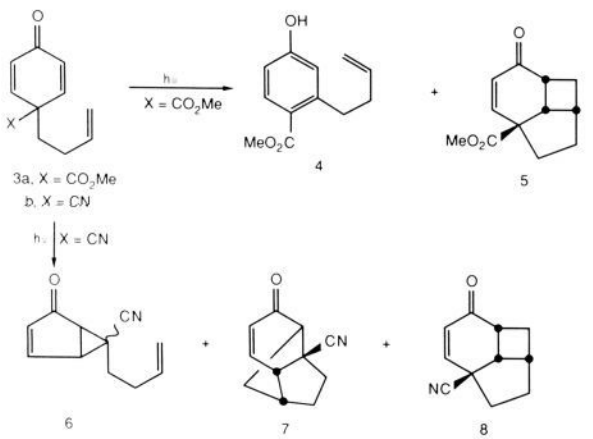


1 2

In the course of an investigation of the photoreactivity of **1**, we discovered an intramolecular 2 + 2 photocycloaddition occurring from 4-(3′-butenyl)-2,5-cyclohexadien-1-ones.[4] Thus, irradiation of **3a** gave an approximately equivalent distribution of phenol **4**, the product of carbomethoxy group rearrangement in zwitterion **2**,[5] and 1-carbomethoxytricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (**5**). The nitrile derivative **3b** was prepared to suppress the undesired migration tendency of the carbomethoxy group.[5] Irradiation of **3b** produced bicyclo[3.1.0]hexenone **6** (the type A photorearrangement product), 1-cyanotricyclo[4.3.1.^{1,5}0^{7,10}]dec-4-en-3-one (**7**) derived from photochemical zwitterionization–cycloaddition of **6**, and the tricyclodecenone **8**.

The intramolecular 2 + 2 photocycloaddition of an α,β-unsaturated carbonyl compound to an alkene has become an important method for construction of acyl-substituted cyclobutanes.[6] However, the inter- and intramolecular photocycloadditions of 2,5-cyclohexadien-1-ones appear not to have been reported. The potential synthetic value of the formation of tricyclodecenones **5** and **8** follows from (1) the recent availability of 4,4-disubstituted 2,5-cyclohexadien-1-ones in racemic or enantiomerically pure form, (2) the diverse functionality in **5**, **8**, and readily conceived analogues that would be available for subsequent synthetic manipulation, and (3) the wide range of synthetic conversions of acyl-substituted cyclobutanes already available.[6b,7] The first experimental data defining structural requirements for the intramolecular process and preliminary chemical characterization of the excited state responsible for cyclobutane formation are presented in this paper.



6 7 8

Results and Discussion

The Birch reduction of methyl benzoates **9a–f** and alkylation of the resulting ester enolates with 4-bromo-1-butene[8] provided

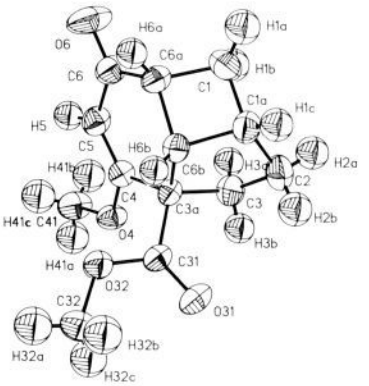
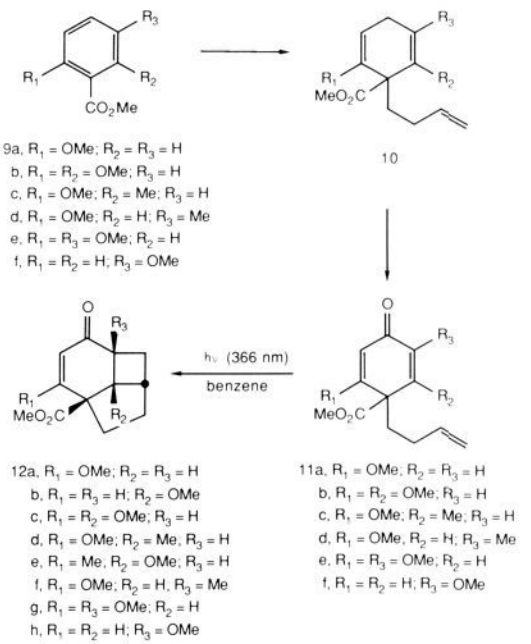


Figure 1. Molecular structure of **12a**.

Scheme I



9a, R_1 = OMe; R_2 = R_3 = H
b, R_1 = R_2 = OMe; R_3 = H
c, R_1 = OMe; R_2 = Me; R_3 = H
d, R_1 = OMe; R_2 = H; R_3 = Me
e, R_1 = R_3 = OMe; R_2 = H
f, R_1 = R_2 = H; R_3 = OMe

12a, R_1 = OMe; R_2 = R_3 = H
b, R_1 = R_3 = H; R_2 = OMe
c, R_1 = R_2 = OMe; R_3 = H
d, R_1 = OMe; R_2 = Me; R_3 = H
e, R_1 = Me; R_2 = OMe; R_3 = H
f, R_1 = OMe; R_2 = H; R_3 = Me
g, R_1 = R_3 = OMe; R_2 = H
h, R_1 = R_2 = H; R_3 = OMe

11a, R_1 = OMe; R_2 = R_3 = H
b, R_1 = R_2 = OMe; R_3 = H
c, R_1 = OMe; R_2 = Me; R_3 = H
d, R_1 = OMe, R_2 = H; R_3 = Me
e, R_1 = R_3 = OMe; R_2 = H
f, R_1 = R_2 = H; R_3 = OMe

Table I. Effect of Solvent on the Regioselectivity of Intramolecular 2 + 2 Photocycloaddition of **11c**

solvent	distribution **12d/12e**
benzene	87:13
methanol	67:33
acetic acid	64:36
trifluoroethanol	40:60 (~30% completion)

1,4-cyclohexadienes **10a–f** (Scheme I). Allylic oxidation of **10a–f**, as previously described,[5] gave the 4-(3′-butenyl)-2,5-cyclohexadien-1-ones **11a–f**.

Irradiation of **11a** at 366 nm in deaerated (N_2) benzene solution for 3 h gave **12a** in >95% yield. A ^{1}H NMR spectrum of the photolysis mixture indicated that less than 5% of the regioisomeric tricyclodecenone **12b** had formed. Crystallization of this mixture from *n*-hexane provided material suitable for X-ray diffraction studies; the molecular structure of **12a** is shown in Figure 1. A combination of the X-ray characterization of **12a** (and **16a**) and a careful inspection of ^{1}H NMR spectroscopic data for the 1-carbomethoxy together with the 1-(acetoxymethyl)tricyclodec-2-en-4-ones was required for the assignment of fused rather than bridged cyclobutanes to all of the 2 + 2 adducts obtained in this study.

The excellent chemical efficiency for the intramolecular 2 + 2 photocycloaddition of **11a**, relative to that for **3a**, is considered to be directly related to the presence of the β-methoxy substituent in **11a**. We have reported that the 3,5-dimethoxy-2,5-cyclohexadienone **13** is unreactive when irradiated with 366-nm light.[5]

(2) Schultz, A. G.; Macielag, M.; Plummer, M. *J. Org. Chem.* **1988**, *53*, 391.
(3) Schultz, A. G.; Puig, S.; Wang, Y. *J. Chem. Soc., Chem. Commun.* **1985**, 785.
(4) Schultz, A. G.; Plummer, M., manuscript in preparation.
(5) Schultz, A. G.; Lavieri, F. P.; Macielag, M.; Plummer, M. *J. Am. Chem. Soc.* **1987**, *109*, 3991.
(6) For reviews, see: (a) Baldwin, S. W. *Org. Photochem.* **1982**, *5*, 123. (b) Oppolzer, W. *Acc. Chem. Res.* **1982**, *15*, 135.
(7) (a) de Mayo, P. *Acc. Chem. Res.* **1971**, *4*, 41. (b) Wender, P. A.; Lechleiter, J. C. *J. Am. Chem. Soc.* **1978**, *100*, 4321. (c) Pirrung, M. C. *J. Am. Chem. Soc.* **1979**, *101*, 7130. (d) Crimmins, M. T.: DeLoach, J. A. *J. Org. Chem.* **1984**, *49*, 2076. (e) Demuth, M. *Pure Appl. Chem.* **1986**, *58*, 1233. (f) Crimmins, M. T.; Mascarella, S. W. *J. Am. Chem. Soc.* **1986**, *108*, 3435. (g) Lange, G. L.; Lee, M. *J. Org. Chem.* **1987**, *52*, 325.
(8) Schultz, A. G.; Lavieri, F. P.; Snead, T. E. *J. Org. Chem.* **1985**, *50*, 3086.

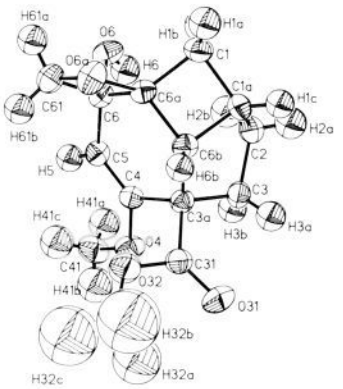
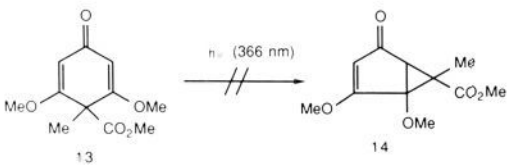


Figure 2. Molecular structure of **16a**.

In contrast, irradiation of 4-(3′-butenyl)-4-carbomethoxy-3,5-dimethoxy-2,5-cyclohexadien-1-one (**11b**) for 3.5 h gave tricyclodecenone **12c** in quantitative yield. These changes in photoreactivity exerted by β-methoxy substituents may be due to a lowering of the energy of the $\pi \rightarrow \pi^*$ triplet state of **13**, **11b**, and related 2,5-cyclohexadienones relative to **3a**. The $n \rightarrow \pi^*$ triplet state is generally considered to be responsible for the type A photoreactivity of 2,5-cyclohexadienones.[9]



While the β-methoxy substituent in **11a** facilitates intramolecular 2 + 2 cycloaddition, cyclobutane formation occurs primarily at the unsubstituted double bond. Regioselectivity appears to be, at least in part, a result of steric effects as indicated by studies with 4-(3′-butenyl)-4-carbomethoxy-3-methoxy-5-methyl-2,5-cyclohexadien-1-one (**11c**). However, Table I shows that product distribution is dependent on the photoreaction solvent; increased quantities of **12e** are obtained in solvents capable of hydrogen bonding to the carbonyl oxygen of **11c**.

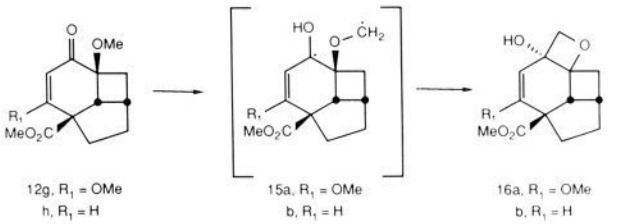
Intramolecular 2 + 2 photocycloaddition of 2,5-cyclohexadien-1-one **11d** appeared to be completely regioselective to give the methyl-substituted cyclobutane **12f** in 93% isolated yield. A high degree of regioselectivity also was exhibited in the case of **11e**, which gave mainly **12g**. Thus, there is little competition from cyclization to the vinylogous ester double bond when C(5) and C(6) are unsubstituted (case **11a**) or when C(5) is unsubstituted and C(6) bears a methyl (case **11d**) or methoxy (case **11e**) substituent.

There is an interesting complication in the photochemistry of **11e**, in that the photoproduct **12g** undergoes a secondary photorearrangement. Conventional spectral analysis did not provide a unique structural assignment for the photorearrangement product. The X-ray determined molecular structure of this material shown in Figure 2 corresponds to the oxetanol **16a**. Oxetanol formation is relatively slow in protic solvents; **12g** was obtained in 83% yield from the photolysis of **11e** in methanolic solution under carefully monitored conditions (~90% conversion of **11e**). A ^{1}H NMR spectrum of the crude photolysate revealed the presence of oxetanol **16a** (8%) and suggested that the cyclobutane resulting from addition to the C(5)–C(6) double bond in **11e** had formed to a minor extent (4%).

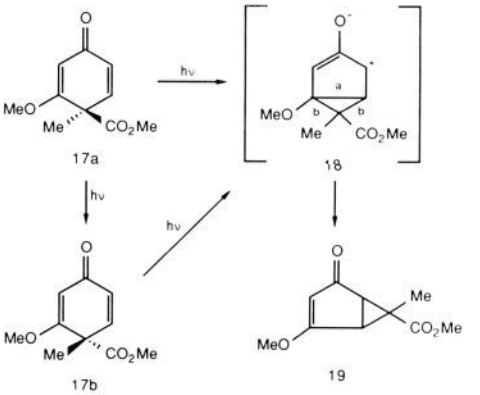
Tricyclodec-2-en-4-one **12g** undergoes quantitative photorearrangement to **16a** in benzene solution. A probable mechanism for this reaction involves γ-hydrogen atom abstraction from the C(5) methoxy substituent by the photoexcited carbonyl group to give the 1,4-biradical **15a** (Scheme II). Radical recombination in **15a** would give the oxetanol **16a**.

(9) Zimmerman, H. E.; Lynch, D. C. *J. Am. Chem. Soc.* **1985**, *107*, 7745.

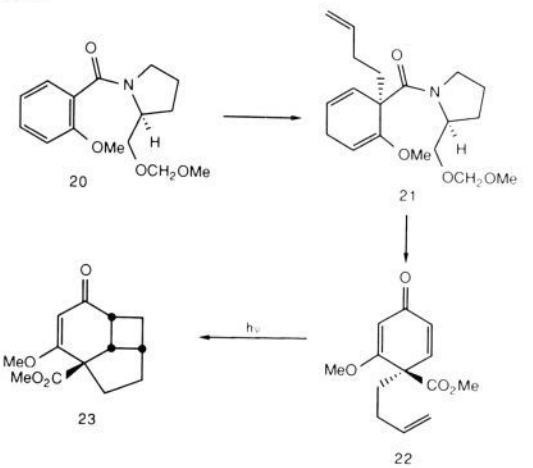
Scheme II



Scheme III



Scheme IV



Oxetanol formation is well-precedented in the photochemical literature of α-methoxyacetophenones and a variety of other α-alkoxy ketones.[10] The photoconversion reported here, however, may be of value in the preparation of structural analogues of the taxane 3-oxetanol ring system.[11] The two-step photoconversion of 4-butenyl-2,5-cyclohexadienones to oxetanols also was applicable to the C(5) desmethoxy analogue **11f**, from which oxetanol **16b** was obtained in 63% isolated yield.

The development of the enantioselective Birch reduction–alkylation[12] has provided an opportunity to examine the stereoselectivity of photorearrangement of 2,5-cyclohexadienones to bicyclo[3.1.0]hexenones.[5] In the course of this study, it was found

(10) (a) Yates, P.; Szabo, A. G. *Tetrahedron Lett.* **1965**, 485. (b) Turro, N. J.; Lewis, F. D. *Tetrahedron Lett.* **1968**, 5845. (c) Anet, F. A. L.; Mullis, D. P. *Tetrahedron Lett.* **1969**, 737. (d) Lewis, F. D.; Turro, N. J. *J. Am. Chem. Soc.* **1970**, *92*, 311. (e) Arnould, J. C.; Pete, J. P. *Tetrahedron Lett.* **1972**, 2415. (f) Gupta, S. C.; Mukerjee, S. K. *Tetrahedron Lett.* **1973**, 5073. (g) Arnould, J. C.; Pete, J. P. *Tetrahedron* **1975**, *31*, 815. (h) Ellis, J. V.; Jones, J. E. *J. Org. Chem.* **1975**, *40*, 485. (i) Hancock, K. G.; Wylie, P. L. *J. Org. Chem.* **1977**, *42*, 1850.

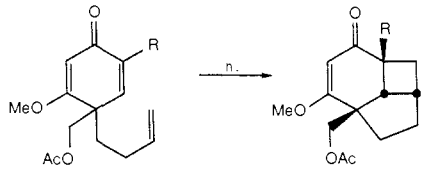
(11) Swindell, C. S.; Britcher, S. F. *J. Org. Chem.* **1986**, *51*, 793 and references cited therein.

(12) (a) Schultz, A. G.; Sundararaman, P. *Tetrahedron Lett.* **1984**, *25*, 4591. (b) Schultz, A. G.; Sundararaman, P.; Macielag, M.; Lavieri, F. P.; Welch, M. *Tetrahedron Lett.* **1985**, *26*, 4575. (c) McCloskey, P. J.; Schultz, A. G. *Heterocycles* **1987**, *25*, 437.

that (4*R*)-4-carbomethoxy-3-methoxy-4-methyl-2,5-cyclohexadien-1-one (**17a**) underwent racemization to the 4*S* isomer **17b** during photorearrangement to bicyclohexenone **19** (Scheme III). Racemization was postulated to occur by reversible cleavage of (1) a ring bond to C(4) in photoexcited **17a** or (2) an external cyclopropane bond (b) in the intermediate zwitterion **18**.

The exclusive formation of products of 2 + 2 photocycloaddition from substrates of type **11** suggested that it would be worthwhile to test the configurational integrity of C(4) in **11a** to photolysis at 366 nm. Enantiomerically pure **22** was prepared from **20** as shown in Scheme IV, and irradiation of **22** in the usual way gave cycloadduct **23**. ^{1}H NMR spectral analysis of **23** and racemic **12a** with the chiral shift reagent tris[3-[(heptafluoropropyl)-hydroxymethylene]-*d*-camphorato]europium(III) (Eu(hfc)$_3$) indicated that no racemization had occurred during the photoconversion **22** → **23**. This result and reactivity data already presented in this paper suggest that the excited state responsible for the photocycloaddition may be different from the n → π^* triplet state normally associated with the type A photorearrangement of 2,5-cyclohexadien-1-ones.[9]

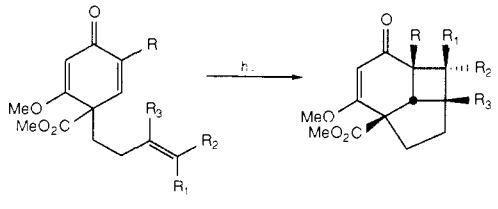
Chemical differentiation between the ester and the vinylogous ester carbonyl groups in cycloadducts **12** might be problematic in certain carbonyl addition processes. We were, therefore, pleased to find that the corresponding acetoxymethyl derivatives **24a** and **24b** could be converted to cycloadducts **25a** and **25b** in essentially quantitative yield. Thus, the presence of a C(4) electron-withdrawing group is not essential for the diversion of photochemical reactivity of 4-butenyl-2,5-cyclohexadienones from the "normal" type A behavior to intramolecular cycloaddition.



24a, R = H
b, R = Me

25a, R = H
b, R = Me

The next series of experiments was designed to examine (1) the stereoselectivity of cyclobutane formation and (2) the compatibility of alkyl group substitution at the butenyl group double bond and C(6) of the 2,5-cyclohexadienone ring. Irradiation of the (*cis*-3′-pentenyl)-2,5-cyclohexadienone **26a** and the *trans*-3′-pentenyl isomer **26b** both provided a 9:1 distribution of the 6β-methyltricyclodec-2-en-4-one **27a** and the 6α-methyl isomer **27b**. The progress of photolysis of the *cis*-3′-pentenyl isomer **26a** was followed by ^{1}H NMR spectroscopy, and isomerization of the C(3′)–C(4′) double bond in the starting material was found to be competitive with photocyclization. At ~40% photocyclization, the distribution of cis and trans olefin isomers was 60:40; at ~70% conversion, olefin isomerization had progressed to a 20:80 mixture favoring the trans isomer. Significantly, the distribution of **27a** and **27b** was ~9:1 even at moderate conversions to cycloadduct.

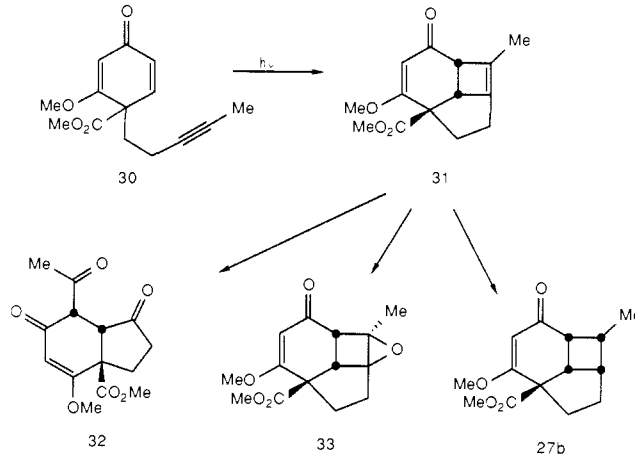


26a, R_1 = Me, R = R_2 = R_3 = H
b, R_2 = Me, R = R_1 = R_3 = H
c, R_3 = Me, R = R_1 = R_2 = H
d, R = R_2 = Me, R = R_3 = H
e, R = R_1 = R_2 = Me, R_3 = H

27a, R_1 = Me, R = R_2 = R_3 = H
b, R_2 = Me, R = R_1 = R_3 = H
c, R_3 = Me, R = R_1 = R_2 = H
d, R_1 = R_2 = Me, R = R_3 = H
e, R = R_1 = R_2 = Me, R_3 = H

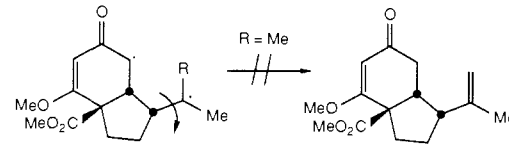
A loss of configurational integrity of the olefinic double bond is typical of enone–olefin cycloadditions.[6] Intermediate 1,4-biradicals that are sufficiently long-lived to allow conformational relaxation are generally proposed to account for the stereochemical results, but rarely have these biradicals been trapped by chemical

Scheme V



30 31 32 33 27b

methods.[13] In view of literature precedent, therefore, the stereoselectivity exhibited by **26a** and **26b** is suggestive of the intermediacy of 1,4-biradical **28a**. Initial formation of the cyclopentane ring as shown in **28a** is in keeping with the "rule of five", an experimentally determined structure–photoreactivity correlation that is often quite useful in predicting regiocontrol in intramolecular olefin cycloadditions.[14,15] The isomerization of the C(3′)–C(4′) double bond observed during irradiation of **26a** may be a result of reversible formation of biradical **28a**.[16a]



28a, R = H
b, R = Me

29

Irradiation of **26c** gave the tricyclodecenone **27c** in 93% isolated yield; once again, type A products were not observed. The high chemical efficiency for this cyclization is noteworthy because of the potential for 1,3-steric interactions between the carbomethoxy group at C(4) and the 3′-methyl substituent that might have reduced the rate of 2 + 2 cycloaddition from the excited state of **26c**. For this same reason, photocycloadditions of **26d** and **26e** also are interesting, especially that of **26e** in which adjacent quaternary centers in the product **27e** are generated. While we do not have information concerning relative rates of cyclization of 4-(3′-butenyl)-2,5-cyclohexadienones at this time, it is already clear that all are much greater than the rates of zwitterionization when there is a methoxy group at C(3) of the cyclohexadienone ring. In the absence of the methoxy group, the rates of zwitterionization and cycloaddition are comparable; cf. **3a** → **4** + **5** and **3b** → **6** + **7** + **8**.

Also of interest is the absence of the bicyclic olefin **29** in the photolysis of **26d**. Olefin **29** would have been formed by a hydrogen atom shift in the intermediate biradical **28b**. This kind of hydrogen atom transfer has been observed for related C(3) and C(4) alkenyl substituted 2-cyclohexenones.[16b,17] However, a

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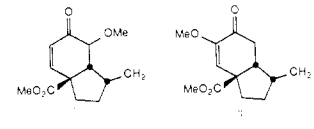
(15) The formation of tricyclodecenone **12h** from photocyclization of **11f** is consistent with the preferred generation of intermediate biradical i, in which the radical center adjacent to the carbonyl group is stabilized by the methoxy substituent, instead of biradical ii.



(16) (a) See photorearrangement of **43** to **44** in ref 6b. (b) See photorearrangement of **62** and **64** to **65** in ref 6b.

significant difference between the literature examples and the present case is the β-methoxy enone chromophore in **26d**, which might alter the reactivity of the derived biradical **28b** by conformational and/or electronic effects.

The pioneering work of Koft and Smith has provided examples of the intramolecular 2 + 2 photocycloaddition of C(3)- and C(4)-substituted (4′-pentynyl)-2-cyclohexenones.[18] We have tested the ability of acetylenes to participate in intramolecular cycloadditions to 2,5-cyclohexadienones with 4-carbomethoxy-3-methoxy-4-(3′-pentynyl)-2,5-cyclohexadien-1-one (**30**). Irradiation of **30** at 366 nm gave the unstable cyclobutene **31**, obtained as a colorless solid (Scheme V). Hydrogenation of this material gave cyclobutane **27b**, which proved to be identical with the minor product obtained from photocyclization of **26a** and **26b**. Thus, the intramolecular enone–acetylene photocycloaddition and cyclobutene hydrogenation provides a stereospecific complement to the opposite stereoselectivity observed with the C(3′),C(4′)-disubstituted enone–olefin cycloaddition demonstrated in the conversions of **26a** and **26b** to **27a** and **27b**.

Attempted crystallization of **31** from a warm hexane–ethyl acetate solution gave a mixture of oxidation products, from which chromatographic separation on silica gel gave crystalline hydrindane **32** (34%) and epoxide **33** (28%). These materials also were prepared by rational oxidation procedures involving (1) *m*-chloroperbenzoic acid treatment of **31** to give epoxide **33** in 86% overall yield from 2,5-cyclohexadienone **30** and (2) oxidative cleavage of **31** with OsO_4–$NaIO_4$ to give **32** in moderate yield.

Triplet sensitization of the photoreactivity of **24a** by benzophenone was demonstrated by irradiation of **24a** such that benzophenone absorbed 95% of the incident light at 366 nm. Under these conditions, the conversion of **24a** to **25a** proceeded somewhat slower than the unsensitized reaction. The use of xanthone as triplet sensitizer was more efficient, despite the fact that xanthone absorbed only 39% of the light at 366 nm. After 30 min of irradiation, the unsensitized reaction was 58% complete while the xanthone-sensitized reaction was 86% complete.

A possible explanation for the difference between the benzophenone- and the xanthone-sensitized reactions may reside in the triplet energies of these sensitizers. Benzophenone and xanthone have triplet energies of 69 and 74 kcal/mol, respectively.[19] The experimentally determined triplet energies for 2,5-cyclohexadienones, without substituents at C(3), have been reported to be 67–71 kcal/mol.[20] Thus, xanthone may be more efficient than benzophenone in triplet-energy transfer to 2,5-cyclohexadienone **24a**.

The photoreactivity of **24a** is not significantly depressed by the presence of up to 1.5 M piperylene. Generally, triplet-quenching studies of 2,5-cyclohexadienones have used extremely high concentrations of quenchers.[21b,c] Piperylene, when used as a solvent, has been shown to completely retard the santonin to lumisantonin interconversion.[21a] Schuster and Fabian have suggested that triplet quenching of a 2,5-cyclohexadienone is inefficient because the triplet state is short lived.[22] It is not surprising, therefore, that piperylene is ineffective at quenching the photoreactivity of **24a**.

The reactivity data gathered thus far would suggest that significant mixing of the $\pi \rightarrow \pi^*$ triplet state with the $n \rightarrow \pi^*$ triplet state normally associated with type A reactivity is required for efficient diversion of the photochemistry of 2,5-cyclohexadienones from the type A process to the intramolecular 2 + 2 cycloaddition. However, the possibility that direct irradiation also might result in photocycloaddition from an excited singlet state should not be eliminated from future considerations. Entropic factors also operate to shift the reaction profile; preliminary studies with the C(4) allyl and 4′-pentenyl analogues of **11a** indicate that such substrates will not undergo photoconversions to the 2 + 2 cycloadducts under conditions utilized in this study.

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Experimental Section

Birch Reduction and Alkylation of Methyl Benzoates (Procedure A). The methyl benzoate (1.0 g, ~6 mmol) was dissolved in 10 mL of tetrahydrofuran (THF) containing *tert*-butyl alcohol (1.0 equiv). To this solution was added 75 mL of distilled ammonia. Small pieces of potassium metal (~2.5 equiv) were added at −78 °C until a blue coloration persisted for 15 min. The alkyl halide (2 equiv) was added to the ammonia solution at −78 °C. After the mixture was stirred at −33 °C for several hours, solid ammonium chloride was added and the reaction mixture was allowed to warm to room temperature. Brine and ethyl acetate were added, and the organic layer was separated. After the organic layer was dried over magnesium sulfate, the solvent was removed under reduced pressure to give the desired product.

Procedure B. The methyl benzoate was reduced as outlined in procedure A, after which several drops of piperylene were added to disperse the blue coloration. Anhydrous lithium bromide (~2.0 equiv) was added, and the ammonia was removed under a stream of nitrogen to give a suspension of the lithium enolate in THF. The suspension was cooled to −78 °C, and the alkyl halide (1.5–2.0 equiv) in THF at −78 °C was added. The reaction workup was the same as that used in procedure A.

6-(3′-Butenyl)-6-carbomethoxy-1-methoxy-1,4-cyclohexadiene (10a) was prepared from **9a** and 4-bromo-1-butene (procedure **B**). The reaction gave a mixture of alkylated and protonated material (~2:1), which was used without further purification: ^{1}H NMR ($CDCl_3$) (60 MHz) δ 6.0–4.7 (m, 6 H), 3.70 (s, 3 H), 3.55 (s, 3 H), 2.75 (m, 2 H), 2.05–1.50 (m, 4 H); IR (film) 1730, 1680, 1640, 1430, 1200 cm^{-1}.

6-(3′-Butenyl)-6-carbomethoxy-1,5-dimethoxy-1,4-cyclohexadiene (10b) was prepared from **9b** and 4-bromo-1-butene (procedure A), but lithium metal was employed, and the lithium enolate was alkylated at −33 °C after removal of ammonia; **10b** was obtained as a colorless solid (237 mg, 61%) after chromatography on silica gel (hexane–ethyl acetate, 15:1). An analytical sample was prepared by recrystallization from hexane–dichloromethane: mp 57–58 °C; ^{1}H NMR ($CDCl_3$) δ 5.86 (m, 1 H), 5.02 (m, 2 H), 4.92 (m, 2 H), 3.71 (s, 3 H), 3.53 (s, 6 H), 2.91 (m, 2 H), 2.12 (m, 2 H), 1.82 (m, 2 H); IR (film) 1745, 1695, 1664, 1642, 1210 cm^{-1}; CIMS, *m/z* (relative intensity) 253 (M^+ + 1, 77), 221 (100), 193 (93), 169 (75). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.24; H, 8.08.

6-(3′-Butenyl)-6-carbomethoxy-1-methoxy-5-methyl-1,4-cyclohexadiene (10c) was prepared from **9c** and 4-bromo-1-butene (procedure **B**). Flash chromatography of the crude reaction mixture on silica gel (hexane–ethyl acetate, 20:1) provided **10c** (6.43 g, 57%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 6.01–5.68 (m, 2 H), 5.14–4.86 (m, 3 H), 3.74 (s, 3 H), 3.57 (s, 3 H), 3.00–2.67 (m, 2 H), 2.24–1.70 (m, 4 H), 1.61 (d, 3 H, J = 1.5 Hz); IR (film) 1729, 1694, 1664, 1643 cm^{-1}; CIMS, *m/z* 237 (M^+ + 1).

6-(3′-Butenyl)-6-carbomethoxy-1-methoxy-4-methyl-1,4-cyclohexadiene (10d) was prepared from **9d** and 4-bromo-1-butene (procedure **B**) (colorless oil, 1.12 g, 85%); ^{1}H NMR ($CDCl_3$) δ 6.80 (m, 1 H), 5.06 (s, 1 H), 4.90 (m, 2 H), 4.81 (t, 1 H, J = 3.5 Hz), 3.64 (s, 3 H), 3.51 (s, 3 H), 2.71 (m, 2 H), 2.20–1.50 (m, 4 H), 1.71 (s, 3 H); IR (film) 2945, 1735, 1695 1665, 1640, 1440, 1228, 1208, 1170, 1040, 910 cm^{-1}; CIMS, *m/z* (relative intensity) 237 (M^+ + 1, 12.11), 205 (100.00), 181 (20.67), 173 (20.71), 135 (83.64).

3-(3′-Butenyl)-3-carbomethoxy-1,4-dimethoxy-1,4-cyclohexadiene (10e) was prepared from **9e** and 4-bromo-1-butene (procedure A), but lithium metal was used and the enolate was alkylated at −33 °C after removal of the ammonia; **10e** was obtained as a colorless oil (29.6 g, 96%) after flash chromatography on silica gel (hexane–ethyl acetate, 15:1): ^{1}H NMR ($CDCl_3$) δ 5.88 (m, 1 H), 5.00 (m, 2 H), 4.82 (m, 1 H), 4.38 (s, 1 H), 3.70 (s, 3 H), 3.58 (s, 3 H), 3.56 (s, 3 H), 2.89 (m, 2 H), 2.24–1.68 (m, 4 H); IR (film) 1730, 1660, 1640, 1220 cm^{-1}; CIMS, *m/z* (relative intensity) 253 (M^+ + 1, 17), 221 (100). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.79; H, 8.05.

3-(3′-Butenyl)-3-carbomethoxy-1-methoxy-1,4-cyclohexadiene (10f) was prepared from **9f** and 4-bromo-1-butene (procedure A), but lithium metal was employed and the lithium enolate was alkylated at −33 °C after removal of the ammonia. The reaction provided **10f** as a colorless oil (615 mg, 66%) after flash chromatography on silica gel (hexane–ethyl acetate, 17:1): ^{1}H NMR ($CDCl_3$) δ 5.84 (m, 3 H), 5.03 (m, 2 H), 4.73 (br s, 1 H), 3.72 (s, 3 H), 3.64 (s, 3 H), 2.73 (m, 2 H), 2.10–1.72 (m, 4 H); IR (film) 1722, 1687, 1640, 1220 cm^{-1}; CIMS, *m/z* 233 (M^+ + 1).

(6*R*)-6-(3′-Butenyl)-6-carbomethoxy-1-methoxy-1,4-cyclohexadiene[23] was prepared in the manner of (6*R*)-1-methoxy-6-(methoxycarbonyl)-6-methyl-1,4-cyclohexadiene.[5,12] The ^{1}H NMR and IR spectra of the product were identical with the racemic material **10a**. The optical rotation of the enantiomerically pure material is $[\alpha]^{23}_D$ −51.9° (*c* 0.29, $CHCl_3$).

6-Carbomethoxy-1-methoxy-6-(*trans*-3′-pentenyl)-1,4-cyclohexadiene was prepared from methyl 2-methoxybenzoate and *trans*-1-iodo-3-pentene (procedure **B**). The reaction provided the 1,4-cyclohexadiene as a colorless oil (1.07 g, 75%) after chromatography on silica gel (hexane–ethyl acetate, 4:1): ^{1}H NMR ($CDCl_3$) δ 5.90 (dt, 1 H, *J* = 9 Hz, *J* = 3 Hz), 5.39 (m, 3 H), 4.82 (t, 1 H, *J* = 3 Hz), 3.65 (s, 3 H), 3.50 (s, 3 H), 2.80 (m, 2 H), 2.06 (m, 1 H), 1.90–1.50 (m, 3 H), 1.51 (br s, 3 H); IR (film) 2945, 1735, 1687, 1650, 1430, 1367, 1225, 1205, 1160 cm^{-1}; EIMS, *m/z* (relative intensity) 236 (M^+, 1.57), 177 (16.00), 168 (22.43), 135 (17.91), 121 (100.00).

6-Carbomethoxy-6-(3′-methyl-3′-butenyl)-1-methoxy-1,4-cyclohexadiene was prepared from methyl 2-methoxybenzoate and 1-iodo-3-methyl-3-butene (procedure **B**). The reaction provided the 1,4-cyclohexadiene as a colorless oil (1.30 g, 91%): ^{1}H NMR ($CDCl_3$) δ 5.90 (dt, 1 H, *J* = 9.4 Hz, *J* = 3 Hz), 5.38 (dt, 1 H, *J* = 9.4 Hz, *J* = 1.5 Hz), 4.84 (t, 1 H, *J* = 2.5 Hz), 4.65 (s, 2 H), 3.66 (s, 3 H), 3.52 (s, 3 H), 2.82 (m, 2 H), 2.16 (m, 1 H), 1.88–1.60 (m, 3 H), 1.68 (s, 3 H); IR (film) 1735, 1690, 1650, 1430, 1230, 1205, 1160, 1020 cm^{-1}; CIMS, *m/z* (relative intensity) 237 (M^+ + 1, 30), 205 (54), 177 (18), 169 (100).

6-Carbomethoxy-1-methoxy-6-(4′-methyl-3-pentenyl)-1,4-cyclohexadiene was prepared from methyl 2-methoxybenzoate and 1-bromo-4-methyl-3-pentene (procedure **B**). The reaction provided the 1,4-cyclohexadiene as a colorless oil (1.12 g, 74%) after chromatography on silica gel (hexane–ether, 4:1): ^{1}H NMR ($CDCl_3$) δ 5.90 (dt, 1 H, *J* = 10 Hz, *J* = 3 Hz), 5.40 (dt, 1 H, *J* = 10 Hz, *J* = 1.5 Hz), 5.10 (m, 1 H), 4.83 (t, 1 H, *J* = 3 Hz), 3.65 (s, 3 H), 3.52 (s, 3 H), 2.81 (m, 2 H), 2.00 (m, 1 H), 1.85–1.60 (m, 3 H), 1.62 (s, 3 H), 1.52 (s, 3 H); IR (film) 2945, 1735, 1690, 1650, 1430, 1225, 1205, 1160 cm^{-1}; CIMS, *m/z* (relative intensity) 250 (M^+ + 1, 9.76), 219 (100.00), 191 (45.28), 168 (98.87).

6-Carbomethoxy-1-methoxy-4-methyl-6-(4′-methyl-3′-pentenyl)-1,4-cyclohexadiene was prepared from methyl 2-methoxy-5-methylbenzoate and 1-bromo-4-methyl-3-pentene (procedure **B**). The reaction provided the 1,4-cyclohexadiene as a colorless oil (0.67 g, 48%) after chromatography on silica gel (hexane–ether, 4:1): ^{1}H NMR ($CDCl_3$) δ 5.08 (s, 2 H), 4.81 (t, 1 H, *J* = 3 Hz), 3.64 (s, 3 H), 3.51 (s, 3 H), 2.71 (m, 2 H), 1.90–1.50 (m, 4 H), 1.72 (s, 3 H), 1.62 (s, 3 H), 1.52 (s, 3 H); IR (film) 1735, 1690, 1665, 1430, 1360, 1222, 1165 cm^{-1}; CIMS, *m/z* (relative intensity) 264 (M^+ + 1, 8), 233 (90), 205 (40), 182 (85).

6-Carbomethoxy-1-methoxy-6-(3′-pentynyl)-1,4-cyclohexadiene was prepared from methyl 2-methoxybenzoate and 1-iodo-3-pentyne (procedure **B**). The reaction provided the 1,4-cyclohexadiene (0.88 g, 63%) as a colorless oil after chromatography on silica gel (hexane–ethyl acetate, 3:1): ^{1}H NMR ($CDCl_3$) δ 5.90 (dt, 1 H, *J* = 9.8 Hz, *J* = 1.0 Hz), 5.35 (dt, 1 H, *J* = 9.8 Hz, *J* = 2.1 Hz), 4.83 (t, 1 H, *J* = 3.7 Hz), 3.66 (s, 3 H), 3.50 (s, 3 H), 2.79 (m, 2 H), 2.26 (m, 1 H), 2.02–1.80 (m, 3 H), 1.73 (t, 3 H, *J* = 2.4 Hz); IR (film) 2945, 1730, 1685, 1648, 1430, 1355, 1225, 1160, 1110, 1060, 1040, 1010 cm^{-1}; CIMS, *m/z* (relative intensity) 235 (M^+ + 1, 43.02), 205 (39.49), 175 (100.00).

6-(3′-Butenyl)-6-(hydroxymethyl)-1-methoxy-4-methyl-1,4-cyclohexadiene. The reduction of 6-(3′-butenyl)-6-carbomethoxy-1-methoxy-4-methyl-1,4-cyclohexadiene with lithium aluminum hydride (1 equiv) in THF provided the alcohol (100%) as a colorless oil that was used without further purification: ^{1}H NMR ($CDCl_3$) δ 5.76 (m, 1 H), 4.84 (m, 4 H), 3.61 (dd, 1 H, *J* = 10.2 Hz, *J* = 8.4 Hz), 3.52 (s, 3 H), 3.24 (dd, 1 H, *J* = 10.2 Hz, *J* = 4.0 Hz), 2.66 (s, 2 H), 1.94–1.60 (m, 3 H), 1.70 (s, 3 H), 1.02 (m, 1 H); IR (film) 3410, 2925, 1655, 1635, 1440, 1205, 1155, 1040, 1015, 990 cm^{-1}; CIMS, *m/z* (relative intensity) 209 (M^+ + 1, 13.79), 191 (26.35), 177 (38.46), 159 (38.46), 135 (100.00).

6-(Acetoxymethyl)-6-(3′-butenyl)-1-methoxy-4-methyl-1,4-cyclohexadiene. The acetylation of 6-(3′-butenyl)-6-(hydroxymethyl)-1-methoxy-4-methyl-1,4-cyclohexadiene with acetic anhydride (2 equiv) in pyridine and several crystals of 4-(dimethylamino)pyridine provided the acetoxymethyl derivative (86%) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 5.76 (m, 1 H), 4.85 (m, 3 H), 4.73 (t, 1 H, *J* = 1.5 Hz), 4.00 (s, 2 H), 3.47 (s, 3 H), 2.63 (m, 2 H), 2.04–1.57 (m, 3 H), 1.97 (s, 3 H), 1.69 (s, 3 H), 1.16 (m, 1 H); IR (film) 2930, 1740, 1660, 1640, 1440, 1370, 1230, 1160, 1040 cm^{-1}; CIMS, 1040 *m/z* (relative intensity) 251 (M^+ + 1, 17.25), 219 (12.24), 191 (100.00), 177 (8.49), 159 (40.74).

General Procedure for the Preparation of 2,5-Cyclohexadien-1-ones. The 1,4-cyclohexadiene was dissolved in ethanol-free chloroform (0.1 M). To this solution was added 3 equiv of pyridinium dichromate. The mixture was refluxed until the reaction was determined to be complete by the use of thin-layer chromatographic analysis (3–10 h). During this time water was removed via a Dean–Stark apparatus. The reaction mixture was filtered through a pad of Florisil, and the pad was washed with solvent. The filtrate was concentrated under reduced pressure to provide the crude product.

4-(3′-Butenyl)-4-carbomethoxy-3-methoxy-2,5-cyclohexadien-1-one (11a). The oxidation of 6-(3′-butenyl)-6-carbomethoxy-1-methoxy-1,4-cyclohexadiene provided **11a** (90 mg, 22%) after chromatography on silica gel (ethyl acetate–dichloromethane, 1:9): ^{1}H NMR ($CDCl_3$) δ 6.46 (d, 1 H, *J* = 9.9 Hz), 6.30 (dd, 1 H, *J* = 9.9 Hz, *J* = 1.3 Hz), 5.69 (d, 1 H, *J* = 1.3 Hz), 5.69 (m, 1 H), 4.96 (m, 2 H), 3.73 (s, 3 H), 3.68 (s, 3 H), 2.30 (m, 1 H), 2.08 (m, 1 H), 1.75 (m, 2 H); IR (film) 1740, 1655, 1595, 1430, 1360, 1210, 990 cm^{-1}; CIMS, *m/z* (relative intensity) 237 (M^+ + 1, 100.00), 223 (18.24), 195 (96.93), 183 (31.14). Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.82. Found: C, 66.26; H, 7.09.

4-(3′-Butenyl)-4-carbomethoxy-3,5-dimethoxy-2,5-cyclohexadien-1-one (11b) was prepared in 70% yield from **10b** as described for **11c**. Flash chromatography on silica gel (hexane–ethyl acetate, 1:1) provided **11b** as a solid. An analytical sample was prepared by recrystallization from hexane–ethyl acetate to give a colorless solid: mp 114–115 °C; ^{1}H NMR ($CDCl_3$) δ 5.76 (m, 1 H), 5.64 (s, 2 H), 5.01 (m, 2 H), 3.74 (s, 9 H), 2.34 (m, 2 H), 1.77 (m, 2 H); IR (film) 1755, 1655, 1635, 1600 cm^{-1}; CIMS, *m/z* 267 (M^+ + 1). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.22; H, 6.89.

4-(3′-Butenyl)-4-carbomethoxy-3-methoxy-5-methyl-2,5-cyclohexadien-1-one (11c). Alternative Procedure for Preparation of 2,5-Cyclohexadienones. A solution of chromium trioxide (14.1 g, 141 mmol), acetic anhydride (53 mL), and acetic acid (66 mL) was cooled to 0 °C and diluted with benzene (40 mL). To the stirred solution was added **10c** (5.87 g, 24.8 mmol) in benzene (25 mL). After 1 h at 5 °C, the reaction mixture was diluted with ethyl acetate (400 mL) and carefully quenched with a saturated solution of sodium bicarbonate (800 mL). The organic phase was separated, and the aqueous phase was extracted with ethyl acetate (3 × 200 mL). The combined organic layers were washed with water (2 × 100 mL) and brine (100 mL), and after the mixture was dried over magnesium sulfate, the solvent was removed under reduced pressure. Flash chromatography on silica gel (hexane–ethyl acetate, 1:1) gave **11c** (4.39 g, 71%) as a solid. An analytical sample was prepared by recrystallization from hexane–ethyl acetate to give colorless plates: mp 83 °C; ^{1}H NMR ($CDCl_3$) δ 6.26 (d, 1 H, *J* = 1.5 Hz), 5.81 (m, 1 H), 5.75 (d, 1 H, *J* = 1.5 Hz), 5.05 (m, 2 H), 3.76 (s, 3 H), 3.72 (s, 3 H), 2.28 (m, 2 H), 1.91 (d, 3 H, *J* = 1.5 Hz), 1.71 (m, 2 H); IR (film) 1745, 1664, 1637, 1610 cm^{-1}; CIMS, *m/z* 251 (M^+ + 1). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.24; H, 7.28.

4-(3′-Butenyl)-4-carbomethoxy-3-methoxy-6-methyl-2,5-cyclohexadien-1-one (11d). The oxidation of 6-(3′-butenyl)-6-carbomethoxy-1-methoxy-4-methyl-1,4-cyclohexadiene provided **11d** (0.24 g, 44%) as a colorless solid after chromatography on silica gel (hexane–ethyl acetate, 1:1): mp 72–73 °C; ^{1}H NMR ($CDCl_3$) δ 6.21 (s, 1 H), 5.69 (s, 1 H), overlapping 5.69 (m, 1 H), 4.94 (m, 2 H), 3.71 (s, 3 H), 3.66 (s, 3 H), 2.24 (dt, 1 H, *J* = 14 Hz, *J* = 6 Hz), 2.02 (dt, 1 H, *J* = 14 Hz, *J* = 6 Hz), 1.89 (s, 3 H), 1.80 (m, 2 H); IR (KBr) 1738, 1660, 1630, 1605, 1445, 1360, 1210, 1160, 985, 915, 890 cm^{-1}; CIMS, *m/z* (relative intensity) 251 (M^+ + 1, 100.00), 237 (22.82), 219 (21.10), 209 (100.00), 197 (17.30). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.24. Found: C, 67.03; H, 7.35.

4-(4′-Butenyl)-4-carbomethoxy-2,5-dimethoxy-2,5-cyclohexadien-1-one (11e) was prepared in 40% yield from **10e** as described for **11c**. Flash chromatography on silica gel (hexane–ethyl acetate, 7:3) provided **11e** as an oil that solidified on standing. An analytical sample was prepared by recrystallization from hexane–ethyl acetate to give a colorless solid: mp 90.5–91.5 °C; ^{1}H NMR ($CDCl_3$) δ 5.80 (s, 1 H), 5.78 (m, 1 H), 5.36 (s, 1 H), 5.02 (m, 2 H), 3.80 (s, 3 H), 3.73 (s, 6 H), 2.46–1.60 (m, 4 H); IR (film) 1735, 1655, 1640, 1610 cm^{-1}; CIMS, *m/z* 267 (M^+ + 1). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.31; H, 6.94.

4-(3′-Butenyl)-4-carbomethoxy-2-methoxy-2,5-cyclohexadien-1-one (11f) was prepared in 21% yield from **10f** as described for **11c**. Flash chromatography on silica gel (hexane–ethyl acetate, 7:3) provided **11f** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 7.12 (dd, 1 H, *J* = 10 Hz, *J* = 3 Hz), 6.46 (d, 1 H, *J* = 10 Hz), 5.98 (d, 1 H, *J* = 3 Hz), 5.80 (m, 1 H), 5.07 (m, 2 H), 3.78 (s, 3 H), 3.74 (s, 3 H), 2.36–1.90 (m, 4 H); IR (film) 1732, 1670, 1640, 1612 cm^{-1}; CIMS, *m/z* (relative intensity) 237

(23) Lavieri, F. P. Ph.D. Thesis, Rensselaer Polytechnic Institute, 1986.

(24) **Note added in proof**: The bis(allylic) oxidations of 1,4-cyclohexadienes with *tert*-butyl hydroperoxide and pyridinium dichromate give 2,5-cyclohexadien-1-ones in good to excellent yields. This discovery significantly increases the overall efficiency of the conversion of benzoic acid derivatives to the 2,5-cyclohexadien-1-ones reported herein: Schultz, A. G.; Taveras, A. G.; Harrington, R. E., manuscript submitted for publication.

($M^+ + 1$, 91), 195 (100). Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 65.96; H, 6.84.

(4*R*)-4-(3′-Butenyl)-4-carbomethoxy-3-methoxy-2,5-cyclohexadien-1-one (22). The oxidation of (6*R*)-6-(3′-butenyl)-6-carbomethoxy-1-methoxy-1,4-cyclohexadiene[23] provided **22** (192 mg, 66%) as a colorless oil after chromatography on silica gel (hexane–ethyl acetate, 1:1). The ^1H NMR and IR spectra of **22** are identical with the racemic material **11a**, $[\alpha]^{24}_D$ −75.3° (*c* 0.17, $CHCl_3$). The enantiomeric purity of **22** was verified by comparing the ^1H NMR signals of **22** and racemic **11a** under the influence of the chiral shift reagent Eu(hfc)$_3$. With racemic **11a**, after the addition of several aliquots of Eu(hfc)$_3$ in $CDCl_3$, the resonances from the C(2) and C(6) vinyl protons of each enantiomer are cleanly resolved. In an identical experiment, **22** was treated with Eu(hfc)$_3$ in $CDCl_3$, and no signal corresponding to the 4*S* enantiomer was observed.

4-(Acetoxymethyl)-4-(3′-butenyl)-3-methoxy-2,5-cyclohexadien-1-one (24a). The oxidation of 6-(acetoxymethyl)-6-(3′-butenyl)-3-methoxy-1,4-cyclohexadiene provided **24a** (0.31 g, 26%) as a colorless oil after chromatography on silica gel (ethyl acetate–dichloromethane, 1:9): ^1H NMR ($CDCl_3$) δ 6.48 (d, 1 H, J = 10 Hz), 6.28 (dd, 1 H, J = 10 Hz, J = 1.6 Hz), 5.66 (m, 1 H), 5.66 (d, 1 H, J = 1.6 Hz), 4.96 (m, 2 H), 4.24 (s, 2 H), 3.72 (s, 3 H), 1.93 (s, 3 H), 2.0–1.5 (m, 4 H); IR (film) 1740, 1660, 1635, 1590, 1365, 1215, 1035 cm^{-1}; CIMS, *m/z* (relative intensity) 251 ($M^+ + 1$, 39.13), 221 (20.56), 191 (49.04), 163 (25.78). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.24. Found: C, 67.00; H, 7.24.

4-(Acetoxymethyl)-4-(3′-butenyl)-3-methoxy-6-methyl-2,5-cyclohexadien-1-one (24b). The oxidation of 6-(acetoxymethyl)-6-(3′-butenyl)-1-methoxy-4-methyl-1,4-cyclohexadiene provided **24b** (0.12 g, 41%) as a colorless oil after chromatography on silica gel (hexane–ethyl acetate, 1:1): ^1H NMR ($CDCl_3$) δ 6.24 (d, 1 H, J = 1.4 Hz), 5.67 (s, 1 H), 5.66 (m, 1 H), 4.91 (m, 2 H), 4.19 (AB quartet, 2 H, J = 11 Hz, J = 9 Hz), 3.71 (s, 3 H), 1.93 (s, 3 H), 1.89 (d, 3 H, J = 1.3 Hz), 1.95–1.40 (m, 4 H); IR (film) 2940, 1740, 1665, 1625, 1605, 1440, 1368, 1210, 1165, 1038, 990 cm^{-1}; EIMS, *m/z* (relative intensity) 264 (M^+, 0.12), 222 (1.09), 204 (2.39), 176 (5.24), 151 (100.00).

3-Methoxy-4-(methoxycarbonyl)-4-(*cis*-3′-pentenyl)-2,5-cyclohexadien-1-one (26a). To a solution of **30** (54 mg, 0.22 mmol) in ethyl acetate (8 mL) was added Lindlar's catalyst (20 mg). This mixture was placed under hydrogen at 1 atm for 3 h. The catalyst was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was chromatographed on silica gel (hexane–ethyl acetate, 2:1) to give **26a** as a colorless oil (47 mg, 86%): ^1H NMR ($CDCl_3$) δ 6.48 (d, 1 H, J = 9.9 Hz), 6.32 (dd, 1 H, J = 9.9 Hz, J = 1.5 Hz), 5.70 (d, 1 H, J = 1.5 Hz), 5.50–5.18 (m, 2 H), 3.74 (s, 3 H), 3.67 (s, 3 H), 2.22 (m, 1 H), 2.01 (m, 1 H), 1.65 (m, 2 H), 1.48 (d, 3 H, J = 6.6 Hz); IR (film) 2950, 1740, 1660, 1630, 1600, 1430, 1365, 1225, 1170 cm^{-1}. Anal. Calcd for $C_{14}H_{18}O_2$: C, 67.18; H, 7.24. Found: C, 67.11; H, 7.15.

4-Carbomethoxy-3-methoxy-4-(*trans*-3′-pentenyl)-2,5-cyclohexadien-1-one (26b). The oxidation of 6-carbomethoxy-1-methoxy-6-(*trans*-3′-pentenyl)-1,4-cyclohexadiene provided **26b** (0.55 g, 49%) as a colorless oil after chromatography on silica gel (hexane–ethyl acetate, 1:1): ^1H NMR ($CDCl_3$) δ 6.46 (d, 1 H, J = 10 Hz), 6.29 (dd, 1 H, J = 10 Hz, J = 1.4 Hz), 5.67 (d, 1 H, J = 1.4 Hz), 5.31 (m, 2 H), 3.72 (s, 3 H), 3.67 (s, 3 H), 2.25 (dt, 1 H, J = 12 Hz, J = 6 Hz), 2.00 (dt, 1 H, J = 12 Hz, J = 6 Hz), 1.90–1.70 (m, 2 H), 1.59 (d, 3 H, J = 4.8 Hz); IR (film) 2945, 1740, 1660, 1630, 1600, 1430, 1365, 1225, 1170 cm^{-1}; EIMS, *m/z* (relative intensity) 250 (M^+, 1.04), 191 (10.86), 182 (63.42), 150 (100.00).

4-Carbomethoxy-3-methoxy-4-(3′-methyl-3′-butenyl)-2,5-cyclohexadien-1-one (26c). The oxidation of 6-carbomethoxy-1-methoxy-6-(3′-methyl-3′-butenyl)-1,4-cyclohexadiene provided **26c** (0.37 g, 44%) as a colorless solid after chromatography on silica gel (hexane–ethyl acetate, 2:1): mp 60–61 °C; ^1H NMR ($CDCl_3$) δ 6.46 (d, 1 H, J = 9.9 Hz), 6.30 (dd, 1 H, J = 9.9 Hz, J = 1.4 Hz), 5.69 (d, 1 H, J = 1.4 Hz), 4.68 (s, 1 H), 4.64 (s, 1 H), 3.74 (s, 3 H), 3.69 (s, 3 H), 2.35 (dt, 1 H, J = 12 Hz, J = 6 Hz), 2.08 (dt, 1 H, J = 12 Hz, J = 6 Hz), 1.80–1.60 (m, 2 H), 1.66 (s, 3 H); IR (film) 2940, 1740, 1660, 1630, 1600, 1430, 1360, 1225, 1170 cm^{-1}; CIMS, *m/z* (relative intensity) 251 ($M^+ + 1$, 100), 223 (26.33), 195 (46.09), 183 (39.78). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.24. Found: C, 67.10; H, 7.20.

4-Carbomethoxy-3-methoxy-4-(4′-methyl-3′-pentenyl)-2,5-cyclohexadien-1-one (26d). The oxidation of 6-carbomethoxy-1-methoxy-6-(4′-methyl-3′-pentenyl)-1,4-cyclohexadiene produced **26d** (0.43 g, 37%) as a colorless oil after chromatography on silica gel (dichloromethane–ethyl acetate, 9:1): ^1H NMR ($CDCl_3$) δ 6.45 (d, 1 H, J = 9.9 Hz), 6.35 (dd, 1 H, J = 9.9 Hz, J = 1.4 Hz), 5.69 (d, 1 H, J = 1.4 Hz), 4.98 (m, 1 H), 3.73 (s, 3 H), 3.67 (s, 3 H), 2.22 (m, 1 H), 2.00 (m, 1 H), 1.64 (m, 2 H), 1.61 (s, 3 H), 1.47 (s, 3 H); IR (film) 2960, 1740, 1660, 1630, 1600, 1430, 1365, 1225, 855 cm^{-1}; CIMS, *m/z* (relative intensity) 265 ($M^+ + 1$, 70.81), 233 (18.40), 211 (13.00), 195 (40.71), 183 (100.00), 182 (61.40).

4-Carbomethoxy-3-methoxy-6-methyl-4-(4′-methyl-3′-pentenyl)-2,5-cyclohexadien-1-one (26e). The oxidation of 6-carbomethoxy-1-methoxy-4-methyl-6-(4′-methyl-3′-pentenyl)-1,4-cyclohexadiene provided **26e** (0.20 g, 55%) as a colorless oil after chromatography on silica gel (hexane–ethyl acetate, 1:1): ^1H NMR ($CDCl_3$) δ 6.23 (d, 1 H, J = 1.4 Hz), 5.69 (s, 1 H), 4.99 (t, 1 H, J = 8 Hz), 3.71 (s, 3 H), 3.65 (s, 3 H), 2.19 (m, 1 H), 1.98 (m, 1 H), 1.90 (d, 3 H, J = 1.4 Hz), 1.61 (m, 2 H), overlapping 1.61 (s, 3 H), 1.46 (s, 3 H); IR (film) 2950, 1740, 1665, 1632, 1610, 1430, 1365, 1220, 1170 cm^{-1}; CIMS, *m/z* (relative intensity) 279 ($M^+ + 1$, 100.00), 247 (16.13), 225 (14.79), 209 (30.47), 197 (89.87).

4-Carbomethoxy-3-methoxy-4-(3′-pentynyl)-2,5-cyclohexadien-1-one (30). The oxidation of 6-carbomethoxy-1-methoxy-6-(3′-pentynyl)-1,4-cyclohexadiene provided **30** (0.29 g, 69%) as a colorless oil after chromatography on silica gel (hexane–ethyl acetate, 1:1); ^1H NMR ($CDCl_3$) δ 6.45 (d, 1 H, J = 9.9 Hz), 6.29 (dd, 1 H, J = 9.9 Hz, J = 1.3 Hz), 5.68 (d, 1 H, J = 1.3 Hz), 3.73 (s, 3 H), 3.67 (s, 3 H), 2.42 (m, 1 H), 2.20 (m, 1 H), 1.90 (m, 2 H), 1.71 (t, 3 H, J = 2.5 Hz); IR (film) 2950, 1740, 1660, 1620, 1600, 1428, 1362, 1220, 1170, 855 cm^{-1}; CIMS, *m/z* (relative intensity) 249 ($M^+ + 1$, 100.00), 217 (50.00), 195 (35.04), 189 (29.21). Anal. Calcd for $C_{14}H_{16}O_4$: C, 67.73; H, 6.49. Found: C, 67.54; H, 6.52.

General Procedure for the Irradiation of 2,5-Cyclohexadien-1-ones. The 2,5-cyclohexadienones were dissolved in spectrophotometric grade benzene unless otherwise indicated. The solutions were purged with dry nitrogen for 15 min prior to photolysis. The light source was a medium-pressure water-cooled 450-W Hanovia mercury arc lamp. The light was filtered through an uranyl glass sleeve to give predominantly the 366-nm ultraviolet emission of the mercury arc lamp, and irradiation times are as indicated. The crude photoproducts were isolated by removing the solvent under reduced pressure.

1-Carbomethoxy-2-methoxytricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (12a). Irradiation of **11a** for 3.5 h provided cycloadduct **12a** in nearly quantitative yield: mp 76–78 °C; ^1H NMR ($CDCl_3$) δ 5.41 (s, 1 H), 3.70 (s, 3 H), 3.64 (s, 3 H), 3.15 (m, 2 H), 3.04–2.82 (m, 2 H), 2.60 (m, 1 H), 2.06–1.58 (m, 4 H); IR (film) 1735, 1640, 1600, 1430, 1350, 1250, 1210 cm^{-1}; CIMS, *m/z* 237 ($M^+ + 1$); ^{13}C NMR ($CDCl_3$) δ 198.75, 178.15, 173.46, 101.00, 56.08, 55.98, 52.43, 46.20, 37.98, 37.69, 35.35, 31.00, 30.03. Less than 5% of **12b** was estimated (^1H NMR spectroscopy) to have been present in the photolysis mixture. Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.82. Found: C, 66.05; H, 6.72.

1-Carbomethoxy-2,10-dimethoxytricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (12c). Irradiation of **11b** (714 mg, 2.68 mmol) in benzene (30 mL) for 66 h provided **12c** in quantitative yield. An analytical sample was prepared by recrystallization from hexane–ethyl acetate–dichloromethane to give a colorless solid: mp 140–141 °C; ^1H NMR ($CDCl_3$) δ 5.52 (s, 1 H), 3.80 (s, 3 H), 3.74 (s, 3 H), 3.36 (dd, 1 H, J = 12 Hz, J = 8 Hz), 3.28 (s, 3 H), 3.03 (m, 1 H), 2.88 (m, 1 H), 2.44 (m, 1 H), 2.36–1.93 (m, 2 H), 1.61 (m, 1 H), 1.41 (m, 1 H); IR (film) 1740, 1650, 1610, 1218 cm^{-1}; CIMS, *m/z* 267 ($M^+ + 1$). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.16; H, 6.90.

1-Carbomethoxy-2-methoxy-10-methyltricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (12d) and 1-Carbomethoxy-10-methoxy-2-methyltricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (12e). Irradiation of **11c** (102 mg, 0.41 mmol) in benzene (20 mL) for 3.5 h provided **12d** as a colorless solid (89 mg, 87%) after chromatography on silica gel (hexane–ethyl acetate, 3:2). An analytical sample was prepared by recrystallization from hexane–ethyl acetate: mp 81–82 °C; ^1H NMR ($CDCl_3$) δ 5.58 (s, 1 H), 3.75 (s, 3 H), 3.71 (s, 3 H), 2.81–2.35 (m, 4 H), 2.13 (m, 2 H), 1.73–1.37 (m, 2 H), 1.21 (s, 3 H); IR (film) 1740, 1650, 1615, 1217 cm^{-1}; CIMS, *m/z* 251 ($M^+ + 1$). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.04; H, 7.34.

Compound **12e** was obtained as a colorless solid (13 mg, 13%): mp 76–78 °C; ^1H NMR ($CDCl_3$) δ 6.00 (s, 1 H), 3.75 (s, 3 H), 3.36 (dd, 1 H, J = 12 Hz, J = 8 Hz), 3.23 (s, 3 H), 3.02 (m, 1 H), 2.83 (m, 1 H), 2.53–2.15 (m, 2 H), 2.05 (d, 3 H, J = 1.5 Hz), 1.94 (m, 1 H), 1.61 (m, 1 H), 1.41 (m, 1 H); IR (film) 1735, 1662, 1112 cm^{-1}; EIMS, *m/z* (relative intensity) 222 (82), 181 (100), 168 (95). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.25. Found: C, 67.12; H, 7.31.

1-Carbomethoxy-2-methoxy-5-methyltricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (12f). Irradiation of **11d** for 2.5 h provided **12f** (81 mg, 93%) as a colorless solid after flash chromatography on silica gel (hexane–ethyl acetate, 1:1): mp 96–97 °C; ^1H NMR ($CDCl_3$) δ 5.38 (s, 1 H), 3.70 (s, 3 H), 3.68 (s, 3 H), 2.97 (t, 1 H, J = 8 Hz), 2.83–2.74 (m, 2 H), 2.10–1.62 (m, 5 H), 1.43 (s, 3 H); IR ($CDCl_3$) 2940, 1730, 1630, 1605, 1230 cm^{-1}; CIMS, *m/z* (relative intensity) 251 ($M^+ + 1$, 100.00), 191 (33.59). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.24. Found: C, 67.25; H, 7.31.

1-Carbomethoxy-2,5-dimethoxytricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (12g). Irradiation of **11e** (316 mg, 1.19 mmol) in methanol (25 mL) for

65 h (~90% conversion) produced **12g**, oxetanol **16g** (8%, ^{1}H NMR analysis), and possibly the regioisomeric tricyclodecenone **11e** (4%). In contrast to this relatively slow conversion of **11e** to **12g**, irradiation of **11e** in benzene for 25 h gave complete conversion to **16a**. Flash chromatography of the photolysate from methanol on silica gel (hexane–ethyl acetate, 7:3) gave **12g** as a colorless solid (263 mg, 83%). An analytical sample was prepared by recrystallization from a hexane–dichloromethane–ethyl acetate mixture (colorless solid): mp 114 °C; ^{1}H NMR ($CDCl_3$) δ 5.66 (s, 1 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.28 (s, 3 H), 3.19–2.95 (m, 2 H), 2.86–2.66 (m, 1 H), 2.57–2.38 (m, 1 H), 2.26–1.90 (m, 3 H), 1.72–1.48 (m, 1 H); IR (film) 1730, 1656, 1607, 1236, 1228, 1206 cm^{-1}; CIMS, m/z 267 (M^+ + 1). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.10; H, 6.76.

(1*R*)-2-Methoxy-1-methoxycarbonyltricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (23). Irradiation of **22** for 2.0 h provided **23**. The ^{1}H NMR and IR spectra of **23** were identical with racemic **12a**, $[\alpha]^{22.5}_D$ +30.2° (*c* 0.695, $CHCl_3$). The enantiomeric purity of **23** was verified by comparing the ^{1}H NMR signals of **23** and racemic **12a** under the influence of Eu(hfc)$_3$. In the racemic material, after the addition of several aliquots of Eu(hfc)$_3$ in $CDCl_3$, several unidentified resonances become resolved and the resonance for the C(3) vinyl proton was markedly broadened. In an identical experiment, **23** was treated with Eu(hfc)$_3$ in $CDCl_3$, and no signals corresponding to the 1*S* enantiomer were observed and the C(3) vinyl proton remained a sharp singlet.

1-(Acetoxymethyl)-2-methoxytricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (25a). Irradiation of **24a** for 3 h provided **25a** (19 mg, 95%): mp 81–83 °C; ^{1}H NMR ($CDCl_3$) δ 5.40 (s, 1 H), 4.34 (d, 1 H, J = 10.7 Hz), 3.80 (d, 1 H, J = 10.7 Hz), 3.71 (s, 3 H), 3.12–2.80 (m, 3 H), 2.60 (m, 1 H), 2.18–1.98 (m, 1 H), superimposed on 1.99 (s, 3 H), 1.82–1.44 (m, 4 H); IR (film) 1740, 1645, 1600, 1455, 1360, 1220 cm^{-1}; CIMS, m/z (relative intensity) 251 (M^+ + 1, 100.00), 191 (8.82); ^{13}C NMR ($CDCl_3$) δ 199.52, 180.21, 170.86, 101.83, 66.76, 55.99, 48.58, 43.64, 38.71, 37.91, 36.15, 30.43, 20.12 (one carbon missing). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.24. Found: C, 67.00; H, 7.24.

1-(Acetoxymethyl)-2-methoxy-5-methyltricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (25b). Irradiation of **24b** for 3 h provided **25b** (0.12 g, 99%) as a colorless solid: mp 124–126 °C; ^{1}H NMR ($CDCl_3$) δ 5.48 (s, 1 H), 4.33 (d, 1 H, J = 10.5 Hz), 3.80 (d, 1 H, J = 10.5 Hz), 3.70 (s, 3 H), 2.94 (t, 1 H, J = 8 Hz), 2.44 (dd, 1 H, J = 2 Hz, J = 8 Hz), 2.13–1.40 (m, 6 H), 2.00 (s, 3 H), 1.39 (s, 3 H); IR ($CDCl_3$) 2950, 1730, 1630, 1605, 1440, 1365, 1235, 1035 cm^{-1}; EIMS, m/z (relative intensity) 264 (2.88), 204 (14.58), 176 (15.08), 151 (100.00). Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.62. Found: C, 67.90; H, 7.67.

1-Carbomethoxy-2-methoxy-7β-methyltricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (27a). Irradiation of **26a** for 2 h gave a mixture (9:1) of **27a** and **27b** (^{1}H NMR analysis). Chromatography on silica gel (hexane–ethyl acetate, 1:1) afforded **27a** as a colorless solid (50 mg, 50%): mp 88–90 °C; ^{1}H NMR ($CDCl_3$) δ 5.40 (s, 1 H), 3.66 (s, 3 H), 3.64 (s, 3 H), 3.06 (t, 1 H, J = 8 Hz), 2.84 (m, 1 H), 2.61 (t, 1 H, J = 9 Hz), 2.48 (q, 1 H, J = 7 Hz), 2.04–1.50 (m, 4 H), 1.19 (d, 3 H, J = 7 Hz); IR ($CDCl_3$) 2940, 1730, 1630, 1605, 1435, 1152, 1250, 1220 cm^{-1}; EIMS, m/z (relative intensity) 250 (M^+, 25.04), 192 (27.62), 182 (65.42), 169 (100.00); ^{13}C NMR ($CDCl_3$) δ 198.96, 178.15, 173.81, 100.94, 56.13, 55.64, 52.52, 46.58, 44.04, 43.24, 39.66, 38.51, 30.01, 21.48.

Irradiation of **26b** for 2 h and chromatography as described above also provided cycloadduct **27a**.

2-Methoxy-1-(methoxycarbonyl)-7α-methyltricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (27b). To the crude cyclobutene **31** (42 mg, 0.17 mmol) in ethyl acetate (5 mL) was added 5% platinum on carbon (4 mg). This mixture was stirred under hydrogen at 1 atm for 1 h. The catalyst was removed by filtration, and the filtrate was concentrated under reduced pressure. Chromatography of the residue on silica gel (hexane–ethyl acetate, 1.5:1) provided **27b** as a colorless oil (27 mg, 63%): ^{1}H NMR ($CDCl_3$) δ 5.54 (s, 1 H), 3.69 (s, 3 H), 3.67 (s, 3 H), 3.16 (m, 2 H), 2.94 (m, 2 H), 2.58 (ddd, 1 H, J = 13 Hz, J = 8 Hz, J = 6 Hz), 2.06 (m, 1 H), 1.72 (m, 2 H), 0.87 (d, 3 H, J = 7.0 Hz); IR (film) 2950, 1740, 1643, 1608, 1430, 1350, 1215, 1153 cm^{-1}; EIMS, m/z (relative intensity) 250 (M^+, 4.79), 191 (22.32), 182 (50.25), 169 (46.25), 68 (100.00); ^{13}C NMR ($CDCl_3$) δ 198.10, 176.44, 173.77, 104.16, 56.04, 52.49, 43.45, 41.83, 38.35, 32.80, 25.27, 11.88; a resonance for the C(1) quaternary carbon could not be located. Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.24. Found: C, 67.02; H, 7.23.

1-Carbomethoxy-2-methoxy-7-methyltricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (27c). Irradiation of **26c** for 1.5 h provided **27c** (121 mg, 93%) as a colorless solid after chromatography on silica gel (hexane–ethyl acetate, 1:1): mp 77–79 °C; ^{1}H NMR ($CDCl_3$) δ 5.41 (s, 1 H), 3.70 (s, 3 H), 3.69 (s, 3 H), 3.07 (dt, 1 H, J = 10.1 Hz, J = 8.7 Hz), 2.84 (dt, 1 H, J = 13.1 Hz, J = 4.8 Hz), 2.67 (dd, 1 H, J = 8.9 Hz, J = 2.2 Hz), 2.02 (dt, 1 H, J = 12.1 Hz, J = 2.4 Hz), 1.89 (m, 2 H), 1.56 (m, 2 H), 1.27 (s, 3 H); IR (film) 2920, 1738, 1650, 1605, 1440, 1350, 1215 cm^{-1}; CIMS, m/z (relative intensity) 251 (M^+ + 1, 100.00), 191 (6.55). Anal. Calcd for $C_{14}H_{18}O_4$: C, 67.18; H, 7.24. Found: C, 67.06; H, 7.30.

1-Carbomethoxy-2-methoxy-6,6-dimethyltricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (27d). Irradiation of **26d** for 2 h provided **27d** (31 mg, 34%) as a colorless oil after flash chromatography on silica gel (hexane–ethyl acetate, 1:1); dienone **26d** also was recovered: ^{1}H NMR ($CDCl_3$) δ 5.23 (s, 1 H), 3.69 (s, 3 H), 3.67 (s, 3 H), 3.13 (t, 1 H, J = 9.5 Hz), 2.71 (dd, 1 H, J = 9.7 Hz, J = 1.1 Hz), 2.51 (m, 2 H), 2.01 (m, 1 H), 1.86–1.44 (m, 2 H), 1.30 (s, 3 H), 0.84 (s, 3 H); IR (film) 2945, 1738, 1640, 1605, 1440, 1355, 1215, 1155 cm^{-1}; CIMS, m/z (relative intensity) 265 (M^+ + 1, 100.00), 233 (3.97), 183 (51.98). Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.62. Found: C, 67.95; H, 7.74.

1-Carbomethoxy-2-methoxy-5,6,6-trimethyltricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (27e). Irradiation of **26e** for 2.25 h provided **27e** (61 mg, 76%) as a colorless solid after flash chromatography on silica gel (hexane–ethyl acetate, 3:2). An analytical sample was prepared by recrystallization from hexane: needles; mp 106–108 °C; ^{1}H NMR ($CDCl_3$) δ 5.49 (s, 1 H), 3.68 (s, 3 H), 3.67 (s, 3 H), 2.66 (d, 1 H, J = 9.5 Hz), 2.40 (m, 2 H), 2.04 (m, 1 H), 1.82–1.42 (m, 2 H), 1.22 (s, 3 H), 1.10 (s, 3 H), 0.83 (s, 3 H); IR ($CDCl_3$) 1730, 1615, 1430, 1335, 1230 cm^{-1}; CIMS, m/z (relative intensity) 279 (M^+ + 1, 100.00), 247 (9.52), 219 (10.24), 197 (56.14). Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.96. Found: C, 69.09; H, 7.93.

Methyl (2aα,4aβ,6aβ,7bβ)-2,2a,5,6,6a,7b-Hexahydro-2a-hydroxy-4-methoxycyclobut[3,4]indeno[4,5-*b*]oxete-4a(7*H*)-carboxylate (16a). A solution of **12g** (52 mg, 0.20 mmol) in benzene (10 mL) was irradiated for 24 h. Evaporation of the benzene afforded **16a** as a solid in quantitative yield. An analytical sample was prepared by recrystallization from hexane–ethyl acetate: colorless prisms; mp 186 °C; ^{1}H NMR ($CDCl_3$) δ 4.85 (s, 1 H), 4.54 (dd, 2 H, J = 16 Hz, J = 6 Hz), 3.76 (s, 3 H), 3.64 (s, 3 H), 3.43 (d, 1 H, J = 8 Hz), 2.80–2.20 (m, 4 H), 1.92 (s, 1 H), 1.86 (m, 2 H), 1.54 (m, 1 H); IR (KBr) 3375, 1728, 1667, 1152 cm^{-1}; CIMS, m/z (relative intensity) 267 (M^+ + 1, 17), 249 (100). Anal. Calcd for $C_{14}H_{18}O_5$: C, 63.15; H, 6.81. Found: C, 63.21; H, 6.82.

Methyl (2aα,4aβ,6aβ,7bβ)-2,2a,5,6,6a,7b-Hexahydro-2a-hydroxy-cyclobut[3,4]indeno[4,5-*b*]oxete-4a(7*H*)-carboxylate (16b). Irradiation of **11f** (69 mg, 0.29 mmol) in benzene (10 mL) for 21 h and flash chromatography on silica gel (hexane–ethyl acetate, 4:1) provided **16b** as a colorless oil (44 mg, 63%). An analytical sample was prepared by crystallization from hexane–dichloromethane to afford colorless blades: mp 92.5–93.5 °C; ^{1}H NMR ($CDCl_3$) δ 6.42 (d, 1 H, J = 10 Hz), 5.87 (d, 1 H, J = 10 Hz), 4.45 (dd, 2 H, J = 18 Hz, J = 6 Hz), 3.76 (s, 3 H), 3.43 (d, 1 H, J = 8 Hz), 2.77 (m, 1 H), 2.63–2.17 (m, 3 H), 2.05 (s, 1 H), 1.88 (m, 2 H), 1.52 (m, 1 H); IR (film) 3373, 1730 cm^{-1}; CIMS, m/z (relative intensity) 237 (M^+ + 1, 4), 219 (64), 191 (80), 177 (100), 159 (83), 131 (55). Anal. Calcd for $C_{13}H_{16}O_4$: C, 66.09; H, 6.83. Found: C, 65.88; H, 6.83.

1-Carbomethoxy-2-methoxy-6-methyltricyclo[4.3.1.0^{7,10}]dec-2,6-dien-4-one (31). Irradiation of **30** for 3 h provided **31** as a colorless solid in high yield (^{1}H NMR analysis). Attempted chromatography on silica gel (hexane–ethyl acetate, 1:1) resulted in low recovery (72 mg, ~30%) of **31**. Attempted recrystallization of the cycloadduct from a hot hexane–ethyl acetate mixture resulted in decomposition: ^{1}H NMR ($CDCl_3$) δ 5.28 (s, 1 H), 4.64 (s, 3 H), 4.63 (s, 3 H), 4.41 (s, 1 H), 3.92 (s, 1 H), 3.94 (m, 1 H), 2.24 (m, 3 H), 1.54 (s, 3 H). ^{1}H NMR spectroscopic and thin-layer chromatographic examination of the hexane–ethyl acetate mixture revealed two new products had formed. Chromatography on silica gel (hexane–ethyl acetate, 1:1) gave **33**; **32** crystallized from the solution used for the chromatography.

5-Acetyl-1-carbomethoxy-4,7-dioxo-2-methoxybicyclo[4.3.0^{1,6}]non-2-ene (32) was isolated as a colorless solid (28.1 mg, 34%): mp 156–157 °C; ^{1}H NMR ($CDCl_3$) δ 5.44 (s, 1 H), 3.77 (s, 3 H), 3.71 (s, 3 H), 3.53 (d, 1 H, J = 1.0 Hz), 2.85 (dd, 1 H, J = 11.7 Hz, J = 9.1 Hz), 2.56–2.22 (m, 3 H), 2.08 (s, 3 H), 2.02 (m, 1 H); IR ($CDCl_3$) 1730, 1610, 1430, 1360, 1220 cm^{-1}; CIMS, m/z (relative intensity) 281 (M^+ + 1, 100.00). Anal. Calcd for $C_{14}H_{16}O_6$: C, 60.00; H, 5.75. Found: C, 60.11; H, 5.73.

1-Carbomethoxy-6-epoxy-2-methoxy-6-methyltricyclo[4.3.1.0^{7,10}]dec-2-en-4-one (33) was isolated as a colorless solid (21.5 mg, 28%): mp 106 °C; ^{1}H NMR ($CDCl_3$) δ 5.50 (s, 1 H), 3.72 (s, 3 H), 3.68 (s, 3 H), 3.03 (m, 1 H), 2.86 (d, 1 H, J = 5.1 Hz), 2.51 (d, 1 H, J = 5.1 Hz), 2.44–2.06 (m, 2 H), 1.75 (m, 1 H), 1.32 (s, 3 H); IR (film) 2950, 1738, 1645, 1610, 1430, 1355, 1220, 1155 cm^{-1}; ^{13}C NMR ($CDCl_3$) δ 193.99, 174.96, 172.78, 102.38, 75.58, 67.18, 56.44, 53.05, 51.81, 49.83, 46.10, 31.87, 21.31, 11.49; CIMS, m/z (relative intensity) 265 (M^+ + 1, 100), 233 (30), 205 (10), 169 (20). Anal. Calcd for $C_{14}H_{16}O_5$: C, 63.63; H, 6.10. Found: C, 63.48; H, 6.14.

Rational Preparation of 32 and 33. To the crude cyclobutene **31** (50 mg, 0.20 mmol) in dioxane–water (3:1, 4 mL) was added osmium tetraoxide (2.6 mg, 5%) in *tert*-butyl alcohol. The solution was stirred at room temperature. To this solution was added sodium metaperiodate

Table II

entry	irradiation time, min	sensitizer	% product
1	30	none	58.6
2	60	none	>80.3
3	30	benzophenone	43.6
4	60	benzophenone	75.1
5	30	xanthone	85.8
6	60	xanthone	>90.0

Table III

entry	irradn time, min	% **24a**	equiv of piperylene
1	30	43.8	0
2	30	42.9	1
3	30	42.4	10
4	60	16.1	10
5	30	54.6	100
6	60	25.4	100

(0.22 g, 1.0 mmol). The now tan-colored solution was stirred at room temperature for 2 h, and then ethyl acetate was added. The organic phase was washed with water and brine. After the mixture was dried over magnesium sulfate, the solvent was removed under reduced pressure to give a black solid (53 mg, 94%). Chromatography on silica gel (dichloromethane–ethyl acetate, 9:1) provided a colorless solid (25 mg, 45%) identical with the previously isolated hydrindane **32**. The crude cyclobutene **31** (25 mg) was dissolved in dichloromethane (2 mL) and cooled to 0 °C, *m*-chloroperbenzoic acid (17 mg, 1.0 equiv) was added, and the solution was stirred for 1.5 h. Additional dichloromethane was then added, the solution was washed with saturated sodium bicarbonate solution and then brine. After drying over magnesium sulfate, the solvent was removed under reduced pressure to give **33** as a colorless solid (23 mg, 86%) identical with that previously isolated.

Triplet-State Sensitization of the Conversion of 24a to 25a. A solution of **24a** (10 mg) and benzophenone (22 mg) in benzene (2 mL) was prepared. Benzophenone absorbed 95% of the light of wavelength 366 nm while the remainder of this light was absorbed by **24a**. Similarly, a solution of **24a** (10 mg) and xanthone (6.6 mg) in benzene (2 mL) was prepared. Xanthone absorbed 39% of the 366-nm light and 86% of the 357-nm light. A control sample containing **24a** (10 mg) in benzene (2 mL) also was prepared. All samples were purged with dry nitrogen for 15 min prior to irradiation and then were simultaneously irradiated by a 400-W Hanovia medium-pressure mercury arc lamp fitted with a uranyl glass filter sleeve. Irradiations were performed for 30 and 60 min, and analyses were carried out with a Hewlett-Packard HP-5710A gas chromatograph fitted with a 16 ft × $^1/_8$ in. stainless steel column. The column was packed with 80–100 mesh Chromosorb G-HP coated with 0.5% QF-1. A flame-ionization detector and a HP-3380A integrator were used for the quantitative analyses.

Attempted Quenching of the Conversion of 24a to 25a. Samples were prepared by dissolving **24a** (10 mg) and 4, 40, or 400 μL (1, 10, 100 equiv) of piperylene in benzene to a total volume of 2.5 mL. A control sample was prepared by dissolving **24a** (10 mg) in benzene (2.5 mL). All samples were purged with dry nitrogen for 15 min prior to irradiation and then were simultaneously irradiated by a 400-W Hanovia medium-pressure mercury arc lamp fitted with the uranyl glass filter sleeve for 30 or 60 min. The samples were analyzed by use of the gas chromatograph.

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Supplementary Material Available: Tables of crystal structure data, atomic coordinates, bond lengths, bond angles, anisotropic parameters, and hydrogen atom coordinates for **12a** and **16a** (12 pages). Ordering information is given on any current masthead page.

Stereochemical Profile of the Dehydrogenases of *Drosophila melanogaster*

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Abstract: A "stereochemical profile" has been experimentally constructed for dehydrogenases from *Drosophila melanogaster*, an organism known to contain an enzyme with an "unusual" stereospecificity. Three of the enzymes examined (malate dehydrogenase, isocitrate dehydrogenase, malic enzyme) catalyze the transfer of the *pro-R* (A) hydrogen from NAD(P)H. Three other enzymes (glucose 6-phosphate dehydrogenase, alcohol dehydrogenase, glycerol 3-phosphate dehydrogenase) catalyze the transfer of the *pro-S* (B) hydrogen from NAD(P)H. The stereospecificity of alcohol dehydrogenase is notable because it is the opposite of that of alcohol dehydrogenases from yeast and mammals, with respect both to cofactor and to the enantiotopic hydrogens on ethanol. These results, together with published data, suggest a general working hypothesis regarding natural selection and the cryptic stereospecificity of enzymes. Natural selection will not distinguish between "locally enantiomeric" transition states; enzymes catalyzing analogous reactions via both transition states should be found in nature. In contrast, natural selection in general will distinguish between enzymes catalyzing analogous reactions via "locally diastereomeric" transition states; in general, only a single diastereomeric transition state should be found in naturally occurring enzymes.

Interest in the stereospecificity of dehydrogenases dependent on nicotinamide cofactors has undergone a renaissance since the proposal of several new functional, structural, and historical models explaining what previously was regarded as a nonfunctional behavior.[1-4]

Distinguishing between these models is challenging, as it requires an assignment of the relative importance of natural selection, conservation, and neutral drift in the recent evolution of modern proteins.[5-7] Nevertheless, the distinction is important, as the

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