manner shown. The lower homologous peptides can then properly be designated as nordidemnins A–C, in which norstatine replaces the statine unit of **1–3**.

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Regioselectivity in the Intramolecular Ene Reaction of Cyclopropene Derivatives

Albert Padwa* and William F. Rieker

Department of Chemistry, Emory University
Atlanta, Georgia 30322
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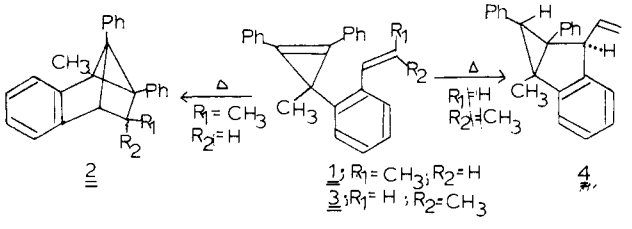
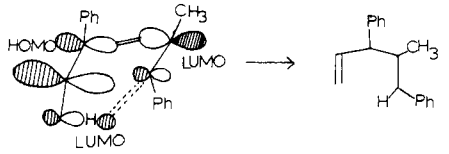
The thermal addition of an alkene to another olefin possessing an allylic hydrogen, the so-called "ene" reaction, is one of the most simple and versatile reactions of organic chemistry.[1] Though radical[2] and other mechanisms[3] have been advanced, the addition is usually considered to proceed in a symmetry-allowed concerted process[4-8] involving a six-membered cyclic transition state, unless prohibited by steric factors.[9] Olefins with strained double bonds seem particularly prone to enter into ene reactions. For example, cyclopropene derivatives are known to undergo ready dimerization via the ene process.[10,11] Considerable interest has recently been focused on intramolecular examples of this reaction.[12] In this communication, we wish to describe a novel regiochemical effect associated with the intramolecular ene reaction of tetrasubstituted cyclopropene derivatives.

As an extension of our studies dealing with intramolecular cycloaddition reactions of cyclopropene derivatives,[13] we have examined the thermal and triplet sensitized behavior of a series of 3-(*o*-alkenylphenyl)-substituted cyclopropenes. Thermolysis of the trans-substituted cyclopropene **1** at 175 °C resulted in a [2 + 2] cycloaddition reaction to produce a 4.6:1 mixture of exo and endobenzotricycloheptene **2**.[14] In marked contrast, heating

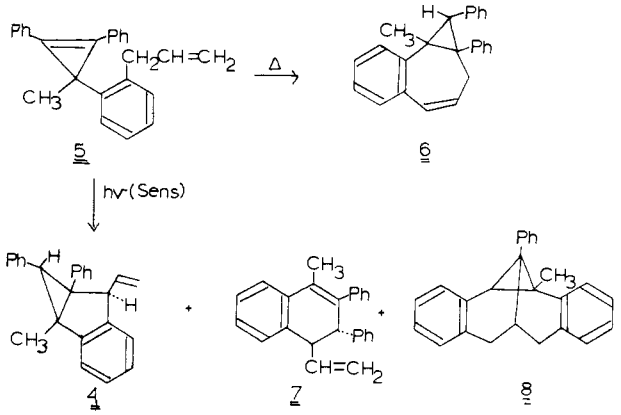


Scheme I



a sample of the isomeric cis-isomer **3** gave rise to benzobicyclohexane **4** in quantitative yield. We suggest that **4** most reasonably arises from **3** by a concerted ene reaction. The geometry necessary for this type of reaction is easily achieved with the *Z*-substituted cyclopropene. Although bimolecular ene reactions of cyclopropenes are known,[10,11] the above case constitutes the first example of an intramolecular version of this reaction.

Additional examples which would establish the generality and scope of the intramolecular ene reaction were sought. With this in mind we investigated the thermolysis of the closely related 3-(*o*-allylphenyl)-substituted cyclopropene **5**. Heating a sample of **5** gave rise to the ene product **6** in quantitative yield.[15] The



NMR spectrum (C_6D_6, 90 MHz) of **6** consists of signals at δ 1.19 (s, 3 H), 2.14 (ddd, 1 H, *J* = 13.3, 6.1, and 2.0 Hz), 2.54 (dd, 1 H, *J* = 13.3 and 7.4 Hz), 2.62 (s, 1 H), 6.01 (ddd, 1 H, *J* = 10.7, 7.4, and 6.1 Hz), 6.62 (d, 1 H, *J* = 10.7 Hz), and 6.72–7.58 (m, 14 H). The sensitized irradiation of **5** was also studied and was found to produce a mixture of three products. Chromatography of the mixture on silica gel gave benzobicyclohexene **4**[15] (60%) together with dibenzotricyclodecane **8** (30%) and dihydronaphthalene **7** (10%). Assignment of the minor component as dihydronaphthalene **7** was made on the basis of its NMR spectrum and by its oxidation to the corresponding aromatic hydrocarbon: NMR **7** ($CDCl_3$, 90 MHz) δ 2.07 (s, 3 H), 3.55 (d, 1 H, *J* = 7.5 Hz), 3.79 (s, 1 H), 4.89–5.15 (m, 2 H), 6.21 (ddd, 1 H, *J* = 17.5, 10.0, and 7.5 Hz), 6.88–7.54 (m, 14 H). The structure of **8** was easily assigned on the basis of its straightforward spectral data:[16] NMR ($CDCl_3$, 90 MHz) δ 1.37 (s, 3 H), 2.22 (d, 1 H, *J* = 15.5 Hz), 2.37 (d, 1 H, *J* = 15.5 Hz), 2.60 (s, 1 H), 2.92 (t, 1 H, *J* = 6.6 Hz), 3.20 (dd, 1 H, *J* = 15.5) and 6.6 Hz), 3.42 (dd, 1 H, *J* = 15.5 and 6.6 Hz), and 6.73–7.49 (m, 13 H).

The triplet state of cyclopropene **5** can readily abstract a hydrogen from the neighboring benzylic carbon to produce a biradical intermediate which either collapses to give **4** or undergoes cyclopropyl ring opening in competition with coupling.[17] The ring-opened species **10** would be expected to cyclize in a disrotatory fashion to give dihydronaphthalene **7**. The formation of dibenzotricyclodecane **8** in the sensitized irradiation represents an

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(15) The NMR spectrum of structures **4** and **6** suggest that the phenyl group is located in the exo position of the cyclopropyl ring. Satisfactory spectral and analytical data were obtained for each new compound.
(16) Attack of the ortho position of the triplet state of **5** on the adjacent double bond can occur in two ways. The NMR data obtained fits structure **8** better than the alternative regioisomer.
(17) Padwa, A.; Blacklock, T. J.; Chou, C. S.; Hatanaka, N. *J. Am. Chem. Soc.* **1979**, *101*, 5743.

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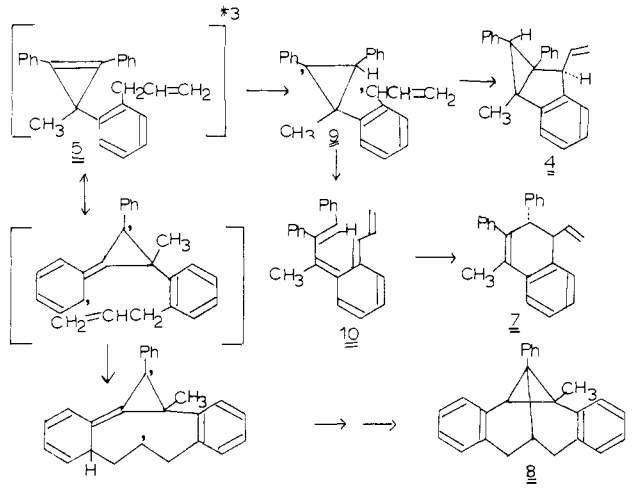
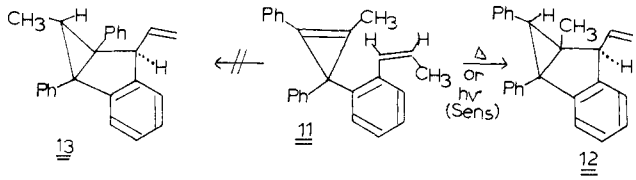
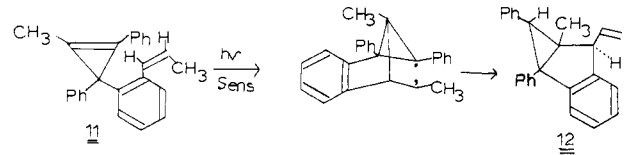


interesting reaction which merits some comment. The mechanism of this transformation may be pictured as proceeding by attack of the ortho position of the triplet state of **5** on the terminal vinyl carbon followed by diradical coupling and subsequent aromatization.[18]

We have also investigated the ene reaction of an unsymmetrically substituted cyclopropene. Thermolysis of (*Z*)-1,3-diphenyl-2-methyl-3-(*o*-1-propenylphenyl)cyclopropene (**11**) gave benzobicyclohexene **12** as the exclusive product in 98% yield: NMR (C_6D_6, 90 MHz) δ 1.35 (s, 3 H), 2.15 (s, 1 H), 4.10 (d, 1 H, J = 8.0 Hz), 5.17–5.46 (m, 2 H), 6.03 (ddd, 1 H, J = 16.7, 9.8, and 8.0 Hz) and 6.51–7.28 (m, 14 H). This reaction is completely regiospecific and involves hydrogen transfer to the carbon bearing the phenyl group. The sensitized irradiation of **11** afforded benzobicyclohexene **12** in 80% yield.[19] No signs of



the isomeric benzobicyclohexane **13** could be detected in the crude photolysate. A mechanism involving hydrogen transfer from the allylic methyl group to the triplet π–π^* excited state followed by diradical coupling cannot rationalize the regiochemistry obtained. This process would be expected to give rise to benzobicyclohexene **13**. We had previously demonstrated that unsymmetrically substituted cyclopropenes transfer hydrogen exclusively to the carbon bearing the methyl group.[17] The regiospecificity associated with the hydrogen-transfer reaction was attributed to formation of the most stable diradical intermediate.[17] The exclusive formation of bicyclohexene **12** in the sensitized irradiation is best explained by a mechanism involving π–π bridging to give the most stable diradical which undergoes a subsequent disproportionation reaction.



Frontier molecular orbital theory nicely rationalizes the exclusive formation of benzobicyclohexene **12** from the thermolysis of **11**. The thermal "ene" reaction has been described in terms of a three-orbital interaction among the HOMO of the π bond in the alkyl olefin, the LUMO of the π bond of the enophile, and the LUMO of the C–H bond of the olefin.[8] Recent MO calculations concerning the ene process suggest that C–C bond formation is much more developed in the transition state than C–H bond formation. According to perturbation theory, the regioselectivity associated with the ene reaction is the result of best orbital overlap,[20] i.e., the atoms with the largest orbital coefficients combine preferentially. The orbital coefficients of the HOMO and LUMO of 1-phenylpropene are presented in generalized form by the size of the orbital lobes in Scheme I. The large coefficient is found at the methyl substituted carbon atom in both the HOMO and LUMO.[20] The coefficient on the carbon end of the ene component is much larger than on the hydrogen atom.[8] Consequently, the MO perturbation treatment of the frontier orbital interaction of 1-phenylpropene with itself predicts that hydrogen transfer will occur on the carbon atom bearing the phenyl group. This is exactly what happens in the thermal ene reaction of the unsymmetrical cyclopropene **11**.

Acknowledgment. We gratefully acknowledge support of this work by the National Science Foundation.

(18) An alternate possibility involves initial bond formation via a six-membered transition state to give a primary radical which undergoes subsequent cyclization onto the ortho position of the aromatic ring.

(19) Benzotricycloheptene **12** was obtained as a mixture of exo and endo isomers. In addition, a 20% yield of a [2 + 2] intramolecular cycloadduct was obtained as the minor component. Complete details will be provided in a later publication.

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Azide Photoaffinity Analogues for Acridine Dye Binding Sites[1]

David M. Mueller, Richard A. Hudson,* and Chuan-pu Lee*

Department of Biochemistry, Wayne State University Detroit, Michigan 48201

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The antimalarial agent and flavin antagonist quinacrine[2] (I, 3-chloro-9-[[4-(diethylamino)-1-methylbutyl]amino]-7-methoxyacridine) interacts with enzyme active sites, notably those which use flavin as a cofactor, e.g., D-amino acid oxidase.[3-5] We report here the synthesis and some chemical and photochemical properties of a quinacrine analogue (II, 3-azido-9-[[4-(diethylamino)-1-methylbutyl]amino]-7-methoxyacridine). This molecule may act as a photoaffinity label at quinacrine binding sites. Also there is potential for the use of the acridine azide intermediates in the synthesis of compounds which can act both as photoaffinity labels in enzyme systems binding quinacrines or similar acridines and as photoactivatable mutagenic agents.[6,7]

Quinacrine and a variety of related acridine derivatives exhibit changes in intrinsic fluorescence on binding with enzymes and other macromolecular systems. These and subsequent changes in fluorescence of the bound acridine associated with interactions at other nearby sites in a macromolecular complex provide useful information about the system. For example, the fluorescence changes for quinacrine associated with energy transducing membranes, e.g., submitochondrial particles,[8,9] chloroplasts, and chromatophores,[10] appear to report on an energy-linked function

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