Origin of Regioselectivity in Paternò-Büchi Reactions of Benzoquinones with Alkylidenecycloalkanes

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Abstract: Paternò-Büchi reactions of benzoquinones with alkylidenecycloalkanes proceed regioselectively. The sense of regioselectivity is determined by the ring size of the olefin, and it appears to be controlled by the conformational properties of the substrate. Oxetane formation is likely to occur through concerted collapse of an exciplex that possesses considerable charge-transfer character.

Introduction

We have recently disclosed[3] that Paternò-Büchi reactions[4] of 1,4-benzoquinone (BQ) with small-ring alkylidenecycloalkanes proceed regioselectively. This stands in sharp contrast to the behavior of acyclic olefins, which react with poor selectivity is such reactions,[5,6] even if strong electronic or steric bias is present. Interestingly, the sense of regioselectivity was found to be a function of the ring size of the substrate. This prompted us to explore the origin of the selectivity observed in our reactions and to further probe their mechanisms. Extensive experimental and computational studies suggest that the sense of regioselectivity is controlled by the tendency of olefinic substrates to minimize eclipsing interactions at or near the transition state of the reaction. Available data seem consistent with a mechanism involving a singlet "preoxetane" diradical intermediate, which arises through collapse of a singlet exciplex. A possibility also exists that oxetane formation might occur through concerted, asynchronous collapse of the exciplex. Details of our work are presented herein.

Background

Irradiation of BQ in the presence of olefins leads to oxetanes. This process is believed to involve formation of an exciplex from the triplet excited state of BQ and the olefin. This exciplex exhibits considerable charge-transfer character,[7] and it may possess a Caldwell-like[8] structure (cf. **1**). It is further believed that collapse of the exciplex through C-O bond formation gives 1,4-diradical intermediates, **2** and **3**, which apparently form without localization of charge or spin density at either of the former olefinic C atoms,[9] i.e., through a highly exothermic step with a very early transition state, and which subsequently cyclize to give oxetanes. Under these conditions, greater or lesser stabilization of radical or ionic intermediates would have no influence on regioselectivity,[10] even in the reaction of electronically and/or sterically biased olefins (strict kinetic control), hence the lack of regioselectivity observed with ordinary olefins.

Indeed, apparent "preoxetane" diradical intermediates of the type **2** have been trapped, e.g. with O_2 (Scheme 1).[11] These experiments were conducted by running the photochemical reaction under oxygen pressure, and increasing O_2 pressure caused increased production of trioxane **4** and a parallel decrease in the yield of oxetane. A diradical pathway is also consistent with the observation that the same 1:1 ratio of *stereoisomeric* oxetanes is obtained when benzoquinone is irradiated in the presence of either *cis*- or *trans*-2-butene,[7] a phenomenon attributable to free internal rotation of the diradical prior to oxetane formation.[12]

A serious problem with this mechanistic picture is that only diradicals arising through formal "Markownikov" collapse of the exciplex (i.e. **2**) have ever been trapped from these reactions, which nevertheless proceed with simultaneous formation of oxetanes in nonselective fashion. The "anti-Markownikov" diradicals such as **3** have been postulated to cyclize to the the oxetane faster than they can be trapped by O_2, as a result of steric (less hindrance) and electronic (less hyperconjugative stabilization) effects. However, the rates of isc of other triplet Paternò-Büchi diradicals (the rate-limiting event for oxetane formation) are rather insensitive to substituent effects.[13] The lifetimes of **2** and **3** should thus be similar.

Results

Irradiation[14] of a degassed benzene solution of BQ and a suitable olefin[15] gave the results summarized in Table 1. Structural type B is the dominant product in the reactions of cyclopropane, -butane, and -pentane substrates. Furthermore, product ratios are uniformly about 1:3 in all cases. Cyclohexanes exhibit reversal

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(3) Ciufolini, M. A.; Rivera-Fortin, M. A.; Byrne, N. E. *Tetrahedron Lett.* **1993**, *34*, 3505.

(4) Review: Jones, G., II. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker, Inc.: New York, 1981; Vol. 5, pp 1-122.

(5) This behavior was first described by: Bryce-Smith, D.; Gilbert, A.; Johnson, M. G. *J. Chem. Soc. C* **1967**, 383.

(6) Quinones thus deviate in behavior from other carbonyl compounds, which tend to react quite regioselectively in Paternò-Büchi processes: ref 4.

(7) Bunce, N. J.; Hadley, M. *Can. J. Chem.* **1975**, *53*, 3240. Strong evidence for the intervention of exciplexes has been garnered through dissociation/trapping experiments from methanolic solutions.

(8) Caldwell, R. A.; Sovocool, G. W.; Gajewski, R. P. *J. Am. Chem. Soc.* **1973**, *95*, 2549. In these exciplexes, the former olefin now possesses radical cationic character, and the former quinone, radical anionic character.

(9) Wilson, R. M.; Musser, A. K. *J. Am. Chem. Soc.* **1980**, *102*, 1720.

(10) In accord with the Hammond postulate.

(11) Wilson, R. M.; Wunderly, S. W.; Walsh, T. F.; Musser, A. K.; Outcalt, R.; Geiser, F.; Gee, S. K.; Brabender, W.; Yerino, L., Jr.; Conrad, T. T.; Tharp, G. A. *J. Am. Chem. Soc.* **1982**, *104*, 4429.

(12) For an excellent review of quinone photochemistry, see: Maruyama, K.; Osuka, A. In *The Chemistry of Quinonoid Compounds*; Patai, S., Rappoport, Z., Eds.; John Wiley & Sons: Chichester, U. K., 1988; Vol. 2, Part 1, Chapter 13.

(13) Caldwell, R. A.; Majima, T.; Pac, D. *J. Am. Chem. Soc.* **1982**, *104*, 629.

(14) (a) The light source was either an argon ion laser or a battery of common fluorescent tubes. Identical regiochemical outcomes, product ratios, and yields are observed with either source, though laser-promoted reactions proceed somewhat faster. (b) Details of the photochemical apparati are provided in the supplementary material.

(15) It has been pointed out already that a ring is necessary for selectivity, but an allylic acetate or a substituent on the olefin is not: see ref 3.

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Scheme 1

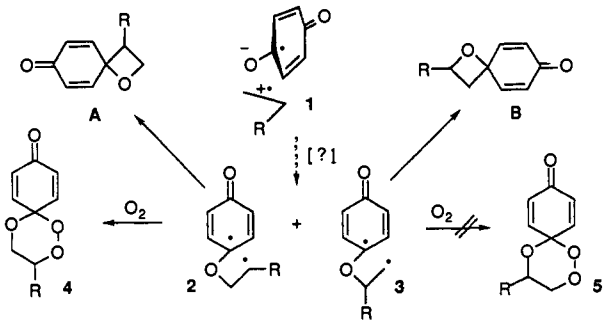
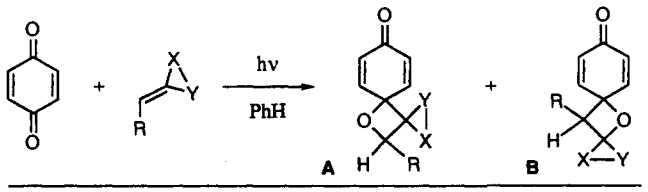


Table 1. Reaction of Benzoquinone with Alkylidenecycloalkanes



entry	X	Y	R	ratio A:B	yield, %[a]
6	CH_2	CH_2	n-C_9H_{19}	1:3.7	50[b]
7	CH_2	$(CH_2)_2$	CH_2OAc	1:3.8	55[b]
8	$(CH_2)_2$	$(CH_2)_2$	CH_2OAc	1:2.3	63[c]
9	$(CH_2)_2$	$(CH_2)_3$	CH_2OAc	9:1	90[c]
10	$(CH_2)_2$	$(CH_2)_3$	CH_3	7:1	86[c]
11	$(CH_2)_3$	$(CH_2)_3$	CH_2OAc	4:1	50[c]

[a] Chromatographed yields. [b] Unoptimized: the reaction was worked up before completion. [c] Optimized.

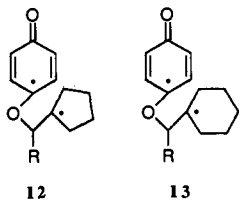
of selectivity in substantial favor of structural type **A**,[16] as do cycloheptane substrates. Regioselectivity, however, is significantly eroded in the seven-membered ring series.[17] In all cases, the two regioisomers of the cycloadduct may be readily distinguished by ^1H NMR. While the absorption of the oxetane methine proton in **A** is observed at around 4.70 ppm, in the isomeric **B** this signal appears at about 3–3.3. ppm. Careful integration of these resonances in the spectra of crude reaction mixtures defined the regioisomeric ratio afforded by each photoreaction.

Discussion

The hypothesis that photocycloadditions of quinones with olefins proceed under kinetic control is supported by molecular mechanics calculations.[18] Products of the type **A** are about 2 kcal/mol more energetic than the isomeric **B**. The preferential formation of **A** with alkylidenecyclohexanes, or the absence of regiocontrol in reactions of acyclic olefins, must be the result of kinetic control, because energy differences among various isomers do not seem to influence product distributions. The selective formation of adducts of the type **B** with alkylidenecyclopentane and smaller-ring substrates *might* be a thermodynamic effect; however, it is difficult to account for the switch from kinetic to thermodynamic control in going from the cyclohexane/acyclic series to the cyclopentane and smaller-ring manifold. It is more likely that reactions of small-ring substrates also proceed under kinetic control and that the formation of thermodynamically more stable adducts is coincidental.

The literature on mechanistic aspects of the Paternò–Büchi reaction of BQ appears to tacitly accept the proposal by Bunce and Hadley[7] that a triplet diradical mechanism operates.

Scheme 2



However, it is difficult to reconcile our results and the lack of regioselectivity observed in reactions of quinones with acyclic olefins with a triplet diradical mechanism for oxetane formation. In the cyclic series, the regioselectivity of formation of the hypothetical triplet diradical is clearly not directed by radical stabilization. While cyclohexanes provide preferentially adducts **A**, the regioselectivity of the photoprocess is reversed with substrates such as **8** (Table 1). Reaction of the latter molecule would be predicted to form even greater proportions of adducts of the type **A** if radical stabilization were involved, because the hypothetical cyclopentyl radical intermediate **12** would be even more highly stabilized than the cyclohexyl analogue **13** (Scheme 2).[19]

Bunce and Hadley hypothesized[7] that lack of selectivity, at least in the acyclic series, may result from either (i) indiscriminate attack upon the alkene by the photoexcited BQ; (ii) random or symmetrical orientation of alkene and BQ before the first bond forms, in accord with the Caldwell hypothesis;[8] or (iii) retardation of the rate of cyclization of a radical like **2** by unfavorable steric interaction and consequent reversal to starting materials more often than **3**, implying that the nearly equal yields of adducts **A** and **B** are fortuitous. However, these arguments are inconsistent with experimental results. The first two proposals fail to explain why lack of regioselectivity is observed only with acyclic olefins or large-ring alkylidenecycloalkanes.[17] It unlikely that the properties or reactivity of benzoquinone (or its excited state) are responsible for this phenomenon. Rather, the small-ring alkylidenecycloalkanes must be endowed with some properties that are absent in other substrates. Moreover, these properties must operate in opposite directions in the cyclohexane and in the cyclopentane (or smaller ring) series. The third explanation was taken as being particularly likely, but all available evidence rules it out. If steric effects were important, formation of the highly congested structures of the type **A** from cyclohexane and cycloheptane substrates (Table 1) would be greatly disfavored.

An important result that Bunce and Hadley discuss only briefly[7] is that the low-energy quencher, 3,3,4,4-tetramethyl-1,2-diazetine 1,2-dioxide ($E_T \approx 40$ kcal/mol), which can quench triplet but not singlet states,[20] did not repress oxetane formation. Furthermore, they were able to exclude that this was due to some other reaction of the quencher with BQ. These observations suggest that there may well exist a singlet diradical pathway to the oxetanes. Nevertheless, the triplet mechanism was ultimately proposed on the basis of other evidence. The conflict remains unresolved to this date.

A major piece of evidence in support of the triplet diradical mechanism was the trapping of presumed biradical intermediates with O_2 or other suitable scavengers.[11] However, the diradical that was trapped was always the product of apparent thermodynamic addition of the oxygen atom of the quinone to the olefin, i.e. **2**, even though the same reaction mixtures that formed trioxanes **4** also gave the expected oxetanes nonregioselectively. This observation would indicate either that (i) the regioisomeric diradical **3** closes to the oxetane much faster than it reacts with

(16) Reference 3 contains several other examples of reactions of alkylidenecyclohexanes.

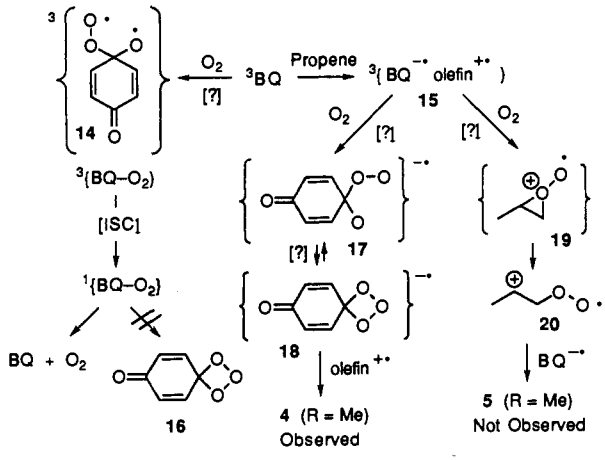
(17) Preliminary observations indicate that selectivity vanishes altogether with 2-(acetoxy-1-ethylidene)cyclooctane, which therefore reacts like acyclic olefins.

(18) All computational work described herein was carried out with the Hyperchem package, available from Autodesk, Inc., Sausalito, CA. Details of computational work are provided as supplementary material.

(19) Rüchardt, C.; Beckhaus, H.-D.; Bonnekessel, J.; Böck, H.; Dempewolf, E.; Groeger, F. A.; Golzke, V.; Hamprecht, G.; Herwig, K.; Hinz, J.; Lorenz, P.; Mayer-Ruthardt, I.; Müller, J.; Oberlinner, A.; Schacht, E. *XXII International Congress of Pure and Applied Chemistry*; Butterworths: London, U.K., 1971; Vol. 4, pp 223 ff.

(20) Ullman, E. F.; Singh, P. *J. Am. Chem. Soc.* **1972**, *94*, 5077.

Scheme 3

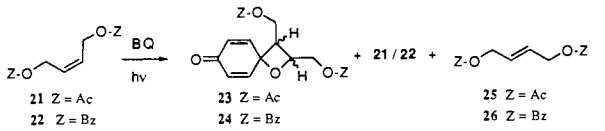


external traps, or that (ii) the trapping experiment does not involve capture of the putative preoxetane diradical, or that (iii) the triplet diradical mechanism is not solely responsible for oxetane formation.

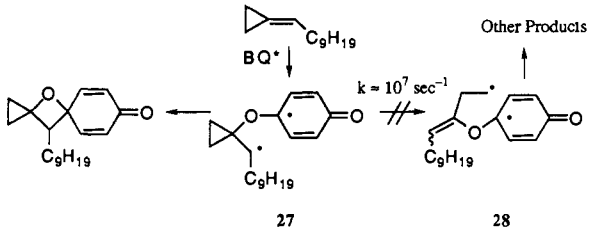
It is difficult to accept the first explanation, because (*vide supra*) the rates of isc of either regioisomeric diradical should be essentially the same, and consensus has it, isc should be the rate-limiting step for oxetane formation. The second possibility was initially raised by Wilson,[11] who was able to exclude reaction pathways involving species **14**/**16** or **17**/**18** on the basis of elegant trapping experiments with $^{18}O_2$. MNDO calculations fully support those conclusions. Trapping of a BQ triplet by O_2 leads to an endothermic diradical **14** that is relatively stable only in the triplet state. Intersystem crossing to the singlet should cause immediate decomposition to a molecule of benzoquinone plus elemental oxygen, rather than formation of trioxetane **16** (Scheme 3). Alternative trapping modes may involve interaction of oxygen with either the radical-cation portion of the exciplex (the former olefin) or its radical-anion moiety (the former quinone). The MNDO-optimized structure of the hypothetical perepoxy radical cation **19** derived from propene revealed that no bonding is present at equilibrium between the inner oxygen atom and C-2 of the olefin and that the species is more accurately described as the peroxy radical cation **20**. Aside from the fact that reaction of O_2 with a cationic entity would be unusual, intermediates **19**/**20** cannot be involved in Wilson's trapping experiments, because they would lead to that regioisomer of the trioxane which is not observed. Oxetane formation through reaction of peroxy radical anion **17** with the radical cation from the olefin may also be ruled out. MNDO revealed that formation of **17** from benzoquinone radical anion plus O_2 is strongly endothermic (ΔH_{react} = +75.15 kcal/mol). Because **17** forms through the merger of two molecules, ΔS_{react} must be negative, rendering the ΔG for the overall process very positive. Not surprisingly (recall the results obtained for **16**), the calculated ΔH_{react} for formation of trioxetane radical anion **18** from BQ radical anion and O_2 is also +75.15 kcal/mol. Thus, the trioxetane and peroxyalkoxide isomers **17**/**18** are isoenergetic, and neither is likely to exist. It seems indeed that trapping of the exciplex itself by O_2 is unlikely and that Wilson's inference that some sort of a "preoxetane diradical" is the most likely candidate for trapping[11] is fully supported by calculations. *This, however, implies that the triplet diradical mechanism cannot be solely responsible for oxetane formation.*

Nature of the Trappable Diradical and Case for Alternative Mechanisms. It will be recalled that no isomerization of 2-butenes is allegedly observed during photocycloaddition with benzoquinone,[7] despite the fact that adducts from such olefins are always formed in the same diastereomeric ratio regardless of the geometry of the starting material. In conflict with this claim, we have discovered that excess diacetate **21** and dibenzoate **22** recovered

Scheme 4



Scheme 5



from a reaction that formed the expected adducts **23** and **24** as 1:1 mixtures of syn and anti diastereomers (Scheme 4) *had not retained their stereochemical integrity*.[21] Isomerization of the olefins must result from triplet sensitization by photoexcited BQ (triplet energy ≈ 50 Kcal/mol),[22] an event that probably involves reversible, thermodynamically controlled addition of the quinone to the olefin (Schenck mechanism, see Scheme 7)[23] and consequent formation of a diradical, which is presumably the species trapped by Wilson.[11]

An even more significant result is that cyclopropyl substrate **6** (Table 1) yields the expected adducts but no detectable amounts of products of cyclopropane ring opening, implying that if a triplet 1,4-diradical intermediate **27** (Scheme 5) were involved in the formation of the major product, its cyclization to an oxetane must be quite fast ($k \geq 10^8$ s^{-1}).[24] We note that lifetimes of Paternò–Büchi diradicals arising from aryl ketones ("2-oxatetramethylenes") are on the order of 1–5 ns,[13] so that a rate constant of 10^8 s^{-1} may not seem unusual. However, while experimental lifetime values for quinone-derived diradicals appear to be unavailable, one would surmise that, because of resonant stabilization of the semiquinone portion of these diradicals, their lifetimes should be considerably longer than 5 ns.

We also note that the hypothetical radical-cationic species arising from olefin **6** through electron transfer to photoexcited BQ should be stable in the cyclopropyl form, rather than open up to the "trimethylenemethane-like" tautomer. This surmise is a direct consequence of experiments described by Miyashi and Roth,[25] whose work appears to imply that diaryl substitution on the cyclopropane ring is required for ring opening.

The above observations, together with quenching experiments by Bunce and Hadley,[7] seem to provide good evidence against the tacitly accepted triplet diradical mechanism, suggesting that there might exist either a singlet diradical mechanism or even a concerted avenue for product formation. Either of these mechanisms would evolve from a singlet exciplex. In this new light,

(21) Benzoquinone is necessary to induce isomerization, which will not occur if irradiation of the olefin is carried out *without* BQ under conditions otherwise identical to those of the photocycloaddition reaction. Spectra of starting/recovered olefins are provided as supplementary material.

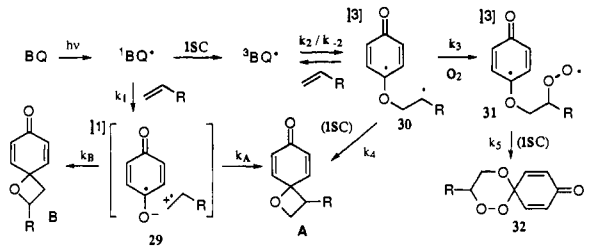
(22) Engel, P. S.; Monroe, B. M. In *Advances in Photochemistry*; Pitts, J. N., Jr., Hammond, G. S., Noyes, A. W., Jr., Eds.; John Wiley & Sons: New York, 1971; Vol. 8, p 245 ff and table on p 305.

(23) Schenck, G. O.; Steinmetz, R. *Bull. Soc. Chim. Belg.* **1962**, *71*, 781. For an excellent discussion see also ref 22, p 269 ff.

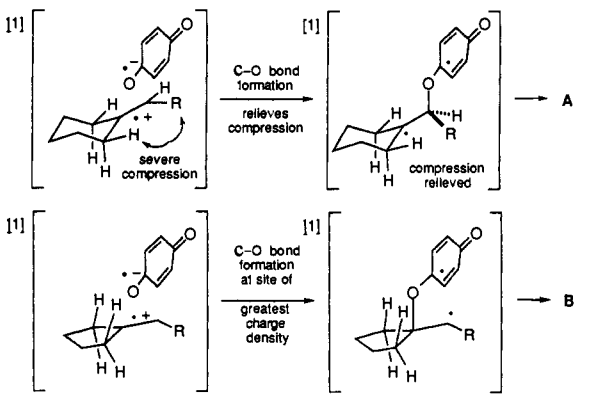
(24) Unimolecular rate constants for opening of similar cyclopropylcarbinyl radicals are on the order of 10^7 s^{-1}: Bowry, V. W.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1991**, *113*, 5687. We presume that 300-MHz NMR spectroscopy should be able to easily reveal less than 1 part in ten of products arising from **28**, hence the estimate of 10^8 s^{-1} as the lower limit for the rate constant for cyclization of the alleged diradical. Experiments with even faster-cleaving substrates (cf. Newcomb, M.; Manek, M. B. *J. Am. Chem. Soc.* **1990**, *112*, 9662. Newcomb, M. *Tetrahedron* **1993**, *49*, 1151) are currently underway.

(25) Takahashi, Y.; Miyashi, T.; Mukai, T. *J. J. Am. Chem. Soc.* **1983**, *105*, 6511. (b) Miyashi, T.; Takahashi, Y.; Mukai, T.; Roth, H. D.; Schilling, M. L. M. *J. Am. Chem. Soc.* **1985**, *107*, 1079.

Scheme 6



Scheme 7

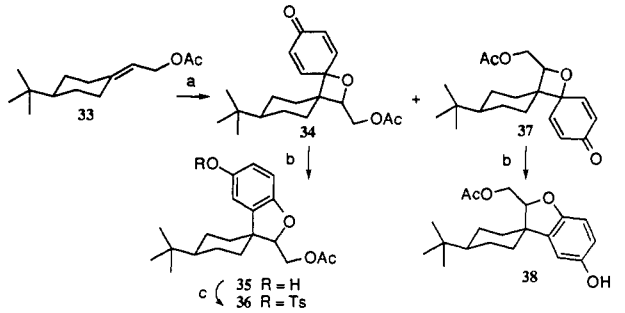


a kinetic scheme for the reaction begins to emerge as shown above (Scheme 6). The photoexcited quinone either forms a singlet exciplex (**29**) with the olefin, or it undergoes isc to the triplet state, which then adds rapidly and reversibly to the olefin to selectively form triplet diradical **30**. It is likely that closure of **30** to oxetane type **A** is rather slow compared to reversal to quinone + olefin. In the presence of O_2 (or other traps), **30** is intercepted to furnish the Wilson trioxanes. Clearly, removal of **30** will necessarily reduce the yield of oxetane, even though this triplet diradical is not part of the major oxetane-producing reaction channel. The oxetane would arise primarily from the singlet exciplex, and the regioselectivity of this process would be controlled by the precise mode of collapse of **29** to the products. A discussion of this aspect of the mechanism follows.

Origin of Regioselectivity in Reactions of Alkylidenecycloalkanes. Consider collapse of the singlet exciplex described above to a singlet diradical, through initial formation of a C–O bond. It may be argued that, because the radical-cationic portion of the exciplex (the former olefin) possesses greater charge density at the ring carbon, the oxygen atom of the semiquinone segment of the exciplex (the former quinone) would be naturally inclined to bind there. In the cyclohexane series, however, allylic strain resulting from compression of the R group against the equatorial hydrogen (Scheme 7) might force C–O bond formation at the exocyclic carbon, so as to relieve much of this steric strain. A similar phenomenon would explain the regiochemical outcome observed with the cycloheptyl substrate, which, on the other hand, possesses greater flexibility than its six-membered ring analogue. This would reduce the severity of the allylic interactions, resulting in a decrease in regioselectivity. In the cyclopentane and lower-homologue substrates, allylic interactions are considerably less severe, as the R group is comfortably situated in between the ring H atoms.[26] With these substrates, regioselectivity would be directed by preferential C–O bond formation at the site of greater charge density. In all cases, the singlet diradical would cyclize to the final oxetane very rapidly and exothermically, through a strongly reactant-like transition state.

The foregoing argument implies that a conformationally constrained alkylidenecyclohexane should participate in the photoaddition reaction with *facial selectivity*. The sense of such selectivity would be directed by the conformational constraints

Scheme 8[a]



[a] Reagents: (a) BQ, hν, 88%; (b) BF_3·OEt_2, CH_2Cl_2, 94%; (c) TsCl, NaOH, THF, 70%; then recrystallization from hexane.

present in the molecule. For instance, the *tert*-butyl substituent in olefin **33** should force the alkylidene group to move toward the equatorial position as the transition state is reached (recall, the transition state must be very early and reactant-like). This is indeed the case. The product of the type **A** obtained from the reaction of **33** with benzoquinone was formed as a 7:1 ratio of facial isomers favoring diastereomer **34** (Scheme 8). This assignment rests on an X-ray crystal structure of compound **36**, mp 128–129 °C, obtained by dienone–phenol rearrangement of **34** and tosylation of the intermediate phenol. Notice that dienone–phenol rearrangements proceed with retention of configuration at the migrating carbon.[27] Furthermore, molecular mechanics calculations indicated that the major product of dienone–phenol rearrangement (**35**) is 1.1 kcal/mol more energetic than the isomeric **38**. Thus, one may confidently assume that the stereochemical integrity of the primary product of photocycloaddition was conserved during the rearrangement, i.e., **34** was indeed the major isomer formed in the photocycloaddition.[28]

A singlet diradical mechanism would also account for the lack of regioselectivity observed with acyclic/macrocyclic olefins. It may be assumed that in these conformationally flexible substrates

(26) These arguments parallel the rationale offered by Brown for the 20-fold faster reduction of cyclohexanone vs cyclopentanone by $NaBH_4$: Brown, H. C.; Muzzio, J. *J. Am. Chem. Soc.* **1966**, *88*, 2811. Similar considerations rationalize a large number of seemingly unrelated phenomena. For instance: (i) the rate of formation of cyclopentyl radicals through decomposition of azocyclopentanes is considerably faster than the rate of formation of cyclohexyl radicals from azocyclohexanes (Rüchardt, C.; Beckhaus, H.-D.; Bonnekessel, J.; B"öck, H.; Dempewolf, E.; Groeger, F. A.; Golzke, V.; Hamprecht, G.; Herwig, K.; Hinz, J.; Lorenz, P.; Mayer-Ruthardt, I.; Müller, J.; Oberlinner, A.; Schacht, E. In *XXII International Congress of Pure and Applied Chemistry*; Butterworths: London, U. K., 1971; Vol. 4, pp 223 ff); (ii) coupling of an activated (DCC or 2-chloropyridinium salt) acid to methyl prolinate is facile, while coupling to methyl pipecolinate is difficult (Ciufolini, M. A.; Xi, N. Unpublished); (iii) enamine formation is faster with cyclopentanone than with cyclohexanone, and (iv) it is faster with pyrrolidine than with piperidine as the amine; (v) pyrrolidine enamines react with CH_3I to give C-methylated derivatives, while piperidine enamines undergo N-methylation under the same conditions (Stork, G.; Brizzolara, A.; Landesman, H.; Szmuszkowicz, J.; Terrell, R. *J. Am. Chem. Soc.* **1963**, *85*, 207); (vi) cyclopentyl substrates generally solvolyze faster than analogous cyclohexyl substrates (Brown, H. C. *J. Chem. Soc.* **1956**, 1248); (vii) cyclopentyl substrates react well in S_N2 reactions, while cyclohexyl substrates tend to eliminate under S_N2 conditions. Additional examples of the profound influence of eclipsing interactions on chemical reactivity may be garnered from the work of Isobe, who has taken full advantage of such effects in a number of brilliant syntheses (Isobe, M.; Kitamura, M.; Goto, T. *J. Am. Chem. Soc.* **1982**, *104*, 4997. Kitamura, M.; isobe, M.; Ichikawa, Y.; Goto, T. *J. Am. Chem. Soc.* **1984**, *106*, 3252).

(27) Perkins, M. J.; Ward, P. *Mech. Mol. Migr.* **1971**, *4*, 55–112. Miller, B. *Mech. Mol. Migr.* **1968**, *1*, 247–313. For a discussion, see: March, J. *Advanced Organic Chemistry*, 3rd ed.; McGraw-Hill: New York, 1985; p 969.

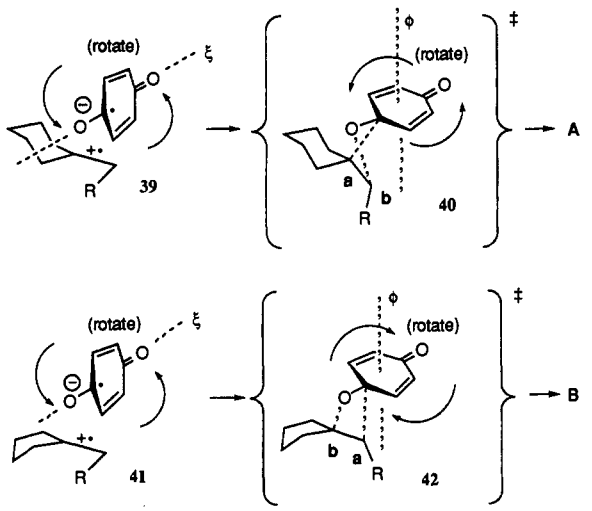
(28) (a) The X-ray structure of **49** is provided as supplementary material. (b) Similar reactions of 2-methyl-2-(acetoxyethylidene)cyclohexane (mixture of geometric isomers) and of its 3-methyl analogue are mentioned in our original report (ref 3). These substrates also appeared to react with facial selectivity, though lethis selectivity was less pronounced than with the *tert*-butyl substrate. Unfortunately, a multitude of stereoisomeric products were obtained from such olefins, and spectra of crude reaction mixtures were extremely complex. Facial selectivity was difficult to measure accurately, but it was estimated as about 3:1 in favor of an isomer believed to result from axial attack of the quinone, by analogy with the *tert*-butyl series.

the various forces discussed above accidentally cancel each other out. Therefore, formation of nearly equal amounts of oxetanes **A** and **B** with those substrates would be indeed a fortuitous event.[7]

We note that the regioselectivity of singlet diradical formation is not likely to result from the fact that the radical-cationic portion of the exciplex (the former olefin) has somehow undergone pyramidalization. One might argue that since radicals generated on carbons bearing strongly electronegative substituents tend to be pyramidal,[29] in a radical cation the cationic character of one of the carbon atoms may well provide the driving force for pyramidalization of the radical center. This question was addressed computationally by studying the structure of the radical cations of 2-methyl-2-butene, ethylidenecyclopropane, ethylidenecyclopentane, and ethylidenecyclohexane, at the MNDO level.[30] As expected,[30] significant twisting was observed about the (former) C=C bond, but no evidence was found for pyramidalization of the relevant carbon atoms.[18]

In closing, we would like to comment on the possibility of a concerted mechanism for oxetane formation. Concerted collapse of the singlet exciplex could determine regioselectivity through an asynchronous bond-forming process, which would proceed with preferential/faster pyramidalization of one of the carbon atoms in the (former) olefin relative to the other. Cyclohexylidene-based radical cations would tend to pyramidalize at the ring carbon to relieve allylic strain. It is less energetically demanding to pyramidalize a radical than a cation;[32] thus, the ring carbon would acquire more radical character, and the side-chain carbon, more ionic character during bond formation. The side-chain carbon would then become bonded preferentially to the oxygen atom of the quinone radical anion (the site of greatest charge density), while the ring carbon would become connected to the carbon atom of that intermediate. The opposite outcome would be expected with cyclopentylidene, and lower homologue substrates, wherein almost perfect staggering exists between the olefinic structure and adjacent ring hydrogens and wherein pyramidalization of the ring carbon is disfavored: faster pyramidalization would now occur at the side-chain carbon. Macrocyclic or acyclic olefins would be insensitive to such effects, because of their conformational flexibility. A perhaps naive picture of the events leading to bond formation envisions evolution of singlet Caldwell exciplexes such as **39** and **41** preferentially toward transition states **40** and **42**, respectively (Scheme 9). Simultaneous rotation of the (former) quinone about axes ξ and ϕ would occur so that the sense of rotation is dictated by the relative rates of pyramidalization of the (former) olefinic carbon atoms. Such a mechanism would not necessarily be in conflict with the results of Scheme 4. Formation of both syn- and anti-**23** and -**24** may be due, at least in part, to isomerization of the olefin prior to the events leading to oxetane formation. However, the extent of olefin isomerization appears to be too small (25% or less) to justify formation of a 1:1 ratio of isomers. It is doubtful that one geometric isomer of the olefin reacts much faster with photoexcited

Scheme 9[a]



[a] A possible course of events leading to oxetanes through concerted collapse of the BQ–olefin exciplex. Bond formation from the singlet Caldwell-like exciplexes **39** and **41** begins with simultaneous rotation of the (former) quinone about axes ξ and ϕ. The sense of rotation about ϕ is dictated by the relative rates of pyramidalization of the (former) olefinic carbon atoms. In either case, carbon atom **a** pyramidalizes faster than **b**. Therefore, **a** acquires more radical character and becomes bound to the C atom of the quinone, whereas **b** acquires more ionic character and becomes bound to the O atom of the quinone.

benzoquinone than the other.[33] A more plausible alternative is that the radical-cationic portion of the exciplex (the former olefin) might itself have a low internal rotation barrier. A very rough upper limit (*vide infra*) for such a barrier in the radical cation of *cis*-1,4-diformyloxy-2-butene may be estimated (MNDO) to be approximately 14.9 kcal/mol.[31] Internal rotation might therefore be relatively facile, and a diradical intermediate may not be absolutely required to explain loss of stereochemistry in such reactions. Conversely, a rotational barrier of that magnitude translates (Arrhenius equation) into a rate constant for cis–trans isomerization (298 K) $k \approx 10^2\ s^{-1}$, assuming a preexponential factor $A \approx 10^{13}$.[34] This value of k appears to be insufficient to permit formation of 1:1 ratios of stereoisomers, as the precursor to the oxetane, whichever its nature, is likely to cyclize with rate constants on the order of *at least* $10^8\ s^{-1}$ (cf. Scheme 5). Of course, one should be mindful that MNDO may calculate rotational barriers that are too large, especially for open-shell systems. Furthermore, exciplex formation may proceed with strong local exothermicity, and if collapse of **29** to the oxetane were to occur under nonthermal conditions (i.e., if the exciplex were "hot": a distinct possibility for a very fast, concerted process), the temperature term in the Arrhenius equation may not correspond to the average temperature of the system. Nonetheless, the above difficulties force us to regard a concerted mechanism as unlikely, at this time.[35]

Conclusions

All aspects of quinone–olefin photocycloaddition reactions, regioselectivity (or lack thereof), loss of olefin stereochemistry during oxetane formation, and results of trapping experiments, appear to be consistent with a singlet diradical mechanism. While

(29) Pauling, L. *J. Chem. Phys.* **1969**, *51*, 2767. For a discussion, see: March, J. *Advanced Organic Chemistry*, 3rd ed.; McGraw-Hill: New York, 1985; p 167.

(30) MNDO appears to be particularly successful in predicting the structure of radical cations: (a) Bauld, N. L. *J. Am. Chem. Soc.* **1992**, *114*, 5800. (b) Bellville, D. J.; Bauld, N. L. *Tetrahedron* **1986**, *42*, 6167. (c) Pabon, R. A.; Bauld, N. L. *J. Am. Chem. Soc.* **1984**, *106*, 1145. (d) Bellville, D. J.; Bauld, N. L. *J. Am. Chem. Soc.* **1982**, *104*, 294.

(31) In complete accord with previous theoretical and experimental work (ref 30), MNDO predicts a twisted conformation for this radical cation. The calculated twist angles about the (former) C–C double bond are ca. 21° for the cis isomer and 176° for the trans isomer. Further details are provided in the supplementary material. Similar rotational barriers were estimated for 2-butene and ethylene.

(32) Lorand, J. P.; Chodroff, S. D.; Wallace, R. W. *J. Am. Chem. Soc.* **1968**, *90*, 5266. Fort, R. C. Jr.; Franklin, R. E. *J. Am. Chem. Soc.* **1968**, *90*, 5267. Humphrey, L. B.; Hodgson, B.; Pincock, R. E. *Can. J. Chem.* **1968**, *46*, 3099. Danen, W. C.; Tipton, T. J.; Saunders, D. G. *J. Am. Chem. Soc.* **1971**, *93*, 5186. Fort, R. C., Jr.; Hiti, J. *J. Org. Chem.* **1977**, *42*, 3968. For a discussion, see: March, J. *Advanced Organic Chemistry*, 3rd ed.; McGraw-Hill: New York, 1985; p 167.

(33) Experiments using *cis*- and *trans*-2-butene have been described by Bunce and Hadley (ref 7). These workers do not mention any rate difference between the two geometric isomers.

(34) Values of the frequency parameter in this range seem to apply rather broadly to unimolecular processes. Cf., e.g.: (a) Saunders, M.; Schleyer, P. V. R.; Olah, G. A. *J. Am. Chem. Soc.* **1964**, *86*, 5680. (b) Saunders, M.; Hagen, E. L. *J. Am. Chem. Soc.* **1968**, *90*, 2436.

(35) This issue is difficult to resolve. Even more sophisticated *ab initio* methods are notoriously unable to produce meaningful data for rotational barriers, especially in open-shell systems.

a concerted mechanism may not be positively ruled out at this time, it may be regarded as unlikely.

Experimental Section[36]

General Procedure for the Cycloaddition Reaction. A degassed (argon) mixture of the olefinic substrate (2.6 mmol), freshly sublimed benzoquinone (2 mmol), solid K_2CO_3 (0.3 mmol), and benzene (6 mL) was subjected to irradiation either with an argon ion laser (cooling to 0 °C required) or with a battery of common fluorescent tubes (room temperature).[14b] The reaction was followed by TLC. After 5 h, the reaction was worked up even though some starting material still remained. The benzene was evaporated, and a ^{1}H spectrum of the crude sample was recorded to determine the ratio of regioisomers of the oxetane. The crude residue was chromatographed over silica gel by eluting first with 5% EtOAc/hexanes (elution of nonpolar starting materials) and then with 50% EtOAc/hexanes (elution of the considerably more polar photoadduct). Yields ranged from 50 to 90%.

Cycloadduct 6B. 50%. R_f (5% EtOAc/hexanes): 0.38. ^{1}H NMR: 7.36 (B′ part of AA′BB′, app dd, 1H, J_1 = 10.2 Hz, J_2 = 2.8 Hz), 7.18 (B part of AA′BB′, app dd, 1H, J_1 = 10.1 Hz, J_2 = 2.8 Hz), 6.29–6.07 (AA′ part of AA′BB′, cm, 2H), 4.9–4.87 (m, 1H), 3.3 (t, 2H, J = 7.74 Hz), 1.7–0.3 (cm, 23H). ^{13}C NMR: 185.5, 149.2, 148.1, 147.9, 145.8, 129.4, 128.5, 128.0, 127.8, 83.8, 70.2, 48.9, 35.7, 31.8, 31.7, 29.6, 29.5, 29.4, 29.3, 29.2, 29.1, 27.7, 26.6, 24.4, 22.6, 14.0, 9.0, 6.8, 6.6, 4.7. IR: 2927, 2855, 1671, 1631, 1507, 1461, 1389, 1252, 1219, 1167, 1075, 931, 853. MS: 288 (M^+), 235, 149, 133, 110, 107 (100%), 91, 55, 41, 29. Anal. Calc for $C_{19}H_{28}O_2$: C, 79.12; H, 9.78. Found: C, 78.77; H, 9.79.

Cycloadduct 7B. 50%. R_f (20% EtOAc/hexanes): 0.34. ^{1}H NMR: 7.09–6.95 (m, 2H), 6.22–6.07 (cm, 2H), 6.22–6.07 (cm, 2H), 4.32–4.12 (AB part of ABX, m, 2H), 3.19 (X part of ABX, m, 1H), 2.5–1.4 (br m, 6H), 1.96 (s, 3H). ^{13}C NMR: 184.7, 170.4, 149.2, 145.2, 129.9, 129.1, 128.7, 127.7, 85.6, 83.9, 75.3, 60.3, 50.3, 38.7, 32.8, 26.0, 20.5, 12.1. IR: 2938, 1742, 1669, 1629, 1510, 1430, 1370, 1231, 1032. MS: 248 (M^+), 188, 178, 150, 136, 107, 79, 43. HRMS: calc 248.1048, obs 248.1039.

Cycloadduct 8B. 63%. R_f (15% EtOAc/hexanes): 0.14. ^{1}H NMR: 7.4–7.0 (cm, 2H), 6.22–6.07 (cm, 2H), 4.122 (dd, 2H, J_1 = 8.1 Hz, J_2 = 1.5 Hz), 3.3 (t, 1H, J = 8.0 Hz), 2.3–1.3 (cm, 11H). IR: 2957, 2878, 1742, 1669, 1629, 1510, 1443, 1370, 1238, 1032, 965, 859. MS: 262 (M^+), 156, 153, 151, 120, 111, 110, 107, 93, 81, 79, 43. HRMS: calc 262.1205, obs 262.1210.

Cycloadduct 9A. 90%. R_f (10% EtOAc/hexanes): 0.06. ^{1}H NMR: 7.37 (B′ part of AA′BB′, app dd, 1H, J_1 = 10.2 Hz, J_2 = 3.2 Hz), 7.20 (B part of AA′BB′, app dd, 1H, J_1 = 10.2 Hz, J_2 = 2.9 Hz), 6.26–6.19 (AA′ part of AA′BB′, cm, 2H), 4.66 (X part of ABX, dd, 1H, J_{AX} = 7.3 Hz, J_{BX} = 4.6 Hz), 4.46–4.32 (AB part of ABX, d AB q, 2H, J_{AB} = 12.0 Hz, J_{AX} = 7.3 Hz, J_{BX} = 4.6 Hz), 2.10 (s, 3H), 1.90–1.60 (br m, 4H), 1.45–1.30 (br m, 6H). ^{13}C NMR: 184.5, 170.6, 147.8, 147.4, 129.3, 128.9, 84.0, 81.5, 64.3, 52.0, 34.8, 28.6, 25.0, 23.0, 22.5, 20.8. IR: 2938, 2861, 1743, 1673, 1623, 1455, 1370, 1236, 1033, 955, 927, 906, 857. MS: 276 (M^+), 216, 187, 174, 145, 131, 108, 107 (100%), 93, 91, 79, 43. HRMS: calc 276.1361, obs 276.1338.

Cycloadduct 10A. 86%. R_f (15% EtOAc/hexanes): 0.30. ^{1}H NMR: 7.38 (B′ part of AA′BB′, app dd, 1H, J_1 = 10.7 Hz, J_2 = 3.2 Hz), 7.17 (B part of AA′B″, app dd, 1H, J_1 = 10.7 Hz, J_2 = 3.2 Hz), 6.23–6.16 (A and A′ part of AA′BB′, cm, 2H), 4.70 (q, 1H, J = 6.5 Hz), 1.8–1.3 (cm, 10H), 1.43 (d, 3H, J = 6.5 Hz). ^{13}C NMR: 184.9, 149.2, 148.4, 128.9, 128.4, 83.9, 81.1, 52.3, 34.6, 28.6, 25.2, 23.0, 22.6, 22.5, 18.2. IR: 2952, 2882, 1743, 1673, 1623, 1511, 1448, 1370, 1230, 1110, 1040. MS: 218 (M^+), 175, 174, 110 (100%), 107, 95, 81, 70, 69. HRMS: calc 218.1307, obs 218.1306.

Cycloadduct 11A. 50%. R_f (15% EtOAc/hexanes): 0.20. ^{1}H NMR: 7.4–7.1 (cm, 2H), 6.30–6.1 (cm, 2H), 4.22 (dd, 2H, J_1 = 8.1 Hz, J_2 = 1.7 Hz), 3.34 (t, 1H, J = 8.0 Hz), 2.3–1.3 (cm, 15H). IR: 2924, 2858, 1742, 1656, 1457, 1370, 1238, 1198, 1045, 096, 866, 806. MS: 290 (M^+), 242, 229, 214, 201, 187, 173, 161, 147 (100%), 123, 107, 95, 91, 81. HRMS: calc 290.1517, obs 290.1518.

Cycloadduct 34. 88%. R_f (20% EtOAc/hexanes): 0.27. ^{1}H NMR: 7.42 (B′ part of AA′BB′, app dd, 1H, J_1 = 10.8 Hz, J_2 = 3.3 Hz), 7.24 (B part of AA′BB′, app dd, 1H, J_1 = 10.8 Hz, J_2 = 3.4 Hz), 6.3–6.21 (AA′ part of AA′BB′, cm, 2H), 4.6 (t, 1H, J = 6.3), 4.33 (d, 2H, J = 6.3), 2.09 (s, 2.10) 2.5–0.7 (cm, 9H), 0.72 (s, 9H). ^{13}C NMR: 194.5, 170.1, 147.9, 147.2, 129.5, 128.0, 105.0, 103.2, 83.5, 80.9, 64.2, 51.9, 46.9, 34.8, 32.2, 31.8, 28.5, 28.1, 23.1, 20.5, 14.5. IR: 2945, 2882, 1743, 1476, 1377, 1230, 1195, 1166, 1096, 1040, 885, 829, 745. MS: 332 (M^+), 290, 230, 201, 173, 146, 120, 107 (100%), 79, 57, 44. HRMS: calc 332.1987, obs 332.1994.

Phenol 35. BF_3·OEt_2 (12.0 μL, 0.12 mmol) was added to a solution of cycloadduct **34** (0.4139 g, 1.25 mmol) in 8 mL of CH_2Cl_2 in a dry 25-mL round-bottom flask. The solution was stirred at room temperature for 2 h. Saturated aqueous $NaHCO_3$ solution (3 mL) was added to the stirring reaction mixture. The layers were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined extracts were passed over a short plug of Na_2SO_4, and the solvent was evaporated to give 0.389 g (94%) of a light-brown solid. R_f (20% EtOAc/hexanes): 0.33. ^{1}H NMR: 7.00–6.50 (cm, 3H), 4.5–4.1 (m, 3H), 2.15 (s, 3H), 2.1–0.9 (cm, 10H), 0.92 (s, 9H). IR: 3409, 2952, 2868, 1743, 1497, 1370, 1237, 1040. MS: 332 (M^+), 272, 231, 215, 201, 187, 173, 161, 147, 123, 107, 57 (100%), 43, 29.

Tosylate 36. Solid tosyl chloride (0.196 g, 1.03 mmol) was added portionwise to a mixture of phenol **35** (0.34 g, 1.03 mmol), THF (5 mL), and 10% aqueous NaOH (3 mL). The mixture was stirred for 8 h. The THF was evaporated, and the aqueous mixture was extracted three times with CH_2Cl_2. The combined extracts were passed over a short plug of Na_2SO_4, and the solvents were evaporated to give 0.35 g (70%) of a white solid. A sample recrystallized from hexane had mp 128–129 °C. R_f (30% EtOAc/hexanes): 0.64. ^{1}H NMR: 7.65 (app d, 2H, J = 8.3 Hz), 7.29 (app d, 2H, J = 8.3 Hz), 6.87–6.63 (cm, 3H), 4.41 (X part of ABX, dd, 1H, J_{AX} = 11.5 Hz, J_{BX} = 2.5 Hz), 4.34–4.15 (AB part of ABX, m, 2H, J_{AB} = 8.4 Hz, J_{AX} = 11.4 Hz, J_{BX} = 2.51 Hz), 2.43 (s, 3H), 2.11 (s, 3H), 2.1–0.7 (cm, 9H), 0.85 (s, 9H). ^{13}C NMR: 170.9, 142.8, 135.9, 132.2, 129.6, 128.7, 122.4, 120.3, 110.2, 90.2, 62.9, 47.2, 46.5, 36.2, 31.3, 27.4, 22.8, 21.7, 21.5, 20.9. IR: 3180, 2958, 2457, 1742, 1587, 1461, 1366, 1048, 894, 709, 672. MS: 486 (M^+ + 1), 426, 331 (100%), 215, 201, 187, 173, 155, 91, 57, 43. HRMS: calc 486.2076, obs 486.2068.

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Supplementary Material Available: Description of photochemical apparatus, details of computational studies, experimental protocols, preparation of various intermediates, spectra of cis olfeins **21**/**22** and of the of cis and trans mixtures **21**/**25** and **22**/**26**, and X-ray structure of **36** (12 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.

(36) General protocols and procedures for the preparation of starting olefins are provided as supplementary material.