Mechanistic and Preparative Studies of the Intramolecular Photocyclization of Methylated 2-(4-Pentenyl)tropones

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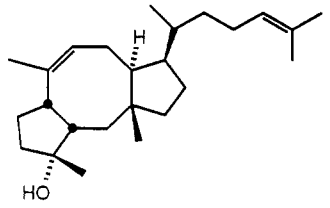
Irradiation of various methylated 2-(4-pentenyl)tropones affords regioisomeric formal [6π + 2π] and [8π + 2π] cycloadducts. The cyclooctadiene-containing [6π + 2π] adducts are produced as mixtures of stereoisomers. A self-consistent mechanistic scheme based upon evidence accumulated through the study of regioselectivity and stereoselectivity as a function of reaction conditions has been proposed. This mechanism includes several discrete intermediates en route to the final cycloadducts. Attempts to functionalize [6π + 2π] cycloadducts through vinyllithium addition led to unconventional products through unanticipated reaction pathways.

Introduction

The identification of numerous biologically active natural products containing eight-membered rings, typically having a bicyclo[6.3.0]undecane substructure,[1] has recently stimulated considerable interest in the development of methodology for cyclooctane synthesis. For example, synthesis of the natural products ophiobolin F (**1**),[1a] dactylol (**2**),[1h] or pleuromutilin (**3**)[1o] will depend critically on an efficient strategy for the construction of the cyclopentannulated cyclooctane nucleus.



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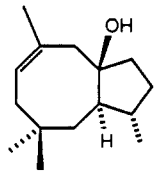

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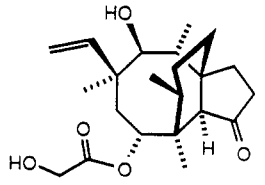

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Many model studies, and in rarer cases completed total syntheses, have been recorded in this area. For example, *acyclic closure* of an appropriately functionalized cyclopentane precursor has delivered the eight membered ring portion of the bicyclo[6.3.0]undecane skeleton.[2] In addition, *fragmentation* of the bicyclo[4.2.0]octane,[3] bicyclo[3.3.1]nonane,[4] bicyclo[3.3.0]octane,[5] and bicyclo[5.1.0]octane[6] ring systems has been exploited for the synthesis of functionalized cyclopentanocyclooctane carbocycles. Finally, *ring expansion* via Cope rearrangement of cyclopentannulated divinylcyclobutanes[7] or Claisen rearrangement of 2-vinyl-5-methylenetetrahydropyrans[8] also affords the 5-8 fused ring system characteristic of these natural products. However, conspicuously absent from this roster of carbocycle-forming reactions is a *cycloaddition* approach to the bicyclo[6.3.0]undecane system. While the strategies cited above furnish the 5-8 fused ring system with varying levels of efficiency, we felt that a direct cycloaddition reaction has the potential for even greater economy of effort. Furthermore, the prospects for regiochemical and stereochemical control in a cycloaddition process may facilitate entry into functionally complex natural product systems.

Documented examples of cyclooctanoid synthesis via formal cycloaddition of two unsaturated precursors fall into

(1) Representative examples include the following. (a) Ophiobolins A-F: Cordell, G. A. *Phytochemistry* **1974**, *13*, 2343 and references cited therein. (b) Ophiobolins G-H: Cole, J. R.; Cole, P. D. *J. Agric. Food Chem.* **1984**, *32*, 778. (c) Cycloaraneosene: Borschberg, H. J. *Diss. ETH* **1975**, 5578. (d) Ceroplastol I: Iitake, Y.; Watanabe, I.; Harrison, I. T.; Harrison, S. *J. Am. Chem. Soc.* **1968**, *90*, 1092. (e) Albolic acid: Rios, T.; Gomez, F. *Tetrahedron Lett.* **1969**, 2929. (f) Fusicoccin A: Barrow, K. D.; Barton, D. H. R.; Chain, E.; Ohnsorge, U. F. W.; Thomas, R. *J. Chem. Soc. C* **1971**, 1265. (g) Cotylenol: Sassa, T. *Agric. Biol. Chem.* **1972**, *36*, 2037. (h) Dactylol: Schmitz, F. J.; Hollenbeak, K. H.; Vanderah, D. J. *Tetrahedron* **1978**, *34*, 2719. (i) Poitediol: Fenical, W.; Schulte, G. R.; Finer, J.; Clardy, J. *J. Org. Chem.* **1978**, *43*, 3630. (j) Precapnelladiene: Ayanoglu, E.; Gebreyesus, T.; Beechan, C. M.; Djerassi, C. *Tetrahedron* **1979**, *35*, 1035. (k) Basmenone: Wahlberg, I.; Eklund, A. M.; Nishida, T.; Enzell, C. R.; Berg, J. E. *Tetrahedron Lett.* **1983**, *24*, 843. Epoxydictymene: Enoki, N.; Furusaki, A.; Suehiro, K.; Ishida, R.; Matsumoto, T. *Tetrahedron Lett.* **1983**, *24*, 4341. (m) Longipenol: Prestwich, G. D.; Tempesta, M. S.; Turner, C. *Tetrahedron Lett.* **1984**, *25*, 1531. (n) Roseatoxide: Adesomoju, A. A.; Okogun, J. I. *J. Nat. Prod.* **1984**, *47*, 308. (o) Pleuromutilin: Kavanagh, F.; Hervey, A.; Robbin, S. W. J. *Proc. Natl. Acad. Sci. U.S.A.* **1951**, *37*, 570. (p) Asterisconolide: San Feliciano, A.; Barrero, A. F.; Medarde, M.; Miguel del Corral, J. M.; Aramburu, A.; Perales, A.; Fayos, J. *Tetrahedron Lett.* **1985**, *26*, 2369.

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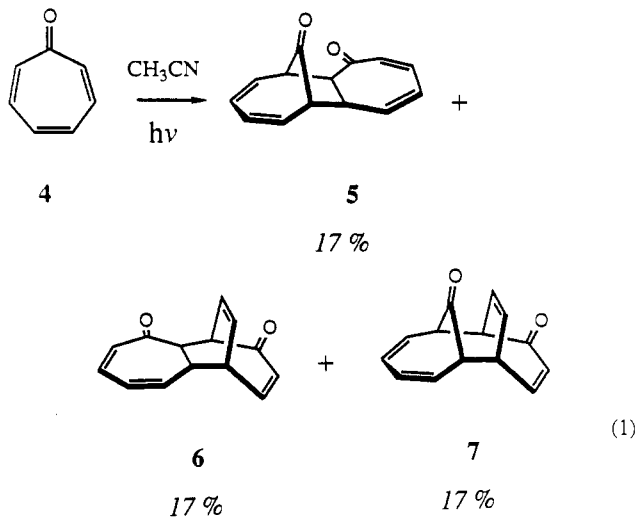
two categories: [4π + 4π] and [6π + 2π] additions. Examples of the former process can be found in the photochemical dimerization of anthracene[9] and naphthalene[10] derivatives, 2-pyridones[11] and 2-pyrones,[12] and the thermal dimerization of 2,3-dimethylenefuran.[13] More recently, Wender et al.[14] have disclosed an intramolecular version of the nickel(0)-catalyzed dimerization of 1,3-dienes[15] to yield, inter alia, the bicyclo[6.3.0]undecane skeleton. In each case, these formal [4π + 4π] dimerization reactions produce a functionalized 1,5-cyclooctadiene carbocycle.

Examples of formal [6π + 2π] cycloadditions encompass far less scope but can be accomplished either photochemically, thermally, or through transition-metal mediation. For example, Ziegler-type titanium–aluminum compounds catalyze the [6π + 2π] addition of olefins (as part of dienes) to cycloheptatriene,[16] while thermal addition of very reactive dienophiles to cycloheptatriene derivatives leads to formal [6π + 2π] adducts, admixed with the products of other competitive pericyclic pathways.[17] Lastly, irradiation of cycloheptatriene in the presence of naphthoquinone affords various 1:1 adducts, including a [6π + 2π] adduct (13%).[18a] Photochemical dimerization of tropone (4) (eq 1) also furnishes the formal [6π + 2π] adduct **5**, along with

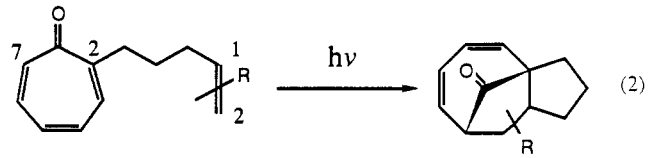


4 **5** 17 % **6** 17 % **7** 17 % (1)

[4π + 2π] and [4π + 6π] adducts **6** and **7**, respectively, in equal amounts.[18b] However, complex product mixtures or the requirement for special activating functionality diminishes the potential utility of these processes in organic synthesis.

The wealth of strategically located functionality that would result from [6π + 2π] cycloaddition of an alkene to a tropone derivative (cf. **5**) motivated us to focus on the possible development of this type of cycloaddition process for bicyclo[6.3.0]undecane synthesis. However, the stereochemical and regiochemical complexity that would potentially result from intermolecular combination of unadorned tropone molecules would mitigate against application of this process to natural product synthesis. Therefore, a successful tropone/alkene addition strategy would depend critically on the olefinic addend intercepting an excited state of tropone in the desired regiochemical orientation prior to the intervention of other competitive photochemical options. An intramolecular variant of the tropone/alkene photocycloaddition seemed a reasonable way to provide sufficient kinetic and regiochemical advantages to allow the desired reaction to occur and selectively provide the desired bicyclo[6.3.0]undecane skeleton.

With this as background, we initially sought to prepare alkenyltropones of the general structure **8** and study their photochemical behavior under a variety of experimental conditions (eq 2). The [6π + 2π] adduct **9**, resulting from



(2)

8 **9**

bond formation between C(1) of the alkene and C(2) of the tropone ring, and C(2) of the alkene and C(7) of the tropone, contains the desired bicyclo[6.3.0]undecane ring system along with functionality appropriate for eventual conversion to various natural product systems. In this report we describe our successful execution of this strategy[19] and detail the results of experiments designed to probe the mechanistic course of this novel process.

Results and Discussion

Synthesis of Substituted Tropones. The addition of alkyl Grignard reagents to 2-chlorotropone, first reported by Doering,[20] proved to be an effective method for the synthesis of the 2-alkyltropones necessary for this study.[19] However, attempts to prepare dialkylated tropones from combination of methylated 2-chlorotropones and Grignard reagents were unsuccessful. These disubstituted species were accessible through the recently reported methodology developed by Funk,[21] which commences with sulfone-stabilized alkyl anion addition to tropone (or alkyltropones), followed by in situ loss of the elements of sulfinic acid to directly afford the alkylated tropone nucleus **12** (eq 3). This chemistry compares quite favorably with the classical method of Doering and was employed in the synthesis of the alkylated tropones used in this study.[22]

Photochemical Studies. Irradiation of the alkenyltropones **13a–f** at 350 nm either in aqueous acidic methanol at room temperature, or in aprotic solvents at low temperature (−30 to −70 °C) in the presence of Lewis or protic acids, afforded various stereoisomeric and regioisomeric cyclization products. In all cases, the desired [6π + 2π] adduct was the major product, although identifi-

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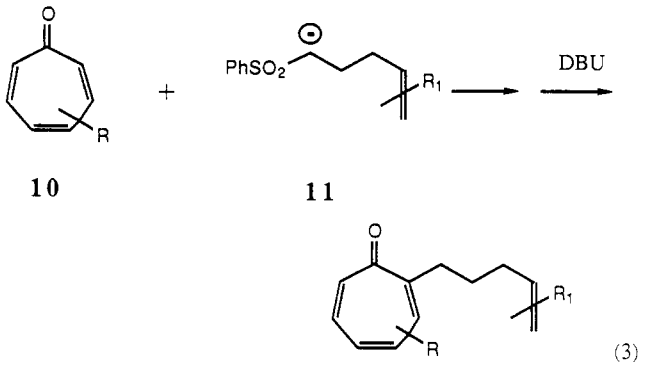
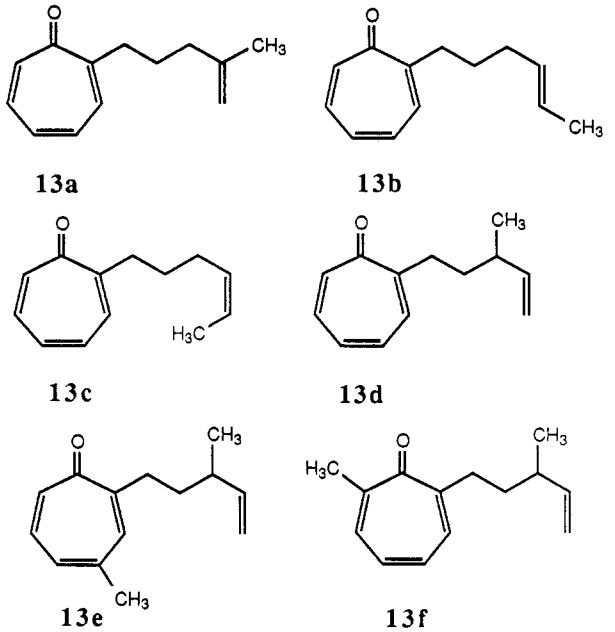


cation of other minor reaction components provided revealing mechanistic clues about the course of this complex transformation (vide infra).



Room-temperature irradiation of alkenyltropone **13a** in acidic methanol with a 350-nm light source furnished a mixture of diastereomeric [6π + 2π] cycloadducts **15a** and **15b** in 45% yield (eq 4).[36] It is particularly important to

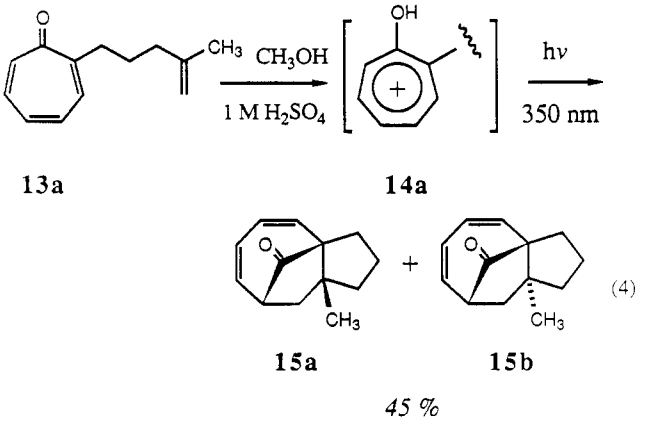


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Table I. Irradiation of Tropone 13a (0.018 M) at Differing Acidities

$[H_2SO_4]$, M	% 14a[a]	15a/15b	% 13a remaining after 45-min irradn
0.02	0.3		75
0.06	0.4		70
0.08	0.6		30
0.10	0.8	1.6	
0.20	0.9	1.8	25
0.40	3.7	2.0	0
0.60	5.4	2.5	

[a] Calculated from the pK_a of the parent hydroxytropylium species.[23]

Table II. Regioisomer Ratio as a Function of Acidity for Tropone 13c

$[H_2SO_4]$, M	(16a + 16b)/17
0.06	0.7:1
0.12	1.6:1
0.20	1.8:1
0.50	2.2:1

note the crucial role that the acidic medium plays in the alkene–tropone photocycloaddition reaction. For example, irradiation of tropone **13a** under neutral conditions in various solvents (hexane, benzene, acetonitrile, methylene chloride, or methanol) resulted in complex reaction mixtures from which only trace amounts of cycloadducts could be detected (GLC). Addition of acid (0.1–0.7 M aqueous H_2SO_4) to a methanolic solution of **13a** generates an equilibrium concentration of hydroxytropylium ion **14a** [pK_a (hydroxytropylium) = −1],[23] a species whose chemical reactivity upon electronic excitation apparently is quite distinct from that of tropone.

Further evidence implicating the hydroxytropylium ion **14a** as the reactive species can be found in Table I. Thus, the consumption of starting tropone **13a** was more rapid as acid concentration, and thus the population of the hydroxytropylium species, increased. Control experiments indicated that the product cycloadducts **15a** and **15b** did not equilibrate or revert to starting material under the reaction conditions. However, at total acid concentrations greater than 0.6 M H_2SO_4, the exo isomer **15a** was selectively destroyed.

(27) Parallel-plane exciplexes have been invoked as obligate intermediates in arene–olefin [6π + 2π] photochemistry. See: Wender, P. A.; Howbert, J. J. *J. Am. Chem. Soc.* **1981**, *103*, 688 and references cited therein.
(28) A similar argument has been advanced to rationalize the stereoselectivity observed upon [4π + 2π] cycloaddition of cyclopentadiene and tropylium tetrafluoroborate in water. See: Ito, S.; Itoh, I. *Tetrahedron Lett.* **1971**, 2969. Clemans, G. B.; Dobbins, M. A. *Tetrahedron Lett.* **1982**, *23*, 387.
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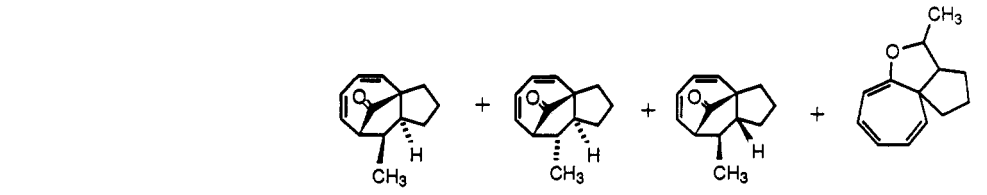
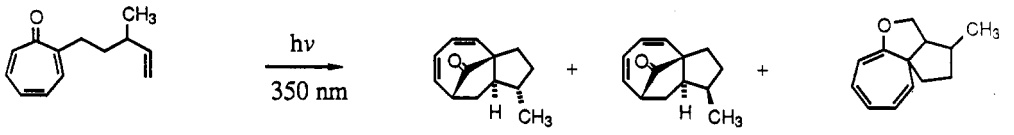
(36) Throughout this paper, photocyclization yields are reported as: GLC yield (isolated yield).

Scheme I



	16a	16b	16c	17	
13b	5[36]	37 (18)	10 (5)	31 (15)	(5)
13c	8 (5)	43 (22)	----	31 (14)	

Scheme II



	18a	18b	19	
a) 4 : 1 CH_3OH / 1 M H_2SO_4 (25°C)	28(19)[36]	13(4)	29(14)	(6)
b) 4 : 1 CH_3OH / 1 M H_2SO_4 (-78°C)	55(24)	9(4)	30(16)	
c) toluene / CF_3CO_2H (10 eq.) (-25°C)	49(21)	7(3)	30(6)	
d) toluene / CF_3CO_2H (10 eq.) (-45°C)	54(22)	7(3)	23(5)	
e) toluene / CF_3CO_2H (10 eq.) (-60°C)	49(26)	5(3)	28(9)	
f) CH_2Cl_2 / CF_3CO_2H (10 eq.) (-45°C)	**59(34)**	**11(6)**	**<5**	

The stereochemical outcome of this photocyclization is quite surprising—the major adduct **15a**, as determined by X-ray crystallographic analysis,[19] contains a *trans*-bicyclo[3.3.0]octane substructure! Molecular mechanics calculations[24] indicate that isomer **15a** is approximately 9 kcal/mol less stable than isomer **15b**. Furthermore, the ratio of the more strained to the less strained species increases as the acidity of the medium increases (Table I). The fact that there are no documented examples of *trans*-bicyclo[3.3.0]octane construction via concerted cycloaddition,[25] and that the stereoisomer ratio appears to be responsive to acidity, raises the possibility that a nonconcerted pathway for alkene–tropone photocyclization operates (vide infra).

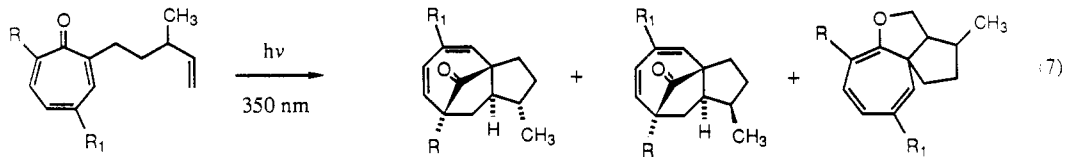
Photocyclization of either (*E*)-alkenyltropone **13b** or (*Z*)-alkenyltropone **13c** resulted in *loss* of olefin geometry upon cycloadduct formation. Thus, irradiation of either the *E* or *Z* species with a 350-nm light source at room temperature in acidic methanol led to nearly identical mixtures of endo $[6\pi + 2\pi]$ adducts **16a,b** and the formal $[8\pi + 2\pi]$ adduct **17** (eq 5, Scheme I). In addition, the (*E*)-alkenyltropone provided small amounts of the *trans*-bicyclo[3.3.0]octane-containing exo $[6\pi + 2\pi]$ adduct **16c**. Control experiments indicated that the starting (*E*)- or (*Z*)-alkenes in **13b** and **13c** do not equilibrate under the reaction conditions and that the product ratios do not change during the course of the reaction.

Formal $[8\pi + 2\pi]$ photochemical addition of alkenes to tropone is precedented.[26] Thus, the isolation and characterization of adduct **17**, as a single (unassigned) stereoisomer, was not surprising. Nevertheless, eventual applications of this methodology to cyclooctanoid natural product synthesis would benefit from suppressing this undesired reaction mode. Increasing the acidity of the medium led to a corresponding monotonic increase in the ratio of the $[6\pi + 2\pi]$ to the $[8\pi + 2\pi]$ adducts in the photocyclization of (*Z*)-alkenyltropone **13c** (Table II). Although this approach is limited by the instability of the cycloadducts in media greater than ~0.7 M sulfuric acid, the observed trend demonstrates that cyclization regioselectivity is responsive to medium effects and that formation of the desired $[6\pi + 2\pi]$ adducts can be maximized by this protocol.

The issue of relative asymmetric induction was probed with the methyl-bearing alkenyltropone **13d**. Irradiation of this tropone in acidic methanol at 350 nm led to a disappointing mixture of cycloadducts **18a,b** and **19** (eq 6, entry a, Scheme II). The partitioning between the regioisomeric $[8\pi + 2\pi]$ adduct **19** and the $[6\pi + 2\pi]$ adducts **18a,b** was similar to that observed for the tropones **13b** and **13c** (ca. 1:1.5). Furthermore, the pendant secondary methyl group had only marginal influence on the stereochemistry of bond formation, leading to production of the diastereomeric $[6\pi + 2\pi]$ adducts **18a** and **18b** in a 2:1 ratio. As with the previous tropone cycloaddition products, resubmission of either pure adduct to the reaction conditions did not lead to equilibration.

In addition to the $[6\pi + 2\pi]$ and $[8\pi + 2\pi]$ adducts, small amounts (~5% GLC, ~1% isolated) of a formal $[4\pi + 2\pi]$ cycloadduct **20a** could be isolated from irradiation of **13d** at room temperature in aqueous acidic methanol. The structural characterization of this product was confirmed by comparison with the spectral data available for the desmethyl analogue **20b** formed through a thermal $[4\pi$

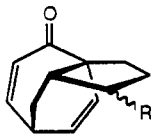
Scheme III



(7)

		21a	21b	22
13e	*a)* CH_2Cl_2, -45 °C, CF_3CO_2H (10 eq.)	*32 (14)* [36]	*11 (5)*	----
R = H, R_1 = CH_3	*b)* toluene, -70 °C, $BF_3 \cdot Et_2O$ (0.5 eq.)	*49 (29)*	*9 (5)*	----
		23a	**23b**	**24**
13f	*c)* CH_2Cl_2, -45 °C, CF_3CO_2H (11 eq.)	*56 (35)*	*9 (5)*	*2*
R = CH_3, R_1 = H	*d)* CH_2Cl_2, -70 °C, CF_3CO_2H (1.1 eq.)	*70 (62)*	*7 (6)*	*7*

+ 2π] cycloaddition.[21] This trace adduct **20a** could not be detected (GLC) in the low-temperature irradiations of tropone **13d**.



20a R = CH_3
20b R = H

Maximizing the production of the particular stereoisomer **18a** was crucial to related studies in natural product synthesis. Therefore, the effects of a systematic variation in reaction conditions (solvent, acid, temperature) on reaction stereochemistry and regiochemistry were explored. Examination of a selection of these results shown in eq 6 revealed that both regio- and stereoselectivity could be significantly improved by choice of an aprotic solvent at low temperature. In general, using less than 10 equiv of acid led to substantially more of the [8π + 2π] regioisomer **19**, while greater than 10 equiv of acid resulted in product decomposition. The reaction displayed the best stereoselectivity in toluene for the [6π + 2π] adduct series (10:1 **18a** to **18b**, entry e), although the regioselectivity was still unsatisfactory (2:1 [6π + 2π] adducts **18a,b** to [8π + 2π] adduct **19**). In methylene chloride (entry f), virtually none of the [8π + 2π] adduct could be detected (GLC) while the stereoselectivity of [6π + 2π] adduct formation was reasonably high (5.6:1 ratio of **18a** to **18b**).

Investigation of the photochemistry of the dialkylated tropones **13e** and **13f** helped to define the scope of tropone substitution permissible in this reaction (eq 7, Scheme III). Both species undergo photocyclization to give mixtures of stereoisomeric [6π + 2π] adducts **21a/b** and **23a/b** and the regioisomeric [8π + 2π] adducts **22** and **24**, respectively, in a qualitatively similar manner to the monosubstituted tropone **13d**. However, the photochemistry of **13e** and **13f** was characterized in general by higher chemical yields and greater stereoselectivity and regioselectivity than those for any of the monosubstituted tropones studied. The methylation pattern and stereochemistry of major isomers **21a** and **23a** are characteristic of several marine sesquiterpenes, and so the results of the photochemistry of **13d–f**, taken together, constitute a model study for syntheses in this area.

Irradiation of either disubstituted tropone **13e** or **13f** under the optimal conditions for monosubstituted analogue **13d** was unsatisfactory (eq 7, entries a and c). However, the use of boron trifluoride etherate in toluene at −70 °C (entry b) resulted in complete regiochemical control and acceptable stereocontrol (**21a:21b** ≅ 5.5:1) upon cyclization of the 4-methyltropone **13e**. Likewise, optimization studies on the 7-methyltropone **13f** suggested that using much less acid resulted in higher product yields (68% total isolated yield of **23a** and **23b**), satisfactory regiocontrol ([6π + 2π]:[8π + 2π] = 11:1), and excellent stereochemical control (**23a:23b** = 10:1). That cyclizations of these dialkylated tropones require less acid than the monoalkylated analogues supports our contention that a hydroxytropylium cation is the photoactive species. Dialkyl substitution should incrementally stabilize an intermediate hydroxytropylium species relative to the monoalkyl case and, hence, provide a higher concentration of this reactive intermediate for photocyclization under experimental conditions which lead to less product destruction.

Mechanistic Considerations. Evaluation of the stereochemical and regiochemical features of this photocyclization process should permit the development of a working mechanistic hypothesis. The accumulated evidence can be summarized as follows:

1. Cyclization of tropone **13a** leads to a preponderance of a more highly strained *trans*-bicyclo[3.3.0]octane-containing stereoisomer **15a**.

2. Stereochemistry of the starting alkene is lost upon cyclization.

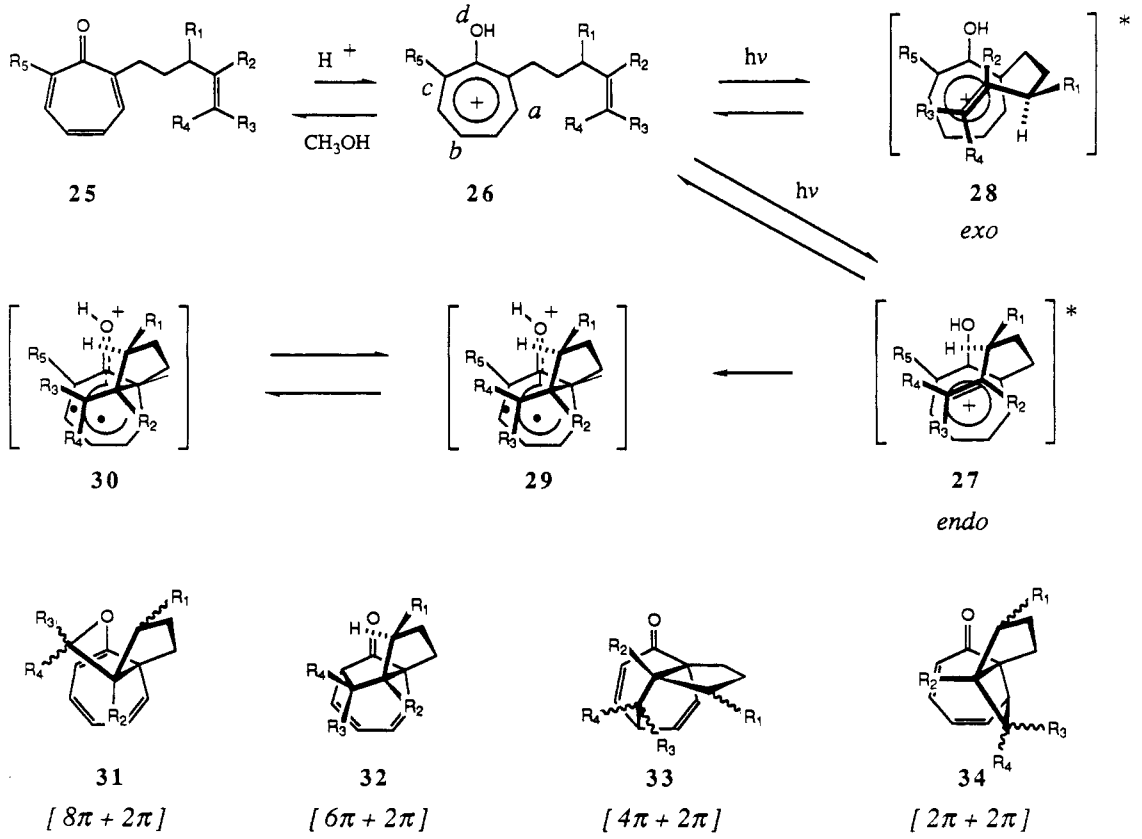
3. The ratio of [6π + 2π] to [8π + 2π] regioisomers varies directly with acid concentration.

4. A substantial level (5.6:1) of relative asymmetric induction is seen upon cyclization of **13d**, and this stereocontrol is even further enhanced (10:1) upon reaction of the 7-methyl analogue **13f**.

5. Trace amounts of a formal [4π + 2π] cycloadduct are isolated from photocyclization of tropone **13d**.

Taken together, these observations can be accommodated by the mechanistic description shown in Scheme IV.

Scheme IV



Reaction through the diastereomeric excited-state geometries depicted by **27** and **28** leads to either the endo or the exo product configuration, respectively. Although these excited states could in fact correspond to exciplexes, we have no experimental evidence that bears directly on this issue.[27] Nevertheless, this parallel-plane model for reactive excited-state geometries provides a convenient framework for rationalizing both the formation of the highly strained *trans*-bicyclo[3.30]octane-containing adducts **15a** and **16c** and the stereoselectivity observed upon cyclization of tropones **13d** and **13f**. Rapid collapse from these excited-state conformations with carbon–carbon bond formation sets the π-facial (endo–exo) selectivity of the cyclization. Therefore, in the Curtin–Hammet limit where equilibrium is established between **27** and **28**, we speculate that the relative stabilities of these species should govern the endo:exo product ratio. One factor that plausibly confers differential stabilization to one member of the pair of diastereomeric excited-state conformers derives from the role that the alkenyl substituents R_2–R_4 play in preventing access of the stabilizing nucleophilic solvent (H_2O, CH_3OH) to the cationic tropylium ring.[28] Note that the strain inherent in the product cycloadducts is not imparted until after the second bond-closure step (vide infra).

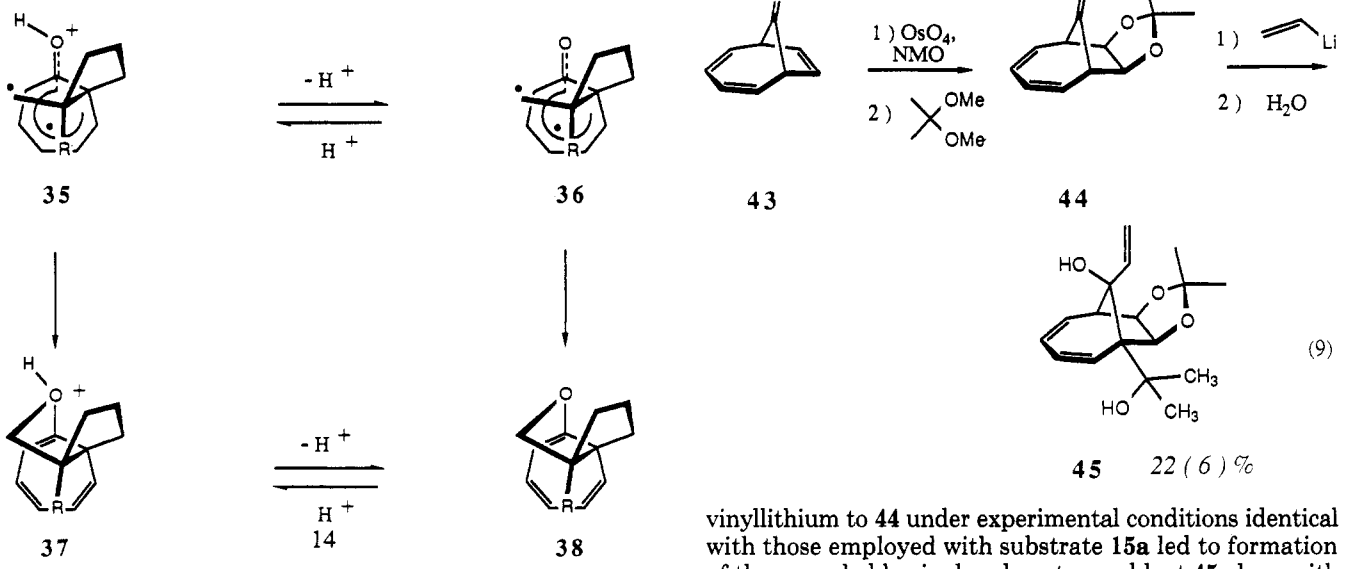
Finally, relative asymmetric induction can be rationalized if the propane tether adopts a conformation that places the secondary methyl groups of **13d** and **13f** in pseudoequatorial positions, thus avoiding moderate steric interactions with the tropylium hydroxyl moiety (**27**, R_1 = CH_3) in **13d** and preventing even greater unfavorable interactions with both the hydroxyl and 7-methyl groups (**27**, R_1 = R_5 = CH_3) in **13f**. Thus, by invoking these parallel-plane conformers as precursors to bond formation from the excited state, both the initial stereoselectivity (**18a**:**18b** = 5.6:1) and the enhanced selectivity (**23a**:**23b** = 10:1) seen upon cyclization of tropones **13d** and **13f**, respectively, can be understood.

Collapse of these excited states with concomitant carbon–carbon bond formation results in a radical/radical cation intermediate **29**. For simplicity, the remainder of the pathway is detailed only for the endo species **27**. Rapid equilibration of this species with its diastereomeric rotamer **30** affords a plausible mechanism for the loss of olefin geometry seen upon irradiation of the (*E*)- and (*Z*)-alkenyltropones **13b** and **13c**.

The regiochemistry of addition in this photocyclization process might arise through partitioning from the putative radical/radical cation intermediate **29**. Bond formation to sites a, b, c, or d (cf. **26**) would lead to formal [$2\pi + 2\pi$], [$4\pi + 2\pi$], [$6\pi + 2\pi$], and [$8\pi + 2\pi$] adducts, respectively, following proton loss. The formal [$2\pi + 2\pi$] adduct **34** could not be detected in any alkenyltropone irradiation. However, if it were formed, it might suffer a facile [1,5] sigmatropic shift to produce a formal exo [$6\pi + 2\pi$] adduct. A small amount of the formal [$4\pi + 2\pi$] adduct **33** (R_1 = CH_3) could be isolated from irradiation of tropone **13d** under a singular set of reaction conditions. The formal [$8\pi + 2\pi$] adduct **31** was formed in substantial amounts (5–30%) in most cyclization reactions. The obligate carbon–oxygen bond forming step en route to **31** could occur either before (**35** → **37**) or after (**36** → **38**) proton loss from the hydroxyl moiety (Scheme V). Although no direct precedent in support of either sequence is known, several relevant cases, in which proton loss from a radical–radical cation pair *precedes* coupling, have been reported.[29] The direct relationship between acidity of the media and [$6\pi + 2\pi$]:[$8\pi + 2\pi$] ratio observed in the photochemistry of tropone **13c** (Table II) is consistent with this interpretation and suggests a rational means to suppress the unwanted [$8\pi + 2\pi$] cycloaddition.

Vinyllithium Addition Studies. We had hoped that

Scheme V



(9)

the utility of the [6π + 2π] photoadduct **15a** in the synthesis of ceroplastol-type natural products (cf. **40**) might be expressed through a [3,5] sigmatropic rearrangement[30] of the derived vinyl alkoxide **39** (eq 8, Scheme VI). However, vinyllithium addition to **15a** did not lead to alcohol formation, but rather resulted in a modest yield of the formal diene addition products **42a/b**.

This remarkable transformation, formally a bis homo Michael addition, must result from an interplay of both unfavorable steric factors inhibiting direct nucleophilic attack at the carbonyl group and a favorable overlap of the carbonyl and diene orbitals. Although a cyclopropyl alkoxide **41**, or the corresponding allylically transposed cyclobutyl alkoxide, might be logical intermediates, efforts to detect these species by trapping experiments (TMSCl addition after TLC indicated complete consumption of **15a**) led only to recovery of the ketones **42a/b**.

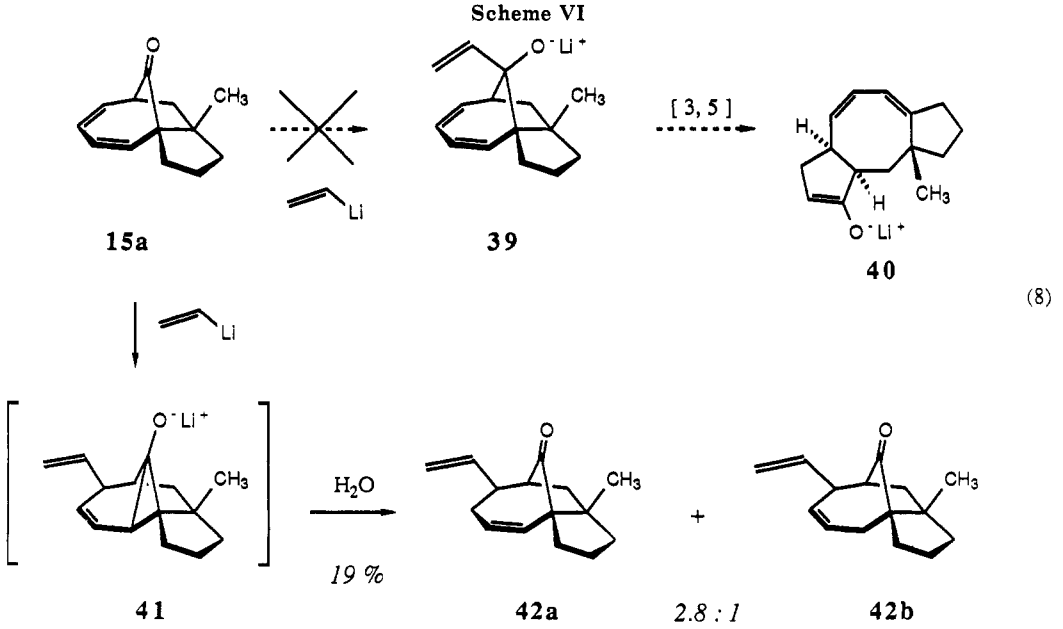
The surprising reactivity of the keto diene **15a** suggested that investigation of the vinyl anion addition chemistry of the simple analogue **44** would be worthwhile. Toward this end, the acetonide **44**, featuring the same bicyclo[4.2.1]nonadienone substructure, was prepared from the known trienone **43**[31] as indicated in eq 9. Addition of vinyllithium to **44** under experimental conditions identical with those employed with substrate **15a** led to formation of the remarkable vinyl and *acetone* adduct **45** along with small amounts of several other uncharacterized products. The structure of diol **45** was suggested by spectroscopic data and confirmed by X-ray crystallographic analysis.[32]

Diol **45** conceivably might arise through the following series of transformations: (1) bridgehead deprotonation of ketone **44** followed by decomposition of the resulting anion to liberate a molecule of acetone; (2) bridgehead deprotonation of a second molecule of ketone **44**, and addition of that anion to the liberate acetone; (3) addition of vinyllithium to the aldol product of step 2. In any event, no products of direct addition of vinyllithium to trienone **43**, either at the diene or the carbonyl, were isolated.

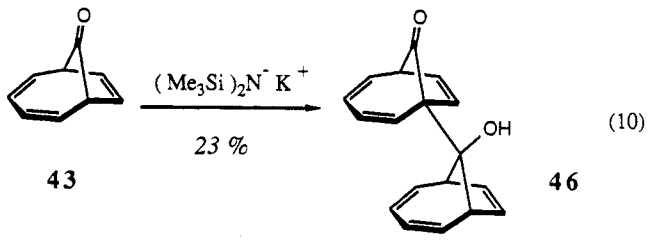
The apparent ease of bridgehead deprotonation[33] in the bicyclo[4.2.1]nonadienone system was emphasized by the results shown in eq 10. Thus, treatment of trienone **43** with potassium hexamethyldisilazide at low temperature led to formation of the aldol dimer **46** as a single (unassigned) diastereomer. The putative bridgehead carbanion could not be intercepted by D_2O or TMSCl quenching experiments—apparently the aldol condensation was too rapid.

The multitude of reaction pathways available to the bicyclo[4.2.1]nonadienone system upon combination with

Scheme VI



(8)



(10)

vinyllithium is a notable aspect of this work. However, lack of predictability for any given species suggested that this approach toward functionalizing the [6π + 2π] photoadducts will not be profitable.

Conclusion

The photocyclization of methylated 2-(4-pentenyl)tropones in acidic solution appears to be a complex process from which many regioisomeric and stereoisomeric cycloadducts can be obtained. Indirect evidence that implicates several discrete intermediates, including excited states and radical/radical cation and/or diradical species, has been obtained primarily through product analysis studies. Judicious choice of reaction conditions ensures that the formal [6π + 2π] regioisomer predominates over the undesired [8π + 2π] or [4π + 2π] isomers. Furthermore, acceptable levels of stereochemical control can be achieved within the [6π + 2π] manifold by the simple expedient of resorting to photochemistry at low temperatures. Attempts to functionalize a representative [6π + 2π] adduct by vinyllithium addition led to a wholly unexpected reaction course, suggesting that the unique juxtaposition of functionality in these adducts must be fully considered before using these bicyclo[6.3.0]undecane species in natural product synthesis.

Experimental Section

Infrared (IR) spectra were recorded on a Perkin-Elmer 281B infrared spectrophotometer. Magnetic resonance spectra (^{1}H NMR, ^{13}C NMR) were recorded on either Bruker WP-200, AM-300, or WM-360 spectrometers. Chemical shifts are reported in δ units, with tetramethylsilane (TMS) as an internal standard. Low- and high-resolution mass spectra (MS, HRMS) were obtained on a Kratos MS9/50 hexapole focusing mass spectrometer. Gas–liquid chromatography (GLC) was performed on a Hewlett-Packard 5890A instrument equipped with a capillary cross-linked methyl silicone column (25 m; i.d. 0.20 mm; film thickness 0.33 mm) and a flame-ionization detector. Helium was used as carrier gas, and the chromoatograms were recorded on an HP 3390A integrator. Liquid (flash)[34] chromatography was carried out by using 32–63-μm silica gel (Woelm-Pharma) and the indicated solvent. Analytical thin-layer chromatography was performed by using precoated silica gel (60 F_{254}) plates (E. Merck). High-pressure liquid chromatography (HPLC) was performed on a Waters 6000A semipreparative instrument equipped with an R-400 refractometer and 440 UV detector, using a ZORBAX-SIL silica gel column (25 cm × 20 mm, Dupont). Elemental analyses were performed by Micro-Tech Laboratories, Inc., Skokie, IL. Photochemical reactions were carried out either in a Rayonet photochemical reactor equipped with a 350-nm light source or with a 450-W Hanovia medium-pressure lamp filtered through uranium glass (Corning). Ether, tetrahydrofuran, and benzene were purified by distillation from sodium/benzophenone under nitrogen, while methylene chloride was distilled from CaH_2 under nitrogen. Moisture-sensitive reactions were carried out in predried glassware and under an inert atmosphere (N_2, Ar).

Photocyclization of Alkenyltropones. General Procedure A. A 50–100-mg sample of alkenyltropone[22] was dissolved in 15–30 mL of a 4:1 CH_3OH/1 M H_2SO_4 (0.2 M acid) solution in a Pyrex test tube and purged with N_2 for 10 min (final concentration ~0.02 M). The test tube was stoppered with a rubber septum and placed in a Rayonet photochemical reactor equipped with 350-nm bulbs. The solution was irradiated at room temperature until GLC indicated consumption of starting material (30–120 min). At this time, the reaction solution was poured into an equal volume of saturated $NaHCO_3$ solution and extracted with 3 × 20 mL of ether. The combined ether extracts were washed with brine, dried over sodium sulfate, filtered, and concentrated in vacuo, and the residue was purified by flash chromatography using 3–8% ether in hexane as eluent. In some cases, HPLC was required to obtain pure samples of photoadducts. The yields (GLC, isolated) are given in the text. Reactions in media of different acidity (Tables I and II) were conducted in an identical manner as described above, with the amount of 1 M H_2SO_4 being varied accordingly.

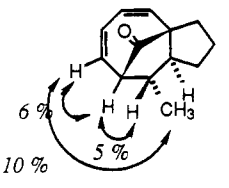
General Procedure B. A 50–100-mg sample of alkenyltropone[22] was dissolved in 15–30 mL of the indicated solvent (CH_2Cl_2 or toluene), leading to a final concentration of 0.02 M. This solution was transferred to the reaction chamber of a Hanovia Pyrex photochemical apparatus, and the entire reactor assembly was immersed in an isopropyl alcohol bath held at the indicated temperature. The appropriate (cf. eq 7) amount of Lewis acid was added, and the solution was slowly purged with a stream of inert gas (N_2 or Ar) for 10 min. The solution was continuously purged and irradiated with a medium-pressure 450-W mercury lamp filtered through uranium glass (ca. 340-nm cutoff) until GLC indicated consumption of starting material. Products were recovered by using the workup procedure described above, and yields are given in the text.

15a: IR (neat) 1740 cm^{-1} (C=O); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.97–5.74 (m, 3 H, =C(H)), 5.25 (d, J = 11.1 Hz, 1 H, =C′(H)), 3.10 (m, 1 H, COC(H)), 2.70 (dd, J = 12.1, 6.4 Hz, 1 H, C(*H*)H), 1.93–1.50 (m, 2 H), 1.72 (dd, J = 12.2, 8.7 Hz, 1 H, C(H)*H*), 1.45 (m, 1 H), 1.30 (m, 1 H), 0.97 (s, 3 H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.5, 132.3, 128.7, 125.8, 125.3, 71.7, 63.5, 53.5, 37.7, 27.8, 27.4, 24.6, 21.6; MS, m/z (relative intensity) 188 (M^+, 4), 131 ($M^+ - C_4H_9$, 23). Anal. Calcd for $C_{13}H_{16}O$: C, 82.92; H, 8.58. Found: C, 82.70; H, 8.71.

15b: IR (CCl_4) 1746 cm^{-1} (C=O); ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.85–5.65 (m, 3 H, =C(H)), 5.20 (d, J = 11.1 Hz, 1 H, =C′(H)), 2.88 (m, 1 H, COC(H)), 2.55 (m, 1 H), 2.15 (dd, J = 13.2, 3.0 Hz, 1 H, C(*H*)H), 1.89 (dd, J = 13.2, 8.4 Hz, 1 H, C(H)*H*), 1.57 (m, 5 H), 1.29 (s, 3 H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 131.5, 129.0, 125.6, 124.5, 66.3, 59.5, 50.5, 44.3, 43.0, 32.2, 23.4, 23.2; MS, m/z (relative intensity) 188 (M^+, 28), 173 ($M^+ - CH_3$, 13), 160 ($M^+ - CO$, 18); HRMS calcd for $C_{13}H_{16}O$ 188.1202, found 188.1190.

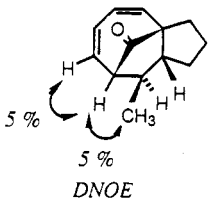
16a: IR (CCl_4) 1748 cm^{-1} (C=O); ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.77 (m, 2 H, =C(H)), 5.66 (dd, J = 10.6, 8.3 Hz, =C′(H)), 5.44 (dd, J = 9, 1 Hz, 1 H, =C″(H)), 3.22 (m, 1 H), 2.82 (td, J = 7.4, 2.3 Hz, 1 H, C(CH_3)*H*), 2.59 (dd, J = 8.3, 2.1 Hz, 1 H, COC(H)), 2.38 (m, 1 H), 1.75–1.4 (m, 5 H), 0.94 (d, J = 7.5 Hz, 3 H, CH_3); HRMS calcd for $C_{13}H_{16}O$ 188.1202, found 188.1208.

16b: IR (CCl_4) 1746 cm^{-1} (C=O); ^{1}H NMR (360 MHz, $CDCl_3$) δ 5.93 (dd, J = 11.6, 7.0 Hz, 1 H, =C(H)), 5.71 (dd, J = 10.7, 7.0 Hz, 1 H, =C′(H)), 5.53 (d, J = 10.7 Hz, 1 H, =C″(H)), 5.36 (dd, J = 11.6, 7.0 Hz, 1 H, =C‴(H)), 2.78 (t, J = 6.6 Hz, 1 H, COC(H)), 2.71 (m, 1 H), 2.51 (m, 1 H), 1.87 (dqd, J = 9.8, 6.5, 5.8 Hz, 1 H, C(CH_3)*H*), 1.82–1.3 (m, 5 H), 1.18 (d, J = 6.7 Hz, 3 H, CH_3); MS, m/z (relative intensity) 188 (M^+, 100), 160 ($M^+ - CO$, 70); HRMS calcd for $C_{13}H_{16}O$ 188.1202, found 188.1194.



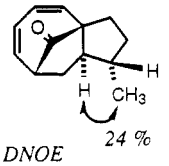
DNOE

16c: IR (CCl_4) 1746 cm^{-1} (C=O); ^{1}H NMR (360 MHz, $CDCl_3$) δ 6.30 (dd, J = 12.5, 6.5 Hz, 1 H, =C(H)) 6.14 (d, J = 12.5 Hz, 1 H, =C′(H)), 6.01 (dd, J = 11.5, 6.3 Hz, 1 H, =C″(H)), 5.78 (dd, J = 11.5, 6.4 Hz, 1 H, =C‴(H)), 2.99 (t, J = 9.1 Hz, 1 H), 2.66 (tq, J = 9.8, 7.0 Hz, 1 H, C(CH_3)*H*), 2.46 (dd, J = 9.9, 6.5 Hz, 1 H, COC(H)), 1.95–1.70 (m, 6 H), 0.96 (d, J = 7.0 Hz, 3 H, CH_3); MS, m/z (relative intensity) 188 (M^+, 100), 173 ($M^+ - CH_3$, 41), 160 ($M^+ - CO$, 21); HRMS calcd for $C_{13}H_{16}O$ 188.1202, found 188.1185.

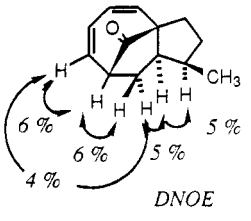


17: IR (CCl_4) 1630 cm^{-1} (C=C); ^1H NMR (360 MHz, $CDCl_3$) δ 6.39 (dd, J = 11.4, 6.8 Hz, 1 H, =C(H)), 6.24 (dd, J = 10.4, 6.4 Hz, 1 H, =C′(H)), 6.18 (dd, J = 9.4, 6.2 Hz, 1 H, =C″(H)), 5.70 (d, J = 6.8 Hz, 1 H, =C‴(H)), 5.50 (d, J = 9.5 Hz, 1 H, =C⁗(H)), 4.38 (m, 1 H, OC(CH_3)H), 2.55 (m, 1 H), 1.80–1.15 (m, 6 H), 1.39 (d, J = 6.5 Hz, 3 H, CH_3); MS, m/z (relative intensity) 188 (M^+, 82) 173 ($M^+ - CH_3$, 69), 145 ($M^+ - C_3H_7$, 100); HRMS calcd for $C_{13}H_{16}O$ 188.1202, found 188.1197.

18a: IR (CCl_4) 1745 cm^{-1} (C=O); ^1H NMR (360 MHz, $CDCl_3$) δ 5.80 (dd, J = 11.0, 7.0 Hz, 1 H, =C(H)), 5.71 (dd, J = 10.6, 7.0 Hz, 1 H, =C′(H)), 5.53 (d, J = 10.6 Hz, 1 H, =C″(H)), 5.51 (dd, J = 11.0, 7.1 Hz, 1 H, =C‴(H)), 2.91 (t, J = 7.2 Hz, 1 H, COC(H)), 2.75 (td, J = 8.4, 3.4 Hz, 1 H, C(CH_3)HC(H)), 2.46 (ddd, J = 12.9, 8.6, 1.3 Hz, 1 H, COC(H)C(H)H), 2.37 (m, 1 H), 1.72–1.4 (m, 5 H), 0.95 (d, J = 6.8 Hz, 3 H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.0, 128.0, 124.7, 124.1, 61.7, 60.6, 53.9, 41.8, 39.2, 33.2, 31.9, 19.9; MS, m/z (relative intensity) 188 (M^+, 100), 160 (M^+ - CO, 25); HRMS calcd for $C_{13}H_{16}O$ 188.1202, found 188.1211.



18b: IR (neat) 1740 cm^{-1} (C=O); ^1H NMR (360 MHz, $CDCl_3$) δ 5.84 (dd, J = 11.1, 6.9 Hz, 1 H, =C(H)), 5.73 (dd, J = 10.5, 6.9 Hz, 1 H, =C′(H)), 5.56 (d, J = 10.6 Hz, 1 H, =C″(H)), 5.42 (dd, J = 11.1, 6.9 Hz, 1 H, =C‴(H)), 3.18 (dt, J = 8, 6 Hz, 1 H, C(CH_3)HC(H)) 2.91 (t, J = 6.6 Hz, 1 H, COC(H)), 2.48 (m, 1 H), 2.06 (dd, J = 12.7, 8.3 Hz, 1 H, COC(H)C(H)H), 1.60 (m, 1 H), 1.46 (m, 1 H), 1.0–0.98 (m, 3 H), 0.89 (d, J = 6.9 Hz, 3 H, CH_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 194.0, 135.9, 127.8, 125.4, 124.3, 54.5, 53.4, 37.4, 34.6, 33.7, 32.8, 29.7, 12.8; MS, m/z (relative intensity) 188 (M^+, 70), 160 (M^+ - CO, 29); HRMS calcd for $C_{13}H_{16}O$ 188.1202, found 188.1206.



19: IR (CCl_4) 1630 cm^{-1} (C=C); ^1H NMR (360 MHz, $CDCl_3$) δ 6.38–6.10 (m, 3 H), 5.70 (d, J = 6.8 Hz, 1 H, =C(H)), 5.42 (d, J = 9.5 Hz, 1 H, =C′(H)), 4.19 (dd, J = 9.0, 7.5 Hz, 1 H, OC(H)H), 4.07 (dd, J = 9.0, 4.0 Hz, 1 H, OC(H)H), 2.32 (m, 1 H), 1.93 (m, 1 H), 1.74 (m, 1 H), 1.48 (m, 2 H), 1.32 (m, 1 H), 1.09 (d, J = 6.8 Hz, 3 H, CH_3); MS, m/z (relative intensity) 188 (M^+, 100), 173 ($M^+ - CH_3$, 36), 160 ($M^+ - C_2H_4$, 10); HRMS calcd for $C_{13}H_{16}O$ 188.1202, found 188.1210.

20a: IR (CCl_4) 1725, 1667 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 6.90 (dd, J = 11.0, 8.0 Hz, 1 H, CH=C(H)C(H)), 6.51 (dd, J = 8, 7 Hz, 1 H, =C(H)), 5.73 (d, J = 11.0 Hz, 1 H, COC(H)=C(H)), 5.55 (d, J = 8.0 Hz, 1 H, C(H)=C(H)C(H)), 3.26 (m, 1 H, C(H)=C(H)C(H)), 2.92 (ddd, J = 13.6, 9.5, 2.6 Hz, 1 H, C(H)H), 2.17 (ddd, J = 11.9, 8.8, 3.0 Hz, 1 H, C(H)C(H)C(H)H), 1.8–1.2 (m, 6 H), 0.98 (d, J = 6.4 Hz, 3 H, CH_3).

21a: IR (CCl_4) 1740 cm^{-1} (C=O); ^1H NMR (360 MHz, $CDCl_3$) δ 5.78–5.63 (m, 2 H, =C(H)), 5.56 (d, J = 10.2 Hz, 1 H, =C′(H)), 5.21 (d, J = 11.1 Hz, 1 H, =C″(H)), 2.68–2.58 (m, 2 H), 2.39–2.32 (m, 1 H), 1.84–1.23 (m, 5 H), 1.16 (s, 3 H, CH_3), 0.94 (d, J = 7.1 Hz, 3 H, C′H_3); ^{13}C NMR (75 MHz, $CDCl_3$) δ 216.6, 136.2, 134.1, 124.5, 122.7, 61.9, 57.2, 56.4, 48.6, 32.9, 32.8, 20.2, 19.6; MS, m/z (relative intensity) 202 (M^+, 82), 187 ($M^+ - CH_3$, 55), 174 (M^+ - CO, 50); HRMS calcd for $C_{14}H_{18}O$ 202.1358, found 202.1356.

23a: IR (CCl_4) 1745 cm^{-1} (C=O); ^1H NMR (360 MHz, $CDCl_3$) δ 5.67 (d, J = 11.5 Hz, 1 H, =C(H)), 5.46 (dd, J = 11.3, 7.2 Hz, 1 H, =C′(H)), 5.33 (s, 1 H, =C″(H)), 2.90 (t, J = 7 Hz, 1 H, COC(H)), 2.74–2.67 (m, 1 H), 2.42–2.30 (m, 2 H), 1.73 (d, J = 1.5 Hz, =C(CH_3)), 1.69–1.63 (m, 5 H), 0.95 (d, J = 6.1 Hz, 3 H, CH_3); ^{13}C NMR (90 MHz, $CDCl_3$) δ 215.6, 132.6, 130.8, 128.2, 127.8, 60.5, 58.8, 54.6, 41.7, 39.1, 32.9, 32.6, 24.9, 20.3; MS, m/z (relative intensity) 202 (M^+, 73), 174 (M^+ - CO, 51) 159 (M^+ - CO, CH_3, 93); HRMS calcd for $C_{14}H_{18}O$ 202.1358, found 202.1356.

Vinyllithium Addition to Dienone 15a. An ethereal solution of vinyllithium[35] (860 μL of a 0.6 M solution, 0.52 mmol) was added dropwise with stirring to an ice-cooled solution of dienone **15a** (80 mg, 0.43 mmol) in 2 mL of THF under argon. After addition, the ice bath was removed, and the homogeneous orange solution was warmed to room temperature. Aftrer 4.5 h, GLC indicated complete consumption of starting material, and the reaction solution was poured into 10 mL of ice-cold 1 M H_3PO_4 and extracted with 2 × 10 mL of ether. The combined ethereal layers were washed with brine, dried over sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography using 40% ether/hexane as eluent to afford 18 mg of a colorless oil (19%, 2.8:1 ratio of **42a** to **42b** by GLC). Pure samples of the olefin isomers **42a** and **42b** could be obtained by HPLC purification using 10% ether/hexane as eluent.

42a: IR (CCl_4) 1740 cm^{-1} (C=O); ^1H NMR (360 MHz, $CDCl_3$) δ 5.93 (ddd, J = 17.1, 10.1, 8.1 Hz, 1 H, C(H)=CH_2), 5.78 (ddd, J = 11.9, 7.3, 4.8 Hz, 1 H, C(H)=C(H)), 5.42 (dd, J = 11.9, 2.0 Hz, 1 H, C(H)=C(H)), 4.98 (dt, J = 17.1, 1.3 Hz, 1 H, C(H)=C(H)H), 4.93 (dt, J = 10.2, 0.7 Hz, 1 H, C(H)=C(H)H), 2.90 (t, J = 8 Hz, 1 H, COC(H)), 2.38 (dd, J = 10.1, 7.7 Hz, 1 H, H_2C=C(H)C(H)), 2.23 (m, 4 H), 2.06 (dd, J = 12.0, 7.0 Hz, 1 H, COC(H)C(H)H), 1.91 (dd, J = 11.9, 8.9 Hz, 1 H, COC(H)C(H)H), 1.8–1.55 (m, 3 H), 1.4–1.2 (m, 2 H), 0.94 (s, 3 H, CH_3).

42b: IR (CCl_4) 1740 cm^{-1} (C=O); ^1H NMR (360 MHz, $CDCl_3$) δ 5.92 (ddd, J = 17.5, 9.6, 7.8 Hz, 1 H, C(H)=CH_2), 5.61 (m, 1 H, C(H)=C(H)), 5.42 (dt, J = 12.5, 2.0 Hz, 1 H, C(H)=C(H)), 5.03 (m, 2 H, C(H)=CH_2), 2.95 (m, 2 H, COC(H), H_2C=C(H)-C(H)), 2.55 (dt, J = 19, 2.0 Hz, 1 H, C(H)=C(H)C(H)H), 2.2 (m, 4 H), 1.8–1.6 (m, 3 H), 1.4 (m, 1 H), 1.2 (m, 1 H), 0.98 (s, 3 H, CH_3).

7,8-Isopropylidenedioxybicyclo[4.2.1]nona-2,4-dien-9-one (44). *N*-methylmorpholine *N*-oxide (4.9 g, 42 mmol) and then osmium tetraoxide (0.4 g of a 2.5 wt % solution in *tert*-butyl alcohol, 1.6 mmol) were added sequentially to a solution of trienone **43**[31] (5.07 g, 38 mmol) in 200 mL of acetone at room temperature. This dark brown solution was stirred overnight, and then sodium sulfite (1.1 g, 8.8 mmol) was added. After 30 min, the solution was filtered through charcoal and Celite, concentrated in vacuo, and purified by flash chromatography with 70% ether/hexane as eluent to yield 1.74 g (28%) of a brown solid: IR (CCl_4) 3400 (OH), 1740 (C=O), 1650 (C=C) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.97–5.72 (m, 4 H), 4.56 (s, 2 H, HOC(H)), 3.12 (s, 2 H, D_2O exchangeable), 2.94 (dd, J = 9.2, 2.5 Hz, 2 H, COC(H)); MS, m/z (relative intensity) 166 (M^+, 1), 120 (M^+ - CO, H_2O, 2). 2,2-Dimethoxypropane (0.65 g, 6.2 mmol) and pyridinium *p*-toluenesulfonate (0.11 g, 0.4 mmol) were added to the above diol (0.69 g, 4.2 mmol) in 20 mL of methylene chloride. The mixture was stirred overnight at room temperature and poured into 5 mL of a 50% saturated brine solution. This solution was extracted with 2 × 20 mL of ether, and the organic extracts were combined, washed sequentially with saturated $NaHCO_3$ and brine, dried with sodium sulfate, filtered, concentrated in vacuo, and purified by flash chromatography with 30% ether/hexane as eluent to afford 0.67 g (78%) of acetonide **44** as a light brown oil: IR (CCl_4) 1760 (C=O), 1650 (C=C) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.92–5.66 (m, 4 H), 4.75 (s, 2 H, OC(H)), 3.00 (dd, J = 8.3, 2.1 Hz, 2 H, COC(H)), 1.4 (s, 3 H, CH_3), 1.31 (s, 3 H, C′H_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ 210.0, 125.6, 123.3, 108.6, 84.6, 56.4, 26.6, 24.5; MS, m/z (relative intensity) 206 (M^+, 38), 191 (M^+ - CH_3, 22). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.87; H, 6.86. Found: C, 70.17; H, 7.11.

1-(1-Hydroxy-1-methylethyl)-7,8-isopropylidenedioxy-9-hydroxy-9-ethenylbicyclo[4.2.1]nona-2,4-diene (45). An ethereal solution of vinyllithium[35] (2.27 mL of a 0.46 M solution, 1.05 mmol) was added dropwise with stirring to an ice-cooled solution

of acetonide 44 (0.20 g, 0.96 mmol) in 3 mL of THF under nitrogen. The orange reaction solution was allowed to warm to room temperature and, after 12 h, poured into 20 mL of ice-cold 1 M H_3PO_4 and extracted with 2 × 20 mL of ether. The combined organic extracts were washed sequentially with saturated $NaHCO_3$ and brine, dried over sodium sulfate, filtered, and concentrated in vacuo to afford 0.15 g of an orange oil, which contained 38% of the adduct 45 (GLC). Purification of this residue by repeated flash chromatography with 50% ether/hexane as eluent, followed by HPLC with 15% ethyl acetate/hexane, furnished an analytically pure sample of diol 45: IR (CCl_4) 3580 cm^{-1} (OH); ^1H NMR (200 MHz, $CDCl_3$) δ 6.58 (ddd, J = 17.0, 10.9, 1.8 Hz, 1 H, C(H)=CH_2), 6.05 (m, 3 H), 5.74 (m, 1 H), 5.34 (dd, J = 17.0, 2.0 Hz, 1 H, C(H)=C(H)H), 4.95 (dd, J = 10.9, 2.0 Hz, 1 H, C(H)=C(H)H), 4.59 (d, J = 6.8 Hz, 1 H, OC(H)=), 4.33 (d, J = 6.8 Hz, 1 H, OC′(H)), 3.92 (s, 1 H), 2.92 (d, J = 7.6 Hz, 1 H, C(OH)C(H)), 2.77 (d, J = 1.8 Hz, 1 H), 1.61 (s, 3 H, CH_3), 1.48 (s, 3 H, C′H_3), 1.27 (s, 6 H, C(OH)(CH_3)$_2$); ^{13}C NMR (50 MHz, $CDCl_3$) δ 132.0, 131.6, 126.5, 123.8, 107.2, 89.0, 85.5, 83.3, 82.1, 67.0, 49.9, 29.6, 28.1, 25.6, 23.8, 23.0, 14.7; MS, m/z (relative intensity) 274 ($M^+ - H_2O$, 3). Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.82; H, 8.29. Found: C, 69.38; H, 8.34.

Aldol Condensation of Trienone 43. A THF solution of potassium hexamethyldisilazide (0.8 mL of a 1.5 M solution, 1.2 mmol) was added dropwise with stirring to a solution of trienone 43 (0.12 g, 0.9 mmol) in 4 mL of THF under an argon atmosphere at −78 °C. The dark brown reaction solution was warmed to 0 °C, poured into 5 mL of ice-cold 1 M H_3PO_4, and extracted with 3 × 20 mL of ether. The combined ether extracts were washed with brine, dried with sodium sulfate, filtered, and concentrated in vacuo. The residue was purified by flash chromatography using 20% ether/hexane as eluent to afford 27 mg (23%) of aldol product 46 as a pale yellow oil: IR (CCl_4) 3510 (OH), 1745 (C=O) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.27–5.8 (m, 8 H), 5.68 (dd, J = 7.0, 0.7 Hz, 1 H, C(H)=C(H)), 5.53 (dd, J = 7.0, 2.3 Hz, 1 H, C(H)=C(H)), 5.23 (dd, J = 6.1, 2.7 Hz, 1 H, C′(H)=C′(H)), 5.14 (ddd, J = 6.2, 2.7, 0.4 Hz, 1 H, =C′(H)), 3.38 (dd, J = 7.7, 2.7 Hz, 1 H, C(H)C(OH)), 3.34 (s, 1 H, OH), 3.20 (dd, J = 7.8, 2.0 Hz, 1 H, COC(H)), 2.82 (dd, J = 7.5, 2.7 Hz, 1 H, C′(H)C(OH)); MS, m/z (relative intensity (CI)), 265 (M^+ + 1, 45), 264 (M^+, 15), 247 (M^+ − OH, 100).

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Steric Inhibition of Photochemical Reactions: The [2 + 2]-Cycloaddition Reaction

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Photochemical [2 + 2]-cycloaddition reactions of a number of diphenylcycloalkenes to tetrachloroethylene (TCE) have been examined. 1,2-Diphenylcyclobutene (1) reacts efficiently with TCE to yield the cyclobutane anticipated for a [2 + 2]-photocycloaddition reaction. In contrast, 1,2-diphenyl-3,3,4,4-tetramethylcyclobutene (**1TM**), 1,2-diphenylcyclopentene (2), and 1,2-diphenylcyclohexene (3) yield only phenanthrene products. Photochemical quantum yields have been determined for all four reactions. For 1 and **1TM**, excited-state lifetimes have been measured as a function of the concentration of added TCE and 2,5-dimethyl-2,4-hexadiene (DMHD). The observed data indicate that the methyl groups in **1TM** effectively inhibit the interaction of possible [2 + 2]-reactants with the **1TM*** excited state.

Steric effects are a well-known and widely investigated phenomenon in ground-state chemistry. Unequivocal observations of the same effects in excited-state chemistry are, however, rare.[1] This is mainly due to the large number of mechanisms by which excited-state energy can be dissipated. In our current investigation of the photochemical and photophysical properties of sterically modified stilbenes,[2,3] we have now found an example that clearly demonstrates steric hindrance in photochemical [2 + 2]-cycloaddition reactions of olefins.

1,2-Diphenylcyclobutene (1) is a model *cis*-stilbene where the four-membered ring strongly limits twisting of the central double bond. Contrary to sterically less constrained stilbenes, the first excited singlet state of 1 cannot relax into a "perpendicular" geometry where the p orbitals of the central double bond form an angle of about 90°.[4-12] The stabilization of the "planar" excited state through the steric constraint of the cyclobutene ring leads to unusual photochemical behavior for 1. Irradiation under high dilution conditions in solvents like hexane[13] or acetonitrile[14] leads to a ring cleavage reaction (eq 1). In the presence of appropriate substrates, however, 1 undergoes efficient photoinduced [2 + 2]-cycloaddition reactions as shown in eq 2.[3,13-15] The first step of this reaction is most likely

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