Cobalt-Based Route to Highly Functionalized Hydrazulenes

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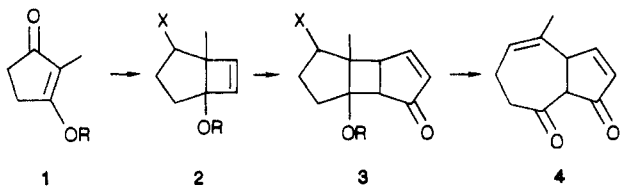
Utilization of a highly stereo- and regioselective $Co_2(CO)_8$-mediated cyclopentenone synthesis allows preparation of the versatile, highly functionalized tricyclic enone **3c** in four steps from 2-methyl-3-methoxy-2-cyclopentenone (**1**). This is, in turn, the key intermediate in both the synthesis of hydrazulenic dione **14** (seven steps from **1**, 27% overall yield) bearing a pseudoguaianolide-type substitution pattern and the synthesis of hydrazulenic ketone **28b** (ten steps from **1**, 17% overall yield) bearing a guaianolide-type substitution arrangement. Both systems possess sufficient functionality to be potentially well-suited for application in natural product synthesis.

Introduction

The many members of the guaianolide and pseudoguaianolide families of hydrazulenic natural products have been the objects of attention of synthetic chemists for many years.[1] As part of a program to explore the applicability of the Pauson–Khand reaction[2] to the synthesis of complex polycyclics, we have investigated its use in incorporating several types of alkenes as the seven-membered ring in a hydrazulene system. Cycloheptene itself is reactive in the Pauson–Khand process at elevated temperature (120 °C), although the yields of hydrazulenes are on the low side.[3] We envisioned that any of a number of strained bicyclic alkenes might serve effectively as the synthetic equivalents of cycloheptenes in the cyclization process. We recently reported the first such alkenes, derivatives of 8-oxabicyclo[3.2.1]oct-6-ene, which give rise to a variety of highly functionalized tricyclic cyclopentenones upon submission to Pauson–Khand cyclization conditions [$Co_2(CO)_8$, various alkynes, 60 °C, inert solvent].[4] Herein we describe the synthesis of a suitably substituted and functionalized bicyclo[3.2.0]hept-6-ene system that shows considerable promise as a precursor, via Pauson–Khand cycloaddition, for the synthesis of natural products in both the guaianolide and pseudoguaianolide families.

Scheme I



1 2 3 4

Results and Discussion

The general strategy we chose to explore is outlined in Scheme I. Starting with a suitable derivative (**1**) of 2-methyl-1,3-cyclopentanedione, we envisioned preparation of a bicyclic alkene **2** that would possess two key elements: a strained double bond, to impart useful Pauson–Khand-type reactivity,[2] and appropriate substitution to allow subsequent opening of an internal cyclobutane bond in the subsequent adduct **3**, revealing the seven-membered ring of the hydrazulene skeleton. Although tricyclics such as **3** have been prepared and used as hydrazulene precursors in the past,[5] the particular approach shown appeared to offer the opportunity to incorporate considerably more functionality at an early stage than had been achieved before. Thus the final product **4** possesses in the seven-membered ring methyl substitution in the proper place as well as functionality at two of the three carbons typically found in oxidized form in the naturally occurring systems. In addition, an enone is already present in the five-membered ring, potentially allowing greater flexibility in subsequent manipulations. Key questions at this stage include choice of approach to the bicyclic alkene, the likelihood of obtaining the desired regiochemistry in the cyclopentenone-forming cycloaddition step, and the nature of the fragmentation to be chosen for final ring-opening.

Syntheses and Cycloadditions of Bicyclo[3.2.0]-hept-6-enes. In choosing the specific systems to approach within the general confines of Scheme I, we considered first systems in which the R group could be readily removed in **3**, forming an alkoxide. Ample precedent existed for Grob-type fragmentations initiated in this way with R = H, Ac, and Me_3Si and X = halide or sulfonate.[5a,b,6] We therefore began with an investigation of the conversion of **1** (R = Ac and Me_3Si) into **2** via photochemical means. Although substituted alkynes typically give [2 + 2] pho-

(1) (a) Marshall, J. A.; Snyder, W. R. *J. Org. Chem.* **1975**, *40*, 1656. (b) Kretchmer, R. A.; Thompson, W. J. *J. Am. Chem. Soc.* **1976**, *98*, 3379. (c) Marshall, J. A.; Ellison, R. H. *J. Am. Chem. Soc.* **1976**, *98*, 4312. (d) Grieco, P. A.; Ohfune, Y.; Majetich, G. *J. Am. Chem. Soc.* **1977**, *99*, 7393. (e) Lansbury, P. T.; Serelis, A. K. *Tetrahedron Lett.* **1978**, 1909. (f) Semmelhack, M. F.; Yamashita, A.; Tomesch, J. C.; Hirotsu, K. *J. Am. Chem. Soc.* **1978**, *100*, 5565. (g) Ohfune, Y.; Grieco, P. A.; Wang, C.-L. J.; Majetich, G. *J. Am. Chem. Soc.* **1978**, *100*, 5946. (h) Wender, P. A.; Eissenstat, M. A.; Filosa, M. P. *J. Am. Chem. Soc.* **1979**, *101*, 2196. (i) Grieco, P. A.; Ohfune, Y.; Majetich, G. *J. Org. Chem.* **1979**, *44*, 3092. (j) Roberts, M. R.; Schlessinger, R. H. *J. Am. Chem. Soc.* **1979**, *101*, 7626. (k) Quallich, G. J.; Schlessinger, R. H. *J. Am. Chem. Soc.* **1979**, *101*, 7927. (l) Lansbury, P. T.; Hangauer, D. G., Jr.; Vacca, J. P. *J. Am. Chem. Soc.* **1980**, *102*, 3964. (m) Greene, A. E. *J. Am. Chem. Soc.* **1980**, *102*, 5337. (n) Posner, G. H.; Babiak, K. A.; Loomis, G. L.; Frazee, W. J.; Mittal, R. D.; Karle, I. L. *J. Am. Chem. Soc.* **1980**, *102*, 7498. (o) Ziegler, F. E.; Fang, J. M. *J. Org. Chem.* **1981**, *46*, 825. (p) Grieco, P. A.; Majetich, G. F.; Ohfune, Y. *J. Am. Chem. Soc.* **1982**, *104*, 4226. (q) Heathcock, C. H.; Del Mar, E. G.; Graham, S. L. *J. Am. Chem. Soc.* **1982**, *104*, 1907. (r) Heathcock, C. H.; Tice, C. M.; Germroth, T. C. *J. Am. Chem. Soc.* **1982**, *104*, 6081. (s) Rigby, J. H.; Wilson, J. Z. *J. Am. Chem. Soc.* **1984**, *106*, 8217. (t) Lansbury, P. T.; Mazur, D. J.; Springer, J. P. *J. Org. Chem.* **1985**, *50*, 1632. (u) Hudlicky, T.; Govindan, S. V.; Frazier, J. O. *J. Org. Chem.* **1985**, *50*, 4166. (v) Saha, M.; Muchmore, S.; van der Helm, D.; Nicholas, K. M. *J. Org. Chem.* **1986**, *51*, 1960. See also: Heathcock, C. H.; Graham, S. C.; Pirrung, M. C.; Plavac, F.; White, C. T. In *The Total Synthesis of Natural Products*; ApSimon, J., Ed.; Wiley: New York, 1983; Vol. 5, pp 1–541.

(2) General references for the Pauson–Khand reaction: (a) Khand, I. U.; Knox, G. R.; Pauson, P. L.; Watts, W. E.; Foreman, M. I. *J. Chem. Soc., Perkin Trans. 1* **1973**, 977. (b) Pauson, P. L.; Khand, I. U. *Ann. N.Y. Acad. Sci.* **1977**, *295*, 2. (c) Pauson, P. L. *Tetrahedron* **1985**, *41*, 5855.

(3) Alkynes react with cycloheptene and $Co_2(CO)_8$ to give hydrazulenones as follows: PhC≡CH (which tends to give higher than usual yields), 41%; MeC≡CH, 17%; PhC≡CPh, 7%; and HC≡CCMe=CH_2, 5%: Khand, I. U.; Pauson, P. L. *J. Chem. Res., Miniprint* **1977**, 0168.

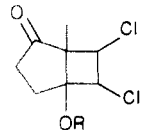
(4) La Belle, B. E.; Knudsen, M. J.; Olmstead, M. M.; Hope, H.; Yanuck, M. D.; Schore, N. E. *J. Org. Chem.* **1985**, *50*, 5215.

(5) E.g. (a) Challand, B. D.; Hikino, H.; Kornis, G.; Lange, G.; de Mayo, P. *J. Org. Chem.* **1969**, *34*, 794. (b) Liu, H. J. *Synth. Commun.* **1974**, 237. (c) Tietze, L.-F.; Reichert, U. *Angew. Chem. Int. Ed., Engl.* **1980**, *19*, 830; (d) Oppolzer, W.; Wylie, R. D. *Helv. Chim. Acta* **1980**, *63*, 1198; (e) Devreese, A. A.; Demuynck, M.; De Clercq, P. J.; Vandewalle, M. *Tetrahedron* **1983**, *39*, 3039, 3049.

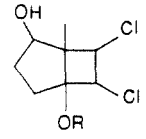
(6) Corey, E. J.; Mitra, R. B.; Uda, H. *J. Am. Chem. Soc.* **1964**, *86*, 485.

0022-3263/87/1952-3595$01.50/0

toadducts with enones[7] and isolated examples of success with ethyne itself are reported,[8] incidents of either failure[9] or anomalous results[5a] in such processes convinced us that an equivalent sequence based on the work of Cargill[10] would be more likely to serve our purpose and be simpler experimentally as well. Thus, photolysis of either **1** (R = Ac[5a] or Me_3Si[11]) in the presence of *trans*-1,2-dichloroethylene gave adducts **5a** and **5b**, which were immediately subjected to reduction to the corresponding alcohols **6a** ($NaBH_4$) and **6b** (LAH) in overall yields of 88% and 59%, respectively. Unfortunately, attempts to dechlorinate either system met with only partial success. Treatment of **6a** with either NaI/acetone, $AgNO_3/Et_3N/CH_3CN$, or $Zn/ZnCl_2$/MeOH returned starting material. Reaction with Zn(Cu)/MeOH led to partial conversion to **2a** (R = Ac; X = OH), but attempts to drive the process to completion also caused loss of the acetate, presumably by transesterification. Similarly, we found it impossible to dechlorinate **6b** under conditions that would leave the silyl ether intact.[12] Since the integrity of the OR group had to be maintained at least until cyclization to form **3** was achieved, we turned to the methyl ether to provide the needed stability in these early steps.



5a, R = Ac
5b, R = Me_3Si



6a, R = Ac
6b, R = Me_3Si

Photocycloaddition of *trans*-1,2-dichloroethylene to the O-methyl derivative of 2-methyl-1,3-cyclopentanedione followed by immediate reduction with $NaBH_4$ gives an 83% yield of a mixture of stereoisomeric alcohols. Provided that *strict* control of the temperature of the reduction is maintained (≤0 °C), only products with *endo*-hydroxyl groups are obtained. The major product, representing about 75% of the mixture, was assigned structure **6c**, and the only other significant component was assigned structure **6d** on the basis of the following ^1H NMR evidence. In both molecules the hydroxyl and C-2 methine protons showed coupling (J = 9.9 and 11.5 Hz, respectively) at all but the highest concentrations in $CDCl_3$, indicative of a comparatively hindered environment and slow intermolecular exchange (vide infra). Relative stereochemistries of the Cl substituents were inferred from the vicinal couplings between the C-6 and C-7 hydrogens: 6.5 Hz in **6c** and 9.8 Hz in **6d**.[13] Finally, the presence of long-range ("W-type") coupling between the proton on C-6 and the exo proton on C-4 in **6d**, but not in **6c**, suggested the C-5/C-6 relationships shown. Additional support for these assignments was obtained through the isolation of an exo alcohol in up to 20% yield when strict temperature control in the reduction was not maintained. In this case no coupling between the hydroxyl and C-2 methine was seen under any circumstances. At this point dechlorination

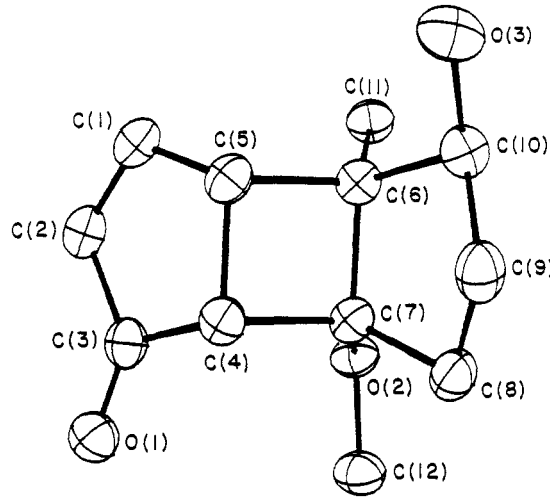
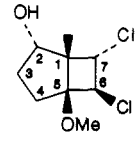
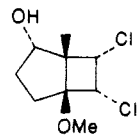


Figure 1. Representation of compound **3c** using 50% thermal ellipsoids.

was achieved readily by submitting **6c/d** to treatment with the reagent derived from adding Na to naphthalene in 1,2-dimethoxyethane (DME) ("sodium dihydronaphthalide"[14]). As expected, the methyl ether survived this procedure and a single product, **2c** (R = Me, X = *endo*-OH), was obtained in 73% yield. Thus the substrate for the key reaction, cycloaddition to a tricyclic enone **3c** (R = Me, X = *endo*-OH), was available in three steps and a 61% overall yeild.

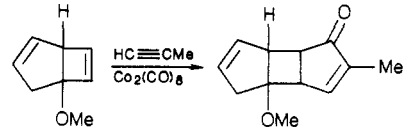


6c



6d

As early as 1977 Pauson's group had demonstrated the suitability of bicyclo[3.2.0]hept-6-enes as cyclization substrates.[15] However, in the cases most closely related to ours, the regiochemical outcome appeared to be exactly the opposite of what we required (e.g., eq 1). Careful



(1)

NMR analyses of the products of several reactions conclusively established an anti disposition of the enone carbonyl and the ring-fusion methoxyl group as the only product of cyclization. At the time it was impossible to evaluate the relative importance of possible electronic, steric, or intramolecular coordination effects in contributing to this result. Given these uncertainties, we attempted the cycloaddition reaction of **2c** in the presence of $Co_2(CO)_8$ in DME under an acetylene/CO atmosphere, obtaining after 3 days at 65 °C a product mixture consisting of a small amount of the cyclopentadienone Diels–Alder dimer[16] together with a 65–85% yield of a single crystalline ketone analyzing correctly for the expected cyclization product. Both NMR and IR confirmed the presence of the cyclopentenone moiety and the tolerance of the free secondary hydroxyl to the procedure: as

(7) E.g. (a) Criegee, R.; Furrer, H. *Chem. Ber.* **1964**, *97*, 2949. (b) Cargill, R. L.; Beckham, M. E.; Siebert, A. E.; Dorn, J. *J. Org. Chem.* **1965**, *30*, 3647. (c) Hanifin, J. W.; Cohen, E. *J. Am. Chem. Soc.* **1969**, *91*, 4494.

(8) E.g. Sunder-Plassman, P.; Nelson, P. H.; Boyle, P. H.; Cruz, A.; Iriarte, J.; Crabbé, P.; Zderic, J. A.; Edwards, J. A.; Fried, J. H. *J. Org. Chem.* **1969**, *34*, 3779.

(9) Owsley, D. C.; Bloomfield, J. J. *J. Chem. Soc. C* **1971**, 3445.

(10) Cargill, R. L.; Crawford, J. W. *J. Org. Chem.* **1970**, *35*, 356.

(11) Torkelson, S.; Ainsworth, C. *Synthesis* **1976**, 722.

(12) The corresponding dibromo compound, which might have been easier to dehalogenate, was inaccessible via photolysis of **1** in the presence of 1,2-dibromoethylene.

(13) Typically J_{vic}(cis) > J_{vic}(trans) in 1,2-disubstituted cyclobutanes: Servis, K. L.; Roberts, J. D. *J. Phys. Chem.* **1963**, *67*, 2885.

(14) Scouten, C. G.; Barton, F. E., Jr.; Burgess, J. R.; Story, P. R.; Garst, J. F. *J. Chem. Soc., D* **1969**, 78.

(15) Bladon, P.; Khand, I. U.; Pauson, P. L. *J. Chem. Res., Miniprint* **1977**, 0153.

(16) Schore, N. E.; LaBelle, B. E.; Kundsen, M. J.; Hope, H.; Xu, X.-J. *J. Organomet. Chem.* **1984**, *272*, 435.

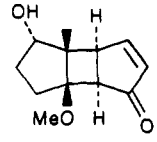
Table I. Proton NMR Spectral Data for Ketones 3[a]

	3a[b]	3b[c]	3c[c]
H-5	7.65 (3.0, 5.0)	7.68 (3.4, 5.5)	7.68 (3.2, 5.6)
H-4	6.40 (5.0)	6.47 (5.5)	6.42 (1.0, 5.6)
H-8_{exo}	4.00 (m)	4.95 (6.5, 10.5)	4.00 (4.2, 6.5, 10.1)
H-6	3.25 (m)	3.27 (3.4, 5.1)	3.22 (1.0, 3.2, 5.0)
H-2	*d*	3.01 (5.1)	2.78 (5.0)
Me-7	1.00 (s)	0.99 (s)	1.00 (s)

[a] $CDCl_3$ solvent. Chemical shifts are followed by coupling constants in parentheses. [b] 90 MHz. [c] 360 MHz. [d] Part of unresolved signal envelope.

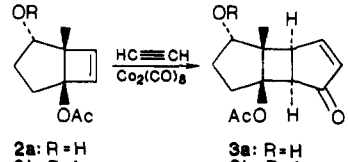
was the case for **2c**, the hydroxyl proton appeared in the ^1H NMR as a sharp doublet at δ 2.31, coupled to the adjacent methine hydrogen with J = 4.2 Hz. Due, however, to the presence of a ring fusion with two adjacent quaternary centers, it was not possible to unequivocally establish the all-important regiochemical outcome of the cyclization by spectroscopic analysis alone. To this end, therefore, an X-ray crystallographic determination was carried out.

Crystals of **3c** suitable for X-ray were readily obtained and were found to be monoclinic with a = 12.261 (3), b = 7.525 (1), and c = 12.699 (3) Å. Data collection was carried out at 140 K. The structure was solved by direct methods and refined to R = 0.043. The result (Figure 1), remarkably enough, shows that the regiochemical outcome of the cyclization of **2c** is exactly the opposite of that observed in the Pauson system with respect to the methoxyl and carbonyl groups. Especially noteworthy is the fact that both of these reactions appear to be totally regioselective. Not a trace of any other regio- or stereoisomer of **3c** was detected in cyclizations of **2c**. Rationalizations of the regio- and stereochemical preferences in the Pauson–Khand reaction have recently been presented elsewhere,[4,17] and it is now clear that steric effects are of the greatest importance. In the case of **2c** it appears that the presence of the angular methyl group is the distinguishing factor in reversing the direction of cycloaddition with respect to the Pauson system: both results place the larger allylic substituent anti to the cyclopentanone carbonyl. Unlike results with other bicyclic substrates,[4] however, this is the first instance where total regioselectivity has been observed.



3c

The generality of this effect has been confirmed in cyclization experiments on alkenes derived from **6a**. Thus both **2a** and **2b** cyclize with acetylene in the presence of $Co_2(CO)_8$ to give single regioisomeric enones, whose NMR spectra are virtually identical in all relevant respects with that of **3c** (Table I). We therefore assume that these products have the same regiochemistry with respect to cyclopentenone annelation (eq 2).



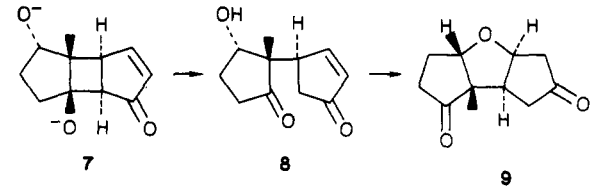
(2)

2a: R = H
2b: R = Ac

3a: R = H
3b: R = Ac

(17) (a) Magnus, P.; Principe, L. M. *Tetrahedron Lett.* **1985**, *26*, 4851. (b) Magnus, P.; Exon, C.; Albaugh-Robertson, P. *Tetrahedron* **1985**, *41*, 5861.

Scheme II



7 **8** **9**

Having established the feasibility of selective synthesis of these tricyclics, it became possible to consider the development of routes from **3c** toward various hydrazulenoid natural products.

Controlled Fragmentation of 3c: An Approach toward Pseudoguaianolides. Given the problems uncovered in the preparations of **3a** and **3b**, methyl ether **3c** was the logical choice for further study. Upon inspection of the system, it is clear that successful fragmentation of the internal cyclobutane bond (cf. Scheme I) requires application of a sequence that will turn the 2° hydroxyl into a leaving group and cleave the methyl ether linkage. However, the additional functionality in the remaining five-membered ring introduces a complication that was absent in other related syntheses, namely, the risk of unwanted cleavage of an external cyclobutane bound in a retro-aldol manner. Reasoning initially (and, as it turned out, quite incorrectly) that cleavage of the methyl ether would require attack by a relatively good nucleophile, we carried out several reactions on **3c** with reagents capable of supplying halide in a Lewis acidic medium. The results with $NaI/Me_3SiCl/CH_3CN$[18] (followed by F^-) were typical: the enone was completely consumed with 2 h at room temperature, leading to a single major product in nearly quantitative yield. This crystalline material lacked a methoxy signal in the ^1H NMR but also displayed no olefinic signals and a single carbonyl absorption in the IR at 1740 cm^{-1}, characteristic of a *saturated* cyclopentanone. The extreme complexity of the NMR spectrum prevented assignment of a structure to this product, necessitating again the use of X-ray diffraction. The result[19] (Scheme II, compound **9**) is quite an unusual system, an *oxa* triquinane structure.

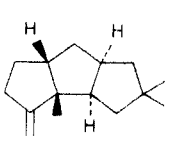
This ring system has appeared only twice before in the literature,[20] having been derived in low yield from either cationic or pyrolytic transformations of bis(cyclopentenyl) ethers. In light of recent interest in linearly fused triquinane natural products in general,[21] it is intriguing to note the points of similarity between **9** and members of the hirsutane class of sesquiterpenes, notably hirsutene itself (**10**) and the antitumor agent coriolin (**11**). In particular, the three compounds show striking parallels in the locations of substitution and functionality; thus the ease of access to the ring system in **9** makes its derivatives attractive targets for further synthetic study. Whether the structural similarities might extend to biological activity, e.g., of an oxa analogue of coriolin, remains to be determined. One is reminded, however, of the comparability of biological activities between the prostacyclins and their carba analogues.[22]

(18) Olah, G. A.; Narang, S. C.; Gupta, B. G. B.; Malhotra, R. *J. Org. Chem.* **1979**, *44*, 1247.

(19) Olmstead, M. M., unpublished results.

(20) Levina, R. Y.; Tantsyreva, T. I.; Vinogradova, V. N.; Treschova, E. G. *Dok. Akad. Nauk. SSSR* **1952**, *85*, 107. Alder, K.; Flock, F. H. *Chem. Ber.* **1956**, *89*, 1732.

(21) E.g., see: Paquette, L. A. *Top. Curr. Chem.* **1979**, *79*, 41; **1984**, *119*, 1.



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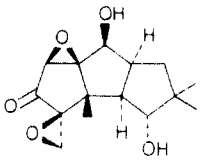


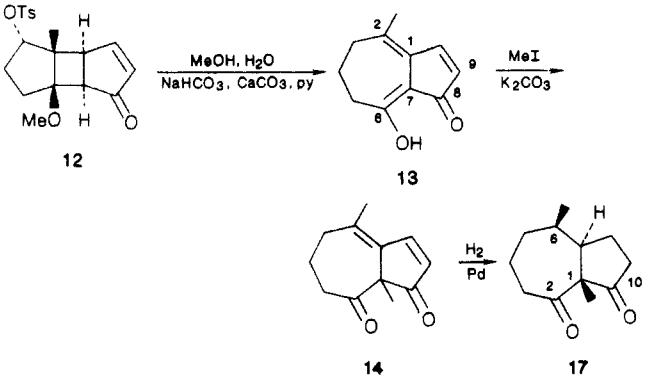
11

The origin of **9** clearly lies in precisely the retro-aldol process that we had hoped to avoid. Thus, instead of converting the 2° alcohol to an iodide, we presume that the reagent mixture converted **3c** to a bis(trimethylsilyl) ether, which upon treatment with fluoride produced an intermediate, perhaps **7**, set up to open only to bis(cyclopentyl) system **8**. Internal Michael addition would then complete the transformation to **9**. These results imply that enones of the general structure **3** are not compatible with acid and, indeed, this has been found to be the case. Direct support for the intermediacy of **8** in the above process comes from the observation by NMR of analogous products in similar ring-opening reactions where subsequent closure of the ether ring is prevented (vide infra).

Given this situation, it appeared that a more fruitful approach would involve initial conversion of the secondary alcohol into a leaving group under neutral conditions. The tosylate of **3c** was therefore prepared (**12**), but it was found to again open in the retro-aldol sense upon treatment with the $NaI/Me_3SiCl/CH_3CN$ reagent. The product mixture thus obtained appeared by NMR and IR to contain the tosylate corresponding to **8** together with a second enone tosylate, most likely the isomeric 2-cyclopentenone with the trisubstituted double bond. At this point the need to find conditions that would favor initial loss of the tosylate group was clear. We therefore initiated a series of experiments aimed at determining optimal conditions for solvolysis of this system. Reflux of a methanol solution of **12** was found to slowly give rise to the same products as those described above. Reasoning that this result might be a consequence of the liberation of free *p*-toluenesulfonic acid from the desired solvolysis process, we explored a number of sets of buffered conditions. It was thus empirically found that complete solvolysis of **12** leading to the cleavage of the required internal cyclobutane bond could be achieved by extended reflux in methanol containing small amounts of pyridine, aqueous $NaHCO_3$, and solid $CaCO_3$. With this recipe it proved possible to reproducibly obtain high (ca. 90%) yields of conjugated dienone **13** as a yellow oil. This material has an extremely simple proton NMR, an apparent consequence of the fact that, being totally enolic, it is on the average a planar molecule. Application of Woodward's rules[23] to the tautomer shown leads to a predicted λ_{max} of 348 nm in the ultraviolet, which compares favorably with the actual spectrum of the compound, which shows peaks at λ_{max} 226, 275, and 349 nm.

Finally, alkylation of **13** at the ring fusion with iodomethane gives rise in high yield to **14**, containing the requisite features necessary to serve as a pseudoguaianolide precursor (Scheme III). Characterization of **14** as the conjugated dienone shown is supported by the presence of a UV absorption at 295 nm (calculated[23] λ_{max} 291 nm). The overall yield in the seven steps from **1** (R = Me) to

Scheme III



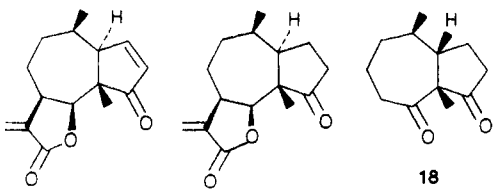
12 13 14 17

Table II. Carbon NMR Spectral Data of Hydrazulenediones[a]

	17[b]	18[c]
C-1	51.6	52.8
C-2 (7-ring C=O)	208.1	*d*
C-3	42.6	40.4
C-4	29.8	26.5
C-5, C-8	23.0, 24.8	23.5, 23.9
C-6	31.0	32.1
C-7, C-9	33.9, 37.5	37.8, 38.4
C-10 (5-ring C=O)	216.5	*d*
CH_3 groups	19.8, 21.0	both 21.5

[a] $CDCl_3$ solvent, room temperature. [b] This work. [c] Reference 1r. [d] Value not given.

14 is a remarkable 27% (calculated by using the 65% yield figure for the cobalt cyclization reaction). This dione possesses an array of functionality that should be well-suited for conversion to systems such as ambrosin (**15**) and damsin (**16**)[1a,d,k] via alkylation α to the saturated ketone. We have found in a preliminary study that catalytic hydrogenation of **14** leads to a single major product. We assign to it structure **17** primarily on the basis of its proton and carbon NMR spectra, which are similar but not identical with that of **18**[1r] (Table II), and the expectation of hydrogenation being directed by the angular methyl group primarily to the opposite face of the molecule.



15 16 18

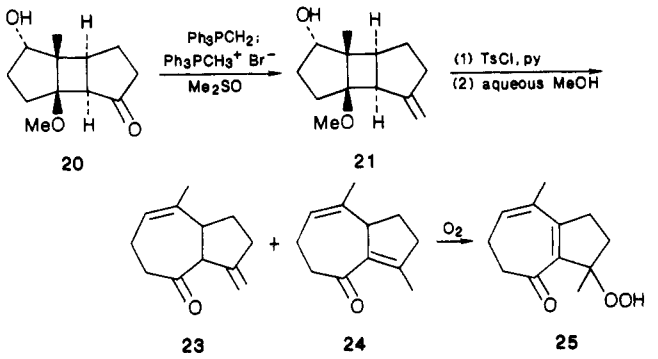
Reversing the Sequence: An Approach toward Guaianolides. The guaianolides possess a one-carbon substituent on the five-membered ring instead of at the ring fusion. This, in principle, may be readily accommodated by introducing nucleophilic carbon at the enone carbonyl of **3c** *prior* to fragmentation, instead of adding electrophilic carbon after ring opening, as was appropriate to the pseudoguaianolide approach above. Having in mind the type of functionality array exemplified by the natural product eremanthrin (**19**),[24] the enone was subjected to catalytic hydrogenation to give **20**, in preparation for

(22) Morton, D. R., Jr.; Brocaw, F. C. *J. Org. Chem.* **1979**, *44*, 2880. See also: Nicolaou, K. C.; Magolda, R. L.; Claremon, D. A. *J. Am. Chem. Soc.* **1980**, *102*, 1404. Johnson, R. A.; Lincoln, F. H.; Nidy, E. G.; Schneider, W. P.; Thompson, J. L.; Axen, U. *J. Am. Chem. Soc.* **1978**, *100*, 7690.

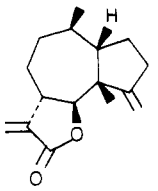
(23) Woodward, R. B. *J. Am. Chem. Soc.* **1941**, *63*, 1123; **1942**, *64*, 72, 76.

(24) (a) Baker, P. M.; Fortes, C. C.; Fortes, E. G.; Gassinelli, G.; Gilbert, B.; Lopes, J. N. C.; Pelligrino, J.; Tomassini, T.; Vichnewski, W. *J. Pharm. Pharmacol.* **1972**, *24*, 853. (b) Corbella, A.; Gariboldi, P.; Jommi, G.; Orsiui, F.; Ferrari, G. *Phytochemistry* **1974**, *13*, 459. (c) Vichnewski, W.; Sarti, S. J.; Gilbert, B.; Herz, W. *Phytochemistry* **1976**, *15*, 191. (d) Herz, W.; Kumar, N.; Vichnewski, W.; Blount, J. F. *J. Org. Chem.* **1980**, *45*, 2503.

Scheme IV



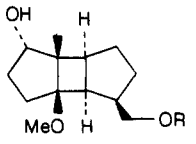
Wittig methylenation. Initial attempts to accomplish the latter by using KCH_2SOCH_3 as the base gave only poor yields of the expected product, returning considerable amounts of starting material. Assuming that competing enolization was occurring, several alternatives were tried, including a "cycling" procedure (adding alternating portions of ylide and water to the ketone),[25] other bases (e.g., *tert*-amylate in toluene[26]), and Peterson olefination,[27] all with similar results. A solution to this problem was found in the use of a very large ratio of ylide to ketone in the presence of a small *additional* excess of *free phosphonium salt* which, we presume, allows continuous equilibrium reprotonation of enolate as the reaction proceeds. In this way yields of **21** were raised from the 25–50% range to nearly 90%.



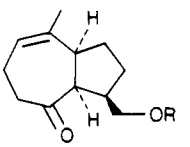
19

On the basis of the results of ring-opening attempts on **3c**, the tosylate (**22**) of **21** was prepared and conditions for solvolysis explored. In this case the use of a buffered system proved to be unsuitable. Instead, simple reflux of **22** in CD_3OH/D_2O (monitored by ^1H NMR) led to replacement of the original methyl signal at δ 0.80 with a new one at δ 1.63 and simultaneous appearance of a new vinyl absorption at δ 5.5 (δ 5.31 in C_6D_6). Isolation of the product on a preparative scale gave a mixture (three materials with m/z 176 by GC-MS) with the major component having a single vinyl hydrogen and two allylic methyl groups by ^1H NMR and a carbonyl stretch in the IR at 1675 cm^{-1}, strongly suggestive of enone **24**, a result of double-bond isomerization. This substance was found to deposit large crystals over a period of several days in which the vinyl region of the ^1H NMR had simplified to a triplet at δ 6.26 (J = 6.6 Hz). Due to certain peculiarities of the NMR spectrum, which included an enigmatic one-proton singlet at δ 9.84, an X-ray structure determination was carried out,[28] revealing the hydroperoxy dienone structure **25**, no doubt the O_2 trapping product of the radical obtained by hydrogen abstraction from the bis-allylic position in **24**. Subsequent solvolysis experiments showed that rigorous exclusion of air prevented peroxide formation but that double-bond migration (**23** → **24**) could not be stopped (Scheme IV). In order to preserve the functionality array in **23** protection of the double bond prior to ring opening was deemed necessary.

Hydroboration of **21** with either $BH_3{\cdot}SMe_2$ at 0 °C or 9-BBN at room temperature gives a single diol (**26**), the primary alcohol of which may be selectively protected with either *t*-$BuMe_2SiCl$ or *t*-$BuPh_2SiCl$ in the presence of catalytic 4-(dimethylamino)pyridine (DMAP) in Et_3N/CH_2Cl_2.[29,30] Both products, **27a** and **27b**, were subjected to the same tosylation/solvolysis sequence established for **21**. In the case of **27a**, near-total loss of the silyl group was observed under unbuffered conditions. Use of conditions similar to those established for **12** allowed isolation of a mixture of the protected hydrazulenone **28a** together with varying amounts of the free alcohol **28c**. Treatment of the crude mixture with *t*-$BuMe_2SiCl$/DMF/imidazole permitted isolation of **28a** in overall yields of up to ca. 45%. As expected, the presence of the more stable protecting group[31] in **27b** proved to be advantageous in that the solvolysis could be carried out much more cleanly under buffered conditions, giving a 76% yield of ketone **28b**, without any observable cleavage of the silyl ether. The assumption that the cis ring fusion is retained under these conditions is supported by the chemical shift of the ring fusion proton α to the carbonyl in each of these ketones: δ 2.98 for **28a** and δ 3.09 for **28b**. In an NMR study of several 4-ketohydrazulenes House and co-workers[32] found that the signal for this proton in the cis series typically falls well downfield (i.e., δ 3.0–3.2) of that in the trans series (δ 2.5–2.8).



26, R = H
27a, R = $SiMe_2$-*t*-Bu
27b, R = $SiPh_2$-*t*-Bu

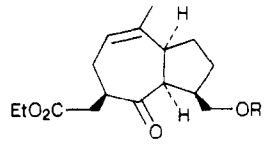


28a, R = $SiMe_2$-*t*-Bu
28b, R = $SiPh_2$-*t*-Bu
28c, R = H

The six-step sequence from cobalt cyclization product **3c** affords **28b** in an overall yield of 43%; thus from the beginning (**1**), this protected ketone is available in 10 steps and a 17% overall yield. The additional manipulations and the need for functional group protection render the approach to **28b** somewhat less efficient than that to the potential pseudoguaianolide precursor **14**. However, **28b** does contain fully differentiated functionality in an arrangement that should render it extremely useful as a guaianolide precursor. In preliminary studies of the latter point we have found that both **28a** and **28b** may be alkylated very selectively and in quite high (80–90%) yield with ethyl iodoacetate using lithium hexamethylsilazide in THF/HMPA. The conditions are those previously defined by Vandewalle and co-workers[5e] as giving rise to predominant alkylation trans to the ring fusion hydrogens in cis-fused 4-ketohydrazulenes. Indeed, in each case only a single product is formed to which we tentatively assign the structures **29a** and **29b**, respectively. We are currently attempting to obtain suitable crystalline derivatives of several of these compounds for X-ray analysis to unambiguously answer these stereochemical questions. In ad-

(25) Adlercreutz, P.; Magnusson, G. *Acta Chem. Scand., Ser. B* **1980**, 647.
(26) (a) Schow, S. R.; McMorris, T. C. *J. Org. Chem.* **1979**, *44*, 3760. (b) Smith, A. B., III; Jerris, P. J. *J. Org. Chem.* **1982**, *47*, 1845.
(27) Petersen, D. J. *J. Org. Chem.* **1968**, *33*, 780.
(28) Hope, H.; Xu, X.-J., unpublished results.
(29) Chaudhary, S. K.; Hernandez, O. *Tetrahedron Lett.* **1979**, 99.
(30) Reaction in DMF with imidazole as catalyst at 45 °C protects both alcohols; reaction at lower temperatures is selective for the primary alcohol, but yields are low.
(31) Hanessian, S.; Lavallee, P. *Can. J. Chem.* **1975**, *53*, 2975.
(32) House, H. O.; Nomura, G. S.; VanDerveer, D.; Wissinger, J. E. *J. Org. Chem.* **1986**, *51*, 2408 and references therein.

dition, an extensive study of alkylation and lactone-formation strategies has been initiated in order to evaluate the full scope of the applicability of both of these routes to natural product synthesis. The results of these studies will be reported in due course.



29a, R = $SiMe_2$-*t*-Bu
29b, R = $SiPh_2$-*t*-Bu

Experimental Section

General. Solvents. For procedures carried out under anhydrous conditions, tetrahydrofuran (THF), benzene, ether, and dimethoxyethane (DME) were vacuum distilled from sodium benzophenone ketyl and stored over 4-Å molecular sieves under argon. Isooctane, hexamethylphosphoric triamide (HMPA), pyridine, dimethylformamide (DMF), triethylamine, acetonitrile, and dimethyl sulfoxide (Me_2SO) were distilled from calcium hydride before use. Cyclohexane, carbon tetrachloride, and dichloromethane were dried over 4-Å molecular sieves.

Reagents. Literature procedures were employed for the preparations of 2-methyl-3-[(trimethylsilyl)oxy]cyclopent-2-en-1-one (1, R = Me_3Si)[11] 2-methyl-3-acetoxycyclopent-2-en-1-one (1, R = Ac),[33] and 2-methyl-3-methoxycyclopent-2-en-1-one (1, R = Me).[34] Unless otherwise noted, other reagents were obtained commercially and used without further purification. All reactions were carried out under an atmosphere of dried argon or nitrogen.

Separation and Purification. Neutral alumina (Mallinckrodt), silica gel (Baker), and Florisil (Sigma) for column chromatography were used as received. Commercially prepared silica gel columns (LiChroprep Si60, EM Reagents) were used for medium pressure liquid chromatography (MPLC) with a Waters differential refractometer detection system (Model R403). Other chromatographic separations were carried out on a Chromatotron (Harrison Research) using silica gel with calcium binder (E. Merck). Analytic thin layer chromatography was done on fluorescent indicating silica gel sheets (Merck). Iodine was used to visualize nonchromophoric bands.

Analysis. Analytical samples were purified by chromatography followed by GC using the columns and conditions indicated. Nuclear magnetic resonance spectra (^1H) were recorded on a Varian EM-390 (90 MHz) spectrometer. High field NMR spectra were recorded on a Nicolet NT-1180 360-MHz FT-NMR spectrometer. Chemical shifts are expressed in parts per million relative to tetramethylsilane (δ = 0.00) or residual chloroform in deuteriochloroform (δ 7.26 relative to Me_4Si). Listed NMR data are given in the following order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constants, and number of protons (by integrated intensity). IR spectra were recorded on a Beckman IR-8 spectrophotometer. Mass spectral data were obtained at the Facility for Advanced Instrumentation (FAI) at the University of California, Davis. Microanalyses were performed at the microanalytical laboratory facility at the University of California, Berkeley.

1-Methyl-5-acetoxy-6,7-dichlorobicyclo[3.2.0]heptan-2-ol (6a). A solution of 0.50 g (3.25 mmol) of 1 (R = Ac) in 150 mL of 1:2 *trans*-dichloroethylene–cyclohexane was irradiated by using a 450-W medium pressure Hanovia lamp for 3 h. Unreacted alkene and solvent were removed at room temperature and high vacuum (and saved for reuse), leaving 1.98 g of a semisolid mixture which was taken up in 37.5 mL of MeOH. This solution was added dropwise to a precooled (0 °C) solution of 0.369 g (9.74 mmol) of $NaBH_4$ in 30 mL of 1:5 H_2O–MeOH under N_2, and the mixture was stirred for an additional 1.5 h at 0 °C. After dilution with water (600 mL), extraction with ethyl acetate (6 × 200 mL), drying ($MgSO_4$), and removal of solvent, a pale yellow oil remained which was chromatographed (silica gel). After removal of nonpolar side products (hexane) elution with 3:1 hexane–ethyl acetate afforded 0.758 g of a mixture of stereoisomers of **6a** as a pale yellow oil (88% yield). A single major component (83% of the mixture) was collected by GC (7% FFAP, chromosorb W, AW, DMCS, 10 ft × $^1/_4$ in. 170 °C). NMR data were consistent with the *endo*-OH *trans*-dichloride stereoisomer (cf. text, structure **6c**): NMR (360 MHz, $CDCl_3$) δ 1.40 (s, 3 H), 2.00 (m, 2 H), 2.12 (s, 3 H), 2.20 (m, 1 H), 2.66 (m, 2 H), 3.96 (ddd, J = 5.9, 9.6, and 9.6 Hz, 1 H), 4.18 (d, J = 5.6 Hz, 1 H), 4.39 (d, J = 5.6 Hz, 1 H); IR ($CHCl_3$) 1735 (s), 3350–3550 (br), 3640 (sharp) cm^{-1}; high-resolution mass spectrum, calcd for $C_{10}H_{14}O_3{}^{35}Cl$ 217.0632, found 217.0614; calcd for $C_{10}H_{14}O_3{}^{37}Cl$ 219.0602, found 219.0639.

1-Methyl-5-[(trimethylsilyl)oxy]-6,7-dichlorobicyclo[3.2.0]heptan-2-ol (6b). Following the general procedure as described for **6a**, a solution of 0.372 g (2.02 mmol) of 1 (R = Me_3Si) in 150 mL of dry, Ar-purged 1:4 *trans*-1,2-dichloroethylene–cyclohexane was photolyzed for 1.75 h. The crude product was taken up in 10 mL of ether and added dropwise to a suspension of 0.10 g of $LiAlH_4$ in 5 mL of ether at 0 °C under N_2. After 2 h at 0 °C the reaction mixture was quenched with saturated Na_2SO_4 and filtered, the residue was washed with ethyl acetate, and the combined filtrates were dried (Na_2SO_4). Removal of solvent and chromatography (Florisil) gave 0.267 g of a mixture containing 78% **6b** (mixture of stereoisomers, net yield 59%) and 22% desilated material (i.e., **6** with R = H): NMR of **6b** ($CDCl_3$, 90 MHz) δ 0.1–0.3 (singlets, 9 H), 1.0–3.2 (m, 8 H), 3.7–5.0 (m, 3 H). As all attempts to use this crude material in subsequent procedures led to loss of the silyl group, no attempts at further purification were made.

1-Methyl-5-methoxy-6,7-dichlorobicyclo[3.2.0]heptan-2-ol (6c). Following the general procedure as described for **6a**, a solution of 0.307 g (2.44 mmol) of 1 (R = Me) in 160 mL of dry, Ar-purged 1:3 *trans*-1,2-dichloroethylene–cyclohexane was photolyzed for 6 h. The crude product (1.06 g) was taken up in 25 mL of MeOH and reduced with 0.277 g (7.31 mmol) of $NaBH_4$ in 30 mL of 1:5 H_2O–MeOH, again, as described for **6a**. *Strict internal temperature control (0 °C) was essential in the reduction to achieve high stereoselectivity.* Workup and purification as before afforded 0.455 g of a heavy, pale yellow oil, a 3:1 mixture of **6c** and **6d** (total yield 83%), suitable for use in all subsequent procedures. For this mixture: IR ($CHCl_3$) 3350–3550 (br), 3640 (sharp) cm^{-1}. Separation by GC (7% FFAP on Chrom W, AW, DMCS, 5 ft × $^1/_4$ in., 145 °C), gave the pure isomers, collected in the order listed below.

For **6c**, a colorless oil: NMR ($CDCl_3$, 360 MHz) δ 1.31 (s, 3 H), 1.89 (m, 3 H), 2.20 (m, 1 H), 2.75 (d, J = 9.9 Hz, 1 H), 3.38 (s, 3 H), 3.90 (m, 1 H), 4.19 (s, 2 H); NMR (C_6D_6, 360 MHz) δ 1.15 (s, 3 H), 1.27 (m, 2 H), 1.54 (m, 1 H), 1.74 (m, 1 H), 2.54 (br s, 1 H), 3.04 (s, 3 H), 3.64 (m, 1 H), 3.91 (d, J = 6.5 Hz, 1 H), 4.10 (d, J = 6.5 Hz, 1 H); high-resolution mass spectrum, calcd for $C_9H_{14}O_2{}^{35}Cl$ 189.0683, found 189.0703; calcd for $C_9H_{14}O_2{}^{37}C$ 191.0653, found 191.0670. Anal. Calcd for $C_9H_{14}O_2Cl_2$: C, 48.02; H, 6.27. Found: C, 47.76; H, 6.29.

For **6d**, a colorless oil: NMR ($CDCl_3$, 360 MHz) δ 1.31 (s, 3 H), 1.60 (m, 1 H), 2.15 (m, 2 H), 2.48 (m, 1 H), 2.53 (d, J = 11.5 Hz, 1 H), 3.20 (s, 3 H), 3.89 (m, 1 H), 4.49 (d, J = 9.8 Hz, 1 H), 4.73 (d, J = 9.8 Hz, 1 H); high-resolution mass spectrum, calcd for $C_9H_{14}O_2{}^{35}Cl$ 189.0683, found 189.0703; calcd for $C_9H_{14}O_2{}^{37}Cl$ 191.0653, found 191.0670.

When strict temperature control was not maintained in the reduction step, a third isomer was obtained with the *exo*-hydroxyl *trans*-dichloride configuration, comprising up to 20% of the product mixture: NMR ($CDCl_3$, 360 MHz) δ 1.21 (s, 3 H), 1.63 (m, 3 H), 2.12 (m, 1 H), 2.41 (m, 1 H), 3.20 (s, 3 H), 4.00 (br m, 1 H), 4.14 (d, J = 7.3 Hz, 1 H), 4.34 (dd, J = 1.0, 7.3 Hz, 1 H).

1-Methyl-5-methoxybicyclo[3.2.0]hept-6-en-*endo*-2-ol (2c). To 40 mL of dry, distilled DME was added 4.50 g (35.2 mmol) of naphthalene. After stirring at 25 °C under N_2 for 5 min, 0.370 g (16.1 mmol) of freshly cut sodium was added in small pieces over a period of 10 min. This deep bluish green mixture was stirred at 25 °C for 30 h and then treated dropwise with a solution of 0.450 g (2.00 mmol) of a mixture of **6c** and **6d** in 10 mL of DME. The mixture was stirred 30 min under N_2 and then carefully exposed to the air. After 30 min excess Na in the now reddish brown mixture was quenched by dropwise addition of MeOH

(33) Cimarusti, C. M.; Wolinsky, J. *J. Org. Chem.* **1966**, *31*, 4188.
(34) Quesada, M. L.; Schlessinger, R. H.; Parsons, W. H. *J. Org. Chem.* **1978**, *43*, 3968.

under N_2, followed by addition of 1 mL of NH_4Cl-saturated 1:1 H_2O–MeOH. After removal of solvent the product was extracted with ethyl acetate (400 mL) and dried ($MgSO_4$). After evaporation the residue was chromatographed first to remove naphthalene (silica gel, 600 mL of hexane) and then (3:1 hexane–ethyl acetate) to isolate the product, 0.226 g of a pale tan oil (73% yield). Final purification of **2c** was effected by GC (7% FFAP, Chrom W, AW, DMCS, 10 ft × $^1/_4$ in., 125 °C): IR ($CHCl_3$) 1585 (m), 3350–3550 (br), 3640 (sharp) cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.23 (s, 3 H), 1.33 (d, J = 5.7 Hz, 1 H), 1.43 (m, 2 H), 1.77 (m, 1 H), 1.98 (m, 1 H), 3.34 (s, 3 H), 3.67 (m, 1 H), 6.26 (d, J = 3.0 Hz, 1 H), 6.30 (d, J = 3.0 Hz, 1 H); high resolution mass spectrum, calcd for $C_9H_{14}O_2$ 154.0994, found 154.0997. Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.85; H, 9.04.

***cis*,*anti*,*cis*-1-Methoxy-7-methyl-*endo*-8-hydroxytricyclo[5.3.0.0^{2,6}]dec-4-en-3-one (3c).** To 20 mL of dry DME under N_2 was added 0.250 g (0.719 mmol) of $Co_2(CO)_8$, and the solution was then stirred under an acetylene atmosphere for 1 h at 25 °C. The formation of the acetylenehexacarbonylcobalt complex was accompanied by vigorous gas (CO) evolution and a color change from yellowish brown to reddish violet. A solution of 0.154 g (1.00 mmol) of **2c** in 5 mL of DME was added and the mixture heated to 60–65 °C for 4 days under an atmosphere of CO and acetylene. After cooling and removal of solvent, the residue was precoated on silica gel and chromatographed. Hexane elution removed residual organometallics and 1:1 hexane/ether eluted a small amount of the cyclopentadienone Diels–Alder dimer.[16] Upon further elution 0.135 g (65% yield) of ketone **3c** was isolated as a white crystalline solid: mp 136.0–136.5 °C; IR ($CHCl_3$) 1690–1705 (vs), 3350–3550 (br) cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.00 (s, 3 H), 1.66 (m, 2 H), 2.06 (m, 2 H), 2.31 (d, J = 4.2 Hz, 1 H), 2.78 (d, J = 5.0 Hz, 1 H), 3.22 (m, 1 H), 3.30 (s, 3 H), 4.00 (m, 1 H), 6.42 (dd, J = 1.0, 5.6 Hz, 1 H), 7.68 (dd, J = 3.2, 5.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 25.1 MHz) δ 15.7, 29.8, 32.7, 37.1, 51.9, 52.4 (2 carbons), 79.1, 83.5, 138.1, 166.1, 209.3. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.19; H, 7.73.

X-ray Crystal Structure Determination for 3c. Crystals were obtained as colorless needles from ether–dichloromethane. The crystal selected for data collection measured 0.325 × 0.225 × 0.625 mm. Cell constants measured at 140 K (Mo Kα, λ 0.71069 Å, graphite monochromator) and computed from a least squares fit of 18 reflections with 29° < 2θ < 40° were a = 12.261 (3), b = 7.525 (1), and c = 12.699 (3) Å, β = 116.15 (2)°; space group $P2_1/c$; Z = 4; d_{calcd}(140 K) = 1.31 g cm^{-1}; d_{meas}(298 K) = 1.29 g cm^{-1}; Syntex $P2_1$ diffractometer. Intensity data were collected to $2\theta_{max}$ = 50° by using a variable speed ω scan of 1° width at 15–60° min^{-1} with 1° offset for background counts. A total of 1862 unique reflections were collected of which 1572 with $I > 3\sigma(I)$ were used in solution and refinement of the structure. Two check reflections showed only random fluctuations. Data reduction to F_o and $\sigma(F_o)$ was carried out as previously described.[35] Solution of the structure was by direct methods. Computer programs were those of SHELXTL, version 3, July 1981, run on a Data General Eclipse computer. Neutral atom scattering factors and corrections for anomalous dispersion were taken from common sources.[36] Non-hydrogen atoms were assigned anisotropic thermal parameters, and hydrogen atoms, located from a difference map, were assigned an isotropic U of 0.035 in the blocked-cascade least-squares refinement. The final difference map was featureless. The mean (shift/esd)$_{max}$ in the last cycle of refinement was 0.007. The function minimized during refinement was $\sum w(|F_o| - |F_c|)^2$ with $w = 1(\sigma^2(F_o) + 0.001F_o^2)$. The final agreement factor was R = 0.043 (184 parameters).

***cis*,*anti*,*cis*-7b-Methyl-3,3a,4a,5,7a,7b-hexahydro-2*H*,7*H*-dicyclopenta[*b*,*d*]furan-1,6-dione (9).** A rapidly stirred solution of 0.050 g (0.24 mmol) of **3c** and 0.036 g (0.24 mmol) of NaI in 0.30 mL of dry CH_3CN was treated at room temperature under N_2 with 0.031 mL (0.24 mmol) of Me_3SiCl. After 2 h an additional equivalent each of NaI, Me_3SiCl, and CH_3CN was added to the yellowish mixture, bringing about a color change to red-brown. After stirring for 10 h at room temperature, excess tetra-*n*-butylammonium fluoride in THF was added dropwise and the mixture was stirred an additional 90 min. Solvent was removed, the residue taken up in 200 mL of ethyl acetate, and the solution washed twice with saturated aqueous sodium thiosulfate and once with brine. After drying ($MgSO_4$), concentration gave a pale yellow oil (0.059 g) the major component of which was isolated by GC (7% FFAP on Chrom W, AW, DMCS, 10 ft × $^1/_4$ in., 210 °C) as a white crystalline solid in 0.036-g yield (77%): IR ($CHCl_3$) 1740 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.10 (s, 3 H), 2.05 (dddd, J = 3.8, 10.3, 10.3, 14.1 Hz, 1 H), 2.17 (dd, J = 9.1, 19.1 Hz, 1 H), 2.27 (ddd, J = 5.0, 5.0, 14.1 Hz, 1 H), 2.37–2.55 (m, 5 H), 3.05 (ddd, J = 5.0, 5.0, 9.1 Hz, 1 H), 4.42, (d, J = 3.8 Hz, 1 H), 4.56 (dd, J = 5.0, 5.0 Hz, 1 H). Structural characterization of this material as **9** ultimately required X-ray crystallographic analysis. This analysis is presented in full detail elsewhere.[37]

2-Methylbicyclo[5.3.0]deca-1,9-diene-6,8-dione (13). A mixture of 0.162 g (0.85 mmol) of *p*-toluenesulfonic acid and 0.94 mL (11.7 mmol) of pyridine was cooled to 0 °C, and 0.107 g (0.051 mmol) of **3c** was added. The mixture was brought to room temperature and allowed to stir for 66 h, at which time TLC showed complete disappearance of starting material (R_f 0.44) and a single spot for the corresponding tosylate **12** (R_f 0.62). At this point **12** can be isolated in nearly quantitative yield as a sensitive white solid by partitioning of the reaction mixture between water and ethyl acetate, washing with 0.01 N HCl, saturated aqueous $NaHCO_3$, and brine, drying ($MgSO_4$), and removal of solvent: IR ($CHCl_3$) 1705 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 0.83 (s, 3 H), 1.60 (m, 1 H), 1.82 (m, 1 H), 2.10 (m, 2 H), 2.46 (s, 3 H), 2.77 (d, J = 5.2 Hz, 1 H), 3.19 (dd, J = 3.3, 5.2 Hz, 1 H), 3.28 (s, 3 H), 4.49 (m, 1 H), 6.41 (d, J = 5.5 Hz, 1 H), 7.62 (dd, J = 3.3, 5.5 Hz, 1 H), 7.36 (d, J = 8.1 Hz, 2 H), 7.82 (d, J = 8.1 Hz, 2 H). In practice tosylate **12** was submitted directly to solvolysis without isolation as follows. Pyridine was pumped away from the crude tosylate at high vacuum. The residue was then heated to reflux with 5 mL of MeOH, 0.042 mL (0.51 mmol) of dry pyridine, and 0.513 g (0.51 mmol) of solid $CaCO_3$ for 2 days. Then 0.90 mL of 2.3% aqueous $NaHCO_3$ and 0.10 mL of MeOH were added and reflux continued for an additional 3 days. Solvents were removed at high vacuum and the residue was extracted with 4 × 25 mL of ether. After drying briefly (Na_2SO_4) and removing solvent, 0.083 g (90% yield) of **13** was obtained as a yellow oil: IR ($CHCl_3$) 1600, 1635, 1655, 1710 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.93 (m, 2 H), 2.06 (s, 3 H), 2.50 (dd, J = 5.4, 5.9 Hz, 2 H), 2.66 (dd, J = 5.4, 5.9 Hz, 2 H), 6.23 (d, J = 5.7 Hz, 1 H), 7.49 (d, J = 5.7 Hz, 1 H), 14.44 (br s, 1 H); ^{13}C NMR ($CDCl_3$, 25.1 MHz) δ 21.9 (2 carbons), 36.2, 37.6, 108.2, 127.1, 130.0, 142.1, 144.7, 178.6, 196.4; UV (ether) λ_{max} 226, 275, 349 nm; high resolution mass spectrum, calcd for $C_{11}H_{12}O_2$ 176.0838, found 176.0821.

2,7-Dimethylbicyclo[5.3.0]deca-1,9-diene-6,8-dione (14). To a solution containing 0.035 g (0.20 mmol) of **13** in 5 mL of dry acetone was added 0.026 g of anhydrous K_2CO_3. Then 0.016 mL (0.25 mmol) of dry methyl iodide was added and the system heated to reflux for 4 h. The solution was filtered and the solids were washed with acetone. Combined filtrates were concentrated and the residue extracted with 3 × 25 mL of ether. Evaporation afforded 0.031 g (82% yield) of **14** as a somewhat impure pale yellow oil: IR ($CHCl_3$) 1680, 1720 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.49 (s, 3 H), 1.90 (m, 1 H), 2.06 (s, 3 H), 2.19 (m, 1 H), 2.24–2.65 (m, 4 H), 6.17 (d, J = 5.4 Hz, 1 H), 8.09 (d, J = 5.4 Hz, 1 H); UV (ether) λ_{max} 222, 295 nm; high resolution mass spectrum, calcd for $C_{12}H_{14}O_2$ 190.0994, found 190.0970. This substance is rather sensitive, and attempts at further purification by chromatographic means led to mixtures whose proton NMR spectra showed increased intensities for peaks associated with uncharacterized decomposition products. Therefore hydrogenation was carried out on the crude material (ca. 80–85% pure) as follows. To a suspension of 0.040 g of 5% Pd–C in 5 mL of MeOH was added a solution of 0.052 g of crude **14** in 5 mL of MeOH. The mixture was stirred at room temperature under 1 atm of H_2 for 72 h whereupon TLC showed complete disappearance of the starting compound. Filtration through a Celite pad and concentration led to 0.050 g (96% yield) of 1,6-dimethylbicyclo[5.3.0]decane-2,10-dione (**15**) as a pale yellow oil: ^{13}C NMR ($CDCl_3$, 25.1 MHz)

(35) Balch, A. L.; Benner, L. S.; Olmstead, M. M. *Inorg. Chem.* **1979**, *18*, 2996.

(36) *International Tables for X-ray Crystal* raphy; Kynoch Press: Birmingham, England, 1974; Vol. IV.

(37) Olmstead, M. M.; Sampath, V.; Schore, N. E. *Acta Crystallogr., Sect. C*, in press.

δ 19.8, 21.0, 23.0, 24.8, 29.8, 31.0, 33.9, 37.5, 42.6, 51.6, 208.1, 216.5.

***cis,anti,cis*-1-Methoxy-7-methyl-*endo*-8-hydroxytricyclo[5.3.0.0^{2,6}]decan-3-one (20).** Following a procedure similar to that described for the hydrogenation of **14** (above), 0.099 g (0.48 mmol) of **3c** was reduced by stirring over 0.060 g of 5% Pd–C for 60 h. After filtration and concentration 0.098 g of **20** was obtained as an analytically pure crystalline solid (98% yield): IR ($CHCl_3$) 1740 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.16 (s, 3 H), 1.59–2.67 (m, 11 H), 3.21 (s, 3 H), 3.87 (m, 1 H). Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.55; H, 8.63. Found: C, 68.41; H, 8.62.

***cis,anti,cis*-1-Methoxy-7-methyl-3-methylenetricyclo[5.3.0.0^{2,6}]decan-*endo*-8-ol (21).** To 1.94 g (48.5 mmol) of KH in a 250-mL three-neck flask under Ar was added 60 mL of dry Me_2SO slowly via syringe. After evolution of H_2 had ceased (ca. 10 min) 18.55 g (51.9 mmol) of methyltriphenylphosphonium bromide was added in one portion and the resulting deep red solution was heated to 60 °C. After 10 min, 0.721 g (3.46 mmol) of **20** in 5 mL of dry Me_2SO was added and heating was continued for 6 h. After cooling, the mixture was poured into 800 mL of water and extracted with 4 × 100 mL of ether. The extracts were washed with 6 × 50 mL of water 50 mL of brine, and dried. Concentration and distillation (Kugelrohr, 125 °C at 0.01 mmHg) yielded 0.633 g of **21** (88% yield): IR (film) 1650, 3080 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.10 (s, 3 H), 1.26 (br s, 1 H), 1.50–1.70 (m, 4 H), 1.81 (dd, J = 4.0, 6.8 Hz, 1 H), 1.96 (m, 1 H), 2.25 (dd, J = 8.1, 10.0 Hz, 1 H), 2.34 (dd, J = 7.1, 8.1 Hz, 1 H), 2.50 (br s, 1 H), 2.72 (d, J = 7.2 Hz, 1 H), 3.15 (s, 3 H), 3.75 (dd, J = 7.0, 10.8 Hz, 1 H), 4.80 (br s, 1 H), 4.96 (br s, 1 H). Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 74.78; H, 9.63.

Tosylation of 21 and Subsequent Solvolysis. To 0.204 g (0.98 mmol) of **21** in 5 mL of pyridine was added 0.325 g (1.70 mmol) of *p*-toluenesulfonyl chloride. After 2 days of stirring at room temperature, the mixture was poured into water and extracted with 4 × 25 mL of ether. Washing with 4 × 25 mL of 5% HCl, 2 × 25 mL of saturated aqueous $NaHCO_3$, drying, and concentration afforded 0.280 g (79% yield) of tosylate **22**, which was used directly in the next step: NMR ($CDCl_3$, 360 MHz) δ 0.80 (s, 3 H), 1.49–1.74 (m, 4 H), 1.88 (m, 1 H), 2.05 (m, 1 H), 2.26 (m, 1 H), 2.38–2.51 (m, 5 H incl tosyl-CH_3, s at δ 2.45), 2.77 (d, J = 7.1 Hz, 1 H), 3.15 (s, 3 H), 4.37 (m, 1 H), 4.83 (br s, 1 H), 5.00 (br s, 1 H), 7.30 (d, J = 8.1 Hz, 2 H), 7.80 (d, J = 8.1 Hz, 2 H).

A mixture containing 0.327 g (0.903 mmol) of **22**, 90 mL of MeOH, and 5 mL of water was heated to reflux for 12 h, concentrated, extracted with 2 × 100 mL of ether, and dried. Removal of solvent and separation on the Chromatotron (CH_2Cl_2, then 1:1 hexane/ether) gave 0.125 g (79% yield) of a colorless oily mixture of unstable dienones **23** and **24**. For **24**, the major component: IR (film) 1600, 1675 cm^{-1}; NMR (C_6D_6, 360 MHz) δ 1.58 (finely split m, 3 H), 1.92 (finely split m, 3 H), 1.94–2.60 (m, 8 H), 3.54 (br m, 1 H), 5.31 (br s, 1 H); ^{13}C NMR (C_6D_6, 50.3 MHz) δ 17.0, 23.8, 24.2, 29.2, 39.9, 43.2, 49.2, 123.7, 128.5, 133.4, 153.1, 201.5; high-resolution mass spectrum, calcd for $C_{12}H_{18}O$ 176.1247, found 176.1228. Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found (for a sample handled in air; see below): C, 68.15; H, 7.40.

Upon standing in an open flask, the **23**/**24** mixture slowly turned yellow and deposited large pale yellow crystals: NMR ($CDCl_3$, 360 MHz) δ 1.52 (s, 3 H), 1.90 (s, 3 H), 1.91 (ddd, J = 3.9, 8.3, 13.5 Hz, 1 H), 2.33 (m, 2 H), 2.47 (ddd, J = 6.5, 8.3, 18.2 Hz, 1 H), 2.63 (m, 3 H), 2.74 (ddd, J = 3.9, 9.2, 18.2 Hz, 1 H), 6.26 (dt, J_d = 1.3 Hz, J_t = 6.6 Hz, 1 H), 9.84 (br s, 1 H); UV (ether) λ_{max} 241, 289, 350 nm. The crystals were suitable for immediate structural determination by X-ray diffraction without further manipulation. The result[28] was **25**, 2,8-dimethyl-8-hydroperoxybicyclo[5.3.0]deca-1(7),2-dien-6-one. In view of the potential hazards associated with organic hydroperoxides, once the structure was established all samples containing any quantity of **25** were immediately destroyed; no attempt to isolate **25** in analytically pure form was made. For comparison with data above: UV (calcd[23]) λ_{max} 349 nm. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74.

***cis,anti,cis*-1-Methoxy-7-methyl-*endo*-3-[[(*tert*-butyldimethylsilyl)oxy]methyl]tricyclo[5.3.0.0^{2,6}]decan-*endo*-8-ol (27a).** To 0.404 g (1.94 mmol) of **21** in 20 mL of THF at 0 °C was added 7.78 mmol of BH_3·SMe_2. The reaction was allowed to warm to room temperature and then stirred for 4 h. Oxidation was effected by addition of 20 mL of ethanol, 4 mL of 6 M NaOH, and 4 mL of 30% H_2O_2 followed by heating to 60 °C for 1 h. The solution was poured into water and extracted with $CHCl_3$. Drying and concentration gave 0.396 g of diol **26** (90% yield), which was used without further purification: NMR ($CDCl_3$, 360 MHz) δ 1.06 (s, 3 H), 1.25 (br s, 1 H), 1.63–1.88 (m, 6 H), 1.92–2.13 (m, 3 H), 2.28 (t, J = 7.8 Hz, 1 H), 2.38 (t, J = 7.3 Hz, 1 H), 3.22 (s, 3 H), 3.45 (br s, 1 H), 3.80 (d, J = 6.0 Hz, 2 H), 3.85 (dd, J = 4.1, 11.3 Hz, 1 H); high-resolution mass spectrum, calcd for $C_{13}H_{22}O_3 - H_2O$ 208.1464, found 208.1475; calcd for $C_{13}H_{22}O_3 - 2H_2O$ 190.1358, found 190.1358.

A solution of 0.386 g (1.71 mmol) of diol **26** in 10 mL of Et_3N and 20 mL of CH_2Cl_2 was treated with 1.17 g (7.76 mmol) of *t*-$BuMe_2SiCl$ and 0.024 g (0.19 mmol) of DMAP. After 12 h, the mixture was concentrated onto silica gel and the product extracted with ether. MPLC (silica gel, ether) gave 0.419 g (72% yield) of **27a** as a colorless oil: NMR ($CDCl_3$, 360 MHz) δ 0.04 (s, 6 H), 0.89 (s, 9 H), 1.01 (s, 3 H), 1.20–2.05 (m, 10 H), 2.23 (t, J = 7.4 Hz, 1 H), 2.34 (t, J = 7.2 Hz, 1 H), 3.13 (s, 3 H), 3.78 (m, 1 H), 3.89 (d, J = 7.3 Hz, 2 H). Anal. Calcd for $C_{19}H_{36}O_3Si$: C, 67.01; H, 10.65. Found: C, 67.24; H, 10.43.

***cis,anti,cis*-1-Methoxy-7-methyl-*endo*-3-[[(*tert*-butyldiphenylsilyl)oxy]methyl]tricyclo[5.3.0.0^{2,6}]decan-*endo*-8-ol (27b).** Following the same procedure as for **27a**, 0.396 g of diol **26** was converted into monosilyl ether **27b** by reaction with 2.13 g (7.76 mmol) of *t*-$BuPh_2SiCl$. Yield, 0.686 g (76%), of **27b**, a colorless oil: NMR ($CDCl_3$, 360 MHz) δ 0.99 (s, 3 H), 1.06 (s, 9 H), 1.17–2.18 (m, 10 H), 2.25 (t, J = 7.3 Hz, 1 H), 2.40 (t, J = 7.3 Hz, 1 H), 3.04 (s, 3 H), 3.78 (dd, J = 6.0, 10.5 Hz, 1 H), 3.95 (AB of ABX, 2 H), 7.29–7.45 (m, 6 H), 7.63–7.75 (m, 4 H). Anal. Calcd for $C_{29}H_{40}O_3Si$: C, 74.95; H, 8.68. Found: C, 74.61; H, 8.69.

***cis*-2-Methyl-*endo*-8-[[(*tert*-butyldimethylsilyl)oxy]methyl]bicyclo[5.3.0]dec-2-en-6-one (28a).** Following the procedure previously described for the preparation of tosylate **22**, 0.296 g (0.867 mmol) of **27a** was converted to 0.401 g (94% yield) of the corresponding tosylate. To this were added 20 mL of pyridine, 50 mL of 15% aqueous MeOH, and 0.163 g (1.63 mmol) of $CaCO_3$, and the mixture was heated to reflux under Ar for 24 h. Then 10 mL of saturated aqueous $NaHCO_3$ was added and the reflux continued for another 48 h. After concentration, extraction into 4 × 50 mL of ether, drying, and removal of solvent, 0.196 g of a mixture of **28a** and **28c** was obtained. This mixture was dissolved in 5 mL of DMF, treated with 0.192 g (1.27 mmol) of *t*-$BuMe_2SiCl$ and 0.432 g (6.35 mmol) of imidazole, and left at room temperature for 24 h. The solution was then poured into water, extracted with ether, dried, and concentrated. MPLC purification (ether) gave 0.123 g of **28a** (46% yield): IR ($CHCl_3$) 1690 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 0.08 (s, 3 H), 0.23 (s, 3 H), 0.87 (s, 9 H), 1.45–1.70 (m, 3 H), 1.73 (s, 3 H), 1.95 (m, 1 H), 2.10 (m, 1 H), 2.35–2.60 (m, 4 H), 2.74 (m, 1 H), 2.98 (dd, J = 8.0, 11.6 Hz, 1 H), 3.48 (dd, J = 3.4, 5.3 Hz, 2 H), 5.59 (m, 1 H). Anal. Calcd for $C_{18}H_{32}O_2Si$: C, 70.07; H, 10.45. Found: C, 70.42; H, 10.61.

***cis*-2-Methyl-*endo*-8-[[(*tert*-butyldiphenylsilyl)oxy]methyl]bicyclo[5.3.0]dec-2-en-6-one (28b).** Silyl ether **27b** (0.686 g, 1.48 mmol) was converted to the corresponding tosylate (0.883 g, 96% yield) by the method previously described for **22**. To this were added 25 mL of pyridine, 70 mL of 15% aqueous MeOH, and 0.284 g (2.84 mmol) of $CaCO_3$, and the mixture was heated to reflux for 24 h. Then 10 mL of saturated aqueous $NaHCO_3$ was added and reflux continued for 48 h. The mixture was concentrated, added to 200 mL of water, and extracted with 4 × 50 mL of $CHCl_3$. After drying and concentration, MPLC purification (ether) gave 0.460 g (72% yield) of **28b**: IR ($CHCl_3$) 1701 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.03 (s, 9 H), 1.61–1.69 (m, 3 H), 1.73 (s, 3 H), 2.00–2.10 (m, 2 H), 2.35–2.55 (m, 4 H), 2.86 (m, 1 H), 3.09 (dd, J = 7.9, 11.6 Hz, 1 H), 3.56 (d, J = 5.6 Hz, 2 H), 5.60 (br s, 1 H), 7.40 (m, 6 H), 7.64 (m, 4 H). Anal. Calcd for $C_{28}H_{36}O_2Si$: C, 77.73; H, 8.38. Found: C, 77.40; H, 8.49.

***cis*-2-Methyl-*endo*-8-[[(*tert*-butyldimethylsilyl)oxy]methyl]-*endo*-5-(carbethoxymethyl)bicyclo[5.3.0]dec-2-en-6-one (29a).** To 0.156 g (0.506 mmol) of ketone **28a** in 10 mL of THF at −78 °C was added 0.127 g (0.76 mmol) of $LiN(SiMe_3)_2$. After 1.5 h, 0.325 g (1.52 mmol) of ethyl iodoacetate was added, followed by 1.5 mL of HMPA. The mixture was warmed to room temperature and left for 20 h. It was then poured into brine and extracted with 4 × 25 mL of ether. The combined extracts were

stirred with 25 mL of a 5% solution of diethylenetriamine for 2 h. The organic layer was separated, washed with 1 N HCl and 25 mL of saturated aqueous $NaHCO_3$, dried, and concentrated. MPLC separation (1:1 hexane/ether) afforded 0.160 g of **29a**: IR ($CHCl_3$) 1690, 1728 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 0.00 (s, 3 H), 0.01 (s, 3 H), 1.23 (t, J = 7.1 Hz, 3 H), 1.29 (s, 9 H), 1.43–1.54 (m, 2 H), 1.54–1.67 (m, 3 H), 1.71 (s, 3 H), 1.94–2.00 (m, 1 H), 2.40 (dd, J = 6.9, 16.4 Hz, 1 H), 2.50–2.60 (m, 2 H), 2.67 (m, 1 H overlapping dd, J = 5.6, 16.4 Hz, 1 H), 3.00 (dd, J = 8.0, 11.6 Hz, 1 H), 3.43 (dd, J = 5.9, 9.7 Hz, 1 H), 3.57 (dd, J = 4.2, 9.7 Hz, 1 H), 4.10 (AB of ABX_3, J_q = 7.1 Hz, 2 H), 5.50 (br d, J = 9.1 Hz, 1 H). Anal. Calcd for $C_{22}H_{38}O_4Si$: C, 66.96; H, 9.71. Found: C, 67.01; H, 9.85.

***cis*-2-Methyl-*endo*-8-[[(*tert*-butyldiphenylsilyl)oxy]methyl]-*endo*-5-(carbethoxymethyl)bicyclo[5.3.0]dec-2-en-6-one (29b).** Following the procedure described above for the synthesis of **29a** (scaled up ×4), 0.877 g (2.03 mmol) of ketone **28b** was alkylated to give 0.937 g (89% yield) of **29b**: IR ($CHCl_3$) 1701, 1728 cm^{-1}; NMR ($CDCl_3$, 360 MHz) δ 1.08 (s, 9 H), 1.22 (t, J = 7.1 Hz, 3 H), 1.50–1.72 (m, 2 H), 1.74 (br s, 3 H), 1.95–2.15 (m, 3 H), 2.34 (dd, J = 7.1, 16.4 Hz, 1 H), 2.40–2.60 (m, 2 H), 2.68 (dd, J = 5.6, 16.4 Hz, 1 H), 2.80 (m, 1 H), 3.00 (m, 1 H), 3.14 (dd, J = 7.8, 11.6 Hz, 1 H), 3.56 (m, 1 H), 3.65 (dd, J = 4.5, 9.8 Hz, 1 H), 4.10 (AB of ABX_3, J_q = 7.1 Hz, 2 H), 5.50 (br d, J = 8.0 Hz, 1 H), 7.30–7.45 (m, 6 H), 7.60–7.75 (m, 4 H). Anal. Calcd for $C_{32}H_{42}O_4Si$: C, 74.09; H, 8.16. Found: C, 73.97; H, 8.10.

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Supplementary Material Available: Tables of atomic coordinates, thermal parameters, bond lengths, and bond angles for **3c** (3 pages). Ordering information is given on any current masthead page.

Mechanism of Intramolecular Photocycloadditions of Cyclooctenones

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The intramolecular photochemical [2 + 2] cycloadditions of a number of 4'-substituted (3'-butenyloxy)-cyclooctenones have been studied. Two classes of substrates were found. One class (phenyl- and vinyl-substituted) forms [2 + 2] adducts in an efficient reaction, while the rest of the compounds form photoproducts slowly and in low yield. The behavior of a carbon analogue shows that rotational relaxation of the cyclooctenone triplet is faster than [2 + 2] cycloaddition. Based on quenching and sensitization studies, it has been suggested that the substituent effect is indicative of an enhanced rate of cyclization to form a 1,4-biradical.

Introduction

Since Corey's initial report[1] of the photochemical enone [2 + 2] cycloaddition, the reaction has been subject to considerable mechanistic scrutiny.[2-7] One of the early observations made on the limitations of the reaction was that enones in flexible systems do not cycloadd successfully. The π,π^* triplet state can relax by rotation about the C_2–C_3 bond,[7] and this rotation about the ethylene linkage allows the T_1 and S_0 surface to cross, the "free rotor effect".[8] In this manner, vibronic coupling allows rapid intersystem crossing to the ground state. An enone–alkene triplet exciplex that undergoes C–C bonding to generate a biradical has been postulated as a key intermediate in the cycloaddition.[4] While exciplex and biradical intermediates are still a matter of some controversy, they do provide a framework in which new results can be discussed without necessarily endorsing their existence. The initial bond formation can occur either α or β to the enone in intermolecular photoannelations.[2,9-12] For intramolecular photoannelations, it is postulated that the biradical is formed from 1,5-closure (the "rule of five"[13]) of the triplet enone to the olefin.

Pulsed laser techniques have provided insight into the enone [2 + 2] cycloaddition. Bonneau has observed transient absorptions at 280 nm assigned to the twisted triplet π,π^* excited state on laser excitation of a number of conjugated enones.[14] The angle of torsion around the double bond, and consequently the triplet energy, varies with the rigidity of the molecule. Constraints to twisting result in higher triplet energies and longer triplet lifetimes, due to the larger gap between the T_1 and S_0 surfaces. Schuster, in collaboration with Bonneau,[15] has integrated the flash and steady-state photochemical behavior of these enones and shown that the excited states involved in the rearrangement[16,17] and cycloaddition reactions are the same

(1) Corey, E. J.; Bass, J. D.; LeMahieu, R.; Mitra, R. B. *J. Am. Chem. Soc.* **1964**, *86*, 5570.
(2) Cantrell, T. S.; Haller, W. S.; Williams, J. C. *J. Org. Chem.* **1969**, *34*, 509.
(3) Weedon, A. C. In *Synthetic Organic Photochemistry*; Horspool, W. M., Ed.; Plenum Press: New York, 1984; p 61.
(4) Loutfy, R. O.; de Mayo, P. *J. Am. Chem. Soc.* **1977**, *99*, 3559.
(5) de Mayo, P.; Nicholson, A. A.; Tchir, M. F. *Can. J. Chem.* **1969**, *47*, 711.
(6) Wagner, P. J.; Buchek, D. J. *Can. J. Chem.* **1969**, *47*, 713.
(7) de Mayo, P. *Acc. Chem. Res.* **1970**, *4*, 41.
(8) Turro, N. J. *Modern Molecular Photochemistry*; Benjamin Cummings Publishing Co.: Menlo Park, CA, 1978.
(9) Wexler, A. J.; Hyatt, J. A.; Reynolds, P. W.; Cottrell, C.; Swenton, J. S. *J. Am. Chem. Soc.* **1978**, *100*, 512.
(10) Dilling, W. L.; Tabor, D. E.; Boer, F. P.; North, P. P. *J. Am. Chem. Soc.* **1970**, *92*, 1399.
(11) Loutfy, R. O.; de Mayo, P. *Can. J. Chem.* **1969**, *50*, 509.
(12) Hanifin, J. W.; Cohen, E. *J. Am. Chem. Soc.* **1969**, *91*, 4494.
(13) Srinivasan, R.; Carlough, K. H. *J. Am. Chem. Soc.* **1967**, *89*, 4932.
(14) Bonneau, R. *J. Am. Chem. Soc.* **1980**, *102*, 3816.
(15) Schuster, D. I.; Bonneau, R.; Dunn, D. A.; Rao, J. M.; Joussiet-Dubieu, J. *J. Am. Chem. Soc.* **1984**, *106*, 2706.
(16) Chan, C. B.; Schuster, D. I. *J. Am. Chem. Soc.* **1982**, *104*, 2928.

0022-3263/87/1952-3603$01.50/0