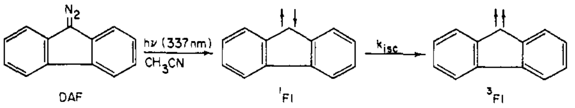
Chemistry of Fluorenylidene. Direct Observation of, and Kinetic Measurements on, a Singlet and a Triplet Carbene at Room Temperature

Sir:

The chemical and physical properties of carbenes continue to provoke widespread interest.[1] Physical techniques, such as low-temperature absorption[2] and EPR[3] spectroscopy, and CIDNP[4] studies have shown the electronic ground state of most carbenes to be the triplet. Product studies, however, have shown that chemical reactions can originate from either the singlet or the triplet state of the carbene.[5] This reactive duality complicates the mechanistic interpretation of the chemistry of carbenes since, most commonly, the product mixture obtained is the result of an unknown combination of reaction from the singlet and the triplet. In this report, we describe the results of our pulsed-laser spectrophotometric investigation of the chemistry of both singlet (^{1}Fl) and triplet (^{3}Fl) fluorenylidene. These carbenes are conveniently



(1)

generated by photolysis of diazofluorene (DAF) in acetonitrile.[6] With these techniques, we are able to observe spectroscopically both the singlet and triplet carbenes, to measure the rate of intersystem crossing for the singlet carbene, and to evaluate the rate constants for reaction of both carbenes with olefins, hydrocarbons, and alcohols. These kinetic and spectroscopic findings permit for the first time a detailed analysis of the chemistry of reacting singlet and triplet carbenes in solution.

Irradiation of DAF at 77 K in a frozen glass produces ^{3}Fl, which has been characterized by absorption[8] and EPR spectroscopy.[3] Our laser flash photolysis of a 6×10^{-4} M solution of DAF in acetonitrile at room temperature with a 10-ns light pulse at 337 nm[9] generates two transient products. The longer lived product[10] exhibits an absorption spectrum, recorded 200 ns after the laser pulse, that is identical with the spectrum previously reported for ^{3}Fl. We therefore can confidently assign the structure of this product to ^{3}Fl. The spectrum of the shorter lived product, recorded 10 ns after the pulse, has an absorption maximum at 470 nm. These spectra, and those recorded at an intermediate time, are shown in Figure 1.

The spectral and temporal differences of the two transient products permit us to measure their rates of reaction and interconversion. By monitoring the rate of growth of the absorption of ^{3}Fl, we have obtained the rate constant for its formation. This rate constant is independent of the wavelength used to monitor the concentration of ^{3}Fl. Similarly, by measuring the change of the absorption at 470 nm of the short-lived product, we have obtained the rate constant for its disappearance. Within experimental error, the consumption of the short-lived product occurs with the same rate constant as that obtained for the formation of ^{3}Fl. Thus, the short-lived product is the precursor to ^{3}Fl, and, therefore, we tentatively assign the structure of this product to ^{1}Fl.[11] The rate constant for intersystem crossing (k_{isc}) of ^{1}Fl is thus 4.07×10^7 s^{-1}, which corresponds to a half-life of 17 ± 2 ns.

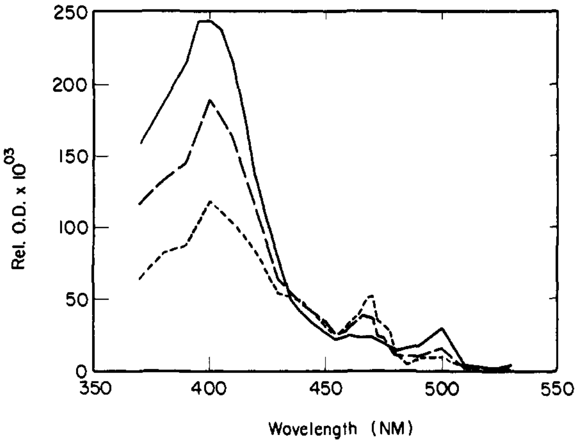


Figure 1. Absorption spectra of the transient products resulting from irradiation of DAF in acetonitrile. The solid curve was recorded 200 ns after the laser pulse, the dashed at 30 ns, and the dotted at 10 ns. The maxima at 400 and 500 nm are due to ^{3}Fl, and the maximum at 470 nm is due to ^{1}Fl.

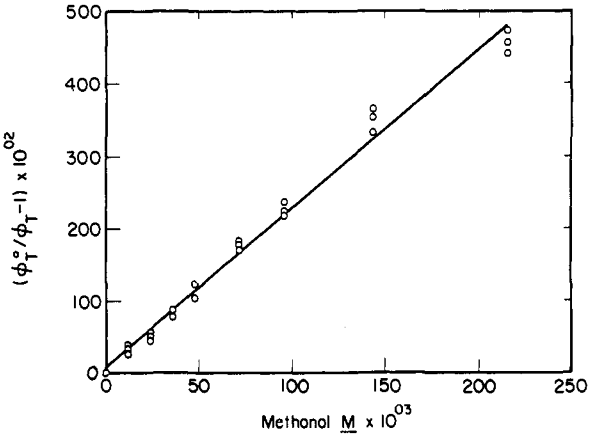


Figure 2. Initial yield of ^{3}Fl in the presence of CH_3OH plotted according to eq 2.

Further evidence that the short-lived product is ^{1}Fl follows from the analysis of its reaction with methanol. It is generally accepted that alcohols react with singlet carbenes to give ethers.[13] Photolysis of DAF under the conditions of the spectroscopic study in acetonitrile containing methanol gives only methyl fluorenyl ether in greater than 95% yield. Analysis of the spectra of the transient products shows that ^{3}Fl reacts very slowly with methanol, indicating that, in this case, intersystem crossing is unidirectional.[14] However, the short-lived transient product reacts with methanol

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(1) R. A. Moss and M. Jones, Jr., *React. Intermed.*, **1**, 69 (1978), and references cited therein.

(2) A. M. Trozzolo, *Acc. Chem. Res.*, **1**, 329 (1968).

(3) A. M. Trozzolo, R. W. Murray, and E. Wasserman, *J. Am. Chem. Soc.*, **84**, 4990 (1962); R. W. Brandon, G. L. Closs, C. E. Davoust, C. A. Hutchison, Jr., B. E. Kohler, and R. Silbey, *J. Chem. Phys.*, **43**, 2006 (1965).

(4) H. D. Roth, *Acc. Chem. Res.*, **10**, 85 (1977).

(5) M. Jones, Jr., and K. R. Rettig, *J. Am. Chem. Soc.*, **87**, 4013 (1965); *ibid.*, **87**, 4015 (1965); N. Shimizu and S. Nishida, *J. Chem. Soc., Chem. Commun.*, 389 (1972); Y. Yamamoto, S.-I. Murahashi, and I. Moritani, *Tetrahedron*, **31**, 2663 (1975); W. J. Baron, M. E. Hendrick, and M. Jones, Jr., *J. Am. Chem. Soc.*, **95**, 6286 (1973); X. Creary, *ibid.*, **102**, 1611 (1980).

(6) W. von E. Doering and M. Jones, J., *Tetrahedron. Lett.*, 791 (1963); S.-I. Murahashi, I. Moritani, and T. Nagai, *Bull. Chem. Soc. Jpn.*, **40**, 1655 (1967). As has been previously noted,[7] unanticipated ground-state reaction of DAF and these olefins to form pyrazolines may complicate this study. We have found that the half-life of DAF with 1.3×10^{-1} M maleic anhydride is 600 s. Thus, pyrazoline formation is rapid. We have carried out our spectroscopic investigation on pyrazoline-free solutions.

(7) D. Bethell, *Adv. Phys. Org. Chem.*, **7**, 153 (1969).

(8) G. L. Closs, C. A. Hutchison, Jr., and B. Kohler, *J. Chem. Phys.*, **44**, 413 (1966).

(9) The laser flash photolysis apparatus has been described previously: J. J. Zupancic, K. A. Horn, and G. B. Schuster, *J. Am. Chem. Soc.*, in press.

(10) The lifetime of this transient, in the absence of trapping reagent, is probably controlled by a combination of reactions, including slow abstraction of hydrogen from the solvent, dimerization, reaction with DAF, and reaction with trace water and O_2 contaminants. The products of this irradiation include the ketazine, fluorene, and solvent-incorporation products. The half-life of the transient under these conditions is ca. 30 μs.

(11) There have been several reports[12] on the direct optical detection of triplet carbenes at room temperature, but, to the best of our knowledge, this is the first report of the observation of a singlet carbene in solution.

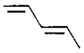
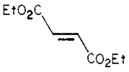
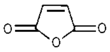
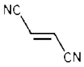
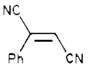
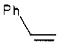
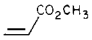
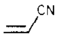
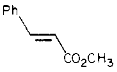
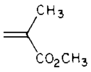
(12) (a) Y. Yamamoto, I. Moritani, Y. Maeda, and S. Murahashi, *Tetrahedron*, **26**, 251 (1970); (b) I. Moritani, S.-I. Murahashi, H. Ashitaka, K. Kimura, and H. Tsubomura, *J. Am. Chem. Soc.*, **90**, 5918 (1968); (c) G. L. Closs and B. E. Rabinow, *ibid.*, **98**, 8190 (1976).

(13) W. Kirmse, "Carbene Chemistry", 2nd ed., Academic Press, New York, 1971; R. A. Moss and M. Jones, Jr., *Carbenes 1973-1975*, **1**, 2.

(14) The notion that singlet and triplet states of some aromatic carbenes are in dynamic equilibrium has apparently been demonstrated for diphenylmethelene.[12c]

0002-7863/80/1502-5958$01.00/0

Table I

reactant[a]	k_s, M^{-1} s^{-1}	k_t, M^{-1} s^{-1}
CH_3OH	8.95×10^8	*b*
$(CH_3)_3COH$	1.51×10^8	*b*
	1.03×10^9	*b*
	*c*	9.17×10^7
	1.27×10^8	6.63×10^6
	*c*	9.81×10^8
	*c*	4.70×10^7
	*c*	2.21×10^7
	9.36×10^8	$<2 \times 10^5$ [d]
	3.51×10^8	*b*
	3.24×10^8	*b*
	3.85×10^8	2.03×10^6
	2.65×10^8	7.11×10^5
	4.38×10^8	$<2 \times 10^5$ [d]
	6.44×10^8	*b*

[a] DAF (6.4×10^{-4} M) in acetonitrile at 25 °C irradiated at 337 nm with the output of a Molectron UV24 nitrogen laser. Spectral changes were monitored at 400 nm. Standard deviations of the rate constants are less than 5% of the reported value. [b] These reactants consume ^3Fl too slowly for us to conveniently measure k_t with our apparatus. [c] Rapid reaction of ^3Fl with these olefins prohibits our determination of ϕ_t and thereby thwarts our application of eq 2 in these cases. [d] Reaction of ^3Fl with DAF, ^3Fl, and trace impurities is competitive with its reaction with these olefins. This rate constant should be viewed as an upper limit only to k_t.

quite rapidly. Moreover, as the methanol content of the solvent increases, the amount of ^3Fl formed decreases, becoming zero at high methanol concentration. These results show that the short-lived product reacts with methanol in competition with intersystem crossing to ^3Fl and that the short-lived product is the sole precursor to ^3Fl. These findings are consistent with our contention that the short-lived product is ^1Fl.

Our spectroscopic analyses permit the determination of the rate of reaction of ^1Fl and ^3Fl with a variety of reagents. For example, the rate constant for reaction of ^1Fl (k_s) with methanol can be determined from the plot (Figure 2) of the yield of ^3Fl (ϕ_t) against methanol concentration, according to eq 2, where ϕ_t^0 is the triplet

$$\left(\frac{\phi_t^0}{\phi_t} - 1\right) = \frac{k_s}{k_{isc}}[CH_3OH] \qquad (2)$$

yield in the absence of methanol. This analysis gives k_s for methanol equal to 8.95×10^8 M^{-1} s^{-1}, about 18 times less than the diffusion-limited rate in acetonitrile. In a similar fashion, we have obtained the value of k_s for a variety of reagents. These data are summarized in Table I.

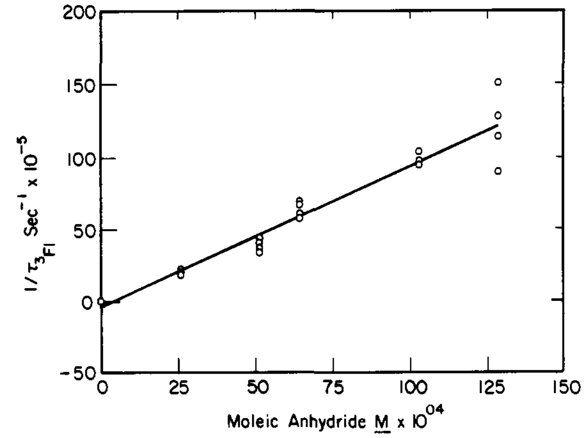
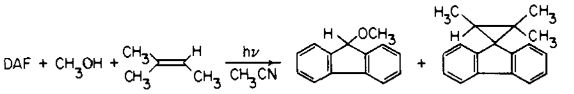


Figure 3. Pseudo-first-order rate constant for decay of ^3Fl in acetonitrile containing various concentrations of maleic anhydride.

Final verification that the short-lived product is ^1Fl comes from the analysis of some quantitative competitive trapping experiments. The kinetic results (Table I) give a ratio of k_s for trapping of ^1Fl by methanol and 2-methyl-2-butene equal to 2.9. Photolysis with the laser apparatus of DAF in acetonitrile containing 0.94 M methanol and 1.15 M 2-methyl-2-butene gives only two products, methyl fluorenyl ether and the appropriate cyclopropanation product (eq 3). At the reagent concentrations employed, the



(3)

kinetic analysis shows that the trapping reaction proceeds 27 times faster than intersystem crossing to ^3Fl. Thus, the observed products derive almost exclusively from the reaction of methanol or 2-methyl-2-butene with the transient product whose structure we have assigned to ^1Fl. The ratio of ether to cyclopropane product, determined by integration of the ^1H NMR spectrum, is 1.40 ± 0.05. This ratio is within the experimental error of the ratio predicted from the kinetic analysis (1.45 ± 0.06). Similarly, competition between methanol and methyl methacrylate for the short-lived product gives the expected ratio of ether and cyclopropane. These findings, and those described above, demonstrate that the short-lived product is ^1Fl and that k_s is the rate-determining factor in the formation of its products.

The rate constant for reaction of ^3Fl (k_t) with trapping reagent can be determined directly by following the rate of change of its characteristic absorption. For example, a plot of the reciprocal of the measured ^3Fl lifetime ($\tau_{^3Fl}$) against maleic anhydride concentration is shown in Figure 3. The slope of this line gives k_t for maleic anhydride. Data from similar experiments with various olefins and other reagents are compiled in Table I. The value of k_t for styrene is so small that we can obtain no more than its upper limit. This limit can be compared to the rate constant obtained indirectly by Closs and Rabinow[12c] for the reaction they have arbitrarily assigned to diphenylmethylene triplet with this olefin.

Access to k_s and k_t for a wide variety of reactants permits a detailed analysis of structure and reactivity for ^1Fl and ^3Fl. From the limited set of data in Table I, some reactivity trends are apparent. Despite the fact that singlet and triplet carbenes have similar energies, for a given olefin, ^1Fl is more reactive than ^3Fl. Also, over the range of olefins we have investigated, k_s appears to be rather insensitive to structure; all rate constants are within a factor of about ten. This may indicate that the major component of $\Delta G^{\ddagger}$ for these reactions is the entropy term.[15] However, k_t is remarkably structure dependent; diethyl fumarate is about ten times more reactive than diethyl maleate. This dichotomy points to the fundamental difference in the mechanism for reaction of singlet and triplet carbenes with olefins.

Finally, we have observed that the photolysis of DAF in pentane or cyclohexane leads to a result that is strikingly different from that obtained in acetonitrile solution. The eventual products of this reaction are characteristic of hydrogen atom abstraction (or insertion). The laser spectroscopy reveals that the sole observable transient product is formed instantaneously on the timescale of

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(15) P. S. Skell and M. S. Cholod, *J. Am. Chem. Soc.*, **91**, 7131 (1969).

the experiment, has an absorption maximum at 497 nm, and a half-life of 3 μs. We assign the structure of this product to the 9-fluorenyl radical.[16] This finding suggests that there is either a large solvent effect on carbene reactivity or the fluorenyl radical is formed through rapid hydrogen abstraction by electronically excited DAF.[17] We are continuing to examine the structure, solvent, and temperature dependence of the reactions of ^{1}Fl and ^{3}Fl with the expectation that these studies will lead to a fuller understanding of their chemistry.

Acknowledgments. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation for their support of this work. Special thanks also to James Wehmer for his assistance in setting up and using the laser apparatus.

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(16) I. Norman and G. Porter, *Trans. Faraday Soc.*, **230A**, 399 (1955).

(17) Reactions of electronically excited diazo compounds have been suggested previously: W. J. Baron, M. R. DeCamp, M. E. Hendrick, M. Jones, J., R. H. Levin, and M. B. Sohn, *Carbenes 1973-1975*, **1**, 1 (1973); H. Tomioka, H. Kitagawa, and Y. Izawa, *J. Org. Chem.*, **44**, 3072 (1979). A referee has suggested that the short-lived product we observe in CH_3CN solution may be ^{3}DAF. We cannot absolutely rule out this possibility. However, if this is the case, then the chemistry previously attributed to singlet carbenes, ether formation and cyclopropanation of olefins in particular, must also proceed from the triplet-excited diazo compound. This conclusion is apparently inconsistent with the observation that carbenes generated from a variety of thermal or photochemical sources give similar products.[18]

(18) R. A. Moss, *Carbenes 1973-1975*, **1**, 1 (1973).

(19) Fellow of the Alfred P. Sloan Foundation 1977-1979; Dreyfus Teacher-Scholar 1979-1984.

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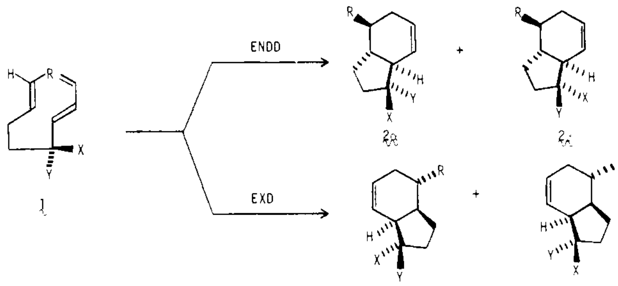
Received March 31, 1980

Cytochalasin Support Studies.[1] Chiral and Stereochemical Control via an Intramolecular Diels-Alder Reaction of a (*Z*)-Diene

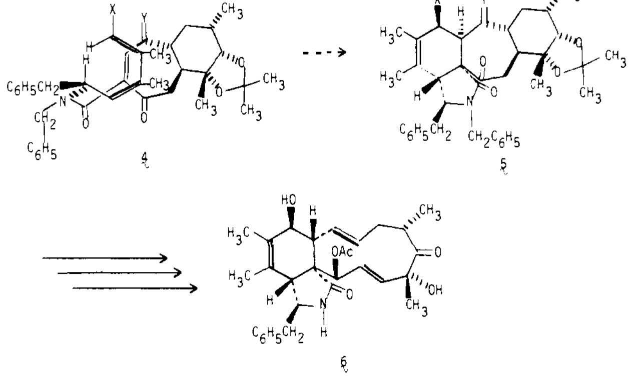
Sir:

The intramolecular Diels-Alder reaction of (*E*)-dienes has become a valuable and often employed strategy at the disposal of the synthetic chemist.[2] A limitation associated with this expedient is that (*E*)-dienes have two relatively easily accessible transition states which, in many instances, afford mixtures of cis and trans fused products (**2** and **3**).[2-5] This situation is further exacerbated by the introduction of an additional asymmetric center at the pentadienylic position of the diene (**1**, X ≠ Y).[6]

Dienes possessing *Z* stereochemistry appear far more amenable for product prediction. Because of its geometry, a (*Z*)-diene can only attain a single transition state in the intramolecular Diels-Alder reaction; more importantly, the stereochemical constraints of the reaction are very strongly transmitted to the carbon which is allylic to the diene moiety. Specifically, in the requisite planar *s*-cis conformation, substitutents at the pentadienylic center experience substantial nonbonded interactions with the *Z* hydrogen at the diene terminus.[7] In the case of an unsymmetrically substituted diene (**4**, **15**), it seems apparent that the reaction will follow the pathway which best minimizes this destabilizing interaction. *For chiral dienes, this effect translates into asymmetric induction by the reaction occurring from a single diastereomeric face of the dienophile.*[8-11]



A useful illustration of this concept would be cyclization of *Z*-amide **4** to lactam **5**. Lactam **5** is a potential substrate for an enolate-promoted fragmentation[1] approach to cytochalasin C **6**.[12]



(X = H; OR / Y = O; β-OH, α-H)

As a prelude to the **4** → **5** transformation, we have examined the simpler model system **15**. Synthesis of this material is accomplished as follows: Treatment of the *N*-tosyl derivative of L(−)-phenylalanine **7**[13] with borane–dimethyl sulfide[14] followed

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(1) Paper 2 in this series; for paper 1, see: Clark, D. A.; Fuchs, P. L. *J. Am. Chem. Soc.* **1979**, *101*, 3567.

(2) Recent reviews: (a) Carlson, R. G. *Annu. Rep. Med. Chem.* **1974**, *9*, 270. (b) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10. (c) Brieger, G.; Bennett, J. N. *Chem. Rev.* **1980**, *80*, 63.

(3) Often the product (**2**) derived from the "endo" transition state (**1a**) is highly favored; however, there are numerous cases[4,5] where mixtures of products or products (**3**) derived only from the "exo" transition state (**1b**) are formed.

(4) (a) Wenkert, E.; Naemura, K. *Synth. Commun.* **1973**, *3*, 45. (b) Bajorek, J. J. S.; Sutherland, J. K. *J. Chem. Soc., Chem. Commun.* **1975**, 1559. (c) Frater, G. *Tetrahedron Lett.* **1976**, 4517. (d) Oppolzer, W.; Achini, R.; Pfenninger, E.; Weber, H. P. *Helv. Chim. Acta* **1976**, *59*, 1186. (e) Oppolzer, W.; Frostle, W. *Ibid.* **1975**, *58*, 590.

(5) (a) Gschwend, H. W.; Lee, A. O.; Meier, H. P. *J. Org. Chem.* **1973**, *38*, 2169. (b) Gschwend, H. W.; Meier, H. P. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 294. (c) Gschwend, H. W. *Helv. Chim. Acta* **1973**, *56*, 1763.

(6) The Roush dendrobine synthesis provides a well-characterized example of all four possible products being isolated: Roush, W. R. *J. Am. Chem. Soc.* **1978**, *100*, 3599.

(7) It is this interaction that is responsible for the 10^5 times reactivity difference between *trans*- and *cis*-pentadiene: (a) Onishchenko, A. S. In "Diene Synthesis"; Monson, S., Ed.; Jerusalem, 1964; pp 11-18. (b) Sauer, J., *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 211. (c) *Ibid.* **1967**, *6*, 16.

(8) There are only three examples of intramolecular Diels-Alder reactions with Z-dienes.[9-11] In their landmark paper, House and Cronin demonstrated that a *Z,E* pair of triene esters cyclize to bicyclic products *at competitive rates*.[9] Their finding indicates that for the (*Z*)-diene the presence of both the diene and dienophile within the same molecule minimizes the steric destabilization of the requisite *s*-cis conformation which is so pronounced in intermolecular Diels-Alder reactions of (*Z*)-dienes.[7] That is, whenever the diene attains the *s*-cis conformation in the intramolecular reaction, it already has the dienophile in close proximity ready to undergo unimolecular cyclization. This must be compared to the intermolecular case where a second-order reaction must be superimposed upon the *s*-cis ⇄ *s*-trans conformational equilibrium. Borch has shown that an unreactive (*Z*)-diene undergoes cis → trans equilibration in preference to direct Diels-Alder cyclization.[10] In another study, Oppolzer has found that a racemic (*Z*)-diene bearing a substituent at the pentadienylic center undergoes a low-yield cyclization at 245 °C to afford a cis-fused bicyclic product (stereochemistry resulting from the pentadienylic center unspecified).[11]

(9) House, H. O.; Cronin, T. H. *J. Org. Chem.* **1965**, *30*, 1061.

(10) Borch, R. F.; Evans, A. J.; Wade, J. J. *J. Am. Chem. Soc.* **1977**, *99*, 1612.

(11) Oppolzer, W.; Fehr, C.; Warneke, J. *Helv. Chim. Acta* **1977**, *60*, 48.

(12) For other synthetic efforts in the cytochalasin area, see ref 4a of Clark, D. A.; Furhs, P. L. *J. Am. Chem. Soc.* **1979**, *101*, 3567. See also: Kim, M. Y.; Wienreb, S. M. *Tetrahedron Lett.* **1979**, 579.

(13) McChesney, E. W.; Swann, W. K. *J. Am. Chem. Soc.* **1937**, *59*, 1116.

(14) Review on BH_3-$(CH_3)_2S$: Lane, C. F. *Aldrichimica Acta* **1975**, *8*, 20.