[91⁻] [IR (IBr) 1135, 1100, 1030, 950, 845 cm^{-1}]. The solid shows signs of decomposition overnight even when stored under argon.

Sodium 2-Phenyl-1,3-dioxolan-2-thiolate ([92⁻]). This solid was prepared from hydroxy thiono ester **37** (292 mg, 1.60 mmol) and NaH (38.5 mg, 1.60 mmol) in dry CH_3CN (51 mL): yield 254 mg (77.6%); mp (sealed tube) 115 °C dec; IR (KBr) 1210, 1035, 925 cm^{-1}. Anal. Calcd for $C_9H_9O_2SNa$: C, 52.93; H, 4.44. Found: C, 52.60; H, 4.61.

Sodium 2-Methyl-1,3-dioxane-2-thiolate ([93⁻]). This solid was obtained from hydroxy thiono ester **38** (163 mg, 1.21 mmol) and NaH (29.2 mg, 1.21 mmol) in dry CH_3CN (15 mL): yield 66.4 mg (35%); IR (KBr) 1120, 1060, 890, 800 cm^{-1}. The solid decomposes on storing overnight.

Sodium 2-Phenyl-1,3-dioxane-2-thiolate ([94⁻]). The salt was prepared in 66.8% yield (223 mg) from hydroxy thiono ester **39** (300 mg, 1.53 mmol) and NaH (36.75 mg, 1.53 mmol) in dry CH_3CN (50 mL): mp (sealed tube) 115 °C dec; IR (KBr) 1210, 1060, 1015, 950, 900 cm^{-1}.

Sodium (2*R,4a*S**,8a*R**)-Hexahydro-2-methyl-1,3-benzodioxan-2-thiolate ([20⁻]).** Sodium hydride (33.4 mg, 1.39 mmol) was added in 1 portion, under a nitrogen atmosphere, to a stirring ice-cold solution of a freshly prepared mixture of thionoacetates **62** and **63** (262 mg, 1.39 mmol) in dry CH_3CN (27.5 mL). After stirring for 30 min, the flask was tightly stoppered and placed in the freezing compartment of a refrigerator (−4 °C) overnight. The precipitated white solid was filtered under nitrogen, washed with anhydrous ether, and dried: yield 102.3 mg (35.0%); IR (KBr) 1440, 1200, 1160, 1065, 1000, 940, 805 cm^{-1}.

(2*R,4a*S**,8a*R**)-Hexahydro-2-methyl-2-(methylthio)-1,3-benzodioxan (99).** Methyl iodide (64.9 mg, 0.45 mmol) was added, under a nitrogen atmosphere, to a suspension of the freshly obtained anionic intermediate [**20**⁻] (96.0 mg, 0.45 mmol) in dry CH_3CN (1.9 mL) at 0 °C. The mixture was stirred for 1 h at 0 °C after which it was diluted with dry CH_2Cl_2 (5.0 mL) and filtered under nitrogen. Concentration of the filtrate gave 93.0 mg (100%) of the title compound: NMR ($CDCl_3$) δ 1.10–2.20 (9 H, m, ring methylenes), 1.75 (3 H, s, CH_3), 2.00 (3 H, s, SCH_3), 3.40–4.00 (3 H, m, OCH and OCH_2); IR (neat) 1450, 1380, 1210, 1160, 1140, 1065, 940, 830 cm^{-1}. (An analytical sample was prepared by short-path distillation: oil bath temperature 120–140 °C, pressure 20 torr). Anal. Calcd for $C_{10}H_{18}O_2S$: C, 59.36; H, 8.96. Found: C, 59.55; H, 8.86.

Acknowledgment. We thank the Research Corporation, the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Biomedical Research Support Program (BRS6 Grant RR 7150), Division of Research Resources, National Institutes of Health, for financial support. We are also grateful to Dr. Kurt Loening for prompt and courteous assistance with the nomenclature. Our sincere thanks also go to Prof. E. Burgess who generously provided us with the results of his MNDO trajectory analysis.

Supplementary Material Available: Syntheses and spectral data for compounds **32–39**, **44–48**, **60–61**, **65–67**, **70–76**, and **95–98** (20 pages). Ordering information is given on any current masthead page.

Thermal Reactions of Cyclopropenone Ketals. Key Mechanistic Features and Scope of the Cycloaddition Reactions of Delocalized Singlet Vinylcarbenes: Three-Carbon 1,1-/1,3-Dipoles

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Abstract: Full details of the key mechanistic features and the preparative scope of the thermal reactions of cyclopropenone ketals which proceed by the thermal generation and subsequent cycloaddition reactions of π-delocalized singlet vinylcarbenes, three-carbon 1,1-/1,3-dipoles lacking octet stabilization, are described and include $_{\omega}2_a$ participation in cheletropic [$_{\pi}2_s + _{\omega}2_a$] nonlinear cycloadditions with an observable endo effect suitable for a one-step, stereoselective construction of *cis*-cyclopropaneacetic acid esters, formal $_{\pi}2_a$ participation in [$_{\pi}2_s + _{\pi}2_a$] cycloadditions suitable for the preparation of functionalized cyclopentenes in which each of the five carbons of the newly formed five-membered ring may bear functionality capable of additional transformations, and $_{\pi}2_s$ participation in [$_{\pi}4_s + _{\pi}2_s$] cycloadditions with selected dienes in direct [3 + 4] cycloadditions suitable for the preparation of functionalized cycloheptadienes capable of further elaboration to tropones/tropolones. The full scope of the thermal reactions of cyclopropenone ketals is demonstrated with the preparation of the complete range of (methoxycarbonyl)tropones, 2-, 3-, and 4-(methoxycarbonyl)tropone and tropone, utilizing the appropriate choice of starting diene and complementary choice of conditions for promoting the thermal [3 + 4] or [4 + 2] cycloaddition of a cyclopropenone ketal. Additional details of a preliminary study of the scope of the cycloaddition reactions of the apparent π-delocalized singlet vinylcarbenes with carbon-heteroatom double bonds are described.

Extensive efforts have focused on the investigation, development, and subsequent application of 1,3-dipolar cycloaddition processes,[2] and the studies in recent years have been characterized by the variety of ways in which the processes can be implemented in the total synthesis of natural products or utilized for the preparation of heterocycles.[2,3] Despite these efforts, the development or use of simple three-carbon 1,3-dipoles in *thermal* cycloaddition reactions has not been described, and their expectant utility remains unrealized.[2,4] The potential participation of three-carbon 1,3-

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(2) *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley-Interscience: New York, 1984; Vol. 1 and 2.

(3) Desimoni, G.; Tacconi, G.; Barco, A.; Pollini. G. P. *Natural Products Synthesis through Pericyclic Reactions*; American Chemical Society: Washington, DC, 1983.

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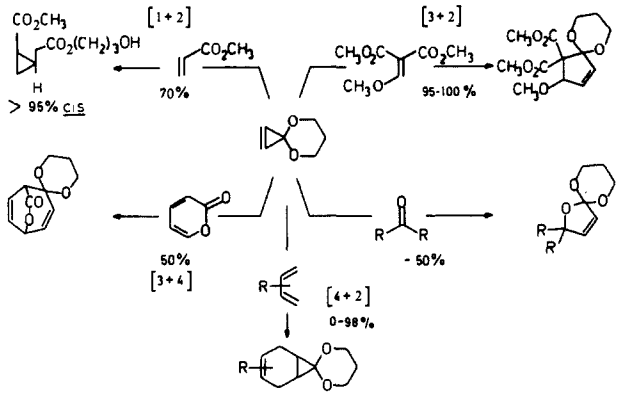
Scheme I



dipoles in a cycloaddition process for the preparation of functionalized cyclopentanes continues to be of particular interest since a general, thermal [3 + 2]-cycloaddition process might be expected to provide an effective complement to the [4 + 2] Diels–Alder cycloaddition reaction employed in the regio- and stereocontrolled preparation of functionalized six-membered rings. However, since simple three-carbon 1,3-dipoles lack octet stabilization and are isoelectronic with vinylcarbenes, their generation and subsequent participation in cycloaddition processes have been discounted from practical application.[5]

Cycloaddition processes employing three-carbon ionic components, e.g., three-carbon delocalized allylic anions[6] or cations,[7] have been extensively investigated and include a select set of three-carbon allylic cations which possess external stabilization and which do participate in general cycloaddition reactions. The most widely recognized of these processes include the extensive work of Noyori[7,8a] and Turro.[7,8b] Related and recent work includes Hoffman's direct utilization of three-carbon allylic cations[7,8c] as 2π components of $[{}_{\pi}4_s + {}_{\pi}2_s]$-cycloaddition processes and the demonstrated utilization of a select set of 4π three-carbon allylic anions in $[{}_{\pi}4_s + {}_{\pi}2_s]$-cycloaddition processes.[6,9] Additional, pertinent work on the development of effective cycloaddition approaches for the introduction of five-membered rings includes Little's applications of the diyl trapping reaction[10] and Danheiser's Lewis acid catalyzed allenylsilane addition–cyclization[11] or two-step alkoxycarbene insertion/alkoxy-accelerated vinylcyclopropane rearrangement.[12]

Additional efforts have focused on the development and utilization of reaction processes equivalent to the use of three-carbon 1,3-dipoles. For this purpose transition-metal-promoted reactions have emerged as the single most explored approach to the effective mediation of three-carbon plus two-carbon addition reactions[13] and include Trost's palladium-promoted cycloaddition of ((acetoxymethyl)allyl)silanes as well as Binger and Noyori's palladium(0)- and nickel(0)-promoted cyclizations of methylenecyclopropanes.

In preceding work we have detailed preliminary investigations of the thermal reactions (70–80 °C) of cyclopropenone ketals with electron-deficient olefins possessing one electron-withdrawing substituent ([1 + 2] cycloaddition),[14a] electron-deficient olefins bearing two, geminal electron-withdrawing substituents ([3 + 2] cycloaddition),[14b] selected carbon–heteroatom double bonds ([3 + 2] cycloaddition),[14c] and α-pyrones ([3 + 4],[14d] [3 + 2],[14b] and [4 + 2][14e] cycloadditions) as well as full details of their dual participation in normal ($HOMO_{diene}$-controlled) and inverse electron-demand ($LUMO_{diene}$-controlled) Diels–Alder reactions with electron-rich, neutral, and electron-deficient dienes under

(5) (a) The initial classification of 1,3-dipoles included 1,3-dipoles without octet stabilization (cf.: Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 565) and included vinylcarbenes, ketocarbenes, ketonitrenes, as well as stabilized allylic cations. These systems today are regarded as ${}_{\pi}2$ reactants and no longer constitute members of the ${}_{\pi}4$ class of 1,3-dipoles customarily employed in 1,3-dipolar cycloadditions. For a full discussion of this and related topics, see: ref 2, Chapter 1. (b) *Carbenes*; Moss, R. A., Jones, M., Jr., Eds.; Wiley-Interscience: New York, 1982; Vol. 1 and 2. For related and recent work on the structure or reactivity of vinylcarbenes, see: (c) Steinmetz, M. G.; Srinivasan, R.; Leigh, W. J. *Rev. Chem. Intermed.* **1984**, *5*, 57. (d) Steinmetz, M. G.; Mayes, R. T. *J. Am. Chem. Soc.* **1985**, *107*, 2111. (e) Davis, J. H.; Goddard, W. A., III; Bergman, R. G. *J. Am. Chem. Soc.* **1977**, *99*, 2427. Hutton, R. S.; Manion, M. L.; Roth, H. D.; Wasserman, E. *J. Am. Chem. Soc.* **1974**, *96*, 4680. Chapman, O. L. *Pure Appl. Chem.* **1974**, *40*, 511. (f) Franck-Neumann, M.; Lohmann, J.-J. *Tetrahedron Lett.* **1978**, 3729. Franck-Neumann, M.; Lohmann, J.-J. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 323. Pincock, J. A.; Boyd, R. J. *Can. J. Chem.* **1977**, *55*, 2482. Yoshida, H.; Kato, M.; Ogata, T.; Matsumoto, K. *J. Org. Chem.* **1985**, *50*, 1145. (g) Gothling, W.; Keyaniyan, S.; de Meijere, A. *Tetrahedron Lett.* **1984**, *25*, 4101, 4105. Weber, W.; de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 138. Weber, W.; de Meijere, A. *Angew. Chem.* **1980**, *92*, 135. Padwa, A.; Cohen, L. A.; Gingrich, H. L. *J. Am. Chem. Soc.* **1984**, *106*, 1065. Zimmerman, H. E.; Fleming, S. A. *J. Am. Chem. Soc.* **1983**, *105*, 622. Padwa, A. *Acc. Chem. Res.* **1979**, *12*, 310. (h) Davies, H. M. L.; Clark, D. M.; Smith, T. K. *Tetrahedron Lett.* **1985**, *26*, 5659. For recent and related work with nucleophilic, singlet carbenes including dimethoxycarbene[5j] and dithiocarbenes,[5j] see: (i) Hoffmann, R. W.; Hauser, H. *Tetrahedron Lett.* **1964**, 197. Hoffmann, R. W.; Hauser, H. *Tetrahedron* **1965**, *21*, 891. Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1971**, *10*, 529. Hoffmann, R. W.; Lilienblum, W.; Dittrich, B. *Chem. Ber.* **1974**, *107*, 3395. Hoffmann, R. W.; Steinbach, K.; Dittrich, B. *Chem. Ber.* **1973**, *106*, 2174. Lemal, D. M.; Gosselink, E. P.; McGregor, S. D. *J. Am. Chem. Soc.* **1966**, *88*, 582. Lemal, D. M.; Gosselink, E. P.; Ault, A. *Tetrahedron Lett.* **1964**, 579. (j) Schollkopf, U.; Wiskott, E. *Justus Liebigs Ann. Chem.* **1966**, *694*, 44. Schollkopf, U.; Wiskott, E. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 485. Lemal, D. M.; Banitt, E. H. *Tetrahedron Lett.* **1964**, 245.

(6) For a discussion of the participation of 4π three-carbon allylic anions in $[{}_{\pi}4_s + {}_{\pi}2_s]$ cycloadditions to provide cyclopentenes, see ref 4a, pp 86–87 and ref 4b, pp 131–135.

(7) For a discussion of the participation of 2π three-carbon allylic cations in $[{}_{\pi}4_s + {}_{\pi}2_s]$ cycloadditions, see ref 4a, p 86, and ref 4b, pp 165–167.

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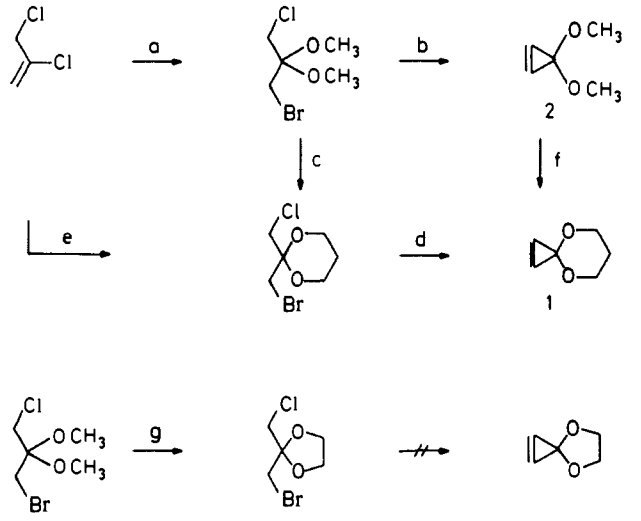
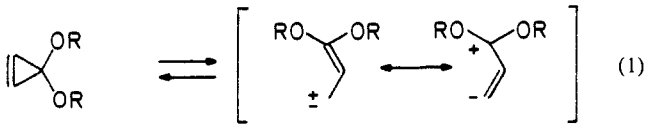
Scheme II[a]



[a] (a) 1.0 equiv of NBS, CH_3OH, catalytic H_2SO_4, 25 °C, 1 h, 40–45%;[20a,b] (b) KNH_2, NH_3, −50 °C, 3 h, 40–65%;[20a,b] (c) 1.0 equiv of 1,3-propanediol, catalytic H_2SO_4, 140 °C ($-CH_3OH$), 8 h, 88%;[19] (d) KNH_2, NH_3, −50 °C, 3 h, 68%;[19] (e) 1.0 equiv of NBS, 4 equiv of 1,3-propanediol, catalytic H_2SO_4, 25 °C, 4.5 h, 12–15%; (f) 1–2 equiv of 1,3-propanediol, $CHCl_3$, 25 °C, 45 min; (g) 1.2 equiv of ethylene glycol, catalytic H_2SO_4, 100 °C, 6 h, 79%.[19a]

room-temperature (25 °C), thermal (70–80 °C), or pressure-promoted (25 °C, 6.2 kbar) reaction conditions,[14e] Scheme I. The factors responsible for the recognition of the thermal and reversible generation of a reactive intermediate derived from the cyclopropenone ketal **1**, which is best characterized as a nucleophilic and π-delocalized singlet vinylcarbene, are detailed herein, eq 1.



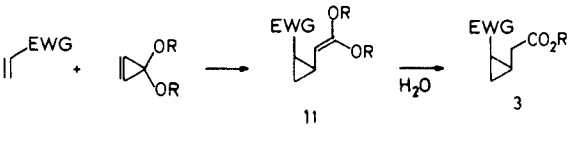
(1)

1 R/R = $(CH_2)_3$

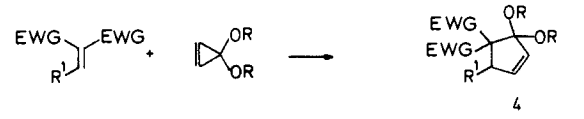
2 R = CH_3

The thermal reactions of cyclopropenone ketals which proceed through the apparent generation of a π-delocalized singlet vinylcarbene include its participation as a 2π component (localized singlet vinylcarbene) in cheletropic $[{}_{\pi}2_s + {}_{\omega}2_a]$ nonlinear cycloadditions to provide cyclopropane ketene acetals with an observable endo effect, its participation as a 2π component (2π three-carbon allylic cation) in $[{}_{\pi}4_s + {}_{\pi}2_s]$ cycloadditions to provided cycloheptadienes, and its formal participation as a 2π component (2π three-carbon allylic cation) in $[{}_{\pi}2_s + {}_{\pi}2_a]$ cycloadditions to provide functionalized cyclopentenes. This last class of thermal reactions of a cyclopropenone ketal may represent the potential but unconfirmed participation of the transient π-delocalized singlet vinylcarbene as a 2π component in cheletropic $[{}_{\pi}2_s + {}_{\omega}2_a]$ nonlinear cycloadditions followed by an accelerated and undetected vinylcyclopropane rearrangement.[15,16]

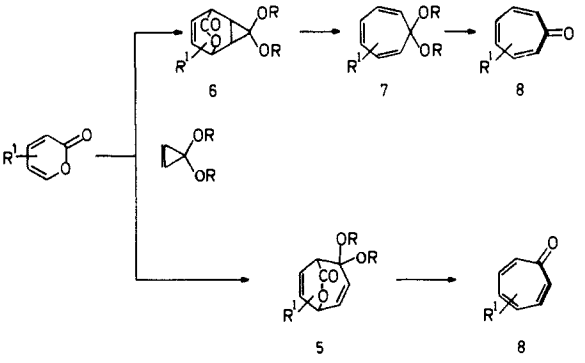
The preparative scope of the cycloaddition reactions of the apparent, transient π-delocalized singlet vinylcarbenes, three-carbon 1,1-/1,3-dipoles, generated in the thermal opening of the cyclopropenone ketals **1** and **2** includes a one-step, stereoselective construction of *cis*-cyclopropaneacetic acid esters (eq 2),[17] a one-step, thermal cycloaddition for the preparation of functionalized cyclopentenes[8-13] in which each of the five carbons of the newly formed five-membered ring bears functionality suitable for additional transformation (eq 3), and a direct [3 + 4] cycloaddition for the preparation of functionalized cycloheptadienes suitable for further elaboration to tropones/tropolones (eq 4).[18] The



(2)

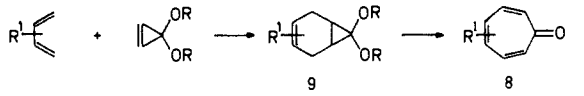


(3)



(4)

complementary scope of the thermal reactions of cyclopropenone ketals is demonstrated with the preparation of a complete range of (methoxycarbonyl)tropones utilizing the appropriate choice of starting diene and complementary choice of conditions for promoting a thermal [3 + 4] or [4 + 2] cycloaddition of a cyclopropenone ketal, eq 4 and 5. Additional details of a preliminary study of the scope of the cycloaddition reactions of the apparent delocalized singlet vinylcarbenes with carbon–heteroatom double bonds are described (eq 6).



(5)

(6)

The successful observation of the intermolecular cycloaddition reactions of the π-delocalized singlet vinylcarbenes can be attributed to the reversible nature of the thermal generation of the apparent, unstabilized three-carbon 1,1-/1,3-dipole. In the presence of suitable electron-deficient substrates, intermolecular cycloaddition reactions of the π-delocalized singlet vinylcarbene may be observed. In the absence of reaction with an effective substrate, reclosure to the starting cyclopropenone ketal is observed. This reversible generation of the three-carbon 1,1-/1,3-dipole permits the observation of effective intermolecular cycloaddition processes and represents a general, and perhaps exclusive,[16] method for the generation and *productive* utilization of

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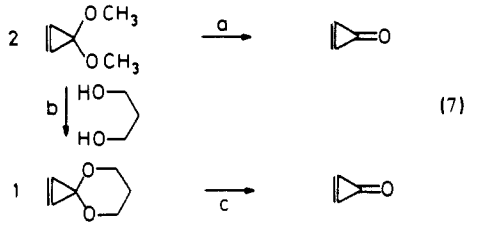
(16) The principal reaction of vinylcarbenes generated by conventional methods[5b] is the intramolecular closure to the corresponding cyclopropene. Consequently, conventional efforts to generate and subsequently trap vinylcarbenes in effective intermolecular cycloaddition processes have been unsuccessful.

(17) (a) Binger, P.; McMeeking, J.; Schafer, H. *Chem. Ber.* **1984**, *117*, 1551. Cocker, W.; Lauder, H. J.; Shannon. P. V. R. *J. Chem. Soc., Perkin Trans. 1* **1974**, 194. Kawashima, M.; Fujisawa, T. *Chem. Lett.* **1983**, 1273. Mitani, M.; Yamamoto, Y.; Koyama, K. *J. Chem. Soc., Chem. Commun.* **1983**, 1446. Weber, W.; de Meijere, A. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 139. (b) Takaya, H.; Suzuki, T.; Kumagai, Y.; Hosoya, M.; Kawauchi, H.; Noyori, R. *J. Org. Chem.* **1981**, *46*, 2854. Bauer, S.; Neupert, M.; Spiteller, G. *J. Chromatogr.* **1984**, *309*, 243.

unstabilized three-carbon 1,1-/1,3-dipoles, eq 1.

Preparation and Reactivity of Cyclopropenone Ketals.[19,20] The prior investigations on the preparation and reactivity of cyclopropenone ketals are limited to the studies of Butler and Breslow.[19,20] Our own observations on the preparation of the cyclopropenone ketal **1**[19] and 3,3-dimethoxycyclopropene (**2**)[20] are detailed in Scheme II and follow the procedures and results detailed in this earlier work.[19,20] As previously described, the attempted extension of the results of these studies to the preparation of cyclopropenone ethylene ketal using the sodium amide closure successfully employed in the preparation of **1** and **2** failed to provide the desired cyclopropenone ketal. Initial studies on the reactions of cyclopropenone ketals have characterized the rapid ketal hydrolysis,[20a,b,f] eq 7, and a mild ketal exchange reaction,



(7)

(a) $CDCl_3$–H_2O, 25 °C, 5 min; (b) 1–2 equiv of 1,3-propanediol, $CHCl_3$, 25 °C, 45 min; (c) $CDCl_3$–H_2O, 25 °C, 30 min.

Scheme II and eq 7. Additional, initial studies on the Diels–Alder [4 + 2]-cycloaddition reactions of 3,3-dimethoxycyclopropene (**2**),[20c] one example each of the reactions of **2** with electron-deficient carbonyls proceeding by an apparent [3 + 2] cycloaddition and a [2 + 2] cycloaddition,[20c] and the reactions of **2** with nucleophiles (amines[20c] and alcohols,[19a] 25 and 70 °C) have been detailed. With the exception of reactions clearly proceeding through the cyclopropenium cation (hydrolysis, ketal exchange), the mechanistic interpretation for the course of the reaction necessarily invoked the nucleophilic or electrophilic character of the strained double bond. Herein we detail studies which provide the evidence of an additional reaction pathway available to the reactive cyclopropenone ketals: the reversible, thermal generation of a nucleophilic and π-delocalized singlet vinylcarbene capable of effective insertion or cycloaddition reactions.

The majority of the work detailed herein has been conducted using the cyclopropenone ketal **1**[19] because of its unusual stability relative to the cyclopropenone ketal **2**.[20] The cyclopropenone ketals **1** and **2** appear to be comparable in the facility with which they participate in thermal cycloaddition reactions which proceed by way of a π-delocalized singlet vinylcarbene.

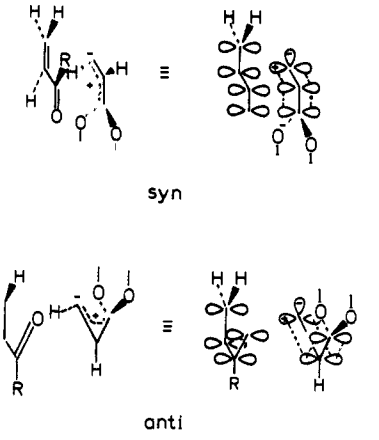
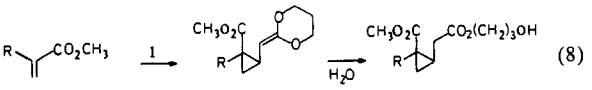


Figure 1.

Results and Discussion

(I) Olefins. (A) Electron-Deficient Olefins Bearing One Geminal Electron-Withdrawing Substituent. Thermal [1 + 2] Cycloaddition (Cheletropic $[_\pi2_s + _\omega2_a]$ Nonlinear Cycloaddition) of π-Delocalized Singlet Vinylcarbenes: Cyclopropane Formation. The results of a full study of the scope of the thermal reaction of cyclopropenone ketals **1** and **2** with electron-deficient olefins bearing one electron-withdrawing substituent, eq 2, are detailed in Table I (entries 1–13).[14a] The reaction proceeds at effective rates at 70–80 °C, and most of the examples detailed in Table I were conducted in nonpolar solvents including benzene or toluene. The cyclopropenone ketals are particularly stable in benzene, and consequently, most of the initial studies have been conducted in this solvent. A subsequent aqueous acid hydrolysis of the initial cyclopropane ketene acetal cycloadducts **11**, which could be detected in the course of the reactions monitored by ^1H NMR spectroscopy,[21] provided the final cycloaddition products **3a–3j** in the yields (0–80%) detailed in Table I. The absolute reaction rate of the [1 + 2] cycloaddition, while being sensitive to the type and extent of olefin substitution, is insensitive to the polarity of the reaction solvent [approximate relative rate for a given substrate: DMF (2.4–1.5) > CH_3CN (1.5–1.4) > C_6H_6 (1.0), eq 8]. The lack



(8)

solvent	equiv of **1**	temp, °C	reaction time	% yield
	[substrate] = 1.0–1.2 M			
R = H				
C_6D_6	2.5	75	12 h	**3a**, 66–70%
CD_3CN	2.3	75	8 h	**3a**, 72%
DMF-d_7	2.3	75	5 h	**3a**, 69%
	approximate relative rates: DMF (2.4) > CH_3CN (1.5) > C_6H_6 (1.0)			
R = CH_3				
C_6D_6	2.0	75	20 h	**3d**, 36–49%
CD_3CN	2.8	75	13 h	**3d**, 49%
DMF-d_7	2.7	75	13 h	**3d**, 50%
CD_3NO_2	2.0	75	little/no reaction	

of a pronounced solvent effect on the observed rate of reaction is consistent with the thermal generation and subsequent rate-limiting cycloaddition of a π-delocalized singlet vinylcarbene in a cheletropic $[_\pi2_s + _\omega2_a]$ nonlinear cycloaddition and is contrary to expectations if a pronounced charge develops in the transition state of the rate-determining step of the reaction.[22] This is further substantiated by the observed endo effect operative in the course

(18) (a) Nozoe, T. *Prog. Org. Chem.* **1961**, *5*, 132. Pauson, P. L. *Chem. Rev.* **1955**, *55*, 9. Pietra, F. *Chem. Rev.* **1973**, *73*, 293. (b) Chapman, O. L.; Fitton, P. *J. Am. Chem. Soc.* **1963**, *85*, 41. Takaya, H.; Hayakawa, Y.; Makino, S.; Noyori, R. *J. Am. Chem. Soc.* **1978**, *100*, 1778. Noyori, R.; Makino, S.; Takaya, H. *Tetrahedron Lett.* **1973**, 1745. Noyori, R. *Acc. Chem. Res.* **1979**, *12*, 61. Evans, D. A.; Hart, D. J.; Koelsch, P. M. *J. Am. Chem. Soc.* **1978**, *100*, 4592. Read, G.; Ruiz, V. M. *J. Chem. Soc., Perkin Trans. 1* **1973**, 1223. Tanaka, K.; Yoshikoshi, A. *Tetrahedron* **1971**, *27*, 4889. Bartlett, P. D.; Ando, T. *J. Am. Chem. Soc.* **1970**, *92*, 7518. (c) Evans, D. A.; Tanis, S. P.; Hart, D. J. *J. Am. Chem. Soc.* **1981**, *103*, 5813. Schreiber, J.; Leimgruber, W.; Pesaro, M.; Schudel, P.; Tlirelfall, T.; Eschenmoser, A. *Helv. Chim. Acta* **1961**, *44*, 540. van Tamelen, E. E.; Spencer, T. A., Jr.; Allen, D. S., Jr.; Orvis, R. L. *Tetrahedron* **1961**, *14*, 8. Martel, J.; Toromanoff, E.; Huynh, C. *J. Org. Chem.* **1965**, *30*, 1752. Kato, M.; Kido, F.; Wu, M. D.; Yoshikoshi, A. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 1516. Kotani, E.; Miyazaki, F.; Tobinaga, S. *J. Chem. Soc., Chem. Commun.* **1974**, 3000.

(19) (a) Butler, G. B.; Herring, K. H.; Lewis, P. L.; Sharpe, V. V., III; Veazey, R. L. *J. Org. Chem.* **1977**, *42*, 679. (b) Boger, D. L.; Brotherton, C. E.; Georg, G. I. *Org. Synth.*, in press.

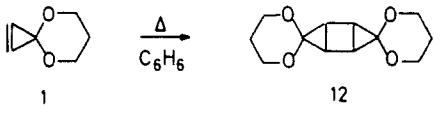
(20) (a) Baucom, K. B.; Butler, G. B. *J. Org. Chem.* **1972**, *37*, 1730. (b) Breslow, R.; Pecoraro, J.; Sugimoto, T. *Org. Synth.* **1977**, *57*, 41. (c) For the first disclosure of the [4 + 2] and selected thermal [3 + 2] cycloadditions of cyclopropenone ketals, see: Albert, R. M.; Butler, G. B. *J. Org. Chem.* **1977**, *42*, 674. (d) For the first observation of [3 + 2] cycloaddition of cyclopropenone ketals with carbon–heteroatom double bonds, see ref 20c. (e) For a description of the dimerization and [2 + 2] cycloadditions of cyclopropenone ketals **1** and **2**, see ref 19a and 20a. (f) Breslow, R.; Oda, M. *J. Am. Chem. Soc.* **1972**, *94*, 4787. Breslow, R.; Oda, M.; Pecoraro, J. *Tetrahedron Lett.* **1972**, 4415, 4419. (g) Eicher, T.; Weber, J. L. *Top. Curr. Chem.* **1975**, *57*, 1.

(21) For example, see experiment detailing the reaction of **1** with methyl methacrylate.

(22) Steiner, G.; Huisgen, R. *J. Am. Chem. Soc.* **1973**, *95*, 5056. Huisgen, R. *Acc. Chem. Res.* **1977**, *10*, 117. Reference 2, Chapter 1.

of the cheletropic nonlinear cycloaddition which provides predominantly the thermodynamically less stable cis isomer of the cyclopropane ketene acetal products. The observed stereoselectivity of the [1 + 2]-cycloaddition reaction decreases with increasing solvent polarity (Table I, entries 1a–d), and this observation is consistent with expectations if the endo effect is derived from a proximal stabilizing interaction of the substrate electron-withdrawing substituent and the allylic cation component of the π-delocalized singlet vinylcarbene, Figure 1.[23] The initial and tentative stereochemical assignments of the major (cis) and minor (trans) isomers of the cyclopropane products were based on spectroscopic properties,[24] and the unambiguous confirmation of the assignments was derived from a comparison of the cycloaddition products of 3,3-dimethoxycyclopropene (**2**) with methyl acrylate (entry 2, Table I, 85% cis, 15% trans; 49% combined yield) with authentic samples.[25] The remainder of the assignments in Table I are based on analogy with this result and are confirmed by the comparable spectroscopic properties of the cyclopropane products.[24] Control studies assured that the cis:trans ratio of the isolated cyclopropane products **3** represented the stereoselectivity of the cycloaddition process. The cycloaddition products **3** were found to be stable to the conditions of workup ($HOAc-H_2O$–THF, 25 °C; hydrolysis of the ketene acetal) as well as purification (SiO_2 chromatography).[26]

In certain instances, solvent participation in reactions with the delocalized singlet vinylcarbenes precluded their use as a medium for the cycloaddition reactions of the cyclopropenone ketals with marginal electron-deficient olefins (e.g., $CHCl_3$, CH_3OH, and CH_3NO_2; cf. Table I, entries 5d, 18g, 18i, and 24c).[27] In addition, a dimerization reaction[19,20] of the cyclopropenone ketals will compete with the reversible generation and subsequent cycloaddition reactions of the π-delocalized singlet vinylcarbene in instances of attempted cycloaddition reactions with marginal electron-deficient substrates, eq 9. The disappearance ($t_{1/2}$ =

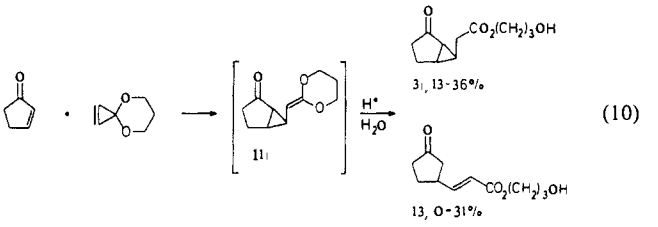


1 12 (9)

10 h, 80 °C, benzene) of the cyclopropenone ketal **1** in the absence of a suitable substrate coincides with the generation of **12**, which can be isolated in yields up to 25% (80 °C, benzene, 21 h). Dimer **12** is the only characterizable product observed or isolated.

The sluggish reactivity of the π-delocalized singlet vinylcarbene with electron-deficient olefins bearing one electron-withdrawing substituent has prevented the attempts to demonstrate unambiguously the maintenance/loss of olefin geometry in the cycloaddition process. For instance, treatment of dimethyl fumarate with cyclopropenone ketal **1** provided **3h** as the exclusive product, and no reaction was observed in the treatment of dimethyl maleate with **1** under identical conditions (Table I, entries 10 and 11).

In only one instance in the complete study of the scope of the [1 + 2]-, [3 + 2]-, and [3 + 4]-cycloaddition reactions has a reaction product been isolated which would suggest a stepwise addition–cyclization reaction proceeding through a detectable dipolar or diradical intermediate, eq 10. The product **13** was

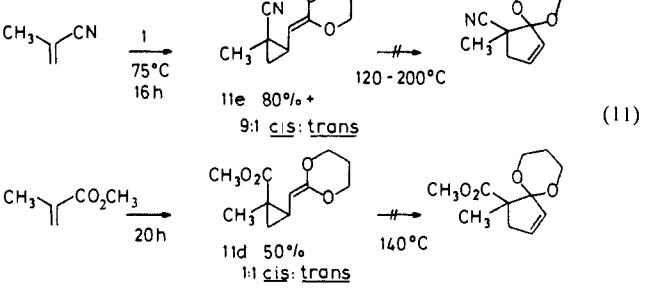


(10)

isolated in erratic yields and occasionally was absent from the reaction mixture. This suggests that **13** represents a secondary product derived from the initial insertion product, and its detection does not constitute firm evidence for a stepwise addition–cyclization process.[28]

Substrates which failed to react productively with the cyclopropenone ketal include phenyl vinyl sulfoxide, ethyl 2-(phenylthio)prop-2-enoate, and dimethyl maleate (Table I, entries 4, 9, and 11) as well as 2-(phenylthio)cyclopent-2-enone, methyl cyclohexene-1-carboxylate, methyl vinyl ketone,[29] and maleic anhydride.[29] The thermal reactions of the cyclopropenone ketal **1** with substrates containing sulfur functionality (e.g., entry 9, Table I) lead to the consumption of starting materials without the production of characterizable products. Similar reactions of singlet carbenes with organosulfur compounds have been described previously.[30]

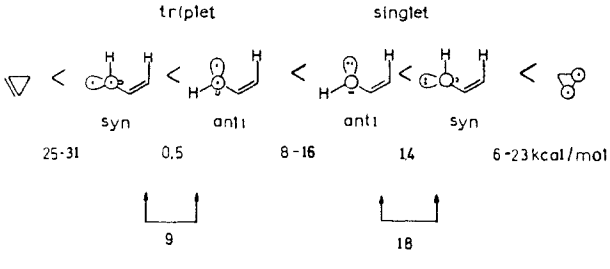
One prominent application of this stereoselective preparation of the *cis*-cyclopropane ketene acetals **11** is the potential of effecting a subsequent thermal vinylcyclopropane rearrangement to provide the corresponding functionalized cyclopentenes.[15] Although this potential has not been investigated to its full extent, attempts to induce the cyclopropane ketene acetals **11d,e** to undergo a vinylcyclopropane rearrangement at modest temperatures (<200 °C) were not successful and provided recovered, unchanged starting material, eq 11.



(11)

Finally, it is important to note that of the cycloaddition processes detailed herein, [1 + 2], [3 + 2], and [3 + 4] cycloadditions, the [1 + 2] cycloaddition of the π-delocalized singlet vinylcarbene in which the 1,1-/1,3-dipole participates as a 2π component in a cheletropic [$_\pi 2_s$ + $_\omega 2_a$] nonlinear cycloaddition represents the slowest and perhaps least effective process described. This may reflect the fact that the transient three-carbon 1,1-/1,3-dipole is

(23) The syn and anti representations of the π-delocalized singlet vinylcarbene follow the accepted nomenclature illustrated below along with the calculated, relative stabilities[5] of the lowest lying triplet and singlet states of the parent vinylmethylene. Syn and anti refer to the relative arrangement of the hydrogens included below.



(24) The cis:trans isomer ratios of the cyclopropane products were determined by ^1H NMR integration of the product $-CH_2CO_2R$ signal. The presence of a vicinal electron-withdrawing substituent cis to this methylene produces a downfield (ca. 0.2 ppm) shift in this signal. This characteristic shift was used to distinguish the cis isomers.

(25) Takaya, H.; Suzuki, T.; Kumagai, Y.; Hosoya, M.; Kawauchi, H.; Noyori, R. *J. Org. Chem.* **1981**, *46*, 2854. Bauer, S.; Neupert, M.; Spiteller, G. *J. Chromatogr.* **1984**, *309*, 243.

(26) Doering, W. E.; Robertson, L. R.; Ewing, E. E. *J. Org. Chem.* **1983**, *48*, 4280.

(27) Turro, N. J.; Cha, Y.; Gould, I. R. *Tetrahedron Lett.* **1985**, *26*, 5951.

(28) It is likely that **13** is generated from **11i** in the acidic aqueous workup and is the result of competitive keto–carbonyl vs. ketene acetal protonation.

(29) The thermal reaction of the π-delocalized singlet vinylcarbene generated from **1** with methyl vinyl ketone and maleic anhydride leads to the consumption of substrate without the isolation of characterizable products. For potential competing reactions with these two substrates, see Table II.

(30) Franck-Neumann, M.; Lohmann, J. J. *Tetrahedron Lett.* **1978**, 3729; **1979**, 2075.

Table I. Thermal Reactions of Cyclopropenone Ketals: Cycloaddition Reactions of Three-Carbon 1,1-/1,3-Dipoles

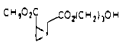
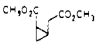
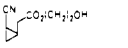
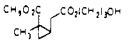
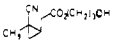
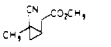
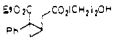
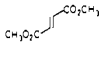
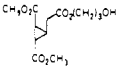
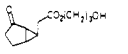
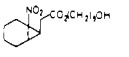
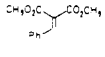
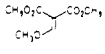
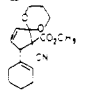
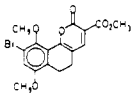
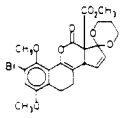
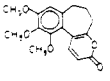
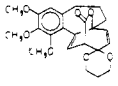
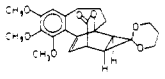
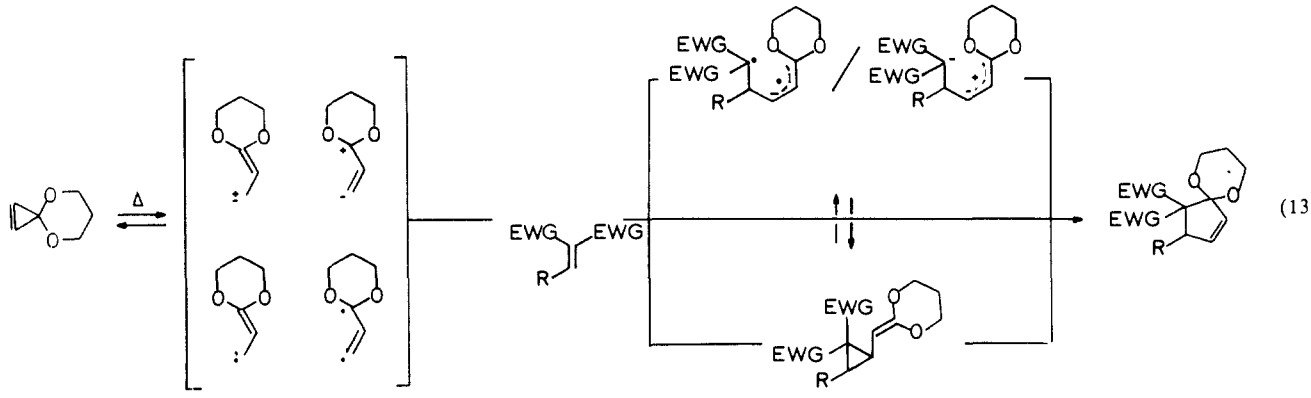
entry	cyclopropenone ketal	substrate[a]	conditions[b] equiv of **1**, temp °C (time, h), solvent	product[c]	yield[d,e]
Electron-Deficient Olefins Bearing One Electron-Withdrawing Substituent: [1 + 2] Cycloaddition[14a] with Cyclopropane Formation					
1a	**1**		2.0, 80 (20), benzene		**3a**, 69% (95:5)
1b			2.5, 75 (12), benzene[g]		**3a**, 66% (nd)
1c			2.3, 75 (8), CH_3CN[g]		**3a**, 72% (60:40)
1d			2.3, 75 (5), DMF[g]		**3a**, 69% (65:35)
2	**2**		2.0, 80 (16), benzene		**3b**, 49% (5–6:1)[25]
3	**1**		2.0, 80 (16), benzene		**3c**, 65% (10:1)
4[a]	**1**		1.8, 80 (16), benzene		no reaction[j]
5a	**1**		2.0, 75 (20), benzene		**3d**, 49% (1:1)
5b			2.8, 75 (13), CH_3CN[h]		**3d**, 49% (2:3)
5c			2.7, 75 (13), DMF[g]		**3d**, 50% (2:3)
5d			2.0, 75 (13), CH_3NO_2		**3d**, trace[m]
6	**1**		2.0, 80 (16), benzene		**3e**, 80% (9:1)
7	**2**		2.0, 75 (16), benzene		**3f**, 63% (5:1)
8[a]	1		2.0, 80 (12), benzene		**3g**, 40% (1:1)
9[a]	**1**		2.0, 80 (20), benzene		0%[f]
10	**1**		1.3, 75 (20), benzene		**3h**, 36% (100:0)
11a	**1**		1.3, 75 (20), benzene		no reaction[j]
11b			1.3, 75 (12), neat		no reaction[j]
12	**1**		2.0, 75 (12–16), benzene		**3i**, 13–36%[k] (nd)
13[a]	**1**		2.0, 75 (12), benzene		**3j**, 24% (nd)
Electron-Deficient Olefins Bearing Two, Geminal Electron-Withdrawing Substituents: [3 + 2] Cycloaddition with Cyclopentene Formation					
14[a]	**1**		1.0, 75 (13), benzene		**4a**, 45%
15[a]	**1**		1.5, 75 (13), benzene		**4b**, 53%[f]
16a[a]	1		1.5, 75 (10), benzene		**4c**, 48%
16b			2.7, 75 (36), toluene		**4c**, 54%
16c			2.5, 75 (32), toluene[l]		4c, 60%
16d			2.0, 25–45 (24–72), CH_2Cl_2		trace
17	**1**		1.5, 75 (15), benzene		**4d**, 57%
18a[a]	**1**		2.0, 80 (5), benzene		**4e**, 95–100%
18b			2.4, 75 (3.5), CD_3CN		**4e**, 85%
18c			2.9, 75 (2.5), DMF-d_7		**4e**, 82%
18d			2.0, 75 (7), $C_6D_5NO_2$		**4e**, 73%
18e			2.1, 75 (5.5), pyridine-d_5		**4e**, 61%
18f			2.0, 75 (12), C_6D_{14}		no reaction[j]
18g			2.0, 75 (12), CD_3NO_2		no reaction[m]
18h			2.0, 45 (24), CD_2Cl_2		trace
18i			2.0, 75 (12), $CDCl_3$		no reaction[m]
19a[a]	**1**		2.0, 80 (4), benzene		**4f**, 86%[n]
19b			1.6, 25 (36), toluene, 6.2 kbar		no reaction
20a[a,o]	**1**		1.6, 80 (12), benzene		no reaction[j]
20b			1.8, 80 (15), heptane		
21a[a,o]			2.2, 80 (3), benzene		
21b			2.2, 80 (16), heptane		
22[a,o]			2.2, 80 (3), benzene		
22b			2.2, 80 (16), heptane		
23[a]	**1**		1.9, 80 (15), benzene		0%[f]
Electron-Deficient Dienes and α-Pyrones Bearing One or Two Electron-Withdrawing Substituents: [3 + 2].[14b] [3 + 4].[14d] and [4 + 2][14e] Cycloaddition					
24a[a]	**1**		1.2, 80 (15), benzene		4g, 62%
24b			1.2, 25 (24–240), neat/benzene		trace[o]
24c			2.0, 60 (48), benzene, 2 equiv of CH_3OH		no reaction[m]
25a[a]	1		5.0, 80 (12), benzene		**4h**, 58% (9:1)

Table I (Continued)

entry	cyclopropenone ketal	substrate[a]	conditions[b] equiv of **1**, temp °C (time, h), solvent	product[c]	yield[d,e]
26[a]	**1**		1.0–2.0, 80 (12), benzene[f]		**4i**, 42%[f]
27a	1		1.2, 80 (8), benzene		**4j**, 10[60]%[f]
27b			3.0, 25 (7 days), CH_2Cl_2,[p] 6.2 kbar		**7a**, 47%[f,q]
28[a]	**1**		2.0, 80 (3), benzene		**4k**, 11[70]%[f]
29a	**1**		1.5, 80 (12), benzene		no reaction[j]
29b			2.6, 25 (48), CH_2Cl_2, 6.2 kbar		**7b**, 59%[f,q]
30a	**1**		2.0, 70 (22), benzene		**5c**, 50%[r]
30b			2.0, 25 (332), CH_2Cl_2, 6.2 kbar		**6c–8c**, 50% conversion[s]
31a[a]	**1**		2.0–3.0, 75 (21–36), benzene		**5d**, 72%[t]
31b			2.0, 25 (5 days), CH_2Cl_2, 6.2 kbar		**6d**, 88%[t]
32[a]	**1**		1.9, 25 (72), neat		**9a**, 60–80%[u]
33a	**1**		1.5, 25 (40), neat		**9b**, 65%[u]
33b			1.0, 75 (4.5), benzene		**9b**, 56%[u]
34	**1**		2.0, 35 (60), neat		**9c**, 70%[u]
			Neutral and Electron-Rich Olefins		
35	**1**		1.0, 80 (20), benzene		no reaction[j]
36	**1**		1.0, 80 (20), benzene		no reaction[j]
37	**1**		1.0, 80 (20), benzene		no reaction[j]
			Alkynes		
38	**1**		1.8, 80 (3), benzene		**10**, 54%
39	**1**		1.7, 80 (17), benzene		no reaction[j]
40	**1**		1.6, 80 (20), benzene		0%[t]

[a] All substrates were obtained from commercial sources, prepared as previously described, or prepared by using procedures adopted from the preparation of closely related structures as detailed in ref 44b. [b] All reactions were run under an inert atmosphere (argon) in the solvent indicated (0.5–2.0 M substrate) as described in the Experimental Section. In entries 1–14, 17, and 18 the crude reaction mixture was exposed to 9:1 tetrahydrofuran–water containing acetic acid (10–12 μL/mL, 25 °C, 15–30 min). Entries 1a–d, 5a–c, 6, 15–19a, 26, and 30a were run in the dark, protected from light, and no qualitative differences in the observed rate of reaction were detected. [c] All products exhibited the expected or reported ^1H NMR, ^{13}C NMR, IR, and MS characteristics consistent with the assigned structure. [d] All yields are based on purified product isolated by chromatography (SiO_2) or recrystallization. [e] The cis:trans isomer ratio in parentheses; was determined by ^1H NMR spectroscopy. [f] The product is unstable to the conditions required for purification, and the actual yield of product, in brackets, was determined by ^1H NMR spectroscopy using an internal standard. [g] Addition of **1** (1.3–1.7 equiv, 2 h, 75 °C) followed by subsequent treatment with additional 1 (1.0 equiv). [h] Addition of **1** (1.8 equiv, 7 h, 75 °C) followed by subsequent treatment with additional **1** (1.0 equiv). [i] The substrate was consumed, and no identifiable product was isolated. [j] The substrate was recovered unchanged, and the cyclopropenone ketal **1** was consumed, dimerizing to afford **12**, with no evidence of the appearance of reaction products from substrate. [k] In several instances, 3-hydroxypropyl 3-(3-oxocyclopentyl)propenoate (**13**) was isolated in variable yields (0–31%). Addition of **1** (1.5 equiv, 75 °C, 20 h) followed by subsequent treatment with additional **1** (1.0 equiv, 75 °C, 12 h). [m] The solvent participates in reactions with the delocalized singlet vinylcarbene. [n] See ref 19b for a detailed procedure (25-mmol scale) for the preparation of **4f**. [o] No trace of the [4 + 2] Diels–Alder cycloaddition product could be detected. [p] No attempt was made to minimize the reaction time. [q] The product is not completely stable to the methods of purification, SiO_2, or Florisil chromatography. The purified yields represent a minimum yield for the conversion; see ref 14e. [r] The structure was confirmed by a single-crystal X-ray structure determination; see ref 32. [s] For a full discussion of this reaction and the isolated products, see ref 14e. [t] For full details and discussions of this work, see ref 14d. [u] Full details of this conversion may be found in ref 14e. [v] For entry 20, R = CH_3; 21, R = $-(CH_2)_5-$; and 22, R = Ph.

Chart I

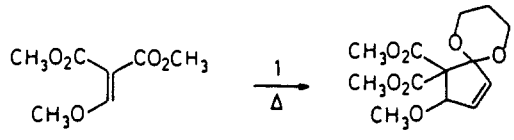


(13)

participating in the cycloaddition process as a localized singlet carbene independent of the conjugative stabilization.[31]

(B) Electron-Deficient Olefins Bearing Two, Geminal Electron-Withdrawing Substituents. Thermal [3 + 2] Cycloaddition (Formal $[_\pi 2_s + _\pi 2_a]$ Cycloaddition) of π-Delocalized Singlet Vinylcarbenes: Cyclopentene Formation. Full details of an investigation of the scope of the thermal reaction of the cyclopropenone ketals **1** and **2** with electron-deficient olefins bearing two, geminal electron-withdrawing substituents, eq 3, are summarized in Table I (entries 14–28, 0–100%).[14b] The observed [3 + 2]-cycloaddition reaction of the transient π-delocalized singlet vinylcarbenes with olefins bearing two, geminal electron-withdrawing substituents proceeds at exceptionally effective rates at 70–80 °C (2–12 h) without the detection of additional reaction intermediates. The initial structure identification of the [3 + 2] cyclopentenone ketal cycloadducts **4** rested on their spectroscopic properties and was confirmed in early studies with a single-crystal X-ray structure determination of **4b**.[14b,32a]

The absolute reaction rate of the [3 + 2] cycloaddition, while being sensitive to the type and extent of olefin substitution, is insensitive to the polarity of the reaction solvent [approximate relative rate for a given substrate: DMF (2) > CH_3CN (1.4) > C_6H_6 (1.0) > C_5H_5N (0.9) > $C_6H_5NO_2$ (0.7), eq 12]. These



(12)

solvent	equiv of **1**	temp, °C	reaction time	yield of **4e**
		[substrate] = 1.0–1.2 M		
C_6D_6	2.0	80	5 h	95–100%
CD_3CN	2.4	75	3.5 h	85%
DMF-d_7	2.9	75	2.5 h	82%
$C_6D_5NO_2$	2.0	75	7 h	73%
C_5D_5N	2.1	75	5.5 h	61%
C_6D_{14}	2.0	75	no reaction	
CD_3NO_2	2.0	75	little/no reaction	
CD_2Cl_2	2.0	45	slow reaction	
$CDCl_3$	2.0	75	solvent participation in thermal reactions of **1**	

approximate relative rates: DMF (2) > CH_3CN (1.4) > C_6H_6 (1.0) > C_5H_5N (0.9) > $C_6H_5NO_2$ (0.7)

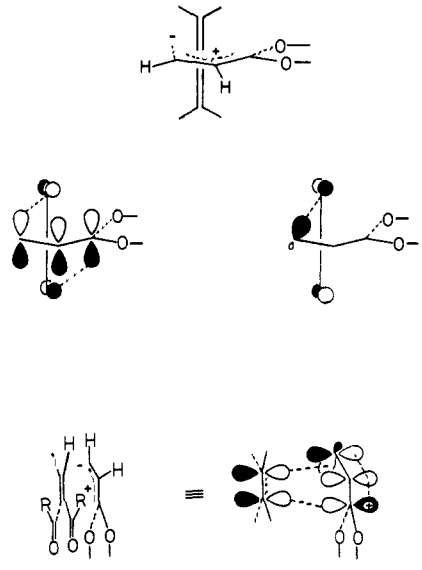


Figure 2.

results do represent an accurate account of the effect of solvent polarity on a rate-determining cycloaddition process since the [3 + 2]-cycloaddition reaction does proceed at a rate much slower than that of the π-delocalized singlet vinylcarbene generation, cf. eq 28. This lack of a pronounced solvent effect on the observed rate of [3 + 2] reaction is consistent with the thermal generation and rate-limiting cycloaddition of a π-delocalized singlet vinylcarbene[33] and is contrary to expectations if the reaction were proceeding by a rate-limiting stepwise addition–cyclization process with the generation of dipolar intermediates,[22] eq 13 (Chart I). Efforts to trap or detect a vinylcyclopropane ketene acetal [1 + 2] cycloadduct and efforts to detect additional products derived from dipolar or diradical intermediates in the course of the observed [3 + 2]-cycloaddition reaction have been unsuccessful.[34] No spectroscopic evidence for the initial generation of a [1 + 2] vinylcyclopropane ketene acetal cycloadduct **11** could be detected in the constant or periodic monitoring of the reaction detailed in Table I, entries 14–28, by ^1H NMR using deuterated solvents as the reaction solvent. The cyclopropane proton adjacent and cis to the ketene acetal of the cycloadducts **11** characteristically appears at 0.5 ppm, and no evidence (<2%) of the appearance of this or other cyclopropane proton signals was observed in the course of the [3 + 2]-cycloaddition reactions that were monitored by ^1H NMR. In addition, no cyclopropane products derived from a vinylcyclopropane ketene acetal cycloadduct **11** (e.g., **3**) were detected upon purification of the [3 + 2] cycloadducts **4**. These unsuccessful efforts and the failure of the related vinylcyclo-

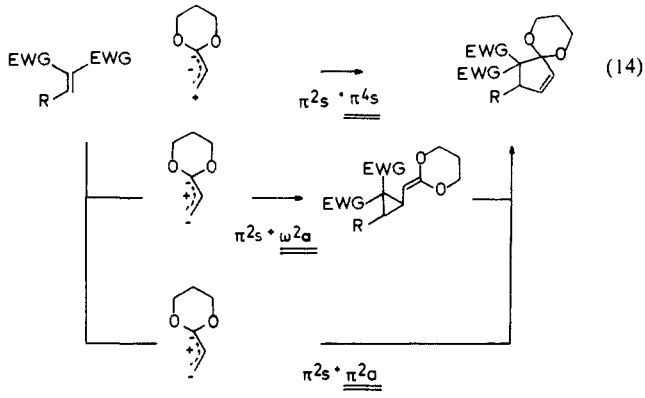
(31) In each of the cycloaddition processes observed with the apparent delocalized singlet vinylcarbene it is only the $[_\pi 2_s + _\omega 2_a]$ cycloaddition which cannot involve the participation of the 2π allylic cation component of the delocalized singlet vinylcarbene.

(32) (a) The single-crystal X-ray structure determination of **4b** was performed by Crystalytics Co., Lincoln, NE. Full details of the work are provided as supplementary material (**15** pages) to ref 14b. (b) The single-crystal X-ray structure determination of **5c** was performed by Prof. Fusao Takusagawa, Department of Chemistry, University of Kansas, and full details (19 pages) are provided as supplementary material.

(33) The experimental results are also consistent with the rate-determining stepwise addition–cyclization of a partially delocalized triplet vinylcarbene.

(34) For related observations: Huisgen, R. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 633. Huisgen, R.; Sustmann, R.; Bunge, K. *Tetrahedron Lett.* **1966**, 3603. Huisgen, R.; Sustmann, R.; Bunge, K. *Chem. Ber.* **1962**, *105*, 1324.

propanes **11d,e**, eq 11, to participate in a vinylcyclopropane rearrangement at temperatures below 200 °C suggest that the initial and obvious assumption that the [3 + 2]-cycloaddition process proceeds in two stages, an initial cheletropic [$_\pi2_s$ + $_\omega2_a$] nonlinear cycloaddition followed by a low-temperature vinylcyclopropane rearrangement, may not be operative,[35] eq 13. Further, no evidence could be secured which would suggest that the reaction proceeds by a diradical, stepwise addition–cyclization sequence which would be an expectant characteristic of a partially delocalized triplet vinylcarbene, eq 13. The fact that no evidence could be secured for a rate-limiting cheletropic [$_\pi2_s$ + $_\omega2_a$] nonlinear cycloaddition and the unlikelihood that the π-delocalized singlet vinylcarbene participates as the conventional 4π allylic anion component of a [$_\pi4_s$ + $_\pi2_s$] cycloaddition suggest the potential $_\pi2_a$ participation of the π-delocalized singlet vinylcarbene in a [$_\pi2_s$ + $_\pi2_a$] two-carbon plus three-carbon cycloaddition, eq 14. In-

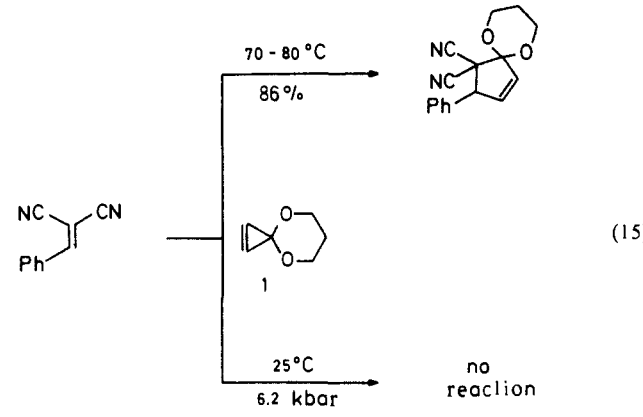


(14)

spection of this possibility reveals that the π-delocalized singlet vinylcarbene possesses an orthogonal filled sp^2 orbital which may contribute an additional bonding interaction in the transition state for the cycloaddition which would be expected to facilitate the reaction. This and the added feature that the π-delocalized singlet vinylcarbene possesses a three-carbon backbone (compared to the two-carbon backbone of the symmetry-allowed but unobserved [$_\pi2_s$ + $_\pi2_a$] olefin dimerization) suggest that it may be ideally suited for participation as a three-carbon $_\pi2_a$ component of a two-carbon plus three-carbon [$_\pi2_s$ + $_\pi2_a$] cycloaddition, Figure 2.[36] The transition state for an unprecedented but attractive and alternative 4π participation of the π-delocalized singlet vinylcarbene in a nonlinear [3 + 2] cycloaddition is also represented in Figure 2. Efforts to distinguish among the possibilities are in progress.

The [3 + 2] cycloaddition of the π-delocalized singlet vinylcarbenes is sensitive to the extent of olefin substitution, and β,β-disubstituted olefins bearing two, geminal electron-withdrawing substituents failed to participate in cycloaddition reactions with the cyclopropenone ketals (Table I, entries 20–22). Additional substrates for which little or no detectable [3 + 2]-cycloaddition reaction was observed include dimethyl ((dimethylamino)-methylene)malonate (no reaction) and thermally unstable, readily enolizable electron-deficient substrates.[37]

Control studies confirmed that observation of the [3 + 2] cycloaddition, as well as the [1 + 2] and [3 + 4] cycloadditions, of the cyclopropenone ketal **1** requires thermal activation. The thermal [3 + 2]-, [1 + 2]-, and [3 + 4]-cycloaddition reactions are equally effective when run in the absence of light and are ineffective under pressure-promoted reaction conditions (6.2 kbar, 25 °C), eq 15.[38]



(15)

Of the cycloaddition processes described herein, [1 + 2], [3 + 2], or [3 + 4] cycloadditions, the apparent [$_\pi2_s$ + $_\pi2_a$] cycloaddition[36] of the transient, π-delocalized singlet vinylcarbenes with electron-deficient olefins bearing two, geminal electron-withdrawing substituents proceeds with the greatest facility. It usually proceeds without competitive cyclopropenone ketal dimerization, eq 9, and is the exclusive course of observed reaction with any substrate bearing two, geminal electron-withdrawing substituents (cf. Table I, entries 24–28). This dominance of the [3 + 2]-cycloaddition reaction over all competitive cycloaddition processes of the π-delocalized singlet vinylcarbene *or* the cyclopropenone ketals themselves (e.g., [4 + 2] cycloaddition) is discussed below. The [3 + 2]-cycloaddition reaction will proceed satisfactorily in nearly any solvent (cf. Table I, entry 18), although benzene or toluene have proven to be the most convenient.

(C) Electron-Deficient Dienes and α-Pyrones. Thermal [3 + 2] and [3 + 4] Cycloaddition of π-Delocalized Singlet Vinylcarbenes vs. [4 + 2] Cycloaddition of Cyclopropenone Ketals: Selective, Competitive Reactions. Complementary Approaches to Cycloheptatrienone (Tropone) Introduction. In expectation of the potential utility of inverse-electron-demand ($LUMO_{diene}$-controlled) Diels–Alder reactions of cyclopropenone ketals,[14e,39] in the initiation of studies designed for the development of direct processes for tropone/tropolone[18] introduction suitable for utilization in the total synthesis of tropoloalkaloids,[14d,40] and in the continued exploration of the thermal reactions of the cyclopropenone ketals, three complementary approaches to cycloheptatrienone formation based on the thermal cycloaddition reactions of **1** have been investigated, eq 4 and 5. The basis for the three approaches is the $_\pi2_s$ participation of the strained olefin of **1** in inverse-electron-demand [$_\pi4_s$ + $_\pi2_s$] Diels–Alder reactions with suitable electron-deficient dienes and α-pyrones (eq 4 and 5) and the three-carbon $_\pi2_s$ participation of a delocalized singlet vinylcarbene in thermal [$_\pi4_s$ + $_\pi2_s$] four-carbon plus three-carbon cycloadditions (eq 4) and

(35) The vinylcyclopropane ketene acetals **11d,e** (eq 11) would be expected to rearrange at higher temperatures than those derived from olefins bearing two, geminal electron-withdrawing groups. However, the [3 + 2] cycloadducts **4** are formed at 70–80 °C (entries 14–28, Table I), and this is at temperatures 120 °C lower than that at which no vinylcyclopropane rearrangement for **11d,e** is observed. Further, in one instance (entry 24b, Table I) a trace of [3 + 2] cycloaddition was detected at 25 °C with no evidence of initial [1 + 2] cycloaddition. If the cycloadduct **4g** is derived by an initial [1 + 2] or [$_\pi2_s$ + $_\omega2_a$] cycloaddition followed by an undetected vinylcyclopropane rearrangement, the rearrangement must be proceeding at 25 °C.

(36) For discussions of the [$_\pi2_s$ + $_\pi2_a$] cycloaddition and factors capable of facilitating the reaction, see ref 4a, pp 163–168, and ref 4b, pp 193–200. Klein, H.; Mayr, H. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 1027. Klein, H.; Erbe, A.; Mayr, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 82. Noyori, R.; Yokoyama, K.; Hayakawa, Y. *J. Am. Chem. Soc.* **1973**, *95*, 2722. Hayakawa, Y.; Yokoyama, K.: Noyori, R. *J. Am. Chem. Soc.* **1978**, *100*, 1791.

(37) Methyl 2,5-dihydro-2-oxo-3-furancarboxylate and 2-(methoxycarbonyl)cyclohex-2-enone both showed a tendency to enolize competitive with participation in thermal (70–80 °C) reactions with the cyclopropenone ketal **1**.

(38) (a) Isaacs, N. S. *Liquid High Pressure Chemistry*; Wiley-Interscience: New York, 1981. (b) The pressure-promoted reactions were carried out in a AGP-10002 Pressure Generator manufactured by Leco Corp., Tenn-Pres Division, Bellefonte, PA 16823. DeShong, P.; Dicken, C. M.; Perez, J. J.; Shoff, R. M. *Org. Prep. Proceed. Int.* **1982**, *14*, 369.

(39) (a) Houk, K. N. *J. Am. Chem. Soc.* **1973**, *95*, 4092. Houk, K. N. *Acc. Chem. Res.* **1975**, *8*, 361. (b) Deem, M. L. *Synthesis* **1971**, 675; **1982**, 701.

(40) (a) For a discussion of colchicine and its related congeners, see: Capraro, H. G. *The Alkaloids*; Academic: Orlando, FL, 1984; Vol. 23, pp 1–70. (b) For a discussion of imerubrine and grandirubrine, see: Buck, K. T. in ref 40a, pp 301–325. (c) For a discussion of rubrolone, see: Palleroni, N. J.; Reichelt, K. E.; Mueller, D.; Epps, R.; Tabenkin, B.; Bull, D. N.; Schuep, W.; Berger, J. *J. Antibiot.* **1978**, *31*, 1218. Schuep, W.; Blount, J. F.; Williams, T. H.; Stempel, A. *J. Antibiot.* **1978**, *31*, 1226.

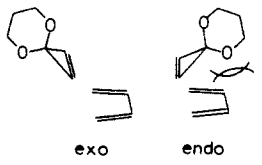
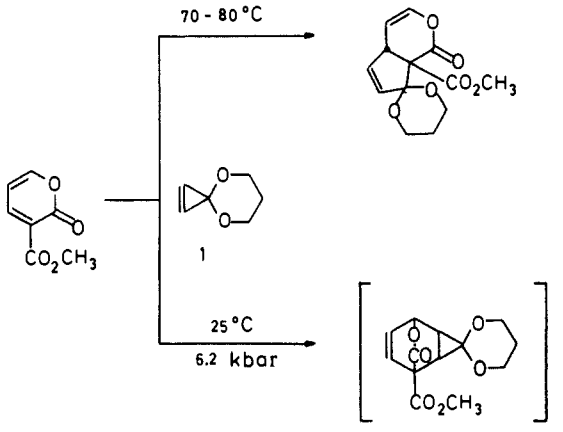


Figure 3.

illustrates two complementary reaction pathways available to the reactive cyclopropenone ketals.

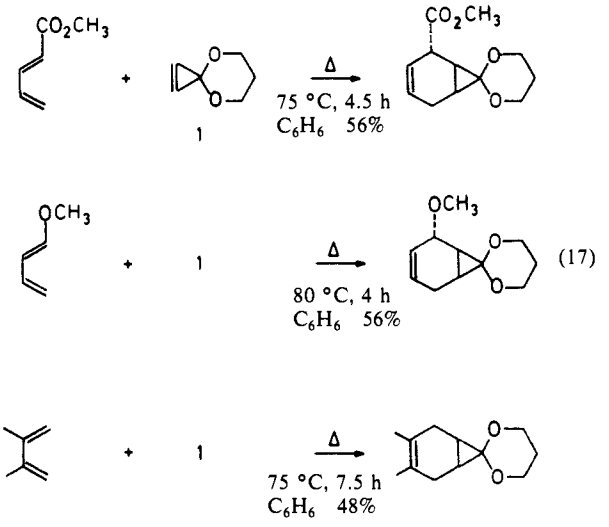
The room-temperature and thermal reactions of the cyclopropenone ketal **1** with electron-deficient dienes and α-pyrones are detailed in Table I (entries 24–34). All substrates containing an electron-deficient olefin bearing two, geminal electron-withdrawing substituents have been found to participate only in a [3 + 2]-cycloaddition reaction with cyclopropenone ketals under thermal reaction conditions (70–80 °C) with exclusive participation of the π-delocalized singlet vinylcarbene. This includes the thermal reaction of the cyclopropenone ketal **1** with electron-deficient dienes which possess two, geminal electron-withdrawing substituents (Table I, entries 24–28). For example, conducting the reaction of 3-(methoxycarbonyl)-2-pyrone with the cyclopropenone ketal **1** under thermal reaction conditions (80 °C, benzene) provided the [3 + 2] cyclopentenone ketal **4j** as the principal product, and conducting the reaction under pressure-promoted reaction conditions (6.2 kbar, 25 °C) provided products derived exclusively from [4 + 2] cycloaddition, eq 16. In addition



(16)

to suggesting that the use of pressure-promoted reaction conditions is the preferred method of accelerating the [4 + 2]-cycloaddition reaction of the cyclopropenone ketals, this observation of clean temperature-dependent reaction products firmly establishes the thermal generation of a reactive intermediate responsible for the [3 + 2]-, as well as the [1 + 2]- and [3 + 4]-, cycloaddition products. If a substrate does not contain an olefin bearing two, geminal electron-withdrawing substituents, [3 + 2] cycloaddition is not observed and competitive thermal cycloaddition reactions of the substrate with the cyclopropenone ketals are observed.

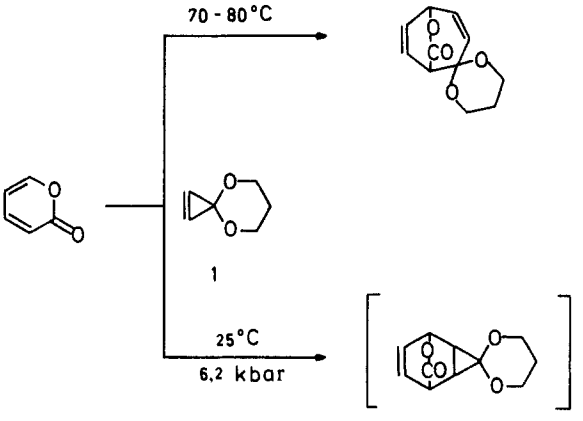
The Diels–Alder reaction of cyclopropenone ketals is subject to a strong steric preference for an exo transition state leading to the [4 + 2] cycloadducts. This preference for exo approach is the result of an unfavorable steric interaction of the geminal dialkoxy substituents of the cyclopropenone ketal with the diene present in the endo transition state, Figure 3. Only in instances in which the endo transition state is comparable with or less sterically demanding than the exo transition state have products derived from endo approach been observed.[14e] In such instances the [4 + 2] cycloaddition proceeds at reduced rates and usually requires the use of pressure-promoted Diels–Alder conditions for observable reaction. Consequently, sterically unhindered (exo transition-state unhindered) electron-deficient, electron-rich, and neutral dienes participate in [4 + 2] Diels–Alder reactions under room-temperature (25 °C, 1 atm), pressure-promoted (25 °C, 6.2 kbar), or thermal (70–80 °C) Diels–Alder conditions at the effective exclusion of products which might be derived from the reversible, thermal generation and subsequent cycloaddition of a π-delocalized singlet vinylcarbene (70–80 °C). Table I (entries 32–34) and eq 17[14e] detail such examples. These reactions proceed



(17)

at rates (70–80 °C, benzene, 4–8 h) competitive with those of many of the thermal [3 + 2]-, [1 + 2]-, and [3 + 4]-cycloaddition reactions of the cyclopropenone ketal **1** with substrates incapable of a Diels–Alder reaction. These observations and the apparent efficiency with which the cyclopropenone ketal **1** *or* the thermally generated π-delocalized singlet vinylcarbene may be trapped in the thermal reactions of **1** confirm that the thermal generation of the π-delocalized singlet vinylcarbene must be reversible.

Sterically hindered (endo and exo transition-state-hindered) electron-deficient dienes including α-pyrone participate in effective [4 + 2] cycloadditions only under pressure-promoted (25 °C, 6.2 kbar)[14e] Diels–Alder conditions (Table I, entries 27b–31b). Further, the thermal reaction of hindered electron-deficient dienes including α-pyrone with the cyclopropenone ketals (70–80 °C, 1 atm) affords products derived from [3 + 4] cycloaddition with three-carbon $_{\pi}2_s$ participation of the π-delocalized singlet vinylcarbene in a [$_{\pi}4_s$ + $_{\pi}2_s$] cycloaddition at the effective exclusion of detectable products derived from Diels–Alder [4 + 2] cycloaddition, Table I (entries 30a–31a) and eq 18.

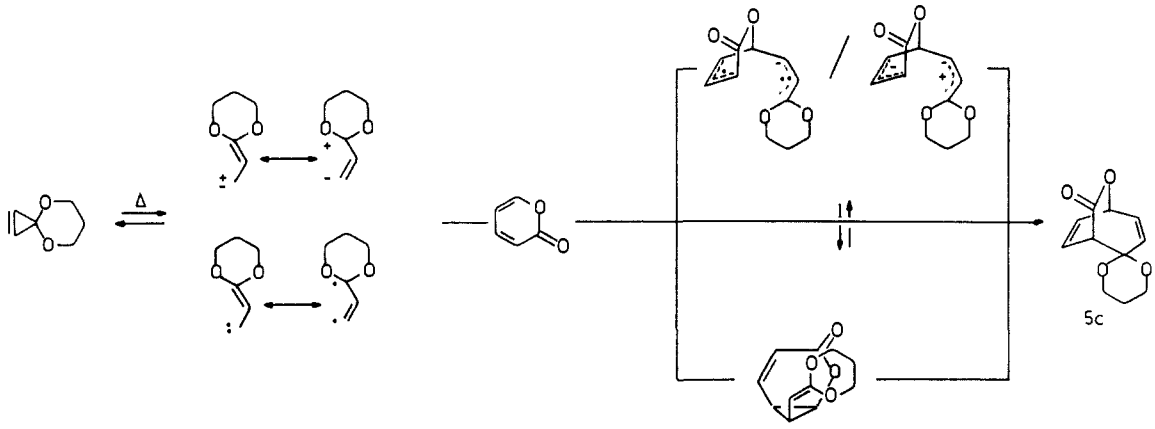


(18)

This selective and complementary behavior of the cyclopropenone ketal is illustrated with the preparation of a complete range of (methoxycarbonyl)tropones utilizing the appropriate choice of diene and α-pyrone and the complementary choice of conditions conducive to promoting [4 + 2] or [3 + 4] cycloaddition, Scheme III.

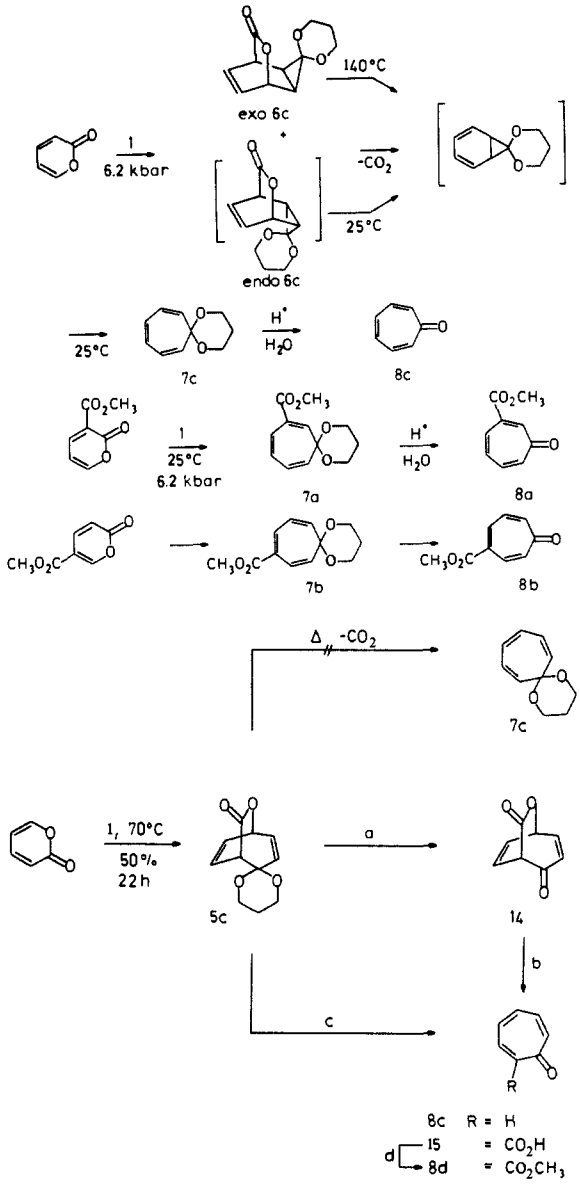
The pressure-promoted [4 + 2] cycloaddition of α-pyrone with cyclopropenone ketal **1** (25 °C, 6.2 kbar)[14e] afforded a mixture of reaction products: *exo*-**6c**, cycloheptatrienone ketal **7c**, and cycloheptatrienone **8c** (resulting from SiO_2 hydrolysis of **7c**), each representing a product derived from the Diels–Alder reaction of **1** with α-pyrone, eq 19. The **6c** endo adduct loses carbon dioxide upon depressurization, and the exo adduct is thermally stable.[41]

Chart II



(21)

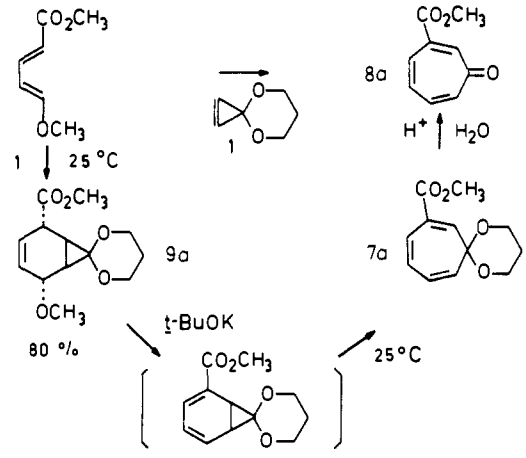
Extensions of these observations to the substituted α-pyrones, 3- and 5-(methoxycarbonyl)-2-pyrone, each possessing an additional electron-withdrawing substituent, provided the cycloheptatrienone ketals **7a** and **7b** directly (6.2 kbar, 25 °C), without the detection or isolation of the intermediate [4 + 2] cycloadducts **6a,b** or the norcaradiene intermediates, eq 19. Decarboxylation of the initial Diels–Alder adducts (25 °C, 1 atm) could be observed upon depressurization of the reaction mixtures, indicating that the conversion of the initial [4 + 2] cycloadducts to the cycloheptatrienone ketals **7a** and **7b** was occurring upon depressurization. The cycloheptatrienone ketals **7a** and **7b**, which are prone to mild hydrolysis, could be purified and characterized prior to conversion to the corresponding 3- and 4-(methoxycarbonyl)-cycloheptatrienones (**8a** and **8b**).[14e]



(19)

(20)

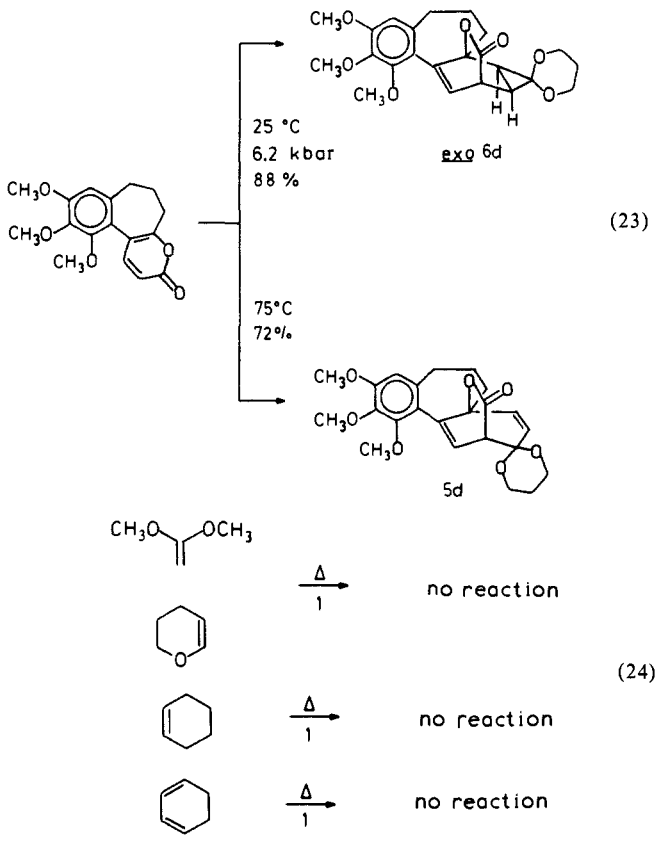
(a) 0.1% aqueous H_2SO_4–CH_3OH (3:1), 4 h, 47%; (b) mesitylene, 140 °C, 4 h; (c) 0.1% aqueous H_2SO_4–CH_3OH (4:1), 14 h; (d) CH_2N_2, ether–THF (1:1), 5 min.



(22)

The thermal reaction (70 °C, benzene, 22 h) of α-pyrone with cyclopropenone ketal **1** provided the [3 + 4] cycloadduct **5c** (50%) at the exclusion of [4 + 2]-cycloaddition products, eq 20. The structure of **5c** was initially assigned on the basis of the spectroscopic properties and was confirmed unambiguously in a single-crystal X-ray structure determination.[32b] Although a number of reaction pathways may account for the formation of **5c** in the thermal reaction of α-pyrone with **1**, the direct $[{}_{\pi}4_s + {}_{\pi}2_s]$ cycloaddition with three-carbon ${}_{\pi}2_s$ participation of a delocalized singlet vinylcarbene in a four-carbon plus three-carbon cycloaddition is most consistent with the results to date and is an expectant behavior of the π-delocalized singlet vinylcarbene, eq 21 (Chart II) and Figure 4. The [3 + 4] cycloadduct **5c** proved resistant to thermolysis, eq 20. Mild, aqueous acid treatment of **5c** provided the bicyclolactone **14**, the product of an unexpectantly selective hydrolysis of the 1,3-propanediol ketal without lactone hydrolysis. Thermolysis of **14** provided cycloheptatrienone (**8c**, tropone), and the elimination of carbon dioxide was observed only at temperatures in excess of 120 °C. Extensive aqueous acid

(41) The observed difference in the rate of decarboxylation of *exo/endo*-**6c** may be attributed to an accelerated rate of decarboxylation of *endo*-**6c** rather than a slowed rate of decarboxylation of *exo*-**6c**. Examples of the thermolysis of related compounds have been compiled; see: Burnier, J. S.; Jorgensen, W. L. *J. Org. Chem.* **1984**, *49*, 3001. For related observations, see: Harvey, J. A.; Ogliaruso, M. A. *J. Org. Chem.* **1976**, *41*, 3374. Kwart, H.; King, K. *Chem. Rev.* **1968**, *68*, 415. Latypova, M. M.; Plemenkov, V. V.; Tuzova, V. B.; Giniyatov, Kh. Z.; Bolesov, I. G. *J. Org. Chem. USSR* (*Engl. Transl.*) **1983**, *82*, 1442. Latypova, M. M.; Plemenkov, V. V.; Kalinina, V. N.; Bolesov, I. G. *J. Org. Chem. USSR* (*Engl. Transl.*) **1984**, *84*, 489. Simmons, H. E.; Fukunaga, T. *J. Am. Chem. Soc.* **1967**, *89*, 5208.



(23)

(24)

treatment of **5c** provided cycloheptatrienone-1-carboxylic acid **15** which upon esterification afforded 2-(methoxycarbonyl)cycloheptatrienone (**8d**).

Treatment of methyl 4-methoxy-1,3-butadiene-1-carboxylate[42] with cyclopropenone ketal **1** (25 °C, 72 h) afforded the [4 + 2] cycloadduct **9a** as the single trans stereoisomer which results from exclusive exo approach of **1** in the Diels–Alder reaction, eq 22. Treatment of **9a** with strong base (KOtBu, THF, 25 °C) effected elimination of methanol, and subsequent rearrangement of the norcaradiene (25 °C) provided **7a**. Hydrolysis of **7a** provided 3-(methoxycarbonyl)cycloheptatrienone (**8a**) identical with the material previously described.[14e]

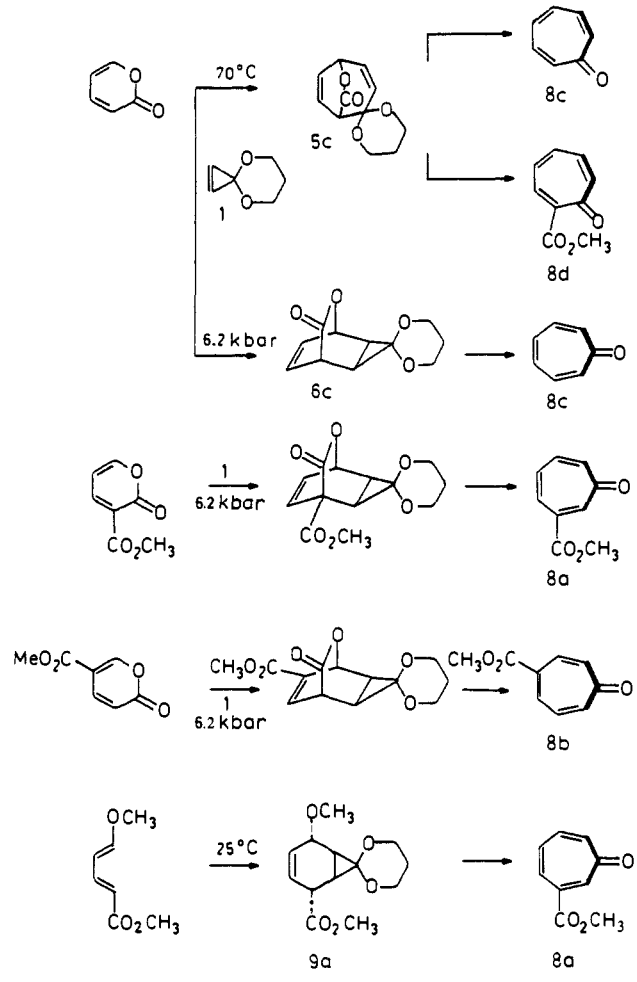
The generality of the [4 + 2]- and thermal [3 + 4]-cycloaddition reactions of the cyclopropenone ketal **1** has been further confirmed in initial studies on their application to the total synthesis of colchicine[14d] utilizing Eschenmoser's α-pyrone, Table I (entry 31) and eq 23. The facility and apparent selectivity with which this highly substituted α-pyrone participates in the thermal [3 + 4]-cycloaddition process further suggests that the reaction constitutes the direct $_{\pi}2_s$ participation of the π-delocalized singlet vinylcarbene in a $[_{\pi}4_s + _{\pi}2_s]$ cycloaddition.

(D) Neutral and Electron-Rich Olefins. A series of representative electron-rich and neutral olefins (Table I, entries 35–37) showed no tendency to participate in addition–cyclization or cycloaddition reactions with the thermally generated vinylcarbenes. This lack of reactivity of the unactivated and electron-rich olefins with the apparent vinylcarbene is an expectant characteristic of a π-delocalized singlet vinylcarbene and is contrary to the expected reactivity of a partially delocalized triplet vinylcarbene. This behavior of the vinylcarbene and its additional lack of reaction with cyclohexadiene, eq 24, provide further confirmation that the thermally generated cyclopropenone ketal derived reactive intermediate may be best characterized as a π-delocalized singlet vinylcarbene.

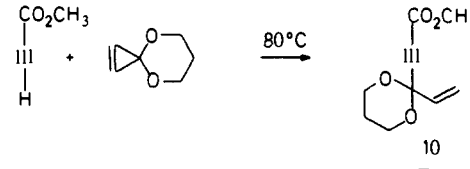
(II) Alkynes. Electron-deficient and neutral alkynes failed to participate in thermal reactions with the cyclopropenone ketals (Table I, entries 38–40). Only the unsubstituted electron-deficient alkyne methyl propiolate (eq 25) was found to participate in an

(42) Maddaluno, J.; d'Angelo, J. *Tetrahedron Lett.* **1983**, *24*, 895. Smithers, R. H. *J. Org. Chem.* **1978**, *43*, 2833.

Scheme III



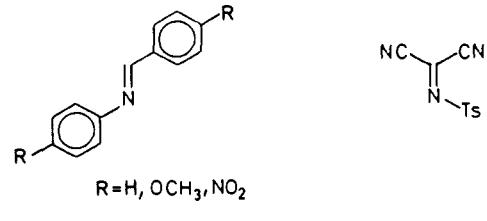
insertion reaction with a thermally generated π-delocalized singlet vinylcarbene. The thermal reaction of methyl propiolate with **1** provided the selectively protected ketoalkyne **10** cleanly.



(25)

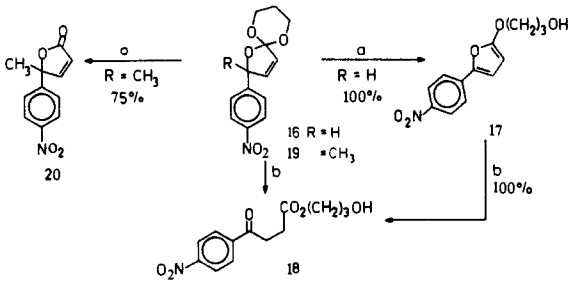
(III) Substrates Bearing Carbon–Heteroatom Double Bonds. Thermal [3 + 2] Cycloaddition of π-Delocalized Singlet Vinylcarbenes: Butenolide, Furan, and γ-Keto Ester Formation. The facility with which the nucleophilic, π-delocalized singlet vinylcarbenes may be trapped in the thermal reactions of cyclopropenone ketals with electron-deficient olefins (C=C) suggested that a comparable investigation of the potential reactivity of systems bearing carbon–heteroatom double bonds (C=O, C=N) be conducted.[43] Table II details the results of a preliminary investigation of the potential scope of the thermal reaction of the cyclopropenone ketals **1** and **2** with representative carbonyl (C=O) containing substrates which proceeds by way of the thermal generation and subsequent, apparent [3 + 2] cycloaddition of a

(43) For the first observation of a [3 + 2] cycloaddition of cyclopropenone ketals with a carbonyl group, see ref 20c. (b) The imines shown below failed to react with the cyclopropenone ketal **1** (80 °C, 12 h, benzene/heptane).



delocalized singlet vinylcarbene, Scheme IV. The initial [3 + 2] cycloadducts serve as viable precursors to furans, γ-keto esters, and butenolides, Scheme IV. In each of the examples detailed in Table II, cycloaddition proceeds under mild conditions (70–80 °C, 12 h), with solvent playing little apparent role in determining the course or rate of cycloaddition.

In initial studies conducted with *p*-nitrobenzaldehyde and *p*-nitroacetophenone, the butenolide ortho ester [3 + 2] cycloadducts **16** and **19** were isolated in pure form by rapid chromatography on silica gel (method A). Mild aqueous acid hydrolysis of **16** afforded the furan **17**, and mineral acid treatment of cycloadduct **16** or furan **17** provided the γ-keto ester **18**. A similar mild aqueous acid treatment of **19** provided the butenolide **20**, eq 26.



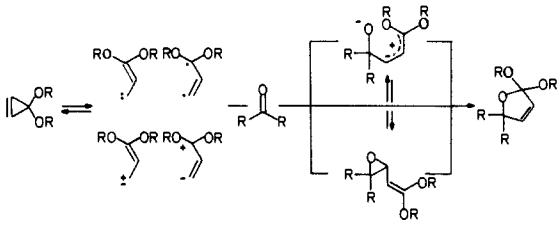
(26)

(a) HOAc, THF–H_2O, 25 °C; (b) HCl, acetone, 25 °C.

In the subsequent studies detailed in Table II no attempt was made to isolate the unstable butenolide ortho ester cycloadducts, and the crude reaction mixtures were subjected to mineral acid (HCl, acetone, method B) or mild aqueous acid (HOAc–H_2O–THF, method C) hydrolysis conditions to afford the γ-keto esters or furan/butenolides directly.

The potential cycloadditions of the π-delocalized singlet vinylcarbenes with additional substrates bearing carbon–heteroatom double bonds were unsuccessfully investigated and include benzophenone, cyclohexanone, 1,3-diphenylacetone, *p*-nitrobenzyl glyoxylate, and 2,2-diphenylacetaldehyde (C=O), as well as imines[43b] (C=N). The results suggest that only selected substrates with carbon–heteroatom double bonds are sufficiently reactive to participate in an observed [3 + 2]-cycloaddition reaction with the π-delocalized singlet vinylcarbenes.

No evidence could be secured which would confirm or eliminate the clear potential that the observed [3 + 2] thermal cycloaddition reaction of the cyclopropenone ketals with substrates bearing carbon–heteroatom double bonds proceeds by a stepwise dipolar addition–cyclization or initial [1 + 2] insertion of the delocalized singlet vinylcarbene followed by subsequent dipolar rearrangement to the observed [3 + 2] cycloadducts, eq 27.



(27)

Summary. The key mechanistic features of the reversible, thermal generation and subsequent cycloaddition reactions of π-delocalized singlet vinylcarbenes detailed herein included the following: (i) The thermal generation of a reactive intermediate responsible for the observed [1 + 2]-, [3 + 2]-, and [3 + 4]-cycloaddition reactions of the cyclopropenone ketals was firmly established with the demonstration of temperature-dependent reaction products (cf. eq 16, 18, 23, and 28). (ii) Control studies confirmed that thermal activation is required for generation of the reactive intermediate (cf. eq 15). (iii) The reversible (cf. eq 5 and 17 vs. eq 2–4) thermal generation of the reactive intermediate was occurring at an unexpectedly productive rate, eq 28. (iv) The reactive intermediate displayed chemical properties characteristic only of a π-delocalized singlet vinylcarbene (cf. eq 8, 12, 23, 25, and 28, Figure 1 endo effect and Figure 4) and displayed no typical properties characteristic of a partially delocalized triplet vinylcarbene (cf. eq 24) consistent with expectations based on the observations that factors which stabilize empty p-orbitals provide the necessary stabilization for observable ground-state singlet carbenes. (v) The mild thermal generation of the π-delocalized singlet vinylcarbene from cyclopropenone ketals is distinct from the behavior of unactivated cyclopropenes, eq 29.

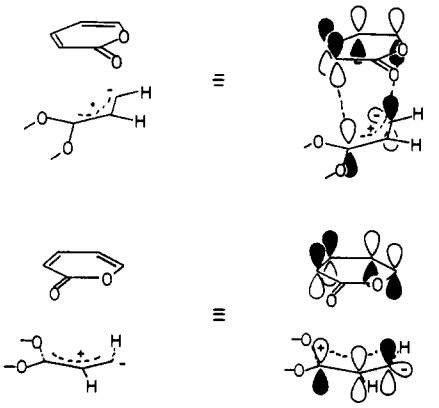
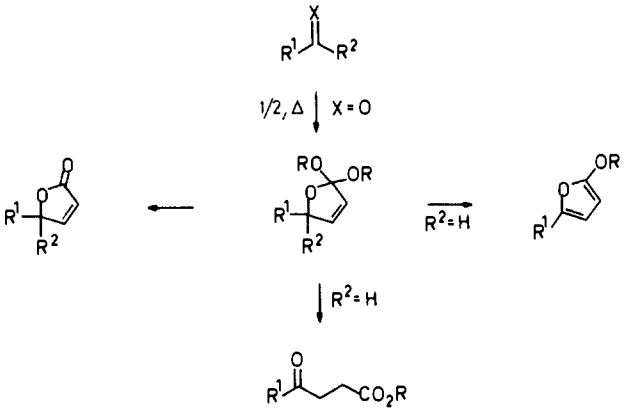
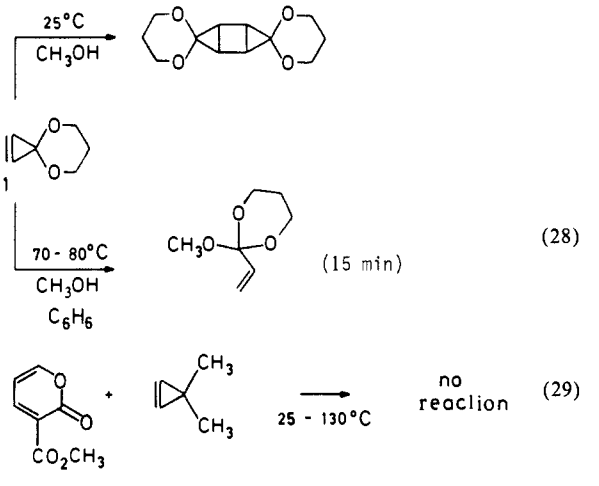


Figure 4.

Scheme IV





(28)

(29)

The scope of the cycloaddition processes of π-delocalized singlet vinylcarbenes, three-carbon 1,1-/1,3-dipoles, has been investigated and include [1 + 2] cycloaddition with electron-deficient olefins bearing one electron-withdrawing substituent with the stereoselective preparation of cyclopropaneacetic acid esters (cheletropic $[\pi 2_s + \omega 2_a]$ nonlinear cycloaddition of the delocalized three-carbon 1,1-/1,3-dipole), thermal [3 + 2] cycloaddition with electron-deficient olefins bearing two geminal electron-withdrawing substituents with the direct preparation of cyclopentenone ketals (formal $[\pi 2_s + \pi 2_a]$ cycloaddition of the delocalized three-carbon 1,1-/1,3-dipole), thermal [3 + 4] cycloaddition with selected

α-pyrones with the direct preparation of cycloheptadienone ketals suitable for conversion to cycloheptatrienones (tropones)/tropolones ([$_{\pi}4_s$ + $_{\pi}2_s$] cycloaddition of the delocalized three-carbon 1,1-/1,3-dipole), as well as [3 + 2] cycloaddition with selected carbon–heteroatom double bonds (C=O). The reversible, thermal generation of π-delocalized singlet vinylcarbenes from cyclopropenone ketals constitutes a general and perhaps exclusive approach to the generation and *productive* utilization of three-carbon 1,1-/1,3-dipoles.

Experimental Section[44]

3,3-Dimethoxycyclopropene (**2**)[20] and 2-(bromomethyl)-2-(chloromethyl)-1,3-dioxolane[19,20] were prepared as described. The preparation of 3-(methoxycarbonyl)cycloheptatrienone 1,3-propanediyl ketal (**7a**),[14e] 3-(methoxycarbonyl)cycloheptatrienone (**8a**),[14e] 4-(methoxycarbonyl)-cycloheptatrienone 1,3-propanediyl ketal (**7b**),[14e] and 4-(methoxycarbonyl)cycloheptatrienone (**8b**)[14e] and the pressure-promoted [4 + 2]-cycloaddition reactions of α-pyrone,[14e] Eschenmoser's α-pyrone[44] (Table I, entry 31),[14d] methyl 2,4-pentadienoate,[14e] methyl 5-methoxy-2,4-pentadienoate,[14e] ethyl sorbate,[14e] 1-methoxy-1,3-butadiene,[14e] and 2,3-dimethyl-1,3-butadiene[14e] have been described previously.

Cyclopropenone 1,3-Propanediyl Ketal (1).[19] A 100-mL, round-bottom flask equipped with a 10-mL Dean-Stark apparatus and a condenser was charged with 30.0 g (0.138 mol) of 1-bromo-3-chloro-2,2-dimethoxypropane,[20b] 10.0 mL (0.138 mol) of 1,3-propanediol, and 3 drops of concentrated sulfuric acid. The resulting solution was heated (bath temperature 140 °C) for 8 h with distillative removal of methanol (ca. 11 mL). The mixture was allowed to cool to room temperature and the crude product partitioned in 150 mL of pentane and 40 mL of water. The organic phase was dried with magnesium sulfate and the solvent removed under reduced pressure. Distillation (1 mm, 90–95 °C) yielded 27.7 g (88%) of 2-(bromomethyl)-2-(chloromethyl)-1,3-dioxane: mp 61–62.5 °C; ^{1}H NMR δ 3.96 (4 H, t, J = 6 Hz, OCH_2), 3.80 (2 H, s, CH_2Br), 3.70 (2 H, s, CH_2Cl), 1.78 (2 H, p, J = 6 Hz, CH_2); IR ($CHCl_3$) ν_{max} 3030, 3000, 2900, 1485, 1430, 1245, 1202, 1158, 1135, 1105 (s), 1020 cm^{-1}.

A 1000-mL, three-necked round-bottom flask was equipped with a gas inlet, an acetone–dry ice condenser with a drying tube containing potassium hydroxide pellets, a stopper, and a magnetic stirrer. An acetone–dry ice bath was placed under the flask, and anhydrous ammonia was condensed into the flask (400 mL). A small piece of potassium metal (ca. 0.5 g) was introduced into the liquid ammonia and the cooling bath removed. A catalytic amount of anhydrous ferric chloride was then added, and the reaction mixture was allowed to warm to reflux temperature, at which time the deep-blue color turned to gray. The remaining potassium metal (12.2 g, 0.31 mol total) was added in 0.5-g pieces over ca. 30 min. The reaction mixture was allowed to stir until a gray suspension resulted. A −50 °C cooling bath was placed under the flask, and the stopper was replaced with a 125-mL, pressure-equalized dropping funnel containing 22.9 g (0.1 mol) of 2-(bromomethyl)-2-(chloromethyl)-1,3-dioxane in 50 mL of anhydrous ether. This solution was added dropwise to the solution of freshly generated potassium amide over 15 min while the temperature was maintained at −50 °C. After the mixture stirred for 3 h at −50 to −60 °C, solid ammonium chloride was added slowly to quench the excess potassium amide. The cooling bath was removed and the ammonia allowed to evaporate. During the course of the evaporation, anhydrous ether (350 mL total) was added dropwise through the addition funnel to replace the ammonia. After the temperature had reached 0 °C, the brown reaction mixture was filtered to remove the inorganic salts, and the salts were washed twice with 25 mL of anhydrous ether. The combined ethereal filtrate and washes were concentrated under reduced pressure (30 mm, <25 °C) to a constant weight. Distillation (1.25 mm, 30–35 °C, cooling the receiver in an ice bath) afforded cyclopropenone 1,3-propanediyl ketal (**1**) as a colorless liquid: 7.6 g, 68% yield; ^{1}H NMR ($CDCl_3$) δ 7.84 (2 H, s, CH=CH), 4.01 (4 H, t, J = 6 Hz, OCH_2), 1.83 (2 H, p, J = 6 Hz, CH_2); ^{13}C NMR ($CDCl_3$) δ 125.6 (d), 81.0 (s), 66.0 (t), 25.8 (t); IR (film) ν_{max} 3101, 2980, 2870, 1600, 1475, 1460, 1435, 1370, 1300, 1275, 1155, 1090, 1030, 935, 910, 865, 740 cm^{-1}.

General Procedure for the Thermal Reactions of Cyclopropenone Ketal 1 with Olefins Possessing One Electron-Withdrawing Substituent. Preparation of 3a. Methyl acrylate (45 μL, 43 mg, 0.50 mmol) and cyclopropenone ketal **1** (115 mg, 1.0 mmol, 2 equiv) were combined in benzene (0.5 mL) under argon, and the resulting solution was warmed at 80 °C (20 h). The crude reaction mixture was concentrated in vacuo, and the crude product was taken up in tetrahydrofuran (1 mL) and treated with 3:1 acetic acid–water (0.1 mL) at 25 °C (20 min). The reaction mixture was diluted with water and extracted with ethyl acetate (1×) and methylene chloride (2×). The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. Chromatography (MPLC, 7 × 250 mm, 50% ethyl acetate–hexane eluant) afforded 75 mg (108 mg theoretical, 69%) of **3a** (95:5 cis:trans isomers) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 4.20 (2 H, t, J = 7 Hz, CO_2CH_2), 3.65 (5 H, s and overlapping t, J = 7 Hz, OCH_3, CH_2OH), 2.65 (2 H, dd, J = 7, 1 Hz, CH_2CO), 2.1–1.5 (4 H, m, two CH, $OCH_2CH_2CH_2O$), 1.3–0.9 (2 H, br m, cyclopropyl CH_2); ^{13}C NMR ($CDCl_3$) δ 173, 172.9 (two s, two C=O), 61.4 (t, CO_2CH_2), 59.2 (t, CH_2OH), 51.6 (q, OCH_3), 32.3, 31.8 (two t, CH_2CO_2, $OCH_2CH_2CH_2O$), 17.5, 16.7 (two d, two cyclopropyl CH), 13.4 (t, cyclopropyl CH_2); IR (film) ν_{max} 3460 (OH), 2955, 2896. 1734 (C=O), 1441, 1389, 1358, 1329, 1304, 1271, 1242, 1196, 1174, 1136, 1078, 1035 cm^{-1}; CIMS (isobutane), m/e (rel intensity) 217 (M + 1, 93), 199 (17), 185 (19), 141 (100); HRMS, $C_{10}H_{17}O_5$ requires m/e 217.1075, found, 217.1083.

3b:[25] ^{1}H NMR ($CDCl_3$) δ 3.68 (6 H, s, two CO_2CH_3), 2.65, 2.38 (2 H, dd, J = 7, 1 Hz; d, J = 7 Hz, 5:1 cis:trans CH_2CO_2), 2.0–1.3 (1 H, br m, $CHCO_2CH_3$), 1.4–0.9 (3 H, br m, $CH_3O_2CCHCH_2CHCH_2$); ^{13}C NMR ($CDCl_3$) δ 173.1, 173.0 (two s, two C=O), 51.5, 51.4 (two q, two OCH_3), 32.1 (t, $CH_2CO_2CH_3$), 17.5, 16.7 (two d, cyclopropyl CH's), 13.3 (t, cyclopropyl CH_2); IR (film) ν_{max} 3030, 2975, 1738 (C=O), 1448, 1390, 1339, 1275, 1200, 1142, 1090, 1009, 952, 880, 840 cm^{-1}.

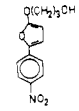
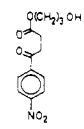
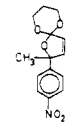
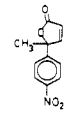
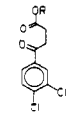
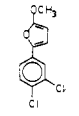
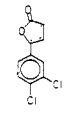
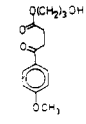
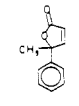
3c: ^{1}H NMR ($CDCl_3$) δ 4.25 (2 H, t, J = 7 Hz, CO_2CH_2), 3.65 (2 H, t, J = 7 Hz, CH_2OH), 2.55, 2.30 (2 H, m and d, 10:1, J = 6 Hz, cis:trans CH_2CO_2), 2.05 (s, OH), 1.87 (2 H, p, J = 7 Hz, $OCH_2CH_2CH_2O$), 1.7–1.1 (3 H, m, $CHCH_2CH$ and $CHCN$), 0.90 (1

(44) (a) Melting points were determined on a Thomas-Hoover capillary melting point apparatus. Infrared spectra (IR) were obtained on a Beckman IR-33, Perkin-Elmer 710B, or IBM FTIR 32 spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian FT-80A or Varian XL-300 spectrometer in $CDCl_3$ unless otherwise noted. Electron impact (EI), chemical ionization (CI), mass spectra (MS), and high-resolution mass spectra (HRMS) were obtained on a Varian CH-5 or Ribermag R10-10 mass spectrometer by Charles Judson and Robert Drake. Microanalyses were performed by Tho I. Nguyen on a Hewlett-Packard Model 185 CHN analyzer at the University of Kansas. Medium-pressure liquid chromatography (MPLC) was performed on silica gel 60 (230–240 mesh).[45] Dry tetrahydrofuran was distilled immediately before use from sodium benzophenone ketyl. Toluene and mesitylene were distilled from powdered calcium hydride. Benzene was distilled from sodium benzophenone ketyl. Benzene-d_6 and *N,N*-dimethylformamide-d_7 were obtained from Stohler Isotopes. Nitrobenzene-d_5, nitromethane-d_3, and cyclohexane-d_{12} were obtained from Thompson Packard, Inc. Extraction and chromatography solvents (CH_2Cl_2, EtOAc, hexane) were distilled before use. All reactions were run under an argon atmosphere. (b) Methyl acrylate, methyl methacrylate, acrylonitrile, phenyl vinyl sulfoxide, methacrylonitrile, diethyl ethylidenemalonate, dimethyl maleate, dimethyl fumarate, cyclopentenone, 1-nitrocyclohexene, benzylidenemalononitrile, *p*-nitrobenzaldehyde, 3,4-dichlorobenzaldehyde, *p*-nitroacetophenone, and methyl propiolate were obtained from Aldrich Chemical Co. Dimethyl (methoxymethylene)malonate was obtained from Fluka Chemicals and distilled under vacuum. 3-(Methoxycarbonyl)-2-pyrone and α-pyrone were purchased from Fluka Chemicals and used without further purification. 5-(Methoxycarbonyl)-2-pyrone was supplied by Chemical Service and was recrystallized (EtOH) before use. 1,1-Dimethoxyethylene was purchased from Wiley Organics. For the preparation of ethyl 2-phenylpropenoate (Table I, entry 8) and application to the synthesis of ethyl 2-(phenylthio)propenoate (Table I, entry 9), see: Ksander, G. M.; McMurry, J. E.; Johnson, M. *J. Org. Chem.* **1977**, *42*, 1180. For the preparation of (1*R*,5*R*)-(+)-ethyl 6,6-dimethyl-2-oxobicyclo[3.1.1]hept-3-ene-3-carboxylate (Table I, entry 14), see: Boger, D. L.; Mullican, M. D.; Hellberg, M. R.; Patel, M. *J. Org. Chem.* **1985**, *50*, 1904. Dimethyl benzylidenemalonate and diethyl benzylidenemalonate (Table I, entries 15 and 16) were prepared as described: Allen, C. F. H.; Spangler, F. W. *Organic Syntheses*; Horning, E. C., Ed.; Wiley: New York, 1955; Collect. Vol. III, p 377. For the preparation of diethyl (1-methylethylidene)malonate, diethyl cyclohexylidenemalonate, and diethyl (diphenylmethylene)malonate (Table I, entries 20–22), see: Lehnert, W. *Tetrahedron* **1973**, *29*, 635. For the preparation of methyl 2-(phenylsulfinyl)propenoate (Table I, entry 23), see: Monteiro, H. J.; Gemal, A. L. *Synthesis* **1975**, 437. Leyendecker, F.; Comte, M.-T. *Tetrahedron Lett.* **1982**, *23*, 5031. Fleming, I.; Goldhill, J.; Perry, D. A. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1563. (Cyclohexen-1-ylmethylene)malononitrile (Table I, entry 24) and methyl 2-(cyclohexene-1-ylmethylene)-2-cyanoacetate (Table I, entry 25) were prepared following the procedure of Foucaud: see: Texier-Boullet, F.; Foucaud, A. *Tetrahedron. Lett.* **1982**, *23*, 4927. For the preparation of methyl 2-oxo-5,6,7,8-tetrahydro-2*H*-1-benzopyran-3-carboxylate (Table I, entry 26) and the methodology for the preparation of methyl 9-bromo-5,6-dihydro-7,10-dimethoxy-2-oxo-2*H*-naphtho[1,2-*b*]pyran-3-carboxylate (Table I, entry 28), see: Boger, D. L.; Mullican, M. D. *J. Org. Chem.* **1984**, *49*, 4033. For the preparation of Eschenmoser's α-pyrone (Table I, entry 31), see: Schreiber, J.; Liemgruber, W.; Pesaro, M.; Schudel, P.; Threlfall, T.; Eschenmoser, A. *Helv. Chim. Acta* **1961**, *44*, 540. For the preparation of methyl 4-methoxy-1,3-butadiene-1-carboxylate (Table I, entry 33), see ref 42.

(45) Meyers, A. I.; Slade, J.; Smith, R. K.; Mihelich, E. D.; Hershenson, F. M.; Liang, C. D. *J. Org. Chem.* **1979**, *44*, 2247.

(46) Assignments are based on the ^{13}C NMR spectrum of nopinone: Holden, C. M.; Whittaker, D. *Org. Magn. Reson.* **1975**, *7*, 125.

Table II. Thermal Reaction of Cyclopropenone Ketals **1** and **2** with C=O Double Bonds

cyclopropenone ketal	substrate R^1COR^2	conditions method,[a] equiv of **1**/**2**, solvent	product[b]	yield[c]
1	R^1 = H, R^2 = *p*-$NO_2C_6H_4$	A, 1, *n*-heptane		**17**, 45%[d]
		A, 2, *n*-heptane		**17**, 42%
		A, 2, *n*-heptane[e]		**17**, 44%
		A, 1, neat		**17**, 3%
1		B, 2, *n*-heptane		**18**, 44%
1	R^1 = CH_3, R^2 = *p*-$NO_2C_6H_4$	A, 2, *n*-heptane		**19**, 22%[f]
1		C, 2, *n*-heptane		**20**, 31%
1	R^1 = H, R^2 = 3,4-$Cl_2C_6H_3$	B, 2, *n*-heptane		**21**,[g] 53%
		B, 1, CH_3CN		**21**, 37%
		B, 3, CH_3CN		**21**, 52%
		B, 2, benzene		**21**, 46%
2		B, 2, *n*-heptane		**22**,[h] 49%
2		A, 2, *n*-heptane		**23**, 30%
1		C, 2, *n*-heptane		**24**, 38%
1	R^1 = H, R^2 = *p*-$CH_3OC_6H_4$	B, 2, *n*-heptane		**25**, 28%
1	R^1 = CH_3, R^2 = C_6H_5	A, 2, *n*-heptane		**26**, 15%[f]
1	R^1 = R^2 = CO_2Et	A, 2, *n*-heptane		**27**, 13%
		A, 1, *n*-heptane		**27**, 12%
		A, 1, benzene		**27**, 8%

[a] Thermal addition–cyclizations were run in 0.2–0.6 M substrate (80 °C, 12 h) under nitrogen. Method A: chromatography on SiO_2. Method B: catalytic concentrated HCl, acetone, 25 °C, 0.5 h. Method C: HOAc, THF, H_2O (1:3:1), 25 °C, 3 h (for **24**), 72 h (for **20**). [b] All products exhibited the expected ^1H NMR, IR, and MS characteristics consistent with the assigned structure and gave satisfactory CHN analysis or HRMS information. [c] All yields are based on purified product isolated by chromatography (SiO_2). [d] Variable amounts of **16** could be isolated. Upon standing at 25 °C, **16** is converted to **17** (100%). [e] The reaction was run with slow addition of **1** (18 h) to the reaction mixture. [f] Compounds **19** and **26** are unstable to the conditions of isolation. [g] R = $(CH_2)_3OH$. [h] R = CH_3.

H, dt, J = 5, 6 Hz, CH_2CHCH_2); ^{13}C NMR ($CDCl_3$) δ 171.4 (s, C=O), 119.7 (s, C≡N), 61.9 (t, CO_2CH_2), 59.0 (t, CH_2OH), 35.2, 31.6 (two t, CH_2CO_2, $OCH_2CH_2CH_2O$), 14.1 (d, CHCN), 13.2 (t, $CHCH_2CH$), 2.6 (d, CH_2CHCH_2); IR (film) ν_{max} 3475 (OH), 2975, 2900, 2250 (C≡N), 1730 (C=O), 1455, 1420, 1402, 1325, 1265, 1185, 1055 cm^{-1}; ClMS (isobutane), *m/e* (rel intensity) 184 (M + 1, 100), 166 (38); HRMS, $C_9H_{14}O_3N$ requires *m/e* 184.0973, found 184.0995.

3d: ^1H NMR ($CDCl_3$) δ 4.22, 4.19 (2 H, two t, 1:1, J = 7 Hz, cis:trans CO_2CH_2), 3.65 (5 H, s and overlapping t, J = 7 Hz, OCH_3, CH_2OH), 2.60, 2.40 (2 H, two d, 1:1, J = 7 Hz, cis:trans CH_2CO_2), 2.05–1.6 (3 H, m, $OCH_2CH_2CH_2O$, OH), 1.5–1.05 (5 H, two s and overlapping m, 1:1 trans:cis CH_3 and cyclopropyl CH's, respectively), 0.90, 0.45 (2 H, rough q, J = 4 Hz, two d, J = 4 Hz, each, cyclopropyl CH_2's); ^{13}C NMR ($CDCl_3$) δ 173.0, 172.4 (two s, cis and trans C=O), 61.6, 61.4 (two t, cis and trans CO_2CH_2), 59.2 (t, CH_2OH), 51.9, 51.7 (two q, cis and trans OCH_3), 34.0, 33.0 (two t, cis and trans CH_2CO_2), 31.8 (t, $OCH_2CH_2CH_2O$); IR (film) ν_{max} 3495 (OH), 2957, 2888, 1725 (C=O), 1464, 1437, 1402, 1391, 1333, 1273, 1231, 1192, 1165, 1096, 1055 cm^{-1}; EIMS, *m/e* (rel intensity) 230 (M^+, 3), 199 (OCH_3, 4), 180 (2), 155 (17), 141 (11), 127 (17), 126 (13), 123 (16), 122 (24), 113 (78), 112 (69), 111 (14), 97 (11), 96 (11), 95 (31), 94 (11); HRMS, $C_{11}H_{18}O_5$ requires *m/e* 230.1153, found 230.1137.

3e: ^1H NMR ($CDCl_3$) δ 4.27 (2 H, t, J = 7 Hz, CO_2CH_2), 3.70 (2 H, t, J = 7 Hz, CH_2OH), 2.55, 2.40 (2 H, two d, 9:1, J = 7 Hz, cis:trans CH_2CO_2), 1.90 (3 H, p, J = 7 Hz, $OCH_2CH_2CH_2O$, OH), 1.40, 1.35 (4 H, two s, 9:1 and overlapping m, cis:trans CH_3 and cyclopropyl CH), 1.01, 1.0, 0.63, 0.55 (2 H, four d, 9:9:1:1, J = 7, 8, 7 Hz, cis CH_2 and trans CH_2, respectively); ^{13}C NMR ($CDCl_3$) δ 171.5, 171.2 (two s, trans and cis C=O), 121.9 (s, C≡N), 61.8 (t, CO_2CH_2), 58.9 (t, CH_2OH), 35.7 (t, cis CH_2CO_2), 33.0 (t, trans CH_2CO_2), 31.6 (t, $OCH_2CH_2CH_2O$), 21.8 (d, cyclopropyl CH), 20.9 (s, CCN), 20.7 (q, cis CH_3), 20.0 (d, trans cyclopropyl CH), 15.4 (q, trans CH_3), 10.44 (t, cis cyclopropyl CH_2), 7.9 (t, trans cyclopropyl CH_2); IR (film) ν_{max} 3480 (OH), 2990, 2960, 2905, 2250 (C≡N), 1740 (C=O), 1462, 1405, 1335, 1270, 1185, 1055 cm^{-1}; CIMS (NH_3), *m/e* (rel intensity) 215 (M + 18, 100), 198 (M + 1, 70), 180 (65).

3f: ^{1}H NMR ($CDCl_3$) δ 3.70 (3 H, s, OCH_3), 2.52, 2.35 (2 H, two d, 5:1, J = 7 Hz, cis:trans CH_2CO_2), 1.9–1.6, 1.5–1.3 (1 H, two br m, 5:1, cis:trans cyclopropyl CH), 1.40, 1.33 (3 H, two s, 5:1, cis:trans CH_3), 1.01, 1.0, 0.60, 0.53 (2 H, four d, 5:5:1:1, J = 7, 8, 7, 7 Hz, cis:trans cyclopropyl CH_2); ^{13}C NMR ($CDCl_3$) δ 171.6, 171.4 (two s, cis and trans C=O), 121.8 (s, C≡N), 51.7 (q, OCH_3), 35.4 (t, cis CH_2CO_2), 32.8 (t, trans CH_2CO_2), 21.7 (d, cyclopropyl CH), 20.9 (s, CCN), 20.7 (q, cis CH_3), 20.1 (d, trans cyclopropyl CH), 15.5 (q, trans CH_3), 10.5 (t, cis cyclopropyl CH_2), 7.9 (t, trans cyclopropyl CH_2); IR (film) ν_{max} 2955, 2236 (C≡N), 1740 (C=O), 1439, 1335, 1267, 1200, 1179 cm^{-1}; EIMS, m/e (rel intensity) 154 (3), 153 (M^+, 3), 138 (1), 122 (5), 94 (41), 93 (100); HRMS, $C_8H_{11}NO_2$ requires m/e 153.0789, found 153.0799.

***cis*-3g**: ^{1}H NMR ($CDCl_3$) δ 7.43 (1 H, d, J = 7 Hz, aromatic CH), 7.28 (4 H, m, aromatic), 4.30 (2 H, t, J = 6 Hz, $CO_2CH_2CH_2CH_2OH$), 4.05 (2 H, q, J = 7 Hz, OCH_2CH_3), 3.69 (2 H, t, J = 6 Hz, $CO_2CH_2CH_2CH_2OH$), 2.75, 2.85 (two overlapping dd, J = 6, 17, 9, 16 Hz, CH_2CO_2), 1.89 (3 H, m, $OCH_2CH_2CH_2OH$, CCH_THCH), 1.72 (1 H, br s, OH), 1.59 (1 H, dd, J = 7, 5 Hz, $CCHHCH$), 1.40 (1 H, dd, J = 9, 5 Hz, CCH_CHCH), 1.13 (3 H, t, J = 7 Hz, OCH_2CH_3). ***trans*-3g**: ^{1}H NMR δ 7.27 (5 H, m, phenyl CH), 4.23, 4.21 (2 H, two overlapping t, J = 6 Hz, $CO_2CH_2CH_2CH_2OH$), 4.10 (2 H, q, J = 7 Hz, OCH_2CH_3), 3.65 (2 H, t, J = 6 Hz, $OCH_2CH_2CH_2OH$), 2.30–2.10 (2 H, m, CH_2CO_2), 1.82 (4 H, m, $OCH_2CH_2CH_2OH$, cyclopropyl CH_2), 1.60 (1 H, br s, OH), 1.22 (1 H, dd, J = 6, 4 Hz, $CHCH_2CO_2$), 1.16 (3 H, t, J = 7 Hz, OCH_2CH_3); 1:1 *cis*:*trans*-**3g** IR (film) ν_{max} 3513, 3065, 3042, 3013, 2968, 1722 (C=O), 1447, 1399, 1370, 1325, 1264, 1184, 1095, 1053, 1028 cm^{-1}; EIMS, m/e (rel intensity) 306 (M^+, 25), 260 (9), 231 (5), 189 (12), 184 (19), 173 (9), 160 (26), 156 (37), 129 (100), 115 (42), 103 (21), 77 (24); HRMS, $C_{17}H_{22}O_5$ requires m/e 306.1466, found 306.1465.

3h: ^{1}H NMR ($CDCl_3$) δ 4.23 (2 H, dt, J = 6, 4 Hz, CO_2CH_2), 3.70 (6 H, s, two CO_2CH_3), 3.66 (2 H, t, J = 6 Hz, CH_2OH), 2.77 (1 H, dd, J = 7, 16 Hz, $CHHCO_2$), 2.65 (1 H, dd, J = 8, 16 Hz, $CHHCO_2$), 2.39 (1 H, dd, J = 9, 5 Hz, *cis*-$CH_3O_2CCHCHCH_2CO_2$), 2.17 (1 H, dd, J = 6, 5 Hz, *trans*-$CH_3O_2CCHCHCH_2CO_2$), 2.08 (1 H, m, $CHCH_2CO_2$), 1.95 (1 H, br s, OH), 1.84 (2 H, p, J = 6 Hz, $OCH_2CH_2CH_2OH$); ^{13}C NMR ($CDCl_3$) δ 171.9, 171.6, 170.5 (three s, three C=O), 61.6 (t, CO_2CH_2), 58.9 (t, CH_2OH), 52.3, 52.2 (two q, two OCH_3), 31.6, 31.0 (two t, CH_2CO_2, $OCH_2CH_2CH_2OH$), 27.4, 26.3 (two d, two $CHCO_2CH_3$), 24.0 (d, $CHCH_2CO_2$); IR (film) ν_{max} 3524, 3457, 2959, 2890, 1732 (C=O), 1458, 1379, 1335, 1312, 1227, 1196, 1173, 1098, 1053, 984, 903 cm^{-1}; EIMS, m/e (rel intensity) 275 (M + 1, 1), 257 (OH, 1), 243 (OCH_3, 6), 215 (CO_2CH_3, 30), 199 (40), 198 (23), 185 (33), 170 (31), 167 (36), 166 (58), 157 (46), 139 (55), 127 (33), 113 (41), 111 (100), 81 (87); HRMS, $C_{12}H_{19}O_7$ requires m/e 275.1129, found 275.1140.

3i: ^{1}H NMR ($CDCl_3$) δ 4.26, 4.24 (2 H, two t, J = 6 Hz, cis and trans CO_2CH_2), 3.72 (2 H, t, J = 6 Hz, CH_2OH), 2.35 (2 H, d, J = 7 Hz, CH_2CO_2), 2.5–1.25 (10 H, m, two cyclopentane CH_2, three cyclopropyl CH, $OCH_2CH_2CH_2O$, OH); IR ($CHCl_3$) ν_{max} 3500 (OH), 3025, 2970, 2900, 1720 (C=O), 1460, 1420, 1350, 1275, 1235, 1185, 1055 cm^{-1}; EIMS, m/e (rel intensity) 212 (M^+, 2), 155 (11), 136 (19), 110 (10), 109 (26), 108 (53), 95 (29), 94 (27), 81 (53), 80 (21), 79 (32), 67 (100); HRMS, $C_{11}H_{16}O_4$ requires m/e 212.1048, found 212.1018.

13: ^{1}H NMR ($CDCl_3$) δ 6.85 (1 H, dd, J = 15, 7 Hz, $CHCH$=CH), 5.80 (1 H, dd, J = 15, 2 Hz, CHCH=CH), 4.28 (2 H, t, J = 7 Hz, CO_2CH_2), 3.68 (2 H, t, J = 7 Hz, CH_2OH), 2.5–1.5 (10 H, three cyclopentane CH_2, cyclopentane CH, $OCH_2CH_2CH_2O$, OH); IR (film) ν_{max} 3450 (OH), 2963, 2896, 1734 (C=O), 1717 (C=O), 1653 (C=C), 1404, 1362, 1310, 1273, 1240, 1196, 1155, 1088, 1055, 988 cm^{-1}; CIMS (NH_3), m/e (rel intensity) 230 (M + 18, 16), 213 (M + 1, 100), 195 (9), 137 (22), 109 (9), 81 (18).

3j: ^{1}H NMR ($CDCl_3$) δ 4.25 (2 H, t, J = 7 Hz, CO_2CH_2), 3.70 (2 H, t, J = 7 Hz, CH_2OH), 2.75, 2.70 (2 H, two d, J = 7 Hz, 1:1 cis:trans CH_2CO_2), 2.4–1.1 (13 H, m, nine cyclohexane protons, one cyclopropyl CH, $OCH_2CH_2CH_2O$, OH); IR (film) ν_{max} 3500 (OH), 2940, 2863, 1734 (C=O), 1449, 1399, 1347, 1331, 1314, 1273, 1210, 1177, 1092, 1053, 986, 938, 864 cm^{-1}.

General Procedure for Thermal Reaction of Cyclopropenone Ketals with Olefins Possessing Two Geminal Electron-Withdrawing Substituents. Preparation of 5,5-Dicyano-4-phenylcyclopent-2-enone 1,3-Propanediyl Ketal (4f). Benzylidenemalononitrile (49 mg, 0.32 mmol) and cyclopropenone ketal **1** (75 mg, 0.67 mmol, 2 equiv) were combined in benzene (0.3 mL), and the resulting solution was warmed at 80 °C until the reaction was judged to be complete by ^{1}H NMR spectroscopy (4 h). Chromatography (MPLC, 15 × 500 mm, 3:1:1 hexane–methylene chloride–ethyl acetate eluant) afforded 73 mg (85 mg theoretical, 86%) of pure **4f** as a white solid: mp 139–141 °C (ethanol); ^{1}H NMR ($CDCl_3$) δ 7.46 (5 H, s, phenyl), 6.72 (1 H, dd, J = 6, 3 Hz, CHCH=CHC), 6.32 (1 H, dd, J = 6, 2 Hz, CHCH=CHC), 4.69 (1 H, dd, J = 3, 2 Hz, allylic CH), 4.4–3.7 (4 H, m, $OCH_2CH_2CH_2O$), 2.5–1.9 (1 H, br m, OCH_2CHHCH_2O), 1.70 (1 H, dt, J = 13, 4 Hz, OCH_2CHHCH_2O); ^{13}C NMR ($CDCl_3$) δ 135.3 (d, CHCH=CHC), 134.4 (s, phenyl C), 129.1, 128.9, 128.6 (three d, three phenyl CH, $CHCH$=CHC), 113.5, 111.7 (two s, two C≡N), 109.5 (s, OCO), 63.0, 62.8 (two t, $OCH_2CH_2CH_2O$), 57.1 (d, allylic CH), 53.4 (s, N≡CCC≡N), 24.3 (t, $OCH_2CH_2CH_2O$); 2D HETCOR ^{13}C–^{1}H NMR ($CDCl_3$, ^{13}C/^{1}H, ppm) 135.3/6.32 (CHCH=CHC), 129.1/6.72 ($CHCH$=CHC), 128.9, 128.6/7.46 (phenyl CH), 63.0, 62.8/4.4–3.7 ($OCH_2CH_2CH_2O$), 57.1/4.69 (allylic CH), 24.3/2.3, 1.7 ($OCH_2CH_2CH_2O$); IR ($CHCl_3$) ν_{max} 3070, 2920, 2290 (C≡N), 1510, 1465, 1365, 1350, 1260, 1210, 1175, 1140, 1100, 1080, 1040, 870, 705 cm^{-1}; EIMS, m/e (rel intensity) 266 (M^+, 64), 208 (31), 207 (11), 189 (16), 182 (10), 181 (26), 180 (68), 179 (46), 154 (23), 153 (63), 152 (18), 141 (12), 140 (25), 138 (14), 131 (39), 127 (23), 126 (15), 116 (22), 115 (100), 114 (10), 113 (70), 112 (34), 105 (13), 103 (22), 102 (16), 89 (21), 77 (42), 76 (27); HRMS, $C_{16}H_{14}O_2N_2$ requires m/e 266.1054, found 266.1051.

This procedure was adapted to a preparative scale:[19b] benzylidenemalononitrile (3.85 g, 25 mmol) and cyclopropenone ketal (5.6 g, 50 mmol) were combined in 25 mL of dry distilled toluene in a sealed tube, and the resulting solution was warmed (80 °C) with stirring for 6.5 h. The crude reaction mixture was filtered, and chromatography (MPLC, 2.5 × 100 cm, 3:1:1 hexane–ethyl acetate–methylene chloride eluant) afforded 4.47 g (6.65 theoretical, 67%) of **4f**.

4a: ^{1}H NMR ($CDCl_3$) δ 6.40 (1 H, dd, J = 7, 1 Hz, CHCH=CHC), 6.0 (1 H, dd, J = 7, 3 Hz, $CHCH$=CHC), 4.2 (2 H, q, OCH_2CH_3), 4.1–3.7 (5 H, m, $OCH_2CH_2CH_2O$, allylic CH), 2.60 (1 H, q, J = 7 Hz, OCH_2CHHCH_2O), 1.4–2.4 (5 H, m, OCH_2CHHCH_2O, $CCHCH_2CH$), 1.3 (3 H, s, CH_3), 1.2 (3 H, t, J = 7 Hz, OCH_2CH_3), 0.80 (3 H, s, CH_3); ^{13}C NMR ($CDCl_3$)[46] δ 203.0 (s, C=O ketone), 168.6 (s, C=O ester), 138.0 (d, CHCH=CHC), 126.6 (d, $CHCH$=CHC), 113.0 (s, OCO), 67.9 (s, O=CCC=O), 61.6, 61.2, 60.6 (three t, $OCH_2CH_2CH_2O$, CO_2CH_2), 59.6 (d, O=CCH), 50.5 (d, allylic CH), 43.0 (d, CH_2CHCH), 41.4 (s, CH_3CCH_3), 26.3 (q, CH_3), 24.4, 22.9 (two q, $OCH_2CH_2CH_2O$, $CHCH_2CH$), 21.6 (q, CH_3), 13.8 (q, OCH_2CH_3); IR (film) ν_{max} 2980, 2880, 1760 (ketone C=O), 1730 (ester C=O), 1460, 1370, 1350, 1290, 1240, 1210, 1150, 1090, 1060 cm^{-1}; EIMS, m/e (rel intensity) 320 (M^+, 2), 292 (4), 275 (3), 237 (7), 223 (7), 219 (4), 177 (3), 154 (100), 139 (10), 113 (29), 100 (28); HRMS, $C_{18}H_{24}O_5$ requires m/e 320.1622, found 320.1625.

4b: ^{1}H NMR ($CDCl_3$) δ 7.20 (5 H, rough s, phenyl), 6.75 (1 H, dd, J = 7, 3 Hz, $CHCH$=CHC), 6.15 (1 H, dd, J = 7, 1 Hz, CHCH=CHC), 4.95 (1 H, rough t, J = 1 Hz, allylic CH), 4.50–3.0 (8 H, m, two CO_2CH_2, $OCH_2CH_2CH_2O$), 2.1 (1 H, br m, OCH_2CHHCH_2O), 1.35 (1 H, m, OCH_2CHHCH_2O), 1.30 (3 H, t, J = 7 Hz, OCH_2CH_3), 0.70 (3 H, t, J = 7 Hz, OCH_2CH_3); ^{13}C NMR ($CDCl_3$) δ 168.2 (s, C=O), 165.2 (s, C=O), 138.3 (s, phenyl C), 136.3 (d, CHCH=CHC), 129.1 (d, phenyl CH), 127.6 (d, phenyl CH), 127.0, 126.8 (two d, phenyl CH, $CHCH$=CHC), 110.3 (s, OCO), 76.0 (s, O=CCC=O), 62.8, 61.3, 60.8, 60.2 (four t, two OCH_2CH_3, $OCH_2CH_2CH_2O$), 52.3 (d, allylic CH), 25.1 (t, $OCH_2CH_2CH_2O$), 14.0, 13.0 (two q, two OCH_2CH_3); IR (film) ν_{max} 3000, 2880, 1735 (C=O), 1500, 1455, 1370, 1355, 1340, 1275, 1255, 1220, 1155, 1125, 1105, 1090, 1055, 1020, 990, 750, 700 cm^{-1}; EIMS, m/e (rel intensity) 360 (M^+, 8), 315 (-OEt, 17), 314 (-EtOH, 40), 288 (20), 287 (-CO_2Et, 100), 269 (6), 256 (5), 241 (7), 228 (14), 201 (23), 184 (23), 183 (65), 157 (17), 156 (22), 155 (24), 144 (11), 131 (12), 129 (25), 128 (48), 127 (34), 115 (55), 91 (20); HRMS, $C_{20}H_{24}O_6$ requires m/e 360.1571, found 360.1567. Unambiguous confirmation of the structure of **4b** was derived from a single-crystal X-ray structure determination.[32a]

4c: ^{1}H NMR ($CDCl_3$) δ 7.29 (5 H, s, phenyl), 6.79 (1 H, dd, J = 7, 3 Hz, $CHCH$=CHC), 6.23 (1 H, dd, J = 7, 1 Hz, CHCH=CHC), 5.03 (1 H, dd, J = 3, 1 Hz, allylic CH), 4.0 (4 H, two overlapping t, $OCH_2CH_2CH_2O$), 3.86 (3 H, s, OCH_3), 3.04 (3 H, s, OCH_3), 1.8–2.5 (1 H, br m, OCH_2CHHCH_2O), 1.4 (1 H, rough dt, J = 10, 1 Hz, OCH_2CHHCH_2O); ^{13}C NMR ($CDCl_3$) δ 168.8 (s, C=O), 165.7 (s, C=O), 138.0 (s, phenyl C), 136.2 (d, CHCH=CHC), 128.8 (d, phenyl CH), 127.6 (d, phenyl CH), 127.0, 126.7 (two d, phenyl CH, $CHCH$=CHC), 110.2 (s, OCO), 76.4 (s, O=CCC=O), 62.8, 61.3 (two t, $OCH_2CH_2CH_2O$), 52.2 (d, allylic CH), 52.0, 51.0 (two q, two OCH_3), 25.0 (t, $OCH_2CH_2CH_2O$); IR ($CHCl_3$) ν_{max} 3030, 2950, 2870, 1730 (C=O), 1490, 1450, 1430, 1345, 1330, 1275, 1255, 1215, 1205, 1145, 1115, 1100, 1080, 1050, 1005, 990, 895, 840 cm^{-1}; EIMS, m/e (rel intensity) 332 (M^+, 12), 301 (OCH_3, 14), 300 (CH_3OH, 36), 274 (25), 273 (CO_2CH_3, 100), 242 (12), 215 (23), 214 (42), 213 (17), 183 (51), 155 (28), 128 (33), 127 (35), 115 (41), 102 (12); HRMS, $C_{18}H_{20}O_6$ requires m/e 332.1259, found 332.1294.

4d: ^{1}H NMR ($CDCl_3$) δ 6.50 (1 H, dd, J = 7, 3 Hz, $CHCH$=CHC), 5.80 (1 H, dd, J = 7, 1 Hz, CHCH=CHC), 4.5–3.5 (9 H, m, two CO_2CH_2, $OCH_2CH_2CH_2O$, allylic CH), 2.10 (1 H, br m,

OCH_2CHHCH_2O), 1.35 (1 H, m, OCH_2CHHCH_2O), 1.30 (3 H, t, J = 7 Hz, OCH_2CH_3), 1.20 (3 H, t, J = 7 Hz, OCH_2CH_3), 1.05 (3 H, d, J = 7 Hz, $CHCH_3$); ^{13}C NMR ($CDCl_3$) δ 168.2 (s, C=O), 166.7 (s, C=O), 138.7 (d, CHCH=*CH*C), 125.0 (d, CH*CH*=CHC), 110.1 (s, OCO), 73.5 (s, O=C*C*C=O), 62.7, 61.1, 60.6, 60.5 (four t, two O*C*-H_2CH_3, $OCH_2CH_2CH_2O$), 42.6 (d, allylic CH), 25.1 (t, $OCH_2CH_2CH_2O$), 14.4, 14.0, 13.8 (three q, two OCH_2CH_3, $CHCH_3$); IR (film) ν_{max} 3000, 2900, 1730 (C=O), 1625, 1470, 1370, 1350, 1310, 1300, 1265, 1235, 1165, 1150, 1100, 1075, 1045, 1020, 980, 930, 860, 720 cm^{-1}; EIMS, *m/e* (rel intensity) 298 (M^+, 6), 283 (CH_3, 8), 253 (OEt, 26), 252 (EtOH, 46), 226 (16), 225 (CO_2Et, 100), 207 (8), 194 (11), 179 (16), 167 (35), 153 (10), 152 (15), 139 (30), 121 (51), 111 (13); HRMS, $C_{15}H_{22}O_6$ requires *m/e* 298.1415, found 298.1413.

4e: ^1H NMR ($CDCl_3$) δ 6.67 (1 H, dd, J = 6, 2 Hz, CH*CH*=CHC), 6.08 (1 H, dd, J = 6, 1 Hz, CHCH=*CH*C), 5.09 (1 H, dd, J = 2, 1 Hz, allylic CH), 3.85 (4 H, m, $OCH_2CH_2CH_2O$), 3.86 (3 H, s, OCH_3), 3.68 (3 H, s, OCH_3), 3.46 (3 H, s, OCH_3), 2.40–1.80 (1 H, br m, OCH_2CHHCH_2O), 1.35 (1 H, rough dt, J = 10, 1 Hz, OCH_2CHHCH_2O); ^{13}C NMR ($CDCl_3$) δ 168.6 (s, C=O), 165.8 (s, C=O), 135.0 (d, CHCH=*CH*C), 127.0 (d, CH*CH*=CHC), 108.1 (s, OCO), 85.5 (d, allylic CH), 75.7 (s, O=C*C*C=O), 62.4, 61.4 (two t, $OCH_2CH_2CH_2O$), 58.9 (q, OCH_3), 52.2, 51.8 (two q, two CO_2CH_3), 24.9 (t, $OCH_2CH_2CH_2O$); IR (film) ν_{max} 2975, 2900, 2860, 1735 (C=O), 1630, 1440, 1365, 1315, 1275, 1235, 1160, 1120, 1100, 1060, 1010, 980, 920, 855, 805, 780, 740 cm^{-1}; EIMS, *m/e* (rel intensity) 286 (M^+, 2), 255 (OCH_3, 19), 254 (CH_3OH, 10), 228 (14), 227 (CO_2CH_3, 100), 196 (9), 169 (64), 137 (28), 107 (10), 79 (11), 75 (33), 59 (34); HRMS, $C_{13}H_{18}O_7$ requires *m/e* 286.1051, found 286.1033.

4g: mp 120–121 °C; ^1H NMR ($CDCl_3$) δ 6.42 (1 H, dd, J = 7, 3 Hz, CH*C*H=CHC), 6.02 (1 H, dd, J = 7, 2 Hz, CHCH=*CH*C), 5.72 (1 H, br s, C=*CH*), 4.10 (5 H, m, $OCH_2CH_2CH_2O$, *C*HCH=CHC), 2.10 (5 H, m, OCH_2CHHCH_2O, allylic CH_2's), 1.65 (5 H, OCH_2CHHC-H_2O, $CCH_2CH_2CH_2CH_2CH$); ^{13}C NMR ($CDCl_3$) δ 135.0 (d, CHCH=*CH*C), 132.7 (s, *C*=CH), 129.1 (d, C=*CH*), 128.0 (d, CH*CH*=CHC), 114.4, 112.0 (two s, two C≡N), 109.7 (s, OCO), 62.7, 62.6 (two t, $OCH_2CH_2CH_2O$), 59.2 (d, *CH*CH=CHC), 51.1 (s, N≡CC*C*≡N), 28.1, 25.3 (two t, allylic CH_2's), 24.4 (t, $OCH_2CH_2CH_2O$), 22.5, 21.7 (two t, $CCH_2CH_2CH_2CH_2CH$); IR ($CHCl_3$) ν_{max} 3027, 2936, 2880, 2838, 2256 (C≡N), 1622, 1478, 1466, 1448, 1435, 1348, 1244, 1215, 1200, 1167, 1123, 1088, 1069, 1042, 1028 cm^{-1}; EIMS, *m/e* (rel intensity) 270 (M^+, 20), 230 (4), 205 (11), 189 (10), 184 (15), 183 (16), 169 (10), 157 (9), 156 (14), 155 (11), 144 (10), 142 (11), 131 (45), 126 (26), 100 (64), 91 (29), 79 (36), 77 (36).

Anal. Calcd for $C_{16}H_{18}N_2O_2$: C, 71.09; H, 6.71; N, 10.37. Found: C, 71.40; H, 6.80; N, 10.24.

4h: ^1H NMR ($CDCl_3$) δ 6.38 (1 H, 9:1, dd, overlapping m, J = 7, 3 Hz, 9:1, trans:cis CH*CH*=CHC), 6.05 (1 H, m, CHCH=*CH*C), 5.57 (1 H, br s, *C*H=C), 4.00 (5 H, $OCH_2CH_2CH_2O$, *CH*CH=CHC), 3.87, 3.67 (3 H, two s, 9:1. trans:cis isomers, CO_2CH_3), 2.05 (5 H, allylic CH_2's, OCH_2CHHCH_2O), 1.55 (5 H, $CCH_2CH_2CH_2CH_2CH$, OCH_2CHHCH_2O); IR ($CHCl_3$) ν_{max} 2936, 2880, 1750 (C=O), 1246, 1196, 1152, 1115, 1098, 1073, 1017 cm^{-1}; EIMS, *m/e* (rel intensity) 303 (M^+, 15), 245 (24), 244 (CO_2CH_3, 100), 232 (19), 222 (19), 205 (14), 186 (23), 164 (14), 158 (25), 116 (24), 100 (41); HRMS, $C_{17}H_{21}O_4N$ requires *m/e* 303.1469, found 303.1490.

4i: ^1H NMR ($CDCl_3$) δ 6.55 (1 H, dd, J = 7, 1 Hz, CHCH=*CH*C), 6.20 (1 H, dd, J = 7, 3 Hz, CHC*H*=CHC), 3.90 (4 H, m, $OCH_2CH_2CH_2O$), 3.72 (3 H, s, OCH_3), 3.55 (1 H, m, bis allylic CH), 2.05 (5 H, br m, $CH_2C{=}CC{H_2}$, OCH_2CHHCH_2O), 1.65 (5 H, br m, $CH_2CH_2CH_2CH_2$, OCH_2CHHCH_2O); ^{13}C NMR ($CDCl_3$) δ 167.9 (s, C=O), 162.1 (s, C=O), 142.5 (s, O*C*=CC), 135.4 (d, CHCH=*CH*C), 126.8 (d, CH*CH*=CHC), 112.1 (s, OCO), 107.1 (s, OC=*C*C), 64.8 (s, O=C*C*C=O), 62.6, 61.2, (two t, $OCH_2CH_2CH_2O$), 52.7 (q, OCH_3), 50.2 (d, bis allylic CH), 25.7, 25.0, 24.6 (three t, $CH_2CH_2CH_2CH_2$, $OCH_2CH_2CH_2O$), 21.9 (t, $CH_2CH_2CH_2CH_2$); IR ($CHCl_3$) ν_{max} 3050, 2970, 2900, 1760, 1442, 1370, 1350, 1335, 1280, 1260, 1205, 1190, 1180, 1160, 1105, 1020, 920 cm^{-1}; EIMS, *m/e* (rel intensity) 320 (M^+, 3), 289 (2), 288 (4), 262 (19), 261 (CO_2CH_3, 100), 203 (30), 175 (12), 140 (15), 91 (25); HRMS, $C_{17}H_{20}O_6$ requires *m/e* 320.1259, found 320.1257.

4j: ^1H NMR ($CDCl_3$) δ 6.63 (1 H, dd, J = 7, 1 Hz, CHCH=*CH*C), 6.33 (1 H, dd, J = 7, 3 Hz, OCH=CH), 6.15 (1 H, dd, J = 7, 3 Hz, CH*CH*=CHC), 5.05 (1 H, dd, J = 7, 3 Hz, OCH=*CH*), 4.12 (1 H, rough q, J = 3 Hz, bis allylic CH), 3.90 (4 H, m, $OCH_2CH_2CH_2O$), 3.75 (3 H, s, OCH_3), 2.5–1.9 (1 H, br m, OCH_2CHHCH_2O), 1.45 (1 H, dt, J = 14, 3 Hz, OCH_2CHHCH_2O); ^{13}C NMR (Me_2SO-d_6) δ 167.4 (s, C=O), 160.9 (s, C=O), 137.1 (d, CH=*C*HO), 135.6 (d, CHCH=*CH*C), 127.1 (d, CH*CH*=CHC), 112.2 (s, OCO), 104.0 (d, OCH=*CH*), 63.9 (s, O=C*C*C=O), 62.3, 60.7 (two t, $OCH_2CH_2CH_2O$), 52.4 (q, OCH_3), 46.0 (d, bis allylic CH), 24.5 (d, $OCH_2CH_2CH_2O$); IR ($CHCl_3$) ν_{max} 3035, 2960, 2880, 1765 (C=O), 1430, 1340, 1268, 1232, 1151, 1138, 1090, 1062, 1018, 997 cm^{-1}; EIMS, *m/e* (rel intensity) 266 (M^+, 2), 238 (23), 237 (28), 234 (CH_3OH, 12), 208 (16), 207 (CO_2CH_3, 100), 206 (30), 179 (28), 177 (12), 176 (17), 151 (26), 150 (10), 149 (72), 121 (63), 100 (87), 93 (26), 92 (26), 77 (35); HRMS, $C_{13}H_{14}O_6$ requires *m/e* 266.0789, found 266.0811.

4k: ^1H NMR ($CDCl_3$) δ 6.94 (1 H, s, aromatic CH), 6.55 (1 H, dd, J = 7, 1 Hz, CHCH=*CH*C), 6.23 (1 H, dd, J = 7, 3 Hz, CH*CH*=CHC), 4.0 (5 H, m, $OCH_2CH_2CH_2O$, bis allylic CH), 3.80 (3 H, s, OCH_3), 3.75 (6 H, s, two OCH_3), 2.75 (1 H, br m, OCH_2CHHCH_2O), 2.22, 2.20 (4 H, two rough t, CCH_2CH_2O), 1.40 (1 H, br m, OCH_2CHHCH_2O); ^{13}C NMR ($CDCl_3$) δ 167.7 (s, C=O), 161.2 (s, C=O), 152.0, 147.2 (two s, two aromatic *C*OCH_3), 140.0 (s, O*C*=CCH), 134.6 (d, CHCH=*CH*C), 128.1 (d, CH*CH*=CHC), 125.6, 124.1 (two s, two aromatic C), 117.0 (s, aromatic CBr), 115.4 (d, aromatic CH), 112.2 (s, OCO), 112.0 (s, OC=*C*CH), 64.5 (s, O=C*C*C=O), 62.7, 61.3 (two t, $OCH_2CH_2CH_2O$), 61.9 (q, OCH_3), 56.0 (q, OCH_3), 53.0 (q, CO_2CH_3), 50.0 (d, bis allylic CH), 24.7 (t, $OCH_2CH_2CH_2O$), 23.6, 20.4 (two t, CCH_2CH_2C); EIMS, *m/e* (rel intensity) 508/506 (M^+, $^1/_1$, 1), 449/447 (CO_2CH_3, 1/1, 20), 391/389 (1/1, 10), 140 (100), 112 (43), 100 (19); HRMS, $C_{23}H_{23}O_8Br$ requires *m/e* 506.0575, found 506.0555.

Solvent Effects on the Rate of Reaction of Methyl Acrylate with 1. Methyl acrylate (30 μL, 29 mg, 0.33 mmol) and **1** (58 mg, 0.51 mmol, 1.5 equiv) were combined in benzene-d_6, *N,N*-dimethylformamide-d_7, or acetonitrile-d_3 (0.4 mL) in a ^1H NMR tube under argon, and the resulting solution was warmed at 75 °C with exclusion of light. The progress of the reaction was monitored by ^1H NMR spectroscopy until judged complete. An additional 1.0 equiv of **1** (37 mg, 0.33 mmol) was added after 2 h to maintain the original concentration of **1**. Workup and purification of the reaction mixture as previously described provided **3a**, and the results are summarized in eq 8.

Solvent Effects on the Rate of Reaction of Methyl Methacrylate with 1. Methyl methacrylate (35 μL, 32 mg, 0.32 mmol) and **1** (74 mg, 0.6 mmol, 2.0 equiv) were combined in benzene-d_6, *N,N*-dimethylformamide-d_7, or acetonitrile-d_3 (0.4 mL) in a ^1H NMR tube under argon, and the resulting solution was warmed at 75 °C with the exclusion of light until the reaction was judged complete by ^1H NMR spectroscopy (20 h).

An additional 1.0 equiv of **1** (36 mg, 0.32 mmol) was added after 2 and 7 h, respectively, to maintain the initial cyclopropenone ketal concentration. The disappearance of methyl methacrylate and the appearance of cyclopropane ketene acetal **11d** (1:1 cis:trans) were monitored by ^1H NMR spectroscopy. Crude **11d**: ^1H NMR (benzene-d_6) δ 4.0–3.6 (m), 3.52, 3.48 (two s, 1:1, cis:trans CO_2CH_3), 1.8–1.5 (m), 1.35 (s, CH_3), 0.90 (dd, J = 4, 12 Hz, cis $CHH_cC(CH_3)CO_2CH_3$), 0.53 (dd, J = 4, 7 Hz, trans $CHH_tC(CH_3)CO_2CH_3$). The crude reaction mixture was worked up as described for **3a**, and purification by chromatography (SiO_2) afforded **3d**. The results are summarized in eq 8.

Solvent Effects on the Rate of Reaction of Dimethyl (Methoxymethylene)malonate with 1. Dimethyl (methoxymethylene)malonate (40.5 mg, 0.23 mmol) and **1** (61.3 mg, 0.55 mmol, 2.4 equiv) were combined in acetonitrile-d_3 (0.4 mL) in a ^1H NMR tube under argon, and the resulting solution was warmed (75 °C) with the exclusion of light until the reaction was judged complete by ^1H NMR spectroscopy (3.5 h). Chromatography (SiO_2, 50% ethyl acetate–hexane eluant) afforded 56 mg (66 mg theoretical, 85%) of pure **4e**.

Concurrently, the reaction was run under identical conditions in benzene-d_6, *N,N*-dimethylformamide-d_7, nitrobenzene-d_5, pyridine-d_5, cyclohexane-d_{12}, nitromethane-d_3, methylene-d_2 chloride, and $CDCl_3$, and the results are detailed in eq 12.

Dimerization of the Cyclopropenone Ketal 1: Isolation and Characterization of 12. A solution of cyclopropenone ketal **1** (64 mg, 0.57 mmol) in benzene-d_6 (2 M) was warmed at 80 °C until no **1** remained as judged by ^1H NMR spectroscopy (21 h). Chromatography (50% ethyl acetate–hexane eluant) afforded 16 mg (64 mg theoretical, 25%) of pure **12** as a white solid: ^1H NMR ($CDCl_3$) δ 4.01, 3.93 (8 H, two t, J = 6 Hz, OCH_2), 1.85 (4 H, p, J = 6 Hz, $OCH_2CH_2CH_2O$), 1.90 (4 H, s, CH); ^{13}C NMR ($CDCl_3$) δ 101.6 (s, OCO), 66.9 and 65.3 (two t, OCH_2), 26.1 (d, *C*H), 25.9 (t, $OCH_2CH_2CH_2O$).

Thermal [3 + 4]-Cycloaddition Reaction of 1 with α-Pyrone: Preparation of 5c. α-Pyrone (94 mg, 0.98 mmol) in benzene (0.5 mL) under argon was treated with cyclopropenone ketal **1** (165 mg, 1.47 mmol), and the resulting solution was warmed at 70 °C for 22 h. Chromatography (SiO_2, 50% ethyl acetate–hexane eluant) afforded 102 mg (204 mg theoretical, 50%) of pure **5c** as a white amorphous solid: mp 118–120 °C; ^1H NMR ($CDCl_3$) δ 6.65 (1 H, ddd, J = 9, 6, 2 Hz, CHCH=*CH*CHO), 6.35 (1 H, dd, J = 11, 7 Hz, CCH=*CH*CHO), 6.20 (1 H, ddd, J = 8, 7, 1 Hz, CH*CH*=CHCHO), 5.75 (1 H, ddd, J = 11, 2, 1 Hz, C*C*H=CHCHO), 4.95 (1 H, dddd, J = 7, 6, 1, 1 Hz, CHO), 4.0 (5 H, m, *CH*CO_2, $OCH_2CH_2CH_2O$), 1.80 (2 H, p, J = 5 Hz,

$OCH_2CH_2CH_2O$); ^{13}C NMR ($CDCl_3$) δ 170.1 (s, C=O), 135.8 (d, C*CH*=CHCHO), 131.0, 130.6 (two d, two CH=*CH*CHO), 126.1 (d, CH=*C*HCO$_2$), 92.3 (s, OCO), 71.6 (d, CHO), 60.5, 59.6 (two t, O*CH*$_2$CH$_2$*CH*$_2$O), 48.7 (d, *C*HCO$_2$), 24.6 (t, OCH$_2$*C*H$_2$CH$_2$O); IR (KBr) ν_{max} 2980, 2772, 1744 (C=O), 1686, 1646, 1391, 1368, 1354, 1273, 1246, 1202, 1136, 1102, 1090, 1034, 1009, 990 cm^{-1}; EIMS, *m/e* (rel intensity) 208 (M$^+$, 12), 180 (CO_2, 15), 179 (11), 163 (7), 140 (7), 122 (22), 121 (20), 113 (90), 112 (22), 107 (30), 106 (52), 100 (59), 95 (32), 94 (34), 93 (36), 78 (100); HRMS, $C_{11}H_{12}O_4$ requires *m/e* 208.0735, found 208.0739.

Anal. Calcd for $C_{11}H_{12}O_4$: C, 63.45; H, 5.81. Found: C, 63.08; H, 5.90.

Unambiguous confirmation of the structure **5c** was derived from a single-crystal X-ray structure determination.[32b]

Thermal Reaction of Methyl Propiolate with 1: Preparation of 10. Methyl propiolate (50 μL, 47.3 mg, 0.56 mmol) and cyclopropenone ketal **1** (115 mg, 1.03 mmol, 1.8 equiv) were combined in benzene-d_6 (0.3 mL) in a ^1H NMR tube, and the resulting solution was warmed at 80 °C under argon until judged complete by ^1H NMR spectroscopy (3 h). MPLC (15 × 250 mm, 25% ethyl acetate–hexane eluant) afforded 59 mg (109.8 mg theoretical, 54%) of pure **10** as a colorless oil: ^1H NMR ($CDCl_3$) δ 5.92 (1 H, dd, J = 17, 10 Hz, *CH*=CH$_2$), 5.71 (1 H, d, J = 17 Hz, CH=CH$_A$H), 5.36 (1 H, d, J = 10 Hz, CH=CH*H*$_B$), 4.27 (2 H, dt, J = 13, 2 Hz, OC*H*$_2$CH$_2$CH$_2$O), 4.01 (2 H, dd, J = 11, 5.5 Hz, OCH$_2$CH$_2$*CH*$_2$O), 3.82 (3 H, s, CO$_2$CH$_3$), 2.22–2.04 (1 H, br m, OCH$_2$C*H*HCH$_2$O), 1.42 (1 H, rough d, J = 14 Hz, OCH$_2$CH*H*CH$_2$O); ^{13}C NMR δ 153.2 (s, C=O), 136.0 (d, *CH*=CH$_2$), 118.1 (t, CH=*CH*$_2$), 93.9 (s, OCO), 81.3 (s, C≡*C*CO$_2$CH$_3$), 78.6 (s, *C*≡CCO$_2$CH$_3$), 62.9 (t, O*CH*$_2$CH$_2$*CH*$_2$O), 52.8 (q, OCH$_3$), 24.7 (t, OCH$_2$*CH*$_2$CH$_2$O); IR (film) ν_{max} 2959, 2874, 2234 (C≡C), 1719 (C=O), 1460, 1435, 1410, 1294, 1256, 1213, 1148, 1119, 1092, 1053, 1044, 982, 957, 926 cm^{-1}; EIMS, *m/e* (rel intensity) 196 (M$^+$, 1), 195 (2), 169 (CH$_2$=CH, 12), 165 (OCH$_3$, 2), 151 (3), 138 (9), 137 (11), 123 (14), 113 (48), 111 (31), 110 (21), 107 (34), 98 (19), 95 (18), 80 (29), 79 (100); HRMS, $C_{10}H_{13}O_4$ requires *m/e* 197.0812, found 197.0831.

Mild Hydrolysis of 5c: Preparation of 14 and Conversion to Tropone (8c). A stirred solution of **5c** (18.9 mg, 0.09 mmol) in methanol (0.2 mL) was treated with dilute aqueous sulfuric acid (0.1%), and the resulting solution was stirred at 25 °C (4 h). The crude reaction mixture was made basic (5% NaHCO$_3$) and extracted with methylene chloride (3×), and the combined organic phases were dried (Na$_2$SO$_4$) and concentrated in vacuo. ^1H NMR analysis of the crude product showed a 1:1 mixture of enone **14** and starting **5c**. Chromatography (SiO$_2$, 50% ethyl acetate–hexane eluant) afforded 6.3 mg (13.5 mg theoretical, 47%) of **14**: ^1H NMR ($CDCl_3$) δ 7.22 (1 H, dd, J = 8, 11 Hz, C*H*=CHC=O), 6.70 (1 H, ddd, J = 8, 6, 2 Hz, CHC*H*=CHCHO), 6.45 (1 H, ddd, J = 8, 7, 1 Hz, CHCH=C*H*CHO), 5.65 (1 H, dd, J = 11, 2 Hz, CH=C*H*—C=O), 5.28 (1 H, rough dd, J = 8, 7 Hz, CHO), 4.37 (1 H, dt, J = 6, 1 Hz, O=C—CH—C=O); IR (film) λ_{max} 3083, 1755 (CO$_2$), 1682 (C=O), 1634, 1381, 1362, 1244, 1228, 1183, 1148, 1123, 1024, 1005, 947, 818 cm^{-1}; EIMS *m/e* (rel intensity) 150 (M$^+$, 4), 123 (4), 122 (CO$_2$, 53), 106 (6), 95 (34), 82 (50), 78 (66); HRMS, $C_8H_6O_3$ requires *m/e* 150.0317, found 150.0313.

A solution of **14** (4.9 mg, 0.033 mmol) in mesitylene (0.3 mL) under argon was warmed at 140 °C until conversion to tropone (**8c**) was complete (4 h). Chromatography (SiO$_2$, 25–75% ether–pentane gradient) afforded 2 mg (3.5 mg theoretical, 58%) of **8c** as a colorless oil identical in all respects with authentic tropone.

Preparation of 2-(Methoxycarbonyl)cycloheptatrienone (8d) from 5c. A solution of **5c** (8 mg) in methanol (0.1 mL) was treated with 0.5 mL of dilute aqueous sulfuric acid (ca. 1%) and was stirred at 25 °C for 14 h. The crude reaction mixture was extracted with methylene chloride (2×), and the combined organic phases were dried (Na$_2$SO$_4$) and concentrated in vacuo. The resulting white solid was dissolved in a 1:1 mixture of tetrahydrofuran–ether and was treated with excess diazomethane. After concentration of the solvent under nitrogen, the resulting orange oil was dissolved in methylene chloride, washed with 5% NaHCO$_3$ (3×), dried (Na$_2$SO$_4$), and concentrated in vacuo. Chromatography on Florisil (25–50% ethyl acetate–hexane gradient) afforded 2-(methoxycarbonyl)cycloheptatrienone (**8d**): ^1H NMR ($CDCl_3$) δ 7.55 (1 H, m, C*H*CO$_2$CH$_3$), 7.06 (4 H, m, four CH), 3.88 (3 H, s, OCH$_3$); IR (film) λ_{max} 2953, 2922, 2853, 1732 (C=O), 1634, 1590, 1530, 1464, 1435, 1291, 1266, 1237, 1073, 1032 cm^{-1}; EIMS *m/e* (rel intensity) 164 (M$^+$, 8), 133 (OCH$_3$, 11), 106 (15), 105 (CO$_2$CH$_3$, 100), 77 (89); HRMS, $C_9H_8O_3$ requires *m/e* 164.0473, found 164.0471.

General Procedure for the Reaction of Cyclopropenone Ketals with C=O Double Bonds. Preparation of Furans and Butenolide Ortho Esters: Reaction of *p*-Nitrobenzaldehyde with Cyclopropenone Ketal 1. Method A. Preparation of 16 and 17. *p*-Nitrobenzaldehyde (205 mg, 1.36 mmol) and cyclopropenone ketal **1** (152 mg, 1.36 mmol) were suspended in heptane (5 mL) and warmed at reflux (80 °C, 12 h) under nitrogen. The crude reaction mixture was concentrated in vacuo, and chromatography (SiO$_2$, ethyl acetate–hexane gradient) afforded 133 mg of **17** and 27 mg of **16** (358 mg theoretical, 45% overall). **17**: mp 103 °C; ^1H NMR (benzene-d_6) δ 7.96 (2 H, d, J = 9 Hz, ArC2–H, ArC6–H), 7.21 (2 H, d, J = 9 Hz, ArC3–H, ArC5–H), 6.37 (1 H, d, J = 3.5 Hz, ArC=C*H*CH=C), 5.08 (1 H, d, J = 3.5 Hz, ArC=CHC*H*=C), 3.89 (2 H, t, J = 6 Hz, O*CH*$_2$CH$_2$CH$_2$OH), 3.43 (2 H, t, J = 6 Hz, OCH$_2$CH$_2$*CH*$_2$OH), 1.65 (2 H, p, J = 6 Hz, OCH$_2$*CH*$_2$CH$_2$OH); EIMS, *m/e* (rel intensity) 263 (M$^+$, 18), 205 (base, 100), 175 (15), 159 (24), 131 (14), 130 (11), 103 (23), 76 (22); HRMS, $C_{13}H_{13}NO_5$ requires *m/e* 263.0793, found 263.0783. **16**: mp 108 °C; ^1H NMR (benzene-d_6) δ 7.94 (2 H, d, J = 9 Hz, ArC2–H, ArC6–H), 7.08 (2 H, d, J = 9 Hz, ArC3–H, ArC5–H), 5.87 (1 H, dd, J = 6, 2 Hz, CH*CH*=CHC), 5.57 (1 H, dd, J = 6, 1 Hz, CHCH=*CH*C), 5.40 (1 H, m, *CH*CH=CHC), 4.6–4.0 (2 H, m, O*CH*$_2$CH$_2$CH$_2$O), 4.0–3.6 (2 H, m, OCH$_2$CH$_2$*CH*$_2$O), 2.3–1.8 (1 H, m, OCH$_2$C*H*HCH$_2$O), 1.20–0.80 (1 H, m, OCH$_2$CH*H*CH$_2$O).

Upon standing at room temperature **16** converts to **17** (100%).

19: ^1H NMR ($CDCl_3$) δ 8.19 (2 H, d, J = 9 Hz, ArC2–H, ArC6–H), 7.61 (2 H, d, J = 9 Hz, ArC3–H, ArC5–H), 6.27 (1 H, d, J = 6 Hz, C*CH*=CHCO$_3$), 5.79 (1 H, d, J = 6 Hz, CCH=*CH*CO$_3$), 4.50 (2 H, dt, J = 12, 4 Hz, O*CH*$_2$CH$_2$CH$_2$O), 4.20–3.80 (2 H, m, OCH$_2$CH$_2$*CH*$_2$O), 2.4–1.9 (1 H, m, OCH$_2$C*H*HCH$_2$O), 1.75 (3 H, s, CH$_3$), 1.60 (1 H, rough d, J = 12 Hz, OCH$_2$CH*H*CH$_2$O); IR (film) ν_{max} 2970, 2885, 1680, 1595, 1508, 1340, 1260, 1240, 1162, 1138, 1104, 1060, 995, 845 cm^{-1}; EIMS, *m/e* (rel intensity) 277 (M$^+$, 2), 262 (CH$_3$, 4), 220 (4), 204 (73), 176 (67), 158 (15), 146 (18), 130 (23), 102 (31); HRMS, $C_{14}H_{15}NO_5$ requires *m/e* 277.0949, found 277.0938.

23: mp 65 °C; ^1H NMR ($CDCl_3$) δ 7.59 (1 H, br s, ArCH), 7.35 (2 H, m, two ArCH), 6.54 (1 H, d, J = 3.5 Hz, ArC=*CH*CH=C), 5.26 (1 H, d, J = 3.5 Hz, ArC=CH*CH*=C), 3.90 (3 H, s, OCH$_3$); EIMS, *m/e* (rel intensity) 244/242 (M$^+$, 2/3 50), 229/227 (CH$_3$, 2/3, 100), 201/199 (2/3, 17), 175 (22), 173 (44), 17 (14), 147 (18), 145 (24); HRMS, $C_{11}H_8Cl_2O_2$ requires *m/e* 241.9901, found 241.9878.

26: ^1H NMR ($CDCl_3$) δ 7.63 (1 H, d, J = 5 Hz, C*CH*=CHCO$_2$), 7.63 (5 H, s, aromatic), 6.05 (1 H, d, J = 5 Hz, CCH=*CH*CO$_2$), 1.84 (3 H, s, CH$_3$); IR ($CHCl_3$) ν_{max} 3050, 3010, 2960, 2895, 1760 (C=O), 1455, 1420, 1385, 1260, 1235, 1130, 1105, 1085, 975, 835 cm^{-1}; EIMS, *m/e* (rel intensity) 174 (M$^+$, 26), 159 (CH$_3$, 53), 131 (53), 115 (18), 105 (46), 103 (61), 77 (100); HRMS, $C_{11}H_{10}O_2$ requires *m/e* 174.0680, found 174.0680.

27: ^1H NMR ($CDCl_3$) δ 6.34 (1 H, d, J = 6 Hz, C*CH*=CHCO$_3$), 5.96 (1 H, d, J = 6 Hz, CCH=*CH*CO$_3$), 4.8–3.7 (8 H, m, two CO$_2$*CH*$_2$, O*CH*$_2$CH$_2$*CH*$_2$O), 2.6–1.3 (2 H, m, OCH$_2$*CH*$_2$CH$_2$O), 1.29 (6 H, t, J = 7 Hz, two OCH$_2$*CH*$_3$); IR ($CHCl_3$) ν_{max} 3020, 1745, 1375, 1370, 1080, 990 cm^{-1}; EIMS, *m/e* (rel intensity) 287 (M + 1, 1), 256 (4), 229 (13), 213 (100), 185 (30), 99 (97).

General Procedure for the Preparation of γ-Keto Esters: Reaction of 3,4-Dichlorobenzaldehyde with Cyclopropenone Ketal 1. Method B. Preparation of 21. 3,4-Dichlorobenzaldehyde (108 mg, 0.625 mmol) and cyclopropenone ketal **1** (140 mg, 1.25 mmol, 2 equiv) were combined in heptane (5 mL), and the resulting suspension was warmed at reflux (80 °C) for 12 h. The crude reaction mixture was concentrated in vacuo, dissolved in acetone (5 mL), and treated with concentrated HCl (3 drops). After the mixture stood at 25 °C (1 h) and was concentrated in vacuo, chromatography (SiO$_2$, ethyl acetate–hexane gradient) afforded 101 mg (190 mg theoretical, 53%) of **21** as a white solid: mp 78 °C; ^1H NMR ($CDCl_3$) δ 8.04 (1 H, d, J = 1 Hz, ArC3–H), 7.83 (1 H, dd, J = 8, 1 Hz, ArC5–H), 7.58 (1 H, d, J = 8 Hz, ArC6–H), 4.27 (2 H, t, J = 6 Hz, O*CH*$_2$CH$_2$CH$_2$OH), 3.71 (2 H, t, J = 6 Hz, OCH$_2$CH$_2$*CH*$_2$OH), 3.25 (2 H, t, J = 6 Hz, COC*H*$_2$CH$_2$CO$_2$), 2.75 (2 H, t, J = 6 Hz, COCH$_2$*CH*$_2$CO$_2$), 1.6 (1 H, br s, OH), 1.87 (2 H, p, J = 6 Hz, OCH$_2$*CH*$_2$CH$_2$OH); IR ($CHCl_3$) ν_{max} 1730, 1690 cm^{-1}.

Anal. Calcd for $C_{13}H_{14}Cl_2O_4$: C, 51.17; H, 4.62. Found: C, 51.08; H, 4.67.

18: ^1H NMR (benzene-d_6) δ 7.81 (2 H, d, J = 9 Hz, ArC2–H, ArC6–H), 7.48 (2 H, d, J = 9 Hz, ArC3–H, ArC5–H), 4.22 (2 H, t, J = 6 Hz, O*CH*$_2$CH$_2$CH$_2$OH), 3.49 (2 H, t, J = 6 Hz, OCH$_2$CH$_2$*CH*$_2$OH), 2.63, 2.62 (4 H, two overlapping t, J = 6 Hz, CO*CH*$_2$*CH*$_2$CO), 1.67 (2 H, p, J = 6 Hz, OCH$_2$*CH*$_2$CH$_2$OH); IR ($CHCl_3$) ν_{max} 1730, 1690 cm^{-1}; CIMS (NH_3), *m/e* (rel intensity) 299 (M + 18, 19), 282 (M + 1, 49), 264 (15), 223 (40), 208 (55), 206 (base, 100); HRMS, $C_{13}H_{14}NO_5$ requires *m/e* 264.0871, found 264.0836.

22: mp 73 °C; ^1H NMR ($CDCl_3$) δ 8.08 (1 H, d, J = 1 Hz, ArC3–H), 7.83 (1 H, dd, J = 8, 1 Hz, ArC5–H), 7.57 (1 H, d, J = 8 Hz, ArC6–H), 3.73 (3 H, s, OCH$_3$), 3.27 (2 H, t, J = 6 Hz, COC*H*$_2$CH$_2$CO$_2$CH$_3$), 2.78 (2 H, t, J = 6 Hz, COCH$_2$*CH*$_2$CO$_2$CH$_3$); IR ($CHCl_3$) ν_{max} 3050, 2980, 1730, 1690, 1595, 1450, 1400, 1385, 1365, 1335, 1240, 1185, 1040, 920 cm^{-1}; EIMS, *m/e* (rel intensity) 262/260

(M^+, 2/3, 7), 231/229 (OCH_3, 2/3, 9), 203/201 (2/3, 2), 175/173 (2/3, base), 147/143 (2/3, 25), 109 (17); HRMS, $C_{11}H_{10}Cl_2O_3$ requires *m/e* 260.0003, found 259.9980.

25: ^1H NMR ($CDCl_3$) δ 7.95 (2 H, d, J = 9 Hz, aromatic), 6.93 (2 H, d, J = 9 Hz, aromatic), 4.18 (2 H, t, J = 6 Hz, CO_2CH_2), 3.86 (3 H, s, OCH_3), 3.77 (2 H, t, J = 6 Hz, CH_2OH), 3.26 (2 H, t, J = 6 Hz, $COCH_2CH_2CO_2$), 2.73 (2 H, t, J = 6 Hz, $COCH_2CH_2CO_2$), 2.2 (1 H, br s, OH), 1.87 (2 H, p, J = 6 Hz, $OCH_2CH_2CH_2O$); IR ($CHCl_3$) ν_{max} 3500 (OH), 1720 (C=O), 1675, 1580, 1508, 1260, 1170, 1035 cm^{-1}; EIMS *m/e* (rel intensity) 266 (M^+, 2), 236 (1), 209 (4), 191 (10), 163 (2) 135 (base, 100); HRMS, $C_{14}H_{18}O_5$ requires *m/e* 266.1153, found 266.1148.

General Procedure for the Preparation of Butenolides: Reaction of *p*-Nitroacetophenone with Cyclopropenone Ketal 1. Method C. Preparation of 20. *p*-Nitroacetophenone (103 mg, 0.625 mmol) and cyclopropenone ketal **1** (140 mg, 1.25 mmol, 2 equiv) were combined in heptane (5 mL), and the resulting suspension was warmed at reflux (12 h). The crude product was concentrated in vacuo and treated with acetic acid-tetrahydrofuran-water (1:3:1) at 25 °C (72 h). Chromatography (SiO_2, ethyl acetate-hexane gradient) afforded 42 mg (137 mg theoretical, 31%) of **20** as a white solid: mp 69 °C; ^1H NMR ($CDCl_3$) δ 8.24 (2 H, d, J = 9 Hz, ArC2-H, ArC6-H), 7.65 (1 H, d, J = 6 Hz, CCH=$CHCO_2$), 7.58 (2 H, d, J = 9 Hz, ArC3-H, ArC5-H), 6.13 (1 H, d, J = 6 Hz, CCH=$CHCO_2$), 1.86 (3 H, s, CH_3); IR ($CHCl_3$) ν_{max} 1780 cm^{-1}; EIMS, *m/e* (rel intensity) 219 (M^+, 5), 204 (CH_3, 100), 177 (61), 176 (83), 160 (16), 158 (19), 150 (18), 146 (23), 130 (33), 102 (32), 76 (53); HRMS, $C_{11}H_9NO_4$ requires *m/e* 219.0531, found 219.0527.

24: ^1H NMR ($CDCl_3$) δ 7.72 (1 H, d, J = 1 Hz, ArC3-H), 7.49 (2 H, m, ArC5-H, ArC6-H), 5.84 (1 H, t, J = 3 Hz, C=CH), 3.46 (2 H, d, J = 3 Hz, C=$CHCH_2$); IR ($CHCl_3$) ν_{max} 3050, 1800 (C=O), 1480, 1395, 1305, 1140, 1005, 1000, 920 cm^{-1}; EIMS, *m/e* (rel intensity) 230/228 (M^+, 2/3, 61), 193 (34), 175/173 (base, 2/3, 100), 165 (72), 149 (15), 147 (28), 145 (31), 109 (31); HRMS, $C_{10}H_6Cl_2O_2$ requires *m/e* 227.9744, found 227.9757.

Acknowledgment. This work was assisted financially by the Searle Scholars Fund and the National Institutes of Health (CA 00898/01134, CA 33668/42056). We thank Prof. G. I. Georg for her contribution to this work (Table II) and for stimulating discussions. We thank Profs. G. E. Keck, D. A. Hart, A. R. Chamberlin, T. A. Engler, A. W. Burgstahler, and R. S. Givens for valuable discussions and suggestions on aspects of this work.

Registry No. **1**, 60935-21-9; **2**, 23529-83-1; *cis*-**3a**, 94922-97-1; *trans*-**3a**, 94922-98-2; *cis*-**3b**, 77462-53-4; *trans*-**3b**, 77462-54-5; *cis*-**3c**, 94922-99-3; *trans*-**3c**, 94923-00-9; *cis*-**3d**, 103384-75-4; *trans*-**3d**, 94923-06-5; *cis*-**3e**, 103384-76-5; *trans*-**3e**, 94923-02-1; *cis*-**3f**, 94923-03-2; *trans*-**3f**, 94923-04-3; *cis*-**3g**, 103384-77-6; *trans*-**3g**, 103384-88-9; **3h**, 103384-78-7; **3i**, 103384-79-8; **3j**, 103384-80-1; **4a**, 88442-07-3; **4b**, 88442-08-4; **4c**, 88442-09-5; **4d**, 88442-10-8; **4e**, 88442-11-9; **4f**, 88442-12-0; **4g**, 103422-00-0; *cis*-**4h**, 103384-81-2; *trans*-**4h**, 103384-89-0; **4i**, 88442-05-1; **4j**, 103384-82-3; **4k**, 103384-84-5; **5c**, 103384-86-7; **7a**, 103384-83-4; **7b**, 103384-85-6; **10**, 103384-87-8; **12**, 60935-26-4; **14**, 103384-92-5; **16**, 95652-68-9; **17**, 95652-70-3; **18**, 95652-71-4; **19**, 95652-69-0; **20**, 95652-72-5; **21**, 95652-73-6; **22**, 95652-74-7; **23**, 95652-75-8; **24**, 95609-49-7; **25**, 103384-90-3; **26**, 53774-21-3; **27**, 103384-91-4; CH_2=$CHS(O)Ph$, 20451-53-0; $PhSC(CO_2Et)$=CH_2, 56685-62-2; $PhCH$=$C(CO_2Et)_2$, 5292-53-5; $PhCH$=$C(CO_2Me)_2$, 6626-84-2; CH_3CH=$C(CO_2Et)_2$, 1462-12-0; $PhCH$=$C(CN)_2$, 2700-22-3; $(CH_3)_2C$=$C(CO_2Et)_2$, 6802-75-1; Ph_2C=$C(CO_2Et)_2$, 24824-36-0; $PhS(O)C(CO_2CH_3)$=CH_2, 85908-47-0; CH_2=$C(OCH_3)_2$, 922-69-0; $CH_3(CH_2)_2C$≡CCO_2CH_3, 18937-79-6; CH_3O_2CC≡CCO_2CH_3, 762-42-5; CH_2=$CHCO_2CH_3$, 96-33-3; CH_2=$CHCN$, 107-13-1; $CH_3C(CO_2CH_3)$=CH_2, 80-62-6; CH_2=$C(CN)CH_3$, 126-98-7; $PhC(CO_2Et)$=CH_2, 22286-82-4; (*E*)-CH_3O_2CCH=$CHCO_2CH_3$, 624-49-7; $CH_3O_2CC(CO_2CH_3)$=$CHOCH_3$, 22398-14-7; CH≡CCO_2CH_3, 922-67-8; *p*-$NO_2C_6H_4CHO$, 555-16-8; *p*-$NO_2C_6H_4COCH_3$, 100-19-6; 3,4-$Cl_2C_6H_3CHO$, 6287-38-3; *p*-$CH_3OC_6H_4CHO$, 123-11-5; $PhCOCH_3$, 98-86-2; $EtOCOCOCO_2Et$, 609-09-6; $HO(CH_2)_3OH$, 504-63-2; 2-cyclopenten-1-one, 930-30-3; 1-nitrocyclohexene, 2562-37-0; 2-pyrone, 504-31-4; 6,6-dimethyl-3-carbethoxy-3-norpinen-2-one, 88442-04-0; diethyl cyclohexylidenemalonate, 41589-43-9; cyclohexene, 110-83-8; 3,4-dihydro-2*H*-pyran, 110-87-2; 1-(cyclohexenylmethylene)malonitrile, 103384-73-2; methyl 3-(1-cyclohexenyl)-2-cyano-2-propanoate, 103384-74-3; 5,6,7,8-tetrahydro-3-methoxycarbonyl-2*H*-benzopyran-2-one, 85531-80-2; 3-methoxycarbonyl-2*H*-pyran-2-one, 25991-27-9; 3-methoxycarbonyl-7,10-dimethoxy-9-bromo-2*H*-naphtho[1,2*b*]pyran-2-one, 88442-03-9; 5-methoxycarbonyl-2*H*-pyran-2-one, 6018-41-3; 2-(bromomethyl)-2-(chloromethyl)-1,3-dioxane, 60935-30-0; 1-bromo-3-chloro-2,2-dimethoxypropane, 22089-54-9.

Supplementary Material Available: Figures showing atom numbering and views of **5c**, tables of fractional coordinates, thermal parameters, and bond distances and angles, and a listing of structure factor analysis (16 pages). Ordering information is given on any current masthead page.

Thermal Reactions of Cyclopropenone Ketals. Application of the Cycloaddition Reactions of Delocalized Singlet Vinylcarbenes: Three-Carbon 1,1-/1,3-Dipoles. An Alternative Synthesis of Deacetamidocolchiceine: Formal Total Synthesis of Colchicine

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Abstract: An alternative preparation of deacetamidocolchiceine, constituting a formal total synthesis of colchicine, is detailed and is based on the thermal [3 + 4] cycloaddition of Eschenmoser's α-pyrone with cyclopropenone 1,3-propanediyl ketal in a process which proceeds via the reversible, thermal generation of a delocalized singlet vinylcarbene, a three-carbon 1,1-/1,3-dipole, and its subsequent $_\pi2_s$ participation in a $[_\pi4_s + _\pi2_s]$ cycloaddition.

Colchicine (**1**), a potent mitotic inhibitor which exhibits a characteristic and specific binding with tubulin preventing microtubule assembly, spindle formation, and consequently cell division, has been the focus of initial extensive and subsequent

0002-7863/86/1508-6713$01.50/0