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# DIELS–ALDER CYCLOADDITION REACTIONS OF CYCLOPROPENONE KETALS

## DUAL PARTICIPATION IN INVERSE ELECTRON DEMAND ($LUMO_{diene}$ CONTROLLED) AND NORMAL ($HOMO_{diene}$ CONTROLLED) DIELS–ALDER REACTIONS. APPROACHES TO THE PREPARATION OF TROPONES

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**Abstract**—Diels–Alder cycloadditions of the cyclopropenone ketal **1** with representative electron-deficient, electron-rich and neutral dienes are presented. The results observed are consistent with the potential for the strained olefin of the cyclopropenone ketal to exhibit accelerated participation in both inverse electron demand ($LUMO_{diene}$ controlled) and normal ($HOMO_{diene}$ controlled) Diels–Alder reactions. Approaches to the introduction of cycloheptatrienones, tropones, based on the room temperature and pressure-promoted Diels–Alder reactions of the cyclopropenone ketal **1** are presented.

### INTRODUCTION

The rate of the Diels–Alder reaction is determined by the lowest HOMO–LUMO energy separation attainable by the reacting diene/dienophile components, $HOMO_{diene}$–$LUMO_{dienophile}$ or $LUMO_{diene}$–$HOMO_{dienophile}$, of the [4+2] cycloaddition.[1] Factors which are responsible for lowering the magnitude of this energy separation accelerate the rate of the Diels–Alder reaction. Two distinct classifications of the Diels–Alder reaction have been described in which the factors affecting the two individual components, the 2-$\pi$ and 4-$\pi$ component, of the reaction act in a complementary manner to reduce the magnitude of a HOMO–LUMO energy separation and result in suitable reaction rates (25–200°) for the [4+2] cycloaddition. These are the normal ($HOMO_{diene}$ controlled) Diels–Alder reaction customarily employing an electron-rich diene (increased $HOMO_{diene}$)/electron-deficient dienophile (decreased $LUMO_{dienophile}$) and the inverse electron demand ($LUMO_{diene}$ controlled) Diels–Alder reaction employing an electron-deficient diene (decreased $LUMO_{diene}$)/electron-rich dienophile (increased $HOMO_{dienophile}$). This complementary choice of diene/dienophile partners for [4+2] cycloaddition and the recognition of the origin of the accompanying rate acceleration have played a major role in the development, predictive success and application of the Diels–Alder reaction.[1-3]

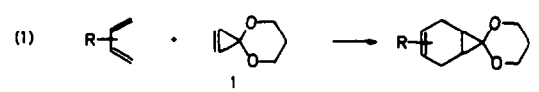
In most instances, factors which accelerate the participation of an olefin in a normal ($HOMO_{diene}$ controlled) Diels–Alder reaction would be expected to slow its participation in an inverse electron demand Diels–Alder reaction. A potential exception to this generalization would be the participation of strained olefins in [4+2] cycloaddition reactions, and experimental studies have detailed examples of their Diels–Alder reactions with electron-rich, electron-deficient as well as neutral dienes.[1-4] This behavior has been attributed to the reactivity of strained olefins, the release of strain energy, which intuitively would suggest high reactivity in the Diels–Alder reaction.[4,5] Qualitatively, strained olefins would be expected to possess an increased HOMO and a decreased LUMO, relative to ethylene, and thus possess the potential for accelerated participation in both normal ($HOMO_{diene}$ controlled) *and* inverse electron demand ($LUMO_{diene}$ controlled) Diels–Alder reactions.[5]

Herein we describe full details of studies designed to investigate the scope of the Diels–Alder reactions of cyclopropenone ketals[6,7] which realize and illustrate this dual participation of strained olefins in $LUMO_{diene}$ *and* $HOMO_{diene}$ controlled Diels–Alder reactions at rates comparable to those customarily associated with useful [4+2] cycloadditions. An anticipated and designed extension of these studies for the preparation of cycloheptatrienones,[8] tropones, suitable for use in the total synthesis of tropoloalkaloids,[9] is described.

### RESULTS AND DISCUSSION

*Scope of the Diels–Alder reactions of the cyclopropenone ketal* **1**[7]

Table 1 details the results of a full study of the scope of the Diels–Alder reaction of the cyclopropenone ketal **1** with representative electron-deficient, electron-rich and neutral dienes (Eq. 1). In accordance with

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expectations, the reactions of the cyclopropenone ketal **1** with electron-deficient olefins (Table 1, entries 1–3)

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proceed at suitable rates (25 and 80°, or 25°/6.2 kbar) consistent with an accelerated inverse electron demand ($LUMO_{diene}$ controlled) Diels–Alder reaction and at a rate in excess of that customarily associated with a normal ($HOMO_{diene}$ controlled) Diels–Alder reaction.

Similarly, the electron-rich diene, 1-methoxy-1,3-butadiene, undergoes smooth [4+2] cycloaddition with the cyclopropenone ketal **1** (25 or 80°, Table 1, entry 4) at a rate consistent with an accelerated normal ($HOMO_{diene}$ controlled) Diels–Alder reaction.

Neutral dienes including isoprene (Table 1, entries 6–10) similarly participate in [4+2] cycloaddition reactions with the cyclopropenone ketal **1** and the reactions may be conducted neat (25°), thermally (solvent, 80°)[10] or under pressure-promoted Diels–Alder conditions (25°, 6.2 kbar).[11]

A full range of experimental conditions for conducting the [4+2] cycloaddition reactions of the cyclopropenone ketal **1** and the results are detailed in Table 1. The results confirm the potential for the strained olefin of **1** to behave as an effective 2-π component in either a $HOMO_{diene}$ controlled or a $LUMO_{diene}$ controlled Diels–Alder reaction. While the initial rationale for the anticipated participation of the cyclopropenone ketal **1** in a normal ($HOMO_{diene}$ controlled) Diels–Alder reaction rested on the lowered $LUMO_{cyclopropenone\ ketal}$, relative to ethylene, a second potential explanation cannot be ruled out. The observed participation of **1** in the normal ($HOMO_{diene}$ controlled) Diels–Alder reaction may be initiated by the reversible formation of the cyclopropenium cation **i** and the subsequent participation of **i** in a normal ($HOMO_{diene}$ controlled) Diels–Alder reaction or in a two-step addition–cyclization reaction (Eq. 2).[12] Either interpretation accurately predicts the observed accelerated reaction of **1** with electron-rich dienes.

In addition, the cyclopropenone ketal **1** is subject to an apparent, reversible and thermal generation of a reactive three-carbon 1,3-dipole best represented as a nucleophilic vinylcarbene (Eq. 3).[13a] This appears

Table 1. Diels–Alder cycloadditions of the cyclopropenone ketal **1**

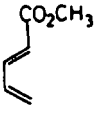
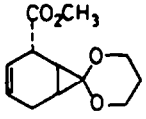
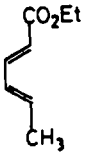
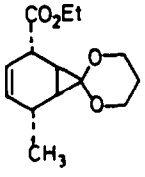
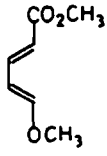
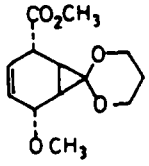
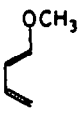
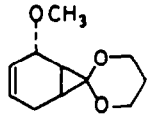
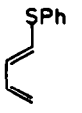
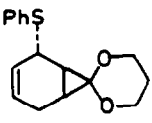
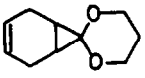
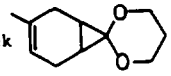
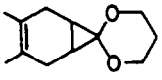
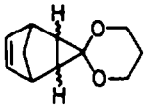
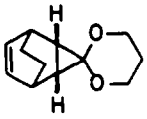
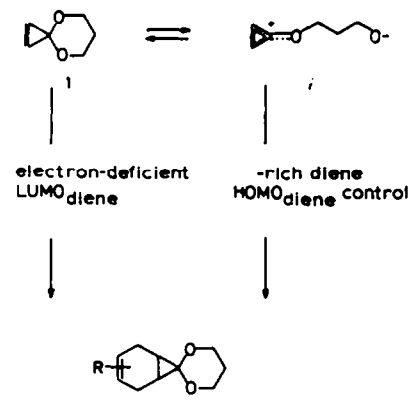
| Entry | Diene | Conditions,[a] (Equiv **1**) | Product[b] | % Yield[c] |
|---|---|---|---|---|
| Electron-Deficient Dienes | | | | |
| 1 |  | (1.5), neat, 25 °C, 40 h |  | **2**, 65% |
| | | (0.9),[d] $C_6H_6$, 75 °C, 4.5 h | | 56% |
| 2 |  | (0.3),[d] neat, 25 °C, 120 h |  | **3**, 46% |
| | | (2.0), neat, 35 °C, 60 h | | 70% |
| | | (2.0), heptane, 35 °C, 168 h | | 62% |
| | | (2.0), $C_6H_6$, 35 °C, 144 h | | 41% |
| | | (1.0), $CH_2Cl_2$, 25 °C, - | | slow |
| | | (1.2), $CH_2Cl_2$, 6.2 kbar, 25 °C, 24 h | | 45% |
| 3[e] |  | (1.9), neat, 25 °C, 72 h |  | **4**, 60% |
| | | (3.0),[f] neat, 25 °C, 168 h | | 80% |
| Electron-Rich Dienes | | | | |
| 4 |  | (1.9), neat, 25 °C, 60 h |  | **5**, 72% |
| | | (1.6), $C_6H_6$, 80 °C, 4 h | | 56% |
| 5[g] |  | (1.4), neat, 25 °C, 160 h |  | **6**, 33% |

Table 1—*continued*

| | | | | |
|---|---|---|---|---|
| **Neutral Dienes** | | | | |
| 6 |  | (0.2),[d] neat, 25 °C, 62 h |  | 7, 69% |
| 7 |  | (0.2),[d] neat, 25 °C, 113 h |  | 8, 57% |
| | | (0.67),[d] $CH_2Cl_2$, 25 °C, 2 week | | 44% |
| | | (0.67),[d] $C_6H_6$, 25 °C, 132 h | | 28% |
| | | (0.67),[d] $CH_3CN$, 25 °C, 132 h | | 23% |
| | | (1.0), $CH_2Cl_2$, 6.2 kbar, 25 °C, 48 h | | 83% |
| | | (1.2), neat, 6.2 kbar, 25 °C, 40 h | | 96% |
| 8 |  | (0.2),[d] neat, 25 °C, 66 h |  | 9, 57% |
| | | (0.5),[d] $C_6H_6$, 75 °C, 7.5 h | | 48% |
| 9 |  | (0.5),[d] neat, 25 °C, 144 h |  | 10, 57% (1:1, exo:endo) |
| 10 |  | (0.6),[d] neat, 25 °C, 2 week |  | 11, 0% |
| | | (2.0), $C_6H_6$, 80 °C, 22 h | | 0% |
| | | (0.6),[d] neat, 6.2 kbar, 25 °C, 1 week | | 25% |

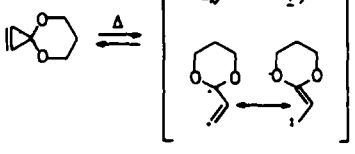
[a] All reactions were run neat or in the indicated solvent (1–3.0 M in substrate) under argon.
[b] All products exhibited the expected $^1$H-NMR, $^{13}$C-NMR, IR and MS characteristics consistent with the assigned structure.
[c] All yields are based on purified products isolated by chromatography ($SiO_2$).
[d] The yield is based on cyclopropenone ketal **1**.
[e] J. Maddaluno and J. d'Angelo, *Tetrahedron Lett.* **24**, 895 (1983); R. H. Smithers, *J. Org. Chem.* **43**, 2833 (1978).
[f] 2.0 Equiv **1** (25°, 66 h) then an additional 1.0 equiv **1** (25°, 96 h).
[g] P. B. Hopkins and P. L. Fuchs, *J. Org. Chem.* **43**, 1208 (1978).

(2)

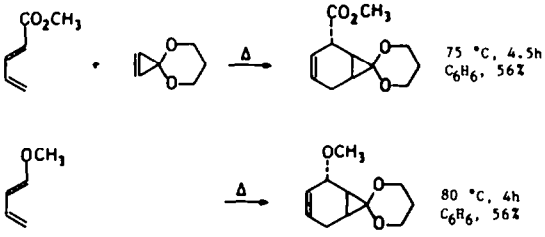



to be an effective and reversible process at 70–80° and products derived from the reaction of the nucleophilic carbene are observed in the presence of appropriate substrates.[13b–d] The ability of **1** to participate in

(3)

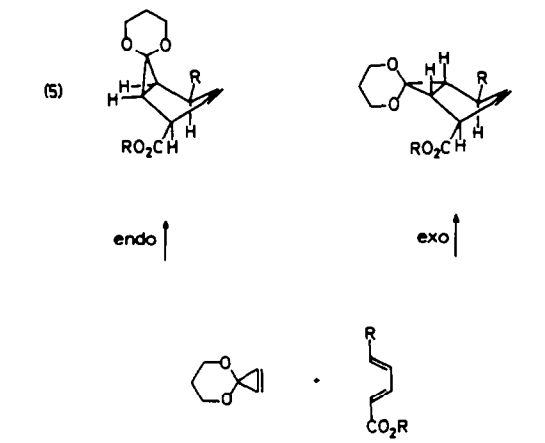


Diels–Alder reactions with the electron-rich, electron-deficient and neutral dienes detailed in Table 1 under thermal conditions (80°) represents an effective trap of the strained olefin of the cyclopropenone ketal in a [4+2] cycloaddition in competition with products which might be derived from the nucleophilic vinylcarbene (Eq. 4). The potential competition of the Diels–Alder reactions of cyclopropenone ketal **1** with the reactions of the transient vinylcarbene under thermal conditions further suggests that the preferred method of accelerating the rate of the Diels–Alder reactions of **1** involves the use of pressure-promoted Diels–Alder conditions (25°, 6.2 kbar).[11]

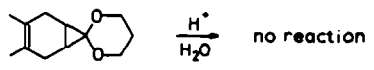



(4)

In nearly all the examples, the isolated Diels–Alder products derived from the cyclopropenone ketal **1** consisted of a single, pure stereoisomer. Although unambiguous proof of the stereochemistry is not available, spectroscopic[14] as well as chemical evidence suggests that the products possess the *trans* stereochemical relationship indicating a preference for an *exo* transition state leading to the [4+2] products (Eq. 5). This preference for an *exo* transition state in the Diels–Alder reactions of **1** is apparently determined by steric factors.[15] Only in instances in which an *endo* transition state is comparably or less sterically demanding than the *exo* transition state are products derived from the *endo* approach observed (Table 1, entries 9 and 10). In such instances, the [4+2] cycloaddition reaction generally proceeds at a reduced rate and in certain instances requires the utilization of pressure-promoted Diels–Alder conditions for an observable reaction (Table 1, entry 10). Additional examples of these observations are detailed below in the [4+2] cycloaddition reactions of **1** with α-pyrones.



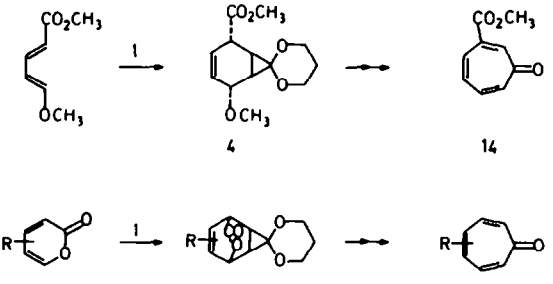

Preliminary studies on the reactivity of the cyclopropenone ketal Diels–Alder adducts revealed an expected and unusual level of stability. Adduct **8** was resistant to ketal hydrolysis upon treatment with a variety of standard and harsh conditions (HOAc–$H_2O$–THF, 3:2:1, 100°, 12 h, no reaction) customarily employed for ketal hydrolysis[16] (Eq. 6). Studies on these and related chemical aspects of the Diels–Alder adducts of the cyclopropenone ketal **1** are currently under investigation.




9

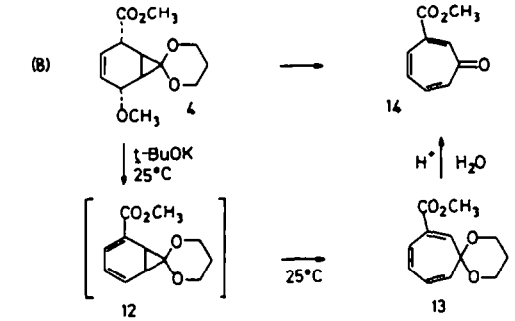
*Tropone introduction*

In expectation of the potential utility of the inverse electron demand Diels–Alder reactions of the cyclopropenone ketal **1** and in initial studies on the development of a process for tropolone introduction[17] suitable for direct utilization in the synthesis of tropoloalkaloids,[8,9] two complementary approaches for cycloheptatrienone, tropone, formation based on the use of **1** were investigated and developed. The basis for the two approaches—the participation of **1** in a room-temperature inverse electron demand Diels–Alder reaction with methyl 4-methoxy-1,3-butadiene-1-carboxylate (Table 1, entry 3) and the participation of **1** in a pressure-promoted Diels–Alder reaction with α-pyrones (Eq. 7)—are detailed below.




(7)

Treatment of methyl 4-methoxy-1,3-butadiene-1-carboxylate with the cyclopropenone ketal **1** (Table 1, entry 3) afforded the [4+2] adduct **4** as a single stereoisomer which possesses the *trans* relative configuration and results from exclusive *exo* approach in the Diels–Alder reaction (Eq. 8). Treatment of **4** with a strong base (t-BuOK, THF, 25°, 10 min)[18] effected elimination of methanol, and a subsequent rearrangement of the norcaradiene **12** (25°) in a room temperature, disrotatory electrocyclic reaction[19]



provided **13** without the detection of the diene **12**. Hydrolysis of **13** (AcOH–$H_2O$–THF, 3:1:4, 25°, 30 min) provided 3-methoxycarbonylcycloheptatrienone (**14**) in a good overall yield.

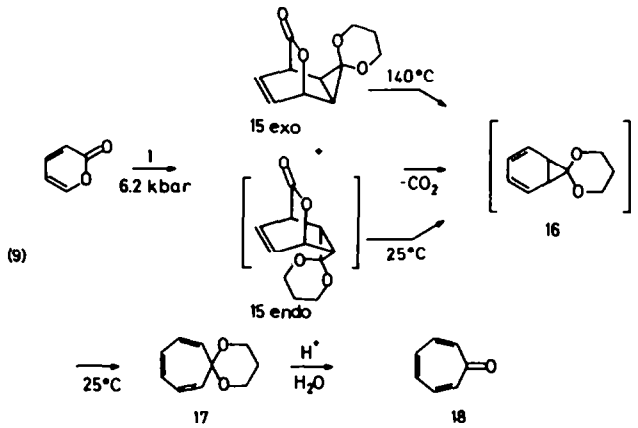
Efforts to reduce this two-step process for tropone introduction to a single operation by employing α-pyrone in a sequence initiated by the [4+2] cycloaddition of the cyclopropenone ketal **1** which would be followed by the loss of carbon dioxide and a subsequent electrocyclic rearrangement of the resultant norcaradiene[19] were successful only under pressure-promoted Diels–Alder conditions.[20] Clean [4+2] cycloaddition was observed (25°, 6.2 kbar) and afforded a mixture of reaction products: *exo*-**15**, cycloheptatrienone ketal (**17**)[21] and cycloheptatrienone (resulting from $SiO_2$-promoted hydrolysis of **17**); each representing a product derived from the Diels–Alder reaction of **1** with α-pyrone (Eq. 9). The **15** *endo* adduct loses carbon dioxide upon depressurization (25°, 1 atm) of the reaction mixture and the *exo* adduct is thermally stable.[22] This observed difference in the rate of decarboxylation of *exo*/*endo*-**15** may be attributed to an accelerated rate of decarboxylation of *endo*-**15** rather than a slowed rate of decarboxylation of *exo*-**15**.[23]

that conversion of the initial [4+2] cycloadducts to the cycloheptatrienone ketals **13** and **19** was occurring upon work-up (25°, 1 atm). The cycloheptatrienone ketals **13** and **19**, which are prone to mild and rapid hydrolysis, could be purified[25] and characterized prior to conversion to the corresponding 3- and 4-methoxycarbonylcycloheptatrienones (**14** and **20**).

Applications of the [4+2] cycloaddition reactions of cyclopropenone ketals as well as additional studies and applications of the thermal reactions of **1** and related species are in progress.

## EXPERIMENTAL

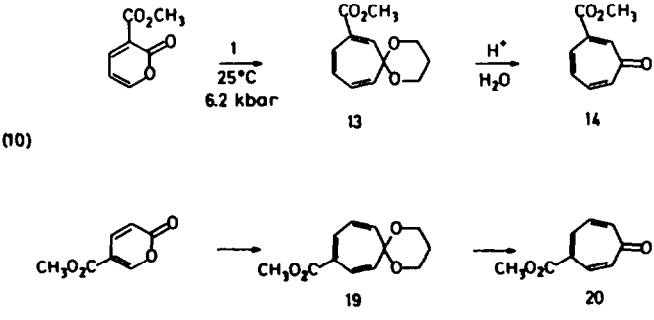
IR spectra were obtained on an IBM FTIR 32 spectrophotometer. $^1$H-NMR spectra were recorded on a Varian FT-80A spectrometer in $CDCl_3$ with TMS internal standard. $^{13}$C-NMR spectra were recorded on a Varian XL-300 spectrometer in $CDCl_3$. Mass spectra (MS) and high-resolution mass spectra (HRMS) 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. All high-pressure reactions were performed in a Leco hydraulically pressurized apparatus[11] containing a castor oil media using Teflon




(9)

Extensions of these observations to the substituted α-pyrones 3-methoxycarbonyl-2-pyrone[24] and 5-methoxycarbonyl-2-pyrone,[24] each possessing an additional electron-withdrawing substituent, provided the cycloheptatrienone ketals **13** and **19** directly (25°, 6.2 kbar)[20b] without the detection or isolation of the intermediate [4+2] cycloadducts or norcaradiene intermediates[19] (Eq. 10). Decarboxylation of the initial Diels–Alder adducts (25°) could be observed upon depressurization of the reaction mixture, indicating

vessels sealed at both ends with brass screw clamps. Dry tetrahydrofuran (THF) was distilled immediately before use from sodium benzophenone ketyl. Acetonitrile was distilled from powdered calcium hydride. $CH_2Cl_2$ was distilled immediately before use from $P_2O_5$. 3-Methoxycarbonyl-2-pyrone, α-pyrone and methyl 2,4-pentadienoic acid were obtained from Fluka Chemicals. 5-Methoxycarbonyl-2-pyrone was supplied by Chem. Service. 1-Methoxy-1,3-butadiene, 2,3-dimethylbutadiene and 1,3-cyclohexadiene were obtained from Aldrich Chemicals. Extraction and chromatographic solvents ($CH_2Cl_2$, EtOAc, hexane) were




(10)

distilled before use. All reactions were run under an argon atmosphere.

*Methyl 7,7 - (trimethylenedioxy) - norcarn - 3 - ene - 2 - carboxylate* (**2**)

*General procedure for the cycloaddition reactions of* **1** *at* 25°. Methyl 2,4-pentadienoic acid[24] (60 mg, 62 μl, 0.54 mmol) and **1**[6] (89 mg, 0.8 mmol, 1.5 equiv) were combined in a 1 ml Kontes vessel under argon atmosphere. The resulting soln was stirred at 25° until no diene remained as determined by $^1$H-NMR (40 h). Chromatography ($SiO_2$, 1.2 × 15 cm, 25% EtOAc–hexane eluant) afforded 78 mg (120 mg theoretical, 65%) of **2** as a colorless oil: $^1$H-NMR ($CDCl_3$) δ 5.68 (2H, br s, CH=CH), 3.95 (4H, t, J = 6 Hz, two $OCH_2$'s), 3.75 (3H, s, $OCH_3$), 3.22 (1H, m, $CHCO_2CH_3$), 2.25 (2H, m, CH=CH—$CH_2$), 1.85 (2H, p, J = 6 Hz, $OCH_2CH_2CH_2O$), 1.90–1.25 (2H, br m, cyclopropyl CH's); IR (film) $\nu_{max}$ 2957, 2865, 1738 (C=O), 1435, 1273, 1244, 1196, 1170, 1156, 1119, 1082, 1059 cm$^{-1}$; EIMS *m/z* (rel. int.) 224 ($M^+$, 16), 209 ($-CH_3$, 6), 165 ($-CO_2CH_3$, 100), 151 (8), 107 (62), 87 (19), 79 (92). (Found: C, 64.10; H, 7.55. Calc for $C_{12}H_6O_4$: C, 64.27; H, 7.19%.)

*General procedure for the cycloaddition reactions of* **1** *at* 80°. Methyl 2,4-pentadienoic acid[24] (103 mg, 106 μl, 0.91 mmol) and **1**[6] (94 mg, 0.83 mmol) were combined in $C_6H_6$ (0.3 ml) in a small reaction vessel under argon. The reaction mixture was warmed at 75° until the reaction was judged complete by $^1$H-NMR (4.5 h). Chromatography ($SiO_2$, 1.2 × 15 cm, 25% EtOAc–hexane eluant) afforded 104 mg (186 mg theoretical, 56%) of **2**.

*Compound* **3**. $^1$H-NMR ($CDCl_3$) δ 5.62 (2H, d, J = 1 Hz, CH=CH), 4.15 (2H, q, J = 7 Hz, $CO_2CH_2$), 3.95 (4H, t, J = 6 Hz, two $OCH_2$'s), 3.20 (1H, m, $CHCO_2Et$), 2.30 (1H, br m, $CHCH_3$), 1.80 (2H, dp, J = 6 Hz, J = 2 Hz, $OCH_2CH_2CH_2O$), 1.65 (1H, dt, J = 9 Hz, J = 2 Hz, cyclopropyl CH), 1.30 (3H, t, J = 7 Hz, $OCH_2CH_3$), 1.25 (3H, d, J = 7 Hz, $CHCH_3$), 1.5–1.0 (1H, m, cyclopropyl CH); IR (film) $\nu_{max}$ 2965, 2930, 2870, 1736 (C=O), 1472, 1456, 1431, 1370, 1287, 1260, 1242, 1181, 1156, 1121, 1071, 1036 cm$^{-1}$; EIMS *m/z* (rel. int.) 252 ($M^+$, 8), 237 ($-CH_3$, 8), 180 (12), 179 ($-CO_2Et$, 100), 121 (41), 93 (67), 91 (54), 87 (35), 79 (19), 78 (14), 77 (53); HRMS, $C_{14}H_{20}O_4$ requires: *m/z* 252.1360; found: 252.1369.

*Compound* **4**. $^1$H-NMR ($CDCl_3$) δ 5.88 (2H, br s, CH=CH), 3.98, 3.94 (5H, two t's, m, J = 6 Hz, $OCH_2CH_2CH_2$, $CHOCH_3$), 3.75 (3H, s, $CO_2CH_3$), 3.39 (3H, s, $OCH_3$), 3.05 (1H, m, $CHCO_2CH_3$), 1.85 (2H, p, J = 6 Hz, $OCH_2CH_2CH_2O$), 1.77 (1H, t, cyclopropyl CH), 1.59 (1H, t, cyclopropyl CH); $^{13}$C-NMR ($CDCl_3$) δ 172.8 (s, C=O), 127.9 (d, CH=CH—$CHOCH_3$), 125.8 (d, CH=CH—$CHOCH_3$), 87.0 (O—C—O), 67.6 (d, $CHOCH_3$), 65.5, 65.1 (two t, $OCH_2CH_2CH_2O$), 54.7 (q, $CO_2CH_3$), 51.9 (q, $OCH_3$), 35.8 (d, $CHCO_2CH_3$), 25.9 (t, $OCH_2CH_2CH_2O$), 24.1 (d, $CHCHOCH_3$), 20.5 (d, $CHCHCO_2CH_3$); IR (film) $\nu_{max}$ 2990, 2895, 1740 (C=O), 1600, 1440, 1385, 1325, 1275, 1200, 1160, 1100, 1065, 1025, 985 cm$^{-1}$; EIMS *m/z* (rel. int.) 254 ($M^+$, 4), 239 ($-CH_3$, 9), 224 (19), 223 ($-OCH_3$, 100), 195 ($-CO_2CH_3$, 60), 163 (43), 137 (16), 117 (50), 105 (31), 77 (54). (Found: C, 61.39; H, 7.50. Calc for $C_{13}H_{18}O_5$: C, 61.40; H, 7.13%.)

*Compound* **5**. $^1$H-NMR ($CDCl_3$) δ 5.73 (2H, br s, CH=CH), 3.95 (5H, t and underlying m, J = 5 Hz, $OCH_2CH_2CH_2O$, $CHOCH_3$), 3.40 (3H, s, $OCH_3$), 2.35 (2H, m, CH=CH—$CH_2$), 1.83 (2H, p, J = 5 Hz, $OCH_2CH_2CH_2O$), 1.47 (2H, br s, cyclopropyl CH's); IR (film) $\nu_{max}$ 3029, 2971, 2926, 2897, 2865, 2820, 1472, 1428, 1266, 1240, 1154, 1132, 1105, 1088, 1057, 1007, 976 cm$^{-1}$; EIMS *m/z* (rel. int.) 196 ($M^+$, 1), 181 ($-CH_3$, 11), 165 ($-OCH_3$, 37), 123 (18), 117 (100), 109 (34), 100 (31), 95 (32), 87 (32), 79 (70), 77 (65); HRMS, $C_{11}H_{16}O_3$ requires: *m/z* 196.1099; found: 196.1087.

*Compound* **6**. $^1$H-NMR ($CDCl_3$) δ 7.25 (5H, m, phenyl), 5.60 (2H, s, CH=CH), 3.95 (5H, m, $OCH_2CH_2CH_2O$, CHSPh), 2.12 (2H, br s, CH=CH—$CH_2$), 1.75 (2H, dp, J = 5 Hz, J = 2 Hz, $OCH_2CH_2CH_2O$), 1.35 (2H, m, cyclopropyl CH's); $^{13}$C-NMR ($CDCl_3$) δ 135.1 (s, phenyl C), 133.1 (d, phenyl CH), 128.7 (d, phenyl CH), 127.3, 126.1, 124.1 (three d's, CH=CH, phenyl CH), 89.6 (s, O—C—O), 66.2, 65.3 (two t's, $OCH_2CH_2CH_2O$), 38.7 (d, CHSPh), 26.2 (t, $OCH_2CH_2CH_2O$), 26.0 (d, $PhSCHCHCOCH_2$), 19.6 (d, $CH_2CH$—$COCH_2$), 18.8 (t, CH=CH—$CH_2$); IR (film) $\nu_{max}$ 3031, 2971, 2892, 1673, 1472, 1439, 1424, 1269, 1242, 1154, 1121, 1055 cm$^{-1}$; EIMS *m/z* (rel. int.) 274 ($M^+$, 1), 241 (1), 208 (1), 187 (1), 165 (100), 107 (34), 87 (28), 79 (46); HRMS, $C_{16}H_{18}O_2S$ requires: *m/z* 274.1027; found: 274.1035.

*Compound* **7**. $^1$H-NMR ($CDCl_3$) δ 5.50 (2H, s, CH=CH), 3.95, 3.90 (4H, two t's, J = 6 Hz, $OCH_2CH_2CH_2O$), 2.2 (4H, br s, CH=CH—$CH_2$), 1.80 (2H, p, J = 6 Hz, $OCH_2CH_2CH_2O$), 1.31 (2H, rough t, J = 1 Hz, cyclopropyl CH's); IR (film) $\nu_{max}$ 3025, 2967, 2915, 2892, 2867, 2836, 1472, 1429, 1269, 1242, 1221, 1156, 1121, 1102, 1057, 997, 976, 934 cm$^{-1}$; EIMS *m/z* (rel. int.) 166 ($M^+$, 27), 151 (14), 124 (12), 123 (8), 108 (28), 107 (25), 100 (31), 80 (36), 79 (100), 78 (19), 77 (27); HRMS, $C_{10}H_{14}O_2$ requires: *m/z* 166.0994; found: 166.0981.

*Compound* **8**. $^1$H-NMR ($CDCl_3$) δ 5.24 (2H, br s, CH=CH), 3.93 (4H, t, J = 5 Hz, $OCH_2CH_2CH_2O$), 2.09 (4H, m, CH=C—$CH_2$, $CH_2CH$=C), 1.79 (2H, p, J = 5 Hz, $OCH_2CH_2CH_2O$), 1.62 (3H, s, C—$CH_3$), 1.33 (2H, m, cyclopropyl CH's); IR (film) $\nu_{max}$ 2965, 2923, 2878, 2836, 1472, 1441, 1428, 1267, 1240, 1154, 1127, 1103, 1078, 1067, 976 cm$^{-1}$; EIMS *m/z* (rel. int.) 180 ($M^+$, 6), 165 (5), 93 (100), 79 (60), 77 (32); HRMS, $C_{11}H_{16}O_2$ requires: *m/z* 180.1149; found: 180.1152.

*Compound* **9**. $^1$H-NMR ($CDCl_3$) δ 3.95 (4H, t, J = 6 Hz, two $OCH_2$'s), 2.11 (4H, br s, two C—$CH_2$'s), 1.80 (2H, p, J = 6 Hz, $OCH_2CH_2CH_2O$), 1.62 (6H, s, $CH_3$), 1.34 (2H, t, J = 2 Hz, cyclopropyl CH's); IR (film) $\nu_{max}$ 2967, 2917, 2863, 2832, 1474, 1443, 1428, 1375, 1267, 1240, 1146, 1127, 1082, 1057, 976, 932 cm$^{-1}$; EIMS *m/z* (rel. int.) 194 ($M^+$, 6), 179 (4), 121 (15), 108 (11), 107 (base, 100), 100 (28), 93 (35), 91 (36), 87 (14), 79 (29), 77 (25); HRMS, $C_{12}H_{18}O_2$ requires: *m/z* 194.1306; found: 194.1284.

*Compound* **10** (endo-*isomer*). $^1$H-NMR ($CDCl_3$) δ 5.90 (2H, t, J = 1 Hz, CH=CH), 3.87 (2H, t, J = 6 Hz, *anti*-$OCH_2$), 3.60 (2H, t, J = 6 Hz, *syn*-$OCH_2$), 3.03 (2H, br s, bridgehead CH's), 1.82, 1.86 (2H, two d's, J = 4 Hz, $CHCH_2CH$), 1.72 (2H, p, J = 6 Hz, $OCH_2CH_2CH_2O$), 1.5–2 (2H, underlying m, cyclopropyl CH's); IR (film) $\nu_{max}$ 3017, 2967, 2930, 2861, 1470, 1397, 1374, 1333, 1258, 1225, 1154, 1105, 1086, 1061, 1021, 976, 953 cm$^{-1}$; EIMS *m/z* (rel. int.) 178 ($M^+$, 1), 177 ($M-1$, 4), 163 (8), 120 (13), 119 (11), 113 (19), 105 (20), 91 (92), 77 (29).

*Compound* **10** (exo-*isomer*). $^1$H-NMR ($CDCl_3$) δ 6.42 (2H, s, CH=CH), 3.90 (4H, t, J = 5 Hz, $OCH_2CH_2CH_2O$), 3.02 (2H, s, bridgehead CH's), 2.0 (1H, d, J = 8 Hz, $CHCHHCH$), 1.83 (2H, p, J = 5 Hz, $OCH_2CH_2CH_2O$), 1.30 (2H, s, cyclopropyl CH's), 0.85 (1H, d, J = 8 Hz, $CHCHHCH$); IR (film) $\nu_{max}$ 3056, 3021, 2971, 2928, 2896, 2863, 1456, 1389, 1372, 1256, 1154, 1105, 1086, 1064, 1022, 962 cm$^{-1}$; EIMS *m/z* (rel. int.) 178 ($M^+$, 5), 177 ($M-1$, 8), 120 (21), 119 (21), 113 (25), 92 (34), 91 (100), 66 (80); HRMS, $C_{11}H_{14}O_2$ requires: *m/z* 178.0993; found: 178.0971.

*Compound* **11**. $^1$H-NMR ($CDCl_3$) δ 5.93 (2H, dd, J = 5 Hz, J = 4 Hz, CH=CH), 3.85, 3.67 (4H, two t's, J = 6 Hz, $OCH_2CH_2CH_2O$), 2.93 (2H, br s, bridgehead CH's), 1.75 (2H, p, J = 6 Hz, $OCH_2CH_2CH_2O$), 1.4 (8H, m, two bridgehead CH's, two cyclopropyl CH's, $CHCH_2CH_2CH$); $^{13}$C-NMR ($CDCl_3$) δ 131.1 (d, CH=CH), 90.0 (s, O—C—O), 65.0, 64.7 (two t's, $OCH_2CH_2CH_2O$), 28.6, 28.2 (two d's, bridgehead CH's, cyclopropyl CH's), 25.8 (t, $OCH_2CH_2CH_2O$), 24.7 (t, $CHCH_2CH_2CH$); IR (film) $\nu_{max}$ 2940, 2863, 1418, 1374, 1327, 1298, 1284, 1258, 1157, 1100, 1090, 1075, 1009, 901, 708 cm$^{-1}$; EIMS *m/z* (rel. int.) 192 ($M^+$, 12), 191 (16), 164 (22), 163 (25), 134 (11), 133 (17), 105 (96), 100 (100), 91 (80).

*3 - Methoxycarbonylcycloheptatrienone 1,3 - proponediol ketal* (**13**)

*From* **4**. A solution of **4** (19 mg, 0.075 mmol) in 0.2 ml dry THF under argon was treated with t-BuOK in dry THF (1.1 equiv) at 25°. The mixture was stirred at 25° for 10 min before the addition of 1 ml of sat $NH_4Cl$. The mixture was extracted with EtOAc (3 ×), dried ($MgSO_4$) and concentrated *in vacuo* to

yield 14 mg (16.7 mg theoretical, 84%) of essentially pure **13** as a yellow oil. Chromatography on Florisil (25% EtOAc–hexane eluant) afforded 9 mg of **13** as a yellow oil: $^1$H-NMR ($CDCl_3$) $\delta$ 7.23 (1H, rough d, J = 11 Hz, $CHCHCO_2CH_3$), 6.74 (1H, s, $CCHC$), 6.70 (1H, dd, J = 11 Hz, J = 7 Hz, $CHCHCO_2CH_3$), 6.38 (1H, dd, J = 6 Hz, J = 10 Hz, $CHCHCOO$), 5.73 (1H, rough d, J = 11 Hz, J = 7 Hz, $CHCHCOO$), 3.82 (4H, t, J = 5 Hz, $OCH_2CH_2CH_2O$), 3.75 (3H, s, $CO_2CH_3$), 1.70 (2H, p, J = 5 Hz, $OCH_2CH_2CH_2O$); $^{13}$C-NMR ($CDCl_3$) $\delta$ 167.1 (s, C=O), 132.4 (d, CH), 130.6 (d, CH), 128.4 (s, $CO_2CH_3$), 127.6, 127.3 (two d's, CH), 126.4 (d, CH), 95.0 (s, OCO), 60.7 (t, $OCH_2CH_2CH_2O$), 52.2 (q, $CO_2CH_3$), 25.7 (t, $OCH_2CH_2CH_2O$); IR (film) $\nu_{max}$ 2957, 2930, 2869, 1721 (C=O), 1460, 1435, 1395, 1327, 1289, 1262, 1213, 1196, 1144, 1117, 1078, 1059, 997, 712 cm$^{-1}$; EIMS *m/z* (rel. int.) 222 ($M^+$, 1), 221 (M − 1, 5), 163 (− $CO_2CH_3$, 34), 149 (14), 133 (21), 106 (12), 105 (base, 100), 77 (55).

*Compound* **13** *from 3-carbomethoxy-2-pyrone*

*General procedure for pressure-promoted cycloaddition* reactions. 3-Carbomethoxy-2-pyrone (19 mg, 0.12 mmol) was dissolved in a minimal volume of $CH_2Cl_2$ (0.1 ml) in a Teflon tube sealed with a brass screw clamp at one end. Cyclopropenone ketal **1** (41 mg, 0.37 mmol) was added and the tube was sealed with a brass screw clamp with exclusion of air. The tube was placed under pressure (6.2 kbar)[11] for 7 days (25°). Upon depressurization, gas evolved on standing. Rapid chromatography ($SiO_2$, EtOAc–hexane eluant) afforded 13 mg (27 mg theoretical, 47%) of **13** as a colorless oil identical to the material described above.

*3-Methoxycarbonylcycloheptatrienone* (**14**). A soln of **13** (10.5 mg, 0.047 mmol) in 0.1 ml dry THF was treated with 3:1 AcOH–$H_2O$ (0.1 ml) under argon. After stirring at 25° for 30 min the mixture was treated with sat $NH_4Cl$ (adjusted to pH 8.5 with $NH_4OH$) and the product was extracted into EtOAc (2 ×) and dried ($MgSO_4$). Concentration of the resulting colorless soln gave 7.5 mg (7.7 mg theoretical, 97%) of **14** as a dark oil. Chromatography on Florisil (25% EtOAc–hexane eluant) followed by rapid concentration under a stream of argon and trituration with heptane under an argon atmosphere afforded 5.2 mg (67% overall recovery) of pure **14** as a white solid. $^1$H-NMR of this solid was identical to that of the crude material: $^1$H-NMR ($CDCl_3$)[26] $\delta$ 7.85 (1H, s, $O{=}C{-}CH{-}CO_2CH_3$), 7.63 (1H, rough d, J = 11 Hz, $CHCHCO$), 7.12 (3H, m, $CHCHCH$), 3.95 (3H, s, $OCH_3$); $^{13}$C-NMR ($CDCl_3$) $\delta$ 187.4 (s, C=O), 166.9 (s, $CO_2CH_3$), 143.8 (d, C2), 142.5 (d, C4), 137.0 (s, C3), 136.4 (d, C7), 133.8 (d, C5), 133.4 (d, C6), 53.5 (q, $OCH_3$); IR ($CHCl_3$) $\nu_{max}$ 1728 (C=O), 1642, 1586, 1275, 1239 cm$^{-1}$; EIMS *m/z* (rel. int.) 164 ($M^+$, 19), 163 (7), 105 (− $CO_2CH_3$, 100), 77 (85); HRMS, $C_9H_8O_3$ requires: *m/z* 164.0473; found: 164.0472.

*Reaction of α-pyrone with* **1**. A neat soln of α-pyrone (40 mg, 0.42 mmol) was mixed with **1** (94 mg, 0.84 mmol, 2 equiv) in a Teflon tube. The tube was sealed and placed under pressure (6.2 kbar) for 2 weeks (25°). $^1$H-NMR of the crude soln showed a mixture of approximately 2:2:1 of *exo*-**15**, **17** and unreacted α-pyrone, respectively. Chromatography ($SiO_2$, 25–50% EtOAc–hexane gradient) afforded of *exo*-**15**, **17** and tropone (resulting from ketal hydrolysis of **17** on $SiO_2$). For *exo*-**15**: $^1$H-NMR ($CDCl_3$) $\delta$ 6.70 (2H, m, CH=CH), 5.42 (1H, dd, J = 7 Hz, J = 3 Hz, $CO_2CH$), 3.94 (4H, t, J = 6 Hz, $OCH_2CH_2CH_2O$), 3.72 (1H, m, $CHCO_2$), 1.85 (5H, p and overlapping m, J = 6 Hz, $OCH_2CH_2CH_2O$, $CO_2CHCH$), 1.71 (1H, dd, J = 5 Hz, J = 3 Hz, $CHCHCO_2$); $^{13}$C-NMR ($CDCl_3$) $\delta$ 172.8 (s, C=O), 136.0 (d, $CO_2CHCH{=}CH$), 133.9 (d, $CO_2CHCH{=}CH$), 99.7 (s, O—C—O), 70.6 (d, $CO_2CH$), 67.0, 65.9 (two t's, $OCH_2CH_2CH_2O$), 41.0 (d, $CHCO_2$), 31.0, 30.8 (two d's, cyclopropyl CH's), 25.4 (t, $OCH_2CH_2CH_2O$); IR ($CHCl_3$) $\nu_{max}$ 3026, 1757 (C=O), 1408, 1375, 1354, 1261, 1174, 1152, 1121, 1104, 1087, 1079, 1013, 1002, 968 cm$^{-1}$; EIMS *m/z* (rel. int.) 208 ($M^+$, 1), 180 (4), 164 (− $CO_2$, 7), 163 (52), 152 (3), 151 (6), 126 (6), 105 (28), 94 (23), 78 (53), 66 (38); HRMS, $C_{11}H_{12}O_4$ requires: *m/z* 208.0735; found: 208.0727. For cycloheptatrienone 1,3-propanediol ketal (**17**):[21] $^1$H-NMR ($CDCl_3$) $\delta$ 6.50 (4H, m, $CHCHCHCHCH$), 5.75 (2H, dd, J = 12 Hz, J = 1 Hz, $CHCCH$), 3.90 (4H, t, J = 6 Hz, $OCH_2CH_2CH_2O$), 1.75 (2H, p, J = 6 Hz, $OCH_2CH_2CH_2O$).

*4-Methoxycarbonylcycloheptatrienone 1,3-propanediol ketal* (**19**). A soln of methyl coumalate (37.7 mg, 0.25 mmol) in $CH_2Cl_2$ (0.1 ml) was treated with **1** (75 mg, 0.67 mmol, 2.6 equiv) in a Teflon tube. The tube was sealed with exclusion of air and placed under pressure (6.2 kbar) for 48 h (25°). Rapid chromatography ($SiO_2$, 1.2 × 15 cm, 35% EtOAc–hexane eluant) afforded 32 mg (54 mg theoretical, 59%) of **19** as a colorless oil: $^1$H-NMR ($CDCl_3$) $\delta$ 7.72 (1H, d, J = 7 Hz, C5-H), 7.04 (1H, d, J = 11 Hz, C3-H), 6.55 (1H, dd, J = 11 Hz, J = 7 Hz, C6-H), 5.97 (2H, rough t, J = 11 Hz, C2-H, C7-H), 3.89 (4H, dt, J = 6 Hz, J = 1 Hz, $OCH_2CH_2CH_2O$), 3.84 (3H, s, $CO_2CH_3$); IR ($CHCl_3$) $\nu_{max}$ 3021, 2977, 2955, 2872, 1715 (C=O), 1437, 1406, 1271, 1217, 1190, 1144, 1113, 1096, 1055, 1021 cm$^{-1}$; EIMS *m/z* (rel. int.) 222 (2), 221 (13), 163 (− $CO_2CH_3$, 29), 105 (100). (Found: C, 64.50; H, 6.30. Calc for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35%.)

*4-Methoxycarbonylcycloheptatrienone* (**20**). A soln of **19** (12.1 mg, 0.055 mmol) in dry THF (0.1 ml) was treated with 3:1 AcOH–$H_2O$ (0.1 ml) under an argon atmosphere. The resulting mixture was stirred at 25° for 2 h, diluted with $CH_2Cl_2$, neutralized with 5% $NaHCO_3$ aq and extracted into $CH_2Cl_2$ (2 ×). The combined organic phases were washed sequentially with 5% $NaHCO_3$ aq and water, dried ($Na_2SO_4$), diluted with heptane and concentrated rapidly under a stream of argon affording 9.2 mg (9.2 mg theoretical, 100%) of **20** as a white solid. $^1$H-NMR ($CDCl_3$) $\delta$ 7.8 (2H, d and overlapping m, J = 11 Hz, C3-H, C6-H), 7.15 (3H, m, C2-H, C5-H, C7-H), 3.90 (3H, s, $OCH_3$); $^{13}$C-NMR ($CDCl_3$) $\delta$ 187.4 (s, C=O), 166.2 (s, $CO_2CH_3$), 145.5 (d, C5), 141.2 (d, C3), 137.8 (d, C6), 135.3 (s, C4), 134.4, 134.1 (two d's, C2, C7), 53.2 (q, $OCH_3$); IR ($CHCl_3$) $\nu_{max}$ 3001, 1725 (C=O), 1638, 1588, 1457, 1438, 1273 cm$^{-1}$; EIMS *m/z* (rel. int.) 164 ($M^+$, 24), 105 (100), 77 (99); HRMS, $C_9H_8O_3$ requires: *m/z* 164.0473; found: 164.0473.

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## REFERENCES

[1a] K. N. Houk, *J. Am. Chem. Soc.* **95**, 4092 (1973); [b] J. S. Burnier and W. L. Jorgensen, *J. Org. Chem.* **48**, 3923 (1983); for recent reviews, see: [c] K. N. Houk, *Accts Chem. Res.* **8**, 361 (1975); [d] K. Fukui, *Fortschr. Chem. Forsch.* **15**, 1 (1970); *Idem*, *Accts Chem. Res.* **4**, 57 (1971); [e] J. Sauer and R. Sustmann, *Angew. Chem. Int. Ed. Engl.* **19**, 779 (1980); [f] J. Sauer, *Ibid.* **6**, 16 (1967); **5**, 211 (1966); [g] R. Huisgen, *Ibid.* **2**, 565 (1963); **7**, 321 (1968); [h] R. Sustmann and G. Binsch, *Mol. Phys.* **20**, 9 (1971). The classifications of the Diels–Alder reaction are: type I [normal ($HOMO_{diene}$ controlled)], type III [inverse electron demand ($LUMO_{diene}$ controlled)], and type II [neutral ($HOMO/LUMO_{diene}$ controlled)]. The neutral Diels–Alder reaction has been customarily represented by the reaction of butadiene with ethylene. For the first experimental verification of a type II Diels–Alder reaction which proceeds at suitable accelerated rates and which is further accelerated by the addition of electron-donating or electron-withdrawing substituents to the dienophile, see: M. Yasuda, K. Harano and K. Janematsu, *J. Org. Chem.* **45**, 659 (1980); T. Sasaki, K. Kanematsu and K. Iizuka, *Ibid.* **41**, 1105 (1976). For further discussions of this topic, see Ref. 1e.

[2] H. Wollweber, *Methoden Org. Chem.*, Houben-Weyl (Edited by E. Muller), Teil 3, V/lc, p. 1040. Georg Thieme, Stuttgart (1970); V. Jager and H. G. Viehe, *Ibid.* Teil 4, V/2a, p. 807 (1970); R. Huisgen, R. Grashey and J. Sauer, *The Chemistry of Alkenes* (Edited by S. Patai), p. 739. Interscience, London (1964).

[3a] J. Fleischhauer, A. N. Asaad, W. Schleker and H.-D. Scharf,

*Justus Liebigs Annln Chem.* 306 (1981); [b]J. Sauer, *Naturwissenschaften* **71**, 37 (1984); [c]S. Danishefsky, *Accts Chem. Res.* **14**, 400 (1981); [d]M. Petrzilka and J. I. Grayson, *Synthesis* 753 (1981); [e]S. M. Weinreb and R. R. Staib, *Tetrahedron* **38**, 3087 (1982); [f]D. L. Boger, *Tetrahedron* **39**, 2869 (1983).

[4] The Diels–Alder reactions of strained olefins and the factors responsible for the observed rate accelerations including the release of ring strain have been extensively investigated. See: [a]K. N. Houk, *Methods in Stereochemical Analysis* (Edited by W. H. Watson), p. 1. Verlag Chemie, Deerfield, Florida (1983); [b]R. Huisgen, P. H. J. Ooms, M. Mingin and N. L. Allinger, *J. Am. Chem. Soc.* **102**, 3951 (1980); [c]N. G. Rondan, M. N. Paddon-Row, P. Caramella, J. Mareda, P. H. Mueller and K. N. Houk, *Ibid.* **104**, 4974 (1982) and refs cited therein.

[5] In simple qualitative considerations, olefin strain would be expected to reduce the strength and extent of $\pi$-bonding resulting in a decreased $HOMO_{olefin}$–$LUMO_{olefin}$ separation: $HOMO_{ethylene} < HOMO_{strained\ olefin}$ and $LUMO_{ethylene} > LUMO_{strained\ olefin}$. Although a correlation of cycloalkene ring size and the UV $\lambda_{max}$ indicate that increasing strain shifts the absorption maximum bathochromically, [5e]*ab initio* calculations and experimentally determined IP values for ethylene and cyclopropene suggest that the quantitative differences may be much smaller than anticipated from a qualitative analysis: $HOMO_{ethylene}$ (−10.1 to −10.3 eV calculated with 4–31G,[5a] 3–21G,[5b] and 6–21G,[5b] −10.5 eV experimental IP[5c,d]), $HOMO_{cyclopropene}$ (−9.5 to −9.7 eV calculated with 4–31G;[5e] −9.7 eV experimental IP[5d]), $LUMO_{ethylene}$ (5.0–5.1 eV calculated with 3–21G[1b,5b] and 6–31G;[5b] 1.5–1.8 eV experimental EA[1e–c]), $LUMO_{cyclopropene}$ (4.9–5.05 eV calculated with 4–31G[5e]). [a]T. A. Halgren, D. A. Kleier, J. H. Hall, Jr., L. D. Brown and W. N. Lipscomb, *J. Am. Chem. Soc.* **100**, 6595 (1978); [b]R. D. Bach, G. J. Wolber and H. B. Schlegel, *Ibid.* **107**, 2837 (1985); [c]D. W. Turner, C. Baker, A. D. Baker and C. R. Brundle, *Molecular Photoelectron Spectroscopy*. Wiley-Interscience, New York (1970); [d]G. Bieri, F. Burger, E. Heilbronner and J. P. Maier, *Helv. Chim. Acta* **60**, 2213 (1977); [e]J. Kao and L. Radom, *J. Am. Chem. Soc.* **100**, 379 (1978). The observed rate acceleration in the Diels–Alder reactions of **1** may be attributed, in a large part, to the release of strain energy [*ca* 25 kcal $mol^{-1}$; cyclopropane strain energy = 27.5 kcal $mol^{-1}$ and cyclopropene strain energy = 52.6 kcal $mol^{-1}$; cf. M. J. S. Dewar, *The Molecular Orbital Theory of Organic Chemistry*, p. 461. McGraw-Hill, New York (1969)] and the classification of the reaction type ($HOMO_{diene}$ vs $LUMO_{diene}$ controlled Diels–Alder reaction) follows from the Frontier orbital energies presented in the work of Houk[1a,c] substituting the IP cyclopropene (9.7 eV)[5e] and EA ethylene (1.5–1.8 eV)[4a–c] for **1**.

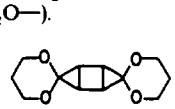
[6] G. B. Butler, K. H. Herring, P. L. Lewis, V. V. Sharpe and R. L. Veazey, *J. Org. Chem.* **42**, 679 (1977).

[7] The Diels–Alder reactions of 3,3-dimethoxycyclopropene (25°, neat) with 1,3-butadiene (20 equiv +, 13 days), isoprene (4 equiv, 13 days), 2,3-dimethyl-1,3-butadiene (1.5 equiv, 4 weeks), and 1-methoxy-1,3-butadiene (3 equiv, 9 days, 41%) have been described: R. M. Albert and G. B. Butler, *J. Org. Chem.* **42**, 674 (1977). Our initial comparison of the rate of [4 + 2] cycloaddition of 3,3-dimethoxycyclopropene vs **1** with isoprene revealed a marked improvement in the reaction utilizing **1**. For additional studies on the preparation and reactions of cyclopropenone ketals, see: K. B. Baucom and G. B. Butler, *J. Org. Chem.* **37**, 1730 (1972); R. Breslow, J. Pecoraro and T. Sugimoto, *Org. Synth.* **57**, 41 (1977); R. Breslow and M. Oda, *J. Am. Chem. Soc.* **94**, 4787 (1972); R. Breslow, M. Oda and J. Pecoraro, *Tetrahedron Lett.* 4415, 4419 (1972).

[8] For a review of the cycloaddition reactions of cyclopropenes, see: [a]M. L. Deem, *Synthesis* 675 (1972); 701 (1982). For additional examples of the utilization of the Diels–Alder reactions of cyclopropenes in the preparation of cycloheptatrienes, see: [b]M. M. Latypova, V. V. Plemenkov, V. B. Tuzov, Kh. Z. Giniyatov and I. G. Bolesov, *J. Org. Chem. USSR* **82**, 1442 (1983); M. M. Latypova, V. V. Plemenkov, V. N. Kalinina and I. G. Bolesov, *Ibid.* **84**, 489 (1984); [c]D. N. Reinhoudt, P. Smael, W. J. M. Van Tilborg and J. P. Visser, *Tetrahedron Lett.* 3755 (1973); W. J. M. Van Tilborg, P. Smael, J. P. Visser, C. G. Kouwenhoven and D. N. Reinhoudt, *Recl. Trav. Chim. Pays-Bas* **94**, 85 (1975); A. Steigel, J. Sauer, D. A. Kleier and G. Binsch, *J. Am. Chem. Soc.* **94**, 2770 (1972).

[9] Tropoloalkaloids include [a]colchicine and its released congeners, see: H. G. Capraro and A. Brossi, *The Alkaloids* (Edited by A. Brossi), Vol. 23, pp. 1–70. Academic Press, Florida (1984); [b]imerubrine, grandirubrine, see: K. T. Buck, *Ibid.* pp. 301–325; [c]rubrolone, see: N. J. Palleroni, K. E. Reichelt, D. Mueller, R. Epps, B. Tabenkin, D. N. Bull, W. Schuep and J. Berger, *Antibiotics* **31**, 1218 (1978); W. Schuep, J. F. Blount, T. H. Williams and A. Stemple, *Ibid.* **31**, 1226 (1978).

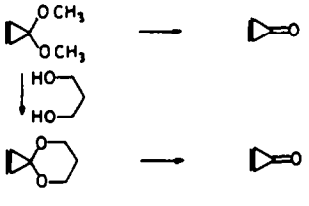
[10] Thermal dimerization of cyclopropenone ketal **1** will compete with slow reactions at 80°. The dimerization product **i**, which has been previously characterized,[6] exhibits the following properties: $^1$H-NMR ($CDCl_3$, ppm) 4.01, 3.93 (two t's, J = 6 Hz, 8H, $-OCH_2-$), 1.85 (p, J = 6 Hz, 4H, $-OCH_2\underline{CH_2}CH_2O-$), 1.40 (s, 4H, $-\underline{CH}-$); $^{13}$C-NMR ($CDCl_3$, ppm) 101.6 (s, O—C—O), 66.9 and 65.3 (two t's, $-O\underline{CH_2}-$), 26.1 (d, $-\underline{CH}-$), 25.9 (t, $-OCH_2\underline{CH_2}CH_2O-$).



[11] For recent reviews, see: Ref. 2e and [a]T. Asano and W. J. le Noble, *Chem. Rev.* **78**, 407 (1978); W. J. le Noble and H. Kelm, *Angew. Chem. Int. Ed. Engl.* **19**, 841 (1980); K. Matsumoto, *Heterocycles* **16**, 1367 (1981); N. S. Isaacs, *Liquid Phase High Pressure Chemistry*. Wiley-Interscience, New York (1981); [b]the pressure-promoted Diels–Alder reactions were carried out in an AGP-10002 Pressure Generator manufactured by Leco Corporation, Tem-Pres Division, Bellefonte, PA 16823, U.S.A. The unit has been described: P. DeShong, C. M. Dicken, J. J. Perez and R. M. Shoff, *Org. Prep. Proc. Int.* **14**, 369 (1982).

[12] [a]Although no direct evidence has been secured to suggest the intermediacy of the cyclopropenium cation **i** in the Diels–Alder reactions of **1**, indirect evidence suggests it is a possible consideration. The hydrolysis of 3,3-dimethoxycyclopropene (5 min, 25°, $CDCl_3$–$H_2O$) and cyclopropenone ketal **1** (30 min, 25°, $CDCl_3$–$H_2O$) proceeds under mild conditions in the absence of added catalyst and must be facilitated by the ease of cyclopropenium cation formation. Further, a similarly mild ketal exchange reaction of 3,3-dimethoxycyclopropene with 1,3-propanediol (1.5 equiv, 45 min, 25°, $CDCl_3$) provides **1** (90–100%) in the absence of added catalyst and apparently is facilitated by the reversible formation of the cyclopropenium cation.

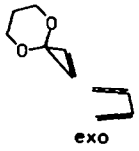
Attempts to accelerate the [4+2] cycloaddition reactions of **1** with the use of conventional Lewis acid catalysts and a radical cation catalyst, tris(*p*-bromophenyl)ammonium hexachloroantimonate [$(p\text{-}BrC_6H_4)_3NSb^+Cl_6^-$],[12b] were not successful and resulted in the consumption of **1** without Diels–Alder catalysis. [b]R. A. Pabon, D. J. Bellville and N. L. Bauld, *J. Am. Chem. Soc.* **105**, 5158 (1983).



[13a] D. L. Boger and C. E. Brotherton, unpublished observations. Full investigations of this and related work are in progress. The ease of the generation of the apparent vinylcarbene (70–80°) from the cyclopropenone ketal **1** and its nucleophilic character are consistent with past observations in which stabilization of an empty *p*-orbital provides the necessary stabilization for observable ground-state singlet carbenes. The observed chemical behavior of the vinylcarbene thermally generated from **1** is consistent with stepwise addition–cyclization reactions which might be expected to be characteristic of a partially delocalized triplet vinylcarbene. However, the instances of 2-$\pi$ insertions, $[{}_{\pi}2_s + {}_{\omega}2_a]$ cycloadditions, with an observable *endo* effect and the observed $[{}_{\pi}4_s + {}_{\pi}2_s]$ cycloadditions are expectant characteristics of a delocalized singlet vinylcarbene.[13c,e] The reversible generation of the vinylcarbene is implicated by the past observations that the principal products derived from vinylcarbenes are cyclopropenes and our observations on the apparent efficiency with which **1** *or* the vinylcarbene may be trapped in the thermal reactions of **1**. For descriptions of the thermal reactions of the cyclopropenone ketal **1** with electron-deficient olefins, see: [b]D. L. Boger and C. E. Brotherton, *J. Am. Chem. Soc.* **104**, 805 (1984); [c]*Idem*, *Tetrahedron Lett.* **25**, 5611 (1984). For reactions with carbon–heteroatom double bonds, see: [d]D. L. Boger, C. E. Brotherton and G. I. Georg, *Ibid.* **25**, 5615 (1984); for the thermal [3 + 4] cycloaddition of **1** with electron-deficient dienes, see: [e]D. L. Boger and C. E. Brotherton, *J. Org. Chem.* **50**, 3425 (1985).

[14] The stereochemical assignments are based on the absence of a detectable $^1$H-NMR upfield shielding shift of the *syn* —$CH_2O$— ketal signal relative to the *anti* —$CH_2O$— ketal signal characteristic of the *endo*-cyclopentadiene adduct. For *endo*-**10**: $^1$H-NMR ($CDCl_3$) $\delta$ 3.87 (*anti* —$CH_2O$—) and 3.60 (*syn* —$CH_2O$—) (two t's, J = 6 Hz, 2H each) and for *exo*-**10**: $^1$H-NMR ($CDCl_3$) $\delta$ 3.90 (t, J = 5 Hz, 4H, *syn* and *anti* —$CH_2O$—). The assignments of *endo*/*exo*-**10** were verified by comparison of their spectroscopic properties with those of related structures: K. B. Wiberg and W. J. Bartley, *J. Am. Chem. Soc.* **82**, 6375 (1960); H. C. Volger, H. Hogeveen and M. M. P. Gaasbeek, *Ibid.* **91**, 218 (1969).

[15] The Diels–Alder reactions of cyclopropene have been shown to occur with a preference for *endo* approach, see: Refs 2*e* and 9*a* and I. G. Bolesov, L. G. Zaitseva, V. V. Plemenkov, I. B. Avezov and L. S. Surmina, *J. Org. Chem. USSR* **78**, 64 (1978); I. G. Bolesov, L. G. Zaitzeva, V. V. Plemenkov and L. S. Surmina, *Ibid.* **78**, 260 (1978) and refs cited therein. The preferred *exo* approach observed with **1** may be attributed to the increased steric congestion that **1** suffers in an *endo* approach.


exo


endo

[16] T. W. Greene, *Protective Groups in Organic Chemistry*. Wiley-Interscience, New York (1981).

[17a] T. Nozoe, *Prog. Org. Chem.* **5**, 132 (1961); P. L. Pauson, *Chem. Rev.* **55**, 9 (1955); F. Pietra, *Chem. Rev.* **73**, 293 (1973).

[18] Treatment of **4** with mild base (1.1 equiv DBU, THF, 25°, 5 min) provided the $\alpha,\beta$-unsaturated ester resulting from double-bond migration without promoting the elimination of methanol.

[19] G. Maier, *Angew. Chem. Int. Ed. Engl.* **6**, 402 (1967); E. Vogel and H. Gunther, *Ibid.* **6**, 385 (1967); E. Vogel, *Pure Appl. Chem.* **20**, 237 (1969); J. M. Schulman, R. L. Disch and M. L. Sabio, *J. Am. Chem. Soc.* **106**, 7696 (1984). The norcaradiene **16** depicted in the conversion of **15** to **17** (Eq. 9) and the corresponding norcaradienes in the conversions detailed in Eq. (10) are not required intermediates. The initial [4 + 2] cycloadducts (e.g. **15**) may be participating in $[\sigma_{2s} + \sigma_{2a} + \sigma_{2a}]$ or $[\sigma_{2s} + \sigma_{2s} + \sigma_{2s}]$ processes to afford the tropone ketals **17**, **13** and **19** directly.

[20a] Reaction of an $\alpha$-pyrone with the cyclopropenone ketal **1** at 25° (neat, 1 atm, no reaction) or 80° (benzene, [3 + 4] cycloaddition observed) failed to provide observable [4 + 2] cycloaddition. The utilization of these observations in the development of a complementary approach to cycloheptatrienone introduction and its application in the total synthesis of tropoloalkaloids are in progress (see Ref. 13). [b]Reaction of 3-methoxycarbonyl-2-pyrone with cyclopropenone ketal **1** at 25° (neat, 1 atm, no reaction) or 80° (benzene, [3 + 2] cycloaddition observed) provided no evidence for observable [4 + 2] cycloaddition (see Ref. 13*b*).

[21] H. E. Simmons and T. Fukunaga, *J. Am. Chem. Soc.* **89**, 5208 (1967).

[22] See Ref. 8*b* and J. A. Harvey and M. A. Ogliarusa, *J. Org. Chem.* **41**, 3374 (1976); H. Kwart and K. King, *Chem. Rev.* **68**, 415 (1968).

[23] Examples of the thermolysis of related compounds have been compiled, see: J. S. Burnier and W. L. Jorgensen, *J. Org. Chem.* **49**, 3001 (1984). Thermolysis of *exo*-**15** in benzene (80°, 20 h) or toluene (120°, 24 h) provided recovered, unchanged starting material and thermolysis in mesitylene (140°, 12 h) provided complete conversion to cycloheptatrienone ketal.

[24] 3-Methoxycarbonyl-2-pyrone (Fluka) and 5-methoxycarbonyl-2-pyrone (Chem. Services) were obtained from commercial sources.

[25] The cycloheptatrienone ketals **13**/**19**, which are unstable to chromatography on silica gel, could be isolated and purified by rapid passage through Florisil (**13**) or silica gel (**19**) and characterized.

[26] M. E. Garst and V. A. Roberts, *J. Org. Chem.* **47**, 2188 (1982).