(GM 24144) and the University of Illinois Research Board for financial support.

**Registry No.** **1a**, 98-03-3; **1b**, 13679-70-4; **1c**, 5834-16-2; **1d**, 498-62-4; **2a**, 77295-66-0; **2b**, 81294-08-8; **2c**, 77386-41-5; **2d**, 81294-09-9; **3a**, 4298-52-6; **3b**, 81294-10-2; **3c**, 81294-11-3; **3d**, 67237-53-0; **4a**, 16900-51-9; **4b**, 81294-12-4; **4c**, 81294-13-5; **4d**, 81294-14-6; **5a**, 1081-34-1; **5b**, 59949-61-0; **5c**, 81294-15-7; **5d**, 81294-16-8.

# Relative Reactivities of Substituted Allenes toward Cycloaddition with Tetraphenylcyclopentadienone. Further Implications on the Viability of the Concerted ($_\pi2_s$ + $_\pi2_a$) Cycloaddition Process

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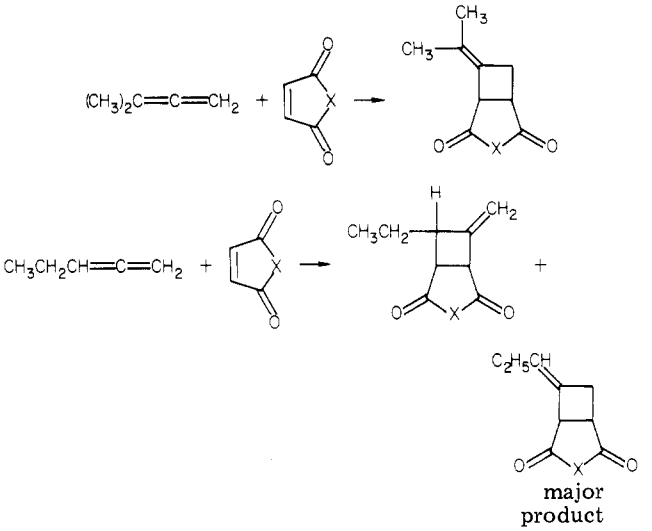
*Received October 29, 1981*

Recent studies in our laboratories have been directed toward gaining a better understanding of the mechanistic details of the cycloaddition and cyclodimerization reactions of allenes. As an alternative to the previously proposed nonconcerted, diradical-intermediate and concerted ($_\pi2_s$ + $_\pi2_a$) mechanisms, a concerted six-electron [$_\pi2_s$ + ($_\pi2_s$ + $_\pi2_s$)] process has been discussed.[1] A comparison of the two concerted processes using PMO theory suggested that the six-electron process should be favored over the four-electron process, and that in cycloaddition reactions with unsymmetrically substituted allenes differences in chemoselectivities should be observed.[1] For example, the cycloaddition of 1,1-dimethylallene via the ($_\pi2_s$ + $_\pi2_a$) process is predicted to be strongly favored across the more highly substituted double bond, while in the six-electron process cycloaddition across the less highly substituted double bond is favored.[1] In the case of monosubstituted allenes the same trends are predicted, although to a lesser degree. The predictions for the [$_\pi2_s$ + ($_\pi2_s$ + $_\pi2_s$)] process were in agreement with the chemoselectivities reported in the cycloaddition reactions of 1,1-dimethylallene and ethylallene with maleic anhydride[2] and those later obtained with *N*-phenylmaleimide (NPMI),[3] suggesting that the ($_\pi2_s$ + $_\pi2_a$) process was not operative in these cases.[1]

The results observed with maleic anhydride and NPMI suggested that it might not be possible to determine the chemoselectivity features of the ($_\pi2_s$ + $_\pi2_a$) concerted process of allenes with two-electron, electron-poor (LUMO controlled) reagents. Since according to PMO theory ($_\pi4_s$ + $_\pi2_s$) cycloaddition reactions of allenes with four-electron, electron-poor (also LUMO controlled) reagents should show the same trends in chemoselectivities and relative reactivities as in the ($_\pi2_s$ + $_\pi2_a$) process, a study of the cycloaddition reactions of allenes with such reagents was undertaken. Preliminary experiments were carried out with hexachlorocyclopentadiene and tetraphenylcyclopentadienone (TPCD). In the attempted reactions with hexachlorocyclopentadiene rearrangement reactions were encountered which could not be circumvented.[4] Preliminary results describing the chemoselectivities observed in the cycloaddition reactions of 1,1-dimethylallene and ethylallene with TPCD have been reported[5] and were consistent with the predictions based on PMO theory. The present note describes further extensions of these studies and focuses, in particular, on the results of relative reactivity studies for comparison with those results obtained in the cycloaddition reactions of allenes with NPMI[3] and 1,1-dichloro-2,2-difluoroethene.[6]




X = O, $NC_6H_5$

The overall reactions of the substituted allenes with TPCD are illustrated in Scheme I. The chemoselectivities observed in the cycloaddition reactions of isobutyl- and *tert*-butylallene are similar to those observed with ethylallene (see Table I). Attempts were also made to observe the cycloadditions with 1-ethyl-1-methylallene and 1-*tert*-butyl-1-methylallene. Under the reaction conditions, however, the former underwent prior rearrangement to form a mixture of conjugated dienes and no products of expected structure could be detected, while in the case of the latter no reaction was observed even over an extended period of time.

The relative reactivities of the substituted allenes toward cycloaddition with TPCD have been determined by competitive reaction techniques and are presented in Table II. (The relative reactivity of 1-*tert*-butyl-1-methylallene represents an upper limit and, in fact, may be very much lower.) For comparison purposes the relative reactivities observed in the cycloaddition reactions with NPMI[3] are also included in Table II. It should be noted that the relative reactivities of the monosubstituted allenes in the two cycloaddition reactions are quite similar; however, the relative reactivity of 1,1-dimethylallene is dramatically different in the two reactions. *Thus, both the chemoselectivity and relative reactivity data indicate that the cycloaddition reactions of allenes with NPMI do not occur via the ($_\pi2_s$ + $_\pi2_a$) process.*

The partial relative reactivities for cycloaddition across the $C_1$–$C_2$ and $C_2$–$C_3$ $\pi$ systems (Table III) in the monoalkylallene series provide a basis for a detailed analysis of the factors affecting both the chemoselectivities and total relative reactivities. The partial relative reactivities for attack on the two $\pi$ systems of ethyl- and isobutylallene are similar and decrease significantly on going to *tert*-butylallene. The reasons for the observed trends become apparent on consideration of the steric effects developed

(1) Pasto, D. J. *J. Am. Chem. Soc.* **1979**, *101*, 37.
(2) Alder, K.; Ackermann, O. *Chem. Ber.* **1957**, *90*, 1697.
(3) Pasto, D. J.; Heid, P. F.; Warren, S. E. *J. Am. Chem. Soc.* **1982**, *104*, in press.
(4) The treatment of 1,1-dimethylallene with freshly distilled hexachlorocyclopentadiene (from sodium carbonate) resulted in the rapid rearrangement of the allene to 3-methyl-1,3-butadiene, which then underwent cycloaddition predominantly across the least substituted double bond (9:1 ratio).
(5) Pasto, D. J. *Tetrahedron Lett.* **1980**, *21*, 4787.
(6) Pasto, D. J.; Warren, S. E. *J. Am. Chem. Soc.* **1982**, *104*, in press.

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Scheme I

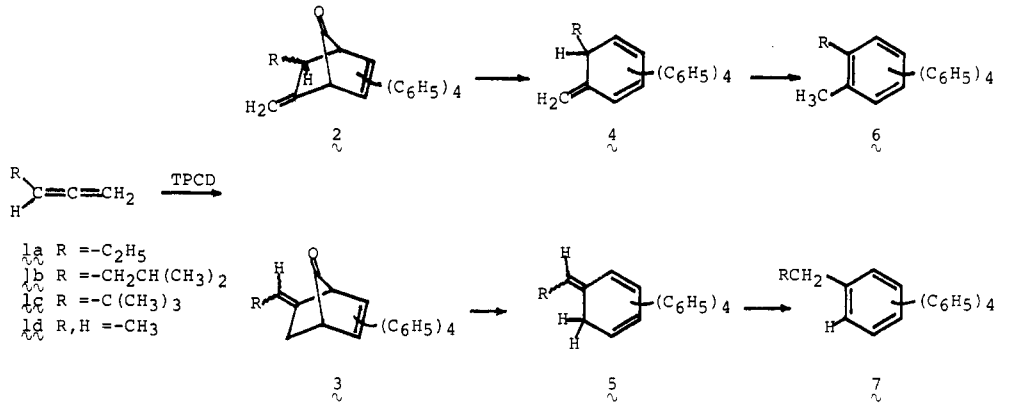


Table I. Chemoselectivities in the Cycloaddition Reactions of Substituted Allenes with TPCD

| allene R(R')C=C=CH$_2$ | | product | |
|---|---|---|---|
| R | R' | 4 (6) | 7 |
| $CH_2CH_3$ | H | 63 | 37 |
| $CH_2CH(CH_3)_2$ | H | 68 | 32 |
| $C(CH_3)_3$ | H | 57 | 43 |
| $CH_3$ | $CH_3$ | 100 | 0 |

Table II. Relative Reactivities of Substituted Allenes toward Cycloaddition with TPCD and NPMI[3]

| allene R(R')C=C=CH$_2$ | | $k_{rel}$[a] | |
|---|---|---|---|
| R | R' | TPCD | NPMI |
| $CH_2CH_3$ | H | 1.00 | 1.00 |
| $CH_2CH(CH_3)_2$ | H | 1.00 | 0.86 |
| $C(CH_3)_3$ | H | 0.45 | 0.72 |
| $CH_3$ | $CH_3$ | 0.65 | 2.8 |
| $C(CH_3)_3$ | $CH_3$ | <0.03 | 0.48 |

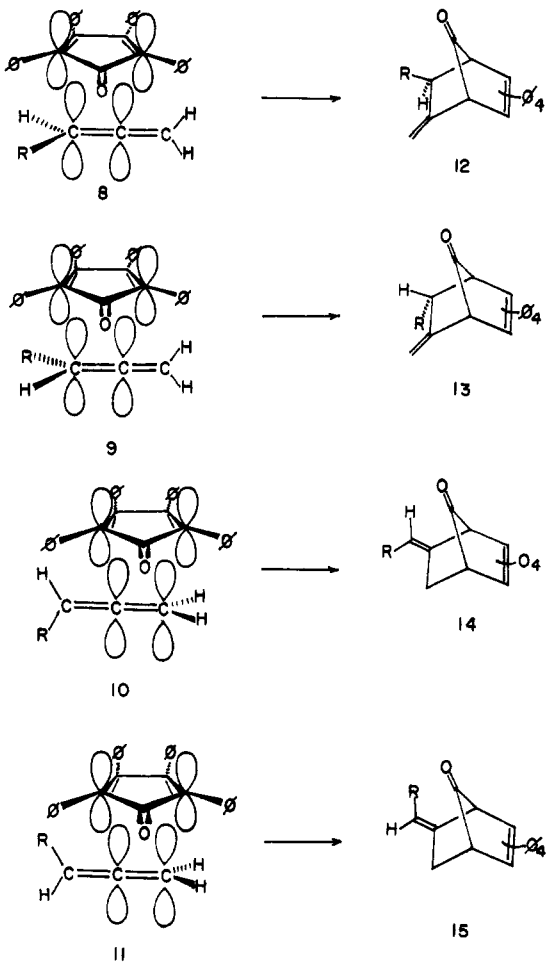
[a] Relative to $k$ for ethylallene = 1.00.

Table III. Partial Relative Reactivities for Cycloaddition across the $C_1$-$C_2$ and $C_2$-$C_3$ $\pi$ Systems of Substituted Allenes

| | partial relative reactivity | |
|---|---|---|
| allene | $C_1$=$C_2$ | $C_2$=$C_3$ |
| ethyl- | 0.63 | 0.37 |
| isobutyl- | 0.68 | 0.32 |
| *tert*-butyl- | 0.26 | 0.19 |
| 1,1-dimethyl- | 0.65 | 0.0 |

in the transition states for cycloaddition across the two $\pi$ systems. Cycloaddition across the $C_1$–$C_2$ $\pi$ system of a monosubstituted allene can occur via the two configurations shown in **8** and **9**, giving rise to the stereoisomeric adducts **12** and **13** (see Scheme II). Inspection of a model of **8** indicates that there is a rather severe steric interaction between the $\alpha$-phenyl of TCPD and the R group which is not present in **9**, particularly if one tilts the back side of the TPCD ring away from the allene, thus favoring reaction via **9**. (Unfortunately, differentiation between the two modes of cycloaddition is lost in the decarbonylation steps with **12** and **13**). When R is ethyl or isobutyl, the alkyl groups can adopt conformations in which the methyl and isopropyl portions are oriented away from the TPCD, presenting identical environments to the approaching TPCD. However, when the R group is *tert*-butyl, the hydrogen atoms on the $\alpha$-carbon which are oriented toward the TPCD in both **8** and **9** are replaced by methyl groups, producing greater steric hindrance and a reduction in the partial relative reactivity.

Scheme II



In the two modes of attack on the $C_2$–$C_3$ $\pi$ system, approach to the face opposite the alkyl group on $C_1$ (configuration **10**) should be strongly favored and should occur with equal ease regardless of the size of the R group. Reaction via configuration **11** is sterically retarded due to a severe interaction generated between the $\alpha$-phenyl and the R group. The ethyl and isobutyl groups can again adopt conformations which present identical environments to the approaching TPCD. The model of **11** when R is *tert*-butyl suggests that the transition state is so sterically congested that little or no reaction should occur via that configuration. Comparison of the partial relative reactivity data for addition across the $C_2$–$C_3$ $\pi$ system suggests that some reaction ooccurs via **11** with ethyl- and isobutylallene. Again, unfortunately, the decarbonylation of the stereoisomeric adducts **14** and **15** precludes a direct assessment

Table IV. Proton Chemical Shifts in 6 and 7[a]

| | R = $CH_2CH_3$ | R = $CH_2CH(CH_3)_2$ | R = $C(CH_3)_3$ |
|---|---|---|---|
| | | Compound 6 | |
| $CH_3$ | 2.17 | 2.17 | 3.88 |
| ArH | 6.78, 7.17 | 6.78, 7.10 | 6.86, 7.11<br>6.30, 7.58 (d, 7.4) |
| R | 0.54 (t, 6.7)<br>2.54 (m)[b] | 0.72 (d, 6.5)<br>1.74 (m)<br>2.59 (m)[b] | 1.12 |
| | | Compound 7 | |
| ArH[c] | 7.41 | 7.41 | 7.46 |
| ArH | 6.83, 7.13 | 6.85, 7.13 | 6.86, 7.14 |
| $-CH_2-$ | 2.49 (m)[b] | 2.49 (m)[b] | 2.69 |
| R | 1.66 (m)<br>0.85 (t, 6.8) | 1.43 (m, 3 H)<br>0.75 (d, 5.9) | 0.85 |

[a] Multiplicities and coupling constants (hertz) are given in parentheses. [b] The resonances of the protons attached to the carbon atoms directly bonded to the aromatic ring appear as complex multiplets, apparently due to hindered rotation about the alkyl carbon-aryl carbon bond. [c] Isolated proton on the central substituted aromatic ring.

of the extent of reaction via **10** and **11**.

1,1-Dimethylallene undergoes cycloaddition only across the $C_1$–$C_2$ $\pi$ system with a partial relative reactivity comparable with those for ethyl- and isobutylallene. Normally, one would have expected 1,1-dimethylallene to react significantly faster than a monoalkylallene due to the higher energy of the $\pi$ MO.[7] The apparent reduction in rate must be due to the adverse steric interaction present in **8** which cannot be avoided with 1,1-dimethylallene. Replacement of a methyl group by a *tert*-butyl group, as in 1-*tert*-butyl-1-methylallene introduces further steric hindrance and reduction in reactivity.

It is interesting to note that no cycloaddition occurs across the $C_2$–$C_3$ $\pi$ system of 1,1-dimethylallene. The introduction of an alkyl group at $C_1$ also raises the energy of the $C_2$–$C_3$ $\pi$ system,[7] which should increase its reactivity. However, approach to either face of the $C_2$–$C_3$ double bond is sterically hindered by the alkyl groups attached to $C_1$. This apparently more than offsets the expected increase in reactivity due to the higher energy of the $\pi$ MO.

## Experimental Section

**Cycloaddition of Substituted Allenes with Tetraphenylcyclopentadienone (TPCD).** In an NMR tube were placed 0.6 mmol of the allene, 0.4 mmol of TPCD, and 1 mL of xylene. The contents of the tube were triply freeze-degassed. The tube was sealed under a vacuum and was placed in a sand bath at 160 °C until the color of the TPCD had disappeared (3–7 days). The contents of the tube were moved and the unreacted allene and the xylene were removed on a vacuum line. A portion of the residue was subjected to preparative HPLC on a 30 × 1 cm column of 5 $\mu$m of silica, using 95% hexane–5% dichloromethane as eluent. The 100-MHz NMR spectra of the separated fractions were recorded by FT techniques (see Table IV). Product compositions were determined by integration of the NMR spectra obtained on the crude product mixtures. Elemental compositions were determined by high-resolution *m/e* measurements (see Table V). Insufficient quantities of the pure were obtained to recrystallize and determine melting points.

**Measurement of Relative Reactivities.** Mixtures were prepared containing 200 $\mu$L of ethylallene (the standard allene), 200 $\mu$L of the other substituted allene, and 100 $\mu$L of heptane or octane (as an internal standard). The mixtures were analyzed by GC to determine standard allene/internal standard and substituted allene/internal standard area ratios. One hundred microliters (~0.7 total mmol of allene) of the mixtures was reacted with 0.17 mmol of TPCD as described above. After the color of the TPCD had disappeared, the tubes were opened and the final standard allene/internal standard and substituted allene/internal standard area ratios were determined by GPC. The changes in area ratios were converted to moles of allene consumed, and the relative rate constants were calculated with an iterative computer program.

Table V. High-Resolution *m/e* Values for Adducts 6 and 7

| adduct | mol formula | calcd *m/e* | obsd *m/e* |
|---|---|---|---|
| **6a** | $C_{33}H_{28}$ | 424.219 | 424.218 |
| **7a** | $C_{33}H_{28}$ | 424.219 | 424.221 |
| **6b** | $C_{35}H_{32}$ | 452.250 | 452.252 |
| **7b** | $C_{35}H_{32}$ | 452.250 | 452.250 |
| **6c + 7c**[a] | $C_{35}H_{32}$ | 452.250 | 452.250 |

[a] Isolated in an inseparable mixture by HPLC.

**Acknowledgment.** We thank the National Science Foundation for partial support of the research (Grant No. CHE77-08627).

**Registry No.** **1a**, 591-95-7; **1b**, 13865-36-6; **1c**, 26981-77-1; **1d**, 598-25-4; TPCD, 479-33-4; hexachlorocyclopentadiene, 77-47-4.

(7) For a discussion of the effect of alkyl substitution on the energy of the $\pi$ systems of an allene, and on the chemical reactivity of the $\pi$ systems, see: Pasto, D. J.; Warren, S. E. *J. Org. Chem.* **1981**, *46*, 2842.

# Crystal Structure and Stereochemistry of Frutescin†[1]

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*Received December 7, 1981*

The sesquiterpene lactone frutescin was the first[2] and long remained the only C-8 lactonized melampolide isolated from natural sources;[3] its occurrence in an *Iva* species is somewhat of an anomaly. Our assumption[2] that its lactone ring was cis fused as in **1** (Chart I) was based primarily on an empirical rule[4] which relates the sign of the Cotton effect associated with the lactone n,$\pi^*$ transition to the stereochemistry of the lactone ring if the absolute configuration is known. However, it has since been shown[5] that the rule is frequently violated and is only applicable to a limited number of sesquiterpene lactone types, with melampolides presenting a particularly confusing picture.[3]

In such cases a better guide to the mode of lactone ring fusion may be Samek's rule which, as modified recently,[6] relates the magnitude of $J_{7,13}$ to the conformation of the lactone ring. For a C-8 lactonized melampolide like frutescin where $J_{7,13}$ = 3 Hz[2], model considerations, deceptive though these can be, then suggest the presence of a trans lactone ring as in **2**. Indeed, in a recent publication dealing with the melampolide schkuhriolide (**4**), Samek and coworkers,[7] commenting on differences in the $^1H$ NMR spectra of frutescin and **4**, suggested that frutescin either differed from **4** conformationally or possessed a trans lactone ring fusion. To resolve this question, we have

† Dedicated to the memory of Zdeněk Samek, deceased Nov 25, 1980.

0022-3263/82/1947-2206$01.25/0 