# Stereochemical Aspects of the Cycloaddition of Alkenylidenecyclopropanes with 4-Phenyl-1,2,4-triazoline-3,5-dione. Evidence in Support of a Concerted Cycloaddition Pathway[1]

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Abstract: The stereochemical features of the cycloaddition reactions of alkenylidenecyclopropanes with 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) have been determined using $(-)$-(R)-2-phenylisobutenylidenecyclopropane $((-)$-(R)-**4**) and (E)-2-phenyl-1-(2,4-dimethyl-1-pentenylidene)cyclopropane (**10**). The reaction of $(-)$-(R)-**4** with PTAD produces $(+)$-(S)-**5** in a stereospecific manner with inversion of configuration and the chiral diene $(+)$-**6**. The assignment of stereochemistry and the stereochemical interrelations are discussed. The results of the reaction of (E)-**10** with PTAD define the orbital selectivity of the reaction and the direction of rotation of the 2,4-dimethyl-1-pentenylidene group. The combined results derived with $(-)$-(R)-**4** and (E)-**10** are totally consistent with the earlier proposed concerted cycloaddition pathway involving an "eight-electron" (*i.e.*, Möbius) transition state in which both double bonds of the allene chromophore are intimately involved.

Prior studies in our laboratories on cycloaddition reactions of cyclopropane-containing compounds have provided considerable information on the reactivity and mode of reaction of such compounds. One class of compounds which has proven to be exceptionally reactive is the alkenylidenecyclopropanes. Alkenylidenecyclopropanes (**1**) react with 4-phenyl-1,2,4-triazoline-
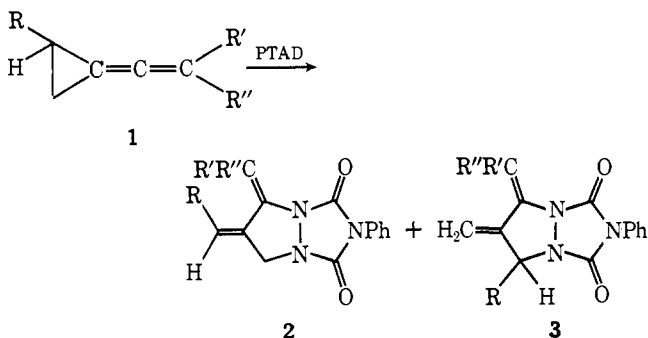
3,5-dione (PTAD) to form adducts of general structure **2** and **3** in which the PTAD has formally added across the methylenecyclopropane portion of **1**.[2] In contrast, however, simple methylenecyclopropenes do not undergo similar cycloaddition reactions, undergoing instead $_\pi2 + _\pi2$ cycloaddition.[3] The possibility that **1** reacts
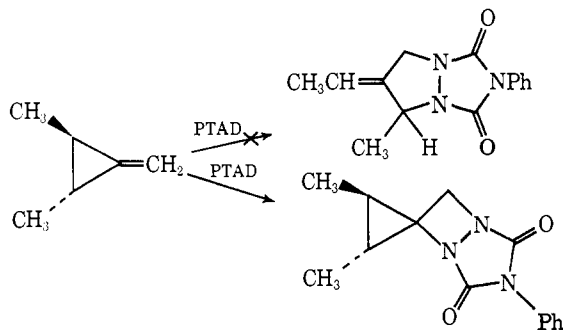
with PTAD to produce dipolar[4] or diradical intermediates which collapse to **2** and **3** has also been investigated. A comparison of the reactions of chlorosulfonyl isocyanate (CSI) with alkenylidenecyclopropanes[5] and *cis*- and *trans*-2,3-dimethylmethylenecyclopropane[6] with those with PTAD[2,3] revealed substantial differences in the stereochemistry and mode of reaction, strongly implying that the reactions of **1** with PTAD do not involve formation of dipolar intermediates. More recently, we have obtained evidence that diradical intermediates are similarly not formed, the reaction of 2-phenylisobutenylidenecyclopropane with 1,1-dichloro-1,1-difluoroethene proceeding in an entirely different manner.[7]

The comparison of all of the existing data led us to propose that the reaction of **1** with PTAD occurred *via* a concerted $[(_\pi2 + _\pi2 + _\sigma2) + _\pi2]$ pathway, *i.e.*, an eight-electron transition state involving both of the double bonds of **1** along with the C_2–C_3 σ-bond. The proposed transition state predicts several intimately related stereochemical features of the cycloaddition reaction: (1) the direction of rotation of the R–C_2–H resulting in formation of a single stereoisomer about the C_7 alkylidene group in **2**, (2) the stereochemistry of attack by PTAD at C_2, (3) the direction of rotation of the R'–C_5–R'' group, and (4) the orbital selectivity of attack at C_4. Of these, only the first was indicated in our prior work. We have now completed a stereochemical study of the reactions of PTAD with **1** using $(-)$-(R)-2-phenylisobutenylidenecyclopropane (**4**)[8] and (E)-2-phenyl-1-(2,4-dimethyl-1-pentenylidene)cyclopropane (**10**) which has provided definitive information concerning each of the stereochemical features indicated above.

(1) Part VIII of Cycloaddition Reactions of Cyclopropane-Containing Compounds. For part VII see D. J. Pasto and J. K. Borchardt, *J. Amer. Chem. Soc.*, **96**, 6937 (1974).

(2) D. J. Pasto and A. F.-T. Chen, *J. Amer. Chem. Soc.*, **93**, 2562 (1971); D. J. Pasto, A. F.-T. Chen, and G. Binsch, *ibid.*, **95**, 1553 (1973).

(3) D. J. Pasto and A. F.-T. Chen, *Tetrahedron Lett.*, 2995 (1972).

(4) For an example of proposed dipolar intermediate formation in a cycloaddition reaction of PTAD see R. Huisgen, W. E. Konz, and U. Schnegg, *Angew. Chem., Int. Ed. Engl.*, **11**, 715 (1972).
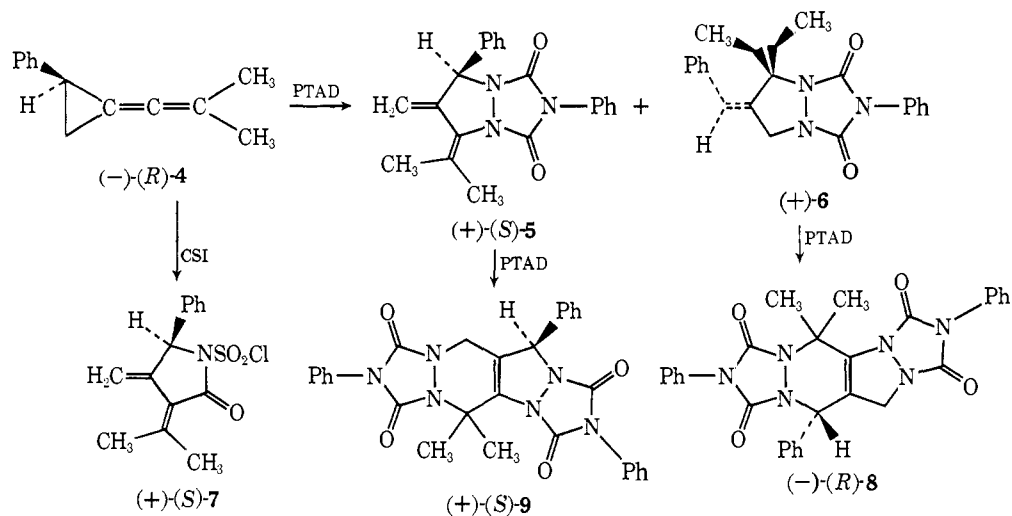
(5) D. J. Pasto, A. F.-T. Chen, G. Ciurdaru, and L. A. Paquette, *J. Org. Chem.*, **38**, 1015 (1973).

(6) D. J. Pasto, A. F.-T. Chen, L. A. Paquette, and G. Ciurdaru, *Amer. Chem. Soc., Div. Petrol. Chem., Prepr.*, **18** (1), 131 (1973).

(7) D. J. Pasto and D. Wampfler, *Tetrahedron Lett.*, 1933 (1974).

(8) D. J. Pasto and J. K. Borchardt, *Tetrahedron Lett.*, 2517 (1973).

Scheme I

(−)-(R)-4   PTAD   (+)-(S)-5 + (+)-6

CSI

(+)-(S)-7

(+)-(S)-9

(−)-(R)-8

Results

Reaction of (−)-(R)-2-Phenylisobutenylidenecyclopropane (4) with PTAD. The reaction of (−)-(R)-4 (64.2% enantiomeric purity)[8] with PTAD in dichloromethane at 0° produces adducts 5 and 6 which are separable by column chromatography. Both adducts are optically active. The absolute configuration of (+)-5 is assigned by comparison with the sign of rotation of (+)-(S)-7, which has been directly converted to (+)-(S)-phenylglycine,[9] and has identical attachment atoms at the chiral carbon atom as in (+)-5.[10] The enantiomeric purity of (+)-5 was determined by nmr techniques. In the presence of tris(trifluoroacetyl-camphorato)europium(III) (Eu(tfac)₃), the hydrogen atoms attached to the chiral carbon atoms in the R and S enantiomers of 5 become diastereotopically related, and integration of the resonances facilitates the direct determination of enantiomeric purity. Using this technique (+)-5 was shown to be 63.4 ± 1.1% enantiomerically pure specifying that the reaction of (−)-(R)-4 with PTAD to produce 5 occurs in a completely stereoselective manner with inversion of configuration (Scheme I).

The chirality of the skewed diene in (+)-6 is assigned on the basis of three lines of evidence.[11] The positive sign of rotation is consistent with the presence of a right-handed helical diene,[12] although in the case of

(9) See reference in footnote 1.
(10) The configurational assignment must for the present time be considered tentative; attempts to degrade 5 to phenylglycine or to a derivative of phenylglycine have thus far not been successful. All of the stereochemical correlations involving compounds reported in this and the companion article,[9] as well as the other stereochemical and mechanistic arguments presented herein, are totally consistent with the stereochemical assignments.
(11) The extremely sterically conjested and skewed nature of the diene chromophores has been demonstrated by an X-ray structural analysis carried out on i (D. J. Pasto and W. R. Scheidt, unpublished results).
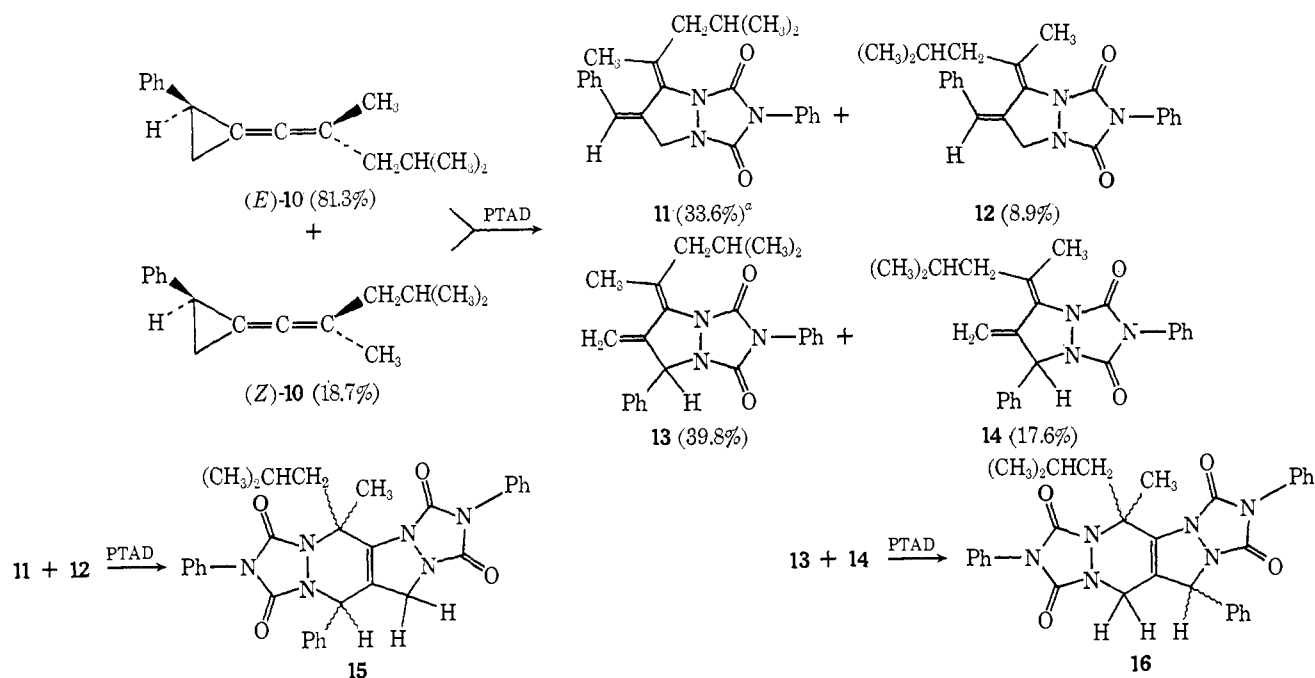
i
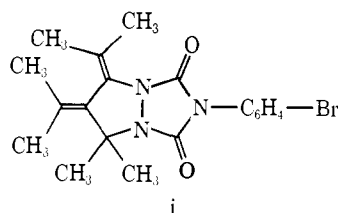
(12) A. W. Burgstahler, H. Ziffer, and U. Weiss, *J. Amer. Chem. Soc.*, **83**, 4660 (1961); A. Moscowitz, E. Charney, U. Weiss, and H. Ziffer, *ibid.*, **83**, 4661 (1961).

(+)-6 the presence of the many functions attached to the diene chromophore could conceivably make the correlation inapplicable. Secondly, the indicated chirality is predicted from the mechanistic considerations and is internally consistent with the other stereochemical features of the reaction (*vide infra*). Thirdly, the chiral diene can be converted to a system containing a chiral carbon atom by reaction with PTAD in which the atoms attached to the chiral center are the same as in 5. In our previous studies it was shown that further cycloaddition of the 1:1 adducts with PTAD occurred by a highly facial selective attack by PTAD on the diene, the group(s) attached to the C₇-alkylidene group exerting the dominant steric influence.[2] In the case of (+)-6, PTAD is predicted to approach the face of the diene opposite the phenyl to produce the 2:1 adduct 8 in which the absolute configuration at the chiral center is opposite that in (+)-5. Commensurate with this prediction is the observation that the sign of rotation of 8 is opposite that in (+)-(S)-5.

The enantiomeric purity of (−)-8 was shown to be 58.3 ± 1.0% by nmr techniques using Eu(tfac)₃. This value is considerably lower than that for (−)-(R)-4 or (+)-(S)-5 and might be due to partial racemization of (+)-5 during the separation and purification procedures or a lack of facial specificity in the cycloaddition reaction of (+)-6 with PTAD. Two lines of evidence indicate the latter to be true. The reaction of (−)-(R)-4 with 2 molar equiv of PTAD (15 min at 0°) produces a mixture of the 2:1 adducts 8 and 9 which were separated by column chromatography. Adduct 8 was shown to be 57.9 ± 0.8% enantiomerically pure, identical with that derived from (+)-6, while adduct 9 was 63.4 ± 0.8% enantiomerically pure. In this sequence (+)-6 reacts immediately with PTAD but yet produces product of nearly the same enantiomeric purity as in the separate reaction steps. Secondly, (+)-6 does not undergo any loss of optical activity at 25° over the course of 10 days which also militates against partial racemization during the separation and purification procedures. It must be concluded, therefore, that the reaction of (+)-6 with PTAD occurs in an ~80% facial selective manner.

Stereochemical analysis of the products formed by reaction of (−)-(R)-4 with PTAD at 61° shows no

Scheme II

CH₂CH(CH₃)₂

Ph—CH=C(CH₃)— ... (E)-10 (81.3%)

(Z)-10 (18.7%)

PTAD

11 (33.6%)ᵃ

12 (8.9%)

13 (39.8%)

14 (17.6%)

11 + 12 $\xrightarrow{\text{PTAD}}$ 15

13 + 14 $\xrightarrow{\text{PTAD}}$ 16

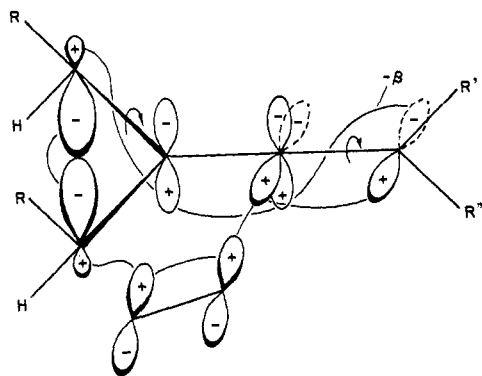ᵃ Percentages represent the composition of the 1:1 adduct fraction.

Figure 1. Orbital interactions in an "eight-electron" (i.e., Möbius) process for cycloaddition.

change in stereoselectivities. This is in contrast with that observed in the reaction of (−)-(R)-4 with chlorosulfonyl isocyanate[1] which proceeds via formation of a dipolar intermediate.

Reaction of 2-Phenyl-1-(2,4-dimethyl-1-pentenylidene)cyclopropane (10) with PTAD. The reaction of 10 (81.3 ± 1.5% (E))[9] with PTAD in methylene chloride at 0° results in the formation of a mixture of unreacted 10 and 1:1 and 2:1 PTAD-10 adducts. The unreacted 10 was separated from the adducts by column chromatography and was shown to be 78.1 ± 1.6% E by nmr analysis. The four 1:1 adducts 11–14 could not be fully separated (the elution sequence being 11 > 13 > 12 > 14). The assignment of the structures of 11–14 was made on the basis of chemical shift comparisons with the similar protons in the 1:1 adducts 5 and 6 derived from 4,[2] the chemical shifts in the two series being within ±0.02 ppm. The 1:1 adduct fractions were combined, and the composition was determined by integration of the expanded high-field region. The ratio of 11 to 12 was 79.1:20.9 (±1.5).

The nmr spectrum of the 2:1 adduct fraction displayed a triplet (J = 1.8 Hz) at δ 5.86 characteristic of

the five-membered ring methine proton in the 2:1 adduct 16. The 1:1 adduct mixture 11–14 was treated with a deficient amount of PTAD, and the 1:1 and 2:1 adducts were separated by column chromatography. The nmr spectrum of the 2:1 adduct fraction displayed two triplets at δ 5.86 and 5.94 (J = 1.3 Hz) (characteristic of the six-membered ring methine proton in 15) in an approximate ratio of 2.7:1. (The 2:1 adducts 16 and 17 undoubtedly are composed of two stereoisomers; however, the nmr spectra of the stereoisomers are not sufficiently different such that the individual spectra can be resolved.) Integration of the nmr spectrum of the recovered 1:1 adduct mixture showed the presence of 40% 11, 15% 12, 33% 14, and 12% 14 indicating the reactivity sequence 13 > 14 ≫ 11 > 12 (Scheme II). This reactivity sequence is consistent with the steric effects on the reactivity of the diene chromophores in the 1:1 adducts as discussed earlier.[2]

Discussion

The stereochemical results described in the foregoing section are consistent with the earlier suggested "eight-electron" (i.e., a Möbius system) concerted cycloaddition reaction occurring via the transition state pictured in Figure 1. The stereochemical features of the reaction demanded by the transition state, all of which are intimately coupled are (1) attack by the π-system of the dienophile on the in-plane p orbital on C₄ of the C₄–C₅ double bond (i.e., orbital selectivity), (2) attack by the dienophile at C₂ with inversion of configuration, (3) outward rotation of the R group of C₃ (the direction of rotation of least steric interference), and (4) the direction of rotation of the R'–C₅–R'' group.

The orbital selectivity of attack is clearly indicated by the results derived with 10. Attack on the in-plane p orbital on C₄ will not result in a difference in reactivity between (E)-10 and (Z)-10, the approach occurring perpendicular to the plane of the methyl and isobutyl

groups.[13] In contrast, attack on the perpendicular p orbital on C_4 of the C_1-C_4 double bond is expected to result in pronounced differences in reactivity between (E)-10 and (Z)-10, as well as facial selective attacks within (E)-10 and (Z)-10 owing to the differing steric effects of the methyl and isobutyl groups and the presence of the phenyl group. This is clearly demonstrated by the steric courses of the reactions of (E)- and (Z)-10 with dicyclohexylborane and chlorosulfonyl isocyanate[9] and 4 with dialkylboranes and diimide.[8] In the reaction of 10 with PTAD the stereochemical composition of the recovered unreacted 10 and the ratio of 11:12 was the same as that of the starting alkenylidenecyclopropane; thus, attack by the dienophile must have occurred on the in-plane p orbital on C_4 of the C_4-C_5 double bond.

The direction of rotation of the R'-C_5-R'' group is also clearly evident from the results derived with 10. Cycloaddition across C_4 and C_3 of (E)-10 results in rotation of the methyl group to the inside of the diene to form 11, while with (Z)-10 the isobutyl group rotates to the inside to produce 12. The ratio of 11:12, being the same as that of the starting (E)- and (Z)-10, is also consistent with the proposed transition state model illustrated in Figure 1.

Finally, the reaction of (−)-(R)-4 with PTAD to produce (+)-(S)-5 in a stereospecific manner requires inversion of configuration at C_2 as predicted.

The transition state model also leads to the prediction of the chirality of the diene chromophore of 6. Considering that all of the rotational processes in proceeding from (−)-(R)-4 to (+)-6 occur in concert, the orientation of the phenyl group away from the plane perpendicular to the three-membered ring provides an advantage in the rotational process about C_2 over that about C_5 ultimately producing the right-handed helical diene in 6. The similar sign of rotation of the chiral diene formed in the reaction of (−)-(R)-4 with chlorosulfonyl isocyanate[9] adds further support for the right-handed helicity of the diene chromophore in 6.

Summary

A comparison of the reaction of PTAD with alkenylidenecyclopropanes with the reactions with other reagents known to proceed via dipolar or diradical intermediates, and the stereochemical results reported in this article, fully support our earlier proposal that the cycloaddition of alkenylidenecyclopropanes with PTAD occurs in a fully concerted manner in which both double bonds of the allene moiety are involved.

Experimental Section

Melting points are uncorrected and were determined using a Mel-Temp melting point apparatus. Optical rotations were determined in chloroform using an O. C. Rudolf and Sons polarimeter. Infrared absorption spectra were determined using a Perkin-Elmer Model 457 infrared spectrophotometer. All nuclear magnetic resonance spectra were recorded using a Varian XL-100 nuclear magnetic resonance spectrometer. Enantiomeric purities were determined by integration of the nmr resonances in the presence of ca. 0.4 molar equiv of tris(trifluoroacetylcamphorato)europium(III) [Eu(tfac)₃].

Reaction of (−)-(R)-4 with PTAD. A solution of 0.49 g (2.8 mmol) of PTAD in 10 ml of dichloromethane was added slowly to

(13) The phenyl group of 10 does not affect the relative reactivities of (E)-10 and (Z)-10. It does, however, affect the facial selectivity of the approach to the C_4-C_5 double bond, attack at the syn face resulting in the formation of 5, while reaction at the anti face results in the formation of 6.

a stirred solution of 0.48 g (2.8 mmol) of (−)-(R)-4[8] ($[\alpha]^{25}$D −19°, 64.2 ± 1.0% enantiomeric purity) in 15 ml of dichloromethane at 0°. After loss of the red color of the PTAD (ca. 1 hr) the solvent was removed under reduced pressure and the residue was chromatographed on a 1 × 20 in. silica gel column. Elution with carbon tetrachloride gave unreacted (−)-(R)-4 (4.2%); $[\alpha]^{25}$D −19°. Further elution with 2:1 benzene–dichloromethane gave 6 (26.2%) followed by 5 (38.0%). Elution with 1:1 benzene–dichloromethane gave the 2:1 adduct 9 (6.1%). The physical properties of 5, 6, and 9 were identical with those reported earlier.[2] The optical rotations and enantiomeric purities are given in Table I.

The reaction of (−)-(R)-4 with PTAD was also carried out at 61° and worked up in an identical manner giving 4 (12.0%), 5 (1.7%), 6 (12.4%), and 9 (31.6%). The optical rotations and enantiomeric purities are given in parentheses in Table I.

Table I. Optical Rotation and Enantiomeric Purities of Adducts of (−)-(R)-4 and PTAD[a]

Compound	$[\alpha]^{25}$D (CHCl₃)	% enantiomeric purity
5	+26.4°	63.3 ± 1.1
6	+3.7° (+2.4°)	
8[b]	−16.8°	58.3 ± 0.8
8[c]	−17.0° (−17.9°)	57.9 ± 0.8 (60.9 ± 1.1)
9	+43.8°	65.2 ± 1.1 (63.9 ± 0.9)

[a] Values in parentheses refer to products formed at 61.2°. [b] From the reaction of PTAD with (+)-6. [c] Directly from the reaction of (−)-(R)-4 with 2 equiv of PTAD.

Reaction of (+)-6 with PTAD. A solution of 0.023 g (0.13 mmol) of PTAD in 10 ml of dichloromethane was added to a solution of 0.046 g (0.13 mmol) of (+)-6 in dichloromethane at 25°. The solvent was removed under reduced pressure and the residue was recrystallized from ethyl acetate. The optical rotation and enantiomeric purity of 8 were determined and appear in Table I.

Reaction of (−)-(R)-4 with 2 Molar Equiv of PTAD. A solution of 0.072 g (0.42 mmol) of (−)-(R)-4 in 15 ml of dichloromethane was cooled to 0° in an ice bath and a solution of 0.149 g (0.85 mmol) of PTAD in 5 ml of dichloromethane at 25° was added rapidly. After 1 hr the temperature was allowed to come to room temperature and the reaction mixture was allowed to stand for 30 min. The solvent was removed under reduced pressure and the residue was fractionally recrystallized from ethyl acetate giving pure 8 and 9 (35:65 ratio by nmr of original product mixture). The optical rotation of 8 and the enantiomeric purities of 8 and 9 were determined and appear in Table I.

Reaction of (E)- and (Z)-10 with PTAD. To a solution of 0.72 g (3.4 mmol) of an 81.3 ± 1.5% (E)-10 and 18.7 ± 1.5% (Z)-10[9] in 10 ml of dichloromethane at 0° was added 0.60 g (3.4 mmol) of PTAD dissolved in 15 ml of dichloromethane. The color of PTAD was rapidly discharged and the solvent was removed under reduced pressure. The residue was chromatographed on a 1.5 × 25 cm silica gel column. Elution with benzene gave 250 mg of unreacted 10. Analysis by nmr indicated the presence of 78.1 ± 1.6% (E)-10 and 21.9 ± 1.6% (Z)-10. Elution with 50–93% methylene chloride–benzene gave a series of 20 50-ml fractions which contained varying amounts of adducts 11–14, the elution sequence being 11 > 13 > 14 > 12. The nmr spectra of intermittent fractions allowed assignment of the individual fractions (no adduct was obtained free of any other adduct). All of the 1:1 adduct fractions were combined (208 mg), and the nmr spectrum of the mixture was integrated showing the presence of 33.6% 11, 8.9% 12, 39.8% 13, and 17.6% 14.

Adduct 11. Nmr (CDCl₃) δ 0.93 (d, J = 6.3 Hz, 6 H), 1.32 (s, 3 H), 2.1 (m, 1 H), 2.42 (d, J = 7.0 Hz, 2 H), 4.43 (d, J = 1.6 Hz, 2 H), 6.56 (t, J = 1.6 Hz, 1 H), 7.47 (m, 5 H).

Adduct 12. Nmr (CDCl₃) δ 0.62 (d, J = 6.3 Hz, 6 H), 1.9 (m, 1 H), 2.06 (s, 3 H), 2.11 (d, J = 7.0 Hz, 2 H), 4.38 (d, J = 1.5 Hz, 2 H), 6.49 (t, J = 1.5 Hz, 1 H), 7.4 (m, 5 H).

Adduct 13. Nmr (CDCl₃) δ 0.98 (d, J = 6.5 Hz, 6 H), 1.8 (m, 1 H), 1.97 (s, 3 H), 2.42 (d, J = 7.0 Hz, 2 H), 5.36 (m, 1 H), 5.48 (m, 1 H), 5.67 (t, J = 1.5 Hz, 1 H), 7.48 (s, 5 H).

Adduct 14. Nmr (CDCl₃) δ 0.82 (d, J = 6.5 Hz, 6 H), 1.9 (m, 1 H), 2.17 (s, 3 H), 2.42 (d, J = 7.0 Hz, 2 H), 5.36 (m, 1 H), 5.48 (m, 1 H), 5.67 (t, J = 1.5 Hz, 1 H), 7.42 (s, 5 H).

Elution with 10% methanol–methylene chloride gave 861 mg of 2:1 adduct (99% total recovery): nmr (CDCl₃) δ 5.88 (t, $J = 3.7$ Hz).

Reaction of the 1:1 Adduct Mixture with PTAD. To a solution of 200 mg (0.52 mmol) of the combined 1:1 adducts in 5 ml of dichloromethane was added 30 mg (0.17 mmol) of PTAD dissolved in 3 ml of dichloromethane. The color of the PTAD was discharged slowly (10 min at 25°), after which the solvent was removed and the residue was separated by chromatography as described above.

1:1 Adduct Fraction. Integration of the nmr spectrum showed the presence of 40% **11**, 15% **12**, 33% **13**, and 12% **14**.

2:1 Adduct Fraction. The nmr spectrum (CDCl₃) showed triplets at δ 5.88 and 5.94 ($J = 3.7$ Hz) in an intensity ratio of ~2.7:1.0.
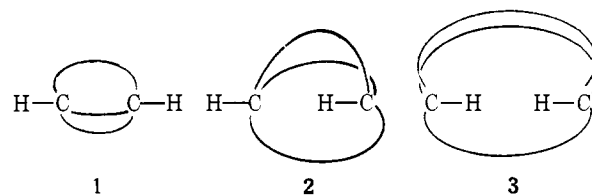
Cycloadditions to Cyclic 1,3-Dienes. A Diels-Alder Route to Inside-Outside Bicyclics[1]

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Abstract: The *cis,cis*-, *cis,trans*-, and *trans,trans*-1,3-cyclododecadienes have been prepared and characterized. The reaction of *cis,trans*-1,3-cyclododecadiene with hexafluoro-2-butyne has been studied in detail. The major product of this reaction was found to be a [2π + 4π] cycloadduct, which appeared to form in the traditional Diels–Alder sense. No [2π + 4π] cycloadducts could be detected or identified from exploratory reactions of perfluoro-2-butyne with either *cis,cis*-1,3-cyclododecadiene or *trans,trans*-1,3-cyclododecadiene. The minor product of the reaction of perfluoro-2-butyne with *cis,trans*-1,3-cyclododecadiene was found to be an unusual "ene" type product. The structures of both products were established through the extensive use of ¹³C, ¹⁹F, and ¹H magnetic resonance spectroscopy and mass spectrometry. The [2π + 4π] cycloaddition to *cis,trans*-1,3-cyclododecadiene provided a simple route to inside-outside (i,o) bicyclics. The rearrangement of 11,12-bis(trifluoromethyl)-(i,o)-bicyclo[8.2.2]-tetradeca-11,13-diene in the presence of base and *n*-bromosuccinimide is discussed.

In line with our general interest in the effect of bond distortion on chemical reactivity, we have investigated various aspects of the chemistry of compounds containing small rings. As part of our overall concern with this relationship between C–C bond distortion and chemical behavior, we questioned whether highly reactive "bent" carbon–carbon σ bonds might exist in aliphatic systems which did not contain any small rings.[3,4] In order to achieve such a goal, a molecular type would be required in which the bonds between carbon atoms are distorted as a result of the total molecular geometry. In principle, it seemed likely that bicyclic molecules with inverted bridgeheads might fulfill our desires. Theoretically, bridged bicyclic molecules can exist in any one of three catagories relative to the stereochemistry at the bridgehead carbons. These can be classified as outside–outside (o,o), inside–outside (i,o), and inside–inside (i,i) bicyclics, which are represented by the general formulas **1**, **2**, and **3**, respec-

tively.[5] If the chains connecting the bridgeheads are small enough, the nonbonded steric interaction of the inverted bridgehead(s) with the rest of the molecule should cause significant perturbations in the bonding in certain parts of the molecule. Thus, we embarked on an exploration of the synthetic routes to inside–outside and inside–inside bicyclics. This paper provides a detailed report of our initial investigations.

At the inception of our studies, several examples of inside–outside and inside–inside bicyclics had already appeared in the literature. However, these were almost entirely limited to macrobicyclic systems having nitrogen at both bridgeheads.[2,6,7] Upon quaternization, these diazamacrobicyclic systems gave double salts which could exist in all three possible stereo-

(1) Paper XLIII on "The Chemistry of Bent Bonds." For the previous paper in this series see P. G. Gassman and E. A. Armour, *J. Amer. Chem. Soc.*, **95**, 6129 (1973).

(2) (a) To whom correspondence concerning this investigation should be addressed at the Department of Chemistry, University of Minnesota, Minneapolis, Minn. 55455. (b) The Ohio State University Postdoctoral Fellow, 1971–1972; National Institutes of Health Postdoctoral Fellow, 1972–1973.

(3) Some unusual reactivity has been noted for the paracyclophanes. For a review see B. H. Smith, "Bridged Aromatic Compounds," Academic Press, New York, N. Y., 1964.

(4) Cyclic trans olefins such as *trans*-cyclooctene and *trans*-cycloheptene might also be expected to exhibit some characteristics of molecules containing "bent" carbon–carbon σ bonds. Unfortunately, the reactivity of the olefinic linkage overshadows any chemical reactivity of the rest of the molecule which might be associated specifically with strained σ bonds.

(5) For a discussion of the concept of bicyclic molecules with inverted bridgeheads, see H. E. Simmons, C. H. Park, R. T. Uyeda, and M. F. Habibi, *Trans. N. Y. Acad. Sci.*, **32**, 521 (1970).

(6) H. E. Simmons and C. H. Park, *J. Amer. Chem. Soc.*, **90**, 2428, 2429, 2431 (1968); *Chem. Eng. News*, **46** (July 3, 1967); C. H. Park and H. E. Simmons, U. S. Patent 3,531,468 (1970); *Chem. Abstr.*, **74**, 13189w (1971); J. M. Lehn, J. P. Sauvage, and B. Dietrich, *J. Amer. Chem. Soc.*, **92**, 2916 (1970); *Tetrahedron Lett.*, 2885, 2889 (1969); B. Dietrich, J. M. Lehn, J. P. Sauvage, and J. Blanzet, *Tetrahedron*, **29**, 1629 (1973); B. Dietrich, J. M. Lehn, and J. P. Sauvage, *ibid.*, **29**, 1647 (1973); see also B. Metz, D. Moras, and R. Weiss, *Chem. Commun.*, 217 (1970).

(7) For exceptions see ref 5.