2_6CH_2COOH exhibit extremely high selectivity factors, $10^{10.6}$-$10^{17.0}$!

Here, it is worth mentioning that the K_{uranyl} values for 2_6H and 2_6CH_2COOH are greater only by 2.3-2.8 log units than that for **1**, whereas the selectivity factors are improved by 10^8-10^{15} log units. This means that the high selectivity factors stem from the unusually low $K_{M^{n+}}$ values: that is, 2_6H and 2_6CH_2COOH are moderately rigid and therefore would firmly maintain the pseudoplanar hexacoordination geometry. This structure is very favorable for the binding of UO_2^{2+} but quite unfavorable for the binding of other metal cations, which usually requires either square-planar or tetrahedral coordination geometry. In 1976 Alberts and Cram[7c] synthesized macrocyclic systems containing one to three β-diketone units and determined the stability constants for several metal cations including UO_2^{2+}. The β-diketone units are linked by the crown-type ethylene oxide chains.[7] The stability constants (25 °C, water:dioxane = 1:1 (v/v)) for a macrocycle containing two β-diketone units are $10^{11.0}$ M^{-1} for UO_2^{2+}, $10^{11.3}$ M^{-1} for Cu^{2+}, $10^{4.8}$ M^{-1} for Ni^{2+}, $10^{9.7}$ M^{-1} for Zn^{2+}, etc.[7] These values are greater by about 1.8 to 6.3 powers of ten than those for the noncyclic analogues, but the significant UO_2^{2+} selectivity was not seen (although their purpose in this paper was not the molecular design of uranophiles). This is probably due to the flexibility of the ring system. In Tabushi's uranophile (**1**), the carboxylate groups are linked by three octamethylene chains, allowing a more flexible conformation. Therefore, it is originally designed so that hexacarboxylate groups can arrange themselves in a suitable way for hexacoordination but also may provide the square-planar or tetrahedral geometry according to an "induce-fit" manner.

Conclusion. We have thus demonstrated that calix[5]arene and calix[6]arene, which can be readily synthesized from cheap starting materials, serve as an excellent basic skeleton for the design of pseudoplanar penta- or hexadentate uranophiles. In general, there are two possible strategies for improving the metal selectivity of macrocyclic ligands: the first one is to enhance the stability constant for the target metal cation and the second one is to lower the stability constants for competing metal cations. If the first strategy is employed, one should design some very rigid macrocycles on the basis of the "hole-size selectivity" rule. Hence, this approach is frequently accompanied by the disadvantage that the dynamic process becomes very slow and is not necessarily recommended for the design of uranophiles. In contrast, the second strategy does not have this disadvantage, and the uranophiles would be applicable as carriers in dynamic processes such as solvent extraction and membrane transport. Calixarenes provide an ideal basic skeleton for the second strategy: they are moderately rigid, allowing the high metal selectivity to be realized, but their conformational freedom still remains. We now believe that modification of calixarenes should lead to a further enhancement in the stability constant and the selectivity factor not only as uranophiles but also more in general as metallocalixarenes.[35,36] Detailed characterization of these and related calixarene derivatives and applications to solvent extraction and immobilization in polymer matrices are now under investigation.

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Reaction of 4-Phenyl-1,2,4-triazoline-3,5-dione with Substituted Butadienes. A Nonconcerted Diels-Alder Reaction

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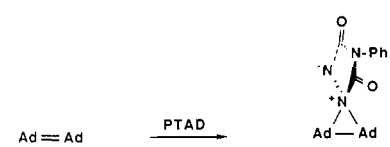
Abstract: The reaction of 4-phenyl-1,2,4-triazoline-3,5-dione with substituted 1,3-butadienes (1,3-butadiene, (*E*,*E*)-, (*Z*,*E*)-, and (*Z*,*Z*)-2,4-hexadiene, and 2,5-dimethyl-2,4-hexadiene) has been investigated. In CH_2Cl_2, 1,3-butadiene, (*E*,*E*)-2,4-hexadiene, and (*Z*,*E*)-2,4-hexadiene give the expected Diels-Alder products with high stereospecificity (>200:1). Surprisingly, (*Z*,*Z*)-2,4-hexadiene gives a mixture of two Diels-Alder products, with the major isomer having the "wrong" stereochemistry. 2,5-Dimethyl-2,4-hexadiene gives mainly (~70%) the ene product. For both (*Z*,*Z*)-2,4-hexadiene and 2,5-dimethyl-2,4-hexadiene, the reactions proceed via observable intermediates to which we assign diazetidine structures. In MeOH, (*Z*,*Z*)-2,4-hexadiene and 2,5-dimethyl-2,4-hexadiene give mainly solvent adducts. (*Z*,*E*)-2,4-Hexadiene gives ~12% MeOH adduct together with the expected Diels-Alder product, while (*E*,*E*)-2,4-hexadiene and 1,3-butadiene give less than 0.05% of the solvent adducts. A mechanism involving initial formation of an aziridinium imide which subsequently opens to a 1,4-zwitterion can account for all the observations and is consistent with force-field calculations. The proposed mechanism may also hold for reactions of other electrophilic reagents such as $^1O_2$ and polycyanoethylenes.

The Diels-Alder (DA) reaction is one of the most popular synthetic tools because of the high control over regio- and stereochemistry it provides. Because the reaction usually proceeds with complete stereospecificity with respect to both the diene and the dienophile, it is generally believed to be concerted. There are a few exceptions, which are mainly limited to halogenated reactants[1] and DA reactions involving very polar components.[2-4]

Scheme I



Triazolinediones are often used as the dienophile in DA reactions to introduce nitrogen functionality and are among the most reactive dienophiles known.[5,6] Triazolinediones and other azo-

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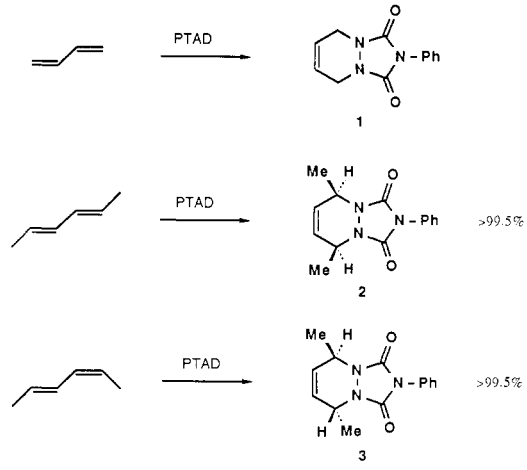
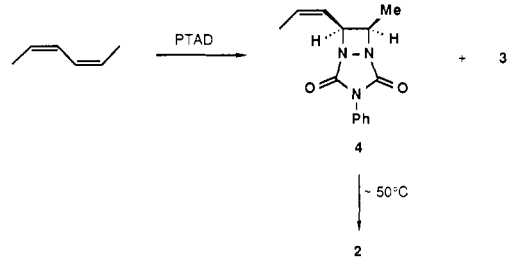
Scheme II



dicarboxyl compounds undergo the same classes of reactions as singlet oxygen, namely [2 + 2] and [4 + 2] (DA) addition and the ene reaction.[7,8] In the ene reaction,[9,10] it has been demonstrated by deuterium substitution of the substrate that both triazolinediones and singlet oxygen react via intermediates that have the stereochemical characteristics of an aziridinium imide[7,11,12] (AI) or perepoxide,[13,14,15] respectively. Recently it has been reported that [2 + 2] adduct formation from triazolinediones and adamantylideneadamantane also proceeds via an intermediate with spectra that suggest an AI structure (Scheme I).[16]

Diazetidines, the [2 + 2] adducts from azodicarboxyl compounds and olefins, are usually formed only when the olefin is fairly electron-rich and lacks allylic hydrogens.[7,17,18-21] A concerted [2 + 2] cycloaddition is forbidden by the Woodward–Hoffmann rules,[22] and the mechanism is usually formulated as proceeding via a zwitterionic or diradical intermediate. In some cases it has been shown that intermediates can be trapped with nucleophiles or ketones.[4,17,19,23-26]

Scheme III



In an early paper by Gillis and Hagarty[27] exploring the reactivity of 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) with dienes, it was noted that PTAD reacts very rapidly with a number of different dienes to give DA products in high yields. In these experiments, PTAD was generated in situ by $Pb(OAc)_4$ oxidation of the urazole. When the diene was 2,5-dimethyl-2,4-hexadiene, none of the DA product was observed, but a low yield of a product containing an acetoxy group was isolated. This compound was suggested to arise from trapping of a dipolar or diradical intermediate by acetate, but the mechanism was not investigated further.

Clennan and L'Esperance have investigated the reaction of (*Z*,*Z*)-, (*Z*,*E*)-, and (*E*,*E*)-1,4-di-*tert*-butoxy-1,3-butadienes with singlet oxygen.[28] The major products in all cases are dioxetanes, the [2 + 2] adduct. For all isomers, a loss of stereochemistry indicates that the reaction proceeds, at least in part, via intermediates. They propose two different mechanisms, a concerted $2_s + 2_a$ cycloaddition competing with formation of a perepoxide intermediate.

Results

We studied the reaction of PTAD with 1,3-butadiene, (*Z*,*Z*)-, (*Z*,*E*)-, and (*E*,*E*)-2,4-hexadiene, and 2,5-dimethyl-2,4-hexadiene. The reactions were carried out by adding a solution of PTAD[29] in CH_2Cl_2 to a stirred solution of the diene in either CH_2Cl_2 or MeOH at different temperatures. In the absence of a diene, PTAD reacts with MeOH to give several unidentified products. However, PTAD reacts much more rapidly with the diene than with MeOH under the reaction conditions, and only diene-containing products were observed.

In CH_2Cl_2, 1,3-butadiene and (*E*,*E*)- and (*Z*,*E*)-2,4-hexadiene react with PTAD to give DA adducts with the expected stereochemical integrity[30] (Scheme II). (*E*,*E*)-2,4-Hexadiene gives an

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adduct, **2**, with cis methyl groups, while (*Z,E*)-2,4-hexadiene gives an adduct, **3**, with trans methyl groups. Analysis of the adducts by capillary GC shows that the reaction is >99.5% stereospecific in both cases. Both adducts show only one methyl resonance in the NMR; the stereochemistry was proved by converting them to their corresponding epoxides with MCPBA. The cis adduct gives two epoxides in approximately a 1:10 ratio, while the trans adduct gives only one. The NMR spectral data for the epoxides support the stereochemical assignments.

Surprisingly, reaction between (*Z,Z*)-2,4-hexadiene and PTAD gave a mixture of both DA adducts **2** and **3**; the major isomer is **3**, with methyl groups trans. There was no diene isomerization during the reaction, as shown by GC analysis. The relative ratio of the two adducts depends on the temperature, with low temperatures favoring the cis isomer (the cis:trans ratio changes from 20:80 at −40 °C to 6:94 at 40 °C). However, solvent polarity has only a minor effect (the ratio at 0 °C is 11:89 in CH_2Cl_2 and 8:92 in acetonitrile). When the two reactants are mixed at −78 °C and allowed to warm while the reaction is monitored by NMR, no reaction is observed until approximately −55 °C. At this temperature, signals from the trans-Diels–Alder adduct **3** appear together with signals from a new compound, **4**. None of the cis-Diels–Alder adduct **2** is present at this temperature. Upon warming, compound **4** rearranges to **2**. The rearrangement occurs with a half-life of a few minutes at 50 °C and is stereospecific within the accuracy of the NMR integration (>85%). The integration accuracy is limited because **4** and **2** are minor products in the mixture. These reactions are shown in Scheme III.

Spectral data for **4** were obtained from the mixture by subtraction of the spectra of **3**. The ^1H NMR has two olefinic resonances at 5.80 and 5.63 ppm, with a vicinal coupling constant of 11.8 Hz, showing that one of the double bonds in the starting material is intact and that the configuration is still *Z*.[31] Besides resonances from the methyl groups (1.54 and 1.23 ppm) and the phenyl group, there are peaks at 5.11 and 4.68 ppm. The coupling constant between these protons is approximately 6.7 Hz. The FTIR spectrum in the carbonyl region was also obtained by subtraction in $CHCl_3$. Strong peaks of **3** are present in the spectrum in the region 1690–1730 cm^{-1}, and the only observable subtraction band is at 1749 cm^{-1}. It is likely that additional peaks are present and obscured by the absorptions of **3**, but the quality of the subtraction spectrum was too poor to assign further peaks to **4**. The ^{13}C NMR has aliphatic resonances at 57 and 78 ppm, among others. The ^{13}C–H coupling constant ($^1J_{C-H}$) for these resonances were determined to be 143 and 154 Hz, respectively.

On the basis of these data, we assign the diazetidine structure to **4**; the spectral data are consistent with those of other diazetidines reported. The ^1H NMR of the diazetidine from PTAD and indene[19,32] has resonances at 4.07 and 4.61 ppm, and the IR has absorptions at 1712 and 1782 cm^{-1}. The diazetidine from adamantylideneadamantane and MeTAD[11] has carbonyl absorptions at 1675 and 1730 cm^{-1}. The $^1J_{C-H}$ coupling constants for the aliphatic methine carbons clearly indicate that they are part of a four-membered ring. Much larger coupling constants would be expected if the intermediate had an aziridinium imide structure. For example, the $^1J_{C-H}$ constants for the α-hydrogens in the saturated cyclic hydrocarbons and the corresponding oxygen and nitrogen heterocycles increase by 38, 36, and 34 Hz in the three-membered rings relative to the six-membered rings, but by only 11, 6, and 6 Hz in the four-membered rings.[34] Since $^1J_{C-H}$ for the hydrogen α to the nitrogen in the six-membered Diels–Alder adduct **2** is 145 Hz, a reasonable estimate for the diazetidine would be 151–157 Hz, close to the observed values, and 177–183 Hz for the AI, much higher than observed. Most of the other diazetidine structures reported[17,18,20,21,24,35,36] have ether substituents and are thus poorer models. The coupling constant between cis protons in diazetidines usually falls in the range 5.6–6.8 Hz, while the trans coupling constant is between 3.7–4.6 Hz.[19,20,24] We therefore assign cis stereochemistry to the diazetidine ring.

Several attempts were made to reduce either the C=C or the C—N bond of **4** in order to further secure the structure. The reactions were done on the mixture of **3** and **4** generated from PTAD and (*Z,Z*)-2,4-hexadiene in CH_2Cl_2 at −45 °C. Reduction with a 20-fold excess of diimide (generated from potassium azodicarboxylate and acetic acid[37]) at 0 °C gave only the two DA products, **2** and **3**. Catalytic hydrogenation using palladium on carbon at 0–25 °C over 12 h reduced the double bond of **3**, but **4** rearranged to **2** more rapidly than it was reduced (**2** was observed after 12 h).

Rhodium on carbon at 0–25 °C did reduce **4** more rapidly than it rearranged to **2** but gave 4–6 products in addition to **3**, none of which could be isolated. Reduction with $NaBH_4$ in CH_2Cl_2/THF at −30 to 0 °C gave **3** together with a new compound which was stable upon heating to 70 °C for 30 min (NMR). However, all attempts to isolate this product by chromatography or recrystallization resulted only in the formation of a white polymeric substance.

The reaction between (*Z,E*)-2,4-hexadiene and PTAD was also followed by low-temperature NMR, but the two reactants formed the trans-Diels–Alder adduct without any observable intermediate in this case. The stereospecificity of the reaction of (*Z,E*)-2,4-hexadiene with PTAD did not change when acetonitrile was used as a solvent instead of CH_2Cl_2, and none of the cis-DA product could be detected.

Reaction between PTAD and 2,5-dimethyl-2,4-hexadiene gave ene product **6** as the major product (approximately 70%). Several other products are present in small amounts, as judged by the ^1H and ^{13}C NMR. No attempt was made to isolate or identify these products. Low-temperature NMR revealed that an intermediate, **5**, is again formed, in nearly quantitative yield in this case. However, **5** is much less stable than **4**, and has a half-life of only a few minutes at −10 °C before rearranging to **6**. The ^1H NMR at −40 °C shows the following resonances (besides the phenyl group): 5.69 (d, J = 10.3, 1 H), 5.38 (dd, J = 10.3, 1.2, 1 H), 1.88 (d, J = 1.1, 3 H), 1.84 (d, J = 1.2, 3 H), 1.60 (s, 3 H), 1.32 (s, 3 H). The presence of four different Me resonances rules out an open zwitterionic structure (which should have a maximum of three methyl resonances) for **5**. The chemical shifts for the two downfield Me resonances suggest that one of the olefinic bonds is still intact and that the PTAD is bonded to C_2 and C_3. The doubling of the one of the proton and two of the methyl resonances is probably due to either the presence of a chiral center in the molecule or to the fact that two different isomers are present. If the doubling were due to long-range coupling, the olefinic proton should be a doublet of quartets or some more complex pattern. Since the intensities of the two peaks in each doublet are the same within a few percent, if the splitting is due to two isomers, they would have to be present in almost equal amounts. It is therefore likely that a chiral center is present. The ^{13}C NMR has resonances at 66, 95, and 113 ppm, among others. The resonance at 66 ppm is a quaternary center and that at 95 ppm is a methine carbon with a $^1J_{C-H}$ coupling constant of 153 Hz.

There are two reasonable structures to consider for intermediate **5**. One is a diazetidine, analogous to **4**, and the other is an aziridinium imide. Both of these have a chiral center, and the AI can also exist as two isomers (outer nitrogen syn or anti to the $(CH_3)_2C{=}C$ group). The strong differences in the chemical

(31) The corresponding coupling constant for (*Z,Z*)-2,4-hexadiene was determined by spectral simulation (treating the data as an AA′BB′$X_3X'_3$ spin system) to be 10.1 Hz.

(32) Note that the adduct from indene and diethyl azodicarboxylate does not have the diazetidine structure as claimed in ref 33a, but rather an oxadiazine structure.[33b,c]

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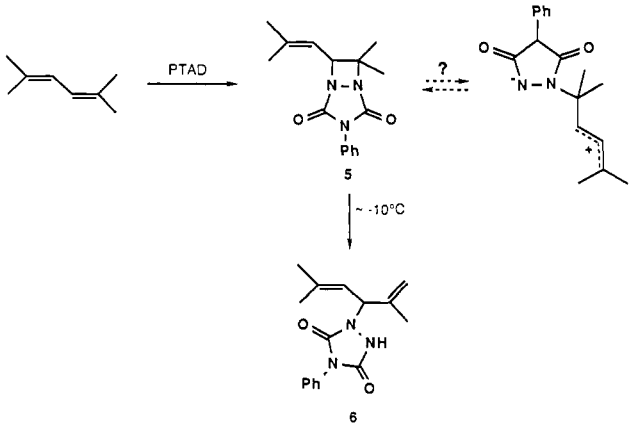
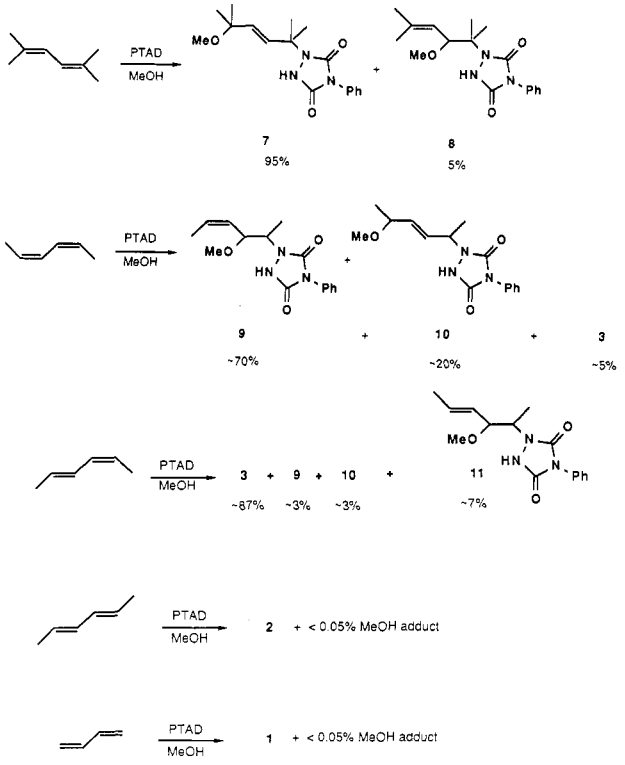
Scheme IV



Scheme V

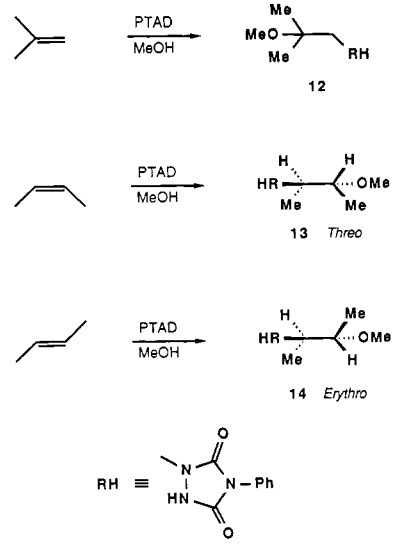


shifts of the two upfield methyl protons caused us to consider a possible aziridinium imide structure for **5**, especially since the methyl groups on C_2 for the dioxetane from 2,5-dimethyl-2,4-hexadiene and singlet oxygen have almost identical chemical shifts.[38] However, the $^1J_{C-H}$ coupling constant of 153 Hz is very close to what would be expected for a diazetidine and does not agree with the estimated value ($^1J_{C-H} \sim 180$ Hz) for an aziridinium imide structure (see above). We therefore assign the diazetidine structure to **5**. These reactions are shown in Scheme IV.

We next turned to MeOH as solvent. 2,5-Dimethyl-2,4-hexadiene gave a 1:20 mixture of two products, both of which contain 1 mol of MeOH. The major isomer, **7**, comes from addition of MeOH at the 5-position while the minor product, **8**, has added MeOH at the 3-position (Scheme V) (see Experimental Section for spectroscopic details). The structure of the major trapping product is analogous to that suggested for the acetate product when PTAD is generated in situ by $Pb(OAc)_4$ oxidation.[27] (*Z,Z*)-2,4-Hexadiene reacts with PTAD in MeOH to give two MeOH adducts together with 5% of the unexpected trans-Diels–Alder product (**3**). The major MeOH adduct (**9**, 75%) comes from

(38) Gollnick, K.; Griesbeck, A. *Tetrahedron* **1984**, *40*, 3235.

Scheme VI



trapping at the 3-position while the minor isomer **10** has the methoxy group at the 5-position. (*Z,E*)-2,4-Hexadiene gives 87% of the normal trans-Diels–Alder adduct (**3**) together with 13% of three isomeric MeOH adducts. The major MeOH adduct (**11**, approximately 60%) has the methoxy group at the 3-position and *E* stereochemistry around the double bond. The remaining 40% of the MeOH adducts consist of approximately equal amounts of **9** and **10**. In the reaction of $^1O_2$ or PTAD with 1,2-disubstituted olefins to give the ene product, it is well established that *Z* isomers react faster than the *E* isomers.[5] In this case PTAD also attacks the *Z* double bond preferentially. The presence of DA products in the above reactions is not an artifact of adding PTAD as a solution in CH_2Cl_2, since addition of solid PTAD to the dienes in MeOH gave the same ratios. For (*E,E*)-2,4-hexadiene and 1,3-butadiene, we were unable to detect any MeOH adducts (<0.05% by GC) and only the Diels–Alder adducts with the usual stereochemistry were observed.

In order to test whether intermediates **4** and **5** were precursors for the MeOH adducts, we carried out the reaction in $CDCl_3$ at low temperature and added a small amount of CD_3OD as a trap. NMR clearly shows that **4** is unaffected by CD_3OD while **5** is slowly (half-life ~ 10 min at −40 °C) trapped to give **7** and **8** in approximately the same ratio as when MeOH was used as solvent.

We also briefly investigated the reaction of *cis*- and *trans*-2-butene and 2-methylpropene (isobutene) with PTAD in CH_2Cl_2 and MeOH. We have previously shown that the butenes cleanly give the ene product in CH_2Cl_2[12,39] and that there probably is an intermediate with an AI structure along the reaction coordinate. In MeOH, all three butenes give MeOH adducts when PTAD is added (Scheme VI). 2-Methylpropene gives ~30% ene product and ~70% of a single MeOH adduct, **12**, while *cis*- and *trans*-2-butene give ~15% ene product and ~85% of stereospecific MeOH adducts, **13** and **14**, respectively (Scheme VI). NMR clearly shows that the *cis*-2-butene adduct **13** is different from the *trans*-2-butene adduct **14**.[40] We believe that the stereochemistries of **13** and **14** are threo and erythro, respectively, but the spectral data are insufficient to make this assignment with certainty. The formation of these adducts is further evidence for an intermediate in the ene reaction of PTAD with olefins; the

(39) The reaction between MeTAD and *cis*- and *trans*-2-butene has been reported earlier: Pirkle, W. H.; Stickler, J. C. *J. Chem. Soc., Chem. Commun.* **1967**, 760.

(40) GC analysis showed that there is a small amount (1–2%) of the "other" MeOH adduct from *cis*- and *trans*-2-butene (i.e., 1–2% of **14** in the reaction of *cis*-2-butene and 1–2% of **13** in the reaction of *trans*-2-butene). However, we were unable to obtain sufficient separation by GC of *cis*- and *trans*-2-butene to quantitatively determine the isomeric purity of our olefins. We believe that the presence of a few percent of the "other" isomer is due to isomeric impurity of our 2-butenes.

Scheme VII

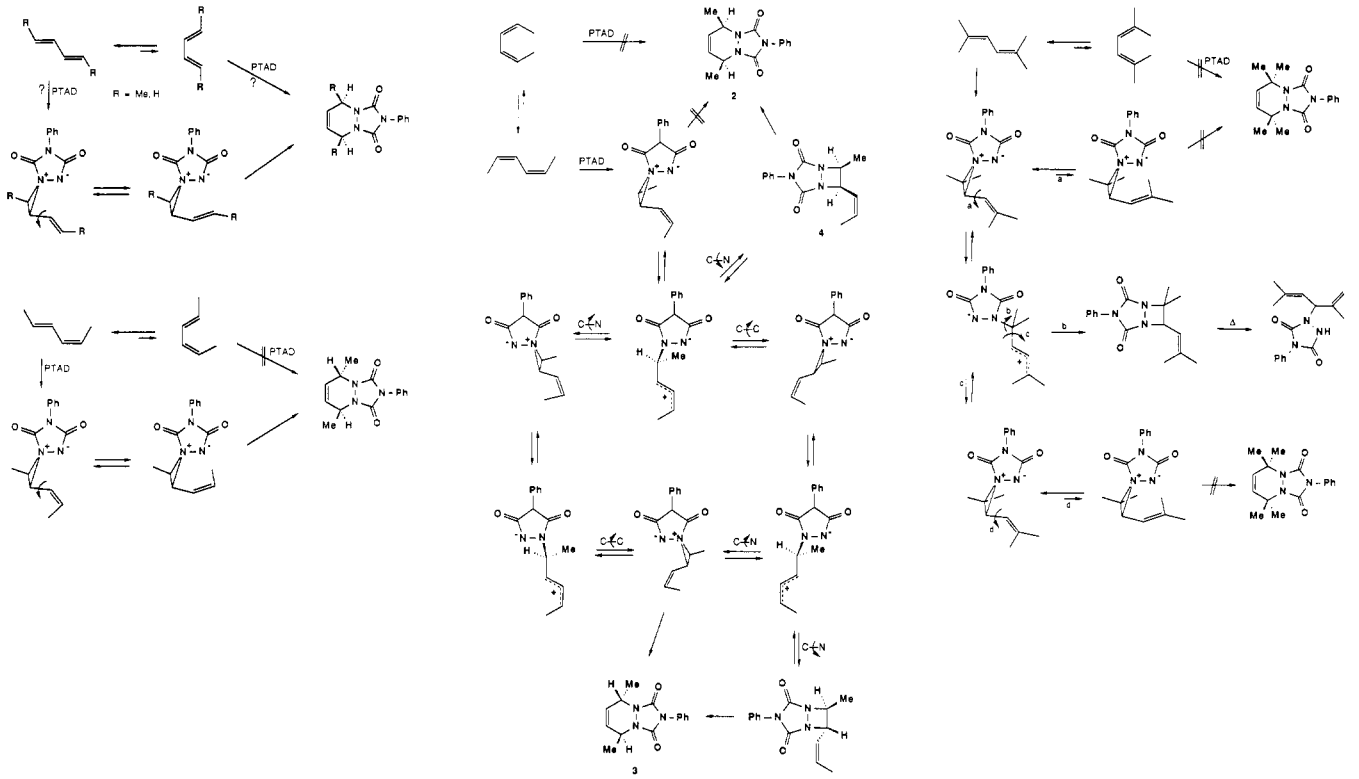


Table I. Relative Rates of Disappearance of Diene[a]

compd	$k_{rel}(CH_2Cl_2)$	k_{rel}(MeOH)
(*Z*,*Z*)-2,4-hexadiene	1	1
(*Z*,*E*)-2,4-hexadiene	6.0 ± 1.1	6.1 ± 1.6
(*Z*,*E*)-2,4-hexadiene	15.2 ± 1.9[b]	
(*E*,*E*)-2,4-hexadiene	>600	

[a] Error limits are one standard deviation. At 24 °C unless otherwise indicated. [b] At −30 °C.

formation of different products from *cis*- and *trans*-2-butene rules out an open zwitterionic intermediate with a long enough lifetime for rotational equilibration. However, it is consistent with the intermediacy of a structurally rigid aziridinium imide, as proposed previously.[12] An attempt to observe an intermediate by low-temperature NMR in $CDCl_3$ proved unsuccessful; the reaction proceeds directly to the ene product at approximately −25 °C without any observable intermediates. We also attempted to observe the reaction between 2,3-dimethyl-2-butene and PTAD, but this reaction is so fast (a few seconds at −80 °C) that we were unable to follow it by NMR.

The relative rates for disappearance of diene were measured by competition experiments. Assuming that the dienes are removed by a second-order process[41] (first order in both diene and PTAD), the relative rates shown in Table I were obtained.

Discussion

The novel results of these reactions are the nonstereospecificity of the reaction with (*Z*,*Z*)-hexadiene and the formation of methanol adducts from several of the substrates. The formation of MeOH adducts in the diene reactions clearly points to a polar intermediate.[43] Similar solvent adducts have often been observed with singlet oxygen and hindered dienes and indenes and have been interpreted as arising from perepoxides or zwitterions.[44] It is significant that we observe MeOH adducts even for (*Z*,*E*)-2,4-hexadiene, which yields only stereospecific DA product. This indicates that this isomer reacts at least partly by the same pathway as (*Z*,*Z*)-2,4-hexadiene. The intermediate could be either an open zwitterion or an aziridinium imide (or both).

There is always the possibility that a change in external parameters (e.g., solvent) can change the preferred reaction pathway.[45] Although a more polar solvent should favor reaction via a zwitterionic intermediate over a concerted reaction, we note that the use of acetonitrile as a solvent instead of CH_2Cl_2 has very little influence on the observed products (e.g., ca. the same ratio of **2** to **3** with (*Z*,*Z*)-2,4-hexadiene and no loss of stereochemistry with (*Z*,*E*)-2,4-hexadiene). The relative rate of reaction of (*Z*,*Z*)- and (*Z*,*E*)-2,4-hexadiene is also insensitive to a solvent change from CH_2Cl_2 to MeOH (Table I).

There are several possible explanations for the formation of the trans-DA adduct as the major product from (*Z*,*Z*)-2,4-hexadiene. Since this adduct is already formed at −55 °C, the intermediate that causes the loss of stereochemistry has already disappeared at this temperature. One mechanism could be that PTAD causes (*Z*,*Z*)-2,4-hexadiene to isomerize to the *Z*,*E* isomer, which then is trapped to give the trans-Diels–Alder adduct. The isomerization would compete with the formation of intermediate **4** (which gives

(41) Since (*Z*,*Z*)- and (*Z*,*E*)-2,4-hexadiene form the same DA product, the relative rates had to be measured by observing the disappearance of diene. Assuming that both dienes are removed by second-order kinetics,[5a,8a,24,42] first-order in both PTAD and diene, we get $-d[ZZ]/dt = k_1[ZZ][PTAD]$ and $-d[ZE]/dt = k_2[ZE][PTAD]$. This gives $d[ZZ]/d[ZE] = k_1/k_2 \times [ZZ]/[ZE] \rightarrow \Rightarrow \ln [ZZ]/[ZZ]_0 = k_1/k_2 \times \ln [ZE]/[ZE]_0$. The relative concentrations were measured by GC using heptane as an internal standard. The above kinetic assumption holds both for an irreversible reaction and for a reaction that occurs via a reversibly formed intermediate (using the steady-state approximation).

(42) Franzus, B. *J. Org. Chem.* **1963**, *28*, 2954.

(43) It should be noted that the terms "zwitterionic" and "diradical" refer to limiting Lewis structures and that real intermediates can have various degrees of zwitterionic or diradical character depending on the specific system and experimental conditions. We prefer to view the intermediates in the present discussion as having largely zwitterionic character based on the structure of the trapping products.

(44) (a) Manring, L. E.; Kanner, R. C.; Foote, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 4707. (b) Manring, L. E.; Foote, C. S. *J. Am. Chem. Soc.* **1983**, *105*, 4710. (c) Zhang, J.; Foote, C. S. *Tetrahedron Lett.* **1986**, *27*, 6153. (d) Burns, P. A.; Foote, C. S. *J. Am. Chem. Soc.* **1974**, *96*, 4339. (e) Fenical, W.; Kearns, D. R.; Radlick, P. *J. Am. Chem. Soc.* **1969**, *91*, 2655, 3396, 7771. (f) Hatsui, T.; Takeshita, H. *Bull. Soc. Chem. Jpn.* **1980**, *53*, 2655. (g) Hasty, N. M.; Kearns, D. R. *J. Am. Chem. Soc.* **1973**, *95*, 3380. (h) Gollnick, K.; Kuhn, H.-J. In *Singlet Oxygen*; Wasserman, H. H., Murray, R. W., Eds.; Academic: New York, 1979.

(45) For a discussion, see: Yamaguchi, K.; Ikeda, Y.; Fueno, T. *Tetrahedron* **1985**, *41*, 2099.

Table II. Energy Differences between Planar Cisoid and Transoid Conformations Calculated by MM2

compd	ΔE, kcal/mol
1,3-butadiene	2.6
(*E*,*E*)-2,4-hexadiene	2.8
(*Z*,*E*)-2,4-hexadiene	5.9
(*Z*,*Z*)-2,4-hexadiene	11.5
2,5-dimethyl-2,4-hexadiene	12.9

the cis-Diels–Alder adduct **2** upon warming). There are three arguments against this mechanism: (1) There is no detectable isomerization of (*Z*,*Z*)-2,4-hexadiene during the reaction. The relative rates in Table I show that the *Z*,*E* isomer reacts only 6 times faster than the *Z*,*Z* isomer, and we would have been able to detect even a few percent isomerization. (2) There is little solvent effect on the formation of the trans-Diels–Alder adduct **3** and **4**, and it is unlikely that two competing pathways should be equally sensitive to a change in solvent. (3) MeOH trapping shows that the reaction of (*Z*,*E*)-2,4-hexadiene goes through an intermediate similar to that from the *Z*,*Z* isomer. We therefore conclude that both the trans-DA adduct and **4** come from an earlier intermediate, a zwitterion or an aziridinium imide.

It is well-known that rotation around an allylic cation has a substantial barrier (~22 kcal/mol),[46] so that simple rotation in a zwitterion should not cause loss of stereochemistry around one of the original double bonds at −55 °C. An allylic radical would also be expected to have a high barrier to rotation.[47] The aziridinium imide would only be able to rotate around the C_3–C_4 single bond, and that rotation can lead only to the cis-Diels–Alder adduct. Therefore *neither* of these two intermediates *alone* can explain the loss of stereochemistry required for the formation of trans-adduct **3**. However, equilibration between them would provide a mechanism in which rotation around single bonds could account for the stereochemistry.

We propose the following reaction scheme (Scheme VII). The dienes exist in an equilibrium between an s-trans and s-cis conformation, which may or may not be planar. The following discussion assumes for simplicity that the s-cis conformation is planar, but the same qualitative arguments can be used if it is gauche.[48] 1,3-Butadiene and (*E*,*E*)-2,4-hexadiene have a fairly small energy difference between the s-trans and s-cis conformations (Table II) and they could react directly from the s-cis conformation to give the observed DA products without any intermediate(s). However, they could also react via an intermediate, as will be discussed in more detail later.

For (*Z*,*E*)-, (*Z*,*Z*)-, and 2,5-dimethyl-2,4-hexadiene, the s-cis conformation is further destabilized by steric interaction of the methyl group(s) on the *Z* olefin, and we suggest that the favored reaction is formation of an aziridinium imide. The C_2 center becomes hybridized between sp^2 and sp^3 and the energy difference between s-cis and s-trans conformations becomes less than in the starting diene. Rotation around the C_3–C_4 single bond to a near-planar conformation allows the *Z*,*E* AI to rearrange to the observed DA product with the methyl groups trans. This rearrangement competes with solvent trapping of the AI in MeOH. An alternative mechanism where (*Z*,*E*)-2,4-hexadiene reacts via two competing pathways, a concerted reaction to the DA product and formation of an aziridinium imide, is less likely since the relative disappearance rates of *Z*,*Z* and *Z*,*E* dienes are the same in both CH_2Cl_2 and MeOH, and these two reaction modes would be expected to differ in solvent dependence, as discussed above.

The same rotation/rearrangement for (*Z*,*Z*)- and 2,5-dimethyl-2,4-hexadiene is disfavored relative to the *Z*,*E* isomer because of the larger steric repulsion caused by the two methyl groups in the s-cis conformation. The opening of the AI to a zwitterion now becomes the favored reaction mode. Either an AI or a zwitterion can account for the trapping products observed in MeOH. The open zwitterion is expected to have almost free rotation around the C_2–C_3 bond and the C_2–N bond. Rotation around these bonds can lead to either a diazetidine or to a new aziridinium imide with trans stereochemistry around the three-membered ring as shown in Scheme VII. This aziridinium imide is identical with the one proposed from (*Z*,*E*)-2,4-hexadiene and should lead to the trans-DA product, as observed. As illustrated in Scheme VII, an alternative diazetidine with the trans stereochemistry around the four-membered ring should also be formed. However, this *trans*-diazetidine would have a much lower barrier for attaining a near-planar conformation than the *cis*-diazetidine **4**, and therefore rearranges to **3** with a low activation barrier. This mechanism rationalizes the observation of only the cis isomer of diazetidine **4**.

We believe that the AI rather than the zwitterion is the first-formed intermediate, since we are unable to detect any loss of stereochemistry of the Diels–Alder adduct from (*Z*,*E*)-2,4-hexadiene. Rotation around the C_2–C_3 single bond in the open zwitterion would be expected to have a very low barrier (~1 kcal/mol), and some loss of stereochemistry would be expected if it were formed first. The open zwitterion probably has a transoid conformation[49] and would therefore be unable to form a DA product, which would have a trans double bond in the six-membered ring.

This mechanism accounts for the lack of a solvent effect on the ratio of trans- to cis-DA product observed from the (*Z*,*Z*)-2,4-hexadiene. The *direction* of the rotation, which should be very solvent independent, determines what product is formed.

The diazetidine **4** is fairly stable but can assume a cisoid conformation upon warming, from which it can rearrange (stereospecifically) to the cis-DA product. 2,5-Dimethyl-2,4-hexadiene has two methyl groups at the terminal carbon, and rotation of the resulting AI (there is only one syn isomer possible) to an s-cis conformation should be energetically impossible, and no DA adduct results.[50] The diazetidine **5** is thus formed quantitatively.[51] However, the open zwitterion from 2,5-dimethyl-2,4-hexadiene is further stabilized over that from (*Z*,*Z*)-2,4-hexadiene by the additional methyl group, and there could well be an equilibrium between the diazetidine and the open zwitterionic form. This would explain the trapping by MeOH at −50 °C and the much lower stability of **5** relative to **4**. The stability of diazetidines toward ring opening is very dependent on the substitution.[52] In some cases, the diazetidine is recovered unchanged after refluxing in acetone for 22 h, while in other systems the diazetidine polymerizes below 0 °C.[24] Acid-catalyzed ring opening with MeOH or H_2O has also been reported.[19,20] Diazetidines from vinyl ethers and azodicarboxyl compounds are known to rearrange to oxadiazines at room temperature.[20] The rearrangement of vinylcyclobutanes from dienes and tetra-

(46) (a) Bollinger, J. M.; Brinich, J. M.; Olah, G. A. *J. Am. Chem. Soc.* **1970**, *92*, 4025, structure **37**. (b) Deno, N. C.; Haddon, R. C.; Nowak, E. N. *J. Am. Chem. Soc.* **1970**, *92*, 6691.

(47) For the parent allyl radical the barrier is 15.7 kcal/mol and for the 1,1-dimethyl-substituted case, >14 kcal/mol. (a) Korth, H.-G.; Trill, H.; Sustmann, R. *J. Am. Chem. Soc.* **1981**, *103*, 4483. (b) Krusic, P. J.; Meakin, P.; Smart, B. E. *J. Am. Chem. Soc.* **1974**, *96*, 6211.

(48) For the parent 1,3-butadiene there is some controversy as to whether the cisoid conformation is planar or gauche. For 1,3-butadienes with substituents *Z* on the terminal carbon(s), the cisoid conformation is probably gauche; see, e.g., Figure 1. For a recent discussion, see: Squillacote, M. E.; Semple, T. C.; Mui, P. W. *J. Am. Chem. Soc.* **1985**, *107*, 6842 and references therein.

(49) The dienes exist largely in the transoid conformation and the zwitterion(s) should thus be formed with a transoid conformation around the central C–C bond. The observation that only products with the *E* stereochemistry at the double bond (**7** and **10**) are formed from MeOH trapping at C_5 is consistent with this assumption.

(50) When the 2,5-dimethyl-2,4-hexadiene system is held in a fixed cisoid conformation by a cyclobutane ring between the 3 and 4 position, only the DA product is formed. Levek, T. J.; Kiefer, E. F. *J. Am. Chem. Soc.* **1976**, *98*, 1875.

(51) The mechanism is here discussed as if the AI is the first-formed intermediate, based on analogy with the *Z*,*Z* isomer. However, it is possible that an open zwitterion is the first intermediate in this case (and that this leads directly to the diazetidine). The open zwitterion should be stabilized more than the AI by the additional two methyl groups and may become lower in energy. The preference for trapping at the C_5 position by MeOH is consistent with the open zwitterion being lower in energy.

(52) For a review of diazetidine chemistry, see: Richter, R.; Ulrich, H. In *Small Ring Heterocycles, Part 2* **1983**, 443.

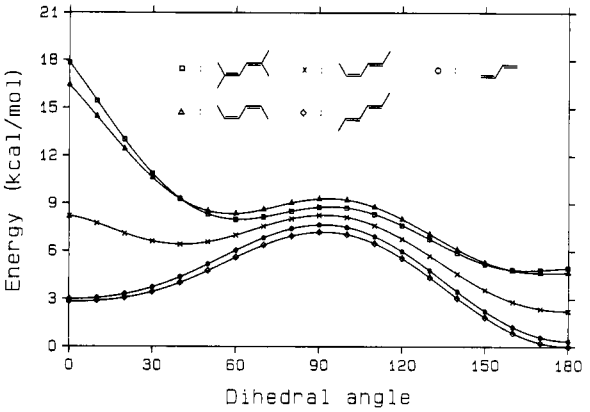


Figure 1. Results of MM2 calculation (see text) on dienes.

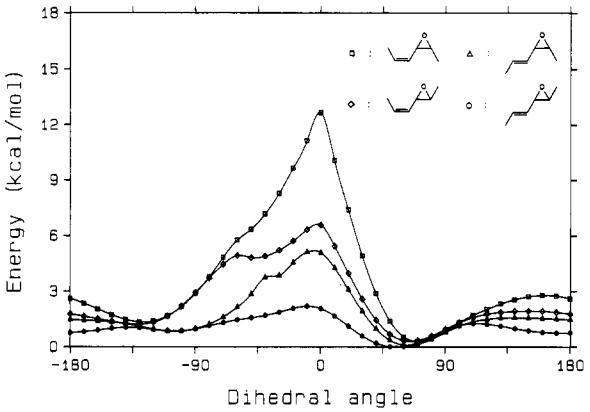


Figure 2. Results of MM2 calculation (see text) on epoxides.

cyanoethylene to cyclohexenes has also been reported.[20,53]

The formation of the ene product from this diazetidine in the case of 2,5-dimethyl-2,4-hexadiene, in contrast to (*Z*,*Z*)-2,4-hexadiene, where the DA product is formed, is rationalized as follows. Breaking the C_2–N_1 bond in diazetidine **4** (leading to the DA product) would give a disubstituted allylic cation, while breaking the C_3–N_2 bond (leading an ene product) would give a secondary carbonium ion. The same bond disconnection for diazetidine **5** would lead to a trisubstituted allylic cation or a tertiary carbonium ion, respectively. Since the stabilization energy increase on going from a secondary to a tertiary carbonium ion probably is larger than that for going from a disubstituted to a trisubstituted allylic cation, breaking the C_3–N_2 bond with consequent formation of the ene product should be more favorable for **5** than **4**.

The above discussion is only valid for the AI isomers that have the imide nitrogen syn to the olefin. Anti-AI isomers should not be able to give DA products directly because the imide nitrogen is on the wrong side. These isomers then have two options: ring opening to the zwitterion or dissociation to the starting diene and PTAD. Since (*Z*,*E*)-2,4-hexadiene forms a polar intermediate (MeOH trapping) but does not lose stereochemistry, we rule out opening to the zwitterion and conclude that the AI's are formed reversibly.[12] The AI's should be structurally rigid, and no loss of stereochemistry is expected if they are formed reversibly.

To further test these ideas, we carried out force-field calculations using Allinger's MM2 program.[54] For the aziridinium imide structure, we had to define some parameters (see Experimental Section for details). Since the validity of some of these assumptions is difficult to test, we also carried out MM2 calculations

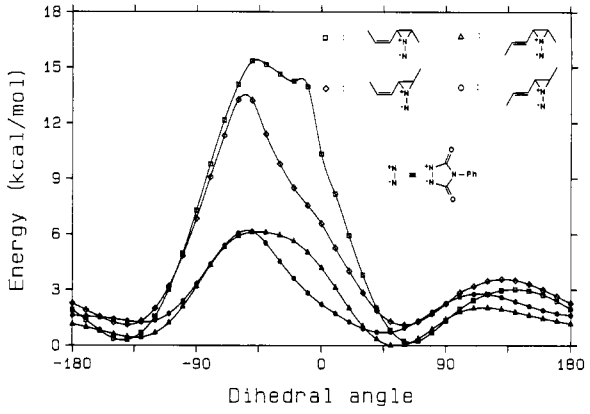


Figure 3. Results of MM2 calculation (see text) on aziridinium imides.

Table III. Energy Differences (kcal/mol) between Cisoid Conformation (θ = 0°) and the Global Minimum Calculated by MM2 for the Structures in Figures 2 and 3

structure[a]	epoxide	aziridinium imide
Z,*Z*	12.4	10.1
Z,*E*	6.2	5.5
E,*Z*	5.0	4.2
E,*E*	2.1	1.5

[a] The first label refers to the stereochemistry of the double bond, and the second to that around the three-membered ring.

on the corresponding compounds where an epoxide group replaces the AI moiety. In Figures 1–3 are shown the calculated steric energies of the dienes, the monoepoxides, and the aziridinium imides as a function of rotational angle around the central C–C bond. The zero point for the dihedral angle is the cisoid conformation, and negative angles refer to conformations where the terminal olefinic carbon is on the same side as the epoxide or AI. Some relative conformational energies are given in Tables II and III. The positions of the minima and the overall features are very similar for the AI's and epoxides. The two energy curves differ mainly for angles in the range $-100° < \theta < -20°$, where the Me group is close to the imide N and where the AI structure is higher in energy due to the steric interaction. The relative energy differences for cisoid conformations are very similar for the two systems, as seen in Table III. The AI's with the *Z* stereochemistry around the three-membered ring are slightly lower in energy than those with the *E* stereochemistry. Although one should not put too much emphasis on small differences, this order is consistent with the observation that the major MeOH trapping product **11** from (*Z*,*E*)-2,4-hexadiene has *E* stereochemistry of the olefinic bond.

We postulated above that the parent 1,3-butadiene and (*E*,*E*)-2,4-hexadiene could react with PTAD either directly from the s-cis conformation or via an aziridinium imide intermediate. (*Z*,*E*)-2,4-Hexadiene gives approximately 12% trapping product in MeOH, but (*E*,*E*)-2,4-hexadiene gives less than 0.05%. If an AI is formed from (*E*,*E*)-2,4-hexadiene, it must therefore have a much shorter lifetime than that from (*Z*,*E*)-2,4-hexadiene. If the difference in activation energy for the AI to DA rearrangement is assumed to be close to the energy difference for obtaining a near-planar conformation, we would expect that the AI from the *E*,*E* isomer would rearrange to the DA product ~100–1000 times faster than the AI from the *Z*,*E*, based on our MM2 calculations (Table III; activation energy difference ~2.7–4.0 kcal/mol). If rearrangement and MeOH trapping are the only paths by which the AI's can disappear, we would expect 0.14–0.014% MeOH trapping product from (*E*,*E*)-2,4-hexadiene. These numbers are based on relative energies calculated by MM2 and are too close to the experimental detection limits to give a definite answer.[55]

(53) (a) Eisch, J. J.; Husk, G. R. *J. Org. Chem.* **1966**, *31*, 589. (b) Drexler, J.; Lindermayer, R.; Hassan, M. A.; Sauer, J. *Tetrahedron Lett.* **1985**, 2555, 2559. (c) Kataoka, F.; Shimizu, N.; Nishida, S. *J. Am. Chem. Soc.* **1980**, *102*, 711.

(54) (a) Allinger, N. L.; Yuh, Y. *QCPE* **1980**, *12*, 395. (b) Burkert, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington, DC, 1982.

(55) Preliminary results for the reaction of the three 2,4-hexadiene isomers with singlet oxygen indicate products analogous to those obtained with PTAD in the present study. With singlet oxygen, MeOH trapping products are obtained for all three hexadiene isomers: O'Shea, K.; Foote, C. S., in progress.

From the competition experiments, we know that (*Z,E*)-2,4-hexadiene reacts approximately 6 times faster than the *Z,Z* isomer but that the *E,E* isomer reacts at least 600 times faster. The $\Delta G°$ values for the 2,4-hexadienes have been measured[56] to be *E,E*:*Z,E*:*Z,Z* = 0.0:0.43:1.63 kcal/mol. The difference in energy of the AI's from the three hexadienes (stereochemistry around the three-membered ring and the terminal olefin) would be expected to be very small (MM2 calculations suggest values <1.0 kcal/mol). Based on the Bell–Evans–Polanyi principle,[57] the relative reaction rates for the first step should be related to the difference in energy between the starting dienes and the AI's (the more exothermic, the faster the reaction). If all three 2,4-hexadienes first form an AI which rearranges to the DA products in a subsequent step, we would expect all three isomers to have approximately the same rate constant for the first step (within a factor of 10, the *Z,Z* isomer being the fastest).

For the second step, rearrangement of the AI to DA product, the relative rates using the above assumption would be *Z,E*:*E,E* $\sim$ 1:(10^2–10^3). If the *Z,Z* olefin also gave the DA product directly from the first-formed AI, this isomer should react $\sim 10^{-3}$ times as fast as the *Z,E* isomer (Table III shows that the difference in activation energy $\sim$4.6–5.9 kcal/mol). However, the *Z,Z* isomer probably reacts via an open zwitterionic form, as argued above. If the first step is reversible and the second step rate determining, the observed relative rates of disappearance of diene (1:6:>600) are consistent with the formation of an AI intermediate for all three dienes.

An alternative mechanism is that (*E,E*)-2,4-hexadiene and 1,3-butadiene react directly from a s-cis conformation without formation of any intermediate(s) (i.e., a "normal" concerted DA reaction). (*E,E*)-2,4-Hexadiene has a smaller energy difference for assuming a s-cis conformation than the two other isomers ($\sim$3.1–3.3 kcal/mol, Table I), and a one-step mechanism for this isomer could equally well explain the kinetic data. The relative rates of disappearance of diene therefore cannot be used to distinguish between the two alternatives.

Conclusion

The present study shows that all three reaction modes, [4 + 2], [2 + 2], and ene, can be observed with simple dienes and PTAD. We propose a mechanism that can account for all the observed products and relative reaction rates. In this mechanism, the rotational barrier for assuming a planar conformation determines what product is observed.

For dienes with at least one *Z* methyl group, the reaction proceeds through one or more intermediates that can be trapped by MeOH. For the parent diene and (*E,E*)-2,4-hexadiene, either a one- or a two-step reaction mechanism is consistent with the experimental data. The formation of diazetidines from vinyl ethers is usually rationalized as proceeding via an open zwitterion,[23,24] while the aziridinium imide has been postulated as an intermediate in the ene reaction.[12,13,15,58] A homotropylium zwitterion intermediate has also been postulated[8k] in the reaction of PTAD with cyclooctatetraene, which gives the Diels–Alder product arising from the open form of cyclooctatetraene at low temperatures. We suggest that the aziridinium imide can play a role in the formation of all three types of products, diazetidines, ene, and Diels–Alder. Although the AI probably is the first-formed intermediate with simple dienes, an open zwitterion is probably only a few kcal/mol higher in energy.[59] The relative ordering in other systems will probably depend on the substituents. Finally, numerous reports in the literature suggest that the mechanism proposed in this paper may also be applicable to other electrophilic reagents such as singlet oxygen[10,28,37,44,55] and polycyanoethylenes.[63]

After we completed the manuscript, we were informed by Prof. E. Clennan of results with *tert*-butoxylated butadienes and PTAD that strikingly parallel those reported here, including the observation of intermediates at low temperature.[64]

Experimental Section

Melting points are uncorrected. NMR spectra were obtained at 500 MHz for ^1H and 125 MHz for ^{13}C, using $CDCl_3$ or $CDCl_3/CFCl_3$ mixtures (low temperature) as solvent, except when noted otherwise. Chemical shifts are given in ppm (δ) relative to internal TMS. Assignment of the number of directly bound hydrogens to carbons was done by using the INEPT pulse sequence[65] or from the multiplicity of the undecoupled spectrum. $^1J_{C-H}$ values (in hertz) were determined from ^{13}C spectra obtained with a gated ^1H decoupling procedure (^1H decoupled during relaxation delay to build up NOE, but turned off during acquisition of the FID).

(*Z,Z*)-, (*Z,E*)-, and (*E,E*)-2,4-hexadiene were obtained from Wiley Organics in isomeric purities >99%. The absolute isomeric purity was determined by capillary GC. PTAD was synthesized by oxidation of 4-phenylurazole (Aldrich) with *tert*-butyl hypochlorite[66] according to a literature procedure.[29]

General Procedure for the Reactions. A solution of PTAD in CH_2Cl_2 was added dropwise to a stirred solution of the diene in either CH_2Cl_2 or MeOH at the desired temperature. After the characteristic red color of PTAD had disappeared, the solutions were stirred an additional 1–2 h. The solvent was removed under reduced pressure, and the products were separated by column chromatography on silica gel using mixtures of ethyl acetate and hexane as eluent and recrystallized from ethyl acetate/hexane mixtures. Product ratios were determined by NMR and capillary GC.

Diels–Alder adduct 1 from 1,3-butadiene and PTAD:[30] mp = 158–159 °C; exact mass calculated for $C_{12}H_{11}N_3O_2$ 229.0851, found 229.0838;

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(58) It should be noted that a clear distinction between an AI and a open zwitterion is not always possible. Consider a series of olefins ranging from the parent (symmetric) compound to one unsymmetrically mono- or disubstituted at one of the olefinic carbons, with the substituents having different abilities to stabilize a cationic center. Let us assume that the parent system (e.g., 2,3-dimethyl-2-butene) forms an AI and that an open zwitterion is highr in energy. For a substituted olefin (e.g., 2-methoxy-3-methyl-2-butene), the zwitterion with a positive charge on C_2 is lower in energy than the zwitterion with the charge on C_3. The AI in this case is probably unsymmetrical, with the $N-C_2$ bond being longer and weaker than the $N-C_3$ bond. The barrier for opening the AI to the zwitterionic structure should be smaller than for the parent compound. For a system where one of the zwitterionic structures is substantially favored over the other (e.g., 2,3-dimethoxy-2-methyl-2-propene), the AI should be very unsymmetrical, and the barrier for opening to a zwitterion may disappear. In this case there is only one intermediate with "open" zwitterionic structure. See also ref 21.

(59) The direct formation of an aziridinium imide from olefins and azodicarboxyl compounds is probably only possible when the stereochemistry of the N=N bond is *Z*. For compounds like dialkyl azodicarboxylates, the favored configuration is *E*. These compounds are known to undergo the same reactions as the triazolinediones, where the N=N bond is locked in a *Z* configuration, but at a slower rate.[5] The ene reaction for acyclic azodicarboxyl compounds is believed to be concerted,[8b,c,39,60] in contrast to the reaction with *Z* azodicarboxyl compounds like PTAD.[7,11,12] The irradiation of azodicarboxyl compounds having the *E* stereochemistry of the N=N bond can cause an isomerization to the *Z* isomer. It is often observed that irradiation results in a much faster reaction[29a,61] and, in some cases, a shift in the observed products.[62] This could be because the *Z* isomer is higher in energy (and thus more reactive) than the *E* isomer. We note that it could also be due to a change in mechanism, where only the *Z* isomer is able to form an aziridinium imide. The *E* isomer would have to react via a concerted or open zwitterionic/diradical mechanism. See ref 7 and 19 for relevant discussions.

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^{1}H NMR 7.35–7.54 (m, 5 H), 5.92 (s, 2 H), 4.15 (s, 4 H); ^{13}C NMR 152.4, 131.2, 129.1, 128.1, 125.4, 120.8, 43.4.

Diels–Alder adduct 2 from (*E*,*E*)-2,4-hexadiene and PTAD:[30] mp = 135–136 °C; exact mass calculated for $C_{14}H_{15}N_3O_2$ 257.1164, found 257.1155; ^{1}H NMR 7.32–7.54 (m, 5 H), 5.75 (s, 2 H), 4.45 (q, J = 6.6, 2 H), 1.51 (d, J = 6.6, 6 H); ^{13}C NMR ($^1J_{C-H}$ coupling constants were obtained in acetone-d_6) 152.1, 131.4, 129.0, 127.9, 126.5, 125.4, 50.6 (CH, $^1J_{C-H}$ = 145), 19.0 (CH$_3$, $^1J_{C-H}$ = 128).

Diels–Alder adduct 3 from (*Z*,*E*)-2,4-hexadiene and PTAD:[30] mp = 169.5–170.5 °C; exact mass calculated for $C_{14}H_{15}N_3O_2$ 257.1164, found 257.1173; ^{1}H NMR 7.28–7.56 (m, 5 H), 5.83 (d, J = 2.3, 2 H), 4.56 (dq, J = 2.3, 6.6, 2 H), 1.32 (d, J = 6.6, 6 H); ^{13}C NMR 152.4, 131.3, 129.0, 127.9, 126.0, 125.2, 50.1, 16.6; IR (CHCl$_3$, cm^{-1}) 1601, 1609, 1710, 1737 (sh).

The Diels–Alder adducts **2** and **3** were converted to their corresponding epoxides by heating (50 °C) with a 10-fold excess of MCPBA in CHCl$_3$ for 10 h. The CHCl$_3$ was extracted with an aqueous NaHCO$_3$ solution to remove the benzoic acid and dried with MgSO$_4$.

Major epoxide from *cis*-dimethyl Diels–Alder adduct 2: ^{1}H NMR 7.25–7.40 (m, 5 H), 4.54 (q, J = 6.8, 2 H), 3.31 (s, 2 H), 1.56 (d, J = 6.8, 6 H).

Epoxide from *trans*-dimethyl Diels–Alder adduct 3: ^{1}H NMR 7.25–7.40 (m, 5 H), 4.63 (m, 1 H), 4.48 (m, 1 H), 3.51 (m, 1 H), 3.36 (m, 1 H), 1.44 (d, J = 6.4, 3 H), 1.34 (d, J = 6.6, 3 H).

Intermediate 4 was generated by dropwise addition of a solution of PTAD in CH$_2$Cl$_2$ to a stirred solution of (*Z*,*Z*)-2,4-hexadiene in CH$_2$Cl$_2$ at −45 °C. After the characteristic red color of PTAD has disappeared, the CH$_2$Cl$_2$ was removed under high vacuum at 0 °C. The solid residue was redissolved in deuteriated solvent and the NMR was obtained at 0 °C. The solution contains approximately a 1:4 mixture of **4**:**3** under these conditions. Spectral data for **4** were obtained by subtracting the spectrum of **3** from the mixture: ^{1}H NMR 5.80 (dd with fine structure observed, partly buried under resonances from **3**, J = 11.8, 6.1, 1 H), 5.63 (dd, J = 11.8, 4.8, 1 H), 5.11 (distorted, J = 6.0, 1 H), 4.68 (quintet, J = 6.7, 1 H), 1.54 (dd, J = 7.0, 1.2, 1 H), 1.23 (probably dd, but partly buried under the resonance from **3**, two lines observed with J = 1.3); ^{13}C NMR ($^1J_{C-H}$ in acetone-d_6) 154.4, 144.6, 77.9 (CH, $^1J_{C-H}$ = 154), 56.7 (CH, $^1J_{C-H}$ = 143), 20.0 (CH$_3$, $^1J_{C-H}$ = 128), 19.7 (CH$_3$, $^1J_{C-H}$ = 130) (no peaks could be assigned in the region 120–130 ppm because of the resonances from the phenyl groups); IR (CHCl$_3$, cm^{-1}) 1749 (the region 1690–1730 cm^{-1} was obscured by strong absorptions from the Diels–Alder adducts).

Reduction of 4 with NaBH$_4$. A solution of PTAD in CH$_2$Cl$_2$ was added dropwise to a stirred solution of (*Z*,*Z*)-2,4-hexadiene in CH$_2$Cl$_2$ at −45 °C. The solution was warmed to −30 °C and THF was added, keeping the temperature at −30 °C. An excess of NaBH$_4$ was added and the solution was allowed to warm to 0 °C. The reaction was quenched with water, and the excess NaBH$_4$ was destroyed by dropwise addition of acetic acid. The aqueous phase was extracted with CH$_2$Cl$_2$, which was dried with Na$_2$SO$_4$. NMR of the crude mixture showed **3** and a new compound instead of **4**. This compound was stable to heating to 70 °C for >30 min. However, all attempts to isolate the compound resulted in the formation of a white polymeric material.

Intermediate 5 was generated by adding 1 equiv of 2,5-dimethyl-2,4-hexadiene (20 μL) in CDCl$_3$ to a solution of PTAD (25 mg) in CDCl$_3$ at −40 °C in a 10-mm NMR tube. The NMR tube was transferred without warming to a precooled probe and the spectrum was obtained at −40 °C: ^{1}H NMR 7.31–7.63 (m, 5 H), 5.69 (d, J = 10.3, 1 H), 5.38 (dd, J = 10.3, 1.2, 1 H), 1.88 (d, J = 1.1, 3 H), 1.84 (d, J = 1.2, 3 H), 1.60 (s, 3 H), 1.32 (s, 3 H); ^{13}C NMR 150.6, 148.2, 113.4 (CH, $^1J_{C-H}$ = 154), 94.7 (CH, $^1J_{C-H}$ = 153), 66.3 (quaternary C), 26.7 (CH$_3$), 23.5 (CH$_3$), 20.1 (CH$_3$), 18.9 (CH$_3$) (no peaks were assigned in the region 120–130 ppm because of the phenyl group resonances). Intermediate **5** is fairly unstable and some decomposition (~10%) was observed during accumulation of the ^{13}C NMR (3 h).

Ene product 6 from 2,5-dimethyl-2,4-hexadiene and PTAD: mp = 151.5–152.5 °C; exact mass calculated for $C_{16}H_{19}N_3O_2$ 285.1477, found 285.1483; IR (CHCl$_3$, cm^{-1}) 1715, 1607, 1598; ^{1}H NMR 7.83 (bs, 1 H), 7.35–7.54 (m, 5 H), 5.35 (AB, Δδ = 0.059 ppm, J = 9.1, 2 H), 5.07 (s, 1 H), 5.03 (s, 1 H), 1.83 (s, 3 H), 1.78 (s, 3 H), 1.73 (s, 3 H); ^{13}C NMR 153.7, 152.3, 141.4, 139.3, 131.4, 128.9, 127.9, 125.3, 118.1, 114.5, 58.8, 25.7, 20.4, 18.5.

Major MeOH adduct 7 from 2,5-dimethyl-2,4-hexadiene and PTAD: mp = 137–138 °C; no molecular ion observed, exact mass calculated for $C_{17}H_{22}N_3O_3$ (M − CH$_3$OH) 285.1477, found 285.1469; ^{1}H NMR 9.39 (bs, 1 H), 7.35–7.47 (m, 5 H), 5.72 (AB, Δδ = 0.15 ppm, J = 16.2, 2 H), 3.09 (s, 3 H), 1.59 (s, 6 H), 1.19 (s, 6 H); ^{13}C NMR 154.1, 152.7, 136.0, 132.2, 131.1, 129.1, 128.3, 125.9, 74.6, 62.2, 50.4, 25.4, 25.1.

Minor MeOH adduct 8 from 2,5-dimethyl-2,4-hexadiene and PTAD: exact mass calculated for $C_{17}H_{22}N_3O_3$ (M − H) 316.1649, found 316.1661; ^{1}H NMR 8.25 (bs, 1 H), 7.32–7.48 (m, 5 H), 5.09 (d, J = 9.8, 1 H), 4.09 (d, J = 9.8, 1 H), 3.26 (s, 3 H), 1.83 (s, 3 H), 1.74 (s, 3 H), 1.56 (s, 3 H), 1.48 (s, 3 H).

Major MeOH adduct 9 from (*Z*,*Z*)-2,4-hexadiene and PTAD: mp = 137–138 °C; exact mass calculated for $C_{15}H_{19}N_3O_3$ 289.1426, found 289.1433; IR (CHCl$_3$, cm^{-1}) 3358, 1773, 1707, 1503, 1430; ^{1}H NMR 8.76 (bs, 1 H), 7.35–7.50 (m, 5 H), 5.86 (ddq, J = 11.1, 7.1, 0.9, 1 H), 5.29 (ddq, J = 11.1, 9.5, 1.8, 1 H), 4.21 (quintet, J = 6.9, 1 H), 4.12 (ddd, J = 9.5, 6.3, 0.9, 1 H), 3.21 (s, 3 H), 1.69 (dd, J = 7.1, 1.8, 3 H), 1.25 (d, J = 7.0, 3 H); ^{13}C NMR 154.2, 153.8, 132.2, 131.3, 129.3, 128.4, 127.9, 126.2, 77.6, 56.3, 56.2, 14.8, 13.8.

Minor MeOH adduct 10 from (*Z*,*Z*)-2,4-hexadiene and PTAD: mp = 107–109 °C; exact mass calculated for $C_{15}H_{19}N_3O_3$ 289.1426, found 289.1428; ^{1}H NMR 8.20 (bs, 1 H), 7.37–7.48 (m, 5 H), 5.70 (AB, Δδ = 0.04 ppm, J = 16.3, 2 H), 4.87 (sextet, J = 6.5, 1 H), 3.73 (sextet, J = 6.5, 1 H), 3.24 (d, J = 3.6, 3 H), 1.41 (dd, J = 3.7, 3.2, 3 H), 1.21 (dd, J = 3.4, 3.0, 3 H).

Major MeOH adduct 11 from (*Z*,*E*)-2,4-hexadiene and PTAD: exact mass calculated for $C_{15}H_{19}N_3O_3$ 289.1426, found 289.1445; ^{1}H NMR 7.67 (bs, 1 H), 7.34–7.54 (m, 5 H), 5.78 (dq, J = 15.4, 6.5, 1 H), 5.41 (ddq, J = 15.4, 8.3, 1.7, 1 H), 4.32 (dq, J = 6.9, 3.6, 1 H), 3.64 (dd, J = 8.1, 3.2, 1 H), 3.29 (s, 3 H), 1.76 (dd, J = 6.5, 1.4, 3 H), 1.35 (d, J = 6.9, 3 H).

Ene product from *cis*- and *trans*-2-butene with PTAD:[39] mp = 86.5–87.5 °C; exact mass calculated for $C_{12}H_{13}N_3O_2$ 231.1008, found 231.1005; ^{1}H NMR 7.36–7.51 (m, 5 H), 5.88 (m, 1 H), 5.32 (dd, J = 17.3, 0.8, 1 H), 5.26 (dd, J = 10.5, 0.8, 1 H), 4.83 (m, 1 H), 1.38 (d, J = 7.0, 3 H); ^{13}C NMR 154.1, 152.6, 135.1, 131.2, 129.1, 128.2, 125.5, 118.4, 54.3, 16.3.

Ene product from 2-methylpropene with PTAD: mp = 104–105 °C; exact mass calculated for $C_{12}H_{13}N_3O_2$ 231.1008, found 231.0994; ^{1}H NMR 7.37–7.52 (m, 5 H), 4.98 (s, 1 H), 4.96 (s, 1 H), 4.12 (s, 2 H), 1.74 (s, 3 H); ^{13}C NMR 153.5, 152.6, 138.5, 131.3, 129.2, 128.3, 125.6, 115.5, 52.5, 20.0.

MeOH adduct 12 from 2-methylpropene and PTAD: exact mass calculated for $C_{13}H_{17}N_3O_3$ 263.1270, found 263.1274; ^{1}H NMR 7.34–7.53 (m, 5 H), 3.57 (s, 2 H), 3.21 (s, 3 H), 1.24 (s, 6 H); ^{13}C NMR 152.8, 152.1, 131.5, 129.1, 128.1, 125.6, 76.0 (4 °C), 54.8 (CH$_2$), 49.4 (CH$_3$), 21.4 (CH$_3$).

MeOH adduct 13 from *cis*-2-butene and PTAD: exact mass calculated for $C_{13}H_{17}N_3O_3$ 263.1270, found 263.1269; ^{1}H NMR 7.32–7.53 (m, 5 H), 4.22 (dq, J = 7.0, 3.5, 1 H), 3.43 (dq, J = 6.2, 3.5, 1 H), 3.32 (s, 3 H), 1.32 (d, J = 7.0, 3 H), 1.21 (d, J = 6.2, 3 H); ^{13}C NMR 152.9, 152.5, 131.4, 128.9, 127.9, 125.5, 79.0, 56.9, 55.6, 16.2, 15.1.

MeOH adduct 14 from *trans*-2-butene and PTAD: exact mass calculated for $C_{13}H_{17}N_3O_3$ 263.1270, found 263.1254; ^{1}H NMR 7.25–7.53 (m, 5 H), 4.32 (dq, J = 7.0, 3.2, 1 H), 3.72 (dq, J = 6.4, 3.2, 1 H), 3.35 (s, 3 H), 1.28 (d, J = 7.0, 3 H), 1.19 (d, J = 6.4, 3 H); ^{13}C NMR 152.8, 151.4, 131.3, 128.9, 128.0, 125.5, 79.1, 55.9, 54.9, 15.1, 10.8.

Force-field calculations were done with Allinger's MM2 program.[54] The torsional parameters for rotation around the central C–C bond in the dienes (V_1 = 0.96, V_2 = 7.54, V_3 = 1.28 kcal/mol) were chosen so that the rotational energy profile for 1,3-butadiene matched that determined from experimental data.[67] Force-field parameters for the aziridinium imide structure were obtained as follows. The five-membered-ring system was assigned equilibrium bond lengths and angles modeled after the X-ray structure of a similar compound.[68] Force constants for stretching and bending were assigned reasonable values based on comparison with standard MM2 parameters. The torsional parameters were assigned values keeping the ring flat with a substantial barrier to puckering. A lone pair on the outer nitrogen in the plane was used to model the partial negative charge associated with this atom.

The structure and force constants for the three-membered ring in the AI were calculated at the ab initio HF/STO-3G level on a model system ($C_2H_4N_2H_2$), where ethylene serves as a model for the olefin and diimide for the triazoline ring. The singlet oxygen analogue, the perepoxide, has been calculated both at the HF/STO-3G level[70] and at the much better MCSCF/DZ + P level.[71] The structures at the two different levels are slightly different (bond, bond length (HF/STO-3G, Å), bond length (MCSCF/DP + P, Å), (O–O, 1.58, 1.52), (C–C, 1.48, 1.46), (C–O,

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1.45, 1.48)). We assumed that the changes in structure in the AI would be similar, and the HF/STO-3G results were then scaled accordingly. This gave the following stretching parameters (bond, r_0 (Å), force constant (mdyn/Å)): (C–C, 1.470, 5.88), (C–N, 1.520, 5.43), (N–N, 1.553, 1.42). The bending and torsional parameters were modeled after cyclopropane parameters.

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Supplementary Material Available: Listing of all nonstandard parameters used in the force-field calculations (3 pages). Ordering information is given on any current masthead page.

Transition-Metal-Catalyzed Cyclization of Alkynoic Acids to Alkylidene Lactones

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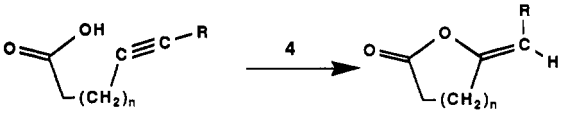
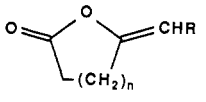
Abstract: Alkynoic acids I–IV can be effectively cyclized to the corresponding exocyclic enol lactones with a new Rh(I) complex, $[(cycphos)RhCl]_2$ (**4**) (cycphos = 1,2-bis(dicyclohexylphosphino)ethane), that we have developed. The high-yield lactonizations can be performed at room temperature, and methylene chloride appears to be the best solvent for the cyclization. Exclusive



I R=H, n=1
II R=CH_3, n=1
III R=Ph, n=1
IV R=H, n=2

formation of *Z*-olefinic isomers was observed, i.e., trans addition of the carboxylate OH across the triple bond. There is also a strong preference for the formation of five- vs six-membered rings in the substituted pentynoic acid systems. Other electron-rich group VIII transition-metal complexes and mercuric salts were tested for catalytic activity under similar reaction conditions and were found to be less effective. The proposed mechanism involves initial OH activation by the metal center followed by nucleophilic attack of carboxylate anion on the metal-coordinated alkyne of the intermediate, and subsequent reductive elimination from the resulting hydrido–vinyl complex releases the lactone product and regenerates the catalyst.

Interest in the chemistry of exocyclic enol lactones **1** has emerged in recent years because of the biological activities of a number of natural products shown to contain this moiety.[1-3] For example, compounds such as obtusilactone (**2**)[4] and cyanobacterin (**3**)[5] are reported to possess cytotoxic and antibiotic properties.



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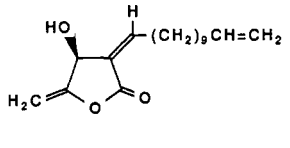

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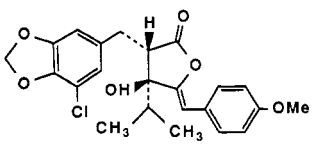

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Due to their ready availability, the cyclization of α,ω-acetylenic acid precursors represents one of the most effective synthetic approaches to these enol lactone systems (eq 1). Indeed, the

(1)

cyclizations of 4-pentynoic acids to alkylidenebutyrolactones catalyzed by conventional Lewis acids such as silver nitrate,[6] mercuric acetate,[2,7a] mercuric trifluoroacetate,[7b-d] and mercuric oxide[3] have been reported. However, the utility of these catalysts

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