Reactions of Phenyltriazolinedione with Alkenes. Stereochemistry of Methanol Adducts to Aziridinium Imide Intermediates

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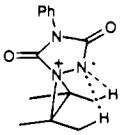
Abstract: The addition of 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) and the stereochemistry of methanol/PTAD adduct formation with *cis*- and *trans*-2-butenes, 1-methylcyclopentene, (*E*)-2-methyl-2-butene-*1,1,1-d*$_3$, and substituted indenes (indene, 2-methylindene, 2,3-dimethylindene) have been investigated. There is no loss of stereochemistry in the addition of MeOH and PTAD to butenes, 1-methylcyclopentene, 2-methyl-2-butene, and indene. However, in methyl-substituted indenes **9** and **14**, loss of stereochemistry at the reaction center is observed. An aziridinium imide (AI) is proposed as an intermediate in all these systems. The stability of the AI intermediate and its equilibration with an open zwitterion depend on the particular system. Only in the benzylically-stabilized tertiary indenes is the open zwitterion stable enough to cause loss of stereochemistry.

Reactions of 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD) with conjugated dienes[1] and alkenes[2,3] have recently attracted considerable mechanistic attention. A recent examination of the [4 + 2] addition of PTAD to 1,4-dimethylbutadienes suggested that a nonconcerted Diels−Alder reaction takes place. An intermediate aziridinium imide (AI) was suggested for all three isomers, which is trappable by nucleophiles in the case of the (*Z,Z*)- and (*Z,E*)-isomers but not with the (*E,E*)-isomer, and which subsequently opens to a 1,4-zwitterion in the case of the (*Z,Z*)-isomer.[1] A 1,4-dipolar intermediate was proposed earlier by Butler et al. in the reaction of PTAD with vinyl esters[4,5] and ethers.[6]

Deuterium isotope effects[7,8] and stereochemical studies[9,10] have shown that PTAD reacts in the ene reaction through an intermediate with the stereochemical characteristics of an aziridinium imide (AI), **1**. In an elegant experiment, Squillacote and co-workers studied the reaction of PTAD with *trans*-cycloheptene.[11] The ^{1}H and ^{13}C NMR spectra demonstrated



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the existence of an AI at −135 °C and its subsequent conversion to the ene product at higher temperatures. Intermediacy of an unstable AI was also demonstrated by ^{13}C NMR in the reaction of adamantylideneadamantane with PTAD.[12] An intermediate analogous to the AI, a perepoxide, has been implicated in the ene reaction of singlet oxygen with olefins.[13−16]

In this paper, we report the structure and stereochemistry of products formed in the reaction of PTAD with *cis*- and *trans*-2-butene, 1-methylcyclopentene, (*E*)-2-methyl-2-butene-*1,1,1-d*$_3$, and indenes, including trapping the AI intermediate with methanol. We also discuss the substrate dependence of the preference for AI and zwitterion intermediates.

Results

Adducts from PTAD and *cis*- and *trans*-Butenes. Reactions of PTAD with *cis*- and *trans*-butenes were carried out by adding solid PTAD or a solution of PTAD in CH_2Cl_2 to a stirred

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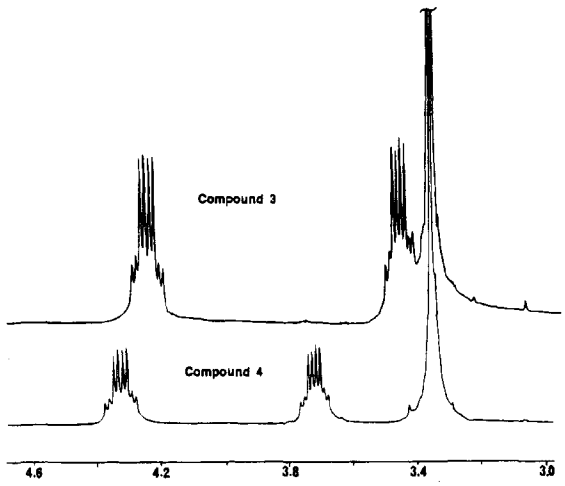


Figure 1. ^{1}H NMR spectra of MeOH adducts **3** and **4** from *cis*- and *trans*-2-butene and PTAD.

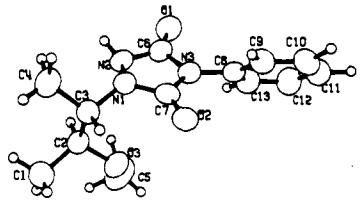
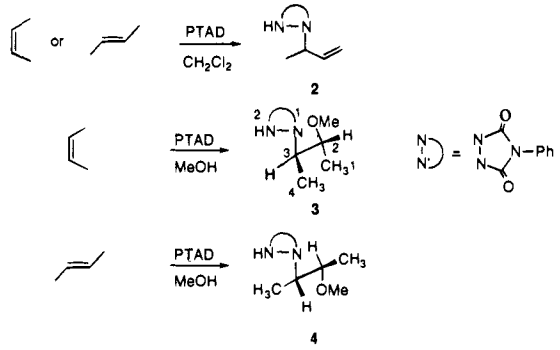


Figure 2. ORTEP drawing of the PTAD + MeOH adduct (**3**) of *cis*-2-butene. Selected interatomic distances (Å): C1−C2 = 1.527, C2−C3 = 1.523, C3−C4 = 1.527, C2−O3 = 1.423; C5−O3 = 1.414, C3−N1 = 1.464, N1−N2 = 1.421, N1−C7 = 1.347, N2−C6 = 1.371, C6−N3 = 1.399, C7−N3 = 1.409, C8−N3 = 1.419, C6−O1 = 1.213, C7−O2 = 1.225, mean C−C distance of the phenyl group 1.382.

solution of the alkene in either CH_2Cl_2 or $MeOH/CH_2Cl_2$ at different temperatures. In CH_2Cl_2, ene adduct **2** is the only product.[17,18]

However, in methanol, the reaction gives different diastereoisomeric solvent addition products, **3** and **4**, from *cis*- and *trans*-2-butene, respectively, with >97% stereospecificity. ^{1}H



NMR shows substantial chemical shift differences for **3** and **4** (Figure 1). Hydrogens next to the very electron-withdrawing nitrogen resonate at 4.24 and 4.32 ppm, respectively, in **3** and **4**, whereas hydrogens next to oxygen appear at 3.44 and 3.70 ppm. The structure of **3** was shown by X-ray crystallography (Figure 2). Hydrogens HC_2 and HC_3 are *anti* (dihedral angle 175°), while the methyl groups C1 and C4 are staggered (dihedral angle 60°). The triazolinedione ring is essentially planar (mean deviation from the least-squares plane 0.024 Å) with the nitrogen atoms N1 and N2 deviating the most, and the

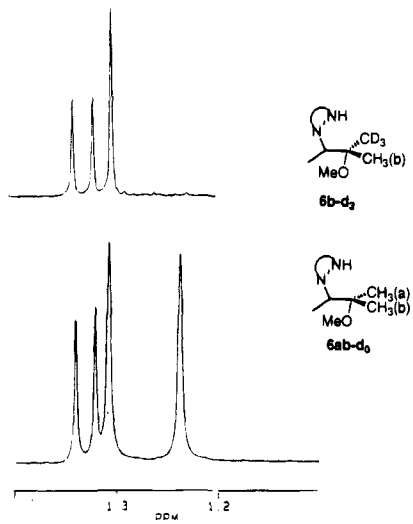
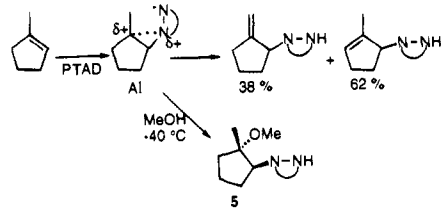


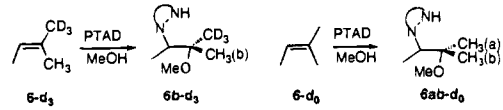
Figure 3. ^{1}H NMR spectra of MeOH adducts **6b-*d*$_3$** and **6ab-*d*$_0$** from **6-*d*$_3$**/ and **6-*d*$_0$**/trimethylethylene and PTAD.

corresponding atoms C3 and HN2 being out of plane by −0.38 and 0.39 Å, respectively. The dihedral angle between the plane and the phenyl ring is 51.7°.

As with *cis*- and *trans*-2-butenes, the addition of PTAD to 1-methylcyclopentene in methanol is stereospecific to produce Markovnikov adduct **5**, as shown by the shift of the hydrogen α to N, 4.34 ppm. ^{1}H NMR of **5** showed only one methoxy resonance at 3.25 ppm. We assign the *trans* stereochemistry by analogy to the butenes.



PTAD and MeOH Adducts of (*E*)-2-Methyl-2-butene-*1,1,1-d*$_3$ and -*d*$_0$. In methanol, the reaction of PTAD with 2-methyl-2-butene gives the Markovnikov adduct **6ab-*d*$_0$** as the only product. The two geminal methyl groups a and b of adduct



6ab-*d*$_0$ are diastereotopic and resonate at 1.24 and 1.31 ppm, respectively (Figure 3). To test the stereospecificity of this reaction, (*E*)-2-methyl-2-butene-*1,1,1-d*$_3$ was prepared in high stereochemical purity. Wittig coupling of acetaldehyde and the corresponding stabilized ylide gave the (*E*)-α,β-unsaturated ester in >97% stereochemical purity. Subsequent reduction of the ester with $LiAlD_4$ followed by reduction of the mesylate gave (*E*)-2-methyl-2-butene-*1,1,1-d*$_3$ (**6-*d*$_3$**). ^{1}H NMR spectra of the product of reaction of this olefin with PTAD in methanol showed only one singlet methyl at 1.30 ppm. This result again indicates stereospecific formation of the Markovnikov adduct **6b-*d*$_3$** (Figure 3). Again, the stereochemistry is assigned by analogy with the butenes.

Indenes. The reaction between PTAD and indene in both CH_2Cl_2 and methanol has been studied.[7,19] In dichloromethane,

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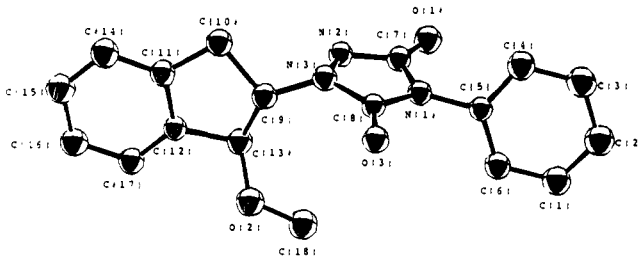
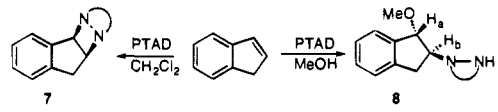


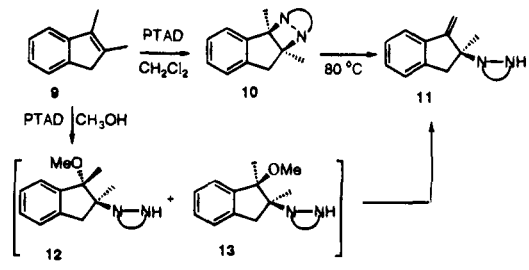
Figure 4. ORTEP view of compound **8**. Selected interatomic distances (Å) and angles (deg) (estimated standard deviations are in parentheses): distances. C9–C13 = 1.546(5), C9–N3 = 1.453(5), C12–C13 = 1.507(5), C12–C17 = 1.378(5), C15–C16 = 1.391(5), N2–N3 = 1.426(4), C8–O3 = 1.232(4), N1–C5 = 1.436(4), C3–C4 = 1.388-(6); angles, C8–N3–N2 = 110.75, C7–N1–C5 = 123.40, C6–C5–C4 = 121.68, C17–C12–C11 = 120.76.

the reaction affords the [2 + 2] diazetidine **7**, whereas in methanol the reaction gives the *trans* methanol adduct **8**. The structure of **8** was confirmed by X-ray crystallography (Figure 4).



^{1}H NMR spectra of the crude reaction mixture showed only one methoxy peak at 3.52 ppm. This result indicates regiospecific formation of the Markovnikov adduct **8**, and rules out an open zwitterionic intermediate in the reaction. If nonregiospecific, nonstereospecific addition had occurred, there should have been a maximum of four different methoxy resonances. Markovnikov directivity through an open ion should have given two products. Besides resonances from the methylene hydrogens and the phenyl rings, there are peaks at 5.14 (H_a) and 4.76 (H_b) ppm, resolved in DMSO-d_6. The coupling constant between these protons is 5.82 Hz, consistent with the *trans* configuration indicated by the crystal structure.

Surprisingly, reaction between 2,3-dimethylindene (**9**) and PTAD in CH_2Cl_2 or $CDCl_3$ at −60 °C gave only the [2 + 2] adduct **10**, not the ene product. Diazetidine **10** is stable only when isolated as a white crystalline solid by slow crystallization from CH_2Cl_2 at −15 °C over a period of several days. The ^{1}H NMR spectrum at −50 °C shows, besides the phenyl groups, methyl resonances at 1.93 and 1.86 ppm and methylene hydrogens at 4.07 (d, J = 18.5 Hz, 1H) and 3.00 (d, J = 18.5 Hz, 1H). Upon warming the sample to 80 °C for 5 h, **10** rearranges completely to ene product **11**, Figure 5 and 6.



When the PTAD reaction was carried out in a mixture of CH_2Cl_2 and MeOH at −60 °C, two stereoisomeric Markovnikov solvent addition products, **12** (Figure 7) and a very small amount (~10%) of **13**, were formed along with a small amount of ene product **11**. The major isomer was assigned the *trans* structure

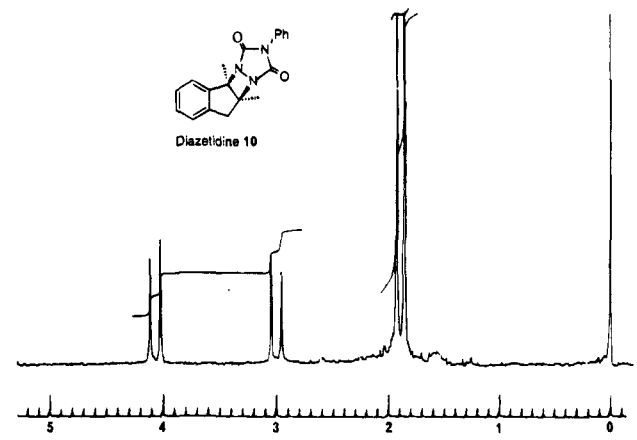


Figure 5. ^{1}H NMR spectrum of diazetidine **10** in $CDCl_3$.

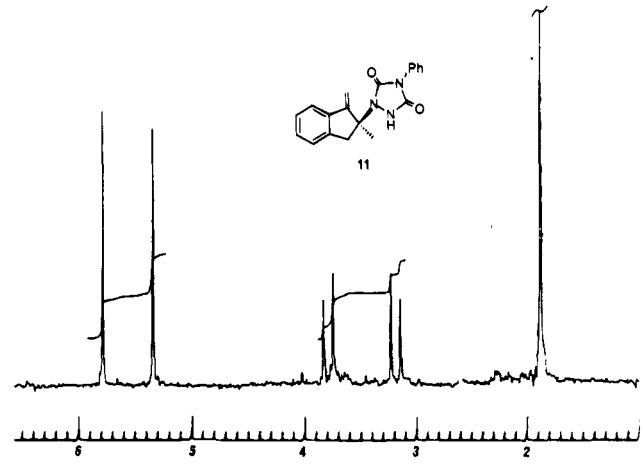


Figure 6. ^{1}H NMR spectrum of the ene product **11** from rearrangement of diazetidine **10**.

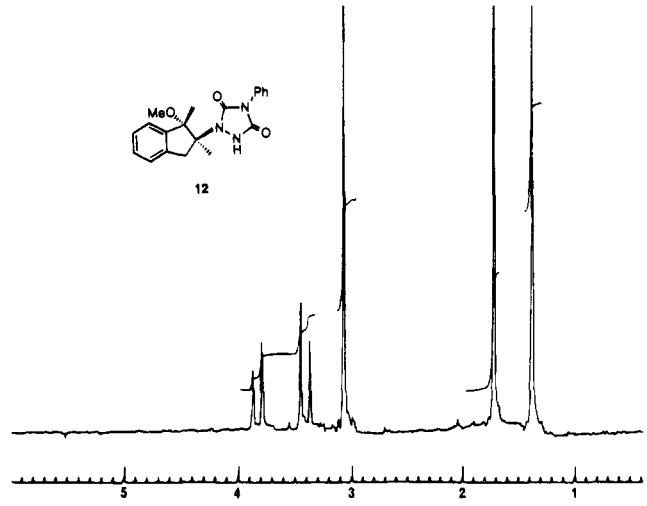


Figure 7. ^{1}H NMR spectra of *trans* MeOH adduct **12** from 2,3-dimethylindene and PTAD.

by analogy to the structure of adduct **8** from indene, confirmed to be *trans* by X-ray crystallography. Adducts **12** and **13** are not stable in solution and on standing in $CDCl_3$ for a few days at room temperature are completely transformed to **11** by elimination of methanol. However, **12** and **13** are stable in the solid state.

Similar results were obtained in the reaction of PTAD with 2-methylindene (**14**). When the reaction was carried out at −60 °C in CH_2Cl_2, [2 + 2] and ene products **15** and **16** were formed in a ratio of 75:25, respectively. Compound **15** isomerizes to

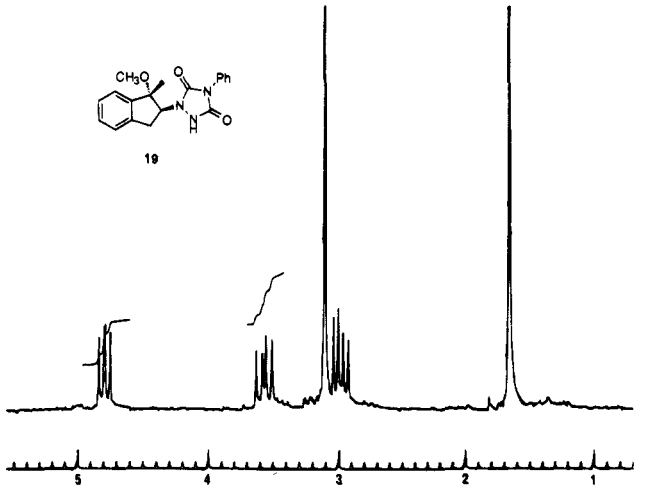
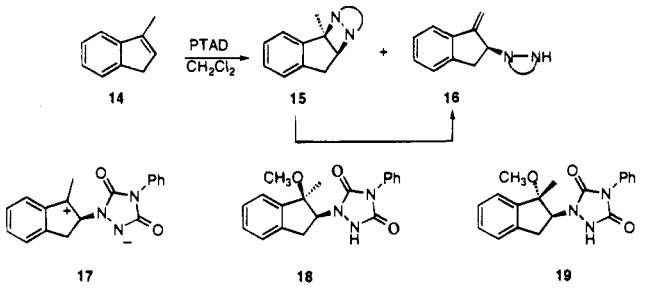


Figure 8. ^{1}H NMR spectra of *trans* MeOH adduct **19** from 2-methylindene and PTAD.

16 more rapidly than **10** to **11**. Upon heating an NMR sample at 80 °C, complete isomerization of diazetidine **15** to ene product **16** was observed in 3 h. However, when the reaction was run in a MeOH/CH_2Cl_2 mixture, two regiospecific methanol adducts were formed, in a ratio of 68:32. These adducts are the *cis* and *trans* Markovnikov stereoisomers **18** and **19**, respectively; see the ^{1}H NMR spectrum of isomer **19** (Figure 8).

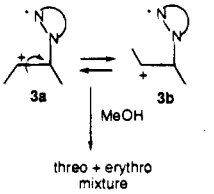


Upon standing at room temperature, the ratio of these products reverses to 34:66, followed by slow elimination of methanol to give ene product **16**. These results suggest the formation of a zwitterionic intermediate such as **17**. This carbocation is tertiary and benzylically stabilized and leads to the regiospecific addition of methanol at C_2 with loss of stereochemical integrity to produce adducts **18** and **19**. These adducts slowly isomerize to ene product **16** by loss of methanol. Although the stereochemistry of **18** and **19** is not established (many attempts to obtain suitable crystals for X-ray crystallographic analysis failed), we believe that the major product is the *cis* methanol adduct **18** because an NOE experiment on **19** gave no enhancement of the hydrogen next to the irradiated CH_3. Insufficient purified **18** was available to permit a comparable experiment.

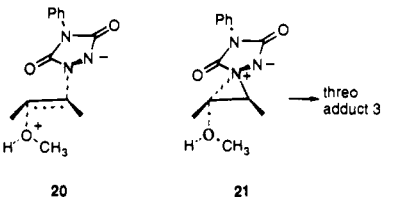
Discussion

The exclusive formation of the *threo*-isomer from *cis*-2-butene and the *erythro*-isomer from the *trans*-isomer requires stereospecific *anti* addition of methanol. These results eliminate the possibility of an open dipolar intermediate, **3a** or **4a**, since free rotation of the methyl group around the former double bond should yield a mixture of *threo*- and *erythro*-isomers from both butenes.

Two possible mechanisms could account for the ^{1}H NMR data: (a) a synchronous one-step mechanism, demonstrated in structure **20**, where PTAD and methanol add from the opposite face of the double bond to afford adduct **3** (b) the mechanism

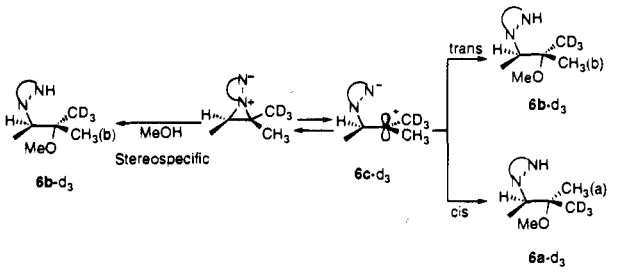


demonstrated in structure **21**, with nucleophilic addition of



methanol to a rigid AI intermediate, giving the same stereochemistry. However, concerted addition without an intermediate is excluded by secondary isotope effects in the reaction of *cis*- and *trans*-2-butene-*1,1,1-d*$_3$ with PTAD in methanol. These results showed a normal secondary isotope effect ($k_H/k_D \approx 1.1$ per atom); in a concerted reaction where an sp^2-hybridized carbon changes to sp^3, an inverse or no isotope effect would be expected.[20] The direct detection of aziridine imides in several reactions, mentioned in the Introduction, makes the latter the more plausible intermediates.[11,12] In principle, diazetidine intermediates could give comparable stereochemical results, but in cases where they were isolated do not react under the very mild conditions under which most of these adducts are formed.

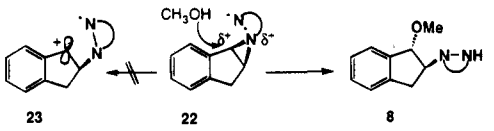
To test the stereospecificity of PTAD and methanol addition to trialkyl-substituted alkenes, **6-*d*$_3$** was prepared. This substrate is ideal for this purpose because it bears two geminal methyl groups that could stabilize a possible open Markovnikov zwitterion from reaction of PTAD and **6-*d*$_3$**. Subsequent nucleophilic attack of methanol on the two faces of the carbocation **6c-*d*$_3$** would produce two adducts **6a-*d*$_3$** and **6b-*d*$_3$**.



In this case, two methyl resonances (a and b) would be expected in the ^{1}H NMR spectrum, but only one methyl resonance (a) was observed (Figure 3), indicating that even in acyclic trialkyl-substituted alkenes, the addition of PTAD in methanol is stereospecific.

As in the case of *cis*- and *trans*-butene and trialkyl-substituted alkenes, the addition of PTAD to the double bond of indene is stereospecific in methanol and gives only *anti*-adduct **8**. Although in this case the AI intermediate **22** could give the secondary benzylically-stabilized cation **23**, these results show retention of stereochemical integrity in the reaction center and are consonant with a "tight" AI intermediate with some degree of positive charge at the benzylic position, not an open 1,4-dipolar zwitterion.[21] Charge separation as in **22** was proposed earlier by Greene and co-workers.[8]

(20) Elemes, Y.; Orfanopoulos, M. Manuscript in preparation.



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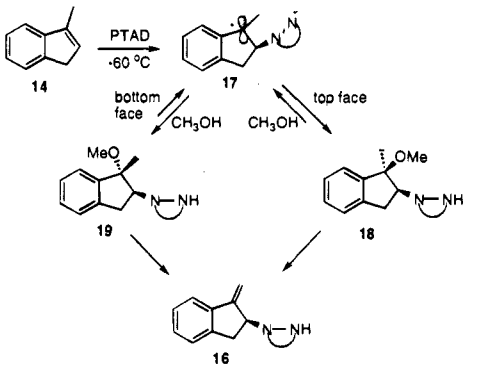
The addition of PTAD to 2,3-dimethylindene in aprotic solvents produces diazetidine **10**, which subsequently isomerizes cleanly to ene product **11**. In the reaction of singlet oxygen with indenes, dioxetane, ene, and [2 + 4] products can be formed, depending on the conditions.[22,23] However, there is no evidence that analogous dioxetanes rearrange to ene product in this series.[22,24]

In order to explain the lack of stereospecificity with substituted indenes, we suggest that nucleophilic attack of methanol captures carbocation **17** nonstereospecifically and produces *cis*- and *trans* adducts **18** and **19** in a kinetic ratio of 68:32. Upon standing at room temperature for several hours, adducts **18** and **19** equilibrate through zwitterion **17**, giving the thermodynamic ratio 36:64.



14 17 19 18 16

AI and zwitterionic intermediates have also been suggested in the reaction of PTAD and substituted butadienes.[1] In this case, unstable diazetidines were formed which rearranged at moderate temperatures to Diels–Alder or ene products, depending on the system; in methanol, solvent trapped the zwitterion in some cases but not others.

It is worth noting that, in trisubstituted alkenes, the ene reaction of PTAD with 1-methylcyclopentene follows Markovnikov selectivity by abstracting allylic hydrogens only from the geminal alkyl groups. The charge separation in the AI intermediate proposed by Greene[8] is consistent with the regio- and stereospecific addition of methanol at the tertiary carbon in 1-methylcyclopentene and deuterated 2-methyl-2-butene. These results suggest that the fused benzene ring in the methyl-substituted indenes stabilizes the tertiary carbonium ion enough to give an open zwitterionic intermediate similar to **17** and allows nonspecific attack of methanol.

In an earlier paper Hoye et al. suggested dipolar or diradical intermediates to rationalize the regio- and stereoselectivity in the ene reaction of PTAD with α,β-unsaturated carbonyl compounds.[25] In the present system, diradical intermediates cannot be ruled out, but would not account for the solvent adducts. Methanol adducts are also formed in the reaction of singlet oxygen and substituted dienes[26,27] and indenes.[28] Such adducts have been interpreted as arising from perepoxides or zwitterions.[22,24,25,28–30]

Conclusion

The stability of the AI intermediate and its equilibration with the open intermediate depend on the particular system. In the addition of MeOH and PTAD to *cis*- and *trans*-butene, 1-methylcyclopentene, (*E*)-2-methyl-2-butene-*1,1,1-d*$_3$, and indene, there is no loss of stereochemistry. In this case, a tight AI is proposed which does not equilibrate to any significant extent with an open zwitterion. However, in methyl-substituted indenes **9** and **14**, the AI intermediate can give a tertiary benzylic cation, stabilizing the zwitterion and causing loss of stereochemical integrity at this center. The interconversion of the methanol adducts and the ready conversion of these compounds and diazetidine adducts to the ene products are also consistent with the relative stability of zwitterions in this system.

Experimental Section

Nuclear magnetic resonance (NMR) spectra were determined on Brucker WP-200 MHz and AM-500 MHz spectrometers. All spectra were taken in $CDCl_3$, except as noted. Chemical shifts are reported in δ (ppm) relative to internal tetramethylsilane. Analytical gas chromatography was done using a Hewlett-Packard Model 5880 instrument equipped with a 50 ft OV-100 capillary column and an FID detector. Mass spectra were obtained on an AEI MS-902 instrument. *cis*- and *trans*-2-butene, indene, and indanone were obtained from Aldrich Chemical Co. PTAD was prepared by oxidation of 4-phenylurazole (Aldrich) with *tert*-butyl hypochloride according to a literature procedure.[31]

General Procedure for the Reactions. Solid PTAD or a solution in CH_2Cl_2 was added to a stirred solution of the alkene in CH_2Cl_2, $CDCl_3$, or MeOH/CH_2Cl_2 at the desired temperature, in a round-bottomed flask or an NMR tube. After the characteristic red color of PTAD disappeared, ^{1}H NMR spectra were obtained at −60 °C or room temperature. Where possible, the product was separated by flash 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 ^{1}H NMR analysis.

Preparation of 2,3-Dimethylindene. The title compound was prepared by a Grignard reaction between 3-methylindanone (prepared in good yield according to a literature method)[32] and methylmagnesium iodide. To a Grignard reagent prepared from CH_3I (2.02 g) and Mg (0.41 g) in absolute ether was added a solution of 3-methylindanone (1.3 g) in ether at 0 °C. After 1/2 h the mixture was warmed to room temperature and then refluxed for an additional 1 h. The reaction mixture was worked up with NH_4Cl solution and extracted three times with Et_2O. The organic layers were combined, dried ($MgSO_4$), filtered, and concentrated to afford 2,3-dimethylindene as an oil in 85% yield. TLC (hexane/ethyl acetate, 2:1) showed only one product. This compound decomposes slowly on standing and is purified by silica gel flash column chromatography (hexane/ethyl acetate, 2:1) before use. ^{1}H NMR: 2.02 (s, 3H), 2.05 (s, 3H), 3.24 (s, 2H), 7.06–7.36 (m, 4H).

2-Methylindene. To the Grignard reagent from methylmagnesium iodide (3.1 g of CH_3I and 0.72 g of Mg) in Et_2O was added a solution of indanone (2.4 g) in Et_2O. After the usual procedure, the reaction mixture was worked up with a saturated solution of NH_4Cl. Evapora-

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tion of Et_2O left a residue, identified as 2-methylindene, in 80% yield. This compound polymerizes on standing at room temperature. It is purified by silica gel flash column chromatography (hexane/ethyl acetate, 2:1) before use. ^1H NMR: 2.15−2.17 (m, 3H), 3.29−3.31 (m, 2 H), 6.18 (d, J = 1.5 Hz, 1 H), 7.29−7.42 (m, aromatic, 4H).

MeOH Adduct 3 from *cis*-2-Butene and PTAD. Crystals of compound **3** were obtained from chloroform/hexane. ^1H NMR: 7.34−7.52 (m, 5 H), 4.24 (dq, J = 7.0, 3.2 Hz, 1 H), 3.44 (dq, J = 6.2, 3.5 Hz, 1 H), 3.32 (s, 3 H), 1.32 (d, J = 7.0 Hz, 3 H), 1.21(d, J = 6.2 Hz, 3 H). Exact mass for $C_{13}H_{17}N_3O_3$: calcd 263.1270, found 263.1288.

MeOH Adduct 4 from *trans*-2-Butene and PTAD. Crystals of **4** were recrystallized from ethyl acetate/hexane. Mp: 124.5−125.5 °C. ^1H NMR: 7.25−7.52 (m, 5 H) 4.32 (dq, J = 7.0, 3.2 Hz, 1 H), 3.70 (dq, J = 6.4, 3.2 Hz, 1 H), 3.35 (s, 3 H), 1.28 (d, J = 7.0 Hz, 3 H), 1.19 (d, J = 6.4 Hz, 3 H). Exact mass for $C_{13}H_{17}N_3O_3$: calcd 263.1270, found 263.1286.

MeOH Adduct 5 from 1-Methylcyclopentene and PTAD. ^1H NMR: 7.37−7.55 (m, 5 H), 4.34 (dd, J = 8.3, 8.3 Hz, 1 H), 3.25 (s, 3 H), 2.31−1.59 (m, 6 H), 1.25 (s, 3 H). Exact mass for $C_{15}H_{19}N_3O_3$: calcd 289.1426, found 289.1422.

Preparation of (*E*)-2-Methyl-2-butene-*1,1,1-d*$_3$ (6-*d*$_3$). **(a) 2-[(Triphenylphosphino)methyl]propionate.** To 80 g (300 mmol) of triphenylphosphine in 20 mL of benzene was added 50 g (300 mmol) of methyl 2-bromopropionate in 70 mL of benzene. After 24 h of reflux, the solution was filtered and washed twice with warm benzene to yield the phosphonium salt (90%). To 115 g (260 mmol) of the above salt in 100 mL of water was added a 20% solution of NaOH. A yellow ylide separated immediately and was extracted from the water layer with dichloromethane. Evaporation of the solvent gave 70 g (80%) of yellow stabilized ylide. Mp: 144−147 °C. ^1H NMR: 1.70 (d, J = 13.6 Hz, 3H), 3.25 (s, 3H), 7.30 (m, 15H).

(b) Methyl (*E*)-2-Methyl-2-butenoate. To 15 g (45 mmol) of the above ylide in 50 mL of dichloromethane was added dropwise 2.9 g (60 mmol) of acetaldehyde in 10 mL of dichloromethane. After stirring overnight at room temperature, the solvent was evaporated to give the esters in 95% yield and 97% (*E*)-isomeric purity. ^1H NMR: 1.78 (d, partially overlapped, 3H), 1.82 (s, 3H), 3.8 (s, 3H), 6.85 (m, 1H).

(c) 1-Hydroxy-2-methyl-2-butene-*1,1-d*$_2$. To 1.46 g (35 mmol) of $LiAlD_4$ (Aldrich, 98% D) in 60 mL of dry ether cooled to 0 °C was added dropwise 4.7 g (46 mmol) of the previously prepared (*E*)-ester in 10 mL of dry ether. After 12 h of reflux, the reaction was worked up with base in the usual manner (0.8 mL of water, 1.0 mL of 20% NaOH, 1.2 mL of water). This solution was filtered, and the organic layer was washed twice with a saturated solution of NH_4Cl and once with brine and dried over sodium carbonate. Evaporation of solvent gave the title product in 70% yield. ^1H NMR: 1.64 (br d, partially overlapped, 3H), 1.67 (s, 3H), 5.5 (br m, 1H).

(d) (*E*)-1-(Methylsulfonyl)-2-methyl-2-butene-*1,1-d*$_2$. To a solution of 2.42 g (24 mmol) of triethylamine and 1.9 g (22 mmol) of the allylic-d_2 alcohol in 30 mL of dry dichloromethane cooled to −5 °C was added dropwise 2.74 g (24 mmol) of methanesulfonyl chloride. After 30 min of additional stirring, the reaction mixture was treated with ice cold 5% HCl aqueous solution, ice cold saturated sodium carbonate solution, and brine. After drying the organic layer over magnesium sulfate, the solvent was evaporated to yield 3.2 g 80% of the allylic-d_2 mesylate. The mesylate was unstable and was kept cold and reduced immediately to the corresponding olefin-d_3. ^1H NMR: 1.66 (d, partially overlapped, 3H), 1.70 (s, 3H), 2.95 (s, 3H), 5.65 (m, 1H).

(e) (*E*)-2-Methyl-2-butene-*1,1,1-d*$_3$. To 0.29 g (6.6 mmol) of $LiAlD_4$ in 10 mL of dry diglyme was added dropwise 3.1 g (17 mmol) of the above mesylate in 10 mL of dry diglyme. After 1 h of stirring at room temperature, the product was recovered by direct distillation from the reaction mixture. The temperature was slowly raised to 150 °C. The olefin was collected in a 2-isopropanol/dry ice cooled flask in 70% yield. ^1H NMR: 1.53 (d, partially overlapped, 3H), 1.58 (s, 3H), 5.2 (m, 1H). ^{13}C NMR: 13.4, 17.2, 118.5, 132.0. ^{13}C NMR of the protio olefin: 13.4, 17.3, 25.7, 118.7, 132.0.

MeOH Adduct 6b-*d*$_3$ from (*E*)-2-Methyl-2-butene-*1,1,1-d*$_3$ and PTAD. This adduct was prepared at −45 °C and recrystallized from ethyl acetate/hexane. Exact mass for $C_{14}H_{16}D_3N_3O_3$: calcd 281.1663, found 281.1661. ^1H NMR: 1.30 (s, 3H), 1.32 (d, 3H), 3.24 (s, 3H), 4.22 (q, 1H), 7.25−7.56 (m, 5H). ^1H NMR of the protio adduct **6ab-*d*$_0$**: 1.24 (s, 3Ha), 1.31 (s, 3Hb), 1.33 (d, 3H), 3.26 (s, 3H), 4.2 (q, 1H), 7.26−7.55 (m, 5H), 7.80 (br s, 1H).

Diazetidine 7 from Indene and PTAD.[7,19] ^1H NMR: 7.03−7.60 (m, 9H), 5.97 (d, J = 5.9 Hz, 1 H), 5.37 (dd, J = 5.9, 5.9 Hz, 1 H), 3.91 (d, J = 18.5 Hz, 1 H), 3.13 (dd, J = 6.3, 18.5 Hz, 1 H).

MeOH Adduct 8 from Indene and PTAD. This adduct has limited solubility in both polar and nonpolar solvents. DMSO was the best solvent. The adduct was separated by column chromatography on silica gel using mixtures of ethyl acetate and hexane (2:1) and recrystallized from ethyl acetate/hexane to give white needles. Mp: 205−206 °C. Exact mass for $C_{18}H_{17}N_3O_3$: calcd 323.1270, found 323.1296. ^1H NMR: 7.21−7.53 (m, 9H), 4.92−5.03 (m, 2H), 3.52 (s, 3H), 3.42 (dd, J = 7.6, 16 Hz, 1H), 3.05 (dd, J = 5.9, 16.5 Hz, 1H). ^1H NMR in DMSO-d_6: 7.29−7.49 (m, 9H), 5.14 (d, J = 5.8 Hz, 1H), 4.76 (m, 1 H), 3.46 (s, 3H), 3.21−3.41 (m, 1H), 3.11 (dd, J = 16.5, 8.0 Hz, 1H). ^{13}C NMR in DMSO-d_6: 152.55, 152.37, 139.97, 139.10, 131.61, 128.84, 128.56, 127.89, 126.90, 126.07, 124.78, 124.60, 84.52, 61.90, 56.42, 31.96.

Diazetidine 10 from 2,3-Dimethylindene and PTAD. This compound was crystallized from CH_2Cl_2 at −15 °C for a few days. Exact mass for $C_{19}H_{17}N_3O_2$: calcd 319.1321, found 319.1312. ^1H NMR: 7.26−7.51 (m, 7H), 6.78−6.83 (m, 2H) 4.07 (d, J = 19 Hz, 1H), 3.00 (d, J = 19 Hz, 1H), 1.93 (s, 3H), 1.86 (s, 3H). ^{13}C NMR: 161.08, 159.49, 140.77, 137.86, 131.12, 130.63, 129.12, 128.54, 128.05, 126.04, 125.84, 125.50, 83.64, 77.83, 39.07, 21.04, 19.41.

Ene Adduct 11 from 2,3-Dimethylindene and PTAD. ^1H NMR: 7.27−7.47 (m, 9H), 5.74 (s, 1H), 5.32 (s, 1H), 3.79 (d, J = 17 Hz, $1H_a$), 3.17 (d, J = 17 Hz, $1H_b$), 1.86 (s, 3 H). ^{13}C NMR: 153.12, 152.06, 141.56, 137.87, 131.04, 129.50, 128.88, 128.03, 127.12, 125.46, 125.14, 121.20, 106.41, 69.39, 42.78, 24.58. The resonance at 127.12 appears to be for two carbons. Exact mass for $C_{19}H_{17}N_3O_2$: calcd 319.1321, found 319.1322.

***Trans*-MeOH Adduct 12 from 2,3-Dimethylindene and PTAD.** Compound **12** was recrystallized from ethyl acetate and hexane. Mp: 187.5−189 °C. ^1H NMR: 7.88 (br s, 1H), 7.26−7.56 (m, 9H), 3.83 (d, J = 16 Hz, 1H), 3.41 (d, J = 16 Hz, 1H), 3.07 (s, 3H), 1.72 (s, 3H), 1.38 (s, 3 H). ^{13}C NMR: 154.44, 152.98, 142.04, 139.32, 131.34, 129.78, 129.59, 129.07, 128.10, 125.52, 125.35, 124.98, 88.82, 71.11, 51.26, 44.91, 19.10, 17.71. A small amount (~10%) of an isomer, believed to be **13**, was also present along with a small amount of **11** and other impurities. Because of the number of small peaks in the spectrum, the structure of **13** could not be confidently assigned.

Diazetidine 15 from 2-Methylindene and PTAD. ^1H NMR: 7.29−7.55 (m, 7H), 6.77−6.84 (m, 2H), 5.15 (d, J = 5.9 Hz, 1H), 3.93 (d, J = 18.6 Hz, 1H), 3.29 (dd, J = 18.0, 6.0 Hz, 1H), 2.11 (s, 3H).

Ene Adduct 16 from 2-Methylindene and PTAD. Crystals were obtained. Mp: 116.5−118 °C. Exact mass for $C_{18}H_{15}N_3O_2$: calcd 305.334, found 305.1159. ^1H NMR: 7.25−7.52 (m, 9H), 5.68 (d, J = 2.2 Hz, 1H), 5.50−5.55 (m, 1H), 5.25 (d, J = 2 Hz, 1H), 3.27−3.40 (dd, J = 8.6, 16.8 Hz, 1H), 3.02−3.13 (dd, J = 5.3, 16.8 Hz, 1H).

MeOH Adduct 18 from 2-Methylindene and PTAD. ^1H NMR: 7.24−7.56 (m, 9H), 5.05 (t, J = 7.1, Hz, 1H), 3.42−3.10 (m, 2H), 3.20 (s, 3H), 1.46 (s, 3H).

MeOH Adduct 19 from 2-Methylindene and PTAD. Attempts to recrystallize the white solid from adducts **18** and **19** from absolute ethanol gave isomer **19** as a white powder. Mp: 213−216 °C dec. ^1H NMR analysis showed only one stereoisomer: 7.29−7.59 (m, 9H), 4.77 (dd, J = 7.3, 9.8 Hz, 1H), 3.56 (dd, J = 9.8, 15.1 Hz, 1H), 3.06 (s, 3H), 2.96 (dd, J = 7.8, 15.1 Hz, 1H), 1.64 (s, 3H). An NOE experiment on **19** gave no enhancement of the hydrogen next to CH_3.

Structure Determination by X-ray Diffraction. MeOH Adduct 3 from *cis*-Butene and PTAD. Crystals of the PTAD and methanol adduct of *cis*-2-butene were obtained by recrystallization from chloroform/hexane. Data were collected on an elongated prism, 0.9 × 0.2 × 0.2 mm.

Crystal data: orthorhombic, $P2_12_12_1$, a = 7.095(1) Å, b = 10.05(1) Å, c = 19.793(4) Å, V = 1411.4 Å^3, Z = 4, λ (Cu Kα) = 1.5418 Å, $C_{13}H_{17}N_3O_3$, M_r = 263.3, D_c = 1.24 g cm^{-1}, μ = 6.57 cm^{-1}, $F(000)$ = 560. Lattice parameters were measured by the least-squares method for the angular coordinates of 15 reflections, 49° < 2θ < 52°. Data

were collected at room temperature with a Syntex P21 autodiffractometer by a $\theta 2\theta$ scan method with a scan rate of 1.0−10.0 deg min^{-1}. The scan range was 1.8° plus the $\alpha_1 - \alpha_2$ divergence in 2θ. The background was measured for 1/4 of the scan time at the start and end of each scan. Crystal stability and X-ray damage were monitored by 3 reflections measured every 67 reflections. No damage to the crystal was observed. Of the 1351 reflections measured in the range $3° < 2\theta < 125°$, 21 were found systematically absent and 57 with $I < 3\sigma(I)$ suppressed. Therefore, 1273 unique reflections were used. Intensities were corrected by Lorentz and polarization factors.

Structures were solved and refined with SHELX76.[33] Scattering factors were taken from ref 34. Refinement was done by full-matrix, unit-weight least squares ($\sum(F_o - F_c)^2$ minimized). The best E map ($E > 1.2$) revealed 14 out of 19 non-H atoms. The additional five atoms were found by a difference Fourier map. Hydrogen atoms were similarly located at the end of isotropic refinement. Final refinement of the positional parameters of all atoms, anisotropic thermal parameters for non-H atoms, and isotropic thermal parameters for H-atoms gave $R = 0.0381$, $wR = 0.0403$. The alternative enantiomeric structure converged to $R = 0.0384$, $wR = 0.0403$.[35] The final difference Fourier map showed no features, maximum and minimum residual electron densities 0.0004 and −0.0002 e Å^{-3}, respectively.

MeOH Adduct 8 from Indene and PTAD. Crystals of methanol adduct **8** from indene and PTAD ($C_{18}H_{17}N_3O_3$), $M_r = 323$, were obtained from ethyl acetate/hexane. Data measured on a crystal of dimensions 0.3 × 0.15 × 0.12 mm are $P2_1/n$, $a = 7.693(3)$ Å, $b = 10.650(5)$ Å, $c = 19.793(4)$ Å, $\beta = 90.79(1)°$, $V = 1554$ Å^3, $Z = 4$, λ(Mo Kα) = 0.7107 Å, $D_c = 1.38$ g cm^{-1}. Lattice parameters were measured by the least-squares fit of the angular coordinates of 20 reflections in the range $10° < 2\theta < 20°$. Data were collected at 128 K with a modified Picker diffractometer equipped with a graphite monochromator, by a $\theta-2\theta$ method with a scan rate of 4.5 deg min^{-1}. Crystal stability and X-ray damage were monitored by 3 reflections measured every 97 reflections. No damage to the crystal was observed. Of the 3128 reflections measured up to 50.0° in 2θ, 1457 were considered observed with a criterion for observation $I \geq 3\sigma(I)$. Intensities were corrected for Lorentz and polarization factors, but not for absorption. Structures were solved by the direct methods program MULTAN.[36] Scattering factors were taken from ref 34. Refinement was done by full-matrix weighted least squares [$\sum w(F_o - F_c)^2$ minimized, $w = 1/\sigma^2(F)$]. Hydrogen atom positions were calculated but not refined. Final refinement of the positional and anisotropic thermal parameters (217 parameters) of non-H atoms gave $R = 0.051$, $wR = 0.057$. The average shift to esd ratio in the final cycle of refusement was 0.017 (maximum 0.088). The maximum and minimum residual electron densities were 0.30 and 0.20 e Å^{-3}, respectively.

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