Further Studies of the Thermal and Photochemical Diels−Alder Reactions of *N*-Methyl-1,2,4-triazoline-3,5-dione (MeTAD) with Naphthalene and Some Substituted Naphthalenes

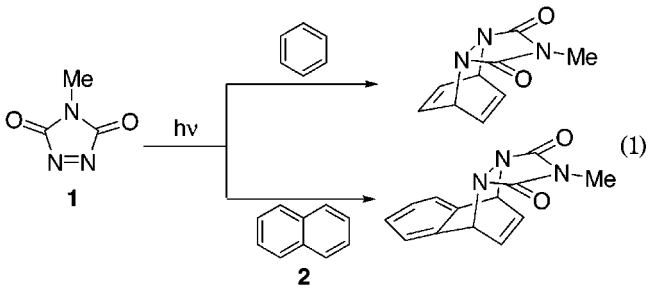
Gary W. Breton* and Kristy A. Newton

Berry College, Department of Chemistry, P.O. Box 495016, Mount Berry, Georgia 30149-5016

Received April 19, 1999

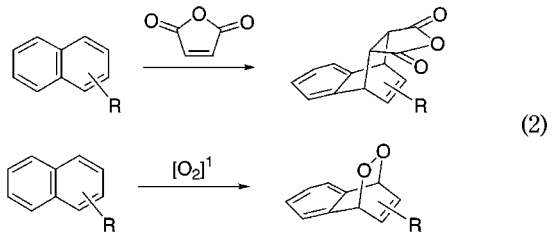
MeTAD thermally reacted with naphthalene (**2**) and methylated naphthalenes to give equilibrium mixtures of starting materials and [4 + 2] cycloadducts. Methyl substitution on the naphthalene ring generally increased both the amount of cycloadduct formed and the rate of cycloaddition relative to **2**. The isolated cycloadducts were all thermally labile and quantitatively reverted to the parent naphthalene in the presence of 2,3-dimethyl-2-butene as a trap for liberated MeTAD. The rates of the cycloreversion reactions were affected by substitution patterns but not appreciably by solvent. A mechanism for the cycloaddition reaction is presented that proposes the involvement of a charge-transfer complex. Photochemically, MeTAD demonstrated lower regioselectivity in its reactions with substituted naphthalenes relative to the corresponding thermal reactions.

Several years ago Sheridan described the photochemical reaction of MeTAD (**1**) with a number of aromatic compounds including benzene and naphthalene (**2**).[1,2] The reactions with benzene and **2** afforded novel Diels−Alder cycloadducts (eq 1) that have served as precursors to several theoretically interesting molecules.[2−4]



(1)

While more reactive in a Diels−Alder sense than benzene, naphthalenes are generally poor diene components in the classical Diels−Alder cycloaddition reaction.[5] Cycloaddition has been reported, therefore, only with strong dienophiles such as maleic anhydride and singlet oxygen in addition to MeTAD (eq 2).[6,7] Herzog and co-workers reported that equilibria were established between starting materials and Diels−Alder cycloadducts when naphthalene and substituted naphthalenes were heated (typically 100 °C for 24 h) in the presence of excess maleic anhydride.[6] Cycloadducts were generally formed in poor yields with simple mono- and disubstituted naphthalenes (1−47%),[6a,b] but higher conversions were reported at high pressures (∼9000 atm) or with polyalkylated naphthalenes.[6c,d] The cycloadducts reverted to starting materials upon heating. Singlet oxygen does not react with **2**, but it does react readily with naphthalene compounds that are at least disubstituted with alkyl groups (e.g., 1,4- or 1,8-dimethylnaphthalene).[7]



(2)

While the photochemical reactions of MeTAD with **2** and some substituted naphthalenes have already been reported,[1,3,4] the corresponding thermal reactions of triazolinediones with naphthalenes have only been briefly mentioned in the literature.[4] Herein we provide a more detailed report on the thermal and photochemical reactions of MeTAD with **2** and a series of methylated naphthalenes (compounds **3**−**9** in Chart 1). We also report on our studies of the thermal cycloreversions of the [4 + 2] adducts.

Results

1. Thermal Reactions of MeTAD with Naphthalene and Substituted Naphthalenes. A. Reaction with Naphthalene (2). When MeTAD is mixed with **2** in $CDCl_3$ (initially 0.40 M each) at 29 °C in the absence

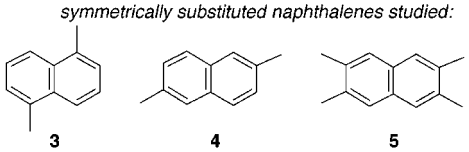
* To whom correspondence should be addressed. e-mail: gbreton@berry.edu. office: (706)-290-2661. fax: (706)-238-7855.

(1) (a) Kjell, D. P.; Sheridan, R. S. *J. Am. Chem. Soc.* **1984**, *106*, 5368. (b) Kjell, D. P.; Sheridan, R. S. *J. Photochem.* **1985**, *28*, 205.
(2) Hamrock, S. J.; Sheridan, R. S. *J. Am. Chem. Soc.* **1989**, *111*, 9247.
(3) Kjell, D. P.; Sheridan, R. S. *J. Am. Chem. Soc.* **1986**, *108*, 4111.
(4) Burger, U.; Mentha, Y.; Thorel, P. J. *Helv. Chim. Acta* **1986**, *69*, 670.
(5) Biermann, D.; Schmidt, W. *J. Am. Chem. Soc.* **1980**, *102*, 3163.
(6) (a) Kloetzel, M. C.; Herzog, H. L. *J. Am. Chem. Soc.* **1950**, *72*, 1991. (b) Kloetzel, M. C.; Dayton, R. P.; Herzog, H. L. *J. Am. Chem. Soc.* **1950**, *72*, 273. (c) Plieninger, H.; Wild, D.; Westphal, J. *Tetrahedron* **1969**, *25*, 5561. (d) Oku, A.; Ohnishi, Y.; Mashio, F. *J. Org. Chem.* **1972**, *37*, 4264.
(7) (a) Wasserman, H. H.; Larsen, D. L. *J. Chem. Soc., Chem. Commun.* **1972**, 253. (b) Adam, W.; Prein, M. *Acc. Chem. Res.* **1996**, *29*, 275.
(8) For comparison, Burger et al. (ref 4) reported a value of K_{eq} = 0.4 for the reaction of *N*-phenyl-1,2,4-triazoline-3,5-dione with naphthalene at 25 °C in $CDCl_3$.

10.1021/jo9906429 CCC: $19.00
Published on Web 04/27/2000

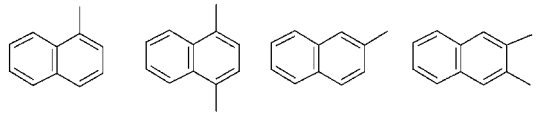
Chart 1

symmetrically substituted naphthalenes studied:



3 **4** **5**

unsymmetrically substituted naphthalenes studied:



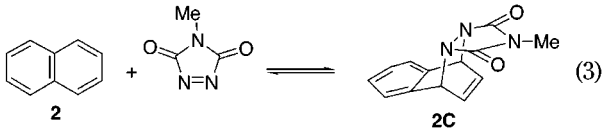
6 **7** **8** **9**

Table 1. Reaction of MeTAD with Symmetrically Substituted Naphthalenes[a]

cmpd	solvent	K_{eq} [b]	yield of cycloadduct, %[c]
2	$CDCl_3$	2.0	34 (21)
	C_6D_6	0.3	10
	CD_3CN	0.1	4
	$(CD_3)_2CO$	0.1	4
3	$CDCl_3$	2.8	40
	$(CD_3)_2CO$	0.1	3
4	$CDCl_3$	17.7	69 (63)
	$(CD_3)_2CO$	0.2	7
5	$CDCl_3$	351	89 (69)

[a] Conducted at 29 °C with initial concentrations of naphthalene and MeTAD at 0.40 M each. [b] Determined by relative integrations of appropriate signals in the ^{1}H NMR spectrum. Values are reliable to within ±5% [c] Determined by ^{1}H NMR spectroscopy. Values in parentheses are isolated yields.

of light, an equilibrium is established within 18 h in which a 34% yield (K_{eq} = 2.0) of cycloadduct **2C** (where **C** denotes a [4 + 2] cycloadduct with MeTAD) is formed as the only product (eq 3 and Table 1).[8] No change in



2 **2C** (3)

the equilibrium ratio was observed even after an additional 7 days of reaction time. The equilibrium constant for the reaction was determined at a series of temperatures over the range 26−50 °C. A van't Hoff plot (Figure 1) afforded $\Delta H° = -44$ kJ/mol and $\Delta S° = -141$ J/mol. The identity of the reaction solvent had a strong impact on the extent of the reaction (Table 1). Reaction was observed to readily take place in nonpolar (e.g., benzene) and weakly polar (e.g., $CDCl_3$) solvents, but strongly polar solvents (e.g., acetone) discouraged adduct formation. Adduct **2C** quantitatively reverted to starting material (as a solution in $CDCl_3$) in the presence of 2,3-dimethyl-2-butene as a trap for liberated MeTAD.[9]

B. Reaction of MeTAD with Symmetrically Substituted Methylated Naphthalenes. Reactions of MeTAD with symmetrically substituted naphthalenes **3**−**5** to afford cycloadducts **3C**−**5C** were conducted in the dark at 29 °C in $CDCl_3$, and were followed by periodic monitoring of the reaction using ^{1}H NMR spectroscopy. The results are summarized in Table 1. The reactions were monitored at least 24−48 h past the time required

(9) The alkene 2,3-dimethyl-2-butene reacts rapidly and quantitatively with MeTAD in an ene reaction to afford a relatively inert urazole product. See: Ohashi, S.; Leong, K.-W.; Matyjaszewski, K.; Butler, G. *J. Org. Chem.* **1980**, *45*, 3467.

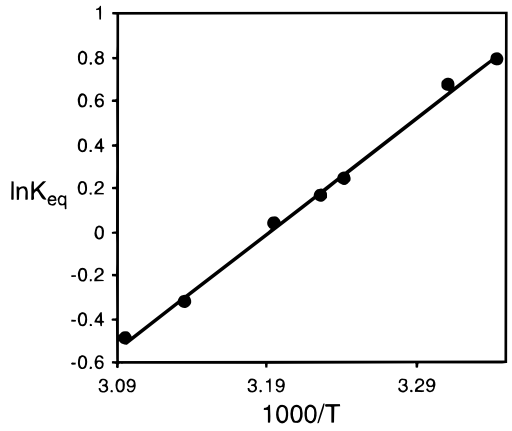


Figure 1. van't Hoff plot for the reaction of MeTAD with naphthalene (**2**).

Table 2. Thermal Reaction of MeTAD with Unsymmetrically Substituted Naphthalenes[a]

			yield of cycloadduct, %[c]	
naphthalene	solvent	K_{eq} [b]	**C$_A$**	**C$_B$**
6	$CDCl_3$	2.1	10	29
	$(CD_3)_2CO$	0.1	*d*	5
7	$CDCl_3$	4.5	6	43 (21)
	$(CD_3)_2CO$	0.1	*d*	4
8	$CDCl_3$	12.8	58 (39)	6
	$(CD_3)_2CO$	0.2	8	*d*
9	$CDCl_3$	110	86 (60)	*d*
	$(CD_3)_2CO$	0.8	21	*d*

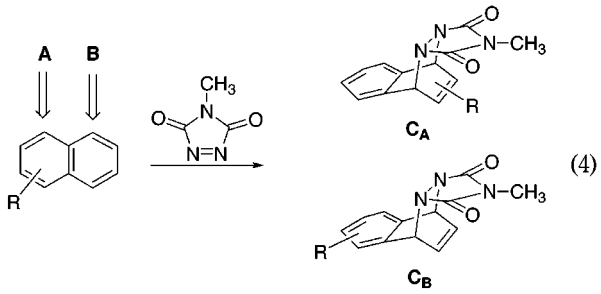
[a] Conducted at 29 °C with initial concentrations of naphthalene compound and MeTAD at 0.40 M each. [b] Determined by relative integrations of appropriate signals in the ^{1}H NMR spectrum. Values are reliable to within ±5%. [c] Determined by ^{1}H NMR spectroscopy. Values in parentheses are isolated yields. [d] No cycloadduct observed in the ^{1}H NMR spectrum.

for attainment of the maximum yield of cycloadduct to ensure that an equilibrium had been established. Reaction of MeTAD with 1,5-dimethylnaphthalene (**3**) afforded an equilibrium mixture of starting materials and cycloadduct **3C** with K_{eq} = 2.8 within 10 min. Reaction with 2,6-dimethylnaphthalene (**4**) required approximately 8 h to attain equilibrium although the exent of the equilibrium in favor of cycloadduct was much greater than that of compound **3**. When the reactions of **3** and **4** were conducted in acetone-d_6 as solvent, lesser equilibrium amounts of cycloadduct were observed. Reaction of MeTAD with 2,3,6,7-tetramethylnaphthalene (**5**) in $CDCl_3$ afforded the greatest yield of cycloadduct (89%) observed with all of the naphthalenes investigated requiring approximately 5 h of reaction time to reach equilibrium.

Cycloadducts **4C** and **5C** were isolated by quenching excess MeTAD in the reaction mixture with 2,3-dimethyl-2-butene and isolating the product via preparative thin-layer chromatography. The adducts were thermally labile and reverted quantitatively back to starting naphthalene in the presence of 2,3-dimethyl-2-butene as a trap for the liberated MeTAD. Adduct **3C** was especially labile, however, and resisted all of our efforts at its isolation employing preparative TLC as well as HPLC (see below). Rate studies on its cycloreversion indicated a half-life of approximately 9 min at 29 °C. A more detailed discussion of the cycloreversion process of the adducts is presented below.

C. Reaction of MeTAD with Unsymmetrically Substituted Methylated Naphthalenes. Unsymmetri-

cally substituted naphthalenes (**6**−**9**) present two nonequivalent aromatic rings as possible sites of attack by MeTAD. For the purposes of discussion and comparison, cycloadducts $\mathbf{C_A}$ and $\mathbf{C_B}$ will be defined as the [4 + 2]-cycloadducts resulting from reaction at the substituted ring (1,4-addition) and the unsubstituted ring (5,8-addition), respectively (eq 4). The results of these reactions are summarized in Table 2.



(4)

The reaction of MeTAD with 1-methylnaphthalene (**6**) in the dark at 29 °C in $CDCl_3$ was followed by periodic monitoring of the reaction using ^{1}H NMR spectroscopy. Within the first 10 min of reaction a 15% yield of cycloadduct $\mathbf{6C_A}$ was observed. As the reaction proceeded, however, the yield of $\mathbf{6C_A}$ dropped slightly while cycloadduct $\mathbf{6C_B}$ began to form. The yield of $\mathbf{6C_B}$ increased over the course of 24 h to a maximum yield of 29%, while $\mathbf{6C_A}$ was afforded with a final yield of 10%. No further change was observed with extended reaction times. The combined yield of cycloadduct corresponded to $K_{eq} = 2.1$ which was comparable to the equilibrium constant obtained with naphthalene itself ($K_{eq} = 2.0$), but slightly lower than that obtained with compound **3** ($K_{eq} = 2.8$). A lesser equilibrium amount of cycloadduct was observed when the reaction was conducted in acetone-d_6.

A similar trend was observed during the course of reaction of MeTAD with 1,4-dimethylnaphthalene (**7**). At very short reaction times (<2 h), cycloadduct $\mathbf{7C_A}$ was predominant (e.g., at $t = 0.5$ h, there was 11% $\mathbf{7C_A}$ and 7% $\mathbf{7C_B}$) while at longer reaction times cycloadduct $\mathbf{7C_B}$ was predominant. The final ratio of 7:1 for $\mathbf{7C_B}$ to $\mathbf{7C_A}$ after 24 h was greater than that observed for compound **6** (3:1).

Methyl substitution at the 2-position, such as in 2-methylnaphthalene (**8**) or 2,3-dimethylnaphthalene (**9**) favored formation of cycloadduct $\mathbf{C_A}$. At short reaction times (<0.5 h) the reaction of MeTAD with **8** afforded similar amounts of cycloadducts $\mathbf{8C_A}$ (9%) and $\mathbf{8C_B}$ (6%). The yield of $\mathbf{8C_B}$ increased to a maximum within 5 h (11%) and then began to decline to a final equilibrium value of 6%. The yield of $\mathbf{8C_A}$, however, continued to increase to a final equilibrium value of 58% over 48 h. Similarly, compound **9** afforded a final equilibrium value of 86% of $\mathbf{9C_A}$ with no observance of $\mathbf{9C_B}$ in the final equilibrium mixture (after 48 h), although cycloadduct $\mathbf{9C_B}$ was observed in small amounts (5−6% at its maximum) during the course of the reaction. When the reaction of **9** was conducted in acetone-d_6 a lower yield of $\mathbf{9C_A}$ (21%) was observed in the final equilibrium mixture than was observed in $CDCl_3$. There was no evidence (within limits of detection) for the formation of $\mathbf{9C_B}$ even at short reaction times.

Many of the cycloadducts were isolated in the same manner as was described previously for symmetrically substituted naphthalenes. Generally the regioisomeric cycloadducts $\mathbf{C_A}$ and $\mathbf{C_B}$ were not separable by analytical or preparative TLC using conventional SiO_2 plates. Although some separation was possible utilizing analytical SiO_2 plates that had been impregnated with $AgNO_3$, attempts at the corresponding preparative method failed. However, we were able to separate and purify the regioisomeric cycloadducts formed from compounds **8** and **9** utilizing preparative HPLC (see the Experimental Section). Regioisomers were readily differentiated by their characteristic vinyl and bridgehead proton absorptions in the ^{1}H NMR spectra. The vinyl protons of the cycloadducts consistently absorbed between 6.3 and 6.8 ppm while the bridgehead protons absorbed between 5.4 and 6.0 ppm. From the number and multiplicities of the various absorptions, assignment of structure to that of cycloadduct $\mathbf{C_A}$ or $\mathbf{C_B}$ was straightforward (see Experimental Section).

Unfortunately, the 1,4-adducts of all of the 1-methyl-substituted naphthalenes (**3**, **6**, and **7**) were too thermally unstable for isolation and complete characterization as they all experienced severe degradation during attempts at preparative TLC or HPLC. However, the ^{1}H NMR spectra of these cycloadducts (obtained via subtraction of the signals of the starting materials from the spectrum of the reaction mixture [see Experimental Section]) are completely consistent with the proposed structures. Furthermore, each of the adducts underwent quantitative cycloreversion to afford MeTAD and the starting naphthalene in the same manner as the more well-characterized cycloadducts. For these reasons we are quite confident in the correctness of the structures proposed.

D. Observation of Charge-Transfer Intermediates. Sheridan reported that UV−vis spectroscopy of CCl_4 solutions of MeTAD (0.6 mM) in the presence of an excess (0.6 M) of naphthalene revealed a new absorption band that was attributed to a 1:1 charge-transfer complex between the two reactants.[1] In our hands at these initial concentrations, a broad unstructured absorption with $\lambda_{max} = 378$ nm was observed. Sheridan further reported that selective irradiation of this complex (formed in only small amounts) led directly to cycloadduct formation, suggesting that the ground-state charge-transfer complex initiated at least one pathway toward product formation.[1] Charge-transfer complexes have been implicated as product precursors in a number of reactions between triazolinediones and electron-rich alkenes and aromatics.[1,10−12] Their intermediacy in reactions with aromatics has been readily ascertained by the formation of characteristic blood-red solutions upon mixing reactants.

Mixing of MeTAD with all of the substituted naphthalenes in chloroform resulted in the formation of deep blood-red solutions characteristic of MeTAD charge-transfer complexes. New absorptions in the UV−vis spectra attributed to charge-transfer complexes were observed when MeTAD (0.6 mM) was mixed with compounds **6** and **8** (each initially 0.6 M). The λ_{max} values for these absorptions (413 nM for **6** and 394 nM for **8**) were red-shifted from that observed for **2**, which was consistent with the presence of electron-donating methyl

(10) Hall, H. J. *J. Org. Chem.* **1983**, *48*, 1708.
(11) Hall, H. J.; Kaler, L.; Herring, R. *J. Org. Chem.* **1984**, *49*, 2579.
(12) Hall, H. J.; Jones, M. L. *J. Org. Chem.* **1983**, *48*, 822.
(13) The change in λ_{max} of the charge-transfer complexes of MeTAD with **6** and **8** relative to that of **2** (35 and 16 nm, respectively) correlate well with the corresponding shifts reported for the TCNE complexes of these same compounds (36 and 25 nm, respectively). See ref 18.

Table 3. Rate Constants for the Thermal Cycloreversion of Cycloadduct 2C[a,b]

solvent (ϵ)	temp/°C	rate/10^{-5} s^{-1}
C_6D_6 (2.3)	29	2.93 ± 0.26
$CDCl_3$ (4.8)	29	3.24 ± 0.02
$(CD_3)_2CO$ (21)	29	3.94 ± 0.03
CD_3CN (38)	29	5.34 ± 0.02
$(CD_3)_2SO$ (47)	29	4.92 ± 0.05
$CDCl_3$	35	6.01 ± 0.02
$CDCl_3$	40	12.4 ± 0.12
$CDCl_3$	45	23.3 ± 0.4
$CDCl_3$	50	43 ± 2

[a] Conducted according to the general procedure provided in the Experimental Section. [b] Each independent run was performed at least twice and the results averaged.

groups on the rings.[13] When this process was repeated with compound **7**, no charge-transfer complex and no free MeTAD were observed. Apparently, under these conditions, all of the MeTAD was quickly converted to cycloadduct.

2. Photochemical Reactions of MeTAD with Substituted Naphthalenes. Sheridan has reported the formation of cycloadduct **2C** in 40% isolated yield upon irradiation of a solution of MeTAD and **2** in CCl_4.[1] We repeated this reaction in acetone (in which only small amounts of **2C** were formed thermally) and isolated compound **2C** in 48% yield. Irradiation of an equimolar solution of MeTAD and compound **6** in CCl_4 afforded only cycloadduct $\mathbf{6C_B}$ in 38% yield after purification by preparative TLC.[14] There was no indication of the presence of cycloadduct $\mathbf{6C_A}$ in the ^{1}H NMR spectrum of the crude reaction mixture. Irradiation of an equimolar solution of MeTAD and **6** in acetone also afforded cycloadduct $\mathbf{6C_B}$ as the only detected product. Irradiation of an equimolar solution of MeTAD and **8** in CCl_4 afforded a 46% isolated yield of a mixture of cycloadducts $\mathbf{8C_A}$ and $\mathbf{8C_B}$ in a 58:42 ratio, respectively, reflecting a mild preference for reaction at the more electron-rich ring.[14] Finally, photochemical reaction of MeTAD with **9** in CCl_4 afforded a mixture of cycloadducts $\mathbf{9C_A}$ and $\mathbf{9C_B}$ in a ratio of 68:32, respectively. The ratio was little affected by solvent, affording a 60:40 ratio of $\mathbf{9C_A}$ to $\mathbf{9C_B}$ under identical conditions in the more polar solvent acetone.

3. Thermal Cycloreversion of Cycloadducts. Colorless solutions of purified cycloadducts began to turn pink within seconds of dissolution in $CDCl_3$ due to liberation of MeTAD from the cycloadduct in a retro Diels−Alder process. In the absence of a chemical trap for MeTAD, an equilibrium was again established between cycloadduct, naphthalene, and MeTAD which severely complicated attempts at measuring rates of cycloreversion. However, by conducting the reaction in the presence of a suitable trap for MeTAD, the forward cycloaddition process was halted, and the rate of cycloreversion was more conveniently measured. Thus, 2,3-dimethyl-2-butene was employed as a chemical trap for liberated MeTAD in all of the cycloreversion experiments studied.[9]

Rate constant determinations for the cycloreversion of **2C** were made at a series of temperatures (Table 3) using ^{1}H NMR spectroscopy. First-order kinetics over several half-lives were observed in all cases examined. Cycloadduct **2C** exhibited a half-life of 1.5 h in $CDCl_3$ at 40 °C,

(14) Sheridan (ref 1a) provided some initial experimental results on this reaction.

Table 4. Rate Constants for the Thermal Cycloreversion of Various Cycloadducts[a]

cycloadduct	rate/ 10^{-5} s^{-1}	rel rate
2C	3.24 ± 0.02	1
3C	132 ± 2	41
4C	2.41 ± 0.01	0.74
5C	1.79 ± 0.02	0.55
$\mathbf{6C_A}$	223 ± 2	69
$\mathbf{6C_B}$	1.99 ± 0.02	0.6
$\mathbf{7C_B}$	1.13 ± 0.02	0.35
$\mathbf{8C_A}$	1.09 ± 0.01	0.34
$\mathbf{8C_B}$	4.83 ± 0.02	1.5
$\mathbf{9C_A}$	0.55 ± 0.05	0.17
$\mathbf{9C_B}$	10.6 ± 0.1	3.3

[a] Conducted at 29 °C according to the general procedure provided in the Experimental Section. [b] Each independent run was performed at least twice, and the results were averaged.

Table 5. Calculated Rate Constants (k_2 in Scheme 1) for the Cycloaddition Reactions of MeTAD with Various Naphthalenes[a,b]

naphthalene	solvent	rate/10^{-5} s^{-1}
2	$CDCl_3$	6.6 (1)
	C_6D_6	0.9 (0.14)
	$(CD_3)_2CO$	0.4 (0.06)
	CD_3CN	0.5 (0.08)
3	$CDCl_3$	370
4	$CDCl_3$	4.3
5	$CDCl_3$	630

[a] Calculated using the K_{eq} values in Table 1 and the cycloreversion rates in Table 4. [b] In parentheses are provided the rates relative to the reaction conducted in $CDCl_3$.

which is qualitatively similar to that previously reported by Sheridan ($t_{1/2} \cong 45$ min at 40 °C in benzene).[1] Activation parameters for the cycloreversion process were determined to be $\Delta H^{\ddagger} = 23.6$ kcal/mol and $\Delta S^{\ddagger} = -0.8$ cal/deg·mol (at 25 °C). The rate was relatively insensitive to solvent polarity (Table 3), exhibiting a change in rate of a factor of less than 2 from the least polar solvent tested (benzene-d_6) to the most polar (dimethyl sulfoxide-d_6).

The rates of cycloreversion of several other cycloadducts in $CDCl_3$ were conducted in the same manner as described above, and the results are summarized in Table 4. As with **2C**, all of the cycloreversion reactions exhibited first-order kinetics.

Discussion

1. Thermal Reactivity. A. The Reaction Mechanism. Rate constants for the cycloaddition reactions of MeTAD with naphthalene in various solvents were calculated (Table 5) by assuming K_{eq} for the reaction to be simply the ratio of the rate constant for the cycloaddition process and the rate constant for the cycloreversion process. The relative rates are remarkably similar to those previously reported for the Diels−Alder cycloaddition of MeTAD with 1,3-cyclooctadiene (1:0.14:0.03:0.12 for CH_2Cl_2, benzene, acetone, and acetonitrile, respectively).[15] Recent theoretical studies on the cycloaddition of MeTAD to dienes suggested that for dienes in which an s-cis conformation is readily obtained (as is the case with the naphthalenes) a concerted cycloaddition pathway is favored.[16a] In several cases in which inter-

(15) Isaksen, H.; Snyder, J. P. *Tetrahedron Lett.* **1977**, 889.
(16) (a) Chen, J. S.; Houk, K. N.; Foote, C. S. *J. Am. Chem. Soc.* **1988**, *120*, 12303. (b) Jansen, F.; Foote, C. S. *J. Am. Chem. Soc.* **1987**, *109*, 6376.

Scheme 1

Mechanism A

$$\text{MeTAD + NAP} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [\text{MeTAD•NAP}]_{CT} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \text{Cycloadduct}$$

Mechanism B

$$[\text{MeTAD•NAP}]_{CT} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{MeTAD + NAP} \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} \text{Cycloadduct}$$

NAP = naphthalene or substituted naphthalene

mediates were involved in the cycloaddition process the intermediates proved trappable by the addition of external nucleophiles.[16] However, when the reaction between compound **3** and MeTAD was conducted in a solvent mixture of 3:1 $CDCl_3/CD_3OD$—a mixture that has been successful in the past for trapping dipolar intermediates involved in MeTAD reactions—no new adducts were observed so that a long-lived dipolar intermediate (e.g., a zwitterion or an aziridinium imide) may be ruled out as a possible intermediate.[16] Given this evidence, it is likely that the formation of cycloadducts occur via concerted [4 + 2] cycloaddition processes. The lower yields of cycloadduct obtained in the reaction of MeTAD with naphthalene and substituted naphthalenes in the more polar solvents (e.g., acetone) may be attributed to selective solvation of the polar triazolinedione which shifts the equilibrium toward starting materials.[17]

The role of charge-transfer intermediates in these reactions has proven difficult to elucidate. Two reasonable mechanisms for the reaction of MeTAD with naphthalene and substituted naphthalenes are presented in Scheme 1. The two proposed mechanisms differ in their description of the involvement of a charge-transfer complex in the overall reaction pathway. On one hand, the formation of charge-transfer complex intermediates of naphthalene and substituted naphthalenes with strong dienophiles such as MeTAD,[1] maleic anhydride,[6d] TCNE,[18] and singlet oxygen[19] have all been reported. In addition, reactions of MeTAD with several electron-rich aromatic compounds have been demonstrated to proceed via initial formation of charge-transfer complexes.[10−12] These observations would suggest the intermediacy of a charge-transfer complex as a fast equilibrium step prior to cycloadduct formation (mechanism A). Alternatively, the charge-transfer complex could exist simply as a nonproductive equilibrium process independent of the cycloaddition process (as in mechanism B). In support of this is the observation that the extent and rate of the reactions have little dependence on the ionization energy of the reacting naphthalenes. Unfortunately, therefore, given the available evidence we are unable at this point to satisfactorily distinguish between these two mechanistic possibilities.

B. Effect of Substitution on K_{eq}. The extent of formation of cycloadduct in the established reaction equilibria depends on the amount and pattern of substitution on the naphthalene ring. In all cases investigated, methyl substitution increased the amount of cycloadduct formed at equilibrium. Substitution at the 2-position appears to be more effective at promoting cycloadduct formation than does substitution at the 1-position (e.g., compare the K_{eq} values obtained for the compounds **3** and **6** with those of **4** and **8** in Tables 1 and 2). Monosubstitution at the 2-position of a single ring of the naphthalene nucleus is approximately equally effective at promoting cycloadduct formation as is monosubstitution at both rings (e.g., compare the K_{eq} values obtained for compound **4** with that of **8**). However, disubstitution on the same ring is more effective than is disubstitution on separate rings (i.e., compare the K_{eq} values obtained for compound **9** with that of **4**). It would therefore appear that the rings act essentially independent of each other in their reactions with MeTAD since greater electron-density at the reacting ring is more important a factor than is electron-density of the entire naphthalene core. This is further borne out when comparing the reactivity of compound **6** with that of **2**. Compound **6** contains an electron-donating methyl group while **2** does not. Despite this, the K_{eq} values for the two reactions (K_{eq} = 2.0 and 2.1 for **2** and **6**, respectively) are essentially equivalent because MeTAD is directed toward reaction with the unsubstituted ring of **6** (see discussion below for a rationalization of this behavior) where the distant methyl group apparently has little effect.

C. The Cycloaddition Process. Table 5 summarizes the calculated cycloaddition rates for reaction of MeTAD with symmetrically substituted naphthalenes in $CDCl_3$. Methyl substitution at the 1-position of the naphthalene nucleus as in **3** has a dramatic rate-enhancing effect and increases the rate of cycloaddition by a factor of 50 over that of **2**. Consistent with this was the observation that the reaction of **6** with MeTAD at short reaction times (<30 min) revealed an initial preference for attack of MeTAD at the substituted aromatic ring to afford adduct $\mathbf{6C_A}$. Similarly, in the reaction of MeTAD with compound **7**, adduct $\mathbf{7C_A}$ was the only product formed at short reaction times (<20 min). In both cases the electron-donating effect of the 1-methyl substituent activates the rings toward cycloaddition relative to the unsubstituted ring.

Substitution at the 1-position is more effective at increasing the rate of cycloaddition than is substitution at the 2-position as is observed from comparison of the rates of cycloaddition of MeTAD with compounds **3** and **4**. The poorer activating effect of the 2-methyl substituent is further illustrated by the reactions of MeTAD with compounds **8** and **9** where, unlike the reactions with **6** and **7**, effective competition by both rings for reaction with MeTAD occurred, and both regioisomeric adducts $\mathbf{C_A}$ and $\mathbf{C_B}$ were observed throughout the reactions.

D. The Cycloreversion Process. Examination of the thermal cycloreversion data reported in Tables 3 and 4 reveals some interesting trends. For example, it is apparent that methyl substitution at the 1- and 6-positions has a rate-accelerating effect on the reversion process (e.g., $\mathbf{6C_A}$ cycloreverts 69 times faster than **2C**, and $\mathbf{8C_B}$ 1.5 times faster) while methyl substitution at the 2- and 5-positions has a rate retarding effect (e.g., $\mathbf{8C_A}$ cycloreverts 2.9 times slower than **2C**, and $\mathbf{6C_B}$ 1.7 times slower).[20] In addition, the substituents exert their

(17) Burrage, M. E.; Cookson, R. C.; Gupte, S. S.; Stevens, D. R. *J. Chem. Soc., Perkin Trans. 2* **1975**, 1325.

(18) Frey, J. E.; Andrews, A. M.; Combs, S. D.; Edens, S. P.; Puckett, J. J.; Seagle, R. E.; Torreano, L. A. *J. Org. Chem.* **1992**, *57*, 6460.

(19) Aubry, J.-M.; Mandard-Cazin, B.; Rougee, M.; Bensasson, R. V. *J. Am. Chem. Soc.* **1995**, *117*, 9159.

(20) The stabilizing effect of a 2- and 5-methyl substituent toward cycloreversion has also been observed in a series of 1,4-endoperoxides formed via singlet oxygenation of 1,4-dimethylnaphthalene, 1,4,5-trimethylnaphthalene, and 1,2,4-trimethylnaphthalene. See ref 7a and also: Turro, N. J.; Chow, M.-F.; Rigaudy, J. *J. Am. Chem. Soc.* **1981**, *103*, 7218.

activating or deactivating effects in concert. For example, the relative rate of cycloreversion of **3C** was estimated by multiplying the relative rate of $\mathbf{6C_A}$ by that of $\mathbf{6C_B}$ to afford a value of 41 in excellent agreement with the experimentally determined value (Table 1). In the same manner, relative rates for the following cycloadducts were estimated: **4C** (0.51), **5C** (0.56), $\mathbf{7C_B}$ (0.36), $\mathbf{9C_B}$ (2.3), and $\mathbf{9C_A}$ (0.12) in reasonable agreement with the experimentally determined values. Using this method, the relative rate of cycloreversion of $\mathbf{7C_A}$ (a compound that we were unable to isolate) is estimated to be 4800 (i.e., 69[2]).

The rate-accelerating effect of a 1-substituent in the cycloreversion process may be accounted for by evoking a destabilizing steric interaction between the carbonyl group of the urazole ring with the naphthalene methyl substituent which would be severe for cycloadducts substituted at the 1-position but minimal for those substituted at the 2(3)-, 5(8)-, or 6(7)-positions. In support of this, molecular mechanics calculations (MM2) on compound $\mathbf{6C_A}$ indicated an unsymmetrical structure with a significantly longer C_1-N bond (1.481 Å) than the C_4-N bond (1.472 Å).[21] Modeling of $\mathbf{6C_B}$, $\mathbf{8C_A}$, $\mathbf{8C_B}$ suggested symmetrical structures, indicating the lack of steric interactions of the urazole ring with the methyl groups in these positions. Interestingly, asymmetry is not nearly so marked in the 1,4-cycloadduct of singlet oxygen and 1-methylnaphthalene (C_1-O bond = 1.435 Å and C_4-O bond = 1.431 Å) where a steric interaction is expected to be considerably less. This would explain why the reported singlet oxygenation of 1,4-dimethylnaphthylene afforded the 1,4-cycloadduct contrary to the regioselectivity of MeTAD. However, it was also reported that singlet oxygenation of a 1,4-dialkylnaphthylene containing particularly bulky alkyl groups *did* direct reaction to the 5,8-positions.[22] In addition, it was observed that the resulting oxygenated 1,4-cycloadduct of this naphthalene was 10 times less stable than the 5,8-adduct in qualitative agreement with our findings for the relative stabilities of the corresponding MeTAD adducts.

E. Conclusions. The observed equilibria established between each of the naphthalenes and MeTAD may be rationalized in terms of kinetic versus thermodynamic control of the reactions. For example, reaction of MeTAD with naphthalenes substituted at the 1-position afforded poorer equilibrium amounts of cycloadduct than naphthalenes substituted at the 2-position (e.g., compare the K_{eq} values for the reactions of compounds **3** and **4**) despite the superior rate-enhancing effect of a 1-substituent in the cycloaddition process. This is explained by the fact that whereas the 1-substituted methyl group kinetically favors formation of the 1,4-cycloadducts in the cycloaddition reaction, the same methyl group destabilizes these adducts in a thermodynamic sense as a result of the steric interaction with the urazole ring. Owing to the reversibility of the cycloaddition process, the thermodynamics of the system eventually predominates. However, a methyl substituent at the 2-position (e.g., **4**) kinetically favors formation of the 1,4-cycloadduct, is located far enough away to have little destabilizing steric interaction with the urazole ring of the product and retards cycloreversion of the adduct. All of these factors favor a greater K_{eq} value for **4** than that of **3** as is observed. For unsymmetrically substituted compound **8**, methyl substitution at the 2-position kinetically activates the A-ring toward cycloaddition relative to the B-ring and it also retards cycloreversion of the resulting adduct. Thus, reaction of **8** occurs predominantly at ring A. This effect is even more pronounced for the 2,3-dimethylated compound **9**. For compound **6**, however, despite the rate-enhancing effect of the 1-methyl group in the cycloaddition reaction, the resulting 1,4-cycloadduct is thermodynamically less stable that the 5,8-cycloadduct and reactivity is ultimately directed predominantly to the B-ring. A similar effect is observed for the 1,4-dimethylated compound **7**.

The reported reactions of maleic anhydride with substituted naphthalenes are also reversible processes, and demonstrated similar selectivities.[6c] Thus, reaction of maleic anhydride with 1-methyl and 1,4-dimethylnaphthalene afforded 5,8-cycloadducts while reaction with 2-methyl and 2,3-diethylnaphthalene afforded 1,4-cycloadducts.

2. Photochemical Reactivity. A viable reaction mechanism for the photochemical reaction of MeTAD with naphthalenes has already been proposed in which both singlet and triplet photoexcited MeTAD cycloadd to the naphthalene through the intermediacy of a contact radical-ion pair.[1] Unlike the behavior of MeTAD in its thermal reactions, MeTAD displayed only mild regioselectivity in its photochemical reactions with substituted naphthalenes. Reaction with compounds **8** and **9** yielded mixtures of isomeric cycloadducts with a small preference for reaction at the more electron-rich ring. Uncharacteristically, however, reaction with **6** afforded only product from reaction at the unsubstituted ring (i.e., $\mathbf{6C_B}$). However, this result may be attributed to a difference in cycloreversion rates of the two initially formed products. Reaction at the substituted ring would form cycloadduct $\mathbf{6C_A}$ which is less stable than that of $\mathbf{6C_B}$. Cycloreversion of the less stable adduct would continually diminish the concentration of $\mathbf{6C_A}$ while restocking the supply of MeTAD that may add to form the more stable adduct $\mathbf{6C_B}$. As the reaction progresses, therefore, adduct $\mathbf{6C_B}$ continues to accumulate while the concentration of $\mathbf{6C_A}$ is eventually depleted.

Experimental Section

Materials were obtained commercially and used without further purification unless otherwise specified. *N*-Methylurazole was oxidized to MeTAD according to literature procedure, and sublimed under vacuum for final purification.[23,24] Acetone used in photochemical reactions was dried over $CaCl_2$ and distilled just prior to use. ^1H NMR spectra were obtained at 60 MHz and ^{13}C NMR spectra at 15.1 MHz. The compound 2,3,6,7-tetramethylnaphthalene was obtained as a gift.

General Procedure for the Thermal Reactions of MeTAD with Naphthalene and Substituted Naphthalenes. To a solution of MeTAD (25 mg, 2.21 mmol) in 0.50 mL of deuterated solvent (see Tables 1 and 2) away from sources of direct light was added the naphthalene compound (2.21 mmol). The resulting solution was mixed well and transferred to a clean dry NMR tube which was wrapped with aluminum foil to prevent exposure to light. A ^1H NMR spectrum was generally taken immediately afterward, and the sample then placed in a water bath (usually set at 29 °C to

(21) MM2 calculations performed with CS Chem3D Pro, CambridgeSoft Corporation.

(22) Pierlot, C.; Aubry, J.-M. *Chem. Commun.* **1997**, 2289.

(23) Mallakpour, S. E. *J. Chem. Ed.* **1992**, *69*, 238.

(24) Cookson, R. C.; Gupte, S. S.; Stevens, I. D. R.; Watts, C. T. *Org. Synth.* **1971**, *51*, 121.

coincide with the NMR probe temperature). The sample was removed at regular intervals for analysis by ^{1}H NMR. If the cycloadduct was to be isolated, the sample was rinsed with 2 mL of CH_2Cl_2 into a separatory funnel containing 20 mL of CH_2Cl_2 and the excess MeTAD was quenched by the addition of a few drops of 2,3-dimethyl-2-butene. The organic layer was washed once with 20 mL saturated aq $NaHCO_3$, dried over Na_2SO_4, filtered, and concentrated. The solid residue was then purified by preparative TLC (20 × 20 cm SiO_2 plates) using an appropriate solvent mixture of ethyl acetate and hexane. Regioisomeric adducts were generally purified by preparative HPLC on a 25 cm × 10 mm 5 μm Supelcosil SPLC-Si column eluting with 10% 2-propanol in hexane at a flow rate of 3 mL/min (UV detector set at 255 nm). Purified products were characterized by IR and NMR spectroscopy.

1,4-Cycloadduct with Naphthalene (2C).[1] ^{1}H NMR ($CDCl_3$): δ 7.26 (m, 4H), 6.81 (dd, J = 3.1, 4.0 Hz, 2H), 5.81 (dd, J = 3.1, 4.0 Hz, 2H), 2.93 (s, 3H). IR (KBr): 1760, 1705, 1460 cm^{-1}.

1,4-Cycloadduct with 1,5-Dimethylnaphthalene (3C). ^{1}H NMR data were obtained by difference on an equilibrium mixture of MeTAD, **3**, and cycloadduct due to the thermal lability of the adduct which prevented its isolation (see Results section above): ^{1}H NMR ($CDCl_3$): δ 7.09 (m, 3H), 6.79 (dd, J = 5.7, 7.7 Hz, 1H), 6.44 (dd, J = 1.7, 7.7 Hz, 1H), 6.0 (dd, J = 1.7, 5.7 Hz, 1H), 2.83 (s, 3H), 2.43 (s, 3H), 2.3 (s, 3H).

1,4-Cycloadduct with 2,6-Dimethylnaphthalene (4C). ^{1}H NMR ($CDCl_3$): δ 7.2 (m, 3H), 6.30 (dp, J = 5.8, 1.8 Hz, 1H), 5.65 (d, J = 5.8 Hz, 1H), 5.47 (d, J = 1.8 Hz, 1H), 2.89 (s, 3H), 2.31 (s, 3H), 1.95 (d, J = 1.9 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 157.4, 144.1, 137.1, 133.7, 132.9, 127.1, 124.6, 123.5, 122.9, 61.4, 57.8, 26.0, 21.8, 19.8. IR (KBr): 1760, 1720, 1460 cm^{-1}.

1,4-Cycloadduct with 2,3,6,7-Tetramethylnaphthalene (5C). ^{1}H NMR ($CDCl_3$): δ 7.07 (s, 2H), 5.40 (s, 2H), 2.90 (s, 3H), 2.22 (s, 3H), 1.86 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 155.2, 134.0, 132.7, 123.6, 121.7, 60.0, 23.6, 17.8, 13.8. IR (KBr): 1765, 1710, 1455 cm^{-1}.

1,4-Cycloadduct with 1-Methylnaphthalene (6C$_A$).[1] ^{1}H NMR data were obtained by difference on a mixture of MeTAD, **6**, and **6A** (at short reaction times) due to the thermal lability of the adduct which prevented its isolation (see Results section above): ^{1}H NMR ($CDCl_3$): δ 6.78 (dd, J = 5.8, 7.7 Hz, 1H), 6.44 (dd, J = 1.7, 7.7 Hz, 1H), 5.73 (dd, J = 1.7, 5.8 Hz, 1H), 2.87 (s, 3H), 2.31 (s, 3H). The aromatic protons of compound **6A** were obscured by the aromatic protons of compound **6**.

5,8-Cycloadduct with 1-Methylnaphthalene (6C$_B$).[1] ^{1}H NMR ($CDCl_3$): δ 7.08 (br m, 3H), 6.81 (dd, J = 3.1, 4.0 Hz, 2H), 6.06 (dd, J = 3.1, 4.0 Hz, 1H), 5.77 (dd, J = 3.1, 4.0 Hz, 1H), 2.90 (s, 3H), 2.43 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 157.4 (2 C), 136.1, 134.6, 132.9 (2 C), 131.8, 128.7, 126.6, 120.8, 57.3, 53.8, 25.9, 18.3. IR (KBr): 1765, 1715, 1460 cm^{-1}.

1,4-Cycloadduct with 1,4-Dimethylnaphthalene (7C$_A$). ^{1}H NMR data were obtained by difference on a mixture of MeTAD, **7**, and **7A** (at short reaction times) due to the thermal lability of the adduct which prevented its isolation (see Results section above): ^{1}H NMR ($CDCl_3$): δ 7.25 (br s, 4H), 6.43 (s, 2H), 2.78 (s, 3H), 2.30 (s, 3H).

5,8-Cycloadduct with 1,4-Dimethylnaphthalene (7C$_B$). ^{1}H NMR ($CDCl_3$): δ 6.96 (m, 2H), 6.86 (dd, J = 4.1, 3.2 Hz, 2H), 6.06 (dd, J = 3.2, 4.1 Hz, 1H), 2.94 (s, 3H), 2.44 (s, 6H). IR (KBr): 1765, 1705, 1460 cm^{-1}.

1,4-Cycloadduct with 2-Methylnaphthalene (8C$_A$).[1] ^{1}H NMR ($CDCl_3$): δ 7.24 (m, 4H), 6.33 (dp, J = 5.3, 1.8 Hz, 1H), 5.73 (d, J = 5.3 Hz, 1H), 5.52 (d, J = 1.9 Hz, 1H), 2.92 (s, 3H), 1.97 (d, J = 1.8 Hz, 3H). ^{13}C NMR ($CDCl_3$): δ 157.3, 143.5, 137.0, 135.7, 126.9, 126.5, 124.4, 122.9, 122.3, 61.3, 57.6, 25.7, 19.5. IR (KBr): 1765, 1715, 1455 cm^{-1}.

5,8-Cycloadduct with 2-Methylnaphthalene (8C$_B$).[1] ^{1}H NMR ($CDCl_3$): δ 7.3−7.0 (m, 3H), 6.79 (dd, J = 3.2 Hz, 2H), 5.76 (br t, J = 3.8 Hz, 2H), 2.93 (s, 3H), 2.33 (s, 3H). IR (KBr): 1750, 1710, 1450 cm^{-1}.

1,4-Cycloadduct with 2,3-Dimethylnaphthalene (9C$_A$). ^{1}H NMR ($CDCl_3$): δ 7.22 (m, 4H), 5.47 (s, 2H), 2.88 (s, 3H), 1.87 (s, 6H). ^{13}C NMR ($CDCl_3$): δ 159.5, 138.6, 135.5, 128.8, 124.4, 64.4, 27.7, 18.0. IR (KBr): 1760, 1710, 1450 cm^{-1}.

5,8-Cycloadduct with 2,3-Dimethylnaphthalene (9C$_B$). ^{1}H NMR ($CDCl_3$): δ 7.10 (m, 2H), 6.78 (dd, J = 3.1, 4.0 Hz, 2H), 5.72 (dd, J = 3.1, 4.0 Hz, 2H), 2.93 (s, 3H), 2.23 (s, 6H). IR (KBr): 1770, 1705, 1450 cm^{-1}.

General Procedure for the Photochemical Reactions of MeTAD with Naphthalene and Substituted Naphthalenes. Solutions of MeTAD (50 mg) and the naphthalene compound (15 mM each) in CCl_4 or acetone were deoxygenated with a stream of dry nitrogen gas and irradiated through a sealed water-jacketed Pyrex flask using three 300 W incandescent bulbs until the solution became colorless (between 10 min to 1 h depending on the naphthalene compound). The solutions were concentrated, analyzed by ^{1}H NMR spectroscopy, and subjected to purification by preparative TLC or HPLC as described above.

General Procedure for the Kinetics Measurements of the Thermal Cycloreversions. A solution of cycloadduct (approximately 0.30 M), dichloroethane (1 equiv), and 2,3-dimethyl-2-butene (2 equiv) in 0.5 mL of $CDCl_3$ (or otherwise indicated solvent) in an NMR tube was heated in a waterbath maintained at the desired temperature. Periodic determinations of the extent of the reaction were made by examining the integration of the N-Me signals of the adduct (approximately δ 2.9) and the ene-product (δ 3.02) versus the signal of dichloroethane (δ 3.70) as an internal standard. Clean first-order kinetics was observed over at least 3 half-lives in all cases. An average value of two or more runs was taken for each rate constant.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. The NMR upgrade used in this work was made possible by the National Science Foundation's Division of Undergraduate Education (ILI-IP) through DUE Grant no. 9750684. The UV-vis spectrophotometer used in this work was made possible by the 1998 Camille and Henry Dreyfus Special Grant Program in the Chemical Sciences. We also thank Dr. Yoshio Aso of the Department of Applied Chemistry, Hiroshima University, for the generous gift of 2,3,6,7-tetramethylnaphthalene.

Supporting Information Available: ^{1}H NMR spectra for cycloadducts **2C**, **4C**, **5C**, **6C$_B$**, **7C$_B$**, **8C$_A$**, **8C$_B$**, **9C$_A$**, and **9C$_B$**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9906429