Supplementary Material Available: Details of the crystal structures of **1–3** including experimental procedures, ORTEP drawings, and tables of atomic positional parameters, bond distances, bond angles, anisotropic thermal parameters, hydrogen atom positions, and data collection parameters (33 pages); listing of observed and calculated structure factors for **1–3** (32 pages). Ordering information is given on any current masthead page.

Cyclobutene Photochemistry.[1] Partial Orbital Symmetry Control in the Photochemical Ring Opening of a Constrained Cyclobutene

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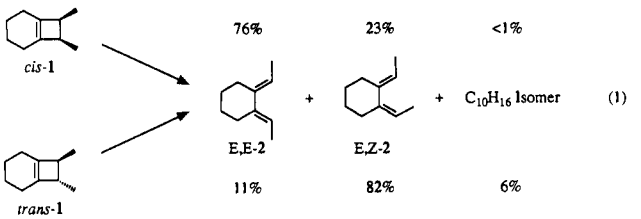
Direct photolysis of alkyl-substituted cyclobutenes in solution results in competing, nonstereospecific ring opening to the corresponding conjugated dienes and fragmentation to the corresponding alkene and alkyne.[3-8] We have recently suggested that a nonconcerted mechanism best accounts for the results observed to date,[5] but there are alternative pericyclic pathways that cannot be completely ruled out. For example, if excited-state ring opening occurs entirely by the disrotatory route, then formally forbidden products could result if competing internal conversion to vibrationally excited levels of the cyclobutene ground state occurs or if excited-state ring opening proceeds adiabatically to yield diene(s) in the first excited singlet state.[3,5] Ring opening by the latter mechanism would be expected to yield a distribution of isomeric dienes that is determined by the excited-state torsional decay characteristics of the specific diene isomer(s) formed in the primary (disrotatory) step. In principle, this mechanism can be tested by comparing the diene distribution obtained from cyclobutene ring opening with that expected on the basis of the independently characterized excited-state behavior of the dienes, *if* the stable conformations of the dienes are similar to the (planar s-cis) conformers that would be initially obtained upon concerted ring opening.[3,5] With this goal in mind, we have initiated a study of the photochemistry of a series of polycyclic cyclobutene derivatives and their isomeric, conformationally constrained (s-cis) conjugated dienes. Our initial results, which are reported herein, reveal a fascinating structural dependence on the stereospecificity and efficiency of this prototypical excited-state pericyclic reaction.

Direct photolysis of deoxygenated 0.02 M pentane solutions of *cis*- and *trans*-7,8-dimethylbicyclo[4.2.0]oct-1(6)-ene (**1**)[9] with 193- or 214-nm light[11] results in the formation of (*E*,*E*)- and (*E*,*Z*)-1,2-diethylidenecyclohexane (**2**)[12] and one additional $C_{10}H_{16}$ isomer in the yields shown in eq 1.[13] No other products were detected, in either case, in yields greater than 2% relative to that of the major product.[14] The relative product yields from photolysis of *cis*- and *trans*-**1** were independent of excitation wavelength in both cases.



Product quantum yields (Table I) were determined with the 193-nm light source. The photolysis of bicyclo[4.2.0]oct-7-ene, which yields *cis*,*cis*-1,3-cyclooctadiene with a quantum yield of 0.14 ± 0.02,[3] was used as actinometer. The additional isomer formed on photolysis of *trans*-**2** could not be isolated owing to its low yield.

Quantum yields for cis,trans photoisomerization of (*E*,*E*)- and (*E*,*Z*)-**2** were determined by using a 254-nm light source and the direct photoisomerization of *cis*,*cis*-1,3-cyclooctadiene as actinometer ($\phi_{cc \rightarrow ct} = 0.27$).[15] Under these conditions, direct photolysis of a deaerated 0.02 M pentane solution of (*E*,*E*)-**2** yields (*E*,*Z*)-**2** and *cis*-**1** with quantum yields of 0.27 ± 0.03 and 0.07 ± 0.01, respectively. Photolysis of (*E*,*Z*)-**2** under identical conditions yields (*E*,*E*)-**2** and *trans*-**1** with quantum yields of 0.28 ± 0.03 and 0.025 ± 0.005, respectively.[16] We note that ring closure of (*E*,*E*)- and (*E*,*Z*)-**2** occurs with >90% stereospecificity and with quantum yields similar to those reported for other s-cis dienes.[17] From the quantum yields for photoisomerization of **2**, the distributions of (*E*,*E*)- and (*E*,*Z*)-**2** that would be formed if ring opening of **1** occurs by the disrotatory adiabatic pathway can be calculated;[18] these are roughly (*E*,*E*)-**2**/(*E*,*Z*)-**2** = 2.4 and

Table I. Product Quantum Yields from Photolysis (193 nm) of Deaerated 0.02 M Pentane Solutions of *cis*- and *trans*-**1** at 23 °C[a]

cyclobutene	(*E*,*E*)-**2**	(*E*,*Z*)-**2**	$C_{10}H_{16}$ isomer
cis-**1**	0.57 ± 0.08	0.19 ± 0.03	
trans-**1**	0.09 ± 0.02	0.63 ± 0.09	0.05 ± 0.01

[a] Calculated from the slopes of concentration vs excitation dose plots, using the ring opening of bicyclo[4.2.0]oct-7-ene as actinometer.[3]

(1) Part 7 of the series. Part 6: see ref 7.

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(9) Compounds *cis*- and *trans*-**1** were synthesized as a 1:12 mixture by acetophenone-sensitized cycloaddition of 1,2,3,4-tetrahydrophthalic anhydride with 2-butene,[10] followed by hydrolysis and decarboxylation according to standard procedures.[4,5] The two isomers were separated and purified by semi preparative vapor-phase chromatography. Additional quantities of *cis*-**1** were prepared by direct photolysis (254 nm) of (*E*,*E*)-**2** (see ref 12). They were identified on the basis of their 500-MHz ^1H and ^{13}C NMR, IR, UV, and mass spectra. The ^1H NMR and UV spectra were particularly helpful in distinguishing between the two isomers.[4] *cis*-**1**: ^1H NMR (CCl_4) δ 0.94 (d, 6 H, J = 6.7 Hz), 1.62 (m, 4 H), 1.75 (d, 2 H), 1.86 (d, 2 H), 2.78 (complex q, 2 H); UV (pentane) λ_{max} 191 nm (ϵ 9400). *trans*-**1**: ^1H NMR (CCl_4) δ 1.08 (d, 6 H, J = 6.8 Hz), 1.60 (m, 2 H), 1.66 (m, 2 H), 1.77 (d, 2 H, $J \approx 16$ Hz), 1.85 (d, 2 H, $J \approx 16$ Hz), 2.19 (complex q, 2 H, J = 6.5 Hz); UV (pentane) λ_{max} 187 nm (ϵ 6300). Complete data will be reported in the full paper.

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(11) Photolyses employed the pulses of an ArF excimer laser (193 nm, ca. 15 ns, 20 mJ, 0.5 Hz repetition rate) or a 16-W zinc resonance lamp (214 nm). Solutions were deoxygenated prior to photolysis with a stream of dry nitrogen.

(12) Compound (*E*,*E*)-**2** was prepared by semipreparative (ca. 300 mg) gas-phase thermolysis of *trans*-**1** at 180 °C. It was isolated by preparative vapor-phase chromatography after bulb-to-bulb distillation of the reaction mixture: ^1H NMR (CCl_4) δ 1.58 (d, 6 H, J = 6.8 Hz), 1.59 (m, 4 H), 2.16 (br s, 4 H), 5.26 (q, 2 H, J = 6.8 Hz); UV (pentane) λ_{max} 221 nm (ϵ 7500). Compound (*E*,*Z*)-**2** was isolated from the direct photolysis of (*E*,*E*)-**2** (see ref 9): ^1H NMR (CCl_4) δ 1.60 (d, 3 H, J = 6.8 Hz), 1.60 (m, 4 H), 1.67 (d, 3 H, J = 6.8 Hz), 2.10 (m, 2 H), 2.74 (m, 2 H), 5.12 (complex m, 2 H); UV (pentane) λ_{max} 216 nm (ϵ 8200). Complete spectroscopic data for these compounds will be reported in the full paper.

(13) Product yields were determined from the slopes of product concentration vs excitation dose plots, which were linear over the 0.5–4% conversion range. No other products were observed in yields greater than 3%. Control experiments in which 0.02 M solutions of **1** containing 5×10^{-4} M *cis*,*cis*-1,3-cyclooctadiene were photolyzed (193 and 214 nm) to ca. 5% conversion demonstrated that secondary diene photolysis does not occur under these conditions (no isomerization of the cyclooctadiene occurs).[3,5,8]

(14) The clean formation of only ring-opening products from **1** is noteworthy. In the other cases that have been studied, fragmentation competes effectively with ring opening;[3-8] in the case of **1**, however, this process would yield products of relatively high energy and is thus suppressed.

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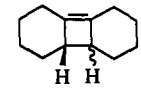
(*E*,*Z*)-**2**/(*E*,*E*)-**2** = 2.4 from *cis*- and *trans*-**1**, respectively. Comparison of these ratios with those observed from photolysis of *cis*-**1** [(*E*,*E*)-**2**/(*E*,*Z*)-**2** = 3.3] and *trans*-**1** [(*E*,*Z*)-**2**/(*E*,*E*)-**2** = 7.5] indicates that if ring opening occurs by the adiabatic disrotatory pathway, it does so only partially; in both cases, the relative yield of the formally allowed diene isomer is too high to be accounted for solely by this mechanism.

The degree of stereospecificity associated with photochemical ring opening of *cis*- and *trans*-**1** is substantially higher than that observed for any of the mono-,[3,4] bi-,[5-7] or tricyclic alkylcyclobutenes[8] that have now been studied, and the reaction is unusually efficient.[3,4,6] From both isomers of **1**, the major diene product is that of orbital symmetry allowed,[19] disrotatory ring opening. The present results should be compared to those obtained for the monocyclic analogues (*cis*- and *trans*-**3**) under similar conditions: these compounds afford mixtures of isomeric 3,4-dimethyl-2,4-hexadienes with only a slight preference for the formally allowed product(s).[4] The substantial difference between the ring-opening behavior of **1** and **3** is inconsistent with a nonconcerted mechanism for the reaction. In fact, the present results provide the strongest indication to date that *orbital-symmetry factors do play a role* in the photochemical ring opening of cyclobutenes.

3



4

Fully orbital symmetry controlled ring opening would be expected to proceed via a pathway involving partial disrotatory ring opening in the excited state followed by internal conversion to the ground state at a geometry corresponding to the pericyclic maximum in the ground state potential energy surface for disrotatory ring opening.[20] Evidence is available to suggest that the reaction is in fact initiated with disrotatory motions along the reaction coordinate, viz., the substantially higher quantum yield for ring opening of *cis*-tricyclo[6.4.0.0^{2,7}]dodec-1(2)-ene (*cis*-**4**) compared to that of the trans isomer.[8,21] Presumably, the ultimate formation of forbidden diene isomers[5-8] is due to some intervening process (of relatively minor importance in **1**) which diverts reactivity away from the "normal" pericyclic pathway. Possibilities include internal conversion to upper vibrational levels of ground-state cyclobutene, complete ring opening on the excited-state surface to yield singlet (vertical) excited dienes, or conversion to biradicaloid ground-state configurations.

The present results for **1** indicate that the overall course of the reaction, and its efficiency, can be altered as a result of specific structural features present in the cyclobutene (or perhaps the product dienes). One possible factor is ring strain (the activation energies for thermal ring opening of systems like **1** are 2-3 kcal/mol lower than those for the monocyclic analogues[17c]). However, the conformational rigidity of the product dienes or the alkyl substituents on the cyclobutene double bond might also play a role in altering the course of the reaction. Further studies of the effects of structural rigidity on the photochemical ring opening of cyclobutene derivatives are in progress.

Acknowledgment. We thank Dr. D. Hughes and Mr. B. Sayer (McMaster University) for acquiring high-field ^{1}H and ^{13}C NMR spectra. Acknowledgment is made to the Natural Sciences and Engineering Research Council of Canada for financial support of this research.

(18) For *cis*-**1**, the predicted ratio is given by $E,E/E,Z = (1 - \sum\phi_{EE\rightarrow})/\phi_{EE\rightarrow EZ}$, where $\phi_{EE\rightarrow EZ}$ is the quantum yield for photoisomerization of (*E*,*E*)-**2** to (*E*,*Z*)-**2** and $\sum\phi_{EE\rightarrow}$ is the sum of the quantum yields for all the products of photolysis of (*E*,*E*)-**2**.

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Unusual Dynamic Features of the *trp* Repressor from *Escherichia coli*

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The *trp* repressor from *Escherichia coli* (a 25-kD symmetric dimer) is a DNA-binding protein that regulates the tryptophan biosynthetic pathway.[1] In the absence of Trp, the repressor has a low affinity for DNA and the transcription of the three operons involved in the de novo synthesis of Trp can proceed. At high Trp concentration, a stable ternary complex between the repressor, two Trp molecules, and operator DNA is formed, and the transcription of the *trp* operon is inhibited. Both the crystal structures[2,3] and the NMR solution structures[4,5] for both the aporepressor (Trp free) and the holorepressor (Trp bound) are known, and a structure of a DNA-repressor complex has been reported[6] and challenged.[7] The structural differences between the apo and holo forms of the repressor are relatively small, and the precise mechanism of repressor action is as yet not completely understood.

In an effort to better define this mechanism, we report herein amide-proton exchange rate data which point to significant differences in dynamics *between* and *within* the two repressor species. In preliminary one-dimensional NMR studies, the backbone NH population of the aporepressor could be classified into three classes according to their exchange rates in D_2O: rapid (lifetimes <10 min at 35 °C) = ~40% of total, intermediate (30-90 min) = ~10%, and slow (24-48 h) = ~50%. This was somewhat surprising, as the protein is 70% helical, and conventional wisdom would lead one to expect relatively slow exchange rates for all backbone NH's in helices. Approximate individual exchange rates were measured in a series of heteronuclear multiple quantum (HMQC)[8] experiments on a uniformly ^{15}N labeled holorepressor for a period of 27 h after dissolving in D_2O. A plot of individual lifetimes ($\tau = 1/k$) as a function of residue number is shown in Figure 1A, along with the secondary structure (helices A-F) of the monomer chain.[5] The striking result is that the exchange rates of backbone NH's in the DNA-binding region (D and E) are 2 orders of magnitude faster than for the ABCF dimeric core of the molecule.

A detailed comparison of the exchange rates in the presence and in the absence of tryptophan was carried out in similar experiments on a repressor selectively labeled with [^{15}N]leucine. We chose to label Leu because the 19 Leu residues are distributed throughout the repressor sequence with at least one residue residing in each of the α-helices. Furthermore, with only 19 amide protons to monitor, even the 1D ^{15}N-edited spectra were readily interpreted. Figure 1B shows the lifetimes of the leucine NH's of the aporepressor measured in a series of 1D ^{15}N-edited proton spectra recorded at 35 °C for a period of 44 h after dissolving in D_2O. Several of the Leu NH's had almost completely exchanged within the 10 min it took to dissolve the sample, put it in the spectrometer, and acquire the first spectrum ($\tau \leq 0.2$ h). For the holorepressor many of the exchange rates were slow enough that a series of 2D

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