Table I. Rise Time of transient absorbance

complex	$\tau \times 10^{12}$, s	
	H_2O	D_2O
trans-$Cr(en)_2(NCS)_2^+$	16 ± 3 (4)[a]	24 ± 2 (2)
trans-$Cr(NH_3)_2(NCS)_4^-$	22 ± 2 (4)	11 ± 2 (3)
$Cr(NCS)_6^{3-}$	16 ± 2 (2)	12 ± 6 (2)

[a] The value in parentheses represents the number of measurements from which the standard deviation was calculated. In cases where an average is presented for only two measurements, the uncertainty reflects arbitrarily twice the difference between the two experimental values.

reasonably well with previously reported values.[12,16b] The rise times of excited-state absorbance (ESA) were independent of probe wavelength and are listed in Table I. By measuring the rate of appearance of excited singlet absorbance (S_1) in Rhodamine 6-G (6 ± 2(4) ps), we established that our measured rise times of transient absorbance observed for the Cr(III) complexes were within our experimental time resolution and also provided an independent measure of the width of our picosecond pulse. Rate plots were linear for 1 to 2 lifetimes and were not corrected for the influence of the pump pulse.

There are two notable features apparent in the data in Table I. First, there is very little change in the transient rise time from one complex to another. The transient has been assigned as the lowest doublet excited state on the basis of the close similarity in the lifetimes for the decay of ESA and the decay of phosphorescence intensity in *trans*-$Cr(NH_3)_2(NCS)_4^-$ at low temperature.[16b] If the rise in ESA reflects intersystem crossing (ISC) from the vibrationally equilibrated first excited quartet state to the doublet state, the lifetime might be expected to be dependent on the energy gap between the minima in the doublet and the excited quartet potential energy surfaces. The data show little or no dependence on 10 *Dq*, the value of which should reflect that gap. An alternative interpretation is consistent with evidence reported by Kane-Maguire et al.[18] that intersystem crossing may compete with vibrational equilibration in Cr(III) complexes. Since the energy of the lowest doublet is relatively insensitive to 10 *Dq*, the rise time may reflect a combination of intersystem crossing from the initially formed quartet state to the doublet state and relaxation within the doublet manifold from the vibrational level isoenergetic with the Franck-Condon state produced in the excited quartet at the energy of the laser pulse (1.88 μm^{-1} or 530 nm). The energy separation between the initially attained vibrational level in the doublet and the zeroth vibrational level would then be relatively independent of the nature of the complex. Consequently, the observed lifetime might not be sensitive to changes in 10 *Dq* if intersystem crossing were comparable with or faster than vibrational decay. A similar explanation was used recently to explain excited-state relaxation in *trans*-$Cr(NH_3)_2(NCS)_4^-$.[13] If this is the correct model, the observed lifetime might depend on the energy of the Franck-Condon state in the excited quartet manifold. Picosecond studies as a function of excitation wavelength would be helpful in examining this possibility.

Second, there is a modest but definite isotope effect. The expected effect of D_2O on the rate constant (a reduction) is observed, however, only in the case of *trans*-$Cr(en)_2(NCS)_2^+$. The reverse effect is observed in *trans*-$Cr(NH_3)_2(NCS)_4^-$ and perhaps in $Cr(NCS)_6^{3-}$, the rates in these cases being accelerated. Isotope exchange for coordinated ammine protons may be responsible for changes in the measured lifetimes, but still would be expected to lengthen quartet lifetimes in each complex regardless of whether the perturbarion was inner or outer sphere. However, the opposite effects on doublet risetimes may reflect a charge dependence similar to that reported in the photochemistry of *trans*-$Cr(en)_2NCSF^+$ and *trans*-$Cr(NH_3)_2(NCS)_4^-$,[19] and in photophysical studies of ESA decay on the nanosecond time scale for $Cr(NH_3)_5NCS^+$, *trans*-$Cr(NH_3)_2(NCS)_4^-$, and $Cr(NCS)_6^{3-}$.[12] Additional studies of the medium dependence of excited-state decay in Cr(III) complexes are underway.

In conclusion, we have shown that the rise time of excited-state absorbance is measurable and longer than the earlier estimate of <10 ps. We believe that the available evidence favors the doublet-state assignment for the observed ESA. However, the precise details of the relaxation mechanism from the initially excited quartet state to the doublet manifold remain to be unraveled.

Acknowledgment. The authors gratefully acknowledge discussions with Professors G. B. Porter and A. D. Kirk and also thank them for samples of [*trans*-$Cr(en)_2(NCS)_2]ClO_4$ and [*trans*-$Cr(en)_2(NCS)_2]Cl$. This work was supported by the U.S. Army Research Office under Grant DAAG 29-76-9-0275.

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Intramolecular Diels–Alder Reactions. A New Entry into Bridgehead Bicyclo[3.*n*.1]alkenes

Sir:

Intramolecular Diels–Alder reactions have proven to be of considerable value in the synthesis of complex polycyclic molecules.[1] When the diene and dienophile are joined at the 2 position of the diene, the reaction can result in formation of a bridgehead alkene[2] (eq 1). We are not aware of any examples


(1)

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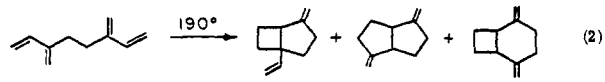
of this reaction to date, although several reports of retro-Diels–Alder reactions that involve precursors to highly strained bridgehead alkenes have recently appeared.[3] We report here the first examples of intramolecular Diels–Alder cycloadditions that result in formation of bridgehead alkenes.

We have previously found that thermal rearrangement of 3,6-dimethylidine-1,7-octadiene (**1**) at 190 °C results in the formation of bicyclic dienes **2–4**[4] (eq 2). When tetraene **1** is



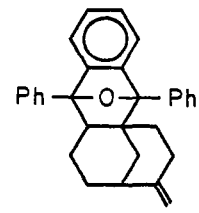
(2)

1 2 3 4

subjected to more severe conditions (7 s, 400 °C), two new products, **5** (9.5%) and **6** (11.8%), are formed in addition to bicyclic dienes **2–4**.[5] The structures of these compounds were established as follows. Bridgehead diene **5**, 6-methylidinebi-

5 6

cyclo[3.3.1]non-1-ene, has a characteristic pungent odor and exhibits the following spectral properties: ^{1}H NMR ($CDCl_3$) δ 5.47 (t, 1 H, J = 6 Hz), 4.65 (br s, 2 H), 2.9–1.0 (m, 11 H); IR (CS_2) 3065, 3020, 2945-2855, 1633, 890, 883, 840, 830, 818, 799, 790 cm^{-1}; UV (hexanes) λ_{max} 206 nm. Compound **5** reacts readily with diphenylisobenzofuran to produce an adduct (**7**, stereochemistry was undetermined) which no longer



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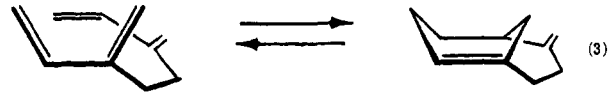
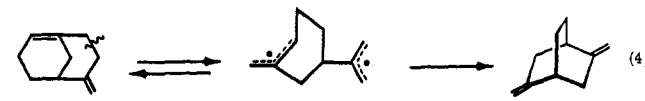
exhibits a triplet at δ 5.47. The ^{1}H NMR spectrum of **6** is deceptively simple: ^{1}H NMR ($CDCl_3$) δ 4.77 (d, 2 H, J = 1.8 Hz), 4.62 (d, 2 H, J = 1.8 Hz), 2.36 (s, 6 H), 1.65 (s, 4 H). The carbon spectrum confirms the presence of a C_2 axis and two exocyclic methylenes: ^{13}C NMR ($CDCl_3$) δ 155.5, 105.8, 36.7, 36.2, 26.6. The IR spectrum (CS_2) (3062, 2930, 2855, 1651, 908, 876 cm^{-1}) exhibits many similarities to the spectrum reported for 2-methylenebicyclo[2.2.2]octane.[6] Final confirmation was obtained by treatment of 2,5-dioxobicyclo[2.2.2]-octane[7] with 2 equiv of methylenetriphenylphosphorane; the resulting product was indistinguishable from **6**. Compound **6** was recovered unchanged when it was subjected to the reaction conditions. Similar treatment of **5**, however, resulted in the formation of **6** (83%) together with smaller amounts of **3** (9%) and **1** (8%). Bridgehead diene **5** is the product of an intramolecular Diels–Alder cycloaddition (eq 3). Although there are



(3)

1 5

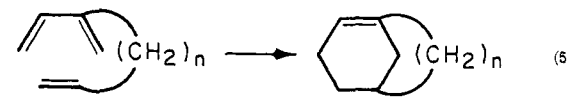
two stereoisomers of **6**, the constraints imposed by the intramolecularity of the cycloaddition predict exclusive formation of the more stable Z isomer (*cis*-cyclohexene and *trans*-cyclooctene) as shown in eq 3. Accumulation of bridgehead alkene (**5**) under the reaction conditions is precluded because it is rapidly partitioned between starting material (**1**) and thermodynamically more stable bicyclooctane **6**. The rearrangement, **5** → **6**, can be formally viewed as a stepwise cleavage of the bond between carbons 7 and 8 to produce diradical **8** which then undergoes transannular ring closure to **6** (eq 4).



(4)

5 8 6

To establish if the Diels–Alder route to bridgehead alkenes is merely a novelty associated with tetraene **1** or rather a method of general synthetic utility, the following studies were undertaken. Inspection of the molecular model of **1** indicates that, in all likely conformations for Diels–Alder reaction, simultaneous coplanarity of both diene units would be difficult; thus, activation of the dienophile by conjugation with the adjacent methylidine group is probably not a requirement for reaction. This was confirmed by a study of 3-methylidine-1,7-octadiene (**9**).[8] Thermolysis of **9** (8 s, 405 °C) results in formation of the prototype anti-Bredt compound, bicyclo[3.3.1]non-1-ene (**10**) in 16% yield[9] (eq 5). The product,

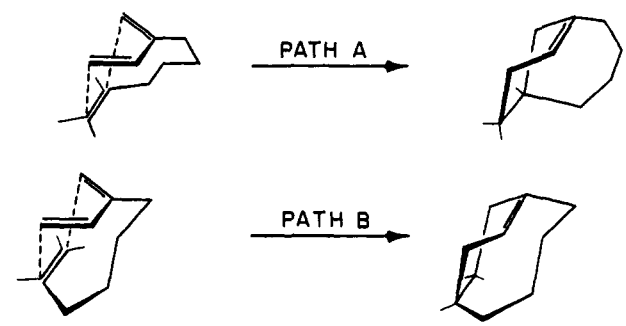


(5)

9 n = 3
11 n = 4
10 n = 3
12 n = 4

isolated by preparative VPC, was characterized by comparison of spectroscopic properties (NMR, UV, IR) with those reported in the literature,[10] and by preparation and characterization of its diphenylisobenzofuran adduct. In a similar manner, 3-methylidine-1,8-nonadiene (**11**)[8] (5 s, 455 °C) gives bicyclo[4.3.1]dec-1(9)-ene (**12**) in 55% yield.[11] Interestingly, two stereoisomeric transition states are accessible to triene **11**, each of which leads to a different product (Scheme I). Con-

Scheme I



firmation of the proposed structure of the major product was obtained by catalytic hydrogenation of **12**; the ^{13}C NMR spectra exhibits six distinct carbon resonances consistent with the expected product, bicyclo[4.3.1]decane.[12] The major product from this cycloaddition is derived, therefore, from the conformation that produces the less strained *trans*-cyclononene ring (path A) rather than one that produces a *trans*-cyclooctene ring (path B).

The preceding examples establish that intramolecular Diels–Alder cycloadditions provide one of the quickest and most direct synthetic entries into bridgehead bicyclo[3.n.1]-alkenes.[2,14] The scope of these reactions and the chemistry of bicyclo[3.n.1]alkenes are currently under investigation.

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(5) A flow apparatus consisting of a 30 cm × 10 mm quartz tube heated by a cylindrical tube furnace was employed for all high temperature work. The alkenes were swept through the hot zone by a stream of dry nitrogen at atmospheric pressure. Reactions were monitored by VPC using an internal standard. The complete product distribution, after correction for unreacted starting material (33.7%), was as follows: **2**, 4.1%; **3**, 65.1%; **4**, 9.5%; **5**, 9.5%; **6**, 11.8%.
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(9) The yield was determined by VPC and represents the fraction of the total pyrolysis mixture (84% mass balance). In addition to **10** and starting material (81%), 3% of an as yet unidentified material is also formed. Bridgehead diene can be isolated in 11% overall yield based upon starting triene. The yield of **10** is not an equilibrium value. When **10** is subjected to the reaction conditions, triene **9** was formed in 51% yield. We are currently attempting to obtain equilibrium values for this system to establish the thermodynamic relationship between reactants and products.
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(11) Bicyclo[4.3.1]dec-1(9)-ene (**12**): ^{1}H NMR δ ($CDCl_3$) 5.63 (t, 1 H, J = 5 Hz), 2.4–0.8 (m, 15 H); IR (CS_2) 3030, 2995, 2840, 1650, 1435, 1355, 1210, 1283, 1272, 1010, 987, 970, 925, 895, 825, 795, 788, 682 cm^{-1}; UV (hexane) λ_{max} 204 nm: P. A. Gassman, G. M. Lein, Jr., and R. Yamaguchi, *Tetrahedron Lett.*, 3113 (1976). A small amount (<3%) of an as yet unidentified product is also observed.
(12) Bicyclo[4.3.1]decane: ^{13}C NMR ($CDCl_3$) δ 34.55, 32.66, 32.01, 30.37, 27.86, 19.31; mp 94.5–95.5 °C (lit.[13] 95–97 °C).
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A New Fluorescence Technique to Measure the Permeation of Water Molecules across Bilayer Membranes

Sir:

The influence of proteins, lipid composition, and various additives on the permeability of water molecules across biological membranes is still not understood in great detail. This is partly due to a lack of versatile techniques allowing routine measurements. The existing methods (NMR,[1-5] osmotic gradient,[6-13] and measurements of the permeating tritium-labeled water across cellular membranes in a fast-flow tube[8,12,14,15]) have both merits and disadvantages. The new method to be described is especially applicable to phospholipid vesicles, and uses only minimal quantities of material both in volume and concentration so that routine measurements should be possible. The method is based on the solvent-isotope effect of the fluorescence quantum yield of indole chromophores.[16-20] The physical reason why, e.g., indole chromophores, have higher quantum yields in D_2O than in H_2O is still open for discussion[16-19] and will not be persued here. With few exceptions[20,21] the solvent-isotope effect of the fluorescence quantum yield has been overlooked by most molecular biologists. When combined with fast mixing devices, this effect offers a broad field of application; the permeation of water molecules across biological membranes and the accessibility of endogeneous tryptophan residues to water molecules[20] under various experimental conditions are just two examples.

The adaption of this isotope effect to measurements of water permeation across vesicular bilayers includes the following steps: (i) the preparation of an aqueous (H_2O) vesicle solution containing, e.g., tryptamine (3-(2-aminoethyl)indole), both intra- and extravesicularly, (ii) the removal of the extravesicular tryptamine either by dialysis or by chromatographic methods, and (iii) the fast mixing of this H_2O vesicle solution with an equivalent D_2O solvent while the tryptamine fluorescence is monitored. As a consequence of the fast mixing of these solutions the observed fluorescence intensity will first drop within the short mixing time owing to the dilution of the chromophore containing vesicle solution. With increasing exchange of the intravesicular H_2O by the extravesicularly offered D_2O molecules, the fluorescence intensity will then increase again until it reaches a plateau reflecting a statistical distribution of the H_2O and D_2O molecules around the chromophore. Thus, the time course of this increase in the fluorescence intensity becomes a direct measure of the permeating D_2O (or HDO) molecules.

The above-outlined idea has been realized by the following preliminary experiments. Dipalmitoylphosphatidylcholine (~10 mg/mL) together with 0.3 M tryptamine HCl were sonified in aqueous (H_2O) 20 mM $CaCl_2$ at neutral pH above the crystalline to liquid-crystalline phase transition temperature (T_c). Tryptamine HCl was chosen instead of the amino acid tryptophan because of the higher water solubility of tryptamine. As result of the sonication above T_c, usually small and unilamellar vesicles are formed which are almost impermeable to ions at moderate temperatures.[22,23] Subsequently the extravesicular tryptamine was removed either by dialysis (24–48 h at $T < T_c$) against 20 mM $CaCl_2$ or the vesicle solution was passed through a preequilibrated sepharose 4B column[24] and eluted with 20 mM $CaCl_2$ also below T_c, or both methods were employed. Except for a small leakage the extravesicular tryptamine molecules were almost quantitatively removed. This vesicle solution was diluted (1:5 to 1:20) and then put into syringe 1 of a stopped-flow apparatus. Syringe 2 contained 20 mM $CaCl_2$ in D_2O. After thermal equilibration the two solutions were rapidly mixed within 1 ms while the time-dependent fluorescence intensity was recorded (λ_{ex} 280, 295 nm, λ_{em} >340 nm by cut-off filter, or 340 ≤ λ_{em} ≤ 400 nm by band-pass filter). A typical record (using a transient recorder) of these experiments together with the experimental setup is shown in Figure 1. Additionally, Figure 1 contains a plot of the logarithm of the fluorescence intensity vs. time, starting after the mixing period. The latter curve reveals that the fluorescence intensity reaches its new equilibrium value in an almost single-exponential manner, so that the rate constant k describing the permeation of D_2O (HDO) can easily be deduced. Electron micrographs (by staining methods) show rather large vesicles with a radius r of ~5000 Å; thus, a permeability coefficient P_d (according to $P_d = r(k/3)$) of 1.4×10^{-4} cm s^{-1} is calculated which corresponds well with the data measured by the NMR relaxation technique on unilamellar vesicles.[2]

The validity of the above method and the interpretation of the resultant data in terms of a water (here D_2O, HDO) permeation are based on the following assumptions.

(i) The tryptamine molecules are entrapped within the aqueous phase of the intravesicular compartment. This point raises the critical question about the location and permeability of the probe molecule. The experiments were carried out at neutral pH where tryptamine is positively charged and the lipids are zwitterionic. As the pK values are far from neutral,

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