change of the carbonyl stretching frequency (by up to 40 cm^{-1}),[10] whereas the formation of a bicyclic hemiaminal ether with an N—C bond length of 1.50 Å[11] results in an additional upfield shift of 84 ppm.[12] Within this frame of reference, the 105-ppm upfield shift observed for the adducts, e.g., **3**, indicates that one of the Dabco nitrogen atoms has moved to within bonding distance. This assignment is further supported by a comparison with the corresponding hydrate and methanolate[13] which have very similar chemical shifts (Table I).

The interaction between ketone and amine does not result in quantitative adduct formation as documented, for example, by the observation of two distinct ^{19}F resonances. The ratio of ketone to adduct signals shows the concentration and temperature dependence typical for an equilibrium. The NMR data gave a considerably better fit for the 1:1 adduct than for a species with other than 1:1 stoichiometry. These results may not completely eliminate the possibility of 2:1 adducts, particularly not for very high concentrations of one of the reactants, but they render them unlikely under the conditions of our experiments.

For the pair, trifluoroacetophenone-Dabco, the observed ratio of CF_3 resonances indicates an equilibrium constant, $K_{292} = 1.5$ L/mol, and the temperature dependence of the equilibrium constant between 257 and 337 K yields the thermodynamic parameters, $\Delta H° = -9.3$ kcal/mol and $\Delta S° = -32$ eu. The adducts of trifluoroacetophenone with 1-azabicyclo[2.2.2]octane (Abco) and triethylamine (TEA) are less stable than the adduct with Dabco, with equilibrium constants, $K_{292} = 0.6$ L/mol for the abco adduct and $K_{292} = 0.07$ L/mol for the TEA adduct. The reduced stabilities of these complexes precluded accurate determinations of $\Delta H°$ and $\Delta S°$ by the NMR method.

Thermodynamic parameters for all three adducts were determined calorimetrically by thermometric titration procedures[14] in acetonitrile solution.[15] The results follow: Dabco adduct, $K_{298.2} = 0.893$, $\Delta H° = -9.03$ kcal/mol, $\Delta S° = -30.5$ eu; Abco adduct, $K_{298.2} = 0.362$, $\Delta H° = -8.73$ kcal/mol, $\Delta S° = -31.3$ eu; TEA adduct, $K_{298.2} = 0.037$, $\Delta H° = -8.66$ kcal/mol, $\Delta S° = -35.6$ eu. On the basis of these results, an electronic stabilizing factor involving lone-pair interactions[16] in the Dabco complex is not discernible. The relative equilibrium constants of the Dabco and Abco adducts can be attributed to a statistical factor, whereas the much lower stability of the TEA complex can be ascribed to unfavorable steric factors.

Although the thermodynamic stabilities of the zwitterionic adducts are similar to those of molecular complexes such as the π complexes between aromatic hydrocarbons and ketones,[17] the NMR spectra of the two types of adducts reveal fundamental differences. The π molecular complexes show weighted averages of the chemical shifts of free and complexed reactants indicating that the barrier between the reactants and the complex is low and that the rate of equilibration is fast on the NMR time scale. In contrast, the observation of separate signals for the ketone and the zwitterionic adducts indicates that, in these systems, the rate of exchange is slow and the barrier between reactants and adduct is high. Further experiments are being carried out to investigate similar adducts in related systems and to determine the time scale of the association/dissociation processes.[18]

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Experimental Evidence for Nonsquare Cyclobutadiene as a Chemically Significant Intermediate in Solution

Sir:

After decades of dispute[1] most experimentalists and theoreticians now seem to agree on a D_{2h} (rectangular) singlet description for the ground state of cyclobutadiene. A crucial experiment leading to the new accord was the matrix isolation infrared study of Masamune et al.[1z] This work showed that cyclobutadiene and cyclobutadiene-d_4, prepared from a variety of precursors, had infrared spectra which were inconsistent with a D_{4h} equilibrium geometry but were consistent with a D_{2h} structure.

We felt that it would be desirable to obtain independent experimental support for nonsquare cyclobutadiene as a chemically significant[2] intermediate in solution. Such an experiment might be a progenitor to the determination of the energy difference between D_{2h} and D_{4h} geometries of singlet cyclobutadiene as well as serving to demonstrate that non-

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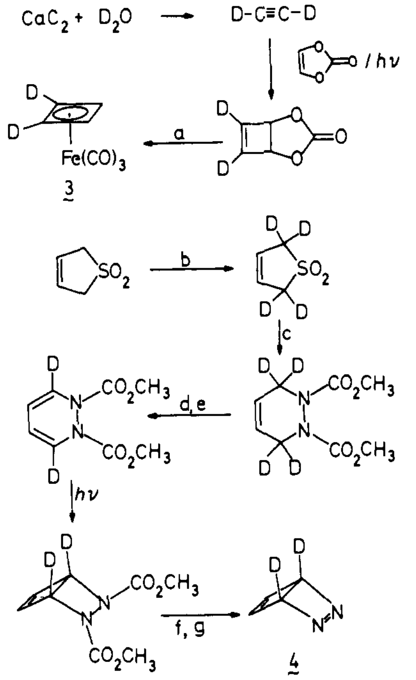

Figure 1. (a) $Na_2Fe(CO)_4$; (b) K_2CO_3/D_2O; (c) $CH_3CO_2N{=}NCO_2CH_3/\Delta$; (d) *N*-bromosuccinimide; (e) 2,6-lutidine; (f) $KOBu^t/Me_2SO$; (g) $Pb(OAc)_4$.

square equilibrium geometry is an intrinsic property of cyclobutadiene and not just an artifact of matrix isolation.[3] In this communication we describe an experiment which fulfills the second goal and promises to fulfill the first.

If cyclobutadiene does indeed have a D_{2h} geometry, then its labeled analogue cyclobutadiene-*1,2*-d_2 would have two isomers (**1** and **2**, Figure 2). Barring an unprecedented isotope effect, **1** and **2** would be expected to have virtually identical concentrations at equilibrium. The crucial observation for the present experiment is that, among the possible precursors to cyclobutadiene-*1,2*-d_2, there is one which would necessarily produce **1** and **2** in their equilibrium proportions while another could, in principle, generate a nonequilibrium distribution of the two isomers. These precursors are cyclobutadiene-*1,2*-d_2 iron tricarbonyl (**3**) and 2,3-diazabicyclo[2.2.0]hexa-2,5-diene-*1,4*-d_2[4] (**4**), respectively. We have prepared both by the routes outlined in Figure 1.[5,6]

Since the ring in cyclobutadiene iron tricarbonyl is known to be square,[7] **3** must necessarily give equal proportions of **1** and **2** upon oxidation. By contrast, only coincidence would allow **4** to give equal proportions of **1** and **2**, provided that both C–N bonds break simultaneously. A $_\sigma2_s + {_\sigma2_s}$ mechanism for deazetation of **4** would give exclusively **2** as the initial product while the more probable $_\sigma2_s + {_\sigma2_s} + {_\pi2_s}$ would give exclusively **1** (Figure 2).

If **1** and **2** could be trapped in a concerted two-bond-forming process,[8] then the ratio of **1**:**2** would be reflected in the deuterium distribution of the products, provided that the rate of trapping was greater than the rate of **1** ⇌ **2** interconversion. Our experimental results confirm this hypothesis.

When cyclobutadiene is trapped with an acrylic acid derivative, the resulting endo adduct can be iodolactonized. The iodolactone shows $J \simeq 6$ Hz between H_a and H_b but $J \simeq 0$ Hz between H_b and H_c in the ^1H NMR spectrum (Figure 3).

Of the four label-isomeric iodolactones derived from cyclobutadiene-*1,2*-d_2, only two (**5a** and **5c**) have a proton at the site corresponding to H_b. In **5c** this proton appears as a 6-Hz doublet in the NMR, whereas in **5a** it is a singlet, somewhat broadened by residual coupling to the deuterium at the H_a site. The ratio of singlet to doublet components for the H_b proton resonance thus provides a measure of the ratio of **5a**:**5c**. Since **5a** comes originally from **1**[8] while **5c** comes from **2**, measurement of the **5a**:**5c** ratio can provide important information about the relative rates of trapping and **1** ⇌ **2** interconversion, provided that **1** and **2** are generated in a nonequilibrium distribution.

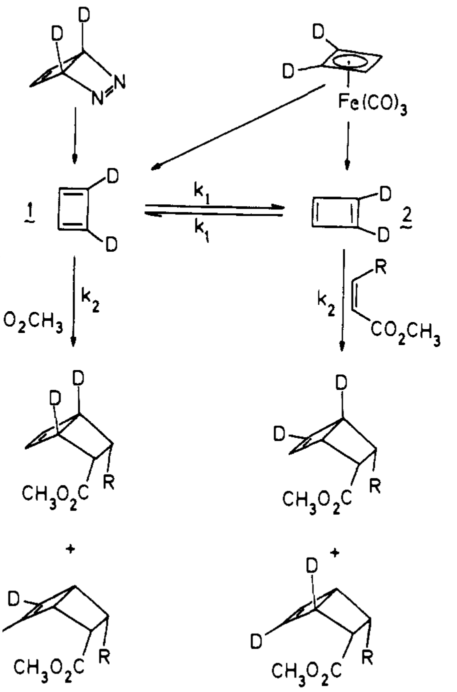

Figure 2.

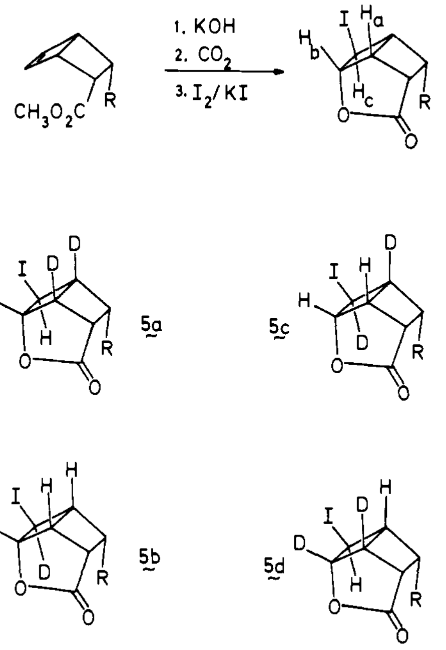

Figure 3.

When **4** is generated and deazetized in the presence of 3.6 M methyl acrylate at 10 °C, the iodolactones (Figure 3, R = H) derived from the resulting adducts show a "triplet" (singlet + doublet) resonance for H_b. Deuterium decoupling and integration of the spectrum at 270 MHz shows an area ratio of (1.07 ± 0.11):1 for the singlet:doublet components, indicating essentially complete equilibration of the cyclobutadiene-*1,2*-d_2 isomers before trapping. This result is confirmed by obtaining a similar spectrum from a reaction in which the cyclobutadiene-*1,2*-d_2 is generated by oxidation of **3**.

With 2.8 M methyl (*Z*)-3-cyanoacrylate[9] as trapping reagent, a strikingly different result is obtained. The iodolactones (Figure 3, R = CN) derived from the products of oxidation of **3** in the presence of the dienophile still show a "triplet" resonance for H_b. However, when the cyclobutadiene-*1,2*-d_2 is generated from **4**, the corresponding iodolactones show only *a singlet resonance for* H_b.[10a]

Three important conclusions follow.[10b] (1) Singlet cyclobutadiene cannot have a D_{4h} equilibrium geometry in solution. If it did, the two sources of cyclobutadiene-*1,2*-d_2 would have given identical label distributions in the adducts with methyl (*Z*)-3-cyanoacrylate. (2) The $\Delta G^{\ddagger}$ for interconversion of isomeric (presumably rectangular) cyclobutadienes is comparable with that for trapping. With 3.6 M methyl acrylate as trap, geometrical isomerism is faster than adduct formation, whereas with 2.8 M methyl (*Z*)-3-cyanoacrylate trapping appears to be the faster process. (3) The formation of cyclobutadiene-*1,2*-d_2 from **4** and the subsequent trapping with methyl (*Z*)-3-cyanoacrylate must both be concerted pericyclic processes since involvement of a biradical intermediate in either step would have resulted in formation of **5a** and **5c** in equal amounts.[11]

The mechanism in Figure 2 requires that the ratio of **5a**:**5c** vary with the concentration of trapping reagent (T) according to the equation[11,12]

$$[\mathbf{5a}]/[\mathbf{5c}] = 1 + (k_2/k_1)[\mathrm{T}]$$

Measurement of the **5a**:**5c** ratio as a function of [T] should, therefore, provide a quantitative determination of k_2/k_1. Independent measurement of k_2 for a variety of dienophiles would then yield several estimates of k_1, the rate constant for geometrical isomerism of cyclobutadiene-*1,2*-d_2. This in turn could lead to evaluation of the activation parameters for the process, by studies at several different temperatures. Experiments of this kind are in progress.

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(2) If geometrical isomerism were faster than *all* other processes, then cyclobutadiene would exhibit *effective* D_{4h} symmetry even though D_{4h} may not represent a local minimum in the potential energy surface. By "chemically significant" we mean that the reactive intermediate can undergo chemical reactions with rates comparable with or greater than the rate of its isomerism.

(3) Recent experiments[1y,z] show that, when CO_2 is produced as a byproduct in the formation of cyclobutadiene in an argon matrix, its infrared spectrum shows abnormal symmetry, apparently because of complex formation between the CO_2 and cyclobutadiene. The spectrum of the cyclobutadiene does not appear to be seriously perturbed by this interaction, however.

(4) For an alternative preparation of the unlabeled azo compound see: Masamune, S.; Nakamura, N.; Spadaro, J. *J. Am. Chem. Soc.* **1975,** *97*, 918.

(5) The synthesis of the 5,6-dicarbomethoxy-5,6-diazabicyclo[2.2.0]hex-2-ene-*1,4*-d_2 is based on Altman, L. J.; Semmelhack, M. F.; Hornby, R. B.; Vederas, J. C. *Chem. Commun.* **1968,** 686.

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(7) Davis, M. L.; Speed, C. S. *J. Organomet. Chem.* **1970,** *21*, 401.

(8) The experimental results presented in this communication do not distinguish between ${}_{\sigma}2_s + {}_{\sigma}2_s$ and ${}_{\sigma}2_s + {}_{\sigma}2_s + {}_{\pi}2_s$ mechanisms for the deazetation and trapping. Figure 2 arbitrarily depicts the latter mechanism.

(9) Sauers, C. K.; Cotter, R. J. *J. Org. Chem.* **1961,** *26*, 6.

(10) (a) The signal to noise ratio in the NMR spectrum is such that up to 5% of the doublet component would have been undetectable. (b) We cannot absolutely rule out the possibility of adduct formation by direct attack of the dienophile on azo compound **4**. However, in all trapping reactions studied thus far, the total amount of deuterium at the bridgehead sites in the primary products is equal[11] to the total amount of deuterium at the vinyl sites. We have been unable to find a mechanism for direct reaction between **4** and a dienophile which would lead to this result without coincidental equality of rate for two different processes. Note also that the equal amounts of **5**a and **5c** obtained with methyl acrylate as trap would require coincidental equality of rate for three different processes.

(11) We have found no evidence for a significant isotope effect on the product distribution. The most easily measured case comes from trapping cyclobutadiene-*1,2*-d_2 with diethyl azodicarboxylate. The resulting adduct shows two singlets for the bridgehead and vinyl protons ($J \simeq 0$ Hz between vicinal bridgehead and vinyl protons). The integral ratio of these two singlets is 1.00 ± 0.05. It seems reasonable to expect that cyclobutadiene cycloadditions would have early transition states with relatively little rehybridization and consequent small secondary isotope effects.

(12) This equation is derived on the assumption that the initially formed cyclobutadiene-*1,2*-d_2 from **4** consists of only a single isomer.

(13) NSF Predoctoral Fellow, 1978–1981.

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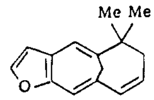
Total Synthesis of (±)-Dihydrospiniferin-1: A Furanosesquiterpene with a 1,6-Methano[10]annulene Carbon Skeleton

Sir:

Spiniferin-1, an unstable furanosesquiterpene from the Mediterranean sponge *Pleraplysilla spinifera*, was recently reformulated as I or, less likely, II through careful NMR spectral analysis.[1,2] Accordingly, spiniferin-1 would appear to be the first known natural product incorporating the novel 1,6-methano[10]annulene carbon framework.[3]



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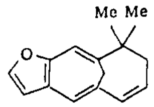

II

Its unique carbon skeleton, its chemical instability, and the unresolved ambiguity between structures I and II[2] stimulated our interest in developing a structurally definitive synthesis of spinferin-1. In this report we offer support for structure I through a rational total synthesis of the known[2] dihydro derivative **11** (Scheme I).

Dienone **2**[4] was prepared by an improved sequence through addition of methyllithium to 6-methoxy-1-tetralone (**1**), Birch reduction,[5] and acid-catalyzed hydrolysis–elimination. Conjugate addition of lithium dimethylcuprate afforded the unsaturated ketone **3**. Attempted Simmons-Smith cyclopropanation[6] of enone **3** caused conjugation of the double bond. As expected,[6] the related alcohol yielded to cyclopropanation, but even here the reaction proved capricious and numerous trials were needed to optimize conditions.[7] Jones oxidation[8] of the derived tricyclic alcohol led to the corresponding ketone **4**: ν_{max} 1710, 1465 cm^{-1}; δ 2.5 (s, H-1), 2.1 (m, H-3), 1.1, 1.0 (s, CH_3's), 0.4 ppm (s, H-11).

Formylation[9a] of ketone **4** occurred as planned at the less hindered (C-3) α position[9b] to give the hydroxymethylene

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