The data in Table I for the reaction of $PA^{\bullet+}$ with 4-methylpyridine illustrate the excellent fit of experimental data with theory for rate-determining reaction 3 and the overall stoichiometry shown in (5).[11] The apparent rate constants were observed to be independent of voltage sweep rate (ν) and essentially independent of the temperature (average value equal to 4.0 (±0.3) × 10^7 M^{-1} s^{-1}) indicating a very low or zero activation energy. Kinetic data for the reactions of $PA^{\bullet+}$ with pyridine, 4-methylpyridine, and piperidine, obtained by the prepeak method, in both acetonitrile and dichloromethane are summarized in Table II. Data for the reaction of $PA^{\bullet+}$ with 4-cyanopyridine obtained by conventional double-potential-step chronoamperometry in acetonitrile are included as well.

$$2PA^{\bullet+} + 2Nu \rightarrow PA(NU)_2^{2+} + PA \qquad (5)$$

The features of the data of most interest are the very large rate constants, low activation energies, and high selectivities. A plot of log k vs. pK_a (of the nitrogen bases) for the reactions in acetonitrile is curved, indicating decreased selectivity as the rate approaches diffusion control.[13] The data show that reactions 3 are not only "allowed" but also quite facile. The relative rate constants for the reactions of $PA^{\bullet+}$ and 9,10-diphenylanthracene cation radical (k_{PA}/k_{DPA}) suggest a substantial steric effect for reactions 3 when $DPA^{\bullet+}$ reacts with the nitrogen-centered nucleophiles.

The near zero or very low apparent activation energies suggest that the formation and dissociation of of the π complex (eq 6) must be taken into account in the detailed rate law (7). This sequence can give rise to low or even negative activation energies.

$$PA^{\bullet+} + Nu \underset{k_b}{\overset{k_f}{\rightleftharpoons}} PA^{\bullet+}/Nu \xrightarrow{k_p} PA^{\bullet}\text{-}Nu^{+} \qquad (6)$$

$$-d[PA^{\bullet+}]/dt = 2k_p(k_f/k_b)[PA^{\bullet+}][Nu] \qquad (7)$$

The fact that the rate constants obtained for Nu being 4-cyanopyridine by the direct kinetic method, which would detect $PA^{\bullet+}/Nu$ as well as $PA^{\bullet+}$, are in accord with the expectation based on the log k vs. pK_a plot confirms that the reaction is going to completion on the time scale of the kinetics. Thus, relationship 8 is valid. This rules out the unlikely possibility that K $(=k_f/k_b)$ is large and thus k_p does not contribute to the kinetics. Complexes such as $PA^{\bullet+}/Nu$ have been proposed to account for kinetic observations in numerous other cases,[1] but it has not yet been possible to observe them. This has been attributed to small equilibrium constants for their formation. The results reported here are consistent with these observations and suggest that the low activation energies are a consequence of a negative $\Delta H°$ associated with the preequilibrium masking the positive E_a of the bond-forming step.

$$-d([PA^{\bullet+}] + [PA^{\bullet+}/Nu])/dt = -d[PA^{\bullet+}]/dt = k_{app}[PA^{\bullet+}][Nu] \qquad (8)$$

Our general conclusion is that cation radical–nucleophile reactions can be very rapid, approaching diffusion control, and have low activation energies. The rapid reactions are first order in cation radical. The detailed structures of the initial products of the reactions are not known and the products may or may not form via a kinetically observable intermediate π complex. In any event, it would appear that the general conclusion[5] that cation radical–nucleophile reactions are high-energy reactions is not correct.

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[11] The products of the reactions are pyridinium salts.[12] The two mechanisms considered previously,[7] both involving the loss of the second electron to the electrode (eCe) can only apply in cases where the rate constants are 10^8 M^{-1} s^{-1} or greater (at ν = 0.1 V/s).

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Intramolecular Photoinduced Diene–Diene Cycloadditions: A Selective Method for the Synthesis of Complex Eight-Membered Rings and Polyquinanes

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The photoinduced [$2\pi + 2\pi$] cycloaddition of alkenes is one of the most commonly used strategy-level reactions for complex molecule synthesis. Its utility has been established for cycloadditions of ground-state alkenes with excited-state alkenes, dienes, and chromophores incorporating these groups.[2] Intermolecular diene–diene cycloadditions have also been studied[3] and a few have practical value[3b] but most are reported to produce complex mixtures. Sensitized dimerization of isoprene, for example, gives seven products and at least 15 dimers are obtained from piperylene.[3c] While unexplored, the intramolecular version of this reaction has the potential for circumventing these selectivity problems and for providing a facile route to substitutionally complex eight-membered rings[4] through rearrangement of the divinylcyclobutane photoproducts.[5] Described herein are the first examples of this photochemical reaction which delineate its scope and stereoselectivity and establish its merit in cyclooctane and polyquinane synthesis, the latter through a formal synthesis of the antitumor, antibiotic coriolin (**20**).[6]

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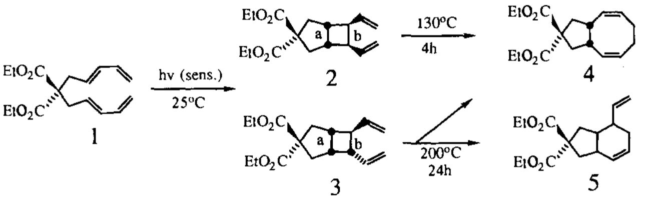
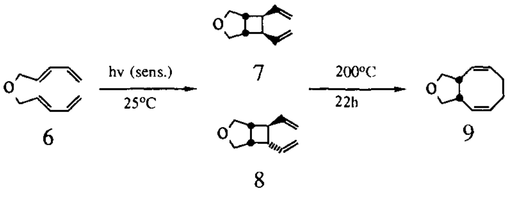
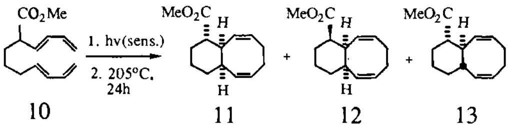
Our initial investigation of this reaction class was conducted with tetraene **1**, readily prepared in quantitative yield from diethyl malonate and pentadienyl bromide.[4a] Irradiation (Hanovia 450W source, Pyrex filter) of a solution of this tetraene (0.02 M in hexane) and benzophenone (sensitizer, 20 mol %) gave after 6 h (100% conversion) two major products (1:1)[7] in 80% yield. *p*-(Dimethylamino)benzophenone proved even more effective in sensitizing this reaction, providing complete conversion of **1** in 3 h when present in only 10 mol %. The complete selectivity for *cis*-fused products in these reactions is consistent with initial, reversible formation of a five-membered ring (bond a) with two allylic radical subunits.[2b,h] When these subunits are cis related, ring closure (formation of bond b) would give the observed cis-fused products (**2** and **3**), while the corresponding trans-related diradical intermediates, if formed, would presumably fragment preferentially to starting tetraene rather than cyclize to the more strained, trans-fused products. Six- and eight-membered ring products (**4** and **5**), which could also arise from these diradical intermediates, were formed but only in trace amounts.



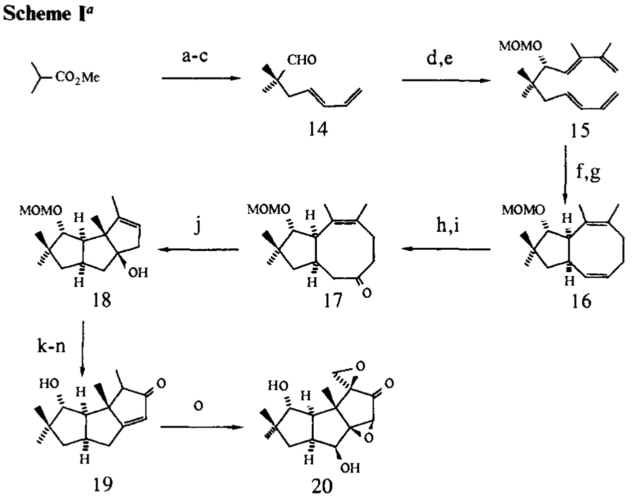
The utility of cycloadducts **2** and **3** in the preparation of cyclooctadienes was tested next. Thermolysis (130 °C, 4 h) of cycloadduct **2** in benzene was found to give only the *cis*-fused cyclooctadiene **4**[4a] (ca. 100%). More vigorous conditions (200 °C, 24 h) were required for the rearrangement of **3** but cyclooctadiene **4** was again the major product (50%).[8] Four minor cyclohexene products were also obtained (**5**; combined yield ca. 50%) and were assigned by comparison with Diels–Alder products derived from thermolysis (200 °C, 4 h) of tetraene **1**. For preparative synthetic purposes, cyclooctadiene **4** can be conveniently and efficiently obtained by direct thermolysis of the photolysis mixture.

Further studies revealed that the above results are general for other undeca-1,3,8,10-tetraenes and heteroatom analogues. For example, benzophenone-sensitized excitation of tetraene ether **6**[9] gave, after 16 h, cycloadducts **7** and **8** (1:1, 50%), which upon thermolysis (200 °C, 22 h) afforded the cis-fused, heterobicyclic product **9** (75%). For substrates with a four-atom tether between dienes, e.g., **10**,[4a] the benzophenone-sensitized cycloaddition was slower (93% conversion after 26 h), presumably due to the less favorable entropy for the formation of six- relative to five-membered rings. Thermolysis of these cycloadducts gave cyclooctadienes **11**, **12**, and **13** (5:1:2, respectively) in 42% overall yield.





Scheme I^a



^{a}(a) LDA, THF, −78 °C; BrCH$_2$CH=CHCH=CH$_2$, −78 → 0 °C, 71%; (b) LAH, Et$_2$O, 0 °C to room temperature, 90%; (c) (COCl)$_2$, Me$_2$SO, Et$_3$N, CH$_2$Cl$_2$, −78 °C, 81%; (d) LiCH=C(CH$_3$)C(CH$_3$)=CH$_2$,[12] 64%; (e) MOMCl, KH, THF, 0 °C to room temperature, 77%; (f) hν, benzophenone, hexane, 12 h; (g) 200 °C, 12 h, hexane, 60% overall; (h) 9-BBN, C$_5$H$_{12}$/C$_6$H$_{14}$, 45 °C, 8 h; H$_2$O$_2$, NaOH, EtOH, 74%; (i) PDC, CH$_2$Cl$_2$, 80%; (j) BF$_3$·Et$_2$O, CH$_2$Cl$_2$, 0 °C, 66%; (k) B$_2$H$_6$, THF, room temperature; NaOH, H$_2$O$_2$, 79%; (l) PDC, CH$_2$Cl, 90%; (m) MsCl, Et$_3$N, CH$_2$Cl$_2$, 0 °C to room temperature, 82%; (n) 6 M HCl/THF/H$_2$O (1:2:1), 55 °C, 6 h, 66%; (o) ref 11.

The minor but significant amount of trans-fused product **13** in this case and the absence of the trans-fused products in the sequences originating from **1** and **6** reflect the relative strain involved in the formation of cis- and trans-fused cycloadducts of the bicyclo[4.2.0] and -[3.2.0] series.

The foregoing studies provide the basis for the design of new approaches to bicyclo[6.*n*.0]alkanes and polycycles derived from their transannular closure.[10] For example, the triquinane coriolin (**20**) could be elaborated from closure of the bicycle **17**. In order to evaluate this strategy and to test the stereoinduction and substitution sensitivity of the above methodology, the synthesis and reactions of **17** were investigated. Toward this end, tetraene **15** which contains all of the carbon atoms of coriolin (**20**) was prepared in five steps from methyl isobutyrate. Photolysis (benzophenone sensitizer, 12 h, 23 °C) of this tetraene in multigram quantities followed by thermolysis of the photoproducts gave cyclooctadiene **16** in 60% overall yield. The formation of only one stereoisomer in this sequence is again consistent with the initial, reversible formation of diradical intermediates under photolysis conditions and their preferential closure to the cis-fused photoproducts in which the ether group is on the sterically less congested convex face.

Elaboration of the rearrangement product **16** was achieved in a highly chemo-, regio-, and stereoselective fashion with 9-BBN which provided predominantly (42:1) one alcohol from which ketone **17** was obtained upon oxidation. The second key stage of this synthesis, transannular closure of ketone **17**, proceeded smoothly to give the cis-anti-cis triquinane **18**, through selective reaction of the less strained (extended) ketone conformer. Finally, triquinane **18** was converted in four steps to enone **19** which has previously been transformed to coriolin (**20**) (Scheme I).[11]

In summary, the intramolecular photocycloaddition of bis dienes provides the basis for an efficient and preparative route to cyclooctadienes and triquinanes. It can be conducted with a variety of substituents and exhibits a high degree of inherent and induced

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(7) Satisfactory NMR, IR, and low-resolution mass spectra and combustion analysis or exact mass determination were obtained for all new compounds.

(8) The thermolysis of **3** presumably involves formation of a diradical which could directly give **4** and **5** or their respective precursors **2** and **1**.

(9) Ether **6** was prepared by reaction of the potassium salt of 2,4-pentadienol with 2,4-pentadienyl bromide.

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stereoselectivity, consistent with a mechanism involving selective closure of reversibly formed diradical intermediates to the less strained cycloadducts. Finally, this method provides an important complement to the recently reported nickel-mediated cycloaddition[4a] in servicing problems in bicyclo[6.n.0]alkane synthesis.

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Supplementary Material Available: Analytical data for compounds **2**, **3**, **6–9**, **11**, **12**, **15**, and **16** (5 pages). Ordering information is given on any current masthead page.

Unusual Asymmetry of Methyl ^{2}H EFG in Thymine: A Solid State Deuterium NMR and ab Initio MO Study

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Solid-state ^{2}H NMR spectroscopy is a powerful method of studying molecular motion in the solid state.[1-4] The power of this technique derives from the facts that quadrupole coupling is the dominant interaction and the electric field gradient (EFG) tensor is usually axially symmetric for a deuteron bonded to carbon, with the unique axis along the C–D bond. In the case of a methyl group, rapid 3-fold rotation yields an averaged EFG whose symmetry axis is along the rotation axis, and the corresponding powder pattern is axially symmetric ($\eta \leq 0.01$) with a quadrupole splitting of ca. 40 kHz.[5]

We are interested in obtaining spectra of thymidine and ribothymidine, deuteriated at the methyl positions, to study motion of nucleotide bases in DNA and tRNA, respectively. In our initial work we are studying the dynamics of the model compound, thymine-*methyl*-d_3.[6] Inversion-recovery ^{2}H NMR spectra of this compound clearly showed the T_1 anisotropy predicted for 3-fold methyl jumps.[5,7] The linear Arrhenius plot of correlation time, τ_c, against $1/T$ (where $\tau_c = \tau_0 \exp(E/RT)$) yielded an apparent activation energy of 6.9 kJ/mol and a preexponential factor, τ_0, of 2×10^{-13} s. These results show that the ^{2}H spin–lattice relaxation is determined by the 3-fold methyl motion. However, this motion does not account for the asymmetry in the observed line shape, Figure 1. A computer simulation of this lineshape showed that the asymmetry parameter was 0.07–0.08, unusually large for a methyl deuteron, while the splitting, 36 kHz, was several kilohertz less than expected. The goal of the work reported herein was to determine the cause of this unusual methyl line shape.

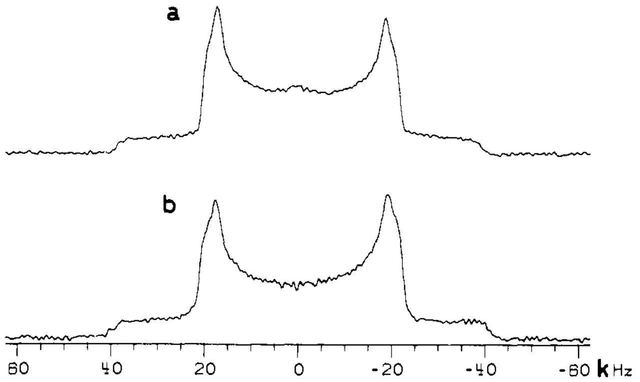

Figure 1. Powder ^{2}H NMR spectra, 38.45 MHz, of methyl deuteriated thymine: (a) at 295 K; (b) at 148 K. No line broadening is added.

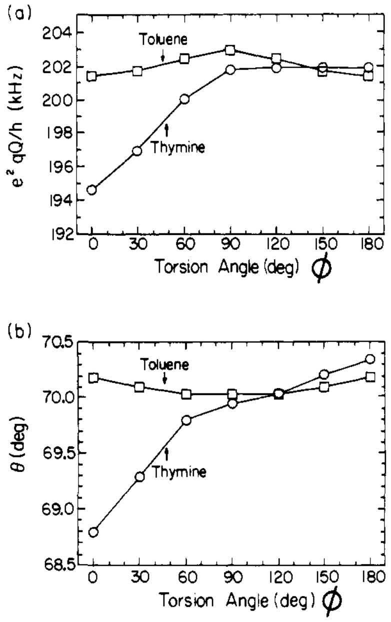

Figure 2. Calculated deuterium electric field gradient tensor for C–^{2}H in methyl group of thymine (○) and toluene (□). Torsion angle, ϕ, is defined by the atoms C_{carbonyl}–C_{ring}–C_{methyl}–D. (a) Deuterium coupling constant vs. ϕ; (b) the orientation of the z-axis, θ, with respect to the C_3 rotation axis.

Although the thymine-*methyl*-d_3 T_1 data are completely accounted for by the 3-fold rotation of the methy group, an additional rapid ($\tau_c < 10^{-11}$ s), small amplitude (rms angle <15°) motion cannot be excluded, since it would not significantly affect the ^{2}H spin–lattice relaxation. Such a small amplitude motion could explain the observed 7% asymmetry parameter and the 36-kHz splitting. For example, an excellent computer simulation of the observed line shape is obtained assuming that a Pake pattern ($\eta = 0$) with 40-kHz splitting is averaged by a 12° (rms) libration of the C_5–C_{methyl} bond axis.

If such a small-amplitude motion occurs at the C_5–C_{methyl} site, then it should also occur at the N–H sites, because the aromatic ring is rigid and neutron and X-ray diffraction studies of thymine moieties have shown that thermal parameters of methyl carbons are no larger than those of ring carbons.[8] The measured ^{2}H T_1 of N–^{2}H sites in (NH-d_2, methyl protonated) thymine was about 4000 s at 295 K. The ^{2}H relaxation is mostly determined by

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