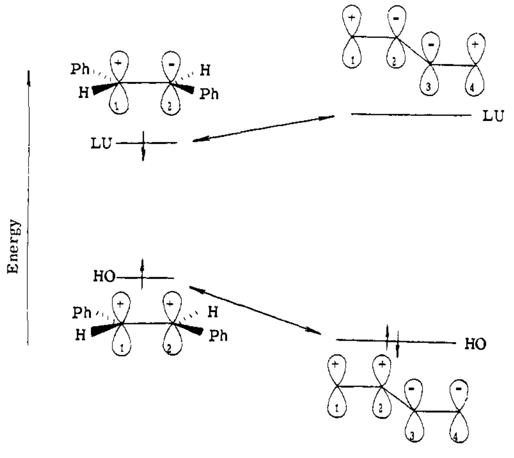

Figure 1. Orbital interaction diagram for excited *trans*-stilbene with butadiene. Relative energies are estimated from ionization potentials and singlet energies.[17a]

dicative of reversible exciplex formation.[16] We observe neither an inverse temperature dependence of the rate constant for quenching *trans*-stilbene fluorescence by dienes nor exciplex emission; however, irreversible exciplex formation cannot be excluded.

Frontier orbital theory[10] has proven useful in predicting the preferred regioisomers and relative reactivities in the Diels–Alder and other cycloaddition reactions.[17] Concerted photochemical 2 + 2 cycloaddition of *trans*-stilbene(s) with a conjugated diene (d) involves the interaction of both the highest occupied (HO–HO) and lowest unoccupied (LU–LU) molecular orbitals (Figure 1). Second-order perturbation theory provides eq 2 for the stabilization energy upon

$$\Delta E = \frac{(C_{\mathrm{HOs1}}C_{\mathrm{HOd1}} + C_{\mathrm{HOs2}}C_{\mathrm{HOd2}})^2\gamma^2}{E_{\mathrm{HOs}} - E_{\mathrm{HOd}}} + \frac{(C_{\mathrm{LUs1}}C_{\mathrm{LUd1}} + C_{\mathrm{LUs2}}C_{\mathrm{LUd2}})^2\gamma^2}{E_{\mathrm{LUs}} - E_{\mathrm{LUd}}} \qquad (2)$$

π-orbital interaction; where C_{HOd1} is the coefficient of the diene C-1 HO orbital, γ is the resonance integral between interacting orbitals, and $E_{\mathrm{HOs}} - E_{\mathrm{HOd}}$ is the energy separation between interacting orbitals (Figure 1). The preferred regioisomers will be determined by the magnitude of the diene HO and LU coefficients. Results of CNDO/2 calculations are given in Table I for several dienes. The HO coefficients for 1,3-pentadiene and 2-methyl-1,3-butadiene are similar to those recently reported for INDO calculations.[17f] Consideration of either the HO or LU coefficients leads to the prediction of preferred addition to the more substituted double bond, in agreement with the experimental results.

There remains the intriguing problem of explaining the preference for addition to the less substituted double bond observed in most diene 1,2-cycloadditions.[1-4] Stepwise (radical or ionic) reactions can be rationalized on the basis of formation of the more stable bifunctional intermediate.[1] The transition states for 1,3-dipolar and ketene additions are most likely asymmetric with substantial polar character.[18] Steric effects may also mitigate against addition to the more substituted double bond. Ketene [$_\pi 2_s + _\pi 2_a$] cycloaddition reactions are subject to severe steric demand.[19] The lower regioselectivity of singlet diphenylvinylene carbonate[9] vs. *trans*-stilbene could also be steric in origin. Thus preferred cycloaddition to the more substituted diene double bond may only be observed for concerted reactions with minimal steric demand. Electrophilic singlet carbenes or nitrenes may fulfill these requirements; however, the available evidence is inconclusive.[5-7]

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Nuclear Magnetic Resonance of Photoexcited Triplet States. I. The Measurement of the Rate of Degenerate Singlet–Triplet Exchange for Anthracene in Solution[1]

Sir:

The NMR spectroscopy of molecules undergoing rapid exchange between diamagnetic and paramagnetic environments is well understood and is exemplified in studies of fast electron transfer between an organic radical ion and its diamagnetic precursor.[2] An entirely equivalent process can be envisioned when molecules undergo photoexcitation, intersystem cross to a triplet state, and decay to the ground state. Indeed, in a little noticed paper, Cocivera reported line broadening in the ^{1}H NMR spectrum of pyrene when the sample was irradiated with ultraviolet light.[3] On the basis of limited experimental data he proposed what is proven here to be an essentially correct mechanism for the line broadening.

In the theory of spin exchange processes it is convenient to distinguish between strong and weak pulse limits depending on the degree of dephasing the rf induced x–y nuclear

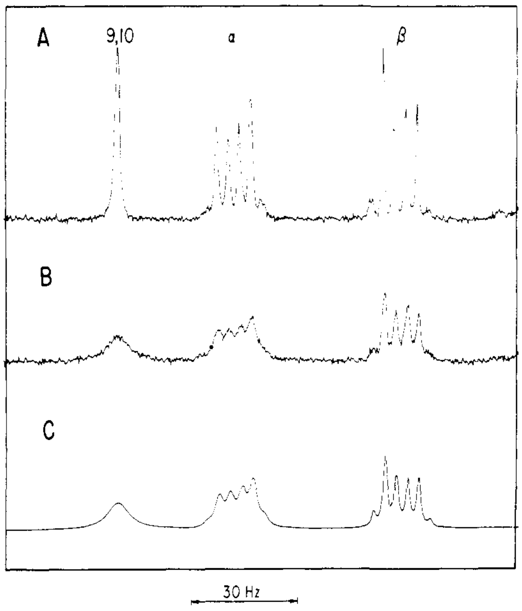

Figure 1. A 90-MHz FT ^1H NMR spectrum (16 pulses) of 0.042 *M* anthracene in bromobenzene-d_5. (A) dark; (B) during irradiation (λ >310 nm); (C) composite computer simulation of B.

magnetization experiences while in a paramagnetic environment.[2] In Cocivera's experiment dephasing of the proton spins was complete and consequently all information on the electron spin distribution in the triplet state was lost. In such cases the observed line broadening amounts to uncertainty broadening caused by the shortened *ground state* life time.

In this communication we wish to report results demonstrating that it is possible to choose conditions corresponding to the weak pulse limit and thus to extract useful information on photoexcited triplet states from high resolution NMR spectra.

Figures 1A and 1B show respectively the NMR spectra of 0.042 *M* anthracene in bromonzene-d_5 in the dark and during irradiation with a 1000-W Xe-Hg arc lamp (degassed, λ >310 nm).[4] It is apparent on inspection that line broadening occurs to a different degree for the resonances associated with the three types of protons in a sequence corresponding to the isotropic hyperfine coupling constants in the triplet state of anthracene: $a_{9,10} > a_\alpha > a_\beta$.[5] The observed differential broadening implies that the strong pulse limit has not been reached and requires that $\frac{2}{3}a_i^2\tau_p^2 < 1$; where a_i (in rad/sec) is the isotropic hyperfine coupling constant for the ith proton and τ_p is the lifetime of the paramagnetic molecule. Using the known hyperfine coupling constants this implies $\tau_p < 10^{-8}$ sec, a time many orders of magnitude shorter than the triplet excitation lifetime. This consideration strongly suggests a bimolecular degenerate singlet-triplet exchange process of the type

$$T_1 + S_0 \overset{k}{\rightleftharpoons} S_0 + T_1$$

predicting a concentration dependent residence time for the triplet excitation on an individual molecule.[6] The correctness of this interpretation was confirmed by running experiments over a range of concentrations and observing substantially increased line broadening with increasing dilution.[7] The results of these experiments for anthracene are shown in Figure 2 where the incremental line width ($1/T_2'$—corrected for diamagnetic line width and inhomogeneous broadening during irradiation) for the three different protons is plotted against $1/[C]$. The line widths were measured by matching computer synthesized spectra of specified line width with the experimental spectra (e.g., Figure 1C).

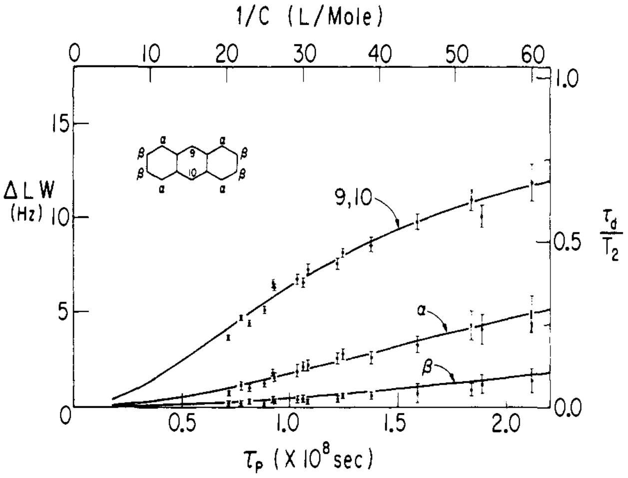

Figure 2. The effect of concentration on the incremental line broadening observed for the three types of protons in anthracene on irradiation. Solid lines are best fit curves based on eq 1 giving the parameters discussed in the text.[9] The error bars represent an estimate of the confidence limits for computer simulation of the line widths of experimental spectra as in Figure 1C.

Using a simplified formalism the line width is given by[8]

$$\left(\frac{1}{T_2'}\right)_i = \frac{1}{\tau_d}\,\frac{\frac{2}{3}a_i^2\tau_p^2}{1 + \frac{2}{3}a_i^2\tau_p^2 + \tau_p T_{1e}^{-1}} \qquad (1)$$

where τ_d is the diamagnetic lifetime and T_{1e} is the electron spin-lattice relaxation time in the triplet state. For anthracene the isotropic components of the hyperfine interaction in the triplet state are known from ENDOR experiments,[5] making it possible to fit the experimental line widths to theoretical curves generated from eq 1. As shown in Figure 2 (solid lines) good fits are obtained with $\tau_d = 0.018$ sec, $T_{1e} = 3.1 \times 10^{-8}$ sec, and values of τ_p as shown in the abscissa of the graph.[9] From the known concentrations and τ_p, a bimolecular exchange rate constant of $k = 2.8 \times 10^9$ l M^{-1} sec^{-1} is obtained.[10] This value strongly suggests that the degenerate triplet-singlet exchange is diffusion controlled, a result we suspect to be rather general for molecules with extended π-electron systems.[11]

No direct measurements of T_{1e} in organic triplet molecules in solution have been made, and therefore it is not possible to compare the value determined in our experiment with values derived by other methods. However, a check on the order of magnitude is possible by the following procedure. Assuming that T_{1e} is mostly governed by electron dipole-dipole interactions it should be given by

$$\frac{1}{T_{1e}} = \frac{2}{15}{*D}^2\tau_c\left(\frac{1}{1 + \omega_e^2\tau_c^2} + \frac{4}{1 + 4\omega_e^2\tau_c^2}\right) \qquad (2)$$

where τ_c is the rotational correlation time, $*D$ is the zero-field splitting parameter ($|*D| = 0.072$ cm^{-1} for anthracene[5]), and ω_e is the Larmour frequency of the electron. Since to a good approximation the same correlation time, τ_c, enters into an equation describing the nuclear spin-lattice relaxation time for protonated ^{13}C nuclei relaxing via fluctuating C-H dipole-dipole interactions, ^{13}C T_1 measurements can provide an estimate for T_{1e}. Measurements of T_1 for the α and β ^{13}C nuclei of anthracene in bromobenzene lead to a value of 3.3×10^{-8} sec for T_{1e}, not a bad agreement considering the diversity of the methods involved.

Preliminary experiments have shown that this method is applicable to a wide variety of molecules in photoexcited triplet states and should be of general value in photochemistry. For example it is possible to use photosensitization to produce the triplet state of a molecule whose line broadening is of interest as has been shown for the naphthalene-benzophenone system, where little broadening is observed on direct irradiation of naphthalene in the absence of benzophenone. The application of this method to determine hyperfine interactions and thus structural information as well as relative triplet energies for biologically important molecules such as chlorophyll will be reported shortly.

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(7) The concentration of anthracene in these experiments was high enough over the range studied so that the number of light quanta absorbed did not change significantly.
(8) This equation is strictly valid only for one nuclear spin.[2] However, for systems where the nuclear spin-spin coupling constants are small compared to chemical shift differences, it provides a good approximation to the line widths obtained from a solution of the equation of motion of the total density matrix for the coupled system.
(9) Best fit curves were obtained by a direct search method using "Subroutine Stepit" written by J. P. Chandler and available from the Quantum Chemistry Program Exchange.
(10) Another computer fitting was attempted in which the a_i's were also treated as variables. It is interesting to note that the program converged to values which deviate by less than 15% from the known a_i's,[5] and the remaining three parameters determined by the more restricted search procedure. Of course, the determination of both hyperfine coupling constants and τ_p is only possible if T_{1e} is comparable to or smaller than τ_p.
(11) The value of k corresponds to a diffusion rate constant of $2k$ since the maximum probability for degenerate exchange is 0.5.
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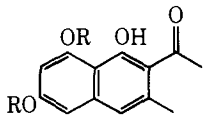
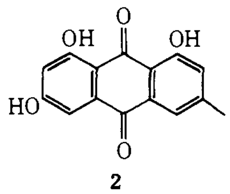
Biogenetic-Type Syntheses of Polycyclic Polyketide Metabolites Using Partially Protected β-Hexa- and β-Heptaketones: 6-Hydroxymusizin, Barakol, Emodin, and Eleutherinol

Sir:

Biogenetically modeled syntheses of polyketide-type aromatic natural products have recently attracted attention.[1] Numerous syntheses of monocyclic compounds have been reported which involve free or partially protected β-tetracarbonyl compounds as precursors, but the corresponding use of higher polycarbonyl compounds or their derivatives has not, as yet, led to any naphthalenoid or anthracenoid natural products.[2] We now report biogenetic-type syntheses of 6-hydroxymusizin (**1**) and emodin (**2**), as well as the related heterocyclic metabolites barakol (**3**) and eleutherinol (**4**). The present approach involves polyketones having the two terminal carbonyl groups protected as ketals; these facilitate synthesis of the polycarbonyl compounds and direct their subsequent cyclizations.



1, R = H
10, R = $COCH_3$



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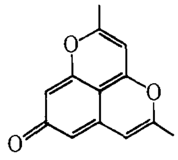

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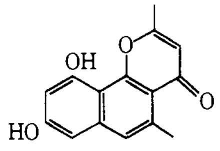
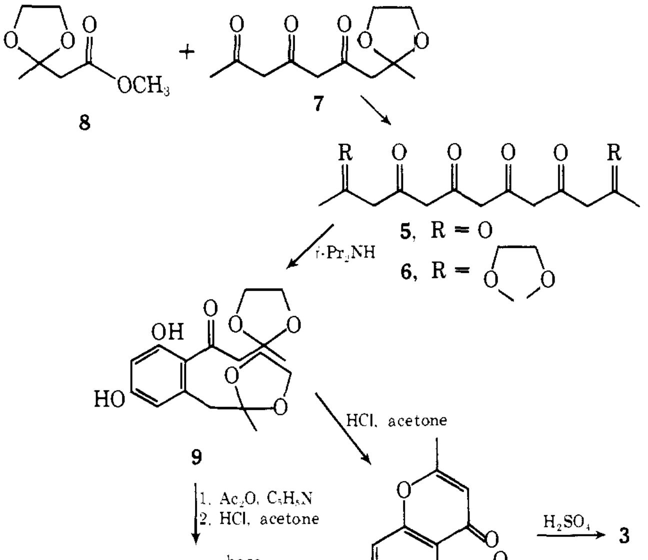


4

Scheme I



Bis(ethylene ketal) **6**[3] of hexaketone **5** was employed for the synthesis of **1** and **3** and was prepared by acylation (30-45%) of the trilithium salt (0.03 mol, prepared with *i*-Pr_2NLi) of protected tetraketone **7**[3,4] with ester **8** (0.015 mol) in THF at −78° (Scheme I). The only cyclization pathway readily available to **6** is formation of resorcinol **9**; an 80% yield of **9**[3] was obtained when **6** was treated with *i*-Pr_2NH (C_6H_6, reflux, 0.5 hr). After acetylation (Ac_2O, C_6H_5N, 25°, 40 hr) of **9**, the ketal groups were removed, and the second ring was closed to give naphthol **10**[3] (55%) by treatment with 1:40 hydrochloric acid-acetone (25°, 10 hr). Saponification of **10** under N_2 (4 *M* KOH, 25°, 25 min) gave 70% of 6-hydroxymusizin (**1**), identical with an authentic sample.[5]

If **9** was not acylated prior to removal of the ketal groups, chromone **11** was formed instead (87%). Chromone **11**, on treatment with concentrated H_2SO_4 (1 hr, 25°), cyclized further to give barakol (**3**, 80%), which was identical with an authentic sample.[6,7] Both **3** and **11** are constituents of *Cassia siamea*.[8]

The initial approach to **2** involved bis(ethylene ketal) **13a** of heptaketone **12** (Scheme II). Acylation of the trilithium salt (0.03 mol, formed with *i*-Pr_2NLi) of **7** with the sodium salt (0.015 mol, formed with NaH) of ester **14**[3,9] gave **13a** (THF, 18 hr, 25°, 17%),[10] which, although relatively stable at ambient temperature, could not be purified fully by chromatography on silica gel. Cyclization of **13a** could give either resorcinol **15a** or **17a**, but under all conditions examined **15a** was the major product, only traces of **17a** being formed. For example, treatment with Et_3N in toluene (3 min, reflux) gave 57% of **15a** (which cyclized spontaneously