Photocycloaddition of β-Methylstyrenes to Some 9-Cyanophenanthrenes. Chemical Consequences of Exciplex Formation

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Abstract: Photocycloaddition of 9-cyanophenanthrene (**1a**) and β-methylstyrene (**2j**) occurs both from S_1 and T_1 of **1a**. The existence of a triplet component depends on whether reaction can compete with triplet excitation transfer to the styrene. The head-to-head endo-phenyl product **3aj**, with retention of the olefin configuration, is the only product detected. With *trans*-anethole (p-methoxy-β-methylstyrene, **1k**), its cis isomer **2l**, and β-anisylisobutylene (**2m**), products are similar; in each case, substantially stereospecific formation of an endo-aryl, head-to-head product results. The introduction of remote cyano and methoxy substituents in **1a** has little effect on the product distribution if the substituents are in the 6 position (i.e., in 3-substituted 10-cyanophenanthrenes). However, head-to-tail adducts are observed in reaction mixtures, and isolated in two cases, when the substituent pattern is 3.9. Singlet exciplex fluorescence is observed when charge transfer is pronounced, and in one case (**1a** + **2k**) the exciplex is demonstrated to be a product precursor. A CNDO study of the addend models and PMO analysis rationalizes the stereochemistry well and gives mixed success in rationalizing regiochemistry. Concerted collapse of the exciplex to cycloadduct appears the most likely mechanism of reaction.

Introduction

There has been considerable recent interest in the [2 + 2] photocycloaddition of olefins. Following a proposal by Corey[1] some years ago, numerous investigators have concluded that excitation of one partner is followed by its formation of a complex with the other. This *exciplex* may then collapse, either directly or through a 1,4-biradical, to the cyclobutane products. The mechanism is exemplified below.
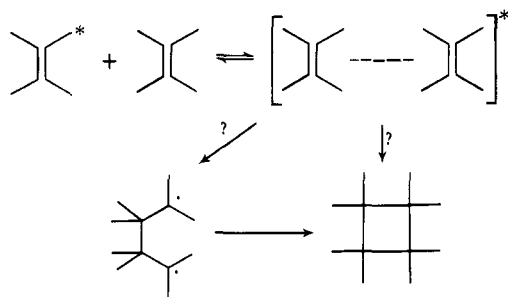
A substantial number of exciplex luminescences or excimer luminescences resulting from photoassociation have been observed,[2] and on the basis of these it is often assumed that bimolecular photoreactions usually originate from such species. However, only recently have examples become available in which exciplex luminescence and product formation occur simultaneously.[3-17] It has seemed critical to us to locate photocycloadditions where both exciplex emission and its intermediacy in the reaction can be documented.

In this paper, we describe the photoadditions of several styrene derivatives to substituted 9-cyanophenanthrenes. In several cases, exciplex emissions occur, and in one case a kinetic experiment demonstrates that the exciplex is an obligatory intermediate. Stern–Volmer slopes, structural and solvent dependence of the exciplex emissions, and product stereochemistry all point to a coherent mechanistic picture in which exciplexes quite similar to those now familiar in photoassociation[2] are product precursors. We here present the product structures and rationalization of cycloadduct regiochemistry; detailed quantitative studies will be presented separately.

Experimental Section

General. Solvents used were typically AR grade; for quantitative work, selected experiments were done in benzene purified by washing

with concentrated H_2SO_4 and distillation from P_2O_5. Melting points were uncorrected. Isoprene was freshly distilled before use. Gas chromatographic analyses were performed on an F & M Model 700 thermal conductivity gas chromatograph. Microanalyses were performed either by Gailbraith or by MHW Laboratories.

Spectra. Nuclear magnetic resonance spectra were performed on a Jeolco C60HL 60-MHz spectrometer, ultraviolet spectra on a Bausch and Lomb Spectronic 505 double-beam recording spectrophotometer, and fluorescence and phosphorescence spectra on a Farrand MK-1 ratio recording spectrofluorimeter.

Reagents when commercially available were used as received for preparative experiments unless stated otherwise. For quantitative experiments, solid compounds were chromatographed and recrystallized; liquids were passed through activity I alumina. The only observed effect of purification was removal of a yellow, quenching impurity from β-methylstyrene (**2j**).

cis-**Anethole (2l)** was prepared by Michler's ketone sensitized isomerization of *trans*-anethole (**2k**). Distillation of the reaction mixture on a Teflon spinning band column afforded *cis*-anethole (**2l**) containing ca. 6% of the trans isomer (by GLC on Carbowax 20M).

β-**Anisylisobutylene (2m)** was prepared by the reaction of anisaldehyde with isopropylmagnesium bromide in ether, followed by dehydration of the crude carbinol in warm 85% phosphoric acid. Extraction and distillation afforded **2m**: bp 75 °C (1 mm); NMR ($CDCl_3$) δ 1.87 (6 H), 3.75 (s, 3 H), 6.24 (m, 1 H), 6.85 (d, J = 9 Hz, 2 H), and 7.19 (d, J = 9 Hz, 2 H).

α,p'-**Dicyanostilbene** was prepared from p-cyanobenzaldehyde and phenylacetonitrile. Reflux of 0.1 mol of each for 0.5 h in 65 mL of ethanol containing 0.7 g of NaOH afforded a crude precipitate of α,p'-dicyanostilbene. Recrystallization from ethanol afforded material pure to TLC (19.5 g, 85%), mp 170 °C.

3,9-Dicyanophenanthrene was prepared by Mallory photocyclization[18] of 5 g of α,p'-dicyanostilbene utilizing 0.3 g of I_2 in 1 L of oxygen-saturated AR benzene in a standard irradiation well, employing a 450-W lamp and a Pyrex filter sleeve. The reaction was stopped after 72 h, the crude precipitate was collected, the reaction mixture was washed with basic thiosulfate to remove I_2, and all product-containing materials were combined. Chromatography on silica gel with benzene as solvent afforded a mixture of the phenanthrene and another material. Sublimation of this mixture at 200–240 °C and 0.2 mm gave only the phenanthrene. We presume the other compound to be its dimer,[19,22] which fragmented to the phenanthrene during the sublimation. The crude phenanthrene was recrystallized from chlorobenzene to afford 3,9-dicyanophenanthrene (4.25 g, 85%), mp 288.5 °C. Anal. Calcd for $C_{16}H_8N_2$: C, 84.19; H, 3.52; N, 12.27. Found: C, 84.11; H, 3.37; N, 12.07.

α-**Cyano-p-methoxystilbene** was similarly prepared from p-

Table I. Properties of Cycloadducts

Adduct	Mp, °C	Yield, %	H_a	H_b	H_c	and	H_d	R_1	R_2	H_e	H_f	Recrystn solvent
3aj	125.5–126.5	10	6.36		3.62	and	4.09	2.8[a]	1.18[b]			Methanol
3bj	186	47	6.32		3.66	and	4.0	2.8[a]	1.22[b]			Ethanol
3cj	185	87	6.42		3.68	and	4.16	2.8[a]	1.24[b]			Ethanol
3ak	126–128	90	6.38		3.56	and	3.98	2.6[a]	1.19[b]			Methanol
3bk	184	87	6.36		3.64	and	4.06	2.7[a]	1.20[b]			Ethanol
3ck	185	80	6.52		3.70	and	4.15	2.75[a]	1.22[b]			Ethanol
3al	131–132		6.52		4.36	and	4.52	0.76[b]	3.28[a]			Methanol
3am	103	54	6.6		4.00	and	4.23	0.68[b]	1.38[b]			Hexane
4bj	224	9		6.29			4.05		1.32[c]	4.45	3.1	Ethanol
3dk	99–102	27	6.27		3.7–4				2.7[a]	1.10[b]		Hexane–ether
4dk	173–174.5	0.8		6.03			4.0		1.24[c]	4.27	2.95	Hexane–benzene
4dj	*d*	*d*	5.98				4.17		1.25[c]	4.26	2.9	*d*
3ej	175–176	57	6.13		3.53	and	3.96	2.6[a]	1.17[b]			Ethanol
3ek	134.5–135	20	6.22		3.53	and	3.97	2.7[a]	1.20[b]			Hexane–benzene

[a] Methine hydrogen. [b] Methyl group. [c] Methyl group analogous to R_2 in structures **3**. [d] Detected in reaction mixture but not isolated.

Table II

Compd	Calcd, %			Found, %		
	C	H	N	C	H	N
3aj	89.80	5.93	4.36	89.49	5.99	4.31
3bj	86.67	5.23	8.08	85.95	5.52	7.96
3cj	86.67	5.23	8.08	86.35	5.31	8.19
3ak	85.44	6.02		85.67	6.09	
3bk	82.95	5.35	7.44	83.05	5.22	7.47
3ck	82.95	5.35	7.44	82.95	5.35	7.31
3al	85.44	6.02		85.57	6.12	
3am	85.44	6.34	3.83	85.65	6.42	3.65
4bj	86.67	5.23	8.08	85.99	5.36	8.14
3dk	81.86	6.08	3.67	82.04	6.36	3.47
4dk	81.86	6.08	3.67	81.66	5.95	3.61
3ej	85.44	6.02	3.99	85.62	6.00	3.94
3ek	81.86	6.08	3.67	81.77	6.00	3.68

methoxyphenylacetonitrile and benzaldehyde, mp 94 °C (18 g, 77%).

3-Methoxy-10-cyanophenanthrene was prepared by Mallory photocyclization as above, mp 158 °C (2.5 g, 50%). Anal. Calcd for $C_{16}H_{11}NO$: C, 82.38; H, 4.74; N, 6.00. Found: C, 81.79; H, 4.86; N, 5.98.

α-Cyano-*p*-methoxystilbene was similarly prepared from anisaldehyde and phenylacetonitrile, mp 94.5 °C (20 g, 85%).

3-Methoxy-9-cyanophenanthrene prepared by Mallory photocyclization weighed 3.0 g (60%), mp 125 °C. Anal. Calcd for $C_{16}H_{11}NO$: C, 82.38; H, 4.74; N, 6.00. Found: C, 82.4; H, 4.86; N, 6.17.

Photocycloadditions were performed using a Hanovia 450-W medium-pressure mercury arc lamp. Sensitized irradiations utilized a Corning 3320 filter sleeve. The absorption of 9-cyanophenanthrene (**1a**) ($\epsilon \simeq 47$ at the 366-nm mercury line) permitted direct irradiations when necessary to utilize the 3320 filter. Some direct irradiations were performed with a Pyrex filter.
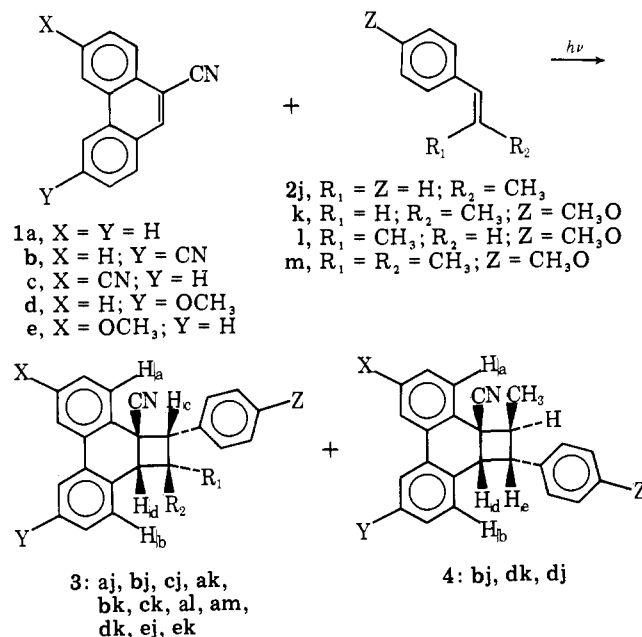
In general, solutions 0.02 M in each addend were irradiated. After most of the starting material had disappeared (by TLC or by NMR of an aliquot of the reaction mixture), the reaction mixture was subjected to column chromatography on silica gel utilizing a benzene-hexane mixture. The cycloadduct fractions, when a substantially pure adduct resulted, were crystalline upon evaporation of solvent. In the case of product mixtures, careful rechromatographing of the adduct fraction, utilizing less benzene than in the initial separation, was required for separation. The cycloadducts were recrystallized as indicated in Table I. No effort was made to optimize isolated yields; since products other than cycloadducts or phenanthrene dimers were undetected by TLC, and since dimerization could be suppressed by increasing the olefin concentration, we suspect that yields could be made virtually quantitative. Analytical data for the adducts are given in Table II.

The structures of products **3** and **4** are here indicated by the substitution pattern of the reactants. Thus, **1p** + **2q** → **3pq** and/or possibly **4pq**. Table I summarizes physical properties, particularly the NMR spectra, and yields.

Results

Preparative scale irradiation led to the following photoproducts.

1a, X = Y = H
b, X = H; Y = CN
c, X = CN; Y = H
d, X = H; Y = OCH₃
e, X = OCH₃; Y = H

2j, R_1 = Z = H; R_2 = CH_3
k, R_1 = H; R_2 = CH_3; Z = CH_3O
l, R_1 = CH_3; R_2 = H; Z = CH_3O
m, R_1 = R_2 = CH_3; Z = CH_3O

3: aj, bj, cj, ak,
    bk, ck, al, am,
    dk, ej, ek

4: bj, dk, dj

Additionally, the dimers **5a** and **5d** were isolated in some cases, particularly in the reactions with **2j**. The structure **5d**

5d
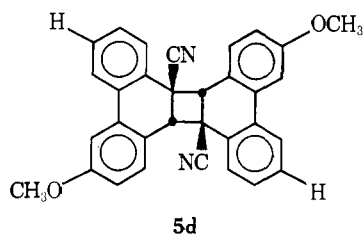
was determined from its NMR spectrum, which was analogous to that of the known[19] **5a**.

The NMR spectra in Table I are adequate to specify a unique structure for each adduct isolated. Most crucial is the observation of H_a at δ ca. 6.3–6.6, a position surprisingly far upfield for an aromatic proton. The shift of this signal with either Eu(fod)$_3$ or Pr(fod)$_3$ was similar to that for the benzylic cyclobutane protons H_c and H_d for **3aj** and **3ak**. Since coordination of the lanthanide should occur at the nitrile group and collinearly with it, and the only aromatic proton expected from observation of models to be nearly as close to the nitrile as H_c and H_d is H_a, the assignment of H_a is thus meaningful: *its pronounced upfield shift requires an endo phenyl group*, since the only reasonable explanation is that H_a lies in the shielding region of an endo-phenyl ring current. Inspection of Dreiding models confirms that this should indeed be the case.

Adduct regiochemistry was assigned by the benzylic cyclobutane protons and in some cases confirmed by the splitting pattern of H_a. All the adducts of type **3** have benzylic protons H_c and H_d as simple doublets ($J = 9$–11.5 Hz). Structures of type **4** show a more complex pattern for H_d and H_e. Regiochemical assignments with adducts of **1b–e** were confirmed by the splitting pattern of the upfield aromatic proton H_a or H_b. In adducts of **1a**, H_a appears as a double doublet, $J = 8$ and 1.5 Hz, as expected for ortho and meta aromatic coupling, respectively. With adducts of **1b–e** meta coupling is not observed for the upfield aromatic hydrogen H_a (in **3**) or H_b (in **4**) when the aryl group of the styrene is proximate to the ring bearing the remote substituent X or Y.

The stereochemistry of the methyl group can be assigned by its chemical shift. The "normal" position for a methyl on quaternary carbon, δ ca. 1.2, is observed with all adducts derived from *trans*-**2j** and **2k**. In contrast, **3al** shows its methyl significantly shifted upfield and its nonbenzylic methine significantly shifted downfield compared to **3ak**. These results are rationalized by consideration of the effect of the ring current of the proximate aromatic ring of the phenanthrene moiety. In **3am**, both a high-field and a low-field methyl are observed, as would be expected.

The approximate triplet for H_e at δ 4.45 further confirms the head-to-tail assignment of **4bj**. Its δ 4.05 doublet for H_d suggests (but does not prove) that the downfield cyclobutane hydrogen in adducts of type **3** is also H_d.

Excited State Precursors. Multiplicity. The styrenes **2** do not absorb appreciably at the wavelengths transmitted by the Corning 3320 filter sleeve ($\lambda \gtrsim 330$ nm). Accordingly, all direct photoreactions are initiated from S_1 of the phenanthrene derivative. All phenanthrenes phosphoresce strongly in EPA at 77 K; accordingly, T_1 reached via intersystem crossing is a potential intermediate as well. Table III presents the excited state energies of **1a–e**.

Table IV presents the results of relative rate studies with **1a** and some of the styrenes. Isomerizations were monitored by GC and cycloadduct formation was monitored by NMR. For **2j**, the comparison of adduct formation and trans–cis isomerization is most informative. Isoprene at 0.2 M virtually eliminates isomerization; isomerization is thus a triplet-state reaction, since isoprene hardly quenches **1a** fluorescence ($k_Q\tau < 0.1$ M^{-1}) but is expected to be a good quencher for triplet **1a**. Since >97% of the isomerization was quenched in an ex-

Table IV. Relative Reactivities with **1a** and **2** in Benzene[a]

Styrene	Conditions[b]	Relative rate of adduct formation	Relative rate of cis–trans isomerization
2j		1.3	13
	4×10^{-4} M MK	1.0	13
	0.2 M isoprene	0.6	0.5
2k		12	10
	5×10^{-5} M MK	6	
	4×10^{-4} M MK	1.3	
	1.2×10^{-3} M MK	0.36	
	0.2 M isoprene	12	4
	0.2 M **2k**	30	
2l	0.2 M isoprene	8	

[a] All reactions performed in a 1-L flask with a Corning 3320 filter sleeve. [b] Solutions 0.02 M in each cycloaddend except as noted.

periment in which only about half the adduct formation was quenched, there must be a substantial fraction of **3aj** arising from S_1 of **1a**. Conversely, since the triplet sensitizer, Michler's ketone (MK), absorbs some 88% of the light ($\epsilon \sim 18\,000$ at the predominant exciting wavelength of 365 nm vs. ϵ 47 for **1a** at 365 nm) when added at 4×10^{-4} M, the rate decrease of only ca. 25% requires a triplet component also. The quenching effect of isoprene on the cycloaddition (Table IV) confirms this conclusion.

With **2k**, the rate of cycloaddition to **1a** is completely unaffected by isoprene and is very strongly quenched by MK. The observed attenuation in the presence of 1.2×10^{-3} M MK is very nearly that which we estimate would be expected, based on the hypothesis that S_1 is the only state reactive toward **2k** and on consideration of the following relevant parameters: (1) absorption spectra and of **1a** MK, (2) absorption spectrum of 2-mm thickness of the Corning 3320 glass filter, (3) spectral output of the lamp, and (4) Forster quenching of S_1 of **1a** by MK. While a precise calculation would not be possible without more exacting work, we estimate a residual relative rate from S_1 of 0.29 ± 0.1 vs. 0.36 observed. We conclude that formation of **3ak** from **2k** is almost exclusively a singlet process, a conclusion recently confirmed by Dr. D. Creed in these laboratories.

The presence or absence of a triplet component may be due to the relative instability of a (putative) triplet exciplex toward collapse to the triplet of the styrene derivative. The methoxy group shifts S_1 of the β-methylstyrene chromophore from 293 nm (97.6 kcal) to 307 nm (93.1 kcal); while we have not determined the triplet energy of **2k**, if the known triplet energy of **2j** (59.8 kcal[23]) were shifted by a comparable amount, triplet excitation transfer from **1a** to **2k** could be exothermic instead of the 2 kcal endothermic for **2j**. Such an energy ordering would also obviously account for the rather less efficient isoprene quenching of **2k** isomerization relative to **2j** (Table III). The absence of a triplet component to **3ak** formation thus might arise because formation of **2k** triplet completely dominates the chemistry of the **1a**:**2k** triplet exciplex.

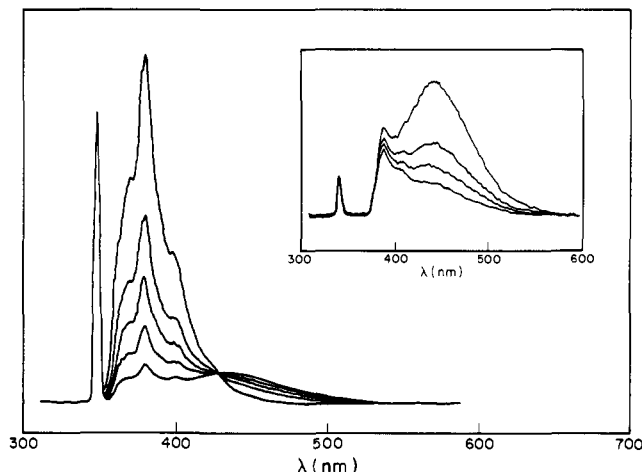Both singlet and triplet components are present in the **1b** +

Figure 1. Quenching of 1a fluorescence by 2k. Insert: quenching of the 1a:2k exciplex fluorescence by dimethyl acetylenedicarboxylate.

2j → 3bj + 4bj reaction. Sensitization by Michler's ketone affords **3bj** as the sole isolated product, while direct irradiation affords both. Clearly, **4bj** is a singlet product; whether **3bj** is exclusively a triplet product or is formed from both triplet and singlet pathways is as yet undetermined.

Stereochemistry. The reactions of **1a** with **2j** or **2k** proceed, within observation limits, with complete retention of configuration of the olefin. It was, however, necessary to employ 0.2 M isoprene to minimize sensitized **2k** ⇌ **2l** isomerization. Although the employment of a triplet quencher for enhancing stereoselectivity in such cases seems an obvious notion, we are unaware of any other synthetic applications.

Examination of reaction mixtures involving **1a** and either **2j** or **2k** by NMR, especially in the δ 1.5–0.5 region where only the methyl groups of the adducts appear, shows ≲2% of adducts with different chemical shifts. This is true even for the triplet component of the reaction with **2j**. We were able to show that *cis*-**2j** is unreactive by noting the expected downward break in a plot of **3aj** formation with time at the point where isomerization to *cis*-**2j** neared completion in a MK-sensitized reaction.

With **2l**, the analysis of stereochemistry is more complicated. We have never obtained **2l** completely free of **2k**, and we have already reported[4] that the rate of quenching of S_1 of **1a** by **2k** is substantially faster than quenching by **2l**. In preparative experiments in the presence of isoprene, we have easily obtained **3al** crystalline and free of **3ak**. By NMR examination of such reaction mixtures, however, we have always detected at least 15% of **3ak**. Consideration of the isomeric composition and the kinetic parameters for the reaction leads us to estimate 95% stereoselectivity for the **1a** + **2l** reaction.

Another possible explanation for this small loss of stereochemistry is that exciplex substitution[24] is occurring. If the (**1a:2k**) exciplex is more stable than the (**1a:2l**) exciplex, as would be inferred from their fluorescence spectra, the reaction[1] (**1a:2l**) + **2k** → [1](**1a:2k**) + **2l** is exothermic. The small amount of **2k** in the **2l** could then lead to even more **3ak** than would be calculated on the basis of competitive quenching of **1a** singlet by **2k** and **2l**.

Another stereochemical feature of these reactions is particularly striking: the bulky phenyl group of the styrene derivative invariably is found in the more crowded endo position in the adduct. It is relatively common for singlet photodimers to exhibit such "maximum-overlap" behavior,[20,25–29] presumably arising from a singlet excimer mechanism. However, the triplet product in the **1a** + **2j** reaction is in contrast to the "minimum-overlap" less crowded products commonly observed[26,27,30,31] in triplet state reactions. Note the marked

contrast in singlet vs. triplet behavior in coumarin[25] dimerization, acenaphthylene dimerization,[26,27] and dimerization of substituted phenanthrenes.[20,31] In each case, syn dimers are obtained in the singlet state and anti dimers dominantly[26,27] or exclusively[25,31] from the triplet state. It may be that triplet exciplexes, as in the present case, derive either greater stability or greater propensity for reaction from orbital overlap than do triplet excimers. We must regard the role of triplet excimers (exciplexes) in photoreactions as somewhat clouded at present. Further studies of reactivity and product structure as a function of reactant structure, together with further search for triplet exciplex (excimer) intermediates by physical means, are needed.

It is of interest that a single adduct is formed even in the triplet state reactions (**3aj, 3bj**). One might have expected a triplet 1,4-biradical to be produced, even if a triplet exciplex intermediate intervenes.[1,3,32] While the "most stable biradical" hypothesis would satisfactorily explain the *regio*chemistry regardless of triplet exciplex intermediacy, significant *stereo*randomization could be expected. We advance three hypotheses in rationalization of the absence of an exo-phenyl product. First, triplet exciplex collapse may occur concertedly with concomitant spin inversion. Such a result would to our knowledge be unprecedented. Second, the 1,4-biradical precursor may be constrained from rotation by the presence of the bulky aromatic moieties and consequently can afford only the product corresponding to its initial structure, presumably the maximum overlap one derivable from a sandwich exciplex. Third, the endo-phenyl compound **3aj** may actually not be the more hindered, since it can have four of the five nonhydrogen substituents on the puckered cyclobutane ring in pseudoequatorial positions, while the exo-phenyl analogue can have at most three. Distinction among these three is not now possible; much more must be learned about the dynamics of triplet exciplexes and 1,4-biradicals first.

Exciplex Intermediates. Excimers and exciplexes have long been postulated as intermediates in photocycloadditions. Dimerization of anthracene,[9,28] of acenaphthylene,[26] of substituted cyanophenanthrenes,[21] and of coumarin[25] were proposed to proceed through excimers, while the additions of tetramethylethylene to stilbene,[33] of benzophenone to 2-butene,[32a] of acrylonitrile to naphthalene,[34] of various alkenes to cyclohexenones,[35] of two differently substituted anthracenes,[36] of alkenes to benzene,[37] (possibly) of dienes to acenaphthylene,[38] and a host of other reactions have been proposed to proceed through exciplexes. In these examples, no direct spectroscopic evidence was initially available which indicated the presence of excimers or exciplexes under the reaction conditions. In recent years, however, in an increasing number of cases, there have been simultaneous observations of exciplex emission and cycloadduct formation; noteworthy are the reactions of phenanthrene with dimethyl fumarate,[3,39] various alkenes and dienes,[12c] and 9-cyanophenanthrene with 2,5-dimethyl-2,4-hexadiene.[11]

Figure 1 shows the fluorescence spectrum of **1a** with varying concentrations of **2k**. The quenching of **1a** fluorescence is accompanied by the growing in of a new, structureless emission (λ_{max} 435 nm). The isoemissive point at 427 nm is clear evidence for a stoichiometric relation between the two, and there is essentially no doubt that the 435-nm emission is the fluorescence of the **1a:2k** exciplex.

Although exciplex formation and photoreaction occur in the same system, it requires a separate experiment to demonstrate exciplex intermediacy in the reaction. The insert in Figure 1 shows the effect of dimethyl acetylenedicarboxylate on the exciplex fluorescence. *The marked attenuation* ($k_q\tau$ in air-saturated benzene = 64 ± 5 M^{-1}] is *accompanied by identical attenuation of photocycloaddition* ($k_Q\tau$ = 62 ± 5 M^{-1}). Dimethyl acetylenedicarboxylate is not an efficient quencher of

Table V. Estimated Rate Constants for Fluorescence Quenching of Phenanthrenes by Styrenes

		$10^{-9} S/\tau^{air}$, M^{-1} s^{-1}			
Phenanthrene	τ^{air}, ns	βMS	*t*-An	c-An	*p*-BA
1a (9CP)	15.3	0.1	5.0	1.0	4.4
1b (3,9-DCP)	9.4	0.7	17.3		
1c (3,10-DCP)	11.3	1.2	12.0		
1d (3-MeO-9CP)	12.2	0.1	1.0		
1e (3-MeO-10CP)	19.7	0.1	1.5		

Table VI. Exciplexes Observed between Phenanthrene and Styrene Derivatives

	Exciplex λ_{max}[a] and intensity[b] in benzene			
Phenanthrene	βMS	*t*-An	c-An	*p*-BA
1b (3,9-DCP)	428 (++)	485 (++)		
1c (3,10-DCP)	(+)	469 (++)		
1a (9CP)	0	432 (++)[c]	420 (+)	448 (++)
1d (3-MeO-9CP)	0	(+)		
1e (3-MeO-10CP)	0	425 (+)		

[a] Uncorrected, nm. [b] (++): intensity ca. 10% of phenanthrene. (+): intensity ca. 1% of phenanthrene. 0: undetected. [c] 418 (++) in isooctane; 468 (+) in acetone.

Figure 2. A probable structure for the **1a:2k** exciplex.

1a singlet, $k_Q\tau = 2.2$ M^{-1}, and the quenching must result from interaction with the exciplex. The quenching result could thus only be obtained if the exciplex is either a direct precursor of product or in *equilibrium* with a species which is. The former is clearly the simpler assumption.
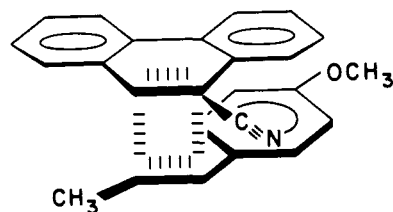
Figure 2 suggests a structure for the **1a:2k** exciplex. It involves maximum overlap of the chromophores and permits the stereospecific collapse to products that we observe.

Nature of the Exciplex Intermediates. The existence of an exciplex in the reaction of **1a** with **2k** seems virtually certain, and the involvement of related exciplexes in the other **1 + 2 →** **3** reactions therefore seems highly probable in view of their similarity. Even in the cases of triplet reactions, **1a** or **1b + 2j** sensitized by Michler's ketone, the analogous regiochemistry and stereochemistry suggests a triplet exciplex.[40] We undertook a fluorimetric study of the singlet exciplexes via substituent and solvent effects, from which we conclude that they are charge transfer (CT) in nature, and that their properties are quite similar to those of unreactive exciplexes. Tables V and VI list the results obtained.

First, the quantity S/τ^{air}, where S is the Stern–Volmer slope for quenching of phenanthrene fluorescence by the styrene and τ is the phenanthrene singlet lifetime, is markedly sensitive to substituent. *trans*-Anethole is an order of magnitude better quencher than β-methylstyrene and the dicyanophenanthrenes are an order of magnitude better quenchees than methoxycyanophenanthrenes. The quantities S/τ^{air} are rather complex functions of rate constants for exciplex formation, feedback (reversion) rates for exciplex → phenanthrene singlet, and the lifetimes of the phenanthrene and exciplex. They nonetheless should qualitatively increase as exciplex stability increases. Evidently, increasing charge transfer (CT) stabilizes these exciplexes as it does many others.[2,41]

Second, the λ_{max} for exciplex fluorescence when seen (Table VI) is sharply red shifted both by substituents which would enhance CT between the partners and by an increase in solvent polarity. Such behavior is readily expected, based on the work of Weller.[41] Our solvent shift in fact approximates those for arene–amine exciplexes, where dipole moment estimates of ca. 12 D have been interpreted to mean that those exciplexes possess substantial CT character.[41]

As the expected CT character of the exciplex decreases, so does the intensity of exciplex emission. Thus, the dicyano-

phenanthrene–anethole exciplexes emit most strongly, and the methoxycyanophenanthrene–β-methylstyrene exciplexes are essentially nonemissive. The emission intensity may be taken as a rough inverse measure of exciplex reactivity. We have already noted[42] that radiative rate constants for nearly all known exciplexes are rather similar. The relation $\phi_F = k_F\tau$ for the exciplex then requires τ to be relatively long if ϕ_F is large. Since τ for these exciplexes[42] is dominated by nonradiative pathways (reaction, decay, and intersystem crossing), we conclude qualitatively that increasing stability of the exciplex by addition of polar substituents inhibits the nonradiative exit channels. Recent theoretical treatments[43] suggest that the exciplex → product path involves passage of the highly polar exciplex over a less polar transition state to a "nonpolar pericyclic minimum", from which reaction and decay ensue. Lewis and Hoyle[12c] have reported solvent effects which largely support this theory. We note that the substituent effects on our exciplex emission intensities are consistent, in that emission is negligible when reaction (decay) is expected to be fastest.

Unreactivity of *cis*-β-Methylstyrene. In no case have we isolated a product related to *cis*-**2j**, and (vide supra) we have demonstrated that it is unreactive in the triplet reaction. It is relatively easy to understand lowered singlet reactivity by analogy to the lowered S/τ value of *cis*-**2k** relative to *trans*-**2k** (Table V), presumably a consequence of increased ionization potential[4] for the cis isomer. An increased ionization potential will diminish the ability of the cis isomer to quench S$_1$ of **3** via electron donation.

Before the lack of triplet reactivity of *cis*-**2j** is well understood, triplet exciplexes must be better understood. We previously[32b] were unable to decide whether CT or exciton-resonance (ER) binding dominated the phenanthrene–dimethyl fumarate and phenanthrene–dimethyl maleate triplet exciplexes. In the present case, the rather similar ionization potentials[4] of **1a** and **2j** would suggest a diminished CT contribution relative to that for the phenanthrene–dimethyl fumarate (maleate) system. The triplet excitation energies for *trans*-**2j** (59.8) and **1a** (58.0) are a close match, a situation which should maximize ER. That *trans*-**2j** → *cis*-**2j** isomerization results efficiently from the triplet **1a**–*trans*-**2j** interaction, presumably a consequence of excitation transfer, may confirm the importance of ER in this case. If so, the much higher triplet energy of *cis*-**2j** (ca. 70) and consequent poorer triplet energy match with **1a** would militate against significant ER.

Whether or not the diminished cis isomer reactivity relative to the trans results from diminished ER, diminished CT, or from as yet undiscerned causes, it is interesting that both *cis*-**2j** and dimethyl maleate show it. The origin of the effect need not be the same in the two cases, however,

CNDO Studies of Stereochemistry and Regiochemistry. We have performed CNDO studies on the addends, using a program kindly supplied by Professor Lionel Raff. By using a frontier orbital approach, we hoped to gain insight into the factors influencing product structure. Our success is mixed.

Consider the differing approaches of the reactants to give rise to four products: head-to-head products of type **3**, head-to-tail products of type **4**, and the (unobserved) products with the aryl group from the styrene derivative exo. These can be

Table VII. FMO Calculations of Styrene (S)–Phenanthrene (P) Excited-State Interaction Energies[a]

	9CP (1a)	3,9-DCP (1b)	3,10-DCP (1c)	3-HO-9CP	3-HO-10CP
			Styrene		
ΔE_{HOMO}, eV	0.18	0.37	0.37	0.24	0.44
ΔE_{LUMO}, eV	0.95	1.29	1.23	0.71	0.41
$E_{head-to-head}$, endo phenyl	3.203	1.538	1.929	2.574	2.403
$E_{head-to-tail}$, endo phenyl	3.997	1.944	1.876	3.421	2.705
$E_{head-to-head}$, exo phenyl	0.872	0.447	0.478	0.743	0.637
			Hydroxystyrene		
ΔE_{HOMO}, eV	0.73	0.92	0.92	0.31	0.11
ΔE_{LUMO}, eV	1.50	1.84	1.78	1.26	0.96
$E_{head-to-head}$, endo phenyl	0.900	0.627	0.796	1.574	4.973
$E_{head-to-tail}$, endo phenyl	1.116	0.756	0.784	2.199	4.597
$E_{head-to-head}$, exo phenyl	0.245	0.169	0.186	0.433	1.135

[a] ΔE_{HOMO} values obtained from vertical ionization potential differences. We thank Professor K. N. Houk and Dr. J. N. A. Ridyard for photoelectron spectra. ΔE_{LUMO} values obtained as IP $- E_s$, where E_s is the ^1L_a excitation energy. These values are for the compounds we studied and not for the models used in the calculations. Perturbation energies are given in units of γ^2/eV.

treated theoretically by assuming interaction exclusively between superposed AOs in the π system; for example, formation of **3aj** would involve interaction of the C-9 p orbital of **1a** with the α p orbital of **2j**, the C-10 p orbital of **1a** with the β p orbital, and six remote p orbitals of **1a** with the six p orbitals of the phenyl ring of **2j**. A different set of eight p orbital pairs would be involved in formation of type **4** products, and only two pairs (phenanthrene C-9 and styrene α, and phenanthrene C-10 and styrene β, for example) would be involved in the formation of exo-phenyl products. We had hoped to predict our results by computation of the perturbation energy E:

$$E = \frac{\gamma^2}{\Delta E_{HOMO}} \left(\sum_i C_i^{HOMOP} C_i^{HOMOS} \right)^2$$
$$+ \frac{\gamma^2}{\Delta E_{LUMO}} \sum_i \left(C_i^{LUMOP} C_i^{LUMOS} \right)^2$$

where γ expresses the energy of interaction between two superposed AOs, each given the same subscript, and the summation is over all superposed pairs of orbitals from the phenanthrene (P) and the styrene (S). We modeled **2j** as styrene, **2k** as *p*-hydroxystyrene, and methoxy substituents as hydroxy. Table VII summarizes our calculations.

The preference for endo phenyl is readily discernible from our results. The perturbation energy is considerably greater in all cases for endo vs. exo phenyl.

The calculations predict that, whether methoxy or cyano is the remote substituent, the type **4** (head-to-tail) product should dominate with the 3,9 substituent pattern in all but one case and type **3** (head-to-head) with the 3,10 in all cases. Indeed, we have only observed type **4** products with the 3,9 pattern and have observed them with remote cyano or methoxy; however, they never dominate. With the 3,10 compounds, only type **3** has been detected, in agreement with prediction. The calculations incorrectly predict that 9CP (**1a**) itself should prefer head-to-tail product. Further, the calculations do not consider spin, so the apparent multiplicity effect on the **4bj:3bj** ratio cannot be studied.

Although the success of the calculations seems fair, we note that the predictions are often based on quite small differences in calculations of E. We would encourage further comparison of theory and experiment only where predicted differences are more clearcut. Finally, these calculations obviously assume minimal perturbation of the two reactants. It may be that the

product is determined not by the exciplex structure but by the structure of the preferred transition state for reaction. If so, both our calculations and those of Lewis, Hoyle, and Johnson, who used a similar approach for the reaction of *trans*-stilbene with conjugated dienes,[45] should be considered only qualitative and suggestive.

Exciplex Collapse to Product. Collapse of exciplexes to product (1) may be concerted, (2) may proceed through 1,4-biradicals, or (3) may proceed through zwitterions (1,4-dipoles). The third possibility seems unlikely, because remote methoxy and cyano groups would be expected to exhibit opposite effects on regiochemistry, where in reality they are qualitatively similar. Distinction between the first two is not possible with the data at hand. An "ordinary" singlet biradical, i.e., one generated thermally, might well exhibit detectable loss of stereochemical integrity,[46] and thus seems unlikely. We consequently believe that these reactions probably involve concerted collapse of exciplex either directly to product or to a "nonpolar pericyclic minimum" as suggested[43] in current theory. However, experimental probes of the [2 + 2] excited state cycloaddition surfaces currently fall far behind theory, and a detailed description of exciplex decay channels remains an intriguing problem for the future.

References and Notes

(1) E. J. Corey, J. D. Bass, R. LeMahieu, and R. B. Mitra, *J. Am. Chem. Soc.*, **86**, 5570 (1964).
(2) B. Stevens, *Adv. Photochem.*, **8**, 161 (1971), and references cited therein.
(3) S. Farid, S. E. Hartman, J. C. Doty, and J. L. R. Williams, *J. Am. Chem. Soc.*, **97**, 3697 (1975).
(4) See R. A. Caldwell and L. Smith, *J. Am. Chem. Soc.*, **96**, 2994 (1974), for a preliminary report of some of the present work.
(5) N. C. Yang, K. Srinivasachar, B. Kim, and J. Libman, *J. Am. Chem. Soc.*, **97**, 5006 (1975).
(6) (a) J. Saltiel and D. Townsend, *J. Am. Chem. Soc.*, **95**, 6140 (1973); (b) B. D. Watson, D. E. Townsend, and J. Saltiel, *Chem. Phys. Lett.*, **43**, 295 (1976).
(7) J. Saltiel, D. E. Townsend, B. D. Watson, P. Shannon, and S. L. Finson, *J. Am. Chem. Soc.*, **99**, 884 (1977).
(8) N. C. Yang, D. M. Shold, and B. Kim, *J. Am. Chem. Soc.*, **98**, 6587 (1976).

(9) (a) A. Chandross and C. J. Dempster, *J. Am. Chem. Soc.*, **92**, 704 (1970); (b) E. A. Chandross and C. J. Dempster, *ibid.*, **92**, 3586 (1970); (c) E. A. Chandross and A. H. Scheibel, *ibid.*, **95**, 611, 1671 (1973).

(10) T. Hagashi, N. Mataga, Y. Sakata, S. Misumi, M. Morita, and J. Tanaka, *J. Am. Chem. Soc.*, **98**, 5910 (1976).

(11) K. Mizuno, C. Pac, and H. Sakurai, *J. Am. Chem. Soc.*, **96**, 2993 (1974), and references cited therein.

(12) (a) F. D. Lewis and R. H. Hirsch, *J. Am. Chem. Soc.*, **98**, 5914 (1976); (b) F. D. Lewis, R. H. Hirsch, P. M. Roach, and D. E. Johnson, *ibid.*, **98**, 8438 (1976); (c) F. D. Lewis and C. E. Hoyle, *ibid.*, **99**, 3779 (1977).

(13) J. J. McCullough, R. C. Miller, D. Fang, and W-S. Wu, *J. Am. Chem. Soc.*, **97**, 5942 (1975).

(14) T. Sugihara, C. Pac, and H. Sakurai, *Chem. Lett.*, 667 (1972).

(15) J. Ferguson, A. W-H. Mau, and M. Puza, *Mol. Phys.*, **27**, 377 (1974); **28**, 1457, 1467 (1974).

(16) S. Farid and K. A. Brown, *J. Chem. Soc., Chem. Commun.*, 564 (1976).

(17) F. C. De Schryver et al., *Pure Appl. Chem.*, **49**, 237 (1977), and references cited therein.

(18) C. S. Wood and F. B. Mallory, *J. Org. Chem.*, **29**, 3373 (1964).

(19) M. V. Sargent and C. V. Timmons, *J. Chem. Soc.*, 5544 (1964).

(20) H. Bouas-Laurent, R. Lapouyade, A. Castellan, A. Nourmamode, and E. A. Chandross, *Z. Phys. Chem. (Frankfurt am Main)*, **101**, 39 (1976).

(21) R. Lapouyade, A. Castellan, J. P. Morand, and H. Bouas-Laurent, *C. R. Acad. Sci., Ser. C*, **277**, 837 (1973).

(22) A. Castellan, Ph.D. Thesis, University of Bordeaux, 1974. We thank Professor Bouas-Laurent for a copy of this thesis.

(23) (a) A. A. Lamola and G. S. Hammond, *J. Chem. Phys.*, **43**, 2129 (1965); (b) P. M. Crosby, J. M. Dyke, J. Metcalfe, A. J. Rest, K. Salisbury, and J. R. Sodeau, *J. Chem. Soc., Perkin Trans. 2*, 182 (1977).

(24) H. Ohta, D. Creed, P. H. Wine, R. A. Caldwell, and L. A. Melton, *J. Am. Chem. Soc.*, **98**, 2002 (1976).

(25) R. Hoffman, P. Wells, and H. Morrison, *J. Org. Chem.*, **36**, 102 (1971), and references cited therein.

(26) D. O. Cowan and R. L. E. Drisko, *J. Am. Chem. Soc.*, **92**, 6281, 6286 (1970).

(27) I.-M. Hartmann, W. Hartmann, and G. O. Schenck, *Chem. Ber.*, **100**, 3146 (1967).

(28) A. Schonberg, "Preparative Organic Photochemistry", Springer-Verlag, New York, N.Y., 1968.

(29) See also K. Mizuno, C. Pac, and H. Sakurai, *J. Chem. Soc., Chem. Commun.*, 648 (1974), for an unsymmetrical example.

(30) A. G. Anastassiou and G. W. Griffin, *J. Org. Chem.*, **33**, 3441 (1968); C. D. De Boer, *J. Am. Chem. Soc.*, **91**, 1855 (1969).

(31) G. Sugowdz, P. J. Collin, and W. H. F. Sasse, *Tetrahedron Lett.*, 3843 (1969).

(32) (a) R. A. Caldwell, G. W. Sovocool, and R. P. Gajewski, *J. Am. Chem. Soc.*, **95**, 2549 (1973); (b) R. A. Caldwell, *ibid.*, **95**, 1690 (1973).

(33) (a) O. L. Chapman and R. D. Lura, *J. Am. Chem. Soc.*, **92**, 6352 (1970); (b) J. Saltiel, J. T. D'Agostino, O. L. Chapman, and R. D. Lura, *ibid.*, **93**, 2804 (1971).

(34) R.M Bowman, T. R. Chamberlain, C. W. Huang, and J. J. McCullough, *J. Am. Chem. Soc.*, **96**, 692 (1974).

(35) P. De Mayo, *Acc. Chem. Res.*, **4**, 41 (1971), and references cited therein.

(36) H. Bouas-Laurent and R. Lapouyade, *Chem. Commun.*, 817 (1969).

(37) W. Ferree, Jr., J. B. Grutzner, and H. Morrison, *J. Am. Chem. Soc.*, **93**, 5502 (1971), and references cited therein.

(38) W. I. Ferree, Jr., B. F. Plummer, and W. W. Schloman, Jr., *J. Am. Chem. Soc.*, **96**, 7741 (1974); the authors consider an exciplex intermediate but find the evidence more convincing for a biradical intermediate.

(39) R. A. Caldwell and D. Creed, *J. Am. Chem. Soc.*, **96**, 7369 (1974).

(40) See ref 12a for a cogent discussion of the stereochemical and regiochemical consequences of singlet or triplet exciplex formation on cycloaddition products.

(41) (a) H. Leonhardt and A. Weller, *Ber. Bunsenges. Phys. Chem.*, **67**, 791 (1973); (b) H. Knibbe, D. Rehm, and A. Weller, *ibid.*, **73**, 839 (1969); (c) H. Beens, H. Knibbe, and A. Weller, *J. Chem. Phys.*, **47**, 1183 (1967); (d) see also ref 2.

(42) D. Creed, P. H. Wine, R. A. Caldwell, and L. A. Melton, *J. Am. Chem. Soc.*, **98**, 621 (1976).

(43) J. Michl, *Photochem. Photobiol.*, **25**, 141 (1977), and references cited therein.

(44) (a) K. Fukui, *Fortschr. Chem. Forsch.*, **15**, 1 (1970); (b) N. D. Epiotis, *J. Am. Chem. Soc.*, **94**, 1924, 1935, 1941 (1972); (c) K. N. Houk, *Acc. Chem. Res.*, **8**, 361 (1975).

(45) F. D. Lewis, C. E. Hoyle, and D. E. Johnson, *J. Am. Chem. Soc.*, **97**, 3267 (1975).

(46) P. D. Bartlett, *Q. Rev., Chem. Soc.*, **4**, 473 (1970).

Structural Studies of Tetracyclines.[1]
Crystal and Molecular Structure of
Tetracycline Methyl Betaine Pentahydrate

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Abstract: The crystal structure of tetracycline methyl betaine pentahydrate was determined by x-ray diffraction techniques. Crystals of the betaine are orthorhombic, with space group $P2_12_12_1$ and unit cell dimensions of $a = 9.608$ (2), $b = 12.143$ (2), and $c = 21.036$ (4) Å. The unit cell and space group are surprisingly similar to those of tetracycline hexahydrate. The structure was solved by direct methods and refined by least-squares procedures to a final unweighted residual of 0.036 for the 1791 reflections used in the analysis. The conformation of tetracycline methyl betaine is virtually identical with that found for tetracycline (in the hexahydrate), as well as in the biologically active amide-protonated tetracyclines. Consequently, the loss of antibacterial activity with quaternization is not due to conformational changes. The differences in the biological activity of tetracycline are explicable on the basis of the loss of the hydrogen bonding potential of the amino group. Therefore, models for the mechanism of inhibition of protein synthesis by tetracyclines will most likely require hydrogen bonding to the dimethylamino group and the zwitterionic form of the drug.

Tetracyclines are widely used antibiotics. Their antimicrobial action appears to be related to the inhibition of protein synthesis by interference with the binding of aminoacyl-t-RNA to the ribosome.[5] However, on a molecular level the nature of the mechanism is not known. In fact, the conformation and state of the tetracycline molecule (i.e., neutral, protonated, or zwitterionic) at the active site has been the subject of much speculation. Our previous studies[2,3] suggested that the conformation found for both the active protonated and zwitterionic species was most likely the conformation at the active site. The next step in developing a molecular model for the mode of action of tetracyclines was to ascertain the relative importance and role of the various functional groups in the molecule.

There are a number of chemical modifications of tetracyclines which occasionally improve the therapeutic usefulness of these drugs but the majority of the chemical changes destroy the antimicrobial properties.[4] One such destructive modification is the quaternization of the dimethylamino group. Both tetracycline methyl iodide and tetracycline methyl betaine have relatively little useful antibacterial activity.[6] The structure of one of these two compounds was deemed essential for determining whether a conformational change was responsible for the loss of biological activity. We decided to study the methyl betaine derivative since the molecular dimensions determined in this equal-atom compound would be more precise than from the iodide salt.