Chemistry of Benzene–Anthracene Cyclodimers[1]

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Abstract: Synthesis of the formal $[4\pi_s + 4\pi_s]$ and $[4\pi_s + 2\pi_s]$ adducts of benzene and anthracene (**1** and **2**) has made possible the observation of features on the potential-energy surfaces that govern Woodward–Hoffmann-allowed and -forbidden cycloreversions. The thermal dissociation of **1** is not chemiluminescent in spite of favorable kinetic and thermodynamic parameters, and its photochemical dissociation yields excited anthracene in very high efficiency ($\Phi_{An^*} = 0.80$). The entropy of activation in the thermal dissociation of **2** is negative, and the photochemical dissociation of **2** yields excited anthracene in low but appreciable efficiency ($\Phi_{An^*} = 0.08$). Comparison of these data clearly demonstrates orbital symmetry control of both the ground- and excited-state reactions.

Energy-rich cyclodimers[2] of aromatic hydrocarbons are expected to display novel chemistry in their reversions to their parent arenes. The synthesis of both the $[4\pi_s + 4\pi_s]$ and the $[4\pi_s + 2\pi_s]$ meso adducts of benzene to anthracene[1] has allowed a study of orbital and state symmetry control[3] in their thermal and photochemical cycloreversions. The pair of compounds, **1** and **2**, is unique in that its clean dissociation to the parent arenes, though similar energetically and otherwise, proceeds via reaction pathways governed by different rules of conservation of orbital symmetry. Mechanistic information deduced from product distribution sheds light on important features of the ground- and first-excited-state surfaces that govern cycloaddition reactions.

Results

Compounds **1** and **2** were synthesized (Scheme I) by an application of the photocycloaddition of substituted 1,3-cyclohexadienes to anthracene,[4] followed by conversion of the oxy substituents to an olefinic bond. That conversion was effected under mild conditions by using the base-induced fragmentation of a 2-phenyl-1,3-dioxalane moiety.[5] Final purities of better than 99.8% after column chromatography and low-temperature recrystallization were ascertained by UV spectroscopy. The kinetics of the thermal decompositions of **1** and **2** in *n*-octane solution were determined by monitoring the growth of anthracene absorption in the UV spectrum at five temperatures. Quantum yields for fluorescence at 273 K were determined by using a Perkin-Elmer MPF-4 spectrofluorimeter with a corrected spectra unit. Quantum yields for photodissociation were measured with a ferrioxalate actinometer to calibrate the light intensity.

Discussion

A. Thermal Dissociations. 1. Kinetics and Activation Parameters. Appearance of anthracene absorption on the UV spectra of **1** and **2** followed good first-order kinetics, from which activation parameters were extracted with conventional transition-state theory. The data in Table I for the thermolysis of **1** and **2** show behavior predicted by the Woodward–Hoffmann rules. The thermally allowed cycloreversion of **2** has a lower enthalpy of activation than the thermally forbidden reaction of **1**. More interestingly, the negative entropy of activation of **2** indicates a highly ordered transition state characteristic of a concerted reaction; the large positive entropy of activation of **1** indicates that, rather than surmounting a symmetry-imposed barrier along a concerted path, thermal dissociation proceeds in a stepwise fashion.

Scheme I

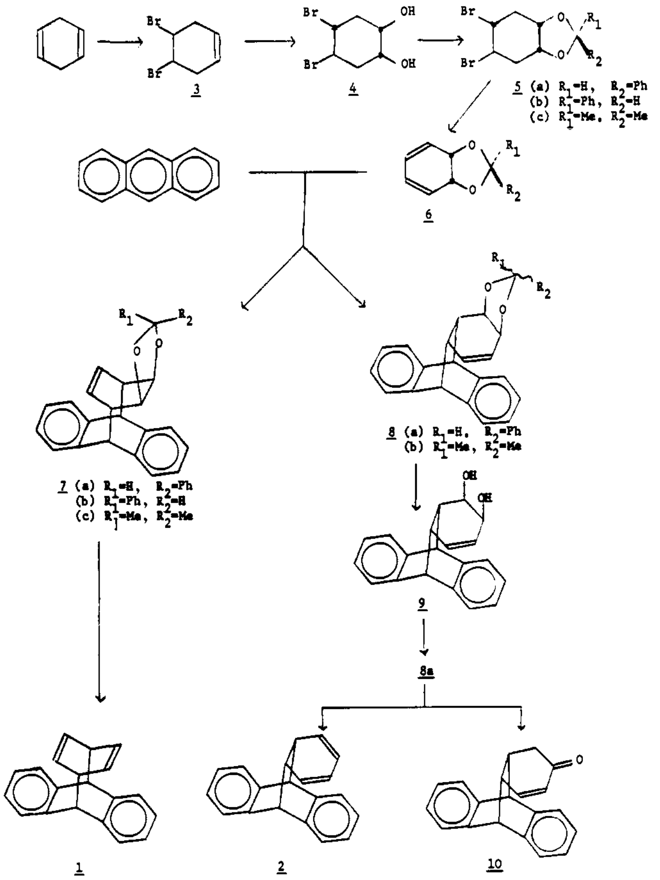

Table I

	thermolysis		photolysis	
compd	ΔH^*, kcal/mol	ΔS^*, eu	Φ_{An}	Φ_{An^*}
1	33.0 ± 0.9	16.4 ± 2.4	0.86 ± 0.06	0.80 ± 0.08
2	24.3 ± 0.2	−3.0 ± 0.6	0.71 ± 0.05	0.08 ± 0.01

2. Thermodynamic Parameters. Although very few thermochemical data are available for **1**, the enthalpy of thermal dissociation of **1** (reaction 1) into anthracene and benzene may be estimated from the enthalpy of thermal dissociation of anthracene

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(1) A preliminary account of this work has been published: Yang, N. C.; Chen, M. J.; Chen, P.; Mak, K. T. *J. Am. Chem. Soc.* **1982**, *104*, 853–855. This work is also identified as "Chemistry of Exciplexes 18."

(2) For a few known cyclodimers of benzene, see: (a) Schröder, C.; Martin, W.; Röttele, H. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 69–70. (b) Berson, J. A.; Davis, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 3658–3659. (c) Grimme, W.; Köser, H. G. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 307–308. (d) Mak, K. T.; Srinivasachar, K.; Yang, N. C. *J. Chem. Soc., Chem. Commun.* **1979**, 1038–1039. (e) Shinmyozu, T.; Inazu, T.; Yoshino, T. *Chem. Lett.* **1978**, 405–408.

(3) Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Academic Press: New York, 1970.

(4) Mak, K. T. Ph.D. Thesis, University of Chicago, 1980.

(5) (a) Hines, J. N.; Peagram, M. J.; Thomas, E. J.; Whitman, G. H. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2332–2337. (b) Berlin, K. D.; Rathore, B. S.; Peterson, M. *J. Org. Chem.* **1965**, *30*, 226–228. (c) Wharton, P. S.; Hiegal, G. A.; Ramaswami, S. *J. Org. Chem.* **1964**, *29*, 2441–2442.

(6) Birks, J. B. "Photophysics of Aromatic Molecules"; Wiley: New York, 1970.

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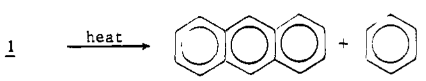
photodimer **11a** into two anthracene (reaction 2), assuming the strain energy of **1** is similar to that of the anthracene photodimer.



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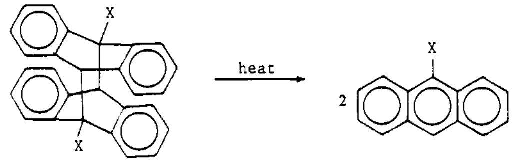
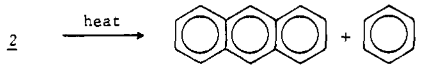


(2)

11, a X = H
b X = CN
c X = CH_3

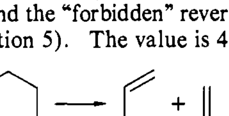


(3)

The difference in enthalpy changes between these two reactions will then be the difference in delocalization energies of products formed, that of benzene and those of anthracene less two benzenes or −22 kcal/mol. Although the high heat of fusion of anthracene interferes with the direct measurement of the enthalpy of thermal dissociation of **11a** by calorimetry, the enthalpy of thermal dissociation of the photodimer of 9-cyanoanthracene (**11b**) and related compounds has been measured to be −20 kcal/mol.[7] This value does not vary appreciably with substitution and is used for our estimation.[7] Therefore, we estimated the ΔH of reaction to be −42 kcal/mol.

The enthalpy of thermal dissociation of **2** (reaction 3) cannot be readily estimated. Since $[4\pi_s + 2\pi_s]$ adducts derived from anthracene and 1,3-dienes are generally more stable than the corresponding $[4\pi_s + 4\pi_s]$ adducts,[8,9] the ΔH of reaction 3 will be less negative than that of reaction 1.

There is also very little thermochemical data available for the entropy changes in these reactions. However, entropy changes in cycloreversions of simple organic systems may be readily calculated from Benson's thermochemical values,[10] both for the symmetry-allowed reversion of cyclohexene to 1,3-butadiene and ethylene (reaction 4) and the "forbidden" reversion of cyclobutane to two ethylenes (reaction 5). The value is 46.1 eu for reaction



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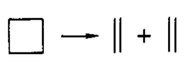


(5)

4 and 41.4 eu for reaction 5. The results merely suggest that the entropy of unimolecular dissociation of a molecule into two components is highly positive. Since both **1** and **2** possess ring systems more rigid than these simple analogues, we assign the average of these two values of 44 eu as a reasonable lower limit for entropy changes in our reactions.

3. Implications of Thermochemical Data. One of the original goals of our research was to show that the thermal dissociation of **1** might be chemiluminescent. Since **1** decomposes as a reasonable rate around 80 °C (353 K), the free-energy change of reaction 1 is −57.5 kcal/mol and the free energy of activation is 27.2 kcal/mol. Thus, the total amount of energy available at the transition state of this reaction is 84.7 kcal/mol. The amount of energy needed to excite anthracene to its first excited state is only 76.3 kcal/mol.[11] Therefore, there is sufficient energy available in the thermal decomposition of **1** to generate excited anthracene which is highly fluorescent. However, neither rapid heating of a solution of **1** in *n*-octane to its boiling point nor rapid heating of a crystal of **1** to above 200 °C generates a detectable amount of fluorescence to eyes accustomed to darkness in a dark room. The results imply that **1** at the transition state of its thermal decomposition does not cross over to the singly excited surface of anthracene in spite of the amount of energy available. The results suggests that a thermally forbidden pericyclic reaction which generates sufficient energy to excite its product is not necessarily chemiluminescent.[12] Geometrical factors and orbital symmetry must also play important roles in this crossing. These points will be discussed in connection with the photochemical decomposition of **1** (vide infra).

B. Photochemical Dissociations. The results of the photochemical dissociations of **1** and **2** are notable in four respects:

(1) Both **1** and **2** display product luminescence. Anthracene fluorescence from traces of anthracene present in the sample was ruled out by taking excitation spectra before and after quantum yield measurements. The absorbing species that gave anthracene fluorescence showed xylene-like absorption.[13]

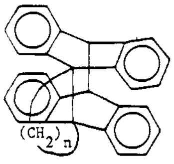
(2) At 273 K, no xylene-like fluorescence was observed for either compound; all product fluorescence was from excited anthracene.

(3) The quantum yields for the formation of excited anthracene differ markedly for **1** and **2** although the overall quantum yield for photodissociation to benzene and anthracene is high in both cases (Table I).

(4) The quantum yield for formation of excited anthracene from excited **1** is very efficient and, within experimental error, identical with the quantum yield for photodissociation.

From these observations, some elementary features of the first excited singlet surface, as well as mechanistic details for photocycloadditions, can be deduced. The initial barrier along the reaction coordinate for either compound must be small. Fluorescence lifetimes for *o*-xylene and related compounds are about 32 ns, and their quantum yields are about 0.16.[14] The absence of xylene-like fluorescence indicates that reaction occurs at least 2 orders of magnitude faster than the radiative decay.

A comparison of the results for **1** and **2** with previously published work on other arene cyclodimers draws some interesting contrasts. Systematic studies of the adiabatic photocycloreversions have been done by Ferguson[15] for the anthracene dimer **11a**, 9-methylanthracene photodimer **11c**, a number of intramolecular cycloadducts of α, ω-(bis-9-anthryl)-*n*-alkanes with linking chains from *n* = 2–4 **12**, [2.4](9,10)-anthracenophane cycloadduct **13**, and the intramolecular heterodimer of 1-(9-anthryl)-3-(1-naphthyl)propane **14**. The anthracene photodimer and 9-methylanthracene photodimer have also been studied by Förster[16] and by Yamamoto and their co-workers.[17] Empirically, adducts



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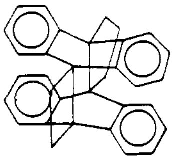

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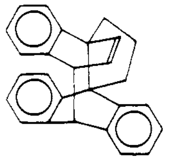

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[7] (a) Guarini, G.; Sarti-Pantoni, P. *Mol. Cryst. Liq. Cryst.* **1970**, *6*, 423–426. (b) Dontai, D.; Guarini, G.; Sarti-Pantoni, P. *Ibid.* **1972**, *17*, 187–195.

[8] Okada, T.; Kida, K.; Mataga, N. *Chem. Phys. Lett.* **1982**, *88*, 157–160.

[9] Wang, T.; Ni, J.; Masnovi, J.; Yang, N. C. *Tetrahedron Lett.* **1982**, *23*, 1231–1234.

[10] Benson, S. W. "Thermochemical Kinetics", 2nd ed.; Wiley-Interscience: New York, 1976.

[11] Murov, S. L. "Handbook of Photochemistry"; Marcel Dekker: New York, 1973.

[12] For a review on pericyclic chemiluminescent reactions, see: Turro, N. J.; Ramamurthy, V. In "Rearrangements in Ground and Excited States"; de Mayo, P., Ed.; Academic Press: New York, 1980; pp 1–23.

[13] For a review on adiabatic photochemical reactions, see: Turro, N. J.; McVey, J.; Ramamurthy, V.; Lechtken, P. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 572–586.

[14] Reference 6, p 126.

[15] (a) Ferguson, J.; Puza, M. *Chem. Phys. Lett.* **1978**, *53*, 215–218. (b) Ferguson, J. *Chem. Phys. Lett.* **1980**, *76*, 398–402.

[16] Menter, J.; Förster, Th. *Photochem. Photobiol.* **1971**, *15*, 289–296.

[17] (a) Yamamoto, S.; Grellman, K.-H.; Weller, A. *Chem. Phys. Lett.* **1980**, *70*, 241–245. (b) Yamamoto, S.; Grellman, K.-H. *Chem. Phys. Lett.* **1982**, *85*, 73–80.

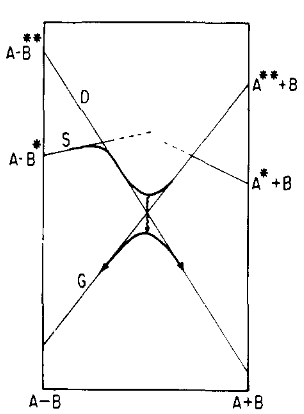
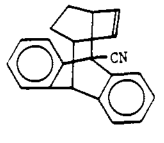


Figure 1. Schematic representation of potential surfaces of a $[4\pi_s + 4\pi_s]$ photocycloaddition and its reversion.

11 through **12b** show behavior very similar to the unsubstituted anthracene dimer. All of the anthracene-anthracene adducts dissociate adiabatically to a fluorescent excimer upon photolysis although the quantum yields are of the order of 0.003 or less at room temperature. The naphthalene–anthracene heterodimer **14** is the only heterodimer system for which fluorescence data were previously reported. For **14**, fluorescence quantum yield exceeded 0.2 at 273 K.[15]

Recently, the photolyses of several photocycloadducts of substituted anthracenes and 1,3-dienes have been investigated by Mataga and Saltiel and their co-workers. Mataga's group reported that the photolysis of adduct **15** from 9-cyanoanthracene to its components is adiabatic with an efficiency better than 10% while the irradiation of **16** yields only the parent fluorescence under the same condition.[8] Saltiel's group reported that the photolyses adducts **17** and **18** from 9,10-dichloroanthracene are adiabatic to yield excited 9,10-dichloroanthracene with efficiencies ranging from 0.002 to 0.013 under a variety of conditions.[18]



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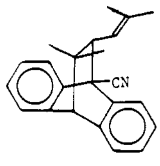

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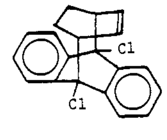

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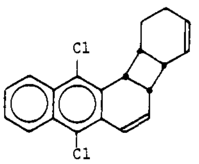

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1. Photodissociation of 1. In the general model for photochemically allowed cycloadditions (Figure 1),[19] the photoexcited starting material crosses over from the singly excited surface (S) to the doubly excited surface (D). It proceeds along this surface to a pericyclic minimum, deactivates from the minimum- to the ground-state surface (G), and partitions from the maximum (or near the maximum) on the ground surface to the product or the starting material. In the case of photocycloaddition of 1,3-cyclohexadiene (CHD) to 9-cyanoanthracene (CNA) to adduct **15** and its reversion, it is known that CHD quenches the fluorescence of CNA at a rate approaching the diffusion-controlled limit and the adduct formation is the major nonradiative pathway in this quenching process, $\Phi_{CNA} = 0.65$.[20] However, the photolysis of adduct **15** yields excited CNA adiabatically with an efficiency higher than 10%.[8] Hence, in the photoreversion of **15**, excited **15** in its dissociation approaches the pericyclic minimum with excess vibrational energy and the formation of CNA* is indicative of escape from the minimum along the adiabatic excited-state surface.

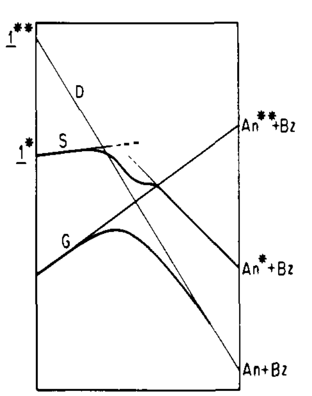

Figure 2. Schematic representation of potential surfaces of decompositions of **1**.

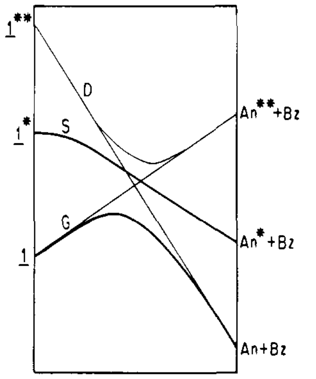

Figure 3. Alternative schematic representation of potential surfaces of decompositions of **1**.

Data from the photoreversions of **15**, **17**, and cyclodimers of arenes support a model where, as the energy difference between adducts or dimers and their parent components is increased, secondary maxima along the reaction coordinate are decreased, leading to greater efficiency in photodissociation as well as more efficient adiabatic photodissociation.

On the basis of the available kinetic, spectroscopic, and thermodynamic data, possible two-dimensional potential surface diagrams for the decomposition of **1** may be constructed (Figures 2 and 3). In the construction, we also take the conservation of orbital symmetry into consideration among the orbitals involved in the chemical transformations and assume that the six bonding orbitals in the two benzene nuclei in **1** have the same symmetry properties as ψ_1 through ψ_6 of anthracene formed. Thus, the ground state of **1** correlates with a double excited anthracene ($\psi_7^2 \rightarrow \psi_8^2$) plus benzene, while the doubly excited state ($\pi_2^2 \rightarrow \pi_3^{*2}$) of **1** correlates with the ground state of anthracene plus benzene. In the state correlation for a $[4\pi_s + 4\pi_s]$ cycloaddition, the singly excited state of the adduct (a S → A transition) correlates with a singly excited state of one of the substrates (an A → S transition). In the photodissociation of **1** into anthracene plus benzene, there are a number of possible excitations for both **1** and its components have similar symmetry properties which make the exact assignment difficult. Compound **1** exhibits a xylene-like absorption spectrum with a somewhat anomalous fine structure;[21]

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(18) Smothers, W. K.; Saltiel, J. *J. Am. Chem. Soc.* **1983**, *105*, 2794–2799.

(19) (a) Michl, J. *Pure Appl. Chem.* **1975**, *41*, 507–534 and references therein. (b) Carr, R. V.; Kim, B.; McVey, J. K.; Yang, N. C.; Gerhartz, W.; Michl, J. *Chem. Phys. Lett.* **1976**, *39*, 57–60. (c) van der Lugt, W. Th. A. M.; Oosterhoff, L. J. *J. Am. Chem. Soc.* **1969**, *91*, 6042–6049. (d) Caldwell, R. A. *J. Am. Chem. Soc.* **1980**, *102*, 4004.

(20) Yang, N. C.; Srinivasachar, K.; Kim, B.; Libman, J. *J. Am. Chem. Soc.* **1975**, *97*, 5006–5008. Shold, D. M. Ph.D. Thesis, University of Chicago, 1975.

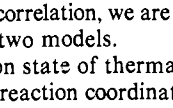
(21) This anomalous fine structure, λ_{max} 284.5 (ϵ 3850), is similarly noted in its dihydro analogue. Yang, N. C.; Libman, J. *J. Am. Chem. Soc.* **1972**, *95*, 1405–1406. It may be attributed to an intramolecular charge-transfer interaction.

we may assign the photoexcited **1** to have the same symmetry as an anthracene in its upper excited state (an A $\rightarrow$ S transition, a possible candidate will be the forbidden $^1A \rightarrow {}^1K_a$ state involving a $\psi_5 \rightarrow \psi_8$ transition)[22] or the allowed fluorescent state of anthracene ($\psi_7 \rightarrow \psi_8$, $^1B_{2u}$ state plus benzene). Similarly, the allowed fluorescent state of anthracene plus benzene may also correlate with an upper excited state of benzene (any A $\rightarrow$ S transition) in **1**.

Due to the highly exothermic nature of photodissociation of **1**, all pathways along the reaction coordinates become unsymmetrically tilted. Assuming the photoexcited **1** has the same symmetry as an upper excited anthracene plus benzene (Figure 2), nearly quantitative formation of singlet excited anthracene in the photodissociation of **1** represents the extreme case of the general model[19b] where the exothermic nature of this reaction tilts the reaction coordinate enough to effectively remove any barrier to escape from the pericyclic minimum. An alternative explanation would be that photoexcited **1** may cross directly over to the singly excited surface that relates to the fluorescent state of anthracene bypassing the doubly excited surface, since each additional surface crossing may lower the adiabatic transformation (Figure 3). Due to the lack of experimental data on some of the excited states involved in this correlation, we are unable to express any preference between these two models.

The transition state of thermal dissociation of **1** comes fairly early along the reaction coordinate according to these correlation diagrams and has a substantially different geometry from that of the pericyclic minimum on the double excited surface. This difference in geometry will reduce both the probability of deactivation from the excited-state surface and the probability of chemiluminescence (Figure 2). Furthermore, the lack of symmetry correlation between the ground-state surface with the singly excited surface will also reduce the probability of chemiluminescence (Figures 1 and 2).

2. Photodissociation of 2. Data from the photodecomposition of **2** indicate that large exothermicity alone is insufficient to promote efficient adiabatic conversion and that symmetry control necessitates a correlation among singly excited states. The degree of concertedness and the question of intermediates in photocycloadditions have been subjects of much current dispute. The photocycloreversions of **1** and **2** provide some mechanistic insights into these questions. The intermediacy of a common singlet biradical in both reactions, as suggested by Kaupp,[23] is excluded by this argument. Biradicals **19** and **20**, derived from **1** and **2**, differ only in initial conformation. The barrier to rotation around the remaining bridging σ bond is insignificant compared to thermal energy available at 273 K, so rapid loss of memory concerning origin is expected. This leads to the prediction, in Kaupp's scheme, of similar quantum yield results in the photolyses of **1** and **2**.



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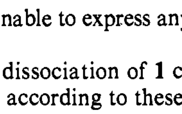

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The present data, coupled with general models for photochemically allowed cycloadditions, present an adequate and consistent picture for reactions of **1**. Picosecond laser spectroscopy[8] has detected a transient species in the $[4\pi_s + 2\pi_s]$ photocycloaddition of 2,5-dimethyl-2,4-hexadiene to 9-cyanoanthracene. No intermediates were observed in the $[4\pi_s + 4\pi_s]$ photocycloaddition of 1,3-cyclohexadiene to 9-cyanoanthracene. However, $[4\pi_s + 2\pi_s]$ cycloadducts are generally more stable than the corresponding $[4\pi_s + 4\pi_s]$ adducts; e.g., photolysis of adduct **15** to its components is adiabatic while adduct **16** is stable under the same condition. Therefore, adduct **2** is an ideal mechanistic probe if one assumes that the cycloreversion proceeds by a reversal of the cycloaddition mechanism because of the following.

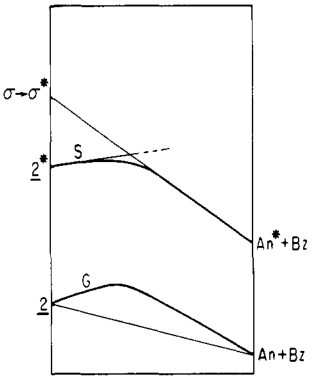

Figure 4. Schematic representation of potential surfaces of allowed decompositions of **2**.

(1) The exothermicity of the reaction ensures that little or no return to the initially excited species occurs.

(2) Intersystem crossing rates for $S_1 \rightarrow T_1$ in *o*-xylenes are comparable to radiative decay rates.[14] Lack of xylene-like fluorescence implies that intersystem crossing and triplet reactions play no major role in the photochemistry of **2**.

(3) Being a photocycloreversion, the reaction is uncomplicated by initial complex formation that can occur in studies of photocycloadditions.

(4) Being a photocycloreversion, there is no ambiguity as to the supra, supra overlap of orbitals in the separated components. This eliminates a symmetry-allowed concerted $[4\pi_s + 2\pi_a]$ or $[4\pi_a + 2\pi_s]$ reaction as an explanation for this photo-Diels–Alder reaction.

(5) The absence of product exciplex fluorescence rules out a concerted symmetry-allowed dissociation to a low-lying charge-transfer state.[24]

According to the Woodward–Hoffmann rules, $[4\pi_s + 2\pi_s]$ cycloaddition and its reversion are allowed processes in the ground state. This correlation may be extended to the doubly excited state as well, thus there is no dip in the doubly excited surface as opposed to the $[4\pi_s + 4\pi_s]$ systems. There is a correlation between the singly excited state as well; however, the low-lying singly excited state of the adduct correlates with an upper excited state of the substrate while the low-lying singly excited state of the substrate correlates with an upper excited state of the adduct.[25] The photolysis of **2** may be treated as a general case of $[4\pi_s + 2\pi_s]$ systems; i.e., the low-lying singlet of **2**, a $\pi \rightarrow \pi^*$ state (a $\psi_2 \rightarrow \psi_3$ excitation of the cyclohexadienyl chromophore or an A $\rightarrow$ S transition), correlates with an upper excited state of benzene plus anthracene, while the fluorescent state of anthracene plus benzene correlates with an upper excited state of **2**, and A $\rightarrow$ S transition such as the $\sigma \rightarrow \sigma^*$ state of **2**. Due to the exothermic nature of this photolysis, photoexcited **2** may access the singly excited surface of anthracene plus benzene which correlates with the upper excited state of **2** in competition against its stepwise dissociation and its nonradiative decay (Figure 4). The adiabatic photodecomposition of the 1,4-peroxide of 1,4-dimethyl-9,10-diphenylanthracene may proceed via a similar mechanistic pathway.[26] The lack of a dip in the doubly excited surface as well as the higher thermodynamic stability of other $[4\pi_s + 2\pi_s]$ adducts contribute to the photostability of these adducts.

Conclusion

Synthesis of the formal $[4\pi_s + 4\pi_s]$ and $[4\pi_s + 2\pi_s]$ adducts of benzene and anthracene (**1** and **2**) has made possible observations of features on the potential energy surfaces that govern Woodward–Hoffmann-allowed and -forbidden cycloreversions. Comparison of the thermal and photochemical decompositions

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of **1** and **2** to the parent arenes clearly demonstrates orbital symmetry control of both the ground- and excited-state reactions.

Experimental Section

Preparation of 4,5-Dibromo-1,2-cyclohexanediol. The procedure of Mak[27] was used to convert 1,4-cyclohexadiene to **4**. 1,4-Cyclohexadiene (51.59 g) was brominated[28] in 100 mL of anhydrous chloroform at −78 °C to give a white precipitate. Insolubility of the dibromide at low temperatures prevents addition of a second equivalent of bromine. Evaporation of the solvent and distillation at reduced pressure gave 137.86 g of white crystals; mp 34–37 °C, 90% isolated yield. **3** (28.77 g) was oxidized in 3.0 L of buffered (60 g of $MgSO_4$) $EtOH/H_2O$ at −5 °C by slow, dropwise addition of aqueous potassium permanganate over a period of 5.5 h. Continued stirring at −15 °C for an additional 15 h and discharge of brown MnO_2 with SO_2 gave a slurry that was filtered to remove inorganic salts. Reduction of volume to 1 L and 1 week storage at 5 °C afforded white, crystalline precipitate. Repeated concentration and harvesting gave a total of 14.75 g, 45% yield, of **4**, recrystallized from hot chloroform, mp 103–105 °C.

Formation of Cyclic Acetals 5a–c. The isopropylidene and benzylidene derivatives were made conventionally by an acid-catalyzed reaction with a large excess of 2,2-dimethoxypropane or benzaldehyde dimethyl acetal. The endo, **5b**, and exo, **5a**, isomers of the benzylidene derivative were separated by repeated washing with petroleum ether, **5a** remaining behind as a crystalline solid, recrystallized from hot chloroform to give white needles, mp 127.5 °C. The isopropylidene derivative **5c** was used without further purification; characterization has been previously reported.[27]

5a: mp 127.5 °C; IR (KBr) 3036, 2910, 1495, 1462, 1442, 1097, 1073, 770 cm^{-1}; NMR ($CDCl_3$) δ 7.44 (m, 2 H, Ar*H*), 7.37 (m, 3 H, Ar*H*), 6.19 (s, 1 H, ArC*H*), 4.50 (m, 1 H, C*H*Br), 4.41 (m, 2 H, C*H*–O), 4.23 (m, 1 H, C*H*Br), 2.85 (m, 2 H, BrCC*H*CHO), 2.49 (m, 1 H, BrCC*H*CHO), 2.29 (m, 1 H, BrCC*H*CHO); UV (*n*-hexane) λ_{max} (ϵ) 267 (88), 263 (185), 257 (237), 251 (211), 245 (197), 204 (15 800); mass spectrum *m/z*: 364 (P + 4, 5.3%), 363 (P + 3, 15.0%), 362 (P + 2, 11%), 361 (P + 1, 31%), 360 (**P**, 5%), 105 (100%);

Anal. Calcd for $C_{13}H_{14}O_2Br_2$: C, 43.12; H, 3.90. Found: C, 43.07; H, 3.85.

5b: colorless oil; NMR ($CDCl_3$) 7.54 (m, 2 H, Ar*H*), 7.40 (m, 3 H, Ar*H*), 5.87 (s, 1 H, ArC*H*), 4.53–4.23 (m, 4 H, C*HX*), 2.85 (m, 2 H, CHBrC*H*CHO), 2.53 (m, 1 H, CHBrC*H*CHO), 2.33 (m, 1 H, CHBrC*H*CHO).

Preparation of Dienes 6a–c. All three dibromides were dehydrobrominated to the respective dienes by the same procedure shown for the exo isomer **6a**. **5a** (6.88 g) in 200 mL of anhydrous benzene was treated with 10.54 g of freshly distilled DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) and refluxed for 6 h. Removal of the hydrobromide salt by filtrating, extracting 3 times with aqueous $NaHCO_3$, drying over $MgSO_4$, and evaporating left 3.31 g of diene, colorless oil, crude yield 87%. Unreacted dibromide was removed by precipitation from petroleum ether. Diene **6a** was not purified further; it decomposed rapidly on Activity I silica, evolving heat and producing a mixture of benzaldehyde and phenol. Attempts at vacuum distillation resulted in Diels–Alder dimerization. Diene **6c** can be purified further by distillation, 40 °C/1 torr.

6a: colorless oil; IR (KBr) 3050, 2930, 2890, 1650, 1083, 1063 cm^{-1}; NMR ($CDCl_3$) 7.52 (m, 1 H, Ar*H*), 7.38 (m, 4 H, Ar*H*), 6.08 (m, 2 H, CH=C*H*—C*H*=CH), 5.93 (m, 2 H, C*H*=CH—CH=C*H*), 5.85 (s, 1 H, ArC*H*), 4.90 (s, 2 H, OHCC*H*O); UV (MeOH) λ_{max} (ϵ) 266 (4200), 260 (4710), 257 (4740), 252 (4340), 202 (16 800).

Photocycloadditions of 6a–c to Anthracene. All photocycloadditions were conducted by using a 450-W Hanovia medium-pressure mercury lamp through a uranyl filter. Substrate and solvent were varied in an attempt to control the regiospecificity of addition in each case. Addition of anthracene in 100–500-mg portions was followed by 20-min deaeration with bubbling dry nitrogen. After 0.5–1.5 h of irradiation, all anthracene was consumed either by adduct formation or by photodimerization. Filtration to remove dianthracene and repetition of the process until yield, followed by NMR, did not result in an increase in [$4\pi_s + 4\pi_s$] and [$4\pi_s + 2\pi_s$] cycloadducts. Results are summarized in Table II. Workup by evaporation followed by chromatography on silica with petroleum ether/methylene chloride gave, in each case, clear oils pure by NMR. Recrystallization of **7a** from benzene/hexane gave white needles, mp 241.5 °C. Recrystallization of **8b** from petroleum ether gave white prisms, mp 155–155.5 °C.

7a: mp 241.5 °C; IR (KBr) 3040, 2940, 1472, 1451, 1340, 1092, 1085, 733 cm^{-1}; NMR ($CDCl_3$) 7.26–7.07 (m, 13 H, Ar*H*), 5.98 (s, 1 H, ArC*H*), 5.77 (m, 2 H, C*H*=C*H*), 4.36 (s, 2 H, C*H*O), 4.28 (d, 2 H, ArC*H*Ar, *J* = 11.4 Hz), 3.49 (m, 2 H, C*H*—CH=CH—C*H*); UV (MeOH) λ_{max} (ϵ) 279 (1520), 275 (1050), 271 (1150), 268 (872), 263 (872), 256.5 (797).

Table II

diene	solvent	anthracene added, g	irradiat time, h	yield of adducts,[a] %	[4 + 4]/[4 + 2]
6a	3.31 g of CH_3CN, 400 mL	7.27	36.6	31	5:1
6a,b	0.42 g of CH_2Cl_2, 50 mL	4.40	19.0	46	>10:1
6c	5.65 g of CH_2Cl_2, 400 mL	10.47	24.0	27	3:5
	2.55 g of CH_2Cl_2, 125 mL	4.30	16.0		

[a] Based on diene.

Anal. Calcd for $C_{27}H_{22}O_2$: C, 86.32; H, 5.87. Found: C, 85.68; H, 5.86.

7b: mp 269 °C; IR (KBr) 3050, 2950, 1473, 1403, 1085, 1058, 767 cm^{-1}; NMR ($CDCl_3$) 7.35 (m, 2 H, Ar*H*), 7.29 (m, 5 H, Ar*H*), 7.14 (m, 6 H, Ar*H*), 5.74 (m, 2 H, C*H*=C*H*), 5.42 (s, 1 H, ArC*H*), 4.27 (d, 2 H, ArC*H*Ar, *J* = 11.3 Hz), 4.22 (s, 2 H, C*H*O), 3.42 (m, 2 H, C*H*—CH=CH—C*H*); UV (MeOH) λ_{max} (ϵ) 279 (1490), 275.5 (973), 271 (1110), 267 (894), 262.5 (840), 261 (800), 256.5 (764); mass spectrum *m/z* 378 (P, 0.1%), 377 (0.2%), 178 (100%).

7c: mp 241.5 °C; IR (KBr) 3050, 2935, 1474, 1457, 1385, 1378, 1050, 744 cm^{-1}; NMR ($CDCl_3$) 7.52 (m, 2 H, Ar*H*), 7.44–7.28 (m, 6 H, Ar*H*), 5.61 (m, 2 H, C*H*=C*H*), 4.22 (d, 2 H, ArC*H*Ar, *J* = 11.0 Hz), 4.18 (s, 2 H, C*H*O), 3.24 (m, 2 H, C*H*—CH=CH—C*H*), 1.24 (s, 3 H, C*H*$_3$), 1.06 (s, 3 H, C*H*$_3$), UV (*n*-hexane) λ_{max} (ϵ) 279.5 (1910), 276 (1140), 271 (1330), 264 (760), 255 (282), 211 (30800); mass spectrum 330 *m/z* (P, 0.1%), 178 (100%).

Anal. Calcd for $C_{23}H_{22}O_2$: C, 83.61; H, 6.71. Found: C, 83.60; H, 6.62.

8b: mp 155–155.5 °C; IR (KBr) 1270, 765, 750, 740 cm^{-1}; NMR ($CDCl_3$) 7.33–7.06 (m, 8 H, Ar*H*), 5.65 (d of d, 1 H, CH=C*H*—CHO, J_1 = 10.3, J_2 = 4.3 Hz), 5.29 (d, 1 H, C*H*=CH—CHO, *J* = 10.3 Hz), 4.27 (d, 1 H, ArC*H*Ar, *J* = 2.1 Hz), 4.22 (d, 1 H, CH=CH—C*H*O, *J* = 4.7 Hz), 4.17 (d, 1 H, ArA*H*Ar, *J* = 2.0 Hz), 3.01 (m, 1 H, C*H*O), 2.72 (m, 1 H, C*H*—CH=CH—CHO), 2.58 (d, 1 H, C*H*—CHO, *J* = 8.5 Hz), 1.30 (s, 3 H, C*H*$_3$), 1.28 (s, 3 H, C*H*$_3$); UV (*n*-hexane) λ_{max} (ϵ) 272 (1700), 265 (1340), 259 (800), 251 (550), 208 (44560).

Anal. Calcd for $C_{23}H_{22}O_2$: C, 83.61; H, 6.71. Found: C, 83.82; H, 6.69.

Preparation of Cycloadducts 1 and 2. The thermally allowed [$4\pi_s + 2\pi_s$] retrocycloaddition of the 2-phenyl-1,3-dioxalane anion systems to yield a benzoate anion and an olefin, described by Hines, Peagram, Thomas, and Whitham,[5] was used to convert **7a** and **8a** to the corresponding cyclodimers. **8b** was converted to **8a**, a mixture of stereoisomers, by hydrolysis in $AcOH/CH_2Cl_2/H_2O$ (3:3:1), followed by acetalation with benzaldehyde dimethylacetal catalyzed by toxic acid in chloroform solution. Similar treatment of **7c** gave only the endo isomer **7b**. Further treatment of **7a**, **7b**, and **8a** was parallel; elimination of benzoate ion from **8a** is illustrative of the general procedure. **8a** (430.0 mg), dried at <0.04 torr for 16 h in 100 mL of tetrahydrofuran and freshly distilled from metallic sodium, was treated with 9.7 equiv. of *tert*-butyllithium (three portions) at −15 °C. After 20 h TLC showed no starting material, so the reaction mixture was quenched with 1 mL of water and evaporated under reduced pressure. The residue was taken up in diethyl ether and extracted 3 times with water. After the residue was dried over $MgSO_4$ and evaporated, the organic material was chromatographed at 0 °C on Activity I silica, using petroleum ether/methylene chloride as eluent to afford 75.5 mg of [$4\pi_s + 2\pi_s$] cyclodimer, crude yield 26%. Further elution gave 156 mg of a yellow oil, yield 51%, identified spectroscopically as the enone **10**. Presumably, it results from the fragmentation of the anion following abstraction of an allylic proton[5a] from **8a**. A petroleum ether solution of crude **2** was saturated at room temperature and chilled to −20 °C to give white prisms, found free of anthracene by NMR and UV spectroscopy. Identical treatment of **7a** gave 98% yield of the [$4\pi_s + 4\pi_s$] cyclodimer **1**, based on consumed **7a**. The other stereoisomer **7b** was unreactive under the same conditions, probably for conformational reasons.[5a]

9: mp 101–107 °C; IR (KBr) 3350, 3030, 2930, 2850, 1470, 1450, 1060, 1040, 760, 750 cm^{-1}; NMR ($CDCl_3$) 7.36–7.07 (m, 8 H, Ar*H*), 5.85 (d of d, 1 H, CH=C*H*—CHO, J_1 = 9.7 Hz, J_2 ; 2.7 Hz), 5.66 (m, 1 H, C*H*=CH—CHO), 4.47 (d, 1 H, ArC*H*Ar, *J* = 2.4 Hz), 4.22 (d, 1 H, ArC*H*Ar, *J* = 2.1 Hz), 3.60 (m, 1 H, CH=CH—C*H*O), 3.18 (m,

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1 H, C*H*O), 2.77 (m, 1 H, C*H*—CHO), 2.33 (d of d of d, 1 H, C*H*—CH=CH—CHO, J_1 = 9.7, J_2 = 7.7, J_3 = 2.5 Hz), 2.03 (d, 1 H, O*H*, J = 8.3 Hz), 1.77 (d, 1 H, O*H*, J = 4.5 Hz); UV (MeOH) $\lambda_{\max}$ (ϵ) 272 (1190), 265 (920), 259 (570), 251 (412).

Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 81.90; H, 7.24.

1: mp (melts at 214 °C dec); IR (KBr) 3027, 2942, 1625, 1600, 1470, 1492 cm^{-1}; NMR ($CDCl_3$) 7.09 (m, 4 H, Ar*H*), 7.03 (m, 4 H, Ar*H*), 5.91 (m, 4 H, C*H*=C*H*), 4.25 (d, 2 H, ArC*H*Ar, J = 11.5 Hz), 3.52 (m, 2 H, CH=CH—CH—CH=CH); UV (MeOH) $\lambda_{\max}$ (ϵ) 284.5 (3850), 276 (2140), 268 (1080), 256 (1150), 219 (24 100).

Mass spectrum and elemental analysis were not attempted because of the low thermal stability of **1**.

2: mp (melts at 214 °C dec); IR (CCl_4) 3070, 3035, 2940, 2890, 1468, 1459 cm^{-1}; NMR ($CDCl_3$) 7.35–7.06 (m, 8 H, Ar*H*), 5.42–5.32 (m, 4 H, C*H*=C*H*—C*H*=C*H*), 4.21 (s, 2 H, ArC*H*Ar), 3.06 (s, 2 H, CH=CH—C*H*—C*H*—CH=CH); UV (MeOH) $\lambda_{\max}$ (ϵ) 291 (1150), 279 (2310), 272 (3610), 266 (3230), 260 (2570).

Mass spectrum and elemental analysis were not attempted because of the low thermal stability of **2**.

10: yellow oil; IR (KBr) 3020, 2920, 1680, 1470, 1460, 1390, 765, 740 cm^{-1}; NMR ($CDCl_3$) 7.30–3.00 (m, 8 H, Ar*H*), 6.62 (d of d, 1 H, C*H*=CH—CO, J_1 = 10.5, J_2 = 3.6 Hz), 5.71 (d of d, 1 H, CH=C*H*—CO, J_1 ; 9.6 Hz, J_2 = 2.1 Hz), 4.26 (d, 1 H, ArC*H*Ar, J = 2.0 Hz), 4.06 (br s, 1 H, ArC*H*Ar), 2.88 (m, 1 H, C*H*—CH=CH—CO), 2.61 (m, 2 H, C*H*$_2$—CO), 2.17 (d of d, C*H*—CH$_2$—CO, J_1 = 14.0, J_2 = 3.6 Hz); UV (MeOH) $\lambda_{\max}$ (ϵ) 272 (1310), 265 (1442), 219 (9960).

Thermolyses of 1 and 2. Thermal decomposition of **1** (1.88×10^{-5} to 4.69×10^{-5} M) and **2** (1.34×10^{-5} M) in *n*-octane was followed by appearance of anthracene absorption at 375 nm. Measurements were made in 1-cm path length quartz cuvettes by using a Cary 219 UV/VIS spectrophotometer equipped with a thermostatic cell compartment. Temperature was measured simultaneously with a copper-constantan thermocouple placed in an identical cell. Kinetic plots were analyzed by the Guggenheim method[29] with time intervals optimized for linearlity, giving first-order rate constants. Arrhenius plots were linear, giving experimental activation energies which were converted to activation parameters with conventional transition-state theory.

Quantum Yield for Total Anthracene Formation. A ferrioxalate actinometer was made according to the procedure by Murov;[11] the procedure was tested until consistent results could be obtained. Stock solutions of **1** and **2** were adjusted to optical densities of 0.1 at 284 and 291 nm, respectively. Aliquots (0.5 mL) were deaerated and irradiated in 1-mL volume, 1-cm path length, narrow cells to minimize uneven stirring effects. The length of irradiation was 0.5–5.0 min. All sample trials were done by using the Perkin-Elmer MPF-4 spectrometer as the light source; the excitation slit was set at 10.0-nm band-pass. Samples were run at 0 ± 0.5 °C. Exposure of the actinometer solutions was done under identical conditions at 23.0 ± 0.5 °C for 15–40 min.

Quantum Yield for Excited Anthracene Formation. Stock solutions of **1** and **2** in spectrophotometric-grade methanol were adjusted to optical densities of 0.1 at 284 and 291 nm, respectively. Solutions were degassed by multiple freeze–thaw cycles at 0.01 torr. Emission and excitation spectra were taken on a Perkin-Elmer MPF-4 spectrofluorimeter with corrected spectra unit at 0 ± 0.5 °C from 220 to 600 nm. The excitation slit was set at 1.0-nm band-pass; the emission slit was 1.0 nm for **1** and 2.0 nm for **2**. Each sample was used only once to prevent interference from anthracene produced during the fluorescence measurement. Standards[30] of 9,10-diphenylanthracene in ethanol and quinine sulfate in 1 N H_2SO_4 were used to calibrate the emission quantum yield.

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Registry No. 1, 80409-72-9; **2**, 80409-73-0; **3**, 42846-36-6; **4**, 80446-29-3; **5a**, 92241-42-4; **5b**, 92241-43-5; **5c**, 92241-44-6; **6a**, 80409-74-1; **6b**, 92241-45-7; **6c**, 80409-75-2; **7a**, 92343-32-3; **7b**, 80409-76-3; **7c**, 80409-77-4; **8a** (isomer 1), 80409-79-6; **8a** (isomer 2), 80446-28-2; **8b**, 80409-78-5; **9**, 92241-46-8; **10**, 92241-47-9; $CH_3C(OMe)_2CH_3$, 77-76-9; $PhCH(OMe)_2$, 1125-88-8; 1,4-cyclohexadiene, 628-41-1; anthracene, 120-12-7.

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Artificial Intelligence Approach to Structure–Activity Studies. Computer Automated Structure Evaluation of Biological Activity of Organic Molecules

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Abstract: A new program is introduced to study the relationship between structure and biological activity of organic molecules. The computer-automated structure evaluation program automatically recognizes molecular structures from the KLN code, a molecular linear coding routine, and proceeds automatically to identify, tabulate, and statistically analyze biophores, i.e., substructures believed to be responsible for known or anticipated biological activity of groups of molecules. The method is applied to the study of the carcinogenicity of polycyclic aromatic hydrocarbons, the carcinogenicity of *N*-nitrosamines in rats, and the pesticidal activity of some ketoxime carbamates.

The evaluation and prediction of the biological effect of chemicals has been at the center of preoccupation of chemists involved in drug development as well as of those concerned about the effect that chemicals may have on the environment.

In the last decade, several methods have emerged that have the potential of helping to solve the problem. They all, in one form or another, revolve around the basic concept that some correlation exists between structure and activity. Among those methods that

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