

raphy on a diglycerol column served to preparatively separate the deuterated isomers.

In addition, deuterium was incorporated at the isopropyl group by treatment of α -methyl-*p*-methoxystyrene with deuterioborane followed by refluxing acetic acid.¹¹ This procedure was followed by the synthesis outlined above substituting hydroborane for deuterioborane. The overall procedure is exhibited in Scheme I.

Table I shows the analysis for the loss of DOH and HOH from the molecular ions of the various deuterated alcohols and clearly demonstrates that there are hidden in the apparent nonspecific loss of water⁵ processes which are highly stereospecific. In detail, the isomers

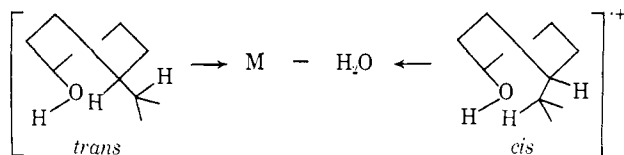
Table I^a

Compd	% M - DOH	% M - HOH
III	13	87
IV	81	19
III'	82	18
IV'	17	83

^a The deuterium incorporation was determined by mass spectral analysis of the derived ketones. It was $d_0/d_1 = 43/57$ (III and IV) and 9/91 (III' and IV'). Rigorous exclusion of oxygen produced the incorporation shown for III and IV. Less exacting conditions allowed only trace deuterium incorporation. The conditions for III' and IV' were far less critical. All figures shown here are corrected to 100% from these deuterium incorporation data. The method of preparation requires identical position and amount of deuterium within each isomer pair. All the data were taken on a CEC-103 mass spectrometer at 70 eV and *ca.* 130°. Corresponding runs on an MS-902 mass spectrometer gave closely similar results.

with deuterium accessible through either a 1,4 or 1,5 elimination show appreciable (>80%) loss of DOH (IV and III'), thereby requiring that the *cis* and *trans* isomers of 4-isopropylcyclohexanol eliminate water in the highly stereospecific manner exhibited in Scheme II.

Scheme II^a



^a This is one of various transition states which may be adduced to fit the determined stereospecificity.

Even more important than this finding of a highly stereospecific elimination of water in these molecules is the implication that deuterium labeling studies of electron impact induced elimination reactions ($M - HX$) are the likely road to gain the so-far unrealized but expected¹² potential for mass spectrometry in stereochemical studies. Thus, while there is no question of the stereochemical assignments in these well-studied cyclohexanols, there is little doubt that the present tools for determining stereochemistry in related compounds

S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1965, pp 115-116 and 177-178, and references therein.

(11) The *p*-methoxy as well as the α -methyl group assure deuterium incorporation at the resultant tertiary position. See: H. C. Brown, "Hydroboration," W. A. Benjamin, New York, N. Y., 1962, pp 115 and 118. The *p*-methoxy- α -methylstyrene was prepared according to R. L. Huang and F. Morsingh, *J. Chem. Soc.*, 160 (1953). It gave an nmr spectrum in accord with its structure.

(12) See ref 10, pp 187-188.

are weak. Indeed, in substituted cyclooctanols, only unequivocal synthesis made available the configurations of the 5-substituted isomers,¹³ while the application of nmr to assign configuration to these flexible ring systems has been challenged.¹⁴ Other methods including the often used relative retention times on chromatography are equivocal and may be subject to unexpected breakdowns. The combination of deuterium labeling in conjunction with mass spectrometry may therefore serve a useful function in this regard and our present work is directed to accomplishing this goal in systems less well defined than the model studied herein.

(13) See for example: A. C. Cope and R. B. Kinnel, *J. Amer. Chem. Soc.*, 88, 752 (1966); A. C. Cope and D. L. Nealy, *ibid.*, 87, 3122 (1965).

(14) F. A. L. Anet and M. St. Jacques, *ibid.*, 88, 2586 (1966).

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Aromatic Substitution. XXVII.^{1a,b} Friedel-Crafts Benzoylation of Toluene and Benzene with Substituted Benzyl Chlorides. Substituent Effects in the Electrophilic Substituting Agent Affecting the Nature of the Transition State as Reflected by Substrate and Positional Selectivity

Sir:

Electrophilic aromatic substitution is one of the most thoroughly studied types of organic reactions.² Still many of the mechanistic aspects remain undecided and controversial. In our previous studies³ we reported a series of electrophilic aromatic substitutions involving strongly electrophilic reagents which showed low substrate selectivity as reflected by $k_{\text{toluene}}/k_{\text{benzene}}$ rate ratios, but at the same time high positional selectivity (generally high *ortho*:*para* ratios with only a small amount of *meta* isomer formed). We expressed our view that in these systems the rate-determining transition state that lies early on the reaction coordinate thus has substantial π character. Our conceptions gained interest⁴ but were also repeatedly criticized⁵ and it was suggested that the low substrate selectivity observed was

(1) (a) Part XXVI: G. A. Olah, J. Lukas, and E. Lukas, *J. Amer. Chem. Soc.*, 91, 5319 (1969). (b) Presented in part at the joint Meeting of the American Chemical Society and the Chemical Institute of Canada, Toronto, Ontario, May 1970, Abstract ORGN 21.

(2) For recent reviews see: (a) R. Breslow, "Organic Reaction Mechanisms," W. A. Benjamin, New York, N. Y., 1969; (b) L. Stock, "Aromatic Substitution Reactions," Prentice-Hall, Englewood Cliffs, N. J., 1968; (c) L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, 1, 35 (1963); (d) G. A. Olah, "Friedel-Crafts and Related Reactions," Vol. I-IV, Wiley-Interscience, New York, N. Y., 1963-1964.

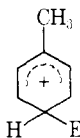
(3) G. A. Olah, S. J. Kuhn, and S. Flood, *J. Amer. Chem. Soc.*, 83, 4571 (1961); G. A. Olah, S. J. Kuhn, S. Flood, and J. C. Evans, *ibid.*, 84, 3687 (1962); G. A. Olah, S. J. Kuhn, and S. Flood, *ibid.*, 84, 1688 (1962); G. A. Olah and N. Overchuk, *ibid.*, 87, 5786 (1965).

(4) For example, R. Breslow "Organic Reaction Mechanism," W. A. Benjamin, New York, N. Y., 1969, Chapter 5.

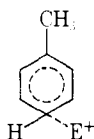
(5) C. D. Ritchie and H. Win, *J. Org. Chem.*, 29, 3093 (1964); W. S. Tolgyesi, *Can. J. Chem.*, 43, 343 (1965) (for a rebuttal, see G. A. Olah and N. Overchuk, *ibid.*, 43, 3279 (1965)); P. Kreienbühl and H. C. Zollinger, *Tetrahedron Lett.*, 1739 (1965); J. H. Ridd in "Studies on Chemical Structure and Reactivity," Methuen, London, 1965, p 152; H. Cerfontain and A. Telder, *Recl. Trav. Chim. Pays-Bas.*, 86, 37 (1967); S. W. Caille and J. P. Corriu, *Chem. Commun.*, 1251 (1967); *Tetrahedron*, 25, 2005 (1969); and most notably C. K. Ingold in "Structure and Mechanism in Organic Chemistry," 2nd ed, Cornell University Press, Ithaca, N. Y., 1969, p 290.

a consequence of incomplete mixing of the reagents before reactions with the very reactive electrophilic reagent.

We wish to report now the first of a series of studies proving that *the position of the transition state in electrophilic aromatic substitutions is not a rigidly fixed one resembling always the Wheland intermediate* (benzenonium ion, σ complex) as generally assumed, but fre-



quently represents a much earlier state on the reaction coordinate of the potential energy diagram of the reaction *resembling not the intermediate but the starting aromatics* (oriented π complex, using Dewar's π -complex terminology but with substantially different definition concerning the orientation and nature of the interaction).



Our previous work provided, we believe, well-documented examples of "early transition states" of electrophilic aromatic substitutions using strongly electrophilic reagents (stable nitronium ions, incipient alkyl-carbonium ions, and halonium ions). We felt that it also should be possible in a systematic way through suitable substituents in the same reagent to effect the electron deficiency of the substituting agent and thus observe a regular shifting of the position of the transition state from a late one resembling the σ complex (Wheland intermediate) to an early one resembling starting aromatics. In order to achieve our objectives we studied the titanium tetrachloride catalyzed benzylation of toluene and benzene with *substituted* benzyl chlorides, a system where the effect of electron-donating substituents will tend to decrease the electron deficiency of the benzylic carbon in the alkylating agent (*e.g.*, the benzyl chloride-Lewis acid catalyst complex) and electron-withdrawing substituents will increase it. Table I summarizes the data obtained.⁶ Data of Table I prove the effect of substituents both on substrate selectivity (as reflected in the $k_{\text{toluene}}/k_{\text{benzene}}$ rate ratios) and on positional selectivity (as shown with isomer distributions, primarily in the ortho:para ratios). Electron-donating substituents ortho and para to the benzylic center increase the k_t/k_b ratio and at the same time decrease the ortho:para isomer ratio in the methyldiphenylmethanes formed, *e.g.*, para substitution is becoming predominant. On the other hand, electron-withdrawing substituents decrease k_t/k_b and increase the ortho:para isomer ratio.

(6) $k_{\text{toluene}}/k_{\text{benzene}}$ relative rate data were generally obtained by the competitive method of rate determination. The ratio of reagents was: 0.1 mol of toluene, 0.1 mol of benzene, 0.01 mol of benzyl chloride, 0.001 mol of titanium tetrachloride. The reaction temperature was 30° and experiments were run for 10 min. Analyses were carried out by capillary gas-liquid chromatography. It was also possible to measure absolute rates for toluene and benzene separately using an internal standard method. Agreement between reactivities obtained from competitive and absolute rate data were excellent. Details will be published in our forthcoming full paper.

Table I. TiCl_4 -Catalyzed Benzylation of Benzene and Toluene with $\text{XC}_6\text{H}_4\text{CH}_2\text{Cl}$ at 30°

$\text{XC}_6\text{H}_4\text{CH}_2\text{Cl}$	$k_{\text{toluene}}/k_{\text{benzene}}$	Methyldiphenylmethane isomer				ortho:para
		ortho	meta	para	1:2	
<i>p</i> -NO ₂	2.5	59.6	6.2	34.2	0.87	
<i>o</i> -F	4.8	39.3	7.8	52.9	0.37	
<i>m</i> -F	4.6	37.7	7.8	54.5	0.35	
<i>p</i> -F	8.7	43.0	6.5	50.5	0.43	
<i>o</i> -Cl	4.6	38.8	7.2	54.0	0.36	
<i>m</i> -Cl	6.4	43.1	6.5	50.4	0.43	
<i>p</i> -Cl	6.2	40.1	5.0	54.9	0.37	
H	6.3	40.5	4.3	55.2	0.37	
<i>o</i> -CH ₃	19.1	24.6	3.4	72.0	0.17	
<i>m</i> -CH ₃	7.8	41.3	2.5	56.2	0.37	
<i>p</i> -CH ₃	29.0	31.4	2.1	66.5	0.24	
2,4,6-(CH ₃) ₃	37.4	16.1	3.1	80.8	0.10	
<i>o</i> -CH ₃ O	60.3	23.2	1.3	75.5	0.15	
<i>m</i> -CH ₃ O	13.2	47.5	2.3	50.2	0.47	
<i>p</i> -CH ₃ O	97.0	28.6	1.5	69.9	0.20	

Meta substituents have relatively little effect. Experimental data clearly indicate that with decreasing electrophilicity of the reagent the transition state increasingly resembles the Wheland intermediate. As the para-substituted benzenonium ion has greater stability than the ortho (meta being the least stable), para substitution is becoming predominant, 66.5–80.8% (with $k_{\text{toluene}}/k_{\text{benzene}}$ being as high as 97). The incipient benzyl cation (*e.g.*, benzyl chloride-catalyst complex) is a strong electrophile, and k_t/k_b and isomer distribution obtained in the reaction of unsubstituted benzyl chloride itself with benzene and toluene indicate an early transition state, resembling starting materials (toluene or benzene) and not the benzenonium ion intermediates. Consequently k_t/k_b is low and the 1:2 ortho:para isomer ratio relatively high (although due to some bulkiness of the reagent complex the ortho:para ratio is not as high as values found with smaller strong electrophiles, where the 1:2 ortho:para ratio can reach or exceed 1).

The position of the transition state in electrophilic aromatic substitutions is not fixed and can resemble in limiting cases either the Wheland intermediate or starting aromatics (the Hammond postulate⁷ thus is experimentally well verified for these reactions). One of the major factors, demonstrated in this work, which influences the position of the transition state is the electrophilicity of the reagent. Substituent effects in the benzylic reagents including those for ortho substituents give excellent linear relationship with Brown's σ^+ constants (which were indeed derived to reflect substituent effects in the related cumyl systems) and were found to be additive. The Brown selectivity relationship relating to ring-substituted benzenes seems to hold well with reactions where late transition states are indicated (as reflected by high k_t/k_b values and low 1:2 ortho:para ratios). Reactions indicating early transition states resembling starting aromatics and not intermediates show no relationship with σ^+ , but could be better related to Hammett σ or Taft σ^* constants which better reflect ground-state inductive effects of the aromatic substrates. No single set of substituent constants or, for the same reason, reaction constants can correlate reactions of both early and later transition-

(7) G. S. Hammond, *J. Amer. Chem. Soc.*, **77**, 334 (1955).

state nature. This explains the correlation of numerous electrophilic aromatic substitutions of the "late transition state" type with σ^+ in the linear free energy relationship⁸ (frequently called the "Brown Selectivity Relationship"). This relationship fails, however, when more reactive electrophiles are involved giving increasingly "early transition states" with structures resembling starting materials. For these cases, σ^+ constants are obviously not suited, because they are derived from benzylic systems reflecting primarily conjugative effects and not ground-state inductive effects.

The realization that the extent of resonance and inductive interaction in the transition state depends on the electron demand of the reagent has indeed led to the view that satisfactory correlation of electrophilic substitutions requires the introduction of more than one parameter which measures the importance of these interactions. The most successful treatment of this type so far is that of Yukawa and Tsuno⁹ and it indeed correlates the widely varying erratic electrophilic substitution reactions much better than the Hammett-Brown treatment.

In conclusion, our work proves for the first time in a well-defined electrophilic aromatic substitution reaction where all parameters are kept constant and only the electrophilicity of the reagent is changed systematically through substituents in the reagent itself that the position and thus the nature of the transition state is not a fixed one and can be changed with ease from a late one resembling intermediate (σ complex) to an early one resembling starting material (π complex). The general implications of this concept for the mechanism of electrophilic aromatic substitution will be further emphasized in subsequent publications, including reports of similar effects in other electrophilic reactions of aromatics (acylations, sulfonylations, etc.)

Acknowledgment. Partial support of the work by the Petroleum Research Fund administered by the American Chemical Society is gratefully acknowledged.

(8) For a summary see L. M. Stock and H. C. Brown, *Advan. Phys. Org. Chem.*, **1**, 35 (1963).

(9) Y. Yukawa and Y. Tsuno, *Bull. Chem. Soc. Jap.*, **32**, 971 (1959).

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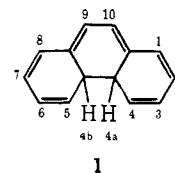
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Received July 6, 1970

Photocyclization of α,α' -Diethyl-4,4'-stilbenediol. Isolation of a Stable Tautomer of the Elusive Dihydrophenanthrenes

Sir:

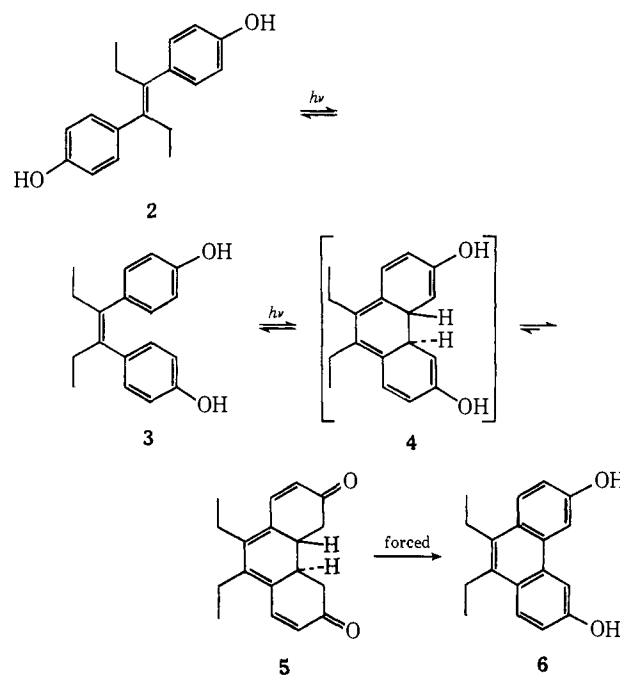
The photochemical oxidative cyclization of stilbenes to phenanthrenes has been the subject of numerous mechanistic studies and has found wide applicability in the synthesis of aromatic and heteroaromatic compounds.¹ Most workers accept a reaction mechanism in which *cis*-stilbene is converted to 4a,4b-dihydrophenanthrene (DHP, **1**) prior to dehydrogenation.

(1) For recent reviews see (a) F. R. Stermitz in "Organic Photochemistry," Vol. I, O. L. Chapman, Ed., Marcel Dekker, New York, N. Y., 1967, p 247; (b) E. V. Blackburn and C. J. Timmons, *Quart. Rev., Chem. Soc.*, **23**, 482 (1969).



Stermitz, *et al.*,² presented evidence that the transient visible absorption observed during photolysis of stilbene was caused by intermediate **1**. However, the DHP was not isolated, not only because of oxidation to phenanthrene,² but also because of reverse reaction to stilbene.³ A recent attempt to prepare stable DHP's from styrylnaphthalenes was unsuccessful.⁴

In view of the continuing interest in the intermediate dihydrophenanthrenes, we were prompted to reinvestigate the work of one of us⁵ concerning the isolation of stable, crystalline 3,4,4a,4b,5,6-hexahydro-3,6-dioxo-9,10-diethylphenanthrene (**5**) from the irradiation of synthetic estrogenic hormone diethylstilbestrol (*trans*- α,α' -diethyl-4,4'-stilbenediol) (**2**). We now (**1**) present complete analytical evidence for structure **5**, (**2**) reformulate the mechanism in terms of a stilbene photocyclization in which intermediate DHP **4** is stabilized by keto-enol tautomerism to the isolable diketone **5**, (**3**) emphasize that the aromatic hydrogens of **2** which become 4a and 4b in **5** remain intact, *i.e.*,



attached to the same carbon atoms,⁶ and (**4**) present indirect evidence that these hydrogens are in a *trans* configuration.

Diketone **5** was prepared by irradiating diethylstilbestrol in aqueous methanol at 254 m μ . Chloroform extraction and recrystallization from toluene-heptane afforded golden-yellow crystals of **5**, which

(2) W. M. Moore, D. D. Morgan, and F. R. Stermitz, *J. Amer. Chem. Soc.*, **85**, 829 (1963).

(3) K. A. Muszkat and E. Fischer, *J. Chem. Soc. B*, 662 (1967).

(4) E. V. Blackburn, C. E. Loader, and C. J. Timmons, *ibid.*, **C**, 163 (1970).

(5) D. Baner, *J. Ass. Offic. Agr. Chem.*, **44**, 323 (1961).

(6) Rearranged 9,10-dihydrophenanthrene isomers have been isolated: M. V. Sargent and C. J. Timmons, *J. Amer. Chem. Soc.*, **85**, 2186 (1963).