

THE MODEL FOR THE TRANSITION STATE OF ELECTROPHILIC  
AROMATIC SUBSTITUTIONS:  $\sigma$ -COMPLEX OR EXCITED  
CHARGE-TRANSFER COMPLEX? A MISE AU POINT

E. Baciocchi\* and L. Mandolini\*,\*\*

Dipartimento di Chimica, Università La Sapienza

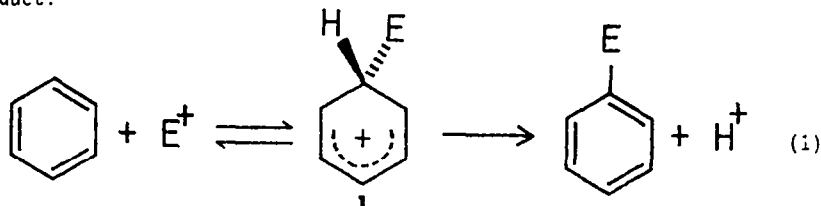
00185 Roma (Italy)

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**ABSTRACT:** Two models are presently available for a description of transition states in electrophilic aromatic substitutions, namely, the  $\sigma$ -complex model and the excited charge-transfer model. A critical evaluation of the relative merits of the two models has been carried out in the light of the wealth of quantitative data available in the field of electrophilic aromatic substitutions of the methylbenzenes. It is shown that virtually all known effects of structure on the rates of electrophilic attack to the methylbenzenes are explainable in terms of the  $\sigma$ -complex model, whereas are inconsistent with the charge-transfer model.

INTRODUCTION

Aromatic electrophilic substitutions are among the most important of all organic reactions. The mechanism of these reactions has been the subject of intensive research ever since.<sup>1,2</sup> The mechanism more widely accepted at present is one involving a two-step sequence where the firstly formed cationic  $\sigma$ -complex  $\frac{1}{2}$  is deprotonated in the second step to give the reaction product.<sup>3</sup>



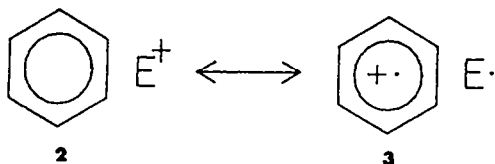
A more detailed version of this mechanism includes the fast and reversible formation of a charge-transfer (CT) complex between the aromatic substrate and the electrophile prior to the formation of the  $\sigma$ -complex. Because of their low stability constants, CT-complexes are usually not taken explicitly into account in discussions of the overall energetics of electrophilic aromatic substitutions. Therefore, the occurrence of CT-complexes does not limit the essential validity of the two-step mechanism of eq (1).

By assuming that the transition state of the slow step of the reaction closely resembles the high energy  $\sigma$ -complex intermediate, the orientation properties of the substituents, as well as the observed relationship between inter- and intramolecular selectivity (Brown's selectivity relationship)<sup>1b</sup> have been satisfactorily rationalized. Furthermore, a wealth of direct experimental evidence concerning the formation of  $\frac{1}{2}$  has been collected in reactions

\*\* and Centro di Studio C.N.R. sui Meccanismi di Reazione, Roma.

between electrophiles and aromatic substrates.<sup>4</sup>

From time to time, however, arguments and conjectures have been presented which, although not excluding the possibility that the  $\sigma$ -complex is an actual reaction intermediate, tend to lessen its role as a good model for comprehending the transition state.<sup>2,5</sup> It has been suggested, with an emphasis which has been increasingly stronger in recent times, that interaction of an electrophile with an aromatic substrate may be characterized by a significant electron transfer component. In other words, in the reaction path leading from the weakly bound CT-complex to the covalently bonded  $\sigma$ -intermediate, a sizable electron transfer component may play a significant role, radical cations being involved or not as discrete intermediates. In the language of resonance, it would mean that the transition state is significantly stabilized by the dative structure 3, which closely represents the excited state of the CT-complex, whose ground state is approximately described by the no bond structure 2.



This is clearly equivalent to the notion that in the transition state electron transfer has progressed further than covalent bonding between the aromatic carbon and the electrophile. Interestingly, this hypothesis appears to fit in with the recent proposal by Pross that many polar processes between an acceptor A (e.g. an electrophile) and a donor D (e.g. an arene) may be interpreted as the result of avoided crossing of DA and D<sup>+</sup>A<sup>-</sup> configurations.<sup>6</sup> According to this proposal the barrier for the polar reaction is "in some way related to the energetics of a single electron transfer from one reactant to the other".<sup>6b</sup>

The idea that the (ArH<sup>+</sup>E<sup>·</sup>) pair 3 can replace the  $\sigma$ -complex as the model for the transition state of electrophilic aromatic substitutions is undoubtedly of great theoretical interest. It would imply, *inter alia*, the unification of stepwise (oxidation, one electron transfer) and concerted (electrophilic addition, two electron transfer) mechanisms, ever since considered to belong to entirely distinct domains.

With the aim at getting insight into this important problem we have carried out a critical evaluation of the relative merits of the two models in the light of the consistent body of information now available.

#### THE RELEVANCE OF THE MODEL

According to Leffler,<sup>7</sup> a description of the transition state can be given in terms of the known structure of reactants and products by comparing the effect of structural variations on the rate constant with their effect on the overall equilibrium constant of the reaction.

Because well-behaved systems for which the relevant data required for a rate-equilibrium relationship to be tested are more the exception than the rule, it is a common practice to compare substituent effects on the rate of a given reaction with the corresponding effects on standard processes related as close as possible to the reaction at hand.

Thus, strong support to the suggestion that the energetics of an aromatic electrophilic substitution is that associated to the process of  $\sigma$ -complex formation has come from the observation that substituent effects on the reaction rate closely parallel those on the Brönsted basicity, that is on the stability of the  $\sigma$ -complexes formed by proton addition to the aromatic moiety.<sup>3</sup>

However, the significance of this parallelism has been dismissed by the advocates of the electron transfer model on the basis that similar parallelism can also be found when reactivity data are compared with other molecular properties such as oxidation potentials ( $E^\circ$ ), charge transfer complexes transition energies ( $h\nu_{CT}$ ) and ionization potentials ( $I_D$ ), all related to processes where an electron is lost from the aromatic substrate.<sup>2,5</sup> From here the belief that a clear choice between the two transition state models is difficult since both predict identical structure dependence of reactivity.<sup>2</sup>

Clearly, there is a part of truth in this statement since in both models the aromatic ring is positively charged and it is therefore quite reasonable that in several cases they can respond even to a remarkably similar extent to substituent electronic effects. However, specific directive effects exist in the  $\sigma$ -complex model which are absent in the excited charge transfer complex model, which lead to systematic and significant differences in the response of the two models to structural effects when di- and polysubstituted benzenes are considered.

This is well illustrated by the data reported in Table 1 for the methylbenzenes series. If we look at the pattern exhibited by the  $\sigma$ -basicities ( $\log K_B$ ) we note that among the subsets of dimethyl-, trimethyl-, and tetramethylbenzenes there is an isomer, namely, m-xylene, mesitylene and isodurene, respectively, whose basicity far exceeds that of the other isomers. We also note that the basicity of mesitylene is significantly greater than that of durene. These findings are the result of the high sensitivity of the  $\sigma$ -complexes energy to the directive effects of substituents, which makes particularly stable those complexes where the electron donating methyl groups are ortho and (or) para to the position of attack. A different situation holds with the  $E^\circ$ ,  $h\nu_{CT}$  and  $I_D$  values which appear to depend much more on the number of methyl groups than on their relative position. This is quite reasonable as the three sets of data provide a measure of the ability of the methylbenzenes to assume a positive charge which is not localized at any particular position of the aromatic backbone. As a consequence of the above observations it turns out that a close scrutiny of structure effects on reactivity in reactions of typical electrophiles with the methylbenzenes has the potential of providing a criterion for the choice of the more appropriate model for the transition state of electrophilic aromatic substitutions, as well as for a meaningful comparison with electron transfer reactions.

Table 1

Standard Oxidation Potentials ( $E^\circ$ ), Ionization Potentials ( $I_D$ ), Charge-Transfer Transition Energies ( $h\nu_{CT}$ ), and  $\sigma$ -Basicities of the Methylbenzenes.

Compound	$E^\circ(V)^a$	$I_D(eV)^b$	$h\nu_{CT}(kcal/mol)^c$	$\sigma$ -Basicity $^d$
toluene	2.67	8.82	71.0	-6.3
<u>o</u> -xylene	2.37	8.56	67.3	-5.3
<u>m</u> -xylene	2.38	8.56	66.7	-3.2
<u>p</u> -xylene	2.30	8.44	66.4	-5.7
hemimellitene	2.23	8.42	63.0	-2.8
pseudocumene	2.13	8.27	63.2	-2.9
mesitylene	2.35	8.42	63.0	-0.4
prehnitene	2.06	8.14	59.5	-1.9
isodurene	2.07	8.07	60.0	+0.1
durene	2.07	8.05	58.8	-2.2
pentamethylbenzene	1.99	7.92	56.0	+0.1

a) In  $CF_3CO_2H$  vs. NHE. Data from J.O. Howell et al. *J. Am. Chem. Soc.*, **106**, 3968 (1984).

b) Data quoted in the ref. reported in footnote a.

c) CT-complexes with tetracyanoethylene in  $CCl_4$  solution. Data from R.K. Chan, and S.C. Liao, *Can. J. Chem.*, **48**, 299 (1970).

d) Log  $K_B$  for protonation in HF. Data from ref. 4, p 851.

#### THE TRANSITION STATE STRUCTURE

In Table 2 the reactivity of m-xylene, mesitylene and isodurene has been compared with that of the other dimethyl-, trimethyl- and tetramethylbenzenes, respectively, for those electrophilic aromatic substitutions for which data were available. These include some of the most typical electrophilic aromatic substitutions: hydrogen deuterium exchange, bromination, chlorination, acetylation, and mercuration.\*

We immediately see that for the reactions of hydrogen deuterium exchange, bromination (in AcOH and  $CF_3CO_2H$ ), chlorination, and mercuration (in  $CH_2Cl_2$  and AcOH), all the results are those predicted by the  $\sigma$ -model for the transition state structure. Thus, the reactivity of m-xylene, mesitylene and isodurene always exceeds that of the respective isomers and mesitylene is always more reactive than durene. The differences in rate range from one to two orders of magnitude and greatly exceed the experimental uncertainties in the rate constants

\* The nitration of methylbenzenes by methyl nitrate has also been studied [G.Olah and H.Lin, *J. Am. Chem. Soc.*, **96**, 2892 (1974)]. In this case the reactivity of the higher members of the series may be at least partially diffusion controlled, thus making the data of doubtful significance for the present discussion. An excellent discussion of the role of electron transfer in aromatic nitration is available [L.Eberson and F. Radner, *Acc. Chem. Res.*, **20**, 53 (1987)]

Table 2  
Reactivity Ratios between pairs of methylbenzenes for some electrophilic aromatic substitutions (1-8) and electron transfer processes (9,10).

Reaction	Reactivity Ratios									
	m-xylene	p-xylene	m-xylene	mesitylene	mesitylene	mesitylene	isodurene	isodurene	mesitylene	mesitylene
	o-xylene	p-xylene	pseudocumene	hemimellitene	hemimellitene	prehnitene	durene	durene	durene	durene
1. Deuterium exchange in $D_2O-CF_3CO_2H^a$	29.8	36.0	113	87.1	87.1		89.9	89.9	34.2	34.2
2. Chlorination in acetic acid <sup>a</sup>	88.2	89.0	58.9	66.7	66.7	29.2	37.2	37.2	18.8	18.8
3. Bromination in acetic acid <sup>a</sup>	96.6	204	124	113	113	38	148	148	66	66
4. Bromination in $CF_3CO_2H^b$	92.5	217								
5. Acetylation <sup>a</sup>	16	14.8	1.7	0.35	0.35	1.0	73	73	28.6	28.6
6. Mercuration in $CH_2Cl_2$	8.9	11.0	6.7	4.2	4.2	2.7	12.2	12.2	6.4	6.4
7. Mercuration in acetic acid <sup>a</sup>	2.1	4.2	4.3	3.1	3.1	2.0	8.6	8.6	7.0	7.0
8. Mercuration in $CF_3CO_2H^c$	1.1	8.8	8.5	7.1	7.1	0.6	17.3	17.3	7.3	7.3
9. Oxidation by CAN in acetic acid <sup>d</sup>			0.7				0.2	0.2	0.005	0.005
10. Reaction with 9-Arylfluorenyl cation <sup>e</sup>						0.7			0.11	0.11

a) Data from E. Baciocchi and G. Illuminati, *Prog. Phys. Org. Chem.*, **5**, 1 (1967).

b) Data from ref. 2a.

c) Data from ref. 2b.

d) Data from E. Baciocchi, L. Mandolini, and C. Rol, *Tetrahedron Letters*, 3343 (1976).

e) Data from D. Bethell, P. N. Clare and G. J. Hare, *J. Chem. Soc. Perkin II*, 1889 (1983).

(generally very low in these systems). The reactivity ratios for the mercuriation reactions are smaller than those observed in the other reactions, most likely as a result of a reduced selectivity in the former process.

The same situation also holds for acetylation where, because of the high steric requirements of this reaction, we can compare only substrates with similar steric hindrance at the position of attack (m-xylene versus p-xylene and mesitylene and isodurene versus durene).

There is therefore no doubt that for the above reactions the observed structural effects on reactivity are exactly those expected on the basis of a transition state closely resembling the  $\sigma$ -complex model. In contrast, the data in Table 2 cannot be accounted for by the excited CT-complex model. According to this model we would expect durene to be more reactive than mesitylene and that similar reactivity in each subset should be exhibited by the isomeric dimethyl-, trimethyl- and tetramethylbenzenes. Actually this reactivity pattern is indeed observed in the reactions of polymethylbenzenes with cerium (IV) ammonium nitrate and with 9 - arylfluorenyl cations (two last entries of Table 2). For the former reaction an electron transfer mechanism has been clearly established whereas for the latter there is convincing evidence for a transition state  $\bar{3}$ -like.

A particular comment is devoted to mercuriation in  $\text{CF}_3\text{CO}_2\text{H}$ . Whereas most of the reactivity ratios are consistent with the  $\sigma$ -model, the anomalies encountered with the m-xylene/o-xylene and isodurene/prehnitene ratios make a clear-cut distinction between the two models less easy to trace.

#### THE ORIENTATION PROBLEM

The above discussion has clearly shown that, at least for the electrophilic aromatic substitutions reported in Table 2, the  $\sigma$ -complex is far a superior model than the excited charge transfer complex  $\bar{3}$  for the transition state structure. However, on this basis only it cannot be excluded that an intermediate like  $\bar{3}$  is formed en route to the  $\sigma$ -complex.

Information in this respect can be obtained by data of isomeric distribution in the reactions of substituted benzenes. Accordingly, it has been pointed out by Pedersen et.al.<sup>5</sup> first and by Fukuzumi and Kochi<sup>2</sup> later, that if the  $\sigma$ -complex forms from collapse of  $\bar{3}$ , the isomeric distribution should be determined by the ring distribution of the odd-electron spin density in the radical cation.

Fortunately, Ramakrishna Rao and Symons<sup>8</sup> have recently been able to measure the hyperfine coupling constants (G) for a large number of monosubstituted radical cations and a check of this hypothesis becomes thus possible. For m-xylene radical cation Ramakrishna Rao and Symons report that all ring protons have the same G values, that is the same odd-electron spin density. In contrast, in electrophilic aromatic substitutions of m-xylene the 5-position is markedly less reactive than the other three positions. Moreover, in benzonitrile radical cation a large spin density at the para position is observed, in line with photoelectron spectroscopy measurements<sup>9</sup> and theoretical calculations<sup>10</sup> but in striking contrast with the well recognized meta orienting power of the CN group. The same situation holds with other electron withdrawing group like COR,  $\text{CO}_2\text{R}$  and CHO.

It appears therefore that the idea that an electron transfer component may play a significant role somewhere along the reaction coordinate of electrophilic aromatic substitution reactions is mechanistically unsound.

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