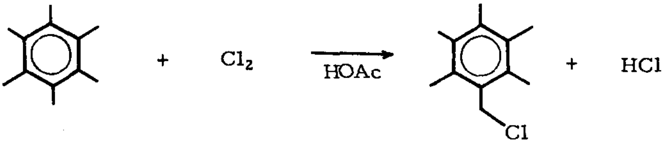
Tetrahedron Letters No. 49-50, pp 4305 - 4308, 1974. Pergamon Press. Printed in Great Britain.

ELECTROPHILIC AROMATIC SUBSTITUTION:
ELECTRON TRANSFER ROUTES IN SIDE CHAIN SUBSTITUTION

by Jay K. Kochi
Department of Chemistry, Indiana University, Bloomington, Indiana 47401

(Received in UK and accepted for publication 25 October 1974)

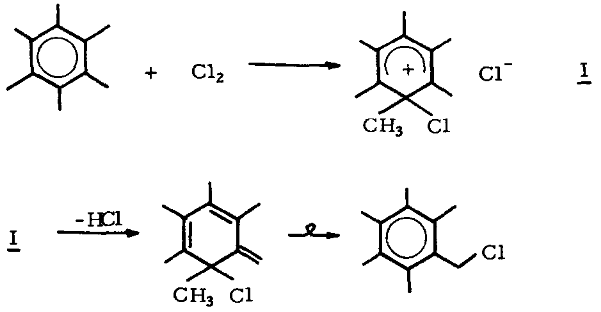
In a continuing series of interesting reports, Baciocchi, Illuminati and coworkers have described the side chain substitution of alkyl-aromatics under a variety of electrophilic conditions.[1-3] For example, hexamethylbenzene is converted to pentamethylbenzyl chloride by chlorine in acetic acid in the dark.[2] The scope of these non-conventional substitution reactions comprise a variety of electrophilic reactions including halogenation, (chlorine, bromine and iodine), nitration and thiocyanation which proceed generally on polyalkylbenzenes and other electron-rich aromatics such as thiophenes, etc.[3-4]



(1)

The heterolytic mechanism in Scheme I which they propose for side chain substitution under electrophilic conditions include: first, the formation of a σ-adduct I between the electrophile and arene in eq 2, followed by either a stepwise or synchronous α-proton loss and rearrangement (eq 3), e. g.,[2]

Scheme I

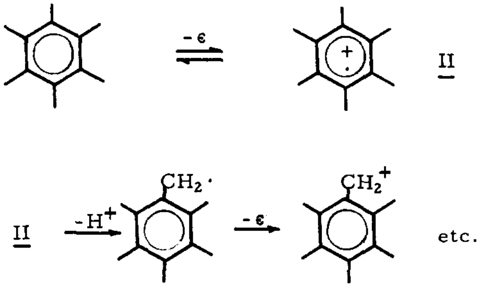


(2)

(3)

It has recently been shown, however, that aromatic substitution, either in the nuclear or side chain positions, may proceed by electron-transfer processes.[5] The electron transfer steps in Scheme II have been effected either electrochemically or by metal oxidants such as cobalt(III), manganese(III), cerium(IV) capable of effecting one-electron changes.[5,6] The formation of the aromatic cation-radical **II** is the key to the electron transfer mechanism, since side chain substitution follows directly from the loss of an α-proton as shown in eq 5. Two factors are important in facilitating the electron transfer process in Scheme II: a relatively low oxidation potential for the aromatic compound and the availability of a one-electron oxidant. We feel that both conditions are fulfilled in a number of the side chain substitution reactions reported by Illuminati *et al.* In particular, many of the electrophiles available for aromatic substitution are also capable of performing as one-electron oxidants. Thus, chlorine, bromine and iodine readily undergo one-electron reduction and are also highly effective electron acceptors in charge transfer complexes with a variety of arenes.[7] Similarly, nitronium ions involved directly or indirectly in nitration have a reasonable high reduction potential relative to nitrogen dioxide.[8]

Scheme II

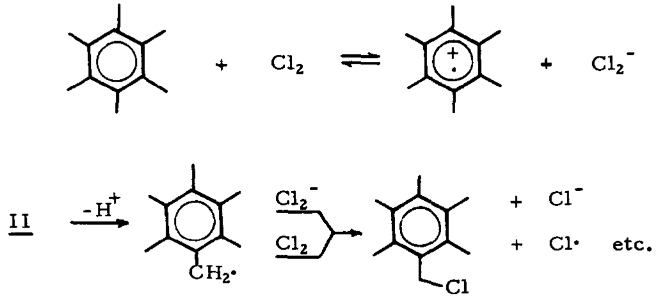


(4)

(5)

We wish to show that chlorination of hexamethylbenzene under conditions described by Illuminati *et al.* may proceed by an electron transfer mechanism. Thus, acetic acid solutions of chlorine and hexamethylbenzene were mixed directly in the cavity of an electron spin resonance spectrometer. The intense and well-resolved esr spectrum of hexamethylbenzene cation-radical shown in Figure 1 was readily obtained at room temperature. Other arenes such as pentamethylbenzene and durene showed similar behavior. The facile formation of the radical-cation is consistent with an electron-transfer mechanism described in Scheme III.

Scheme III



(6)

(7)

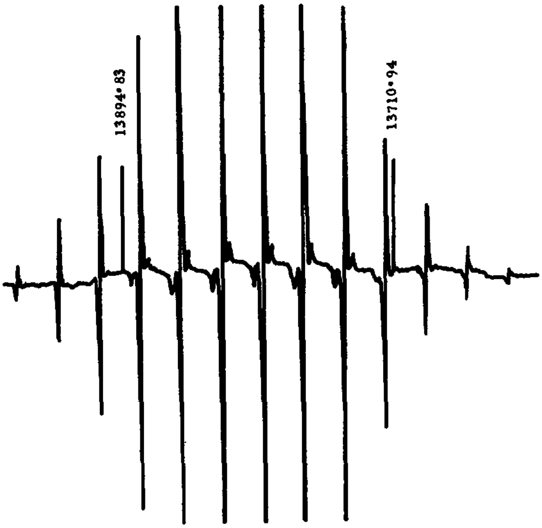


Figure 1. Esr spectrum of the hexamethylbenzene radical-cation (central portion) obtained during the reaction of hexamethylbenzene and chlorine in acetic acid at 25 °C. Proton nmr field markers are in kHz.

The electron transfer mechanism in Scheme III involves readily accessible intermediates and avoids the postulation of cyclohexadienes and their rearrangement. A rigorous distinction between heterolytic and electron transfer pathways in Schemes I and III, respectively, is difficult to make since electrophilic addition (eq 2) and electron transfer (eq 7) have much the same electronic requirements.[5b] In some electrophilic substitutions, such as proton exchange,[9] acceptors are unavailable for an electron transfer process to occur, and the reaction must perforce take a heterolytic pathway.

In addition to side chain substitutions, there are a number of other types of non-conventional reactions of aromatic compounds carried out under electrophilic conditions, including: nuclear ipso substitution, rearrangement, addition and other reactions.[10] Interestingly, the reactivity patterns found in many of these aromatic reactions are closely akin to those presented above for side chain substitutions. Thus, it may also be worthwhile to recast the mechanisms of these transformations in the light of electron transfer processes.

References

1. E. Baciocchi, P. Faggioni and G. Illuminati, Gazz. Chim. Ital., 103, 1311 (1973).

2. E. Baciocchi, A. Ciana, G. Illuminati and C. Pasini, J. Amer. Chem. Soc., 87, 3953 (1965).

3. (a) G. Illuminati, L. Mandolini and A. Patara, Tetrahedron Letters, 4161 (1972),
   (b) K. Nakamura, Bull. Chem. Soc., Japan, 44, 133 (1971),
   (c) H. Suzuki, Ibid., 43, 879 (1970),
   (d) R. Astolfi, E. Baciocchi and G. Illuminati, La Chim. e Ind., 53, 1153 (1971).

5. (a) E. I. Heiba, R. M. Dessau and W. J. Koehl, J. Amer. Chem. Soc., 91, 6830 (1969).
   (b) J. K. Kochi, R. T. Tang and T. Bernath, Ibid., 95, 7114 (1973),
   (c) L. Eberson, Ibid., 89, 4669 (1967).

6. It is also possible with apparent 2-electron oxidants such as Tl(III). [I. H. Elson and J. K. Kochi, J. Amer. Chem. Soc., 95, 5061 (1973)].

7. L. J. Andrews and R. N. Keefer, "Molecular Complexes in Organic Chemistry", Holden-Day, San Francisco, Calif., 1964.

8. F. A. Cotton and G. Wilkinson "Advanced Inorganic Chemistry", Third Ed., Interscience Pub., 1972, p. 357.

9. (a) V. G. Shubin, A. A. Tabatskaya and V. A. Koptyug, Zhur, Org. Khim., 6, 2081 (1970),
   (b) C. Eaborn and G. J. Wright, J. Chem. Soc., B, 2262 (1971).

10. For recent reviews see:
    (a) S. R. Hartshorn, Chem. Soc., Revs., 3, 167 (1974).
    (b) P. B. D. de la Mare, Accounts. Chem. Research, in press.