MECHANISMS OF ELECTROPHILIC SUBSTITUTION IN METALLOCENES:

THE INSIDE-OUTSIDE RELATIONSHIP

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A popular mechanism for electrophilic substitution in metallocenes is one in which ring substitution occurs through rate-limiting transfer of electrophile from a metal-complexed cation (I) to a sigma-complex, followed by fast removal of proton (1,2).


I
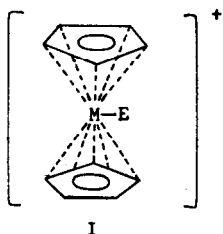
There are a number of observations in the literature which are at variance with such a mechanism (3,4). Recently Rosenblum and Abbate (5) have demonstrated that for the intramolecular cyclization of the epimeric acids (IIa and IIb), there appears to be no preference for the endocyclic substitution involving attack upon the metal atom.
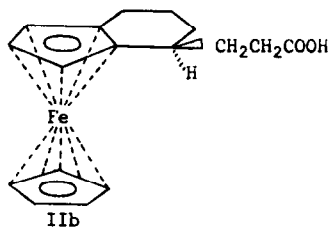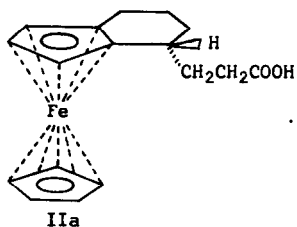
It has been suggested (6) that electrophilic reactions in metallocenes can be explained on the basis of direct formation of sigma-complex without metal participation. In the present report we wish to communicate a general treatment of electrophilic substitution in metallocenes based on this suggestion and upon the assumption that the mechanisms of reactions in these systems parallel those of other organometallic compounds (7,8).

The starting point of our treatment lies in the two mechanisms seen in equations
1 and 2, and pictured in terms of an energy profile in figure 1. Mechanism 1 involves
a two-step process in which electrophile cleaves the metal-carbon bond in an S_E2 reac-
tion with retention of configuration, followed by rate-limiting removal of proton from
the outside in a second step. This step constitutes an S_E2 reaction with inversion.
Concurrent with this process, a second mechanism involves rate-limiting attack of
electrophile from the outside in an S_E2 displacement with inversion of configuration,
followed by fast removal of proton from the inside, with retention of configuration.
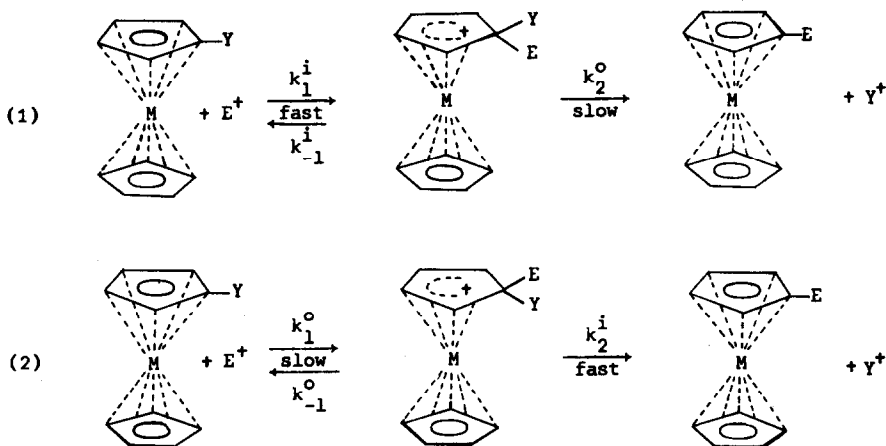

In those cases where E = Y (e.g. proton exchange or radiomercury exchange) reaction (1)
is the microscopic reverse of reaction (2). Thus any process with similar entering and
leaving groups will proceed in both senses. The major pathway for those substitutions
having widely different entering and leaving groups (e.g. acylation) will depend on the
relative rate constants for the individual steps and thus on the nature of electrophile
and substrate.[*] It is possible to correlate reactivities of metallocenes with the data
for benzenoid aromatics by developing two different electrophilic, σ^+, substituent param-
eters. One of these, σ^+_{INSIDE}, is that constant for attack on the metal side of the ring

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[*] We picture the role of the metal-complexed cation (I) (if it exists) as being the
counterpart of the π-complex in benzenoid substitution and have excluded it from our
scheme.

(k_1^i), i.e. utilization of the higher electron density found on this side, and should correlate those substitutions occurring by reaction 1. A second constant, $\sigma^+_{OUTSIDE}$, is for those substitutions in which the electrophile interacts with substrate on the side of the ring opposite the metal atom in the rate-limiting step (k_1^o) and should correlate those substitutions occurring by reaction 2.

We propose that the availability of sigma-bond electrons for carbon-metal hyperconjugation (or E_2 elimination) should be related to the availability of these electrons for electrophilic attack. Thus equation 1 should correlate with equation 3, which also makes use of the inside electrons (in an E_2 sense), and equation 2 should correlate with equation 4, since these two reactions make similar use of the carbon-metal bond.

(3)

(4)
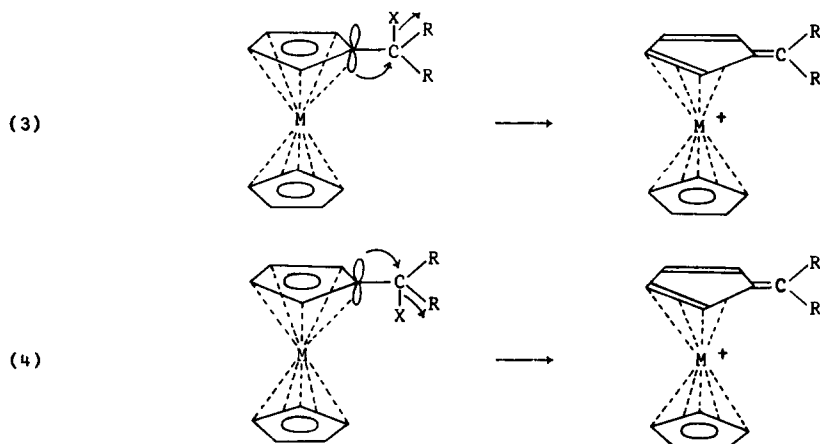
A σ^+_{Fer} = -1.4 has been defined (8) in terms of equation 3 and is very similar to the earlier value of -1.3 from protonation of ketones (9). We will call this the inside value, σ^+_{INSIDE} = -1.4. The outside value, $\sigma^+_{OUTSIDE}$, may be obtained by correcting the inside value for the exo/endo solvolysis ratio obtained by Trifan and Backsai (10) and Hill and Richards (11) with α-acetoxy-1,2-tetramethyleneferrocenes. The ratio k_{exo}/k_{endo} = 2500, after correction for a steric factor of about 8 (10,11) gives k_{exo}/k_{endo} ≅ 300. This results in a $\sigma^+_{OUTSIDE}$ = -1.4 - [log k_{exo}/k_{endo}]/-6.1 ≅ -1.0.

In figure 1, if a stronger electrophile is substituted for $^*H^+$ the activation energy for outside attack will be lowered more (to A) than that for outside removal of proton (to B) tending to channel the reaction through pathway 2. The opposite may be said of weak electrophiles. Therefore, according to our proposal, substitutions proceeding exclusively through reaction 2 will be those in which the attacking reagent is more electrophilic than the leaving group. They will show no primary isotope effect and will correlate with $\sigma^+_{OUTSIDE} \cong -1.0$. Those proceeding through reaction 1 will have the opposite relationship of entering and leaving groups. They should show a primary isotope effect and should correlate with $\sigma^+_{INSIDE} = -1.4$.
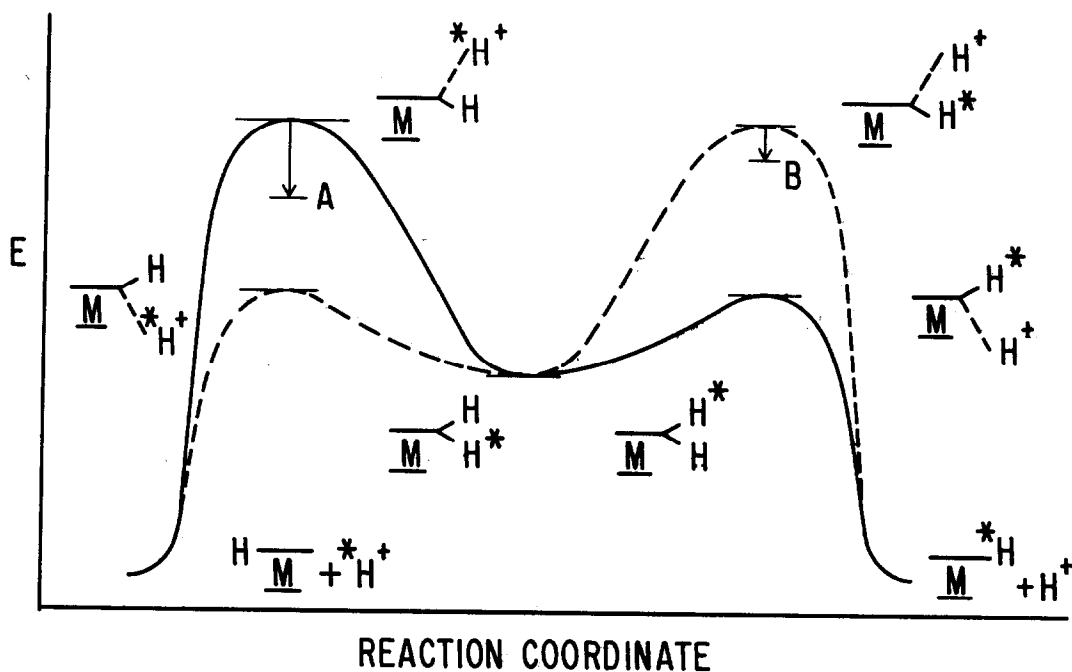

REACTION COORDINATE

FIG. 1

Reaction coordinate for proton exchange by reactions 1 and 2. Dotted line, reaction 1; full line, reaction 2. The points A and B represent the extent of the lowering of the respective activation energies when the strongly electrophilic reagent E^+ is substituted for $^*H^+$.

Proton exchange in ferrocene must proceed equally by equations 1 and 2. It, therefore, should show an isotope effect and does (k_H/k_D = 1.8) (12),[*] its rate should correlate with σ^+ = -1.0 and actually correlates with σ^+ = -1.1 (12). Acetylation, which involves the very electrophilic species, Ac^+, shows no isotope effect (k_H/k_D = 1.0) (12), and correlates with σ^+ = -0.8 to -1.0. On the other hand, the weak electrophile, $Hg(OAc)_2$, reacts with ferrocene with a rate in excess of that calculated from σ^+ = -1.4 and shows an isotope effect (k_H/k_D = 3.2) indicating inside attack.

In addition, limited solvolysis data of Plesske and Richards (14) indicates that $[\sigma^+_{INSIDE} - \sigma^+_{OUTSIDE}]$, (i.e. the k_{exo}/k_{endo} solvolysis ratio mentioned above) increases in the order ferrocene < ruthenocene < osmocene. This observation combined with our mechanism explains why in solvolysis of α-metallocenylmethyl acetates the reactivity order is osmocene > ruthenocene > ferrocene, whereas in acylation, the order ferrocene > ruthenocene > osmocene prevails. The former reactions go according to σ^+_{INSIDE}, and the latter by $\sigma^+_{OUTSIDE}$.

The mechanistic schemes and experimental details will be presented in full at a later time.

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[*] Yakusin (13) reports a somewhat lower value than ours, k_H/k_D = 1.4. The reasons for this discrepancy will be discussed in the full paper.

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