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A COMPARISON OF THE RELATIVE ENERGIES OF ISOMERIC INTERMEDIATES FORMED IN ELECTROPHILIC, RADICAL, AND NUCLEOPHILIC AROMATIC SUBSTITUTION REACTIONS[1]

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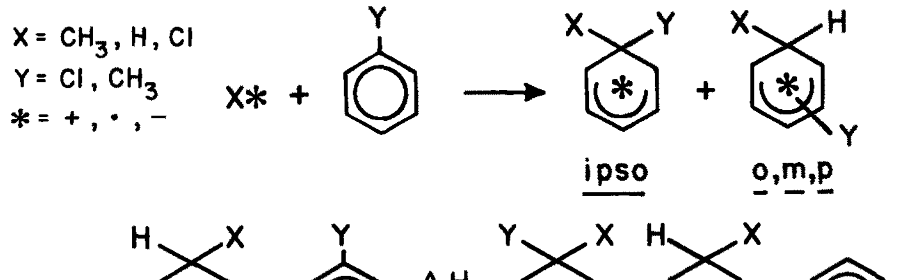
Abstract—The relative energetics of isomeric σ-complex intermediates formed in electrophilic, free radical, and nucleophilic attack of Cl, H, and Me on PhCl and PhMe are compared for all positions: *o*, *m*, *p*, and *ipso*. The results are presented as ΔH, computed by the MINDO/3 method, for the appropriate isodesmic reaction with benzene. For the chlorobenzene intermediates, there is a marked increase in the relative preference for the *ipso*-position as the reactions change from electrophilic to free radical to nucleophilic. For toluene intermediates, the order of stability—$p > o > m > ipso$—is seen in all reactions except for one case, free radical methylation. In general, the free radical intermediates show the smallest range of energy differences. Comparison of predictions from these calculations with experimental results (largely partial rate factors and product ratios) shows some qualitative agreement.

EXPLANATIONS of selectivity in aromatic substitution reactions have frequently been given in the language of resonance theory (the number and stability of the various resonance contributors to the possible isomeric resonance hybrids that depict the σ-complex intermediates). Resonance theory has been accurate in predicting *o,p* vs *m* orientation in substitution reactions of mono- and di-substituted benzenes. On the other hand, simple resonance theory fails to explain variations in *o*/*p* ratios. Furthermore, during the past decade, the importance of attack at the *ipso*-position (the position bearing the substituent) has been realized.[2,3] *ipso*-Attack can lead to several results: (1) replacement of the substituent by the electrophile, (2) migration of either the attacking electrophile or the substituent to some other position, (3) formation of a cyclohexadiene by addition of a nucleophile, and (4) loss of the electrophile to form reactants. Since an *ipso*-intermediate can rearrange to give *o*-product, the conventional *o*, *p*, vs *m* product distribution can no longer be taken as a reliable indicator of the relative energies of isomeric intermediates or of the transition states leading to them. Finally, resonance theory has little to say about the relative energies of *ipso*-intermediates formed from different substituted benzenes.

A recent report by Everly and Traynham,[4] establishes the formation and rearrangement of an *ipso*-intermediate in the photoinitiated chlorination of *p*-bromonitrobenzene. Although replacements of a substituent during aromatic free radical substitution reactions have been reported by several investigators during the past 75 yr,[5-8] an *ipso*-intermediate has not been proposed until recently.[9] In fact, it is this proposal by Traynham[9] that has served as the impetus for the study described below.

In order to achieve insight into the factors influencing the relative energies of isomeric σ-complex intermediates that may be found in electrophilic, radical, and nucleophilic aromatic substitution reactions, calculations have been done utilizing the MINDO/3 method.[10] These calculations have been performed on the *o*-, *m*-, *p*- and *ipso*-intermediates formed in the attack of Me, H, or Cl on PhCl and PhMe, eqn (1).

The data are presented as energies relative to the corresponding σ-complex intermediate formed in the attack on benzene. This relative energy relationship can be described as ΔH for the isodesmic reaction shown in eqn (2). Treatment of the results in this fashion serves two purposes—correction of systematic errors that may be present in MINDO/3 and facilitation of comparison with experimental data. The bonds being made and



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broken in the reactants and products of eqn (2) are of the same type. Differences in ΔH of eqn (2) are a reflection of the position and nature of the substituent, Y.

To establish the validity of MINDO/3 for these reactions, comparisons of the computed relative stabilities with the appropriate experimental data are made. Ideally gas-phase data should be used for comparison. (In the one case where data are available, MINDO/3 does quite well; see *X-Methylcyclohexadienyl intermediates*). However, since the objective of this study is to develop an overview, no attempt is made to be quantitative and data from the solution phase are used for comparison as well. Most of the experimental data cited are partial rate factors. It is not expected that rates of substitution parallel localization energies. Apart from the fact that the rate data are usually from solution phase, the steric factors in substitution reactions are usually more pronounced in activation energies than in ΔH's. Yet, this report shows that many of the *trends* in the rate data parallel the *trends* in the computational data, when comparing the three types of substitution reactions juxtaposed to each other.

It is the intent in this report to summarize the theoretical and experimental data in such a way that these *trends* as a function of electronic character, ($* = +$, $\cdot$, $-$), become apparent. Of special interest is the trend for the relative stability of the *ipso*-intermediate, i.e. what conditions favor *ipso*-attack. The results are presented by reaction type: Me, H, and Cl addition to PhCl, then similar additions to PhMe. In each reaction-type section, the discussion follows the sequence; electrophilic, radical, and nucleophilic addition. The general format is a presentation of the theoretical and experimental data followed by a comparison of the two. The discussion section ends with a summary of the major *trends* observed in the study, caveats concerning MINDO/3, and conclusions about the stability of *ipso*-intermediates.

Computational procedure

Calculations were performed by use of the MINDO/3 program obtained from Quantum Chemical Program Exchange in Bloomington, Indiana—QCPE No. 279. Computations were carried out on an IBM 360 computer at the LSU System Network Computer Center or an IBM 370 computer at the Louisiana Department of Highways, Baton Rouge, LA. In general, all structures, except those noted in the text, were fully optimized until the criteria established for Herbert's test were satisfied.

RESULTS AND DISCUSSION

X-Chloro-6-methylcyclohexadienyl intermediates

Figure 1 displays the relative energies of all possible intermediates, 2, formed from the addition of Me$^+$, Me$^\cdot$, and Me$^-$ to PhCl. The energies are displayed relative to the energy of the corresponding 6-methylcyclohexadienyl intermediate, 1, as the energy of the following isodesmic reaction, eqn (3).

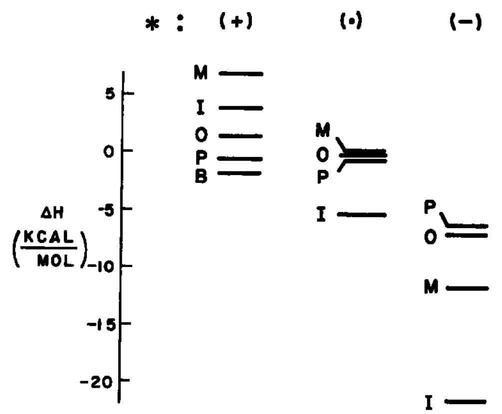
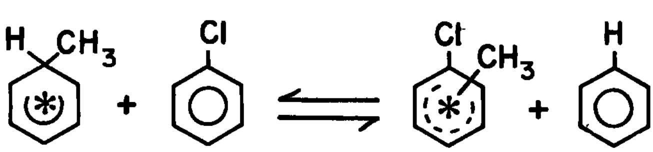


Fig. 1. Plot of ΔH values of eqn (3). O, M, P, and I represent 1-, 2-, 3-, and 6 - chloro - 6 - methylcyclohexadienyl intermediates, respectively. B represents a bridged chloronium ion which results from a 1,2 chlorine shift in the 6 - chloro - 6 - methylcyclohexadienyl cation. The ΔH value for the 6 - chloro - 6 - methylcyclohexadienyl cation is obtained by restricting the optimization procedure to prevent the 1,2 chlorine shift. The ΔH value for 6 - chloro - 6 - methylcyclohexadienyl anion is an approximation. Since no stable structure can be found in the calculational procedure, a representative structure has been chosen (see text) and the ΔH has been computed with this structure.

For 2 ($* = +$), the stability order among the conventional intermediates is $p > o > m$. This ordering agrees nicely with the experimental observation that a Cl substituent is an *o,p*-director in electrophilic substitution. According to the calculations, the *ipso*-intermediate will not be formed at all, since optimization of a structure with Me attached to the *ipso*-C leads to a minimum only at a bridged chloronium ion between the *ipso*- and *o*-positions. If the *ipso*-intermediate is restricted from rearrangement, by fixing the *ipso*-C-Cl and *ipso*-C-CH$_3$ bonds, its relative stability lies between *o*- and *m*-intermediates.

Relevant experimental data[11] on electrophilic alkylation of PhCl are summarized below. The *p*-derivative has been reported as the exclusive or predominant product in almost every case. However, an isomeric mixture has been observed[12a] in ethylation by C$_2$H$_4$ and AlCl$_3$, $m > o = p$, and by EtBr and GaBr$_3$ (partial rate factors, $o_f/m_f/p_f$: .271/.102/.538).[12b] The former product mixture possibly resulted from equilibration of the products.[13] Intramolecular shifts are known in electrophilic aromatic substitutions.[14,15] Support for *ipso*-attack would also come from observation of dehalogenation. Dehalogenation has not been reported in alkylations of chlorobenzenes, but has been observed in alkylations[16] of PhBr.

Comparison of experiment and theory reveals both similarities and differences. The partial rate factors show that attack at all positions of PhCl is slower than attack of benzene, but the calculations predict the formation of *p* and bridged intermediates should be slightly



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faster. This difference could be attributed to the facts the calculations represent the gas phase and do not include entropy effects. However, the error is small and the calculations do predict the correct order of stabilities, excluding the bridged intermediate. Even so, it is concluded that there is not very good agreement between the calculations and experiment.

The calculations suggest the stability order for **2** (* = ·) for the typical positions of substitution to be $p > o > m$. The energy differences among these three intermediates are very small so essentially no selectivity should be observed at these positions. The *ipso*-intermediate is predicted to be the most stable. In addition, the calculations predict that a rearrangement from *ipso* to *o* can occur by a Cl shift.[17]

The striking result from experiment is the high percentage of *o* product. The *o*, *m*, *p* ratio is essentially the same for homolytic methylation of PhCl by three methods: decomposition[18] of $(t\text{-BuO})_2$ (64, 25, 11), decomposition[19] of t-BuOOAc·(69, 21, 10), and photolysis[20] of MeHgI (62, 28, 11). Partial rate factors have been calculated for the t-BuOOAc decomposition[19]: $o_f/m_f/p_f$: 3.0/0.9/0.9. A speculation is that the high percentage of *o* product might arise from rearrangement of the *ipso* intermediate, as suggested by Traynham.[9] Experimental verification of rearrangement for this reaction has not yet been found.[21] Another point concerning the *ipso*-intermediate would be the possibility of dechlorination. In a competition experiment between PhCl and benzene for methyl radicals, no PhMe could be found.[17] Although the authors were looking for PhMe produced by reaction of Me· with benzene, the absence of PhMe would seem to rule out methyl substitution of Cl in PhCl. In contrast to methylation, homolytic cyclohexylation of PhCl does produce small amounts of cyclohexylbenzene.[22] An *ipso*-intermediate is proposed.[23]

Comparison of experiment and theory shows fair agreement. The calculations predict methylation of PhCl at all positions to be equal to or slightly more reactive than benzene. Experiment reveals a slight deactivation at the *m* and *p* positions. Although the calculations overestimate the importance of *ipso*-attack, they do support Traynham's explanation[9] for a large *o*/*p* ratio.

The stabilities of **2** (* = −) are calculated to be $ipso > m > o > p$. The *ipso*-structure is not a stable intermediate at all. A search of the energy surface reveals that Me^- would displace Cl^- directly. The energy value shown is for a structure with a C–Cl bond length of 1.95 Å and $C\text{–}CH_3$ bond length of 1.65 Å.

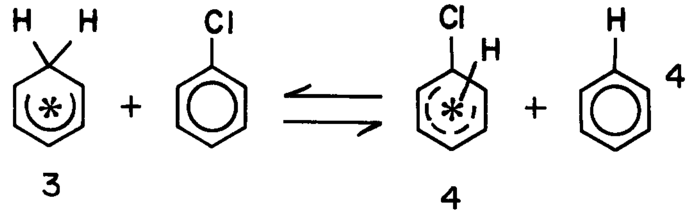
Anionic substitution *o*, *m*, or *p*, is an unknown reaction, since the leaving group would be H^-. Loss of Cl^- would occur but likely via a benzyne mechanism or by halogen–metal exchange[24] depending on the reagents employed to generate Me^-. A direct displacement mechanism has been proposed for the formation of cyclopropylbenzene[25] from PhCl and $c\text{-}C_3H_5Li$.

Since displacement is the predominant reaction in nucleophilic aromatic substitution, it is no surprise in the calculations that the *ipso* position is energetically favored for attack. However, it is questionable whether or not a direct displacement of Cl^- by methide involving no barrier would occur even in the gas phase.

On an individual reaction basis, the calculations give only a fair representation of experimental results. However, there are two important trends that are reflected by the calculations when considering the three reactions together. First, as the intermediates become more electron-rich, the *ipso*-intermediate becomes favored. Second, the change from highly selective electrophilic alkylation to less selective radical alkylation to highly selective nucleophilic alkylation is reflected in the calculated relative stabilities of the intermediates.

X-Chlorocyclohexadienyl intermediates

Figure 2 illustrates the relative energies of all possible intermediates formed in the reaction of a H^+, $H^\cdot$ and H^- with PhCl. The data are presented as ΔH for the isodesmic reaction, eqn (4), in order to compare the stabilities of the X-chlorocyclohexadienyl intermediates, **4**, with the corresponding cyclohexadienyl intermediates, **3**.



Intermediates formed by the reaction of H^+ with PhCl have an order of relative stability $p > o > ipso > m$. The differences in energy of *p*, *o*, and *m* for protonation are virtually identical with those for electrophilic methylation (see Figs. 1 and 2). All positions except *p* are predicted to be deactivated.

In super acid solution, protonation occurs exclusively at the *p*-position.[26] Detritiation of labeled PhCl[27] has given the following partial rate factors: $o_f/m_f/p_f$: 0.036/0.001/0.161, whereas deuteroexchange[28] of PhCl in OBr has given: o_f/p_f: 0.06/0.73. Gas phase tritiodeprotonation[29] shows less selectivity in the position of exchange. Gas phase tritiodechlorination[30] is seen, but likely occurs via attack on Cl, not on the *ipso*-C.

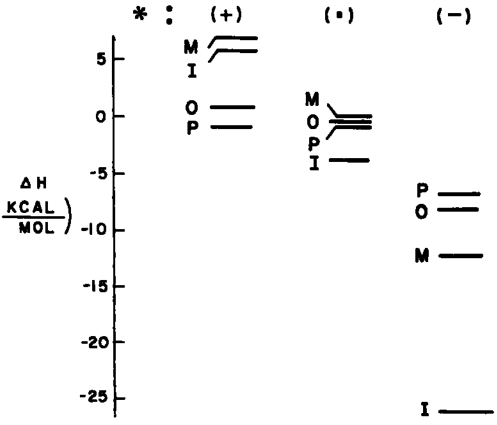


Fig. 2. Plot of ΔH values for eqn (4). O, M, P, and I represent 1-, 2-, 3-, and 6-chlorocyclohexadienyl intermediates, respectively.

As in methylation of PhCl, the calculations predict the correct order of positional reactivity but overestimate the reactivity of the *p*-position. The calculations do not coincide with the reduced selectivity seen in the gas-phase experiments.

Combining $H^{\cdot}$ with PhCl gives a set of intermediates whose relative energies imply that little selectivity should be observed. The *ipso*-intermediate is calculated to be significantly more stable, similar to what is predicted for homolytic methylation.

A statistical distribution is observed in the exchange reaction of hot tritium atoms with PhCl, and PhCl is slightly more reactive than benzene.[31] Furthermore, dechlorination accounts for eleven percent of the product mixture.[32]

The calculations are in good agreement with experiment from the standpoint of the lack of positional selectivity and reactivity. Furthermore, the prediction of high reactivity at the *ipso* position is suggested by the observation of a significant amount of dechlorination product.

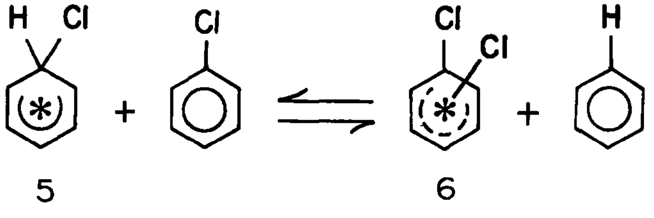
The calculations predict that relative energies of intermediates formed by attack of H^- on PhCl are similar to those predicted in methide addition, $ipso \gg m > o > p$. Furthermore, the calculations predict an enhanced stability for the isomeric intermediates, **4** ($* = -$), compared to **3** ($* = -$).

The calculations are consistent with the known dechlorination of PhCl by hydride reagents.[33] The mechanism is likely direct displacement, but other mechanisms have not been ruled out.

In summary, the trend for **4** parallels the trend seen for **2**; viz., as the number of electrons increase in the intermediate, the more relatively stable the *ipso*-intermediate becomes compared to the *p*, *m*, and *o* intermediates and the more stable all these intermediates become compared to **3** and **1**, respectively. The experimental data corroborate this trend.

X,6-Dichlorocyclohexadienyl intermediates

An illustration of the relative energies of the intermediates formed in the addition of Cl^+, $Cl^{\cdot}$, and Cl^- to PhCl is presented in Fig. 3. The ΔH values have been computed for the isodesmic reaction, eqn 5, of PhCl with 6-chlorocyclohexadienyl intermediates, **5**, to form benzene and X,6-dichlorocyclohexadienyl intermediates, **6**.



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The calculations indicate that addition of Cl^+ to PhCl forms intermediates with the following stability order: $p > o > m > ipso$. The *m*-isomer is not a stable structure (unless restricted) and rearranges to a chloronium ion, bridging the *m* and *p* positions. As seen in methylation and protonation of PhCl, the calculations predict the *p*-position to be activated.

An extensive amount of experimental work on electrophilic chlorination of PhCl has been reported.[34,35] These data can be summarized in the following way. The *o*/*m*/*p* ratios fall in the range of 28–40/0–6/55–72, except for one report[36] where the ratio is 15/1/84. Partial rate factors for molecular chlorination[35c] of PhCl in $MeNO_2$ are $o_f/m_f/p_f$: 0.08/0.0/0.189.

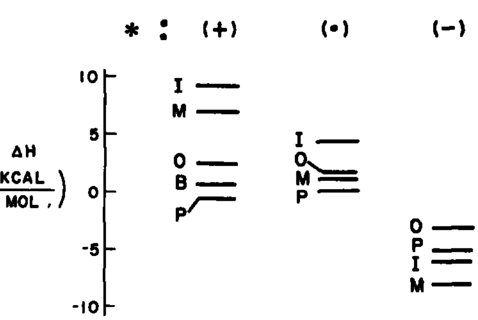


Fig. 3. Plot of ΔH values for eqn (5). O, M, P, and I represent 1, 2, 3, and 6,6-dichlorocyclohexadienyl intermediates, respectively. B represents a bridged chloronium ion resulting from a 1,2 chlorine shift in the 2,6-dichlorocyclohexadienyl cation. The ΔH value for the 2,6-dichlorocyclohexadienyl cation is obtained by restricting the optimization procedure to prevent the 1,2 chlorine shift.

The calculations agree with the order of reactivity, especially the deactivation at the *m*-position. However, the failure of MINDO/3 to account for the deactivation at the *p*-position in all cases discussed, is a more serious discrepancy. MINDO/3 apparently overestimates the donating ability of Cl.

For radical chlorination of PhCl, the calculations predict a narrowing of the relative energy differences and a change in the stability order compared to electrophilic chlorination, $p > m > o > ipso$. This is in contrast to the relative stabilities of similar intermediates in the homolytic methylation, **2** ($* = \cdot$), and hydrogen atom addition, **4** ($* = \cdot$). Another contrast among **2**, **4**, and **6** ($* = \cdot$) is the relative stability of the *ipso*-intermediate. In **6** ($* = \cdot$), *ipso* is the least stable and in **2** and **4** ($* = \cdot$), *ipso* is the most stable.

Homolytic chlorination of PhCl in the gas phase[37] gives a predominance of *m*-product (*o*/*m*/*p*: 11/65/24) with one exception.[38] In contrast to these data, hot homolytic chlorination of PhCl by recoil Cl atoms[40] yields a 41/26/33 ratio of *o*/*m*/*p* products. Partial rate factors have also been reported,[40] m_f/p_f: 0.63/1.57. However, the major reaction in hot homolytic chlorination is chlorine replacement, a well-known reaction in certain aryl halide and nitro compounds.[41]

Although the calculations reveal the *m*-isomer to be second in stability, they do agree with the trend that shows an increase in *m*-product in going from electrophilic to homolytic chlorination. The calculations predict that exchange should not be the major reaction if the *ipso*-intermediate is involved. In fact, the high proportion of ^{38}Cl-for-Cl exchange in the hot homolytic reaction has been explained[40] as coming not from a mechanism via an *ipso*-intermediate but instead from a mechanism involving attack of $^{38}Cl^{\cdot}$ on PhCl to produce $Ph^{\cdot}$ and ^{38}Cl–Cl followed by the reverse reaction to form $Ph^{38}Cl$ and $^{\cdot}Cl$.

The calculations predict that the stabilities of **6** (* = −) are $m > ipso > p > o$. All positions are predicted to be activated.

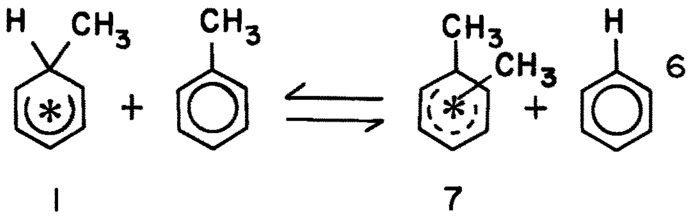
There is a report of an attempted anodic chlorination[42] of PhCl with $Cl_2^{-\cdot}$. No products are formed under these conditions.

In summary, the calculations are consistent with the trends in substitution pattern on going from electrophilic to homolytic chlorination of PhCl. However, the agreement does not seem to be quite as good as in the methylation and protonation examples. Homolytic chlorination by two different methods[37,39] gives markedly different ratios. The high proportion of *m* in the product ratio of the high temperature gas-phase chlorination is more indicative of the stability order calculated for anionic intermediates. In fact, the product ratio from this homolytic reaction is referred to[37b] as the "nucleophilic pattern". The likely possibility is that different mechanisms are involved in these two homolytic reactions, perhaps not involving intermediates like **6** (* = ·).

Comparison of Figs. 1–3 reveals an interesting contrast. Calculations of intermediates formed by attack of $Me^{\cdot}$ and $H^{\cdot}$ on PhCl predict the *ipso*-intermediate as most stable, whereas in attack of $Cl^{\cdot}$, the *ipso*-intermediate is the least stable. This comparison suggests that there is a possible correlation between the favorability of the *ipso*-intermediate and the difference in electronegativity of the attacking and leaving groups, viz, *ipso* is favored when the attacking group has a lower electronegativity than the leaving group. This suggestion agrees with an experimental study[7b], which indicates that *ipso*-substitution in a series of substituted benzothiazoles by 1-adamantyl radical occurs more easily when the substituent is electron-withdrawing.

X,6-Dimethylcyclohexadienyl intermediates

The relative energies of the intermediates formed in the addition of Me^+, $Me^{\cdot}$, and Me^- to PhMe are presented in Fig. 4. The ΔH values represent the reaction, eqn (6), of **1** and PhMe to form X,6-dimethylcyclohexadienyl intermediates, **7**, and benzene.



The calculations suggest a relative stability order for **7** (* = +) to be $p > o > m \gg ipso$. Except for attack at the *ipso*-position, all of the intermediates are more stable than **1** (* = +).

Experimentally, methylation occurs with a predominance of *o*-product under the conventional conditions.[43–45] The partial rate factors,[45] corrected for isomerization, are $o_f/m_f/p_f$: 8.3/1.8/9.4. Recently, a report has appeared on the methylation of PhMe in the liquid phase by "free" methyl cations.[46] These experiments have given partial rate factors[47] showing a greater preference for formation of the *p*-intermediate—$o_f/m_f/p_f$: 2.7/1.9/4.7. In addition, a significant portion (14%) of the reaction products has resulted from Me exchange. In a gas-phase methylation[48] of PhMe, the partial rate factors are quite different, $o_f/m_f/p_f$: 1.50/3.50/1.67; and methyl-methyl exchange also occurs.

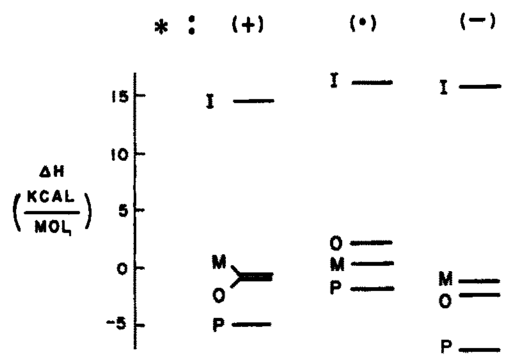


Fig. 4. Plot of ΔH values for eqn (6). O, M, P, and I represent 1, 2, 3, and 6,6-dimethylcyclohexadienyl intermediates, respectively.

The positional selectivity predicted by the calculations ($p > o > m$) reflects the correct order of that observed experimentally ($p \geq o > m$). The nearly equal preference for *o* and *p* observed experimentally is not seen in the calculations. The calculations do agree with the enhanced reactivity of PhMe over benzene, but appear to overestimate the stability of the *p*-intermediate.

Relative stabilities of **7** (* = ·) are clearly indicated by calculations to be $p > m > o \gg ipso$. The calculations predict further that the *p*-position is slightly activated, the *o*-position is slightly deactivated and the *m*-position is the same in reactivity compared to benzene.

Experimentally, there are two reports of homolytic methylation of PhMe. Partial rate factors for radical methylation are $o_f/m_f/p_f$: 1.6/0.96/0.90 by decomposition[19] of t-BuOOAc. Although partial rate factors have not been determined, methylation by decomposition of AcOOAc[49] yields a similar ratio of *o*-, *m*-, and *p*-products.

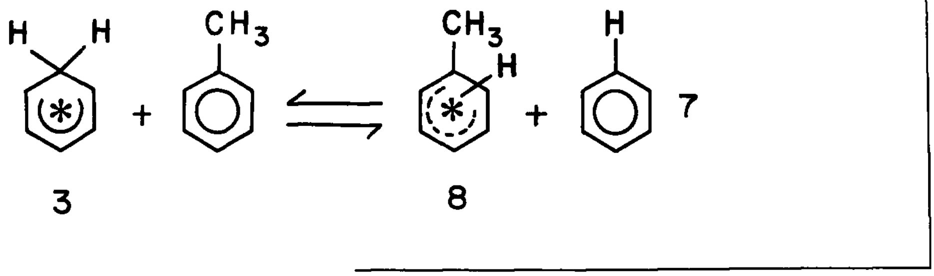
The calculations are not in agreement with the results with respect to positional selectivity. The calculations do reflect the trend of decreased reactivity when comparing homolytic and electrophilic methylation of PhMe.

For **7** (* = −), the order of stability is $p > o > m \gg ipso$. This is somewhat contrary to what might have been expected, since Me is generally considered as electron donating from the experience of structure-reactivity studies in aromatic electrophilic and radical substitutions. Recent studies[50,51] have revealed that Me can stabilize certain anions in the gas phase.

The likely result of mixing Me^- and PhMe would be formation of $PhCH_2^-$. In fact, the reaction of alkylmetallics with PhMe give metalation[52] predominantly at the benzyl position and no alkylation is observed.

X-Methylcyclohexadienyl intermediates

The relative energies of the intermediates formed in the addition of a H^+, $H^\cdot$, and H^- to PhMe are shown in Fig. 5. As before, the energy values are given relative to 3. This relationship is expressed as an isodesmic reaction, eqn (7), of 3 and PhMe to give benzene and X-methycyclohexadienyl intermediates, 8.



The calculations suggest that the relative order of the stability of 8 (* = +) is *p* > *o* > *m* ≫ *ipso*. This ordering is similar to 7 (* = +). However, a closer comparison indicates two significant differences (see Figs. 4 and 5). One is that the *ipso*-intermediate is relatively closer in energy to the conventional intermediates in 8 (* = +) than in 7 (* = +). The other is that the *o*-intermediate is closer in stability to the *p* for protonation than for methylation. Both of these differences are likely a reflection of the reduced steric effect of H compared to Me. All positions except *ipso* are predicted to be activated.

Experimental results on proton exchange in solution[28,53] are too numerous to cite individually. Examination of the partial rate factors suggest that there is a dependence on the acid used. Solutions of H_2SO_4 and CF_3COOH give ratios of $o_f/m_f/p_f$: 234–541/3.2–9.2/250–702 with the increase in p_f showing up in solutions with higher concentrations of CF_3COOH. Exchanges of PhMe with HBr[53] and DBr[28] give ratios of $o_f/m_f/p_f$: 1060–1600/5.4–9/3800–6200. Gas-phase exchange studies[54] yield a product ratio, *o*/*m*/*p*: 46/17/32. Thus, in all these exchange reactions the *o*- and *p*-positions are the most reactive.

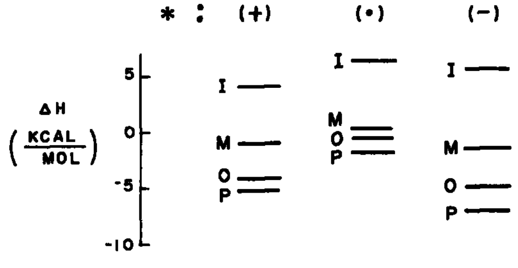


Fig. 5. Plot of ΔH values for eqn (7). O, M, P, and I represent 1-, 2-, 3-, and 6-methylcyclohexadienyl intermediates, respectively.

Studies designed to measure the stabilities of 8 (* = +) indicate the *p*-intermediate is most stable. Low temperature PMR studies[55] indicate that the *p*-intermediate is the only one formed in super acid media. An ICR study[56] supports the conclusion that in the gas phase the *p*-position is most likely protonated.

These proton affinity measurements[56] allow for a quantitative comparison of theory and experiment. The experimental ΔH-values (kcal/mole) for eqn (7) are: *ipso*, *m*, *o*, *p*; ≥ −1.2, −2.4, −6.0, −7.2. The computed values by MINDO/3 are: *ipso*, *m*, *o*, *p*; 4.1, −0.9, −4.0, −5.1.

In summary, the calculations are compatible with the equilibrium studies that indicate *p* as most stable, and are in good agreement with kinetic studies that show the *p*-position is more reactive than the *o*-position, and both are considerably more reactive than the *m*-position. A quantitative comparison reveals that MINDO/3 underestimates ΔH for eqn (7) for all isomers but does give an excellent prediction of the energy difference between the *o*-, *m*-, and *p*-isomers.

The relative energetics of 8 (* = ·) are similar to 8 (* = +); i.e. the stability order is *p* > *o* > *m* ≫ *ipso*. Again, as in methylation a reduction in relative reactivity, eqn (7) (* = ·) vs eqn (7) (* = +), is predicted by ΔH-values closer to zero.

Experimental exchange studies with tritium atoms generated by irradiation of PhSH[57] and PrSH[58] show partial rate factors of $o_f/m_f/p_f$: 2.0/1.76/1.14 and 4.41/3.11/2.97, respectively. In a study[31] with "hot" tritium atoms, the approximate partial rate factors are $o_f/m_f/p_f$: 4.6/1.0/4.0. An ESR study[59] at 77 K of 8 (* = ·) indicates that the *o*-isomer is predominant. Exchange of ring-labeled toluenes[60] at 700°C with $H^\cdot$ occurs with the following approximate partial rate factors: $o_f/m_f/p_f/i_f$: 1.02/0.92/0.85/0.7.

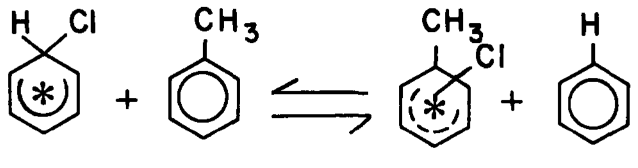
In summary, experiment indicates the *o*-position to be most reactive. The calculations predict that *p* should be more reactive than *o*, and thus the calculations underestimate the stability of the *o*-intermediate. The calculations do support the reduced values of the partial rate factors seen for the radical reaction compared to protonation.

Again the anionic intermediates are included for completeness. The stability order of 8 (* = −) is identical to both 8 (* = +) and (* = ·); thus indicating the dual role of Me as a donor and acceptor.[50,51] A reaction of H^- with PhMe, if it is to occur,[61] would likely involve benzyl anion formation.

6-Chloro-X-methylcyclohexadienyl intermediates

Figure 6 reveals the calculated relative energies of the intermediates formed in the addition of Cl^+, $Cl^\cdot$, and Cl^-

to PhMe. The ΔH-values represent the relative stability of the 6 - chloro - X - methylcyclohexadienyl intermediates, **9**, defined by an isodesmic reaction, eqn (8).



5 **9** 8

Calculations on **9** (* = +) suggest a stability order of $p > o > m \gg ipso$. All positions are predicted to be activated except for *ipso*. The *ipso*-intermediate is not stable by these calculations and spontaneously rearranges to a bridged intermediate (Cl spanning the *ipso*- and *o*-positions) equal in stability to the *o*-intermediate.

Experimental results on electrophilic chlorination of PhMe in solution are quite abundant.[35a,b; 62,63] The data can be generalized as follows: Lewis acid-catalyzed chlorinations show partial rate factors of $o_f/m_f/p_f$: 134/4/82; molecular chlorinations show $o_f/m_f/p_f$: 534–617/0–5/552–820, except for chlorinations in MeCN (1830/9.1/6250) and $MeNO_2$ (2420/8.3/9500).

The calculations are consistent with the observation that the *p*, *o*, and *m* are activated. The calculations are in best agreement with the data in MeCN and $MeNO_2$. The calculations do not agree with the preference for the *o*-position in Lewis acid-catalyzed chlorinations.

The calculated relative energies of **9** (* = ·) indicate a stability order: $p > o > m > ipso$. The ΔH values for eqn (8) (* = ·) suggest a reduction in reactivity compared to electrophilic chlorination, eqn (8) (* = +).

Experimental results on radical chlorination giving ring substitution are sparse. Free radical chlorination[64] of PhMe at 0° gives 70% α-, 20% *o*-, and 10% *p*-products. Themolysis or photolysis of $PbCl_4$ in the presence of PhMe yields equal parts *o*- and *p*-product. Hot atom chlorination[65] of PhMe in 11% CCl_4 yields 41% α-, 26% *o*-, 16% *m*-, and 17% *p*-products.

The calculations are more consistent with the product distribution in hot-atom chlorination, but the competition from α-hydrogen abstraction makes any conclusion tentative until exact mechanistic details are resolved.

The anionic intermediates, **9** (* = −), are included for completeness. The calculations suggest the same order of stability as seen for **9** (* = +) and (* = ·). *ipso*-Attack does not form a stable intermediate. The structure used for methide displacement of Cl^- on PhCl (see above) is used for comparison purposes. It is not surprising that *ipso*-attack is disfavored as Me^- is a poor leaving group.

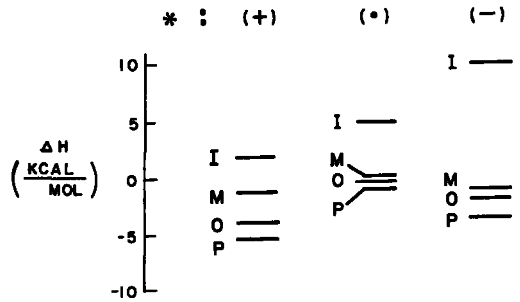


Fig. 6. Plot of ΔH for eqn (8). O, M, P, and I represent 1-, 2-, 3-, and 6 - chloro - 6 - methylcyclohexadienyl intermediates, respectively. See legend of Fig. 1 for a discussion of the 6 - chloro - 6 - methylcyclohexadienyl anion.

There is an experimental report of anodic chlorination[42] of PhMe. The active chlorinating agent is postulated to be $Cl_2^{\div}$. Product ratios are not given but it is stated that "...chemical and electrochemical halogenation are not distinguishable on the basis of products obtained".

SUMMARY AND CONCLUSIONS

The major trends revealed in this study can be summarized as follows:

(1) For intermediates derived from attack on chlorobenzene, the calculations predict an increase in the relative stability of the *ipso*-intermediates as the reaction changes from electrophilic to free radical to nucleophilic attack.

(2) For free radical reactions of PhCl, *ipso*-attack is most likely with radicals that are less electronegative than $Cl^{\cdot}$.

(3) For intermediates derived from attack on PhMe, the calculations predict the same stability order, $p > o > m > i$, except for intermediates formed in free radical methylation, $p > m > o > i$.

(4) In all reaction types examined, the calculations predict that the intermediates formed in attack of radicals show the smallest range of energy differences.

Although the calculations make a few predictions that accurately reflect experimental data, in general, the MINDO/3 method cannot be used quantitatively and some qualitative problems exist as well. Based on the prediction that the *p*-position is activated for electrophilic attack in PhCl, it would appear from experimental data in solution that MINDO/3 overestimates the electron-donating ability of the chloro group. However, this may not be an overestimate in the gas phase, where delocalization of the positive charge is more important. Since the *ipso*-intermediate is predicted by MINDO/3 to be the most stable in attack of $Me^{\cdot}$ and $H^{\cdot}$ on PhCl [**2** and **4** (* = ·), respectively], it can only be concluded that MINDO/3 overestimates the stability of the *ipso* intermediate because there is no experimental support for *ipso*-attack in these two reactions of PhCl. Part of this overestimation of the *ipso*-intermediate's stability is due to MINDO/3's error in predicting the relative stabilities of C(sp^3)–Cl and C(aromatic)–Cl bonds.[66] Correcting for this error of 6.2 kcal/mol, would make only two significant changes in the analysis. Where *ipso* is the most stable structure for **2** and **4** (* = ·), it would become the least stable and thus in better agreement with experiment.

The reasons for the enhanced stability of the *ipso*-

intermediate in these reactions are not totally clear. One possibility is that by bonding to the *ipso* carbon the *p-pi* electronic-interaction of the chloro group and the aromatic nucleus is reduced. The destabilizing effect of this interaction on anions and perhaps on radicals is not present in the *ipso* intermediate. A manifestation of the loss of *p-pi* interaction is seen as increase in the calculated *ipso* C–Cl bond length compared to the calculated C–Cl bond length in PhCl, 1.77 Å. For **2**, **4**, and **6**, respectively, the calculated *ipso*-C–Cl bond lengths are: (* = +) 1.84, 1.80, and 1.78; (* = ·) 1.92, 1.86, and 1.82; and (* = −) unstable, 2.04 and 1.89 Å. Thus, a trend exists for a longer C–Cl bond as the electronic character changes from cationic to anionic and as the attacking group changes from Me to Cl.

The prediction of high relative stability for bridged intermediates in **2** (* = +) and **6** (* = +) is of interest and warrants further study. The discussion of these intermediates is being postponed until a more systematic study is completed.

In conclusion, the most promising general result in the calculations is the small ΔH values for all radical reactions examined. This result predicts very little dependence of the reaction rate on the substituent in substituted benzenes. This prediction is in excellent agreement with experimental findings.[19,57] The prediction that *ipso*-intermediates are relatively more stable in radical than in electrophilic attack appears to have some experimental support but not enough examples have been reported to adequately verify the prediction. The likelihood of radical attack at the *ipso* position in PhCl appears to be linked to the relative electronegativity of the attacking radical.

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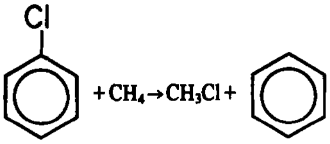

(i)