Relative Leaving Abilities and Isotope Effects in Electrophilic Aromatic Substitution

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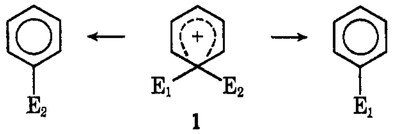
Received August 18, 1970

In acetic acid–acetic anhydride containing HCl, 1-chloro-1-nitro-2-keto-1,2-dihydronaphthalene (**2**, X = Cl) undergoes both migration and loss of NO_2^+, rather than Cl^+. In contrast, the bromo analog (**2**, X = Br) loses Br^+. We therefore conclude that the leaving abilities of these electrophiles increase in the order $Cl^+ < NO_2^+ < Br^+$. An order of relative leaving abilities for most of the common electrophiles is presented and justified. The factors that govern relative leaving abilities are considered. The implications of these relative leaving abilities for isotope effects and other aspects of electrophilic aromatic substitution are discussed.

For some time we have been interested in relative leaving abilities of electrophiles in electrophilic aromatic substitution. We may state the general question as follows. In the intermediate **1**, which of the two electrophiles, E_1^+ or E_2^+, is cleaved more rapidly (or migrates more readily), and why? Notice that this question concerns the leaving abilities of cationic species, rather than the anionic ones that are involved in nucleophilic substitutions at saturated carbon.



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For the special case that one of the electrophiles is H^+, hydrogen isotope effects[2-7] provide the answer to this question. In the reaction

$$E^+ + ArH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} EArH^+ \xrightarrow{k_2} ArE + H^+$$

ArD will be observed to react at nearly the same rate as ArH if $k_2 \gg k_{-1}$. If this condition is not met, then loss of H^+ must compete with loss of E^+ and the second step becomes partly or completely rate limiting. We may thus conclude that the electrophile E^+ is more rapidly lost than H^+ if and only if electrophilic substitution by E^+ shows an isotope effect appreciably greater than 1. For example, since iodinations, nitrosations, and mercurations all proceed with appreciable isotope effects, we may conclude that I^+, NO^+, and Hg^{2+} are all lost at least as readily as H^+. In contrast, NO_2^+, Cl^+, and R^+ must be lost much less readily than H^+, since nitrations, chlorinations, and alkylations rarely show appreciable isotope effects. (The alternative explanation for the small isotope effects in these reactions is considered in the Discussion.) Aromatic substitutions by still other electrophiles, such as ArN_2^+, Br^+, SO_3, and RCO^+, which are usually lost less readily than H^+, show higher isotope effects under special circumstances, usually when steric effects hinder swinging the substituent into the plane of the aromatic and thus decrease k_2.

Of course, these relative leaving abilities are not intrinsic properties of the electrophiles. For example, we must keep in mind that proton loss is an SN2 displacement on hydrogen, whereas loss of NO_2^+ or NO^+ is an SN1 process. Here we are invoking the principle of microscopic reversibility to conclude that, since nitration and nitrosation proceed *via* attack by NO_2^+ and NO^+, loss of NO_2^+ or NO^+ from the intermediate does not occur *via* SN2 attack on nitrogen. Whether loss of some other electrophile is an SN1 or SN2 process may likewise be determined on the basis of the mechanism of attack by that electrophile. Thus we may conclude that I^+, Br^+, and Cl^+ are never lost as such, but are removed by nucleophiles, among which halides seem to be especially effective, and the isotope effect in mercuration varies from 3.2 to 6.8, depending on the state of the water that must discriminate between H^+ or Hg^{2+}. Therefore it is necessary to recognize that the reaction conditions can have a considerable effect on leaving abilities of species that react by an SN2 process. An excellent example of this phenomenon was furnished by Zollinger,[4] who demonstrated that under some conditions a diazonium ion is more readily lost than H^+, but that this order is reversed by bases. Finally, we must keep in mind that leaving ability is also affected by substitution: *tert*-Bu^+ is clearly a better leaving group than *i*-Pr^+, and p-$MeOC_6H_4N_2^+$ is better than p-$O_2NC_6H_4N_2^+$.

If we take the magnitude of the hydrogen isotope effect[8] (or the extent to which steric effects must be introduced in order to produce an appreciable isotope effect) as a quantitative reflection of the ratio k_{-1}/k_2, we may list the substituents in approximate order of increasing leaving ability: $Cl^+ \sim NO_2^+ \sim R^+ < Br^+ < D^+ \sim ArN_2^+ \sim SO_3 \sim RCO^+ < NO^+ \sim H^+ \sim I^+ < Hg^{2+}$. Furthermore, we shall assume transitivity. If E_1ArH^+ loses E_1^+ much less readily than it loses H^+, and if E_2ArH^+ loses E_2^+ about as readily as it loses H^+, then intermediate **1** loses E_1^+ much less readily than it loses E_2^+, etc. Then we may also take the above sequence as a list of electrophiles in order of increasing leaving ability relative to each other (subject to the qualifying statements of the previous paragraph).

We consider the order for those electrophiles that are lost readily to be rather secure, since it is based on isotope effects (k_H/k_D) ranging from 3 to 7. On the other hand, we cannot be so certain about the relative leaving abilities of those electrophiles that are lost much less readily than protons, since substitutions with these electrophiles generally show isotope effects $k_H/k_D < 2$.

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[1] Alfred P. Sloan Research Fellow, 1967–1969.

[2] L. Melander, "Isotope Effects on Reaction Rates," The Ronald Press, New York, N. Y., 1960, Chapter 6.

[3] E. Berliner, *Progr. Phys. Org. Chem.*, **2**, 253 (1964).

[4] H. Zollinger, *Advan. Phys. Org. Chem.*, **2**, 163 (1964); *Ann. Rev. Phys. Chem.*, **13**, 400 (1962).

[5] H. Cerfontain, H. J. Hofmann, and A. Telder, *Recl. Trav. Chim. Pays-Bas*, **83**, 493 (1964).

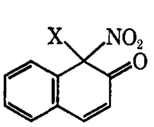
[6] G. A. Olah, *J. Tenn. Acad. Sci.*, **40**, 77 (1965).

[7] R. O. C. Norman and R. Taylor, "Electrophilic Substitution in Benzenoid Compounds," Elsevier, Amsterdam, 1965.

[8] These have been tabulated in ref 5 and 6, and citations of the original references may be found there.

Even the observation of an isotope effect that is produced by steric effects does not necessarily bear upon relative leaving abilities. For example, we have inferred that Br^+ and ArN_2^+ are inherently better leaving groups than Cl^+ and NO_2^+ because brominations and diazo couplings of sterically hindered aromatics more often show isotope effects. However, it is possible (though unlikely) that Br^+ and ArN_2^+ are ordinarily the poorer leaving groups, but that they are more sensitive to steric effects.

Therefore we decided that direct comparison of the relative leaving abilities of these poorer leaving groups is necessary, rather than inferences based on isotope effects. In particular, we have been especially interested in the relative leaving abilities of Cl^+, Br^+, and NO_2^+ in acetic acid–acetic anhydride mixtures. As a *model* for an intermediate **1** having two of these substituents, we chose the conjugate acids of the 1-halo-1-nitro-2-keto-1,2-dihydronaphthalenes (**2**, X = Cl, Br),



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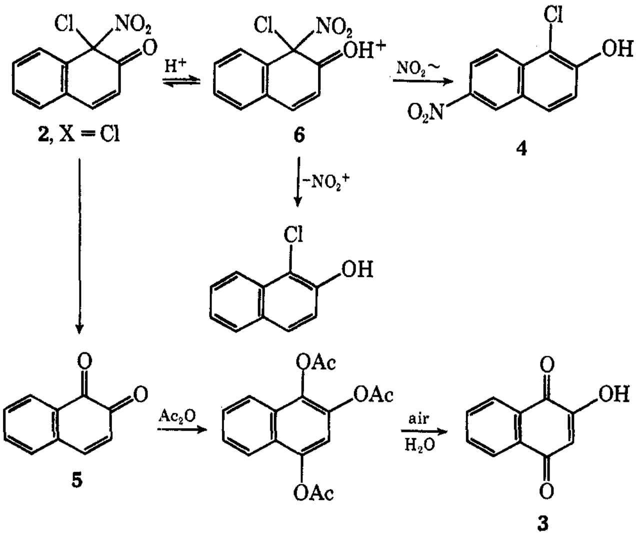
and we have investigated their behavior both in the presence and in the absence of chloride. Also, since it is known[9] that these ketones readily decompose to 1,2-naphthoquinone, with liberation of nitrous fumes, we have included urea in the reaction mixture, in an attempt to prevent nitration through nitrosation. (1,6-Dinitro-2-naphthol has been isolated[9] from solutions of the bromonitro ketone in acetic acid.)

Results

A solution of 1-chloro-1-nitro-2-keto-1,2-dihydronaphthalene (**2**, X = Cl) in chloroform was prepared according to Fries.[9] This very sensitive material was not isolated or purified, but its solution was added immediately to an acetic acid–acetic anhydride mixture containing HCl and urea. On work-up, both 2-hydroxy-1,4-naphthoquinone (**3**) and 1-chloro-6-nitro-2-naphthol (**4**), mp 197.5–198°, were obtained, the latter as its acetate. The former presumably arises *via* 1,2-naphthoquinone (**5**), which is formed on heating **2** in inert solvents, and which we have found to be converted to **3** under the conditions employed. The latter arises from the conjugate acid **6** (or its acetate) by migration of NO_2^+, and not by an intermolecular process, since under the reaction conditions 1-chloro-2-naphthol is not nitrated by 1 equiv of acetyl nitrate.



The 1-chloro-6-nitro-2-naphthol (**4**) is an unknown compound, although it may be the same as the chloronitronaphthol, mp 192°, of Gaess[10] and the chloronitronaphthol, mp 190–191°, of Kaneko.[11] Our structure proof rests on elemental analysis, a consistent infrared spectrum, inertness to nitrosation, monobromination to a ketone, and oxidation by alkaline permanganate to 4-nitrophthalic acid. Thus we conclude that this is another example of the rare migration of a nitro group.[12]

A small amount of 1-chloro-2-naphthol was also detected among the products. This arises through competing loss of NO_2^+ from **6**. The alternative possibility, that this represents material that did not undergo the initial nitration, is excluded, since appreciable 1-chloro-2-naphthol was also detected by tlc in the products from **6** prepared by chlorination of 1-nitro-2-naphthol in base.

No 1-nitro-2-naphthol or 1,6-dinitro-2-naphthol was detected. Therefore, we conclude that even in the presence of HCl and acetic acid the loss of Cl^+ does not compete with loss and migration of NO_2^+.

In contrast, the bromo analog, 1-bromo-1-nitro-2-keto-1,2-dihydronaphthalene (**2**, X = Br), undergoes loss of Br^+ and forms 1-nitro-2-naphthol, even in the absence of HCl. Therefore we conclude that loss or migration of NO_2^+ does not compete with S_N2 displacement on bromine by acetic acid or chloride.

Discussion

Relative Leaving Abilities of the Poor Leaving Groups Br^+, Cl^+, and NO_2^+.—From the experiments here reported, we may conclude that the leaving abilities of these electrophiles increase in the order, $Cl^+ < NO_2^+ < Br^+$. In particular, we may now conclude that a species like **1** (E_1 = Cl, E_2 = NO_2) is more likely to react by loss or migration of NO_2^+ rather than Cl^+. Also, we have substantiated the expectation based on isotope effects that a species like **1** (E_1 = Br, E_2 = NO_2) is more likely to lose Br^+ than NO_2^+, and, if our assumption of transitivity is valid, then we would expect a species like **1** (E_1 = Br, E_2 = Cl) to lose (or migrate) Br^+ rather than Cl^+. Of course, this result has already been obtained[13] for 1-bromo-1-chloro-2-keto-1,2-dihydronaphthalene, which with HCl or HBr gives 1-chloro-6-bromo-2-naphthol and 1-chloro-2-naphthol. Indeed, the preferential loss and migration of Br^+ is just what chemical intuition would lead one to expect. Also, we note that, with HBr in acetic acid, 1-chloro-1-methyl-2-keto-1,2-dihydronaphthalene was found to undergo halogen migration, rather than loss or migration of methyl;[13] so we may further conclude that methyl is a poorer leaving group than even chlorine.

Berliner[8] has suggested that under the proper condi-

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[9] K. Fries, *Justus Liebigs Ann. Chem.*, **389**, 315 (1912).

[10] F. Gaess, *J. Prakt. Chem.*, **45**, [2] 616 (1892); through Elsevier's "Encyclopaedia of Organic Chemistry," 1950, Vol. 12B, p 1565.

[11] T. Kaneko, *Yakugaku Zasshi*, **68**, 179 (1948).

[12] P. H. Gore, *J. Chem. Soc.*, **1957**, 1437.

[13] K. Fries and K. Schimmelschmidt, *Justus Liebigs Ann. Chem.*, **484**, 245 (1930).

tions practically all substitutions except nitration may proceed with an appreciable isotope effect, and he has expected that even chlorination should do so. On the basis of our results, we conclude that nitration is more likely than chlorination (or methylation) to proceed with an appreciable isotope effect. Myhre[14] has tentatively reached this same conclusion.

General Considerations of Leaving Abilities of Electrophiles.—First we must demonstrate that kinetic isotope effects observed in electrophilic aromatic substitution really do reflect relative leaving abilities. It seems to be generally accepted that "the most important factor which determines the occurrence of an isotope effect is the relative magnitude of k_{-1} and k_2, and hence the heights of the transition state barriers leading from the intermediate to reactants and products."[3] However, there have also been suggestions[3,6,15,16] that a small isotope effect does not necessarily mean that $k_2 \gg k_{-1}$, but that it may be due to an asymmetry in the transition state, which is quite likely for these very exothermic proton transfers. Despite the general validity of this argument and its widespread acceptance, we reject it as the explanation for the low isotope effects sometimes observed in electrophilic aromatic substitution. Although the isotope effect on proton loss from the intermediate does vary[16,17] with the acidity of $EArH^+$, the range seems to be only from 3 to 7. Indeed, observations of $k_H/k_D > 6$ in diazo couplings and hydrogen isotope exchanges where $EArH^+$ is a relatively weak acid and in mercurations where $EArH^+$ is probably a strong acid suggest that the isotope effect on proton transfer from $EArH^+$ can approach and even surpass the limiting value of *ca.* 7. Also, calculations[18] show that, even when the transition state is so asymmetric that the proton is bound seven times as strongly to the carbon atom as it is to the base, k_H/k_D drops only to 3.3. Such extreme asymmetry seems quite unlikely in these reactions. Therefore we contend that the isotope effect *is* determined almost entirely by the ratio k_{-1}/k_2, that values of $k_H/k_D \sim 1$ do correspond to reactions with $k_2 \gg k_{-1}$, and that we are justified in estimating relative leaving abilities from magnitudes of k_H/k_D.

Next we consider the factors that govern relative leaving abilities of electrophiles. Both Berliner[3] and Olah[6] have stated, "It is by no means always clear why in some reactions the proton loss becomes part of the rate-determining step and in others not. Many factors seems to contribute to where exactly the transition state for the rate-controlling step occurs." On the contrary, we feel that the above order of relative leaving abilities is not so baffling but is in fact a reasonable one for the relative rates of breaking the carbon-electrophile bond. It seems to parallel what might be expected for the order of stability[19] (lack of reactivity and electrophilicity, "happiness") of the various electrophiles. For example, NO_2^+ is an especially powerful electrophile; it forms a strong C–N bond that is quite difficult to cleave. Likewise, ionization of R^+ (data are for benzhydryl and isopropyl) from the intermediate would not be expected to be a fast reaction unless R^+ is an extremely stable carbonium ion. Species of intermediate leaving ability, such as SO_3, RCO^+, and ArN_2^+, are also species of greater ease of formation through routes other than from **1**, and the good leaving groups, such as Hg^{2+}, H^+, and NO^+, are particularly stable species, of low electrophilicity; it is therefore understandable that C–Hg^+, C–H, and C–NO bonds are readily cleaved. Similarly, iodine is not very electrophilic; so it is not surprising that C–I bonds are also readily cleaved. Of course, species such as Cl^+, Br^+, I^+, H^+, Hg^{2+}, and some R^+ (*e.g.*, methyl) do not ionize from the intermediate in an SN1 process, but are removed in an SN2 process. Therefore the relative leaving abilities of these species depend on the nature and concentration of the nucleophiles present, so that comparisons involving such species cannot be absolute but are applicable only under whatever conditions are specified. Nevertheless, it is obvious that the rate of nucleophilic attack by either oxygen or halogen nucleophiles must increase in the order $CH_3 < Cl < Br < I$, inasmuch as this is the order of increasing polarizability.

Alternative Explanations for Leaving Abilities of Electrophiles.—It is instructive to consider other factors that have been suggested as important in determining leaving abilities.

Several researchers[20] have suggested that the strength of the carbon–electrophile bond is important. For example, C–Hg and C–I bonds are especially weak; so they are readily cleaved. This explanation is quite close to ours, except that considerations of bond strengths are more relevant to homolytic cleavages, rather than the heterolytic ones that are involved here. (For SN1 processes this suggestion may be made equivalent to ours if the electron affinity of the electrophile is also included as an important factor. We prefer to focus on the "heterolytic" bond strength.) Besides, for those substituents that are removed in an SN2 process, it is necessary to consider the strengths of both the bond to be broken and the bond to be made (just as for free radicals, which prefer to abstract hydrogen atoms, rather than halogen atoms, even though the C–H bond is stronger than the C–X bond).

We have already mentioned that steric effects are important, as has long been recognized.[4] Clearly, large groups flanking the reaction center will hinder the approach of a bulky electrophile into the plane of the aromatic and thus decrease k_2. (Many previous interpretations of these steric effects stressed an increase in k_{-1}, but it seems quite likely that bulky substituents may even decrease this rate in some cases.) As the leaving ability of protons is thus decreased relative to that of the electrophile, reversal of the electrophilic attack can compete with loss of proton, thereby leading to a hydrogen isotope effect.

It has also been suggested[3,6] that the selectivity of the reaction is important, with reactions involving powerful electrophiles showing no isotope effect. In some respects this approach is quite similar to ours, in that a powerful electrophile will be one whose leaving ability

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[14] P. C. Myhre, M. Beug, and L. L. James, *J. Amer. Chem. Soc.*, **90**, 2105 (1968); P. C. Myhre and J. W. Tilley, Abstracts, 156th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1968, Organic Division No. 107; P. C. Myhre, personal communication.

[15] G. S. Hammond, *J. Amer. Chem. Soc.*, **77**, 334 (1955); F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961).

[16] R. P. Bell and D. M. Goodall, *Proc. Roy. Soc., Ser. A*, **294**, 273 (1966).

[17] J. L. Longridge and F. A. Long, *J. Amer. Chem. Soc.*, **89**, 1292 (1967); A. J. Kresge, D. S. Sagatys, and H. L. Chen, *ibid.*, **90**, 4174 (1968).

[18] R. A. More O'Ferrall and J. Kouba, *J. Chem. Soc. B*, 985 (1967).

[19] A. V. Willi, *Chimia*, **15**, 239 (1961).

[20] L. G. Cannell, *J. Amer. Chem. Soc.*, **79**, 2932 (1957); H. G. Kuivila and K. V. Nahabedian, *ibid.*, **83**, 2164 (1961); A. J. Kresge and J. F. Brennan, *Proc. Chem. Soc.*, 215 (1963).

is quite poor, so that proton loss is always favored and no isotope effect is observed. Nevertheless, there does not seem to be a very good correlation between selectivity and isotope effect, mercuration being a rather unselective reaction that shows a large isotope effect. It has also been suggested[3,6] as a corollary that reactions involving reactive aromatics should also show no isotope effects. However, we would expect that the reactivity of the aromatic cannot affect the *relative* leaving abilities (except insofar as a reactive intermediate formed from an unreactive aromatic should be less selective as to which electrophile is lost). Thus we reject the suggestions[4,21] that formation of a stable quinonoid intermediate is somehow associated with the occurrence of an isotope effect.

We also reject the suggestions[2,22] that iodinations and sulfonations show isotope effects because the intermediate (**1**, $E_1 = H$, $E_2 = SO_3^-$, or one resulting from iodination of a phenoxide) is neutral and therefore a weaker acid. What is important in determining whether there is an isotope effect is the ratio k_{-1}/k_2; thus, even though k_2 is smaller for a neutral species, so is k_{-1}.

It has long been recognized that reactants and reaction conditions affect the isotope effect. Now we may readily understand these observations in terms of relative leaving abilities. For example, bromination of anisole-*m*-sulfonate with $BrOH_2^+$ or BrOH shows no isotope effect whereas bromination with Br_2 shows $k_H/k_D = 2.6$. Of course, this is not really due to the change in brominating agent, but to the change in reaction conditions; attack by H_2O on Br^+ does not compete with attack by H_2O on H^+, but attack of Br^- on Br^+ can compete. Another example is the remarkable $k_H/k_D = 6.1$ for nitration of anthracene in acetonitrile;[23] in so weakly basic a solvent, the proton becomes a very poor leaving group, in this case even poorer than NO_2^+, which needs no nucleophile to remove it. Notice that this result demonstrates that the product-forming step must be proton transfer from the σ-complex intermediate, and *not* formation of an NO_2BF_4 π complex or separation of an HBF_4 π complex.[6]

Further Aspects of Leaving Abilities.—We may include some other electrophiles whose relative leaving abilities may be gauged. From kinetic studies and/or isotope effects in protodecarboxylation,[24] protodeboronation,[25] and protodesilylation,[26] we may conclude that H^+ is a poorer leaving group than CO_2, $B(OH)_3$ (or Ph_3B), and Me_3Si^+. By transitivity we conclude that I^+ and Br^+ are also poorer leaving groups than these. This conclusion is consistent with the kinetics of bromodecarboxylation[27] and halodeboronation.[28] We also note that the kinetics of bromodesulfonation[29] show that loss of Br^+ is also competitive with cleavage of SO_3, as suggested above by isotope effects and the assumption of transitivity. Likewise, in the presence of Br^-, loss of Br^+ has been found [30] to be competitive with cleavage of $ArCHOH^+$. The well-known occurrences of nitrodealkylation,[31] halode-*tert*-butylation,[32] and diazodehydroxyalkylation[33] suggest further relative leaving abilities, as indicated below.

Finally, we indicate how simple considerations of leaving abilities can clarify some previously puzzling features of aromatic reactivity.

Whereas bromination of dianisylcarbinol leads to considerable cleavage and formation of *p*-bromoanisole, bromination of dianisylmethane produces very little cleavage product.[34] This result is readily understood in terms of the poorer leaving ability to be expected for $p\text{-}MeOC_6H_4CH_2^+$, relative to $p\text{-}MeOC_6H_4CHOH^+$.

Whereas nitration of phenylmercuric ion leads primarily to nitrophenylmercuric ions,[35] nitrosation leads to nitrosobenzene, *via* nitrosodemercuration.[36] This contrast may be attributed to the reversibility of NO^+ attack, which is perhaps faster than proton loss, but slower than loss of Hg^{2+} from **1** ($E_1 = Hg^+$, $E_2 = NO$).

The variations in the mechanism of protodecarboxylation[24] are readily understood in terms of the variations in the relative leaving abilities of H^+ and CO_2. In dilute acid, intermediate **1** ($E_1 = H$, $E_2 = CO_2^-$) loses CO_2 more readily than H_2O removes H^+. In buffer solutions, general base catalysis increases the rate of proton removal, but does not affect the rate of CO_2 loss. In strong acid, there is very little such intermediate, since it is present almost entirely as a species protonated on carboxyl oxygen, which readily loses H^+ but cannot lose CO_2. Similar phenomena are apparently involved in protodecarbonylation,[37] protodeformylation,[38] and protodesulfonation.[39]

Finally, for a test of our understanding of relative leaving abilities, we wish to make the following prediction. Since $ArCHOH^+$ (and possibly CH_2OH^+) have leaving abilities comparable with that of Br^+, steric effects should create a situation in which they also have a leaving ability comparable with that of H^+. Therefore we predict that hydroxyalkylation and chloromethylation[40] of tri-*tert*-butylbenzene (or perhaps even mesitylene) should show a hydrogen isotope effect, $k_H/k_D > 3$.

Conclusions

Thus we have demonstrated that considerations of the relative leaving abilities of electrophiles are sufficient

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[23] H. Cerfontain and A. Telder, *Recl. Trav. Chim. Pays-Bas*, **86**, 371 (1967).

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[25] H. G. Kuivila and K. V. Nahabedian, *ibid.*, **83**, 2159, 2164 (1961); J. N. Cooper and R. E. Powell, *ibid.*, **85**, 1590 (1963).

[26] C. Eaborn, P. M. Jackson, and R. Taylor, *J. Chem. Soc. B*, 613 (1966).

[27] E. Grovenstein, Jr., and U. V. Henderson, Jr., *J. Amer. Chem. Soc.*, **78**, 569 (1956); E. Grovenstein, Jr., and G. A. Ropp, *ibid.*, **78**, 2560 (1956).

[28] H. G. Kuivila and E. J. Soboczenski, *ibid.*, **76**, 2675 (1954); H. G. Kuivila and R. M. Williams, *ibid.*, **76**, 2679 (1954).

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to provide a simple basis for understanding why some reactions proceed with an isotope effect and others do not, and we have shown how this approach is applicable to understanding why a particular step in a general aromatic substitution is rate limiting.

In summary, we may list the electrophiles here considered in order of increasing leaving ability, as judged from isotope effects, from reactions of model compounds, and from other kinetic studies. We list those that ionize in an S_N1 process separately from those that are cleaved in an S_N2 process.

$$\begin{gathered}NO_2^+ < i\text{-}Pr^+ \sim SO_3 < tert\text{-}Bu^+ \sim ArN_2^+ < ArCHOH^+ < \\ NO^+ < CO_2 < B(OH)_3\end{gathered}$$

$$\begin{gathered}CH_3^+ < Cl^+ < Br^+ < D^+ \sim RCO^+ > \\ H^+ \sim I^+ < Hg^{2+} < Me_3Si^+\end{gathered}$$

It is possible to compare S_N1 and S_N2 processes, but they vary more strongly with conditions. For example, we have demonstrated that a frequent order is $Cl^+ < NO_2^+ < Br^+$. We suggest that these relative leaving abilities can provide a useful basis for considering any electrophilic substitution. Furthermore we maintain that these sequences of leaving abilities are reasonable ones to be expected for the relative rates of heterolysis of a carbon–electrophile bond. And variations in leaving ability are readily understood in terms of steric effects and effects of reaction conditions. Finally, we suggest that study of the reactions of an appropriate 2-keto-1,2-dihydronaphthalene system can provide a general method for determining more relative leaving abilities and for further testing of the applicability of the above sequences.

Experimental Section

Melting points were determined on a Fisher–Johns block and are uncorrected. Microanalysis was by Galbraith Laboratories, Inc. Thin layer chromatography on Eastman chromagram sheets (silica) with chloroform, methanol, or absolute ethanol eluent, followed by development with NH_3 vapor, was found suitable for separating the compounds of interest.

Materials.—1-Chloro-2-naphthol was prepared according to Franzen and Stäuble[41] and recrystallized from ligroin, mp 66.5–67.5 (lit.[42] 70–71°). 1,6-Dinitro-2-naphthol was prepared according to published methods,[43] mp 195.5–197.5° (lit.[44] 195 dec). 1-Bromo-2-naphthol (Aldrich) was recrystallized from ligroin, mp 81–82° (lit.[45] 84°).

Preparation of 1-Bromo-1-nitro-2-keto-1,2-dihydronaphthalene (2, X = Br).[9]—To a cooled, stirred solution of 1.00 g of 1-bromo-2-naphthol in 5 ml of $HCCl_3$ was added 1 ml of chilled 90% HNO_3. After 2 min, ice was added and the lower layer was removed, washed with cold water, and dried with Na_2SO_4. Hexane was added to the chilled solution until crystals appeared. The mixture was immediately filtered and the filtrate was cooled to −78° and then allowed to warm to *ca.* −20°. The yellow crystals were collected and dried to obtain 525 mg of product: mp 60–62.5° (lit.[9] 74°); ir ($HCCl_3$) prominent bands at 5.92 (C=O), 6.35 (NO_2), 7.50 (NO_2), and 12.3 μ (CH); nmr ($DCCl_3$) τ 2.50 (d) + 2.57 (m) (5 H total), 3.68 (d, *J* = 10 Hz, 1 H). On standing at room temperature this material slowly decomposed with evolution of nitrous fumes and formation of 1,2-naphthoquinone: ir ($HCCl_3$) 5.99 μ (C=O) [lit.[46] 1678 cm^{-1} (CCl_4)]. Therefore, this ketone was not generally isolated, but its freshly prepared $HCCl_3$ solution was immediately reacted. This solution showed the same ir and nmr (prepared in $DCCl_3$) peaks as did the solution of the crystalline material, and no OH, $ArNO_2$, or quinone peaks could be detected.

A $HCCl_3$ solution showing these same ir peaks could also be prepared by rapidly adding a solution of 83 mg of Br_2 in 1 ml of $HCCl_3$ to a cooled stirred solution of 95 mg of 1-nitro-2-naphthol in 25 ml of 0.1 *M* Na_2CO_3 containing 0.1 g of NaBr, removing the $HCCl_3$ layer after 2 min, and washing with water.

Preparation of 1-Chloro-1-nitro-2-keto-1,2-dihydronaphthalene (2, X = Cl).[9]—To a cold solution of 80 mg of 1-chloro-2-naphthol in 500 μl of $HCCl_3$ was added 100 μl of chilled 90% HNO_3, and the mixture was swirled vigorously. After 2 min, ice was added and the $HCCl_3$ was washed with cold water and dried with Na_2SO_4. The ir spectrum of this solution was quite similar to that of the bromo analog (2, X = Br), with prominent bands at 5.91, 6.34, 7.50, and 12.2 μ. A solution of this product in $DCCl_3$ was also prepared: nmr τ 2.50 (d) + 2.57 (m), (5 H total), 3.72 (d, *J* = 9 Hz, 1 H). However, as Fries[9] also found, no pure ketone could be isolated from these solutions. Indeed, the solution of this material readily evolved nitrous fumes even at room temperature, and formed 1,2-naphthoquinone. Therefore this ketone was never isolated or purified, but its freshly prepared solution was immediately reacted.

A $HCCl_3$ solution showing these same ir peaks could also be prepared by rapidly adding 1 ml of 0.7 *M* NaOCl to a cooled stirred solution of 95 mg of 1-nitro-2-naphthol in 25 ml of 0.1 *M* Na_2CO_3 containing 0.35 ml of 10% H_2SO_4, removing the $HCCl_3$ layer after 2 min, and washing with water.

Reaction of 1-Chloro-1-nitro-2-keto-1,2-dihydronaphthalene (2, X = Cl) with Acid.—A fresh $HCCl_3$ solution of this material, prepared from 3.20 g of 1-chloro-2-naphthol, was filtered through Na_2SO_4 into a cooled, stirred solution of 1.20 of g of urea and 3.0 ml of concentrated HCl in 40 ml of redistilled Ac_2O plus 20 ml of AcOH. The mixture was allowed to stand for 2.5 hr at 25° and then for 2.5 hr at 60°; 1 ml of concentrated H_2SO_4 was then added; and the mixture was held 0.5 hr more at 60°. The mixture was then poured into 600 ml of H_2O and stirred gently overnight to hydrolyze the Ac_2O.

The mixture was extracted with ether and the ether layer washed with H_2O and 1 *N* NaOH. Evaporation of the ether gave 1.80 g of yellowish solid whose nmr and ir were characteristic of a nitronaphthyl acetate. Recrystallization of this material from 95% EtOH furnished a tan powder, mp 152–153.5°. The crude acetate was hydrolyzed in refluxing aqueous methanolic NaOH; work-up led to 1.20 g of crude 1-chloro-6-nitro-2-naphthol (**4**) as a brown solid. Thin layer chromatography indicated that the crude 1-chloro-6-nitro-2-naphthol contained a small amount of 1-chloro-2-naphthol (also detected by odor), but no 1-nitro-2-naphthol or 1,6-dinitro-2-naphthol.

Acidification and extraction of the NaOH washings of the original reaction mixture led to 700 mg of dark red powder, whose principal component was identified as 2-hydroxy-1,4-naphthoquinone by tlc, by ir (6.04 μ), and by melting point (195–197 dec) and mixture melting point of a sublimed sample. Formation of 2-hydroxy-1,4-naphthoquinone was also indicated by the uv spectrum of the aqueous washings of the original reaction mixture. No 1-nitro-2-naphthol or 1,6-dinitro-2-naphthol could be detected by tlc or ir. It was also found that under the conditions employed, both 1,2-naphthoquinone and 1,2,4-triacetoxynaphthalene are partially converted to 2-hydroxy-1,4-naphthoquinone. Also, treating the original ether extract with *o*-phenylenediamine gave the characteristic uv spectrum of benzo[*a*]phenazine, so that some 1,2-naphthoquinone does survive.

Reaction of 1-chloro-1-nitro-2-keto-1,2-dihydronaphthalene (2, X = Cl) prepared by chlorination of 1-nitro-2-naphthol gave the same products, as evidenced by tlc. Also these same products were detected from decomposition in aqueous HOAc.

Characterization of 1-Chloro-6-nitro-2-naphthol (4).—The crude product from the reaction of 2 (X = Cl) was purified by precipitating it from alkali with HOAc and repeated recrystallization from 50% EtOH, to give orange needles: mp 197.5–198°; ir 2.72 m, 2.81 m, 6.15 m, 6.52 m, 7.47 μ s.

Anal. Calcd for $C_{10}H_6ClNO_3$: C, 53.71; H, 2.705; Cl, 15.85. Found: C, 53.81; H, 2.75; Cl, 16.05.

With benzoyl chloride in dry THF, the lithium salt of **4** could be converted to a benzoate, mp 221–222°. Under conditions[47]

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[41] H. Franzen and G. Stäuble, *J. Prakt. Chem.*, **103** [2], 379 (1921–1922).

[42] T. Zincke, *Ber.*, **21**, 3378 (1888).

[43] C. Graebe, *Justus Liebigs Ann. Chem.*, **335**, 1239 (1904).

[44] O. Wallach and H. Wichelhaus, *Ber.*, **3**, 846 (1870).

[45] A. J. Smith, *J. Chem. Soc.*, **35**, 789 (1879).

[46] M.-L. Josien, N. Fuson, J.-M. Lebas, and T. M. Gregory, *J. Chem. Phys.*, **21**, 331 (1953).

[47] R. Henriques and M. Ilinski, *Ber.*, **18**, 704 (1885).

such that 1-naphthol, 2-naphthol, or 6-bromo-2-naphthol was readily nitrosated, **4** was unreactive, just as 1-chloro-2-naphthol or 1-bromo-2-naphthol. Also, with 1 equiv of Br_2 in HOAc containing NaOAc, followed by quenching with ice and extraction with $HCCl_3$, **4** gave a solution that exhibited strong absorption at 5.89 μ and that liberated iodine from aqueous KI. This behavior was the same as that of 1-chloro-2-naphthol or 1-bromo-2-naphthol, and quite different from that of 2-naphthol. Oxidation of **4** with alkaline $KMnO_4$ led to 4-nitrophthalic acid, identified by melting point and mixture melting point.

Intramolecularity of the Rearrangement.—1-Chloro-2-naphthol (320 mg) in 3 ml of $HCCl_3$ was added to a solution of 120 mg of urea, 0.2 ml of H_2SO_4, and 0.11 ml of 70% HNO_3 in 4 ml of Ac_2O and 2 ml of AcOH. The mixture was allowed to stand at 60° for 3 hr and was then treated as above. Tlc of the hydrolyzate showed only 1-chloro-2-naphthol.

Reaction of 1-Bromo-1-nitro-2-keto-1,2-dihydronaphthalene (2, X = Br).—A fresh $HCCl_3$ solution of this material, prepared by nitration of 1.00 g of 1-bromo-2-naphthol, was filtered through Na_2SO_4 into a cooled, stirred solution of 0.6 g of urea, 1 ml of concentrated H_2SO_4, 10 ml of redistilled Ac_2O, and 5 ml of AcOH. Work-up as for the chloro analog gave 480 mg of crude acetate, which was hydrolyzed to 320 mg of brown solid. Recrystallization of this material from $HCCl_3$ gave orange crystals of 1-nitro-2-naphthol, identified by melting point and mixture melting point. Tlc of the crude material indicated that 1-nitro-2-naphthol was the principal product. No 1-bromo-2-naphthol could be detected, but tlc indicated the presence of a small amount of another substance, presumably 6-bromo-1-nitro-2-naphthol, which was not investigated. Acidification of the NaOH extract led to 130 mg of brown solid containing chiefly 2-hydroxy-1,4-naphthoquinone.

Registry No.—2, X = Br, 26885-81-4; 2, X = Cl, 26885-82-5; **4**, 26885-83-6.

Acknowledgments.—We are indebted to Dr. F. Thomas Bond for helpful suggestions and to Mr. Jerome F. Keeton for some preliminary experiments.

Substituent Effects on Solvolyses of 1,4-Ethano-1,2,3,4-tetrahydronaphthalen-2(*exo* and *endo*)-yl (Benzobicyclo[2.2.2]octen-2(*exo* and *endo*)-yl) Derivatives[1,2]

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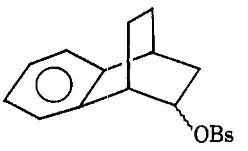
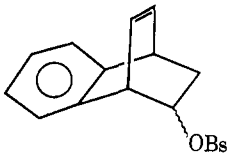
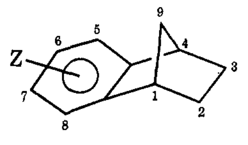
Received September 3, 1970

Series of aromatic-substituted 1,4-ethano-1,2,3,4-tetrahydronaphthalen-2(*exo*)-yl *p*-bromobenzenesulfonates (Z-**A**-OBs) or chlorides and the corresponding endo epimers (Z-**B**-OBs) were prepared and the solvolysis reactions studied. In the exo series, the relative rates of acetolysis of 6-CH_3O, H, 7-CH_3O, 7-NO_2, 6-NO_2, and 6,7-$(NO_2)_2$ derivatives at 77.6° were 224, 1, 0.58, 3.4 × 10^{-3}, 2.4 × 10^{-3}, and 2.1 × 10^{-4}, respectively. The solvolyses of 6-CH_3O, H, and 7-CH_3O lead to products entirely controlled by the neighboring aryl group, **A** alcohols (or esters) of retained configuration, and 1,5-methanobenzocyclohepten-2(ax)-ols (or esters) (Z-**C**-X) by rearrangement. In contrast, the acetolysis of deactivated 7-NO_2-**A**-OBs gave, besides **A** and **C** derivatives, the inverted 7-NO_2-**B**-OAc, 7-nitro-1,4-methanobenzocyclohepten-5(ax and eq)-yl acetates (7-NO_2-**D**-OAc), and minor hydrocarbons. Also, the **A**-OAc:**C**-OAc product ratio for the 7-NO_2 compound was different from the constant ratio obtained from the 6-CH_3O, H, and 7-CH_3O compounds. From the 6,7-$(NO_2)_2$ brosylate, **B** and **D** derivatives and hydrocarbons were obtained, but not **A** and **C** derivatives. The results from the 7-NO_2 compound are interpreted in terms of concurrence of the aryl-assisted path (k_Δ) and the solvent-assisted path (k_s); those from the 6,7-$(NO_2)_2$ compound suggest no participation and the products are explained in terms of a k_s process and its leakage. The rates of the 6-CH_3O, H, 7-CH_3O, 7-NO_2, and 6-NO_2 brosylates are well correlated with σ^+ constants, yielding a ρ of -3.25, but that of the 6,7-$(NO_2)_2$ brosylate is not. The relative rates in acetolysis of the endo brosylates were 0.34 for H, 2.7 × 10^{-2} for 7-NO_2, 2.4 × 10^{-2} for 6-NO_2, and 2.0 × 10^{-3} for 6,7-$(NO_2)_2$. No notable substituent effect on the distribution of products was observed. The predominant products in these cases were **D** acetates. The ρ–σ treatment of the endo rates yields a straight line with a ρ of -1.50. The apparent exo:endo rate ratios decrease from 2.9 for the H compounds to 0.13 for the 7-NO_2 compounds, but those for the 7-NO_2, 6-NO_2, and 6,7-$(NO_2)_2$ compounds are essentially constant at ~0.1.

In a previous paper solvolyses of the parent 1,4-ethano-1,2,3,4-tetrahydronaphthalen-2(*exo* and *endo*)-yl brosylates and of 1,4-ethano-1,4-dihydronaphthalen-9-(*exo* and *endo*)-yl (benzobicyclo[2.2.2]octadien-2(*exo* and *endo*)-yl) brosylates were reported.[3] Since our initial work on the benzonorbornen-9-yl system,[4] interest in substituent effects on the solvolysis of this ring system has remained at a high level.[5-8] The study of cationic intermediates of bicyclo[2.2.2]octyl







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[1] The terms endo and exo are defined as follows: substituents on the side of the benzene ring are endo and those on the other side are exo. Axial and equatorial indicate the configuration of a substituent on the cyclohexane moiety and are abridged as ax and eq, respectively.

[2] The numbering used in this paper is shown in the charts.

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(7) (a) H. Tanida, H. Ishitobi, T. Irie, and T. Tsushima, *ibid.*, **91**, 4512 (1969); (b) H. Tanida, T. Irie, and T. Tsushima, *ibid.*, **92**, 3404 (1970), and a series of our papers cited therein.

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