SUPERELECTROPHILES AND THEIR CHEMISTRY

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DOUGLAS A. KLUMPP

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PREFACE

Our book is about the emerging field of "Superelectrophiles and Their Reactions." It deals first with the differentiation of usual electrophiles from superelectrophiles, which show substantially increased reactivity. Ways to increase electrophilic strength, the classification into gitionic, vicinal, and distonic superelectrophiles, as well as the differentiation of superelectrophilic solvation from involvement of *de facto* dicationic doubly electron deficient intermediates are discussed. Methods of study including substituent and solvent effects as well as the role of electrophilic solvation in chemical reactions as studied by kinetic investigations, spectroscopic and gas-phase studies, and theoretical calculations are subsequently reviewed. Subsequently, studied superelectrophilic systems and their reactions are discussed with specific emphasis on involved gitionic, vicinal, and distonic superelectrophiles. A brief consideration of the significance of superelectrophilic chemistry and its future outlook concludes this book.

Results of substantial experimental and theoretical work of the field accumulated in recent years warrant a comprehensive review and discussion. This should be of general use to chemists not only with academic and research fields interest but also to advanced students. Because of relevance to potential significant practical applications (including the pharmaceutical and petrochemical fields), industrial chemists should also benefit from it.

We believe that continuing work will result in much further progress and practical applications. If our book will be of help toward this endeavor, our goal will be achieved.

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GENERAL ASPECTS

Electrophiles (i.e., electron-deficient species) are of fundamental importance to chemistry. The concept of nucleophiles (lit. "nucleus seeking") and electrophiles (lit. "electron seeking") was suggested by Ingold following similar views implied by Lapworth's description of "anionoid" and "cationoid" reagents, Robinson's concepts, and Lewis's theory of bases (electron donors) and acids (electron acceptors).[1]

The realization of carbon electrophiles or carbocations dates back to 1901, with the reports of the ionization of triphenylmethyl alcohol in concentrated sulfuric acid and triphenylmethyl chloride with aluminum and tin chlorides.[1b,2] These reactions gave deeply colored solutions, which are now attributed to the formation of the π-conjugatively delocalized triphenylmethyl cation. In later studies by Meerwein, Ingold, Hughes, Whitmore, Roberts, Winstein, Schleyer, and others, using kinetic, stereochemical, and varied experimental methods, carbocation electrophiles were recognized as intermediates in reactions. It was Olah who discovered in the early 1960s methods to prepare and study long-lived persistent carbocations, for which he received the Nobel Prize in 1994. The topic was well reviewed and there is no need for further discussion here.[3] Varied diverse electrophilic reagents, functionalities, and intermediates have been further studied in detail.[3] They were reviewed in preceding monographs, which are referred to for the interested reader.[3b,d] With the advance of our

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structural and mechanistic understanding, it became clear that electrophilic reactivity is an important driving force in many chemical reactions.

Extensive efforts have been made to characterize nucleophile and electrophile strengths. Hammett first correlated[4a] the acidities of substituted benzoic acids (**1**)
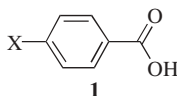
with the structures of the substituent groups and set up his equation as $\log k/k_o = \sigma p$ (where k_o is the rate or equilibrium constant for X=H, k is the rate or equilibrium constant for the substituted benzoic acid, p is a constant for the given reaction, and σ (Hammet's constant) is the value characteristic for the substituent).[4] In their linear free-energy studies, Swain and Scott characterized nucleophiles and electrophiles in kinetic experiments by comparing reaction rates according to the equation 1,

$$\log k_x/k_{H_2O} = sn_x \tag{1}$$

where s is the parameter characteristic for the electrophile and n_x is the parameter characteristic for the nucleophile.[5] More recently, Mayr and co-workers have conducted extensive kinetic studies in estimating the electrophilicities and nucleophilicities of a wide variety of reactants (Figure 1).[6] Using equation 2,

$$\log k(20^\circ C) = s(N + E) \tag{2}$$

the rate constants k for nucleophile-electrophile reactions may be calculated from three parameters (N the nucleophilicity parameter, E the electrophilicity parameter, and s the nucleophile-dependent slope parameter). By analyzing pseudo-first order rate constants with various types of nucleophiles, the electrophilicities of many cationic and neutral species have been established. These electrophiles include dithiocarbenium ions, iminium ions, cationic organometallic complexes (such as propargyl cations with cobalt carbonyl stabilization, cationic palladium complexes, and others), and quinone methides. When experimentally observed, rate constants k are compared with those values of k predicted from the three parameter equation (eq 2), they are generally accurate to within a factor of 10 to 100, excluding reactions with bulky reagents or multi-centered reactions (like S_N2). Moreover, the three-parameter equation may be used to
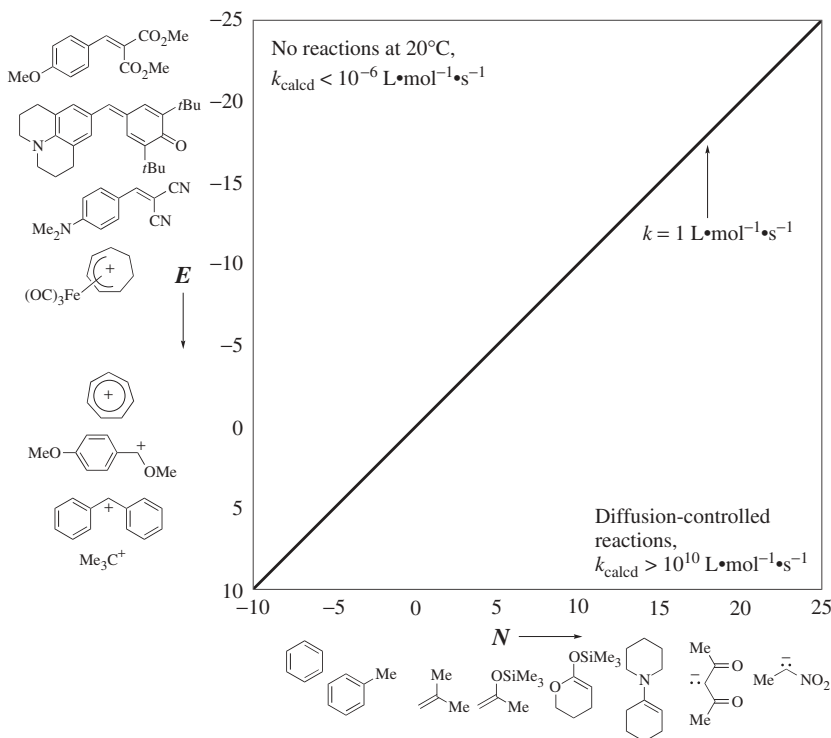
Figure 1. Estimated reaction rates, k_{calcd}, using nucleophilicity parameter N and electrophilicity parameter E.

describe numerous types of reactions involving electrophiles in such reactions as Michael additions, Mannich aminoalkylations, palladium-catalyzed allylations, Freidel-Crafts alkylations, and others.

In addition to the linear free energy studies discussed, there have been many attempts to estimate the thermodynamic stabilities of electrophilic species, such as carbocations.[7] The pK_{R+} values for carbocations reveal trends in relative stability and is defined as, according to the equilibrium established between the carbinol

$$pK_{R+} = \log([R^+]/ROH) + H^+$$

and carbocation in acidic solution. The pK_{R+} value for triphenylmethyl cation is -6.63 and that of the tri(p-nitrophenyl)methyl cation is -16.27, which is consistent with the resonance destabilization of the cationic center by the nitrophenyl substituents. Gas-phase ionization techniques have also been used to provide thermodynamic data for a variety of electrophiles.[8]

It has been recognized that electrophiles must have sufficiently high reactivity in order to react with weak nucleophiles. This concept of electrophilic reactivity is well demonstrated in the carbonyl chemistry of aldehydes and ketones. The carbonyl group is a reactive electrophilic center when encountering strong nucleophiles like Grignard and organolithium reagents (eq 3). The rapidly formed alkoxide product is thermodynamically heavily favored. With weaker nucleophiles like water or alcohols, reaction rates are considerably slower and the equilibria often favor the starting carbonyl compounds. However, protonation or complexation of a carbonyl group increases its electrophilic reactivity, and weaker nucleophiles may then react with the resulting carboxonium ion (eq 4).

$$(3)$$

$$(4)$$
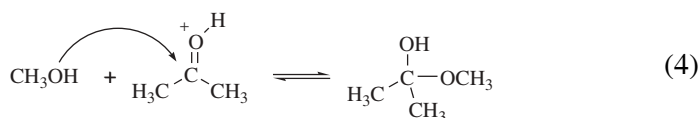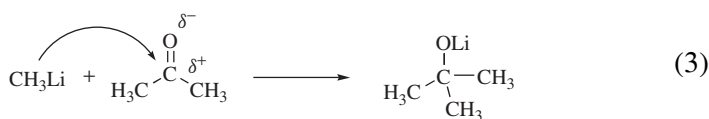
Examples of acid-catalyzed carbonyl chemistry are abundant in synthetic organic chemistry, biochemistry, industrial processes (such as in the synthesis of malachite green; eq 5), and in polymer chemistry (such as in the synthesis of bisphenols of derived epoxy and polycarbonate resins; eq 6).[9]

$$(5)$$

$$(6)$$
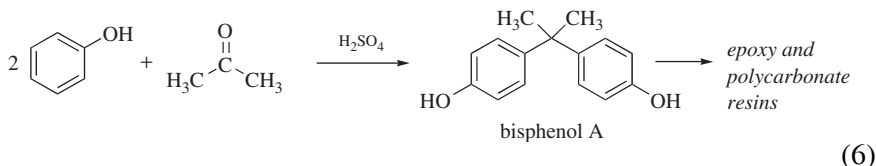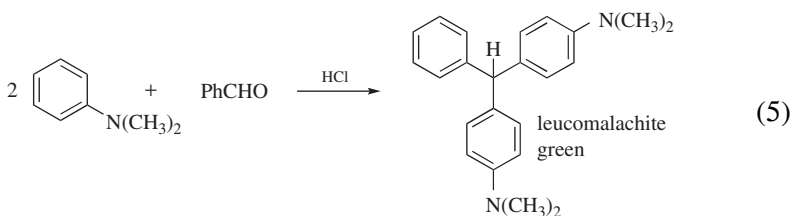
Without protonation of the carbonyl group, weak nucleophiles (*N,N*-dimethylaniline and phenol) would only react slowly or not at all with the carbonyl groups. Similarly, complexation with Lewis acids can enhance the electrophilic reactivities of carbonyl compounds. This occurs by decreasing participation (using Winstein's concept) of the neighboring oxygen

into the developing carbocationic center and thus increasing the polarized character of the (complexed) carbonyl group and lowering the energy of the LUMO (as described by the frontier molecular orbital theory). It has also been shown that substitution by electron withdrawing groups can significantly increase the electrophilic reactivity of carbonyl groups and their related protonated carboxonium ions. Whereas protonated acetophenone (**2**) is unreactive towards benzene (a weak π-nucleophile), the carboxonium ion from 2,2,2-trifluoroacetophenone reacts to give the condensation product in high yield (eqs 7–8).[10]

$$(7)$$

$$(8)$$
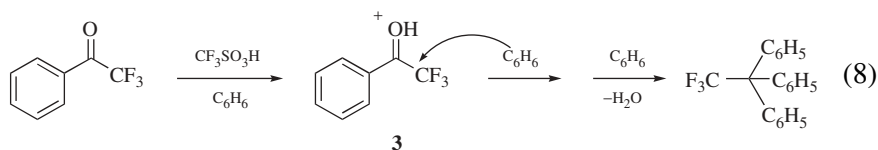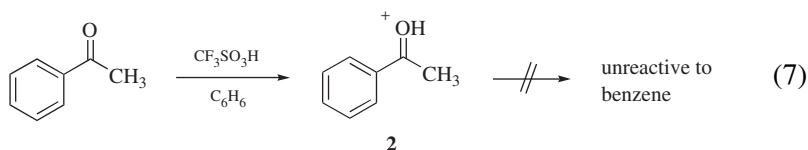
The electron withdrawing inductive effects of the fluorine substituents render the carboxonium ion **3** more electrophilic than carboxonium ion **2**, and consequently it reacts with benzene. Thus, the electrophilic reactivity of the carbonyl group can be greatly enhanced by Brønsted or Lewis acid solvation and by substitution with electron withdrawing groups.

Although increased electrophilicity can lead to reactions with weak nucleophiles, highly electrophilic cations can exist as stable, long-lived speci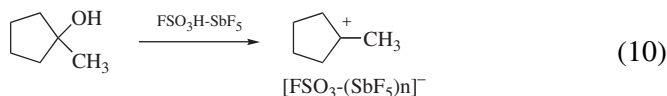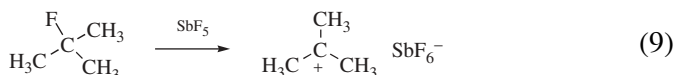es in solutions of low nucleophilicity.[11] Superacidic media are especially well suited for studies of such highly electrophilic species. Superacids and their chemistry, a topic extensively reviewed in a previous monograph,[11] have enabled the preparation and study of varied long-lived cationic electrophiles such as carbocations, acyl and carboxonium cations, and varied onium ions such as oxonium, sulfonium, halonium, nitronium, and azonium ions.[3d] Whereas these electrophilic species react instantaneously with many common electron donor solvents, the superacidic media is essentially an environment of very low nucleophilicity. For example, efficient routes to carbocation electrophiles include the ionization of alkyl fluorides in SbF_5 and the ionization of alcohols in magic acid, $FSO_3H\text{-}SbF_5$ (eqs 9–10).[12,13]

$$\underset{\substack{H_3C}}{\overset{\substack{F}}{C}}\underset{CH_3}{\overset{CH_3}{}} \xrightarrow{SbF_5} \underset{H_3C\;+\;CH_3}{\overset{CH_3}{C}}\quad SbF_6^- \tag{9}$$

$$\overset{OH}{\underset{CH_3}{}} \xrightarrow{FSO_3H\text{-}SbF_5} \overset{+}{}-CH_3 \tag{10}$$

$$[FSO_3\text{-}(SbF_5)n]^-$$

In the superacids, the resulting counterions are weak nucleophiles: SbF_6^- or $[SbF_6^-(SbF_5)_n]^-$, $[FSO_3\text{-}(SbF_5)_n]^-$, etc.

Gillespie proposed the widely accepted definition of superacids as those being stronger than 100% H_2SO_4 for Brønsted acids (i.e., $H_0 \leq -12$).[11] Similarly, according to Olah, Lewis acids stronger than anhydrous $AlCl_3$ are considered superacidic. Brønsted superacids span the logarithmic Hammett acidity scale from $H_0 -12$ for anhydrous H_2SO_4, to -27 for FSO_3H-SbF_5 (9:1) and ca. -30 for HF-SbF_5(1:1) (Figure 2). The isolated ("naked") proton is unobtainable in solution chemistry, but by comparing gas phase data with superacid solution chemistry, its acidity has been estimated to be in the -50 to -60 H_0 range. Superacids can react with weak base-sites like the n-electrons of carbonyl and other groups, the π-electrons of unsaturated groups (alkenes, alkynes, and arenes), and even with σ-electrons of alkanes. Not only carbocationic but also other varied reactive electrophiles can be generated as long-lived species in the superacids, and these electrophiles can often be studied directly by spectroscopic methods. They can also participate in many superacid-catalyzed reactions.
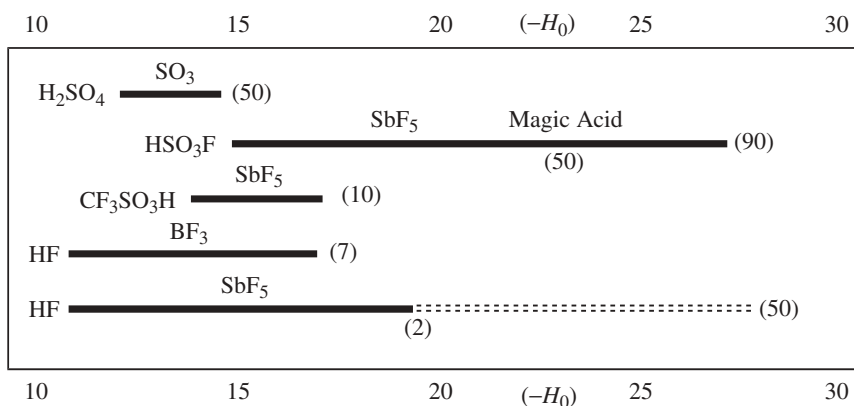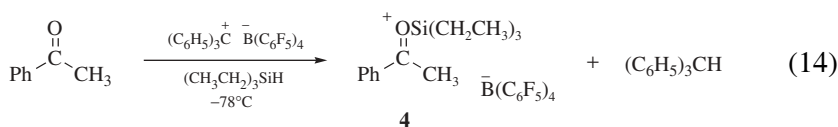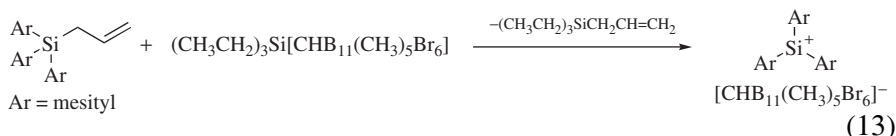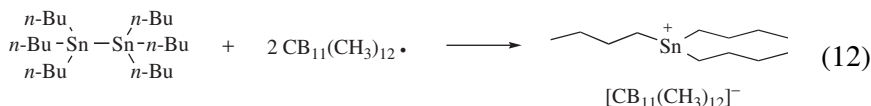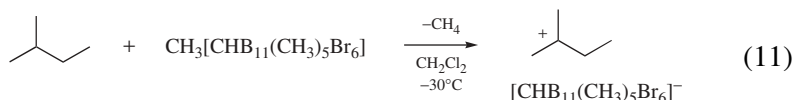

Figure 2. Acidity ranges for several common superacids. The solid bars are measured using indicators, while the broken bar is estimated by kinetics measurements; in (%) mol Lewis acid.

With respect to electrophiles and electron-deficient varied species, there have been suggestions of "non-coordinating solvents" and "non-coordinating anions." Of course, by definition anions are electron donors. In order to prepare highly electron-deficient species such as trialkylsilyl cations, claims were made for the use of non-nucleophilic or non-coordinating anions.[14] Even more surprisingly, some of these reactive ions have been prepared from toluene solution, referred to as a "non-nucleophilic solvent."[14] It should be mentioned that "the myth of non-coordinating anions" was discussed as early as 1973 by Rosenthal, who concluded that "it is clear that the notion of the non-coordinating anion should be put to rest alongside the notion of non-coordinating solvent."[15] Olah et al. subsequently discussed this point critically. As a result, the terms "least coordinating" and more correctly "weakly coordinating" anions were substituted.

Much effort has been made recently to find new weakly coordinating anions as counter ions for strong electrophiles and acids.[16] Like the conjugate bases of superacids, these weakly coordinating anions are generally characterized by the anionic charge being delocalized over the entirety of large anions, with no individual atom bearing a substantial part of the charge. Many of the most useful weakly coordinating anions have hydrogen and fluorine atoms on their periphery, thus avoiding the presence of strongly Lewis basic-sites. Among the most common low or weakly coordinating anions are borate anions, such as Meerwein's BF_4^- (which is of course the conjugate base of the important superacid $HF\text{-}BF_3$), Wittig's $B(C_6H_5)_4^-$, and the more recent $B(C_6F_5)_4^-$, and $[B(OTeF_5)_4]^-$, as well as Olah's SbF_6^- or $SbF_6^-\text{-}(SbF_5)_n$. The weakly coordinating borates are of particular practical importance to the activity of the electrophilic, one-component Ziegler-Natta olefin polymerization catalysts.[17] These cationic, metallocene catalysts have been shown to have high activities as polymerization catalysts, due in large part to their electrophilic metal center and weakly coordinating anions. It has been shown that for a given type of catalytic site, the more weakly coordinating anions result in more active polymerization catalysts. Another class of less coordinating anions are Reed's 1-carba-*closo*-dodecaborate monoanions ($CB_{11}H_{12}^-$ and related halogenated analogs). In addition to being used as counter ions in active, cationic polymerization catalysts, these anions have also been shown to be useful in the preparation of salts of varied electrophilic cations.[18] These include four-coordinate Fe(III)porphyrins, crystalline salts of carbocations (eq 11), a weakly coordinated, highly crowded stannyl cation (eq 12) and highly stabilized silicenium cations (eq 13), and other salts, despite the high electrophilic reactivities of the cations. Reactive electrophilic salts

$$\text{(isobutane)} \quad + \quad CH_3[CHB_{11}(CH_3)_5Br_6] \quad \xrightarrow[\substack{CH_2Cl_2 \\ -30°C}]{-CH_4} \quad \overset{+}{\text{(tert-butyl cation)}} \quad [CHB_{11}(CH_3)_5Br_6]^- \tag{11}$$

$$\underset{n\text{-Bu}}{\overset{n\text{-Bu}}{n\text{-Bu}-Sn}}-\underset{n\text{-Bu}}{\overset{n\text{-Bu}}{Sn-n\text{-Bu}}} \quad + \quad 2\,CB_{11}(CH_3)_{12}\bullet \quad \longrightarrow \quad \overset{+}{Sn} \quad [CB_{11}(CH_3)_{12}]^- \tag{12}$$

$$\underset{Ar}{\overset{Ar}{Ar-Si}}\diagup \quad + \quad (CH_3CH_2)_3Si[CHB_{11}(CH_3)_5Br_6] \quad \xrightarrow{-(CH_3CH_2)_3SiCH_2CH=CH_2} \quad \underset{Ar}{\overset{Ar}{Ar-Si^+}}$$

$$Ar = \text{mesityl} \qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad\qquad [CHB_{11}(CH_3)_5Br_6]^- \tag{13}$$

$$\underset{Ph}{\overset{O}{\underset{\|}{C}}}CH_3 \quad \xrightarrow[\substack{(CH_3CH_2)_3SiH \\ -78°C}]{(C_6H_5)_3\overset{+}{C}\ \bar{B}(C_6F_5)_4} \quad \underset{Ph}{\overset{+OSi(CH_2CH_3)_3}{\underset{\|}{C}}}CH_3 \quad \bar{B}(C_6F_5)_4 \quad + \quad (C_6H_5)_3CH \tag{14}$$

$$\mathbf{4}$$

such as the silylated carboxonium ion (**4**, eq 14) and the tris-mesityl silicenium ion have been prepared as tetra(pentafluorophenyl)borate salts. Recent reviews have been published on weakly coordinating anions, especially with respect to polymerization catalysts.[16,17]

Although monocationic carbon electrophiles have been involved in chemical reactions for many years, multiply charged organic electrophiles (dications, trications, etc.) have only been studied recently.[19] It was the high reactivity of dicationic vicinal and geminal electrophiles that led to the concept of superelectrophilic activation as proposed by Olah in the 1970s.[20] In 1973, Brouwer and Kiffen reported the results of superacid-catalyzed reactions between protonated aldehydes and ketones (carboxonium ions) and alkanes, as well as the reactions of the acetyl cation with alkanes (Scheme 1).[21] In solutions of HF−SbF$_5$ or HF−BF$_3$, reaction products are formed that are consistent with hydride transfer between the acetyl cation (generated *in situ* from acetic acid) and isobutane. Earlier studies by Olah and co-workers showed, however, that acetyl salts like acetyl hexafluoroantimonate do not abstract hydride from alkanes in aprotic solvents (SO$_2$, SO$_2$ClF, or CH$_2$Cl$_2$). In order to explain the enhanced reactive of the acetyl cation in superacid, Olah proposed the formation of a protosolvated, superelectrophilic intermediate (**5**).[20] Despite the fact that the acetyl cation has a positive charge, it has nonbonding oxygen electron pairs, which are capable of interacting with the superacidic media. In the limiting case, the hydrogen-bonded species (**7**) can lead toward the formation of the highly electrophilic, doubly electron deficient, dicationic
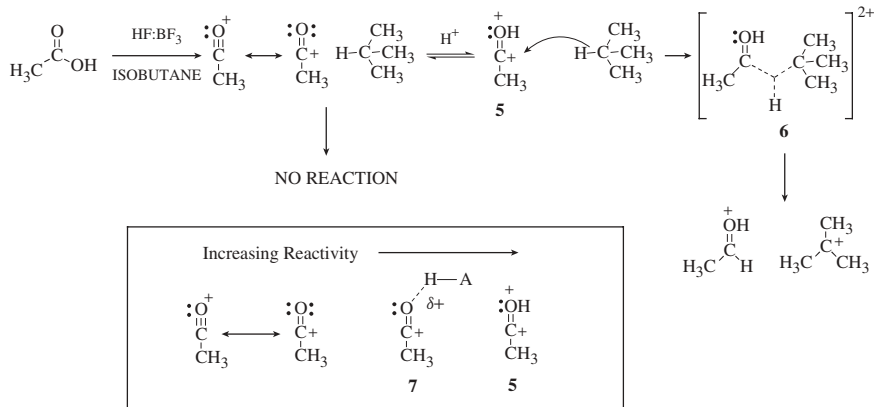
Scheme 1. Protosolvation of the acetyl cation and its reaction with isobutane.

species **5**. It is the superelectrophilic intermediate (**5** or **7**) that is capable of reacting with the C−H bond of the hydrocarbon substrate (isobutane). Subsequently, the complex **6** then leads to the formed hydride abstraction products. As described more thoroughly in Chapter 5, the proposed superelectrophilic activation is also supported by thermodynamic calculations.

About the same time, a similar type of activation was observed in the reactions of nitronium salts.[20] Nitronium salts (such as $NO_2^+BF_4^-$ or $NO_2^+PF_6^-$) show little or no tendency to react with deactivated arenes or alkanes in aprotic media. However, in fluorosulfuric acid or HF-BF₃ solution, nitration takes place giving nitration products even nitromethane (eq 15).
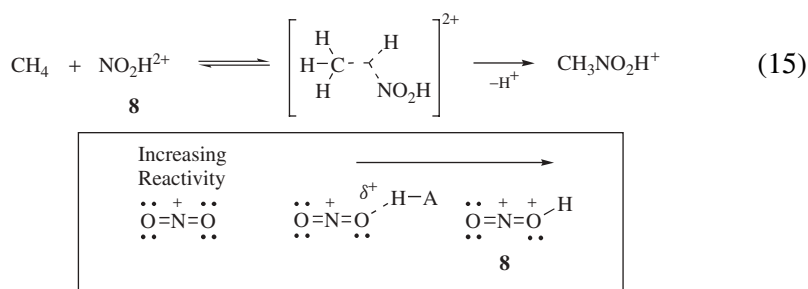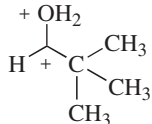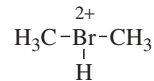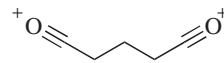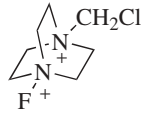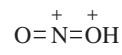

These results can be interpreted in terms of protosolvation of the nitronium ion. While the monocationic nitronium ion is a sufficiently polarizible electrophile to react with strong nucleophiles such as olefins and activated arenes, it is generally not reactive enough to react with weak nucleophiles including methane. Partial or complete protonation of the nitronium oxygen then leads to the superelectrophilic species **8**. The

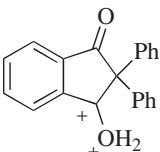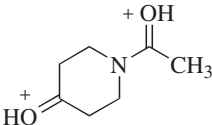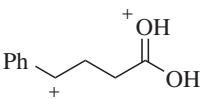heightened electrophilic reactivity of **8** allows the reactions with deactivated aromatics and alkanes.

The protionitronium ion (**8**, NO_2H^{2+}) and the protioacetyl cation (**5**, CH_3COH^{2+}) were the first examples of superelectrophilic intermediates. Their electrophilic reactivities are much greater than that of the corresponding parent monocations.[22] As such, these superelectrophiles are capable of reacting with weaker nucleophiles than the nitronium (NO_2^+) and acetyl (CH_3CO^+) cations. A defining feature of these superelectrophiles (and those described subsequently) is the further complexation (solvation) of the monocationic electrophile by Brønsted or Lewis acids. As a result of this interaction, neighboring group participation with the electrophilic center is decreased and the resulting electrophiles are increasingly electron deficient and reactive.[22] In the limiting cases, multiply charged *de facto* dications (even multications) may result. As discussed in Chapter 7, superelectrophiles are distinguished from such distant dications in which the two charged groups are isolated. Distant onium dications exhibit chemistry no different than the monocationic onium ions. The term "superelectrophile" previously has been applied occasionally to a number of other chemical systems, including metal complexes in high oxidation states, electrophiles bearing multiple electron-withdrawing groups, and other highly reactive electrophiles. While these systems may exhibit unique chemistry, they are not superelectrophiles within the context of discussed acid-base interactions. Consequently, their chemistry will not be included in our discussions in this book.

Superelectrophilic intermediates have been categorized into two distinct groups: the *distonic* (distant) and the *gitonic* (close) superelectrophiles (Table 1).[22] Distonic superelectrophiles are defined as electrophiles in

**Table 1. Classes and examples of superelectrophiles**

Gitonic Superelectrophiles	Distonic Superelectrophiles

which the positive charge centers are separated by two or more carbon or hetero atoms, while gitonic superelectrophiles are characterized by the positive charge centers being in close proximity. Both types of superelectrophiles and their chemistry will be discussed in subsequent chapters.

Theoretical calculations have been done on varied superelctrophilic species. They are often found in deep potential energy wells on the energy surfaces, although others are higher lying minima. Moreover, the calculated gas-phase structures are often only kinetically stable species but with sizable energy barriers to proton loss or other fragmentations. These calculations have been verified by the observation of a number of superelectrophiles by gas-phase mass spectroscopy studies (*vide infra*). Reactions of superelctrophiles in the condensed phase frequently involve discreetly formed dicationic (or tricationic) species. However, as noted with the protioacetyl dication (CH_3COH^{2+}, **5**) and the protionitronium dication (NO_2H^{2+}, **8**), formation of effective dications may be the limiting case. Partial protonation or weaker donor-acceptor interaction with a Lewis acid, what we now call electrophilic solvation, can also activate electrophiles to produce superelectrophiles. Along these same lines, there has been kinetic evidence to suggest varying degrees of protonation in the transitions states involving superelectrophiles.[23] For many superelectrophiles, it has not been possible to de facto directly observe these species, even with fast spectroscopic methods. It has been proposed in several of these studies that superelectrophiles are formed in only low concentrations. As an explanation for these reactions, superelectrophilic transition states may be involved with no persistent intermediates.

Two types of interactions have been shown to be involved in superelectrophilic species. Superelectrophiles can be formed by the further interaction of a conventional cationic electrophile with Brønsted or Lewis acids (eq 16).[23] Such is the case with the further protonation (protosolvation) or Lewis acid coordination of suitable substitutents at the electron deficient site, as for example in carboxonium cations. The other involves further protonation or complexation formation of a second proximal onium ion site, which results in superelectrophilic activation (eq 17).[24]

$$(16)$$

$$(17)$$

10
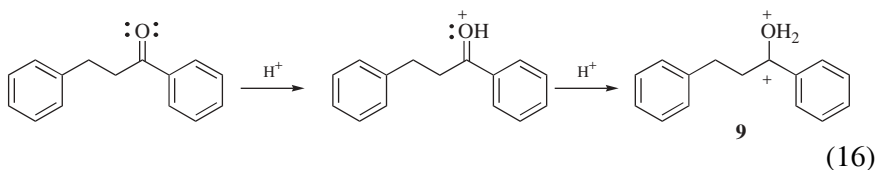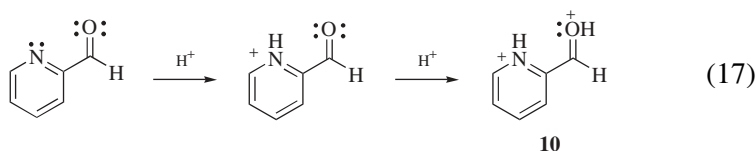
Both types of dicationic species (**9–10**) exhibit the properties and reactivities of superelectrophiles.

It should be noted that it was Pauling who predicted the viability of a doubly charged molecular structure in the 1930s by suggesting the kinetic stability of the helium dimer dication ($He_2{}^{2+}$).[25] Despite the large estimated exothermic energy of dissociation (200 kcal/mol), theoretical calculations predicted a substantial energy barrier to dissociation (33.2 kcal/mol). The recent mass spectrometric observation of the helium dimer dication, $He_2{}^{2+}$, confirms Pauling's prediction.[25b] The kinetic stability of the helium dimer dication can be understood by the bonding interaction ($He_2{}^{2+}$ is isoelectronic with the hydrogen molecule) offsetting the large electrostatic charge-charge repulsion. Molecular orbital theory also predicted the stability of aromatic dications, including the cyclobutadiene dication, the biphenylene dication, and the cyclooctatetrene dication. These dicationic species (**11–13**),
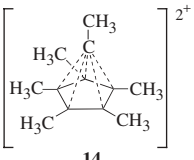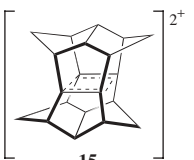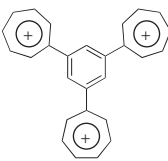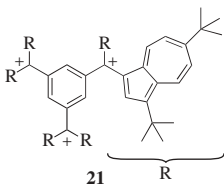

11   **12**   **13**
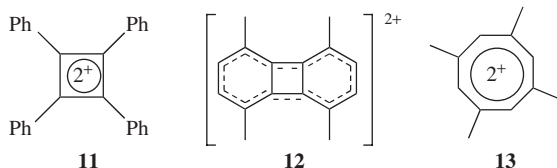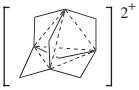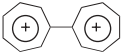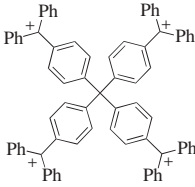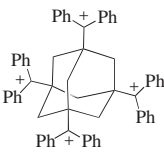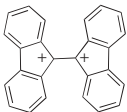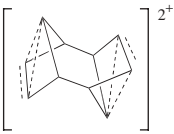
as well as many other related systems, have since been observed as stable ions in under high-acidity, low nucleophilicity conditions.[19a,b]

Superelectrophilic onium dications have been the subject of extensive studies and their chemistry is discussed in chapters 4–7. Other multiply charged carbocationic species are shown in Table 2. These include: Hogeveen's bridging, nonclassical dication (**14**)[26]; the pagodane dication (**15**)[27]; Schleyer's 1,3-dehydro-5,7-adamantane dication (**16**)[28]; the bis(fluroenyl) dication (**18**)[29]; dications (**17** and **19**);[19a] trications (**20–21**)[19a,30]; and tetracations (**22–23**).[31] Despite the highly electrophilic character of these carbocations, they have been characterized as persistent ions in superacids.

In solutions of low nucleophilicity, multiply charged electrophiles can frequently exhibit deep-seated rearrangements and fragmentation reactions. These reactions often stem from the electrostatic repulsive effects involving the charge centers, and they have precluded the observation of

Table 2. Some persistent multiply charged carbocations

Dications		Higher Cations

14   15   16   17   18   19   20   21   22   23

some multi-charged ions. For example, a long-sought goal in carbocation studies was the generation of an aliphatic 1,3-carbodication. Whereas ionization of 2,5-dichloro-2,5-dimethylhexane gives the stable 1,4-dication (**24**, eq 18) ionization of 2,4-dichloro-2,4-dimethylpentane (**25**) leads only to the 2-pentenyl cation (**27**, eq 19).[32] It is thought that the 1,3-dication (**26**) if formed undergoes rapid deprotonation to give ion **27**. Similarly, ionization of the diol (**28**) gives the two monocations instead of the expected 1,3-dication (eq 20).[32] Other reactions of dicationic species are described in chapters 4–7.

$$\text{Cl}\cdots\text{Cl} \xrightarrow[\substack{SO_2ClF \\ -78°C}]{SbF_5} \mathbf{24} \tag{18}$$

$$\mathbf{25} \xrightarrow[\substack{SO_2ClF \\ -78°C}]{SbF_5} \mathbf{26} \longrightarrow \mathbf{27} \tag{19}$$

$$\mathbf{28} \xrightarrow[\substack{SO_2ClF \\ -78°C}]{\substack{HSO_3F \\ SbF_5}} + \tag{20}$$
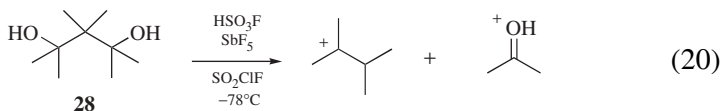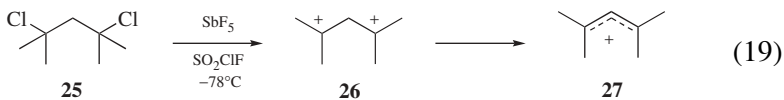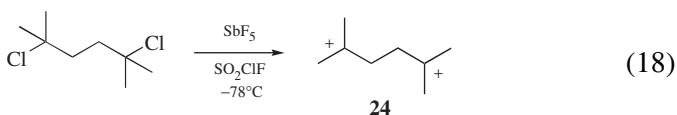
The concept of superelectrophilic activation was first proposed 30 years ago.[20] Since these early publications from the Olah group, superelectrophilic activation has been recognized in many organic, inorganic, and biochemical reactions.[22] Due to the unusual reactivities observed of super-electrophiles, they have been exploited in varied synthetic reactions and in mechanistic studies. Superelectrophiles have also been the subject of numerous theoretical investigations and some have been directly observed by physical methods (spectroscopic, gas-phase methods, etc.). The results of kinetic studies also support the role of superelectrophilic activation. Because of the importance of electrophilic chemistry in general and super-acidic catalysis in particular, there continues to be substantial interest in the chemistry of these reactive species. It is thus timely to review their chemistry.

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2

STUDY OF SUPERELECTROPHILES

2.1 INTRODUCTION

Many of the methods used in the study of electrophiles can also be applied
in studies of superelectrophiles. As noted in the introduction, superelec-
trophiles often exhibit very high reactivities when compared with conven-
tional electrophiles. The heightened reactivities can consequently be used
to estimate the degree of superelectrophilic activation in the chemistry
of superelectrophiles. In this respect, several reports have characterized
superelectrophiles based on kinetic studies. Reaction rates were shown
to increase with acidity for certain types of acid-catalyzed conversions
indicative of superelectrophilic activation. Although superelectrophiles
affecting reactions are generally present only in low concentrations, some
persistent superelectrophiles have been studied using varied spectroscopic
techniques. Low-temperature NMR and gas-phase techniques have been
used in studies of several types of superelectrophiles. Theoretical calcula-
tions have been used to characterize many superelectrophilic systems. In
addition to proving their intermediate nature as energy minima, they also
have provided ground state geometries and energies. Calculations have
also indicated significant energy barriers to dissociation for a variety of
dicationic and tricationic superelectrophiles. This chapter describes the

various methods of study of characteristic superelectrophilic systems that have been studied. Other techniques, such as isotopic labeling studies, calorimetric measurements, and various physical measurements, are also discussed when relevant.

2.2 REACTIVITY PROFILES

One of the defining features of superelectrophiles is the often-observed high level of reactivity towards nucleophiles of low strength.[1] This experimental observation is frequently used as an indication for the involvement of a superelectrophiles. To illustrate, the following examples show how the electrophile's reactivity can be characterized to indicate superelectrophilic chemistry.

It was the enhanced reactivities of nitronium and acetylium salts in superacidic media that lead Olah to first propose in 1975 the concept of superelectrophilic activation.[2] As mentioned in Chapter 1, nitronium salts exhibit markedly enhanced reactivities in strong acids when compared with reactions in aprotic solvents. Even the slow nitration of methane can be accomplished using nitronium hexafluorophosphate ($NO_2^+PF_6^-$) in superacidic FSO_3H, while nitronium salts in aprotic solvents are unreactive. This increased reactivity in superacid was suggested to involve protosolvation of the nitronium cation, forming the limiting superelectrophile NO_2H^{2+}. In a similar respect, nitration of strongly deactivated arenes is only effected by nitronium salts in superacidic media. For example, nitronium tetrafluoroborate ($NO_2^+ BF_4^-$) does not nitrate m-dinitrobenzene in nitromethane solvent, but in FSO_3H it gives 1,3,5-trinitrotoluene (eq 1).[3]

$$(1)$$
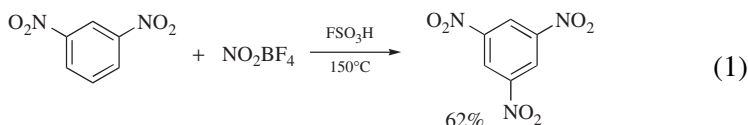
When nitronium tetrafluoroborate was attempted to be reacted with pentafluorobenzene in the triflic acid, CF_3SO_3H (H_0 −14.1), no nitration occured. However, using the much stronger superacid, triflatoboric acid (2 CF_3SO_3H-$B(O_3SCF_3)_3$, H_0 −20.5), nitration occurs in high yield (the nitronium ion being in $situ$ generated from nitric acid; eq 2).[3]

$$(2)$$
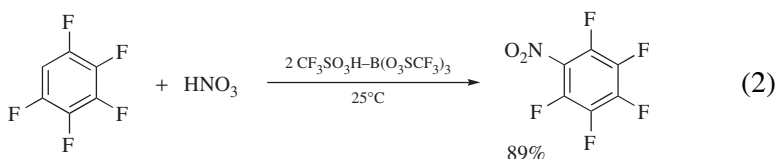
Even the trityl cation has been successfully nitrated using superacidic activation of nitronium salts (eq 3).[4]


$$\text{(3)}$$
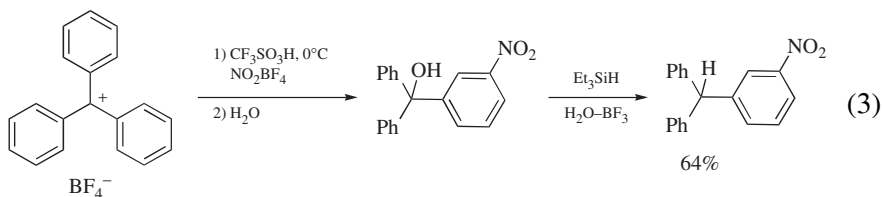
Due to the delocalization of the cationic charge into the phenyl rings, they are only very weakly nucleophilic. The reaction of nitronium tetrafluoroborate with triphenylcarbenium tetrafluoroborate in excess CF_3SO_3H, however, gives the mononitration product, which can then be reduced using ionic hydrogenation (Et_3SiH). The same reaction in an aprotic medium (CH_2Cl_2) gives no nitration product. These results are all consistent with the protolytic activation of the nitronium cation in the superacids. Methane, m-dinitrobenzene, pentafluorobenzene, and the trityl cation, are all weak nucleophiles, and the nitronium cation (**1**) does not possess sufficient electrophilic reactivity to attack these nucleophiles. Increasing the acidity of the reaction medium, however, leads to an equilibrium with the protosolvated nitronium ion (**2**) (or even the protonitronium ion, **3**),
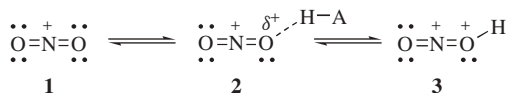

which is a significantly more reactive electrophile. Thus, nitration of these weak nucleophiles suggest the involvement of the superelectrophilic species (**2** or **3**). A more detailed discussion of the superelectrophilic nitronium ion is found in Chapter 5.

Friedel-Crafts type reactions of strongly deactivated arenes have been the subject of several recent studies indicating involvement of superelectrophilic intermediates. Numerous electrophilic aromatic substitution reactions only work with activated or electron-rich arenes, such as phenols, alkylated arenes, or aryl ethers.[5] Since these reactions involve weak electrophiles, aromatic compounds such as benzene, chlorobenzene, or nitrobenzene, either do not react, or give only low yields of products. For example, electrophilic alkylthioalkylation generally works well only with phenolic substrates.[6] This can be understood by considering the resonance stabilization of the involved thioalkylcarbenium ion and the delocalization of the electrophilic center (eq 4). With the use of excess Lewis acid, however, the electrophilic reactivity of the alkylthiocarbenium ion can be

greatly enhanced, indicating superelectrophilic activated species (**4**).[6c] The greater electrophilic reactivity allows for the electrophilic alkylthioalkylation of even benzene and halogenated arenes in good yields (eq 5).

$$(4)$$

$$(5)$$
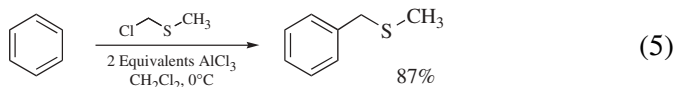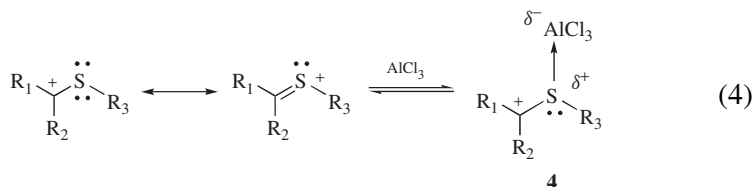
Similarly, hydroxyalkylation with aldehydes or ketones is best accomplished with activated aromatic compounds, such as phenols.[7] However, reaction even with chlorobenzene has been carried out with either parabanic acid or isatin using triflic acid (eqs 6–7).[8,9]

$$(6)$$

$$(7)$$
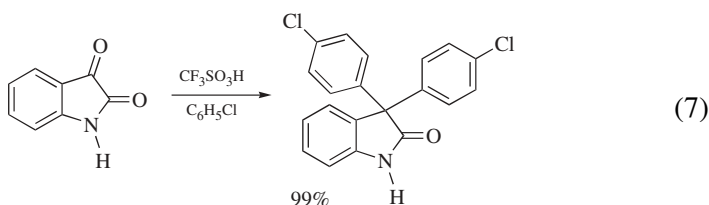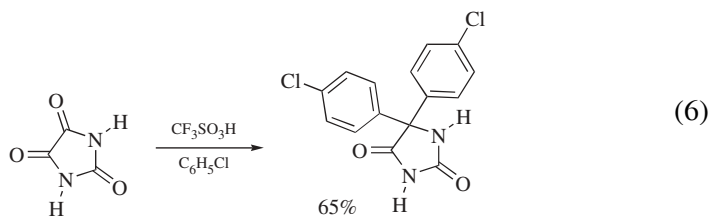
Diprotonated, superelectrophilic intermediates were suggested to be involved in both conversions. Considering protonated aldehydes, benzaldehyde gives a carboxonium ion that is significantly resonance stabilized and thus unreactive towards aromatic substrates such as o-dichlorobenzene or nitrobenzene. Pyridinecarboxaldehydes, however, show much higher electrophilic reactivities due to their ability to form via N-protonation the superelectrophile (**5**, eq 8).[10] A similar situation is seen in the hydroxyalkylation reactions of acetyl-substituted arenes. Acetophenone is fully protonated in excess triflic acid, but the resulting carboxonium ion (**6**) is