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Deciphering a 20-Year-Old Conundrum: The Mechanisms of Reduction by the Water/Amine/Sml₂ Mixture

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Abstract: The reaction of Sml₂ with the substrates 3-methyl-2-butanone, benzyl chloride, *p*-cyanobenzyl chloride, and anthracene were studied in the presence of water and an amine. In all cases, the water content versus rate profile shows a maximum at around 0.2 M H₂O. The rate versus amine content profile shows in all cases, except for benzyl chloride, saturation behavior, which is typical of a change in the identity of the rate-determining step. The mechanism that is in agreement with the observed data is that electron transfer occurs in the first step. With substrates that are not very electrophilic, the intermediate radical anions lose the

Introduction

Following the introduction of Sml₂ as a single-electron-transfer reducing agent to organic chemistry by Kagan et al.,^[1] many researchers have striven to develop means to control its chemoselectivity and enhance its reactivity.^[2] This was usually achieved by using additives, which either complexed to the substrate or, more frequently, to Sml₂. Examples of the first group are iron, copper, and nickel salts.^[3] However, most efforts focused on additives that coordinated to the Sml₂ itself. Ligands for the samarium cation can affect the course of the reaction in several ways.^[4] For example, hexamethylphosphoramide (HMPA), which is one of the most commonly used ligands,^[5] substantially increases the reduction potential of Sml₂. This results from greater energy gain upon coordination of HMPA to samarium(III) than that to samarium(II). $^{\mbox{\tiny [6]}}$ Proton donors, such as MeOH and water, also coordinate to Sml₂, but without having a significant effect on its reduction potential.^[7,8] Their added value stems from the ability to trap efficiently shortlived radical anions generated by electron transfer from Sml₂ to the substrate before back electron transfer takes place.^[7a,9]

In 1995, Cabri et al. discovered that the addition of water and amine to the reaction mixture significantly enhanced the reactions of Sml_2 .⁽¹⁰⁾ This discovery lay dormant for seven years until it was brought to the public's attention by Hilmersson et al.⁽¹¹⁾ The group of Hilmersson contributed significantly to added electron back to samarium(III) relatively quickly and the reaction cannot progress efficiently. However, in a mixture of water/amine, the amine deprotonates a molecule of water coordinated to samarium(III). The negatively charged hydroxide, which is coordinated to samarium(III), reduces its electrophilicity, and therefore, lowers the rate of back electron transfer, which allows the reaction to progress. In the case of benzyl chloride, in which electron transfer is rate determining, deprotonation by the amine is coupled to the electron-transfer step.

the development of this area, which was further developed by Procter et al. $^{\left[12\right] }$

Despite its synthetic importance,^[11h] the mechanism of the reaction in question remains unclear, although several attempts have been made to explain it. Suggestions include coordination of the amine to $Sml_{2'}^{[10]}$ precipitation of $Sm(OH)_3$ to provide the driving force for pushing the reaction to the right,^[11a] nucleophilic assistance by the amine in the reduction of benzyl halides,^[11e] and deprotonation of the water molecule to generate a better reducing agent^[12f] (hydroxide ion coordinated to SmI₂). Moreover, contradictory information on the kinetic rate order of water and amine has been reported.^[12e] A statement made by Procter et al. in a recent paper describes faithfully the state of the art of this interesting reaction: "the mechanistic details of this process, including the critical role of amine and H_2O additives, remained unclear". $^{[12f]}$ Herein, we report a mechanistic study of this reaction with the substrates 3-methyl-2-butanone, benzyl chloride, p-cyanobenzyl chloride, and anthracene and show the role of the amine and water in this often verbally referred to as "magic mixture".

Results and Discussion

It seems most likely that a mechanism that necessitates the presence of both water and amine must involve proton transfer between these two parties, as suggested by Procter et al.^[12f] This is supported by the fact that a correlation was found between the basicity of the amines and their activity.^[11h,12f] In addition, Kudo and Kamochi showed that the K(Na)OH/water system was also an efficient combination,^[13] this demonstrated the importance of the presence of a hydroxide ion. It is clear that of the two components, water and

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Figure 1. UV/Vis spectra of Sml₂ in the presence of water.

amine, water will usually preferentially complex to samarium. This is evidenced from spectral changes of Sml₂ caused by the incremental addition of water (Figure 1; similar behavior was observed also by Hilmersson and Dahlén^[11h]) and the lack of any spectral changes in the presence of Et₃N. The absence of isosbestic points in Figure 1 indicates the involvement of an intermediate structure(s) between noncomplexed and fully water-complexed Sml₂. However, a close examination of Figure 1 shows that isosbestic points do exist within the low (0–100 mm) and higher water concentration range (200–500 mm), as shown in Figure 2. This implies that at a low con-



Figure 2. UV/Vis spectra of Sml₂ in the presence of water at a concentration of 0–100 mm. The inset shows the spectrum in the presence of 200–500 mm of water.

centration of water Sml₂ is converted into one type of absorbing species (which may represent several different complexes with the same absorption) and upon increasing the concentration of water this intermediate(s) is converted into the final complex without going through an additional intermediate with a different spectral absorption.

We first examined the effect of varying the water concentration on the reaction kinetics in the presence of a constant concentration of amine. All reactions were carried out under pseudo-first-order conditions and the reaction rate was monitored by following the disappearance of the Sml₂ absorption at $\lambda = 570$ nm. The following concentrations were used in all



Figure 3. Rate constants as a function of water concentration in the reaction of ${\sf Sml}_2$ with benzyl chloride in the presence of ${\sf Et}_3{\sf N}.$

cases: $[Sml_2] = 1 \text{ mM}$, [substrate] = 10 mM, and [amine] = 20 mM. In Figure 3, the effect of varying the water concentration over the range of 0.001-1 m in the reaction of Sml_2 with benzyl chloride in the presence of Et_3N is shown.

The reaction rate increases rapidly at the beginning of the reaction and reaches a maximum at around 0.2 M. Further addition of water results in a gradual decrease of the rate constants. Similar results were obtained by Procter^[12f] and Hilmersson and Anker.^[11] This rate decrease may be the result of two possible causes. The first is that, as the water concentration is increased, second and even third solvation shells are built. This may hamper inner-sphere electron transfer, and thus, lower the rate. However, this should affect only substrates such as carbonyl derivatives, which are known to react with Sml₂ by an inner-sphere mechanism.^[14] However, it was suggested that polyaromatic compounds, such as anthracene, react by an outer-sphere mechanism,^[14] and yet, anthracene exhibits the same phenomenon (see the Supporting Information). Moreover, for all substrates examined, 3-methyl-2-butanone (with Et₃N and tetramethylethylenediamine (TMEDA)), benzyl chloride (with Et₃N), p-cyanobenzyl chloride (with ethyldiisopropylamine (EDIPA), since it was too fast with Et₃N), and anthracene (with Et₃N; see the Supporting Information), the maximum effect is achieved at the same water concentration (0.2 M). This implies that the rate drop is not substrate dependent. A more likely explanation is based on the rate of the deprotonation reaction. A water molecule or any other proton donor, when attached directly to the samarium cation, will enjoy a significant acidity increase. In MeOH, this acidity increase amounts to about 11 pK_a units.^[15] In THF, a solvent with a lesser ability to stabilize anions, this effect may even be doubled. As a result, deprotonation by the amine will be significantly enhanced. However, the acidification of water molecules in the secondary and tertiary solvation shells will be much diminished. Because the amine cannot access the more acidic bound water molecules in the primary solvation shell, the rate of deprotonation will be drastically decreased and because, as we show below, deprotonation rates play a crucial role in the reduction process, the overall rate will be diminished.

We now turn to the effect of the amine on the reaction rate. Again, all reactions were carried out under pseudo-first-order conditions and the rate was monitored at $\lambda = 619$ nm. The following concentrations were used in all cases: [Sml₂] = 1 mm, [substrate] = 10 mm, and [water] = 50 mm. This concentration



of water was chosen because at higher concentrations the reactions with high amine concentrations were too fast to follow. The effect of varying the amine concentration over the range of 0.001-0.4 M in the reaction of Sml₂ with 3-methyl-2-butanone is shown in Figure 4. The rate profile exhibits a satu-



Figure 4. Rate constants as a function of Et_3N concentration in the reaction of Sml_2 with 3-methyl-2-butanone in the presence of water.

ration effect. The kinetic order in amine before the onset of levelling off is one (slope = 0.99, r^2 = 1.00). The corresponding figures for other substrates and amines appear in the Supporting Information.

The rate profiles for water and amine provide a clear indication of the reaction mechanism and of the role these two components have in the reaction. Assuming that the amine deprotonates a water molecule complexed to samarium, there are three possible scenarios for this deprotonation of water by the amine. The first is that deprotonation takes place before electron transfer [Eq. (1)]. In other words, the amine will deprotonate either partly or fully complexed Sml₂. The coordination of $OH^{\scriptscriptstyle -}$ to $Sm^{\scriptscriptstyle \parallel}$ will render the latter a better donor, and hence, enhance the reaction. The second scenario is that deprotonation takes place after electron transfer. This will generate a hydroxide anion bound to Sm^{III} [Eq. (2)] and will enhance the reaction by virtue of diminishing the electrophilicity of Sm^{III}I₂, and hence, reduce the rate of back electron transfer. The third possibility [Eq. (3)] is that deprotonation occurs simultaneously with electron transfer (proton-coupled electron transfer (PCET)).^[16] For the sake of simplicity, in Equations (1)-(3), A is the substrate, R is a general substituent on nitrogen, and only one water molecule is shown to be complexed to the samarium cation.

$$\begin{array}{c} \mathrm{Sm}^{+2} + \mathrm{NR}_{3} & \longrightarrow & \mathrm{Sm}^{+2} + \mathrm{HNR}_{3}^{\textcircled{\Theta}} & \xrightarrow{\mathrm{A}} & \mathrm{A}^{\overleftarrow{}} + & \mathrm{Sm}^{+3} + \mathrm{HNR}_{3} & (1) \\ \downarrow & \downarrow & \downarrow \\ H_{2}\mathrm{O} & & \mathsf{OH} & & \downarrow & \mathsf{OH} \end{array}$$

$$A + \underbrace{Sm^{+2}}_{H_2O} \underbrace{k_1}_{K_1} A^{\overline{}} + \underbrace{Sm^{+3}}_{H_2O} \underbrace{k_2}_{NR_3} A^{\overline{}} + \underbrace{Sm^{+3}}_{OH} + \underbrace{MNR_3}_{OH} (2)$$

$$A + \underbrace{Sm^{+2}}_{H_2O} + NR_3 \xrightarrow{PCET} A^{\overline{+}} + \underbrace{Sm^{+3}}_{I \oplus \Theta} + \underbrace{HNR_3}_{P}$$
(3)

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The aforementioned results suggest that the second option [Eq. (2)] is the actual scenario. The "magic mixture" is used in cases in which, under normal conditions, that is, in the absence of water and amine, the reaction does not (or hardly) take place. This usually means that the electron-transfer step is highly endothermic, and therefore, is highly reversible. In the absence of a rapid successive step that prevents back electron transfer from the radical anion to samarium(III) and pushes the reaction to completion, the reaction will not take place. We have embarked upon this problem previously and for cases in which the "locking" step was protonation of the radical anion, the simple solution we devised was to enhance the protonation step.^[7a,9] This was achieved by replacing inefficient bimolecular protonation by a proton donor from the bulk, through efficient unimolecular protonation within the ion pair by a proton donor already complexed to the samarium cation. We realize that the magic mixture provides an alternative mechanism. Instead of locking the substrate radical anion by protonation, it prevents it from dispensing the added electron by reducing the electrophilicity of the acceptor: Sm^{III}. Reduced electrophilicity is the outcome of the partial neutralization of the effective charge by the negatively charged hydroxide. As a result, the lifetime of the radical anion is increased, which enables it to proceed further towards the products. Saturation observed in the rate profile of the amine is in agreement with this mechanism. At relatively low amine concentrations, the reaction is first order in the amine. As the amine concentration increases, the deprotonation rate is enhanced until the rate of the back electron transfer step in Equation (2) and the rate of deprotonation become similar. At this point, the bend in the rate profile is achieved and electron transfer starts to become the rate-determining step. Further increasing the amine concentration will therefore not affect the rate because deprotonation becomes a post-rate-determining step (Figure 5).



Figure 5. A rate profile showing electron transfer followed by deprotonation. Amine concentration increases from a to c. The bend occurs at b.

Because the bend in the rate profile indicates a point at which the rate of deprotonation by the amine is equal to the rate of back electron transfer, one could expect that in less electrophilic substrates, in which back electron transfer is faster, the rate will be matched only at a higher amine concen-

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tration. Indeed, whereas the reaction with 3-methyl-2-butanone has its bend at $[Et_3N]\!\approx\!0.05\,\,\text{m}$ (Figure 4), with a much less electrophilic anthracene the bend is achieved at only around 0.6 $\,\text{m}$ (see the Supporting Information).

It should be pointed out that the amine rate profile not only supports deprotonation as a post-electron-transfer step, it also rules out deprotonation as the first step [Eq. (1)]. Such a mechanism necessitates kinetics that are first order in amine at all concentrations. A leveling off may be achieved only in the unlikely event that complete deprotonation of all samariumwater complexes is achieved. Needless to say, in this kind of scenario, the magic mixture should have exhibited a significant increase in the reduction potential of Sml₂, which was not observed.^[11e]

The suggested mechanism can be further supported thanks to the fact that, for several decades, the mechanism of protontransfer reactions was intensively studied. Thus, the arsenal of physical organic chemistry contains a very useful tool to investigate the case in hand. In terms of proton-transfer chemistry, the topic is referred to as "specific versus general base catalysis" and the diagnostic tool developed is aimed to distinguish between cases in which proton transfer takes place at the preequilibrium stage (specific catalysis) or at the rate-determining step (general catalysis).^[17] In the first case, the concentration of the deprotonated species (OH⁻ complexed to SmI₂) is pH dependent. In the second case, the rate depends on the concentration of the individual bases present in solution and their kinetic basicity. Thus, working in a buffered solution and changing the concentration of the buffer without changing the buffer ratio will keep the pH constant. Nevertheless, the concentration of individual bases present in solution will increase with increasing buffer concentration. Hence, if the reaction is a specific base-catalyzed reaction, a plot of the rate versus buffer concentration will be linear with a slope of zero because the pH remains constant. Whereas if the reaction is general base catalysis, that is, deprotonation is the rate-determining step, since the free-base concentration increases with concentration of buffer, while that of the hydroxide ion remains constant, the plot will exhibit a positive slope. By using the couple Et₃N/Et₃N·HI as the buffer (see the Supporting Information for details) and varying its concentration, while the pH was maintained constant, a straight line with a positive slope was obtained (Figure 6). This indicates that proton transfer takes place at the rate-determining step.



Figure 6. General base-catalyzed experiment with 3-methyl-2-butanone (20 mm) and Sml_2 (2 mm) in THF/water (1/1 v/v).

librium between water and amine. Their order of reactivity is hydroxide ≥ amine > water. However, because the water and hydroxide concentrations are constant in the buffer experiment, their effect will be reflected in the intercept of the plot shown in Figure 6, whereas the slope is governed by increasing amine concentration. We have performed an experiment at the same water concentration in the absence of buffer with a varied concentration of Et₃N. In this case, the concentration of hydroxide ions is expected to increase in parallel to the amine concentration and, indeed, the slope obtained was much higher, which showed that the high reactivity of the hydroxide ion overcompensated for its low concentration (see the Supporting Information). It should be pointed out that the hydroxide, in this case, may function both as a general base and/or as a ligand for Sml₂. In the latter case, it may produce a very strong reducing agent, which is in agreement with the suggestion by Procter et al.^[12f] However, due to its minute concentration, it cannot be electrochemically detected. We now turn to the feasibility of the third scenario, in which

It should be pointed out that there are three bases present

in the reaction mixture: water, amine, and the minute amounts

of free hydroxide ion present in the solution due to the equi-

electron transfer and deprotonation are concerted [Eq. (3)]. The highest probability for such a mechanism is with a substrate for which electron transfer is rate determining with no possibility of back electron transfer. Benzyl chloride fits this requirement because electron transfer is concomitant with the departure of the leaving group. Indeed, in this case, no saturation kinetics were observed and a first-order reaction in amine was observed up to $1.2 \,\mathrm{M}$ (Figure 7).



Figure 7. Amine kinetic order in the reaction of benzyl chloride (10 mm) with Sml_2 (1 mm) and water (50 mm).

To exclude other mechanistic options, we performed the buffer experiment on this system as well. The positive slope obtained (1.6, $r^2 = 0.9947$; see the Supporting Information) clearly shows a general base catalysis mechanism in which the proton is transferred in the rate-determining step. Because the aforementioned buffer diagnostic tool rules out the possibility of pre-deprotonation as the first step [Eq. (1)] and since electron transfer is irreversible, we conclude that proton transfer is coupled to the electron-transfer step (PCET) in the rate-determining step.

Savéant et al. convincingly showed that the introduction of an electron-withdrawing substituent on the benzyl halides

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caused the mesolytic cleavage to be a stepwise reaction.^[18] We therefore investigated the reaction of *p*-cyanobenzyl chloride. As expected, the rate constant versus [amine] plot did not display a straight line up to high amine concentration, as found for benzyl chloride, but rather showed leveling-off behavior (see the Supporting Information), which was typical of reversible electron-transfer reduction.

We have shown herein that, in the Cabri-Hilmersson reactions, electron transfer could occur either concomitantly with proton transfer (PCET) or could precede it. The only substrate in this study in which the two processes are merged into a single transition state is benzyl chloride. Other substrates reacted in the sequential mode. The advantage of coupling in PCET is that the system avoids high-energy species on the reaction path. On the other hand, there are two probability obstacles: one that is embedded in the entropy factor, whereas the other is the encounter probability, which is concentration dependent. The activation entropy reflects the reduction in the degrees of freedom upon arriving at the transition state. It is probably similar for both process, although probably slightly more demanding for PCET. However, the major difference is in the concentration-dependent encounter probability. In enzymes, when all reacting parties are at the active site, the probability is, of course, very high. For example, in cytochrome c oxidase,^[19] electron transfer is accompanied by proton transfer from tyrosine 244 cross-linked to histidine 240. Needless to say, if protonation were external (bimolecular), the probability for a coupled process would be drastically diminished. Clearly, benzyl chloride reacts through PCET, although proton transfer is bimolecular because it offers a lower energy path. Why then would the other substrates not also benefit from this? We believe that they do and there is also a PCET component in the other cases. The fact that it is not so dominant results again from probability considerations.

To clarify the above assertion, let us assume, for the sake of simplicity, that the substrate pairs first with Sml₂, which transfers to it an electron in an equilibrium reaction. A longer lifetime of the ion pair produced in this reaction results in a greater probability for its encounter with an amine and deprotonation of a water molecule bound to Sml₂. As a result, the electron affinity of the substrate, and hence, the lifetime of its radical anion increases, along with the contribution of the sequential component to the overall reaction at the expense of the PCET component. This conclusion is evidenced by the shape of the plateau section for the various substrates. We have two substrates that differ markedly in their electron affinity: anthracene and 3-methyl-2-butanone. One can clearly see in log-log plots that the slope at the plateau region is not zero (Figures 8 and 9). With anthracene it is about 0.42 (Figure 8), whereas for 3-methyl-2-butanone it is much smaller (0.18; Figure 9). This is, of course, in agreement with the higher stability of the radical anion of the ketone, which favors the stepwise reaction. The latter occurs through increased probability of an encounter between the ion pair and the amine compared with that of anthracene, for which this probability is smaller and leaves more room for PCET.



Figure 8. A log–log plot showing the amine kinetic order in the reaction of Sml_2 with 3-methyl-2-butanone.



Figure 9. A log–log plot showing the amine kinetic order in the reaction of $\mathsf{Sml}_{\mathsf{z}}$ with anthracene.

We now turn to a quantitative analysis of the kinetic results, which is enabled mainly because of the fortunate existence of the saturation phenomenon in the rate versus amine concentration profile. The overall rate equation is $rate = k[A][NR_3]$ [Sml₂]. By assuming a steady-state concentration for the radical anionic intermediate in Equation (2), Equation (4) is obtained:

$$rate = \frac{k_1 k_2 [NR_3]}{k_{-1} + k_2 [NR_3]} [A] [Sml_2]$$
(4)

When Equation (4) is applied to the uprising limb of Figure 4, $k_{-1} \gg k_2$ [NR₃], the equation will acquire the form given in Equation (5):

rate =
$$\frac{k_1 k_2 [NR_3]}{k_{-1}} [A] [SmI_2]$$
 (5)

Therefore, the first-order rate constant (k) in Figure 4 is equal to Equation (6):

$$k = \frac{k_1 k_2 [\text{NR}_3]}{k_{-1}} [\text{A}]$$
(6)

The slope of the uprising limb in Figure 4 is given by Equation (7):

$$\frac{\Delta k}{\Delta[\mathsf{NR}_3]} = \frac{k_1 k_2}{k_{-1}} [\mathsf{A}] \tag{7}$$

Because the slope can be measured in each case and the concentration of the substrate is known, the value of k_1k_2/k_{-1} could be determined. In the plateau region, $k_{-1} \ll k_2[NR_3]$, the rate is equal to that given by Equation (8):

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tions between the radical anions

p-dimethylaminobenzophenone and [Sm^{III}][2I], amounts to about 30 kcal mol^{-1.[20]} Because the radical anion of the aliphatic ketone of the present study is much "harder" than the highly delocalized benzophenone radi-

rate = k_1 [A][Sml₂]

Namely, electron transfer is the rate-determining step and the rate constant (k_1) can be determined by back extrapolation of the data from the plateau region to an amine concentration of zero. Once k_1 is known, the ratio k_2/k_{-1} [Eq. (7)] can be determined. Relevant data is presented in Table 1.

water molecule may transfer a proton either to the carbonyl radical anion or to the amine. In both cases, proton transfer takes place between two heteroatoms. Why then is proton transfer to the amine of the magic mixture more facile than proton transfer from water to the oxygen atom in the radical anion? The answer lies, most probably, in the realm of electrostatic interactions. We have shown that electrostatic interac-

of

Table 1. Kinetic analysis for the reactions with Sml ₂ under Cabri–Hilmersson conditions.				
Entry	Substrate (amine) ^[a]	$\Delta k/\Delta$ (NR ₃)	$k_1 \; [M^{-1} s^{-1}]$	k ₂ /k ₋₁ [м ⁻¹]
1	3-methyl-2-butanone (Et ₃ N)	4130	19900	21
2	3-methyl-2-butanone (TMEDA)	2920	17400	18
3	<i>p</i> -cyanobenzyl chloride (EDIPA)	14390	26000	55
4	anthracene (Et ₃ N)	250	9400	3

(8)

The electron-transfer rate constant (k_1) for 3-methyl-2-butanone was determined in two experiments, each with a different amine (Table 1, entries 1 and 2): $(18700 \pm 1250) \text{ m}^{-1} \text{s}^{-1}$. This value is slightly lower than that for *p*-cyanobenzyl chloride and, as expected, significantly higher than that for anthracene. The k_2/k_{-1} value in Table 1 is slightly higher for Et₃N than that for TMEDA. Because k_{-1} is independent of the amine, this reflects the relative kinetic basicity of the two amines. A comparison of the results given in Table 1, entries 1 and 4, keeping in mind that the deprotonation rate constants are identical in the two cases, shows that the rate constant for back electron transfer, k_{-1} , is seven times larger for anthracene than that for 3-methyl-2-butanone.

Finally, we would like to discuss the differences between the two methods that enhance the reaction by competing with or effectively reducing the back electron transfer step $[k_{-1};$ Eq. (4)]. The first one is unimolecular protonation by proton donors such as water or a molecule of methanol complexed to Sml₂. The complexed proton donor protonates efficiently the radical anion within the ion pair [increasing k_2 in Eq. (9)], pushing the reaction forward.

$$A + Sm^{+2} \xrightarrow{k_1} A^{\overline{}} + Sm^{+3} \xrightarrow{k_2} P$$
(9)

The fact that, despite the ability of water molecules complexed to Sml₂ to unimolecularly protonate the radical anion, there is a strong dependence of the rate on the amine concentration. This indicates that the magic mixture is more effective at preventing back electron transfer than protonation of the radical anion, despite the fact that deprotonation is bimolecular. When protonation is supposed to take place on a carbon atom, as is the case with anthracene, the explanation is rather simple. Protonation on carbon, even if thermodynamically favored, is known to be slow and usually cannot compete with proton transfer between two heteroatoms, such as between amine and water.^[17] Therefore, in these cases, the first method (internal protonation) is not expected to successfully compete with the magic mixture. However, the case of carbonyl compounds presents a more difficult problem. In this case, the

cal anion, its interaction with "hard" Sm^{III} may be 5–10 kcal mol⁻¹ stronger.^[21] Thus, protonation of the carbonyl radical anion will result in a loss of stabilization energy of at least 35 kcal mol⁻¹ relative to proton transfer to the amine. This rough estimate provides a good explanation for the superiority of the magic mixture over direct proton transfer to the carbonyl radical anion.

Conclusion

Based on the evidence gathered, the most probable main reaction mechanism for reduction by a mixture of water/amine/ Sml₂, is deprotonation of a water molecule complexed to Sml₂ by an amine molecule after the electron-transfer step. This deprotonation, which binds a negatively charged hydroxide ion to Sm^{III} reduces its electrophilicity, and therefore, reduces the rate of back electron transfer within the ion pair. By conducting a buffer experiment, it was shown that all reactions, at relatively low amine concentration, were general base catalyzed. In other words, deprotonation can be effected by any base in the system, including water and hydroxide. The case of benzyl chloride, for which electron transfer and cleavage of the C-CI bond take place in a single step [Eq. (3)], is unique among the substrates, since no saturation is observed in the plot of rate versus [amine]. Because electron transfer is irreversible and deprotonation is rate determining, the reaction must be PCET.

Experimental Section

General

All reagents were purified prior to use by following standard procedures.^[22] Liquid reagents (substrates, water, and amines) were degassed with argon prior to use. THF was dried and freshly distilled from sodium/benzophenone under an argon atmosphere. Sml₂ was freshly prepared prior to use by stirring samarium metal and 1,2-diiodoethane at room temperature.^[1b] The concentration of Sml₂ was determined by UV/Vis spectroscopic measurements (λ = 619 nm; ε = 635). Kinetic and preparative reactions were carried out in clean and dry glassware under a nitrogen atmosphere. NMR spectra were recorded by using 300/400 MHz Bruker instruments.

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Kinetics

Stopped-flow kinetic measurements were carried out by using a Hi-Tech stopped-flow spectrometer. All reactions were performed under pseudo-first-order conditions. Rates of reactions were monitored by following the disappearance of the Sml₂ absorbance at $\lambda = 619$ (for the amine profile) and 570 nm (for the water profile). To ensure that the expected products were also obtained under kinetic conditions, preparative reactions were conducted with reactant concentrations similar to those used in the kinetic measurements.

General procedure for preparative reactions under kinetic conditions

A solution (10 mL) of the substrate (benzyl chloride (0.63 g; 4.98 mmol), 3-methyl-2-butanone (0.43 g; 4.98 mmol), anthracene (0.44 g; 2.47 mmol), or p-cyanobenzyl chloride (0.75 g; 4.98 mmol)) in THF containing triethylamine (0.20 g, 1.97 mmol) and $\rm H_2O$ (0.054 g, 3 mmol) was added to a solution of SmI_2 (10 mL) in THF (0.1 M) in a volumetric flask. The final concentrations of the different reactants in the reaction mixture were as follows: Sml₂, 0.05 m; substrates, 0.25 м (except for anthracene, which was 0.125 м); Et₃N, 0.1 M; and H₂O, 0.15 M). After the decolorization of Sml₂, the reaction mixture was filtered and the filtrate was diluted with chloroform (25 mL). The organic solution was washed with a 0.1 M solution of HCl (10 mL). The aqueous layer was extracted with chloroform $(3 \times 10 \text{ mL})$. The solutions in chloroform were combined, dried over anhydrous sodium sulfate, concentrated under reduced pressure, and analyzed by NMR spectroscopy and ESI-MS. The products for 3-methyl-2-butanone, benzyl chloride, p-cyanobenzyl chloride, and anthracene were 3-methyl-2-butanol, toluene, p-cyanotoluene, and 9,10-dihydroanthracene, respectively.

General procedure for buffer experiments

The rate of reduction of 3-methyl-2-butanone and benzyl chloride was measured in the presence of buffer. Buffer solutions were prepared in water with a 1:1 mixture of Et₃N and its corresponding iodide salt, [Et₃NH][I]. Kinetic measurements were performed in a 1:1 (v/v) mixture of THF and H₂O. The solution of Sml₂ and substrate in THF was placed in one syringe and the buffer solution in the other. The reactions rates were monitored by following the decay of the Sml₂ absorbance at $\lambda = 560$ nm.

Preparation of [Et₃NH][I]

HCl (0.154 g, 4.21 mmol; 0.48 mL of 32% HCl in H₂O) was added to Et_3N (0.426 g, 4.21 mmol) in THF (5 mL). The product [Et_3NH][Cl] was filtered and dried by applying high temperature and vacuum. It was then dissolved in acetonitrile and Nal (0.63 g, 4.21 mmol) was added to the solution. This resulted in the precipitation of NaCl, which was separated through filtration. The filtrate was concentrated under reduced pressure and dried in vacuum.

Keywords: electron transfer • kinetics • proton transfer • reaction mechanisms • samarium iodide

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