Kinetics

Reversed Electron Apportionment in Mesolytic Cleavage: The Reduction of Benzyl Halides by Sml₂

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Abstract: The paradigm that the cleavage of the radical anion of benzyl halides occurs in such a way that the negative charge ends up on the departing halide leaving behind a benzyl radical is well rooted in chemistry. By studying the kinetics of the reaction of substituted benzylbromides and chlorides with Sml₂ in THF it was found that substrates *para*-substituted with electron-withdrawing groups (CN and CO₂Me), which are capable of forming hydrogen bonds with a proton donor and coordinating to samarium cation, react in a reversed electron apportionment mode. Namely, the halide departs as a radical. This conclusion is based on the

Introduction

This paper weds two important topics, the chemistry of benzyl halides and of Sml₂. The benzylic system is one of the most important model systems. The vicinity of the α -carbon to the aromatic π system is, most probably, the major cause for its proliferated use in the exploration of a multitude of effects and phenomena. Selected examples of this are the determination of substituent parameters,^[1] substituent effects on rates of reactions such as S_N2,^[2] and steric inhibition of resonance.^[3] Sml₂, which was introduced into organic chemistry much later,^[4] became a pivotal player among the electron-transfer reducing agents due to several advantages it has over the others. Its popularity lies in is its versatility and ability to affect chemoselectivity by appropriate ligation.^[5]

In most of the papers reporting the reaction of Sml₂ with benzyl halides, the benzylic system was used as a model or a vehicle to explore the landscape of Sml₂ capabilities. A number of examples of these are the lifetime of excited Sml₂,^[6] the issue of inner sphere versus outer sphere electron transfer,^[7] as a mechanistic probe for the reactions of Sml₂-water,^[8] the effect of crown ethers on Sml₂ reactions,^[9] the effect of water,^[10] glyme,^[11] hexamethylphosphoramide (HMPA)^[12] and so on.

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found convex Hammett plots, element effects, proton donor effects, and the effect of tosylate (OTs) as a leaving group. The latter does not tend to tolerate radical character on the oxygen atom. In the presence of a proton donor, the tolyl derivatives were the sole product, whereas in its absence, the coupling dimer was obtained by a S_N2 reaction of the benzyl anion on the neutral substrate. The data also suggest that for the *para*-CN and CO₂Me derivatives in the presence of a proton donor, the first electron transfer is coupled with the proton transfer.

When Sml₂ is allowed to react with benzyl halides, an electron is transferred from the Sml₂ to the substrate. The electron transfer may merge with the departure of the halide into a single step (dissociative electron attachment). Alternatively, the electron transfer may produce a radical anion with a finite lifetime (of at least several molecular vibrations) and the departure of the leaving group occurs in a second step. This point was addressed several years ago by Jensen and Daasbjerg^[13] and Saveant et al.,^[14] but not within the context of Sml₂. Jensen and Daasbjerg suggested the involvement of a carbonium ion configuration when electron-donating substituents are used. The contribution of this configuration is diminished when strong electron-accepting substituents are present such as in the case of dicyanobenzene. Saveant et al. concluded that in the case of a strong electron-withdrawing substituent, such as the nitro group, the reaction is stepwise with the first step being a reversible electron transfer and the departure of the leaving group is rate-determining. With electron-donating substituents the reaction is most probably a concerted one, similar to $S_N 2$ and the addition of the electron and the expulsion of the halide take place simultaneously.

In this paper we report on the mechanism of the reaction of benzyl halides with Sml₂. As will be shown later, this study led to some interesting and unexpected results.

Results and Discussion

The kinetics of the reactions of substituted benzyl bromide with Sml_2 in THF [Eq. (1)] was investigated under pseudo first order conditions, in which the concentration of Sml_2 was 2.5 mm and that of the substrate was 50 mm.



$$X \longrightarrow CH_2-Br + Sml_2 \longrightarrow X \longrightarrow CH_2-CH_2-CH_2 \longrightarrow X$$
(1)

X=p-Me, H, p-OMe, p-Cl, m-CF₃, p-CF₃, m-CN, p-CO₂Me

For all the substituents used, the reaction rates were followed spectroscopically by monitoring the disappearance of Sml_2 at 619 nm. The reactions were found to be first order in Sml_2 . The kinetic order in the substrate was determined for the *p*-Me, *p*-Cl, and *p*-CN derivatives, as representatives of the whole series, and was found to be also first order (Figure 1). The first (*k*I) and second (*k*II=kI/[substrate] order rate constants for all the substrates are given in Table 1. The reaction



Figure 1. Kinetic order in the *p*-Me, *p*-Cl, and *p*-CN benzyl bromide derivatives.

Table 1. Rate constantwith Sml2 in THF.	for the reaction of subst	ituted benzyl bromide
Substituent	<i>k</i> I [s ⁻¹]	<i>k</i> II [м ⁻¹ s ⁻¹]
<i>p</i> -Me	0.17	3.4
н	0.2	3.9
<i>m</i> -OMe	0.22	4.35
p-Cl	0.29	5.8
m-CF ₃	0.29	5.8
p-CF ₃	0.50	10.4
<i>m</i> -CN	0.54	10.8
p-CN	17	340

of the p-CO₂CH₃ derivative was too fast to follow by using stopped flow spectroscopy and was estimated to be $\geq 200 \text{ s}^{-1}$.

The rate constants for most of the derivatives do not vary much ($(6.35 \pm 3) \text{ m}^{-1} \text{s}^{-1}$). Yet, the data in the Table show that the *p*-CN derivative reacts nearly two orders of magnitude faster than most other derivatives. Thus, the two strong electron-withdrawing substituents, *p*-CN and *p*-CO₂Me deviate significantly from the rest of the substituents. The origin of this deviation will be discussed later. We will first focus on the departure step of the leaving group.

An important diagnostic tool for the participation of a leaving group departure in the rate-determining step is the element effect. Hence, we determined the rate constants for the reaction of substituted benzyl chlorides under the same conditions. The reactions were much slower, enabling us to determine also the rate constant for the p-CO₂CH₃ derivative. The Table 2. Rate constant for the reaction of substituted benzyl chloride with Sml_2 in THF.

Substituent	<i>k</i> I [s ⁻¹]	<i>k</i> II [м ⁻¹ s ⁻¹]
<i>p</i> -Me	0.0050	0.1
Н	0.0035	0.07
<i>m</i> -OMe	0.0053	0.105
p-Cl	0.007	0.14
m-CF ₃	0.007	0.13
p-CF ₃	0.011	0.215
<i>m</i> -CN	0.015	0.3
p-CN	0.25	4.9
<i>p</i> -CO ₂ Me	8	160

Table 3. The Br/Cl element effect in the reaction halides with Sml_{2} .	of substituted benzyl
Substituent	k(ArCH ₂ Br) k(ArCH ₂ Cl)
<i>p</i> -Me H <i>m</i> -OMe <i>p</i> -Cl <i>m</i> -CF ₃ <i>p</i> -CF ₃ <i>m</i> -CN	34.0 55.7 41.4 41.4 44.6 48.4 36.0 69.4

first and second order rate constants are given in Table 2 and the element effect for the various substituents is given in Table 3.

The element effect shows clearly that the departure of the leaving group occurs at the rate-determining step. Interestingly, this element effect is significantly smaller than that observed by other investigators for benzyl halide although in different systems. For example, Jansen and Daasberg^[13] studied the reduction of benzyl bromide and chloride in DMF by using 1,4-dicyanonaphthalene radical anion as a donor. The element effect in this case was 359. An element effect of 496 was reported^[15] for the reactions with tri-*n*-butylstannane in benzene and a value of 670 was found for the same system in another report.^[16] The low element effect observed in our case may indicate a relatively early transition state. The difference in the transition state position along the reaction coordinate may stem from the difference in the solvents used or, more likely, from the nearby presence of the Sm³⁺. Namely, the triply charged samarium cation may electrophilically assist, through electrostatic stabilization, the expulsion of the leaving group. Molecular beam studies show that the electron donor may use a front side approach to the substrate,^[17] unlike the anti-approach of a nucleophile in the classical S_N2 reaction. This is explained as resulting from an electrostatic stabilization of the product. It is not unlikely that the samarium cation is located in a way that enables it to interact both with the π system and the leaving group simultaneously as shown in Figure 2. As will be explained later on, this transition state structure does not apply to the *p*-CN and the *p*-COOMe derivatives.





Sm⁺³ The data bled us to ρ values of 0.63 ($r^2 = 0$ ArCH₂Cl, re We will

Н

Figure 2. Transition state for the electrophilically assisted departure of the leaving group from benzyl chloride. The data in Tables 1 and 2, enabled us to calculate the Hammett ρ values of 0.66 (r^2 =0.873) and 0.63 (r^2 =0.705) for ArCH₂Br and ArCH₂Cl, respectively (Figure 3).

We will now discuss the mechanism of the *p*-CN and *p*-COOMe derivatives. As we have mentioned before, these two substituents deviate positively by orders of magnitude from the shallow Hammett



Figure 3. Hammett plots for the reaction of benzyl bromides and chlorides with Sml₂. Data points for *p*-CN and *p*-COOMe were omitted.

plot. The meaning of a convex Hammett plot is that at the bending zone, a mechanism change takes place.^[18] Thus, in the present case, the two substituents react by a mechanism different from that of the other substituents. Convex Hammett plots for benzyl halides radical anions were previously observed by Jensen and Daasbjerg^[13] and Huang and Wayner^[19] by using aromatic radical anions as the electron donors. Jensen and Daasbjerg explained the deviation (by using the valance bond model) as a change from an S_N 1-like mechanism for the electron-donating substituents to a S_N 2-like mechanism for the electron-withdrawing substituents. Based on product analysis, Huang and Wayner had shown that there is a shift from electron transfer to the S_N 2 mechanism [Eq. (2)].



The present work differs phenomenologically from the aforementioned reports in the behavior of the electron-withdrawing substituents. This is best demonstrated by comparison with Wayner's work, in which the break in the Hammett plot occurs at H and all the electron-withdrawing substituents (m-CF₃, *p*-CF₃, *m*-CN, and *p*-CN), fit nicely on the same ascending limb with a ρ^- value of 2.6 (Figure 4).



Figure 4. Hammett plot of log(k) versus σ^- for the reaction of DCN radical anion with some substituted benzyl bromides in DMF. Data from ref. [18].

Yet, in our case, the only deviating substituent is p-CN (and the p-CO₂Me, which was not included in Wayner's study), whereas the substituents; m-CF₃, p-CF₃, and m-CN do not lie on an ascending limb but are rather in line with the electrondonating substituents (Figure 3). It is therefore, unlikely that the above explanations apply to the case at hand. We suggest that, in the present case, the change in the mechanism, results from a change in the mesolytic mode of cleavage. In principle, regardless of whether the reaction is a dissociative electron attachment or consists of two successive steps, there are two options for electron apportionment as shown in Equation (3).

$$ArCH_2 - X \xrightarrow{Sml_2} ArCH_2 + X^{\Theta}$$
(3a)

In one mode (3 a), the departing halogen carries the negative charge leaving behind a benzyl radical. In the other (3 b), the benzylic system becomes negatively charged and the halogen departs as a radical. We suggest that for most of the substituents in our case the reaction is through pathway 3a, whereas the CN and CO_2Me derivatives react through 3b.

The halogen atoms, CI and Br, are capable of stabilizing both a radical and a negative charge. To support the suggested mechanism, we have looked for a leaving group that tolerates radicals to a much lesser extent than Br and Cl and therefore will not react through the 3b path. We assume that an oxygen-based leaving group will serve our purpose because the bond energy, which reflects on the stability of the radical, is considerably higher for the O-C bond than for the CI-C and Br-C bonds (for HO-Me, Cl-Me and Br-Me, the bond energies are 92, 83.7, and 70.3 kcal mol⁻¹, respectively).^[20] This is also in line with the commonplace experience that oxygen is the ultimate chain carrier in fires, whereas bromine derivatives, due to the relative stability of the bromine radical, were used as an essential component in fire-extinguishing compounds. A conceivable candidate for such a leaving group is *p*-toluenesulfonate. We have calculated^[21] the O–Me bond energy in Me–OSO₂Ph as well as the bond energies of the halides; Me--Cl and Me--Br. The data is given in Table 4.

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Table 4. The X–Me bond energy [kcal mol ^{-1}] ^[a] .			
	B3LYP/6- 31+G*	M06/AUG— cc-pVDZ	M06/AUG —cc-pVTZ
PhSO ₃ Me	84.2	93.8	92.0
Cl–Me	82.8	88.0	87.8
Br–Me	74.8	74.1	74.0
[a] Calculated as $E_{\rm X} + E_{\rm Me} - E_{\rm MeX}$.			

Table 5. Ab initio computed reaction energies for Equations (4) and (5).			
Eq.	B3LYP/6-31+G*	M06/AUG-cc-pVDZ	M06/AUG-cc-pVTZ
4 5		-17.0 -26.1	-20.3 -29.3

The data in the Table and the two isodesmic reactions below [Eqs. (4) and (5)] for which the data is presented in Table 5 show that sulfonate is a suitable candidate for this purpose.

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Therefore, we have synthesized benzyl tosylate with the *p*-CN substituent, and the corresponding *m*-CN and *p*-Cl derivatives as reference points. The kinetics of the reactions of these compounds with Sml_2 was followed and the reaction rates determined. The *m*-CN and *p*-Cl derivatives displayed an autocatalytic-zero order behavior, whereas the *p*-CN derivative gave a clean first order reaction (Figure 5 and the Supporting Infor-

0.2 0.18 0.15 0.12 Abs 0.09 0.06 0.03 습 Ś 100 150 z'n 250 300 360 400 450 500 Time (s)

Figure 5. Kinetic trace for the reaction of *p*-Cl benzyl tosylate with Sml₂.

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 Table 6. First and second rate constants for the reaction of substituted benzyl tosylates.

Substituent	<i>k</i> I [s ⁻¹]	<i>k</i> II [м ⁻¹ s ⁻¹]
p-Cl m-CN p-CN	0.02 ^[a] 0.01 ^[a] 0.03	$0.4^{[a]}$ $0.2^{[a]}$ 0.6
[a] Rate constants derived from initial rates.		

mation). To enable a comparison of the *p*-CN derivative rate constant with that of the two other substituents, their reaction rate constants were determined by using the initial rates method.

The data presented in Table 6 clearly show that the p-cyanobenzyl tosylate does not deviate from the two other substituents (p-Cl and m-CN). Namely, when the "inverse" mesolytic cleavage mode is energetically too costly, no rate deviation and no convex Hammett plot are observed.

This strongly supports the assumption that the positive deviation exhibited by the Cl and the Br (but not by OTs) is due to their stability as radicals and therefore their ability to exploit the inverse mesolytic mode. Thus, in the case of the *p*-CN substituent, the expulsion of these halogens as radicals is faster than their departure as anions, whereas the aversion of the tosylate to become a radical compels it to leave as an anion.

It is interesting to compare the reactivity of the *p*-CN tosylate with that of the corresponding halides. In Table 7 the rate constants for the benzylic system with the three leaving groups Br, Cl, and OTs are given.

Table 7. Rate constants for the reaction of the <i>p</i> -CN Cl, Br, and OTs (X) as leaving groups.	benzyl system with
х	<i>k</i> II [м ⁻¹ s ⁻¹]
CI	4.9
Br	340
OTs	0.6

The data clearly show that although tosyl group is generally considered to be a better leaving group than Cl and Br in unimolecular heterolytic reactions,^[22] it reacts much slower than the chloride and the bromide derivatives, further supporting the inverse mesolytic cleavage for the two halides.

We will turn now to the autocatalytic reactions and its cause. We have reported in the past cases of zero order-autocatalytic reactions of imines with Sml₂.^[23] These were interpreted as resulting from catalysis on the surface of micro Sml₃ crystals. In light of the similarity between the three OTs substrates, and the absence of such catalysis in the chloride and bromide derivatives, it is unlikely that the present case is also a surface catalysis case. Moreover, addition of externally prepared Sml₃ enhanced the reactions, causing the autocatalytic behavior to vanish and the reactions became first order in the disappearance of Sml₂. These results suggest that a displacement of the OTs by an iodide ion of Sml₃ is causing this behavior. Indeed,



Table 8. Products obtained in the reaction of some benzyl bromides and tosylates with Sml_3 .	
Substrate	Product
p-CN BnBr p-Me BnBr m-CN BnOTs p-CN BnOTs	Starting material Starting material 70 <i>% m-</i> CN Bnl 100 <i>% p-</i> CN Bnl

when the $ArCH_2X$ compounds shown in Table 8 were allowed to react with Sml_3 for 2 h, only the tosylates were converted to the corresponding iodides.

The fact that the *p*-CN tosylate does not show the autocatalytic behavior, stems, apparently, from the fact that its reaction with Sml_2 is faster than its reaction with Sml_3 .

Of crucial importance is the question; what causes the reduction by Sml₂ to differ so markedly from the reduction by aromatic radical anions? The explanations given to the Hammett curvature by Daasbjerg and Wayner were the degree of inclusion or its absence of a carbonium like the valence bond (VB) structure at the transition state^[13] and a switch from an $S_N 2$ mechanism to an electron transfer one.^[19] Whereas, in the Sml₂ reactions, the cause for the rate enhancement, as we have shown, is the change from the normal to the inverse mesolytic cleavage mode. To be more specific, the question is, why does our system involve the inverse cleavage mode whereas the other systems do not? In his work on the SRN1 mechanism, Rossi and Bunnett suggested that in a mesolytic bond cleavage, the negative charge will reside with the group that is most capable of stabilizing it.^[24] Yet, the benzylic systems are identical in all of the three scenarios and only in the present case, the cleavage direction is reversed. The most plausible reason for the difference seems to be rooted in the nature of the countercation. In the present study, the countercation is Sm³⁺. In the cases in which the donors were electrochemically generated, the countercation was the carrier tetrabutylammonium cation. An additional clue is the fact that unlike in the Wayner system (in which all electron-withdrawing substituents are on the same line), in the reaction with Sml_2 , only the *p*-CN and p-CO₂Me substituents deviate from the line, whereas the other substituents are "well behaved". These two substituents differ from the others by two features. The first is that these two substituents are capable of delocalizing the negative charge from the benzylic position onto themselves, and the second is that they are capable of binding to the samarium cation.^[10a, 25] Although it is unlikely that the electron-withdrawing power of the *p*-CN and *p*-CO₂Me substituents alone is sufficient to overcome the electronegativity of Cl and Br, their pairing with the triply charged samarium cation, apparently results in more efficient negative charge stabilization on the benzylic fragment than by its localization on the nucleofuge. Hence, according to the Bunnett paradigm,^[24] the mode of cleavage will be reversed. This cannot happen with the sterically hindered tetrabutylammonium cation, neither can it happen with the p-CF₃ substituent nor with meta substituents in which the molecular π orbital is orthogonal to the one relevant to the benzylic



Scheme 1.

position. The suggested mechanism is shown in Scheme 1 for the *p*-CN case.

Additional support for this mechanism comes from the effect of proton donors on the reaction rates. Proton donors, either by hydrogen bonding or by protonation on the substituent, can provide the same effect as that of Sm^{3+} . In the absence of a proton donor, the product, as we have shown, is the corresponding dimer. In the presence of MeOH, at concentrations as low as 25 mm, the product is the corresponding toluene.^[26] Despite the difference in the products, MeOH did not have any effect on the reaction rates of all the substrates (see the Supporting Information) except for the *p*-CN and *p*-CO₂Me-substituted ones. For these two substituents, a significant rate enhancement was observed (Table 9).

Table 9. Effect of added MeOH on the rates of the reaction between Sml_2 and benzyl bromide, chloride, and tosylate.			
Substrate	С (МеОН) [м]	<i>k</i> (rel.)	
<i>p</i> -CN BnBr	0	1	
	0.5	2.3	
	1	3.6	
p-CN BnCl	0	1	
	0.5	3.5	
	1	6.9	
p-CN BnOTs	0	1	
	0.5	5.3	
	1	23.3	
p-CO ₂ MeBnCl	0	1	
	0.5	15	
	1	28.75	

The suggested mechanism is, therefore, as follows. A Sml₂ molecule, to which several MeOH molecules are coordinated, approaches the substrate and the MeOH molecule forms a hydrogen bond with the nitrogen atom of the cyano group or with one of the ester oxygen atoms. Subsequently, two events follow: One is electron transfer and the other is the tightening of the H-bond to form a covalent bond. The possible sequences of the two events are shown in Scheme 2 for the CN derivative. The proton-coupled electron transfer (PCET),^[27] which avoids the high energy corner is the most likely route. Reaching directly from the hydrogen-bonded ground state to the *para* quinoidic structure avoids the formation of the high energy radical anion and the high energy protonated nitrile, and the negative charge ends up on the methoxide anion coordinated to the Sm³⁺ cation.

The structure in the lower right hand side of the diagram is depicted as a quinoidic structure in which the bromine radical



Scheme 2.

has left. However, it could also be that the reaction is stepwise and species at this corner is the radical, which in the next step expels the halogen radical and provides, after prototropy, the final *para*-cyanotoluene. The kinetic H/D isotope effect measured in the 0.1 to $4 \,\mathrm{M}$ concentration range of MeOH(D) was 0.9 ± 0.17 , in line with a proton transfer between two heteroatoms.

As can be seen from Table 9, the effect of MeOH is inversely proportional to the ability of the leaving group to stabilize a radical. According to the Hammond postulate,^[28] within a family of reactions, the more endothermic the reaction is, the later its transition state. Thus, Br, which is capable of stabilizing the product radical, will have an earlier transition state than CI and OTs and will therefore enjoy to a lesser extent the enhancing effect of the methanol. The interpretation of the effect with the OTs leaving group depends on the assigned mechanism for the OTs. Assuming that this derivative reacts in the inverse mesolytic mode, since the tosyl radical is less stable than the two halogen radicals, its transition state will be achieved much later featuring a well-developed negative charge on the benzylic unit. This, in turn will result in a much larger rate enhancement by the added MeOH, as is indeed shown in the Table. In this case, the fact that the *p*-cyanobenzyl tosylate rate constant is similar to that of all the other derivatives that react through the normal cleavage mode, must be fortuitous. If, as we have suggested above, the OTs derivative reacts in the normal mode, the rate acceleration by MeOH results from a higher ability to exploit the solvation of the leaving group by MeOH, through the formation of hydrogen bonds to two oxygen atoms of the leaving group (the third oxygen will probably be too hindered).

The final point that we would like to address is the relative rates of the *p*-CN and *p*-CO₂Me derivatives. It turns out that the *p*-CO₂Me substituent is significantly faster than the *p*-CN. Yet, both σ and σ^- suggest that *p*-CN is a more powerful electron-withdrawing group than the *p*-CO₂Me (σ values are 0.53 and 0.64 and σ^- values are 0.63 and 1.0 for *p*-CO₂Me and *p*-CN, respectively). The reason for this discrepancy lies in the unique nature of the electron-withdrawing capability of the cyano group. Although it is considered a strong electron-withdrawing group, its electronic effect, in a significant part, is inductive. This was realized rather early when it was discovered that cyano carbon acids behave like "normal" acids (in the Eigen sense)^[29] similar to chloroform, and unlike regular carbon acids, in which the negative charge is delocalized away from the carbon atom onto the activating group.^[30] This behavior was also confirmed computationally.^[31] Thus, the nitrogen atom of the cyano group, unlike that of the carbonyl in the ester, will not carry much negative charge in its frontier orbital. This will result in a diminished binding to the samarium cation or to a proton, at the transition state, relative to the binding to the p-CO₂Me group, and therefore to a lower rate enhancement.

Conclusion

We have shown that the classical course of electron apportionment in the Sml₂-induced mesolytic cleavage of substituted benzyl chlorides and bromides is not retained when *para* substituents capable of delocalizing the negative charge onto themselves are used. In these cases, because of the ability of these substituents to bind the samarium cation or to undergo an efficient protonation within a PCET process, placing the negative charge on the departing halide will render the reaction energetically less favored. As a result, these halides will leave as radicals and the negative charge will be delocalized onto the benzyl-Sm³⁺ system. The above conclusions are based on the specific features of the substituents deviating from the Hammett plots, on the ability of the leaving group to depart as an anion or as a radical, and on the effect of MeOH.

Experimental Section

General methods

THF was dried over Na wire, in the presence of benzophenone, and distilled under an argon atmosphere. The freshly distilled THF was used for all kinetic experiments as well as for the preparative reactions. MeOH was dried according to known procedures.^[32] Water content was determined to be lower than 20 ppm. Sml₂ solutions were prepared as needed from a freshly prepared 0.1 M THF solution.^[33] The concentration of the Sml₂ solution was spectroscopically determined ($\lambda = 619$ nm; $\varepsilon = 635$). The ArCH₂OTs was prepared using the following procedure for *p*-cyanobenzyl bromide. p-Cyanobenzyl bromide (0.49 gr, 2.5 mм) was dissolved in acetonitrile (50 mL) and Ag-p-toluenesulfonate (0.71 gr, 2.5 mм) was introduced into the solution. After 5 h at 50 °C the solution was filtered, evaporated, and extracted with diethyl ether. p-Cl BnOTs, and m-CN BnOTs were prepared in a similar manner. The identity of the products were confirmed by ¹H (300 MHz) and ¹³C (75 MHz) NMR spectroscopies, and HRMS analyses and their melting point were compared with the literature values.[34]

Kinetics

The kinetics of the reactions was followed by using a stopped flow spectrophotometer in a glovebox under nitrogen atmosphere at room temperature. The reactions were monitored at the λ_{max} of the Sml₂ (619 nm). Whenever a proton donor was used, it was mixed with the substrate solution. Each set of experiments was repeated two to three times. Within a set, each measurement was

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routinely repeated three times. At the end of each series, the first measurement was repeated to ensure reproducibility within a set. The deviation usually observed was about 5%. First-order kinetics was analyzed by using Kinet Asyst (v. 2.2 Hi-Tech Ltd.).

General Procedure: Product preparation under conditions similar to the kinetic measurements: A freshly prepared solution of Sml₂ (0.1 m) in THF was added in the glovebox to a homogeneous solution of the ArCH₂X in dry THF. The total volume of the reaction was 16 mL, and the final concentrations were $[Sml_2] = 50 \text{ mM}$ and $[ArCH_2X] = 50 \text{ mM}$. After the reaction is completed, the reaction mixture was dissolved in diethyl ether (40 mL) and washed three times with potassium dihydrogen phosphate buffer (15 mL). After washing by brine (20 mL) and drying over anhydrous Na₂SO₄, the solvent was filtered and evaporated under reduced pressure (isolated yield > 95%). The dimer (ArCH₂CH₂Ar) was the sole product. With the addition of one equivalent of methanol to the reaction, the monomer (ArCH₃) was isolated as the only product (yield > 95%).

Keywords: electron transfer \cdot kinetics \cdot radicals \cdot reduction \cdot samarium

- [1] H. H. Jaffe, Chem. Rev. 1953, 53, 191-261.
- [2] a) S. R. Hartshorn, Aliphatic Nucleophilic Substitution, Cambridge University Press, Cambridge, **1973**, and references therein. b) G. Kohnstam, Advances in Physical Organic Chemistry, Vol. 5, Academic Press, London, New York, **1967**, pp. 121–172; c) R. A. Sneen, Acc. Chem. Res. **1973**, 6, 46–53; d) R. A. Y. Jones, Physical and Mechanistic Organic Chemistry, 2nd ed., Cambridge University Press, Cambridge, **1984**, pp. 155–158, and references therein.
- [3] E. C. Anslyn, D. A. Doughert, *Modern Physical Organic Chemistry* University Science Books, Sausalito, CA, USA, 2004.
- [4] J. L. Namy, P. Girard, H. B. Kagan, New J. Chem. 1977, 1, 5-7. For recent reviews on the chemistry of SmI₂, see: a) M. Szostak, D. J. Procter, Angew. Chem. Int. Ed. 2012, 51, 9238-9256; Angew. Chem. 2012, 124, 9372-9390; b) B. Sautier, D. J. Procter, Chimia 2012, 66, 399-403; c) D. J. Procter, R. A. Flowers, T. Skrydstrup, Organic Synthesis Using Samarium Diiodide: A Practical Guide, The Royal Society of Chemistry, Cambridge, 2010; d) J. M. Concellón, H. Rodríguez-Solla, C. Concellón, V. Amo, Chem. Soc. Rev. 2010, 39, 4103-4113; e) T. Honda, Heterocycles 2010, 81, 2719-2747; f) T. Nakata, Chem. Soc. Rev. 2010, 39, 1955-1972; g) K. C. Nicolaou, S. P. Ellery, J. S. Chen, Angew. Chem. Int. Ed. 2009, 48, 7140-7165; Angew. Chem. 2009, 121, 7276-7301; h) K. Gopalaiah, H. B. Kagan, New J. Chem. 2008, 32, 607-637; i) S. Ichikawa, Chem. Pharm. Bull. 2008, 56, 1059-1072; j) V. Faugeroux, Y. Genisson, Curr. Org. Chem. 2008, 12, 751-773; k) D. Y. Jung, Y. H. Kim, Synlett 2005, 3019-3032; I) J. M. Concellón, H. Rodríguez-Solla, Chem. Soc. Rev. 2004, 33, 599-609; m) A. Dahlén, G. Hilmersson, Eur. J. Inorg. Chem. 2004, 3393-3403; n) D. J. Edmonds, D. Johnston, D. J. Procter, Chem. Rev. 2004, 104, 3371-3403; o) M. Szostak, M. Spain, D. J. Procter, Chem. Soc. Rev. 2013, 42, 9155-9183; p) M. Szostak, N. J. Fazakerley, D. Parmar, D. J. Procter, Chem. Rev. 2014, 114, 5959-6039; a) K. A. Choquette, R. A. Flowers in Comprehensive Organic Synthesis, Vol. 1 (Eds.: G. A. Molander, P. Knochel), 2nd ed., Elsevier, Oxford, 2014, pp. 279.
- [5] R. Yella, S. Hoz, Org. Lett. 2014, 16, 3876-3879.
- [6] W. G. Skene, J. C. Scaiano, F. L. Cozens, J. Org. Chem. 1996, 61, 7918– 7921.
- [7] R. J. Enemærke, K. Daasbjerg, T. Skrydstrup, Chem. Commun. 1999, 343 344.

- [8] M. Szostak, M. Spain, D. J. Procter, J. Am. Chem. Soc. 2014, 136, 8459– 8466.
- [9] S. Maity, K. A. Choquette, R. A. Flowers II, E. Prasad, J. Phys. Chem. A 2012, 116, 2154-2160.
- [10] a) M. Szostak, M. Spain, K. A. Choquette, R. A. Flowers, D. J. Procter, J. Am. Chem. Soc. 2013, 135, 15702–15705; b) E. Prasad, R. A. Flowers, J. Am. Chem. Soc. 2005, 127, 18093–18099.
- [11] J. A. Teprovich, Jr., M. N. Balili, T. Pintauer, R. A. Flowers, Angew. Chem. Int. Ed. 2007, 46, 8160-8163; Angew. Chem. 2007, 119, 8308-8311.
- [12] K. A. Choquette, D. V. Sadasivam, R. A. Flowers, J. Am. Chem. Soc. 2010, 132, 17396–17398.
- [13] H. Jensen, K. Daasbjerg, J. Chem. Soc. Perkin Trans. 2 2000, 1251-1257.
- [14] C. P. Andrieux, A. L. Gorande, J.-M. Saveant, J. Am. Chem. Soc. **1992**, *114*, 6892–6904 and references therein.
- [15] E. V. Blackburn, D. D. Tanner, J. Am. Chem. Soc. 1980, 102, 692-697.
- [16] L. W. Menapace, H. G. Kuivila, J. Am. Chem. Soc. 1964, 86, 3047-3051.
- [17] B. Jia, J. Laib, R. F. M. Lobo, P. R. Brooks, J. Am. Chem. Soc. 2002, 124, 13896–13902.
- [18] a) J. E. Leffler, J. Org. Chem. 1951, 16, 1785; b) O. Exner in Advances in Linear Free Energy Relationships (Eds.: N. B. Chapman, J. Shorter), Plenum, New York, 1972, pp. 12.
- [19] Y. Huang, D. D. M. Wayner, J. Am. Chem. Soc. 1994, 116, 2157-2158.
- [20] Y-R. Luo, Handbook of Bond Dissociation Energies in Organic Compounds, CRC press, New York, 2003.
- [21] Gaussian 09, Revision A.02, M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, G. Scalmani, V. Barone, B. Mennucci, G. A. Petersson, H. Nakatsuji, M. Caricato, X. Li, H. P. Hratchian, A. F. Izmaylov, J. Bloino, G. Zheng, J. L. Sonnenberg, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, T. Vreven, J. A. Montgomery, Jr., J. E. Peralta, F. Ogliaro, M. Bearpark, J. J. Heyd, E. Brothers, K. N. Kudin, V. N. Staroverov, R. Kobayashi, J. Normand, K. Raghavachari, A. Rendell, J. C. Burant, S. S. Iyengar, J. Tomasi, M. Cossi, N. Rega, J. M. Millam, M. Klene, J. E. Krnox, J. B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, K. Morokuma, V. G. Zakrzewski, G. A. Voth, P. Salvador, J. J. Dannenberg, S. Dapprich, A. D. Daniels, O. Farkas, J. B. Foresman, J. V. Ortiz, J. Cioslowski, D. J. Fox, Gaussian, Inc., Wallingford CT, **2009**.
- [22] H. M. R. Hoffmann, J. Chem. Soc. 1965, 6762-6765.
- [23] C. N. Rao, S. Hoz, J. Am. Chem. Soc. 2011, 133, 14795-14803.
- [24] R. A. Rossi, J. F. Bunnett, J. Am. Chem. Soc. 1974, 96, 112.
- [25] C. N. Rao, S. Hoz, J. Org. Chem. 2012, 77, 4029-4034.
- [26] This shows that the dimer formation does not result from a radical combination but rather from an S_N2 reaction of the benzyl anion on ArCH₂-X.
- [27] R. Yella, S. Hoz, Org. Lett. 2013, 15, 5262-5265.
- [28] G. S. Hammond, J. Am. Chem. Soc. 1955, 77, 334-338.
- [29] M. Eigen, Angew. Chem. Int. Ed. Engl. 1964, 3, 1–19; Angew. Chem. 1963, 75, 489–508.
- [30] A. C. Lin, Y. Chiang, D. B. Dahlberg, A. J. Kresge, J. Am. Chem. Soc. 1983, 105, 5380.
- [31] a) R. P. Bell, The Proton in Chemistry, Chapman and Hall, London, 1973, Chapter 10; b) S. Hoz, Z. Gross, D. Cohen, J. Org. Chem. 1985, 50, 832.
- [32] D. D. Perrin, W. L. F. Armarego, Purification of Laboratory Chemicals, 3rd ed., Pergamon Press, New York, 1989.
- [33] P. Girard, J. L. Namy, H. B. Kagan, J. Am. Chem. Soc. 1980, 102, 2693– 2698.
- [34] S. Yoh, Y. Tsuno, M. Sawada, Y. Yukawa, J. Chem. Soc. Perkin Trans. 2 1989, 7–13.

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