

On the Role of Samarium/HMPA in the Post Electron-Transfer Steps in SmI_2 Reductions

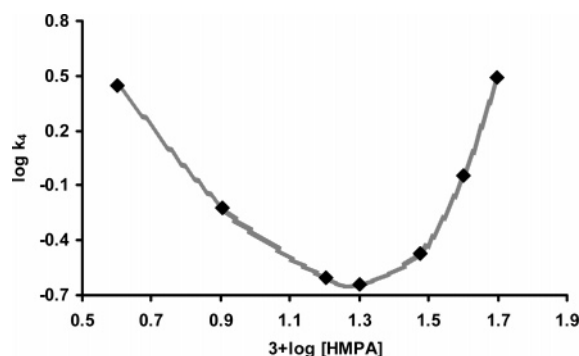
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ABSTRACT



The reaction of *p,p'*-dichlorobenzophenone with SmI_2 was studied in the presence of variable amounts of HMPA. The electron-transfer step takes place instantaneously. In the presence of excess substrate, the addition of HMPA retarded the rate of coupling to pinacol by a factor of 250. In the presence of an excess of SmI_2 , the initial rate retardation is followed by a dramatic increase in rate.

The chemistry of SmI_2 is highly sensitive to various additives. Therefore, one of the main foci of studies in recent years has been the improvement of reactivity, chemoselectivity, and stereoselectivity by additives.¹ Since the discovery by Inanaga,² HMPA became one of the most important additives in the chemistry of SmI_2 .³

The principal findings regarding this agent are: (a) the formation of a tetra-coordination complex⁴ and hexa-coordination complex⁵ with SmI_2 , which has a dramatic effect on the rate of electron transfer and regio and stereo selec-

tivities;^{1b,6} (b) the work by Flowers,⁷ by Hilmersson,⁸ and by Skrydstrup and Daasbjerg⁹ indicated that complexation by HMPA is accompanied by a marked increase (0.90 V) in the reduction potential of the SmI_2 ; (c) the reactivity order is hexa > tetra > 0 HMPA coordinated SmI_2 ;⁹ and (d) evidence was provided for the ionic character of these complexes.⁹

Contrary to the consensus that HMPA facilitates the reactions of SmI_2 , we show in this paper that, in certain cases,

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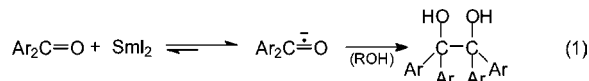
(7) (a) Shabangi, M.; Flowers, R. A. *Tetrahedron Lett.* **1997**, *38*, 1137–1140. (b) Shotwell, J. B.; Sealy, J. M.; Flowers, R. A. *J. Org. Chem.* **1999**, *64*, 5251–5255.

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HMPA slows down the reactions and also changes their course.

One of the classical uses of SmI_2 is the reduction of carbonyl compounds. Herein we present results obtained in the reduction (eq 1) of *p,p'*-dichlorobenzophenone (**1**). The reactions were followed at the λ_{max} (580 nm) of the radical anion using stopped flow spectroscopy.



This substrate was chosen for this study rather than the unsubstituted benzophenone because of its high electron affinity, which results in its complete conversion to the radical anion at the dead time of the mixing. (Concentrations used: $[\text{SmI}_2] = 2.5 \text{ mM}$; $[\text{Ar}_2\text{C}=\text{O}] = 50 \text{ mM}$ in THF.)

The reaction in the absence of a proton donor was second order (k_1) in the radical anion, as expected for a coupling reaction. Addition of trifluoroethanol (TFE) to the reaction mixture resulted in first-order kinetics in the radical anion (k_2) and first order in the TFE.

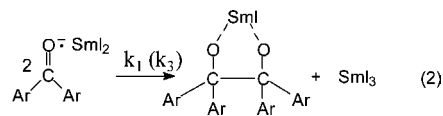
Table 1 and Figures S1 and S2 (see Supporting Information) demonstrate the unusual effect HMPA has on the rate of the reaction of **1** in the presence of excess substrate over SmI_2 .

Table 1. Rate Constants for the Reaction of SmI_2 (2.5 mM) with **1** (50 mM) in the Presence and in the Absence of TFE as a Function of HMPA Concentration

no TFE		[TFE] = 25 mM	
[HMPA] (mM)	$k_1 (\text{M}^{-1}\text{s}^{-1})$	[HMPA] (mM)	$k_2 (\text{s}^{-1})$
0	1500	0	5.8
8	30	8	0.4
16	7	16	0.08
20	6.5	20	0.075
30	6.2	30	0.07
40	6.15	40	0.064
50	6.1	50	0.065

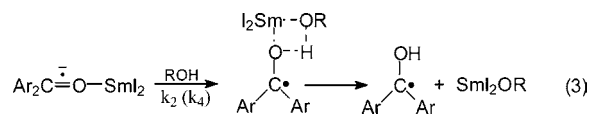
Increasing the concentration of HMPA results in a dramatic decrease of rates. The coupling reaction in the absence of proton donor is slowed down by a factor of ca. 250 and in the presence of TFE by a factor of ca. 80. The most plausible explanation of this is that the Sm^{+3} generated in the electron-transfer step is essential for the subsequent steps of the reactions, and its intensive complexation of HMPA apparently prevents it from fulfilling its role in these steps.

Reactions in the Absence of TFE. Because of the Coulombic repulsion between the two negatively charged oxygen atoms in the radical anions, in the absence of protons to neutralize the negative charges,¹⁰ bridging by a di- or trivalent metal cation (eq 2) is essential for pinacol formation. Mono-valent cations such as Na^+ fail to produce “even a trace of pinacol.”¹¹

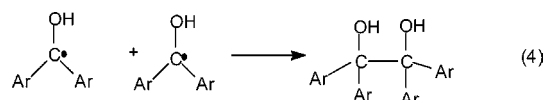


In the present case, the Sm^{+3} provides the necessary bridging. However, an increased amount of HMPA coordinating to the Sm^{+3} reduces the concentration of Sm^{+3} available for the bridging, and therefore, ultimately, the reaction rates decrease. At the plateau ($[\text{HMPA}] \geq 20 \text{ mM}$), the bridging is achieved, probably by an addition–elimination sequence displacing some HMPA molecules from the samarium in a rate determining step.

Reactions in the Presence of TFE. In previous work,¹² we have shown that because of the weak basicity of the radical anion, protonation by TFE in this relatively apolar medium (THF) is highly endothermic. The protonation is energetically enabled by the Sm^{+3} cation stabilization of the generated alkoxide. This stabilization is equivalent to an increase of the acidity of the alcohol by ca. 11 orders of magnitude.¹³ Most likely, the hard Sm^{+3} departs from the soft radical anion, in a square transition state, and moves to the hard alkoxide generated in the course of the protonation (eq 3). However, relatively high concentrations of HMPA reduce the concentration of the Sm^{+3} available to sustain the protonation process, and therefore, the reaction rate is decreased.



In the presence of 25 mM TFE, the radical obtained mainly dimerizes to furnish pinacol (eq 4).



It should be noted that a ca. 10 fold rate drop was also observed in the reduction of 1-iodobutane by $[\text{Sm}\{\text{N}(\text{SiMe}_3)_2\}_2]$ as a result of adding HMPA to the reaction mixture. However, it was concluded that the rate retardation originates from hindered access at the electron-transfer step.¹⁴

The picture becomes more complicated when SmI_2 is present in excess.¹⁵ The drop in reaction rates is still observed. However, this rate depression is followed by an upward surge of the rate as the concentration of the HMPA is further increased (Table 2, Figures 1 and 2).

In the absence of proton donor and for low concentration of HMPA, the reaction is second order in the radical anion

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Table 2. Rate Constants for the Reaction of SmI₂ (10 mM) with **1** (2 mM), in the Presence and in the Absence of TFE, as a Function of HMPA Concentration

no TFE		[TFE] = 25 mM	
[HMPA] (mM)	k_3 (M ⁻¹ s ⁻¹)	[HMPA] (mM)	k_4 (s ⁻¹)
0	100	0	3.6
4	80	4	2.8
8	21	8	0.6
16	18	16	0.25
	k_5 (s ⁻¹)	20	0.23
30	0.28	30	0.34
40	2.3	40	0.9
50	5.8	50	3.1

(k_3), in line with the above discussion for the coupling reaction. However, at higher concentrations of HMPA, the reaction becomes first order (k_5) in the radical anion.

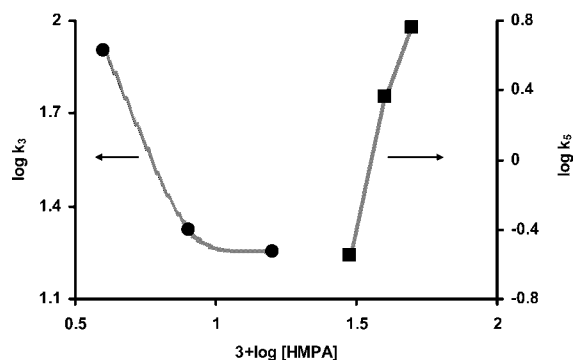


Figure 1. Log–log plot of the dependence of the rate constants for the reaction of SmI₂ with **1** as a function of HMPA concentration.

Addition of small quantities of HMPA reduces the rate because of the depletion of “free” Sm⁺³ as stated above.

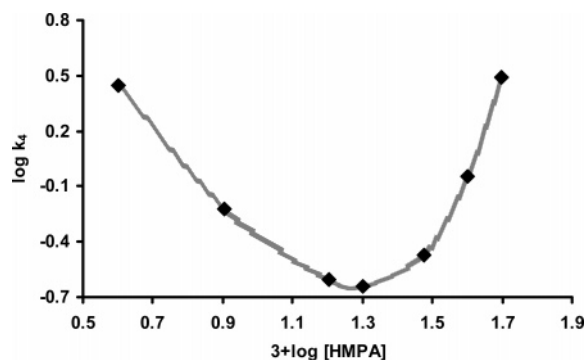
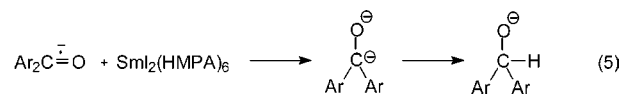


Figure 2. Log–log plot of the dependence of the rate constants for the reaction of SmI₂ with **1** as a function of HMPA concentration in the presence of TFE.

However, a further increase in the HMPA concentration induces the formation of SmI₂(HMPA)₆ with an increased reduction potential,⁹ which leads to the formation of the dianion (eq 5). The latter, presumably, rapidly abstracts a proton from THF¹⁶ to yield the hydrol as the major product (93% + 7% starting material) at 40 mM HMPA.

In the presence of TFE, a similar mechanistic variation takes place. At low HMPA concentrations, there is enough “free” Sm⁺³ to enable efficient protonation, hence the first order in the radical anion (k_4) and in the proton donor. At higher concentrations of HMPA, protonation of the radical anion becomes relatively inefficient due to the depletion of the “free” Sm⁺³ to support it, and as a result of this, the rate decreases. A further increase of the concentrations of HMPA induces the formation of the very basic dianion. This step becomes rate determining because the protonation of this highly basic species is very rapid and does not necessitate any assistance from Sm⁺³, thus rendering the reaction to be zero order in the proton donor.



An additional indication for the involvement of SmI₂(HMPA)₆ (or other complexes with reducing power higher than that of SmI₂(HMPA)₄) is the rate retardation observed; when at a high concentration of HMPA (40 mM), the concentration of SmI₂ is increased. Thus, in the absence of a proton donor, the rate constant for [SmI₂] = 12 mM is 0.86 s⁻¹ and it decreases to 0.52 s⁻¹ for [SmI₂] = 19 mM. This is simply because the surplus of HMPA used to generate the SmI₂(HMPA)₆ is used now to coordinate the added SmI₂.

To the best of our knowledge, this is the first report on the kinetics of the post electron-transfer events in the reduction of carbonyl compounds by SmI₂. This work shows that both Sm⁺³ and HMPA play an important role in this regime of the reaction and that *it is possible to control the interplay between the effects of “free” and complexed Sm⁺³ using HMPA to affect the rates, the mechanistic course, and the products obtained in these reactions.* This is nicely exemplified by the fact that high quantities of pinacol are always obtained in the absence of HMPA. However, in the presence of an excess of HMPA and SmI₂, hydrol is the only product, even in the absence of TFE.

Supporting Information Available: Technical data and Figures S1 and S2. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(15) The reactions in this case were analyzed as first order reactions. In an ideal situation, a 10-fold excess is needed for a pseudo first order analysis. However, because reliable kinetic measurements could be obtained only below 1 O.D., the maximum concentration of SmI₂ that could be used in these reactions was 0.01 M. Moreover, because of traces of water present in the solution, the concentration of the substrate was maintained above 0.002 M. Thus, the relative change in the reagent in excess SmI₂, instead of changing from 10 to 9, is changed from 8 to 6. In spite of that, reasonable first order rate constants were obtained.

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