

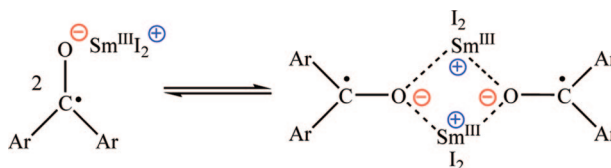
Reduction of Benzophenones with SmI₂. Post Electron Transfer Processes

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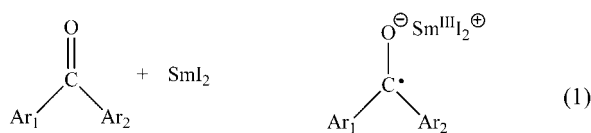
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The kinetics of the reaction of several substituted benzophenones with SmI₂ in THF was studied by using stopped flow spectrometry. The electron transfer takes place during the dead time of mixing and for most derivatives it is nearly quantitative. In the presence of an excess of substrate and in the absence of proton donors the dimerization reaction to pinacol is second order in the radical anion and has a negative order in SmI₂. Similarly, in reactions in the presence of excess SmI₂, the reaction shows negative order in the concentration of the substrate. It is concluded that the radical anions exist as a mixture of monomeric ion pairs and Streitwieser dimers. In the presence of trifluoroethanol, protonation of the Streitwieser dimer occurs with a rate constant an order of magnitude larger than that of the monomer.

Introduction

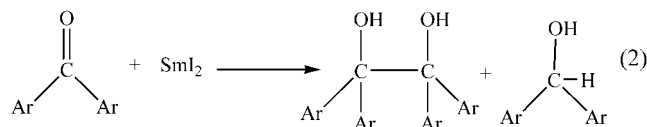
The majority of the reductions which employ SmI₂ are those of carbonyl compounds.¹ In most of these reactions the radical anion generated has a very short lifetime and does not accumulate to an appreciable extent such as to enable a kinetic examination of its reactions.² The relative stability of the radical anions of substituted benzophenones enables their direct monitoring and investigation.³ In a recently published paper we took advantage of this and determined the equilibrium constant for the electron transfer reaction (eq 1). This led to the quantitative assessment of the electrostatic interaction between the Sm³⁺ and the radical anion (ca. 25 kcal/mol).⁴



DCI: Ar₁ = Ar₂ = p-ClC₆H₄-
Cl: Ar₁ = p-ClC₆H₄-; Ar₂ = Ph-
H: Ar₁ = Ar₂ = Ph-
DMe: Ar₁ = Ar₂ = p-Tol-
DA: Ar₁ = Ar₂ = p-MeO-C₆H₄-
DMA: Ar₁ = p-Me₂N-C₆H₄-; Ar₂ = Ph-

In the present paper we explore the kinetics and the mechanism of the reactions at the post electron transfer step

domain. The two products which are obtained in these reactions are pinacol and benzhydrol (eq 2), the ratio of which depends on the reaction conditions.⁵



Results and Discussion

The reactions were followed with use of stopped flow spectroscopy. The radical anions are formed during the dead time of mixing (<3 ms) and have λ_{max} in the range of 570 to 590 nm depending on their substitution. The substrates absorb in the 350 nm range with no absorption above 400 nm. The progress of the reactions was monitored at the λ_{max} of the radical anions (Figure 1).

We first discuss the reactions in the absence of proton donors. Usually, the reactions were performed under pseudo-first-order

(1) For some recent reviews, see: (a) Flowers, R. A., II. *Synlett* **2008**, 1427–1439. (b) Edmonds, D. J.; Johnston, D.; Procter, D. J. *Chem. Rev.* **2004**, *104*, 3371–3403. (c) Kagan, H. B. *Tetrahedron* **2003**, *59*, 10351–10372. (d) Steel, P. G. *J. Chem. Soc., Perkin Trans. 1* **2001**, 2727–2751. (e) Dahlen, A.; Hilmersson, G. *Tetrahedron Lett.* **2001**, *42*, 5565–5569. (f) Krief, A.; Laval, A.-M. *Chem. Rev.* **1999**, *99*, 745–777. (g) Molander, G. A.; Harris, C. R. *Tetrahedron* **1998**, *54*, 3321–3354. (h) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307–338.

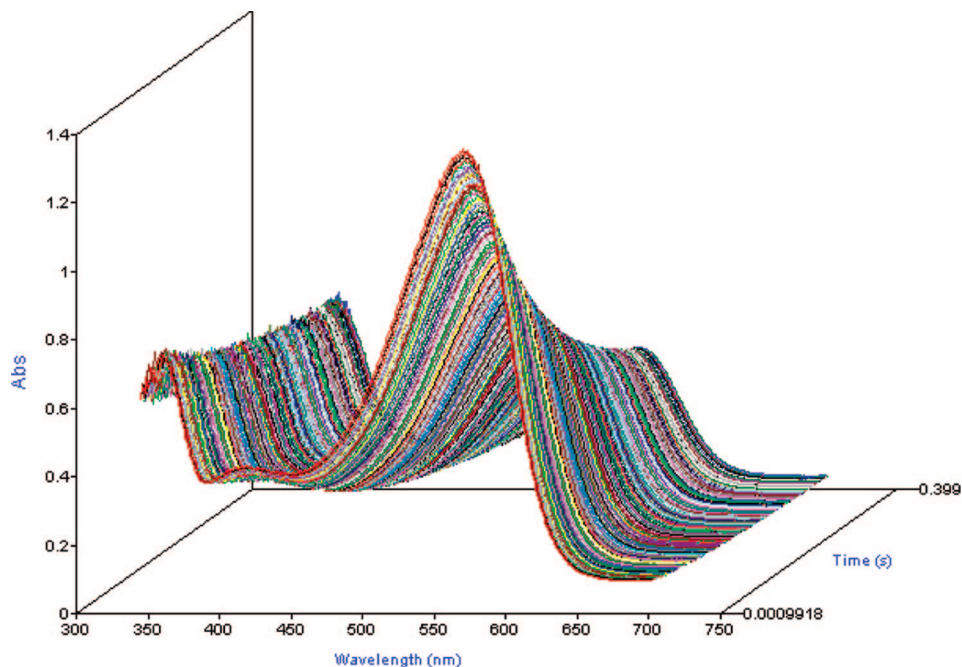


FIGURE 1. Diode array monitoring of the reaction of H radical anion (50 mM) with SmI₂ (2.5 mM).

TABLE 1. Second-Order Rate Constants for the Reaction of the Substituted Substrates (50 mM) with Various Concentrations of SmI₂

SmI ₂ mM	<i>k</i> ₃ (M ⁻¹ s ⁻¹)					
	DCl	Cl	H	DMe	DA	DMA
1.25	960	2400	4600	6010	1840	15760
2.5	480	1300	2673	2620	940	11950
5	140	533	842	1680	610	8760

conditions with large excesses of the benzophenone. Typically, the initial substrate concentration was 50 mM and that of the SmI₂ was 2.5 mM. After substituting the equilibrium constants of the reactions of eq 1 into the kinetic equations, the kinetic traces gave good correlation with second order in the concentration of the radical anion (eq 3, see, for example, Figure S1 in the Supporting Information).

$$\text{rate} = k_3[\text{radical anion}]^2 \quad (3)$$

We have also examined the kinetic order of SmI₂ in the reactions. The concentration of SmI₂ was varied between 1.25 to 5 mM. The data for the various substrates are given in Table 1 and in Figure 2 the log–log plot is given for H.⁶

As can be seen from the data in all cases, the kinetic order in SmI₂ is negative. We have encountered a negative order in SmI₂ previously, in the reactions of 1,1-diphenyl-2,2-dicyanoethylene.⁷ We believe that the origin of the phenomenon is the same for both substrates, namely, inhibition by free Sm³⁺. Because of the Coulomb repulsion between the two negatively charged

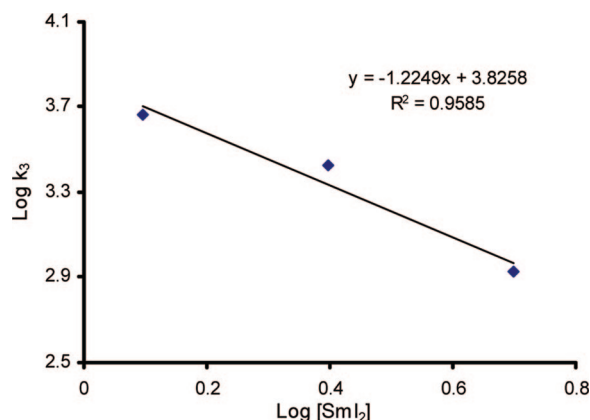


FIGURE 2. A log–log plot showing the negative order in the SmI₂ ([H] = 50 mM).

oxygen atoms in the radical anions, bridging by a di- or trivalent metal cation is essential for pinacol formation. It is well established in the literature that no coupling is observed when reduction of benzophenone is carried out under conditions yielding monovalent cations such as Na⁺.⁸ Since the radical anions and Sm³⁺ are highly paired, it is necessary that one of the two ion pairs which combine to give the pinacol shed its Sm³⁺I₂, namely, the reaction takes place between a paired radical anion and the minute amount of *free radical anion*. (This point will be somewhat modified later on in the discussion.) The free Sm³⁺ slows down the reaction by shifting backward the equilibrium of eq 4. Thus, reducing the amounts of free radical anion necessary for the coupling reaction (eq 5), leads to the negative order in SmI₂.

(2) (a) Chopade, P. R.; Prasad, E.; Flowers, R. A. *J. Am. Chem. Soc.* **2004**, *126*, 44–45. (b) Dahle'n, A.; Hilmersson, G. *Tetrahedron Lett.* **2002**, *43*, 7197–7200. (c) Prasad, E.; Flowers, R. A., II. *J. Am. Chem. Soc.* **2002**, *124*, 6357–6361. (d) Prasad, E.; Flowers, R. A. *J. Am. Chem. Soc.* **2002**, *124*, 6895–6899. (e) Enemaerke, R. J.; Hertz, T.; Skrydstrup, T.; Daasbjerg, K. *Chem. Eur. J.* **2000**, *6*, 3747–3754. (f) Miller, R. S.; Sealy, J. M.; Shabangi, M.; Kuhlman, L. M.; Fuchs, J. R.; Flowers, R. A. *J. Am. Chem. Soc.* **2000**, *122*, 7718–7722. (g) Molander, G. A.; Harris, C. R. *J. Am. Chem. Soc.* **1996**, *118*, 4059–4071. (h) Nomura, R.; Matsuno, T.; Endo, T. *J. Am. Chem. Soc.* **1996**, *118*, 11666–11667. (i) Kagan, H. B. *New J. Chem.* **1990**, *14*, 453. (j) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236–8246.

(3) Farran, H.; Hoz, S. *Org. Lett.* **2008**, *10*, 865–867.

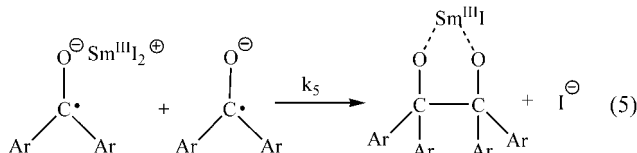
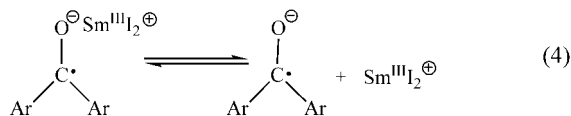
(4) Farran, H.; Hoz, S. *Org. Lett.* **2008**, *10*, 4875–4877.

(5) Kleiner, G.; Tarnopolsky, A.; Hoz, S. *Org. Lett.* **2005**, *7*, 4197–4200.

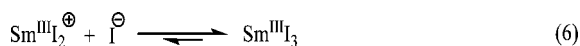
(6) The straight trend line drawn through the points is to enable the reader to get a feeling for the inhibitive effect. However, it is clear that it should not be linear over the whole range due to the equilibrium for the radical anion formation as is indeed the case for some of the other substrates.

(7) Tarnopolsky, A.; Hoz, S. *J. Am. Chem. Soc.* **2007**, *129*, 3402–3407.

(8) Bachmann, W. E. *J. Am. Chem. Soc.* **1933**, *55*, 1179–1188.



The total concentration of Sm³⁺ that is generated during the mixing time remains constant throughout the reaction. However, as the reaction progresses, and more pinacol dianion chelated to an Sm³⁺ is formed, the concentration of the free Sm³⁺ should increase and the inhibition should become more effective. Yet the fitting to a second order is very good throughout the whole reaction, implying that the concentration of the inhibitor remains nearly constant during the reaction. The equilibrium reaction that is responsible for maintaining a nearly constant concentration of Sm³⁺I₂ is probably its pairing with the I⁻ ion as shown in eq 6, and as shown in eq 5 the concentration of this ion increases with the formation of the pinacol dianion–Sm³⁺I⁻ chelate.



As mentioned before, these reactions were carried out with an excess of substrate. Using excess of SmI₂ we can control the concentration of Sm³⁺. Increasing the concentration of the substrate will increase the fraction of Sm³⁺ formed from the excess SmI₂. As a result, the inhibition will increase. In this case, the reaction will be zero order in the SmI₂ but will show a negative order for the substrate. As can be seen from Figure 3, the kinetic order in benzophenone is indeed negative, reflecting the indirect inhibition it causes by increasing the concentration of the inhibitor Sm³⁺I₂.

CHART 1

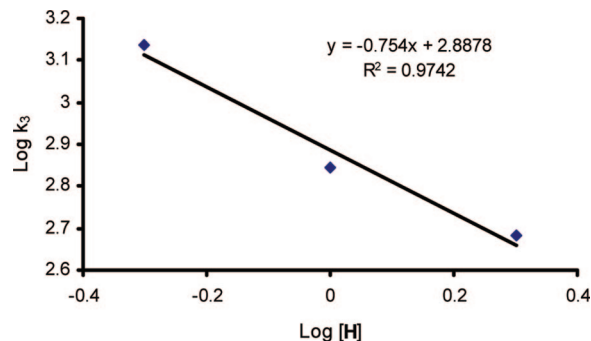
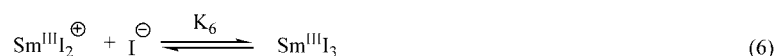
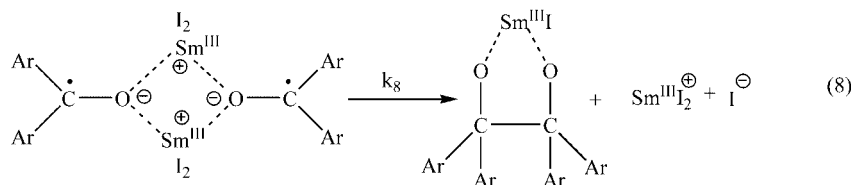
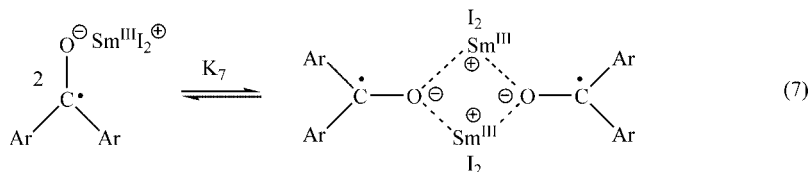
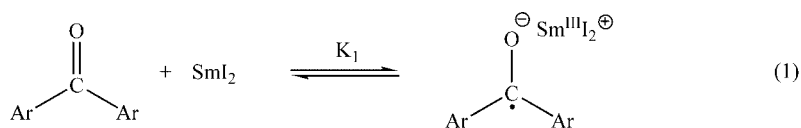


FIGURE 3. A log–log plot showing the negative order in H ([H] = 0.5, 1.0, 2.0 mM; [SmI₂] = 10 mM).

At this point we have to modify somewhat the reaction scheme. In the previous paper⁴ we have shown that the Coulombic interaction between the Sm³⁺ and the radical anion of benzophenones amounts to ca. 25 kcal/mol. This implies that the dissociation of Sm³⁺I₂ from an ion pair (eq 4) will be endothermic by ca. 25 kcal/mol. Evidently, in light of the fast rate of the reactions, a 25 kcal/mol hurdle cannot be a part of the reaction mechanistic scheme. We therefore suggest that the ion pairs aggregate to give dimers of the type suggested a long time ago by Streitwieser.⁹ Streitwieser had shown that the arrangement of four charges together leads to a significant electrostatic energy gain, especially in solvents of low polarity. It is reasonable to assume that the dissociation of Sm³⁺ from such a dimer is energetically much less costly. The suggested mechanism is given in Chart 1.

The first step is an electron transfer (eq 1). This is followed by the formation of the Streitwieser dimer (eq 7) from which, after dissociation of Sm³⁺, the product is obtained (eq 8). Concomitantly, the equilibrium described in eq 6 is established.

We have simulated this reaction scheme using the SPECFIT program¹⁰ for all the substrates and the concentrations used. The equilibrium constants for the electron transfer (eq 1) were

TABLE 2. Coupling Rate Constants for the Radical Anions of Substituted Benzophenones

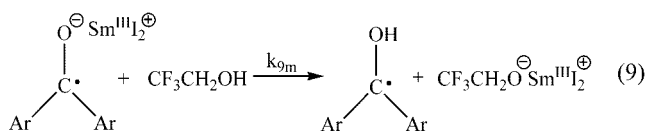
substrate	k_8 ($M^{-1} s^{-1}$)
DCl	19.4
Cl	35.4
H	62.6
DMe	125.6
DA	186
DMA	206.3

previously determined and were used in the simulation as constants. The equilibrium constants K_7 and K_6 and the rate constant k_8 were obtained from the simulation. The value of the equilibrium constant was practically independent of the substituents ($K_7 = 60 M^{-1}$). The equilibrium constant K_6 was found to be $10^4 M^{-1}$ and the values for k_8 are given in Table 2. A very good fit was obtained with the experimental data as shown in Figure 4 for the case of the unsubstituted substrate and in Figures S2–S6 in the Supporting Information for the other substrates.

Moreover, using the obtained rate and equilibrium constants and implementing different initial concentrations of SmI_2 , the negative order in SmI_2 was reconstructed for electron donating DA and electron withdrawing Cl derivatives (Figures S7 and S8 in the Supporting Information).

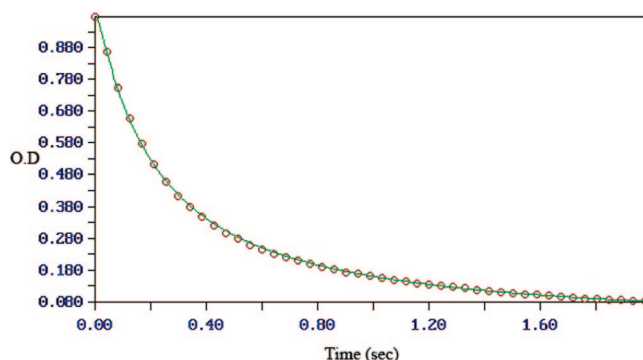
Shown in Figure 5 is the Hammett plot¹¹ for k_8 . The negative slope ($\rho = -0.91$) reflects the reduced amount of negative charge sensed by the substituents at the transition state of the coupling reaction.

When the reactions were carried out in the presence of trifluoroethanol (TFE), two regimes could be discerned. At low concentrations of TFE, the reaction is second order in the radical anion reflecting the dimerization reaction. As the concentration of TFE increases (>50 mM), the reaction kinetics approach more first order in the radical anion (no dimerization at the radical anion level) and first order in the TFE. Unlike the reactions in the absence of TFE, the reaction is now of zero order (not negative) in SmI_2 since there is no need to bridge between two radical anions and get rid of one Sm^{3+} prior to their coupling. Moreover, the presence of the Sm^{3+} in the vicinity of the radical anion is rather essential to stabilize the incipient alkoxide generated in the course of the protonation. Since trifluoroethoxide is harder than the radical anion, its interaction with the hard Sm^{3+} further enhances the reaction.^{3,7} A refined model must involve protonation on the ion pair as well as on the Streitwieser dimer (eqs 9 and 10).

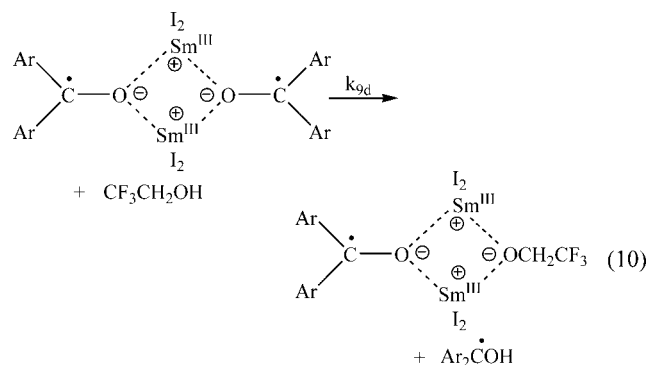


By using the equilibrium constant for the Streitwieser dimer formation previously determined, SPECFIT analysis results in protonation rate constants for the two protonation reactions (Table 3).

As can be seen from the table, the dimer protonation rate constant is ca. an order of magnitude larger than that of the mono ion pair. A reasonable explanation of that is based on the assumption that a correlation exists between the kinetics and the thermodynamics¹² of the protonation reaction. In the protonation of the dimer, the trifluoroalkoxide ion replaces a benzophenone radical anion moiety in the dimer. Since the

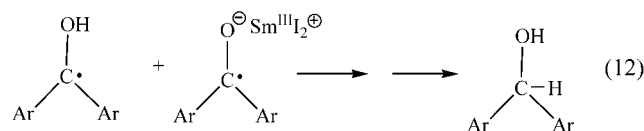
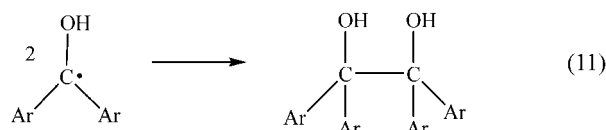
**FIGURE 4.** Reaction of H (50 mM) with SmI_2 (1.25 mM). Points are experimental and the line is SPECFIT results based on the reaction scheme shown in Chart 1.**TABLE 3. Rate Constants for Protonation of the Monomeric and Dimeric Radical Anions of the Substituted Benzophenones**

substrate	k_{9m} ($M^{-1} s^{-1}$)	k_{9d} ($M^{-1} s^{-1}$)
DCl	97	1119
Cl	197	1824
H	375	2404
DMe	574	7000
DA	706	12000
DMA	1200	14923



negative charge is very localized on the alkoxide oxygen whereas it is highly delocalized in the benzophenone radical anion, it is reasonable to assume that the exchange of the two will increase the stability of the new Streitwieser dimer. Partial expression of this stabilization at the transition state is probably responsible for the lower barrier to the protonation of the dimer relative to that of the monomer.

Following the protonation step could either be a radical coupling to produce pinacol (eq 11) and/or electron transfer from another radical anion (in the excess of substrate or from SmI_2 in the case of excess SmI_2) followed by a second protonation (eq 12).



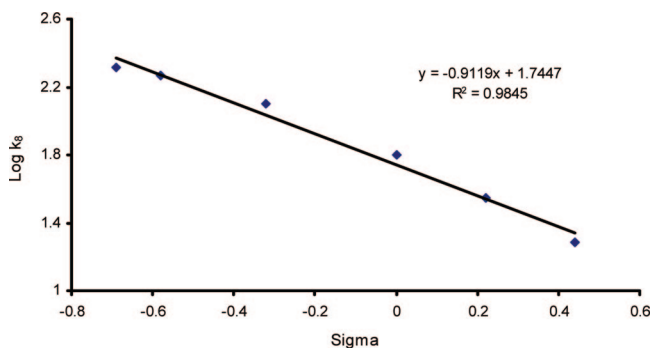


FIGURE 5. Hammett plot for the coupling of the radical anions of substituted benzophenones.

Either of these processes, as a rate-determining step, would imply a second order in the radical anion. The fact that the kinetic order in the radical anion is 1 implies that the first protonation is the rate-determining step. It should be noted that in the presence of TFE, large amounts of pinacol are obtained. The reason for it is that large amounts of the radical anion are converted over a short period of time to the corresponding radical. As a result, the concentration of the radical anion available for the second electron transfer is reduced while the concentration of the radical for the bimolecular coupling increases.

The ρ value for the protonation step k_{9m} is -0.86 (Figure 6) and that for the protonation of the Streitwieser dimer is -1.0 (Figure S9 in the Supporting Information).

This is a relatively small value especially in light of the fact that the negative charge is completely annihilated in this step unlike the case in the coupling reaction where the molecules remain charged ($\rho = -0.91$). However, the location of the transition state along the reaction coordinate may also affect the ρ value. In addition, in the ground state, the radical anions are probably highly paired to the samarium cations and therefore the change in the negative charge sensed by the substituents is not so large.

Summary and Conclusions

The instantaneous reaction of SmI₂ with benzophenones enabled us to investigate the post electron transfer events. We

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(10) SPECFIT Global Analysis System (v. 2.11, Spectrum Software Associates).

(11) Hammett, L. P. *Physical Organic Chemistry*; McGraw-Hill: London, UK, 1970; Chapter 11.

(12) Leffler, J. E.; Grunwald, E. *Rates and Equilibria of Organic Reactions*; Wiley: New York, 1963.

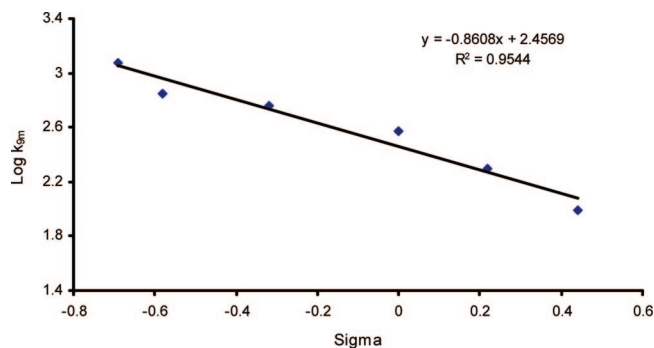


FIGURE 6. Hammett plot for the protonation of the radical anion monomer k_{9m} by TFE.

suggest that the radical anion of benzophenone, which is highly paired to Sm³⁺I₂, exists either as a monomer or as a Streitwieser dimer, which gains its stability from the interactions between two pairs of charges. The radical anions undergo two processes: coupling in the absence of proton donor and protonation in its presence. The protonation takes place on the dimer at a rate that is about an order of magnitude larger than that on the monomer. For all three processes, the ρ value is around -1 , which probably reflects the discontinuation of the negative charge delocalization onto the aromatic rings at the radical anion level.

Experimental Section

THF was refluxed over Na wire with benzophenone and distilled under argon. Water content was determined to be lower than 20 ppm. All substrates are commercially available and were recrystallized from petroleum ether. SmI₂ was diluted as needed from a 0.1 M commercial THF solution. The concentration of the SmI₂ solution was spectroscopically determined ($\lambda = 615$ nm; $\epsilon = 635$). The kinetics of the reactions was followed with a stopped flow spectrophotometer in a glovebox under nitrogen atmosphere. The reactions were monitored at the λ_{max} of the radical anions. In cases where a proton donor was used, the proton donor was mixed with the substrate solution. At the end of each series, the first measurement was repeated to ensure reproducibility within a set. The deviation usually did not exceed 8%. The kinetics were analyzed by using KinetAsyst (v. 2.2 Hi-Tech Ltd.) and the SPECFIT Global Analysis System (v. 2.11, Spectrum Software Associates).¹⁰ See details in the Supporting Information.

Supporting Information Available: SPECFIT analysis protocol. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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