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Guidelines for the Use of Proton Donors in SmI_2 Reactions: Reduction of α-Cyanostilbene

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Abstract: The reduction of a series of α-cyanostilbenes with SmI_2 was studied in THF in the presence of various proton donors. No reaction occurred in the presence of the alcohols TFE, *i*-PrOH and *t*-BuOH. In the presence of MeOH, water and ethylene glycol the reactions occurred; however in the presence of water and ethylene glycol they were too fast for kinetic determinations ($\tau_{1/2} < 1$ ms). Reactions with MeOH were first order in SmI_2 and first order in the substrate. The order in MeOH varies as a function of its concentration and the plot of log k vs log [MeOH] is sigmoidal. Comparison of the kinetic isotope effect and the incorporation isotope effect suggests that, counterintuitively, protonation of the radical anion takes place on the carbon β to the cyano group. It is concluded that proton donors that form complexes with SmI_2 expand the range of substrates that can be reduced by SmI_2. This is due to their proximity to the radical anion as it is formed. This short-lived radical anion cannot be efficiently trapped by a proton donor from the bulk medium. A protocol is herein suggested as to when proton donors which complex to SmI_2, e.g. MeOH, water and ethyleneglycol should be used, and when it is recommended to use noncomplexing proton donors, e.g. TFE, *i*-PrOH and *t*-BuOH, to induce reaction.

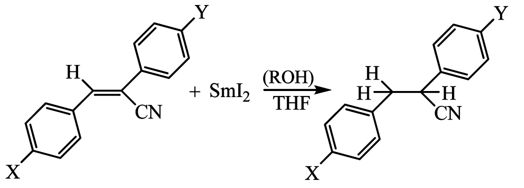
Introduction

There is no doubt that SmI_2 is one of the most versatile reducing agents in organic chemistry.[1] Its major advantages are that it is a mild reagent, can be solubilized in a variety of solvents and coordinates effectively a variety of cosolvents and additives. The reactivity scope of SmI_2 reductions is governed largely by the additives used.[2] In many cases, it is essential to add a proton source to the reaction mixture. In the present paper we show that the identity of the proton donor is critical to the synthetic outcome of the reduction. It is suggested that proton donors should be classified into two categories: those which form complexes with SmI_2, and those that do not. Glycols,[3,1d] MeOH[4] and water[5,4b,f] exemplify the first group; whereas EtOH, *t*-BuOH and TFE are examples of the second.

Regarding the first group, since ethylene glycol and water accelerated our model reaction beyond our measuring capabilities, we focused on MeOH as our proton donor. We show that this additive can expand the activity scope of SmI_2 to substrates which could not be reduced by a combination of SmI_2 and proton donors of the second category, and (with the exception of water) that this is *not* the outcome of an increase in the reduction potential of SmI_2. We also suggest that using the "wrong" class of proton donors may lead to the formation of an undesired product. Thus, in case of doubt, a representative proton donor of each category should be used followed by fine-tuning within the group.

Results and Discussion

The reduction of a series of α-cyanostilbenes with SmI_2 was studied in THF (eq 1) in the presence and absence of proton donors.



(1)

1: X=H, Y=H
MeO-1: X=MeO, Y=H
1-OMe: X=H, Y=MeO
Cl-1: X=Cl, Y=H
1-Cl: X=H, Y=Cl
Cl-1-Cl: X=Cl, Y=Cl

The reactions were followed using a stopped flow spectrophotometer under a nitrogen atmosphere. The reactions were examined under pseudo first order conditions using an excess of substrate or an excess of SmI_2. In the first case the reactions were followed at the λ_{max} of the SmI_2 (618 nm) or its complex with MeOH at 590 nm and in the second case at the λ_{max} of the substrate (315 nm-340 nm). In the presence of the alcohols trifluoroethanol (TFE), *i*-PrOH and *t*-BuOH at concentrations of up to 3.25M, no reaction was observed even after 2000 s. However, in the presence of 3 M MeOH, product isolation studies showed a practically complete conversion of the substrate

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

(2) (a) Flowers, R. A., II. *Synlett* **2008**, 1427–1439. (b) Dahlen, A.; Hilmersson, G. *Eur. J. Inorg. Chem.* **2004**, 3393–3403.

(3) (a) Vestergren, M.; Gustafsson, B.; Johansson, A.; Håkansson, M. *J. Organomet. Chem.* **2004**, *689*, 1723–1733. (b) Dahlen, A.; Hilmersson, G. *Tetrahedron Lett.* **2001**, *42*, 5565–5569. (c) Yoshida, A.; Manamoto, T.; Inanaga, J.; Mikami, K. *Tetrahedron Lett.* **1998**, *39*, 1777–1780.

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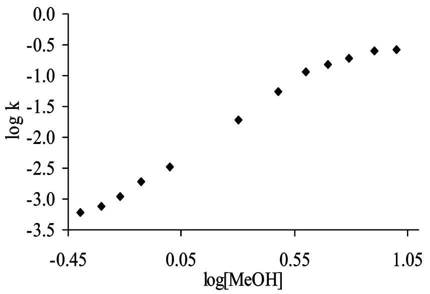


Figure 1. A plot of log k as a function of log [MeOH] for the reaction of **1** (25 mM) with SmI$_2$ (2.5 mM).

Table 1. Second Order Rate Constants in the Presence of MeOH (2 M)

substrate	1	MeO-1	1-OMe	Cl-1	1-Cl	Cl-1-Cl
k(M^{-1}s^{-1})	0.74	0.063	0.185	4.64	4.75	38.5

to the reduced product (eq 1) within 20 s at room temperature. It should be noted that, of the four alcohols used, TFE is the most acidic,[6] yet MeOH is the only alcohol which complexes appreciably to SmI$_2$.[7]

In all cases, the reactions were first order in SmI$_2$ or its complex with MeOH and first order in the substrate. The order in MeOH varies as a function of its concentration and the plot of log k vs log [MeOH] is sigmoidal as shown for example for the reaction of **1** (Figure 1).

The chlorinated substrates were too reactive to enable the measurement of their rate constants at high concentration of MeOH. As a result, the upper plateau could not be reached. The first order rate constants are given in the Supporting Information section. Usually the kinetic measurements were repeated three times, and the error in the rate constants is in the range of 4−10%. Second order rate constants are given in Table 1. These were determined at [MeOH] = 2 M, a concentration which enabled convenient rate measurements for all the substrates.

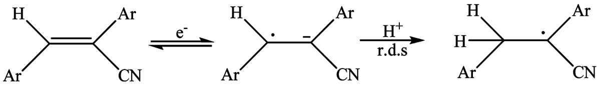
Table 2. Kinetic H/D Isotope Effects

substrate	1	MeO-1	1-MeO	Cl-1	1-Cl
k_H/k_D	6.6 ± 0.2[a]	6.6 ± 0.6[b]	6.4	7.6 ± 0.2[b]	6

[a] Average of 9 experiments. [b] Average of 4 experiments.

The aforementioned sigmoidal plots, as well as the fact that proton donors that do not complex with SmI$_2$ do not induce a reaction, indicate that the SmI$_2$−MeOH complex is vital for these reactions. The enabling of the reaction by this complex could be due either to an increase in the reduction potential of SmI$_2$ or to efficient trapping of a minute amount of radical anion formed. The first cause is a viable option since it was shown by Flowers et al. that water complexation to SmI$_2$ increases the reduction potential of SmI$_2$ from −1.33 V to −1.9 V.[8] It is conceivable that MeOH may also act in the same manner although tetraglyme complexation to SmI$_2$ has been reported not to affect the SmI$_2$ reduction potential.[9] Based on our results (below) we suggest that an efficient trapping of the radical anion by protonation is the cause of the reaction. The H/D kinetic isotope effect obtained in our reactions (Table 2) show that protonation is involved in the rate controlling step.

The large kinetic isotope effect indicates that proton transfer is rate determining. Assuming the classical Birch reduction[10] mechanism of the sequence electron, proton, electron, proton transfer steps, the rate determining step could be either the first or the second protonation. Since the second protonation comes after two electron transfer steps, if rate determining, it dictates second order kinetics in SmI$_2$. Since the kinetics are first order in SmI$_2$, the first protonation has to be the rate determining step as shown in eq 2.



(2)

If the only role of MeOH in inducing reduction were limited to enhancing the electron transfer step by increasing the reduction potential of the SmI$_2$ complex, then addition of TFE along with MeOH should speed the reaction by enhancing the protonation rate of the radical anion by TFE from the bulk medium (since TFE is significantly more acidic than MeOH). However, experiments performed with **1** in the presence of 3 M MeOH showed that addition of 1.7 M TFE did not affect the reaction rate. It must therefore be concluded that the MeOH in the complex is the protonating agent.[11]

The rate equation should therefore be (eq 3)

$$\text{rate} = k[\text{substrate}][\text{SmI}_2(\text{MeOH})_n] \qquad (3)$$

This equation is somewhat simplified, since at any given concentration of MeOH there is a range of SmI$_2$−MeOH complexes and "n" in the equation may acquire values of 1, 2, 3, ... The contribution of each complex to the reaction will depend on its concentration and rate constant. Complex composition is expected to be more homogeneous at the initial and final plateau zones.

Hence, the mechanism of the reaction is as follows: electron transfer from the SmI$_2$(MeOH)$_n$ to the substrate followed by protonation of the radical anion by the MeOH from within the ion pair.

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(4) (a) Tarnopolsky, A.; Hoz, S. *J. Am. Chem. Soc.* **2007**, *129*, 3402–3407. (b) Tarnopolsky, A.; Hoz, S. *J. Org. Biomol. Chem.* **2007**, *5*, 3801–3804. (c) Kleiner, G.; Tarnopolsky, A.; Hoz, S. *Org. Lett.* **2005**, *7*, 4197–4200. (d) Chopade, P. R.; Davis, T. A.; Prasad, E.; Flowers, R. A., II. *Org. Lett.* **2004**, *6*, 2685–2688. (e) Edmonds, D. J.; Muir, K. W.; Procter, D. J. *J. Org. Chem.* **2003**, *68*, 3190–3198. (f) Keck, G E.; Wager, C. A.; Sell, T.; Wager, T. T. *J. Org. Chem.* **1999**, *64*, 2172–2173. (g) Yacovan, A.; Bilkis, I.; Hoz, S. *J. Am. Chem. Soc.* **1996**, *118*, 261–262. (h) Hasegawa, E.; Takahashi, M.; Horaguchi, T. *Tetrahedron Lett.* **1995**, *36*, 5215–5218. (i) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236–8246.

(5) (a) Chopade, P. R.; Prasad, E.; Flowers, R. A., II. *J. Am. Chem. Soc.* **2004**, *126*, 44–45. (b) Dahlén, A.; Hilmersson, G.; Knettle, B. W.; Flowers, R. A., II. *J. Org. Chem.* **2003**, *68*, 4870–4875. (c) Hasegawa, E.; Curran, D. P. *J. Org. Chem.* **1993**, *58*, 5008–5010. It should be noted that water is also a critical component of the SmI$_2$/water/amine reducing system developed by Hilmersson and co-workers. Dahln, A.; Nilsson, A.; Hilmersson, G. *J. Org. Chem.* **2006**, *71*, 1576–1580. Dahln, A.; Hilmersson, G. *J. Am. Chem. Soc.* **2005**, *127*, 8340–8347. Dahln, A.; Hilmersson, G. *Chem.−Eur. J.* **2003**, *9*, 1123–1128.

(6) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456–463.

(7) Complexation is evident from the change in the spectrum of SmI$_2$. None of the other alcohols affect its spectrum (see refs 3−5). However, other alcohols may also complex to SmI$_2$ although not to they same extent. It is reasonable to assume that the order of complexation would be a function of the steric size of R in ROH. e.g. EtOH > *i*-PrOH > *t*-BuOH.

(8) Prasad, E.; Flowers, R. A., II. *J. Am. Chem. Soc.* **2005**, *127*, 18093–18099.

(9) Pedersen, H. L.; Christensen, T. B.; Enemærke, R. J.; Daasbjerg, K.; Skrydstrup, T. *Eur. J. Org. Chem.* **1999**, 565–572.

(10) (a) Dryden, H. L.; Webber, G. M.; Burtner, R. R.; Cella, J. A. *J. Org. Chem.* **1961**, *26*, 3237–3245. (b) Allinger, N. L.; Cava, M. P.; DeJonj, D.; Johnson, C. R.; Lebel, N. A.; Stevens, C. L. *Organic Chemistry*; Worth Publishing: New York, 1973; p 382.

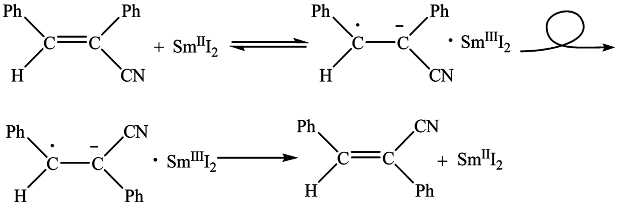
(11) The upper plateau in Figure 1 signifies that MeOH from the bulk medium is not protonating the radical anion.

The question to be answered at this stage is: why does MeOH promote the reaction whereas the other alcohols fail to do so. We assume that the reason is the following. The radical anion generated in the first step has a short lifetime before it reverts back to SmI_2 and the neutral substrate. Because of this short lifetime, the probability of an encounter between this short-lived radical anion and a proton donor coming from the bulk solution is very low. The advantage of MeOH is that "riding on the back" of the samarium it resides in the close proximity of this short-lived radical anion and can efficiently trap it. The importance of the proximity on reaction rates is self-evident and is also well documented in the literature, mainly by the work of Mandolini,[12] who reported effective molarities as high as 10^6.

A variation of this stepwise mechanism is a coupled electron−proton transfer reaction. That is, the electron transfer from SmI_2 and the proton transfer from an accompanying Sm-complexed MeOH molecule may merge into a single step.[13] Formally, the samarium methanol complex thus transfers the equivalent of a hydrogen radical to the substrate. In order to account for this possibility we reacted the cis isomer of **1** with SmI_2. It was assumed that the cis isomer of **1** could be used as a probe for the existence of a distinct electron transfer if its isomerization to the more stable trans isomer is significantly faster than the back electron transfer to the Sm^{3+}. The preparation of the cis isomer of **1** was achieved by simply exposing a trans isomer solution in benzene to sunlight for several days.[14] Equilibrium was reached at about 84% conversion. Since various attempts to reach a much higher purity of the cis isomer were not successful, the mixture of the two isomers, after the evaporation of the benzene, was used in the following experiments.

In the first experiment we reacted the cis−trans mixture (12 mM, 5.25:1 respectively) with SmI_2 (17 mM) in the absence of any proton source for 100 s, following which the reaction mixture was quenched and analyzed. NMR analysis showed that the composition changed to 50% cis and 50% trans. After 1000 s reaction, the cis isomer vanished and only the trans isomer was observed. In another experiment, a catalytic amount of SmI_2 (1.6 mM) was added to the mixture of the isomers (8 mM) in THF and the analysis performed after 1000 s revealed a mixture of 50% cis and 50% trans.

The isomerization apparently follows the sequence of steps shown in eq 4.



(4)

In order to show that the cis isomer could serve as a good model for the trans isomer in terms of electron acceptance, we determined the reduction potential of the two isomers using cyclic voltammetry. The cyclic voltammetry was performed using platinum mesh counter electrodes, platinum wire working electrodes, and ribbon of lithium metal reference electrodes. The electrolyte used was NBu_4PF_6 (0.2 M) + NBu_4I (0.02 M), and the sweep rate was 0.02 V s^{-1}. The two voltammograms are shown in Figure 2.

The reduction potential of the cis isomer (in the equilibrium mixture described above) was 1.339 V, and that of the trans isomer was nearly the same (1.309 V). This shows that the cis isomer could indeed serve as a good model for the trans isomer.

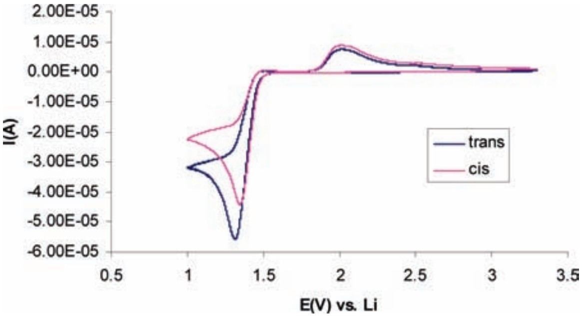


Figure 2. CV of cis and trans isomers of **1** in scan rate of 20 mV/s.

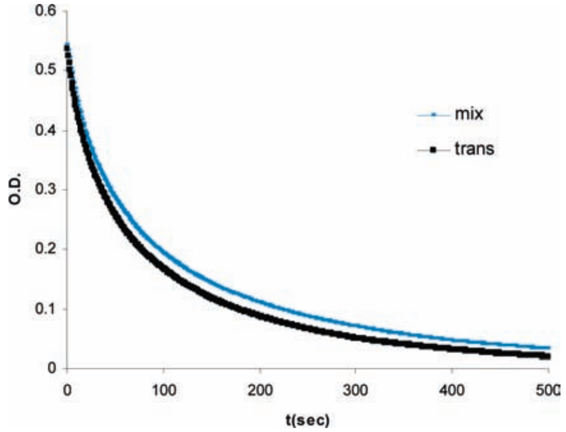


Figure 3. Kinetic traces at 590 nm for the reaction of the mixture of isomers of **1** and of the pure trans isomer (5 mM), SmI_2 7.5 mM and MeOH (3 M).

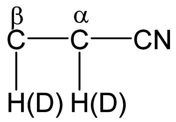
The similarity of the two isomers of **1** is evidenced also by a comparison of the reduction rates of the mixture containing mostly the cis isomer with that of the pure trans isomer. The kinetic traces are shown in Figure 3.

Based on the above it would seem that the coupled mechanism is not likely although it cannot be totally excluded.

We will focus now on the protonation site. It will be shown that the first protonation site is as depicted in eq 2, although this may be counterintuitive. As mentioned above, the reactions display a significant kinetic H/D isotope effect. In addition we have also determined the incorporation isotope effect at the positions α and β to the cyano group. This was facilitated by the difference in the chemical shifts of these protons in the NMR. The incorporation ratio was determined in a competition experiment in which the reaction medium contained both MeOH and MeOD. A solution of **1** (25 mM) was allowed to react with SmI_2 (5 mM) in the presence of 3 M methanol with the composition ratio 9:1 MeOD:MeOH. The conditions were identical to those used in the determination of the kinetic isotope effect. The incorporation of H relative to D at the α and β positions was evaluated by NMR. The results of four experiments are depicted in Chart 1. The data show that at the carbon α to the cyano group the incorporation ratio was 4.5 ± 0.2 whereas at the β position it was 6.8 ± 0.6. The kinetic isotope effect at 3 M MeOH was 6.7 ± 0.3 suggesting that the rate determining protonation of the radical anion takes place at the β rather than at the α carbon.

This result seems to be counterintuitive since most organic chemist will draw the major resonance structure of the radical

Chart 1



Incorporation isotope effects H/D	6.0	4.3
	6.7	4.4
	7.2	4.6
	7.4	4.7
Atomic charges		
NBO	-0.25	-0.28
CHELPG	-0.35	-0.25

anion with the negative charge on the α carbon. Assuming protonation of the radical anion to be charged controlled, one would expect it to be on the α carbon. However, it turns out that protonation at the β carbon of radical anions is a rather general phenomenon. The radical anion of acrylonitrile generated by pulse radiolysis undergoes protonation at 77 K exclusively on the β carbon. At 300 K, protonation is believed to occur also at the α position.[15] Protonation occurs preferentially at the β carbon also in cases where the stabilizing function is not a cyano group. This is true for example for acrylic acids,[16] esters and amides,[17]although in this case the first and fast protonation was shown to be on the oxygen atom. This protonation is reversible, and a slow rate determining protonation takes place on the β carbon of the acrylates.[18]

In light of the contradistinction between the back of an envelope resonance structure approach which places the negative charge on the α carbon, and the observed β protonation, we have probed the charge distribution in the radical anion using the Gaussian suit of programs at the B3LYP/6-31+G* level.[19] The geometries and energy data are given in the Supporting Information. It should be kept in mind that atomic charges are not physical observables and the results depend on the computational method. In the present case, the data (see Chart 1) are somewhat inconclusive as NBO analysis showed similar charges on both carbons, whereas CHELPG localized more charge on the β carbon, in line with the observed protonation on the β carbon.

Supportive of the higher charge concentration on C_β is the substituent effect. The monosubstituted substrates can be divided into two groups one with X = H and the other with Y = H, with the unsubstituted substrate common to both. Hammett ρ value[20] for variation of substituents on the aromatic ring α to the cyano group is 2.7 whereas that for the β position is 3.7 (Figure 4) suggesting that charge density is indeed higher on the part remote from the cyano group. Thus, both the ρ values are in concert with the CHELPG analysis suggesting that the charge reside more heavily on the β carbon. It should be noted that two other factors may contribute to the β protonation: steric preference and product stability. It may be assumed that the Sm^{3+} ion interacts preferentially with the less hindered carbon. In previous work we have shown that this interaction with benzophenone radical anion amounts to ca. 25 kcal/mol.[21] This interaction will direct the electrophilic replacement of the Sm^{3+} by proton to the β position. *Ab initio* calculations of the two radicals shown below showed that the radical α to the cyano group (formed by protonation at the β-carbon) is more stable than its isomer by ca. 10 kcal/mol. Thus, if the transition state for the protonation reaction is not too early, product stability will also direct the protonation to the β position.

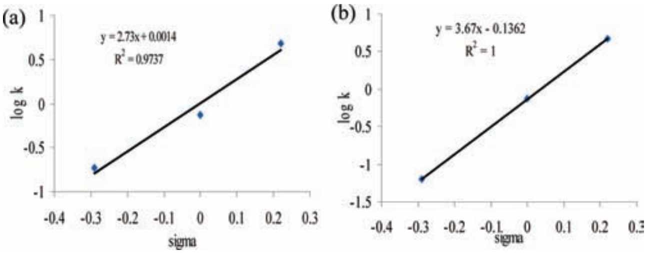
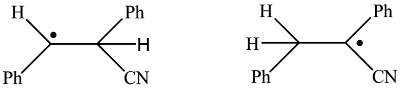


Figure 4. ρ values for variation of subsistent on the aromatic rings: (a) α to the cyano group; (b) β to the cyano group.



E = -633.53979 a. u.   E = -633.55527 a. u.

To sum up, the protonation at the β carbon could be the outcome of several sources: charge distribution, steric crowdedness and a late transition state which reflects the stability of the products.

Conclusions

In addition to the unexpected protonation site of the radical anion, the major conclusion of this study is that the range of substrates that react with SmI_2 can be expanded by using proton donors which complex efficiently to SmI_2. As a result of this complexation, the proton donor dwells, within the ion pair, in the proximity of the short-lived radical anion, and can therefore successfully trap it. On the other hand, the probability of the encounter of this short-lived radical anion with a proton donor from the bulk solution is rather low. Hence, the radical anion may revert quickly to the starting material with no reaction effected, as is the case with the series of substrates reported here. Thus, in syntheses involving substrates of low reduction potential, MeOH, ethylene glycol or water should be used as proton donors. However, these efficient proton donors should be avoided when it is necessary for the negative charge to react further.

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(12) (a) Mandolini, L. *Adv. Phys. Org. Chem.* **1986**, *22*, 1–111. (b) Illuminati, G.; Mandolini, L. *Acc. Chem. Res.* **1981**, *14*, 95–102. (c) Kirby, A. *J. Adv. Phys. Org. Chem.* **1980**, *17*, 183. (d) Illuminati, G.; Mandolini, L.; Masci, B. *J. Am. Chem. Soc.* **1977**, *99*, 6308–6312.

(13) (a) Irebo, T.; Reece, S. Y.; Daniel, M. S.; Nocera, G.; Hammarstrom, L. *J. Am. Chem. Soc.* **2007**, *129*, 15462–15464. (b) Fecenko, C. J.; Thorp, H. H.; Meyer, T. J. *J. Am. Chem. Soc.* **2007**, *129*, 15098–15099. (c) Meyer, T. J.; Huynh, M. V.; Thorp, H. H. *Angew. Chem., Int. Ed.* **2007**, *46*, 5284–5304. (d) Mayer, J. M. *Annu. Rev. Phys. Chem.* **2004**, *55*, 363–390. (e) Hammes-Schiffer, S. *Acc. Chem. Res.* **2001**, *34*, 273–281.

(14) Codington, J. F.; Mosettig, E. *J. Org. Chem.* **1952**, *17*, 1027–1034.

(15) Buxton, G. V.; Ellis, P. G.; McKillop, T. F. W. *J. Chem. Soc., Faraday Trans. 1* **1979**, *75*, 1050.

(16) Madhavan, V.; Lichtin, N. N.; Hayon, E. *J. Org. Chem.* **1976**, *41*, 2320.

(17) (a) Wojnárovits, L.; Takács, E.; Dajka, K.; D'Angelantonio, M.; Emmi, S. S. *Radiat. Phys. Chem.* **2001**, *60*, 337. (b) Madhavan, V.; Lichtin, N. N.; Hayon, E. *J. Am. Chem. Soc.* **1975**, *97*, 2989.

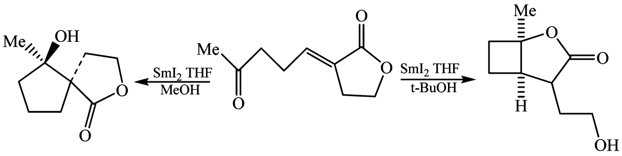
(18) The likelihood of protonation on a nitrile nitrogen is, in general, much smaller than on a lone pair of oxygen because of the difference in the lone pairs' energies. Moreover, protonation on a heteroatom does not display an H/D isotope effect (because of the Eigen mechanism). Thus, the large isotope effect observed in our case indicates that, even if a reversible protonation exists, it is a side reaction which is irrelevant to the major reaction path.

(19) Frisch, M. J.; et al. *Gaussian 03, Revision B.04* (see Supporting Information).

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

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

A beautiful demonstration of this principle is the elegant report of Procter et al.[22] describing a dramatic effect on the course of the reaction caused by changing the proton donor from MeOH to *t*-BuOH (eq 5).



(5)

The authors suggested that the formation of the cyclobutanol derivative involves the action of the negative charge of the radical anion. The spiro product would seem to be formed by protonation of the radical anion and further reduction to give an enolate. Thus, when a reaction involves a series of steps in which the negative charge participation is essential, such as the formation of the cyclobutanol derivative in eq 5, the use of MeOH will hamper the reaction. In such a case it is recommended to use a noncomplexing proton donor such as *t*-BuOH. On the other hand, using MeOH in the reaction will quench the negative end (by protonation) allowing further steps leading to spiro products. It should be clear that this is not a binary decision since between these two extremes there is a continuum. Thus, despite of the lack of spectroscopic evidence, EtOH could probably also complex SmI_2 to some extent and present an intermediate behavior.

Hence, for synthetic purposes, the knowledge of the mechanism will assist the chemist in choosing the suitable category of proton donor to be employed. In cases where the mechanism is not known, it may be worthwhile to try a representative donor from each group, e.g. MeOH vs *t*-BuOH followed by fine-tuning within the selected group. This fine-tuning should be carried out not only for the identification of the most suitable proton donor but also to determine its optimal concentration. In complexing proton donors, the latter has an important effect on the size of the coordination sphere of the SmI_2, which may in turn affect the rate and the course of the reaction.

Experimental Section

General. THF was dried and freshly distilled over Na wire + benzophenone under an argon atmosphere. TFE, *i*-PrOH, *t*-BuOH and MeOH were dried according to known procedures.[23] Water content was determined (K. F. Coulometer 652) to be lower than 20 ppm. SmI_2 was diluted as needed from a 0.1 M commercial THF solution. The concentration of the SmI_2 solution was spectroscopically determined ($\lambda = 615$ nm; $\varepsilon = 635$). The reactants and products were synthesized according to published procedures.[24] Products of the reduction are known compounds and were also synthsized.[25] Structures were confirmed by NMR and melting point determinations.

Kinetics. The kinetics of the reactions was followed using a stopped flow spectrophotometer in a glovebox under nitrogen atmosphere. The reactions were monitored at the λ_{max} of the complex $SmI_2(MeOH)_n$ or the substrate depending on the reaction conditions. In cases where a proton donor was used, the proton donor was first mixed with the substrate solution and then with the SmI_2. At the end of each series, the first measurement was repeated to ensure reproducibility within a set. The deviation usually did not exceed 10%. The kinetic measurements were repeated three times, and the error in the rate constants is in the range of 4−10%. The kinetics were analyzed by using KinetAsyst (v. 2.2 Hi-Tech Ltd.).

Reactions in the Presence of Water or Ethylene Glycol. Kinetic experiments using water or ethylene glycol as additives were too fast to be measured. Reaction between **1** (25 mM) and SmI_2 (2.5 mM) in the presence of 125 mM water was complete in less than 0.01 s. Reaction using the same conditions with ethylene glycol (12.5 mM) finished within 0.03 s.

Kinetic Isotope Effect. The kinetic isotope effect was determined by measuring reaction rate constants in the presence of MeOH and MeOD. All the reactions were performed in a glovebox under nitrogen. A solution of the substrates (25 Mm) was allowed to react with SmI_2 (2.5 mM) in the presence of MeOH or MeOD (3 M). Each experiment was repeated 4 or 9 times depending on the substrate.

Incorporation Isotope Effect. The incorporation ratio was determined in a competition experiment in which the reaction medium contained both MeOH and MeOD. A solution of **1** (25 mM) was allowed to react with SmI_2 (2.5 mM) in the presence of 3 M proton donor with the composition ratio 9:1 MeOD:MeOH. The conditions were identical to those used in the determination of the kinetic isotope effect. After 1000 s, the reaction mixture was quenched by I_2 and a few drops of sodium thiosulfate (0.1 N) were added to remove excess iodine. Water was added, and the solution was extracted with dichloromethane (25 mL × 3). The combined organic layer was washed with water (25 mL × 3) and brine, dried over $MgSO_4$, filtered and evaporated under vacuum. The residue was purified by column chromatography using CH_2Cl_2 as eluent.

The incorporation of H relative to D at the α and β positions was evaluated by NMR. ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 3.99$ (dd, $J = 6.6$, 8.4 Hz, $1H_\alpha$), $\delta = 3.19$ (dd, $J = 8.4$, 13.6 Hz, $1H_\beta$), $\delta = 3.14$ (dd, $J = 6.6$, 13.6 Hz, $1H_\beta$) ppm.

Cis Isomer of 1. The cis isomer of **1** was synthesized according to a published procedure[14] and was obtained as a mixture of 84% cis and 16% trans.

The cis−trans mixture (12 mM) was allowed to react with SmI_2 (17 mM) in the absence of any proton source for various lengths of time, after which the reaction mixture was quenched by I_2. The workup procedure was similar to the one described above, and the residue after evaporation was analyzed by NMR. (Trans isomer: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.33{-}8$ (m, 8H), 7.56 (s, $1H_{olef}$) ppm. Cis isomer: ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.16{-}7.33$ (m, 8H), 7.31 (s, $1H_{olef}$) ppm.) Mesitylene was used as an external standard.

In another experiment, a catalytic amount of SmI_2 (1.6 mM) was added to the mixture of the isomers (8 mM) in THF and the analysis performed after 1000 s.

Cyclic Voltammetry. We have determined the reduction potential of the cis and trans isomers using cyclic voltammetry. All experiments were carried out in a glovebox (M. Braun) under an argon atmosphere. Oxygen and moisture levels were below 5 ppm and 1 ppm, respectively. THF was dried using molecular sieve zeolite over a period of a few days. The electrochemical experiments were carried out in a standard three electrode cell, in which platinum wire, platinum mesh and a ribbon of lithium metal served as the working, counter and reference electrodes, respectively. The electrolyte used was NBu_4PF_6 (0.2 M) + NBu_4I (0.02 M). A solution of 2 mM potassium ferricyanide, $K_3Fe(CN)_6$, with 0.2 M NBu_4PF_6 was used to calibrate the reference electrode's potential. Cyclic voltammetry experiments were carried out using an Autolab potentiostat (Echochemie, The Netherlands), and the sweep rate was 0.02 V s^{-1}.

Supporting Information Available: First order rate constants for the reactions of substituted **1** (Tables S1−S6), complete ref 15, Gaussian archives for the computed structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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(22) Hutton, T. K.; Muir, K. W.; Procter, D. J. *Org. Lett.* **2003**, *5*, 4811–4814.

(23) Perrin, D. D.; Armarego, W. L. F. *Purification of laboratory chemicals*, 3rd ed.; Pergamon Press: New York, 1989.

(24) (a) Ladher, F.; Gharbi, R. E. *Synth. Commun.* **1991**, *21*, 413–417. (b) *Organic syntheses*; Collect. Vol. III; p 715.

(25) Kulp, S. S.; Caldwell, C. B. *J. Org. Chem.* **1980**, *45*, 171–173.