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Hydroxylated HMPA Enhances both Reduction Potential and Proton Donation in SmI_2 Reactions

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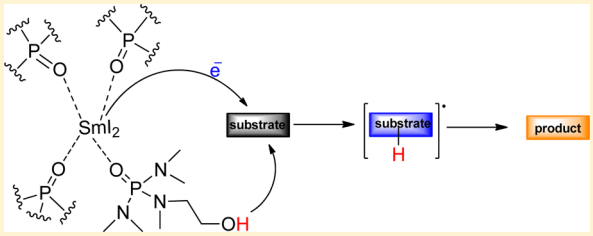
Supporting Information

ABSTRACT: HMPA is known to increase the reduction potential of SmI_2. However, in many cases, the transferred electron returns from the radical anion of the substrate back to the Sm^{3+}. This could be avoided by an efficient trapping of the radical anion: e.g., by protonation. However, bimolecular protonation by a proton donor from the bulk may be too slow to compete with the back electron transfer process. An efficient unimolecular protonation could be achieved by using a proton donor which complexes to SmI_2, in which case the proton is unimolecularly transferred within the ion pair. A derivative of HMPA in which one of the methyl groups was substituted by a CH_2CH_2OH unit was synthesized. Cyclic voltammetry studies have shown that it resembles HMPA in its ability to enhance the reduction potential of SmI_2, and reactivity studies show that it has also efficient proton shift capabilities. The various aspects of this additive were examined in the reactions of SmI_2 with three substrates: benzyl chloride, methyl cinnamate, and anthracene.

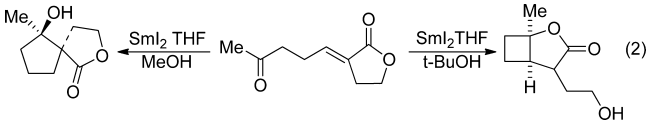


INTRODUCTION

Samarium iodide is one of the most useful reducing reagents employed in synthetic chemistry.[1,2] An important advantage of this reagent is that its reactivity and product distribution can be tuned and modulated by various additives.[3] A classical example is the use of MeOH in photocatalyzed reactions.[4] When SmI_2 is excited in the visible region, it becomes a much better reducing agent than it is in the ground state.[5] However, once the electron transfer takes place, the back electron transfer is highly exothermic because it produces Sm^{2+} in its ground state. Therefore, unless there is an efficient process competing with the back electron transfer, no net reaction will take place. Such a competing reaction is the mesolytic cleavage of alkyl halides (eq 1).

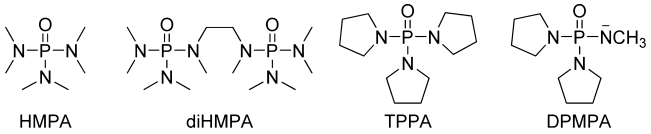
$$R{-}X + e^- \rightarrow R^{\bullet} + X^- \qquad (1)$$

We have shown that protonation of the radical anion could also compete with the back electron transfer, provided it is done unimolecularly.[4] Protonation of the highly unstable radical anion by a proton donor from the bulk is a bimolecular reaction. However, the lifetime of the radical anion is too short to enable such a protonation and, therefore, protonation cannot prevent the fast back electron transfer. However, if a proton donor such as MeOH is complexed to the SmI_2,[6] the protonation takes place unimolecularly within the ion pair efficiently, trapping the radical anion before it transfers its electron back to the Sm^{3+}. Using this strategy, we have broadened the range of photocatalyzed reduction to include substrates which previously were not amenable to photocatalytic reduction.[4] Another example is the work of Procter et al.,[7] in which MeOH and t-BuOH lead to different products (eq 2). We have suggested that the reason for this dissimilarity is that MeOH, in sharp contradistinction to t-BuOH, complexes



to SmI_2 and is, therefore, present in the vicinity of the radical anion as it is formed. Hence, in the first case, cyclization occurs at the radical level, whereas in the second case it is driven by the negative charge (because of the sluggishness of the bimolecular protonation), giving rise to a different cyclization product.

A second important additive is HMPA. The reduction potential of SmI_2 can be significantly boosted by complexing it with HMPA.[8] When four molecules of HMPA are complexed to SmI_2, its reduction potential is increased from −1.3 to −2.1 V, increasing significantly the range of substrates which can be reduced by this reagent.[9] Several derivatives of HMPA have been described in the literature. These include a dimer of HMPA (diHMPA)[10] and TPPA[11] as well as the anionic derivative DPMPA.[12]



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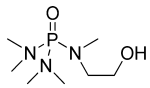
The last compound was recently successfully employed by Reissig[13] and was found to be better for γ-aryl ketone cyclizations.

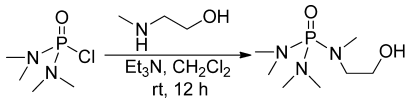
Thus, the additives HMPA and its derivatives and MeOH (or other ligands that complex to SmI_2 such as water and glycols) are both found to be very useful in SmI_2 reductions. Unfortunately, however, these additives compete with each other for the binding sites of SmI_2 and, as a result, they mutually reduce each other's efficiency. In this paper we report the effect obtained by the combination of these two functions into a single molecule. This molecule is a derivative of HMPA (HOMPA) in which, one of the NMe_2 units is replaced by *N*-methylethanolamine.



HOMPA

RESULTS AND DISCUSSION

HOMPA was synthesized (eq 3) following a synthesis similar to that in the literature.[14]



(3)

We have quantified its effect on the reduction potential of SmI_2 in two ways: (a) measuring its reduction potential by cyclic voltammetry and (b) measuring its effect on the reactivity of SmI_2 toward benzyl chloride. The latter was chosen because the cleavage of the C−Cl bond does not necessitate protonation; therefore, only the "HMPA like" properties are examined.[15]

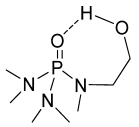
Cyclic voltammetry was performed under the following conditions: working electrode, glassy carbon; reference electrode, $Ag/AgNO_3$ in THF; counter electrode, Pt wire; electrolyte, 0.1 M tetrabutylammonium hexafluorophosphate; 2 mL electrochemical cell at a scan rate of 100 mV/s. The results are given in Table 1.

Table 1. Oxidation Potential of SmI_2 in THF in the Presence of Various Concentrations of HOMPA and HMPA[a]

[additive] (mM)	HOMPA (V)	HMPA (V)	HMPA[b] (V)
5	−1.15	−1.3	−1.46
10	−1.18	−2.05	−2.05
15	−1.42	−1.99	−2.05
20	−1.99	−2.08	

[a]$[SmI_2]$ = 2.5 mM. [b]Data from Flowers et al.[9]

We have also measured the reduction potential of HMPA itself in order to calibrate our results against the original data of Flowers. Table 1 shows that our measured potentials are in reasonable agreement with those reported by Flowers. The data show that HOMPA lags behind HMPA in enhancing the reduction potential of SmI_2 at low concentrations. However, at higher concentrations (20 mM; 8 equiv)[16] it exhibits a reduction potential close to that of HMPA. This suggests that HOMPA's complexation constant to SmI_2 is smaller than that of HMPA. However, once it occupies all the sites[17] it induces an effect similar to that of HMPA. The smaller complexation constant may be due to an internal hydrogen bond within HOMPA.



HOMPA with an internal H-bond

An additional experiment was performed in order to assess the origin of the increased reduction potential of the HOMPA−SmI_2 complex. We have found that this increase is most probably due to the fact that HOMPA complexes more strongly to the product Sm^{3+} than to Sm^{2+} in a way similar to that for HMPA.[18] Figure 1 shows the spectra of (a) SmI_2, (b) SmI_2 to which 2.5 mM of HOMPA was added, (c) SmI_2 to which 5 mM of HOMPA was added, and (d) the solution where to the composition presented in (c) 2.5 mM of SmI_3 was added. When HOMPA complexes to SmI_2, its spectrum is changed in a manner similar to that of the HMPA complex. Figure 1d shows clearly that, upon the addition of Sm^{3+}, the SmI_2 retains its original spectrum, indicating a stronger ligation of HOMPA to Sm^{3+} than to Sm^{2+}. This enhanced affinity for Sm^{3+} is probably the primary cause for the increased reduction potential.

Next, the kinetics of the reaction of SmI_2 with benzyl chloride in the presence of HOMPA were measured with HMPA as a reference point. As mentioned above, this reaction was chosen because its rate is independent of proton donor concentration and, therefore, reflects only the ability of complexed SmI_2 to donate an electron. In addition, it should be pointed out that Flowers has found that in the reduction of alkyl halides by SmI_2 a unique mechanism is operative.[19] That is, HMPA forms a complex with primary alkyl halides activating the C−X bond, thereby enhancing reaction rate. However, the early leveling off of the rate with respect to HMPA concentration described by Daasbjerg et al. for the reactions of benzyl chloride suggests that there is no such effect with benzyl chloride.[17]

In the reaction with benzyl chloride, its concentration was 25 mM, that of SmI_2 was 2.5 mM, and that of the additives ranged from 5 to 20 mM. At the low concentrations (5 and 10 mM) of HOMPA and HMPA, the reactions obeyed pseudo-first-order kinetics only for the first part of the reaction because the affinity of the two phosphoramides toward the Sm^{3+} generated in the first part is, as we have shown above, much higher than that to Sm^{2+}. Therefore, the ability of the SmI_2 to reduce the substrate was reduced as the reaction progressed, due to the diminishing concentrations of the chelating phosphoramides. First-order analysis was successfully conducted only on the first 40−70% of reaction for the two concentrations, respectively. Pseudo-first-order rate constants are given in Table 2. Kinetic traces are shown in the Figure S1 (Supporting Information).

Interestingly, in spite of the lack of linearity in the reduction potentials of SmI_2 between the two additives, the rate constants are linearly related (Figure 2).

The next substrate in our investigation was methyl cinnamate. It reacts very quickly, and the reduction is completed in less than 1 min. Methyl cinnamate was chosen in order to demonstrate the different effect the two additives have on the product distribution. In the preparative reactions we have used the following concentrations: methyl cinnamate, 0.04 M; SmI_2, 0.084 M, phosphoramide additives, 0.34 M each.

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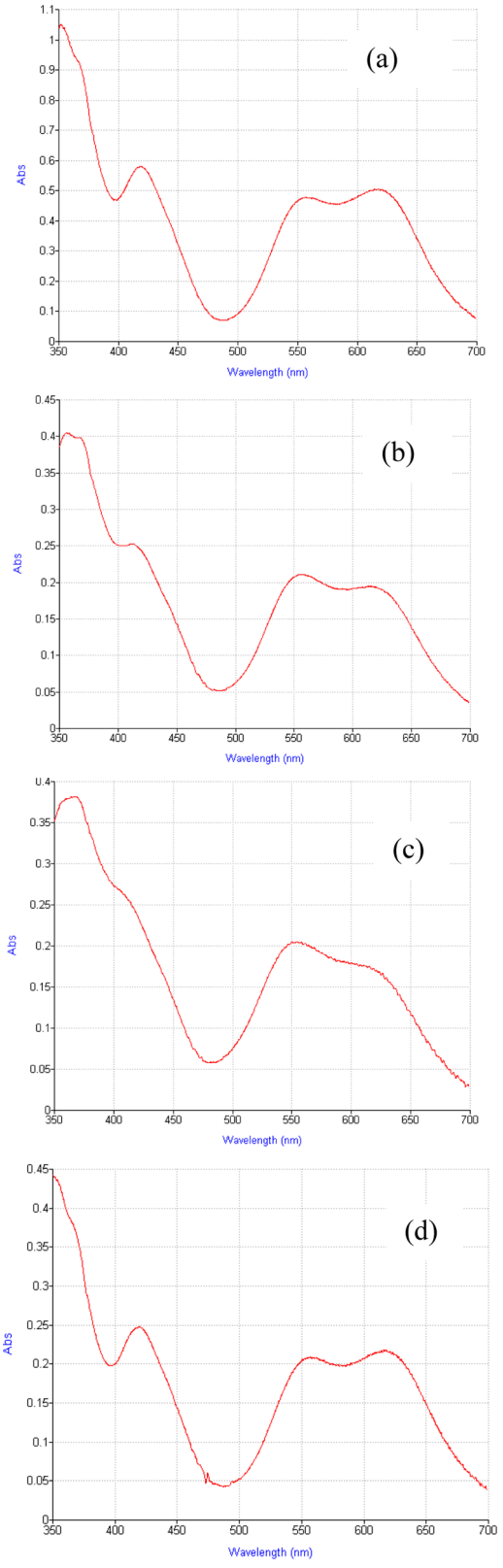


Figure 1. Visible spectra of (a) 5 mM SmI_2, (b) 2.5 mM SmI_2 + 2.5 mM HOMPA, (c) 2.5 mM SmI_2 + 5 mM HOMPA, and (d) 2.5 mM SmI_2 + 5 mM HOMPA + 2.5 mM SmI_3.

When MeOH was added to the reactions in the presence of HMPA, its concentration was 0.5 M. When only MeOH was used as a reference additive, its concentration was 2 M.

Table 2. Pseudo-First-Order Rate Constants for the Reactions of SmI_2 (2.5 mM) with Benzyl Chloride (25 mM) in the Presence of Various Concentrations of Phosphoramide Additives[a]

[phosphoramide] (mM)	k_{HOMPA} (s^{-1})	k_{HMPA} (s^{-1})
5	0.04	0.26
10	0.13	0.70
15	0.19	1.02
20	0.26	1.32

[a]The pseudo-first-order rate constant in the absence of phosphoramide is 0.0017 s^{-1}.

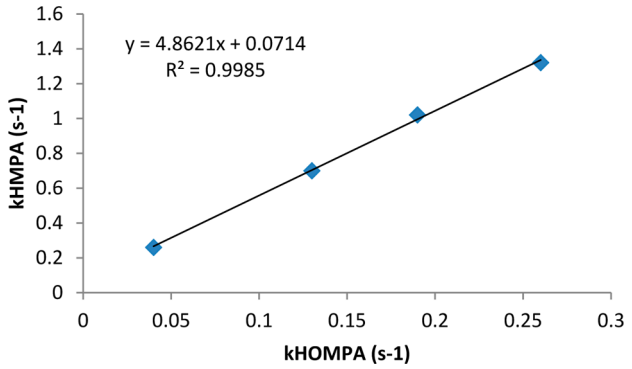
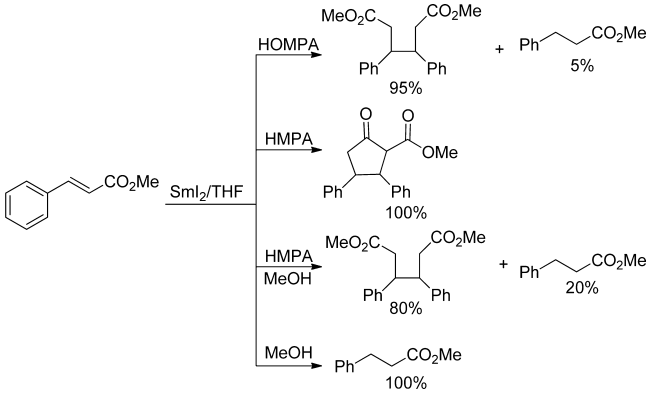


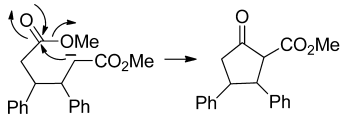
Figure 2. Plot of the pseudo-first-order rate constants for the reduction of benzyl chloride in the presence of HMPA as a function of the rate constants in the presence of HOMPA.

Scheme 1 shows the product distribution under each set of conditions used. As can be seen, the reactions of HOMPA and

Scheme 1



HMPA are entirely different. The cyclization reaction observed in the presence of HMPA is documented in the literature,[20] and its absence in the reaction with HOMPA is most probably due to the efficient protonation of the carbanion α to the ester group by the OH of HOMPA, thus preventing the cyclization step (eq 4).



(4)

The equivalence of HOMPA to the combination of HMPA and MeOH is evident from the similarity in their product

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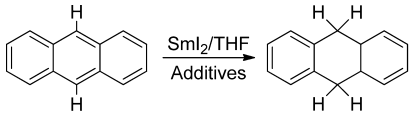
distributions, showing that HOMPA can fulfill both functions simultaneously. In the presence of only MeOH the reduced monomer was the sole product.

Because of its complexity, the reaction was not amenable to simple kinetic analysis. However, determination of the reaction half-life using stopped flow spectroscopy showed that under the conditions [methyl cinnamate] = 25 mM, [SmI_2] = 2.5 mM and [phosphoramide additives] = 10 mM each, the half-life for the HMPA in the presence of 0.5 M MeOH was 0.005 s, that for HMPA itself was 0.014 s, that for 0.5 M MeOH was 7.8 s, and for HOMPA the reaction was over in the dead time of the instrument (Figure S2, Supporting Information). Thus, although these reactions are relatively fast, that of HOMPA is faster than that of the combination of HMPA and MeOH.

The last substrate to be examined was anthracene. Unlike the case for methyl cinnamate, this substrate gives a single product, 9,10-dihydroanthracene (eq 5).

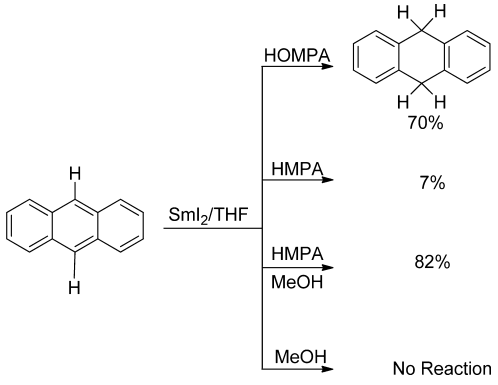


(5)

This substrate was used because, unlike the case for methyl cinnamate, trapping the radical anion and preventing the back electron transfer can be achieved only by protonation, whereas in the case of methyl cinnamate, dimerization may also prevent the back electron transfer. We therefore expect this case to be a good demonstration of the importance of the capabilities of HOMPA as a proton donor in a comparison with HMPA itself.

Scheme 2 shows the product distribution as a function of the added additive(s).

Scheme 2



Concentrations were the same as those used to generate the data of Scheme 1. Yields reported are NMR yields. All of the reactions were quenched with I_2 solution after 1 min. As can be seen, HOMPA yielded after 1 min ca. 70% of 9.10-dihydroanthracene, while HMPA yielded only 7% (probably due to a trace of water in the solution or to proton transfer from THF). The combination of HMPA and MeOH gave results similar to those of HOMPA, while MeOH did not enable any reaction. Thus, a comparison of the HOMPA reaction with that of MeOH shows HOMPA's ability to increase the reduction potential of SmI_2, and a comparison with the HMPA reaction demonstrates that it utilizes its ability to function as a proton donor.

It should be pointed out that HOMPA has a technical advantage over HMPA. Usually, because HMPA is highly soluble in many solvents, it is very difficult to get rid of in the course of the reaction workup. However, using water with sodium bicarbonate and ether in the workup leaves the organic ethereal solution free of HOMPA, which is quantitatively transferred to the aqueous phase. We found out that it is possible to recover it (60%) from the reaction mixture and reuse it without seriously affecting its efficacy. On the other hand, HOMPA has the disadvantage that, like other proton donors, it enhances the decay of SmI_2.[21]

In conclusion, HOMPA increases the reduction potential of SmI_2 and at the same time serves also as a proton donor. It competes effectively with the combination of HMPA and MeOH. To the best of our knowledge, there is no information regarding its carcinogenic[22] nature relative to that of HMPA.

EXPERIMENTAL SECTION

General Procedures. All reagents were purified prior to use following literature procedures.[23] All of the reactions were carried out in oven-dried glassware under a nitrogen or argon atmosphere using anhydrous solvents. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded at 400 and 700 MHz. Carbon nuclear magnetic resonance (^{13}C NMR) and phosphorus nuclear magnetic resonance (^{31}P) spectra were recorded at 100 MHz and at 175 and 162 MHz, respectively. Mass spectra (MS) were obtained using EI/CI mass spectrometers. SmI_2 solutions (0.1 M in THF) were prepared according to a reported procedure[24,25] and diluted as needed. The concentration of the SmI_2 solutions was determined by spectroscopic techniques (λ 619 nm; ε = 635). The reactions of SmI_2 with the various substrates were performed in volumetric flasks (10/20 mL) under a nitrogen atmosphere in the glovebox.

The cyclic voltammetry experiments were performed using a standard glassy-carbon electrode as a working electrode with Pt wire as an auxiliary electrode and silver/silver nitrate electrode as a reference electrode at a 100 mV/s scan rate. A 0.1 M solution of tetrabutylammonium hexafluorophosphate (NBu_4PF_6) in THF was used as electrolyte. The concentration of SmI_2 was 2.5 mM for all experiments.

The kinetics experiments were performed using a stopped-flow spectrophotometer inside the glovebox under a nitrogen atmosphere at room temperature. The reactions were monitored at the λ_{max} value of SmI_2 (619 nm). The additive and substrate were contained in one syringe, and the SmI_2 solution was contained in the other. Each set of experiments was repeated two to three times. Within a set, each measurement was 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 less than 5%. First-order kinetics were analyzed using Kinet Asyst (v. 2.2, Hi-Tech Ltd.).

Synthesis of HOMPA. To a solution of *N*-methylethanolamine (2.82 mL, 35.17 mmol) and triethylamine (6.6 mL, 46.9 mmol) in 20 mL of dry dichloromethane was slowly added *N*,*N*,*N*′,*N*′-tetramethylphosphorodiamidic chloride (3.47 mL, 23.45 mmol) at room temperature and the mixture was stirred for 12−14 h. After completion of the reaction as monitored by TLC (silica gel 60 F_{254} precoated plates), the reaction mixture was filtered to remove the triethylamine hydrochloride salt. The organic layer was washed with water and brine solution and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the crude reaction mixture was purified by column chromatography on silica gel (60−120 mesh) using 4% methanol in chloroform to afford 2.95 g of pure HOMPA (60% yield) as a colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.58−2.60 (m, 15H), 3.04−3.05 (m, 2H), 2.02 (br s, 2H), 4.62 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 33.89, 33.93, 36.21, 36.25, 52.2, 51.3, 59.0; ^{31}P NMR (162 MHz, $CDCl_3$) δ 28.4; HRMS (Q-TOF ESI positive mode) calcd 210.1371 for $C_7H_{21}N_3O_2P$, found 210.1369. For spectral data, see the Supporting Information.

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Reaction of Methyl Cinnamate and SmI_2 in the Presence of HOMPA. A solution of methyl cinnamate (32.4 mg, 0.04 M) in THF and HOMPA (355.7 mg, 0.34 M) was mixed in a volumetric flask inside the glovebox. Then 0.1 M SmI_2 in THF solution (4.2 mL, 0.084 M) was added to the reaction mixture. The total volume of the reaction mixture was 5 mL. There was immediate decolorization of the SmI_2 solution. Then the reaction mixture was diluted to 20 mL with diethyl ether and quenched with 5% aqueous $NaHCO_3$. The organic and aqueous layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 5.0 mL). The combined organic layer was washed with 5% aqueous phosphate buffer solution (2 × 5.0 mL) and brine solution (10 mL) and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the crude reaction mixture was analyzed by ^1H (400 MHz) and ^{13}C (100 MHz) NMR. The NMR data matched the data reported in the literature for the monomer and the dimer.[24] The ratio of dimer to monomer in the product mixture was 95:5.

Recovery of HOMPA from the Aqueous Layer. After the workup the aqueous layer was again extracted with 10% MeOH in $CHCl_3$ (3 × 10 mL) and the combined organic layer was washed with brine and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure the crude product (212.5 mg, 60% recovery) was analyzed by ^1H (400 MHz) and ^{13}C (100 MHz) NMR spectra.

Reaction of Methyl Cinnamate and SmI_2 in the Presence of HMPA. A solution of methyl cinnamate (129.7 mg, 0.04 M) in THF and HMPA (1.2 mL, 0.34 M) were mixed. Then 0.1 M SmI_2 in THF solution (16.8 mL, 0.084 M) was added to the reaction mixture. The total volume of the reaction mixture was 20 mL. The reaction was stopped after a given time, and the excess SmI_2 was quenched with iodine solution. The reaction mixture was then diluted to 40 mL with diethyl ether and quenched with 5% aqueous $NaHCO_3$ and 5% aqueous $Na_2S_2O_3$ solution. The organic and aqueous layers were separated, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic layer was washed with 5% aqueous phosphate buffer solution (2 × 10 mL) and brine solution (20 mL) and dried over anhydrous Na_2SO_4. After removal of the solvent under reduced pressure, the crude reaction mixture was purified by column chromatography on silica gel (60−120 mesh) using 10% ethyl acetate in petroleum to afford pure product (73.0 mg) in 62% yield as a white solid: mp 122−124 °C (lit.[26] mp 126 °C), analyzed by ^1H (700 MHz) and ^{13}C (175 MHz) NMR and mass spectra.

Reaction of Methyl Cinnamate and SmI_2 in the Presence of HMPA and MeOH. This reaction was performed with methyl cinnamate (129.7 mg, 0.04 M) in the presence of 0.1 M SmI_2 in THF solution (4.2 mL, 0.084 M), HMPA (0.3 mL, 0.34 M), and MeOH (0.1 mL, 0.5 M) as additive. The workup procedure was same as that mentioned above. The crude reaction mixture was analyzed by ^1H (400 MHz) and ^{13}C (100 MHz) NMR; it contained a mixture of dimer and monomer product in a ratio of 80:20.

Reaction of Methyl Cinnamate and SmI_2 in the Presence of MeOH. This reaction was performed with methyl cinnamate (129.7 mg, 0.04 M) in the presence of 0.1 M SmI_2 in THF solution (4.2 mL, 0.084 M) and MeOH (0.4 mL, 2.0 M) as additive. The workup procedure was same as that mentioned above. The crude reaction mixture was analyzed by ^1H (400 MHz) and ^{13}C (100 MHz) NMR. It contained only the monomer.

Reaction of Anthracene and SmI_2. The procedure was similar to that of the reactions of methyl cinnamate. The crude reaction mixture was analyzed by ^1H (400 MHz) and ^{13}C (100 MHz) NMR, and the analytical data of the product 9,10-dihydroanthracene matched the values reported in the literature.[27]

■ ASSOCIATED CONTENT

Supporting Information

Figures giving kinetic traces for the reactions of benzyl chloride and methyl cinnamate and spectral data for HOMPA. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ REFERENCES

(1) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693−2698.

(2) For some recent reviews, see: (a) Szostak, M.; Spain, M.; Procter, D. J. *Chem. Soc. Rev.* **2013**, *42*, 9155−9183. (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) Krief, A.; Laval, A.-M. *Chem. Rev.* **1999**, *99*, 745−777. (f) Molander, G. A.; Harris, C. R. *Tetrahedron* **1998**, *54*, 3321−3354. (g) Molander, G. A.; Harris, C. R. *Chem. Rev.* **1996**, *96*, 307−338.

(3) (a) Flowers, R. A., II. *Synlett* **2008**, *10*, 1427−1439. (b) Dahlén, A.; Hilmersson, G. *Eur. J. Inorg. Chem.* **2004**, 3393−3403.

(4) Amiel-Levy, M.; Hoz, S. *Chem. Eur. J.* **2010**, *16*, 805−809.

(5) Ogawa, A.; Ohya, S.; Hirao, T. *Chem. Lett.* **1997**, 275−276.

(6) Yacovan, A.; Bilkis, I.; Hoz, S. *J. Am. Chem. Soc.* **1996**, *118*, 261−262.

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

(8) Inanaga, J.; Ishikawa, M.; Yamaguchi, M. *Chem. Lett.* **1987**, 1485−1486.

(9) (a) Shabangi, M.; Flowers, R. A., II *Tetrahedron Lett.* **1997**, *38*, 1137−1140. (b) Enemærke, R. J.; Daasbjerg, K.; Skrydstrup, T. *Chem. Commun.* **1999**, 343−344.

(10) McDonald, C. E.; Ramsey, J. D.; Grant, J. A.; Howerter, K. A. *Tetrahedron Lett.* **2009**, *50*, 5308−5310.

(11) McDonald, C. E.; Ramsey, J. D.; Sampsell, D. G.; Butler, J. A.; Cecchini, M. R. *Org. Lett.* **2010**, *12*, 5178−5181.

(12) McDonald, C. E.; Ramsey, J. R.; Sampsell, D. G.; Anderson, L. A.; Krebs, J. E.; Smith, S. N. *Tetrahedron* **2013**, *69*, 2947−2953.

(13) Berndt, M.; Hölemann, A.; Niermann, A.; Bentz, C.; Zimmer, R.; Reissig, H.-U. *Eur. J. Org. Chem.* **2012**, 1299−1302.

(14) Du, D.-M.; Fang, T.; Xu, J.; Zhang, S.-W. *Org. Lett.* **2006**, *8*, 1327−1330.

(15) A similar approach was used by Flowers et al.: Teprovich, J. A., Jr.; Balili, M. N.; Pintauer, T.; Flowers, R. A., II *Angew. Chem.* **2007**, *46*, 8160−8163.

(16) It is important to note that the number of equivalents by itself is not a sufficient parameter and must be accompanied by the concentration of one of the components. The same number of equivalents may cause a near-saturation in complex formation at high concentrations but very little complexation for a very dilute reaction.

(17) These might be four or six; see: Enemaerke, R. J.; Hertz, T.; Skrydstrup, T.; Daasbjerg, K. *Chem. Eur. J.* **2000**, *6*, 3747−3754.

(18) Rao, C. N.; Hoz, S. *J. Am. Chem. Soc.* **2011**, *133*, 14795−14803.

(19) (a) Prasad, E.; Flowers, R. A., II *J. Am. Chem. Soc.* **2002**, *124*, 6895−6899. (b) Choquette, K. A.; Sadasivam, D. V.; Flowers, R. A., II *J. Am. Chem. Soc.* **2010**, *132*, 17396−17398.

(20) Shinohara, I.; Okue, M.; Yamada, Y.; Nagaoka, H. *Tetrahedron Lett.* **2003**, *44*, 4649−4652.

(21) It is well-known that SmI_2 has a natural decay. Therefore, in the commercial product the SmI_2 is stabilized with Sm metal flakes. This decay is enhanced in the presence of proton donors: Rao, C. N.; Hoz, S. *J. Org. Chem.* **2012**, *77*, 4029−4034. However, it should be noted that Matsukawa and Flowers managed to run the reaction of Sm^{2+} in water as a solvent: Matsukawa, S.; Hinakubo, Y. *Org. Lett.* **2003**, *5*, 1221−1223. Prasad, E.; Flowers, R. A., II *J. Am. Chem. Soc.* **2005**, *127*, 18093−18099.

(22) (a) Jackson, H.; Jones, A. R.; Cooper, E. R. A. *J. Reprod. Fert.* **1969**, *20*, 263−269. (b) Lee, K. P.; Trochimowicz, H. J. *J. Natl. Cancer Inst.* **1982**, *68*, 157−171. (c) Lo, C.-C.; Chao, P.-M. *J. Chem. Ecol.* **1990**, *16*, 3245−3253.

(23) Perrin, D. D.; Armarego, W. L. F. *Purification of Laboratory Chemicals*, 3rd ed.; Pergamon Press: New York, 1989.
(24) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693−2698.
(25) For the dimer: (a) Banik, B. K.; Venkatraman, M. S.; Banik, I.; Basu, M. K. *Tetrahedron Lett.* **2004**, *45*, 4737−4739. For the monomer: (b) Kleinke, A. S.; Jamison, T. F. *Org. Lett.* **2013**, *15*, 710−713.
(26) Nishiguchi, I.; Hirashima, T. *Angew. Chem., Int. Ed.* **1983**, *22*, 52−53.
(27) Nandi, P.; Dye, J. L.; Jackson, J. E. *J. Org. Chem.* **2009**, *74*, 5790−5792.