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Dipyrrolidinomethylaminophosphoric acid triamide (DPMPA) as an activator for the samarium diiodide-mediated reduction of alkyl and aryl halides

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ABSTRACT

The use of the conjugate base of dipyrrolidinomethylaminophosphoric triamide (DPMPA$^-$) as an activator of samarium diiodide is reported. This phosphoramidate has been shown to be a very potent ligand, allowing for the efficient, low-temperature reduction of alkyl and aryl chlorides. Reductive cyclizations of haloalkenylnaphthalenes are also reported.

1. Introduction

Samarium diiodide is one of the most useful reagents employed by organic chemists.[1] The utility of this reductant can be extended with the use of additives such as electron-rich cosolvents or certain transition metal salts.[2] The most commonly used activating cosolvent is the phosphoramide HMPA.[3] Addition of HMPA to a deep blue solution of SmI_2 in THF results in the formation of a purple, soluble complex. An X-ray structure reveals the complex contains four HMPA molecules bound to a central Sm^{2+}.[4] The HMPA ligands are believed to increase the reactivity of the Sm^{2+}species by donating electron density to the metal center. The synthetic utility of SmI_2 is so greatly enhanced by the use of HMPA that the majority of modern SmI_2 chemistry is accomplished with HMPA as the activating cosolvent.

It should also be noted that HMPA has been shown to affect the course of many SmI_2 reductions in ways other than coordination to Sm(II). Flowers and co-workers have demonstrated that HMPA activates alkyl halide bonds to reduction by Sm(II) species.[5] Hoz and Farran have shown that HMPA actually *inhibits* diaryl ketones from forming pinacol products.[6] This effect is thought to be a result of the complexation of Sm(III) by HMPA. HMPA-complexed Sm(III) species can no longer perform their necessary bridging function, thus dimerization cannot occur.

Although of great synthetic value, HMPA is known to have untoward biological effects. HMPA is antispermatogenic and mutagenic.[7] Rats develop nasal tumors when HMPA is inhaled,[8] but tumor formation is not observed when HMPA is administered orally.[9] There is evidence that this carcinogenicity is related to *multiple* hydroxylations at *N*-methyl positions of HMPA by cytochrome P450 enzymes. The resultant di- and tri-hydroxylated HMPA metabolites are thought to be the agents responsible for the nucleic acid damage.[10] In spite of this harmful biological activity, chemists use SmI_2 with HMPA as a cosolvent on a routine basis. A modest number of potential HMPA replacements have been examined. Electron-rich ligands such as *N*,*N*-dimethylpropyleneurea (DMPU),[11] 1,1,3,3-tetramethylguanidine (TMG), and 1,8-diazabicyclo[5.4.0]undec-7ene (DBU),[12] hexamethydisilazide[13] and recently, 1,3-dimethyl-2-imidazolidinone (DMI)[14] have shown promise as alternatives to HMPA. None of these, however, have been demonstrated to be generally applicable to the wide range of synthetic applications for which HMPA has proven useful.

We have been engaged in a program to develop safer and hopefully better organic ligands for SmI_2 activation. Our initial focus was the dehydro dimer of HMPA, diHMPA (Fig. 1). We presume that diHMPA poses less of a risk than HMPA due to its lower volatility. It proved to be approximately 1/3 as reactive as HMPA in most applications.[15] We recently reported that tripyrrolidinophosphoric acid triamide (TPPA) is on average an order of magnitude more reactive than HMPA as an activator of SmI_2.[16] This enhanced reactivity of the SmI_2/4TPPA complex (presumably

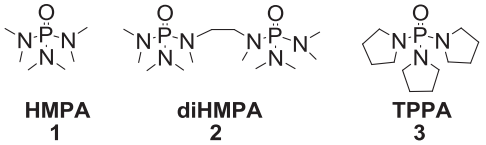

Fig. 1. Phosphoramide activators of SmI_2.

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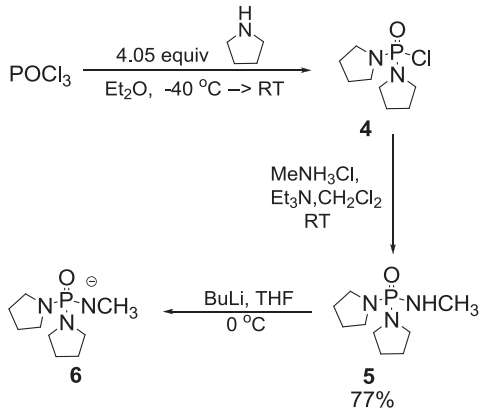
$[Sm(TPPA)_4(THF)_2]^{2+}2I^-$) was observed for the reduction of alkyl bromides and chlorides as well as in C–C bond forming reactions with iodides and ketones as radical precursors. Reissig has recently reported that SmI_2/TPPA is often superior to SmI_2/HMPA for γ-aryl ketone cyclizations.[17] The increased ability of TPPA relative to HMPA to function as an activator for SmI_2 may be due to the increased basicity of pyrrolidine (pK_b=2.8) relative to dimethylamine (pK_b=3.6).[18] This suggests that pyrrolidino may be more electron releasing than dimethylamino to the P=O moiety. The steric compactness of pyrrolidine is undoubtedly beneficial as well. These findings are of importance because HMPA is banned in several countries while TPPA is not currently known to have any deleterious health effects.[19]

2. Results and discussion

We are now examining the use of anionic phosphoramides (phosphoramidates) in the hope that they will deliver even more electron density to the Sm(II) center and thus further enhance the reductive capabilities of the resultant complex.[20] The synthesis of our first phosphoramidate, **6** is shown in Scheme 1. This phosphoramidate was designed with a single *N*-methyl group, to minimize mutagenicity,[8] and two pyrrolidino groups, because of their proven utility in the case of TPPA. Addition of 4.05 equiv of pyrrolidine to $POCl_3$ at −40 °C, followed by slow warming to room temperature selectively forms dipyrrolidinophosphoryl chloride (**4**) and 2 equiv of pyrrolidinium hydrochloride (removed by filtration). A very slight impurity (<1%) of TPPA is formed as well. Addition of CH_3NH_3Cl and Et_3N affords the crude phosphoramide, dipyrrolidinomethylaminophosphoric triamide (**5**, DPMPA). Purification is accomplished by distillation followed by sequential (5×) washes with hexane to selectively remove the less polar TPPA impurity. In this manner the neutral phosphoramide DPMPA is produced from $POCl_3$ in 77% yield as a hygroscopic, white powdery solid. Addition of *n*-BuLi to a THF solution of DPMPA affords the desired anionic species, $DPMPA^-$.



Scheme 1. The synthesis of $DPMPA^-$.

Addition of 4 equiv of $DPMPA^-$ in THF to 1 equiv of SmI_2 in THF yields a dark brown (not blue or purple) THF-soluble complex. Initial experiments designed to characterize SmI_2/$DPMPA^-$ mixtures suggest that they have significant reductive capabilities. 1-Chlorodecane, a reluctant substrate for reduction by most Sm(II) species, was chosen for these initial tests.[3,16] Complexes were formed from SmI_2 and the indicated ligand (Table 1). One minute after the addition of 1-chlorodecane and tetradecane (internal standard), an aliquot was removed and quenched with I_2.[21] A second aliquot was removed at 1 h. Both aliquots were analyzed by gas chromatography using internal standardization techniques.

Table 1
Relative reactivity of SmI_2 and additive with 1-chlorodecane

$$Cl(CH_2)_9CH_3 \xrightarrow[\text{Additive, 2 equiv } t\text{-BuOH, 0 °C}]{\text{3 equiv } SmI_2\text{, (0.050 M in THF)}} CH_3(CH_2)_8CH_3$$

Entry	Additive/SmI_2 (equiv)	Yield (%) at 1 min[a]	Yield (%) at 1 h[a]
1	4 equiv HMPA	< 1	< 1
2	4 equiv TPPA	< 1	< 1
3	4 equiv DPMPA	< 1	< 1
4	2 equiv diHMPA	0	0
5	1 equiv $DPMPA^-$	0	3
6	2 equiv $DPMPA^-$	47	66
7	3 equiv $DPMPA^-$	72	93
8	4 equiv $DPMPA^-$	90	96
9[b]	15 equiv H_2O, 12 equiv Et_3N	< 1	2
10	4 equiv LiBr	0	0

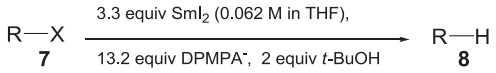
[a] Yield determined by GC.
[b] *t*-BuOH was not used.

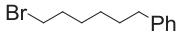
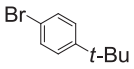
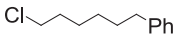
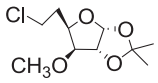
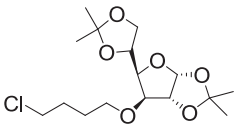
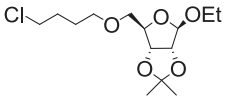
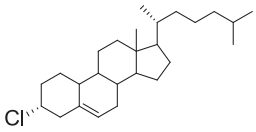
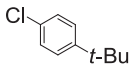
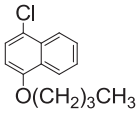
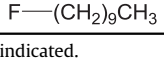
Complexes formed from SmI_2 and 4 equiv of the neutral phosphoramides HMPA, TPPA, and DPMPA produced a 0–1% yield of decane at the 1 min and 1 h marks (entries 1–3). No decane was produced in the case of the less reactive diHMPA (entry 4). Complexes formed from SmI_2 and $DPMPA^-$ were substantially more reactive. The 1:2 complex affords significant amounts of decane (47% yield) even at the 1 min mark (entry 6). With the 1:4 complex, the reaction is nearly complete (90% yield) at the 1 min mark (entry 8). Hilmersson and co-workers have used 7 SmI_2/35H_2O/28Et_3N to reduce 1-chlorodecane (14 h, 20 °C, 95%).[22] These conditions were modified to more closely match the other entries in this study (3SmI_2/15H_2O/12Et_3N, 0 °C). At the 1 min mark this samarium aquo complex produced a <1% yield of decane (entry 9). A 2% yield was found at the 1 h mark. These results indicate that the SmI_2/4$DPMPA^-$ complex is dramatically more reactive with 1-chlorodecane than any Sm(II) complex previously reported.

To ensure that the observed rate enhancements were due to $DPMPA^-$, a pair of additional experiments were undertaken. The effect of the presence of Li^+ was examined by adding 3 equiv of SmI_2 to 12 equiv of LiBr.[23] The resultant violet solution was exposed to 1 equiv of 1-chlorodecane. No decane was observed at either the 1 min or 1 h mark (entry 10). It was deemed important to ensure that unreacted *n*-BuLi was not present in the reaction mixture. To this end, 1 equiv of *n*-BuLi was added to an equimolar amount of DPMPA in THF at 0 °C, and stirred for 5 min. One equivalent of 3-phenylpropanal was added, and this mixture was stirred for 1 h at 0 °C, then quenched with water. Analysis of the crude reaction mixture reveals only DPMPA and 3-phenylpropanal, indicating free *n*-BuLi was not present in the reaction mixture at the time of addition of the aldehyde.

The obvious first synthetic application of SmI_2/4$DPMPA^-$ is for the reduction of carbon–halogen bonds. A series of more reactive organobromine and less reactive organochlorine compounds were successfully reduced as shown in Table 2. Both alkyl and aryl bromides can be efficiently reduced (entries 1 and 2). Primary (entries 3–6), secondary (entry 7), and tertiary (entry 8) alkyl chlorides were reduced in high yields. Aryl chlorides (entries 9–11) were also amenable to reduction. Alkenes, aryl groups, acetals, and ethers are compatible with this reducing system. These reactions were performed by addition of a THF solution of the organochlorine substrate to a THF solution of the SmI_2/4$DPMPA^-$ complex at −66 °C. This solution was then allowed to warm to room temperature over 2 h. It was determined that 3.3 equiv of SmI_2 was required to reliably take the reduction to completion. The color of the reaction mixture was observed to change from dark brown to light brown beginning typically at −30 °C. These conditions are substantially milder than Inanaga's original

Table 2
The reduction of alkyl halides with SmI_2/4DPMPA$^-$

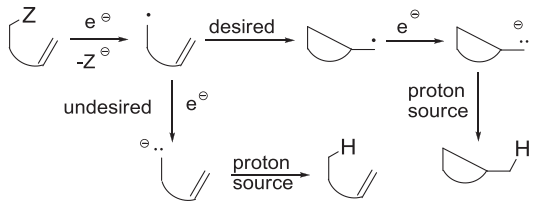


Entry	R–X		Yield[a] (%)
1	**7a**		80[a]
2	**7b**		94[a,b,c]
3	**7c**		82
4	**7d**		76
5	**7e**		93
6	**7f**		90
7	**7g**		82
8	**7h**		89[c]
9	**7i**		93[c]
10	**7j**		91[c]
11	**7k**		95
12	**7l**		0[c]

[a] Isolated yield unless otherwise indicated.
[b] Organobromine compounds required 3.0 equiv SmI_2 and 12 equiv DPMPA$^-$.
[c] Yield determined by GC.

conditions for the reduction of primary alkyl chlorides with SmI_2/4HMPA, which require 8 h at 60 °C.[3] The ease of reduction of organochlorine compounds suggests that it would be reasonable to determine if SmI_2/4DPMPA$^-$ can reduce organofluorine bonds, which have proven to be very difficult to reduce.[24] Attempts were made to reduce 1-fluorodecane with SmI_2/4DPMPA$^-$ at 21 °C and under reflux conditions. Decane was not produced under either set of conditions.

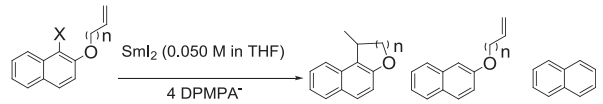
It is a concern that SmI_2/4DPMPA$^-$ may be *too* reactive for many transformations for which other SmI_2/phosphoramide complexes are useful. In particular, reactions that require an initial one-electron reduction followed by ring closure onto a radical acceptor with a subsequent second one-electron reduction may not be possible with this highly reactive reductant (Scheme 2). If the initial radical is further reduced prior to its reaction with the radical many such reactions will be rendered untenable.



Scheme 2. Reduction/cyclization of radical precursors with a pendant alkene.

This question was examined with the *O*-allyl[25] and *O*-butenyl[26,27] substrates shown below (Table 3). Using radical precursors with different rates of radical generation (ArBr vs ArCl) and 5- and 6-*exo-trig* cyclizations allowed for the assessment of the viability of this reaction pathway using SmI_2/4DPMPA$^-$. Three different modes of addition are reasonable. Addition of a THF solution of the substrate all at once (method A) would seem to be the one in which premature reduction of the incipient carbon radical could be most problematic. Slow addition of a THF solution of SmI_2 to a solution of the substrate and DPMPA$^-$ (method B) or slow addition of the preformed, soluble SmI_2/4DPMPA$^-$ reductant to a THF solution of the substrate (method C) should offer better results.

Table 3
Reductive cyclization of 1-halo-2-alkenyloxynaphthalenes



9a X = Br, n = 1
9b X = Cl, n = 1
9c X = Br, n = 2
9d X = Cl, n = 2

10a n = 1 **11a** n = 1 **12**
10b n = 2 **11**b n = 2

Entry	Compd	SmI_2 (equiv)	Method[a]	Addition temp (°C)	Yield (%)		
					10[b]	**11**[b]	**12**[c]
1	**9a**	3.0	A	−66	96	0	0
2	**9a**	3.0	B	−66	88	0	0
3	**9a**	3.0	C	−66	67	7	0
4	**9b**	3.3	A	−66	79	0	0
5	**9b**	3.3	B	0	80	0	0
6	**9b**	3.3	C	−66	59	0	0
7	**9c**	3.0	A	−66	59	24	2
8	**9c**	3.0	B	−66	67	6	0
9	**9c**	3.0	C	−66	63	35	0
10	**9d**	3.3	A	−66	67	18	5
11	**9d**	3.3	B	−66	70	29	0
12	**9d**	3.3	B	−23	83	2	0
13	**9d**	3.3	B	0	78	5	5
14	**9d**	3.3	C	−66	66	17	0

[a] Method A: add substrate toSmI_2/4DPMPA$^-$ in THF; method B: add SmI_2 to substrate/DPMPA$^-$ in THF; method C: add SmI_2/DPMPA$^-$ to substrate in THF.
[b] Isolated yield.
[c] Yield determined by GC.

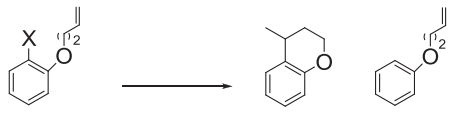
Method A, adding the substrate to the preformed complex, worked well for both *O*-allyl substrates **9a** and **9b** (entries 1 and 4). The reduced but uncyclized byproduct **11a** was not observed. As in the case of the simple organochlorine reductions, slightly more reductant (3.3 equiv) was required to consume the chloro substrates. Loss of the brown color characteristic of SmI_2/4DPMPA$^-$ occurred more rapidly and at lower temperatures in the case of the bromo substrates. It was anticipated that further reduction of the initially formed radical prior to cyclization would be more of an issue for **9c** and **9d**. It was determined that significant quantities of the reduced but uncyclized byproduct **11b** were observed in the cases of the *O*-butenyl substrates **9c** and **9d** (entries 7 and 10). Interestingly, small quantities of the reductive elimination product naphthalene were also observed by ^{1}H NMR of the crude reaction

mixtures. The yield of naphthalene in each of the reactions in Table 3 was determined by gas chromatography.

Method B, addition of a THF solution of SmI_2 over 4 min to a THF solution of the substrate, worked well for all four substrates (entries 2, 5, 8, 11–13). Method B worked best for the chloro *O*-butenyl substrate **9c** when the SmI_2 was added at −23 °C (entry 12), as opposed to the initial effort at −66 °C (entry 11). This can be understood based on the observation that color changes associated with reduction of C–Cl bonds by SmI_2/4DPMPA$^-$ are typically observed in the −20 to −30 °C range. A large concentration of reductant is not building up during the 4 min addition process. Addition times for method B were standardized at 4 min. It was noted that longer addition times resulted in increased quantities of naphthalene. When a 12 min addition of SmI_2 at −66 °C to **9c** was attempted (modified method B), the yield of cyclized product **10b** decreased to 52% and the yield of naphthalene increased to 13%.

Method C, a 4 min addition of the preformed complex to the substrate, is clearly the least effective of the three procedures. In the cases of the two butenyl substrates, lower yields of **10b** and higher yields of **11b** were noted (entries 9 and 14). No naphthalene was observed using this method.

The best of these procedures Method B, compares favorably to results obtained by other reductive cyclization methods (Scheme 3). Bardagi has reported that **9c** affords an 89:11 ratio of **10b** to **11b** upon treatment with the radical anion of ethyl benzoate in liquid ammonia.[27] The related 1-iodo-2-*O*-butenylbenzene (**13a**) was treated with the SmI_2/Et_3N/H_2O reducing system and gave a 60:40 ratio of **14** to **15**.[28] Exposure of 1-bromo-2-*O*-butenylbenzene (**13b**) to Bu_3SnH/hν provides **14** and **15** in a 57:23 ratio.[29]



13a X = I
13b X = Br

14 **15**

Scheme 3. Cyclization of halo-(*O*)-butenylbenzenes.

Cyclic voltammetry was utilized to quantify the reducing power of SmI_2/DPMPA$^-$complexes. As evidenced by the results contained in Table 4, the electron-rich DPMPA$^-$ ligands significantly lower the reduction potential of SmI_2. Comparison with ligands at the same degree of coordination (1 equiv of diHMPA[15] and 2 equiv of TPPA[16]) indicates that DPMPA$^-$ is donating significantly more electron density to the SmI_2 than any known, neutral phosphoramide ligand. In fact, only two coordinated DPMPA$^-$ ligands activate the samarium diiodide to a similar extent as 4 equiv of HMPA or 2 equiv of diHMPA. Because SmI_2 saturated with DPMPA$^-$ was expected to possess a standard potential even more negative based on the synthetic examples described elsewhere in the paper, attempts were made to characterize SmI_2 with three or four coordinated DPMPA$^-$. However, instrumental limitations and electrochemical irreversibility prevented the measurement of their standard potentials. Indeed, difficulties were also noted by Hilmersson and co-workers in their characterization of SmI_2/H_2O/amine complexes by cyclic voltammetry.[22]

Table 4
Effect of various phosphoramides on the standard potential of SmI_2[a]

Entry	Reductant	Cosolvent SmI_2	Standard potential (V) versus Ag/$AgNO_3$	Δ*E* versus SmI_2
1	SmI_2	—	−1.329±0.005	—
2	SmI_2/DPMPA$^-$	1	−1.51±0.01	0.17
3	SmI_2/DPMPA$^-$	2	−1.93±0.01	0.59
4	SmI_2/diHMPA	1	−1.43±0.02	0.09
5	SmI_2/diHMPA	2	−2.03±0.06	0.69
6	SmI_2/TPPA	2	−1.41±0.02	0.07
7	SmI_2/HMPA	4	−2.07±0.01	0.74
8	SmI_2/TPPA	4	−1.94±0.05	0.61

[a] Cyclic voltammograms were recorded at 5 mM SmI_2 with *n*-Bu_4NPF_6 (0.025 M) and *n*-BU_4NI (0.020 M) at 100 mV/s.

The intense brown color of the SmI_2/4DPMPA$^-$ solution is unique. When neutral phosphoramides (HMPA, diHMPA, TPPA) are added to SmI_2, violet solutions are produced, and the two absorption maxima at 553 and 621 nm merge to a broad band centered at about 540 nm. A peak centered around 380 nm is also present.[15,16,22,31] In the case of neutral DPMPA the same behavior is noted, with absorption maxima present at 388 and 539 nm. A series of experiments were undertaken to examine the change in the UV–vis spectrum of SmI_2 upon addition of increasing amounts of DPMPA$^-$. The UV–vis spectrum that results from the addition of 1 equiv of DPMPA$^-$ to 10 mM SmI_2 forming a blue-black solution is remarkably similar to the SmI_2/4HMPA spectrum (Fig. 2). Merging of the 553 and 621 nm peaks to a new broader peak at 546 nm is noted. Upon addition of 2, 3, or 4 equiv of DPMPA$^-$ (producing deep brown solutions), the absorption maxima at 553 and 621 nm diminished to a shoulder of the single broad peak centered at λ_{max}=405 nm. Although the electronic characteristics of these three solutions appear to be similar by UV–vis, their relative reactivities (Table 1) and their voltammograms (Table 4) indicate that the 'higher ratio' complexes are substantially more reductive (Fig. 2).

3. Conclusion

In summary, we have synthesized a novel complex of samarium diiodide and an anionic phosphoramide (phosphoramidate). This complex has been exploited for the efficient reduction of carbon–chlorine bonds under extremely mild conditions. We have also used this complex to reductively cyclize halogenated *O*-allyl and *O*-butenyl substrates efficiently. Cyclic voltammetry indicates that the addition of the DPMPA$^-$ to SmI_2 results in a significant decrease in the standard potential of the resultant complex. The addition of sequential equivalents of DPMPA$^-$ to SmI_2 was monitored also by UV–vis spectrometry.

4. Experimental section

4.1. General information

Pyrrolidine, DMF, Et_3N, HMPA, TPPA, toluene, and *t*-BuOH, were distilled from CaH_2 prior to use. Tetrahydrofuran was distilled from Na/benzophenone and sparged with argon for 10 min prior to use. DPMPA and diHMPA were azeotropically dried with toluene in Schlenkware prior to use. The concentration of SmI_2 in THF was confirmed by titration with I_2.[32] All reactions were performed under a nitrogen or argon atmosphere in oven-dried glassware. Organohalide substrates **7a**,[33] **7c**,[34] **7e**,[35] **7l**,[36] and **9a**–**d**[25,27] were synthesized by the literature methods. NMR spectra were recorded at room temperature on a Bruker Avance spectrometer (300 MHz for ^{1}H, 75 MHz for ^{13}C, and 121 MHz for ^{31}P) in $CDCl_3$. Chemical shifts are reported on the δ scale in parts per million (ppm) referenced to the residual solvent proton resonance of $CDCl_3$ (7.28 ppm) or the solvent carbon resonance of $CDCl_3$ (77.0 ppm). Phosphoric acid (0.00 ppm) was used as an external standard for ^{31}P spectra. Infrared spectra were recorded on a Thermoelectron IR100. Ultraviolet–visible spectra were recorded on an Ocean Optics USB-4000 spectrometer coupled to an Ocean Optics DT-Mini-2 UV–Visible–NIR source and a 300 μm transmission dip probe. The dip probe tip allows for a transmission pathlength of 2 mm. Column chromatography was accomplished using silica gel (70–230 mesh) as the stationary phase and mixtures of hexanes and ethyl acetate as the mobile phase. Thin-layer chromatography was performed on Analtech silica gel

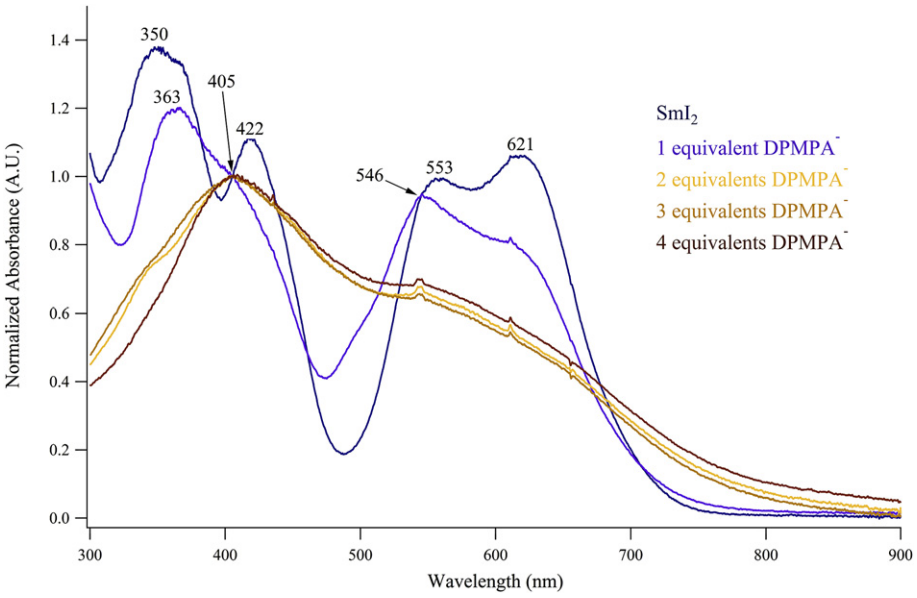


Fig. 2. Normalized (at 405 nm) UV–vis spectra recorded at 10 mM SmI_2 in THF.

plates with fluorescent indicator. Gas chromatography was performed with a Shimadzu GC-2014 equipped with a 30 m Restek Rx1-5ms column. High-resolution mass spectrometry was performed at the University of Buffalo using a ThermoFinnigan MAT 95 XL with ESI II source. A three-electrode system was utilized for the voltammetry measurements. The working electrode was glassy carbon, while the auxiliary and reference were a platinum wire and Ag/Ag^+ non-aqueous reference electrode, respectively. Prior to analysis, the glassy carbon working electrode was prepared by polishing sequentially in 1.0, 0.3, and 0.05 μm alumina that had been slurried with 18 MΩ water. The polished glassy carbon electrode was subsequently sonicated in isopropanol containing activated carbon, rinsed with 18 MΩ water, and dried under a stream of nitrogen. Following measurement, the voltammetric data were semi-integrated[37] and the standard potential was estimated according to the method of Oldham and Myland.[38]

4.2. Preparation of dipyrrolidinomethylaminophosphoric acid triamide (5)

A mechanically stirred mixture of $POCl_3$ (6.00 mL, 0.0644 mmol) in Et_2O (100 mL) was cooled to −40 °C (CH_3CN/liquid N_2). Pyrrolidine (21.7 mL, 0.261 mmol) was added over a 5 h period via syringe pump. The resultant mixture was allowed to warm to room temperature overnight. Hexanes (100 mL) was added, and the mixture was cooled to 0 °C. The precipitate was removed by vacuum filtration. Solvent was removed under reduced pressure. Dichloromethane (50 mL), CH_3NH_3Cl (17.5 g, 0.259 mmol), and Et_3N (71 mL, 0.51 mmol) were added, and the mixture was stirred for 48 h. Water (40 mL) was added and the mixture was extracted with $CHCl_3$ (6×30 mL). The resultant extract was washed with 10% NaOH (20 mL) and water (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Distillation (0.5 mmHg, 215–218 °C) afforded a white solid, which was washed with hexanes (5×8 mL) yielding 10.78 g (0.04948 mmol, 77%) of white solid, mp 66.0–67.0 °C. IR (ATR, cm^{-1}) 3200, 2968, 2846, 1429, 1207, 1183, 1096. ^1H NMR (300 MHz) δ 3.18–3.15 (m, 8H), 2.61 (dd, J=11.6, 5.8 Hz, 3H), 2.16 (br, 1H), 1.84–1.80 (m, 8H). ^{13}C NMR (75 MHz) δ 46.5 (d, J=4.2 Hz), 27.2 (s), 26.4 (d, J=8.0 Hz). ^{31}P NMR (121 MHz) δ 17.3. HRMS (ESI) m/z $[M+H]^+$ calcd for $C_9H_{21}N_3OP$ 218.1423, found 218.1417.

4.3. General procedure for the reduction of 1-chlorodecane with SmI_2/phosphoramide

The appropriate phosphoramide (1.75 mmol) was added followed by THF (4.0 mL), tetradecane (10.0 μL, 0.0384 mmol), *t*-BuOH (27 μL, 0.29 mmol), and 4.7 mL of a 0.093 M solution of SmI_2 (0.44 mmol) in THF. The resultant mixture was cooled to 0 °C. After stirring for 5 min, 1-chlorodecane (29.4 μL, 0.144 mmol) was added. Aliquots were removed at 1 min and 1 h and immediately quenched with 0.1 M I_2 in hexane. Each aliquot was mixed with 0.1 mL of 0.1 M HCl and 1.0 mL of Et_2O. The Et_2O extract was analyzed by gas chromatography.

4.4. General procedure for the reduction of 1-chlorodecane with SmI_2/$DPMPA^-$

A 0.50 M solution of $DPMPA^-$ was made by adding DPMPA (1.392 g, 6.411 mmol), to THF (10.2 mL), cooling to 0 °C, and adding 2.6 mL of a 2.5 M solution of *n*-BuLi in hexane (3.2 mmol). In a separate flask 4.7 mL of a 0.093 M solution of SmI_2 (0.44 mmol) in THF was added along with *t*-BuOH (27 μL, 0.29 mmol), and tetradecane (10.0 μL, 0.0384 mmol) and the resultant mixture cooled to 0 °C. The appropriate amount of THF (3.1 mL for 1:1, 2.3 mL for 2:1, 1.4 mL for 3:1, 0.5 mL for 4:1) and $DPMPA^-$ solution (0.87 mL for 1:1, 1.7 mL for 2:1, 2.6 mL for 3:1, and 3.5 mL for 4:1) were added to the SmI_2 flask. After stirring for 5 min, 1-chlorodecane (29.4 μL, 0.144 mmol) was added. Aliquots were removed at 1 min and 1 h and immediately quenched with 0.1 M I_2 in hexane. Each aliquot was mixed with 0.1 mL of 0.1 M HCl, and 1.0 mL of Et_2O. The Et_2O extract was analyzed by gas chromatography.

4.5. Synthesis of organochlorine substrates

*4.5.1. 5,6-Dideoxy-6-chloro-1,2-O-isopropylidene-3-O-methyl-α-D-xylo-hexofuranose (**7b**).* THF (1 mL) was added to 5-deoxy-1,2-*O*-isopropylidene-3-*O*-methyl-α-D-*xylo*-hexofuranose[39] (68 mg, 0.31 mmol). PPh_3 (98 mg, 0.37 mmol) was added, and the stirred mixture was cooled to 0 °C. *N*-Chlorosuccinimide (50 mg, 0.37 mmol) was added, and the mixture was allowed to warm overnight. Saturated $Na_2S_2O_3$ was added and the mixture was extracted with Et_2O (3×2 mL). The concentrated mixture was

purified by column chromatography (SiO_2, solvent gradient ranging from 3% ethyl acetate in hexanes to 6% ethyl acetate in hexanes) to provide **7b** (71 mg, 0.30 mmol, 96% yield) as a colorless oil. IR (ATR, cm^{-1}) 2992, 1374, 1020. ^1H NMR (300 MHz) δ 5.87 (d, J=3.9 Hz, 1H), 4.59 (d, J=3.9 Hz, 1H), 4.38–4.32 (m, 1H), 3.68–3.62 (m, 1H), 3.41 (s, 3H), 2.27–2.18 (m, 1H), 2.10–1.98 (m, 1H), 1.50 (s, 3H), 1.32 (s, 3H). ^{13}C NMR (75 MHz) δ 111.5, 104.6, 84.6, 81.5, 77.3, 57.7, 42.0, 31.2, 26.7, 26.2. HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{10}H_{17}O_4ClNa$ 259.0712, found 259.0708.

*4.5.2. 1-O-ethyl-5-O-(4′-chlorobutyl)-2,3-O-isopropylidene-β-D-ribofuranose (**7d**).* Acetone (2.5 mL) and ethanol (7.5 mL) were added to ribose (0.500 g, 3.33 mmol) with stirring. To this mixture were added $CuSO_4$ (1.99 g) and H_2SO_4 (0.1 mL) This mixture was refluxed for 3 h, cooled, and filtered. Water (10 mL) was added, and the mixture was extracted with Et_2O (3×15 mL). The combined extracts were dried with Na_2SO_4, filtered, and the solvent removed under reduced pressure to afford 0.566 g (2.62 mmol, 79% crude yield) of 1-*O*-ethyl-2,3-*O*-isopropylidene-β-D-ribofuranose as a light yellow syrup. DMF (2.9 mL) was added to 1-*O*-ethyl-2,3-*O*-isopropylidene-β-D-ribofuranose (0.500 g, 2.29 mmol). This mixture was cooled to 0 °C, and a 60% dispersion of NaH in mineral oil (110 mg, 2.75 mmol) was added. After stirring for 20 min, 1-bromo-4-chlorobutane (340 μL, 2.96 mmol) was added. This mixture was allowed to warm to room temperature, and stirred for 12 h. Water (5 mL) was added, and the mixture was extracted with 2:1 Et_2O/hexanes (3×10 mL). The concentrated mixture was purified by column chromatography (SiO_2, solvent gradient ranging from 2% ethyl acetate in hexanes to 4% ethyl acetate in hexanes) to provide **7d** (412 mg, 1.34 mmol, 58% yield) as a colorless oil. IR (ATR, cm^{-1}) 2939, 2870, 1373, 1210, 1086. ^1H NMR (300 MHz) δ 5.08 (s, 1H), 4.68 (d, J=6.0 Hz, 1H), 4.60 (d, J=6.0 Hz, 1H), 4.31 (t, J=7.6 Hz, 1H), 3.75–3.69 (m, 1H), 3.56 (t, J=3.4 Hz, 2H), 3.58–3.40 (m, 5H), 1.95–1.85 (m, 2H), 1.76–1.71 (m, 2H), 1.50 (s, 3H), 1.34 (s, 3H), 1.19 (t, J=7.1 Hz, 3H). ^{13}C NMR (75 MHz) δ 112.3, 107.8, 85.3, 85.0, 82.2, 71.8, 70.4, 62.9, 45.0, 29.4, 27.0, 26.5, 25.0, 14.9. HRMS (ESI) m/z $[M+Na]^+$ calcd for $C_{14}H_{25}O_5ClNa$ 331.1285, found 331.1283.

*4.5.3. 4-Chloro-1-n-butoxynaphthalene (**7i**).* To a solution of DBU (626 μL, 4.20 mmol) in DMF (1.4 mL) was added 4-chloro-1-naphthol (0.500 g, 2.80 mmol). 1-Bromobutane (450 μL, 4.20 mmol) was added, and the mixture was heated to 50 °C overnight. After cooling to room temperature, water (10 mL) was added, and the mixture was extracted with hexanes (3×10 mL). The concentrated mixture was purified by column chromatography (SiO_2, 1% ethyl acetate in hexanes) to provide **7i** (498 mg, 2.12 mmol, 76% yield) as a colorless oil. IR (ATR, cm^{-1}) 3080, 2958, 2933, 2871, 1591, 1456, 1424, 1375. ^1H NMR (300 MHz) δ 8.35 (d, J=8.3 Hz, 1H), 8.24 (d, J=8.4 Hz, 1H), 7.67–7.54 (m, 2H), 7.47 (d, J=8.3 Hz, 1H), 6.73 (d, J=8.3 Hz, 1H), 4.14 (t, J=6.3 Hz, 2H), 1.99–1.89 (m, 2H), 1.69–1.57 (m, 2H), 1.06 (t, J=7.4 Hz, 3H). ^{13}C NMR (75 MHz) δ 155.0, 132.2, 128.3, 127.7, 126.8, 126.7, 125.1, 123.8, 123.5, 105.5, 69.0, 32.2, 20.4, 14.9. HRMS (EI) m/z $[M]^+$ calcd for $C_{14}H_{15}OCl$ 234.0817, found 234.0810.

4.6. General procedure for the reduction of organochlorine compounds

To an ice-cold mixture of DPMPA (816 mg, 3.76 mmol) and THF (3.0 mL) was added 1.50 mL of a 2.5 M solution of *n*-BuLi (3.8 mmol) in hexane. This mixture was stirred for 5 min, and 9.7 mL of a 0.097 M solution of SmI_2 (0.94 mmol) in THF was added, and stirred for 5 min. After cooling the reductant to −66 °C, a solution of the organochlorine substrate (0.285 mmol) and *t*-BuOH (54 μL, 0.57 mmol) in THF (1.4 mL) was added. The mixture was allowed to warm to 21 °C over 2 h and, where appropriate, tetradecane (10.0 μL, 0.0384 mmol) was added. Water (8 mL) was added, and the mixture was extracted with a 2:1 mixture of hexanes and Et_2O (5×5 mL). The concentrated mixture was purified by silica gel column chromatography.

4.7. General procedures for cyclization of 1-chloro-2-alkenyloxynaphthalenes

4.7.1. Method A. To an ice-cold mixture of DPMPA (816 mg, 3.76 mmol) and THF (6.0 mL) was added 1.50 mL of a 2.5 M solution of *n*-BuLi (3.8 mmol) in hexane. This mixture was stirred for 5 min, and 9.7 mL of a 0.097 M solution of SmI_2 (0.94 mmol) in THF was added, and stirred for 5 min. After cooling the reductant to −66 °C, a solution of the 1-chloro-2-(*O*)-alkenylnaphthalene (0.285 mmol) in THF (1.4 mL) was added. The mixture was allowed to warm to 21 °C over 2 h and tetradecane (10.0 μL, 0.0384 mmol) was added. Water (8 mL) is added, and the mixture was extracted with a 2:1 mixture of hexanes and Et_2O (5×5 mL). The concentrated mixture was purified by column chromatography (SiO_2, solvent gradient ranging from 100% hexanes to 1% ethyl acetate in hexanes) to provide the corresponding reduced products.

4.7.2. Method B. To an ice-cold mixture of DPMPA (816 mg, 3.76 mmol) and THF (6.0 mL) was added 1.50 mL of a 2.5 M solution of *n*-BuLi (3.8 mmol) in hexane. This mixture was stirred for 5 min. After cooling to the appropriate temperature, a solution of 1-chloro-2-(*O*)-alkenylnaphthalene (0.285 mmol) in THF (1.4 mL) was added. Over 4 min, 9.7 mL of a 0.097 M solution of SmI_2 (0.94 mmol) in THF was added. The mixture was allowed to warm to 21 °C over 2 h and tetradecane (10.0 μL, 0.0384 mmol) was added. The mixture was worked up and purified as described in method A.

4.7.3. Method C. To an ice-cold mixture of DPMPA (816 mg, 3.76 mmol) and THF (6.0 mL) was added 1.50 mL of a 2.5 M solution of *n*-BuLi (3.8 mmol) in hexane. This mixture was stirred for 5 min, and 9.7 mL of a 0.097 M solution of SmI_2 (0.94 mmol) in THF was added. Into a separate flask 1-chloro-2-(*O*)-alkenylnaphthalene (0.285 mmol) in THF (1.4 mL) was added, and cooled to −66 °C. The preformed reductant was added over 4 min to the substrate. The resultant mixture was allowed to warm to 21 °C over 2 h, and tetradecane (10.0 μL, 0.0384 mmol) was added. The mixture was worked up and purified as described in method A.

4.8. Analytical data for compounds 8–12

*4.8.1. 1-Phenylhexane (**8a**).*[40] Colorless oil. ^1H NMR (300 MHz) δ 7.22–7.08 (m, 5H), 2.52 (t, J=7.6 Hz, 2H), 1.53 (m, 2H), 1.3 (m, 6H), 0.82 (br, 3H). ^{13}C NMR (75 MHz) δ 142.9, 128.4, 128.2, 125.5, 36.0, 31.7, 31.5, 29.0, 22.6, 14.1.

*4.8.2. 5,6-Dideoxy-1,2-O-isopropylidene-3-O-methyl-α-D-xylo-hexofuranose (**8d**).*[41] Colorless oil. ^1H NMR (300 MHz) δ 5.90 (d, J=4.0 Hz, 1H), 4.59 (d, J=4.0 Hz, 1H), 4.07 (dt, J=7.3, 3.1 Hz, 1H), 3.58 (d, J=3.1 Hz, 1H), 3.42 (s, 3H), 1.76–1.65 (m, 3H), 1.51 (s, 3H), 1.34 (s, 3H), 0.97 (t, J=7.5 Hz, 3H). ^{13}C NMR (75 MHz) δ 111.1, 104.6, 84.1, 81.7, 81.5, 57.8, 26.6, 26.2, 20.9, 10.4.

*4.8.3. 3-O-n-Butyl-1,2:5,6-di-O-isopropylidene-α-D-glucofuranose (**8e**).*[42] Colorless oil. ^1H NMR (300 MHz) δ 5.85 (d, J=3.7 Hz, 1H), 4.50 (d, J=3.7 Hz, 1H), 4.31–4.25 (m, 1H), 4.12–4.03 (m, 1H), 3.95–3.82 (m, 1H), 3.94 (d, J=3.1 Hz, 1H), 3.60–3.47 (m, 2H), 1.55–1.50 (m, 2H), 1.47 (s, 3H), 1.41–1.29 (m, 10 H), 0.89 (t, J=7.3 Hz, 3H). ^{13}C NMR (75 MHz) δ 111.7, 108.8, 105.2, 82.5, 82.1, 81.2, 72.5, 70.3, 67.2, 31.7, 26.8, 26.7, 26.2, 25.4, 19.2, 13.8.

*4.8.4. 1-O-Ethyl-5-O-n-butyl-2,3-O-isopropylidene-β-D-ribofuranose (**8f**).* Colorless oil. ^1H NMR (300 MHz) δ 5.06 (s, 1H), 4.67 (d,

J=6.5 Hz, 1H), 4.59 (d, *J*=6.9 Hz, 1H), 4.30 (t, *J*=6.9 Hz, 1H), 3.76–3.66 (m, 1H), 3.51–3.37 (m, 5H), 1.60–1.48 (m, 2H), 1.48 (s, 3H), 1.43–1.31 (m, 2H), 1.31 (s, 3H), 1.16 (t, *J*=7.1 Hz, 3H), 0.91 (t, *J*=7.3 Hz, 3H). ^{13}C NMR (75 MHz) δ 112.2, 107.7, 85.3, 85.0, 82.3, 71.7, 71.2, 62.8, 31.7, 26.4, 25.0, 19.3, 14.9, 13.9. HRMS (ESI) *m*/*z* $[M+Na]^+$ calcd for $C_{14}H_{26}O_5Na$ 297.1672, found 297.1672.

*4.8.5. Cholest-5-ene (**8g**).*[43] White solid. ^{1}H NMR (300 MHz) δ 5.30–5.28 (m, 1H), 2.32–2.18 (m, 1H), 2.10–1.93 (m, 3H), 1.90–1.81 (m, 2H), 1.79–1.69 (m, 1H), 1.63–0.92 (m, 23H), 1.00 (s, 3H), 0.92 (d, *J*=6.4 Hz, 3H), 0.90 (d, *J*=1.3 Hz, 3H), 0.88 (d, *J*=1.3 Hz, 3H), 0.70 (s, 3H). ^{13}C NMR (75 MHz) δ 143.7, 119.0, 56.8, 56.1, 50.6, 42.31, 39.9, 39.8, 39.5, 37.5, 36.2, 35.8, 32.9, 31.9, 31.8, 28.2, 28.0, 28.0, 24.3, 23.8, 22.8, 22.5, 20.7, 19.5, 18.7, 11.8.

*4.8.6. 1-n-Butoxynaphthalene (**8k**).*[44] Colorless oil. ^{1}H NMR (300 MHz) δ 8.21 (m, 1H), 7.70 (m, 1H), 7.40–7.24 (m, 4H), 6.69 (d, *J*=7.2 Hz, 1H), 4.04 (t, *J*=6.3 Hz, 2H), 1.82 (m, 2H), 1.52 (m, 2H), 0.94 (t, *J*=7.4 Hz, 3H). ^{13}C NMR (75 MHz) δ 154.9, 134.5, 127.5, 126.3, 126.0, 125.8, 125.1, 122.1, 120.0, 104.5, 67.8, 31.4, 19.6, 14.0.

*4.8.7. 1-Methyl-1,2-dihydronaphtho[2,1-b]furan (**10a**).*[45] Colorless oil. ^{1}H NMR (300 MHz) δ 7.86 (d, *J*=8.3 Hz, 1H), 7.78 (d, *J*=8.4 Hz, 1H), 7.72 (d, *J*=8.8 Hz, 1H), 7.51 (m, 1H), 7.34 (m, 1H), 7.16 (d, *J*=8.8 Hz, 1H), 4.82 (t, *J*=10.1 Hz, 1H), 4.41 (dd, *J*=8.7, 3.8 Hz, 1H), 3.94 (m, 1H), 1.50 (d, *J*=6.3 Hz, 3H). ^{13}C NMR (75 MHz) δ 157.0, 130.5, 129.6, 129.3, 129.0, 126.6, 123.6, 122.7, 122.3, 112.3, 79.4, 36.2, 20.4.

*4.8.8. 1-Methyl-1,2-dihydronaphtho[2,1-b]pyran (**10b**).*[27] Colorless oil. ^{1}H NMR (300 MHz) δ 7.95 (d, *J*=8.2 Hz, 1H), 7.79 (d, *J*=8.1Hz, 1H), 7.64 (d, *J*=9.5 Hz, 1H), 7.54–7.48 (m, 1H), 7.38–7.32 (m, 1H), 7.06 (d, *J*=9.5 Hz, 1H), 4.39–4.34 (m, 2H), 3.62–3.53 (m,1H), 2.35–2.23 (m, 1H), 1.91–1.85 (m, 1H), 1.50 (d, *J*=7.7 Hz, 3H). ^{13}C NMR (75 MHz) δ 151.3, 132.6, 128.7, 127.9, 126.2, 122.9, 122.0, 119.1, 118.7, 61.5, 28.7, 24.4, 22.0.

*4.8.9. 2-(But-3-enyloxy)naphthalene (**11**).*[27] Colorless oil. ^{1}H NMR (300 MHz) δ 7.82–7.75 (m, 3H), 7.51–7.46 (m, 1H), 7.40–7.35 (m, 1H), 7.22–7.18 (m, 1H), 7.18 (s, 1H), 6.07–5.93 (m, 1H), 5.29–5.17 (m, 2H), 4.18 (t, *J*=6.7 Hz), 2.66 (m, 2H). ^{13}C NMR (75 MHz) δ 156.8, 134.5, 134.4, 129.3, 128.9, 127.6, 126.7, 126.3, 123.5, 118.9, 117.0, 106.6, 67.1, 33.6.

4.9. UV–vis spectrum of SmI_2/4DPMPA complex

THF (7.4 mL) was added to a flask equipped with the UV–vis probe, and a background spectrum was taken. A 0.095 M solution of SmI_2 in THF (1.9 mL, 0.18 mmol) was added. DPMPA (182 mg, 0.839 mmol) was dissolved in THF (8.0 mL), and 7.2 mL of this solution was transferred to the SmI_2-containing flask. After stirring for 1 min, the spectrum was acquired.

4.10. General procedure,UV–vis spectrum of SmI_2/$DPMPA^-$ complexes

A 0.10 M solution of $DPMPA^-$ was made by adding DPMPA (391 mg, 1.80 mmol) to THF (17.3 mL), cooling to 0 °C and adding 0.72 mL of a 2.5 M solution of *n*-BuLi in hexane (1.80 mmol). In a separate flask equipped with the UV–vis probe, THF was added (14.3 mL for 1:1, 12.5 mL for 2:1, 10.7 mL for 3:1, 8.9 mL for 4:1), and a background spectrum was taken. A 0.095 M solution of SmI_2 in THF (1.9 mL, 0.18 mmol) was added. The appropriate amount of the 0.10 M solution of $DPMPA^-$ in THF (1.8 mL for 1:1, 3.60 mL for 2:1, 5.4 mL for 3:1, 8.9 mL for 4:1) was transferred to the SmI_2-containing flask. After stirring for 1 min, the spectrum was acquired.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.02.025.

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