ORGANOMETALLICS

Silylium Ion Promoted Reduction of Imines with Hydrosilanes

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Supporting Information

ABSTRACT: The silvlium ion promoted reduction of imines yielding the corresponding amines is reported. Both tert-butylferrocenylmethylsilane and triethylsilane are efficient hydride donors for the reduction of intermediate silyliminium ions, thereby regenerating the catalytically active silylium ion and closing the catalytic cycle.



The use of silylium ions in catalysis is currently enjoying growing interest.¹ Now that the long controversy on the issue of the isolation and characterization of these tricoordinate silicon cations in free form in the condensed phase is settled,² their application as potent catalysts in organic chemistry has become a new challenge. The obvious choice of transformations for these extremely electron-deficient compounds was a typical Lewis acid catalyzed reaction such as the Diels-Alder reaction,^{3,4} where the silylium ion catalyst is released unchanged from the adduct to maintain a catalytic cycle. Also, the combination of a silicon cation with a bulky phosphine Lewis base resulted in the formation of a frustrated Lewis pair capable of activating dihydrogen (albeit irreversibly and not yet catalytically).⁵ Another class of reactions promoted by silylium ions consumes the active catalyst by formation of a covalent bond. To close the catalytic cycle, the regeneration of the silicon cation from a suitable precursor in a later step is essential.¹ An isolated example of self-regenerating silvlium ion catalysis was presented by Lambert⁶ during his efforts directed toward the generation of silicon-stabilized carbenium ions: diphenylethene was hydrosilylated using a catalytic amount of $[Et_3Si(C_6D_6)]^+[B(C_6F_5)_4]^-$ and Et_3SiH as the stoichiometric hydride source. The same concept was successfully used by Ozerov⁷ and Müller⁸ in hydrodefluorination reactions of various substrates containing $C(sp^3)$ -F bonds. Siegel extended the scope of this reaction to $C(sp^2)$ -F bonds and trapped the intermediate carbenium ion by an intramolecular Friedel-Crafts reaction, yielding polycyclic aromatic hydrocarbons.⁹ The regeneration of the silvlium ion catalyst was achieved by protodesilylation of dimesityldimethylsilane in the latter case. Different pathways of catalyst regeneration are also discussed for silicon cation promoted Mukaiyama aldol^{3,10,11} and polymerization reactions.¹² Aside from Lambert's early alkene hydrosilylation,⁶ pioneering work on the reduction of carbonyl compounds using a silvlium ion as promoter was reported by Kira before.¹³ However, the hydrosilylation of different ketones did not afford the expected silvl ethers but, as a result of deoxygenation, alkanes or even alkenes instead. This

observation was rationalized by the facile formation of disiloxane as a good leaving group and independently confirmed by the group of Piers.¹⁴ Recently, our group employed the ferrocene-stabilized silylium ion 1¹⁵ (Figure 1)



Figure 1. Ferrocene-stabilized silylium ion 1.

in a hydrosilylation reaction of ketones¹⁶ that stops at the alcohol oxidation level, likely due to the unusual stabilization of the cationic silicon center by the ferrocene backbone¹⁵ and the related hydride donor strength of the corresponding ferrocenylsubstituted silane 2.1

Intrigued by these results, we became interested in the extension of this catalysis to other carbonyl derivatives, namely imines.¹⁸ We began screening the representative benzaldehydederived aldimines 4a-f to probe the influence of the nitrogen protecting group (Table 1, entries 1-6). These reactions were performed at room temperature rather than -60 °C (cf. C=O reduction¹⁶), and therefore, we decided to use either 1,2-F2C6H4 or 1,2-Cl2C6H4 instead of CH2Cl2 as solvent. Catalyst 1 is perfectly stable in these solvents¹⁵ but not in CH₂Cl₂^{4a} at room temperature (for the use of the cheaper toluene as solvent, see below). A catalytic amount of silylium ion 1 was generated in situ from a slight excess of tBuFcMeSiH(2) and $[Ph_3C]^+[B(C_6F_5)_4]^-$ (3) prior to the addition of the imine. Using preformed 1 (5.0 mol %),¹⁹ diphenylphosphinoyl- (entry 1), tert-butoxycarbonyl- (entry 2), and benzyl-protected (entry 3) imines 4a-c showed no conversion to the corresponding

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Table 1. Silylium Ion Promoted Reduction of Aldimines a	ınd
Ketimines: Screening of the Nitrogen Protecting Group'	1

		1. [Ph ₃ C]⁺[E	B(C ₆ F ₅) ₄] [−]			
	N	$_{-}R^{1}$	(3 , 5.0 mol %)			$HN^{-}R^{1}$	
			fBuFcMeSiH (2)				
	Ũ	R ² 1,2	-F ₂ C ₆ H ₄ 2. hydr	, r.t., time olysis		→ R ²	
	4a–4f		oreforma	reformation of		5a–5f	
	(aldimine and 61 (ketimin	es) [tBuFc prior to ti e)	MeSi]⁺[E he additi	B(C ₆ F ₅) ₄] [−] (1 on of the im) ine	and 7f	
entry	imine	\mathbb{R}^1	\mathbb{R}^2	time (h)	amine	yield (%) ^b	
1	4a	$P(O)Ph_2$	Н	70	5a	no conversn ^c	
2	4b	C(O)OtBu	Н	70	5b	no conversn ^c	
3	4c	CH ₂ Ph	Н	70	5c	no conversn ^c	
4	4d	CHPh ₂	Н	142	5d	40 ^{<i>d</i>}	
5	4e	Ph	Н	46	5e	84	
6 ^e	4f	$S(O_2)Tol$	Н	16	5f	90	
7^e	6f	$S(O_2)Tol$	Me	119	7f	19^d	

^{*a*}All reactions were performed according to the general procedure (cf. the Supporting Information) on a 0.20 mmol scale. ^{*b*}Analytically pure product after flash column chromatography on silica gel. ^{*c*}Conversion determined by GLC analysis using in situ formed Ph₃CH as internal standard. ^{*d*}Full conversion was not achieved. ^{*e*}1,2-Cl₂C₆H₄ as solvent.

amines 5a-c at room temperature and prolonged reaction times. A switch to the benzhydryl protection group (entry 4) then enabled the reduction, but conversion of imine 4d to amine 5d was incomplete, and the isolated yield was only 40% after hydrolysis. Phenyl substitution (entry 5) resulted in full conversion of 4e after 46 h, and amine 5e was obtained in 84% isolated yield. Sulfonyl-protected imine 4f (entry 6) reacted at an even faster reaction rate (16 h), affording amine 5f in 90% yield after hydrolysis. Conversely, sulfonyl-substituted acetophenone-derived ketimine 6f reacted sluggishly under otherwise identical reaction conditions (entry 7).

We interpret these results according to the catalytic cycle previously proposed by us for the related C=O reduction (Scheme 1).¹⁶ It commences with formation of silyliminium ion V from silylium ion I and imine IV. However, it is at least conceivable that, in the presence of excess II (silane reagent), I (silylium ion catalyst) also seeks stabilization through η^1 Si-H

Scheme 1. Simplified Catalytic Cycle for the Silylium Ion Promoted Reduction of Imines a



 ${}^{a}[B(C_{6}F_{5})_{4}]^{-}$ as counteranion omitted for clarity.

coordination of another molecule of II, thereby forming nearly linear hydride-bridged III. Reed and co-workers had even provided crystallographic evidence of the existence of such intermolecular adducts.²⁰ Transfer of I onto the imine nitrogen atom of IV would then occur from III, resembling the mechanism described for Si-H bond activation with the Lewis acids $B(C_6F_5)_3^{21}$ and Brookhart's iridium(III) pincer complex²² (not shown).^{23,24} That alternative pathway seems a bit more unlikely with our sterically hindered, ferrocene-stabilized silicon cation 1 substituted with a tert-butyl group but is certainly possible with the conventional $[Et_3Si]^+[B(C_6F_5)_4]^-$ as catalyst. Moreover, we are aware of the availability of another Lewis basic coordination site in nonreacting aldimines 4a,b as well as reacting sulfonyl-substituted 4f and 6f, and these oxygen donors might possibly compete with the imine nitrogen atom for Lewis pair formation with I (or III). That was further verified in a stoichiometric NMR experiment, where tertbutoxycarbonyl-protected 4b was shown to form a stable complex with 1 (²⁹Si NMR (1,2-Cl₂C₆D₄): δ 114.6 ppm for 1 but 33.0 ppm for 4b·1), not resulting in any decomposition. Hydride transfer from silane II onto the carbon atom of V regenerates catalyst I and releases the silvlated amine VI, which is later hydrolyzed to amine VII. The reduction step will be highly sensitive toward the electronic situation in V. Electronwithdrawing groups on the nitrogen atom destabilize V and enhance its reactivity and will, therefore, facilitate the hydride abstraction step. Aldimine 4f combines both the stability of the protecting group in Lewis acidic media and the high reactivity of V, resulting in full conversion (cf. Table 1, entry 6). In turn, the additional substituent in ketimine 6f lends further stabilization to the positive charge and increases steric bulk in V, resulting in poor conversion (cf. Table 1, entry 7). To prove that II is the actual hydride source, we applied deuterated silane d-2 to the reduction of imine 4f, yielding amine d-5f in 90% yield (not shown; see the Supporting Information for details).

After identification of the optimal imine protection group, we turned our attention toward the substrate scope of our silvlium ion promoted reduction of imines with tBuFcMeSiH (2) (Table 2, column 5). Aryl-substituted N-tosylated imines 9f-13f (entries 2-6, column 5) performed well, producing the corresponding amines 17f-21f in moderate to good yields. Alkyl-substituted imines 14f-16f showed even better results (entries 7-9, column 5) with excellent yields of over 95% for amines 22f-24f. Neither steric hindrance (entries 4, 5, and 8) nor enolizable imines (entries 7 and 9) were a limitation. This C=N reduction is, however, different from the related C=O reduction, where the use of tBuFcMeSiH (2) prevented overreduction (alcohol formation)¹⁶ and the use of Et₃SiH (8) resulted in full deoxygenation (alkane formation).^{13,14} Exhaustive reduction is not an option here, as the disilazanide anion as opposed to neutral disiloxane is a poor leaving group. We, therefore, concluded that our ferrocenyl-substituted silane (2) might be replaced by readily available $Et_3SiH(8)$ in this silylium ion catalysis (Table 2, column 6). Gratifyingly, similar results were obtained using 8 and a catalytic amount of $[Ph_3C]^+[B(C_6F_5)_4]^-$ (entries 1–9, column 6). We note here that Ph₃SiH worked equally well in the reduction of 4f to 5f (94% isolated yield after 2 h, not included in Table 2).

The catalyses were routinely run for 16 h (overnight), but full conversion was achieved in 4 h with *t*BuFcMeSiH (2) and in 1 h with Et₃SiH (8) for the model substrate 4f (Table 2, entry 1, columns 5 and 6). Also, the expensive 1,2-Cl₂C₆H₄ as solvent was successfully replaced by toluene in these reactions,

Table 2. Reduction of Aryl- and Alkyl-Substituted N-Tosylated Aldimines Using either tBuFcMeSiH (2) or Et₃SiH (8) as Hydride Source^a



1-naphthyl 90 5 12f 20f 93 2-naphthyl 6 63 66 13f 21f 7 cyclohexyl 98 99 14f 2.2f 8 15f tert-butyl 23f 95 96 g 16f pentan-3-yl 24f 97 96

^{*a*}All reactions were performed according to the general procedure (cf. the Supporting Information) on a 0.20 mmol scale. ^{*b*}Analytically pure product after flash column chromatography on silica gel.

and the corresponding amine **5f** was isolated in 95% yield (after 8 h) and 88% (after 1 h), respectively. The higher reactivity of the triethylsilylium ion based system relative to **1** is rationalized by its reduced steric hindrance, and that prompted us to reinvestigate the reduction of *N*-tosylated ketimine **6f**, where the reduction catalyzed by the ferrocene-stabilized silylium ion 1 had failed before (Table 1, entry 7). That reduction was now successful, forming amine **7f** in 76% yield within 1 h (Scheme 2).

Scheme 2. Triethylsilylium Ion Promoted Reduction of an N-Tosylated Alkyl Aryl Imine



In summary, we have demonstrated the potential of silylium ions to act as promoters for the reduction of imines. Several *N*-tosylated aldimines were readily reduced to the corresponding amines at room temperature using either our *t*BuFcMeSiH (2) or commercially available Et₃SiH (8) as the stoichiometric hydride source. With Et₃SiH (8), even an *N*-tosylated ketimine was reduced under these mild reaction conditions. The catalyst performance is, however, inferior to that of the $B(C_6F_5)_3/R_3SiH$ combination, where hydrosilylation is faster and less reactive imines do react at an elevated temperature of 70 °C.^{24a} That might be due to the intermediacy of a borohydride as the actual reductant.²¹ The crucial step of the present catalysis, that is the regeneration of the silicon cation, is the hydride transfer from a less hydridic silane to the intermediate silyliminium ion, and for the catalysis to proceed, the hydride donor strength and

the electrophilicity of the silyliminium ion must be well balanced.

ASSOCIATED CONTENT

Supporting Information

Text and figures giving general procedures and characterization data as well as ¹H, ¹³C, and ²⁹Si NMR spectra for amines **5d–f**, *d*-**5f**, **7f**, and **17f–24f** as well as the deuterated silane *d*-**2**. 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.

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