Lewis Superacid Catalysis

DOI: 10.1002/anie.200906036

N-Acyliminium Ion Chemistry: Highly Efficient and Versatile Carbon–Carbon Bond Formation by Nucleophilic Substitution of Hydroxy Groups Catalyzed by $Sn(NTf_2)_4$

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N-acyliminium ions are widely used as electrophiles in α-amidoalkylation reactions. These stabilized carbenium ion intermediates are typically generated from cyclic N,O-acetals in acidic medium and usually lead to useful α-functionalized amino derivatives after intra- or intermolecular trapping by nucleophiles.[1] Despite the great synthetic possibilities of such chemistry, catalytic versions have been developed only quite recently. Indeed, some examples of amidoalkylation with silicon-based nucleophiles have been reported,[2–5] though with generally moderate catalytic activity, while $HNTf_2$ (Tf = trifluoromethanesulfonyl)[6] has proven to be a more efficient catalyst allowing a broader combination of donor–acceptor partners under milder reaction conditions. Although challenging and of practical significance to the organic chemist, the catalytic α-amidoalkylation of C–H nucleophiles has been less explored[7,8] with only a few examples dealing with intermolecular coupling with β-keto esters or β-diketones,[7] or intramolecular arylation.[8]

The apparent need for an alkoxy or acetoxy aminal derivative in all these catalytic reactions requires an additional step which lengthens the procedures. It would therefore be desirable to use the parent hydroxy aminals themselves as amidoalkylating agents for more efficient and atom-economical processes. Owing to the increasing demand for efficient and environmentally friendly procedures, the development of catalytic and direct carbon–carbon bond-forming reactions of unmodified reaction partners is an exciting challenge. To this end, considerable achievements towards the direct S_N1-type alkylation between carbon nucleophiles and alcohols have been recently developed despite the poor leaving-group ability of the hydroxy group.[9–12] However, while most of the subclasses of stabilized carbenium ions (e.g. benzyl, allyl, indenyl) have been alkylated using this strategy, similar reactions using *N*-acyliminium ions remain unexplored.[13] Given their ability to catalyze an amidoalkylation process starting from common N,O-acetals, silyltriflates[2,3] and metal triflate salts[4,8a,b] may be valuable candidates for this purpose. However, as the catalytic performance displayed by $Sc(OTf)_3$ was inferior to that of $HNTf_2$ in some challenging amidoalkylations,[6a] and the use an acetoxy lactam was necessary to reach a good overall performance with $Bi(OTf)_3$,[8b] we were prompted to use stronger σ Lewis acids.

Recognizing the Lewis superacidity generally associated with the metal triflimidate species[14–16] and encouraged by the excellent activity and broad applicability displayed by $HNTf_2$ in the catalytic α-amidoalkylation of common N,O-acetals,[6] we explored the activity of triflimidate-based catalysts for the nucleophilic substitution reaction of the hydroxy group of hemi-N,O-acetals. We report herein a highly efficient and general tin(IV) triflimidate[17] catalyzed α-amidoalkylation reaction of the simplest *N*-acyliminium ion precursors, that is, hydroxy aminals, with various carbon-centered nucleophiles including silicon-based derivatives, β-dicarbonyl compounds, and electron-rich arenes. Rewardingly, we also document the first examples of the use of simple ketones as donor components as a significant bonus in catalytic *N*-acyliminium ion chemistry.

In a first set of reactions, 5-hydroxypyrrolidin-2-one **1** was used as the electrophilic precursor. Because of the lower stabilizing effect of the lone pair of electrons on nitrogen, N,O-acetals such as compound **1** are less prone to provide iminium ions than their 2-alkoxy carbamate analogues. Hence, the reaction of **1** with the weakly nucleophilic allyl trimethylsilane was chosen as an inherently difficult benchmark coupling reaction in order to identify the best catalytic systems.[18] Preliminary optimization studies unambiguously indicated that $Sn(NTf_2)_4$[19] used at a loading of 1 mol%, (Table 1, entry 1) outperforms other triflimidate salts and $Sc(OTf)_3$[4] as well.[20] With $Sn(NTf_2)_4$ as the catalyst and CH_3CN as solvent, reactions of **1** with the more nucleophilic silyl enol ethers **2b**–**d** were then undertaken, and excellent yields of the desired adducts **3b**–**d** were uniformly obtained at room temperature (Table 1, entries 2–6). The inherent weak reactivity of the hydroxylactams was reflected by the requirement of 2–3 equivalents of the sensitive silyl enol ethers to provide high yields of adducts **3** (cf. entries 3 and 4, Table 1).[21] We next extended these studies to the reactions

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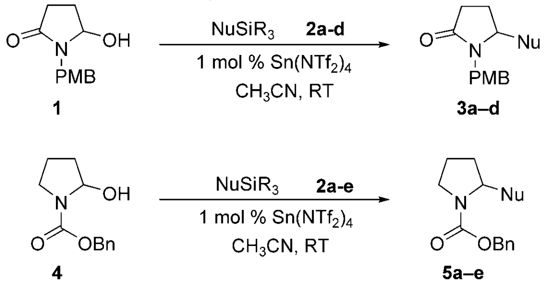
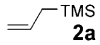
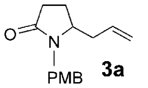
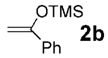
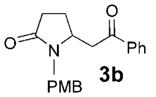
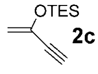
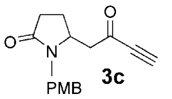
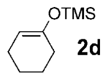
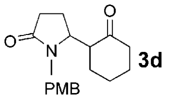
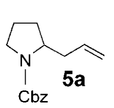
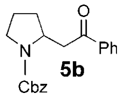
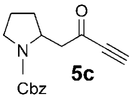
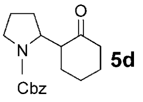
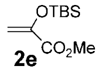
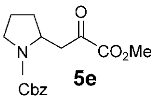
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/anie.200906036.

Table 1: $Sn(NTf_2)_4$-catalyzed amidoalkylation of N,O-acetals **1** and **4** with various silicon-based nucleophiles **2a–e**.



Entry	Substrate	$NuSiR_3$	Time	Product	Yield [%]
1[a,b]	**1**		3 h		81
2[c]	**1**		4 h		88
3[a]	**1**		4 h		68
4[d]	**1**	**2c**	3.5 h	**3c**	90
5[d]	**1**		2.25 h		93[e]
6[c]	**1**	**2d**	2.25 h	**3d**	93
7[a]	**4**	**2a**	1 h		94
8[f]	**4**	**2b**	6 h		92
9[a]	**4**	**2b**	6 h	**5b**	95
10[a]	**4**	**2c**	3.5 h		95
11[a]	**4**	**2d**	2 h		95[g]
12[f]	**4**	**2d**	2 h	**5d**	98[g]
13[a]	**4**		2 h		67

[a] Conducted with 2 equiv of the nucleophile. [b] Conducted at 50 °C. [c] Conducted with 2.5 equiv of the nucleophile. [d] Conducted with 3 equiv of the silyl enol ether. [e] Mixture of diastereoisomers 3:1. [f] Conducted with 1.5 equiv of the silyl enol ether. [g] Mixture of diastereoisomers 2.3:1. Abbreviations: Cbz = carbobenzoxy, PMB = *para*-methoxybenzyl, TBS = *tert*-butyldimethylsilyl, TES = triethylsilyl, TMS = trimethylsilyl.

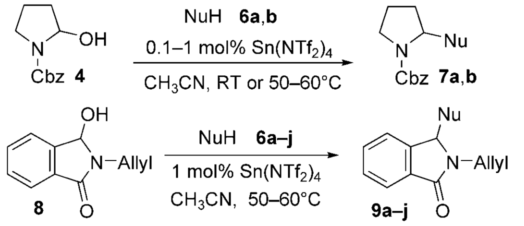
of the more reactive 2-hydroxy carbamate **4**, and the results of coupling with several nucleophiles **2a–e** using $Sn(NTf_2)_4$ as the catalyst are summarized in Table 1, entries 7–13. In almost all of the examples high efficiency was observed examined (92–98 % yields) with 1.5–2 equivalents of the nucleophile; this emphasizes that **4** is more reactive than **1** (Table 1, entries 6–12). When methyl pyruvate derivative **2e** was used, the desired adduct **5e** was isolated in only 67 % yield, most likely because of a retro-Mannich addition triggered by the extreme strength of the Lewis acidic catalyst.[23] Other metal triflimidate salts such as $Bi(NTf_2)_3$, $Cu(NTf_2)_2$, $In(NTf_2)_3$, and $Mg(NTf)_2$ were also tested as catalysts (1 mol %) with the more reactive electrophilic precursor **4**. With the particular exception of $Mg(NTf)_2$, which remained totally inefficient, these reagents displayed excellent catalytic activity.[22]

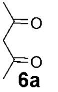
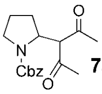
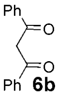
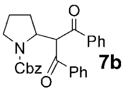
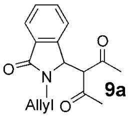
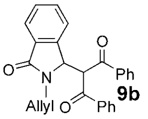
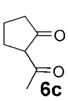
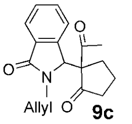
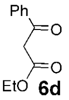
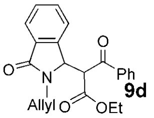
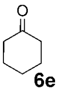
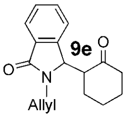
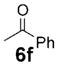
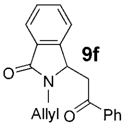
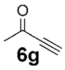
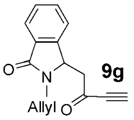
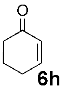
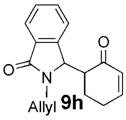
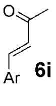
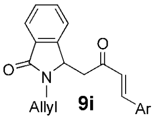
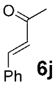
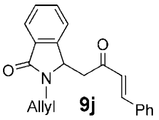
In addition to the enolation of **4** with silicon-based nucleophiles, $Sn(NTf_2)_4$ was also found to efficiently catalyze the alkylation with active methylene derivatives (Table 2, entries 1 and 2). In terms of eco-compatibility, these transformations are of great interest, as water is the only by-product released. Good yields of the Mannich-type adducts **7a**,**b** were obtained. Interestingly, the result presented in entry 2 points out that the extremely high acidic strength of the tin salt enabled isolation of the Mannich adducts **7b** in synthetically useful yields at a catalyst loading as low as 0.1 mol %.[23] The synthetic potential of this improved protocol is further exemplified by the fact that the reaction was performed on a 500 mg scale. For comparison purpose, a poor conversion (ca. 20 % conv.) was observed when the same reaction was carried out in the presence of 0.1 mol % $HNTf_2$.

On the other hand, the less reactive hydroxyphtalimide **8** gave the desired β-dicarbonylated adducts **9a–d** in almost quantitative yields with 1 mol % of $Sn(NTf_2)_4$ at 60 °C (Table 2, entries 3–6).[24] The excellent reaction profiles observed with **8** at this elevated temperature, even with the weakly nucleophilic components **6c** and **6d** (Table 2, entries 5 and 6), may be attributed to the high stability of the phtalimidic *N*-acyliminium ion. The distinct advantage of $Sn(NTf_2)_4$ in catalytic *N*-acyliminium ion chemistry was further emphasized by the use of ketones as a challenging class of nucleophiles. We indeed discovered that when we used only a slight excess amount (2–3 equiv) of six different and representative ketones, complete conversions and high yields of the Mannich adducts **9e–j** were systematically obtained after short reaction times (Table 2, entries 7–12). These remarkable results are the first examples of this type of direct catalytic α-amidoalkylations, indicating that also simple ketones could now be considered as adequate donors in catalytic intermolecular *N*-acyliminium ion chemistry.[25] Overall, our results highlight the distinct advantage of $Sn(NTf_2)_4$ in these transformations as the reaction of acetophenone (see Table 2, entry 8) catalyzed by 5 mol % $HNTf_2$ and 1 mol % $Bi(NTf_2)_3$ over 9 h in refluxing acetonitrile gave only moderate conversions of 60 % and 43 %, respectively.

To further demonstrate the general applicability of tin triflimidate in these direct alkylations, we briefly investigated the intramolecular Friedel–Crafts-type reactions of hydroxy lactams **10a–c**. These reactions were carried out using 1 mol % of $Sn(NTf_2)_4$ in acetonitrile at room temperature. The nucleophilic substitution proceeded rapidly with high efficiency affording the desired arylated products **11a–c** in 90–99 % yields under unprecedented extremely mild conditions (Table 3). The high reactivity observed with the Sn^{IV} triflimidate Lewis superacid at room temperature is note-

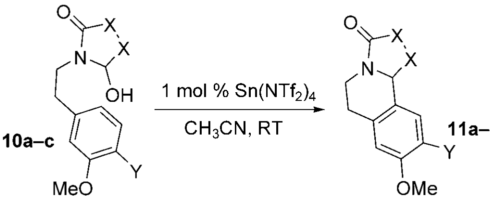
Table 2: Sn(NTf$_2$)$_4$-catalyzed amidoalkylation of N,O-acetals **4** and **8** by various enol nucleophiles **6a–j**.

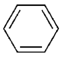
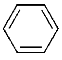


Entry	Aminal	NuH	*t*, *T*	Product	Yield [%]
1	**4**	 **6a**	30 min, RT	 **7a**	75
2	**4**	 **6b**	1 h 40, RT 40 min,[a] RT	 **7b**	38 81
3[b]	**8**	**6a**	4 h, 60 °C	 **9a**	>99
4[b],	**8**	**6b**	3 h, 60 °C	 **9b**	>99
5[b]	**8**	 **6c**	3 h, 60 °C	 **9c**	>99
6[c]	**8**	 **6d**	5 h, 50 °C	 **9d**	93
7[b,d]	**8**	 **6e**	4 h, 60 °C	 **9e**	>99
8[b,d]	**8**	 **6f**	3 h, 60 °C	 **9f**	>99
9[b,d]	**8**	 **6g**	4 h, 60 °C	 **9g**	95
10[b,d]	**8**	 **6h**	4 h, 60 °C	 **9h**	76
11[b,e,f]	**8**	 **6i**	2 h, 60 °C	 **9i**	79
12[b,e]	**8**	 **6j**	6 h, 60 °C	 **9j**	93

[a] Conducted with 0.1 mol% of the catalyst. [b] The reaction was carried out at 60 °C. [c] The reaction was carried out at 50 °C. [d] Conducted with 3 equiv of the ketone. [e] Conducted with 2 equiv of the ketone. [f] Ar = 3,4-(MeO)$_2$-C$_6$H$_3$.

Table 3: Sn(NTf$_2$)$_4$-catalyzed Friedel–Crafts-type cyclization of hydroxy lactams **10a–c**.



Entry	X–X	Y	Time	Product (yield [%])
1 2		OMe (**10a**)	30 min 20 min[a]	**11a** (99) **11a** (>99)
3		H (**10b**)	1 h	**11b** (91)[b]
4	CH$_2$–CH$_2$	OMe (**10c**)	1 h	**11c** (96)

[a] The reaction was carried out in CDCl$_3$ and was monitored by ^{1}H NMR spectroscopy; a similar reaction rate was measured in CD$_3$CN. [d] The regioisomer of **11b** was obtained in 4% yield.

worthy, given the weak reactivity displayed by hydroxy lactams in catalytic intermolecular alkylations.[24,26]

In summary, we have found that the extremely active Sn^{IV} triflimidate was able to efficiently catalyze the nucleophilic substitution reaction of hydroxy groups of unprotected hydroxy N,O-acetals. The catalytic system relies on the Lewis superacid properties of triflimidate-based reagents and requires low catalyst loadings (0.1–1 mol%) and mild conditions. The coupling reaction shows unprecedented applicability in terms of carbon nucleophiles, including allyltrimethylsilane, silyl enol ethers, active methylene derivatives, arenes and even ketones. The scope of catalytic *N*-acyliminium ion chemistry is broaden as well as the field of application of the promising Lewis superacidic tin(IV) triflimidate catalyst.[27] We believe that this readily available reagent should now be considered as a privileged candidate for developing highly efficient Lewis acid catalyzed transformations.

Received: October 27, 2009

Keywords: acetals · catalysis · Lewis acids · *N*-acyliminium ions

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[1] For some reviews, see: a) W. N. Speckamp, M. J. Moolenaar, *Tetrahedron* **2000**, *56*, 3817; b) B. E. Maryanoff, H.-C. Zhang, J. H. Cohen, I. J. Turchi, C. A. Maryanoff, *Chem. Rev.* **2004**, *104*, 1431.

[2] For a list of catalytic nucleophilic substitution reactions of *N*-acyliminium ion precursors using TMSOTf: see Ref. [3].

[3] R. Ben Othman, A. Fousse, T. Bousquet, M. Othman, V. Dalla, *Org. Lett.* **2005**, *7*, 2825.

[4] a) O. Okitsu, R. Suzuki, S. Kobayashi, *Synlett* **2000**, 989; b) O. Okitsu, R. Suzuki, S. Kobayashi, *J. Org. Chem.* **2001**, *66*, 809; c) M. K. S. Vink, C. A. Schortinghuis, J. Luten, J. H. van Maarseveen, H. E. Schoemaker, H. Hiemstra, F. P. J. T. Rutjes, *J. Org. Chem.* **2002**, *67*, 7869; d) P. N. M. Botman, F. J. Dommerholt, R. de Gelder, Q. B. Broxterman, H. E. Schoemaker, F. P. J. T. Rutjes, R. H. Blaauw, *Org. Lett.* **2004**, *6*, 4941; e) S. S. Kinder-

man, R. de Gelder, J. H. van Maarseven, H. E. Schoemaker, H. Hiemstra, F. P. J. T. Rutjes, *J. Am. Chem. Soc.* **2004**, *126*, 4100.

[5] a) D. Russowsky, R. Zen Petersen, M. N. Godoi, R. A. Pilli, *Tetrahedron Lett.* **2000**, *41*, 9939; b) L. A. F. de Godoy, N. Soares Camilo, R. A. Pilli, *Tetrahedron Lett.* **2006**, *47*, 7853.

[6] a) R. Ben Othman, T. Bousquet, M. Othman, V. Dalla, *Org. Lett.* **2005**, *7*, 5335; b) M. J. Tranchant, C. Moine, R. Ben Othman, T. Bousquet, M. Othman, V. Dalla, *Tetrahedron Lett.* **2006**, *47*, 4477.

[7] a) N. Soares Camilo, R. A. Pilli, *Tetrahedron Lett.* **2004**, *45*, 2821; b) O. Onomura, Y. Kanda, Y. Nakamura, T. Maki, Y. Matsumara, *Tetrahedron Lett.* **2002**, *43*, 3229; c) Y. Matsumura, T. Ikeda, O. Onomura, *Heterocycles* **2006**, *67*, 113.

[8] a) S. S. Kinderman, M. M. T. Wekking, J. H. van Maarseveen, H. E. Schoemaker, H. Hiemstra, F. P. J. T. Rutjes, *J. Org. Chem.* **2005**, *70*, 5519; b) F. Pin, S. Comesse, B. Garrigues, Š. Marchalín, A. Daïch, *J. Org. Chem.* **2007**, *72*, 1181; c) I. T. Raheem, P. S. Thiara, E. A. Peterson, E. N. Jacobsen, *J. Am. Chem. Soc.* **2007**, *129*, 13404; d) I. T. Raheem, P. S. Thiara, E. N. Jacobsen, *Org. Lett.* **2008**, *10*, 1577.

[9] For references on catalytic methods for C–C bond formation using allyl alcohols: *Silicon-based nucleophiles* a) T. Saito, Y. Nishimoto, M. Yasuda, A. Baba, *J. Org. Chem.* **2006**, *71*, 8516; b) R. Sanz, A. Martínez, D. Miguel, J. M. Álvarez-Gutiérrez, F. Rodríguez, *Adv. Synth. Catal.* **2006**, *348*, 1841; c) K. Motokura, N. Nakagiri, T. Mizugaki, K. Ebitani, K. Kaneda, *J. Org. Chem.* **2007**, *72*, 6006. β-Dicarbonyl nucleophiles without any additive: d) F. Ozawa, H. Okamoto, S. Kawagishi, S. Yamamoto, T. Minami, M. Yoshifuji, *J. Am. Chem. Soc.* **2002**, *124*, 10968; e) M. Yasuda, T. Somyo, A. Baba, *Angew. Chem.* **2006**, *118*, 807; *Angew. Chem. Int. Ed.* **2006**, *45*, 793. Nucleophilic (hetero)arenes: f) T. Tsuchimoto, K. Tobita, T. Hiyama, S.-I. Fukuzawa, *J. Org. Chem.* **1997**, *62*, 6997; g) M. Kimura, M. Futamata, R. Mukai, Y. Tamaru, *J. Am. Chem. Soc.* **2005**, *127*, 4592; h) S. Podder, J. Choudhury, S. Roy, *J. Org. Chem.* **2007**, *72*, 3129; i) I. Usul, S. Schmidt, M. Keller, B. Breit, *Org. Lett.* **2008**, *10*, 1207; j) K. Namba, H. Yamamoto, I. Sasaki, K. Mori, H. Imagawa, M. Nishizawa, *Org. Lett.* **2008**, *10*, 1767.

[10] Representative references on the catalytic alkylation of propargyl alcohols: Silicon-based nucleophiles: a) Y. Nishibayashi, I. Wakiji, Y. Ishii, S. Uemura, M. Hidai, *J. Am. Chem. Soc.* **2001**, *123*, 3393; b) M. R. Luzung, F. D. Toste, *J. Am. Chem. Soc.* **2003**, *125*, 15760; c) R. Sanz, A. Martinez, J. M. Álvarez-Guttiérez, F. Rodríguez, *Eur. J. Org. Chem.* **2006**, 1383; d) Z.-P. Zhan, J.-L. Yu, H.-J. Liu, Y.-Y. Cui, R.-F. Yang, W.-Z. Yang, J.-P. Li, *J. Org. Chem.* **2006**, *71*, 8298; e) Y. Nishibayashi, A. Shinoda, Y. Miyake, H. Matsuzawa, M. Sato, *Angew. Chem.* **2006**, *118*, 4953; *Angew. Chem. Int. Ed.* **2006**, *45*, 4835. β-Dicarbonyl nucleophiles: f) R. Sanz, D. Miguel, A. Martinez, J. M. Álvarez-Guttiérez, F. Rodríguez, *Org. Lett.* **2007**, *9*, 727. Nucleophilic (hetero)arenes: g) Y. Nishibayashi, M. Yoshikawa, Y. Inada, M. Hidai, S. Uemura, *J. Am. Chem. Soc.* **2002**, *124*, 11846; h) J. J. Kennedy-Smith, L. A. Young, F. D. Toste, *Org. Lett.* **2004**, *6*, 1325; i) H. Matsuzawa, Y. Miyake, Y. Nishibayashi, *Angew. Chem.* **2007**, *119*, 6608; *Angew. Chem. Int. Ed.* **2007**, *46*, 6488; j) H. Matsuzawa, K. Kanao, Y. Miyake, Y. Nishibayashi, *Org. Lett.* **2007**, *9*, 5561.

[11] For references on catalytic alkylation of benzyl alcohols: Silicon-based nucleophiles: a) M. Yasuda, T. Saito, M. Ueba, A. Baba, *Angew. Chem.* **2004**, *116*, 1438; *Angew. Chem. Int. Ed.* **2004**, *43*, 1414; b) G. V. M. Sharma, K. L. Reddy, P. S. Lakshmi, R. Ravi, A. C. Kunwar, *J. Org. Chem.* **2006**, *71*, 3967; β-Dicarbonyl nucleophiles: c) S. Shirakawa, S. Kobayashi, *Org. Lett.* **2007**, *9*, 311; d) M. Rueping, B. J. Nachtsheim, A. Kuenkel, *Org. Lett.* **2007**, *9*, 825; e) R. Sanz, D. Miguel, A. Martínez, J. M. Álvarez-Gutiérrez, F. Rodríguez, *Org. Lett.* **2007**, *9*, 2027; f) M. Noji, Y. Konno, K. Ishii, *J. Org. Chem.* **2007**, *72*, 5161; g) P. N. Liu, Z.-Y. Zhou, C. P. Lau, *Chem. Eur. J.* **2007**, *13*, 8610; (Hetero)arenes: h) K. Mertins, I. Novel, J. Kischel, A. Zapf, M. Beller, *Angew. Chem.* **2005**, *117*, 242; *Angew. Chem. Int. Ed.* **2005**, *44*, 238; i) I. Iovel, K. Mertins, J. Kischel, A. Zapf, M. Beller, *Angew. Chem.* **2005**, *117*, 3981; *Angew. Chem. Int. Ed.* **2005**, *44*, 3913; j) Ref. [10e]; k) M. Rueping, B. J. Nachtsheim, W. Ieawsuwan, *Adv. Synth. Catal.* **2006**, *348*, 1033; l) S. Lin, X. Lu, *J. Org. Chem.* **2007**, *72*, 9757.

[12] For references on the direct catalytic alkylation of saturated secondary and tertiary alcohols, see references [9a,c] and [11a,g].

[13] We are aware of only one example of a catalytic α-amidoalkylation from a hydroxy N,O-acetal, see reference [7a].

[14] For some references on the use of metal triflimidate salts as catalysts: a) H. Kobayashi, J. Nie, T. Sonoda, *Chem. Lett.* **1995**, 307; b) K. Mikami, O. Kotera, Y. Motoyama, H. Sakaguchi, M. Maruta, *Synlett* **1996**, 171; c) K. Ishihara, M. Kubota, H. Yamamoto, *Synlett* **1996**, 265; d) K. Ishihara, Y. Karumi, M. Kubota, H. Yamamoto, *Synlett* **1996**, 839; e) K. Ishihara, M. Kubota, H. Yamamoto, *Synlett* **1996**, 1045; f) P. A. Grieco, S. T. Handy, *Tetrahedron Lett.* **1997**, *38*, 2645; g) K. Ishihara, Y. Hiraiwa, H. Yamamoto, *Synlett* **2000**, 80; h) A. Marx, H. Yamamoto, *Angew. Chem.* **2000**, *112*, 182; *Angew. Chem. Int. Ed.* **2000**, *39*, 178; i) M. P. Sibi, G. Petrovic, *Tetrahedron: Asymmetry* **2003**, *14*, 2879; j) R. F. Sweis, M. P. Schramm, S. A. Kozmin, *J. Am. Chem. Soc.* **2004**, *126*, 7442; k) M. B. Boxer, H. Yamamoto, *Org. Lett.* **2005**, *7*, 3127; l) A. K. Chakraborti, Shivani, *J. Org. Chem.* **2006**, *71*, 5785; m) A. K. Buzas, F. M. Istrate, F. Gagosz, *Angew. Chem.* **2007**, *119*, 1159; *Angew. Chem. Int. Ed.* **2007**, *46*, 1141.

[15] Metal triflimide salts have often been recognized as presenting higher Lewis acid activity than the corresponding triflates. See the references [14a–e,g,j] and [16a].

[16] For our previous contribution in the use of metal triflimide salts in catalysis, see: a) F. Grau, A. Heumann, E. Duñach, *Angew. Chem.* **2006**, *118*, 7443; *Angew. Chem. Int. Ed.* **2006**, *45*, 7285; b) P. Lemechko, F. Grau, S. Antoniotti, E. Duñach, *Tetrahedron Lett.* **2007**, *48*, 5731; c) S. Antoniotti, E. Duñach, *Tetrahedron Lett.* **2009**, *50*, 2536.

[17] For our recent reports documenting a simple, efficient and broadly applicable water-free procedure for the preparation of anhydrous metal triflimidate and metal triflate salts, see: a) I. Favier, E. Duñach, *Tetrahedron Lett.* **2003**, *44*, 2031; b) S. Antoniotti, E. Duñach, *Chem. Commun.* **2008**, 993.

[18] This allylation reaction progressed very smoothly at room temperature, but complete conversions of **1** were achieved within short reaction times when the reaction was performed at 50 °C. See the Supporting Information for details.

[19] This catalyst was prepared according to the method reported in Ref. [17b] and used as a solvate $Sn(NTf_2)_4 \cdot 6\,DMSO$.

[20] Yields of **3a**: 53 % with $Bi(NTf_2)_3$, 27 % with $In(NTf_2)_3$, 24 % with $Cu(NTf_2)_2$, 0 % with $Mg(NTf_2)_2$, 5 % with $Sc(OTf)_3$. See the Suporting Information for more details.

[21] Yields were also typically above 90 % when only 2 equiv of silyl enol ethers **2b–d** was used with the methoxy lactam derived from **1** under similar reaction conditions.

[22] $Bi(NTf_2)_3$- and $In(NTf_2)_3$-catalyzed allylation of **4**: 94 % and 93 % yield, respectively ; $Cu(NTf_2)_2$-catalyzed amidoalkylation of cyclohexanone trimethylsilyl enol ether **2d**: 98 % yield.

[23] When 1 mol % of $Sn(NTf_2)_4$ was used, several side products formed and **7b** was isolated in only 40 % yield. A control experiment proved that $Sn(NTf_2)_4$ (1 mol % in CH_3CN) mediates the rapid decomposition of the Mannich adduct **7b**, most likely through retro-Mannich pathway triggered by the Lewis superacidity of the catalyst.

[24] The reaction between **8** and acetylacetone gave a nearly 70 % conversion after 24 h of reaction at room temperature in

acetonitrile. Under similar conditions, the more reactive acetoxylactame gave the Mannich adduct **9a** quantitatively.

[25] Our results complement the recent development of a copper-catalyzed oxidative Mannich reaction between tertiary amines and methyl ketones: Y. Shen, M. Li, S. Wang, T. Zhan, Z. Tan, C. C. Guo, *Chem. Commun.* **2009**, 953.

[26] The α-amidoalkylation of the trimethylsilyl enol ether of acetophenone (3 equiv) by the phtalimidic hydroxy lactam **8** does not exceed 30 % conversion over 24 h in the presence of 1 mol % of $Sn(NTf_2)_4$ or $HNTf_2$.

[27] During the preparation of this manuscript, Dixon and coworkers published a thermal, catalytic enantioselective Friedel—Crafts-type intramolecular amidoalkylation of in situ generated hydroxy lactames: M. C. Muratore, C. A. Holloway, A. W. Pilling, R. I. Storer, G. Trevitt, D. J. Dixon, *J. Am. Chem. Soc.* **2009**, *131*, 10796.