Tetrahedron Letters 53 (2012) 1843–1846

Contents lists available at SciVerse ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

$Yb(OTf)_3$-promoted effective benzylation and allylation with *N*-tosyl amino group as a stable leaving group

Jinqian Liu, Limin Wang *, Xingzhou Zheng, Aili Wang, Mengyun Zhu, Jianjun Yu, Qiang Shen

Shanghai Key Laboratory of Functional Materials Chemistry and Institute of Fine Chemicals, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, PR China

ARTICLE INFO

Article history:
Received 28 October 2011
Revised 13 January 2012
Accepted 31 January 2012
Available online 8 February 2012

Keywords:
Benzylation and allylation
Alkylation
$Yb(OTf)_3$
1,3-dicarbonyl compounds
N-tosyl amino group

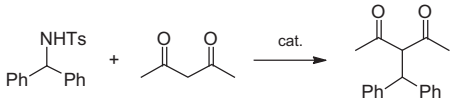
ABSTRACT

A simple, inexpensive, environmentally friendly, and highly efficient benzylation and allylation of 1,3-dicarbonyl compounds with sulfonamides in the presence of $Yb(OTf)_3$ is described. $Yb(OTf)_3$ was proved to be a good catalyst for the cleavage of sp^3 carbon–nitrogen bond. Various 1,3-dicarbonyl compounds can couple with a broad range of tosyl-activated benzylic and allylic amines to give diversely functionalized products in good to excellent yields.

Introduction

Following the rapid expansion of organic synthesis to the area of biomolecules, which ubiquitously possess amino groups, the research for the substitution of an amino group or its protected group at an ordinary sp^3 carbon with a protic carbon to form new functional groups is more and more urgent.[1] Benzylation and allylation are important for the formation of carbon–carbon bonds, in general, the cleavage of carbon–halogen bonds or carbon–oxygen bonds under acidic conditions has been widely applied to the formation of carbon–carbon bonds in chemical synthesis, benzylic and allylic halides and the corresponding sulfonates are frequently employed as the alkylating agents.[2] Nevertheless, strongly acidic hydrogen halides are inevitably generated as byproducts in the reaction and these acids are able to promote undesired side reactions such as elimination, overalkylation, or some other reactions. One of the methods to solve this problem is using alcohols as the substrates,[3] and another approach is making tosyl amino group as a leaving group.[4] Whereas, it is still a challenge for chemists to find suitable acids for the efficient substitution of an amino group or its protected group at an ordinary sp^3 carbon with a protic carbon to form new functional groups. In 2009, Tian and his co-workers developed a $ZnCl_2$–TMSCl double Lewis acid catalytic system for the sp^3 carbon–nitrogen cleavage.[4j] Recently, they also reported a $FeCl_3$-catalyzed cleavage of sp^3 carbon–nitrogen bonds to generate benzyl cation intermediates.[5]

Table 1
Catalyst Screening and Reaction Optimization[a]



1a **2a** **3aa**

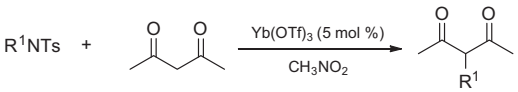
Entry	Catalyst	Solvent	Amount (mol %)	Yield[b] (%)
1	None	CH_3NO_2		<5
2	TsOH	CH_3NO_2	5	<5
3	H_2SO_4	CH_3NO_2	50	61
4	$AlCl_3$	CH_3NO_2	20	<5
5	$CuCl_2{\cdot}3H_2O$	CH_3NO_2	5	<5
6	$Sc(OTf)_3$	CH_3NO_2	5	99
7	$La(OTf)_3$	CH_3NO_2	5	97
8	$Yb(OTf)_3$	CH_3NO_2	2	59
9	$Yb(OTf)_3$	CH_3NO_2	4	89
10	$Yb(OTf)_3$	CH_3NO_2	5	99
11	$Yb(OTf)_3$	^{i}PrOH	5	<5
12	$Yb(OTf)_3$	DCE	5	65
13	$Yb(OTf)_3$	DMF	5	<5
14	$Yb(OTf)_3$	CH_3CN	5	60
15	$Yb(OTf)_3$	Toluene	5	0

[a] Reaction conditions: Compound **1a** (0.50 mmol), **2a** (0.60 mmol). The reaction was conducted at 100 °C for 18 h.
[b] Isolated yield.

* Corresponding author. Tel./fax: +86 21 64253881.
E-mail address: wanglimin@ecust.edu.cn (L. Wang).

0040-4039/$ - see front matter © 2012 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2012.01.141

Table 2
Catalytic alkylation of acetyl acetone with sulfonamides[a]



1a-1m **2a** **3aa-3am**

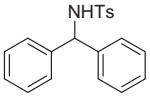
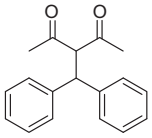
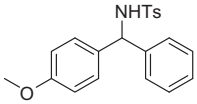
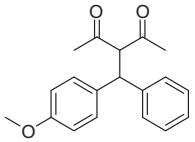
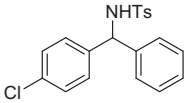
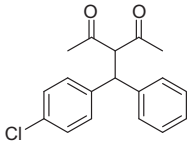
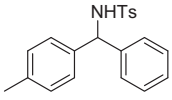
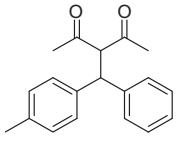
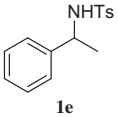
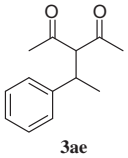
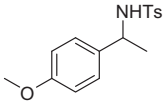
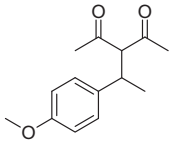
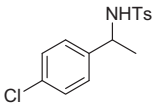
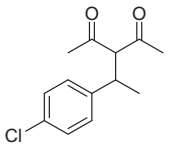
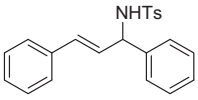
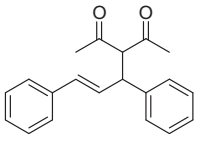
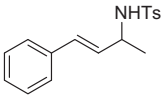
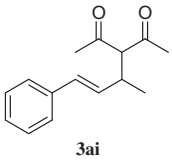
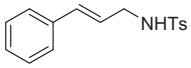
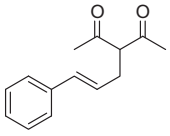
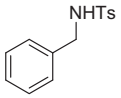
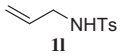
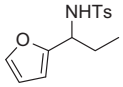
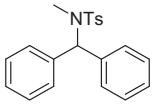
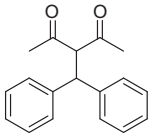
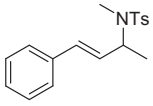
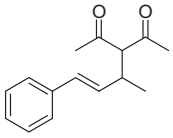
Entry	1	Time (h)	T (°C)	3	Yield[b] (%)
1	 **1a**	18	100	 **3aa**	99
2	 **1b**	6	rt	 **3ab**	94
3	 **1c**	18	100	 **3ac**	96
4	 **1d**	18	100	 **3ad**	99
5	 **1e**	18	100	 **3ae**	99
6	 **1f**	6	rt	 **3af**	95
7	 **1g**	18	100	 **3ag**	93
8	 **1h**	8	rt	 **3ah**	99
9	 **1i**	8	rt	 **3ai**	96

Table 2 (*continued*)

Entry	1	Time (h)	T (°C)	3	Yield[b] (%)
10	 **1j**	24	100	 **3aj**	66[c]
11	 **1k**	24	100		0
12	 **1l**	24	100		0
13	 **1m**	24	100		0
14	 **1n**	24	100	 **3aa**	99
15	 **1u**	8	rt	 **3ai**	96

[a] Reaction conditions: Compound **1** (0.50 mmol), **2a** (0.60 mmol), $Yb(OTf)_3$ (5 mol %), CH_3NO_2 (2 ml).
[b] Isolated yield.
[c] Keto/Enol = 1:2.

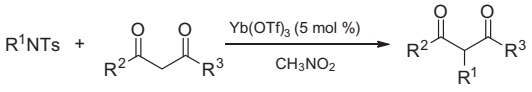
$Yb(OTf)_3$, as a relative inexpensive and representative lanthanide salts, with advantage of catalytic use, strong Lewis acidity even in pure water, preformed efficient catalytic activity in various organic transformations.[6] In continuation of our studies on the use of lanthanide salts,[7] we decided to investigate $Yb(OTf)_3$ for the reaction of protic carbon with sulfonamides.

Results and discussion

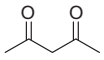
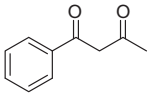
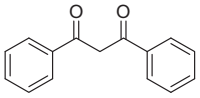
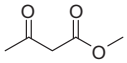
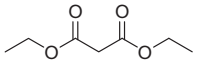
First, the model reaction of *N*-tosyl benzhydrylamine (**1a**) with acetyl acetone (**2a**) was examined in order to study the reaction conditions (Table 1). The reaction was carried out at 100 °C for 18 h. There was almost no product without catalysts (Table 1, entry 1). Various traditional Brønsted or Lewis acids, such as TsOH, H_2SO_4, $AlCl_3$, and $CuCl_2{\cdot}3H_2O$ were tried (Table 1, entries 2–5), but the yields were unsatisfactory. However, the remarkable improvement of the yield (99%) was obtained in the presence of $Yb(OTf)_3$ (Table 1, entry 10) or $Sc(OTf)_3$ (Table 1, entry 6) as catalyst in $MeNO_2$. We chose to carry out the reaction with $Yb(OTf)_3$ because of its lower cost compared to $Sc(OTf)_3$.[8] The loading of $Yb(OTf)_3$ for the reaction was examined (Table 1, entries 8–10), when the loading is 5 mol %, the best results were acquired. The Screening of solvents, such as CH_3CN, CH_3NO_2, ^{i}PrOH, DCE, DMF, and toluene (Table 1, entries 10–15), have also been explored. CH_3NO_2 was proved to be the best solvent at 100 °C for 18 h (Table 1, entry 10).

Based on the optimized reaction conditions, a broad range of tosyl-activated amines were examined in the $Yb(OTf)_3$-catalyzed alkylation of acetyl acetone (**2a**) (Table 2). The cross-coupling reaction of tosyl-activated benzylic amines with acetyl acetone (**2a**) proceeded smoothly to give the corresponding substituted 1,

Table 3
Reaction of 1,3-dicarbonyl compounds with sulfonamides[a]



1 **2** **3**

Entry	1	2	Time (h)	T (°C)	3	Yield[b] (%)
1	**1a**	 **2a**	18	100	**3aa**	99
2	**1e**		18	100	**3ae**	99
3	**1h**		8	rt	**3ah**	99
4	**1a**	 **2b**	18	100	**3ba**	97
5	**1e**		18	100	**3be**	84
6	**1h**		8	rt	**3bh**	96[c]
7	**1a**	 **2c**	18	60	**3ca**	91
8	**1e**		18	60	**3ce**	80
9	**1h**		8	rt	**3ch**	92
10	**1a**	 **2d**	18	100	**3da**	99
11	**1h**		6	rt	**3dh**	96
12	**1a**	 **2e**	24	100		0
13	**1h**		18	rt		0

[a] Reaction conditions: Compound **1** (0.50 mmol), **2** (0.60 mmol), $Yb(OTf)_3$ (5 mol %), CH_3NO_2 (2 ml).
[b] Isolated yield.
[c] *trans*/*cis* = 1:1.

3-diketones in good to excellent yields (Table 2, entries 1–7). The substrates bearing electron-donating groups on their aromatic rings reacted more easily even at room temperature for 6 h (Table 2, entry 2 and entry 6). With regard to the allylic alkylation of acetyl acetone (**2a**), tosyl-activated allylic amines were found to serve as suitable substrates at room temperature for 8 h (Table 2, entries 8–10). *N*-tosyl phenylmethanamine (**1k**),[9] *N*-tosyl prop-2-en-1-amine (**1l**)[10] and *N*-tosyl 1-(furan-2-yl)propan-1-amine (**1m**) did not couple with acetyl acetone probably because of the unstability of the carboncation. The use of **1j** obtained a mixture of enol and keto.[11] The third amines, such as **1n** and **1u**, also proved to be suitable substrates to this reaction (Table 2, entry 14 and 15).

A variety of 1,3-dicarbonyl were tried for the cross-coupling reaction with tosyl-activated benzylic and allylic amines (Table 3). The cross-coupling reaction of **1a** and **1e** with most 1,3-diketones proceeded smoothly with excellent yield (Table 3, entries 1–2, 4–5, 7–8). **2c** was more active, it coupled at a lower temperature (60 °C) for 18 h (Table 3, entries 7–8).

In addition, we tried some other 1,3-dicarbonyl compounds, such as **2d** and **2e**, which were thought to be less active for this kind of alkylation.[12] The coupling of **2e** with benzylic (**1a**) or allylic amines (**1h**) was disappointing, but the reaction of **2d** with benzylic (**1a**) and allylic amines (**1h**) could get high yield (up to 99%).

Conclusions

In summary, we have successfully reported the benzylation and allylation of various 1,3-dicarbonyl compounds with sulfonamides in the presence of $Yb(OTf)_3$. The cross-coupling reactions proceeded through a cleavage of sp^3 carbon–nitrogen bonds. The advantages of this reaction are broad scope, high yield, mild conditions, use of inexpensive catalyst, and simplicity of operation with the only side product.

Acknowledgments

This research was financially supported by the National Nature Science Foundation of China (20672035) and Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2012.01.141.

References and notes

1. (a) *Amino Acids, Peptides and Proteins in Organic Chemistry*; Hughes, A. B., Ed.; Wiley-VCH: Weinheim, 2009; Vols 1 and 2, (b) Dewick, P. M. *Medicinal Natural Products*, 3rd ed.; Wiley: Chichester, 2009; (c) Trauner, D. *Chem. Rev.* **2008**, *108*, 1499–1796; (d) Gladysz, J. A. *Chem. Rev.* **2005**, *105*, 4235–4812; (e) Walsh, C. T.; Wright, G. D. *Chem. Rev.* **2005**, *105*, 391–774.
2. For a review, see: Olah, G. A.; Krishnamurti, R.; Surya, G. K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, 1991; Vol. 3, pp 293–339.
3. (a) Yasuda, M.; Somyo, T.; Baba, A. *Angew. Chem., Int. Ed.* **2006**, *45*, 793–796; (b) Sanz, R.; Miguel, D.; Martinez, A.; Alvarez-Gutierrez, J. M.; Rodriguez, F. *Org. Lett.* **2007**, *9*, 2027–2030; (c) Sanz, R.; Martinez, A.; Miguel, D.; Alvarez-Gutierrez, J. M.; Rodriguez, F. *Adv. Synth. Catal.* **2006**, *348*, 1841–1845; (d) Noji, M.; Konno, Y.; Ishii, K. *J. Org. Chem.* **2007**, *72*, 5161–5167; (e) Rueping, M.; Nachtsheim, B. J.; Kuenkel, A. *Org. Lett.* **2007**, *9*, 825–828; (f) Motokura, K.; Fujita, N.; Mori, K.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *Angew. Chem., Int. Ed.* **2006**, *45*, 2605–2609; (g) Motokura, K.; Nakagiri, N.; Mizugaki, T.; Ebitani, K.; Kaneda, K. *J. Org. Chem.* **2007**, *72*, 6006–6015; (h) Kischel, J.; Mertins, K.; Michalik, D.; Zapf, A.; Beller, M. *Adv. Synth. Catal.* **2007**, *349*, 865–870; (i) Babu, S. A.; Yasuda, M.; Tsukahara, Y.; Yamauchi, T.; Wada, Y.; Baba, A. *Synthesis* **2008**, *11*, 1717–1724; (j) Funabiki, K.; Komeda, T.; Kubota, Y.; Matsui, M. *Tetrahedron* **2009**, *65*, 7457–7463; (k) Thirupathi, P.; Kim, S. S. *Tetrahedron* **2010**, *66*, 2995–3003.
4. (a) Seong, M. R.; Lee, H. J.; Kim, J. N. *Tetrahedron Lett.* **1998**, *39*, 6219; (b) Enders, D.; Narine, A. A.; Toulgoat, F.; Bisschops, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 5661; (c) Li, H.-H.; Dong, D.-J.; Tian, S.-K. *Eur. J. Org. Chem.* **2008**, 3623; (d) Liu, C.-R.; Li, M.-B.; Cheng, D.-J.; Yang, C.-F.; Tian, S.-K. *Org. Lett.* **2009**, *11*, 2543; (e) He, Q.-L.; Sun, F.-L.; Zheng, X.-J.; You, S.-L. *Synlett* **2009**, 1111; (f) Sun, F.-L.; Zheng, X.-J.; Gu, Q.; He, Q.-L.; You, S.-L. *Eur. J. Org. Chem.* **2010**, 47; (g) Esquivias, J.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2006**, *45*, 629; (h) Alonso, I.; Esquivias, J.; Carretero, J. C. *J. Org. Chem.* **2008**, *73*, 6401; (i) Liu, C.-R.; Li, M.-B.; Yang, C.-F.; Tian, S.-K. *Chem. Commun.* **2008**, 1249; (j) Liu, C.-R.; Li, M.-B.; Yang, C.-F.; Tian, S.-K. *Chem. Eur. J.* **2009**, *15*, 793.
5. (a) Liu, C.-R.; Li, M.-B.; Yang, C.-F.; Tian, S.-K. *Org. Lett.* **2010**, *12*, 3832–3835; (b) Wang, J.-Y.; Yang, C.-F.; Tian, S.-K. *Chem. Commun.* **2011**, *47*, 8343–8345.
6. (a) Curini, M.; Epifano, F.; Genovese, S.; Marcotullio, M. C.; Rosati, O. *Org. Lett.* **2005**, 1331–1333; (b) Curini, M.; Epifano, F.; Genovese, S. *Tetrahedron Lett.* **2006**, *47*, 4697–4700; (c) Curini, M.; Epifano, F.; Genovese, S. *Tetrahedron Lett.* **2007**, *48*, 2717–2720; (d) Genovese, S.; Epifano, F.; Pelucchini, C.; Curini, M. *Eur. J. Org. Chem.* **2009**, 1132–1135; (e) Genovese, S.; Epifano, F.; Pelucchini, C.; Procopio, A.; Curini, M. *Tetrahedron Lett.* **2010**, *51*, 5992–5995; (f) Epifano, F.; Genovese, S.; Rosati, O.; Tagliapietra, S.; Pelucchini, C.; Curini, M. *Tetrahedron Lett.* **2011**, *52*, 568–571; Dharma Rao, G. B.; Kaushik, M. P. *Tetrahedron Lett.* **2011**, *52*, 5104–5106.
7. (a) Ma, Y.; Wang, L.-M.; Shao, J.-H.; Tian, H. *Curr. Org. Chem.* **2007**, *11*, 1570–1573; (b) Wang, L.-M. et al *J. Fluorine Chem.* **2009**, *130*, 406–409; (c) Wang, L.-M.; Tang, J., et al *Tetrahedron* **2011**, *67*, 8465–8469.
8. Price from Strem Chemicals: $Yb(OTf)_3$ = $38.00/5 g, $Sc(OTf)_3$ = $172.00/5 g.
9. Cui, X.-J.; Shi, F.; Tse, M.-K.; Goerdes, D.; Thurow, K.; Beller, M.; Deng, Y.-Q. *Adv. Synth. Catal.* **2009**, *351*, 2949–2958.
10. Sun, W.-S.; Ma, X.-Z.; Hong, L.; Wang, R. *J. Org. Chem.* **2011**, *76*, 7826–7833.
11. This cross-coupling reaction is hard to proceed and rarely researched: Rueping, M.; Nachtsheim, B.-J.; Kuenkel, A. *Org. Lett.* **2007**, *9*, 825–828.
12. The examples of the similar products: Yuan, Y.; Feng, X.; Liu, X.-N.; Shi, Z.-Z. *Appl. Organomet. Chem.* **2007**, *21*, 958–964.