

ORGANIC CHEMISTRY

FRONTIERS

Accepted Manuscript



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this *Accepted Manuscript* with the edited and formatted *Advance Article* as soon as it is available.

You can find more information about *Accepted Manuscripts* in the [Information for Authors](#).

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard [Terms & Conditions](#) and the [Ethical guidelines](#) still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

ARTICLE

Addition of carbon nucleophiles to hemiaminals promoted by a Lewis acidic polyoxotungstate

Cite this: DOI: 10.1039/x0xx00000x

Wen-Jing Xuan, Candice Botuha, Bernold Hasenknopf and Serge Thorimbert*

Received 00th January 2012,

Accepted 00th January 2012

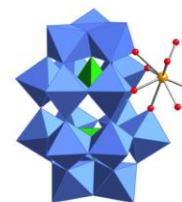
DOI: 10.1039/x0xx00000x

www.rsc.org/

A Lewis acidic hafnium(IV) ion incorporated in a polyoxotungstate (POM/Hf) was successfully employed as recoverable catalyst in the nucleophilic addition of carbon nucleophiles, such as silyl enol ethers, silyl ketene acetals, β -diketones and β -diketoesters, to unprotected hydroxy aminal at room temperature. The corresponding α -substituted heterocycles were obtained in good yields and the recovered POM catalyst could be reused up to three times without significant loss of activity.

In the synthesis of nitrogen-containing heterocycles, *N*-acyliminium ions have been widely used as efficient electrophiles.¹ Most often these stabilized ionic intermediates are generated from precursors such as amino nitrile, *N,O* acetals in acidic medium in the presence of stoichiometric quantities of Brønsted acids or traditional Lewis acids, such as $\text{BF}_3 \cdot \text{OEt}_2$, TiCl_4 , SnCl_4 , InCl_3 , NbCl_5 and $\text{Zn}(\text{OTf})_2$, which are environmentally harmful.^{2,3,4} More recently, catalytic versions have been reported that take advantage of the Lewis acidic properties of lanthanides triflates⁵ or *N*-trimethyl silyl-bis-(trifluoromethanesulfonyl)imide derivatives (HNTf_2 ; $\text{Zn}(\text{NTf}_2)_2$)⁶ or Brønsted organocatalysts.⁷ Even if those conditions are efficient for synthetic purpose,⁸ the need of alkoxy- or acetoxy-aminals lengthen the overall process. Indeed, from the point of view of atom economy and environmental reasons, the direct use of unprotected hemiaminals, which are more easily available, would be better.⁹ Some results in this field, including those with activated benzylic alcohols have been reported^{9d} but to our knowledge, none of them reports the recovery of the catalyst.

Polyoxometalates (POMs) as rapidly expanding green catalysts, are widely used in oxidation and acid catalyzed transformations.¹⁰ In a previous work, organic soluble Lanthanide complexes of POMs were synthesized by grafting Lewis acidic cations (Y^{3+} , Yb^{3+} , La^{3+} , Hf^{3+} , Sc^{3+} ...) onto monolacunary Dawson polyoxotungstates [$\text{P}_2\text{W}_{17}\text{O}_{61}$]¹⁰ and used as Lewis acid catalysts for Mannich type reactions.¹¹ We demonstrated that the coordination between the metal atoms and water molecules allows an indirect Brønsted acidity useful to catalyze Mukaiyama-aldol reactions.¹² In order to expand the application of those catalysts, the hafnium(IV) complex $\text{TBA}_5\text{K}[\alpha_1\text{-Hf}(\text{H}_2\text{O})_4\text{P}_2\text{W}_{17}\text{O}_{61}]$ (POM/Hf) (scheme 1) was selected as a representative species and used in the challenging nucleophilic addition reactions to *in situ* generated cyclic *N*-acyliminium ions from 5-*N*-Boc-2-hydroxypyrrolidine **1a** and *N*-Boc-2-hydroxypiperidine **1b** respectively.



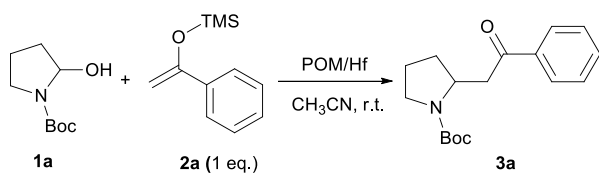
Scheme 1 Representation of the anion of $\text{TBA}_5\text{K}[\alpha_1\text{-Hf}(\text{H}_2\text{O})_4\text{P}_2\text{W}_{17}\text{O}_{61}]$. The phosphotungstic framework is shown as coordination polyhedra (blue W, green P). The Hf^{4+} ion (yellow) is coordinated to four terminal oxo ligands and four water molecules (red).

The choice for the α_1 isomer was dictated by steric and electronic considerations. Indeed, the $\text{Hf}(\text{IV})$ atom is a large cation that can be coordinated to the four oxido ligands in the lacunary site of the POM, and still has open coordination sites. It has been demonstrated that its α_2 isomer was more prone to dimerization which may lead to less active catalysts.^{11a} The chiral α_1 framework is also of particular interest for its potential as chiral catalyst.

We report herein our results concerning the POM/Hf-mediated nucleophilic additions of silyl enol ethers, ketene-acetals and activated methylene C-nucleophiles to hemiaminals that provide an easy access to substituted pyrrolidines and piperidines derivatives *via* cyclic *N*-acyliminium ions at room temperature.

We initially chose to examine the addition of 1-Phenyl-1-trimethylsilyloxyethylene **2a** to *N*-Boc-2-hydroxypyrrolidine **1a** as a model reaction in the presence of 10 mol % catalyst at room temperature in CH_3CN . The expected product **3a** was isolated in 69 % yield after 20 min. (Table 1, entry 2).

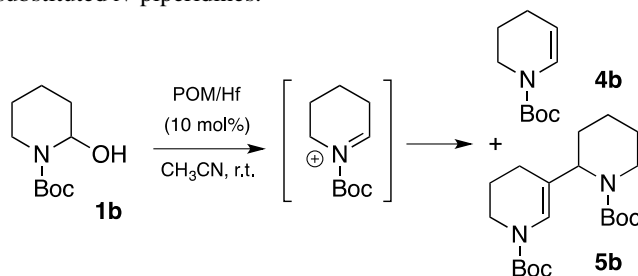
Table 1 Optimization of the Amount of Catalyst



Entry	POM/Hf (mol%)	Time	Yield (%)
1	-	24 h	-
2	10	20 min	69
3	1	1 h	72
4	0.25	17 h	80

It is possible to decrease the loading of catalyst down to 0.25 mol% albeit the reaction time should be increased up to 17 h to achieve a similar yield (Table 1, entry 4). However, the amount of 1 mol% of POM/Hf was chosen to extend the scope of the nucleophilic addition as well as the use of *N*-Boc-2-hydroxypiperidine **1b** as electrophile.

Unfortunately, the reaction of 1-Phenyl-1-trimethylsilyloxyethylene **2a** with *N*-Boc-2-hydroxypiperidine **1b** was not as efficient as for **1a**. Indeed, in the previous conditions a low yield of the expected product **3b** together with a total consumption of the starting material **1b** was observed (Table 2, entry 2), a pattern that results from the elimination of water from the corresponding iminium. Actually, the *in-situ* formed *N*-acyliminium intermediate resulting from the interaction of the *N*-Boc-2-hydroxypiperidine **1b** and POM/Hf can lead to the relatively stable enecarbamate by-product **4b**, or can undergo self-condensation to further form the “dimeric” enecarbamate **5b** which proved to be inert to the nucleophile **2a**.^{13,14} Both forms of enecarbamate cause the competitive loss of starting materials, which can explain the relatively low yield for all the 2-substituted *N*-piperidines.

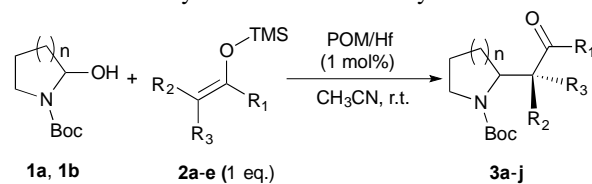


Scheme 2 Competitive elimination and dimerization of *N*-Boc-2-hydroxypiperidine **1b** via *N*-acyliminium.

Thereafter, the scope of the reaction was investigated with different substrates *N*-Boc pyrrolidine **1a** and *N*-Boc piperidine **1b** and a series of nucleophiles such as silyl enol ethers or ketene-acetals. The 1-(trimethylsilyloxy)-cyclohexene **2c** acts as a good nucleophile with **1a** and gives the corresponding 2-substituted *N*-Boc pyrrolidine **3e**, in 63% yield after 4h. Interestingly, an excellent yield of 98% as a 70:30 mixtures of diastereomers could be obtained by the use of 10 mol % of catalyst (Table 2, entry 5). Both 1- and 2-(trimethylsilyloxy) butadiene **2d** and **2e** reacted moderately with pyrrolidine **1a** (Table 2, entries 7 and 9).

Attempts to employ methyl trimethylsilyl dimethylketene acetal **2b** and 1-(trimethylsilyloxy)-cyclohexene **2c** as nucleophiles with *N*-Boc-2-hydroxypiperidine **1b** failed, which might be attributed to the relative steric hindrance of the secondary or tertiary reactive C-atom whereas the less substituted nucleophiles **2d-e** reacted in low yields. The competitive elimination of water on **1b** (vide supra) simultaneously to the partial hydrolysis of the nucleophiles should be responsible of these unproductive results. In conclusion, our investigation on the addition of trimethylsilyl enol ethers to the 5-membered *N*-acyliminium precursor **1a** under Lewis acidic POM/Hf revealed that moderate to high yields of the corresponding 2-substituted *N*-Boc pyrrolidines were obtained. Lower yields were observed for the reaction between the same nucleophiles and the 6-membered precursor **1b**.

Table 2. POM-catalyzed Reaction with Silylenol Ethers **2**.



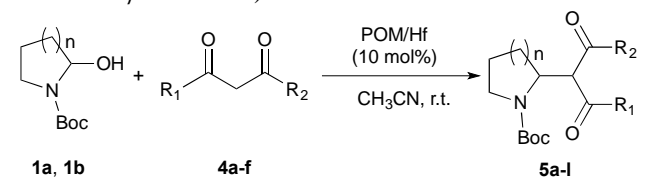
Entry	1	Nucleophile	Time (h)	Product	Yield (%)
1	1a		1	3a	72
2	1b	2a	0.3	3b	16
3	1a		18	3c	58 ^a
4	1b		16	3d	-
5	1a		4	3e ^b	63 ^c
6	1b	2c	4	3f	-
7	1a		24	3g	69
8	1b	2d	15	3h	11 ^d
9	1a		4	3i	45 ^a
10	1b	2e	4	3j	10 ^a

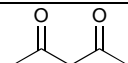
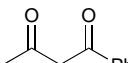
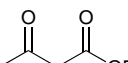
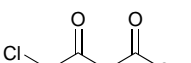
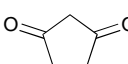
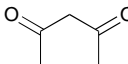
^a 10 mol% catalyst was used. ^b Diastereomeric ratio of **3e** (70 : 30). ^c 98% yield after 18 min. when 10 mol% catalyst was used. ^d 24% yield after 1.5 h when 4 mol% catalyst was used.

To further expand the scope of the reaction, the use of 1,3-dicarbonyl compounds **6** as nucleophiles was also investigated. Such enolizable C-nucleophiles are expected to react smoothly in such slightly acidic conditions. In the presence of POM/Hf,

they provided the corresponding 2-substituted pyrrolidine adduct **7** in moderate to good yields as illustrated by the representative examples in Table 3. Acyclic diketones or keto esters reacted with electrophile **1a** in yields ranging from 49 to 64% (Table 3 entries 1-6). Excellent yields were achieved in the reactions with 1,3-cyclopentanedione **6e** or 1,3-cyclohexanedione **6f**. The 2-substituted *N*-Boc-pyrrolidines **7i** and **7k** were isolated in 96 and 85 % yields respectively with 1 mol% of POM/Hf as catalyst (Table 3, entries 9 and 11). The desired products **7i-k** exist mainly in their corresponding enolic form as revealed by the corresponding ¹H and ¹³C NMR spectra (see SI). The products **7c**, **7e** and **7g** were formed as difficultly separable mixture of diastereoisomers. While the purification of **7d** allowed its isolation as a single, analytically pure diastereomer, **7h** and **7l** could not be obtained as pure products. Besides, the attempt to employ diethyl malonate as nucleophile failed so far. As previously observed with silylenol ethers as nucleophiles, lower yields were noticed with hydroxypiperidine **1b** in comparison to hydroxypyrrolidine **1a** (Table 3, compare entries 1,3,5,9 vs 2,4,6,10). The lower reactivity of the 6-membered iminium in comparison to the 5-membered one, should be responsible for the presence of elimination products.¹³⁻¹⁶

Table 3. POM-catalyzed Reaction with 1,3-dicarbonyls (β -diketones or β -ketoesters).

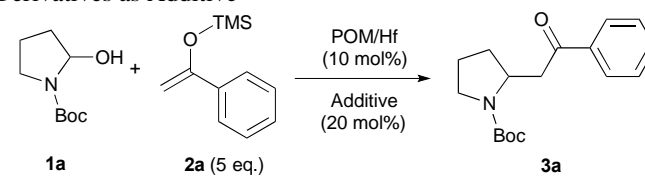


Entry	1	Nucleophile	Time (h)	Product	Yield (%)
1	1a		3	7a	63
2	1b	6a	1	7b	57
3	1a		20	7c	64
4	1b	6b	39	7d	8 ^a
5	1a		6.5	7e	55
6	1b	6c	22	7f	35
7	1a		5.5	7g	49
8	1b	6d	5.5	7h	-
9	1a		5.5	7i	96 ^b
10	1b	6e	4	7j	83 ^b
11	1a		2	7k	85 ^b
12	1b	6f	2	7l	-

^a only one diastereomer was successfully separated. ^b 1 mol% catalyst was used.

The Hf⁴⁺ ion in the catalyst has four coordinated water molecules which could either act as proton donor or could exchange with the reactive organic molecules. Indeed, in previous work, the POM/Hf demonstrated Lewis acidity in Mannich type reactions (Nitrogen type electrophiles) and induced Brønsted acidity for Mukaiyama-aldol reactions (oxygen type electrophiles). We thus decided to explore the acidity involved in the present activation of hemiaminals **1a,b**. For that purpose, pyridine and 2,6-di-*tert*-butylpyridine were used as additives during the POM/Hf catalyzed nucleophilic addition.¹⁷ Both bases are strong enough to capture protons and should inhibit any Brønsted acid-catalyzed reaction. While pyridine can also bind to metal centers, thus inhibiting strongly Lewis acid-catalyzed reactions, 2,6-di-*tert*-butylpyridine is highly hindered and should less coordinate to the Lewis acidic Hafnium ion located in our bulky POM. Therefore its effect on Lewis acid catalysis is expected to be weak. In our experiments, when pyridine (20 mol%) was added, the reaction between 1-phenylvinyl trimethylsilyl ether **2a** (5 equiv.) and *N*-Boc-2-hydroxypyrrolidine **1a** was totally halted, while no influence was observed in the presence of 2,6-di-*tert*-butylpyridine (Table 4).

Table 4. Mechanism Consideration, Inhibition with Pyridine Derivatives as Additive



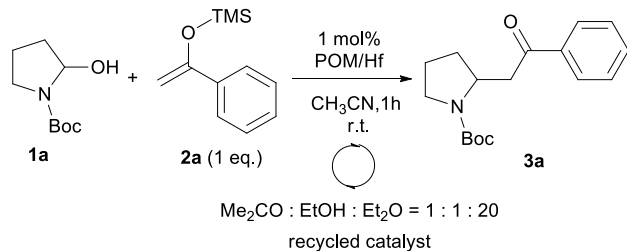
Entry	Additive	Time (h)	Yield (%)
1	-	1	69
2	2,6-di- <i>tert</i> -butylpyridine	1	72
3	pyridine	1	-

We conclude that the reaction is catalyzed by the POM/Hf in a Lewis acidic manner. First, one water molecule initially coordinated to the Hf atom is exchanged with the substrates. Then, the hydroxyaminal **1a,b** that is coordinated to the POM/Hf *via* its hydroxy group is converted into its corresponding iminium by the departure of the anionic POM/Hf-OH that could itself activated the pronucleophiles **2** and **6**.

We also examined the possible recovery of our catalyst. Due to the specific solubility of POMs, the catalyst should be easily recovered. Indeed, at the end of the reaction the addition of a solvent mixture of acetone/ethanol/diethyl ether (1/1/20) resulted in the precipitation of the POM/Hf as a white powder (with a recovery of >95% yield). In this study, the recyclability of catalyst has been tested on the 1 mol% scale, and its purity was checked by ³¹P NMR after each round. The catalyst can be

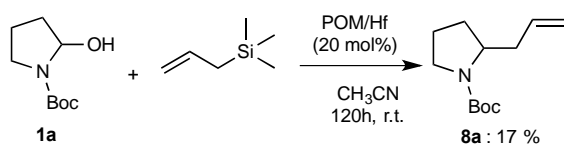
reused at least for three times without losing its reactivity. Slow decrease was then observed due to the few mg handled as well as probable slow decomposition and/or dimerization of the catalyst as time going.¹⁸

Table 5 Recyclability of the Catalyst.



Cycle	1	2	3	4
Yield (%)	72	74	69	49

Finally, we also examined the addition of allyltrimethylsilane to the reagent **1a**. By using 20 mol% of POM/Hf catalyst, a 17% yield of the expected 2-allyl carbamate product **8a** was obtained after 120 h. Although the yield is relatively low, this is the first time such kind of polyoxometalate complex (POM/Hf) allows the nucleophilic addition of allyltrimethylsilane onto emiaminal via the *in situ* formation of *N*-acyliminium ions.



Scheme 3 : Reaction with allyl silane

In summary, we used a Hafnium containing Dawson polyoxometalate as soluble catalyst for the carbon nucleophilic addition of silyl ether and methylene activated pro-nucleophiles to cyclic hemiaminals. The *in-situ* formed *N*-acyliminium ions reacted smoothly at room temperature giving the desired pyrrolidine and piperidine products in moderate to good yields. The POM/Hf has been proved to catalyze the reaction in a Lewis acidic pathway. It is playing a dual catalysis: activation of the nucleophile and the electrophile.. It can be easily precipitated and removed taking advantage of its specific solubility. Recycling of the catalyst is possible for a limited number of cycles. Studies are still underway for its further application in other organic reactions and its asymmetric versions.

Acknowledgements

We thank the Université P. et M. Curie (UPMC) and CNRS for funding. The Fédération de Recherche (FR2769) provided technical access for analysis. M. Forêt Jacquard kindly tested the reproducibility of the reactions. W.J.X. acknowledges the China Scholarship Council (CSC) for a PhD fellowship.

Notes and references

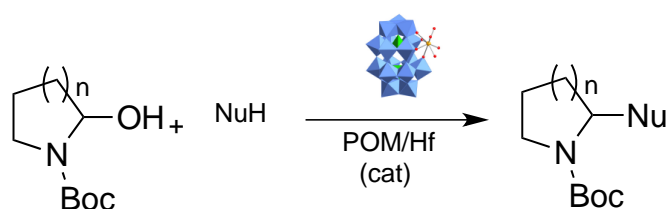
- Sorbonne Université, UPMC Univ Paris 06. UMR 8232, Institut Parisien de Chimie Moléculaire. F-75005 Paris, France.
- CNRS, UMR 8232, IPCM, F-75005 Paris, France.
- † Dedicated to Professor Max Malacria on the occasion of his 65th birthday.
- †† Electronic Supplementary Information (ESI) available: See DOI: 10.1039/b000000x/
- Selected reviews : (a) B.E. Maryanoff, H.-C. Zhang, J. H. Cohen, I. J. Turchi and C. A. Maryanoff, *Chem. Rev.*, 2004, **104**, 1431. (b) A. Yaziri and S. G. Pyne *Synthesis*, 2009, 339. (c) A. Yaziri and S. G. Pyne, *Synthesis*, 2009, 513. (d) N. R. Candeias, L. C. Branco, P. M. P. Gois, C. A. M. Afonso and A. F. Trindade, *Chem. Rev.*, 2009, **109**, 2703. (e) U. Martinez-Estibalez, A. Gomez-SanJuan, O. Garceia-Calvo, E. Aranzamendi, E. Lete and N. Sotomayor, *Eur. J. Org. Chem.*, 2011, 3610. (f) P.-Q. Huang, *Synlett*, 2006, 1133-1149. (g) P. M. Weintraub, J. S. Sabol, J. M. Kane and D. R. Borchering, *Tetrahedron*, 2003, **59**, 2953-2989. (g) D. Enders and J. P. Shillock, *Chem. Soc. Rev.*, 2000, **29**, 359.
- (a) C. J. Li, *Chem. Rev.*, 1993, **93**, 2023.
- (a) D. Russowsky, R. Z. Petersen, M. N. Godoi and R. A. Pilli, *Tetrahedron Lett.*, 2000, **41**, 9939. (b) C. K. Z. Andrade and R. A. F. Matos, *Synlett.*, 2003, 1189.
- R. A. Pilli and L. G. Robello, *Synlett.* 2005, 2297.
- (a) S. Kobayashi, M. Sugiura, H. Kitagawa and W. W.-L. Lam, *Chem. Rev.*, 2002, 102, 2227. (b) S. Kobayashi, *Eur. J. Org. Chem.*, 1999, 15. (c) for a recent application of Bi(OTf)₃ see A. E. Schneider, T. Beisel, A. Shemet and G. Manolikakes, *Org. Biomol. Chem.*, 2014, **12**, 2356.
- (a) H. Yamamoto, *Proc. Jpn. Acad. Ser. B.*, 2008, **84**, 134-146. (b) B. Mathieu and L. Ghosez, *Tetrahedron Lett.*, 1997, **38**, 5497. (c) R. Ben Othman, T. Bousquet, M. Othman and V. Dalla, *Org. Lett.*, 2005, **7**, 5335.
- (a) Y. S. Lee, Md. M. Alam and R. S. Keri, *Chem. Asian J.*, 2013, **8**, 2906. (b) T. Akiyama, J. Itoh and K. Fuchibe, *Adv. Synth. Catal.*, 2006, **348**, 999. (c) see a special issue of *Chem. Rev.*, 2007, **107**, n°12.
- Selected examples (a) M. E. Muratore, C. A. Holloway, A. W. Pilling, R. I. Storer, G. Trevitt and D. J. Dixon, *J. Am. Chem. Soc.*, 2009, **131**, 10796. (d) A. C. Breman, J. Dijkink, J. H. van Maarseveen, S. S. Kinderman and H. Hiemstra *J. Org. Chem.*, 2009, **74**, 6327. (c) H. Sun, C. Martin, D. Kesselring, R. Keller and K. D. Moeller, *J. Am. Chem. Soc.*, 2006, **128**, 13761. (c) U. Albrecht, H. Armbrust, P. Langer, *Synlett*, 2004, **143**. (d) J.-C. Adelbrecht, D. Craig, B. W. Dymock and S. Thorimbert, *Synlett*, 2000, 467. (e) J.-C. Adelbrecht, D. Craig and S. Thorimbert, *Tetrahedron Lett.*, 2001, **42**, 8369.
- (a) N. S. Camilo and R. A. Pilli, *Tetrahedron Lett.*, 2004, **45**, 2821. (b) R. Ben Othman, R. Affani, M.-J. Tranchant, S. Antoniotti, V. Dalla and E. Dunach, *Angew. Chem. Int. Ed.*, 2010, **49**, 776. (c) for an original copper catalyzed version see S.-L. Shi, X.-F. Wei, Y. Shimizu and M. Kanai, *J. Am. Chem. Soc.*, 2012, **134**, 17019. (d) M. Hamon, N. Dickinson, A. Devineau, D. Boliën, M.-J. Tranchant, C. Taillier, I. Jabin, D. C. Harrowven, R. J. Whitby, A. Ganesan and V. Dalla, *J. Org. Chem.*, 2014, **79**, 1900. (e) M. Szostak, B. Sautier and D. J. Procter *Chem. Commun.*, 2014, **50**, 2518.

- 1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60
- 10 (a) M. Misono, *Catal. Today*, 2005, **100**, 95. (b) "Applications of Polyoxometalates in Homogeneous Catalysis": R. Neumann in *Polyoxometalate Molecular Science*, Vol. 98; J. J. Borrás-Almenar, E. Coronado, A. Müller, M. T. Pope, Eds.; Kluwer, Dordrecht, **2003**, p. 327. (c) "Heterogeneous Catalysis by Heteropoly Compounds", I. V. Kozhevnikov, *ibid.*, p. 351. (d) X. Fang and C. L. Hill, *Angew. Chem. Int. Ed.*, 2007, **46**, 3877. (e) J. Geboers, S. Van de Vyver, K. Carpentier, K. de Blochouse, P. Jacobs and B. Sels, *Chem. Commun.*, 2010, **46**, 3577. see also (f) S. Luo, J. Li, H. Xu, L. Zhang and J. P. Cheng, *Org. Lett.*, 2007, **9**, 3675. (g) J. Li, S. Hu, S. Luo and J. P. Cheng, *Eur. J. Org. Chem.*, 2009, 132. (h) A. E. Kuznetsov, Y. V. Geletii, C. L. Hill, K. Morokuma and D. G. Musaev, *Inorg. Chem.*, 2009, **48**, 1871. (i) A. Sartorel, M. Carraro, A. Bagnò, G. Scorrano and M. Bonchio, *Angew. Chem. Int. Ed.*, 2007, **119**, 3319. (j) A. Sartorel, P. Miro, E. Salvadori, S. Romain, M. Carraro, G. Scorrano, M. Di Valentini, A. Llobet, C. Bo and M. Bonchio, *J. Am. Chem. Soc.*, 2009, **131**, 16051. (k) B. P. Burton-Pye and L. C. Francesconi, *Dalton Trans.*, 2011, **40**, 4421. (l) M. R. Antonio, J. Jing, B. P. Burton-Pye and L. C. Francesconi, *Dalton Trans.*, 2010, **39**, 7980. (m) S. Kosuke, M. Sugawa, Y. Kikukawa, K. Kamata, K. Yamaguchi and N. Mizuno, *Inorg. Chem.*, 2012, **51**, 6953. (n) H. G. T. Ly, G. Absillis, and T. N. Parac-Vogt, *Dalton Trans* 2013, **42**, 10929.
- 11 (a) C. Boglio, G. Lenoble, C. Duhayon, B. Hasenknopf, R. Thouvenot, C. Zhang, R. C. Howell, B. P. Burton-Pye, L. C. Francesconi, E. Lacôte, S. Thorimbert, M. Malacria, C. Afonso and J.-C. Tabet, *Inorg. Chem.*, 2006, **45**, 1389. (b) C. Boglio, G. Lemière, B. Hasenknopf, S. Thorimbert, E. Lacôte, and M. Malacria, *M. Angew. Chem. Int. Ed.*, 2006, **45**, 3324; (c) C. Boglio, K. Micoine, P. Rány, B. Hasenknopf, S. Thorimbert, E. Lacôte, M. Malacria, C. Alfonso and J.-C. Tabet, *Chem. Eur. J.*, 2007, **13**, 5426. (d) M. Bosco, S. Rat, N. Dupré B. Hasenknopf, E. Lacôte, M. Malacria, P. Rány, J. Kovensky, S. Thorimbert and A. Wadouachi, *ChemSusChem*, 2010, **3**, 1249. see also some other pioneer references : (e) Y. Kikukawa, S. Yamaguchi, K. Tsuchida, Y. Nakagawa, K. Uehara, K. Yamaguchi and N. Mizuno, *J. Am. Chem. Soc.*, 2008, **130**, 5472. (f) X. Zhang, J. Li, Y. Chen, J. Wang, L. Feng, X. Wang and F. Cao *Energy Fuels*, 2009 **23**, 4640. (g) J. Li, X. Zhang, W. Zhu and F. Cao, *ChemSusChem*, 2009, **2**, 177. (h) K. Nomiya, K. Ohta, Y. Sakai, T. Hosoya, A. Ohtake, A. Takakura, and S. Matsunaga *Bull. Chem. Soc. Jpn.* 2013, **86**, 80
- 12 (a) E. Derat, E. Lacôte, B. Hasenknopf, S. Thorimbert and M. Malacria, *J. Phys. Chem. A*, 2008, **112**, 13002. (b) N. Dupré P. Rány, Pauline, K. Micoine, C. Boglio, S. Thorimbert, E. Lacôte, B. Hasenknopf and M. Malacria, *Chem. Eur. J.*, 2010, **16**, 7256.
- 13 D. F. Oliveira, P. C. M. L. Miranda and R. D. C. Carlos, *J. Org. Chem.*, 1999, **64**, 6646.
- 14 (a) A. R. Pinder, *Nat. Prod. Rep.*, 1989, 515. (b) G. J. Koomen and M. J. Wanner, *J. Org. Chem.*, 1996, **61**, 5581.
- 15 R. A. Pilli, L. G. Robello, N. S. Camilo, J. Dupont, A. A. Moreira Lapis and B. A. da Silveira Neto, *Tetrahedron Lett.*, 2006, **47**, 1669.
- 16 (a) R. A. Pilli, M. A. Böckelmann and C. F. Alves, *J. Braz. Chem. Soc.* 2001, **12**, 634. (b) M. G. M. D'Oca, L. A. B. Moraes, R. A. Pilli and M. N. J. Eberlin. *J. Org. Chem.*, 2001, **66**, 3854.
- 17 (a) H. C. Brown and R. B. Johannesen, *J. Am. Chem. Soc.*, 1953, **75**, 16. (b) A. Corma, *Chem. Rev.*, 1995, **95**, 559. (c) Y. Kikukawa, S. Yamaguchi, Y. Nakagawa, K. Uehara, S. Uchida, K. Yamaguchi, N. Mizuno, *J. Am. Chem. Soc.*, **2008**, *130*, 15872.
- 18 (a) M. N. Sokolov, N. V. Izarova, E. V. Peresypkina, D. A. Mainichev and V. P. Fedin, *Inorg. Chim. Acta*, 2009, **362**, 3756. (b) Y. Saku, Y. Sakai, K. Nomiya, *Inorg. Chim. Acta*, 2010, **363**, 967.

ARTICLE

Table content abstract

Organic soluble $\text{TBA}_5\text{K}[\alpha_1\text{Hf}(\text{H}_2\text{O})_4\text{P}_2\text{W}_{17}\text{O}_{61}]$ (POM/Hf) catalyzes the addition of pronucleophiles (Silylenolethers, diketones, ketoesters, allylsilane) to unactivated hemiaminals.



Nu-H : Silylenolethers, diketones, ketoesters, allylsilane