Tetrahedron Letters 50 (2009) 1180–1183

Contents lists available at ScienceDirect

Tetrahedron Letters

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

Selective synthesis of sulfoxides and sulfones by tantalum(V) catalyzed oxidation of sulfides with 30% hydrogen peroxide

Masayuki Kirihara[a,*], Junya Yamamoto[a], Takuya Noguchi[a,b], Yoshiro Hirai[b]

[a] *Department of Materials and Life Science, Shizuoka Institute of Science and Technology, 2200-2 Toyosawa, Fukuroi, Shizuoka 437-8555, Japan*
[b] *Faculty of Science, Department of Chemistry, Toyama University, 3190 Gofuku, Toyama 930-8555, Japan*

ARTICLE INFO

Article history:
Received 8 October 2008
Revised 4 December 2008
Accepted 8 December 2008
Available online 24 December 2008

Keywords:
Oxidation
Hydrogen peroxide
Tantalum(V) chloride
Sulfide
Sulfoxide
Sulfone

ABSTRACT

The reaction of sulfides with 30% hydrogen peroxide catalyzed by tantalum(V) chloride in acetonitrile, *i*-propanol, or *t*-butanol selectively provided the corresponding sulfoxides in high yields. On the other hand, the reaction of sulfides with 30% hydrogen peroxide-catalyzed by tantalum(V) chloride or tantalum(V) ethoxide in methanol effectively gave the sulfones.

Sulfoxides and sulfones are useful synthetic intermediates for the construction of several important organic molecules.[1] Moreover, there are many biologically important compounds containing a sulfoxide- or sulfone moiety. Sulfoxides and sulfones are generally prepared via oxidation of the corresponding sulfide; however, it is often very difficult to stop the oxidation at the sulfoxide stage. For the synthesis of sulfones from sulfides, other oxidizable functional groups, such as alcohols or olefins, sometimes react as well producing undesirable compounds.[1]

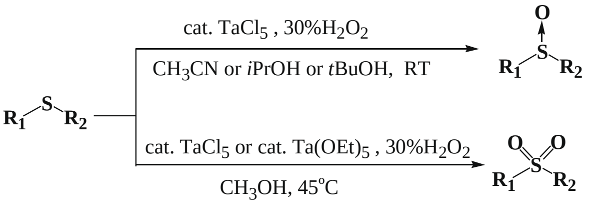
A large number of methods have been developed to overcome this drawback; however, most of these reactions require a stoichiometric amount of oxidant, resulting in undesirable waste.[2] Aqueous 30% hydrogen peroxide has recently been utilized as an attractive and environmentally benign oxidant[3] for the oxidation of sulfides, because it is inexpensive, easy to handle, safely stored, and produces only water as a side-product. Since the oxidation of sulfides with aqueous hydrogen peroxide in the absence of any catalysts requires a long reaction time, several transition metal (Ti,[4b] Mo,[4c] Fe,[4d] V,[4e,f] W,[4g,h] Re,[4i] Cu,[4j] Mn,[4k,l] and Au[4m]) compounds have been used as catalysts.[4a]

Although transition metal-catalyzed reactions produce the products in high yields, there are still some problems such as the use of acidic or base conditions (Mn), long reaction times (Fe and Mo), using hazardous solvents and/or reagents (Mo, V, Cu, and Mn), low chemoselectivity (Ti, Fe, V, W, and Re), and rare elements in the earth (Re and Au).

Recently, we reported several new synthetic methods for environmentally benign reactions using aqueous 30% hydrogen peroxide.[5] During the course of these studies, it was found that tantalum(V) chloride and tantalum(V) ethoxide are excellent catalysts for the oxidation of sulfides using aqueous 30% hydrogen peroxide (Scheme 1).

Higher valent vanadium compounds [V(V) or V(IV)] have been used as catalysts for hydrogen peroxide oxidation, utilizing various synthetic methods.[6] In contrast, although tantalum is a group 5 element like vanadium, tantalum compounds have seldom been used as oxidation catalysts despite being ideal for 'green chemistry', because they are far less toxic than vanadium compounds.[7a,b]

Recently, we found that the treatment of 1,3-dithianes with 30% hydrogen peroxide in the presence of a catalytic amount of tantalum(V) chloride and sodium iodide provided the carbonyl

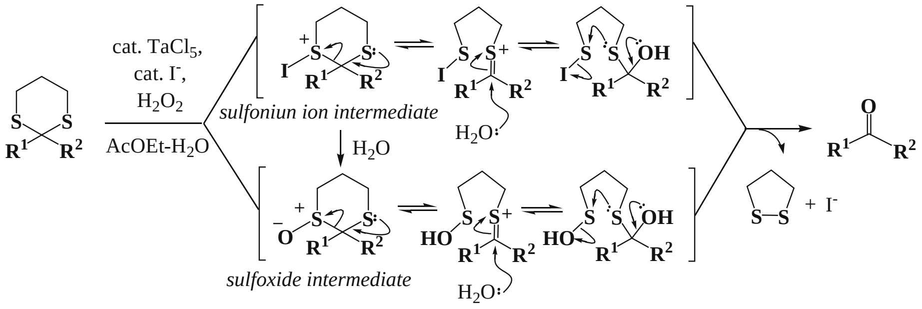


Scheme 1.

---

* Corresponding author. Tel.: +81 538 45 0166; fax: +81 538 45 0110.
E-mail address: kirihara@ms.sist.ac.jp (M. Kirihara).

0040-4039/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetlet.2008.12.064



Scheme 2.

compounds in high yield.[5b] This reaction is the result of oxidation of the sulfur atom of the 1,3-dithianes via sulfonium ion intermediates and/or sulfoxide intermediates (Scheme 2), and therefore by extension, it would be possible to oxidize sulfides under similar reaction conditions.

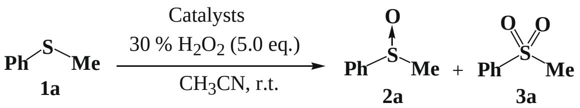
The oxidation of thioanisole (**1a**) with 30% hydrogen peroxide using tantalum(V) chloride as a catalyst in acetonitrile in the presence or absence of sodium iodide was investigated first (Table 1). Thioanisole was oxidized with hydrogen peroxide in the absence of catalysts to produce the sulfoxide (**2a**); however, it took quite some time to complete the oxidation (run 1). Tantalum(V) chloride was an excellent oxidation catalyst, and was effective even in the absence of sodium iodide (runs 2–4). The sulfoxide (**2a**) was efficiently obtained in all cases. The sulfone (**3a**) was the minor product (less than 10% yield) even for a long reaction time (24 h, run 4). Urea hydrogen peroxide (UHP) was not a good oxidant for the oxidation of sulfide catalyzed by tantalum(V) chloride (run 5).[8] Interestingly, a stoichiometric amount of sodium iodide inhibited the oxidation of thioanisole with hydrogen peroxide catalyzed by tantalum(V) chloride (run 7).

The oxidation of **1a** with 30% hydrogen peroxide was then investigated using several tantalum(V) compounds as catalysts in acetonitrile (Table 2). Tantalum(V) chloride and tantalum(V) ethoxide have catalytic activity for the oxidation of **1a** with hydrogen peroxide. However, tantalum(V) oxide was ineffective.

The oxidation of **1a** with 30% hydrogen peroxide using tantalum(V) chloride as a catalyst was examined in several solvents (Table 3). The less polar solvents constituting a heterogeneous solvent system with aqueous hydrogen peroxide were not effective (runs 1–3). In the polar solvents, **1a** was efficiently oxidized into the corresponding sulfoxide (**2a**) and/or sulfone (**3b**) (runs 4–14). The oxidative ability of this reaction system in more polar (or sterical less hindered) solvents (run 4: CH_3CN, run 7: MeOH, and run 10: EtOH) is greater than that in less polar (or sterical more hindered) solvents (run 5: CH_3CH_2CN, run 11: *i*PrOH, and run 13: *t*BuOH). The best conditions to prepare the sulfoxide (**2a**) selectively are the reaction in CH_3CN at room temperature (run 4), in *i*PrOH at 45 °C (run 12), or in *t*BuOH at 45 °C (run 14). The ideal condition to synthesize the sulfone (**3a**) is the reaction in MeOH at 45 °C (run 9).

In order to further examine the synthesis of sulfoxides (**2**), several sulfides (**1**) were treated with 30% hydrogen peroxide in

Table 1

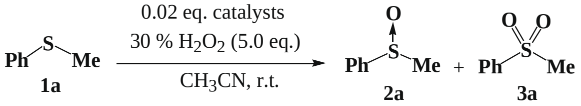


Run	$TaCl_5$ (equiv)	NaI (equiv)	Time (h)	Yield[a] (%)		
				1a	2a	3a
1	—	—	20.0	0	98.0	2.0
2	0.10	—	0.5	0	93.8	6.2
3	0.02	—	1.75	0	95.2	4.8
4	0.02	—	24.0	0	90.8	9.2
5[b]	0.02	—	30.0	43.2	56.8	0
6	0.10	0.10	1.0	0	88.2	11.8
7	0.10	1.00	24.0	94.9	5.1	0

[a] Determined by ^1H NMR (methyl protons).

[b] UHP was used instead of 30% H_2O_2.

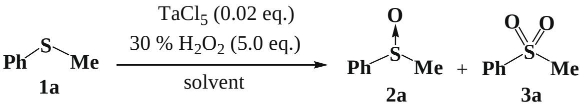
Table 2



Run	Catalyst (equiv)	Time (h)	Yield[a] (%)		
			1a	2a	3a
1	**$TaCl_5$**	1.75	0	96	4
2	**$Ta(OEt)_5$**	5.0	0	72	28
3	**Ta_2O_5**	20.0	0	94	6
4	**—**	20.0	0	98	2

[a] Determined by ^1H NMR (methyl protons).

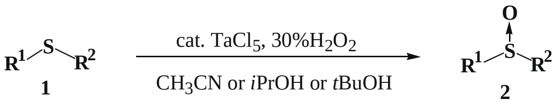
Table 3

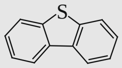


Run	Solvent	Time (h)	Temp.	Yield[a](%)		
				1a	2a	3a
1	CH_2Cl_2	5.5	rt	28	23	49
2	Toluene	e.5	rt	50	2	48
3	AcOEt	5.5	rt	17	58	25
4	CH_3CN	3.0	rt	0	95	5
5	CH_3CH_2CN	3.0	rt	11	82	7
6	CH_3CH_2CN	7	rt	0	79	21
7	MeOH	0.5	rt	0	86	14
8	MeOH	8.5	rt	0	3	97
9	MeOH	1.5	45 °C	0	1	99
10	EtOH	0.5	rt	7	87	6
11	*i*PrOH	0.5	rt	34	66	0
12	*i*PrOH	0.3	45 °C	0	95	5
13	*t*BuOH	0.5	rt	36	64	0
14	*t*BuOH	1.5	45 °C	1	96	**3**

[a] Determined by ^1H NMR (methyl protons).

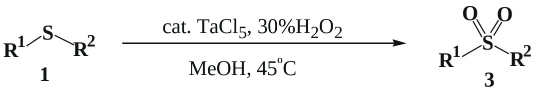
Table 4

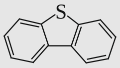


Entry	R^1	R^2	Solvent	$TaCl_5$ (equiv)	H_2O_2 (equiv)	Time (h)	Temp.	Yield[a](%)
1	Ph	$CH_2{=}CH_2CH$	CH_3CN	0.02	5	5.5	rt	95
2	Ph	$PhCH_2$	CH_3CN	0.02	5	2	rt	95
3			*i*PrOH	0.02	5	3.25	45 °C	94
4			*t*BuOH	0.02	5	3	45 °C	99
5	$PhCH_2$	$PhCH_2$	CH_3CN	0.02	5	1	rt	99
6			*i*PrOH	0.02	5	0.3	45 °C	94
7			*t*BuOH	0.02	5	5.7	45 °C	92
8	$PhCH_2$	CH_3	CH_3CN	0.02	5	0.5	rt	96
9	Ph	Ph	CH_3CN	0.1	20	2	rt	90
10			*i*PrOH	0.1	20	1.25	45 °C	83
11			*t*BuOH	0.1	20	2	45 °C	81
12			CH_3CN	0.1	20	8.5	50 °C	76

[a] Isolated yields.

Table 5

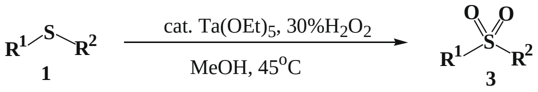


Entry	R^1	R^2	$TaCl_5$ (equiv)	H_2O_2 (equiv)	Time (h)	Yield[a] (%)
1	Ph	$CH_2{=}CH_2CH$	0.02	5	3	99
2	Ph	$PhCH_2$	0.02	5	2.5	96
3	$PhCH_2$	$PhCH_2$	0.02	5	2.5	99
4	$PhCH_2$	CH_3	0.02	5	0.25	97
5	Ph	Ph	0.1	20	3.5	90
6			0.1	20	20	98

[a] Isolated yields.

the presence of catalytic amounts of tantalum(V) chloride in acetonitrile, *i*-propanol, and *t*-butanol (Table 4). The sulfoxides were selectively obtained in all cases. It is notable that the olefin moiety was not oxidized at all (entry 2). Although 0.1 equiv of tantalum chloride and 20 equiv of hydrogen peroxide were required for the diaromatic sulfides, the corresponding sulfoxides were still obtained in relatively high yield (entries 9–12).

Table 6



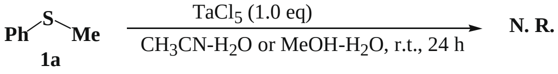
Entry	R^1	R^2	$TaCl_5$ (equiv)	H_2O_2 (equiv)	Time (h)	Yield[a] (%)
1	Ph	CH_3	0.02	5	1	99
2	Ph	$CH_2{=}CH_2CH$	0.02	5	1.3	100
3	Ph	$PhCH_2$	0.02	5	2.5	99
4	$PhCH_2$	$PhCH_2$	0.02	5	2.5	97
5	Ph	Ph	0.1	20	3	98

[a] Isolated yields.

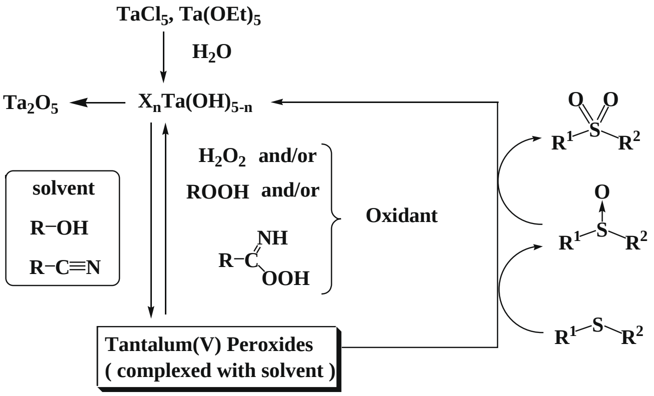
The treatment of several sulfides with 30% hydrogen peroxide in the presence of catalytic amounts of tantalum(V) chloride in methanol at 45 °C effectively afforded the corresponding sulfones (**3**) in all cases (Table 5). The olefin was inert under the reaction condition (entry 1). For the diaromatic sulfides, 0.1 equiv of tantalum chloride and 20 equvi of hydrogen peroxide were required to produce **3** in high yields (entries 5 and 6).

The oxidation of sulfides (**1**) with 30% hydrogen peroxide using tantalum(V) ethoxide as a catalyst was further examined in methanol (Table 6). The corresponding sulfones (**3**) were obtained in high yield.

To investigate the reaction mechanism, **1a** was treated with an equimolar amount of tantalum(V) chloride in aqueous acetonitrile



Scheme 3.



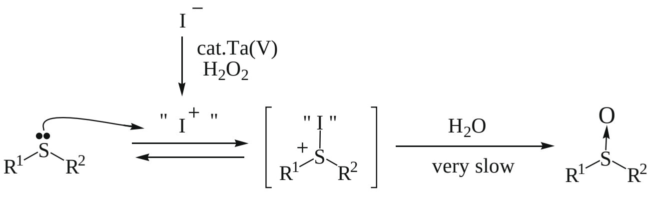
Scheme 4.

or aqueous methanol in the absence of hydrogen peroxide. In this case, **1a** was completely unreacted and was quantitatively recovered. This result means that tantalum(V) chloride itself is not the oxidizing agent in the reaction system (Scheme 3).[8]

A plausible reaction mechanism is shown in Scheme 4. Tantalum(V) chloride or tantalum(V) ethoxide immediately reacts with water to form tantalum(V) hydroxides. The resulting hydroxides react with hydrogen peroxide or peroxides derived from the reaction of hydrogen peroxide with the solvents (alcohols or nitriles) to produce tantalum(V) peroxides. Since tantalum(V) compounds act as Lewis acid,[11e–o] alcohols and nitriles coordinate with tantalum(V) peroxides to produce tantalum(V) peroxide complexes. The tantalum(V) peroxide complexes oxidize sulfides or sulfoxides, and revert to tantalum(V) hydroxides (or their complex of the solvent). The resulting tantalum(V) hydroxides react with peroxides to form the tantalum(V) peroxide complexes again. Unfortunately, the chemistry of tantalum(V) peroxides is almost unknown even in inorganic chemistry. Therefore, the exact structure of tantalum(V) peroxide complexes is unclear.[9] Although the solvent effect is not perfectly clear, it is assumed that the coordinative properties of the solvents affect the oxidative ability of the tantalum(V) peroxides. Further details of this reaction and the structure of tantalum(V) peroxide complexes are currently under investigation.

In the presence of sodium iodide, iodo cation equivalents or iodine derived from the oxidation of the iodo anion reacts with a sulfide to produce an iodosulfonium ion intermediate. The intermediate subsequently reacts with water to form the sulfoxide (Scheme 5). It has been reported that the first step is fast and reversible, and the second step is very slow.[10] The formation of the iodosulfonium ions prevents the reaction of sulfides with tantalum(V) peroxide complexes, therefore sulfides did not produce the oxidized products in the presence of the molar equivalent of sodium iodide.

A general experimental procedure for the oxidation of sulfides is thus the following: A mixture of sulfide (1.0 mmol), tantalum chloride (7.1 mg, 0.02 mmol), and 30% hydrogen peroxide (0.5 mL, 5 mmol) in a solvent (2 mL, acetonitrile or methanol) is stirred at room temperature (acetonitrile) or 45 °C (methanol). The reaction is monitored by thin layer chromatography (TLC). After **1** disappears from the TLC, saturated aqueous sodium thiosulfate (15 mL) is added to the reaction mixture, followed by extraction with ethyl acetate (20 mL × 3). The combined organic phase is washed with brine, dried over anhydrous magnesium sulfate, and evaporated. Chromatography on silica gel gives pure products (**2** or **3**).



Scheme 5.

References and notes

1. (a) Drabowicz, J.; Kielbsinski, P.; Mikolajczyk, M.; in Patai, S.; Rappoport, Z.; Stirling, C. (Eds.), The Chemistry of Sulphone and Sulphoxide, John Wiley and Sons, NY, 1988.; (b) Carreno, M. C. *Chem. Rev.* **1995**, *95*, 1717–1760; (c) Frenanez, I.; Khiar, N. *Chem. Rev.* **2003**, *103*, 3651–3706.
2. (a) Oae, S.; Kawai, T.; Furukawa, N. *Tetrahedron Lett.* **1984**, *35*, 69–72; (b) Nicolaous, K. C.; Magolda, R. L.; Sipio, W. J.; Lysenko, W. E.; Joullie, M. M. *J. Am. Chem. Soc.* **1980**, *102*, 3784–3793; (c) Leonard, N. J.; Johnson, C. R. *J. Org. Chem.* **1962**, *27*, 282–284; (d) Iranpoor, N.; Firouzabadi, H.; Pourali, A.-R. *Synlett* **2004**, 347–349; (e) Hajipour, A. R.; Kooshki, B.; Ruoho, A. E. *Tetrahedron Lett.* **2005**, *46*, 5503–5506; (f) Ozanne-Beaudenon, A.; Quideau, S. *Tetrahedron Lett.* **2006**, *47*, 5869–5873.
3. Jones, C. W. in Application of Hydrogen Peroxide and Derivatives, RCS Crean Technology Monographs. Formerly of Solvay Interox R&D, Windnes, UK. 1999.; Noyori, R.; Aoki, M.; Sato, K. *Chem. Commun.* **2003**, 1977–1986.
4. (a) Kaczorowska, K.; Kolarska, Z.; Mitka, K.; Kowalski, P. *Tetrahedron* **2005**, *61*, 8315–8327; (b) Mba, M.; Prins, L. J.; Licini, G. *Org. Lett.* **2007**, *9*, 21–24; (c) Jeyakumar, K.; Chand, K. *Tetrahedron Lett.* **2006**, *47*, 4573–4576; (d) Egami, H.; Katsuki, T. *J. Am. Chem. Soc.* **2007**, *129*, 8940–8941; (e) Blakemore, P. R.; Burge, M. S. *J. Am. Chem. Soc.* **2007**, *129*, 3068–3069; (f) Mohammadpoor-Baltork, I.; Hill, M.; Caggiano, L.; Jackson, R. F. W. *Synlett.* **2006**, 3540–3544; (g) Sato, K.; Hyodo, M.; Aoki, M.; Zheng, X.-Q.; Noyori, R. *Tetrahedron* **2001**, *57*, 2469–2476; (h) Shi, X.-Y.; Wei, J.-F. *J. Mol. Catal. A* **2008**, *280*, 142–147; (i) Yamazaki, S. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2955–2959; (j) Kelly, P.; Lawrence, S. E.; Maguire, A. R. *Synlett* **2007**, 1501–1506; (k) Hosseinpoor, F.; Golchoubian, H. *Tetrahedron Lett.* **2006**, *47*, 5195–5197; (l) Alonso, D. A.; Nájera, C.; Varea, M. *Tetrahedron Lett.* **2002**, *43*, 3459–3461; (m) Yuan, Y.; Bian, Y. *Tetrahedron Lett.* **2007**, *48*, 8518–8520.
5. (a) Kirihara, M.; Okubo, K.; Koshiyama, T.; Kato, Y.; Hatano, A. *ITE Lett.* **2004**, *5*, 279–281; (b) Kirihara, M.; Harano, A.; Tsukiji, H.; Takizawa, R.; Uchiyama, T.; Hatano, A. *Tetrahedron Lett.* **2005**, *46*, 6377–6380; (c) Kirihara, M.; Ogawa, S.; Noguchi, T.; Okubo, K.; Monma, Y.; Shimizu, I.; Simosaki, R.; Hatano, A.; Hirai, Y. *Synlett* **2006**, 2287–2289; (d) Kirihara, M.; Asai, Y.; Ogawa, S.; Noguchi, T.; Hatano, A.; Hirai, Y. *Synthesis* **2007**, 3286–3289; (e) Noguchi, T.; Hirai, Y.; Kirihara, M. *Chem. Commun.* **2008**, 3040–3042.
6. Hirao, T.; in ACS Symposium Series 974 (Vanadium: The Versatile Metal), American, pp 2–27.
7. (a) Zenz, C.; Bartlett, J. P.; Thiede, W. H. *Arch. Environ. Health* **1962**, *5*, 542–546; (b) Browning, E. *Toxicity of industrial Metals*, 2nd ed.; Appleton-Century-Crofts: New York, 1969. 340–347.
8. A referee asked what could be the effect of oxygen and other oxidizing agents such as Oxone on the selectivity. We think that oxygen cannot be an oxidant in this reaction system, because the sulfide (**1a**) is inert without hydrogen peroxide as shown in Scheme 3. We examined the reaction depicted in Scheme 3 under air and oxygen atmosphere. Since it has been reported that Oxone rapidly oxidizes sulfides to the corresponding sulfones without any catalysts, we did not examine the reaction of sulfides with oxone in the presence of $TaCl_5$. Chemical Society, 2007 and references cited therein.
9. A referee pointed out that it would be better if comments on experimental results and mechanistic aspects are discussed throughout the manuscript, instead of having this listing of tables of results followed by some discussions in the last part of the manuscript. We think that the active species of this oxidation must be tantalum(V) peroxide complexes. Unfortunately, the chemistry of tantalum(V) peroxide is almost unknown even in inorganic chemistry, it is impossible to discuss the mechanistic aspects throughout the manuscript.
10. Higchi, T.; Gensch, K.-H. *J. Am. Chem. Soc.* **1966**, *5*, 5486–5487.
11. Recent reports of organic syntheses using tantalum reagents: (a) Takai, K.; Yamada, M.; Odaka, H.; Utimoto, K. *J. Org. Chem.* **1994**, *59*, 5852–5853; (b) Aoyagi, Y.; Tanaka, W.; Ohta, A. *J. Chem. Soc., Chem. Commun.* **1994**, 1225–1226; (c) Takai, K.; Yamada, M.; Odaka, H.; Utimoto, K.; Fujii, T.; Furukawa, I. *Chem. Lett.* **1995**, 315–316; (d) Takai, K.; Yamada, M.; Utimoto, K. *Chem. Lett.* **1995**, 851–852; (e) Chandrasekhar, S.; Takhi, M.; Uma, G. *Tetrahedron Lett.* **1997**, *38*, 8089–8092; (f) Chandrasekhar, S.; Takhi, M.; Reddy, Y. R.; Mohapatra, S.; Rao, C. R.; Reddy, K. V. *Tetrahedron* **1997**, *53*, 14997–15004; (g) Chandrasekhar, S.; Reddy, B. V. *Synlett* **1998**, 851–852; (h) Chandrasekhar, S.; Ramachander, T.; Takhi, M. *Tetrahedron Lett.* **1998**, *39*, 3263–3266; (i) Chandrasekhar, S.; Mohanty, P. K.; Raza, A. *Synth. Commun.* **1999**, *29*, 257–262; (j) Chandrasekhar, S.; Ramachandar, T.; Prakash, S. J. *Synthesis* **2000**, 1817–1818; (k) Chandrasekhar, S.; Prakash, S. J.; Jagadehwar, V.; Narsihmulu, C. *Tetrahedron Lett.* **2001**, *42*, 5561–5563; (l) Andes, C.; Harkins, S. B.; Murtuza, S.; Oyler, K.; Sen, A. *J. Am. Chem. Soc.* **2001**, *123*, 7423–7424; (m) Shibata, I.; Nose, K.; Sakamoto, K.; Yasuda, M.; Baba, A. *J. Org. Chem.* **2004**, *69*, 2185–2187; (n) Chandrasekhar, S.; Ramachandar, T.; Shyamsunder, T. *Indian J. Chem., Sect. B* **2004**, *43B*, 813–838; (o) Chandrasekhar, S.; Jaya Prakash, S.; Shyamsunder, T.; Ramachandar, T. *Synth. Commun.* **2005**, *35*, 3127–3131.