

Article

SnCl₄·5H₂O: A Highly Efficient Catalyst for Hydration of Alkyne

Dongxue Chen ^{1,2,3}, Dantong Wang ^{1,2,3}, Wei Wu ^{1,2,3,*} and Linfei Xiao ^{1,2,3,*}

¹ Key Laboratory of Chemical Engineering Process & Technology for High-efficiency Conversion, College of Heilongjiang Province, Heilongjiang University, Harbin 150080, China;

E-Mails: yaoyaoacry@163.com (D.C.); dantwang@163.com (D.W.)

² International Joint Research Center of Catalytic Technology, Heilongjiang University, Harbin 150080, China

³ School of Chemistry and Material Sciences, Heilongjiang University, Harbin 150080, China

* Authors to whom correspondence should be addressed; E-Mails: wuwei@hlju.edu.cn (W.W.); xiaolf@hlju.edu.cn (L.X.); Tel./Fax: +86-451-8660-9227 (W.W. & L.X.).

Academic Editor: Rajender S. Varma

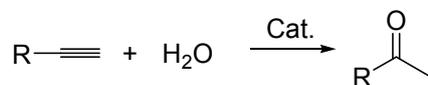
Received: 20 March 2015 / Accepted: 13 May 2015 / Published: 21 May 2015

Abstract: SnCl₄·5H₂O is a highly efficient catalyst in the hydration of terminal alkynes that affords carbonyl compounds in high to good yields. Under the optimized reaction conditions, the moderate to excellent yields of corresponding ketones were obtained when the aromatic and aliphatic terminal alkynes were used as substrates. With using diphenylacetylene as an internal alkyne, the corresponding ketone was not detected in the reaction mixture.

Keywords: hydration; alkynes; ketones; stannic chloride pentahydrate

1. Introduction

The hydration of alkyne is one of the most important methods for the synthesis of ketone (Scheme 1) [1,2]. The addition of water to the alkyne, with a perfect atom economy, is regarded as a convenient and efficient access to carbonyl compound in modern organic synthesis [3,4].



Scheme 1. The hydration of alkyne.

The classical methods for the hydration of alkynes have been carried out using mercury (II) salts as Lewis acidic catalysts in aqueous sulfuric acid [5]. However, the toxicity of mercury (II) and the requirement of strong acid have produced pollution problems that have limited its applications [6]. As possible alternative catalysts, transition-metal complexes containing Rh [7], Ir [8], Pb [9], Pt [10], Au [11–16], Ag [17,18], Fe [19], Co [20] have been reported to catalyze the hydration of alkyne in good yields. At the same time, anti-Markovnikov hydration of terminal alkyne have been carried out in the presence of ruthenium complex [21,22]. It was noted that the strong Brønsted acid such as TfOH or Tf₂NH [23] or concentrated H₂SO₄ [24], HCO₂H [25] or PTSA [26] has to be used as a cocatalyst in order to obtain a good yield of ketone when the transition-metal complex was employed as a catalyst in the hydration of alkyne. Recently, it was found that the metal salts were effective at activating the carbon-carbon triple bond in the presence of protonic acids, for instance, In(OTf)₃ with PTSA [27], FeCl₃ with AcOH [28] and FeCl₂·4H₂O with MsOH [29]. These methods use non-noble metal salts as catalysts, but the stoichiometric amount of Brønsted acid as a cocatalyst was still necessary for the hydration of alkyne. Therefore, the development of a general, efficient, inexpensive and readily available catalyst for the hydration of alkyne to corresponding carbonyl compound is very much in demand [30–33].

It is well known that SnCl₄ is a common, cheap, easy-handling Lewis acid, and has much lower toxicity. Recently, as a Lewis acid catalyst, SnCl₄ has been used widely in reduction of glycopyranosyl azides [34], the ring-opening reaction of 4, 5-dihydropyrroles [35], conversion of glucose [36] and intermolecular polyene cyclization [37]. In this work, we found that SnCl₄·5H₂O was a highly efficient and environmentally benign catalyst for the hydration of terminal alkyne to generate methyl ketone without using liquid Brønsted acid as a cocatalyst. To the best of our knowledge, this is the first example of Sn-catalyzed hydration of alkyne. In this manuscript, the reaction conditions and the substrate scope of hydration of alkyne were investigated when SnCl₄·5H₂O was employed as a catalyst.

2. Results and Discussion

2.1. Effects of Varying the Catalyst

Initially, the catalytic activity of transition metal salt was investigated in the hydration of phenylacetylene (1a) when using MeOH as a solvent, and the results are listed in Table 1.

Table 1. Hydration of phenylacetylene catalyzed by transition metal salt ^a.

Entry	Catalyst	Yield ^b %
1	CuCl	15
2	CuCl ₂ ·2H ₂ O	31
3	Cu(NO ₃) ₂ ·3H ₂ O	26
4	FeCl ₃	4
5	SnCl ₂ ·2H ₂ O	66
6	SnCl ₄ ·5H ₂ O	70
7 ^c	SnCl ₄ ·5H ₂ O	91

^a Reaction conditions: phenylacetylene (2 mmol), catalyst (10 mol %), MeOH (1 mL), reaction temperature 120 °C, reaction time 18 h; ^b GC yield; ^c 15 mol % of catalyst was used.

It is shown in Table 1 that acetophenone (2a) was given in 15% yield when the 10 mol % of CuCl was used as a catalyst in MeOH at 120 °C for 18 h (entry 1), and the better yield of acetophenone (2a) was obtained when the Cu²⁺ salts were used as catalysts (entries 2 and 3). It was probably due to the Lewis acid property of Cu²⁺. The same tendency was found when different valence states of stannic salts were used as catalysts in the hydration of phenylacetylene (1a) (Table 1, entries 5 and 6). In the presence of SnCl₂·2H₂O, the acetophenone (2a) was yield to 66%. The yield of acetophenone (2a) was increased to 70% when employing SnCl₄·5H₂O (10 mol %) as a catalyst for the hydration of phenylacetylene (1a). When the amount of SnCl₄·5H₂O was increased to 15 mol %, the yield of product was increased to 91% (Table 1, entry 7). However, when using FeCl₃ with the strong Lewis acidity as a catalyst, only 4% of acetophenone (2a) was obtained (Table 1, entry 4), which could be caused by the strong and hard Lewis acidity of FeCl₃ [26].

2.2. Optimum Reaction Conditions

The effect of solvent on the hydration of phenylacetylene (1a) was also investigated by screening different solvents, and the results showed that the solvent played a key role in this process (Table 2, entries 1–9). When the reaction was carried out in 1,4-dioxane or DMF, a trace amount of acetophenone (2a) was detected in the reaction mixture (Table 2, entries 1 and 2). Other common solvents such as toluene, DMSO, CH₃CN, DCM and acetone gave moderate yield of acetophenone (2a) (Table 2, entries 3–7). When the methanol with active proton was used as a solvent for the hydration of phenylacetylene (1a), the yield of acetophenone (2a) was increased to 91%, respectively. It was noted that the addition of water in solvent did not accelerate this reaction, and the yield of acetophenone (2a) was decreased slightly when the mixture of methanol and water was used as a solvent (Table 2, entry 10). When using ethanol alternative methanol, a similar yield of acetophenone (2a) was obtained (Table 2, entry 8). This indicates that protic solvent could accelerate the hydration of alkyne.

Table 2. Optimization of solvents and reaction conditions for the hydration of phenylacetylene ^a.

Entry	Solvent	Temperature °C	Time h	Yield ^b %
1	1,4-dioxane	120	18	1
2	DMF	120	18	<1
3	Toluene	120	18	46
4	DMSO	120	18	49
5	CH ₃ CN	120	18	37
6	DCM	120	18	42
7	CH ₃ COCH ₃	120	18	66
8	EtOH	120	18	90
9	MeOH	120	18	91
10 ^c	MeOH	120	18	84
11	MeOH	110	18	60
12	MeOH	130	18	90
13	MeOH	120	14	80
14	MeOH	120	16	88
15	MeOH	120	20	90

^a Reaction conditions: phenylacetylene (2 mmol), SnCl₄·5H₂O (15 mol %), solvent (1 mL); ^b GC yield;

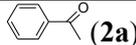
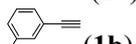
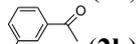
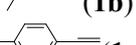
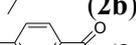
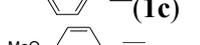
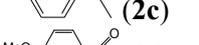
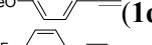
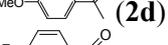
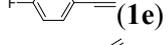
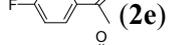
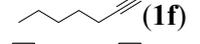
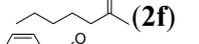
^c 2 mmol H₂O was added in the reaction mixture.

In this work, the effect of reaction temperature on the hydration of alkyne was evaluated. When the reaction temperature was decreased to 110 °C, the yield of acetophenone (2a) was decreased to 60% (Table 2, entry 11). Increasing the reaction temperature to 130 °C did not improve the yield of acetophenone (2a), which indicates that 120 °C was the optimal reaction temperature (Table 2, entry 12). The yield of acetophenone (2a) was increased with prolonging the reaction time, but the yield was not further improved when the reaction time was increased more than 18 h. The acetophenone (2a) was yield to 90% when the reaction time was prolonged to 20 h (Table 2, entry 15).

2.3. Hydration of Other Alkynes

Under the optimal reaction conditions, the scope and limitation of the hydration with $\text{SnCl}_4 \cdot 5\text{H}_2\text{O}$ were investigated with using a series of terminal aromatic alkynes with different substituent groups on the aromatic ring, aliphatic alkynes, and internal alkyne as substrates, and the results are listed in Table 3.

Table 3. Hydration of other alkynes using $\text{SnCl}_4 \cdot 5\text{H}_2\text{O}$ as a catalyst ^a.

Entry	Alkyne	Product	Yield ^b %
1	 (1a)	 (2a)	91 ^c
2	 (1b)	 (2b)	98
3	 (1c)	 (2c)	93
4	 (1d)	 (2d)	>99
5	 (1e)	 (2e)	49
6	 (1f)	 (2f)	81
7	 (1g)	 (2g)	-

^a Reaction conditions: alkyne (2 mmol), $\text{SnCl}_4 \cdot 5\text{H}_2\text{O}$ (15 mol %), MeOH (1 mL), reaction temperature 120 °C, reaction time 18 h; ^b ¹HNMR yield; ^c GC yield.

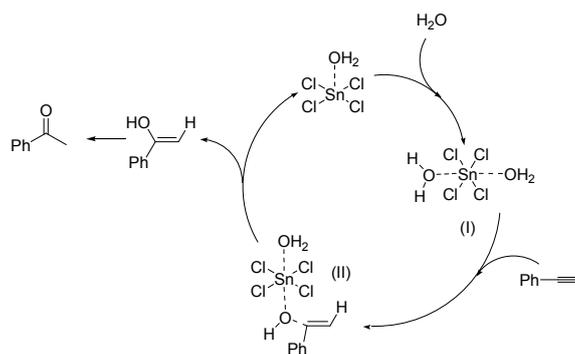
From Table 3, it can be seen that liquid aromatic alkynes were efficiently converted to the corresponding ketones. Electron rich aromatic alkynes (Table 3, entries 2–4) showed better conversion in comparison to alkyne that contain electron withdrawing group (Table 3, entry 5). When 4-fluorophenylacetylene was used as a substrate, the corresponding ketone was yield to 49%. The results in Table 3 also indicate that the steric hindrance of substituent on benzene had very little influence on the catalytic efficiency in the hydration of terminal aromatic alkynes, and a substituent on the *m*-position of benzene, with more steric hindrance, showed 98% yields for the corresponding product (Table 3, entry 2). To our delight, not only aromatic alkyne, but also aliphatic alkyne (Table 3, entry 6) was converted effectively to the corresponding aliphatic ketone in 81% yield.

Hydration of internal alkyne was also investigated under the optimal reaction conditions. Unfortunately, the corresponding ketone was not found (Table 3, entry 7) in the reaction mixture.

2.4. Possible Reaction Mechanism

Based on previous reports [38,39] and the results in our study, a probable catalytic cycle was proposed for the hydration of alkyne using $\text{SnCl}_4 \cdot 5\text{H}_2\text{O}$ as a catalyst, as shown in Scheme 2.

Generally, the hydration of alkyne may follow pathways: one is proposed based on Hg^{2+} salts as catalysts and another is proposed using Brønsted acids as catalysts. Sn^{4+} salts show strong Lewis acidity, so SnCl_4 could form hydrates with water and the proton in H_2O was activated. In this process, the carbon-carbon triple bond of alkyne was protonated by H^+ which was produced by the activated H_2O which was contained in solvent and catalyst and then coordinated with $\text{SnCl}_4(\text{H}_2\text{O})\text{OH}^-$ to form intermediate II. Then intermediate II was reductive elimination and rapid tautomerization to produce methyl ketone.



Scheme 2. The possible mechanism for the hydration of alkyne in the presence of $\text{SnCl}_4 \cdot 5\text{H}_2\text{O}$.

3. Experimental Section

3.1. Chemicals

All the chemicals were commercially available and were used without further purification. ^1H NMR spectra were recorded on a Bruker 400 MHz instrument using 0.5 mL CDCl_3 as solvent containing TMS as internal standard. The products were analyzed by a HP 6890/5973 GC-MS and a gas chromatography (GC, Techcomp, 7900; Techcomp Ltd.: Shanghai, China) equipped with a flame-ionized detector (FID).

3.2. Hydration Reaction

General procedure for hydration of alkyne: The $\text{SnCl}_4 \cdot 5\text{H}_2\text{O}$ (0.3 mmol, 15 mol %) and phenylacetylene (1a, 2 mmol) were added to 1 mL methanol in a 25 mL sealed tube. The reaction mixture was heated up to 120 °C and stirred at refluxed for 18 h. After completion of the reaction, the crude mixture was allowed to cool at room temperature and filtered through celite to give acetophenone (2a) as yellow filtrate. The products were qualitatively analyzed by a HP 6890/5973 GC-MS and quantitatively analyzed by a gas chromatography (GC, Techcomp, 7900; Techcomp Ltd.: Shanghai, China) equipped with a flame-ionized detector (FID) or a Bruker 400 MHz instrument with using 0.5 mL CDCl_3 as solvent containing TMS as internal standard.

4. Conclusions

In summary, a general, efficient and non-noble metal method using $\text{SnCl}_4 \cdot 5\text{H}_2\text{O}$ as a catalyst without using Brønsted acid as a cocatalyst for the transformation of various alkynes to the corresponding ketones in high yields has been successfully developed. Under optimized reaction

conditions, substrates with electron-withdrawing groups or electron-donating groups were performed smoothly and gave moderate to excellent yields. It should be noted that aliphatic alkyne also afforded the ketone in good yield.

Acknowledgments

We are grateful to the Foundation for Youth Science and Technology Innovation Talents of Harbin of China (RC2013LX018002) for financial support.

Author Contributions

Dongxue Chen and Dantong Wang performed the experiment. Wei Wu and Linfei Xiao analyzed and discussed the experimental results. Dongxue Chen, Linfei Xiao and Wei Wu wrote the paper.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Alonso, F.; Beletskaya, I.P.; Yus, M. Transition-metal-catalyzed addition of heteroatom-hydrogen bonds to alkynes. *Chem. Rev.* **2004**, *104*, 3079–3160.
2. Corma, A.; Leyva-Pérez, A.; Sabater, M.J. Gold-catalyzed carbon-heteroatom bond-forming reactions. *Chem. Rev.* **2011**, *111*, 1657–1712.
3. Li, L.; Zeng, M.S.; Herzon, S.B. Broad-spectrum catalysts for the ambient temperature anti-markovnikov hydration of alkynes. *Angew. Chem. Int. Ed.* **2014**, *53*, 7892–7895.
4. Hintermann, L.; Labonne, A. Catalytic hydration of alkynes and its application in synthesis. *Synthesis* **2007**, doi:10.1055/s-2007-966002.
5. Mello, R.; Alcalde-Aragonés, A.; González-Núñez, M.E. Silica-supported HgSO₄/H₂SO₄: A convenient reagent for the hydration of alkynes under mild conditions. *Tetrahedron Lett.* **2010**, *51*, 4281–4283.
6. Liu, W.J.; Li, J.H. Cerium (IV) sulfate-catalyzed hydration of alkynes. *Chin. J. Org. Chem.* **2006**, *26*, 1073–1078.
7. Blum, J.; Huminer, H.; Alper, H. Alkyne hydration promoted by RhCl₃ and quaternary ammonium salts. *J. Mol. Catal.* **1992**, *75*, 153–160.
8. Kanemitsu, H.; Uehara, K.; Fukuzumi, S.; Ogo, S. Isolation and crystal structures of both enol and keto tautomer intermediates in a hydration of an alkyne-carboxylic acid ester catalyzed by iridium complexes in water. *J. Am. Chem. Soc.* **2008**, *130*, 17141–17147.
9. Imi, K.; Imai, K.; Utimoto, K. Regioselective hydration of alkynones by palladium catalysis. *Tetrahedron Lett.* **1987**, *28*, 3127–3130.
10. Hartman, J.W.; Hiscox, W.C.; Jennings, P.W. Catalytic hydration of alkynes with platinum(II) complexes. *J. Org. Chem.* **1993**, *58*, 7613–7614.
11. Mizushima, E.; Sato, K.; Hayashi, T.; Tanaka, M. Highly efficient Au^I-catalyzed hydration of alkynes. *Angew. Chem. Int. Ed.* **2002**, *41*, 4563–4565.

12. Casado, R.; Contel, M.; Laguna, M.; Romero, P.; Sanz, S. Organometallic gold(III) compounds as catalysts for the addition of water and methanol to terminal alkynes. *J. Am. Chem. Soc.* **2003**, *125*, 11925–11935.
13. Wang, W.L.; Zheng, A.M.; Zhao, P.Q.; Xia, C.G.; Li, F.W. Au-NHC@Porous organic polymers: Synthetic control and its catalytic application in alkyne hydration reactions. *ACS Catal.* **2014**, *4*, 321–327.
14. Rostamizadeh, S.; Estiri, H.; Azad, M. Au anchored to (α -Fe₂O₃)-MCM-41-HS as a novel magnetic nanocatalyst for water-medium and solvent-free alkyne hydration. *Catal. Commun.* **2014**, *57*, 29–35.
15. Zhou, Y.; Liu, Q.J.; Lv, W.F.; Pang, Q.Y.; Ben, R.; Qian, Y.; Zhao, J. Indazolin-s-ylidene-*N*-heterocyclic carbene complexes of rhodium, palladium, and gold: Synthesis, characterization, and catalytic hydration of alkynes. *Organometallics* **2013**, *32*, 3753–3759.
16. Xu, X.Y.; Kim, S.H.; Zhang, X.; Das, A.K.; Hirao, H.; Hong, S.H. Abnormal *N*-heterocyclic carbene gold(i) complexes: Synthesis, structure, and catalysis in hydration of alkynes. *Organometallics* **2013**, *32*, 164–171.
17. Sayantani, S.; Abir, K.B. Bulky, spherical, and fluorinated anion BArF₄ induces ‘on-water’ activity of silver salt for the hydration of terminal alkynes. *Tetrahedron Lett.* **2014**, *55*, 1444–1447.
18. Thuong, M.B.T.; Mann, A.; Wagner, A. Mild chemo-selective hydration of terminal alkynes catalysed by AgSbF₆. *Chem. Commun.* **2012**, *48*, 434–436.
19. Wu, X.F.; Bezier, D.; Darcel, C. Development of the first iron chloride-catalyzed hydration of terminal alkynes. *Adv. Synth. Catal.* **2009**, *351*, 367–370.
20. Tachinami, T.; Nishimura, T.; Ushimaru, R.; Noyori, R.; Naka, H. Hydration of terminal alkynes catalyzed by water-soluble cobalt porphyrin complexes. *J. Am. Chem. Soc.* **2013**, *135*, 50–53.
21. Breit, B.; Gellrich, U.; Li, T.; Lynam, J.M.; Milner, L.M.; Pridmore, N.E.; Slattery, J.M.; Whitwood, A.C. Mechanistic insight into the ruthenium-catalysed anti-Markovnikov hydration of alkynes using a self-assembled complex: A crucial role for ligand-assisted proton shuttle processes. *Dalton Trans.* **2014**, *43*, 11277–11285.
22. Zeng, M.S.; Li, L.; Herzon, S.B. A highly active and air-stable ruthenium complex for the ambient temperature anti-Markovnikov reductive hydration of terminal alkynes. *J. Am. Chem. Soc.* **2014**, *136*, 7058–7067.
23. Tsuchimoto, T.; Joya, T.; Shirakawa, E.; Kawakami, Y. Brønsted acid-catalyzed hydration of alkynes: A convenient route to diverse carbonyl compounds. *Synlett* **2000**, 1777–1778.
24. Allen, A.D.; Chiang, Y.; Kresge, A.J.; Tidwell, T.T. Substituent effects on the acid hydration of acetylenes. *J. Org. Chem.* **1982**, *47*, 775–779.
25. Menashe, N.; Shvo, Y. Hydration of alkynes in anhydrous medium with formic acid as water donor. *J. Org. Chem.* **1993**, *58*, 7434–7439.
26. Maud, J.; Olivier, P.; Jean-François, P.; Abdallah, H.; Jean-Daniel, B.; Mouad, A. A ring-closing metathesis based synthesis of bicyclic nucleosides locked in S-type conformations by hydroxyl functionalised 3',4'-trans linkages. *Tetrahedron* **2010**, *66*, 3775–3786.
27. Gao, Q.; Li, S.Y.; Pan, Y.M.; Xu, Y.L.; Wang, H.S. *p*-Toluenesulfonic acid-promoted selective functionalization of unsymmetrical arylalkynes: A regioselective access to various arylketones and heterocycles. *Tetrahedron* **2013**, *69*, 3775–3778.

28. Mauro, B.; Samuele, C.; Federico, L.; Chiara, P. Hydration of aromatic terminal alkynes catalyzed by iron(III) sulfate hydrate under chlorine-free conditions. *Tetrahedron Lett.* **2014**, *55*, 1608–1612.
29. Park, J.; Yeon, J.; Lee, P.H.; Lee, K. Iron-catalyzed indirect hydration of alkynes in presence of methanesulfonic acid. *Tetrahedron Lett.* **2013**, *54*, 4414–4417.
30. Chen, Z.W.; Ye, D.N.; Ye, M.; Liu, L.X. Highly efficient AgBF₄-catalyzed synthesis of methyl ketones from terminal alkynes. *Tetrahedron* **2013**, *69*, 6116–6120.
31. Das, R.; Chakraborty, D. AgOTf catalyzed hydration of terminal alkynes. *Appl. Organomet. Chem.* **2012**, *26*, 722–726.
32. Cabrero-Antonino, J.R.; Leyva-Pérez, A.; Corma, A. Regioselective hydration of alkynes by iron(III) Lewis/Brønsted catalysis. *Chem. Eur. J.* **2012**, *18*, 11107–11114.
33. Cabrero-Antonino, J.R.; Leyva-Pérez, A.; Corma, A. Iron(III) Triflimide as a catalytic substitute for gold(I) in hydroaddition reactions to unsaturated carbon-carbon bonds. *Chem. Eur. J.* **2013**, *19*, 8627–8633.
34. Sahoo, L.; Singhamahapatra, A.; Paul, K.J.V.; Loganathan, D. SnCl₄/Sn catalyzed chemoselective reduction of glycopyranosyl azides for the synthesis of diversely functionalized glycopyranosyl chloroacetamides. *Tetrahedron Lett.* **2013**, *54*, 5361–5365.
35. Zhang, Z.G.; Wang, D.; Wang, B.; Liu, Q.F.; Liu, T.X.; Zhang, W.; Yuan, B.B.; Zhao, Z.J.; Han, D.D.; Zhang, G.S. SnCl₄ mediated synthesis of γ -amino ketones derivatives via the ring-opening reaction of 4, 5-dihydropyrroles. *Tetrahedron* **2013**, *69*, 9063–9067.
36. Hu, S.Q.; Zhang, Z.F.; Song, J.L.; Zhou, Y.X.; Han, B.X. Efficient conversion of glucose into 5-hydroxymethylfurfural catalyzed by a common Lewis acid SnCl₄ in an ionic liquid. *Green Chem.* **2009**, *11*, 1746–1749.
37. Zhao, Y.J.; Loh, T.P. Bio-inspired polyene cyclization: Synthesis of tetracyclic terpenoids promoted by steroidal acetal-SnCl₄. *Chem. Commun.* **2008**, 1434–1436.
38. Toman, L.; Lukas, R.; Spevacek, J. Isobutylene polymerization in the presence of *t*-BuCl/SnCl₄. *Polym. Bull.* **1992**, *28*, 175–180.
39. Han, J.K.; Lee, K.W.; Lee, C.E. Proton dynamics in SnCl₄·5H₂O. *J. Korean Phys. Soc.* **2000**, *37*, L487–L489.