Chem. Pharm. Bull. 52(7) 864—865 (2004) Vol. 52, No. 7

Facile Characterization of Polymer-Supported Reagents Using Cross Polarization Magic Angle Spinning Method in Solid State ^{13}C-NMR

Kazuaki Shikii,[a,c] Hiroko Seki,*[a,d] Kentaro Yamaguchi,*[a,d] Wannaporn Disadee,[b]
Toshiko Watanabe,[b] and Tsutomu Ishikawa[b]

[a] *Chemical Analysis Center, Chiba University; and* [b] *Graduate School of Pharmaceutical Science, Chiba University; 1–33 Yayoi, Inage-ku, Chiba 263–8522, Japan:* [c] *Nissan Chemical Industries, Ltd.; 722–1 Tsuboi, Funabashi, Chiba 274–8507, Japan: and* [d] *CREST, Japan Science and Technology Agency (JST); Kawaguchi Center Building, 4–1–8, Honcho, Kawaguchi, Saitama 332–0012, Japan.*

Received February 12, 2004; accepted May 6, 2004; published online May 18, 2004

Polymer-supported (PS) reagents can be easily characterized using a cross polarization magic angle spinning method in solid state ^{13}C-NMR. The technique was applied to the characterization of PS-dimethylimidazolidinone, analogue to potential heterogeneous dehydrating agent.

Key words PS reagent; solid state NMR; cross polarization magic angle spinning; energy dispersive X-ray spectroscopy; PS-dimethylimidazolidinone

Polymer-supported (PS) reagents and catalysts attract much attention as new tools in organic synthesis and may be applicable in industrial processes because of their advantages over conventional agents on easier handlings, reusability, and detoxiability.[1,2] Many applications of Merrifield beads have been developed in chemistry and related fields. The use of such reactants in flow systems[3] could bring the development to a future stage. Thus, solid state chemistry is very important in high throughput chemistry as well as green chemistry. IR and swollen resin magic angle spinning (SR MAS) NMR have been used for the characterization of PS-molecules.[4—6] However it is not so easy to simply characterize PS-compounds in conventional methods because of their amorphous and/or insoluble properties.

In the preceding paper,[7] we described the preparation of PS-dimethylimidazolidinone analogue (PS-DMI) **3** as a potential dehydrating agent and its application to esterification and amidation after conversion to the corresponding PS-chloroimidazolinium chloride (PS-DMC) salt **4** by chlorination, as shown in Chart 1. In this paper, we present simple and rapid characterization of **3** using an easily operative cross polarization magic angle spinning (CP MAS) method in solid state ^{13}C-NMR. This technique can be used as an alternative approach for the characterization of PS-molecules.

Experimental

Materials **1** and **2** were purchased from Tokyo Kasei Kogyo CO. Ltd. and ACROS, respectively. **3** was prepared by the reaction of 4-chloromethylpolystyrene–1% divinylbenzene copolymer resin (PS-Cl) **1**[8] (200—400 mesh chloride contents *ca.* 1.74 mmol/g) with 1-methyl-2-imidazolidinone **2**. **5** was obtained from procedure in reference 7. All reagents were not purified.

NMR Measurements Cross polarization magic angle spinning (CP MAS) solid state ^{13}C-NMR were performed on a JEOL JNM LA400 spectrometer at room temperature. Samples were placed in a zirconia roter 4 mm I.D. These PS-compounds were subjected to ^{13}C-NMR measurement using a CP MAS method focusing on carbonyl and *N*-methyl carbon signals. The spinning rate was controlled without overlapping SSB and other peaks. After preliminary examination, solid state NMR measurement conditions were determined as follows; contact time: 5 ms, acquisition time: 20 ms, pulse delay: 5 s, spinning rate: 6000 Hz, and measurement time: 10 h. The liquid ^{13}C-NMR of **5** in $CDCl_3$ was carried out on a JEOL JNM ECP-400 spectrometer at room temperature, where pulse delay of 1.5 s and 1000 scans were collected.

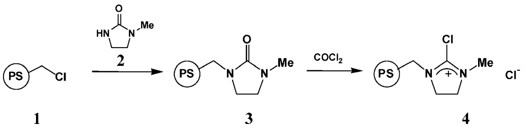

Chart 1. Preperation of **3** and **4** from **1**

Elemental Analysis Elemental analysis was performed on the product having the largest carbonyl peak integral ratio. Carbon, hydrogen, nitrogen, and oxygen contents in the product molecules were determined using a PE2400 series II (Perkin Elmer), and chlorine was quantified by ion chromatography DX-500 (DIONEX) under the oxygen flask combustion method. Moreover, the elemental analysis by energy dispersive X-ray spectroscopy (EDAX) was also carried out on a DX-prime+1 with scanning electron microscopy ESEM-2700 (Nikon) and confirmed the existence of residual chloride in **3**. Good accordance between theoretical and experimental values indicated the quantitative conversion of **1** to **3**.

Procedure In this case, we evaluated the peak integral ratio between the carbonyl and the aromatic (120—140 ppm) carbons in solid state ^{13}C-NMR on five selected specimens of **3**, which we prepared under various reaction conditions,[7] to determine the conversion yield. A peak at 145 ppm was excluded because the accuracy of conversion yields might be decreased by considerably large value of the peak area based on the aromatic carbons comparing to the carbonyl ones. The carbonyl carbon peak was selected as standard because it was separated more clearly than the *N*-methyl carbon peak. We investigated accurate integral ratio between carbonyl and aromatic carbon with peak separation by using ALICE (JEOL) software, and compared samples of **3** with the best conversion yield 98% as standard.

Results and Discussions

Solid state ^{13}C-NMR measurement by using CP MAS method was performed to avoid reduction of the resolution. It is thought that this method can be used for the relative comparison of peak integral.

Solid ^{13}C-NMR spectra of compounds **1** and **3** are compared to the liquid ^{13}C-NMR spectrum of *N*-benzyl-*N*′-methyl-2-imindazolidinone (**5**) (Fig. 1).

These spectra are in good agreement for each signal patterns. Clearly separated signals in **3** at δ *ca.* 160 and 30 ppm due to carbonyl and *N*-methyl carbons support its structural profile. An elemental analysis for the sample, which has the largest carbonyl peak integral, was performed to confirm its composition (Table 1). A little residual chlorine indicated that the reaction proceeded quantitatively. Absolutely no residual of **2**, soluble in organic solvent was observed in this

---

* To whom correspondence should be addressed. e-mail: yamaguchi@cac.chiba-u.ac.jp

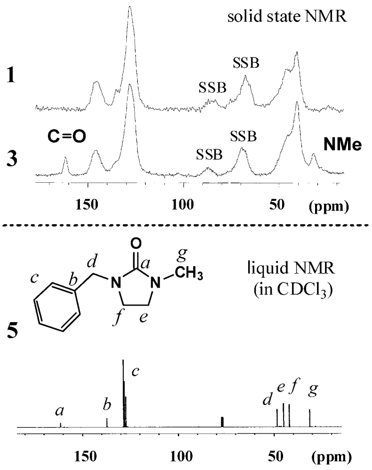

Fig. 1. Solid State ^{13}C-NMR Spectra of **1** and **3** and Liquid ^{13}C-NMR Spectrum of **5**

SSB: spinning side band.

Table 1. Elemental Analysis of **1** and **3**

	1 (Cl contents: 1.74 mmol/g)		**3**	
	Theoretical (%)	Experimantal (%)	Theoretical (%)	Experimantal (%)
C	86.5	85.61[a)]	85.5	84.27[a)]
H	7.2	7.12[a)]	7.6	7.42[a)]
N	0	0.43[a)]	4.4	4.62[a)]
O	0	—	2.5	2.62[a)]
Cl	6.2	6.45[b)]	0	0.11[b)]
Total	99.9	99.61	100	99.04

a) By elemental analysis. *b*) By ion chromatography.

reaction because the product after reaction was sufficiently washed with 1 N HCl, methanol, water and methylenedichloride. The highest conversion yield is calculated as follows; $1-0.11/6.45=0.98$, 98%.

In general, CP method is not adapted to the absolute quantitation because the efficiency of cross polarization might be different depends on the compounds. When the target peak overlaps with other larger peak, this method is not available for quantitation. Moreover, it is necessary for quantitation that the purity of the reference compound is assured.

Table 2. Conversion Yields of **3** Prepared from **1** under Different Condition

Run	Conversion yield (%)
1*	98
2	49
3	92
4	87
5	69

The data 1* was estimated from the elemental analysis in Table 1 and the data 2—5 were estimated from the CP MAS method.

A conversion yields ranging from 51 to 98% were observed for the samples produced in various conditions (Table 2).

Thus, this reaction proceeded quantitatively in some cases, whereas in other cases incompletely, indicating that our method could offer speedy and easy quantitative analysis in screening reaction condition.

In conclusion, we showed that, even with a slightly lower resolution, CP MAS method in solid state ^{13}C-NMR can be not only a powerful but also simple and rapid method for the characterization of PS-molecules.

References

1) Booth S., Hermkens P. H. H., J. Ottenheijm H. C., Rees D. C., *Tetrahedron*, **54**, 15385—15443 (1998).
2) Ley S. V., Baxendale I. R., Brusotti G., Caldarelli M., Massi A., N. Nesi, *Il Farmaco*, **57**, 321—330 (2002).
3) Hodge P., *Curr. Opinion Chem. Biol.*, **7**, 362—373 (2003).
4) Krajnc P., Toplak R., *Reactive Funct. Polymers*, **52**, 11—18 (2002).
5) Zhu X., Blough B. E., Carroll I., *Tetrahedron Lett.*, **41**, 9219—9222 (2000).
6) Rentsch D., Hany R., Barthelemy S., Steinauer R., *Tetrahedron Lett.*, **44**, 6987—6990 (2003).
7) Disadee W., Watanabe T., Ishikawa T., *Synlett*, **1**, 115—117 (2003).
8) Ford W. T., Yacoub S. A., *J. Org. Chem.*, **46**, 819—821 (1981).