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Ring Opening and Expansion of Aziridines in a Silica−Water Reaction Medium

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Ring-opening reactions of *N*-tosylaziridines with water-soluble nucleophiles proceeded in a silica−water reaction medium. The system is applicable to a ring expansion of an aziridine with potassium thiocyanate, leading to a thiazolidine derivative.

The replacement of current organic chemical processes with more environmentally benign alternatives is an important goal from an ecological point of view.[1] A great deal of interest has developed regarding the use of aqueous media in organic transformations because water is nontoxic, nonflammable, and inexpensive and environmentally benign.[2] Prompted by this, we previously reported on the iodine-catalyzed aziridination of olefins using chloramine-T (CT)[3] in aqueous media by the addition of a phase-transfer catalyst (PTC).[4] Since CT has an ionic character, a PTC is generally used to permit the reaction to proceed in water. An alternative potential process in aqueous media has recently been devised based on the adsorptive nature of silica gel.[5] Silica is effective as an organic reaction medium in water because the organic substrate is adsorbed to the silica by hydrophobic interactions between the surface of the silica and the organic molecule. In addition, the surface area available for a reaction (surface area of the silica) in such a system should be quite large compared with that of the interface in a conventional liquid−liquid biphasic system. In our preliminary work,[5] we described the ring opening of an aziridine and indicated that the use of silica−water reaction media had great potential for use in a variety of chemical reactions. Although some examples of the ring opening of aziridines with nucleophiles in water have been reported to date, a catalyst[6] and/or water-soluble organic solvents[7] are required for the reaction to proceed. From these points of view, to expand the utility of this potentially valuable strategy, we herein report on the reaction of aziridines with water-soluble nucleophiles leading to ring-opening and ring-expansion products. Since the efficiency of the ring opening of an aziridine with sodium azide was satisfactory in our preliminary study,[5] cyanides and iodides as water-soluble nucleophiles were investigated for ring opening of aziridines.

Although silica gel was found to be an effective solid medium for the iodine-catalyzed aziridination of olefins with CT and ring opening of aziridines with NaN_3 in water, a variety of porous materials were examined for the ring opening of an aziridine with KCN to improve the efficiency of our preliminary result (Table 1). The reaction of aziridine **1a** with KCN in water in the absence of a porous material at 80 °C did not proceed at all (entry 1). When Silica Gel 60 was employed, regioselective ring-opening product **2a** was obtained in 69% yield. The silica gel was found to be reusable without any special treatment, and **2a** was produced in 65% yield in the second cycle and in 65% in the third cycle under the same conditions. When mesoporous silica with a hexagonal array, MCM-41,[8] was used in the reaction, the desired ring-opening product was produced in moderate yield. Neutral and basic alumina, 4 Å molecular sieves, Celite 545, and Montmorillonite K10 were also positive for the reaction, but Silica Gel 60 was found to be a very useful solid medium.

The ring opening of various *N*-tosylaziridines with KCN was investigated in water in the presence of Silica Gel 60, and the results are shown in Table 2. Aziridine **1b** was readily converted to the ring-opening product in good yield with complete regioselectivity (entry 1). When the reaction of *sec*-butyl-substituted aziridine **1c** was examined under the same conditions, the reaction proceeded in moderate yield. Although the efficiencies of the reactions of **1d** and **1e** could be improved, the complete regioselective ring opening of both aziridines was observed, and the method was found to be applicable to the ring opening of a hydroxylated aziridine. The bicyclic aziridines **1f** and **1g** were transformed to the corresponding ring-opening products with trans configurations, respectively. Thus, the presence of Silica Gel 60 enhanced the performance of all of the ring-opening reactions.

Although the ring opening of **1a** with metal chlorides and bromides did not proceed at all, even in the presence of silica,

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[1] (a) Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: New York, 1998. (b) Eissen, M.; Metzger, J. O.; Schmidt, E.; Schneidewind, V. *Angew. Chem., Int. Ed.* **2002**, *41*, 414−436. (c) Special Topic Issue on Green Chemistry: *Acc. Chem. Res.* **2002**, *35*, 685−816.

[2] (a) Li, C.-J.; Chan, T.-H. *Organic Reactions in Aqueous Media*; Wiley: Chichester, UK, 1997. (b) *Organic Synthesis in Water*; Grieco, P. A., Ed.; Blake Academic and Professional: London, 1998.

[3] Ando, T.; Kano, D.; Minakata, S.; Ryu, I.; Komatsu, M. *Tetrahedron* **1998**, *54*, 13485−13494.

[4] Kano, D.; Minakata, S.; Komatsu, M. *J. Chem. Soc., Perkin Trans. 1* **2001**, 3186−3188.

[5] Minakata, S.; Kano, D.; Oderaotoshi, Y.; Komatsu, M. *Angew. Chem., Int. Ed.* **2004**, *43*, 79−81.

[6] (a) Reddy, M. A.; Reddy, L. R.; Bhanumathi, N.; Rao, K. R. *Chem. Lett.* **2001**, 246−247. (b) Chandrasekhar, S.; Narsihmulu, C.; Sultana, S. S. *Tetrahedron Lett.* **2002**, *43*, 7361−7363.

[7] (a) Fitremann, J.; Pureault, A.; Depezay, J.-C. *Synlett* **1995**, 235−237. (b) Maligres, P. E.; See, M. M.; Askin, D.; Reider, P. J. *Tetrahedron Lett.* **1997**, *38*, 5253−5256.

[8] (a) Kresge, C. T.; Leonowicz, M. E.; Roth, W. J.; Vartuli, J. C.; Beck, J. S. *Nature* **1992**, *359*, 710−712. (b) Beck, J. S.; Vartuli, J. C.; Roth, W. J.; Leonowicz, M. E.; Kresge, C. T.; Schmitt, K. D.; Chu, C. T.-W.; Olson, D. H.; Shepard, E. W.; McCullen, S. B.; Higgins, J. B.; Schlenker, J. L. *J. Am. Chem. Soc.* **1992**, *114*, 10834−10843. (c) Grun, M.; Unger, K. K.; Matsumoto, A.; Tsutsumi, K. *Microporous Mesoporous Mater.* **1999**, *27*, 207−216.

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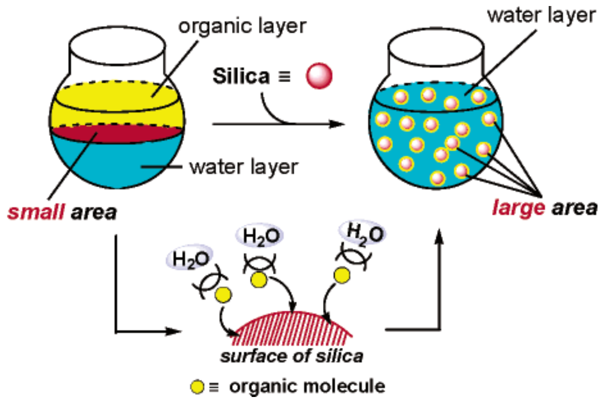
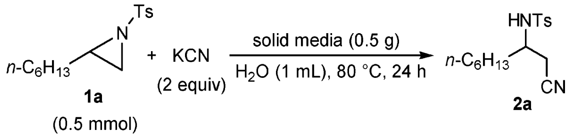


FIGURE 1. Schematic of an organic reaction using a silica−water system.

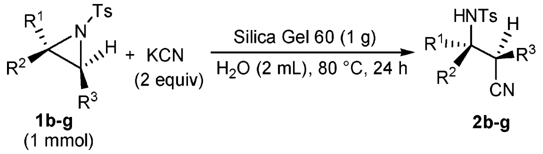
TABLE 1. Ring Opening of Aziridine 1a with KCN in Solid Media



entry	solid media	yield (%)
1	none	0
2	Silica Gel 60[a]	69
3	MCM-41	60
4	neutral alumina	33
5	basic alumina	10
6	MS 4A	36
7	Celite 545	45
8	Montmorillonite K10	36

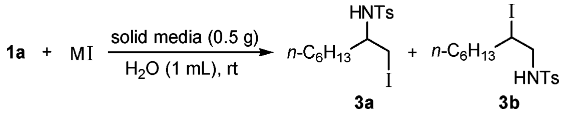
[a] Purchased from Nacalai Tesque, spherical, neutral.

TABLE 2. Ring Opening of Aziridines with KCN Using a Silica−Water System



entry		Aziridine				yield (%)
		R^1	R^2	R^3		
1	**(1b)**	CH_2Ph	H	H	**(2b)**	72
2	**(1c)**	*sec*-C_4H_9	H	H	**(2c)**	57
3	**(1d)**	Ph	H	H	**(2d)**	24
4	**(1e)**	CH_2OH	H	H	**(2e)**	32
5	**(1f)**	H	$-(CH_2)_3-$		**(2f)**	58
6	**(1g)**	H	$-(CH_2)_4-$		**(2g)**	88

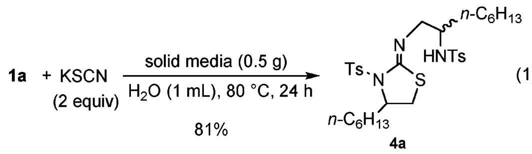
TABLE 3. Ring Opening of an Aziridine with Metal Iodides Using a Silica−Water System



MI (equiv)	time (h)	Yield (%)	
		3a	**3b**
LiI (5)	24	7	15
NaI (5)	24	14	15
KI (5)	24	27	0
CuI (5)	24	0	0
ZnI_2 (2.5)	24	67	6
ZnI_2 (2.5)	48	90	6

some iodide salts were found to open the ring under mild conditions. As listed in Table 3, a series of metal iodide salts were screened, and gratifyingly, ZnI_2 was found to bring about the desired transformation to **3a** in high yield. In these reactions, the formation of the regioisomer **3b** was observed, indicating that Lewis acidity or the hard/soft character of the metal ions might have an influence on the selectivity.

To obtain a ring-expansion product, potassium thiocyanate was employed in the reaction of **1a** (eq 1). As was expected, a ring-expansion product, thiazolidine derivative **4a** consisting of one thiocyanate and two aziridine moieties, was produced in good yield as a mixture of two diastereomers. The ring opening of aziridines with potassium thiocyanate in water using β-cyclodextrin was reported quite recently by Rao and co-workers.[9] In contrast to their results, although heating conditions were employed, the ring-expansion product was obtained selectively by our method.



(1)

In summary, the unique ring opening and expansion of aziridines using a silica−water system is described herein. The results demonstrate the generality of the system, which is directly connected to an environmentally benign synthetic organic process. Further investigation of the scope of the system is currently underway.

Experimental Section

Representative Experimental Procedure. To a mixture of potassium cyanide (65 mg, 1 mmol) and Silica Gel 60 (0.5 g) in distilled water (1.5 mL) was added aziridine **1a** (141 mg, 0.5 mmol). The mixture was stirred at 80 °C for 24 h under an ambient atmosphere. After the addition of acetone (5 mL), the mixture was passed through a short Celite column using acetone (10 mL) and Et_2O (10 mL) as eluents. The filtrate was dried over Na_2SO_4, and the solution evaporated to give the crude product. Purification by flash column chromatography (silica gel; 10% ethyl acetate in hexane) gave 107 mg (69%) of ring-opening product **2a** as a colorless oil. The characteristics of the products in this reaction (**2a**−**g**, **3a**) were found to be identical to those reported previously.[10]

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Supporting Information Available: Copies of ^{1}H NMR spectra for compounds **3a** and **3b**. Copies of ^{1}H NMR and ^{13}C NMR spectra for compound **4a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) (a) Reddy, M. S.; Narender, M.; Nageswar, Y. V. D.; Rao, K. R. *Tetrahedron Lett.* **2005**, *46*, 6437−6439. (b) Das, B.; Ramu, R.; Ravikanth, B.; Reddy, K. R. *Tetrahedron Lett.* **2006**, *47*, 779−782.

(10) Minakata, S.; Okada, Y.; Oderaotoshi, Y.; Komatsu, M. *Org. Lett.* **2005**, *7*, 3509−3512.