Reaction Media

Silica–Water Reaction Media: Its Application to the Formation and Ring Opening of Aziridines[**]

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In recent years, the demand for environmentally benign organic-chemical processes has increased and this issue must be considered, from the ecological point of view, in the future design and implementation of new synthetic methodologies.[1] Organic reactions in aqueous media have been the subject of considerable attention in terms of achieving more environmentally friendly synthetic transformations.[2] On the other hand, aziridines[3] are useful synthetic intermediates for a variety of organic syntheses and they are frequently present as important substructures of biologically active compounds. Thus, the development of an efficient synthetic route to aziridines represents an attractive task for organic chemists and, as a result, a variety of methodologies have been exploited.[4]

We recently reported on the iodine-catalyzed formation of aziridines from olefins by using chloramine-T (CT)[4k] in aqueous media by the addition of a phase-transfer catalyst (PTC).[4l] The use of PTC to permit the reaction in aqueous media is a general method because of the ionic character of CT. An alternative potential process in water was devised based on the adsorptive nature of silica gel. Although the application of silica gel to organic synthesis has been widely investigated,[5] to the best of our knowledge its use in organic reactions in aqueous media has not been exploited.[6] Silica would be effective as organic reaction media in water because the organic molecule as a substrate would be expected to be adsorbed to the silica by hydrophobic interactions between the surface of the silica and the organic molecule (Figure 1). Herein we report on the iodine-catalyzed formation of aziridines from olefins by using CT and the ring opening of the resulting product in a silica–water system, in which the use of silica (silica gel or MCM-41) showed unique results.

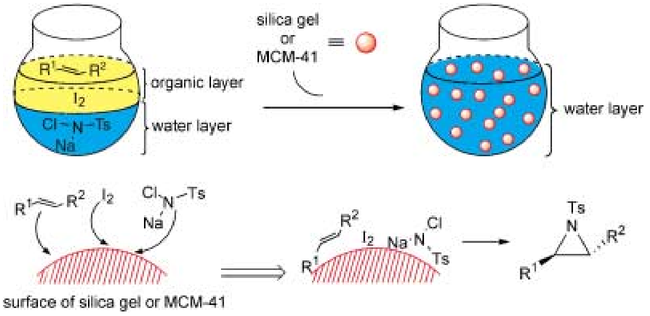
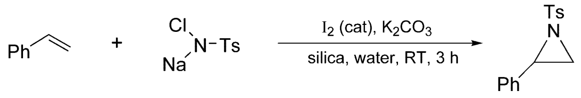


Figure 1. Proposed path for the formation of aziridines in a water–silica system.

Table 1: A comparison of silica gel 60 and MCM-41 as surface media for the formation of aziridine from styrene by using CT in Water.[a]



Entry	Silica [g]	CT [mmol]	Specific surface area [$m^2 g^{-1}$]	Yield [%]
1	silica gel 60 (0.25)	2.0	640	32
2	silica gel 60 (0.5)	2.0	640	55
3	silica gel 60 (0.5)	4.0	640	85
4	MCM-41 (0.25)	2.0	1060	80

[a] Reaction conditions: styrene (1.0 mmol), CT (2.0 or 4.0 mmol), I_2 (10 mol%), K_2CO_3 (2.0 mmol), silica (0.25 or 0.5 g), H_2O (1.5 mL), RT, 3 h. Ts = *p*-toluenesulfonyl.

Although the reaction of styrene with CT in the presence of K_2CO_3 and a catalytic amount of I_2 in water did not proceed at all, the addition of silica gel to the system led to the production of the desired aziridine (Table 1). For example, when styrene (1.0 mmol) was treated with CT (2.0 mmol), K_2CO_3 (2.0 mmol), and I_2 (10 mol%) in the presence of silica gel 60[7] (0.25 g) in water, *N*-(*p*-toluenesulfonyl)-2-phenylaziridine was obtained in 32% yield (entry 1). An increase in the amount of the silica gel used to 0.5 g improved the yield of the product (entry 2), but additional amounts failed to improve the efficiency of the reaction. The use of four equivalents of CT under the conditions of entry 2 gave the best result, an 85% yield of the aziridine (entry 3). From the difference in efficiency of the reactions (entry 1 versus entry 2), the product yield appears to be dependent on the specific surface area of the silica gel. Recently, mesoporous materials have attracted considerable attention in organic synthesis as solid acids or supports.[8] MCM-41,[9] one of such mesoporous silicas with a hexagonal array of uniform mesopores, was evaluated in the present aqueous system to synthesize aziridines. The use of MCM-41 led to a positive result, even when the reaction was carried out with two equivalents of CT and 0.25 g of silica (entry 4). A reaction using MCM-41 might proceed effectively because of its larger specific surface area, which is nearly double that of silica gel 60.

A variety of olefins were examined for this silica-mediated preparation of aziridines in water by using the iodine catalyst-CT system (Table 2). In the presence of MCM-41 (0.25 g), K_2CO_3 (2.0 mmol), and an iodine catalyst (20 mol%), 1,2-dihydronaphthalene was reacted with CT (2.0 mmol) to afford the corresponding aziridine in 75% yield. Other

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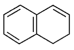
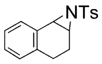
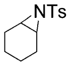
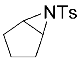
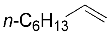
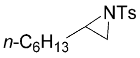
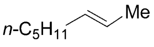
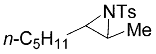
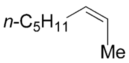
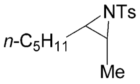
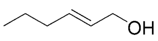
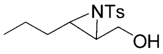
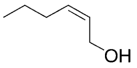
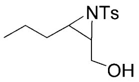
Table 2: Silica–water-mediated formation of aziridines from various olefins.[a]

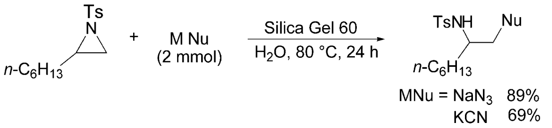
olefin	aziridine	yield [%] MCM-41	Silica gel 60
		75	68
		75	68
		64	53
		7	26[b] 49
		4[c]	42[c]
		27[d]	70[d]
		56[c]	58[c]
		72[d]	61[b,d] 59[d]

[a] Reaction conditions: olefin (1.0 mmol), CT (2.0 mmol), I_2 (20 mol%), K_2CO_3 (2.0 mmol), silica (MCM-41; 0.25 g or silica gel 60; 1.0 g), H_2O (1.5 mL), RT, 3 h. [b] Silica gel 60 (0.5 g). [c] *Trans* only. [d] *Cis* only.

cyclic olefins such as cyclohexene and cyclopentene were also used with the MCM-41 system resulting in the formation of aziridines in good yields. When these reactions were carried out with silica gel 60 (1.0 g), aziridines were also obtained in good yields. In spite of the fact that a larger amount of silica gel 60 (1 g; surface area: 640 m^2) was employed, compared to that of MCM-41 (0.25 g; surface area: 265 m^2), better results were achieved when the latter system was used, thus indicating that specific properties of MCM-41, which is a mesoporous solid and has an hexagonal array, may have played a role in these reactions. Although the formation of aziridines from acyclic olefins mediated by MCM-41 proceeded with a low yield, the same reactions with silica gel 60 gave the desired aziridines in moderate to good yields. The origin of this might be differences of the pore sizes of the MCM-41 and silica gel 60. As the average pore size of the MCM-41 used in this system is 25 Å, about half that of silica gel 60 (60 Å), we assume that the high degree of freedom of acyclic olefins suffers from difficulty in interacting with the surface of the MCM-41. On the other hand, allylic alcohols gave the corresponding aziridines in good yields with either MCM-41 or silica gel 60. It is possible that the hydroxyl group of these olefins may assist in the adsorption of olefins to the surface of the silicas.[10] This prediction is supported by the fact that the aziridination of *trans*-2-hexene scarcely proceeded under the same conditions.

To understand the different efficiencies for the aziridination, the amount of cyclohexene and 1-octene adsorbed to the two types of silicas were investigated in MeOH. Although there was little difference between silica gel 60 and MCM-41 in terms of the amount of cyclohexene adsorbed, a remarkable difference was observed for 1-octene.[11] As a result, the efficiency of the reaction is dependent on the extent of adsorption of olefins to the silicas, strongly suggesting that the reaction occurs on the surface of the silicas.

To show the generality of this media in organic synthesis, the ring opening of *N*-(*p*-toluenesulfonyl)-2-*n*-hexylaziridine with NaN_3 or KCN was examined. The reaction of the aziridine with NaN_3 or KCN in water in the absence of silica did not proceed. When silica gel 60 was added, however, the reaction proceeded to afford the regioselective ring-opening products (Scheme 1).



Scheme 1. Application of silica–water system to the ring opening of 2-hexyl-*N*-(*p*-toluenesulfonyl)aziridine with NaN_3 or KCN.

In summary, a new organic transformation in water by exploiting the adsorptive nature of silica is demonstrated; the formation of aziridines and their ring opening are used as examples. Applications of the present system to other organic reactions are now in progress, as the use of this system represents an environmentally benign organic synthesis.

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Keywords: aziridines · cyclization · nitrogen heterocycles · silicates · water chemistry

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[10] Although substrates that have only an olefin moiety are adsorbed to the surface of silica in water by hydrophobic repulsion, the substrates with functional groups such as a hydroxy group have an ability to interact with the surface (terminal) of silica (HO−Si), if they are not highly soluble in water.

[11] See Supporting Information.