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Ru/C catalyzed cyclization of linear α,ω-diamines to cyclic amines in water

Thomas M. Gädda, Xiao-Yan Yu, Akira Miyazawa *

Nanotechnology Research Institute (NRI), National Institute of Advanced Industrial Science and Technology (AIST), Central 5, Higashi, Tsukuba, Ibaraki 305-8565, Japan

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ABSTRACT

A facile and convenient way to prepare cyclic amines in water was achieved by the catalyst system composed of Ru/C and Al powder. The α,ω-diaminoalkanes, 1,4-diaminobutane, 1,5-diaminopentane, and 1,6-diamino-heptane were converted to corresponding cyclic amines in good yields. The use of D_2O provided a novel route to obtain deuterated cyclic amines in good yields.

1. Introduction

Alkylations of primary and secondary amines to obtain secondary- or tertiary amines are of considerable importance in organic synthesis. Conventionally such compounds have been prepared by reductive amination of the condensation products from amino compounds and carbonyl compounds or by amino dehalogenation from amines and halo-alkanes.[1] It is also known that amines themselves can be used as alkylating reagents to prepare secondary- or tertiary amines from primary amines. Murahashi and his co-workers reported an inter- and intramolecular coupling reaction of alkyl amines and diamines to secondary-, tertiary-, and cyclic amines using heterogeneous Pd black as a catalyst.[2] In a similar manner, α,ω-aminoalcohols can also be used to prepare heterocyclic amines.[3] Some related reports on the transition metal catalyzed synthesis of cyclic amines from aliphatic α,ω-diamines can be found in the literature. Raney nickel catalyzed intramolecular cyclization of aliphatic α,ω-diamines have been investigated in preparations of pyrrolidine and piperidine.[4] Kagiya, Ohtani, and his co-workers reported that TiO_2/Pt catalysts in water can transform α,ω-diamines to cyclic amines upon prolonged UV irradiation.[5] Some studies of the same have been carried out in the gas phase at high temperatures using zeolites as catalysts for the cyclic amine conversion.[6] Also, homogeneous late transition metal catalyst can also catalyze the intramolecular cyclization of α,ω-diamines in organic solvents.[7] Hydroamination can be considered as a further approach to prepare cyclic amines from alkyl amines bearing alkenyl- or alkynyl group at the terminal position of the starting materials. However, achieving control on the selectivity may be difficult as the addition to the C–C double or triple bonds usually favors the Markovnikov rule.[8] Additionally, there are a number of other ways to prepare nitrogen containing heterocycles such as intramolecular ring-closure of *N*-(ω-haloalkyl)imines, δ- and γ-alkenylimines, aminoalkanes, and *N*-chloroalkylamines.[9] Thus, most of the above reactions are carried out at high temperatures for prolonged reaction times, utilize organic solvents, and usually convert with less favorable selectivities, despite the use of transition metals catalyst.

Recently, we reported a novel, environmentally more benign way to convert primary amines to secondary amines.[10] A change of reaction conditions transforms amines on secondary alkyl groups to corresponding ketones. Herein, we would like to report the extension of this synthetic method for the conversion of aliphatic α,ω-diamines to corresponding cyclic amines. Contrary to previous investigations, our method uses heterogeneous catalysts and water is employed as a solvent and reagent. The use of water allows a different reaction pathway, which results in faster, more selective transformations.

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* Corresponding author. Tel.: +81 29 861 9388; fax: +81 29 861 4566.
E-mail address: a.miyazawa@aist.go.jp (A. Miyazawa).

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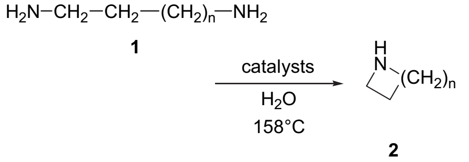
2. Results and discussion

We tested four different metal catalysts (Ru/C, Rh/C, Pd/C, and Pt/C) for the intramolecular catalytic cyclization of α,ω-diaminoalkanes, 1,4-diaminobutane and 1,6-daiaminohexane, to their corresponding cyclic amines, pyrrolidine and azepane, in water at 158 °C (Table 1). These reactions gave the desired cyclic amines along with side products. In the reactions with 1,4-diaminobutane, the cyclic imine, 1-pyrroline, was observed as a major side product together with small amounts of pyrrole and linear oligomeric products (entries 1–5). Adiponitrile, on the other hand, was observed in the reactions with 1,6-diaminohexane (entries 6–10). The formations of side products were confirmed by GC and GC–MS analysis. The results of these preliminary experiments suggested that Ru/C and Pd/C were effective catalysts for the reaction in terms of conversion and both showed better selectivity (entries 1, 2, 4, 6, 7, and 9) in comparison to Rh/C (entries 3 and 8). The Pt/C catalyst gave similar conversions compared to Ru/C and Pd/C, however selectivity of **2** was poor in 1,4-diaminobutane reaction (entry 5). Comparing Ru/C and Pd/C, the Ru/C catalyst showed higher selectivity than Pd/C in 1,6-diaminohexane cyclization. From above results we finally chose Ru/C as a suitable catalyst for the cyclization of α,ω-diaminoalkanes under the condition.

Table 1
Catalytic cyclization of α,ω-diaminoalkane



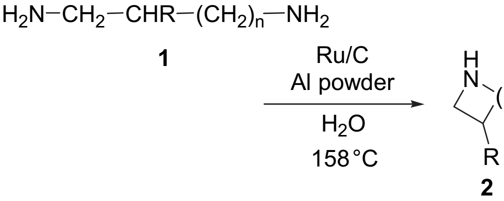
Entry	Diamine **1** n	Catalysts (mol %)	Time (h)	Conv.[a] (%)	Selectivity[a] **2** (%)
1	2	Ru/C (2.7)	1	7	39
2	2	Ru/C (2.7)	4	18	90
3	2	Rh/C (2.6)	1	7	—
4	2	Pd/C (2.6)	1	11	47
5	2	Pt/C (1.4)	1	8	—
6	4	Ru/C (2.9)	1	31	89
7	4	Ru/C (2.9)	4	43	95
8	4	Rh/C (2.8)	4	2	44
9	4	Pd/C (2.8)	4	39	72
10	4	Pt/C (1.5)	4	37	84

Reaction conditions; α,ω-diaminoalkane (100 mg), catalyst (50 mg), and water (2 mL) were placed in a 10 mL pressure resistant glass vessel.

[a] Conversions and selectivities were determined by GC and GC–MS analysis.

As the conversion and the selectivity of the reaction was relatively poor, aluminum powder was added to the reaction mixture. Previously, the addition of aluminum powder to the reactions where primary amines were converted to secondary amines has been found to drastically accelerate the reaction and enhance the selectivity of the secondary amine formation.[10b] Therefore we studied the Ru/C catalyzed cyclizations of 1,4-diaminobutane, 1,5-diaminopentane, 2-methyl-1,5-diaminopentane, and 1,6-diamino-heptane in the presence of aluminum powder. The addition of aluminum powder was found to dramatically facilitate the reaction and improve selectivity of the cyclization reaction. The starting diamines were almost completely consumed within 2 h and cyclic amine selectivities were over 88% in all cases (Table 2). While Pd/C gave similar results as Ru/C in the absence of Al, addition of it significantly slowed the reaction. Low conversions, less than 3%, of the starting material of 1,4-diaminobutane and 1,6-diaminohexane, respectively, were recorded.

Table 2
Ru/C catalyzed cyclization of α,ω-diaminoalkane in the presence of aluminum powder



Entry	Diamine **1**		Time (h)	Conv.[a] (%)	Selectivity[a] **2** (%)
	R	n			
1	H	2	0.5	42	95
2	H	2	2	99	88
3	H	3	0.5	46	86
4	H	3	1	99	98
5	Me	3	1.5	98	95
6	H	4	0.5	75	96
7	H	4	1	99	95

Reaction conditions; α,ω-diaminoalkane (100 mg), catalyst (50 mg, 2.6–2.9 mol % Ru), water (2 mL), and Al powder (30 mg) were placed in a 10 mL pressure resistant glass vessel.

[a] Conversions and selectivities were determined by GC and GC–MS analysis.

The conversion of 1,4-diaminobutane and 1,4-diaminohexane, plotted as a function of reaction time are shown in Figure 1. It is evident that the *in-situ* generated H_2 from the reaction of aluminum with water facilitates the hydrogenation of the imine intermediates to amines.[11] Similarly, dehydrogenation of imine intermediates were found to have significantly decreased as formation of side products such as adiponitrile were strongly suppressed. No reaction was seen when the reaction was carried out with aluminum in the absence of catalyst on carbon.

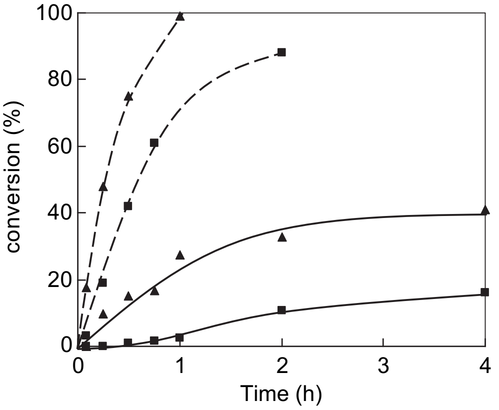


Figure 1. Plots of conversion of 1,4-diaminobutane (■) and 1,6-diaminohexane (▲) with (- - -) and without aluminum (—) vs reaction time. Conditions are the same as described in Table 1 and Table 2.

Some reports indicate that the ease of cyclization in the formation cyclic amines follows the order of ring size 5>3>6>7>4.[8,12] The results obtained for α,ω-diaminobutane, -pentane and -hexane cyclization in this study seems to disagree with earlier findings. The results obtained suggest that the reaction follow the order 7>6>5 in ring size. Although the detailed reaction pathway is not clear, the results suggests that the intramolecular cyclization of α,ω-diaminoalkane in water run through a different reaction