



The conversion of an aziridine plus an iminium salt to a 1,2-diamine

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Received 17 June 2003; revised 23 July 2003; accepted 28 July 2003

Abstract—The conversion of an aziridine to a 1,2-diamine using lithium iodide and an iminium salt is discussed. We have found that when the aziridine is substituted by only alkyl groups, it is the less substituted carbon–nitrogen bond that is broken; whereas, when the aziridine is substituted by a phenyl group at either the nitrogen or the carbon, it is the more substituted carbon–nitrogen bond that is broken. For a 2,3-disubstituted aziridine, the reaction sequence goes with net retention of stereochemistry.

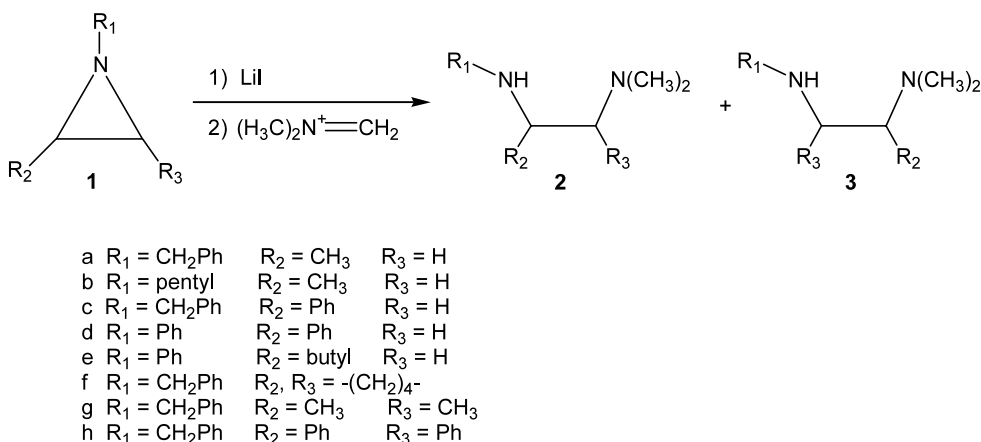
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1,2-Diamines, also known as vicinal diamines, are biologically and medically important compounds. In addition, they are prominent in organic synthesis as starting materials, as chiral auxiliaries, and as chiral ligands to a variety of metal complexes.^{1–5}

Although there are known conversions of aziridines to 1,2-diamines, the number is rather small.^{1,6–11} In addition, to open the ring, most of these conversions require electron-withdrawing groups on the nitrogen and a strong nucleophile, such as azide. Alternatively, the aziridine can be converted to an aziridinium ion, which can then be ring-opened with a large variety of nucleophiles.^{12–14}

Previously, we have shown that a ring-opened aziridine will react with a metal carbonyl complex, such as $\text{Fe}(\text{CO})_5$, to generate a metallacyclic complex,¹⁵ and will react with CO_2 to generate an oxazolidinone.¹⁶ In this manuscript, we will show that a ring-opened aziridine will react with a readily available¹⁷ iminium salt to generate, after an aqueous work-up, a 1,2-diamine. We have studied the regiochemistry and the stereochemistry of this reaction.

As shown in Scheme 1, we used $(\text{CH}_3)_2\text{N}^+=\text{CH}_2$ as the iminium salt and varied the substituents on the aziridine. These reactions were run by heating aziridine **1** with LiI in THF to affect a ring opening, and then,



Scheme 1.

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adding the iminium salt and stirring at room temperature. For compounds **1a** and **1b**, in which the nitrogen and a carbon are both substituted by alkyl groups, it is the less substituted carbon–nitrogen bond which is broken to give products **2a** and **2b**, respectively, in 70–80% yield. Only a trace of regioisomer **3** can be detected by ^1H NMR spectroscopy or gas chromatography/mass spectrometry.

When carbon-2 is substituted by a phenyl group as in **1c**, it is the more substituted carbon–nitrogen bond that is broken to give **3c** in over 70% isolated yield. When $\text{R}_1 = \text{Ph}$, as in **1d** and **1e**, the more substituted carbon–nitrogen bond is broken to give **3d** and **3e**, but unfortunately in very low isolated yield (about 20%).

Next, we wanted to determine the stereochemistry of this transformation. Aziridine **1f** gives 1,2-diaminocyclohexane **2f** as the product. If the two amine groups are *trans*, a large diaxial coupling between H_1 and H_2 should be observed. In contrast, if the two amines are *cis*, the J value will be small.¹⁸ A J value of 2.4 Hz was obtained, which indicates that the two amino groups are *cis*. Thus, this transformation goes with net retention of stereochemistry.

For aziridine **1g**, the reaction is stereospecific, i.e. the *cis* stereoisomer of the starting material gives one stereoisomer of the product and the *trans* stereoisomer of the starting material gives the other stereoisomer of the product. This was determined by the differences in the chemical shifts of the two products. (The product from *cis*-**1g** has its methyl groups at 1.09 and 1.14 ppm and H_1 and H_2 at 2.3 and 2.9 ppm. The product from *trans*-**1g** has its methyl groups at 0.8 and 1.0 ppm and H_1 and H_2 at 2.2 and 2.3 ppm.) The stereochemistry of the product diamine was determined by the chemical shifts and coupling constants of H_1 and H_2 .¹⁹ We found that *cis*-**1g** generates *erythro*-**2g** and that *trans*-**1g** generates *threo*-**2g**. Thus, as above, this reaction goes with net retention of stereochemistry.

When the aziridine ring is substituted by two phenyl groups as in **1h**, as we have shown previously, for

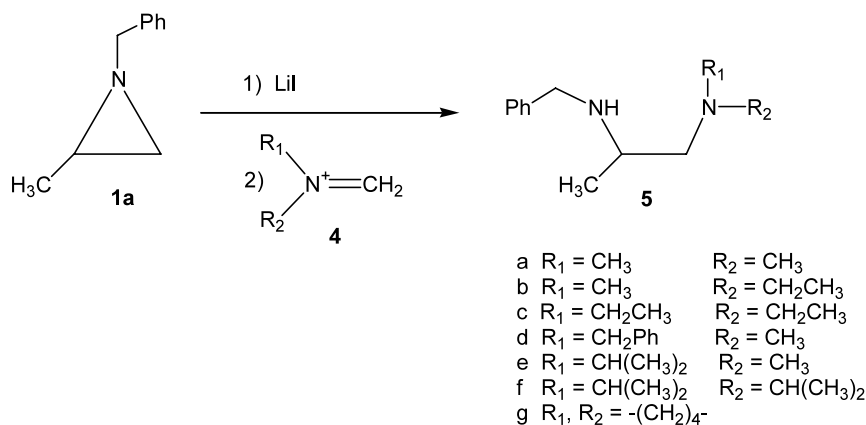
reasons that are unknown to us,¹⁶ the ring opening reaction does not occur.

Next, as shown in Scheme 2, we used aziridine **1a** and varied the iminium salt (**4**). These reactions were done to determine the variety of substituents that could be used.

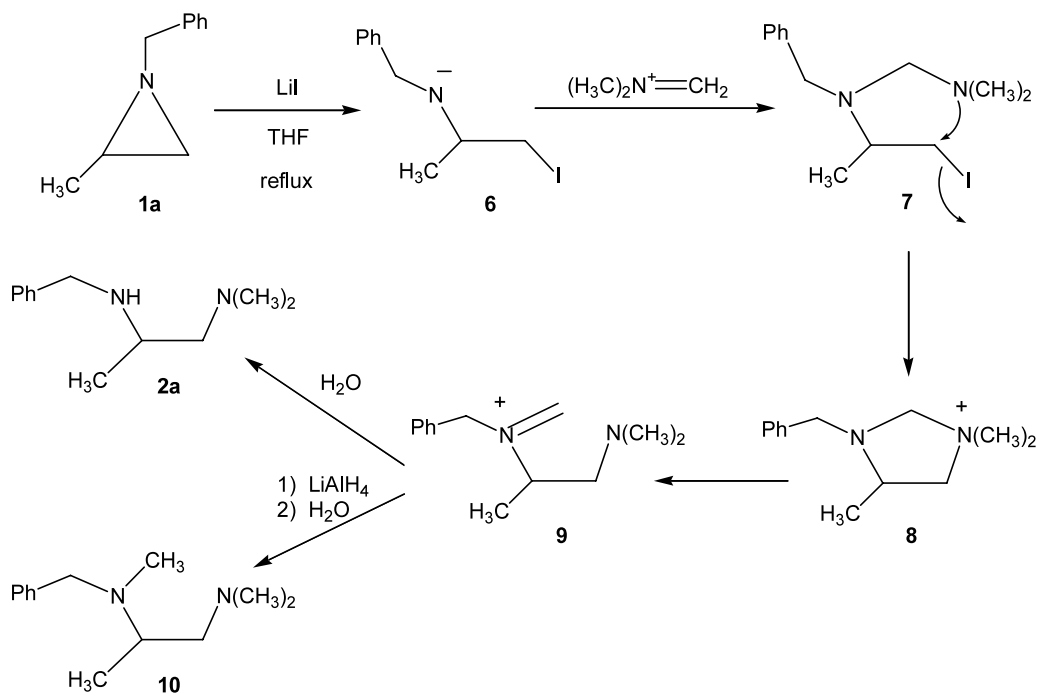
In all cases, the methylene is lost and the two alkyl groups are retained in the product diamine (**5**). This result implies that the iminium salts are stable to hydrogen scrambling under our reaction conditions. All reactions proceed in good yield (65–85%) except for the di-isopropyl case (**4f**), which does not react at all. We suspect this lack of reactivity is due to the large size of the two isopropyl groups.

Because a *gem*-aminoether is the immediate precursor to each iminium salt, we were curious if a *gem*-aminoether would undergo a similar reaction with a LiI ring-opened aziridine. Although the aminoethers have the advantage of being less air-sensitive than the iminium salts, in most cases, they were very difficult to isolate due to their volatility. The exception is the aminoether corresponding to iminium salt **4d**, which has a benzyl substituent. For this reaction, the yield was higher when using the iminium salt than when using the aminoether.

Taking into account the above data, we propose the mechanism shown in Scheme 3, which is drawn for the conversion of aziridine **1a** to diamine **2a**. As mentioned previously,¹⁶ in the first step, LiI opens the aziridine ring to give **6**. (Although we have no spectroscopic data for **6**, we believe it is present because when the solution is concentrated, we isolate a six-membered ring dimer of **6**. This dimer is not observed upon concentration of **1**.) Compound **6** then reacts with the iminium salt to give **7**, which immediately ring closes to give **8**. We have NMR data consistent with compound **8**. Upon hydrolysis of the reaction solution, diamine **2a** is generated.



Scheme 2.



Scheme 3.

Though we have no direct proof, our results are consistent with compound **8** isomerizing to compound **9**. When the reaction solution is treated with LiAlH_4 prior to the aqueous work-up, diamine **10** is generated.

This mechanism explains the net retention of stereochemistry that is observed. In the first step, the stereochemistry is inverted by the $\text{S}_{\text{N}}2$ addition of I^- , and in the third step, the stereochemistry is again inverted by the $\text{S}_{\text{N}}2$ addition of an amine.

The conversion of an aziridine plus an iminium salt to a 1,2-diamine was studied. We found that the reaction is regiospecific (when the aziridine is substituted by only alkyl groups, it is the less substituted carbon–nitrogen bond that is broken; whereas, when the aziridine is substituted by a phenyl group, it is the more substituted carbon–nitrogen bond that is broken) and stereospecific (a 2,3-disubstituted aziridine reacts with net retention of stereochemistry). Although the yields are not quantitative, they are usually between 70 and 80%. In addition, most products are very clean after simple extractions, i.e. either no chromatography or a short column in a disposable pipette is all that is needed.^{20,21}

Acknowledgements

M.T.H. thanks the Department of Chemistry of the University of Cincinnati for a Laws-Shubert Fellowship. The authors thank Professor Paul Lahti of the University of Massachusetts for suggesting the LiAlH_4 experiments.

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20. General procedure for the conversion of an aziridine to a diamine. A mixture of the aziridine (1.0 mmol) and lithium iodide (0.20 g, 1.5 mmol) in 30 mL of THF was allowed to reflux for 15 min. This reaction was cooled to room temperature. Then the iminium salt (1.0 mmol) was added and the solution was stirred at 25°C. After at least 20 h, the reaction mixture was added to 50 mL of ether. Then the mixture was treated with 100 mL of water and made acidic (pH 2 or 3, as determined by pH paper) with HCl. The water was removed and made basic (pH 10 or 11, as determined by pH paper) with NaOH. Finally, the water was extracted with 150 mL of ether, in three portions. The ether solutions were mixed together, dried with anhydrous K₂CO₃, and evaporated to dryness. The remaining oil easily was purified (when necessary) by using a short alumina column in a disposable pipette, eluting with methylene chloride and ethyl acetate, to give the corresponding 1,2-diamine. Spectroscopic data for compounds **2**, **3** and **5** have been reported previously.¹⁵
21. Isolation of the reaction intermediate **8g**. The reaction using aziridine *trans*-**1g** and iminium salt **4a** was run as discussed in Ref. 20. After 20 h, the reaction mixture was added to 50 mL of ether and the solid that precipitated from the solution was collected: ¹H NMR δ 1.21 (d, J =6.1 Hz, 3H), 1.38 (d, J =7.0 Hz, 3H), 2.87–2.93 (m, 1H), 2.96 (s, 3H), 3.10 (s, 3H), 3.41–3.47 (m, 1H), 3.71 (d, J =14.2 Hz, 1H), 4.03 (d, J =8.6 Hz, 1H), 4.08 (d, J =14.4 Hz, 1H), 4.24 (d, J =8.3 Hz, 1H), 7.31–7.36 (m, 5H).