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Aza-pinacol rearrangement: acid-catalyzed rearrangement of aziridines to imines†

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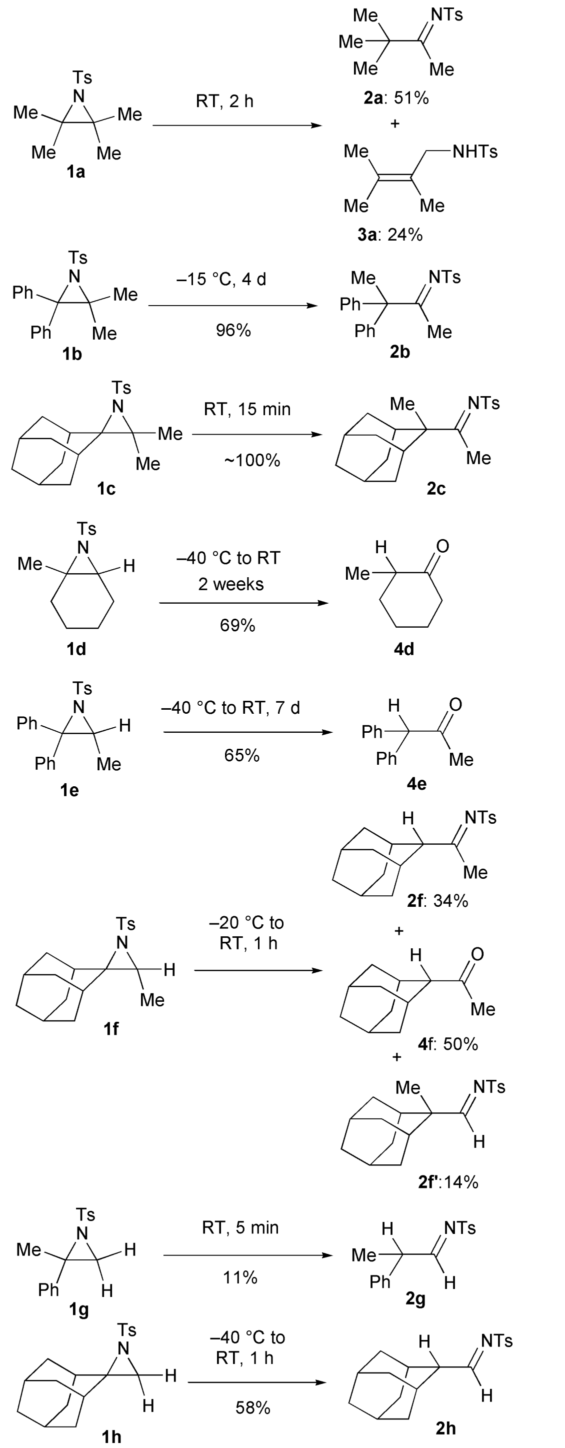
A series of di-, tri-, and tetra-substituted *N*-tosylaziridines [*N*-(toluene-*p*-sulfonyl)aziridines] 1, prepared by aziridination of the corresponding alkenes with *N*-[(tolyl-*p*-sulfonyl)-imino]phenyliodinane (TsN = IPh), was found to undergo a BF_3-catalyzed rearrangement (aza-pinacol rearrangement) under mild conditions to give the corresponding *N*-tosylimines 2 generally in satisfactory yields.

Acid-catalyzed rearrangement of epoxides to carbonyl compounds, which is interpreted as a type of pinacol rearrangement in a wide sense, has been extensively investigated mainly from the viewpoints of the mechanism and application to organic syntheses.[1] Rather surprisingly, however, acid-catalyzed rearrangement of aziridines to imines (aza-pinacol rearrangement) has not hitherto been reported.[2,3] We have now found that *N*-tosylazridines [*N*-(toluene-*p*-sulfonyl)aziridines] undergo an acid-catalyzed aza-pinacol rearrangement under mild conditions to give the corresponding *N*-tosylimines generally in satisfactory yields.[4]

A series of di-, tri-, and tetra-substituted *N*-tosylaziridines **1a–h**, many of which are new compounds, was synthesized by aziridination of the corresponding alkenes with *N*-[(tolyl-*p*-sulfonyl)imino]phenyliodinane (TsN=IPh).[5] Rearrangement of **1** was examined by using $BF_3{\cdot}Et_2O$, which is the most common Lewis acid applied to the rearrangement of epoxides. The results, summarized in Scheme 1, show that the rearrangement is general and takes place under mild conditions. Thus, treatment of the aziridine **1a** with 0.3 molar amount of $BF_3{\cdot}Et_2O$ in $CHCl_3$ at rt for 2 h provided the imine **2a** in 51% yield in addition to the sulfonamide **3a**[6] in 24% yield. Similar treatment of **1b** and **1c** with $BF_3{\cdot}Et_2O$ resulted in the exclusive methyl migration to afford **2b** and **2c**, respectively, in excellent yields. Rearrangement of **1c** to **2c** took place also by use of other acid catalysts such as $AlCl_3$, $MgBr_2{\cdot}Et_2O$, $CF_3SO_3SiMe_3$, concentrated H_2SO_4, and CF_3CO_2H in 100, 91, 100, 100, and 97% yields, respectively. *N*-Tosylimines are generally susceptible to hydrolysis and are used as prepared *in situ* for synthetic purposes.[7] Thus, treatment of a trisubstituted aziridine **1d** with $BF_3{\cdot}Et_2O$ gave a 69% yield of ketone **4d**, the hydrolysis product of the corresponding imine,[8] which was produced by a hydrogen migration. When, for comparison, the corresponding epoxide **5** was treated with $BF_3{\cdot}Et_2O$ under similar conditions, hydrogen migration and ring-contraction took place in a comparable ratio to give a mixture of **4d** (45%) and **6** (43%) (Scheme 2).Preferential hydrogen migration was also observed with trisubstituted aziridines **1e**[8] and **1f**. The preferential hydrogen migration, therefore, seems to be one characteristic of the present aza-pinacol rearrangement, thus providing a good flavor for synthetic use. Even disubstituted aziridines **1g** and **1h** underwent the rearrangement to give **2g** and **2h**, respectively. *N*-Tosylimines are known to undergo a BF_3-catalyzed hetero-Diels–Alder reaction.[9] Thus, when the rearrangement of **1h** was carried out in the presence of 2,3-dimethylbuta-1,3-diene, the

† Electronic supplementary information (ESI) available: experimental procedure and characterization data. See http://www.rsc.org/suppdata/cc/b1/b109445a/



Scheme 1 BF_3-catalysed aza-pinacol rearrangement of *N*-tosylaziridines in $CHCl_3$.

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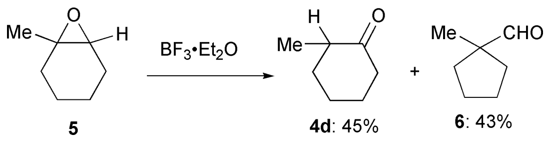
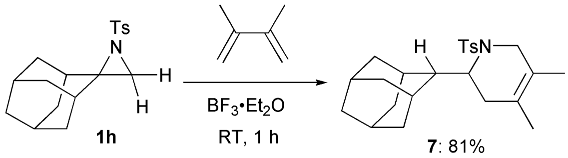
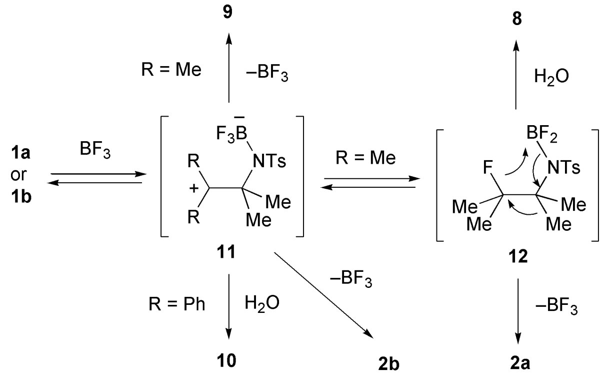


Scheme 2



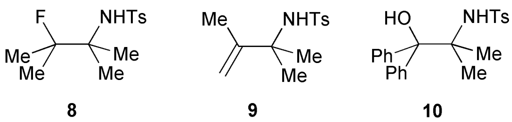
Scheme 3



Scheme 4

Diels–Alder adduct **7** of **2h** and the diene was obtained in 81% yield in a one-pot reaction (Scheme 3).

The progression of the rearrangements of **1a** and **1b** to **2a** and **2b**, respectively, was monitored by ^{1}H NMR spectroscopy in order to look into the mechanism. For the reaction of **1a**, new signals, which are neither assigned to **1a** nor **2a** and originate probably from two compounds, began to develop immediately after mixing of **1a** and $BF_3{\cdot}Et_2O$ at 20 °C and these signals were completely replaced largely by those of **2a** and its hydrolysis product (pinacolone) after 1 h. Indeed, the reaction, carried out at −18 °C and quenched at the early stage, allowed us to isolate two new products **8** and **9** in 70 and 27% yields, respectively.



Furthermore, on treatment with $BF_3{\cdot}Et_2O$, **8** was converted to **2a** quantitatively (obtained as the corresponding ketone in 96% yield). Also, for the reaction of **1b**, ^{1}H NMR analysis revealed the appearance of new signals which are neither assigned to **1b** nor **2b**. When the reaction of **1b** with $BF_3{\cdot}Et_2O$, carried out at −18 °C, was quenched after 6 h by addition of aq. $NaHCO_3$, the aminoalcohol **10** was isolated in 39% yield in addition to **2b** in 55% yield.

On the basis of the above findings, the following are presented concerning the mechanism of the rearrangement of **1a** and **1b** (Scheme 4). The initial step would involve the formation of carbocation intermediates **11** just as in the case of the rearrangement of many epoxides.[1] In the case of **1a**, **11** would produce **9** by deprotonation, while the intramolecular fluorine migration would lead to **12**,[10,11] the probable intermediate that was observed by ^{1}H NMR spectroscopy and would produce **8** through hydrolysis.[12] The formation of **12** from **11** is regarded as an aliphatic version of the well-known Schiemann reaction.[13] Finally, the methyl migration of **12** occurs to produce **2a**. On the other hand, in the case of **1b**, the intermediate, observed by ^{1}H NMR spectroscopy, might be assigned to the carbocation **11**,[14] which affords **10** by hydrolysis. In this case, the carbocation **11** is stable enough to suppress the fluorine migration, and hence **2b** would be directly formed from **11** by methyl migration.

In conclusion, the aza-pinacol rearrangement developed here, which takes place under mild conditions and prefers hydrogen migration to alkyl group migration, is synthetically promising since recently *N*-tosylaziridines have become readily obtainable.[5,15]

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11 Treatment of **1a** with $AlCl_3$ at rt afforded **2a** in 60% yield, whereas quenching of the reaction at the early stage allowed the isolation of the chloride that corresponds to the fluoride **8**.

12 The ^{1}H NMR spectrum of **8** closely resembles that of the probable intermediate **12** in the methyl chemical shift values.

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