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Ring opening of Phenylaziridines with Allylsilanes.

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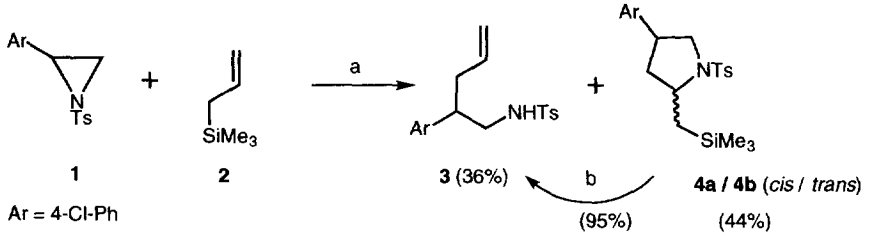
Abstract : N-tosyl phenylaziridines are opened regioselectively with allylsilanes in presence of $BF_3.Et_2O$ to form γ-amino olefins. During the reaction a formal [3+2] cycloaddition produced the corresponding pyrrolidines, amenable to the open chain compounds with TBAF. Copyright © 1996 Published by Elsevier Science Ltd

N-Activated aziridines are versatile intermediates for the synthesis of compounds bearing nitrogen functionnalities.[1] Their synthetic utility as building blocks originates from the capability to undergo regioselective ring-opening reactions with a wide range of nucleophilic reagents such as Grignard, Wittig, organolithiums, or cuprates reagents.[2-6] Pursuing our interest in the construction of biological important compounds with aziridines, we decided to experiment the reactivity of phenylaziridines with allylsilanes.[7] The advantage in using allylsilanes instead of organometallic nucleophiles is that the reaction conditions tolerate the presence of functionnalities, attached to their backbone.[8,9] A recent communication regarding the *intra*molecular ring opening of aziridines[10] with allylsilanes prompt us to describe our results on the *inter*molecular version. In this letter we present the reactivity of phenylaziridines against various allylsilanes in presence of Lewis acids, as well as some transformations of the obtained adducts. The nucleophilic ring opening of activated aziridines is generally assisted by the presence of Lewis acids. A good compromise between assistance and intrinsic reactivity is concentrated in $BF_3.OEt_2$.

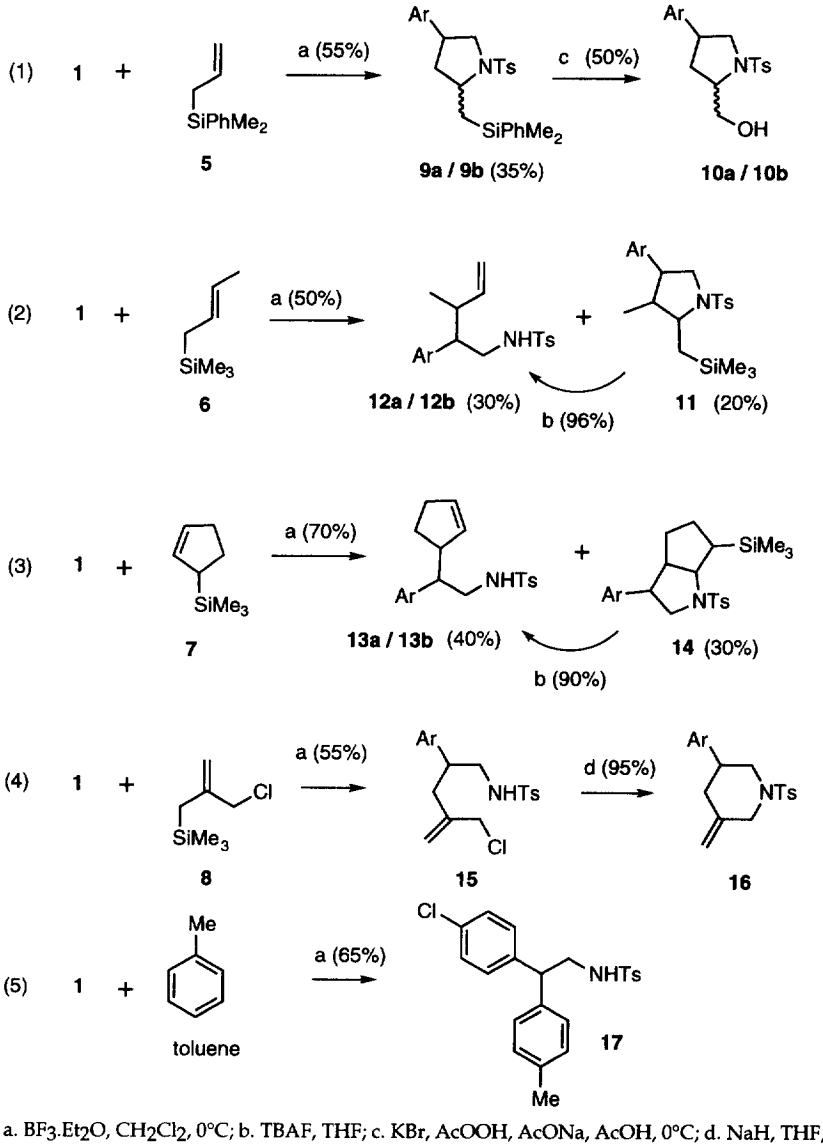


Reagents: a. $BF_3.Et_2O$, CH_2Cl_2, 0°C; b. TBAF, THF.

Scheme 1

The starting aziridine **1** was prepared from p-chlorostyrene with PhINTs by catalyzed aziridination according to Evans.[11] In the first attempt of the ring opening reaction with allyltrimethylsilane **2**, we found that, at 0°C in CH_2Cl_2, and in presence of a threefold excess of $BF_3.Et_2O$, p-Cl-phenylaziridine **1** was totally transformed in 1 h. Two compounds were isolated after the usual work up and purification by column chromatography :[12] the compound

corresponding to the slow running spot in TLC, isolated in 36% yield was identified as the expected amino olefin **3**; the one corresponding to the fast running spot, isolated in 44% yield was identified, after analysis of the ^{1}H and ^{13}C NMR spectra and MS analysis, as a 1/1 mixture of two pyrrolidines **4a/b** (*cis* and *trans*), inseparable in TLC. The observed reactivity at the benzylic position of aziridine **1** is consistent with the stability of the corresponding carbocation.



Reagents : a. $BF_3.Et_2O$, CH_2Cl_2, 0°C; b. TBAF, THF; c. KBr, AcOOH, AcONa, AcOH, 0°C; d. NaH, THF, reflux.

Scheme 2

As anticipated we could transform quantitatively the mixture of pyrrolidines **4a/4b** in the amino olefin **2** by a brief heating in THF in presence of TBAF. This fluoride induced silicon fragmentation is similar to the fragmentation reported by Langlois[13] and recently by Harmata.[14]

The formation of the pyrrolidines ring which is formally the result of a non concerted [3+2] cycloaddition, may be explained in the following way : during the S_E2' reaction the silicon stabilised β-carbocation is trapped by the transient amide anion, forming the 5 membered ring. Similar examples are reported with oxygen as well as with nitrogen.[15-16] Additionnally we have experimented different solvents, temperature and stoechiometry of $BF_3.Et_2O$. In our hands Et_2O or toluene are not suitable media, we observed respectively the fluorinated adduct at the benzylic position and an other ring opening reaction of aziridine **1** (vide infra). The temperature is not a critical factor at -78, 0 or 20°C the same results either in reaction rate or product composition are roughly obtained. Concerning the stoechiometry of $BF_3.Et_2O$, 0.2 equivalent are sufficient in order to perform the reaction, however the yields are lower in some extent : 17% for **3** and 50% for **4a/4b**. These results suggest a possible asymmetric catalysis if the appropiate Lewis acid is found. Finally we checked that the Lewis acid is necessary to perform the reaction, and without the presence of allylsilane no reaction was detectable.

In order to determine the scope and limitations of this reaction, we decided to examine the reactivity of other allylsilanes, such as allylphenyldimethylsilane **5**, crotyltrimethylsilane **6**, cyclopentenyltrimethylsilane **7**, or 2-chloromethyl-3-trimethylsilylpropene **8** with aziridine **1**. The results are reported on Scheme 2 (entry 1 to 5). (Entry 1) The reaction of aziridine **1** with allylsilane (**5**) gave only the cyclic adducts **9a/9b** (inseparable *cis* and *trans* mixture) in 55% yield. Interestingly the mixture **9a/9b** was converted to the corresponding prolinols **10a/10b** using the Fleming's procedure,[17] again as an unseparable mixture in 50% yield. (Entry 2) The reaction with crotylsilane **6** gave a global yield of 50%, 20% for the cyclic adducts, a mixture of three compounds **11**, amenable with TBAF to the open chain analogues, and 30% for the open chain adduct as mixture of two diastereomers **12a/12b** in a 1 to 1 ratio. (Entry 3) With allylsilane (**7**) the same reactivity was observed but the open chain compounds **13a/13b** were the major adducts in 40%, the mixture of the bicyclic adducts **14** contains several diastereomers isolated in 30% yield, which could be cleanly transformed to the open chain derivatives **13a/13b** in quantitative yield. (Entry 4) With allylsilane **8**, under the normal conditions only the open chain adduct **15** was formed in 40% yield (non optimized). A brief treatment with NaH afforded the arylpiperidine **16** in quantitative yield. This two step sequence allowed a direct preparation of 3,4-substituted piperidines with the exocyclic methylene waiting for further transformation. (Entry 5) During our preliminary experiment, when CH_2Cl_2 was replaced with toluene, the formation of a product different from **3** was observed. After purification by column chromatography, and ^1H and ^{13}C NMR studies, we identified *N*-tosyl-2-(4'-chloro)-2-(4"-methyl)diphenylethylamine **17**. The reaction was repeated without allylsilane but **17** was the only compound formed.[18] This result revealed that toluene is an excellent nucleophile for the ring opening of activated phenylaziridines.

In conclusion, we have found that N-tosyl phenylaziridines react smoothly with allylsilanes in presence of $BF_3.Et_2O$ regioselectively at the benzylic position given simultaneously the amino olefinic adducts and the five membered pyrrolidines, easily transformable in the former. Furthermore as homochiral phenylaziridines are accessible,[19,20] the above reaction should be rendered enantioselective. Finally the obtained amino olefins are suitable for further transformations, work in this direction is underway in our laboratory.

References and Notes.

1. Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599-619.
2. Kozikowski, A. P.; Ishida, H.; Isobe, K. *J. Org. Chem.* **1979**, *44*, 2788-2790.
3. Baldwin, J. E.; Adlington, R. M.; Robinson, N. G. *J. Chem. Soc., Chem. Commun.* **1987**, 153-155.
4. Osborn, H. M. I.; Sweeney, J. B.; Howson, B. *Synlett* **1993**, 676-677.
5. Ibuka, T.; Nakai, K.; Habashita, H.; Fujii, N.; Garrido, F.; Mann, A.; Chounan, Y.; Yamamoto, Y. *Tetrahedron Lett.* **1993**, *34*, 7421-7424.
6. Ezquerra, J.; Pedregal, C.; Lamas, C.; Pastor, A.; Alvarez, P.; Vaquerro, J. J. *Tetrahedron Lett.* **1996**, *37*, 683-686.
7. Ibuka, T.; Schoenfelder, A.; Bildstein, P.; Mann, A. *Synth. Commun.* **1995**, 25, 1777-1782.
8. Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293-1316.
9. Langkopf, E. Schinzer, D. *Chem. Rev.* **1995**, 95, 1375-1408.
10. Bergmeir, S. C.; Seth, P. P. *Tetrahedron Lett.* **1995**, *36*, 3793-3796.
11. Evans, D. ; Faul, M. M.; Bilodeau, M. T. *J. Org. Chem.* **1991**, *56*, 6744-6746.
12. Experimental procedures: To a solution of **1** (100 mg, 0.32 mmol) and **2** (0.20 mL, 0.98 mmol, 3 eq.) in CH_2Cl_2 (5 mL) was added dropwise at 0°C a solution of freshly distilled $BF_3.Et_2O$ (0.10 mL, 0.98 mmol, 3 eq.) in CH_2Cl_2 (5 mL). After stirring at 0°C for 1 h, the reaction mixture was quenched with saturated NH_4Cl, extracted with ether (3 x 10 mL), dried (Na_2SO_4) and concentrated in vacuo. The residue was purified by chromatography eluting with hexane/ether : 5/5 to give **3**[7] (36%) and **4a/4b** (44%), as mixture of two diastereomers. Physical data for **4a/4b** : ^1H NMR (200 MHz, $CDCl_3$) δ 0.06 (s, 9H), 0.08 (s, 9H), 0.99 (dd, J = 14.5 and 2.5 Hz, 1H), 1.05 (dd, J= 14.5 and 2.5 Hz, 1H), 1.48 (dd, J = 14.5 and 3.5 Hz, 1H), 1.59 (dd, J = 12 and 2.5 Hz, 1H), 1.70 (q, J = 3 Hz, 1H), 1.76-1.86 (m, 2 H), 2.28-2.46 (m, 1H), 2.46 (s, 6H), 2.53-2.64 (m, 1 H), 2.95 (t, J = 10 Hz, 1H), 3.30 (t, J = 11.5 Hz, 1H), 3.40-3.57 (m, 1 H), 3.70-3.96 (m, 4H), 6.95-7.25 (m, 8H), 7.32-7.75 (m, 8H).
13. Bac, N. V.; Langlois, Y. *J. Am. Chem. Soc.* **1982**, *104*, 7666-7667.
14. Harmata, M.; Jones, D. E. *Tetrahedron Lett.* **1995**, *36*, 4769-4772.
15. Osumi, K.; Sugimura, H. *Tetrahedron Lett.* **1995**, *36*, 5789-5792.
16. Kiyooka, S.; Shiomi, Y.; Kira, H.; Kaneko, Y.; Tanimori, S. *J. Org. Chem.* **1994**, *59*, 1958-1960.
17. Fleming, I.; Sanderson, P. E. J. *Tetrahedron Lett.* **1987**, *28* ,4229-4232.
18. Experimental procedure : To a solution of **1** (50 mg, 0.16 mmol) and toluene (0.05 mL, 0.48 mmol, 3 eq.) in CH_2Cl_2 (3 mL) was added $BF_3.Et_2O$ (0.02 mL, 0.18 mmol, 1 eq.) at -78°C. The reaction mixture was stirred for 2 h at -78°C, quenched with NH_4Cl and extracted with Et_2O (3 x 10 mL). The combined organic layers were dried and concentrated under reduced pressure. The residue was purified by chromatography on silica gel eluting with hexane/ether : 4/6 to yield **17** (54 mg, 84%) as white solid m.p. 148°C. ^1H NMR (200 MHz, $CDCl_3$) δ 2.32 (s, 3 H), 2.46 (s, 3 H), 3.50 (t, J = 7.5 Hz, 1H)), 4.03 (t, J = 8 Hz, 1H), 4.49 (t, J = 6 Hz, 1H), 6.95-7.33 (m, 10H), 7.68 (d, J = 8 Hz, 2H). ^{13}C NMR (50 MHz, $CDCl_3$) δ 90.9, 21.5, 47.1, 49. 5, 127.1, 128.8, 129.2, 129.7, 131.2, 132.7, 136.9, 137.1, 139.5, 143.5.
19. Li, Z.; Conser, K. R.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1993**, *115*, 5326-5327.
20. Evans, D. ; Faul, M. M.; Bilodeau, M. T.; Anderson, B. A.; Barnes, D. M. *J. Am. Chem. Soc.* **1993**, *15*, 5328-5329.

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