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INTRAMOLECULAR VARIANTS OF AMINOMETHANO DESILYLATION: REACTIONS OF IN SITU GENERATED IMMONIUM IONS WITH ALLYLSILANES

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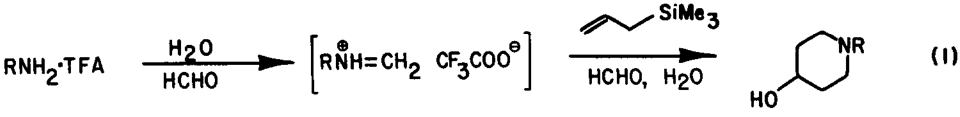
Summary: Intramolecular condensation of immonium ions with allylsilanes in aqueous tetrahydrofuran at ambient temperature gives rise to five, six, seven, and eight-membered rings containing nitrogen.

A previous report from our laboratory has demonstrated that simple immonium ions, generated *in situ* under Mannich-like conditions, upon exposure to allylsilanes in the presence of excess formaldehyde gives rise to piperidines via a novel aminomethano desilylation-cyclization process (cf eq. 1).[1] Despite the relatively acidic conditions required to generate immonium ion 1 in water, protodesilylation of the allyltrimethylsilane is not a competitive process. We detail below an intramolecular variation of the aminomethano desilylation process which permits access to five, six, seven and eight-membered rings containing nitrogen.



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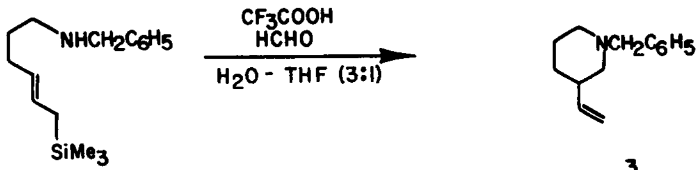
In a preliminary study, amino allylsilane 2[2] as its trifluoroacetate salt was treated at



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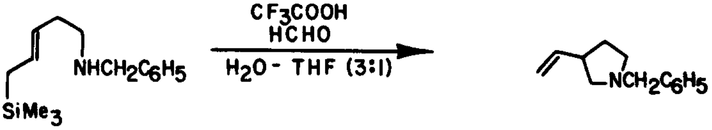
ambient temperature with 1.2 equiv of aqueous formaldehyde in water:tetrahydrofuran (3:1). After 56 h a 94% yield of N-benzyl 3-vinylpiperidine 3[5] was obtained. Examination of amino allylsilane 4[6] possessing one less carbon atom in the tether provided the 3-vinyl pyrrolidine 5 in 81% under essentially identicial conditions described above for the transformation of 2 into 3. Despite the long reaction times observed in the two cases cited above, no products derived from protodesilylation were detected.



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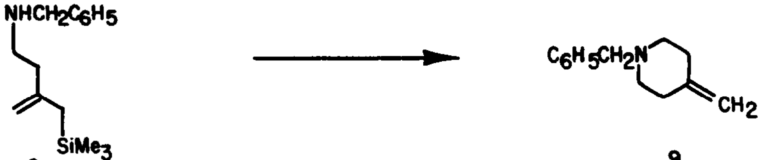
In an effort to examine the generality of this intramolecular process, amino allylsilanes 6-8[7] were subjected to the standard reaction conditions [CF_3COOH (1.0 equiv), HCHO (1.2 equiv), H_2O-THF (3:1)]. In the case of substrate 6, a 73% yield of 9 was isolated after 19 h at ambient temperature. Much to our surprise, amino allylsilane 7 smoothly underwent aminomethano desilylation over a 42 h period giving rise to the seven-membered ring system 10 in



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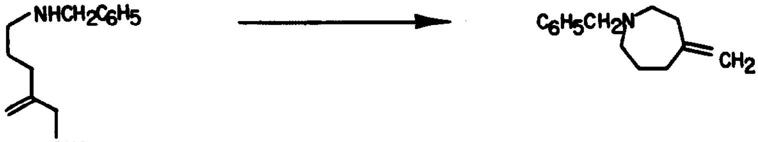

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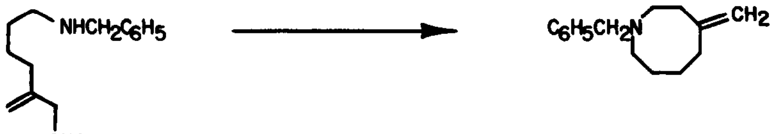

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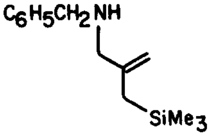
96% isolated yield. Less spectacular, but noteworthy, was the observation that amine 8 provided a 64% yield of the eight-membered ring compound 11 after 5 days at 50°C. During the course of this investigation amine 12 was subjected to aminomethano desilylation. Not suprisingly, none of five-membered ring product 13 could be detected.[10]



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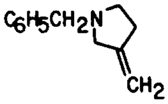

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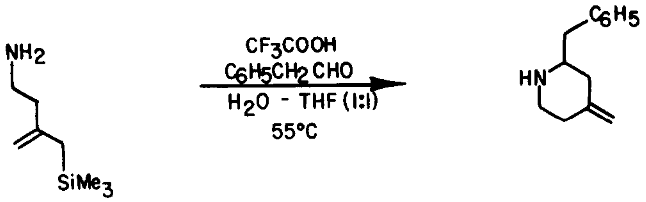
Finally, in order to shed light on the ability to employ aldehydes other than formaldehyde the reaction of primary amine 14 with the phenylacetaldehyde was examined. Addition of 2.0 equiv of phenylacetaldehyde to an 0.8 M solution of the amine as its trifluoroacetate salt in a 1:1, water-tetrahydrofuran mixture at 55°C afforded after 24 h a 71% of piperidine 15.[11]



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The intramolecular aminomethano desilylation process should prove exceedingly useful in the construction of naturally occurring alkaloids. Efforts along these lines are currently in progress.

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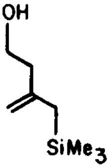
REFERENCES

1. S.D. Larsen, P.A. Grieco, and W.F. Fobare, J. Am. Chem. Soc., 108, 3512 (1986).
2. Amino allylsilane 2 was prepared via a four-step sequence in approximately 60% overall yield starting from 4-tetrahydropyranyloxybutanal [1. $(C_6H_5)_3P{=}CHCH_2SiMe_3$,[3] THF; 2. PPTS,[4] EtOH; 3. TsCl, Et_3N, CH_2Cl_2; 4. $C_6H_5CH_2NH_2$, THF].
3. I. Fleming and I. Paterson, Synthesis, 446, (1979).
4. M. Miyashita, A. Yoshikoshi, and P.A. Grieco, J. Org. Chem., 42, 3772, (1978).
5. All new compounds have been fully characterized spectrally and have elemental composition determined by high-resolution mass spectrometry and/or combustion analysis.
6. Amino allylsilane 4 was prepared from 3-tetrahydropyranyloxypropanal in 46% overall yield using the scheme detailed in reference 2.
7. Amino allylsilane 5 was prepared in a straightforward manner from the known alcohol i.[8]



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Substrates 6 and 7 were prepared directly via a three-step procedure from γ-butyrolactone and δ-valerolactone respectively according to the method of Fujita.[9]

8. M. Ochiai, E. Fujita, M. Arimoto, and H. Yamaguchi, Chem. Pharm. Bull., 31, 86, (1983).
9. M. Ochiai, E. Fujita, M. Arimoto, and M. Yamaguchi, J. Chem. Soc., Chem. Commun., 1108, (1982).
10. cf. J.E. Baldwin, J. Chem. Soc., Chem. Commun., 734, (1976).
11. The long reaction times and good to excellent yields observed for the intramolecular variants of aminomethano desilylation are in accord with previous observations on the intermolecular process.

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