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A NOVEL RING-OPENING REACTION OF AZIRIDINE INDUCED BY THE FORMATION OF NITROGEN-SUBSTITUTED CARBANION OF NONSTABILIZED TYPE

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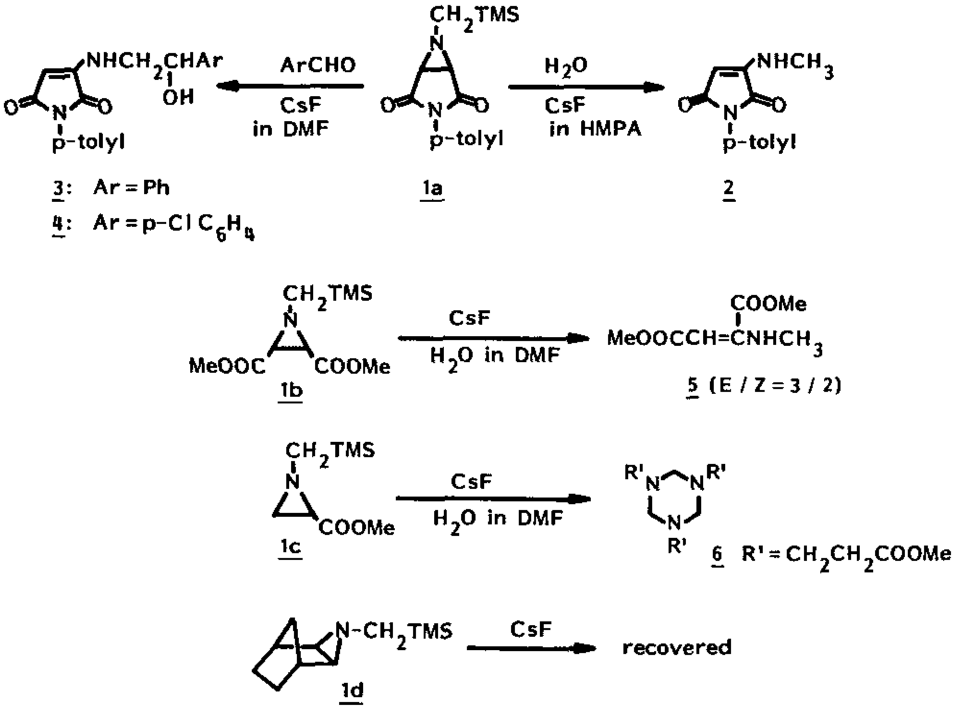
Abstract —— Desilylation of 1-(trimethylsilylmethyl)aziridines causes a novel ring-opening reaction of aziridine. Only aziridines whose ring bears at least one anion-stabilizing moiety undergo the desilylation, and the resultant carbanion of nonstabilized type changes into a stabilized one inviting the ring-opening. The types of products depend upon the number of anion-stabilizing moieties as well as the quenching reagents employed.

Although a silicon-carbon bond is smoothly cleaved by the action of silylophile forming a carbanion species if the carbon is substituted with at least one anion-stabilizing moiety[1], generation of the nonstabilized carbanion by desilylation is quite difficult[2]. We have recently found that the silicon-carbon bond of N-(trimethylsilylmethyl)triazoles can be readily cleaved on the treatment with a fluoride ion[3]. To evaluate the anion-stabilizing ability of a heteroaromatic triazole ring or a nitrogen atom[4], we have investigated the desilylation reactions of some related nonaromatic heterocycles such as triazolines and aziridines with a trimethylsilylmethyl substituent on the nitrogen. During the course of this study, we came across a novel ring-opening reaction of aziridine.

As trimethylsilylmethyl azide is a ready-to-prepare and inexplosive alkyl azide with a silyl functionality[5], it may be used for the introduction of a trimethylsilylmethyl moiety on the nitrogen of aziridines. Thus the 1,3-dipolar cycloaddition reactions[6] of the azide with N-(p-tolyl)maleimide, dimethyl fumarate, methyl acrylate, and bicyclo[2.2.1]hept-2-ene and the followed nitrogen elimination reactions[7] give several N-(trimethylsilylmethyl)aziridines 1a to 1d in good yields[8]. When the fused aziridine 1a was treated with an equivalent of cesium fluoride in hexamethylphosphoric triamide (HMPA) at room temperature under nitrogen, the reaction mixture gradually turned orange then to deep red. Usual work-up with water gave a yellow-colored solid of 2 (mp 225-227 °C) in 80% yield (Scheme 1). This product 2 carries no longer both an aziridinyl and a silyl moieties and was assigned as 3-methylamino-1-(p-tolyl)maleimide on the basis of the spectral data as well as the elemental analysis[9]. The reactions using at least an equivalent of cesium fluoride in HMPA or dimethylformamide (DMF) gave better yields of 2 than those using tetrabutylammonium fluoride as a silylophile in tetrahydrofuran or 1,2-dimethoxyethane.

Instead of water, benzaldehyde was employed as a quenching reagent for an intermediate involved in the reaction (at room temperature in dry DMF for 1 h using two equivalents of the aldehyde and each an equivalent of 1a and cesium fluoride). The product 3 (mp 188-190 °C) given in 85% yield was assigned as 3-(2-hydroxy-2-phenylethyl)amino-1-(p-tolyl)maleimide[10] as shown in Scheme 1. Similarly, the reaction with p-chlorobenzaldehyde under the same conditions provided 4 (mp 229-231 °C) in 75% yield.

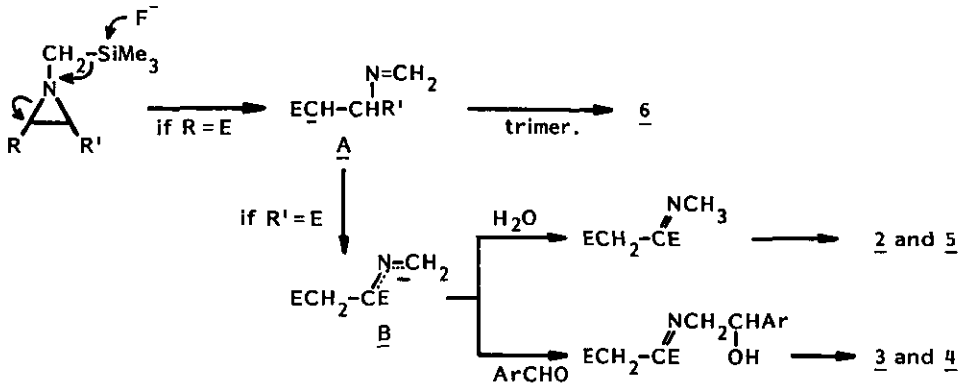


Scheme 1.

In the reaction between each equivalent of 1b and cesium fluoride in DMF at room temperature for 15 h, the aziridine ring of 1b was also opened up giving a mixture of E and Z isomers of enamine 5 as yellow viscous oil (E/Z = 3/2) in 76% yield. The structure and the ratio of isomers were based on the spectral data[11].

On the other hand, the aziridine 1c carrying only one anion-stabilizing substituent gave, unexpectedly, a different type of desilylated and also aziridine-opened product 6 (colorless oil) in 88% yield, which corresponded to the trimer of desilylated species of 1c[12].

Under various conditions (CsF in DMF at 60 °C for 68 h; CsF in DMF at 100 °C for 41 h; CsF-PhCHO in DMF at 100 °C for 41 h), the aziridine 1d with no anion-stabilizing group was quantitatively recovered. This result shows that the scission of the silicon-carbon bond is dominated by the stabilization of formed anionic species.



Scheme 2.

The reaction mechanism for the above mentioned results is given in Scheme 2. If the substituent R in 1 is capable of stabilizing an anionic center, the attack of the fluoride ion onto the silicon atom drives the cleavage of the silicon-carbon bond and causes the concurrent ring-opening of the aziridine ring to form a stabilized anionic intermediate A. When another stabilizing substituent exists (R'=E), a 1,2-proton migration occurs to give a more stabilized species B. The reactions of B with water and aldehydes at the sterically less hindered position form the intermediates C and D, which then tautomerize into the isolated products 2 to 5. On the other hand, when no more stabilizing substituent exists (R'≠E) in A, this anion is quenched with water and then trimerizes (or in the reverse order) to give the product 6. As 1d has no anion-stabilizing substituent on the ring, such a desilylation has not been observed.

It should be noted that the ring-opening of aziridine has been induced by the formation of a carbanion of nonstabilized type, and that the cleavage of the silicon-carbon bond has been assisted by the stabilization of the resultant carbanion through the ring-opening of aziridine ring. Such a ring-opening is a new pattern of reaction in the aziridine chemistry[13].

REFERENCES AND NOTES

1. As a recent review: W. P. Weber, "Silicon Reagents for Organic Synthesis", as Vol. 14 in "Reactivity and Structure Concepts in Organic Chemistry", ed by K. Hafner, J. -M. Lehn, C. W. Rees, P. von R. Schleyer, B. M. Trost, R. Zahradnik, Springer-Verlag, Berlin, Heiderberg, New York (1983), Chap. 25, pp. 391-404.
2. Some examples for the desilylative generation of nonstabilized azomethine

ylides, pyridinium and thiazolium methylides are known: O. Tsuge, S. Kanemasa, S. Kuraoka, and S. Takenaka, Chem. Lett., 1984, 279 and 281, and the references cited therein; O. Tsuge, S. Kanemasa, and S. Kuraoka, submitted.

3. O. Tsuge, S. Kanemasa, and K. Matsuda, Chem. Lett., 1983, 1131.
4. Nothing is known on the nature of nitrogen-substituted carbanion of non-stabilized type.
5. Its versatility has been demonstrated in recent years (O. Tsuge, S. Kanemasa and K. Matsuda, J. Org. Chem., in press and Ref. 3).
6. The reactions were carried out between the azide (1.2 equiv.) and the dipolarophiles under reflux in dry benzene.
7. The crude mixtures of cycloadditions were irradiated with a high pressure mercury lamp (13-17 h).
8. Isolated yields are given as follows: 1a (100%); 1b (93%); 1c (75%); 1d (53%). All the yields are based on the dipolarophiles.
9. All the new compounds reported herein gave satisfactory elemental analyses. 2: IR (KBr) 3300 (NH), 1700, and 1625 cm^{-1} (CO); ^1H-NMR ($CDCl_3$) δ 2.33 (3H, s, p-Me), 2.91 (3H, d, J=5.0 Hz, NMe), 4.92 (1H, s, =CH), 5.55 (1H, br, NH), and 7.18 ppm (4H, s, ArH); ^{13}C-NMR ($CDCl_3$) δ 21.08 (q, p-Me), 30.53 (q, NMe), 84.01 (d, =CH), 125.88 (d), 129.52 (s), 129.52 (d), 137.27 (s), 150.30 (s, =CNH-), 166.27 (s, CO), and 171.26 ppm (s, CO); MS m/e 216 (M^+, base peak).
10. 3: IR (KBr) 3300 (OH), 3125 (NH), 1700, and 1625 cm^{-1} (CO); ^1H-NMR (DMSO-d_6) δ 2.30 (3H, s, p-Me), 3.32 (2H, m, CH_2), 4.84 (1H, dt, CH), 5.04 (1H, s, =CH), 5.62 (1H, d, OH), 7.08-7.48 (9H, m, ArH), and 7.72 ppm (1H, t, NH); ^{13}C-NMR (DMSO-d_6) δ 20.55 (q, p-Me), 51.84 (t, CH_2), 70.28 (d, CH), 83.13 (d, =CH), 125.99, 126.11, 127.17, 127.99, 129.12, 129.40, 136.33 (s), 142.84 (s), 150.12 (s, =CNH-), 165.73 (s, CO), and 170.61 ppm (s, CO); MS m/e 322 (M^+) and 216 (base peak).
11. 5: ^1H-NMR ($CDCl_3$) δ 2.75 (3H x 3/5, d, J=5.0 Hz, NMe (E)), 3.00 (3H x 2/5, d, J=5.0 Hz, NMe (Z)), 3.64-3.84 (6H, three singlets, COOMe (E + Z)), 4.65 (1H x 3/5, s, =CH (E)), 5.05 (1H x 2/5, s, =CH (Z)), and 7.95 ppm (1H, br, NH (E + Z)); ^{13}C-NMR ($CDCl_3$) δ 29.80, 31.70 (each q, NMe), 50.68, 52.60 (each q, COOMe), 86.48 (d, =CH), 152.18 (s, =CNH-), 164.03, and 170.55 ppm (each s, CO).
12. 6: IR (neat) 1725 cm^{-1} (CO); ^1H-NMR ($CDCl_3$) δ 2.35-2.85 (12H, m, CH_2CH_2), 3.36 (6H, s, NCH_2N), and 3.65 ppm (9H, s, COOMe); ^{13}C-NMR ($CDCl_3$) δ 33. 11 (t, OC-CH_2-), 47.97 (t, CH_2-N), 51.55 (q, COOMe), 73.68 (t, NCH_2N), and 172.67 ppm (s, CO); MS m/e 345 (M^+), 301, 230, and 116.
13. Aziridine rings open at the carbon-nitrogen bond in the influence of nucleophiles, usually via aziridinium salts (D. R. Crist and N. J. Leonard, Angew. Chem., 1969, **81**, 953; I. O. Sutherland, "Nitrogen Compounds, Carboxylic Acids, Phosphorous Compounds", as Vol. 2 in "Comprehensive Organic Chemistry", ed by Sir D. Barton, W. D. Ollis, Pergamon Press, Oxford, New York, Tronto, Sydney, Paris, Frankfurt (1979), pp. 52-55.).

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