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Regiospecific ring opening of *N*-acylaziridines by neutral hydrolysis

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Abstract

The neutral hydrolysis of *N*-acyl-2,2-dimethylaziridines gave rise to the amidoalcohols in 76–91% overall yields. These products resulted from the specific cleavage of the C-2–N bond.

N-Acyl-2,2-dimethylaziridines were quantitatively isomerised by sodium iodide into three isomers; the major products were derived by cleavage of the C-2–N bond. Stamm has previously reported that those aziridines gave, with a very low yield, the ethoxyamides by reaction with ethanol at reflux; the nucleophile attacks the same more substituted carbon.[1] In this paper, we used another nucleophile such as water in a neutral medium at room temperature.

So, the reaction of *N*-benzoylethylenimine (unsubstituted aziridine) with distilled water for 11 days leads to the *N*-(2-hydroxyethyl) benzamide (29% yield). However, the substitution of the C-2 carbon atom by two methyl groups, in the aziridines **1a–e**, accelerated the hydrolysis (3 days) and considerably increased the yields of the corresponding amidoalcohols **2a–e**[5] (76–91% yields).

An ionic mechanism, undergone by a tertiary carbocation which is formed by heterolytic cleavage of the C-2–N bond of the *O*-protonated aziridine, appears excluded to explain the specific ring opening on the C-2 side[2] (Scheme 1). Indeed, we have obtained the starting materials when, on the one hand we treated *N*-benzoyl-2,2-dimethyl-3-phenylaziridine **1f** and *N*-benzoyl-2,3-diphenylaziridine **1g** with neutral water; and on the other hand, we treated the aziridine **1b** with basic water (NaOH; 0.1N).[3] We may suggest, then, another hydrolysis mechanism such as the possibility of hydrogen bonding between the oxygen atom of the acyl group and the hydrogen atom of the first water molecule which weakened the C-2–N bond; the donor inductive effect of the two methyl groups stabilised this C-2 carbon atom and made the attack of the second water molecule easy (Scheme 1).

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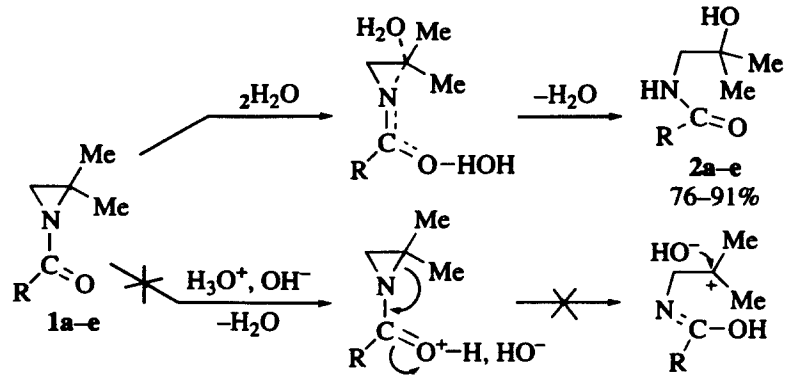

a: R = Ph–; **b**: R = p, MeOPh–; **c**: R = Ph–CH_2–; **d**: R = Ph–CH=CH–
e: R = Ph–CH_2–CH_2–

Scheme 1.

The specific ring opening at the more hindered carbon atom of the same *N*-acyl-2,2-dimethylaziridines by different amines has also been reported by Stamm.[4] From these results, we can conclude that the protic nucleophile attacks the more positive carbon atom of the aziridine heterocycle.

References

1. (a) Besbes, N. *Tetrahedron Lett.* **1998**, *39*, 4275–4276. (b) Buchholz, B.; Stamm, H. *Isr. J. Chem.* **1988**, *27*, 17–23.
2. (a) Heine, H. W.; Fetter, M. F.; Nicholson, E. A. *J. Am. Chem. Soc.* **1959**, *81*, 2202–2204. (b) Pittmann, C. U.; McManus, S. P. *J. Org. Chem.* **1970**, *35*, 1187–1192.
3. (a) The two aziridines **1f** and **1g** were isomerised by the concentrated sulphuric acid into the corresponding oxazolines undergoing intramolecular *O*-alkylation at the C-2 carbon. (b) Besbes, N. *J. Soc. Alger. Chem.* **1997**, *7*, 313–315. (c) McManus, S. P.; Hearn, R. A. *J. Org. Chem.* **1976**, *41*, 1895–1899.
4. Buchholz, B.; Onistchenko, A.; Stamm, H. *Z. Naturforsch, B: Anorg. Chem., Org. Chem.* **1986**, *41*, 1311–1314.
5. Spectral data IR (CH_2Cl_2); ^1H NMR ($CDCl_3$, 60 MHz); ^{13}C NMR ($CDCl_3$, 25.2 MHz) and SM (70 ev): **1a**: R=Ph; IR: (C=O) 1665. ^1H NMR: 1.23 (s, 6H), 2.30 (s, 2H), 7.33–8.20 (m, 5H). **1b**: R=pMeOPh; IR: (C=O) 1650. ^1H NMR: 1.26 (s, 6H), 2.28 (s, 2H), 3.86 (s, 3H), 7.00 (d, *J*=9, 2H), 8.03 (d, *J*=9, 2H). **1c**: R=$PhCH_2$; IR: (C=O) 1655. ^1H NMR: 1.23 (s, 6H), 2.10 (s, 2H), 3.60 (s, 2H), 7.20 (s, 5H). **1d**: R=PhCH=CH; IR: (C=C) 1620, (C=O) 1655. ^1H NMR: 1.33 (s, 6H), 2.20 (s, 2H), 6.60 (d, *J*=17, 1H), 7.35–7.90 (m, 6H). **1e**: R=$PhCH_2CH_2$; IR: (C=O) 1675. ^1H NMR: 1.26 (s, 6H), 2.05 (s, 2H), 2.40–3.20 (m, 4H), 7.30 (s, 5H). **2a**: yield: 91%. IR: (C=O) 1650, (NH) 3440, (OH) 3590. ^1H NMR: 1.16 (s, 6H), 3.35 (t, *J*=6, 2H), 3.86 (s, 1H), 7.13 (t, *J*=6, 1H), 7.15–7.86 (m, 5H). **2b**: yield: 84%. IR: (C=O) 1655, (NH) 3440, (OH) 3580. ^1H NMR: 1.20 (s, 6H), 3.38 (t, *J*=6, 2H), 3.76 (s, 2H), 4.00 (s, 1H), 6.85 (d, *J*=8, 2H), 7.23 (t, *J*=6, 1H), 7.76 (d, *J*=8, 2H). **2c**: yield: 76%. IR: (C=O) 1655, (NH) 3440, (OH) 3600. ^1H NMR: 1.10 (s, 6H), 3.15 (t, *J*=6, 3H), 3.52 (s, 2H), 4.15 (s, 1H), 6.40 (t, *J*=6, 1H), 7.28 (s, 5H). **2d**: yield: 87%. IR: (C=C) 1625, (C=O) 1660, (NH) 3440, (OH) 3590. ^1H NMR: 1.23 (s, 6H), 3.40 (t, *J*=6, 2H), 3.68 (s, 1H), 6.60 (d, *J*=17, 1H), 7.06 (t, *J*=6, 1H), 7.20–7.66 (m, 5H), 7.70 (d, *J*=17, 1H). **2e**: yield: 87%. IR: (C=O) 1660, (NH) 3440, (OH) 3590. ^1H NMR: 1.10 (s, 6H), 2.30–3.10 (m, 4H), 3.16 (t, *J*=6, 2H), 3.36 (s, 1H), 6.25 (t, *J*=6, 1H), 7.26 (s, 5H); ^{13}C NMR: 27.0 (q), 31.7 (t), 38.2 (t), 50.3 (t), 70.6 (s), 126.1 (d), 128.1 (d), 128.3 (d), 140.5 (s), 173.1 (s). SM *m/z* (%): 221 (M+, 11), 163 (100), 133 (28), 105 (65), 104 (58), 91 (93), 72 (54), 71 (44), 59 (36). Anal. calcd: C, 70.55; H, 8.64; N, 6.33; O, 14.46. Found: C, 70.68; H, 8.84; N, 6.54; O, 14.69.