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Rearrangement of 3-Methyl-2-(4-substituted phenyl)-1,3-oxazolinium 3-Methylides

Tomoko KITANO, Naohiro SHIRAI, and Yoshiro SATO*

Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467, Japan. *Received August 28, 1991*

2-(4-Substituted phenyl)oxazolidinium 3-methylides (5), prepared by fluoride ion-induced desilylation of 3-methyl-2-(4-substituted phenyl)-3-(trimethylsilyl)methyl-1,3-oxazolinium iodides (4), rearranged to 4-methyl-2-(4-substituted phenyl)morpholines (8, Stevens rearrangement products) as the main products.

Keywords nitrogen ylide; Sommelet–Hauser rearrangement; Stevens rearrangement; ring enlargement; cyclic amine; organosilicon compound; ammonium salt; fluoride ion

The Sommelet–Hauser rearrangement has rarely been used in organic synthesis, because the Hofmann elimination occurs in competition with the ylide formation under strongly basic conditions.[1-3] We previously reported that the fluoride-ion induced desilylation reaction of *N*-(trimethylsilylmethyl)benzylammonium salts regioselectively gave benzylammonium *N*-methylides in quantitative yields under non-basic conditions.[4-12] The five- to seven-membered cyclic 2-phenylammonium *N*-methylides thus produced were rearranged to give the eight- to ten-membered cyclic amines in high yields.[7,10,12] As a further extension of our work, we attempted the synthesis of 5-methyl-8-substituted 3,4,5,6-tetrahydro-1*H*-2,5-benzoxazocine (7) from 3-methyl-2-(4-substituted phenyl)-3-(trimethylsilyl)methyl-1,3-oxazolinium iodides (4).

Oxazolidinium iodide (**4a**) was prepared by the reaction of benzaldehyde (**1a**) with 2-[(trimethylsilyl)methylamino]-ethanol (**2**) followed by quaternization with iodomethane. 2-(4-Methoxyphenyl)-3-methyl-3-[(trimethylsilyl)methyl]-1,3-oxazolidinium iodide (**4b**), similarly prepared, was used for the reaction with cesium fluoride without isolation because of its high hygroscopicity.

Reaction of **4a** with cesium fluoride in dimethylformamide (DMF) at room temperature gave only 2-phenyl-4-methylmorpholine (**8a**, Stevens rearrangement product) (entry 2 in Table I). Similar treatment of **4b** afforded a mixture of morpholine **8b** and 8-methoxy-5-methyl-3,4,6,6a-tetrahydro-5*H*-benzoxazocine (**6b**, [2, 3] sigmatropic rearrangement product from **5b**; conjugated triene compound) (entry 5). When both reactions were quenched after 1 h at 0 °C, the ratios of **6a, b** to **8a, b** increased (entries 1 and 4).

We reported earlier that the stability of the conjugated triene compounds is affected by the nature of the substituents on the triene moiety; electron-donating groups such as methoxy stabilize the triene functionality.[7-11] The Stevens rearrangement products are not produced directly from the ylides by a [1, 2] radical rearrangement, as mentioned previously,[1,2,13] but are formed by a [2, 3] sigmatropic rearrangement followed by a [1, 3] radical rearrangement; that is, the conjugated triene compounds are

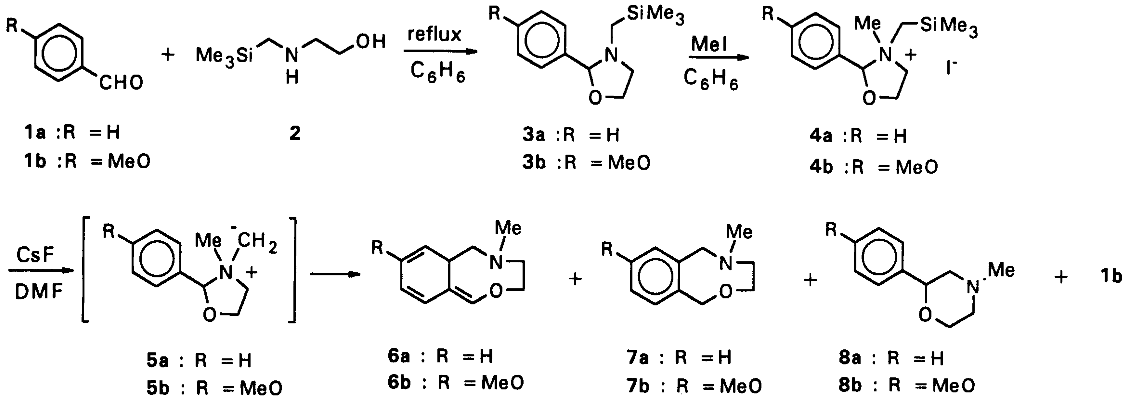

Chart 1

TABLE I. Reaction of 3-Methyl-2-(substituted phenyl)-3-[(trimethylsilyl)methyl]oxazolidinium Iodides (**4a**, **b**) with CsF

Entry		R	Reaction conditions			Products	
			Temperature (°C)	Time (h)	DBU (mol eq)	Total yield (%)	Ratio[a] **6**:**7**:**8**:**1**
1	**4a**	H	0	1	—	49	8: 0: 92: 0
2	**4a**	H	r.t.	48	—	71	0: 0:100: 0
3	**4a**	H	r.t.	48	5	57	0: 0:100: 0
4	**4b**	MeO	0	1	—	46[b]	43: 0: 54: 3
5	**4b**	MeO	r.t.	24	—	69[b]	24: 0: 71: 5
6	**4b**	MeO	r.t.	24	10	45[b]	0:20: 70:10

a) Determined from the proton ratios of the ^{1}H-NMR. *b*) The yield is based on **3b**. r.t. = room temperature.

intermediates not only in the Sommelet–Hauser rearrangement but also in the Stevens rearrangements.[8] The trienes, which rearrange to the Stevens products in non-basic media, were converted to the Sommelet–Hauser products in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as a result of acceleration of a [1, 3] proton transfer pathway in some cases.[11,12] The addition of DBU to the reaction mixture of **4**, however, did not result in a change of the product from **8** to tetrahydro-1*H*-2,5-benzoxazocines **7** (Sommelet–Hauser products), although **6b** was transformed into **7b**. We are currently attempting to clarify the mechanism of these unexpected results.

Experimental

DMF was dried over BaO and distilled under reduced pressure. CsF was dried (P_2O_5) at 180 °C under reduced pressure. Proton nuclear magnetic resonance (^{1}H-NMR) spectra were recorded at 100 or 400 MHz. Aluminum oxide (Merck, Aluminumoxide 90, 70—230 mesh) was used for column chromatographies. All melting and boiling points are uncorrected.

2-Phenyl-3-[(trimethylsilyl)methyl]-1,3-oxazolidine (3a) and 2-(4-Methoxyphenyl)-3-[(trimethylsilyl)methyl]-1,3-oxazolidine (3b) A solution of ethanolamine (27.15 g, 444 mmol) and (chloromethyl)trimethylsilane (5.56 g, 45 mmol) in MeCN (100 ml) was heated at reflux for 8 h and then poured into H_2O (100 ml). The AcOEt extract of the reaction mixture was dried ($MgSO_4$), concentrated, and distilled to give 2-[(trimethylsilyl)methylamino]ethanol (**2**, 5.74 g, 86%), bp 95 °C (15 mmHg). IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 3400 (OH and NH). ^{1}H-NMR ($CDCl_3$) δ: 0.04 (9H, s, $SiCH_3$), 1.78 (2H, br s, OH and NH), 2.05 (2H, s, $SiCH_2$), 2.78 (2H, t, J=5.7 Hz, NCH_2), 3.60 (2H, t, J=5.7 Hz, OCH_2).

A solution of **2** (16.20 g, 110 mmol) and benzaldehyde (**1a**, 10.61 g, 100 mmol) or *p*-anisaldehyde (**1b**, 13.62 g, 100 mmol) in benzene (170 ml) was placed in a flask equipped with a Dean–Stark water-separator and heated at reflux for 6 h. The mixture was concentrated under reduced pressure and the residue was distilled to give **3a** (13.12 g, 56%) or **3b** (15.40 g, 58%).

3a: bp 109—110 °C (2.1 mmHg). IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 1250 ($SiMe_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.03 (9H, s, $SiCH_3$), 1.68, 2.01 (2H, ABq, J=14.1 Hz, $SiCH_2$), 2.57 (1H, dd, J=16.7, 9.1 Hz, 4-H), 3.35 (1H, ddd, J=9.1, 6.6, 2.9 Hz, 5-H), 3.98—4.08 (2H, m, 4-H and 5-H), 4.60 (1H, s, 2-H), 7.31—7.38 (3H, m, ArH), 7.46—7.50 (2H, m, ArH). *Anal.* Calcd for $C_{13}H_{21}NOSi$: C, 66.33; H, 8.99; N, 5.95. Found: C, 66.10; H, 9.06; N, 5.87.

3b: bp 121 °C (0.6 mmHg). IR $\nu_{\max}^{\text{film}}$ cm^{-1}: 1250 ($SiMe_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.03 (9H, s, $SiCH_3$), 1.62, 1.98 (2H, ABq, J=14.1 Hz, $SiCH_2$), 2.54 (1H, dd, J=16.9, 9.3 Hz, 4-H), 3.35 (1H, ddd, J=9.3, 6.8, 2.8 Hz, 5-H), 3.79 (3H, s, OCH_3), 3.96—4.07 (2H, m, 4-H and 5-H), 4.52 (1H, s, 2-H), 6.88, 7.40 (4H, A_2B_2, J=8.8 Hz, ArH). *Anal.* Calcd for $C_{14}H_{23}NO_2Si$: C, 63.35; H, 8.73; N, 5.28. Found: C, 63.36; H, 8.95; N, 5.24.

3-Methyl-2-phenyl-3-(trimethylsilyl)methyl-1,3-oxazolidinium Iodide (4a) A solution of **3a** (12.28 g, 52 mmol) and MeI (11.76 g, 83 mmol) in benzene (27 ml) was heated at reflux for 10 h. The precipitated crystals were collected by filtration. Yield 18.25 g (93%), mp 142—144 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.35 (9H, s, $SiCH_3$), 2.40, 4.24 (2H, ABq, J=14.4 Hz, $SiCH_2$), 2.76 (3H, s, NCH_3), 4.32—4.37 (1H, m, 4-H), 4.58—4.69 (3H, m, 4-H and 5-H), 6.51 (1H, s, 2-H), 7.49—7.70 (5H, m, ArH). *Anal.* Calcd for $C_{14}H_{24}INOSi$: C, 44.56; H, 6.41; N, 3.71. Found: C, 44.27; H, 6.51; N, 3.81.

Reaction of 4a with CsF The ammonium salt **4a** (1.13 g, 3 mmol) was placed in a 30-ml flask equipped with a magnetic stirrer, a septum, and a test tube which was connected by a short piece of rubber tubing. CsF (2.0 g, 13 mmol) was put into the test tube. The apparatus was dried under reduced pressure and was flushed with N_2. DMF (10 ml) was added by a syringe, and then the CsF was added. The mixture was stirred under the conditions listed in Table I and then poured into 1% $NaHCO_3$ (100 ml). The ethereal extract of the reaction mixture was washed with 1% $NaHCO_3$, dried ($MgSO_4$), and concentrated. Distillation of the residue gave 4-methyl-2-phenylmorpholine (**8a**), bp 110—115 °C (2 mmHg) [lit.[14] bp 95 °C (5 mmHg)]. The ^{1}H-NMR spectrum of the residue after 1 h of stirring at 0 °C showed the presence of 5-methyl-3,4,6,6a-tetrahydro-5*H*-2,5-benzoxazocine (**6a**) with **8a** (entry 1). Compound **6a** could not be isolated due to its instability on a column.

6a: ^{1}H-NMR ($CDCl_3$) δ: 2.52 (3H, s, NCH_3), 2.69 (1H, dd, J=13.8, 9.7 Hz, 6-H), 2.76 (1H, dd, J=13.8, 3.0 Hz, 6-H), 2.83 (1H, ddd, J=15.2, 3.7, 2.8 Hz, 4-H), 2.95 (1H, ddd, J=15.2, 10.6, 4.1 Hz, 4-H), 3.70 (1H, ddd, J=12.0, 4.1, 2.8 Hz, 3-H), 3.80—3.90 (1H, m, 6a-H), 4.27 (1H, ddd, J=12.0, 10.6, 3.7 Hz, 3-H), 5.65 (1H, ddd, J=9.5, 5.4, 0.9 Hz, 9-H), 5.71 (1H, ddd, J=9.4, 5.5, 0.9 Hz, 7-H), 5.94 (1H, dddd, J=9.4, 5.4, 1.3, 0.9 Hz, 8-H), 5.98 (1H, dd, J=9.5, 0.9 Hz, 10-H), 6.28 (1H, d, J=1.8 Hz, 1-H).

Reaction of 4b with CsF A solution of **3b** (0.80 g, 3 mmol) and MeI (4.26 g, 30 mmol) in DMF (15 ml) was heated at 75 °C for 2 h. In order to remove excess MeI, the solution was concentrated under reduced pressure to about 10 ml. After the addition of CsF (2.0 g, 13 mmol), the mixture was stirred under the conditions shown in Table I. The reaction was quenched and the mixture was treated in a manner similar to that described for **4a**. The ^{1}H-NMR spectrum of the residue showed the presence of 8-methoxy-5-methyl-3,4,6,6a-tetrahydro-5*H*-benzoxazocine (**6b**), 4-methyl-2-(4-methoxyphenyl)morpholine (**8b**), and **1b**. Compound **6b** could not be isolated due to its instability on a column.

6b: ^{1}H-NMR ($CDCl_3$) δ: 2.52 (3H, s, NCH_3), 2.65 (1H, dd, J=13.6, 9.6 Hz, 6-H), 2.72 (1H, dd, J=13.6, 3.1 Hz, 6-H), 2.82 (1H, ddd, J=15.0, 3.6, 2.8 Hz, 4-H), 2.93 (1H, ddd, J=15.0, 10.5, 4.2 Hz, 4-H), 3.54 (3H, s, OCH_3), 3.70 (1H, ddd, J=12.1, 4.2, 2.8 Hz, 3-H), 3.80—3.90 (1H, m, 6a-H), 4.26 (1H, ddd, J=12.1, 10.5, 3.6 Hz, 3-H), 4.53 (1H, dd, J=6.0, 2.5 Hz, 7-H), 5.60 (1H, dd, J=9.8, 2.5 Hz, 9-H), 6.04 (1H, d, J=9.8 Hz, 10-H), 6.31 (1H, d, J=2.0 Hz, 1-H).

8b: bp 180—185 °C (19 mmHg) [lit.[14] bp 137 °C (3 mmHg)].

Reaction of 4a, b with CsF in the Presence of DBU DBU was added by a syringe through the septum to a solution of **4a, b** in DMF, prepared in a manner similar to that described above, and then the mixture was treated with CsF. The residue from **4a** was purified on an aluminum oxide column (hexane : Et_2O = 9 : 1) to give **8a**. The residue from **4b** was chromatographed on an aluminum oxide column (hexane : Et_2O = 9 : 1) to give 8-methoxy-5-methyl-3,4,5,6-tetrahydro-1*H*-2,5-benzoxazocine (**7b**) and **8b**.

7b: bp 170 °C/6 mmHg. ^{1}H-NMR ($CDCl_3$) δ: 2.40 (3H, s, NCH_3), 2.64—2.68 (2H, m, 4-H), 3.82 (3H, s, OCH_3), 3.80—3.85 (2H, m, 3-H), 3.98 (2H, s, 6-H), 4.74 (2H, s, 1-H), 6.73 (1H, d, J=2.6 Hz, 7-H), 6.82 (1H, dd, J=8.2, 2.6 Hz, 9-H), 7.14 (1H, d, J=8.2 Hz, 10-H). *Anal.* Calcd for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.40; H, 8.52; N, 6.50.

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