Rearrangement of *N,N*-Dimethyl(1- or 2-naphthylmethyl)ammonium *N*-Methylide

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***N,N*-Dimethyl-(1- or 2-naphthylmethyl)ammonium *N*-methylide (2a, b) produced from *N,N*-dimethyl-*N*-[(trimethylsilyl)methyl] (1- or 2-naphthylmethyl)ammonium iodide (1a, b) with CsF in *N,N*-dimethylformamide, was rearranged to 2-[(dimethylamino)methyl]-1,2-dihydro-1-naphtholidene (3a) or 1-[(dimethylamino)methyl]-1,2-dihydro-2-naphtholidene (3b), respectively, in high yield. Aromatization of 3a, b to the Sommelet–Hauser products (4a, b) occurred with the aid of KOH or heating.**

Keywords ammonium ylide; Sommelet–Hauser rearrangement; Stevens rearrangement; organosilicon compound; [2,3]sigmatropic rearrangement

Sommelet–Hauser rearrangement of benzylammonium ylides is a useful method for synthesizing *ortho*-methylbenzylamines. However, base-promoted ylide formation, which is usually employed, often gives complex mixtures of amines because plural ylides are formed simultaneously.[1,2] In fluoride ion-induced desilylation reaction of *N*-[1-(trimethylsilyl)alkyl]benzylammonium salts, the ylide-anions were located regioselectively on the carbons with which the silyl groups had been linked. Thus the yields of the products were remarkably improved.[3-19] This paper reports the reaction of *N,N*-dimethyl-*N*-[(trimethylsilyl)methyl](1- or 2-naphthylmethyl)ammonium iodides (**1a, b**) with cesium fluoride.

Ammonium iodides (**1a, b**) were prepared starting from α- or β-naphthoyl chloride with *N*-methyl(trimethylsilyl)-methylamine followed by lithium aluminum hydride reduction, then quaternization with iodomethane. Treatment of **1a, b** with cesium fluoride in *N,N*-dimethyl formamide (DMF) gave a high yield of 2-[(dimethylamino)methyl]-1,2-dihydro-1-naphtholidene (**3a**, [2,3]-sigmatropic rearrangement product) or 1-[(dimethylamino)methyl]-1,2-dihydro-2-naphtholidene (**3b**) after 40 min of stirring at room temperature (Table I, entries 1 and 3). However, the product **3a** changed to 1-methyl-2-[(dimethylamino)methyl]naphthalene (**4a**, Sommelet–Hauser rearrangement product) after 2 d (entry 2). Conversion of **3b** to 2-methyl-1-[(dimethylamino)methyl]-naphthalene (**4b**) was not completed after 3 d (entry 4). Pure **4b** was obtained after 13 d but the yield was decreased by polymerization of **3b**.

Hauser *et al.*[20] obtained **4a** (75%) and **4b** (84%) from *N,N,N*-trimethyl(1-naphthylmethyl)ammonium chloride and a 2-naphthylmethyl analogue by treatment with sodium amide in liquid ammonia. The difference of the

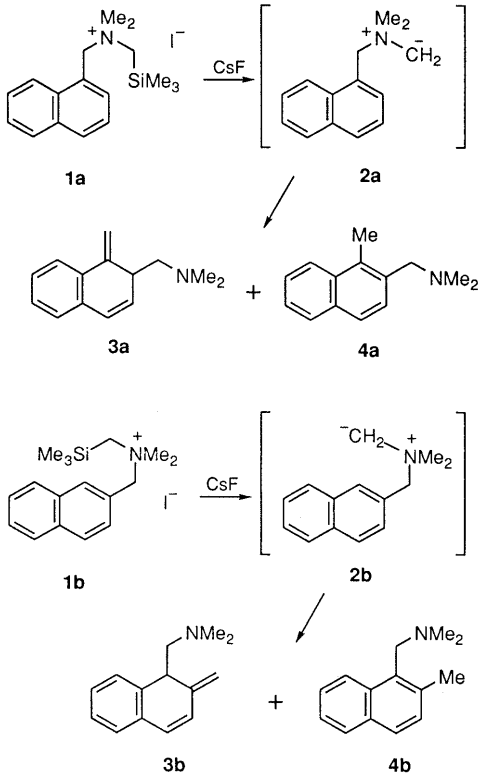

Chart 1

TABLE I. Reaction of *N,N*-Dimethyl-*N*-[(trimethylsilyl)methyl](1- or 2-naphthylmethyl)ammonium Iodides (**1a, b**) with CsF

Entry	Ammonium salt (**1**)	Reaction time	Total yield (%)	Ratio[a] of **3** : **4**
1	**1a**	40 min	85	91 : 9
2	**1a**	2 d	70	0 : 100
3	**1b**	40 min	92	98 : 2
4	**1b**	3 d	79	35 : 65
5	**1b**	13 d	26	0 : 100

a) Determined from the integration of the signals in the ^{1}H-NMR spectra.

TABLE II. Reaction of Naphtholidene Derivatives **3a** and **3b**

Entry		Reaction conditions	Ratio[a] of **4**	**5**	**6**	Total yield (%)
1	**3a**[b]	5% KOH/EtOH, r.t., 3 h	100	0	0	88
2	**3a**	Xylene, reflux, 6 h	78	22	0	94
3	**3b**[c]	5% KOH/EtOH, r.t., 5 h	100	0	0	80
4	**3b**	Xylene, reflux, 44 h	14	0	86	75

a) Determined from the integration of the signals in the ^{1}H-NMR spectra. *b*) A mixture of **3a** and **4a** (91 : 9) was used. *c*) A mixture of **3b** and **4b** (98 : 2) was used. r.t. = room temperature.

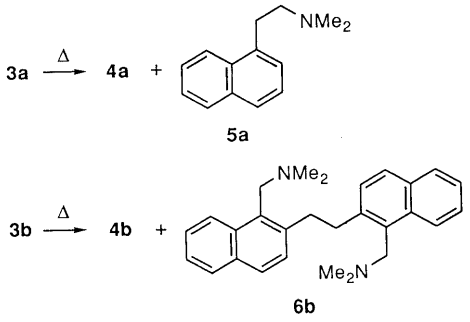

Chart 2

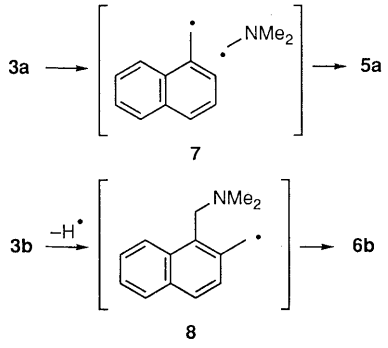

Chart 3

products between the two ylide reactions indicates that aromatization of **3** to **4** is slow in non-basic media but occurs quickly in the presence of a strong base. An antarafacial [1,3]hydrogen shift at the 2-position of **3a** (or 1-position of **3b**) to the exomethylene group is required in non-basic media. The π framework should be twisted far from planarity at the transition stage.[21] Conjugation of the benzene ring with the triene portion may pose an obstacle to such a twisting conformation.

Indeed, **3a**, **b** were respectively changed to **4a**, **b** in 5% KOH solutions in high yields (Table II). Heating at 140°C in xylene, **3a** converted to a mixture of **4a** and *N*,*N*-dimethyl-2-(1-naphthyl)ethylamine (**5a**, Stevens rearrangement product), whereas **3b** gave 1,2-bis[1-(dimethylamino)methyl-2-naphthyl)ethane (**6b**) as the main product. The Stevens product **5a** is formed as a result of [1,3] radical migration *via* a radical pair (**7** in Chart 3).[7] The dimerization product **6b** may be formed from a β-naphthylmethyl radical (**8**) which is produced by elimination of the C1-hydrogen from **3b**. However, it is still unclear what is the cause of the difference in thermal isomerization of **3a** and **3b**.

Experimental

All reactions were carried out in N_2. DMF was dried over BaO and distilled under reduced pressure. Ether was distilled from Na benzophenone ketyl. CsF was dried over P_2O_5 at 180 °C under reduced pressure. ^{1}H-NMR spectra were recorded at 270 or 400 MHz. Mass spectra were obtained using electron impact (EI) ionization (70 eV). All melting and boiling points are uncorrected.

***N*,*N*-Dimethyl-*N*-(trimethylsilyl)methyl(1-naphthylmethyl)ammonium Iodide (1a)** A solution of *N*-methyl(trimethylsilyl)methylamine (2.45 g, 20.9 mmol) and 1-naphthoyl chloride (8.56 g, 45.3 mmol) in benzene (130 ml) was stirred vigorously with 10% NaOH (30 ml) for 40 min at room temperature. The benzene layer was separated, washed with water, then dried ($MgSO_4$), and the solvent was evaporated under reduced pressure to give a colorless oil. The oil was added to a suspension of $LiAlH_4$ (1.50 g, 39.5 mmol) in ether (50 ml), and the mixture was heated at reflux for 2.5 h. The reaction was quenched with EtOAc (5 ml) and 5% HCl (50 ml), and then the mixture was extracted with ether. The extract was washed with water, dried ($MgSO_4$), and concentrated under reduced pressure to give *N*-methyl-*N*-[(trimethylsilyl)methyl](1-naphthylmethyl)-amine (4.24 g, 79%), bp 135 °C (1.5 mmHg, oven temperature of Kugelrohr distillation apparatus). ^{1}H-NMR ($CDCl_3$) δ: 0.02 (9H, s), 1.96 (2H, s), 2.18 (3H, s), 3.82 (2H, s), 7.36—8.40 (7H, ArH). *Anal.* Calcd for $C_{16}H_{23}NSi$: C, 74.65; H, 9.00; N, 5.44. Found: C, 74.59; H, 9.10; N, 5.35.

A solution of the 1-naphthylmethylamine (0.71 g, 2.8 mmol) and iodomethane (3.26 g, 23 mmol) in MeCN (10 ml) was heated at reflux for 2.5 h and then concentrated. The residue was recrystallized from MeCN–ether to give **1a** (2.22 g, 80%), mp 184—187 °C. ^{1}H-NMR ($CDCl_3$) δ: 0.28 (9H, s), 3.34 (6H, s), 3.68 (2H, s), 5.61 (2H, s), 7.36—8.00 (7H, m). *Anal.* Calcd for $C_{17}H_{26}INSi$: C, 51.13; H, 6.56; N, 3.51. Found: C, 51.31; H, 6.78; N, 3.28.

***N*,*N*-Dimethyl-*N*-(trimethylsilyl)methyl(2-naphthylmethyl)ammonium Iodide (1b)** In a manner similar to that described above, a mixture of *N*-methyl(trimethylsilyl)methylamine (2.67 g, 22.8 mmol) and 2-naphthoyl chloride (3.64 g, 19.1 mmol) in benzene (60 ml) was stirred with 10% NaOH (10 ml) and treated to give *N*-methyl-*N*-[(trimethylsilyl)-methyl]-2-naphthamide (4.24 g, 82%), mp 51—52 °C (hexane). ^{1}H-NMR ($CDCl_3$) δ: 0.20 (9H, s), 3.02 (3H, s), 3.15 (2H, s), 7.45—7.87 (7H, m). *Anal.* Calcd for $C_{16}H_{21}NOSi$: C, 70.80; H, 7.80; N, 5.16. Found: C, 70.56; H, 7.86; N, 4.99.

Reduction of the naphthamide (6.00 g, 22 mmol) with $LiAlH_4$ (0.85 g, 22 mmol) in ether (40 ml) gave *N*-methyl-*N*-[(trimethylsilyl)methyl](2-naphthylmethyl)amine (4.16 g, 73%), bp 140 °C (2.5 mmHg, Kugelrohr). ^{1}H-NMR ($CDCl_3$) δ: 0.11 (9H, s), 2.02 (2H, s), 2.31 (3 H, s), 3.70 (2H, s), 7.25—7.82 (7H, ArH). *Anal.* Calcd for $C_{16}H_{23}NSi$: C, 74.65; H, 9.00; N, 5.44. Found: C, 74.48; H, 9.21; N, 5.20.

Treatment of the 2-naphthylmethylamine (0.73 g, 2.8 mmol) with iodomethane (4.5 g, 32 mmol) in MeCN (10 ml) gave **1b** (1.09 g, 97%), mp 184—185 °C (MeCN–ether). ^{1}H-NMR ($CDCl_3$) δ: 0.30 (9H, s), 3.37 (6H, s), 3.50 (2H, s), 5.31 (2H, s), 7.50—8.19 (7H, m). *Anal.* Calcd for $C_{17}H_{26}INSi$: C, 51.13; H, 6.56; N, 3.51. Found: C, 51.02; H, 6.80; N, 3.18.

General Procedure for the Reaction of 1a or 1b with CsF The ammonium salt **1** (824 mg, 2.06 mmol) was placed in a 20-ml flask equipped with a magnetic stirrer, septum, and a test tube which was connected to the flask by a short piece of rubber tubing. CsF (1.52 g, 10 mmol) was placed in the test tube. The apparatus was dried under reduced pressure and was flushed with N_2. DMF (10 ml) was added to the flask by syringe. CsF was added from the test tube. The mixture was stirred at room temperature for the time listed in Table I. The reaction mixture was poured into 1% $NaHCO_3$ (200 ml) and extracted with Et_2O (4 × 100 ml). The ethereal extract was washed with 1% $NaHCO_3$ (200 ml), dried ($MgSO_4$), and concentrated under reduced pressure to give a pale yellow oil. The ^{1}H-NMR spectrum of the oil from **1a** showed the presence of **3a** or **4a**, and that of the oil from **1b** revealed **3b** and **4b**. Samples were separated by HPLC (Merck, Hibar LiChrosorb NH_2, 250 × 10 mm, hexane–ether). The results are listed in Table I.

3a: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 2.21 (1H, dd, J= 7.2, 11.9 Hz, CH_2N), 2.25 (6H, s, CH_3N), 2.43 (1H, dd, J=8.6, 11.9 Hz, CH_2N), 3.28—3.33 (1H, m, 2-H), 5.07 (1H, s, CH_2=), 5.49 (1H, s, CH_2=), 6.13 (1H, dd, J=5.3, 9.6 Hz, 3-H), 6.46 (1H, d, J=9.6 Hz, 4-H), 7.04 (1H, d, J=7.2 Hz, 5-H), 7.16—7.26 (2H, m, 6-H, 7-H), 7.53 (1H, d, J=7.5 Hz, 8-H). UV λ_{max}^{hexane} nm (log ε): 283 (3.77), 240 (4.43), 229 (4.45). *Anal.* Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60; N, 7.03. Found: C, 84.35; H, 8.81; N, 6.92.

4a: ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 2.28 (6H, s, CH_3N), 2.70 (3H, s, CH_3), 3.60 (2H, s, CH_2N), 7.41—8.09 (6H, m, ArH). *Anal.* Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60; N, 7.03. Found: C, 84.23; H, 8.74; N, 6.79.

3b: ^{1}H-NMR ($CDCl_3$, 400 MHz) δ: 2.21 (1H, dd, J=6.4, 12.3 Hz, CH_2N), 2.25 (6H, s, CH_3N), 2.45 (1H, dd, J=8.9, 12.3 Hz, CH_2N), 3.65 (1H, dd, J=6.4, 8.9 Hz, 1-H), 5.05 (1H, s, CH_2=), 5.15 (1H, s, CH_2=), 6.28 (1H, dd, J=9.6 Hz, 3-H), 6.38 (1H, d, J=9.6 Hz, 4-H), 7.06—7.17 (4H, m, ArH). UV λ_{max}^{hexane} nm (log ε): 301 (4.04), 221 (4.29). *Anal.* Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60; N, 7.03. Found: C, 84.36; H, 8.80; N, 6.65.

4b: ^{1}H-NMR ($CDCl_3$, 270 MHz) δ: 2.33 (6H, s, CH_3N), 2.56 (3H, s, CH_3), 3.80 (2H, s, CH_2N), 7.28 (1H, d, J=8.6 Hz), 7.76 (1H, d,

$J=8.6$ Hz), 7.35—7.51 (2H, m), 7.76 (1H, d, $J=10.7$ Hz), 8.23 (1H, d, $J=8.6$ Hz). *Anal.* Calcd for $C_{14}H_{17}N$: C, 84.37; H, 8.60; N, 7.03. Found: C, 84.21; H, 8.71; N, 6.83.

Reaction of 3a and 3b in 5% KOH A mixture of **3a** and **4a** (91 : 9, 384 mg) or **3b** and **4b** (98 : 2, 45 mg) was dissolved in 5% KOH in EtOH (3 ml) and stirred at room temperature. After **3a** or **3b** had disappeared (3 h for **3a**, 5 h for **3b**), the solution was mixed with water (20 ml) and extracted with ether (3×20 ml). The extract was dried ($MgSO_4$) and concentrated to give **4a** (338 mg, 88%) and **4b** (36 mg, 80%).

Thermal Isomerization of 3a and 3b A solution of **3a** (451 mg, 2.26 mmol) or **3b** (256 mg, 1.28 mmol) in xylene (5 ml) was heated at 140 °C for 6 or 44 h and extracted with 10% HCl (4×5 ml). The aqueous extract was made alkaline with 10% NaOH and extracted with Et_2O (4×50 ml). The extract was washed with H_2O, dried ($MgSO_4$), and concentrated to give a mixture (423 mg) of **4a** and **5a**[22] or a mixture (192 mg) of **4b** and **6b**. The product ratios were determined from the proton signal ratios in the ^{1}H-NMR spectra.

Compound **6b** was isolated by Al_2O_3 column chromatography (Et_2O–hexane).

6b: ^{1}H-NMR ($CDCl_3$) δ: 1.58—1.67 (1H, m, $C\underline{H}_2CH_2$), 1.71—1.82 (1H, m, $C\underline{H}_2CH_2$), 2.61 (2H, d, $J=7.3$ Hz, $CH_2C\underline{H}_2$), 2.66—2.69 (1H, m), 2.88—3.00 (1H, m), 3.07—3.12 (1H, m), 3.81 (1H, s), 2.26 (6H, s, CH_3N), 2.29 (6H, s, CH_3N), 6.08—6.13 (1H, m), 6.54 (1H, d, $J=9.6$ Hz, 4-H), 7.04—7.23 (4H, m), 7.28 (1H, d, $J=8.4$ Hz, 4-H′), 7.29—7.41 (1H, m), 7.44—7.50 (1H, m), 7.67 (1H, d, $J=8.4$ Hz, 5-H), 7.75 (1H, d, $J=7.9$ Hz, 5-H′), 8.24 (1H, d, $J=8.6$ Hz, 8-H). ^{13}C-NMR ($CDCl_3$) δ: 31.5, 31.7, 36.9, 38.6, 45.3, 46.2, 55.8, 59.2, 124.7, 124.8, 125.9, 125.9, 126.3, 126.4, 127.0, 127.7, 128.0, 128.2, 133.0, 131.1, 132.4, 133.5, 133.9, 138.5, 139.9. *Anal.* Calcd for $C_{28}H_{34}N_2$: C, 84.37; H, 8.60; N, 7.03. Found: C, 84.36; H, 8.68; N, 6.57. MS *m/z*: 398 (M^+, relative intensity, 0.46), 340 (8.83), 141 (0.76).

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References

1) S. H. Pine, *Org. Reactions*, **18**, 403 (1970).
2) A. R. Lepley, "Mechanisms of Molecular Migrations," Vol. 3, ed. by B. S. Thyagarajan, Wiley-Interscience, New York, 1971, pp. 297—440.
3) M. Nakano, Y. Sato, *J. Org. Chem.*, **52**, 1844 (1987).
4) N. Shirai, Y. Sato, *J. Org. Chem.*, **53**, 194 (1988).
5) H. Sugiyama, Y. Sato, N. Shirai, *Synthesis*, **1988**, 988.
6) N. Shirai, F. Sumiya, Y. Sato, M. Hori, *J. Org. Chem.*, **54**, 836 (1989).
7) S. Okazaki, N. Shirai, Y. Sato, *J. Org. Chem.*, **55**, 334 (1990).
8) N. Shirai, Y. Watanabe, Y. Sato, *J. Org. Chem.*, **55**, 2767 (1990).
9) F. Sumiya, N. Shirai, Y. Sato, *Chem. Pharm. Bull.*, **39**, 36 (1991).
10) Y. Machida, N. Shirai, Y. Sato, *Synthesis*, **1991**, 117.
11) T. Kitano, N. Shirai, Y. Sato, *Synthesis*, **1991**, 996.
12) T. Tanaka, N. Shirai, Y. Sato, *Chem. Pharm. Bull.*, **40**, 518 (1992).
13) T. Kitano, N. Shirai, Y. Sato, *Chem. Pharm. Bull.*, **40**, 768 (1992).
14) T. Tanaka, N. Shirai, J. Sugimori, Y. Sato, *J. Org. Chem.*, **57**, 5034 (1992).
15) T. Usami, N. Shirai, Y. Sato, *J. Org. Chem.*, **57**, 5419 (1992).
16) Y. Sato, N. Shirai, Y. Machida, E. Ito, T. Yasui, Y. Kurono, K. Hatano, *J. Org. Chem.*, **57**, 6712 (1992).
17) T. Kitano, N. Shirai, M. Motoi, Y. Sato, *J. Chem. Soc., Perkin Trans. 1*, **1992**, 2851.
18) A. Sakuragi, N. Shirai, Y. Sato, Y. Kurono, K. Hatano, *J. Org. Chem.*, **59**, 148 (1994).
19) Y. Maeda, N. Shirai, Y. Sato, *J. Chem. Soc., Perkin Trans. 1*, **1994**, 393.
20) C. R. Hauser, D. N. Van Eenam, P. L. Bayless, *J. Org. Chem.*, **23**, 354 (1958).
21) R. T. Morrison, R. N. Boyd, "Organic Chemistry," Allyn and Bacon, Inc., Boston, 1987, pp. 1156—1160.
22) E. E. Smissman, A. C. Makriyannis, E. J. Walaszek, *J. Med. Chem.*, **13**, 640 (1970).