Sommelet-Hauser or Stevens Rearrangement of 1-Methyl-2-(substituted-phenyl)piperazinium 1-Methylides. Ring Enlargement of Piperazines to Seven- or Nine-membered Cyclic Amines

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Fluoride ion-induced desilylation of 4-acetyl-1-methyl-2-(4-substituted phenyl)-1-trimethylsilylmethylpiperazinium iodides **5** gave 5-acetyl-2-methyl-10-substituted 1,3,4,5,6,11a-hexahydro-2*H*-2,5-benzodiazonines **7** and/or 5-acetyl-2-methyl-10-substituted 2,3,4,5,6,7-hexahydro-1*H*-2,5-benzodiazonines **8** (Sommelet–Hauser rearrangement products). However, a similar treatment of 1-methyl-3-oxo-2-phenyl-1-trimethylsilylmethylpiperazinium iodide **10** afforded 1-methyl-6-phenyl-2,3,6,7-tetrahydro-1*H*-diazepine-5-one **12** (Stevens rearrangement product).

Sommelet–Hauser rearrangement of ammonium ylides is an attractive method in ring enlargement reactions of cyclic amines.[1] However, this method has rarely been used in organic synthesis because base-promoted ylide formation often results in a mixture of the rearrangement products due to the difficulty in specifying the location of the ylide anion.[2]

In ylide formation by fluoride ion-induced desilylation of 1-(trimethylsilyl)alkylammonium salts, the ylide anions locate regioselectively on carbons with which the silyl groups had linked.[3,4] We earlier reported the application of this method to ring enlargement.[4d,g,i,k] We report herein the synthesis of new 9-membered cyclic amines, 2,3,4,5,6,7-hexahydro-1*H*-2,5-benzodiazonines starting from 2-phenylpiperazines.

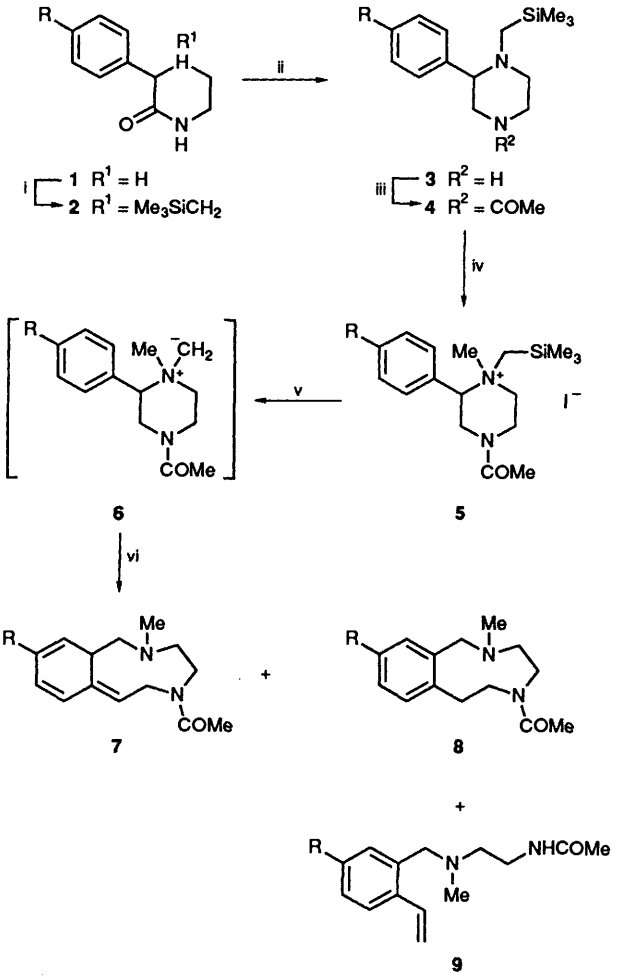
2-Phenyl-1-trimethylsilylmethylpiperazine **3a** and a 2-(4-methoxyphenyl)-analogue **3b** were prepared by reaction of 3-(4-substituted phenyl)piperazin-2-ones **1a**, **b** with (iodomethyl)-trimethylsilane followed by reduction with lithium aluminium hydride. Amines **3a**, **b** were acetylated with acetic anhydride and then quaternized with iodomethane to give a mixture of *cis*- and *trans*-4-acetyl-1-methyl-2-(4-substituted phenyl)-1-trimethylsilylmethylpiperazinium iodides **5a**, **b**.†

Reaction of **5a**, **b** with caesium fluoride was carried out in dimethylformamide (DMF) at room temperature. Spectroscopic analysis of the reaction mixture from **5a** showed the presence of 5-acetyl-2-methyl-1,3,4,5,6,11a-hexahydro-2*H*-2,5-benzodiazonine **7a**, 5-acetyl-2-methyl-2,3,4,5,6,7-hexahydro-1*H*-2,5-benzodiazonine **8a**, and 6-methyl-7-(2-vinylphenyl)-3,6-diazaheptan-2-one **9a** (entries 1 and 2, Table 1). The conjugated triene compound **7a**, which is a [2,3]-sigmatropic rearrangement product of ylide **6a**, still remained after 48 h. However, isolation of **7a** failed because of its partial isomerization on a silica or an aluminium oxide column. Similar treatment of **5b** gave only the conjugated triene compound **7b** after 24 h (entry 4).

We previously reported that [2,3]-sigmatropic rearrangement products of *para*-methoxy-substituted benzylammonium ylides were isolable at room temperature but aromatized to the Sommelet–Hauser products with the aid of strongly basic amines such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU).[4l] When the reaction of **5** was carried out in the presence of DBU, the products changed from **7** to **8** (entries 3 and 5).

When piperazinone **2a** was converted into 1-methyl-3-oxo-2-phenyl-1-trimethylsilylmethylpiperazinium iodide **10** and similarly treated with CsF, 1-methyl-6-phenyl-2,3,6,7-tetrahydro-1*H*-diazepin-5-one **12** (Stevens rearrangement product) was obtained in 43% yield (Scheme 2). The formation of Stevens products from benzylammonium *N*-alkylides produced in non-basic media was depressed in the presence of DBU.[4l] In the reaction of **10**, however, no change to the Sommelet–Hauser product was observed with the addition of DBU.

The restricted rotation around the amide C(O)–N bonds complicated the ^1H and ^{13}C NMR spectra of **4**, **5**, **7** and **8** at room temperature. The assignment of **4**, **7** and **8** was performed



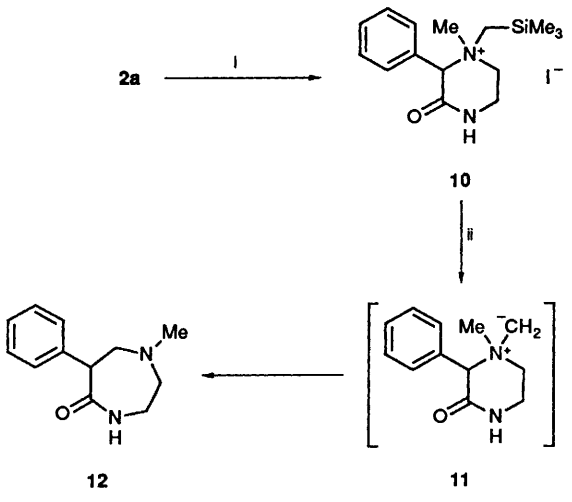
Scheme 1 *Reagents and conditions:* i, Me_3SiCH_2I, MeCN, reflux, 10–72 h; ii, $LiAlH_4$, THF, reflux, 2 h; iii, Ac_2O, Et_2O, room temp., 1 h; iv, MeI, MeCN, reflux, 10 h; v, CsF, DMF, room temp. 24–48 h

† We temporarily assigned the major product to the *trans*-isomer and the minor product to the *cis*-isomer.

Table 1 Reaction of 4-acetyl-1-methyl-2-(4-substituted phenyl)-1-trimethylsilylmethylpiperazinium iodide **5** with CsF

Entry	R	Reaction time (h)	Additive[b]	Total yield (%)	Ratio[a] 7:8:9
1 **a**	H	24	—	59	26:64:10
2 **a**	H	48	—	83	16:68:16
3 **a**	H	48	DBU	70	0:100:0
4 **b**	MeO	24	—	59	100:0:0
5 **b**	MeO	48	DBU	74	0:100:0

[a] Determined from the proton ratios of ^{1}H NMR spectra. [b] Five mole equivalents for **5** were added.



Scheme 2 *Reagents and conditions:* i, MeI, benzene, reflux, 10 h; ii, CsF, DMF, room temp., 20 h

with the aid of H–H and C–H COSY, however, that of **5** was difficult because the (*E*) and (*Z*) isomers existed in the *cis*- and *trans*-isomers, respectively. In confirmation of the structures, **4b** and **8b** were converted into the corresponding *N*-ethyl derivatives by lithium aluminium hydride reduction.

Experimental

DMF was dried by distillation from BaO under reduced pressure. CsF was dried (P_2O_5) at 180 °C under reduced pressure. Aluminium oxide (Merck, Aluminium oxide 90, 70–230 mesh) was used for column chromatographies. All melting and boiling points are uncorrected. *J* Values are given in Hz.

3-*Phenyl*-4-*trimethylsilylmethylpiperazin*-2-*one* **2a**.—A solution of 3-phenylpiperazin-2-one[5] **1a** (14.10 g, 80 mmol) and (iodomethyl)trimethylsilane[6] (8.60 g, 40 mmol) in MeCN (100 cm^3) was heated at reflux for 10 h and concentrated. The residue was dissolved in ethyl acetate (100 cm^3), washed with water (100 cm^3), and concentrated. The residue was recrystallized from hexane to give the *title compound* **2a** (8.63 g, 80%), m.p. 98–102 °C (Found: C, 64.05; H, 8.25; N, 10.6. $C_{14}H_{22}H_2OSi$ requires C, 64.08; H, 8.45; N, 10.67%); ν_{max}(Nujol)/cm^{-1} 3170 (NH), 1680 (CO) and 1250 ($SiMe_3$); δ_H(400 MHz; $CDCl_3$; Me_4Si) −0.03 (9 H, s, SiMe), 1.71 and 1.97 (2 H, AB q, *J* 14.7, $SiCH_2$), 2.51 (1 H, ddd, *J* 12.1, 10.3 and 3.7, 5-H), 2.98 (1 H, ddd, *J* 12.1, 3.7 and 3.5, 5-H), 3.23 (ddd, 1 H, *J* 11.5, 3.7 and 3.5, 6-H), 3.44–3.55 (1 H, m, 6-H), 3.79 (1 H, s, 3-H) and 7.24–7.43 (6 H, m, NH and Ph).

3-(4-*Methoxyphenyl*)-4-*trimethylsilylmethylpiperazin*-2-*one* **2b**.—A solution of sodium (3.22 g, 140 mmol) in ethanol (80 cm^3) was added to a solution of ethyl 2-bromo-2-(4-methoxyphenyl)acetate[7] (32.70 g, 120 mmol) and ethylenediamine (15.05 g, 251 mmol) in ethanol (150 cm^3), and the mixture was heated at reflux for 4 h. The mixture was filtered and concentrated. The residue was recrystallized from benzene to give 3-(4-*methoxyphenyl*)*piperazin*-2-*one* **1b** (15.27 g, 62%), m.p. 136–139 °C (Found: C, 63.85; H, 6.85; N, 13.55. $C_{11}H_{14}N_2O_2$ requires C, 64.06; H, 6.84; N, 13.58%); ν_{max}(Nujol)/cm^{-1} 3250, 3200 (NH) and 1680 (CO); δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.83 (1 H, br s), 3.06 (1 H, ddd, *J* 4.4, 8.8 and 12.6, 5-H), 3.16 (1 H, ddd, *J* 4.4, 8.8 and 12.6, 5-H), 3.37 (1 H, ddd, *J* 4.4, 8.8 and 11.6, 6-H), 3.53 (1 H, ddd, *J* 4.4, 8.8 and 11.6, 6-H), 3.80 (3 H, s, Me), 4.52 (1 H, s, 3-H), 6.49 (1 H, br s, NH), 6.88 (2 H, d, *J* 8.8, Ph) and 7.33 (2 H, d, *J* 8.8, Ph).

In the same way as described for **2a**, a solution of **1b** (13.01 g, 63 mmol) and (iodomethyl)trimethylsilane (7.56 g, 35 mmol) in MeCN (100 cm^3) was heated at reflux for 3 days and worked up. The residue was chromatographed on silica gel (methanol–ether, 5:95) to give the *title compound* **2b** (6.03 g, 65%), m.p. 130–133 °C (recrystallized from ethyl acetate–hexane) (Found: C, 61.4; H, 8.55; N, 9.35. $C_{15}H_{24}N_2O_2Si$ requires C, 61.60; H, 8.27; N, 9.58%); ν_{max}(Nujol)/cm^{-1} 3200 (NH), 1680 (CO) and 1260 (SiMe); δ_H(400 MHz; $CDCl_3$; Me_4Si) −0.02 (9 H, s, Me_3Si), 1.69 and 2.20 (2 H, AB q, *J* 14.7, $SiCH_2$), 2.52 (1 H, ddd, *J* 3.7, 10.6 and 12.7, 5-H), 3.00 (1 H, m, 5-H), 3.25 (1 H, m, 6-H), 3.53 (1 H, m, 6-H), 3.79 (1 H, s, 3-H), 3.80 (3 H, s, MeO), 6.73 (1 H, br s, NH), 6.88 (2 H, d, *J* 8.2, Ph) and 7.31 (2 H, d, *J* 8.2, Ph).

2-*Phenyl*-1-*trimethylsilylmethylpiperazine* **3a**.—To a mixture of lithium aluminium hydride (1.00 g, 26 mmol) in THF (90 cm^3) was added **2a** (6.46 g, 25 mmol). After 1 h of reflux, the reaction was quenched with 5% NaOH (4 cm^3) and the mixture was filtered. The filtrate and washings of the precipitate with ether were concentrated and distilled to give the *title compound* **3a** (4.88 g, 80%), b.p. 132 °C/0.3 Torr* (Found: C, 67.5; H, 9.95; N, 11.15. $C_{14}H_{24}N_2Si$ requires C, 67.68; H, 9.74; N, 11.28%); ν_{max}(film)/cm^{-1} 3260 (NH) and 1250 ($SiMe_3$); δ_H(400 MHz; $CDCl_3$; Me_4Si) −0.02 (9 H, s, SiMe), 1.36 and 2.02 (2 H, AB q, *J* 14.5, $SiCH_2$), 1.72 (1 H, br s, NH), 2.11 (1 H, ddd, *J* 11.2, 9.3 and 5.1), 2.67 (1 H, dd, *J* 12.1 and 9.9), 2.85–3.05 (5 H, m) and 7.18–7.38 (5 H, m, Ph).

2-(4-*Methoxyphenyl*)-1-*trimethylsilylmethylpiperazine* **3b**.—In the same way, **2b** (5.51 g, 19 mmol) and lithium aluminium hydride (2.23 g, 59 mmol) were allowed to react in THF (100 cm^3) to give the *title compound* **3b** (5.00 g, 95%), m.p. 40–42 °C (Found: C, 64.6; H, 9.4; N, 9.85. $C_{15}H_{26}N_2OSi$ requires C, 64.70; H, 9.41; N, 10.06%); ν_{max}(Nujol)/cm^{-1} 1250 ($SiMe_3$); δ_H(400 MHz; $CDCl_3$; Me_4Si) −0.03 (9 H, s, SiMe), 1.33 and 2.02 (2 H, AB q, *J* 14.4, $SiCH_2$), 1.61 (1 H, br s, NH), 2.10 (1 H, ddd, *J* 5.1, 9.5 and 11.3), 2.64 (1 H, dd, *J* 10.9 and 12.8), 2.85 (2 H, m), 2.96 (3 H, m), 3.80 (3 H, s, OMe), 6.84 (2 H, d, *J* 8.1, Ph) and 7.22 (2 H, d, *J* 8.1, Ph).

4-*Acetyl*-2-*phenyl*-1-*trimethylsilylmethylpiperazine* **4a**.—Ac_2O (2.89 g, 28 mmol) was added to a chilled solution of **3a** (4.78 g, 19 mmol) in Et_2O (20 cm^3). After 10 min of stirring, the mixture was poured into water (100 cm^3) and made alkaline with 10% NaOH. The Et_2O (4 × 50 cm^3) extract of the mixture was washed with water (3 × 50 cm^3), dried ($MgSO_4$), concentrated, and distilled to give the *title compound* **4a** (5.06 g, 90%), b.p. 200–205 °C/0.6 Torr [a mixture of (*E*) and (*Z*) isomers, 57:43] (Found: C, 65.95; H, 9.15; N, 9.4. $C_{16}H_{26}N_2OSi$ requires C, 66.16; H, 9.02; N, 9.64%); ν_{max}(film)/cm^{-1} 1660 (CO) and 1250 ($SiMe_3$); δ_H(400 MHz; $CDCl_3$; Me_4Si) −0.02 (9 H, s, SiMe), 1.36 and 2.00 (2 H, AB q, *J* 14.5, $SiCH_2$) and 7.34 (5 H, m, Ph);

* 1 Torr = 133.322 Pa.

(*E*): 2.04 (3 H, s, COMe), 2.00–2.05 (1 H, m, 6-H), 2.84 (1 H, m, 5-H), 3.00–3.10 (3 H, m, 2-H, 3-H and 6-H), 3.58 (1 H, m, 3-H) and 4.55 (1 H, m, 5-H); (*Z*): 2.11 (3 H, s, COMe), 2.08–2.14 (1 H, m, 6-H), 2.44–2.62 (1 H, m, 3-H), 2.95 (1 H, m, 2-H), 3.03 (1 H, m, 6-H), 3.37 (1 H, m, 5-H), 3.73 (1 H, m, 5-H) and 4.45 (1 H, m, 3-H); δ_C(67.8 MHz; $CDCl_3$; Me_4Si) −1.2 (SiMe), 21.2 (COMe), 127.6 (Ph), 127.9 (Ph), 128.1 (Ph), 128.2 (Ph), 128.5 (Ph), 128.7 (Ph), 141.1 (Ph) and 168.5 (CO); (*E*): 41.9 (C-5), 46.6 (Si–C–N), 54.0 (C-3), 54.9 (C-6) and 71.3 (C-2); (*Z*): 46.5 (SiC–N), 46.7 (C-5), 48.9 (C-3), 55.5 (C-6) and 70.5 (C-2).

4-*Acetyl*-2-(4-*methoxyphenyl*)-1-*trimethylsilymethylpiperazine* **4b**.—In the same way, **3b** (3.98 g, 14 mmol) and acetic anhydride (2.34 g, 23 mmol) were allowed to react in ether (25 cm^3) to give **4b** (4.48 g, 98%), viscous oil [a mixture of (*E*) and (*Z*) isomers, 56:44] (Found: C, 63.8; H, 8.85; N, 8.7. $C_{17}H_{28}N_2O_2Si$ requires C, 63.71; H, 8.81; N, 8.74%); δ_H(400 MHz; $CDCl_3$; Me_4Si); (*E*): −0.03 (9 H, s, MeSi), 1.32 and 2.00 (2 H, AB q, *J* 14.5), 2.04 (3 H, s, MeCO), 2.10 (1 H, m, 6-H), 2.88 (2 H, m, 2-H and 5-H), 3.05 (2 H, m, 3-H and 6-H), 3.55 (1 H, dt, *J* 13.2 and 2.8, 3-H), 3.81 (3 H, s, MeO), 4.53 (1 H, m, 5-H), 6.88 (2 H, d, *J* 8.6, Ph) and 7.24 (2 H, d, *J* 8.6, Ph); (*Z*): −0.02 (9 H, s, MeSi), 1.32 and 2.05 (2 H, AB q, *J* 14.5, $SiCH_2$), 2.10 (3 H, s, MeCO), 2.13 (1 H, dd, *J* 12.5 and 3.1, 6-H), 2.53 (1 H, dd, *J* 12.5 and 11.0, 3-H), 2.80 (1 H, dd, *J* 12.5 and 2.9, 2-H), 3.05 (1 H, m, 6-H), 3.34 (1 H, ddd, *J* 12.5, 12.5 and 2.9, 5-H), 3.71 (1 H, m, 5-H), 3.80 (3 H, s, MeO), 4.42 (1 H, m, 3-H), 6.84 (2 H, d, *J* 8.6, Ph) and 7.22 (2 H, d, *J* 8.6, Ph); δ_C(67.8 MHz; $CDCl_3$; Me_4Si) −1.2 (SiMe), 21.2 (MeCO), 129.1 (Ph), 168.5 (CO); (*E*): 41.9 (C-5), 46.3 (Si–C–N), 54.0 (C-3), 54.9 (C-6), 55.3 (MeO), 70.4 (C-2), 114.0 (Ph) 133.1 (Ph) and 159.2 (Ph); (*Z*): 46.2 (SiC–N), 46.8 (C-5), 49.0 (C-3), 55.2 (MeO), 55.5 (C-6), 69.7 (C-2), 113.8 (Ph), 133.3 (Ph) and 159.0 (Ph).

4-*Acetyl*-1-*methyl*-2-*phenyl*-1-*trimethylsilylmethylpiperazinium Iodide* **5a**.—A solution of **4a** (7.43 g, 26 mmol) and iodomethane (18.9 g, 133 mmol) in acetonitrile (30 cm^3) was heated at reflux for 10 h and concentrated. The residue was recrystallized from a mixture of ethyl acetate and acetone to give the *title compound* **5a** (8.71 g, 79%), m.p. 225–228 °C (Found: C, 47.1; H, 7.05; N, 6.2. $C_{17}H_{29}IN_2OSi$ requires C, 47.22; H, 6.76; N, 6.48%); ν_{max}(Nujol)/cm^{-1} 1660 (CO) and 1250 ($SiMe_3$). Assignment of the ^1H NMR spectrum (400 MHz; $CDCl_3$) was difficult because (*E*) and (*Z*) isomers existed in *cis*-**5a** and *trans*-**5a**, respectively.

4-*Acetal*-1-*methyl*-2-(4-*methoxyphenyl*)-1-*trimethylsilylmethylpiperazinium Iodide* **5b**.—In the same way, **4b** (3.41 g, 10.7 mmol) and iodomethane (7.75 g, 54.6 mmol) were heated in acetonitrile (15 cm^3) and worked up to give the *title compound* **5b** (4.19 g, 88%), m.p. 150–153 °C (ethyl acetate–acetone) (Found: C, 46.8; H, 6.7; N, 5.75. $C_{18}H_{31}IN_2O_2Si$ requires C, 46.75; H, 6.77; N, 6.06%); ν_{max}(Nujol)/cm^{-1} 1660 (CO) and 1250 ($SiMe_3$). Assignment of the ^1H NMR spectrum (400 MHz; $CDCl_3$) was difficult because (*E*) and (*Z*) isomers existed in *cis*-**5b** and *trans*-**5b**, respectively.

Reaction of **5a** *with* CsF.—Ammonium salt **5a** (1.30 g, 3 mmol) was placed in a 30 cm^3 flask equipped with a magnetic stirrer, a septum, and a test tube connected with the flask by a short piece of rubber tube. CsF (2.0 g, 13 mmol) was placed in the test tube. The apparatus was dried under reduced pressure and was flushed with N_2. DMF (10 cm^3) was added *via* syringe, and then CsF was added from the test tube. The mixture was stirred for the time listed in Table 1 at room temp., poured into 1% $NaHCO_3$ (100 cm^3), and extracted with ethyl acetate (4 × 100 cm^3). The extract was washed with 1% $NaHCO_3$ (3 × 50 cm^3), dried ($MgSO_4$), and concentrated under reduced pressure. ^1H NMR spectroscopy of the residual oil indicated the presence of 5-acetyl-2-methyl-1,3,4,5,6,11a-hexahydro-2*H*-2,5-benzodiazonine **7a**, 5-*acetyl*-2-*methyl*-2,3,4,5,6,7-*hexahydro*-1H-2,5-*benzodiazonine* **8a** and 6-*methyl*-7-(2-*vinylphenyl*)-3,6-*diazaheptan*-2-*one* **9a**. The samples of **8a** and **9a** were isolated on an HPLC column (Merck Hibar LiChrosorb NH_2, 250 × 10 mm, Et_2O). The ratio was calculated on the basis of the proton ratios of ^1H NMR spectra (Table 1).

7a; (not isolated); δ_H(400 MHz; $CDCl_3$; Me_4Si) 3.80–3.87 (1 H, m, 4-H), 3.97–4.07 (1 H, m, 6-H), 4.30 (1 H, dd, *J* 17.4 and 7.3, 6-H), 5.45–5.51 (1 H, m, 11a-H), 5.59–5.71 (3 H, m, 9-H, 10-H and 11-H) and 5.84–5.96 (2 H, m, 7-H and 8-H), the other signals were not assigned due to overlapping with those of **8a** and **9a**.

8a; b.p. 175 °C/0.6 Torr (Kugelrohr) (Found: C, 72.45; H, 9.0; N, 12.0. $C_{14}H_{20}N_2O$ requires C, 72.38; H, 8.68; N, 12.06%); ν_{max}(film)/cm^{-1} 1660 (CO). The presence of (*E*) and (*Z*) isomers was observed on the ^1H NMR spectrum but the assignment was difficult (*isomer*-1/*isomer*-2, 53:47); δ_H(400 MHz; $CDCl_3$; Me_4Si) 7.10–7.24 (4 H, m, Ph); *isomer*-1: 2.01 (3 H, s, COMe), 2.49 (3 H, s, NMe), 2.55 (2 H, t, *J* 5.1, 3-H), 3.24 (2 H, m, 7-H), 3.28 (2 H, m, 4-H), 3.62 (2 H, m, 6-H) and 3.72 (2 H, s, 1-H); *isomer*-2: 2.09 (3 H, s, COMe), 2.45 (2 H, t, *J* 5.1, 3-H), 2.56 (3 H, s, NMe), 3.09 (2 H, m, 7-H), 3.28 (2 H, m, 4-H), 3.62 (2 H, m, 6-H) and 3.75 (2 H, s, 1-H).

9a; b.p. 165 °C/0.5 Torr (Kugelrohr) (Found: M^+, 232.1572. $C_{14}H_{20}N_2O$ requires *M*, 232.1575); δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.87 (3 H, s, COMe), 2.23 (3 H, s, NMe), 2.44 (2 H, t, *J* 5.7, $MeNCH_2$), 3.25 (2 H, q, *J* 5.7, 4-H), 3.56 (2 H, s, 7-H), 5.31 (1 H, dd, *J* 11.0 and 1.3, =CH_2), 5.71 (1 H, dd, *J* 17.5 and 1.3, =CH_2), 5.95 (1 H, br s, NH), 7.12 (1 H, dd, *J* 17.5 and 11.0, PhCH=), 7.16–7.32 (3 H, m, ArH) and 7.53 (1 H, dd, *J* 7.5 and 1.1, Ph).

Reaction of **5b** *with* CsF.—In the same way, **5b** (0.92 g, 1.99 mmol) and CsF (1.52 g, 10.0 mmol) were allowed to react in DMF (10 cm^3) and worked up to give 5-acetyl-2-methyl-10-methoxy-1,3,4,5,6,11a-hexahydro-2*H*-2,5-benzodiazonine **7b**, an undistillable viscous oil [a mixture of (*E*) and (*Z*) isomers, 66:34]; λ_{max}(hexane)/nm 310; δ_H(400 MHz; $CDCl_3$; Me_4Si) (*E*): 2.10 (3 H, s, MeCO), 2.35 (3 H, s, NMe), 2.40 (2 H, m, 1-H), 2.50 (1 H, m, 3-H), 2.83 (1 H, m, 3-H), 3.01 (1 H, m, 4-H), 3.42 (1 H, m, 11a-H), 3.53 (3 H, s, OMe), 3.93 (1 H, m, 4-H), 4.05 (1 H, m, 6-H), 4.39 (1 H, m, 6-H), 4.56 (1 H, d, *J* 5.9, 11-H), 5.55 (1 H, m, 7-H), 5.62 (1 H, d, *J* 9.9, 9-H) and 6.01 (1 H, d, *J* 9.9, 8-H); (*Z*): 2.11 (3 H, s, MeCO), 2.37 (3 H, s, NMe), 2.40 (2 H, m, 1-H), 2.55 (1 H, m, 3-H), 2.83 (1 H, m, 3-H), 3.31 (1 H, m, 4-H), 3.40 (1 H, m, 4-H), 3.54 (3 H, s, OMe), 3.60 (1 H, m, 11a-H), 3.93 (1 H, m, 6-H), 4.52 (1 H, m, 6-H), 4.56 (1 H, d, *J* 5.9, 11-H), 5.62 (1 H, d, *J* 9.9, 9-H), 5.80 (1 H, m, 7-H) and 6.05 (1 H, d, *J* 9.9, 8-H).

Reaction of **5a, b** *with CsF in the Presence of DBU*.—In a manner similar to that described for the reaction of **5a** or **5b** with CsF, a solution of **5a** or **5b** (2 mmol) in DMF (10 cm^3) was prepared and DBU (1.52 g, 10 mmol) was added *via* syringe. Then, CsF (1.52 g, 10 mmol) was added. The residual oil was purified on an aluminium oxide column (hexane–ethyl acetate) to give **8a** or 5-*acetal*-10-*methoxy*-2-*methyl*-2,3,4,5,6,7-*hexahydro*-1H-2,5-*benzodiazonine* **8b**. The results are shown in Table 1.

8b; b.p. 188 °C/1 Torr (Kugelrohr) (Found: C, 68.6; H, 8.55; N, 10.65. $C_{15}H_{22}N_2O_2$ requires C, 68.67; H, 8.45; N, 10.68%); ν_{max}(film)/cm^{-1} 1640 (CO). The presence of (*Z*) and (*E*) isomers was observed on the ^1H NMR spectrum but the assignment was difficult (*isomer*-1/*isomer*-2, 58:42); δ_H(400 MHz; $CDCl_3$; Me_4Si); *isomer*-1: 2.01 (3 H, s, COMe), 2.49 (3 H, s, NMe), 2.56 (2 H, t, 5.1, 3-H), 3.18 (2 H, br s, 7-H), 3.28 (2 H, m, 4-H), 3.58 (2 H, m, 6-H), 3.69 (2 H, s, 1-H), 3.78 (3 H, s, OMe), 6.71–6.78 (2 H, m, 9-H and 11-H) and 7.03 (1 H, d, *J* 8.4, 8-H); *isomer*-2: 2.09 (3 H, s, COMe), 2.46 (2 H, d, *J* 5.0, 3-H), 2.55 (3 H, s,

NMe), 3.02 (2 H, d, *J* 5.4, 7-H), 3.28 (2 H, m, 4-H), 3.58 (2 H, m, 6-H), 3.71 (2 H, s, 1-H), 3.79 (3 H, s, OMe), 6.71–6.78 (2 H, m, 9-H and 11-H) and 7.09 (1 H, d, *J* 8.2, 8-H).

1-Methyl-3-oxo-2-phenyl-1-trimethylsilylmethylpiperazinium Iodide **10**.—A solution of **2a** (3.94 g, 15 mmol) and MeI (10.6 g, 75 mmol) in benzene (10 cm^3) was heated at reflux for 10 h and concentrated. The residue was recrystallized from a mixture of acetone and methanol to give the *title compound* **10** (4.09 g, 67%), m.p. 225–230 °C (a mixture of *cis* and *trans* isomers, 17:83)* (Found: C, 44.45; H, 6.35; N, 6.8. $C_{15}H_{25}IN_2OSi$ requires C, 44.55; H, 6.23; N, 6.93%); ν_{max}(Nujol)/cm^{-1} 1680 (CO) and 1260 ($SiMe_3$); δ_H(400 MHz; $CDCl_3$; Me_4Si) *cis*-**10**: 0.22 (9 H, s, SiMe), 2.50 and 3.17 (2 H, AB q, *J* 14.8, $SiCH_2$), 3.53 (3 H, s, NMe), 3.77–3.93 (2 H, m, 6-H), 4.05–4.15 (1 H, m, 5-H), 4.20–4.24 (1 H, m, 5-H), 6.27 (1 H, s, 2-H), 7.44–7.84 (5 H, m, Ph) and 8.26 (1 H, s, NH); *trans*-**10**: 0.27 (9 H, s, SiMe), 3.14 and 3.87 (2 H, AB q, *J* 14.8, $SiCH_2$), 3.01 (3 H, s, NMe), 3.77–3.93 (2 H, m, 6-H), 4.05–4.15 (1 H, m, 5-H), 4.30–4.40 (1 H, m, 5-H), 6.15 (1 H, s, 2-H), 7.44–7.84 (5 H, m, Ph) and 8.18 (1 H, s, NH).

Reaction of **10** *with* CsF.—In a manner similar to that described for the reaction of **5** with CsF, **10** (1.21 g, 3 mmol) and CsF (2.0 g, 13 mmol) were allowed to react in DMF (10 cm^3). The reaction mixture was poured into 1% $NaHCO_3$ (100 cm^3) and extracted with $CHCl_3$ (4 × 100 cm^3). The extract was washed with 1% $NaHCO_3$ (2 × 100 cm^3), dried ($MgSO_4$), and concentrated. The residue was recrystallized from ethyl acetate to give *1-methyl-6-phenyl-2,3,6,7-tetrahydro-1H-diazepin-5-one* **12** (262 mg, 43%), m.p. 123–125 °C (Found: C, 70.15; H, 8.0; N, 13.7. $C_{12}H_{16}N_2O$ required C, 70.56; H, 7.89; N, 13.71%); ν_{max}(Nujol)/cm^{-1} 1660 (CO); δ_H(400 MHz; $CDCl_3$; Me_4Si) 2.33–2.45 (1 H, m, 2-H), 2.39 (3 H, s, NMe), 2.78–2.93 (3 H, m, 2-H and 7-H), 3.14–3.26 (1 H, m, 3-H), 3.50–3.63 (1 H, m, 3-H), 3.95 (1 H, dd, *J* 1.98 and 8.25, 6-H), 6.09 (1 H, br s, NH) and 7.20–7.38 (5 H, m, Ph).

Lithium Aluminium Hydride Reduction of **4b**.—A mixture of **4b** (31 mg, 0.097 mmol) and lithium aluminium hydride (12 mg, 0.316 mmol) in THF (5 cm^3) was heated at reflux for 3.5 h. The reaction was quenched with saturated potassium sodium tartrate (25 cm^3) and the mixture was extracted with Et_2O (3 × 15 cm^3). The extract was dried ($MgSO_4$) and concentrated to give *4-ethyl-2-(4-methoxyphenyl)-1-trimethylsilylmethylpiperazine* (25 mg, 86%), yellow oil; δ_H(400 MHz; $CDCl_3$; Me_4Si) −0.03 (9 H, s, SiMe), 1.06 (3 H, t, *J* 7.2, CH_3CH_2), 1.35 and 2.02 (2 H, AB q, *J* 14.4, $SiCH_2$), 1.95 (1 H, t, *J* 10.6, 3-H), 2.18 (1 H, m, 6-H), 2.29 (1 H, m, 5-H), 2.37 (2 H, q, *J* 7.2, CH_2CH_3), 2.78 (1 H, dt, *J* 2.5 and 11.4, 6-H), 2.88 (1 H, dd, *J* 2.9 and 10.6, 3-H), 3.01 (1 H, dt, *J* 2.5 and 11.4, 5-H), 3.07 (1 H, dd, *J* 2.9 and 10.6, 2-H), 3.80 (3 H, s, OMe), 6.84 (2 H, d, *J* 7.5, Ph) and 7.24 (2 H, d, *J* 7.5, Ph); EIMS *m/z* 306 (M^+, 20%) and 233 (100) [Found: M^+, 306.2129. Calc. for $C_{17}H_{30}N_2OSi$: *M*, 306.2126].

Lithium Aluminium Hydride Reduction of **8b**.—In a manner similar to that described above, a mixture of **8b** (46 mg, 0.175 mmol) and lithium aluminium hydride (14 mg, 0.369 mmol) in THF (5 cm^3) was allowed to react to give *5-ethyl-10-methoxy-2-methyl-2,3,4,5,6,7-hexahydro-1H-2,5-benzodiazonine* (31 mg, 69%), pale yellow oil; δ_H(400 MHz; $CDCl_3$; Me_4Si) 1.08 (3 H, t, *J* 7.1), 2.35 (2 H, dd, *J* 5.9 and 4.8), 2.55 (3 H, s, NMe), 2.54–2.57 (2 H, m), 2.60 (2 H, q, *J* 7.1), 2.64 (2 H, m), 2.80 (2 H, m), 3.80 (3 H, s, OMe), 4.08 (2 H, s, 1-H), 6.75 (1 H, dd, *J* 8.2 and 2.7, 9-H), 6.86 (1 H, d, *J* 2.7, 11-H), 6.97 (1 H, d, *J* 8.2, 8-H); EIMS *m/z* 248 (M^+, 41%), 190 (100) and 134 (86) [Found: M^+, 248.1903. Calc. for $C_{15}H_{24}N_2O$: *M*, 248.1887].

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* See footnote on page 2851.