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REACTION OF (DIALKYLAMINOMETHYL)TRIMETHYLSILANES WITH BENZYNE

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Summary

Reactions of (dialkylaminomethyl)trimethylsilanes [dimethylamino-, diethylamino-, pyrrolidino- and morpholino-] with benzyne in THF gave two types of aniline derivatives: *N*-alkyl-*N*-(1-trimethylsilylalkyl)anilines and *N*-alkyl-*N*-trimethylsilylmethylanilines. From (piperidinomethyl)trimethylsilane, however, unexpected 1-(α-trimethylsilylbenzyl)piperidine was obtained together with *N*-(4-pentenyl)-*N*-trimethylsilylmethylaniline.

Introduction

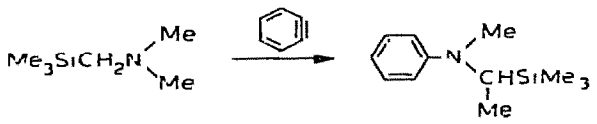
It has been reported that benzyne reacts with tertiary aliphatic amines to give arylamine intermediates which subsequently rearrange via Stevens [1] and/or Sommelet-Hauser [2] pathways to give corresponding aniline derivatives. In the present paper, the reaction of several (dialkylaminomethyl)trimethylsilanes with benzyne [3] are described.

Results and discussion

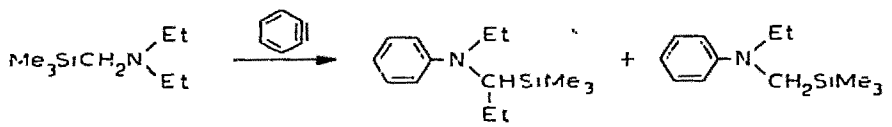
The reaction of (dimethylaminomethyl)trimethylsilane (Ia) with bromobenzene in the presence of sodium amide [3] in boiling tetrahydrofuran gave a pale yellow oil as the sole basic product. The ^{1}H NMR spectral and elemental analyses confirmed the structure of this oil as *N*-methyl-*N*-(1-trimethylsilylethyl)-aniline (IIa) (60% yield), which resulted from the addition of Ia to benzyne to give an intermediate which rearranged by methyl migration from nitrogen to carbon (the Stevens rearrangement).

Two kinds of basic products were isolated from the reaction of benzyne with (diethylaminomethyl)trimethylsilane (Ib), (pyrrolidinomethyl)trimethylsilane (Ic), and (morpholinomethyl)trimethylsilane (Id) under the same reaction condition as for Ia. Analytical data of the isolated products revealed that these products were grouped into two types of aniline derivatives. One group com-

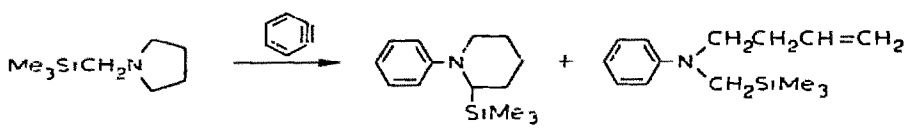
prised Stevens rearrangement products, i.e., *N*-ethyl-*N*-(1-trimethylsilylpropyl)-aniline (IIb) (3%) from Ib, 1-phenyl-2-trimethylsilylpiperidine (IIc) (36%) from Ic, and 4-phenyl-5-trimethylsilylperhydro-1,4-oxazepine (9%) from Id, respectively. The other group comprised Hofmann elimination products, i.e., *N*-ethyl-*N*-trimethylsilylmethylaniline (IIIb) (39%) from Ib, *N*-(3-butenyl)-*N*-trimethylsilylmethylaniline (IIIc) (15%) from Ic, and *N*-(2-vinyloxyethyl)-*N*-trimethylsilylmethylaniline (IIId) (9%) from Id, respectively (see eqns. 1-4). Detrimethyl-



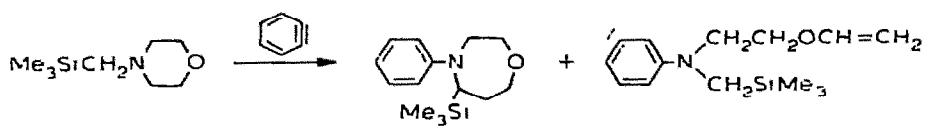
(Ia) (IIa) (1)



(Ib) (IIb) (IIIb) (2)



(Ic) (IIc) (IIIc) (3)



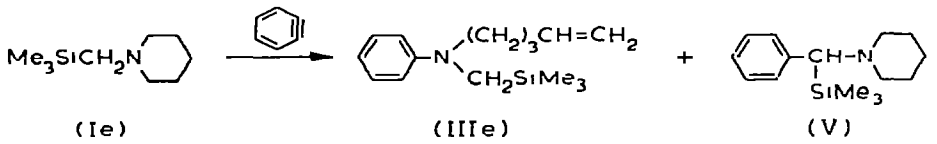
(Id) (IId) (IIId) (4)

(IV) (5)

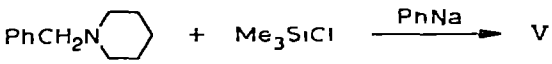
silylation of IId by 47% hydrobromic acid gave 4-phenylperhydro-1,4-oxazepine (IV), which was identified by comparison of its properties with an authentic sample synthesized from a reaction of 3-(2-chloroethoxy)propyl chloride with aniline (eqn. 5).

The reaction of (piperidinomethyl)trimethylsilane (Ie) with benzyne also gave two basic products. One of them was determined to be a ring opened product, *N*-(4-pentenyl)-*N*-trimethylsilylmethylaniline (IIIe) (19%). An NMR spectrum of the other compound was not consistent with the expected ring expanded product, 1-phenyl-2-trimethylsilylperhydroazepine (IIe), but was in accord with the unexpected 1-(α-trimethylsilylbenzyl)piperidine (V) (24%) (see eqn. 6). Compound V was identified by comparison of its properties with an authentic

sample prepared from a reaction of 1-benzylpiperidine with trimethylchlorosilane in the presence of phenylsodium (eqn. 7).

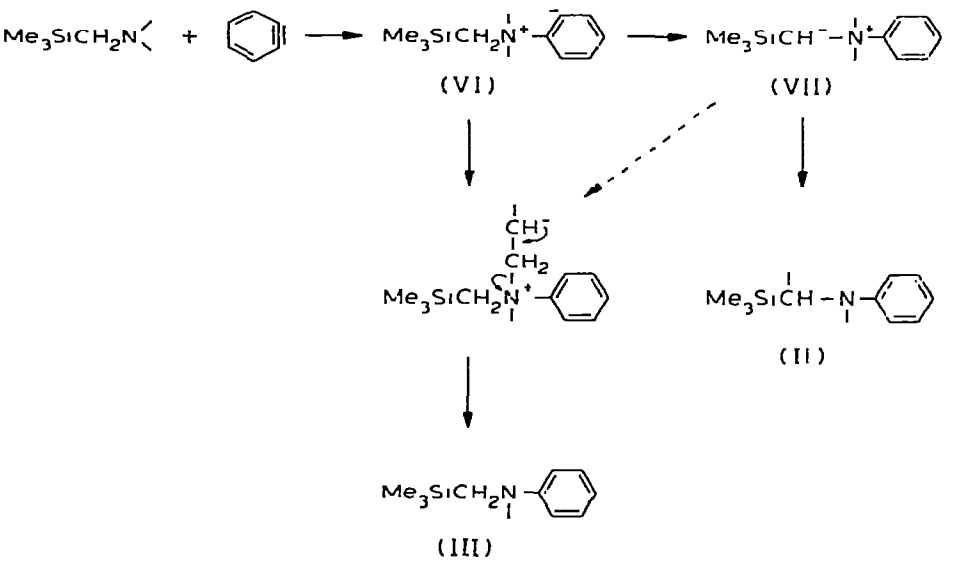


(Ie) (IIIe) (V) (6)



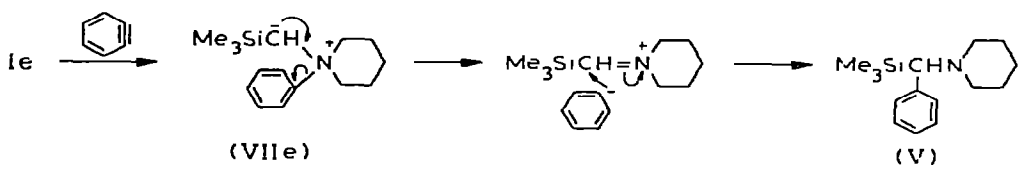
(7)

The reactions presumably take place by two discrete steps. First, electrophilic attack of benzyne on the tertiary amine gives a betaine (VI). Second, an intramolecular proton transfer of the betaine leads to an ylide (VII)* which subsequently rearranges (Stevens rearrangement) to give the *N*-alkyl-*N*-(1-trimethylsilylalkyl)aniline derivative (II). When the *N*-alkyl group of the (dialkylaminomethyl)silane has a β-hydrogen, the Hofmann elimination reaction competes with the rearrangement reaction and the *N*-alkyl-*N*-trimethylsilylmethylaniline derivative (III) is produced (see eqn. 8).



(VI) (VII) (II) (III) (8)

The result with Ie to give V suggests that perhaps reaction 9 occurs. A similar type of rearrangement occurs with the ammonium ylide system [5] (eqn. 10).



(VIIe) (V) (9)

* Miller [4] has determined that $Me_3SiCHNMe_3$ rearranges via methyl migration to (1-dimethylaminoethyl)trimethylsilane.

(10)

However, this still does not explain the anomalous behavior of Ie.

Experimental

NMR spectra were recorded on a JNM-MH-60 (JEOL) spectrometer and ^1H chemical shifts are given directly or indirectly relative to tetramethylsilane. IR spectra were obtained using an IR-A-2 (JASCO) spectrometer. All boiling points and melting points are uncorrected.

(Dialkylaminomethyl)trimethylsilane (Ia-Ie). A mixture of chloromethyltrimethylsilane (80 mmol) and the dialkylamine (dimethylamine, diethylamine, pyrrolidine, morpholine, or piperidine) (200 mmol) was heated in a sealed tube at 120-140° for 8 h. After the addition of 100 ml of 10% sodium hydroxide solution, the mixture was extracted with ether. The ethereal extract was dried, concentrated, and distilled to give the corresponding aminomethylsilane (Ia-Ie). The properties and analyses of these compounds are summarized in Table 1.

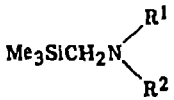
The reaction of (dimethylaminomethyl)trimethylsilane (Ia) with benzyne. A solution of bromobenzene (3.45 g, 22 mmol) in 5 ml of THF was added dropwise to a boiling suspension of Ia (2.6 g, 20 mmol) and sodium amide (0.96 g, 25 mmol) in 20 ml of THF. The reaction mixture was stirred at reflux for 2 h, and then hydrolyzed (saturated ammonium chloride solution) and extracted with ether. The ethereal extract was dried, concentrated, and distilled under reduced pressure to give 2.45 g (60%) of *N*-methyl-*N*-(1-trimethylsilylethyl)aniline (IIa): b.p. 136-140°/21 mm; NMR ($CDCl_3$): δ 0.16 (s, 9H, $SiCH_3$), 1.31 (d, *J* 7.5 Hz, 3H, $CHC\underline{H}_3$), 2.96 (s, 3H, NCH_3), 3.63 (q, *J* 7.5 Hz, 1H, $C\underline{H}CH_3$), 6.55-7.20 ppm (m, 5H, aromatic protons). (Found: C, 69.38; H, 10.19; N, 6.70. $C_{12}H_{21}NSi$ calcd.: C, 69.50; H, 10.21; N, 6.75%.)

The reaction of (diethylaminomethyl)trimethylsilane (Ib) with benzyne. Ib (3.10 g, 20 mmol), bromobenzene (3.45 g, 22 mmol), and sodium amide (0.94 g, 24 mmol) were allowed to react in 25 ml of THF using the above procedure. The fraction of b.p. 75-85°/2 mm of the ethereal extract was converted to the hydrochloride and recrystallized from ethanol/ether to give 1.86 g (39%) of *N*-ethyl-*N*-trimethylsilylmethylaniline hydrochloride (IIIb—HCl): m.p. 159-163° (decomp.). (Found: C, 59.09; H, 9.28; N, 5.71. $C_{12}H_{21}NSi \cdot HCl$ calcd.: C, 59.11; H, 9.09; N, 5.74%.) NMR (free base in $CDCl_3$): δ 0.22 (s, 9H, $SiCH_3$), 1.27 (t, 3H, CH_3), 3.00 (s, 2H, $SiCH_2$), 3.54 (q, 2H, NCH_2), 6.60-7.42 ppm (m, 5H, aromatic protons).

After concentration of the mother liquor, the residue was made basic and extracted with ether. Preparative thin layer chromatography (silica gel/n-hexane) of the extract gave 0.16 g (3%) of *N*-ethyl-*N*-(1-trimethylsilylpropyl)aniline (IIb). NMR ($CDCl_3$): δ 0.06 (s, 9H, $SiCH_3$), 1.09 (t, 3H, CH_3), 1.19 (t, 3H, CH_3), 1.64 (quintet, *J* 6.5 Hz, 2H, $CHC\underline{H}_2$), 3.13-3.40 (m, 1H, SiCH), 3.46 (q, 2H, NCH_2), 6.53-7.36 ppm (m, 5H, aromatic protons). IIb—HCl, m.p. 157-158° (recrys-

TABLE 1

(DIALKYLAMINOMETHYL)TRIMETHYLSILANE (Ia-Ie)



(I)

	R^1	R^2	B.p. (°C/mmHg)	Yield (%)	M.p. (°C) (oxalate)[a]	Formula	Analysis found (calcd.) (%)		
							C	H	N
Ia	CH_3	CH_3	115–118	55	147–149	$C_6H_{17}NSi \cdot C_2H_2O_4$	43.09 (43.41)	8.43 (8.65)	6.27 (6.33)
Ib	C_2H_5	C_2H_5	144–146[b]	53					
Ic	$-(CH_2)_4-$		65–67/25	61	127–129	$C_8H_{19}NSi \cdot C_2H_2O_4$	48.31 (48.56)	8.41 (8.56)	5.66 (5.66)
Id	$-(CH_2)_2O(CH_2)_2-$		79–80/20	73	131–132	$C_8H_{19}NOSi \cdot C_2H_2O_4$	45.31 (45.61)	8.06 (8.04)	5.31 (5.32)
Ie	$-(CH_2)_5-$		74–76/22[c]	58					

[a] Recrystallized from ethanol/ether. [b] Lit. b.p. 145-150° [6]. [c] Lit. b.p. 59° /9 mm [6].

tallized from i-propanol/ether). (Found: C, 61.68; H, 9.79; N, 5.00. $C_{14}H_{25}NSi \cdot HCl$ calcd.: C, 61.84; H, 9.64; N, 5.15%.)

The reaction of (pyrrolidinomethyl)trimethylsilane (Ic) with benzyne. Ic (3.10 g, 20 mmol), bromobenzene (3.45 g, 22 mmol), and sodium amide (0.94 g, 24 mmol) were allowed to react in 25 ml of THF using the above procedure. The fraction of b.p. 115-130°/4 mm of the ethereal extract was converted to the hydrochloride and recrystallized from i-propanol/ether to give 1.93 g (36%) of 1-phenyl-2-trimethylsilylpiperidine hydrochloride (IIc—HCl): m.p. 191-193°. (Found: C, 62.10; H, 9.18; N, 5.18. $C_{14}H_{23}NSi \cdot HCl$ calcd.: C, 62.30; H, 8.96; N, 5.19%.) NMR (free base in $CDCl_3$): δ 0.07 (s, 9H, $SiCH_3$), 1.51-2.02 [m, 6H, $(CH_2)_3$], 2.93-3.42 (m, 1H, SiCH), 3.45-3.72 (m, 2H, NCH_2), 6.61-7.44 ppm (m, 5H, aromatic protons).

After concentration of the mother liquor, the residue was made basic and extracted with ether. Silica gel column chromatography (n-hexane) of the extract gave 0.70 g (15%) of *N*-(3-butenyl)-*N*-trimethylsilylmethylaniline (IIIc). IR (film): ν 1635 cm^{-1} (C=C). NMR ($CDCl_3$): δ 0.17 (s, 9H, $SiCH_3$), 2.66 (q, 2H, CH_2CH=), 3.02 (s, 2H, $SiCH_2$), 3.55 (t, 2H, NCH_2), 5.09-5.49 (m, 2H, $C=CH_2$), 5.69-6.20 (m, 1H, CH=), 6.62-7.50 ppm (m, 5H, aromatic protons). (Found: C, 72,34; H, 10.02; N, 5.99. $C_{14}H_{23}NSi$ calcd.: C, 72.04; H, 9.93; N, 6.00%.)

The reaction of (morpholinomethyl)trimethylsilane (Id) with benzyne. Id (3.46 g, 20 mmol), bromobenzene (3.45 g, 22 mmol), and sodium amide (0.94 g, 24 mmol) were allowed to react in 25 ml of THF using the above procedure. The fraction of b.p. 110-120°/1 mm of the ethereal extract was chromatographed on an alumina column. The first fraction of n-hexane afforded 0.43 g (9%) of *N*-(2-vinyloxyethyl)-*N*-trimethylsilylmethylaniline (IIId). IR (film): ν1638 cm^{-1} (C=C). NMR ($CDCl_3$): δ 0.10 (s, 9H, $SiCH_3$), 3.04 (s, 2H, $SiCH_2$), 3.78 (t, 2H, NCH_2). 3.92 (t, 2H, OCH_2), 4.07 (d,d, *J* 7.5, 1.8 Hz, 1H, = CH_2), 4.27 (d,d, *J* 13.5 1.8 Hz, 1H, = CH_2), 6.53 (d,d, *J* 13.5, 7.5 Hz, 1H, CH=), 6.71-7.37 ppm (m, 5H, aromatic protons). (Found: C, 67.44; H, 9.31; N, 5.66. $C_{14}H_{23}NOSi$ calcd.: C, 67.42; H, 9.29; N, 5.62%.)

The second fraction gave 0.47 g (9%) of 4-phenyl-5-trimethylsilylperhydro-1,4-oxazepine (IId). NMR ($CDCl_3$): δ 0.10 (s, 9H, $SiCH_3$), 2.03-2.40 (m, 2H, $SiCHCH_2$), 3.10-4.20 (m, 7H, NCH_2, CH_2OCH_2, SiCH), 6.39-7.20 ppm (m, 5H, aromatic protons). IId—HCl, m.p. 119-121° (recrystallized from ethanol/ether). (Found: C, 58.76; H, 8.39; N, 5.10. $C_{14}H_{23}NOSi \cdot HCl$ calcd.: C, 58.82; H, 8.46; N, 4.90%.)

The reaction of (piperidinomethyl)trimethylsilane (Ie) with benzyne. Ie (5.13 g, 30 mmol), bromobenzene (5.18 g, 33 mmol), and sodium amide (1.40 g, 36 mmol) were allowed to react in 40 ml of THF using the above procedure. The fraction of b.p. 95-105°/1 mm of the ethereal extract was converted to the hydrochloride and recrystallized from ethanol/ether to give 2.06 g (24%) of 1-(α-trimethylsilylbenzyl)piperidine hydrochloride (V—HCl): m.p. 221-222° (decomp.). (Found: C, 63.40; H, 9.23; N, 4.83. $C_{15}H_{25}NSi \cdot HCl$ calcd.: C, 63.46; H, 9.23; N, 4.93%.) NMR (free base in $CDCl_3$): δ 0.04 (s, 9H, $SiCH_3$), 1.36-1.86 [m, 6H, $(CH_2)_3$], 2.36-2.73 (m, 4H, NCH_2), 2.91 (s, 1H, SiCH), 7.23 ppm (s, 5H, aromatic protons.)

After concentration of the mother liquor, the residue was made basic and extracted with ether. Alumina column chromatography (n-hexane) of the extract

gave 1.40 g (19%) of *N*-(4-pentenyl)-*N*-trimethylsilylmethylaniline (IIIe). IR (film): ν 1640 cm^{-1} (C=C). NMR ($CDCl_3$): δ 0.19 (s, 9H, $SiCH_3$), 1.60-2.45 (m, 4H, CH_2CH_2), 2.99 (s, 2H, $SiCH_2$), 3.46 (t, 2H, NCH_2), 5.05-6.44 (m, 2H, $=CH_2$), 5.70-6.44 (m, 1H, =CH), 6.52-7.42 ppm (m, 5H, aromatic protons). (Found: C, 72.46; H, 10.05; N, 5.46. $C_{15}H_{25}NSi$ calcd.: C, 72.81; H, 10.18; N, 5.66%.)

4-Phenylperhydro-1,4-oxazepine (IV) (*a*) A mixture of IId (0.29 g, 1 mmol), 47% hydrobromic acid (6 ml), and acetic acid (4 ml) was heated at 115° for 6 h and then concentrated under reduced pressure. The residue was neutralized with potassium hydroxide and extracted with ether. After removal of the ether, the residue was chromatographed on a silica gel column (chloroform) to give 0.16 g (78%) of IV. NMR ($CDCl_3$): δ 2.10 (quintet, 2H, C—CH_2—C), 3.50-4.01 (m, 8H, NCH_2, OCH_2), 6.50-7.42 ppm (m, 5H, aromatic protons). IV—HCl, m.p. 170-173° (decomp. recrystallized from i-propanol/ether). (Found: C, 61.65; H, 7.49; N, 6.58. $C_{11}H_{15}NO \cdot HCl$ calcd.: C, 61.82; H, 7.55; N, 6.55%.)

(*b*) A suspension of aniline (0.77 g, 8 mmol), 3-(2-chloroethoxy)propyl chloride (1.30 g, 8 mmol), sodium bicarbonate (1.68 g, 20 mmol) in DMF (20 ml) was heated under reflux for 8 h, then concentrated under reduced pressure. The residue was extracted with ether. After removal of the ether, the residue was chromatographed on a silica gel column to give 0.24 g (16%) of IV, which was identical to the sample described in (*a*).

1-(α-Trimethylsilylbenzyl)piperidine (V). A mixture of *N*-benzylpiperidine (1.75 g, 10 mmol), phenylsodium (13 mmol) [7], benzene (39 ml), and n-octane (10 ml) was refluxed for 2 h and cooled to 30°. After the addition of trimethylchlorosilane (1.80 g, 16 mmol), the mixture was stirred for 30 min then heated at 55° for 1.5 h. Water was added to the chilled reaction mixture and the organic layer was separated, dried, and concentrated. Silica gel column chromatography (chloroform) of the residue gave 0.15 g (6%) of V, which was identified by spectroscopic comparison with the compound obtained from the benzyne reaction of Ie.

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