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SYNTHESIS AND REACTIONS OF 1,1-DIMETHYL-3-SUBSTITUTED-1,2,3,4-TETRAHYDROBENZO[*d*]-1,3-AZASILINES AND THEIR METHIODIDES

YOSHIRO SATO, YUJI FUKAMI and HIDEAKI SHIRAI

Faculty of Pharmaceutical Sciences, Nagoya City University, Tanabe-dori, Mizuho-ku, Nagoya 467 (Japan)

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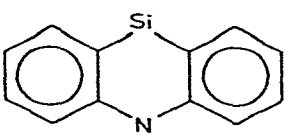
Summary

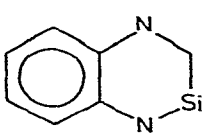
1,1-Dimethyl-3-substituted-1,2,3,4-tetrahydrobenzo[*d*]-1,3-azasilines (III) and 1,1,3-trimethyl-3-substituted-1,2,3,4-tetrahydrobenzo[*d*]-1,3-azoniasiline iodides (IV) were synthesized by reactions of (2-bromomethylphenyl)chloromethyldimethylsilane (II) with primary amines or secondary amines. In liquid ammonia II led to 3,3'-spirobi(1,1-dimethyl-1,2,3,4-tetrahydrobenzo[*d*]-1,3-azoniasiline) iodide (VI) as a major product. Lithium aluminum hydride reduction of IV gave predominantly *N*-methyl-*N*-substituted-2-trimethylsilylbenzylamines (VIII).

Introduction

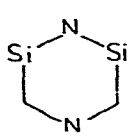
Several six-membered ring systems containing nitrogen and silicon as heteroatoms have been reported as follows:



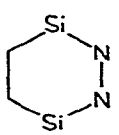
Gilman et al. [1a]



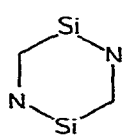
Wieber et al. [1b]



Niederprüm et al. [1c]



Pitt et al. [1d]



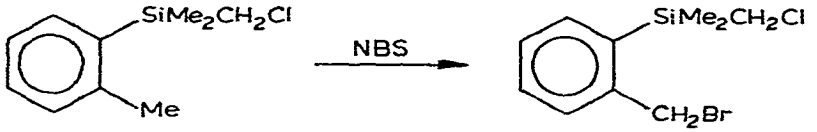
Mironov et al. [1e]

Mironov et al. [1f]

In the present paper a new ring system, 1,2,3,4-tetrahydrobenzo[*d*]-1,3-azasiline, is reported. Reduction of the related 1,2,3,4-tetrahydrobenzo[*d*]-1,3-azoniasiline iodide by lithium aluminum hydride is described.

Results and discussion

A starting compound, (2-bromomethylphenyl)chloromethyldimethylsilane (II), was prepared by bromination of chloromethyldimethyl(2-methylphenyl)-silane (I) in a 62% yield.



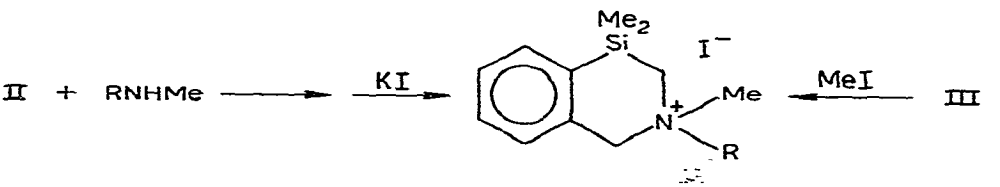
(I) (II)

Three, 1,1-dimethyl-3-substituted-1,2,3,4-tetrahydrobenzo[*d*]-1,3-azasilines (IIIa, R = Me; IIIb, R = Ph; IIIc, R = $PhCH_2$) were synthesized in 73—76% yields from reactions of II with the corresponding primary amines (methylamine, aniline and benzylamine, respectively).

(IIIa) R = Me 74%
(IIIb) R = Ph 73%
(IIIc) R = $PhCH_2$ 76%

Their structures were confirmed by ^1H NMR spectral and elemental analyses.

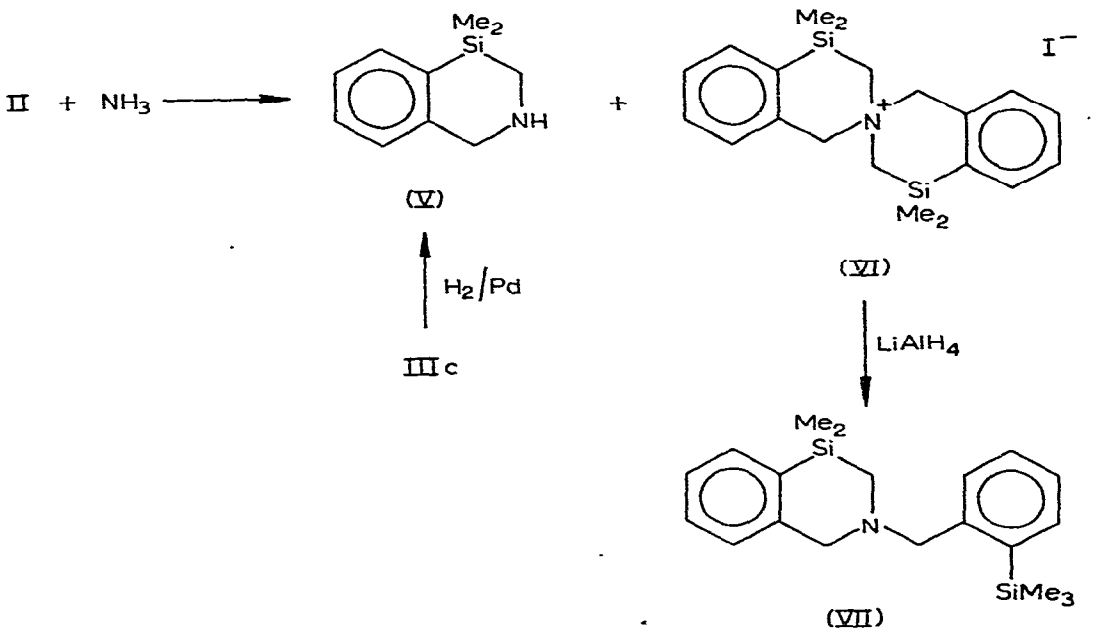
The reaction of II with dimethylamine, *N*-methylaniline or *N*-methylbenzylamine gave a mixture of 1,1,3-trimethyl-3-substituted-1,2,3,4-tetrahydrobenzo[*d*]-1,3-azoniasiline chloride and bromide, respectively. These were converted to the corresponding iodides (IVa, R = Me; IVb, R = Ph; IVc, R = $PhCH_2$) by treatment with potassium iodide. The methiodides thus prepared also were obtained by methylation of IIIa, IIIb and IIIc with methyl iodide.



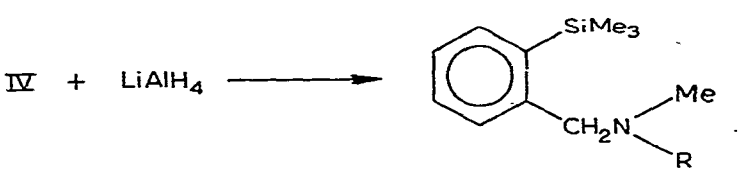
(IVa) R = Me 28%
(IVb) R = Ph 68%
(IVc) R = $PhCH_2$ 41%

In liquid ammonia II gave low yield of 1,1-dimethyl-1,2,3,4-tetrahydrobenzo[*d*]-1,3-azasiline (V) accompanied by a large quantity of a solid product. Amine V also was obtained from IIIc by catalytic reduction. Treatment of the

solid product with potassium iodide gave a crystalline solid whose elemental and NMR spectral analyses suggested that it was 3,3'-spirobi(1,1-dimethyl-1,2,3,4-tetrahydrobenzo[*d*]-1,3-azoniasiline) iodide (VI).



Lithium aluminum hydride reduction of VI yielded 1,1-dimethyl-3-(2-trimethylsilylbenzyl)-1,2,3,4-tetrahydrobenzo[*d*]-1,3-azasiline (VII) by reductive cleavage of the $SiCH_2—N^+$ bond. It is interesting that this bond was cleaved more readily by lithium aluminum hydride than a $ArCH_2—N^+$ bond. Treatment of several IV with an excess of lithium aluminum hydride gave the corresponding *N*-methyl-*N*-substituted-2-trimethylsilylbenzylamines (VIII) in high yields, thus establishing the general nature of such preferential $SiCH_2—N^+$ cleavage. Cope et al [2] have shown that in the reaction of tetrasubstituted ammonium salts with lithium aluminum hydride, methyl or benzyl groups are cleaved faster than other alkyl groups. Therefore, the order of the reductive cleavage of the $C—N^+$ bond is $SiCH_2 > CH_3 \approx PhCH_2 >$ alkyl.



(VIIIa) R = Me 79%
(VIIIb) R = Ph 80%
(VIIIc) R = $PhCH_2$ 84%

Experimental

NMR spectra were recorded using a JNM-MH-60 (JEOL) spectrometer with tetramethylsilane as internal standard. IR spectra were recorded on a IRA-2 (JASCO) spectrometer. All melting points were determined on a Yanagimoto Micro Melting Point Apparatus, and are uncorrected. Vapor-pressure molecular weight data were taken on a Perkin—Elmer 115 Molecular Weight Apparatus.

(2-Bromomethylphenyl)chloromethyldimethylsilane (II)

A solution of I [3] (51.4 g, 258 mmole), *N*-bromosuccinimide (46.0 g, 258 mmole) and benzoyl peroxide (783 mg) in 1000 ml of carbon tetrachloride was heated at reflux for 2.5 h. The mixture was filtered and the filtrate distilled, giving 46.9 g (62.0%) of II; b.p. 124-126° (3 mm), NMR($CDCl_3$): δ 0.59 (*s*, 6H, $SiCH_3$), 3.22 (*s*, 2H, CH_2Cl), 4.72 (*s*, 2H, CH_2Br), and 7.2-7.8 ppm (*m*, 4H, aromatic protons). (Found: C, 43.41; H, 5.38. $C_{10}H_{14}BrClSi$ calcd.: C, 43.26; H, 5.08%.)

1,1,3-Trimethyl-1,2,3,4-tetrahydrobenzo[d]-1,3-azasiline (IIIa)

To a solution of methylamine in benzene (10%, 60 ml) was added II (7.83 g, 28.2 mmole). The mixture was stirred at room temperature for 2 h, then at 50° for 2 h, and then was extracted with 5% hydrochloric acid. The aqueous extract was made basic with sodium hydroxide and the product was recovered by extraction with benzene. The benzene extract was dried and distilled to give 3.99 g (73.9%) of IIIa; b.p. 94-95° (6 mm), NMR ($CDCl_3$): δ 0.28 (*s*, 6H, $SiCH_3$), 2.18 (*s*, 2H, $SiCH_2N$), 2.53 (*s*, 3H, NCH_3), 3.55 (*s*, 2H, $ArCH_2N$), and 6.8-7.5 ppm (*m*, 4H, aromatic protons). (Found: mol. wt., 196.2. $C_{11}H_{17}NSi$ calcd.: mol. wt., 191.3.) IIIa hydrochloride, m.p. 238-239°. (Found: C, 58.02; H, 7.69; N, 6.25. $C_{11}H_{18}ClNSi$ calcd.: C, 58.00; H, 7.96; N, 6.15%.)

1,1-Dimethyl-3-phenyl-1,2,3,4-tetrahydrobenzo[d]-1,3-azasiline (IIIb)

A solution of II (10.01 g, 36.1 mmole) and aniline (13.45 g, 144.4 mmole) in 50 ml of ethanol was heated at reflux for 2 h. After the evaporation of the solvent, the residue was suspended in benzene and extracted with 5% hydrochloric acid. The aqueous extract was treated in the same manner as described above to give 6.67 g (73.0%) of IIIb; b.p. 121-126° (0.2 mm), m.p. 51-53°, NMR ($CDCl_3$): δ 0.29 (*s*, 6H, $SiCH_3$), 3.20 (*s*, 2H, $SiCH_2N$), 4.51 (*s*, 2H, $ArCH_2N$), and 6.7-7.7 ppm (*m*, 9H, aromatic protons). (Found: C, 75.73; H, 7.63; N, 5.49; mol. wt., 243.8. $C_{15}H_{19}NSi$ calcd.: C, 75.83; H, 7.56; N, 5.53%; mol. wt., 253.4.)

1,1-Dimethyl-3-benzyl-1,2,3,4-tetrahydrobenzo[d]-1,3-azasiline (IIIc)

A solution of II (6.01 g, 21.7 mmole) and benzylamine (11.6 g, 108 mmole) in 60 ml of benzene was stirred at 70° for 2 h and then extracted with 5% hydrochloric acid. The aqueous extract was treated in the same manner as described for IIIa to give 4.42 g (76.2%) of IIIc; b.p. 119-123° (0.11 mm), NMR ($CDCl_3$): δ 0.24 (*s*, 6H, $SiCH_3$), 2.20 (*s*, 2H, $SiCH_2N$), 3.80 (*s*, 2H, $ArCH_2N$), 3.83 (*s*, 2H, $ArCH_2N$), and 7.0-7.8 ppm (*m*, 9H, aromatic protons). (Found: C, 76.55; H, 7.67; N, 5.30; mol. wt., 286.3. $C_{17}H_{21}NSi$ calcd.: C, 76.35; H, 7.91; N, 5.24%; mol. wt., 267.5.)

1,1,3,3-Tetramethyl-1,2,3,4-tetrahydrobenzo[d]-1,3-azoniasiline (IVa)

To a solution of dimethylamine in benzene (7%, 60 ml) was added II (5.08 g, 19.3 mmole). The mixture was allowed to stand at room temperature for 24 h. After the addition of a saturated sodium carbonate solution, the aqueous layer and precipitated crystals were separated and extracted with chloroform. The extract was dried and evaporated and the residue dissolved in a solution of potassium iodide (5 g) in aqueous ethanol. After the evaporation of the solvent under reduced pressure, the product was extracted with chloroform and then recrystallized from ethanol to give 1.68 g (27.5%) of IVa; m.p. 232-234°, NMR ($CDCl_3$—DMSO-d_6): δ 0.49 (*s*, 6H, $SiCH_3$), 3.48 (*s*, 6H, NCH_3), 3.64 (*s*, 2H, $SiCH_2N$), 4.96 (*s*, 2H, $ArCH_2N$), and 7.2-7.7 ppm (*m*, 4H, aromatic protons). (Found: C, 43.23; H, 6.00; N, 4.09. $C_{12}H_{20}INSi$ calcd.: C, 43.24; H, 6.05; N, 4.20%.)

The reaction of IIIa (2.18 g, 11.4 mmole) with methyl iodide (2.0 g, 14.1 mmole) in 18 ml of ethanol afforded 3.34 g (88.2%) of IVa. That the products from both of these reactions were identical was confirmed by comparison of their m.p.'s and IR spectra.

1,1,3-Trimethyl-3-phenyl-1,2,3,4-tetrahydrobenzo[d]-1,3-azoniasiline iodide (IVb)

A solution of II (15.00 g, 54.0 mmole) and *N*-methylaniline (29.0 g, 271 mmole) in 40 ml of benzene was stirred at room temperature for 24 h. Treatment of the reaction mixture in a similar manner as described for IVa gave 14.57 g (68.2%) of IVb; m.p. 185-187° (decomp.), NMR ($CDCl_3$—DMSO-d_6): δ 0.18 (*s*, 3H, $SiCH_3$), 0.48 (*s*, 3H, $SiCH_3$), 4.28 and 4.55 (*AB*-quartet, *J* 15 Hz, 2H, $SiCH_2N$), 5.72 (*s*, 2H, $ArCH_2N$), and 7.0-7.9 ppm (*m*, 9H, aromatic protons). (Found: C, 51.63; H, 5.64; N, 3.46. $C_{17}H_{22}INSi$ calcd.: C, 51.64; H, 5.62; N, 3.54%.)

The same methiodide was obtained from the reaction of IIIb with methyl iodide in a 27.8% yield.

1,1,3-Trimethyl-3-benzyl-1,2,3,4-tetrahydrobenzo[d]-1,3-azoniasiline iodide (IVc)

To a boiling suspension of *N*-methylbenzylamine (6.17 g, 50.9 mmole) and potassium carbonate (2.0 g) in 10 ml of benzene was added dropwise a solution of II (4.71 g, 17.0 mmole) in 10 ml of benzene for 30 min. After additional stirring for 1.5 h, the reaction mixture was treated in a similar manner as described for IVa to give 2.82 g (40.5%) of IVc; m.p. 195-197°, NMR ($CDCl_3$): δ 0.46 (*s*, 3H, $SiCH_3$), 0.49 (*s*, 3H, $SiCH_3$), 3.30 (*s*, 3H, NCH_3), 3.56 and 3.98 (*AB*-quartet, *J* 15 Hz, 2H, $SiCH_2N$), 5.08 and 5.24 (*AB*-quartet, *J* 15 Hz, 2H, $ArCH_2N$), 5.39 (*s*, 2H, $PhCH_2$), and 7.2-8.0 ppm (*m*, 9H, aromatic protons). (Found: C, 52.63; H, 5.74; N, 3.29. $C_{18}H_{24}INSi$ calcd.: C, 52.80; H, 5.92; N, 3.42%.)

The same methiodide was obtained from the reaction of IIIc with methyl iodide in a 88.6% yield.

Reaction of II with ammonia

A mixture of II (5.93 g, 21.3 mmole) and liquid ammonia (about 25 g) was allowed to stand in an autoclave at room temperature for 24 h. The excess ammonia was vented and the residue extracted with benzene and then with chloro-

form. The benzene extract was evaporated and the residue was distilled, giving 221 mg (5.8%) of V; b.p. 101-103° (3 mm), NMR (CCl_4): δ 0.31 (*s*, 6H, $SiCH_3$), 2.32 (s, 1H, NH), 2.48 (*s*, 2H, $SiCH_2N$), 3.90 (*s*, 2H, $ArCH_2N$), and 6.9-7.5 ppm (aromatic protons). (Found: C, 67.59; H, 8.81; N, 7.76; mol. wt., 184.6. $C_{10}H_{15}NSi$ calcd.: C, 67.74; H, 8.53; N, 7.90%; mol. wt., 177.3.)

The chloroform extract was evaporated and the residue dissolved in hot aqueous ethanol and treated with a saturated KI (4 g) solution. The resulting crystals were recrystallized from ethanol to give 3.26 g (65.7%) of VI; m.p. 294-295° (decomp.), NMR ($CDCl_3$—DMSO-d_6): δ 0.37 (*s*, 6H, $SiCH_3$), 0.43 (*s*, 6H, $SiCH_3$), 3.26 and 3.46 (*AB*-quartet, *J* 15 Hz, 4H, $SiCH_2N$), 4.93 (*s*, 4H, $ArCH_2N$), and 6.9-7.7 ppm (*m*, 8H, aromatic protons). (Found: C, 51.54; H, 6.06; N, 3.03. $C_{20}H_{28}INSi$ calcd.: C, 51.60; H, 6.06; N, 3.01%.)

1,1-Dimethyl-1,2,3,4-tetrahydrobenzo[d]-1,3-azasiline (V)

A mixture of IIIc hydrochloride (m.p. 226-228°, 1.00 g, 3.3 mmole), 10% palladium-charcoal (200 mg) and ethanol (15 ml) was shaken with hydrogen at atmospheric pressure for 2 days. The mixture was filtered and concentrated. Recrystallization of the residue from ethanol—ether gave 497 mg (70.6%) of V hydrochloride; m.p. 209-211°. Its free base was identical to the reaction product of II with ammonia.

1,1-Dimethyl-3-(2-trimethylsilylbenzyl)-1,2,3,4-tetrahydrobenzo[d]-1,3-azasiline (VII)

A mixture of VI (4.03 g, 8.7 mmole), lithium aluminum hydride (1.63 g, 43.0 mmole) and 200 ml of THF was heated at reflux for 2 h and then hydrolyzed with a saturated ammonium chloride solution. The THF layer was separated and the aqueous layer was extracted with ether. The combined organic layer was dried and distilled, giving 2.64 g (89.7%) of VII; b.p. 123-137° (0.2 mm), NMR ($CDCl_3$): δ 0.25 (*s*, 6H, $SiCH_3$), 0.30 (*s*, 9H, $SiCH_3$), 2.20 (*s*, 2H, $SiCH_2N$), 3.64 (*s*, 2H, $ArCH_2N$), 3.82 (*s*, 2H, $ArCH_2N$), and 6.8-7.5 ppm (*m*, 8H, aromatic protons). (Found: C, 70.90; H, 8.44; N, 4.10; mol. wt., 343.9. $C_{20}H_{29}NSi_2$ calcd.: C, 70.73; H, 8.61; N, 4.12%; mol. wt., 339.6.)

N,N-Dimethyl-2-trimethylsilylbenzylamine (VIIIa)

In a similar manner as described above, the reaction of IVa (3.00 g, 9.0 mmole) with lithium aluminum hydride (1.4 g, 36.9 mmole) in 150 ml of THF gave 1.47 g (78.8%) of VIIIa; b.p. 77-83° (5mm), NMR ($CDCl_3$): δ 0.33 (*s*, 9H, $SiCH_3$), 2.32 (*s*, 6H, NCH_3), 3.69 (*s*, 2H, $ArCH_2N$), and 7.3-7.9 ppm (*m*, 4H, aromatic protons). (Found: mol. wt., 207.5. $C_{12}H_{21}NSi$ calcd.: mol. wt., 207.4.) VIIIa picrate, m.p. 198-200°. (Found: C, 49.63; H, 5.41; N, 12.95. $C_{18}H_{24}N_4O_7Si$ calcd.: C, 49.53; H, 5.54; N, 12.84%.)

N-Methyl-N-phenyl-2-trimethylsilylbenzylamine (VIIIb)

In a similar manner as described for VII, the reaction of IVb (3.02 g, 7.6 mmole) with lithium aluminum hydride (1.1 g, 29.0 mmole) in 150 ml of THF gave 1.63 g (79.6%) of VIIIb; b.p. 104-114° (0.12 mm), NMR ($CDCl_3$): δ 0.39 (*s*, 9H, $SiCH_3$), 3.11 (*s*, 3H, NCH_3), 4.83 ($ArCH_2N$), and 6.8-7.9 ppm (*m*, 9H, aromatic protons). (Found: C, 75.88; H, 8.77; N, 5.47; mol. wt., 264.0. $C_{17}H_{23}NSi$ calcd.: C, 75.76; H, 8.62; N, 5.20%; mol. wt., 269.5.)

N-Benzyl-N-methyl-2-trimethylsilylbenzylamine (VIIIc)

In a similar manner as described for VII, the reaction of IVc (3.00 g, 7.3 mmole) with lithium aluminum hydride (1.3 g, 34.3 mmole) in 150 ml of THF gave 1.74 g (83.9%) of VIIIc; b.p. 127-131° (0.6 mm), NMR ($CDCl_3$): δ 0.37 (*s*, 9H, $SiCH_3$), 2.21 (*s*, 3H, NCH_3), 3.64 (*s*, 2H, $ArCH_2N$), 3.77 (*s*, 2H, $ArCH_2N$), and 7.0-7.7 ppm (*m*, 9H, aromatic protons). (Found: mol. wt., 286.5. $C_{18}H_{25}NSi$ calcd.: mol. wt., 283.5.) VIIIc hydrochloride, m.p. 169-171°. (Found: C, 67.35; H, 8.01; N, 4.32. $C_{18}H_{26}ClNSi$ calcd.: C, 67.57; H, 8.19; N, 4.38%.)

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