Journal of Organometallic Chemistry, 118 (1976) 1—6

SYNTHESIS AND REACTIONS OF 1-SUBSTITUTED 3,3-DIMETHYLBENZO-[*d*]-1,3-AZASILOLINES

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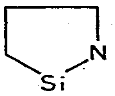
(Received March 22nd, 1976)

Summary

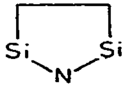
1-Substituted 3,3-dimethylbenzo[*d*]-1,3-azasilolines (III) were synthesized by intramolecular cyclization of the corresponding (3-chlorophenyl)(*N*-substituted aminomethyl)dimethylsilanes (II) by the use of phenyllithium. Reaction of III with benzyne generated from *o*-fluorobromobenzene and n-butyllithium gave 1-phenyl-2-substituted-3,3-dimethylbenzo[*d*]-1,3-azasilolines (VIII).

Introduction

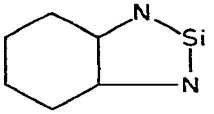
Several five-membered ring systems containing nitrogen and silicon as heteroatoms have been reported as follows:



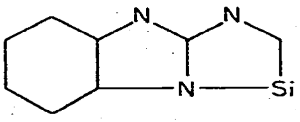
Nametkin et al. [1a]



Andrianov et al. [1b]

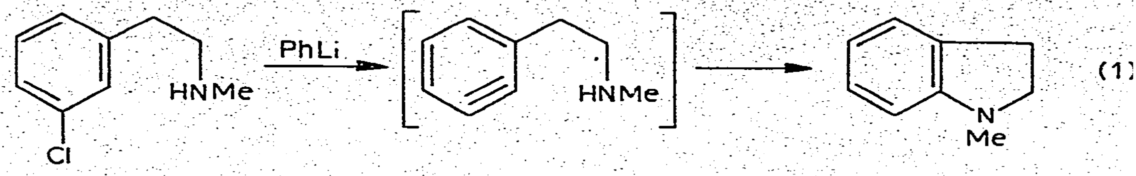


Kummer et al. [1c]



Alper et al. [1d]

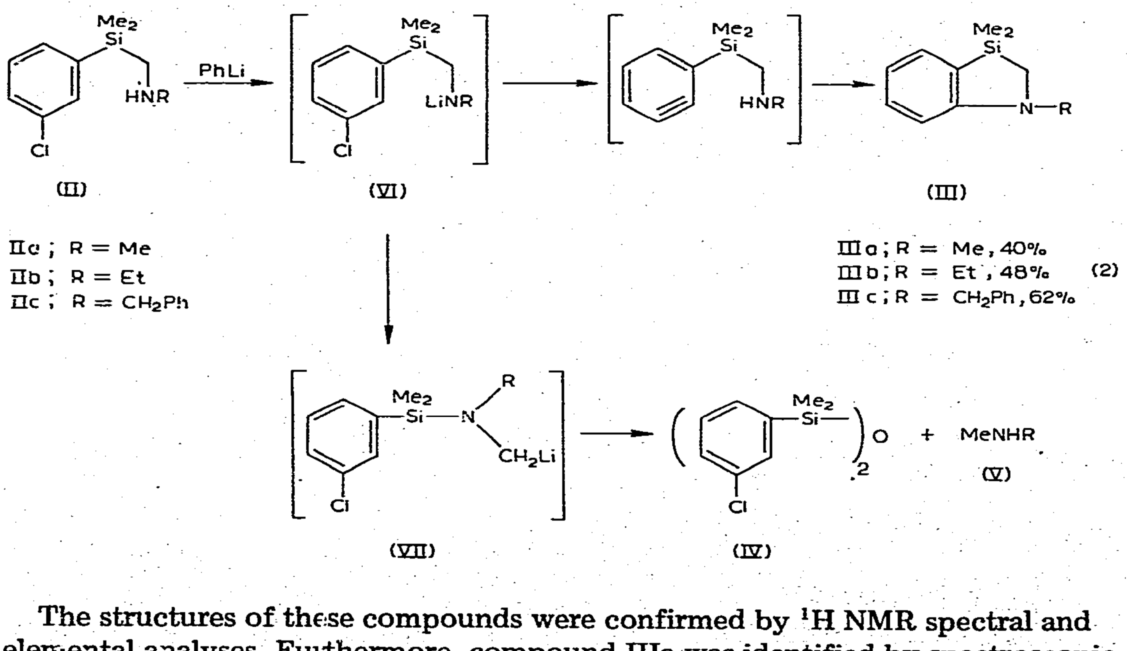
The intramolecular addition of nucleophiles to benzyne intermediates has provided a useful method for the synthesis of heterocyclic systems, e.g., *N*-methylindoline was prepared by the reaction of *N*-methyl-2-(3-chlorophenyl)-ethylamine with phenyllithium [2] (eq. 1).



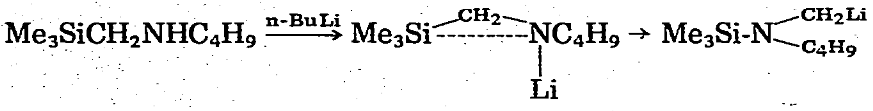
In the present paper, the synthesis of 1-substituted 3,3-dimethylbenzo[*d*]-1,3-azasiloline (III) using the above method is reported. As an extention of the benzyne reaction of aminoalkylsilanes [3], the reaction of III with benzyne also is described.

Results and discussion

When (3-chlorophenyl)(*N*-substituted aminomethyl)dimethylsilanes (IIa, R = Me; IIb, R = Et and IIc, R = CH_2Ph) were allowed to react with phenyllithium in boiling ether, the corresponding cyclization products, 1-substituted 3,3-dimethylbenzo [*d*]-1,3-azasilolines (IIIa, R = Me, IIIb, R = Et and IIIc, R = CH_2Ph), were obtained in a 40—60% yield together with small amounts of 1,3-bis(3-chlorophenyl)tetramethyldisiloxane (IV) and a secondary amine (V) (eq. 2).

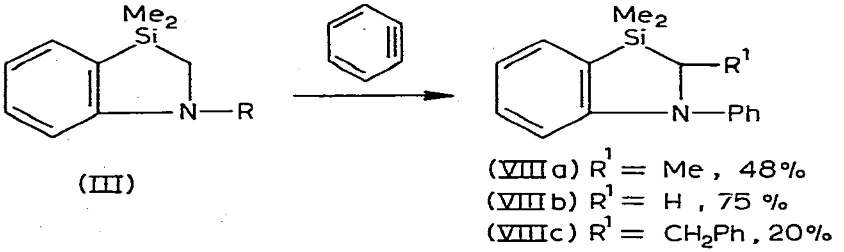


The structures of these compounds were confirmed by ^{1}H NMR spectral and elemental analyses. Furthermore, compound IIIa was identified by spectroscopic comparison with one of the reaction products obtained by reaction of *N,N*-dimetl yl-2-dimethylphenylsilylethylamine with benzyne in the presence of excess n-butyllithium [3c]. The formation of IV and V is presumably a result of the hydrolysis of silylamine (VII) produced by competitive migration of the silyl group from carbon to nitrogen in the intermediate VI. Nametkin et al. [1a] have shown that n-butylaminomethyltrimethylsilane is rearranged to trimethylsilylmethylbutylamine via an *N*-metallated intermediate in the presence of n-butyllithium (eq. 3)



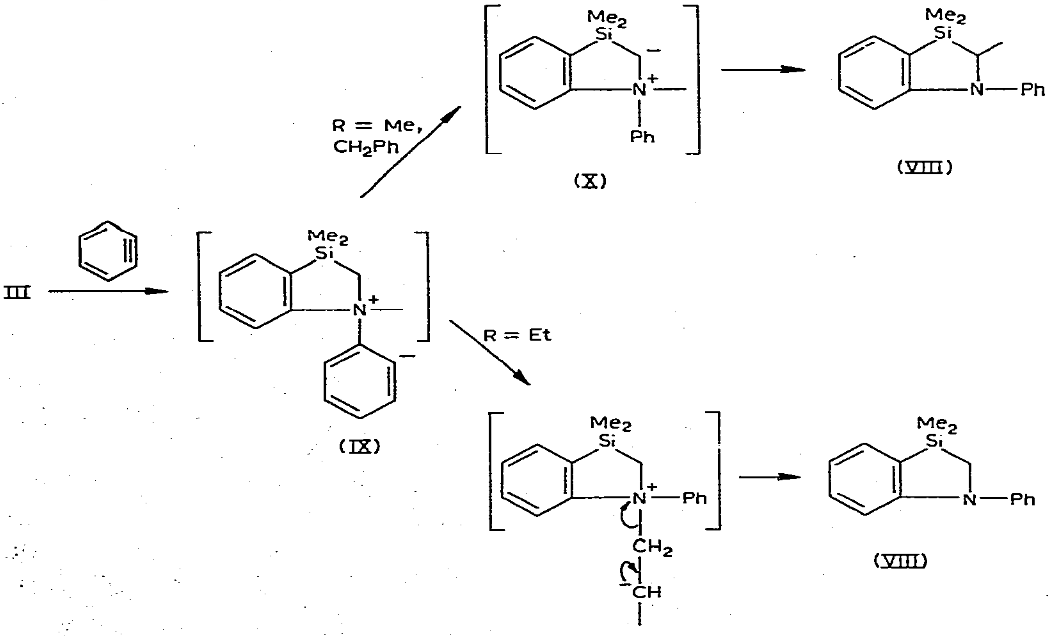
$$\mathrm{Me_3SiCH_2NHC_4H_9} \xrightarrow{\text{n-BuLi}} \mathrm{Me_3Si\overset{CH_2}{\cdots\cdots}\underset{\displaystyle Li}{N}C_4H_9} \rightarrow \mathrm{Me_3Si\text{-}N}\begin{smallmatrix}\mathrm{CH_2Li}\\ \mathrm{C_4H_9}\end{smallmatrix} \qquad (3)$$

The reaction of 1-methyl(or benzyl)-3,3-dimethylbenzo[*d*]-1,3-azasiloline (IIIa or IIIc) with benzyne, generated from *o*-fluorobromobenzene and n-butyllithium, gave a single basic product. The ^{1}H NMR spectral and elemental analyses of these compounds comfirmed the structures as 1-phenyl-2-methyl(or benzyl)-3,3-dimethylbenzo[*d*]-1,3-azasiloline (VIIIa or VIIIc) (Stevens rearrangement product). However, the reaction of 1-ethyl-3,3-dimethylbenzo[*d*]-1,3-azasiloline (IIIb) with benzyne under the same reaction conditions as those used for IIIa gave a Hofmann elimination product, 1-phenyl-3,3-dimethylbenzo[*d*]-1,3-azasiloline (VIIIb) and no Stevens rearrangement product (eq. 4).



(4)

The reaction presumably takes place by two discrete steps. First, nucleophilic attack of amine III to benzyne gives a betaine intermediate IX. Second, an intramolecular proton transfer in the betaine intermediate leads to an ylide intermediate X which subsequently is rearranged to VIII. When a *N*-substituent of III has a *β*-hydrogen, the Hofmann elimination reaction occurs predominantly and VIII is produced (eq. 5).



(5)

Experimental

NMR spectra were recorded using a JNM-MH-100 (JEOL) spectrometer with tetramethylsilane as internal standard. GLC analyses were performed on a JGC-1100 (JEOL) chromatograph. Fractional distillation was carried out using a GKR-50 (Büchi) Kugelrohr distillation apparatus. Vapor-pressure molecular weight data were taken on a Perkin—Elmer 115 molecular weight apparatus. All boiling points and melting points are uncorrected. n-Butyllithium, 15% in hexane, was obtained from Nakarai Chemicals Ltd., Kyoto. Ether was dried by distillation from lithium aluminum hydride prior to use.

(3-Chlorophenyl)chloromethyldimethylsilane (I)

A solution of chloromethyldimethylchlorosilane (20 g, 130 mmol) in ether (50 ml) was added to a solution of 3-chlorophenylmagnesium bromide [4] prepared from 3-bromochlorobenzene (25 g, 130.5 mmol) and magnesium turnings (3.17 g, 130.5 mg-atom) in ether (150 ml). After 11 h of stirring at reflux, the reaction mixture was hydrolyzed with saturated aqueous NH_4Cl, and extracted with ether. The ethereal extract was dried, concentrated, and distilled to give 15.2 g (53%) of I, b.p. 85—89°C/ 5 mmHg. NMR (CCl_4): δ 0.40 (s, 6H, $SiCH_3$), 2.83 (s, 2H, $SiCH_2$), 7.20—7.44 ppm (m, 4H, aromatic protons). (Found: C, 49.30; H, 5.37. $C_9H_{12}Cl_2Si$ calcd.: C, 49.32; H, 5.52%.)

(3-Chlorophenyl)(N-substituted aminomethyl)dimethylsilane (IIa—IIc)

A mixture of primary amine (methylamine, ethylamine, or benzylamine) (200 mmol) and I (8.76 g, 40 mmol) was heated at 130—140° C for 3—6 h. After the addition of 10% NaOH (50 ml), the reaction mixture was extracted with ether. The ethereal extract was dried, concentrated, and distilled to give corresponding IIa (64%), IIb (71%), and IIc (76%). These compounds were charactarized as follows.

(3-Chlorophenyl)methylaminomethyldimethylsilane (IIa); b.p. 81—83° C/ 5 mmHg. (Found: C, 55.96; H, 7.38; N, 6.44. $C_{10}H_{16}ClNSi$ calcd.: C, 56.18; H, 7.57; N, 6.55%.)

(3-Chlorophenyl)ethylaminomethyldimethylsilane (IIb); b.p. 82—83° C/ 3 mmHg. (Found: C, 57.82; H, 8.03; N, 5.82. $C_{11}H_{18}ClNSi$ calcd.: C, 58.00; H, 7.96; N, 6.15%.)

(3-Chlorophenyl)benzylaminomethyldimethylsilane (IIc): b.p. 127—130°C/ 0.1 mmHg (Found: C, 66.45; H, 7.20; N, 4.92. $C_{16}H_{20}ClNSi$ calcd.: C, 66.29; H, 6.95; N, 4.83%.)

Reaction of IIa with phenyllithium

A solution of phenyllithium [5] prepared from bromobenzene (5.20 g, 33 mmol) and lithium clippings (0.60 g, 86 mg-atom) in ether (20 ml) was added to a boiling solution of IIa (6.40 g, 30 mmol) in ether (130 ml). After 2 h of stirring at reflux, the reaction mixture was hydrolyzed with saturated NH_4Cl, and extracted with ether. The ethereal extract was dried and concentrated. Distillation of the residue gave 2.10 g (40%) of 1,3,3-trimethylbenzo[*d*]-1,3-azasiloline (IIIa), b.p. 90—92° C/ 4 mmHg. NMR (CCl_4): δ 0.31 (s, 6H, $SiCH_3$), 2.56 (s, 2H, $SiCH_2$), 2.84 (s, 3H, NCH_3), 6.28—7.20 ppm (m, 4H, aromatic protons). (Found: C, 67.45; H, 8.40; N, 7.85. $C_{10}H_{15}NSi$ calcd.: C, 67.74; H, 8.53; N, 7.90%.)

The higher boiling fraction (b.p. 105—120°C/ 4 mmHg) was chromatographed on silica gel (n-hexane) to give 0.26 g (5%) of 1,3-bis(3-chlorophenyl)tetramethyldisiloxane (IV). b.p. 125—128°C/ 4 mmHg. NMR (CCl_4): δ 0.32 (s, 12H, $SiCH_3$), 7.20—7.43 ppm (m, 8H, aromatic protons). (Found: C, 54.46; H, 5.47; mol.wt., 348.2. $C_{16}H_{20}Cl_2OSi_2$ calcd.: C, 54.07; H, 5.67%; mol. wt., 355.4.)

Reaction of IIb with phenyllithium

In a similar manner as described for IIa, IIb (6.84 g, 30 mmol) and phenyllithium (prepared from bromobenzene (5.20 g, 33 mmol) and lithium clippings (0.60 g, 86 mg-atom)) were allowed to react in ether (150 ml), and then the reaction mixture was treated. Distillation of the ethereal extract gave 2.75 g (48%) of 1-ethyl-3,3-dimethylbenzo[*d*]-1,3-azasiloline (IIIb), b.p. 94—96°C/ 4 mmHg. NMR (CCl_4): δ 0.32 (s, 6H, $SiCH_3$), 1.12 (t, 3H, $C—CH_3$), 2.56 (s, 2H, $SiCH_2$), 3.28 (q, 2H, $N—CH_2—C$), 6.32—7.24 ppm (m, 4H, aromatic protons). (Found: C, 68.79; H, 8.85; N, 7.21. $C_{11}H_{17}NSi$ calcd.: C, 69.05; H, 8.96; N, 7.32%.)

The higher boiling fraction (b.p. 100—115°C/ 4 mmHg) was chromatographed on a silica gel column (n-hexane) to give 0.22 g (4%) of IV.

Reaction of IIc with phenyllithium

In a similar manner as described for IIa, IIc (8.70 g, 30 mmol), and phenyllithium (prepared from bromobenzene (5.20 g, 33 mmol) and lithium clippings (0.60 g, 86 mg-atom)) were allowed to react in ether (150 ml), and then the reaction mixture was worked up as above. Distillation of the ethereal extract gave 4.16 g (62%) of 1-benzyl-3,3-dimethylbenzo[*d*]-1,3-azasiloline (IIIc), b.p. 114—116°C/ 0.09 mmHg. NMR (CCl_4): δ 0.32 (s, 6H, $SiCH_3$), 2.60 (s, 2H, $SiCH_2$), 4.40 (s, 2H, $N—CH_2$), 6.19—7.28 ppm (m, 9H, aromatic protons). (Found: C, 75.92; H, 7.26; N, 5.24. $C_{16}H_{19}NSi$ calcd.: C, 75.83; H, 7.56; N, 5.53%.)

The lower boiling fraction (b.p. 30—60°C/ 0.03 mmHg) was chromatographed on an alumina column. The first eluate (benzene) gave 0.31 g (6%) of IV. The second eluate (10% ethanol/benzene) gave 0.28 g (8%) of *N*-methylbenzylamine (V) which was identified by spectroscopic comparison with an authentic sample.

Reaction of IIIa with benzyne

n-Butyllithium (6 ml, 9.4 mmol) was added to a solution of IIIa (1.40 g, 7.9 mmol) and *o*-fluorobromobenzene (1.65 g, 9.5 mmol) in ether (50 ml) at —40 to —45°C. The mixture was stirred at the same temperature for 2 h, and then at room temperature for 1 h. After the addition of saturated aqueous NH_4Cl, the reaction mixture was extracted with ether. The ethereal extract was dried, concentrated, and distilled to give 0.95 g (48%) of 1-phenyl-2,3,3-trimethylbenzo-[*d*]-1,3-azasiloline (VIIIa), b.p. 107—110°C/ 0.07 mmHg. NMR (CCl_4): δ 0.32 (s, 3H, $SiCH_3$), 0.36 (s, 3H, $SiCH_3$), 1.16 (d, J 8 Hz, 3H, $C—CH_3$), 3.20 (q, J 8 Hz, 1H, N—CH), 6.32—7.44 ppm (m, 9H, aromatic protons). (Found: C, 75.62; H, 7.61; N, 5.28. $C_{16}H_{19}NSi$ calcd.: C, 75.83; H, 7.56; N, 5.53%.)

Reaction of IIIb with benzyne

In a similar manner as described for IIIa, IIIb (1.91 g, 10 mmol), *o*-fluorobromobenzene (2.10 g, 12 mmol), and n-butyllithium (7.6 ml, 12 mmol) were allowed to react in ether (50 ml), and then the reaction mixture was worked up. Distillation of the ethereal extract gave 1.80 g (75%) of 1-phenyl-3,3-dimethylbenzo[*d*]-1,3-azasiloline (VIIIb), b.p. 97—100°C/ 0.15 mmHg, m.p. 48—49°C (recrystallized from ethanol). NMR (CCl_4): δ 0.36 (s, 6H, $SiCH_3$), 3.06 (s, 2H, $SiCH_2$), 6.40—7.33 ppm (m, 9H, aromatic protons). (Found: C, 75.41; H, 7.39; N, 5.77. $C_{15}H_{17}NSi$ calcd.: C, 75.26; H, 7.16; N, 5.85%.)

Reaction of IIIc with benzyne

In a similar manner as described for IIIa, IIIc (2.30 g, 9.1 mmol), *o*-fluorobromobenzene (1.91 g, 12 mmol), and n-butyllithium (7 ml, 11 mmol) were allowed to react in ether (50 ml), and then the reaction mixture was worked up as above. GLC analysis (10% AN-600)of the ethereal extract showed the presence of 1-phenyl-2-benzyl-3,3-dimethylbenzo[*d*]-1,3-azasiloline (VIIIc) (20%) and unchanged IIIc (38%).

A sample of VIIIc was isolated by distillation (b.p. 150—155°C/ 0.05 mmHg) followed by column chromatography on alumina (1% ether/n-hexane) and characterized as follows.

VIIIc: m.p. 79—80°C (recrystallized from methanol). NMR (CCl_4): δ 0.04 (s, 3H, $SiCH_3$), 0.20 (s, 3H, $SiCH_3$), 2.46 (d d, J 12.1, 13.6 Hz, 1H, A component of AMX, $CHCH_2Ph$). 3.11 (d d, J 5.3, 13.6 Hz, 1H, M component of AMX, $CHCH_2Ph$), 3.50 (d d, J 5.3, 12.1 Hz, 1H, X component of AMX, $CHCH_2Ph$), 6.28—7.48 ppm (m, 14H, aromatic protons). (Found: C, 79.94; H, 6.99; N, 4.19. $C_{22}H_{23}NSi$ calcd.: c, 80.19; H, 7.04; N, 4.25%.)

Acknowledgement

The authors are grateful to the Shin-Etu Chemical Industry Co., Ltd. for a generous gift of chlorosilanes.

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