BENZOPYRIDOSILAAZEPINES AND BENZOPYRIDOSILAAZEPINONES

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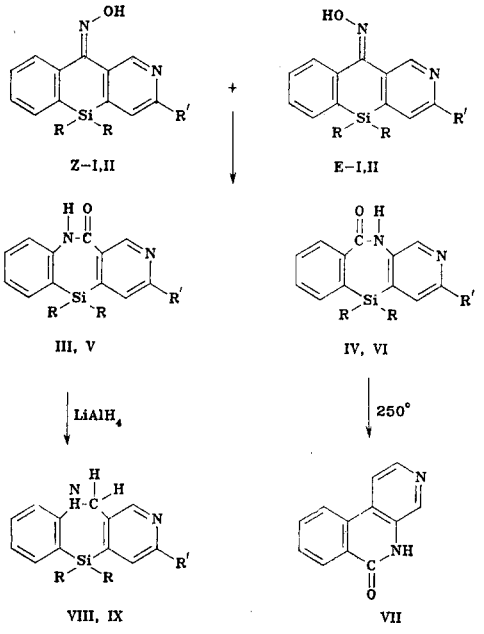
The Beckmann rearrangement of dihydrosilazatone oximes yields benzopyridosilaazepinones which are isomeric relative to the position of the amide fragment in the central ring. One of these isomers is converted upon thermolysis at 250°C to the lactam of o-(3-aminopyridyl-4)benzoic acid. The reduction of benzopyridosilaazepinones yields benzopyridosilaazepines.

The first reported benzopyridosilaazepine, namely, 3-methyl-5,5-diphenyl-5-sila-5H,10H,11H-benzo[b]pyrido[4,5-e]azepine, was described in our previous work [1]. In order to construct the benzopyridosilaazepine system, we used the Beckmann rearrangement of dihydrosilaazatrone oximes [1] which was carried out in absolute ether in the presence of phosphorus pentachloride. Since the oximes of 10,10-dimethyl- and 3-methyl-10,10-diphenyl-9,10-dihydro-10-sila-2-azatrones (I and II) exist as a mixture of Z- and E-isomers [1], the formation of benzopyridosilaazepinones with different orientation of the amide fragment between the benzene and pyridine rings should have been expected as a result of this rearrangement.



I, III, IV, VIII R=CH_3, R′=H; II, V, VI, XI R=C_6H_5, R′=CH_3

A thin-layer chromatographic study showed the formation of two compounds in the rearrangement. Oxime I yielded a mixture of 11-oxo-5,5-dimethyl-5-sila-5H,10,11H-benzo[b]pyrido[4,3-e]azepine (III) and 10-oxo-5,5-dimethyl-5-sila-5H,10H,11H-benzo[e]pyrido[3,4-b]azepine (IV), while oxime II yields a mixture of 11-oxo-3-methyl-5,5-diphenyl-5-sila-5H,10H,11H-benzo[b]-pyrido[4,5-e]azepine (V) and 10-oxo-3-methyl-5,5-diphenyl-5-sila-5H,10H,11H-benzo[e]pyrido[5,4-b]azepine (VI). Lactams III and IV were separated as individual compounds. Lactam III is unchanged upon heating to 250°C, while its isomer IV is converted quantitatively under these conditions with the loss of the dimethylsilyl group to the lactam of o-(3-aminopyridyl-4)-benzoic acid (VII). Individual isomers were isolated chromatographically from the mixture of III and VII.

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The structures of isomeric lactams III and IV were established using the position of 1-H and 9-H in their PMR spectra. The chemical shifts of these protons should be most sensitive to change in the orientation of the carbonyl group in the amide fragment. As a result of the effect of the carbonyl group, the 1-H signal in lactam II is found further downfield (δ 8.68 ppm) than in IV (δ 8.46 ppm), while the 9-H signal in III is further upfield (in the 7.48-6.95 ppm region, it coincides with the aromatic proton signals) than in isomer IV (δ 7.66 ppm). The 3-H proton is found at δ 8.46 and 8.23 ppm, respectively.

In order to prepare benzopyridosilaazepines, we reduced mixtures of isomeric lactams III and IV with lithium aluminum hydride in ether. A complex mixture of products is formed. Chromatography of this mixture gave 5,5-dimethyl-5-sila-5H,10,11H-benzo[b]-pyrido[4,3-e] azepine (VIII), which was also obtained in the reduction of a pure individual isomer of lactam III by lithium aluminum hydride. By analogy, reduction of a mixture of V and VI gave only 3-methyl-5,5-diphenyl-5-sila-5H,10H,11H-benzo[b]pyrido[4,5-e]azepine (IX). The position of the nitrogen atom in the azepine ring of IX was established by analogy to azepine VIII. Azapine IX and the azepine obtained by the reduction of a mixture of isomeric oximes II by lithium aluminum hydride were identical in their physicochemical indices.

EXPERIMENTAL

The PMR spectra were taken on a Tesla BS-497 spectrometer at 100 MHz and on a Bruker WP-80 spectrometer at 80 MHz with acetone-d_6 (III and IV) and $CDCl_3$ (VII-IX) as the solvents. The internal standard was TMS. The IR spectra were taken on a UR-20 spectrophotometer in KBr pellets. The column and thin-layer chromatography was carried out on silica gel A 100/160 and developed with iodine vapor.

11-Oxo-5,5-dimethyl-5-sila-5H,10H,11H-benzo[b]pyrido[4,3-e]azepine (III) and 10-Oxo-5,5-dimethyl-5-sila-5H,10H,11H-benzo[e]pyrido[3,4-b]azepine(IV). A. A sample of 6 g (28.8 mmoles) phosphorus pentachloride was added in 0.5-g portions over 2 h to a solution of 4 g (15.7 mmoles) oxime I in 400 ml absolute ether and maintained with strong stirring for 10 h at 20°C. The reaction mass was treated with saturated aqueous sodium carbonate until basic. The ethereal layer was separated and dried over magnesium sulfate. The residue (3.1 g) was crystallized from heptane–ethyl acetate to yield 2.91 g (72%) of a mixture of lactams III and IV, R_f 0.42 and 0.31 (ethyl acetate). Found, %: C 66.2; H 5.7; N 11.0, M^+ 254. $C_{14}H_{14}N_2OSi$. Calculated, %: C 66.1; H 5.5; N 11.0, M 254.

The aqueous layer after separation of the ethereal layer was acidified with acetic acid to pH 6 and lactam IV was extracted with chloroform. The residue (0.6 g) after distilling off the chloroform solvent was crystallized from heptane–ethyl acetate to yield 0.56 g (14%) IV as white crystals with mp 196.5-197°C, R_f 0.31 (ethyl acetate). IR spectrum: 820 and 1255 [$Si(CH_3)_2$], 1655 (C=O), 3180-3200 cm^{-1} (bound NH). PMR spectrum (80 MHz): 9.33 (s, 1H, NH), 8.46 (s, 1H, 1-H), 8.23 (d, 1H, 3-H), 7.66 (m, 1H, 9-H), 7.25-7.51 (m, 4H, aromatic protons), 0.67 ppm (s, 6H, Si–CH_3). Found, %: N 11.1, M 254. $C_{14}H_{14}N_2OSi$. Calculated, %: N 11.0, M 254.

B. A mixture of lactams III and IV (1.5 g, 5.9 mmoles) was heated at 230-250°C for 15 min. The reaction mass was subjected to chromatography on a 20 × 2-cm column using 5:1 heptane–ethyl acetate as eluent. Initially, 0.69 g (46%) lactam III was separated as white crystals with mp 211-212°C from heptane–ethyl acetate, R_f 0.42 (ethyl acetate). IR spectrum: 820 and 1255 [$Si(CH_3)_2$], 1653 (C=O), 3180-3200 cm^{-1} (bound NH). PMR spectrum (80 MHz): 9.38 (s, 1H, NH), 8.68 (s, 1H, 1-H), 8.46 (d, 1H, 3-H), 7.48-6.96 (m, 5H, aromatic protons), 0.67 ppm (s, 6H, $SiCH_3$). Found, %: C 66.2; H 5.2; N 11.1, M 254. $C_{14}H_{14}N_2OSi$. Calculated, %: C 66.1; H 5.5; N 11.0, M 254. Then, 0.54 g (48%) lactam VII was separated as white crystals with mp 291-292°C (from ethyl acetate), R_f 0.18 (ethyl acetate). IR spectrum: 1695 (CO), 3160 cm^{-1} (bound NH). Mass spectrum, m/z (%): 196 (100) M^+, 168 (25) $[M - CO]^+$, 167 (50.2) $[M - HCO]^+$. Found, %: C 73.4; H 4.0; N 14.3. $C_{12}H_8N_2O$. Calculated, %: C 73.5; H 4.1; N 14.3, M 196.

C. A sample of 0.2 g (0.79 mmole) lactam IV was heated at 230-250°C for 10 min. The reaction mass was crystallized from ethyl acetate to give 0.15 g (96%) lactam VII, mp 291-292°C. The mixed melting point with the same sample obtained by method B was undepressed.

3-Methyl-11-oxo-5,5-diphenyl-5-sila-5H,10H,11H-benzo[b]pyrido[4,5-e]azepine (V) and 3-Methyl-10-oxo-5,5-diphenyl-5-sila-5H,10H,11H-benzo[e]pyrido[5,4-b]azepine (VI). The method described above was used to obtain 0.93 g (84.5%) of a mixture of isomers V and VI from 1.1 g (2.8 mmoles) oxime II. These isomers had R_f 0.56 and 0.51 (ethyl acetate). IR spectrum:

1108 and 1429 (Si—C_6H_5), 1652 (CO), 3280-3300 cm^{-1} (bound NH). Found, %: C 76.6; H 5.3; N 7.0, M^+ 392. $C_{25}H_{20}N_2OSi$. Calculated, %: C 76.5; H 5.1; N 7.1, M 392.

5,5-Dimethyl-5-sila-5H,10H,11H-benzo[b]pyrido[4,3-e]azepine (VIII). A solution of 3.9 g (102.6 mmoles) lithium aluminum hydride in 200 ml absolute ether was added to a solution of 2.6 g (10.2 mmoles) of a mixture of isomeric lactams III and IV in 200 ml absolute ether over 1 h. The mixture was heated at reflux for 30 h and then decomposed with 15 ml ethyl acetate and 25 ml 20% aqueous NaOH. The ethereal layer was decanted and dried over magnesium sulfate. The residue (2.4 g) after distilling off the ether solvent was subjected to chromatography on a 40 × 3 cm column with 5:1 heptane—ethyl acetate as eluent to yield 0.91 g (37%) VIII as white crystals with mp 157-157.5°C (from ethyl acetate—heptane), R_f 0.42 (ethyl acetate). IR spectrum: 820 and 1260 [$Si(CH_3)_2$], 1525 and 3275 cm^{-1} (NH). PMR spectrum (11 MHz): 8.50 (d, 1H, 3-H), 8.43 (s, 1H, 1-H), 7.44 (m, 2H, 4- and 6-H), 7.12 (m, 1H, 8-H), 6.82 (m, 1H, 7-H), 6.67 (m, 1H, 9-H), 4.45 (s, 3H, NH and CH_2); 0.70 ppm (s, 6H, $SiCH_3$); J_{98} = 8, J_{97} = 1.2, $J_{78} \simeq J_{76} \simeq 7.5$, J_{86} = 1.5 Hz. Found, %: C 70.1; H 6.9; N 11.9, M^+ 240. $C_{14}H_{19}N_2Si$. Calculated, %: C 70.0; H 6.7; N 11.7; M 240.

B. A sample of 0.22 g (43%) VIII with mp 157-157.5°C (from ethyl acetate) was obtained by an analogous procedure by reduction from 0.54 g (2.1 mmoles) lactam III. A mixed melting point with a sample obtained by method A was undepressed.

3-Methyl-5,5-diphenyl-5-sila-5H,10H,11H-benzo[b]pyrido[4,5-e]azepine (IX). The reduction of 2 g (5.1 mmoles) of a mixture of lactams V and VI by the method described above gave 0.6 g (31%) IX as white crystals with mp 193-194°C (from hexane), R_f 0.5 (1:4 hexane—ethyl acetate). IR spectrum: 1108 and 1429 (Si—C_6H_5), 1548 and 3270 cm^{-1} (NH). PMR spectrum (100 MHz): 7.78 (s, 1H, 1-H), 6.83 (s, 1H, 4-H), 4.44 (-, 1H, NH), 4.22 (s, 2H, CH_2), 2.22 ppm (s, 3H, CH_3). Found, %: C 79.7; H 6.0; N 7.2, M^+ 378. $C_{25}H_{22}N_2Si$. Calculated, %: C 79.4; H 5.8; N 7.4, M 378.

LITERATURE CITED

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AMINATION OF ISOMERIC BROMO-1-METHYLNITROPYRAZOLES

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A method was developed for the synthesis of 5-bromo-1-methyl-4-nitropyrazole from 1-methylpyrazole. In the reaction with 25% aqueous ammonia at 180-190°C, 5-bromo-1-methyl-4-nitropyrazole is readily converted to 5-amino-1-methyl-4-nitropyrazole; the production of 4-amino-1-methyl-5-nitropyrazole from 4-bromo-1-methyl-5-nitropyrazole requires the presence of a copper catalyst; under the same conditions in the amination of 4-bromo-1-methyl-3-nitropyrazole, 4-amino-1-methyl-3-nitro- and 1-methyl-3-nitropyrazoles are formed in a 2:3 ratio.

The ability of halopyrazoles to enter into nucleophilic substitution reactions depends on the mutual arrangement of the halogen and substituent that activates its substitution in the heterocycle. Such reactions are used chiefly for the production of 5-substituted pyrazoles, containing an electron acceptor group in the 4-position. There are no data in the literature on the amination of halopyrazoles; the 3- and 5-amino-1-methyl-4-nitropyrazoles described were synthesized by other methods [1, 2].

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