REACTIONS OF 2,5-DIMETHYL-4-TRIPHENYLSILYLPYRIDINE AT THE α-METHYL GROUP

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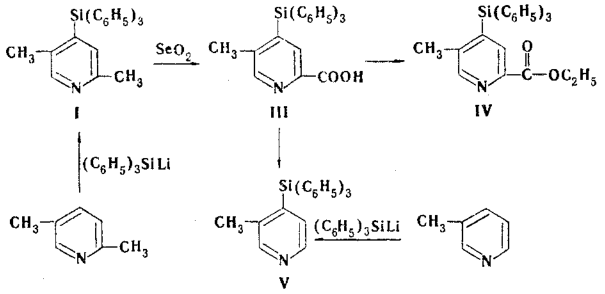
5-Methyl-4-triphenylsilylpyridine-2-carboxylic acid was synthesized, esterified, and decarboxylated. Several transformations of trans-5-methyl-4-triphenylsilyl-2-styrylpyridine were examined.

2,5-Dimethyl-4-triphenylsilylpyridine (I) and 5-methyl-4-triphenylsilyl-2-styrylpyridine (II), which were previously described in [1], were used to synthesize some new substituted pyridine bases with a triphenylsilyl grouping in the pyridine ring.

In the present communication we present the transformations of I at the active α-methyl group. The triphenylsilyl grouping in the 4 position apparently does not have a substantial effect on the activity of the α-methyl group of I as compared with its activity in 2,5-dimethyl-4-phenylpyridine. Compound I was oxidized by means of selenium dioxide to 5-methyl-4-triphenylsilylpyridine-2-carboxylic acid (III), from which the ethyl ester (IV) was obtained by the usual method [2]. Decarboxylation of substituted picolinic acid III gave 3-methyl-4-triphenylsilylpyridine (V) in 55% yield.



The structures of pyridine bases I and V were confirmed by alternative synthesis via the Gilman method [3], which established that the addition of triphenylsilyllithium to the pyridine proceeds to give 1,4-dihydro-4-triphenylsilylpyridine. The oxidation of the latter with alcoholic hydrochloric acid solution or nitrobenzene gives 4-triphenylsilylpyridine. Compounds I and V were obtained by the action of triphenylsilyllithium on 2,5-dimethylpyridine and β-picoline in tetrahydrofuran in yields of 0.5 and 18.4%, respectively. 2,6-Dimethyl-4-triphenylsilylpyridine (VI) was similarly obtained in 9% yield from 2,6-dimethylpyridine. The low yields of silyl-substituted pyridine bases I, V, and VI are probably caused by the effect of the methyl groups attached to C_2 and C_5 of the pyridine ring on the addition of triphenylsilyllithium. We were unable to isolate the corresponding 1,4-dihydropyridines – they are apparently oxidized to the corresponding pyridine bases on workup of the reaction mixture.

We have previously obtained stilbazole II by condensation of I with benzaldehyde in the presence of acetic anhydride in acetic acid [1]. Its isolation from the reaction mixture presents considerable difficulties. An attempt was therefore made to obtain II by condensation of I with benzaldehyde in the presence of anhydrous zinc chloride at 190-210°. A complex of stilbazole II with zinc chloride $(C_{32}H_{27}NSi)_2ZnCl_2 \cdot HCl$

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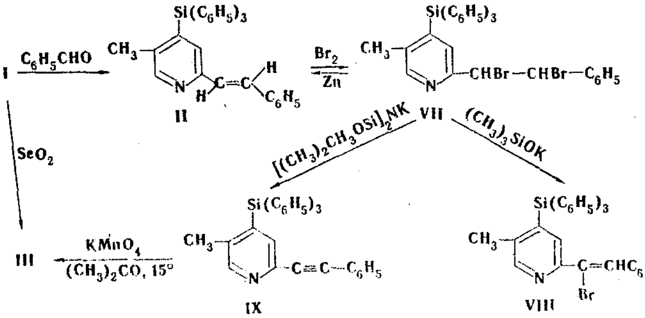
was isolated from the reaction mixture and decomposed with saturated potassium hydroxide solution to give II. A band at 1642 cm^{-1}, which corresponds to the stretching vibrations of the double bond, is present in the IR spectrum of II. The absorption bands at 970 and 982 cm^{-1}, which correspond to the out-of-plane deformation vibrations of the C–H bonds, indicate a trans configuration for II [4].

Stilbazole II was converted to substituted ethynyl derivative IX. Bromination of II in chloroform gave 1,2-dibromo-1-phenyl-2-(5-methyl-4-triphenylsilyl-2-pyridyl)ethane (VII). The IR spectrum of VII contains an intense band at 560 cm^{-1}, which is related to the stretching vibrations of the C–Br bond.



The debromination of VII by means of zinc dust in ethanol gave a complex of II with zinc bromide, which, according to the analytical data, has the composition $C_{32}H_{27}NSi \cdot ZnBr_2$, which is in agreement with the literature data [5]. The decomposition of this complex in a column filled with aluminum oxide gave only stilbazole II, as indicated by the identical character of the IR and UV spectra and the absence of a melting-point depression in mixtures with a genuine sample of the compounds.

The reaction of dibromoethane VII with bis[(dimethylmethoxy)silyl]amide* and potassium trimethylsilanolate was accomplished. It might have been expected that the bromine atoms would be replaced by amino or hydroxyl groups, respectively. However, under the conditions we used to carry out the experiments, we noted only dehydrobromination, which is in agreement with the results obtained by Ruhlmann [6], who observed dehydrochlorination of chlorocyclohexane in the reaction of it with potassium bis(trimethylsilyl)amide. Only one molecule of hydrogen bromide is cleaved in the case of the reaction of VII with potassium trimethylsilanolate, and 5-methyl-4-triphenylsilyl-2-(β-bromostyryl)pyridine (VIII) is apparently formed. The absorption bands at 1624, 1205, 942, and 795 cm^{-1} in the IR spectrum of VIII correspond to trisubstituted ethylene derivatives. The low frequency of the stretching vibrations of the C=C bond (1624 cm^{-1}) is due to the presence of bromine attached to the double bond [7].

Complete dehydrobromination occurs during treatment of VII with potassium bis[(dimethylmethoxy)silyl]amide, and 5-methyl-4-triphenylsilyl-2-phenylethynylpyridine (IX) is isolated in 51% yield. The difference in the dehydrobromination reactions is associated with the different basicities of potassium trimethylsilanolate and potassium bis[(dimethylmethoxy)silyl]amide. Dehydrobromination occurs rapidly in tetrahydrofuran but is accompanied by cleavage of a triphenylsilyl group. The oxidation of IX at the acetylene bond gave benzoic acid and pyridine carboxylic acid III. A weak band of the C≡C bond at 2220 cm^{-1}, which is characteristic for a structure of the ArC≡CAr type [8], is observed in the IR spectrum of IX.

EXPERIMENTAL

Thin-layer chromatography (TLC) was carried out using a mixture of equal amounts of activity II and III aluminum oxide with elution with hexane–ethyl acetate (3 : 1 by volume).

2,5-Dimethyl-4-triphenylsilylpyridine (I). A solution of triphenylsilyllithium, obtained from 76.7 g (0.26 mole) of triphenylchlorosilane in 460 ml of absolute tetrahydrofuran, was added with cooling to 0° in the course of 50 min to a solution of 40 g of 2,5-lutidine in 60 ml of absolute tetrahydrofuran. The reaction mixture was refluxed for 1 h (until the Gilman test was negative), and the next day it was treated with 18% hydrochloric acid (with respect to Congo Red). The tetrahydrofuran was removed by vacuum distillation, and the neutral reaction products were extracted with ether. The residual salts of organic bases were treated with saturated aqueous potassium hydroxide solution, and the organic bases were extracted with ether. The extract was dried with magnesium sulfate, and the ether and excess lutidine were removed by distillation

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to give 20.6 g of a viscous, dark-brown mass, which was refluxed for 6 h in 30 ml of nitrobenzene. The residue after removal of the nitrobenzene by vacuum distillation was chromatographed with a column (25 by 700 mm) filled with activity II aluminum oxide with elution by heptane to give 0.5 g of I with mp 156.5-157.8° (from heptane) and R_f 0.63. This product did not depress the melting point of the compound obtained by the method in [1]. The picrate had mp 179-181° (from alcohol) and did not depress the melting point of the picrate obtained in [1].

5-Methyl-4-triphenylsilyl-2-styrylpyridine (II). A. A mixture of 5.38 g (14.8 mmole) of I, 3.15 g (29.8 mmole) of benzaldehyde, and 2 g of anhydrous zinc chloride was heated at 180-190° for 12 h. The mixture was cooled, 20 ml of alcohol was added, the resulting precipitate (4.23 g) was treated with an aqueous alcohol solution of hydrochloric acid and washed successively with alcohol and benzene to give 2.24 g of a complex of II with zinc chloride with mp 252-256° (from alcohol). Found: C 70.1; H 5.5; N 2.6; Cl 9.5%. $C_{64}H_{54}Si_2N_2 \cdot ZnCl_2 \cdot HCl$. Calculated: C 71.2; H 5.1; N 2.6; Cl 9.9%. The complex was decomposed with sodium hydroxide, and II was extracted with five 50-ml aliquots of ether. The ether was removed by distillation, and the residue was crystallized from hexane to give 1.1 g (29%) of II with mp 166-167° and R_f 0.73 [1]. UV spectrum (in alcohol), λ_{max}, nm (log ε): 224 (4.83), 244 (4.33), 274 (4.52), 310 (4.50). IR spectrum, cm^{-1}: 3075 (w), 3055 (w), 1642 (m), 1582 (m), 1432 (s), 1355 (s), 1310 (m), 1115 (vs), 1080 (m), 982 (s), 970 (s), 767 (s), 747 (vs), 715 (vs), 697 (vs).

B. A mixture of 0.36 g (0.59 mmole) of VII, 0.42 g (0.0064 g-atom) of freshly activated zinc dust, 20 ml of absolute alcohol, and 15 ml of absolute dioxane was refluxed for 8 h. The solvents were removed by distillation, and the residue was washed with hot chloroform and, at the end, with hot dioxane. The solvents were removed by distillation to give 0.55 g of complex of II with zinc bromide as colorless crystals with mp 310-312° (from alcohol). Found: N 2.1%. $C_{32}H_{27}NSi \cdot ZnBr_2$. Calculated: N 2.1%. A solution of 0.5 g (0.74 mmole) of the complex in chloroform was passed through a column filled with activity II aluminum oxide with elution by ethyl acetate–hexane (1 : 1) to give 0.16 g (59%) of II with mp 167-168° (from heptane).

5-Methyl-4-triphenylsilylpyridine-2-carboxylic Acid (III). A. A mixture of 3 g (8.24 mmole) of I and 1.37 g (12.34 mmole) of selenium dioxide in 40 ml of absolute pyridine was refluxed with vigorous stirring for 4 h. The selenium was removed by filtration, the pyridine was removed by distillation, and the residue was treated with hot water to decompose the unchanged selenium dioxide. The aqueous layer was decanted, and acid III was extracted from the residue with boiling heptane to give 1.41 g (43%) of colorless crystals of III with mp 189-190° (dec., from alcohol). Found: C 75.9; H 5.7; N 3.9%. $C_{25}H_{21}NO_2Si$. Calculated: C 75.9; H 5.3; N 3.5%. Partial evaporation of the mother liquor gave 1.5 g of a mixture of I and III.

B. A 0.75-g (1.7 mmole) sample of ethynyl derivative IX was dissolved in a mixture of 25 ml of acetone and 1 ml of water, and 0.72 g (4.54 mmole) of potassium permanganate was added in portions (a new portion was added after decolorization of the previous portion) with vigorous stirring. The precipitated manganese dioxide was removed by filtration, the acetone was evaporated from the filtrate, and the residue (0.09 g) was worked up to give a substance with mp 243-245° (from alcohol–acetic acid) and R_f 0.29, the structure of which could not be established. The precipitated manganese dioxide was washed repeatedly on the filter with hot water followed by methanol. The solution was evaporated on a water bath to 30 ml and acidified with 15% hydrochloric acid until it was weakly acidic to give 0.37 g of III with mp 185-186° (from alcohol). This product did not depress the melting point of the III obtained (mp 189-190°). The filtrate after separation of III was evaporated to 4-5 ml, and the mixture was filtered to give 0.05 g of benzoic acid with mp 117-118.5° (from water).

Ethyl 5-Methyl-4-triphenylsilylpyridine-2-carboxylate (IV). A 0.72-g (1.8 mmole) sample of III was heated for 1.5 h with 2 ml of thionyl chloride. The excess thionyl chloride was removed by vacuum distillation, 10 ml of absolute ethanol was added to the residue, and the mixture was refluxed for 3 h. The alcohol was removed by distillation, and the residue was treated with aqueous sodium carbonate solution. The organic bases were extracted with ether (four 20-ml portions), and the extract was dried with sodium sulfate. The ether was removed by distillation, and the residue was passed through a column (2 by 10 cm) filled with activity II aluminum oxide with elution by ethyl acetate–hexane (1 : 10) to give 0.15 g (19%) of 5-methyl-4-triphenylsilyl-2-carbethoxypyridine (IV) as colorless crystals with mp 171.5-172.5° (from ethyl acetate–hexane) and R_f 0.27. Found: C 76.5; H 6.4; N 3.6%. $C_{27}H_{25}NO_2Si$. Calculated: C 76.6; H 5.9; N 3.3%.

3-Methyl-4-triphenylsilylpyridine (V). A. A 0.22-g (0.56 mmole) sample of III was heated with 6 ml of water in an autoclave at 200° for 3.5 h. The organic bases were extracted with ether, and the extract was dried with magnesium sulfate. The ether was removed by distillation, and the residue (0.17 g), which, according to TLC, was a mixture of III and V, was passed through a column filled with activity II aluminum oxide with elution by hot heptane to give 0.11 g (55%) of colorless crystals of V with mp 198-198.7° (from heptane) and R_f 0.48. Found: C 82.2; H 6.1; N 3.7%. $C_{24}H_{21}NSi$. Calculated: C 82.0; H 6.0; N 4%. The picrate had mp 212-214° (from alcohol–acetone). Found: N 9.6%. $C_{24}H_{21}NSi \cdot C_6H_3N_3O_7$. Calculated: N 9.6%.

B. A solution of triphenylsilyllithium, obtained from 14.5 g (0.05 mole) of triphenylchlorosilane in 120 ml of absolute tetrahydrofuran, was added to a solution of 5 g (0.053 mole) of 3-methylpyridine in 30 ml of absolute tetrahydrofuran. The mixture was heated at 70° for 1.5 h and worked up in the same way as in the preparation of I. The basic extract yielded 0.95 g of V with mp 195-197.3° (ligroin–benzene) and R_f 0.47, which did not depress the melting point of V obtained in the manner described above. The filtrate remaining from the separation of V was vacuum-evaporated, and the residue was refluxed with 20 ml of nitrobenzene for 4 h. The nitrobenzene was removed by vacuum distillation, and the residue (9.81 g) was chromatographed with a column (2.5 by 40 cm) filled with activity II aluminum oxide with elution by heptane to additionally give 2.08 g of V with mp 196-197° and R_f 0.48. The overall yield of V was 3.23 g (18%). The picrate had mp 216-218°. A mixture of this picrate with the picrate described above had mp 212-216°.

2,6-Dimethyl-4-triphenylsilylpyridine (VI). A solution of triphenylsilyllithium, obtained from 14.7 g (0.05 mole) of triphenylchlorosilane and 1.45 g (0.21 g-atom) of lithium in 120 ml of absolute tetrahydrofuran, was added in the course of 20 min to 6.45 g (0.06 mole) of 2,6-dimethylpiperidine, and the reaction mixture was refluxed for 1.5 h (until it gave a negative Gilman reaction). The mixture was worked up as in the preparation of I. The ether extract of the organic bases gave 3.85 g of residue, which was crystallized from ligroin containing a small amount of alcohol to give 1.64 g (9%) of VI with mp 157-160° and R_f 0.66. Found: C 82.1; H 6.6; N 3.6%. $C_{25}H_{23}NSi$. Calculated: C 82.3; H 6.3; N 3.8%. The picrate had mp 163-164.5° (from alcohol–acetone). Found: N 9.3%. $C_{25}H_{23}NSi \cdot C_6H_3N_3O_7$. Calculated: N 9.5%.

1,2-Dibromo-1-phenyl-2-(5-methyl-4-triphenylsilyl-2-pyridyl)ethane (VII). A solution of 0.49 g (3 mmole) of bromine in 6 ml of absolute chloroform was added gradually to a solution of 1.37 g (3 mmole) of II in 20 ml of absolute chloroform, and the mixture was stirred at room temperature for 1.5 h and refluxed for 2 h. The chloroform was removed by distillation, and the residue was recrystallized to give 1.17 g of colorless crystals of VII with mp 162-163° (from heptane–benzene) and R_f 0.74. Found: C 62.6; H 4.2; Br 26.4; N 2.2%. $C_{32}H_{27}Br_2NSi$. Calculated: C 62.6; H 4.4; Br 26.1; N 2.3%. IR spectrum, cm^{-1}: 3070 (w), 1587 (w), 1139 (w), 1110 (vs), 1080 (s), 1035 (w), 1004 (w), 750 (s), 714 (vs), 622 (s), 611 (s), and 560 (vs).

5-Methyl-4-triphenylsilyl-2-(β-bromostyryl)pyridine (VIII). A solution of 0.3 g (0.65 mmole) of VII in 50 ml of absolute benzene was added to 0.17 g (1.3 mmole) of potassium trimethylsilanolate, and the mixture was refluxed for 7 h and filtered. The benzene was removed by distillation, and the residue (0.29 g) was repeatedly recrystallized from heptane to give 0.06 g (27%) of VIII with mp 170-172° and R_f 0.67. Found: C 71.7; H 5.2; Br 14.5; N 2.9%. $C_{32}H_{26}BrNSi$. Calculated: C 72.2; H 4.9; Br 15.0; N 2.6%. IR spectrum, cm^{-1}: 3065 (w), 3045 (w), 1624 (w), 1578 (w), 1318 (w), 1308 (w), 1205 (w), 1110 (vs), 1080 (s), 1035 (m), 942 (s), 868 (s), 830 (m), 795 (s), 758 (vs), 742 (s), 710 (vs), and 700 (vs). The picrate had mp 230-233° (from alcohol–acetone). Found: N 7.7%. $C_{32}H_{26}BrNSi \cdot C_6H_3N_3O_7$. Calculated: N 7.4%.

5-Methyl-4-triphenylsilyl-2-phenylethynylpyridine (IX). A 1.8-g (8.2 mmole) sample of hexamethylcyclotrisilazan was added to 1.12 g of a 27.5% solution of potassium hydroxide in methanol, and, after the mixture had heated up and solidified, it was heated on a bath for 2 h at 100-110°, and 50 ml of absolute benzene (freshly distilled over lithium aluminum hydride) was added. All of the operations were carried out with protection from air moisture. A solution of 1.6 g (2.54 mmole) of VII in 50 ml of absolute benzene was added to the resulting solution of potassium bis[(dimethylmethoxy)silyl]amide, and the mixture was refluxed for 12 h. Absolute methanol (45 ml) was added, and the mixture was refluxed for 1 h. The solvents and volatile products were removed by distillation, and 50 ml of water was added to the residue. The aqueous mixture was extracted with ether, and the extract was dried with magnesium sulfate. The ether was removed by distillation, and the residue was treated with a mixture of 5 ml of hexane containing 0.5 ml of alcohol to give 0.94 g of crystals. Crystallization from alcohol–hexane gave 0.6 g (51%) of IX with mp 157-158° and R_f 0.70. Found: C 85.0; H 5.8; N 3.1%. $C_{32}H_{25}NSi$. Calculated: C 85.1; H 5.5; N 3.1%. UV spectrum (in alcohol), λ_{max}, nm (log ε): 222 (4.74), 283 (4.46), 320 (4.52), 330 (4.51). IR spectrum, cm^{-1}: 3070 (w), 3050 (m), 3020 (w), 2220 (w), 1600 (w), 1570 (m), 1340 (s), 1300 (w), 1270 (w), 1229 (w), 1195 (w), 1161 (w), 1113 (vs), 1070 (s), 1035 (m), 1002 (w), 895 (w), 763 (vs), 750 (s), 715 (vs), 697 (vs). The picrate had mp 193-194.5° (from alcohol–acetone). Found: N 8.2%. $C_{32}H_{25}NSi \cdot C_6H_3N_3O_7$. Calculated: N 8.2%.

The IR spectra of mineral-oil suspensions were recorded with a UR-20 spectrophotometer. The UV spectra of alcohol solutions were recorded with an SF-4a spectrophotometer.

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