

Reactions of Alkyl- and Phenylpiperidones with Benzene in the presence of AlBr_3

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Received March 1, 2004

3-Bromo- and 5-bromo-4-piperidones were used mainly in dehydrobromination reactions [1], in Faworsky reaction [2], and in nucleophilic substitutions [3]. We attempted to use 5-bromo-4-piperidones as alkylating agents for benzene derivatives in Friedel–Crafts reactions in the presence of aluminum bromide. As alkylating agents served hydrobromides of 5-bromo-1,2,5-trimethyl-4-piperidone (**I**) and 3-bromo-2,6-diphenyl-4-piperidone (**II**).

The reaction of 5-bromo-1,2,5-trimethyl-4-piperidone hydrobromide (**I**) with excess benzene in the presence of AlBr_3 at 65°C alongside the replacement of the bromine by benzene involved the heterocycle opening to afford 2-methyl-1-(methylamino)-2-phenyl-4-hexen-3-one (**III**) in a 58% yield.

Inasmuch as in the molecule of compound **III** the conjugation system includes the double bond, the carbonyl group, and the aromatic ring, in the IR spectrum the frequency of the carbonyl group vibrations is shifted to 1650 cm^{-1} ; also are observed characteristic absorption bands of the phenyl substituent at 3060 , 1600 , 1485 , 690 cm^{-1} , a strong band of the $\text{C}=\text{C}$ bond at 1620 cm^{-1} , and a band of NH group at 3300 cm^{-1} .

Since the benzene did not show high reactivity in this reaction we isolated after treatment of the reaction mixture with aqueous sodium carbonate alongside compound **III**

also products obtained from compound **I** by dehydrobromination [1,2,5-trimethyl-1,2,3,4-tetrahydropyridin-4-one (**IV**) (yield 17%)] and hydrolysis [5-hydroxy-1,2,5-trimethyl-4-piperidone (**V**) (yield 20%)] (Scheme 1).

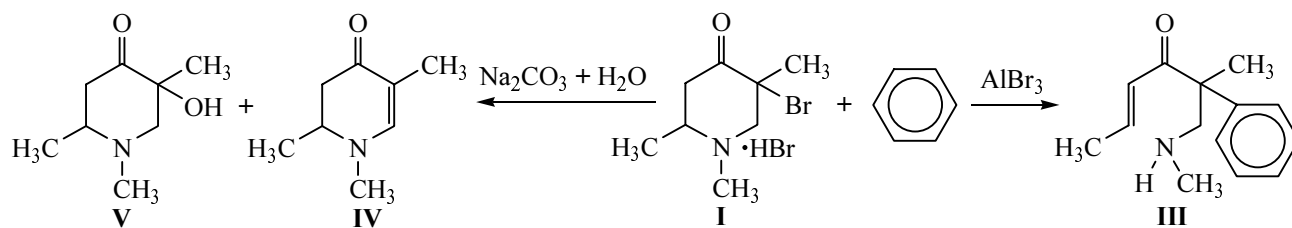
In reaction of 3-bromo-2,6-diphenyl-4-piperidone (**II**) with excess benzene in the presence of aluminum bromide at room temperature followed by heating at $60\text{--}65^\circ\text{C}$ for 3 h an oily unstable compound **A** was obtained that on treating with ether solution of hydrogen chloride yielded (3-oxo-1,2,5-triphenyl-4-chloro)pentylammonium chloride (**VI**), mp $212\text{--}213^\circ\text{C}$.

The formation of compounds **III** and **A** occurred as a result of Friedel–Crafts benzene alkylation with piperidone bromo derivatives **I** and **II** and of heterocycle opening at the $\text{C}\text{--}\text{N}$ bond effected by AlBr_3 .

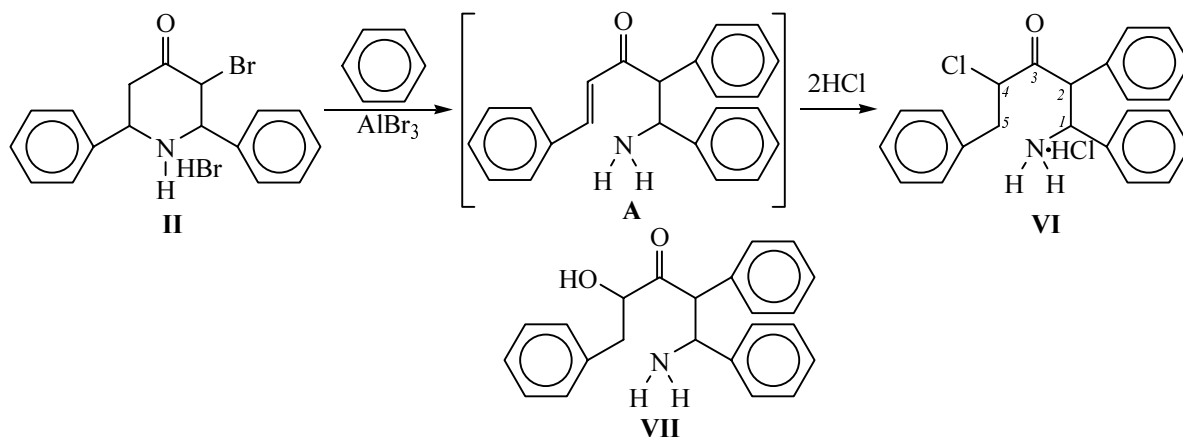
At the treatment of 5-amino-1,4,5-triphenyl-1-penten-3-one (**A**) with the ether solution of HCl the hydrogen chloride apparently added at the double bond. The IR spectrum of compound **VI** contains absorption band of $\text{C}\text{--}\text{Cl}$ band with a maximum at 780 cm^{-1} , a broad band corresponding to the ammonium group N^+H_3 ($2720\text{--}2400\text{ cm}^{-1}$), and overtones characteristic of a mono-substituted benzene ring in the region $2000\text{--}1660\text{ cm}^{-1}$.

The ^{13}C NMR spectrum is also in sufficient agreement with the assumed structure of compound **VI**. The char-

Scheme 1.



Scheme 2.



acteristic peak of carbon atom of the C=O group appears at 192 ppm, of CCl group at 39.82 ppm, and the multiplet of aromatic carbons in the region 128.03–143.93 ppm

At treating compound VI with aqueous ammonia a nucleophilic substitution occurred of the chlorine atom by a hydroxy group affording 5-amino-2-hydroxy-1,4,5-triphenylpentan-3-one (VII).

Thus in reactions of 3- and 5-bromo-4-piperidones AlBr₃ promoted the electrophilic substitution and the heterocycle opening at the C–N bond leading to formation of new compounds.

Reactions of hydrobromide I in benzene in the presence of AlBr₃. At room temperature 3.8 g (14 mmol) of aluminum bromide was mixed with 10 ml of benzene and 9.0 g (29 mmol) of hydrobromide I, and to this thick mass was added 50 ml of benzene. The reaction mixture was stirred at 60–65°C for 3 h. Excess benzene was distilled off, and the residue was treated with a saturated water solution of sodium carbonate. The reaction products were extracted into ether, the extract was dried over MgSO₄. On distilling off the solvent the residue was subjected to fractional distillation in a vacuum. First fraction. 2.0 g (17%) of compound IV, bp 40–42°C (1 mm Hg), n_D^{20} 1.4620 [3]. Second fraction. 0.4 g (20%) of compound V, bp 73–74°C (1 mm Hg), d_4^{20} 1.0248, n_D^{20} 1.4650; MR_D 42.37, calc. 42.63. IR spectrum, ν , cm⁻¹: 1738 (C=O), 3490 (OH). Found, %: C 61.27; H 9.16; N 8.99. C₈H₁₆NO₂. Calculated, %: C 61.16; H 9.54; N 8.91. Third fraction, amine III, 3.8 g (58%), bp 75–78°C (1 mm Hg), d_4^{20} 0.9840, n_D^{20} 1.5220; MR_D 63.22, calc. 63.34. Found, %: C 77.33; H 8.90; N 6.72. C₁₄H₁₉NO. Calculated, %: C 77.42; H 8.76; N 6.44

3-Oxo-1,2,5-triphenyl-4-chloropentylammonium chloride (VI). Likewise from 3.4 g (12 mmol) of AlBr₃, 3.5 g (8 mmol) of hydrobromide II, and 55 ml of benzene

after heating at 60–65°C for 2 h and distilling off the solvent we obtained 2.5 g of oily substance that was treated with an ether solution of hydrogen chloride. The reaction product was recrystallized from ethanol. Yield of compound VI 2.7 g (86%), colorless crystals, mp 212–213°C. Found, %: C 68.68; H 6.05; N 3.67; Cl 17.70. C₂₃H₂₃Cl₂NO. Calculated, %: C 69.00; H 5.75; N 3.50; Cl 17.75.

5-Amino-2-hydroxy-1,4,5-triphenylpentan-3-one (VII). In acetone was dissolved 2.9 g of hydrochloride VI, to the solution was added aqueous ammonia till neutral reaction, and the reaction product was extracted into benzene. On distilling off the solvent and recrystallization of the residue from ethanol we obtained 2.4 g of compound VII. Yield 93%, mp 86–87°C. Found, %: C 79.18; H 7.89; N 4.23. C₂₃H₂₃NO₂. Calculated, %: C 80.01; H 6.67; N 4.05.

IR spectra were measured in the range 4000–400 cm⁻¹ on a spectrophotometer Specord IR-75. The ¹³C NMR spectra were registered on spectrometer Bruker MX-400 from solutions of compounds in CDCl₃, internal reference TMS. The reaction progress was monitored by TLC on plates with unfixed layer of aluminum oxide of the II activity grade, development in iodine vapor.

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