# INVESTIGATIONS IN THE DIPIPERIDYL SERIES

## XI.* REACTION OF 2,2'-DIPIPERIDYL WITH PHOSGENE

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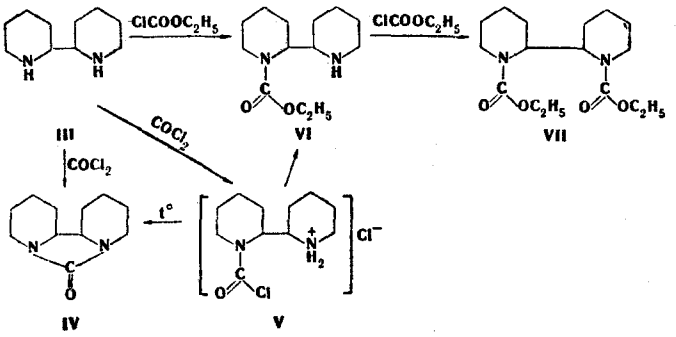
The reduction of 2-(2-piperidyl)pyridine gives diastereomers of 2,2'-dipiperidyl (III and IIIa). The action of phosgene on III gave tricyclo[1.6.7.12]-1,12-diaza-13-tridecanone and 1-chlorocarbonyl-2,2'-dipiperidyl. The latter reacts with sodium ethoxide to give 1-ethoxycarbonyl-2,2'-dipiperidyl, which is also obtained by alternative synthesis from III and ethyl chlorocarbonate.

The available information on 2,2'-dipiperidyl (I) is extremely limited [2]. We have previously described the preparation of 2-(2-piperidyl)pyridine (II) [3].

In the present communication, we reduced II with sodium in isoamyl alcohol in order to obtain I and its derivatives. The reaction proceeds with the formation of two diastereomers (III and IIIa). These compounds were separated by preparative chromatography on aluminum oxide.

The reaction of III with phosgene gave tricyclo[1.6.7.12]-1,12-diaza-13-tridecanone (IV) and 1-chlorocarbonyl-2,2'-dipiperidyl hydrochloride (V) via the following scheme:




The reaction of equimolecular amounts of III and phosgene leads to hydrochloride V, while in the presence of excess phosgene the reaction gives primarily IV, which is also readily obtained on vacuum distillation of hydrochloride V under nitrogen. Compound V reacts with sodium ethoxide to give 1-ethoxycarbonyl-2,2'-dipiperidyl (VI), which is also obtained by alternative synthesis from III and ethyl chlorocarbonate. Compound VI reacts with ethyl chlorocarbonate to give 1,1'-diethoxycarbonyl-2,2'-dipiperidyl (VII).

The IR spectra of III and IIIa in the region of the stretching and deformation vibrations of the NH groups display two bands each at 3250, 3340 and 1440, 1460 $cm^{-1}$, respectively. The spectra of VI and VII contain frequencies of the stretching vibrations of the C=O groups at 1670 and 1695 $cm^{-1}$. The disappearance of NH absorption bands and the appearance of the absorption band of the C=O group of the carbamide ring at 1732 $cm^{-1}$ are characteristic for IV.

*See [1] for communication X.

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A comparative analysis of III, IV, and VII by thin-layer chromatography (TLC) on $Al_2O_3$ shows that IV and VII lose their basic character. While a system of solvents saturated with dry ammonia is used for the chromatography of III, a low-polarity toluene–chloroform system is used for IV and VII.

## EXPERIMENTAL

2,2'-Dipiperidyls III and IIIa. A 50-g (0.3 mole) sample of II with bp 124° (2 mm) and $n_D^{20}$ 1.5412 (bp 256-266° [1]) was dissolved in 600 ml of freshly distilled isoamyl alcohol, and 46 g (2 g-atom) of sodium was added in one lump (!) to the cold mixture, after which the mixture was heated to the boiling point on a sand bath. At the end of the reaction, the mixture was cooled, hydrochloric acid was added (pH 5-5.5), and the isoamyl alcohol was removed by steam distillation. The hydrochlorides of the bases were treated with 40% KOH solution until the mixture was strongly alkaline, and the bases were extracted with ether. The ether extract was dried with sodium sulfate, the solvent was removed by distillation, and the residue was vacuum-distilled with collection of the fraction with bp 108-112° (1 mm) and $n_D^{20}$ 1.5011. Two substances with $R_f$ 0.12 and 0.27 were detected by TLC on activity II $Al_2O_3$ with elution by ammonia-saturated $CHCl_3$–benzene–methanol (15:18:1.5). The substances were separated by preparative TLC on activity II $Al_2O_3$ with elution with ammonia-saturated $CHCl_3$–benzene–methanol (120:144:12). A 0.5-g sample of the mixture of III and IIIa dissolved in 3 ml of chloroform was applied to a 75-by-35-cm plate. The $Al_2O_3$ sections containing the substances were collected and washed out with methanol. Removal of the solvent gave chromatographically homogeneous III and IIIa.

Compound III was a colorless liquid with mp 30° (in a sealed capillary, bp 110-111° (1 mm), $n_D^{20}$ 1.4993, and $R_f$ 0.12. Found: C 71.4; H 11.8; N 16.8%. $C_{10}H_{20}N_2$. Calculated: C 71.4; H 11.9; N 16.7%. The dihydrochloride was obtained as colorless crystals with mp 299-300° (from alcohol). Found: Cl 24.4%. $C_{10}H_{20}N_2 \cdot 2HCl$. Calculated: Cl 24.5%. The picrate had mp 221-222° (from water).

Compound IIIa had mp 44° (from petroleum ether) and $R_f$ 0.27. Found: C 71.3; H 11.8; N 16.8%. $C_{10}H_{20}N_2$. Calculated: C 71.4; H 11.9; N 16.7%. The dihydrochloride was obtained as colorless crystals with mp 310-311° (from alcohol). Found: Cl 24.4%. $C_{10}H_{20}N_2 \cdot 2HCl$. Calculated: Cl 24.5%. The picrate had mp 230-231° (from water).

Tricyclo[1.6.7.12]-1,12-diaza-13-tridecanone (IV). A 3.36-g (0.02 mole) sample of III was dissolved in 15 ml of anhydrous toluene, the solution was cooled to −15°, and 1 g (0.01 mole) of phosgene dissolved in 20 ml of toluene was added. The solution was heated on a water bath for 6 h, and the solid product (A) was separated. The toluene was removed by distillation, and the residue was vacuum-distilled to give 1.4 g (71%) of IV as a colorless liquid (the material darkened in air) with bp 126° (1 mm), $n_D^{20}$ 1.5150, and $R_f$ 0.34 [toluene–chloroform–methanol (18:15:1.5)]. Found: C 66.8; H 9.4; N 14.2%. $C_{11}H_{18}N_2O$. Calculated: C 66.9; H 9.3; N 14.4%. The picrate had mp 175-176° (from alcohol). Found: N 16.41%. $C_{11}H_{18}N_2O \cdot C_6H_3N_3O_7$. Calculated: 16.5%.

1-Chlorocarbonyl-2,2'-dipiperidyl Hydrochloride (V). A 2-g sample of A in 50 ml of acetone was heated on a water bath for 3 h, solid portion B was separated, and one-third of the solvent was removed by distillation. Petroleum ether (50 ml) was added to the residue to give 0.4 g of colorless crystals with mp 293-294° (from acetone) and $R_f$ 0.18 [chloroform–benzene–acetone (15:10:5)]. Found: C 49.4; H 7.2; Cl 29.3; N 15.0%. $C_{11}H_{19}ClN_2O \cdot HCl$. Calculated: C 49.4; H 7.5; Cl 29.0; N 14.6%. Product B yielded 0.3 g of the dihydrochloride of III with mp 299-300° (from alcohol).

1-Ethoxycarbonyl-2,2'-dipiperidyl (VI). A 2.7-g (0.01 mole) sample of hydrochloride IV in 100 ml of acetone was heated for 5 h with 1.3 g (0.02 mole) of sodium ethoxide. The solvent was removed by distillation to give 1.5 g (86%) of VI with bp 127-128° (2 mm), $n_D^{20}$ 1.4988, and $R_f$ 0.52 [chloroform–benzene–methanol (15:18:1.5)]. Found: C 69.7; H 10.6; N 12.4%. $C_{13}H_{24}N_2O$. Calculated: C 69.7; H 10.7; N 12.5%. The hydrochloride had mp 247-248° (from alcohol). Found: Cl 12.7%. $C_{13}H_{24}N_2O \cdot HCl$. Calculated: Cl 12.8%. The picrate had mp 168-169° (from ether). Reaction of 0.5 g (3 mmole) of III in 10 ml of toluene with 0.32 g (3.5 mmole) of ethyl chlorocarbonate gave 0.1 g (30%) of VI with $R_f$ 0.52. The picrate had mp 168-169° (from ether).

1,1'-Diethoxycarbonyl-2,2'-dipiperidyl (VII). A solution of 2.5 g (0.01 mole) of VI in 30 ml of anhydrous ether was mixed with cooling with 0.54 g (0.005 mole) of ethyl chlorocarbonate. The ether solution was separated, and the solvent was removed by distillation to give prisms of VII with mp 44° (from petroleum ether at −10°). Found: C 68.5; H 10.1; N 10.2%. $C_{16}H_{28}N_2O_2$. Calculated: C 68.6; H 10.0; N 10.0%.

## LITERATURE CITED


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