THE PRODUCT OF THE CONDENSATION OF LUPININIC ACID WITH PIPERIDINE*

Kh. A. Aslanov, T. K. Kasymov, A. S. Sadykov, and A. I. Ishbaev

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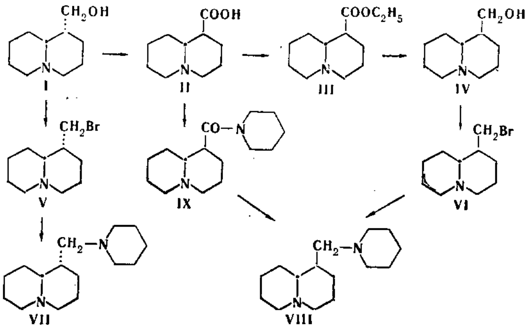
The condensation of lupininic acid with piperidine in the presence of phosphorus pentoxide forms d-epilupininoylpiperidine. The reduction of d-epilupininoylpiperidine with lithium aluminum hydride has given piperidino-d-epilupinane.

In previous work [1, 2], on performing the reaction of lupininic acid (II) with piperidine we isolated a colorless substance with mp 240-241°C and a liquid substance with bp 228-230°C (5 mm).

A study of the reaction products has shown that the crystalline substance is a mixture of the hydrochlorides of piperidine and of the product of the condensation of lupininic acid with piperidine.

The liquid base with bp 228-230°C (5 mm) has the composition $C_{15}H_{26}N_2O$. Its spectrum had the characteristic bands of a lactam group (1623 cm^{-1}) and of a trans quinolizidine nucleus (2800-2700 cm^{-1}). Acid hydrolysis gave lupininic acid (II) and piperidine. Thus, the base, $C_{15}H_{26}N_2O$, is lupininoylpiperidine (IX).

It is known that lupinine forms two series of derivatives, corresponding to 1-lupinine (I) and d-epilupinine (IV). During some reactions, epimerization of the lupinine derivatives takes place. In order to establish which epimer substance IX is we reduced it with lithium aluminum hydride. This gave a base $C_{15}H_{28}N_2$, corresponding to piperidinolupinane. The stereoisomeric lupinanes, for comparison, we synthesized by a published method [3] from 1-lupinine (I) and d-epilupinine (IV).



The latter was obtained by the reduction of ethyl d-epilupininic acid (III) with lithium aluminum hydride. The action of phosphorus pentabromide on lupinine and epilupinine gave, respectively, bromolupinane (V) and bromoepilupinane (VI) [4]. By heating the bromolupinanes with piperidine in sealed tubes at 150-160°C, we obtained piperidino-1-lupinane (VII) and piperidino-d-epilupinane (VIII).

A comparison of their physicochemical constants and IR spectra showed that the base that we obtained by the reduction of the product of the condensation of lupininic acid with piperidine corresponded completely to piperidino-d-epilupinane (VIII). Thus, the product of the condensation of lupininic acid with piperidine has the structure of d-epilupinopiperidine (IX).

EXPERIMENTAL

d-Epilupininoylpiperidine (IX). Some 11 g of finely ground lupininic acid with mp 255°C was dissolved in 120 ml of piperidine, and 46 g of phosphorus pentoxide was added in portions with cooling. The reaction mixture was boiled for

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*The lupininic acid described in the literature is d-epilupininic acid. So as not to produce confusion, we also call it lupininic acid.

3 hr. The excess of piperidine was distilled off in vacuum. The residue was dissolved in cold water, and the solution was made alkaline with potassium carbonate and extracted with ether. The ethereal solution was dried with sodium sulfate. After the ether had been distilled off, 11 g (75.5%) of a viscous oily substance was obtained with bp 228-230°C (5 mm), $[\alpha]_D$ +54.2° (c 2.13; ethanol); R_f 0.78 [density 85 paper of the Leningrad no. 2 mill; n-butanol acetic acid water (5 : 1 : 4)]. Found %: C 72.22, 72.19; H 10.46, 10.50; N 11.01, 11.15. $C_{15}H_{26}N_2O$. Calculated %: C 72.00; H 10.40; N 11.20. The perchlorate was obtained by mixing a saturated solution of sodium perchlorate with a solution of the base with 5% HCl. Mp 199-200°C (from water). Found %: C 51.59, 51.65; H 7.86, 7.55; N 8.07, 8.20. $C_{15}H_{26}N_2O \cdot HClO_4$. Calculated %: C 51.50; H 7.76; N 8.00.

Hydrochloride. Mp 114-115°C (from acetone). Found %: Cl 12.40, 12.41. $C_{15}H_{26}N_2O \cdot HCl$. Calculated %: Cl 12.39.

Saponification of d-epilupininoylpiperidine (IX). A solution of 2 g of the base in 15 ml of 20% H_2SO_4 was boiled for 16 hr. The reaction mixture was made alkaline with barium hydroxide to pH ~12 and extracted with ether. Gaseous hydrogen chloride was passed through the ethereal solution. The white precipitate that deposited was filtered off with suction and recrystallized from a mixture of ethanol and ether. This yielded the hydrochloride with mp 243-244°C giving no depression of the melting point with piperidine hydrochloride. Gaseous carbon dioxide was passed through the alkaline solution. The barium carbonate that deposited was filtered off and was twice washed with water. The filtrate and the wash-waters were combined and evaporated to dryness. The residue was recrystallized from a mixture of water and acetone. The colorless crystals isolated had mp 254-255°C and gave no depression of the melting point with d-epilupininic acid.

Reduction of d-epilupininoylpiperidine (IX). To a hot solution of 1 g of lithium aluminum hydride in 150 ml of absolute ether was added, dropwise, 3 g of d-epilupininoylpiperidine in 50 ml of absolute ether. The reaction mixture was heated for 3 hr and was cooled, and the excess of lithium aluminum hydride was decomposed first by the addition of moist ether and then with a saturated solution of potassium carbonate. The reaction product was extracted with ether. The ethereal extract was dried with sodium sulfate. After the ether had been driven off, the reduction product was distilled at 158-160°C (10 mm), $[\alpha]_D$ +96.5° (c 2.05; ethanol); R_f 0.73. Found %: C 76.23, 76.20; H 11.98, 11.86; N 11.70, 11.89. $C_{15}H_{28}N_2$. Calculated %: C 76.14; H 11.94; N 11.84. Picrate. mp 205-206°C. A mixture with piperidino-d-epilupinane picrate gave no depression of the melting point.

Ethyl d-epilupininate (III). A solution of 10 g of the acid in 200 ml of absolute ethanol was saturated with gaseous hydrogen chloride for 8 hr and was then left for 24 hr and finally boiled for 4 hr. Then the ethanol was distilled off, the residue was dissolved in 50 ml of water, and the solution was made alkaline with potassium carbonate, with cooling, and was extracted with ether. The ethereal solution was dried over sodium sulfate, and after the ether had been driven off the residue was distilled at 139-140°C (4 mm). Yield 5.52 g (55%), $[\alpha]_D$ +48° (c 2.42; ethanol); R_f 0.77.

d-Epilupinine (IV). A solution of 4.7 g of ethyl d-epilupininate in 70 ml of absolute ether was added dropwise to a hot solution of 2 g of $LiAlH_4$ in 300 ml of absolute ether. The mixture was heated for another 4 hr and left overnight. On the following day, the excess of $LiAlH_4$ was decomposed with moist ether and the solution was made alkaline with saturated potassium carbonate solution and was extracted with ether. The ethereal solution was dried over calcined sodium sulfate, and the ether was distilled off. The yield of IV was 3.7 g (98.4%) (from petroleum ether). Mp 79-80°C, $[\alpha]_D$ +36.8° (c 2.00; ethanol); R_f 0.55.

Bromo-d-epilupinane (VI). With stirring and cooling, 15 g of powdered phosphorus pentabromide was added in portions to a solution of 3.5 g of d-epilupinine in 60 ml of dry benzene. The reaction mixture was heated for 2 hr. The benzene was distilled off to dryness. The residue was decomposed with water and was washed three times with ether and then the solution was made alkaline and was extracted with ether. The ethereal solution was dried over sodium sulfate and evaporated. The yield of VI was 5.2 g (98.5%). Bp 126-130°C (2 mm); $[\alpha]_D$ +61° (c 2.08; ethanol).

Piperidino-d-epilupinane (VIII). A mixture of 3.9 g of bromoepilupinane and 20 ml of piperidine was heated in a sealed tube at 150-160°C for 6 hr. The reaction mixture was diluted with water, made alkaline with potassium carbonate, and extracted with ether. The ethereal solution was dried and evaporated. The residue, which formed a viscous oil, distilled at 158-160°C (10 mm). Yield 3.7 g (93%), $[\alpha]_D$ +97.3° (c 2.05; ethanol); R_f 0.73. Found %: C 76.23, 76.13; H 11.98, 11.86; N 12.12, 12.21. $C_{15}H_{28}N_2$. Calculated %: C 76.20; H 11.94; N 11.84. Picrate. mp 205-206°C (from ethanol).

Bromo-*l*-lupinane (V). Some 11 g of lupinine was brominated under the conditions for the bromination of d-epilupinine. The yield of V was 15 g (99%). Bp 126-130°C (2 mm); $[\alpha]_D$ −27.2° (c 3.10; ethanol); R_f 0.76. Picrate. mp 134-135°C (from water). Found %: N 11.90, 12.22. $C_{10}H_{18}NBr \cdot C_6H_3N_3O_7$. Calculated %: N 12.14.

Piperidino-*l*-lupinane (VII). This was obtained in a similar manner to piperidino-d-epilupinane (VIII). Yield 97%. Bp 158-160°C (10 mm); $[\alpha]_D$ −37° (c 2.32; ethanol). Found %: C 76.32, 76.20; H 11.92, 11.80; N 12.00, 12.07. $C_{15}H_{28}N_2$. Calculated %: C 76.20; H 11.94; N 11.84. Picrate. mp 113-114°C (from ethanol).

REFERENCES

1. A. S. Sadykov, Kh. A. Aslanov, and T. Tursunbaev, ZhOKh, 30, 3496, 1960.
2. Kh. A. Aslanov, T. Kasymov, A. S. Sadykov, and A. I. Ishbaev, KhPS [Chemistry of Natural Compounds], 3, no. 6, 412, 1967.
3. F. Bohlmann, E. Winterfeld and U. Frise. Chem. Ber., 96, 2251, 1963.
4. Bartholomäus and Schaumann, German patent no. 386936, 1923; 1, 2636, 1924.

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Lenin Tashkent State University