

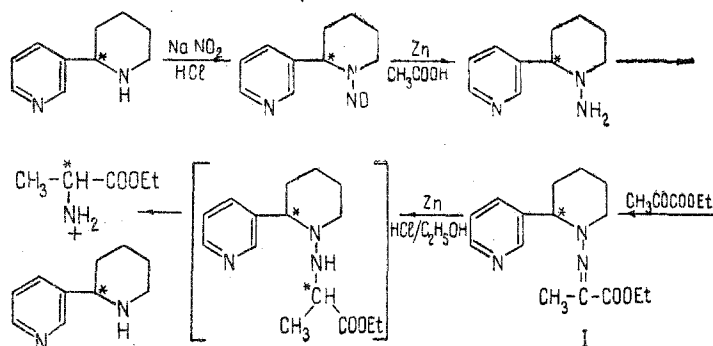
# A NEW SYNTHESIS OF OPTICALLY ACTIVE $\alpha$ -ALANINE

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In the synthesis of optically active amino acids, optically active bases can be used as asymmetrizing agents. For example, the interaction of optically active  $\alpha$ -phenylethylamine and  $\alpha, \beta$ -unsaturated acids takes place stereospecifically and by subsequent hydrogenolysis of the carbon-nitrogen bond it is possible to obtain amino acids with a high specific optical purity [1]. However, from the biochemical point of view the starting materials for the synthesis of amino acids must be  $\alpha$ -keto acids. Consequently, it is desirable to find a stereospecific route for the reductive amination of ketones.

We have obtained optically active  $\alpha$ -alanine by using anabasine (the alkaloid of *Anabasis aphylla*) as the optically active agent; it is converted by nitrosation and subsequent reduction of the nitroso group into the corresponding N-amino compound. The reaction of N-aminoanabasine with ethyl pyruvate led to the corresponding optically active hydrazone (I).



Reduction of the double carbon-nitrogen bond with zinc in alcoholic hydrogen chloride formed a second asymmetric center. The hydrogenolysis of the nitrogen-nitrogen bond takes place simultaneously (or successively, in a second stage). In this way we have obtained optically active  $\alpha$ -alanine with a yield of 10%,  $[\alpha]_D^{20} -6.1^\circ$ , which corresponds to 40% optical purity and have recovered the initial anabasine (90% of the original optical activity).

## Experimental

**Hydrazone from  $\alpha$ -aminoanabasine and ethyl pyruvate (I).** A solution of 57 mmole of N-aminoanabasine obtained by the usual method [2] from N-nitrosoanabasine [3] in 50 ml of alcohol was treated with 58 mmole of ethyl pyruvate. The reaction mixture was evaporated in vacuum. The residual oil crystallized. After recrystallization, 14.8 g of substance (I) (95%) was obtained with mp  $71-72^\circ\text{C}$  (from isooctane)  $[\alpha]_D^{20} +605.8^\circ$  (c 2.7; alcohol).

**$\alpha$ -Alanine.** A mixture of 12 mmole of (I), 50 ml of alcohol, and 45 mmole of zinc dust was slowly treated with a saturated alcoholic solution of hydrogen chloride. Then, when all the zinc had dissolved, another 22 mmole of zinc dust and the corresponding volume of alcoholic hydrogen chloride solution were added. The solution was filtered, the filtrate was evaporated in vacuum, and the residue was dissolved in water. When the zinc ion had been precipitated with hydrogen sulfide (the pH was kept at 4-5 by the addition of small amounts of NaOH solution), the mixture was centrifuged and the solution was made alkaline (hydrolysis of the ester taking place simultaneously) and extracted with ether until thin-layer chromatography no longer gave a spot for anabasine [ $\text{Al}_2\text{O}_3$ , benzene-methanol (9:1)]. The alanine was isolated from the aqueous layer by means of chromatography on a column of Dowex 1  $\times$  2 resin ( $\text{OH}^-$  form) and was eluted with 5% acetic acid. This gave 100 mg of  $\alpha$ -alanine (10%) with mp  $295^\circ\text{C}$  (decomp.),  $[\alpha]_D^{20} -6.1^\circ$  (c 0.8; 6 N HCl). According to a paper chromatogram the substance was identical with an authentic sample.

## Summary

Optically active  $\alpha$ -alanine has been synthesized from pyruvic acid using N-aminoanabasine as the asymmetrizing agent.

## REFERENCES

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