SEPARATION OF RACEMIC ALANINE INTO ITS OPTICAL ANTIPODES

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Numerous methods are known for the separation of racemic amino acids based on the formation of diastereoisomeric derivations [1-4]. However, these methods are fairly laborious, the yield of product does not exceed 50%, and partial racemization is possible even in the process of obtaining the free optically active amino acids from their derivatives.

Another method of separating racemates is based on the difference in the crystallization of molecular compounds of DL-amino acids with optically inactive compounds and similar molecular compounds of the D- and L-amino acids [2, 5]. This method has proved to be the most successful for separating racemic amino acids, in particular, DL-alanine. The procedure for separating this substance is simple and does not require additional operations, i.e., the conversion of the amino acids into N-acetyl derivatives and hydrolysis. All the operations take place without racemization, in contract to the method of separation through diastereoisomers, and the yield of amino acids is not less than 95%.

We have developed a method for separating racemic alanine into the optically active D- and L-alanines which is simple to perform and ensures a high yield and complete optical separation.

The essence of the method developed is that the DL-alanine is converted into DL-alanine p-toluenesulfonate and, on the basis of the different solubilities of the racemic salt and of an optically active salt of alanine in 97% aqueous acetone, by keeping the solution of DL-alanine p-toluenesulfonate at 22°C for 2 h and adding a seed of D- or L-alanine p-toluenesulfonate (0.01 g) crystalline D- or L-alanine p-toluenesulfonate is obtained.

The process of separating the racemate was performed in steps (Table 1). To maintain the equilibrium of the substances in solution, after the precipitation of the crystals of the D- or L- isomer, the DL-isomer was added to the solution in an amount equal to the amount of crystals that had deposited.

The D- and L-alanines were obtained by passing their salts through KU-2 resin, optically pure products the specific rotations of which agreed with literature data being obtained in 100% yield.

The advantage of the method that we have proposed in comparison with the known method of separating DL-alanine with the aid of benzenesulfonic acid [5] is the simplicity of the preparation of the salt DL-alanine p-toluenesulfonate, the rapidity of the method (2 h instead of 20 h), and the higher yield of product.

EXPERIMENTAL

The p-toluenesulfonic acid was obtained by a published method [6].

DL-Alanine p-Toluenesulfonate. A solution of 5 g of alanine and 9.7 g of p-toluenesulfonic acid in 20 ml of water was stirred for 1 h. On evaporation of the solvent, white crystals deposited with mp 155°C (decomp.). DL-Alanine p-toluenesulfonate does not dissolve in acetone, chloroform, or ethyl acetate on heating. It dissolves on heating in ethanol and 97% aqueous acetone and is readily soluble in water.

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TABLE 1. Separation of DL-Alanine p-Toluenesulfonate into D- and L-Alanine p-Toluenesulfonates

Amount added		Comp. of the solution		Amount of seed	Yield of D- and L-alanines, g
DL form	active form	DL form	active form		
5	(*D*)—0,1	5	(*D*)—0,1	(*D*) 0,01	(*D*) 1,8
1,79	0	4,99	(*L*) 1,6	(*L*) 0,01	(*L*) 2,2
2,1	0	4,98	(*D*) 2	(*D*) 0,01	(*D*) 2,8

D- and L-Alanine p-Toluenesulfonates. These were obtained in a similar manner to the preceding case: mp 175°C (decomp.), $[\alpha]_D^{25}$ −2° (c 4.5; water) for D-alanine p-toluenesulfonate, and $[\alpha]_D^{25}$ +1.96° (c 4.5; water) for L-alanine p-toluenesulfonate.

D-and L-Alanine p-toluenesulfonates dissolve in 97% aqueous acetone to a considerably smaller extent than DL-alanine p-toluenesulfonate.

Separation of DL-Alanine p-Toluenesulfonate into D- and L-Alanine p-Toluenesulfonates. With heating, 5 g of DL-alanine p-toluenesulfonate and 0.1 g of D-alanine p-toluenesulfonate were dissolved in 45 ml of 97% aqueous acetone. After the solution had been cooled, a seed of 0.01 g of D-alanine p-toluenesulfonate was added. After 2 h, crystals of D-alanine p-toluenesulfonate (1.8 g) were obtained. The filtrate was evaporated, 1.79 g of DL-alanine p-toluenesulfonate was added to the residue, and the whole was dissolved with heating in 45 ml of 97% aqueous acetone and the solution was cooled and treated with a seed of 0.01 g of L-alanine p-toluenesulfonate. After 2 h, crystals of L-alanine (2.2 g) had deposited. Then the experiment was repeated similarly, adding DL-alanine p-toluenesulfonate each time in an amount equal to the amount of active alanine salts that had been isolated.

Separation of D- and L-Alanine p-Toluenesulfonate into D- or L-Alanine and p-Toluenesulfonic Acid. A solution of 2 g of D- or L-alanine p-toluenesulfonate in 20 ml of water was passed through a column of KU-2 cation-exchange resin. The weight ratio of substance to resin was 1:10. The alanine was eluted with 1 N HN_4OH. The eluate was evaporated in vacuum to dryness, giving a crystalline precipitate of D- or L-alanine (0.68 g) with a yield of ~100%. It was recrystallized from methanol, mp 297°C; for D-alanine, $[\alpha]_D^{25}$ −14.7° (c 2; 5 N HCl), and for L-alanine, $[\alpha]_D^{25}$ +14.5° (c 2; 5 N HCl).

SUMMARY

A new method for separating racemic alanine into its optical antipodes via alanine p-toluenesulfonate has been developed.

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