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Abstract

Full Text

CHEMISTRY

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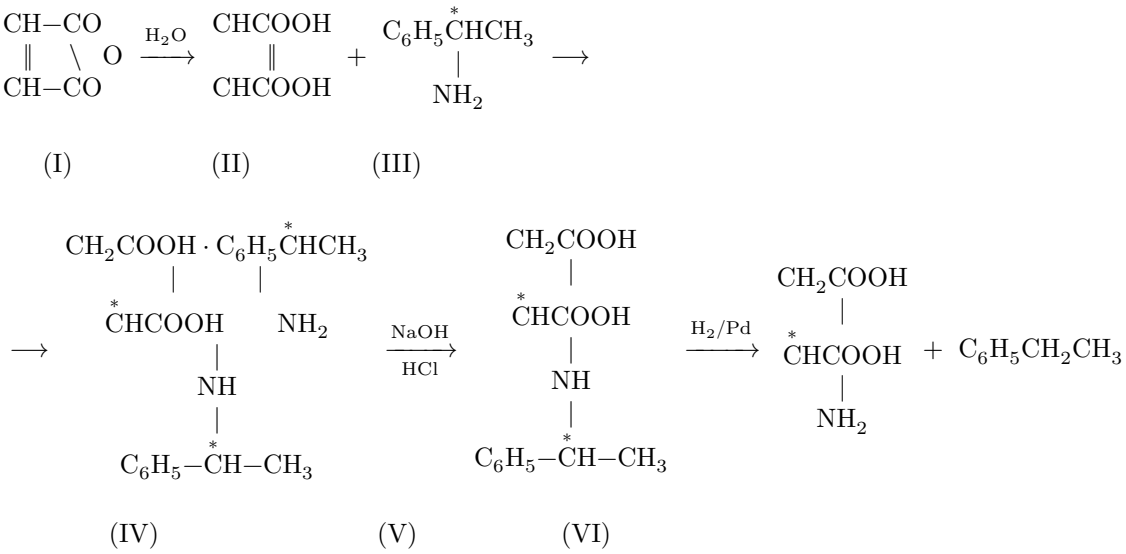
A NEW METHOD FOR OBTAINING OPTICALLY ACTIVE ASPARTIC ACID

Optically active aspartic acid, one of the first amino acids to have been isolated in the individual state, is usually obtained by hydrolysis of protein substances. In this process $L(+)$-aspartic acid is formed. Enzymatic methods for obtaining amino acids also lead to optically active aspartic acid. Possessing a high stereospecific action, enzymes make it possible to obtain amino acids with a high degree of optical purity. Thus, for example, DL-aspartic acid in the form of the chloroacetyl derivative was resolved into optical antipodes with the aid of renal acylase ([1]). D- and L-aspartic acids can also be obtained with the aid of other optically active substances. Among recent reports in this field one may note the work on the resolution of N-benzylaspartic acid with L-leucinamide ([2]). The authors succeeded in obtaining both forms of N-benzylaspartic acid in good yield.

In 1961 a report appeared on the synthesis of optically active α-amino acids from α-keto acids by interaction of the latter with optically active α-phenylethylamine ([3]). In that case the asymmetric center of the amino acid arose at the stage of hydrogenation of the C = N bond of the Schiff base. We obtained both antipodes of aspartic acid by adding optically active α-phenylethylamine to maleic acid. It should be noted that in our case the asymmetric center of the amino acid arises at the stage of addition of the optically active amine



(I) (II) (III) (IV) (V) (VI)

On addition to maleic acid of α-phenylethylamine with $[\alpha]_D^{20} - 39^\circ$, salt IV is separated in the form of a semicrystalline mass, representing a mixture of diastereomers, since salt IV has three asymmetric carbon atoms. The analogous compound with benzylamine is a racemate with m.p. 180°.

Decomposition of salt IV with alkali and acidification with hydrochloric acid to pH 2.7 leads to *N*-substituted aspartic acid V. Since this acid contains two asymmetric carbon atoms, upon the action

one form of α-phenylethylamine, the formation of two diastereomers may be expected. Since the phenylethylamine used by us is not of 100% optical purity, the formation of an inactive compound may also be expected. Indeed, upon addition of α-phenylethylamine with $[\alpha]_D^{20} - 39^\circ$ to maleic acid, two types of crystals of acid II precipitated upon acidification—large, well-formed crystals and small ones collected in the form of spheres. The crystals differ so sharply that, in small quantities, they can be separated with tweezers. In addition, the isomers formed have different solubilities and precipitate successively at several different pH values; therefore it is possible to separate them by gradual acidification. When an amine with $[\alpha]_D^{20} - 39^\circ$ is used, acid V is formed mainly in the form of large crystals; from it, by hydrogenation over palladium black, *D*(−)-aspartic acid with $[\alpha]_D^{20} - 22.4^\circ$ was obtained (c 0.05, 1 *N* HCl) (88% optically pure).

Upon further acidification, mainly the second form of acid V precipitates (small crystals), hydrogenation of which gives *DL*-aspartic acid.

Addition to maleic acid of α-phenylethylamine with $[\alpha]_D^{20} + 10^\circ$ leads to the formation of two crystalline forms of acid V in approximately equal amounts,

Fig. 1

Figure 1: Fig. 1

which precipitate successively at pH 2.7. In this case, upon hydrogenation of the form of acid V (large crystals), $L(+)$-aspartic acid was obtained, $[\alpha]_D^{20} + 4.83$ (C 0.4, 1 N HCl).

Hydrogenation of the second isomer leads to DL-aspartic acid.

In the transformations carried out, two molecules of optically active α-phenylethylamine participate, one of which adds across the double bond, while the other forms a salt. Whether partial asymmetric synthesis takes place here, or whether we are dealing with resolution of diastereomers, will be shown by our further investigations. Figure 1 gives the dispersion curves of optical rotation for N-phenylethylaminosuccinic (2) and aspartic acids (1).

Fig. 1

Experimental Part

α-Phenylethylamine was obtained by reductive amination of acetophenone according to Leuckart (5). Resolution into optical antipodes was carried out with tartaric acid in methanol (6).

Salt of phenylethylaminosuccinic acid (IV). 0.03 mole (2.6 g) of maleic anhydride was boiled for 30 min in 8 ml of water. Then 0.06 mole (6.9 g) of phenylethylamine with $[\alpha]_D^{20} - 39^\circ$ was added dropwise to the reaction mixture with stirring. The reaction proceeded with heating. The mixture was heated for 1 h. After cooling, the salt obtained was precipitated with acetone. Yield 8 g (85%).

Found, %:	N 7.96, 8.03
$C_{20}H_{26}O_4N_2$. Calculated, %:	N 7.82

(−) N-phenylethylaminosuccinic acid (V). 3 g of IV was dissolved in 5 ml of 15% sodium hydroxide. The phenylethylamine that separated was extracted with ether; the residue was acidified with hydrochloric acid to pH 2.7. Two forms of acid V precipitated successively—large crystals, 1 g (51%),

m.p. 179-181°, $[\alpha]_D^{20} - 13.43^\circ$ (R_f 4.5, 1 N HCl) and small crystals, 0.2 g (10%), m.p. 200-203°, $[\alpha]_D^{20} - 6.08^\circ$ (R_f 1.7, 1 N HCl), R_f 0.058 (butanol : water : acetic acid = 4 : 5 : 1). The large crystals were analyzed.

Found, %:	N 5.83, 5.69
$C_{12}O_5O_4N$. Calculated, %:	N 5.9

$D(-)$-aspartic acid (VI). 0.4 g of the N-substituted acid V with m.p. 179-181° was dissolved in a minimum amount of 30% alcohol and hydrogenated over palladium black at $t = 20°$ for 3 hours. The catalyst was filtered off and the solution was evaporated. This gave 0.3 g (100%) of $D(-)$-aspartic acid, 88% optical purity. M.p. 196-200° (in a sealed tube), $[\alpha]_D^{20} - 22.4°$ (C 0.5, 1 N HCl), R_f 0.14 (butanol : water : acetic acid = 4 : 5 : 1), R_f of the reference 0.14.

Found, %:	N 8.99, 8.94
$C_4H_7O_4N \cdot H_2O$. Calculated, %:	N 9.00

Literature data: m.p. 271° (in a sealed tube), $[\alpha]_D^{20} - 25.5°$ (C 2.3N HCl).

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named after M. V. Lomonosov

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Note: Figure translations are in progress. See original paper for figures.