A Temperature Effect in an Asymmetric Synthesis by Hydrogenolytic Asymmetric Transamination

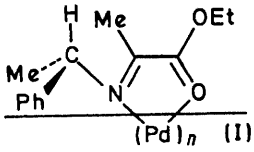
By KAORU HARADA* and TAKAO YOSHIDA

(*Institute of Molecular Evolution, Department of Chemistry, University of Miami, 521 Anastasia Avenue, Coral Gables, Florida* 33134)

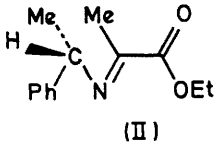
Summary The asymmetric synthesis of alanine by hydrogenolytic asymmetric transamination at varying temperatures shows a definite temperature effect.

OPTICALLY ACTIVE α-amino-acids have been synthesized from the Schiff bases of α-keto-acids with optically active α-alkylbenzylamines by catalytic hydrogenation and subsequent hydrogenolysis.[1-5] In a previous study in this laboratory, a solvent effect in the asymmetric synthesis was reported and a possible steric course was suggested.[2,4,5] During the course of further investigation on the steric course, a definite temperature effect was observed.

The Schiff bases of ethyl pyruvate with *S*-(−)-α-methylbenzylamine and with *R*-(+)-α-methylbenzylamine were hydrogenated at 1 atm. in alcohol by using palladium hydroxide on charcoal at temperatures from −20° to +65°. The resulting *N*-alkylalanine ethyl ester was hydrolysed with 6N-hydrochloric acid. The *N*-alkylalanine, isolated by the use of a Dowex 50 column, was hydrogenolysed by using palladium hydroxide on charcoal under relatively low pressure, 35—40 lb/in². The resulting optically active alanine was isolated by the use of a Dowex 50 column. The yields of alanine are in the range of 50—75%. A part of the alanine was converted into the 2,4-dinitrophenyl (DNP) derivative and the resulting DNP-alanine was purified by using celite column chromatography without fractionation of optical isomers.[1] The configurations and optical purities of DNP-alanine obtained are summarized in the Figure.



(I)



(II)

Under the conditions employed, the configuration of alanine obtained by the use of *S*-(−)-amine at lower temperatures was *S* (optical purity 60% at −20°). The optical activity decreased sharply with rise of the reaction temperature, becoming zero at about 17°. Then the configuration of alanine was inverted and the optical activity of *R*-alanine increased steadily until it reached a maximum at about 45—50° (optical purity 43% at 50°). Finally, the optical activity of the alanine decreased at higher temperatures. The results obtained by the use of *R*-(+)-α-methylbenzylamine were almost identical in magnitude with those obtained on *S*-(−)-α-methylbenzylamine, but were opposite in sign (Figure).

These findings may be explained on the basis of the steric course suggested earlier.[2,4,5] The preferred conformation of the substrate on the catalyst surface at lower temperatures could be structure (I). The five-membered-ring structure (I) could then be absorbed at the less bulky side of the molecule and hydrogenation could take place (two-step mechanism). The participation of structure (I) would decrease with rise of the reaction temperature and the participation of structure (II) would increase. At higher temperatures the preferred conformation could be structure (II), which is hydrogenated directly without forming a five-membered-ring substrate–catalyst complex (one-step mechanism). The fall of optical purity at high temperatures could be explained by the thermal agitation of the conformation of the substrate molecule.

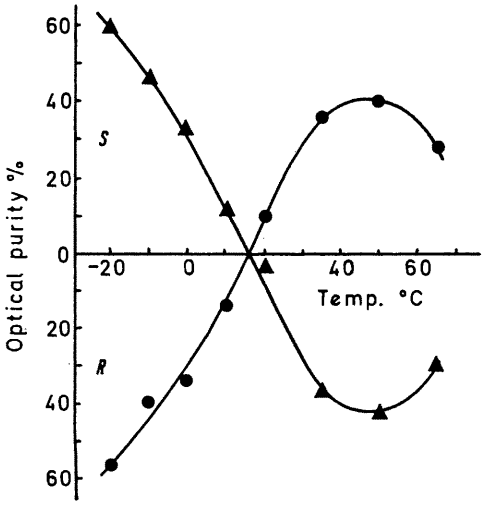


FIGURE. ● *DNP-Alanine prepared from* R-(+)-α-*methylbenzylamine.* ▲ *DNP-Alanine prepared from* S-(−)-α-*methylbenzylamine.*

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