HYDROGENATION OF 2-PHENYLACRYLIC ACID

Kotova M., Bachmaier J., Vyskočilová E., Červený L.

Department of Organic Technology, University of Chemistry and Technology, Prague 6, CZ 166 28, Czech Republic

Ibuprofen or (*RS*)-2-(4-(2-methylpropyl)phenyl)propionic acid (Fig. 1) is a nonsteroidal anti-inflammatory drug. It is typically found in many over-the-counter drugs. Ibuprofen is used to reduce fever and treat the pain or inflammation. Ibuprofen is a 2-arylpropionic acid derivative with a chiral center, which can be obtained by hydrogenation of corresponding acrylic acid. A racemic mixture or single enantiomer can be formed as a product based on the type of used catalyst and reaction conditions.
2-Phenylacrylic acid was chosen as a model substance to study the conditions for hydrogenation of 2-arylacrylic acids. Hydrogenation of 2-phenylacrylic acid was performed, and 2-phenylpropionic acid, which has a structure very similar to ibuprofen, was obtained as a product (Fig. 2).

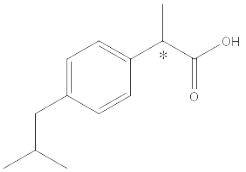

Fig. 1. Ibuprofen

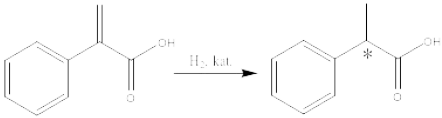

Fig. 2. Hydrogenation of 2-phenylacrylic acid

Hydrogenation of 2-phenylacrylic acid was performed using both supported metal catalysts (Ru/C Johnson Mathey 605, Pd/C Clariant) and chiral ruthenium catalysts. The influence of temperature (25-100 °C), pressure (2-8 MPa), amount of catalyst (1-10 wt. %), solvent type (methyl *tert*-butyl ether, methanol, hexane, dichloromethane) on the selectivity to the desired 2-phenylpropionic acid and reaction rate was studied. As we expected, the reaction rate increased with increasing temperature, pressure, and amount of catalyst. The selectivity was significantly dependent on the selected parameters. With increasing temperature and pressure, the relative concentration of 2-cyclohexylpropanoic acid increased. It can be explained because the latter mentioned compound was formed by the subsequent hydrogenation of the benzene ring of our desired product. Enantioselective hydrogenations of 2-phenylacrylic acid to (*R*)- or (*S*)-2-phenylpropionic acid using chiral ruthenium catalysts were performed at 50 °C and 2 MPa in methanol. The amount of catalyst was 5% by weight. The selectivity and reaction rate were significantly affected by the ligands present in the catalyst structure. The catalysts were compared concerning the parameter ee (enantiomeric excess) of obtained 2-phenylpropionic acid. Based on the obtained results, optimal conditions for the hydrogenation of 2-(4-isobutylphenyl)prop-2-enoic acid to (*RS*)-ibuprofen or single enantiomers might be proposed.