# TETRAHYDROINDOLE: PROMISING TECHNOLOGICAL DECISIONS

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The possibility of industrial production tetrahydroindole (THI) opens up, firstly, a new direction of pharmaceutical fine chemicals, as some of its derivatives are biologically and DNA-active substances, secondly, the prospect of inexpensive synthesis of indole stimulates an expansion of the production of stern amino acids.

Industrial implementation of THI technology is a joint development o Irkutsk Institute of Chemistry SB RAS and Lithuanian research company «Waldis». They sought to get an inexpensive indole as raw materials for the booming market of tryptophan. The originality of their decision consists in that an exotic tetrahydroindole, the market cost of which is reached 240 euros per gram, is transformed into a cheap raw material for the production of indole because reactants for its manufacture are the products of large-scale productions and readily available in the market.

This technology, which is based on the Trofimov reaction, was tested in vitro in a glass vessel and also at the pilot plant in a 6-liter and 10-liter steel reactors using industrial raw materials of companies «Azoty Tarnow» (Poland) and "Sayanyhimprom" (Russia), also industrial solvents of company "Arkema" (France). Chemical yield of THI to reacted cyclohexanone oxime (CHO) is 98% per pass with a product purity of 99.7%. Conversion degree CHO in this process is over 75%, but unreacted CHO can easy be recycled, since it remains with the solvent during a THI extraction.

Furthermore, unique technology of manufacture indole on an industrial scale was worked out in the research. Problem of dehydrogenation THI to indole was solved effectively using sulfide nano-catalyst. This technology allows to regulate nanostructures growth on the alumina substrate is by changing the filtration rate of the catalyst solution. Thereby, it is possible to get an optimal structure of the core of nano-catalyst and to achieve a high yield of indole (96%), almost 100% selectivity of the process and the product purity over 99.7%. Other known catalysts for dehydrogenation THI are obviously inferior to him in the efficiency. So, the yield of indole is 65.7% in process with catalyst containing chromium and rare-earth elements . There are 1-ethylindole (1.3%), 2-ethylindole (8.9%), unidentified products (5.8%) and tetrahydroindole (1.2%) in the reaction mixture. These substance have a similar boiling temperatures and solubility. Therefore, the desired reaction product (indole) is obtained in a complex mixture that is technologically inseparable. It is one of disadvantages of this method. Another disadvantage is the use of catalyst systems containing high concentrations of expensive palladium (1-1.5%) and rare earth elements (5%).

The catalyst system used by us has nano-sized nickel sulfide as the active ingredient. The uniqueness of this system is that such catalysts were not used for aromatization nitrogenous heterocycles with saturated nano-fragments up to present studies. According to conventional opinion, sulfur compounds were considered as catalyst poisons in relation to the heterogeneous dehydrogenation catalysts based on Ni, Pt, and Pd. It was believed that they lose activity in the presence of even trace of hydrogen sulphide, mercaptans and sulfides. The typical catalysts for such processes are the supported catalysts based on palladium and rare earth elements, and platinum and rhodium. Chrome, iron, molybdenum, copper, cadmium, zinc compounds or metalic nickel are used less commonly.

It is known that pyrrolidine is converted into pyrrole on a rhodium catalyst (0.5% Rh on $Al_2O_3$, $650^0$C) with a small yield (about 45%) of product, and it is decreased to 17% on chromia-alumina catalyst (33.5% $Cr_2O_3$ on $Al_2O_3$, $400^0$C). Also palladium on carbon (5% Pd/C, $200^0$C) can be used for dehydrogenation THI to indole. The same catalytical system is used for the aromatization of products of indole series(for example, 3,4-dihydro-carbolines and β-tetrahydro-β-carboline) with a small yield of β-carbolines (up to 25%) .

During the development of the new nano-catalyst using nickel sulfide as active component, it was found that the doping of ions $Na^+$ and $Cl^-$ increases a polarization of alumina amphoteric molecules and strengthens the interaction between the mesopores of supporting structure of catalyst and nickel sulfide. The affinity of the catalyst to nickel sulfide, in turn, affects the size and number of nanoclusters (NiS) on the fractal surface of supporting structure of catalyst (γ-$Al_2O_3$). A decrease in their size increases the yield of indole on this catalyst. It was found that the optimum size of the NiS nanocrystal clusters is 300-800 nm.