Green Chemistry: New Methods for Organic Synthesis and Applications

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Abstract:
Organic chemistry chemicals are some of the important starting materials for a great number of major chemical industries. The production of organic chemicals as raw materials or reagents for other applications is a major sector of manufacturing polymers, pharmaceuticals, pesticides, paints, artificial fibres, food additives, etc. Organic synthesis on a large scale, compared to the laboratory scale, involves the use of energy, basic chemical ingredients from the petrochemical sector, catalysts and after the end of the reaction, separation, purification, storage, packaging, distribution etc. During these processes there are many problems of health and safety for workers in addition to the environmental problems caused by their use and disposition as waste. Green Chemistry with its 12 principles would like to see changes in the conventional ways that were used for decades to make synthetic organic chemical substances and the use of less toxic starting materials. Green Chemistry would like to increases the efficiency of synthetic methods, to use less toxic solvents, reduce the stages of the synthetic routes and minimize waste as far as practically possible. In this way, organic synthesis will be part of the effort for sustainable development.

Keywords: *Old synthesis of Ibuprofen, New synthesis of Adipic Acid, The efficiency of the GREEN method of Adipic Acid*

1. Introduction

REACH (Registration, Evaluation, Authorisation and Restriction of Chemical substances) is the new European Community Regulation on chemicals and their safe use (EC 1907/2006). The aim of REACH is to improve the protection of human health and the environment through the better and earlier identification of the intrinsic properties of chemical substances. At the same time, REACH aims to enhance innovation and competitiveness of the European Union chemicals industry. Chemical industries all over the world are competing for innovation and safer products. Green Chemistry and Green Engineering provide the tools and alternative materials, processes and systems which will change not only the sustainability of the production of chemical materials, but also their environmental credentials by reducing toxicity and increase recyclability.

2. Old Synthesis of Ibuprofen

Ibuprofen was synthesized in 1960 by the pharmaceutical company Boot (England) and sold under the commercial name Aspro, Panadol and Nurofen. The synthesis of Ibuprofen was performed in six steps with the production of secondary by-products and waste. The main problem according to the scientists at the time was that this synthesis had a very “poor atom economy”.

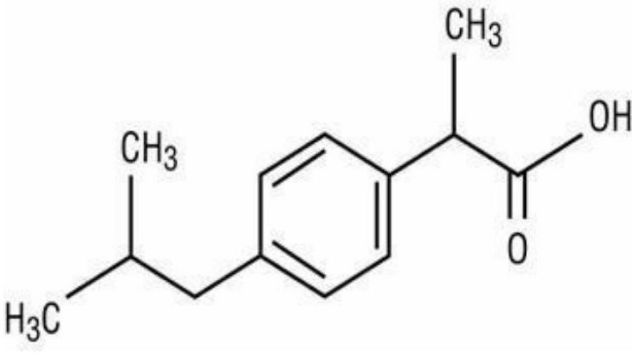

Figure: 1 Ibuprofen

A new synthetic route with only three steps and increased efficiency. The atoms of the starting chemicals are incorporated into the products of the reactions and waste is minimised. In both synthetic routes the starting chemical is 2-methylpropylbenzene, which is produced from the petrochemical industry. The innovation in the new method was in the second step. A catalyst of Nickel (Raney nickel) was used thus decreasing substantially the steps of the synthesis.

In the old synthetic route, each step had a yield of 90% so that the final product came to be 40% yield compared to the starting chemical. This resulted in the increased production of by-products as waste. The drug was produced annually (only in Great Britain) in 3.000 tones and we understand that substantial amounts of chemicals were lost as waste. Energy also was lost by the low efficiency of the reaction method. In the "greener' method of three steps the final yield is 77%, whereas the Raney nickel catalyst (Nickel, CO/Pt) can be recycled and reused. In the old synthetic route, the $AlCl_3$ used as a catalyst had to be thrown away as waste. The energy requirements of the second method were much lower than the first.

The new synthetic route of Ibuprofen is a classic example of how Green Chemistry ideas can influence to the better the industrial synthetic methods, not only from the point of economic efficiency, but also from the point of more effective science and technology methods

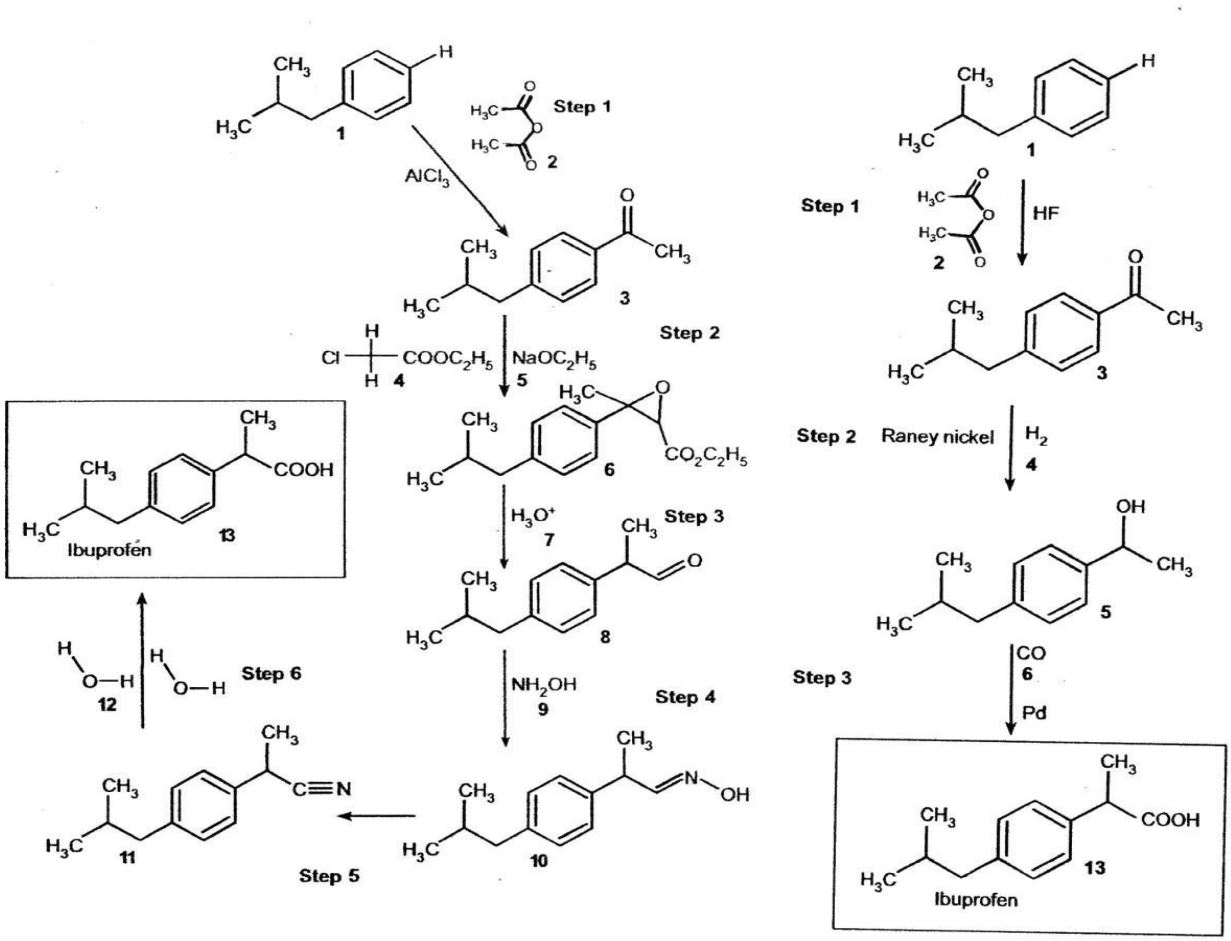

Figure: 2 the two synthetic routes of Ibuprofen

3. New Synthesis of Adipic Acid

Adipic acid is a very important starting material for Nylon-6,6 and cakehole (which is used in the pharmaceutical and pesticide industries). Adipic acid is produced annually in more than 2.000 million kg.

The industrial production of Adipic acid used benzene as a starting material. Benzene is one of the basic chemicals for industrial reactions and a solvent. It is known that derives mainly from the refining processes of the petrochemical industry. Be3nzene is also known for its carcinogenic properties (it causes leukemia to highly exposed workers). Afterwards the starting material became cyclohexanone or a mixture of cyclohexanone and cyclohexanol. For the oxidation process it was used nitric acid, producing toxic fumes of nitric oxides, NOx, which are also contributors to the greenhouse effect and the destruction of the ozone layer in the stratosphere. It was Inevitable that the method had to be changed again with more environmentally benign reactions.

Finally, chemical engineers and synthetic organic chemists researched for alternatives. The "greener" method of adipic acid uses a new generation of catalysts. The starting chemical is cyclohexene and its oxidation is performed by 30% hydrogen peroxide (H_2O_2). The catalyst is dissolved in a special organic solvent (Aliquat 336). The catalyst is a salt of the metal Wolframs or Tungsten (W) [Tungsten catalysts (Na2WO4 /KHSO4/ Aliquat 336).

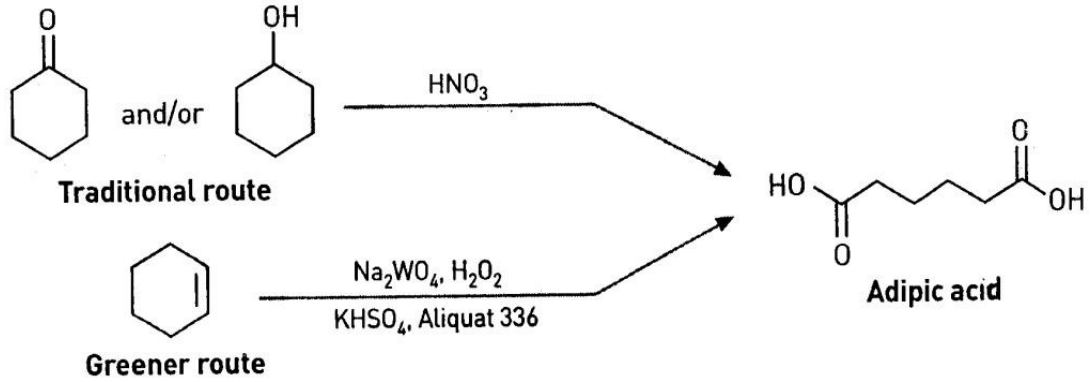

Figure: 3 adipic acid

4. The Efficiency of the Green Method of Adipic Acid

The Adipic acid synthesis by the two methods can be used as a good example for the "atom economy" (atom or mass efficiency) of reactions in synthetic routes.

A. **The "old", traditional method** for the Adipic acid with cyclohexanone/cyclohexanol oxidation by Nitric acid. In the presence of catalyst copper/vanadium [Cu(0.1-05% & V (0.02-0.1%)] The reaction is:

$$C_6H_{12}O + 2\ HNO_3 + H_2O \square C_6H_{10}O_4 + NO_x\ (NO, NO_2, N_2O, N_2)$$

In this method the negative aspect is the release of nitrogen oxides. The Yield is 93% If we take into account the mass of the atoms, for reactants and product, we can have the following calculations:

Product mass = (6C) (12) (10H) (1) (4O) (!6) = 146 g Reactant mass = (6C) (12) (18H) (1) (9O) (16) (2N) (14) = 262 g

Yield or Mass efficiency of the reaction, is the ratio of product/reactants X 100 = 146/262 X 100 = 55,7%

B. The new "greener" method The preparation from cyclohexene oxidized by H_2O_2 in the presence of the catalyst $N\alpha_2WO_4.2H_2O$ (1%) with solvent Aliquat 336 [CH_3 (ν-$C_8H_{17})_3N$] HSO_4 (1%)].

$$C_6H_{10} + 4\ H_2O_2 \xrightarrow{\text{catalysts}} C_6H_{10}O_4 + 4\ H_2O$$

The new "greener" method does not produce toxic waste and its yield is 90%.

Product mass = (6C) (12) (10H) (1) (4 O) (16) (2N) (14) =146 g

Reactant mass = (6C) (12) (18H) (1) (8 O) (16) = 218 g **Reaction**
Mass efficiency = 146/218 X 100 = 67%.

The reaction mass efficiency of the "greener" method is 11% higher than the first method.

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