A CARTRIDGE REACTOR FOR A FLOW-TYPE LABORATORY HYDROGENATION APPARATUS

The invention relates to a cartridge reactor for a flow-type hydrogenation apparatus, wherein the reactor has a casing equipped with an inlet, an outlet and a closed expanded portion enclosing a reaction volume spreading between the inlet and the outlet.

Hydrogenating processes (from now on, hydrogenation) are used in the chemical synthesis of organic compounds: hydrogen is incorporated into starting molecules – optionally in the presence of a catalyst – at given positions and thereby qualitatively different molecules are generated from the starting molecules. Hydrogenation is widely used by the modern chemical industry (including also pharmaceutical industry). Accordingly, a variety of apparatuses, so-called hydrogenation reactors have been developed for implementing the hydrogenation. These apparatuses serve, however, for carrying out generally hydrogenation on industrial scale and hence one of their common features is the relatively large size and the immobility originating from the size.

Due to the rapid spread of combinatorial chemical methods, nowadays the synthesis used by the pharmaceutical industry and the laboratory assaying are increasingly becoming the potential application fields of hydrogenation. In case of these new fields of application the emphasis is laid on the derivatisation of several (or many) substances in tiny amounts separately but rapidly and, if possible, in an automated manner, instead of preparing a single substance in a great amount. The hydrogenation apparatuses that satisfy the requirements concerned should have a small size and, in case of need, be suitable for accomplishing several, even highly different types of homogeneous or inhomogeneous catalytic hydrogenation within a short period of time. In order to achieve the realizability of the various types of reactions rapidly after each other, besides a fast change of the substance to be hydrogenated (from now on, sample material) – especially in case of a selective catalytic hydrogenation process – there is also a need for the exchange of the catalyst itself which, if possible, should be accomplished without interrupting the operation of the hydrogenation apparatus. Therefore, the catalyst should be easily accessible

and rapidly removable, and it should promote the chosen hydrogenation reaction at the highest possible efficiency in a relatively small volume.

It is a well-known fact, that the course of hydrogenation reactions is greatly affected by the temperature and pressure existing within the reactor used for accomplishing the reactions, as well as the extent to which the sample material and the gaseous hydrogen (together reactants) added to the sample material mix. In case of a continuous flow-type hydrogenation, the length of the time period spent by the reactants in the reactor, that is the so-called residence time is also of special importance: the longer it is, the more complete the planned hydrogenation reaction is. By providing a suitable flow resistance within the reactor, the level of mixing and the residence time can be significantly increased which finally improves the yield of the hydrogenation process.

U.S. Patent No. 4,847,016 discloses an industrial scale, flow-type heterogeneous hydrogenation in the presence of a catalyst. The catalyst is fixed on a support being insoluble in a sample material or in a solution thereof (from now on, sample solution), and the thus fixed catalyst suspended in the sample material/solution is fed into the reactor together with the hydrogen gas essential for the reaction. The reactor is packed with a geometrically regularly arranged elements of a material chemically inert to the reactants and the catalyst particles fed thereinto. The packing elements are preferably spheres of glass or ceramic. The geometrical structure created by the packing elements significantly increases the mixing of the reactants with each other and with the catalyst particles. Furthermore, as a consequence of the flow resistance due to the geometrical structure, the residence time of the sample material within the reactor increases. A disadvantage of this solution is, that part of the catalyst particles leaves the reactor with the liquid-phase reaction product (that is the hydrogenated product), and hence its recovery requires the usage of various additional units.

International Publication No. WO 2004/007414 also describes an industrial scale flow-type hydrogenation process and an arrangement for accomplishing the process. In this solution, the catalyst being suspended also in the liquid-phase sample material is fed into the reactor in the presence of hydrogen gas required for the reaction. To hinder the transport of the catalyst from the reactor or to reduce its transport to a minimum, a device which mechanically retains the catalyst particles and transmits the reactants/hydrogenate is arranged within the reactor. The said device is provided by a bulk material, a fabric

material, an open-celled foam or a packing used in distillation columns. The reactor is fixedly coupled into the hydrogenation system, and hence when the mechanical catalyst retaining ability of the device exhausts, its replacement requires the disassembling of the hydrogenation system. Furthermore, as a consequence of the size differences of the suspended catalyst particles said device will retain only a part of the catalyst within the reactor, and therefore in this solution the full clearance of the hydrogenate from the catalyst also requires the application of an additional unit(s).

The fixation of the catalyst on a support and then its addition to the sample material or the sample solution in a suspended form is fully acceptable when industrial scale hydrogenation apparatuses are considered. As the experiments show, this is, nevertheless, unsuitable (eg. because of the tiny (about 0.5 mm in size) cross-sections of the liquid transporting elements used in the apparatus) in the case of a laboratory scale hydrogenation apparatus: sooner or later the suspended catalyst particles clog the apparatus' liquid transporting elements which might result in a stop, or in a serious case, a failure of the apparatus.

In view of the above, the aim of the present invention is to construct such a small-sized hydrogenation apparatus which meets the requirements appearing in continuous laboratory scale hydrogenation (eg. replaceability when different substances are synthesized after each other and provision of long residence times), as well as makes all kinds of handling of the catalyst, that is its suspending, feed and optionally its removal from the hydrogenate, unnecessary.

The above aim is achieved by creating a cartridge reactor, which is formed in a laboratory size, and its reaction volume is at most 10 cm^3 and is filled with an immobilized packing medium that increases flow resistance and facilitates mixing, and the inlet and the outlet are formed with a structure enabling detachable connection to the hydrogenation apparatus.

Preferably, the packing medium comprises a catalyst.

Preferably, the inner diameter of the expanded portion is 5 to 10 times as large as that of the inlet, more preferably the inner diameter of the expanded portion is at most 10 mm.

Preferably, the inlet and the outlet are formed as the male elements of a flare joint.

Preferably, the immobility of the packing medium is achieved by filter elements arranged in opposite ends of the expanded portion and extending in a full cross-section thereof and a packing of individual particles, wherein wherein the size of the openings of the filter elements is smaller than the average particle size of the packing. The packing medium is preferably made up of a granulated catalyst.

In a possible further embodiment of the cartridge reactor according to the invention, the immobility of the packing medium is achieved by providing a packing medium having a spatially contiguous geometrical structure.

The invention will now be explained in detail with reference to the accompanied drawing, wherein Figure 1 shows a sectional view of a replaceable cartridge reactor according to the invention in its assembled form, along its longitudinal axis.

Figure 1 illustrates a cartridge reactor 10 for a laboratory scale hydrogenation apparatus. The cartridge reactor 10 has a casing equipped with an inlet 18 and an outlet 20, wherein the casing is formed from an envelope 12 and an end-plate 14 being combined preferably by means of a pressure-tight connection, eg. a welding or a brazing/soldering joint 15. The casing of the cartridge reactor 10 is preferably pressure-tight and is made of acid- and corrosion-resistant steel, and encloses a reaction volume 16. When assembled, the cartridge reactor 10 forms preferentially a tubular (preferably a cylindrical) element.

The cartridge reactor 10 is formed with a structure which enables the cartridge reactor 10 to be connected into the flow path a flow-type laboratory scale hydrogenation apparatus. Accordingly, in a possible embodiment of the cartridge reactor 10, the outer surfaces of the inlet 18 and the outlet 20 are provided with threads 22 and 24, respectively, for the connection with the laboratory scale apparatus via a flare joint equipped with a proper sealing. Other detachable joining mechanisms (eg. an instant fitting system made of acid- and corrosion-resistant steel) known by a person skilled in the relevant field can equally be used for the replaceable connection of the cartridge reactor 10 into the flow path.

The cartridge reactor 10 is equally appropriate for performing homogeneous and heterogeneous hydrogenation. An immobilized packing medium 29 (that is, a medium being incapable of leaving the cartridge reactor 10 together with the through-flowing sample solution) is arranged within the reaction volume 16 of the cartridge reactor 10 which significantly increases the residence time spent by the fed sample solution within

the cartridge reactor 10. The immobility of the packing medium 29 is accomplished eg. by arranging filter elements 26, 28 in the cartridge reactor 10 at the opposite ends thereof, which filter elements 26, 28 do not transmit the packing medium 29. Another way of assuring the immobility of the packing medium 29 is that it is fabricated with a spatially contiguous porous geometrical structure, eg. in the form of a (thick) web built up of a plurality of fibers.

In case of a homogeneous hydrogenation, the packing medium 29 contains no solid catalyst, however, it exerts an increased flow resistance (relative to the one exerted by the empty reaction volume 16) that facilitates the hydrogenation reactions due to the intensive mixing of the fed sample solution and the hydrogen gas.

In case of heterogeneous reactions, the packing medium 29 comprises eg. solid catalyst particles, a web or a mesh of fibers coated with a catalyst or made of a catalyst, tiny beads coated with a catalyst, or any combination thereof, wherein the catalyst supporting elements are preferably inert to the hydrogenation reaction to be carried out. A variant of the packing medium 29 comprising a plurality of tiny beads being in contact with each other and a fine powder of a catalyst filling the empty contiguous space among the beads is especially preferred. Any catalyst can be used as the packing medium 29 or as a part thereof; the catalyst actually used is chosen in accordance with the given hydrogenation process.

The inlet 18 and the outlet 20 are preferentially formed with identical inner diameters, which inner diameter, for maintaining continuously a homogeneous material distribution in cross-section, preferably corresponds to that of the liquid transporting elements used in the hydrogenation apparatus. Accordingly, the inner diameter of the inlet 18 is 0.05 to 1.0 mm, preferably 0.5 mm. The inner diameter of the cartridge reactor 10 is preferably 5 to 10 times as large as that of the inlet 18, it is preferably 4 to 6 mm. The length of the cartridge reactor 10 is 30 to 100 mm, preferably 40 to 60 mm.

The fabrication of the cartridge reactor 10 according to the invention is extremely simple and inexpensive. The envelope 12 equipped with the inlet 18 and the end-plate 14 having the outlet 20, both of the cartridge reactor 10, are manufactured on a production line by a simple mechanical working. After having formed the envelope 12, first the filter element 26 is inserted into the reaction volume 16 and then the packing medium 29 is filled onto it. Then the filter element 28 is arranged on top of the packing medium 29, the

end-plate 14 is fitted on the envelope 12 and then these last two elements are combined by a suitable manner, eg. by means of welding, brazing or laser fusing. As a next step, the cartridge reactor 10 is provided by threads 22 and 24 on its inlet 18 and outlet 20, respectively, and the cartridge reactor 10 is closed in an airtight manner for a later use by screwing a cap on each of the threads 22, 24. The airtight closure of the cartridge reactor 10 can also be accomplished by applying a closing foil onto the inlet 18 and the outlet 20 each. Within the framework of a serial fabrication of the cartridge reactor 10, the continuous monitoring of the packing medium's 29 quality (for example, of the maintenance of a constant amount of the catalyst included in the packing medium 29) is also possible. In this way a large-scale manufacturing of such replaceable cartridge reactors 10 is achieved, which reactors after being installed into the flow-type laboratory scale hydrogenation apparatuses allow the production of hydrogenated product with identical characteristics, provided that the other parameters affecting the course of hydrogenation are left unchanged.

CLAIMS

1. A cartridge reactor (10) for a flow-type laboratory scale hydrogenation apparatus, wherein the reactor comprises a casing equipped with an inlet (18), an outlet (20) and a closed expanded portion enclosing a reaction volume (16) extending between the inlet (18) and the outlet (20), *characterized in* that it is formed in a laboratory size, and its reaction volume (16) is at most 10 cm^3 and is filled with an immobilized packing medium (29) that increases flow resistance and facilitates mixing, and the inlet (18) and the outlet (20) are formed with a structure enabling detachable connection to the hydrogenation apparatus.

2. The cartridge reactor (10) according to Claim 1, *characterized in* that the packing medium (29) comprises a catalyst.

3. The cartridge reactor (10) according to Claim 1, *characterized in* that the inner diameter of the expanded portion is 5 to 10 times as large as that of the inlet (18).

4. The cartridge reactor (10) according to Claim 3, *characterized in* that the inner diameter of the expanded portion is at most 10 mm.

5. The cartridge reactor (10) according to Claim 1, *characterized in* that the inlet (18) and the outlet (20) are formed as the male elements of a flare joint.

6. The cartridge reactor (10) according to Claim 1, *characterized in* that the immobility of the packing medium (29) is achieved by filter elements (26, 28) arranged in opposite ends of the expanded portion and extending in a full cross-section thereof and a packing of individual particles, wherein the size of the openings of the filter elements (26, 28) is smaller than the average particle size of the packing.

7. The cartridge reactor (10) according to Claim 1, *characterized in* that the immobility of the packing medium (29) is achieved by providing a packing medium having a spatially contiguous geometrical structure.

8. The cartridge reactor (10) according to Claim 6, *characterized in* that the packing medium (29) is made up of a granulated catalyst.