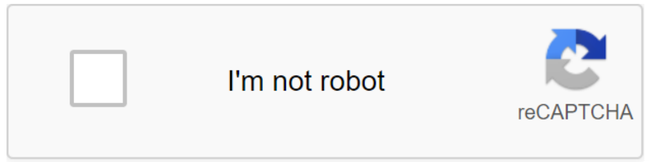

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The turbulent flow through carbon felt, on which catalysts were supported contributed to scaling to production levels, as it awarded reactors large-scale independent, flow plugs like the distribution of residency time and high mass transmission rates. Equipping cells with micro-reference electrodes allows the transfer of reaction conditions, first developed in batch systems, to continuous flow reactors. Catalysts prepared by the nascent impregnation of the humidity of metallic salts in a lightly oxidized carbon supports, were easily easy 3A self-sufficient two in one whole cell biocatalitis, combining ketorreduca and cofactor regenerative enzyme activity, was developed and successfully used for synthesis (R)-3-quinuclidinol with a 3-fold increase in reaction rate over local enzymes at low load of biocatalitis (∼1.65%), excellent enoricion, impressive substrate concentration 486 g L-1, as well as high yield space-time (R)-3-quinuclidinol up to 1505.5 g L-1 d-1 which was the highest ever reported. These results showed that the newly developed self-sufficient biocatalite may be useful for synthetic and industrial applications in synthesis (R)-3-quinuclidinol, essential for the production of soyphenacin, revatropate and acyndinia, with a better clinical outcome than those currently available. Page 4 (S)-2-Chloro-1- (2.4-dichlorophenyl) ethanol (3) is a chiral intermediate in the synthesis of luliconazole ((R)-E-1). Here we report on the new bioreparation 3 by bioreducting 2-chloro-1- (2.4-dichlorophenil) ethanolone (2) using recombinant Escherichiichi coli expressing LK08, a ketorodoctase mutant from Lactobacillus kefiri as biocatalitis. To improve the performance of the process, the conditions of response to biotransformation, including pH, temperature and concentration of isopropanol and NADPH, as well as the number of recombinant E. coli cells, were optimized. When the ensimatic process was carried out on a scale of 300 g in optimized conditions, ketone 2 was completely converted into chiral alcohol 3 with a product value of ee 99%. In addition, 3 was isolated and used for the chemical synthesis of luliconazole with 38% yield and 99% ee. This study is an efficient and cost-effective chemo-enzyme manufacturing process (R)-E-1. Page 5Worked and improved second-generation synthesis of the Nav1.7 GDC-0276 inhibitor based on first-generation synthesis experience. The first-generation synthesis was carried out with the help of SNAr's regioslective reaction to the advanced starting material t-butyl 5-chloro-2.4-difluorbenzoate with 1-adamantanemetaneman. In the newly developed second-generation synthesis, the significantly improved SNAr regioslective response was performed on the easily accessible source material 1-chloro-2.4-diphtorbenzene, followed by the installation of a

group of carboxylates of electrophilic aromatic bromination and palloxycarbonylation of palladium-catalise. The subsequent reaction of the Suzuki-Mia cross compound was then telethanized directly into the hydrolysis of phase transmission. Amida resulting acid intermediate with 1-Azetydine sulfamide, in turn, provided GDC-0276 in high total yield and purity of a scale of 100 kg. Page 6LEARN about THESE METRICSArticle Views are COUNTER-compatible amount of full text article download from November 2008 HTML) in all institutions and individuals. These metrics are regularly updated based on usage prior to the last days. The quotes number of other articles with reference to this article are calculated by Crossref and updated daily. Find more information on Crossref citation counts. Altmetric Attention Assessment is a quantitative indicator of the attention that a research article has received online. Clicking on the doughnut icon will download the page to altmetric.com with more information about the account and the presence of social media for this article. Learn more about Altmetric Attention Score and how the score is calculated. Page 7 Supplemental production refers to production methods that are used to create 3D (3D) structures, adding a certain material step by step to support. Currently, these production methods can be more material- and cost-effective than conventional methods and allow for the production of a wide range of 3D structures using computer design (CAD). A wide range of materials can be additively manufactured (AM), resulting in specific properties and a very diverse structure, making them a promising matrix for use as carriers of enzymes. The variety of materials makes it possible to choose materials with the properties necessary for specific biocatalytic processes. This is especially true of hybrid reactor concepts, where several operations, including catalytic reactions and downstream processes, are combined into a single vehicle. For the enzymatic decarboxylation of ferulic acid, polyethylene terephthalate (PET) was selected as an additively manufactured carrier material for the immobilization of phenolic acid decarboxylase (PAD) from Microbacteria Columtinium. The genetic fusion of PAD with anchor peptides allowed for adorptive immobilization on PET. Starting with immobilized activity of 0.39 and 0.19 U m-2 and conversion 19.2 and 3.7% after 2 hours of optimize peptide and sequence of the spacer between the anchor Peptide and PAD led to immobilisates with activity up to 1.80 and 0.41 U-2 and conversions of 59.9 and 3.9% after 2 hours as part of this study integrating the removal of the product in situ, included extraction with n-heptan, a change in the hydrophobic surface of the PET and a conversion of 88.0 and 3.8% after 2 hours could be observed. Page 8 The widespread use of amydin and guanidin bases in synthetic chemistry deserves a deep understanding of their chemical properties. The propensity of these reagents to hydrolysis in mild conditions and to generate aminelactam and amineunei, respectively, was not adequately described earlier. During the synthesis of urifosbuvir (MK-3682) we became aware of this responsibility for the 1.8-diazabicyclo 5.4.0-undec-7-ene (DBU), watching the formation of an unexpected and traced the root cause of the low level of N-(3-ainopropil)-caprolactam, present in the commercial bottle. A controlled study of stability for two months at 25 degrees Celsius showed that, above the water threshold, DBU is steadily hydrolyzed over time. Hydrolysis tariffs for DBU, 1.5-diazabicyclo 4.3.0-non-5-ene (DBN), 7-methyl-1.5.7-triazabicyclo 5-ene (MTBD), 1.5.7-triazabicyclo 4.4.0'dec-5-ene (TBD), and N.N.N. N,N'-tetramethylguanidine (TMG) in organic, aqueous, mixed solvents were then measured in order to gain a more general understanding of what conditions should be avoided in order to maintain their integrity. Our findings show that these bases are hydrolytically unstable in unsettled and very basic solutions, but become significantly more stable in buffer solutions at pH values below 11.6.Page 9A scalable process for PF-06651600 (1) was developed thanks to the successful provision of the first generation synthesizer. Synthesis highlights include: (1) replacing the expensive PtO2 with a less expensive 5% Rh/C catalyst for pyridine hydrogenation, (2) identification of the crystallization of diasteromer salt to isolate the enantiomesically pure cis isomer directly from the racial mix of cis/trans isomers, (3) high-yielding amide through Schutten-Baumann conditions and (4) the critical development of a reproducible crystallization procedure for stable crystalline salt (1) TsOH), which is suitable for long-term storage and pill development. All chromatographic cleaners, including two chiral chromatographic divisions of SFC, have been eliminated. Combined with other improvements at each stage of synthesis, the overall yield was increased from 5% to 14%. Several multi-kilogram APIs were delivered to support clinical trials. Page 10 Is Improved and The Practical Method is reported here for access to 3,4.5 -trifluoro---1.1-biphenyl-2-amin (1), a key intermediate for Fluxapyroxad. The total yield for preparation 1 was 73%, with a purity of 99.88%, after a three-step process. More importantly, this process has been improved in the production of Suzuki-Mia compound biphenyl compounds, allowing the catalyst to load as low as 0.04 maul. This method could provide an economic and environmentally friendly process leading to broad prospects for industrial application. Page 11Page 12Integrated continuous production has become a promising device for the rapid production of active pharmaceutical ingredients (API). This report reports on a newly developed continuous flow system for the rapid production of celecoxib, a selective non-steroidal anti-inflammatory drug. This approach has been proven generally to synthesize several alkyls and aril replace In order to minimize the tedious process process Intermediate/products, we have developed a continuous platform to extract flow and separate the platform to perform the entire sequence of reactions as a result of short living time with good yields. The current process was further extended to the gram-wide synthesis of the API associated with COX-2, viz. celecoxib, in the process of continuous flow. Page 13 High-end experiments is a method for screening multiple reaction conditions parallel to micro or nanoscrate without depleting precious start materials. However, assembling a comprehensive screening kit often involves the distribution of large numbers of solid reagents with a variety of physical properties in small quantities. Automated distribution of solids, especially on a submilligram scale, has long been a problem without practical and reliable solutions. This paper describes the use of our newly developed chemical-coated bead technology to provide a one-size-fits-all approach to a solid processing problem. This technology, combined with an automated solid dosing platform or calibrated measuring spoons, can distribute submilligrams of a variety of solids with efficiency and adequate accuracy. Page 14Soling reliable synthesis 2-methyl-2-4--3-methyl-2-oxo-8-(quinolin-3-il)-2.3-dihydro-1H-imidaso 4.5-kekinolin-1-il-phenyl-propionilie (dactoly) on a commercial scale. The key step is the Pd-Catalise Suzuki Compound 2-'4-(8-bromo-3-methyl-2-oxo-2,3-dihydro-1H-imidazo-4.5-c'quinolin-1-yl)-phenyl-2-methyl-propionitrille-to-3-quinolinic acid. Particular attention is paid to reducing the amount of pd catalyst used in Suzuki and cleaning up the raw drug, including the removal of traces of Pd.Page 15Page 16 Practically and financially viable use of immobilized enzymes in the production of pharmaceutical and bulk chemicals requires highly catalytically active enzymes and effective mass transmission of substrate to the active area. The significant cost of immobilized enzymes also requires increased reuse of enzymes to keep operating costs down. The degree of reuse of immobilized enzymes depends on parameters such as long-term enzyme stability in process conditions, media integrity and depletion due to mechanical stress, as well as ease of operation and recovery at scale. In this case, we report the use of the SpinChem (RBR) rotating reactor for Novozim 435 mediated kinetic resolution (cis)-isoppil 3-aminecyclolexancarboxilat as an alternative to the traditional reaction using free-flowing immobilized lipases in a conventional batch reactor. Reuse has been studied in addition to parameters such as the type of immobilized enzyme, loading, arousal speed, temperature and scalability. Using SpiChem RBR technology, we found that the processing of the immobilized enzyme was easy with preserved enantioslectiveness and catalytic activity. Final Final the process was successfully demonstrated on a scale of 1 kg with 39% isolated yield and 98.8% enantiometric purity. Page 17LEARN ABOUT THESE METRICSArticle Views are a COUNTER-compatible amount of the full text of the download article from November 2008 (both PDF and HTML) across all agencies and individuals. The quotes number of other articles with reference to this article are calculated by Crossref and updated daily. Find more information on Crossref citation counts. Altmetric Attention Assessment is a quantitative indicator of the attention that a research article has received online. Clicking on the doughnut icon will download the page to altmetric.com with more information about the account and the presence of social media for this article. Learn more about Altmetric Attention Score and how the score is calculated. Page 18 This article refers to 53 other publications. 1Han, S.; Ma, C. Y.; Mahmoud, T.; Penchev, R.Y.; Roberts, KJ; Morris, J.; Ozkan, L.; White, G.; Grieve, B.; Hall, A.; Boozer, P.; Gibson, N.; Keller, P.; Shuttleworth, P.; Price, CJ In the process of monitoring and controlling supersaturation in the seed cooling package of glutamic acid crystallization: from the laboratory to the industrial experimental plant. Org. Process Res. 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Clicking on the doughnut icon will download the page to altmetric.com with more information about the account and the presence of social media for this article. Learn more about Altmetric Attention Score and about how the score is calculated. Page 21Analytic spectrograms and data, including 1H NMR, 13C NMR, HRMS and HPLC HPLC connections 6, 6a, 7, 7a, 8, 9, 9a, 10, 1 (OSA), original OCA, Imp-1, Imp-2, Imp-3, Imp-4, Imp-5, Imp-6, Imp-7, Imp-8, Imp-9, Imp-10, Imp-11, Imp-12, Imp-13 and Imp-14 (PDF)Page 22Page 23When oiling-out occurs, a second liquid phase is formed, and the composition of the parent phase, where the crystals are nucleied and grow, changes because the target material and impurities are distributed in each according to their own distribution factor. Although oiling is generally considered undesirable, if oiling changes in the composition of impurities and reduces the content of impurities in the maternal phase, then it may be effective for cleaning. In this article, we investigated the effect of oiling on the cleaning of the intermediate compound and found the following: the time of addition of long water and a large number of seeds each reduced the content of impurities A (Imp-A) and Imp-B. On the other hand, the Imp-C content has not been changed for a long time adding water and has been increased with a large number of seeds. Technological data show that oiling is suppressed by a large number of seeds. These results suggest that the oilings altered the composition of the maternal phase and prevented the inclusion of Imp-C in the crystals. Our findings can be developed into a new cleaning technique using oiling during crystallization. Page 24Detinmetion control of the crystallization process requires a clear understanding of the kinetics of nucleation. The interpretation of the secondary nucleation threshold (CST) of this crystallization process in optimized hydrodynamic conditions can highlight the impact of critical process variables on the distribution of product particle size (PSD). This paper proposes a new approach in the development of an industrial crystallization process, in which a quantitative link has been developed between the crystallization of the structural cooling of the batch and the force of the turbulent haircut fluid (TSS). Experiments include crystallization of paracetamol solution in isopropanol. A new method was adopted, in which a large single paracetamol seed crystal was held still in the agitation reactor. Using velocimetric imaging of particles, constant TSS was obtained at various scales, leading to permanent SNT due to the reproduction of crystalline nuclei. This led to better control over the crystallization process, which eventually led to a consistent PSD, regardless of scale. Each scale had a single PSD, which was evident when scanning electron microscopy. The investigation explains that IT is possible to control PSD on a variety of scales by controlling SNT using hydrodynamics. It is suggested that this is a reliable approach in the process of crystallization by breeding crystal cores, which gives a potential opportunity to improve the production process. Page 25Scal projections from continuous micro flow (laboratory) to (pilot or production) are important, but not trivial. To overcome the need for labor-intensive testing on an experimental or production scale, this work is a model approach based on previous laboratory experiments. However, it also improves understanding of the involved chemical process. The process of highly exothermic organetal reaction is being fully developed. Kinetic studies on a laboratory scale using stationary FT-IR measurements form the basis for a systematic approach to scaling. Subsequently, scaling from microreactors (internal diameter 0.5 mm) to milli-scale experimental reactors (internal diameter 2 mm) by increasing the diameter of the channel and the speed of flow was investigated. Model-based scaling forecasts are presented, including heat and mass balances. Page 26 This article refers to 37 other publications. 1Jakki, J.; Colle, A. Enantiomers, Racial Comrades and Resolutions; John Wylie and Sons, 1981.2K'llges, T.; Vetter, T. Model-based analysis of continuous crystallization/reactionary processes separating the conglomerate forming enantiomers. Cryst. Growth Des. 2017, 17 (1), 233- 247, DOI: 10.1021/acs.cgd.6b01487 3Chhabra, N.; Aseri, M.L.; Padmanabhan, D. Review of Drug Addiction and Its Significance. Int. J. Appl. basic Med. Res. 2013, 3 (1), 16-18, DOI: 10.4103/2229-516X.112233 4Maier, N. M.; Franco, P.; Lindner, W. Separation of enantiomers: Needs, Challenges, Perspectives. D. 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