

Review Article

Reactive Chromatography: A Review of Process Technology

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Abstract: Chemical Industries are primarily intended for conversion of raw materials into desired products. It develops new products for human lives. The challenge for chemical companies is to cut their costs. The chemical industries have high rate of technological change. Chemical industries use separate processes for converting raw material into product. Now day's the technology that is adopted is reactive separation. In this technology, the emphasis is given on combining separate units in one single unit. Advantageous of this technology is like reducing energy use, increase efficiency etc. Reactive separation uses different techniques like Reactive Chromatography, Reactive Distillation and Reactive Extraction, Reactive Membrane Separation, Reactive Crystallization. Out of this, Reactive chromatography is a attractive alternative since it employs differences in adsorption - desorption of chemical reagents on external solid phase, which can also act as catalyst. It is possible to obtain high purity of product from this process, also downstream purification is reduced or even eliminated. Fixed bed reactor or simulated bed reactors are mainly used for this purpose. Many researchers have studied reactive chromatography. This review is focused in development in reactive chromatography processes.

Keywords: Reactive Separation, Reactive Chromatography, Fixed Bed Chromatography Reactor, Simulated Bed Chromatography Reactor

1. Introduction

Chemical Industries are the primarily, intended for conversion of raw materials into desired products that we use in our daily life. It is necessary for us to understand the importance of the chemical industry which includes a wide range of industries from the large chemical, petrochemical and fertilizer industries to the smaller and light industries like paint and varnishes. The chemical industry is undergoing huge changes worldwide. The challenge for chemical companies is to cut their costs while ensuring that they conform to the best practices in protecting the environment. Currently, chemical production is a high-tech industry, where the competitiveness is more based on investment on research and development than the labor cost. Conventionally physical separation methods having several drawback mainly high cost. So it is necessary to explore alternative methods. Reactive separations (RS) are integrated operations that combine conveniently the

reaction and separation into a single unit that allows the simultaneous production and removal of products thus improving the productivity and selectivity, reducing the energy use, eliminating the need for solvents and leading to intensified, high efficiency systems with green engineering attributes [1]. The designs of reactive separation process involve the reactor and separation operation in single process with simultaneous reaction and separation [2].

Any chemical process involves unit operations and reaction, combinations of this comes under the term of reactive separation processes. Some of advantage of reactive separation are by using reaction to improve separation (overcoming azeotropes, while others are realized by using separation to improve reactions (increasing rates, overcoming equilibrium limitations, minimizing side reaction). As both operations occur in the same unit, there must be match between pressure and temperature. If there is no significant difference between the operating conditions of reaction and separation, then the combination of reaction and separation is

not possible. Further, it has few inherent disadvantages like new technology, limited application, extensive experimental development, complex modeling requirement.

The coupling of mass transfer with reaction mechanism improves catalyst life. Increased mass transfer driving forces realized in reactive separation lead to better surface renewal by moving inhibitors from catalyst surface. The coupling with heat transfer lead to alternate design option for heat addition and heat removal in reactive separation process.

Reactive separations are applied reactions, such as esterification, etherification, hydrolysis and alkylation, trans-esterification. The applications of reactive separation are numerous and has wide range of operations. There are different reactive separation process such as reactive extraction, reactive distillation and reactive absorption, reactive membrane separation, reactive crystallization, reactive chromatography.

Organization of the article thus: section 1 introduces to reaction separation. Section 2 describes the importance of reactive Chromatography. Section 3 describes the different case studies in the area of reactive Chromatography, and the paper is concluded in section 4.

2. Reactive Chromatography

Chromatographic reactor, which uses differences in absorptivity of the different components involved. It is alternative to reactive distillation when the reaction involves non-volatile and temperature sensitive component, as is the case of pharmaceutical industry, a reaction occurs inside a chromatographic column catalyzed by a catalytic adsorbent, and the product is separated by the difference in the affinity to the same catalytic adsorbent packed in the column. Chromatographic reactors are valuable when the reaction is equilibrium-limited. Chromatography can separate complex mixtures with great precision [3].

The purity requirements of the products are often easier to meet in chromatography compared to other separation methods. Lastly, chromatography can be used to separate delicate products that require special care to avoid harsh process conditions. Reactive chromatography is well suited to a variety of uses in the field of biotechnology, such as separating the mixture of proteins or production of biodiesel. Reactive chromatography, as of today, has developed into an invaluable laboratory tool and an industrial unit for the synthesis and purification of compounds. Over the last four decades, research has focused on the development of continuous chromatographic reactor in order to enhance productivity and reduce solvent consumption.

2.1. Principle of Reactive Chromatography

The reactive chromatography process is a combination of reaction and chromatographic separation inside a single column. Chromatography is an adsorptive separation process, where the components are separated based on their different affinity towards the adsorbent. For simultaneous reaction and separation, the packing material must be a

catalyst that has different affinity towards the reactants and products.

Figure 1 illustrates the batch reactive chromatography process for the reaction between reactants A and B that produces products C and D. In this process, the limiting reactant (A) is injected into the column that is initially saturated with excess reactant (B). Reactant B is continuously supplied as a desorbent.

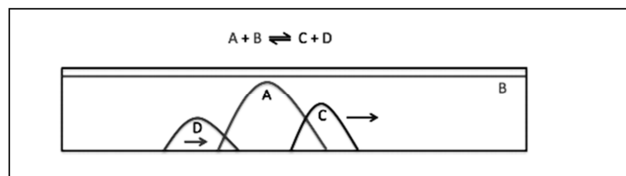


Figure 1. Principle of reactive chromatography [4].

Two components (A and B) react inside the column with the presence of catalyst and produce two products (C and D). Among the two products, weakly adsorbed component (C) moves faster in comparison to the strongly adsorbed component (D). Based on the different elution time, the products are collected separately by fractionation.

2.2. Classification of Reactive Chromatography

Based on the phase situations and the principles used, the reactive chromatography identified in the literature can be classified as shown in Figure 2.

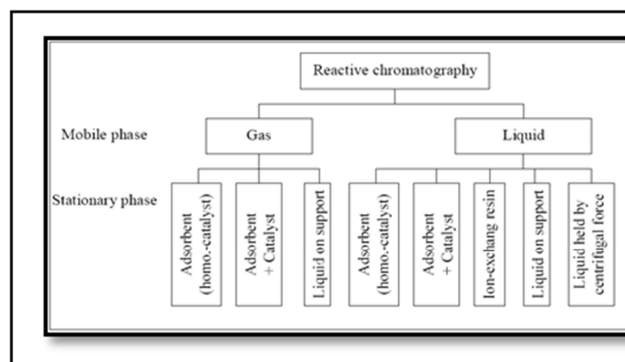


Figure 2. Classification of Reactive Chromatography Based on Phase Situation [5].

Depending on the mobile phase, the reactive chromatography can be distinguished between gas chromatographic reactors or liquid chromatographic reactors as Figure 2. The stationary phases are solids typically in the form of porous media with large specific surface areas. The solid phases can be individual adsorbent for self catalytic or homogeneous catalyzed reactions. The stationary phase may be a liquid coated on a solid support or a liquid retained by centrifugal force [5].

The chromatographic reactors can be classified as gas chromatographic reactors or liquid chromatographic reactors, depending on gases or liquids used as mobile phase. The gas chromatographic reactors are not as developed due to the deficiency of interesting reactions from the application point

of view in the gas phase, compared to the very interesting reactions in the liquid phase.

Also the reactive chromatography can be classified depending on the operation modes and the principles used as continuous or discontinuous depending on whether the

reactant or the reactant mixture is fed continuously or discontinuously into the reactor. The classification of reactive chromatography based on operation mode is as shown in Figure 3.

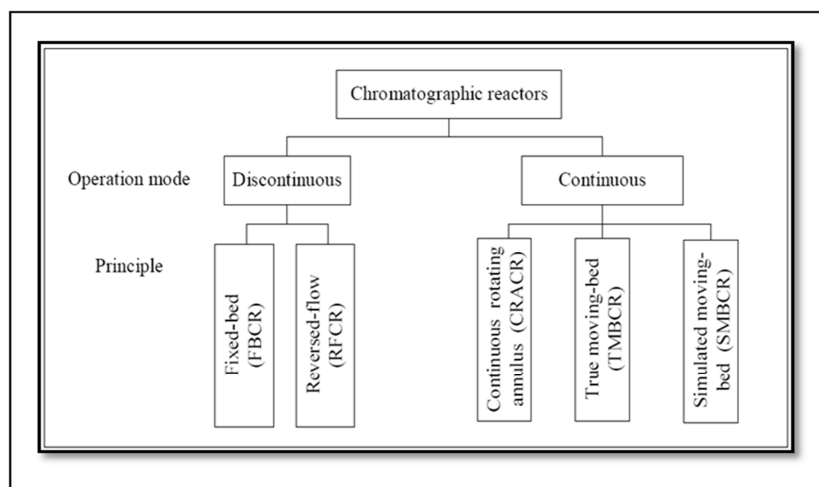


Figure 3. Classification of Reactive Chromatography Based on Operation Mode [5].

This paper focus on mainly on liquid chromatography methods and the next section describes the types of chromatographic reactor that are used in reactive chromatography. Chromatographic reactors are mainly of two types 1) Fixed bed chromatographic reactor (FBCR). 2) Simulated Moving Bed Reactor (SMBR). These types of chromatographic reactor are discussed below.

2.3. Fixed Bed Chromatographic Reactor (FBCR)

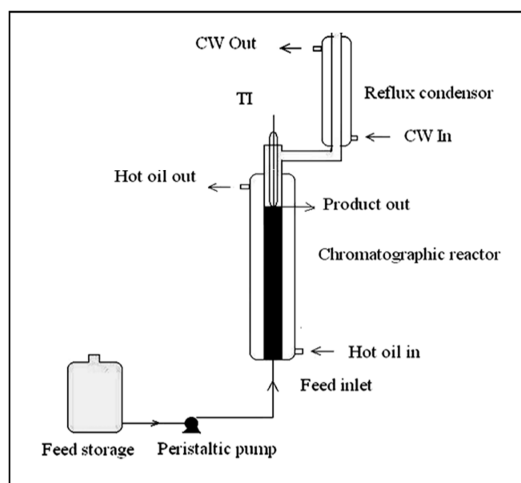


Figure 4. Fixed bed chromatographic reactor [7].

The Figure 4 shows fixed bed chromatographic reactor (FBCR). This reactor can be used to evaluate the practicality of RC. The performance of FBCR is analyzed using the breakthrough curves. Once the feasibility is proven, the reaction can be conducted in a continuous mode reactor like simulated moving bed reactor [6]. In RC, packing material is an important factor as it should not only act as a catalyst for the reaction

but also adsorb one of the products.

2.4. Simulated Moving Bed Reactor (SMBR)

Simulated moving bed reactor (SMBR) is an extension of the reactive chromatography process that performs in a continuous and counter-current fashion. Figure 5 shows the standard SMBR unit where chromatographic columns are connected in a cyclic configuration. In single chromatographic reactors, each column is packed with resins that function both as a catalyst and an adsorbent. For a standard four-zone SMBR, four streams are present: a feed stream, a desorbent stream, the extract phase and the raffinate phase.

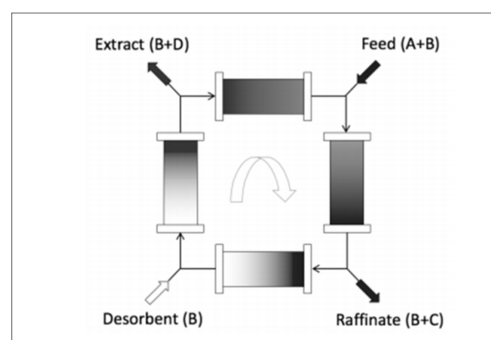


Figure 5. Simulated Moving Bed Reactor unit for the production of component C through the reaction of A and B ($A+B \leftrightarrow C+D$) [19].

For reversible and equilibrium limited reactions in Figure 5, such as $A+B \leftrightarrow C+D$, both reactants are injected through the feed port and one of the reactants (B) is used as a desorbent. Two reactants, injected through the feed port, react inside the column catalyzed by the packing material. Two products, C and D, have different affinities towards the packing material. The faster moving component is recovered from the raffinate outlet while the strongly retained component, D is obtained in

the extract outlet. As the reaction proceeds inside the SMBR, the products are continuously removed from the system.

3. Case Studies of Reactive Chromatography

Lode [6] investigated synthesis of methyl acetate, catalyzed by using a sulfonated polystyrene divinylbenzene resin. SMBR was used for this purpose. Data obtained from experimentally determined adsorption thermodynamics and reaction kinetics represented mathematically and, a model for a reactive chromatographic column is developed and validated.

Deshmukh [7] studied esterification of butyl cellosolve with acetic acid using cation exchange resin Amberlyst - 15 is using chromatographic reactor. The study determining the appropriate kinetic model for the reaction by performing experiments at different parameters. Adsorption capacity of the resin for different components involved in the reaction is performed through adsorption experiments. The combined process is experimentally investigated using a fixed bed chromatographic column. Mathematical model is developed experimental data and mathematical model having good match.

Reed [8] studied the kinetics of continuous sucrose inversion catalyzed by fixed beds of acid form ion exchange resin. For this study reactor was used 1 inch in diameter flow rate and catalyst particle sizes adjusted to such that cover a modified Reynolds number is less. Reaction temperature was varied from 323 K to 348 K. The order of reaction was first. The study indicates that the observed rate of reaction is strongly depending on diffusion within the resin particles and that external mass transfer is not major effect for given condition.

Mazzotti [9] showed complex dynamical behavior of chromatography reactors. The reaction was synthesis of ethyl acetate and water from ethanol and acetic acid by using polystyrene-divinylbenzene acidic resin. The chromatographic reactor used for the reaction change in of composition was observed in the fixed bed column at different flow rate By the obtained results from experiment the dynamical behavior of the chromatographic reactor was achieved.

Gelosa [10] investigated the synthesis of triacetine, starting from glycerol and acetic acid, using reactive chromatography on acidic polymeric resins. The study include e adsorption equilibria of the involved multicomponent mixtures and then to the study of the kinetics of reactions using a batch reactor. Next, the separation and reaction process is investigated using FBRC. The obtained data is compared with the predictions of a mathematical model. It was shown that, although this synthesis requires three steps in series, the chromatographic reactor can produce high-purity triacetine with high conversions.

Vu [11] investigated ester hydrolysis reactions by chromatography reactor using equilibrium theory and rate

model. Theory was introduced as study the possibility of chromatographic reactors. It also decides whether total conversion and total separation in a chromatographic fixed-bed reactor with a pulse injection of the reactants is possible. Reactions of the type $2A \leftrightarrow B + C$ or $A \leftrightarrow B + C$ used. Total conversion and separation was only possible if the reactant has intermediate adsorptivity. For the second reaction, total conversion separation is always possible for any order of adsorptivities, provided that the chromatographic column is sufficiently long. Ester hydrolysis reactions with water in excess are considered as a practical application for the second type of reaction. Then length of column required for total conversion separation is estimated.

Strohleina [12] studied the esterification of acrylic acid with methanol using Amberlyst 15 as a stationary phase has been investigated using a chromatographic reactor. Kinetic model for the catalytic reaction has been developed. Dispersion of concentration by density gradient effects also taken. The parameters of model determined. In general, a good match between experimental and calculated results is obtained. Based on the detailed batch column model, a complete model of a simulated-moving-bed reactor has been implemented.

Ali [13] studied the kinetics of the esterification reaction between propionic acid and methanol, ethanol, and 1- butanol using Amberlyst -15 as catalyst. Using a fixed - bed plug flow reactor over the different temperature range and different acid to alcohol molar ratios reaction was carried were out. Several kinetic models were tested like the pseudo- homogeneous (PH), Eley - Rideal (ER), Langmuir - Hinshelwood (LH), and Popken (PP) models. In all cases, the activity coefficients were estimated using the UNIFAC model to account for the non ideal thermodynamic behavior of the reactants and products. The P - P model was found suitable.

Gyani [14] studied application of RC for the synthesis of 2-ethylhexyl acetate through esterification of acetic acid with 2-ethylhexanol. Amberlyst-15 has been used as a catalyst. Batch reactor was used for this purpose. The effects of various parameters have been investigated. Activity based Langmuir-Hinshelwood-Hougen-Watson (LHHW) model was used for regression. Non - reactive binary adsorption experiments were performed to determine the parameters of Langmuir adsorption isotherm. Mathematical model and experimental data were compared.

Pereira [15] studied novel process for the ethyl lactate synthesis in a simulated moving bed reactor. By using SMBR purity of 95% can be obtained. External and internal mass - transfer resistances and variable velocity due to change of liquid composition was taken in to account while developing model.

Dakdouki [16] investigated solid-phase reactive chromatography (SPRC), which combines reaction, separation, and purification into a single unit This method was used the synthesis of some natural bioactive compounds, like methoxylated analogues of resveratrol, alkylresorcinols, and 5 - aryl-2, 4 - pentadienoates, over a column of alumina - KF under microwave irradiation by using the Wittig and Horner - Emmons reactions. SPRC gives high purity in less times.

Patel [17] investigated esterification reactions of acetic acid and *n* - hexanol were studied in batch and continuous chromatographic reactors in the presence of a gelular ion-exchange resin catalyst (Purolite CT-124) to synthesize *n*-hexyl acetate. Experiments were carried out using different parameters such as feed flow rate, feed mole ratio of *n* - hexanol to acetic acid, desorbent flow rate, in batch and continuous chromatography reactor. Complete conversion of acetic acid achieved.

Reddy [18] showed the study of 2 - Ethylhexyl Acetate using Simulated Moving Bed Reactor. To act as true moving bed system inlet and outlet ports are switched at different time interval. SMBR was employed for heterogeneously catalyzed reversible reactions, in which one of the reactants works as a solvent and the catalyst. The different such as conversion, raffinate purity, and extract purity are chosen. The model reaction considered is the esterification of acetic acid with 2 - ethylhexanol catalyzed by cation exchange resin. This work was carried out to represent complete algorithm for the design of SMBR.

Gyani [19] studied SMBR for the Synthesis of 2 - Ethylhexyl Acetate. Modeling also carried out. The simulation indicate that an SMBR unit containing eight columns gives high conversion and purity with a typical desorbent requirement of 46.35 mol of acetic acid per mole of product and a productivity of 32.01 mol of product per kilogram of adsorbent per day.

Oh [20] indicated use of reactive chromatography for catalytic Synthesis of Propylene Glycol Methyl Ether Acetate. By using chromatographic reactor at different flow rates, injection volumes, and different temperatures esterification carried out. Model for isothermal equilibrium dispersive model was executed and parameters were determined by fitting the model to the experimental data. It was observed that when volume of single component was too large, two reaction sites were formed inside the column, resulting in a deformed peak shape of the product in the outlet chromatogram. High conversion was achieved when the flow rate and the injection volume was small. The results point out that the chromatographic reactor enhanced the reaction beyond the equilibrium.

Ghodke [21] studied both reactive distillation and reactive chromatography stabilization of bio - oil, along with several oxygenated organic compounds, contains substantial amounts of carboxylic acids. For stabilization of bio-oil through esterification of acid with alcohol in the presence of ion-exchange resin catalyst multifunctional reactors can be used. Reactive distillation is carried at higher temperature. Reactive chromatography can perform reaction at low temperatures and with lower alcohols. The limitation is that the catalyst used for esterification also catalyzes simultaneous polymerization of furfural-like components which deactivate the catalyst. Deactivation of Amberlyst - 15 with ethanol after 20 h of continuous run in a FBRC. RC is a promising candidate for this particular application.

Bibi [22] analyzed of models for reactive chromatography using irreversible and reversible reactions. Rectangular

reactant pulses are injected into initially empty or pre-equilibrated columns assuming both Dirichlet and Danckwerts boundary conditions. Model uses two partial differential equations for convection, longitudinal dispersion and first order chemical reactions. Mechanisms on solute transport, analytical and numerical solutions of the models could be helpful to understand and design chromatographic reactors. The Laplace transformation is applied to solve the model equations analytically for linear adsorption isotherms. Results are compared with numerical predictions using a high-resolution finite volume scheme for two sets of boundary conditions.

Ma [23] investigated theoretical analysis and digital simulation for multiphase reactive chromatography. Multiphase reaction chromatography equations are established considering the coupling effect between chemical reaction and multiphase chromatography. The reversible chromatographic process of two-phase four-component was discussed using the second order form with flux limiting factor. The fluctuation with initial and boundary conditions was analyzed, and the formation mechanism of the wave image was discussed. The results show when the fluid enters the chromatography, the shock wave will be generated due to the difference of the adsorption property of the component, thus affecting the concentration distribution diagram of the chromatogram.

4. Conclusion

This review has attempted to cover major process technology available. Reactive separation combines several unit operations and processes. RC can be used for many processes like bio-oil, Synthesis of 2 - Ethylhexyl Acetate, esterification of acrylic acid, sucrose inversion, esterification reactions of acetic acid and *n* - hexanol, synthesis of some natural bioactive compounds, ethyl lactate synthesis, esterification of butyl cellosolve with acetic acid, esterification reaction between propionic acid and methanol, ethanol, and 1- butanol, synthesis of ethyl acetate and water, esterification of acrylic acid with methanol, synthesis of methyl acetate, synthesis of triacetone. Reactive chromatography has few drawbacks like scale up, conducting reaction and separations at same conditions, but it works easily for given applications.

Abbreviations

CW in: cold water inlet
CW out: cold water outlet
RC: reactive chromatography
RD: reactive distillation
RE: reactive extraction
RS: reactive separation
TI: temperature indicator
PH: Pseudo - homogeneous
ER: Eley - Rideal
LH: Langmuir-Hinshelwood

PP: Popken

LHHW: Langmuir-Hinshelwood - Hougen - Watson

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