



Reactive separations: more ways to skin a cat

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Abstract

The integration of an in-situ separation function within the reactor holds the promise of increased conversion, higher selectivity and reduced capital investment. We survey recent developments in reactive separations technology and emphasise the breadth of potential applications and possibilities for innovations. © 2002 Elsevier Science Ltd. All rights reserved.

Keywords: Reactive distillation; Reactive extraction; Membrane reactors; Adsorptive reactors

1. Introduction

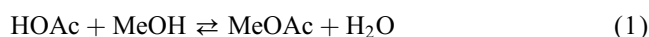
The traditional flow sheet of a chemical process consists of a reactor followed by a separation unit to remove the unconverted reactants from the desired product and recycle these to the reactor; see Fig. 1. Innovative reactor configurations and choice of operating conditions can be used to maximise the conversion of reactants and improve selectivity to the desired product, thereby reducing the costs associated with the separation step. Strategies for arriving at the “ideal” reactor configuration have been discussed in the literature (Krishna & Sie, 1994). In recent years there has been considerable academic and industrial interest in the area of reactive separations wherein the separation function is integrated within the reactor; a variety of separation principles and concepts can be incorporated into the reactor; see Fig. 2. The term multi-functional reactor is often used to embrace reactive separations technology, which promises reduction in capital costs, increased conversion and reduced by-product formation.

In this paper we survey recent developments in reactive separations technology, emphasising the available alternatives and pointing out obstacles in the way of successful implementation of this technology. We begin with a success

story of reactive distillation (RD) technology for methyl acetate production.

2. Reactive distillation

High-purity methyl acetate is used in large amounts as an intermediate in the manufacture of a variety of polyesters such as photographic film base and cellulose acetate. The manufacture of high-purity methyl acetate by the acid-catalysed esterification reaction of acetic acid with methanol



is made difficult by a variety of factors:

- reaction equilibrium limitations,
- difficulty of separating AcOH and H₂O, and
- presence of MeOAc–H₂O and MeOAc–MeOH azeotropes.

Conventional processes use one or more liquid-phase reactors with large excess of one reactant in order to achieve high conversions of the other. A typical flowsheet of a conventional process is shown in Fig. 3 in which the reaction section is followed by eight distillation columns, one liquid–liquid extractor and a decanter. This process requires a large capital investment, high energy costs and a large inventory of solvents.

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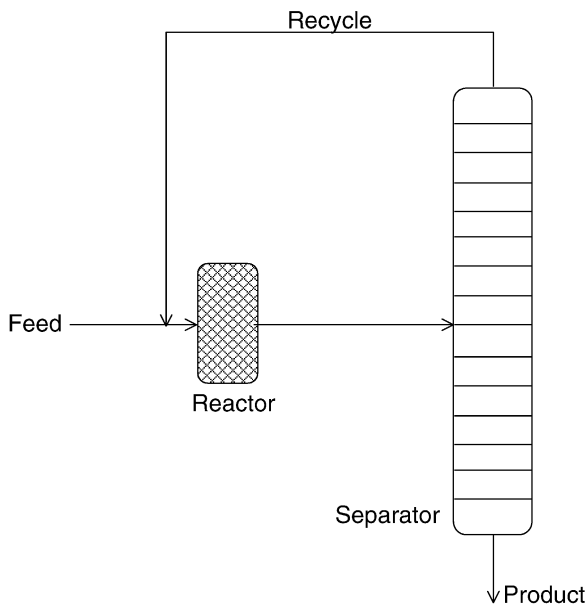


Fig. 1. Conventional flowsheet of a process consisting of a reactor followed by a separation unit.

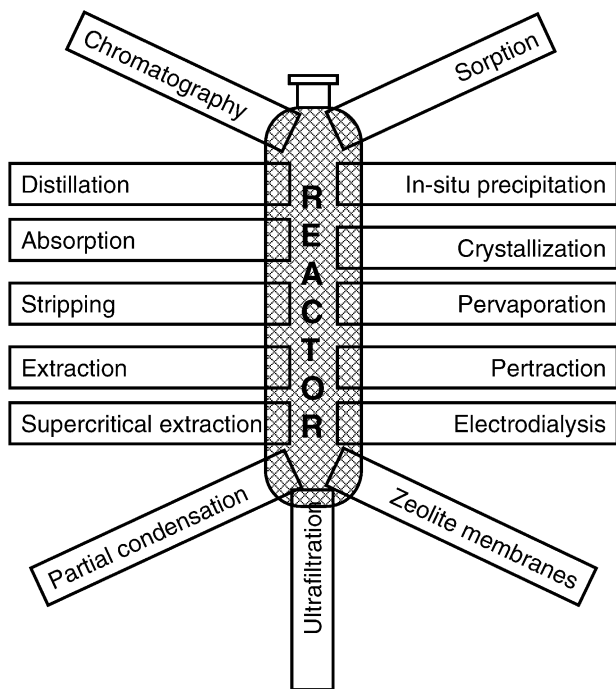


Fig. 2. Various in-situ separation function integrated into the reactor.

In the RD process for methyl acetate, invented by Eastman Chemical Company (Agreda, Partin, & Heise, 1990; Sirola, 1996), the entire process is carried out in a single column as shown in Fig. 4. In this single column high-purity methyl acetate is made with no additional purification steps and with no unconverted reactant streams to be recovered. By flashing off the methyl acetate from the reaction mixture, conversion is increased without using excess of one

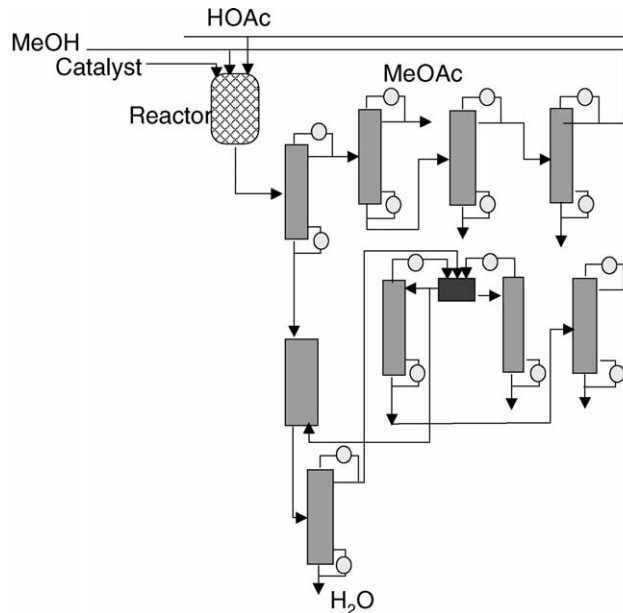


Fig. 3. Conventional processing schemes for carrying out the esterification reaction $\text{MeOH} + \text{AcOH} \rightleftharpoons \text{MeOAc} + \text{H}_2\text{O}$, consisting of one reactor followed by nine distillation columns.

of the reactants. The reactive column has stoichiometrically balanced feeds and is designed so that the lighter reactant MeOH is fed at the bottom section and the heavier acetic acid is fed at the top. The column consists of three sections. The reaction takes place predominantly in the middle section, shaded grey below the point of sulphuric acid injection. The bottom section, serves to strip off the MeOH from water and return it to the reaction zone. The vapours leaving the reactive section consists of the MeOAc–MeOH azeotrope which is “broken” in the rectifying section by addition of AcOH which acts as entrainer. The RD column represents an entire chemical plant and costs one-fifth of the capital investment of the conventional process and consumes only one-fifth of the energy.

The successful commercialisation of RD technology requires special attention to hardware design that does not correspond to those for conventional (non-reactive) distillation. On any reactive tray, the requirements of the chemical reaction (i.e. high liquid hold-up for maximising conversion) are not in consonance with the requirement for good separation (i.e. high interfacial area). For conventional distillation, the preferred regime of operation is the spray regime whereas for reactive trays, we need to increase the liquid holdup and so the preferred regime of operation is the bubbly flow or froth regime; see Fig. 5. High liquid hold-ups could be realised by use of bubble caps, reverse flow trays with additional sumps to provide ample tray residence time. In the Eastman process for methyl acetate manufacture specially designed high liquid hold-up trays are used (Agreda et al., 1990; Sirola, 1996). If we carry out a detailed hardware design for the RD column for MeOAc production, we see that a much larger

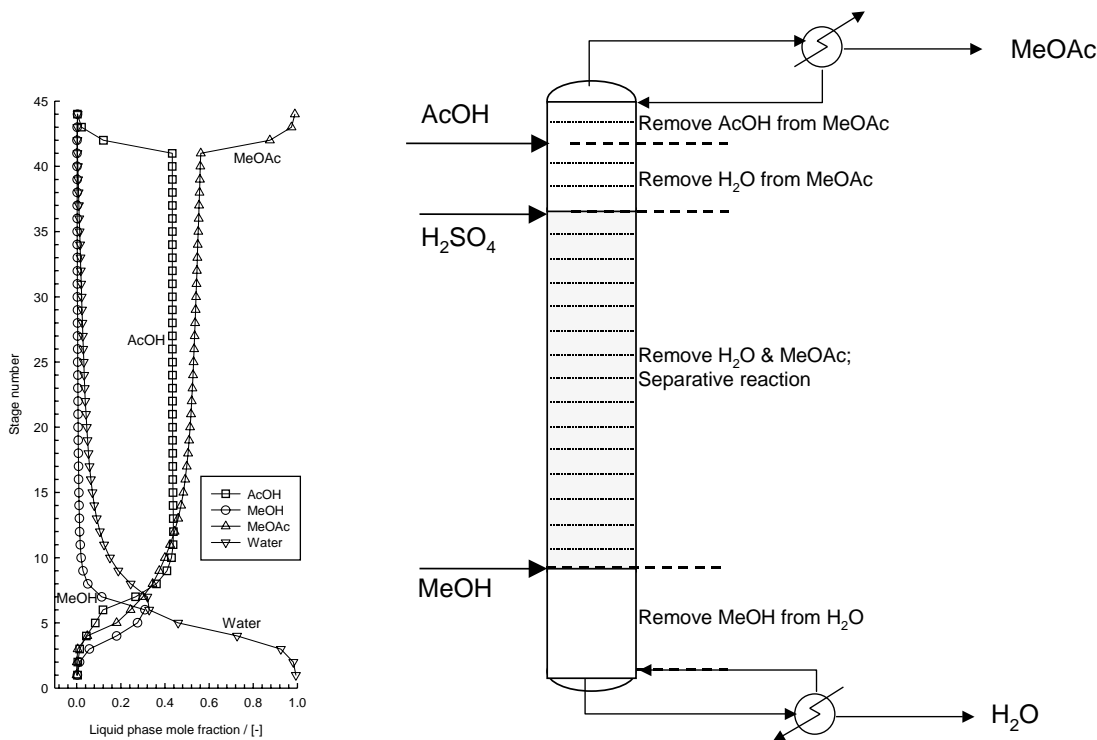


Fig. 4. The Eastman reactive distillation process for methyl acetate manufacture. Adapted from Agreda et al. (1990).

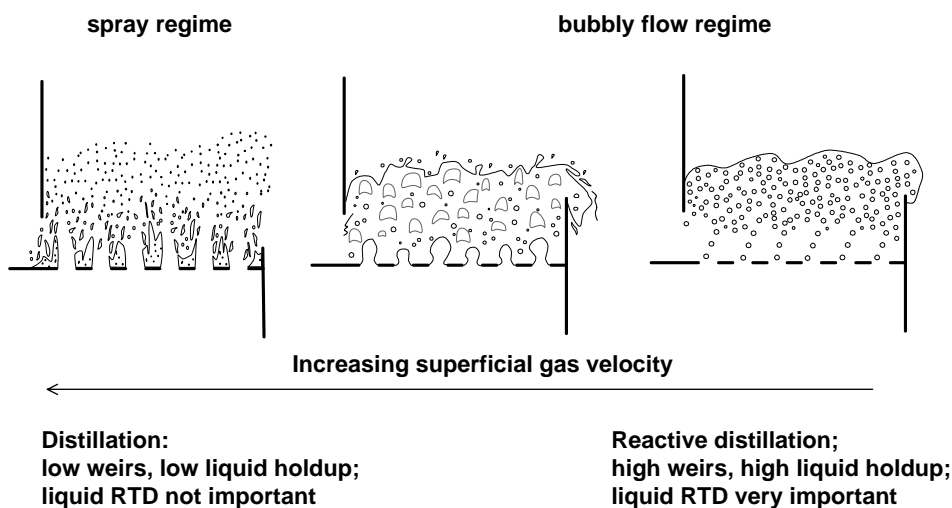


Fig. 5. Choice of hydrodynamic flow regimes on reactive and non-reactive trays.

column diameter is required for the reactive section in order to allow lower superficial vapour velocities and the bubbly froth regime; see Fig. 6. Furthermore, the weir heights used for reactive trays need to be significantly higher than those for conventional distillation.

For heterogeneously catalysed RD columns, hardware design poses considerably more challenges. The catalyst particle sizes used in such operations are usually in the 1–3 mm range; larger particle sizes lead to intra-particle diffusion limitations. To overcome the limitations of flooding the

catalyst particles have to be enveloped within wire gauze envelopes. Two commonly used structures are catalyst bales (Subawalla, Gonzalez, Seibert, & Fair, 1997) and catalyst sandwiches such as the KATAPAK-S structure (van Baten, Ellenberger, & Krishna, 2001); see Fig. 7. The catalyst loading in such structures is only 20–25% of the column (reactor) volume. This underlines the non-compatibility of requirements of chemical reaction (small particle sizes and high catalyst loadings), separation (large interfacial area between gas and liquid phases) and pressure drop (higher

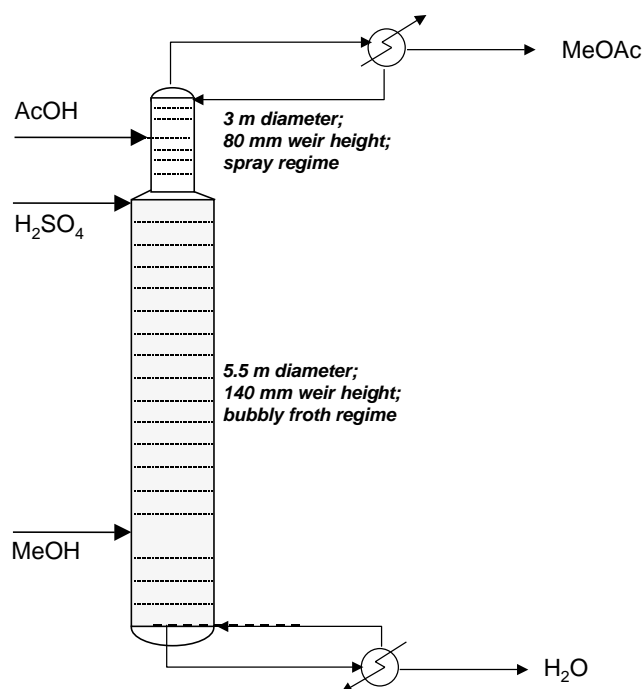


Fig. 6. Column configuration and tray hardware design for RD column for methyl acetate manufacture.

“open” areas for gas–liquid flow). One way to overcome the hardware design conflicts for heterogeneous catalysed RD is to employ the side-reactor or external reactor concept (Schoenmakers & Buehler, 1982; Jakobsson, Pyh  lahti, Pakkanen, Keskinen, & Aittamaa, 2001). Fig. 8 shows the different arrangements that are possible. The external liquid-phase packed-bed reactors operate either in (a) direct passage, or (b) recycle-loop around one or more distillation trays. In the direct passage case, the liquid phase is completely withdrawn from the column and, after reaction, returned to the next tray down the column. This layout is equivalent to an arrangement of the reactor between two distillation trays. If designed properly, it is the only arrangement that does not require sumps or buffer vessels; the hydrostatic height between the two trays is sufficient to overcome the pressure drop in the catalyst bed. In the recycle-loop operation (reactive pump-around) the liquid is withdrawn from the downcomer on any tray and returned to a tray further up the column. In this case we need buffer vessels and a liquid circulation pump.

The side-reactors concept has been suggested for production of methyl tertiary butyl-ether, tertiary amyl-ether and iso-octene (Jakobsson et al., 2001).

The petroleum industry offers another potential candidate for the use of RD technology. Co-current gas–liquid downflow trickle bed reactors are widely applied for hydrodesulphurization (HDS) of gasoil and heavier oils; See Fig. 9(a). The removal of sulphur can generally be described by a second order reaction in total sulphur. This high reaction order is not a consequence of a specific reaction

mechanism, but reflects the presence of a variety of organic sulphur compounds with different reactivities. A large proportion consists of more reactive compounds that are removed in an early stage of the reaction, whereas conversion of a smaller amount of progressively more refractory compounds occurs more slowly in later stages. Hydrogen sulphide, a by-product of the HDS reaction, is therefore generated in large quantities already in the inlet part of the catalyst bed and in co-current operation the generated H_2S passes through the remaining downstream part of the bed, leading to concentration profiles as shown in Fig. 9(a). It can be seen that in the usual co-current operation the major part of the bed operates in a H_2S -rich regime. Hydrogen sulphide suppresses the activity of HDS catalysts. Co-current operation is therefore clearly sub-optimal, since activity is suppressed in the major downstream part of the bed where high catalyst activity is needed for conversion of the more refractory compounds. Much more favourable H_2S profiles can be obtained in counter-current operation; the main part of the bed now operates under H_2S -lean conditions; see Fig. 9(b). The fresh hydrogen entering the catalyst bed at the bottom also serves to strip the dissolved H_2S in gasoil. Only a relatively small part of the catalyst bed (near the top) operates under H_2S -rich conditions, and suppression of catalyst activity in this part is of lesser consequence since the sulphur compounds to be converted here react easily. A similar situation exists in hydrocracking. The by-product of conversion of nitrogen-containing organic compounds, viz., ammonia, is a very strong inhibitor for hydrogenation and particularly for hydrocracking reactions.

Removal of aromatics in petroleum fractions by hydrogenation is an example where chemical equilibria play a role. Due to the presence of sulphur in most petroleum fractions, only sulphur tolerant catalysts, e.g., catalysts of the Ni/Mo/alumina type are generally applied. Catalysts of this type are only moderately active, and consequently need relatively high temperatures to achieve industrially acceptable conversion rates. Since equilibria for aromatics hydrogenation are unfavourable at high temperature, increasing the temperature to enhance reaction rates cannot go beyond a certain level, and this sets a limit to the depth of aromatics removal. For the hydrogenation of aromatics too the co-current operation is unfavourable. This is not only so from a kinetic point of view (inhibition by H_2S and NH_3), but also because of thermodynamics (Trambouze, 1990). Deep removal of aromatics from an oil fraction generally is limited by thermodynamic equilibrium. In the co-current mode of operation the partial pressure of H_2 at the exit end of the reactor is lowest because of the combined effects of pressure drop, hydrogen consumption and build up of gaseous components other than H_2 (H_2S , NH_3 , H_2O , light hydrocarbons).

The counter-current reactor shown in Fig. 9(b) is essentially an RD column wherein the H_2S is stripped from the liquid phase at the bottom and carried to the top. The quantitative advantages of the RD implementation for hydroprocessing are brought out in a design study carried out

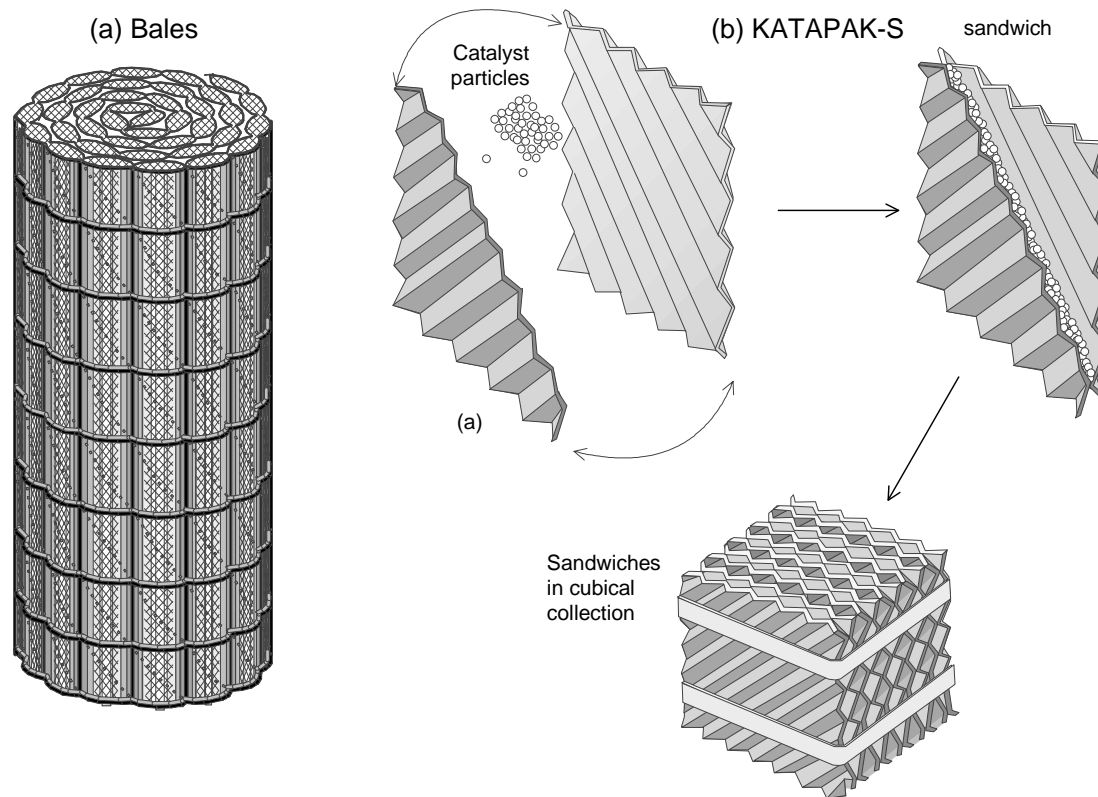


Fig. 7. (a) Catalyst bales licensed by Chemical Research and Licensing. (b) Structured catalyst-sandwiches licensed by Sulzer and Koch-Glitsch.

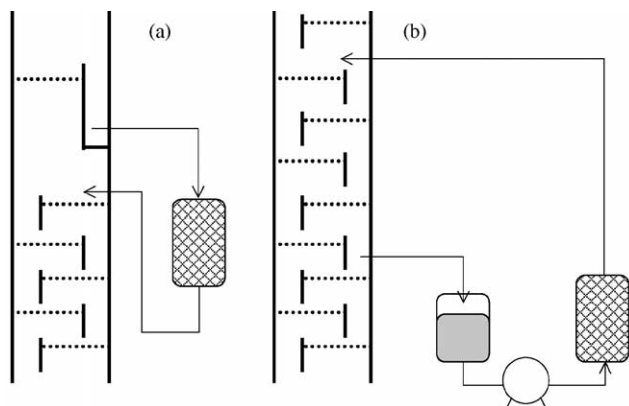


Fig. 8. External side-reactor configurations. (a) Direct passage, (b) reactive pump-around. Adapted from Schoenmakers and Buehler (1982).

by Van Hasselt (1999). For a 20,000 bbl/day hydrodesulphurisation unit with a target conversion of 98% conversion of sulphur compounds, the catalyst volume required for a conventional trickle bed reactor is about 600 m^3 . For counter-current RD implementation the catalyst volume is reduced to about 450 m^3 .

The major bottleneck to the implementation of RD technology for counter-current hydroprocessing in commercial practice relates to hardware limitations. The catalyst loading in structures such as catalytic bales and KATAPAK-S

are only 20–25% by volume; this compares unfavourably with the conventional trickle bed in which catalyst loadings of around 60% by volume are achieved. There is a need to develop improved hardware configurations that allow counter-current contacting of gas and liquid, in the presence of 1–1.5 mm catalyst particles, wherein the catalyst loadings are in the region of 50–60%.

The spectacular success of RD technology for methyl acetate does not appear to have been realised for other processes, at least on the basis of the published literature. One reason for this could be the fact that the reaction temperatures have necessarily to be lower, and operating pressures higher, for RD operation as compared to say vapour-phase fixed bed reactors. Stitt (2001) has performed a detailed comparison of the economics of conventional technology with RD technology for the toluene disproportionation reaction. He has shown that though RD technology leads to significantly simpler flowsheet; this advantage is offset due to the higher cost of the RD column, in view of the higher operating pressures employed.

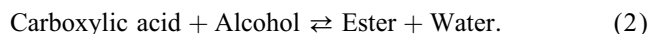
3. Alternative reactive separation processes for esterifications

For a given reaction, there may be various possibilities for in-situ separations; we illustrate this for the esterification

reaction for which the candidature of RD has been firmly established in the foregoing section.

3.1. Membrane pervaporation reactor

The pervaporation membrane reactor has been developed by several workers for carrying out the reaction between an alcohol and a carboxylic acid to produce esters (Okamoto, Yoshikawa, Ying, Tanaka, & Kita, 2001; Zhu, Minet, & Tsotsis, 1996; Sanchez & Tsotsis, 2001):



The reaction is carried out in a tubular reactor in the liquid phase; see Fig. 10. In the construction used by Zhu et al. (1996) the walls of the tube were made of a ceramic support material that was impregnated with polyetherimide, which allows selective permeation of water vapour through the membrane tube walls. Zhu et al. (1996) obtained a significant improvement in the conversion when compared to a conventional tubular reactor and supra-equilibrium conversions were achieved. Okamoto et al. (2001) and Bernal, Coronas, Menéndez, and Santamaría (2001) use zeolite membranes for selective pervaporation of water vapour for a variety of esterification reactions. For comparison with RD technology, it needs to be stressed that even though supra-equilibrium conversions are achieved in a pervaporation membrane reactor, the conversion does not quite reach 100%; this means that the (raffinate) product contains the product ester, along with water and unreacted carboxylic acid and alcohol. In order to obtain pure ester, a further distillation step is required. In the case of methyl acetate production, this distillation step could be rather complex (see Fig. 3). In biotechnology, the combination of the bioreactor and a separate membrane pervaporation unit for selective permeation of the desired product say ethanol or butanol, leads to a very efficient process because of the suppression of product inhibition (Lipnizki, Hausmanns, Laufenberg, Field, & Kunz, 2000).

3.2. Pulsed chromatographic reactor

Sardin, Schweich, and Villermaux (1992) describe the use of a pulsed chromatographic reactor for carrying out the reaction between acetic acid and ethyl alcohol to produce ethyl acetate. The reactor consists of a mixed alumina and cation exchange resin in acidic form to separate the products and catalyse the reaction. The composition of the solids mixture is chosen to avoid separating the reactants. A pulse containing the feed mixture of acetic acid and ethanol, in stoichiometric proportions, is injected into the reactor. An eluant (i.e. solvent) is fed continuously to the reactor. The product ethyl acetate is not adsorbed and is therefore eluted first out of the reactor. Water, on the other hand is very strongly adsorbed. The principle of separation is illustrated

in Fig. 11. Conversions exceeding the equilibrium limit are obtained in pulse-mode operation. The frequency of feed pulsing must be adjusted to allow the efficient separation of the ester from the reaction mixture—continuous feed injection policy offers no advantage over conventional fixed bed reactors. A comparison of the performance of a pulsed chromatographic reactor and a conventional fixed bed reactor for carrying out ester *hydrolysis* is given by Falk and Seidel-Morgenstern (1999).

In practice, the product ester from a pulsed chromatographic reactor is obtained in the presence of the eluant (solvent) and a further separation step (e.g., distillation) will be necessary to recover the product in pure form. The eluant can be chosen to be one of the reactants, say alcohol, but the choice must be such as to avoid the complexity of product recovery. It is clear that pulsed chromatographic reactors will not be able to produce the desired ester product in pure form in one step and therefore this technology will not normally be able to compete with the alternative RD technology. However, pulsed reaction chromatography offers a useful technological solution for low-volume high-cost chemicals associated with say the pharmaceutical, perfumery and fragrance industries.

3.3. Continuous (simulated) moving bed adsorber–reactor

For continuous operation and implementation of the in-situ adsorption–reaction principle we must resort to the simulated moving bed adsorber technology. Carr and Dandekar (2001) describe a liquid phase simulated moving bed adsorption-with-reaction process for methyl acetate synthesis; see Fig. 12. The process consists of eight discrete beds, which are divided into three different zones. Amberlyst-15 is used both as adsorbent and catalyst. Amberlyst-15 is made up of cross-linked polystyrene divinyl benzene polymer with functionalised sulphonic groups. The sulphonic groups catalyse the esterification reaction and the polymer preferentially adsorbs water by swelling. The feed consists of pure AcOH and the second reactant MeOH is used as desorbent. Of the two products, water is more strongly adsorbed, and MeOAc less strongly adsorbed. A raffinate stream containing predominantly methyl acetate, and an extract stream containing mostly water and methanol are withdrawn. By continuously switching the ports of the feed and effluent streams in the direction of fluid flow, a simulated movement of solid is created that is countercurrent to the direction of liquid flow.

AcOH is fed to the centre of the reactor, where it encounters a downward flow liquid stream containing MeOH. In the presence of Amberlyst-15 reaction takes place to form MeOAc and H₂O. Amberlyst-15 preferentially adsorbs water and carries the water upwards. The separation of MeOAc from H₂O causes a complete conversion of AcOH. As the adsorbent travels upward it

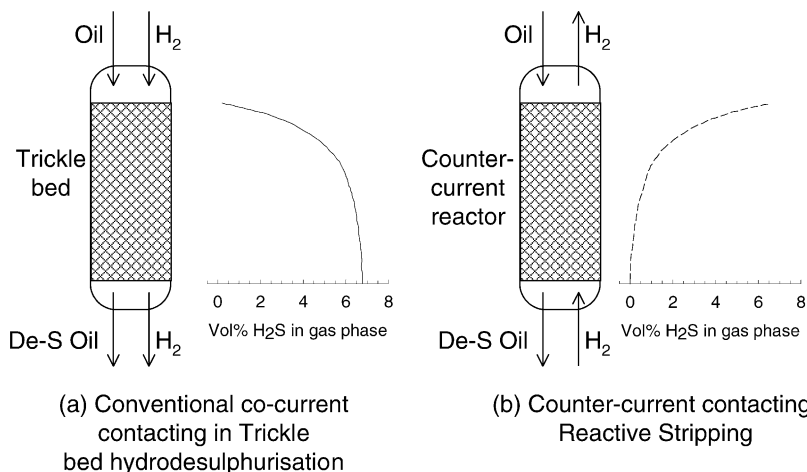


Fig. 9. Hydrodesulphurisation of gas oil carried out in (a) co-current trickle bed reactor and (b) counter-current RD unit.

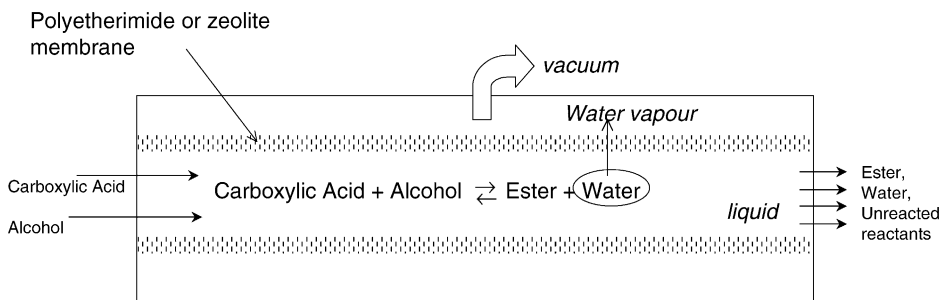


Fig. 10. The membrane pervaporation reactor concept for esterifications.

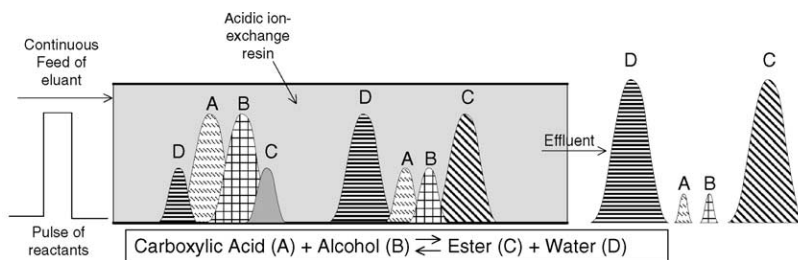


Fig. 11. The pulsed chromatographic reactor concept for esterifications.

encounters the downward flowing liquid MeOH, which strips the water from the adsorbent. An extract stream containing MeOH and water is removed. Any remaining water carried by Amberlyst-15 is stripped by the entering MeOH feed in the topmost zone. The adsorbent leaving the top of the reactor and entering the bottom of the reactor, contains practically no water. This minimises the back-reaction of MeOAc and H₂O, thus preventing any reduction in conversion. Thus the raffinate stream contains mostly MeOAc and MeOH.

Although the simulated moving bed in-situ adsorption technology realises 100% conversion of AcOH with 99.9% recovery of MeOAc, the process cannot compete with the RD technology of Eastman Chemical Company because the raffinate stream of MeOAc and MeOH forms an

azeotrope which poses a difficult separation problem (Carr & Dandekar, 2001).

The simulated moving bed adsorber–reactor concept is being developed for carrying out catalytic isomerisation of *n*-paraffins to produce branched isomers; this process is gaining in importance in the petroleum industry because of the need to increase the octane number of gasoline while reducing the benzene and olefins content (Carr & Dandekar, 2001).

4. Which product to separate?

When considering in-situ separation of product, it is important to stress that often removing only *one* of the products

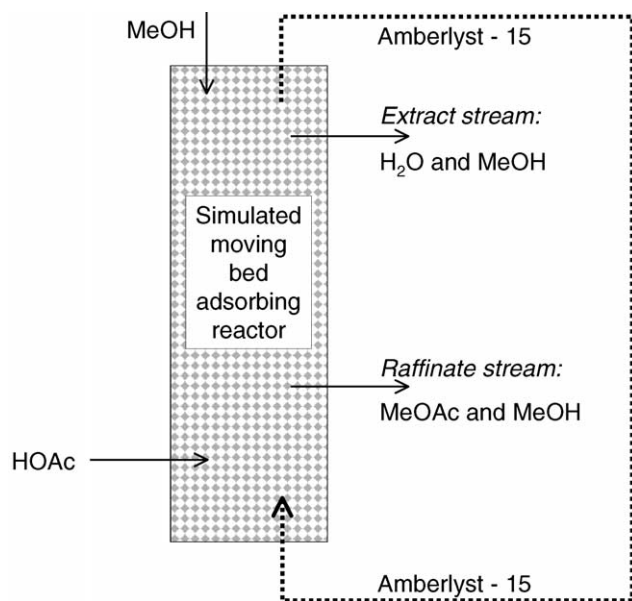


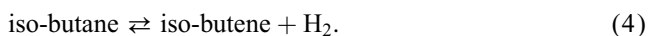
Fig. 12. Operation of a simulated moving bed adsorber and chemical reactor for methyl acetate manufacture. Adapted from Carr and Dandekar (2001).

of the reaction is sufficient to drive the equilibrium to the right or prevent unwanted side reactions. There is usually a choice with respect to the product to separate from the reaction zone. Let us consider the Claus reaction for production of sulphur following the reversible reaction scheme:



Conventional technology for carrying out the Claus reaction consists of a series of fixed bed catalytic reactors, with interstage removal of sulphur by condensing the product vapour stream; see Fig. 13(a). An alternative strategy, that is much more thermodynamically efficient, is in-situ adsorption of water inside the reactor (Agar, 1999; Elsner, Ditrach, & Agar, 2001) by using a packed bed with a mixture of catalyst and zeolite adsorbent; see Fig. 13(b). The sulphur formed would then be separated from the almost completely converted gas emerging from the adsorptive reactor in a single condensation step. The sulphur-free gas from the condenser could subsequently be reheated and employed for the regeneration of the second adsorptive reactor.

Now consider the dehydrogenation reaction:



This is an equilibrium-limited reaction and in-situ removal of either the *isobutene* or H_2 is sufficient to drive the reaction to the right. If we carry out the reaction in a packed bed membrane reactor, the separation of H_2 from the reaction products is easier if we use Knudsen selectivity as separation principle. Hydrogen has the smallest molecular weight and therefore its flux through the membrane will be the highest; see Fig. 14.

The permeation of components across a (nanoporous) zeolite, or carbon molecular sieve (CMS) membrane is dictated by both (competitive) sorption and mobility of the species. For example, for permeation of a mixture of *n*-butane and hydrogen across a silicalite membrane, the steady-state permeation flux of *n*-butane is much higher than that of hydrogen, whose flux is virtually zero (Kapteijn, Bakker, van de Graaf, Zheng, Poppe, & Moulijn, 1995). Hydrogen is virtually excluded from the nanopores by the more strongly sorbed *n*-butane; see Fig. 15(a). The sorption–diffusion principle of transport within nanopores provides a basis for separating hydrogen from a mixture of light hydrocarbons (methane, ethane, propane and butane) from refinery fuel gases by allowing the mixture to permeate through a carbon molecular sieve membrane (Rao & Sircar, 1993). The hydrocarbons are much more strongly adsorbed than hydrogen and permeate selectively across the membrane. Propane and butanes are nearly completely removed in the permeate stream. Final purification of hydrogen by pressure swing adsorption is required before recycling back to the refinery. The advantage of this membrane separation process is that the hydrogen rich stream is recovered from the retentate (feed) side of the membrane and can be re-used in the refinery without the need for further recompression.

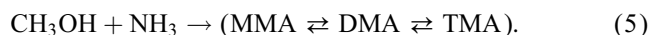
Silicalite membranes also offer more subtle separation possibilities, exploiting configurational entropy effects (Krishna & Smit, 2001). For example for permeation of a mixture of hexane isomers, the selectivity is heavily in favour of the linear isomer; see Fig. 15(b). The high permeation selectivity towards the linear isomer is not due to sieving effects (both isomers can enter the silicalite matrix) but to configurational entropy effects caused due to the higher “packing efficiency” of the linear isomer. To exploit configurational entropy effects we need to operate above a total mixture loading of 4 molecules per unit cell. Below this loading there is very little competition between the linear and branched isomers.

The zeolite membrane reactor deserves further research attention.

5. Separation at the catalyst level

Almost all separation principles for in-situ product removal can be applied at the level of the catalyst by clever catalyst design and modifying the morphology (pore size, connectivity), accessibility to and from active sites, and sorption characteristics of sites.

Consider the reaction of ammonia and methanol to form methyl amines. The equilibrium product consists of a mixture of mono-, di- and tri-methylamines, denoted by MMA, DMA and TMA, respectively.



In conventional catalyst design with Si-Al-oxide catalyst the product consists of a mixture of MMA, DMA and

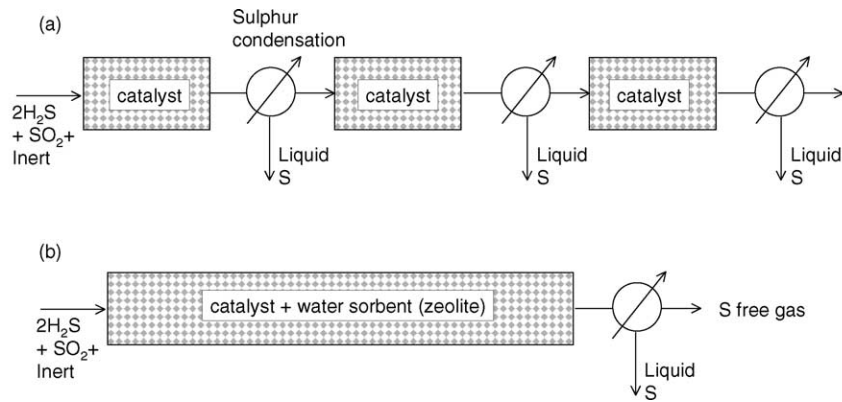


Fig. 13. (a) Conventional fixed-bed reactor train, with inter-stage sulphur removal by condensation, for Claus process. (b) Fixed bed reactor, with in-situ sorption of water by zeolite adsorbent. Adapted from Agar (1999).

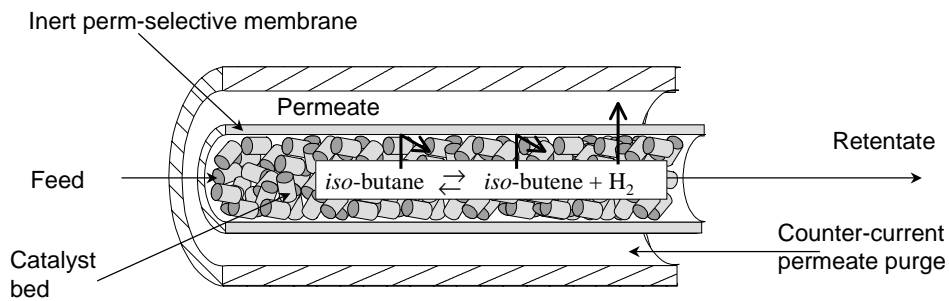


Fig. 14. Membrane reactor for dehydrogenation of *iso*-butane–*iso*-butene.

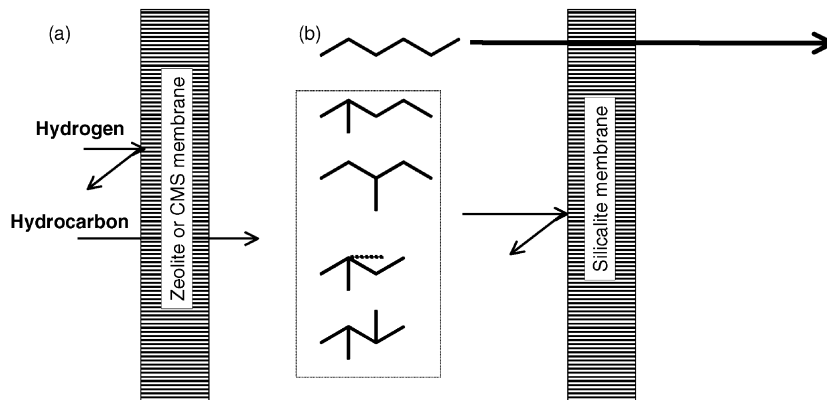


Fig. 15. (a) Permeation of hydrogen–hydrocarbon mixture across a zeolite or CMS membrane. (b) Permeation of hexane isomers across silicalite membrane. The process is highly selective to the linear isomer provided the loading inside the membrane is maintained higher than 4 molecules per unit cell (Krishna & Smit, 2001).

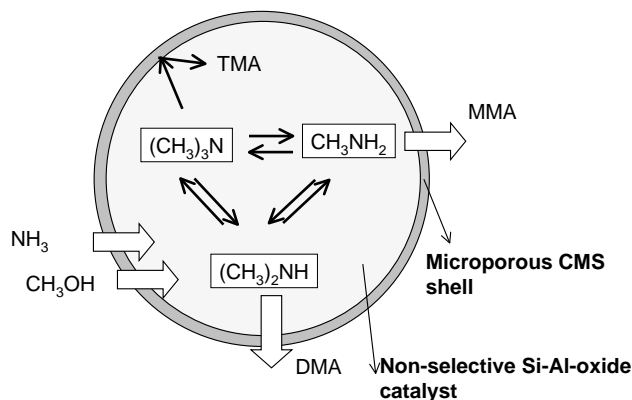


Fig. 16. A carbon molecular sieve (CMS) shell covering a conventional catalyst allows prevents TMA from diffusing out (Foley et al., 1994).

TMA at a composition that are in thermodynamic equilibrium, giving $(\text{MMA} + \text{DMA})/\text{TMA} = 2$. Foley, Lafyatis, Mariwala, Sonnichsen, and Brake (1994) have developed a novel catalyst consisting of Si-Al-oxide catalyst encapsulated within a shell of carbon molecular sieve (CMS). The CMS membrane layer is permeable to the reactants ammonia and methanol as well as to the smaller molecules of the desired products MMA and DMA. The larger molecules of the unwanted by-product TMA, the formation of which is thermodynamically favoured, are retained within the catalyst pellet where they undergo further equilibrium reaction back to the desired products; see Fig. 16. With the CMS membrane shell concept, the product distribution is favourably altered to yield $(\text{MMA} + \text{DMA})/\text{TMA} = 5$.

With zeolite catalysts, in-situ separation can be achieved by proper choice of pore size. Consider the toluene disproportionation reaction to produce benzene and xylenes using a ZSM-5 catalyst (Haag, Lago, & Weisz, 1981). The relative diffusivity values of benzene and ortho-, meta- and para-xylenes are 10000, 1, 1 and 10000, respectively. Therefore, only the products benzene and *p*-xylene can effectively be transported out of the zeolite catalyst. Without diffusional control the relative proportions of the xylene isomers will correspond to the thermodynamic equilibrium between the xylene isomers. As the diffusion of the xylene molecules becomes more limiting the differences in diffusivity of the isomeric xylenes gain importance, resulting in increased selectivity to the para isomer.

Another interesting strategy which has been adopted is the introduction of an aqueous layer around the catalyst before dispersing this (wet) catalyst into an organic reaction medium. This strategy has been applied for selective hydrogenation of benzene to cyclohexene with powdered Pt or Ru catalyst (Wismeijer, Kieboom, & van Bekkum, 1986). The powdered catalyst is first wetted with aqueous ZnSO₄ solution before dispersing it into liquid benzene reactant. Gaseous hydrogen is bubbled into this liquid-liquid-solid dispersion. The desired product cyclohexene distributes preferentially into the organic phase

and is thus prevented from further hydrogenation to cyclohexane; see Fig. 17. Asahi Chemicals are believed to utilise such a concept in their commercial process.

6. Separate feeding of reactants

Partial oxidation of hydrocarbons, a highly exothermic reaction, is usually carried out in a fixed bed reactor. The problems in such reactors are hot-spot formation and selectivity loss due to the high propensity of desired partially oxidised product to react further to yield combustion products (CO₂ and H₂). One of the ways to increase the selectivity towards the intermediate product is to control the oxygen concentration along the reactor length. This can be conveniently implemented by means of the membrane reactor concept; see Fig. 18. The oxygen concentration along the reactor length can be carefully controlled to favourably influence the reactor selectivity (Sanchez & Tsotsis, 2001; Coronas & Santamaria, 1999; Julbe, Farrusseng, & Guizard, 2001; Saracco, Neomagus, Versteeg, & Van Swaij, 1999; Drioli & Romano, 2001; Sirkar, Shanbag, & Kovvali, 1999). This, of course, is not possible in the case of the conventional fixed-bed reactors, where the oxygen concentration is maximum at the entrance and decreases monotonically along the length of the reactor. As a result the selectivity is typically low at the reactor inlet, where the reaction rate is the highest, which negatively impacts on the overall yield. An additional benefit of the membrane reactor concept is that the separation of the oxidant and organic substrate creates reactor conditions less prone to explosions and other undesirable safety effects, that are typically associated with the oxidation of gaseous hydrocarbons, thus potentially broadening the range of feasible operation (Lafarga & Varma, 2000). Of concern are diminished reaction rates, due to the decreased oxygen partial pressures, and reactant hydrocarbon back-diffusion (Sanchez & Tsotsis, 2001).

Both dense and porous membranes have been used in experimental studies (Sanchez & Tsotsis, 2001). Dense membranes are made, typically, of metallic silver and its alloys, various stabilised zirconias, as well as perovskites and brownmillerites. These materials are useful in preparing membranes because they are capable of transporting oxygen selectively. Porous membranes that have been utilised include zeolite and alumina either intact or impregnated by a variety of catalytic materials, including LaOCl, various perovskites, etc. Depending on their pore size and pore size distribution they have been used, with a varying degree of success, in order to maintain a controlled concentration of oxygen in the reaction side.

The membrane reactor concept is finding increasing application in biotechnology (Sanchez & Tsotsis, 2001). For enzymatic conversions, in particular, one often utilises a hollow-fibre reactor, where enzymes are immobilised in the porous part of the hollow fibre membrane. One important advantage that this type of membrane reactor offers over the

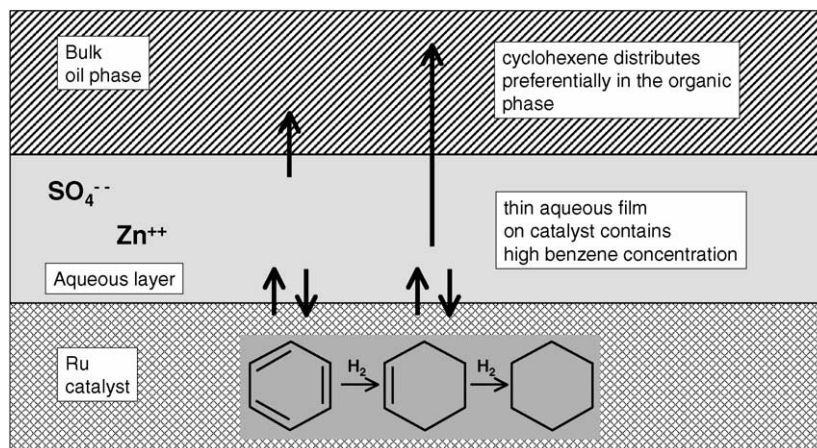


Fig. 17. Use of aqueous layer on catalyst particles to enhance the selectivity towards cyclohexene during hydrogenation of benzene. Adapted from Wismeijer et al. (1986).

more conventional enzymatic conversion bioreactors, is the longer contact times of the reactants with the enzymes, due to the high membrane surface/to reactor volume ratio. Another important and growing application of membrane bioreactors is in waste water treatment. Conventional treatment of waste-water is often carried-out by aerobic or anaerobic biological processes. These processes transform the complex organic contaminants, typically found in the wastewater, into simpler and harmless gaseous or water soluble metabolites, together with some residual sludge. This type of conventional biological treatment has the disadvantage that one must, at some point, physically separate the biocatalyst from the treated water. Membrane-based bioreactor processes present an attractive solution to the problem of biomass separation from the wastewater to be treated, since the membranes provide an effective barrier for microbes and other particles. The use of the membrane, furthermore, provides for a more effective process control, since one can independently adjust the residence time in the fermentation vessel and the permeation rate through the membrane. One important advantage of the membrane-based bioreactor process is in the reduction of the size of the industrial unit.

7. In-situ extraction

By deliberate addition of a second liquid phase containing a selective solvent we may extract the desired product from the reaction zone and prevent further side reactions (Brändström, 1983). For example, in the bromination of dialcohols in aqueous phase the problem is to prevent the second OH group from reacting with HBr to form the dibromide. This can be solved by adding a hydrocarbon to the reaction mixture. The hydrocarbon extracts the monobromide, but not the dihydroxy compound or the HBr, from the reaction mixture. The monobromide is thus removed from the reaction mixture as soon as it is formed and is thereby prevented from the action of HBr by phase separation. In the

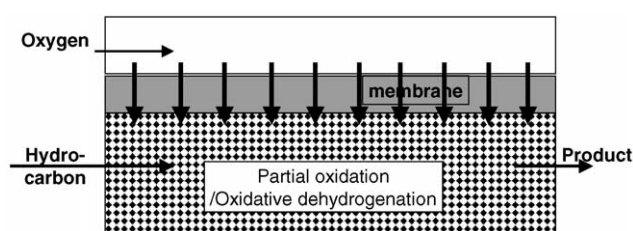


Fig. 18. Staged addition of oxygen to packed bed reactor carrying out partial oxidation of a hydrocarbon.

Hofmann reaction of an amide with hypochlorite the intermediate isocyanate can be extracted out to make isocyanates with high yields. In photochemical sulphoxidation of paraffins water is used to extract sulphonic acid to prevent formation of poly-sulphonic acids. In the Ruhrchemie—Rhône Poulenc process for the production of butanal by hydroformylation of olefin, the in-situ extraction of the desired product from the aqueous reaction phase prevents the formation of heavy ends (Kuntz, 1987); see Fig. 19. Sharma (1988) has considered several examples of reactions which would profit from introduction of an additional extractant phase.

In equilibrium limited biocatalysed reactions removal of the desired product, which are often thermally labile, in-situ supercritical extraction with carbon dioxide can lead to substantial benefits. In the lipase catalysed interesterification of triglycerides, a high degree of incorporation of required fatty acids into triglyceride cannot be obtained because of its reverse reaction. Adschiri, Akiya, and Chin (1992) have applied supercritical carbon dioxide extraction to the removal of products from a liquid-phase reaction system as a means of solving the problem. Supercritical CO₂ is nontoxic, and its critical temperature (304.2 K) is both sufficiently low for dealing with thermally labile materials and close to the optimal temperature for the enzymatic reaction. Significant improvement in the degree of incorporation of oleic acid into

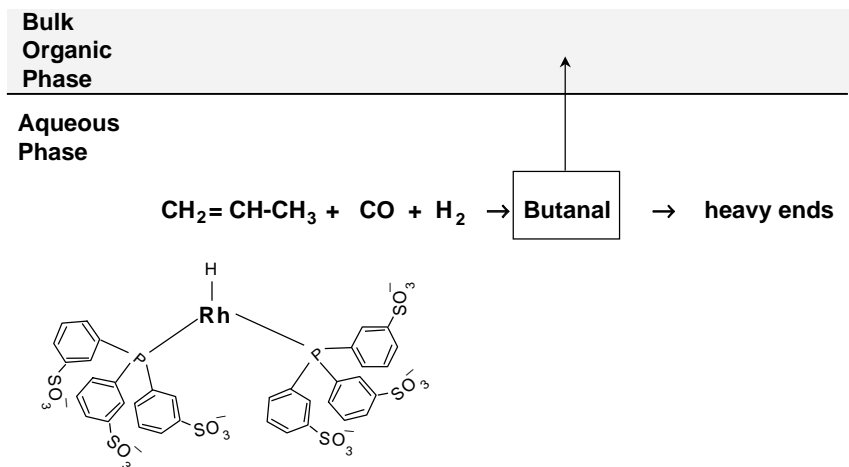


Fig. 19. In-situ extraction of desired butanal in hydroformylation of olefins.

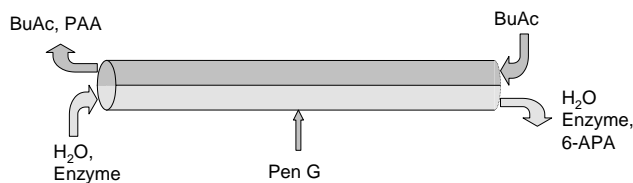


Fig. 20. Counter-current enzymatic biphasic reactor for hydrolysis of Penicillin G; Adapted from Straathof et al. (2001).

the triglyceride, above equilibrium values, was achieved in a batch reactor (Adschiri et al., 1992). Aaltonen and Rantakylä (1991) have listed the various advantages of using supercritical CO₂ as a solvent in enzymatically catalysed reactions, as compared to aqueous media.

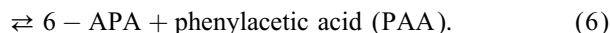
8. Converting batch to continuous counter-current operations

In text books of chemical reaction engineering the analogy is often drawn between batch reactors and plug flow reactors with regard to attainment of conversions. When two liquid phases, say, are contacted in a batch reactor (e.g., a stirred vessel), this is equivalent to a *co-current* plug flow reactor. For equilibrium limited reactions, there is a distinct advantage when converting from batch operations to continuous *counter-current* operation. For the equilibrium limited reaction of ammonia with phthalic anhydride to yield phthalimide a continuously operated multi-stage counter-current reactor offers significant advantages over batch operation (Bartholomé, Hetzel, Horn, Molzahn, Rotermund, & Vogel, 1978) and a high purity product containing negligible amount of unreacted anhydride is obtained.

Enzymatic reactions are often carried out in industry in batch operations. Consider, for example, the enzymatic hydrolysis of penicillin G to produce 6-aminopenicillanic acid

(6-APA), one of the main precursors towards semisynthetic β -lactam antibiotics.

Penicillin G + water

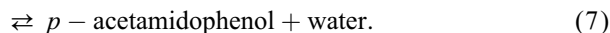


Straathof, den Hollander, and van der Wielen (2001) have demonstrated the advantages of a continuous *counter-current* chromatographic reactor for carrying out this reaction: see Fig. 20. The conversion in the counter-currently contacted biphasic system (water and butyl acetate) is significantly higher than the conversion that can be reached in an equivalent batch system.

9. In-situ crystallisation

Seidlitz, Mathieu, Breysse, and Houzelot (2001) have presented a novel reactor concept for in-situ product separation by crystallisation. They consider the equilibrium-limited synthesis of synthesis of *p*-acetamidophenol:

p - aminophenol + acetic acid



The solvent (mother liquor) for both reaction and crystallisation is (acetic acid + water). Reaction and crystallisation temperatures have been set, respectively, to 100° and 30°C. The apparatus consists if an upper section is dedicated to reaction, working at high temperature, and crystallisation takes place in a bottom section, working at low temperature. The two sections are linked together and the reaction product is directed to the crystallisation section, and mother liquor is recycled to the top so as to improve conversion. The apparatus is fed with reactants in reaction section, while solid-liquid suspension of product is extracted from crystallisation section; see Fig. 21.

Because fouling, or encrustation, is one of the major problems in industrial crystallisation, special care has been taken

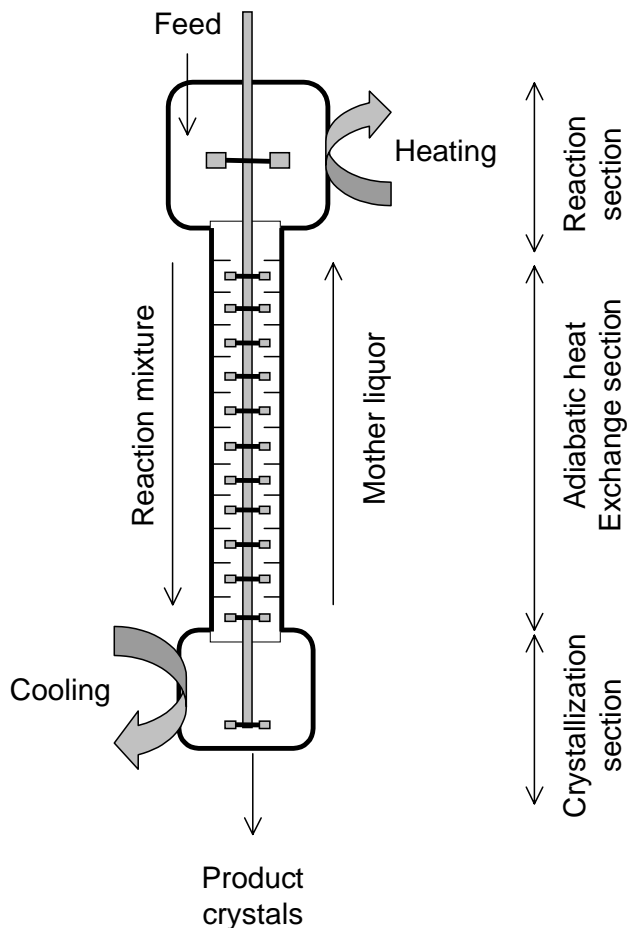


Fig. 21. Simultaneous synthesis and separation of a product by cooling crystallisation. Adapted from Seidlitz, et al. (2001).

to design the apparatus regarding internal heat exchange between both sections. Indeed, it is impossible to avoid fouling on surfaces, particularly for *p*-acetamidophenol, when introducing directly the hot supersaturated stream of product, coming from reaction section into the cold crystallisation section. Consequently, an adiabatic heat exchange section is inserted between reaction and crystallisation section, in order to cool the hot stream by the cold recycling stream of mother liquor coming from the crystallisation section. The adiabatic heat exchange section consists of a multistage agitated Kühni column with perforated plates. The circulation of fluid between reaction and crystallisation sections is created by the effect of backmixing, resulting from the rotation of the radial turbines in the column.

This process concept has two limitations: (1) reaction and crystallisation media must be identical because mother liquor is recycled to reaction section, (2) the solubility of the product must be lower than solubility of reactants or by-products at crystallisation temperature. A lot of industrial syntheses can fit these rules and take advantage of this in-situ crystallisation concept.

10. Concluding remarks

The integration of an in-situ separation function within the reactor holds the promise of increased conversion, higher selectivity and reduced capital costs. Reactive separations have therefore attracted the attention of academic researchers and industrial practitioners alike. While surveying the highlights of recent developments, the following major points emerge:

- For any given reaction scheme there is often of the choice regarding the separation principle to adopt, e.g., distillation, pervaporation, sorption, etc.
- In some cases there may be a choice regarding which of the products is to be separated from the reaction zone.
- The in-situ separation function could be incorporated into the heterogeneous catalyst by altering the catalyst morphology and design.
- Separately feeding the reactants to the reaction zone could be beneficial in many cases.
- For successful commercial implementation of reactive distillation technology, increased attention needs to be paid to the development of the proper hardware.
- The use of membrane reactor technology is already being commercially used in the biotechnology area. Its use in the mainstream chemical industry is imminent.
- New developments in materials technology such as solid oxides and nanoporous materials (zeolites, carbon molecular sieves, nanoporous carbon) have opened new separation-with-reaction avenues, hitherto not possible.

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