On the optimal design of gas-expanded liquids based on process performance

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A B S T R A C T

Gas-expanded liquids (GXLs) are mixed solvents composed of an organic solvent and a compressible gas, usually carbon dioxide (CO2) due to its environmental and economic advantages. The best choice of GXL, as defined by the specific organic solvent and the CO2 composition, depends strongly on the process in which the solvent is to be used. Given the large range of possible choices, there is a need to predict the impact of GXL design on process performance from economic and environmental perspectives. In this work, we present a design methodology in which limited experimental data are used to build a predictive model which allows a wider design space to be assessed. The proposed methodology for the integrated design of CO2-expanded solvent and process is applied to the Diels–Alder reaction of anthracene and 4-phenyl-1,2,4-triazoline-3,5-dione (PTAD). Three organic co-solvents are studied: acetonitrile, methanol and acetone. Given that the process cost is sensitive to the operating pressure and reactor volume, a trade-off between reaction rate constant and solubility is required in order to design an optimal process from a cost perspective. From a total cost perspective and in terms of energy consumption, it is found that designs with small amounts of CO2 or, in the case of acetone, without any CO2, offer the best performance. However, CO2 use is found to lead to a significant reduction in organic solvent inventory, up to 70% in some cases. In this work the importance of taking multiple performance criteria, including process metrics, into account when designing GXLs is demonstrated.

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1. Introduction

Liquid-phase chemical reactions are important both in industrial processes and at the laboratory scale. In many cases, a solvent is used as the medium in which liquid-phase chemical reactions take place. The solvent plays a significant role in determining the reactor performance, especially in the control of reaction rates and temperature; a change of solvent can affect the rate constant(s) by several orders of magnitude and can change the mechanism and hence the order of a chemical reaction (Reichardt and Welton, 2011; Buncel et al., 2003; Gani et al., 2005). Millions of tons of solvent are used in industrial processes every year and the impact of solvents on the environment and on energy consumption cannot be neglected. For example, 20 million tons of volatile organic compounds are released annually and are responsible for 50% of greenhouse gas emissions from typical pharmaceutical processes (Jiménez-González et al., 2005). Furthermore, solvents have been found to be responsible for 60% of the energy used in the production of an active pharmaceutical ingredient (Jiménez-González et al., 2005). Thus, there is a pressing need to minimise...
the quantity of organic solvents used in industrial processes, and to search for alternative, more environmentally friendly solvents. According to Jiménez-González et al. (2011), solvent selection or optimisation is one of the major green engineering research areas for sustainable manufacturing, as the potential impact of advances in this area is high and there is significant room for improvement.

An interesting category of “green” solvents is that of gas-expanded liquids (GXLs) (Jessop and Subramaniam, 2007), which are mixed solvents composed of an organic solvent and a compressible gas, usually CO₂ due to the low risk associated with its use and its economic advantages. GXLs have recently generated great interest, because of their distinct behaviour, which is due to the combination of gas and liquid characteristics; for example, CO₂ enhances gas solubility and mass transfer, while organic solvents increase the solubility of liquid and solid solutes. The properties of a gas-expanded solvent can be tuned by exploiting the properties of the organic solvent and those of the gas, simply by varying the pressure of the system. Ye et al. (2012) studied and successfully predicted the vapour-liquid equilibrium (VLE) of twelve multi-component systems including CO₂-expanded liquids using cubic equations of state with excess Gibbs free energy based mixing rules. GXLs have been shown to be effective solvents for many processes such as oil recovery, where Hwang and Ortiz (2000) showed that by adding an amount of organic solvent in supercritical CO₂ the solvation power of the resulting mixture was significantly enhanced, leading to increased extraction efficiency and reduced asphaltene deposits. They have also been investigated in the context of gas recrystallization (Chang and Randolph, 1991), as mobile phases for HPLC (high-performance liquid chromatography) (Wen and Olesik, 2001), as solvents for post-reaction separations, e.g. in homogeneous catalysis where efficient recovery and recycle of the catalyst is required and where GXLs offer mild operating temperatures and pressures (West et al., 2004), or for particle formation (Jung and Perrut, 2001; Fages et al., 2004). GXLs have also been studied in the context of reactions (Wei et al., 2002), where their performance is also remarkable, as discussed in two extensive reviews on this subject (Akien and Poliakoff, 2009; Subramaniam, 2010). Their advantages include recovery and recycle of both the organic compound and CO₂ through depressurization, which is less energy intensive than standard separation techniques, moderate operating pressures compared to the use of supercritical CO₂, and enhanced transport rates and reaction rates, compared to pure organic solvents. Overall, they are environmentally friendly, as the amount of the organic species in a given volume of GXL solvent is reduced, thanks to the addition of CO₂. Thus, gas-expanded solvents satisfy several green chemistry and process engineering requirements.

When designing a GXL for a given process that includes reaction and separation tasks, one must decide both on the nature of the organic solvent and the composition of the GXL. While there is a growing body of work demonstrating the benefits of GXLs for specific processing steps, and assessing the economic and environmental performance of GXL and supercritical fluid-based processes (Fang et al., 2007; Gong et al., 2008; Ghanta et al., 2012a, 2012b), the question of how to identify the best GXL has not been addressed, although there have been few systematic comparisons of the performance of a GXL compared to that of a pure organic solvent (Akien and Poliakoff, 2009). In fact, the optimal choice is closely linked to the process of interest, as trade-offs must be made between the productivity of the reactor and the cost and effectiveness of any subsequent separations, in order to achieve the best overall process performance. This has been amply demonstrated in the literature on solvent design for separations, in which organic solvents have been the main focus (Buxton et al., 1999; Marcoulaki and Kokossis, 2000; Giovangliou et al., 2003; Eden et al., 2004; Karantzi et al., 2007; Lek-Utaiwan et al., 2008; Bardow et al., 2010; Pereira et al., 2011). In order for a systematic approach to GXL design to be feasible, one must be able to relate mathematically process performance to solvent properties and thus to quantify the impact of solvent choice on physico-chemical phenomena such as reaction rates and phase equilibrium. In this context, there have been several advances in the design of mixtures of organic solvents or aqueous organic solutions (Klein et al., 1992; Buxton et al., 1999; Sinha et al., 2003; Gani, 2004; Karunanithi et al., 2005; Akula et al., 2012), in which both the nature of the co-solvent(s) and the composition of the mixture are considered as part of the design problem.

Of relevance to the design of GXLs for reactive processes, there has been a growing body of work in the area of solvent design for reactions, using chemometrics (Carlson, 1992) as well as computer-aided molecular design (CAMD) techniques. Some of the approaches proposed have been based on empirical models to relate solvent structure to reaction kinetics, maximising the rate constant for a single-step reaction based on the availability of experimental reaction rate data in a few solvents (Folic et al., 2004, 2005; Sheldon et al., 2006; Folic et al., 2006, 2007). This work has been extended to more complex reaction systems (Folic et al., 2008a). Other approaches have been based on a broader range of solvent properties and their impact on reactions, while using database information to include the impact of the solvent on the rate constant (Gani et al., 2005; Harper et al., 2003). Such an approach can be used to tackle multi-step reactive systems (Gani et al., 2008) and has been applied to solvent selection for an enzymatic glycerolysis reaction (Folic et al., 2008b). Stanescu and Achenie (2006) have proposed a methodology based on the generation of candidate solvents by CAMD using a range of solvent properties, followed by quantum mechanical (QM) predictions of the solvent-dependent reaction rate constant to rank the most promising solvents. Recently, Strubing et al. (2013) have proposed a QM-CAMD methodology, in which continuum solvation (Marenich et al., 2009) quantum mechanical calculations of the rate constant are integrated within the design problem formulation and the resulting computational complexity is handled through the use of a surrogate model. No experimental data on the reaction are required to arrive at candidate solvents. The effectiveness of the approach has been demonstrated on a Menschutkin reaction, in which a 40% increase in the rate constant upon using the best reaction solvent identified by QM-CAMD has been observed experimentally.

Despite these advances, existing approaches cannot be applied directly to the design of GXLs for use in reactive processes. A specific challenge arises in the presence of solid reactants, where it is necessary to trade-off the increase in reaction rate as the CO₂ content of the GXL increases, against the resulting decrease in the solubility of the reactants. The objective of this paper is thus to develop a methodology for the design of GXLs based on the consideration of GXL performance within a process. The best GXL is chosen based on the overall economic performance of a conceptual process, where the key processing steps in which the GXL is to be involved are taken into account. The effect of the addition of CO₂ on the organic solvent inventory can also be investigated, and compared to the case where pure organic solvent is used. The nature of the organic co-solvent and the composition of the GXL are key decisions, whose optimal values are affected by reactor volume and energy requirements. Although the design of mixed solvents has been addressed in the literature (Klein et al., 1992; Buxton et al., 1999; Sinha et al., 2003; Karunanithi et al., 2005), attention has so far been focused mainly on low-pressure separation processes and high pressure and reactive systems remain challenging. In particular, the effect of GXL design on the reaction rate, through changes in the reaction rate constant and in
the solubility of the reactants as a function of composition or pressure, cannot be quantified using the models that form the basis of existing CAMD approaches. These issues are tackled here by embedding within the design problem empirical models that link the properties of the mixed solvent to the reaction rate constant as well as a predictive equation of state that can capture pressure effects. The proposed methodology is illustrated on the design of a process to produce a Diels–Alder adduct; it is equally applicable to the design of any other mixed solvent.

The design problem under consideration and the overall methodology are discussed in more detail in Section 2.1. In Sections 2.2.1 and 2.2.2, the models that are used in formulating the GXL design problem are introduced. The process model is introduced in Section 2.2.3 and the cost calculations are presented in Section 2.2.4; finally, the application of the methodology to a Diels–Alder reaction is discussed in Section 3.

2. Problem definition and formulation

2.1. General design problem formulation

The proposed methodology for the integrated design of a CO2-expanded solvent for a given reaction and the conceptual design of the associated reactor-separation system is based on an optimisation framework. The design problem can be expressed as

\[
\begin{align*}
\text{min} & \quad f(x, y) \\
\text{subject to} & \quad h(x, y) = 0 \\
& \quad g(x) \leq 0 \\
& \quad x \in X \subseteq \mathbb{R}^n \\
& \quad y \in [0, 1]^q \quad (1)
\end{align*}
\]

where \( x \) is a \( n \)-dimensional vector of process variables such as flowrates, volumes, compositions and \( y \) is a \( q \)-dimensional vector of binary variables used to specify the choice of organic co-solvent. The objective function, \( f(x, y) \), is an overall performance index, such as the total annualised cost of the process, which needs to be minimized for a specific production rate. The equality constraints, \( h(x, y) \), correspond to the property, process and cost models and the inequalities, \( g(x) \), represent the design constraints. The property constraints include the relationship between the GXL design (nature of the co-solvent and composition) and the reaction rate constant and phase equilibria, while the process model constraints include conservation equations.

A key challenge in GXL design is to develop a modelling framework which allows all the quantities necessary to obtain the performance index to be computed for a range of design choices. A conceptual flowsheet is used to link the GXL make-up to the process performance, taking into account the most significant contributions to performance in reaction and separation steps. To facilitate exposition of the model, it is introduced based on the consideration of a single bimolecular reaction:

\[ A + B \rightarrow C. \]

The flowsheet is shown in Fig. 1. It consists of a CSTR, a separation system and a compressor, illustrating the need to capture solvent and pressure effects on kinetics and phase equilibria. In the separation section, it is assumed that CO2 is recovered by simple depressurization, and that the separation of the organic solvent, reactants and products is effected by evaporation and subsequent condensation of the solvent. In practice, more cost-effective ways to recover the components may be suitable, such as the further addition of CO2 in order to take advantage of its anti-solvent properties. However, given the high energy requirements associated with the proposed evaporation/condensation, it provides a significant cost penalty on the use of organic solvent and hence a best-case assessment of the performance of a GXL relative to the pure organic solvent. The identification of the optimal GXL that results in the minimum total cost of the process as a function of operating pressure, reactor volume and energy costs, is investigated.

2.2. Model development

The model used for GXL design is divided into several sub-models that capture different physical aspects:

- a kinetic model that captures the dependence of the reaction rate constant on the GXL;
- a thermodynamic relationship between the solvent make-up, pressure, temperature and density;
- the material and energy balances;
- the dependence of the performance indices (cost and organic solvent inventory) on process variables.

These different components of the model are described in more detail in the remainder of this section.

2.2.1. Reaction rate constant

In order to study solvent effects on the reaction rate, the solvatochromatic equation (Kamlet and Taft, 1976; Taft and Kamlet, 1976), an empirical model which correlates the reaction rate constant to specific solvent properties, is used. The solvatochromatic equation is a linear free-energy relationship which has been used to correlate a number of free energy-based properties such as rate constants, solubility, octanol–water partition coefficients (Kamlet et al., 1984; Taft et al., 1985). Several forms of the equation, involving different solvent properties, have been proposed. In this work, and without loss of generality, the original form of the equation is used:

\[
\ln k_{r,i} = \ln k_{r,0} + s_i \alpha_i + a_i \beta_i + b_i, \quad (2)
\]

where \( k_{r,i} \) is the rate constant for a reaction \( r \) in a solvent \( i \), \( k_{r,0} \) is the rate constant for reaction \( r \) in a reference solvent, the Greek symbols denote the solvatochromic parameters \( \beta_i \) is the polarity of the solvent, \( \alpha_i \) is the hydrogen bond acidity of the solvent, \( \beta_i \) is the hydrogen bond basicity of the solvent) and \( s_i, a_i, b_i \) are coefficients that depend on the reaction of interest. These coefficients are typically regressed based on experimental kinetic data in several solvents.
The most common application of the solvatochromic equation for chemical reactions has been to investigate the effect of using different pure solvents as a medium. Many solvatochromic parameters have been obtained experimentally for pure solvents (Abraham et al., 1991; Abraham, 1993b, 1993a; Zissimos et al., 2002) and predictive methods have been proposed for solvents for which no data are available (Platts et al., 2006; Sheldon et al., 2005). There has also been some interest in mixed solvents (Barbosa et al., 1996a; Reta et al., 2001: Ray and Bagchi, 2005) but the prediction of mixed solvent parameters as a function of composition, which are needed for GXL design, remains challenging.

There have been some successful attempts to correlate the solvatochromic parameters of binary solvent mixtures to their composition, based on preferential solvation models (Ráfols et al., 1995, 1997; Bosch et al., 1996a, 1996b; Ortega et al., 1996; Rosés et al., 1997; Buhvestov et al., 1998; Herodes et al., 1999; Hari-Mood et al., 2007). Such relationships are key to enabling the design of a GXL in which the optimal solvent make-up must be found. The preferential solvation model of Ráfols et al. (1995) is used in this work. The standard experimental approach for measuring solvatochromic parameters, based on the colour shifts caused by the interactions between a solvent and an indicator probe or solute, is taken into account in developing the model. Indeed, the expected differences in the interactions of a given solute with the two solvent components are considered via local composition variables that correspond to a microsphere of solvation around the solute. In the Ráfols et al. (1995) model, a specific solvent property of interest (i.e., one of the solvatochromic parameters), $Y$, in a mixed solvent consisting of components $i$ and $j$, can be expressed implicitly as a function of the mole fraction of solvent $x_i$, $Y(x_i)$ is obtained as a function of the corresponding property in the pure solvents, $Y_i$ in solvent $i$ and $Y_j$ in solvent $j$:

$$Y(x_i) = x_i Y_i + x_j Y_j + x_i x_j Y_{ij},$$

where subscripts $i$ and $j$ correspond to the pure solvents and $x_i$ (or $x_j$) is the local mole fraction of solvent $i$ (or $j$) in the microsphere of solvation, which in turn depends on the bulk composition, as defined by $x_i$. $x_i x_j$ is the local mole fraction of a hypothetical solvent that forms a microsphere of solvation around the indicator and consists of the same number of $i$ and $j$ molecules. $Y_{ij}$ is the value of property $Y$ for the hypothetical solvent. The preferential solvation parameters $f_{ij}$ and $f_{ji}$, which are composition-independent, are introduced to measure the tendency of the indicator (or solute) to be solvated by solvent $j$ and the hypothetical solvent $ij$, respectively, rather than solvent $i$, and are defined as

$$f_{ij} = \frac{x_i Y_i}{x_i X_i},$$

$$f_{ji} = \frac{x_j Y_j}{x_j X_j}.$$

Thus, the dependence of the solvent property, $Y$, on the bulk composition $x_i$ is given explicitly by the following expression:

$$Y(x_i) = \frac{Y_i (1-x_i)^2 + x_j Y_j (1-x_i) + x_j Y_{ij}(1-x_i)x_i}{(1-x_i)^2 + f_{ij} x_j (1-x_i) + f_{ji} (1-x_i)x_i}.$$

This final equation has three parameters, $f_{ij}$, $f_{ji}$, and $Y_{ij}$, which are estimated based on experimental data, in order to calculate the solvatochromic parameters $Y$ at different compositions. Unfortunately, there are currently limited data for the solvatochromic parameters of GXLs in the literature. We consider three organic solvents in combination with CO$_2$ here: acetonitrile (Ford et al., 2008b), acetone and methanol (Ráfols et al., 1997). In Figs. 2–4, results from parameter estimation for the model described are shown for the three mixed solvents. The solvatochromic parameters are given as a function of mole fraction of CO$_2$ in the mixture (i.e., $j=\text{CO}_2$), at a temperature $T=40\, ^\circ\text{C}$. The globally optimal values for parameters $f_{ij}$, $f_{ji}$ and $Y_{ij}$, as determined by the BARON

![Fig. 2](image2.png)  
**Fig. 2.** Calculated solvatochromic parameters for CO$_2$+acetonitrile at $T=40\, ^\circ\text{C}$ (curves) compared to experimental data (symbols) (Wyatt et al., 2005). Solid curve, diamonds: $\alpha$; dashed curve, squares: $\beta$; dash–dot curve, triangles: $\gamma$.

![Fig. 3](image3.png)  
**Fig. 3.** Calculated solvatochromic parameters for CO$_2$+acetone at $T=40\, ^\circ\text{C}$ (curves) compared to experimental data (symbols) (Wyatt et al., 2005). Solid curve, diamonds: $\alpha$; dashed curve, squares: $\beta$; dash–dot curve, triangles: $\gamma$.

![Fig. 4](image4.png)  
**Fig. 4.** Calculated solvatochromic parameters for CO$_2$+methanol at $T=40\, ^\circ\text{C}$ (curves) compared to experimental data (curves) (Wyatt et al., 2005). Solid curve, diamonds: $\alpha$; dashed curve, squares: $\beta$; dash–dot curve, triangles: $\gamma$. 

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software (Tawarmalani and Sahinidis, 2005; GAMS Development Corporation, 2011) and using a lower bound 0.01 for the parameters $f_{ij}$ and $f_{ji}$, are given in Table 1; an excellent fit is obtained over the entire range of CO2 compositions for the three organic solvents, even in the case of $\alpha$ for methanol + CO2, which exhibits highly nonlinear behaviour.

### 2.2.2. Thermodynamic model

The use of GXLs or other solvents is especially desirable when some of the reactants are solid at the reaction conditions. In such cases, when operating at maximum capacity, the reactor mixture is expected to be at solid–vapour–liquid equilibrium (SVLE) so that the limiting (solid) reactant is present at maximum concentration in the liquid phase, as defined by its solubility. For simplicity, it is assumed that reactant A is a solid.

The isofugacity condition is satisfied for vapour–liquid equilibrium (VLE) and solid–liquid equilibrium (SLE), expressed in terms of fugacity coefficients:

$$
\tilde{y}_i \phi_i(T, P, \tilde{x}) = \tilde{x}_i \phi_i(T, P, \tilde{y}), \quad i = \text{CO}_2, \text{CS}
$$

and

$$
\tilde{f}_A(T, P) = \tilde{x}_A \phi_A(T, P, \tilde{y}),
$$

where the index $i$ runs over the components present in the liquid and vapour phases (here CO2 and the organic co-solvent, referred to as CS above), $\phi_i$ denotes the fugacity coefficient of component $i$ for the vapour phase and $\phi_i$ that for the liquid phase. Component A, the solid, is assumed involatile and is only present in the solid and liquid phases. The isofugacity condition in this case can be written as shown in Eq. (8), where $f_{A}$ is the fugacity of species A in the solid phase (dependent only on temperature and pressure as it is assumed to be pure), $\tilde{x}$ is the vector of liquid phase mole fractions and $\tilde{y}$ that of vapour phase mole fractions, $T$ the temperature and $P$ the pressure. The fugacity coefficients are calculated using the group-contribution volume translated Peng–Robinson equation of state (GC-VTPR EoS) (Ahlers et al., 2004).

The fugacity of the solid phase can be expressed as a function of the fugacity coefficient of the pure solid, $\phi_A^s$, the sublimation pressure of reactant A, $P_{sub}^A$, and the Poynting correction factor, $P_{\text{Po}}^A$, so that

$$
\tilde{f}_A^s(T, P, P_{\text{sub}}^A, P_{\text{Po}}^A) = \tilde{x}_A \phi_A^s(T, P, \tilde{y}).
$$

The Poynting factor, $P_{\text{Po}}^A$, is given by the relation

$$
P_{\text{Po}}^A = \exp \left( \frac{v_i (P - P_{\text{sub}}^A)}{RT} \right),
$$

where $v_i$ is the molar volume of component $i$ in the solid phase. The fugacity coefficient of the pure solid is assumed to be unity at the very low pressure $P_{sub}^A$.

We note that the solubility of the solid could alternatively be obtained based on a thermodynamic route that involves a solid–liquid transition (Sandler, 1999; Poling et al., 2007), rather than the solid–gas transition used above. Both routes are applicable provided that data for the transitions can be found.

#### 2.2.2.3. Process model

The process flowsheet is given in Fig. 1. For this conceptual process, it is assumed that the separation is perfect, so that no product is recycled and there are no losses of reactants or solvents. Thus, there is no need for a fresh solvent feed. The desired production flowrate, $N_{A,4}$, and the reaction temperature are taken as fixed. The optimal co-solvent, defined by vector $y$, the optimal composition of the GXL, as given by the molar fraction of CO2 relative to that of co-solvent, $x_{CO2}$, and the optimal single-pass conversion, $\epsilon$, are sought.

The reaction rate $r$, in mol m$^{-3}$ s$^{-1}$, is given by

$$
r = r(k, C_{A,2}, C_{B,2}),
$$

where $k$ is the reaction rate constant given by Eq. (2), in m$^3$ mol$^{-1}$ s$^{-1}$, and $C_{A,2}$, $C_{B,2}$ are the concentrations of reactants A and B, respectively, in the reactor in mol m$^{-3}$. The reactor mole balance for species $i$ is

$$
N_i + N_{i,3} - N_{i,2} + \nu_i V_R = 0, \quad i = A, B, C, \text{CO}_2, \text{CS},
$$

where $N_i$ is the fresh feed of $i$ (with $N_{C,1} = N_{CO_2,1} = N_{CS,1} = 0$), $N_{i,2}$ is the molar flowrate of $i$ in the stream leaving the reactor, $N_{i,3}$ is the recycle flowrate of $i$ (with $\nu_{CO_2} = \nu_{CS} = 0$) and $V_R$ is the reactor volume in m$^3$.

The single-pass conversion, $\epsilon$, is defined by

$$
N_{A,2} = (1 - \epsilon)(N_{A,1} + N_{A,3}).
$$

Reactant B is assumed to be present in excess by a factor $f_r$

$$
N_{B,2} = f_r N_{A,2}.
$$

The mole fractions in the reactor are the same as in the reactor outlet and given by

$$
x_{R,i} = \sum_{i} \frac{N_{i,2}}{N_{A,2} + N_{B,2}}, \quad i = A, B, C, \text{CO}_2, \text{CS}.
$$

The concentrations of A and B in the reactor, $C_{A,2}$ and $C_{B,2}$, are given by the relations

$$
C_{A,2} = \frac{x_{R,A} M_{A}}{V_R}, \quad i = A, B,
$$

where $M_{R,i}$ is the number of moles of component $i$ in the reactor and $x_{R,i}$ is the mole fraction of component $i$ in the reactor. The GXL composition is given by

$$
x_{CO2} = \frac{x_{R,CO2}}{x_{R,CO2} + x_{R,CS}}
$$

For the phase equilibrium calculations, it is assumed that species B and C behave ideally and are present only in the liquid phase, so that the phase equilibrium calculations are carried out for three components only: component A, the organic co-solvent, and CO2, on the basis of scaled mole fractions $x_i$, such that $x_A + x_{CO2} + x_{CS} = 1$. The mixture is denoted by A+GXL. The scaled mole fractions are therefore defined as

$$
x_i = \frac{x_{R,i}}{x_{R,A} + x_{R,CO2} + x_{R,CS}}.
$$
The mole numbers in the reactor (in mol), $M_{Ri}$, for component $i$, $M_R$ for total number, are related by

$$M_{Ri} = x_RiM_R, \quad i = A, B, C, CO_2, CS,$$

(19)

The volume of the mixture of A and GXL (in $m^3$), $V_{A+GXL}$ is

$$V_{A+GXL} = (M_A + M_{CO_2} + M_{CS})/\rho_{A+GXL},$$

(20)

where $V_{A+GXL}$ is the molar volume of the liquid phase of the $A+GXL$ mixture (in $m^3$ mol$^{-1}$), as calculated in the phase equilibrium model, and $V_{A+GXL}$ is the corresponding volume in the reactor (in $m^3$). $V_R$ and $V_C$, the volumes of reactant B and product C, respectively, are calculated from their pure component densities under the assumption of ideal mixture behaviour:

$$V_i = \frac{M_{Ri}}{\rho_i} \quad i = B, C,$$

(21)

where $M_r$ is the molar mass of $i$ (in $g$ mol$^{-1}$) and $\rho_i$ is the mass density of $i$ (in $g$ m$^{-3}$). The volume of the reactor is therefore given by

$$V_R = V_{A+GXL} + V_B + V_C.$$

(22)

The mass balances for the separator are as follows:

$$N_{i1} = N_{i3}, \quad i = A, B, CO_2, CS,$$

$$N_{C2} = N_{C4}. $$

(23)

The specific co-solvent used is determined by defining binary variables $\gamma_{ACN}$, $\gamma_{DMK}$ and $\gamma_{MEOH}$, which take a value of 1 if acetonitrile, acetone or methanol, respectively, is present in the GXL, and a value of 0 otherwise. To ensure that exactly one co-solvent is selected, they are such that

$$\gamma_{ACN} + \gamma_{DMK} + \gamma_{MEOH} = 1.$$  

(24)

All coefficients relating to the co-solvent CS in the model are set through linear relations to these binary variables. For example,

$$f_{CO_2/CS} = \gamma_{ACN}f_{CO_2/ACN} + \gamma_{DMK}f_{CO_2/DMK} + \gamma_{MEOH}f_{CO_2/MEOH}.$$

(25)

### 2.2.4. Estimating process costs

The results of the material balances can be used to estimate the size of the units and the utility requirements. On this basis, the total cost of the process can be evaluated by considering capital and operating costs. For the flowsheet considered here, the main items of capital cost consist of the costs arising from the reactor, the separation unit, the compressor and the organic solvent, while the cost of the steam and the cooling water for the separation and of the electricity for the compressor contribute to the operating cost.

Correlations from Douglas (1988) are used to obtain the relevant costs and are listed here for completeness. The annualised installed cost of the reactor, $C_{R}$, is thus given by

$$C_{R} = \left(\frac{M_{R}S}{280}\right)^{0.6287}(2.18 + F_P F_m),$$

(26)

where $M_{R}$ is the Marshall and Swift equipment index for 2010, $F_P$ is a correction factor that depends on the pressure. The value of $F_m$ is set to be 1 (assuming carbon steel), while for $F_P$, a second order polynomial is used:

$$F_P = 0.0255P^2 + 0.0387P + 1.0136.$$  

(27)

The annualised cost of the organic solvent is calculated using the following expression:

$$C_{CS} = \frac{1}{\gamma} C_{CS} m_{CS}.$$  

(28)

where subscript $CS$ corresponds to the organic co-solvent, $m_{CS}$ is the inventory of co-solvent (in kg), derived by multiplying the mass of co-solvent in the reactor by 2, and $C_{CS}$ is the cost of the co-solvent per kg, which is obtained from Sigma-Aldrich. Values for cost coefficients and other design data are listed in Table 2.

The capital cost of the separator, $C_{SEP}^{(S)}$, is calculated as the cost of two heat exchangers, namely an evaporator to vapourise the organic solvent and recover the solid product and a condenser to condense the organic solvent again. The overall temperature change is from the reactor temperature of 40 $\degree C$ to the boiling point of the solvent. The installed cost of each heat exchanger is calculated from the following equation (Douglas, 1988):

$$C_{SEP}^{(S)} = \frac{M_{R}S}{280} 23.71(A_{evap}^{0.65} + A_{cond}^{0.65}).$$  

(29)

where $A_{evap}$ and $A_{cond}$ are the areas of the evaporator and condenser respectively, in $m^2$. The areas are obtained by assuming that evaporation is achieved using saturated steam at 15 psig, and condensation is achieved with cooling water.

The annualised installed capital cost of the compressor, $C_{COMP}$, is given as follows (Douglas, 1988):

$$C_{COMP}^{(S)} = \frac{M_{R}S}{280} 536.475 bhp^{0.82}.$$  

(30)

The brake horsepower, bhp, in units of hp, is given by

$$bhp = \frac{P_{hp}}{\eta}.$$  

(31)

where $P_{hp}$ is the utility requirement assuming 100% efficiency in hp units, and $\eta$ is the efficiency of the compressor. The utility requirement is related to the flowrate of $CO_2$ as follows:

$$P_{hp} = \frac{3.0310^{-5} \gamma}{\gamma} P_m Q_{in} \left(\frac{P_m}{P_{in}} \right)^{7} - 1.$$

(32)

### Table 2

| Quantity          | Value | Units |
|-------------------|-------|-------|
| $\gamma_{ACN}$, acetonitrile price | 108   | $ kg^{-1}$ |
| $\gamma_{DMK}$, acetone price        | 40    | $ kg^{-1}$ |
| $\gamma_{MEOH}$, methanol price      | 36    | $ kg^{-1}$ |
| Heat transfer coefficients (Douglas, 1988) | | |
| Condensing gas to vapourising liquid  | 1400  | W m$^{-2}$ K$^{-1}$ |
| Condensing gas to liquid            | 850   | W m$^{-2}$ K$^{-1}$ |
| Liquid to liquid                    | 300   | K$^{-1}$ |
| M&S cost factor (Chemical Engineering Magazine, 2010) | | |
| $\gamma_{ACN}$, steam price          | 0.03  | $ kW h^{-1}$ |
| $\gamma_{DMK}$, cooling water price  | 0.005 | $ kW h^{-1}$ |
| $\gamma_{MEOH}$, electricity price   | 0.06  | $ kW h^{-1}$ |
| Cooling water inlet temperature      | 298.15| K |
| Cooling water outlet temperature     | 313.15| K |
| $\eta$, compressor efficiency        | 0.9   | - |
| Operating hours                    | 8000  | h per year |
where $Q_a$ is the flow that enters the compressor in ft$^3$/min (based on N$\times$CO$_2$;3), $P_a$ and $P_{out}$ are the initial and final pressures, respectively, in lb/in$^2$ and $\gamma = 0.23$, Douglas (1988).

The operating cost includes the cost of the steam, $C_{st}$, and the cooling water, $C_{cw}$, for the separation unit and the electricity, $C_{ele}$, used by the compressor on an annual basis:

$$C_{st}(S) = Q_{st}C_{st},$$

$$C_{cw}(S) = Q_{cw}C_{cw},$$

$$C_{ele}(S) = P_{ele}C_{ele},$$

where $Q_{st}$ is the heating requirement for evaporation, $Q_{cw}$, the cooling requirement for condensation and $Q_{ele}$ the compressor energy requirement.

The total cost, $C_{total}$, in $ per annum, is

$$C_{total} = C_{st} + C_{sep} + C_{cond} + C_{st} + C_{cw} + C_{ele}. $$

(36)

### 3. Case study

The methodology presented for the design of a GXL is applied to the Diels–Alder reaction of anthracene with 4-phenyl-1,2,4-triazine-3,5-dione (PTAD) to form the adduct (8,9,10,11-dibenzo-4-phenyl-2,4,6-triaza[5,2,2,0]tricyclo-undeca-8,10-diene-3,5-dione (adduct). Fig. 5, based on a production rate of 1 mol s$^{-1}$ of adduct. The kinetics of this reaction have been studied in acetonitrile + CO$_2$ mixtures by Ford et al. (2008b) who obtained data at a temperature of $T = 40$ °C, under pseudo first-order conditions, by using an excess of PTAD. Anthracene, a non-polar compound, has limited solubility in the polar co-solvents considered here and its solubility is a determining factor in identifying the optimal GXL composition and equipment size. Given the higher expected solubility of PTAD, it is assumed to be present in excess in the reactor by a factor of five so that $f_e = 5$. The density of the adduct is assumed to be equal to 1.2 g cm$^{-3}$. Other physical properties are listed in Table 3.

#### 3.1. Reaction rate constant

The solvatochromatic equation proposed by Ford et al. (2008b), based on the form of equation (37) and their kinetic data in acetonitrile + CO$_2$ is used to obtain the pseudo first-order rate constant $k_i$ as a function of the properties of a GXL containing the co-solvent i and mole fraction $x_{CO_2}$.

$$k_i(x_{CO_2}) = 1.9 - 2.62r_i^2(x_{CO_2}) - 4.68\alpha_i(x_{CO_2}) + 1.58/\delta_i(x_{CO_2}).$$

(37)

The application of this equation to calculate the reaction rate constant in the three mixed solvents is shown in Fig. 6, where $k_i$ is given as a function of the mole fraction of CO$_2$ in the mixture. The solvatochromatic equation provides a good fit for the acetonitrile co-solvent data for CO$_2$ mole fractions up to 0.85, but significant differences can be seen for the two data points with the highest CO$_2$ content. Due to the low solubility of anthracene at such high CO$_2$ concentrations, larger errors can be expected in the reported rate constants; indeed, this would explain the surprising decrease in rate constant at about 0.95 CO$_2$ mole fraction. This indicates that greater model uncertainty can be expected at high CO$_2$ concentration, and care should be taken in interpreting any solution of the design problem around such values. In all mixed solvents, the rate constant is predicted to increase with increasing the mole fraction of CO$_2$, up to about 0.95. The calculated increase is greater when the co-solvent is acetonitrile than when it is acetone. In contrast, the Diels–Alder reaction is predicted to be very slow in CO$_2$ + methanol at most concentrations, with a sharp increase as the pure-CO$_2$ limit approaches, consistent with the behaviour of $\alpha$ for this mixture. It should be noted that the coefficients of the solvatochromatic equation are based only on acetonitrile + CO$_2$ data and, although the solvatochromatic parameters of the other solvent mixtures are accurate (Figs. 3 and 4), the extrapolated rate constants for the other solvents can be expected to be less accurate.

$\begin{array}{cccccc}
\text{component} & \Delta H_{vap} (\text{J mol}^{-1}) & T_c (\text{K}) & P_c (\text{MPa}) & z_i & \omega & T_b (\text{K}) & C_p (\text{J mol}^{-1} \text{K}^{-1}) & D & E & F & \nu_i (\text{cm}^3 \text{mol}^{-1}) \\
\hline
\text{Acetonitrile} & 29,840^a & 545.5^a & 4.83^b & 0.184^c & 0.321^d & 354.71^e & 82^f & - & - & - & - \\
\text{Acetone} & 29,100^g & 509.5^g & 4.76^h & 0.234^i & 0.311^j & 329.45^k & 131^l & - & - & - & - \\
\text{Methanol} & 35,200^m & 512.6^m & 8.096^n & 0.224^o & 0.559^p & 337.8^q & 88^r & - & - & - & - \\
\text{Water} & 40,670^s & - & - & - & - & 75.3^t & - & 10.08^u & 3741.9^v & 219.2^w & 142.5^x \\
\text{Anthracene} & - & - & - & - & - & - & - & - & - & - & - \\
\end{array}$

$^a$ Antosik et al. (2004), $^b$ Ewing and Ochoa (2004), $^c$ Simmrook et al. (1986), $^d$ Khurma et al. (1983), $^e$ Misra et al. (1987), $^f$ Hopfe (1990) accessed via the DETHERM (2013) database. $^g$ Liessmann et al. (1995) accessed via the DETHERM (2013) database. $^h$ Rastorguev and Ganiev (1967). $^i$ Matynshov and Schmid (1994). $^j$ Ahlers et al. (2004). $^k$ Davila and Trusler (2009). $^l$ Antosik et al. (2004). $^m$ Anouti et al. (2009). $^n$ Ahlers et al. (2004).
3.2. Thermodynamic model

The reactor contains a gas-expanded liquid which consists of anthracene, PTAD, the adduct, CO2 and the organic co-solvent. Anthracene is assumed to be at its solubility limit, so that the solid–liquid equilibrium equation (Eq. (9)) is applied. The excess reactant, PTAD, and the adduct are assumed to be present only in the liquid phase and to behave ideally. CO2 and the organic co-solvent are at vapour–liquid equilibrium.

The predictions of the group-contribution VTPR EoS are compared against available experimental data for vapour–liquid equilibrium for the three GXLs of interest as shown in Fig. 7. The VLE predictions are in reasonable agreement with experimental data over the whole range of CO2 compositions. The percentage average absolute deviations in pressure for the three mixtures are as follows: 15.3% for acetonitrile + CO2, 1.8% for acetone + CO2 and 17.2% for methanol + CO2. In the case of the methanol + CO2 mixture, the onset of vapour–liquid–liquid equilibrium (VLLE) is seen at high pressures, for an overall CO2 mole fraction of approximately 0.6. In Fig. 8, the solubility of anthracene in each binary solvent, as calculated by applying the solid–vapour–liquid equilibrium model to the three component mixtures, is shown as a function of pressure (equivalently xCO2). The model provides a good prediction of the solubility of anthracene in pure acetone and in pure acetonitrile. These results clearly show that the behaviour of solubility as a function of pressure is the opposite of that of the rate constant, with solubility tending to decrease with increasing CO2 mole fraction. Slight solubility maxima are predicted in the case of CO2 with acetonitrile and with methanol. This indicates that the optimal GXL design may require a trade-off between solubility and rate constant.

3.3. GXL design

The mixed-integer design problem consists of identifying the optimal co-solvent, composition for the GXL and conversion for a fixed production rate of adduct. Since in this case study, only three

![Graphs](image-url)
organic solvents are considered, the MINLP is solved by enumeration. An implementation of the model in gPROMS (Process Systems Enterprise, 1997) is used.

The total cost of the process is given in Fig. 9, for the case of a single-pass conversion of 50%. Mole fractions of CO₂ of up to 0.6 are investigated in the case of methanol + CO₂, in order to avoid the occurrence of VLE. The cost with methanol + CO₂ is considerably higher than with the other two mixed solvents, since the reaction in methanol + CO₂ is much slower than in the other solvents (Fig. 6) and the solubility of anthracene is lower (Fig. 8). In all mixed solvents, the cost is seen to increase with increasing CO₂ content in the GXL, although shallow minima are exhibited in the case of acetonitrile + CO₂ and methanol + CO₂. These occur at a low CO₂ mole fraction of $x_{CO_2} = 0.04$; for the acetonitrile co-solvent a minimum cost of approximately $9.3$ million per annum is found, while for the methanol co-solvent the minimum cost is approximately $12.9$ million per annum. In the case of acetonitrile co-solvent, the minimum occurs when no CO₂ is used. However, acetone exhibits a competitive cost over a large region of mole fraction of CO₂ (up to 0.8), when compared to the other co-solvents.

The performance of the process can be investigated for different single-pass conversions, as shown in Fig. 10 for the case of acetone + CO₂. The total cost decreases with increasing conversion, since a smaller amount of organic co-solvent is needed and thus the costs of the separation unit and the compressor, which dominate the total cost, decrease. Qualitatively, the overall dependence of the cost on CO₂ content remains the same at all conversions.

The analysis of the overall cost indicates that the cost is minimised when little or no CO₂ is present (Tables 4 and 5). In this particular case study, pure acetone leads to the best performance. For methanol and acetonitrile, the use of a small amount of CO₂ (4–7 mol%) brings an economic benefit. Nevertheless, in order to design a process with low environmental impact, it is desirable to find a trade-off between the amount of organic solvent and the total costs. This is investigated by considering a single-pass conversion of 95%, which affords the best economic performance, and examining the total cost and the solvent inventory as a function of GXL composition. For methanol, the minimum solvent mass is reached at the upper bound on CO₂ mole fraction of 0.6
The results for acetone and acetonitrile are shown in Fig. 11. As can be seen, the mass of solvent shows a minimum towards higher CO2 mole fractions, specifically, $x_{CO2} = 0.595$ for acetone and $x_{CO2} = 0.855$ for acetonitrile. In the latter case, the high mole fraction of CO2 corresponds to the region of larger uncertainty in kinetic model (cf Fig. 6), which may lead to an underestimation of the amount of solvent required. Nevertheless, the trend in acetonitrile is clear and the use of a GXL has a significant impact on the solvent requirement, with a decrease of around 77% for acetonitrile and of around 17% in the case of acetone. Details of the key design and economic metrics for processes based on minimising the use of organic solvent are listed in Tables 6 and 7. The reduction in solvent use comes at a significant cost, as can be seen by comparing Tables 5 and 7, and incurs a large increase in energy consumption (cf Tables 4 and 6).

The capital and operating costs associated with the use of the compressor are seen to be the largest contributors to the overall cost based on the simple process analysis carried out here. We highlight that accounting for solvent losses and introducing less costly separation techniques may also have an impact on the overall behaviour of the process. The data in Fig. 11 provides a useful illustration of the trade-off between economic and environmental performance indicators. Moderate amounts of CO2, up to 10–15 mol% are found to yield a reasonable trade-off. Naturally, in order to establish a firm comparison of the environmental performance of the three co-solvents, quantitative cradle-to-grave environmental impact analysis should be considered, e.g., following the approach adopted for GXL systems (Fang et al., 2007; Ghanta et al., 2012a, b) and supercritical CO2 systems (Gong et al., 2008).

### 4. Conclusions

Solvents play a vital role in industry and novel solvent classes such as gas-expanded liquids have been the subject of growing interest, thanks especially to their relatively benign environmental impact. An assessment of their benefits must necessarily include process considerations, and take into consideration changes in capital and operating costs. A methodology for the design of a CO2-expanded solvent and an associated conceptual process design was presented and applied to a case study for which kinetic data are available, namely the Diels–Alder reaction of anthracene and PTAO.

Three organic co-solvents were considered: acetonitrile, acetone and methanol. The effect of co-solvent choice on the reaction kinetics was modelled by using a solvatochromic equation in combination with a preferential solvation model, while solid–vapour–liquid phase equilibrium was modelled using the group-contribution volume-translated Peng Robinson (GC-VTPR) equation of state for the fluid phases, and sublimation data for the solid phase. Model calculations were compared to available data and found to offer a good description of the kinetic and thermodynamic properties. On this basis, the GXL designs that achieve minimum process cost or minimum solvent inventory were considered and the impact of solvent composition was investigated.

It was found that the use of pure acetone as a solvent results in a lower cost than any GXL, but both acetonitrile and acetone offer good performance for the process over a range of CO2 concentrations, giving the designer the option to decrease organic solvent use by tuning the operating pressure of the reactor. Effective designs are based on balancing anthracene solubility (highest in the organic solvent) and rate constant (highest at high CO2 content). Methanol was found to be an inappropriate co-solvent for the reaction studied, as the rate of the reaction is predicted to be very low, leading to very high costs.

The proposed methodology highlights the importance of taking multiple process performance indicators into account when designing GXLs and assessing their benefits. The approach can be applied to other processes and can be used to guide the investigation of improved solvent mixtures. Indeed, greater advantages may be derived when applying the proposed approach to other reaction systems, as enhanced reaction rates have also been observed for a Menschutkin reaction in CO2-expanded acetonitrile (Ford et al., 2008a). However, further application of the design approach requires predictive models not only for the rate constant, but also for the phase equilibria of the reactants and GXL mixtures. Such a model is not yet available for methyl p-nitrobenzenesulfonate (MNBS), one of the reactants in the reaction studied by Ford et al. (2008a). Finally, additional benefits may be derived by extending the range of solvents that can be investigated—this will necessitate the measurement of new data on the solvatochromatic behaviour of GXLs.

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