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METHASOL
CO₂ TO CH₃OH

**INTERNATIONAL COOPERATION FOR SELECTIVE CONVERSION
OF CO₂ INTO METHANOL UNDER SOLAR LIGHT**



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Nature of the Deliverable

R	Document, report (excluding the periodic and final reports)	X
DEM	Demonstrator, pilot, prototype, plan designs	
DEC	Websites, patents filing, press & media actions, videos, etc.	
OTHER	Software, technical diagram, etc.	

Dissemination Level

PU	Public, fully open, e.g. web	X
CO	Confidential, only for members of the consortium (including the Commission Services)	

Quality procedure

Date	Version	Reviewers	Comments
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Project Summary

This report is part of the deliverables from the project "METHASOL" which has received funding from the European Union's Horizon 2020 research and innovation program under grant agreement No. 101022649.

Methanol is an appealing energy vectors, with attractive volumetric and gravimetric energy values, storable in liquid phase at ambient conditions of pressure and temperature, and that can be used as fuel directly or converted into chemicals or gasoline. However, its production lacks a sustainable route. Thus, the METHASOL project aims to produce methanol through a sustainable and cost-effective process based on the selective visible light driven gas phase CO₂ reduction, with a solar to methanol energy conversion efficiency of 5%. During 42 months, METHASOL will gather 14 partners from EU/Associated MS, China and the USA, including some of the world's most recognized researchers on artificial photosynthesis, to achieve a ground-breaking combination of a CO₂ reduction reaction (CO₂RR) system based on Metal-Organic Framework (MOF) and a graphitic Carbon Nitride (g-CN) for photocatalytic oxygen evolution reaction (OER), through a Z-scheme heterojunction. Following the definition of the system specifications (WP1), a first set of materials for OER and CO₂RR will be synthesised and their photocatalytic activity and stability will be screened (WP2). The most promising materials will be further analysed thanks to experimental characterisation and modelling (WP3), leading to guidelines used for designing an enhanced CO₂RR and OER materials (WP4). The best systems will then be integrated through a Z-scheme heterojunction, either with or without a mediator, and tested in tailored reactors operating in the gas phase under different conditions (WP5). A complete sustainability analysis will be conducted (WP6) to ensure the clean production of methanol. The cooperation between European and Chinese research entities will be consolidated to last beyond the project lifetime through the creation of a common exploitation plan (WP7). Through its ambitious activities on photocatalyst developments for solar to methanol conversion, METHASOL will propose a new path for decarbonizing Europe.

More information on the project can be found at <https://www.methasol.eu>.

Objective and Executive Summary

The objective of this deliverable is to present the Green Chemistry-based guidelines that can be used for the choice of materials at the early stage of the project. This guide is based on the literature, where the benefits of Green Chemistry have been presented through a number of examples. In this guide, we have used the 12 Principles of Green Chemistry as a framework to structure the guidelines that can be used for the choice of materials. These Green Chemistry-based guidelines have addressed the variety of strategies available for choosing the materials, highlighting the broad spectrum of Green Chemistry. Although the 12 Principles are a helpful framework, the 12 Principles are not independent of each other but rather work in a cross-disciplinary and interconnected framework in which synergies are expected to be realized.

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1. Introduction

Green Chemistry in 1991 was presented to eliminate or reduce hazardous components, in order to reduce the exposure of environment and humans to chemicals (Kharissova et al, 2019). In literature (e.g. Erythropel et al. 2018), the benefits of Green Chemistry have been presented through a number of examples. In this guide, which is based on Erythropel et al. (2018), we use the 12 Principles of Green Chemistry (Figure 1) as a framework to present the guidelines that can be used for the choice of materials.

In this guide, we use the 12 Principles of Green Chemistry as a framework to present the guidelines.



Figure 1. Principles of Green Chemistry (Erythropel et al. 2018)

2. Green Chemistry-based Guidelines

2.1 Guidelines based on Principle 1 (prevent waste)

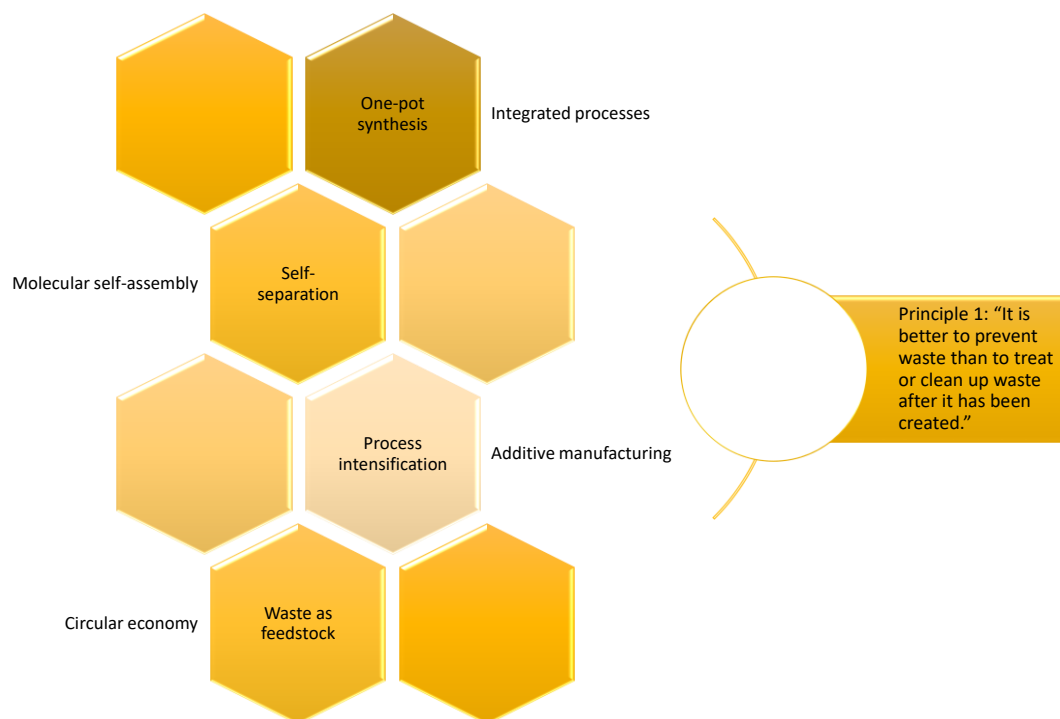


Figure 2. Principle 1 of Green Chemistry

Waste prevention (Principle 1) is a basis of Green Chemistry. The chemical waste has serious environmental, economic, and social impacts (UNEP, 2015).

Based on Principle 1 of Green Chemistry, the guidelines listed below are extracted:

See the concept of
“Industrial Ecology”

Shift from conventional “end-of-pipe” to avoid waste in the first place: To do so, new methods need be used across the lifecycle (starting from extraction, manufacturing, use, up to disposal/recycling), most of which are the main focus of specific Principles of Green Chemistry explained in their sections.

Reduce waste of chemical synthesis via simplification and dematerialization (e.g. one-pot synthesis): The one-pot synthesis avoids purification of intermediates, thus

lowering solvents and separation aids. This can be done via progresses in catalyst design, for instance selective activation of carbon–hydrogen bonds (Gunanathan et al. 2011; Milstein 2010), aryl–aryl bond formation (McGlacken et al. 2009; Klusmann and Sureshkumar 2011; Su et al. 2015; Girard et al. 2014), and olefin metathesis (Seigal 2005).

Design reactions where the products or reagents undertake further roles that are ordinarily done by auxiliaries (e.g. self-separation or molecular self-assembly): This lead to autonomous reactions with less resource that is needed for driving the system (Whitesides 2002). The main elements in this strategy are designing at the system level as well as benefiting intrinsic chemical and physical properties (Zimmerman 2006).

Apply the concept of Process Intensification: It focuses on re-design for better quality, yield, and efficiency, which is done via reduction in complexity of process or size of plant (Zimmerman 2006; DOE 2015).

Closed loop (“waste as feedstock”) systems if the waste generation is not completely avoidable: Metallic chemistry is an example where toxicity of waste streams are considerable under the conditions that energy and material requirements for virgin (and scarce) material are high. (Izatt 2014). Waste-as-feedstock study has made considerable progresses in valorisation of renewables (Principle 7). Many approaches to quantify waste and efficient application of materials are presented e.g. Environmental Factor, or *E*-factor (Sheldon 2007, 2008, 2012) (Principle 2), Life Cycle Assessment (LCA) (Swarr et al. 2017).

Anticipate end-of-life options to make sure that processes are sustainable: This falls in the “circular economy” concept, which can be applied at the interface of engineering and chemistry (O'Connor, 2016).

E-factor and LCA are examples of the approaches that are available to quantify waste and efficient application of materials.

2.2 Guidelines based on Principle 2 (atom economy)

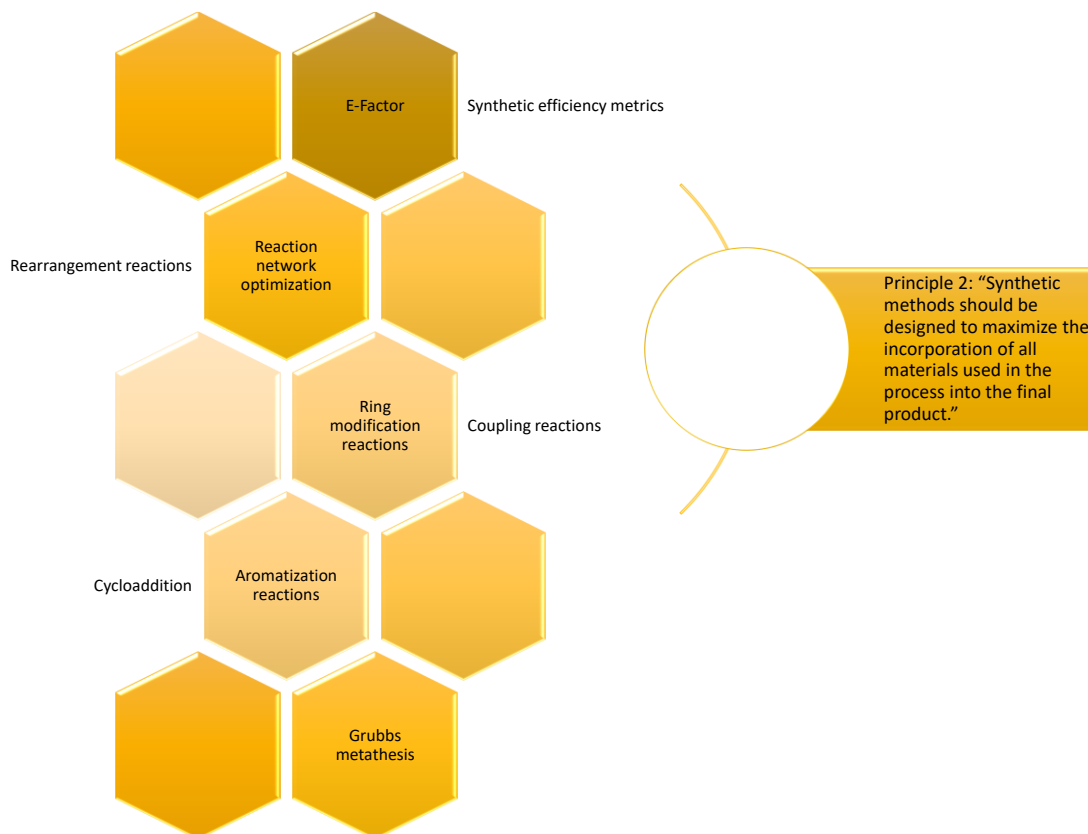


Figure 3. Principle 2 of Green Chemistry

Traditionally, selectivity and yield as a measure of success were used. Today, “atom economy” (Trost, 1991) is used as it is adapted as a supplement to the E-factor.

Based on Principle 2 of Green Chemistry, the guidelines listed below are extracted:

Apply atom economy’s metrics: The concept of atom economy is established on the conventional philosophy of yield by dividing the molecular weight of the product(s) by the reactants, hence the generated waste is considered (Table 1).

Table 1. Metrics of atom economy (adapted from Erythropel et al. 2018)

Metric	Equation
Percent yield	$\frac{\text{Actual yield}}{\text{Theoretical yield}} \times 100\%$
% Atom economy	$\frac{\text{MW atoms utilized}}{\text{MW of reactants}} \times 100\%$
% Experimental atom Economy	$\frac{\text{Theoretical yield}}{\text{Mass of reactants}} \times 100\%$
%PE EAE	$\frac{\text{Actual yield}}{\text{Mass of reactants}} \times 100\%$
<i>E</i> -Factor	$\frac{\text{Waste generated}}{\text{Actual yield}}$
<i>F</i> -Factor	$\frac{\text{Value of metric of interest}}{\text{Functionality}}$

Metrics of atom economy are not limited to E-Factor.

Use chemical reactions with high atom economy:

- Rearrangement chemical reactions e.g. the Cope rearrangement (Kurti and Czako, 2005), the Claisen rearrangement (Li and Trost, 2008), the Curtius rearrangement (Bräse et al. 2005), and the Schmidt reaction (Bräse et al. 2005; Nyfeler and Renaud 2006)
- Coupling reactions e.g. the Suzuki–Miyaura cross-coupling (Miyaura et al. 1979)

- Ring contraction/expansion reactions (Troost et al. 2005; Song et al. 2011) e.g. the Buchner reaction (Reisman et al. 2011) and the benzilic acid rearrangement (Yamabe et al. 2006)
- Cycloaddition/aromatization reactions e.g. the Biginelli reaction (Marson 2012) and the Diels–Alder cycloaddition (Kotha et al 2015)
- Catalytic reaction pathways (Dicks and Hent, 2015) (Principle 9)
- Approached for protecting group-free synthesis result in considerable benefits (Young and Baran, 2009) (Principle 8)

Minimize the number of reaction steps (step-economy): Chemical production often depends on multiple synthetic steps (Marth et al 2015). One approach to enhance efficiency is via step-economy, where step-economical synthesis can be developed to target molecular function or structure (Wender 2014). In this context, Computer-Aided Organic Synthesis (CAOS) models (Todd 2005) can be beneficial in terms of optimizing step economy, improving atom economy and minimizing formation of byproduct(s).

Measure the impact of improvements in synthetic efficiency on other aspects of the lifecycle of chemical: For instance, extraction of metals utilized in catalysts, can offset the advantages in chemical synthesis. In addition to resource efficiencies (e.g. energy), efficiency metrics need to be used to measure the health and environmental effects of new methods via LCA.

Extraction of metals used in catalysts, can offset the overall benefits.

2.3 Guidelines based on Principle 3 (less hazardous synthesis)

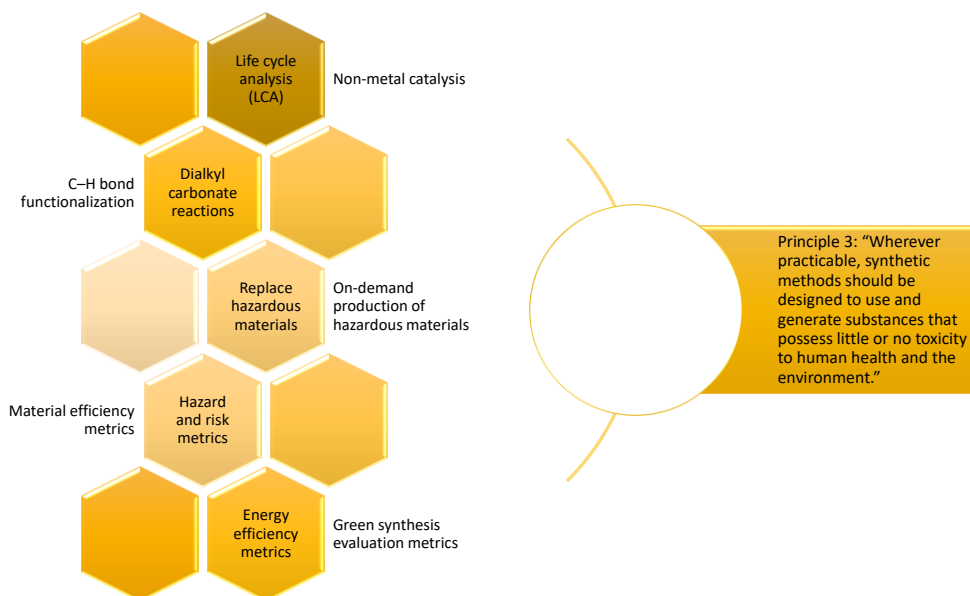


Figure 4. Principle 3 of Green Chemistry

Principle 3 of Green Chemistry, which is linked to Principle 4, take into account aspects other than efficiency when assessing social and environmental effects.

Based on Principle 3 of Green Chemistry, the guidelines listed below are extracted:

Adapt concepts from related areas (e.g. environmental chemistry, toxicology) and to take into account impacts across the whole lifecycle: One of the central philosophies of Green Chemistry is reduction of risk (U.S. National Research Council, 1983) by lowering hazards listed in Table 2 (Mihelcic and Zimmerman 2010).

Table 2. Hazard categories (Mihelcic and Zimmerman, 2010)

Human toxicity hazards		Environmental toxicity hazards	Physical hazards	Global hazards
Carcinogenicity	Immunotoxicity	Aquatic toxicity	Explosivity	Acid rain
Neurotoxicity	Reproductive toxicity	Avian toxicity	Corrosivity	Global warming
Hepatotoxicity	Teratogenicity	Amphibian toxicity	Oxidizers	Ozone depletion
Nephrotoxicity	Mutagenicity (DNA toxicity)	Phytotoxicity	Reducers	Security threat
Cardiotoxicity	Dermal toxicity	Mammalian toxicity (nonhuman)	pH (acidic or basic)	Water scarcity/flooding
Hematological toxicity	Ocular toxicity		Violent reaction with water	Persistence/bioaccumulation
Endocrine toxicity	Enzyme interactions			Loss of biodiversity

Principle 3 needs collaborations across Environmental Chemistry, Toxicology, and Environmental Engineering.

Reduce or eliminate hazardous chemical intermediates: This involves drop-in substitutions for problematical reagents; for instance, dimethyl carbonate has a better environmental index in carbonylation and methylation reactions than phosgene, dimethyl sulphate, or methyl halides (Fiorani et al 2018).

Find alternatives to important intermediates such as organohalogenes: This can be done through improvement in design of catalyst, especially regarding selectivity. For the case of carbon–hydrogen bond activation, which is conventionally performed via halogen-mediated functionalization (Hartwig 2016). As greener alternatives, the selective and direct transition metal catalyst-mediated carbon–hydrogen bond activation approaches were developed to avoid toxic byproducts, with further enhancements in step- and atom-efficiencies (Gensch et al 2016).

Use less toxic and abundant metals in catalytic approaches: This is detailed in Principle 9 (Polshettiwar and Varma, 2010).

On-demand or in situ production and consumption of toxic components: This can be an option to decrease risks linked with synthetic systems (Principle 12) as proved for phosgene in amide synthesis (Fuse et al 2011).

Use of quantitative and robust measures: One of the main challenges in developing less hazardous synthetic approaches is weak characterization of toxicity properties of wastes. In addition, even after toxic hazards are well-identified, it is more challenging to perform quantitative comparisons. In this regards, quantitative and robust measures were developed such as:

i) Environmental Quotient, which take into accounted both the *E*-factor of a process and its inherent hazard (Sheldon, 1994);

ii) Environmental Assessment Tool for Organic Synthesis (EATOS), which take into accounts the quantity of waste and reactants as well as their relative toxicity effects (Eissen and Metzger 2002).

iii) EcoScale, which scores the safety of chemicals and also process details (Van Aken et al 2006).

Besides, LCA methodology is also utilized to assess chemical synthesis pathways (Eckelman, 2016) although gaps in data about toxicity of chemicals is still a concern.

Environmental Quotient, EATOS, and EcoScal are examples of the measures for Principle 3.

Industry, government entities and NGOs have built and adapted tools to evaluate hazard such as what is listed below:

**USEtox: A tool to
evaluate ecotoxicity
and human toxicity**

- “LifecycleInitiative” presented the USEtox model to evaluate ecotoxicity and human toxicity (Rosenbaum et al 2008)
- BASF presented an eco-efficiency assessment tool to evaluate ecological effects versus cost-savings (Saling et al 2002)

2.4 Guidelines based on Principle 4 (design benign chemicals)

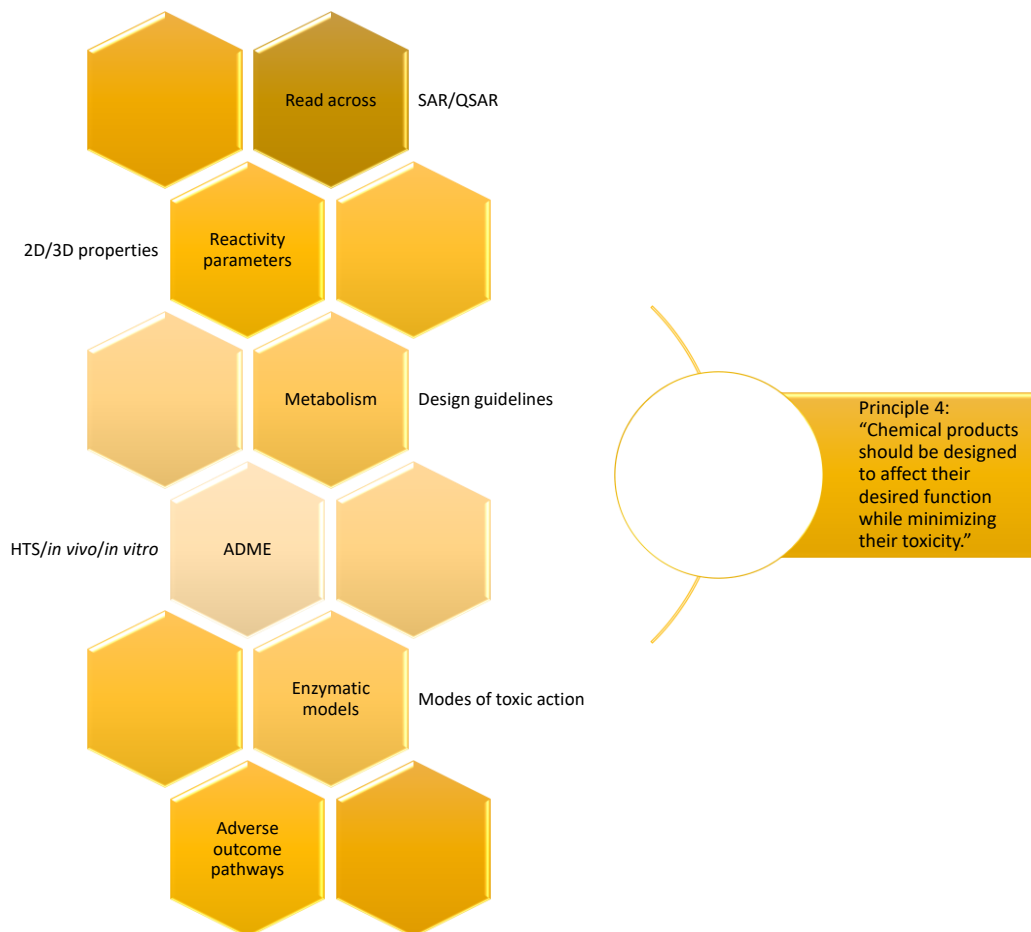


Figure 5. Principle 4 of Green Chemistry

Principle 4 is one of the least developed Green Chemistry's Principles,

Principle 4 is one of the least developed Green Chemistry's Principles, which might be due to the fact that Principle 4 needs knowledge of both chemical function and toxicity properties (Voutchkova et al 2012), as well as the knowledge of environmental and chemical engineering to mitigate any of the other hazards listed in Table 2. The objective is to pinpoint hazardous components and then substitute them with less hazardous components.

Based on Principle 4 of Green Chemistry, the guidelines listed below are extracted:

Design chemical alternatives based on molecular design guidelines: The lack of toxicity information on potential substitutions may result in the substitution of one hazardous components with another due to regrettable replacement (Zimmerman and Anastas, 2015). Hence, developments of chemical alternatives can be assisted by the molecular design guidelines in order to pinpoint areas of chemical space with lower hazard (Tickner et al. 2015) while take into accounting functional performance.

Use the approaches for prediction of chemical activity from structure: Predictive toxicity models are established on the basis that linked molecular properties and chemical structure are connected to both biological effects and chemical function (Jaworska and Nikolova-Jeliazkova, 2007). Approaches to predict activity from structure are in use for more than one hundred years (Meyer, 1901) and were mainly applied as read-across and structure–activity relationships (SAR) models (Schultz et al 2006).

Develop molecular design guidelines based on 3D structure: This can be achieved by density functional theory (DFT) (Shen et al 2016). Furthermore, computational power allowed to include new descriptors e.g. electron affinity in *in silico* models (Knudsen et al 2015). For instance, rigorous toxicity models based on three-dimensional reactivity properties were proved to have better performance than conventional two-dimensional QSAR (Melnikov et al 2016).

Apply the adverse outcome pathway (AOP) and molecular initiating events (MIEs): The objective of “*in silico*” models is to integrate chemical's absorption, distribution, metabolism, and excretion (ADME). These complex mechanisms depend on properties and structure, as well as on individual variability, target endpoint, and species (European Chemicals Agency 2011). The concepts of AOP and MIEs were presented to aid model biological cascades via main steps of initiation and propagation (Vinken, 2013). From the perspective of chemical properties, there are two types of processes: i) toxicokinetic: how a component reaches the site of toxic impact and ii) toxicodynamic: which biological interactions result in unfavourable impacts (Melnikov et al 2016). The 3D chemical features aid build interpretable models for toxicokinetic and toxicodynamic impacts (Enoch 2011) and can be linked to chemicals' modes of action in order to enhance performance of models (Nendza 2014).

Tox21 and ToxCast are databases that can be used to identify properties related to mechanisms of toxic action.

Identify structures and properties related to mechanisms of toxic action and toxic endpoints: This is needed to address chemical function in the molecular design guidelines (Phillips et al 2017). New medium and high throughput screening (HTS) platforms have been developed (Knudsen et al 2015). Large *in vitro* databases (e.g. Tox21 and ToxCast) are built to help elucidate modes of toxic action (Hsieh et al 2015).

2.5 Guidelines based on Principle 5 (benign solvents & auxiliaries)

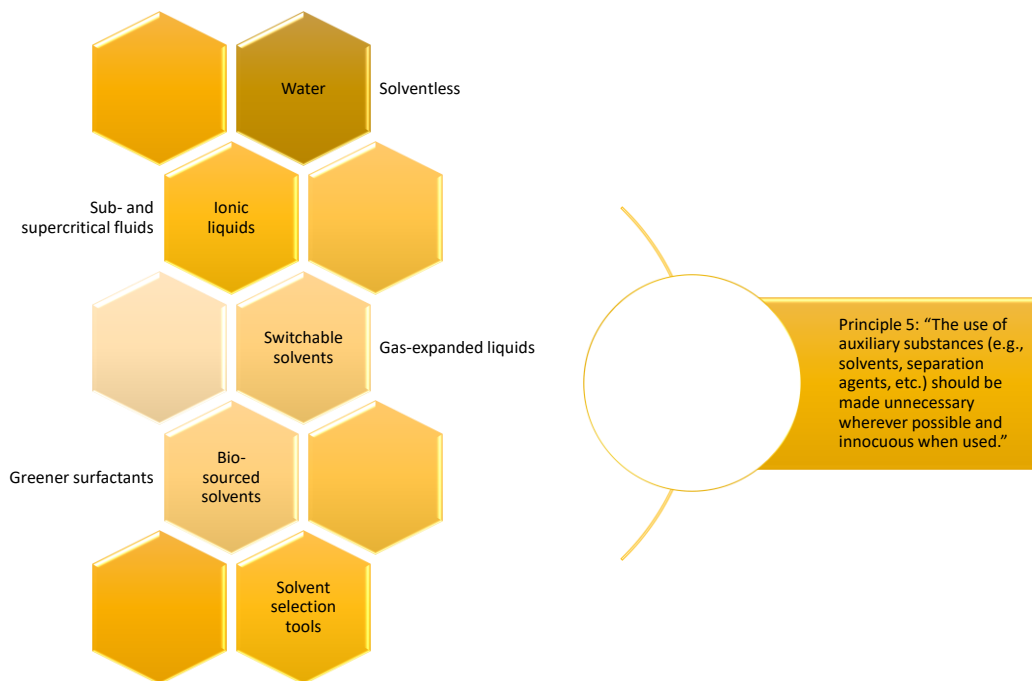


Figure 6. Principle 5 of Green Chemistry

Solvents are very important factor in the environmental impact of chemicals and pharmaceuticals (Slater et al 2010). Conventional volatile solvents have high potential for exposures, which increase risk when are toxic as well (Breslow 2010). That is why solvent use minimization and replacement was a dynamic field in Green Chemistry (Alder et al 2016).

Based on Principle 5 of Green Chemistry, the guidelines listed below are extracted:

Use of water as solvent: As water is innocuous, it has received considerable attention as a green solvent. Many reactions can occur in water, and the application of miscible organic co-solvents expanded the scope to incorporate electrochemical synthesis, nucleophilic substitutions, oxidations and reductions (Simon and Li, 2012). Nevertheless, there remain challenges regarding lifecycle take into account e.g. socioeconomic effects of trans-national water “embedded” in final products and imbalances in quantity (and quality) of water (Wang et al 2016).

Several solvent selection guides are available online.

Use solvent selection guides: Several guides for choice of solvents are already available (Byrne et al 2016), which facilitate the identification of targets for substitution and take into account of candidates for replacement. Options for solvent alternatives are expanding thanks to progresses in bio-based solvents e.g. 2-methyltetrahydrofuran and glycerol derivatives (Santoro et al 2017).

Design solvents taking downstream process steps into consideration (switchable solvents (Kerton et al 2013)): It consists of three main categories: switchable-hydrophilicity solvent (SHS), switchable water (SW), and switchable-polarity solvents (SPS) (Jessop et al 2012). The idea of these is to allow the chemical reaction in one mode, then swap modes helping the separation of final product.

Supercritical carbon dioxide is very attractive solvent.

Use gas expanded liquids and subcritical and supercritical fluids: Within available subcritical/supercritical (Leitner, 2002) and gas expanded liquid (Soh et al 2014) regions, conditions can be adjusted to enhance energy efficiency and yield (Jessop and Subramaniam, 2007). Supercritical carbon dioxide is very attractive solvent due to its simple separation from reaction mixtures through depressurization (Jessop et al 2012).

Use room-temperature ionic liquids (ILs): ILs (Lozano et al 2015) are organic salts made of cations and anions. The main benefits of ILs are their thermal stability, their very low vapour pressure, and the ability to match libraries of cations and anions (Zhang et al 2012). This resulted in making ILs that are comparable to the most-commonly used solvents (e.g. acetone) in a range of uses (Villar-Garcia et al 2014). Note that ILs' manufacturing and disposal are typically more resource-intensive than the conventional solvents (Wasserscheid and Joni, 2010).

Try to eliminate the application of solvents with unconventional ways of mixing or supplying energy (Gawande 2014): For instance, the application of ball bearings to blend solids at high speeds (Friscic, 2012) exhibits much potential, along with microwave assisted reactions (Kappe et al 2013).

2.6 Guidelines based on Principle 6 (design for energy efficiency)

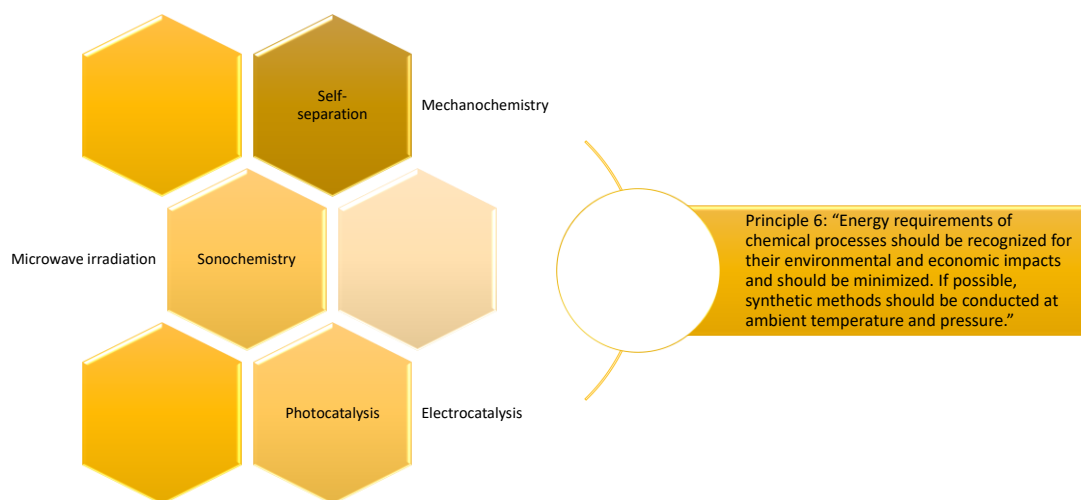


Figure 7. Principle 6 of Green Chemistry

Separation of the final product is the most energy-intensive step of chemical synthesis.

On one hand, catalyst is utilized as an effective way of lowering the energy demand of a reaction (Principle 9). On the other hand, Green Chemistry has played an important role regarding the establishing methods that decrease the total energy demand for reactions, concentrating particularly on separation and work-up because they require high-energy demand.

Within synthesis, the most energy demanding stage is the separation of product (Sholl and Lively, 2016). There are huge rooms to reduce energy demand if separations can be done without energy-intensive methods. As mentioned in Principles 1 and 5, there are many examples in this regard: i) Example 1: the application of a switchable solvent make it possible to separate the final product from the solvent by the addition of carbon dioxide and water (Jessop et al 2010).; ii) Example 2: Benefiting from the change in solubility of a catalysis in reactants against products paves the way for self-separation toward the termination of the chemical reaction (Leng et al 2009).

Based on Principle 6 of Green Chemistry, the guidelines listed below are extracted:

Benefit from progresses in unconventional mechanisms of energy delivery: Enhancements in shorter reaction times, milder reaction conditions, and energy

efficiency can result in considerable benefits (Polshettiwar and Varma 2008) through the unconventional energy delivery mechanisms listed below:

- **Microwave irradiation:** Heating of chemical reactions that need hours at high temperature can be done very quickly using this method (Moseley and Kappe, 2011). The method is compatible with a wide variety of solvents and even solvent-free systems (de la Hoz et al 2016). It should be noted that the finding whether process is more efficient when done with this system than traditional heating, have to be evaluated on a case-by-case assessment (Moseley and Kappe, 2011).
- **Sonochemistry** utilize ultra-high frequency waves in order to resonate air cavities until implosion takes place, which convert electric into mechanical energy (Mason and Peters 2002). The obtained energy can heat the local surrounding up to several thousand Kelvins (Cravotto and Cintas, 2006). Other uses of the sonochemistry system are coupling with other methods to build synergistic impacts e.g. with microwave-aided heating particularly in heterogenous catalyst where sonochemistry effects the surface of the most commonly used metals (Cravotto and Cintas, 2006), and also in microfluidic reactors, in which sonochemistry can avoid solids build-up in process intensification (Fernandez Rivas and Kuhn, 2016). Sonochemical oxidation was shown to efficiently degrade organic polymers (Adewuyi, 2001).
- **Electrocatalyst** works by using a potential difference between an anode and a cathode in a conductive medium (a conductive polymer or a solution-based supporting electrolyte) allowing electron transport. Electrochemical reactions typically do not need pressurization or heating, but convert the electricity into chemical energy. The benefits of this method were shown for many environmental uses such as water treatment (Matilainen and Sillanpaa, 2010), water splitting (Han et al, 2016), and carbon dioxide reduction (Qiao et al 2014).
- **Photocatalyst** can be used without any need for electrolyte and also can be performed homogeneously allowing for the application of enantioselective catalysis in synthesis of fine chemicals (Prier et al 2013). Heterogeneous

See Ramyashree et al. (2020) regarding metal-organic framework-based photocatalysts for carbon dioxide reduction to methanol

The name of the photocatalysis itself is related to two of principles of Green Chemistry: Principles 6 and 9 (Carlos and Quintero 2011).

photocatalyst benefits from the application of semiconducting materials in various redox transformations.

- Photo-assisted electrochemistry: The two methods of electrochemical photocatalytic are supplementary because both perform redox chemistry on a surface with a potential from external sources e.g. technology for water splitting or carbon dioxide reduction (White et al 2015).

2.7 Guidelines based on Principle 7 (use of renewable feedstocks)

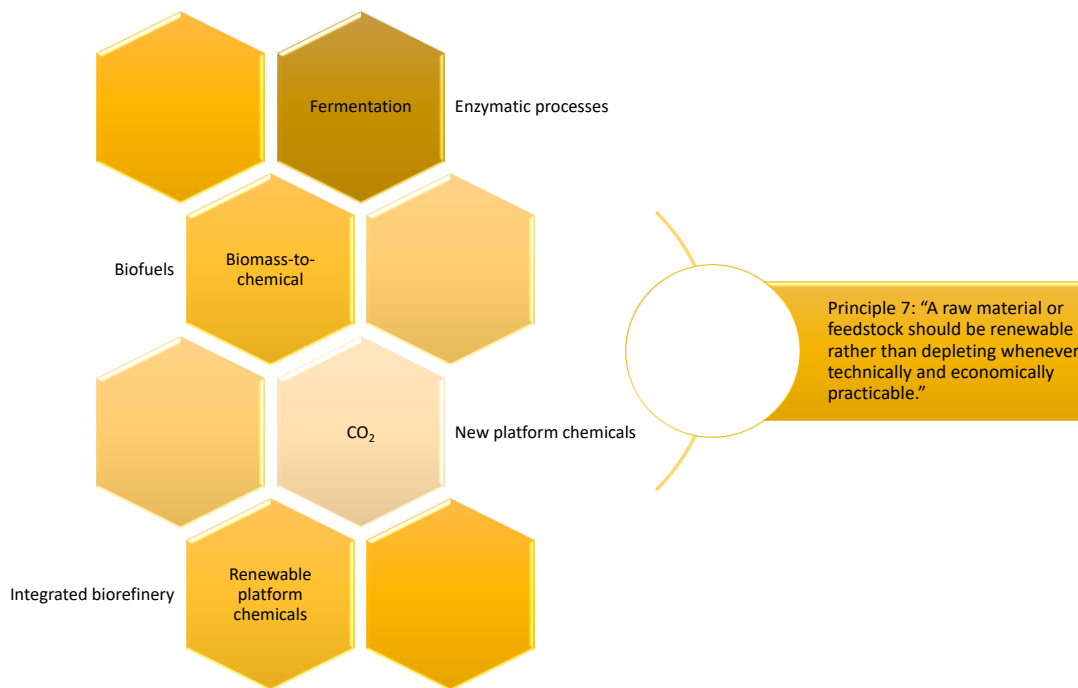


Figure 8. Principle 7 of Green Chemistry

As biomass-to-chemical technology development is more and more guided by LCA, many of the fundamental concerns (e.g. land transformation, water use) lead to investment in renewables that are seen as low value or waste.

Based on Principle 7 of Green Chemistry, the guidelines listed below are extracted:

“Redox Economy” vs. “Atom Economy”

Redox economy: Crude petroleum has 85–89% C, 10–14% H, and less than 1% O while renewables have only 50–75% C, 6–13% H, and 11–45% O (Hirth and Busch, 2003). Consequently, new processes must be developed to valorise these materials, including carbon dioxide. Similar to the idea of atom economy (Principle 2), the concept of “redox economy”, is a helpful way to assess chemical processing of renewables (Burns et al 2009).

Take into account the importance of intermediate “building block” chemicals: On one side, many of “building block” bio-based chemicals are identical to considerable

petrochemical feedstocks (Gallezot, 2012). On the other side, biobased feedstock can also provide routes to various building blocks that are difficult to get from crude oil, thus providing new opportunities (Spevacek, 2017) e.g. C2–C3 olefins from carbon dioxide as well as C1 molecules (methanol, formic acid, formaldehyde) (Centi et al 2013).

Biotechnology vs. “classic” organic synthesis: Biotechnology has several advantages as molecules can be generated through only a single step, products are usually pure stereoisomers, and side chemical reactions seldom happen because of the specificity of the enzymatic conversion (see bio-catalyst in Principle 9) (Keasling et al 2012). Nevertheless, there are several drawbacks linked with enzymatic/ fermentation process: carbon sources are usually mono- or disaccharides, which either originates from crops (e.g. corn) or must be made from lignocellulosic material, adding a typically energy-intensive step (Agbor et al 2011). Furthermore, microbial synthesis yields are usually lower than chemical synthesis (Jang et al 2012).

Use self-cycling fermenter to “synchronize” cell growth: This can enhance microbe productivity (Storms et al 2012). An final objective can be the co-production of chemicals and food through a “bio-refinery” (Brar et al 2016).

Apply “the six principles of Green extraction”: Microalgae were the subject of intense study interest (Foley et al 2011), which led to Green Chemistry-guided improvements in method for lipid extraction (Kwan et al 2016) and bio-fuel production (Mata et al 2010). The guidelines on green extraction methods are not limited to microalgae, and presented as “the six principles of Green extraction” (Chemat et al 2012).

**The Six Principles
of Green Extraction
are not limited to
microalgae.**

2.8 Guidelines based on Principle 8 (reduce derivatives)

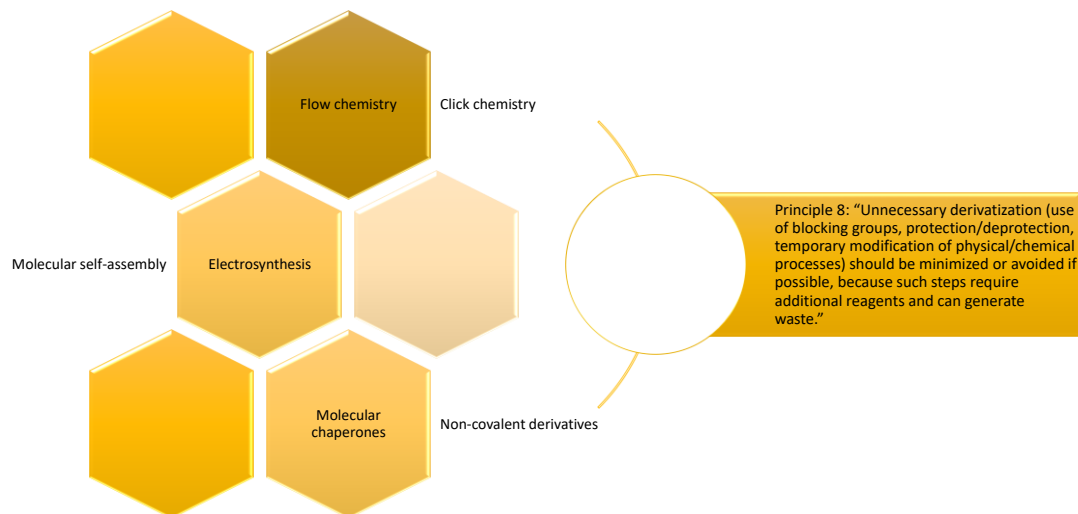


Figure 9. Principle 8 of Green Chemistry

Preferably, chemical synthesis is better to be done without protecting groups whenever feasible as they consumes further raw materials, which increases the number of intermediate separation stages (Anastas and Warner, 1998). This can be done by improving reaction selectivity (chemoselectivity) or by using non-covalent interactions (Shenvi et al 2009) as detailed in the following guidelines:

- *Non-covalent modification technique:* It employs H bonding, lipophilic–lipophilic, pi-stacking or electrostatic exchanges to control the components’ properties in chemical reactions (Stoler and Warner, 2015). One common method is co-crystallization (Qiao et al 2011).
- *Self-assembly:* Chemical chaperones help in self-assembly of polymers via H bonding, host–guest interactions, metal–ligand coordination, and pi–pi stacking interactions. Molecular chaperones pave the way for greener reaction as well (Chi et al 2013). Catalysed molecular assembly (“*catassembly*”) was

utilized to help chemical reactions that are slower or need elevated activation energy. In addition, catalysis is a helpful way of obtaining chirality (Wang et al 2014).

- *Protecting group-free chemistry*: One typical example of a catalyst-enabled method is synthesis of conjugated polymers through metallic-catalysed direct (hetero)arylation of aromatic components (Bura et al 2016), eliminating intermediate steps, which allows straightforward separation, as well as waste reduction (Bura et al 2016). *In situ* protecting groups is another method which were described for chemical reactions in supercritical carbon dioxide (Mohammed and Kitchens, 2016).
- *Electrochemical synthesis*: This is another way of eliminating intermediate synthetic steps, in which selective electron transfer helps in carbon-carbon bond formation or functional group interconversions for electroactive/electro-responsive reagents (Schäfer, 2011). Redox-umpolung chemical reactions help considerably simplified reaction sequences (Frontana-Urbe et al 2010).
- *Flow chemistry*: It was utilized to reduce derivatisation in synthesis and also in analytical methods (Plutschack et al 2017). Microfluidics in flow reactors reduce side chemical reactions through more accurate control of thermic conditions. It can be utilized in combination with packed-bed columns of immobilized reagents to perform several purposes in only a single unit (Li and Trost, 2008).
- *“Click chemistry”*: This concept was coined by Barry Sharpless (Kolb et al 2001), based on modular chemical reactions seen in the nature, where tiny units are combined to make bigger structures (Kolb et al 2001). As mainly click chemistry is done in water, protecting groups for amide or hydroxy functionalities can be avoided (Kolb et al 2001). An example is the copper(I)-catalysed 1,2,3-triazole forming chemical reaction between azides and terminal alkynes without protecting groups (Thirumurugan et al 2013). When derivatisation is inevitable, it is straightforward to make a comparison of avoidance of temporary modifications using atom economy (Principle 2). It is important to take into account that synthetic efficiencies might lead to the expense of other lifecycle effects.

2.9 Guidelines based on Principle 9 (catalyst)

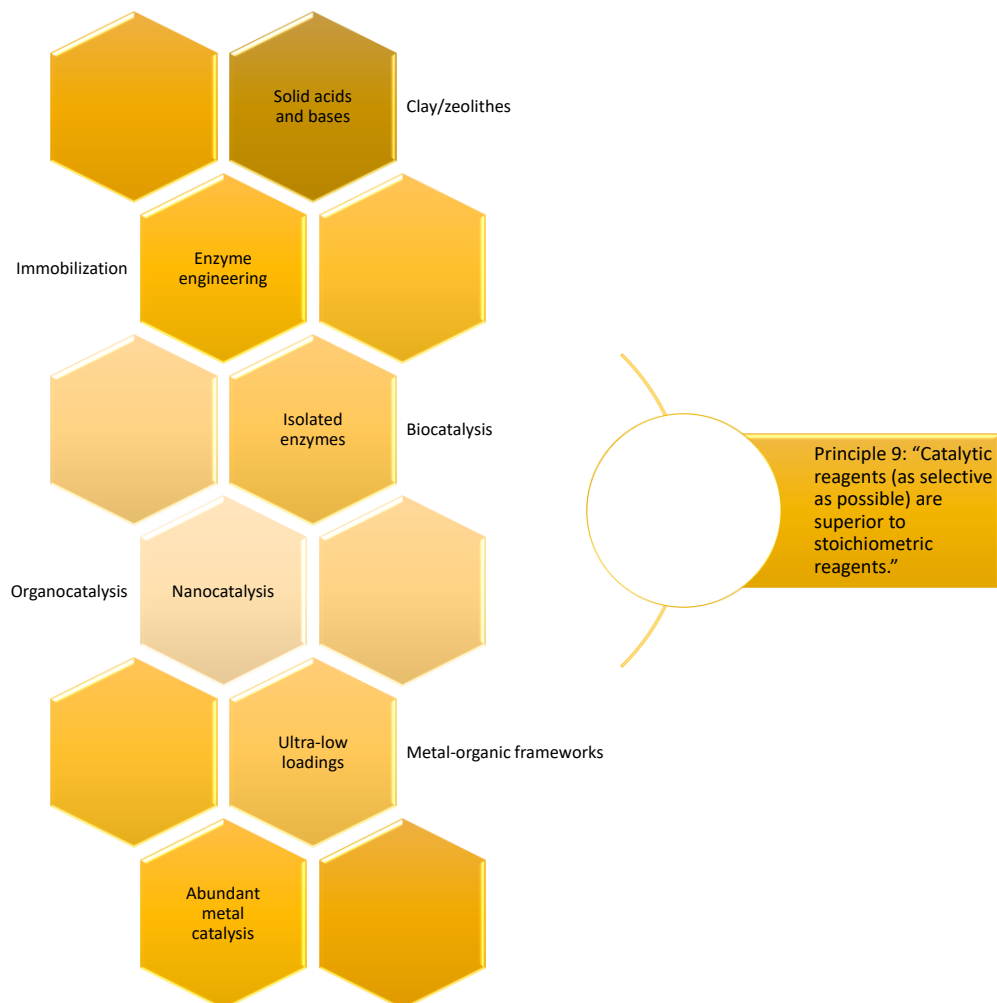


Figure 10. Principle 9 of Green Chemistry

The application of catalyst is a way to increase selectivity, lower energy demand, reduce waste, and also to improve atom economy, and thus, catalyst address several Principles. Consequently, catalysts are one of the most multipurpose means that is available for Green Chemistry (Sheldon et al 2007).

Based on Principle 9 of Green Chemistry, the guidelines listed below are extracted:

Take into account toxicity and hazard (Egorova and Ananikov 2016), as well as relative abundance of metals utilized (Bullock 2010): The "metal criticality" was developed to

See Albo et al. (2015) regarding active metals for the electrochemical transformation of CO₂ into CH₃OH

Precious metals are not only toxic, but their low natural abundancies lead to volatile market prices and increased cost of product (Phan and Luscombe, 2019).

assess metals beyond their abundance in order to consider ecological impacts of mining operations and vulnerability to supply constraints (Graedel et al 2015). Use of plants for phytoextraction of metals from polluted sites for catalytic application (Deyris and Grison, 2018) is an innovative method in this regard.

Operate under ambient conditions: This lead to reduce energy demand.

Increase stability, reduce loading, and recyclability: The ways to reach these objectives are latency, immobilization, and tandem or undirected protocols.

Gear selectivity towards specific products: This can be done by consideration of regio- and enantioselectivity (Ye et al 2016).

In the following paragraphs, several examples of catalyst systems are given: homogeneous catalytic systems, heterogeneous catalytic systems, and biocatalyst.

- **Homogeneous catalytic systems:** One of the most studied homogeneous systems is palladacycles and used as one of the most efficient systems for carbon–carbon bond formation (Dupont and Flores 2009). Recent reports exhibit considerably improved turnover numbers while application of ultra-low loadings (Consorti et al 2003). Main research are focused on getting high performance from non-precious metals, especially abundant first-row transition metals (e.g. copper manganese, iron) (Junge et al 2011), and application of biomimetic methods (e.g. enzymes) as inspiration to obtain similar efficiency and reactivity . Examples in the literature are a Mn/Na-based catalyst for oxidative cleavage of 1,2-diols (Escande et al 2017), and Fe-tetraamido macrocyclic ligand (TAML) activator for oxidation processes (Kirchhoff, 2003). Performance improvements of homogeneous catalysts were achieved via immobilization and simplifying separation (McMorn and Hutchings, 2004). This concept was shown with supramolecular architectures, solid supports, and ionic liquids in combination with supercritical carbon dioxide (Müller and Vogt, 2009). There have also been considerable progresses in organocatalyst, which utilizes no metals, hence leading to economic and toxicological benefits (McCort-Tranchepain, et al 2009). For instance, one of the common categories of organocatalysts is amino acids, which are known to be mainly non-hazardous (Dondoni and Massi, 2008). There have been studies to enhance the efficiency and activity of

metal-free catalysts (Hernandez and Juaristi, 2012). Nevertheless, this is challenging due to catalyst loadings (Wende and Schreiner, 2012) and catalyst recycling (Shaikh 2014).

- **Heterogeneous catalysts:** Although heterogeneous catalysts are harder to study than homogenous one, heterogeneous catalysts have numerous pros e.g. simplified catalyst recycling, ease of sideling, and superior stability and separation (Lin et al 2001). Nevertheless, the application of abundant non-precious metals is interesting because of increasing awareness of toxicity (*Egorova and Ananikov 2016*), and scarcity issues during the lifecycle (Graedel et al 2015). Zeolites (Ma et al 2000), clays (Dasgupta and Torok, 2009), and solid acid or base catalysts are examples of the catalysts that are based on abundant materials. The latter two can provide better safety than common aqueous systems (Principles 3 and 12) (Gupta and Paul, 2014). A category of robust silica-supported porous Brønsted acid catalysts was made that can be adjusted with different active metals in order to obtain certain reactions (Kadib et al 2013). Nanoparticle catalyst has also been studied with a particular emphasis on non-precious metals of copper and nickel (Hudson et al 2012). Nevertheless, there is some debate regarding the human health and environmental concerns linked with the exposure and fate of nanoparticles (Lin et al 2010).
- **Biocatalyst:** Natural catalysts (e.g. catalytic antibodies and enzymes) outperform synthetic catalysts in terms of kinetics and selectively (e.g. enantioselectivity) (Bommarius and Riebel-Bommarius 2007). Biocatalyst can be done under mild conditions and the catalysts utilized are usually biocompatible, renewable and biodegradable (Anastas et al 2001). Enzymatic systems use the chiral nature of enzymes in making stereo- and regiochemical reaction products for use in production of complex components (Koeller and Wong, 2001). Enzyme-based catalysts use modified or unmodified recombinant enzymes in isolated reactions or whole cell processes (Mulvihill et al 2011). Technology of isolated enzymes to control synthesis is already proven, and thanks to progresses in protein engineering and DNA technology, enzymes can today be made for a precise synthesis (Bornscheuer et al 2012). However, its design still needs a detailed mechanistic analysis of enzyme processes (Bornscheuer et al 2012). Many biocatalyst need further study to

enhance stability as it is constrained by “mild” conditions. In addition, cofactor or substrate incompatibilities, inhibition, and reaction rate limitations are challenging, which can be avoided by the application of isolated enzymes (Schmidt-Dannert and Lopez-Gallego 2016). Performance improvements are being studied through the coupling of chemical and biological mechanisms and immobilization e.g. combining nanotechnology with enzymatic processes (Bornscheuer et al 2012).

2.10 Guidelines based on Principle 10 (design for degradation)

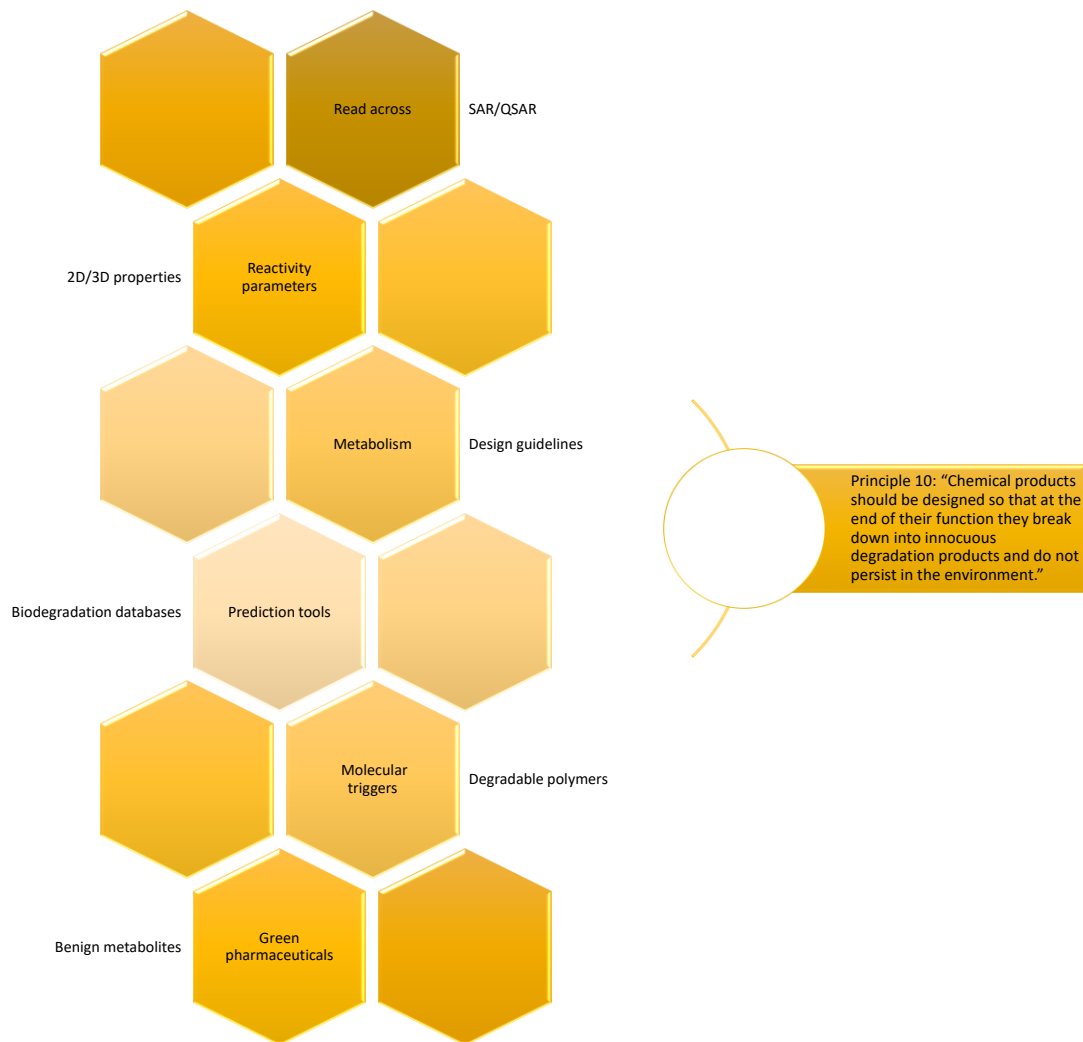


Figure 11. Principle 10 of Green Chemistry

Green Chemistry tries to find an equilibrium between the stability of components during use phase(s) , and their biodegradability when are released to the nature.

Based on Principle 10 of Green Chemistry, the guidelines listed below are extracted:

**Biodegradation
database: UMBBD**

Use biodegradation databases: There are several biodegradation databases that contain data about environmental fate of molecules (Howard and Boethling 2010) e.g.

the University of Minnesota Biocatalyst/Biodegradation Database (UMBBD) (Gao et al 2010). Furthermore, there are tools for predicting ecological fate, which are considerable regarding molecular design e.g. the UMBBD Pathway Prediction System (PPS) (Hou et al 2004) and the CATABOL program (Jaworska et al 2002).

Take into account “rules of thumb”: There is a set of “rules of thumb” regarding the functional groups that reduce molecules particularly recalcitrant: quaternary carbons, tertiary amines, halogenated molecules (except for iodine), polycyclic structures with more than three rings, aliphatic ether bonds and heterocycles. However, the integration of amides, ester bonds, phenyl rings, and unbranched terminal alkyl chains enhances the degradability (Howard et al 2008).

Use models for to predict biodegradation: QSAR/SAR in *silico* models were presented to predict biodegradability based on the electronic and chemical structure as well as the properties of molecules (Principle 4). QSAR/SAR models were developed to predict biodegradation (Jaworska et al 2003), atmospheric degradation (Öberg, 2005), and hydrolysis (Rücker and Kümmerer, 2012). The U.S. EPA EpiSuite™ software (Environmental Protection Agency, 2017) has tools for prediction of degradation i.e. BIOWIN and BioHCwin for biodegradation, HYDROWIN for hydrolysis, and AOPWIN for atmospheric degradation (Howard and Boethling 2010).

Integrate a “molecular switch” into components that activate under certain ecological conditions: This can promote the degradation of chemicals (Khetan and Collins, 2007) e.g. using non-covalent derivatives (Stoler and Warner, 2015)

Take into account the produced metabolites in terms of their potential for human toxicity, their degradation kinetics, and ecotoxicity effects: There are many cases where apparently innocuous components decompose to problematic stable components. For instance, nonylphenol ethoxylate surfactants decompose to nonylphenol in the nature, which is a toxic xenobiotic component, and also endocrine disruptor (Soares et al 2008).

Develop biodegradable polymer: Numerous new biodegradable polymer classes were made with the objective of reducing the overall environmental burdens of plastic wastes (Chen and Patel, 2012) e.g. cellulose and starch derivatives (Averous 2004), poly(lactic acid) (PLA) (Vink and S. Davies, 2015), poly(vinyl alcohol) (PVA) (Chiellini et al 2003), poly(hydroxyalkanoates) (PHA) (Lee 1996), poly(butylene succinate) (PBS) (Xu and Guo, 2010), and poly(caprolactone) (PCL) (Shah et al 2014).

U.S. EPA EpiSuite™
has tools for
prediction of
degradation.

Learn from pharmaceutical chemistry: A frontier of development for biodegradation is in the field of pharmaceutical. Active Pharmaceutical Ingredient (API) and API metabolites are challenging because of chemical complexity and design regarding long shelf-lives (Jagiello et al 2015). As APIs are biologically active, they can make a considerable threat after entering the nature e.g. antibiotic resistance (Kümmerer, 2009), or a massive decrease in vulture population because of exposure to diclofenac (Oaks et al 2004).

2.11 Guidelines based on Principle 11 (real-time analysis for pollution prevention)

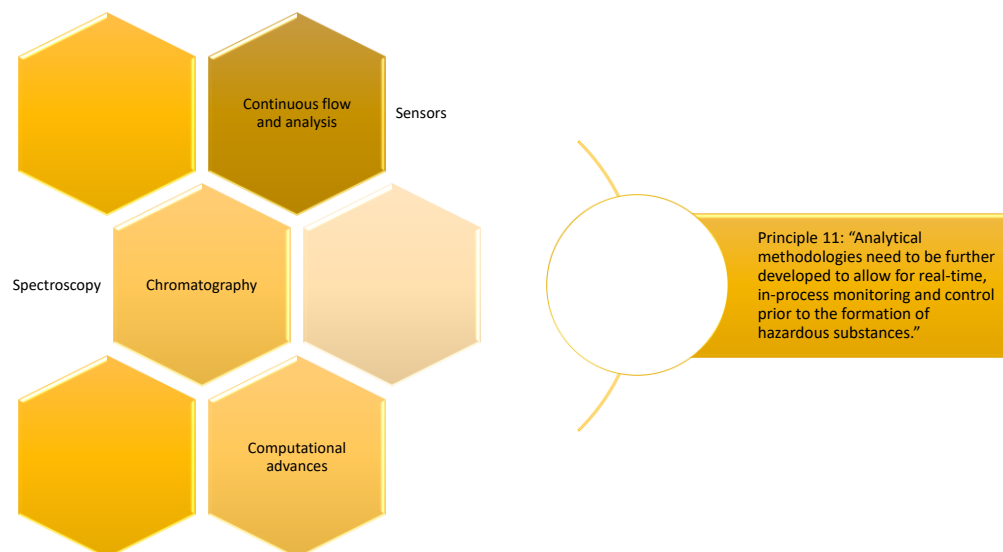


Figure 12. Principle 11 of Green Chemistry

Principle 11 of Green Chemistry emphasises the significance of monitoring in controlling safety and hazards. Real-time monitoring can be utilized in order to gain enhanced synthetic efficiency, waste prevention, aid catalyst design, and support solvent-free chemistry and also bio-chemical processing. It is particularly helpful in optimisation of continuous-flow reactors (Sans and Cronin, 2016).

Based on Principle 11 of Green Chemistry, the guidelines listed below are extracted:

Apply monitoring methods: A wide variety of methods are developed, “in-line” or “on-line” (Browne et al 2012). Many spectroscopic approaches were adapted for in-line measurement (Sans and Cronin, 2016), e.g. microfluidic “lab on a chip”. Typical examples in the literature are UV/VIS (Sans et al 2014), IR and attenuated total reflection (ATR-IR) (Chan et al 2009), Raman (Hamlin and Leadbeater, 2013), Mass (Petucci et al 2007), and NMR spectroscopy (Gomez et al 2015). Gas chromatography (GC) and

liquid chromatography (LC) are other considerable monitoring means. Nevertheless, these have to be utilized on-line instead of in-line, and LC is usually combined with solid phase extraction (SPE) before injection, and mass spectroscopy post-separation (Hamilton et al 2014). Sensor technology has a considerable role, for instance monitoring headspace or dissolved gas concentrations by luminescence, electrochemical sensors or IR (Friedrich et al 2013). There are also examples regarding the application of feedback loops to monitor chemical reaction (Sans and Cronin, 2016) e.g. parameters for a methylation reaction in supercritical carbon dioxide using Matlab[®] (Bourne et al 2011), as well as LabView[®]-based optimization tools (Sans et al 2015). Other applications are Raman spectroscopy and X-ray powder diffraction to monitor solventless mechanochemical reactions (Friščić et al 2013).

Use sensors: Design of sensors, such as electrochemical sensing (voltammetric, potentiometric or conductimetric) provide quantitative or qualitative measurements of isolated species or analytes (Brett and Oliveira-Brett, 2011). Electrochemical sensing gives special versatility as it is based on the charge transfer phenomena linked with chemical reactions (Brett and Oliveira-Brett, 2011). Optical (fluorometric and colorimetric) sensors for a specific component have been studied toward their greener synthesis (Askim et al 2013).

Encompass the environmental effects of analytical approaches (beyond process chemistry): There is need for assessment of methods for time and convenience as well as hazard, material intensity, energy demand, occupational exposures (e.g., emission of vapours to lab space), and fate of the waste for each sample (Koel, 2016). For instance, liquid chromatography can be improved by adjusting stationary or mobile phases, introducing additives, or application of high-temperature separations (Olives et al 2017). Another example is the application of supercritical carbon dioxide rather than organic solvents in chiral separations (McClain et al 2014).

2.12 Guidelines based on Principle 12 (inherently benign chemistry for accident prevention)

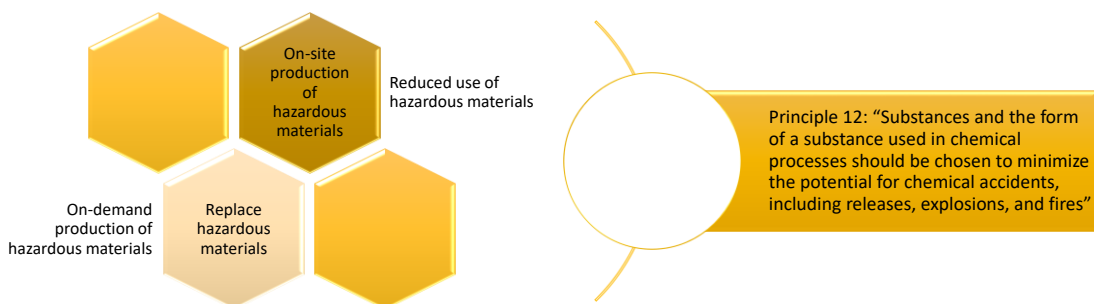


Figure 13. Principle 12 of Green Chemistry

In accordance with a study by the ACS GCI Chemical Manufacturer's Roundtable (Giraud et al 2014), Principle 12 (along with Principle 1) is one of the most implemented Principles. This is because of the high linked environmental, social and economic costs of both waste generation and chemical accidents, and their weight to the important social drivers (e.g. worker safety) (Anastas and Hammond 2016).

One of the key concept in the context of Principle 12 of Green Chemistry, is the concept of Inherently Safer Processes (ISP), based on which the two following guidelines are extracted:

- *Apply the ISP concept:* ISP concept was first presented by Kletz (1978): “What you don't have can't leak” (Kletz, 1978). Since then, numerous studies have lead to safer processes, most of which were presented in *Inherently Safer Chemical Processes* (Center for Chemical Process Safety 2010).
- *Apply ISP metrics:* There are several ISP metrics and assessment tools (Khan et al 2015) e.g.the MERITT by AIChE and INSET (EU INSIDE 2001).

Furthermore, referring to Anastas and Hammond (2016), the following guidelines are extracted:

- *Replace hazardous components in the chemical synthesis processes*
- *Limit transportation of hazardous components by switching to on-site production*
- *Limit storage of hazardous components by on-demand production*
- *Reduce the reliance on irreplaceable hazardous components*

Principle 12 and Principle 1 are one of the most implemented Principles.

ISP assessment tools: MERITT and INSET

3. Conclusion

The 12 Principles provide a useful way of structuring the Green Chemistry-based guidelines addressing the variety of strategies available for choosing the materials, which have also highlighted the broad spectrum of Green Chemistry.

Although the 12 Principles are a helpful framework, it should be noted that the 12 Principles are not independent from each other but rather work in a cross-disciplinary and interconnected framework in which synergies are expected to be realized. Through this framework, it is more straightforward to choose the materials that avoid tradeoffs between Principles of Green Chemistry and/or lifecycle impacts.

References

- Adeyuyi, Y. G. (2001). Sonochemistry: environmental science and engineering applications. *Industrial & Engineering Chemistry Research*, 40(22), 4681–4715.
- Agbor, V. B., Cicek, N., Sparling, R., Berlin, A., & Levin, D. B. (2011). Biomass pretreatment: fundamentals toward application. *Biotechnology advances*, 29(6), 675–685.
- Albo, J., Alvarez-Guerra, M., Castaño, P., & Irabien, A. (2015). Towards the electrochemical conversion of carbon dioxide into methanol. *Green Chemistry*, 17(4), 2304–2324.
- Albo, J., & M Alvarez-Guerra, P. C., A Irabien. *Green Chemistry*. 2015;17(4):2304-24.
- Alder, C. M., Hayler, J. D., Henderson, R. K., Redman, A. M., Shukla, L., Shuster, L. E., & Sneddon, H. F. (2016). Updating and further expanding GSK's solvent sustainability guide. *Green Chemistry*, 18(13), 3879–3890.
- Anastas, P. T., & Hammond, D. G. (2016). Inherent Safety at Chemical Sites. In: Elsevier.
- Anastas, P. T., & J. C. Warner. *Green Chemistry: Theory and Practice*, Oxford University Press, Oxford, 1998.
- Anastas, P. T., Kirchoff, M. M., & Williamson, T. C. (2001). Catalysis as a foundational pillar of green chemistry. *Applied Catalysis A: General*, 221(1-2), 3–13.
- Askim, J. R., Mahmoudi, M., & Suslick, K. S. (2013). Optical sensor arrays for chemical sensing: the optoelectronic nose. *Chemical Society Reviews*, 42(22), 8649–8682.
- Averous, L. (2004). Biodegradable multiphase systems based on plasticized starch: a review. *Journal of Macromolecular Science, Part C: Polymer Reviews*, 44(3), 231–274.
- Bommarius, A. S., & Riebel-Bommarius, B. R. (2004). *Biocatalysis: fundamentals and applications*: John Wiley & Sons.
- Bornscheuer, U. T., Huisman, G. W., Kazlauskas, R. J., Lutz, S., Moore, J. C., & Robins, K. (2012). Engineering the third wave of biocatalysis. *Nature*, 485(7397), 185–194.
- Bourne, R. A., Skilton, R. A., Parrott, A. J., Irvine, D. J., & Poliakoff, M. (2011). Adaptive process optimization for continuous methylation of alcohols in supercritical carbon dioxide. *Organic Process Research & Development*, 15(4), 932–938.
- Brar, S. K., Sarma, S. J., & Pakshirajan, K. (2016). Platform chemical biorefinery: future green chemistry.
- Bräse, S., Gil, C., Knepper, K., & Zimmermann, V. (2005). Organic azides: an exploding diversity of a unique class of compounds. *Angewandte Chemie International Edition*, 44(33), 5188–5240.
- Breslow, R. in *Handbook of Green Chemistry: Vol.5 Green Solvents: Reactions in Water*, ed. P. T. Anastas and C. J. Li, Wiley-VCH, Weinheim, Germany, 2010, ch. 1, vol. 5, pp. 1–25.
- Brett, C. M., & Oliveira-Brett, A. M. (2011). Electrochemical sensing in solution—origins, applications and future perspectives. *Journal of Solid State Electrochemistry*, 15(7), 1487–1494.
- Browne, D. L., Wright, S., Deadman, B. J., Dunnage, S., Baxendale, I. R., Turner, R. M., & Ley, S. V. (2012). Continuous flow reaction monitoring using an on-line miniature mass spectrometer. *Rapid Communications in Mass Spectrometry*, 26(17), 1999–2010.
- Bullock, R. M. (2011). *Catalysis without precious metals*: John Wiley & Sons.

- Bura, T., Blaskovits, J. T., & Leclerc, M. (2016). Direct (hetero) arylation polymerization: trends and perspectives. *Journal of the American Chemical Society*, 138(32), 10056–10071.
- Burns, N. Z., Baran, P. S., & Hoffmann, R. W. (2009). Redox economy in organic synthesis. *Angewandte Chemie International Edition*, 48(16), 2854–2867.
- Byrne, F. P., Jin, S., Paggiola, G., Petchey, T. H., Clark, J. H., Farmer, T. J., . . . Sherwood, J. (2016). Tools and techniques for solvent selection: green solvent selection guides. *Sustainable chemical processes*, 4(1), 1–24.
- Carlos, J., & C. Quintero. *Activation of heterogeneous nanocatalysts by solar light: principles, synthesis and applications*, In: *Catalysis: Principles, Types and Applications* ISBN: 978-1-61209-654-4, Editor: Minsuh Song, pp. 101-165, 2011 Nova Science Publishers.
- Center for Chemical Process Safety, *Inherent Safer Chemical Processes: A Life Cycle Approach*, John Wiley & Sons, Hoboken, NJ, 2nd edn, 2010.
- Centi, G., Quadrelli, E. A., & Perathoner, S. (2013). Catalysis for CO₂ conversion: a key technology for rapid introduction of renewable energy in the value chain of chemical industries. *Energy & Environmental Science*, 6(6), 1711–1731.
- Chan, K. A., Gulati, S., Edel, J. B., de Mello, A. J., & Kazarian, S. G. (2009). Chemical imaging of microfluidic flows using ATR-FTIR spectroscopy. *Lab on a Chip*, 9(20), 2909–2913.
- Chemat, F., Vian, M. A., & Cravotto, G. (2012). Green extraction of natural products: concept and principles. *International journal of molecular sciences*, 13(7), 8615–8627.
- Chen, G.-Q., & Patel, M. K. (2012). Plastics derived from biological sources: present and future: a technical and environmental review. *Chemical reviews*, 112(4), 2082–2099.
- Chi, X., Xu, D., Yan, X., Chen, J., Zhang, M., Hu, B., . . . Huang, F. (2013). A water-soluble, shape-persistent, mouldable supramolecular polymer with redox-responsiveness in the presence of a molecular chaperone. *Polymer Chemistry*, 4(9), 2767–2772.
- Chiellini, E., Corti, A., D'Antone, S., & Solaro, R. (2003). Biodegradation of poly (vinyl alcohol) based materials. *Progress in Polymer Science*, 28(6), 963–1014.
- Consorti, C. S., Zanini, M. L., Leal, S., Ebeling, G., & Dupont, J. (2003). Chloropalladated propargyl amine: a highly efficient phosphine-free catalyst precursor for the Heck reaction. *Organic letters*, 5(7), 983–986.
- Cravotto, G., & Cintas, P. (2006). Power ultrasound in organic synthesis: moving cavitation chemistry from academia to innovative and large-scale applications. *Chemical Society Reviews*, 35(2), 180–196.
- Dasgupta, S., & Toeroek, B. (2008). Application of clay catalysts in organic synthesis. A review. *Organic Preparations and Procedures International*, 40(1), 1–65.
- de la Hoz, A., Díaz-Ortiz, A., & P. Prieto. in *RSC Green Chemistry Series: Vol. 47 Alternative Energy Sources for Green Chemistry*, ed. G. Stefanidis and A. Stankiewicz, Royal Society of Chemistry, Cambridge, UK, 2016, ch. 1, vol. 47, pp. 1–33.
- Dicks, A. P., & Hent, A. (2014). *Green chemistry metrics: a guide to determining and evaluating process greenness*: Springer.
- DOE 2015; US Dept. of Energy, *Quadrennial Technology Review 2015: Chapter 6 - Technology Assessments: Process Intensification*, Washington, DC, 2015.

- Dondoni, A., & Massi, A. (2008). Asymmetric organocatalysis: from infancy to adolescence. *Angewandte Chemie International Edition*, 47(25), 4638–4660.
- Eckelman, M. J. (2016). Life cycle inherent toxicity: a novel LCA-based algorithm for evaluating chemical synthesis pathways. *Green Chemistry*, 18(11), 3257–3264.
- Egorova, K. S., & Ananikov, V. P. (2016). Which metals are green for catalysis? Comparison of the toxicities of Ni, Cu, Fe, Pd, Pt, Rh, and Au salts. *Angewandte Chemie International Edition*, 55(40), 12150–12162.
- Eissen, M., & Metzger, J. O. (2002). Environmental performance metrics for daily use in synthetic chemistry. *Chemistry—A European Journal*, 8(16), 3580–3585.
- El Kadib, A., Finiels, A., & Brunel, D. (2013). Sulfonic acid functionalised ordered mesoporous materials as catalysts for fine chemical synthesis. *Chemical Communications*, 49(80), 9073–9076.
- Enoch, S. J., Ellison, C. M., Schultz, T. W., & Cronin, M. T. D. (2011). A review of the electrophilic reaction chemistry involved in covalent protein binding relevant to toxicity. *Critical reviews in toxicology*, 41(9), 783–802.
- Erythropel, H. C., Zimmerman, J. B., de Winter, T. M., Petitjean, L., Melnikov, F., Lam, C. H., . . . Tu, Q. (2018). The Green ChemisTREE: 20 years after taking root with the 12 principles. *Green Chemistry*, 20(9), 1929–1961.
- Escande, V., Lam, C. H., Grison, C., & Anastas, P. T. (2017). EcoMnOx, a biosourced catalyst for selective aerobic oxidative cleavage of activated 1, 2-diols. *ACS Sustainable Chemistry & Engineering*, 5(4), 3214–3222.
- EU INSIDE, The INSET Toolkit - INherent SHE Evaluation Tool, Brussels, Belgium, 2001.*
- European Chemicals Agency, The Use of Alternatives to Testing on Animals for the REACH Regulation, Helsinki, Finland, 2011.*
- Fernandez Rivas, D., & Kuhn, S. (2016). Synergy of microfluidics and ultrasound: Process intensification challenges and opportunities. *Topics in Current Chemistry*, 374(5).
- Fiorani, G., Perosa, A., & Selva, M. (2018). Dimethyl carbonate: a versatile reagent for a sustainable valorization of renewables. *Green Chemistry*, 20(2), 288–322.
- Foley, P. M., Beach, E. S., & Zimmerman, J. B. (2011). Algae as a source of renewable chemicals: opportunities and challenges. *Green Chemistry*, 13(6), 1399–1405.
- Friščić, T. (2012). Supramolecular concepts and new techniques in mechanochemistry: cocrystals, cages, rotaxanes, open metal–organic frameworks. *Chemical Society Reviews*, 41(9), 3493–3510.
- Friščić, T., Halasz, I., Beldon, P. J., Belenguer, A. M., Adams, F., Kimber, S. A., . . . Dinnebier, R. E. (2013). Real-time and in situ monitoring of mechanochemical milling reactions. *Nature chemistry*, 5(1), 66–73.
- Frontana-Uribe, B. A., Little, R. D., Ibanez, J. G., Palma, A., & Vasquez-Medrano, R. (2010). Organic electrosynthesis: a promising green methodology in organic chemistry. *Green Chemistry*, 12(12), 2099–2119.
- Fuse, S., Tanabe, N., & Takahashi, T. (2011). Continuous in situ generation and reaction of phosgene in a microflow system. *Chemical Communications*, 47(47), 12661–12663.

- Gallezot, P. (2012). Conversion of biomass to selected chemical products. *Chemical Society Reviews*, 41(4), 1538–1558.
- Gao, J., Ellis, L. B., & Wackett, L. P. (2010). The University of Minnesota biocatalysis/biodegradation database: improving public access. *Nucleic acids research*, 38(suppl_1), D488–D491.
- Gawande, M. B., Bonifacio, V. D., Luque, R., Branco, P. S., & Varma, R. S. (2014). Solvent-free and catalysts-free chemistry: a benign pathway to sustainability. *ChemSusChem*, 7(1), 24–44.
- Gensch, T., Hopkinson, M. N., Glorius, F., & Wencel-Delord, J. (2016). Mild metal-catalyzed C–H activation: examples and concepts. *Chemical Society Reviews*, 45(10), 2900–2936.
- Girard, S. A., Knauber, T., & Li, C.-J. (2014). The Cross-Dehydrogenative Coupling of C–H Bonds: A Versatile Strategy for C–C Bond Formations. *Angewandte Chemie International Edition*, 53(1), 74–100.
- Giraud, R. J., Williams, P. A., Sehgal, A., Ponnusamy, E., Phillips, A. K., & Manley, J. B. (2014). Implementing green chemistry in chemical manufacturing: A survey report. In: ACS Publications.
- Gomez, M. V., Rodriguez, A. M., de la Hoz, A., Jimenez-Marquez, F., Fratila, R. M., Barneveld, P. A., & Velders, A. H. (2015). Determination of kinetic parameters within a single nonisothermal on-flow experiment by nanoliter NMR spectroscopy. *Analytical chemistry*, 87(20), 10547–10555.
- Graedel, T. E., Harper, E. M., Nassar, N. T., Nuss, P., & Reck, B. K. (2015). Criticality of metals and metalloids. *Proceedings of the National Academy of Sciences*, 112(14), 4257–4262.
- Gunanathan, C., & Milstein, D. (2011). Metal–ligand cooperation by aromatization–dearomatization: a new paradigm in bond activation and “Green” catalysis. *Accounts of chemical research*, 44(8), 588–602.
- Gupta, P., & Paul, S. (2014). Solid acids: Green alternatives for acid catalysis. *Catalysis Today*, 236, 153–170.
- Hamilton, S. E., Mattrey, F., Bu, X., Murray, D., McCullough, B., & Welch, C. J. (2014). Use of a miniature mass spectrometer to support pharmaceutical process chemistry. *Organic Process Research & Development*, 18(1), 103–108.
- Hamlin, T. A., & Leadbeater, N. E. (2013). Raman spectroscopy as a tool for monitoring mesoscale continuous-flow organic synthesis: Equipment interface and assessment in four medically-relevant reactions. *Beilstein journal of organic chemistry*, 9(1), 1843–1852.
- Han, L., Dong, S., & Wang, E. (2016). Transition-metal (Co, Ni, and Fe)-based electrocatalysts for the water oxidation reaction. *Advanced materials*, 28(42), 9266–9291.
- Hartwig, J. F. (2016). Evolution of C–H bond functionalization from methane to methodology. *Journal of the American Chemical Society*, 138(1), 2–24.
- Hernández, J. G., & Juaristi, E. (2012). Recent efforts directed to the development of more sustainable asymmetric organocatalysis. *Chemical Communications*, 48(44), 5396–5409.
- Hirth, T., & Busch, R. *CHEManager*, 2003, 3, 20–21.
- Hou, B. K., Ellis, L. B., & Wackett, L. P. (2004). Encoding microbial metabolic logic: predicting biodegradation. *Journal of Industrial Microbiology and Biotechnology*, 31(6), 261–272.
- Howard, P. H., & Boethling, R. S. in *Handbook of Green Chemistry: Vol.9 Green Processes: Designing Safer Chemicals*, ed. P. T. Anastas, R. S. Boethling and A. M. Voutchkova, Wiley-VCH, Weinheim, Germany, 2010, ch. 16, vol. 9, pp. 453–484.

- Hsieh, J.-H., Sedykh, A., Huang, R., Xia, M., & Tice, R. R. (2015). A data analysis pipeline accounting for artifacts in Tox21 quantitative high-throughput screening assays. *Journal of biomolecular screening*, 20(7), 887–897.
- Hudson, R., Li, C.-J., & Moores, A. (2012). Magnetic copper–iron nanoparticles as simple heterogeneous catalysts for the azide–alkyne click reaction in water. *Green Chemistry*, 14(3), 622–624.
- Izatt, R. M., Izatt, S. R., Bruening, R. L., Izatt, N. E., & Moyer, B. A. (2014). Challenges to achievement of metal sustainability in our high-tech society. *Chemical Society Reviews*, 43(8), 2451–2475.
- Jagiello, K., Mostrag-Szlichtyng, A., Gajewicz, A., Kawai, T., Imaizumi, Y., Sakurai, T., . . . Aoki, Y. (2015). Towards modelling of the environmental fate of pharmaceuticals using the QSPR-MM scheme. *Environmental Modelling & Software*, 72, 147–154.
- Jang, Y.-S., Kim, B., Shin, J. H., Choi, Y. J., Choi, S., Song, C. W., . . . Lee, S. Y. (2012). Bio-based production of C2–C6 platform chemicals. *Biotechnology and bioengineering*, 109(10), 2437–2459.
- Jaworska, J., Dimitrov, S., Nikolova, N., & Mekenyan, O. (2002). Probabilistic assessment of biodegradability based on metabolic pathways: CATABOL system. *SAR and QSAR in Environmental Research*, 13(2), 307–323.
- Jaworska, J., & Nikolova-Jeliazkova, N. (2007). How can structural similarity analysis help in category formation? *SAR and QSAR in Environmental Research*, 18(3-4), 195–207.
- Jaworska, J. S., Boethling, R. S., & Howard, P. H. (2003). Recent developments in broadly applicable structure-biodegradability relationships. *Environmental Toxicology and Chemistry: An International Journal*, 22(8), 1710–1723.
- Jessop, P. G., Mercer, S. M., & Heldebrant, D. J. (2012). CO₂-triggered switchable solvents, surfactants, and other materials. *Energy & Environmental Science*, 5(6), 7240–7253.
- Jessop, P. G., Phan, L., Carrier, A., Robinson, S., Dürr, C. J., & Harjani, J. R. (2010). A solvent having switchable hydrophilicity. *Green Chemistry*, 12(5), 809–814.
- Jessop, P. G., & Subramaniam, B. (2007). Gas-expanded liquids. *Chemical reviews*, 107(6), 2666–2694.
- Junge, K., Schröder, K., & Beller, M. (2011). Homogeneous catalysis using iron complexes: recent developments in selective reductions. *Chemical Communications*, 47(17), 4849–4859.
- Kappe, C. O., Pieber, B., & Dallinger, D. (2013). Microwave effects in organic synthesis: myth or reality? *Angewandte Chemie International Edition*, 52(4), 1088–1094.
- Keasling, J. D., Mendoza, A., & Baran, P. S. (2012). A constructive debate. *Nature*, 492(7428), 188–189.
- Kerton, F., & R. Marriott, G. K., A. Stankiewicz, Y. Kou, P. Seidl and J. H. Clark. *Alternative Solvents for Green Chemistry, The Royal Society of Chemistry, Cambridge, UK, 2nd edn, 2013.*
- Kharissova, O. V., Kharisov, B. I., Oliva González, C. M., Méndez, Y. P., & López, I. (2019). Greener synthesis of chemical compounds and materials. *Royal Society open science*, 6(11), 191378.
- Khetan, S. K., & Collins, T. J. (2007). Human pharmaceuticals in the aquatic environment: a challenge to green chemistry. *Chemical reviews*, 107(6), 2319–2364.
- Kirchhoff, M. M. (2003). Promoting green engineering through green chemistry. *Environmental science & technology*, 37(23), 5349–5353.
- Kletz, T.A. *Chem. Ind.*, 1978, 6, 287–292.

- Klussmann, M., & Sureshkumar, D. (2011). Catalytic oxidative coupling reactions for the formation of carbon-carbon bonds without carbon-metal intermediates. *Synthesis*, 2011(03), 353–369.
- Knudsen, T. B., Keller, D. A., Sander, M., Carney, E. W., Doerrer, N. G., Eaton, D. L., . . . Tice, R. R. (2015). FutureTox II: in vitro data and in silico models for predictive toxicology. *Toxicological Sciences*, 143(2), 256–267.
- Koel, M. (2016). Do we need green analytical chemistry? *Green Chemistry*, 18(4), 923–931.
- Koeller, K. M., & Wong, C.-H. (2001). Enzymes for chemical synthesis. *Nature*, 409(6817), 232–240.
- Kolb, H. C., Finn, M. G., & Sharpless, K. B. (2001). Click chemistry: diverse chemical function from a few good reactions. *Angewandte Chemie International Edition*, 40(11), 2004–2021.
- Kümmerer, K. (2009). Antibiotics in the aquatic environment—a review—part I. *Chemosphere*, 75(4), 417–434.
- Kurti, L., & Czako, B. (2005). *Strategic applications of named reactions in organic synthesis*: Elsevier.
- Kwan, T. A., Tu, Q., & Zimmerman, J. B. (2016). Simultaneous extraction, fractionation, and enrichment of microalgal triacylglycerides by exploiting the tunability of neat supercritical carbon dioxide. *ACS Sustainable Chemistry & Engineering*, 4(11), 6222–6230.
- Lee, S. Y. (1996). Bacterial polyhydroxyalkanoates. *Biotechnology and bioengineering*, 49(1), 1–14.
- Leitner, W. (2002). Supercritical carbon dioxide as a green reaction medium for catalysis. *Accounts of chemical research*, 35(9), 746–756.
- Leng, Y., Wang, J., Zhu, D., Ren, X., Ge, H., & Shen, L. (2009). Heteropolyanion-based ionic liquids: reaction-induced self-separation catalysts for esterification. *Angewandte Chemie*, 121(1), 174–177.
- Li, C.-J., & Trost, B. M. (2008). Green chemistry for chemical synthesis. *Proceedings of the National Academy of Sciences*, 105(36), 13197–13202.
- Lin, D., Tian, X., Wu, F., & Xing, B. (2010). Fate and transport of engineered nanomaterials in the environment. *Journal of environmental quality*, 39(6), 1896–1908.
- Lin, G.-Q., Li, Y.-M., & Chan, A. S. (2001). *Principles and applications of asymmetric synthesis*: John Wiley & Sons.
- Lozano, P., Bernal, J. M., Garcia-Verdugo, E., Sanchez-Gomez, G., Vaultier, M., Burguete, M. I., & Luis, S. V. (2015). Sponge-like ionic liquids: a new platform for green biocatalytic chemical processes. *Green Chemistry*, 17(7), 3706–3717.
- Ma, Y., Tong, W., Zhou, H., & Suib, S. L. (2000). A review of zeolite-like porous materials. *Microporous and mesoporous materials*, 37(1-2), 243–252.
- Marson, C. M. (2012). Multicomponent and sequential organocatalytic reactions: diversity with atom-economy and enantiocontrol. *Chemical Society Reviews*, 41(23), 7712–7722.
- Marth, C. J., Gallego, G. M., Lee, J. C., Lebold, T. P., Kulyk, S., Kou, K. G. M., . . . Sarpong, R. (2015). Network-analysis-guided synthesis of weisaconitine D and liljestrandinine. *Nature*, 528(7583), 493–498.
- Mason, T. J., & Peters, D. (2002). *Practical sonochemistry: Power ultrasound uses and applications*: Woodhead Publishing.
- Mata, T. M., Martins, A. A., & Caetano, N. S. (2010). Microalgae for biodiesel production and other applications: a review. *Renewable and sustainable energy reviews*, 14(1), 217–232.

- Matilainen, A., & Sillanpää, M. (2010). Removal of natural organic matter from drinking water by advanced oxidation processes. *Chemosphere*, 80(4), 351–365.
- McCort-Tranchepain, I., & M. Petit and P. I. Dalko. in *Handbook of Green Chemistry: Vol.1 Green Catalysis: Homogenous Catalysis*, ed. P. T. Anastas and R. H. Crabtree, Wiley-VCH, Weinheim, Germany, 2009, ch. 9, vol. 1, pp. 255–309.
- McGlacken, G. P., & Bateman, L. M. (2009). Recent advances in aryl–aryl bond formation by direct arylation. *Chemical Society Reviews*, 38(8), 2447–2464.
- McMorn, P., & Hutchings, G. J. (2004). Heterogeneous enantioselective catalysts: strategies for the immobilisation of homogeneous catalysts. *Chemical Society Reviews*, 33(2), 108–122.
- Melnikov, F., Kostal, J., Voutchkova-Kostal, A., Zimmerman, J. B., & Anastas, P. T. (2016). Assessment of predictive models for estimating the acute aquatic toxicity of organic chemicals. *Green Chemistry*, 18(16), 4432–4445.
- Mihelcic, J. R., & Zimmerman, J. B. (2021). *Environmental engineering: Fundamentals, sustainability, design*: John Wiley & Sons.
- Milstein, D. (2010). Discovery of environmentally benign catalytic reactions of alcohols catalyzed by pyridine-based pincer Ru complexes, based on metal–ligand cooperation. *Topics in Catalysis*, 53(13), 915–923.
- Miyaura, N., Yamada, K., & Suzuki, A. (1979). A new stereospecific cross-coupling by the palladium-catalyzed reaction of 1-alkenylboranes with 1-alkenyl or 1-alkynyl halides. *Tetrahedron Letters*, 20(36), 3437–3440.
- Mohammed, F. S., & Kitchens, C. L. (2016). Reduced reactivity of amines against nucleophilic substitution via reversible reaction with carbon dioxide. *Molecules*, 21(1), 24.
- Moseley, J. D., & Kappe, C. O. (2011). A critical assessment of the greenness and energy efficiency of microwave-assisted organic synthesis. *Green Chemistry*, 13(4), 794–806.
- Müller, C., & Vogt, D. in *Handbook of Green Chemistry: Vol.1 Green Catalysis: Homogenous Catalysis*, ed. P. T. Anastas and R. H. Crabtree, Wiley-VCH, Weinheim, Germany, 2009, ch. 6, vol. 1, pp. 127–149.
- Mulvihill, M. J., Beach, E. S., Zimmerman, J. B., & Anastas, P. T. (2011). Green chemistry and green engineering: a framework for sustainable technology development. *Annual review of environment and resources*, 36, 271–293.
- Nendza, M., Müller, M., & Wenzel, A. (2014). Discriminating toxicant classes by mode of action: 4. Baseline and excess toxicity. *SAR and QSAR in Environmental Research*, 25(5), 393–405.
- Nyfeler, E., & Renaud, P. (2006). Intramolecular Schmidt reaction: Applications in natural product synthesis. *CHIMIA International Journal for Chemistry*, 60(5), 276–284.
- O'Connor, M. P., Zimmerman, J. B., Anastas, P. T., & Plata, D. L. (2016). A strategy for material supply chain sustainability: Enabling a circular economy in the electronics industry through green engineering. In: ACS Publications.
- Oaks, J. L., Gilbert, M., Virani, M. Z., Watson, R. T., Meteyer, C. U., Rideout, B. A., . . . Arshad, M. (2004). Diclofenac residues as the cause of vulture population decline in Pakistan. *Nature*, 427(6975), 630–633.

- Öberg, T. (2005). A QSAR for the hydroxyl radical reaction rate constant: validation, domain of application, and prediction. *Atmospheric Environment*, 39(12), 2189–2200.
- Olives, A. I., Gonzalez-Ruiz, V., & Martín, M. A. (2017). Sustainable and eco-friendly alternatives for liquid chromatographic analysis. *ACS Sustainable Chemistry & Engineering*, 5(7), 5618–5634.
- Othman, S. N., Noor, Z. Z., Abba, A. H., Yusuf, R. O., & Hassan, M. A. A. (2013). Review on life cycle assessment of integrated solid waste management in some Asian countries. *Journal of Cleaner Production*, 41, 251–262.
- Petucci, C., Diffendal, J., Kaufman, D., Mekonnen, B., Terefenko, G., & Musselman, B. (2007). Direct analysis in real time for reaction monitoring in drug discovery. *Analytical chemistry*, 79(13), 5064–5070.
- Phan, S., & Luscombe, C. K. (2019). Recent advances in the green, sustainable synthesis of semiconducting polymers. *Trends in Chemistry*, 1(7), 670–681.
- Phillips, K. A., Wambaugh, J. F., Grulke, C. M., Dionisio, K. L., & Isaacs, K. K. (2017). High-throughput screening of chemicals as functional substitutes using structure-based classification models. *Green Chemistry*, 19(4), 1063–1074.
- Plutschack, M. B., Pieber, B., Gilmore, K., & Seeberger, P. H. (2017). The hitchhiker's guide to flow chemistry. *Chemical reviews*, 117(18), 11796–11893.
- Polshettiwar, V., & Varma, R. S. (2008). Microwave-assisted organic synthesis and transformations using benign reaction media. *Accounts of chemical research*, 41(5), 629–639.
- Polshettiwar, V., & Varma, R. S. (2010). Green chemistry by nano-catalysis. *Green Chemistry*, 12(5), 743–754.
- Prier, C. K., Rankic, D. A., & MacMillan, D. W. (2013). Visible light photoredox catalysis with transition metal complexes: applications in organic synthesis. *Chemical reviews*, 113(7), 5322–5363.
- Qiao, J., Liu, Y., Hong, F., & Zhang, J. (2014). A review of catalysts for the electroreduction of carbon dioxide to produce low-carbon fuels. *Chemical Society Reviews*, 43(2), 631–675.
- Qiao, N., Li, M., Schlindwein, W., Malek, N., Davies, A., & Trappitt, G. (2011). Pharmaceutical cocrystals: an overview. *International journal of pharmaceutics*, 419(1-2), 1–11.
- Ramyashree, M. S., Priya, S. S., Freudenberg, N. C., Sudhakar, K., & Tahir, M. (2020). Metal-organic framework-based photocatalysts for carbon dioxide reduction to methanol: A review on progress and application. *Journal of CO2 Utilization*, 101374.
- Reisman, S. E., Nani, R. R., & Levin, S. (2011). Buchner and beyond: Arene cyclopropanation as applied to natural product total synthesis. *Synlett*, 2011(17), 2437–2442.
- Rosenbaum, R. K., Bachmann, T. M., Gold, L. S., Huijbregts, M. A., Jolliet, O., Juraske, R., . . . Margni, M. (2008). USEtox—the UNEP-SETAC toxicity model: recommended characterisation factors for human toxicity and freshwater ecotoxicity in life cycle impact assessment. *The International Journal of Life Cycle Assessment*, 13(7), 532–546.
- Rücker, C., & Kümmerer, K. (2012). Modeling and predicting aquatic aerobic biodegradation—a review from a user's perspective. *Green Chemistry*, 14(4), 875–887.

- Saling, P., Kicherer, A., Dittrich-Krämer, B., Wittlinger, R., Zombik, W., Schmidt, I., . . . Schmidt, S. (2002). Eco-efficiency analysis by BASF: the method. *The International Journal of Life Cycle Assessment*, 7(4), 203–218.
- Sans, V., & Cronin, L. (2016). Towards dial-a-molecule by integrating continuous flow, analytics and self-optimisation. *Chemical Society Reviews*, 45(8), 2032–2043.
- Sans, V., Glatzel, S., Douglas, F. J., Maclaren, D. A., Lapkin, A., & Cronin, L. (2014). Non-equilibrium dynamic control of gold nanoparticle and hyper-branched nanogold assemblies. *Chemical Science*, 5(3), 1153–1157.
- Sans, V., Porwol, L., Dragone, V., & Cronin, L. (2015). A self optimizing synthetic organic reactor system using real-time in-line NMR spectroscopy. *Chemical Science*, 6(2), 1258–1264.
- Santoro, S., Ferlin, F., Luciani, L., Ackermann, L., & Vaccaro, L. (2017). Biomass-derived solvents as effective media for cross-coupling reactions and C–H functionalization processes. *Green Chemistry*, 19(7), 1601–1612.
- Schäfer, H. J. (2011). Contributions of organic electrosynthesis to green chemistry. *Comptes Rendus Chimie*, 14(7-8), 745–765.
- Schmidt-Dannert, C., & Lopez-Gallego, F. (2016). A roadmap for biocatalysis—functional and spatial orchestration of enzyme cascades. *Microbial biotechnology*, 9(5), 601–609.
- Schultz, T. W., Carlson, R. E., Cronin, M. T. D., Hermens, J. L. M., Johnson, R., O’Brien, P. J., . . . Veith, G. D. (2006). A conceptual framework for predicting the toxicity of reactive chemicals: modeling soft electrophilicity. *SAR and QSAR in Environmental Research*, 17(4), 413–428.
- Schwarz, H. (2017). On the usefulness of useless knowledge. *Nature Reviews Chemistry*, 1(1), 1–3.
- Seigal, B. A., Fajardo, C., & Snapper, M. L. (2005). Tandem catalysis: generating multiple contiguous carbon-carbon bonds through a ruthenium-catalyzed ring-closing metathesis/kharasch addition. *Journal of the American Chemical Society*, 127(46), 16329–16332.
- Shah, A. A., Kato, S., Shintani, N., Kamini, N. R., & Nakajima-Kambe, T. (2014). Microbial degradation of aliphatic and aliphatic-aromatic co-polyesters. *Applied microbiology and biotechnology*, 98(8), 3437–3447.
- Shaikh, I. R. *J. Catal.*, 2014, 402860, 1–35.
- Sheldon, R. A. (1994). Consider the environmental quotient. *CHEMTECH;(United States)*, 24(3).
- Sheldon, R. A. (2007). The E factor: fifteen years on. *Green Chemistry*, 9(12), 1273–1283.
- Sheldon, R. A. (2008). E factors, green chemistry and catalysis: an odyssey. *Chemical Communications(29)*, 3352–3365.
- Sheldon, R. A. (2012). Fundamentals of green chemistry: efficiency in reaction design. *Chemical Society Reviews*, 41(4), 1437–1451.
- Sheldon, R. A., Arends, I., & Hanefeld, U. (2007). *Green chemistry and catalysis*: John Wiley & Sons.
- Shen, L. Q., Judson, R. S., Melnikov, F., Roethle, J., Gudibanda, A., Zimmerman, J. B., & Anastas, P. T. (2016). Probabilistic diagram for designing chemicals with reduced potency to incur cytotoxicity. *Green Chemistry*, 18(16), 4461–4467.
- Shenvi, R. A., O’Malley, D. P., & Baran, P. S. (2009). Chemoselectivity: the mother of invention in total synthesis. *Accounts of chemical research*, 42(4), 530–541.

- Sholl, D. S., & Lively, R. P. (2016). Seven chemical separations to change the world. *Nature News*, 532(7600), 435.
- Simon, M.-O., & Li, C.-J. (2012). Green chemistry oriented organic synthesis in water. *Chemical Society Reviews*, 41(4), 1415–1427.
- Slater, C. S., M. J. Savelski, Carole, W. A., & Constable, D. J. C. in *Green Chemistry in the Pharmaceutical Industry*, ed. P. J. Dunn, A. S. Wells and M. T. Williams, Wiley-VCH, Weinheim, Germany, 2010, ch. 3, pp. 49–81.
- Soares, A., Guieysse, B., Jefferson, B., Cartmell, E., & Lester, J. N. (2008). Nonylphenol in the environment: a critical review on occurrence, fate, toxicity and treatment in wastewaters. *Environment international*, 34(7), 1033–1049.
- Soh, L., Curry, J., Beckman, E. J., & Zimmerman, J. B. (2014). Effect of system conditions for biodiesel production via transesterification using carbon dioxide–methanol mixtures in the presence of a heterogeneous catalyst. *ACS Sustainable Chemistry & Engineering*, 2(3), 387–395.
- Song, Z.-L., Fan, C.-A., & Tu, Y.-Q. (2011). Semipinacol rearrangement in natural product synthesis. *Chemical reviews*, 111(11), 7523–7556.
- Stoler, E., & Warner, J. C. (2015). Non-covalent derivatives: cocrystals and eutectics. *Molecules*, 20(8), 14833–14848.
- Storms, Z. J., Brown, T., Sauvageau, D., & Cooper, D. G. (2012). Self-cycling operation increases productivity of recombinant protein in *Escherichia coli*. *Biotechnology and bioengineering*, 109(9), 2262–2270.
- Su, B., Cao, Z.-C., & Shi, Z.-J. (2015). Exploration of earth-abundant transition metals (Fe, Co, and Ni) as catalysts in unreactive chemical bond activations. *Accounts of chemical research*, 48(3), 886–896.
- Swarr, T. E., & D. Cespi, J. F. a. P. N. in *Handbook of Green Chemistry: Vol.10 Tools for Green Chemistry*, ed. P. T. Anastas, E. S. Beach and S. Kundu, Wiley-VCH, Weinheim, Germany, 2017, ch. 1, vol. 10, pp. 1–27.
- Thirumurugan, P., Matosiuk, D., & Jozwiak, K. (2013). Click chemistry for drug development and diverse chemical–biology applications. *Chemical reviews*, 113(7), 4905–4979.
- Tickner, J. A., Schifano, J. N., Blake, A., Rudisill, C., & Mulvihill, M. J. (2015). Advancing safer alternatives through functional substitution. *Environmental science & technology*, 49(2), 742–749.
- Todd, M. H. (2005). Computer-aided organic synthesis. *Chemical Society Reviews*, 34(3), 247–266.
- Trost, B. M. (1991). The atom economy—a search for synthetic efficiency. *Science*, 1471–1477.
- Trost, B. M., Frederiksen, M. U., & Rudd, M. T. (2005). Ruthenium-catalyzed reactions—a treasure trove of atom-economic transformations. *Angewandte Chemie International Edition*, 44(41), 6630–6666.
- U.S. Environmental Protection Agency, *Estimation Programs Interface Suite™ for Microsoft® Windows*, v 4.11., <https://www.epa.gov/tsca-screening-tools/epi-suitetm-estimation-program-interface>, .
- U.S. National Research Council, *“The Red Book”: Risk Assessment in the Federal Government: Managing the Process*, The National Academies Press, Washington, DC, 1983. Retrieved from
- Van Aken, K., & L. Streckowski and L. Patiny. *Total syntheses of oxygenated brazanquinones via regioselective homologous anionic Fries rearrangement of benzylic O-carbamates*, *Beilstein J. Org. Chem.*, 2006, 2, 1–7.

- Villar-Garcia, I. J., Lovelock, K. R., Men, S., & Licence, P. (2014). Tuning the electronic environment of cations and anions using ionic liquid mixtures. *Chemical Science*, 5(6), 2573–2579.
- Vink, E. T., & Davies, S. (2015). Life cycle inventory and impact assessment data for 2014 Ingeo™ polylactide production. *Industrial Biotechnology*, 11(3), 167–180.
- Voutchkova, A. M., Kostal, J., & P. T. Anastas. in *Handbook of Green Chemistry: Vol.9 Green Processes: Designing Safer Chemicals*, ed. P. T. Anastas, R. S. Boethling and A. M. Voutchkova, Wiley-VCH, Weinheim, Germany, 2012, ch. 13, vol. 9, pp. 349–373.
- Wang, R., Hertwich, E., & Zimmerman, J. B. (2016). (Virtual) water flows uphill toward money. *Environmental science & technology*, 50(22), 12320–12330.
- Wang, Y., Lin, H.-X., Chen, L., Ding, S.-Y., Lei, Z.-C., Liu, D.-Y., . . . Tian, Z.-Q. (2014). What molecular assembly can learn from catalytic chemistry. *Chemical Society Reviews*, 43(1), 399–411.
- Wasserscheid, P., & J. Joni. in *Handbook of Green Chemistry: Vol.6 Green Solvents: Ionic Liquids*, ed. P. T. Anastas, P. Wasserscheid and A. Stark, Wiley-VCH, Weinheim, Germany, 2010, ch. 2, vol. 6, pp. 41–59.
- Wende, R. C., & Schreiner, P. R. (2012). Evolution of asymmetric organocatalysis: multi- and retrocatalysis. *Green Chemistry*, 14(7), 1821–1849.
- White, J. L., Baruch, M. F., Pander III, J. E., Hu, Y., Fortmeyer, I. C., Park, J. E., . . . Yan, Y. (2015). Light-driven heterogeneous reduction of carbon dioxide: photocatalysts and photoelectrodes. *Chemical reviews*, 115(23), 12888–12935.
- Whitesides, G. M., & Grzybowski, B. (2002). Self-assembly at all scales. *Science*, 295(5564), 2418–2421.
- Xu, J., & Guo, B.-H. (2010). Poly (butylene succinate) and its copolymers: Research, development and industrialization. *Biotechnology journal*, 5(11), 1149–1163.
- Yamabe, S., Tsuchida, N., & Yamazaki, S. (2006). A FMO-Controlled Reaction Path in the Benzil- Benzilic Acid Rearrangement. *The Journal of organic chemistry*, 71(5), 1777–1783.
- Ye, R., Hurlburt, T. J., Sabyrov, K., Alayoglu, S., & Somorjai, G. A. (2016). Molecular catalysis science: Perspective on unifying the fields of catalysis. *Proceedings of the National Academy of Sciences*, 113(19), 5159–5166.
- Young, I. S., & Baran, P. S. (2009). Protecting-group-free synthesis as an opportunity for invention. *Nature chemistry*, 1(3), 193–205.
- Zhang, Q., Vigier, K. D. O., Royer, S., & Jerome, F. (2012). Deep eutectic solvents: syntheses, properties and applications. *Chemical Society Reviews*, 41(21), 7108–7146.
- Zimmerman, J. B., & Anastas, P. T. (2015). Toward designing safer chemicals. In: American Association for the Advancement of Science.
- Zimmerman, J. B., & P. T. Anastas. in *Sustainability Science and Engineering*, ed. M. A. Abraham, Elsevier, Amsterdam, 2006, ch. 10, vol. 1, pp. 201–221.