Trends in Analytical Chemistry 61 (2014) 1–10

Contents lists available at ScienceDirect

Trends in Analytical Chemistry

journal homepage: www.elsevier.com/locate/trac

Greener derivatization in analytical chemistry

I. Lavilla *, V. Romero, I. Costas, C. Bendicho

Departamento de Química Analítica y Alimentaria, Área de Química Analítica, Facultad de Química, Universidad de Vigo, Campus As Lagoas-Marcosende s/n, 36310 Vigo, Spain

ARTICLE INFO

Keywords:
Derivatization
Electrochemical derivatization
Energy efficiency
Enzymatic derivatization
Greener derivatization
Microwave-assisted derivatization
Photoderivatization
Reagent
Solvent
Ultrasound-assisted derivatization

ABSTRACT

Principle 8 of Green Chemistry recommends eliminating derivatization, yet it is difficult to fulfill in analytical chemistry, so we consider the design of environment-friendly derivatization procedures in this article. We provide an overview on the main strategies for achieving greener derivatization procedures, emphasizing the use of less hazardous reagents and solvents and more efficient forms of energy. We consider using alternative media, such as water, bio-derived solvents, natural deep eutectic solvents, supercritical fluids, ionic liquids and organic solvents instead of classical undesirable solvents. We highlight derivatization with natural compounds and enzymes. We also discuss use in derivatization of different forms of energy, such as microwaves, ultrasound, photochemical or electrochemical. We present numerous examples where the overall green profile of the analytical methodology can be enhanced by focusing on the derivatization steps.

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Abbreviations: AE, Atom economy; CE, Capillary electrophoresis; DES, Deep eutectic solvent; DLLME, Dispersive liquid-liquid microextraction; DNPH, 2,4-dinitrophenylhydrazine; E-factor, Environmental factor; EHS, Environmental, health and safety; EMMA, Electrophoretically-mediated microanalysis; EMY, Effective mass yield; EPA, Environmental Protection Agency; EQ, Environmental quotient; ES-MS, Electrospray-mass spectrometry; FI, Flow injection; GAC, Green analytical chemistry; GC, Gas chromatography; GC-MS, Gas chromatography-mass spectrometry; GSK, GlaxoSmithKline; HFBA, Heptafluorobutyric anhydride; IC, Ionic chromatography; IL, Ionic liquid; LC, Liquid chromatography; LCA, Life-cycle assessment; LOD, Limit of detection; LPME, Liquid-phase microextraction; MALDI-MS, Matrix-assisted laser desorption/ionization mass spectrometry; NADES, Natural deep eutectic solvents; NEMI, National environmental methods index; PBT, Persistent, bioaccumulative and toxic reagent; OSHA, Occupational Safety and Health Administration; Photo-VG, Photochemical-vapor generation; PLE, Pressurized liquid extraction; RCRA, Resource Conservation and Recovery Act; RME, Reaction mass efficiency; SF, Supercritical fluid; SPME, Solid-phase microextraction; TRI, Toxic release inventory; US, Ultrasound; UV, Ultraviolet.

* Corresponding author. Tel.: +34 986-812291; Fax: +34 986-812556.
E-mail address: isela@uvigo.es (I. Lavilla).

http://dx.doi.org/10.1016/j.trac.2014.05.007
0165-9936/

1. Introduction

Ideally, according to Principle 8 of Green Chemistry, when a green analytical method is designed: "Unnecessary derivatization (blocking group, protection/deprotection, temporary modification of physical/chemical processes) should be avoided whenever possible" [1]. Principle 8 of Green Chemistry, focused mainly on organic synthesis, was adapted to analytical laboratories by Namieśnik et al. [2], becoming Principle 6 of Green Analytical Chemistry (GAC) ("Derivatization should be avoided"). Nevertheless, this is difficult to apply in analytical chemistry, particularly when enhancement of the sensitivity and/or selectivity of measurements are required [3,4]. Even with the most sophisticated and advanced instrumentation, such as that used in emerging fields {e.g., proteomics [5]}, derivatization is exploited in order to improve quantitative and qualitative aspects of the analytical methodology.

Undoubtedly, derivatization involves, to some extent, an environmental impact due to the increased amounts of reagents, solvents and energy consumed and/or waste generated [6]. Derivatization processes can be considered a special type of microscale synthetic chemistry [7], and they can entail several steps that are time consuming and use of hazardous reagents/solvents under extreme conditions of temperature and pressure. Other principles of Green Chemistry [1] and GAC [2] can therefore be directly applied to those procedures, particularly reduction of the waste generated, use of safer solvents and reagents, preference for reagents obtained from renewable source, efficient energy use and minimization of risk of accidents.

There is a broad literature concerning analytical derivatization procedures. Numerous books and reviews have been published on this matter. These mainly focus on functional groups and/or techniques used in determination. Some trends in derivatization have been pointed out in order to obtain faster and simpler procedures, especially through automation and miniaturization [3,4,8].

Although the main goal of current approaches to derivatization is not to obtain greener developments, they can be considered under this perspective. As noted, automation and miniaturization are two important keys to designing greener procedures for derivatization (e.g., on-chip derivatization integrates all principles of Green Chemistry). In this case, the amounts of reagents used and waste generated are reduced by at least four to five orders of magnitude in comparison with conventional methodologies [9]. Completely automated methods are a reality in routine laboratories [e.g., when using liquid chromatography (LC)] [10].

Table 1 shows different approaches to derivatization assessed according to the green benefits achieved. As can be seen, special efforts have been made to eliminate and/or reduce organic solvents via novel developments in miniaturization, such as solid-phase microextraction (SPME) or liquid-phase microextraction (LPME) techniques, both with the possibility of simultaneous extraction and derivatization. Greener approaches to derivatization include some instrumental configurations, such as on-column/in-capillary derivatization with LC and capillary electrophoresis (CE), respectively. In these approaches, derivatization takes place during the separation stage, so they are advantageous over the most conventional pre-column, post-column or capillary modes of derivatization, since consumption of sample and derivatizating agents is low and full automation occurs without additional equipment. The introduction of sample and derivatization agent in the injection port (i.e., in-port derivatization) in gas chromatography (GC), especially when it is combined with SPME, simplifies sample preparation, avoids the use of hazardous conditions and reduces solvent and waste generation. Also worth mentioning is use of more efficient forms of energy, such as microwaves, ultrasound (US) and UV radiation, which soften derivatization conditions. In recent years, the use of reagents and solvents that are less toxic in order to reduce their impact on the environment and laboratory staff has received increasing attention.

Table 1
Some approaches to greener derivatization in analytical laboratories

Most important benefits achieved	Approaches
Less toxic reagents and more soft conditions	• Derivatization with natural products • Derivatization in aqueous media • Derivatization in supercritical fluids • Derivatization in ionic liquids • Enzymatic derivatization
Reduction of energy consumption Save time, reagents and waste	• Microwave assisted derivatization • Ultrasound assisted derivatization • Photochemical derivatization • Electrochemical derivatization
Reduction of the work scale Miniaturization	• On-chip derivatization
Derivatization in the instrument Reduction of labor, save time, energy, risks and reagents	• In-port derivatization • On-column/in-capillary derivatization
Automation	• On-line derivatization
Reduction of analytical steps, Simultaneous derivatization and extraction Elimination or reduction of organic solvents Reduction of the work scale	• Solid-phase derivatization • In-fiber derivatization • In-drop derivatization • In-hollow fiber derivatization • In-membrane derivatization

In this article, we discuss different derivatization procedures involving less toxic and hazardous reagents/solvents and more efficient forms of energy. Both questions directly relate to the environmental impact and can be considered important factors in order to minimize negative effects from the analytical laboratory. Table 2 shows examples of greener procedures for derivatization.

2. The need to use reagents and solvents that are less toxic

In general, reagents and solvents used in derivatization are often irritant, corrosive and toxic, so their replacement by others more environment friendly could have positive benefits from the standpoint of the environment. There are different tools for evaluating the environmental, health and safety (EHS) hazards in a chemical process [52], namely, holistic life-cycle assessment (LCA) technique, environmental factor (E-factor), environmental quotient (EQ), effective mass yield (EMY), atom economy (AE), reaction mass efficiency (RME) and eco-scale. Nonetheless, these general tools are difficult to implement in GAC.

A simple way to evaluate EHS impacts in analytical laboratories is use of the National Environmental Methods Index (NEMI) [53], a project of the American Chemical Society's Green Chemistry Institute aiming to "define, identify, and promote analytical chemistry methods that use fewer harmful solvents, use safer chemicals, and minimize waste". An analytical method is not considered green when:

- it uses a persistent, bioaccumulative and toxic (PBT) reagent;
- it uses a hazardous reagent;
- it uses a corrosive pH (when pH is less than 2 or greater than 12); and
- the waste generated is greater than 50 g.

PBT and hazardous reagents are listed in the Toxic Release Inventory (TRI) [54]. Apart from their toxicity, PBT chemicals pose special risks because they remain in the environment for long periods of time and can be accumulated in biological tissues. More