



## Deep Eutectic Solvents (DESS): Emerging viable solvent systems for transition-metal-catalyzed cross-coupling reactions

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### ABSTRACT

The worth of solvents in organic synthesis is often underestimated and misunderstood. The utilization and introduction of newer solvents are encouraged over traditional solvents. Thanks to green chemistry regulations, they are becoming increasingly reported for cross-coupling reactions and all other organic reactions. Deep eutectic solvents (DESS) have become a trend in the current green millennium and are worth exploring for their role in cross-coupling reactions. A brief overview of the history, classification, methods of preparation, and applications of DESS towards cross-coupling reactions are deliberated; the appropriate explanations from the Hole theory are used to explain the efficiency of these esoteric media and the catalysts in cross-coupling reactions. The crucial accomplishments relating to the multiple roles of DESS, like a catalyst, solvent, nucleophile, substrate, or ligand, are highlighted through the embodiment of carbon-heteroatom, carbon-carbon cross-coupling reactions reported between 2020 and 2024. A wide variety of transition-metal-catalysts (TMC) based on Pd, along with inexpensive transition-metal-catalysts like Fe, Co, Cu, Ni, etc., are also summarized in this paper. The review demonstrates the utility of DES that obviated the use of toxic exogenous bases and ligands, minimized homocoupling product in cross-coupling reactions, eliminated harsh reaction conditions, improved yields and product selectivity, and reduced the use of toxic solvents for purifications. The DESS could also stabilize air and water-sensitive TM catalysts, thus improving catalytic efficiency. This review underscores the use of DESS in transition-metal-catalyzed cross-coupling reactions, promoting green and sustainable chemistry for the future.

### 1. Introduction

By utilizing the expertise ideas of green chemistry, Chemists, chemical engineers, and the pharmaceutical industry are increasingly adopting novel strategies to significantly aid in resolving the long-standing problems that affect our environment, economy, and health [1–3]. The primary tactics undertaken during the reaction/process design are using catalysts, encouraging low catalyst loading and recyclability, employing green media, and minimizing the usage of toxic solvents for purification. These approaches provide environment-friendly, safe, and economically feasible processes to accomplish the performance of chemical reactions and manufacturing of value-based products.

#### 1.1. Deep eutectic solvents

tial, etc., traditional solvents like toluene, acetonitrile, dimethyl formamide (DMF), etc., are currently discouraged [6]. Since they constitute a significant portion of chemical waste produced in the chemical and pharmaceutical industries, solvents adversely affect the environment and health. Therefore, a search for alternative or greener solvents is the need of the hour. The solvents can be deemed green if the requirements, such as widespread availability, non-volatility, recyclability, non-toxicity, biodegradability, biorenewability, low cost, and recyclability, among others, are satisfied [7–11]. Supercritical fluids (SCFs) and gas-expanded fluids [12], ionic liquids (ILs) [13,14], bio-based solvents [15], water [16], and fluorinated solvents [17] are just a few of the neoteric greener solvents that have garnered significant interest. However, high toxicity and unavailability of fluorinated solvents, the procedural requirements for using SCFs, and the higher costs, toxicity, and te-