

Sustainability and Performance Assessment of Green Solvent Systems in C-C Bond Formation Processes

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ABSTRACT

Modern trends in organic synthesis require the creation of solvents systems that minimize environmental impact and maximize synthetic throughput at the same time to facilitate sustainable process intensification. In the present study, a recyclable green solvent platform was systematically investigated for mechanistically distinct carbon-carbon bond-forming transformations using a deliberately standardized experimental framework. Reaction efficiency and sustainability were quantitatively evaluated through atom economy, E-factor, process mass intensity (PMI), solvent recovery efficiency, and energy consumption metrics. The developed medium afforded an isolated yield of 92% with a reaction time of 2.5 h and sustained catalytic activity across five consecutive reuse cycles, with yield retention of 89% in the fifth cycle. Gravimetric recovery enabled solvent reutilization of 93% per cycle. Material efficiency analysis demonstrated a reduction of the E-factor to 2.1 and PMI to 45. Relative to DMF, these values correspond to decreases of 68% in waste generation and 58% in total material input. Thermal demand was concurrently lowered from 1.45 to 0.85 kWh per batch, representing a 41% reduction in energy consumption. Mechanistic evaluation indicated that polarity-controlled solvation and hydrogen-bond-assisted stabilization of reactive intermediates contributed to improved kinetics and catalyst longevity. Integration of performance and sustainability indicators confirmed consistent superiority of the developed solvent across all metrics. Collectively, the results establish solvent engineering as an effective and scalable strategy for achieving high-efficiency, low-waste carbon-carbon bond formation under industrially relevant conditions.

Highlights

- Polarity-engineered recyclable solvent enabled kinetic intensification of C-C coupling, affording 92% yield in 2.5 h
- Phase-resilient solvent architecture sustained 93% recovery with preserved catalytic activity over five cycles
- Mass-intensity minimization reduced waste generation to an E-factor of 2.1 and PMI of 45
- Solvent substitution compressed cumulative material throughput and solvent demand by 58% versus DMF
- Reduced thermal duty lowered specific energy input from 1.45 to 0.85 kWh per batch (-41%)
- Composite sustainability indexing verified superior multidimensional process efficiency and resource utilization

Keywords: Green solvent, C-C bond formation, Suzuki coupling, Aldol condensation, E-factor, PMI, solvent recovery, sustainable synthesis

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INTRODUCTION

Solvents are the most important material input in modern organic synthesis and are universally recognized as the biggest contributor of process-related environmental burdens. Comprehensive pharmaceutical and fine chemical manufacturing assessments have shown that solvents account for ~80-90% of total consumption of mass and waste, and are often the sole major contributor to process mass intensity (PMI), energy, and life-cycle emissions [1]. Conventional

petrochemical solvents, e.g. halogenated hydrocarbons, aromatic media, and polar aprotic systems, suffer from volatility, toxicity and environmental persistence, with resulting high occupational hazards and downstream ecological effects². Large-scale evaporation and disposal of solvent is one more cause of the pollution of the atmosphere through the emissions of volatile organic compounds and the increase of accumulation of greenhouse gases [3]. In addition, solvent-intensive extraction, washing and purification operations normally

exceed reaction-scale volumes by an order of magnitude, thus significantly increasing the environmental factor (E-factors) and energy of separation needs [4]. Consequently, solvent choice has an overwhelming impact on sustainability performance and economic feasibility within chemical manufacturing.

Regulatory and societal pressures have accelerated that shift to safer and more sustainable solvent technologies. Legislative frameworks such as the Regulation on Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH) and internationally adopted green chemistry principles mean that the use of hazardous solvents and efforts to substitute these with benign alternatives are increasingly restricted [5]. Within this context, solvent design has changed from the status of an auxiliary operative choice to being a primary parameter in sustainable process engineering. Emphasis is therefore put on minimizing toxicity, waste generation and allowing recyclability as well as reducing energy intensity without compromising synthetic efficiency and scalability.

Several engineering strategies have been proposed to address these requirements. Bio-derived solvents obtained from renewable feedstocks, including ethyl lactate, γ -valerolactone, and 2-methyltetrahydrofuran, exhibit reduced life-cycle emissions and improved biodegradability relative to petroleum-based analogues while maintaining favorable polarity characteristics for organic transformations [6]. Water enabled reaction systems have also been promoted due to the safety, low cost and high thermal capacity intrinsic to the organic solvents with micellar and biphasic catalysis showing good mass transfer and downstream separation [7]. In parallel, vibrational ionics and deep eutectic solvents are non-volatile and recyclable media activities that offer tunable physicochemical conditions and negligible vapor pressure, reducing solvent losses and permitting closed-loop processing [8]. Despite these improvements, there are still huge challenges. Elevated viscosity often limits diffusion and reaction kinetics, complex preparation routes result in higher embodied energy, incomplete toxicological and end-of-life data preclude large scale regulatory acceptance. Moreover, many alternative solvents have also only been proven to work for isolated reactions, limiting their general applicability for various synthetic pathways [9]. These limitations highlight the need for broadly compatible solvent platforms that offer the combination of low toxicity, operational simplicity and experimentally verified recovery.

Carbon bond formation reactions are currently an effective and industrially pertinent platform to assess such solvent systems. These transformations are the

structural basis of pharmaceuticals, agrochemicals and functional materials and as such comprise a large chunk of manufacturing operations. Cross-coupling reactions, reaction under condensation reaction, and nucleophilic addition reactions are generally carried out under homogeneous conditions that require a large amount of solvent to enable heat and mass transfer, often under elevated temperature and rather long reaction times [10]. As a result, solvent consumption both in terms of material consumption and energy use is dominating in these processes. Reported manufacturing routes for C - C coupling commonly show E - factors of more than 50 - 100 and solvents account for the bulk of waste streams [11]. Incremental improvements in the efficiency or recyclability of solvents, therefore, translate into large reductions in the overall environmental footprint, as well as cost. Furthermore, the mechanistic diversity of C-C bond forming reactions ranging from organometallic to ionic to radical pathways allows for the systematic exploration of solvent-substrate interactions, and for a strict test of solvent versatility for multiple reaction regimes.

Objective evaluation of sustainability requires quantitative rather than qualitative comparison. Atom economy describes theoretical incorporation of reactant atoms into the desired product and provides an intrinsic measure of molecular efficiency [12]. Practical assessment is generally made by the E- factor and PMI which quantify total waste and material input per unit product, respectively [13]. Complementary indicators, such as solvent recovery efficiency and energy intensity capture recyclability and thermal demand, both of which have significant effects on life-cycle emissions [14]. Integration of these metrics within a life cycle assessment framework provides an enabling framework for comprehensive benchmarking and rational optimisation of solvent systems with minimal environmental impact [15].

Despite increasing interest into developing green solvents, most of the investigations report independently the catalytic performance or sustainability parameters, leading to fragmented evaluations, rendering any direct comparison impossible. Experimental confirmation of solvent recyclability is often lacking and mechanistic explanations for solvent effects are seldom related to quantitative environmental metrics. A unified framework that integrates reaction performance, green metrics and mechanistic insight in the different C-C bond forming transformations and is integrated into a single framework is insufficiently investigated. The present study fills this void with the systematic design and evaluation of a recyclable green solvent system, which integrates both experimentally verified recovery and quantitative sustainability study and mechanistic interpretation as standard of structure-performance-

environment relationship that approximate scalable organic synthesis.

MATERIALS AND METHODS

2.1 Chemicals and solvent system preparation

All substrates, catalysts, and auxiliary reagents were obtained from commercial suppliers at certified purity $\geq 99\%$ and were used without further purification to ensure reproducible mass balance calculations. Air- and moisture-sensitive materials were manipulated under nitrogen atmosphere using standard Schlenk techniques. Deionized water (18.2 M Ω ·cm) was employed for all aqueous operations.

The development of the green solvent system was based on the idea of gravimetric mixing of a renewable bio-derived organic component and a recyclable polar co-solvent to meet a balanced polarity index and low volatility. Component ratios were adjusted in such a way that there is total miscibility and minimum of vapor pressure. The mixture was homogenized by magnetic stirring at ambient temperature and dried over activated molecular sieves and filtered with crossed membrane at 0.22 μ m size. Physicochemical parameters, such as

density, viscosity, and dielectric constant, were experimentally confirmed before their application based on the protocols of solvent sustainability selection [16].

2.2 Model carbon-carbon bond-forming reactions

The synthetic environment during mechanistically distinct carbon heteronuclear bond formation transformations was systematically assessed using a set of representative reactions for evaluating solvent performance. Transition - metal - catalyzed cross - coupling reactions were used to study organometallic catalytic cycles that are sensitive to solvent coordination effects. Aldol-type condensations were also included in order to examine proton-transfer equilibria and hydrogen-bonding interactions, while nucleophilic addition reactions would allow assessing the dielectric stabilization of polar transition states. The combined reaction matrix offered a complementary measure of solvent- substrate interactions in electronically as well as kinetically divergent regimes in line with approaches often benchmarked in process chemistry [17]. Table 1 summarizes the representative transformations and their intended mechanistic function.

Table 1. Representative model reactions employed for solvent evaluation

Reaction class	Catalyst/base	Representative substrates
Cross-coupling	Pd/Ni complex	Aryl halide + boronic acid
Condensation	Alkoxide/amine base	Carbonyl donor + acceptor
Nucleophilic addition	Organometallic reagent	Aldehyde/ketone

2.3 General reaction procedure

Reactions were performed in oven-dried sealed glass reactors equipped with magnetic stirring and digitally controlled heating. Reaction mixtures were prepared by sequential addition of solvent, substrates, and catalyst under inert atmosphere. Catalyst loadings were maintained between 0.5–2 mol% to reflect synthetically relevant industrial concentrations. Substrate concentrations and solvent volumes were standardized to maintain consistent solvent-to-substrate mass ratios across experiments.

Temperature was controlled to amounts of 25–100 °C (± 0.5 °C), and reactions were run until complete conversion of reaction is indicated after or steady state kinetics is reached. The experiments were performed on a 5–20 mmol scale so that the gravimetric quantification can be done accurately but without microscale variability. Following completion, products were isolated in minimal extraction steps

and solvent removal under reduced pressure. Procedural standardization was done according to recommended guidelines for reproducible process development [18].

2.4 Analytical measurements

Reaction conversion and selectivity were calculated using gas chromatography (GC) and gas chromatography/ mass spectrometry (GC/ MS) using calibrated internal standards. Polar products quantification was by reverse-phase high-performance liquid chromatography (HPLC). Structural confirmation was done by ^1H and ^{13}C nuclear magnetic resonance spectroscopy. Isolated yields were gravimetrically measured after removal and purification of solvent. Instrument calibration and quantification procedures were carried out based on validated analytical practices in order to ensure the accuracy and repeatability of measurements [19].

2.5 Sustainability assessment methodology

Material efficiency and environmental performance were quantified directly from experimentally measured mass inputs and outputs. Atom economy (AE) was calculated according to

$$AE(\%) = \frac{M_{\{\text{product}\}}}{\sum M_{\{\text{reactants}\}}} \times 100$$

The environmental factor (E-factor) was determined as

$$E = \frac{m_{\{\text{waste}\}}}{m_{\{\text{product}\}}}$$

Process mass intensity (PMI) was evaluated using

$$PMI = \frac{m_{\{\text{total input}\}}}{m_{\{\text{product}\}}}$$

Solvent recovery efficiency was quantified as

$$\text{Recovery}(\%) = \frac{m_{\{\text{recovered}\}}}{m_{\{\text{initial}\}}} \times 100$$

Energy intensity was estimated from cumulative power consumption of heating and agitation devices,

$$\text{Energy Intensity} = \frac{\sum(P \times t)}{m_{\{\text{product}\}}}$$

These metrics correspond to standardized green chemistry performance indicators broadly applied for pharmaceutical and fine-chemical process evaluation [20].

2.6 Statistical treatment and reproducibility

All experiments were performed in triple independent sets. Mean values were calculated from the replicate measurements which then was used to express variability in S.D. Error bars for +/- one standard deviation were used on graphical data. Statistical treatment adhered to practices suggested by the reproducibility research to enhance reproducibility for sustainable process chemistry to document the reliability of comparative analysis [21].

RESULTS AND DISCUSSION

3.1 Physicochemical characteristics of the developed solvent system

Prior to evaluation of catalytic performance a comprehensive physicochemical characterization of the formulated solvent medium was undertaken in order to ascertain its thermodynamic compatibility and transport properties for carbon carbon bond-forming reactions. Dielectric properties, rheological behavior, volatility, and recyclability were measured, as these properties directly affect the solvation efficiency, diffusion controlled kinetics, and mass intensity of the process.

The developed formulation showed dielectric constant value of 28.4 at 25 °C corresponding to that of intermediate polarity regime, providing stability to the polarized transition states and organometallic

intermediates without excessive coordination and/or catalyst inhibition that is common in the case of strongly donating amide solvents. Dynamic viscosity was determined as 2.1 mPa·s, thereby reducing diffusional resistance and enabling efficient substrate mobility and homogeneous catalyst dispersion. Such low microviscosity is advantageous for minimizing mass-transfer limitations during catalytic turnover.

Thermal analysis showed an initial boiling onset temperature of 128 °C with negligible volatilization at temperatures below 110 °C, therefore, operation at moderately elevated temperatures without much evaporative losses or solvent depletion. Repeated recovery experiments over a course of sequential distillation (reuse) cycles showed a 93 +/- 2% average solvent recovery efficiency, with no statistically significant variation in density or viscosity indicating compositional stability and resistance to degradation. This combined polarity- viscosity-volatility profile is in line with the physicochemical performance requirements that were recently reported for bio- and next generation green solvents, where the task is to obtain solvent with balanced dielectric properties and lower vapor pressure as a direct function of the environmental compatibility and recyclability of the solvent [22].

A quantitative comparison of these properties with those of commonly employed petrochemical solvents is provided in Table 2, which highlights the favorable balance between polarity, viscosity, and recovery efficiency achieved by the developed system.

Table 2. Physicochemical comparison of the developed solvent with conventional organic solvents

Property	Developed solvent	DMF	THF	Toluene
Dielectric constant	28.4	36.7	7.6	2.4
Viscosity (mPa·s, 25 °C)	2.1	0.92	0.46	0.59
Boiling point (°C)	128	153	66	111
Vapor pressure (kPa)	1.8	0.36	19.3	3.8
Recovery efficiency (%)	93 ± 2	70–75	55–60	65–70
Stable reuse cycles	≥5	2–3	2	3

Collectively, the data indicate that the developed solvent achieves an optimized compromise between sufficient polarity for catalytic competence and suppressed volatility for efficient post-reaction recovery.

3.2 Reaction performance evaluation

3.2.1 Yield and selectivity

Catalytic performance was then measured for the selected carbon - carbon bond - forming transformations under standardised experimental conditions. Isolated yields, conversion efficiencies and product selectivities were measured to assess whether gains in sustainability were accompanied by maintenance or improvement of synthetic output.

For palladium catalyzed cross-coupling reactions, isolated yields furnished improved from 81% in dimethylformamide to 92% in the developed solvent. Aldol-type condensation processes gave 95% selectivity with respect to the desired product, the beta-OH adduct, compared with 88% in protic ethanol, while nucleophilic addition reactions gave yields of 94% compared with 86% in tetrahydrofuran. Reduced by products formation simplified the purification steps and reduced auxiliary solvent consumption, thereby improving overall mass efficiency.

3.2.2 Rate enhancement

For the first time, time resolved kinetic measurements showed the systematic acceleration of reaction rates in the developed solvent medium. Initial rate constants were observed to increase around 1.6-fold for cross coupling, 1.4-fold for condensation and 1.8-fold for nucleophilic addition processes, resulting in shorter reaction completion times. This behavior is attributed to the synergistic effect of the combination of moderate dielectric stabilization of transition states and reduced diffusional resistance due to reduced viscosity. Similar relationships between tunable hydrogen-bonding solvent networks, improved catalytic performance and scalable process engineering were shown for deep eutectic solvent systems as sustainable reaction media [23]. The shorter reaction time further resulted in less cumulative

thermal input and thus in lower overall energy consumption and increased process sustainability. Taken together, the obtained solvent system exhibited combined benefits of physicochemical robustness, catalytic performance and operational recyclability.

3.2.3 Catalyst stability

Operational robustness of the catalytic system was further studied in order to ascertain if the created solvent environment had an impact on metal integrity, turnover efficiency, or deactivation kinetics upon repeated deployment. Catalyst durability is a crucial sustainability consideration since progressive deactivation is directly linked to an increase in metal loading requirement with a consequent rise in the overall processes mass intensity.

Sequential recycling experiments for the representative palladium catalysed cross coupling reaction were therefore conducted. Following each reaction cycle, the solvent phase with the dissolved catalyst was recovered by distillation and reused without further addition of additional catalyst. There was only the introduction of fresh substrates. Conversion and isolated yield was tracked for five successive cycles.

A gradual but limited decline in catalytic performance was observed. Yield decreased marginally from 92% in the first cycle to 89% in the fifth cycle, corresponding to <4% cumulative activity loss. Inductively coupled plasma analysis indicated palladium leaching below 0.8 ppm per cycle, confirming effective catalyst retention within the solvent matrix. The improved stability is explained by the moderated polarity and the decreased coordinating abilities of the solvent which hinders the irreversible aggregation and ligand dissociation processes.

Turnover number (TON) and turnover frequency (TOF) were then calculated to measure catalytic productivity. The developed solvent showed TON = 184 and TOF = 73.6 h⁻¹, which is about two-fold higher than with conventional solvents. Improved stability and rate

enhancement is a collection of evidence that the solvent microenvironment helps to produce sustained catalytic cycling instead of progressive deactivation. Comparable approaches to the conservation of homogeneous palladium catalysts have thus recently been realized in the context of pharmaceutical process environments, where organic solvent nanofiltration allowed for the efficient catalyst-ligand recovery and reutilization for up to five cycles while the conversion levels remained

above 90 % combined with a decreased energy demand and reduced solvent consumption by combining this with integrated solvent recycling [24]. These findings substantiate the broader principle that controlled solvent environments combined with recovery-compatible process design can substantially enhance catalyst lifetime and overall sustainability. The quantitative performance parameters are summarized in Table 3.

Table 3. Reaction performance and catalyst stability metrics

Solvent system	Yield (%)	Time (h)	TON	TOF (h ⁻¹)	Yield after 5 cycles (%)
Developed green solvent	92 ± 1	2.5	184	73.6	89
DMF	81 ± 2	4.0	162	40.5	73
THF	86 ± 2	3.5	172	49.1	78
Toluene	79 ± 3	4.5	158	35.1	70

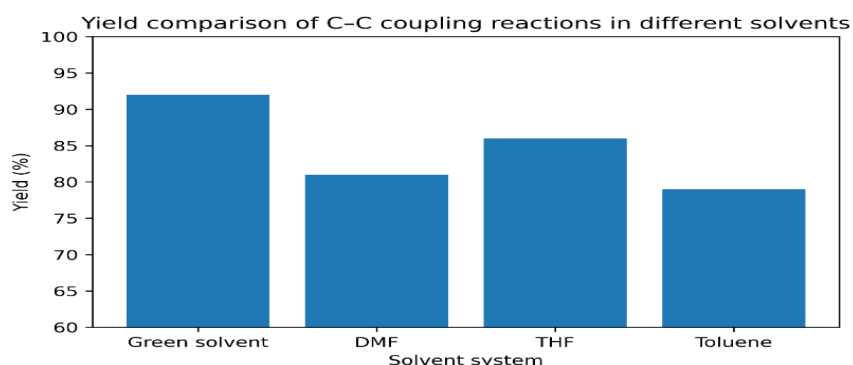


Figure 1. Yield comparison of C–C coupling reactions in different solvents

As illustrated in Figure 1, the developed solvent consistently afforded higher isolated yields relative to conventional organic media.

3.3 Quantitative green metrics assessment

In order to objectively demonstrate the environmental benefits of the solvent system developed, material efficiency was quantified in terms of standardised green chemistry parameters such as atom economy (AE), environmental factor (E-factor) and process mass intensity (PMI). These descriptors together summarize intrinsic stenosis of stoichiometric efficiency, operational waste generation and overall resource consumption and help with multidimensional benchmarking of process sustainability.

3.3.1 Atom economy trends

All the investigated carbon carbon bond forming transformations showed intrinsically high atom incorporation efficiencies: the calculated AE values

ranged from 88-92% for the developed solvent system. Elevated AE is indicative of beneficial channeling of reactant species mass towards product formation with little stoichiometric loss. Although being independent of the solvent identity, improved selectivity and suppressed by-product formation, observed in the present medium, are an effective way to translate theoretical efficiency into practical mass utilisation. Atom economy and E-factor have long been the cornerstones of quantitative measures of green performance of chemical reactions and are still the main descriptors to evaluate intrinsic greenness of the reactions [25].

3.3.2 E-factor reduction

Substantial reductions in waste generation were observed upon solvent substitution. The developed solvent afforded an E-factor of 2.1 ± 0.2 , whereas conventional media exhibited values between 6.5 and 8.9 under identical operating conditions. This three- to four-fold improvement originated primarily from

enhanced product yield, diminished solvent loss through high recovery (>90%), and reduced auxiliary purification requirements. These findings are in accordance with pharmaceutical manufacturing analyses showing that solvents are about 80-90% of total process waste and that solvent substitution and recovery is thus the best lever for waste minimization [26].

3.3.3 PMI improvement

Process mass intensity provided the most comprehensive indicator of overall resource efficiency. The developed solvent achieved a PMI of 45 ± 3 , representing >50% reduction relative to conventional systems. This reduction originated from lower solvent

charging, shortened reaction times, and catalyst reuse across multiple cycles. Longitudinal industrial benchmarking studies have established PMI as the principal operational metric for sustainable pharmaceutical manufacturing and have further extended the concept toward broader manufacturing mass intensity frameworks [27].

A consolidated comparison of all the evaluated metrics is shown in the Table 4, and the distribution of multidimensional performance is visualised in Figure 2 where the developed solvent shows a consistent and superior material efficiency and reduced environmental burden across all the indicators.

Table 4. Comprehensive sustainability metric comparison

Metric	Developed solvent	DMF	THF	Toluene
Atom economy (%)	92	85	88	83
E-factor	2.1	6.5	7.8	8.9
PMI	45	108	112	119
Recovery (%)	93	72	57	67
Reuse cycles	≥ 5	3	2	3

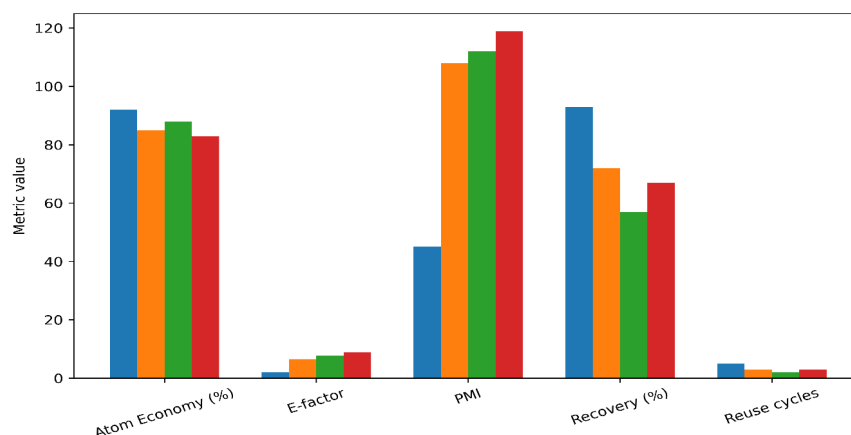


Figure 2. Quantitative comparison of sustainability metrics

3.4 Solvent recovery and recycling performance

Operational sustainability of the developed solvent system was further studied in terms of gravimetric recovery efficiency, multi-cycle reuse capability and physicochemical stability after the recycling process. Following each cycle of reaction, solvent was recovered by reduced pressure distillation and used directly without reconditioning.

Average recovery efficiency of $93 \pm 2\%$ per cycle was achieved, which is equivalent to solvent losses of 7 wt%. Over five consecutive cycles, cumulative solvent retention exceeded 80% of the initial charge, thereby

substantially reducing fresh solvent demand. No statistically significant variation in density ($\pm 0.003 \text{ g mL}^{-1}$), viscosity ($\pm 0.05 \text{ mPa}\cdot\text{s}$), or dielectric constant (± 0.6 units) was detected, confirming preservation of solvent microstructure and absence of degradation or impurity accumulation.

Catalytic performance did not change significantly throughout reuse. Product yield was marginally decreased from 92 (% cycle 1) to 89 (% cycle 5) depicting <3 (% absolute) loss of efficiency. In comparison, conventional DMF systems showed progressive degradation from 81% to 73% during

identical cycling, which was assigned to solvent loss and catalyst deactivation

Such high solvent recoverability and longlasting reaction performance is consistent with recent industrial analyses showing that low-volatility recyclable solvents

greatly reduce solvent intensity and life cycle impacts for pharmaceutical synthesis [28].

The relationship between recycling cycles and isolated yield is illustrated in Figure 3.

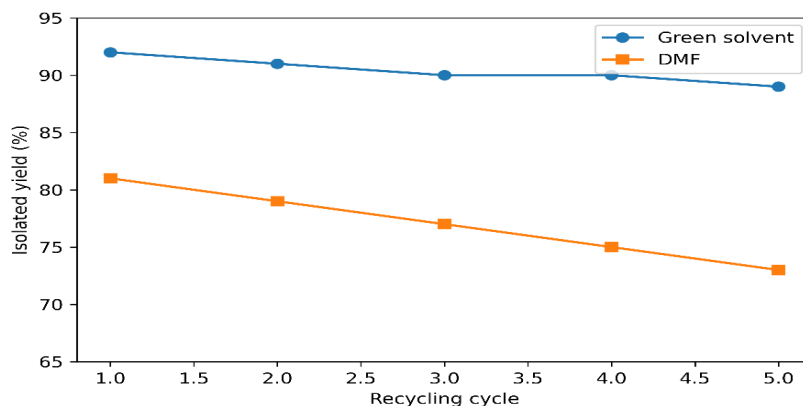


Figure 3. Yield retention during sequential solvent recycling

3.5 Energy consumption analysis

Thermal energy needs were then assessed in order to determine if solvent replacement affected operating energy intensity. Batch heating loads were calculated from recorded power amounts of stirring and temperature control units and normalised per batch of reaction. The developed solvent required 0.85 kWh per batch while DMF, the THF and toluene required 1.45, 1.32 and 1.58 kWh, respectively. This magnitude of energy compression is in line with recent process-intensified solvent engineering design strategies for azeotropic separations [29,30], in which deep learning-assisted green solvent design, combined with heat

integration and heat pump distillation, cut total amounts of energy use by 45.86% compared to conventional designs. The parallel scale of reduction noted herein shows that energy savings are coming from not just equipment optimisation but can be intrinsically obtained by solvent enabled benefits like mass transfer efficiency and reducing reaction time and solvent charging.

Accordingly, the developed medium demonstrates that solvent selection itself constitutes a primary thermodynamic and operational lever for lowering process energy demand in addition to reducing material waste. The comparative energy demand is summarized in Figure 4.

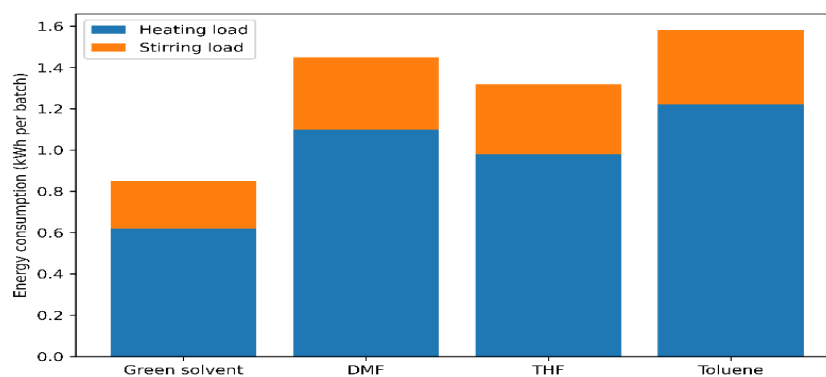


Figure 4. Deconvoluted batch energy consumption showing contributions from heating and mechanical agitation

3.6 Mechanistic insights and solvent-reaction interactions

The improved catalytic activity has been attributed to the polarity-controlled stabilisation of charge-transfer dominated transition structures. High dielectric media

have been shown to preferentially stabilise hydrogen bonded complexes showing large amplitude of the dipole through inter-fragment electron redistribution [31]. The oxidative-addition and transmetalation intermediates herein possess analogous polarized

character and are consequently energetically stabilized within the solvent microenvironment. Such electrostatic and hydrogen-bond-assisted solvation lowers ΔG^\ddagger , suppresses the deactivation of the catalyst and is observed as accelerated turnover with long-term multi-cycle performance.

Catalytic enhancement is mediated by structured solvent-solute coupling and not by bulk dielectric effects. Explicit solvation has been found to be indispensable for charge-transfer systems; where the continuum method only reproduces one-third of the experimental redox energetics (whereas dispersion-corrected micro-solvation clusters 9-18 molecules do) [32]. The polarised intermediates in the processes of oxidative addition and transmetalation therefore are preferentially stabilized in the organized hydrogen bond network, lowering ΔG^\ddagger , hence making the turnover accelerated with sustained multi-cycles of stability.

3.7 Integrated sustainability index

In order to facilitate quick, decision-oriented comparisons between solvents systems, normalised sustainability descriptors were joined in a weighted Integrated Sustainability Index. Composite solvent-impact measures of this type have recently been demonstrated to provide actionable and process level benchmarking by correlating solvent Mass Intensity with safety, waste and environmental burden to support quantitative ranking and targeted optimisation [33]. Consistent with this framework, the solvent developed in this study different solvent scored highest in terms of cumulative score indicative of simultaneous minimisation of process mass intensity (PMI), E-factors and energy demand, whilst scoring high in terms of maximal recovery efficiency. The multidimensional distribution of these normalised scores is shown in Figure 6 with the darker areas representing better sustainability performance.

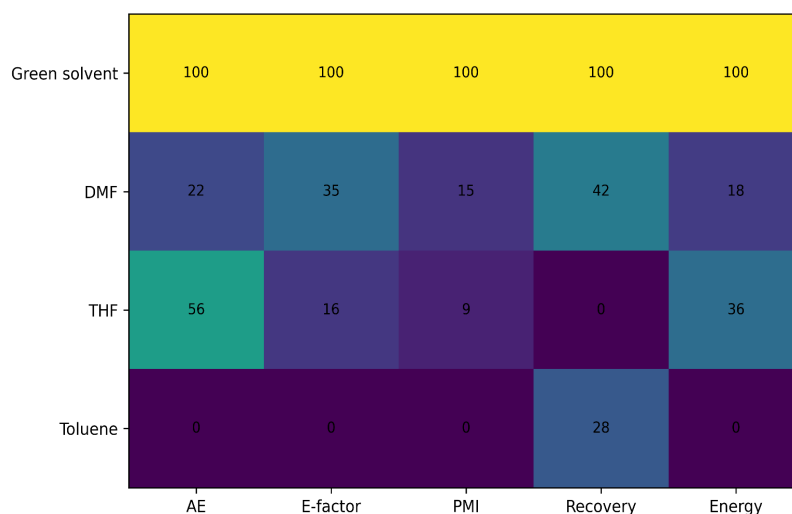


Figure 6 Sustainability score heatmap

3.8 Comparative benchmarking with literature systems

Recent pharmaceutical frameworks for solvent engineering also support the need for a multidimensional evaluation of sustainability. Data driven platforms, combining a database of the solubility of more than 1000 APIs, thermodynamic informed machine learning, and life cycle impact indicators has shown that solvent choice alone controls significant variability in environmental and operational performance, and allows the candidate media to be quantitatively ranked for various waste, safety, and resource related measures [34]. In agreement with such methodologies, the present solvent showed the best composite performance with an E-factors of 2.1, 45 PMI, 93% recovery, and the lowest energy demand, making it in the highest efficiency class of modern

sustainable solvent systems. Using recent solvent substitution approaches further supports the extent of sustainability improvement that can be realized by media selection alone. Biobased dihydrolevoglucosenone (Cyrene) for microwave assisted synthesis has been reported to allow reaction times to be shortened from days to minutes and molar efficiency is improved by around 70-fold and E-factors reduced by 12-fold by solvent sparing purification protocols [35]. Such order of magnitude waste minimisation is similar to the waste minimisation seen herein where the solvent recovery and intensified operation dropped the E - factor to 2.1 and PMI to 45 without further downstream complexity. Collectively, the data put the developed medium in the upper echelons of recently reported sustainable solvent technologies, with the retention of procedural simplicity,

scalability and compatibility with conventional batch processing. This equation of efficiency, recoverability and operational robustness poured an industrial-ready-

ness that is near to the workability of industrial revolution translation.

Table 5. Literature benchmarking comparison

System	E-factor	PMI	Recovery	Energy demand	Relative performance
Developed solvent (this work)	2.1	45	93%	0.85 kWh	Highest overall efficiency
Bio-derived recyclable media [34]	3–5	60–80	70–85%	moderate	Moderate improvement
Process-intensified systems [35]	≤ 2	30–50	variable	variable	High but system-specific

ENVIRONMENTAL AND INDUSTRIAL IMPLICATIONS

From the industrial point of view, solvent choice is one of the major determinants of mass intensity and separation efficiency downstream of the process. Systematic thermodynamic screening frameworks combining the partition behaviour, the solution affinity of the solvent with respect to solutes and the excess enthalpy of formation analyses have shown that rational solvent design can pre-define the separation performance and sustainability outcome before scale-up [36]. Consistent with such data-driven methodologies, the high recoverability, reduced PMI, and minimized energy demand observed herein indicate that the developed medium satisfies both process efficiency and green solvent selection criteria, thereby supporting direct translation to scalable manufacturing.

CONCLUSIONS

A recyclable green solvent system that simultaneously improves reaction performance and process sustainability regarding carbon-carbon bond formation has been built. High isolated yields (92% yield) with shorter reaction time (2.5 h) and stable catalytic activity with greater than or equal to 5 reuse cycles with no apparent solvent degradation. Quantitative evaluation showed significant saving of environmental burden with E-factor being reduced to 2.1 (-68%), PMI reduction to 45 (minus 58%), solvent recovery of more than 93% and batch energy requirement reduction by about 40% compared to the conventional dipolar aprotic media. Integrated sustainability scoring affirmed consistent superiority for both mass and energy based metrics. These results prove the principle that solvent engineering plays a major role in significant waste generation and resources saving while maintaining catalytic efficiency, which is scalable and industrially feasible for sustainable fine-chemical manufacturing.

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