REVIEW

Application of stop-flow micro-tubing reactor system in organic reaction development

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Abstract

Recently demonstrated as a novel reaction screening technology, the stop-flow micro-tubing (SFMT) reactors amalgamate features from continuous micro-flow and conventional batch reactors, resulting in a more logical and rigorous synthesis approach. When compared to traditional batch reactors, SFMT provides a safer and more efficient alternative, particularly suitable for chemical reactions under drastic conditions. The incorporation of commercially available transparent micro-tubing into SFMT makes it an excellent choice for light-mediated reactions, ensuring more uniform exposure to light. And SFMT stands apart from continuous-flow reactors by offering a notably convenient screening approach that is unrestricted by residence time and reactor size, while also effectively eradicating the risk of cross-contamination. The successful reactions developed within the SFMT reactor can be easily translated to continuous-flow synthesis for large-scale production. Overall, the SFMT reactor system exhibits similarities to continuous-flow reactors while surpassing batch reactors, especially for reactions involving gas reagents and/or requiring light illumination. This review aims to provide a comprehensive survey of the synthetic application of SFMT.

Keywords Stop-flow micro-tubing reactor · Reaction development · Flow synthesis · Gas-involved reaction

Introduction

Flow chemistry has emerged as an innovative technique with significant potential for advancing efficient chemical synthesis, garnering considerable attention in fields such as organic chemistry, pharmaceutical manufacturing, and materials science [1–3]. This technique offers several advantages over traditional batch reactions, including precise reaction control, improved safety, easier scalability and enhanced heat and mass transfer due to higher specific surface area [4, 5]. However, to make the system continuously running, a constant pressure must be applied to preserve flow equilibrium,

as any changes in pressure could disrupt the stability of the system. Thus, the evaluation of reaction parameters is different from typical batch set-ups. Several in-line and on-line detection methods can be applied for real-time condition screening, but limited to continuous variables, such as flow rate, temperature, retention time, etc [6]. The screening of discrete parameters, such as reagents, catalysts and solvents using continuous-flow techniques is quite time-consuming, as the whole flow system should be shut-down and restart till the stable [7]. And parallel screening, which is normally used in batch set-up, needs much more equipment (pumps, BPRs, tubing, fittings, and etc.) to support. Therefore, there is a pressing need for streamlined and effective screening methods for continuous-flow synthesis.

Wu and coworkers, in 2017, developed a modular and versatile reactor system named as "stop-flow" microtubing (SFMT) reactor [8]. This innovative system combines features from continuous-flow and batch reactors (Fig. 1). Unlike conventional continuous-flow, the SFMT platform allows for the flow to be stopped when desired. This is made possible by incorporating shut-off valves at both ends of the micro-tubing reactor, creating a "switch in-and-out" mechanism. As illustrated in Fig. 1c, two vessels, containing solutions of reagent 1 and reagent 2 respectively, were affixed to individual

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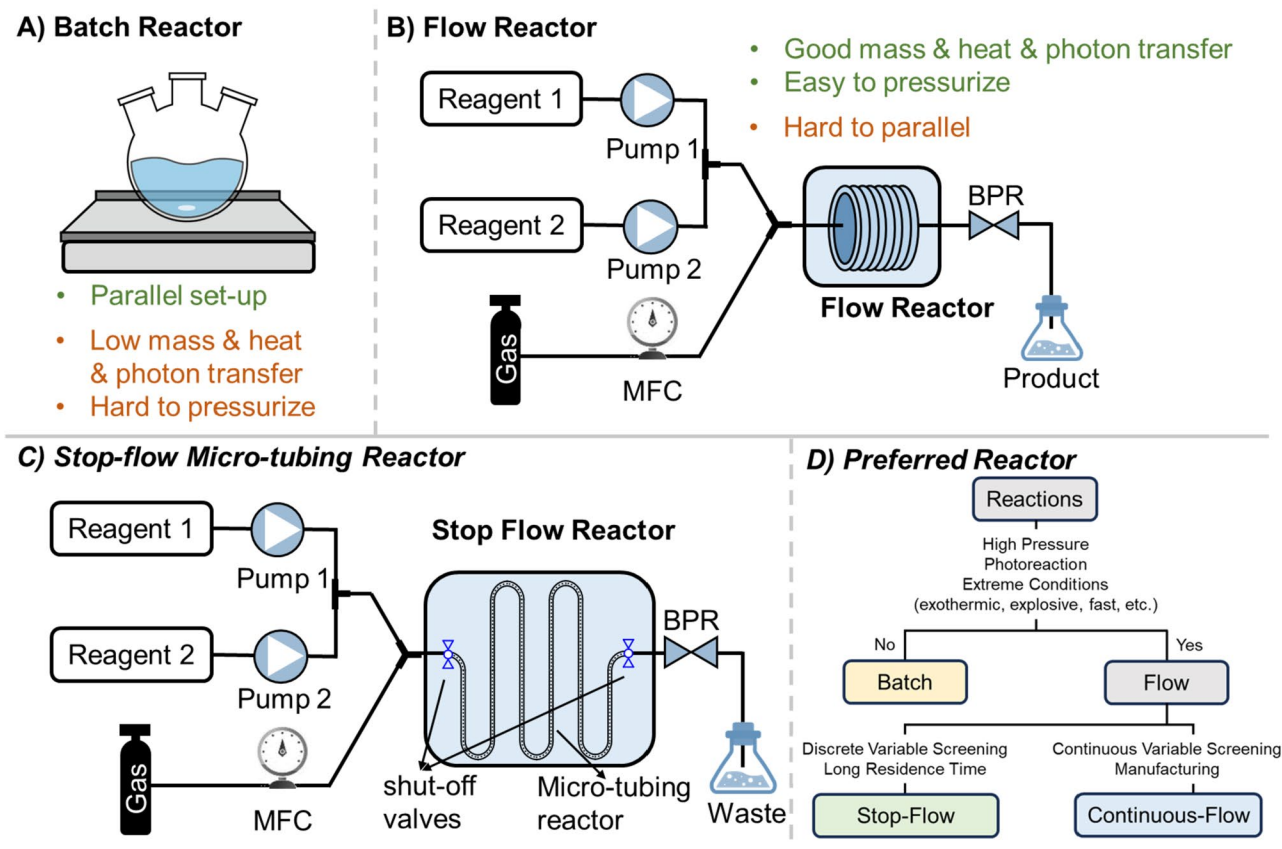3 Department of Chemistry, National University of Singapore, Singapore 117543, Singapore

Fig. 1 **a** Batch reactor. **b** Continuous-flow reactor. **c** SFMT reactor. **d** Decision tree for preferred reactor

pumps, subsequently connected to a T-mixer. And a pressurized gas cylinder and the outlet were attached to a Y-mixer if gaseous reactant was needed. The outlet of Y-mixer was then coupled to the reactor. Termini of the reactor were secured with shut-off valves, while the reactor's outlet was linked to a back-pressure regulator (BPR). The gas cylinder was pressurized slightly beyond the designated back-pressure of the system. Each pump was set up with certain flow rates, and the substrates were introduced into the flow system. Following the complete filling of the tubing reactor, the shut-off valves were closed, and the reactor was subsequently immersed in a hot oil bath or subjected to illumination from a light source to facilitate further reactions. Detailed information on the set-up and various components required for the SFMT system has been provided by Wu's group [9].

With the utilization of micro-tubing reactors, the SFMT system offers numerous advantages, including excellent heat transfer, high-pressure reactions with improved safety, enhanced interfacial contact, efficient light irradiation, and reduced reagent usage and waste production. Compared to continuous-flow reactors, implementing SFMT for reaction screening by straightforward numbering-up saves time and prevents cross-contamination. Rapid screening of reaction

conditions can be achieved without limitations in residence time or reactor size. Besides, during the reaction period, visible lights can be shone on the micro-tubing to facilitate photo-mediated reactions. The inherent good heat transfer performance and narrow residence time distribution of the microtubes, ensured a similar reaction environment between continuous-flow and stop-flow synthesis. As a result, the successful reactions adopting SFMT can be easily transferred to continuous-flow reactors for large-scale production. In contrast to traditional batch or continuous-flow systems that benefit from vigorous stirring or convective mixing through a static mixer, SFMT relies significantly on diffusion for mass transfer, leading to lower mixing efficiency [10]. Nevertheless, in reactions that entail gas/liquid biphasic transformations, the SFMT can guarantee effective reactivities by virtue of its interfacial contact.

Taking into account the characteristics of traditional batch, continuous-flow, and SFMT systems, a preliminary judgment can be formed on the preferred reactors for different reactions (Fig. 1d). Traditional batch processes offer flexibility for a wide range of reactions and still is the most common reaction set-up. Microtubing reactors was preferred while the reaction was carried with high pressure, light

irradiation, and under extreme conditions (e.g. exothermic, explosive, ultra-fast, etc.). Narrowing down to microtubing reactors, continuous flow reactor showed advantages in continuous variable screening and manufacturing, while stop-flow reactor could be a solution for discrete variable screening and long-resident time reactions. This paper aims to comprehensively overview this relatively nascent field of diverse reactions reliant upon the SFMT system.

Applications of SFMT

Reaction involving gaseous reactants

SFMT reactor was firstly used in several reactions utilizing acetylene gas [8]. Acetylene gas was not a traditionally ideal feedstock for research lab discoveries due to its inconvenient handling and explosive properties. And gaseous reagents often suffered from low reactivity, reproducibility, and wastage of excess gas. However, the advent of SFMT presented a remarkable instrument for gas/liquid biphasic transformations. With the assistance of SFMT, Sonogashira coupling achieved 96% yield of terminal alkyne **1** under ambient conditions using Pd(PPh$_3$)$_2$Cl$_2$ and CuI as catalysts in DMSO, with only trace amounts of undesired symmetric internal alkyne detected (Fig. 2). SFMT enabled the screening of 10 different conditions in 3 h, dramatically accelerating the optimization process compared to continuous-flow reactors

that required over 20 h. Under the optimized condition, various aryl iodides were effectively converted to corresponding terminal alkynes, yielding good results, with slightly better selectivity observed for electron-rich substrates compared to electron-poor ones. Notably, when the reaction was performed without a copper co-catalyst, Sonogashira coupling did not occur, and only fulvene **2** as the product was detected with 66% yield, in which three molecules of acetylene were incorporated. In this work, SFMT was also applied for screening the base and catalysts for vinylation of fluorinated aryl bromides under blue LED. Ir(ppy)$_2$(dtbbpy) PF$_6$ proved to be the most effective catalyst, and iPr$_2$NEt was identified as the optimal base. The reaction achieved a good yield of 70% with 10-psi BPR, in contrast to batch flasks where only trace amounts of the fluorinated styrene product **3** were detected. SFMT further proved to be an effective tool for developing visible-light promoted gas/liquid reactions, which is particularly well-suited for screening due to the time-consuming nature of visible-light promoted photoredox transformations in many cases.

In 2018, Wu and coworkers further developed metal-free C-H alkylation and allylation reactions using microtubing reactors. They combined a photocatalyst [Acr$^+$-Mes] ClO$_4$and HCl as the HAT catalyst precursor to enable chlorine-based C-H activation in a catalytic fashion [11]. HCl, produced in chlorine-radical-based HAT processes, enabled C-H activation as expected, making it a suitable HAT catalyst precursor. However, previous attempts at this process

Fig. 2 Utilization of acetylene as a feed stock in transition-metal catalysis and photo-redox catalysis. a Yield in SFMT reactor. b Yield in batch reactor
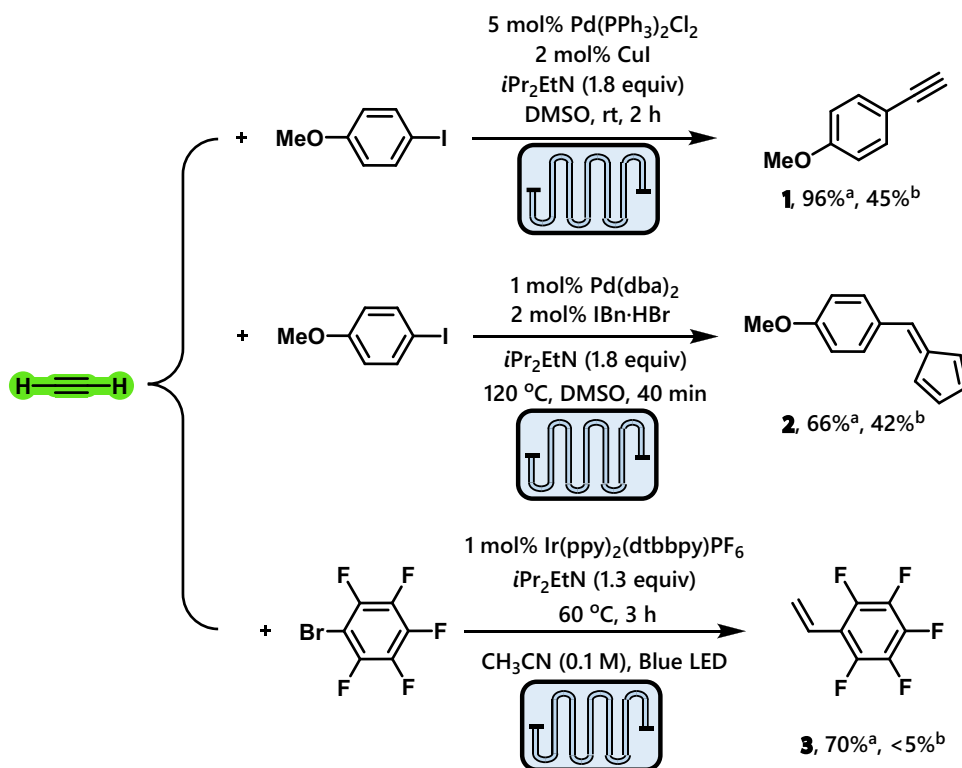
had low conversion and product selectivity due to the volatile feature of HCl [12]. By applying SFMT reactors, the efficiency of the reaction improved due to the unique advantages provided by microflow technologies. At first, the C-H alkylation of cyclohexane using benzylidenemalononitrile in the presence of catalytic [Acr$^+$-Mes]ClO$_4$ and HCl under irradiation with blue LEDs and mild heating was evaluated. The reaction in batch flasks suffered from poor reproducibility (40-95% yield) due to the evaporation of volatile HCl from the heating reaction solution, whereas SFMT reactors prevented HCl from escaping, resulting **4** in almost complete conversion with excellent reproducibility (98% yield) using lesser amounts of cyclohexane (2 vs. 10 equiv) and HCl (5 vs. 20 mol%). This dual catalyst system was extended to activate more challenging molecules, such as ethane, which selectively generated the coupling product **5** in excellent yield (95%) in SFMT reactors, while no product was formed in batch reactors due to low ethane concentration remaining at 50 $^\circ$C and 1 atm pressure (Fig. 3a). The developed alkylation could be scaled up by increasing the volume of the SFMT reactor or directly converting SFMT reactors into continuous-flow microtubing reactors, both achieving good yields. Moreover, this photo-mediated chlorine radical-based HAT process could be applied to allylation with allyl phenyl sulfones as allyl sources to generate allylated products **6**

(Fig. 3b). However, for substrates with more than one reactive site, the selectivity was low to moderate, likely due to the high reactivity of chlorine radicals. To address this, Wu's group developed another bromine-radical-mediated highly selective alkylation of unactivated C(sp^3)–H bonds using an organo-photoredox catalyst with CH$_2$Br$_2$ as the bromine radical precursor and solvent [13]. Hydrogen atom abstraction based on bromine radicals requires a higher activation energy than that required with chlorine radicals, enabling more selective transformations [14]. Thus, the bromine-radical protocol showed excellent reactivity with tertiary C-H bonds and low to moderate reactivity with secondary C-H bonds, with no reactivity towards primary C-H bonds. The selectivity was controlled by the ratio of tertiary to secondary C-H bonds in the substrate, and SFMT reactors were used to enhance the reaction's efficiency and reliability. Conducting the reaction in SFMT reactors under optimized conditions using benzylidenemalononitrile and methylcyclopentane as substrates achieved **7** in 80% yield with a selectivity of 9:1 (Fig. 3c). The scale of the reaction could be further increased by utilizing SFMT reactors with a larger volume, showcasing the practical utility of this strategy.

Recently, Wu and Deng developed an operationally simple protocol for Minisci-type hydrogen-evolution cross coupling of heteroarenes with various C(sp^3) − H partners via
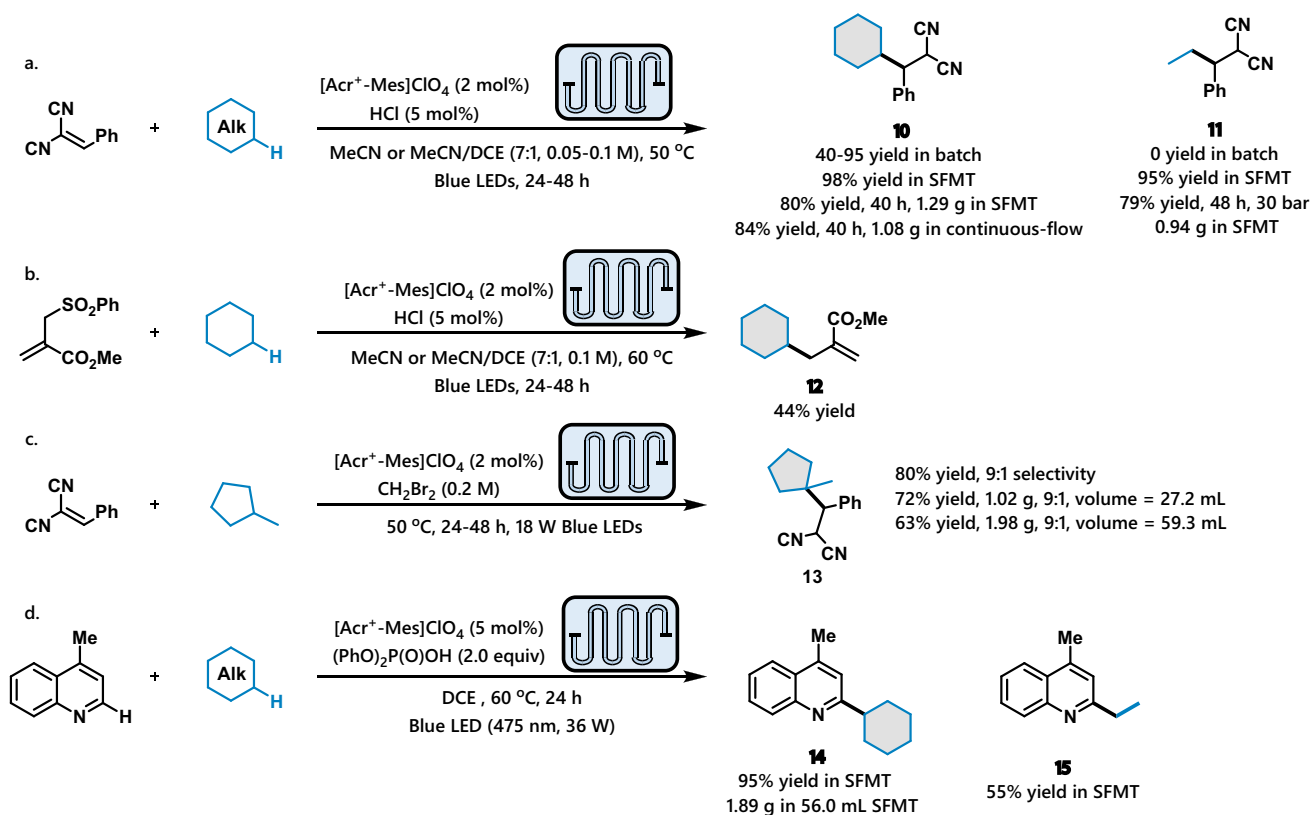
Fig. 3 Visible light induced reactions of unactivated C(sp^3)-H bonds

visible light-induced HAT catalysis with the help of SFMT [15]. In this visible light-mediated transformations, SFMT offered several advantages, such as enhanced light penetration and maintenance of volatile and gaseous reagents and intermediates at elevated temperatures, making them essential for achieving efficient dehydrogenation. The reported reaction involved a catalytic amount (5 mol%) of [Acr$^+$-Mes] ClO$_4$ and two equivalents of diphenyl phosphate in DCE at 60 °C under blue LED light (475 nm, 36 or 72 W) irradiation for 24–48 h, resulting in the desired coupling products **8** in good yield (Fig. 3d). Notably, ethane proved to be an efficient substrate for coupling with heteroarenes using the SFMT reactor, delivering the corresponding ethylation product **9** in moderate yield.

With the assistance of SFMT reactors, methane was directly functionalized through aerobic iodination. To avoid flammable gas-air compositions in the flow system, high methane pressure was utilized. In the SFMT reactor, methane (500 psi) was combined with an air-saturated CH$_3$CN solution containing catalytic [^{n}Bu$_4$N]Cl and I$_2$, resulting in up to 10 turnovers of CH$_3$I using catalytic irradiation (390 nm) [16]. (Fig. 4).

Ethylene, like methane and ethane, is a very simple molecule with a huge annual global production. Despite its abundance, there have been limited reported methods utilizing ethylene as a reactant for producing fine chemicals. This is

likely due to its inherent simplicity, resulting in the formation of molecules with modest complexity, as well as concerns about handling such a flammable gas. However, Wu's group recently developed an innovative approach to utilize ethylene as a starting material for a divergent synthesis of 1,2-diarylethanes, 1,4-diarylbutanes, 2,3-diarylbutanes, and ethylarenes, through the synergistic combination of photoredox and Ni catalysis (Fig. 5) [17]. In the first reaction (condition A), 1,2-diarylethanes were selectively obtained using Ru(bpy)$_3$Cl$_2$ (0.5 mol %), NiCl$_2$-glyme (10 mol %), tetramethylethylenediamine (TMEDA) (2 equiv), and Hünig's base (2 equiv) in DMSO (0.2 M) under blue LED irradiation at 50 °C for 24 h. For the synthesis of 1,4-diarylbutanes (condition B), [Ir(ppy)$_2$(dtbbpy)]PF$_6$ (1 mol %) was used as the photocatalyst in MeCN (0.05 M) at 25 °C under blue LED irradiation, resulting in excellent selectivity and yield. By increasing the reaction temperature to 100 °C and replacing NiCl$_2$-glyme with NiI$_2$ in DMSO (0.1 M) (condition C), 2,3-diarylbutanes were exclusively obtained but only applicable to para-functionalized bromo- and iodoarenes in batch reactors due to ethylene escaping from the DMSO solution at high temperatures. To address this limitation, the SFMT reactor proved efficient for generating 2,3-diarylbutanes from a wide range of para- or meta-substituted aryl iodides and bromides (condition D), as it maintained high temperature and pressure, keeping ethylene in the reaction solution.

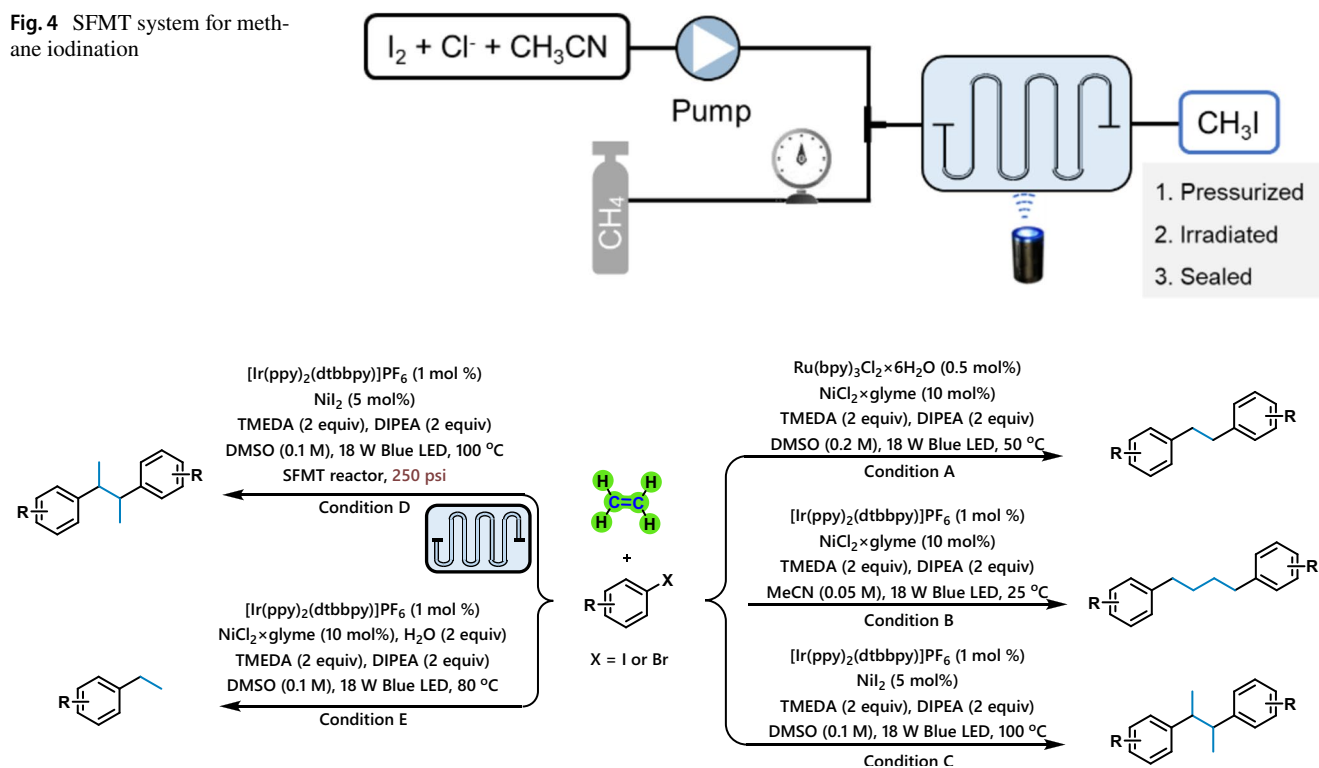**Fig. 4** SFMT system for methane iodination

Fig. 5 Metal catalyzed divergent difunctionalization of ethylene

Additionally, under condition E, reductive-Heck products were generated from arenes bearing electron-deficient substituents when subjected to the Ir/Ni dual catalytic system under blue LED irradiation at 80 °C in the presence of water. These findings demonstrate the versatile and efficient use of ethylene as a valuable starting material in fine chemical synthesis, highlighting the potential of photoredox and Ni catalysis in combination with SFMT reactors.

Photo-mediated reactions

With the assistance of SFMT, Wu's group achieved visible-light-mediated alkylation of allylic sp[3] C–H bonds with electron-deficient alkenes. They used tetramethylethylene and benzylidenemalononitrile under blue LED light ($\lambda_{max} = 425$ nm) with 9-mesityl-10-methylacridinium perchlorate [Acr$^+$-Mes]ClO$_4$ (2.5 mol%) in 1,2-dichloroethane (DCE, 0.05 M) for 18 hours at room temperature, resulting 10 in 91% isolated yield without [2 + 2] cycloaddition byproducts (Fig. 6) [18]. Notably, the use of SFMT reactors instead of traditional batch flasks significantly reduced the reaction time from 18 hours to 5 h while maintaining a similar yield of 90%. Furthermore, SFMT reactors demonstrated effectiveness in oxidizing tetra-substituted alkenes with unhindered allylic C–H bonds, followed by C–C bond formation to generate 11, overcoming slow reactions in batch reactors due to steric hindrance. This alkylation protocol was successfully extended to other benzylic substrates with increased oxidative potential by using SFMT reactor system, such as electron-neutral arenes, electron-poor arenes, and methyl-substituted heterocycles, resulting in accelerated product formation (12-15) with good yields.

In addition to the successful applications mentioned above, Zhang and Wang demonstrated the use of SFMT reactors in an electron donor-acceptor (EDA) complex initiated α-cyanation of tertiary amines (Fig. 7a) [19]. This process involves the association of electron-rich tertiary amines with electron-deficient benzoyl cyanide to generate the EDA complex. Under light excitation, the EDA complex reaches an electronically excited state, leading to electron transfer (ET) from donor to acceptor. This process can trigger the formation of imine species and cyanide anions, enabling α-cyanation of tertiary amines [20]. In their work, benzoyl cyanide 16 and 2-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline 17 were reacted in CH$_3$CN (0.05 M) with Li$_2$CO$_3$ as an additive at room temperature and argon atmosphere under the irradiation of 18 W 390 − 400 nm purple light-emitting diodes (LEDs). This resulted in the desired product 18 being obtained in 97% isolated yield. Moreover, when they applied the same strategy in an SFMT reactor without the additive, the α-amino nitrile product was generated in 81% yield after 4 h.

Through EDA complex photochemistry, the visible light-driven α-alkylation of N-aryl tetrahydroisoquinolines was further achieved by Zhang group without the need for any photocatalysts, transition-metal catalysts, or additional oxidants (Fig. 7b) [21]. The reaction involved Katritzky salt 19 as the electron acceptor and 2-phenyl-1,2,3,4-tetrahydroisoquinoline 20 as the electron donor. It was carried out at room temperature under the irradiation of 390–400 nm purple light-emitting diodes (LEDs) in the presence of K$_2$CO$_3$ as the base and DCM as the solvent (0.2 M). The desired product 21 was obtained in 72% isolated yield. To explore the practical applicability of this EDA complex photochemistry, the reaction was performed in an SFMT reactor. Remarkably, the use of SFMT system reduced the reaction time from 24 h to 10 h, with a yield of 79% achieved.

In 2020, Li and coworkers reported a visible-light photoredox-catalyzed C-O bond cleavage of diary ethers through acidolysis with an aryl carboxylic acid, followed by a one-pot hydrolysis to yield two molecules of phenols (Fig. 8) [22]. For the acidolysis process, they investigated the
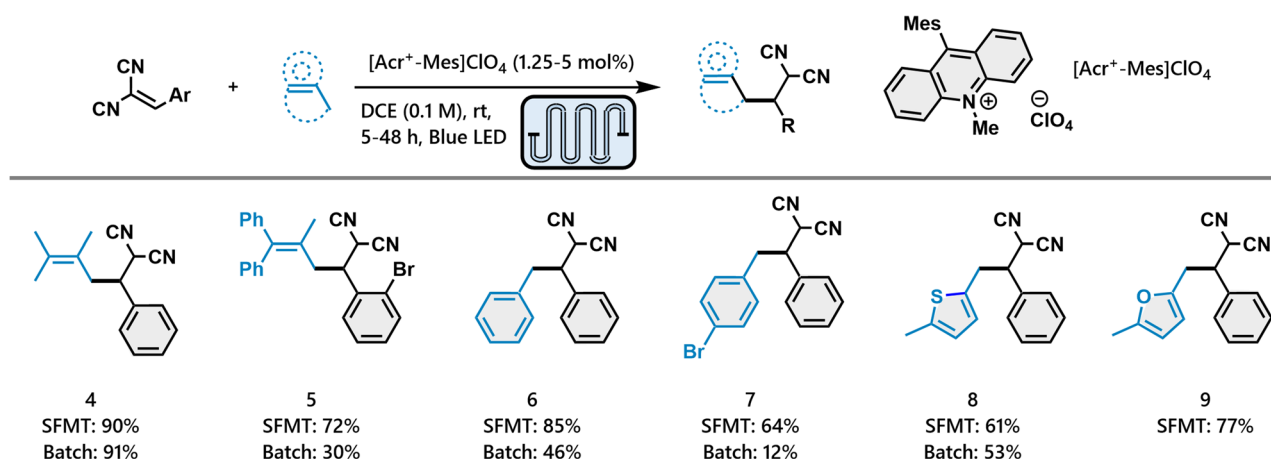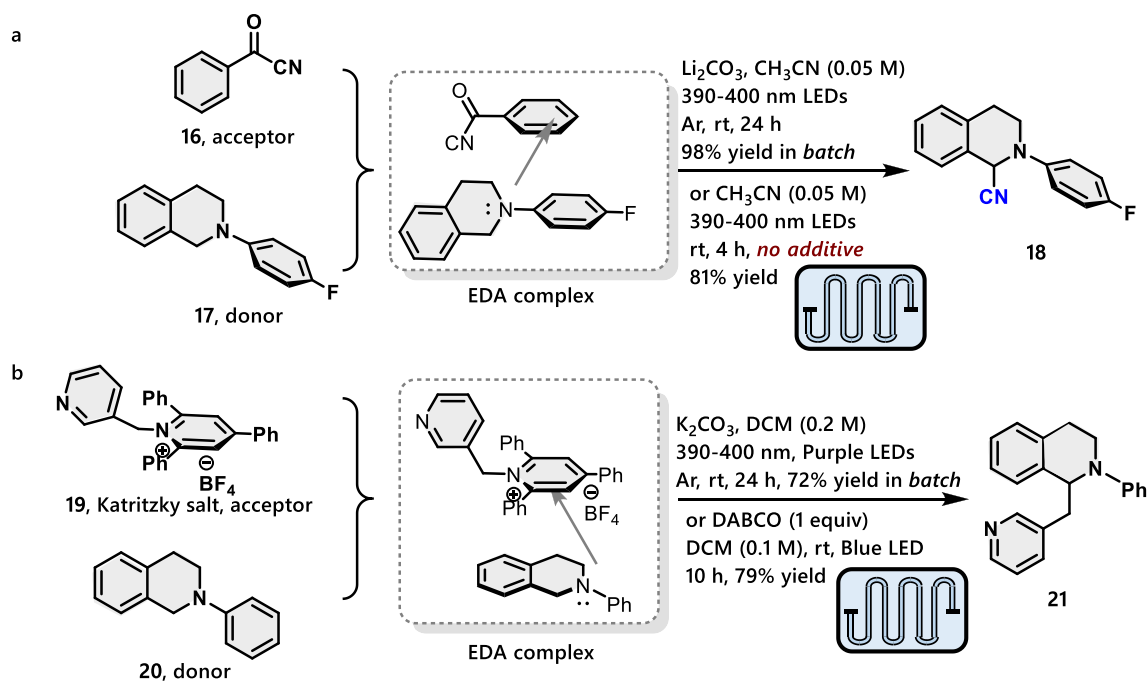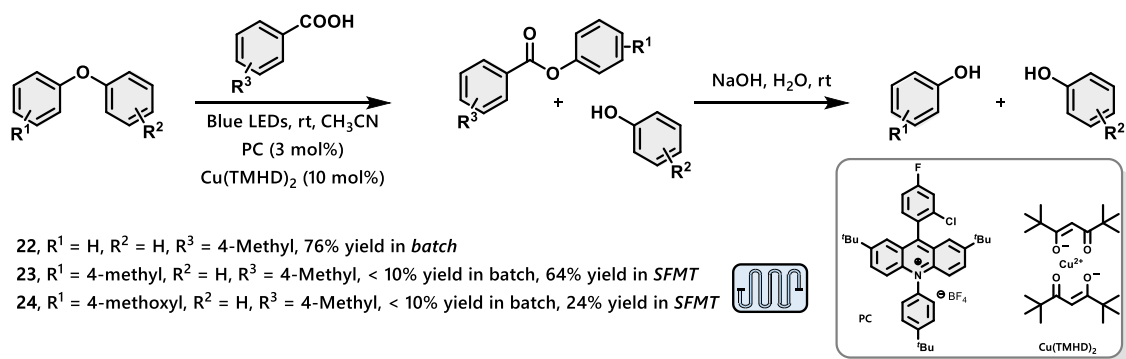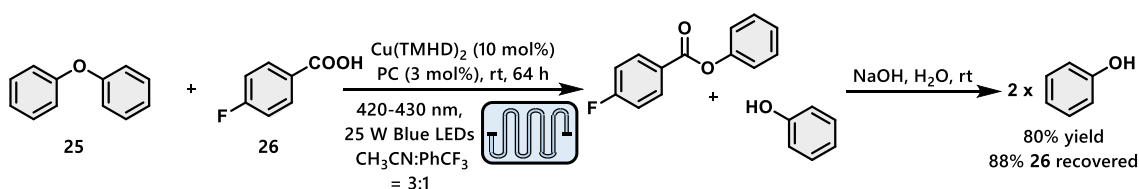

Fig. 6 Alkylation of unfunctionalized allylic/benzylic sp[3] C-H bonds

Fig. 7 Electron donor-acceptor complex-initiated photochemical reactions. **a** Benzoyl cyanide as the acceptor. **b** Katritzky salt as the acceptor

Fig. 8 Selective C-O bond cleavage of diaryl ethers

reaction of diphenyl ether with 4-methylbenzoic acid, using an acridinium photocatalyst (3 mol%) and Cu(TMHD)$_2$ (10 mol%) as a Lewis acid, under 425–430 nm blue LEDs irradiation for 30 h. The reaction resulted in 76% yield of phenyl 4-methylbenzoate **22** and 69% yield of phenol. However, the standard conditions showed very low efficiency (< 10%) for 4-methyl and 4-methoxyl substrates. To

improve the efficiency, they employed SFMT reactors for the reactions, which led to 4-methy ester products **23** in 64% yield with comparable phenol yields. And 4-methoxyl still resulted in low efficiency with **24** in 24% yield. To further demonstrate the practicality of this strategy, a gram-scale reaction of diphenyl ether **25** with 4-fluorobenzoic acid **26** was conducted using flow reactors. The resulting phenol was

obtained in 80% yield, with 4-fluorobenzoic acid showing 88% recovery yield.

Zhu and coworkers previously developed a metal-free photo-induced approach to generate alkoxyl radicals in DCM, enabling C(sp^3)–H functionalization reactions [23]. However, this batch reaction in a non-green chlorinated solvent could not be scaled up. To address this limitation, flow chemistry was employed to develop a green process for the alcohol-mediated Minisci reaction [24]. Initially, 4-chloroquinoline and n-pentanol were investigated via a 1,5-HAT process in SFMT reactors. The reaction utilized phenyliodine bis(trifluoroacetate) (PIFA) as the catalyst, blue LEDs light, and acetonitrile as a green solvent, resulting in 75% yield, higher than the batch reactor yield of 55% (Fig. 9a). Subsequently, the Minisci-type reaction via the β-C–C scission pathway was explored. The reaction of iso-butanol and 4-chloroquinoline using the SFMT system provided 75% yield of the corresponding adduct, again higher than the batch reaction (Fig. 9b). To demonstrate the practicality, gram-scale preparation was conducted in a continuous-flow reactor, affording 1.16 g of **29** and 1.27 g of **30**, which could not be easily achieved in a traditional batch photochemical reaction.

Reaction kinetic study with SFMT

In addition to enhancing the efficiency of the mentioned photo-mediated reaction types, SFMT can also be used to optimize the synthetic process of certain fine chemicals. For example, Xu's group developed an efficient continuous-flow system for the one-stage production of cyclopropylamine (**CPA**) through the Hofmann rearrangement of cyclopropanecarboxamide (**CPCA**) as shown in the Fig. 10a [25].

Initially, two competitively parallel reactions occur during the consumption of **CPCA**: chlorination as the main reaction and hydrolysis as the side reaction. The chlorinated product **31** is then converted to isocyanate **32** with the assistance of a base. Subsequently, **32** undergoes hydrolysis to yield the product **CPA** or reacts with **CPCA** and **CPA** to form by-products **33** and **34**, respectively. Additionally, residual sodium hypochlorite reacts with **CPA**, leading to a reduction in the final yield. To overcome these side reactions and achieve precise control over the reaction conditions to increase selectivity and reactivity, flow chemistry was employed. SFMT reactors were initially used to study the reaction kinetics and explore suitable conditions, which significantly reduced the time required for experimentation. After conducting a comprehensive study on the hydrolysis and chlorination of **CPCA**, along with screening various reaction conditions such as mixing, temperature, and reagent quantities, a residence time of 4 min in the delay loop at 90 °C was selected, resulting in the production of **CPA** in 95–96% yield (Fig. 10b).

In 2020, Lu and coworkers investigated a continuous homogeneous synthesis of hydroxylamine hydrochloride (NH$_2$OH·HCl) using SFMT reactors [26]. The overall synthetic route, starting from nitromethane (NM) through Meyer reaction, was shown in the Fig. 11, with the Nef reaction as a side reaction. The experiments in this paper were performed at less than 120 °C to suppress side reactions. The reaction was heterogeneous under normal pressure in a batch tank. As a result, the by-product formic acid was added to transform the system into a homogeneous state. SFMT was selected to study the kinetic characteristics and develop a corresponding homogeneous kinetic model. Several reaction characteristics were studied on this platform,

Fig. 9 Aliphatic alcohol-mediated Minisci-type reaction. **a** Yield in SFMT reactor. **b** Yield in batch reactor
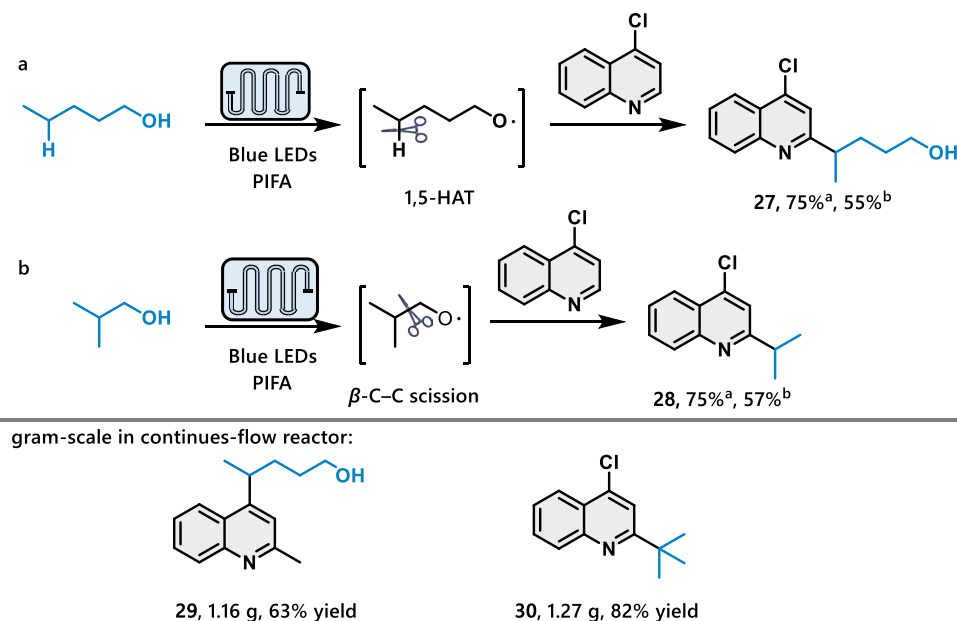
including the effect of temperature, reaction order of NM, and the influence of HCl and water. Based on a wide range of reaction conditions, the established model demonstrated satisfactory agreement with the experimental data, demonstrating its effectiveness as a valuable tool for designing the production process. Consequently, the scale-up experimental results in flow microtubes exhibited high consistency with those in the stop-flow setup, where the conversion of NM (20 wt%) reached 91.7% at 110 °C after 4 h.

Lu's group utilized the SFMT reactor once more to conduct a homogenous kinetic study of the ring-opening reaction [27]. This reaction involves the conversion of ethylene oxide (**EO**) with acrylic acid (**AA**) catalyzed by organochromium(III) complexes to produce the important monomer, 2-hydroxyethyl acrylate (**HEA**). In batch reactors, this reaction typically occurs as a three-phase reaction, requiring long reaction times to achieve significant

conversion. However, by employing SFMT reactors, a homogenous mixture could be achieved through fast mixing of **EO** and **AA** under elevated temperature and pressure, significantly reducing the reaction time and making it a highly efficient platform for investigating the reaction kinetics. To gain a deeper understanding of the reaction kinetics, a reduced kinetic model based on a simplified reaction network with the utilization of parallel SFMT reactors was proposed (Fig. 12). The model showed good calibration results and effectively described the experimental data, demonstrating its strong predictive ability for the continuous synthesis of **HEA**. Furthermore, the study compared four types of organochromium catalysts (chromium(III) acetate, chromium(III) 2-ethylhexanoate, chromium(III) picolinate, and chromium(III) acetylacetonate) for their catalytic features. It was found that the catalytic activity and selectivity depended strongly on the chelating ability and steric
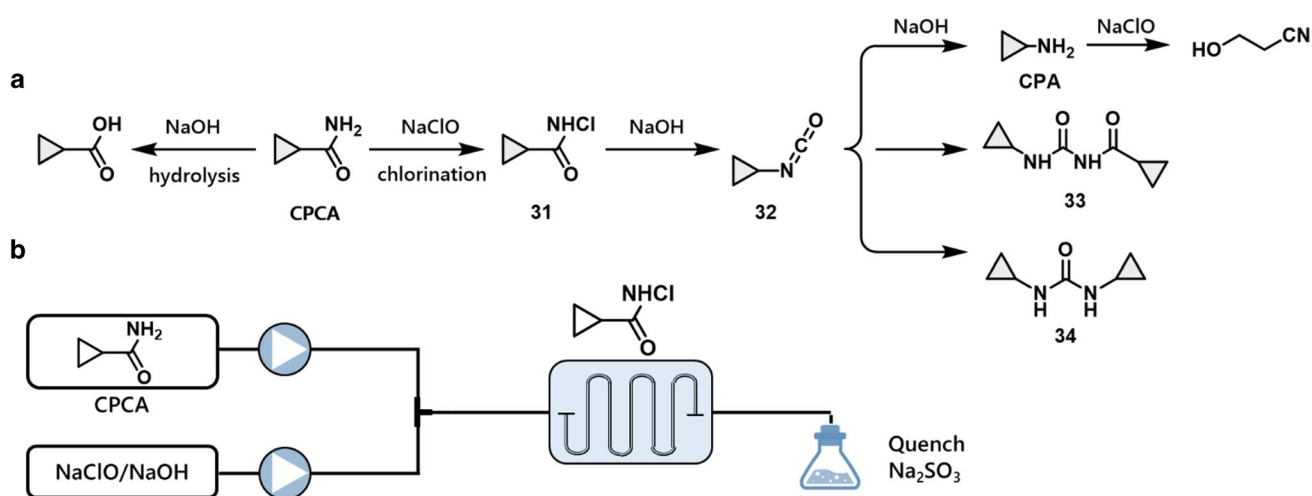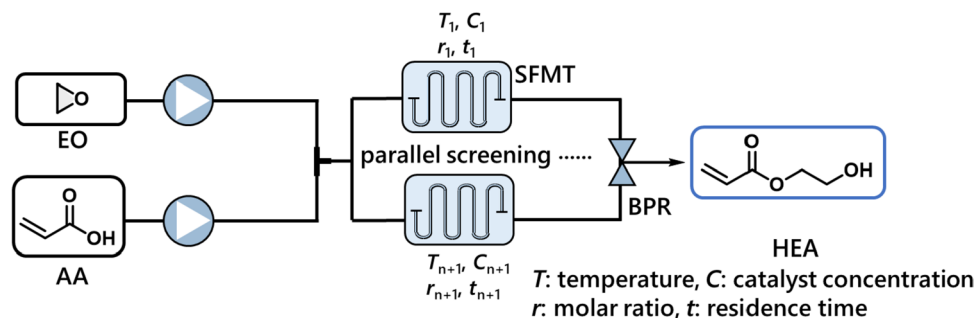
Fig. 10 Hofmann rearrangement of **CPCA** to generate **CPA** and its schematic of the SFMT system. **a** Reaction pathway and possible by-products. **b** Set-up of the SFMT system
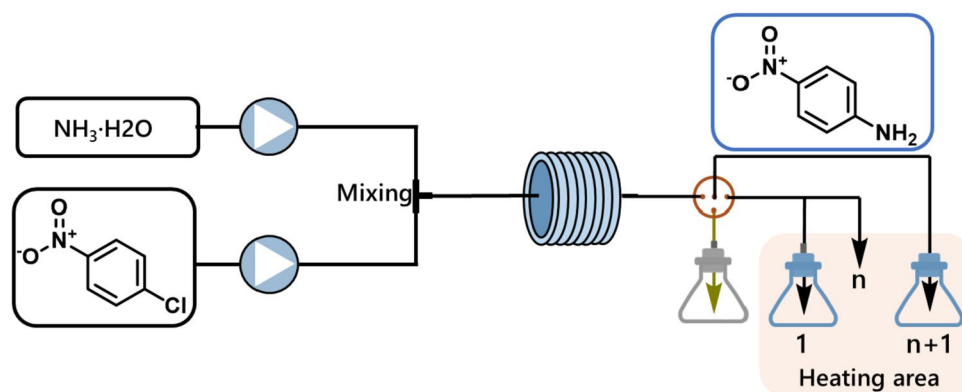
Fig. 11 The synthetic route of Meyer reaction and Nef reaction
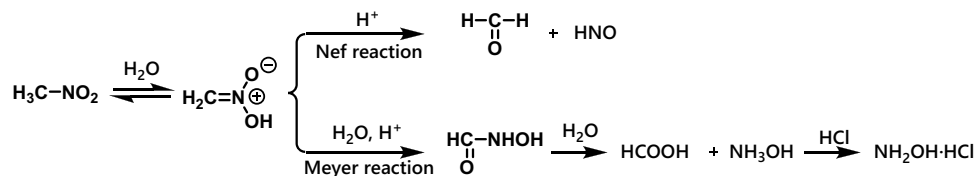
Fig. 12 Parallel screening of reaction conditions based on SFMT

Fig. 13 Set-up of modified SFMT reported by Lu's group

hindrance of the ligand. A high-efficiency catalyst might contain a ligand (or support) with weak interaction with the Cr metal center and considerable steric hindrance.

To enhance the efficiency and safety of the amination reaction of 4-nitrochlorobenzene (**PNA**), a modified SFMT reactor was introduced by Lu and coworkers (Fig. 13) [28]. In this modified setup, continuous feeding of reactants during experiments facilitated the collection of samples with varying residence times by shifting the multiway valve. The process involved collecting the sample with the longest residence time first and then shifting the multi-way valve to direct the effluent to a waste bottle for a specific time interval before returning to collect the second sample. Since the temperature and pressure in the sampling kettle and the entire reaction system remained constant, the collection bottles could be treated as non-stirring reactors until the sampling kettle was moved out of the oven and cooled. Thus, by carefully choosing the entry times of the effluent into the multiple collection bottles, the reaction situation at different reaction times can be observed under steady-state conditions in a single experiment. Besides, this study found consistent results when comparing the typical SFMT and modified SFMT systems, affirming that the modified method accurately reflected the actual flow reaction. Subsequently, reaction conditions (reaction temperature, residence time, ammonia usage, and concentration) were easily screened, and a cost-effective kinetic model was developed. Based on these data, a self-circulation strategy was proposed and verified to reduce the burden of ammonia separation and recovery in a continuous tubular reactor system. This strategy achieved 99% product purity within 2.5 h at a cycle ratio of 90%, showcasing its practical effectiveness.

Conclusion

In summary, the SFMT system is a groundbreaking and versatile technology that enhances efficiency, selectivity, and scalability in various chemical reactions compared to traditional batch reactors. The advantages of SFMT lie in its handling of gaseous reagents, precise reaction control, and facilitation of parallel screening, making it invaluable for reaction optimization and discovery. And SFMT proved to be an efficient platform to study the inherent kinetic characteristics of some industrial process in order to improve the production efficiency. Overall, this significant advancement is hoped to accelerate the development of novel fine compounds and practical chemical synthesis.

Declarations

Conflict of interest Authors have no conflict of interest to declare.

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