Organic Synthesis on Electrowetting-On-Dielectric Digital Microfluidic Device

Novelty / Progress Claim(s)

This paper presents the microfluidic synthetic reaction of organic chemistry using an electrowetting-on-dielectric (EWOD) digital microfluidic (DMF) device. EWOD platform has been used in various applications involving aqueous solutions, hence its fluidic functionalities (e.g., transporting, merging, splitting, and dispensing) of aqueous solutions have been broadly studied. However, chemical synthesis usually requires non-aqueous solvents and they are known to be non-movable in EWOD device. Operating organic fluids in EWOD platform has not been reported yet. Therefore, in this paper, we introduce a novel technique of "engine-and-cargo" that enables the use of non-movable fluids in EWOD DMF device. We selected esterification as the model reaction and demonstrated on-chip characterization and optimization of the organic chemistry reaction.

Background / State of the Art

Integrating the micro systems into the synthetic chemistry has been initiated by establishing continuous flow systems and a range of chemical reactions have been performed. Suzuki coupling, Witting reaction and nitration of benzene are the examples of synthesis carried out in micro channels [1]. Despite the advantages, micro channels suffer from several limitations such as obstruction of the channels, the difficulty of maintaining a constant hydrodynamic pressure, and dependency of flow rates on channel cross-sectional area, which causes unwanted diffusion. EWOD DMF is an alternative to the microchannel reactors because it eliminates the need of mechanical pumps and valves, prevents cross-mixing and inhibits dispersion due to diffusion, and brings the feasibility of performing multistep reactions and synchronize synthesis [2]. However, EWOD has been favorable only to aqueous solutions due to the electrowetting properties of these liquids. There are many applications in which the necessity of using non-movable fluids is undeniable. For example, phenol is used in DNA isolation protocols, but phenol is completely non-movable in an EWOD device. A system of engine-and-cargo will enable the use of non-movable fluids in a typical EWOD without any modification of device architectures. This will provide ways to process biological and chemical protocols on an EWOD device.

Description of the New Method or System

Engine-and-cargo system is a compound droplet system of two immiscible fluids. An engine refers to the fluid that has the electrowetting properties. In this study, we used an ionic liquid, [bmim]PF_6; a cargo is the one without electrowetting properties and it is non-movable in a typical EWOD device. The motion of an engine droplet by electrowetting operation leads motion of an entire compound droplet, thus fluidic functionalities of cargo droplet, too. Fig.1 shows the sequence of generation of a system of engine-and-cargo from the reservoir. Fig. 2(a) confirms the use of the engine did not interfere the esterification reaction. Fig. 2(b) shows the good consistency in volume of dispensed cargo droplets. Therefore, with engine-and-cargo approach, EWOD devices are capable of hosting any organic synthesis. As a case study, we selected the esterification reaction (Fig. 3).

Experimental Results

Menthol, trimethylamine and DMAP were dissolved into toluene to form the cargo fluid. Acetic anhydride separately dispensed from the reservoir to participate with the engine-and-cargo and proceed the reaction. For the kinetic characterization study (Fig. 4), the reaction was quenched at different times. In the case of catalyst loading optimization study (Fig. 5), different concentrations of catalyst were participated in the reaction. Fig. 6 shows the GC-MS results of droplets quenched at five different times. As shown, the conversion from the starting materials to the products increases over the time until 60 s after which trimethylamine evaporated and consequently the reaction did not proceed further. It is evident from Fig. 7 that more concentration of catalyst results in a higher yield the reaction.

Word count: 575

References

[1] Fletcher, P. D., *Tetrahedron*, *58*(24), 4735-4757.
[2] Kim, H. K., *Miniaturized Systems for Chemistry and Life Sciences (μTAS)* (pp. 617-619).

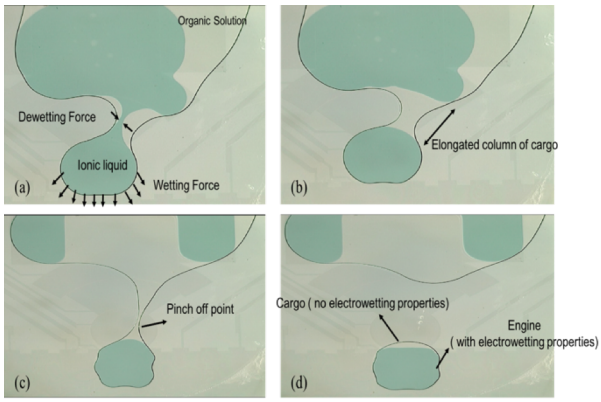


Figure 1: A sequence of generation of a system of engine-and-cargo from the reservoir. The EWOD force generated by the engine forms the elongated column of cargo, Fig. 1(c), and thereby, due to the hydrodynamic instability neck forms and eventually pinch off occurs, Fig. 1(d).

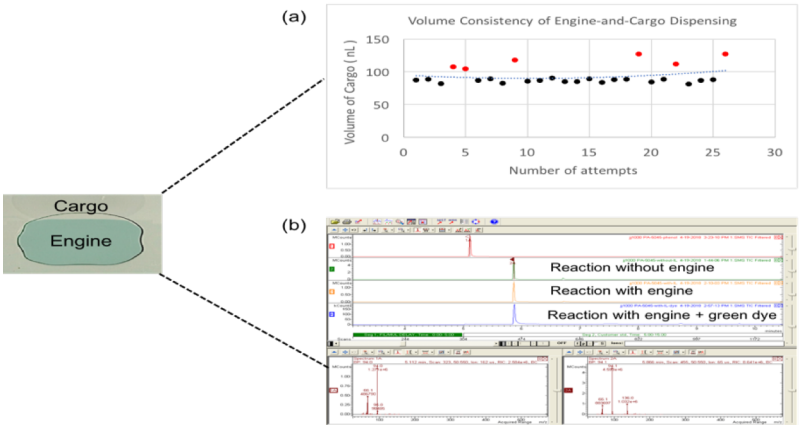


Figure 2: (a): good performance in volume consistency and accuracy where excluding the red dots the inconsistency is ±3%. It has shown a trend in which almost after 3 times dispensing an engine-and-cargo (black dots), the fourth one (red dots) should be discarded. (b) GC-MS confirmed the use of the engine (ionic liquid) did not interfere the Esterification reaction.

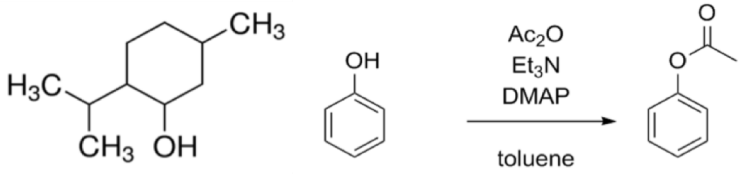


Figure 3: Participating Menthol, Acetic Anhydride, Trimethylamine and DMAP in the presence of Toluene as solvent.5 moles of Menthol, 10 moles of Trimethylamine along with 0.5% of DMAP were dissolved into 1mLToluene. Also, 10 moles of Acetic anhydride were dissolved in Toluene, and located at the designated reservoir.

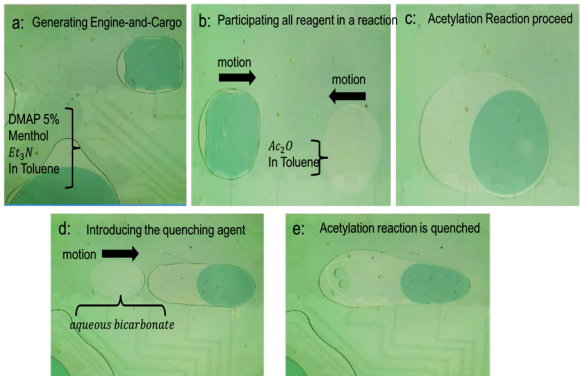


Figure 4: Steps of acylation of menthol on an EWOD. For the kinetic study, the reaction was quenched after the different times (10s, 15s, 30s, 45s, and 60s). The quenching agent is bicarbonate.

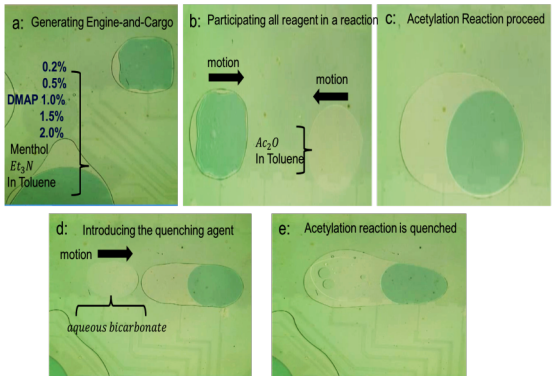


Figure 5: Steps of acylation of menthol on an EWOD. Four different catalyst percentages (0.2%, 0.5%, and 1.0%, and 1.5%) have been tested to demonstrate catalyst loading optimization.

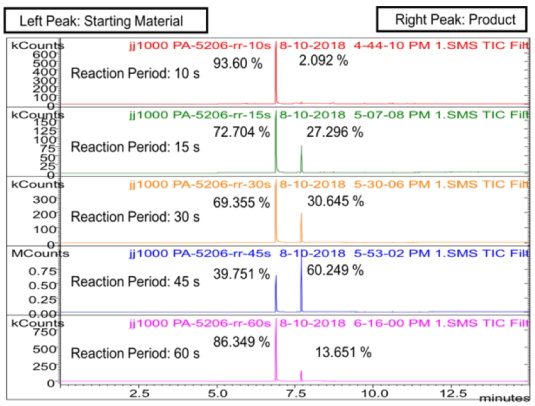


Figure 6: GC-MS of sample products quenched at five different times. As shown, the conversion from the starting materials to the products increases over the time until 60 s after which trimethylamine evaporated and consequently the reaction did not proceed further.

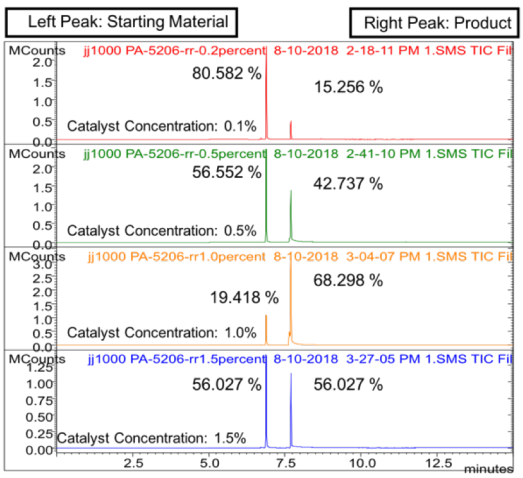


Figure 7: The progress of the mass spectroscopy (GC-MS) of different concentration of Catalyst (DMAP. It is evident that more concentration of catalyst results in a higher yield the reaction.