Supporting Information for

## Efficient Passerini reactions in an aqueous vesicle system

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## Synthesis of *N*-(4-methoxybenzyl)formamide:

Reaction conditions: 4-methoxybenzylamine (30 mmol; 3.8 ml) and ethyl formate (12.5 ml) were heated under reflux overnight. After cooling the reaction mixture to room temperature, 5 ml hexane were added. The precipitate was filtered and washed with hexane. Yield 78 % (3.86 g).



Figure 1 <sup>1</sup>H NMR spectrum of *N*-(4-methoxybenzyl)formamide (200 MHz, CDCl<sub>3</sub>).

## Synthesis of *p*-methoxybenzylisocyanide (3a):

Reaction conditions: To a solution of *N*-(4-methoxybenzyl)formamide (16 mmol; 2.64 g) and triethylamine (48 mmol; 6.7 ml) in dry dichloromethane (20 ml) at -78°C phosphoryl oxychloride (20 mmol; 1.85 ml) was added dropwise. After 1 h of stirring at room temperature, the reaction mixture was quenched by adding a saturated solution of NaHCO<sub>3</sub> (20 mL), then extracted with dichloromethane (2×20 mL). The combined organic layers were dried with MgSO<sub>4</sub> and residuals of solvent were distilled under reduced pressure. The crude product was purified by column chromatography on silica gel using hexane/AcOEt as an eluent. Yield 80 % (1.88 g).



Figure 2 <sup>1</sup>H NMR spectrum of compound 3a (200 MHz, CDCl<sub>3</sub>).

Appearance of the aqueous Passerini multicomponent reaction samples containing DODAB



**Figure 3** Photographic images of the Passerini multicomponent reaction samples (reaction with benzoic acid **1b** (0.2 mmol), dodecyl aldehyde **2a** (0.2 mmol) and *p*-methoxybenzyl isocyanide **3a** (0.2 mmol)) in PBS (2 mL), with the addition of DODAB (0.04 mmol), 25 °C.

Left: milky suspension of DODAB in PBS after 10 minutes of stirring with a magnetic stirrer.

Middle: Reaction mixture 5 minutes after adding the starting materials.

Right: Reaction mixture after 24 h; product precipitation which occurs is not seen on the image.





Figure 4<sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4a (400 MHz, CDCl<sub>3</sub>).



Figure 5 <sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4b (400 MHz, CDCl<sub>3</sub>).

Figure 6 <sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4c (400 MHz, CDCl<sub>3</sub>).





Figure 7<sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4d (400 MHz, CDCl<sub>3</sub>).



Figure 8<sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4e (400 MHz, CDCl<sub>3</sub>).



Figure 9 <sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4f (400 MHz, CDCl<sub>3</sub>).



Figure 10 <sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4g (400 MHz, CDCl<sub>3</sub>).



Figure 11 <sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4h (400 MHz, CDCl<sub>3</sub>).



Figure 12 <sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4i (400 MHz, CDCl<sub>3</sub>).



Figure 13 <sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4j (400 MHz, CDCl<sub>3</sub>).

Figure 14<sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4k (400 MHz, CDCl<sub>3</sub>).



Figure 15 <sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4I (400 MHz, CDCl<sub>3</sub>).



Figure 16<sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4m (400 MHz, CDCl<sub>3</sub>).



Figure 17<sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4n (400 MHz, CDCl<sub>3</sub>).



Figure 18<sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 40 (400 MHz, CDCl<sub>3</sub>).



Figure 19<sup>1</sup>H NMR (above) and <sup>13</sup>C NMR (below) spectra of compound 4p (400 MHz, CDCl<sub>3</sub>).