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Ultra-low Formation of Octahydrophenazine in Beckmann Rearrangement of Cyclohexanone Oxime using a Microreactor

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1. Eliminating the effect of mixing

1.1 Experiment

Figure S1 shows the experiment setup for the measurement of the reaction conversion. Different from the setup in Figure 1, another metering pump that delivered water was used to terminate the reaction together with a ice-water bath. The other adopted devices were as same as Figure 1. Different lengths of delay loops were employed to control the residence time at different flow rates. In order to decrease the temperature rise, 90% amount of the desired cyclohexanone oxime (CHO) was replaced by caprolactam (CPL).

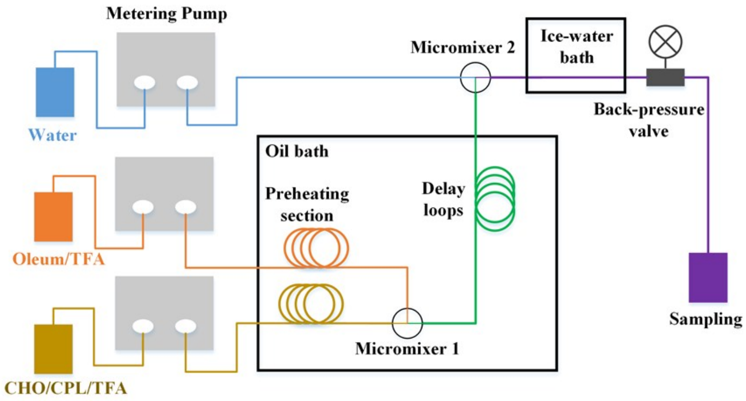

Figure S1. Schematic overview of the experimental setup

0.25 g of the obtained sample was analyzed as following: firstly, the pH was adjusted to 7 by 10 M NaOH solution and then it was extracted by 2 mL dichloromethane. The organic phase was analyzed by GC with the same method. The conversion was calculated by Eq. S1 based on the amount of CHO.

$$X_{\mathrm{CHO}}(\%) = (1 - \frac{m_{\mathrm{CHO}}}{m_{\mathrm{CHO0}}}) \times 100 \tag{S1}$$

1.2 Results and discussion

The mixing performance of adopted T-type micromixer has been described in our previous study[1] and the segregation indexes, X_S, were found in the range of 10^{-2} to 10^{-3}. In order to guarantee the adequate mixing, we investigated the effect of flow rates on the reaction conversion, as outlined in Figure S2. The conversion of CHO increased with the increase of the volume flow rate (Q_C) at low range (< 5 mL/min) and tended to be constant with Q_C larger than 5 mL/min. Thus, Q_C was set at > 7.5 mL/min for further experiments to decrease the effect of mixing.

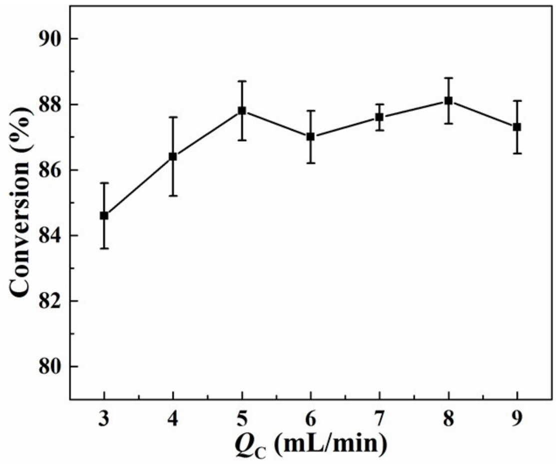

Figure S2. Effect of volume flow rate on the reaction conversion at 30 s. Run conditions: T= 80 °C, T/A ratio: 7.5, A/O ratio: 1.0, SO_3 mass fraction: 10%, D(TFA): 0.2. Q_C: volume flow rate of continuous fluid.

2. Comparison of different bases in the neutralization step

2.1 Materials

Calcium hydroxide (>95%) was purchased from Sinopharm Chemical Reagent Co., Ltd, and dimethylamine (AR, 40wt.% in H_2O) was purchased from Aladdin Industrial Corporation.

2.2 Results and discussion

Calcium hydroxide ($Ca(OH)_2$) and dimethylamine (DMA), were chosen as the typical inorganic and organic bases. The results were shown in Table 1. For the inorganic bases (entries 2&3), the contents of OHP and other two light impurities (2-CYO and 2-HCO) were similar. The content of OHP neutralized by DMA (entry 4) was similar to the inorganic bases but much lower than ammonia (entry 1), verifying that OHP, which was produced in the neutralization process, was mainly due to the using of NH_3. However, the contents of light impurities obtained by DMA were higher than NH_3 (entry 1) but lower than NaOH and $Ca(OH)_2$ (entries 2&3), which was mainly due to the reaction between DMA and reaction intermediates. The difference between DMA and NH_3 may be due to the different reaction activity. Although the reaction products failed to be isolated by GC, the trends that light impurities decreased neutralized by DMA compared to inorganic bases also confirmed the reaction between reaction intermediates and the neutralization reagent.

Table 1. Effect of different bases in the neutralization process on the OHP content. Run conditions of the reaction: Temperature: 80 °C, SO_3 mass fraction: 10%, T/A ratio: 7.5, A/O ratio: 0.8, D(TFA): 0.2. The pH value in the neutralization: 7.0.

Entry	Base	2-CYO (%)	2-HCO (%)	OHP (ppm)
1	Ammonia	0.021	0.028	142
2	10 mol/L NaOH	0.12	0.091	57
3	$Ca(OH)_2$[a]	0.11	0.087	58
4	Dimethylamine	0.064	0.054	54

[a] The corresponding amount of water was calculated by entry 2 based on the concentration of OH^-

and pre-added in the liquid product. $Ca(OH)_2$ was then added as solid.

References

1. J. S. Zhang, K. Wang, Y. C. Lu and G. S. Luo, *Chem. Eng. Process*, 2010, 49, 740-747.