

Supporting Information

Fully Continuous Flow Synthesis of 5-(Aminomethyl)-2-methylpyrimidin-4-amine: A Key Intermediate of Vitamin B₁

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S1. Continuous flow synthesis of 2-(dimethylaminomethylidene)propanedinitrile (4) in a Protrix microchannel reactor

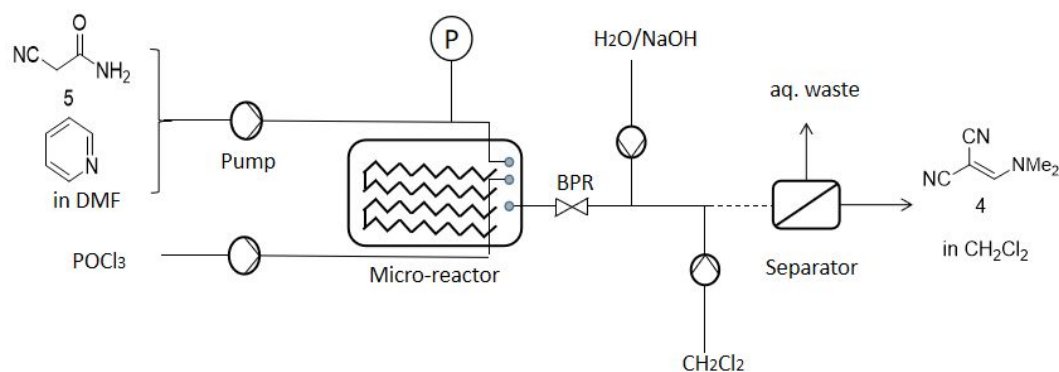


Figure S1. Continuous flow synthesis of compound 4 using a Protrix microchannel reactor

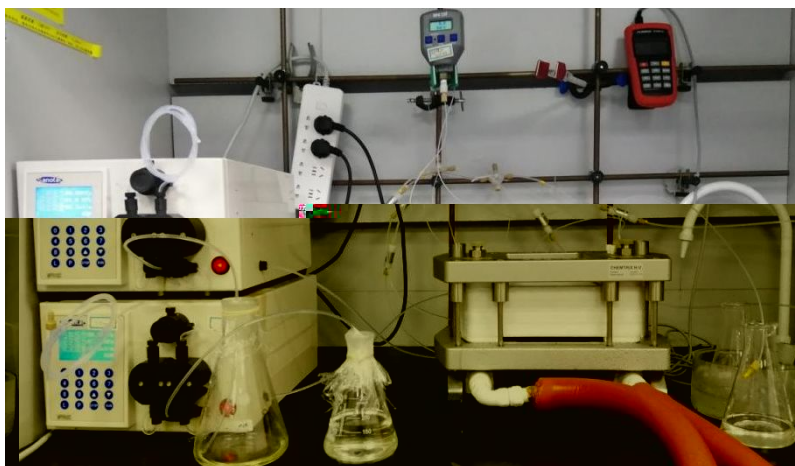


Figure S2. Continuous flow synthesis set- up for compound **4** in a Protix microchannel reactor

Table S1. Effects of temperature and reaction time on reaction conversion

| Entry | Volume (ml) | Residence time (min) | Temperature (°C) | Conversion (%) | Yield (%) |
|-------|-------------|----------------------|------------------|----------------|-----------|
| 1 | 12.6 | 30 | -10 | 84 | / |
| 2 | 12.6 | 30 | -5 | 86 | / |
| 5 | 12.6 | 30 | 0 | 89 | / |
| 6 | 12.6 | 30 | 5 | 88 | / |
| 7 | 12.6 | 30 | 10 | 90 | / |
| 8 | 12.6 | 30 | 15 | 85 | / |
| 9 | 12.6 | 30 | 20 | 88 | / |
| 10 | 12.6 | 30 | 25 | 92 | 78 |
| 11 | 12.6 | 20 | 10 | 78 | / |
| 12 | 12.6 | 20 | 20 | 85 | 72 |
| 13 | 12.6 | 60 | 10 | 91 | 62 |

S2. Clogging in the flow synthesis of 4-amino-2-methylpyrimidine-5-carbonitrile (3)

in a Coflore ACR



Figure S3. Clogging in ACR

S3. Products from 3 single step continuous flow synthesis

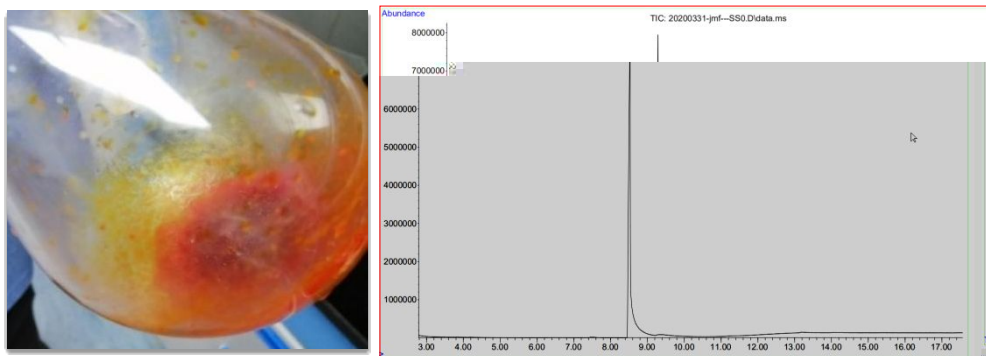


Figure S4. 2-(dimethylaminomethylidene)propanedinitrile (4) generated by continuous flow synthesis in the microchannel coil reactor

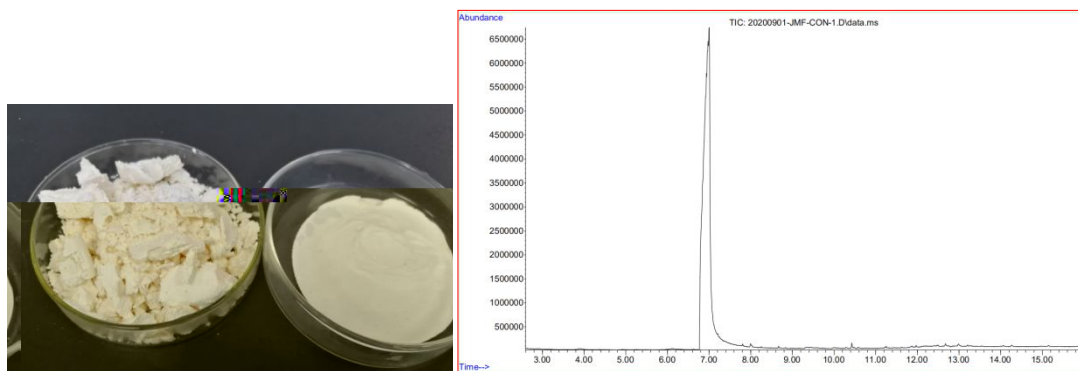


Figure S5. 4-amino-2-methylpyrimidine-5-carbonitrile (**3**) generated by continuous flow synthesis in the ACR

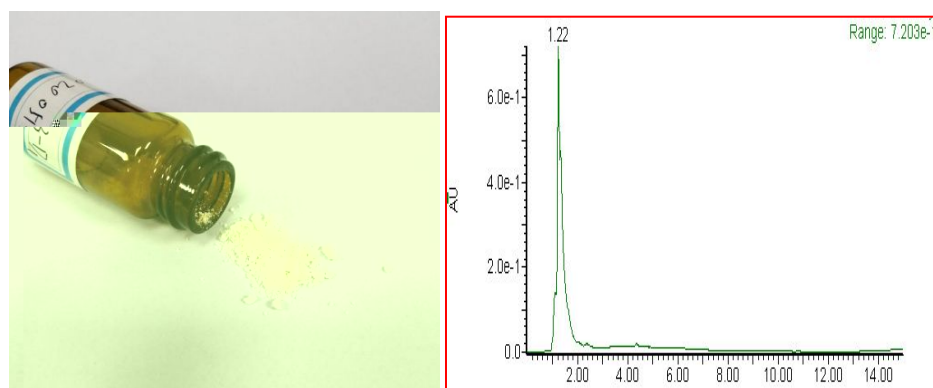


Figure S6. 5-(Aminomethyl)-2-methylpyrimidin-4-amine(**2**) generated by continuous flow synthesis in the fixed-bed reactor

S4. Continuous extraction using a CINC Model-continuous Inline extractor

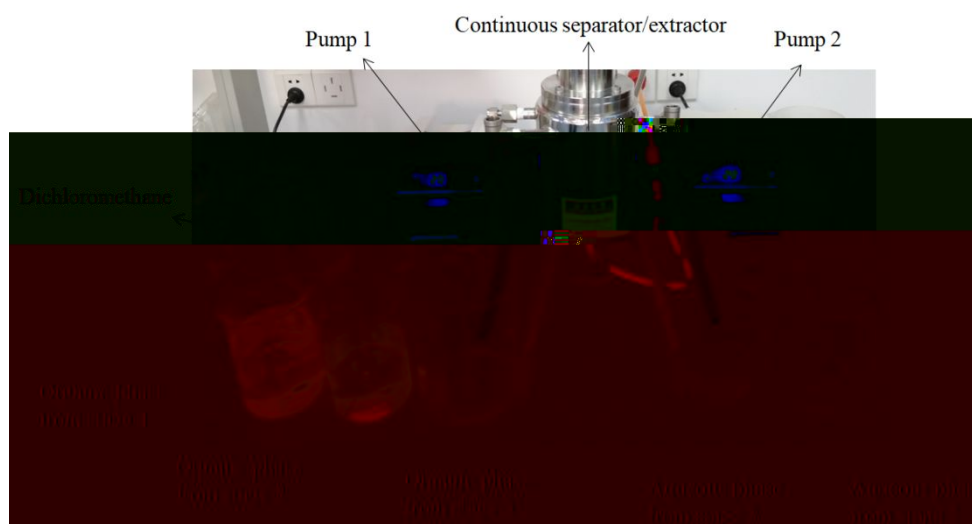


Figure S7. Continuous extraction using a continuous inline extractor by CINC Deutschland GMBH and Co.