Electronic Supplementary Material (ESI) for Polymer Chemistry.


# Supporting Information

# Efficiency Assessment on Single Unit Monomer Insertion Reactions for Monomer Sequence Control: Kinetic Simulations and Experimental Observations

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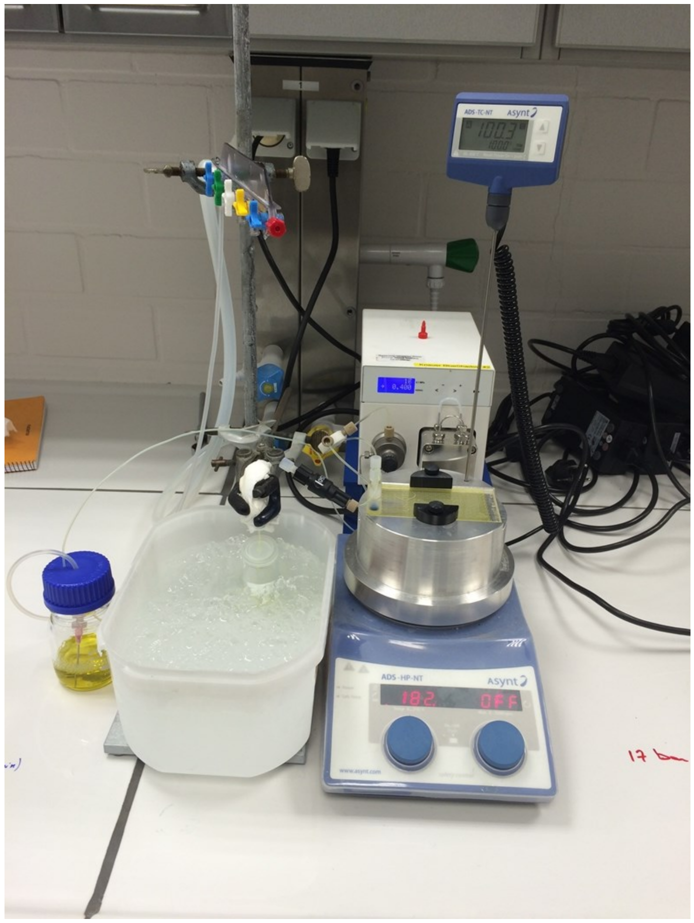



**Figure S1.** Image of the mesoreactor setup utilized for the upscaled SUMI synthesis.

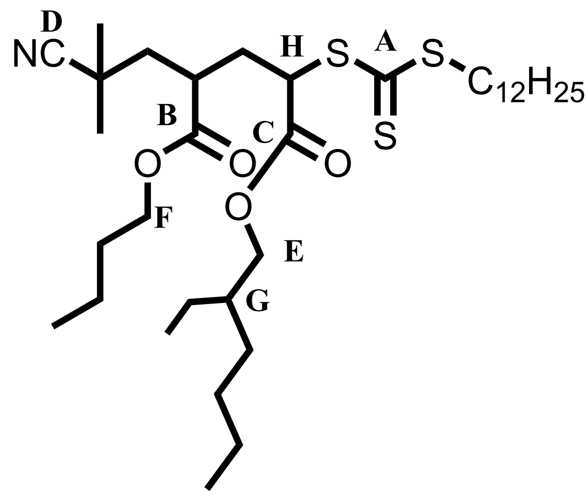



**Figure S2**. [13]CNMR peak assignments of the SUMI-2AB product (see Figure S3, S4 and S5).

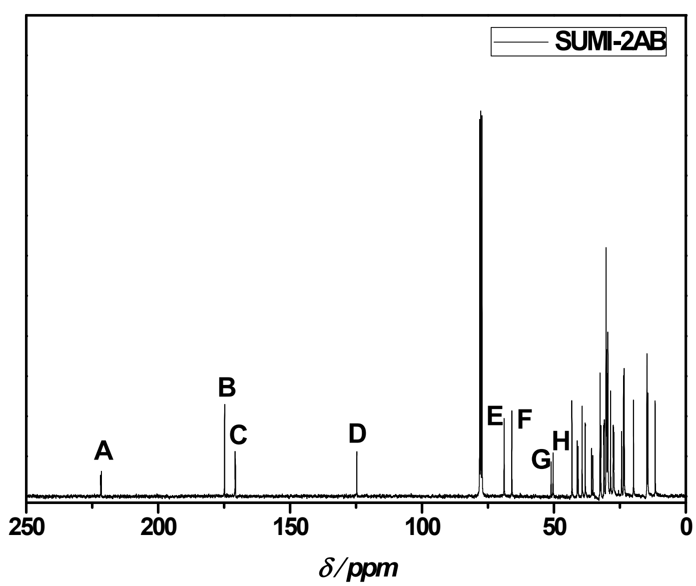



**Figure S3**. $^{13}$C NMR spectrum of **SUMI-2AB** (*n*BA-EHA oligo-RAFT agent).

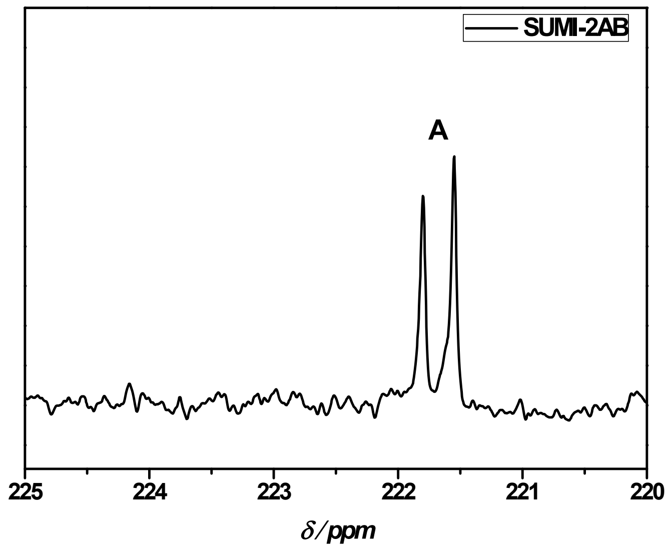



**Figure S4**. Zoom into $^{13}$C NMR spectrum of **SUMI-2AB** (*n*BA-EHA oligo-RAFT agent), The two peaks can be assigned to different diastereomers.

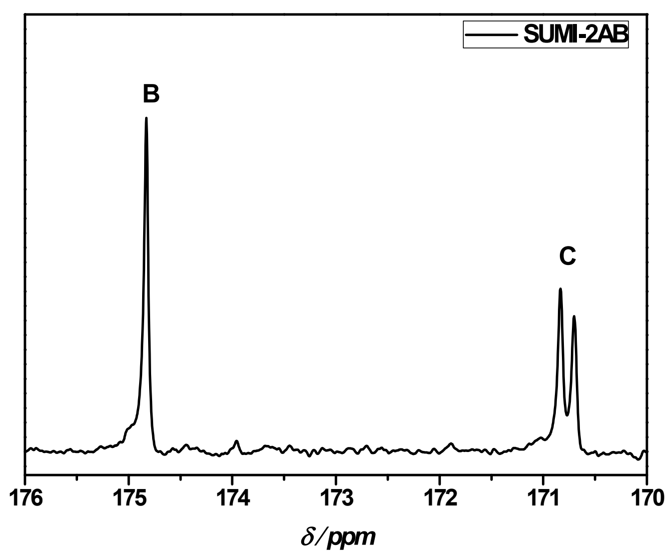



**Figure S5**. Zoom into $^{13}$C NMR spectrum of **SUMI-2AB** (*n*BA-EHA oligo-RAFT agent), the two peaks (C) can be assigned to different diastereomers.

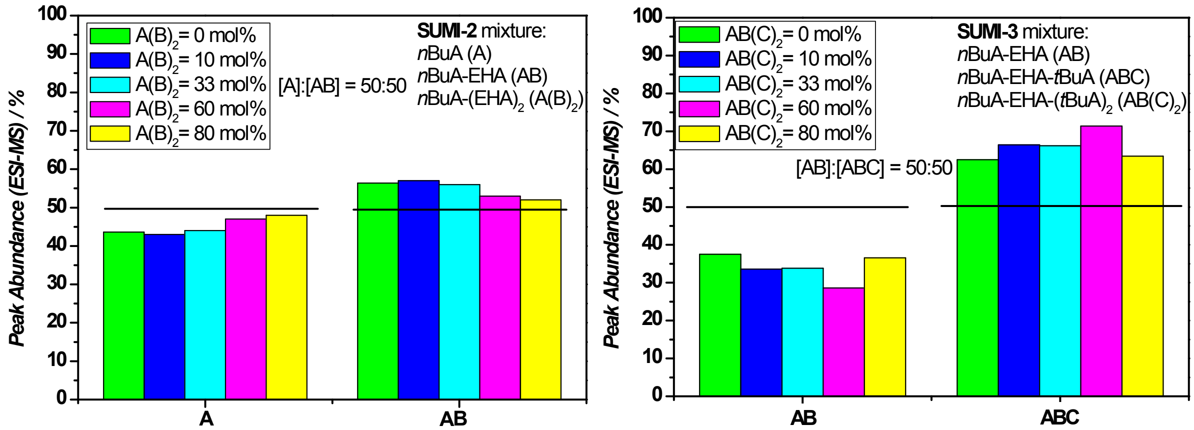



**Figure S6**. Left: ESI-MS peak abundance of A and AB for a constant A:AB molar ratio in the **SUMI-2** calibration mixture while the moles of A(B)$_2$ are varied. Right: ESI-MS peak abundance of AB and ABC for a constant AB:ABC molar ratio in the **SUMI-3** calibration mixture while mol% AB(C)$_2$ is varied.

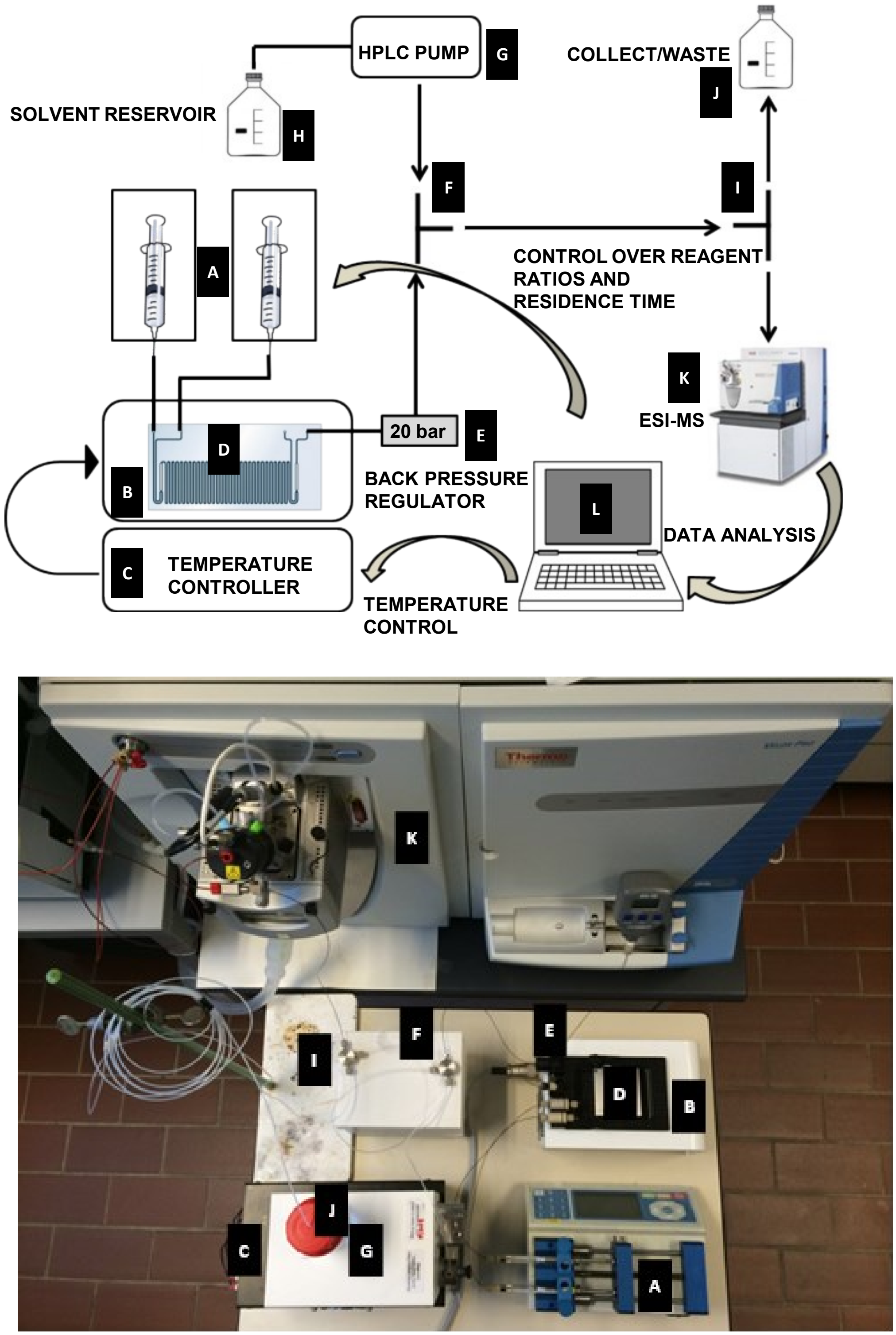



**Figure S7.** Representation of a flow chart of the on-line setup (top) and image of the on-line setup (bottom).

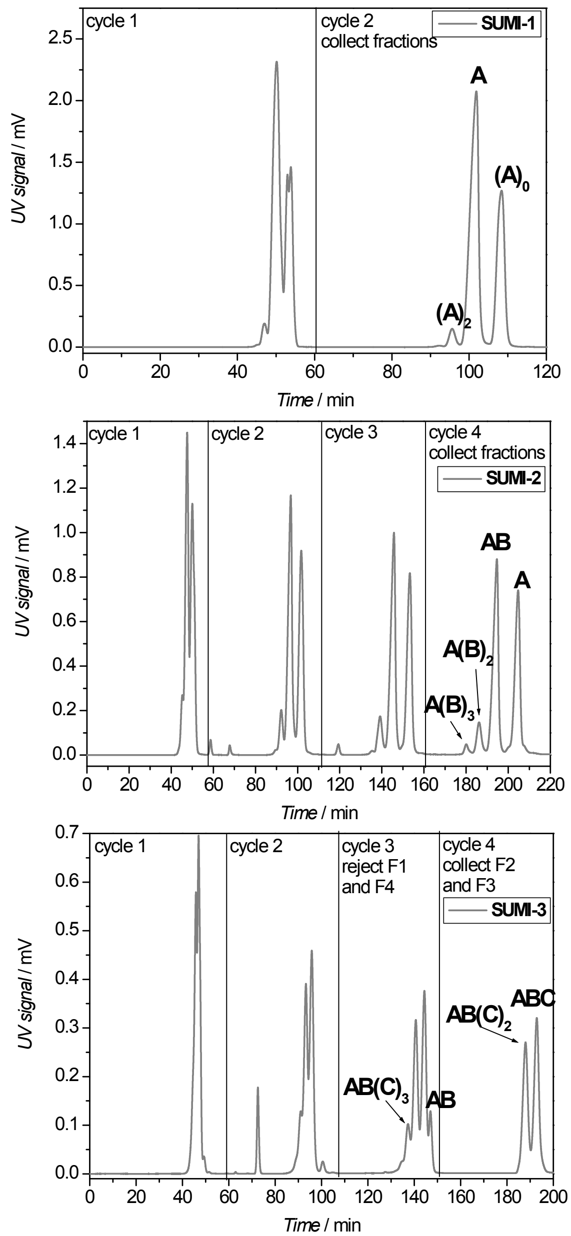
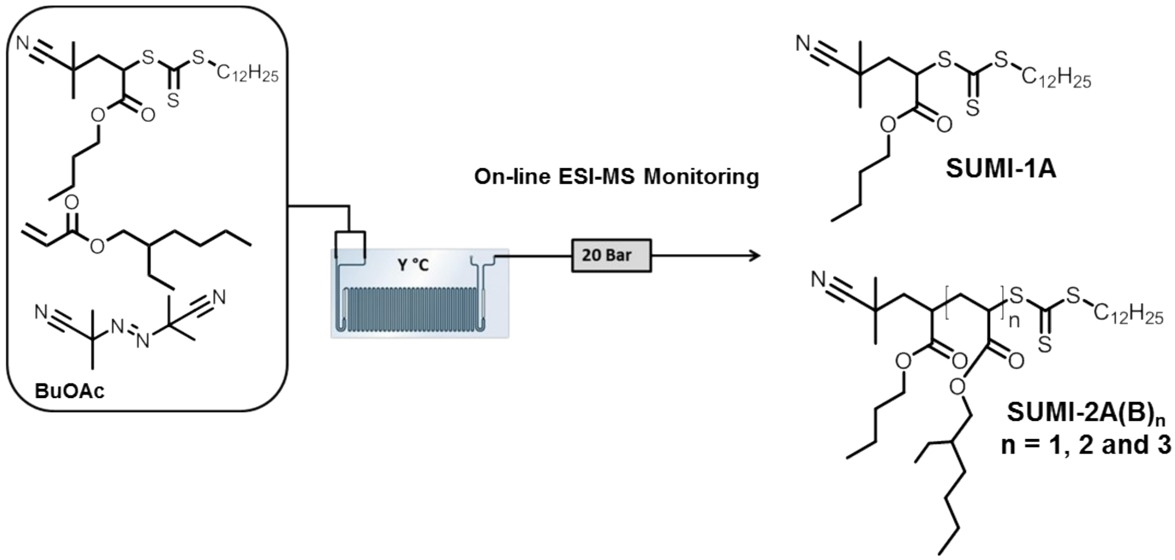



**Figure S8.** Recycling SEC trace recorded during consecutive purification cycles of **SUMI-1**, **SUMI-2** and **SUMI-3**. (data partially previously published in [2])




**Scheme S1.** Schematic representation of the reaction products for the microreactor synthesis of **SUMI-2.** (previously published in [1])

**Table S1.** Microreactor screening conditions and ESI-MS peak abundances for the synthesis of **SUMI-2AB**. (previously published in [1])

| Condition | Temp. (°C) | [EHA] : [**SUMI-1A**] | Residence Time (min) | A (%) | AB (%) | $A(B)_2$ (%) | $A(B)_3$ (%) |
|---|---|---|---|---|---|---|---|
| 1 | 95 | 5:1 | 10 | 50 | 38 | 10 | 2 |
| 2 | 95 | 10:1 | 5 | 41 | 50 | 9 | 0 |
| 3 | 95 | 10:1 | 7,5 | 11 | 58 | 27 | 4 |
| 4 | 100 | 1:1 | 5 | 70 | 30 | 0 | 0 |
| 5 | 100 | 2:1 | 5 | 47 | 49 | 4 | 0 |
| 6 | 100 | 2:1 | 10 | 22 | 62 | 16 | 0 |
| 7 | 100 | 3:1 | 8 | 9 | 61 | 27 | 3 |
| 8 | 100 | 4:1 | 6 | 12 | 60 | 25 | 3 |
| 9 | 100 | 5:1 | 2,5 | 40 | 54 | 6 | 0 |
| 10 | 100 | 5:1 | 4 | 16 | 62 | 20 | 2 |
| **11** | **100** | **5:1** | **5** | **9** | **61** | **26** | **4** |
| 12 | 110 | 3:1 | 2,5 | 19 | 65 | 16 | 0 |
| 13 | 110 | 3:1 | 4 | 9 | 68 | 19 | 4 |
| 14 | 110 | 2:1 | 4 | 28 | 61 | 11 | 0 |
| 15 | 110 | 2:1 | 5 | 20 | 64 | 16 | 0 |

**Table S2.** Microreactor screening conditions and molar ratios of all insertion products for the synthesis of **SUMI-2AB**.* (primary experimental results previously published in [1])

| Condition | Temp. (°C) | [EHA] : [**SUMI-1A**] | Residence Time (min) | A (%) | AB (%) | $A(B)_2$ (%) | $A(B)_3$ (%) |
|---|---|---|---|---|---|---|---|
| 1 | 95 | 5:1 | 10 | 57 | 31 | 10 | 2 |
| 2 | 95 | 10:1 | 5 | 48 | 43 | 9 | 0 |
| 3 | 95 | 10:1 | 7,5 | 13 | 56 | 27 | 4 |
| 4 | 100 | 1:1 | 5 | 78 | 22 | 0 | 0 |
| 5 | 100 | 2:1 | 5 | 56 | 40 | 4 | 0 |
| 6 | 100 | 2:1 | 10 | 27 | 57 | 16 | 0 |
| 7 | 100 | 3:1 | 8 | 11 | 59 | 27 | 3 |
| 8 | 100 | 4:1 | 6 | 13 | 59 | 25 | 3 |
| 9 | 100 | 5:1 | 2,5 | 48 | 46 | 6 | 0 |
| 10 | 100 | 5:1 | 4 | 20 | 58 | 20 | 2 |
| **11** | **100** | **5:1** | **5** | **11** | **59** | **26** | **4** |
| 12 | 110 | 3:1 | 2,5 | 24 | 60 | 16 | 0 |
| 13 | 110 | 3:1 | 4 | 11 | 66 | 19 | 4 |
| 14 | 110 | 2:1 | 4 | 35 | 54 | 11 | 0 |
| 15 | 110 | 2:1 | 5 | 24 | 60 | 16 | 0 |

* It is assumed that peak abundances of $A(B)_2$ and $A(B)_3$ match the true molar ratio.

**Table S3**. Theoretical and isolated yields for **SUMI2** and **SUMI3** products, synthesized with different setups. (part of experimental results already previously published in [1] and [2])

| Setup | Desired SUMI | Theoretical Yield (%) | Isolated Yield (%) |
|---|---|---|---|
| Batch | SUMI-2AB | 50 | 46 |
| Batch | SUMI-3ABC | 30 | 20 |
| Batch | SUMI-2AC | n.a. | 50 |
| Batch | SUMI-3ACB | n.a. | 20 |
| Microflow | SUMI-2AB | 59 | 43 |
| Microflow | SUMI-3ABC | 34 | n.a. |
| Mesoflow | SUMI-2AB | 53 | 48 |
| Mesoflow | SUMI-3ABC | 22 | 20 |

## Overview Predici model

***Coefficients (CL-independent model)***

| | |
|---|---|
| $k_t$ | $1\cdot10^9$ L·mol$^{-1}$·s$^{-1}$ |
| $k_d$ | $A$ = 1.580e+15 s$^{-1}$; $E_A$/R = 1.551e+04 J/mol |
| $k_{p1}$ | $7\cdot10^4$ L·mol$^{-1}$·s$^{-1}$ |
| $k_{p2}$ | $7\cdot10^4$ L·mol$^{-1}$·s$^{-1}$ |
| $k_{p3}$ | $7\cdot10^4$ L·mol$^{-1}$·s$^{-1}$ |
| $k_{ad1}$ | $7\cdot10^6$ L·mol$^{-1}$·s$^{-1}$ |
| $k_{ad2}$ | $7\cdot10^6$ L·mol$^{-1}$·s$^{-1}$ |
| $k_{ad3}$ | $7\cdot10^6$ L·mol$^{-1}$·s$^{-1}$ |
| $k_{ad4}$ | $7\cdot10^6$ L·mol$^{-1}$·s$^{-1}$ |
| $k_{frag1}$ | $7\cdot10^3$ s$^{-1}$ |
| $k_{frag2}$ | $7\cdot10^3$ s$^{-1}$ |
| $k_{frag3}$ | $7\cdot10^3$ s$^{-1}$ |
| $k_{frag4}$ | $7\cdot10^3$ s$^{-1}$ |
| $k_{p1ini}$ | $7\cdot10^4$ L·mol$^{-1}$·s$^{-1}$ |
| $k_{p2ini}$ | $7\cdot10^4$ L·mol$^{-1}$·s$^{-1}$ |
| $k_{p3ini}$ | $7\cdot10^4$ L·mol$^{-1}$·s$^{-1}$ |

***Reaction Modules***

**Initiator decomposition**

AIBN ---> I + I , kd

**Propagation**

I + monomer ---> IM , kini

IM + monomer ---> IMM , kp1ini

IMM + monomer ---> IMMM , kp2ini

IMMM + monomer ---> IMMMM , kp3ini

RM + monomer ---> RMM , kp1

RMM + monomer ---> RMMM , kp2

RMMM + monomer ---> RMMMM , kp3

**SUMI-RAFT equilibria**

I + RMTTC ---> INT(ISMR) , kad1

IM + RMTTC ---> INT(ISMR) , kad1

IMM + RMTTC ---> INT(ISMR) , kad2

IMMM + RMTTC ---> INT(ISMR) , kad3

IMMMM + RMTTC ---> INT(ISMR) , kad4

I + RMMTTC ---> INT(ISMMR) , kad2

IM + RMMTTC ---> INT(ISMMR) , kad2

IMM + RMMTTC ---> INT(ISMMR) , kad2

IMMM + RMMTTC ---> INT(ISMMR) , kad3

IMMMM + RMMTTC ---> INT(ISMMR) , kad4

I + RMMMTTC ---> INT(ISMMMR) , kad3

IM + RMMMTTC ---> INT(ISMMMR) , kad3

IMM + RMMMTTC ---> INT(ISMMMR) , kad3

IMMM + RMMMTTC ---> INT(ISMMMR) , kad3

IMMMM + RMMMTTC ---> INT(ISMMMR) , kad4

I + RMMMMTTC ---> INT(ISMMMMR) , kad4

IM + RMMMMTTC ---> INT(ISMMMMR) , kad4

IMM + RMMMMTTC ---> INT(ISMMMMR) , kad4

IMMM + RMMMMTTC ---> INT(ISMMMMR) , kad4

IMMMM + RMMMMTTC ---> INT(ISMMMMR) , kad4

INT(ISMR) ---> RM + Dead , kfrag1

INT(ISMR) ---> RMTTC + Dead , kfrag1

INT(ISMMR) ---> RMM + Dead , kfrag2

INT(ISMMR) ---> RMMTTC + Dead , kfrag2

INT(ISMMMR) ---> RMMM + Dead , kfrag3

INT(ISMMMR) ---> RMMMTTC + Dead , kfrag3

INT(ISMMMMR) ---> RMMMM + Dead , kfrag4

INT(ISMMMMR) ---> RMMMMTTC + Dead , kfrag4

RM + RMTTC ---> INT(RMSMR) , kad1

RMM + RMTTC ---> INT(RMMSMR) , kad2

RMMM + RMTTC ---> INT(RMMMSMR) , kad3

RMMMM + RMTTC ---> INT(RMMMMSMR) , kad4

INT(RMSMR) ---> RM + RMTTC , kfrag1

INT(RMMSMR) ---> RMM + RMTTC , kfrag2

INT(RMMMSMR) ---> RMMM + RMTTC , kfrag3

INT(RMMMMSMR) ---> RMMMM + RMTTC , kfrag4

INT(RMSMR) ---> RMTTC + RM , kfrag1

INT(RMMSMR) ---> RMMTTC + RM , kfrag1

INT(RMMMSMR) ---> RMMMTTC + RM , kfrag1

INT(RMMMMSMR) ---> RMMMMTTC + RM , kfrag1

RM + RMMTTC ---> INT(RMSMMR) , kad2

RMM + RMMTTC ---> INT(RMMSMMR) , kad2

RMMM + RMMTTC ---> INT(RMMMSMMR) , kad3

RMMMM + RMMTTC ---> INT(RMMMMSMMR) , kad4

INT(RMSMMR) ---> RMMTTC + RM , kfrag1

INT(RMMSMMR) ---> RMMTTC + RMM , kfrag2

INT(RMMSMMR) ---> RMM + RMMTTC , kfrag2

INT(RMMMSMMR) ---> RMMTTC + RMMM , kfrag3

INT(RMMMMSMMR) ---> RMMTTC + RMMMM , kfrag4

INT(RMSMMR) ---> RMTTC + RMM , kfrag2

INT(RMMMSMMR) ---> RMMMTTC + RMM , kfrag2

INT(RMMMMSMMR) ---> RMMMMTTC + RMM , kfrag2

RM + RMMMTTC ---> INT(RMSMMMR) , kad3

RMM + RMMMTTC ---> INT(RMMSMMMR) , kad3

RMMM + RMMMTTC ---> INT(RMMMSMMMR) , kad3

RMMMM + RMMMTTC ---> INT(RMMMMSMMMR) , kad4

INT(RMSMMMR) ---> RMMMTTC + RM , kfrag1

INT(RMSMMMR) ---> RMTTC + RMMM , kfrag3

INT(RMMSMMMR) ---> RMMMTTC + RMM , kfrag2

INT(RMMSMMMR) ---> RMMTTC + RMMM , kfrag3

INT(RMMMSMMMR) ---> RMMMTTC + RMMM , kfrag3

INT(RMMMSMMMR) ---> RMMM + RMMMTTC , kfrag3

INT(RMMMMSMMMR) ---> RMMMTTC + RMMMM , kfrag4

INT(RMMMMSMMMR) ---> RMMMMTTC + RMMM , kfrag3

RM + RMMMMTTC ---> INT(RMSMMMMR) , kad4

RMM + RMMMMTTC ---> INT(RMMSMMMMR) , kad4

RMMM + RMMMMTTC ---> INT(RMMMSMMMMR) , kad4

RMMMM + RMMMMTTC ---> INT(RMMMMSMMMMR) , kad4

INT(RMSMMMMR) ---> RMMMMTTC + RM , kfrag1

INT(RMSMMMMR) ---> RMTTC + RMMMM , kfrag4

INT(RMMSMMMMR) ---> RMMMMTTC + RMM , kfrag2

INT(RMMSMMMMR) ---> RMMTTC + RMMMM , kfrag4

INT(RMMMSMMMMR) ---> RMMMTTC + RMMMM , kfrag4

INT(RMMMSMMMMR) ---> RMMMMTTC + RMMM , kfrag3

INT(RMMMMSMMMMR) ---> RMMMMTTC + RMMMM , kfrag4

INT(RMMMMSMMMMR) ---> RMMMM + RMMMMTTC , kfrag4

**Termination**

I + I ---> Dead , kt

I + RM ---> Dead , kt

I + RMM ---> Dead , kt

I + RMMM ---> Dead , kt

I + RMMMM ---> Dead , kt

IM + RM ---> Dead , kt

IM + RMM ---> Dead , kt

IM + RMMM ---> Dead , kt

IM + RMMMM ---> Dead , kt

IMM + RM ---> Dead , kt

IMM + RMM ---> Dead , kt

IMM + RMMM ---> Dead , kt

IMM + RMMMM ---> Dead , kt

IMMM + RM ---> Dead , kt

IMMM + RMM ---> Dead , kt

IMMM + RMMM ---> Dead , kt

IMMM + RMMMM ---> Dead , kt

IMMMM + RM ---> Dead , kt

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RM + RMM ---> Dead , kt

RM + RMMM ---> Dead , kt

RM + RMMMM ---> Dead , kt

RMM + RMM ---> Dead , kt

RMM + RMMM ---> Dead , kt

RMM + RMMMM ---> Dead , kt

RMMM + RMMM ---> Dead , kt

RMMM + RMMMM ---> Dead , kt

RMMMM + RMMMM ---> Dead , kt

No efficiency factors have been used and all reactions are considered explicitly.

## References


[1] J. Haven, J. Vandenbergh and T. Junkers, *Chem. Commun.*, 2015, 51, 4611−4614.

[2] J. Vandenbergh, G. Reekmans, P. Adriaensens and T. Junkers, *Chem. Commun.*, 2013, **49**, 10358−10360.