Impact of residence time distributions in reacting magnesium packed-beds on Grignard reagent formation – Selectivity of Grignard reagent formation (part 2)

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Electronic Supplementary Information (ESI)

Content

1 Residence time measurements under reactive conditions

1.1 Performing residence time distribution experiments

Exemplary cumulative distribution functions obtained from the normalized measurement data as well as by fitting the dispersion model to the measurement data are presented. The cumulative distribution functions shown represent the results being close to the mean Bodenstein number Bo mentioned or displayed within the publication, unless otherwise specified. The dimensionless residence time distribution functions presented are obtained from the model cumulative distribution functions.

Specific Bodenstein number and hydrodynamic residence time τ are noted.

Pumps used for residence time distribution experiments corresponding to the presented distribution functions are listed in table 1.

Table 1: Details of pumps used during residence time measurements.

pump	pump type	pump name	manufacturer
A	syringe pump	PN1610 syringe dosing system	Postnova Analytics GmbH
C	micro annular gear pump	mzr-7205	HNP Mikrosysteme GmbH
D	valveless rotary piston pump	Reglo-CPF Digital with ISM321 drive and RH1CKC pump head	Ismatec, Cole-Parmer Instrument Company LTD

1.2 Cumulative distribution functions

1.2.1 Coarse magnesium turnings

1.2.1.1 Pump A

Bo = 19

τ = 633 s

Figure 1: Cumulative distribution function, pump A, coarse magnesium turnings, displacement of tracer.

Figure 2: Dimensionless residence time distribution function, pump A, coarse magnesium turnings, displacement of tracer.

Bo = 25

τ = 650 s

Figure 3: Cumulative distribution function, pump A, coarse magnesium turnings, introduction of tracer.

Figure 4: Dimensionless residence time distribution function, pump A, coarse magnesium turnings, introduction of tracer.

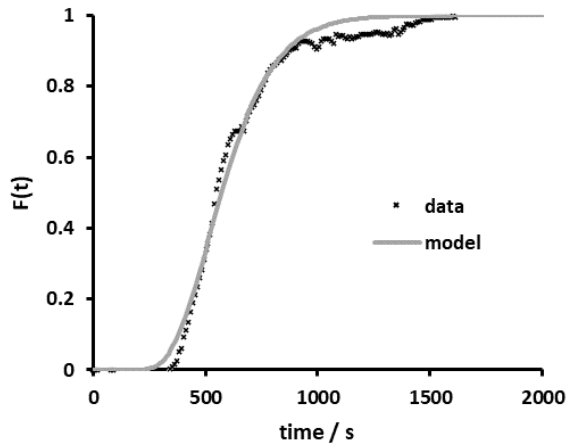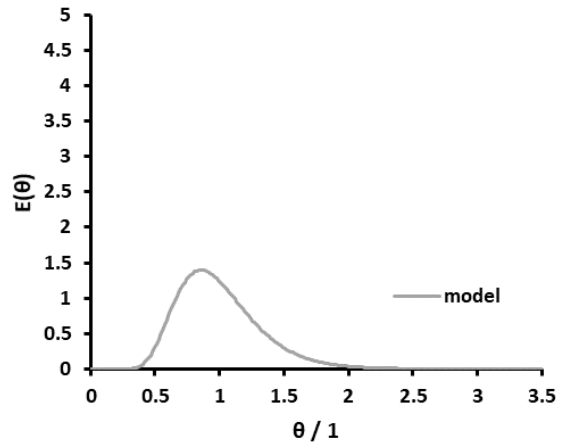**1.2.1.2 Pump C**

Bo = 31

τ = 707 s

Figure 5: Cumulative distribution function, pump C, coarse magnesium turnings, displacement of tracer.

Figure 6: Dimensionless residence time distribution function, pump C, coarse magnesium turnings, displacement of tracer.
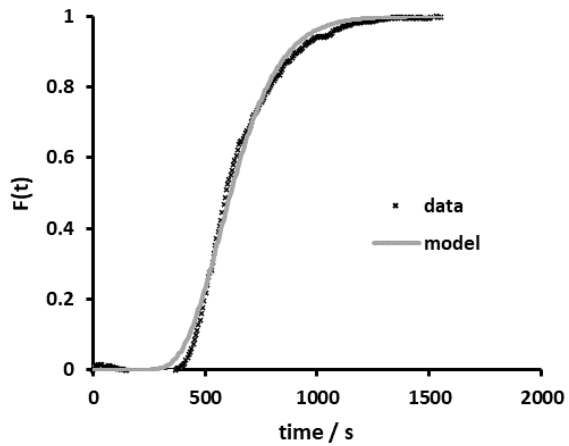
Bo = 14

τ = 708 s

Figure 7: Cumulative distribution function, pump C, coarse magnesium turnings, introduction of tracer.
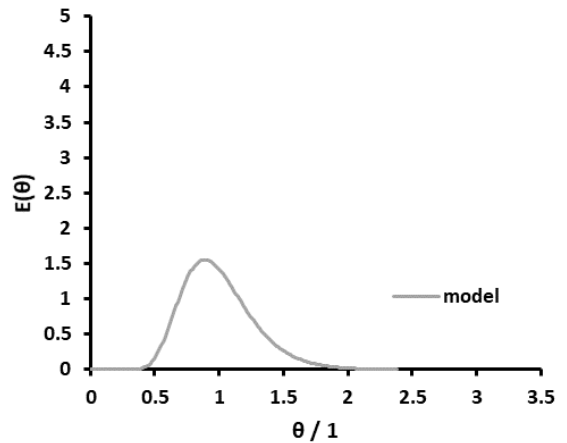

Figure 8: Dimensionless residence time distribution function, pump C, coarse magnesium turnings, introduction of tracer.

1.2.1.3 Pump D

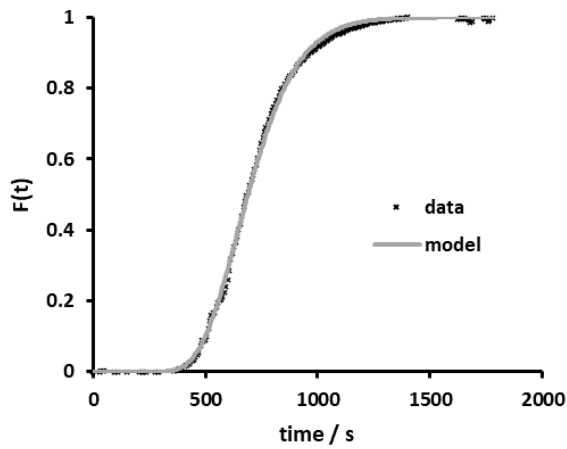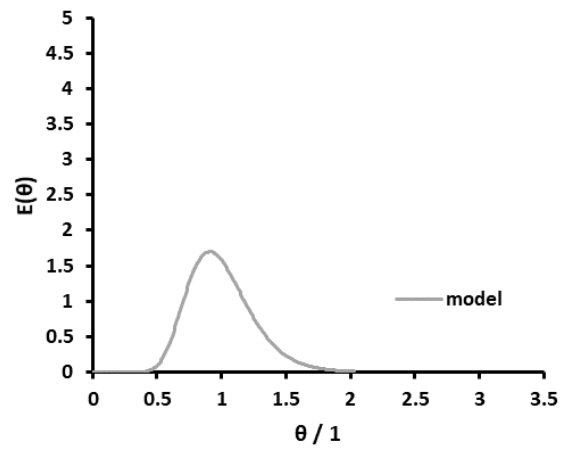**Bo = 26**

τ = 711 s

Figure 9: Cumulative distribution function, pump D, coarse magnesium turnings, displacement of tracer.

Figure 10: Dimensionless residence time distribution function, pump D, coarse magnesium turnings, displacement of tracer.

Bo = 20

τ = 680 s

Figure 11: Cumulative distribution function, pump D, coarse magnesium turnings, introduction of tracer.

Figure 12: Dimensionless residence time distribution function, pump D, coarse magnesium turnings, introduction of tracer.

1.2.2 Fine magnesium turnings
1.2.2.1 Pump A

Bo = 44

τ = 611 s

Figure 13: Cumulative distribution function, pump A, fine magnesium turnings, displacement of tracer.

Figure 14: Dimensionless residence time distribution function, pump A, fine magnesium turnings, displacement of tracer.
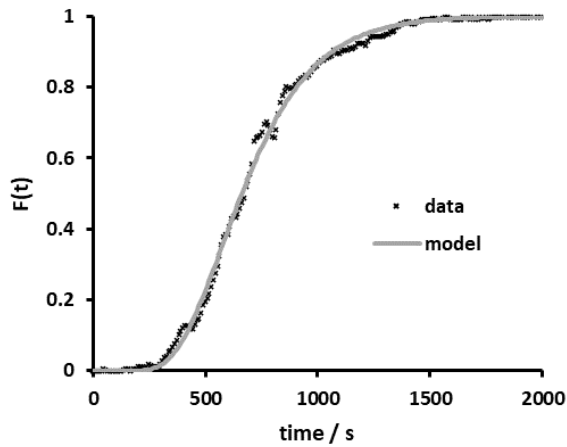
Bo = 44

τ = 608 s

Figure 15: Cumulative distribution function, pump A, fine magnesium turnings, introduction of tracer.
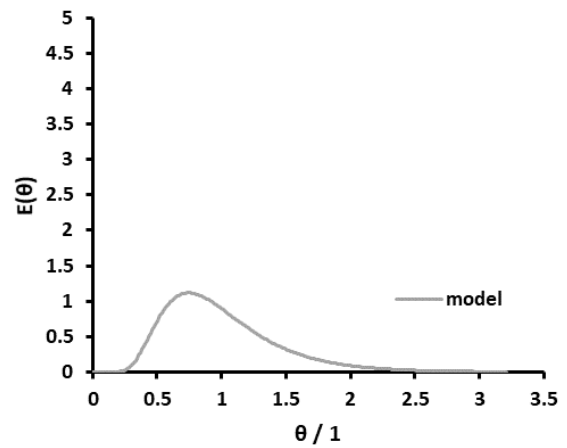

Figure 16: Dimensionless residence time distribution function, pump A, fine magnesium turnings, introduction of tracer.
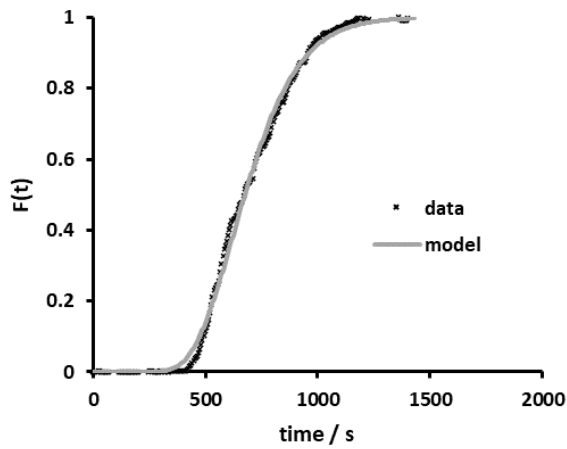
1.2.2.2 Pump C

Bo = 50

τ = 672 s
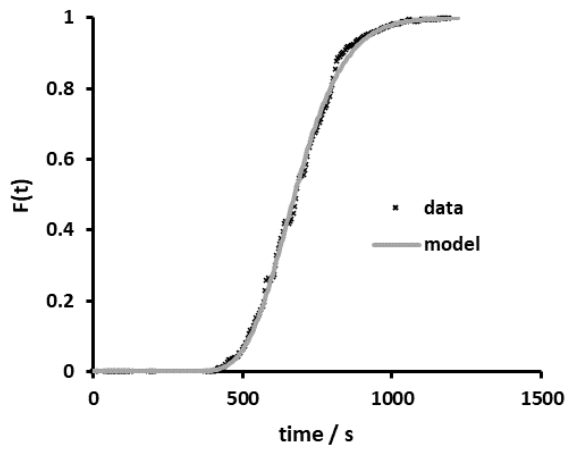
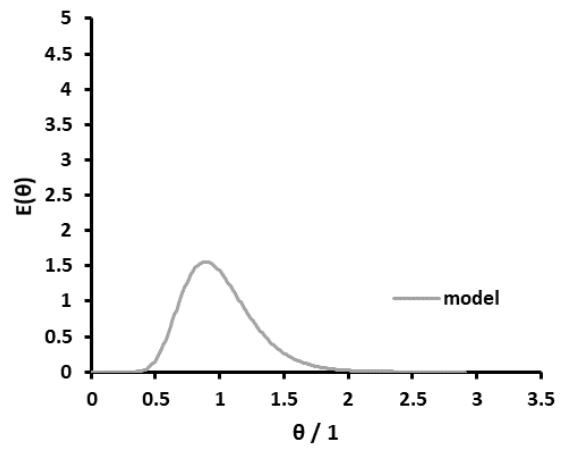Figure 17: Cumulative distribution function, pump C, fine magnesium turnings, displacement of tracer.
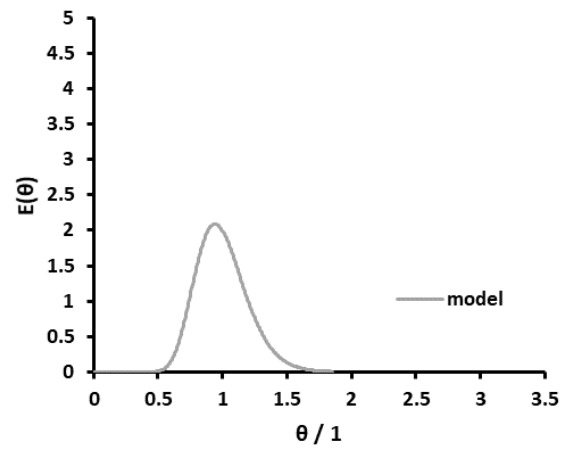
Figure 18: Dimensionless residence time distribution function, pump A, fine magnesium turnings, displacement of tracer.
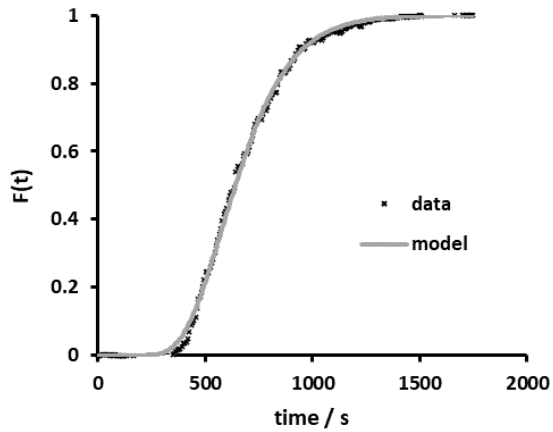
Bo = 61

τ = 641 s
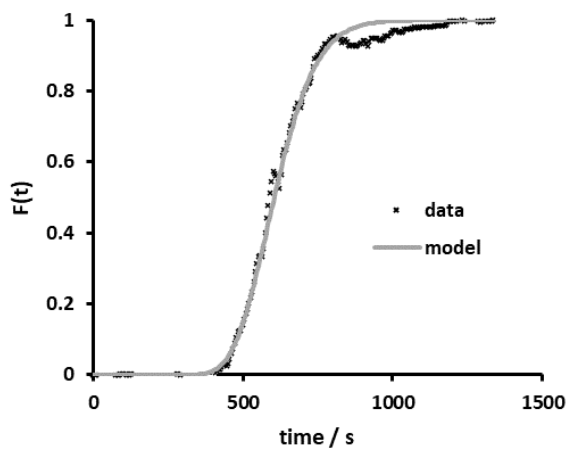
Figure 19: Cumulative distribution function, pump D, fine magnesium turnings, introduction of tracer.
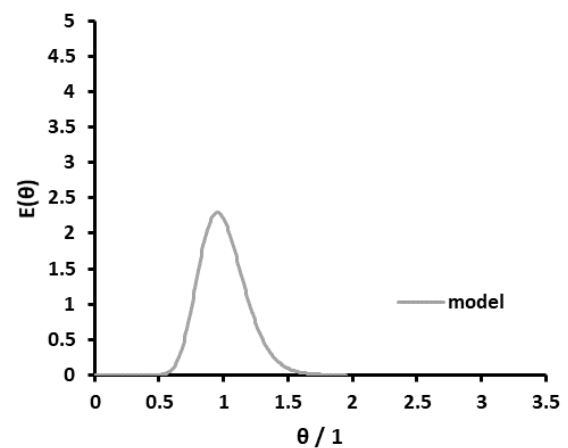
Figure 20: Dimensionless residence time distribution function, pump C, fine magnesium turnings, introduction of tracer.

1.2.2.3 Pump D

Bo = 23

τ = 687 s
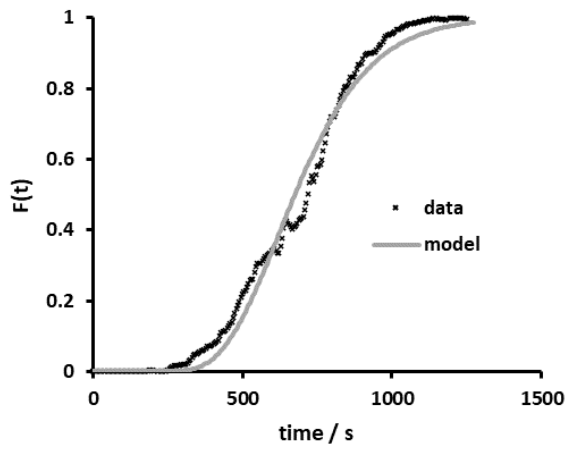
Figure 21: Cumulative distribution function, pump D, fine magnesium turnings, displacement of tracer.
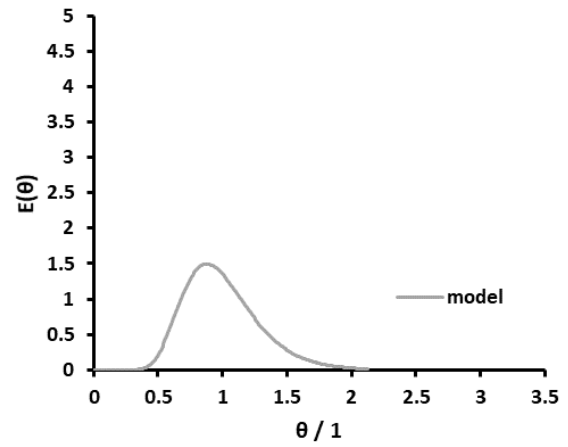
Figure 22: Dimensionless residence time distribution function, pump D, fine magnesium turnings, displacement of tracer.

Bo = 61

τ = 616 s

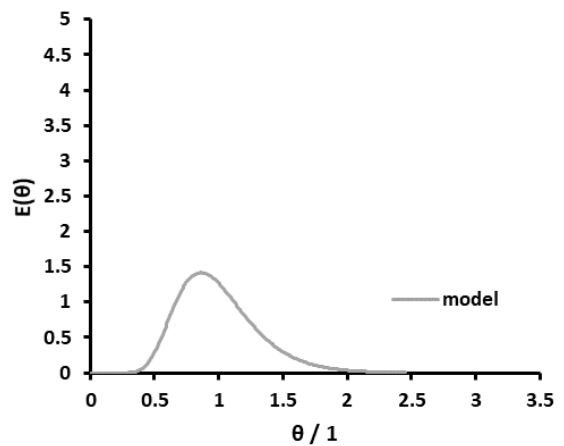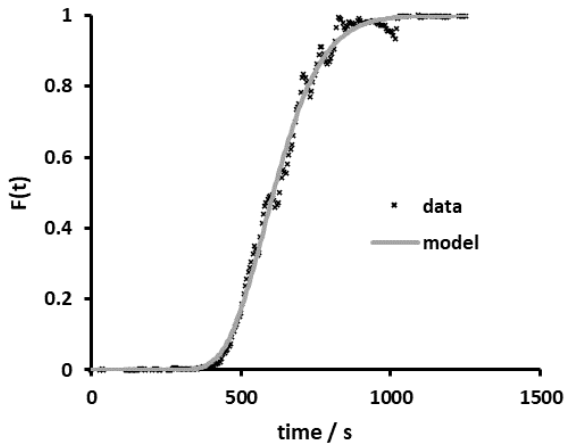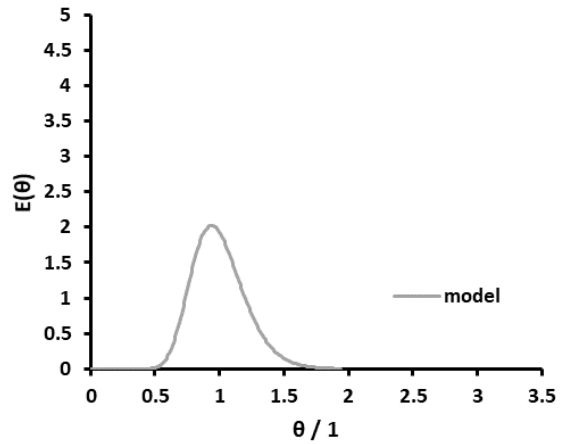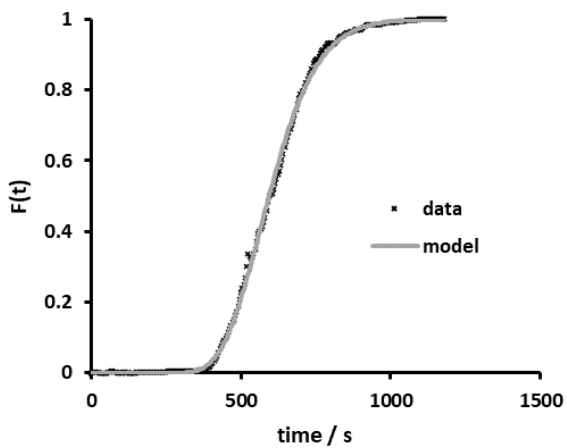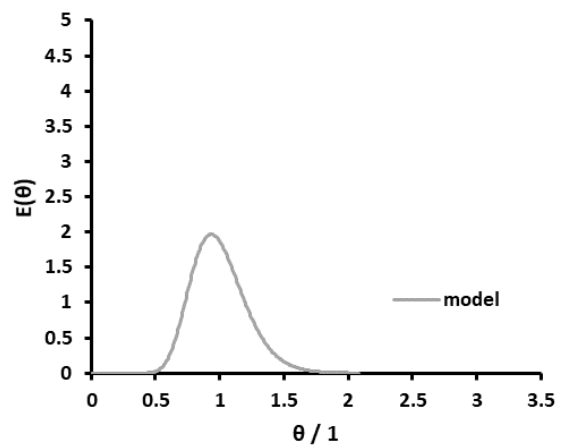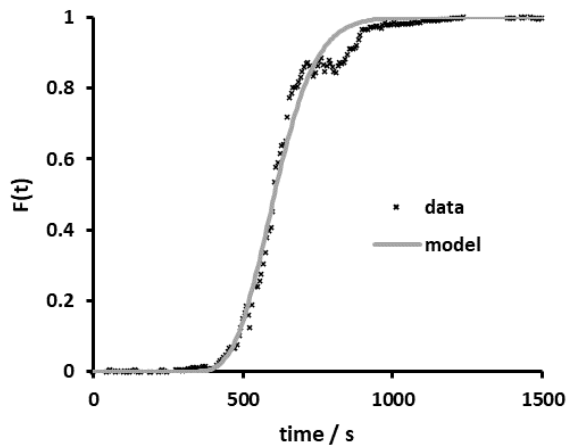Figure 23: Cumulative distribution function, pump D, fine magnesium turnings, introduction of tracer.
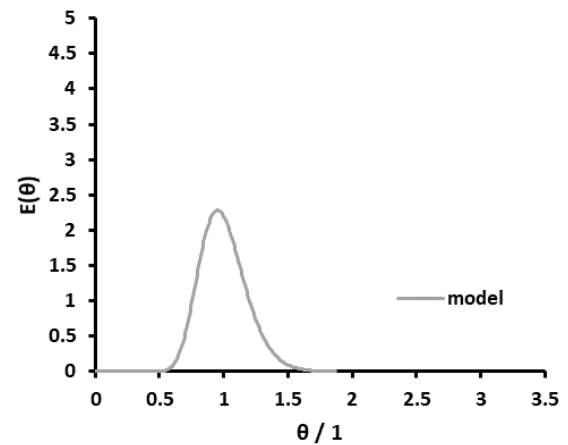
Figure 24: Dimensionless residence time distribution function, pump D, fine magnesium turnings, introduction of tracer.

1.2.3 No use of jogging motor

Bo = 10

τ = 567 s
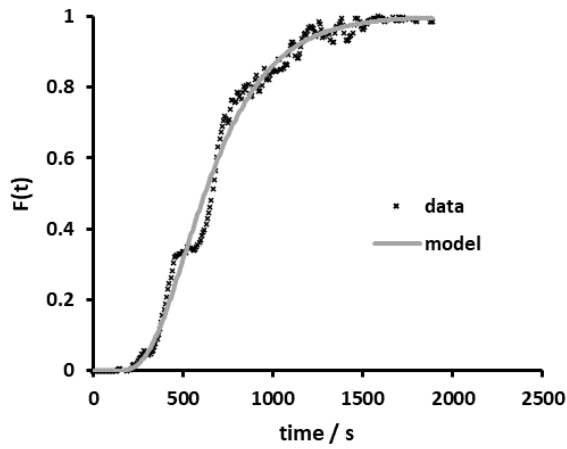
Figure 25: Cumulative distribution function, pump A, coarse magnesium turnings, displacement of tracer, no jogging motor.
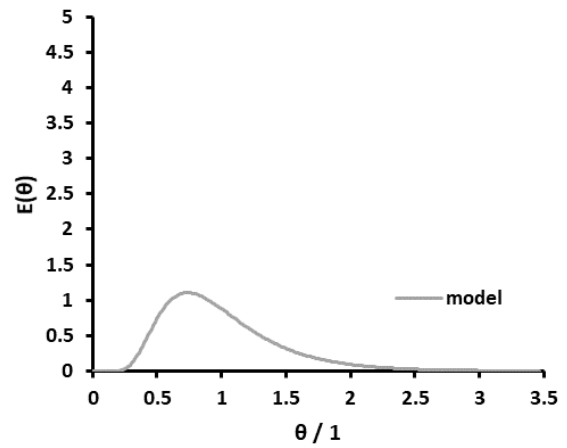
Figure 26: Dimensionless residence time distribution function, pump A, coarse magnesium turnings, displacement of tracer, no jogging motor.

Bo = 9

τ = 785 s
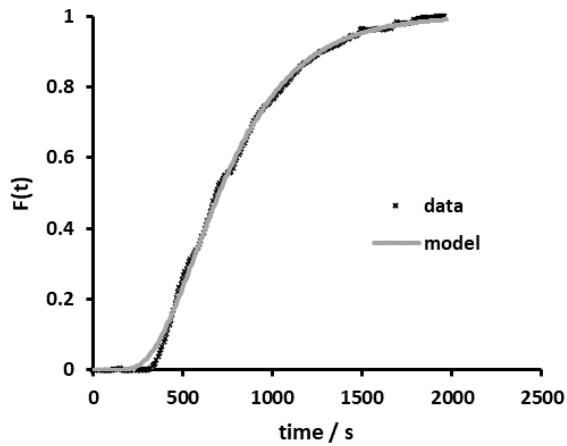
Figure 27: Cumulative distribution function, pump C, coarse magnesium turnings, introduction of tracer, no jogging motor.
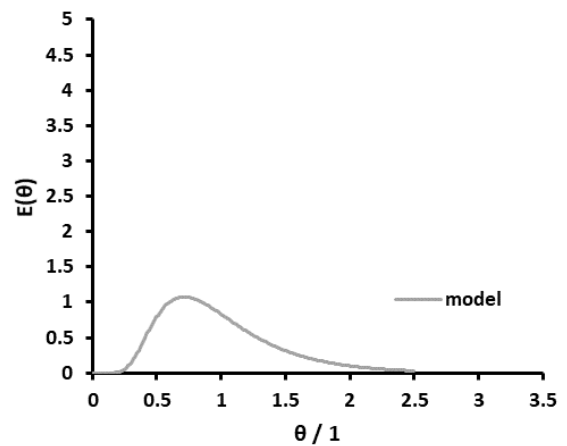
Figure 28: Dimensionless residence time distribution function, pump C, coarse magnesium turnings, introduction of tracer, no jogging motor.

2 Grignard reagent synthesis in a stirred tank (semi-continuous batch mode)

2.1 Batch procedure 1: Literature reaction conditions
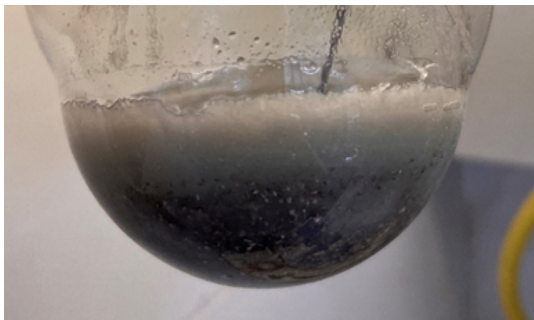
Figure 29: Precipitated bibenzyl during synthesis (batch procedure 1).

2.2 Batch procedure 2: 1:1 transfer of the flow conditions to batch synthesis

Figure 30: High excess of magnesium during synthesis (batch procedure 2, coarse magnesium turnings).
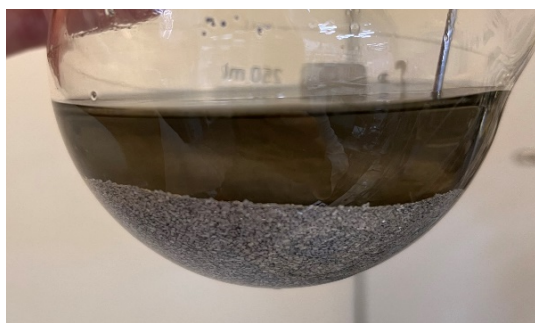
Figure 31: Remaining magnesium turnings after synthesis (batch procedure 2, coarse magnesium turnings).

2.3 Batch procedure 3: Literature reaction conditions adapted to flow conditions
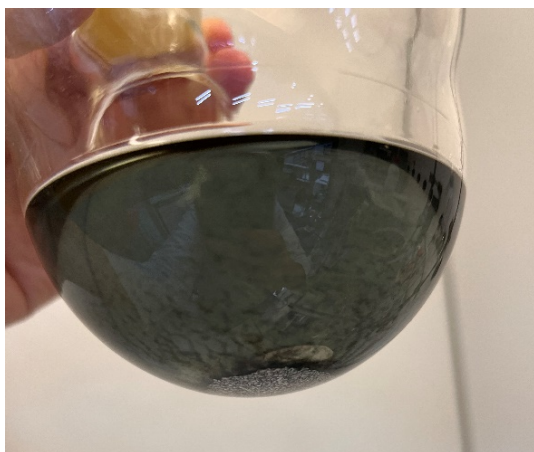
Figure 32: Remaining magnesium turnings after synthesis (batch procedure 3, coarse magnesium turnings).

3 Benzyl alcohol formation

The current understanding on the formation of benzyl alcohol in benzylmagnesium bromide synthesis assumes that this species is formed by oxidation and subsequent hydrolysis of the Grignard reagent.[1]

To clarify whether benzyl alcohol is formed within the Grignard reagent formation itself or afterwards, a control experiment was performed. For this purpose, benzylmagnesium bromide was synthesized from coarse magnesium turnings and (bromomethyl)benzene according to the instruction for the Grignard reagent synthesis in the continuous flow reactor. The pulsation-free micro annular gear pump (pump C) was used. A sample of the reaction solution was collected from the PTFE-tube attached to the reactor outlet and connected to a glass vial filled with argon (sample A). Another sample was directly taken from the reactor cartridge at the inlet for thermocouple T4 (see figure 1 in the manuscript) by means of a syringe (sample B). T4 is located within the magnesium bed just below the reaction solution outlet. This position was chosen because most likely full conversion of the halide educt is obtained by the corresponding residence time and the actual Grignard reagent formation is completed. The samples were taken directly after the other.

Conversion and selectivities of sample A and B are listed in table 2. Sample B (withdrawn from reactor cartridge) does not contain any benzyl alcohol while sample A (collected within argonized vial) does contain benzyl alcohol. This gives evidence that the reaction solution gets into contact with air, upon which the alcohol is formed, at some point in the sample taking procedure and the sample processing.

These experimental results show that the benzyl alcohol is formed after the actual Grignard reagent formation reaction and therefore the benzyl alcohol can be regarded as a fraction of the Grignard reagent that underwent a consecutive reaction. Thus, the benzyl alcohol must be considered as part of the Grignard reagent content to evaluate the impact of the residence time distribution on the selectivity of the benchmark Grignard reagent formation.

Table 2: Conversion of the halide and selectivities of the components within the reaction mixture within the reactor cartridge (sample A) and within the glass vial (sample B).

	component	sample A	sample B
conversion / %	(bromomethyl)benzene	99	100
selectivity / %	benzylmagnesium bromide	58	71
	benzyl alcohol	16	0
	2-phenylethylbenzene	26	29

The chromatograms of the gas chromatography measurements of sample A (top) and sample B (bottom) are displayed in figure 33 and table 3 lists the retention times for the components toluene, (bromomethyl)benzene, benzyl alcohol and 2-phenylethylbenzene. Tetrahydrofuran (solvent) and methanol (quenching agent) are within the solvent cut-off and not shown in these plots.

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[1] A. Kadam et al., Green Chem., 2013, 15, 1880-1888, doi: 10.1039/C3GC40702K
M.T. Goebel et al., J. Am. Chem. Soc., 1933, 55, 4, 1693-1696, doi: 10.1021/ja01331a065
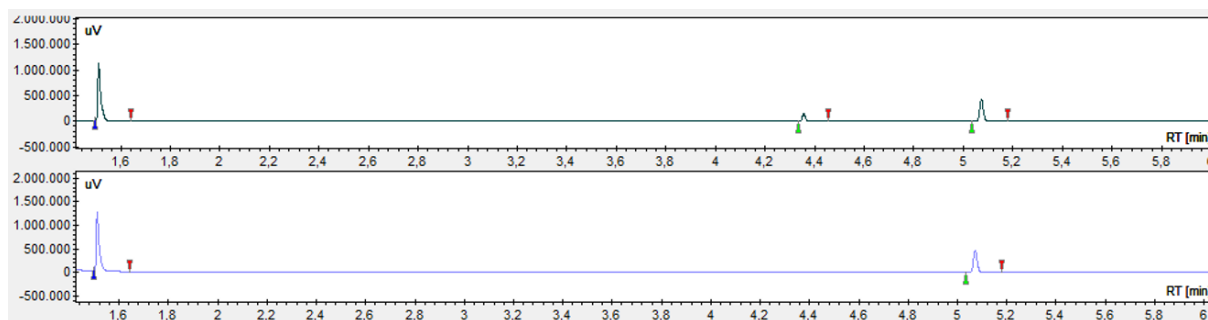
Figure 33: Gas chromatography plots of sample A (top) and sample B (bottom).

Table 3: Retention times for GC analysis of reaction product of benzylmagnesium bromide synthesis according to figure 33.

component	retention time / min
toluene	1.51
(bromomethyl)benzene	3.53
benzyl alcohol	4.35
2-phenylethylbenzene	5.07

4 Conversion and selectivities

Within the following tables, the selectivities of the single components are listed. For the selectivities mentioned or shown in the manuscript, benzylmagnesium bromide and benzyl alcohol are summed up.

4.1 Figure 7 within the manuscript

Table 4: Conversion and selectivities for the synthesis of benzylmagnesium bromide depending on the pump system used (figure 7 within manuscript).

| column | (bromomethyl)benzene conversion / % | selectivity / % | | |
		benzylmagnesium bromide	benzyl alcohol	2-phenylethyl-benzene
1	100	71	12	17
2	100	63	14	22
3	100	63	15	21
4	100	61	13	26
5	100	81	4	14
6	100	74	18	8
7	100	79	6	15
8	100	70	19	11

4.2 Figure 8 within the manuscript

Table 5: Conversion and selectivities for the synthesis of benzylmagnesium bromide and the selectivities of benzylmagnesium bromide (incl. benzyl alcohol) displayed in figure 8 within the manuscript.

| Bo / 1 | (bromomethyl)benzene conversion / % | selectivity / % | | |
		benzylmagnesium bromide	benzyl alcohol	2-phenylethyl-benzene
0	95	60	8	32
0	95	63	11	26
18	100	63	14	22
20	100	63	15	21
21	100	71	12	17
25	100	79	6	15
37	100	81	4	14
46	100	74	18	8

4.3 Figure 9 within the manuscript

Table 6: Conversion and selectivities for the synthesis of benzylmagnesium bromide with fine magnesium turnings and oscillatory flow conditions (pump C + pump D, figure 9 within the manuscript).

osc. Re / 1	frequency / s^{-1}	amplitude / m	(bromomethyl)benzene conversion / %	selectivity / %		
				benzylmagnesium bromide	benzyl alcohol	2-phenylethyl-benzene
0	0	0	100	74	18	8
0.097	0.667	0.000065	100	70	19	11
0.220	1.000	0.000097	100	83	5	12
0.340	1.167	0.000130	99	78	7	14
0.490	1.667	0.000130	99	78	9	12
0.857	1.167	0.000324	99	70	10	19
0.979	0.667	0.000650	100	82	6	12
1.285	1.167	0.000487	99	75	9	16
2.203	1.667	0.000585	100	82	4	14
2.203	1.667	0.000585	100	74	9	18
2.938	2.000	0.000650	100	79	6	15

4.4 Figure 12 within the manuscript

Table 7: Conversion and selectivities for the synthesis of benzylmagnesium bromide with fine magnesium turnings and oscillatory flow conditions (pump C + pump B, figure 12 within the manuscript).

osc. Re / 1	frequency / s^{-1}	amplitude / m	(bromomethyl)benzene conversion / %	selectivity / %		
				benzylmagnesium bromide	benzyl alcohol	2-phenylethyl-benzene
0.122	0.008	0.00650	100	74	5	21
0.245	0.033	0.00325	100	76	4	20
0.367	0.050	0.00325	100	64	11	25
0.490	0.048	0.00455	100	73	6	21
0.612	0.042	0.00650	100	71	6	22

4.5 Figure 13 within the manuscript

Table 8: Conversion and selectivities for the synthesis of benzylmagnesium bromide with coarse magnesium turnings and oscillatory flow conditions (pump C + pump B, figure 13 within the manuscript).

osc. Re / 1	frequency / s⁻¹	amplitude / m	(bromomethyl)benzene conversion / %	selectivity / %		
				benzylmagnesium bromide	benzyl alcohol	2-phenylethyl-benzene
0	0	0	100	63	14	22
0.276	0.008	0.00566	99	60	9	31
0.276	0.004	0.01132	99	67	13	20
0.441	0.027	0.00283	100	68	6	26
0.552	0.033	0.00283	99	80	7	13
0.552	0.033	0.00283	100	66	6	28
0.717	0.043	0.00283	99	80	6	14
0.828	0.013	0.01132	100	77	7	16
0.966	0.010	0.01698	99	59	8	33
1.104	0.022	0.00849	99	58	10	32
1.214	0.073	0.00283	99	67	6	27
1.324	0.080	0.00283	99	60	5	35
1.380	0.021	0.01132	99	63	11	26
1.490	0.090	0.00283	99	61	6	34
1.656	0.050	0.00566	100	77	6	17
1.656	0.033	0.00849	100	64	6	30
1.680	0.042	0.00566	100	61	13	26
1.766	0.107	0.00283	99	69	5	27
1.931	0.058	0.00566	100	62	6	32
1.931	0.117	0.00283	100	81	5	14
1.931	0.058	0.00566	99	63	11	26
2.207	0.067	0.00566	100	79	4	16
2.207	0.067	0.00566	99	69	6	25
2.207	0.083	0.00424	100	68	6	25
2.483	0.150	0.00283	99	62	5	33
2.759	0.167	0.00283	99	80	4	16
2.759	0.028	0.01698	99	58	6	35