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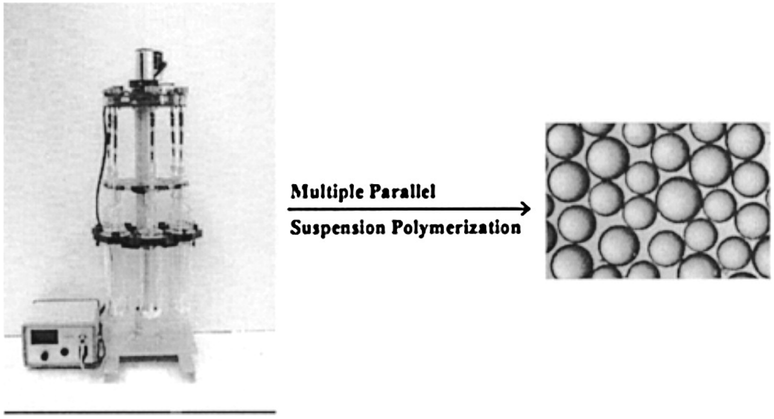

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Synthesis of Resins via Multiparallel Suspension Polymerization

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A system for the multiparallel synthesis of polymer resins for solid-phase synthesis is presented, accelerating the preparation of new resins using standard suspension polymerization protocols. The system was evaluated by preparing a range of polystyrene resins with well-defined characteristics.

Introduction

Combinatorial synthetic strategies have stimulated the development of new types of polymer supports with compositions and properties that enable a broad spectrum of organic transformations[1,2] to be accessed. The use of polymer resins as an aid to synthesis is becoming an increasingly common feature in both academic and industrial laboratories,[3] with the chemical and physical nature of the polymer support playing an integral role in synthesis. In most synthetic applications the cross-link density, physical form, and the relative uniformity of the cross-linked materials are important parameters for efficient synthesis,[4] and scope exists for the development of new supports to facilitate solid-phase organic synthesis.

Traditionally polymer supports have been made by suspension polymerization. Optimization of suspension polymerization conditions are often very time-consuming, an issue that becomes important when research on new polymerization systems is carried out. Moreover, it is well-known that in suspension polymerization processes parameters such as reactor geometry, agitator design, and agitation rate can significantly influence particle size and distribution.[5] Therefore, in most polymerization systems carried out on bench-scale dimensions, particular attention has to be paid to these parameters and their reproducibility. The novel instrument, designed in our laboratories (Figure 1), is an example of a multiple-parallel synthesis system that we have successfully used in suspension polymerization reactions and represents a valid alternative to single polymerization reactions. This methodology facilitates the systematic study of the correlation among polymer structure, properties, and performance. The new system offers the possibility of changing several parameters of a polymerization recipe, for example, in terms of composition of organic and aqueous phases but with constant vessel, stirrer geometry, and agitation rate. This equipment facilitates the optimization of both specific polymer compositions for particular applications and the suspension polymerization conditions (initiator, temperature, colloid stabilizers, agitator design).[6−10]

Results and Discussion

The apparatus shown in Figure 1 comprises a stand to support six glass reaction vessels counterpoised on a vertical column; the system is free to move around the column and up and down by 120 mm and designed to be mounted in a standard water bath. At the top of the system is a low-voltage brushless dc motor that drives the six stirrers through a gearbox and a multishaft belt coupled to six stirrers in the reactions vessels. Motor speed is fully adjustable (stirrer speed between 0 and 800 rpm) without the risk of any significant reduction in speed as the load is increased. The system was initially tested by performing a multiparallel synthesis of a set of polystyrene resins with 2% DVB cross-linking. Suspension polymerization reactions on a 20−40 g scale of organic monomers (500 mL vessels) were conducted and worked up simultaneously. Results of six 2% DVB cross-linked PS resins prepared simultaneously are reported in Table 1, showing the reproducibility of the system in terms of bead size distribution and yields.

Table 1. Size Distribution Percentages of 2% DVB PS Resins

entry	>355 μm	355−250 μm	250−125 μm	125−75 μm	75−45 μm	yield[a] (%)
1	3.5	4.5	82.0	9.0	1.0	60
2	3.5	4.0	78.0	11.0	3.5	65
3	0.0	0.0	81.0	12.5	6.5	60
4	0.5	4.0	90.0	3.5	2.0	64
5	5.0	7.0	84.0	3.0	1.0	70
6	0.5	3.0	85.0	10.0	1.5	60

[a] Yield of beads after sieving.

With these results in hand, two additional batches of resins were prepared, varying the level of DVB, the volume ratios of organic monomers to solvent (toluene) and the loading of the chloromethyl group. The size distributions of the resins

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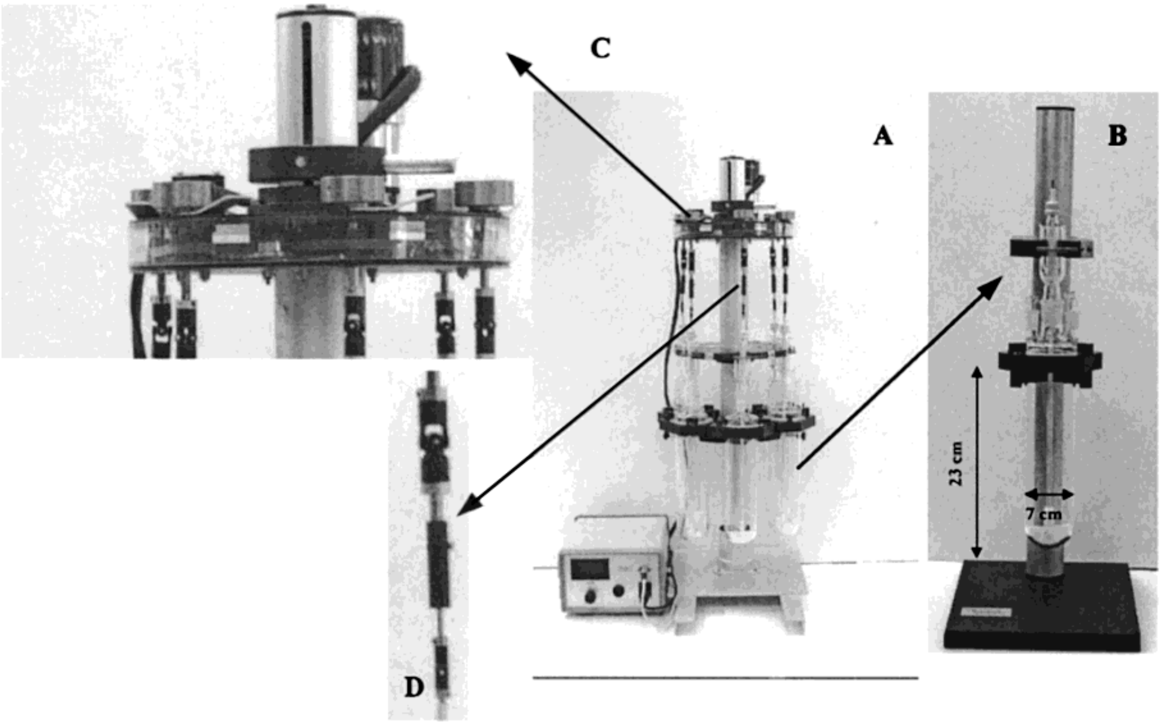

Figure 1. (A) Multiparallel polymerization system showing (B) multiparallel polymerization 500 mL reaction vessel with half-moon stirrer, (C) magnified view of stirring motor assembly and drive-belt system, and (D) magnified view of movable joint connector to join driving spindle to stirrer bar.

Table 2. Size Distribution Percentages of 1−15% DVB PS Resins

entry	DVB (%)	ratio[a] (v/v)	>355 μm	355−250 μm	250−125 μm	125−75 μm	75−45 μm	yield[b] (%)
7	1	3/1	2.0	16.0	78.0	3.0	1.0	70
8	3	2/1		0.5	94.0	4.5	1.0	74
9	4	2/1		3.0	85.0	8.0	4.0	81
10	8	1/1		0.4	87.0	8.5	4.0	73
11	10	1/1		0.1	96.0	3.6	0.3	81
12	15	1/1		2.0	95.0	2.0	1.0	86

[a] Volume ratio between organic monomers and solvent (toluene). [b] Yield of sieved beads.

Table 3. Size Distribution Percentages of 1−8% DVB PS Chloromethylated Resins

entry	loading (mmol/g)	DVB (%)	ratio[a] (v/v)	>355 μm	355−250 μm	250−125 μm	125−75 μm	75−45 μm	yield[b] (%)
13	1	1	3/1	4.0	2.0	89.0	2.0	3.0	80
14	1	2	3/1	0.4	3.0	90.0	6.0	0.6	98
15	2	2	2/1	0.5	0.5	87.0	9.0	3.0	96
16	2	3	2/1	0.6	0.1	86.0	9.3	4.0	95
17	2	4	2/1	6.0	10.0	66.0	10.0	8.0	98
18	1	8	1/1	0.4	0.6	60.0	23.0	16.0	90

[a] Volume ratio between organic monomers and solvent (toluene). [b] Yields of sieved beads.

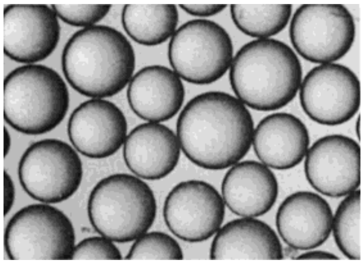

Figure 2. Example of 1% DVB PS resin beads in DMF (size: 250−125 μm).

are given in Tables 2 and 3. The beads produced with variable DVB levels are shown in Table 2 (see Figure 2 for an example of 1% DVB PS resin beads in DMF) and show the clear and expected trend of enhanced yields with increased percentage cross-linking and the good size distribution obtained with this polymerization system, across the whole array.

Conclusions

In conclusion the results clearly illustrate that a multiparallel approach is a valid possibility for suspension polymerization and represents a valid tool to rapidly design new polymeric bead supports and/or optimize polymerization. Considering the time frame and problematic consistency associated with suspension polymerization, this opens up the path to parallel bead production, thus allowing unique new polymer resins to be synthesized and evaluated. The system

Table 4. Stoichiometry of the Premixed Organic Phase in Suspension Polymerization Series

entry	resin cross-linking (%)	styrene (mmol)	DVB (mmol)	vinylbenzyl chloride (mmol)	toluene[a] (mL)
1−6	2	176.6	4.15	0	11.0
7	1	189.7	2.1	0	7.0
8	3	185.1	5.8	0	11.0
9	4	182.7	7.7	0	11.0
10	8	173.1	15.4	0	21.0
11	10	168.3	19.2	0	21.0
12	15	126.0	28.0	0	21.0
13	1	154.2	1.85	24.6	7.0
14	2	152.0	4.15	24.6	10.0
15	2	128.8	3.85	40.0	10.0
16	3	127.0	5.4	40.0	10.0
17	4	125.0	6.9	40.0	10.0
18	8	139.0	16.6	24.6	21.0

[a] Initiator AIBN (1.0% w/w) was added to the organic phase.

is currently being utilized for preparing libraries of novel polymers supports for use in a range of solid-phase organic synthesis.

Experimental Section

Suspension Polymerization. Premixed organic phases (Table 4) were added to the aqueous phases (1.0 g of PVA (poly(vinyl alcohol), 87−89% hydrolyzed, $M_r = 85-146$ kDa), 5−10 g of Na_2SO_4 or 2 g of Na_2HPO_4 (pH = 8), 200 mL of H_2O) while stirring the mixture in the 500 mL cylindrical reaction vessels equipped with mechanical stirring bars connected to a central stirring motor (Figure 1) and purged with N_2. The suspensions were allowed to equilibrate for 30 min, and the temperature was raised to 65 °C for 16 h. The crude polymers were collected in six polypropylene filtration bags and washed with water and water/THF (1:1), THF, THF/MeOH (1:1), MeOH. The resins were extracted via a large Soxhlet in six cups with methanol for 24 h. The beads were dried in vacuo and sieved to afford resins in five size ranges (>355, 355−250, 250−125, 125−75, 75−45μm).

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