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A General Approach to Creating Soluble Catalytic Polymers Heterogenized in Microcapsules

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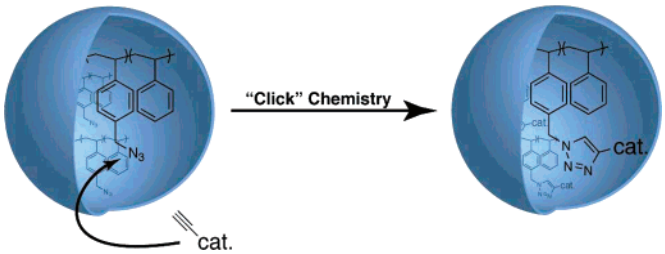
ABSTRACT



A general method for preparing site-isolated polymeric catalysts is presented. Linear chloromethyl and azide polymers have been sequestered within polyurea microcapsules and small molecule catalysts soaked through the shell walls to functionalize the soluble polymers. Reaction onto each type of support is quantitative and MacMillan, DMAP, and TEMPO test catalysts are shown to have faster reaction rates than the analogous resin-supported catalysts.

We recently reported the preparation of encapsulated catalytic linear polymers.[1] When the capsules were swollen in the reaction solvent, polymeric catalysts bound within remained active and in a solution-like environment.[2] We demonstrated that reaction rates were directly dependent on capsule wall thickness, and that the encapsulated catalyst showed greater activity than the same catalyst on cross-linked polystyrene support. This approach may not be widely adopted, however, because a linear polymer-bound catalyst must first be synthesized and then encapsulated within a polymeric shell. This requires that the catalyst be robust enough to survive the encapsulation conditions. Also, differences in the molecular weight and functionality of the polymer-bound catalyst change the nature of the polyurea shell.

Herein, we report general approaches to overcome these barriers by demonstrating that polyurea capsules containing chloromethyl- and azide-functionalized linear polymers can be directly functionalized with small molecule catalysts (Scheme 1). From these premade supports, we prepared three encapsulated catalysts: a MacMillan-type catalyst for Diels−Alder reactions, a 4-(*N*,*N*-dimethylamino)pyridine (DMAP) acylation catalyst, and a 2,2,6,6-tetramethylpiperidinyloxy (TEMPO) oxidation catalyst. Rates for the catalysts were compared to those of analogous resin-supported catalysts.

We first investigated capsules directly analogous to Merrifield resin.[3,4] Poly(chloromethylstyrene-*co*-styrene) was generated by using well-known methods[5,6] and microencapsulated in polyurea shells.[1,7] To determine if an active catalyst could be made from these microcapsules, an imidazolidinone

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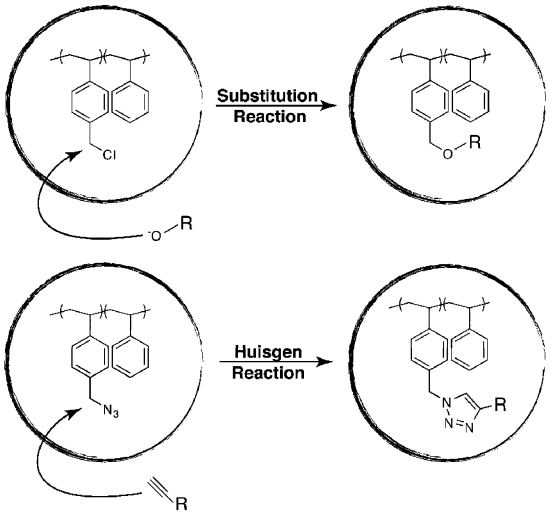
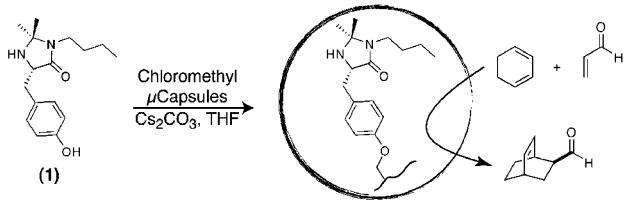
Scheme 1. Functionalization of Preformed Microcapsules



catalyst[8] featuring a phenol group[9] (**1**) was deprotonated and reacted onto the encapsulated polymer (Scheme 2), as well

Scheme 2. Imidazolidinone Functionalization and Catalysis



as onto the commercially available Merrifield resin. Loading was determined by chlorine elemental analysis before and after catalyst functionalization. Reaction rates for the Diels–Alder reaction of 1,3-cyclohexadiene with acrolein increased for the microencapsulated catalyst compared to those for the catalyst on Merrifield resin (Table 1).

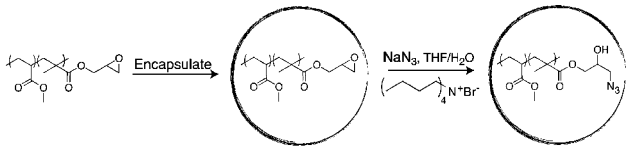
Table 1. Relative Rates of the Diels–Alder Reaction (4 mol % of Catalyst)

catalyst	k_{rel}	yield,[a] %
imidizolidinone on PS-DVB	1.0	52
imidizolidinone in μCapsule	1.7	52
μCapsule (background)	0.4	18

[a] After 24 h.

While the above test case showed that a small molecule catalyst could be functionalized onto a linear polymer in a

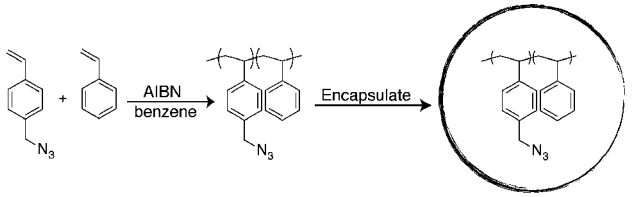
Scheme 3. Synthesis of Encapsulated Azide Polyacrylate



preformed microcapsule, they require a pendant group for attachment, like the phenolic group on **1**. The handle had to be easily deprotonated by a reasonably weak base, since a strong base would be quenched by the polyurea shell of the microcapsules. Also, the chloromethyl capsules could not support a nucleophilic catalyst like DMAP, which cross-links the polymer, negating any rate enhancement from linear polymer solubility. To overcome these limitations, we turned to the copper-catalyzed Huisgen "click" reaction between an azide and a terminal acetylene as a method of functionalization.[10,11]

Because the polymer backbone can play a large role in the rate of catalysis, we decided to make more than one type of soluble polymer support for encapsulation and compare them. To narrow our focus, we looked at a polyacrylate-based system (Scheme 3) versus a polystyrene-based system (Scheme 4). These polymers were functionalized with azide,

Scheme 4. Synthesis of Encapsulated Azide Polystyrene



to be reacted with acetylene-containing small molecule catalysts.

To determine if an active catalyst could be "clicked" into microcapsules, a DMAP analogue with an acetylene (**2**)[12] was synthesized and reacted into the azide-functionalized capsules with a copper(I) catalyst (Scheme 5).[10] The resulting DMAP capsules showed complete loss of the azide by ATR-IR. While DMAP has been shown to ligate to copper, it was found that a simple wash with 1 M HCl, followed by neutralization removed any residual copper present to below detectable limits by elemental analysis.

To test the capsules, we compared them against the pre-"clicked" azide capsules using the method of initial rates for the acylation of 1-phenylethanol. The encapsulated

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(9) Puglisi, A.; Benaglia, M.; Cinquini, M.; Cozzi, F.; Celentano, G. *Eur. J. Org. Chem.* **2004**, 567–573.
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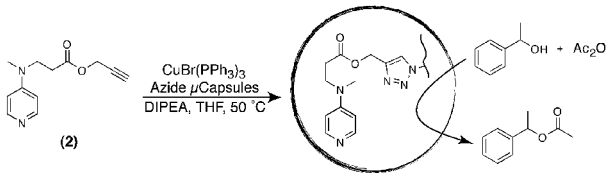
Scheme 5. DMAP Functionalization and Catalysis



DMAP triazole on polyacrylate (PA) was 60 times more active than that of unfunctionalized capsules (Table 2).

Table 2. Relative Acylation Rates of 1-Phenylethanol (0.75 mol % of Catalyst)

catalyst	k_{rel}	conversion,[a] %
DMAP on PS-DVB	1.0	99
DMAP triazole in μCapsule (PA)	0.48	56
DMAP triazole in μCapsule (PS)	2.1	99
DMAP analogue (**2**)	3.9	99
azide μCapsule (background)	0.008	6.0

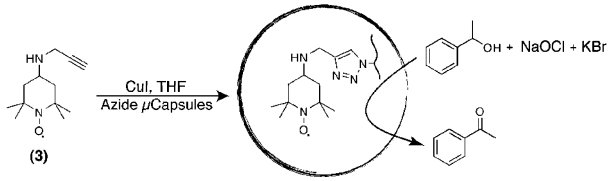
[a] After 20 h.

However, these rates were only about half the rate of commercially available DMAP on PS resin, and we had previously observed high activity for DMAP on a polystyrene-based encapsulated polymer.[1]

In the case of the second, polystyrene-based catalyst (Scheme 4), the azides also survived the encapsulation conditions, as indicated by ATR-IR, and were reacted to completion with **2** with copper catalyst. Notably, the microcapsules showed a greater rate of reaction than commercially available DMAP on Merrifield resin (Table 2). These capsules gave an isolated yield of 89% after chromatography, could be isolated by filtration, and were recycled three times.

To see if this method could be generalized we next functionalized the azide-functionalized capsules with a TEMPO analogue containing a pendant acetylene[13] (**3**) via the Huisgen reaction[14] (Scheme 6). Although the rate of oxidation of *sec*-phenethyl alcohol to acetophenone for the

Scheme 6. TEMPO Functionalization and Catalysis



PA-based TEMPO microcapsules was again sluggish compared to that of the analogous TEMPO-modified Merrifield resin, the PS-based capsules catalyzed the reaction 2.5 times faster than the resin (Table 3). The catalyst gave an isolated

Table 3. Relative Oxidation Rates of 1-Phenylethanol (0.33 mol % of Catalyst)

catalyst	k_{rel}	conversion,[a] %
TEMPO triazole on PS-DVB	1.0	>99
TEMPO triazole in μCapsule (PA)	0.24	61
TEMPO triazole in μCapsule (PS)	2.5	>99
azide μCapsule (background)	0.06	5.0

[a] After 24 h.

yield of 96% and even under fast stirring did not show signs of capsule breakage, allowing the capsules to be recycled three times.

We have developed a new system for preparing site-isolated polymeric catalysts that are more active than resin-supported catalysts. We have also shown that the type of functionalized polymer used as the catalyst backbone in these microcapsules is critical for reasonable reaction rates. Rather than having to develop encapsulation conditions for each new polymer-supported catalyst, any appropriately functionalized small molecule or catalyst can be readily attached to an already encapsulated soluble polymer and quickly assayed.

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Supporting Information Available: Experimental methods, elemental analysis data, ATR-IR and NMR spectra, and rate data. This material is available free of charge via the Internet at http://pubs.acs.org.

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