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Suspension Ring-Opening Metathesis Polymerization: The Preparation of Norbornene-Based Resins for Application in Organic Synthesis

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A series of norbornene-based resin beads were obtained by aqueous suspension ring-opening metathesis polymerization (ROMP) and used as polymeric supports for organic synthesis. These resins were prepared from norbornene, norborn-2-ene-5-methanol, and cross-linkers such as bis-(norborn-2-ene-5-methoxy)alkanes, di(norborn-2-ene-5-methyl)ether, and 1,3-di(norborn-2-ene-5-methoxy)benzene. The resulting unsaturated ROMP (U-ROMP) resins containing olefin repeat units were chemically modified using hydrogenation, hydrofluorination, chlorination, and bromination reactions to produce saturated ROMP resins with different chemical and physical properties. The hydrogenated ROMP (H-ROMP) resin was found to be highly resistant to acidic, basic, Lewis acid, and Birch reduction conditions and was assessed as a polymeric support in a series of solid-phase synthetic applications. The H-ROMP resin was found to have superior performance compared to polystyrene-divinylbenzene (PS-DVB) copolymers in aromatic nitration and acylation reactions. In a conventional five-step solid-phase synthesis of a hydantoin, similar results were obtained for both the H-ROMP and PS-DVB resins. The U-ROMP resin was also shown to be effective in the solid-phase syntheses of benzimidazoles and benzimidazolones.

Introduction

Ring-opening metathesis polymerization (ROMP)[1] is a well-defined living polymerization reaction that was first discovered by Karl Ziegler in the mid-1950s,[2] and the ring-opening polymerization of ring-strained norbornene monomers was later reported by Truett in 1960.[3] The synthesis of polymers with defined molecular weight and polydispersity, as well as of block and graft copolymers, can be easily achieved using ROMP. Since the initial discovery and mechanistic elucidation of ROMP by Chauvin (Chauvin mechanism) in 1970,[4,5] the ROMP reaction has been extensively studied. Many fundamental breakthroughs have accelerated the development of high-performance catalysts with good stability and functional group tolerance. Several transition metals have been investigated for the development of new catalysts;[6] however, most research has been focused on three transition-metal species, namely the molybdenum and tungsten alkylidene complexes developed by Schrock[7] and the ruthenium alkylidene complexes introduced by Grubbs.[8] While tungsten- and molybdenum-based catalysts have higher catalytic activity than ruthenium-based catalysts, they are unstable and rapidly deactivate in moisture and air due to high oxophilicity.[9] These early transition-metal alkylidene complexes also have low tolerance to monomers containing hydroxyl, amine, carboxylic acid, ester, and amide functionalies as well as high sensitivity to protic polar solvents. In contrast, the ruthenium-based systems developed by Grubbs[10] exhibit higher stability toward protic functionalities compared to the molybdenum and tungsten analogues.[7,11]

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With advances in catalysts for ROMP reactions, applications of ROM polymers, especially norbornene-based, have been widened to various fields such as ROM polymer-supported reagents[12] (known as ROMPGELs) and catalysts[13] for organic reactions, high-throughput parallel synthesis,[14] molecular recognition,[15] separation techniques,[16] peptide synthesis,[17] and biological sciences.[18]

Styrene-based polymers such as polystyrene-*co*-divinylbenzene (PS-DVB) resin and more recently *J*anda*J*els[19] are the most popular and commercially available materials for polymer-assisted organic synthesis and are frequently utilized because of their well-defined preparation procedures and properties such as free-flowing handling, good swelling, and physical/chemical stability. Polystyrene resins are inexpensive and can be easily prepared by radical polymerization in a biphasic aqueous suspension system to yield spherical beads that are resistant to mechanical breakdown into fines that could potentially clog automated synthesis equipment or flow through reactors. ROMP methodology offers an alternative route for the preparation of resin beads by biphasic aqueous suspension polymerization. In particular, ruthenium-based Grubbs' catalysts, because of their stability in moisture and air, have been used in the polymerization of functionalized norbornenes and 7-oxanorbornenes even in aqueous media,[20] and examples of cross-linked ROM polymer latexes produced by suspension or emulsion polymerization have been described.[21] However, these latex-type polymers are not in a suitable form to use and handle in a typical solid-phase organic chemistry type setting. Bead-type resins prepared by grafting functionalized norbornenes on the surface of silica and polystyrene resins (called ROMP−Spheres) have been reported by Buchmeiser[22] and Barrett[23] and have found use as solid-supported catalysts and reagents in organic synthesis.

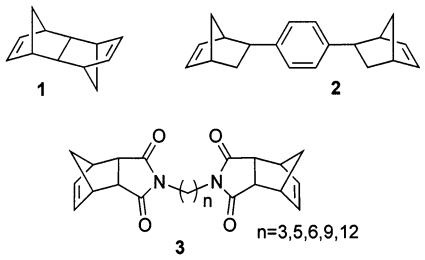

FIGURE 1. Common ROMP cross-linking monomers.

Several cross-linkers with varying degrees of complexity have been reported in the literature to prepare insoluble norbornene-based polymers, Figure 1,[12b] including 1,4,4a,5,8,8a-hexahydro-1,4,5,8-*exo*-*endo*-dimethanonaphthalene **1**[13] and 1,4-di(norborn-2-en-5-yl)benzene **2**.[24] A recent patent details the preparation of ROM polymers with better swelling properties using bis(*N*-alkylenedicarboxyimidonorbornene) **3**[17] as a cross-linker to give the ROM polymer more flexibility. However, we note that resins prepared using a cross-linker exemplified by **3** may not be suitable for general use because the carboximide moiety is not chemically inert.

In considering a new resin design based on norbornene monomers, one must ultimately consider resin reactivity with external reagents and catalysts. The unsaturated ROMP (labeled as U-ROMP) resins obtained from norbornene-based monomers have reactive olefin units in their backbone, thus limiting their application in solid-phase organic synthesis (SPOS). However, these olefin units can be chemically modified by reactions such as hydrogenation and halogenation. In particular, a hydrogenated H-ROMP resin would consist of only aliphatic hydrocarbons and should be stable to many of the harsh reaction conditions that are incompatible with polystyrene resins, and this would greatly expand the repertoire of chemical reactions available to the solid-phase synthetic chemist. For example, polystyrene has aromatic and benzylic groups within its matrix; therefore, common chemical reactions such as electrophilic aromatic substitution and radical substitution and oxidation cannot be easily adapted to these resins. Accordingly, a few reports of nonpolystyrene resins such as polyethers have recently been described and have shown promising results in applications such as Friedel−Crafts acylation and Birch reduction.[25]

Herein, we report the preparation of norbornene-based cross-linkers, the preparation of cross-linked hydroxyl-

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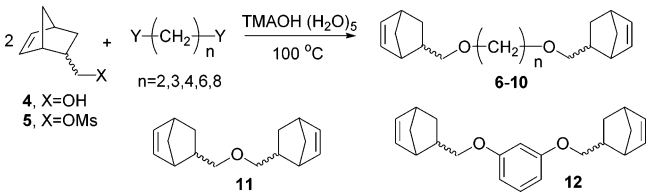
TABLE 1. Yields of Cross-Linkers Prepared

cross- linker	*n*	X	Y	time/h	yield/%
6	2	OMs	OH	12	13
7	3	OH	Br	10	14
8	4	OH	Cl	1.5	66
9	6	OH	Br	12	20
10	8	OH	Br	3	55
11		OMs		16	57
12		OMs	OH	12	59

SCHEME 1



functionalized ROMP resin beads by suspension polymerization, and the chemical modification of these polymers using hydrogenation, hydrofluorination, chlorination, and bromination reactions. In addition, the application of ROMP based resins as supports for electrophilic aromatic substitution reactions and for the synthesis of organic scaffolds is presented.

Results and Discussion

The preparation of norbornene-based cross-linking elements with ether linkages was critical to the development of ROMP resin that possesses the desired physical properties for SPOS applications. For the synthesis of these molecules, several ether formation conditions were investigated;[26] however, in all cases, the reaction did not take place. The only viable route we have found to the norbornene cross-linkers **6**−**10** utilized tetraalkylammonium hydroxide as the base under solvent-free conditions, Scheme 1. Using this procedure, cross-linker **6** was prepared from norborn-2-ene-5-methyl mesylate **5** and ethylene glycol in 13% yield, and a series of cross-linkers **7**−**10** were prepared by reaction of norborn-2-ene-5-methanol **4** (a mixture of *exo*- (38%) and *endo*- (62%) isomers) with the appropriate dihaloalkanes in 14−66% yields, Table 1. Dimerization of **5** gave cross-linker **11** in 57% yield, and **12** was obtained in 59% yield by heating a mixture of **5** and resorcinol in the presence of 5 equiv of K_2CO_3 in DMF. Finally, although the yields for some of the cross-linkers synthesized were marginal, we note that cross-linker **11**, one of the best yielding products prepared in a single step, was ultimately found to provide the most desirable properties (vide infra) for bead preparation and synthetic evaluation. For the suspension-ROMP experiments, we evaluated both the first- and second-generation Grubbs' ruthenium catalysts **13** and **14**, Figure 2. Although the first-generation catalyst **13** gave some polymeric product, it appeared that the cross-linker failed to be incorporated into the polymer and only soluble material was formed.

When the second-generation Grubbs' catalyst **14** was used, the desired cross-linked, insoluble resins were obtained in good yields, Scheme 2, Table 2. A series of polymers with different loading levels and cross-linker ratios were synthesized from norbornene **15**, norborn-2-

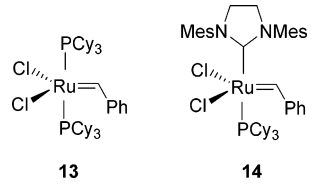
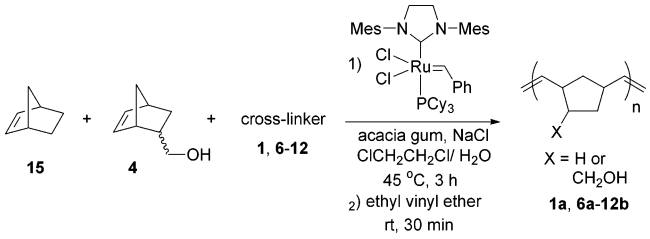


FIGURE 2. Grubbs' first- and second-generation catalysts.

SCHEME 2



ene-5-methanol **5**, and cross-linkers **1** and **6**−**12** using catalyst **14** (monomers/catalyst = 1000:1) in 1,2-dichloroethane. All 14 resins were prepared with 1−2 mol % cross-linker and a theoretical loading of 1 mmol/g of the hydroxy group, except for **8d** (8 mmol/g) and **8c** (5% cross-linker), in yields ranging from 33 to 97%. All the beads were slightly gray in color and were free flowing and spherical, Figure 4.

Some of the important reaction parameters needed for obtaining spherical resin beads were as follows: (i) the method of addition of the catalyst, (ii) the amount of surfactant (acacia gum), (iii) choice of solvent, and (iv) mixing parameters. Since polymerization occurs immediately after the addition of the catalyst, the catalyst was added only after the organic phase was completely suspended in the aqueous phase. When a homogeneous solution of catalyst dissolved in either 1,2-dichloroethane or toluene was added to the suspended monomer mixture, low polymerization yield and a large mass of aggregated beads were obtained. Adding a colloidal suspension of catalyst in methanol into a presuspended monomer mixture was critical to provide optimal yields of the desired resins. The surfactant concentration also played a critical role in the formation of spherical beads, and the optimum concentration of surfactant was found to be 30 g/L. At lower concentrations of surfactant, the droplets were unstable and coalesced, and an aggregated mass of polymer was produced. When larger amounts of surfactants were used, the polymerization yield was low, possibly due to the inability of the catalyst to penetrate the stabilized droplets. When toluene was used as a solvent, the resultant beads aggregated on top of suspension regardless of the amount of surfactant. Consistent with reported observations,[27] when a denser solvent such as 1,2-dichloroethane was used (organic phase occupied lower region), no aggregation was observed. Moreover, mechanical agitation with small blades was also required to avoid aggregation of the beads (Figure 3). A picture of

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TABLE 2. Preparation Yield and Swollen Volumes of U-ROMP Resins

resin	cross-linker (mol %)	yield/%	loading (mmol/g)[a]	volume of swollen resin (mL/g)[b]					
				THF	dioxane	benzene	CH_2Cl_2	DMF	*n*-hex
1a	**1** (1)	72	1	6.7	3.6	6.2	6.0	2.3	3.0
6a	**6** (1)	33	1	10.6	5.1	10.1	9.2	2.7	4.1
5a	**7** (1)	77	1	9.7	4.7	6.5	6.8	3.5	3.5
8a	**8** (1)	46	1	7.5	3.8	5.2	5.8	2.8	4.2
8b	**8** (2)	55	1	6.4	4.2	4.4	4.9	3.1	2.9
8c	**8** (5)	75	1	5.1	3.8	4.6	4.6	2.9	3.0
8d	**8** (1)	97	8[c]	4.6	4.1	3.4	3.9	7.0	2.9
9a	**9** (1)	51	1	6.0	4.1	4.6	4.4	2.8	2.8
9b	**9** (2)	44	1	8.9	3.9	8.0	7.6	2.2	4.1
10a	**10** (1)	63	1	6.1	4.7	6.1	5.9	3.4	2.8
11a	**11** (1)	80	1	12.1	5.8	9.5	9.2	3.1	4.9
11b	**11** (2)	79	1	8.5	4.4	6.6	6.3	3.4	3.9
12a	**12** (1)	66	1	8.0	4.3	7.1	6.3	2.6	3.7
12b	**12** (2)	71	1	7.4	3.5	5.1	4.9	3.1	4.1
MF[d]			1	6.4	6.0	6.6	6.0	4.8	
J-*J*[e]			1	14.0	14.8	14.6	15.0	10.4	

[a] Theoretical mmol of hydroxy group per gram. [b] The swollen volume was determined in a syringe equipped with a frit. [c] Resin was prepared from **5** and cross-linker **8**. [d] PS-DVB resin (1% cross-linked). [e] *J*anda*J*el (1% cross-linked).

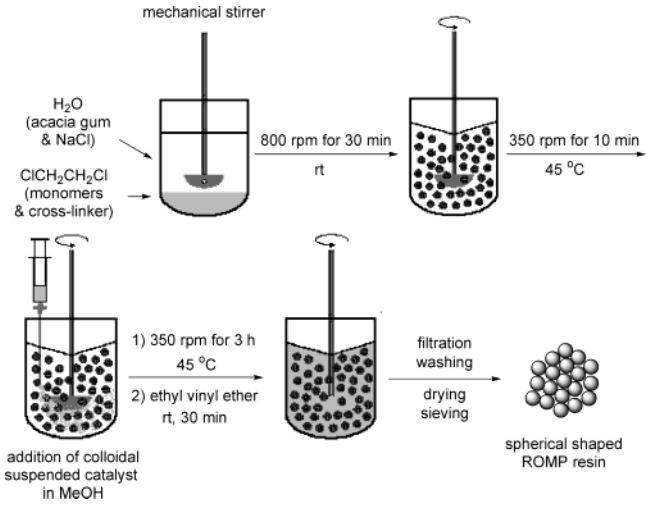

FIGURE 3. Schematic procedure for suspension-ROMP.

the beads isolated from the suspension ROMP reaction is shown in Figure 4.

The swelling of a polymer resin in commonly used solvents is an important criterion to determine if it will be suitable for SPOS applications.[28] Swollen volumes for all 14 ROMP resins in THF, dioxane, benzene, dichloromethane, DMF, and *n*-hexane are presented in Table 2. For comparison, the swelling volumes of 1% cross-linked PS-DVB resin and a 1% cross-linked *J*anda*J*el resin are also shown. The swelling of the new ROMP resins compares favorably to the PS-DVB resin but is lower than *J*anda*J*el. As expected, resin **1a** prepared with the less flexible cross-linker **1** exhibited lower swelling compared to the resins prepared from flexible cross-linkers **6**−**12**. In addition, a higher loading (8 mmol/g) resin **8d** exhibited slightly lower swelling than a similar resin **8a** that was prepared with a loading of 1 mmol/g. The highest swelling resin **11a** that was prepared with 1 mol % cross-linker **11** was selected for further evaluation in a solid-phase application and also for further chemical modification of the residual olefin bonds.

The residual olefin groups in unsaturated resin **11a** (U-ROMP) served as a starting point to chemically and physically tune the properties of the parent polymer. Accordingly, four daughter resins were prepared from the parent unsaturated (U-ROMP) polymer **11a** using hydrogenation, hydrofluorination, chlorination, and bromination reactions, Scheme 3. The fully saturated (H-ROMP) resin **16** was obtained placing U-ROMP **11a** under an atmosphere of hydrogen at high pressure (150 psi) in the presence of Wilkinson's catalyst.[29] Complete reduction of all olefins in the polymer backbone was difficult to achieve, and extended reaction times of 7 days were required to ensure complete hydrogenation. Although alternative conditions for hydrogenation of ROMP materials using diimide reducing agents have been developed,[30] in our application this methodology did not give acceptable conversions into the hydrogenated polymer product. Hydrofluorinated ROMP resin **17** was prepared by direct addition of anhydrous hydrogen fluoride to U-ROMP resin **11a**, performed within a peptide cleavage apparatus. To prepare the chlorinated **20** and brominated ROMP resins **22**, the alcohol functional group of starting U-ROMP resin **11a** was first protected as its trifluoroacetate **18** in order to prevent potential side reactions such as oxidation and alkoxyhalogenation. A suspension of the TFA ester resin **18** was then treated with molecular bromine or chlorine followed by deprotection of the ester group to yield the halogenated polymers **20** and **22**, Scheme 3.

In all cases, complete consumption of the olefin group was confirmed by gel-phase NMR and IR spectroscopy. The loading of the hydroxyl group estimated using DMT quantification[31] was 0.90, 0.77, 0.55, and 0.37 mmol/g for the hydrogenated **16**, hydrofluorinated **17**, chlorinated **20**, and brominated **22** resins, respectively. The resulting beads were all free flowing and had the same spherical shape as U-ROMP resin **11a**. The swollen volumes of

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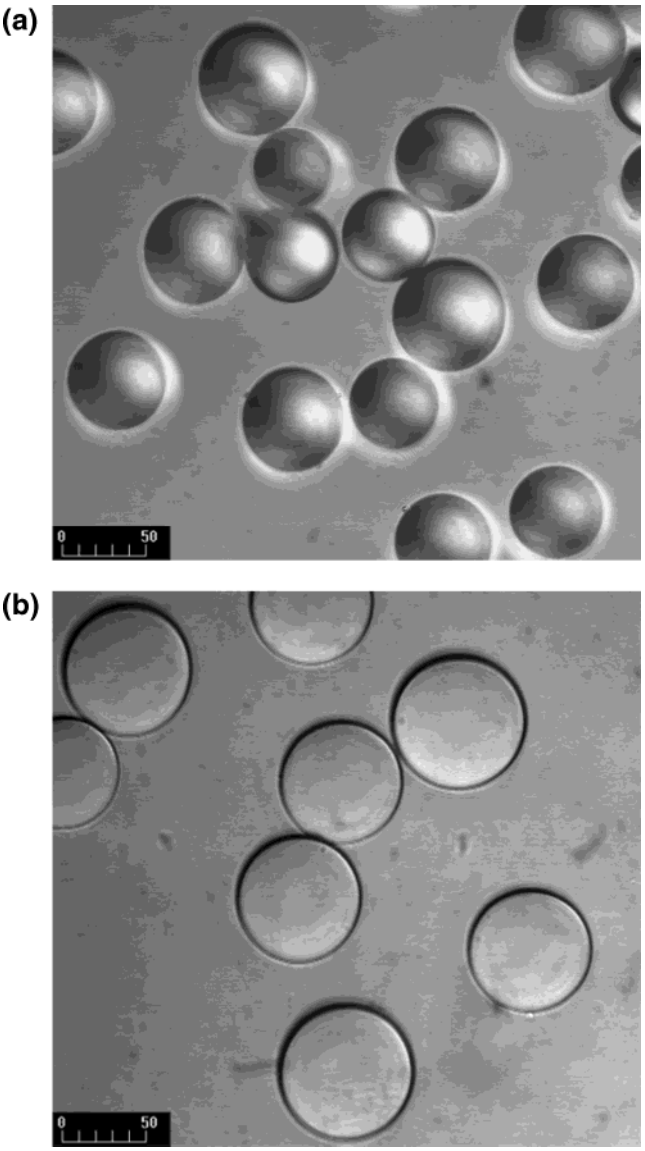
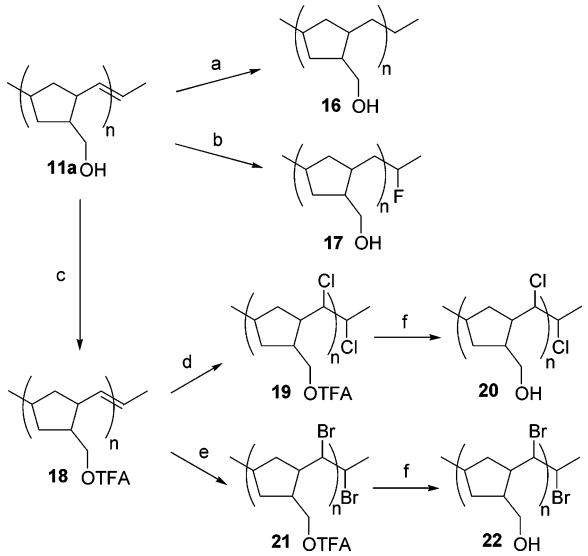


FIGURE 4. (a) Microscope image of beads of unsaturated ROMP resin **11a** obtained by suspension polymerization after sieving. (b) Microscope image of beads of ROMP resin **16** swollen in dioxane.

these saturated ROMP resins and U-ROMP resin in various solvents are shown in Table 3. The ROMP resins **16**, **17**, **20**, and **22** typically have slightly lower swollen volumes compared to the parent U-ROMP resin **11a** in all solvents except DMF, Table 3. These saturated ROMP resins also have lower swollen volumes compared to the PS-DVB and *J*anda*J*el resins (Table 2).

To select a suitable polymeric support that would be chemically durable in SPOS applications, the chemical stability of U-ROMP **11a**, H-ROMP **16**, and chlorinated ROMP **20** resins was tested under harsh acidic and basic conditions. The hydrofluorinated **17** and brominated **22** resins were excluded from these studies because of their poor swelling properties. When subjected to basic conditions such as 10% tetrabutylammonium hydroxide (condition A)[32] and 3% NaH in THF (condition B), U-ROMP and H-ROMP resins remained intact, while the chlorinated resin lost about 30% of the dry weight, presumably because of the elimination of HCl from the resin. All

SCHEME 3 [a]



[a] Reagents and conditions: (a) $RhCl(PPh_3)_3$ (2 mol %), H_2 (150 psi), THF, rt, 7 d; (b) HF, CH_2Cl_2, 0 °C, 2 h; (c) TFAA, Et_3N, CH_2Cl_2, −10 °C to rt, 1 h 30 min; (d) Cl_2, CH_2Cl_2, rt, 1 h; (e) Br_2, CH_2Cl_2, −10 °C to rt, 1 h; (f) K_2CO_3, MeOH/THF (1:10), rt, 15 h.

resins were not affected by 10% piperidine/THF solution (condition C). When these resins were treated with a TFA solution (condition D), addition of TFA to the olefins of U-ROMP resin **11a** occurred on the basis of weight increase as well as the appearance of intense carbonyl peak (1775 cm^{-1}) and the disappearance of olefin absorption (2995 cm^{-1}) in IR spectra.[33] On the contrary, an addition reaction did not occur in 10% H_2SO_4/THF solution (condition E). The H-ROMP and chlorinated ROMP resins were not affected by these acidic conditions. Additional tests were conducted to compare the H-ROMP resin with the two polystyrene resins, PS-DVB resin and *J*anda*J*el. In BBr_3/CH_2Cl_2 solution (condition F), *J*anda*J*el degraded into a homogeneous solution presumably because of the aryl ether cross-linker cleavage, while there were no physical or chemical changes to the PS-DVB and hydrogenated ROMP resin **16**. Both of the polystyrene-based resins were severely degraded in sodium in liquid ammonia solution (condition G) and the resulting polymers exhibited different IR and swelling properties; however, under these conditions, the H-ROMP resin remained intact. These results show that the H-ROMP resin is a robust inert support able to withstand harsh reaction conditions.

The solid-phase synthesis of benzimidazole **27** and benzimidazolone **29** was carried out using the U-ROMP support **11a** according to literature precedent, Scheme 4.[34,35] The olefin functional groups embedded in this resin is not affected by the reaction conditions used in this synthesis. To begin the synthesis, substrate **23** was

(32) Test conditions (50 mg of resin was used in each case): (A) 10% TBAOH/THF, 60 °C, 4 h; (B) 3% NaH/THF (w/v), rt, 4 h; (C) 10% piperidine/THF, 60 °C, 4 h; (D) 50% TFA/toluene, 100 °C, 4 h; (E) 10% H_2SO_4/THF, rt, 4 h; (F) BBr_3, CH_2Cl_2, rt, 1 h; (G) Na, 50% NH_3/THF, −30 °C, 3 h.

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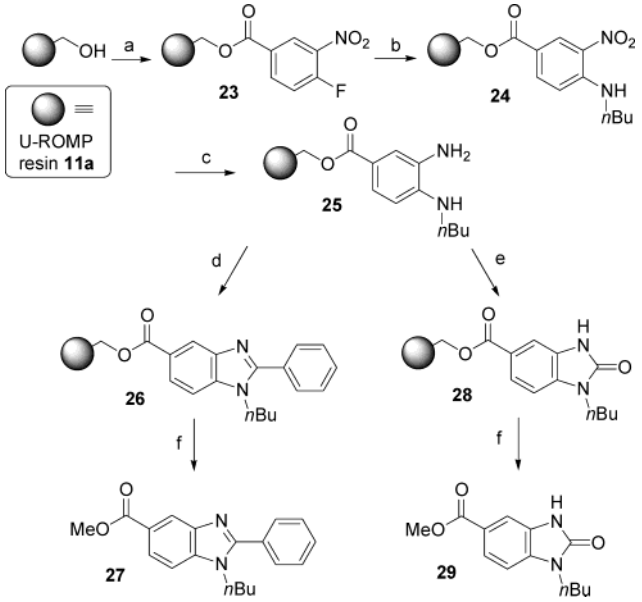
TABLE 3. Swollen Volumes of Saturated ROMP Resins

	resin	loading[a] (mmol/g)	volume of swollen resin (mL/g) THF	dioxane	benzene	CH_2Cl_2	DMF	*n*-hex
16	hydrogenated	0.90	7.3	2.5	5.0	4.1	2.4	2.4
17	hydrofluorinated	0.77	3.8	2.8	3.8	4.1	2.8	3.0
20	chlorinated	0.52	6.2	4.2	3.6	4.2	4.7	1.7
22	brominated	0.37	3.2	1.8	1.8	2.9	3.3	1.4
11a	unsaturated	0.94	12.1	5.8	9.5	9.2	3.1	4.9

[a] Average value determined using DMT quantification.

SCHEME 4[a]

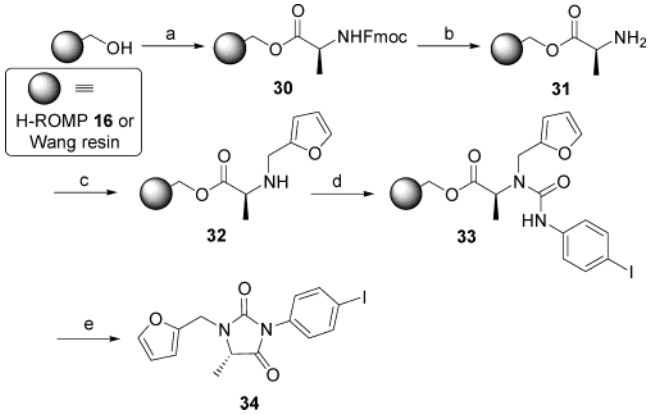


[a] Reagents and conditions: (a) 4-fluoro-3-nitrobenzoic acid, DIC, DMAP, CH_2Cl_2, rt, 12 h; (b) *n*-$BuNH_2$, Et_3N, CH_2Cl_2, rt, 3 h; (c) $SnCl_2{\cdot}(H_2O)_2$, THF, rt, 36 h; (d) PhCHO, CAN, THF, rt, 24 h; (e) triphosgene, Et_3N, CH_2Cl_2, rt, 4 h; (f) 0.5 M NaOMe/MeOH, THF, 50 °C, 1 h 30 min.

prepared by the reaction of hydroxy U-ROMP resin **11a** and 4-fluoro-3-nitrobenzoic acid using diisopropylcarbodiimide (DIC) and a catalytic amount of DMAP. Nucleophilic replacement of fluoride with *n*-$BuNH_2$ generated **24**, which was reduced to 1,2-phenyldiamine **25** by using 10 equiv of tin(II) chloride dihydrate. After reduction, the resulting diamine **25** was treated with benzaldehyde and cerium ammonium nitrate (CAN) to afford the corresponding polymer-bound benzimdazole **26**, and subsequent cleavage with NaOMe gave the desired benzimidazole product **27** in 74% yield and 96% purity. Polymer-bound diamine **25** was also treated with triphosgene and cleaved in a similar fashion to afford benzimadazolone **29** in 82% yield and 87% purity. Both of these results compare well with the reported values for syntheses performed on Lantern[33] and PS-DVB supports.[34]

We also compared the saturated H-ROMP resin **16** with a commercially available styrene-based Wang resin for the solid-phase synthesis of a hydantoin as a model reaction, Scheme 5.[36] This reaction sequence was considered a good testing ground for our resin since a diverse set of solvents such as dichlromethane, THF, DMA, DMF,

SCHEME 5[a]



[a] Reagents and conditions: (a) Fmoc-D-Ala-OH, DIC, DMAP, CH_2Cl_2, rt, 24 h; (b) 10% piperidine/THF, rt, 1 h; (c) (i) 2-furaldehyde, 1% AcOH/DMA, rt, 1 h, (ii) $NaBH_3CN$, rt, 12 h; (d) 4-iodophenyl isocyanate, DMF/toluene (1:1), rt, 5 h; (e) $(i\text{-Pr})_2NH$/THF (1:1), rt, 12 h.

and toluene are used throughout the synthesis. Despite the H-ROMP resin **16** having slightly inferior swelling characteristics compared to the Wang resin, the desired hydantoin **34** was isolated from both resins in comparable yields (80 and 84% yield from H-ROMP **16** and Wang resins respectively) and in similar purity (92%).

Since the norbornene-based H-ROMP resin **16** does not possess olefin or aromatic groups within the polymer matrix, we considered this polymer to be an ideal platform to perform support-bound electrophillic aromatic substitution reactions such as Friedel−Crafts acylation and aromatic nitration reactions. Both the H-ROMP resin and a 5-hydroxypentyl PS-DVB resin[37] were converted to the phenoxy-substituted resins **35** using Mitsunobu conditions,[38] Scheme 6. Acylation of **35** was carried out with 3 equiv of benzoyl chloride and 2 equiv of $AlCl_3$ for 3 h. The product 4-hydroxybenzophenone **37** was obtained by cleavage of the ether linkage using boron tribromide in chloroform at reflux. The regioisomer product, 2-hydroxybenzophenone, was not detected. However, we note that the regioisomer may be more prone to cleavage during acylation because of selective *ortho*-dealkylation.[39] Clearly, these chemical limitations are a disadvantage; however, they are inherent to both resins and still allow a valid comparison between the two supports.

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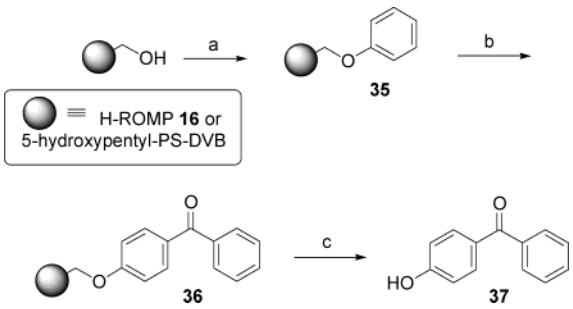
(39) Farkas, L.; Gottsegen, Á.; Nógrádi, M.; Strelisky, J. *Tetrahedron* **1971**, *27*. 5049−5054.

SCHEME 6 [a]



[a] Reagents and conditions: (a) PhOH, DIAD, PPh_3, THF, rt, 24 h; (b) PhCOCl, $AlCl_3$, CH_2Cl_2, rt, 3 h; (c) BBr_3, $CHCl_3$, reflux, 12 h.

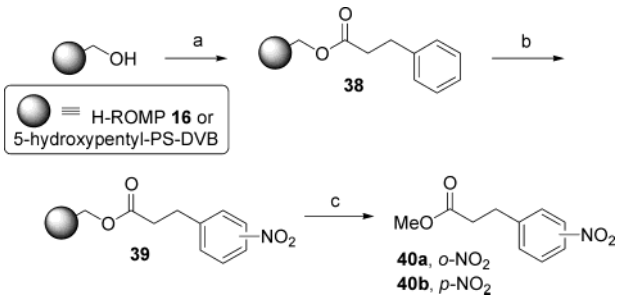
TABLE 4. Acylation of Polymer-Supported Compound 36

	yield (%)		purity (%)	
	H-ROMP	PS-DVB	H-ROMP	PS-DVB
37	42	24	85	42
phenol	6	25	14	38
total	48	49	99	80

Yields of 4-hydroxybenzophenone **37** were 42 and 24% for the H-ROMP **16** and the PS-DVB resins, respectively, Table 4. The lower yields for the PS-DVB resins can be attributed to the competitive acylation of the aromatic backbone of the polystyrene support[40] in addition to the premature cleavage of the ether linkage. Although some phenol impurity originated from the incomplete acylation reaction was observed within the cleavage product **37** (6 and 25% for H-ROMP and PS-DVB resins, respectively), the purity of **37** obtained from the H-ROMP resin (**37**/phenol = 85:14) was significantly higher than the purity of the acylation product **37** cleaved from the PS-DVB resin (**37**/phenol = 42:38). On the basis of yield and purity, the results clearly show the superior performance of the H-ROMP resin as compared to the PS-DVB resin in a solid-phase Friedel−Crafts reaction.

Shackelford and co-workers have recently reported an efficient method for the nitration of aromatic compounds that can be performed under anhydrous conditions.[41] In this reaction, tetramethylammonium nitrate ($TMANO_3$) and triflic anhydride are used in place of the commonly used nitrating reagent HNO_3/H_2SO_4. We utilized this procedure in order to assess the utility of our H-ROMP resin compared to PS-DVB polymer supports in an electrophilic aromatic nitration reaction, Scheme 7. The H-ROMP and PS-DVB polymer-bound hydrocinnamates **38** were obtained by treatment of each resin with hydrocinnamoyl chloride in the presence of triethylamine. Next, each of the polymer-bound hydrocinnamates **38** was treated under our modified conditions whereby 3 equiv of tetrabutylammonium nitrate ($TBANO_3$) and excess triflic anhydride were used. In the case of the PS-DVB resin, additional experiments using 6 equiv of reagents were also carried out. After the nitration reaction was complete, the compounds were cleaved by transesterification using NaOMe in anhydrous THF to provide the nitration products as a mixture of regioisomers, *o*-**40a** and *p*-nitro cinnamates **40b**, Table 5. Using 3 equiv of the nitrating reagent, the combined yield of **40a** and **40b** was 59% (**40a**, 35%; **40b**, 24%) for the H-ROMP resin with 4% unreacted methyl hydrocinnamate in the reaction mixture. Under similar reaction conditions on the PS-DVB resin, the combined yield of **40a** and **40b** was 14% (**40a**, 9%; **40b**, 5%) with 42% unreacted methyl hydrocinnamate in the reaction mixture. For the H-ROMP resin, product purity was 87% (**40a**, 51%; **40b**, 36%) with 4% of methyl hydrocinnamate. For the PS-DVB resin, even when 6 nitrating equivalents were used, the combined yield for products **40a** and **40b** of 28% (**40a**, 18%; **40b**, 10%) was obtained with purity of 49% (**40a**, 27%; **40b**, 22%) containing 24% methyl hydrocinnamate. Thus, even using larger equivalents of the nitrating reagent, the yield and purity of the products was considerably lower using the PS-DVB resin than that obtained with the H-ROMP resins. Again, we attribute the lower yields for the PS-DVB resin to the competitive nitration of the aromatic backbone of the parent polymer as confirmed by the presence of significant nitro peaks (1516, 1343 cm^{-1}) in IR spectra of this resin after cleavage.

SCHEME 7 [a]



[a] Reagents and conditions: (a) hydrocinnamoyl chloride, Et_3N, CH_2Cl_2, 0 °C to rt, 6 h; (b) $TBANO_3$, Tf_2O, CH_2Cl_2, −10 °C to rt, 3 h; (c) (i) 0.5 M NaOMe/MeOH, THF, 50 °C, 3 h, (ii) MeI, rt, 1 h.

Conclusions

A series of spherical, cross-linked polymer resins for application in solid-phase organic synthesis have been successfully prepared by the suspension ROMP reaction of norbornene and functionalized norbornene monomers. The preparation of these resins is straightforward and inexpensive, and therefore, these resins could be produced in bulk. The fully saturated H-ROMP resin was prepared from the unsaturated ROMP resins and has been shown to be chemically inert, and unlike styrene-based resins, the backbone of the hydrogenated ROMP resin does not interfere in electrophilic aromatic substitutions such as Friedel−Crafts acylation and nitration. Potentially, the H-ROMP resin could be utilized as supports under numerous other reaction conditions that are inherently incompatible with polystyrene based polymers. We are currently evaluating this exciting class

(40) After cleavage of the desired product from the PS-DVB resin, this resin exhibited an absorption at 1649 cm^{-1} in IR spectra suggesting the formation of the polymer-bound benzophenone product from the competing acylation reaction.

(41) Shackelford, S. A.; Anderson, M. B.; Christie, L. C.; Goetzen, T.; Guzman, M. C.; Hananel, M. A.; Kornreich, W. D.; Li, H.; Pathak, V. P.; Rabinovich, A. K.; Rajapakse, R. J.; Truesdale, L. K.; Tsank, S. M.; Vazir, H. N. *J. Org. Chem.* **2003**, *68*, 267−275.

TABLE 5. Nitration of Polymer-Supported Compound 39

	yield (%)			purity (%)		
	H-ROMP	PS-DVB		H-ROMP	PS-DVB	
	3 equiv	3 equiv	6 equiv	3 equiv	3 equiv	6 equiv
40a	35	9	18	51	12	27
40b	24	5	10	36	10	22
methyl hydrocinnamate	4	42	20	4	48	24

of resins in multiple applications and these results will be published in due course.

Experimental Section

General Procedure for Preparing Cross-Linkers 6−10. A mixture of norborn-2-ene-5-methanol (**4**, 1.03 g, 8.27 mmol), 1,4-dichlorobutane (0.45 mL, 4.14 mmol), and tetramethylammonium hydroxide (7.49 g, 41.35 mmol) was stirred for 1 h 30 min at 100 °C. Water (200 mL) was added to the mixture before the mixture solidified. The aqueous phase was extracted with EtOAc (30 mL × 3). The combined extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography (eluted with 20% EtOAc/*n*-Hex) to yield 1,4-bis(norborn-2-ene-5-methoxy)butane (**8**, 0.83 g, 66%, the mixture of 6 diastereomers) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ (relative integral) 0.43−0.47 (m, 1.2H), 1.04−1.09 (m, 0.8H), 1.18−1.28 (m, 2.1H), 1.27−1.28 (m, 1.5H), 1.37−1.40 (m, 1.9H), 1.57−1.68 (m, 5.3H), 1.75−1.81 (m, 1.5H), 1.27−2.34 (m, 1.3H), 2.71 (s, 0.7H), 2.75 (br s, 2.1H), 2.88 (br s, 1.3H), 2.98 (t, J = 9.2 Hz, 1.3H), 3.10 (dd, J = 9.2, 6.8 Hz, 1.3H), 3.28 (t, J = 9.0 Hz, 0.9H), 3.32−3.46 (m, 4.9H), 5.90 (dd, J = 5.8, 3.0 Hz, 1.3H), 6.02 (dd, J = 5.8, 3.0 Hz, 0.7H), 6.06−6.09 (m, 2.0H); MS (ESI) m/z 325 [M + Na]$^+$, 304 [M + H]$^+$.

1,2-Bis(norborn-2-ene-5-methoxy)ethane (6). From norborn-2-ene-5-methoxy mesylate (**5**) and ethylene glycol was obtained **6** in 13% yield as a colorless oil (a mixture of six diastereomers): ^{1}H NMR ($CDCl_3$) δ (relative integral) 0.43−0.47 (m, 1.0H), 1.04−1.09 (m, 1.1H), 1.17−1.22 (m, 2.4H), 1.27 (s, 2.1H), 1.36−1.39 (m, 1.1H), 1.74−1.80 (m, 1.1H), 2.31−2.34 (m, 1.0H), 2.72−2.75 (m, 3.0H), 2.87 (br s, 1.0H), 3.05 (td, J = 9.1, 3.5 Hz, 1.0H), 3.14−3.18 (m, 1.0H), 3.34 (td, J = 9.2, 2.3 Hz, 1.0H), 3.46−3.59 (m, 5.1H), 5.89−6.09 (m, 4.0H); MS (EI) m/z 274 [M]$^+$, 209, 143, 107.

1,3-Bis(norborn-2-ene-5-methoxy)propane (7). From norborn-2-ene-5-methanol **4** and 1,3-dibromopropane was obtained cross-linker **7** in 14% yield as a colorless oil (a mixture of 6 diastereoisomers): ^{1}H NMR ($CDCl_3$) δ (relative integral) 0.43−0.47 (m, 1.3H), 1.04−1.09 (m, 0.9H), 1.18−1.25 (m, 2.8H), 1.27 (s, 1.7H), 1.38−1.40 (m, 1.4H), 1.63−1.66 (m, 0.8H), 1.74−1.85 (m, 4.2H), 2.27−2.33 (m, 1.3H), 2.70 (br s, 0.7H), 2.75 (br s, 1.9H), 2.87 (br s, 1.2H), 2.99 (t, J = 9.2 Hz, 1.4H), 3.10 (dd, J = 9.2, 6.8 Hz, 1.4H), 3.28 (t, J = 6.4 Hz, 0.9H), 3.37−3.52 (m, 7.1H), 3.94 (d, J = 5.6 Hz, 1.1H), 5.14 (d, J = 10.0 Hz, 0.5H), 5.24 (d, J = 18.8 Hz, 0.5H), 5.85−6.09 (m, 4.0H); MS (EI) m/z 288 [M]$^+$, 223, 157, 117.

1,6-Bis(norborn-2-ene-5-methoxy)hexane (9). From **4** and 1,6-dibromohexane was obtained cross-linker **9** in 20% yield as a colorless oil (a mixture of six diastereoisomers): ^{1}H NMR ($CDCl_3$) δ (relative integral) 0.41−0.46 (m, 1.4H), 1.03−1.08 (m, 0.9H), 1.17−1.22 (m, 2.4H), 1.27 (m, 1.7H), 1.29−1.39 (m, 6.0H), 1.49−1.57 (m, 4.6H), 1.62−1.65 (m, 1.0H), 1.74−1.80 (m, 1.4H), 2.26−2.32 (m, 1.3H), 2.70 (br s, 0.8H), 2.74 (br s, 2.1H), 2.86 (br s, 1.3H), 2.96 (t, J = 9.0 Hz, 1.4H), 3.09 (dd, J = 9.0, 6.6 Hz, 1.4H), 3.24−3.44 (m, 6.3H), 5.89 (dd, J = 5.6, 2.8 Hz, 1.3H), 6.01 (dd, J = 5.6, 3.2 Hz, 0.8H), 6.06−6.09 (m, 2.0H); HRMS (MALDI-FTMS) m/z = 353.2458 [M + Na]$^+$, calcd for $C_{22}H_{34}O_2Na$ = 353.2451.

1,8-Bis(norborn-2-ene-5-methoxy)octane (10). From **4** and 1,8-dibromooctane was obtained cross-linker **10** in 55% yield as a colorless oil (a mixture of six diastereoisomers): ^{1}H NMR ($CDCl_3$) δ (relative integral) 0.42−0.47 (m, 1.2H), 1.04−1.08 (m, 0.8H), 1.18−1.39 (m, 13.6H), 1.48−1.52 (m, 5.0H), 1.61−1.66 (m, 0.9H), 1.74−1.80 (m, 0.3H), 2.27−2.33 (m, 1.3H), 2.71 (br s, 0.8H), 2.75 (br s, 2.1H), 2.87 (br s, 1.2H), 2.97 (t, J = 9.2 Hz, 1.4H), 3.09 (dd, J = 9.4, 6.6 Hz, 1.4H), 3.24−3.45 (m, 7.2H), 5.88−6.09 (m, 4.0H); MS (EI) m/z 358 [M]$^+$, 227, 107.

Di(norborn-2-ene-5-methyl) Ether (11). From the dimerization of **5** was obtained cross-linker **11** in 57% yield as a colorless oil (a mixture of six stereoisomers): ^{1}H NMR ($CDCl_3$) δ (relative integral) 0.42−0.48 (m, 1.0H), 1.03−1.10 (m, 1.2H), 1.17−1.28 (m, 2.5H), 1.28 (s, 2.3H), 1.38−1.40 (m, 1.1H), 1.53−1.54 (m, 1.8H), 1.74−1.81 (m, 1.1H), 2.29−2.34 (m, 1.1H), 2.71 (br s, 0.7H), 2.76 (br s, 2.5H), 2.86−2.91 (m, 1.2H), 2.93−3.50 (m, 5.3H), 5.90−6.09 (m, 4.0H); MS (EI) m/z 230 [M]$^+$, 165, 107.

1,3-Bis(norbornene-2-methoxy)benzene (12). A mixture of **5** (1.80 g, 8.90 mmol), resorcinol (478 mg, 4.34 mmol), and potassium carbonate (3.00 g, 21.71 mmol) in DMF (30 mL) was heated to 150 °C for 12 h. After being cooled to room temperature, the reaction was quenched by addition of water (150 mL), and this mixture was transferred to a separation funnel. The organic phase was separated, and the aqueous phase was extracted with EtOAc (100 mL × 3). The combined extracts were washed with saturated aqueous ammonium chloride (30 mL × 2), dried over Na_2SO_4, and concentrated under reduced pressure. Cross-linker **12** (830 mg, 59%, the mixture of six diastereomers) was isolated by flash column chromatography (eluted with 10% EtOAc/*n*-Hex) as a colorless oil: ^{1}H NMR ($CDCl_3$) δ (relative integral) 0.56−0.60 (m, 1.1H), 1.19−1.33 (m, 5.0H), 1.43−1.45 (m, 1.2H), 1.84−1.90 (m, 2.2H), 2.81−2.83 (br m, 3.0H), 3.00 (br s, 1.2H), 3.49 (td, J = 9.1, 3.1 Hz, 1.2H), 3.63−3.68 (m, 1.2H), 3.79 (td, J = 9.1, 3.5 Hz, 1.0H), 3.95−4.00 (m, 0.9H), 5.91−6.14 (m, 4.0H), 6.38−6.49 (m, 3.0H), 7.07−7.13 (m, 1.0H); HRMS (MALDI-FTMS) m/z = 323.2012 [M + H]$^+$, calcd for $C_{22}H_{27}O_2$ = 323.2005.

General Procedure for Preparing Cross-Linked U-ROMP Resin (11a). The aqueous phase used for the suspension polymerization reactions was prepared by dissolving acacia gum (30 g) and NaCl (10 g) in deionized water (1 L). This solution was then filtered to remove insoluble impurities and degassed for 15 min under vacuum while being sonicated. A 1 L flange flask equipped with three-necked lid was charged with 600 mL of the above aqueous solution. The apparatus was degassed and then placed under an atmosphere of argon. To this solution was added a solution of norbornene (**15**, 30.0 g, 318.16 mmol), norborn-2-ene-5-methanol (**5**, 4.37 g, 35.18 mmol), and cross-linker **11** (0.82 g, 3.54 mmol) in $ClCH_2CH_2Cl$ (40 mL). The organic suspension was stirred at 600 rpm and 45 °C and monitored for droplet size by microscope. Once the desired droplet size was formed, the stirring rate was reduced to 250 rpm. A colloidal suspension of Grubbs' second-generation catalyst **14** (303 mg, 0.36 mmol) in MeOH (3 mL) was quickly added to the mixture via syringe. After the mixture was stitted for 3 h at 45 °C, the heating bath was removed and the polymerization was terminated by addition of ethyl vinyl ether (10 mL). The reaction solution was cooled to room temperature and stirred for an additional 30 min. The crude resin beads were filtered with a 400-mesh sieve, washed with warm water several times, and then dried under vacuum. The resultant beads were washed by continuous extraction in Soxhlet apparatus with THF overnight, sequentially washed

with 50% MeOH/THF and MeOH, and dried under vacuum to give off-white U-ROMP resin (**11a**, 25.18 g, 72%). The dried resin was sieved in three size ranges: >40 mesh (3.44 g, 10%), 40−100 mesh (6.65 g, 26%), 100−200 mesh (10.67 g, 30%), 200−400 mesh (4.07 g, 12%). The hydroxyl loading of this resin (0.94 mmol/g) was obtained by DMT quantitation: ^{1}H NMR ($CDCl_3$) δ (relative integral) 0.98−1.00 (1.1), 1.31 (2.1), 1.76, 1.82 (3.7), 2.13 (0.5), 2.40 (0.9), 2.75 (1.3), 3.40 (0.1), 3.56 (0.1), 5.16 (1.2), 5.30 (1.0); ^{13}C NMR ($CDCl_3$) δ 32.2, 32.3, 32.9, 33.1, 37.2, 38.6, 41.3, 42.1, 42.7, 43.1, 43.4, 64.5, 133.0, 133.8; FTIR ν_{max} (cm^{-1}) 3380, 2995, 2938, 2861, 1445.

Hydrogenated ROMP resin (16). A mixture of U-ROMP resin (**11a**, 100−200 mesh, 10.00 g, 102.6 mmol of olefin) and $RhCl(PPh_3)_3$ (1.00 g, 1.08 mmol) was suspended in anhydrous THF (100 mL) and placed under hydrogen gas (200 psi) for 7 days at room temperature. The resin was collected by filtration and then washed with THF using a Soxhlet apparatus overnight. Pale yellow H-ROMP resin **16** (7.6 g) was obtained after drying under vacuum. ^{1}H NMR and IR were used to determine the extent of the hydrogenation. The hydroxyl loading of this resin (0.90 mmol/g) was obtained by DMT quantification: ^{1}H NMR ($CDCl_3$) δ (relative integral) 0.58−2.20 (br m, 31.4), 3.71 (br s, 1.0); ^{13}C NMR ($CDCl_3$) δ 31.7, 35.8, 40.4; FTIR ν_{max} (cm^{-1}) 3332, 2906, 2843, 1450.

Hydrofluorinated ROMP Resin (17). CH_2Cl_2 (10 mL) was added to a cylindrical Teflon reaction vessel containing U-ROMP resin **11a** (100 mg, 1.03 mmol of olefin) and a magnetic stirrer. The mixture was allowed to freeze in a liquid nitrogen bath. Excess liquid HF was added to the reaction vessel from an HF container. The mixture was warmed to 0 °C by replacing the liquid nitrogen bath with an ice bath, and the resulting mixture was stirred for 2 h at 0 °C. The resin was collected by filtration, washed with CH_2Cl_2 and MeOH, and dried under vacuum to give 118 mg of hydrofluorinated ROMP resin **17**. ^{1}H NMR and IR were used to determine the extent of the hydrofluorination. The hydroxyl loading of this resin (0.77 mmol/g) was obtained by DMT quantitation: ^{1}H NMR ($CDCl_3$) δ (relative integral) 0.80−0.86 (m, 1.6) 0.93 (d, J = 6.8 Hz, 0.5), 1.20−1.28 (m, 1.8), 1.46−1.70 (m, 1.8), 1.79−1.84 (m, 1.2), 3.69−3.73 (m, 1.0); ^{13}C NMR ($CDCl_3$) δ 14.1, 20.7, 22.7, 25.3, 25.59, 25.62, 34.5, 34.6, 68.0; FTIR ν_{max} (cm^{-1}) 3447, 2911, 2848, 1445.

Chlorinated ROMP Resin (20). Trifluoroacetyl-U-ROMP resin **18** was obtained by treatment of U-ROMP resin **11a** (1.00 g, 0.94 mmol of hydroxy group) with trifluoroacetic anhydride (0.66 mL, 4.70 mmol) in the presence of Et_3N (0.66 mL, 4.70 mmol) in CH_2Cl_2 (20 mL) for 3 h at −10 °C to room temperature, followed by collecting and washing with CH_2Cl_2 and MeOH and drying under vacuum. Chlorine gas was bubbled through a suspension of **18** (500 mg, 4.70 mmol of olefin) in CH_2Cl_2 (10 mL) through a needle from a chlorine cylinder for 30 min at room temperature. The resin was collected by filtration and washed with CH_2Cl_2 and MeOH, followed by drying under vacuum to give 830 mg of chlorinated trifluoroacetyl-ROMP resin **19**. The mixture of **19** (500 mg, 0.26 mmol of trifluoroacetyl group) and potassium carbonate (360 mg, 2.60 mmol) in 15 mL of 10% MeOH/THF was stirred for 12 h at room temperature. The resin was collected by filtration, washed with THF and MeOH, and dried under vacuum to give 440 mg of chlorinated ROMP resin **20**. ^{1}H NMR and IR were used to determine the extent of the chlorination. The hydroxyl loading of this resin (0.52 mmol/g) was obtained by DMT quantitation: ^{1}H NMR ($CDCl_3$) δ (relative integral) 1.20−2.11 (m, 5.6), 2.46 (br, 1.7), 2.76 (br, 0.8), 3.72 (2.0), 4.01−4.43 (1.7); ^{13}C NMR ($CDCl_3$) δ 29.0, 41.8, 45.4, 68.0, 69.2; FTIR ν_{max} (cm^{-1}) 3402, 2935, 2867, 1446.

Brominated ROMP Resin (22). To a suspension of **18** (500 mg, 4.70 mmol of olefin) in CH_2Cl_2 (20 mL) was added dropwise a solution of bromine (0.48 mL, 9.40 mmol) in CH_2Cl_2 (3 mL) at −10 °C. After the addition was completed, the cooling bath was removed, and the reaction was maintained for 30 min at room temperature. The resulting resin was filtered, washed with CH_2Cl_2 and MeOH, and dried under vacuum to give 1.22 g of brominated trifluoroacetyl-ROMP resin **21**. The mixture of **21** (1.00 g, 0.33 mmol of trifluoroacetyl group) and potassium carbonate (455 mg, 3.30 mmol) in 10% MeOH/THF (15 mL) was stirred for 12 h at room temperature. The resin was collected by filtration, washed with THF and MeOH, and dried under vacuum to give 946 mg of chlorinated ROMP resin **22**. ^{1}H NMR and IR were used to determine the extent of the bromination. The hydroxyl loading of this resin (0.37 mmol/g) was obtained by DMT quantitation: ^{1}H NMR ($CDCl_3$) δ (relative integral) 1.83 (m, 3.1), 2.24 (br, 0.9), 2.62 (br, 0.7), 3.71 (m, 2.0), 4.28 (br, 0.6); ^{13}C NMR ($CDCl_3$) δ 14.1, 20.6, 22.6, 25.2, 25.6, 31.6, 34.6, 67.9; FTIR ν_{max} (cm^{-1}) 3417, 2931, 2863, 1445.

Determination of Resin Swelling. A 1 mL syringe equipped with a frit was charged with 50 mg of the resin sample and the solvent (1 mL) was added. After the mixture was shaken for 5 min, the solvent was allowed to drain from the syringe and a second aliquot of solvent was added and the shaking and draining procedure was repeated twice. The swelling volume of resin was then recorded and the swelling volume per gram of material was calculated by multiplying this value by 20.

3-Butyl-2-phenyl-1*H*-benzoimidazole-6-carboxylic Acid Methyl Ester (27). For the preparation of the benzimidazole **27**, a second batch of U-ROMP resin **11a** (1% cross linked, 1.54 mmol/g) was used. Resin **11a** (2.00 g, 3.08 mmol) was suspended in CH_2Cl_2 (40 mL). 4-Fluoro-3-nitrobenzoic acid (1.14 g, 6.16 mmol), diisopropylcarbodiimide (1.44 mL, 9.24 mmol), and DMAP (38 mg, 0.31 mmol) were added, and the resulting mixture was shaken for 12 h. The resin was collected by filtration, washed with THF and MeOH, and dried under vacuum to give 2.82 g of pale yellow resin **23**. Resin **23** was treated with *n*-$BuNH_2$ (1.52 mL, 15.40 mmol) in the presence of Et_3N (2.15 mL, 15.40 mmol) in CH_2Cl_2 (40 mL) for 3 h at room temperature. The resin was collected by filtration, washed with THF, CH_2Cl_2, and MeOH, and then dried under vacuum to give 2.99 g of yellow resin **24**. A mixture of resin **24** (1.500 g, 1.54 mmol) and tin(II) chloride dihydrate (3.49 g, 15.45 mmol) in THF (30 mL) was shaken for 36 h at room temperature. The resin was collected by filtration, washed with THF, 10% Et_3N/THF, 10% Et_3N/MeOH, and MeOH, and dried under vacuum to give 1.55 g of pale yellow resin **25**. Polymer-bound diamine **25** (400 mg, 0.40 mmol) was treated with benzaldehyde (0.12 mL, 1.20 mmol) and ceric ammonium nitrate (CAN) (0.66 g, 1.20 mmol) in THF (15 mL) for 24 h at room temperature with shaking. The resin was collected by filtration, washed with THF and MeOH, and dried under vacuum to give 503 mg of pale brown resin **26**. To a suspension of resin **26** (450 mg, 0.36 mmol) in 10 mL of anhydrous THF under an atmosphere of argon was added 0.5 M NaOMe/MeOH solution (3.6 mL, 1.80 mmol) via syringe at room temperature. The reaction was maintained for 1 h 30 min at 50 °C and then quenched by adding saturated aqueous ammonium chloride (5 mL). The reaction mixture was filtered and washed with THF (5 mL × 3). This filtrate was transferred to a separation funnel, and water (100 mL) was added. The organic phase was separated, and aqueous phase was extracted with EtOAc (20 mL × 3). The combined extracts were concentrated under reduced pressure. Purification of the crude mixture by preparative TLC (eluted with 40% EtOAc/*n*-Hx) gave 67 mg (74% yield, 96% purity by HPLC) of compound **27** as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 0.84 (t, J = 7.4 Hz, 3H), 1.25 (sixtet, J = 7.4 Hz, 2H), 1.77 (quintet, J = 7.7 Hz, 2H), 3.93 (s, 3H), 4.22 (t, J = 7.6 Hz, 2H), 7.41 (d, 8.4 Hz, 1H), 7.50−7.53 (m, 3H), 7.68−7.70 (m, 2H), 8.02 (dd, J = 8.8, 1.6 Hz, 1H), 8.50 (d, J = 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.4, 19.8, 31.7, 44.6, 52.0, 109.7, 122.2, 124.1, 124.4, 128.7, 129.2, 130.0 130.1, 138.8, 142.6, 155.4, 167.6; HRMS (MALDI-FTMS) m/z = 309.1582 $[M + H]^+$, calcd for $C_{19}H_{21}N_2O_2$ = 309.1597.

3-Butyl-2-oxo-2,3-dihydro-1*H*-benzoimidazole-6-carboxylic Acid Methyl Ester (29). To a suspension of resin

25 (400 mg, 0.40 mmol) and Et_3N (0.73 mL, 5.2 mmol) in CH_2Cl_2 (10 mL) under an atmosphere of argon was added dropwise a solution of triphosgene (237 mg, 0.80 mmol) in CH_2Cl_2 (5 mL) at room temperature. After 4 h at room temperature, the resin was collected by filtration, washed with THF, CH_2Cl_2, 10% Et_3N/CH_2Cl_2, and MeOH, and dried under vacuum to give 415 mg of pale brown resin **28**. To a suspension of resin **28** (350 mg, 0.33 mmol) in 10 mL of anhydrous THF under an atmosphere of argon was added 0.5 M NaOMe/MeOH solution (3.3 mL, 1.60 mmol) via syringe at room temperature. The reaction was maintained for 1 h 30 min at 50 °C and then quenched by adding saturated aqueous ammonium chloride (5 mL). The reaction mixture was filtered and washed with THF (5 mL × 3). This filtrate was transferred to a separation funnel, and water (100 mL) was added. The organic phase was separated, and the aqueous phase was extracted with EtOAc (20 mL × 3). The combined extracts were concentrated under reduced pressure. Purification of the crude mixture by preparative TLC (eluted with 40% EtOAc/*n*-Hx) gave 67 mg (82% yield, 96% purity by HPLC) of compound **29** as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 0.94 (t, J = 7.2 Hz, 3H), 1.39 (sextet, J = 7.5 Hz, 2H), 1.73 (quintet, J = 7.5 Hz, 2H), 3.88 (s, 3H), 6.99 (d, J = 8.4 Hz, 1H), 7.81−7.84 (m, 2H), 10.58 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 13.7, 20.1, 30.4, 40.9, 52.1, 107.2, 111.0, 123.4, 123.8, 127.8, 134.1, 156.1, 167.1; HRMS (MALDI-FTMS) m/z = 249.1234 $[M + H]^+$, calcd for $C_{13}H_{17}N_2O_3$ = 249.1234.

1-(Furan-2-ylmethyl)-3-(4-iodophenyl)-5-methylhydantoin (34). A mixture of H-ROMP resin (300 mg, 0.25 mmol), Fmoc-D-Ala-OH (155 mg, 0.50 mmol), diisopropylcarbodiimide (0.14 mL, 0.90 mmol), and DMAP (4 mg, 0.03 mmol) in anhydrous CH_2Cl_2 (20 mL) was shaken for 24 h at room temperature. The resin was collected by filtration, washed with THF and MeOH, and dried under vacuum to give 373 mg of resin **30**. Resin **30** was shaken in 10% piperidine/THF (15 mL) for 1 h at room temperature. The resin was collected by filtration, washed with THF and MeOH, and dried under vacuum to give 317 mg of resin **31**. The suspension of 317 mg of the amino resin **31** and 2-furaldehyde (0.12 mL, 1.25 mmol) in 1% AcOH/DMA (15 mL) was stirred for 1 h at room temperature. To this mixture was added $NaBH_3CN$ (314 mg, 5.00 mmol). The reaction was kept stirring for 12 h at room temperature. The resin was collected by filtration, washed with THF, 10% Et_3N/THF and MeOH, and dried under vacuum to give 330 mg of resin **32**. The mixture of 250 mg of resin **32** and 4-iodophenyl isocyanate (177 mg, 0.72 mmol) in DMF/toluene (1:1) (14 mL) was shaken for 5 h at room temperature. The resin was collected by filtration, washed with THF and MeOH, and dried under vacuum to give 300 mg of resin **33**. Resin **33** (250 mg) was stirred in 50% diisopropylamine/THF (14 mL) for 12 h at room temperature. The reaction mixture was filtered and washed with THF. The combined filtrate and wash was concentrated under reduced pressure. Purification of crude mixture by preparative TLC (eluted with 30% EtOAc/*n*-Hx) gave 54 mg (80% yield, 92% purity by HPLC) of compound **34** as a pale yellow oil. When Wang resin (1.12 mmol/g) was used in the same procedure as above, 93 mg (84% yield and 92% purity by HPLC) of product **34** was obtained: ^{1}H NMR ($CDCl_3$) δ 1.50 (d, J = 7.2 Hz, 3H), 4.02 (q, J = 6.9 Hz, 1H), 4.27 (d, J = 15.6 Hz, 1H), 4.95 (d, J = 16.0 Hz, 1H), 6.32−6.34 (m, 2H), 7.11 (d, 8.4 Hz, 2H), 7.38 (d, J = 0.8 Hz, 1H), 7.75 (d, J = 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 15.1, 30.2, 37.3, 55.0, 93.0, 109.2, 110.5, 127.4, 131.4, 137.9, 142.9, 148.8, 154.2, 171.8; HRMS (MALDI-FTMS) m/z = 397.0027 $[M + H]^+$, calcd for $C_{15}H_{14}IN_2O_3$ = 397.0044.

4-Hydroxybenzophenone (37). To a suspension of H-ROMP resin (300 mg, 0.25 mmol), phenol (235 mg, 2.50 mmol), and PPh_3 (328 mg, 1.25 mmol) in THF (30 mL) was added diisopropyl azodicarboxylate (DIAD) (0.345 mL, 1.75 mmol) at room temperature. After being shaken for 48 h, the resin was collected by filtration, washed with THF and MeOH, and dried under vacuum to give 318 mg of resin **35**. Benzoyl chloride (69 μL, 0.591 mmol) was added to a well-stirred suspension of 250 mg of **35** and $AlCl_3$ (53 mg, 0.39 mmol) in anhydrous CH_2Cl_2 (30 mL) at room temperature under an atmosphere of argon. After being stirred for 3 h, the resin was collected by filtration, washed with CH_2Cl_2 and MeOH, and dried under vacuum to yield acetylated resin **36**. BBr_3 (1.0 M) in CH_2Cl_2 solution (0.87 mL, 0.87 mmol) was added to a suspension of 232 mg of the acylated resin **36** in anhydrous CH_2Cl_2 (20 mL) at room temperature. The mixture was stirred under heating at 60 °C for 12 h and then cooled to room temperature. The reaction mixture was filtered and washed with THF. The combined filtrate and wash was concentrated under reduced pressure. Purification of crude mixture by preparative TLC (eluted with 30% EtOAc/*n*-Hx) gave 14 mg (42%) of compound **37** as a white solid and 1 mg (6%) of phenol. Analysis of the crude product by HPLC gave a purity of **37**/phenol of 85:14. When 5-hydroxypentyl PS-DVB resin (0.97 mmol/g) was used as a polymeric support in the same procedure as above, 8 mg (24%) of product **37** and 4 mg (25%) of phenol were obtained. Analysis of the crude product by HPLC gave a purity of **37**/phenol of 42:38: ^{1}H NMR ($CDCl_3$) δ 6.91 (dt, J = 7.6, 2.4 Hz, 2H), 7.38 (br s, 1H), 7.43−7.46 (m, 2H), 7.55 (tt, J = 6.8, 1.5 Hz, 1H), 7.72−7.77 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 115.4, 128.3, 129.5, 129.9, 132.2, 133.1, 138.0, 160.8, 196.9; HRMS (MALDI-FTMS) m/z = 199.0746 $[M + H]^+$, calcd for $C_{13}H_{11}O_2$ = 199.0754.

3-(2-Nitrophenyl)propionic Acid Methyl Ester (40a). To a well-stirred suspension of H-ROMP resin (500 mg, 0.415 mmol) and Et_3N (174 μL, 1.25 mmol) in CH_2Cl_2 (20 mL) was added dropwise hydrocinnamoyl chloride (185 μL, 1.25 mmol) at room temperature. After being shaken for 6 h, the resin was collected by filtration, washed with THF and MeOH, and dried under vacuum to give 516 mg of resin **38**. Trifluoromethansulfonic anhydride (112 μL, 0.67 mmol) was added to a suspension of 300 mg of resin **38** and tetrabutylammonium nitrate (270 mg, 0.89 mmol) in anhydrous CH_2Cl_2 (30 mL) under an atmosphere of argon at −10 °C. After 30 min, the cooling bath was removed and the reaction was continued for additional 2 h 30 min at room temperature. The resin was collected by filtration, washed with THF and MeOH, and dried under vacuum to give 308 mg of resin **39**. The loaded compounds on the resin were cleaved by adding 0.5 M NaOMe/MeOH solution (0.92 mL, 0.46 mmol) to reaction vessel containing a suspension of resin **39** (215 mg, 0.15 mmol) in anhydrous THF (20 mL) under an atmosphere of argon via syringe at room temperature. The reaction was maintained for 3 h at 50 °C and then quenched by adding saturated aqueous ammonium chloride (5 mL). The reaction mixture was filtered and washed with THF (5 mL × 3). The combined filtrated and wash was transferred to a separation funnel, and water (100 mL) was added. The organic phase was separated, and the aqueous phase was extracted with EtOAc (20 mL × 3). The combined extracts were concentrated under reduced pressure. Purification of the crude mixture by preparative TLC (eluted with 15% EtOAc/*n*-Hx) gave 11 mg (35%) of ortho-nitrated compound **40a** and 8 mg (24%) of para-nitrated compound **40b** and a trace amount of methyl hydrocinnamate. Analysis of the crude product by HPLC gave a purity of **40a**/**40b**/methylhydrocinnamate of 51:36:4. When 5-hydroxypentyl PS-DVB resin (0.97 mmol/g) and two different equivalents of reagents (i.e., 3 and 6 equiv) were used in the same procedure as above, 5 mg [total 14% (9% of *o*-**40a** and 5% of *p*-**40b** by ^{1}H NMR integration) yield; 12% (ortho), 10% (para) purity by HPLC of crude product], and 10 mg [total 28% (18% of *o*-**40a** and 10% of *p*-**40b** by ^{1}H NMR integration) yield; and 27% (ortho), 22% (para) purity by HPLC of crude product] of nitrated compounds were obtained, respectively. **40a**: ^{1}H NMR ($CDCl_3$) δ 2.65 (t, J = 7.6 Hz, 2H), 3.02 (t, J = 7.6 Hz, 2H), 3.63 (s, 3H), 7.33 (d, J = 8.4 Hz, 2H), 8.11 (d, J = 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$) δ 30.6, 34.8, 51.8, 123.8, 129.2, 148.2, 172.5; MS (EI) m/z 209 $[M]^+$, 149.

3-(4-Nitrophenyl)propionic acid methyl ester (40b): ^{1}H NMR ($CDCl_3$) δ 2.69 (t, J = 7.6 Hz, 2H), 3.18 (t, J = 7.6 Hz,

2H), 3.63 (s, 3H), 7.32−7.38 (m, 2H), 7.45−7.52 (m, 1H), 7.90 (d, $J = 8.0$ Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 28.3, 34.6, 51.7, 124.9, 127.6, 132.1, 133.2, 135.5, 172.7; MS (EI) m/z 209 $[M]^+$, 149.

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Supporting Information Available: General methods. NMR and IR spectra of U-ROMP resin and saturated ROMP resins. NMR and HPLC data of **27**, **29**, **34**, **37**, and **40a**,**b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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