Development of Polymer-Supported Benzotriazole as a Novel Traceless Linker for Solid-Phase Organic Synthesis[1]

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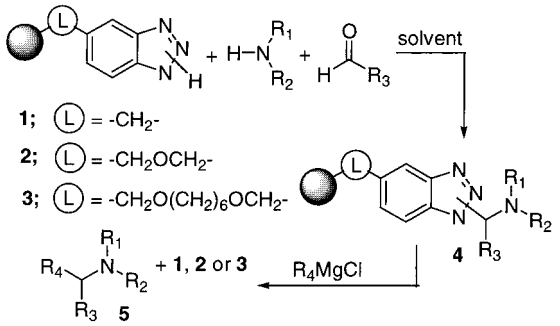
Much of the current effort in solid-phase organic synthesis (SPOS) is being focused on the development of new types of linking strategies,[2] and this includes the introduction of traceless or "clean break" linkers. Recent reports have delineated the development of newer classes of functional groups as traceless linkers for both aliphatic and aromatic C−H bond formation,[3] whereas much of the earlier work focused on silicon-based linkers.[4]

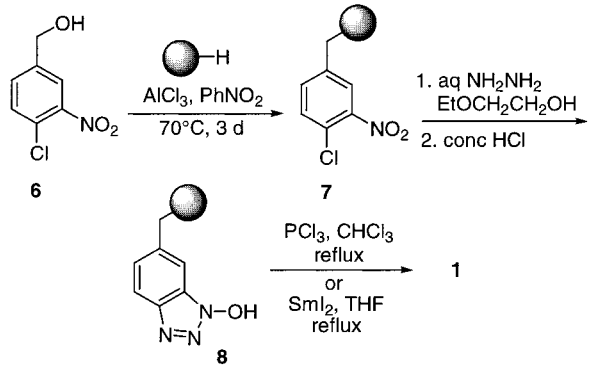
Benzotriazoles are widely used auxiliaries in organic synthesis, and a broad range of synthetic methodologies has been developed around this simple heterocycle.[5] This renders it as an attractive template for the generation of small organic molecule libraries via combinatorial chemistry techniques. Herein, we report the synthesis and characterization of polymer-supported benzotriazoles **1**−**3** as yet another type of traceless linker and their reaction with selected aldehydes and amines to form Mannich-type adducts **4** that were cleaved with Grignard reagents to provide a small library of homologated secondary and tertiary amine products **5** (Scheme 1).

Our initial approach to polymer-supported benzotriazole was to draw upon the known chemistry of polymer-supported 1-hydroxybenzotriazole. Although newer, more versatile polymer-supported anchors to 1-hydroxybenzotriazole have recently been reported, such as the electron-withdrawing 6-sulfonamide moiety,[6] we elected to pursue the more robust, mildly electron-releasing sp^3-carbon

Scheme 1



Scheme 2



linker that would most closely mimic the electronics of benzotriazole itself. Thus, our initial target became **1**, which could be accessed via literature approaches utilizing Friedel−Crafts alkylation[7] (Scheme 2). Following a solution model study utilizing benzene as a surrogate for polystyrene (see Supporting Information), reaction of polystyrene with 4-chloro-3-nitrobenzyl alcohol (**6**)[7a] under Friedel−Crafts conditions gave **7**. Chloride displacement with hydrazine followed by cyclization in ethanolic HCl then provided the polymer-supported 1-hydroxybenzotriazole **8**, upon which reductive cleavage of the 1-OH moiety was readily performed with either phosphorus trichloride[8] or SmI_2.[9] Polymer-supported benzotriazole **1**, determined to have a loading of 1.92 mmol/g by microanalysis, displayed extremely poor swelling properties in a wide range of organic solvents (vide infra). The FTIR spectrum of resin **1** showed a strong band at 1200 cm^{-1}, which is assigned to the ring-stretching vibrations of the heteroring. Attempts were made to gather structural data on compound **1** (as well as **7** and **8**) via gel-phase ^{13}C NMR spectroscopy, but even after long acquisition times (40 000 scans) no peaks were observed. Further attempts to gather spectral information on **1** and **8** via magic-angle spin NMR spectroscopy were similarly unproductive. Resin **1** was also characterized as its *N*-acetyl derivative, which displayed a prominent band at 1739 cm^{-1} in the FTIR that corresponds to the C=O stretch found in *N*-acetyl-1*H*-benzotriazole.[10] We also prepared the acetyl

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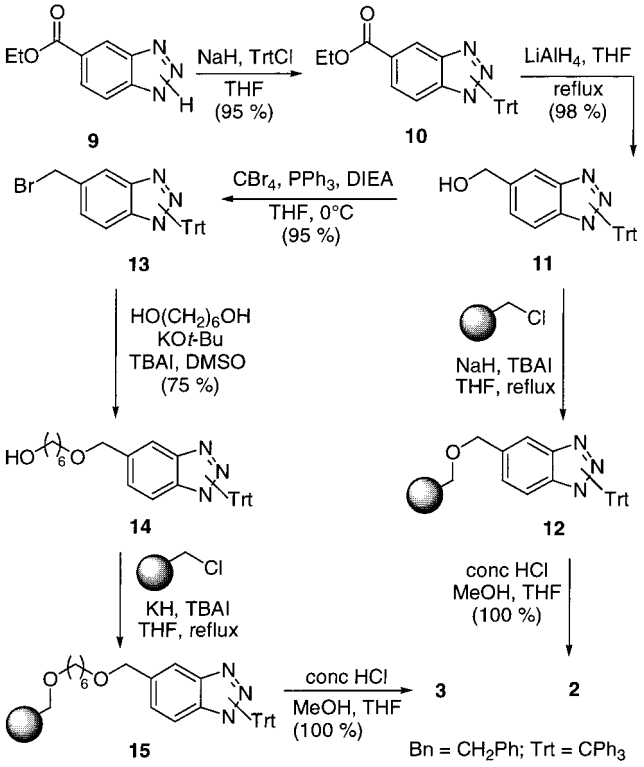
Scheme 3



derivative of the polymer-supported hydroxybenzotriazole (**8**). This showed C═O stretches at 1822 and 1734 cm^{-1} that correspond to the reported stretches of *O*-acetyl-1*H*-hydroxybenzotriazole.[11] Thus, these data suggest that the reduction of **8** to **1** proceeded quantitatively.

Because of the extremely poor swelling properties of **1**, we decided to synthesize and evaluate analogues with longer, more flexible linkers. Toward this end, polystyrene-supported **2** and **3** with mono- and diether anchors, respectively, became our targets (Scheme 3). Initial attempts to O-alkylate 1*H*-benzotriazole-5-methanol[12] with Merrifield resin failed, so an alternative strategy was pursued in which *N*-trityl-protected congener **11** would be utilized instead. Thus, the sodium salt of 1*H*-benzotriazole-5-carboxylic acid, ethyl ester (**9**)[12] was alkylated with trityl chloride under standard conditions to provide compound **10** in 95% yield as a mixture of isomers (ca. 2:1:2 *N*-1:*N*-2:*N*-3) by ^1H and ^{13}C NMR spectroscopy. The mixture of esters was reduced with $LiAlH_4$ in 95% yield to a corresponding mixture of *N*-trityl-protected 5-(hydroxymethyl)benzotriazole **11**. To secure analytical data, the isomers were isolated by either crystallization or column chromatography. The isomers could be easily distinguished by the anisotropic effects of the phenyl groups of the trityl moiety.[13] The benzotriazole protons next to the trityl group of the *N*-1- and *N*-3-isomer showed a downfield shift of about 1.6 ppm compared to the *N*-2-isomer. Intermediate **11** was then subjected to numerous alkylation and trityl deprotection conditions, utilizing benzyl bromide as a surrogate for Merrifield resin, to establish an optimal loading (see Supporting Information). After this, treatment of **11** in THF with NaH followed by addition of 5 mol % tetra-*n*-butylammonium iodide and then Merrifield resin, gave polymer-supported **12**. Target resin **2** was obtained in quantitative yield by cleavage of the *N*-trityl moiety of **12** with concentrated HCl in THF/methanol at 25 °C. The gel-phase ^{13}C NMR spectrum of **2** supported the assigned structure by distinctive peaks that can be assigned to the benzotriazole nucleus at δ 71.7 ppm (C-5 α-methylene carbon), 113.5 and 115.2 ppm (C-4 and C-7, respectively), 136.9 and 138.8 ppm (C-3a and C-7a, respectively), and 145.4 ppm (C-5). Resin **2**, with a loading of 1.27 mmol/g, as determined by microanalysis, shows very good swelling properties in a variety of organic solvents.[14] The loading of **2** also correlates well with that of *N*-trityl precursor **12**, which was determined to be 1.01 mmol/g by microanalysis and 0.99 mmol/g from the weight of recovered triphenylcarbinol in the HCl hydrolysis reaction.

Toward further examination of the effect of an extended linker on the physicochemical behavior and reactivity of polymer-supported benzotriazole, we also synthesized target diether resin **3**. *N*-Trityl-protected 5-(hydroxymethyl)benzotriazole **11** was treated with carbon tetrabromide and triphenylphosphine[15] to provide in good yield the bromide **13**, which was then chain extended to alcohol ether **14**. Further alkylation of **14** with Merrifield resin to **15** followed by hydrolysis of the *N*-trityl protecting group to give target diether resin **3** was carried out as described above for **2**.

The gel-phase ^{13}C NMR spectrum of **3** supported the assigned structure with linker and benzotriazole peaks at δ 26.1 and 29.7 ppm (linker carbons), 70.7 and 72.6 ppm (linker carbons α to oxygen), 113 ppm (C-7), 115.3 ppm (C-4), 137.2, 138.7 ppm (C-3a, C-7a, C-5), and 145.3 ppm (C-5). Resin **3**, with a loading of 0.99 mmol/g as determined by microanalysis, displays superior swelling properties.

We also determined the swelling properties of resins **1**−**3** and their corresponding precursor resins in selected solvents by applying the procedure recently reported by Santini and Griffith.[16] Resin **3** displays extraordinarily good swelling (>7 mL/g) in DMF, THF, and toluene, greater than that for its precursor Merrifield resin in each solvent evaluated (see Table 2, Supporting Information). Similar results were obtained for resin **2**, although the observed values are somewhat less. In contrast, resin **1** was determined to be the worst swelling polymer, and its swelling relative to precursor resin polystyrene was improved only slightly in polar solvents (DMF and EtOH).[17] The improved swelling properties of **1** vs **2** vs **3** as the tether length is increased can be attributed to an overall reduction in polymer cross-linking; thus **3** is much more accessible to solvation than **1**.

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(14) We also synthesized a congener of **2** from ArgoPore-Cl Merrifield resin (poly(ethylene glycol)−polystyrene graft copolymer, 120−230 μm, 1.26 mmol/g Cl) in the same two-step sequence of reactions starting from **11**. Because of the lower loading of the starting resin, the loading of ArgoPore-benzotriazole **2** never exceeded 0.78 mmol/g. The physical properties of this resin are outstanding, and its application toward the synthesis of Mannich-type adducts gave results similar to **2**.
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(17) Besides the solvents listed in Table 1, resin **1** was found to exhibit very poor swelling properties in benzene, chloroform, diethyl ether, and methanol.

Table 1. Amines Synthesized from Mannich Adducts of Polymer-Supported Benzotriazole

no.	resin	R_1, R_2	R_3	R_4	yield (%)
5a	**1**	$-(CH_2)_2O(CH_2)_2-$	*p*-(MeO)C_6H_4	CH_2Ph	56
5b	**1**	$-(CH_2)_2O(CH_2)_2-$	Ph	CH_2Ph	31
5c	**1**	H, $(CH_2)_5CH_3$	$CH(CH_3)_2$	CH_2Ph	20
5d	**1**	$-(CH_2)_2O(CH_2)_2-$	$CH(CH_3)_2$	CH_2Ph	25
5d	**2**	$-(CH_2)_2O(CH_2)_2-$	$CH(CH_3)_2$	CH_2Ph	70
5e	**2**	$-(CH_2)_2O(CH_2)_2-$	$CH(CH_3)_2$	Ph	27
5f	**2**	$-(CH_2)_2O(CH_2)_2-$	*p*-(MeO)C_6H_4	Ph	38
5g	**2**	$-(CH_2)_2O(CH_2)_2-$	Ph	CH_2Ph	63
5h	**2**	H, pyridin-2-yl−	$CH(CH_3)_2$	CH_2Ph	76
5d	**3**	$-(CH_2)_2O(CH_2)_2-$	$CH(CH_3)_2$	CH_2Ph	77
5g	**3**	$-(CH_2)_2O(CH_2)_2-$	Ph	CH_2Ph	55
5h	**3**	H, pyridin-2-yl−	$CH(CH_3)_2$	CH_2Ph	76
	1, 2, 3	H, $(CH_2)_5CH_3$	aromatic[a]	CH_2Ph	0

[a] Phenyl, 3-pyridyl, 4-methoxyphenyl.

In an initial survey of the chemistry of our benzotriazole-linked resins **1**−**3**, we explored well documented Mannich-type reactions previously described by Katritzky[5] (Scheme 1). The derived stable adducts **4** were isolated by the normal techniques of resin filtration, washings, and drying and then cleaved from the resin with Grignard reagents to give the amine products **5a**−**h** shown in Table 1 in variable yields but generally excellent purity (see Supporting Information).

Even though our data set is limited, we observed no general reactivity trends for the aldehyde and amine combinations evaluated, and yields appear to be independent of the choice of resin **1**−**3**, although slightly lower yields were found when utilizing resin **1**. The reaction of primary aliphatic amines with aliphatic or aromatic aldehydes tended to give low yields of **5** (data not shown) or no product at all (e.g., last entry in Table 1). The primary aromatic amine 2-aminopyridine reacted with aliphatic and aromatic aldehydes (e.g., **5h** of Table 1), but aniline did not undergo comparable reactions regardless of the resin used. To directly compare the efficiencies of resins **1**−**3**, compound **5d** was prepared. Good yields were obtained using the better swelling resins **2** and **3**, but only a moderate yield was obtained with **1**, although the total amount of amine **5** cleaved from adduct resin **4** was almost the same as a result of the higher loading of resin **1**. For those cases in which the Mannich condensation worked, gel-phase ^{13}C NMR of the polymer-supported intermediates **4** was used to characterize the adducts. For example, the gel-phase ^{13}C NMR of the Mannich precursor derived from polymer **3**, morpholine, and isobutyryl aldehyde showed distinct signals for the adduct **4** at δ 19.3 and 20.0 ppm for the *gem*-dimethyl carbons, 28.7 ppm for the isopropyl methine carbon, 48.6 and 49.1 ppm for the morpholine carbons α to nitrogen, 66.9 and 67.1 ppm for the morpholine carbons α to oxygen. Signals at 85.6 and 85.8 ppm can be assigned to the C-1 methine carbons of **4** attached at the *N*-1 and *N*-3 positions of the benzotriazole ring, respectively, and one at 92.6 ppm is assigned to attachment at *N*-2. The peak heights of these suggest an approximately 1:1:2 ratio of *N*-1, *N*-3, and *N*-2 isomers, respectively.

In summary, we have developed methodologies for the synthesis of three polymer-supported benzotriazoles and have initially evaluated these in the synthesis of a small library of homologated secondary and tertiary amines via polymer-supported Mannich-type adducts followed by cleavage with Grignard reagents. Although our initial data suggest that resins with better swelling properties may not improve the reactivity of the benzotriazole auxiliary for Mannich-type reactions and that the scope of such reactions may be limited relative to the solution phase, more work needs to be carried out to validate these findings.

Experimental Section

General Methods. See the Supporting Information.

Preparation of 4-(Polystyrene-bound)methyl-1-chloro-2-nitrobenzene (7). To a stirred suspension of poly(styrene-*co*-divinylbenzene) resin (10.0 g; 2% cross-linked, 200−400 mesh; Aldrich) and $AlCl_3$ (13.3 g, 0.10 mol) in nitromethane (100 mL) at 25 °C was added 4-chloro-3-nitrobenzyl alcohol (**6**)[7a] (10.0 g, 53.3 mmol) in small portions. The mixture was stirred for 3 d at 80 °C, and the resin was collected by filtration and then washed successively with 1:1 1 N aqueous HCl/THF (3 × 50 mL), DMF (3 × 50 mL), MeOH (3 × 50 mL), and THF (3 × 50 mL). The product was dried to give 15.1 g of **7** as a dark brown resin. Anal. found: C, 75.82; H, 5.81; N, 2.98; Cl, 7.89; loading = 2.12 mmol/g (based on N analysis), 2.22 mmol/g (based on Cl analysis).

Preparation of 6-(Polystyrene-bound)methylbenzotriazol-1-ol (8). A mixture of 4-(polystyrene-bound)methyl-1-chloro-2-nitrobenzene (**7**) (14.0 g) and anhydrous hydrazine (9.42 mL, 0.30 mol) in 2-methoxyethanol (30 mL) was agitated at reflux for 20 h. The resin was filtered off and washed sequentially with 1:1 H_2O/THF (3 × 50 mL), DMF (3 × 30 mL), MeOH (3 × 30 mL), and THF (3 × 30 mL). The product was dried to give 13.5 g of a dark brown resin. Anal. found: C, 76.90; H, 6.56; N, 9.65; Cl, 1.55; loading = 2.30 mmol/g (based on N analysis). A suspension of the hydrazino resin (13.0 g) and concentrated HCl (40 mL) in dioxane (40 mL) was stirred at reflux for 20 h. The resin was filtered and washed with H_2O/THF (1:1, 2 × 30 mL), DMF (2 × 30 mL), MeOH (2 × 30 mL), and THF (2 × 30 mL). The product was dried to yield **8** (12.5 g) as a dark brown resin. Anal. found: C, 78.78; H, 6.59; N, 8.00; Cl, 1.52; loading = 1.90 mmol/g (based on N analysis). The resin was further characterized as its *O*-acetyl derivative. A suspension of **8** (200 mg), acetic anhydride (80.0 mg, 0.80 mmol), and 2 mL of pyridine was stirred for 14 h at 40 °C. The resin was washed with H_2O/THF (1:1), MeOH, and THF (3 × 52 mL, each) and dried to yield 217 mg of a brownish resin. IR (KBr): 1822, 1734 cm^{-1}.

Preparation of 5-(Polystyrene-bound)methyl-1*H*-benzotriazole (1). (a) From PCl_3 Reduction of 8. 6-(Polystyrene-bound)methylbenzotriazol-1-ol (**8**) (12.0 g) was suspended in $CHCl_3$ (75 mL) and treated with PCl_3 (8.00 mL, 90.0 mmol). The mixture was stirred for 20 h at reflux, and the resin was then collected by filtration and washed successively with 1:1 H_2O/THF (3 × 50 mL), MeOH (3 × 50 mL), and THF (3 × 50 mL). It was suspended in THF (60 mL), treated with concentrated HCl (8 mL), and stirred at reflux for 3 h. The resin was filtered off and washed successively with 1:1 H_2O/THF (2 × 30 mL), DMF (2 × 30 mL), MeOH (2 × 30 mL), and THF (2 × 30 mL). The product was dried to yield **1** (11.7 g) as a dark brown resin. IR (KBr): 3430, 1200 cm^{-1}. Anal. found: C, 78.48; H, 6.34; N, 8.06; Cl, 1.50; loading = 1.92 mmol/g (based on N analysis). The resin was further characterized as its *N*-acetyl derivative by reaction of **1** with acetic anhydride as discussed above for **8**. IR (KBr): 1739 cm^{-1}.

(b) From SmI_2 Reduction of 8. To a solution of SmI_2 (50.0 mL, 5.00 mmol, 0.1 M in THF, Aldrich) was added 6-(polystyrene-bound)methylbenzotriazol-1-ol (**8**) (1.00 g). The mixture was stirred at reflux overnight, during which the color changed from blue to yellow. To the cooled solution was added 0.1 N aqueous HCl (20 mL), and stirring was continued for 5 min at 25 °C. The resin was filtered off and washed successively with 1:1 H_2O/THF (2 × 5 mL), DMF (2 × 5 mL), MeOH (2 × 5 mL), and THF (2 × 5 mL). The product was dried to yield **1** (0.94 g) as a dark brown resin. Anal. found: C, 78.42; H, 6.11; N, 8.03; Cl, 1.21; loading = 1.91 mmol/g (based on N analysis).

Preparation of 5-(Polystyrene-bound)methoxymethyl-*N*-trityl-1*H*-benzotriazole (12). A solution of (*N*-trityl-1*H*-benzotriazol-5-yl)methanol (**11**) (5.00 g, 12.8 mmol) in THF (80

mL) at 25 °C was treated with NaH (291 mg, 12.1 mmol). The mixture was stirred for 30 min, treated with tetra-*n*-butylammonium iodide (447 mg, 1.21 mmol) and Merrifield resin (5.00 g; cross-linked with 1% DVB, 200−400 mesh, 1.78 mmol/g Cl loading; Fluka), and then agitated at reflux for 20 h. The cooled mixture was diluted with 20 mL of 0.5 N aqueous HCl and stirred for 5 min. The resin was collected by filtration and washed successively with 1:1 H_2O/THF (3 × 25 mL), MeOH (3 × 25 mL), and THF (3 × 25 mL). The product was dried to yield 7.45 g of **12** as a yellow resin. Gel-phase ^{13}C NMR: δ 40.41 (br), 72.06, 79.09, 84.28, 117.15, 118.88, 124−133 (br), 141.49, 142.61, 145.39. Anal. found: C, 85.84; H, 6.79; N, 4.26; Cl, 0.05; loading = 1.01 mmol/g (based on N analysis). The filtrate and washings were combined, partially concentrated, and extracted with Et_2O. The combined organic layers were dried and concentrated to leave 2.00 g (5.10 mmol) of starting alcohol **11**.

Preparation of 5-(Polystyrene-bound)methoxymethyl-1*H*-benzotriazole (2). A suspension of 5-(polystyrene-bound)-methoxymethyl-*N*-trityl-1*H*-benzotriazole (**12**) (7.00 g) in 3:2 THF/MeOH (150 mL) at 25 °C was treated with concentrated HCl (18 mL), and the mixture was stirred for 18 h. The resin was collected by filtration and washed sequentially with 1 N aqueous NaOH (15 mL), 1:1 H_2O/THF (3 × 15 mL), MeOH (3 × 15 mL), and THF (3 × 15 mL). The product was dried to yield 5.43 g of **2** as a yellow resin. Gel-phase ^{13}C NMR: δ 40.32 (br), 71.68, 113.50, 115.17, 123−135 (br), 136.85, 138.82, 145.37. IR (KBr): 3436, 1204 cm^{-1}. Anal. found: C, 82.59; H, 6.88; N, 5.34; loading = 1.27 mmol/g (based on N analysis). Processing of the filtrate as described above for **12** provided 1.76 g (6.76 mmol, 96% of theory) of triphenylcarbinol, which corresponds to a loading of 1.24 mmol/g for **12**.

5-[[[6-(Polystyrene-bound)methoxyhexyl]oxy]methyl]-*N*-trityl-1*H*-benzotriazole (15). 6-[(*N*-Trityl-1*H*-benzotriazol-5-yl)methoxy]hexan-1-ol (**14**) (1.77 g, 3.60 mmol) was dissolved in THF (25 mL), and KH (145 mg, 3.60 mmol) was added at 25 °C. The mixture was stirred for 30 min, treated successively with tetra-*n*-butylammonium iodide (37.0 mg, 0.10 mmol) and Merrifield resin (1.00 g; cross-linked with 2% DVB, 200−400 mesh, 1.79 mmol/g Cl loading; Fluka), and then agitated at reflux for 20 h. The cooled mixture was diluted with 10 mL of 0.5 N aqueous HCl and stirred for 5 min. The resin was collected by filtration and washed successively with 1:1 H_2O/THF (3 × 30 mL), MeOH (3 × 30 mL), and THF (3 × 30 mL). The product was dried to give 1.61 g of **15** as a yellow resin. Gel phase ^{13}C NMR: δ 26.08, 29.69, 40.37 (br), 70.17, 72.48, 70.03, 112.06, 113.67, 118.54, 119.89, 123.65, 125−133 (br), 134.59, 137.80, 141.50, 146.16. Anal. found: C, 85.84; H, 7.22; N, 3.39; Cl, 0.40; loading = 0.81 mmol/g (based on N analysis). Processing of the filtrate as described above for **12** provided 0.70 g (1.42 mmol, 40%) of starting alcohol **14**.

5-[[[6-(Polystyrene-bound)methoxyhexyl]oxy]methyl]-1*H*-benzotriazole (3). A suspension of 5-[[[6-(polystyrene-bound)methoxyhexyl]oxy]methyl]-*N*-trityl-1*H*-benzotriazole (**15**) (1.50 g) in 3:2 THF/MeOH (25 mL) at 25 °C was treated with concentrated HCl (1.5 mL), and the mixture was stirred for 2 h. The resin was collected by filtration and washed sequentially with 1 N aqueous NaOH (5 mL), 1:1 H_2O/THF (3 × 5 mL), MeOH (3 × 55 mL), and THF (3 × 10 mL). The product was dried to yield 1.20 g of **3** as an off-white resin. Gel-phase ^{13}C NMR: δ 26.12, 29.71, 40.53 (br), 70.66, 72.61, 112.98, 115.30, 123−134 (br), 137.22, 138.69, 145.30; IR (KBr): 3380, 1203 cm^{-1}. Anal. found: C, 83.73; H, 7.49; N, 4.15; Loading = 0.99 mmol/g (based on N analysis). Workup of the filtrate as described above yielded 290 mg (1.2 mmol, 98% of theory) of recovered triphenylcarbinol, which corresponds to a loading of 1.00 mmol/g for resin **15**.

General Procedure for Formation of Resin-Bound Benzotriazole Adducts (4) Followed by Cleavage with Grignard Reagents to Amines (5). To a 25 °C suspension of polystyrene-bound benzotriazole in THF, EtOH, or DMF (15 mL/g resin) was added the aldehyde and the amine (5 equiv each). The mixture was stirred at reflux (THF, EtOH) or at 70 °C (DMF) for ca. 17 h. The resulting resin was filtered and washed successively with MeOH (3 × 10 mL) and THF (3 × 10 mL). The resin-bound benzotriazole adduct **4** was dried and then suspended in toluene (15 mL/g resin) at 25 °C. Grignard reagent (5 equiv) was added, and the mixture was stirred at reflux overnight. The cooled mixture was treated with 0.5 N aqueous HCl (15 mL) and stirred for 10 min. The resin was collected by filtration, washed successively with 1:1 H_2O/THF (3 × 10 mL), MeOH (3 × 10 mL), and THF (3 × 10 mL), and dried. The combined filtrate and washings were partially concentrated, and then the aqueous layer was extracted with Et_2O (3 × 20 mL). The combined extracts were washed with 1 N aqueous HCl and then disposed. The combined aqueous layers were cautiously basified with saturated aqueous $NaHCO_3$ and extracted with Et_2O. The combined extracts were dried and concentrated to provide the pure amine **5**.

Note Added in Proof. Following submission of the present manuscript, two accounts of the synthesis of polymer-supported benzotriazole, utilizing a linker strategy different from that reported herein, and their application to the generation of Mannich adducts were disclosed by Katritsky et. al. (Katritzky, A. R.; Belyakov, S. A.; Tymoshenko, D. O. *J. Comb. Chem.* **1999**, *1*, 173−176) and a group at GlaxoWellcome (Paio, A. In *Proceedings on High-Throughput Organic Synthesis*; San Diego CA, February 4−5, 1999; see www.healthtech.com).

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Supporting Information Available: Spectral data for compounds **4**, **5a**−**h**; experimental details and spectral data for **10**, **11**, **13**, and **14** and compounds **17**, **19**, **20**, and **21** from surrogate polymer studies; and experimental procedure and Table 2 with calculated swelling properties of **1**−**3** in different solvents. This material is available free of charge via the Internet at http://pubs.acs.org.

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