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Functional Polymers from Vinylpolystyrene. Diels−Alder Reactions with Olefins

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We describe a convenient route toward resins of cross-linked polystyrene bearing large numbers of carboxylic acid or anhydride, imide, acyl halide, or perhaloalkyl functional groups. These result from Diels−Alder reactions involving the site-isolated, residual vinyl aromatic units in divinylbenzene-rich copolymers (including commercial products). As shown by FT IR, solid-phase NMR, titration and elemental analysis, up to 2 mol of a good dienophile such as maleic anhydride bind to polymer beads by consecutive Diels−Alder/ene reactions (Wagner−Jauregg mechanism), while adducts are also possible from electron-poor dienes like hexachlorocyclopentadiene. Afterward, the new functional groups themselves prove accessible toward further modification. Optionally, the porous bead substrates can first be loaded with magnetic iron oxide to yield magnetically separable functional polymers.

Introduction

Conventional ways of making functional polymers often lead to features that are harmful to their use as solid-phase reagents, catalysts, sorbents, and protecting groups: for example, copolymerization of functional monomers can give uneven distribution of functional groups, while many modifications of cross-linked polystyrene using electrophilic and nucleophilic reactions result in labile moieties.[1−4] Typical styrene-based resins containing only 1−2 mol % of cross-linking units also tend to collapse in poor solvents, blocking access to interior functional groups. In contrast, reactive sites inside more highly cross-linked porous beads can remain accessible under a broader range of conditions for their synthesis, use, and regeneration. We have previously described modifying such materials that were divinylbenzene-rich copolymers containing residual vinyl groups (i.e., "vinylpolystyrene", Ps-CH$=$CH$_2$, **1**), by radical addition of thiols and other small molecules H-X, to attach functional groups through stable and protruding dimethylene spacers, as Ps-CH$_2$CH$_2$-X.[5,6] Here we describe how, in a still simpler procedure that does not require initiator, such residual vinyls can also react through cycloaddition mechanisms with either dienes or dienophiles to yield resins now highly functionalized with cyclic anhydride, imide, or acyl or alkyl halide groups. These last, in particular the relatively stable polyhalogenated adducts from hexachlorocyclopentadiene, would provide a convenient way to increase the density of beads for possible upflow fluid-bed applications, as well as change their adsorption properties.[7] Some of the other product functional polymers may be employed as solid-phase protecting groups for solid-phase synthesis, or for ion-exchange or chelation of charged species, or as intermediates toward polymer-supported catalysts or separation media, particularly through irreversible binding by acylating polymer functionalities, out of aqueous solution and without denaturation, of enzymes, antibodies, or other biomolecules.[8,9] To provide alternative means of separation from product mixtures other than filtration, flotation, or decantation, we also demonstrate how such preformed polymer beads can be made magnetic,[10−12] as well as chemically active.

A small-molecule analog of vinylpolystyrene is vinylbenzene, i.e., styrene. In cycloaddition reactions, styrene is known to participate either as diene or dienophile, or sometimes as both, to offer many possible products depending on reagents and conditions.[13,14] Its reactions with dienophiles such as maleic anhydride and fumaric acid have been reviewed.[14,15] These typically result in alternating copolymers, some of which are commercially important;[16] in the presence of free-radical inhibitors, however, these polymerization reactions are suppressed and only cycloaddition (often polycyclic) products are isolated.[14] For similar reactions of vinylpolystyrene, radical inhibitor would not be required since site isolation already prevents polymerization here.[5] The reaction of styrene as electron-rich dienophile with hexachlorocy-

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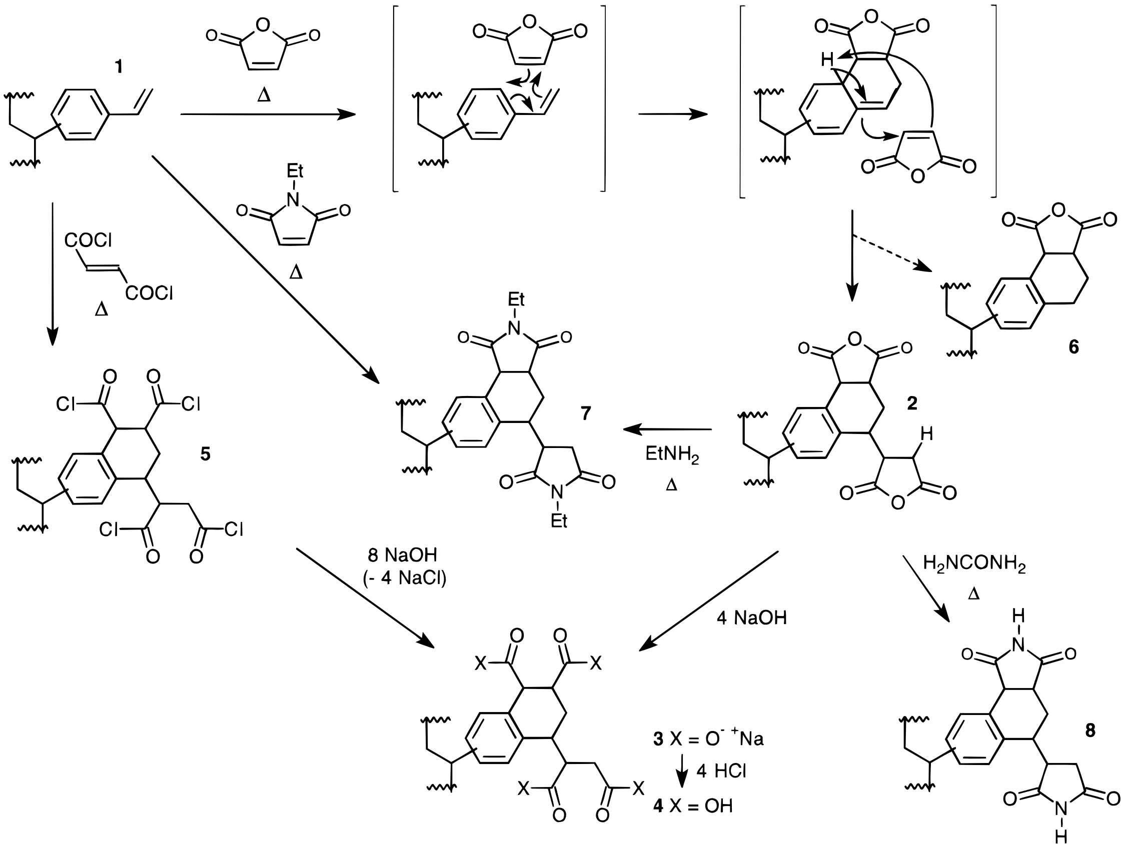
Scheme 1[a]



[a] Stereochemistry not shown. The aryl substitution pattern in **1** may be either 1,3 or 1,4: **2**, **3**, or **4** from the former can be either 1,2,4 or 1,2,6, from the latter, only 1,2,5.

clopentadiene and other electron-poor dienes,[17] which has been cited as an example of a Diels−Alder reaction with "inverse electron demand",[13] provides a model for another possible means of modifying vinylpolystyrene.

Results and Discussion

Heating **1** with excess maleic anhydride gave product **2** containing more than 1 mol of anhydride per starting vinyl, as shown by titration of base-hydrolyzed product **3** to acid **4**. This is consistent with a mechanism in which the first molecule of dienophile reacts by a Diels−Alder reaction that disrupts the aromaticity of one polymeric phenyl, whose re-aromatization then provides the driving force for an ene reaction that links the second molecule (Scheme 1), as is known for vinyl aromatic small molecules under the name of "Wagner−Jauregg reaction".[14] Further evidence for this mechanism and product included the appearance of peaks in the IR and ^{13}C NMR spectra of **2** that were typical of trialkylbenzene (910 cm^{-1} and 135 ppm) and cyclic anhydride (1789 cm^{-1} and 170 ppm for $C{=}O$, shifting on base hydrolysis; 22 ppm for **C**H$_2$CO; also a trace of COOH at 1728 cm^{-1}) groups. Though the low resolutions of these spectra (including ^{13}C NMR, for these sorts of solid samples)[5] precluded direct identification and quantitation of positional and stereoisomers, it would be expected, from the involvement of a Diels−Alder step, that all the 1,2,3,4-tetrahydronaphthyl groups in **2** and other polymer products of *cis* dienophiles were *cis*-1,2-disubstituted and that **5** and others from *trans* dienophiles were exclusively 1,2-*trans*. Other steric and electronic factors (such as the "endo rule" for Diels−Alder reactions in general) undoubtedly affect product distribution. Though such isomerism would not be important for many applications of these products, including biomolecule support,[9] it may affect chelating ability (for example, of **4**, as prepared either 1,2-*cis* via **2** or 1,2-*trans* via **5**).

In fact, the data from product titration corresponded to a conversion of **1** to bis-adduct **2** that, at best, did not proceed beyond the 90% achieved after 48 h at 100−125 °C. This was from a vinyl-bearing polymer that was a commercial resin, also evidently polymerized divinylbenzene, whose faster and more complete reaction may have been due to its vinyl groups being more accessible than in our own precursor made with toluene as porogen. IR spectra showed no vinyls left by then. Even in the absence of initiator that sometimes makes their further cross-linking an important side reaction during radical addition to vinylpolystyrene,[6] some vinyls could have dimerized by a cycloaddition similar to that of styrene during its thermal polymerization.[18] Or, some of the intermediate mono-adduct may have re-aromatized prematurely to stable **6**, forestalling attachment of a second dienophile molecule—such 1,3-rearrangements are formally forbidden by a concerted mechanism[19] but may still occur by other means such as acid catalysis.[20] Either possibility would be very difficult to confirm at the concentrations involved with the techniques available.

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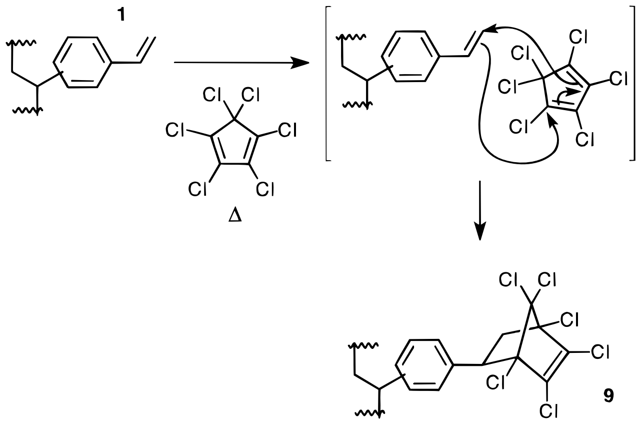
Scheme 2



The addition of an equivalent of aluminum chloride as a Lewis acid did not improve the reaction rate or final conversion and indeed caused competing Friedel–Crafts acylation, as shown by the appearance of aryl ketone FTIR peaks at 1680 and 1670 cm^{-1}. Despite the reactions being done in air, naphthalene autoxidation products of **2** were not observed.

The macroporous resin could easily be loaded with magnetic iron oxide, either before or after Diels–Alder functionalization as above, to yield magnetically recuperable beads.[10,11] This was accomplished by impregnation of the beads with ferrous and ferric salts, followed by mild alkaline autoxidation and washing out any loose particles of synthetic magnetite.[12] However, such *in situ* generation of magnetite within the polymeric pores prior to reaction with maleic anhydride may have blocked access by maleic anhydride reagent to some of the deeper reactive styryl sites and led to materials bearing a lesser amount of functionalities. These magnetized beads were strongly attracted to such permanent magnets as polyfluorocarbon-coated stir bars.

Other dienophiles such as fumaryl chloride and *N*-ethylmaleimide also respectively gave bis-adducts **5** and **7** with good conversion, demonstrating the versatility and scope of the reaction. Spectroscopically similar **7** also resulted by chemical modification of **2** with ethylamine; similar conversion to polymer-supported bis-maleimide **8** also demonstrated the accessibility and reactivity of the polymeric functional groups. However, the reaction of **1** with benzoquinone gave an uncharacterizable black product.

Alternatively, the use of **1** as a dienophile was demonstrated by reaction with the electron-poor diene hexachlorocyclopentadiene[17] to give adduct **9** in good yield (Scheme 2).

Experimental Section

Reagents and solvents were used as received unless otherwise indicated. Vinylpolystyrene **1a** was prepared with toluene as porogen and assayed for vinyl groups by FTIR,[21] as described previously.[6] Samples of commercial Amberlite XAD-4 and XAD-16 were obtained as gifts from Supelco and, after being washed in distilled water, extracted by Soxhlet with methanol, and dried, showed FTIR spectra matching peak-to-peak that of **1a** and indicating comparable degrees of functionalization (X_f), and so were respectively denoted **1b** and **1c**. In general, 100–500 μm beads of **1a**–**c** were degassed under vacuum for 30–60 min and then purged with nitrogen prior to use. FTIR spectra of dry ground samples spread onto IR-transparent silicon wafers were recorded using an IR microscope in transmittance mode. ^{13}C CP-MAS (cross polarization/magic angle spinning) and ^{13}C CP-MAS-DD (also with $\tau = 45$ ms dipolar dephasing; in the peak lists following, those labeled "DD" persist here) NMR spectra were obtained on a 100 MHz solid-phase NMR spectrometer;[5] the program C-13 NMR Module (Softshell, Grand Junction, CO) was used to assign the peaks.[22] Elemental analyses were done by Robertson Microlit Laboratories (NJ). Back titrations of polymeric acid were done by presoaking the polymer beads in a measured excess of 5:1 1.00 N NaOH(aq):THF for 24 h and then titrating aliquots of the supernatant with standardized 1.00 N HCl (aq). The ash was weighed after the sample was heated in a ceramic crucible at 400 °C for 24 h, converting all iron to Fe_2O_3, and then cooling.

***o*-(*cis*-1,2:5,6-Bis(oxydicarbonyl)hexane-1,4-diyl)polystyrene. From Synthesized and Commercial Vinylpolystyrenes 2a–c.** To 0.34 X_f vinylpolystyrene beads prepared with toluene as porogen **1a** (11.46 g, 32.66 mmol) was added a solution of maleic anhydride (3.50 g, 35 mmol) in 50 mL of toluene (bp 111 °C). The mixture was refluxed for 12 h, and the beads were filtered while hot. The beads were then washed with 30 mL of hot toluene 9×, 30 mL of acetone 7×, and then ether and dried in a vacuum oven for 48 h at 60 °C, yielding 14.88 g of **2a** as light beige beads: IR (Si wafer) 1868 (w), 1789 (s), 1728 (w), 1630 (w, weaker than **1a**), 1217, 990 (w, weaker than **1a**), 890–910 (br) cm^{-1}; ^{13}C CP-MAS NMR δ 171 (DD, **C**OO**C**O), 145 (DD, disubstituted aryl **C**-R), 135 (DD, trisubstituted aryl **C**-R), 127 (aryl **C**-H), 40, 30, and 22 (alkyl **C**H and **C**H$_2$), and 15 ppm (DD, **C**H$_3$).[5] Anal. Calcd for $(C_{10}H_{12})_{0.45}(C_{10}H_{10})_{0.37}(C_{18}H_{14}O_6)_{0.18}$ (48% conversion): mmol acid/g, 4.33. Found: mmol acid/g (3 titrations against 1 blank), 4.33 ± 0.17.

Refluxing, with a 10-fold excess of maleic anhydride in *o*-xylene at a higher temperature (bp 120 °C) with commercial Amberlite XAD-4 beads of the same 0.34 X_f vinyl content **1b** and for the same 12 h time, gave **2b** showing titration results (mmol acid/g, 4.33 ± 0.04) and spectra that were not significantly different from those of **1a**, i.e., still corresponding to 0.18 X_f of bis-anhydride groups of structure **2**. With Amberlite XAD-16 beads of 0.35 X_f vinyl-bearing polymer **1c**, titration data showed that the content of bis-anhydride in **2c** continued to increase, past 0.24 X_f (mmol acid/g, 5.75 ± 0.06) at 12 h, 0.28 X_f (mmol acid/g, 5.94 ± 0.04) at 25 h, up to 0.32 X_f (mmol acid/g, 6.66 ± 0.14) at 48 h, with accompanying decrease and eventual disappearance of IR peaks at 1630 and 990 cm^{-1}.

From Magnetite-Impregnated Vinylpolystyrene (2d). Amberlite XAD-16 beads of 0.35 X_f vinyl-bearing polymer **1c** (9.00 g, 26.1 mmol) were soaked in a 100 mL methanol solution containing $FeCl_2$ (5.00g, 40.0 mmol) and $FeCl_3$ (5.00 g, 31.0 mmol) for 12 h at room temperature in air and then filtered. The moist beads were then transferred to an Erlenmeyer flask containing 250 mL of 1 M NH_3(aq) and boiled gently in air for 30 min. The resulting dark brown beads were then filtered over 425 mm wire mesh and washed with boiling water several times until filtrate was clear and colorless. The beads were then dried in vacuo for 3 days at 75 °C until constant weight, giving 10.11 g of dark brown beads, **1d**. To 4.00 g of these was added a solution of maleic anhydride (5.00 g, 50 mmol) in 30 mL of *o*-xylene. The suspension was heated to 120 °C for 48 h, and the beads were filtered off while hot. The beads were then washed with 30 mL of hot toluene 9×, 30 mL of acetone 7×, and then ether and dried in a vacuum oven for 48 h at 60 °C, yielding 4.33 g of **2d** as dark brown beads: FTIR (Si wafer) same as from **2a**. Anal. Calcd for $(C_{10}H_{12})_{0.45}(C_{10}H_{10})_{0.36}(C_{18}H_{14}O_6)_{0.19}(Fe_3O_4)_{0.039}$ (54% conversion, 5 wt % magnetite): mmol acid/g, 4.28; ash, 5.27. Found: mmol acid/g, 4.34; ash, 5.23.

***o*-(Tetrasodium *cis*-1,2,5,6-tetracarboxyhexane-1,4-diyl)polystyrene (3).** A sample of **2a** was treated with aqueous base as for the pH back titration procedure, and the resulting **3a** was examined spectroscopically: FTIR (KBr)

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3600−3100, 1572, 1406, 1217 cm^{-1}; ^{13}C CP-MAS NMR δ 184 (DD), 145 (DD), 138 (DD), 127, 40, 30, 32, 15 (DD).

***o*-(*trans*-1,2,5,6-Tetrakis(chlorocarbonyl)hexane-1,4-diyl)polystyrene (5).** Amberlite XAD-16 beads of 0.35 X_f vinyl-bearing polymer **1c** (9.00 g 26.1 mmol) were soaked in 30 mL of *o*-xylene that had been dried over molecular sieves, and then fumaryl chloride (16.01 g, 105 mmol) was added. The mixture was then heated 24 h at 120 °C and filtered hot, and the residue was washed with toluene 16× and then ether and dried in vacuo for 3 days at 75 °C until constant weight, yielding 11.11g of **5** as tan beads: FTIR (Si wafer) 1792, 1727 cm^{-1}; ^{13}C CP-MAS NMR δ 166, 145 (DD), 127, 40, 28, 15 (DD). Anal. Calcd for $(C_{10}H_{12})_{0.45}(C_{10}H_{10})_{0.38}(C_{18}H_{14}O_4Cl_4)_{0.17}$ (53% conversion): mmol acid/g, 7.43. Found: mmol acid/g, 7.61.

***o*-(*cis*-1,2:5,6-Bis(N-ethyl(iminodicarbonyl)hexane-1,4-diyl)polystyrene (7). By Reaction of 1 with *N*-Ethylmaleimide.** Amberlite XAD-16 beads of 0.35 X_f vinyl-bearing polymer **1c** (2.5 g, 7.25 mmol) was soaked with 10 mL of *o*-xylenes, and *N*-ethylmaleimide (2.50 g, 20.0 mmol) was then added. The mixture was heated at 120 °C for 24 h and then filtered hot and washed with toluene 16× and then ether. The beads were then dried in vacuo for 3 days at 75 °C until constant weight, yielding 3.53 g of **7** as tan beads: FTIR (Si wafer) 1791, 1726 cm^{-1}; ^{13}C CP-MAS NMR δ 166 (DD), 145 (DD), 127, 40, 28, 15 (DD). Anal. Calcd for $(C_{10}H_{12})_{0.45}$-$(C_{10}H_{10})_{0.27}(C_{22}H_{24}O_4N_2)_{0.28}$ (80% conversion): C, 79.77; H, 7.43; N, 3.27. Found: C, 80.67; H, 7.01; N, 3.27.

By Reaction of 2 with *N*-Ethylamine. Beads of 0.32 X_f polymer-supported bis-anhydride **2c** derived from Amberlite XAD-16 (1.00 g, 3.33 mmol anhydride) was added to 70 wt % aqueous ethylamine (2 mL, 30 mmol) and 8 mL of THF and then heated 1 h at 40 °C. The beads were then filtered, transferred to a 25 mL round bottom flask containing 10 mL of *o*-xylene, heated to 120 °C for 2 h, then filtered hot, and washed several times with ethanol and ether. The beads were then dried in vacuo 24 h at 70 °C, yielding 1.05 g of **7** as white beads: FTIR as above, except for more significant peaks at 3400 (m, br) and 1870, and a broader one at 1790 cm^{-1}. Anal. Calcd for $(C_{10}H_{12})_{0.45}(C_{10}H_{10})_{0.23}(C_{18}H_{14}O_6)_{0.05}(C_{22}H_{24}O_4N_2)_{0.27}$ (84% conversion): C, 78.59; H, 7.19; N, 3.63. Found: C, 78.22; H, 7.22; N, 3.61.

***o*-(*cis*-1,2:5,6-Bis(iminodicarbonyl)hexane-1,4-diyl)polystyrene (8).** Beads of 0.18 X_f polymer-supported bis-anhydride **2b** derived from Amberlite XAD-4 (1.00 g, 2.17 mmol anhydride) were suspended in 5 mL of triglyme containing “99% grade” urea (0.70 g, 12 mmol) and heated to 150 °C for 1 h, then filtered hot, and washed with hot toluene, hot ethanol, and then ether. The beads were dried in vacuo, yielding 0.93 g of **8** as light beige beads: FTIR (Si wafer) 1782, 1716 cm^{-1}; ^{13}C CP-MAS NMR δ 169 (DD), 145 (DD), 135 (DD), 127, 40, 30, 22, 15 (DD). Anal. Calcd for $(C_{10}H_{12})_{0.45}(C_{10}H_{10})_{0.37}$-$(C_{18}H_{14}O_6)_{0.08}(C_{18}H_{16}O_4N_2)_{0.10}$ (56% conversion): N, 1.69. Found: N, 1.76.

(1,2,3,4,7,7-Hexachlorobicyclo[2.2.1]hept-2-en-5-yl)polystyrene (9). Amberlite XAD-16 beads of 0.35 X_f vinyl-bearing polymer **1c** (4.0 g, 11.60 mmol) were soaked with 10 mL of toluene, and hexachlorocyclopentadiene (4.1g, 15.0 mmol) was then added. The mixture was heated for 16 h at 125 °C, then filtered hot, washed with toluene 6×, ethanol 4×, and then ether. The beads were then dried in vacuo for 3 days at 75 °C until constant weight, yielding 5.50 g of **9** as tan beads: FTIR (Si wafer) 1269, 1209, 1154, 1097, 1063 cm^{-1}. Anal. Calcd for $(C_{10}H_{12})_{0.45}(C_{10}H_{10})_{0.42}(C_{15}H_{10}Cl_6)_{0.13}$ (38% conversion): Cl, 16.70. Found: Cl, 16.75.

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