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A synthetic approach to pyrazole functionalized polystyrene

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Summary

Polystyrene containing 20 % phenyl rings functionalized with pyrazole was obtained by acylation and subsequent reaction with *N*,*N*-dimethylformamid dimethylacetal and hydrazine and characterized by means of NMR and IR spectroscopy and elemental analysis.

Introduction

The field of solid state synthesis rapidly developed since the first report of R. B. Merrifield on a polymer based peptide synthesis.[1,2,3] Coupling one of the substrates to an organic resin allows to apply a second or third substrate in large excess without running into severe separation problems. Simple filtration and washing removes the unreacted starting materials from the product, which is thus generally obtained in high yields. This procedure has found its major applications in multi step synthesis, automated syntheses and in combinatorial chemistry. The resins used for this purpose are mainly cross-linked copolymers of styrene and divinyl benzene (1-2%) carrying certain functions, like chloromethyl, hydroxymethyl or aminomethyl groups at a discrete number of the aromatic moieties. However, there are some restrictions concerning the use of solvents: Solid state reactions are mainly carried out in the presence of solvents enhancing the accessibility of the functionalized sites for the substrates by swelling.
This may be overcome by using soluble polymers, which can be removed from the reaction mixture by ultra filtration [4,5,6] or by supporting them onto inorganic particles (supported liquid-phase synthesis/catalysis).[7,8] In the present paper we report a general access to soluble pyrazole functionalized polystyrene, which can be used for further modification by organic synthons or for the complexation of catalytically active metal sites like the commercially available polyvinyl pyridine.[9,10,11,12]

Experimental section

*Synthesis of poly(styrene-co-(4-acetylstyrene)) (**2**)*

Polymer **2** was synthesized according to the procedure published by Nasrullah et al. for the synthesis of completely acylated polystyrene.[13] 10 g of polystyrene (96.0 mmol of monomer, Aldrich 43,010-2, average Mw ~230,000 average Mn ~140,000) are dissolved in 400 mL of CS_2 and the mixture is cooled to 0°C. After the addition of 4.44 g (33.0 mmol, 0.34 equiv.) of $AlCl_3$ the solution is stirred for 1 h, whereby the color turns to orange-red. 1.78 ml (25.0 mmol, 0.26 equiv.) of acetylchloride, dissolved in 50 ml of CS_2, are added dropwise. This may result in a solidification of the mixture, which affords the addition of further solvent. The solution is allowed to warm up to r.t., stirred for 2 h and poured onto crushed ice. The resulting solid is treated with concentrated hydrochloric acid to remove precipitated alumina, filtered, washed with methanol and dried in vacuum. Yield: 6.70 g (59 %). Further purification of polymer **2** is performed by dissolving in thf, filtration and precipitation in methanol. ^{1}H NMR (400 MHz, 25°C, $CDCl_3$): 7.55 (0.4 H, m, 11-H), 7.02 (2.3 H, m, 4,6,10-H), 6.54-6.43 (2 H, m, 5-H), 2.50 (0.6 H, s, 14-H), 1.83 (s, 1H, 1,7-H), 1.40 (s, 2H, 2,8-H), all signals are broad. IR (KBr, cm^{-1}): 3082w, 3059w, 3025m, 2922s, 2849w, 1683vs ($\nu_{C=O}$), 1604s, 1493m, 1452s, 1415w, 1358m, 1305w, 1268s, 1182w, 1071w, 1028w, 955w, 906w, 829w, 758m, 698vs, 598w, 538w. Elemental analysis: found C 89.3%, H 7.7%, O 3.0, calcd. for $(C_{42}H_{42}O)_n$ (20% of acylation of styrene) C 89.6, H 7.5, O 2.8.

*Poly(styrene-co-(4-(3-dimethylamino-2-propenone)styrene) (**3**)*

0.63 g of **2** (1.12 mmol of acyl groups) and 10 ml of *N*,*N*-dimethylformamid dimethylacetal are dissolved in 100 ml of toluene in a flask equipped with a reflux condenser and a pressure vent. The solution is stirred for 14 d at a temperature of 95°C, whereby the color of the solution turns to brown. After cooling to r.t., the yellow colored product is precipitated by the addition of 200 ml of methanol and isolated by centrifugation. The product can be further purified by subsequent dissolution in a minimum amount of thf, filtration and precipitation in methanol. It is dried in vacuum. Yield: 0.68 g (85%) of a white powder. ^{1}H NMR (400 MHz, 25°C, thf-D_8): 7.77 (0.13 H, s, 15-H), 7.55-7.50 (0.30 H, m, 11-H), 7.06-7.02 (2.7 H, m, 4,6,10-H), 6.55-6.44 (1.9 H, m, 5-H), 5.69 (0.11 H, s, 14-H), 3.08 and 2.90 (2×0.36 H, 2×s, 16,17-H), 1.80 (1 H, s, 1,7-H), 1.40 (2 H, s, 2,8-H), all signals are broad. IR (KBr, cm^{-1}): 3082w, 3059w, 3025m, 2921m, 2849w, 1645s ($\nu_{C=O}$), 1604m, 1577s, 1551m, 1493m, 1452m, 1434m, 1355m, 1308w, 1261m, 1180w, 1097m, 1050m, 1016m, 900w, 802m, 757m, 698vs, 540w. Elemental analysis: found C 80.8%, H 7.1%, N 1.9, calcd. for $[(C_{45}H_{47}NO)\cdot(CH_3OH)_3]_n$ (20% of 3-dimethylaminopropenone side chains at the phenyl rings) C 80.8, H 8.3, N 2.0.

*Poly(styrene-co-(4-(3-pyrazolyl)styrene) (**4**)*

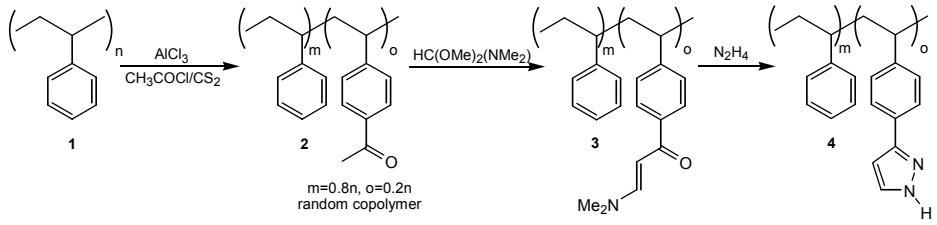
0.20 g of **3** (0.28 mmol dimethylamino-2-propenone groups) and 0.50 g of a 80% solution of hydrazine in water (1.25 mmol) are dissolved in thf. After the solution is heated to reflux for 6 h, it is poured into 50 ml of methanol. Yield: 0.12 g (64%) of a white powder, which is isolated by centrifugation and dried in vacuum. ^{1}H NMR (400 MHz, 25°C, thf-D_8): 7.42 (0.5 H, s, 14,15-H), 6.93 (2.6 H, s, 4,6,10-H). 6.50 (2.1 H,

m, 5-H), 1.80 (1 H, s, 1,7-H), 1.40 (2H, s, 2,8-H), all signals are broad. IR (KBr, cm^{-1}): 3210w (ν_{NH}), 3082w, 3059w, 3025m, 2962m, 2922m, 2849w, 1601w, 1493m, 1452m, 1261m, 1095s, 1027s, 802s, 758m, 698vs, 542w. Elemental analysis: found C 79.6%, H 7.1%, N 3.4, calcd. for $[(C_{42}H_{42}N_2)\cdot(CH_3OH)_3]_n$ (20% of pyrazolyl groups at the phenyl rings) C 80.6%, H 8.1%, N 4.2.

Results and discussion

Since some time, our group is investigating ligands bearing pyrazole rings as coordinating sites for homogeneous catalysis.[14,15,16,17,18,19,20] Pyrazoles can be obtained best by a ring closure reaction with hydrazine and 1,3-diketones. These precursors can easily be generated by a Claisen condensation starting from a ketone possessing at least one α-hydrogen atom and an ester in the presence of a base. Such a reaction sequence is less favorable if one of the components of the Claisen condensation is a polymer, since 1,3-diketonates are formed as intermediates, which will give rise to side reactions and conversions below 100% due to their polyanionic nature. Alternatively synthetic equivalents of 1,3-diketones like 1-aryl-3-dimethylaminopropenones can be applied, which avoids the generation of charged intermediates. These compounds are accessible by condensation of (aromatic) acyl derivatives with *N*,*N*'-dimethylformamide dimethyl- or diethylacetal.[21] Here, the application of this procedure for the functionalisation of polystyrene is reported. Scheme 1 summarizes the synthetic steps which lead to the desired polymeric material. The degree of functionalisation depends on the amount of acyl groups introduced into the polystyrene in the first step. High degrees of funtionalisation have turned out to lead to materials which are insoluble in common organic solvents, probably due to coagulation of the polymer by dominant intra- and intermolecular hydrogen bonding. We therefore focused on the synthesis of a material functionalized at about 20% of the aromatic side chains.

For this, polystyrene (**1**) was reacted in CS_2 solution with 0.26 equiv of CH_3COCl in the presence of an excess of $AlCl_3$ (0.34 equiv.). Following this procedure, about 20% of the phenyl groups were acylated, which can be determined either by elemental analysis or by ^1H NMR spectroscopy. Condensation of the resulting polystyrene/poly(4-acyl)styrene copolymer **2** with *N*,*N*-dimethylformamide dimethylacetal in a pressure tube by heating with microwave irradiation, as reported before for a whole series of analogous compounds,[21] is unfavorable in this case, since the drastic conditions lead to an insoluble, probably cross-linked material. Therefore the acetylated polymer **2** was heated for a long reaction period with a high excess of *N*,*N*'-dimethylformamide dimethylacetal in toluene solution, giving the soluble 4-(3-dimethylaminopropenone) substituted copolymer **3**. Final ring closure with hydrazine hydrate can thus be performed in homogenous phase resulting in the formation of the desired polystyrene/poly[4-(3-pyrazolyl)styrene] copolymer **4**.



Scheme 1.

All compounds were characterized spectroscopically: Figure 1 shows a comparison of the IR spectra of compounds **1–4**.

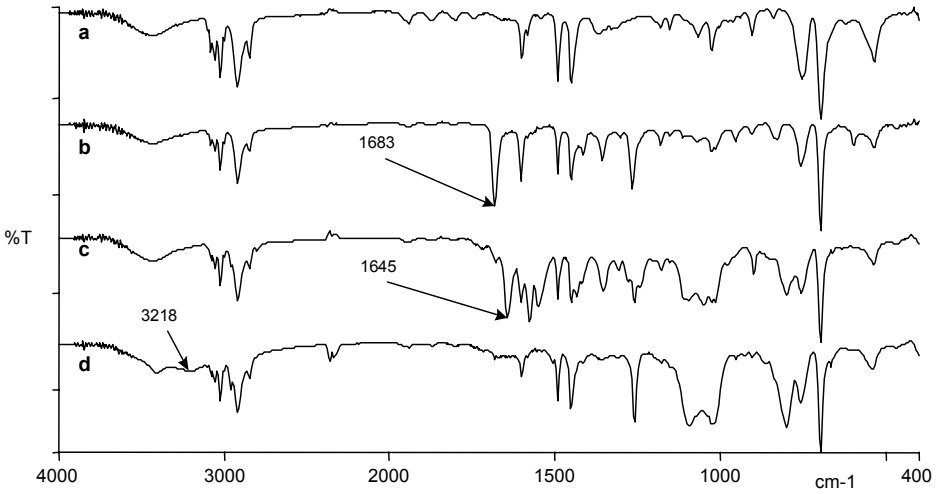


Figure 1. IR spectra of a) polystyrene (**1**), b) poly(styrene-*co*-(4-acetylstyrene)) (**2**), c) poly(styrene-*co*-(4-(3-dimethylamino-2-propenone)styrene) (**3**), d) poly(styrene-*co*-(4-(3-pyrazolyl)styrene) (**4**).

The acetylation of **1** gives rise to an absorption at 1683 cm^{-1}, typical for the C=O stretching vibration of aromatic acyl groups. The conversion of these sites into the 3-aminoprop-2-enone groups of **3** is confirmed by a new C=O stretching vibration at 1645 cm^{-1}.[21] The last step of the reaction sequence results in the disappearance of the C=O absorption and the appearance of the N-H absorption band of pyrazole at 3218 cm^{-1}.

Additionally the success of the reaction was confirmed by ^{1}H NMR spectroscopic investigations of the polymers **1-4**, although the resonances are broader than for systems with low molecular weight. Figure 2 shows the corresponding spectra, the identified signals of residual solvents and reagents were subtracted from the original spectra.

Acylation of polystyrene (**1**) gives rise to two new signals at 2.50 and 7.55 ppm, which we assign to the C*H*$_3$CO group and the *ortho* protons of the acylated phenyl rings. After the introduction of the 3-dimethylaminopopenone sites, the resonance at 2.50 ppm disappeared. Two new signals at 3.08 ppm und 2.90 ppm can be assigned to the chemically and magnetically inequivalent *N*-methyl groups of the side chains. The two signals of the 3-dimethylaminopropenone side chains are observed at about 5.70 and 7.82 ppm, which corroborates excellently with the data we recently published for 1-phenyl-3-dimethylaminopropenone.[21] The ^{1}H NMR spectrum of **4** is less complex. Compared to the ^{1}H NMR spectrum of **1**, a new resonance at 7.42 ppm can be assigned to the proton in the 5-position of the pyrazole ring. A further signal at 2.41 ppm may be assigned to residual dimethylamine, the side product of the ring closure reaction.

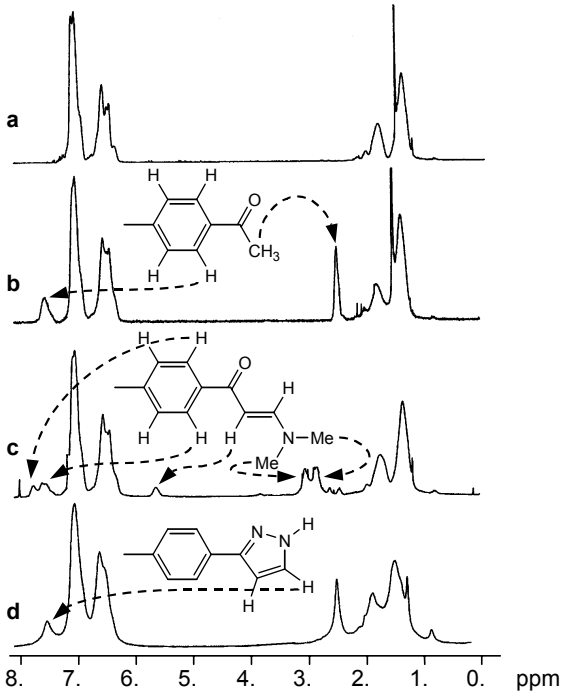


Figure 2. ^{1}H-NMR spectra (from solutions, thf-D$_8$) of a) polystyrene (**1**), b) poly(styrene-*co*-(4-acetylstyrene)) (**2**), c) poly(styrene-*co*-(4-(3-dimethylamino-2-propenone)styrene) (**3**), d) poly(styrene-*co*-(4-(3-pyrazolyl)styrene) (**4**).

The elemental analysis of **2** proves a degree of acylation of about 20 % (C:O = 39.6:1), which corroborates with the data of the further functionalized compounds **3** and **4**. However, owing to the more polar side chains, compounds **3** and **4** tend to absorb the solvent (methanol) employed for the precipitation of the polymers, which can only be removed by keeping the polymers under vacuum for a long time and therefore has to be taken into account for the calculation of the elemental analyses.

Conclusions

Polystyrene can be transferred into a soluble polystyrene / poly[4-(3-pyrazolyl)styrene] copolymer containing about 20% of pyrazole substituted phenyl rings. The final product and the intermediate compounds were characterized by elemental analyses and ^{1}H-NMR and infrared spectroscopy. This procedure opens up an access to a new type of functionalized polymer with applications in metal ion extraction and catalysis.

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