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POLYMERS AS REAGENTS AND CATALYSTS. 39.
INTRODUCTION OF PHENYLAMIDO AND PHENYLHYDRAZIDO GROUPS INTO A CROSSLINKED STYRENE-ACRYLATE MATRIX*

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Abstract

Crosslinked copoly(styrene-p-nitrophenylacrylate) (**1**) was hydrolyzed to copoly(styrene-acrylic acid) (**2**) while further transformation with thionyl chloride gave copoly(styrene-acryloyl chloride) (**3**). Room temperature reaction of copoly(styrene-acryloyl chloride) (**3**) in acetonitrile with aromatic amines (aniline, pentafluoroaniline) and aromatic hydrazines (phenylhydrazine, pentafluorophenylhydrazine) gave the corresponding amides (**4**, **5**) and hydrazides (**6**, **7**). The swelling abilities of these amides and hydrazides depended on the type of functional group (amido, hydrazido), aromatic moiety (phenyl ring, pentafluorophenyl ring) and solvent polarity (chloroform, dimethylformamide, perfluorodecaline, perfluorooctane, perfluorocyclic ethers $C_8F_{16}O$). No significant enhancement in swelling capacity in perfluoro carbonated solvents was achieved by substitution of the phenyl ring by fluorosubstituted rings.

Introduction

Polymer supported reagents and catalysts play an important role in many fields of chemistry [1-9] and chemical technology [10-16], as well as in medicine [17-20] and chemistry related technologies [21-24]. Immobilisation of a reagent on an insoluble crosslinked polymer matrix is usually reflected

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*Dedicated to the memory of Prof. Dr. Anton Šebenik.

in a much easier handling reagent, though reactivity can be changed. The required functionalization of a polymer reagent can be achieved through polymerisation of appropriately functionalized monomers or through further functionalization of polymer resins. Chemical modification of polymer resins therefore represents an important technique for preparation of new reagents, catalysts, separation media, etc. Recently much work in organic synthesis has been devoted to the use of polymer supported reagents, especially with respect to combinatorial chemistry [25-32].

By far the most studied polymer carrier is crosslinked polystyrene, and a number of reports have appeared dealing with additional crosslinking during the introduction of various functional groups into the polymer backbone, and the swelling behaviour of polystyrene based resins. Crosslinked polystyrene has a limited range of solvent compatibility due to its poor swelling capacity in polar solvents. It has, however, been demonstrated that substitution of some styrene units by acrylic esters and amides can substantively change the swelling behaviour [33]. It is known that the swelling ability of a crosslinked resin is an important factor in the selection of reaction conditions and the supported reagent itself. Since most of the reaction sites are positioned inside the crosslinked polymer particle, the accessibility of reactants is hindered in the case of poor swelling.

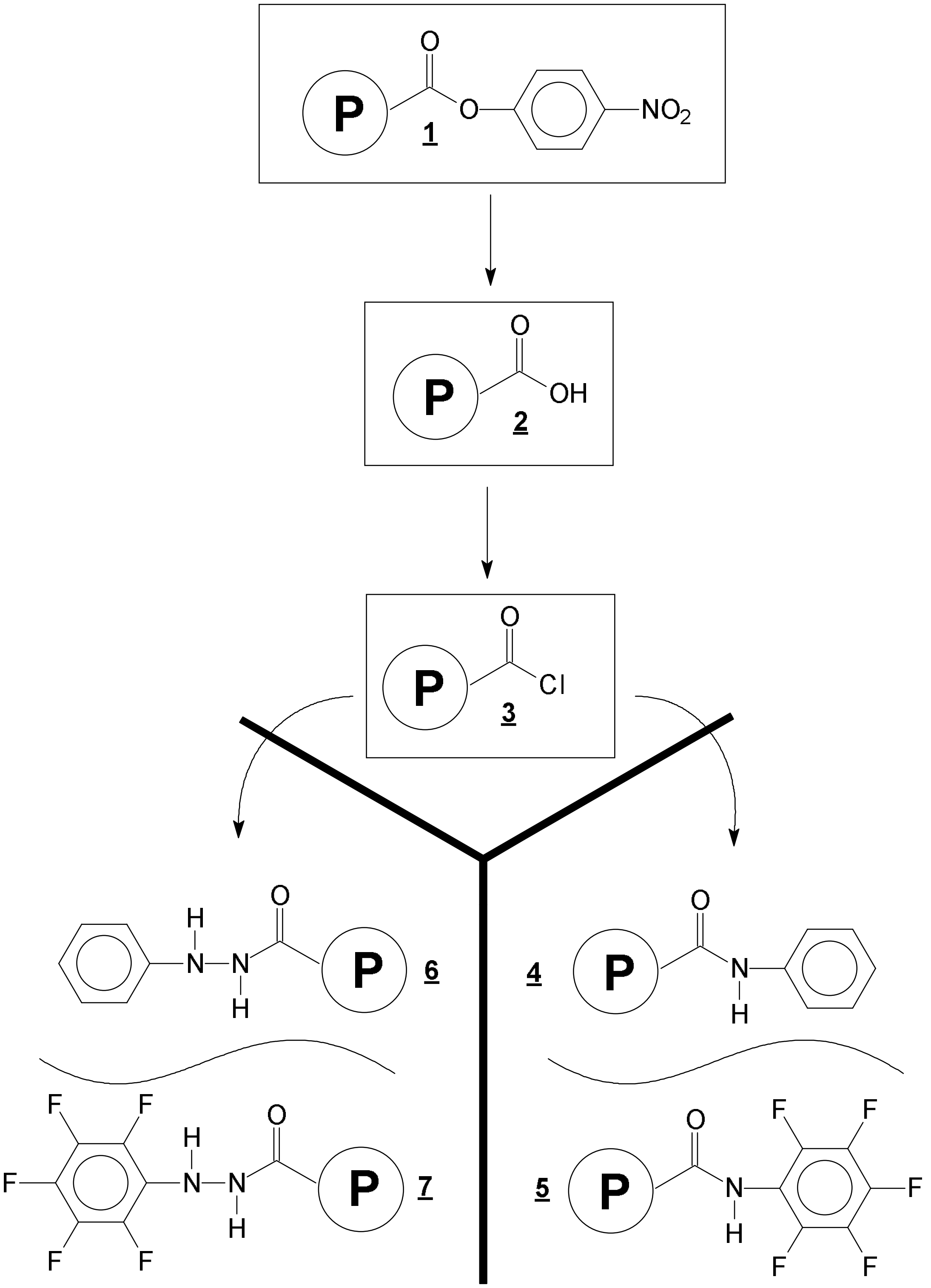
Perfluoro carbonated solvents have become increasingly important and the subject of many studies dealing with their applications in organic synthesis; this is due to some of their unique properties, such as inertness and non-toxicity [34,35]. Some new approaches, such as the fluorous biphasing concept were developed [36-40] and the advantages of such methods were proven, amongst other, by oxidations [41-43] and reductions [44,45]. The use of perfluoro carbonated solvents has also been reported in the context of soluble fluorocarbon polymers with reactive sites that can bind reagents and render them soluble in the fluorous phase [46]. We were interested in the effect of introduction of perfluorophenyl rings into the polymer matrix of crosslinked copoly(styrene-acrylate) on the swelling abilities of perfluorophenyl derivatives in perfluoro carbonated solvents.

In the present paper we report the preparation of perfluorophenylamido, perflurophenylhydrazido, anilido and phenylhydrazido derivatives from copoly(styrene-p-nitrophenylacrylate) (**1**) and of the effect of the polymer structure changes on the swelling abilities of these resins in the perfluoro carbonated solvents perfluorooctane (Fluorinert FC-77), perfluorodecaline and perfluoro cyclic ethers (Fluorinert FC-75), as well as in chloroform and dimethylformamide.

Results and discussion

Several advantages of the crosslinked polystyrene-acrylate matrix for preparation of reagents and catalysts have already been presented [47,48]. We have demonstrated that p-nitrophenolate is a convenient leaving group for functionalization of crosslinked poly(styrene-acrylate) resin [49-52], and thus effectively substituting for 2,4,5-trichlorophenolate which was used in earlier investigations [47,48]. Crosslinked copoly(styrene-p-nitrophenylacrylate) (**1**) readily reacted with primary amines; however additional crosslinking of the polymer matrix was observed with some primary amines [49], bifunctional amines [50] and hydrazines [51]. On the other hand, under similar conditions functionalizations with less basic aromatic amines failed. For the above mentioned reasons we decided to test another synthetic strategy for preparation of anilido and phenylhydrazido derivatives, namely conversion of **1** to the acrylic acid derivative **2** and further transformation to the acid chloride derivative **3** (*Scheme*).

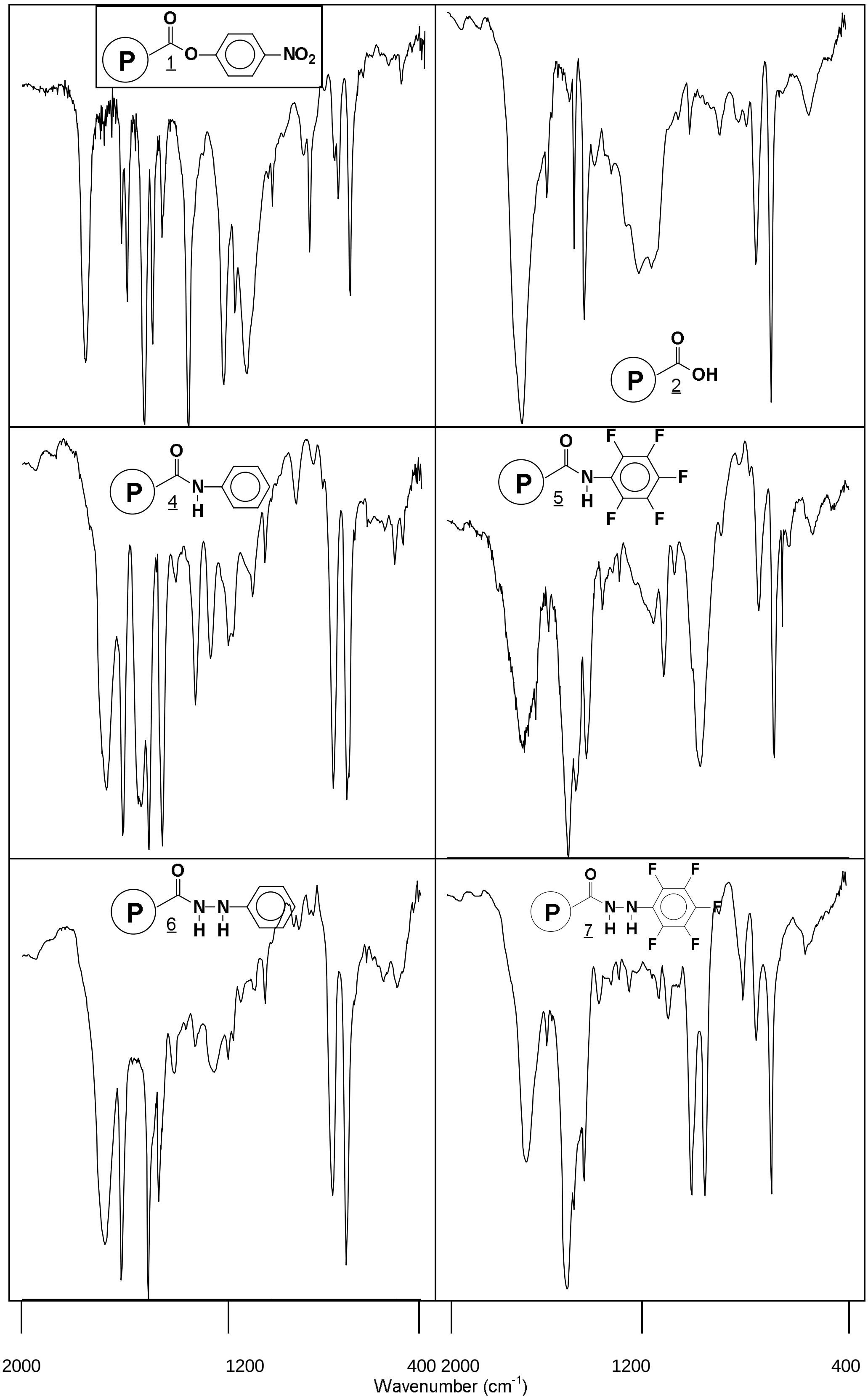
SCHEME



First we studied the reaction conditions for the hydrolysis of crosslinked copoly(styrene-p-nitrophenylacrylate) (**1**). Reaction with a 1.5 M aqueous solution of NaOH gave almost no desired product as the polymer beads sustained their chemical structure even after 10 hours reaction under reflux. We suspected the inertness of the beads was due to their poor swelling in water and thus performed the reaction in the presence of tetrahydrofurane since the swelling capacity of copoly(styrene-p-nitrophenylacrylate) (**1**) in tetrahydrofurane is 6.1 ml/g. The reaction was monitored by FTIR spectroscopy and after 2 hours of stirring under reflux the complete disappearance of nitro peak at 1345 cm^{-1} was observed, as well as the C=O double bond shift from 1760 cm^{-1} to 1650 cm^{-1}. The sodium salt of copoly(styrene-acrylic acid) was converted to acid (**2**) with HCl (C=O double bond shift to 1705 cm^{-1}). The resin was also analysed by combustion elemental analysis, proving complete substitution of p-nitrophenyl groups by hydroxy groups. Further reaction of copoly(styrene-acrylic acid) (**2**) with thionyl chloride in acetonitrile at room temperature resulted in a polymer resin with 13.7% of chlorine which represents more than 80% functionalization. FTIR spectroscopy showed the shift of the C=O double bond peak from 1705 cm^{-1} to 1785 cm^{-1} (*Figure 1*).

It is known that the chemical reactivity of acid chlorides strongly depends on their structure, the nucleophile and reaction conditions, and for this reason we decided to investigate the reactivity of the polymer supported acid chloride. Reactions of crosslinked copoly(styrene-acryloyl chloride) (**3**) with aniline or pentafluoroaniline in acetonitrile at 50°C in the presence of triethylamine as a base gave amides **4** or **5** , respectively, with 3.6 or 2.5 mequiv of amido group per gram (calculated for **4** 3.2 mequiv, calculated for **5** 2.5 mequiv of amido groups per gram). (*Scheme*). Under similar conditions reactions with phenylhydrazine or pentafluorophenylhydrazine resulted in resins **6** or **7**, respectively, with 2.8 mequiv or 2.5 mequiv of hydrazido groups per gram (calculated for **6** 3.0 mequiv, calculated for **7** 2.4 mequiv of hydrazido groups per gram). No additional crosslinking of the polymer matrix was observed during the nucleophile addition-substitution process. The reactions were easily monitored by FTIR spectroscopy (*Figure 1*) and

Figure 1: FTIR spectra of polymer resins

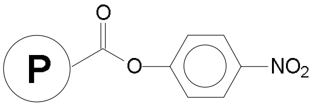
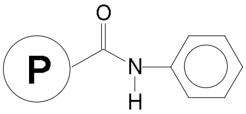
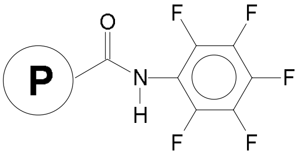
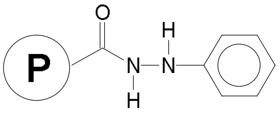
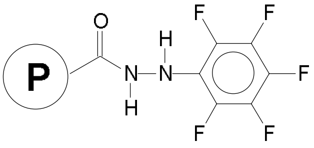


elemental analysis, showing nitrogen was again introduced into the molecules.

As crosslinked polymer beads are usually insoluble in all solvents, it is of vital importance for the polymer beads to swell in the solvent in use so that access of the soluble substrates to polymer supported reagents or catalysts is enabled. The swelling properties of the polymer in question is therefore one of its most important characteristics and can depend on the chemical structure of the backbone and the groups attached, the degree of crosslinking and its physical structure on one hand, and the properties of the solvent on the other. We tested the swelling abilities of resins **4**, **5**, **6** and **7** in dimethylformamide, chloroform and in the perfluorocarbonated solvents perfluorooctane (Fluorinert FC-77), perfluorodecaline and perfluoro cyclic ethers (Fluorinert FC-75). The results are presented in the *Table* and in *Figure 2*. Copoly(styrene-p-nitrophenylacrylate) (**1**) showed no swelling in fluoro solvents but high solvent capacity in dimethylformamide and chloroform. Substitution of the paranitrophenyl moiety in the polymer matrix with hydrazido or anilido groups did not cause significant changes in swelling capacity of the resins in chloroform; however, larger differences were observed in dimethylformamide where a higher decrease in swelling was observed for phenylhydrazido beads (**6**) than for anilido (**4**). Only slight enhancement of swelling was observed in perfluoro carbonated solvents for amido and hydrazido polymers in comparison to ester (**1**). Substitution of the phenyl ring by the pentafluorophenyl group in the polymer matrix enhanced swelling in dimethylformamide (the largest effect), chloroform and Fluorinert FC-75, while the opposite effect was observed in perfluorodecaline. On the other hand, substitution by a pentafluorophenyl group in amido resins diminished swelling in dimethylformamide (the largest effect) and chloroform, while enhancing swelling capacity in all perfluoro carbonated solvents.

The established effect of ester group substitution with amido or hydrazido functional group on swelling capacity of polymer resins (**4**-**7**) on the one hand, and the unpredictability of the effect of phenyl group substitution with pentafluoro analogues on the other, confirmed again how difficult is to foresee the physical properties of new polymeric systems and their behaviour in various solvents.

Table : Effect of polymer structure on swelling in various solvents[a]

POLYMER	mL/g[b]	SOLVENT $CHCl_3$	FC-77	PFD	FC-75	DMF
 **1**	1.9	4.8	1.9	1.9	1.9	7.5
 **4**	1.7	5.0	2.3	1.9	2.2	6.5
 **5**	2.0	4.8	2.5	2.4	2.5	5.9
 **6**	1.8	5.1	2.4	2.5	1.9	4.8
 **7**	2.0	5.7	2.4	2.2	2.4	5.6

[a] Swelling capacity in mL of swollen beads/g of air-dry resin.

[b] Volume of 1g air-dry resin.

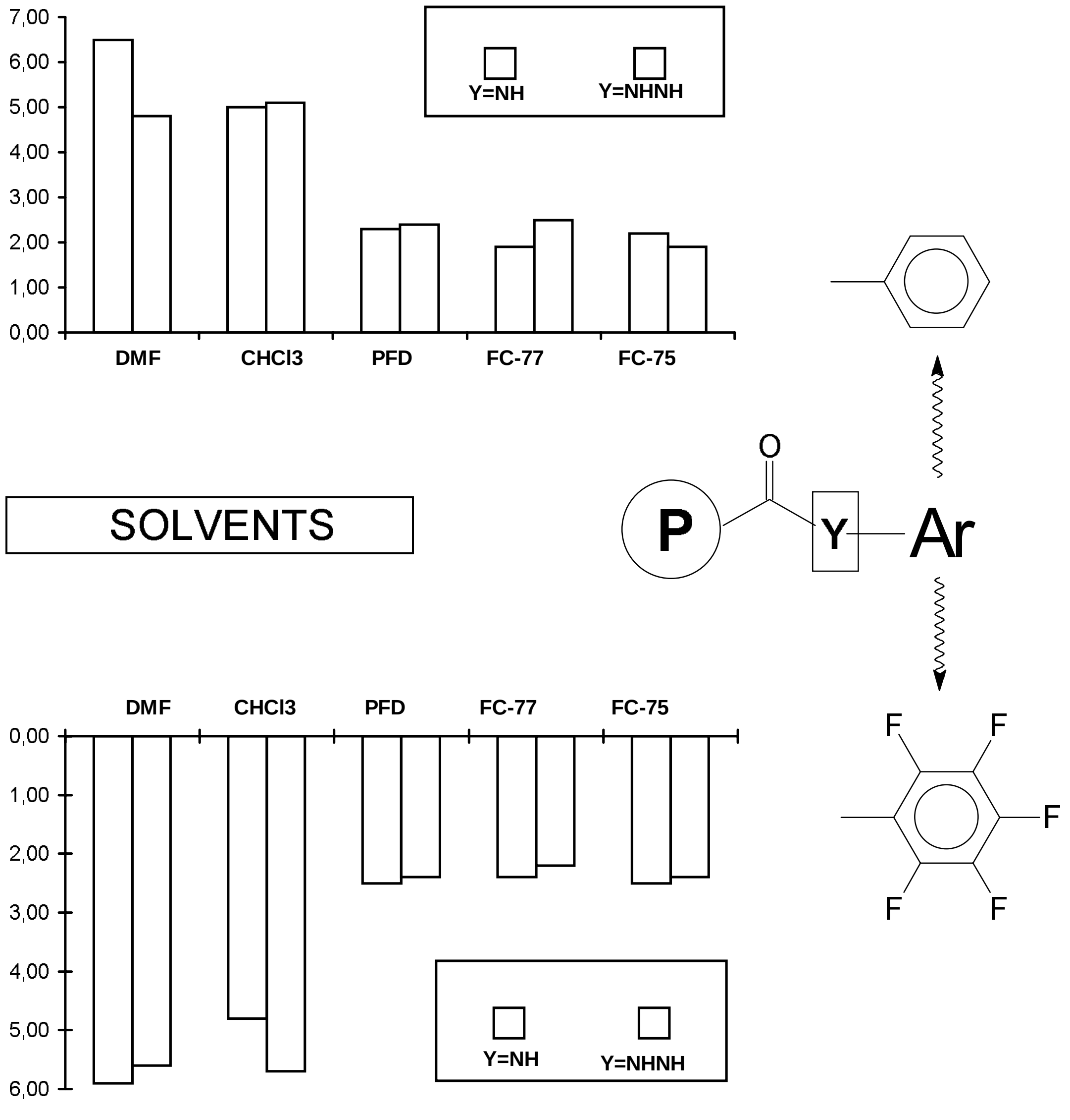
FC-75: trade name for perfluoro carbonated solvent, consisting mainly of perfluorocyclic ethers $C_8F_{16}O$

FC-77: trade name for perfluoro carbonated solvent, consisting mainly of perfluorooctane

PFD: perfluorodecaline

DMF: dimethylformamide

***Figure 2**: Effect of solvent and polymer structure on swelling of derivatives 4,5,6 and 7*



Experimental section

Materials

Commercially available p-nitrophenol (Fluka), acryloylchloride (Fluka), triethylamine (Fluka), azobisisobutyronitrile (Fluka), poly(vinylpyrrolidone) (Fluka), thionylchloride (Fluka), aniline (Aldrich), pentafluoroaniline (Fluorochem), phenylhydrazine (Aldrich), pentafluorophenylhydrazine (Fluorochem), perfluorodecaline (Fluorochem), Fluorinert FC-75 (3M, mainly perfluorocyclic ethers $C_8F_{16}O$), Fluorinert FC-77 (3M, mainly perfluorooctane) were used as received. Divinylbenzene (Merck, consisting also of 45% isomeric ethylvinylbenzenes) was washed with NaOH (5%) and water before use. The degree of functionalization of resins was determined by FTIR spectroscopy (Perkin-Elmer FT-IR 1720X) and combustion analysis (Perkin-Elmer 2400 CHN). Crosslinked copoly(styrene-p-nitrophenylacrylate) **1**, 4% DVB containing 2.61 mequiv of ester groups per gram of air-dry resin (3.2 mequiv of ester groups per gram of resin dried for 3 hours in vacuo at 110°C) was prepared by literature methods [49,51,52].

Preparation of crosslinked copoly(styrene-acrylic acid) (2)

5 g of air-dry copoly(styrene-p-nitrophenylacrylate) (**1**, 4% DVB) was suspended in 50 ml of tetrahydrofurane and 50 ml of a 1.5 M aqueous solution of NaOH was added. The reaction mixture was heated under reflux with stirring for 2 hours. The solid product was filtered off, washed with deionized water (10 x 50 ml), suspended in 50 ml of deionized water and acidified with diluted HCl until pH=4, again filtered off, washed with deionized water (3 x 50 ml), dried at room temperature for 20 hours and in vacuo at 60°C for 3 hours. The progress of the reaction was monitored by FTIR spectroscopy and combustion analysis and 2.24 g of dry polymer beads was obtained with the following composition: %C=76.20, %H=7.12, %N=0.0.

Preparation of crosslinked copoly(styrene-acryloyl chloride) (3)

5 g of dry copoly(styrene-acrylic acid) (**2**) was suspended in 60 ml of acetonitrile and 9.5 g of thionyl chloride was added. The reaction mixture was stirred at room temperature for 30 minutes. The solid product was filtered off, washed with acetonitrile (3 x 10 ml), dried at room temperature for 20 hours and 6.1 g of polymer beads was obtained. 1 g of air-dry product was further dried in vacuo at 60°C for 3 hours and 0.87 g of dry product was obtained with the following composition: %C=72.29, %H=6.27, %Cl=13.7

Reactions of crosslinked copoly(styrene-acryloyl chloride) (3) with amines and hydrazines

2 g of copoly(styrene-acryloyl chloride) (**3**) was suspended in 25 ml of acetonitrile, 1.96 g of triethylamine and the appropriate amount of amine (aniline, pentafluoroaniline) or hydrazine (phenylhydrazine, pentafluorophenylhydrazine) was added (molar ratio of acyl chloride function: amine= 1: 1.2). The reaction mixture was stirred at room temperature for 30 minutes and at 50°C for 5 hours.The solid product was filtered off, washed with acetonitrile (3 x 10 ml) dried at room temperature for 20 hours and the following amounts of products were isolated: anilide derivative (**4**): 2.57 g; pentafluoroanilide derivative (**5**): 3.15 g; phenylhydrazide derivative (**6**): 2.62 g; pentafluorophenyhydrazide derivative (**7**): 3.76 g;

1 g of air-dry product was further dried in vacuo at 100°C for 3 hours to obtain dry samples with the following compositions:

anilide derivative (**4**): 0.91 g, %C=81.16, %H=7.10, %N=5.06; 3.6 mequiv of anilido groups per gram (calculated 3.2 mequiv per gram),

pentafluoroanilide derivative (**5**): 0.95 g, %C=64.38, %H=4.63, %N=3.55; 2.5 mequiv of anilido groups per gram (calculated 2.5 mequiv per gram),

phenylhydrazide derivative (**6**): 0.93 g, %C=76.32, %H=7.44, %N=7.66; 2.8 mequiv of hydrazido groups per gram (calculated 3.0 mequiv per gram), *pentafluorophenyhydrazide derivative* (**7**): 0.89 g, %C=60.97, %H=4.39, %N=7.06; 2.5 mequiv of hydrazido groups per gram (calculated 2.4 mequiv per gram).

Determination of the swelling capacities of polymer resins

1 ml of air-dry polymer resin was weighed, placed in a graduated cylinder, 10 ml of solvent was added and after 24 hours the volume of swollen beads was measured. The swelling capacities per gram are presented in the *Table*.

Acknowledgements

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References

[1] Labana S. S. (Ed.), *Chemistry and Properties of Crosslinked Polymers;* Academic Press, New York, 1977.

[2] Seymour R. B. and Carraher Jr. C. E., *Structure-Property Relationships in Polymers;* Plenum Press, New York, 1984.

[3] Ford W. T. (Ed.), *Polymeric Reagents and Catalysts;* American Chemical Society, Washington, D.C., 1986.

[4] Laszlo P. (Ed.), *Preparative Chemistry Using Supported Reagents;* Academic Press, San Diego, 1987.

[5] Sherrington D. C. and Hodge P. (Eds.), *Synthesis and Separations Using Functional Polymers;* John Wiley & Sons, Chichester, 1988.

[6] Benhaur J. L. and Kinstle J. F. (Eds.), *Chemical Reactions on Polymers;* American Chemical Society, Washington, D.C., 1988.

[7] Epton R. (Ed.), *Innovation and Perspectives in Solid Phase Synthesis. Peptides, Polypeptides and Oligonucleotides. Macro-organic Reagents and Catalysts;* SPCC (UK), Birmingham, 1990.

[8] Tundo P., *Continuous Flow Methods in Organic Synthesis;* Ellis Horwood, Chichester, 1991.

[9] Smith K. (Ed.), *Solid Supports and Catalysts in Organic Synthesis;* Ellis Horwood, Chichester, 1992.

[10] Eisenberg A. and King M., *Ion-Containing Polymers: Physical Properties and Structure;* Academic Press, New York, 1977.

[11] Flett D. S.(Ed.), *Ion Exchange Membranes;* Ellis Horwood, Chichester, 1983.

[12] Naden D and Streat M., *Ion Exchange Technology;* Ellis Horwood, Chichester, 1984.

[13] Lloyd D.R. (Ed.), *Materials Science of Synthetic Membranes;* American Chemical Society, Washington, D.C., 1985.

[14] Collins A.N., Sheldrake G.N., and Crosby J. (Eds.), *The Commercial Manufacture and Applications of Optically Active Compounds;* John Wiley & Sons, Chichester, 1992.

[15] Scranton A. B., Bowman C. N., and Peiffer R. W. (Eds.), *Photopolymerization. Fundamentals and Applications;* American Chemical Society, Washington DC, 1997.

[16] Dyer A., Hudson M. J., and Williams P. A. (Eds.), *Progress in Ion Exchange. Advances and Applications;* The Royal Society of Chemistry, Cambridge, 1997.

[17] Carraher Jr. C. E. and Gebelein C. G. (Eds.), *Biological Activities of Polymers;* American Chemical Society, Washington D.C., 1982.

[18] Wells J. I., *Pharmaceutical Preformulation: The Physicochemical Properties of Drug Substances;* Ellis Horwood, Chichester, 1988.

[19] Peppas N. A. and Langer R. S. (Eds.), *Advances in Polymer Science. 122. Biopolymers II;* Springer-Verlag, Berlin, 1995.

[20] Park K. (Ed), *Controlled Drug Delivery. Challenges and Strategies;* American Chemical Society Washington, DC, 1997.

[21] Davidson T. (Ed.), *Polymers in Electronics;* American Chemical Society, Washington, D.C., 1984.

[22] Guillet J., *Polymer Photophysics and Photochemistry: An Introduction to the Study of Photoprocesses in Macromolecules;* Cambridge University Press, Cambridge, 1985.

[23] Zachmann H.-G. (Ed.), *Advances in Polymer Science. 108. Structure in Polymers with Special Properties*; Springer-Verlag, Berlin, 1993.

[24] Narkis M. and Rosenzweig N. (Eds.), *Polymer Powder Technology;* John Wiley and Sons, Chichester, 1995.

[25] Hermkens P. H. H., Ottenheijm H. C. J., and Rees D. C., *Tetrahedron* **1996**, *52*, 4527-4554.

[26] Hermkens P. H. H., Ottenheijm H. C. J., and Rees D. C., *Tetrahedron* **1997**, *53*, 5643-5678.

[27] Armstrong R. W., Combs A. P., Tempest P. A., Brown S. D., and Keating T. A., *Acc. Chem. Res.* **1996**, *29*, 123-131.

[28] Thompson L. A. and Ellman J. A., *Chem. Rev.* **1996**, *96*, 555-600.

[29] Früchtel J. S. and Jung G., *Angew. Chem.* **1996**, *108*, 19-46.

[30] Lam K. S., Lebl M., and Krchňak V., *Chem. Rev.* **1997**, *97*, 411-448.

[31] Jung G., Ed., *Combinatorial Peptide and Nonpeptide Libraries;* VCH, Weinheim, 1996.

[32] Czarnik A. W. and DeWitt S. H. (Eds.), *A Practical Guide to Combinatorial Chemistry;* American Chemical Society, Washington DC, 1997.

[33] Arshady R. and Ledwith A., *Reactive Polymers* **1983**, *1*, 159-174.

[34] Zhu D.-W., *Synthesis* **1993**, 953-954.

[35] Chambers R. D. and Edwards A. R., *J. Chem. Soc. Perkin Trans. 1*, **1997**, 3623-3627.

[36] Studer A., Hadida S., Ferritto R., Kim S.-Y., Jeger P., Wipf P., and Curran D. P., *Science* **1997**, *275*, 823-826.

[37] DiMagno S. G., Dussault P. H., and Schultz J. A., *J. Am. Chem. Soc.* **1996**, *118*, 5312-5313.

[38] Gladysz J. A., *Science* **1994**, *266*, 55-56.

[39] Horvath I. T. and Rabai J., *Science* **1994**, *266*, 72-75.

[40] Cornils B., *Angew. Chem.* **1997**, *109*, 2147-2149.

[41] Klement I., Lütjens H., and Knochel P., *Angew. Chem.* **1997**, *109*, 1605-1607.

[42] Pozzi G., Cinato F., Montanari F., and Quici S., *J. Chem. Soc. Chem. Commun.* **1998**, 877-878.

[43] Pozzi G., Colombani I., Miglioli M., Montanari F., and Quici S., *Tetrahedron* **1997**, *53*, 6145-6162.

[44] Curran D. P. and Hadida S., *J. Am. Chem. Soc.* **1996**, *118*, 2531-2532.

[45] Juliette J. J. J., Horvath I. T., and Gladysz J. A., *Angew. Chem.* **1997**, *109*, 1682-1684.

[46] Bergbreiter D. E. and Franchina J. G., *J. Chem. Soc. Chem. Commun.* **1997**, 1531-1532.
[47] Arshady R., *Adv. Mater.* **1991**, *3*, 182-190.
[48] Arshady R., *Makromol. Chem.* **1984**, *185*, 2387-2400.
[49] Zupan M., Krajnc P., and Stavber S., *Polymer* **1996**, *37*, 5477-5481.
[50] Zupan M., Krajnc P., and Stavber S., *J. Pol. Sci.: Part A: Polymer Chemistry* **1998**, *36*, 1699-1706.
[51] Zupan M., Krajnc P., and Stavber S., *J. Pol. Sci.: Part A: Polymer Chemistry* **1996**, *34*, 2325-2331.
[52] Zupan M., Krajnc P., Trnovšek R., and Stavber S., *Acta Chim. Slov.* **1996**, *43*, 189-205.

Povzetek

Zamreženi kopoli(stiren-p-nitrofenilakrilat) (**1**) smo hidrolizirali do kopoli(stiren-akrilne kisline) (**2**) ter nadalje s tionil kloridom pretvorili v zamrežen kopoli(stiren-akriloil klorid) (**3**). Pri sobni temperaturi smo v acetonitrilu iz kopoli(stiren-akriloil klorida) (**3**) z aromatskimi amini (anilin, pentafluoroanilin) in aromatskimi hidrazini (fenilhidrazin, pentafluorofenilhidrazin) sintetizirali zamrežene amidne (**4**, **5**) in hidrazidne derivate (**6**, **7**). Stopnja nabrekanja polimernih nosilcev v topilih je odvisna od tipa funkcionalne skupine (amid, hidrazid), aromatskega dela (fenilni obroč, pentafluorofenillni obroč) in polarnosti topila (kloroform, dimetilformamid perfluorodekalin, perfluorooktan, perfluoro ciklični etri). Zamenjava fenilnega obroča s pentafluorofenilnim ne vodi do bistvenega povečanja nabrekanja v perfluoro topilih.