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Synthetic Methods for the Preparation of Polystyrene Resins Containing Chiral Polyamine Chains

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Abstract: The preparation of functionalized polystyrene-divinylbenzene resins containing functional groups derived from polyamine aliphatic chains has been studied. Best results are always obtained by direct alkylation of the polyamine with Merrifield's polymers, but double alkylation at both end of the polyamine is observed. The procedure is useful for the preparation of polymer containing different chiral and non-chiral polyamine functionalities.

INTRODUCTION

Insoluble polymers containing polyamine chains have several important potential aplications.[1] Cyclic and non-cyclic polyamines can interact, sometimes in a selective fashion, with a variety of species such as transition metal cations, organic and inorganic anions and even neutral compounds, the exact behavior being modulated by the pH of the medium.[2] Accordingly, polymers containing such functionalities can be used for separation processes or for the preparation of supported catalysts based on transition metal cations. Several examples of this kind of polymers have been reported as well as their application in hydrometallurgy processes,[3] in environmental applications[4] and in the preparation of some copper catalysts.[5] For the development of novel supported catalysts that could be of interest for the Fine Chemicals industry, chirality has to be always taken into account as an essential factor.[6] This is also important when enantioselective separations are considered.[7] Accordingly, preparation of resins containing chiral polyamine chains is an important target. On the other hand, recent advances in the area of combinatorial chemistry demand further studies on the functionalization of solid supports and on the development of useful synthetic transformations of the attached fragments. In this context, a careful control of the synthetic procedure is needed in order to obtain polymers having structurally well defined chiral sites that could afford reproducible results and allow for a rational design of novel supported systems.

Here we report on our results on the preparation of polymers containing chiral aliphatic polyamine chains. Different approaches have been considered for the grafting of the desired functional groups onto preformed polystyrene-divinylbenzene polymers and their scope and limitations have been studied.

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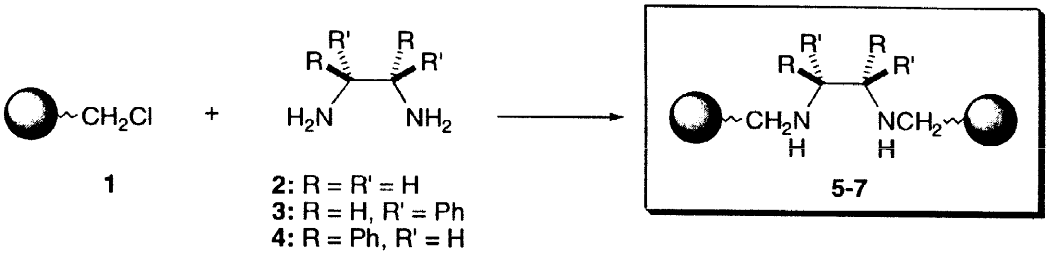
RESULTS AND DISCUSSION

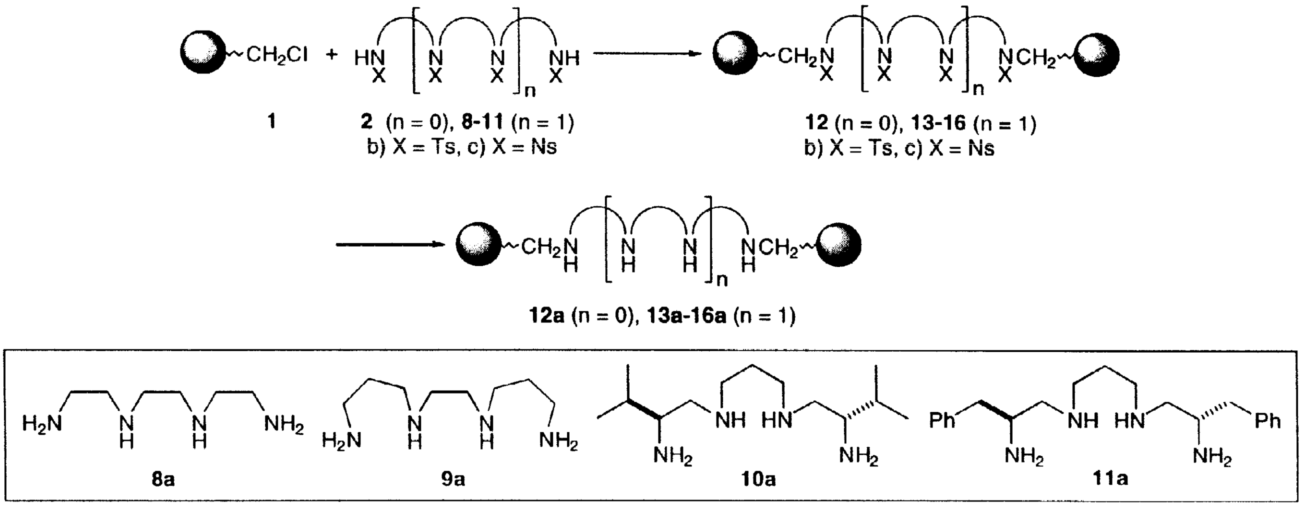
The most simple situation was found when the grafting of ethylenediamines was considered. Ethylenediamine (**2**) and (*R,R*)- or (*S,S*)-1,2-diphenylethylenediamine (**3** and **4**) were supported on crosslinked polystyrene by reaction with a chloromethylated resin under conditions that prevent quaternization (DMF/$NaHCO_3$).[9]



Scheme 1

Complete disappearance of the C-Cl bands at ca. 1260 and 688 cm^{-1} revealed a quantitative transformation of the chloromethyl groups. However, the functionalization degree determined by nitrogen analysis indicated the presence of the general structures **5-7** where both amino groups are linked to the polymeric backbone. Similar crosslinking processes have been described with the use of other difunctional reagents.[9b,10] As a matter of fact, selective grafting through only one of the nitrogen atoms has been reported to require the use of a N,N,N'-trialkyl ethylenediamine.[5] Thus, starting from a Merrifield resin containing 1.08 mmol Cl/g and 1% DVB (DF=0.11), the supported diamines **5-7** were obtained with loadings of 0.4-0.5 mmol/g (DF=0.11).

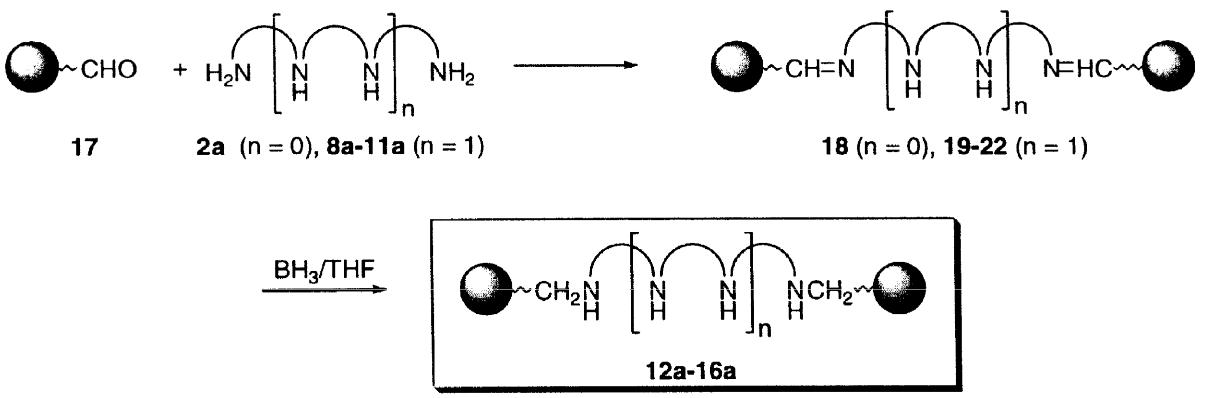
For the introduction of polyamines such as the tetraamines **8a-11a**, direct alkylation with polymers such as **1** does not seem to be appropriate, as side reactions could also take place through the secondary nitrogen atoms.



Scheme 2

Selective alkylation of polyamines at the primary amino groups can be generally obtained by the use of appropriate N-protecting groups like tosyl or related groups.[11] Thus, when pertosylated polyamines **2b, 8b-11b** were reacted with a Merrifield polymer (1.08 mmol Cl/g, 1% DVB, DF=0.11), in the presence of a base, an uncomplete conversion of the chloromethyl groups was observed, giving place to the formation of resins **12b-16b** with loadings of ca. 0.2 mmol/g (DF=0.05, 45% conversion). Additionally, deprotection to give the desired supported polyamines **12a-16a** could not be efficiently accomplished because of the very drastic conditions required for N-detosylation.[11] An obvious alternative was the use of a protective group requiring milder deprotection conditions. Recently, the nitrobenzenesulfonyl (nosyl) group has been shown to be a reasonable alternative for the protection of primary amino groups in N-alkylation processes, requiring very mild conditions for deprotection, conditions that, apparently, were compatible with the polymeric backbone.[12] According to this, the same procedure outlined in the Scheme 2 was carried out starting from polyamines **2c, 8c-11c** (X=Nos). Quantitative conversions were obtained in the preparation of polymers **13c-14c** derived from non-chiral pernosylated polyamines **8c** and **9c**, but lower yields were obtained when chiral compounds **10c** and **11c** were used. Moreover, when elimination of the nosyl groups was attempted under the usual conditions (PhSH, $HSCH_2COOH$,...), a partial loss of the polyamine moiety was always observed.

A second alternative assayed was the one shown in the Scheme 3 which does not require N-protection of the starting polyamines. In solution, this procedure has been shown to be very efficient for the terminal alkylation of linear polyamines.[13]



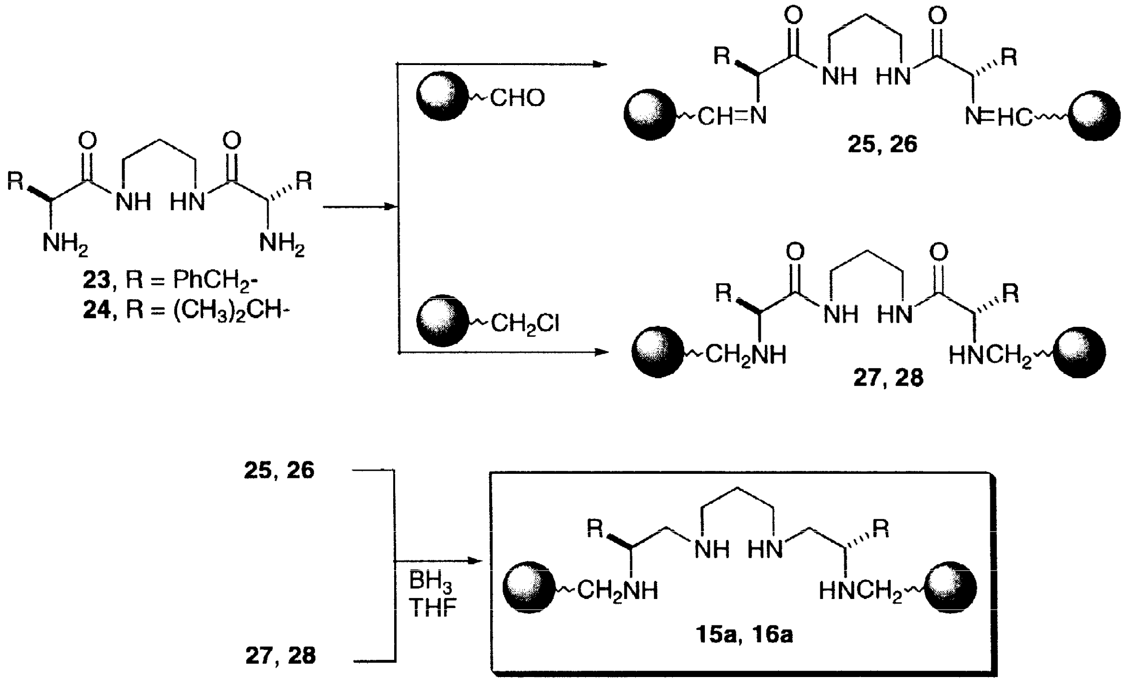
17 **2a** (n = 0), **8a-11a** (n = 1) **18** (n = 0), **19-22** (n = 1) **12a-16a**

Scheme 3

The polymeric benzaldehyde **17** was prepared by oxidation of the chloromethyl groups with DMSO (1.006 mmol/g, 1% DVB, DF=0.11) as has been previously described.[14] Reaction of **17** with polyamines **8a-11a** as well as with diamine **2a** afforded polymeric diimines **18-22**. This reaction can be easily monitored through the complete disappearance of the carbonyl band at 1700 cm^{-1} and the appearance of a new C=N band at 1642 cm^{-1}. Elemental analyses for these polymers showed, however, nitrogen contents slightly lower than expected for resins **18-22**.

Conversion of polymeric diimines **18-22** into supported polyamines **12a-16a** could not be carried out with the use of $NaBH_4$ under different conditions. A quantitative transformation was obtained, however, in all cases with the use of BH_3/THF. Thus, polymer-supported polyamines **12a-16a** were obtained with loadings ranging from 0.5 mmol/g for **12a** to ca. 0.3 mmol/g for resins **13a-16a**.

Chiral polyamines **10a** and **11a** were prepared from 1,3-propylenediamine and aminoacids phenylalanine and valine, diamides **23** and **24** being the synthetic intermediates.[15] This lead us to study the possibility of using such diamides for the preparation of the desired supported chiral polyamines. In this way, two different approaches were used. According to the former results, reaction of compounds **23-24** with polymeric benzaldehyde **17** gave supported diimines **25** and **26**. A complete disappearance of the carbonyl band at 1700 cm^{-1} was observed along with the presence of the new amide band at 1671 cm^{-1}. As in the former case, the nitrogen content was lower than expected.



Scheme 4

Simultaneous reduction of both the imine and the amide groups could be easily achieved, in a quantitative way, with the use of BH$_3$/THF in refluxing THF. The corresponding polymers **15a** and **16a** with loadings of 0.25 mmol/g were thus obtained. Attempts to selectively reduce the imine groups to transform resins **25-26** into polymers **27-28** using milder conditions, were unsuccessful. A partial reduction of the amide group was always obtained along with the complete reduction of the imine functionality as evidenced by FT-IR spectroscopy.

In a second approach, direct reaction of diamides **23-24** with a Merrifield polymer, under conditions similar to those used for ethylenediamines **2-4**, afforded diamides **27-28**. Quantitative conversion of the chloromethyl groups could be monitored through the complete disappearance of the C-Cl band at ca.1260 cm^{-1} in the FT-IR and , specially, in the FT-Raman spectra of those resins (see Figure 1). The presence of the expected functional groups is shown by the observation of the amide C=O band at 1670 cm^{-1} as well as distinct N-H bands (see Figure 1). Reduction of resins **27-28** with BH$_3$/THF gave the desired polymers **15a-16a**, again in quantitative yields.

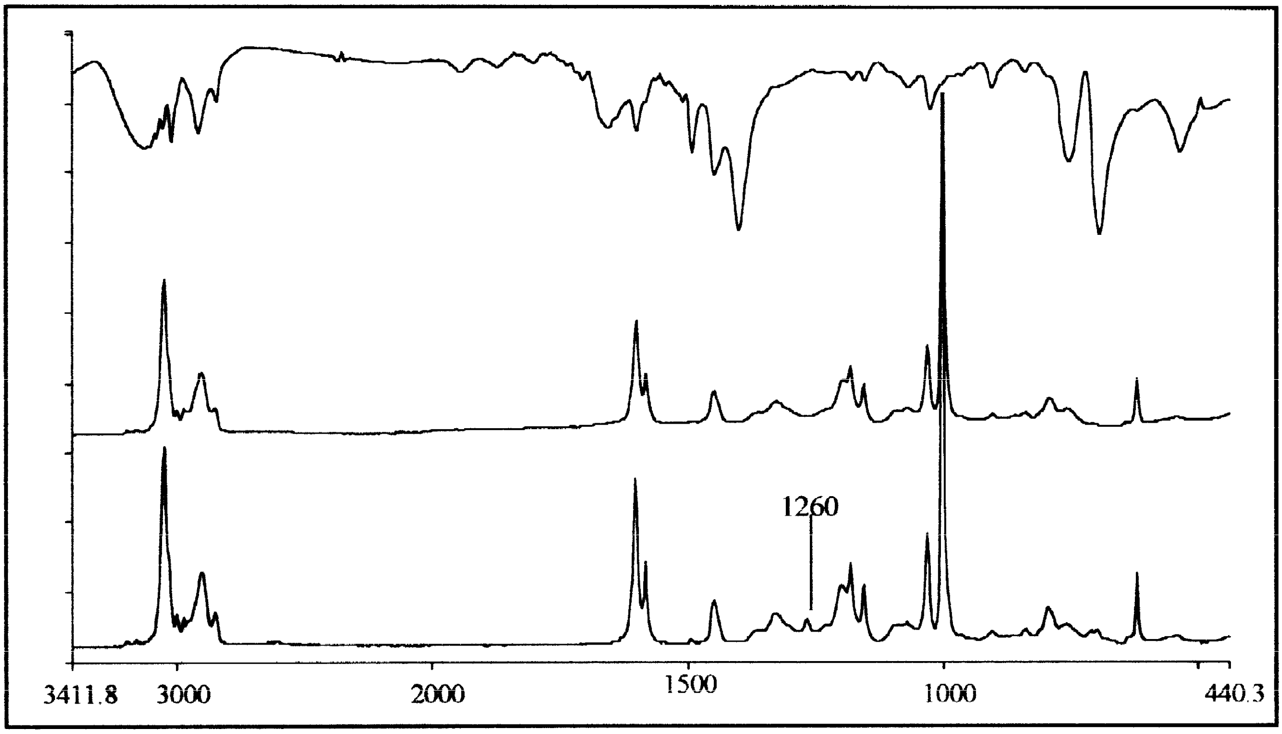


Figure 1

CONCLUSIONS

Polymers containing polyamine chiral groups can be prepared in different ways starting from chloromethylated resins. Direct alkylation at both ends of the polyamine chain can be accomplished when ethylenediamines **2-4** or chiral diamides **23-24** are used. As an alternative, in particular for polyamines **8a-9a**, formation of polymeric diimines **18-22** and **25-26** can be obtained from resin bound benzaldehyde **10**. Reduction of the imine group as well as reduction of the amide functionality in **25-28**, can be easily achieved with the use of BH_3/THF. Preliminary experiments have shown that these polymers containing polyamine chains can form the expected copper complexes in a similar way to that reported for related systems. Copper-loaded resins, however, could not be obtained from polymeric imines, as hydrolysis of such groups seems to be favored by the presence of the metal cation. Additional work in order to study the properties and applications of those resin are currently being carried out.

EXPERIMENTAL

Commercial polystyrene-divinylbenzene copolymers were purchased from Fluka and washed and vacuum dried to constant weight before use. IR spectra of KBr pellets of polymers were recorded on a Perkin-Elmer 2000 FT-IR spectrophotometer. Raman spectra were obtained on the Raman accesory for the same instrument Quantitative elemental analyses were performed in duplicate on a Carlo Erba EA1108 CHNS-O instrument.

General procedure for the preparation of polymer-supported diamines 5-7. Synthesis of 6.

A stirred suspension of a Merrifield polymer (1% crosslinked, 1 mmol Cl/g, DF = 0.11, $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_9H_9Cl)_{0.11}]$) (100 mg, 0.1 mmol) and (*R,R*)-1,2 diphenylethylenediamine **3** (64 mg, 0.3 mmol) in dry DMF (20 mL) containing anhyd. $NaHCO_3$ (25 mg, 0.3 mmol) was heated at 80°C for 24 h. The resulting resin was filtered and washed (3x) with DMF, H_2O, MeOH:H_2O (1:2, 1:1, 2:1), CH_2Cl_2 and vacuum dried at 0°C overnight. IR (KBr): peaks absent at 1260 and 688 cm^{-1}. Anal. calcd. for $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_{16}H_{16}N)_{0.11}]$: C, 91.0; H, 7.6; N, 1.3. Found: C, 90.6; H, 8.0; N, 1.35. The nitrogen content corresponds to 0.48 mmol/g (DF = 0.11).

General procedure for the preparation of polymer-supported diimines 18-22. Synthesis of 18.

A suspension of polymeric benzaldehyde (1% crosslinked, 1 mmol CHO/g, DF = 0.11, $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_9H_8O)_{0.11}]$) (200 mg, 0.2 mmol) and ethylenediamine (36 mg, 0.6 mmol) in dry DMF (20 mL) was heated at 80°C for 24 h. The resulting resin was filtered and washed (3x) with DMF, H_2O, MeOH:H_2O, MeOH and CH_2Cl_2 and vacuum dried at 50°C overnight to give polymer **18**. IR (KBr): peak absent at 1701 cm^{-1}, peak present at 1642 cm^{-1}. Anal. calcd. for $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_{10}H_{11}N)_{0.11}]$: C, 90.1; H, 7.7; N, 1.4. Found: C, 90.0; H, 7.9; N, 1.2. The nitrogen content corresponds to 0.43 mmol/g (DF = 0.11).

General procedure for the preparation of resins 12a-16a by reduction of diimines 18-22. Synthesis of 12a.

To a suspension of resin **18** (1% crosslinked, 0.43 mmol/g, DF = 0.11, $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_{10}H_{11}N)_{0.11}]$) (100 mg, 0.43 mmol) in dry THF (5 mL) a 1 M solution of BH_3/THF was added under an inert atmosphere. The mixture was stirred at rt for 24 h. The resulting resin was filtered and washed (3x) with THF, diluted HCl, MeOH:H_2O, MeOH and CH_2Cl_2 and vacuum dried at 50°C overnight to give polymer **12a**. IR (KBr): peak absent at 1642 cm^{-1}. Anal. calcd. for $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_{10}H_{13}N)_{0.11}]$: C, 90.7; H, 7.8; N, 1.2. Found: C, 90.0; H, 7.9; N, 1.4. The nitrogen content corresponds to 0.5 mmol/g (DF = 0.11).

Preparation of polymer-supported diimines 25 and 26. Synthesis of 25.

A suspension of polymeric benzaldehyde (1% crosslinked, 1 mmol CHO/g, DF = 0.11, $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_9H_8O)_{0.11}]$) (100 mg, 0.1 mmol) and diamide **23** (82 mg, 0.3 mmol) in dry DMF (20 mL) was heated at 80°C for 24 h. After the usual work up, the resin **25** was obtained. IR (KBr): peak absent at 1700 cm^{-1}, peaks present at 1640-1675 cm^{-1}. Anal. calcd. for $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_{15.5}H_{20}N_2O)_{0.11}]$: N, 2.4. Found: N, 1.4. The nitrogen content corresponds to 0.25 mmol/g (DF = 0.11).

Reduction of polymer-supported diimine 25.

To a suspension of resin **25** (0.25 mmol/g, 50 mg, 0.13 mmol) in dry THF (5 mL) a 1 M solution of BH_3/THF was added, and the resulting mixture was refluxed for 24 h under an argon atmosphere. After the same work up described for **12a**, the polymer **15a** was obtained. IR (KBr): peaks absent at 1640-1675 cm^{-1}. Anal. calcd. for $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_{15.5}H_{24}N_2)_{0.11}]$: N, 2.5. Found: N, 1.6. The nitrogen content corresponds to 0.29 mmol/g.

General procedure for the preparation of polymer-supported diamides 27 and 28. Synthesis of 27.

A suspension of a chloromethyladed resin (1% crosslinked, 1 mmol Cl/g, DF = 0.11, $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_9H_9Cl)_{0.11}]$) (100 mg, 0.1 mmol) and diamide **23** (82 mg, 0.3 mmol) in dry DMF (20 mL) containing anhyd. $NaHCO_3$ (25 mg, 0.3 mmol) was heated at 70°C for 24 h. The resulting resin was filtered and washed (3x) with DMF, H_2O, MeOH:H_2O, MeOH and CH_2Cl_2 and vacuum dried at 50°C overnight to give polymer **27**. IR (KBr): peaks absent at 1260 and 688 cm^{-1}, peaks present at 1670 and 3018 3053 and 3081 cm^{-1}. Anal. calcd. for $[(C_{10}H_{10})_{0.01}(C_8H_8)_{0.88}(C_{15.5}H_{22}N_2O)_{0.11}]$: N, 2.4. Found: N, 1.8. The nitrogen content corresponds to 0.32 mmol/g.

Reduction of this polymer with BH_3/THF as described before afforded the corresponding resin **15a** containing 0.34 mmol of functional group/g.

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