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Synthesis of Covalently Bound Polymeric Macrocyclic Amines and Amides

Dieter Wöhrle* and Volker Nicolaus

Organische und Makromoleculare Chemie, Studiengang Chemie, Universität Bremen, Leobener Straße NW II, D-2800 Bremen 33, Federal Republic of Germany

SUMMARY

Covalently bound polymeric macrocyclic amines 3b are prepared by two routes. A macroreticular polystyrene is used as carrier. One route proceeds over the polymer bound macrocyclic amine 6b. Furthermore, the analogous low molecular model compounds are prepared. The polymers are able to bind transition metal ions reversibly.

INTRODUCTION

Macrocyclic amines A and amides B as nitrogen containing analogous of crown ethers are of increasing interest (Ref. 1-5).

A **B**

The multidentate ligands A, B are able to bind transition metal ions. For example, the selectivity decreases in the order Cu(II)>>Zn(II)>Cd(II) >Co(II) (Ref. 6). Macrocyclic dioxotetraamines exist as double deprotonated neutral complexes of the type $[Mt^{II}H_{-2}L]^{\circ}$ with square planar arrangement of the four nitrogen ligand atoms (Ref. 3, 4). In contrast, macrocyclic amines form dicationic chelates with bivalent transition metal ions of the type $[Mt^{II}L]^{2+}$ with octahedral coordination (Ref. 4,7-11). Demetallization may be carried out with acids. Macrocyclic amines can stabilize transition metal ions in unconventional oxidation states such as Ni(III), Cu(III) (Ref. 12). Co(II), Ni(II), Cu(II) chelates of macrocyclic amines may form either binuclear μ-peroxo complexes or mononuclear superoxo complexes with dioxygen in aqueous solution reversibly (Ref. 3, 13, 14).

Covalently bound polymeric macrocyclic amines and amides may combine the advantage of chelate properties with the advantages of polymer immobilization. The need to prepare such compounds is expressed in Ref. 11 (p. 83-107) due to possible enzyme like activity. Till now only two papers shortly describe covalently bound polymeric chelates of type A (Ref. 6,15). The reaction of linear chloromethylated polystyrene with a macrocyclic amine results in multiple N-alkylation under network formation. Additionally, it must be mentioned that N-alkylation reduces the bond strength of metal ions (Ref. 1). Our paper is the first to report on the preparation of covalently bound polymeric macrocyclic amines and amides by C-C connection between the ligands and the polymer chain. In order to direct the investigations towards practical interest a commercial macroreticular polystyrene was used as starting material for the polymer immobilization. The other

* To whom offprint requests should be sent

compounds are also easy available.

SYNTHESES

The preparation of macrocyclic amines of type A and amides of type B was carried out on a macroreticular resin. Starting from an ethenyl group containing precursors of the macrocyclic amines or amides is not advantageous this time because the (C=C)-bond may react during preparation of the macrocycles. The concept of synthesis considers the preparation of the polymers as well as that of the corresponding low molecular model compounds. In this way the synthesis is optimized and identification of the products of the polymer analogous reactions is facilitated. Two ways of preparing covalently bound polymeric macrocyclic amines were followed. Route A leads over the polymer bound macrocyclic amide. Route B includes a polymer bound tosylated macrocyclic amine which exhibits chelating properties and may be used as starting material for other substituted macrocyclic amines (Ref. 2,16).

Route A

The low molecular macrocyclic amide 2a was prepared through the reaction of malonic acid ester (1a) with 1,4,8,11-tetraazaundecane in ethanol. In contrast to the literature on analogous cyclic amides (Ref. 1) the reaction was carried out according the principle of dilution in order to obtain a yield of 2a greater than 10 %. Main products are oligomeric and polymeric amides. For the preparation of the covalently bound polymeric macrocyclic amide, at first 1a was immobilized on a chloromethylated macroreticular resin (Cl content 10.05 %). The preparation of 1b was successfully carried out with the sodium salt of 1a. 98 % of the chloromethyl groups react with 1a under formation of 1b. The subsequent reaction of 1b with tetraazaundecane in pyridine leads to 75 % conversion of ester groups to amide groups of 2b, according to elemental analyses. The reactions in ethanol, DMF and DMSO instead of pyridine were not successful. Formation of polymeric or oligomeric amides is prohibited due to the macroreticular structure of the carrier.

The reduction of the amide groups of 2a,b under formation of macrocyclic amines 3a,b gives nearly quantitative yields.

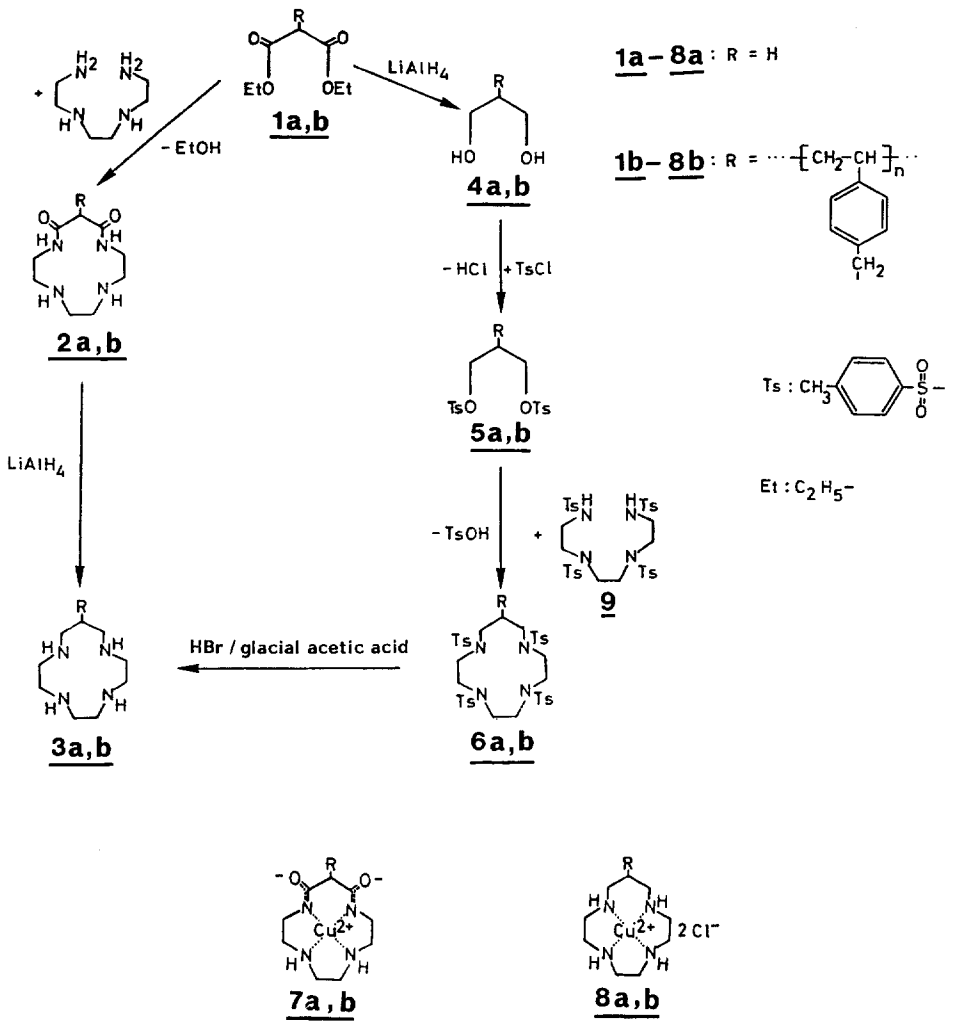
Route B

The preparation of covalently bound polymeric tosylated macrocyclic amines 6a,b was achieved by the reaction of the corresponding ditosylated propandiols 5a,b with the tosylated tetraazaundecane 9. 9 was obtained in 54 % yield. In the case of the polymers the polymer bound propanediol 4b must be prepared first. This was quantitatively achieved by the reduction of (C=O) groups of the polymer 1b. Also the tosylation of the (H-O)groups of 1b under formation of 5b in pyridine proceeds quantitatively. In the reaction of 9 with 5a,b the former was converted into its disodium salt with NaH. Reaction with 5a results in 30 % of low molecular 6a while starting from 5b for the preparation of the polymer 6b all tosylated alcoholic groups reacted.

The low molecular 6a and the analogous polymer 6b could be quantitatively detosylated in HBr/acetic acid via the hydrobromic acid salts. 3a,b were obtained as reaction products.

It must be started that route A is the shorter pathway for the preparation of macrocyclic amines 3. However, as mentioned before, route B is the one of a greater variability.

Scheme 1


Route A
Route B
1a,b
LiAlH4
- EtOH
4a,b
2a,b
- HCl
+ TsCl
5a,b
LiAlH4
- TsOH
9
HBr / glacial acetic acid
3a,b
6a,b
1a - 8a : R = H
1b - 8b : R =
Ts : CH3
Et : C2H5-
7a,b
8a,b
2 Cl-

ANALYSES AND METAL BINDING

Elemental analyses are used to calculate the conversion of functional groups of polymer analogous reactions. Additionally, IR-spectroscopy is most helpful in evaluating the conversion of functional groups.

Through the conversion of chloromethylated polystyrene to polymer 1b the (ν(C-Cl)) at 669 cm^{-1} vanishes and a new very intensive absorption of (ν(C=O)) at 1734 cm^{-1} occurs. The IR-spectrum of the polymer bound macrocyclic amide 2b exhibits an intensive absorption for (ν(C=O) of the amide groups at 1669 cm^{-1}. Weak absorptions at 1734 cm^{-1} show that small amounts of ester groups are still present which is also indicated by N- and O-analysis. In the polymer bound macrocyclic amine 3b no absorptions of (ν(C=O) are found. Beside absorptions of polystyrene 1b, 2b, 3b show those of the corresponding low molecular compounds 1a, 2a and 3a.

The successful reduction 1b to 4b is indicated by the disappearance of the (ν(C=O) at 1734 cm^{-1}. The tosylated product 5b shows an intensive doublet at 1192 and 1176 cm^{-1} which is typical of tosylated alcoholes (Ref. 17). Through the reaction of 5b with 9 to 6b the doublet disappears. 3b obtained by detosylation of 6b, shows the same IR-spectrum as 3b prepared by the other way. 4b, 5b, and 6b exhibit beside the mentioned absorption, other ones which are present in 4a, 5a, and 6a.

The polymers 2b and 3b are able to bind transition metal ions from aqueous solutions although the matrix of the carrier is hydrophobic. In comparison to the white colored ligands 2b and 3b the copper(II) containing chelates 7b and 8b are intensively blue and the cobalt(II) containing ones are red-brown colored. In case of the resin 7b, metal uptake results in lowers of pH from 6 to 4 which agree with the structure of the chelate. From aqueous solutions containing Cu(II) and Co(II) only the former was bound (s. Experimental Part). Demetallization was achieved by handling with 5 % hydrochloric acid for a few minutes.

EXPERIMENTAL

Used instruments. FT-IR (Nicolet 5 DX), ^{1}H-NMR (Bruker WH 360), UV/VIS (Perkin Elmer PE 554).

Starting resin: Macroreticular polystyrene with $\sim$ 20 % crosslinking, pore diameter 800 Å, pore volume unknown, 22-50 mesh (Janssen Nr. 22, 094-9). Chloromethylation was carried out with chloromethylmethylether/$ZnCl_2$ in tetrachloroethylene (Ref. 19). The resin contains 1.62 mmole/g CH_2Cl groups (Cl content 5.81 %). The difference between the total Cl content of 10.05 % and the Cl content of the CH_2Cl groups results from the reaction of unreacted vinyl groups of the resin with the chloromethylation agent (Ref. 22).

Copper analyses: 10 mg of the copper containing compound were heated at 1273 K for 2 h in air. After dissolving the residue in a mixture of 6 ml conc. H_2SO_4 and 4 ml conc. HNO_3 the amount of Cu^{2+} was determined at pH 6 with sodium diethyldithiocarbaminate as described (Ref. 18).

Route A

1,4,7,10-Tetraazacyclotridecane-11,13-dion (2a): This compound was prepared as described (Ref. 1).
Yield: 2.14 g (10 %), mp: 464 K (Ref. 1: 462 K).

IR (KBr, cm^{-1}): 3340, 3315, 3259 (ν(N-H)), 1654 (ν(C=O)), 1569 (δ(N-H)) of the amide groups).

1,4,7,10-Tetraazacyclotridecane (3a): The cyclic amine can be prepared through reduction of 2a with $LiAlH_4$ in diethylether (Ref. 1).
Yield: 0.88 g (47 %) mp: 316 K (Ref. 20: 314 K)

IR (KBr, cm^{-1}): 3295 (ν(N-H)), 2957, 2924, 2905, 2856, 2828 (ν(C-H)).

Polymer 1b: 3.2 g (20 mmole) 1a were added under stirring to a suspension of 0.46 g (20 mmole) sodium in 100 ml dry toluene. The mixture was heated under reflux till all sodium has reacted. 5 g of the chloromethylated macroreticular polystyrene containing 1.62 mmole/g chloromethyl groups were added. After 4 h heating under reflux, the isolated resin was treated with ethanol in a soxhlet apparatus and dried at 353 K i. vac. Yield: 6.54 g.

IR (KBr, cm^{-1}): 1734 (ν(C=O)), no absorption at 669 (ν(C-Cl)).

$[(C_8H_8)_{3.88}(C_{10}H_{10})_{1.54}(C_{16}H_{20}O_4)_{1.62}]_n$ $(1057.1)_n$

Calc.: O 9.81
Found: O 10.19

Polymer 2b: 50 ml pyridine, 1 g polymer 1b containing 1.6 mmole diester groups and 4 g (27 mmole) 1,4,7,10-tetraazadecane were heated for 60 h under reflux. The isolated polymer was treated with ethanol in a soxhlet apparatus and dried at 353 K i. vac.
Yield of white colored polymer 2b: 1.1 g

IR (KBr, cm^{-1}): 1669 (ν(C=O)) of amide, weak absorption at 1734 (ν(C=O)) of ester groups from starting material.

$[(C_8H_8)_{3.88}(C_{10}H_{10})_{1.54}(C_{16}H_{20}O_4)_{0.42}(C_{18}H_{26}N_4O_2)_{1.2}]_n$ $(1117.1)_n$

Calc.: N 6.02 O 5.84
Found: N 6.57 O 6.38

Polymer 3b: 300 mg (2.8 mmole) $LiAlH_4$ were suspended in 50 ml dry diethylether under dry nitrogen. After adding 100 mg of polymer 2b containing 1.17 mmole cyclic amide groups the mixture was heated under reflux for 6 h. The excess of $LiAlH_4$ was destroyed with ice water and the precipitating aluminium hydroxide dissolved with conc. H_2SO_4. The isolated polymer was washed with water, treated with ethanol in a soxhlet apparatus and dried at 353 K. i.vac.

IR (KBr, cm^{-1}): Disappearance of the absorption bands at 1669 (ν(C=O amide)) and 1734 (ν(C=O ester)).

$[(C_8H_8)_{3.88}(C_{10}H_{10})_{1.54}(C_{12}H_{16}O_2)_{0.42}(C_{18}H_{30}N_4)_{1.2}]_n$ $(1050)_n$

Calc.: C 83.6 H 8.56 N 6.5
Found: C 82.22 H 8.53 N 6.08

Route B
1,3-Di(p-toluenesulfonyloxy)propane (5a): this compound was prepared in pyridine in a yield of 67 % according to a method described in Ref. 21. Mp: 363 K (Ref. 21: 364-366 K).

IR (KBr, cm^{-1}): 1192, 1174 (ν(S=O))

1,4,7,10-Tetra(p-toluenesulfonyl)-1,4,7,10-tetraazadecane (9): This compound was also prepared according to a method described in Ref. 21. Yield: 51 g (54 %), mp: 480-482 K.

^{1}H-NMR (DMSO-d^6), δ in ppm: 7.3-7.8 (m, phenylene), 3.18 (m, CH_2), 2.4 (s, CH_3): intensity ratio 16:12:12.

1,4,7,10-Tetra(p-toluenesulfonyl)-1,4,7,10-tetraazacyclotridecane (6a): The cyclisation was carried out as described in Ref. 21. Yield: 2.4 g (30 %), mp: 485 K (Ref. 20: 492 K).

1,4,7,10-Tetraazacyclotridecane (3a): The detosylation of 6a was carried out as described in Ref. 21. The resulting tetrahydrobromide of 3a was dissolved in 50 ml of water and 0.5 g (12.5 mmole) NaOH were added. The mixture was heated at 353 K for 12 h. 3a was extracted from the aqueous phase with chloroform. Working up results in 0.32 g (67 %) of colorless 3a. Mp: 315-317 K (Ref. 20: 314 K).

IR (KBr, cm^{-1}): Analogous to 3a prepared by route A.

Polymer 4b: 100 mg polymer 1b containing 1.6 mmole diester groups/g were added to a suspension of 300 mg (2.8 mmole) $LiAlH_4$ in 50 ml dry diethylether. The mixture was heated 4 h under reflux. Further work up was conducted as described for polymer 3b.

IR (KBr, cm^{-1}): disappearance of the absorption at 1734 (ν(C=O)).

$[(C_8H_8)_{3.88}(C_{10}H_{10})_{1.54}(C_{12}H_{16}O_2)_{1.62}]_n$ $(922.6)_n$

Calc.: O 5.63
Found: O 5.77

Polymer 5b: 5.38 g (78 mmole) p-toluenesulfonic acid chloride in 30 ml dry pyridine were added to a suspension of 100 mg polymer 4b in 20 ml dry pyridine under cooling with ice. Stirring was continued for additional 5 h. The isolated polymer was treated with ethanol in a soxhlet apparatus and dried at 353 k i.vac.

IR (KBr, cm^{-1}): 1192, 1176 (ν(S=O)).

$[(C_8H_8)_{3.88}(C_{10}H_{10})_{1.54}(C_{26}H_{28}O_6S_2)_{1.62}]_n$ $(1415.7)_n$

Calc.: O 10.99 S 7.32
Found: O 11.39 S 7.74

Polymer 6b: The preparation is analogous to that of 6a. 2 g (2.6 mmole) 9, 200 mg (8.3 mmole) NaH and 50 mg polymer 5b were used.

IR (KBr, cm^{-1}): disappearance of the absorption bands at 1192, 1176.

$[(C_8H_8)_{3.88}(C_{10}H_{10})_{1.54}(C_{46}H_{56}N_4O_{12}S_4)_{1.62}]_n$ $(2274.8)_n$

Calc.: N 3.99 S 9.12
Found: N 3.28 S 8.78

Polymer 3b from 6b: The preparation is analogous to those described for 3a from 6a. The polymer exhibits the same IR as that one prepared from 2b.

7a, 8a: The copper(II) complexes of 2a, 3a were prepared by heating of equimolar solutions of the ligands and Cu(II) chloride•$2H_2O$ in ethanol under reflux in nearly quantitative yields as described (Ref. 3,4).

IR (KBr, cm^{-1}): 3266 (ν(N-H)), 1638 (ν(C=O)).

7b, 8b: 100 mg 2b or 6b were added with slow stirring to a solution containing 20 mg Cu(II) chloride•$2H_2O$ in 50 ml water. After 2 h the now blue colored polymers were filtered off, treated with ethanol in a soxhlet apparatus and dried at 353 K i. vac.

Copper analyses results in 0.96 mmole Cu/g for 7b and 0.92 mmole Cu/g for 8b. Employing 20 mg Cu(II) chloride and 20 mg Co(II) chloride together in the reaction with 100 mg 7b, 8b only Cu(II) was found in the chelates after metal analysis.

IR (KBr, cm^{-1}): no significant changes in comparison to 2b and 3b.

REFERENCES

1. I. Tabushi, Y. Taniguchi, H. Kato, Tetrahedron Lett. 12, 1049 (1977).
2. T.A. Kaden; Top. Curr. Chem. 121, 105 (1984).
3. R. Machida, E. Kimura, M. Kodama, Inorg. Chem. 22, 2055 (1983).
4. E. Kimura, T. Kaiko, R. Machida, R. Nagai, M. Kodama, Inorg. Chem. 23, 4181 (1984)
5. D.H. Busch, J. Am. Chem. Soc., 100, 392 (1978).
6. W. Szcepaniak, K. Kuczynski, React. Poly. 3, 101 (1985)
7. B. Bosnich, C.K. Poon, M.L. Tobe, Inorg. Chem. 4, 1102 (1965).
8. L.Y. Martin, C.R. Sperati, D.H. Busch, J. Am. Chem. Soc. 99, 2968 (1977)
9. M. Kato, T. Ito, Inorg. Chem. 24, 504 (1985).
10. M. Kato, T. Ito, Inorg. Chem. 24, 509 (1985).
11. N. Ise, I. Tabushi (Editors) "An Introduction to Speciality Polymers", Cambridge University Press, Cambridge, 1983.
12. G.A. Melson (Editor) "Coordination Chemistry of Macrocyclic Compounds", Plenum Press, New York, 1979.
13. E. Kimura, R. Machida, M. Kodama, J. Am. Chem. Soc. 106, 5497 (1984).
14. M. Kodama, E. Kimura, J. Chem.Soc., Dalton Trans. 7, 327 (1980).
15. V. Louvet, P. Appriou, H. Handel, Tetrahedron Lett. 23, 2445 (1982).
16. M. Ciampolini, M. Micheloni, N. Nardi, P. Paoletti, P. Dapporto, F. Zanobini, J. Chem. Soc., Dalton Trans. 7, 1357 (1984).
17. Fieser u. Fieser, "Reagents for Organic Chemistry", Vol. I, John Wiley and Sons Inc., New York, 1967

18. J. Fries, H. Getrost, Organische Reagenzien für die Spurenanalyse, E. Merck, Darmstadt, 1977.

19. D. Braun, H. Cherdron, W. Kern, Praktikum der makromolekularen organischen Chemie, Hüthig-Verlag, Heidelberg, 1979.

20. H. Stetter, K.-H. Meyer, Chem. Ber. 94, 1410 (1961).

21. G.H. Searle, R.J. Geue, Aust. J. Chem. 37, 957 (1984).

22. J.P.C. Bootsma, B. Eling, G. Challa, React. Poly. 3, 17 (1984).

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