Articles

Polymeric and Macrocyclic Ureas Based on Meta-Substituted Aromatic Diamines

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ABSTRACT: The condensation reactions of the structurally similar monomers 1,3-phenylenediamine (**1a**) and 2,6-diaminopyridine (**1b**) with *N*,*N*-carbonyldiimidazole have been compared. Whereas the reaction of **1a** resulted in an amino terminated oligomeric polyurea, a mixture of two macrocyclic trimers and one macrocyclic tetramer was obtained in the case of **1b**. The three components of the mixture could be isolated by extraction with DMSO at different temperatures. The structure of the macrocyclic compounds was investigated by means of NMR and matrix-assisted laser desorption/ionization time-of-flight mass spectroscopy.

Introduction

Under certain conditions, macrocycle formation has been observed during polymerization. The reasons for this are specific interactions or structural influences. However, high-dilution techniques or metal complex formation also can be specifically utilized in preparing macrocyclic structures.

Very defined cyclic structures with high yields are formed when alkali-metal ions are used as templates.[1] A well-known example is the synthesis of crown ethers, in which 18-membered rings are formed in the coordination sphere of potassium ions. For the preparation of calixarenes, the type of alkaline cation (NaOH, KOH, RbOH) also has a strong influence on the resulting ring size.[2] Without those templates, cyclization proceeds more or less randomly, although kinked monomers or high flexibility of the resulting polymer chains may increase the extent of ring formation.

Segeev et al. pointed out that macrocyclic phenylene sulfides are formed during the synthesis of poly(phenylene sulfides) by conversion of various dihalobenzenes with sodium sulfide.[3] Under certain conditions, macrocycles were the major reaction product. Similar results were reported by Ovchinnikov et al. for the conversion of 4,4′-difluorobenzophenone and sodium sulfide.[4] Apart from the resulting poly(4,4-thiodiphenylene ketone), a defined cyclic compound with six phenyl units was obtained in small amounts. In highly diluted solution the yield could be increased significantly.

Brunelle at al.[5] described a kinetically controlled hydrolysis/condensation reaction of bisphenol A−bis-chloroformate which resulted in a mixture of cyclic oligomeric aromatic carbonates. This reaction did not require high dilution and was mainly influenced by the type of the amine catalyst used.

Recently, we reported on the new cyclotris(2,6-pyridylformamidine) $(-Pyr-N{=}CH-NH-)_3$ which was obtained quantitatively by conversion of 2,6-diaminopyridine with triethylorthoformate whereas the same reaction of the structurally very similar 1,3-phenylenediamine resulted in oligomeric polyformamidines.[6,7] It has to be pointed out that neither high dilution nor the presence of templates were necessary to get a defined cyclic structure without any byproducts in high yield. Both the cyclic and the polymeric formamidines were assumed to interact with various low-molecular compounds to form physical networks. In particular, the cyclic trimer seemed to be a suitable component to build up two-dimensional or even three-dimensional associates. However, one disadvantage of formamidines is their low hydrolytic stability that limits their application.

A promising alternative are urea compounds. Because of their structural similarity to formamidines, it was assumed that the formation of macrocyclic ureas based on 2,6-diaminopyridine should also be possible. Such compounds may interact on three sides with polymers or low-molecular-mass compounds by hydrogen bridge formation resulting in larger associates. An appropriate method for the preparation of ureas is the conversion of amines with *N*,*N*-carbonyldiimidazole.[8] This reaction proceeds at room temperature and resulted in polyureas when diamino compounds were used. In the present publication, the reactions of 2,6-diaminopyridine and 1,3-phenylenediamine with *N*,*N*-carbonyldiimidazole according to Scheme 1 are compared. The tendency of ring

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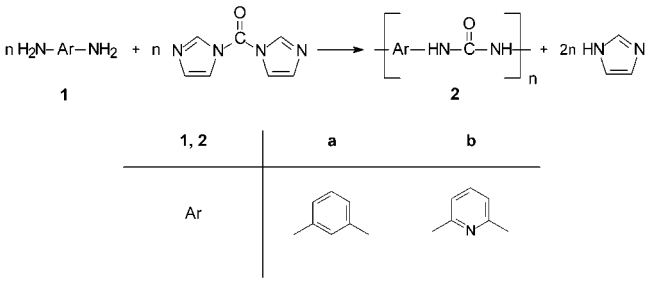
Scheme 1



formation depending on the monomers is discussed. It will be shown that defined cyclic urea structures based on 2,6-diaminopyridine are available which, according to our knowledge, has not been mentioned in the literature before.

Experimental Part

Materials. All chemicals were purchased from Fluka. 1,3-Phenylenediamine (**1a**) and 2,6-diaminopyridine (**1b**) were purified by recrystallization from ethanol. *N,N*-Carbonyldiimidazole and dimethylacetamide p.a. (DMA) were used without further purification. Dimethyl sulfoxide (DMSO) and tetrahydrofuran (THF) were stored over molecular sieves and purified by distillation prior to use.

Condensation Reactions. 2a. An excess of 10 mol % of *N,N*-carbonyldiimidazole (6.24 g, 38.5 mmol) was added to a solution of 1,3-phenylenediamine (**1a**) (3.78 g, 35.0 mmol) in 35 mL of DMSO under a low nitrogen stream. The excess of *N,N*-carbonyldiimidazole was necessary to compensate the decomposition of this compound caused by traces of water. The temperature of the reaction mixture was gradually raised to 140 °C and maintained at 140 °C for 4 h. The reaction temperature was then increased to 180 °C and held for another 4 h. After cooling to room temperature, the reaction mixture was poured into acetone/ethyl ether (9:1). The precipitate was filtered off, extracted with acetone, and dried in a vacuum at 90 °C for 8 h.

Yield: 64%. Mp: no melting until decomposition.

^{1}H NMR (DMSO): δ (ppm) = 7.06 (m, 1H, H_{ar}), 7.17 (m, 1H, H_{ar}), 7.70 (s, 1H, H_{ar}), 8.62 (s, 2H, N*H*−CO−N*H*), NH_2-terminal group: 5.1 (broad, NH_2), 6.20 (d, 1H, H_{ar}), 6.57 (d, 1H, H_{ar}), 6.78 (s, 1H, H_{ar}), 6.90 (t, 1H, H_{ar}), 8.28 (s, 1H, NH−CO−N*H*), 8.57 (s, 1H, N*H*−CO−NH).

2b. The conversion of 2,6 diaminopyridine (**1b**) with *N,N*-carbonyldiimidazole was carried out at room temperature and at 100 °C. The batch size and reactants stoichiometry were the same as for **2a**. The reaction time was 4 h in both cases. After cooling to room temperature, the reaction mixture was poured into acetone/ethyl ether (9:1). The precipitate was filtered off, extracted with acetone, and dried in a vacuum at 90 °C for 8 h. A white powder was obtained. Yield: 91%. Mp: no melting until decomposition.

The crude product was separated into three fractions by subsequent extraction with DMSO at 80 °C and 120 °C. The weight contents of the three fraction were 0.04, 0.48, and 0.48 for fraction 1, fraction 2, and fraction 3, respectively.

Fraction 1 (soluble in DMSO at 80 °C). ^{1}H NMR (TFA-*d*): δ (ppm) = 7.20 (d, 2H, H_{ar}), 8.25 (t, 1H, H_{ar}). Mp: no melting until decomposition, white powder.

Fraction 2 (insoluble in DMSO at 80 °C, soluble in DMSO at 120 °C). ^{1}H NMR (TFA-*d*): δ (ppm) = 7.24 (d, 2H, H_{ar}), 8.27 (t, 1H, H_{ar}). ^{1}H NMR (DMSO-d_6): δ (ppm) = 6.72 (d, 1H, H_{ar}), 7.74 (t, 1H, H_{ar}), 7.93 (d, 1H, H_{ar}), 10.03 (s, 1H, N*H*−CO−NH), 11.27 (s, 1H, NH−CO−N*H*). ^{13}C NMR (DMSO-d_6): δ (ppm) = 106.40 (C_{ar}), 106.72 (C_{ar}), 140.80 (C_{ar}), 149.48 (C_{ar}), 151.17 (C_{ar}), 151.48 (NH−CO−NH). Mp: no melting until decomposition, white powder.

Fraction 3 (insoluble in DMSO at 120 °C). ^{1}H NMR (TFA-*d*): δ (ppm) = 7.44 (d, 2H, H_{ar}), 8.24 (t, 1H, H_{ar}). Mp: no melting until decomposition, white powder.

Measurements. Matrix-assisted laser desorption/ionization time-of-flight mass spectroscopic (MALDI−TOF−MS) experiments were performed on a HP G2030A MALDI−TOF−MS system (Hewlett-Packard). The desorption/ionization was induced by a pulsed N_2 laser The mass spectra were obtained at 28 kV acceleration voltage. The matrix was 2,5-dihydroxybenzoic acid (DHB) for **2a**, **2b**, and fraction 1. The samples were dissolved in DMSO, and the matrix material was dissolved in THF or DMA. Mixtures of the matrix and sample solutions were dropped onto a sample holder and dried under vacuum. In the case of fractions 2 and 3, desorption and ionization could be realized without the matrix. The measurements were carried out in linear mode and positive polarity. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX 500 spectrometer operating at 500.13 MHz for ^{1}H and at 125.77 MHz for ^{13}C, respectively. The samples were measured at ambient temperature. The solvent DMSO-d_6 was used as lock and internal standard (δ(^{1}H) = 2.50 ppm; δ(^{13}C) = 39.6 ppm). Sodium 3-(trimethylsilyl)-3,3,2,2-d_4-propionic acid was used as internal standard (δ(^{1}H) = 0 ppm) for measurements in trifluoroacetic acid-*d* (TFA-*d*).

Calculations. Geometry optimization of the macrocyclic structures and calculations of their Hartree−Fock energies were performed using the software GAMESS[9] for quantum mechanical ab initio calculations with the STO-6G basis set.

Results and Discussion

To estimate the possibility to obtain cyclic trimers based on 2,6-diaminopyridine, ab initio calculations were performed. The calculations revealed that from the energetic point of view the cyclic urea structure (−Pyr-NH−CO−NH−)$_3$ with a Hartree−Fock energy of −1400 hartree is similar to the corresponding cyclic formamidine structure (−Pyr-N=CH−NH−)$_3$ with a Hartree−Fock energy of −1177 hartree. The synthesis of the letter was described earlier.[6,7] The negative Hartree−Fock energies suggest stable ring structures for both compounds.

By analogy with the formamidines,[6] the tendencies of macrocyclic rings formation during the conversion of 1,3-phenylenediamine and 2,6-diaminopyridine with *N,N*-carbonyldiimidazole is discussed in the following. For the purpose of comparison, the temperature regime was chosen similarly as for the preparation of the formamidines although the reaction proceeds at room temperature as well.

The conversion of 1,3-phenylenediamine with *N,N*-carbonyldiimidazole in DMSO according to Scheme 1 resulted in a white powderlike oligomer (**2a**) that precipitated during the reaction. The ^{1}H NMR spectrum of **2a** shown in Figure 1 is in accordance with the expected polyurea. Beside the chain signals, signals of amino terminal groups could be found. From the intensity ratio of the terminal group signals to the chain signals a number-average molecular mass M_n of 1210 g/mol was calculated. The MALDI spectrum shown in Figure 2 verifies the oligomeric nature of the reaction product. M_n calculated from the MALDI spectrum (1210 g/mol) match surprisingly good with the value obtained from the NMR spectrum. Usually, MALDI provides lower M_n values since species with higher molecular weights do not fly as good as low molecular weight ones. The distances between the main signals correspond exactly to the molecular mass of one repetition unit of 134 g/mol. From the signal positions, one can conclude that only amino group terminated oligomers were formed. Splitting of the particular signals is caused by associates with K^+ or Na^+ which most probably come from the glass equipment used for the preparation. Cyclic structures could not be found.

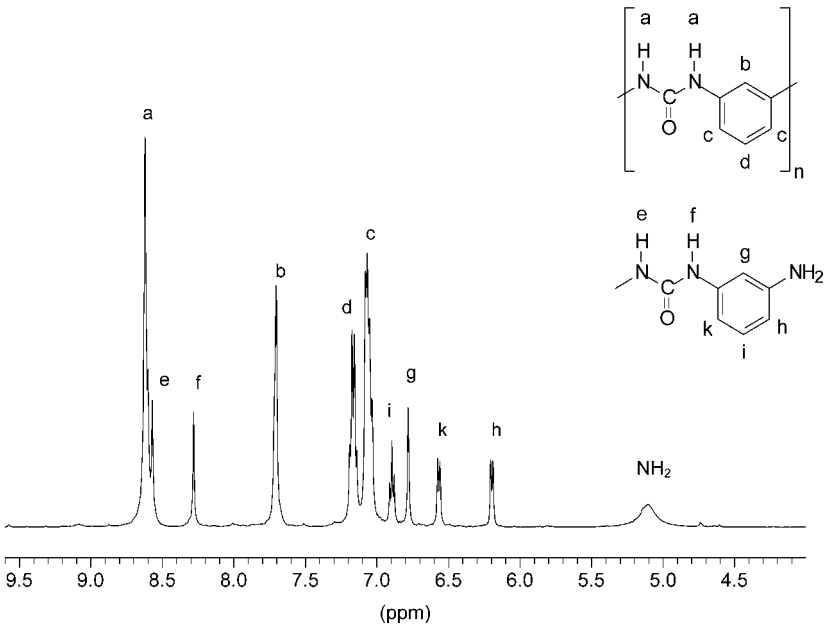


Figure 1. ^{1}H NMR spectra of **2a** in DMSO.

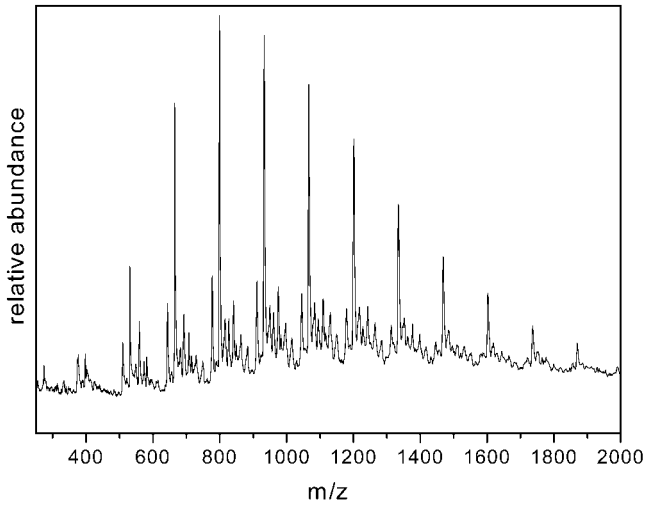


Figure 2. MALDI−TOF−MS spectrum of **2a**.

The conversion of the structurally very similar 2,6-diaminopyridine at 100 °C yielded completely different results. The ^{1}H NMR spectrum of the crude reaction product **2b** shown in Figure 3a contains three well-separated doublets and a signal group in the aromatic region. From ^{1}H-correlated spectroscopy (COSY), it can be concluded that this signal group results from three overlapping triplets. So, three different pyridine rings can be identified for this sample. Since no terminal group signals were observed, it was likely to assume that a mixture of macrocyclic compounds was formed. To get more clarity about that, we tried to separate the mixture by subsequent extraction of **2b** with DMSO at 80 and 120 °C. The three fractions obtained (see Experimental Part) were investigated separately.

The ^{1}H NMR spectra of the three fractions (see Figure 1, parts b−d) confirm the existence of three different compounds which can be distinguished by the position of their H_b signals (H_{b1}: 7.20 ppm; H_{b2}: 7.24 ppm; H_{b3}: 7.44 ppm). The signal positions and the similarity of their ^{1}H NMR spectra allowed to conclude that the repeating unit of the three compounds should be the 2,6-pyridylurea moiety (−Pyr−NH−CO−NH−) in each

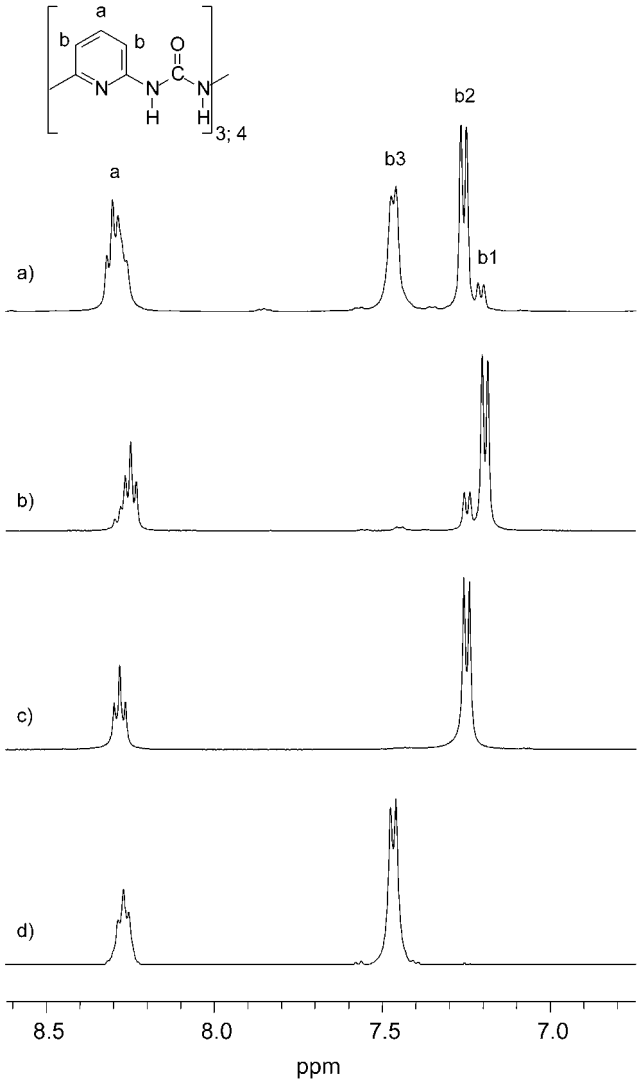


Figure 3. ^{1}H NMR spectra of **2b** in TFA-*d*: (a) virgin sample); (b) first fraction, soluble in DMSO at 80 °C; (c) second fraction, insoluble in DMSO at 80 °C, soluble at 120 °C; (d) third fraction, insoluble in DMSO at 120 °C.

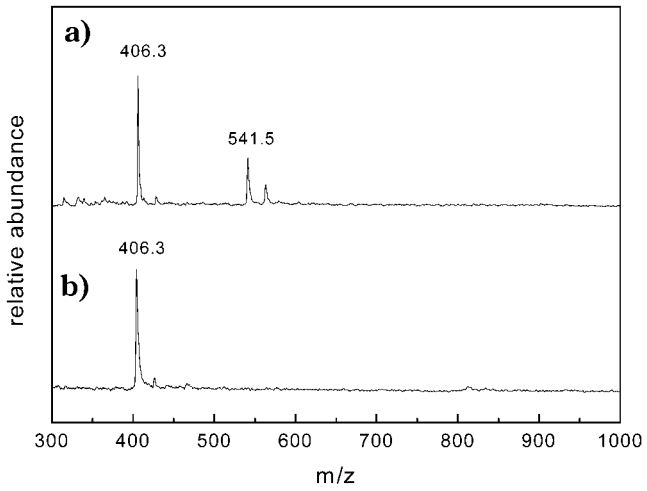


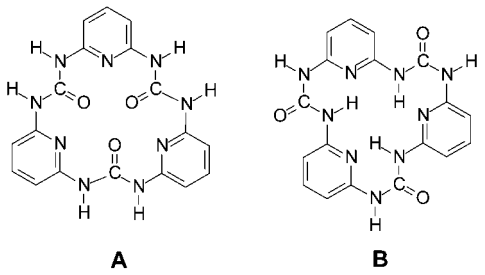
Figure 4. MALDI−TOF−MS spectrum of **2b**: (a) virgin sample; (b) sample after extraction with DMSO at 80 °C.

case. The signal shifts are most probably caused by different ring sizes as well as different conformations of the urea moieties.

In the following, these compounds are named as **M1** (H_{b1}: 7.20 ppm), **M2** (H_{b2}: 7.24 ppm), and **M3** (H_{b3}: 7.44 ppm). Their structures will be discussed below. According to the NMR spectra, fraction 1, which was soluble in DMSO at 80 °C, contains mainly **M1** and traces of **M2** (approximately 20 mol %), whereas fraction 2 and fraction 3, obtained by subsequent extraction with DMSO at 120 °C, proved to be pure compounds **M2** (soluble part) and **M3** (insoluble part), respectively. The molar ratio of **M1**:**M2**:**M3** in **2b** calculated from the ^{1}H NMR signal integrals (H_{b1}:H_{b2}:H_{b3}) was 0.1:0.5:0.4.

A definitive answer about the nature of the mixture was provided by MALDI−TOF−MS. In the MALDI spectrum of **2b** (see Figure 4a), only two signal groups can be observed. The first signal at m/z = 406.3 corresponds exactly with the molecular mass of a protonated cyclic trimer (m = 406.37) whereas the second one at m/z = 541.5 belongs to a protonated cyclic tetramer (m = 541.49). The small signals that are shifted ca. 22 units from the main signals to higher molecular masses are caused by Na^+ associates.

Scheme 2



It was possible to separate the tetramer from the trimers completely by extraction with DMSO at 80 °C (see Figure 4b). From this it can be concluded, that the major component **M1** of the extractable part (first fraction) is a cyclic tetramer and that the two components **M2** and **M3** in the remainder are two different cyclic trimers with equal molecular masses. As mentioned above, **M2** and **M3** were obtained as pure samples by extraction with DMSO at 120 °C. The existence of one tetramer (**M1**) and two different trimers (**M2** and **M3**) were confirmed by MALDI measurements of the three fractions.

The conformation and the structural differences of the two trimers could not be concluded from the NMR spectra since proton exchange with the solvent (TFA) strongly broadens the amide proton signals of the urea group. For **M2**, NMR spectroscopic investigations could be performed in DMSO were the proton exchange rate is low. The ^{1}H NMR spectrum is presented in Figure 5.

The structure of DMSO soluble **M2** could be determined by combination of 1D and 2D NMR techniques. Generally, the two different conformations **A** and **B** shown in Scheme 2 can be assumed for the cyclic trimer **M2**. In the case of structure **A**, the two amide protons (H_e, H_d) as well as the two pyridyl protons next to the substituents (H_a, H_c) are identical. However, since for each of these protons a separated signal was found, the hypothetical structure **A** can be excluded for **M2**. Additionally, 2D rotating-frame Overhauser spectroscopy (ROESY) experiments revealed that proton H_a and proton H_e are situated in immediate vicinity so that structure **B** is proved for **M2**.

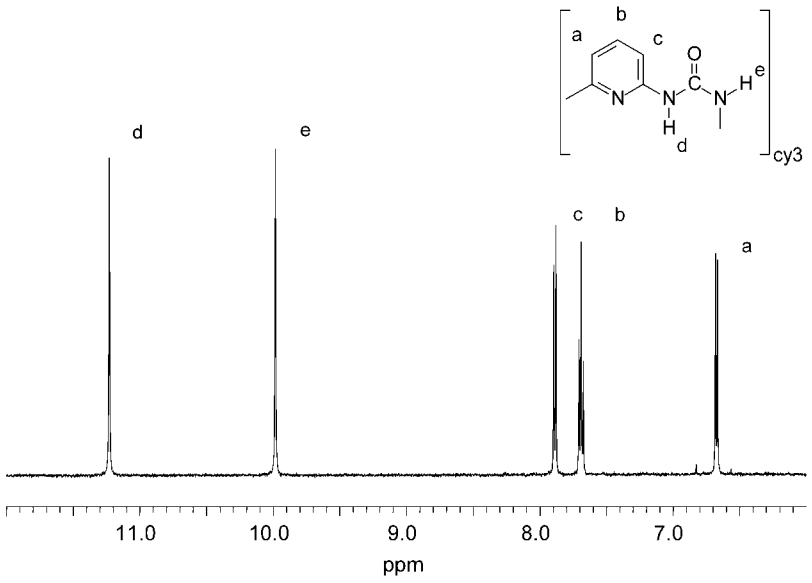


Figure 5. ^{1}H NMR spectra of the cyclic trimer **2b/2** in DMSO-d_6 (at 120 °C, DMSO soluble part of **2b**).

A final proof for the structure of the second cyclic trimer **M3** cannot be given because it could only be dissolved in protic acids like TFA. Protonation and fast proton exchange at the NH group in this solvent limit NMR investigations with respect to the structural differences of the trimers **M2** and **M3**. So, the special arrangement of NH protons cannot be determined by ROESY measurements. From the ^{1}H spectra of both trimers in TFA-*d* (Figure 3), it can be concluded that the structural differences should be caused by the group between the pyridine rings because a significant chemical shift difference is observed for the protons next to this group. Unfortunately, a comparison of the ^{13}C CPMAS spectra of **M2** and **M3** gives no additional information. Both spectra are nearly identical. Assuming that a higher structural symmetry should result in more stable crystals and consequently in a lower solubility, it is reasonable to assume that **M3** represents structure **A**. Alternatively, the cyclic isourea derivative (−NH−COH═N−) which also is assumed to be energetically stable according to ab initio calculations can be supposed.

The main conclusion is that the reaction of 2,6-diaminopyridine with *N*,*N*-carbonyldiimidazole did not yield in polymeric structures. Similarly, as already observed in the reaction with triethylorthoformate,[6,7] cyclic structures were formed. However, whereas the reaction with triethylorthoformate resulted almost quantitatively in a defined cyclic formamidine trimer, a relatively large amount of cyclic tetramers (10 mol % by ^{1}H NMR) were obtained in the reaction with *N*,*N*-carbonyldiimidazole. Obviously, the flexibility of the urea structure is higher than that of the formamidine structure so that deviations from a planar trimer structure are rather possible.

To reduce the molecular mobility of the intermediates formed during the formation of the cyclic ureas, the conversion of 2,6-diaminopyridine with *N*,*N*-carbonyldiimidazole was repeated at ambient temperatures. In this case, the DMSO soluble trimer **M2** was formed predominantly. Only 10 mol % (NMR) of **M3** were found as byproduct. The formation of cyclic tetramers was not observed. The results show that the cyclic trimer **M2** with structure **B** is the energetically most favored one. It is assumed that this structure is stabilized by internal hydrogen bridges between the urea hydrogens and the pyridyl nitrogens.

The main reason for the ring formation of 2,6-diaminopyridine is the *meta*-substitution of the aromatic ring and the lack of a proton between the two substituted carbon atoms of the pyridine ring. It is assumed that in the case of the 1,3-phenylene moiety, sterical hindrance between the proton in 2-position and the urea group results in a nonplanar conformation, so that the formation of a planar cyclic structure is prevented. The missing proton in the respective position of the 2,6-pyridyl moiety allows the urea group to adopt a planar conformation that results in ring formation. Additionally, internal hydrogen bonds between the NH of the urea group and the nitrogen of the pyridyl group may support ring formation too.

Conclusion

On the basis of ab initio calculations, it was assumed that macrocycle formation during the reaction of **1b** with *N*,*N*-carbonyldiimidazole may proceed. The investigations confirmed our expectations. The conversion of **1b** with *N*,*N*-carbonyldiimidazole resulted in a mixture of cyclic trimers and a tetramer (**2b**), whereas with the structurally similar monomer **1a** an oligomer (**2a**) was obtained. Extraction of **2b** with DMSO allowed to separate the sample into two different trimers and one tetramer.

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References and Notes

(1) *Stereochemie*; Hauptmann, S. Mann, G., Eds.; Spektrum, Akad. Verl.: Heidelberg, Germany, Berlin, and Oxford, England, 1996; Kapitel 6, pp 291−325.
(2) Hinton, H. S. *IEEE Spectrum* **1992**, Feb, 42−45.
(3) Sergeev, V. A.; Nedel'kin, V. I.; Astankov, A. V.; Nikiforov, A. V.; Alov, E. M.; Moskvichev, Yu. Ya. *Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1990**, *39*, 763.
(4) Ovchinnikov, Yu. E.; Nedel'kin, V. I.; Ovsyannikova, S. I.; Struchkov, Yu. T. *Russ. Chem. Bull.* **1994**, *43*, 1384−1389.
(5) Brunelle, D. J.; Boden, E. P.; Shannon, T. G. *J. Am. Chem. Soc.* **1990**, *112*, 2399−2402.
(6) Böhme, F.; Rillich, M.; Komber, H. *Macromol. Chem. Phys.* **1995**, *196*, 3209−3216.
(7) Kunert, C.; Voigt, D.; Friedel, P.; Komber, H.; Böhme, F. *J. Polym. Sci. Polym. Chem.* **2001**, *39*, 1280−1287.
(8) Staab, H. A. *Liebigs Ann. Chem.* **1957**, *609*, 75.
(9) Schmidt, M. W.; Baldridge, K. K.; Boatz, J. A.; Jensen, J. H.; Koseki, S.; Gordon, M. S.; Nguyen, K.; Windus, T. L.; Elbert, S. T. *QCPE Bull.* **1990**, *10*, 52−53.

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