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# Synthesis and UV/Vis analysis of amino acid-derived bisurea-type receptors involving anion complexation

**Abstract**: Sixteen new bisurea compounds incorporating versatile proteinogenic amino acids as well as nipecotic acid have been synthesized *via* addition reaction to aryl diisocyanates. The products were analytically characterized and their ability for anion recognition was studied by UV/Vis spectroscopy. In the presence of fluoride, acetate or dihydrogenphosphate ions, hyperchromic and bathochromic peak shifts were determined. By way of contrast, bromide, iodide, or hydrogensulfate ions cause no significant change of absorbance. The special effect of heterocyclic derivatives was explained by molecular modeling calculations. In addition, the crystal structure of the byproduct dimethyl *N*,*N*′-(1,4-phenylene)dicarbamate is discussed.

**Keywords:** amino acids; anion recognition; crystal structure; synthesis; ureas; UV/Vis spectroscopy.

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## 1 Introduction

Due to the important biological role and environmental impact of anions, developing molecular receptors for their recognition and sensing continues to be a topic of current interest [1–11]. Relating to this, a wide variety of anion receptors based on organic frameworks have been designed, including both macrocyclic and acyclic systems [12–15]. Aside from the neutral receptors showing the structure of secondary amides [16–19], urea derived receptor molecules possessing two parallel NH hydrogen bond donor groups have proven highly effective in the recognition and binding of anions [20–28]. Although a great many of receptors of this type have been prepared, mostly featuring a cleft or cyclic structure containing urea molecules as multiple binding sites, corresponding receptor molecules showing an amino acid integral with the urea moiety are rare [29–31] and are used only in very special cases, although seeming promising in this field.

Here, we describe the synthesis of a series of new bisurea compounds **1**–**16** having this structural property. More strictly speaking, their structure is characteristic of two amino acid-derived urea units attached to opposite positions of a benzene (**1**–**8**) or biphenyl (**9**–**16**) core with eight different amino acids being used in this respect (Fig. 1). These compounds were tested regarding their complexation behavior to various anions by means of a UV/Vis spectrometric method. The results of this study are reported indicating developmental possibility in the sensing of acetate, fluoride, and dihydrogenphosphate anions. Moreover, a byproduct **17** (Fig. 1), which has been isolated in the course of the preparation of **4**, has been identified by X-ray crystal structure analysis.

## 2 Results and discussion

### 2.1 Synthesis of compounds

The bisurea compounds **1**–**16** (Fig. 1) were synthesized following the common reaction pattern between isocyanate and an amine [32], considering also a recently described procedure for the preparation of the individual compound **2** [33]. In the present cases, two different diisocyanates, i.e., *p*-phenylene diisocyanate or 3,3′-dimethyl-4,4′-biphenylene diisocyanate, and a selection of amino acids differing in size and polarity were used. They involve L-alanine, L-phenylalanine, L-valine, L-leucine, L-proline, (*R*)-3-piperidinecarboxylic acid, L-threonine, and L-glutamic acid – all being native compounds except for (*R*)-3-piperidinecarboxylic acid (nipecotic acid) – giving rise to formation of the corresponding bisureas (**1**, **9**; **2**, **10**; **3**, **11**; **4**, **12**; **5**, **13**; **6**, **14**; **7**, **15**; **6**, **16**, respectively).

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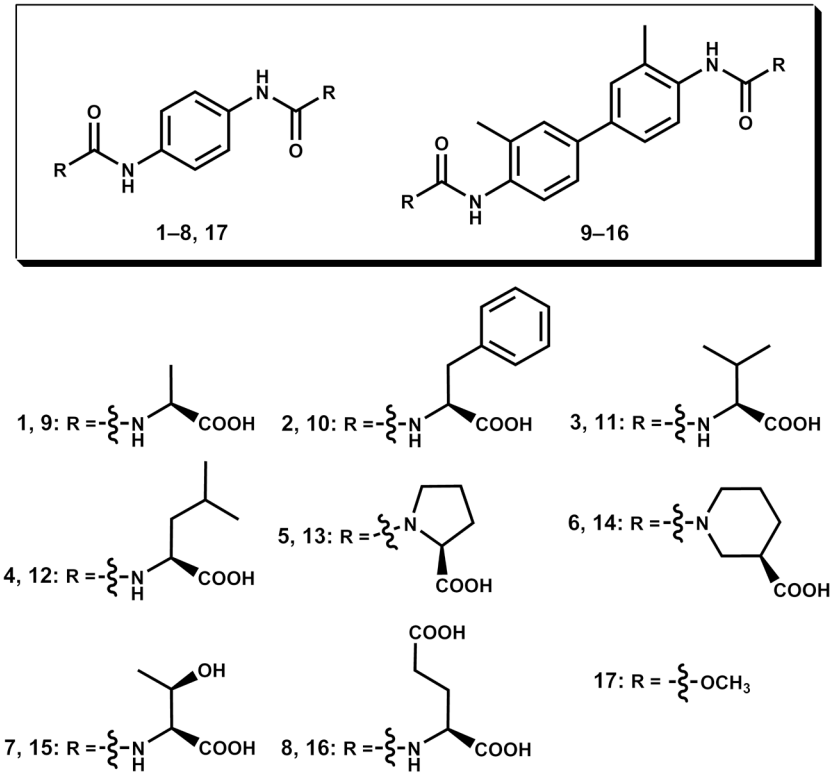


**Fig. 1:** Formula structures of the bisureas **1**–**16** and the dicarbamate **17** studied in this paper.

In order to prevent undesirable side reactions caused by the highly reactive isocyanate function, the reactions were done in a two-phase system composed of a solution of the diisocyanate in toluene and an aqueous alkaline solution of the amino acid. With the exception of **15** and **16**, where 3,3′-dimethyl-4,4′-biphenylene diisocyanate and L-threonine or L-glutamic acid were used, the products could be obtained in moderate to high yields (43–94 %). However, **15** yielded only 12 % and for **16** no product at all was isolated under the given reaction conditions. This is perhaps suggestive of the different polarity of the amino acids having a bearing on the product yield since due to the polar side chains both L-threonine and L-glutamic acid show distinctly higher polarity compared to the other amino acids. In addition, a steric effect caused by the methyl substituents neighboring the isocyanate groups may also interfere with the reaction leading to this specific finding, in particular regarding compound **16.** In such a case, a phase transfer catalyst is expected to overcome the problem. Hence, in separate experiments aliquat 336 and 18-crown-6 were added to the reaction, resulting in the formation of **16** in 4 and 16 % isolated yield, respectively. As expected, no racemization was observed during compound synthesis.

Among the compounds featuring a benzene spacer unit and following the given procedure, **4** was isolated in the lowest yield. Hence the separated toluene phase was evaporated and the residual solid was recrystallized from methanol yielding the byproduct dimethyl *N*,*N*′-(1,4-phenylene)dicarbamate (**17**) which obviously came from reaction of remaining *p*-phenylene diisocyanate with methanol. Characterization of the compound was done *via* melting point and NMR data that correspond to the literature [34, 35]. Nevertheless, getting more detailed structural information, a crystal structure analysis of the compound **17** has been performed.

## 2.2 Crystal and molecular structure of dimethyl *N*,*N*′-(1,4-phenylene)-dicarbamate 17

Crystal growing of **17** from *n*-propanol yields colorless crystals of the triclinic space group $P\bar{1}$ with one molecule in the unit cell (Fig. 2), i.e., the molecule has crystallographic inversion symmetry (Tables 1–3). Bond lengths and angles of the carbamate moiety agree with those found in the crystal structure of *N*-phenylurethane [36]. The least-squares planes of the carbamate moieties are inclined at an angle of 34.4(1) deg with reference to the plane of the aromatic ring. The conformation of the molecule is

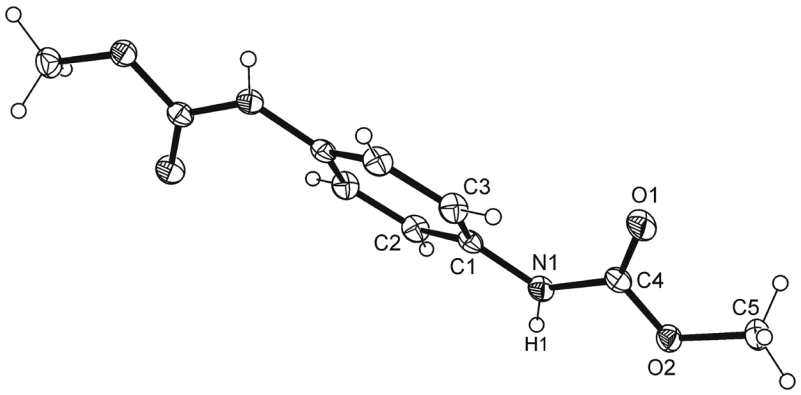


**Fig. 2:** *Ortep* diagram of the molecular structure of **17**; displacement ellipsoids are drawn at the 50 % probability level, H atoms as spheres with arbitrary radii.

stabilized by intramolecular C–H···O hydrogen bond type contacts [37] involving the phenylene hydrogen H3 and the carbonyl oxygen O1 [C3–H3···O1 2.47 Å, 111.0 deg].

The crystal structure is constructed of supramolecular ribbons extending along the crystallographic *a* axis (Fig. 3). Within these aggregates, the molecules are connected by conventional N–H···O=C hydrogen bonds [*d*(H1···O1) 2.09(1) Å, angle N1–H1···O1 157(1) deg]. No stacking of arene rings is observed in the crystal structure. Instead, the displacement of molecules of neighboring ribbons allows formation of weak intermolecular contacts of the C–H···O [*d*(H2···O2) 2.62 Å] and C–H···$\pi$ type [*d*(H5A···C1) 2.80 Å] [38].

**Table 1:** Crystallographic and structure refinement data for **17**.

| | |
|---|---|
| Empirical formula | $C_{10}H_{12}N_2O_4$ |
| Formula weight | 224.21 |
| Crystal system | triclinic |
| Space group | $P\bar{1}$ (No. 2) |
| Unit cell dimensions | |
| *a*, Å | 5.1010(1) |
| *b*, Å | 7.0810(2) |
| *c*, Å | 8.1256(2) |
| $\alpha$, deg | 73.0340(15) |
| $\beta$, deg | 76.8987(15) |
| $\gamma$, deg | 70.6359(14) |
| *V*, Å$^3$ | 262.085 |
| *Z* | 1 |
| *F*(000), e | 118 |
| $D_{calcd.}$, mg m$^{-3}$ | 1.421 |
| $\mu$(Mo$K_\alpha$), mm$^{-1}$ | 0.11 |
| Data collection | |
| Temperature, K | 100(2) |
| Reflections collected | 5723 |
| $\theta$-range for data collection, deg | 3.6–28.1 |
| Index ranges *h*, *k*, *l* | ±6, ±9, ±10 |
| Refl. total/unique/$R_{int}$ | 5068/1265/0.0157 |
| Refinement method | Full-matrix least-squares on all $F^2$ |
| No. of *F* values with $I > 2\sigma(I)$ | 1176 |
| No. of refined parameters | 78 |
| Final *R* indexes | |
| $R_1$ [$I > 2\sigma(I)$]/$R_1$ (all data) | 0.0312/0.0331 |
| $wR_2$ [$I > 2\sigma(I)$]/$wR_2$ (all data) | 0.0883/0.0901 |
| Weighting expression *w*[a] | $[\sigma^2(F_o^2) + (0.0466P)^2 + 0.08P)]^{-1}$ |
| *S* = Goodness-of-fit ($F^2$) | 1.083 |
| Final $\Delta\rho_{max/min}$, e Å$^{-3}$ | 0.32/–0.21 |

[a]$P = (\mathrm{Max}(F_o^2, 0) + 2F_c^2)/3$.

**Table 2:** Selected torsion angles (deg) for **17**.

| | |
|---|---|
| O(1)–C(4)–O(2)–C(5) | –1.5(1) |
| N(1)–C(4)–O(2)–C(5) | 178.5(1) |
| C(1)–N(1)–C(4)–O(1) | –4.5(2) |
| C(1)–N(1)–C(4)–O(2) | 175.5(1) |

## 2.3 Anion complexation studies

Anion complexation was analyzed for each compound **1**–**16** by UV/Vis spectroscopic titration in DMSO solution. This solvent, necessarily required for reason of solubility, was used according to literature references [39–41] although its UV cut-off wavelength is 270 nm [42]. A variety of six different anions were selected involving species of biological relevance. They include the probe anions $F^-$, $Br^-$, $I^-$, $HSO_4^-$, $H_2PO_4^-$, and $AcO^-$. Tetrabutylammonium (TBA) was used as the counter cation (TBA fluoride as its trihydrate). Solutions of each concentration ratio were titrated separately. Thus, the concentration of the receptor was held constant ($5 \times 10^{-5}$ M), and the amount of the anion increased from zero to four mole equivalents.

The free bisureas **1**–**16** show characteristic absorption bands centered for the phenylene derivatives **1**–**8** between 264 and 266 nm and for the biphenylene derivatives **9**–**16** between 284 and 300 nm, i.e., at larger wavelengths for

**Table 3:** Selected hydrogen bond-type interactions in **17**.

| D–H···A | Symmetry operation | Bond lengths (Å) | | | Angles (deg) |
|---|---|---|---|---|---|
| | | D–H | D···A | H···A | D–H···A |
| C(3)–H(3)···O(1) | *x*, *y*, *z* | 0.93 | 2.930(1) | 2.47 | 111 |
| C(2)–H(2)···O(2) | 2 – *x*, 1 – *y*, 1 – *z* | 0.93 | 3.438(1) | 2.62 | 147 |
| N(1)–H(1)···O(1) | 1 + *x*, *y*, *z* | 0.87(1) | 2.909(1) | 2.09(1) | 157(1) |

the biphenylene derivatives. This is a reasonable finding for the bands being assigned to $\pi$–$\pi^*$ transition of the aromatic groups [43]. Though the $n$–$\pi^*$ transition owing to the carbonyl groups may also fall into this range of wavelengths, the corresponding extinction coefficient is expected to be much lower. Actually, absorption is only located in the UV range.

On the addition of bromide, iodide or hydrogensulfate ions to **1**–**16**, no significant spectral shifts can be observed. By way of contrast, the addition of fluoride, acetate or dihydrogenphosphate ions results in each case in a hyperchromic peak shift (i.e., absorbance rises) and a bathochromic shift, which is, however, mostly small. Only the compounds **5**, **13**, and **14** containing a heterocyclic group show total peak shifts >10 nm. Nevertheless, a bathochromic shift clearly indicates that complexation of the anion occurred [44–46].

For a more detailed discussion, the proline derivative **13** was selected as precedent. In the absence of anions, **13** shows an absorption peak at 290 nm (Fig. 4a). On continuous addition of two equivalents of fluoride ions, the peak maximum moves to 305 nm, accompanied by increasing absorbance. Further addition of fluoride ions up to four equivalents did not lead to any significant spectral changes. A clear isosbestic point is indicated at 287 nm. Similar spectral changes can be observed on the addition of $AcO^-$ or $H_2PO_4^-$ (Fig. 4b, c), respectively. To visualize the selectivity of an individual receptor molecule to various anions, the percentage change in absorbance at a defined wavelength is shown dependent on mole ratio [43]. For the compound **13**, it is evident that the addition of fluoride, acetate or dihydrogenphosphate ions results in an increase of absorbance at 320 nm (Fig. 5a). However, for these anions, no clear difference in selectivity could be determined. On the addition of fluoride ions, saturation is observed at a receptor to anion ratio of 1:2 correlating to the complexation of one anion per urea group. Acetate ions give saturation at lower anion concentration, whereas at least three equivalents of anions are necessary for $H_2PO_4^-$.

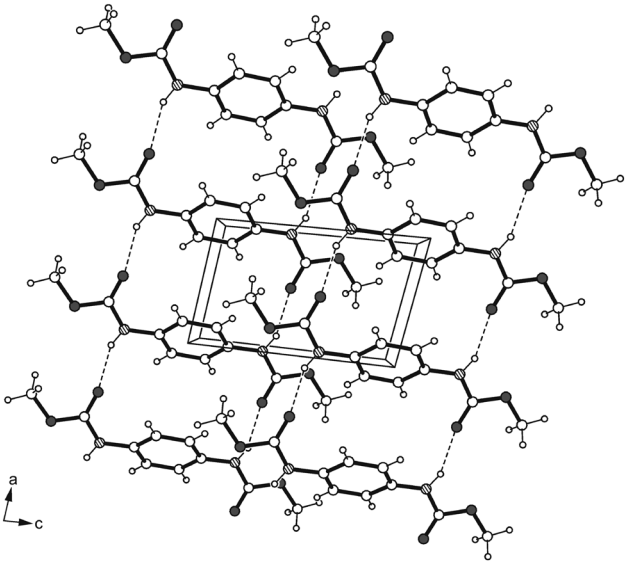


**Fig. 3:** View of the crystal structure of **17** down the crystallographic *b* axis. Oxygen atoms are displayed as grey and nitrogen atoms as hatched circles. Broken lines represent hydrogen bond interactions.

Among the other investigated receptors, only compound **14** behaves similarly, yielding also a percental change >100 % (Figs. 4d–f, 5b); otherwise the change ranges from 12 % (compound **16**, 4 equivalent of fluoride) to 71 % (compound **5**, 4 equivalent of acetate). The prominent effect caused by the receptors **13** and **14** (bearing heterocycles in the lateral groups) strikes as somehow unusual, because both compounds are derived from secondary amines so that each urea moiety possesses only one NH group. In contrast, strong anion complexation of ureas is commonly attributed to the bidentate coordination mode of their two NH groups [47], and thus receptors of the latter mentioned type (**1**–**4**, **7**–**12**, **15**, **16**) are actually expected to show higher affinities toward anions. In this connection, it would be of interest to compare the corresponding behavior of related phenyl mono-urea analogues being known in the literature [48–51]. Unfortunately, however, these compounds have not been studied in this respect. Thus, a respective comparison cannot be done.

For further inspection, molecular modeling calculations (Fig. 6) have been performed for **1**–**16** revealing three interesting findings. First, intramolecular hydrogen bonds

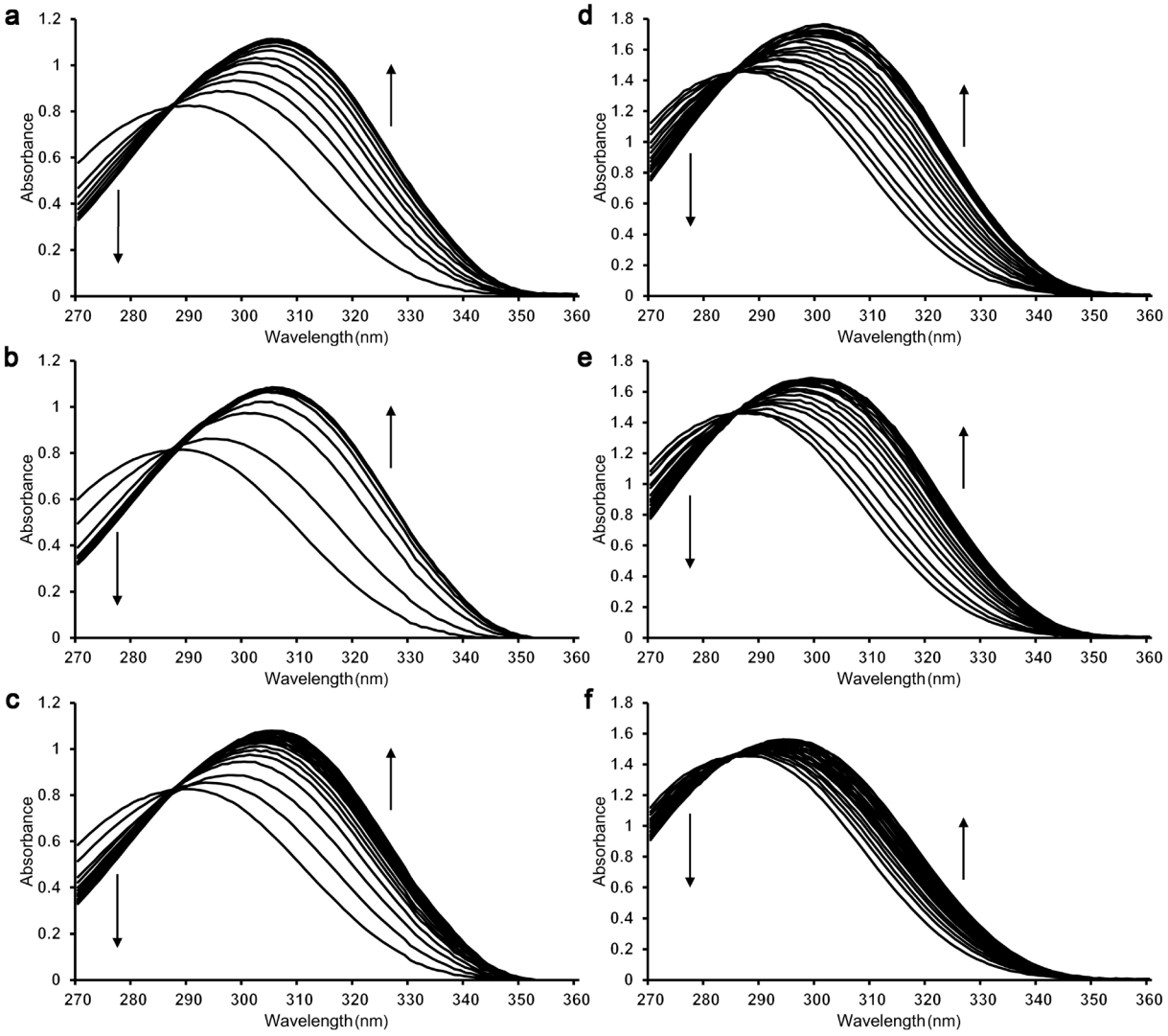


**Fig. 4:** UV/Vis spectral titrations of **13** with fluoride (a), acetate (b) and dihydrogenphosphate ions (c) as well as of **14** with fluoride (d), acetate (e) and dihydrogenphosphate ions (f) in DMSO at 298 K; [**13**] and [**14**] = $5 \times 10^{-5}$ M.

are shown to exist between OH of the carboxyl function and the carbonyl group of the urea moiety, on principle, as specified in Fig. 6a. The corresponding calculated bond lengths are in the range of 1.70–1.77 Å (O–H···O=C) and 2.64–2.70 Å (O···O=C) with O–H···O bonding angles of 162.7–166.7 deg for the compounds **1**–**4**, **7**–**12, 15**, and

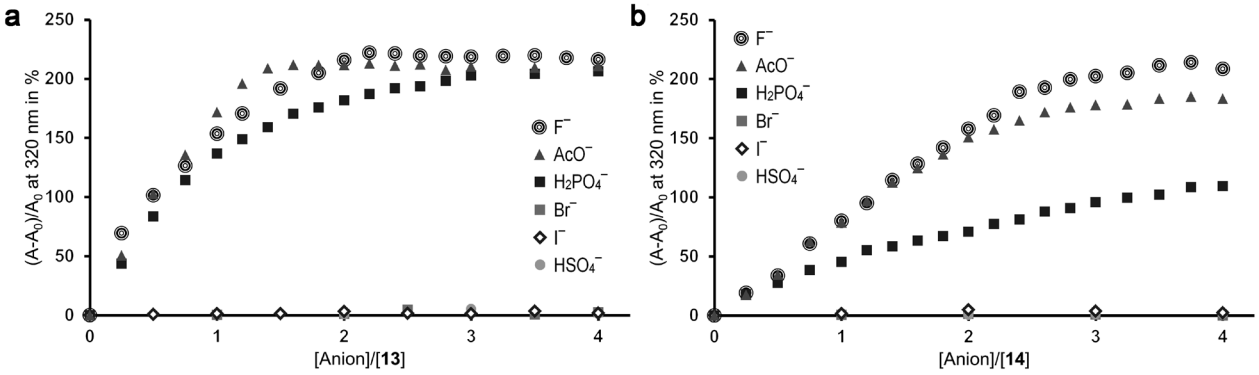


**Fig. 5:** Percental changes of absorbance at 320 nm of **13** (a) and **14** (b) upon the addition of anions at 298 K.

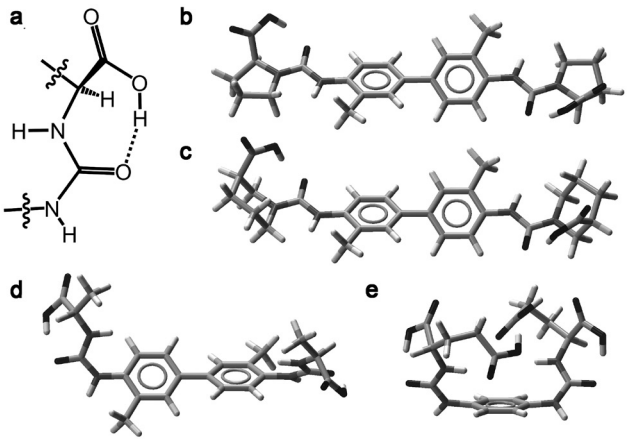


**Fig. 6:** (a) Hydrogen-bonding motif found by molecular modeling in compounds **1–16**; pictured is a detail of **8**; (b–e) energy-minimized structures of **13** (b), **14** (c), **9** (d) and **8** (e). MacroModel V.9.8, OPLS_2001 force field, MCMM, 50.000 steps. Color code: C, light gray; H, white; N, dark gray; O, black.

**16**. In the heterocyclic ring containing compounds **5**, **6**, **13**, and **14**, the angle is slightly smaller (156.4–158.0 deg). The length of the hydrogen bond of **5** and **13** correspond to those of the other $\alpha$-amino acid derivatives. Because nipecotic acid is a $\beta$-amino acid, the hydrogen bonds in **6** and **14** are a little longer (O–H···O=C: 1.88 Å, O···O=C: 2.78 Å).

A second finding relates to the orientation of the urea carbonyl group regarding the NH function next to the aromatic ring. The derivatives of proline and nipecotic acid (**5**, **6**, **13**, **14**) feature an *anti*-arrangement of both the respective units with O=C–N–H torsion angles of 174.8–178.0 deg resulting in an open, stretched molecular structure (Fig. 6b, c). In **13**, the plane of the proline ring as well as the urea moiety are twisted at 12.4 deg with reference to the neighboring phenylene unit. By contrast, in the energy-minimized structures of **1**–**4**, **7**–**12**, and **15**–**16**, the aromatic NH and the urea carbonyl group point into the same direction (O=C–N–H torsion angles: 4.6–11.2 deg) giving rise to an *anti*-orientation of the urea NH groups (Fig. 6a, d, e). As a result, the urea moiety is incapable of acting in a chelate ligand mode and anions can only enter into a single NH contact. Furthermore, the geometry of the urea group causes an angular molecular structure with the urea moiety not being located in the plane of the aromatic ring. We assume that the resulting compact structure of the receptor molecule impedes the NH groups in binding of anions. This also seems plausible, because the introduction of the longer biphenyl spacer additionally supports the ability for anion complexation.

In a third way, for **2**–**4**, **7**, **8**, **10**, and **16**, the molecular modeling studies show that the amino acid side chains are close together involving additional interactions for the stabilization of compact molecular conformations. The contacts result from van der Waals interactions between aliphatic side chains as well as from hydrogen bonding, such as between the hydroxyl groups of threonine or carboxyl groups of glutamic acid (Fig. 6e), respectively. A comparison between the benzene derivatives **1**–**8** and their biphenyl analogues **9**–**16** demonstrates that the conformation of the urea unit is neither affected by the type of the spacer nor by the additional interactions discussed. Hence, conclusions based on the calculations are largely in line with the above experimental findings.

Following another approach, i.e., anion selectivity, the compounds **1**, **2**, **5**, **10**, and **16** show the highest percental change of absorbance in the presence of acetate ions, whereas the other 11 compounds possess preference for fluoride ions. In this respect, no clear correlation can be found between molecular structure and anion preference. Except for compound **13** showing the selectivities $F^- \approx AcO^- \approx H_2PO_4^- >> HSO_4^- \approx Br^- \approx I^-$ (Fig. 5a), the general selectivity trend of anion complexation was found as $F^- \approx AcO^- > H_2PO_4^- >> HSO_4^- \approx Br^- \approx I^-$. The latter order corresponds to the basicity of the anions and is quite similar to published results [41, 43].

Unfortunately, binding constants could not be determined from the measured data because of insufficient curve fitting. Obviously the systems studied are very complex involving a number of equilibria in solution. The urea moieties, for example, are able to bind anions forming different 1:1 and 1:2 complexes because of the two independent urea groups within one molecule [52]. Furthermore, it is known from the literature that the NH groups can be deprotonated by fluoride ions (acting as base) [39, 46, 53–56]. By contrast, addition of acetate or dihydrogenphosphate ions only leads to the formation of hydrogen-bonded complexes and no deprotonation is reported [45, 53]. Regarding the receptors **1**–**16**, the carboxyl groups would be deprotonated rather than the urea moieties, which would result in very similar UV shifts for all compounds. But strong spectral shifts have only been observed for the derivatives **13** and **14** excluding proton transfer as a main or overpowering competition reaction.

## 3 Conclusion

In summary, addition reactions between two aromatic diisocyanates differing in the length of the aromatic unit and various amino acids enabled the preparation of 16 bisureas, normally in moderate to high yields, showing

distinctive structural feature to behave as new potential anion receptors. Respective complexation studies carried out for each compound using UV/Vis titration experiments in DMSO revealed significant changes of absorption on the addition of fluoride, acetate and dihydrogenphosphate ions, whereas bromide, iodide, and hydrogensulfate ions cause only negligible changes. For the compounds **13** and **14**, the largest spectral shifts were found, demonstrating potential applicability as sensor molecules for these specific anions. Molecular modeling studies have been performed for **1**–**16**, as a matter of principle showing hydrogen bonding between carboxylic OH and urea C=O and indicating to some extent further interactions between amino acid side chains. Energy optimization for the proline and nipecotic acid derivatives (**5**, **6**, **13**, **14**) result in stretched structures, which are more suitable for anion complexation in comparison to the other receptors tested (**1**–**4**, **7**–**12**, and **15**–**16**). The calculated structures of the latter compounds suggest an *anti*-orientation of the urea NH groups possibly weakening the formation of bidentate coordination modes to anions. The calculations indicate and the analysis of the spectra of **1**–**16** confirms that the spectral shifts are mainly caused by anion complexation.

For further investigation, future synthesis and spectroscopic analysis of the corresponding methyl esters could be appropriate to add. Another interesting question being open to study is to what extent the new receptors, due to their optical purity, are capable of chiroselective anion recognition. Research along these lines is in the stage of starting.

# 4 Experimental section

## 4.1 General

Melting points were determined on a Büchi Melting Point Unit B-540 (Essen, Germany) and are not corrected. IR spectra were measured as KBr pellets on a Nicolet FT-IR 510 spectrometer (Thermo Fisher Scientific, Waltham, USA). NMR spectra were obtained using an Avance Ultrashield 500 spectrometer (Bruker, Karlsruhe, Germany) at 500.1 MHz ($^1$H) or 125.8 MHz ($^{13}$C) in [D$_6$]DMSO solution. Chemical shifts $\delta$ are reported in parts per million relative to the internal reference TMS. Mass spectra were recorded on a Varian 320 MS (Agilent Technologies, Santa Clara, USA) by electrospray ionization (ESI) and atmospheric pressure chemical ionization (APCI), respectively. Elemental analyses were performed on a Vario Micro Cube (Hanau, Germany). Optical rotation was determined on an automatic digital polarimeter P3002RS (Krüss Optronic, Hamburg, Germany). The UV/Vis measurements were accomplished on a Zeiss Specord M500 spectrometer (Jena, Germany). Reagents and chemicals for the synthesis were used as purchased from chemical suppliers (ABCR, Sigma-Aldrich).

## 4.2 General procedure for the synthesis of compounds 1–16

The amino acid and the equivalent amount of sodium hydroxide were dissolved in water. Under stirring a solution of the diisocyanate in toluene was added at 0 °C. After the reaction period the phases were separated, and the aqueous phase was acidified. The precipitate was filtered off and recrystallized from methanol.

## 4.3 *N*,*N*′-[1,4-Phenylenebis(iminocarbonyl)]-di(L-alanine) (1)

L-Alanine and 1,4-phenylenediisocyanate were used; reaction period: 4 h; white powder (85 %); m. p. 225–227 °C. – $[\alpha]_D^{20}$ = –21.7 ($c$ = 0.14, MeOH). – IR (KBr): $\nu_{max}$ = 3338, 3098, 3041, 2999, 2936, 1701, 1635, 1565, 1515, 1458, 1407, 1378, 1302, 1230, 1185, 1173, 1122, 1086, 916, 821, 764, 641, 587, 523 cm$^{-1}$. – $^1$H NMR: $\delta_H$ = 1.30 (d, 6H, CHC*H*$_3$, $^3J_{HH}$ = 7.2 Hz), 4.16 (m, 2H, C*H*COOH, $^3J_{HH}$ = 7.3 Hz), 6.34 (d, 2H, N*H*, $^3J_{HH}$ = 7.5 Hz), 7.23 (s, 4H, H-Ar), 8.41 (s, 2H, N*H*), 12.56 (br, COO*H*). – $^{13}$C NMR: $\delta_C$ = 18.3, 48.0, 118.4, 134.2, 154.8, 175.0. – MS (ESI): $m/z$ = 339.1 [M+H]$^+$. – $C_{14}H_{18}N_4O_6 \cdot ½\ H_2O$: calcd. C 48.41, H 5.51, N 16.13; found: C 48.65, H 5.44, N 15.72.

## 4.4 *N*,*N*′-[1,4-Phenylenebis(iminocarbonyl)]-di(L-phenylalanine) (2)

L-Phenylalanine and 1,4-phenylenediisocyanate were used; reaction period: 4.5 h; white powder (73 %); m. p. 179–180 °C. Data of compound **2** have recently been published [33].

## 4.5 *N*,*N*′-[1,4-Phenylenebis(iminocarbonyl)]-di(L-valine) (3)

L-Valine and 1,4-phenylenediisocyanate were used; reaction period: 2 h; white powder (87 %); m. p. 209–211 °C. – $[\alpha]_D^{20}$ = +10.5 ($c$ = 0.39, MeOH). – IR (KBr): $\nu_{max}$ = 3386, 3310, 2965, 2930, 2870, 1727, 1603, 1565, 1518, 1473, 1407, 1315, 1296, 1271, 1214, 1150, 1128, 1109, 1033, 1017, 976, 853, 821, 774, 726, 634, 523 cm$^{-1}$. – $^1$H NMR: $\delta_H$ = 0.90 (d, 6H,

$CH(CH_3)_2$, $^3J_{HH}$ = 6.8 Hz), 0.95 (d, 6H, $CH(CH_3)_2$, $^3J_{HH}$ = 6.8 Hz), 2.11 (m, 2H, $CH(CH_3)_2$), 4.15 (dd, 2H, CHCOOH, $^3J_{HH}$ = 8.7 Hz), 6.35 (d, 2H, NH, $^3J_{HH}$ = 8.7 Hz), 7.27 (s, 4H, H-Ar), 8.50 (s, 2H, NH). – $^{13}$C NMR: $\delta_C$ = 17.8, 19.5, 30.5, 57.6, 118.6, 134.4, 155.6, 174.2. – MS (ESI): $m/z$ = 417.1 $[M+Na]^+$. – $C_{18}H_{26}N_4O_6$: calcd. C 54.81, H 6.64, N 14.21; found: C 54.72, H 6.83, N 14.27.

## 4.6 *N,N′*-[1,4-Phenylenebis(iminocarbonyl)]-di(L-leucine) (4)

L-Leucine and 1,4-phenylenediisocyanate were used; reaction period: 8 h; white powder (60 %); m. p. 279–281 °C (dec.); $[\alpha]_D^{20}$ = –12.0 ($c$ = 0.42, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3392, 3345, 3037, 2955, 2870, 1720, 1654, 1606, 1559, 1515, 1470, 1407, 1366, 1309, 1236, 1204, 1163, 1131, 1043, 1021, 926, 831, 764, 720, 609, 523 cm$^{-1}$. – $^1$H NMR: $\delta_H$ = 0.90 (dd, 12H, $CH(CH_3)_2$, $^3J_{HH}$ = 6.5 Hz), 1.50 (m, 4H, $CH_2$, $^3J_{HH}$ = 5.5 Hz, $^3J_{HH}$ = 8.0 Hz), 1.67 (m, 2H, $CH(CH_3)_2$, $^3J_{HH}$ = 6.5 Hz, $^3J_{HH}$ = 7.5 Hz), 4.16 (m, 2H, CHCOOH, $^3J_{HH}$ = 5.5 Hz, $^3J_{HH}$ = 9.0 Hz), 6.28 (d, 2H, NH, $^3J_{HH}$ = 8.0 Hz), 7.22 (s, 4H, H-Ar), 8.37 (s, 2H, NH). – $^{13}$C NMR: $\delta_C$ = 21.6, 22.8, 24.4, 41.0, 50.7, 118.3, 134.1, 155.0, 175.0. – MS (ESI): $m/z$ = 423.2 $[M+H]^+$. – $C_{20}H_{30}N_4O_6 \cdot ½\ H_2O$: calcd. C 55.67, H 7.24, N 12.99; found: C 55.84, H 7.26, N 13.12.

## 4.7 *N,N′*-[1,4-Phenylenebis(iminocarbonyl)]-di(L-proline) (5)

L-Proline and 1,4-phenylenediisocyanate were used; reaction period: 4 h; white powder (94 %); m. p. 336–337 °C (dec.). – $[\alpha]_D^{20}$ = –87.7 ($c$ = 0.39, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3316, 2980, 2958, 2870, 1723, 1682, 1641, 1613, 1594, 1515, 1477, 1416, 1356, 1242, 1226, 1192, 1106, 1087, 976, 922, 812, 758, 723, 644, 558, 520 cm$^{-1}$. – $^1$H NMR: $\delta_H$ = 1.92 (m, 6H), 2.16 (m, 2H), 3.45 (m, 2H, $^3J_{HH}$ = 7.4 Hz), 3.52 (m, 2H), 4.30 (m, 2H, CHCOOH), 7.33 (s, 4H, H-Ar), 8.12 (s, 2H, NH), 12.21 (br, COOH). – $^{13}$C NMR: $\delta_C$ = 24.3, 29.3, 46.1, 58.8, 120.0, 134.7, 154.1, 174.5. – MS (ESI): $m/z$ = 391.3 $[M+H]^+$. – $C_{18}H_{22}N_4O_6 \cdot ½\ H_2O$: calcd. C 54.13, H 5.80, N 14.03; found: C 53.90, H 5.96, N 13.87.

## 4.8 (*R,R*)-*N,N′*-[1,4-Phenylenebis(iminocarbonyl)]-bis(3-piperidinecarboxylic acid) (6)

(*R*)-(–)-3-Piperidinecarboxylic acid and 1,4-phenylenediisocyanate were used; reaction period: 5 h; white powder (87 %); m. p. 219–221 °C. – $[\alpha]_D^{20}$ = –68.8 ($c$ = 0.42, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3376, 2949, 2860, 1720, 1616, 1553, 1518, 1473, 1429, 1309, 1226, 1185, 1131, 1074, 1005, 929, 856, 827, 748, 679, 641, 568, 520 cm$^{-1}$. – $^1$H NMR: $\delta_H$ = 1.41 (m, 2H, $^3J_{HH}$ = 10.0 Hz), 1.57 (m, 2H), 1.64 (m, 2H), 1.97 (m, 2H, $^3J_{HH}$ = 3.2 Hz, $^3J_{HH}$ = 7.8 Hz), 2.37 (m, 2H, CHCOOH, $^3J_{HH}$ = 3.6 Hz, $^3J_{HH}$ = 10.3 Hz, $^3J_{HH}$ = 14.0 Hz), 2.87 (t, 2H, $^3J_{HH}$ = 11.0 Hz), 2.95 (dd, 2H, $^3J_{HH}$ = 10.4 Hz), 3.91 (d, 2H, $^3J_{HH}$ = 13.1 Hz), 4.12 (d, 2H, $^3J_{HH}$ = 10.9 Hz), 7.28 (s, 4H, H-Ar), 8.39 (s, 2H, NH), 12.28 (br, 2H, COOH). – $^{13}$C NMR: $\delta_C$ = 24.1, 27.1, 40.8, 44.1, 45.8, 120.1, 134.8, 155.0, 174.7. – MS (APCI): $m/z$ = 419.2 $[M+H]^+$. – $C_{20}H_{26}N_4O_6 \cdot ½\ H_2O$: calcd. C 56.20, H 6.37, N 13.11; found: C 56.43, H 6.61, N 13.12.

## 4.9 *N,N′*-[1,4-Phenylenebis(iminocarbonyl)]-di(L-threonine) (7)

L-Threonine and 1,4-phenylenediisocyanate were used; reaction period: 10 h; white powder (64 %); m. p. 226–227 °C (dec.). – $[\alpha]_D^{20}$ = +7.9 ($c$ = 0.40, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3544, 3497, 3376, 3322, 3297, 3164, 3104, 2987, 2933, 2623, 1730, 1701, 1628, 1613, 1562, 1508, 1454, 1407, 1321, 1302, 1290, 1226, 1195, 1150, 1116, 1081, 1021, 1002, 954, 878, 856, 824, 812, 748, 672, 647, 615, 533 cm$^{-1}$. – $^1$H NMR: $\delta_H$ = 1.10 (d, 6H, $CH_3$, $^3J_{HH}$ = 6.0 Hz), 4.07 (dd, 2H, CHCOOH, $^3J_{HH}$ = 2.5 Hz, $^3J_{HH}$ = 9.0 Hz), 4.18 (m, 2H, CHOH, $^3J_{HH}$ = 2.5 Hz, $^3J_{HH}$ = 6.0 Hz), 5.08 (br, OH), 6.22 (d, 2H, NH, $^3J_{HH}$ = 9.0 Hz), 7.23 (s, 4H, H-Ar), 8.76 (s, 2H, NH). – $^{13}$C NMR: $\delta_C$ = 20.8, 57.8, 66.4, 118.2, 134.3, 155.5, 173.2. – MS (ESI): $m/z$ = 399.1 $[M+H]^+$. – $C_{16}H_{22}N_4O_8 \cdot 2.5\ H_2O$: calcd. C 43.34, H 6.14, N 12.64; found: C 43.37, H 5.14, N 12.67.

## 4.10 *N,N′*-[1,4-Phenylenebis(iminocarbonyl)]-di(L-glutamic acid) (8)

L-Glutamic acid and 1,4-phenylenediisocyanate were used; reaction period: 4 h; white powder (73 %); m. p. 205–206 °C. – $[\alpha]_D^{20}$ = +17.0 ($c$ = 0.45, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3386, 3050, 2952, 1733, 1698, 1606, 1556, 1524, 1454, 1413, 1302, 1274, 1214, 1176, 1147, 1081, 1062, 1040, 1017, 983, 913, 834, 786, 758, 723, 574, 530, 489 cm$^{-1}$. – $^1$H NMR: $\delta_H$ = 1.81 (m, 2H, $CH_2CH_2COOH$), 2.02 (m, 2H, $CH_2CH_2COOH$), 2.33–2.25 (m, 4H, $CH_2CH_2COOH$), 4.20 (m, 2H, CHCOOH), 6.41 (d, 2H, NH, $^3J_{HH}$ = 7.7 Hz), 7.25 (s, 4H, H-Ar), 8.48 (s, 2H, NH), 12.20 (br, COOH). – $^{13}$C NMR: $\delta_C$ = 27.3, 30.0, 51.7, 118.5, 134.3, 155.1, 173.9, 174.2. – MS (ESI): $m/z$ = 455.1 $[M+H]^+$. – $C_{18}H_{22}N_4O_{10} \cdot ½\ H_2O$: calcd. C 46.65, H 5.00, N 12.09; found: C 46.49, H 5.10, N 12.21.

### 4.11 *N,N′*-[(3,3′-Dimethylbiphenyl-4,4′-diyl)-bis(iminocarbonyl)]-di(L-alanine) (9)

L-Alanine and 4,4′-diisocyanato-3,3′-dimethylbiphenyl were used; reaction period: 9.5 h; white powder (45 %); m. p. 341–342 °C. – $[\alpha]_D^{20}$ = −47.1 (*c* = 0.18, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3322, 2984, 2946, 1742, 1635, 1591, 1546, 1454, 1375, 1302, 1239, 1166, 1128, 1068, 865, 796, 761, 650 $cm^{-1}$. – $^1H$ NMR: $\delta_H$ = 1.31 (d, 6H, CHC*H*$_3$, $^3J_{HH}$ = 7.3 Hz), 2.26 (s, 6H, C*H*$_3$-Ar), 4.17 (m, 2H, C*H*COOH, $^3J_{HH}$ = 7.3 Hz), 7.18 (d, 2H, N*H*, $^3J_{HH}$ = 7.3 Hz), 7.34 (dd, 2H, H-Ar, $^3J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 1.8 Hz), 7.39 (d, 2H, H-Ar, $^4J_{HH}$ = 1.5 Hz), 7.88 (d, 2H, H-Ar, $^3J_{HH}$ = 8.5 Hz), 8.05 (s, 2H, N*H*). – $^{13}C$ NMR: $\delta_C$ = 18.2, 18.3, 48.1, 120.3, 123.7, 126.8, 127.7, 133.4, 137.1, 154.9, 175.0. – MS (ESI): *m*/*z* = 907.4 $[2\cdot M+Na]^+$. – $C_{22}H_{26}N_4O_6 \cdot H_2O$: calcd. C 57.38, H 6.13, N 12.17; found: C 57.57, H 6.13, N 11.83.

### 4.12 *N,N′*-[(3,3′-Dimethylbiphenyl-4,4′-diyl)-bis(iminocarbonyl)]-di(L-phenylalanine) (10)

L-Phenylalanine and 4,4′-diisocyanato-3,3′-dimethylbiphenyl were used; reaction period: 7.5 h; white powder (70 %); m. p. 322–324 °C (dec.). – $[\alpha]_D^{20}$ = +70.9 (*c* = 0.59, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3351, 3088, 3056, 3028, 2927, 1723, 1638, 1591, 1543, 1496, 1454, 1442, 1385, 1302, 1242, 1119, 1081, 1062, 1030, 878, 821, 755, 701, 650 $cm^{-1}$. – $^1H$ NMR: $\delta_H$ = 2.24 (s, 6H, C*H*$_3$-Ar), 2.97 (dd, 2H, C*H*$_2$, $^3J_{HH}$ = 7.7 Hz), 3.09 (dd, 2H, C*H*$_2$, $^3J_{HH}$ = 5.1 Hz), 4.49 (m, 2H, C*H*COOH, $^3J_{HH}$ = 5.4 Hz), 7.01 (d, 2H, N*H*, $^3J_{HH}$ = 7.9 Hz), 7.24 (6H, H-Ar), 7.31 (4H, H-Ar), 7.35 (dd, 2H, H-Ar, $^3J_{HH}$ = 8.5 Hz, $^4J_{HH}$ = 1.8 Hz), 7.40 (d, 2H, H-Ar, $^4J_{HH}$ = 1.7 Hz), 7.85 (d, 2H, H-Ar, $^3J_{HH}$ = 8.5 Hz), 8.04 (s, 2H, N*H*), 12.81 (br, COO*H*). – $^{13}C$ NMR: $\delta_C$ = 18.2, 37.6, 53.9, 120.7, 123.7, 126.5, 127.1, 127.8, 128.3, 129.4, 133.6, 137.0, 137.4, 154.9, 173.6. – MS (ESI): *m*/*z* = 595.4 $[M+H]^+$. – $C_{34}H_{34}N_4O_6 \cdot 2\,H_2O$: calcd. C 64.75, H 6.07, N 8.88; found: C 64.44, H 5.75, N 8.75.

### 4.13 *N,N′*-[(3,3′-Dimethylbiphenyl-4,4′-diyl)-bis(iminocarbonyl)]-di(L-valine) (11)

L-Valine and 4,4′-diisocyanato-3,3′-dimethylbiphenyl were used; reaction period: 6 h; white powder (43 %); m. p. 315–316 °C. – $[\alpha]_D^{20}$ = +12.3 (*c* = 0.20, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3300, 3031, 2961, 2936, 2876, 1739, 1714, 1632, 1587, 1543, 1496, 1445, 1394, 1302, 1245, 1188, 1160, 1128, 1065, 1036, 872, 802, 758, 647 $cm^{-1}$. – $^1H$ NMR: $\delta_H$ = 0.91 (d, 6H, CH(C*H*$_3$)$_2$, $^3J_{HH}$ = 6.8 Hz), 0.94 (d, 6H, CH(C*H*$_3$)$_2$, $^3J_{HH}$ = 6.8 Hz), 2.10 (m, 2H, C*H*(CH$_3$)$_2$, $^3J_{HH}$ = 5.2 Hz), 2.27 (s, 6H, C*H*$_3$-Ar), 4.16 (dd, 2H, C*H*COOH, $^3J_{HH}$ = 4.9 Hz, $^3J_{HH}$ = 8.6 Hz), 6.95 (d, 2H, N*H*, $^3J_{HH}$ = 8.7 Hz), 7.36 (d, 2H, H-Ar, $^3J_{HH}$ = 8.5 Hz), 7.41 (s, 2H, H-Ar), 7.93 (d, 2H, H-Ar, $^3J_{HH}$ = 8.9 Hz), 7.95 (s, 2H, N*H*), 12.55 (br, COO*H*). – $^{13}C$ NMR: $\delta_C$ = 17.7, 18.2, 19.2, 30.4, 57.4, 120.2, 123.8, 126.5, 127.7, 133.3, 137.1, 155.2, 173.9. – MS (ESI): *m*/*z* = 499.5 $[M+H]^+$. – $C_{26}H_{34}N_4O_6 \cdot ½\,H_2O$: calcd. C 61.52, H 6.95, N 11.04; found: C 61.73, H 7.09, N 11.02.

### 4.14 *N,N′*-[(3,3′-Dimethylbiphenyl-4,4′-diyl)-bis(iminocarbonyl)]-di(L-leucine) (12)

L-Leucine and 4,4′-diisocyanato-3,3′-dimethylbiphenyl were used; reaction period: 20 h; white powder (55 %); m. p. 259–260 °C (dec.). – $[\alpha]_D^{20}$ = −5.5 (*c* = 0.53, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3338, 3031, 2955, 2870, 1717, 1647, 1591, 1543, 1496, 1445, 1388, 1369, 1299, 1245, 1169, 1125, 1068, 1036, 878, 821, 758, 653, 574 $cm^{-1}$. – $^1H$ NMR: $\delta_H$ = 0.91 (d, 6H, CH(C*H*$_3$)$_2$, $^3J_{HH}$ = 6.6 Hz), 0.94 (d, 6H, CH(C*H*$_3$)$_2$, $^3J_{HH}$ = 6.6 Hz), 1.53 (m, 4H, C*H*$_2$, $^3J_{HH}$ = 8.5 Hz), 1.72 (m, 2H, C*H*(CH$_3$)$_2$, $^3J_{HH}$ = 6.6 Hz), 2.26 (s, 6H, C*H*$_3$-Ar), 4.20 (m, 2H, C*H*COOH, $^3J_{HH}$ = 8.5 Hz), 6.96 (d, 2H, N*H*, $^3J_{HH}$ = 8.0 Hz), 7.35 (d, 2H, H-Ar, $^3J_{HH}$ = 8.6 Hz), 7.41 (s, 2H, H-Ar), 7.87 (s, 2H, N*H*), 7.91 (d, 2H, H-Ar, $^3J_{HH}$ = 8.4 Hz), 12.52 (br, COO*H*). – $^{13}C$ NMR: $\delta_C$ = 18.1, 21.6, 22.8, 24.4, 41.0, 50.8, 120.2, 123.7, 126.6, 127.7, 133.3, 137.0, 155.0, 175.0. – MS (ESI): *m*/*z* = 527.2 $[M+H]^+$. – $C_{28}H_{38}N_4O_6 \cdot H_2O$: calcd. C 61.75, H 7.40, N 10.29; found: C 61.29, H 7.42, N 10.25.

### 4.15 *N,N′*-[(3,3′-Dimethylbiphenyl-4,4′-diyl)-bis(iminocarbonyl)]-di(L-proline) (13)

L-Proline and 4,4′-diisocyanato-3,3′-dimethylbiphenyl were used; reaction period: 7.5 h; white powder (73 %); m. p. 288–290 °C. – $[\alpha]_D^{20}$ = −76.4 (*c* = 0.20, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3345, 2965, 2927, 2889, 2604, 1723, 1622, 1594, 1515, 1451, 1394, 1366, 1242, 1201, 1131, 1084, 1021, 922, 824, 751, 577, 527 $cm^{-1}$. – $^1H$ NMR: $\delta_H$ = 1.93 (m, 6H), 2.18 (m, 2H, $^3J_{HH}$ = 5.3 Hz, $^3J_{HH}$ = 9.1 Hz, $^2J_{HH}$ = 12.8 Hz), 2.25 (s, 6H, C*H*$_3$-Ar), 3.49 (m, 2H, $^3J_{HH}$ = 7.3 Hz), 3.57 (m, 2H), 4.33 (m, 2H, C*H*COOH), 7.41–7.36 (4H, H-Ar, $^3J_{HH}$ = 8.4 Hz), 7.46 (s, 2H, H-Ar), 7.77 (s, 2H, N*H*), 12.46 (br, COO*H*). – $^{13}C$ NMR: $\delta_C$ = 18.1, 24.0, 29.4, 46.1, 58.8, 123.7, 125.5, 127.9, 132.6, 135.8, 136.9, 154.3, 174.4. – MS (ESI): *m*/*z* = 495.3 $[M+H]^+$. – $C_{26}H_{30}N_4O_6 \cdot H_2O$: calcd. C 60.92, H 6.29, N 10.93; found: C 60.20, H 6.41, N 10.50.

### 4.16 (*R*,*R*)-*N*,*N*′-[(3,3′-Dimethylbiphenyl-4,4′-diyl)-bis(iminocarbonyl)]-bis(3-piperidinecarboxylic acid) (14)

(*R*)-(−)-3-Piperidinecarboxylic acid and 4,4′-diisocyanato-3,3′-dimethylbiphenyl were used; reaction period: 6 h; white powder (71 %); m. p. 286–288 °C. – $[\alpha]_D^{20}$ = −66.9 ($c$ = 0.52, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3294, 3025, 2946, 2863, 1733, 1701, 1625, 1606, 1508, 1445, 1420, 1290, 1252, 1182, 1141, 1074, 1059, 1002, 954, 869, 812, 751, 637, 568 $cm^{-1}$. – $^1H$ NMR: $\delta_H$ = 1.46 (m, 2H, $^3J_{HH}$ = 13.4 Hz), 1.63 (m, 4H, $^3J_{HH}$ = 6.7 Hz), 1.98 (m, 2H), 2.23 (s, 6H, C$H_3$-Ar), 2.43 (m, 2H, C*H*COOH), 2.99 (t, 2H, $^3J_{HH}$ = 10.8 Hz), 3.07 (dd, 2H, $^3J_{HH}$ = 13.2 Hz), 3.84 (d, 2H, $^3J_{HH}$ = 13.1 Hz), 4.08 (d, 2H, $^3J_{HH}$ = 10.7 Hz), 7.26 (d, 2H, H-Ar, $^3J_{HH}$ = 8.3 Hz), 7.38 (m, 2H, H-Ar, $^4J_{HH}$ = 1.7 Hz), 7.46 (d, 2H, H-Ar, $^4J_{HH}$ = 1.2 Hz), 8.09 (s, 2H, N*H*),12.41 (br, COO*H*). – $^{13}C$ NMR: $\delta_C$ = 18.1, 24.1, 27.1, 40.8, 44.3, 46.2, 123.7, 125.8, 128.0, 132.9, 135.9, 137.3, 155.4, 174.8. – MS (ESI): $m/z$ = 523.4 $[M+H]^+$. – $C_{28}H_{34}N_4O_6$: calcd. C 64.35, H 6.56, N 10.72; found: C 63.90, H 6.77, N 10.64.

### 4.17 *N*,*N*′-[(3,3′-Dimethylbiphenyl-4,4′-diyl)-bis(iminocarbonyl)]-di(L-threonine) (15)

L-Threonine and 4,4′-diisocyanato-3,3′-dimethylbiphenyl were used; reaction period: 10 h; white powder (12 %); m. p. 236–237 °C (dec.). – $[\alpha]_D^{20}$ = +12.3 ($c$ = 0.50, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3316, 2977, 2939, 2594, 1723, 1676, 1628, 1591, 1549, 1499, 1486, 1445, 1407, 1378, 1321, 1252, 1194, 1163, 1090, 945, 875, 821, 802, 761, 663 $cm^{-1}$. – $^1H$ NMR: $\delta_H$ = 1.13 (d, 6H, C$H_3$, $^3J_{HH}$ = 6.5 Hz), 2.26 (s, 6H, C$H_3$-Ar), 4.13 (m, 2H, C*H*COOH, $^3J_{HH}$ = 9.0 Hz), 4.21 (m, 2H, C*H*OH, $^3J_{HH}$ = 4.0 Hz), 5.10 (br, 2H, O*H*), 6.90 (d, 2H, N*H*, $^3J_{HH}$ = 8.5 Hz), 7.35 (d, 2H, H-Ar, $^3J_{HH}$ = 8.5 Hz), 7.41 (s, 2H, H-Ar), 7.90 (d, 2H, H-Ar, $^3J_{HH}$ = 8.5 Hz), 8.14 (s, 2H, N*H*), 12.47 (br, COO*H*). – $^{13}C$ NMR: $\delta_C$ = 18.2, 20.8, 58.0, 66.5, 120.4, 123.7, 126.9, 127.7, 133.3, 137.2, 155.6, 173.2. – MS (ESI): $m/z$ = 503.1 $[M+H]^+$. – $C_{24}H_{30}N_4O_8 \cdot ½\ H_2O$: calcd. C 56.35, H 6.11, N 10.95; found: C 56.36, H 6.26, N 11.01.

### 4.18 *N*,*N*′-[(3,3′-Dimethylbiphenyl-4,4′-diyl)-bis(iminocarbonyl)]-di(L-glutamic acid) (16)

In modification of the general procedure potassium hydroxide, 18-crown-6 ether, L-glutamic acid and 4,4′-diisocyanato-3,3′-dimethylbiphenyl were used; reaction period: 31 h; white powder (16 %); m. p. 263–264 °C (dec.). – $[\alpha]_D^{20}$ = –26.2 ($c$ = 0.11, $CH_3OH$). – IR (KBr): $\nu_{max}$ = 3357, 3303, 2917, 1720, 1641, 1584, 1549, 1451, 1404, 1239, 1119, 862, 821, 805, 764, 622 $cm^{-1}$. – $^1H$ NMR: $\delta_H$ = 1.88 (m, 4H, C$H_2$C$H_2$COOH, $^3J_{HH}$ = 7.7 Hz), 2.25 (s, 6H, C$H_3$-Ar), 2.29 (t, 4H, C$H_2$C$H_2$COOH, $^3J_{HH}$ = 7.6 Hz), 4.16 (m, 2H, C*H*COOH, $^3J_{HH}$ = 6.8 Hz), 6.97 (d, 2H, N*H*, $^3J_{HH}$ = 7.1 Hz), 7.34 (d, 2H, H-Ar, $^3J_{HH}$ = 8.4 Hz), 7.39 (s, 2H, H-Ar), 7.87 (d, 2H, H-Ar, $^3J_{HH}$ = 8.5 Hz), 7.99 (s, 2H, N*H*). – $^{13}C$ NMR: $\delta_C$ = 18.2, 28.3, 30.8, 52.3, 120.6, 123.7, 127.0, 127.7, 133.4, 137.2, 155.0, 174.2 (2C). – MS (ESI): $m/z$ = 597.2 $[M+K]^+$. – $C_{26}H_{30}N_4O_{10} \cdot 1.5\ H_2O$: calcd. C 53.33, H 5.68, N 9.57; found: C 53.09, H 5.30, N 9.53.

### 4.19 Dimethyl *N*,*N*′-(1,4-phenylene)dicarbamate (17)

White powder; m. p. 207–208 °C. – $^1H$ NMR: $\delta_H$ = 3.64 (s, 6H, OC$H_3$), 7.34 (s, 4H, H-Ar), 9.50 (s, 2H, N*H*). – $^{13}C$ NMR: $\delta_C$ = 51.5, 118.8, 134.0, 154.1.

### 4.20 X-ray structure determination

Intensity data were collected on a Kappa APEX II diffractometer (Bruker AXS) with Mo$K_\alpha$ radiation (λ = 0.71073 Å) using $\varphi$- and $\omega$-scans. Reflections were corrected for background, Lorentz, and polarisation effects. A preliminary structure model was derived by application of Direct Methods [57, 58] and were refined by full-matrix least-squares calculations based on $F2$ for all reflections [57, 58]. With the exception of the N–H hydrogen, all other hydrogen atoms were included in the models in calculated positions and were refined as constrained to the bonding atoms. Table 1 contains the crystal data and numbers pertinent to data collection and structure refinement, Tables 2 and 3 summarize important torsion angles and selected hydrogen bond parameters, respectively.

CCDC 1044807 contains the supplementary crystallographic data for this article. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

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