AXIALLY CHIRAL BIS(α-AMINO ACID)S AND THEIR DEAMINO ANALOGUES. SYNTHESIS AND CONFIGURATIONAL ASSIGNMENT*

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The axially chiral bis(α-amino acid)s *cis*-**2** and *trans*-**2** as possible building blocks for polymeric structures of novel type of helicity were prepared. Their configuration has been determined by NMR spectroscopy and, in the case of the *trans*-isomer, confirmed by single-crystal X-ray diffraction. Analogous pair of stereoisomeric diacids *cis*-**3** and *trans*-**3**, devoid of the amino groups, was also prepared and their configuration assigned. The observed differences in the NMR spectra of *cis*- and *trans*-isomers of **2** and **3** are discussed from the viewpoint of their different symmetry properties.
Key words: Chiral bis(α-amino acid)s; Axial chirality; Amino acids; NMR spectrometry; X-Ray diffraction.

Many important properties and functions of amino acids depend on their chirality. As a rule, chirality of natural as well as unnatural amino acids depends on the presence of an asymmetric atom[2].

Recently, we have reported[1d] the first[4] α-amino acid **1** whose chirality results from another type of molecular dissymmetry, based on the presence of a biaryl axis. As an extension of the earlier study, we have now investigated the corresponding axially chiral Janus[6] bis(α-amino acid)s **2**. Examination of models indicates that these bis(amino acid)s can give rise to helical rod-like polymers which are exceptional[7] in that their axis of helicity coincides with the polymer backbone. In this way, the novel bis(amino acid)s **2** may provide an interesting access to a very rare type of helical

* This is the seventh of the series of papers dealing with axially chiral amino acids, their derivatives and analogues; for previous papers see ref.[1].

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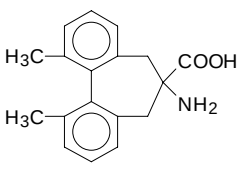
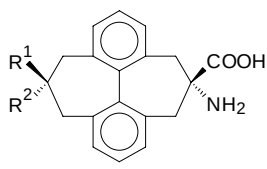
topology that is based on the primary[9] polymer structure. A possible synthetic approach to such an intriguing topology may be based on the interfacial condensation of reactive diesters of bis(amino acid)s **2** providing the corresponding polymeric dioxopiperazines. Both *cis*-**2** and *trans*-**2** should afford analogous (but stereochemically distinct) spiro-polymer architectures (Fig. 1) of unique conformational homogeneity which might find interesting application in enantioselective catalysis as well as in enantiomeric separation.

In this paper we report synthesis and configurational assignment of the starting *cis*- and *trans*-bis(amino acid)s **2**. At the same time, we provide analogous information concerning the corresponding diacids *cis*-**3** and *trans*-**3**, devoid of the amino groups.

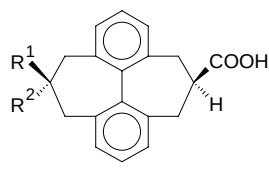


1



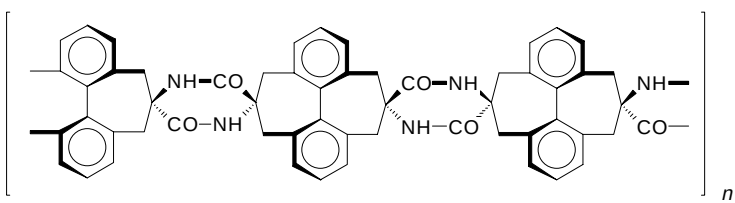
2

cis-**2**, R^1 = COOH; R^2 = NH_2
trans-**2**, R^1 = NH_2; R^2 = COOH

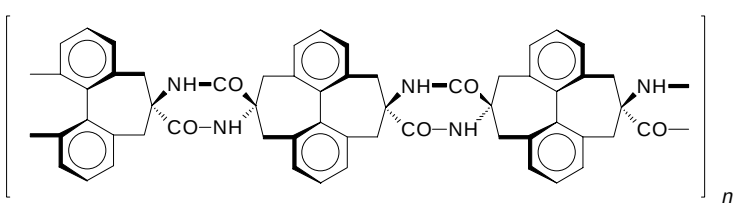


3

cis-**3**, R^1 = COOH; R^2 = H
trans-**3**, R^1 = H; R^2 = COOH



cis



trans

FIG. 1
Polymeric homochiral dioxopiperazines derived from *R*-enantiomers of diacids *cis*-**2** and *trans*-**2**

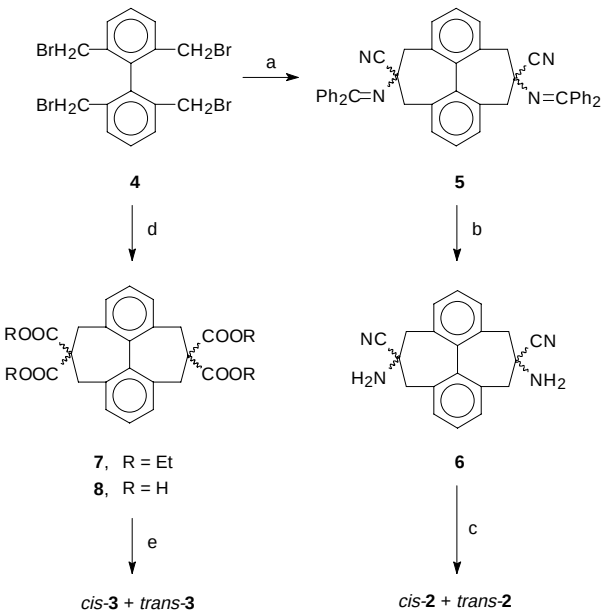
RESULTS AND DISCUSSION

Synthesis

The diamino diacids **2** have been prepared starting from tetrabromide[11] **4** using the straightforward route depicted in Scheme 1. Attempted separation of the isomers at the stages of intermediates **5** and **6** was unsuccessful and we succeeded only in separation of the final compounds **2** by preparative HPLC on a reversed phase (C18) in aqueous methanol, containing 0.1% trifluoroacetic acid. The configuration of the acids was determined by NMR spectral analysis and confirmed by single-crystal X-ray diffraction study of compound *trans*-**2** (*vide infra*). Diacids **3** were synthesized starting also from tetrabromide **4** (Scheme 1). Their configuration was again derived from the NMR spectra of the acids and their dimethyl esters.

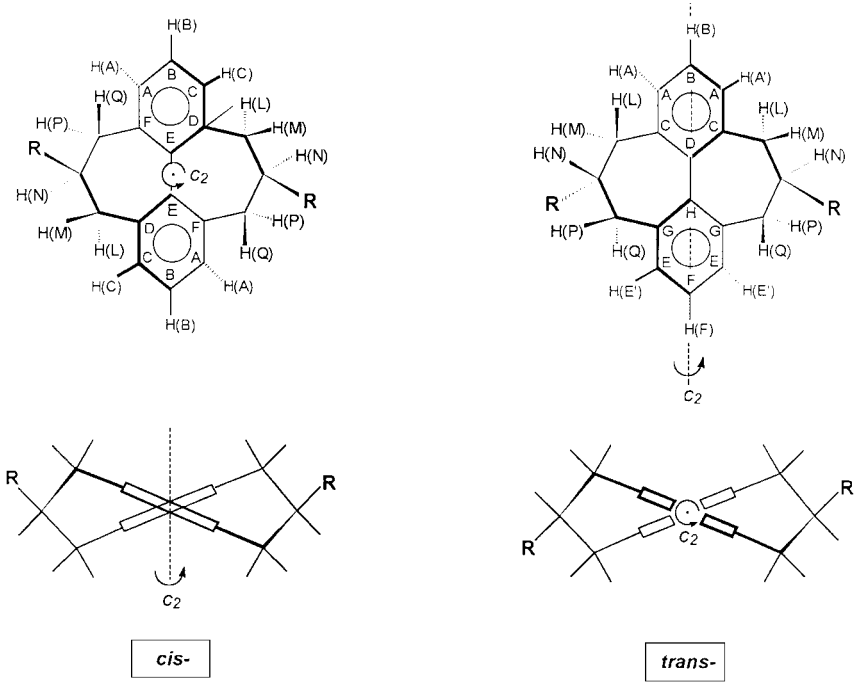
NMR Structural Analysis

The *cis*- and *trans*-isomers of bis(amino acid)s **2**, diacids **3** and dimethyl esters of **3** can be distinguished on the basis of their symmetry properties and corresponding consequences in the NMR spectra. The situation is illustrated on the example of *cis*- and



Reaction steps : a) diphenylmethyleneglycine nitrile, TEBA, 50% aq. NaOH, toluene, r.t., 20 h; b) 2M HCl, r.t., 3 h; c) conc. HCl, reflux, 15 h; d) (i) diethyl malonate, NaOEt, reflux, 3 h, (ii) NaOH/EtOH, reflux, 4 h; e) 220-260 °C, 10 min

SCHEME 1



cis-		*trans*-
3 symm. nonequiv. protons (2 identical ABC-systems)	*aromatic protons*	4 symm. nonequiv. protons (2 different systems: AA′B and EE′F)
5 symm. nonequiv. protons (2 identical LMNPQ-systems)	*alicyclic protons*	5 symm. nonequiv. protons (2 identical LMNPQ-systems)
6 symm. nonequiv. carbons (2 identical ABCDEF-systems)	*aromatic carbons*	8 symm. nonequiv. carbons (2 different systems: A2BC2D + E2FG2H)
3 symm. nonequiv. carbons	*alicyclic carbons*	3 symm. nonequiv. carbons

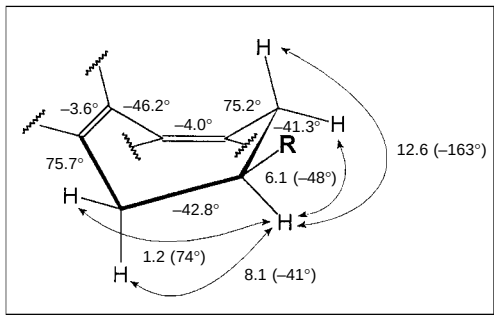


FIG. 2

Structures, symmetry properties and NMR characteristics of *cis*- and *trans*-isomers of diacids **3**. The interproton coupling constants observed for *trans*-**3**, together with the torsion angles derived from the calculated energy-minimized conformation, are shown in the box

trans-diacids **3** in Fig. 2. Both isomers have a two-fold rotation axis of symmetry (C_2) which in the case of the *cis*-isomer is perpendicular to the approximate plane of the molecule and passes through the middle of the central biaryl bond while in the case of the *trans*-isomer it coincides with this bond and passes through the four aromatic carbon atoms in *para*-positions. As the result, the spin systems of aromatic protons and carbons in both isomers are different. Aromatic protons in the *cis*-isomer form two identical ABC systems while in the *trans*-isomer two different AA′B and EE′F systems should be observed. Similarly, aromatic carbons in the *cis*-isomer correspond to two identical ABCDEF systems (6 signals) while in the *trans*-isomer two different A_2BC_2D and E_2FG_2H (8 signals) systems should be observed. The number of signals of alicyclic protons or carbons in *cis*- and *trans*-isomer is identical and therefore they cannot be used for distinguishing the configuration.

Using these theoretical considerations, we could differentiate between the *cis*- and *trans*-isomers of bis(amino acid) **2** from the experimental NMR spectra (aromatic regions of their ^{1}H and ^{13}C spectra are shown in Fig. 3) and analogously between the diacids *cis*-**3** and *trans*-**3** and their dimethyl esters (see data in Tables I and II). It should be noticed that chemical shift differences of some symmetrically nonequivalent protons and carbon atoms are very small even in high-field NMR spectra (^{1}H at 500 MHz and ^{13}C at 125.7 MHz). For example, the signals of aromatic carbons A and C in *cis*-**3**

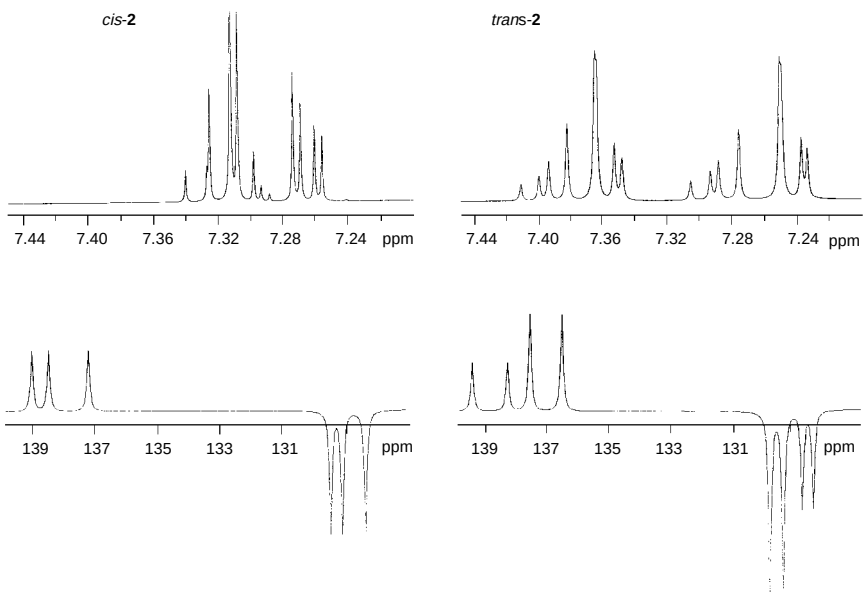


FIG. 3
Aromatic regions of ^{1}H and ^{13}C NMR spectra of *cis*- and *trans*-isomers of bis(amino acid)s **2**

and alicyclic CH_2 carbons in both *cis*-**3** and *trans*-**3** coincide in DMSO and they could be resolved only after addition of CD_3OD (see Tables I and II). Similarly the signals of aromatic protons in dimethyl esters of *cis*-**3** as well as *trans*-**3** in $CDCl_3$ give narrow nonanalyzable multiplets and the configurational assignment could be only based on their ^{13}C NMR spectra. Better resolved spectral patterns of aromatic protons in **2** and **3** were confirmed and NMR parameters refined by spin simulation.

The vicinal coupling constants of the alicyclic protons in diacids **3** and their dimethyl esters (J = 6.1, 12.6, 8.1 and 1.2 Hz ; see Table I and Fig. 2) indicate rigidity of the

TABLE I
Proton NMR data of compounds **2**, **3** and dimethyl esters of **3**

Hydrogen	*cis*-**2** D_2O + NaOD	*trans*-**2** D_2O + NaOD	*cis*-**3** DMSO	*trans*-**3** DMSO	Dimethyl ester	
					cis-**3** $CDCl_3$	*trans*-**3** $CDCl_3$
arom. H	7.32 t (B) 7.31 dd (A) 7.27 dd (C) J(AB) = 7.5 J(BC) = 7.5 J(AC) = 1.4	7.39 m (B) 7.36m (A,A′) 7.29 m (F) 7.24 m (E,E′) J(AB) = 7.5 J(A′B) = 7.5 J(AA′) = 1.5 J(EF) = 7.5 J(E′F) = 7.5 J(EE′) = 1.7	7.25 dd (A) 7.22 t (B) 7.15 dd (C) J(AB) = 7.5 J(AC) = 1.6 J(BC) = 7.3	7.26 m (AA′) 7.24 m (B) 7.19 m (F) 7.13 m (E,E′) J(AB) = 7.5 J(A′B) = 7.5 J(AA′) = 2.5 J(EF) = 7.5 J(EF′) = 7.5 J(EE′) = 2.5	7.20–7.24 m (2 × ABC)	7.20–7.25 m (AA′BEE′F)
CH_2	3.00 d (Q) 2.93 d (L) 2.52 d (P) 2.24 d (M) J(LM) = 13.2 J(PQ) = 13.7	3.06 d (Q) 2.95 d (L) 2.60 d (P) 2.34 d (M) J(LM) = 13.2 J(PQ) = 13.9	2.90 bdd (Q) 2.76 bdd (L) 2.37 dd m (P) 2.35 dd (M) J(LM) = 13.2 J(PQ) = 13.4 J(LN) = 6.1 J(MN) = 12.6 J(PN) = 8.1 J(QN) = 1.2 J(LQ) < 1	2.90 bdd (Q) 2.75 bdd (L) 2.39 dd (P) 2.33 dd (M) J(LM) = 13.2 J(PQ) = 13.4 J(LN) = 6.1 J(MN) = 12.6 J(PN) = 8.1 J(QN) = 1.2 J(LQ) < 1	2.99 bdd (Q) 2.84 bdd (L) 2.56 dd (M) 2.55 dd (P) J(LM) = 13.2 J(PQ) = 13.7 J(LN) = 6.2 J(MN) = 12.8 J(PN) = 8.0 J(QN) = 1.2 J(LQ) < 1	2.98 bdd (Q) 2.84 bdd (L) 2.57 dd (M) 2.56 dd (P) J(LM) = 13.2 J(PQ) = 13.7 J(LN) = 6.2 J(MN) = 12.8 J(PN) = 8.0 J(QN) = 1.2 J(LQ) < 1
CH	–	–	3.14 m (N)	3.14 m (N)	3.23 m (N)	3.22 m (N)
COOR	–	–	12.34 bs	12.33 bs	3.71 s	3.71 s

molecules in solution and can be used to estimate their geometry. Energy minimization of *cis*- and *trans*-diacids **3** using the molecular mechanics method MM2 provided conformations with torsion angle –46° between planes of the two phenyl rings and interproton torsion angles –48, –163, –41 and 74° (see Fig. 2). Using the generalized Karplus relation[12], these angles can be recalculated to the theoretical *J*-values 5.0, 11.5, 6.4 and 1.3 Hz which are in a good agreement with the observed ones.

*Molecular Structure of Bis(amino acid) trans-**2***

The molecular structure of bis(amino acid) *trans*-**2**, as determined by single-crystal diffraction, is shown in Fig. 4, confirming correctness of the configurational assignment attained by NMR (*vide supra*). Some selected torsion angles are given in Table III.

The X-ray analysis shows that the molecule exists as a double zwitterion, bound by three solvating molecules of water into a three-dimensional arrangement. Concerning the torsion angles between the phenyl ring planes, a very satisfactory agreement between the value found by X-ray diffraction for bis(amino acid) *trans*-**2** (about 49°) and

TABLE II
Carbon-13 NMR data of compounds **2**, **3** and esters of **3**

Carbon	*cis*-**2** D_2O + NaOD	*trans*-**2** D_2O + NaOD	*cis*-**3** DMSO	*cis*-**3** DMSO + CD_3OD (9 : 1)	*trans*-**3** DMSO	*trans*-**3** DMSO + CD_3OD (9 : 1)	Dimethyl ester *cis*-**3** $CDCl_3$	Dimethyl ester *trans*-**3** $CDCl_3$
arom. C	139.08(2)	139.50	138.04(2)	138.26(2)	138.07	138.31	138.33(2)	138.67
	138.53(2)	138.36	137.38(2)	137.56(2)	137.98	138.22	137.02(2)	138.03
	137.25(2)	137.59(2)	136.45(2)	136.65(2)	137.63(2)	137.84(2)	136.49(2)	137.49(2)
		136.57(2)			136.19(2)	136.40(2)		136.04(2)
arom. CH	129.51(2)	129.93(2)	128.29(2)	128.47(2)	128.23(2)	128.44(2)	128.54(2)	128.43(2)
	129.10(2)	129.47(2)	127.50(2)	127.67(2)	127.65	127.85	127.53(2)	127.56
	128.37(2)	128.85		127.64(2)	127.52(2)	127.69(2)	127.58(2)	127.53
		128.48			127.35	127.52		127.37(2)
CH_2	44.41(2)	43.06(2)	33.14(4)	33.34(2)	33.13(4)	33.35(2)	33.62(2)	33.62(2)
	42.04(2)	40.92(2)		33.28(2)		33.29(2)	32.92(2)	32.95(2)
CH	–	–	49.00(2)	49.16(2)	48.98(2)	49.16(2)	49.44(2)	49.46(2)
C	70.21(2)	70.65(2)	–	–	–	–	–	–
COOR	183.02(2)	180.65(2)	175.36(2)	175.49(2)	175.34(2)	175.49(2)	174.87(2)	174.84(2)
							51.76(2)	51.76(2)

that calculated by the MM2 method (for acids **3**, 46°; *vide supra*) is apparent. Also the corresponding torsion angles in the alicyclic parts of acid *trans*-**2** found in crystal (Table III) and calculated by energy minimization (using the MM2 method) for diacids *trans*-**2** (Table III) and *trans*-**3** (Fig. 2) fairly agree.

TABLE III
Selected torsion angles (in °) for *trans*-**2** found in crystal and calculated by the MM2 method (in parentheses)

Bonds	Angles		Bonds	Angles	
	Found	MM2		Found	MM2
			7-Membered rings		
C2–C1–C11–C16	–49.1(3)	(–46.4)	C6–C1–C11–C12	–48.8(3)	(–46.5)
C1–C11–C16–C17	0.0(3)	(–3.7)	C1–C11–C12–C9	–2.5(3)	(–3.4)
C11–C16–C17–C18	70.6(3)	(74.4)	C8–C9–C12–C11	77.0(3)	(73.8)
C16–C17–C18–C19	–40.4(3)	(–41.6)	C7–C8–C9–C12	–48.3(3)	(–40.8)
C17–C18–C19–C2	–45.3(3)	(–41.5)	C6–C7–C8–C9	–38.9(3)	(–42.2)
C1–C2–C19–C18	74.5(3)	(74.2)	C1–C6–C7–C8	71.3(3)	(74.5)
C11–C1–C2–C19	–1.8(3)	(–3.4)	C11–C1–C6–C7	–0.9(3)	(–3.5)
			Substituents (NH_3^+, COO^-)		
N2–C18–C19–C2	73.2(2)	(72.3)	C6–C7–C8–N1	79.7(2)	(71.5)
C16–C17–C18–N2	–159.6(3)	(–155.2)	N1–C8–C9–C12	–167.2(3)	(–154.7)
C20–C18–C19–C2	–170.0(3)	(–168.5)	C6–C7–C8–C10	–162.5(3)	(–168.5)
C16–C17–C18–C20	81.8(2)	(85.2)	C10–C8–C9–C12	76.8(2)	(85.7)

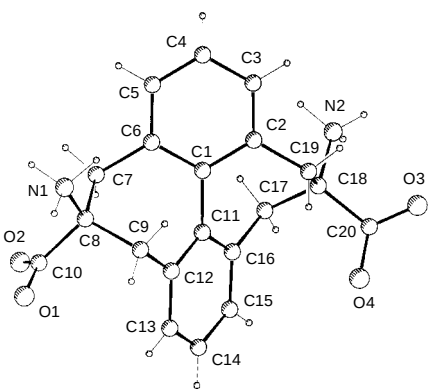


FIG. 4
Perspective view of molecule of bis(amino acid) *trans*-**2** (only one enantiomer of the racemate is shown)

EXPERIMENTAL

NMR spectra were measured on FT-NMR spectrometers Varian UNITY-200 (^{1}H at 200 MHz; compounds **5**–**7**) and UNITY-500 (^{1}H at 500 MHz and ^{13}C at 125.7 MHz; compounds **2**, **3** and dimethyl esters of **3**).

cis- and *trans*-5,11-Diamino-5,6,11,12-tetrahydro-4*H*,10*H*-dibenzo[*ef*,*kl*]heptalene-5,11-dicarbonitrile (**6**)

To a stirred mixture of tetrabromide[11] **4** (3.95 g, 7.5 mmol), (diphenylmethylene)glycinenitrile[13] (3.30 g, 15 mmol), benzyltriethylammonium bromide (0.45 g, 0.15 mmol) and toluene (20 ml) was added 50% aqueous NaOH (6 g, 75 mmol) at 0 °C during 15 min. After stirring at room temperature for 24 h, the mixture was diluted with dioxane (100 ml) and dilute (1 : 5) hydrochloric acid (about 70 ml) was added under vigorous stirring and cooling with ice to strongly acidic reaction. After stirring at room temperature for 3 h, the mixture was concentrated *in vacuo* to half of the original volume, diluted with water (200 ml) and extracted three times with ether. The combined aqueous layers were made alkaline with NaOH and the product was extracted several times into ethyl acetate. The combined organic phases were washed with water, the solvent was evaporated and the residue used in the next reaction step. A small sample of the above solution was dried and the solvent was evaporated to yield the dinitrile **6**. ^{1}H NMR spectrum: 7.50–7.25 m, 6 H (ArH); 3.06–2.44 m, 8 H (CH_2), 1.86 br s, 4 H (NH_2). FAB MS, *m/z*: 315 $(M + 1)^+$.

cis- and *trans*-5,11-Diamino-5,6,11,12-tetrahydro-4*H*,10*H*-dibenzo[*ef*,*kl*]heptalene-5,11-dicarboxylic Acid (*cis*-**2** and *trans*-**2**)

Crude dinitrile **6**, obtained in the preceding experiment, was refluxed with concentrated HCl (30 ml) for 15 h with addition of other concentrated HCl portions (5 ml each) at 3 h intervals. The reaction mixture was then evaporated and the dry residue (2.26 g) was subjected to preparative HPLC on a reverse phase (C18 in 0.1% TFA–water–methanol). Each of the separated salts of the pure *cis*- and *trans*-diamino diacids was dissolved in water (10 ml) and the solution was applied onto a column of Dowex 50 X 2 in H^+ form (30 ml). After washing with water to neutral reaction of the eluate, the acid was eluted with 5% aqueous ammonia, the eluate was evaporated to dryness and the residue was coevaporated three times with water.

cis-**2**: Yield 0.57 g (19% based on tetrabromide **4**), m.p. 360 °C. For the ^{1}H and ^{13}C NMR spectra, see Tables I and II. HR-FAB MS: 353.1524; for ($C_{20}H_{20}N_2O_4$ + H) calculated: 353.1501. For $C_{20}H_{20}N_2O_4 \cdot 3\,H_2O$ (406.4) calculated: 59.10% C, 6.45% H, 6.89% N; found: 59.11% C, 6.16% H, 7.33% N.

trans-**2**: Yield 0.63 g (21% based on tetrabromide **4**), m.p. 360 °C (water). For the ^{1}H and ^{13}C NMR spectra, see Tables I and II. HR-FAB MS: 353.1563; for ($C_{20}H_{20}N_2O_4$ + H) calculated: 353.1501. For $C_{20}H_{20}N_2O_4 \cdot 3\,H_2O$ (406.4) calculated: 59.10% C, 6.45% H, 6.89% N; found: 59.07% C, 6.45% H, 6.87% N.

Tetraethyl 5,6,11,12-Tetrahydro-4*H*,10*H*-dibenzo[*ef*,*kl*]heptalene-5,5,11,11-tetracarboxylate (**7**)

Diethyl malonate (10.2 g, 64 mmol) was added to a solution of sodium ethoxide, prepared from sodium (1.4 g, 61 mmol) and ethanol (100 ml). After addition of tetrabromide **4** (5.2 g, 10 mmol), the stirred mixture was refluxed for 3 h, cooled and partitioned between water and ether. The ethereal layer was dried over sodium sulfate, the solvent evaporated and the residue crystallized from ethanol to give 4.05 g (77%) of tetraester **7**, m.p. 125–126 °C. ^{1}H NMR spectrum ($CDCl_3$): 1.28 t, 12 H, J = 7.1 (C**H**$_3$CH$_2$); 2.82 d, 4 H, J = 14.0; 3.19 d, 4 H, J = 14.0 (CH_2); 4.20–4.34 m, 8 H (C**H**$_2$CH$_3$); 7.18–7.26 m,

6 H (ArH). FAB MS, *m/z*: 523 (M + H). For $C_{30}H_{34}O_8$ (522.6) calculated: 68.95% C, 6.56% H; found: 68.70% C, 6.53% H.

4,5,6,10,11,12-Tetrahydro-4*H*,10*H*-dibenzo[*ef*,*kl*]heptalene-5,5,11,11-tetracarboxylic Acid (**8**)

A solution of sodium hydroxide (11.6 g, 290 mmol) in a mixture of water (35 ml) and ethanol (110 ml) was added to a stirred solution of tetraester **7** (11.0 g, 21.1 mmol) and the mixture was refluxed for 4 h. After standing overnight, the mixture was diluted with water and the clear solution was washed with ether. The aqueous layer was acidified with hydrochloric acid and the product extracted with ether. Washing with water, drying over sodium sulfate and evaporation of the solvent afforded 8.24 g (95%) of tetracarboxylic acid **8**, decomposing above 210 °C. For $C_{22}H_{18}O_8.H_2O$ (428.6) calculated: 61.68% C, 4.71% H; found: 61.59% C, 5.09% H. FAB MS, *m/z*: 411 (M + 1).

cis-5,6,11,12-Tetrahydro-4*H*,10*H*-dibenzo[*ef*,*kl*]heptalene-5,11-dicarboxylic Acid (*cis*-**3**)

Tetracarboxylic acid **8** (1.11 g, 2.7 mmol) was heated at 220–260 °C for 10 min. The cold mixture was boiled with ethyl acetate, cooled, filtered and the solid washed with ethyl acetate. Yield 492 mg of *cis*-**3**, m.p. 328–332 °C, very sparingly soluble in all common solvents. For $C_{20}H_{18}O_4$ (322.3) calculated: 74.53% C, 5.59% H; found: 74.68% C, 5.68% H. For ^{1}H and ^{13}C NMR spectra, see Tables I and II.

The dimethyl ester for the NMR study was prepared by treatment of diacid **3** with diazomethane; its NMR spectra are given in Tables I and II.

trans-5,6,11,12-Tetrahydro-4*H*,10*H*-dibenzo[*ef*,*kl*]heptalene-5,11-dicarboxylic Acid (*trans*-**3**)

The filtrate from the above preparation was evaporated and the residue (350 mg) was several times crystallized from ethyl acetate to give 42 mg of *trans*-**3**, m.p. 215–217 °C. For $C_{20}H_{18}O_4 \cdot 2/3\ C_4H_8O_2$ (381.0) calculated: 73.10% C, 6.07% H; found: 73.30% C, 6.00% H. For ^{1}H and ^{13}C NMR spectra, see Tables I and II.

The dimethyl ester for the NMR study was prepared by treatment with diazomethane; its NMR spectra are given in Tables I and II.

Single-Crystal X-Ray Diffraction Analysis of *trans*-**2**

trans-**2**·3 H_2O, $C_{20}H_{26}N_2O_7$, M = 406.43, monoclinic, space group $P2_1/c$, a = 11.345(1), b = 8.815(1), c = 20.401(3) Å, β = 103.47(1); V = 1 984.1(4) Å^3, D_c = 1.361 Mg m^{-3}, μ = 0.103 mm^{-1}, $F(000)$ = 792, Z = 4. Crystal size was 0.2 × 0.15 × 0.35 mm (grown from water). Measurements were performed on a CAD4 diffractometer at 293(2) K with MoKα radiation, λ = 0.71073 Å. From a total of 3 580 reflections measured in the range h = –13 to 13, k = 0 to 10, l = 0 to 24, 3 484 were independent (R_{int} = 0.026). The structure was solved by direct methods[14] (SHELXS86) and refined by full matrix least squares based[15] on F^2 (SHELXL93). Final R indices were R = 0.0402, and wR = 0.1002. The atomic coordinates, bond lengths and angles were deposited by Cambridge Structural Database. Full crystallographic data in the form of standard CIF files as produced by SHELX are available by e-mail from the author (J. P.).

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REFERENCES AND NOTES

1. a) Tichy M., Ridvan L. Holy P., Zavada J., Cisarova I., Podlaha J.: *Tetrahedron: Asymmetry* **1998**, *9*, 227; b) Vojtisek P., Cisarova I., Podlaha J., Zak Z., Bohm S., Tichy M., Zavada J.: *Z. Kristallor*. **1997**, *212*, 226; c) Tichy M., Ridvan L., Zavada J.: *Collect. Czech. Chem. Commun*. **1997**, *62*, 62; d) Ridvan L., Abdallah N., Holakovsky R., Tichy M., Zavada J.: *Tetrahedron: Asymmetry* **1996**, *7*, 231; e) Tichy M., Zavada J.: *Collect. Czech. Chem. Commun*. **1995**, *60*, 2161; f) Tichy M., Zavada J., Podlaha J., Vojtisek P.: *Tetrahedron: Asymmetry* **1995**, *6*, 1279.
2. Beyond the category of α-amino acids we have traced down a few amino acid structures in the literature that contain other element of chirality than asymmetric carbon atom, including 1,11-diamino-6,6-di(ethoxycarbonyl)-6,7-dihydro-5*H*-dibenzo[*a*,*c*][7] annulene and 6-(aminomethyl)-spiro[3.3]heptane-2-carboxylic acid; *cf.* ref.[3].
3. a) Iffland D. C., Siegel H. J.: *J. Am. Chem. Soc*. **1958**, *80*, 1947; b) Loffler L. J., Britcher S. F., Baumgarten W.: *J. Med. Chem*. **1970**, *13*, 926.
4. Following our report in ref.[1d], Mazaleyrat and coworkers[5] prepared further examples of axially chiral α-amino acids.
5. a) Mazaleyrat J.-P., Gaucher A., Wakselman M., Tchertanov L., Guilham J.: *Tetrahedron Lett*. **1996**, *37*, 2971; b) Mazaleyrat J.-P., Gaucher A., Savrda J., Wakselman M.: *Tetrahedron: Asymmetry* **1997**, *8*, 619; c) Mazaleyrat J.-P., Gaucher A., Goubart Y., Savrda J., Wakselman M.: *Tetrahedron Lett*. **1997**, *39*, 2091.
6. Referring to the double-faced Roman god. For a related case of axially chiral Janus dilactam, see ref.[1f].
7. In common helical polymers such as poly(amino acid)s, polymethacrylates or polyisocyanates, the stereochemistry is entirely different since the polymeric backbone does not coincide with the axis of helicity but, instead, winds up around it; *cf.* ref.[8].
8. Okamoto Y., Nakato T.: *Chem. Rev*. **1994**, *94*, 349.
9. The helical topology of the common polymers[8] is based exclusively on the secondary and/or tertiary structure. To our best knowledge, no authentic polymer with primary helical structure has been reported so far. Synthetic approaches to such structures ("helixates") never exceeded the level of the lowest oligomers (trimers and tetramers); *cf.* ref.[10].
10. a) Gange D., Magnus P., Bass L., Arnold E. V., Clardy J.: *J. Am. Chem. Soc*. **1980**, *102*, 2134; b) Belohradsky M., Budesinsky M., Gunterova J., Hodacova J., Holy P., Zavada J.: *J. Org. Chem*. **1996**, *61*, 1205; c) Belohradsky M., Budesinsky M., Gunterova J., Hodacova J., Holy P., Zavada J.: *Tetrahedron* **1996**, *52*, 11013.
11. Agranat I., Rabinovitz M., Shaw W.-C.: *J. Org. Chem*. **1979**, *44*, 1936.
12. Haasnoot C. A. G., de Leeuw F. A. A. M., Altona C.: *Tetrahedron* **1980**, *36*, 2783.
13. O'Donnell M. J., Bruder W. A., Eckrich T. M., Schullenberger D. F., Staten G. S.: *Synthesis* **1984**, 127; and references therein.
14. Sheldrick G. M.: *Acta Crystallogr., Sect. A: Cryst. Phys., Diffr., Theor. Gen. Crystallogr*. **1990**, *46*, 467.
15. Sheldrick G. M.: *SHELXL93. Program for Crystal Structure Refinement from Diffraction Data*. University of Gottingen, Gottingen 1993.