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Chemo-Enzymatic Approach to the Synthesis of Each of the Four Isomers of α-Alkyl-β-Fluoroalkyl-Substituted β-Amino Acids

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Abstract: Starting from easily available ethyl 2-methyl-4,4,4-trifluoroacetoacetate and benzylamine each of the four stereoisomers of α-methyl-β-trifluoromethyl-β-alanine have been synthesized in optically pure form *via* stereocontrolled chemo-enzymatic procedure including diastereoselective base-catalyzed [1,3]-proton shift reaction and enantioselective penicillin acylase-catalyzed resolution.

The recent upsurge of interest in the carbapenem antibiotics[2] has been accompanied by a great deal of attention to the synthesis of various α-,β-disubstituted β-amino acids[3] which are one of the key structural units in the penem skeleton. However, among the large number of α-,β-disubstituted β-amino acids described, fluorine-containing ones are practically unknown.[4,5] Our recent results on biomimetic [1,3]-proton shift reaction[6] and biocatalytic resolution of β-amino acids[7] prompted us to couple these two methods in one chemo-enzymatic approach that includes stereoselective synthesis of desirable diastereomer and next, biocatalytic resolution of pure diastereomer into the pair of enantiomers. We report here our preliminary results on the application of this methodology to a synthesis of each of the four stereoisomers of hitherto unknown α-methyl-β-trifluoromethyl-β-alanine (Scheme 1).

Previously, we have reported[6a] that the *N*-benzyl imine/*N*-benzyl enamine mixture **2**, prepared from ketoester **1**[8] and benzylamine, on the treatment with triethylamine easily underwent [1,3]-proton transfers to give in a yield of 94% the pair of diastereomers **3a,b** in the 37:63 ratio. Further experiments revealed that this ratio is uninfluenced by the solvent, reaction temperature, and the time of exposition with triethylamine, but sensitive to the nature of base employed. Thus, we have found that catalysis of the isomerization with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) results in the nearly the same ratio of diastereomers **3a,b**,[9] but with domination of the opposite diastereomer. This stereochemical result (ratio **3a**/**3b** as 65/35) was obtained also by the action of catalytic amount (10 mol%) of DBU on the mixture **3a** and **3b** (ratio 37/63) formed in the

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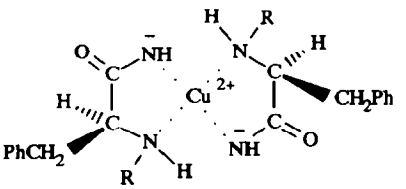
complexes of (S)–phenylalaninamide (Phe–NH_2) and N^2–methyl–(S)–phenylalaninamide (MePhe–NH_2)[4] and, therefore, the mechanism of chiral discrimination involved must be different.



(1): R = C_8H_{17}

(2): R = $C_{12}H_{25}$

These particular structures may lead to "self–assembling" systems spontaneously arising owing to non–covalent forces among the component molecules.[12] With this in mind, we set out to prepare crystals to see how the long hydrocarbon chains would assemble and thus obtaining reasonable clues about the adsorption mode of the chiral selector on the column stationary phase and on the discriminating interactions with the enantiomers.

EXPERIMENTAL

(S)–phenylalaninamide was obtained from Sigma Chemical Co. (St. Louis, MO, U.S.A.). N–octanal and n–dodecanal were obtained from Merck (Darmstadt, Germany). Pd/C (10%) was purchased from Sigma. $Cu(OAc)_2 \cdot H_2O$ (RPE), methanol (RCS–grade) and ethyl ether (RCS–grade) were purchased from Carlo Erba (Milan, Italy). Melting points were recorded on an Electrothermal apparatus and were uncorrected. ^{1}H–NMR and ^{13}C–NMR spectra were recorded on a Bruker AC 100 spectrometer. Infrared spectra were recorded on a Perkin Elmer Mod. 298 spectrophotometer. Mass spectra were recorded on a Finnigan MAT SSQ 710 spectrometer using electron impact ionization (70 eV, EI). Elemental analyses were performed on a Carlo Erba Mod. 1106 elemental analyzer. Optical rotations were measured on an Autopol III Rudolph Research polarimeter with a path length of 1 dm. UV–Vis spectra were recorded on a Kontron Uvikon 860 spectrophotometer. CD spectra were recorded on a Jasco 500A spectropolarimeter.

N^2–n–octyl–(S)–phenylalaninamide hydrochloride: to (S)–Phe–NH_2 (8.2 g, 0.05 mol) dissolved in MeOH (200 mL) Pd/C (10%) (20% w/w, 1.64 g) and n–octanal (7.27 mL, 0.05 mol) were added under nitrogen. Hydrogenation was performed at 40°C for 12 h, the catalyst filtered and the solution evaporated to dryness. The crude product was treated with HCl/MeOH, washed with ethyl ether (100 mL) to remove the residual aldehyde, then washed with a diluted alkali solution to remove the unreacted (S)–Phe–NH_2. The product was recrystallized as the hydrochloride from MeOH/Et_2O. Yield: 70%; m.p. 212°C dec.; $[\alpha]_D^{25}$= +34.0 (*c*=1, EtOH 95%). Found: C, 65.07; H, 9.53; N, 8.64 %. Calc. for $C_{17}H_{29}ClN_2O$: C, 65.26; H, 9.34; N, 8.95 %. ^{1}H–NMR ($CDCl_3$, free amine): δ 0.97 (t, 3H, CH_3–C), 1.18 (m, 17H, C–CH_2–C, NH), 2.44 (m, 2H, C–CH_2–N), 2.69 (dd, 1H, CH_β), 3.20 (dd, 1H, CH_β), 3.30 (dd, 1H, CH_α), 5.66 (broad s, 1H, CO–NH), 7.28 (m, 6H, $H_{arom.}$ + CO–NH) ppm. ^{13}C–NMR ($CDCl_3$, free amine): δ 14.08 (CH_3), 22.60, 26.99, 29.21, 29.32, 29.85, 31.78, 39.31 (CH_2 + CH_β), 48.83 (CH_2N), 64.14 (CH_α), 126.93, 128.74, 129.08, 137.62 ($C_{arom.}$), 177.27 (CO) ppm.

N^2–n–dodecyl–(S)–phenylalaninamide hydrochloride: to (S)–Phe–NH_2 (8.2 g, 0.05 mol) dissolved in 2–propanol (200 mL) Pd/C (10%) (20% w/w, 1.64 g) and n–dodecanal (11 mL, 0.05 mol) were added under

nitrogen. The same work up performed for the other ligand gave the desired product. Yield: 70 %; m.p. 200°C dec.; $[\alpha]_D^{25}$= + 22.8 (*c*=1, EtOH 95%). Found: C, 68.66; H, 10.39; N, 7.30. Calc. for $C_{21}H_{37}ClN_2O$: C, 68.35; H, 10.11; N, 7.59 %. ^{1}H-NMR ($CDCl_3$, free amine): δ 0.88 (t, 3H, CH_3–C), 1.24 (m, 20H, C–CH_2–C), 1.61 (broad s, 1H, NH), 2.41 (m, 2H, C–CH_2–N), 2.69 (dd, 1H, CH_β), 3.25 (m, 2H, CH_β + CH_α), 6.20 (broad d, 1H, CO–NH), 7.27 (m, 7H, $H_{arom.}$ + CO–NH) ppm. ^{13}C-NMR ($CDCl_3$, free amine): δ 14.13 (CH_3), 22.69, 26.98, 29.35, 29.56, 29.63, 29.82, 31.92, 39.34 (CH_2 + CH_β), 48.77 (CH_2N), 64.13 (CH_α), 126.87, 128.73, 129.05, 137.67 ($C_{arom.}$), 177.62 (CO) ppm.

Bis[N^2–n–octyl–(S)–phenylalaninamidato]copper(II) dihydrate, [Cu(NocPhe–NH)$_2$]·2H$_2$O (1). N^2–octyl–(S)–phenylalaninamide hydrochloride (0.624 g, 2 mmol) and $Cu(OAc)_2 \cdot H_2O$ (0.2 g, 1 mmol) were dissolved in methanol/water=9/1 (100 mL). The pH was adjusted to 9.0 (1 M NaOH) and the solution was allowed to stand at room temperature. After 24–48 h red–violet crystals were obtained (m.p. 156°C; Found: C, 62.85, H, 9.03, N, 8.43 %. Calc. for $C_{34}H_{58}CuN_4O_4$: C, 62.79, H, 8.99, N, 8.61 %; CD: λ = 520 nm ([Θ] = –3000), λ = 409 nm ([Θ] = 3100)).

Bis[N^2–n–dodecyl–(S)–phenylalaninamidato]copper(II) dihydrate, [Cu(NdoPhe–NH)$_2$]·2H$_2$O (2). The same procedure used for (1) was followed. Whenever a precipitate was formed, MeOH was added until it was redissolved. After standing for 24 h at room temperature red–violet crystals were formed (m.p. 137°–138° C. Found: C, 66.20, H, 10.41, N, 6.87 %. Calc. for $C_{42}H_{74}CuN_4O_4$: C, 66.15, H, 9.78, N, 7.35 %; CD: λ = 550 nm ([Θ] = –2500), λ = 465 nm ([Θ] = 2375)).

Crystal data. Complex (1): $C_{34}H_{58}CuN_4O_4$, M = 650.4, monoclinic, space group $P2_1$, a = 23.494(8), b = 7.299(2), c = 10.612(3) Å, β = 90.10(5)°, V = 1820(1) Å^3, Z = 2, F (000) = 702, D_c = 1.187 Mg m^{-3}, μ (Cu–Kα) = 11.5 cm^{-1}, λ = 1.54178 Å, 3918 reflections measured, 3257 with $I > 2\sigma(I)$ used in refinement of 619 parameters, $(\Delta\rho)_{max}$ = 0.21, $(\Delta\rho)_{min}$ = –0.41 eÅ^{-3}, max 2θ = 140°. Complex (2): $C_{42}H_{74}CuN_4O_4$, M = 762.6, monoclinic, space group $P2_1$, a = 27.915(8), b = 7.341(2), c = 10.809(3) Å, β = 95.44(5)°, V = 2205(1) Å^3, Z = 2, F (000) = 830, D_c = 1.149 Mg m^{-3}, μ (Cu–Kα) = 9.8 cm^{-1}, λ = 1.54178 Å, 4741 reflections measured, 3179 with $I > 2.5\sigma(I)$ used in refinement of 756 parameters, $(\Delta\rho)_{max}$ = 0.19, $(\Delta\rho)_{min}$ = –0.43 eÅ^{-3}, max 2θ = 140°.

Structure determination. The relevant data concerning the crystal structure analyses are summarized in Table 1. The intensity data of both compounds were collected at room temperature in the θ – 2θ step–scanning mode on a Siemens AED three–circle diffractometer under the control of a General Automation Jumbo 220 Computer with Cu–Kα radiation (λ=1.54056 Å). The intensity of a standard reflection was monitored after every 50 measurement and showed good stability of the crystal and the electronics. The absorption correction was neglected in view of small crystal dimensions (0.33x0.23x0.16 mm for (1) and 0.49x0.33x0.16 mm for (2)). All data were corrected for Lorentz and polarization effects. The structures were solved by Patterson and direct methods using SHELX 86[13] system of computer programs. Refinements were carried out by full–matrix least–squares cycles to R=0.028, R_w=0.078 for (1) and R=0.031, R_w=0.082 for (2) (w= $1/[\sigma^2(Fo^2)+(aP)^2)]$ where P=(Max(F_o^2,0)+2F_o^2)/3 and a=0.0467 for (1) and a=0.1135 for (2)), using SHELXL 92[14] program. The hydrogen atoms, located on a difference map, were all refined isotropically. Atomic scattering factors were taken from ref. 15. The final atomic fractional coordinates are given in Table 1 for both complexes (1) and (2).

All calculations were performed on the GOULD 6040 Powernode and ENCORE 91 computers of the Centro di Studio per la Strutturistica Diffrattometrica del C.N.R. (Parma), using the PARST[16] program for the geometrical description of the structures and ORTEP[17] and PLUTO[18] for the structure drawings.

Table 1. Atomic Fractional Co-ordinates ($x10^4$) for Non-hydrogen Atoms.

Atom	X/a (1)	Y/b (1)	Z/c (1)	X/a (2)	Y/b (2)	Z/c (2)
Cu	-0.23441(2)	0.00000(0)	-0.72254(4)	0.19681(2)	0.42211(9)	0.83002(5)
N(1A)	-0.2404(2)	0.2581(5)	-0.6923(3)	0.2016(1)	0.1710(5)	0.8596(3)
N(2A)	-0.2545(1)	-0.0154(6)	-0.5340(2)	0.2148(1)	0.4442(6)	1.0207(3)
O(1A)	-0.2516(1)	0.4807(5)	-0.5432(2)	0.2111(1)	-0.0539(5)	1.0107(2)
C(1A)	-0.2466(2)	0.3176(5)	-0.5783(4)	0.2072(1)	0.1116(6)	0.9751(4)
C(2A)	-0.2458(2)	0.1685(5)	-0.4773(3)	0.2065(1)	0.2593(5)	1.0746(3)
C(3A)	-0.1894(2)	0.1737(6)	-0.4034(4)	0.1590(2)	0.2557(6)	1.1353(4)
C(4A)	-0.1358(2)	0.1648(6)	-0.4836(4)	0.1136(2)	0.2665(7)	1.0459(4)
C(5A)	-0.1109(2)	-0.0028(10)	-0.5113(4)	0.0931(2)	0.4309(11)	1.0117(4)
C(6A)	-0.0607(2)	-0.0072(13)	-0.5800(5)	0.0504(2)	0.4364(13)	0.9313(5)
C(7A)	-0.0353(2)	0.1497(15)	-0.6189(6)	0.0290(2)	0.2754(14)	0.8851(6)
C(8A)	-0.0601(3)	0.3132(12)	-0.5922(6)	0.0500(2)	0.1137(12)	0.9198(6)
C(9A)	-0.1108(2)	0.3255(8)	-0.5264(5)	0.0925(2)	0.1076(8)	0.9964(6)
C(10A)	-0.3128(2)	-0.0885(6)	-0.5105(4)	0.2648(1)	0.5127(6)	1.0516(4)
C(11A)	-0.3585(2)	0.0105(8)	-0.5834(3)	0.3018(1)	0.4099(8)	0.9866(3)
C(12A)	-0.4179(2)	-0.0575(6)	-0.5525(4)	0.3530(2)	0.4795(6)	1.0188(4)
C(13A)	-0.4644(2)	0.0266(7)	-0.6357(4)	0.3888(1)	0.3921(7)	0.9386(3)
C(14A)	-0.5242(2)	-0.0471(6)	-0.6100(4)	0.4397(1)	0.4688(6)	0.9590(4)
C(15A)	-0.5680(2)	0.0297(7)	-0.6999(4)	0.4736(1)	0.3905(7)	0.8713(4)
C(16A)	-0.6276(2)	-0.0504(7)	-0.6809(4)	0.5238(2)	0.4692(6)	0.8874(4)
C(17A)	-0.6707(2)	0.0228(10)	-0.7751(5)	0.5578(1)	0.3905(7)	0.7978(4)
C(18A)				0.6084(2)	0.4686(6)	0.8134(4)
C(19A)				0.6418(2)	0.3923(7)	0.7228(4)
C(20A)				0.6918(2)	0.4729(7)	0.7361(4)
C(21A)				0.7244(2)	0.3993(11)	0.6441(5)
O(1B)	-0.2104(1)	-0.4692(4)	-0.9074(3)	0.1764(1)	0.8940(5)	0.6420(3)
N(1B)	-0.2298(2)	-0.2522(5)	-0.7564(3)	0.1928(2)	0.6793(5)	0.7954(4)
N(2B)	-0.2138(1)	0.0262(5)	-0.9119(3)	0.1791(1)	0.4012(6)	0.6392(3)
C(1B)	-0.2130(2)	-0.3065(6)	-0.8665(4)	0.1781(2)	0.7322(6)	0.6820(4)
C(2B)	-0.1897(2)	-0.1526(5)	-0.9514(3)	0.1590(1)	0.5789(6)	0.5953(4)
C(3B)	-0.1242(2)	-0.1506(6)	-0.9342(4)	0.1040(2)	0.5772(7)	0.5959(4)
C(4B)	-0.0944(1)	0.0012(9)	-1.0084(3)	0.0790(1)	0.4313(10)	0.5140(3)
C(5B)	-0.0844(2)	-0.0183(10)	-1.1365(4)	0.0724(2)	0.4511(10)	0.3844(4)
C(6B)	-0.0558(2)	0.1210(12)	-1.2019(5)	0.0481(2)	0.3154(12)	0.3125(5)
C(7B)	-0.0370(2)	0.2717(10)	-1.1395(6)	0.0321(2)	0.1601(12)	0.3665(6)
C(8B)	-0.0478(2)	0.2939(9)	-1.0143(6)	0.0396(2)	0.1344(9)	0.4923(6)
C(9B)	-0.0763(2)	0.1587(8)	-0.9481(4)	0.0628(2)	0.2719(8)	0.5650(4)
C(10B)	-0.2618(2)	0.0895(6)	-0.9934(4)	0.2191(2)	0.3344(6)	0.5682(4)
C(11B)	-0.3158(2)	-0.0240(7)	-0.9785(4)	0.2648(1)	0.4465(7)	0.5874(3)
C(12B)	-0.3619(2)	0.0452(6)	-1.0676(4)	0.3025(2)	0.3756(6)	0.5061(4)
C(13B)	-0.4201(2)	-0.0419(6)	-1.0473(4)	0.3514(2)	0.4657(6)	0.5271(4)
C(14B)	-0.4651(2)	0.0294(7)	-1.1361(4)	0.3869(1)	0.3929(7)	0.4400(4)
C(15B)	-0.5248(2)	-0.0421(6)	-1.1153(4)	0.4375(1)	0.4744(6)	0.4580(4)
C(16B)	-0.5684(2)	0.0337(7)	-1.2060(4)	0.4714(1)	0.3955(7)	0.3696(4)
C(17B)	-0.6283(2)	-0.0339(11)	-1.1875(5)	0.5219(2)	0.4731(6)	0.3867(4)
C(18B)				0.5551(1)	0.3920(7)	0.2967(4)
C(19B)				0.6064(2)	0.4651(6)	0.3107(4)
C(20B)				0.6384(2)	0.3833(7)	0.2186(4)
C(21B)				0.6895(2)	0.4532(10)	0.2309(5)
O(1W)	-0.1737(2)	-0.5283(7)	-0.1436(3)	0.1466(1)	0.9510(7)	0.3956(3)
O(2W)	-0.1988(2)	-0.3064(5)	-0.3632(3)	0.1685(1)	0.7350(5)	1.1790(3)

RESULTS AND DISCUSSION

Synthesis of the ligands and of the copper(II) complexes (1) and (2). The synthesis of the ligands was achieved in good yields by reductive alkylation of (S)–phenylalaninamide with *n*–octanal and *n*–dodecanal and hydrogen with Pd/C 10% as catalyst in MeOH, and subsequent treatment with HCl/MeOH. By dissolving the hydrochlorides and copper(II) acetate (2/1 molar ratio) in MeOH/H_2O=9/1, blue solutions were obtained that turned to deep red–violet when the pH was adjusted to 9 by dropwise addition of NaOH (1 M). This is due to the formation of the CuL_2H_{-2} neutral species (**1**) and (**2**), that have a red–violet colour and absorb at λ=491 nm and λ=500 nm, respectively, in agreement with a N_4 coordination sphere, as in the case of the previously studied amino acid amides.[9,10] After standing 24–48 h at room temperature, red–violet needle–shaped crystals were obtained.

X–ray crystallography and description of the structures. For both complexes the structure consists of discrete molecular units (Fig. 1). The Cu(II) ion has an approximate square planar environment involving the four nitrogen atoms from two octyl– and dodecylphenylalaninamidato molecules which are *trans* to each other. The benzyl groups are on the same side with respect to the coordination plane, as it has been found so far only in [Cu(Phe–$NH)_2$], [Cu(MePhe–$NH)_2$]·H_2O, [Cu(Me_2Phe–$NH)_2(OH_2)$][7] and in [Cu(N–Bz–L–Pro)$_2$].[19] One of the phenyl rings is bent towards the coordination plane and it weakly interacts with the copper atom, the other ring stretches out away. The corresponding conformational angles for the complexes (**1**) and (**2**), are, respectively: N(2A)C(2A)C(3A)C(4A) = 69.3(4)°, 69.5(4)°; N(2B)C(2B)C(3B)C(4B) = –58.4(4)°, –59.6(5)°. In both complexes the two chains are situated on the same side with respect to the plane of the nitrogen atoms, in contrast with what reported for copper complexes of N–alkyl–β–alaninates in which the chains were assumed to be on the opposite sides, on the basis of X–ray diffraction patterns obtained by the powder method.[20] The latter situation is observed also for other N–alkyl substituted ligands.[21,22]

In both complexes (**1**) and (**2**), the copper ion lies on the coordination plane as found for the unmodified [Cu(Phe–$NH)_2$] and the chain length does not affect the system planarity. This is confirmed by the fact that the N(1A)–Cu–N(1B) and N(2A)–Cu–N(2B) angles for the octyl– and dodecyl–derivatives are 178.4(2), 177.8(1) and 178.4(2), 179.6(1)°, respectively. In [Cu(Phe–$NH)_2$] the corresponding angles are 175.6(2) and 174.3(2)°, whereas in [Cu(MePhe–$NH)_2$], where the distance of the copper atom from the coordination plane is 0.135(1) Å, they are 178.2(3) and 165.5(2)°. The smaller value between the amino nitrogen atoms was justified in the latter case with the steric hindrance of the methyl groups. The lengthening of the alkyl chains in (**1**) and (**2**) determines a better planarity of the coordination plane, probably because the copper–carbon chain interactions (Cu···C(11A) = 3.271(4), Cu···C(11B) = 3.324(4) and Cu···C(11A) = 3.244(4), Cu···C(11B) = 3.386(4) Å, respectively) compensate the longer interactions (Cu···C(4A) = 3.636(4), Cu···C(5A) = 3.664(5) Å for (**1**) and Cu···C(4A) = 3.636(4), Cu···C(5A) = 3.664(5) Å for (**2**)) between copper and phenyl rings.

The two aliphatic chains are in the axial positions, the torsion angles are: C(10A)N(2A)C(2A)C(1A) = –105.2(4), –102.4(4)° for (**1**) and C(10B)N(2B)C(2B)C(1B) = –100.7(4), –102.2(4)° for (**2**). The absolute configurations of the structures were established in the early stages of the refinement by assigning the (S)–configuration to the phenylalaninamide ligand. In both complexes a new stereogenic centre is formed on the amino nitrogen: the absolute configuration of N(2A) and N(2B) atoms is (R). The Cu–N distances in the two complexes correspond to those expected, the longest being observed for the amino groups and the shortest for

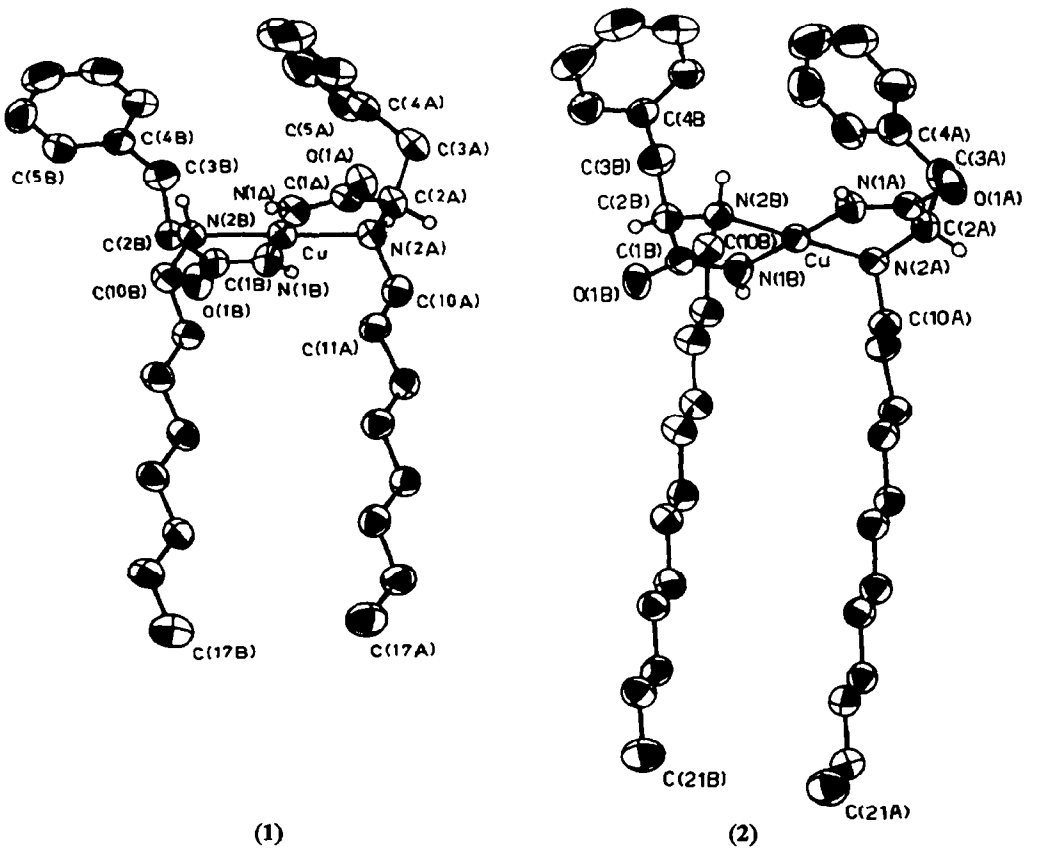


Fig. 1. X-ray molecular structure of $[Cu(NocPhe-NH)_2]\cdot 2H_2O$ (1) and $[Cu(NdoPhe-NH)_2]\cdot 2H_2O$ (2).

the amidates (Cu–N(1A) = 1.917(4), Cu–N(2A) = 2.059(3), Cu–N(1B) = 1.879(3) and Cu–N(2B) = 2.076(3) Å for (1); Cu–N(1A) = 1.874(4), Cu–N(2A) = 2.081(3), Cu–N(1B) = 1.926(4) and Cu–N(2B) = 2.080(3) Å for (2)).[23] The other bond lengths are in good agreement with the literature values.[7,8] In both complexes, the five membered chelate ring on the side of the benzyl group which is bent towards the copper atom shows an envelope conformation [q_2 = 0.212(3), 0.226(3) Å; ϕ_2 = −75(1), −76.0(9)°], while the one on the other side has a twist conformation [q_2 = 0.260(3), 0.254(4) Å; ϕ_2 = −85.8(8), −85.0(9)°].

Projection of the structure of (1) along the *b* axis is presented in Fig. 2. The molecules are arranged in chains with the octyl groups oriented nearly parallel to the *a* axis to give layers of phenyl rings and polar groups [(100) planes] alternated to aliphatic chains [(200) planes]. The alkyl chains inter-penetrate one another by turn, assuming a multibilayer tail-to-tail and head-to-head structure, as shown in Fig. 2. The packing of compound (2) is similar. The lattice is characterized by Cu–Cu distances of 12.52 and 14.26 Å for (1) and 13.05 and 17.37 Å for (2). Thus, the layer-to-layer distances and, in particular, the thickness of the bilayer are affected by the hydrocarbon chain length. Therefore, it is possible to control or to modify the properties of the solid system by simply modulating the chemical features of every single component.

In both complexes the packing along the *z* axis is determined by the hydrogen bonds of the ligands with two water molecules [$O(2)_w \cdots O(1)_w$ = 2.898(5), $O(2)_w \cdots O(1A)$(x, y−1, z) = 2.755(5), $O(1)_w \cdots O(1B)$(x, y, z+1) = 2.687(4) Å for (1); $O(1)_w \cdots O(1B)$ = 2.746(4), $N(2A) \cdots O(2)_w$ = 3.094(5), $O(2)_w \cdots O(1A)$(x, y+1, z) = 2.745(5), $O(2)_w \cdots O(1)_w$(x, y, z+1) = 2.940(5) Å for (2)]. This particular structure is typical of molecular laminates, crystalline solids with alternating layers of metal and hydrocarbon as observed for copper(II) complexes with pyridine or phenantroline derivatives.[24] The hydrophobic interactions between the hydrocarbon chains produce a bilayer structure typical of various long chain compounds.[25,26,27,28] The peculiarity of this kind of compounds is to present layered arrays with polar and apolar alternating zones.

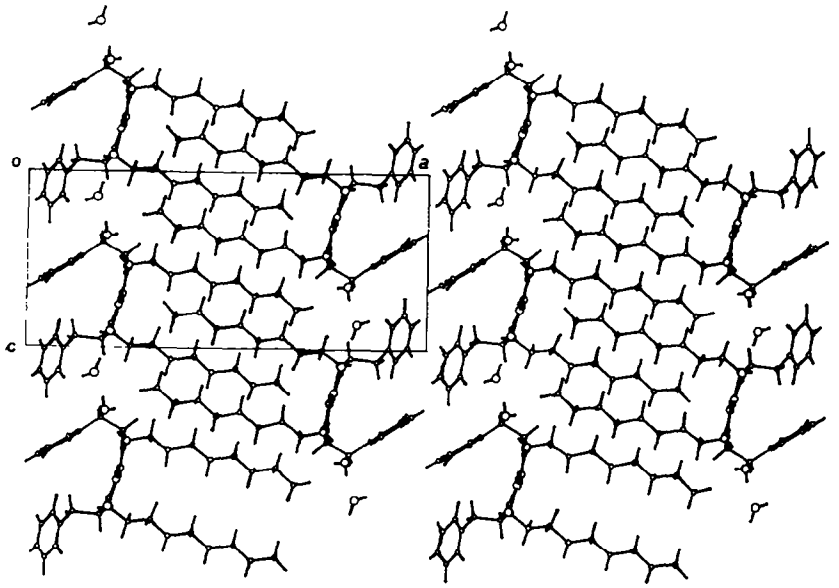


Fig. 2. The packing arrangement of (1) on the (010) plane.

The structures of the complexes (1) and (2) resemble those of compounds that are known to form columnar mesophases.[29] However, at the polarizing microscope analysis (with a variable-temperature unit) these compounds do not appear to be mesogenic. Probably, the presence of the benzyl rings and the stereochemistry of the amino nitrogen (tetrahedrical) are unfavourable to the interconversion to the discotic state. These molecular assemblies may intercalate well with the C_{18} chains of the chromatographic column and lead to asymmetrically modified surfaces for chiral recognition.

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