A C T A U N I V E R S I T A T I S L O D Z I E N S I S
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THE MOLECULAR AND CRYSTAL STRUCTURE OF BENZYLOXYCARBONYL--L,D-PHENYLALANYL-(α,β dehydro)PHENYLALANINE (1)****

$C_{26}H_{24}N_2O_5$, M = 444.49, triclinic, $P\bar{1}$, a = 6.429(4)A, b = 13.225(9)A, c = 14.126(13)A, α= 104.68(7)°, β= 94.44(7)°, γ = 96.49(5)°, V = 1147(2) A^3, Z = 2, D_x = 1.287 gcm^{-3}, μ = = 6.50 cm^{-1}. Diffractometer data, room temperature, λ(CuKα) = = 1.54178 A, F(000) = 468, R = 0.0459 for 3715 reflections with $I > 3\sigma(I)$, max Δ/σ < 1.421 for both positional and thermal parameters.

The molecule has an extended conformation: the angles φ,ψ for L-Phe are -89.5(2)°, 114. 1(1)° respectively; the peptide bond exists in a trans form : ω = -179.8(1)°. The χ1 value = = 3.4(3)° for (α,β -dehydro)Phe indicates a cis conformation of this amino acid with respect to the peptide bond.

Introduction

The title compound (1) was obtained by W a s i a k, K o z i o ł-k i e w i c z (1983) [1], as an intermediate to synthesis of the analogs of the neuropeptide Substance P. The present structural

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work on [1] has been undertaken to determine the structure of (α, β-dehydro)phenylalanine (ΔPhe) and the structure of dipeptide of this amino acid with its natural precursor.

Experimental

Colourless, needle-shaped crystals were obtained from ethanol. Cell parameters and intensity data measured on Enraf Nonius CAD-4 diffractometer. Orientation matrix from 25 carefully centered reflexions with θ-range: 10^{o}-56.4^{o}; graphite monochromatized CuKα, ω/2θ scan; the range of h, k and l: -7 to 7, -16 to 16, -17 to 17 respectively; total 4760 reflexions measured to $\sin\theta/\lambda = 0.63$, data not corrected for absorption (controls: orientation matrix and intensity $4\bar{1}2$ ($\sigma(I_{control})/I_{control} = 0.015$). 3714 reflexions with $I > 3\sigma(I)$ used in refinement. Structure solved by direct methods #SHELX 76 [2] and refined on F by full-matrix least-squares; atomic scattering factors from #SHELX76 [2]. After initial anisotropic refinement a difference Fourier synthesis at R = 0.084 revealed positions of all hydrogen atoms. In subsequent cycles of refinement H atoms allowed to refine isotropically; max and min Δρ in final difference map are 0.17 and - 0.18 eA^{-3} respectively. Final R = 0.0459, S = 0.464, unit weights. Torsion angles were calculated by #FFE3 [3].

Discussion

It is difficult to classify the conformation of the backbone of benzyloxycarbonyl-L,D-Phe-ΔPhe due to only one proper peptide bond in the molecule. However, the torsion angles φ,ψ for L-Phe: -89.5(2), $114.1(1)^{o}$ lie on the φ -ψ Ramachandran diagram [4] within an allowed region for β-structure, indicating rather extended conformation of the backbone around Cα(C9) of this amino acid. These values can be compared, for example, with those of the angles for Phe in Gly-L--Phe-Gly: -119^{o}, 113^{o} [5] or in N-(Haloacetyl)-L-Phe-L-Phe-ethyl esters: $-102^{o}(-100)^{o}$, $106^{o}(110)^{o}$ [6].

The atoms forming the peptide bond (C9, C7, N6, C2) are in a trans configuration, the torsion angle ω about this bond being $-179.8(1)^{o}$. The mentioned peptide group and O8 and H106 atoms from this peptide bond are co-planar, the max. distance from the best plane through these atoms is 0.02(3) A. The amide bond between benzyloxycarbonyl- and - Phe exists in a trans configuration: torsion angle C9-N11-C12-O14 = $171.5(1)^{o}$. The $\chi 1$, $\chi 2$ angles (N11-C9-C10--C30, C9-C10-C30-C31) for L-Phe are $-177.7(2)^{o}$,$79.7(3)^{o}$; it means that C30(C_{γ}) atom is in -ap(trans) position to N11(N) atom, and

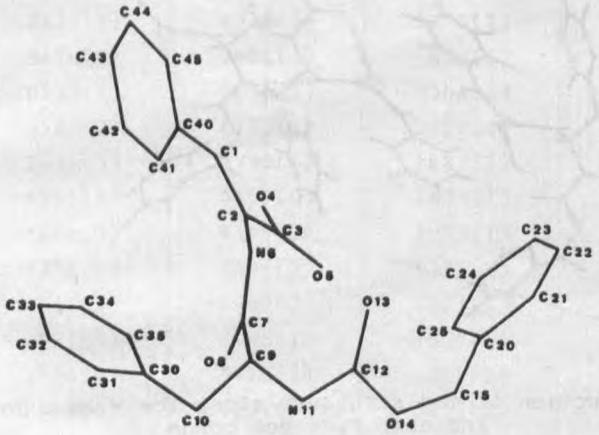

Fig. 1. The atom numbering scheme

C31($C\delta 1$) is in +sc(+g) conformation with respect to C9($C\alpha$) atom. This conformation of the L-Phe side chain, predominant in solution [7], was found, among others, in 31% of cases for Phe, Trp, Tyr in 19 analyzed protein structures: $\chi 1,\chi 2 = 184^{o},76^{o}$ (the data are averaged for Phe, Trp, Tyr)[8]. The $\chi 2 = 79(3)^{o}$ value indicates, that the phenyl ring of Phe is trying to achieve perpendicular arrangement to C9($C\alpha$)-C10($C\beta$)-C30(C_{γ}) plane, resulting in minimum steric hindrance between the α- and δ - carbon atoms.

In ΔPhe: $\chi 1$, $\chi 2$ = 3.4(3)°,-164.2(2)°. The $\chi 1$ value, indicating a +sp(cis) position of C40(Cγ) atom, is not suprising, contrary to $\chi 2$, whose value is rather rare in peptides and proteins [8]. Several systems of π conjugated bonds in ΔPhe cause shortening of the single bonds in this amino acid (see Table 2).

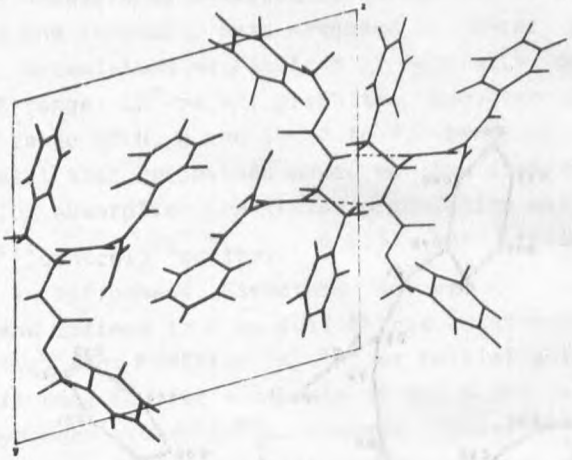

Fig. 2. A projection of the structure along the x axis. Dotted lines indicate hydrogen bonds

Each molecule of (1) participates in three hydrogen bonds. The O4 and H105(O5) atoms from the free carboxyl terminal group of one molecule are interacting with the H106(N6) and O13 atoms from a neighbouring molecule: O13..H105 = 1.78(3) A, O13..H105-O5 = 167(3)°, O.4..H106 = 2.25(2) A, O4..H106-N6 = 162(2)°. Two molecules related by a centre of inversion form a hydrogen bond between H111(N11) and O8 with a distance of H111..O8 = 2.12 A and an angle O8..H111-N11 = = 165(2)°.

The Tables (1-4) in this paper are for molecule with L-isomer of phenylalanine.

Table 1

Final fractional coordinates ($\times 10^4$) and isotropic temperature factors ($\times 10^4$) with e.s.d.'s in parentheses

$$U_{eq} = 1/3 \sum\sum U_{ij} a_i^* a_j^* (\bar{a}_i, \bar{a}_j)$$

Atoms	x	y	z	U_{eq} [A^2]
1	2	3	4	5
N11	2993(3)	5719(1)	833(1)	417(7)
N6	4952(2)	4789(1)	2671(1)	400(7)
O8	6255(2)	4435(1)	1200(1)	478(7)
O13	2185(2)	6920(1)	2174(1)	540(7)
O14	3474(2)	7406(1)	893(1)	518(7)
O4	10533(2)	5054(1)	3304(1)	606(8)
O5	8588(2)	6103(1)	2725(1)	551(7)
C9	2681(3)	4799(1)	1212(1)	397(8)
C7	4795(3)	4657(1)	1692(1)	382(7)
C1	6888(3)	4149(2)	3899(1)	471(9)
C15	3351(4)	8494(2)	1375(2)	604(12)
C2	6818(3)	4687(2)	3223(1)	416(8)
C12	2831(3)	6688(1)	1367(1)	419(8)
C10	1816(4)	3816(2)	382(2)	487(10)
C3	8828(3)	5287(2)	3083(1)	455(9)
C20	5114(4)	8966(2)	2186(2)	577(11)
C21	4903(6)	9880(2)	2870(3)	917(18)
C22	6558(9)	10353(3)	3614(3)	1191(24)
C23	8354(7)	9901(3)	3663(3)	1057(22)
C24	8569(5)	8990(3)	2991(2)	819(16)
C25	6960(4)	8527(2)	2246(2)	667(13)
C30	1373(3)	2838(1)	736(2)	476(9)
C31	-461(4)	2652(2)	1163(2)	608(12)
C32	-886(5)	1737(2)	1465(2)	753(15)
C33	505(5)	1012(2)	1354(3)	859(17)
C34	2352(5)	1207(2)	961(3)	934(18)
C35	2779(4)	2109(2)	652(2)	695(14)
C40	5226(3)	3502(2)	4225(2)	464(9)

Table 1 (contd)

1	2	3	4	5
C41	5686(4)	3256(2)	5114(2)	559(10)
C42	4201(5)	2679(2)	5494(2)	687(13)
C43	2242(5)	2338(2)	4493(2)	741(14)
C44	1754(4)	2542(2)	4103(2)	741(14)
C45	3232(4)	3119(2)	3713(2)	623(12)
H109	1703(30)	4939(15)	1709(14)	442(53)
H115	3390(35)	8829(18)	801(17)	682(70)
H101	8268(34)	4196(16)	4224(16)	561(64)
H210	2829(38)	3705(18)	-122(18)	682(73)
H215	1981(39)	8575(19)	1613(18)	741(77)
H111	3439(35)	5681(18)	308(17)	537(70)
H110	538(36)	3966(17)	64(16)	600(65)
H106	3912(37)	4937(18)	2959(17)	609(73)
H145	2799(37)	3267(18)	3071(18)	695(74)
H144	361(45)	2270(22)	3704(20)	902(92)
H141	6955(39)	3490(19)	5476(18)	695(79)
H131	-1480(39)	3169(20)	1235(18)	751(78)
H143	1345(45)	1877(23)	5221(21)	901(97)
H125	7087(44)	7825(23)	1701(21)	1001(95)
H133	230(43)	363(23)	1542(20)	949(91)
H142	4654(44)	2513(22)	6080(21)	902(95)
H134	3390(57)	613(29)	779(26)	1431(134)
H122	6093(61)	10993(32)	4111(30)	1573(152)
H135	4120(50)	2252(25)	341(23)	1214(115)
H123	9454(55)	10219(27)	4200(26)	1243(123)
H105	9961(57)	6313(28)	2579(26)	1369(138)
H132	-2074(44)	1632(22)	1735(20)	830(95)
H121	3529(55)	10181(27)	2907(26)	1242(139)
H124	9988(56)	8669(27)	3122(26)	1299(135)

Table 2

Bond lengths [A]

C1	C40	1.467(3)	C1	C2	1.329(3)
C2	C3	1.492(3)	C2	N6	1.418(2)
C3	O4	1.211(2)	C3	O5	1.320(2)
C7	C9	1.524(2)	C7	N6	1.343(2)
C7	O8	1.229(2)	C9	C10	1.529(3)
C9	N11	1.450(2)	C10	C30	1.507(3)
C12	N11	1.332(2)	C12	O13	1.222(2)
C12	O14	1.340(2)	C15	O14	1.441(2)
C15	C20	1.504(3)	C20	C21	1.371(3)
C20	C25	1.385(3)	C21	C22	1.404(5)
C22	C23	1.364(6)	C23	C24	1.359(5)
C24	C25	1.383(4)	C30	C31	1.391(3)
C30	C35	1.384(3)	C31	C32	1.387(4)
C32	C33	1.373(4)	C33	C34	1.375(5)
C34	C35	1.377(4)	C40	C41	1.394(3)
C40	C45	1.395(3)	C41	C42	1.380(4)
C42	C43	1.364(4)	C43	C44	1.372(4)
C44	C45	1.386(4)			

Table 3

Bond angles [°]

C2	C1	C40	131.3(2)	C3	C2	C1	117.6(2)
C3	C2	N6	117.6(2)	C1	C2	N6	124.7(2)
C2	C3	O4	122.2(2)	C2	C3	O5	114.5(2)
O4	C3	O5	123.3(2)	C9	C7	N6	116.2(2)
C9	C7	O8	121.1(2)	N6	C7	O8	122.8(2)
C7	C9	C10	110.0(2)	C7	C9	N11	108.2(1)
C10	C9	N11	110.6(2)	C9	C10	C30	113.1(2)
N11	C12	O13	126.4(2)	N11	C12	O14	110.5(2)
O13	C12	O14	123.1(2)	O14	C15	C20	112.6(2)
C7	N6	C2	122.8(2)	C9	N11	C12	122.8(2)
C12	O14	C15	116.9(2)	C15	C20	C21	118.5(2)
C15	C20	C25	122.3(2)	C21	C20	C25	119.1(2)

Table 3 (contd)

C20	C21	C22	119.5(3)	C21	C22	C23	120.3(3)
C22	C23	C24	120.5(3)	C23	C24	C25	119.6(3)
C24	C25	C20	121.0(2)	C10	C30	C31	120.5(2)
C10	C30	C35	121.1(2)	C31	C30	C35	118.4(2)
C30	C31	C32	120.2(2)	C31	C32	C33	120.5(3)
C32	C33	C34	119.6(3)	C33	C34	C35	120.3(3)
C34	C35	C30	120.9(3)	C1	C40	C41	117.2(2)
C1	C40	C45	124.9(2)	C41	C40	C45	117.9(2)
C40	C41	C42	121.3(2)	C41	C42	C43	119.7(2)
C42	C43	C44	120.6(3)	C43	C44	C45	120.2(2)
C44	C45	C40	120.3(2)				

T a b l e 4

Torsion angles [°]

Atoms				Angle
1				2
C22	C21	C20	C15	-177.9(3)
C24	C25	C20	C15	178.8(3)
C21	C20	C15	O14	-162.8(3)
C25	C20	C15	O14	19.2(4)
C20	C15	O14	C12	77.7(3)
C15	O14	C12	N11	178.9(2)
C15	O14	C12	O13	-0.8(3)
O14	C12	N11	C9	171.5(1)
C12	N11	C9	C10	149.9(2)
C12	N11	C9	C7	-85.5(2)
O13	C12	N11	C9	-8.9(3)
N11	C9	C10	C30	-177.7(2)
N11	C9	C7	N6	114.1(1)
N11	C9	C7	O8	-65.9(2)
C9	C10	C30	C31	79.7(2)
C9	C10	C30	C35	-99.8(3)
C9	C7	N6	C2	-179.8(1)
C10	C30	C31	C32	178.4(2)
C10	C30	C35	C34	-178.9(3)
C10	C9	C7	N6	-124.9(2)

Table 4 (contd)

1				2
O8	C7	N6	C2	0.2(2)
O8	C7	C9	C10	55.1(2)
C7	N6	C2	C1	-133.7(2)
C7	N6	C2	C3	50.7(2)
C7	C9	C10	C30	62.8(2)
N6	C2	C1	C40	3.4(3)
N6	C2	C3	O4	-160.2(1)
N6	C2	C3	O5	21.5(2)
C2	C1	C40	C41	-164.2(2)
C2	C1	C40	C45	15.8(4)
C3	C2	C1	C40	179.0(2)
O4	C3	C2	C1	23.8(2)
O5	C3	C2	C1	-154.5(2)
C1	C40	C41	C42	178.0(2)
C1	C40	C45	C44	-177.9(2)
H106	N6	C2	C1	-47(2)
H106	N6	C2	C3	129(2)
H106	N6	C7	C9	1(2)
H106	N6	C7	O8	-179(2)
C2	C3	O4	$H106^{1}$	-146(1)
O5	C3	O4	$H106^{1}$	36(1)
C3	O4	$H106^{1}$	$N6^{1}$	58(7)
O4	$H106^{1}$	$N6^{1}$	$C2^{1}$	148(6)
O4	$H106^{1}$	$N6^{1}$	$C7^{1}$	-33(7)
H111	N11	C12	O13	-179(2)
H111	N11	C12	O14	1(2)
H111	N11	C9	C10	39(2)
H111	N11	C9	C7	-82(2)
C9	C7	O8	$H111^{2}$	-6(1)
N6	C7	O8	$H111^{2}$	174(1)
C7	O8	$H111^{2}$	$N11^{2}$	-159(7)
O8	$H111^{2}$	$N11^{2}$	$C12^{2}$	-94(8)
O8	$H111^{2}$	$N11^{2}$	$C9^{2}$	94(8)
H105	O5	C3	O4	-10(2)

Table 4 (contd)

1				2
H105	O5	C3	C2	172(2)
N11	C2	O13	H105[3]	45(1)
O14	C12	O13	H105[3]	-134(1)
C12	O13	H105[3]	O5[3]	73(12)
O13	H105[3]	O5[3]	C3[3]	-161(11)

Symmetry related atoms:

[1] x' = x - 1, y' = y, z' = z

[2] x' = 1 - x, y' = 1 - y, z' = 2 - z

[3] x' = x + 1, y' = y, z' = z

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STRUKTURA KRYSZTAŁÓW I CZĄSTECZKI BENZYLOKARBONYLO-L,D--FENYLOALANYLO-(α,β dehydro) FENYLOALANINY (1)

$C_{26}H_{24}N_2O_5$, M_{cz} = 444.49, układ trójskośny, PĪ a = 6.429(4), b = 13.225(9), c = 14.126(13) A, α = 104.68(7), β = 94.44(7), γ = 96.49(5)°, V = 1147(2) A^3, Z = 2, D_x = 1.287 gcm^{-3}, μ = 6.50 cm^{-1}. Dane dyfraktometryczne, temperatura pokojowa, λ(CuKα) = 1.54178 A, F(000) = 468, R = 0.0459 dla 3715 refleksów z kryterium obserwowalności $I > 3\sigma(I)$, max $\Delta/\sigma < 1.421$ dla parametrów pozycyjnych i temperaturowych.

Molekuła znajduje się w konformacji rozciągniętej: kąty Ø,Ψ dla L-Fen przyjmują wartości -89.5(2)° i 114.1(1)°. Wiązanie peptydowe tworzy formę trans: ω = -179.8(1)°. Wartość χ1 = 3.4(3)° dla (α, β-dehydro)Fen wskazuje na konformację cis tego aminokwasu w stosunku do wiązania peptydowego.