2003

Crystal Structure of Boc-Trp(CHO)-DPhe-Ile-DPhe-Leu-OCH3, C48H59N6O10

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Crystal structure of Boc-Trp(CHO)-ΔPhe-Ile-ΔPhe-Leu-OCH_3, $C_{48}H_{59}N_6O_{10}$

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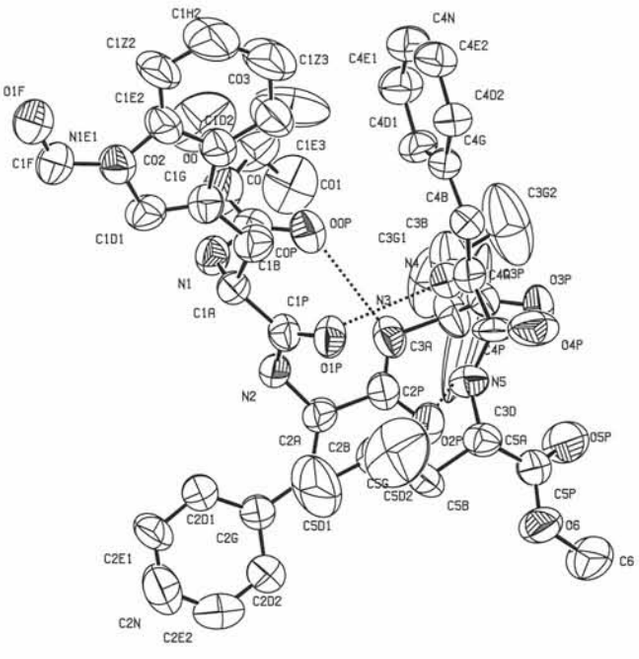
Received November 13, 2002, accepted and available on-line February 3, 2003; CCDC-No. 1267/972



Abstract

$C_{48}H_{59}N_6O_{10}$, orthorhombic, $P2_12_12_1$ (No. 19), a = 19.276(5) Å, b = 19.439(5) Å, c = 13.352(5) Å, V = 5003.1 Å^3, Z = 4, $R_{gt}(F)$ = 0.077, $wR_{ref}(F^2)$ = 0.230, T = 293 K.

Source of material

The title peptide has been synthesised using the mixed anhydride coupling and the azalactone method according to [1] and [2] respectively. The peptide was crystallised from its solution in acetone-water mixture (4:1) by slow evaporation method.

Experimental details

The ratio $N(hkl)_{obs}/N(param)$ is relative low (4.8) which is a result of the relative low crystal quality. The side chains of Ile and Leu are thermally disordered. The atoms C3D and C5D1 were refined isotropically.

Discussion

The specific folded structures can be generated with α,β-dehydro-residues. A set of design rules have been developed with dehydro-residues [3]. However, there have been still some gaps in finalizing some of these rules. In order to generalize the design rules, a new pentapeptide sequence was synthesized with two ΔPhe residues at (i+2) and (i+4) positions. The remaining three positions in the pentapeptide are filled with high constraint generating residues such as Trp, Ile and Leu. This is the first sequence with Trp at (i+1) position and two ΔPhe residues are seperated by a branched β-carbon residue Ile. In the peptide Boc-Trp(CHO)-ΔPhe-Ile-ΔPhe-Leu-OCH_3 the backbone torsion angles φ_1 = –52.3(8)°, ψ_1 = –49.1(7)°, ω_1 = –177.5(6)°, φ_2 = –56.5(8)°, ψ_2 = –31.4(9)°, ω_2 = 179.7(6)°, φ_3 = –69.8(8)°, ψ_3 = –31.3(9)°, ω_3 = 169.9(6)°, φ_4 = –60.3(8)°, ψ_4 = –28.4(9)°, ω_4 = –177.0(6)°, φ_5 = –90.2(8)°, ψ_5^T = 13(1)° indicate that the peptide adopts a 3_{10}-helical conformation. The structure is stabilized by three N(i+3) → O=C(i) hydrogen bonds. The side chain torsion angles of ΔPhe_2 and ΔPhe_4 are χ_2^1 = –8(1)°, $\chi_2^{2,1}$ = –175(1)°, $\chi_2^{2,2}$ = 3(1)° and χ_4^1 = –3(1)°, $\chi_4^{2,1}$ = –175.8(7)°, $\chi_4^{2,2}$ = 1(1)° respectively and indicate that the side chain conformation of two ΔPhe residues are planar. The side chain conformation of sand-witched branched β-carbon residue Ile is found to be favourably staggered to the backbone with torsion angles $\chi_3^{1,1}$ = –67.7(9)°, $\chi_3^{1,2}$ = 167(1)°, χ_3^2 = –64(2)°. It is noteworthy that the side chain conformation of isoleucine in the structure of Boc-Leu-ΔPhe-Ile-ΔPhe-Ile-OCH_3 [4] was not observed in the staggered arrangement thus causing considerable deviations from the planarity in the side chains of neighbouring ΔPhe residues. The side chain conformation of the leucyl residue with torsion angles χ_5^1 = –64.7(8)°, $\chi_5^{2,1}$ = 165(1)° and $\chi_5^{2,2}$ = –61(1)° is one of the most commonly observed conformations for the side chain of leucine [2]. Overall, the 3_{10}-helical conformation of the present peptide has all the side chains favourably aligned. Therefore, it can be stated that the structures of peptides with two ΔPhe residues at alternate positions will always result in the formation of a 3_{10}-helical conformation. In the crystal structure, the molecules are linked through two intermolecular hydrogen bonds d(N1–H1···O5P) = 2.898(8) Å and d(N2–H2···O7) = 2.98(1) Å.

Table 1. Data collection and handling.

Crystal:	colorless prism, size 0.3 × 0.4 × 0.5 mm
Wavelength:	Cu K_α radiation (1.54180 Å)
μ:	6.74 cm^{-1}
Diffractometer, scan mode:	Enraf Nonius CAD4, $\omega/2\theta$
$2\theta_{max}$:	139.96°
$N(hkl)_{measured}$, $N(hkl)_{unique}$:	4783, 4745
Criterion for I_{obs}, $N(hkl)_{gt}$:	$I_{obs} > 2\ \sigma(I_{obs})$, 2762
$N(param)_{refined}$:	574
Programs:	SHELXS-97 [5] SHELXL-97 [6]

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Table 2. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{iso}
H(01A)	4*a*	0.6143	0.5507	0.7866	0.08
H(01B)	4*a*	0.6128	0.4863	0.7160	0.08
H(01C)	4*a*	0.5598	0.4922	0.8046	0.08
H(02A)	4*a*	0.4558	0.5214	0.5987	0.08
H(02B)	4*a*	0.4640	0.4759	0.6948	0.08
H(02C)	4*a*	0.5158	0.4671	0.6052	0.08
H(03A)	4*a*	0.5377	0.6213	0.5724	0.08
H(03B)	4*a*	0.6024	0.5725	0.5734	0.08
H(03C)	4*a*	0.5976	0.6336	0.6498	0.08
H(1)	4*a*	0.4106	0.6568	0.8400	0.08
H(1A)	4*a*	0.4107	0.7529	0.9246	0.08
H(1BA)	4*a*	0.4742	0.8441	0.8527	0.08
H(1BB)	4*a*	0.5094	0.7918	0.7797	0.08
H(1DA)	4*a*	0.3232	0.7795	0.8054	0.08
H(1ZA)	4*a*	0.3041	0.8808	0.4751	0.08
H(1HA)	4*a*	0.4021	0.9237	0.3971	0.08
H(1EA)	4*a*	0.5228	0.8701	0.6281	0.08
H(1F)	4*a*	–0.0016	–0.0013	0.0032	0.08
H(2)	4*a*	0.4815	0.6609	1.0369	0.08
H(2B)	4*a*	0.5854	0.6882	1.2563	0.08
H(2DB)	4*a*	0.5300	0.6950	1.4076	0.08
H(2DA)	4*a*	0.4084	0.6997	1.1639	0.08
H(2EA)	4*a*	0.3143	0.6983	1.2649	0.08
H(2EB)	4*a*	0.4327	0.7084	1.5029	0.08
H(2NA)	4*a*	0.3241	0.7049	1.4328	0.08
H(3)	4*a*	0.6232	0.6488	0.9664	0.08
H(3A)	4*a*	0.7556	0.6625	1.0267	0.08
H(3B)	4*a*	0.7036	0.6285	0.8343	0.08
H(3GA)	4*a*	0.8149	0.6019	0.7805	0.08
H(3GB)	4*a*	0.8455	0.6326	0.8796	0.08
H(3GC)	4*a*	0.8078	0.6807	0.8028	0.08
H(3GD)	4*a*	0.6891	0.5443	0.9485	0.08
H(3GE)	4*a*	0.7411	0.5201	0.8661	0.08
C(3D)	4*a*	0.784(2)	0.530(2)	1.000(2)	0.27(1)
H(4)	4*a*	0.6558	0.7688	0.8816	0.08
H(4B)	4*a*	0.7024	0.9399	0.7973	0.08
H(4DA)	4*a*	0.6669	0.7643	0.7228	0.08
H(4DB)	4*a*	0.6874	0.9607	0.6354	0.08
H(4EA)	4*a*	0.6474	0.7337	0.5557	0.08
H(4EB)	4*a*	0.6696	0.9298	0.4699	0.08
H(4N)	4*a*	0.6454	0.8158	0.4301	0.08
H(5)	4*a*	0.6686	0.8404	1.0577	0.08
H(5A)	4*a*	0.6994	0.9631	1.1411	0.08
H(5BA)	4*a*	0.6175	0.855	1.2225	0.08
H(5BB)	4*a*	0.6312	0.9239	1.2801	0.08
H(5GA)	4*a*	0.5647	0.918	1.0948	0.08
C(5D1)	4*a*	0.4965(8)	0.9061(9)	1.214(1)	0.176(5)
H(5DD)	4*a*	0.5279	1.0290	1.1213	0.08
H(5DE)	4*a*	0.6091	1.0243	1.1162	0.08
H(5DF)	4*a*	0.5719	1.0322	1.2200	0.08
H(6A)	4*a*	0.8091	0.9142	1.4309	0.08
H(6C)	4*a*	0.8577	0.9154	1.3368	0.08
H(6D)	4*a*	0.8214	0.8467	1.3690	0.08
HW(1)	4*a*	0.054(4)	–0.155(4)	–0.091(6)	0.08
HW(2)	4*a*	–0.035(4)	0.165(3)	0.108(5)	0.08

Table 3. Atomic coordinates and displacement parameters (in Å^2).

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(01)	4*a*	0.5849(6)	0.5174(5)	0.755(1)	0.143(9)	0.096(6)	0.16(1)	0.024(6)	–0.006(8)	0.005(7)
C(02)	4*a*	0.4885(8)	0.4995(6)	0.643(1)	0.20(1)	0.14(1)	0.22(2)	0.07(1)	–0.04(1)	–0.09(1)
C(03)	4*a*	0.5716(9)	0.5993(6)	0.6142(9)	0.33(2)	0.118(8)	0.095(7)	0.06(1)	0.06(1)	–0.010(7)
C(0)	4*a*	0.5355(6)	0.5530(5)	0.6879(8)	0.136(8)	0.083(5)	0.104(7)	0.029(5)	–0.013(6)	–0.034(6)
O(0)	4*a*	0.4854(3)	0.5937(3)	0.7477(5)	0.088(3)	0.090(4)	0.130(5)	0.010(3)	–0.012(4)	–0.039(4)
C(0P)	4*a*	0.5057(4)	0.6463(4)	0.8044(6)	0.067(4)	0.072(4)	0.076(5)	0.006(3)	0.005(4)	–0.001(4)
O(0P)	4*a*	0.5656(2)	0.6657(3)	0.8168(4)	0.062(3)	0.094(3)	0.095(4)	0.004(2)	0.008(3)	0.000(3)
N(1)	4*a*	0.4502(3)	0.6769(3)	0.8434(4)	0.066(3)	0.068(3)	0.081(4)	–0.011(3)	–0.006(3)	–0.007(3)
C(1A)	4*a*	0.4553(3)	0.7441(3)	0.8918(5)	0.053(3)	0.071(4)	0.068(4)	0.004(3)	0.000(3)	0.006(3)
C(1B)	4*a*	0.4669(4)	0.8016(4)	0.8161(5)	0.076(4)	0.072(4)	0.066(4)	–0.003(3)	–0.011(3)	0.012(3)
C(1G)	4*a*	0.4107(3)	0.8132(3)	0.7420(5)	0.066(4)	0.064(4)	0.070(4)	0.001(3)	0.002(3)	0.011(3)
C(1D2)	4*a*	0.4208(4)	0.8445(4)	0.6463(6)	0.064(4)	0.111(6)	0.080(5)	0.005(4)	0.005(4)	0.006(5)
C(1D1)	4*a*	0.3438(4)	0.8008(4)	0.7506(5)	0.075(4)	0.093(5)	0.056(4)	0.007(4)	–0.011(3)	0.011(4)
N(1E1)	4*a*	0.3080(3)	0.8242(3)	0.6651(5)	0.063(3)	0.095(4)	0.074(4)	0.006(3)	0.007(3)	–0.003(3)
C(1E2)	4*a*	0.3574(4)	0.8515(5)	0.6012(6)	0.062(4)	0.125(6)	0.071(5)	0.020(4)	0.011(4)	–0.005(5)
C(1Z2)	4*a*	0.3475(5)	0.8788(7)	0.5054(7)	0.080(5)	0.23(1)	0.065(5)	0.023(7)	0.017(4)	0.049(7)
C(1H2)	4*a*	0.4068(6)	0.902(1)	0.4591(9)	0.114(8)	0.36(2)	0.086(7)	0.06(1)	0.001(7)	0.10(1)
CZ(3)	4*a*	0.4735(7)	0.897(1)	0.4990(9)	0.117(8)	0.36(2)	0.087(8)	0.03(1)	0.026(6)	0.09(1)
C(1E3)	4*a*	0.4798(5)	0.8703(6)	0.5965(7)	0.068(5)	0.19(1)	0.099(7)	0.022(6)	0.022(5)	0.034(7)
C(1F)	4*a*	0.2356(4)	0.8186(6)	0.6552(8)	0.066(5)	0.171(9)	0.099(7)	0.016(5)	–0.012(5)	0.009(7)
O(1F)	4*a*	0.2071(3)	0.8430(4)	0.5816(5)	0.070(3)	0.182(6)	0.107(5)	0.011(3)	–0.013(3)	0.008(5)
C(1P)	4*a*	0.5111(3)	0.7463(4)	0.9730(5)	0.046(3)	0.075(4)	0.084(5)	0.003(3)	–0.001(3)	0.003(4)
O(1P)	4*a*	0.5526(2)	0.7938(2)	0.9796(4)	0.055(2)	0.077(3)	0.095(3)	–0.009(2)	–0.006(2)	0.004(3)
N(2)	4*a*	0.5107(3)	0.6942(3)	1.0412(4)	0.056(3)	0.082(4)	0.059(3)	–0.014(3)	–0.005(2)	0.012(3)
C(2A)	4*a*	0.5602(3)	0.6968(4)	1.1197(5)	0.064(3)	0.075(4)	0.059(4)	–0.010(3)	–0.011(3)	0.016(3)
C(2B)	4*a*	0.5462(3)	0.6938(4)	1.2166(6)	0.060(4)	0.118(6)	0.066(5)	–0.016(4)	–0.010(3)	0.023(4)
C(2G)	4*a*	0.4824(3)	0.6974(5)	1.2734(5)	0.057(3)	0.122(6)	0.066(5)	–0.012(4)	–0.005(3)	0.019(4)
C(2D2)	4*a*	0.4868(5)	0.6983(6)	1.3767(7)	0.077(5)	0.19(1)	0.080(6)	–0.008(6)	–0.003(5)	0.007(7)
C(2D1)	4*a*	0.4144(4)	0.6992(5)	1.2330(6)	0.069(4)	0.166(9)	0.066(5)	–0.009(5)	0.000(4)	0.013(5)
C(2E1)	4*a*	0.3582(4)	0.7000(6)	1.2937(7)	0.063(4)	0.20(1)	0.088(6)	–0.006(5)	0.010(4)	0.031(7)
C(2E2)	4*a*	0.4283(6)	0.7039(6)	1.4338(7)	0.117(8)	0.19(1)	0.063(5)	–0.006(7)	–0.003(5)	–0.015(6)
C(2N)	4*a*	0.3634(5)	0.7032(7)	1.3926(9)	0.090(6)	0.20(1)	0.102(8)	–0.013(7)	0.025(6)	0.021(8)

Table 3. Continued.

Atom	Site	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(2P)	4*a*	0.6349(3)	0.6996(4)	1.0876(6)	0.056(3)	0.096(5)	0.075(5)	–0.009(4)	0.005(3)	0.013(4)
O(2P)	4*a*	0.6783(2)	0.7279(3)	1.1430(4)	0.060(3)	0.143(5)	0.091(4)	–0.022(3)	–0.007(3)	0.017(3)
N(3)	4*a*	0.6532(3)	0.6704(3)	1.0022(5)	0.053(3)	0.077(3)	0.086(4)	–0.004(2)	0.004(3)	0.022(3)
C(3A)	4*a*	0.7265(3)	0.6755(4)	0.9696(7)	0.055(3)	0.088(5)	0.107(6)	0.011(3)	0.015(4)	0.030(5)
C(3B)	4*a*	0.7405(4)	0.6227(5)	0.884(1)	0.069(5)	0.092(6)	0.18(1)	0.010(4)	0.015(6)	–0.029(7)
C(3G2)	4*a*	0.8082(6)	0.6356(7)	0.832(1)	0.14(1)	0.15(1)	0.34(2)	–0.035(8)	0.10(1)	–0.10(1)
C(3G1)	4*a*	0.7356(6)	0.5510(6)	0.923(1)	0.110(8)	0.121(9)	0.26(2)	0.014(6)	–0.04(1)	0.00(1)
C(3P)	4*a*	0.7453(3)	0.7496(4)	0.9410(5)	0.055(3)	0.090(5)	0.067(4)	–0.006(3)	0.012(3)	–0.004(4)
O(3P)	4*a*	0.8036(2)	0.7705(3)	0.9548(4)	0.047(2)	0.106(4)	0.098(3)	–0.009(2)	0.001(2)	0.005(3)
N(4)	4*a*	0.6941(2)	0.7880(3)	0.8993(4)	0.054(3)	0.082(4)	0.057(3)	–0.007(3)	0.002(2)	0.005(3)
C(4A)	4*a*	0.7036(3)	0.8591(4)	0.8848(5)	0.057(3)	0.086(5)	0.061(4)	–0.010(3)	–0.003(3)	0.005(4)
C(4B)	4*a*	0.6957(3)	0.8925(4)	0.7943(5)	0.059(3)	0.088(4)	0.062(4)	–0.001(3)	0.005(3)	–0.004(4)
C(4G)	4*a*	0.6791(3)	0.8672(4)	0.6970(4)	0.058(3)	0.089(5)	0.043(3)	–0.008(3)	–0.002(3)	0.010(3)
C(4D1)	4*a*	0.6670(4)	0.7977(4)	0.6730(5)	0.081(4)	0.088(5)	0.057(4)	–0.011(4)	–0.013(3)	0.009(4)
C(4D2)	4*a*	0.6794(3)	0.9147(4)	0.6201(5)	0.076(4)	0.086(4)	0.055(4)	–0.005(4)	–0.001(3)	0.003(4)
C(4E1)	4*a*	0.6551(4)	0.7796(4)	0.5718(6)	0.102(5)	0.087(5)	0.075(5)	–0.012(4)	0.003(4)	–0.007(4)
C(4E2)	4*a*	0.6681(4)	0.8965(5)	0.5198(6)	0.096(5)	0.096(6)	0.063(5)	–0.010(4)	0.005(4)	0.008(4)
C(4N)	4*a*	0.6546(5)	0.8285(5)	0.4959(6)	0.112(6)	0.112(6)	0.053(4)	–0.003(5)	–0.002(4)	0.018(4)
C(4P)	4*a*	0.7176(4)	0.9023(4)	0.9731(4)	0.097(5)	0.089(5)	0.025(3)	–0.004(4)	0.001(3)	0.006(3)
O(4P)	4*a*	0.7488(4)	0.9568(3)	0.9705(4)	0.169(6)	0.110(4)	0.068(3)	–0.066(4)	0.012(4)	–0.006(3)
N(5)	4*a*	0.6903(3)	0.8790(3)	1.0594(4)	0.080(3)	0.068(3)	0.061(3)	0.000(3)	–0.002(3)	–0.002(3)
C(5A)	4*a*	0.6945(3)	0.9138(4)	1.1548(5)	0.069(4)	0.072(4)	0.054(4)	0.010(3)	0.003(3)	0.003(3)
C(5B)	4*a*	0.6260(3)	0.9038(5)	1.2140(6)	0.067(4)	0.125(6)	0.064(4)	0.013(4)	0.017(3)	0.018(4)
C(5G)	4*a*	0.5646(4)	0.9358(6)	1.1635(7)	0.069(4)	0.155(8)	0.080(5)	0.025(5)	–0.007(4)	–0.022(6)
C(5D2)	4*a*	0.5687(8)	1.0121(7)	1.154(1)	0.17(1)	0.18(1)	0.28(2)	0.10(1)	–0.06(1)	–0.01(1)
C(5P)	4*a*	0.7585(3)	0.8910(4)	1.2078(6)	0.059(4)	0.103(5)	0.057(4)	–0.001(4)	0.002(3)	–0.010(4)
O(5P)	4*a*	0.8053(3)	0.8600(4)	1.1751(5)	0.083(4)	0.180(6)	0.093(4)	0.041(4)	–0.011(3)	–0.034(4)
O(6)	4*a*	0.7582(3)	0.9123(4)	1.3027(4)	0.078(3)	0.173(6)	0.069(4)	0.036(4)	–0.012(3)	–0.025(4)
C(6)	4*a*	0.8164(5)	0.8958(7)	1.3650(7)	0.090(6)	0.18(1)	0.091(6)	0.042(6)	–0.023(5)	–0.004(6)
O(7)	4*a*	0.9009(4)	0.9135(4)	0.9662(8)	0.136(5)	0.168(7)	0.193(8)	0.081(5)	–0.003(6)	0.015(7)

Acknowledgments. The authors thank Council of Scientific and Industrial Research, New Delhi for financial support.

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