Crystal Structures of *N*-(Benzyloxycarbonyl)prolylleucine Ethyl Ester and *N*-(*t*-Butoxycarbonyl)prolylleucine Benzyl Ester

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The molecular structures of *N*-(benzyloxycarbonyl)prolylleucine ethyl ester and *N*-(*t*-butoxycarbonyl)-prolylleucine benzyl ester, were determined by the X-ray method. The former belongs to the orthorhombic system $P2_12_12_1$ with $Z=4$, $a=9.917(3)$, $b=21.960(3)$, and $c=9.956(1)$ Å; the latter belongs to the monoclinic system $P2_1$ with $Z=2$, $a=10.475(1)$, $b=17.910(1)$, $c=6.303(1)$ Å, and $\beta=90.213(7)°$. Both structures were determined by the direct method; the final R indexes are 0.062 for the former and 0.072 for the latter. An extended conformation found in both dipeptides shows that in terms of the Pro–Leu unit alone this conformation is preferable to the folded β-turn conformation such as is found in longer peptides. The leucyl side chain conformations found in peptides or amino acids were also studied. For the residues occurring in the peptides the $C'-C^{\alpha}-C^{\beta}-C^{\gamma}-C^{\delta 1}$ trans-zigzag conformation was found overwhelmingly, without any obvious relationships to the main chain torsion angles. On the other hand, for the C-termini leucyl residues and leucines the $N-C^{\alpha}-C^{\beta}-C^{\gamma}-C^{\delta 2}$ trans-zigzag conformation was rather preferred and the ϕ values were restricted to a narrow range.

Several linear oligopeptides containing the Pro–Leu sequence have been studied by the X-ray method. They are benzyloxycarbonyl(Z)–Gly–Pro–Leu–Gly–Pro,[1] Z(*o*-Br)–Gly–Pro–Leu–Gly–Pro,[2] Z(*p*-Br)–Gly–Pro–Leu–Gly,[3] *t*-butoxycarbonyl(Boc)–Pro–Leu–Gly,[4] *S*-benzyl–Cys–Pro–Leu–Gly–NH_2,[5] Pro–Leu–Gly–NH_2,[6] and Z–Gly–Pro–Leu.[7] All the oligopeptides but the last two have the β-turn of type I[8] with a 4→1 hydrogen bond, in which Pro and Leu residues are located at the second and third sites of the β-turn. On the other hand, the Pro–Leu parts in Pro–Leu–Gly–NH_2 and Z–Gly–Pro–Leu take more extended forms, somewhat similar to the poly(L-proline) II.

In this study, Z–Pro–Leu–OEt(ethyl ester) and Boc–Pro–Leu–OBzl(benzyl ester), which cannot have an intramolecular hydrogen bond of the β-turn, were prepared and their crystal structures were worked out by the X-ray method.

Experimental

Z–Pro–Leu–OEt and Boc–Pro–Leu–OBzl were prepared from the corresponding N-protected proline and the C-protected leucine.

The X-ray diffraction data were collected on a Hilger and

TABLE 1. CRYSTAL AND EXPERIMENTAL DATA

		Z–Pro–Leu–OEt	Boc–Pro–Leu–OBzl
Molecular formula		$C_{21}H_{30}N_2O_5$	$C_{23}H_{34}N_2O_5$
Molecular weight		390.48	418.53
Crystal system		Orthorhombic	Monoclinic
Space group		$P2_12_12_1$	$P2_1$
Z		4	2
Cell dimensions	$a=$	9.917(3) Å	10.475(1) Å
	$b=$	21.960(3)	17.910(1)
	$c=$	9.956(1)	6.303(1)
	$\beta=$	—	90.213(7)°
	$U=$	2168.2 Å^3	1182.9 Å
D_m, floatation(NaI_{aq})		1.178 g/cm	1.165 g/cm
D_x		1.197	1.175
Number of reflections		2104	1266
(Non-zero reflections)		(1963)	(1182)
$2\theta_{max}$		130°	100°
Crystal size		0.3×0.15×0.07 mm	0.3×0.2×0.02 mm
μ(Cu $K\alpha$)		6.51 cm^{-1}	6.30 cm^{-1}

TABLE 2. Z–Pro–Leu–OEt. FINAL PARAMETERS
(e.s.d.'s in parentheses)
(a) Fractional co-ordinates (×10^4).

	x	y	z		x	y	z
O(1)	5253(2)	1872(1)	3777(2)	C(8)	6030(3)	1840(1)	4894(3)
O(2)	6893(2)	1454(1)	5061(2)	C(9)	4800(3)	2787(1)	5435(2)
O(3)	6609(2)	3131(1)	3969(2)	C(10)	4761(3)	3150(1)	6760(3)
O(4)	6242(2)	4514(1)	4932(2)	C(11)	6141(3)	3027(1)	7372(3)
O(5)	7213(2)	4611(1)	2914(2)	C(12)	6433(3)	2374(1)	7026(3)
N(1)	5693(2)	2278(1)	5768(2)	C(13)	5420(3)	3178(1)	4324(2)
N(2)	4603(2)	3606(1)	3816(2)	C(14)	5166(3)	4086(1)	2987(3)
C(1)	4571(4)	2191(1)	1089(3)	C(15)	4091(3)	4561(1)	2576(3)
C(2)	3790(4)	2297(1)	−60(3)	C(16)	2920(4)	4338(1)	1760(3)
C(3)	3289(4)	1812(1)	−784(3)	C(17)	1976(4)	4870(2)	1458(4)
C(4)	3536(3)	1237(1)	−361(3)	C(18)	3347(5)	4044(2)	463(4)
C(5)	4283(4)	1131(1)	779(3)	C(19)	6263(3)	4417(1)	3751(3)
C(6)	4807(3)	1608(1)	1504(3)	C(20)	8410(3)	4904(1)	3503(4)
C(7)	5661(3)	1474(1)	2696(3)	C(21)	9329(4)	4422(2)	3996(4)

(b) Anisotropic thermal parameters ($\times 10^4$) expressed in the form: $\exp\{-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+\beta_{12}hk+\beta_{13}hl+\beta_{23}kl)\}$.

	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
O(1)	114(2)	23(1)	108(2)	17(2)	−56(4)	−11(2)
O(2)	103(2)	26(1)	145(3)	23(2)	−52(5)	8(2)
O(3)	92(2)	33(1)	126(2)	15(2)	38(4)	15(2)
O(4)	164(3)	38(1)	121(2)	−21(3)	9(5)	−25(2)
O(5)	101(2)	32(1)	155(3)	−18(2)	22(5)	6(2)
N(1)	107(3)	24(1)	88(2)	13(2)	−33(5)	9(2)
N(2)	81(2)	23(1)	92(2)	−1(2)	6(4)	13(2)
C(1)	202(5)	25(1)	103(3)	−15(4)	−3(8)	−11(3)
C(2)	270(6)	29(1)	103(3)	1(4)	−20(9)	14(4)
C(3)	189(5)	46(1)	91(3)	−21(4)	−41(7)	−11(4)
C(4)	166(5)	31(1)	134(4)	−31(3)	−52(8)	−26(3)
C(5)	181(5)	26(1)	139(4)	−4(3)	−68(8)	−33(3)
C(6)	108(4)	27(1)	110(3)	4(3)	0(6)	−25(2)
C(7)	151(4)	35(1)	154(4)	41(4)	−91(8)	−61(4)
C(8)	91(3)	24(1)	105(3)	−7(3)	−34(6)	14(3)
C(9)	100(3)	24(1)	80(3)	9(3)	−8(5)	11(2)
C(10)	164(4)	35(1)	91(3)	34(4)	40(7)	−2(3)
C(11)	175(5)	39(1)	104(4)	16(4)	−49(8)	−28(3)
C(12)	125(4)	39(1)	100(3)	29(3)	−48(7)	−2(3)
C(13)	100(3)	20(1)	79(3)	5(3)	−16(5)	−4(2)
C(14)	99(3)	20(1)	93(3)	−2(2)	3(6)	9(2)
C(15)	123(4)	24(1)	107(3)	1(3)	−6(6)	17(3)
C(16)	150(4)	30(1)	167(4)	−27(3)	−83(8)	35(4)
C(17)	163(5)	42(1)	216(6)	3(4)	−113(10)	52(4)
C(18)	287(7)	46(1)	250(7)	47(6)	−266(14)	−71(5)
C(19)	96(3)	21(1)	120(3)	8(3)	23(6)	−3(3)
C(20)	112(4)	33(1)	260(6)	−22(4)	−42(10)	−3(4)
C(21)	145(5)	50(1)	278(7)	14(5)	−89(10)	1(5)

(c) Hydrogen positional ($\times 10^3$) and isotropic thermal ($\times 10$) parameters.

	x	y	z	B	Bonded to		x	y	z	B	Bonded to
H(1)	491(3)	253(1)	156(3)	50(8)	C(1)	H(16)	563(3)	390(1)	218(3)	27(6)	C(14)
H(2)	352(3)	272(1)	−28(3)	59(9)	C(2)	H(17)	385(3)	479(1)	343(3)	34(6)	C(15)
H(3)	272(3)	191(1)	−167(3)	56(8)	C(3)	H(18)	473(2)	492(1)	197(3)	29(6)	C(15)
H(4)	318(3)	86(1)	−78(3)	60(8)	C(4)	H(19)	243(3)	404(1)	225(3)	52(8)	C(16)
H(5)	448(3)	65(1)	111(3)	59(8)	C(5)	H(20)	111(3)	469(1)	89(3)	62(8)	C(17)
H(6)	556(4)	98(1)	305(3)	74(9)	C(7)	H(21)	173(4)	512(1)	225(4)	98(11)	C(17)
H(7)	672(3)	153(1)	262(3)	53(8)	C(7)	H(22)	231(3)	521(1)	89(3)	47(8)	C(17)
H(8)	388(2)	263(1)	509(2)	5(4)	C(9)	H(23)	241(4)	386(1)	4(3)	88(11)	C(18)
H(9)	457(3)	365(1)	661(3)	31(6)	C(10)	H(24)	424(5)	428(1)	−17(4)	111(12)	C(18)
H(10)	409(3)	295(1)	728(3)	40(7)	C(10)	H(25)	383(3)	373(1)	62(4)	76(10)	C(18)
H(11)	685(3)	328(1)	700(3)	49(8)	C(11)	H(26)	811(3)	523(1)	431(3)	48(7)	C(20)
H(12)	616(3)	313(1)	836(3)	38(7)	C(11)	H(27)	888(4)	524(1)	287(3)	70(9)	C(20)
H(13)	745(2)	225(1)	693(3)	32(6)	C(12)	H(28)	991(3)	464(1)	453(4)	75(10)	C(21)
H(14)	617(3)	202(1)	771(3)	43(7)	C(12)	H(29)	879(3)	420(1)	492(3)	71(9)	C(21)
H(15)	373(2)	365(1)	418(2)	11(5)	N(2)	H(30)	967(4)	411(1)	312(4)	104(12)	C(21)

Watts four circle diffractometer with Ni-filtered Cu $K\alpha$ radiation and ω-2θ step scan. Lorentz and polarization factors were applied, but no absorption corrections were made. The crystal and experimental data are listed in Table 1.

Structure Determination and Refinement

Both structures were determined by the direct method using the program *MULTAN*[9] and refined by the block-diagonal least-sequares method with the program *HBLS* V.[10] Since the ($\bar{2}01$) reflection of Boc–Pro–Leu–OBzl suffered much from extinction, it was omitted from the refinement. The final R values were 0.062 for Z–Pro–Leu–OEt and 0.072 for Boc–Pro–Leu–OBzl. The minimized function was $\sum\omega(\Delta F)^2$, with $\omega=0.0$ for $|F_o|=0$, and $\omega=(\sigma^2(F)+a|F_o|+b|F_o|^2)^{-1}$ for $|F_o|>0$, where $\sigma(F)$ was the standard deviation based on the counting statistics. The parameters were: $a=-0.157$ and $b=0.008$ for Z–Pro–Leu–

OEt, and $a=-0.073$ and $b=0.004$ for Boc–Pro–Leu–OBzl.

All the atomic scattering factors were taken from International Tables for X-Ray Crystallography.[11] The calculations were made on FACOM 230-60 and 75 of Nagoya University. The final positional and thermal parameters are also listed in Tables 2 and 3.[12]

Results and Discussion

Bond Lengths and Angles. The bond lengths and angles of the two molecules (Figs. 1 and 2) are in

Table 3. Boc–Pro–Leu–OBzl. Final parameters
(e.s.d.'s in parentheses)

(a) Fractional co-ordinates ($\times 10^4$).

	x	y	z		x	y	z
O(1)	6298(4)	4822(2)	12019(6)	C(9)	5949(7)	2890(4)	13517(10)
O(2)	6389(4)	4294(2)	15378(6)	C(10)	4231(6)	3789(4)	9867(10)
O(3)	3438(4)	3742(3)	11328(6)	C(11)	2590(6)	3983(3)	7162(10)
O(4)	2993(5)	2732(2)	6075(8)	C(12)	2191(7)	4705(3)	5952(10)
O(5)	1413(4)	3346(2)	4566(6)	C(13)	2336(8)	5402(4)	7255(13)
N(1)	5996(5)	3607(2)	12426(6)	C(14)	1849(8)	6073(4)	5813(15)
N(2)	3903(5)	4004(2)	7942(7)	C(15)	1680(10)	5399(5)	9392(16)
C(1)	7881(8)	5595(4)	13865(15)	C(16)	2399(6)	3298(3)	5844(11)
C(2)	5532(10)	5865(4)	14102(16)	C(17)	1200(7)	2721(4)	3169(12)
C(3)	6661(9)	6014(4)	10720(12)	C(18)	338(6)	2963(4)	1407(10)
C(4)	6595(8)	5591(3)	12780(12)	C(19)	−220(7)	3656(4)	1308(11)
C(5)	6206(6)	4251(4)	13416(11)	C(20)	−1010(7)	3859(5)	−475(12)
C(6)	5619(6)	3547(3)	10226(8)	C(21)	−1176(7)	3350(5)	−2008(12)
C(7)	5739(7)	2697(3)	9801(10)	C(22)	−686(8)	2650(5)	−1950(12)
C(8)	5401(8)	2354(4)	11915(11)	C(23)	68(9)	2456(4)	−265(13)

(b) Anisotropic thermal parameters ($\times 10^4$) expressed in the form:
$\exp\{-(\beta_{11}h^2+\beta_{22}k^2+\beta_{33}l^2+\beta_{12}hk+\beta_{13}hl+\beta_{23}kl)\}$.

	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
O(1)	154(6)	24(1)	191(14)	−9(6)	−32(15)	6(8)
O(2)	181(7)	34(1)	180(13)	−28(6)	−82(16)	6(9)
O(3)	113(6)	60(2)	280(15)	5(7)	34(15)	51(11)
O(4)	140(7)	28(1)	587(22)	16(6)	−210(20)	14(12)
O(5)	89(5)	34(2)	305(15)	7(5)	−26(15)	15(9)
N(1)	117(7)	23(2)	111(13)	2(6)	−102(16)	−22(10)
N(2)	95(6)	32(2)	186(16)	4(6)	−96(16)	73(10)
C(1)	173(14)	50(4)	600(44)	−93(13)	−180(39)	7(22)
C(2)	235(15)	33(3)	620(43)	34(13)	355(41)	−60(19)
C(3)	219(13)	30(3)	300(28)	−8(10)	−72(32)	36(15)
C(4)	158(11)	21(2)	353(29)	−35(9)	−3(29)	−28(15)
C(5)	118(9)	29(2)	302(24)	−3(9)	12(24)	32(15)
C(6)	84(7)	27(2)	168(17)	0(8)	83(19)	−20(13)
C(7)	131(9)	18(2)	310(24)	1(9)	73(24)	−22(15)
C(8)	193(13)	21(2)	321(26)	−23(9)	−154(30)	9(15)
C(9)	159(11)	24(3)	286(24)	−14(9)	−30(27)	86(14)
C(10)	79(7)	24(2)	334(23)	−4(8)	55(22)	−19(14)
C(11)	79(8)	26(2)	342(25)	14(8)	−79(22)	9(14)
C(12)	142(10)	16(2)	246(23)	0(8)	−88(24)	38(13)
C(13)	135(11)	35(3)	506(36)	8(11)	0(31)	70(18)
C(14)	158(12)	42(3)	572(41)	17(11)	−133(35)	53(20)
C(15)	279(18)	39(4)	614(44)	25(14)	76(45)	−57(22)
C(16)	81(9)	32(3)	410(29)	13(9)	−159(26)	45(15)
C(17)	132(10)	28(3)	436(29)	−28(10)	−75(28)	−57(17)
C(18)	70(8)	41(3)	257(23)	−10(8)	−39(22)	−34(14)
C(19)	110(9)	31(3)	414(27)	25(9)	−53(26)	−28(17)
C(20)	111(10)	45(3)	453(31)	−8(10)	−100(28)	−33(17)
C(21)	97(10)	70(4)	344(27)	−31(11)	−93(26)	−27(19)
C(22)	162(12)	71(4)	274(26)	−32(13)	−110(28)	−97(20)
C(23)	131(10)	54(4)	447(33)	−38(11)	92(29)	−59(20)

(c) Hydrogen positional ($\times 10^3$) and isotropic thermal ($\times 10$) parameters.

	x	y	z	B	Bonded to		x	y	z	B	Bonded to
H(1)	813(6)	618(4)	1412(10)	46(18)	C(1)	H(18)	218(6)	394(3)	885(9)	46(19)	C(11)
H(2)	871(6)	539(3)	1311(10)	43(18)	C(1)	H(19)	131(5)	459(3)	582(9)	34(17)	C(12)
H(3)	780(7)	530(4)	1502(11)	52(19)	C(1)	H(20)	286(6)	471(3)	463(9)	38(17)	C(12)
H(4)	583(7)	645(4)	1489(11)	57(20)	C(2)	H(21)	343(6)	549(3)	776(9)	36(17)	C(13)
H(5)	558(6)	551(3)	1586(9)	34(17)	C(2)	H(22)	187(6)	650(3)	655(10)	43(18)	C(14)
H(6)	438(6)	587(3)	1304(10)	36(17)	C(2)	H(23)	93(5)	609(3)	569(9)	30(16)	C(14)
H(7)	670(6)	659(3)	1108(9)	39(17)	C(3)	H(24)	263(6)	610(3)	483(10)	37(17)	C(14)
H(8)	579(6)	598(3)	1040(10)	44(19)	C(3)	H(25)	175(6)	581(3)	1023(11)	45(19)	C(15)
H(9)	737(6)	574(3)	980(11)	43(18)	C(3)	H(26)	190(6)	489(3)	1070(10)	50(20)	C(15)
H(10)	623(5)	385(3)	927(8)	24(15)	C(6)	H(27)	55(6)	531(4)	872(10)	43(18)	C(15)
H(11)	681(6)	262(3)	938(9)	39(17)	C(7)	H(28)	79(6)	233(4)	407(10)	44(18)	C(17)
H(12)	510(6)	258(3)	833(9)	35(17)	C(7)	H(29)	207(6)	259(3)	228(10)	45(18)	C(17)
H(13)	568(5)	180(3)	1191(8)	29(15)	C(8)	H(30)	−7(5)	410(3)	243(8)	23(15)	C(19)
H(14)	446(6)	226(3)	1251(9)	41(18)	C(8)	H(31)	−157(5)	443(3)	−53(8)	22(15)	C(20)
H(15)	687(6)	269(3)	1444(9)	38(17)	C(9)	H(32)	−175(6)	339(3)	−321(9)	42(18)	C(21)
H(16)	547(5)	292(3)	1489(8)	34(16)	C(9)	H(33)	−74(6)	232(3)	−258(9)	44(19)	C(22)
H(17)	470(6)	413(3)	726(9)	44(18)	N(2)	H(34)	52(6)	204(3)	−19(10)	49(19)	C(23)

TABLE 4. TORSION ANGLES (ϕ, ψ) AND SIDE CHAIN CONFORMATION OF LEUCINE[a]

	ϕ/°	ψ/°	Type[b]	Ref.
N-Acetyl-Leu-isopropylamide	−90	158	I	15
Leu-Pro-Gly	—	153.4	I	16
Benzoyl-DL-Leu-Gly-OEt (A)	−94.2	151.4	I	17
Z-Pro-Leu-OEt	−56.2	147.7	I	
N-Acetyl-DL-Leu-ethylamide	−91	144	I	18
Benzoyl-DL-Leu-Gly-OEt (B)	−64.8	142.6	I	17
N-Acetyl-DL-Leu-*N*-methylamide	−93.8	140.4	I	19
Pro-Leu-Gly-NH_2	−61.2	127.8	I	6
Z-Leu-*p*-nitrophenyl ester	−93.5	48.8	I	20
Boc-Pro-Leu-Gly	−110.8	26.7	I	4
Z-Gly-Pro-Leu-Gly	−115.8	15.4	I	21
Z-Gly-Pro-Leu-Gly-Pro	−107.3	12.0	I	1
Z(*o*-Br)-Gly-Pro-Leu-Gly-Pro	−104.7	8.4	I	2
Z(*p*-Br)-Gly-Pro-Leu-Gly	−104.0	8.0	I	3
S-Benzyl-Cys-Pro-Leu-Gly-NH_2 (A)	−74.1	−8.5	III	5
S-Benzyl-Cys-Pro-Leu-Gly-NH_2 (B)	−71.6	−11.9	II	5
Leu-Tyr Cu(II)	—	−14.7	I	22
D-Leu-Gly	—	−145.4	I	23
Boc-Pro-Leu-OBzl	−99.1	−159.9	I	
Cyclic peptides				
cyclo-(Pro-Leu)	−41.5	33.8	I	24
Ilamycin B_1 (1)	−123	2	I	25
cyclo-(His-Leu)	20.2	−10.4	I	26
C termini residues				
Z-Gly-Pro-Leu	−89.4	(38.1)[c]	I	7
Pro-Leu	−74.8	(−18.9)	I	27
Gly-Leu	−54.9	(−30.2)	II	28
Amino acids				
2Leucine·HCl (A)	—	(−13.1)	II	29
Leucine·HI	—	(−13.3)	II	30
Leucine·HBr	—	(−15.2)	II	31
2Leucine·HCl (B)	—	(−17.7)	II	29
DL-Leucine	—	(−37.1)	II	32
N-methyl-leucines				
N-methyl-DL-Leu-Gly	−57.9	118.3	II	33
Ilamycin B_1 (2)	−128	99	II	25
Ilamycin B_1 (3)	−121	38	I	25
┌D-HyIv-L-MeIleu-D-HyIv-L-MeLeu-┐	77.9	−33.7	I	34

a) All the torsion angles for the L-isomers are listed. b) Type I, II, and III have the trans-zigzag chains of $C'-C^{\alpha}-C^{\beta}-C^{\gamma}-C^{\delta 1}$, $N-C^{\alpha}-C^{\beta}-C^{\gamma}-C^{\delta 2}$, and $C'-C^{\alpha}-C^{\beta}-C^{\gamma}-C^{\delta 2}$, respectively. c) In cases of C termini leucyl residue and leucine amino acid, ψ means the torsion angle $N-C^{\alpha}-C'-O$.

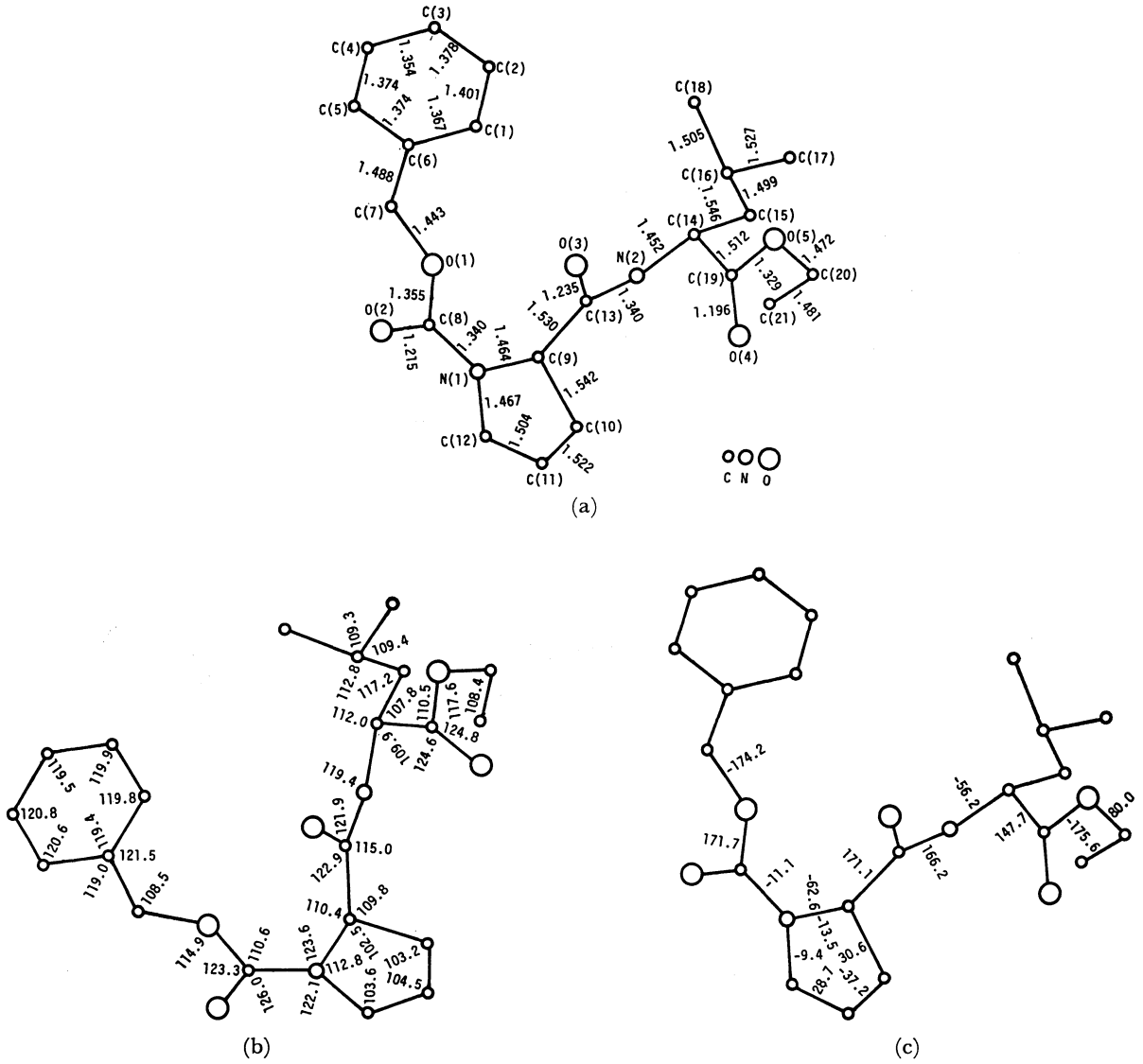

Fig. 1. (a) Bond lengths (Å), (b) angles (°), and (c) torsion angles (°) for Z–Pro–Leu–OEt.

accordance with the average values of the peptides, within the experimental error. Seemingly abnormal large values observed at the C^{β} atoms of the leucyl residues (117.2° in Z–Pro–Leu–OEt and 113.3° in Boc–Pro–Leu–OBzl) are common to all the leucines so far studied. They are attributed to the steric repulsion between the peptide plane and the bulky leucyl side chain.[3]

Prolyl Side Chain. Both pyrrolidine rings are designated as C^{γ}-*endo*, conformation B by the definition of Balasubramanian *et al.*[13] But following the more detailed classification by Ashida and Kakudo,[14] they can be distinguished as C_2–C^{γ}-*endo* for Z–Pro–Leu–OEt and an intermediate state between C_2–C^{γ}-*endo* and C_s–C^{γ}-*endo* for Boc–Pro–Leu–OBzl.

Leucyl Side Chain. Most of the side chain conformations of the leucyl residues so far analyzed can be classified into three trans-zigzag conformations, *i.e.* C′ to $C^{\delta 1}$(type I), N to $C^{\delta 2}$(type II), and C′ to $C^{\delta 2}$(type III).[4] (see Table 4 footnote) The two molecules in this study take a type I conformation.

The main chain torsion angles (ϕ,ψ) and the leucyl side chain conformations are presented in Table 4. For the leucyl residues occurring in the peptides, type I is found overwhelmingly, without any obvious relationships to the main chain torsion angles. On the other hand, for the C termini leucyl residues and leucines, type II is rather preferred and the ψ values seem to be restricted to a narrow range.

Peptide Chain. The main chain torsion angles are shown in Figs. 1 and 2. Both of the peptides analyzed in this study, Z–Pro–Leu–OEt and Boc–Pro–Leu–OBzl, take an extended conformation, in contrast to the folded β-turn conformation of the longer peptides so far analyzed. This observation suggests that an extended conformation is preferable to the folded conformation for the simple Pro–Leu unit. The folded conformation has only been found with the 4→1 hydrogen bond. The conformational difference between the dipeptides and the longer peptides suggests an important role for the semi-local interactions, such as the 4→1 hydrogen bond, in the folding of peptide chains.

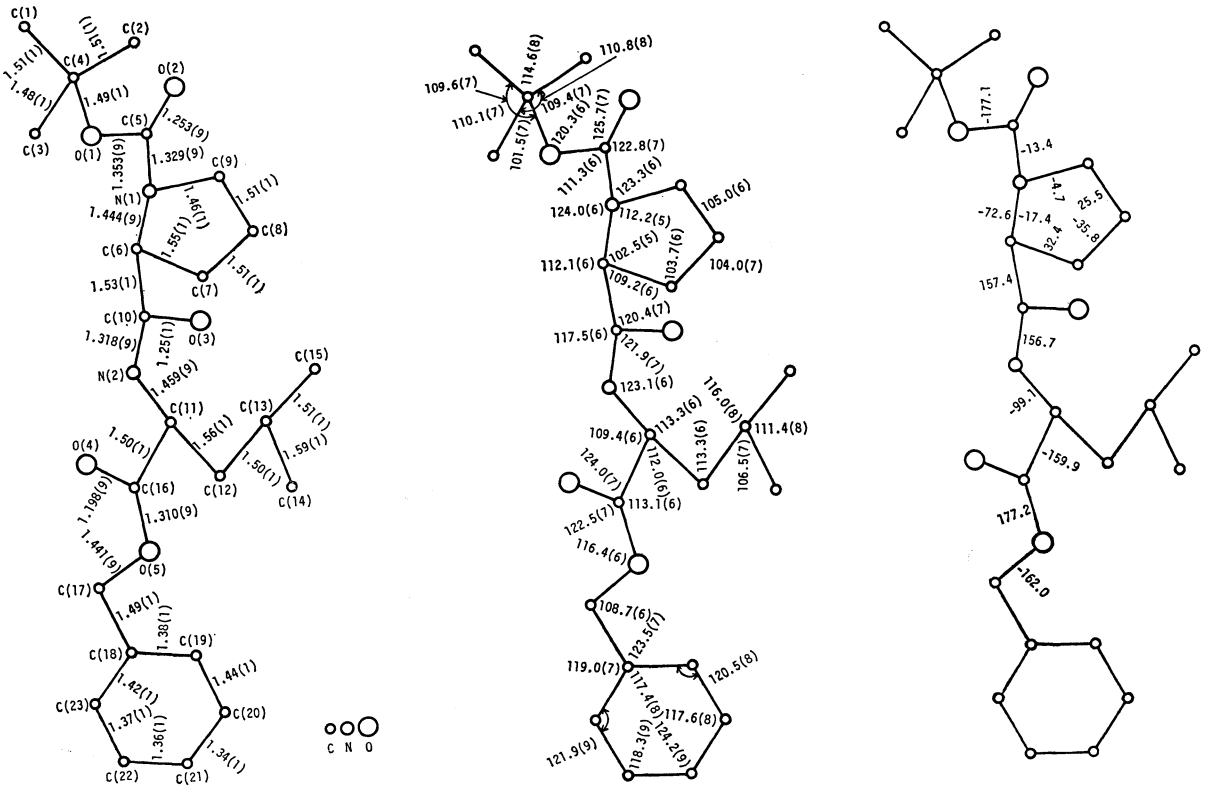

Fig. 2. (a) Bond lengths (Å), (b) angles (°), and (c) torsion angles (°) for Boc–Pro–Leu–OBzl.

Crystral Structure. The crystal structures of the two compounds are shown in Figs. 3 and 4. Although there is no close relationship between the two structures, the hydrogen bonds between the carbonyl oxygen atom of the oxycarbonyl group and the nitrogen atom of the leucyl residue are commonly observed. This fact, together with the clustering of the Boc or Z group and the other hydrophobic groups in each crystal, suggests that the two N-protecting groups, Boc and Z, play a similar role in crystal packing.

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References

1) S. Bando, N. Tanaka, T. Ashida, and M. Kakudo, Ann. Meet. Crystallogr. Soc. Japan, Osaka (1973).
2) T. Ueki, S. Bando, T. Ashida, and M. Kakudo, *Acta Crystallogr., Sect. B*, **27**, 2219 (1971).
3) T. Ueki, T. Ashida, M. Kakudo, Y. Sasada, and Y. Katsube, *Acta Crystallogr., Sect. B*, **25**, 1840 (1969).
4) T. Ashida, I. Tanaka, Y. Shimonishi, and M. Kakudo, *Acta Crystallogr., Sect. B*, **33**, 3054 (1977).
5) A. D. Rudko and B. W. Low, *Acta Crystallogr., Sect. B*, **31**, 713 (1975).
6) L. L. Reed and P. L. Johnson, *J. Am. Chem. Soc.*, **95**, 7523 (1973).
7) T. Yamane, T. Ashida, Y. Shimonishi, M. Kakudo, and Y. Sasada, *Acta Crystallogr., Sect. B*, **32**, 2071 (1976).
8) C. M. Venkatachalam, *Biopolymers*, **6**, 1425 (1968).
9) G. Germain, P. Main, and M. M. Woolfson, *Acta Crystallogr., Sect. A*, **27**, 368 (1971).
10) T. Ashida, The Universal Crystallographic Computing System-Osaka, The Computation Center, Osaka Univ. (1973), p. 55.
11) "International Tables for X-Ray Crystallography," The Kynoch Press, Birmingham (1974), Vol. IV, p. 149.
12) The F_o and F_c tables are kept as Document No. 7832a for Z–Pro–Leu–OEt and No. 7832b for Boc–Pro–Leu–OBzl at the Chemical Society of Japan.
13) R. Balasubramanian, A. V. Lakshminarayanan, M. N. Sabesan, G. Tegoni, K. Venkatesan, and G. N. Ramachandran, *Int. J. Protein Res.*, **3**, 25 (1971).
14) T. Ashida and M. Kakudo, *Bull. Chem. Soc. Jpn.*, **47**, 1129 (1974).
15) A. Aubry, Ph. D. Thesis, University of Nancy, Nancy, France, 1976.
16) Y. C. Leung and R. E. Marsh, *Acta Crystallogr.*, **11**, 17 (1958).
17) P. A. Timmins, *Acta Crystallogr., Sect. B*, **31**, 2240 (1975).
18) A. Aubry, M. Marraud, J. Protas, and J. Neel, *C. R. Acad. Sci., Ser. C*, **278**, 697 (1974).
19) T. Ichikawa and Y. Iitaka, *Acta Crystallogr., Sect. B*, **25**, 1824 (1969).
20) V. M. Coiro, F. Mazza, and G. Mignucci, *Acta Crystallogr., Sect. B*, **30**, 2607 (1974).
21) Y. Matsuura, private communication (1977).
22) D. van der Helm, S. E. Ealick, and J. E. Burks, *Acta Crystallogr., Sect. B*, **31**, 1013 (1975).

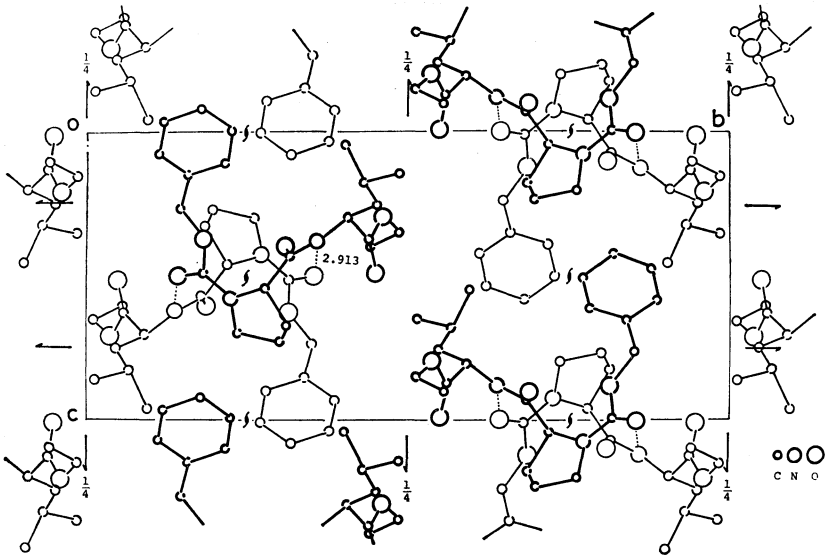

Fig. 3. Crystal structure of Z–Pro–Leu–OEt. Hydrogen bonds are shown with dashed lines.

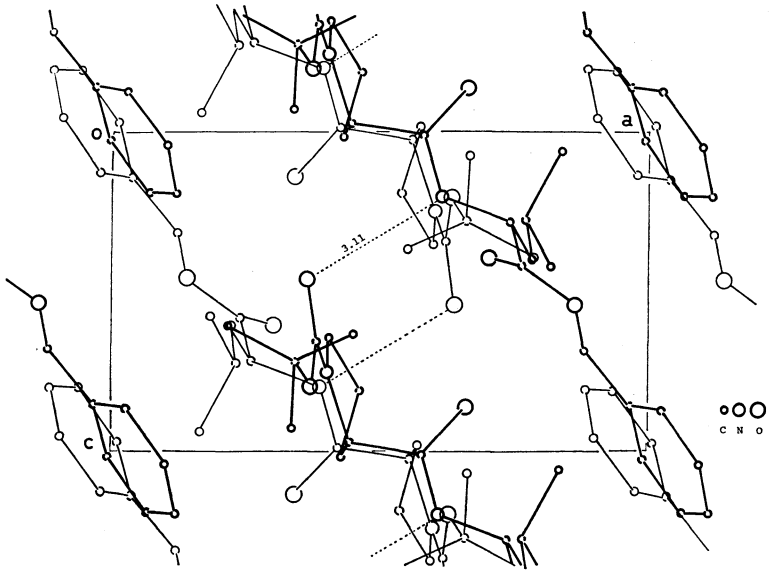

Fig. 4. Crystal structure of Boc–Pro–Leu–OBzl. Hydrogen bonds are shown with dashed lines.

23) S. T. Rao, *Z. Kristallogr.*, **129**, 50 (1969).
24) I. L. Karle, *J. Am. Chem. Soc.*, **94**, 81 (1972).
25) Y. Iitaka, H. Nakamura, K. Takada, and T. Takita, *Acta Crystallogr., Sect. B*, **30**, 2817 (1974).
26) I. Tanaka, T. Iwata, N. Takahashi, T. Ashida, and M. Tanihara, *Acta Crystallogr., Sect. B*, **33**, 3902 (1977).
27) I. Tanaka, Y. Asada, H. Sugino, and T. Ashida, unpublished data.
28) V. Pattabhi, K. Venkatesan, and S. R. Hall, *J. Chem. Soc., Perkin Trans. 2*, **1974**, 1722.
29) L. Golic and W. C. Hamilton, *Acta Crystallogr., Sect. B*, **28**, 1265 (1972).
30) M. O. Chaney, O. Seely, and L. K. Steinrauf, *Acta Crystallogr., Sect. B*, **27**, 544 (1971).
31) E. Subramanian, *Acta Crystallogr.*, **22**, 910 (1967).
32) B. D. Blasio, C. Pedone, and A. Sirigu, *Acta Crystallogr., Sect. B*, **31**, 601 (1975).
33) R. Chandrasekaran and E. Subramanian, *Acta Crystallogr., Sect. B*, **25**, 2599 (1969).
34) J. Konnert and I. L. Karle, *J. Am. Chem. Soc.*, **91**, 4888 (1969).