Recl. Trav. Chim. Pays-Bas **106**, 151–156 (1987) 0165–0513/87/05151–06$2.00

Crystal and molecular structure of *N*-acetyl *N*-hydroxy α-amino acids

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Abstract. The crystal and molecular structures of racemic (DL) *N*-acetyl-*N*-hydroxyvaline and 2-(*N*-acetyl-*N*-hydroxyamino)butyric acid have been determined from three-dimensional X-ray data. The crystals of both compounds are monoclinic, space group $P2_1/a$.
The molecular conformation of these amino acid derivatives is similar, as far as the φ torsion angle is concerned, but the ψ values are significantly different. In the crystal structures of both compounds, two series of intermolecular hydrogen bonds (HB's) are present: N–OH...O=C–OH HB's link the *N*-hydroxy and carboxylic groups, while O=C–OH...O=C–N HB's link the carboxylic and *N*-hydroxyamidic groups.

Introduction

The chemistry of naturally occurring α-amino acids is well established and their biochemical importance is fully understood. Much less is known, however, about the chemical and biochemical behaviour of non-protein amino acids. Among these are the α-amino acids with a functionality in addition to the amino and carboxy groups. These "uncommon" amino acids have been shown to be characteristics structural elements of several naturally occurring compounds. For instance, numerous α,β-dehydro amino acids have been identified as constituents of naturally occurring peptides[1]. Another class of uncommon amino acids, *i.e.* *N*-hydroxy amino acids[2], can be found as structural elements in antibiotics, growth agents, enzyme inhibitors, herbicides, antitumour agents, antifungal agents and siderophores. In general, the nitrogen is acylated in these natural products to form *N*-acyl *N*-hydroxy amino acid derivatives, which can also be regarded as *N*-substituted hydroxamic acids.
We feel that the structure of uncommon amino acids deserves attention. In contrast to the vast amount of work

Table I Experimental details.

Formula unit	$C_6N_1O_4H_{11}$ (**2**)	$C_7N_1O_4H_{13}$ (**1**)
Instrument	Four-circle diffractometer Philips PW 1100	
Radiation (graphite monochromatized)	Mo*K*α	Mo*K*α
Crystal dimensions, mm	0.03 × 0.02 × 1.00	0.03 × 0.02 × 0.40
Scan width (deg)	1.00	1.80
Scan speed (deg s^{-1})	0.020	0.030
ϑ range (deg)	$2° \leqslant \vartheta \leqslant 25°$	$2° \leqslant \vartheta \leqslant 25°$
N° of standard intensity reflections measured at 3-h intervals	3	3
Method used to solve structure	MULTAN	MULTAN
Least-squares refinement based on	*F*	*F*
Weight	unit	unit
N° independent reflections	1791	1623
N° reflections with $I \geqslant 2.5\ (I)$	971	735
R_{int} (%)	1.29	3.90
N° of equivalent reflections	125	83
Final $R = [\Sigma(\|F_o\| - \|F_c\|)/\Sigma\|F_o\|]$ (%)	4.75	6.01
$s = [\Sigma(F_o - F_c)^2/(m - n)]^{1/2}$	0.73	1.00
$(\Delta/\sigma)_{max}$	0.010	0.013
Residual electron density in final difference map (e $Å^{-3}$)	from 0.22 to −0.21	from 0.19 to −0.25
Programs used	*SHELX* 76[9]	*SHELX* 76[9]
	MULTAN 78[10]	*MULTAN* 78[10]
Atomic scattering factors from	International Tables for X-ray Crystallography[11]	

carried out on the structure of protein amino acids and peptides, little attention has been paid thus far to the structure of non-protein amino acids and their derivatives. In the last few years, we have reported the crystal, molecular and electronic structure of *N*-acetyl dehydro amino acids, their esters and cyclic didehydropeptides[3,4].

Subsequently, we undertook an analogous investigation of *N*-acetyl *N*-hydroxy amino acids, which are chemically and biologically related to α,β-didehydro amino acids[5].

We now wish to report the crystal and molecular structure of racemic (DL) *N*-acetyl-*N*-hydroxyvaline [**1**:R = $CH(CH_3)_2$] and 2-(*N*-acetyl-*N*-hydroxyamino)butyric acid (**2**: R = CH_2CH_3).

Results and discussion

Experimental details and crystal data are reported in Tables I and II, respectively. Final positional parameters are reported in Tables III and IV**. The numbering scheme of the atoms is shown in Fig. 1.

Table II Crystallographic data.

Formula unit	$C_6N_1O_4H_{11}$ (**2**)	$C_7N_1O_4H_{13}$ (**1**)
system	monoclinic	monoclinic
space group	$P2_1/a$	$P2_1/a$
a (Å)	14.003(3)	12.573(3)
b (Å)	5.425(2)	6.888(2)
c (Å)	10.495(3)	10.857(3)
α (degrees)	90	90
β (degrees)	93.70(5)	101.08(5)
γ (degrees)	90	90
V (Å^3)	795.6(4)	922.7(5)
M_r	161.16	175.18
Z	4	4
D_c (g·cm^{-3})	1.345	1.261
D_m (g·cm^{-3})[a]	1.330	1.255
F(000)	344	376
λ (Mo$K\alpha$)	0.71069	0.71069
$\mu_{MoK\alpha}$ (cm^{-1})	1.062	0.967
T (°K)	298	298

[a] By flotation in KBr aqueous solutions.

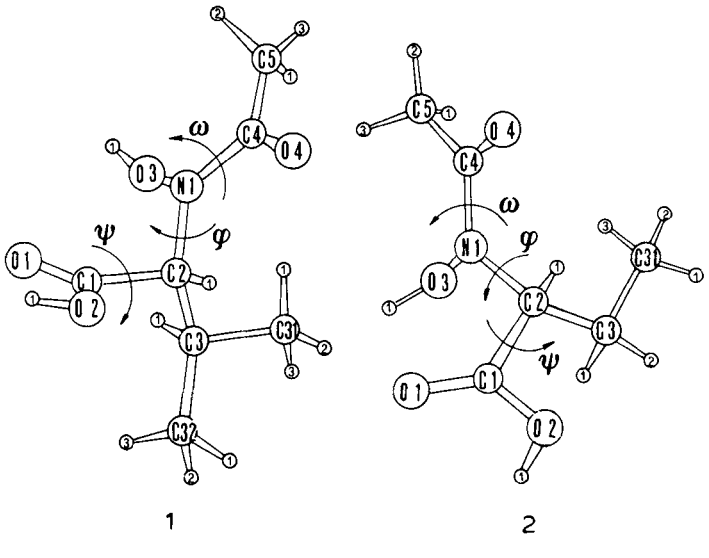


Fig. 1. Conformation of **1** *and* **2**; *the atom numbering scheme and relevant torsion angles are shown.*

Table III Fractional coordinates (× 10^4, for H × 10^3) and equivalent isotropic thermal parameters (e.s.d.'s are given in parentheses), for $C_7N_1O_4H_{13}$ (**1**).

Atom	x	y	z	B_{eq} or B (Å^2)
O(1)	−122(5)	5495(10)	6304(5)	7.2(2)
O(2)	427(5)	7277(13)	8003(8)	6.0(2)
O(3)	1646(4)	3098(9)	5689(7)	5.1(2)
O(4)	3590(4)	5940(8)	7554(5)	5.9(2)
N(1)	2089(4)	4463(8)	6602(5)	3.9(2)
C(1)	513(5)	5840(13)	7229(8)	4.4(2)
C(2)	1529(5)	4594(12)	7648(7)	3.8(2)
C(3)	1269(6)	2618(11)	8147(8)	4.6(2)
C(31)	2317(8)	1438(16)	8519(13)	6.6(4)
C(32)	675(8)	2820(19)	9223(10)	6.9(3)
C(4)	3153(5)	4929(12)	6663(8)	4.3(2)
C(5)	3672(7)	4187(17)	5643(10)	6.0(4)
H(1.2)	188(4)	523(7)	826(5)	4.0
H(1.3)	94(5)	200(9)	736(6)	4.0
H(1.5)	380(6)	277(12)	571(7)	4.0
H(2.5)	337(7)	455(13)	472(9)	4.0
H(3.5)	428(7)	496(13)	578(9)	4.0
H(1.31)	262(8)	108(16)	766(10)	5.0
H(2.31)	214(5)	29(11)	882(6)	5.0
H(3.31)	271(8)	215(14)	933(9)	5.0
H(1.32)	46(8)	150(15)	955(9)	6.0
H(2.32)	106(11)	312(19)	1013(12)	6.0
H(3.32)	0(8)	347(14)	902(8)	6.0
H−O(2)	−21(9)	780(17)	750(12)	6.0
H−O(3)	143(9)	362(13)	514(9)	5.0

Table IV Fractional coordinates (× 10^4, for H × 10^3) and equivalent isotropic thermal parameters (e.s.d.'s are given in parentheses), for $C_6N_1O_4H_{11}$ (**2**).

Atom	x	y	z	B_{eq} or B (Å^2)
O(1)	−2524(2)	3666(5)	5894(2)	3.52(7)
O(2)	−2854(2)	2475(6)	7858(2)	4.01(7)
O(3)	−1288(2)	8270(5)	6313(2)	3.26(6)
O(4)	415(2)	3868(5)	7271(3)	4.09(8)
N(1)	−905(2)	6046(5)	6786(2)	2.55(7)
C(1)	−2341(2)	3571(6)	7025(3)	2.63(8)
C(2)	−1471(2)	4808(7)	7708(3)	2.61(8)
C(3)	−1754(3)	6548(9)	8765(4)	3.79(11)
C(31)	−922(4)	8018(11)	9367(5)	5.00(16)
C(4)	42(2)	5698(7)	6753(3)	2.80(10)
C(5)	605(3)	7555(9)	6067(5)	4.10(12)
H(1.5)	56(3)	907(8)	647(4)	5.3(1)
H(2.5)	123(3)	690(9)	599(4)	6.5(1)
H(3.5)	34(3)	787(8)	522(4)	5.6(1)
H(1.31)	−109(3)	912(10)	1010(5)	8.1(1)
H(2.31)	−43(3)	692(9)	966(4)	6.0(1)
H(3.31)	−59(3)	904(8)	877(4)	5.6(1)
H(1.2)	−107(2)	354(6)	806(3)	2.3(1)
H(1.3)	−225(3)	770(8)	843(4)	4.8(1)
H(2.3)	−206(3)	549(8)	942(4)	5.6(1)
H−O(2)	−339(3)	181(9)	750(4)	7.3(1)
H−O(3)	−162(3)	782(10)	559(5)	8.5(1)

Crystal packing is given in Figs. 2 and 3.

Bond distances and angles are shown in Tables V-VIII: bond distances are within the usual range for amino acid derivatives: in particular, the N−C_α bond lengths are

** Lists of structure factors and anisotropic thermal parameters have been deposited with editorial office Recueil as Supplementary Publication No. Recl. 491. Copies may be obtained from editorial office Recueil, P.O. Box 90613, 2509 LP The Hague.

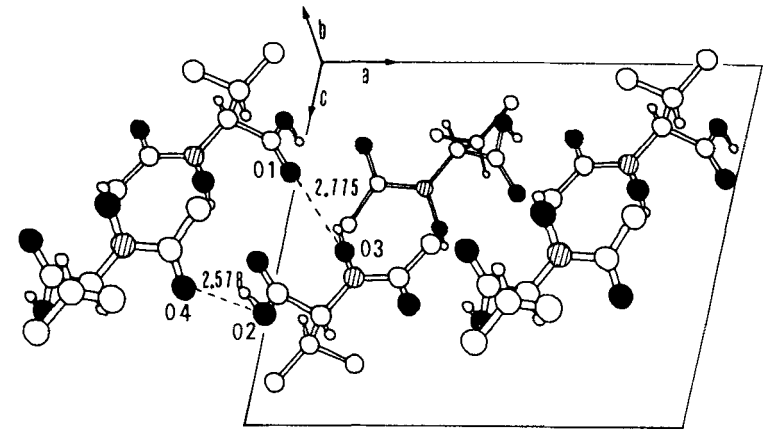


Fig. 2. The crystal packing of **1**.

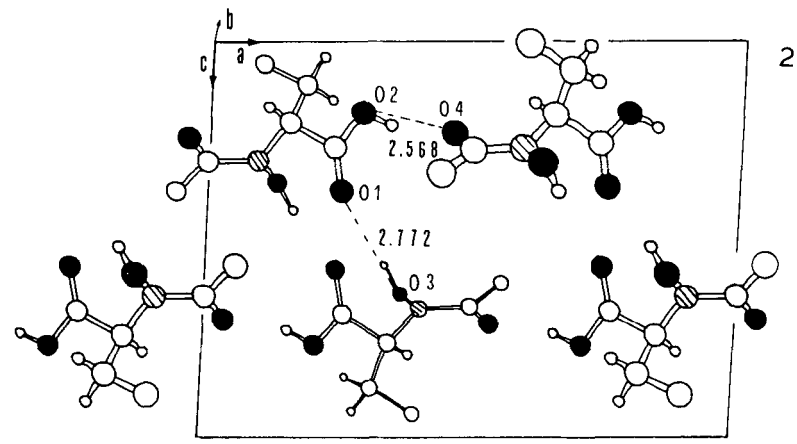


Fig. 3. The crystal packing of **2**.

1.449(9) Å (**1**) and 1.454(4) Å (**2**), to be compared with 1.451 Å reported for 2-(*N*-acetyl-D-amino)butyric acid[6]. The C′–N (amidic) bond lengths are 1.365(8) Å (**1**) and 1.342(4) Å (**2**), to be compared with 1.348[6]: this indicates partial carbon–nitrogen double bonds as found in amides.

The molecular conformation of these amino acid derivatives (which differ only in one β-methyl group) is similar, as far as the φ(C1–C2–N1–C4) torsion angles are concerned ($\phi_1 = \pm 126.1°$, $\phi_2 = \pm 129.2°$), but differs in the ψ(O2–C1–C2–N1) values ($\psi_1 = \mp 128.0°$, $\psi_2 = \pm 179.5°$). The hydroxamic moieties assume a significantly distorted ($\omega_1 = \pm 162.8°$, $\omega_2 = \pm 161.8°$) transoid conformation. According to *Kolasa*[7], only the *trans* (*E*) conformation should be assumed in solution by *N*-acyl *N*-hydroxy amino acid esters. Intramolecular hydrogen bonds (which probably stabilize *Z*- and *E*-isomers in solution[7]) are absent in the crystalline state. Actually, in the crystal structures of both compounds, two series of intermolecular hydrogen bonds (HB's) are present: N–OH...O=C–OH HB's link the N-hydroxy and carboxylic groups, while O=C–OH...O=C–N HB's link the carboxylic and *N*-hydroxyamidic groups (see Table IX).

Such results suggest that these systems should show an interesting conformational behaviour, and encourage us to pursue the investigation of a larger series of *N*-hydroxy amino acids bearing different side chains and terminal groups.

Table V Bond lengths (Å) for $C_7N_1O_4H_{13}$ (**1**).

O(1)–C(1)	1.181(9)	C(4)–C(5)	1.480(14)
O(2)–C(1)	1.316(13)	C(5)–H(1.5)	.99(8)
O(3)–N(1)	1.402(8)	C(5)–H(2.5)	1.04(9)
O(4)–C(4)	1.232(9)	C(5)–H(3.5)	.92(9)
N(1)–C(2)	1.449(9)	C(31)–H(1.31)	1.10(12)
N(1)–C(4)	1.365(8)	C(31)–H(2.31)	.90(7)
C(1)–C(2)	1.537(10)	C(31)–H(3.31)	1.05(9)
C(2)–C(3)	1.524(11)	C(32)–H(1.32)	1.03(10)
C(2)–H(1.2)	.85(5)	C(32)–H(2.32)	1.03(12)
C(3)–C(32)	1.509(15)	C(32)–H(3.32)	.95(9)
C(3)–C(31)	1.535(12)	O(2)–HO(2)	.95(9)
C(3)–H(1.3)	.97(6)	O(3)–HO(3)	.70(9)

Table VI Bond lengths (Å) for $C_6N_1O_4H_{11}$ (**2**).

O(1)–C(1)	1.199(4)	C(3)–C(31)	1.516(7)
O(2)–C(1)	1.310(4)	C(3)–H(1.3)	.98(4)
O(2)–HO(2)	.89(5)	C(3)–H(2.3)	1.01(4)
O(3)–N(1)	1.398(4)	C(31)–H(1.31)	1.02(5)
O(3)–HO(3)	.90(5)	C(31)–H(2.31)	.95(4)
O(4)–C(4)	1.232(4)	C(31)–H(3.31)	.98(4)
N(1)–C(2)	1.454(4)	C(4)–C(5)	1.493(6)
N(1)–C(4)	1.342(4)	C(5)–H(1.5)	.93(4)
C(1)–C(2)	1.528(4)	C(5)–H(2.5)	.96(4)
C(2)–C(3)	1.528(6)	C(5)–H(3.5)	.95(4)
C(2)–H(1.2)	.95(3)		

Table VII Bond angles (°) for $C_7N_1O_4H_{13}$ (1).

O(3)–N(1)–C(4)	116.4(5)
O(3)–N(1)–C(2)	114.1(5)
C(2)–N(1)–C(4)	124.5(6)
O(1)–C(1)–O(2)	124.7(7)
O(2)–C(1)–C(2)	113.4(7)
O(1)–C(1)–C(2)	121.9(8)
N(1)–C(2)–C(1)	107.7(6)
C(1)–C(2)–H(1.2)	103(3)
C(1)–C(2)–C(3)	112.5(6)
N(1)–C(2)–H(1.2)	113(3)
N(1)–C(2)–C(3)	113.1(6)
C(3)–C(2)–H(1.2)	107(3)
C(2)–C(3)–H(1.3)	99(4)
C(2)–C(3)–C(31)	109.6(7)
C(2)–C(3)–C(32)	111.4(7)
C(31)–C(3)–H(1.3)	101(4)
C(32)–C(3)–H(1.3)	122(4)
C(32)–C(3)–C(31)	111.9(8)
O(4)–C(4)–N(1)	117.1(7)
N(1)–C(4)–C(5)	116.8(7)
O(4)–C(4)–C(5)	126.0(7)
C(4)–C(5)–H(3.5)	99(6)
C(4)–C(5)–H(2.5)	121(5)
C(4)–C(5)–H(1.5)	112(4)
H(2.5)–C(5)–H(3.5)	99(7)
H(1.5)–C(5)–H(3.5)	116(7)
H(1.5)–C(5)–H(2.5)	109(7)
C(3)–C(32)–H(3.32)	115(5)
C(3)–C(32)–H(2.32)	123(7)
C(3)–C(32)–H(1.32)	112(6)
H(2.32)–C(32)–H(3.32)	111(9)
H(1.32)–C(32)–H(3.32)	103(8)
H(1.32)–C(32)–H(2.32)	87(9)
C(3)–C(31)–H(3.31)	103(5)
C(3)–C(31)–H(2.31)	107(4)
C(3)–C(31)–H(1.31)	108(6)
H(2.31)–C(31)–H(3.31)	103(7)
H(1.31)–C(31)–H(3.31)	129(8)
H(1.31)–C(31)–H(2.31)	105(7)
C(1)–O(2)–HO(2)	95(7)
N(1)–O(3)–HO(3)	107(7)

Table VIII Bond angles (°) for $C_6N_1O_4H_{11}$ (2).

C(1)–O(2)–HO(2)	112(3)
N(1)–O(3)–HO(3)	103(3)
O(3)–N(1)–C(4)	118.0(3)
O(3)–N(1)–C(2)	114.9(2)
C(2)–N(1)–C(4)	122.3(2)
O(1)–C(1)–O(2)	126.1(3)
O(2)–C(1)–C(2)	109.9(3)
O(1)–C(1)–C(2)	123.9(3)
N(1)–C(2)–C(1)	110.1(2)
C(1)–C(2)–H(1.2)	107(2)
C(1)–C(2)–C(3)	112.0(3)
N(1)–C(2)–H(1.2)	105(2)
N(1)–C(2)–C(3)	112.1(3)
C(3)–C(2)–H(1.2)	110(2)
C(2)–C(3)–H(2.3)	107(2)
C(2)–C(3)–H(1.3)	110(2)
C(2)–C(3)–C(31)	113.5(4)
H(1.3)–C(3)–H(2.3)	106(3)
C(31)–C(3)–H(2.3)	111(2)
C(31)–C(3)–H(1.3)	109(2)
C(3)–C(31)–H(3.31)	114(2)
C(3)–C(31)–H(2.31)	109(3)
C(3)–C(31)–H(1.31)	114(3)
H(2.31)–C(31)–H(3.31)	102(3)
H(1.31)–C(31)–H(3.31)	107(4)
H(1.31)–C(31)–H(2.31)	109(4)
O(4)–C(4)–N(1)	119.6(3)
N(1)–C(4)–C(5)	118.1(3)
O(4)–C(4)–C(5)	122.3(3)
C(4)–C(5)–H(3.5)	113(2)
C(4)–C(5)–H(2.5)	108(2)
C(4)–C(5)–H(1.5)	109(2)
H(2.5)–C(5)–H(3.5)	107(4)
H(1.5)–C(5)–H(2.5)	117(4)
H(1.5)–C(5)–H(3.5)	104(4)

Experimental

Proton magnetic resonance spectra were measured using a Varian Associates Model T-60. Chemical shifts are reported as δ values (parts *per* million, relative to tetramethylsilane as an internal standard); deuterochloroform was used as solvent unless stated otherwise. Melting points were measured on a Köfler hot stage (Leitz-Wetzlar) and are uncorrected. Thin-layer chromatography (TLC) was carried out using Merck precoated silica gel F-254 plates (thickness 0.25 mm). Spots were visualized with a UV hand lamp or iodine vapour. For high pressure LC, the Miniprep LC (Jobin Yvon) was used.

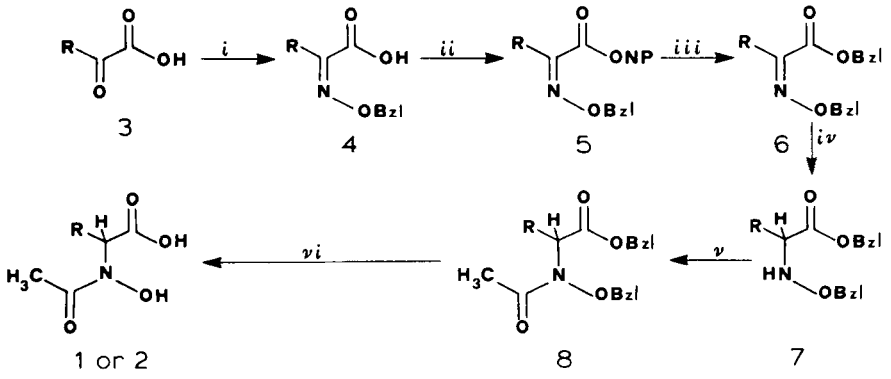
Synthesis

The synthesis of the *N*-Acetyl *N*-hydroxy α-amino acids is depicted in Scheme 1.

α-(Benzyloximino) p-nitrophenyl esters (**5**) were prepared by the procedure described by *Herscheid* et al.[8]: **5** [R = $CH(CH_3)_2$]: see ref. 8; **5** (R = CH_2CH_3): 69% yield; m.p. 79–81 °C. ^{1}H NMR:

Table IX Hydrogen bonds.

Hydrogen bonds for $C_6N_1O_4H_{11}$ (**2**)			
O(2)–HO(2) .89(5)	O(2)....O(4)^{i} 2.568(4)	HO(2)....O(4)^{i} 1.72(5)	O(2)–HO(2)–O(4)^{i} 158.(4)
O(3)^{ii}–HO(3)^{ii} .90(5)	O(1)....O(3)^{ii} 2.772(3)	HO(3)^{ii}....O(1) 1.96(5)	O(1)–HO(3)^{ii}–O(3)^{ii} 150.(5)
Symmetry code: $i = \frac{1}{2} + x, (\frac{1}{2} - y) + 1, z$; $ii = -(\frac{1}{2} + x) + 1, -(\frac{1}{2} - y) + 1, -z + 1$			
Hydrogen bonds for $C_7N_1O_4H_{13}$ (**1**)			
O(2)–HO(2) .95(9)	O(2)....O(4)^{ii} 2.578(9)	HO(2)....O(4)^{ii} 1.75(9)	O(2)–HO(2)–O(4)^{ii} 144.(5)
O(3)–HO(3) .70(9)	O(3)....O(1)^{i} 2.775(8)	HO(3)....O(1)^{i} 2.13(9)	O(3)–HO(3)–O(1)^{i} 153.(5)
Symmetry code: $i = -x, -y + 1, -z + 1$; $ii = (\frac{1}{2} + x) - 1, (\frac{1}{2} - y) + 1, z$			



i $C_6H_5CH_2ONH_2 \cdot HCl$, H_2O
ii p-$NO_2C_6H_4OH$, DCC, AcOEt
iii $C_6H_5CH_2OH$, DBU, CH_2Cl_2
iv $(CH_3)_3N \cdot BH_3$, HCl, Et_2O
v $CH_3C(O)Cl$, pyridine, CH_2Cl_2
vi Pd/C, H_2, CH_3OH

1: R = $CH(CH_3)_2$
2: R = CH_2CH_3

Bzl = $C_6H_5CH_2$
ONP = p-$NO_2C_6H_4O$

Scheme 1

δ 8.22 and 7.28 (AB, 4H, C_6H_4), 7.35 (s, 5H, C_6H_5), 5.35 (s, 2H, $CH_2C_6H_5$), 2.70 (q, 2H, CH_2CH_3), 1.15 (t, 3H, CH_2CH_3).

α-(Benzyloximino)benzyl esters (**6**). A solution of DBU (9.12 g, 60 mmol) in 120 ml of CH_2Cl_2 was added dropwise to a stirred solution of **5** (60 mmol) and benzyl alcohol (6.48 g, 60 mmol) in 240 ml of CH_2Cl_2. Stirring was continued at room temperature until completion of the reaction (3 h) as monitored by TLC (CH_2Cl_2/*n*-hexane 1/1 v/v). The reaction mixture was washed successively with 0.1 N aqueous HCl and 0.1 N aqueous NaOH until the yellow colour of the organic layer had completely disappeared. The organic layer was then separated and dried (Na_2SO_4). The solvent was evaporated to give crude **6**, which could be used in the next reaction without further purification in quantitative yield. Column chromatography on silica gel (Merck, silica gel H (type 60), CH_2Cl_2/*n*-hexane 1/1 v/v as eluent) can be applied to remove traces of impurities.
6 [R = $CH(CH_3)_2$]: 86% yield after purification; oil. ^{1}H NMR: δ 7.35 (s, 10H, C_6H_5), 5.26 and 5.21 (2s, 4H, $CH_2C_6H_5$), 3.43 (m, 1H, CH), 1.16 [d, 6H, $(CH_3)_2$].
6 (R = C_2H_5): oil. ^{1}H NMR: δ 7.40 (s, 10H, C_6H_5), 5.30 (s, 4H, $CH_2C_6H_5$), 2.63 (q, 2H, CH_2CH_3), 1.06 (t, 3H, CH_2CH_3).

N-*(Benzyloxy)α-amino acid benzyl esters* (**7**). Trimethylamine–borane (1.83 g, 25 mmol) was added at room temperature to a stirred solution of **6** (10 mmol) in 100 ml of anhydrous ether, saturated with dry HCl. Stirring was continued at room temperature until completion of the reaction (16 h) as monitored by TLC (CH_2Cl_2). After evaporation of the solvent, the residue was dissolved in 50 ml of CH_3COOEt. This solution was washed three times with 30 ml of a 5% aqueous $NaHCO_3$ solution and then once with brine. The organic layer was separated and dried (Na_2SO_4). The residue, after evaporation of the solvent, was purified by column chromatography (Merck, silica gel H (type 60), diisopropyl ether/*n*-hexane 1/1 v/v as eluent).
7 [R = $CH(CH_3)_2$]: 65% yield;oil. ^{1}H NMR: δ 7.31 and 7.26 (2s, 10H, C_6H_5), 5.93 (br, 1H, NH), 5.20 [s, 2H, $(O)COCH_2$], 4.66 (s, 2H, $NOCH_2$), 3.45 (d, 1H, NCH), 2.13–1.46 [m, 1H, $CH(CH_3)_2$], 0.93 and 0.81 [2d, 6H, $(CH_3)_2$].
7 (R = C_2H_5): 58% yield; oil. ^{1}H NMR: δ 7.33 and 7.30 (2s, 10H, C_6H_5), 5.98 (br, 1H, NH), 5.20 [s, 2H, $(O)COCH_2$], 4.71 (s, 2H, $NOCH_2$), 3.61 (m, 1H, NCH), 1.51 (m, 2H, CH_2CH_3) 0.90 (t, 3H, CH_2CH_3).

N-*Acetyl* N-*(benzyloxy) α-amino acid benzyl esters* (**8**). A solution of pyridine (0.87 g, 11 mmol) in 5 ml of dry CH_2Cl_2 was added to an ice-cooled, stirred solution of **7** (10 mmol) and freshly distilled acetyl chloride (0.86 g, 11 mmol) in 30 ml of dry CH_2Cl_2. Stirring was continued at room temperature for 1 h after which time the salt was removed by filtration. The filtrate was washed with 0.1 N aqueous HCl (2 × 30 ml), 5% aqueous $NaHCO_3$ (2 × 30 ml) and H_2O (1 × 30 ml). The organic layer was separated and dried (Na_2SO_4) and the solvent was evaporated to give pure **8**.

8 [R = $CH(CH_3)_2$]: 90% yield; oil. ^{1}H NMR: δ 7.35 (s, 10H, C_6H_5), 5.21 [s, 2H, $(O)COCH_2$], 4.96 and 4.80 (AB, J_{AB} 11 Hz, 2H, $NOCH_2$), 4.79 (d, 1H, NCH), 2.90–2.11 [m, 1H, $CH(CH_3)_2$], 2.11 [s, 3H, $(O)CCH_3$], 1.03 and 0.90 [2d, 6H, $(CH_3)_2$].
8 (R = C_2H_5): 93% yield; oil. ^{1}H NMR: δ 7.33 (s, 10H, C_6H_5), 5.18 [s, 2H, $(O)COCH_2$], 4.90 (t, 3H, $NOCH_2$ and NCH), 2.36–1.65 (m, 2H, CH_2CH_3), 2.13 [s, 3H, $(O)CCH_3$], 0.096 (t, 3H, CH_2CH_3).

N-*Acetyl* N-*hydroxy α-amino acids* (**1** and **2**)

A solution of **8** (10 mmol) in 100 ml of MeOH was treated at room temperature and atmospheric pressure with H_2 and 10% Pd/C (150 mg) until 450 ml of H_2 (20 mmol) had been consumed. After removal of the catalyst by filtration, the solvent was evaporated to give pure **1** or **2** in quantitative yield. The compound was crystallized from acetone/*n*-hexane.
1 [R = $CH(CH_3)_2$]: m.p. 139–141°C. ^{1}H NMR ($CDCl_3/CD_3OD$ 1/1 v/v): δ 4.86 (d, 1H, NCH), 2.83–1.75 [m, 1H, $CH(CH_3)_2$], 2.18 [s, 3H, $(O)CCH_3$], 1.11 and 0.90 [2d, 6H, $(CH_3)_2$].
2 (R = C_2H_5): m.p. 112–114°C. ^{1}H NMR ($CDCl_3/CD_3OD$ 1/1 v/v): δ 5.41–4.68 (m, NCH and HDO*), 2.21 [s, 3H, $(O)CCH_3$], 2.21–1.60 (m, 2H, CH_2CH_3), 0.95 (t, 3H, CH_2CH_3).

Acknowledgements

We wish to thank Mr. *M. Tognolin* and Mr. *F. De Zuane* for their invaluable technical assistance.
This work was supported by the Italian *Consiglio Nazionale delle Ricerche* (C.N.R.) within a *Progetto di Ricerca Bilaterale* between the University of Nijmegen and the Istituto di Chimica e Tecnologia dei Radioelementi del C.N.R., Padova (Decreti Presidente C.N.R. no. 058055 and no. 019886).

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* CD_3OD is contamined with H_2O.

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