Tetrahedron Vol 44, No 17, pp 5403 to 5414, 1988
Printed in Great Britain

0040-4020/88 $3.00+.00
Pergamon Press plc

NEW SYNTHESES OF α-AMINO ACIDS BASED ON *N*-ACYLIMINO ACETATES

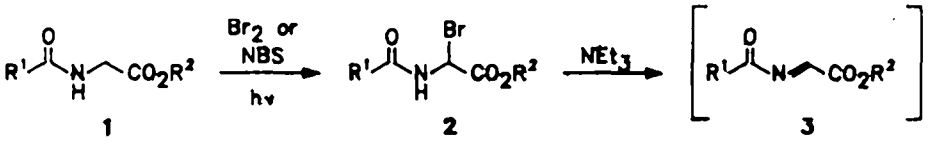
THOMAS BRETSCHNEIDER, WOLFGANG MILTZ,
PETER MÜNSTER and WOLFGANG STEGLICH*

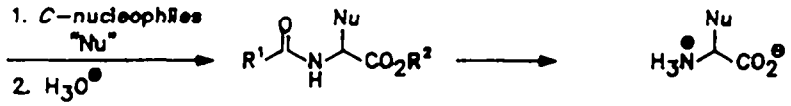
Institut für Organische Chemie und Biochemie der Universität Bonn
Gerhard-Domagk-Straße 1, D-5300 Bonn 1, F.R.G.

(Received in USA 18 January 1988)

Abstract- The reaction of *N*-acylamino-2-bromoacetates 2 (*via* *N*-acylimino acetates 3) with higher order mixed cuprates, trimethylsilyl enol ethers and β-dicarbonyl compounds leads to a variety of α-amino acid derivatives. Their conversion into the free amino acids can be conveniently carried out by the use of *t*-butyl protection. In case of the *N*-acetyl compounds cleavage of the protecting group and optical resolution can be achieved in one step by hog renal acylase.

Electrophilic glycine equivalents are enjoying increasing popularity since *Ben Ishai's* pioneering investigations[1]. In recent years several of these compounds have been introduced for the synthesis of α-amino acids e.g. *N*-acylimino malonates[2], *N*-acylimino acetates[3-5], α-acetoxylated *N*-arylidene glycinates[6] and chiral heterocycles[7,8]. The discovery that a variety of *N*-acylamino acetates 1 can be brominated smoothly to yield the α-bromo derivatives 2 has made this group of glycine equivalents easily available[3,9,10]. On treatment of 2 with *tert.* amines or an excess of organometallic reagents, highly reactive α-acylimino acetates 3 [11] are formed *in situ* which react with a number of *C*-nucleophiles to yield *N*-protected α-amino acid esters.





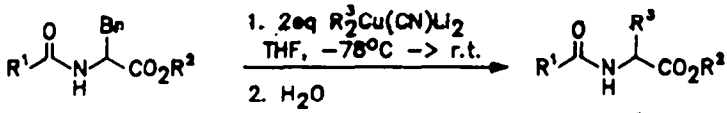
1 – 3	a	b	c	d	e	f	g
R^1	Me	Me	CF_3	Ph	Ph	Ph	OBu^t
R^2	Me	Bu^t	Et	Me	Et	(+)-menthyl	Bu^t

This reaction has been carried out so far with Grignard reagents[3,4,5] and enamines[3,10]. By virtue of its sterically shielded carbonyl groups and the ease of deprotection after C-C-bond formation, *t*-butyl 2-bromo-2-(*t*-butoxycarbonylamino)acetate 2g is the compound of choice for the synthesis of free amino acids[3,12]. We now report on recent progress in the use of *N*-acylimino acetates for α-amino acid synthesis.

A. Reaction of *N*-Acylimino Acetates 3 with Cuprate Reagents

In many cases the reaction of *N*-acylimino acetates with aliphatic Grignard reagents occurs only in modest yield. We therefore tested a variety of alternative organometallic reagents, among which the higher order mixed cuprates, $R_2Cu(CN)Li_2$, developed by *Lipshutz* and coworkers[13] gave by far the best results. This is in agreement with the experience of *O'Donnell*[6] and *Williams*[8] with other electrophilic glycine equivalents.

Reaction of two equivalents of cuprate reagent with one equivalent of 2-acylamino-2-bromoacetate in THF at -78°C leads to the formation of the desired amino acid derivatives in good yield (Table 1). In this way alkyl, alkenyl and aryl groups can be transfered to the *N*-acylimino acetates 3 .



2 4

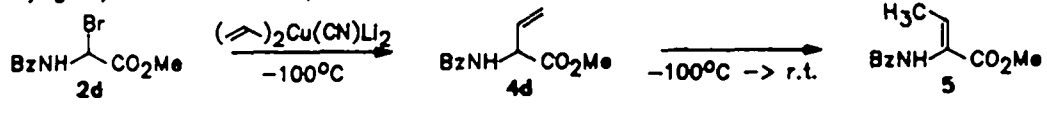
Table 1.

Product No.	R^1	R^2	R^3	yield [%]
4a	Ph	Me	Bu^n	78
4b	Me	Me	Bu^n	64
4c	Ph	Me	Bu^t	30
4d	Ph	Me	$-CH=CH_2$	50
4e	Ph	Me	Ph	83
4f	Ph	Me	1-naphthyl	80
4g	OBu^t	Bu^t	1-naphthyl	75
4h	Me	Me	1-naphthyl	68

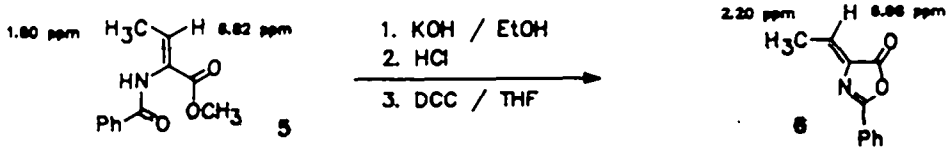
The high selectivity of the higher order mixed cuprates in comparison to other organometallic reagents allows the use of a wide range of protecting groups. Even the use of methyl 2-acetylamino-2-bromoacetate 2a , which fails with Grignard reagents, gives good results. The procedure is suitable for scale-up, which was shown by the synthesis of methyl 2-acetylamino-2-(1-naphthyl)acetate 4h in 60% yield on a 10 gram scale.

Preliminary experiments reacting the chiral *N*-acylimino acetate 3f with $Ph_2Cu(CN)Li_2$ at -100°C resulted in a 'de' of 40% (^1H n.m.r.). The use of other chiral auxiliaries is under active investigation.

The reaction of the corresponding vinyllithium derivative, $(CH_2=CH)_2Cu(CN)Li_2$, with 2-acylamino-2-bromoacetates shows an interesting temperature dependence. At low temperatures the desired vinylglycine derivative is formed and can be isolated by quenching the reaction mixture. On warming to room temperature, however, the vinyl compound undergoes a double bond shift to yield the corresponding (*Z*)-crotonate 5 . The stereochemistry at the double bond was assigned according to ref.[14] by hydrolysis of the ester followed by ring closure to the 2-oxazolin-5-one 6 . The observed diamagnetic shift of the methyl group in the ^1H n.m.r. spectrum of 5 compared to 6 indicates a (*Z*)-stereochemistry.



2d 4d 5



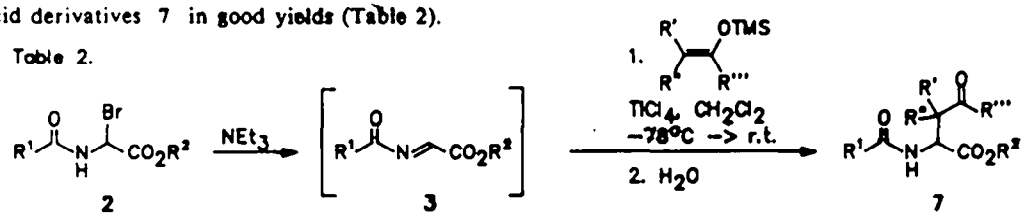
5 6

B. Reaction of *N*-Acylimino Acetates 3 with Silyl Enol Ethers

Previous work has shown[3,10] that *N*-acylimino acetates **3** react smoothly with enamines to yield α-amino-γ-oxo acid derivatives. Because many enamines are difficult to prepare, or are even unaccessible, we extended this method to silyl enol ethers.

The *N*-acylimino acetates **3** react with trimethylsilyl enol ethers in the presence of equimolar amounts of titanium tetrachloride[15] at -78°C to give, after acidic work-up, the desired α-amino-γ-oxo acid derivatives **7** in good yields (Table 2).

Table 2.



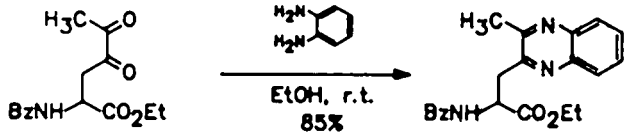
2 **3** **7**

Educts: Bromoester No.	Trimethylsilyl enol ether	Method of prep.	Products: No.	R^1	R^2		yield [%]
2e		A	7a	Ph	Et		58
2e		A	7b	Ph	Et		80
2g		A	7c	OBu^t	Bu^t		60
2b		B	7d	Me	Bu^t		73
2e		A	7e	Ph	Et		50
2e		A	7f	Ph	Et		57
2e		A	7g	Ph	Et		25
2e		A	7h	Ph	Et		83
2e		A	7i	Ph	Et		89
2g		B	7j	OBu^t	Bu^t		78
2b		B	7k	Me	Bu^t		60

In this reaction silyl enol ethers of ketones, β-oxoesters, α-diketones, aldehydes and carboxylic acid esters can be used. Even α-amino acid derivatives with a quarternary β-carbon atom **7h-k** are accessible in high yields. Independently, the reaction of **2g** with the silyl enol ether derived from methyl vinyl ketone has been used by others[13] for the synthesis of a heterocyclic amino acid.

The high diastereoselectivity observed in the reaction with prochiral enamines[3,10] does not occur in the reaction of **3** with silyl enol ethers. Thus the reaction of 1-(trimethylsilyloxy)cyclohexene with **3e** yields a mixture of *syn*- and *anti*-diastereomers in nearly equal amounts.

In the reaction of 3e with 2,3-bis(trimethylsilyloxy)-1,3-butadiene a derivative 7g of the as yet unreported 2-amino-4,5-dioxo-hexanoic acid is formed. By reaction of 7g with 1,2-diaminobenzene the quinoxaline derivative 8 is obtained in high yield.

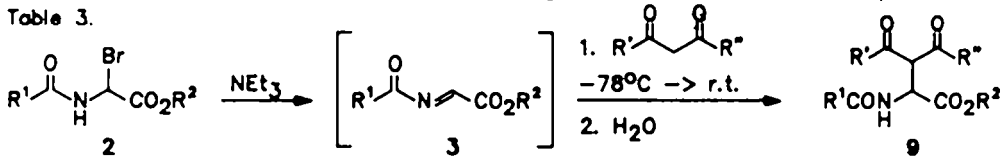


7g 8

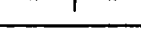
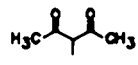
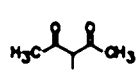
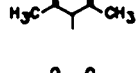
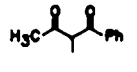
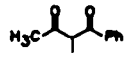
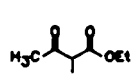
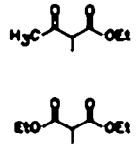
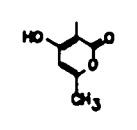
C. Reaction of *N*-Acylimino Acetates 3 with β-Dicarbonyl Compounds

The high reactivity of *N*-acylimines towards CH-acidic compounds[2,16,17] led us to use this reaction for a simple preparation of α-amino acids containing two additional carbonyl groups (table 3). As expected, a great variety of β-diketones, β-oxoesters and malonates reacts smoothly with *N*-acylimino acetates 3 . In the case of unsymmetric β-diketones, a slight diastereomeric excess (≈30%) was observed.

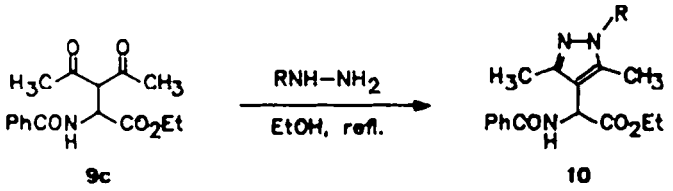
Table 3.



2 3 9

Product No.	R^1	R^2		yield [%]
9a	CF_3	Et		81
9b	OBu^t	Bu^t		82
9c	Ph	Et		92
9d	Ph	Me		62
9e	OBu^t	Bu^t		50
9f	Ph	Me		87
9g	OBu^t	Bu^t		48
9h	Ph	Me		52
9i	Ph	Me		66
9j	OBu^t	Bu^t		60

The products may be converted into heterocyclic compounds by reaction with dinucleophiles. In this manner 9c has been transformed into the pyrazol derivatives 10a and 10b in high yield. For earlier work on similar compounds see *ref.*[1].



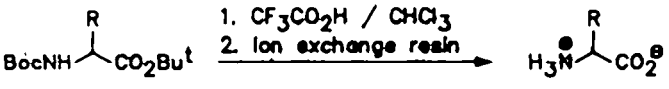
9c 10

No.	R	yield [%]
10a	H	96
10b	Ph	99

D. Deprotection of the derived products

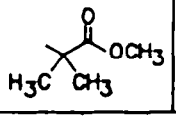
The utility of the described procedures depends critically on the ease of deprotection of the derived amino acid derivatives. This is especially important for compounds containing functional groups such as multiple bonds or carbonyl groups.

Both protecting groups of the *t*-butyl *N*-(*t*-butoxycarbonylamino)acetates are removed easily in one step by treatment with trifluoroacetic acid in chloroform, thus liberating the free amino acids 11 (table 4).

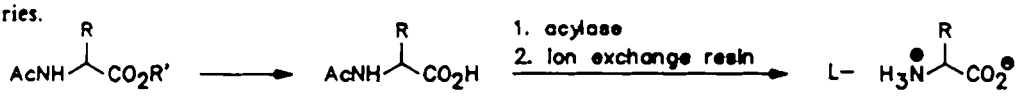


11

Table 4.

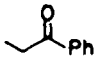
Educt No.	R	Product No.	yield [%]
4g	1-naphthyl	11a	87
7c		11b	61
7j		11c	55

Especially attractive is the combination of an *N*-acetyl protecting group with methyl or *t*-butyl esters. After removal of the ester group, the resulting *N*-acetyl amino acids can be resolved enzymatically by hog renal acylase[18]. This was demonstrated by the synthesis of L-norleucine and L-2-amino-4-oxo-4-phenyl-butanoic acid (table 5). An especially economic, straightforward way to L-amino acids is offered by the route using methyl 2-acetylamino-2-bromoacetate 2a . This is easily available in large quantities from *N*-acetyl glycine in two steps. This synthesis compares favorably to other methods employing chiral auxiliaries.



12 13

Table 5.

Educt No.	R	R'	N-acetyl amino acid No.	N-acetyl amino acid yield [%]	L-amino acid No.	L-amino acid yield [%]
4b	Bu^n	Me	12a	85	13a	82
7d		Bu^t	12b	94	13b	85

Experimental

Melting points were determined with a Büchi melting-point apparatus and are uncorrected. Infrared spectra were obtained using a Perkin Elmer 1420 spectrometer. The proton magnetic resonance spectra were recorded with Varian EM 390, Bruker WH-90 and AC-200 instruments (solutions in deuteriochloroform unless otherwise stated, tetramethylsilane as internal reference). Optical rotations were measured with a Perkin Elmer 241 polarimeter. TLC separations were carried out on silica gel TLC plates Merck 60 F_{254}. Flash chromatography was carried out according to lit.[19] on Merck silica gel (article no. 9385). Organic solutions were dried over unhydrous magnesium sulphate and solvent evaporation was carried out at reduced pressure using a rotatory evaporator. Mass spectra were obtained at 70 eV using an AEI MS 50 spectrometer equipped with a data system. Elemental analyses were performed at the Institut für Organische Chemie und Biochemie, Universität Bonn.

Materials.

Trimethylsilyl Enol Ethers:

1-*Phenyl*-1-(*trimethylsiloxy*)-*ethene* and 1-(*Trimethylsiloxy*)-*cyclohexene* were prepared according to the procedure of *House*[30] by refluxing the carbonyl compound with chlorotrimethylsilane and triethylamine in dimethylformamide. In a similar manner, 2,3-*bis*(*trimethylsiloxy*)-1,3-*butadiene* was prepared according to lit.[31]. 2-*Trimethylsiloxy*-1-*propene* was obtained using the system triethylamine / chlorotrimethylsilane / sodium iodide in acetonitrile[32]. 2-*Methyl*-1-*trimethylsiloxy*-1-*propene* was synthesized using trimethylsilyl triflate / triethylamine in ether[28]. 1-*Methoxy*-2-methyl-1-*trimethylsiloxy*-1-*propene* was prepared by reaction of the corresponding ester enolate with chlorotrimethylsilane[34]. *Methyl* 3-*Trimethylsiloxy*-2-*butenoate* was purchased as an 86% (*E*) / 10% (*Z*) mixture from Fluka AG, Buchs (Switzerland).

Organolithium Compounds:

Vinyllithium was prepared by reaction of tetravinyltin with n-butyllithium in pentane and redissolving the precipitate in THF according to lit.[35].
1-*Naphthyllithium* was synthesized by reaction of 1-bromo-naphthalene with n-butyllithium in ether and redissolving the precipitate in ether / benzene analogous to ref.[36].
The other organolithium compounds used are commercially available.

2-*Acylamino*-2-*bromoacetates* **2**:

t-*Butyl* 2-(*Acetylamino*)*acetate* **1b** was prepared by acetylation of glycine *t*-butylester hydrochloride with acetic anhydride / DMAP in pyridine (2 h, 70°C), usual extractive work up and distillation. (73%) as colorless oil, b.p. 125°C / 0.13 mbar, δ_H 1.45 (9 H, s), 2.00 (3 H, s), 3.87 (2 H, d, *J* 5.5 Hz), 6.38 (1 H, br s), (Found: M^+ + H, 174.1129. $C_8H_{16}NO_3$ requires M + H, 174.1129.

Methyl 2-*Acetylamino*-2-*bromoacetate* **2a** was prepared by esterification of aceturic acid with methanol / $SOCl_2$ and photobromination of the methylester using bromine as decribed in ref.[9]. (95%), m.p. 87 - 90°C, δ_H 2.08 (3 H, s), 3.83 (3 H, s), 6.42 (1 H, d, *J* 10 Hz), 7.08 (1 H, br).

t-*Butyl* 2-*Acetylamino*-2-*bromoacetate* **2b** was obtained by photobromination of **1b** using NBS analogous to lit.[9]. (96%) as slightly yellow oil, δ_H 1.48 (9 H, s), 2.05 (3 H, s), 6.30 (1 H, d, *J* 10.5 Hz), 6.93 (1 H, br).

Methyl 2-*Benzoylamino*-2-*bromoacetate* **2d** and *Ethyl* 2-*Benzoylamino*-2-*bromoacetate* **2e** were prepared by esterification of hippuric acid and photobromination of the resulting esters as described in ref.[9].

t-*Butyl* 2-*Bromo*-2-(t-*butoxycarbonylamino*)*acetate* **2g** was obtained by reaction of glycine *t*-butyl ester hydrochloride with di-*t*-butyl dicarbonate and photobromination of the protected derivate using NBS according to lit.[3].

General Procedure for the Reaction of 2-*Acylamino*-2-*bromoacetates with Higher Order, Mixed Cuprates:*

To a suspension of CuCN (538 mg, 6 mmol, dried azeotropically with toluene (3 ml) at r.t. under reduced pressure) in dry THF (15 ml) under Argon at -78°C is added a solution of the organolithium compound

(12 mmol) in THF *via* syringe. The mixture is allowed to warm to 0°C at which point it becomes homogenous. After 1-2 minutes at 0°C the solution is recooled to -78°C and a solution of the bromoester 2 (3 mmol) in dry THF (8 ml) is added dropwise. After 1 h stirring at -78°C the mixture is allowed to warm to r.t. and quenched with saturated NH_4Cl solution. Extractive work-up with ether, drying of the organic layer over $MgSO_4$ and evaporation of the solvent under reduced pressure leads to the products, which are further purified by flash chromatography on silica gel (eluent: petroleum ether / ethyl acetate).

Methyl 2-(*Benzoylamino*)*hexanoate* **4a** (76%), m.p. 73-74°C, (Found: C, 67.3; H, 7.9; N, 5.5. $C_{14}H_{19}NO_3$ requires C, 67.45; H, 7.7; N, 5.6 %), $\nu_{max.}$(KBr) 3300, 3060, 2950, 1750, 1635, 1535, 1215, 720, 695 cm^{-1}, δ_H 0.70 - 2.10 (9 H, complex), 3.70 (3 H, s), 4.76 (1 H, complex), 6.67 (1 H, d, *J* 7.5 Hz), 7.2 - 7.9 (5 H, complex).

Methyl 2-(*Acetylamino*)*hexanoate* **4b** (64%), m.p. 78-80°C, (Found: C, 57.9; H, 8.9; N, 7.1. $C_9H_{17}NO_3$ requires C, 57.7; H, 9.15; N, 7.5 %), $\nu_{max.}$(KBr): 3280, 3080, 2960, 1750, 1650, 1555, 1220, 1160, 720 cm^{-1}, δ_H 0.73 - 1.90 (9 H, complex), 2.00 (3 H, s), 3.70 (3 H, s), 4.57 (1 H, complex), 6.20 (1 H, br).

Methyl 2-*Benzoylamino*-3,3-*dimethylbutanoate* **4c** (30%), m.p. 65°C, (Found: C, 67.55; H, 7.9; N, 5.4. $C_{14}H_{19}NO_3$ requires C, 67.45; H, 7.7; N, 5.6 %), $\nu_{max.}$(KBr): 3320, 2960, 1740, 1640, 1535, 1370, 1350, 1215, 755, 700 cm^{-1}, δ_H 1.05 (9 H, s), 3.72 (3 H, s), 4.68 (1 H, d, *J* 9.5 Hz), 6.67 (1 H, d, *J* 9.5 Hz), 7.2 - 7.9 (5 H, complex).

Methyl 2-(*Benzoylamino*)*but*-3-*enoate* **4d** (reaction and hydrolysis at -100°C) (50%), m.p. 64-67°C, (Found: C, 65.5; H, 6.05; N, 6.3. $C_{12}H_{13}NO_3$ requires C, 65.7; H, 6.0; N, 6.4 %), $\nu_{max.}$(KBr): 3330, 3010, 2960, 1730, 1655, 1520, 1215, 740, 640 cm^{-1}, δ_H 3.73 (3 H, s), 5.53 (3 H, complex), 5.8 - 6.23 (1 H, complex), 6.93 (1 H, br), 7.22 - 7.93 (5 H, complex).

Methyl 2-*Benzoylamino*-2-*phenyl-acetate* **4e** (83%), m.p. 108-110°C, (Found: C, 71.1; H, 5.7; N, 5.2. $C_{16}H_{15}NO_3$ requires C, 71.4; H, 5.6; N, 5.2 %), $\nu_{max.}$(KBr): 3300, 3030, 2920, 1740, 1615, 1510, 1475, 1150, 725, 680 cm^{-1}, δ_H 3.70 (3 H, s), 5.72 (1 H, d, *J* 6 Hz), 7.0 - 7.9 (11 H, complex).

Methyl 2-*Benzoylamino*-2-(*naphth*-1-*yl*)*acetate* **4f** (80%), m.p. 164-165°C, (Found: C, 75.1; H, 5.4; N, 4.4. $C_{20}H_{17}NO_3$ requires C, 75.2; H, 5.4; N, 4.4 %), $\nu_{max.}$(KBr): 3310, 3030, 2930, 1730, 1620, 1520, 1205, 765, 680 cm^{-1}, δ_H 3.70 (3 H, s), 6.50 (1 H, d, *J* 7.5 Hz), 6.98 (1 H, br), 7.3 - 8.0 (12 H, complex).

t-*Butyl* 2-(t-*Butoxycarbonylamino*)-2-(*naphth*-1-*yl*)*acetate* **4g** (75%), m.p. 101-104°C, (Found: C, 70.2; H, 7.5; N, 3.95. $C_{21}H_{27}NO_4$ requires C, 70.6; H, 7.6; N, 3.9 %), $\nu_{max.}$(KBr): 3400, 2980, 1730, 1705, 1500, 1390, 1365, 1150, 810, 785 cm^{-1}, δ_H 1.33 (9 H, s), 1.40 (9 H, s), 5.45 (1 H, d, *J* 9 Hz), 5.90 (1 H, d, *J* 9 Hz), 7.2 - 8.3 (7 H, complex).

Methyl 2-*Acetylamino*-2-(*naphth*-1-*yl*)*acetate* **4h** (68%), m.p. 150-152°C, (Found: C, 70.2; H, 5.85; N, 5.3. $C_{15}H_{15}NO_3$ requires C, 70.0; H, 5.9; N, 5.4 %), $\nu_{max.}$(KBr): 3320, 3070, 2960, 1750, 1645, 1540, 1225, 1130, 785 cm^{-1}, δ_H 2.02 (3 H, s), 3.73 (3 H, s), 6.36 (2 H, br), 7.39 - 7.63 (4 H, complex), 7.8 - 7.92 (2 H, complex), 8.1 - 8.17 (1 H, complex).

Methyl (Z)-2-(*Benzoylamino*)*but*-2-*enoate* **5** (62%), m.p. 70-72°C, (Found: C, 65.8; H, 6.0; N, 6.3. $C_{12}H_{13}NO_3$ requires C, 65.7; H, 6.0; N, 6.4 %), $\nu_{max.}$(KBr): 3280, 2950, 1730, 1660, 1645, 1510, 1480,1260, 690 cm^{-1}, δ_H 1.80 (3 H, d, *J* 7 Hz), 3.72 (3 H, s), 6.82 (1 H, d, *J* 7 Hz), 7.2 - 8.0 (6 H, complex).

General Procedures for the Reaction of 2-*Acylamino*-2-*bromoacetates with Trimethylsilyl Enol Ethers:*

Method A: To a stirred, cooled (-78°C) solution of the bromoester 2 (5 mmol) in dry dichloromethane (40 ml) is added triethylamine (0.77 ml, 5.5 mmol). After 20 min a solution of titanium tetrachloride (0.60 ml, 5.5 mmol) in dichloromethane (5 ml) is added dropwise, whereby the colour of the solution changes to dark red. After further 10 min of stirring a solution of the trimethylsilyl enol ether (5.5 mmol) in dichloromethane (5 ml) is added dropwise. The mixture is then allowed to warm to r.t. over 12 h and hydrolyzed by addition of dilute aqueous citric acid (40 ml). The organic layer is washed with aqueous $NaHCO_3$, dried with $MgSO_4$ and evaporated to dryness. Purification of the products is achieved by flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 2:1).

Method B: To a stirred, cooled (-78°C) solution of the bromoester 2 (5 mmol) in dry dichloromethane (40 ml) is added successively the trimethylsilyl enol ether (10 mmol) and the titanium tetrachloride (0.60 ml, 5.5 mmol), both dissolved in dichloromethane (5 ml). Then triethylamine (0.77 ml; 5.5 mmol) in dichloromethane (10 ml) is added dropwise, the mixture is allowed to warm to r.t. over 12 h and worked up as described in method A.

Ethyl 2-Benzoylamino-4-oxopentanoate 7a (58%), m.p. 73-74°C, (Found: C, 63.6; H, 6.8; N, 5.6. $C_{14}H_{17}NO_4$ requires C, 63.9; H, 6.5; N, 5.3 %), $\nu_{max.}$(KBr): 3340, 2980, 1725, 1600, 1580, 1530, 1490, 1210, 1025, 760, 715 cm^{-1}, δ_H 1.30 (3 H, t, *J* 7.5 Hz), 2.13 (3 H, s), 3.17 (2 H, complex), 4.18 (2 H, q, *J* 7.5 Hz), 4.90 (1 H, complex), 7.03 - 7.87 (6 H, complex).

Ethyl 2-Benzoylamino-4-oxo-4-phenylbutanoate 7b (80%), m.p. 81-82°C, (Found: C, 70.2; H, 6.1; N, 4.6. $C_{19}H_{19}NO_4$ requires C, 70.1; H, 5.9; N, 4.3 %), $\nu_{max.}$(KBr): 3320, 3060, 2980, 1745, 1690, 1635, 1600, 1575, 1210, 755, 710, 690 cm^{-1}, δ_H 1.22 (3 H, t, *J* 7.5 Hz), 3.75 (2 H, complex), 4.22 (2 H, q, *J* 7.5 Hz), 5.13 (1 H, complex), 7.26 - 8.07 (11 H, complex).

t-*Butyl* 2-(t-*Butoxycarbonylamino*)-4-*oxo*-4-*phenylbutanoate* 7c (60%), m.p. 103-104°C, (Found: C, 65.4; H, 8.0; N, 4.1. $C_{19}H_{27}NO_5$ requires C, 65.3; H, 7.8; N, 4.0 %), $\nu_{max.}$(KBr): 3420, 3050, 2970, 1740, 1700, 1680, 1485, 1390, 1365, 1150, 695 cm^{-1}, δ_H 1.50 (18 H, s), 3.55 (2 H, complex), 4.55 (1 H, complex), 5.55 (1 H, d, *J* 7.5 Hz), 7.2 - 8.0 (5 H, complex).

t-*Butyl* 2-*Acetylamino*-4-*oxo*-4-*phenylbutanoate* 7d (73%) as colourless oil., $\nu_{max.}$(neat): 3300, 3050, 2960, 2920, 1730, 1680, 1520, 1360, 1100, 725, 680 cm^{-1}, δ_H 1.40 (9 H, s), 1.97 (3 H, s), 3.58 (2 H, complex), 4.82 (1 H, complex), 6.62 (1 H, d, *J* 7.5 Hz), 7.3 - 7.7 (3 H, complex), 7.85 - 8.1 (2 H, complex), (Found: M^+ + H 292.1541. $C_{16}H_{22}NO_4$ requires M + H, 292.1549).

Ethyl 2-Benzoylamino-2-(2-*oxocyclohexyl*)*acetate* 7e (50%), 1:1 mixture of two diastereomers, (1'*R*,2*R*)/(1'*S*,2*S*)-(7e) isolated by fractional recrystallization[27]: m.p. 141-142°C, (Found: C, 67.0; H, 7.1; N, 4.8. $C_{17}H_{21}NO_4$ requires C, 67.3; H, 7.0; N, 4.6 %), $\nu_{max.}$(KBr): 3330, 2920, 1730, 1710, 1640, 1530, 1020, 725, 700 cm^{-1}, δ_H 1.27 (3 H, t, *J* 7.5 Hz), 1.50 - 2.60 (8 H, complex), 8.87 (1 H, complex), 4.17 (2 H, q, *J* 7.5 Hz), 4.67 (1 H, dd, *J* 8.5 and 4.0 Hz), 7.10 - 7.60 (4 H, complex), 7.60 - 8.00 (2 H, complex).

Ethyl 2-Benzoylamino-3-*methoxycarbonyl*-4-*oxopentanoate* 7f (57%), 1:1 mixture of two diastereomers, one diastereomer isolated by fractional recrystallisation : m.p. 80-82°C, (Found: C, 60.1; H, 6.0; N, 4.6. $C_{16}H_{19}NO_6$ requires C, 59.8; H, 6.0; N, 4.4 %), $\nu_{max.}$(KBr): 3320, 3060, 2940, 1740, 1730, 1640, 1530, 730, 695 cm^{-1}, δ_H 1.25 (3 H, t, *J* 7.5 Hz), 2.37 (3 H, s), 3.78 (3 H, s), 4.22 (2 H, q, *J* 7.5 Hz), 4.42 (1 H, d, *J* 4.5 Hz), 5.46 (1 H, dd, *J* 9 and 4.5 Hz), 7.25 (1 H, d, *J* 9 Hz), 7.4 - 7.8 (5 H, complex).

Ethyl 2-Benzoylamino-4,5-*dioxohexanoate* 7g .- To hydrolyze the remaining silyl enol ether functionality in the side chain, the crude oil was stirred with THF (30 ml)/1N HCl (1 ml) for 1 h, neutralized with calcium carbonate (2 g), filtered and dried ($MgSO_4$). After solvent evaporation the product was purified by flash chromatography. (25%) as yellow crystalls, m.p. 110-112°C, (Found: C, 61.9; H, 6.0; N, 4.9. $C_{16}H_{17}NO_6$ requires C, 61.85, H, 5.9, N, 4.8 %), $\nu_{max.}$(KBr): 3280, 3050, 2980, 1710, 1630, 1530, 1335, 1090, 725, 690 cm^{-1}, δ_H 1.29 (3 H, t, *J* 7.5 Hz), 2.37 (3 H, s), 3.38 (2 H, complex), 4.25 (2 H, q, *J* 7.5 Hz), 5.05 (1 H, complex), 7.10 (1 H, d, *J* 7 Hz), 7.35 - 7.8 (5 H, complex).

Ethyl 2-Benzoylamino-3,3-*dimethyl*-4-*oxobutanoate* 7h (63%), m.p. 79-80°C, (Found: C, 65.1; H, 6.9; N, 5.1. $C_{16}H_{19}NO_4$ requires C, 65.0, H, 6.9, N, 5.05 %), $\nu_{max.}$(KBr): 3330, 3060, 2960, 1720, 1640, 1600, 1575, 1540, 1340, 705, 690 cm^{-1}, δ_H 1.20 (9 H, complex), 4.22 (2 H, q, *J* 7.5 Hz), 5.17 (1 H, d, *J* 10 Hz), 6.83 (1 H, d, *J* 10 Hz), 7.3 - 8.0 (5 H, complex), 9.68 (1 H, s).

Ethyl 2-Benzoylamino-3-*methoxycarbonyl*-3-*methylbutanoate* 7i (89%), m.p. 45-46°C, (Found: C, 62.4; H, 6.8; N, 4.5. $C_{16}H_{21}NO_6$ requires C, 62.5, H, 6.9, N, 4.6 %), $\nu_{max.}$(KBr): 3350, 3060, 2960, 1730, 1660, 1600, 1575, 1515, 1480, 1200, 710 cm^{-1}, δ_H 1.30 (9 H, complex), 3.70 (3 H, s), 4.18 (2 H, q, *J* 7.5 Hz), 5.00 (1 H, d, *J* 9 Hz), 7.0 - 7.6 (4 H, complex), 7.7 - 8.0 (2 H, complex).

t-*Butyl* 2-(t-*Butoxycarbonylamino*)-3-*methoxycarbonyl*-3-*methylbutanoate* 7j (76%), m.p. 75-76°C, (Found: C, 57.9; H, 8.5; N, 4.4. $C_{16}H_{29}NO_6$ requires C, 58.0, H, 8.8, N, 4.2 %), $\nu_{max.}$(KBr): 3370, 2970, 1730, 1720, 1700, 1510, 1360, 1150, 1040, 880 cm^{-1}, δ_H 1.10 (3 H, s), 1.25 (3 H, s), 1.40 (9 H, s), 1.43 (9 H, s), 3.67 (3 H, s), 4.55 (1 H, d, *J* 10 Hz), 5.23 (1 H, d, *J* 10 Hz).

t-Butyl 2-Acetylamino-3-methoxycarbonyl-3-methylbutanoate **7k** (60%), m.p. 80-82°C, (Found: C, 57.4; H, 8.8; N, 5.05. $C_{12}H_{23}NO_6$ requires C, 57.1, H, 8.5, N, 5.1 %), $\nu_{max.}$(KBr): 3250, 3060, 2970, 1735, 1645, 1550, 1220, 1155, 1135, 865, 840, 790 cm^{-1}, δ_H 1.13 (3 H, s), 1.25 (3 H, s), 1.43 (9 H, s), 2.06 (3 H, s), 3.70 (3 H, s), 4.87 (1 H, d, *J* 10 Hz), 6.20 (1 H, d, *J* 10 Hz).

2-(2-Benzoylamino-2-ethoxycarbonylethyl)-3-methylquinoxaline **8** .- A solution of 1,2-diaminobenzene (11 mg, 0.1 mmol) in ethanol (2 ml) was added to a solution of **7g** (29 mg, 0.1 mmol) in the same solvent (3 ml). After 24 h at r.t. the solvent was evaporated *in vacuo* and the product was purified by recrystallisation from petroleum ether / ethyl acetate. (85%) as greenish-brown crystals, m.p. 130-132°C, (Found: C, 69.0; H, 5.95; N, 11.7. $C_{21}H_{21}N_3O_3$ requires C, 69.4, H, 5.8, N, 11.6 %), $\nu_{max.}$(KBr): 3320, 3060, 2970, 1740, 1625, 1540, 1485, 765, 705, 690 cm^{-1}, δ_H 1.08 (3 H, t, *J* 7.5 Hz), 2.70 (3 H, s), 3.63 (2 H, complex), 4.12 (2 H, q, *J* 7.5 Hz), 5.33 (1 H, complex), 7.26 - 8.11 (10 H, complex).

General Procedure for the Reaction of 2-Acylamino-2-bromoacetates with β-Dicarbonyl Compounds:

The acyliminoester **3** is generated by addition of triethylamine (0.75 ml, 5.5 mmol) to bromoester **2** in dry THF at -78°C. After 30 min the β-dicarbonyl compound (6 mmol), stirred with triethylamine (6 mmol) in dry THF at room temperature for 30 min, is added slowly to the acyliminoester. After warming up the mixture is stirred for 12 h at room temperature. Then aqueous 20% citric acid (5 ml) is added and the solution is neutralised with aqueous sodium hydrogen carbonate. The product is extracted with ethyl acetate (3x) and the dried organic phase is evaporated *in vacuo*. Purification is possible by recrystallisation from ethyl acetate / petroleum ether or by column chromatography on silica gel (eluent: petroleum ether (40 - 60) / ethyl acetate).

Ethyl 2-Trifluoroacetylamino-4-oxo-3-(1-oxoethyl)pentanoate **9a** (81%), m.p. 91°C, $\nu_{max.}$(KBr): 3300, 2980, 1740, 1725, 1700, 1550, 1365, 1320, 1280, 1180, 1020 cm^{-1}, δ_H 1.26 (3 H, t, *J* 4.5 Hz), 2.23 (3 H, s), 2.33 (3 H, s), 4.2 (2 H, q, *J* 4.5 Hz), 4.5 (1 H, d, *J* 3 Hz), 5.16 (1 H, dd, *J* 9 and 3 Hz), 7.43 (1 H, br d, *J* 3 Hz) , (Found: M^+, 297.0826. $C_{11}H_{14}F_3NO_5$ requires M, 297.0868).

t-Butyl 2-(t-Butoxycarbonylamino)-4-oxo-3-(1-oxoethyl)pentanoate **9b** (82%), m.p. 80°C, (Found: C, 58.1; H, 8.2; N, 4.4. $C_{16}H_{27}NO_6$ requires C, 58.3; H, 8.3; N, 4.25 %), $\nu_{max.}$(KBr): 3320, 3000, 2985, 2915, 1735, 1725, 1700, 1685, 1520, 1360, 1310, 1155, 1060 cm^{-1}, δ_H 1.44 (18 H, s), 2.27 (3 H, s), 2.31 (3 H, s), 4.4 (1 H, d, *J* 4.6 Hz), 4.48 (1 H, dd, *J* 9 and 4.6 Hz), 5.58 (1 H, d, *J* 9 Hz).

Ethyl 2-Benzoylamino-4-oxo-3-(1-oxoethyl)pentanoate **9c** (92%), m.p. 117°C, $\nu_{max.}$(KBr): 3300, 2980, 1735, 1720, 1700, 1640, 1530, 1490, 1360, 1330, 1270, 1210, 1170, 1105, 1020, 940, 860, 695 cm^{-1}, δ_H 1.21 (3 H, t, *J* 7.5 Hz), 2.23 (3 H, s), 2.31 (3 H, s), 4.16 (2 H, q, *J* 7.5 Hz), 4.58 (1 H, d, *J* 4.5 Hz), 5.45 (1 H, dd, *J* 9 and 4.5 Hz), 7.33 - 7.5 (4 H, complex), 7.66 - 7.83 (2 H, complex), (Found: M^+, 305.1275. $C_{16}H_{19}NO_5$ requires M, 305.1258).

Methyl 2-Acetylamino-4-oxo-3-(oxophenylmethyl)pentanoate **9d** (62%), m.p. 87°C, (Found: C, 61.85; H, 5.95; N, 4.9. $C_{16}H_{17}NO_5$ requires C, 61.85; H, 5.9; N, 4.8 %), $\nu_{max.}$(KBr): 3280, 3000, 2950, 2920, 1750, 1710, 1675, 1640, 1520, 1440, 1370, 1280, 1210, 1165, 980, 765 cm^{-1}, δ_H 2.4 and 2.43 (3 H, s), 2.68 and 2.8 (3 H, s, ratio: 2.1 : 3.4), 4.1 and 4.13 (3 H, s), 5.3 - 5.53 (2 H, complex), 7.26 - 7.66 (4 H, complex), 7.93 - 8.06 (2 H, complex).

t-Butyl 2-(t-Butoxycarbonylamino)-4-oxo-3-(oxophenylmethyl)pentanoate **9e** (50%) as oil, (Found: C, 64.4; H, 7.5; N, 3.7. $C_{21}H_{29}NO_6$ requires C, 64.4; H, 7.5; N, 3.6 %), $\nu_{max.}$(neat): 3420, 2970, 2920, 1730, 1715, 1700, 1675, 1490, 1365, 1315, 1240, 1230, 1145, 1060 cm^{-1}, δ_H 1.37 (9 H, s), 1.43 (9 H, s), 2.22 (3 H, s), 2.27 (2 H, s), 4.87 (1 H, dd, *J* 9 and 4.5 Hz), 5.23 (1 H, d, *J* 4.5 Hz), 5.42 (0.33 H, d, *J* 9 Hz), 5.70 (0.67 H, d, *J* 9 Hz), 7.33 - 7.69 (3 H, complex), 7.83 - 8.07 (2 H, complex).

Methyl 2-Benzoylamino-3-ethoxycarbonyl-4-oxopentanoate **9f** (87%), m.p. 103°C, (Found: C, 60.1; H, 6.0; N, 4.35. $C_{16}H_{19}NO_6$ requires C, 59.8; H, 6.0; N, 4.4 %), $\nu_{max.}$(KBr): 3320, 2970, 1735, 1710, 1635, 1535, 1330, 1280, 1260, 1180, 1030, 690 cm^{-1}, δ_H (400 MHz) 1.23 and 1.28 (3 H, t, *J* 7 Hz), 2.35 and 2.36 (3 H, s), 3.74 and 3.76 (3 H, s), 4.18 and 4.25 (2 H, q, *J* 7 Hz), 4.40 and 4.41 (1 H, d, *J* 4 Hz), 5.10 and 5.15 (1 H, dd, *J* 9 and 4 Hz), 7.34 and 7.36 (1 H, d, *J* 9 Hz), 7.42 - 7.52 (3 H, complex), 7.76 - 7.95 (2 H, complex).

t-Butyl (t-Butoxycarbonylamino)-3-ethoxycarbonyl-4-oxo-pentanoate **9g** (48%) as oil, (Found: C, 56.45; H, 7.8; N, 3.8. $C_{17}H_{29}NO_7$ requires C, 56.8; H, 8.1; N, 3.9 %), $\nu_{max.}$(neat): 3440, 3380, 2990, 2940, 1725, 1500, 1460, 1390, 1370, 1250, 1155, 1055 cm^{-1}, δ_H 1.27 (3 H, t, *J* 6.5 Hz), 1.43 (18 H, s), 2.27 (3 H, s), 4.1 (1 H, complex), 4.18 (2 H, q, *J* 6.5 Hz), 4.8 (1 H, complex), 5.5 (1 H, complex).

1-Methyl 4-ethyl 2-Benzoylamino-3-(ethoxycarbonyl)butandioate **9h** (52%), m.p. 80°C, (Found: C, 58.45; H, 5.9; N, 4.0. $C_{17}H_{21}NO_7$ requires C, 58.1; H, 6.0; N, 4.0 %), $\nu_{max.}$(KBr): 3260, 2980, 1750, 1650, 1540, 1310, 1260, 1150, 1030, 700 cm^{-1}, δ_H 1.2 (3 H, t, *J* 7.5 Hz), 1.3 (3 H, t, *J* 7.5 Hz), 3.73 (3 H, s), 4.03 - 4.4 (5 H, complex), 5.5 (1 H, dd, *J* 9 and 4.5 Hz), 7.23 - 7.9 (6 H, complex).

Methyl 2-Benzoylamino-2-(4-hydroxy-6-methyl-2-oxo-2H-pyran-3-yl)acetate **9i** (66%), m.p. 170 - 172°C, (Found: C, 60.3; H, 4.9; N, 4.8. $C_{16}H_{15}NO_6$ requires C, 60.6; H, 4.8; N, 4.4 %), $\nu_{max.}$(KBr): 3400, 3050 - 2800, 1750, 1690, 1640, 1600, 1560, 1515, 1480, 1340, 1210, 990, 830, 710 cm^{-1}, δ_H 2.16 (3 H, s), 3.76 (3 H, s), 5.6 (1 H, d, *J* 9 Hz), 5.93 (s, 1 H), 7.33 - 7.56 (3 H, complex), 7.73 - 7.86 (2 H, complex), 8.0 (1 H, br d, *J* 9 Hz), 8.76 (1 H, br).

t-Butyl 2-(t-Butoxycarbonylamino)-2-(1-hydroxy-5,5-dimethyl-3-oxocyclohexen-2-yl)acetate **9j** (60%), m.p. 143°C, (Found: C, 61.6; H, 8.5; N, 3.9. $C_{19}H_{31}NO_6$ requires C, 61.8; H, 8.5; N, 3.8 %), $\nu_{max.}$(KBr): 2990, 2700, 1740, 1725, 1570, 1490, 1390, 1370, 1330, 1260, 1160, 1060 cm^{-1}, δ_H 1.09 (6 H, s), 1.43 (18 H, s), 2.28 (4 H, s), 4.87 (1 H, d, *J* 6.6 Hz), 6.11 (1 H, d, *J* 6.6 Hz), 7.44 (1 H, br).

General Procedure for the Cyclisation of **9** *:*

9c (5 mmol) is dissolved in ethanol (50 ml) and after addition of hydrazine hydrate (100%) or phenylhydrazine (for compounds **10a** or **10b** respectively) (5 mmol) the solution is refluxed for 2 hours. After evaporation to dryness the product may be purified by recrystallisation from ethyl acetate / petroleum ether (40-60) **10a** or by flash-chromatography on silica gel (eluent: ethyl acetate / petroleum ether 1:1) **10b** .

Ethyl 2-Benzoylamino-2-(3,5-dimethylpyrazol-4-yl)acetate **10a** (96%), m.p. 164°C, (Found: C, 63.8; H, 6.6; N, 13.3. $C_{16}H_{19}N_3O_3$ requires C, 63.8; H, 6.35; N, 13.9 %), $\nu_{max.}$(KBr): 3250, 2980, 1745, 1635, 1600, 1575, 1520, 1485, 1335, 1220, 1190, 1150, 1090, 1020, 690 cm^{-1}, δ_H 1.23 (3 H, t, *J* 7.5 Hz), 2.26 (6 H, s), 4.16 (2 H, dq, *J* 7.5 and 3 Hz), 5.63 (1 H, d, *J* 6 Hz), 7.18 (1 H, br d, *J* 6 Hz), 7.26 - 7.5 (3 H, complex), 7.66 - 7.86 (2 H, complex), 9.66 (1 H, br s).

Ethyl 2-Benzoylamino-2-(3,5-dimethyl-N-phenylpyrazol-4-yl)acetate **10b** (99%), m.p. 115°C, (Found: C, 69.8; H, 6.4; N, 11.0. $C_{22}H_{23}N_3O_3$ requires C, 70.0; H, 6.1; N, 11.1 %), $\nu_{max.}$(KBr): 3300, 3060, 2980, 2940, 1740, 1660, 1595, 1520, 1500, 1480, 1365, 1345, 1320, 1215, 1200, 1135, 1080, 1020, 775, 755, 700, 690 cm^{-1}, δ_H 1.26 (3 H, t, *J* 7.5 Hz), 2.36 (3 H, s), 2.4 (3 H, s), 4.23 (2 H, q, *J* 7.5 Hz), 5.7 (1 H, d, *J* 7 Hz), 7.16 (1 H, br d, *J* 7 Hz), 7.26 - 7.5 (8 H, complex), 7.76 (2 H, complex).

General Procedure for the Synthesis of the DL-*Amino Acids:*

The *N*-Boc-amino acid *t*-butyl ester (0.5 mmol) is refluxed for 15 min with trifluoroacetic acid/chloroform 1:1 (20 ml). The solvent is evaporated, the residue dissolved in 0.1N HCl (10 ml) and extracted with ethyl acetate (5 ml). The aqueous phase is applied to an ion exchange column (DOWEX® 50-W-X4, 50-100 mesh, pyridinium form, 25 ml of resin bed). The column is eluted with water followed by 10% aqueous pyridine and the aqueous pyridine fraction is evaporated *in vacuo*.

DL-*2-Amino-2-(naphth-1-yl)acetate* **11a** (87%), m.p. 199-201°C, $\nu_{max.}$(KBr): 3400, 2930, 1655, 1630, 1575, 1515, 1370, 800, 775 cm^{-1}, $\delta_H(CF_3CO_2D)$ 6.42 (1 H, s), 7.57 - 8.33 (7 H, complex).

DL-*2-Amino-4-oxo-4-phenylbutanoic acid* **11b** (61%), m.p. 190-200°C (dec.), (Found: C, 61.9; H, 6.1; N, 7.1. $C_{10}H_{11}NO_3$ requires C, 62.2; H, 5.7; N, 7.25 %), $\nu_{max.}$(KBr): 3320, 3150, 3060, 2910, 2530, 2080, 1690, 1640, 1590, 1530, 755, 690 cm^{-1}, $\delta_H(D_2O)$ 3.79 (2 H, complex), 4.22 (1 H, complex9, 7.4 - 7.8 (3 H, complex), 8.0 - 8.2 (2 H, complex).

DL-2-*Amino*-3-*methoxycarbonyl*-3-*methylbutanoic acid* **11c** (55%), m.p. >250°C (dec.), (Found: C, 47.7; H, 7.5; N, 7.9. $C_7H_{13}NO_4$ requires C, 48.0; H, 7.5; N, 8.0 %), $\nu_{max.}$(KBr): 3400, 3000, 2960, 2610, 1735, 1670, 1620, 1580, 1520, 1400, 1155, 820, 780 cm^{-1}, $\delta_H(D_2O)$ 1.29 (3 H, s), 1.37 (3 H, s), 3.79 (3 H, s), 4.04 (1 H, s).

General Procedures for the Synthesis of the L-*Amino Acids:*

a) *Acidic cleavage of the* t-*butyl esters*:

The *N*-acetylamino acid *t*-butyl ester (1 mmol) is refluxed for 15 min with trifluoroacetic acid / chloroform 1:1 (20 ml). The solvent is evaporated and the crude *N*-acetyl-DL-amino acid is purified by recrystallisation from petroleum ether/ ethyl acetate.

b) *Basic cleavage of the methyl esters*:

The *N*-acetyl amino acid methyl ester (1 mmol) is refluxed for 1 h with a mixture of ethanol (20 ml) and 1N KOH (1.5 ml). Then the solvent is evaporated under reduced pressure, the residue dissolved in water (20 ml), acidified with 1N HCl (2 ml) and extracted with ethyl acetate (3x20 ml). The organic layer is dried with $MgSO_4$ and evaporated to dryness. The crude acid is purified by recrystallisation from petroleum ether/ethyl acetate.

c) *Enzymatic cleavage of the* N-*acetyl amino acids*:

The *N*-acetyl amino acid **12** (1 mmol) is dissolved in water (50 ml) by adjusting the pH to 7.2 with 1N LiOH, immobilized hog renal acylase (500 mg, about 60 units/g) is added and the mixture is stirred at 37°C for 16 h. Then the pH is adjusted to 1-2 with 1N HCl, the enzyme is filtered off and the filtrate is extracted with ethyl acetate. The free L-amino acid **13** is isolated from the aqueous phase using the ion exchange technique described above.

2-(*Acetylamino*)*hexanoic acid* **12a** (85%), m.p. 102-103°C, $\nu_{max.}$(KBr): 3320, 2940, 1705, 1580, 1530, 1200, 990, 780, 700,600 cm^{-1}, δ_H 0.73 - 1.90 (9 H, complex), 2.00 (3 H, s), 4.50 (1 H, complex), 6.40 (1 H, d, *J* 8 Hz), 8.75 (1 H, br).

2-*Acetylamino*-4-*oxo*-4-*phenylbutanoic acid* **12b** (94%), m.p. 165-166°C (dec.), (Found: C, 60.9; H, 5.7; N, 5.6. $C_{12}H_{13}NO_4$ requires C, 61.3; H, 5.6; N, 5.95 %), $\nu_{max.}$(KBr): 3400, 3310, 2300-3200, 1740, 1710, 1655, 1525, 1190, 750, 690 cm^{-1}, $\delta_H(d_6$-DMSO) 1.79 (3 H, s), 3.42 (2 H, complex), 4.71 (1 H, complex), 7.3 - 8.1 (5 H, complex), 8.2 (1 H, d, *J* 8 Hz), 12.1 - 13.2 (1 H, br).

L-2-*Aminohexanoic acid* **13a** (82%), m.p. > 300°C, $[\alpha]_D^{30}$ +22.5° (c 1 in 6N HCl), $\nu_{max.}$(KBr): 2960, 1580, 1405, 1350, 1320, 6650 cm^{-1}, $\delta_H(D_2O)$ 0.87 - 2.13 (9 H, complex), 3.80 (1 H, t, *J* 6 Hz) ppm.

L-2-*Amino*-4-*oxo*-4-*phenylbutanoic acid* **13b** (85%), m.p. 155-160°C (dec.), $[\alpha]_D^{30}$ +42.9° (c 0.105 in 6N HCl), +3.6° (c 0.385 in H_2O), $\nu_{max.}$(KBr): 3050, 2910, 1680, 1590, 1485, 1400, 1210, 745, 680 cm^{-1}, $\delta_H(D_2O)$ 3.79 (2 H, complex), 4.22 (1 H, complex), 7.4 - 7.8 (3 H, complex), 8.0 - 8.2 (2 H, complex) ppm.

Acknowledgements

We thank Prof. Ch. Wandrey, KFA Jülich, for a gift of immobilized hog renal acylase. We are also grateful to Dr. J.-P. Obrecht, SOCAR AG, Dübendorf, Switzerland, for providing us the manuscript of his unpublished results prior to its disclosure. The Theodor Laymann Stiftung is acknowledged for the award of a studentship (T. B.).

References

1 D. Ben-Ishai, J. Altmann, Z. Bernstein and N. Peled, *Tetrahedron* ,1978, 34, 67 and earlier word as cited herein.

2 R. Kober, W. Hammes and W. Steglich, *Angew. Chem.* 1982, 94, 213; *Angew. Chem. Int. Ed. Engl.* 1982, 21, 203.

3 P. Münster and W. Steglich, *Synthesis*, 1987, 223.

4 A. L. Castelhano, S. Horne, R. Billedeau and A. Krantz, *Tetrahedron Lett.*, 1986, 27, 2435.

5 P. Ermert, I. Meyer, Ch. Stucki, J. Schneebeli and J.P. Obrecht, submitted

6 a) M. J. O'Donnell and J.-B. Falmagne, *Tetrahedron Lett.*, 1985, 26, 299.
b) M. J. O'Donnell and J.-B. Falmagne, *J. Chem. Soc., Chem. Commun.*, 1985, 1168.

7 U. Schöllkopf, H.-J. Neubauer and M. Hauptreif, *Angew. Chem.*, 1985, 97, 1065; *Angew. Chem. Int. Ed. Engl.*,1985, 24, 1066.

8 P. J. Sinclair, D. Zhai, J. Reibenspies and R. M. Williams, *J. Amer. Chem. Soc.*, 1986, 108, 1103.

9 R. Kober and W. Steglich, *Liebigs Ann. Chem.*,1983, 599.

10 R. Kober, K. Papadopoulos, W. Miltz, D. Enders and W. Steglich, H. Reuter and H. Puff, *Tetrahedron*, 1985, 41, 1693.

11 I. Malassa and D. Matties, *Chem.-Ztg.*, 1987, 111, 181 and lit. cited in there.

12 P. Hartmann and J.-P. Obrecht, *Synth. Commun.*, in press.

13 B. H. Lipshutz, R. S. Wilhelm and J. A. Kozlowski, *Tetrahedron*, 1984, 40, 5005.

14 V. Austel and W. Steglich, *Chem. Ber.*, 1975, 108, 2361.

15 T. Mukaiyama, *Angew. Chem.*, 1977, 89, 858; *Angew.Chem. Int.Ed.Engl.*,1977, 16, 817.

16 a) F. Weygand and W. Steglich, *Chem.Ber.*,1965, 98, 487.
b) M. Ozaki, T. Iwasaki, M. Miyoshi and K. Matsumoto, *J. Org. Chem.*, 1979, 44, 1714.

17 D. H. Rich and M. K. Dhaon, *Tetrahedron Lett.*,1983, 24, 1671.

18 J. P. Greenstein and M. Winitz, 'Chemistry of the Amino Acids', Chapman and Hall, London, 1985.

19 W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.*, 1978 43, 2925.

20 H. O. House, L. J. Czuba, M. Gall and H. D. Olmstead, *J. Org. Chem.*,1969, 34, 2324.

21 S. Murai, I. Ryu, Y. Kadono, H. Katayama and K. Kondo, *Chem. Lett.*, 1977, 1219.

22 P. Cazeau, F. Moulines, O. Laporte and F. Douboudin, *J. Organomet. Chem.*, 1980, 201, C9.

23 H. Emde, A. Götz, K. Hofmann and G. Simchen, *Liebigs Ann. Chem.*, 1981, 1643.

24 C. Ainsworth, F. Chen and Y. N. Kuo, *J. Organomet. Chem.*, 1972, 46, 59.

25 D. Seyferth and M. A. Weiner, *J.Amer.Chem.Soc.*, 1961, 83, 3583.

26 M. Schlosser and V. Ladenberger, *J. Organomet. Chem.*, 1967, 8, 193.

27 R. Kober, Dissertation, University of Bonn, 1984.