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N-Acyl-α-triphenylphosphonioglycinates: A Novel Cationic Glycine Equivalent and its Reactions with Heteroatom Nucleophiles

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Summary. Two simple and convenient methods of transforming easily accessible 4-phosphoranylidene-5(4*H*)-oxazolones into N-acyl-α-triphenylphosphonioglycinates are described. N-Acyl-α-triphenylphosphonioglycinates react smoothly with heteroatom nucleophiles in the presence of *DBU* or triethylamine yielding the corresponding α-functionalized glycine derivatives.

Keywords. 4-Phosphoranylidene-5(4*H*)-oxazolones; α-Triphenylphosphonioglycinates; Cationic glycine equivalent; Glycine α-functionalization; α-Heterosubstituted glycine derivatives.

N-Acyl-α-triphenylphosphonionoglycinate: Ein neues kationisches Glycinäquivalent und seine Reaktionen mit Heteroatomnucleophilen

Zusammenfassung. Zwei einfache Methoden zur Überführung der leicht zugänglichen 4-Phosphoranyliden-5(4*H*)-oxazolone in N-Acyl-α-triphenylphosphonionoglycinate werden beschrieben. Die N-Acyl-α-triphenylphosphonionoglycinate reagieren leicht mit Heteroatomnucleophilen in Gegenwart von *DBU* oder Triethylamin zu den entsprechenden α-funktionalisierten Glycinderivaten.

Introduction

There is a strong demand for an effective methodology for the synthesis of α-amino acids due to the frequent occurrence of natural, rare, biologically active non-proteinogenic amino acids. Moreover, the synthesis of natural and unnatural non-proteinogenic α-amino acids has become an area of great importance with the advent of peptide-derived chemotherapeutics [1].

A considerable part of α-amino acid synthetic methods makes use of anionic and cationic glycine equivalents (**1** and **2**) [1]. One of the successful approaches to the synthesis of α-heterosubstituted glycine derivatives consists in the reaction of glycine cationic equivalents with heteroatom nucleophiles. N-Acyl-α-hydroxy- and N-acyl-α-methoxyglycinates (**3a**, **b**) have been reported to be the first glycine

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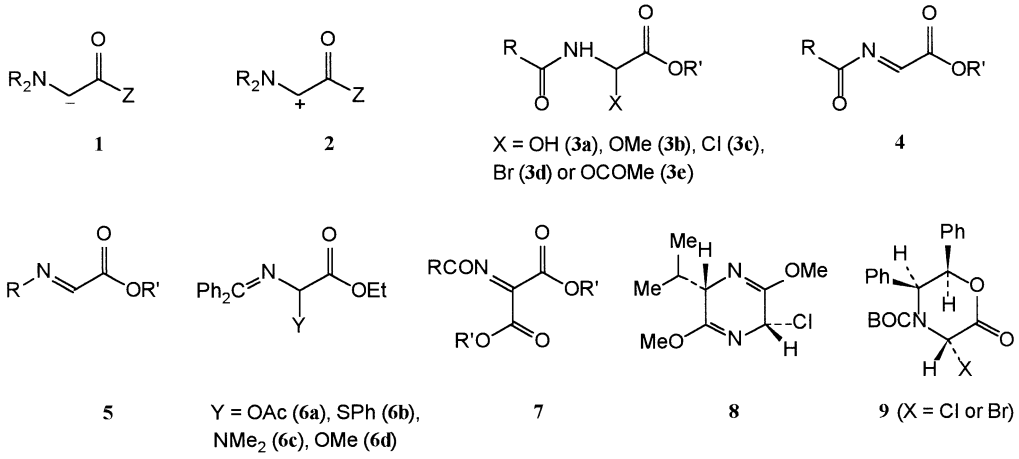


Scheme 1

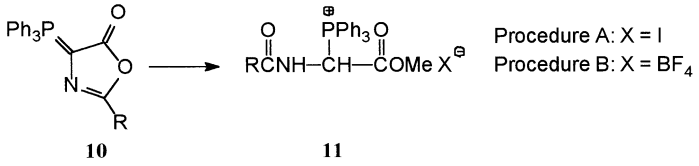
cationic equivalents in the pioneering works of *Ben-Ishai et al.* [2]. During the last two decades, several other electrophilic glycine equivalents have been introduced for the synthesis of α-amino acids, *e.g.* N-acyl-α-chloro- (**3c**) [3] and N-acyl-α-bromoglycinates (**3d**) [3–5] and – obtained *in situ* from them – unstable N-acyliminoacetates (**4**) [4, 5], N-acyl-α-acetoxyglycinates (**3e**) [6], iminoacetates (**5**) [7], α-acetoxy-, α-phenylthio-, α-dimethylamino-, and α-methoxy-N-diphenylmethyleneglycinates (**6a–d**) [8], N-acyliminomalonates (**7**) [9], chlorinated *bis*-lactim ethers (**8**) [10], and 3-chloro- or 3-bromo-2,3,5,6-tetrahydro-4*H*-1,4-oxazin-2-one derivatives (**9**) [11]. The search for new effective synthons of this kind is still an important challenge for organic chemists.

In this contribution, we report the synthesis and properties of N-acyl-α-triphenylphosphonioglycinates as well as their reactions with a variety of heteroatom nucleophiles. These hitherto unknown compounds may be considered as new cationic glycine equivalents.

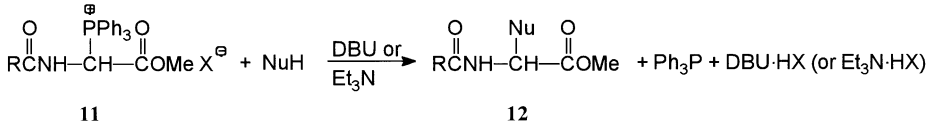
Results and Discussion

Recently, we have described a new convenient and effective synthesis of 4-triphenylphosphoranylidene-5(4*H*)-oxazolones (**10**), a hardly known class of phosphorus ylides derived from 5(4*H*)-oxazolones [12]. Ylides **10** react smoothly with acetyl iodide in acetonitrile at room temperature, yielding crystalline 4-C-acylation products [13] which, in turn, under the influence of methanol undergo deacylation followed by ring opening to give N-acyl-α-triphenylphosphonioglycinate iodides **11a**, **b**. We have also developed a direct, simple synthesis of similar N-acyl-α-triphenylphosphonioglycinate tetrafluoroborates (**11c–e**) from ylides **10** which consists in the treatment of the ylide with an ethereal solution of HBF_4 in methanol (Scheme 2).

N-Acyl-α-triphenylphosphonioglycinates are crystalline compounds, stable at room temperature when protected from moisture, well soluble in CH_2Cl_2, $CHCl_3$, and acetonitrile, but insoluble in diethyl ether. They can be purified by dissolution in CH_2Cl_2 and precipitation with diethyl ether. The structure of N-acyl-α-



Scheme 2



Scheme 3

triphenylphosphonioglycinates **11** was confirmed by their spectroscopic properties (IR, ^{1}H and ^{13}C NMR) as well as by satisfactory results of elemental analyses; in particular, the values of the ^{13}C chemical shifts and the C–P$^+$ coupling constants for the Ph_3P^+ and P$^+$-CH< groups agree very well with the data reported in our previous paper for similar 4-triphenylphosphonio-5(4*H*)-oxazolones [14].

N-Acyl-α-triphenylphosphonioglycinates **11** react easily with a variety of O-, S-, or N-nucleophiles (Nu = PhO, PhS, $PhCH_2S$, *t*-BuS, 4-nitroimidazol-1-yl, imidazol-1-yl, benzotriazol-1-yl, phthalimido, pyrazol-1-yl, cyclohexylamino) in the presence of 1,8-diazabicyclo[5.4.0]undecene-7 (*DBU*) or triethylamine in acetonitrile or methanol at room temperature yielding the corresponding α-heterosubstituted glycine derivatives **12**, usually in a good to excellent yields (Scheme 3).

The structure of α-heterosubstituted N-acyl-glycinates **12** was confirmed by their spectroscopic data (IR, ^{1}H and ^{13}C NMR) as well as by satisfactory elemental analyses. The assignments of carbon signals of the CHNu and OMe groups in compounds **12c**, **12d**, **12h**, and **12i** as well as proton and carbon signals of the pyrazol-1-yl group in **12i** are based on HETCOR experiments.

In summary, the presently reported routes offer an easy access to the hitherto unknown N-acyl-α-triphenylphosphonioglycinates, which, being easily accessible, stable compounds of high reactivity towards heteroatom nucleophiles, seem to be a new, interesting cationic glycine equivalent. Their reactions with heteroatom nucleophiles enable an easy entry to α-heterosubstituted glycine derivatives.

Experimental

Melting points, determined in capillary tubes, are uncorrected. IR spectra were recorded on a Zeiss Specord M 80 spectrophotometer; the measurements were carried out in CH_2Cl_2 (0.2 *M*) using cells of 0.075 mm. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Varian UNITY INOVA-300 spectrometer operating at 300 and 75.5 MHz, respectively, in the FT mode using *TMS* as an internal standard. Elemental analyses proved to be in satisfactory agreement with the calculated values (C, H, N, P).

Ylides **10** (R = Ph, *t*-Bu, Me) were synthesized as described previously [12]. Commercial grade acetonitrile, CH_2Cl_2, diethyl ether, benzene, and ethyl acetate were distilled and dried over molecular sieves (4 Å). Triethylamine was purified according to the procedure given by *Sauer* [15].

Synthesis of N-acyl-α-triphenylphosphonioglycinates **11**

Procedure A

Ylides **10** were acylated with acetyl iodide as described in our previous paper [13]. 20 ml methanol were added to 10 mmol of the acylation product, and the reaction mixture was stirred for the time given and evaporated to dryness. Crude **11** was dissolved in CH_2Cl_2, the pure product was precipitated with a twice as large volume of diethyl ether, filtered, washed with a mixture of CH_2Cl_2 and diethyl ether (1:2; v/v), and dried at 0.02–0.05 mm Hg at 20°C for 1 h.

Procedure B

To a stirred suspension of 10 mmol ylide **10** in 20 ml methanol, an etheral solution of 1.72 ml HBF_4 (54%, 12.5 mmol) was added at 0°C. The mixture was stirred for the time given and worked up as described above for *Procedure A*.

Methyl N-benzoyl-α-triphenylphosphonioglycinate iodide (**11a**, *R* = Ph, *X* = I; $C_{28}H_{25}INO_3P$)

Procedure A, 20°C, 3 h; yield: 84%; m.p.: 137–137.5°C; ^{1}H NMR (δ): 9.48 (dd, 1H, $J_{P\text{-}H} = 5.3$ Hz, $J_{H\text{-}H} = 7.6$ Hz, NH), 8.13–7.29 (m, 20H, Ph_3P^+, Ph), 7.24 (dd, 1H, $J_{P\text{-}H} = 16.3$ Hz, $J_{H\text{-}H} = 7.7$ Hz, CH), 3.61 (s, 3H, OMe) ppm; ^{13}C NMR (δ): 167.1 (d, $J = 0.5$ Hz, CONH), 54.4 (d, $J = 59.5$ Hz, CHP^+), 165.2 (d, $J = 8.6$ Hz, *C*OOMe), 53.8 (OMe), 118.6 (d, $J = 85.2$ Hz, Ph_3P, C_1), 135.0 (d, $J = 10.0$ Hz, Ph_3P, C_2), 129.8 (d, $J = 13.1$ Hz, Ph_3P, C_3), 134.7 (d, $J = 3.0$ Hz, Ph_3P, C_4), 132.6, 130.9, 128.5, 127.6 (Ph) ppm; IR: $\nu = 3200$m, 1771vs, 1730vs, 1663vs, 1522s cm^{-1}.

Methyl N-pivaloyl-α-triphenylphosphonioglycinate iodide (**11b**, *R* = *t*-Bu, *X* = I; $C_{26}H_{29}INO_3P$)

Procedure A, 20°C, 3 h; yield: 81%; m.p.: 138.5–139°C; ^{1}H NMR (δ): 8.80 (dd, 1H, $J_{P\text{-}H} = 13.7$ Hz, $J_{H\text{-}H} = 6.9$ Hz, NH), 8.04–7.52 (m, 15H, Ph_3P^+), 7.18 (dd, 1H, $J_{P\text{-}H} = 16.2$ Hz, $J_{H\text{-}H} = 7.4$ Hz, CH), 3.58 (s, 3H, OMe), 0.93 (s, 9H, *t*-Bu) ppm; ^{13}C NMR (δ): 179.0 (d, $J = 0.5$ Hz, CONH), 53.6 (d, $J = 60.5$ Hz, CHP^+), 165.1 (d, $J = 8.6$ Hz, *C*OOMe), 53.6 (OMe), 119.1 (d, $J = 85.7$ Hz, Ph_3P, C_1), 135.1 (d, $J = 10.1$ Hz, Ph_3P, C_2), 129.7 (d, $J = 14.1$ Hz, Ph_3P, C_3), 134.6 (d, $J = 3.0$ Hz, Ph_3P, C_4), 38.3 (*C*Me$_3$), 27.0 (C*Me*$_3$) ppm; IR: $\nu = 3230$m, 1770vs, 1728vs, 1663vs, 1512s cm^{-1}.

Methyl N-benzoyl-α-triphenylphosphonioglycinate tetrafluoroborate (**11c**, *R* = Ph, *X* = BF_4; $C_{28}H_{25}BF_4NO_3P$)

Procedure B, 0°C, 2 h; yield: 64%; m.p.: 170.5–172°C; ^{1}H NMR (δ): 8.87 (dd, 1H, $J_{P\text{-}H} = 4.7$ Hz, $J_{H\text{-}H} = 8.0$ Hz, NH) 7.98–7.29 (m, 20H, Ph_3P^+, Ph), 6.61 (dd, 1H, $J_{P\text{-}H} = 16.1$ Hz, $J_{H\text{-}H} = 7.6$ Hz, CH), 3.64 (s, 3H, OMe) ppm; ^{13}C NMR (δ): 167.8 (d, $J = 0.5$ Hz, CONH), 55.3 (d, $J = 60.4$ Hz, CHP^+), 165.4 (d, $J = 7.9$ Hz, *C*OOMe), 53.9 (OMe), 118.5 (d, $J = 85.2$ Hz, Ph_3P, C_1), 134.8 (d, $J = 10.1$ Hz, Ph_3P, C_2), 129.8 (d, $J = 13.1$ Hz, Ph_3P, C_3), 134.8 (d, $J = 3.0$ Hz, Ph_3P, C_4), 132.6, 130.9, 128.5, 127.4 (Ph) ppm; IR: $\nu = 3360$m, 1775vs, 1734vs, 1669vs, 1531s cm^{-1}.

Methyl N-pivaloyl-α-triphenylphosphonioglycinate tetrafluoroborate
(**11d**, $R = t$-Bu, $X = BF_4$; $C_{26}H_{29}BF_4NO_3P$)

Procedure B, 0°C, 1.5 h; yield: 77%; m.p.: 179–181°C; ^{1}H NMR (δ): 8.20 (dd, 1H, $J_{P\text{-}H} = 13.6$ Hz, $J_{H\text{-}H} = 6.8$ Hz, NH), 7.95–7.54 (m, 15H, Ph_3P^+), 6.35 (dd, 1H, $J_{P\text{-}H} = 16.1$ Hz, $J_{H\text{-}H} = 7.2$ Hz, CH), 3.60 (s, 3H, OMe), 0.89 (s, 9H, *t*-Bu) ppm; ^{13}C NMR (δ): 179.6 (d, $J = 0.5$ Hz, CONH), 54.5 (d, $J = 61.3$ Hz, CHP^+), 165.2 (d, $J = 7.9$ Hz, *C*OOMe), 53.7 (OMe), 119.0 (d, $J = 85.8$ Hz, Ph_3P, C_1), 134.9 (d, $J = 10.1$ Hz, Ph_3P, C_2), 129.8 (d, $J = 13.1$ Hz, Ph_3P, C_3), 134.7 (d, $J = 3.0$ Hz, Ph_3P, C_4), 38.3 (*C*Me$_3$), 26.6 (C*Me*$_3$) ppm; IR: $\nu = 3378$m, 1772vs, 1732vs, 1668vs, 1522s cm^{-1}.

Methyl N-acetyl-α-triphenylphosphonioglycinate tetrafluoroborate
(**11e**, $R = Me$, $X = BF_4$; $C_{23}H_{23}BF_4NO_3P$)

Procedure B, 0°C, 1 h; yield: 80%; m.p.: 165–167°C; ^{1}H NMR (δ): 8.35 (d, 1H, $J_{H\text{-}H} = 8.2$ Hz, NH), 7.87–7.60 (m, 15H, Ph_3P^+), 6.46 (dd, 1H, $J_{P\text{-}H} = 15.5$ Hz, $J_{H\text{-}H} = 8.5$ Hz, CH), 3.62 (s, 3H, OMe), 1.77 (s, 3H, Me) ppm; ^{13}C NMR (δ): 171.5 (d, $J = 0.5$ Hz, CONH), 54.0 (d, $J = 59.2$ Hz, CHP^+), 165.1 (d, $J = 7.6$ Hz, *C*OOMe), 54.1 (OMe), 117.4 (d, $J = 85.1$ Hz, Ph_3P, C_1), 134.6 (d, $J = 10.1$ Hz, Ph_3P, C_2), 130.1 (d, $J = 12.8$ Hz, Ph_3P, C_3), 135.2 (d, $J = 3.0$ Hz, Ph_3P, C_4), 21.6 (Me) ppm; IR: $\nu = 3342$m, 1771vs, 1737vs, 1687vs, 1525s cm^{-1}.

Reaction of N-acyl-α-triphenylphosphonioglycinates **11** *with heteroatom nucleophiles (general procedure)*

A solution of 20 mmol nucleophile and 1.78 ml *DBU* (12 mmol) or 1.66 ml triethylamine (12 mmol) in 1.6 ml acetonitrile or 1.2 ml methanol was added dropwise to a stirred solution or suspension of 10 mmol **11** in 2.4 ml acetonitrile or 1.8 ml methanol. The mixture was stirred at room temperature for the time given, and the solvent was removed under reduced pressure. The product was isolated from the residue by column chromatography on silica gel (Kieselgel 60 Merck, 0.063–0.200 mm, 45 ml) eluting with ethyl acetate (**12e**), a mixture of ethyl acetate and benzene in a volume ratio of 1:1 (**12g**, **h** and **12j**), 1:5 (**12a**,**d** and **12i**), or with a mixture of ethyl acetate and methanol in a volume ratio of 5:1 (**12f**). The crude product was recrystallized from benzene or from a mixture of benzene and hexane.

Methyl N-pivaloyl-α-phenoxyglycinate (**12a**, $R = t$-Bu, $Nu = PhO$; $C_{14}H_{19}NO_4$)

Starting material: **11b**; MeCN in the presence of Et_3N; 72 h yield: 35%; m.p.: 74–76°C; ^{1}H NMR (δ): 7.27–7.17 (m, 2H, Ph), 7.05–6.91 (m, 3H, Ph), 6.70 (d, br, 1H, $J = 9.3$ Hz, NH), 6.26 (d, 1H, $J = 9.5$ Hz, CH), 3.77 (s, 3H, OMe), 1.12 (s, 9H, *t*-Bu), 7.27–7.17 (m, 2H, Ph), 7.05–6.91 (m, 3H, Ph), 6.70 (d, br, 1H, $J = 9.3$ Hz, NH), 6.26 (d, 1H, $J = 9.5$ Hz, CH), 3.77 (s, 3H, OMe), 1.12 (s, 9H, *t*-Bu) ppm; ^{13}C NMR (δ): 178.3 (CONH), 76.5 (*CH*Nu), 168.2 (*C*OOMe), 53.1 (OMe), 39.0 (*C*Me$_3$), 27.2 (C*Me*$_3$), 156.1, 129.6, 122.9, 116.9, (Ph: C_1, C_3, C_4, C_2) ppm; IR: $\nu = 3440$, 1756vs, 1681vs, 1180s cm^{-1}.

Carrying out the reaction in MeOH in the presence of *DBU* for 1 h afforded 42% **12a**; m.p.: 73.5–75.5°C; IR: $\nu = 3444$m, 1755vs, 1686vs, 1177s cm^{-1}.

Methyl N-pivaloyl-α-phenylthioglycinate (**12b**, $R = t$-Bu, $Nu = PhS$; $C_{14}H_{19}NO_3S$)

Starting material: **11b**; MeCN in the presence of Et_3N; 1 h; yield: 99%; m.p.: 36–37°C; ^{1}H NMR (δ): 7.53–7.29 (m, 5H, Ph), 6.39 (d, br, 1H, $J = 8.4$ Hz, NH), 5.74 (d, 1H, $J = 8.6$ Hz, CH), 3.78 (s, 3H, OMe), 1.15 (s, 9H, *t*-Bu) ppm; ^{13}C NMR (δ): 177.0 (CONH), 56.1 (*CH*Nu), 169.3 (*C*OOMe), 52.9

(OMe), 38.8 ($C\mathrm{Me_3}$), 27.2 ($C\mathit{Me_3}$), 135.5, 130.0, 129.4, 129.1 (Ph: C_2, C_1, C_4, C_3) ppm; IR: $\nu = 3442$m, 1736vs, 1671vs, 1184vs $\mathrm{cm^{-1}}$.

Carrying out the reaction in MeOH in the presence of Et_3N for 1 h afforded 72% **12b** m.p.: 36.5–37.5°C; IR: $\nu = 3442$m, 1738vs, 1671vs, 1180vs $\mathrm{cm^{-1}}$.

Methyl N-pivaloyl-α-benzylthioglycinate (**12c**, $R = t$-Bu, $Nu = \mathrm{PhCH_2S}$; $\mathrm{C_{15}H_{21}NO_3S}$)

Starting material: **11b**; MeCN in the presence of Et_3N; 0.5 h; yield: 89%; m.p.: 52–54°C; ^{1}H NMR (δ): 7.42–7.16 (m, 5H, Ph), 6.32 (d, br, 1H, $J = 7.8$ Hz, NH), 5.55 (d, 1H, $J = 8.3$ Hz, CH), 3.91 (d, 1H, $J = 14.1$ Hz, CH_2), 3.85 (d, 1H, $J = 14.1$ Hz, CH_2), 3.75 (s, 3H, OMe), 1.09 (s, 9H, *t*-Bu) ppm; ^{13}C NMR (δ): 177.5 (CONH), 53.9 (*CHNu*), 169.5 (*C*OOMe), 53.0 (OMe), 38.7 ($C\mathrm{Me_3}$), 27.2 ($C\mathit{Me_3}$), 137.8, 129.0, 128.7, 127.4 (Ph: C_1, C_2 or C_3, C_3 or C_2, C_4), 35.6 (CH_2) ppm; IR: $\nu = 3442$m, 1735vs, 1669vs, 1180vs $\mathrm{cm^{-1}}$.

Methyl N-pivaloyl-α-t-buthylthioglycinate (**12d**, $R = t$-Bu, $Nu = (\mathrm{CH_3})_3\mathrm{CS}$; $\mathrm{C_{12}H_{23}NO_3S}$)

Starting material: **11b**; MeCN in the presence of Et_3N; 1 h; yield: 60%; m.p.: 63–64°C; ^{1}H NMR (δ): 6.33 (d, br, 1H, $J = 7.9$ Hz, NH), 5.56 (d, 1H, $J = 8.7$ Hz, CH), 3.77 (s, 3H, OMe), 1.40 (s, 9H, $\mathrm{SCMe_3}$), 1.21 (s, 9H, $\mathrm{CCMe_3}$) ppm; ^{13}C NMR (δ): 177.2 (CONH), 52.2 (*CHNu*), 170.5 (*C*OOMe), 52.9 (OMe), 38.6 ($C\mathrm{Me_3}$), 27.2 ($C\mathit{Me_3}$), 45.7 ($\mathrm{SCMe_3}$), 31.1 ($\mathrm{SC}\mathit{Me_3}$) ppm; IR: $\nu = 3460$m, 1745vs, 1670vs, 1179vs $\mathrm{cm^{-1}}$.

Methyl N-pivaloyl-α-(4-nitroimidazol-1-yl)glycinate (**12e**, $R = t$-Bu, $Nu = 4$-nitroimidazol-1-yl; $\mathrm{C_{11}H_{16}N_4O_5}$)

Starting material: **11b**; MeCN in the presence of *DBU*; 2 h; yield: 98%; m.p.: 138–138.5°C; ^{1}H NMR (δ): 7.93 (d, 1H, $J = 1.6$ Hz, $\mathrm{CH_{imid}}$, H_5), 7.68 (d, 1H, $J = 1.5$ Hz, $\mathrm{CH_{imid}}$, H_2), 7.35 (d, br, 1H, $J = 6.1$ Hz, NH), 6.43 (d, 1H, $J = 6.8$ Hz, CH), 3.90 (s, 3H, OMe), 1.24 (s, 9H, *t*-Bu) ppm; ^{13}C NMR (δ): 178.8 (CONH), 62.5 (*CHNu*), 165.9 (*C*OOMe), 54.5 (OMe), 38.9 ($C\mathrm{Me_3}$), 27.1 ($C\mathit{Me_3}$), 148.1, 135.7, 117.9 ($\mathrm{C_3H_2N_2NO_2}$: C_4, C_2, C_5) ppm; IR: $\nu = 3430$m, 1758vs, 1686vs, 1182vs $\mathrm{cm^{-1}}$.

Methyl N-pivaloyl-α-(imidazol-1-yl)glycinate (**12f**, $R = t$-Bu, $Nu =$ imidazol-1-yl; $\mathrm{C_{11}H_{17}N_3O_3}$)

Starting material: **11d**; MeCN in the presence of *DBU*; 2 h; yield: 93%; resin; ^{1}H NMR (δ): 7.73 (s, 1H, $\mathrm{CH_{imid}}$, H_2), 7.53 (d, br, 1H, $J = 7.0$ Hz, NH), 7.05 (s, br, 2H, $\mathrm{CH_{imid}}$, H_4 and H_5), 6.45 (d, 1H, $J = 7.3$ Hz, CH), 3.83 (s, 3H, OMe), 1.21 (s, 9H, *t*-Bu) ppm; ^{13}C NMR (δ): 178.4 (CONH), 61.3 (*CHNu*), 167.2 (*C*OOMe), 53.8 (OMe), 38.8 ($C\mathrm{Me_3}$), 27.1 ($C\mathit{Me_3}$), 136.7, 129.2, 117.4 ($\mathrm{C_3H_3N_2}$: C_2, C_4, C_5) ppm; IR: $\nu = 3443$m, 1752vs, 1683vs, 1180vs $\mathrm{cm^{-1}}$.

Methyl N-acetyl-α-(benzotriazol-1-yl)glycinate (**12g**, $R =$ Me, $Nu =$ benzotriazol-1-yl; $\mathrm{C_{11}H_{12}N_4O_3}$)

Starting material **11e**; MeCN in the presence of *DBU*; 0.5 h; yield: 98%; m.p.: 129.5–130.5°C; ^{1}H NMR (δ): 8.06 (d, 1H, $J = 8.4$ Hz, $\mathrm{C_6H_4N_3}$, H_4), 7.88 (d, 2H, $J = 8.1$ Hz, $\mathrm{C_6H_4N_3}$, H_7 and NH), 7.55 (ddd, 1H, $J_1 = 8.2$ Hz, $J_2 = 8.2$ Hz, $J_3 = 0.9$ Hz, $\mathrm{C_6H_4N_3}$, H_6), 7.41 (ddd, 1H, $J_1 = 8.1$ Hz, $J_2 = 8.4$ Hz, $J_3 = 0.9$ Hz, $\mathrm{C_6H_4N_3}$, H_5), 7.28 (d, 1H, $J = 8.4$ Hz, CH), 3.81 (s, 3H, OMe), 2.09 (s, 3H, Me) ppm; ^{13}C NMR (δ): 170.4 (CONH), 61.3 (*CHNu*), 166.0 (*C*OOMe), 53.9 (OMe), 22.8 (Me), 145.5, 132.8, 128.4, 124.6, 119.9, 110.2 ($\mathrm{C_6H_4N_3}$: C_{3a}, C_{7a}, C_6, C_5, C_4, C_7) ppm; IR: $\nu = 3420$m, 1760vs, 1697vs, 1163s $\mathrm{cm^{-1}}$.

Methyl N-acetyl-α-phthalimidoglycinate (**12h**, $R = Me$, $Nu =$ phthalimido; $C_{13}H_{12}N_2O_5$)

Starting material: **11e**; MeCN in the presence of *DBU*; 2.5 h; yield: 58%; m.p.: 145.5–147°C; ^1H NMR (δ): 7.93–7.85 (m, 2H, $C_6H_4(CO)_2N$, H_4 and H_7), 7.81–7.74 (m, 2H, $C_6H_4(CO)_2N$, H_5 and H_6), 7.05 (d, br, 1H, $J = 8.3$ Hz, NH), 6.75 (d, 1H, $J = 8.5$ Hz, CH), 3.80 (s, 3H, OMe), 2.08 (s, 3H, Me) ppm; ^{13}C NMR (δ): 169.9 (CONH), 54.7 (*CHNu*), 166.9 (*C*OOMe or C=O), 54.1 (OMe), 23.3 (Me), 167.6 (C=O or *C*OOMe), 134.9, 132.0, 124.3 (C_6H_4: C_5 and C_6, C_{3a} and C_{7a}, C_4 and C_7) ppm; IR: $\nu = 3435$m, 1785m, 1757vs, 1724vs, 1693s, 1223s cm^{-1}.

Methyl N-benzoyl-α-(pyrazol-1-yl)glycinate (**12i**, $R =$ Ph, $Nu =$ pyrazol-1-yl; $C_{13}H_{13}N_3O_3$)

Starting material: **11a**; MeCN in the presence of Et_3N; 1 h; yield: 71%; m.p.: 115–117°C; ^1H NMR (δ): 8.00 (d, 1H, $J = 8.1$ Hz, NH), 7.86–7.79 (m, 3H, Ph and $C_3H_3N_2$, H_5), 7.56 (d, 1H, $J = 1.8$ Hz, $C_3H_3N_2$, H_3), 7.55–7.38, (m, 3H, Ph), 6.87 (d, 1H, $J = 8.1$ Hz, CH), 6.29 (dd, 1H, $J_1 = 1.9$ Hz, $J_2 = 2.5$ Hz, $C_3H_3N_2$, H_4), 3.83 (s, 3H, OMe) ppm; ^{13}C NMR (δ): 166.9 (CONH or *C*OOMe), 64.7 (*CHNu*), 166.7 (*C*OOMe or CONH), 53.7 (OMe), 132.4, 128.6, 127.8, 127.4 (Ph), 141.1, 131.2, 106.2 ($C_3H_3N_2$: C_3, C_5, C_4) ppm; IR: $\nu = 3430$m, 1758vs, 1675vs, 1157s cm^{-1}.

Methyl N-benzoyl-α-(cyclohexylamino)glycinate (**12j**, $R =$ Ph, $Nu =$ cyclohexylamino; $C_{16}H_{22}N_2O_3$)

Starting material: **11a**; MeCN in the presence of Et_3N; 1 h; yield: 100%; resin; ^1H NMR (δ): 7.82–7.72 (m, 2H, Ph), 7.50–7.32 (m, 3H, Ph), 7.06 (d, br, 1H, $J = 7.9$ Hz, amide NH), 5.53 (d, 1H, $J = 8.1$ Hz, CH), 3.72 (s, 3H, OMe), 3.10 (s, br, 1H, amine NH), 2.64–2.56 (m, 1H, cyclohexyl, H_1), 2.00–0.84 (m, 10H, cyclohexyl) ppm; ^{13}C NMR (δ): 171.5 (CONH), 62.8 (*CHNu*), 167.2 (*C*OOMe), 53.0 (OMe), 131.9, 128.6, 128.3, 127.2 (Ph), 33.95, 32.89, 25.83, 24.73 (cyclohexyl) ppm; IR: $\nu = 3435$m, 3330m, 1743vs, 1669vs, 1211s cm^{-1}.

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