Chemical properties of *N*-(amidomethyl)- and *N*-(imidomethyl)glycine derivatives

1. Reactions of *N*-(amidomethyl)- and *N*-(imidomethyl)glycine esters involving the amino group

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N-Nitroso, *N*-sulfonyl, and *N*-acyl derivatives of *N*-(amidomethyl)- and *N*-(imidomethyl)-glycine esters have been synthesized by the reactions of these esters with HNO_2 or with sulfonylating and acylating reagents.

Key words: alkyl glycinates, Mannich bases, nitrosation, sulfonylation, acylation.

Previously we reported on the preparation of esters of *N*-(amidomethyl)-[1] and *N*-(imidomethyl)glycine,[2] which incorporate the N—CH_2—N fragment. α-Amidomethylamines are known to be cleaved under mild conditions (especially in acid media[3]) to recover amine, amide, and formaldehyde. However, their reactions that occur with retention of the N—CH_2—N group have not yet been studied. Meanwhile, involving *N*-(amidomethyl)- and *N*-(imidomethyl)glycinates in reactions with electrophilic or nucleophilic reagents could open up the way to synthesis of polyfunctional glycine derivatives, including biologically active compounds and intermediates for the preparation of modified peptides.

The purpose of the present work has been to study the reactions of esters of *N*-(amidomethyl)- and *N*-(imidomethyl)glycine with nitrosating, acylating, and sulfonylating reagents.

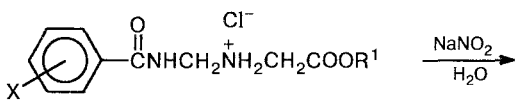
We found that treatment of hydrochlorides of esters of *N*-(amidomethyl)glycine (**1**) with $NaNO_2$ in water at 0 °C affords *N*-(amidomethyl)-*N*-nitrosoglycine esters (**2a—f**) in 41—93 % yields (Scheme 1)

Products **2a—f** precipitate and are thus removed from the reaction zone as they are formed. The higher yields of compounds **2e,f** containing nitro groups in the aromatic ring can be accounted for by the higher stability and/or lower water solubility of these compounds.

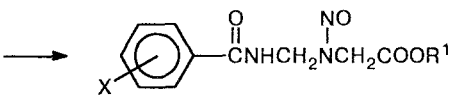
Unlike the reactions involving hydrochlorides of alkyl *N*-(amidomethyl)glycinates, the reactions of *N*-(imidomethyl)glycine esters (**3**) with $NaNO_2$ in the presence of an equimolar amount of HCl result in complex mixtures of products, and we were not able to isolate *N*-nitroso-*N*-(imidomethyl)glycine esters from these mixtures.

Acylation and sulfonylation of *N*-(amidomethyl)- and *N*-(imidomethyl)glycinates was carried out by the action of acyl and sulfonyl halides and by acetic anhydride. In order to trap the acid liberated, the reactions were carried out either in pyridine or in the presence of excess $NaHCO_3$.

Scheme 1



1a—f



2a—f

a: X = H, R^1 = Me
b: X = H, R^1 = Et
c: X = *p*-NO_2, R^1 = Me
d: X = *p*-NO_2, R^1 = Et
e: X = *m*-NO_2, R^1 = Me
f: X = *m*-NO_2, R^1 = Et

The reactions of ester hydrochlorides **1** with *p*-toluene- or methanesulfonyl chloride in pyridine proved to give the corresponding derivatives of *N*-(*p*-tosyl)- (**4a—k**) and *N*-(methanesulfonyl)glycine (**5c**) in 46—96% yields (Scheme 2).

Using Mannich bases prepared by treating hydrochloride **1c** with an equimolar amount of NaOH as an example, we showed that *N*-(amidomethyl)glycine esters as free bases can also be involved in the reaction. The yield of sulfonyl derivative **4c** was 34 %.

Esters **3** also react with the sulfonylating reagent in pyridine; however, these reactions proceed more ambiguously. The yields of the corresponding *N*-(*p*-tosyl)-*N*-(imidomethyl)glycinates (**6a—e**) are 40—44 % (Scheme 3).

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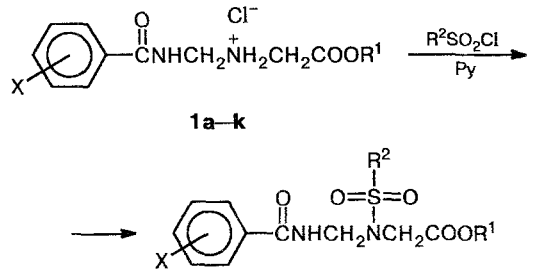
Scheme 2



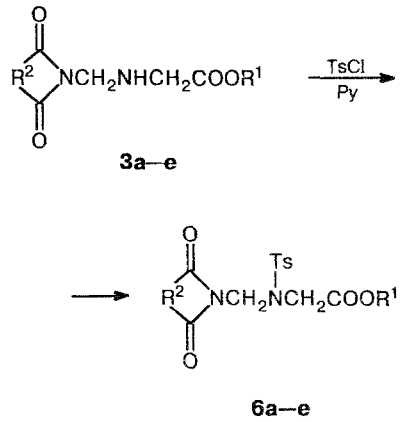
1a—k

4a—k, 5c

a: X = H, R^1 = Me
b: X = H, R^1 = Et
c: X = *p*-NO_2, R^1 = Me
d: X = *p*-NO_2, R^1 = Et
4: R^2 = *p*-MeC_6H_4
5: R^2 = Me
e: X = *m*-NO_2, R^1 = Me
f: X = *m*-NO_2, R^1 = Et
g: X = H, R^1 = CH_2Ph
h: X = *p*-Me, R^1 = Me
k: X = *p*-Br, R^1 = Me

The possibility of introducing acyl substituents to the amine nitrogen atom in esters **1** and **3** was demonstrated by the reactions of the latter with acyl halides derived from aliphatic and aromatic carboxylic acids and also with acetic anhydride. Treating esters **1** with acetyl and benzoyl chlorides in pyridine at 0—20 °C gave esters of *N*-acyl-*N*-(amidomethyl)glycine (**7a,b** and **8a,c,d,g,h,k**) in 48—78 % yields. Compounds **7a—d** and *N*-acyl-*N*-(imidomethyl)glycine esters (**9a,c,d**) were prepared in 78—86 % yields by treatment of the corresponding ester **1** or **3** with acetic anhydride in the presence of 1.5 to 3 molar equivalents of $NaHCO_3$ (Scheme 4).

Scheme 3



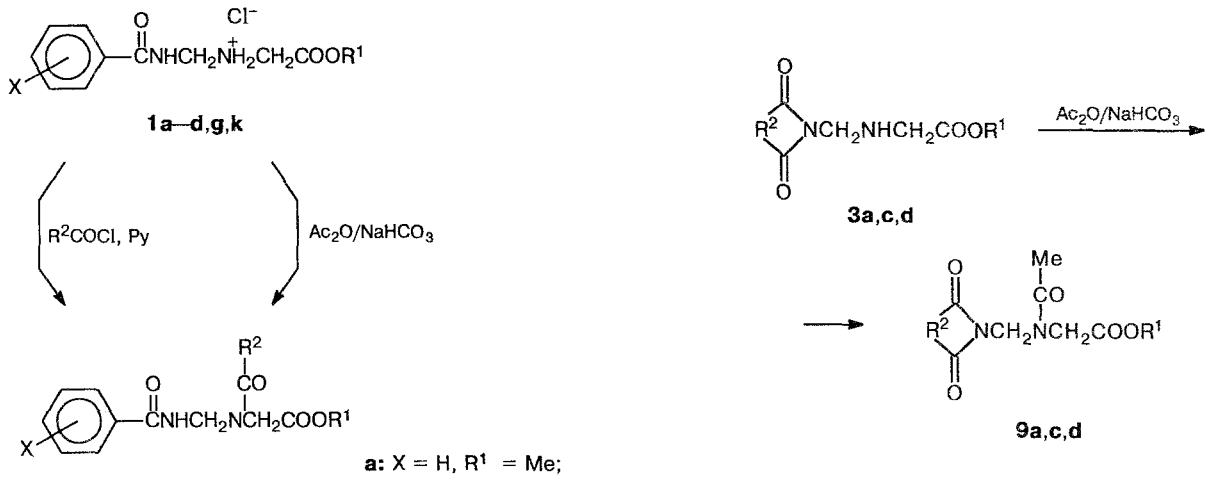
3a—e

6a—e

a: R^1 = Me, R^2 = 1,2-C_6H_4
b: R^1 = Et, R^2 = 1,2-C_6H_4
c: R^1 = Me, R^2 = 3,4-$C_6H_3NO_2$
d: R^1 = Me, R^2 = —$(CH_2)_2$—
e: R^1 = Me, R^2 = —$(CH_2)_3$—

The polyfunctional glycine derivatives synthesized (**2, 4—9**) are stable crystalline or oily compounds. Their structures were confirmed by IR and ^1H and ^{13}C NMR data (Tables 1—6) and mass spectra. The IR spectra of *N*-substituted *N*-(amidomethyl)- and *N*-(imidomethyl)-glycinates exhibit characteristic absorption bands of the amide (1645—1665 cm^{-1}), imide (1690—1780 cm^{-1}), and ester (1730—1755 cm^{-1}) groups. The ^1H and ^{13}C NMR spectra of compounds **2** and **4—9** contain

Scheme 4



1a—d,g,k

7a—d,g,k
8a,c,d

a: X = H, R^1 = Me;
b: X = H, R^1 = Et;
c: X = *p*-NO_2, R^1 = Me;
d: X = *p*-NO_2, R^1 = Et;
g: X = H, R^1 = CH_2Ph;
k: X = Br, R^1 = Me
7: R^2 = Me; **8:** R^2 = Ph

3a,c,d

9a,c,d

a: R^1 = Me, R^2 = 1,2-C_6H_4
c: R^1 = Me, R^2 = 3,4-$C_6H_3NO_2$
d: R^1 = Me, R^2 = —$(CH_2)_2$—

Table 1. Yields, melting points, and data of IR and ^{1}H NMR spectra of *N*-amidomethylglycine esters (**1g—k**)

Compound	Yield (%)	M.p. °C	IR (ν/cm^{-1})			^{1}H NMR, δ (*J*/Hz)						
			O=C(O)	O=C(N)	NH	R		NCH_2C	$NHCH_2N$	NH	NH_2	Ar
						CH_2	Me					
1g	35	153—156	1750	1670	2620—3000	5.21 s	—	4.12 s	4.70 br.s	9.80 t	—	7.36—7.59 (m, 8 H); 8.02—8.07 (m, 2 H, H_o)
1h	65	147—152	1750	1655	2640—3000	—	3.70 s	3.98 s	4.62 (d, *J* = 5.7)	9.52 t	8.44 br.s	7.27 (d, 2 H, H_m, *J* = 7.4); 7.82 (d, 2 H, H_o, *J* = 7.4); 2.32 (s, 3 H, Me)
1k	65	178—181	1755	1670	2980—3320	—	3.66 s	3.96 s	4.54 (d, *J* = 5.7)	9.82 t	8.5 br.s	7.67 (d, 2 H, H_m, *J* = 8.1); 7.85 (d, 2 H, H_o, *J* = 8.1)

Table 2. Yields, melting points, and data of IR and ^{1}H NMR spectra of *N*-nitroso-*N*-(amidomethyl)glycine esters (**2a—f**)

Compound	Yield (%)	M.p. °C	IR (ν/cm^{-1})				^{1}H NMR, δ (*J*/Hz)					
			O=C(O)	O=C(N)	NO_2	NH	R^1		NCH_2C	NCH_2N	NH	Ar
							CH_2	Me				
2a	41	111—112	1750	1650	—	3295	—	3.67 s	4.48 s	5.9 br.s	8.83 br.s	7.59 (m, 3 H, $H_{m,p}$); 7.95 (m, 2 H, H_o)
2b	41	122—124	1750	1660	—	3195—3210	4.1 (q, *J* = 7.1)	1.19 (t, *J* = 7.1)	4.48 s	5.93 (d, *J* = 7.1)	8.88 br.s	7.40—7.73 (m, 3 H, $H_{m,p}$); 7.85—8.20 (m, 2 H, H_o)
2c	61	134—136	1740	1665	1530	3400	—	3.6 s	4.44 s	5.93 s	9.17 br.s	8.15 (d, 2 H, H_o, *J* = 8.5); 8.33 (d, 2 H, H_m, *J* = 8.5)
2d	82	113—115	1730	1665	1520, 1550	3360	4.07 (q, *J* = 7.4)	1.13 (t, *J* = 7.4)	4.44 s	5.87—5.96 m	9.16 m	8.17 (d, 2 H, H_o, *J* = 8.5); 8.34 (d, 2 H, H_m, *J* = 8.5)
2e	87	122—125	1750	1660	1535	3325—3350	—	3.63 s	4.50 s	5.97 (d, *J* = 6.2)	9.18—9.47 br.s	7.75 (t, H_m, *J* = 8.0); 8.34 (d.t, H_o); 8.45 (d.t, H_p); 8.78 (t, H_o, *J* = 1.2)
2f	93	108—110	1755	1650	1530	3320	4.10 (q, *J* = 7.1)	1.20 (t, *J* = 7.1)	4.50 s	5.98 (d, *J* = 7.1)	9.10—9.37 br.s	7.85 (t, H_m, *J* = 8.2); 8.37 (d.t, H_o); 8.49 (d.t, H_p); 8.78 (t, H_o, *J* = 1.9)

Table 3. Yields, melting points, and data of IR and ^{1}H NMR spectra of *N*-amidomethyl-*N*-sulfonylglycine esters (**4a—k, 5c**)

Compound	Yield (%)	M.p. °C	IR (ν/cm^{-1})					^{1}H NMR, δ (*J*/Hz)						
			O=C(O)	O=C(N)	S—N	NH	NO_2	R^1		NCH_2C	NCH_2N	Ar	R^2	
								CH_2	Me				Me	C_6H_4
4a	96	132—133	1755	1660	920	3335	—	—	3.61 s	4.26 s	5.03 br.s	7.79 (d, 2 H, H_o, J = 7.6); 7.43 (t, 2 H, H_m, J = 7.8); 7.52 (t, 1 H, H_p, J = 7.8)	2.25 s	7.32 (d, 2 H, H_m, J = 7.6); 7.76 (d, 2 H, H_o, J = 7.6)
4b	70	98—100	1750	1645	940	3310	—	4.08 (q, J = 7.23)	1.15 (t, J = 7.17)	4.26 s	5.05 (d, J = 7.23)	7.82 (d, 2 H, H_o, J = 7.3); 7.43 (t, 2 H, H_m, J = 7.3); 7.53 (t, 1 H, H_p, J = 7.3)	2.36 s	7.33 (d, 2 H, H_m, J = 7.3); 7.75 (d, 2 H, H_o, J = 7.3)
4c	87	161—163	1750	1650	930	3300	1520—1550	—	3.63 s	4.32 s	5.07 (d, J = 6.4)	8.03 (d, 2 H, H_o, J = 8.2); 8.41 (d, 2 H, H_m, J = 8.2)	2.38 s	7.38 (d, 2 H, H_m, J = 8.2); 7.8 (d, 2 H, H_o, J = 8.2)
4d	87	131—133	1750	1660	940	3300	1520—1550	4.1 (q, J = 7.2)	1.69 (t, J = 6.1)	4.30 s	5.07 (d, J = 6.4)	8.05 (d, 2 H, H_o, J = 9.6); 8.33 (d, 2 H, H_m, J = 9.6)	2.38 s	7.38 (d, 2 H, H_m, J = 9.6); 7.8 (d, 2 H, H_o, J = 9.6)
4e	65	112—114	1755	1650	930	3300	1530—1545	—	3.67 s	4.35 s	5.10 (d, J = 8.1)	7.80 (t, H_m, J = 8.1); 8.24 (dt, H_o, J = 8.1); 8.45 (dt, H_p, J = 8.1); 8.60 (t, H_o, J = 1.7)	2.39 s	7.35 (d, 2 H, H_m, J = 8.1); 7.81 (d, 2 H, H_o, J = 8.1)
4f	95	128—131	1750	1655	945	3310	1530	4.13 (q, J = 7.1)	1.20 (t, J = 6.5)	4.32 s	5.1 (d, J = 6.3)	7.80 (t, H_m, J = 8.5); 8.25 (dt, H_o, J = 8.5); 8.42 (dt, H_p, J = 8.5); 8.62 (t, H_o, J =1.7)	2.37 s	7.37 (d, 2 H, H_m, J = 8.5); 7.82 (d, 2 H, H_o, J = 8.5)

Table 3. (*continued*)

Compound	Yield (%)	M.p. °C	IR (ν/cm^{-1})					^{1}H NMR, δ (*J*/Hz)						
			O=C(O)	O=C(N)	S—N	NH	NO_2	R^1		NCH_2C	NCH_2N	Ar	R^2	
								CH_2	Me				Me	C_6H_4
4g	75	98—99	1750	1660	930	3320	—	5.12 s	—	4.35 s	5.05 (d, *J* = 6.3)	7.29—7.43 (m, 10 H); 7.80 (d, 2 H, H_o, *J* = 8.5)	2.35 s	7.80 (d, 2 H, H_o, *J* = 8.5)
4h	69	135—138	1750	1645	930	3310	—	—	—	3.62 s	4.25 s	5.01 (d, *J* = 6.5)	7.35 (d, 2 H, H_m, *J* = 8.2); 7.81 (d, 2 H, H_o, *J* = 8.2)	2.37 (s, 6 H)	7.25 (d, 2 H, H_m, *J* = 8.2); 7.68 (d, 2 H, H_o, *J* = 8.2)
4k	75	148—149	1760	1665	925	3420	—	—	—	3.62 s	4.28 s	5.02 (d, *J* = 6.3)	7.62 (d, 2 H, H_m, *J* = 8.2); 7.73 (d, 2 H, H_o, *J* = 8.2)	2.37 s	7.33 (d, 2 H, H_m, *J* = 8.2); 7.79 (d, 2 H, H_o, *J* = 8.2)
5c	46	140—142	1745	1660	930	3310	—	—	—	3.60 s	4.19 s	4.85 (d, *J* = 5.7)	7.95 (d, 2 H, H_o, *J* = 9.0); 8.15 (d, 2 H, H_m, *J* = 9.0)	3.00 s	—

signals of the nuclei of the N—CH_2—N group in the 4.8—6.0 and 49—54 ppm regions, respectively. The ^{1}H NMR spectra of *N*-acyl derivatives **7—9** exhibit double sets of signals; the ratio between the integral intensities of these signals for compounds **7a—d,g,k** is 2 : 1, that for **8a,c,d** is 5 : 1, for **9a,d** this ratio is 9 : 1, and for compound **9c** it is 7 : 1. The complication of the ^{1}H NMR spectral pattern observed for compounds **7—9** can be attributed to the restricted character of the rotation around the C—N bond, typical of organic amides, which leads to the presence of two relatively stable geometric isomers in solutions of these compounds.[4]

Thus, we showed for the first time that esters of *N*-(amidomethyl)- and *N*-(imidomethyl)glycine can react with electrophilic reagents with the retention of the N—CH_2—N structural fragment to give the corresponding *N,N*-disubstituted derivatives that cannot be obtained by other methods. In addition, acylation probably opens up the way to the synthesis of peptides containing amido- and imidomethyl substituents.

Experimental

IR spectra of solids were recorded with samples pressed with KBr; those of liquids were recorded in thin films using a Specord IR-75 spectrometer. ^{1}H and ^{13}C NMR spectra were obtained in DMSO-d_6, $(CD_3)_2CO$, or $CDCl_3$ on a Bruker AM-300 spectrometer operating at 300.13 (^{1}H) or 75.5 MHz (^{13}C), and mass spectra were obtained on a Varian CH-6 instrument (EI, 70 eV). TLC was carried out on Silpearl UV-250 silica gel. Compounds **1a—f** and **3a—e** were prepared by previously described procedures.[1,2] Mannich bases **1g—k** were prepared in a similar way; their melting points and spectral characteristics are presented in Tables 1 and 6.

***N*-(Amidomethyl)-*N*-nitrosoglycine esters (2a—f).** At 0—2 °C, a solution of sodium nitrite (0.22 mmol) was added dropwise to a stirred aqueous solution of **1a—f** (0.183 mmol), and the mixture was kept for 8 h at 5 °C. The resulting precipitate of **2a—f** was filtered off, washed with water, and dried in an air flow. The melting points, yields, and IR and ^{1}H NMR spectral data of compounds **2a—f** are presented in Table 2.

***N*-Sulfonyl-*N*-[amido(imido)methyl]glycine esters (4a—k, 5c, 6a—e).** A mixture of **1** or **3** (0.193 mmol), sulfonyl chloride (0.38 mmol), and dry pyridine (0.4 mL) was stirred for 1 h at −10 °C, kept for 48 h at ~20 °C, diluted with cold water (1—2 mL), and carefully acidified with dilute HCl. The precipitate was filtered off, washed with water, and dried in an air flow. Compounds **4a—k**, **5c**, **6a—e** were isolated by TLC on silica gel (using benzene—ether (1 : 1) as the eluent). The yields and physicochemical and spectral characteristics of compounds **4a—k**, **5c**, **6a—e** obtained are presented in Tables 3, 4, and 6.

***N*-Acyl-*N*-[amido(imido)methyl]glycine esters (7—9).** *A.* A mixture of ester **1** or **3** (2.5 mmol), acetic anhydride

Table 4. Yields, melting points, and data of IR and ^{1}H NMR spectra of *N*-imidomethyl-*N*-(*p*-toluenesulfonyl)glycine esters (**6a—e**) and *N*-imidomethyl-*N*-acetylglycine esters (**9a,c,d**)

Compound	Yield (%)	M.p. °C	IR (ν/cm^{-1})			^{1}H NMR, δ (*J*/Hz)						
						R^1				Ts		MeCO
			C=O	S—N	R^2	CH_2	Me	NCH_2C	NCH_2N	Me	C_6H_4	
6a	43	115—118	1720, 1750, 1770	940	7.8 (s, 4 H)	—	3.6 s	4.40 s	5.3 s	2.30 s	7.24 (d, 2 H, H_m, J = 8.0); 7.63 (d, 2 H, H_o, J = 8.0)	—
6b	44	135—138	1720, 1755, 1775	940	7.92 (s, 4 H)	4.1 (q, J = 7.5)	1.2 (t, J = 7.9)	4.44 s	5.38 s	2.37 s	7.30 (d, 2 H, H_m, J = 8.6); 7.78 (d, 2 H, H_o, J = 8.6)	—
6c	16	154—157	1715, 1730, 1745, 1785	940	8.08 (d, 1 H, J = 8.1); 8.65 (d, 1 H, J = 8.1); 8.7 (s, 1 H)	—	3.63 s	4.43 s	5.29 s	2.40 s	7.30 (d, 2 H, H_m, J = 8.1); 7.82 (d, 2 H, H_o, J = 8.1)	—
6d	40	103—104	1710, 1760, 1780	940	2.64 (s, 4 H)	—	3.63 s	4.38 s	5.01 s	2.42 s	7.29 (d, 2 H, H_m, J = 8.1); 7.77 (d, 2 H, H_o, J = 8.1)	—
6e	40	118—120	1690, 1730, 1760	940	1.9 (quint, 2 H, J = 6.8); 2.62 (t, 4 H, J = 6.8)	—	3.62 s	4.44 s	5.28 s	2.43 s	7.32 (d, 2 H, H_m, J = 8.2); 7.80 (d, 2 H, H_o, J = 8.2)	—
9a	77	94—96	1725, 1750, 1775	—	7.72—7.70 (m, 2 H); 7.81—7.90 (m, 2 H)	—	3.6 (s, 2.7 H) 3.67 (s, 0.3 H)	4.21 (s, 1.8 H) 4.30 (s, 0.2 H)	5.28 (s, 1.8 H) 5.37 (s, 0.2 H)	—	—	2.01 (s, 0.3 H) 2.5 (s, 2.7 H)
9c	43	127—131	1730, 1740, 1785	—	8.01—8.12 (m, 1 H); 8.60—8.70 (m, 2 H)	—	3.58 (s, 2.6 H) 3.7 (s, 0.4 H)	4.20 (s, 1.7 H) 4.36 (s, 0.3 H)	5.35 (s, 1.7 H) 5.39 (s, 0.3 H)	—	—	2.03 (s, 0.4 H); 2.51 (s, 2.6 H)
9d	85	Oil	1715 1755 1780	—	2.64 (s, 0.4 H); 2.70 (s, 3.6 H)	—	3.62 (s, 2.7 H) 3.68 (s, 0.3 H)	4.08 (s, 1.8 H) 4.21 (s, 0.2 H)	5.03 (s, 1.8 H) 5.08 (s, 0.2 H)	—	—	2.04 (s, 0.3 H); 2.38 (s, 2.7 H)

(0.1 mmol), and $NaHCO_3$ (7.5 mmol) was stirred at ambient temperature for 1 h and allowed to stand for 3 days. The solvent was removed *in vacuo*, and water was poured over the residue. The aqueous solution was extracted with chloroform, and the organic phase was washed with water and dried with Na_2SO_4. Compounds **7c,d,g,k** and **9a,c** crystallize after treatment with ether (3—4 mL). Compounds **7a,b** and **9d** were isolated using TLC on silica gel (with ethyl acetate as the eluent).

B. A mixture of ester **1** or **3** (0.193 mmol), acyl chloride (0.38 mmol), and dry pyridine (0.4 mL) was stirred for 1 h at −10 °C and kept for 48 h at −20 °C. Cold water (1—2 mL) was added to the reaction mixture, and the resulting mixture was carefully acidified with dilute HCl. In the case of *N*-benzoylglycinates **8**, the precipitate was filtered off, thoroughly washed with water, and dried in an air flow. Products **8** were isolated by TLC on silica gel (with benzene—ether (1:1) as the eluent). In the case of esters **7a,b**, the aqueous solution was extracted with chloroform, and the organic phase was washed with water several times, dried with $MgSO_4$, and subjected to TLC to isolate the products as oils. The yields and spectral characteristics of compounds **7—9** are presented in Tables 4, 5, and 6.

The mass spectrum of **7d**, (*m/z*, I_{rel} (%)): 323 $[M]^+$ (26), 280 (100), 255 (38), 247 (28), 208 (31), 160 (52), 150 (71), 145 (62), 134 (36), 131 (43).

Table 5. Yields, melting points, and data of ^{1}H NMR spectra of *N*-(amidomethyl)glycine esters (**7a—d,g,k, 8a,c,d**)

Compound	Yield (%)	M.p. /°C	^{1}H NMR, δ (*J*/Hz)							
			NCH_2C	NCH_2N	NH	R^1		R^2		Ar
						CH_2	Me	Me	Ph	
7a	78	Oil	4.27 (s, 0.7 H); 4.38 (s, 1.3 H)	4.97 (d, 1.3 H, *J* = 6.6); 5.11 (d, 0.7 H, *J* = 6.1)	—	—	3.74 (s, 1 H); 3.76 (s, 2 H)	2.04 (s, 2 H); 2.27 (s, 1 H)	—	8.37—8.58 (m, (3H); 7.74—7.93 (m, 2 H)
7b	78	Oil	4.37 (s, 1.3 H); 4.26 (s, 0.7 H)	4.93 (d, 1.3 H, 6.1) 5.07 (d, 0.7 H, *J* = 6.1)	—	4.20 (q, *J* = 7.0)	1.25 (t, *J* = 7.0)	2.04 (s, 2 H); 2.26 (s, 1 H)	—	7.41—7.50 (m, 3 H); 7.76 (d, 1.3 H, *J* = 8.7); 7.79 (d, 0.7 H, *J* = 8.7)
7c	86	118—120	4.22 (s, 1.3 H); 4.45 (s, 0.7 H)	4.95 (d, 0.7 H, *J* = 6.1); 5.05 (d, 1.3 H, *J* = 6.1)	9.15 (m, 0.3 H); 9.32 (m, 0.7 H)	—	3.67 (s, 2 H); 3.69 (s, 1 H)	2.03 (s, 1 H); 2.34 (s, 2 H)	—	8.17 (d, 2 H, H_o, *J* = 8.0); 8.34 (d, 2 H, H_m, *J* = 8.0)
7d	78	94—96	4.24 (s, 0.7 H); 4.36 (s, 1.3 H)	4.95 (d, 1.3 H, *J* = 6.3); 5.1 (d, 0.7 H, *J* = 6.3)	8.00 (t, 0.7 H); 8.25 (t, 0.3 H)	2.23 (q, *J* = 7.2)	2.23 (t, *J* = 7.1)	2.00 (s, 2 H); 2.24 (s, 1 H)	—	7.96—7.99 (m, 2 H, H_o); 8.21—8.24 (m, 2 H, H_m)
7g	79	118—120	4.32 (s, 0.7 H); 4.43 (s, 1.3 H)	4.97 (d, 1.3 H, *J* = 6.6); 5.08 (d, 0.7 H, *J* = 6.6)	—	5.14 (s, 1.3 H); 5.17 (s, 0.7 H)	—	2.01 (s, 2 H); 2.27 (s, 1 H)	—	7.30—7.55 (m, 8 H); 7.73 (d, 1.3 H, *J* = 7.2); 7.80 (d, 0.7 H, *J* = 7.2)
7k	56	122—125	4.27 (s, 0.7 H); 4.38 (s, 1.3 H)	4.92 (d, 1.3 H, *J* = 6.6); 5.08 (d, 0.7 H, *J* = 6.6)	7.86 t	—	3.71 (s, 2 H); 3.74 (s, 1 H)	2.03 (s, 2 H); 2.24 (s, 1 H)	—	7.52—7.70 (m, 4 H)
8a	48	118—121	4.33 (s, 1.7 H); 4.21 (s, 0.3 H)	5.12 (br.s, 1.7 H); 5.41 (br.s, 0.3 H)	—	—	3.70 (s, 2 H); 3.79 (s, 1 H)	—	7.30—7.60 (m, 3 H, $H_{m,p}$); 7.70—7.86 (m, 2 H, H_o)	7.30—7.60 (m, (3 H, $H_{m,p}$); 7.70—7.86 (m, (2 H, H_o)
8c	50	135—139	4.37 (s, 1.7 H); 4.41 (s, 0.3 H);	5.10 (d, 0.3 H, *J* = 6.5); 5.17 (d, 1.7 H, *J* = 6.5)	—	—	3.72 (s, 2.6 H); 3.80 (s, 0.4 H)	—	7.33—7.52 (m, 5 H)	7.95 (d, 2 H, H_o, *J* = 9.2); 8.15 (d, 2 H, H_m, *J* = 9.2)
8d	58	104.5—106	3.99 (s, 1.6 H); 4.01 (s, 0.4 H)	4.80 (br.s, (0.4H); 4.87 (d, 1.6 H, *J* = 7.5)	7.85 (br.s, 0.2 H); 8.46 (br.s, 0.8 H)	—	0.90 (t, (3H, 10.5)	—	7.05 (br.s, 5 H)	7.63 (s, 4 H)

Table 6. ^{13}C NMR spectra of derivatives of *N*-(amidomethyl)- and *N*-(imidomethyl)glycine esters (**1h, 4g, 6c, 7b,d, 9a**)

Compound	NCH_2N	NCH_2C	C=O	Aromatic C	Other ^{13}C signals
1h	51.7	44.8	167.0	127.7, 129.0, 129.8 (C-4); 142.5 (CCO)	21.1 (MeC_6H_4); 52.7 (Me)
4g	54.5	49.7	170.1	128.1, 128.3, 129.0, 129.1, 129.3, 129.5, 130.6, 132.7, 135.0, 138.2, 144.5 (C—S)	21.5 (Me); 67.4 (CH_2)
6c	51.3	50.2	169.7, 176.5	143.9 (C—S); 127.8, 129.5, 136.2 (C-4)	21.5 (MeC_6H_4); 28.0 $(OCH_2)_2$; 52.21 (Me)
7b	52.9, 56.5	49.0, 51.7	*	127.0, 127.1, 128.5, 128.6, 131.9, 140.0 (C-4)	13.9, 14.0 (Me); 61.7, 61.8 (OCH_2); 14.0 (MeCO)
7d	52.9, 56.4	49.0, 51.8 169.4, 171.3,	164.9, 166.6, 123.7 (C-2); 171.7, 172.8	138.7, 139.2 (CCO); 123.5, 128.3, 128.5 (C-3); 149.6, 149.9(C-4)	13.9, 14.0 (Me); 20.9, 21.2 (MeCO); 61.7, 61.8 (OCH_2)
9a	50.7, 51.7	47.3, 48.9	167.9, 169.7, 171.3	131.5, 131.9 (CCO); 134.2, 134.5 (C-2); 123.5, 123.7 (C-3)	21.1, 21.4 (MeCO); 52.0, 52.1 (MeO)

* The signals of the carbonyl carbon atoms were not recorded due to the substantial broadening.

References

1. S. G. Zlotin, I. V. Sharova, and O. A. Luk'yanov, *Izv. Akad. Nauk, Ser. Khim.*, 1994, 1078 [*Russ. Chem. Bull.*, 1994, **43** (Engl. Transl.)].
2. S. G. Zlotin, I. V. Sharova, and O. A. Luk'yanov, *Izv. Akad. Nauk, Ser. Khim.*, 1995, 1306 [*Russ. Chem. Bull.*, 1995, **44**, 1260 (Engl. Transl.)].
3. M. Johansen and H. Bundgaard, *Int. J. Pharm.*, 1980, **7**, 119.
4. H. Günter, *NMR spectroscopy. Introduction*, John Wiley and Sons, XIV, 1980.

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