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Alkyl (Z)-2-[(E)-2-ethoxycarbonyl-2-(2-pyridinyl)ethenyl]amino-3-dimethylaminopropenoates **7** and **8** were prepared from ethyl 2-pyridinylacetate (**1**) in two steps. Substitution of the dimethylamino group with alkyl-, aryl-, or heteroaryl amines afforded the corresponding β -alkyl- **22-24**, β -aryl- **25-35**, and β -heteroaryl-amino- α,β -didehydro- α -amino acid **36** and **37** derivatives, intermediates for further preparation of various heterocyclic systems. The orientation around both double bonds were determined by various nmr techniques.

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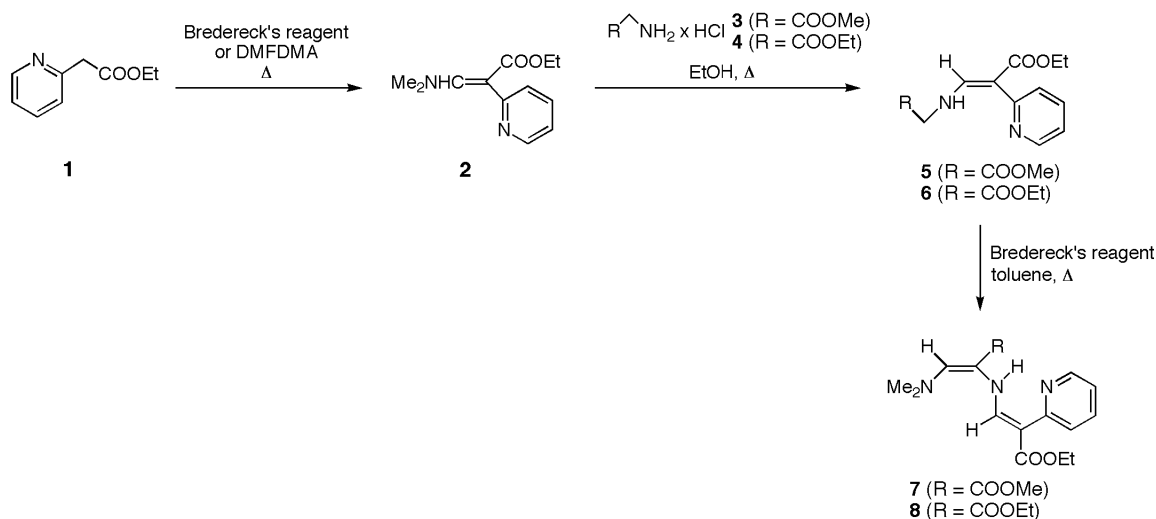
Recently, substituted 2-acylamino- or 2-hydroxy-3-(dimethylamino)propenoates as masked α -formyl- α -amino- or α -formyl- α -hydroxy acid derivatives, and 2-[(2,2-disubstituted ethenyl)amino]-3-(dimethylamino)propenoates and related compounds have been prepared in our laboratory and used as reagents for preparation of various heterocyclic systems, such as 2*H*-pyran-2-ones and fused pyran-2-ones, fused pyridinones, pyrimidinones [1-10], imidazole-4-carboxylates [11], alkyl 1-acyl-3,4-disubstituted pyrrole-2-carboxylates [12,13], dialkyl 3-amino-pyrrole-2,4-dicarboxylates and 5*H*-pyrrolo[3,2-*d*]pyrimidine derivatives [14], and (Z)-aplysinsin analogs in a simple and stereoselective manner [15]. Alkyl 2-[2-cyano-2-(2-pyridinyl)ethenyl]amino-3-dimethylaminopropenoates have been transformed into alkyl 2-[2-cyano-2-(2-pyridinyl)ethenyl]amino-3-[2-methoxycarbonyl-4-(2-pyridinyl)-1*H*-pyrrol-3-yl]aminopropenoates [16]. Chiral 3-(dimethylamino)propenoate analogs derived from L-glutamic and L-pyrroglutamic acid have been used for the preparation of (S)-3-(heteroaryl)alanine and (S)-3-

(heteroaryl)lactic acid derivatives, as well as for the preparation of heterocyclic systems with an α -amino acid structural element incorporated into the cyclic system [17-23].

In continuation of our studies in this area, we report the synthesis of alkyl (Z)-2-[(E)-2-alkoxycarbonyl-2-(2-pyridinyl)ethenyl]amino-3-dimethylaminopropenoates **7** and **8**, and their further transformations with alkyl-, aryl-, and heteroaryl amines into β -alkyl (aryl and heteroaryl)amino- α,β -didehydro- α -amino acid derivatives **22-37** as intermediates for preparation of various heterocyclic systems.

Alkyl (E)-*N*-[2-ethoxycarbonyl-2-(2-pyridinyl)ethenyl]glycinates **5** and **6** were prepared by heating a mixture of ethyl 2-pyridinylacetate (**1**) and *N,N*-dimethylformamid dimethylacetal (DMFDMA) or (*t*-butoxy)bis(dimethylamino)methane (Bredereck's reagent) at 85 °C for 1.5 hours in an argon atmosphere to give ethyl 3-(dimethylamino-2-(2-pyridinyl)propenoate (**2**) followed, without purification, by treatment with an alkyl glycinate hydrochloride **3**, **4** in ethanol by heating at reflux temperature for 1.5 hours in 80-86% yield. They were transformed with (*t*-butoxy)-

Scheme 1



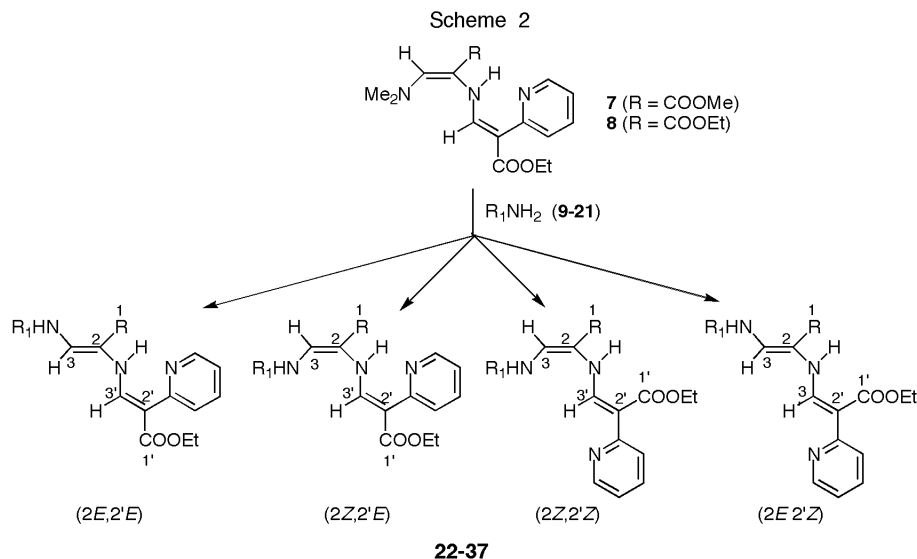
bis(dimethylamino)methane (Bredereck's reagent) in dry toluene by heating under reflux for several hours into alkyl (*Z*)-2-[(*E*)-2-ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-dimethylamino-propenoates **7** and **8** in 91% and 62% yield, respectively. (Scheme 1).

The dimethylamino group in compounds **7** and **8** can be easily substituted with benzyl amines **9-11**, aromatic amines **12-20**, and heteroaromatic amines, such as 2-amino-5-chloropyridine (**21**) in acetic acid at room temperature to form β -alkylamino- α,β -didehydro- α -amino

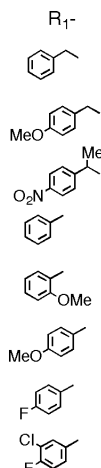
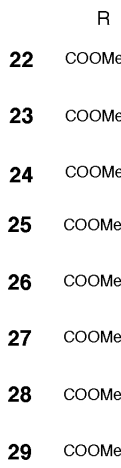
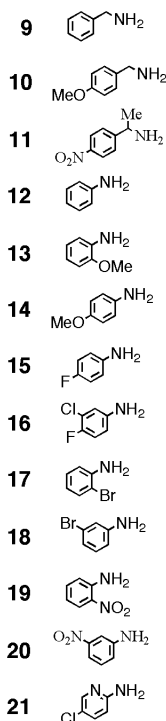
acid derivatives **22-24** in 15-43% yield, β -arylamino- α,β -didehydro- α -amino acid derivatives **25-35** in 13-78% yield, and β -heteroarylamino- α,β -didehydro- α -amino acid derivatives **36** and **37** in 62 and 73% yield, respectively. (Scheme 2). Experimental and analytical data are given in Tables 1, 2, 3, and 4.

Structure Determination.

The structures of the new compounds were determined by ^1H nmr spectra and Heteronuclear Multiple Bond Correlation



amines (R_1NH_2)



products

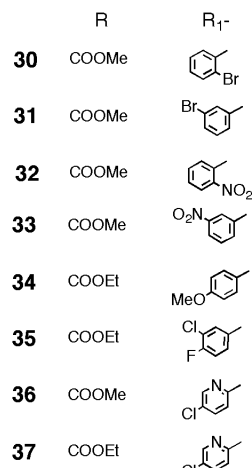


Table 1
Experimental and Analytical Data

Compound	Yield (%)	mp (°C)	Molecular formula Analyses	Number of isomers (ratio)
5	86	95-97 from ethyl acetate/n-heptane (1:6)	C ₁₃ H ₁₆ N ₂ O ₄ Calcd: C, 59.08; H, 6.10; N, 10.60 Found: C, 58.85; H, 5.86; N, 10.40	1
6	80	57-61 from ethyl acetate/n-heptane (1:6)	C ₁₄ H ₁₈ N ₂ O ₄ Calcd: C, 60.42; H, 6.52; N, 10.07 Found: C, 60.43; H, 6.72; N, 10.00	1
7	91	115-117 from ethyl acetate/n-heptane (1:3)	C ₁₆ H ₂₁ N ₃ O ₄ Calcd: C, 60.18; H, 6.63; N, 13.16 Found: C, 60.11; H, 6.88; N, 13.05	1
8	62	63-69 from ethyl acetate/n-heptane (1:3)	C ₁₇ H ₂₃ N ₃ O ₄ Calcd: C, 61.25; H, 6.95; N, 12.60 Found: C, 61.23; H, 7.23; N, 12.57	1
22	36	106-108 from ethanol/water	C ₂₁ H ₂₃ N ₃ O ₄ Calcd: C, 66.13; H, 6.08; N, 11.02 Found: C, 66.31; H, 6.17; N, 10.98	1 [a]
23	43	105-108 from ethanol/water	C ₂₂ H ₂₅ N ₃ O ₅ Calcd: C, 64.22; H, 6.12; N, 10.21 Found: C, 64.43; H, 6.24; N, 10.23	1 [a]
24	15	103-107 from acetone	C ₂₂ H ₂₄ N ₄ O ₆ Calcd: C, 59.99; H, 5.49; N, 12.72 Found: C, 59.63; H, 5.82; N, 11.80	1 [a]
25	23	132-144 from methanol	C ₂₀ H ₂₁ N ₃ O ₄ Calcd: C, 65.38; H, 5.76; N, 11.44 Found: C, 65.31; H, 5.96; N, 11.43	4 [b] (11:9:2:1)
26	17	128-130 from methanol	C ₂₁ H ₂₃ N ₃ O ₅ Calcd: C, 63.47; H, 5.83; N, 10.57 Found: C, 63.75; H, 5.90; N, 10.55	1 [a]
27	78	129-155 from methanol	C ₂₁ H ₂₃ N ₃ O ₅ Calcd: C, 63.47; H, 5.83; N, 10.57 Found: C, 63.54; H, 6.09; N, 10.49	4 [b, c]
28	60	163-178 from methanol/toluene	C ₂₀ H ₂₀ FN ₃ O ₄ Calcd: C, 62.33; H, 5.23; N, 10.90 Found: C, 62.60; H, 5.33; N, 10.96	4 [b] (11:6:1:1)
29	66	144-169 from methanol	C ₂₀ H ₁₉ ClFN ₃ O ₄ Calcd: C, 57.22; H, 4.56; N, 10.01 Found: C, 57.25; H, 4.64; N, 10.02	4 [b] (13:9:2:1)
30	53	156-162 from methanol	C ₂₀ H ₂₀ BrN ₃ O ₄ Calcd: C, 53.82; H, 4.52; N, 9.42 Found: C, 53.75; H, 4.48; N, 9.37	2 [d] (6:1)
31	13	129-132 from methanol/toluene	C ₂₀ H ₂₀ BrN ₃ O ₄ Calcd: C, 53.82; H, 4.52; N, 9.42 Found: C, 54.37; H, 4.56; N, 9.42	2 [d] (7:1)
32	31	138-160 from methanol	C ₂₀ H ₂₀ N ₄ O ₆ Calcd: C, 58.25; H, 4.89; N, 13.58 Found: C, 58.01; H, 4.87; N, 13.52	2 [d] (10:1)
33	45	158-162 from methanol	C ₂₀ H ₂₀ N ₄ O ₆ Calcd: C, 58.25; H, 4.89; N, 13.58 Found: C, 58.19; H, 4.86; N, 13.59	2 [d] (8:1)
34	67	121-135 from ethanol	C ₂₂ H ₂₅ N ₃ O ₅ Calcd: C, 64.22; H, 6.12; N, 10.21 Found: C, 64.20; H, 6.22; N, 10.34	2 [c, d]
35	37	159-165 from ethanol	C ₂₁ H ₂₁ ClFN ₃ O ₄ Calcd: C, 58.14; H, 4.88; N, 9.68 Found: C, 58.07; H, 5.01; N, 9.54	1 [a]
36	62	192-194 from ethanol	C ₁₉ H ₁₉ ClN ₄ O ₄ Calcd: C, 56.65; H, 4.75; N, 13.91 Found: C, 56.67; H, 4.72; N, 13.97	1 [a]
37	73	193-196 from ethanol/water	C ₂₀ H ₂₁ ClN ₄ O ₄ Calcd: C, 57.63; H, 5.08; N, 13.44 Found: C, 57.77; H, 5.10; N, 13.55	1 [a]

[a] (2*E*, 2'*E*). [b] (2*E*, 2'*E*) : (2*Z*, 2'*E*) : (2*Z*, 2'*Z*) : (2*E*, 2'*Z*). [c] The ratio was not determined. [d] (2*E*, 2'*E*) : (2*Z*, 2'*E*).

Table 2
¹H nmr Data

Compound	MHz Solvent	δ (tetramethylsilane)
5	300 CDCl ₃	1.33 (3H, t, COOCH ₂ CH ₃), 3.79 (3H, s, COOMe), 4.12 (2H, d, CH ₂), 4.24 (2H, q, COOCH ₂ CH ₃), 6.97 (1H, ddd, H ₅), 7.62 (1H, ddd, H ₄), 7.92 (1H, d, CHNH), 8.31 (1H, ddd, H ₃), 8.42 (1H, ddd, H ₆), 11.02 (1H, br.s, CHNH), J _{H3H4} = 8.5 Hz, J _{H3H5} = 1.1 Hz, J _{H3H6} = 1.0 Hz, J _{H4H5} = 7.4 Hz, J _{H4H6} = 2.0 Hz, J _{H5H6} = 5.0 Hz, J _{CHNH} = 12.8 Hz, J _{CH2NH} = 6.0 Hz, J _{CH2CH3} = 7.1 Hz.
6	300 CDCl ₃	1.30 (3H, t, COOCH ₂ CH ₃), 1.33 (3H, t, COOCH ₂ CH ₃), 4.10 (2H, d, CH ₂), 4.24 (2H, q, COOCH ₂ CH ₃), 4.25 (2H, q, COOCH ₂ CH ₃), 6.96 (1H, ddd, H ₅), 7.61 (1H, ddd, H ₄), 7.93 (1H, d, CHNH), 8.31 (1H, ddd, H ₃), 8.41 (1H, ddd, H ₆), 11.02 (1H, br.s, CHNH), J _{H3H4} = 8.5 Hz, J _{H3H5} = 1.1 Hz, J _{H3H6} = 1.0 Hz, J _{H4H5} = 7.4 Hz, J _{H4H6} = 2.0 Hz, J _{H5H6} = 5.0 Hz, J _{CHNH} = 12.4 Hz, J _{CH2NH} = 6.0 Hz, J _{CH2CH3} = 7.1 Hz.
7	300 CDCl ₃	1.32 (3H, t, COOCH ₂ CH ₃), 3.03 (6H, s, CHNMe ₂), 3.71 (3H, s, COOMe), 4.23 (2H, q, COOCH ₂ CH ₃), 6.94 (1H, ddd, H ₅), 7.27 (1H, s, CHNMe ₂), 7.60 (1H, ddd, H ₄), 7.90 (1H, d, CHNH), 8.34-8.38 (2H, m, H ₃ , H ₆), 11.52 (1H, br.s, CHNH), J _{H3H4} = 8.6 Hz, J _{H3H5} = 1.1 Hz, J _{H3H6} = 0.7 Hz, J _{H4H5} = 7.2 Hz, J _{H4H6} = 1.7 Hz, J _{H5H6} = 5.0 Hz, J _{CHNH} = 12.5 Hz, J _{CH2CH3} = 7.1 Hz.
	DMSO-d ₆	1.24 (3H, t, COOCH ₂ CH ₃), 3.00 (6H, s, CHNMe ₂), 3.59 (3H, s, COOMe), 4.14 (2H, q, COOCH ₂ CH ₃), 7.07 (1H, ddd, H ₅), 7.30 (1H, s, CHNMe ₂), 7.71 (1H, ddd, H ₄), 7.77 (1H, d, CHNH), 8.28 (1H, d, H ₃), 8.46 (1H, ddd, H ₆), 11.40 (1H, d, CHNH), J _{H3H4} = 8.4 Hz, J _{H3H5} = 1.1 Hz, J _{H3H6} = 1.0 Hz, J _{H4H5} = 7.3 Hz, J _{H4H6} = 1.9 Hz, J _{H5H6} = 5.0 Hz, J _{CHNH} = 13.0 Hz, J _{CH2CH3} = 7.0 Hz.
8	300 CDCl ₃	1.26 (3H, t, COOCH ₂ CH ₃), 1.31 (3H, t, COOCH ₂ CH ₃), 3.03 (6H, s, CHNMe ₂), 4.18 (2H, q, COOCH ₂ CH ₃), 4.25 (2H, q, COOCH ₂ CH ₃), 6.94 (1H, ddd, H ₅), 7.24 (1H, s, CHNMe ₂), 7.60 (1H, ddd, H ₄), 7.93 (1H, d, CHNH), 8.36 (1H, ddd, H ₃), 8.37 (1H, ddd, H ₆), 11.58 (1H, d, CHNH), J _{H3H4} = 8.5 Hz, J _{H3H5} = 1.1 Hz, J _{H3H6} = 1.0 Hz, J _{H4H5} = 7.4 Hz, J _{H4H6} = 1.9 Hz, J _{H5H6} = 4.6 Hz, J _{CHNH} = 12.6 Hz, J _{CH2CH3} = 7.1 Hz.
22	300 CDCl ₃	(2E, 2'E): 1.30 (3H, t, COOCH ₂ CH ₃), 3.72 (3H, s, COOMe), 4.22 (2H, q, COOCH ₂ CH ₃), 4.40 (2H, d, R ₁ CH ₂ NHCH), 5.09 (1H, m, R ₁ CH ₂ NHCH), 6.94-6.97 (1H, m, H ₅ '), 7.26-7.39 (5H, m, 5H(Ph)), 7.44 (1H, d, R ₁ CH ₂ NHCH), 7.59-7.64 (1H, m, H ₄ '), 7.95 (1H, d, CHNH), 8.30-8.41 (2H, m, H ₃ ', H ₆ '), 11.27 (1H, br.s, CHNH), J _{R1CH2NHCH} = 5.6 Hz, J _{R1CH2NHCH} = 13.8 Hz, J _{CHNH} = 9.0 Hz, J _{CH2CH3} = 7.2 Hz.
23	300 CDCl ₃	(2E, 2'E): 1.30 (3H, t, COOCH ₂ CH ₃), 3.72, 3.80 (2x 3H, 2x s, COOMe, OMe), 4.22 (2H, q, COOCH ₂ CH ₃), 4.33 (2H, d, R ₁ CH ₂ NHCH), 5.03 (1H, br.s, R ₁ CH ₂ NHCH), 6.89 (2H, d, H ₃ , H ₅ '), 6.95 (1H, dd, H ₅ '), 7.19 (2H, d, H ₂ , H ₆ '), 7.44 (1H, d, R ₁ CH ₂ NHCH), 7.62 (1H, dd, H ₄ '), 7.93 (1H, br.s, CHNH), 8.31 (1H, d, H ₃ '), 8.37 (1H, d, H ₆ '), 11.28 (1H, br.s, CHNH), J _{H3'H4'} = 8.8 Hz, J _{H4'H5'} = 6.6 Hz, J _{H2H3} = J _{H5H6} = 8.3 Hz, J _{R1CH2NHCH} = 4.9 Hz, J _{R1CH2NHCH} = 13.9 Hz, J _{CH2CH3} = 7.2 Hz.
24	300 CDCl ₃	(2E, 2'E): 1.32 (3H, t, COOCH ₂ CH ₃), 1.59 (3H, d, R ₁ (Me)CHNHCH), 3.69 (3H, s, COOMe), 4.24 (2H, q, COOCH ₂ CH ₃), 4.60 (1H, qd, R ₁ (Me)CHNHCH), 5.07 (1H, dd, R ₁ (Me)CHNHCH), 7.00 (1H, ddd, H ₅ '), 7.26 (1H, d, R ₁ (Me)CHNHCH), 7.46 (2H, dd, H ₂ , H ₆ '), 7.65 (1H, ddd, H ₄ '), 7.96 (1H, d, CHNH), 8.23 (2H, dd, H ₃ , H ₅ '), 8.33 (1H, ddd, H ₃ '), 8.41 (1H, ddd, H ₆ '), 11.31 (1H, d, CHNH), J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.1 Hz, J _{H3'H6'} = 1.0 Hz, J _{H4'H5'} = 7.4 Hz, J _{H4'H6'} = 2.0 Hz, J _{H5'H6'} = 5.0 Hz, J _{H2H3} = J _{H5H6} = 6.6 Hz, J _{H2H6} = J _{H3H5} = 2.0 Hz, J _{R1(Me)CHNHCH} = 7.0 Hz, J _{R1(Me)CHNHCH} = 13.7 Hz, J _{R1(Me)CHNHCH} = 13.6 Hz, J _{CHNH} = 12.7 Hz, J _{CH2CH3} = 7.1 Hz.
(2E,2'E) and (2Z,2'E) isomers of 25 were separated by radial chromatography (petrolether/ethyl acetate = 5:1):		
25	300 CDCl ₃	(2E, 2'E): 1.31 (3H, t, COOCH ₂ CH ₃), 3.79 (3H, s, COOMe), 4.24 (2H, q, COOCH ₂ CH ₃), 6.78 (1H, br.d, R ₁ NHCH), 6.96-7.06 (4H, m, H ₅ ', 3H(Ph)), 7.29-7.35 (2H, m, 2H(Ph)), 7.66 (1H, ddd, H ₄ '), 7.92 (1H, br.d, R ₁ NHCH), 8.01 (1H, br.d, CHNH), 8.36 (1H, ddd, H ₃ '), 8.45 (1H, ddd, H ₆ '), 11.53 (1H, br.s, CHNH), J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.0 Hz, J _{H3'H6'} = 1.0 Hz, J _{H4'H5'} = 7.4 Hz, J _{H4'H6'} = 2.1 Hz, J _{H5'H6'} = 4.9 Hz, J _{R1NHCH} = 12.8 Hz, J _{CHNH} = 12.1 Hz, J _{CH2CH3} = 7.1 Hz. By addition of D ₂ O the doublet at δ = 6.78 ppm and the broad singlet at δ = 11.53 ppm disappear; the doublets at δ = 7.92 ppm and δ = 8.01 change into singlets. (2Z, 2'E): 1.33 (3H, t, COOCH ₂ CH ₃), 3.86 (3H, s, COOMe), 4.26 (2H, q, COOCH ₂ CH ₃), 7.41 (1H, br.d, R ₁ NHCH), 7.63 (1H, ddd, H ₄ '), 8.35 (1H, ddd, H ₃ '), 8.43 (1H, ddd, H ₆ '), 9.62 (1H, br.d, R ₁ NHCH), 12.01 (1H, br.d, CHNH). By addition of D ₂ O the doublet at δ = 9.62 ppm and the broad singlet at δ = 12.01 ppm disappear; the doublet at δ = 7.41 ppm changes into singlet.
25 (2E, 2'E)	CDCl ₃	(2Z, 2'Z) and (2E, 2'Z): 1.36 (6H, t, 2x COOCH ₂ CH ₃), 3.76, 3.83 (6H, 2x s, 2x COOMe), 4.32 (4H, q, 2x COOCH ₂ CH ₃), 1.31 (3H, t, COOCH ₂ CH ₃), 3.79 (3H, s, COOMe), 4.23 (2H, q, COOCH ₂ CH ₃), 6.83 (1H, d, R ₁ NHCH), 6.98-7.06 (4H, m, H ₅ ', 3H(Ph)), 7.29-7.35 (2H, m, 2H(Ph)), 7.66 (1H, ddd, H ₄ '), 7.92 (1H, d, R ₁ NHCH), 7.99 (1H, d, CHNH), 8.36 (1H, ddd, H ₃ '), 8.45 (1H, ddd, H ₆ '), 11.49 (1H, d, CHNH), J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.0 Hz, J _{H3'H6'} = 1.0 Hz, J _{H4'H5'} = 7.4 Hz, J _{H4'H6'} = 2.1 Hz, J _{H5'H6'} = 4.9 Hz, J _{R1NHCH} = 13.2 Hz, J _{CHNH} = 12.2 Hz, J _{CH2CH3} = 7.1 Hz. By addition of D ₂ O the doublets at δ = 6.83 ppm and δ = 11.49 ppm disappear; the doublets at δ = 7.92 ppm and δ = 7.99 change into broad singlets.
25 (2Z, 2'E)	CDCl ₃	1.33 (3H, t, COOCH ₂ CH ₃), 3.86 (3H, s, COOMe), 4.27 (2H, q, COOCH ₂ CH ₃), 6.96-7.05 (4H, m, H ₅ ', 3H(Ph)), 7.30-7.35 (2H, m, 2H(Ph)), 7.41 (1H, d, R ₁ NHCH), 7.63 (1H, ddd, H ₄ '), 8.01 (1H, d, CHNH), 8.35 (1H, ddd, H ₃ '), 8.44 (1H, ddd, H ₆ '), 9.62 (1H, d, R ₁ NHCH), 12.02 (1H, d, CHNH), J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.0 Hz, J _{H3'H6'} = 1.0 Hz, J _{H4'H5'} = 7.4 Hz, J _{H4'H6'} = 2.1 Hz, J _{H5'H6'} = 4.9 Hz, J _{R1NHCH} = 12.5 Hz, J _{CHNH} = 12.2 Hz, J _{CH2CH3} = 7.1 Hz. By addition of D ₂ O the doublets at δ = 9.62 ppm and δ = 12.02 ppm disappear; the doublets at δ = 7.41 ppm and δ = 8.01 change into singlets.
26	300 DMSO-d ₆	(2E, 2'E): 1.25 (3H, t, COOCH ₂ CH ₃), 3.79 (3H, s, OMe), 3.90 (3H, s, COOMe), 4.16 (2H, q, COOCH ₂ CH ₃), 6.95-7.11 (4H, m, 4H(Ph)), 7.51 (1H, ddd, H ₅ '), 7.73 (1H, ddd, H ₄ '), 7.80 (2H, d, R ₁ NHCH, CHNH), 8.26 (1H, ddd, H ₃ '), 8.48 (1H, ddd, H ₆ '), 9.93 (1H, d, R ₁ NHCH), 12.00 (1H, d, CHNH), J _{H3'H4'} = 8.3 Hz, J _{H4'H5'} = 7.5 Hz, J _{R1CHNH} = 12.6 Hz, J _{CHNH} = 12.3 Hz, J _{CH2CH3} = 7.1 Hz.

Table 2 (continued)

Compound	MHz Solvent	δ (tetramethylsilane)
27	300 CDCl ₃	(2 <i>E</i> , 2' <i>E</i>): 1.31 (3H, t, COOCH ₂ CH ₃), 3.79 (6H, s, OMe, COOMe), 4.24 (2H, q, COOCH ₂ CH ₃), 6.69 (1H, br.d, R ₁ NHCH), 6.85-7.03 (5H, m, H ₅ ', 4H(Ph)), 7.66 (1H, ddd, H ₄ '), 7.84 (1H, br.d, R ₁ NHCH), 8.00 (1H, br.d, CHNH), 8.36 (1H, ddd, H ₃ '), 8.44 (1H, ddd, H ₆ '), 11.42 (1H, br.s, CHNH), J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.1 Hz, J _{H3'H6'} = 1.0 Hz, J _{H4'H5'} = 7.4 Hz, J _{H4'H6'} = 2.0 Hz, J _{H5'H6'} = 5.0 Hz, J _{R1NHCH} = 13.0 Hz, J _{CHNH} = 12.5 Hz, J _{CH2CH3} = 7.1 Hz. (2 <i>Z</i> , 2' <i>E</i>): 1.33 (3H, t, COOCH ₂ CH ₃), 3.77, 3.84 (6H, 2x s, OMe, COOMe), 4.26 (2H, q, COOCH ₂ CH ₃), 7.33 (1H, d, R ₁ NHCH), 7.63 (1H, ddd, H ₄ '), 8.34 (1H, ddd, H ₃ '), 8.43 (1H, ddd, H ₆ '), 9.54 (1H, br.d, R ₁ NHCH), 11.93 (1H, br.d, CHNH). The signals for (2 <i>Z</i> , 2' <i>Z</i>) and (2 <i>E</i> , 2' <i>Z</i>) isomers are overlapped.
28	300 CDCl ₃	(2 <i>E</i> , 2' <i>E</i>): 1.31 (3H, t, COOCH ₂ CH ₃), 3.78 (3H, s, COOMe), 4.24 (2H, q, COOCH ₂ CH ₃), 6.78 (1H, br.d, R ₁ NHCH), 6.93-7.06 (5H, m, H ₅ ', 4H(Ph)), 7.66 (1H, ddd, H ₄ '), 7.82 (1H, br.d, R ₁ NHCH), 7.99 (1H, br.d, CHNH), 8.34 (1H, ddd, H ₃ '), 8.43 (1H, ddd, H ₆ '), 11.43 (1H, br.s, CHNH), J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.0 Hz, J _{H3'H6'} = 0.9 Hz, J _{H4'H5'} = 7.4 Hz, J _{H4'H6'} = 2.0 Hz, J _{H5'H6'} = 5.0 Hz, J _{R1NHCH} = 13.3 Hz, J _{CHNH} = 12.5 Hz, J _{CH2CH3} = 7.1 Hz. (2 <i>Z</i> , 2' <i>E</i>): 1.33 (3H, t, COOCH ₂ CH ₃), 3.85 (3H, s, COOMe), 4.26 (2H, q, COOCH ₂ CH ₃), 7.31 (1H, d, R ₁ NHCH), 7.63 (1H, ddd, H ₄ '), 8.33 (1H, ddd, H ₃ '), 8.43 (1H, ddd, H ₆ '), 9.59 (1H, br.d, R ₁ NHCH), 12.00 (1H, br.d, CHNH). (2 <i>Z</i> , 2' <i>Z</i>) and (2 <i>E</i> , 2' <i>Z</i>): 3.76, 3.83 (6H, 2x s, 2x COOMe).
29	300 DMSO-d ₆	(2 <i>E</i> , 2' <i>E</i>): 1.22 (3H, t, COOCH ₂ CH ₃), 3.69 (3H, s, COOMe), 4.14 (2H, q, COOCH ₂ CH ₃), 7.11 (1H, ddd, H ₅ '), 7.20-7.71 (3H, m, 3H(Ph)), 7.76 (1H, ddd, H ₄ '), 7.85 (1H, br.d, R ₁ NHCH), 7.89 (1H, br.d, CHNH), 8.28 (1H, ddd, H ₃ '), 8.50 (1H, ddd, H ₆ '), 9.53 (1H, br.d, R ₁ NHCH), 11.57 (1H, br.d, CHNH), J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.1 Hz, J _{H3'H6'} = 1.0 Hz, J _{H4'H5'} = 7.3 Hz, J _{H4'H6'} = 2.0 Hz, J _{H5'H6'} = 4.9 Hz, J _{R1NHCH} = 12.6 Hz, J _{CHNH} = 12.5 Hz, J _{CH2CH3} = 7.1 Hz. (2 <i>Z</i> , 2' <i>E</i>): 1.25 (3H, t, COOCH ₂ CH ₃), 3.80 (3H, s, COOMe), 4.16 (2H, q, COOCH ₂ CH ₃), 7.09 (1H, ddd, H ₅ '), 7.75 (1H, ddd, H ₄ '), 7.76 (1H, br.d, R ₁ NHCH), 7.99 (1H, br.d, CHNH), 8.25 (1H, ddd, H ₃ '), 8.48 (1H, ddd, H ₆ '), 9.29 (1H, br.d, R ₁ NHCH), 12.02 (1H, br.d, CHNH). (2 <i>Z</i> , 2' <i>Z</i>) and (2 <i>E</i> , 2' <i>Z</i>): 3.68, 3.79 (6H, 2x s, 2x COOMe).
30	300 CDCl ₃	(2 <i>E</i> , 2' <i>E</i>): 1.34 (3H, t, COOCH ₂ CH ₃), 3.89 (3H, s, COOMe), 4.27 (2H, q, COOCH ₂ CH ₃), 6.88 (1H, ddd, H ₅ (Ph)), 7.00 (1H, ddd, H ₅ '), 7.11 (1H, ddd, H ₃ (Ph)), 7.30 (1H, ddd, H ₄ (Ph)), 7.38 (1H, br.d, R ₁ NHCH), 7.56 (1H, dd, H ₆ (Ph)), 7.64 (1H, ddd, H ₄ '), 8.03 (1H, br.d, CHNH), 8.34 (1H, ddd, H ₃ '), 8.45 (1H, ddd, H ₆ '), 10.04 (1H, br.d, R ₁ NHCH), 12.13 (1H, br.d, CHNH), J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.1 Hz, J _{H3'H6'} = 1.0 Hz, J _{H4'H5'} = 7.4 Hz, J _{H4'H6'} = 2.0 Hz, J _{H5'H6'} = 5.0 Hz, J _{H3H4} = 8.2 Hz, J _{H3H5} = 1.5 Hz, J _{H4H5} = 7.4 Hz, J _{H4H6} = 1.5 Hz, J _{H5H6} = 8.0 Hz, J _{R1NHCH} = 12.2 Hz, J _{CHNH} = 11.9 Hz, J _{CH2CH3} = 7.1 Hz. (2 <i>Z</i> , 2' <i>E</i>): 3.91 (3H, s, COOMe), 7.31 (1H, ddd, H ₄ (Ph)).
31	300 CDCl ₃	(2 <i>E</i> , 2' <i>E</i>): 1.34 (3H, t, COOCH ₂ CH ₃), 3.84 (3H, s, COOMe), 4.28 (2H, q, COOCH ₂ CH ₃), 6.89-6.92 (1H, ddd, 1H(Ph)), 6.99 (1H, ddd, H ₅ '), 7.12-7.23 (3H, m, 3H(Ph)), 7.32 (1H, br.d, R ₁ NHCH), 7.64 (1H, ddd, H ₄ '), 8.00 (1H, br.d, CHNH), 8.34 (1H, ddd, H ₃ '), 8.43 (1H, ddd, H ₆ '), 9.61 (1H, br.d, R ₁ NHCH), 12.08 (1H, br.d, CHNH), J _{H3'H4'} = 8.7 Hz, J _{H3'H5'} = 1.1 Hz, J _{H3'H6'} = 1.0 Hz, J _{H4'H5'} = 7.4 Hz, J _{H4'H6'} = 1.9 Hz, J _{H5'H6'} = 5.1 Hz, J _{R1NHCH} = 12.4 Hz, J _{CHNH} = 12.2 Hz, J _{CH2CH3} = 7.2 Hz. By addition of D ₂ O the doublets at δ = 9.61 ppm and δ = 12.08 ppm disappear; the doublets at δ = 7.32 ppm and δ = 8.00 ppm change into singlets. (2 <i>Z</i> , 2' <i>E</i>): 3.86 (3H, s, COOMe).
32	300 CDCl ₃	(2 <i>E</i> , 2' <i>E</i>): 1.30 (3H, t, COOCH ₂ CH ₃), 3.87 (3H, s, COOMe), 4.26 (2H, q, COOCH ₂ CH ₃), 6.99-7.06 (2H, m, H ₅ ', 1H(Ph)), 7.31-7.40 (1H, m, 1H(Ph)), 7.65 (1H, d, R ₁ NHCH), 7.67 (1H, ddd, H ₄ '), 7.78 (1H, d, CHNH), 8.22-8.32 (2H, m, 2H(Ph)), 8.40 (1H, ddd, H ₃ '), 8.47 (1H, ddd, H ₆ '), 10.23 (1H, br.d, R ₁ NHCH), 12.60 (1H, br.d, CHNH), J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.1 Hz, J _{H3'H6'} = 1.1 Hz, J _{H4'H5'} = 7.4 Hz, J _{H4'H6'} = 1.9 Hz, J _{H5'H6'} = 6.0 Hz, J _{R1NHCH} = 12.2 Hz, J _{CHNH} = 12.6 Hz, J _{CH2CH3} = 7.2 Hz. (2 <i>Z</i> , 2' <i>E</i>): 1.35 (3H, t, COOCH ₂ CH ₃), 3.99 (3H, s, COOMe), 4.31 (2H, q, COOCH ₂ CH ₃), 7.62 (1H, d, R ₁ NHCH), 7.63 (1H, ddd, H ₄ '), 7.90 (1H, d, CHNH).
33	300 CDCl ₃	(2 <i>E</i> , 2' <i>E</i>): 1.30 (3H, t, COOCH ₂ CH ₃), 3.82 (3H, s, COOMe), 4.22 (2H, q, COOCH ₂ CH ₃), 7.03 (1H, ddd, H ₅ '), 7.21 (1H, br.d, R ₁ NHCH), 7.29-7.32 (1H, m, 1H(Ph)), 7.45-7.50 (1H, m, 1H(Ph)), 7.67 (1H, ddd, H ₄ '), 7.83-7.88 (2H, m, 2H(Ph)), 7.86 (1H, br.d, CHNH), 7.95 (1H, br.s, R ₁ NHCH), 8.32 (1H, ddd, H ₃ '), 8.45 (1H, ddd, H ₆ '), 11.51 (1H, br.s, CHNH), J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.1 Hz, J _{H3'H6'} = 1.0 Hz, J _{H4'H5'} = 7.4 Hz, J _{H4'H6'} = 1.9 Hz, J _{H5'H6'} = 5.0 Hz, J _{R1NHCH} = 12.9 Hz, J _{CHNH} = 12.9 Hz, J _{CH2CH3} = 7.2 Hz. (2 <i>Z</i> , 2' <i>E</i>): 3.89 (3H, s, COOMe).
34	300 CDCl ₃	(2 <i>E</i> , 2' <i>E</i>): 1.30, 1.31 (6H, 2x t, 2x COOCH ₂ CH ₃), 3.79 (3H, s, OMe), 4.20-4.34 (4H, m, 2x COOCH ₂ CH ₃), 6.69 (1H, d, R ₁ NHCH), 6.86-7.03 (5H, m, H ₅ ', 4H(Ph)), 7.66 (1H, ddd, H ₄ '), 7.81 (1H, d, R ₁ NHCH), 8.02 (1H, d, CHNH), 8.36 (1H, ddd, H ₃ '), 8.44 (1H, ddd, H ₆ '), 11.44 (1H, d, CHNH), J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.0 Hz, J _{H3'H6'} = 0.9 Hz, J _{H4'H5'} = 7.3 Hz, J _{H4'H6'} = 2.0 Hz, J _{H5'H6'} = 5.0 Hz, J _{R1NHCH} = 13.4 Hz, J _{CHNH} = 12.3 Hz, J _{CH2CH3} = 7.1 Hz. (2 <i>Z</i> , 2' <i>E</i>): 1.33, 1.37 (6H, 2x t, 2x COOCH ₂ CH ₃), 7.31 (1H, d, R ₁ NHCH), 7.63 (1H, ddd, H ₄ '), 8.04 (1H, d, CHNH), 8.35 (1H, ddd, H ₃ '), 8.42 (1H, ddd, H ₆ '), 9.52 (1H, d, R ₁ NHCH), 12.16 (1H, d, CHNH).
35	300 CDCl ₃	(2 <i>E</i> , 2' <i>E</i>): 1.35, 1.39 (6H, 2x t, 2x COOCH ₂ CH ₃), 4.28, 4.32 (4H, 2x q, 2x COOCH ₂ CH ₃), 6.80-6.85 (1H, m, 1H(Ph)), 6.99 (1H, ddd, H ₅ '), 7.02-7.12 (2H, m, 2H(Ph)), 7.22 (1H, d, R ₁ NHCH), 7.64 (1H, ddd, H ₄ '), 8.03 (1H, d, CHNH), 8.34 (1H, ddd, H ₃ '), 8.42 (1H, ddd, H ₆ '), 9.57 (1H, d, R ₁ NHCH), 12.26 (1H, d, CHNH), J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.1 Hz, J _{H3'H6'} = 1.0 Hz, J _{H4'H5'} = 7.4 Hz, J _{H4'H6'} = 2.0 Hz, J _{H5'H6'} = 5.0 Hz, J _{R1NHCH} = 12.2 Hz, J _{CHNH} = 12.2 Hz, J _{CH2CH3} = 7.1 Hz.
36	300 CDCl ₃	(2 <i>E</i> , 2' <i>E</i>): 1.30 (3H, t, COOCH ₂ CH ₃), 3.80 (3H, s, COOMe), 4.22 (2H, q, COOCH ₂ CH ₃), 6.77 (1H, dd, H ₃ '), 7.02 (1H, ddd, H ₅ '), 7.46 (1H, d, R ₁ NHCH), 7.55 (1H, dd, H ₄ '), 7.66 (1H, ddd, H ₄ '), 7.97 (1H, br.s, R ₁ NHCH), 8.22 (1H, d, H ₆ '), 8.32 (1H, ddd, H ₃ '), 8.33 (1H, d, CHNH), 8.44 (1H, ddd, H ₆ '), 11.48 (1H, br.s, CHNH), J _{H3H4} = 8.7 Hz, J _{H3H6} = 0.6 Hz, J _{H4H6} = 2.5 Hz, J _{H3'H4'} = 8.5 Hz, J _{H3'H5'} = 1.0 Hz, J _{H3'H6'} = 0.9 Hz, J _{H4'H5'} = 7.3 Hz, J _{H4'H6'} = 2.0 Hz, J _{H5'H6'} = 5.0 Hz, J _{R1NHCH} = 13.4 Hz, J _{CHNH} = 12.5 Hz, J _{CH2CH3} = 7.2 Hz.

Table 2 (continued)

Compound	MHz Solvent	δ (tetramethylsilane)
37	300 CDCl ₃	(2 <i>E</i> , 2' <i>E</i>): 1.29 (3H, t, COOCH ₂ CH ₃), 1.33 (3H, t, COOCH ₂ CH ₃), 4.22 (2H, q, COOCH ₂ CH ₃), 4.27 (2H, q, COOCH ₂ CH ₃), 6.77 (1H, d, H ₃), 7.01 (1H, ddd, H ₅ '), 7.45 (1H, d, R ₁ NHCH), 7.55 (1H, dd, H ₄ '), 7.66 (1H, ddd, H ₄ '), 8.00 (1H, br.s, R ₁ NHCH), 8.22 (1H, dd, H ₆), 8.29 (1H, d, CHNH), 8.32 (1H, ddd, H ₃ '), 8.44 (1H, ddd, H ₆ '), 11.56 (1H, br.s, CHNH), J _{H3H4} = 8.7 Hz, J _{H3H6} = 0.6 Hz, J _{H4H6} = 2.5 Hz, J _{H3'H4'} = 8.6 Hz, J _{H3'H5'} = 1.0 Hz, J _{H3'H6'} = 0.8 Hz, J _{H4'H5'} = 7.4 Hz, J _{H4'H6'} = 1.9 Hz, J _{H5'H6'} = 5.0 Hz, J _{R1NHCH} = 12.7 Hz, J _{CHNH} = 12.6 Hz, J _{CH2CH3} = 7.2 Hz.

Table 3

¹H nmr (CDCl₃) [a] (δ in ppm, J in Hz)

	d _{R1NHCH}	d _{R1NHCH}	d _{CHNH}	d _{CHNH}	J _{R1NHCH}	J _{CHNH}
22 (2 <i>E</i> , 2' <i>E</i>)	7.44	5.09	7.95	11.27	13.8	9.0
23 (2 <i>E</i> , 2' <i>E</i>)	7.44	5.03	7.93	11.28	13.9	-
24 (2 <i>E</i> , 2' <i>E</i>)	7.26	5.07	7.96	11.31	13.6	12.7
26 (2 <i>E</i> , 2' <i>E</i>)	7.80	9.93	7.80	12.00	12.6	12.3
35 (2 <i>E</i> , 2' <i>E</i>)	7.22	9.57	8.03	12.26	12.2	12.2
36 (2 <i>E</i> , 2' <i>E</i>)	7.46	7.97	8.33	11.48	13.4	12.5
37 (2 <i>E</i> , 2' <i>E</i>)	7.45	8.00	8.29	11.56	12.7	12.6
30 [b] (2 <i>E</i> , 2' <i>E</i>)	7.38	10.04	8.03	12.13	12.2	11.9
(2 <i>Z</i> , 2' <i>E</i>)	7.38	10.04	8.03	12.13	12.2	11.9
31 [b] (2 <i>E</i> , 2' <i>E</i>)	7.32	9.61	8.00	12.08	12.4	12.2
(2 <i>Z</i> , 2' <i>E</i>)	7.32	9.61	8.00	12.08	12.4	12.2
32 [b] (2 <i>E</i> , 2' <i>E</i>)	7.65	10.23	7.78	12.60	12.2	12.6
(2 <i>Z</i> , 2' <i>E</i>)	7.62	10.23	7.90	12.60	12.2	12.6
33 [b] (2 <i>E</i> , 2' <i>E</i>)	7.21	7.95	7.86	11.51	12.9	12.9
(2 <i>Z</i> , 2' <i>E</i>)	7.21	7.95	7.86	11.51	12.9	12.9
34 (2 <i>E</i> , 2' <i>E</i>)	7.81	6.69	8.02	11.44	13.4	12.3
(2 <i>Z</i> , 2' <i>E</i>)	7.31	9.52	8.04	12.16	13.4	12.3
25 [b] (2 <i>E</i> , 2' <i>E</i>)	7.92	6.78	8.01	11.53	12.8	12.1
(2 <i>Z</i> , 2' <i>E</i>)	7.41,	9.62	8.01	12.01	12.8	12.1
(2 <i>Z</i> , 2' <i>Z</i>) and (2 <i>E</i> , 2' <i>Z</i>)	7.41, 7.92	6.78, 9.62	2X 8.01	11.53, 12.01	12.8	12.1
27 [b] (2 <i>E</i> , 2' <i>E</i>)	7.84	6.69	8.00	11.42	13.0	12.5
(2 <i>Z</i> , 2' <i>E</i>)	7.33	9.54	8.00	11.93	13.0	12.5
(2 <i>Z</i> , 2' <i>Z</i>) and (2 <i>E</i> , 2' <i>Z</i>)	2X 7.84	6.69, 9.54	2X 8.00	11.42, 11.93	13.0	12.5
28 [b] (2 <i>E</i> , 2' <i>E</i>)	7.82	6.78	7.99	11.43	13.3	12.5
(2 <i>Z</i> , 2' <i>E</i>)	7.31	9.59	7.99	12.00	13.3	12.5
(2 <i>Z</i> , 2' <i>Z</i>) and (2 <i>E</i> , 2' <i>Z</i>)	2X 7.82	6.78, 9.59	2X 7.99	11.43, 12.00	13.3	12.5
29 [b] (2 <i>E</i> , 2' <i>E</i>)	7.85	9.53	7.89	11.57	12.6	12.5
(2 <i>Z</i> , 2' <i>E</i>)	7.76	9.29	7.99	12.02	12.6	12.5
(2 <i>Z</i> , 2' <i>Z</i>) and (2 <i>E</i> , 2' <i>Z</i>)	7.76, 7.85	9.29, 9.53	7.89, 7.99	11.57, 12.02	12.6	12.5

[a] Spectra of compounds **26** and **29** were obtained in dimethyl sulfoxide-*d*₆ as solvent. [b] The similar chemical shifts and coupling constants for R₁NHCH, R₁NHCH, CHNH, and CHNH for (2*E*, 2'*E*) and (2*Z*, 2'*E*) isomers in ¹H nmr spectra of compounds **30-33** and for some isomers in ¹H nmr spectra of compounds **25**, **27-29** result in broad singlets and broad doublets due to overlapping.

(HMBC) experiments. The HMBC nmr experiment of compound **5** in deuteriochloroform solution at room temperature shows that the compound exists in one isomeric form. The orientation around the C=C double bond was deduced from the coupling constant ³J_{C=O, ¹H} = 4.5 Hz, which indicates the (*E*) orientation (Figure 1). The ¹H nmr chemical shifts and coupling constants for compound **5** [δ (CHNH) = 7.92 ppm, δ (CHNH) = 11.02 ppm, J_{CH-NH} = 12.8 Hz] are of similar values as those for compound **6** [δ (CHNH) = 7.93 ppm, δ (CHNH) = 11.02 ppm, J_{CH-NH} = 12.4 Hz].

The ¹H nmr spectra of compounds **7** and **8** in deuteriochloroform exhibit besides the signals characteristic for pyridine ring, ethyl and methyl groups in esters, and

dimethylaminomethylene group, a doublet at δ = 7.90-7.93 ppm for CHNH and δ = 11.52-11.58 ppm for CHNH with the coupling constant J_{CHNH} = 12.5-12.6 Hz, thus indicating

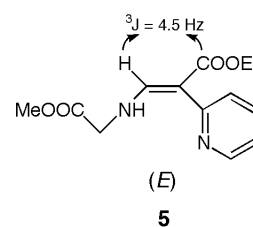


Figure 1

Table 4
 ^{13}C nmr Data

Compound	MHz Solvent	δ (tetramethylsilane)
5	75.5 CDCl_3	14.70 ($\text{COOCH}_2\text{CH}_3$), 50.16 (COOCH_3), 52.51 (CH_2NH), 59.48 ($\text{COOCH}_2\text{CH}_3$), 97.04, 118.73, 122.34, 135.95, 146.19, 153.21, 157.58, 167.92, 170.23.
7	75.5 CDCl_3	15.00 ($\text{COOCH}_2\text{CH}_3$), 43.12 ($\text{N}(\text{CH}_3)_2$), 51.75 (COOCH_3), 59.64 ($\text{COOCH}_2\text{CH}_3$), 96.66, 101.11, 118.75, 122.51, 136.16, 144.81, 146.42, 155.66, 158.28, 168.46, 168.55.
8	75.5 CDCl_3	14.96, 15.00 (2x $\text{COOCH}_2\text{CH}_3$), 43.07 ($\text{N}(\text{CH}_3)_2$), 59.61, 60.36 (2x $\text{COOCH}_2\text{CH}_3$), 96.49, 101.50, 118.72, 122.47, 136.16, 144.27, 146.40, 155.58, 158.34, 167.98, 168.49.
26	75.5 $\text{DMSO}-d_6$	15.05 ($\text{COOCH}_2\text{CH}_3$), 52.20 (COOCH_3), 56.52 (OMe), 59.37 ($\text{COOCH}_2\text{CH}_3$), 96.15, 106.11, 111.83, 113.43, 119.18, 121.69, 121.99, 122.76, 129.91, 136.61, 136.94, 146.89, 147.80, 151.48, 157.62, 166.84, 167.59.
29 [a]	75.5 $\text{DMSO}-d_6$	15.01, 15.05 (2x $\text{COOCH}_2\text{CH}_3$), 52.01, 52.21 (2x COOCH_3), 59.41, 59.66 (2x $\text{COOCH}_2\text{CH}_3$), 96.22, 97.37, 106.86, 107.33, 116.57, 116.66, 116.95, 117.04, 117.75, 117.82, 118.05, 118.16, 119.20, 119.36, 120.39, 120.55, 120.64, 120.80, 122.02, 122.11, 135.03, 136.61, 136.68, 137.04, 138.81, 139.40, 139.43, 146.86, 147.01, 148.84, 151.20, 151.62, 154.07, 154.81, 157.59, 157.68, 166.16, 166.31, 167.47, 167.60.

[a] The assignments of two major isomers in ^{13}C nmr spectrum are based on the signals of aliphatic groups. The assignments of other signals were not possible due to overlapping and ^{13}C - ^{19}F couplings.

that the orientation of protons in NHCH structural element is *trans* (*antiperiplanar*). The orientation around the $\text{C}=\text{C}$ double bonds was determined on the basis of HMBC nmr experiment for compound 7, indicating that compound exists in one isomeric form. Both coupling constants, $^3J^{13}_{\text{CO},^1\text{H}}$ are 3 Hz and 4 Hz, respectively, indicating that the orientation around $\text{C}(2)=\text{C}(3)$ is (*Z*), while the orientation around the $\text{C}(2')=\text{C}(3')$ is (*E*). (Figure 2).

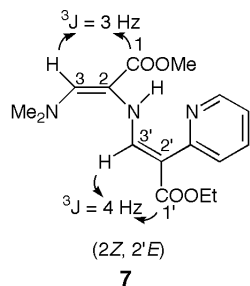


Figure 2

The ^1H nmr spectra of crude compounds 22-37 [24] exhibit one, two or four sets of signals, indicating that these compounds exist in one, two or four isomeric forms. The ratio of isomers was determined on the basis of peaks for methyl and ethyl groups in esters, except for compounds 27 and 34, due to overlapping of signals.

Compound 26 exists as a single isomer. The HMBC nmr experiment in dimethyl sulfoxide- d_6 (at 302 K), shows on the basis of the coupling constants $^3J^{13}_{\text{CO},^1\text{H}} = 9$ Hz for $^1\text{H}-\text{C}(3)=\text{C}(2)-^{13}\text{COOMe}$ and $^3J^{13}_{\text{CO},^1\text{H}} = 4$ Hz for $^1\text{H}-\text{C}(3')=\text{C}(2')-^{13}\text{COOEt}$, that the compound exists in the (*2E,2'E*) form. (Figure 3). In ^1H nmr spectrum, compound 29 shows four sets of signals in the ratio of 13:9:2:1. The HMBC nmr experiment in dimethyl sulfoxide- d_6 (at 302

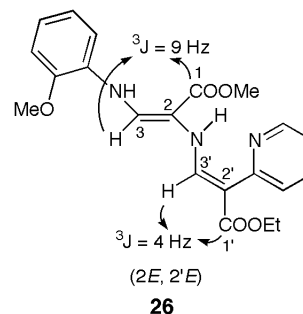


Figure 3

K) indicates (*2E,2'E*) orientation ($^3J^{13}_{\text{CO},^1\text{H}} = 9$ Hz for $^1\text{H}-\text{C}(3)=\text{C}(2)-^{13}\text{COOMe}$, and $^3J^{13}_{\text{CO},^1\text{H}} = 4$ Hz for $^1\text{H}-\text{C}(3')=\text{C}(2')-^{13}\text{COOEt}$) and (*2Z, 2'E*) orientation ($^3J^{13}_{\text{CO},^1\text{H}} = 4$ Hz for $^1\text{H}-\text{C}(3)=\text{C}(2)-^{13}\text{COOMe}$, and $^3J^{13}_{\text{CO},^1\text{H}} = 4$ Hz for $^1\text{H}-\text{C}(3')=\text{C}(2')-^{13}\text{COOEt}$) for two major isomers, respectively. (Figure 4). The determination of orientations around the double bonds for two minor isomers was not possible due to low ratios and overlapping with the signals of major isomers.

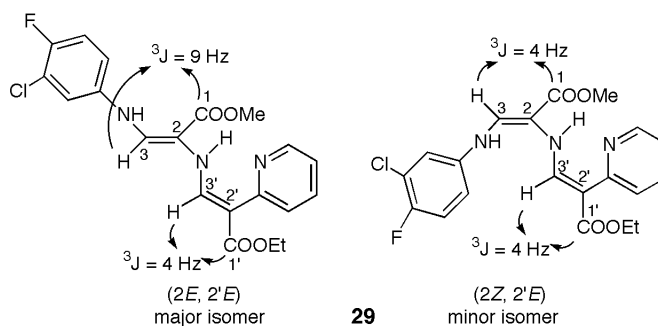


Figure 4

The orientation around the double bonds for all other compounds were determined on the basis of analogous chemical shifts for $CHNH$ and $CHNH$, and J_{CH-NH} coupling constants in 1H nmr spectra. In all cases the orientation in major isomer is (*E*) for $C(2)=C(3)$ and (*E*) for $C(2')=C(3')$ and in the second major isomer (or in the minor isomer for compounds which exist in two isomeric forms, respectively) is (*Z*) around the $C(2)=C(3)$ and (*E*) around the $C(2')=C(3')$ double bonds. Assignments of signals for the two minor isomers, (*2Z*, *2'Z*) and (*2E*, *2'Z*), for those compounds, which exist as four isomeric forms, were not possible. (Table 5).

General Procedure for the Preparation of Alkyl (*Z*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]amino-3-dimethylaminopropenoates **7**, **8**.

To compound **5** or **6** (10 mmol) suspended in dry toluene (10 ml), Bredereck's reagent (20 mmol) was added and the mixture was heated under reflux for several hours. The volatile compounds were evaporated *in vacuo* and the mixture of ethyl acetate (5 ml)/*n*-heptane (15 ml) was added. The precipitate was collected by filtration and washed with ether. The following compounds were prepared in this manner: methyl (*Z*)-2-[(*E*)-2-ethoxycarbonyl-2-(2-pyridinyl)ethenyl]amino-3-dimethylaminopropenoate (**7**) and ethyl (*Z*)-2-[(*E*)-2-ethoxycarbonyl-2-(2-pyridinyl)ethenyl]amino-3-dimethylamino-

Table 5
HMBC nmr Data

Compound	Solvent Temp.	
5	$CDCl_3$ 302 K	One isomer (<i>E</i>): $^3J_{^{13}CO, ^1H} = 4.5$ Hz
7	$CDCl_3$ 302 K	One isomer (<i>2Z</i> , <i>2'E</i>): $^3J_{^{13}CO, ^1H} = 3$ Hz for $^1H-C(3)=C(2)-^{13}COOMe$ $^3J_{^{13}CO, ^1H} = 4$ Hz for $^1H-C(3')=C(2')-^{13}COOEt$
26	$DMSO-d_6$ 302 K	One isomer (<i>2E</i> , <i>2'E</i>): $^3J_{^{13}CO, ^1H} = 9$ Hz for $^1H-C(3)=C(2)-^{13}COOMe$ $^3J_{^{13}CO, ^1H} = 4$ Hz for $^1H-C(3')=C(2')-^{13}COOEt$
29	$DMSO-d_6$ 302 K	Four isomers (13:9:2:1) Major isomer (<i>2E</i> , <i>2'E</i>): $^3J_{^{13}CO, ^1H} = 9$ Hz for $^1H-C(3)=C(2)-^{13}COOMe$ $^3J_{^{13}CO, ^1H} = 4$ Hz for $^1H-C(3')=C(2')-^{13}COOEt$ Minor isomer (<i>2Z</i> , <i>2'E</i>): $^3J_{^{13}CO, ^1H} = 4$ Hz for $^1H-C(3)=C(2)-^{13}COOMe$ $^3J_{^{13}CO, ^1H} = 4$ Hz for $^1H-C(3')=C(2')-^{13}COOEt$

EXPERIMENTAL

Melting points were taken on a Kofler micro hot stage. The 1H nmr spectra were obtained on a Bruker Avance DPX 300 (300 MHz) spectrometer in such solvent as dimethyl sulfoxide- d_6 and deuteriochloroform with tetramethylsilane as internal standard. The elemental analyses for C, H and N were obtained on a Perkin-Elmer CHN Analyser 2400.

General Procedure for the Preparation of Alkyl (*E*)-*N*-[2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]glycinates **5**, **6**.

The mixture of ethyl 2-pyridinylacetate (**1**) (20 mmol, 3 ml) and Bredereck's reagent (25 mmol, 5 ml) was stirred in the oil bath at 85 °C in an argon atmosphere for 1.5 hours. Then ethanol (10 ml) was added and the volatile compounds were evaporated *in vacuo*. The obtained oily residue, ethyl 3-dimethylamino-2-(2-pyridinyl)propenoate (**2**), was without further purification dissolved in ethanol (25 ml), glycine alkyl ester hydrochloride **3** or **4** (20 mmol) was added, and the mixture was heated under reflux for 1.5 hours. The volatile compounds were evaporated *in vacuo* and water (30 ml) was added. The precipitate, which had been formed in refrigerator, was collected by filtration and washed with ether (5 ml). The following compounds were prepared in this manner: methyl (*E*)-*N*-[2-ethoxycarbonyl-2-(2-pyridinyl)ethenyl]glycinate (**5**) from glycine methyl ester hydrochloride (**3**) (20 mmol, 2.5 g) and ethyl (*E*)-*N*-[2-ethoxycarbonyl-2-(2-pyridinyl)ethenyl]glycinate (**6**) from glycine ethyl ester hydrochloride (**4**) (20 mmol, 2.8 g). Experimental and analytical data are given in Tables 1, 2, and 5.

propenoate (**8**). Experimental and analytical data are given in Tables 1, 2, 4, and 5.

General Procedure for the Preparation of β -Alkylamino- α,β -didehydro- α -amino Acid Derivatives **22-24**.

To compound **7** (0.5 mmol, 160 mg) the corresponding aliphatic amine **9-11** (0.5 mmol) and acetic acid (2 ml) were added and stirred at room temperature for 24 hours. The volatile compounds were evaporated *in vacuo*, the appropriate solvent (3 ml) was added and the precipitate was collected by filtration.

Methyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-benzylaminopropenoate (**22**).

This compound was prepared from bezylamine hydrochloride (**9**) (0.5 mmol, 54 mg). The mixture of ethanol (1 ml) and water (1 ml) was used for crystallization. Experimental and analytical data are given in Tables 1, 2, and 3.

Methyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-(4-methoxybenzyl)aminopropenoate (**23**).

This compound was prepared from 4-methoxybezylamine (**10**) (0.5 mmol, 63 mg). The mixture of ethanol (1 ml) and water (1 ml) was used for crystallization. Experimental and analytical data are given in Tables 1, 2, and 3.

Methyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-(4-nitro- α -methylbenzyl)aminopropenoate (**24**).

This compound was prepared from 4-nitro- α -methylbezylamine hydrochloride (**11**) (0.5 mmol, 101 mg). Acetone (2 ml)

was used for crystallization. Experimental and analytical data are given in Tables 1, 2, and 3.

General Procedure for the Preparation of β -Arylamino- α,β -didehydro- α -amino Acid Derivatives 25-35.

To compound **7** (0.5 mmol, 160 mg) or **8** (0.5 mmol, 167 mg) the corresponding aromatic amine **12-20** (0.5 mmol) and acetic acid (2 ml) were added and stirred at room temperature for a few minutes to 24 hours. The volatile compounds were evaporated *in vacuo*, the appropriate solvent (3 ml) was added and the precipitate was collected by filtration.

Methyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-phenylaminopropenoate (**25**) and (*Z*)-2-[(*E*)-, (*Z*)-2-[(*Z*)-, and (*E*)-2-[(*Z*)- Isomers.

This compound was prepared from compound **7** (0.5 mmol, 160 mg) and alanine (**12**) (0.5 mmol, 47 mg), 24 hours, in 11:9:2:1 ratio. The mixture of methanol (1 ml) and water (1 ml) was used for crystallization. Two isomers, (*E*)-2-[(*E*)- and (*Z*)-2-[(*E*)-, were separated with radial chromatography (petroleum/ethyl acetate = 5:1). Experimental and analytical data are given in Tables 1, 2, and 3.

Methyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-(2-methoxyphenyl)aminopropenoate (**26**).

This compound was prepared from compound **7** (0.5 mmol, 160 mg) and 2-methoxyaniline (**13**) (0.5 mmol, 62 mg), 24 hours. The mixture of methanol (1 ml) and water (1 ml) was used for crystallization. Experimental and analytical data are given in Tables 1, 2, 3, and 5.

Methyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-(4-methoxyphenyl)aminopropenoate (**27**) and (*Z*)-2-[(*E*)-, (*Z*)-2-[(*Z*)-, and (*E*)-2-[(*Z*)- Isomers.

This compound was prepared from compound **7** (0.5 mmol, 160 mg) and 4-methoxyaniline (**14**) (0.5 mmol, 61 mg), 24 hours. The ratio was not defined. Methanol (2 ml) was used for crystallization. Experimental and analytical data are given in Tables 1, 2, and 3.

Methyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-(4-fluorophenyl)aminopropenoate (**28**) and (*Z*)-2-[(*E*)-, (*Z*)-2-[(*Z*)-, and (*E*)-2-[(*Z*)- Isomers.

This compound was prepared from compound **7** (0.5 mmol, 160 mg) and 4-fluoroaniline (**15**) (0.5 mmol, 56 mg), 24 hours, in 11:6:1:1 ratio. Methanol (2 ml) was used for crystallization. Experimental and analytical data are given in Tables 1, 2, and 3.

Methyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-(3-chloro-4-fluorophenyl)aminopropenoate (**29**) and (*Z*)-2-[(*E*)-, (*Z*)-2-[(*Z*)-, and (*E*)-2-[(*Z*)- Isomers.

This compound was prepared from compound **7** (0.5 mmol, 160 mg) and 3-chloro-4-fluoroaniline (**16**) (0.5 mmol, 74 mg), 24 hours, in 13:9:2:1 ratio. Methanol (2 ml) was used for crystallization. Experimental and analytical data are given in Tables 1, 2, 3, and 5.

Methyl (*E*)-2-[(*E*)-2-[2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]amino-3-(2-bromophenyl)aminopropenoate (**30**) and (*Z*)-2-[(*E*)- Isomer.

This compound was prepared from compound **7** (0.5 mmol, 160 mg) and 2-bromoaniline (**17**) (0.5 mmol, 83 mg), 24 hours, in

6:1 ratio. Methanol (2 ml) was used for crystallization. Experimental and analytical data are given in Tables 1, 2, and 3.

Methyl (*E*)-2-[(*E*)-2-[2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]amino-3-(3-bromophenyl)aminopropenoate (**31**) and (*Z*)-2-[(*E*)- Isomer.

This compound was prepared from compound **7** (0.5 mmol, 160 mg) and 3-bromoaniline (**18**) (0.5 mmol, 83 mg), 24 hours, in 7:1 ratio. Methanol (2 ml) was used for crystallization. Experimental and analytical data are given in Tables 1, 2, and 3.

Methyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-(2-nitrophenyl)aminopropenoate (**32**) and (*Z*)-2-[(*E*)- Isomer.

This compound was prepared from compound **7** (0.5 mmol, 160 mg) and 2-nitroaniline (**19**) (0.5 mmol, 70 mg), 10 minutes, in 10:1 ratio. Methanol (2 ml) was used for crystallization. Experimental and analytical data are given in Tables 1, 2, and 3.

Methyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-(3-nitrophenyl)aminopropenoate (**33**) and (*Z*)-2-[(*E*)- Isomer.

This compound was prepared from compound **7** (0.5 mmol, 160 mg) and 3-nitroaniline (**20**) (0.5 mmol, 70 mg), 24 hours, in 8:1 ratio. Methanol (2 ml) was used for crystallization. Experimental and analytical data are given in Tables 1, 2, and 3.

Ethyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-(4-methoxyphenyl)aminopropenoate (**34**) and (*Z*)-2-[(*E*)- Isomer.

This compound was prepared from compound **8** (0.5 mmol, 167 mg) and 4-methoxyaniline (**14**) (0.5 mmol, 61 mg), 24 hours. The ratio was not defined. Ethanol (2 ml) was used for crystallization. Experimental and analytical data are given in Tables 1, 2, and 3.

Ethyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-(4-fluoro-3-chlorophenyl)aminopropenoate (**35**).

This compound was prepared from compound **8** (0.5 mmol, 167 mg) and 4-fluoro-3-chloroaniline (**16**) (0.5 mmol, 74 mg), 24 hours. Ethanol (2 ml) was used for crystallization. Experimental and analytical data are given in Tables 1, 2, and 3.

The Preparation of β -Heteroaryl-amino- α,β -didehydro- α -amino Acid Derivatives **36**, **37**.

Methyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-(5-chloro-2-pyridinyl)aminopropenoate (**36**).

To compound **7** (0.5 mmol, 160 mg) 2-amino-5-chloropyridine (**21**) (0.5 mmol, 64 mg) and acetic acid (2 ml) were added and stirred at room temperature for 4 days. The volatile compounds were evaporated *in vacuo* and ethanol (2 ml) was added. The precipitate was collected by filtration and washed with ethanol. Experimental and analytical data are given in Tables 1, 2, and 3.

Ethyl (*E*)-2-[(*E*)-2-Ethoxycarbonyl-2-(2-pyridinyl)ethenyl]-amino-3-(5-chloro-2-pyridinyl)aminopropenoate (**37**).

To compound **8** (0.5 mmol, 167 mg) 2-amino-5-chloropyridine (**21**) (0.5 mmol, 64 mg) and acetic acid (2 ml) were added and stirred at room temperature for 24 hours. The volatile compounds were evaporated *in vacuo* and ethanol (2 ml) was added. The precipitate was collected by filtration and washed with ethanol. Experimental and analytical data are given in Tables 1, 2, and 3.

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