AMINO ACIDS AS SYNTHONS FOR HETEROCYCLES. FORMATION OF 1,2,4-TRIAZINE DERIVATIVES

Janez Smodiš, Rok Zupet, Andrej Petrič, Branko Stanovnik, and Miha Tišler*

Department of Chemistry, E.Kardelj University, 61000 Ljubljana, Yugoslavia

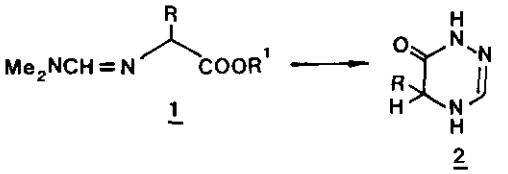
Abstract - Transformation of the amino group of amino acids into an amidine and subsequent treatment with hydrazine leads to 1,2,4-triazine-6(1H)-ones. The method described is a new synthetic approach. Unsaturated amino acids gave imidazol-5-one derivatives after the same reaction sequence.

Our recent interest in heterocyclic amino acids and derivatives [1-6] has prompted us to investigate the possibility of using various amino acids as synthons for the preparation of heterocyclic compounds. Here, we describe the synthetic principle based on amidines for the formation of 1,2,4-triazin-6-ones and imidazol-5-ones.

There are only few synthetic approaches for 1,2,4-triazin-6-ones. They were prepared either by cyclization of α-(acylamino)-carbohydrazides [7-11] or they were obtained as minor products after alkaline hydrolysis of 1-methyl-1,2,4-triazinium iodides.[12] It was also reported that 6-methyl-1,2,4-triazines and related compounds were oxidized to the corresponding 6-ones,[13,14] but for the 3,5-diphenyl analogue it was later shown that the compound is in fact 3,6-diphenyl-1,2,4-triazine-5-one and this probably also holds for some related compounds.[15]

The starting methyl or ethyl esters of amino acids were obtained by a treatment of the corresponding ester hydrochlorides with a base and were transformed under mild reaction conditions into the corresponding amidines 1. These are also obtainable directly by heating the corresponding amino acids with excess of N,N-dimethylformamide dimethyl acetal (DMF-DMA). The obtained amidines reacted smoothly with hydrazine or methyl hydrazine to yield the triazinone derivatives 2 and 3.

Dedicated to the memory of the late Professor Tetsuji Kametani.



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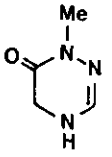
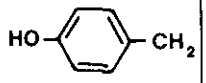
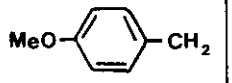


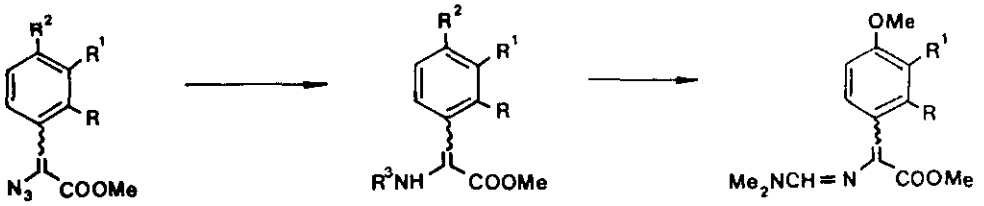
3

	R	R^1
a	H	Et
b	Me	Et
c	Me_2CH	Me
d	Me_2CHCH_2	Me
e	$Me(CH_2)_3$	Me
f	$Me-CH(OH)-$	Me
g	$MeSCH_2CH_2$	Me
h	$PhCH_2SCH_2$	Me
i	$PhCH_2$	Me
j	Ph	Me
k		Me
l		Me
m	COOEt	Et
n	$CONHNH_2$	

For these several tautomeric forms are possible. The eventual structure of the 1-aminoimidazolin-5(4H)-one was easily excluded by nmr data and the fact that the reaction with lead tetraacetate in the presence of dimethyl sulfoxide did not give a S,S-dimethyl sulfoximide as we have shown before for some related compounds.[16] The nmr spectra which reveal a small coupling constant for H_5 and 4-NH group with J_{CHNH} = 1.00-1.47 Hz and a larger one for H_3 and 4-NH group with J_{CHNH} = 3.90 -4.00 Hz, clearly indicate the 1,4,5,6-tetrahydro structure for the obtained triazin-6-ones 2.

The reduced system 2 is apparently stable since an attempt to dehydrogenate compound 2a with DDQ was unsuccessful. Also methylation of either the 1- or 4-NH group with DMF-DMA failed, although we have previously observed such transformations.[17] Moreover, reaction of the imidine 1 with either hydroxylamine or azidotrimethylsilane did no afford defined products.

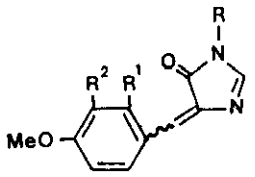
We have also attempted to apply the above sequence of reactions on α,β-didehydro



	R	R^1	R^2
4a	H	H	H
4b	H	H	OMe
4c	OMe	OCH_2Ph	OMe

	R	R^1	R^2	R^3
5a	H	H	H	H
5b	H	H	OMe	H
5c	OMe	OCH_2Ph	OMe	H
5d	H	H	OMe	$COCF_3$
5e	H	H	H	CONHPh
5f	H	H	OMe	CONHPh

	R	R^1
6a	H	H
6b	OMe	OCH_2Ph



	R	R^1	R^2
7a	$PhCH_2$	H	H
7b	NH_2	OMe	OCH_2Ph

amino acids. The azido esters 4 were prepared by condensation of methyl azidoacetate with the corresponding aromatic aldehydes in the presence of sodium methoxide. Althohgh there is no proof for the regiochemistry of 2-azido-3-arylpropenoates, some authors prefer the Z-configuration based on the thermodynamic stability.[18-21] We have attempted to calculate the relative energies of the Z- and E-isomers using MMPMI method [22] but the result revealed that there is very little difference, less than 1 kcal for both configurations. We have tried various reagents for the reduc-

tion of the azido group into an amino and the results are presented in Table 1.

Table 1

Reduction of the azido group in compounds 4

Product	Method of Reduction	Time (h)	Yield, %	mp, °C
5a	H_2S	2	50	oil
	H_2/Pd/C	1	95	
	Al/Hg	1	70	
5b	H_2/Pd/C	1	20	65-66.5
	Al/Hg	1	80	
5c	H_2S	3	37	oil
	Al/Hg	2.5	85	

The amino esters 5 were transformed into the corresponding amidines 6 with *DMF-DMA and further cyclization with either hydrazine or benzylamine* afforded the imidazolin-5-ones 7 and not 1,2,4-triazin-6-ones. The proposed structure is consistent with the obtained nmr spectral data since H_2 in the imidazole ring appears always as singlet. Also in this case the relative energies of the Z- and E-isomer were calculated, but no decision could be reached for the preference of either form. The computer generated perspective drawing of compound 7a is given in Fig. 1.

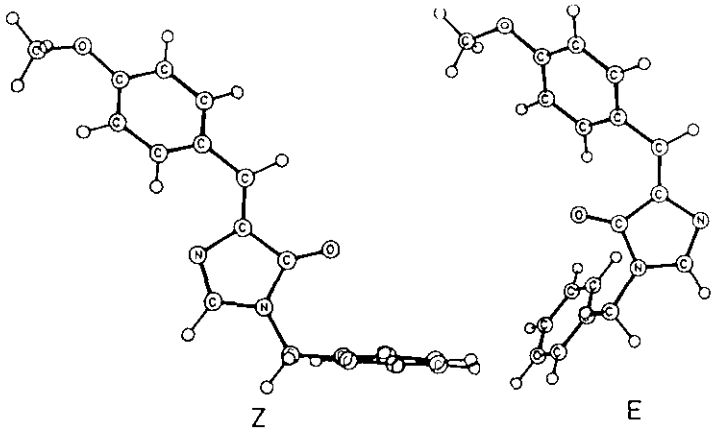


Fig. 1. The computer generated perspective drawing of compound 7a in the Z- and E-configuration

It is most likely that the rigidity, imposed to the amidine 6 by the α,β-double bond results in the non-formation of a triazine ring.

EXPERIMENTAL

^{1}H Nmr spectra were recorded on a JEOL FX 90 Q spectrometer with TMS as an internal standard. Melting points were determined on a Kofler hot stage microscope. Elemental analyses for C, H and N were performed with Perkin-Elmer 240 C analyzer. The progression of the reactions were followed by tlc on Kieselgel 60F_{245} and as mobile phase eiter benzene, a mixture of petroleum ether and benzene (5:1) or chloroform and methanol (5:1) were used. For syntheses commercially available (S)- or (R, S)-amino acids or their methyl or ethyl ester hydrochlorides were used. Ethyl aminoacetate was prepared from its hydrochloride and conc. aqueous sodium hydroxide and was extracted with diethyl ether[23].

Typical procedure for the preparation of N,N-dimethylaminomethylene derivatives of esters of amino acids:

a) Alanine ethyl ester hydrochloride (0.01 mol) was treated with an equivalent amount of sodium ethoxide in ethanol. The solvent was evaporated, tetrahydrofuran (10 ml) was added, the mixture was filtered and the filtrate was treated with DMF-DMA (0.011 mol). The reaction mixture was heated under reflux for 30 min. Evaporation of the solvent afforded an oil (1b) which was distilled at 105-110°C and 2 mm Hg (yield 92%). ^{1}H-Nmr ($CDCl_3$) δ 7.37 (s, CH=N), 3.76 (q, J=6.80 Hz, CH), 1.36 (d, J=6.80 Hz, Me), 2.98 (s, NMe_2). Anal. Calcd for $C_8H_{16}N_2O_2$: C, 55.79; H, 9.36; N, 16.27. Found: C, 55.62; H, 9.12; N, 16.38.

Instead of tetrahydrofuran for the above synthesis also anhydrous benzene may be used. Similarly, compound 1i was prepared in 55% yield after distillation at 155-160°C/2 mm Hg. ^{1}H Nmr ($CDCl_3$) δ 6.97 (s, CH=N), 3.39 (dd, J=5.61 and 13.92 Hz, CH), 2.90-3.30 (dd, J=5.61 and 13.92 Hz, CH_2), 7.22 (s, Ph), 2.81 (s, NMe_2), 3.70 (s, OMe). Anal. Calcd for $C_{13}H_{18}N_2O_2$: C, 66.64; H, 7.74; N, 11.96. Found: C, 66.40; H, 7.94; N, 11.71.

The amidines 1a, 1f, 1h, 1k and 1l were prepared in the same manner, but they were used without purification immediately in the next stage.

b) The corresponding amino acid (0.002 mol) was suspended in DMF-DMA (0.9 ml) and the reaction mixture was heated under reflux for 2 h. After evaporation in vacuo the residual oil was purified by column chromatography using chloroform and methanol (25:1) for elution. By this procedure the amidines 1b, 1c, 1d, 1e (bp. 140°C/1-2 mm Hg), 1g, 1i, 1j and 1l were prepared (yields were 45%, 55%, 82%, 56%, 81%, 55%, 68% and 28%, respectively) and were used without purification for the preparation of triazine derivatives. In the case of tyrosine an excess of DMF-DMA gives 1l, whereas with an equivalent amount of the reagent compound 1k was formed.

5-Methyl-4,5-dihydro-1,2,4-triazin-6(1H)-one (2b).

A mixture of the amidine (1b) (2.08 g), anhydrous ethanol (10 ml) and hydrazine hydrate (0.6 ml of 95%) was heated under reflux for 30 min. The solvent was evaporated and the residue was crystallized from tetrahydrofuran and thereafter from ethyl acetate, mp 136°C (yield 92%). ^{1}H-Nmr ($CDCl_3$) δ 5.35 (d, J=3.91 Hz, CH=N), 3.25 (dq, J=6.60 and 1.22 Hz, CH-Me), 1.16 (d, J=6.60 Hz, Me), 3.69 (broad s, NH), 6.32 (broad s, NH). Anal. Calcd for $C_4H_7N_3O$: C, 42.47; H, 6.24; N, 37.15. Found: C, 42.34; H, 6.35; N, 36.91.

In the same manner the following compounds were prepared:

4,5-Dihydro-1,2,4-triazin-6(1H)-one (2a).

A 48% yield of a solid, mp 188-190°C (from 1-propanol) was obtained. ^{1}H-Nmr (DMSO-d_6) δ 2.94 (s, CH_2), 5.39 (s, H_3). Anal. Calcd for $C_3H_5N_3O$: C, 36.36; H, 5.09; N, 42.41. Found: C, 36.17; H, 5.17; N, 42.85.

5-Isopropyl-4,5-dihydro-1,2,4-triazin-6(1H)-one (2c).

It was obtained in 30% yield, mp 144-146°C (from ethanol and diethyl ether and thereafter from water). ^{1}H-Nmr (DMSO-d_6) δ 0.85 (m, Me_2), 1.9-2.2 (m, CH-Me_2), 3.70 (m, CH-NH), 6.80 (d, J=3.90 Hz, CH=N), 7.00 (broad s, NHCH), 9.98 (s, NHCO). Anal. Calcd for $C_6H_{11}N_3O$: C, 51.01; H, 7.85; N, 29.76. Found: C, 51.07; H, 8.03; N, 29.24.

5-Isobutyl-4,5-dihydro-1,2,4-triazin-6(1H)-one (2d).

It was obtained upon heating the reaction mixture for 2 h in 47% yield, mp 119-122°C. The compound was purified by radial chromatography on Chromatotrone using chloroform and ethanol (25:1) as mobile phase. ^{1}H-Nmr ($CDCl_3$) δ 6.86 (d,

J=3.91 Hz, H_3), 4.02 (m, H_5), 1.60 (m, $Me_2\underline{CH}-CH_2$), 0.96 (m, Me_2), 7.75 (broad s, NH), 5.05 (broad s, NH). Anal. Calcd for $C_6H_{12}N_2O_2$: C, 54.17; H, 8.44; N, 27.07. Found: C, 54.17; H, 8.54; N, 26.95.

5-n-Butyl-4,5-dihydro-1,2,4-triazin-6(1H)-one (2e).

It was obtained after leaving the reaction mixture at room temperature for 2 h. The product was crystallized from aqueous ethanol, mp 145-149°C (78% yield). ^{1}H-Nmr (DMSO-d_6) δ 6.79 (d, J=3.91 Hz, H_3), 3.75 (m, H_5), 1.30 and 1.50 (m, three CH_2), 0.86 (m, Me), 7.00 (broad s, NH). Anal. Calcd for $C_7H_{13}N_3O$: C, 54.17; H, 8.44; N, 27.07. Found: C, 53.81; H, 8.70; N, 26.76.

5-(2'-Hydroxyethyl)-4,5-dihydro-1,2,4-triazin-6(1H)-one (2f).

A 68% yield of a solid was obtained, mp 224-225°C (from 1-propanol). ^{1}H-Nmr (DMSO-d_6) δ 2.81(dd, J=5.60 and 1.00 Hz, H_5), 3.04 (ddd, J=6.50, 6.10 and 5.60 Hz, $C\underline{H}$-Me), 5.32 (d, J=4.00 Hz, H_3), 0.84 (d, J=6.50 Hz, Me), 3.72 (d, J=6.10 Hz, OH), 5.46 (broad s, NH), 7.84 (broad s, NH). Anal. Calcd for $C_5H_9N_3O_2$: C, 41.95; H, 6.34; N, 29.36. Found: C, 42.00; H, 6.38; N, 29.10.

5-(2'-Methylthioethyl)-4,5-dihydro-1,2,4-triazin-6(1H)-one (2g).

It was obtained in 35% yield, mp 122°C (from ethanol - diethyl ether 1:5 and thereafter from water). ^{1}H-Nmr (DMSO-d_6) δ 2.03 (s, Me), 2.4-2.6 (m, SCH_2), 1.7-1.9 (m, $SCH_2\underline{CH_2}$), 6.80 (d, J=3.91 Hz, CH=N), 3.92 (dt, J=5.50 and 1.20 Hz, $C\underline{H}CH_2$), 7.00 (broad s, $N\underline{H}CH$), 10.06 (broad s, NHCO). Anal. Calcd for $C_6H_{11}N_3OS$: C, 41.60; H, 6.40; N, 24.26. Found: C, 41.94; H, 6.46; N, 24.39.

5-Benzylthiomethyl-4,5-dihydro-1,2,4-triazin-6(1H)-one (2h).

The compound was prepared in 52% yield, mp 107-109°C (from aqueous methanol and subsequently from water). ^{1}H-Nmr ($CDCl_3$) δ 3.72 (s, $PhC\underline{H_2}$), 2.67 (dd, J=9.5 and 14.03 Hz, $C\underline{H_2}CH$), 3.10 (dd, J=3.18 and 14.03 Hz, $C\underline{H_2}CH$), 3.93 (ddd, J=3.18, 9.52 and 1.22 Hz, H_5), 6.70 (d, J=3.90, H_3), 7.37 (s, PhH), 8.79 (broad s, NH), 5.37 (dd, J=3.90 and 1.22 Hz, NH). Anal. Calcd for $C_{11}H_{13}N_3OS$: C, 56.16; H, 5.57; N, 17.86. Found: C, 55.98; H, 5.34; N, 17.62.

5-Benzyl-4,5-dihydro-1,2,4-triazin-6(1H)-one (2i).

A 71% yield of a solid was obtained after standing the reaction mixture at room temperature, mp 152-153°C (the product was rinsed with diethyl ether). ^{1}H-Nmr

(DMSO-d_6) δ 6.66 (d, J=3.91 Hz, H_3), 4.10 (dd, J=5.37 and 1.47 Hz, H_5), 2.90 (d, J=5.37 Hz, CH_2), 7.42 (s, PhH), 9.97 (broad s, NH), 6.89 (broad s, NH). Anal. Calcd for $C_{10}H_{11}N_3O$: C, 63.48; H, 5.86; N, 22.21. Found: C, 63.43; H, 6.01; N, 22.54.

5-(p-Hydroxybenzyl)-4,5-dihydro-1,2,4-triazin-6(1H)-one (2k).

It was obtained from the imidine and hydrazine hydrate at room temperature overnight in 91% yield, mp 187-189°C (from chloroform and methanol, 25:1). ^{1}H-Nmr (DMSO-d_6) δ 6.64 (s, H_3), 4.04 (dd, J=1.36 and 5.37 Hz, H_5), 2.78 (d, J=5.37 Hz, CH_2), 6.65 and 6.98 (d, J=8.55 Hz, arom H). Anal. Calcd for $C_{10}H_{11}N_3O_2$: C, 58.53; H, 5.40; N, 20.48. Found: C, 58.57; H, 5.69; N, 20.30.

5-Phenyl-4,5-dihydro-1,2,4-triazin-6(1H)-one (2j).

It was obtained similarly in 50% yield, mp 68-72°C (from water). ^{1}H-Nmr (DMSO-d_6) δ 7.00 (d, J=3.90 Hz, H_3), 4.80 (d, J=1.36 Hz, H_5), 7.33 (s, PhH), 7.57 (broad s, NH). Anal. Calcd for $C_9H_9N_3O$: C, 55.95; H, 5.74; N, 21.75. Found: C, 55.64; H, 5.50; N, 21.80.

5-(p-Methoxybenzyl)-4,5-dihydro-1,2,4-triazin-6(1H)-one (2l).

Tyrosine (0.362 g) was suspended in fivefold excess of DMF-DMA (1 ml) and the mixture was heated under reflux for 3 h. The volatile part was evaporated in vacuo and the residual oil (11) was dissolved in ethanol (3 ml). After addition of hydrazine hydrate (0.15 ml of 80%) the mixture was left to stand at room temperature overnight. The solvent was evaporated and the product was purified by column chromatography and then crystallized from chloroform and diethyl ether (1:5). The product, mp 136-138°C, was obtained in 29% yield. ^{1}H-Nmr ($CDCl_3$) δ 6.91 (s, H_3), 4.17 (dd, J=3.00 and 10.50 Hz, H_5), 3.79 (s, OMe), 7.13 and 6.86 (d, J=8.67 Hz, aromatic H), 3.24 and 2.78 (dd, J=13.92 and 3.00 Hz, CH_2). Anal. Calcd for $C_{11}H_{13}N_3O_2$: C, 60.26; H, 5.98; N, 19.17. Found: C, 60.32; H, 5.99; N, 19.31.

5-Hydrazinocarbonyl-4,5-dihydro-1,2,4-triazin-6(1H)-one (2n).

Diethyl aminomalonate hydrochloride (2.11 g) was treated with an ethanolic solution of sodium ethoxide (prepared from 0.23 g of sodium and 10 ml of absolute ethanol). After evaporation to dryness the oily residue was treated with anhydrous benzene (10 ml), one equivalent of DMF-DMA (1.4 ml) and the mixture was heated under reflux for 15 min.After standing overnight at room temperature, sodium chloride was filtered and the filtrate was evaporated to dryness. The residual oil (1m) was treated with

absolute ethanol (10 ml) and hydrazine hydrate (0.6 ml of 98%) and the mixture was heated under reflux for 30 min. After standing at room temperature overnight the separated crystals were filtered and crystallized from a large amount of ethanol, mp 213-216°C (yield 1.29 g, 90%). The compound can be also crystallized from N,N-dimethylformamide and toluene. ^{1}H-Nmr (DMSO-d_6) δ 3.37 (d, J=1.20 Hz, H_5), 5.38 (d, J=3.90 Hz, H_3), 5.39, 5.78 and 8.06 (broad s, NH groups). Anal. Calcd for $C_4H_7N_5O_2$: C, 30.57; H, 4.49; N, 44.57. Found: C, 30.62; H, 4.65; N, 44.22.

1-Methyl-4,5-dihydro-1,2,4-triazin-6(2H)-one (3).

This compound was prepared from the amidine 1a and methylhydrazine in 72% yield, mp 129-131°C (from ethyl acetate and heptane). ^{1}H-Nmr (DMSO-d_6) δ 2.42 (s, N-Me), 2.96 (s, CH_2), 5.39 (d, J=3.91 Hz, H_3), 5.56 (broad s, NH). Anal. Calcd for $C_4H_7N_3O$: C, 42.47; H, 6.24; N, 37.15. Found: C, 42.73; H, 6.40; N, 37.45.

General procedure for the preparation of methyl 2-azido-3-arylpropenoates (4):

A mixture of the corresponding aldehyde (0.05 mol), methyl azidoacetate (0.15 mol) and anhydrous benzene (50 ml) was cooled to 5°C and during intensive stirring a solution of sodium methoxide (prepared from 3.45 g of sodium and 100 ml of methanol) was added dropwise. After addition was completed, the reaction mixture was stirred at room temperature for 1.5-2.5 h. The conversion was traced with tlc. The solvent was evaporated in vacuo and the residue was neutralized with 0.5 N hydrochloric acid. The mixture was extracted three times with 50 ml of diethyl ether. After drying over $MgSO_4$ the solvent was evaporated and the oily residue was either crystallized from methanol or purified by column chromatography (in the case of the phenyl analogue). In the last case silica (30 g, 70-230 mesh) was used and as mobile phase a mixture of petroleum ether and benzene (5:1) was employed.

In this manner the following aryl derivatives were prepared:

The phenyl derivative (4a) was obtained in 40% yield, mp 34-36°C. Ir: 2150 cm^{-1} (N_3). ^{1}H-Nmr ($CDCl_3$) δ 3.90 (s, Me), 6.31 (s, H_3), 7.36 (m, $H_{3'}$, $H_{4'}$, $H_{5'}$), 7.78 (m, $H_{2'}$, $H_{6'}$). Anal. Calcd for $C_{10}H_9N_3O_2$: C, 59.10; H, 4.46; N, 20.68. Found: C, 59.02; H, 4.22; N, 20.44.

The p-methoxyphenyl derivative (4b) was prepared in 80% yield, mp 68-74°C. Ir: 2150 cm^{-1} (N_3). ^{1}H-Nmr ($CDCl_3$) δ 3.83 (s, Me), 3.89 (s, Me), 6.88 (s, H_3), 6.96

(d, J=8.54 Hz, $H_{2'}$, $H_{6'}$), 7.79 (d, J=8.54 Hz, $H_{3'}$, $H_{5'}$). Anal. Calcd for $C_{11}H_{11}N_3O_3$: C, 56.65; H, 4.75; N, 18.01. Found: C, 56.74; H, 4.93; N, 18.03.

The 2',4'-dimethoxy-3'-benzyloxyphenyl derivative (4c) was obtained in 40% yield, mp 78-80.5°C. Ir: 2150 cm^{-1} (N_3). ^{1}H-Nmr ($CDCl_3$) δ 3.84 (s, Me), 3.87 (s, Me), 3.88 (s, Me), 4.99 (s, CH_2), 6.69 (d, J=9.04 Hz, $H_{6'}$), 7.28 (s, $H_{3'}$), 7.3 (m, PhH), 8.04 (d, J=9.04 Hz, $H_{5'}$). Anal. Calcd for $C_{19}H_{19}N_3O_3$: C, 61.78; H, 5.19; N, 11.38. Found: C, 62.09; H, 5.32; N, 11.59.

General procedure for the reduction of methyl 2-azido-3-arylpropenoates:

a) *With aluminium amalgam.* - *A solution of the corresponding azido compound* (10 mmol) in ethyl acetate (50 ml) was added dropwise to a suspension of aluminium amalgam (prepared from 6 g of aluminium and 6 g of $HgCl_2$)[24] in ethyl acetate (20 ml). The progression of the reduction was monitored by tlc. The solid material was filtered and the filtrate was washed three times with cold water (5 ml). After drying over Na_2SO_4 the solvent was evaporated to dryness. The isolated products, reaction time and yields are presented in Table 1.

b) With palladium carbon. - To a solution of the azido compound in methanol 5% palladium carbon was added and the mixture was stirred in a hydrogen atmosphere for 1 h. Upon filtration and evaporation of the filtrate the products were isolated and characterized (Table 1).

c) With hydrogen sulfide. - Into a solution of the azido compound and some triethylamine in methanol a stream of hydrogen sulfide was introduced for 2-3 h. The separated sulfur was filtered off and the filtrate was evaporated to dryness. The yields are given in Table 1.

Compound 5a: Ir: 3300 and 3450 cm^{-1} (NH_2). ^{1}H-Nmr (DMSO-d_6) δ 3.84 (s, Me), 3.9-4.2 (broad s, NH_2), 6.47 (s, H_3), 7.2-7.4 (m, PhH). Compound 5a was characterized by transformation with phenyl isocyanate in tetrahydrofuran into the urea derivative 5e, mp 251-253°C (from methanol). ^{1}H-Nmr (DMSO-d_6) δ 3.74 (s, Me), 7.26 (s, H_3), 7.3-7.6 (m, PhH), 8.10 and 8.86 (broad s, NH). Anal. Calcd for $C_{17}H_{16}N_2O_3$: C, 68.90; H, 5.44; N, 9.45. Found: C, 69.06; H, 5.53; N, 9.42.

Compound 5b: Ir: 3420, 3500 cm^{-1} (NH_2). ^{1}H-Nmr (DMSO-d_6) δ 3.89 (s, Me), 3.84 (s, Me), 3.9-4.3 (broad s, NH_2), 6.48 (s, H_3), 6.91 (dd, J=9.04 and 1.90 Hz, $H_{2'}$,

$H_{6'}$), 7.41 (dd, J=9.04 and 1.90 Hz, $H_{3'}$, $H_{5'}$). Anal. Calcd for $C_{11}H_{13}NO_3$: C, 63.75; H, 6.32; N, 6.76. Found: C, 63.89; H, 6.48; N, 6.44.

Compound 5b was transformed with phenyl isocyanate in tetrahydrofuran into the corresponding urea derivative (5f), mp 262-265°C (from methanol). ^{1}H-Nmr (DMSO-d_6) δ 3.73 (s, Me), 3.78 (s, Me), 6.98 (d, J=8.79 Hz, $H_{2'}$, $H_{6'}$), 7.25 (s, H_3), 7.65 (d, J=8.79 Hz, $H_{3'}$, $H_{5'}$), 7.30 (m, PhH), 7.91 and 8.83 (broad s, NH). Anal. Calcd for $C_{18}H_{18}N_2O_4$: C, 66.24; H, 5.56; N, 8.58. Found: C, 65.94; H, 5.49; N, 8.67.

Compound 5c: Ir: 3420, 3500 cm^{-1} (NH_2). ^{1}H-Nmr (DMSO-d_6) δ 3.81 (s, Me), 3.84 (two Me), 4.05-4.25 (broad s, NH_2), 5.03 (s, CH_2), 6.54 (s, $H_{3'}$), 6.69 (d, J=8.79 Hz, $H_{6'}$), 7.20 (d, J=8.78 Hz, $H_{5'}$), 7.25-7.45 (m, PhH, H_3). Anal. Calcd for $C_{19}H_{21}NO_5$: C, 66.46; H, 6.16; N, 4.08. Found: C, 66.40; H, 6.01; N, 3.82.

The trifluoroacetyl derivative 5d could be prepared in the following manner. The azido compound 1c (0.466 g) was dissolved in carbon tetrachloride (5 ml), trifluoroacetic anhydride (2 ml) was added and the mixture was treated with zinc powder (0.35 g). Under stirring few drops of trifluoroacetic acid were added and the mixture was cooled externally. After 30 min the reaction mixture was filtered and the filtrate was evaporated in vacuo. The oily residue was crystallized from aqueous methanol, mp 124-126°C (yield 0.125 g, 40%). ^{1}H-Nmr ($CDCl_3$) δ 3.83 (s, Me), 3.86 (s, Me), 6.90 (d, J=8.78 Hz, $H_{2'}$, $H_{6'}$), 7.30 (d, J=8.78 Hz, $H_{3'}$, $H_{5'}$), 7.60 (s, H_3), 7.75-7.85 (broad s, NH). Anal. Calcd for $C_{13}H_{12}F_3NO_4$: C, 51.49; H, 3.98; N, 4.61. Found: C, 51.33; H, 4.09; N, 4.68.

Compound 5c was transformed into its N,N-dimethylaminomethylene derivative (6b) in the following manner. Compound 5c (1.68 g) was dissolved in dry benzene (10 ml), DMF-DMA (0.65 g, 12% excess) was added and the mixture was heated under reflux for 3 h. The reaction mixture was evaporated in vacuo and the residue was treated two times with methanol (5 ml) and the solvent was evaporated. The oily residue was crystallized from aqueous methanol, mp 97-98°C (yield 33%). ^{1}H-Nmr ($CDCl_3$) δ 3.04 (s, NMe), 3.81, 3.84 and 3.90 (s, three OMe), 5.01 (s, CH_2), 6.67 (d, J=9.03 Hz, $H_{6'}$), 7.24 (s, $H_{3'}$), 7.38 (m, PhH), 7.77 (s, CH), 8.29 (d, J=9.03 Hz, $H_{5'}$). Anal. Calcd for $C_{21}H_{26}N_2O_5$: C, 66.31; H, 6.58; N, 7.03. Found: C, 66.77; H, 6.87; N, 7.14.

In a similar manner, compound 6a was prepared in 50% yield, mp 79-81°C (from 1,2-dimethoxyethane). ^{1}H-Nmr ($CDCl_3$) δ 3.06 (s, NMe_2), 3.80 and 3.81 (s, COOMe, s, OMe), 4.85 (dd, J=9.40 and 2.10 Hz, H_2 and H_6), 6.94 (s, CH=Ar), 7.75 (s, CH=N), 7.86 (dd, J=9.40 and 2.10 Hz, H_3 and H_5). Anal. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.10; H, 6.92; N, 10.68. Found: C, 64.35; H, 6.92; N, 10.67.

1-Amino-4-(2',4'-dimethoxy-3-benzoyloxy-1-methylene)-5-imidazolone (7b). The amidine 6b (0.2 g) was dissolved in methanol (5 ml), hydrazine hydrate (25 mg of 98%) was added and the mixture was heated under reflux for 1 h. The product which separated upon cooling was filtered and crystallized from methanol, mp 144-147°C (yield 75 mg, 34%). ^{1}H-Nmr (DMSO-d_6) δ 3.72 and 3.83 (s, two Me), 4.99 (s, CH_2), 6.25 (s, CH), 6.85 (d, J=8.79 Hz, H_5,), 7.00 (s, H_2), 7.16 (d, J=8.79 Hz, H_6,), 7.45 (m, PhH), 9.47 and 10.85 (broad s, NH). Anal. Calcd for $C_{19}H_{19}N_3O_4$: C, 64.58; H, 5.42; N, 11.89. Found: C, 64.58; H, 5.56; N, 11.76.

In a similar manner the amidine 6a reacted with benzylamine in boiling methanol after 2 h to give the imidazolone 7a, mp 153-155°C (from methanol) in 34% yield. ^{1}H-Nmr ($CDCl_3$) δ 3.85 (s, MeO), 4.77 (s, N-Me), 6.94 (d, J=8.78 Hz, H_2,, H_6,), 7.25 (s, CH), 7.32 (broad s, PhH), 7.65 (s, H_2), 8.12 (d, J=8.78 Hz, H_3, H_5,). Anal. Calcd for $C_{18}H_{18}N_2O_2$: C, 73.95; H, 5.52; N, 9.58. Found: C, 73.44; H, 5.68; N, 9.54.

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