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N-Substituted Pyrrolinones from Enamines and α-Dicarbonyls

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Abstract. The reaction between *N*-substituted enamines and phenylglyoxal or glyoxal yielded Δ^2-pyrrolin-5-ones in moderate to good yields. An uncommon pyrrolo [2,1-*b*]thiazole derivative was formed as a minor product when a *N*-(2-mercaptoethyl)enamine was used as the starting reagent. An explanation for the regiochemistry of the reaction is proposed.

The reaction between enamines and carbonylic compounds is a classic method for the synthesis of different types of heterocycles.[1-3] Our interest in this reaction has been focused to the synthesis of new heterocyclic systems from enamines of β-ketoesters and ethanol- or propanol-amines, which allowed us to describe the oxazolo[3,2-*a*]pyridine[4,5] and pyrido[2,1-*b*]oxazine[6] ring systems for the first time. We have also reported a new procedure for the synthesis of pyrroles based on the reaction of β-aminocrotonates or β-aminocrotononitrile with α-ketoaldehydes.[7] The general procedures described for the synthesis of pyrrolinones are based on transformations of γ-ketocarboxylic derivatives, namely the reaction of γ-ketoesters with amines[8] or through cyclization of γ-ketoamides.[9]

In order to get a better knowledge of this methodology and to test the possibilities of synthesizing new pyrrole derivatives, we have studied the reaction between *N*-hydroxyethyl or *N*-hydroxypropyl enamines and α-dicarbonyls. The best results have been obtained with glyoxal and phenylglyoxal, which usually produce 5-oxo-2-pyrroline-3-carboxylates from enamines of β-ketoesters.

METHODS AND RESULTS

The reactions between phenylglyoxal (**1**) or glyoxal (**2**, 40% in water) and the *N*-substituted enamines **3** or **4** (Scheme 1) were carried out in refluxing methanol or at room temperature. In both cases, the main reaction product (45 to 64 % yield in isolated product) was the pyrrolinone (**6-9**). The structures were established from their spectral data. The presence of the γ-lactam was easily detected through its IR absorption

at ~1730 cm^{-1} and the ^{13}C-NMR signal at ~177 ppm. A characteristic feature of the ^{1}H-NMR spectrum of these compounds is the homoallylic coupling between H-4 and the methyl protons at C-2, which is definitive to confirm the regiochemistry of the reaction. Treatment of those pyrrolinones with Ac_2O produced the mixture of 2'-monoacetylated and 5, 2'-diacetylated derivatives, namely **11** and **12** from **6**. This fact was in complete agreement with the structure proposed for the main reaction product. 2-pyrrolin-5-ones are reported to be formed in the reaction of enamines with maleic anhydride derivatives,[9] but the yields attained by this method are substantially lower (15-29 %) than those produced through the procedure described in this paper.

Along with the 2-pyrrolin-5-one several minor products were isolated. Thus, from the reaction of phenylglyoxal (**1**) with enamine **3** , the ketopyrrole **13** was isolated in 16% yield and with enamine **4** the corresponding ketopyrrole **14** was produced in 10% yield. The additional three carbons moiety in **13** was clearly detected in its MS, because the M^+ appeared 40 *m/z* units higher than for the expected 2-pyrrolin-5-one. Furthermore, ^{13}C (29.5, 209.1 and 41.2 ppm) and ^{1}H (2.12 and 3.54 ppm) NMR data confirmed the presence of the 2-oxopropyl residue attached to the pyrrole ring. These products seem to be formed through a condensation step of the starting ketoaldehyde or a reaction intermediate with ethyl acetoacetate, which could have originated from the hydrolytic enamine degradation, followed by decarboxylation during the reaction.

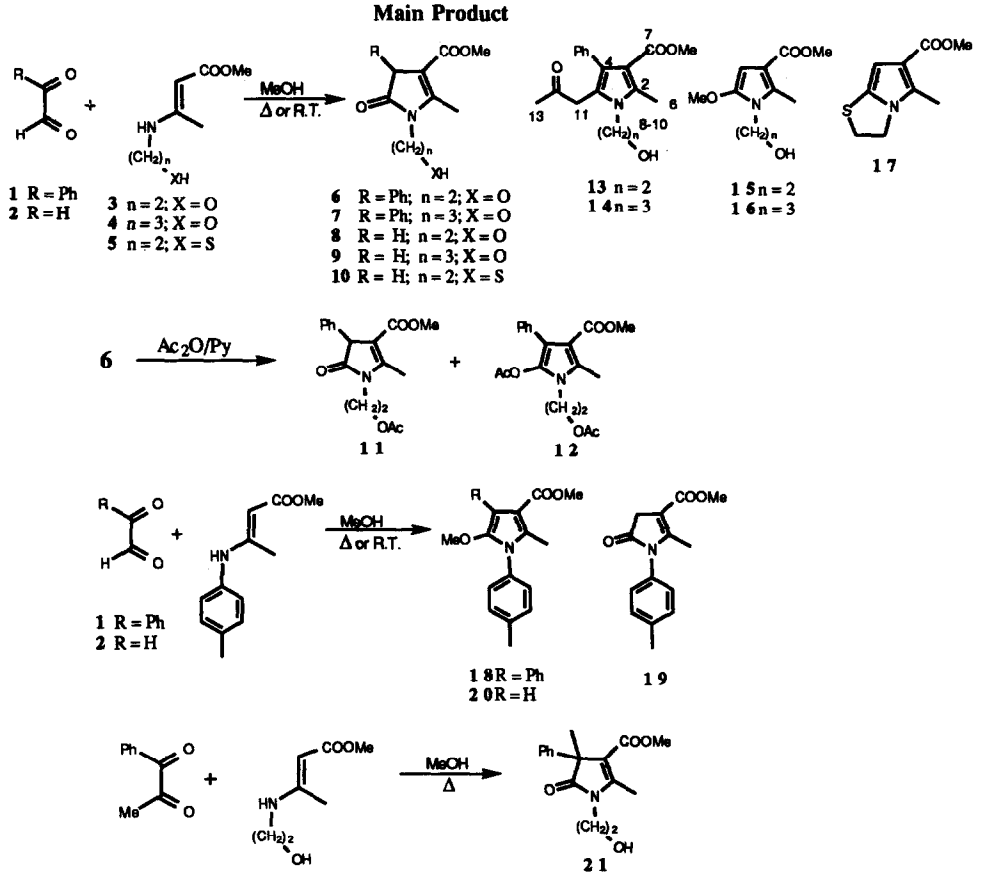
Other minor products resulting from other reactions between glyoxal and enamines are the methoxypyrroles **15** (4%) from **3** and **16** (18%) from **4**. These compounds most probably resulted from addition of one molecule of solvent during the reaction and they were characterized by the presence of methine (^{1}H-NMR ~5.56 ppm *s* and ^{13}C-NMR ~82.9 ppm) and methoxyl signals in their NMR spectra.

Similarly, the reaction of the enamine-thiol **5** with glyoxal produced the 2-pyrrolin-5-one **10** (46%) and a minor product in 8% yield. This unknown compound displayed the M^+ at *m/z* 197, in agreement with the molecular formula $C_9H_{11}NO_2S$, and also showed aromatic absorptions in the IR spectrum. It should contain a methine group at position 3 of the pyrrole moiety due to the presence of a singlet at 6.16 ppm in the ^{1}H NMR spectrum as well as, a methine signal at 100.2 ppm in the ^{13}C spectrum. Thus, its structure was established as that of methyl 5-methyl-2,3-dihydropyrrolo[2,1-*b*]thiazole-6-carboxylate (**17**). There is only one reference in the literature about this kind of fused heterocyclic skeleton,[11] with the description of the tentative structure assignment of a compound resulting from the reaction between 1-(2,2-dimethoxyethyl)pyrrole and thiourea. Unfortunately, the reaction between enamine **5** and phenylglyoxal produced a complex reaction mixture, from which it was not possible to isolate any pure product.

The scope of the reaction was also checked with other *N*-substituted enamines. When methyl 3-*p*-tolylaminocrotonate reacted with ketoaldehydes **1** and **2**, similar reaction products were obtained. From phenylglyoxal the main reaction product (30%) was the methoxy-pyrrole **18**, while from glyoxal the resulting products were the 2-pyrrolin-5-one **19** (44%) and the methoxypyrrole **20** (12.5%).

The synthetic utility of the reaction between *N*-substituted-3-aminocrotonate esters and glyoxal or phenylglyoxal was checked with other substrates (ethyl, isopropyl and benzyl ester analogues of **3**-**5**), which always produced the *N*-substituted 2-pyrrolin-5-ones in 45-70% yield. However, the reaction of *N*-substituted

enamines with other α-dicarbonyl compounds, as pyruvic aldehyde or 1-phenyl-1,2-propanedione gave complex mixtures. Only compound **21** was isolated in 18% yield from the reaction mixture of 1-methyl-2-phenylglyoxal and enamine **3** in refluxing methanol. This compound must arise from a benzilic type rearrangement of the diketone during the reaction producing the required 2-phenyllactic intermediate. 2-pyrrolin-5-ones have been described as starting materials for the synthesis of some interesting derivatives with antifungal and antibacterial properties .[12-14]



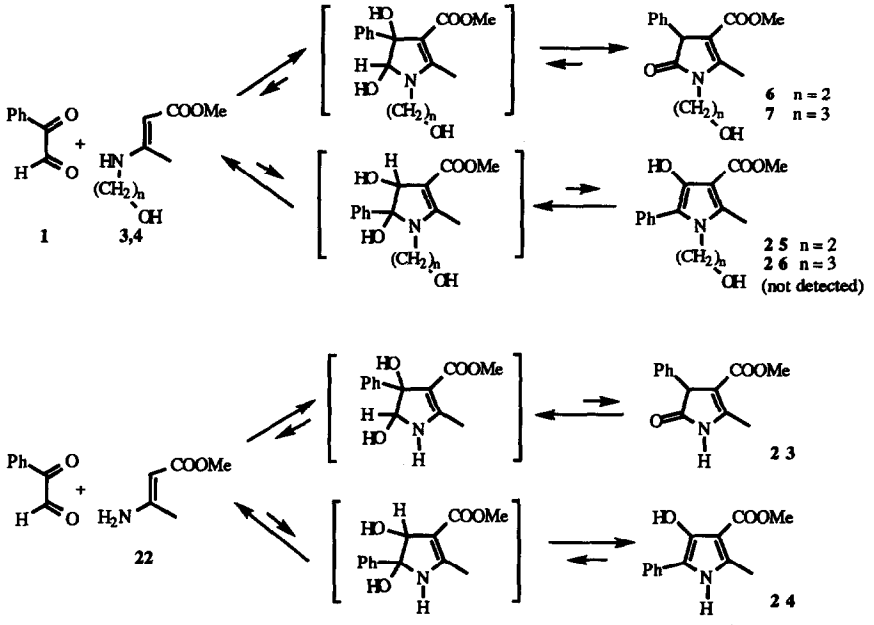
Scheme 1

An intriguing result of the reaction between aldehyde **1** and enamines **3** or **4**, was the different regiochemistry produced with respect to the previously described reaction with the *N*-unsubstituted enamines.[7] In the case of glyoxal, there is not the possibility for the appearance of regioisomers, but in the case of phenylglyoxal instead the 2-pyrrolin-5-ones (**6, 7**) now observed, 5-phenyl-4-hydroxypyrrole derivatives (**24**) were formed from unsubstituted enamines. In order to have a better knowledge of the nature of intermediates, the reactions between **1** and enamines **3, 4** and **22** were carried out in CD_3OD and checked by NMR spectroscopy. The reaction was complete after a few minutes at room temperature with the more reactive enamines **3** and **4**, and took several hours for the consumption of **22**, as it is shown in table 1. The evolution

of the reaction between **1** and **22** showed that the initial product was the 2-pyrrolin-5-one **23**, which was progressively transformed at room temperature into the 5-phenyl-4-hydroxypyrrole **24**. The reaction showed a rapid formation of **24** when heated. These results confirmed the existence of an equilibrium between the pyrrolinone and pyrrole derivatives in the case of unsubstituted enamines. This was not the case for *N*-substituted compounds, for which the attempted transformation of pyrrolinones into the corresponding pyrroles, either in the NMR tube or by heating, was completely unsuccessful (Scheme 2).

Table 1. Kinetics of the reaction between **1** and **22** in CD_3OD controlled by NMR

time (h)	22(%)	Intermediate Product type 23 (%)	24(%)
0.5	38	54	7
2.5	3	71	25
5.0	---	56	43
24.0	---	30	69
Reflux 5 min	---	---	100

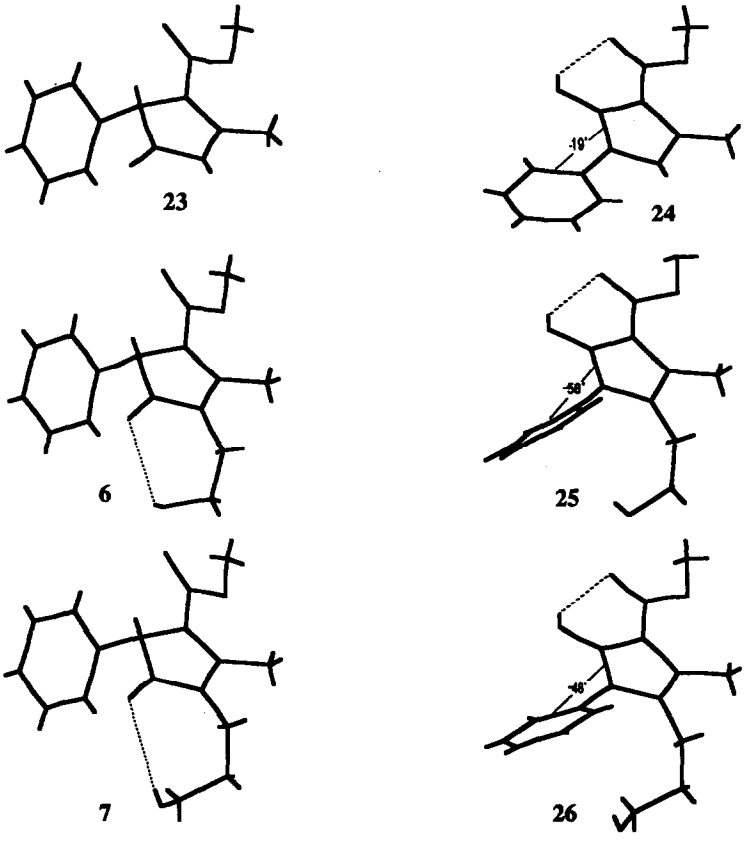


Scheme 2. Proposed mechanistic explanation for the reaction between α-ketoaldehydes and enamines.

A reasonable explanation for this fact could be based on the relative destabilization produced by steric hindrance in *N*-substituted pyrroles (**25-26**) and in the stabilization of pyrrolinones (**6-7**) induced by possible hydrogen bonds linking the hydroxyl group at the side chain and the carbonyl group of the pyrrolinone.

To check the relative stabilities of these compounds semiempirical calculations using AM1 Hamiltonian in MOPAC 6.0 were performed for lower-energy conformations of compounds **6**, **7**, **23**, **24**, **25** and **26** (Scheme 3). Comparatively, the difference in the heat of formation of **23** (ΔH= -72.1 Kcal/mol) and **24** (ΔH= -73.9 Kcal/mol) was much smaller (1.8 Kcal/mol) than those observed for the pairs **6** (ΔH= -122.1 Kcal/mol) / **25** (ΔH= -118.3 Kcal/mol) and **7** (ΔH= -129.3 Kcal/mol) / **26** (ΔH= -124.5 Kcal/mol) whose difference varied from 3.8 Kcal/mol to 4.8 Kcal/mol, respectively. It seems clear that, apart from the presence of hydrogen bonds for the pyrrolinones, the loss of stability of pyrroles is due to a reduced coplanarity of phenyl and pyrrole rings (-58° to -48°) produced by the higher steric interactions between the side chain on the nitrogen atom and the phenyl group for **25** and **26**. In the case of pyrrole **24**, the higher coplanarity (-19°) of both aromatic rings reinforced by the H-bond between the hydroxyl and the carboxylate groups should produce a higher stability of this regioisomer.

As a conclusion, the reported method is general for the rapid synthesis of some kinds of pyrrole derivatives under mild conditions. Although only glyoxal and phenylglyoxal gave good results, many variations can be introduced in the enamine to produce a large number of pyrrole and 2-pyrrolin-5-one derivatives.



Scheme 3. Main conformers of representative 2-pyrrolin-5-ones and their pyrrolic regioisomers (showing hydrogen bonds and selected dihedral angles)

Table 2. ^{13}C NMR data for compounds **6-21**

C	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
2	155.7	154.6	155.1	154.1	153.6	154.2	133.5	132.7	132.6	125.0	129.1	132.2	135.1	154.3	132.9	154.3
3	108.1	108.8	103.3	103.8	103.6	108.2	109.5	110.1	110.6	108.0	108.5	114.8	105.5	103.1	109.1	114.5
4	52.6	52.8	36.5	36.6	36.0	52.3	132.7	137.1	136.3	82.9	83.1	100.2	138.0	36.3	83.2	53.3
5	177.4	178.5	176.8	177.0	175.9	177.0	112.3	115.7	116.0	147.0	147.0	125.9	144.4	174.9	147.5	181.9
6	12.4	12.2	12.4	12.0	12.4	12.0	11.3	12.1	12.0	10.9	10.7	11.4	12.8	13.0	11.8	12.7
7	164.3	164.4	164.3	164.4	164.4	164.0	165.8	166.0	166.2	166.5	166.1	164.4	165.3	164.1	166.0	164.5
8	42.4	38.8	42.7	36.6	39.6	38.8	41.2	46.1	41.2	44.1	38.4	45.2	-	-	-	42.6
9	59.9	31.8	60.7	31.8	36.4	61.7	62.3	61.1	33.4	61.6	32.9	34.6	-	-	-	59.9
10	-	58.5	-	58.6	-	-	-	-	59.5	-	59.4	-	-	-	-	21.1
11	-	-	-	-	-	-	-	41.2	41.2	-	-	-	-	-	-	-
12	-	-	-	-	-	-	-	209.1	208.0	-	-	-	-	-	-	-
13	-		-	-	-	-	-	29.5	29.5		-	-	-	-	-	-
COOMe	50.6	50.9	50.9	50.9	50.9	50.6	50.5	50.4	50.4	50.6	50.6	50.6	50.7	50.6	50.7	50.6
OMe	-	-	-	-	-	-	-	-	-	57.6	57.7	-	62.4	-	57.7	-
Ac	-	-	-	-	-	19.7	20.1	-	-	-	-	-	-	-	-	-
	-		-	-	-	166.7	169.1	-	-	-	-	-	-	-	-	-
	-	-	-	-	-	-	20.7	-	-	-	-	-	-	-	-	-
	-	-	-	-	-		170.6	-	-	-	-	-	-	-	-	-
Ph																
$C_{1'}$	136.4	136.2	-	-	-	136.1	131.3	131.3	131.6	-	-	-	130.4	-	-	139.8
$C_{2'}$ $C_{6'}$	127.7	127.7	-	-	-	127.3	127.6	128.6	128.6	-	-	-	128.4	-	-	126.1
$C_{3'}$ $C_{5'}$	128.5	128.7	-	-	-	128.4	129.7	130.9	130.9	-	-	-	129.7	-	-	128.4
$C_{4'}$	127.1	127.5	-	-	-	127.1	126.4	128.3	128.3	-	-	-	126.3	-	-	127.0
p-tolyl	-	-	-	-	-	-	-	-	-	-	-	-	21.1	21.7	21.1	-
$C_{1''}$	-	-	-	-	-	-	-	-	-	-	-	-	130.4	131.0	138.3	-
$C_{2''}$ $C_{6''}$	-	-	-	-	-	-	-	-	-	-	-	-	128.4	127.5	127.9	-
$C_{3''}C_{5''}$	-	-	-	-	-	-	-	-	-	-	-	-	129.7	129.8	129.7	-
$C_{4''}$	-	-	-	-	-	-	-	-	-	-	-	-	126.3	138.4	128.6	-

Solvent $CDCl_3$. TMS as internal standard, numbering see compounds **13** and **14**.

EXPERIMENTAL

General experimental procedures. Mps were determined in capillaries on a Buchi 510 instrument and are uncorrected. Microanalyses were performed in a Perkin-Elmer 2400 CHN elemental analyzer. UV spectra were recorded in EtOH on a Hitachi 100-60 spectrometer. IR spectra were obtained in CH_2Cl_2 in a Beckman Acculab VIII spectrophotometer. ^1H NMR (200.13 MHz) and ^{13}C NMR (50.3 MHz) spectra were measured in a Bruker WP 200 SY instrument, in deuterochloroform solutions using TMS as internal standard. δ values are expressed in ppm and J in Hz. CG-EIMS were recorded on a Hewlett-Packard 5890 series II, 70 ev. Flash chromatographies were performed in an Eyela EF-10 apparatus.

Reaction of phenylglyoxal with enamines

A solution of phenylglyoxal hydrate (9.7 mmol) and enamine [4] (9.7 mmol) in MeOH (15 ml) was refluxed or allowed to stand at room temperature for 20 h. The solvent was removed and the products were isolated in 16-60% yield by flash chromatography (Hexane-EtOAc) and/or crystallization.

Methyl 4-phenyl-*N*-(2-hydroxyethyl)-2-methyl-5-oxo-2-pyrrolin-3-yl-carboxylate (6). Reflux (45%). IR: 3450, 1730, 1690, 1630, 1500, 1440 cm^{-1}. ^1H NMR δ: 2.54 (3H, d, J=2.3), 3.50-3.80 (4H, m), 3.55 (3H, s), 4.34 (1H, d, J=2.3), 7.10-7.30 (5H, m). UV λmax: 211 and 290 nm (ε=7374 and 7350). MS *m/z* 275 (62, M^+), 244 (18), 216 (100), 198 (19), 184 (17), 128 (20), 105 (21).

Acetylation of 6: Treatment of **6** with Ac_2O-C_5H_5N in the usual way afforded **11**(33%) and **12**(60%).

11: IR: 1740, 1710, 1620, 1500, 1400 cm^{-1}. ^1H NMR δ: 1.94 (3H, s), 2.54 (3H, d, J=2.2), 3.53 (3H, s), 3.95 (2H, m), 4.17 (2H, m), 4.34 (1H, d, J=2.2), 7.10-7.40 (5H, s).

12: IR: 1730, 1700, 1630, 1500, 1400 cm^{-1}. ^1H NMR δ: 2.04 (3H, s), 2.13 (3H, s), 2.55 (3H, s), 3.58 (3H, s), 3.97 (2H, m), 4.22 (2H, m), 7.10-7.40 (5H, s).

Methyl 4-phenyl-*N*-(3-hydroxypropyl)-2-methyl-5-oxo-2-pyrrolin-3-yl-carboxylate (7) Reflux or room temperature (60%) . IR: 3480, 1730, 1640, 1450 cm-^{1}. ^1H NMR δ: 1.74 (2H, m), 2.55 (3H, d, J=2.2), 3.48 (2H, m), 3.55 (3H, s), 3.64 (2H, m), 4.37 (1H, d, J=2.2), 7.10-7.40 (5H, m). UV λmax: 286 and 210 nm (ε=9322 and 9548). MS *m/z* 275 (289, M^+), 257 (19), 230 (100), 212 (37), 184 (48), 128 (29), 102 (12).

Methyl 4-phenyl-*N*-(2-hydroxyethyl)-2-methyl-5-(2-oxopropyl)pyrrol-3-yl-carboxylate (13). Reflux (16%). IR: 3400, 1700, 1610, 1535, 1500 cm^{-1}. ^1H NMR δ: 2.12 (3H, s), 2.55 (3H, s), 3.41 (2H, t, J=5.8), 3.54 (2H, s), 3.70 (3H, s), 3.85 (2H, t, J=5.8), 7.20-7.40 (5H, m). UV λmax: 257 and 236 nm (ε=9257 and 9914). MS *m/z* 315 (35) , 272 (100), 284 (9), 240 (47), 213 (75), 182 (28), 152 (20), 105 (42).

Methyl 4-phenyl-*N*-(3-hydroxypropyl)-2-methyl-5-(2-oxopropyl)pyrrol-3-yl-carboxylate (14). Room temperature (10%). IR: 3650, 3610, 3430, 2400, 1690, 1520 cm^{-1}. ^1H NMR δ: 1.72 (2H, m), 2.12 (2H, s), 2.58 (3H, s), 3.41 (2H, m), 3.57 (2H, s), 3.75 (3H, s), 3.92 (2H, m), 7.20-7.40 (5H, m). UV λmax: 262, 226 and 201 nm (ε=3758, 5310 and 7931). MS *m/z* 315 (35) , 272 (100), 284 (9), 240 (47), 213 (75), 182 (28), 152 (20), 105 (42).

Methyl 4-phenyl-2-methyl-5-methoxy-*N*-(*p*-tolyl)pyrrol-3-yl-carboxylate (18). Reflux (30%). Mp=120-121°C (CH_2Cl_2/MeOH). IR: 1710, 1520, 1450 cm^{-1}. ^1H NMR δ: 2.33 (3H, s), 2.34 (3H, s), 3.66 (3H, s), 3.88 (3H, s), 6.90-7.20 (9H, m). UV λmax: 268 and 234 nm (ε=14744 and 23720). Anal calc.for $C_{21}H_{21}NO_3$: C 75.22, H 6.25, N 4.17 %, found C 75.15, H 6.19, N 4.11%. MS *m/z* 335 (40, M^+) , 320 (23), 304 (64), 288 (100), 272 (13), 230 (16), 115 (8), 91 (10).

Reaction of glyoxal with enamines

A solution of glyoxal (4.8 mmol, 40% in water) and enamine (4.8 mmol) in MeOH (10 ml) was allowed to stand at room temperature for 20 h. The solvent was removed and the products were isolated by flash chromatography (Hexane-EtOAc as eluent).

Methyl *N*-(2-hydroxyethyl)-2-methyl-5-oxo-2-pyrrolin-3-yl-carboxylate (8). (52%). IR: 3430, 1730, 1690, 1450 cm^{-1}. ^1H NMR δ: 2.47 (3H, t, J=2.4), 3.25 (2H, c, J=2.4), 3.60-3.80 (4H, m), 3.72 (3H, s), UV λmax: 281 and 235 nm (ε=6400 and 4380). MS *m/z* 227(100, M^+) , 212 (34), 194 (62), 183(19), 168 (20), 134 (23), 108 (13), 94 (22).

Methyl *N*-(3-hydroxypropyl)-2-methyl-5-oxo-2-pyrrolin-3-yl-carboxylate (9).(64%). IR: 1730, 1690, 1630, 1440 cm^{-1}. ^1H NMR δ: 1.77 (2H, c, J=6.0), 2.47 (3H, t, J=2.4), 3.30 (2H, c, J=2.4), 3.58 (2H, t, J=6), 3.70 (2H, t, J=6), 3.75 (3H, s). UV λmax: 285 and 210 nm (ε=27121 and 21212).

Methyl *N*-(2-mercaptoethyl)-2-methyl-5-oxo-2-pyrrolin-3-yl-carboxylate (10). (46%). Mp=141-143°C (CH_2Cl_2/MeOH). IR: 3400, 1690, 1530 cm^{-1}. ^1H NMR δ: 2.48 (3H, s), 3.70 (2H, t, J=7.9), 3.77 (3H, s), 4.03 (2H, t, J=7.9), 6.16 (2H, s). UV λmax: 281 and 204 nm (ε=16600 and 18030). Anal calc.for $C_9H_{13}NO_3S$: C 50.23, H 6.04, N 6.51 %, found C 50.37, H 6.11, N 6.60 %.

Methyl *N*-(2-hydroxyethyl)-2-methyl-5-methoxypyrrol-3-yl-carboxylate (15). (4%). IR: 3605, 3430, 1690, 1590, 1550, 1440 cm^{-1}. ^1H NMR δ: 2.48 (3H, s), 3.75 (3H, s), 3.80 (3H, s), 3.80-3.90 (4H, m), 5.56 (1H,s).

Methyl *N*-(3-hydroxypropyl)-2-methyl-5-methoxypyrrol-3-yl-carboxylate (16). (18%). IR: 3650, 2400, 1700, 1600, 1550. cm^{-1}. ^1H NMR δ:1.85 (2H, c, J=6.3 Hz), 2.48 (3H, s), 3.58 (2H, t, J=6.3 Hz), 3.77 (3H, s), 3.88 (2H, m), 3.82 (3H, s), 5.58 (1H,s).

Methyl 5-methyl-2,3-dihydropyrrol[2,1-*b*]thiazol-5-yl-carboxylate (17). (8%). Mp = 122 - 124° C (CH_2Cl_2/MeOH). IR: 1690, 1590, 1550 cm^{-1}. ^1H NMR δ: 2.48 (3H, s), 2.89 (2H, t, J=7.0), 3.25 (1H, c, J=2.3), 3.73 (3H, s), 3.80 (2H, m). UV λmax: 238 and 227 nm (ε=3500 and 6260). MS *m/z* 197 (100, M^+), 182 (78), 166 (33), 138 (16), 97 (9), 69 (10). Anal calc.for $C_9H_{11}NO_2S$: C 54.82, H 5.58, N 7.10 %, found C 54.91, H 5.72, N 7.23%.

Methyl 2-methyl-5-oxo-*N*-(*p*-tolyl)-2-pyrrolin-3-yl-carboxylate (19). (44%) . IR: 3400, 1720, 1690, 1640, 1510 cm^{-1}. ^1H NMR δ: 2.23 (3H, t, J=2.4), 2.39 (3H, s), 3.45 (2H, c, J=2.4), 3.76 (3H, s), 7.05 (2H, d, J=8.2), 7.27 (2H, d, J=8.2). UV λmax: 220 and 286 nm (ε=8000 and 5025).

Methyl 2-methyl-5-methoxy-*N*-(*p*-tolyl)-2-pyrrol-3-yl-carboxylate (20). (12%). IR: 1690, 1510, 1440, 1220. cm^{-1}. ^1H NMR δ: 2.30(3H, s), 2.40 (3H, s), 3.72 (3H, s), 3.80 (3H, s), 5.67 (1H, s), 7.09 (2H, d, J=8.2 Hz), 7.26 (2H, d, J=8.2). UV λmax: 249 nm (ε=6000). MS *m/z* 259 (86, M^+), 244 (100), 212(27), 156 (10), 132 (52)

1-phenyl-1,2-propanedione with methyl 3-(2-hydroxyethylamino)crotonate

A solution of 1-phenyl-1,2-propanedione (12.6 mmol) and methyl 3-(2-hydroxyethylamino)crotonate (12.6 mmol) in MeOH (15 ml) was refluxed for 20 h. The solvent was removed and **21**(17%) was isolated from the crude reaction product by flash chromatography (Hexane-EtOAc 1:1) .

Methyl 4-phenyl-*N*-(2-hydroxyethyl)-2,4-dimethyl-5-oxo-2-pyrrolin-3-yl-carboxylate (21). IR: 3450, 1730, 1690, 1630, 1520 cm^{-1}. ^1H NMR δ: 1.74 (3H,s), 2.55 (3H,s), 3.80 (4H,m), 3.54 (3H,s), 7.1-7.3 (5H,m). λmax: 282 and 231 nm (ε=10238 and 10000). MS *m/z* 289 (26, M^+), 258 (6), 230 (100), 212 (19), 198 (5), 128 (8), 115 (8).

Molecular Modelling . Calculations were performed on a Silicon Graphics Indigo computer. Compounds **6, 7, 23, 24, 25** and **26** were built using Macromodel[15] v.4 and energy minimized with the MM2[16] force field. Conformational analysis of each compound was performed by using a Monte Carlo systematic search. Full geometry optimization of the low-energy conformations of every compound was performed using Stewart's AM1 Hamiltonian in MOPAC[17] 6.0. The precise option was used to tighten convergence tolerances.

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