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Synthesis and Reactions of Furo[2,3-*b*]pyrroles

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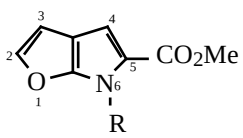
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Abstract: Methyl 6H-furo[2,3-*b*]pyrrole-5-carboxylate (**2a**) was prepared by thermolysis of the corresponding methyl 2-azido-3-(3-furyl)propenoate (**1**). 6-Methyl (**2b**) and 6-benzyl (**2c**) derivatives were obtained using phase-transfer catalysis conditions (PTC). The formylation of 2a-2c gave 2-formylated compounds (**3a**-**3c**). Compounds **4b**, **4c** were prepared by reactions of corresponding esters **2b**, **2c** with hydrazine in refluxing ethanol. By reaction of **3a**-**3c** with hydroxylammonium chloride in acetic anhydride in the presence of pyridine, methyl 2-cyano-6-R[1]-furo[2,3-*b*]pyrrole-5-carboxylates (**5a**-**5c**) were obtained. The reaction of these compounds with sodium azide and ammonium chloride in dimethylformamide led to methyl 2-(5'-tetrazolyl)-6-R[1]-furo[2,3-*b*]pyrrole-5-carboxylates (**6**a-**6c**). A series of 5-methoxycarbonyl-6-R[1]-furo[2,3-*b*]pyrrole-2-carbaldehyde *N,N*-dimethylhydrazones (**7a-7c**) was prepared from methyl 2-formyl-6-R[1]-furo[2,3-*b*]pyrrole-5-carboxylates (**3**a-**3c**) and unsym-dimethylhydrazine. The correlation of the ^{13}C and ^{15}N chemical shifts with the data of the calculated (AM1) net atomic charges is discussed.

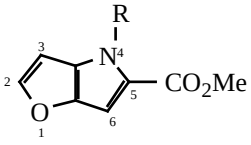
Keywords: Methyl furo[2,3-*b*]pyrrole-5-carboxylates, methyl 2-formylfuro[2,3-*b*]pyrrole-5-carboxylates, methyl 2-cyanofuro[2,3-*b*]pyrrole-5-carboxylates, methyl 2-(5'-tetrazolyl)furo[2,3-*b*]pyrrole-5-carboxylates, 5-methoxycarbonylfuro[2,3-*b*]pyrrole-2-carbaldehydes *N,N*-dimethylhydrazones

Introduction

Furo[2,3-*b*]pyrroles (**2a-2c**) and their positional isomers furo[3,2-*b*]pyrroles (**8a-8c**) belong to A,B-diheteropentalenes, which possess differing degrees of aromaticity based upon chemical behaviour such as their ability to undergo substitution reactions with electrophilic reagents. A,B-diheteropentalenes rank among the electron-rich heterocycles, but a quantitative measurement of their aromaticities is less easily determined [1]. The wide range of potential criteria available for this purpose has been surveyed [1,2].



2a-2c



8a-8c

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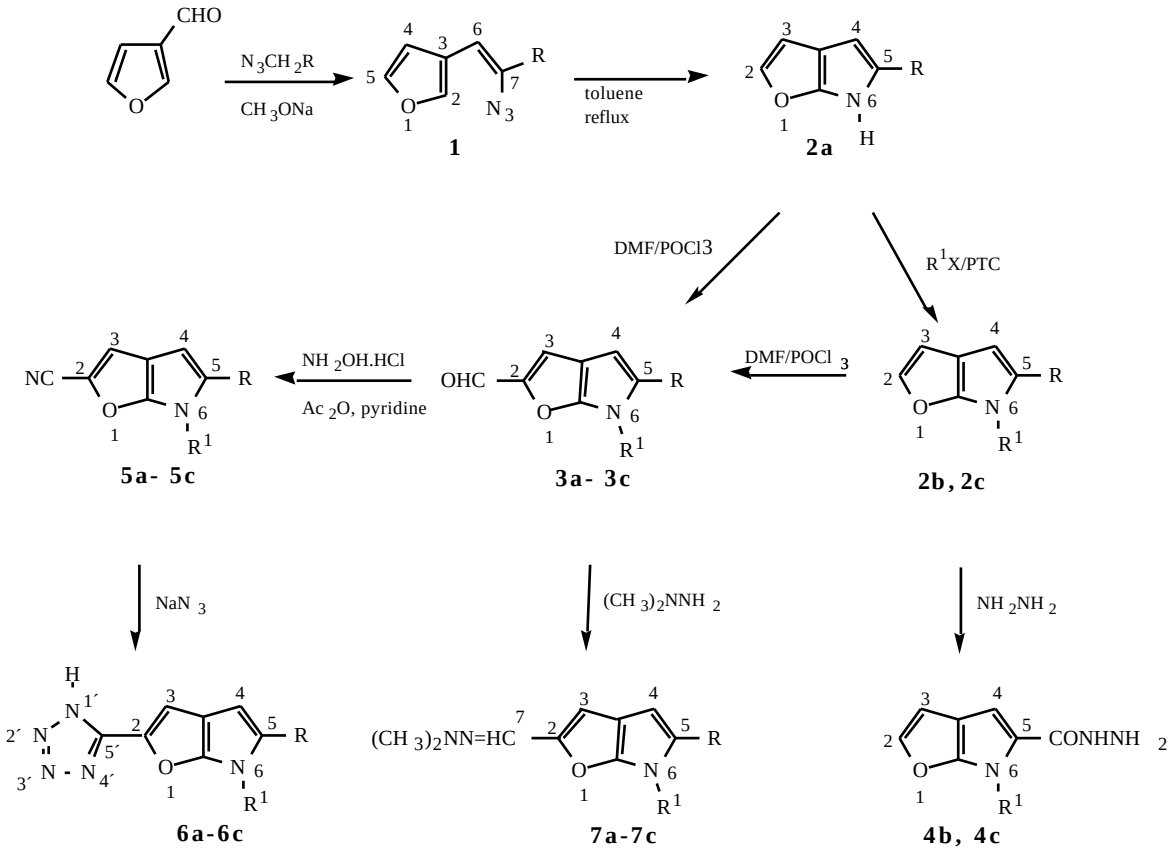
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Most of the available criteria point to an order of decreasing aromaticity of 1,4 > 1,6 ring system which is influenced by the heteroatom in the order S>Se≥N>O. Substituents attached to the A,B-heteropentalene structures can strongly influence the aromaticity. Until recently 1,6-diheteropentalenes containing S, Se heteroatoms had been studied [1,2] and a few derivatives of the furo[2,3-*b*]pyrole system had been prepared [3]. The parent furo[2,3-*b*]pyrrole has not been reported. In the past we were interested in syntheses and studies of the reactions of furo[3,2-*b*]pyrroles and their benzo or dibenzo derivatives [4-9].

In continuation of our programme aimed at developing efficient syntheses of fused oxygen-nitrogen-containing heterocycles, we report here the study of the synthesis of methyl furo[2,3-*b*]pyrrole-5-carboxylate (**2a**) and its utilization in synthesis. Our main interest is a comparison of the behaviour of 1,6-*O*,*N*-diheteropentalene system (**2**) with isomeric 1,4-system (**8**).

Results and Discussion

Reaction of 3-furancarbaldehyde with methyl azidoacetate in the presence of sodium methoxide proceeded smoothly to give the azide **1**, thermolysis of which was carried out in boiling toluene leading to the compound **2a**. Phase transfer catalysis was found to be successful for methylation and benzylation of **2a** giving the derivatives **2b** and **2c** (Scheme 1). The compounds **2a**-**2c** gave under Vilsmeier conditions 2-formylated products **3a**-**3c**. By refluxing the compounds **2b** and **2c** with hydrazine in ethanol the corresponding hydrazides **4b** and **4c** were formed. Our experiments to synthesize 6*H*-furo[2,3-*b*]pyrrole-5-carboxyhydrazide (**4a**) under conditions which were used for preparation of **4b** and **4c** were unsuccessful.



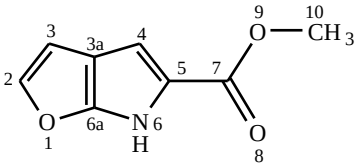
R = CO_2CH_3; R^1 in compounds **2b-7**: **a** = H, **b** = CH_3, **c** = $C_6H_5CH_2$

Scheme 1

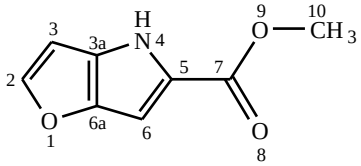
The reaction of **3a**-**3c** with hydroxylammonium chloride in acetic anhydride in the presence of pyridine at 90°C gave the corresponding cyano-substituted compounds **5a**-**5c**. The reaction of the compounds **5a**-**5c** with sodium azide and ammonium chloride in dimethylformamide led to the tetrazoles **6a**-**6c**. *N,N*-Dimethylhydrazones **7a**-**7c** were prepared from the aldehydes (**3a**-**3c**) and *unsym*-dimethylhydrazine in refluxing toluene, using a catalytic amount of 4-methylbenzenesulfonic acid.

During the synthesis and reaction studies of both systems we found out that the 1,4 system (**8**) is more stable than its 1,6 positional isomer (**2**). This empirical conclusion is in agreement with the results of AM1 semiempirical MO calculations that we have carried out for the parent furopyrroles and the ester derivatives **2a** and **8a**. Figure 1 shows the calculated properties for the methyl esters **2a** and **8a** including their heats of formation (ΔH_f). The 1,4 system (**8a**) is calculated to be thermodynamically more stable than the 1,6-isomer (**2a**). The 1,4-system (**8a**) is also calculated to have a significantly larger dipole moment (μ) (Figure 1), which may result in greater solvent stabilisation. Comparable results were obtained for the unsubstituted heterocycles (Figure 2). Calculated net atomic charges and molecular geometries are given in Tables 4-7. The calculated ionisation potentials (using Koopmaan' theorem) (Figure 1) are consistent with the classification of these heterocycles as electron-rich.

The ^{1}H and ^{13}C chemical shifts were assigned after comparison with model compounds [10, 11] and H, C-COSY [12] was used to correlate carbons with directly bonded protons.



2a



8a

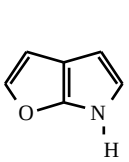
	HOMO	LUMO
e (ev)	-8.88	-0.14
O-1	0.058	0.013
C-2	0.462	0.251
C-3	0.181	-0.258
C-3a	-0.484	-0.030
C-4	0.000	0.520
C-5	0.469	-0.390
N-6	0.166	0.295
C-6a	-0.485	-0.260
C-7	0.038	-0.406
O-8	-0.158	0.317
O-9	-0.068	0.154
C-10	0.018	0.007

μ = 1.45 D
I.P. = 8.88 eV
ΔH_f = -31.27 kcal mol-1

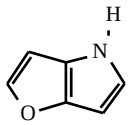
	HOMO	LUMO
e (ev)	-8.79	-0.41
O-1	-0.015	0.180
C-2	0.444	-0.419
C-3	0.235	0.228
C-3a	-0.453	0.317
N-4	-0.046	-0.349
C-5	0.539	0.397
C-6	0.205	-0.374
C-6a	-0.407	-0.122
C-7	0.043	0.333
O-8	-0.183	-0.275
O-9	-0.073	-0.129
C-10	0.019	-0.005

μ = 3.71 D
I.P. = 8.79 eV
ΔH_f = -33.54 kcal mol-1

Figure 1. Calculated (AM1) heats of formation (ΔH_f), dipole moments (μ) and frontier orbital coefficient and energies (ε) for methyl esters **2a** and **8a.**



[2,3-*b*]
ΔH_f = -53.58 kcal.mol^{-1}
μ = 1.28 D
IP = 8.42 eV



[3,2-*b*]
50.97 kcal.mol^{-1}
2.57 D
8.31 eV

Figure 2. Calculated (AM1) heats of formation (ΔH_f) and dipole moments (μ) for parent furopyrroles.

Table 1. ^{13}C Chemical shifts (δ, ppm) of compounds **2a-2c** and **8a-8c** in $CDCl_3$

Carbon	**2a**	**2b**	**2c**	**8a**	**8b**	**8c**
C-2	143.65	143.48	143.72	148.69	148.29	148.30
C-3	105.62	105.71	105.67	98.89	97.83	98.64
C-3a	110.56	107.57	108.05	128.86	133.34	132.99
C-4	106.36	106.86	107.76	-	-	-
C-5	120.70	120.76	120.16	123.77	123.40	123.19
C-6	-	-	-	96.93	97.83	98.80
C-6a	151.60	153.56	153.52	147.93	145.34	145.80
CO	162.75	162.33	162.12	162.61	162.40	162.28
OCH_3	51.60	50.37	50.90	51.58	50.89	51.04
R	-	32.00[a]	48.10[b]	-	34.59[a]	50.62[c]

[a] CH_3
[b] N-CH_2; C_6H_5: 137.33 (C-1'), 128.44 (C-3', C-5'), 127.16 (C-2', C-6'), 127.43 (C-4')
[c] N-CH_2; C_6H_5: 137.60 (C-1'), 128.50 (C-3', C-5'), 127.46 (C-2', C-6'), 127.22 (C-4')

Table 2. Difference of ^{13}C chemical shifts (Δ δ, ppm) [a] of **2a** and **8a** carbons relative to carbons of furan and methyl 2-pyrrolecarboxylate.

Compound	Δ δ(C-2)	Δ δ(C-3)	Δ δ(C-4)	Δ δ(C-5)	Δ δ(C-6)
2a	0.05	-4.78	-7.74	-1.30	-
8a	5.09	-11.51	-	1.77	-18.17

[a] Positive sign denotes a downfield shift from furan and methyl 2-pyrrolecarboxylate, respectively. Chemical shifts for furan [13] are 143.6 (C-2), 110.4 (C-3), for methyl 2-pyrrolecarboxylate [14] 122.0 (C-2), 115.1 (C-3).

The ^{13}C chemical shifts of **2a-2c** and **8a-8**c are reported in Table 1, 1H and ^{13}C NMR data of other compounds are in the experimental part. The different ^{13}C chemical shift values of the corresponding carbon positions for compounds **2a** and **8a** relative to the carbons of furan [13] and methyl 2-pyrrolecarboxylate [14] (Table 2) show, that in the 1,4-isomer **8a** the differences are greater than in 2a. In **8a** carbon C-2 shows a downfield shift Δδ = 5.09

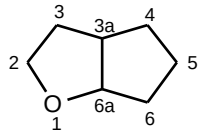
ppm, C-3 an upfield shift Δδ = -11.51 ppm as well as for C-6 Δδ = -18.17 ppm. This demonstrates that the electron density of both compared systems changes due to the annelated ring interaction, but the effect of the annelated ring is greater in the case of the 1,4 system. An analogous upfield shift was observed in 1H,4H-pyrrolo[3,2-*b*]pyrrole [15]. In order to make a direct comparison of both types of furopyrroles we carried out the correlation of the ^{13}C and ^{15}N chemical shifts (Tables 1 and 3) with net atomic charges, calculated using the AM1 method (Tables 4 and 6). In compounds **2a-2c** signals C-2 and C-5 appear at higher magnetic field and C-3 and C-4 at lower field in comparison with corresponding carbons in **8a-8c** (Table 1). The relative values of the calculated net atomic charges for the parent systems (Table 4) and the esters **2a** and **8a** (Table 6) are in good agreement with these experimental data. The comparison of ^{13}C chemical shifts of substituted furo[2,3-*b*]pyrroles shows that the greatest effect of substituents in the 2-position was observed at C-2 and C-3, analogous to the 2-substituted furans [13] and the 1,4-*O*,*N*-system [16].

Table 3. ^{15}N Chemical shifts (δ, ppm and $^{n}J(^{15}N,H)$ coupling constants (Hz) of compounds **2a-2c** and **8a-8c** in $CDCl_3$.

Compound	δ(^{15}N)	$^{1}J(^{15}N,H)$	$^{3}J(^{15}N,H)$[a]	$^{2}J(^{15}N,H)$
2a	-262.1	100.8	3.4	-
2b	-260.4	-	3.3	1.6
2c	-248.3	-	3.3	1.7
8a	-259.2	100.9	3.8	-
8b	-259.0	-	3.6	1.7
8c	-247.6	-	3.5	1.7

[a] ^{3}J(N,H-4) for **2a-2c**, ^{3}J(N,H-6) for **8a-8c**

Table 4. Calculated (AM1) net atomic charges of parent furopyrroles.

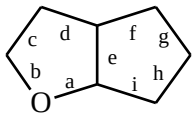


	Position							
Isomer	**1**	**2**	**3**	**4**	**5**	**6**	**3a**	**6a**
[2,3-*b*]	-0.092	-0.116	-0.122	-0.130	-0.141	-0.167[N]	-0.164	-0.001
[3,2-*b*]	-0.074	-0.083	-0.164	-0.153[N]	-0.114	-0.165	-0.121	-0.058

The ^{15}N NMR spectra of the 1,4- and 1,6-*O*,*N*-diheteropentalenes have not previously been published. We measured the ^{15}N NMR spectra of **2a-2c** and **8a-8c** in order to compare both types of *O*,*N*-diheteropentalenes (Table 3). Coupling constants $^{1}J(^{15}N,H)$ and $^{3}J(^{15}N,H)$ were obtained directly from the spectra. Selective excitation was applied to prove that the $^{3}J(^{15}N,H)$ coupling constants are due to the proton on the pyrrole ring; 60 and 100 ms evolution times were used for other compounds and spectral patterns measured were compared with simulated ones using the SIMEPT programme [17]. It was assumed, taking the data for compounds **2a** and **8a** into account, that the greater coupling constants were due to interaction with the proton on the pyrrole ring. The slightly larger negative values of the ^{15}N chemical shifts in **2a-2c** compared to **8a-8c** agree with the relative values of the calculated (AM1) negative charges on nitrogen (Tables 4 and 6).

The configurational assignment of the substituents on the double bond of the hydrazone **7a** has been determined by ^{15}N NMR spectra using the stereospecific coupling constants $^{2}J(^{15}N,H\text{-}7)$. The orientation of the lone-pair of the nitrogen and the corresponding proton has a marked effect on the value of the respective coupling constant. The comparison of the coupling constants $^{2}J(^{15}N,H\text{-}7) = 6.5$ Hz with those of model compounds in ref. [18, 19] confirms the *E*-isomer of **7a**. The same configuration was determined for some hydrazones in our previous paper [20].

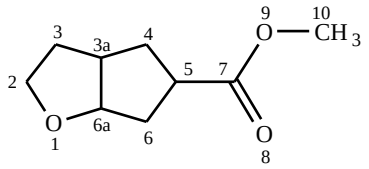
Table 5. Calculated (AM1) geometries of parent furopyrroles.



Isomer	**a**	**b**	**c**	**d**	**e**	**f**	**g**	**h**	**i**
					Bond lengths (Å)				
[2,3-*b*]	1.384	1.420	1.381	1.435	1.443	1.428	1.405	1.413	1.371
[3,2-*b*]	1.380	1.411	1.383	1.436	1.446	1.380	1.399	1.412	1.418

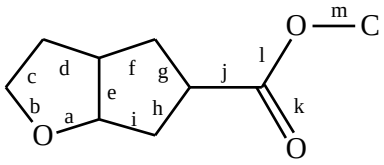
	Bond angles (deg.)					
	bc	cd	de	ef	fg	gh
[2,3-*b*]	113.2	106.5	104.7	105.3	106.8	111.0
[3,2-*b*]	113.1	105.4	106.5	107.6	107.7	111.1

Table 6. Calculated (AM1) net atomic charges of methyl esters **2a** and **8a**.



Isomer	**1**	**2**	**3**	**4**	**5**	**6**	**3a**	**6a**	**7**	**8**	**9**	**10**
[2,3-*b*]	-0.093	-0.104	-0.116	-0.031	-0.148	-0.131[N]	-0.184	+0.04	+0.372	-0.373	-0.265	-0.061
[3,2-*b*]	-0.071	-0.053	-0.180	-0.115[N]	-0.122	-0.069	-0.073	-0.083	+0.371	-0.343	-0.295	-0.058

Table 7. Calculated (AM1) geometries of methyl esters **2a** and **8a**.



Bond lengths (Å)

Isomer	**a**	**b**	**c**	**d**	**e**	**f**	**g**	**h**	**i**	**j**	**k**	**l**	**m**
[2,3-*b*]	1.383	1.425	1.378	1.440	1.450	1.418	1.415	1.422	1.363	1.452	1.237	1.370	1.430
[3,2-*b*]	1.384	1.409	1.382	1.440	1.450	1.369	1.410	1.423	1.410	1.454	1.233	1.374	1.429

Bond angles (deg.)

	bc	cd	de	ef	fg	gh	gj	jl	jk	lm
[2,3-*b*]	112.9	106.9	104.4	105.5	106.7	110.9	128.9	113.8	127.8	116.0
[3,2-*b*]	113.5	105.1	106.5	108.2	107.4	110.7	124.2	114.2	127.9	116.5

Experimental Part

The ^{1}H (360.13 MHz), ^{13}C (90.56) and ^{15}N NMR (36.50 MHz) spectra were recorded on a Bruker AMX 360 spectrometer equipped with a 5 mm broadband probe and a X32 computer using the UX NMR software. ^{1}H and ^{13}C chemical shifts were referred to internal TMS ($\delta = 0.00$).

^{15}N NMR spectra were measured using non-refocused INEPT [21]. The evolution time used was 2.6 ms for compounds **2a** and **8a** and 60 and 100 ms for other compounds. ^{15}N chemical shifts were referred to external nitromethane ($\delta = 0.0$) placed in a coaxial capillary. Negative values of chemical shifts denote upfield shifts with respect to standards.

Melting points were determined on a Kofler hot plate apparatus and are uncorrected. UV spectra were measured on a M-40 (Carl Zeiss, Jena) spectrophotometer in methanol [λ_{max} (log ε); λ_{max} in nm, ε in m^2mol^{-1}]. The IR spectra were taken on a FTIR PU 9802/25 (Philips) spectrophotometer using KBr technique (0.5 mg in 300 mg KBr, ν in cm^{-1}).

Molecular orbital calculations were carried out using the AM1 semiempirical method [22]. The geometry of each molecule studied was found by minimising the energy with respect to all geometrical variables.

*Methyl 2-azido-3-(3-furyl)propenoate (**1a**)*

A solution of 3-furancarbaldehyde (1.92 g, 20 mmol) and methyl azidoacetate (9.2 g, 80 mmol) was added at 0 °C during 30 min to sodium metal (1.84 g, 0.08 gat.) in methanol (60 ml). Stirring was continued for an additional 60 min at a temperature not exceeding 5 °C. The reaction mixture was then cooled to 0 ^{o}C, a solution of ammonium chloride (4.4 g, 80 mmol) in water (10 ml) was added and then the mixture was poured into ice water. The separated precipitate was filtered off and crystallized. Yield 2.55 g (66%); m.p. 40-41 °C (methanol). ^{1}H NMR ($CDCl_3$): 7.91 (dd, 1H, *J*(2,5) = 1.7, *J*(2,4) = 0.9, H-2), 7.42 (t, 1H, *J*(5,2) = *J*(5,4) = 1.7, H-5), 6.78 (2H, H-4, H-6); ^{13}C NMR ($CDCl_3$): 163.56 (C=O), 145.04 (C-2), 143.25 (C-5), 124.57 (C-7), 119.74 (C-3), 116.78 (C-6), 110.71 (C-4), 52.67 (O-CH_3); IR: 1713 (C=O), 2130 (N_3); UV: 299 (3.32), 219 (3.02). Anal. Calcd for $C_8H_7N_3O_3$: C, 49.74; H, 3,65; N, 21.75. Found: C, 49.62; H, 3,55; N, 21.65.

*Methyl 6*H*-furo[2,3-b]pyrrole-5-carboxylate (**2a**)*

Methyl 2-azido-3-(3-furyl)propenoate (**1**) (1 g, 5.2 mmol) was dissolved in toluene (100 ml). The mixture was refluxed under stirring for 1h. The solvent was evaporated in *vacuo* and the product was crystallized. Yield 0.5 g (61%); m.p. 162-166 °C (toluene-isohexane). ^{1}H NMR ($CDCl_3$): 9.80 (bs, 1H, NH), 7.25 (d, 1H, *J* = 2.2, H-2), 6.83 (d, *J*=1.8, 1H, H-4), 6.50 (d, 1H, *J* = 2.2, H-3), 3.88 (s, 3H, O-CH_3); IR: 1682, 1644 (C=O), 3252 (NH); UV: 292 (3.35), 247 (2.81). Anal. Calcd for $C_8H_7NO_3$: C, 58.18; H, 4.27; N, 8.48. Found: C, 58.24; H, 4.36; N, 8.54.

*Methyl 6-methylfuro[2,3-*b*]pyrrole-5-carboxylate (**2b**)*

A solution of sodium hydroxide (50%, 30 ml), methyl iodide (1.56 g, 11 mmol) and triethylbenzylammonium chloride (0.4 g) was added to a stirred solution of **2a** (1.65 g, 10 mmol) in toluene (100 ml). The temperature was then raised to 65 °C, the mixture stirred for 4 h, diluted with water and the organic layer separated. The aqueous layer was extracted with ether and combined with the toluene solution, dried with sodium sulphate and the solvent removed. The residue was crystallized. Yield 0.82 g (45.7%); m.p. 33-35 °C (isohexane). ^{1}H NMR ($CDCl_3$): 7.25 (d, 1H, *J* = 2.2, H-2), 6.84 (s, 1H, H-4), 6.47 (d, 1H, *J* = 2.2, H-3), 3.93 (s, 3H, N-CH_3), 3.80 (s, 3H, O-CH_3); IR: 1701 (C=O) ; UV: 292 (3.30), 253 (2.85). Anal. Calcd for $C_9H_9NO_3$: C, 58.18; H, 4.27; N, 8.48. Found: C, 58.24; H, 4.36; N, 8.54.

*Methyl 6-benzylfuro[2,3-*b*]pyrrole-5-carboxylate (**2c**)*

This was prepared according to the above procedure. Yield 38%; m.p. 52-54 °C (isohexane). ^{1}H NMR ($CDCl_3$): 7.25 (d, 1H, *J* = 2.3, H-2), 6.98 (s, 1H, H-4), 7.34 - 7.18 (m, 5H, H-arom), 6.53 (d, 1H, *J* = 2.3, H-3), 5.69 (s, 2H, N-CH_2), 3.82 (s, 3H, O-CH_3); IR: 1698 (C=O); UV: 293 (3.31), 250 (2.93). Anal. Calcd for $C_{15}H_{13}NO_3$: C, 70.58; H, 5.13; N, 5.43. Found: C, 70.65; H, 5.19; N, 5.37.

*Methyl 2-formyl-6*H*-furo[2,3-*b*]pyrrole-5-carboxylate (**3a**)*

A mixture of dimethylformamide (6 g, 80 mmol) and phosphorus oxychloride (3.4 g, 20 mmol) was stirred at 0 ^{o}C for 20 min. Methyl 6*H*-furo[2,3-*b*]pyrrole-5-carboxylate (**2a**) (3.30 g, 20 mmol) dissolved in dimethylformamide (6g) was added at a temperature not exceeding 10 ^{o}C. The mixture was stirred at 60 ^{o}C for 2h, poured into ice cold water, neutralized with sodium hydrogen carbonate, allowed to stand and the separated substance was filtered off and crystallized from methanol. Yield 2.7 g (70%); m.p. 203-207 °C (methanol). ^{1}H NMR (*DMSO*-d_6): 12.96 (bs, 1H, NH), 9.49 (s, 1H, CH=O), 7.74 (s, 1H, H-3), 6.97 (s, 1H, H-4), 3.82 (s, 3H, O-CH_3); ^{13}C NMR (*DMSO*-d_6): 177.56 (CH=O), 161.08 (C=O), 154.75 (C-2), 153.55 (C-6a), 124.82 (C-5), 120.63 (C-3), 111.21 (C-3a), 107. 01 (C-4), 51.71 (O-CH_3); IR: 1698 (CO), 1644 (CH=O), 3120 (NH); UV: 334 (3.50), 251 (2.74), 228 (3.04). Anal. Calcd for $C_9H_7NO_4$: C, 55.96; H, 3.65; N, 7.25. Found: C, 55.86; H, 3.71; N, 7.45.

According to this procedure the following compounds were prepared:
Methyl 2-formyl-6-methylfuro[2,3-*b*]pyrrole-5-carboxylate (**3b**).

Yield 79.6%; m.p. 157-159 °C (methanol). ^{1}H NMR (*DMSO*-d_6): 9.50 (s, 1H, CH=O), 7.78 (s, 1H, H-3), 7.05 (s, 1H, H-4), 3.81 (s, 3H, O-CH_3), 3.91 (s, 3H, N-CH_3); ^{13}C NMR (*DMSO*-d_6): 177.39 (CH=O), 160.86 (C=O), 155.24 (C-2), 153.48 (C-6a), 124.57 (C-5), 120.96 (C-3), 108.76 (C-3a), 108.20 (C-4), 51.47 (O-CH_3), 32.24 (N-CH_3); IR: 1709 (C=O), 1655 (CH=O); UV: 334 (3.51), 250 (2.74), 231 (3.06). Anal. Calcd for $C_{10}H_9NO_4$: C, 57.97; H, 4.38; N, 6.76. Found: C, 57.83; H, 4.35; N, 6.92.

*Methyl 2-formyl-6-benzylfuro[2,3-*b*]pyrrole-5-carboxylate (**3c**)*

Yield 90.5%; m.p. 194-196 °C (toluene). ^{1}H NMR (*DMSO*-d_6): 9.51 (s, 1H, CH=O), 7.81 (s, 1H, H-3), 7.30 - 7.10 (m, 5H, H-arom), 7.16 (s, 1H, H-4), 5.69 (s, 2H, N-CH_2), 3.78 (s, 3H, O-CH_3); ^{13}C NMR (*DMSO*-d_6): 177.58 (CH=O), 160.79 (C=O), 155.19 (C-2), 153.78 (C-6a), 123.94 (C-5), 120.92 (C-3), 109.28 (C-3a), 109.28 (C-4), 51.60 (O-CH_3), 47.87 (N-CH_2), C-arom: 136.78 (C-1'), 128.72 (C-3', C-5'), 127.66 (C-4'), 126.59 (C-2', C-6'); IR: 1709 (C=O), 1669 (CH=O); UV: 333 (3.48), 252 (2.74), 232 (3.08). Anal. Calcd for $C_{16}H_{13}NO_4$: C, 67.84; H, 4.63; N, 4.94. Found: C, 67.87; H, 4.55; N, 4.74.

*6-Methylfuro[2,3-*b*]pyrrole-5-carboxyhydrazide (**4b**)*

To a solution of **2b** (1.79 g, 10 mmol) in ethanol (30 ml) was added hydrazine hydrate (100%, 3 g), the mixture was refluxed for 40 h and after cooling the separated crystals were filtered off. Yield 0.896 g (50%); m.p. 163-167 °C (methanol). ^{1}H NMR (*DMSO*-d_6): 9.28 (bs, 1H, NH), 7.54 (d, 1H, *J* = 2.0, H-2), 6.74 (s, 1H, H-4), 6.63 (d, 1H, *J* = 2.0, H-3), 4.28 (bs, 2H, NH_2), 3.88 (s, 3H, N-CH_3); ^{13}C NMR (*DMSO*-d_6): 162.34 (C=O), 152.09 (C-6a), 143.34 (C-2), 123.31 (C-5), 106.28 (C-3a), 105.86 (C-3), 100.91 (C-4), 31.84 (N-CH_3); IR: 1618 (C=O), 3281, 3227 (NH); UV: 289 (3.28). Anal. Calcd for $C_8H_9N_3O_2$: C, 53.63; H, 5.06; N, 23.45. Found: C, 53.88; H, 5.22; N, 23.37.

*6-Benzylfuro[2,3-*b*]pyrrole-5-carboxyhydrazide (**4c**)*

This compound was obtained analogously. Yield 71.4%; m.p. 140-143 °C (methanol). ^{1}H NMR (*DMSO*-d_6): 9.37 (bs, 1H, NH), 7.53 (d, 1H, *J* = 2.0, H-2), 7.30 - 7.00 (m, 5H, H-arom), 6.82 (s, 1H, H-4), 6.64 (d, 1H, *J* = 2.0, H-3), 5.70 (s, 2H, CH_2), 4.32 (bs, 2H, NH_2); ^{13}C NMR (*DMSO*-d_6): 162.45 (C=O), 152.11 (C-6a), 143.85 (C-2), 122.91 (C-5), 107.05 (C-3a), 105.97 (C-4), 101.81 (C-3), 47.49 (N-CH_2), C-arom: 138.26 (C-1'), 128.63 (C-3', C-5'), 127.47 (C-4'), 127.07 (C-2', C-6'); IR: 1686, 1609 (C=O), 3316, 3265 (NH); UV: 289 (3.14).

Anal. Calcd for $C_{14}H_{13}N_3O_2$: C, 65.87; H, 5.13; N, 16.46. Found: C, 66.07; H,5.19; N, 16.32.

*Methyl 2-cyano-6*H*-furo[2,3-*b*]pyrrole-5-carboxylate (**5a**)*

To the mixture of **3a** (1.93 g, 10 mmol), pyridine (8 ml) and hydroxylammonium chloride (1.2 g, 17 mmol) in acetic anhydride (5.5 ml) were added under stirring at 95 °C. The reaction mixture was kept at 85-95 °C for 2 h, cooled and poured onto ice. The separated precipitate was filtered off and crystallized. Yield 1.738 g (91.4%); m.p. 212-214 °C (methanol). ^{1}H NMR (*DMSO*-d_6): 13.12 (bs, 1H, NH), 7.82 (s, 1H, H-3), 6.91 (s, 1H, H-4), 3.82 (s, 3H, O-CH_3); ^{13}C NMR (*DMSO*-d_6): 160.99 (C=O), 152.42 (C-6a), 124.94 (C-2), 124.81 (C-5), 119.66 (C-3), 112.51 (CN), 109.28 (C-3a), 105.90 (C-4), 51.63 (O-CH_3); IR: 1690 (C=O), 2222 (CN), 3235 (NH); UV: 303 (3.49), 222 (3.10). Anal. Calcd for $C_9H_6N_2O_3$: C, 56.85; H, 3.18; N, 14,73. Found: C, 56.75; H, 3.24; N, 14,65.

According to this procedure the following compounds were prepared:

*Methyl 2-cyano-6-methylfuro[2,3-*b*]pyrrole-5-carboxylate (**5b**)*

Yield 98.5%; m.p. 181-183 °C (methanol). ^{1}H NMR (*DMSO*-d_6): 7.82 (s, 1H, H-3), 6.98 (s, 1H, H-4), 3.90 (s, 3H, N-CH_3), 3.80 (s, 3H, O-CH_3); ^{13}C NMR (*DMSO*-d_6): 160.91 (C=O), 153.07 (C-6a), 125.24 (C-2), 124.65 (C-5), 119.98 (C-3), 112.34 (CN), 107.01 (C-3a), 107.13 (C-4), 51.47 (O-CH_3), 32.32 (N-CH_3); IR: 1694 (C=O), 2216 (CN); UV: 303 (3.50), 225 (3.10). Anal. Calcd for $C_{10}H_8N_2O_3$: C, 58.82; H, 3.95; N, 13.72. Found: C, 58.63; H, 3.85; N, 13.68.

*Methyl 2-cyano-6-benzylfuro[2,3-*b*]pyrrole-5-carboxylate (**5c**)*

Yield 91%; m.p. 153-156 °C (methanol). ^{1}H NMR (*DMSO*-d_6): 7.87 (s, 1H, H-3), 7.40 - 7.10 (m, 5H, H-arom), 7.09 (s, 1H, H-4), 5.67 (s, 2H, N-CH_2), 3.78 (s, 3H, O-CH_3); ^{13}C NMR (*DMSO*-d_6): 161.08 (C=O), 153.19 (C-6a), 125.79 (C-2), 124.23 (C-5), 120.13 (C-3), 112.36 (CN), 108.34 (C-4), 107.78 (C-3a), 51.75 (O-CH_3), 48.16 (N-CH_2), C-arom: 136.77 (C-1'), 128.89 (C3', C-5'), 127.94 (C-4'), 127.07 (C-2', C-6'); IR: 1717 (C=O), 2220 (CN); UV: 303 (3.49), 226 (3.14). Anal. Calcd for $C_{16}H_{12}N_2O_3$: C, 68.57; H, 4.32; N, 9.99. Found: C, 68.44; H, 4.52; N, 10.02.

*Methyl 2-(5'-tetrazolyl)-6*H*-furo[2,3-*b*]pyrrole-5-carboxylate (**6a**)*

A stirred mixture of **5a** (0.95 g; 5 mmol), sodium azide (0.36 g, 6 mmol), ammonium chloride (0.32 g, 6 mmol) and dimethylformamide (7 ml) was heated at 100 °C for 4 h. The solvent was distilled off *in vacuo*, the residue was dissolved in water, the solution was acidified with hydrochloric acid and the precipitate was filtered off and crystallized. Yield 0.855 g (73.3%); m.p. 270-274 °C (methanol). ^{1}H NMR (*DMSO*-d_6): 13.00 (bs, 1H, NH), 7.44 (s, 1H, H-3), 6.90 (d, 1H, *J* = 1.7, H-4), 3.77 (s, 3H, O-CH_3); ^{13}C NMR (*DMSO*-d_6): 161.18 (C=O), 152.60 (C-6a), 148.60 (C-5'), 140.39 (C-2), 122.47 (C-5), 110.80 (C-3a), 108.45 (C-3), 105.84 (C-4), 51.43 (O-CH_3); IR: 1684 (C=O), 3247 (NH); UV: 313 (3.53), 253 (2.84), 228 (3.07). Anal. Calcd for $C_9H_7N_5O_3$: C, 46.36; H, 3.03; N, 30.03. Found: C, 46.28; H, 3.17; N, 30.12.

According to this procedure the following compounds were prepared:

*Methyl 2-(5'-tetrazolyl)-6-methylfuro[2,3-*b*]pyrrole-5-carboxylate (**6b**)*

Yield 69.5%; m.p. 249-251 °C (methanol). ^{1}H NMR (*DMSO*-d_6): 7.44 (s, 1H, H-3), 6.95 (s, 1H, H-4), 3.97 (s, 3H, N-CH_3), 3.79 (s, 3H, O-CH_3); ^{13}C NMR (*DMSO*-d_6): 161.16 (C=O), 153.54 (C-6a), 149.01 (C-5'), 141.05 (C-2), 122.45 (C-5), 108.59 (C-3a), 108.49 (C-3), 107.07 (C-4), 51.15 (O-CH_3) 32.19 (N-CH_3); IR: 1705 (C=O); UV: 314 (3.54), 253 (2.86), 228 (3.07). Anal. Calcd for $C_{10}H_9N_5O_3$: C, 48.59; H, 3.67; N, 28.33. Found: C, 48.68; H, 3.55; N, 28.22.

*Methyl 2-(5'-tetrazolyl)-6-benzylfuro[2,3-*b*]pyrrole-5-carboxylate (**6c**)*

Yield 66.5%; m.p. 239-244 °C (methanol). ^{1}H NMR (*DMSO*-d_6): 7.49 (s, 1H, H-3), 7.40 - 7.16 (m, 5H, H-arom), 7.06 (s, 1H, H-4), 5.72 (s, 2H, N-CH_2), 3.77 (s, 3H, O-CH_3); ^{13}C NMR (*DMSO*-d_6): 161.20 (C=O), 153.56 (C-6a), 148.98 (C-5'), 141.51 (C-2), 121.81 (C-5), 109.26 (C-3a), 108.74 (C-3), 108.25 (C-4), 51.49 (O-CH_3), 48.06 (N-CH_2), C-arom: 137.19 (C-1'), 128.86 (C-3', C-5') 127.79 (C-4'), 126.84 (C-2', C-6'); IR: 1707 (C=O); UV: 313 (3.52), 257 (2.96), 229 (3.10). Anal. Calcd for $C_{16}H_{13}N_5O_3$: C, 59.44; H, 4.05; N, 21.66. Found: C, 59.47; H, 3.97; N, 21.82.

*5-Methoxycarbonyl-6*H*-furo[2,3-*b*]pyrrole-2-carbaldehyde dimethylhydrazone (**7a**)*

A stirred solution of **3a** (0.96 g, 5 mmol) in toluene (5 ml) containing a catalytic amount of 4-methylbenzene sulphonic acid (3 mg) was treated carefully with *N,N*-dimethylhydrazine (0.30 g, 5 mmol) in toluene (5 ml). The solution was then refluxed for 2 h and the water formed during the reaction was removed in a Dean-Stark trap. The solvent was removed under reduced pressure and the residue was crystallized. Yield 0.882 g (75%); m.p. 191-194 °C (toluene-isohexane). ^{1}H NMR [$(CD_3)_2CO$]: 11.18 (bs, 1H, NH), 7.17 (s, 1H, H-7), 6.75 (s, 1H, H-4), 6.51 (s, 1H, H-3), 3.79 (s, 3H, O-CH_3), 2.92 [s, 6H, N(CH_3)$_2$]; ^{13}C NMR [$(CD_3)_2CO$]: 162.20 (C=O), 155.23 (C-2), 152.60 (C-6a), 123.48 (C-7), 121.63 (C-5), 112.46 (C-3a), 106.18 (C-4), 102.46 (C-3), 51.35 (O-CH_3), 42.73 [(N(CH_3)$_2$)]; ^{15}N NMR (*DMSO*-d_6): -275.5 [(CH_3)$_2$N, ^3J(^{15}N, H-7) = 5.2], -251.8 (N-6, bs), -34.3[N=CH, ^2J(^{15}N, H-7) = 6.5]; IR: 1667 (C=O), 3260 (NH); UV: 341 (3.63), 274 (2.81), 235 (3.03). Anal. Calcd for $C_{11}H_{13}N_3O_3$: C, 56.16; H, 5.57; N, 17.86. Found: C, 56.37; H, 5.47; N, 17.72.

According to this procedure the following compounds were prepared:

*5-Methoxycarbonyl-6-methylfuro[2,3-*b*]pyrrole-2-carbaldehyde dimethylhydrazone (**7b**)*

Yield 73%; m.p. 114-118 °C (toluene-isohexane). ^{1}H NMR (*DMSO*-d_6): 7.21 (bs, 1H, H-7), 6.82 (s, 1H, H-4), 6.45 (bs, 1H, H-3), 3.97 (s, 3H, N-CH_3), 3.81 (s, 3H, O-CH_3), 2.97 [s, 6H, N(CH_3)$_2$]; ^{13}C NMR (DMSO-d6): 162.26 (C=O), 153.88 (C-2), 153.42 (C-6a), C-7 not found, 121.37 (C-5), 109.35 (C-3a), 107.09 (C-4), 103.91 (C-3) 50.92 (O-CH_3), 43.01 [N(CH_3)$_2$], 32.36 (N-CH_3); IR: 1697 (C=O); UV: 341 (3.59), 274 (2.81), 235 (3.00). Anal. Calcd for $C_{12}H_{15}N_3O_3$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.67; H, 5.97; N, 16.72.

*5-Methoxycarbonyl-6-benzylfuro[2,3-*b*]pyrrole-2-carbaldehyde dimethylhydrazone (**7c**)*

Yield 72%; m.p. 129-132 °C (toluene-isohexane). ^{1}H NMR [$(CD_3)_2CO$]: 7.26 (m, 5H, H-arom), 7.15 (s, 1H, H-7), 6.88 (s, 1H, H-4), 6.53 (s, 1H, H-3), 5.73 (s, 2H, N-CH_2), 3.75 (s, 3H, O-CH_3), 2.92 [s, 6H, N(CH_3)$_2$]; ^{13}C NMR [$(CD_3)_2CO$]: 162.41 (C=O), 155.87 (C-2), 154.05 (C-6a), 123.13 (C-7), 120.94 (C-5), 110.59 (C-3a), 108.25 (C-4), 102.46 (C-3), 51.20 (O-CH_3), 48.62 (N-CH_2), 42.69 [N(CH_3)$_2$], C-arom: 138.78 (C-1'), 129.38 (C-3', C-5'), 128.29 (C-4'), 127.68 (C-2', C-6'); IR: 1705 (C=O); UV: 342 (3.58), 270 (2.81), 236 (3.00). Anal. Calcd for $C_{18}H_{19}N_3O_3$): C, 66.45; H, 5.89; N, 12.91. Found: C, 66.54; H, 6.00; N, 12.83.

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