Substituted Vinyl Azides in the Synthesis of Condensed Nitrogen Heterocycles

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Dedicated to Professor Dr. Fritz Sauter, in honour of his 65th birthday

Methyl 4*H*-2-R-furo[3,2-*b*]pyrrole-5-carboxylates were prepared by thermolysis of corresponding methyl 2-azido-3-(5-R-2-furyl)propenoates. *N*-Methyl and *N*-benzyl derivatives were obtained in phase-transfer catalysis conditions. The formylation of methyl furo[3,2-*b*]pyrrole-5-carboxylate and its 4-methyl or 4-benzyl derivative gave 2-formylated compounds, which by hydrolysis afforded the corresponding 2-formyl-4-R-furo[3,2-*b*]pyrrole-5-carboxylic acids. A number of furo[3,2-*c*]pyridines were prepared by reaction of the iminophosphoranes available from corresponding substituted vinyl azides and triphenylphosphine with phenyl or 3-chlorophenyl isocyanates. ^{1}H and ^{13}C NMR, IR, and UV spectra are introduced.

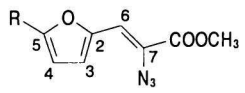
The search for pharmacologically active substances has led to the investigation of indole (furopyrroles, thienopyrroles) and isoquinoline isosters (furopyridines, thienopyridines) in which the benzene ring is replaced by furan or thiophene ring [1]. In addition, new pharmacophores with potential antipsychotic activity possess the thieno[3,2-*c*]pyridine and furo[3,2-*c*]pyridine ring system [2]. For these facts, efficient synthetic methods for these types of heterocycles are highly desirable.

In continuation of our program aimed at developing efficient syntheses of condensed nitrogen-containing heterocycles, we here report on the study of the utilization of substituted vinyl azides (*Ia—Id*) for this purpose. In the past, we used in our work for the preparation of such type azides ethyl azidoacetate and now due to the economic reasons we have turned to methyl azidoacetate and we found out some advantages of this change.

Our previous paper [3] presents some substitution, addition, and cycloaddition reactions of variously substituted furo[3,2-*b*]pyrroles and their condensed derivatives. Several methods have been described for the synthesis of the furo[3,2-*b*]pyridine systems starting either from pyridines or furans [4—7]. Electrophilic [8] and nucleophilic [9] reactions as well as biological properties [2] of the substituted furo[3,2-*c*]pyridines were studied. This paper describes the preparation of methyl 2-azido-3-(2-furyl)propenoate (*Ia*) and its 5-substituted derivatives *Ib—Id*, which are more stable than their ethyl analogues [3]. The thermolysis of *Ia—Id*, which was carried out in boiling toluene was leading to methyl furo[3,2-*b*]pyrrole-5-carboxylate (*IIa*) and to 2-substituted derivatives *IIb—IIc*. This reaction was relatively rapid and afforded the product in very good yield. The phase transfer catalysis was found to be successful for methylation and benzylation of *IIa* giving compounds *IIIa* and *IIIb*. The compounds *Ia, IIIa,* and *IIIb* gave under Vilsmeier condition 2-formylated products *IVa—IVc*, which by hydrolysis furnished the corresponding acids *Va—Vc.* Further substituted vinyl azides *Ia—Id* reacted with triphenylphosphine in dry dichloromethane under nitrogen to give iminophosphoranes *VIa—VId* in good yields. The aza Wittig reaction of *VIa—VId* with phenyl or 3-chlorophenyl isocyanate in dry toluene under reflux leads to triphenylphosphine oxide and corresponding substituted furo[3,2-*c*]pyridines *via* appropriate carbodiimides which were not isolated.

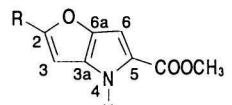
Characteristic data, UV and IR spectra of synthesized compounds are listed in Table 1. The structure of the studied compounds has been confirmed by ^{1}H NMR spectra (Tables 2—4) and ^{13}C NMR spectra (Tables 5—7). Coupling between H-6 and phosphorus in compounds *VIa—VIf* led to a splitting of this signal, the value of the coupling constant $J_{6,P}$ = 6.9—7.2 Hz. The splitting of H-6 signal is shown by the long-range coupling between H-6 and H-3, respectively H-4 protons. The value of stereospecific coupling constant $J_{4,6}$ = 0.7 Hz indicates a preferred s-*cis* conformation of the furan ring relative to the side chain double bond, which is in agreement with earlier study of the stereochemistry of furylethylene derivatives [10, 11].

The ^{1}H NMR spectra of furo[3,2-*b*]pyrroles substituted at C-2 and C-5 display doublets of H-3 and



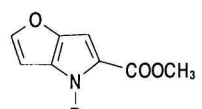
I

	R
a	H
b	C_6H_5
c	4-$CH_3C_6H_4$
d	3,4-$Cl_2C_6H_3$



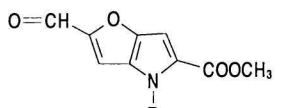
II

	R
a	H
b	C_6H_5
c	4-$CH_3C_6H_4$
d	3,4-$Cl_2C_6H_3$



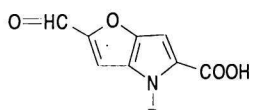
III

	R
a	CH_3
b	$CH_2C_6H_5$



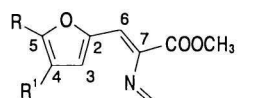
IV

	R
a	H
b	CH_3
c	$CH_2C_6H_5$



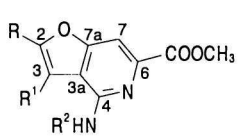
V

	R
a	H
b	CH_3
c	$CH_2C_6H_5$



VI

	R	R^1
a	H	H
b	CH_3	H
c	CH_3	CH_3
d	C_6H_5	H
e	4-$CH_3C_6H_4$	H
f	3,4-$Cl_2C_6H_3$	H



VII

	R	R^1	R^2
a	H	H	C_6H_5
b	CH_3	H	C_6H_5
c	CH_3	CH_3	3-ClC_6H_4
d	C_6H_5	H	3-ClC_6H_4
e	4-$CH_3C_6H_4$	H	3-ClC_6H_4
f	3,4-$Cl_2C_6H_3$	H	C_6H_5
g	3,4-$Cl_2C_6H_3$	H	3-ClC_6H_4

H-6 protons resulting from long-range coupling $^5J_{3,6}$ = 0.8 Hz and for compounds *IIa, IIIa,* and *IIIb* signal H-3 appears as doublet due to interaction with H-2, $^3J_{2,3}$ = 2.2 Hz. The long-range coupling between H-3 and H-7 was observed in ^{1}H NMR spectra of furo[3,2-*c*]pyridines *VIIa—VIIg*, the coupling constant $J_{3,7}$ = 0.9 Hz. The assignment of aromatic protons of all compounds was done on the basis of characteristic splitting and the substituent chemical shift values for substituted benzenes.

For the assignment of carbon signals the selective heteronuclear decoupling and semiselective INEPT experiments were used. In some cases the assignment was based on the characteristic splittings of signals and the values of long-range $J_{C,H}$ coupling constants in proton-coupled ^{13}C NMR spectra. The values of chemical shifts and coupling constants were compared with the data reported for some substituted furo[3,2-*b*]pyrroles [12] and furo[3,2-*c*]pyridines [13]. In the ^{13}C NMR spectra of compounds *VIa—VIf* the splitting of C-6 carbon is observable in $^{13}C\{^1H\}$ experiment as a result of the coupling between this carbon and phosphorus, the coupling constant $J(C_6—P)$ = 20.8 Hz. The splitting of phenyl carbons was also observed.

EXPERIMENTAL

Melting points were determined on a Kofler hot apparatus. ^{1}H NMR (300 MHz) and ^{13}C NMR (75.43 MHz) spectra were recorded on a Bruker AM-300 FT NMR spectrometer at 298 K, *Ia—Id* and *VIa—VIf* in $CDCl_3$, the other compounds in DMSO-d_6. Chemical shifts δ are relative to TMS as internal standard. The UV spectra were measured on a M-40 (Zeiss, Jena) spectrophotometer in methanol, concentration 10^{-4} mol dm^{-3} (see Table 1). The IR spectra were taken on a FTIR PU 9802/25 (Philips) spectrophotometer using KBr technique (0.5 mg /300 mg KBr).

The following starting compounds 5-phenyl-2-furancarbaldehyde, 5-(4-methylphenyl)-2-furancarbaldehyde, and 5-(3,4-dichlorophenyl)-2-furancarbaldehyde were prepared according to [14] and methyl 2-azido-3-(5-methyl-2-furyl)propenoate and methyl 2-azido-3-(4,5-dimethyl-2-furyl)propenoate according to [15].

Methyl 2-Azido-3-(5-R-2-furyl)propenoate *Ia—Id*

A solution of 5-R-2-furancarbaldehyde (20 mmol) and methyl azidoacetate (9.2 g; 80 mmol) was added at 0 °C during 30 min to sodium metal (1.84 g; 80 mmol) in methanol (60 cm^3). Stirring was continued for additional 60 min at temperature not exceeding 5 °C, the reaction mixture was then cooled to 0 °C, a solution of ammonium chloride (4.4 g; 80 mmol) in water (10 cm^3) was added and poured in ice water. The separated precipitate was filtered off and crystallized from methanol.

Methyl 4*H*-2-R-Furo[3,2-*b*]pyrrole-5-carboxylate *IIa—IId*

The corresponding methyl 2-azido-3-(5-R-2-furyl)-propenoate (*Ia—Id*) (1 g) was dissolved in toluene (100 cm^3). The mixture was refluxed under stirring for 1 h, the solvent was evaporated *in vacuo* and the product was crystallized from methanol.

Table 1. Characterization and Spectral Data of Synthesized Compounds

Compound	Formula	w_i(calc.)/% w_i(found)/%			M.p./°C	UV		IR
		C	H	N	Yield/%	λ_{max}/nm	log (ε/(m^{2}mol^{-1}))	$\tilde{\nu}$(ν(C=O))/cm^{-1}
Ia[a]	$C_8H_7N_3O_3$	49.74	3.65	21.76	34—36	333	3.42	1711
	193.1	49.68	3.56	21.92	58			
Ib[a]	$C_{14}H_{11}N_3O_3$	62.45	4.12	15.61	94—97	370	3.55	1707
	269.2	62.42	4.05	15.58	62			
Ic[a]	$C_{15}H_{13}N_3O_3$	63.59	4.63	14.83	101—104	375	3.53	1703
	283.3	63.66	4.66	14.78	73			
Id[a]	$C_{14}H_9Cl_2N_3O_3$	49.73	2.68	12.42	216—220	367	3.56	1715
	338.1	49.78	2.64	12.48	78			
IIa[b]	$C_8H_7NO_3$	58.18	4.27	8.48	137—138	298	3.52	1668
	165.1	57.98	4.30	8.56	58			
IIb[b]	$C_{14}H_{11}NO_3$	69.70	4.59	5.81	192—195	352	3.66	1674
	241.2	69.68	4.44	5.66	61	337	3.72	
IIc[b]	$C_{15}H_{13}NO_3$	70.57	5.13	5.49	216—219	353	3.65	1667
	255.2	70.63	5.44	5.62	72	339	3.72	
IId[b]	$C_{14}H_9Cl_2NO_3$	54.22	2.92	4.52	237—238	361	3.69	1695
	310.1	54.36	2.98	4.56	74	355	3.72	
IIIa	$C_9H_9NO_3$	60.33	5.06	7.81	71—72	300	3.45	1694
	179.1	60.48	5.12	7.84	76			
IIIb	$C_{15}H_{13}NO_3$	70.57	5.13	5.49	99—103	300	3.40	1684
	255.2	70.75	5.43	5.62	66			
IVa[b]	$C_9H_7NO_4$	55.96	3.65	7.25	214—217	342	3.58	1697
	193.1	55.82	3.56	7.18	78			1670
IVb	$C_{10}H_9NO_4$	57.97	4.38	6.76	162—164	342	3.55	1709
	207.2	57.94	4.42	6.79	73			1668
IVc	$C_{16}H_{13}NO_4$	67.84	4.62	4.95	106—107	342	3.55	1709
	283.2	67.94	4.68	5.04	72			1670
Va[b]	$C_8H_5NO_4$	53.65	2.81	7.82	265—270	344	3.56	1684
	179.1	53.74	2.68	7.88	56			1688 sh
Vb	$C_9H_7NO_4$	55.96	3.65	7.25	233—234	344	3.56	1711
	193.1	55.99	3.72	7.32	62			1688 sh
Vc	$C_{15}H_{11}NO_4$	66.91	4.12	5.20	207—212	344	3.49	1686
	268.2	66.98	4.22	5.36	60			
VIa	$C_{26}H_{22}NO_3P$	73.06	5.18	3.27	166—168	355	3.31	1695
	427.4	73.18	5.26	3.48	78			
VIb	$C_{27}H_{24}NO_3P$	73.46	5.48	3.17	146—150	360	3.27	1703
	441.5	73.48	5.62	3.26	80			
VIc	$C_{28}H_{26}NO_3P$	73.82	5.75	3.09	146—150	365	3.32	1692
	455.5	73.88	5.86	3.32	86			
VId	$C_{32}H_{26}NO_3P$	76.32	5.20	2.79	189—192	390	3.53	1687
	503.6	76.22	5.41	2.82	82			
VIe	$C_{33}H_{28}NO_3P$	76.58	5.45	2.72	181—183	392	3.55	1686
	517.6	76.64	5.66	2.88	80			
VIf	$C_{32}H_{24}NO_3P$	76.64	4.82	2.79	228—230	393	–	1690
	501.5	76.64	4.92	2.92	84			
VIIa[c]	$C_{15}H_{12}N_2O_3$	67.15	4.51	10.44	168—171	333	2.83	1693
	268.2	67.28	4.59	10.58	68	295	3.40	
						247	3.19	
VIIb[c]	$C_{16}H_{14}N_2O_3$	68.07	5.00	9.92	185—187	337 sh	2.89	1716
	282.3	68.22	5.12	9.78	66	300	3.42	
						250	3.18	
VIIc[c]	$C_{17}H_{15}ClN_2O_3$	61.73	4.57	8.47	162—164	333 sh	2.99	1716
	330.7	61.84	4.51	8.36	72	302	3.44	
						251	3.14	
VIId[c]	$C_{21}H_{15}ClN_2O_3$	66.58	3.99	7.39	169—171	358	3.38	1713
	378.8	66.72	3.77	7.44	74	315	3.51	
						276	3.29	
VIIe[c]	$C_{22}H_{17}ClN_2O_3$	67.26	4.34	7.13	238—243	359	3.16	1696
	392.8	67.44	4.44	7.34	65	319	3.28	
						273	3.04	
VIIf[c]	$C_{21}H_{14}Cl_2N_2O_3$	61.03	3.41	6.78	231—232	373	3.35	1716
	413.3	61.23	3.45	6.88	76	309	3.46	
						282 sh	3.39	
VIIg[c]	$C_{21}H_{13}Cl_3N_2O_3$	56.34	2.92	6.27	219—224	367	3.39	1699
	447.7	56.52	2.98	6.46	78	309	3.47	
						280 sh	3.35	

For *Ia*—*Id* $\tilde{\nu}$/cm^{-1}: *a*) 2131, 2130, 2112, and 2123 (ν(N_3)); *b*) 3273—3298 (ν(NH)); *c*) 3362—3400 (ν(NH)).

Table 2. ^{1}H NMR Data (δ) of Compounds *Ia*—*Id* and *VIa*—*VIf*

Compound	H-3	H-4	H-6	OCH_3	Other signals, $J_{H,H}$
Ia	7.09 d	6.51 dd	6.85 s	3.88 s	7.48 (d, H-5), $J_{3,4}$ = 3.5 Hz, $J_{4,5}$ = 1.8 Hz
Ib	7.18 d	6.78 d	6.93 s	3.88 s	7.25—7.75 (m, H_{arom}), $J_{3,4}$ = 3.7 Hz
Ic	7.17 d	6.73 d	6.93 s	3.89 s	2.36 (s, CH_3), 7.19, 7.59 (AA'BB' q, H_{arom}), $J_{3,4}$ = 3.7 Hz
Id	7.17 d	6.78 d	6.88 s	3.90 s	7.75 (t, H-2'), 7.46 (m, H-5',H-6'), $J_{3,4}$ = 3.7 Hz
VIa	7.10 dt	6.40 ddd	6.80 dt	3.39 s	7.35 (d, H-5), 7.35—7.80 (m, H_{arom}), $J_{3,4}$ = 3.4 Hz, $J_{3,5}$ = 0.9 Hz, $J_{4,5}$ = 1.8 Hz, $J_{4,6}$ = 0.7 Hz, $J_{6,P}$ = 6.9 Hz
VIb	6.92 d	5.99 d	6.75 d	3.38 s	2.32 (s, CH_3), 7.35—7.80 (m, H_{arom}), $J_{3,4}$ = 3.2 Hz, $J_{6,P}$ = 6.9 Hz
VIc	6.84 m	–	6.72 dd	3.37 s	2.22 (s, CH_3), 1.88 (s, CH_3), 7.35—7.80 (m, H_{arom}), $J_{3,6}$ = 0.7 Hz, $J_{6,P}$ = 6.9 Hz
VId	7.20 d	6.70 dd	6.87 dt	3.41 s	7.35—7.80 (m, H_{arom}), $J_{3,4}$ = 3.5 Hz, $J_{4,6}$ = 0.7 Hz, $J_{6,P}$ = 7.1 Hz
VIe	7.18 dd	6.64 dd	6.87 dt	3.41 s	2.34 (s, CH_3), 7.35—7.80 (m, H_{arom}), $J_{3,4}$ = 3.5 Hz, $J_{3,6}$ = 0.7 Hz, $J_{4,6}$ = 0.9 Hz, $J_{6,P}$ = 7.1 Hz
VIf	7.19 dd	6.72 dd	6.81 dt	3.41 s	7.35—7.80 (m, H_{arom}), $J_{3,4}$ = 3.5 Hz, $J_{3,6}$ = 0.7 Hz, $J_{4,6}$ = 0.7 Hz, $J_{6,P}$ = 7.2 Hz

Table 3. ^{1}H NMR Data (δ) of Compounds *II*—*V*

Compound	H-3	H-6	NH	OCH_3	Other signals, $J_{H,H}$
IIa	6.61 dd	6.76 d	11.70 bs	3.80 s	7.78 (d, H-2), $J_{2,3}$ = 2.2 Hz, $J_{3,6}$ = 0.7 Hz
IIb	7.15 d	6.80 dd	11.80 bs	3.80 s	7.78—7.85 (m), 7.27—7.47 (m, H_{arom}), $J_{3,6}$ = 0.8 Hz, $J_{4,6}$ = 1.7 Hz
IIc	7.07 d	6.78 dd	11.78 bs	3.80 s	2.32 (s, CH_3), 7.24, 7.69 (AA' BB' q, H_{arom}), $J_{3,6}$ = 0.8 Hz
IId	7.35 s	6.78 bs	11.88 bs	3.80 s	8.03 (d, H-2'), 7.76 (dd, H-6'), 7.65 (H-5')
IIIa	6.81 d	6.80 bs	–	3.75 s	7.82 (d, H-2), 3.92 (s, N—CH_3), $J_{2,3}$ = 2.2 Hz
IIIb	6.70 dd	6.90 d	–	3.74 s	7.81 (d, H-2), 5.65 (s, CH_2), 7.10—7.35 (m, H_{arom}), $J_{2,3}$ = 2.2 Hz, $J_{3,6}$ = 0.7 Hz
IVa	7.70 d	6.92 d	12.17 bs	3.92 s	9.64 (s, CHO), $J_{3,6}$ = 0.8 Hz
IVb	7.85 d	6.92 d	–	3.89 s	9.69 (s, CHO), 4.03 (N—CH_3), $J_{3,6}$ = 0.8 Hz
IVc	7.72 d	7.01 d	–	3.86 s	9.63 (s, CHO), 5.77 (s, CH_2), 7.25—7.45 (m, H_{arom}), $J_{3,6}$ = 0.8 Hz
Va	7.69 d	6.87 d	12.11 bs	–	9.63 (s, CHO)
Vb	7.82 d	6.89 d	–	–	9.63 (s, CHO), 4.02 (s, N—CH_3), $J_{3,6}$ = 0.8 Hz
Vc	7.73 d	6.89 d	–	–	9.63 (s, CHO), 5.81 (s, CH_2), 7.25—7.45 (m, H_{arom}), $J_{3,6}$ = 0.8 Hz

Table 4. ^{1}H NMR Data (δ) of Compounds *VIIa*—*VIIg*

Compound	H-3	H-7	NH	OCH_3	Other signals, $J_{H,H}$
VIIa	7.44 dd	7.77 d	9.29 bs	3.89 s	8.15 (d, H-2), 8.07 (d, H-2', H-6'), 7.31 (t, H-3', H-5'), 6.98 (t, H-4'), $J_{2,3}$ = 2.2 Hz, $J_{3,7}$ = 0.9 Hz
VIIb	7.04 m	7.68 d	9.14 bs	3.88 s	8.04 (d, H-2', H-6'), 7.31 (t, H-3', H-5'), 6.96 (t, H-4'), 2.40 (s, CH_3), $J_{3,7}$ = 0.9 Hz
VIIc	–	7.69 s	9.19 bs	3.87 s	8.19 (t, H-2'), 7.63 (dt, H-6'), 7.29 (t, H-5'), 6.97 (t, H-4'), 2.37 (s, 2 × CH_3)
VIId	7.74 s	7.79 s	9.52 bs	3.89 s	8.56 (t, H-2'), 7.00—7.90 (m, H_{arom})
VIIe	*a*	*a*	9.54 bs	3.90 s	8.58 (t, H-2'), 7.34 (t, H-5'), 7.01 (m, H-4'), 7.50—7.80 (m, H_{arom} of R, H-6', H-3, H-7)
VIIf	7.68 d	7.78 d	9.29 bs	3.90 s	R^2: 8.12 (d, H-2', H-6'), 7.33 (t, H-3', H-5'), 6.98 (t, H-4'); R: 7.91 (H-2''), 7.78—7.85 (m, H-5'', H-6''); $J_{3,7}$ = 0.8 Hz
VIIg	*a*	*a*	9.37 bs	3.89 s	R^2: 8.46 (t, H-2'), 7.30 (t, H-5'), 6.98 (dd, H-4'); R: 7.81 (d, H-2''), 7.58—7.78 (m, H-5'', H-6'' and H-3, H-7)

a) Overlapped by multiplet of H_{arom}.

Methyl 4-R-Furo[3,2-*b*]pyrrole-5-carboxylate *IIIa* and *IIIb*

A solution of sodium hydroxide (50 %, 30 cm^3), methyl iodide (1.56 g; 11 mmol), and triethylbenzylammonium chloride (0.4 g) was added to a stirred solution of *IIa* or *IIb* (10 mmol) in toluene (100 cm^3). The temperature was then raised to 65 °C and the mixture stirred for 4 h, diluted with water and the organic layer was separated. The aqueous layer was extracted with ether and combined with toluene solution, dried with sodium sulfate and the solvent was removed. The residue was crystallized from methanol.

Table 5. ^{13}C NMR Data (δ) of Compounds *Ia*—*Id*[a] and *VIa*—*VIf*[a]

Compound	C-2	C-3	C-4	C-5	C-6	C-7	CO	OCH_3
Ia	149.56	115.34	112.58	143.98	113.71	122.77	163.60	52.80
Ib	155.13	117.76	108.20	148.90	113.54	122.19	163.52	52.78
Ic	155.59	117.86	107.58	148.65	113.77	121.96	163.69	52.60
Id	152.56	117.53	109.43	149.77	112.95	123.23	163.45	52.83
VIa	154.43	111.66	109.67	140.16	110.66[b]	134.35	167.54	51.64
VIb	152.77	111.22	107.94	150.24	107.94[b]	133.51	167.60	51.57
VIc	151.32	116.25	114.06	145.77	108.00[b]	133.63	167.74	51.51
VId	151.34	112.32	107.86	154.31	107.12[b]	133.40	167.81	51.71
VIe	151.63	112.35	107.15	153.89	107.30[b]	133.43	167.91	51.68
VIf	148.74	112.18	109.32	155.24	106.30[b]	133.20	167.82	51.78

a) *Ib*: R: 129.86 (C-1'), 128.75 (C-2', C-6'), 124.16 (C-3', C-5'), 128.17 (C-4')
Ic: R: 21.32 (CH_3), 127.32 (C-1'), 129.51 (C-2', C-6'), 124.23 (C-3', C-5'), 138.30 (C-4')
Id: R: 133.24, 125.81, 123.44 (C-2', C-5', C-6'), 131.93, 130.81, 129.87 (C-1', C-3', C-4')
VIa: $(C_6H_5)_3$: 133.41, 132.27, 130.16, 128.13
VIb: R: 13.80 (CH_3); $(C_6H_5)_3$: 132.40, 132.01, 130.91, 128.09
VIc: 11.54 (C_5—CH_3), 10.00 (C_4—CH_3); $(C_6H_5)_3$: 132.62,132.35, 130.86, 128.04
VId: R: 131.17, 128.55, 126.62, 123.52; $(C_6H_5)_3$: 134.73, 132.31, 130.99, 128.19
VIe: R: 21.27 (CH_3), 136.44 (C-4'), 129.24 (C-2', C-6'), 128.51 (C-1'), 123.51 (C-3', C-5'); $(C_6H_5)_3$: 134.30, 132.30, 130.97, 128.17
VIf : R: 132.30, 131.84, 130.51, 129.84, 128.31, 122.53; $(C_6H_5)_3$: 132.74, 132.28, 131.84, 128.24
b) $J(C_6 — P)$ = 20.8 Hz.

Table 6. ^{13}C NMR Data (δ) of Compounds *II*—*V*[a]

Compound	C-2	C-3	C-3a	C-5	C-6	C-6a	CO	OCH_3
IIa	149.29	99.44	129.34	123.22	95.97	146.96	161.63	51.17
IIb	158.77	95.95	130.68	123.33	94.87	146.83	161.40	51.21
IIc	159.12	95.95	130.95	123.05	94.10	146.60	161.43	51.17
IId	155.98	96.86	130.53	124.21	95.85	147.35	161.33	51.31
IIIa	149.42	98.91	133.53	123.21	97.52	144.53	161.56	50.99
IIIb	149.64	98.55	133.21	122.37	99.35	144.94	161.47	51.07
IVa	156.55	111.43	129.78	128.79	95.88	150.85	161.19	52.08
IVb	156.23	110.54	132.68	129.24	97.35	148.34	161.15	51.89
IVc	156.40	110.55	132.25	128.66	98.43	148.70	161.06	51.94
Va	156.30	111.65	131.50	128.40	95.53	151.09	162.26	–
Vb	155.99	110.67	132.42	130.74	97.22	148.53	162.32	–
Vc	156.12	110.86	131.90	130.26	98.31	148.87	162.26	–

a) Other signals: *IIb*: 127.89 (C-1'), 123.63 (C-2', C-6'), 128.85 (C-3', C-5'), 130.82 (C-4'); *IIc*: 20.84 (CH_3), 128.05 (C-1'), 123.64 (C-2', C-6'), 129.42 (C-3', C-5'), 137.46 (C-4'); *IId*: 131.03, 125.05, 123.47 (C-2', C-5', C-6'), 131.81, 131.21, 130.53 (C-1', C-3', C-4'); *IIIa*: 34.60 (N—CH_3); *IIIb*: 49.79 (CH_2), 138.46 (C-3', C-5'), 127.32 (C-4'), 126.93 (C-2', C-6'); *IVa*: 178.87 (CHO); *IVb*: 179.00 (CHO), 34.89 (N—CH_3); *IVc*: 179.06 (CHO), 50.13 (CH_2), 137.65 (C-1'), 128.80 (C-3', C-5'), 127.81 (C-4'), 127.23 (C-2', C-6'); *Va*: 178.76 (CHO); *Vb*: 178.83 (CHO), 34.90 (N—CH_3); *Vc*: 178.98 (CHO), 49.23 (CH_2), 137.95 (C-1'), 128.81 (C-3', C-5'), 127.77 (C-4'), 127.19 (C-2', C-6').

Table 7. ^{13}C NMR Data (δ) of Compounds *VIIa*—*VIIg*[a]

Compound	C-2	C-3	C-3a	C-4	C-6	C-7	C-7a	CO	OCH_3
VIIa	146.91	102.80	114.18	149.24	141.00	104.87	159.35	165.47	52.30
VIIb	156.73	101.90	115.56	148.31	139.71	100.82	158.81	165.50	52.20
VIIc	153.43	109.07	117.37	148.34	139.45	103.58	158.91	165.58	52.56
VIId	156.28	99.59[b]	116.10	148.27	140.45	102.41[b]	159.11	165.19	52.32
VIIe	156.60	98.83[b]	116.23	148.18	140.25	102.43[b]	158.96	165.23	52.32
VIIf	153.18	101.66[b]	115.48	148.95	140.82	101.76[b]	159.24	165.20	52.31
VIIg	153.34	101.26[b]	115.61	148.23	140.89	102.10[b]	159.15	165.00	52.29

a) *VIIa*: R^3: 140.76 (C-1'), 128.49 (C-3', C-5'), 121.35 (C-4'),118.80 (C-2', C-6')
VIIb: 13.79 (CH_3); R^3: 141.14 (C-1'), 128.43 (C-3', C-5'), 121.10 (C-4'), 118.60 (C-2', C-6')
VIIc: 11.70 (C_5—CH_3), 9.38 (C_4—CH_3); R^3: 142.91 (C-1'), 133.32 (C-3'), 130.15 , 120.03, 118.35, 117.37 (C-2', C-4', C-5', C-6')
VIId: R: 129.45 (C-4'), 129.27 (C-3'', C-5''), 128.71 (C-1''); R^3: 142.44 (C-1'), 133.10 (C-3'), 129.95, 120.65, 118.01, 116.73 (C-2', C-4', C-5', C-6')
VIIe: R: 20.95 (CH_3), 139.29 (C-4''), 131.42 (C-2'', C-6''), 129.83 (C-1''), 128.62 (C-3'', C-5''); R^3: 142.48 (C-1'), 133.10 (C-3'), 129.96, 120.63, 117.96, 116.70 (C-2', C-4', C-5', C-6')
VIIf: R: 132.05, 131.50, 131.44, 129.21, 125.91, 124.45 (C_{arom}); R^3: 141.30 (C-1'), 128.48 (C-3', C-5'), 121.38 (C-4'), 118.67 (C-2', C-6')
VIIg: R: 132.01, 131.57, 131.35, 129.00, 125.83, 124.73 (C_{arom}); R^3: 142.25 (C-1'), 133.05 (C-3'), 129.82, 120.86, 118.02, 116.66 (C-2', C-4', C-5', C-6')
b) The values can be interchanged.

Methyl 2-Formyl-4-R-furo[3,2-*b*]pyrrole-5-carboxylate *IVa—IVc*

A mixture of dimethylformamide (6 g; 80 mmol) and phosphorus oxychloride (3.4 g; 20 mmol) was stirred at 0 °C for 20 min. Methyl furo[3,2-*b*]pyrrole-5-carboxylate *IIa*, *IIIa*, *IIIb* (20 mmol) dissolved in dimethylformamide (6 g) was added at a temperature not exceeding 10 °C. The mixture was stirred at 60 °C for 2 h, poured into ice cold water, neutralized with sodium hydrogen carbonate, allowed to stand and the separated substance was filtered off and crystallized from methanol.

2-Formyl-4-R-furo[3,2-*b*]pyrrole-5-carboxylic Acid *Va—Vc*

Ester *IVa—IVc* (10 mmol) in ethanol (50 cm^3) and 5 % solution of sodium hydroxide (20 cm^3) was heated on a steam bath for 1 h and concentrated to half of its original volume. The precipitate was dissolved in dilute ethanol (50 %), acidified with hydrochloric acid (φ_r = 1 : 1) and poured into ice. The precipitate was filtered off and crystallized from methanol.

Methyl 2-Triphenylphosphoimino-3-(4-R^1-5-R-2-furyl)propenoate *VIa—VIf*

A solution of triphenylphosphine (1.31 g; 5 mmol) in dry dichloromethane (20 cm^3) was added dropwise under nitrogen to a stirred solution of *Ia—Id* (5 mmol) in the same solvent (10 cm^3) at 0 °C. The reaction mixture was allowed to warm to the room temperature and stirring was continued for 20 h. The solvent was removed under reduced pressure and the residual solid was recrystallized to give *VIa*, *VId—VIf*. Analogously were prepared *VIb* and *VIc* starting from corresponding 2-azidopropenoates [15].

Methyl 2-R-3-R^1-4-R^2-Aminofuro[3,2-c]pyridine-6-carboxylate *VIIa—VIIg*

A solution of the phenyl isocyanate or 3-chlorophenyl isocyanate (5 mmol) in dry toluene (50 cm^3) was added dropwise under nitrogen to stirred solution of *VIa—VIf* (5 mmol). The reaction mixture was refluxed for 12 h. The solvent was removed under reduced pressure and the solid residue was crystallized.

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REFERENCES

1. Molina, P., Fresneda, P. M., and Hurtado, F., *Synthesis 1987*, 45.
2. New, J. S., Christopher, W. L., Yewich, J. P., Butler, R., Schlemmer, R. F., Jr., Vander Maelen, C. P., and Cipolline, J. A., *J. Med. Chem. 32*, 1147 (1989).
3. Krutošíková, A., *Collect. Czech. Chem. Commun. 55*, 597 (1990).
4. Eloy, F. and Deryckere, A., *J. Heterocycl. Chem. 8*, 57 (1971).
5. Bouzard, J. D. and Bisagni, E., *Bull. Soc. Chim. Fr. 1971*, 1727.
6. Lhommet, G., Sliwa, H., and Maitte, P., *Bull. Soc. Chim. Fr. 1971*, 1442.
7. Krutošíková, A., Dandárová, M., Chylová, J., and Végh, D., *Monatsh. Chem. 123*, 807 (1987).
8. McFarland, J. W., Essary, W. A., Cilenti, L., Cozard, W., and McFarland, P. E., *J. Heterocycl. Chem. 12*, 705 (1975).
9. Koreňová, A., Krutošíková, A., Kováč, J., and Celec, S., *Collect. Czech. Chem. Commun. 52*, 192 (1987).
10. Dandárová, M., Kováč, J., Végh, D., and Žvak, V., *Collect. Czech. Chem. Commun. 47*, 3412 (1982).
11. Dandárová, M., Végh, D., Kováč, J., Goljer I., Pronayová, N., and Špirková, K., *Collect. Czech. Chem. Commun. 51*, 889 (1986).
12. Dandárová, M., Krutošíková, A., and Alföldi, J., *Magn. Reson. Chem. 28*, 830 (1991).
13. Shiotami, S. and Morita, H., *J. Heterocycl. Chem. 28*, 1469 (1991).
14. Frimm, R., Kováč, J., and Krutošíková, A., *Chem. Zvesti 27*, 101 (1973).
15. Krutošíková, A., Dandárová, M., and Bobošík, V., *Collect. Czech. Chem. Commun. 59*, 473 (1994).

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