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SYNTHESIS AND ANTIBACTERIAL ACTIVITY OF 3-PYRROL-1-YLTHIENO[2,3-*b*]PYRIDINE-2-CARBOXYLIC ACID [(PHENYL-,1,3-BENZODIOXOL-5-YL)METHYLENE]HYDRAZIDES

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A series of 3-pyrrol-1-ylthieno[3,2-*b*]pyridine-2-carboxylic acid [(phenyl-, 1,3-benzodioxol-5-yl)methylene]-hydrazides were synthesized by reacting 3-pyrrol-1-ylthieno[2,3-*b*]pyridine-2-carbohydrazides with aromatic aldehydes. The synthesized hydrazides possessed antibacterial properties.

Keywords: 3-(1-pyrrolyl)thieno[2,3-*b*]pyridine derivatives, hydrazides, antibacterial activity.

In continuation of research on the synthesis of compounds with antibacterial activity [1], a series of 22 3-pyrrol-1-ylthieno[2,3-*b*]pyridine-2-carboxylic acid [(phenyl-, 1,3-benzodioxol-5-yl)methylene]hydrazides (**Ia** – **v**) were synthesized and their antibacterial activity was studied. The starting materials for preparing compounds **I** were 3-(1-pyrrolyl)-thieno[2,3-*b*]pyridine-2-carbohydrazides (**IIa** and -**b**) [2] and several aldehydes (**IIIa** – **l**) containing pharmacophores from the chemical-block.com database.

Target compounds **Ia** – **v** were synthesized by refluxing 3-(1-pyrrolyl)thieno[2,3-*b*]pyridine-2-carbohydrazides **II** and aldehydes **III** in EtOH:DMF (1:1, v/v) with *p*-toluenesulfonic acid catalyst. The mixture with DMF was used because the hydrazides were poorly soluble in EtOH. The reaction time depended on the nature of the aldehyde and varied from 10 – 15 min to several hours.

The yields of target compounds **Ia** – **v** reached 98% (Table 1). Compounds **Ia** – **v** were crystalline solids ranging from colorless (**Ia**, **b**, **o**, **p**) to bright yellow (**If** – **h**, **j** – **m**, **q** – **s**) with melting points exceeding those of the corresponding starting hydrazides **II**.

The structures of **Ia** – **v** were confirmed by IR and PMR spectra (Tables 2 and 3). PMR spectra of hydrazones **Ia** – **v** were missing the NH_2 singlet at 4.23 or 4.24 ppm that ap-

TABLE 1. Characteristics of Synthesized Compounds

Compound	Empirical formula	mp, °C	Yield, %
Ia	$C_{22}H_{18}Cl_2N_4O_2S$	266 – 267	96
Ib	$C_{21}H_{16}Cl_2N_4OS$	274 – 275	97
Ic	$C_{22}H_{18}Cl_2N_4O_3S$	278 – 279	96
Id	$C_{21}H_{16}Cl_2N_4O_2S$	264 – 265	90
Ie	$C_{23}H_{21}ClN_4O_4S$	270 – 271	71
If	$C_{22}H_{19}ClN_4O_3S$	279 – 280	75
Ig	$C_{26}H_{22}N_4O_3S$	279 – 280	73
Ih	$C_{25}H_{20}N_4O_2S$	249 – 250	80
Ii	$C_{24}H_{22}N_4O_5S$	268 – 269	87
Ij	$C_{23}H_{20}N_4O_4S$	264 – 265	92
Ik	$C_{25}H_{24}N_4O_6S$	281 – 282	91
Il	$C_{24}H_{22}N_4O_5S$	239 – 240	96
Im	$C_{25}H_{24}N_4O_6S$	283 – 284	97
In	$C_{24}H_{22}N_4O_5S$	252 – 253	95
Io	$C_{28}H_{30}N_4O_6S$	221 – 222	81
Ip	$C_{32}H_{33}N_5O_9S$	194 – 195	77
Iq	$C_{31}H_{31}N_5O_8S$	209 – 210	86
Ir	$C_{36}H_{35}N_5O_8S$	224 – 225	79
Is	$C_{35}H_{33}N_5O_7S$	231 – 232	93
It	$C_{35}H_{32}FN_5O_7S$	234 – 235	84
Iu	$C_{35}H_{32}ClN_5O_7S$	241 – 242	94
Iv	$C_{34}H_{30}ClN_5O_6S$	209 – 210	98

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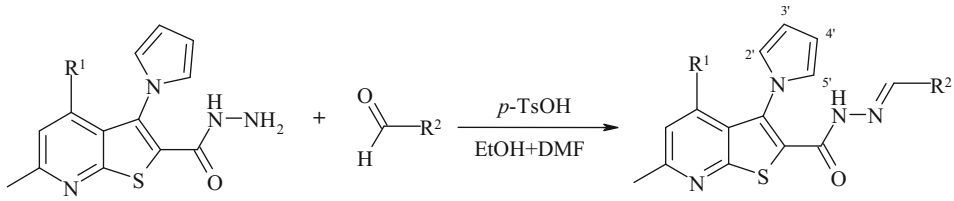


IIa, b **IIIa-l** **Ia-v**

Ia, **c**, **e**, **g**, **i**, **k**, **m**, **o**, **p**, **r**, **t**, **u** and **IIa**: $R^1 = CH_2OCH_3$; **Ib**, **d**, **f**, **h**, **j**, **l**, **n**, **q**, **s**, **v** and **IIb**: $R^1 = CH_3$; **Ia**, **b** and **IIIa**: R^2 = 3,4-dichlorophenyl; **Ic**, **d** and **IIIb**: R^2 = 2-hydroxy-3,5-dichloropheyl; **Ie**, **f** and **IIIc**: R^2 = 4-hydroxy-3-methoxy-5-chlorophenyl.

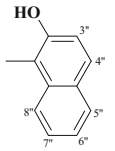
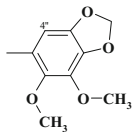
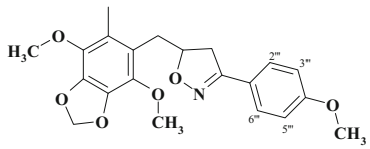
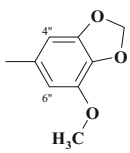
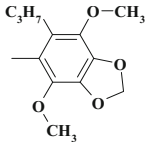
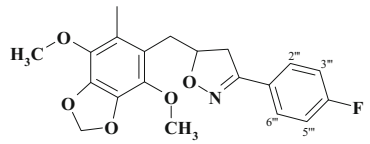
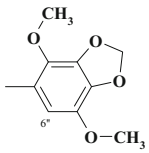
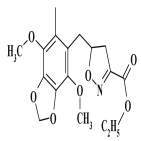
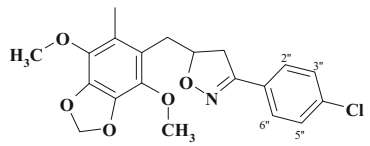
Compound	R^2	Compound	R^2	Compound	R^2
Ig, **h**, **IIId**		**Ii, n, IIIg**		**Ir, s, IIIj**	
Ii, j, IIIe		**Io, IIIh**		**It, IIIk**	
Ik, l, IIIf		**Ip, q, IIIi**		**Is, v, IIIl**	

TABLE 2. PMR Spectra of Synthesized Compounds

Compound	PMR spectrum,(δ, ppm, SSCC, J, Hz)
Ia	2.65 (s, 3H, 6-CH_{3Py}), 3.16 (c, 3H, $CH_2O\underline{CH_3}$), 3.96 (c, 2H, $\underline{CH_2}OCH_3$), 6.20 (s, *anti*-3′-H, 4′-H), 6.38 (s, *syn*-3′-H, 4′-H), 6.86 (s, *anti*-2′-H, 5′-H), 7.08 (s, *syn*-2′-H, 5′-H), 7.44 (c, 1H, H_{Py}), 7.62 – 7.73 (m, 2H, *anti*, *syn*-5-H_{Ar}, N=CH), 7.85 – 8.02 (m, 2H, *anti*, *syn*-2-H_{Ar}, 6-H_{Ar}), 10.74 (c, *syn*-NH), 12.04 (s, *anti*-NH)
Ib	1.89, 2.58 (both s, 3H each, 4-CH_{3Py}, 6-CH_{3Py}), 6.16 (s, *anti*-3′-H, 4′-H), 6.35 (s, *syn*-3′-H, 4′-H), 6.86 (s, *anti*-2′-H, 5′-H), 7.09 (s, *syn*-2′-H, 5′-H), 7.20 (br.s, 1H, H_{Py}), 7.68 – 7.72 (m, 2H, *anti*, *syn*-5-H_{Ar}, N=CH), 7.83 – 8.02 (m, 2H, *anti*, *syn*-2-H_{Ar}, 6-H_{Ar}), 10.60 (c, *syn*-NH),12.10 (s, *anti*-NH)
Ic	2.65 (s, 3H, 6-CH_{3Py}), 3.17 (c, 3H, $CH_2O\underline{CH_3}$), 3.97 (c, 2H, $\underline{CH_2}OCH_3$), 6.22 (s, *anti*-3′-H, 4′-H), 6.36 (s, *syn*-3′-H, 4′-H), 6.84 (s, *anti*-2′-H, 5′-H), 7.06 (s, *syn*-2′-H, 5′-H), 7.44 (c, 1H, H_{Py}), 7.62, (s, 1H, 4-H_{Ar}), 7.65 (s, 1H, 6-H_{Ar}), 8.26 (s, 1H, N=CH), 10.52 (br.s, *anti*-OH), 11.42 (br.s, *syn*-NH), 11.78 (br.s, *syn*-OH), 12.22 (br.s, *anti*-NH)
Id	1.90, 2.59 (both s, 3H each, 4-CH_{3Py}, 6-CH_{3Py}), 6.19 (s, *anti*-3′-H, 4′-H), 6.33 (s, *syn*-3′-H, 4′-H), 6.83 (s, *anti*-2′-H, 5′-H), 7.06 (s, *syn*-2′-H, 5′-H), 7.23 (c, 1H, H_{Py}), 7.63 (s, 1H, 4-H_{Ar}), 7.65 (s, 1H, 6-H_{Ar}), 8.25 (s, 1H, N=CH), 10.50 (br.s, *anti*-OH), 11.35 (c, *syn*-NH), 11.82 (br.s, *syn*-OH), 12.25 (s, *anti*-NH)
Ie	2.64 (s, 3H, 6-CH_{3Py}), 3.16 (c, 3H, $CH_2O\underline{CH_3}$), 3.80 (c, *anti*-OCH_3), 3.87 (c, *syn*-OCH_3), 3.93 (c, *anti*-$\underline{CH_2}OCH_3$), 3.97 (c, *syn*-$\underline{CH_2}OCH_3$), 6.21 (s, *anti*-3′-H, 4′-H), 6.40 (s, *syn*-3′-H, 4′-H), 6.85 (s, *anti*-2′-H, 5′-H), 7.09 (s, *syn*-2′-H, 5′-H), 7.23 (c, 1H, 2-H_{Ar}), 7.25 (s, 1H, 6-H_{Ar}), 7.43 (c, 1H, H_{Py}), 7.78 (s, *syn*-N=CH), 7.93 (s, *anti*-N=CH), 9.97 (br.s, 1H, OH), 10.32 (c, *syn*-NH), 11.89 (s, *anti*-NH)
If	1.90, 2.58 (both s, 3H each, 4-CH_{3Py}, 6-CH_{3Py}), 3.81 (c, *anti*-OCH_3), 3.87 (c, *syn*-OCH_3), 6.18 (s, *anti*-3′-H, 4′-H), 6.37 (s, *syn*-3′-H, 4′-H), 6.83 (s, *anti*-2′-H, 5′-H), 7.09 (s, *syn*-2′-H, 5′-H), 7.20 (c, 1H, H_{Py}), 7.23 (c, 1H, 2-H_{Ar}), 7.25 (c, 1H, 6-H_{Ar}), 7.77 (s, *syn*-N=CH), 7.91 (s, *anti*-N=CH), 9.93 (br.s, 1H, OH), 10.21 (c, *syn*-NH), 11.84 (s, *anti*-NH)

TABLE 2. Continued

Compound	PMR spectrum,(δ, ppm, SSCC, J, Hz)
Ig	2.66 (s, 3H, 6-CH_{3Py}), 3.17 (c, 3H, $CH_2O\underline{CH_3}$), 3.93 (c, *anti*-$\underline{CH_2}OCH_3$), 3.99 (c, *syn*-$\underline{CH_2}OCH_3$), 6.20 (s, *anti*-3′-H, 4′-H), 6.40, (s, *syn*-3′-H, 4′-H), 6.81 (s, *anti*-2′-H, 5′-H), 7.10 (s, *syn*-2′-H, 5′-H), 7.21 (d, 1H, 3″-H_{Ar}), 7.40 (dd, 1H, 6″-H_{Ar}), 7.45 (c, 1H, H_{Py}), 7.60 (dd, 1H, 7″-H_{Ar}), 7.87 (d, 1H, 5″-H_{Ar}), 7.92 (d, 1H, 4″-H_{Ar}), 8.35 (d, 1H, 8″-H_{Ar}), 8.93 (s, *anti*-N=CH), 8.99 (c, *syn*-N=CH), 10.80 (c, *anti*-OH), 10.92 (s, *syn*-OH), 11.99 (s, 1H, NH), $^3J_{3''\text{-}4''}$=8.8, $^3J_{5''\text{-}6''}$=8.0, $^3J_{6''\text{-}7''}$ = 6.4, $^3J_{7''\text{-}8''}$ = 8.4
Ih	1.92, 2.59 (both s, 3H each, 4-CH_{3Py}, 6-CH_{3Py}), 6.17 (s, *anti*-3′-H, 4′-H), 6.37 (s, *syn*-3′-H, 4′-H), 6.81 (s, *anti*-2′-H, 5′-H), 7.11 (s, *syn*-2′-H, 5′-H), 7.21 (d, 1H, 3″-H_{Ar}), 7.22 (c, 1H, H_{Py}), 7.40 (dd, 1H, 6″-H_{Ar}), 7.60 (dd, 1H, 7″-H_{Ar}), 7.88 (d, 1H, 5″-H_{Ar}), 7.93 (d, 1H, 4″-H_{Ar}), 8.36 (d, 1H, 8″-H_{Ar}), 8.93 (s, *anti*-N=CH), 8.98 (s, *syn*-N=CH), 10.88 (c, *anti*-OH), 10.93 (s, *syn*-OH), 12.02 (s, NH), $^3J_{3''\text{-}4''}$ = 8.9, $^3J_{5''\text{-}6''}$ = 8.0, $^3J_{6''\text{-}7''}$ = 6.7, $^3J_{7''\text{-}8''}$ = 8.5
Ii	2.64 (s, 3H, 6-CH_{3Py}), 3.15 (c, *anti*-$CH_2O\underline{CH_3}$), 3.16 (c, *syn*-$CH_2O\underline{CH_3}$), 3.83 (s, *anti*-7″-OCH_3), 3.86 (c, *syn*-7″-OCH_3), 3.92 (c, *anti*-$\underline{CH_2}OCH_3$), 3.96 (c, *syn*-$\underline{CH_2}OCH_3$), 6.05 (c, *anti*-OCH_2O), 6.06 (c, *syn*-OCH_2O), 6.21 (s, *anti*-3′-H,4′-H), 6.39 (s, *syn*-3′-H, 4′-H), 6.85 (s, *anti*-2′-H,5′-H), 6.90 (c, *anti*-6″-H_{Ar}), 6.92 (s, *syn*-6″-H_{Ar}), 6.94 (c, *anti*-4″-H_{Ar}), 6.98 (s, *syn*-4″-H_{Ar}), 7.09 (s, *syn*-2′-H, 5′-H), 7.40 (c, *anti*-H_{Py}), 7.43 (c, *syn*-H_{Py}), 7.81 (s, *syn*-N=CH), 7.92 (s, *anti*-N=CH), 10.43 (c, *syn*-NH), 11.92 (s, *anti*-NH)
Ij	1.86 (c, *anti*-4-CH_{3Py}), 1.90 (c, *syn*-4-CH_{3Py}), 2.58 (s, 3H, 6-CH_{3Py}), 3.83 (s, *anti*-7″-OCH_3), 3.86 (c, *syn*-7″-OCH_3), 6.06 (c, 2H, OCH_2O), 6.18 (s, *anti*-3′-H, 4′-H), 6.37 (s, *syn*-3′-H, 4′-H), 6.84 (s, *anti*-2′-H, 5′-H), 6.89 (c, *anti*-6″-H_{Ar}), 6.92 (s, *syn*-6″-H_{Ar}), 6.93 (s, *anti*-4″-H_{Ar}), 6.98 (s, *syn*-4″-H_{Ar}), 7.10 (s, *syn*-2′-H, 5′-H), 7.16 (c, *anti*-H_{Py}), 7.21 (c, *syn*-H_{Py}), 7.79 (s, *syn*-N=CH), 7.92 (s, *anti*-N=CH), 10.28 (c, *syn*-NH), 11.89 (s, *anti*-NH)
Ik	2.64 (s, 3H, 6-CH_{3Py}), 3.16 (c, 3H, $CH_2O\underline{CH_3}$), 3.70, 3.85 (both s, *anti*-7″-OCH_3, 4″-OCH_3), 3.81, 3.88 (both s, *syn*-7″-OCH_3, 4″-OCH_3), 3.92 (c, *anti*-$\underline{CH_2}OCH_3$), 3.97 (c, *syn*-$\underline{CH_2}OCH_3$), 6.09 (c, 2H, OCH_2O), 6.22 (s, *anti*-3′-H, 4′-H), 6.39 (s, *syn*-3′-H, 4′-H), 6.84 (s, *anti*-2′-H, 5′-H), 7.00 (s, 1H, 6″-H_{Ar}), 7.08 (s, *syn*-2′-H, 5′-H), 7.39 (c, *anti*-H_{Py}), 7.43 (c, *syn*-H_{Py}), 8.09 (s, *syn*-N=CH), 8.20 (s, *anti*-N=CH), 10.39 (c, *syn*-NH), 11.83 (s, *anti*-NH)
Il	1.86 (c, *anti*-4-CH_{3Py}), 1.90 (c, *syn*-4-CH_{3Py}), 2.58 (s, 3H, 6-CH_{3Py}), 3.71, 3.85 (both s, *anti*-7″-OCH_3, 4″-OCH_3), 3.81, 3.88 (both s, *syn*-7″-OCH_3, 4″-OCH_3), 6.10 (c, 2H, OCH_2O), 6.18 (s, *anti*-3′-H, 4′-H), 6.36 (s, *syn*-3′-H, 4′-H), 6.84 (s, *anti*-2′-H, 5′-H), 7.00 (s, 1H, 6″-H_{Ar}), 7.10 (s, *syn*-2′-H, 5′-H), 7.16 (c, *anti*-H_{Py}), 7.22 (c, *syn*-H_{Py}), 8.08 (s, *syn*-N=CH), 8.20 (s, *anti*-N=CH), 10.39 (c, *syn*-NH), 11.85 (s, *anti*-NH)
Im	2.64 (s, 3H, 6-CH_{3Py}), 3.16 (c, 3H, $CH_2O\underline{CH_3}$), 3.74, 3.95 (both s, 3H each, 7″-OCH_3,6″-OCH_3), 3.92 (s, *anti*-$\underline{CH_2}OCH_3$), 3.99 (c, *syn*-$\underline{CH_2}OCH_3$), 6.04 (c, *anti*-OCH_2O), 6.06 (c, *syn*-OCH_2O), 6.21 (s, *anti*-3′-H, 4′-H), 6.40 (s, *syn*-3′-H, 4′-H), 6.84 (s, *anti*-2′-H, 5′-H), 6.85 (s, *anti*-4″-H_{Ar}), 6.90 (s, *syn*-4″-H_{Ar}), 7.10 (s, *syn*-2′-H, 5′-H), 7.39 (c, *anti*-H_{Py}), 7.43 (c, *syn*-H_{Py}), 8.00 (s, *syn*-N=CH), 8.21 (s, *anti*-N=CH), 10.22 (c, *syn*-NH), 11.81 (s, *anti*-NH)
In	1.86 (c, *anti*-4-CH_{3Py}), 1.91 (c, *syn*-4-CH_{3Py}), 2.58 (s, 3H, 6-CH_{3Py}), 3.73, 3.95 (both s, 3H each, 7″-OCH_3, 6″-OCH_3), 6.04 (s, *anti*-OCH_2O), 6.06 (c, *syn*-OCH_2O), 6.17 (s, *anti*-3′-H, 4′-H), 6.38 (s, *syn*-3′-H, 4′-H), 6.84 (s, *anti*-2′-H, 5′-H), 6.90 (s, 1H, 4″-H_{Ar}), 7.12 (s, *syn*-2′-H, 5′-H), 7.17 (c, *anti*-H_{Py}), 7.22 (c, *syn*-H_{Py}), 7.98 (s, *syn*-N=CH), 8.21 (s, *anti*-N=CH), 10.16 (c, *syn*-NH), 11.83 (s, *anti*-NH)
Io	0.36 (br.s, *anti*-$CH_2CH_2\underline{CH_3}$), 0.91 (br.s, *syn*-$CH_2CH_2\underline{CH_3}$), 1.10 (br.s, *anti*-$CH_2\underline{CH_2}CH_3$), 1.38 (br.s, *syn*-$CH_2\underline{CH_2}CH_3$), 2.53 (br.s, *anti*-$\underline{CH_2}CH_2CH_3$), 2.64 (s, 3H, 6-CH_{3Py}), 2.76 (br.s, *syn*-$\underline{CH_2}CH_2CH_3$), 3.16 (c, 3H, $CH_2O\underline{CH_3}$), 3.71 (c, *anti*-4″-OCH_3, 7″-OCH_3), 3.82 (c, *syn*-4″-OCH_3, 7″-OCH_3), 3.91 (c, *anti*-$\underline{CH_2}OCH_3$), 4.00 (s, *syn*-$\underline{CH_2}OCH_3$), 6.06 (c, 2H, OCH_2O), 6.23 (s, *anti*-3′-H, 4′-H), 6.44 (s, *syn*-3′-H, 4′-H), 6.78 (s, *anti*-2′-H, 5′-H), 7.13 (s, *syn*-2′-H, 5′-H), 7.36 (c, *anti*-H_{Py}), 7.43 (c, *syn*-H_{Py}), 7.94 (s, *syn*-N=CH), 8.24 (s, *anti*-N=CH), 9.66 (c, *syn*-NH), 11.79 (s, *anti*-NH)
Ip	1.25 (t, 3H, J = 7.0, $\underline{CH_3}CH_2$), 2.60 (s, *anti*-6-CH_{3Py}),2.65 (s, *syn*-6-CH_{3Py}), 2.95 (dd, 1H, J = 7.3, 17.7, $\underline{CH_2}CH_{isoxazole}$), 3.21 (m, 3H, $\underline{CH_2}CH_{isoxazole}$ and $CH_{2isoxazole}$), 3.13 (c, *anti*-$CH_2O\underline{CH_3}$), 3.17 (c, *syn*-$CH_2O\underline{CH_3}$), 3.77 (c, *anti*-4″-OCH_3, 7″-OCH_3), 3.87 (c, *syn*-4″-OCH_3, 7″-OCH_3), 3.90 (s, *anti*-$\underline{CH_2}OCH_3$), 4.00 (c, *syn*-$\underline{CH_2}OCH_3$), 4.24 (q, 2H, J = 7.0, $CH_3\underline{CH_2}$), 4.57 (br.s, *anti*-$CHO_{isoxazole}$), 4.96 (m, *syn*-$CHO_{isoxazole}$), 6.10 (c, *anti*-OCH_2O), 6.12 (c, *syn*-OCH_2O), 6.22 (s, *anti*-3′-H, 4′-H), 6.42 (s, *syn*-3′-H, 4′-H), 6.80 (s, *anti*-2′-H, 5′-H), 7.12 (s, *syn*-2′-H, 5′-H), 7.35 (c, *anti*-H_{Py}), 7.44 (c, *syn*-H_{Py}), 8.00 (s, *syn*-N=CH), 8.27 (s, *anti*-N=CH), 9.89 (c, *syn*-NH), 11.90 (s, *anti*-NH)
Iq	1.26 (t, 3H, J = 7.0, $\underline{CH_3}CH_2$), 1.84 (c, *anti*-6-CH_{3Py}), 1.94 (c, *syn*-6-CH_{3Py}), 2.54 (s, *anti*-4-CH_{3Py}), 2.58 (s, *syn*-4-CH_{3Py}), 2.95 (dd, 1H, J = 7.6, 16.5, $\underline{CH_2}CH_{isoxazole}$), 3.21 (m, 3H, $\underline{CH_2}CH_{isoxazole}$ and $CH_{2isoxazole}$), 3.78 (c, *anti*-4″-OCH_3, 7″-OCH_3), 3.88 (c, *syn*-4″-OCH_3, 7″-OCH_3), 4.24 (q, 2H, J = 7.0, $CH_3\underline{CH_2}$), 4.57 (br.s, *anti*-$CHO_{isoxazole}$), 4.98 (m, *syn*-$CHO_{isoxazole}$), 6.10 (c, *anti*-OCH_2O), 6.12 (c, *syn*-OCH_2O), 6.20 (s, *anti*-3′-H, 4′-H), 6.42 (s, *syn*-3′-H, 4′-H), 6.81 (s, *anti*-2′-H, 5′-H), 7.13 (s, *syn*-2′-H, 5′-H), 7.22 (c, 1H, H_{Py}), 7.97 (c, *syn*-N=CH), 8.28 (s, *anti*-N=CH), 9.79 (c, *syn*-NH), 11.88 (s, *anti*-NH)

TABLE 2. Continued

Compound	PMR spectrum,(δ, ppm, SSCC, J, Hz)
Ir	2.52 (m, *anti*-$\underline{CH_2}CH_{isoxazole}$), 2.65 (s, 3H, 6-$CH_{3Py}$), 2.69 (m, *anti*-$\underline{CH_2}CH_{isoxazole}$), 2.94 (m, *anti*-$CH_{2isoxazole}$), 3.06 (dd, J = 7.5, 16.8, *syn*-$\underline{CH_2}CH_{isoxazole}$), 3.12 (c, *anti*-$CH_2O\underline{CH_3}$), 3.16 (c, *syn*-$CH_2O\underline{CH_3}$), 3.20 (m, *syn*-$CH_{2isoxazole}$), 3.35 (dd, J = 9.8, 16.8, $CH_2CH_{isoxazole}$), 3.77 (c, 3H, 4‴-OCH_3), 3.79 (s, 6H, 4″,7″-OCH_3), 3.90 (s, *anti*-$\underline{CH_2}OCH_3$), 4.00 (s, *syn*-$\underline{CH_2}OCH_3$), 4.55 (br.s, *anti*-$CHO_{isoxazole}$), 4.83 (m, *syn*-$CHO_{isoxazole}$), 6.10 (c, *anti*-OCH_2O), 6.12 (c, *syn*-OCH_2O), 6.21 (s, *anti*-3′-H, 4′-H), 6.40 (s, *syn*-3′-H, 4′-H), 6.82 (s, *anti*-2′-H, 5′-H), 6.95 (d, J = 8.5, *anti*-3‴, 5‴-H_{Ar}), 6.99 (d, J = 8.5, *syn*-3‴, 5‴-H_{Ar}), 7.10 (s, *syn*-2′-H, 5′-H), 7.31 (br.s, *anti*-H_{Py}, *anti*-2‴, 6‴-H_{Ar}), 7.44 (c, *syn*-H_{Py}), 7.58 (d, J=8.5, *syn*-2‴, 6‴-H_{Ar}), 8.02 (s, *syn*-N=CH), 8.31 (s, *anti*-N=CH), 9.92 (c, *syn*-NH), 11.90 (s, *anti*-NH)
Is	1.83 (c, *anti*-4-CH_{3Py}), 1.93 (c, *syn*-4-CH_{3Py}), 2.44 (c, *anti*-6-CH_{3Py}), 2.53 (m, *anti*-$CH_{2isoxazole}$), 2.59 (c, *syn*-6-CH_{3Py}), 2.67 (m, *anti*-$CH_{2isoxazole}$), 2.96 (m, *anti*-$\underline{CH_2}CH_{isoxazole}$), 3.06 (m, *anti*-$\underline{CH_2}CH_{isoxazole}$), 3.07 (m, *syn*-$CH_{2isoxazole}$), 3.20 (m, *syn*-$\underline{CH_2}CH_{isoxazole}$, *syn*-$CH_{2isoxazole}$), 3.35 (m, *syn*-$\underline{CH_2}CH_{isoxazole}$), 3.77 (c, 3H, 4‴-$OCH_3$), 3.82, 3.88 (both s, 6H, 4″,7″-OCH_3), 4.48 (br.s, *anti*-$CHO_{isoxazole}$), 4.85 (m, *syn*-$CHO_{isoxazole}$), 6.11 (c, *anti*-OCH_2O), 6.12 (c, *syn*-OCH_2O), 6.18 (s, *anti*-3′-H, 4′-H), 6.37 (s, *syn*-3′-H, 4′-H), 6.82 (s, *anti*-2′-H, 5′-H), 6.98 (d, J = 8.4, *anti*-3‴, 5‴-H_{Ar}), 7.05 (br.s, *syn*-3‴, 5‴-H_{Ar}), 7.11 (s, *syn*-2′-H, 5′-H), 7.22 (c, 1H, H_{Py}), 7.32 (br.s, *anti*-2‴, 6‴-H_{Ar}),7.58 (d, J = 8.4, *syn*-2‴, 6‴-H_{Ar}),), 8.01 (s, *syn*-N=CH), 8.32 (s, *anti*-N=CH), 9.81 (c, *syn*-NH), 11.87 (s, *anti*-NH)
It	2.49 (m, *anti*-$\underline{CH_2}CH_{isoxazole}$), 2.60 (s, *anti*-6-$CH_{3Py}$), 2.65 (s, *syn*-6-$CH_{3Py}$), 2.74 (m, *anti*-$\underline{CH_2}CH_{isoxazole}$), 2.94 (m, *anti*-$CH_{2isoxazole}$), 3.10 (m, *syn*-$\underline{CH_2}CH_{isoxazole}$), 3.15 (c, *anti*-$CH_2O\underline{CH_3}$), 3.16 (c, *syn*-$CH_2O\underline{CH_3}$), 3.23 (m, *syn*-$CH_{2isoxazole}$), 3.39 (m, *syn*-$\underline{CH_2}CH_{isoxazole}$), 3.78, 3.80 (both s, *anti*-4″,7″-OCH_3), 3.83, 3.88 (both s, *syn*-4″,7″-OCH_3), 3.89 (s, *anti*-$\underline{CH_2}OCH_3$), 4.00 (s, *syn*-$\underline{CH_2}OCH_3$), 4.49 (br.s, *anti*-$CHO_{isoxazole}$), 4.89 (m, *syn*-$CHO_{isoxazole}$), 6.10 (c, *anti*-OCH_2O), 6.13 (c, *syn*-OCH_2O), 6.22 (s, *anti*-3′-H, 4′-H), 6.40 (s, *syn*-3′-H, 4′-H), 6.82 (s, *anti*-2′-H, 5′-H), 7.10 (s, *syn*-2′-H, 5′-H), 7.27 (m, 2H, 3‴, 5‴-H_{Ar}), 7.30 (c, *anti*-H_{Py}), 7.43 (br.s, 2H, 2‴, 6‴-H_{Ar}), 7.43 (c, *syn*-H_{Py}), 8.05 (s, *syn*-N=CH), 8.31 (s, *anti*-N=CH), 9.97 (c, *syn*-NH), 11.90 (s, *anti*-NH)
Iu	2.49 (m, *anti*-$\underline{CH_2}CH_{isoxazole}$), 2.60 (m, *anti*-$\underline{CH_2}CH_{isoxazole}$), 2.63 (s, 3H, 6-$CH_{3Py}$), 2.96 (m, *anti*-$CH_{2isoxazole}$), 3.11 (c, *anti*-$CH_2O\underline{CH_3}$), 3.15 (m, *syn*-$CH_2O\underline{CH_3}$, *syn*-$\underline{CH_2}CH_{isoxazole}$, *syn*-$CH_{2isoxazole}$), 3.41 (m, *syn*-$\underline{CH_2}CH_{isoxazole}$), 3.69, 3.99 (both s, 6H, 7″, 4″-OCH_3), 3.96 (s, 2H, $\underline{CH_2}OCH_3$), 4.61 (m, *anti*-$CHO_{isoxazole}$), 4.85 (m, *syn*-$CHO_{isoxazole}$), 6.02 (c, *anti*-OCH_2O), 6.04 (c, *syn*-OCH_2O), 6.20 (s, *anti*-3′-H, 4′-H), 6.34 (s, *syn*-3′-H, 4′-H), 6.80 (s, *anti*-2′-H, 5′-H), 7.05 (s, *syn*-2′-H, 5′-H), 7.38 (c, *anti*-H_{Py}), 7.41 (br.s, *anti*-3‴, 5‴-H_{Ar}, *syn*-H_{Py}), 7.48 (d, J = 7.6, *syn*-3‴, 5‴-H_{Ar}, *anti*-2‴, 6‴-H_{Ar}), 7.64 (d, J = 7.6, *syn*-2‴, 6‴-H_{Ar}), 7.98 (s, *syn*-N=CH), 8.19 (s, *anti*-N=CH), 10.00 (c, *syn*-NH), 11.80 (s, *anti*-NH)
Iv	1.83 (c, *anti*-4-CH_{3Py}), 1.89 (c, *syn*-4-CH_{3Py}), 2.54 (m, *anti*-$\underline{CH_2}CH_{isoxazole}$), 2.56 (c, *anti*-4-$CH_{3Py}$), 2.58 (c, *syn*-4-$CH_{3Py}$), 2.83 (m, *anti*-$\underline{CH_2}CH_{isoxazole}$), 2.96 (m, *anti*-$CH_{2isoxazole}$), 3.10 – 3.20 (br.m, *syn*-$CH_{2isoxazole}$, *syn*-$\underline{CH_2}CH_{isoxazole}$), 3.20 (br.m, *syn*-$\underline{CH_2}CH_{isoxazole}$), 3.64 (s, *anti*-7″, 4″-OCH_3), 3.69 (s, *syn*-7″, 4″-OCH_3), 4.60 (m, *anti*-$CHO_{isoxazole}$), 4.86 (m, *syn*-$CHO_{isoxazole}$), 6.03 (c, *anti*-OCH_2O), 6.07 (c, *syn*-OCH_2O), 6.17 (s, *anti*-3′-H, 4′-H), 6.33 (s, *syn*-3′-H, 4′-H), 6.81(s, *anti*-2′-H, 5′-H), 7.07 (s, *syn*-2′-H, 5′-H), 7.11 (c, *anti*-H_{Py}), 7.21 (c, *syn*-H_{Py}), 7.37 (m, *anti*-3‴, 5‴-H_{Ar}), 7.50 (m, *syn*-3‴, 5‴-H_{Ar}, *anti*-2‴, 6‴-H_{Ar}), 7.66 (d, J = 8.4, *syn*-2‴, 6‴-H_{Ar}), 7.95 (s, *syn*-N=CH), 8.20 (s, *anti*-N=CH), 10.03 (c, *syn*-NH), 11.82 (s, *anti*-NH)

peared in spectra of the corresponding starting hydrazones **II** [2]. Instead of it, resonances for protons of the added CH–R^2 group appeared. The CH group resonated at 7.70 – 8.98 ppm. Doubling of this resonance in addition to resonances for CONH and the á-, and â-protons of the pyrrole ring etc. indicated that the solution contained two conformers of target products **Ia** – **v**, i.e., *syn* and *anti*. Another feature of the PMR spectra of the examined compounds was a singlet for the pyrrole protons of both the *syn*- and *anti*-conformers.

IR spectra of products **I** had only one $\acute{\imath}_{N–H}$ stretching band at 3295 – 3260 cm^{-1} (Table 3), in contrast with those of starting hydrazides **IIa** and -**b** [2]. Stretching bands of C–H_{Ar} and C=N groups appeared at 3110 – 3080 and 1580 – 1560 cm^{-1}, respectively. Carbonyl stretching bands shifted from 1620 – 1615 to 1660 – 1640 cm^{-1}.

EXPERIMENTAL CHEMICAL PART

IR spectra were taken in mineral oil on a Specord IR-75 spectrophotometer at room temperature. PMR spectra were recorded in DMSO-d_6 with TMS internal standard on a Bruker DRX-500 spectrometer at operating frequency 500.13 MHz. TLC was performed on Sorbfil plates (PTS-AF-A).

6-Methyl-4-methoxymethyl-3-pyrrol-1-ylthieno[2,3-*b***]pyridine-2-carboxylic acid (3,4-dichlorobenzylidene)-hydrazide (Ia).** A mixture of 6-methyl-4-methoxymethyl-3-pyrrol-1-ylthieno[2,3-*b*]pyridine-2-carbohydrazide (**IIa**, 1.0 g, 3.16 mmol) and 3,4-dichlorobenzaldehyde (**IIIa**, 0.6 g, 3.5 mmol) was dissolved with heating in EtOH:DMF (30 mL, 1:1, v/v), treated with a catalytic amount of *p*-TsOH, and refluxed. The end of the reaction was determined by chromatography (toluene:EtOH eluent, 2:1). The reaction

time was 15 min. The mixture was cooled to room temperature. The precipitate was filtered off, rinsed with H_2O, dried in air, and recrystallized from *i*-PrOH:DMF (1:2, v/v). Yield 1.4 g (96%).

Carbohydrazides **Ib** – **v** were synthesized analogously. The only differences were that the reaction time for **Ig** – **q** was 1 h; for **Ir** – **v**, 3 h.

EXPERIMENTAL BIOLOGICAL PART

The antibacterial properties of the new compounds were screened microbiologically using a qualitative method (diffusion in AGV solid growth medium) and a quantitative method (serial dilutions in growth broth) [3]. The test organisms were *Staphylococcus aureus* and *Escherichia coli*. The tested compounds were dissolved in DMSO. Preliminary screening used compound concentrations of 12 mg/mL (300 μg/25 μL). Antibacterial activity was estimated from the diameter of the growth inhibition zone (DGIZ, mm) and the minimum inhibiting concentration (MIC, μg/mL). These were measured in three repetitions followed by statistical processing using Microsoft Excel software to calculate the mean (*M*), standard deviation of the mean (*m*), and statistical significance (*p*) of the differences from the control. The control was the known broad-spectrum antibacterial drug furazolidone (drug substance, Zhehem Pharmachem Co., P. R. China).

The results showed that several of the synthesized hydrazones **I** and hydrazides **IIa** and -**b** suppressed the growth of the test bacteria (Table 4).

It was found that 3-pyrrol-1-ylthieno[2,3-*b*]pyridine-2-carbohydrazides **IIa** and -**b** exhibited strong antibacterial activity against *E. coli*. Hydrazones **I** that were prepared from them showed different properties depending on the nature of the introduced radical R^2.

Only 11 (**Ia**, -**c**, -**d**, -**e**, -**g**, -**k**, -**m**, -**o**, -**p**, -**r**, -**t**) of the 22 synthesized hydrazones (**Ia** – **v**) displayed antibacterial properties that were characterized as inhibiting growth of the test strains with DGIZ of 10 – 20 mm. The DGIZ for the control was 20 – 26 mm. Compounds **Ia**, -**c**, and -**m** inhibited the growth of only *S. aureus*; **Id** and –**k**, only *E. coli*.

Quantitative assay of the antibacterial activity of **Ia**, -**c**, -**d**, -**e**, -**g**, -**k**, -**m**, -**o**, -**p**, -**r**, and -**t** found (Table 4) that their MIC values fell in the range 62.5 – 1,000 μg/mL. The most active against *S. aureus* were **Ic**, -**g**, -**o**, -**r**, and -**t** with R^2 radicals 2-hydroxy-3,5-dichlorophenyl (**Ic**), 2-hydroxynaphthalene (**Ig**), 4,7-dimethoxy-6-propylbenzo[1,3]dioxol-5-yl (**Io**), 4,7-dimethoxy-6-[3-(4-methoxyphenyl)-4,5-dihydroisoxazol-5-ylmethyl]benzo[1,3]dioxol-5-yl (**Ir**), and 6-[3-(4-fluorophenyl)-4,5-dihydroisoxazol-5-ylmethyl]-4,7-dimethoxybenzo[1,3]dioxol-5-yl (**It**).

The most active antibacterial compound was **Ic**, the MIC of which against *S. aureus* was (62.5 ± 30.62) μg/mL;

TABLE 3. IR Spectra of **Ia**, **b**, **i**, **j**, **l**, **n**, **q**

Compound	IR spectrum, ν_{max}, cm^{-1}				
	N-H	C-H_{Ar}	C=O	C=N	C-O-C
Ia	3260	3110	1640	1560	1090
Ib	3280	3105	1660	1570	1105
Ii	3270	3105	1640	1570	1110
Ij	3280	3090	1640	1580	1080
Il	3290	3100	1640	1570	1090
In	3280	3080	1640	1580	1080
Iq	3295	3105	1640	1580	1090

TABLE 4. Biological Test Results of Synthesized Compounds

Compound	DGIZ, mm		MIC**, μg/mL	
	S. aureus	*E. coli*	*S. aureus*	*E. coli*
Furazolidone	26.0 ± 0.82	20.0 ± 0.82	62.5 ± 30.62	62.5 ± 30.62
IIa	–	10.0 ± 0.82*	–	> 1000
IIb	–	10.0 ± 0.82*	–	> 1000
Ia	10.0 ± 0.82*	18.0 ± 0.82*	> 1000	250.0 ± 176.77
Ib	–	–	–	–
Ic	20.0 ± 1.41*	14.0 ± 0.82*	62.5 ± 30.62	500.0 ± 244.95
Id	–	14.0 ± 1.41*	–	500.0 ± 244.95
Ie	10.0 ± 1.41*	–	> 1000	–
If	–	–	–	–
Ig	17.0 ± 1.41*	–	250.0 ± 176.77	–
Ih	–	–	–	–
Ii	–	–	–	–
Ij	–	–	–	–
Ik	–	15.0 ± 2.16	–	250.0 ± 176.77
Il	–	–	–	–
Im	14.0 ± 1.63*	16.0 ± 2.94	> 1000	250.0 ± 176.77
In	–	–	–	–
Io	30.0 ± 1.41*	–	62.5 ± 30.62	–
Ip	15.0 ± 2.16*	–	500.0 ± 244.95	–
Iq	–	–	–	–
Ir	18.0 ± 2.16*	–	250.0 ± 176.77	–
Is	–	–	–	–
It	17.0 ± 1.41*	–	250.0 ± 176.77	–
Iu	–	–	–	–
Iv	–	–	–	–

* $p < 0.05$ relative to furazolidone;
** the statistical significance is not given because the double-dilution method was used and gave large errors of the mean.

against *E. coli*, (500.0 ± 244.95) μg/mL. The most active compound that inhibited growth of only *S. aureus* was **Io**, the MIC of which was (62.5 ± 30.62) μg/mL; of only *E. coli*, **Ik**, the MIC of which was (250.0 ± 176.77) μg/mL.

Compounds **Ia**, **-c**, **-d**, **-k**, and –**m** were active against *E. coli*. The strongest antibacterial derivatives were **Ia**, **-k**, and **-m** with R^2 radicals 3,4-dichlorophenyl, 4,7-dimethoxybenzo-[1,3]dioxol-5-yl, and 6,7-dimethoxybenzo[1,3]dioxol-5-yl, respectively. Introducing a substituent in the 6-benzo-[1,3]dioxole position could have a drastic effect on the antibacterial activity. Thus, a propyl (**Io**) or 4,5-dihydroisoxazol-5-ylmethyl (**Ip** – **v**) substituent destroyed the activity of the tested compounds against *E. coli*.

The nature of the radical in the pyridine 4-position affected considerably the antibacterial properties of the synthesized compounds. Adding a methoxymethyl group to the 4-position increased the activity against *S. aureus* (**Ia**, **-c**, **-e**, **-g**, **-m**, **-o**, **-p**, **-r**, **-t**) and *E. coli* (**Ia**, **-c**, **-k**, **-m**). Moreover, replacing the methoxymethyl by methyl (**Ib**, **-d**, **-f**, **-h**, **-j**, **-l**, **-n**, **-q**, **-s**, **-v**) caused the antibacterial activity to disappear. The exception was **Id**, which exhibited moderate antibacterial properties against *E. coli*.

Thus, 11 of the 22 new compounds possessed antibacterial activity; 3 of them, against both *S. aureus* (Gram-positive) and *E. coli* (Gram-negative). This characterized them as broad-spectrum compounds. The most promising compounds for further research were **Ic** and **Io**.

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