SYNTHESIS, COMPLEX COMPOUNDS AND ANTIMICROBIAL ACTIVITY OF SOME DERIVATIVES OF FURO[3,2-*C*]PYRIDINE AND THEIR STARTING COMPOUNDS

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Abstract: Some [3,2-*c*]pyridine derivatives were synthesized. 3-(Furan-2-yl)propenoic acid (**1a**) was prepared from furan-2-carbaldehyde under the Perkin's conditions. Obtained acid was converted to the corresponding azide **3**, which in turn was cyclized to give furo[3,2-*c*]pyridin-4(5*H*)-one (**4a**). The reaction of pyridone **4a** with phosphorus oxychloride rendered the chloroderivative **7a**, which was treated in the condition of Suzuki coupling reaction with boronic acid to give 4-phenylfuro[3,2-*c*]pyridine (**8e**) and an unexpected product **10**. Some title compounds have shown moderate to good antimicrobial activity against tested bacteria *Xanthomonas sp.*, *Erwinia amylovora*, and filamentous fungi *Pyrenophora avenae*, *Fusarium graminearum*.

Keywords: furo[3,2-*c*]pyridines, nucleophilic substitution, coupling reaction, ^{1}H and ^{13}C NMR spectra, biological activity

1. Introduction

Compounds with 2-trifluoromethyl group in molecule have interest biological activity. For example 2-(trifluoromethyl)benzimidazoles are known as an important class of compounds due to their wide range of biological activity acting as antiviral, antifungal, antibacterial and anticancer drugs (NAVARRETE-VÁZQUEZ *et al*., 2006). Studies about the antiparasitic activity of 2-(trifluoromethyl)benzimidazole derivatives have shown high potential as antiprotozoal agents (NAVARRETE-VÁZQUEZ *et al*., 2001). The main features of these compounds are the application of the 2-trifluoromethyl group in order to enhance solubility and absorption properties and therefore antiparasitic activity (NAVARRETE-VÁZQUEZ *et al*., 2003). Some 4-substituted furo[3,2-*b*]pyrrole-5-carbohydrazides bearing the 3-(trifluoromethyl)phenyl group at the C-2 position were prepared and their effect on the chlorophyll content in alga suspensions of Chlorella vulgaris and the inhibition of photosynthetic electron transport in spinach chloroplasts were studied (GAŠPAROVÁ *et al*., 2008).

A variety of fused pyridines have been studied for a long time in the field of the chemistry of heterocyclic compounds (SHERMAN 1996; 2008). Furopyridines are very similar to such skeletons as quinoline and isoquinoline which are present in many

DOI 10.2478/v10296-012-0008-x

compounds possessing biological activity. It was reported that some pharmacophores with potential antipsychotic activity contain the thieno- and furo[3,2-*c*]pyridine ring systems (NEW *et al*., 1989). By studying (KENNIS *et al*., 2000) of biological activity of tetrahydrobenzofuropyridines and benzothienopyridines was determined that these two groups of compounds are a part of compounds which show a high affinity in face of subtypes of receptors α_1 and α_2. This fact incites chemists about more complete explication of the structure and functions of these systems. Biological activity of the copper(II) and cobalt(II) 3-methylsufanylnicotinate complexes with furopyridines against various strains of bacteria and filamentous fungi has been investigated (SEGĽA *et al*., 2008; 2009).

For a long time we have been interested in studying of the synthesis and reactivity of various furo[3,2-*c*]pyridines (BOBOŠÍK *et al*., 1995; KRUTOŠÍKOVÁ and SLEZIAK 1996; MOJUMDAR *et al*., 2005; 2009; GAJDOŠ *et al*., 2006; BÚDOVÁ *et al*., 2006; BRADIAKOVÁ *et al*., 2008; 2009; TARABOVÁ *et al*., 2010). This type of the fused heterocycles can be readily coordinated to metal centers through *N*-donor atom. A few from these compounds were used as ligands in the preparation of coordination compounds with transition metals Cu(II), Co(II) and Ni(II). The spectral, magnetic, thermal properties, coordination chemistry and X-ray analysis of these compounds have already been outlined (KRUTOŠÍKOVÁ *et al*., 2001; MIKLOVIČ *et al*., 2004; BARAN *et al*., 2005; TITIŠ *et al*., 2007; VRÁBEL *et al*., 2007a; 2007b; 2007c; BOČA and TITIŠ 2008).

In the past were published synthesis 2-methyl and 2-aryl substituted furo[3,2-*c*]pyridine-4(5*H*)-thiones by reaction of corresponding 2-substituted furo[3,2-*c*]pyridine-4(5*H*)-ones with phosphorus pentasulfide (BOBOŠÍK *et al*., 1995; KRUTOŠÍKOVÁ and SLEZIAK 1996). Methylation of the 2-methylfuro[3,2-*c*]pyridine-4(5*H*)-thione and 1-benzofuro[3,2-*c*]pyridine-1(2*H*)-thione with methyl iodide afforded 4-methylsufanylfuro[3,2-*c*]pyridine or 1-methylsulfanyl-1-benzofuro[3,2-*c*]pyridine but methylation corresponding pyridones gave *N*-methyl compounds (BOBOŠÍK *et al*., 1995; TARABOVÁ *et al*., 2010).

The 4-substituted furo[3,2-*c*]pyridines were prepared by various methods. One method used as the starting compounds of the 4-chlorofuro[3,2-*c*]pyridines in which the chlorine atom was substituted with several nucleophiles (BOBOŠÍK *et al*., 1995; BÚDOVÁ *et al*., 2006; BRADIAKOVÁ *et al*., 2009). The reaction with sodium alkoxides in appropriate alcohol afforded the corresponding 4-alkoxyfuro[3,2-*c*]pyridines (BÚDOVÁ *et al*., 2006). Similarly, utilization of sodium methyltiolate gave methylsufanyl derivatives (BOBOŠÍK *et al*., 1995). Chloro derivatives were converted to 4-amino-substituted furo[3,2-*c*]pyridines by nucleophilic substitution chlorine atom with some heterocyclic secondary amines as piperidine, morpholine or pyrrolidine (BÚDOVÁ *et al*., 2006). The nucleophilic reactions of 1-chloro[1]benzofuro[3,2-*c*]pyridine with secondary heterocyclic amines proceeded analogously (MOJUMDAR *et al*., 2009; TARABOVÁ *et al*., 2010). Suzuki coupling reaction was realized with 1-chloro[1]benzofuro[3,2-*c*]pyridine and phenylboronic acid or pyridin-3-ylboronic acid in the presence of $Pd(PPh_3)_4$ catalyst in dichloromethane 1-phenyl[1]benzofuro[3,2-*c*]pyridine and 1-(pyridin-3-yl)[1]benzofuro[3,2-*c*]pyridine were formed (TARABOVÁ *et al*., 2010).

In the paper (BENCKOVÁ and KRUTOŠÍKOVÁ 1999, MOJUMDAR *et al*., 2009) are described the 4-cyanofuro[3,2-*c*]pyridine and 1-cyano[1]benzofuro[3,2-*c*]pyridine derivatives *via N*-oxides by Reissert-Henze reaction. The alkaline hydrolysis of the cyano derivatives raised the corresponding furo[3,2-*c*]pyridinecarboxylic acids and their amides were prepared by hydrolysis in acid conditions.

The aim of this work was to study the reaction of 4-chlorofuro[3,2-c]pyridine with boronic acid in the condition of Suzuki coupling reaction. The main target of this work were syntheses of the earlier known derivatives of furo[3,2-c]pyridine and their starting compounds for testing their antimicrobial activities.

2. Material and methods

2.1 Chemical, physical methods and instruments

Melting points were determined using Kofler hot plate. All solvents were distilled and dried before use. All reagents were commercially available and were used without purification. Elemental analyses were determined using an EAGER 300 at Institute of Inorganic Chemistry, Technology and Materials, STU in Bratislava. IR spectra were taken on a FTIR Nicolet NEXUS 470 spectrophotometer using KBr pellets (0.5 mg in 300 mg KBr) in region 4000 – 400 cm^{-1} at Institute of Physical Chemistry and Chemical Physics, STU in Bratislava. For interpretation of IR spectra following abbreviations are used s = strong band (a value of transmittance: 0-35%), m = medium band (a value of transmittance: 36-50%) w = weak (a value of transmittance: over 50%). ^{1}H NMR spectra were measured in DMSO-d_6 using Varian INOVA 600 (for ^{1}H 599.782 MHz and for ^{13}C 150.830 MHz) spectrometer, at 25 °C, at Institute of Analytical Chemistry, Department of NMR and MS Spectroscopy, STU in Bratislava. Chemical shifts (δ-scale) are quoted in parts per million and following abbreviations are used: s = singlet; d = doublet; coupling constants (J) are given in Hz.

2.2 Phytopathogene microorganism

In our work phytopathogene bacteria *Xanthomonas sp.* CCM 2888 from Czech collection of microorganism of Masaryk University Brno and *Erwinia amylovora* CPPB A203 obtained from the Collection of Phytopathogenic Bacteria and Referential Antidotes (CPPB) at the Crop Research Institute in Prague-Ruzyně, Czech Republic were used. Bacteria were kept as a stock culture in the refrigerator at the temperature of 8 °C. Isolates of the filamentous fungi *Pyrenophora avenae***,** *Fusarium graminearum* were provided by the Institute of the plants production from Piešťany as pure cultures. Obtained isolates were reinoculated, and stored at temperature 6 ± 2 °C.

2.3 Testing the biocide effect of synthesized compounds

The antimicrobial activity of synthesized compounds was determined *in vitro* against a variety of phytopathogenic microorganism. Antimicrobial activities were

tested by the standard plate diffusion method (PIDDOCK, 1989) and zones of inhibition were measured in mm. The biocide effect was compared with the effect of 1.2 % w/v solution of TMTD (tetramethylthiuram disulfide), active substance of commercial pesticides. The solution of compounds (15 μL) in DMSO (respectively methanol) with concentration 200, 100, 50 and 25 $mg.L^{-1}$ was placed to metal cylinders on the surface of a media inoculated with the tested microorganism. The plates were incubated at 25 °C, and clear zones developed around cylinders indicated the inhibition of microbial growth. The size of the zone of inhibition caused by diffusion of agent into agar is directly related to the degree of susceptibility of an organism. If the tested sample shows microbicidal activity, inhibition zone will appear on agar plate. Tetramethyl tiuram disulfide (TMTD) (1.2% w/w methanol solution) was used as a standard of antimicrobial activity. Tested plates were inoculated with 1 mL of microbial suspension (10^6–10^7 $CFU.mL^{-1}$). Sterile cylinders were placed onto the plates and filled by 15 μL of the solution (DMSO, methanol respectively) of the tested compounds. Plates were incubated at 25 °C for 24 h and 4 d, respectively. The zone inhibition diameter (in millimeters) was recorded. Two parallel tests of the compounds inhibition activity were made.

3. Results and discussion

3.1 Chemistry

3-(Furan-2-yl)propenoic acid (**1a**) was prepared from furan-2-carbaldehyde under the Perkin's conditions. The acid **1a** was converted to the corresponding azide **3a**, which was cyclized by heating in diphenyl ether to furo[3,2-*c*]pyridine-4(5*H*)-one (**4a**). The compound **4a** was aromatized with phosphorus oxychloride to chloroderivative **7a** which was treated in the condition of Suzuki coupling reaction with boronic acid to give 4-phenylfuro[3,2-*c*]pyridine (**8e**) and an unexpected product 4-(furo[3,2-*c*]pyridine-4-yl)furo[3,2-*c*]pyridine (**10**) (Fig. 1). The acids **1b-1d** were synthesized by condensation of the appropriate carbaldehyde with malonic acid under Knoevenagel conditions. The compounds **4b-4f** were prepared analogously by cyclisation of appropriated azides (SLEZIAK and KRUTOŠÍKOVÁ, 1996; GAJDOŠ *et al.*, 2006; MOJUMDAR *et al*., 2009) Reaction of **4b** and **4d** with phosphorus pentasulfide led to corresponding thiones **5a, 5b**, which were methylated in PTC conditions giving **6a** and **6b** (BRADIAKOVÁ *et al*., 2009; TARABOVÁ *et al*., 2010). 2-Methyl[1]benzofuro[3,2-*c*]pyridine-1-one (**4e)** and 5-metyl-2-[3-(trifluoromethyl)-phenyl]furo[3,2-*c*]pyridine-4(5*H*)-one (**4f**) were obtained by reaction of **4b, 4d** with NaH and then methylated with methyl iodide. The compound **4a** was aromatized with phosphorus oxychloride to chloroderivative **7a**. Analogously were synthesized chloroderivatives **7b-7d** and they are described in ref. (SLEZIAK and KRUTOŠÍKOVÁ, 1996; BRADIAKOVÁ *et al*., 2008; GAJDOŠ *et al*., 2006) Refluxing of appropriate chloroderivatives **7b** and **7d** with secondary heterocyclic amines gave **8a-8d** (BRADIAKOVÁ *et al*., 2009; MOJUMDAR *et al*., 2009). The compounds **8f-8j** were prepared according (TARABOVÁ *et al*., 2010; BRADIAKOVÁ *et al*., 2009; BENCKOVÁ and KRUTOŠÍKOVÁ 1999). *N*-Oxides **9a, 9b** were prepared as it is described in (BRADIAKOVÁ *et al*., 2009).

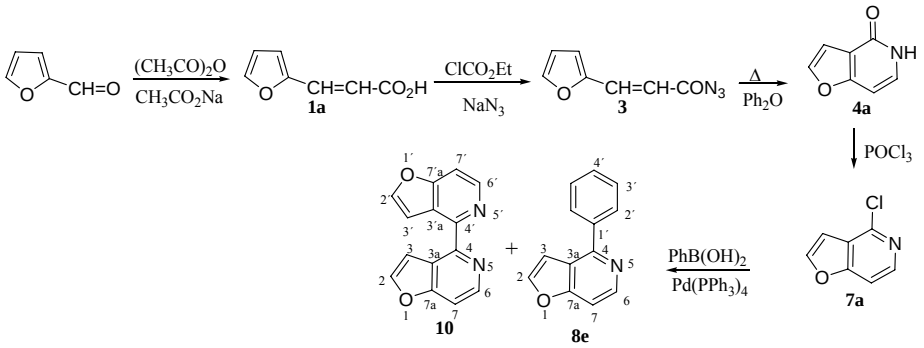


Fig. 1. Synthesis and reaction of 4-chlorofuro[3,2-c]pyridine.

4-Phenylfuro[3,2-*c*]pyridine (8e). The mixture of 4-chlorofuro[3,2-*c*]pyridine (**7a**) (0.767 g; 5 mmol), phenyl boronic acid (0.945 g; 8 mmol), water solution of sodium carbonate (2 M, 7.5 mL) and $Pd(PPh_3)_4$ (0.345 g, 0.3 mmol) in 1.2-dimethoxyethane (9 mL) was heated at 80 °C for 6 h. Then the reaction mixture was poured into mixture dichloromethane and ice water (1:1). The separate organic layer was washed with water and brine, dried with magnesium sulfate, the solvent was evaporated in vacuum. Then from the residue the product **8e** after purification by column chromatography was isolated (silica gel, eluted with $CHCl_3$). Yield 0.2 g, 20.5%, white crystals, m.p. 99-100 °C (methanol); RF = 0.2 ($CHCl_3$). Anal. Calcd. for $C_{13}H_9NO$: C, 79.98; H, 4.65; N, 7.17. Found: C, 80.31; H, 4.55; N, 7.23%. ^{1}H NMR (DMSO-d*6*), δ: 8.56 (d, 1H, $^3J_{(7,6)}$ = 5.8 Hz, H-7), 8.19 (d, 1H, $^3J_{(2,3)}$ = 1.77 Hz, H-2), 8.01 (d, 2H, $^3J_{(2',3')}$ = 7.8 Hz, H-2′, H-6′), 7.67 (d 1H, H-6), 7.55 (dd, 2H, H-3′, H-5′), 7.49 (d 2H, $^3J_{(4',3')}$ = 7.2 Hz, H-4′), 7.32 (d, 1H, H-3). ^{13}C NMR (DMSO-d$_6$), δ: 159.75 (C-7a), 151.88 (C-4), 147.2 (C-2), 144.15 (C-6), 138.61 (C-1′), 128.98 (C-4′), 128.69 (C-3′, C-5′), 128.19 (C-2′, C-6′), 121.44 (C-4′), 106.12 (C-7), 105.58 (C-3). IR / cm^{-1}: 3088s; 3038s; 1602s; 1495m; 1412s; 1260s; 1112m; 1056s; 992w; 818s; 702s; 686m.

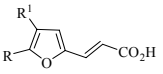
4-(Furo[3,2-*c*]pyridin-4-yl)furo[3,2-*c*]pyridine (10). Yield 12.7%, m.p. 160-165 °C (methanol). Anal. Calcd. for $C_{13}H_9NO$: C, 71.18; H, 3.41; N, 11.86. Found: C, 71.13; H, 3.78; N, 11.48%. ^{1}H NMR (DMSO-d$_6$), δ: 8.68 (d, 2H, $^3J_{(6,7)}$ = 6.0 Hz, H-6, H-6′), 8.21 (d, 2H, $^3J_{(2,3)}$ = 2.4 Hz, H-2, H-2′), 7.86 (dd 2H, $^3J_{(3,2)}$ = 2.4 Hz, $^5J_{(3,7)}$ = 0.6 Hz, H-3, H-3′), 7.78 (dd 2H, $^3J_{(7,6)}$ = 6.0 Hz, $^5J_{(7,3)}$ = 0.6 Hz, H-7, H-7′). ^{13}C NMR (DMSO-d$_6$), δ: 160.0 (C-7a, C-7′a), 150.5 (C-4, C-4′), 147.2 (C-2, C-2′), 143.7 (C-6, C-6′), 122.8 (C-3a, C-3′a), 107.9 (C-3, C-3′), 107.4 (C-7, C-7′). IR/ (cm^{-1}): 3472m; 3453m; 3173w; 3164w; 3140m; 1597m; 1567w; 1532w; 1443m; 1400m; 1317w; 1299w; 1263w; 1194w; 1160w; 1121w; 1111w; 1043w; 1013s; 903w; 879m; 816m; 794w; 783m; 749s; 625w; 607w; 590w; 466w; 425w.

Suzuki coupling reaction was realized with 4-chlorofuro[3,2-*c*]pyridine (**7a**) and phenylboronic acid in the presence of $Pd(PPh_3)_4$ catalyst in dichloromethane, in which 4-phenylfuro[3,2-*c*]pyridine (**8e**) and 4-(furo[3,2-*c*]pyridine-4-yl)furo[3,2-*c*]pyridine (**10**) were formed (Fig. 1). The compounds **8e** and **10** were purified on a silica gel column. Their structures were determined by ^{1}H and ^{13}C NMR spectra. The low yield of **8e** (20.2%) comparing with 1-phenyl[1]benzofuro[3,2-*c*]pyridine (**8f**) (59%)

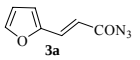
(TARABOVÁ *et al*., 2010) can be explained by the higher [1]benzofuro[3,2-*c*]pyridine system stability. The mechanism of the compound **10** formation is for us until now confused.

3.2 Antimicrobial activity

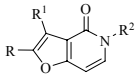
The structures whose biological activity was studied are presented in Fig. 2.



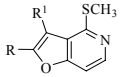
Compound	R	R^1
1a	H	H
1b	3-$CF_3C_6H_4$	H
1c	CH_3	H
1d	CH=CH-CH=CH	



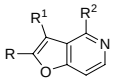
3a



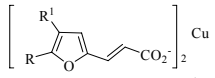
Compound	R	R^1	R^2
4a	H	H	H
4b	3-$CF_3C_6H_4$	H	H
4c	4-$NO_2C_6H_4$	H	H
4d	CH=CH-CH=CH	H	
4e	3-$CF_3C_6H_4$	H	CH_3
4f	CH=CH-CH=CH		CH_3



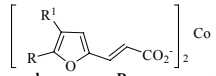
Compound	R	R^1
6a	3-$CF_3C_6H_4$	H
6b	CH=CH-CH=CH	



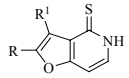
Compound	R	R^1	R^2
8a	3-$CF_3C_6H_4$	H	piperidin-1-yl
8b	3-$CF_3C_6H_4$	H	morpholin-4-yl
8c	CH=CH-CH=CH		piperidin-1-yl
8d	CH=CH-CH=CH		morpholin-4-yl
8e	H	H	phenyl
8f	CH=CH-CH=CH		phenyl
8g	H	H	CO_2H
8h	H	H	CN
8i	H	H	$CONH_2$
8j	3-$CF_3C_6H_4$	H	CO_2H



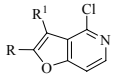
Compound	R	R^1
2a	H	H
2b	CH=CH-CH=CH	H
2c	CH_3	H



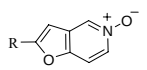
Compound	R	R^1
2d	H	H
2e	CH=CH-CH=CH	H
2f	CH_3	H



Compound	R	R^1
5a	3-$CF_3C_6H_4$	H
5b	CH=CH-CH=CH	



Compound	R	R^1
7a	H	H
7b	3-$CF_3C_6H_4$	H
7c	4-$CH_3OC_6H_4$	H
7d	CH=CH-CH=CH	



Compound	R
9a	H
9b	3-$CF_3C_6H_4$

Fig. 2. Structures of compounds, in which biological activity was studied.

Antimicrobial activity of tested compounds **1a-d** (characterized by MIC) is summarized in Table 1. It was noticed that the tested compounds **1** inhibited growth of microorganism with the lowest concentration 25 $mg.L^{-1}$, except the compound **1d**, in

which the antifungal effect was repressed. Substitution on a furan ring did not influence on antifungal and antibacterial effect.

Table 1. Antimicrobial activity of tested compounds **1a-1d** characterized by MIC [mg.L^{-1}].

Compound	Bacteria				Filamentous fungi			
	***Xanthomonas* sp.**		***E. amylovora***		***F. graminearum***		***P. avenae***	
	Ø[a]	MIC	Ø [a]	MIC	Ø [a]	MIC	Ø [a]	MIC
1a	3.3 ± 1.3	25	1,6 ± 0.1	25	3.3 ± 0.0	25	1.5 ± 0.0	25
1b	3.3 ± 2.3	25	1,6 ± 0.4	25	1.0 ± 0.0	25	3.0 ± 1.3	25
1c	2.8 ± 0.3	25	2.0 ± 0.5	25	2.4 ± 0.1	25	2.0 ± 0.5	25
1d	2.8 ± 1.0	25	1.0 ± 0.0	25	0	N/A	3. 0 ± 0.0	25
TMTD	0.8 ± 0.2	100	1.0 ± 0.0	200	4.6 ± 0.1	200	3.4 ± 0.9	200

[a] zone inhibition diameter expressed in mm over 24 h, 4 d respectively, ± SD
MIC minimal inhibition concentration, N/A compound does not show antimicrobial effect

Antimicrobial activities of tested compounds **2a-2f** are summarized in Table 2. In comparison, the effect of some of this compounds is lower (MIC 50-200 mg.L^{-1}) than tested compounds of group **1a-1d**. The complexes of copper(II) and cobalt(II) shown similar antibacterial effects but the antifungal effects are various. In comparison, copper(II) complexes **2a-2c** are more effective on *F. graminearum* than cobalt(II) complexes. Cobalt(II) complexes **2d-2f** are more effective on *P. avenae*. Sensitivity of microorganism on compounds **2a-2f** decreased in the order: *E. amylovora* > *Xanthomonas* sp. > *P. avenae* > *F. graminearum.*

Table 2. Antimicrobial activity of tested compounds **2a-2f** characterized by MIC [mg.L^{-1}].

Compound	Bacteria				Filamentous fungi			
	***Xanthomonas*. sp.**		***E. amylovora***		***F. graminearum***		***P. avenae***	
	Ø[a]	MIC	Ø [a]	MIC	Ø [a]	MIC	Ø [a]	MIC
2a	1.5 ± 0.5	25	4.5 ± 1.5	25	1.0 ± 0.0	25	1.0 ± 0.0	50
2b	1.0 ± 0.0	25	1.0 ± 0.0	25	1.3 ± 0.0	50	1.5 ± 0.0	25
2c	1.3 ± 0.0	25	4.3 ± 0.0	25	4.3 ± 0.0	25	2.5 ± 0.0	100
2d	5.3 ± 0.0	200	2.0 ± 0.0	25	0	N/A	4.5 ± 0.0	25
2e	2.0 ± 1.0	25	1.3 ± 0.3	25	0	N/A	2.0 ± 0.0	25
2f	2.0 ± 1.0	25	2.8 ± 0.8	25	3.0 ± 0.0	25	1.5 ± 0.5	25
TMTD	0.8 ± 0.2	100	1.0 ± 0.0	200	4.6 ± 0.1	200	3.4 ± 0.9	200

[a] zone inhibition diameter expressed in mm over 24 h, 4 d respectively, ± SD
MIC minimal inhibition concentration, N/A compound does not show antimicrobial effect

The azide **3a** inhibited the growth of bacteria *Xanthomonas* sp. and *E. amylovora* (MIC 25 mg.L^{-1}). The same effect was registered on filamentous fungi *F. graminearum* and *P. avenae* with MIC 25 mg.L^{-1}. In comparison, all of tested

microorganisms are more sensitive to azide **3a** than to previous group of complexes **2a-2f.**

Table 3. Antimicrobial activity of **3a** characterized by MIC [mg.L^{-1}].

Compound	Bacteria				Filamentous fungi			
	***Xanthomonas* sp.**		***E. amylovora***		***F. graminearum***		***P. avenae***	
	Ø[a]	MIC[b]	Ø [a]	MIC	Ø [a]	MIC	Ø [a]	MIC
3a	1.5 ± 0.3	25	2.3 ± 1.0	25	2.3 ± 0.4	25	1.0 ± 0.0	25
TMTD	0.8 ± 0.2	100	1.0 ± 0.0	200	4.6 ± 0.1	200	3.4 ± 0.9	200

[a] zone inhibition diameter expressed in mm over 24 h, 4 d respectively, ± SD
MIC minimal inhibition concentration

From the results we can assumed, that the derivatives of 3-(furan-2 yl)propenoic acid have potential in the development of the new pesticides, effective on bacterial as well as fungal affections of the plants.

Antimicrobial activities of compounds **4a-4f** are summarized in Table 4. In comparison, these compounds are less sensitive to filamentous fungi than in previous groups of compounds **1-3**. Inhibition of the growth of filamentous fungi *P. avenae* is registered only by pyridones **4d** and **4e**. The rest of microorganisms react sensitively on pyridones **4a-4f**, except pyridone **4b** (*Xanthomonas* sp., MIC 100 mg.L^{-1}), **4c** (*E. amylovora,* MIC 100 mg.L^{-1}). Pyridone **4e** has not antifungal effect on *F. graminearum.*

Table 4. Antimicrobial activity of pyridones **4a-4f** characterized by MIC [mg.L^{-1}].

Compound	Bacteria				Filamentous fungi			
	***Xanthomonas* sp.**		***E. amylovora***		***F. graminearum***		***P. avenae***	
	Ø[a]	MIC	Ø [a]	MIC	Ø [a]	MIC	Ø [a]	MIC
4a	3. 0 ± 0.0	25	3.0 ± 0.0	25	1.0 ± 0.0	25	0	N/A
4b	2.0 ± 0.0	100	1.0 ± 0.0	25	2.5 ± 0.2	25	0	N/A
4c	1.0 ± 0.0	25	3.0 ± 0.0	100	4.5 ± 0.0	25	0	N/A
4d	4.2 ± 0.8	25	3.8 ± 0.0	25	4.0 ± 0.0	25	2.0 ± 0.0	50
4e	3.0 ± 0.0	25	4.0 ± 0.0	25	0	N/A	1.0 ± 0.0	25
4f	2.5 ± 0.5	25	1.0 ± 0.0	25	2.8 ± 0.8	25	0	N/A
TMTD	0.8 ± 0.2	100	1.0 ± 0.0	200	4.6 ± 0.1	200	3.4 ± 0.9	200

[a] zone inhibition diameter expressed in mm over 24 h, 4 d respectively, ± SD
MIC minimal inhibition concentration, N/A compound does not show antimicrobial effect

Antimicrobial activities of pyridine-thiones **5a** a **5b** are summarized in Table 5. In comparison, pyridine-thiones are more effective on all microorganisms than in groups **2** and **4.** Both of these compounds have the same effect on microorganisms *Xanthomonas* sp., *E. amylovora,* and *P. avenae*. *F. graminearum* reacts sensitively on pyridine-thione **5b** (MIC 25 mg.L^{-1}).

Table 5. Antimicrobial activity of **5a,b** characterized by MIC [mg.L^{-1}].

Compound	Bacteria				Filamentous fungi			
	***Xanthomonas* sp.**		***E. amylovora***		***F. graminearum***		***P. avenae***	
	Ø[a]	MIC	Ø [a]	MIC	Ø [a]	MIC	Ø [a]	MIC
5a	3.0 ± 0.0	25	1.0 ± 0.0	25	3.5 ± 0.0	50	3.5 ± 0.0	25
5b	2.5 ± 0.5	25	2.5 ± 0.0	25	2.3 ± 0.0	25	3.0 ± 0.0	25
TMTD	0.8 ± 0.2	100	1.0 ± 0.0	200	4.6 ± 0.1	200	3.4 ± 0.9	200

[a] zone inhibtion diameter expressed in mm over 24 h, 4 d respectively, ± SD
MIC minimal inhibition concentration

Antimicrobial effects of chloro derivatives **7a-7d** are summarized in Table 6. Compounds of this group showed various antimicrobial effects. Filamentous fungi are the most sensitive on chloro derivatives **7a** a **7b** (MIC 25 mg.L^{-1}). The biggest effect on bacteria *Xanthomonas* sp. and *E. amylovora* has chloro derivative 7c (MIC 25 mg.L^{-1}).

Table 6. Antimicrobial activity of compounds **7a-7d** characterized by MIC [mg.L^{-1}].

Compound	Bacteria				Filamentous fungi			
	***Xanthomonas* sp.**		***E. amylovora***		***F. graminearum***		***P. avenae***	
	Ø[a]	MIC	Ø [a]	MIC	Ø [a]	MIC	Ø [a]	MIC
7a	3.0 ± 0.0	50	2.3 ± 1.3	25	2.5 ± 0.5	25	3.8 ± 0.0	25
7b	2.7 ± 0.0	25	3.7 ± 0.0	50	3.3 ± 0.0	25	3.0 ± 0.0	25
7c	3.0 ± 0.5	25	2.8 ± 0.0	25	2.0 ± 0.0	100	1.5 ± 0.0	100
7d	2.5 ± 0.2	50	1.0 ± 0.0	100	4.0 ± 0.0	100	1.0 ± 0.0	50
TMTD	0.8 ± 0.2	100	1.0 ± 0.0	200	4.6 ± 0.1	200	3.4 ± 0.9	200

[a] zone inhibition diameter expressed in mm over 24 h, 4 d respectively, ± SD
MIC minimal inhibition concentration

Antimicrobial activities of **8a-8j** are summarized in Table 7. In comparison, this group of compounds **8a-8j** has lower antimicrobial effects than previous groups. Compounds **8a** and **8f** inhibited the growth of bacteria by higher concentrations (MIC 50 mg.L^{-1}) and they are less effective. Compounds 8h and 8i with MIC 25 mg.L^{-1} have antifungal effect on *F. graminearum*, the effect of compounds 8c (MIC 100 mg.L^{-1}), 8f (MIC 200 mg.L^{-1}) and 8g (50 mg.L^{-1}) is registered also. Sensitivity of microorganisms by these compounds decreased in the order: *E. amylovora* > *Xanthomonas* sp. > *P. avenae* > *F. graminearum.*

The antimicrobial activities of tested *N*-oxides **9a, 9b** are summarized in Table 8. Compounds **9a** and **9b** showed the lowest antimicrobial effect of all tested compounds. Inhibition of the growth of bacteria *Xanthomonas* sp. and *E. amylovora* is stronger for *N*-oxide **9b**, which inhibits the growth of filamentous fungi *P. avenae* (MIC 100 mg.L^{-1}) too. However, this compound has not antifungal effect on *F. graminearum*. Antifungal effect is not shown by *N*-oxides **9a**. *N*-oxide **9b** show bigger antimicrobial effect.

Table 7. Antimicrobial activity of compounds **8a-8j** characterized by MIC [mg.L^{-1}].

Compound	Bacteria				Filamentous fungi			
	***Xanthomonas* sp.**		***E. amylovora***		***F. graminearum***		***P. avenae***	
	Ø[a]	MIC	Ø [a]	MIC	Ø [a]	MIC	Ø [a]	MIC
8a	3.0 ± 0.0	50	4.0 ± 0.0	50	0	N/A	2.0 ± 0.0	100
8b	4.6 ± 0.2	50	2.5 ± 0.0	25	0	N/A	2.0 ± 0.0	25
8c	3.6 ± 0.0	25	3.5 ± 0,0	25	1.5 ± 0.5	100	4.3 ± 0.0	50
8d	2.2 ± 0.2	25	3.3 ± 0.3	25	0	N/A	3.5 ± 1.5	50
8e	0.3 ± 0.0	25	6.7 ± 0.0	25	0	N/A	4.9 ± 0.9	25
8f	2.7 ± 0.0	50	3.3 ± 0.0	50	10.3 ± 0.0	200	2.0 ± 0.0	25
8g	1.5 ± 0.3	25	2.3 ± 0.0	25	5.0 ± 1.0	50	1.7 ± 0.2	25
8h	1.7 ± 0.2	25	2.3 ± 0.3	25	1.0 ± 0.5	25	1.8 ± 0.3	25
8i	2.7 ± 0.0	25	2.4 ± 0.2	25	3.1 ± 0.4	25	1.8 ± 0.2	25
8j	3.3 ± 0.0	25	2.3 ± 0.0	25	0	N/A	2.0 ± 0.0	100
TMTD	0.8 ± 0.2	100	1.0 ± 0.0	200	4.6 ± 0.1	200	3.4 ± 0.9	200

[a] zone inhibition diameter expressed in mm over 24 h, 4 d respectively, ± SD
MIC minimal inhibition concentration, N/A compound does not show antimicrobial effect

Table 8. Antimicrobial activity of tested compounds **9a, 9b** characterized by MIC [mg.L^{-1}].

Compound	Bacteria				Filamentous fungi			
	***Xanthomonas* sp.**		***E. amylovora***		***F.graminearum***		***P. avenae***	
	Ø[a]	MIC	Ø [a]	MIC	Ø [a]	MIC	Ø [a]	MIC
9a	2.3 ± 0.8	50	1.0 ± 0.0	200	0	N/A	0	N/A
9b	2.3 ± 1.3	25	1.0 ± 0.0	50	0	N/A	3.0 ± 0.0	100
TMTD	0.8 ± 0.2	100	1.0 ± 0.0	200	4.6 ± 0.1	200	3.4 ± 0.9	200

[a] zone inhibition diameter expressed in mm over 24 h, 4 d respectively, ± SD
MIC minimal inhibition concentration, N/A compound does not show antimicrobial effect.

4. Conclusions

In summary, it was found that during study of the reaction of 4-chlorofuro[3,2-*c*]pyridine with boronic acid in the condition of Suzuki coupling reaction were formed two products. The main expecting product 4-phenylfuro[3,2-*c*]pyridine and the unexpected 4-(furo[3,2-*c*]pyridine-4-yl)furo[3,2-*c*]pyridine. The antimicrobial testing shown that earlier known synthesized derivatives of furo[3,2-c]pyridine and their starting compounds have various potential to inhibit the growth of phytopathogene microorganisms. In general it is shown, that the bacterial strains are more sensitive on these compounds than the fungal strains.

Acknowledgements: This work was supported by the grants VEGA 1/233/12. NMR experimental part of this work was facilitated by support of Slovak National Research and Development Program No. 2003SP200280203. The authors are grateful to Prof. A. Gatial for IR spectra and Dr. N. Pronayová for NMR spectra measurements.

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