# Studies on thiazolopyridines – A novel synthesis of bis-thiazolopyridines as promising antimicrobial agents

MOHAMED E. AZAB¹ GAMEEL A. M. EL-HAG ALI²\* ASHRAF H. F. ABD EL-WAHAB²

<sup>1</sup> Department of Chemistry Faculty of Science, Ain Shams University Cairo, Egypt

<sup>2</sup> Department of Chemistry Faculty of Science, Al-Azhar University Nasr City, P.O. Box 11884, Cairo, Egypt A variety of novel bis-thiazolopyridine derivatives **4a-e** were synthesized *via* the reaction of bis-thiazolinone **3** with different arylcinnamonitrile derivatives (1:2 molar ratio), whereas the reaction of bis-compounds **7a-e** with malononitrile in ethanol solution containing a few drops of piperidine afforded the novel bis-thiazolopyridines **8a-e**. The structures of the synthesized compounds were established by elemental analyses and spectral data. Some of the newly synthesized compounds show moderate to high antimicrobial activity.

*Keywords*: bis-thiazolopyridines, synthesis, antimicrobial activity

Received March 20, 2003 Accepted July 4, 2003

Derivatives of thiazolo[3,2-a]pyridines have been reported to furnish various biological activities such as antimicrobial (1), bactericidal (2), coronary dilating, antihypertensive and muscle relaxing (3). In addition, bis-heterocyclic compounds exhibit various biological activities (4–6) and exert much higher antibacterial activity than heterocyclic compounds (7). It was reported that 2-cyanomethyl-4-thiazolinone (1) was used as starting material for the synthesis of thiazolo[3,2-a]-pyridines (8–11). In view of the above facts and in continuation of our work on the chemistry of thiazolo[3,2-a]pyridines (12–14), we report here on the synthesis of some novel bis-thiazolo[3,2-a]pyridines starting from compound 1 in order to investigate their biological activity.

#### **EXPERIMENTAL**

All melting points are uncorrected (Stuart Scientific Co., UK). The IR spectra were measured in KBr pellets on a Shimadzu IR 200 spectrophotometer (Shimadzu Japan).  $^{1}$ H NMR spectra were recorded in DMSO-d $_{6}$  at 200 MHz on a Varian Gemini NMR spectrometer (Varian, UK), using tetramethylsilane as internal reference. Elemental analyses were carried out at the Microanalytical Center of Cairo University (Egypt).

<sup>\*</sup> Correspondence, e-mail: elahag1970@hotmail.com

The physico-chemical data for the compounds are given in Table I. The spectral data are collected in Table II. Compounds 1 and 6a-e were prepared according to the reported methods (11, 13).

# Syntheses

1,2-Bis[2-(2-cyanomethyl-4-oxo-4,5-dihydrothiazol-5-ylidenemethyl)-phenoxy]-ethane (3). — A mixture of thiazoline 1 (0.02 mol) and bis-aldehyde 2 (0.01 mol) in the presence of abso-

Table I. Physico-chemical data for prepared compounds

Compd. No.	Yield (%)	Crystallization solvent	M.p. (°C)	Mol. formula	Elemental analysis Calcd./found (%)		
				$(M_{\rm r})$	Calc	H	N
3	70	Benzene	> 300	C <sub>26</sub> H <sub>18</sub> N <sub>4</sub> O <sub>4</sub> S <sub>2</sub> (514.57)	60.69 60.60	3.53 3.50	10.89 10.80
4a	65	Benzene	90–92	$C_{46}H_{28}Br_2N_8O_4S_2$ (980.69)	56.32 56.50	2.85 2.90	11.44 11.40
4b	52	Benzene/ethanol	139–140	$C_{46}H_{28}Cl_2N_8O_4S_2$ (891.89)	61.95 61.90	3.16 3.20	12.56 12.50
4c	82	Benzene/ethanol	210–212	$C_{48}H_{34}N_8O_4S_2$ (850.96)	67.75 67.70	4.00 4.00	13.17 13.10
4d	72	Benzene	125–127	$C_{48}H_{34}N_8O_8S_2$ (914.95)	63.01 63.20	3.71 3.62	12.25 11.90
4e	63	Ethanol	245–246	$C_{46}H_{28}F_2N_8O_4S_2$ (858.81)	64.33 64.30	3.26 3.30	13.05 12.90
7a	73	Benzene	270–272	$C_{40}H_{24}Br_2N_4O_4S_2$ (848.57)	56.62 56.60	2.85 2.80	6.60 6.50
7b	74	Benzene/ethanol	271–273	$C_{40}H_{24}Cl_2N_4O_4S_2$ (759.77)	63.24 63.20	3.18 3.10	7.37 7.40
7c	53	Benzene/ethanol	190–191	$C_{42}H_{30}N_4O_4S_2$ (718.84)	70.18 70.20	4.21 4.10	7.79 7.70
7d	59	Benzene	> 300	$C_{40}H_{24}N_6O_8S_2$ (780.77)	61.53 61.50	3.10 3.00	10.76 10.80
7e	62	Ethanol	258–260	$C_{48}H_{30}N_4O_4S_2$ (790.91)	72.89 72.80	3.82 3.80	7.08 7.00
8a	65	Benzene/ethanol	217–219	$C_{46}H_{28}Br_2N_8O_4S_2$ (980.69)	56.34 56.30	2.88 2.92	11.43 11.50
8b	63	Benzene	228-230	C <sub>46</sub> H <sub>28</sub> Cl <sub>2</sub> N <sub>8</sub> O <sub>4</sub> S <sub>2</sub> (891.89)	61.95 62.00	3.16 3.10	12.56 12.48
8c	69	Benzene	179–181	C <sub>48</sub> H <sub>34</sub> N <sub>8</sub> O <sub>4</sub> S <sub>2</sub> (850.96)	67.75 67.80	4.03 4.10	13.17 13.20
8d	80	Benzene	238–240	$C_{46}H_{28}N_{10}O_8S_2$ (912.90)	60.52 60.50	3.09 3.00	15.34 15.30
8e	71	Benzene	218–220	C <sub>54</sub> H <sub>34</sub> N <sub>8</sub> O <sub>4</sub> S <sub>2</sub> (922.03)	70.27 70.30	3.71 3.60	12.14 12.10

Table II. Spectral data of synthesized compounds

Compd.	IR (KBr, cm <sup>-1</sup> )	<sup>1</sup> H NMR (DMSO-d <sub>6</sub> ) (δ, ppm)
3	2923 (CH-aliph.), 2198 (C≡N), 1720 (thiazolinone C=O)	4.01 (s, 4H, 2CH <sub>2</sub> CN), 4.91 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), 7.00–7.40 (m, 10H, 8H Ar-H + 2H-methine)
4a	3417 (NH <sub>2</sub> ), 2923 (CH-aliph.), 2198 (C=N), 1712, 1651 (thiazolinone C=O)	4.35 (s, 4H, pyridine-H), 4.70 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), 7.18–8.03 (m, 18H, 16H Ar-H + 2H-methine), 8.54, 8.57 (2s, 4H, 2NH <sub>2</sub> )
4b	3394 (NH <sub>2</sub> ), 2923 (CH-aliph.), 2198 (C≡N), 1712, 1651 (thiazolinone C=O)	4.18 (s, 2H, pyridine-H), 4.70 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), 7.49–7.69 (m, 18H, 16H Ar-H + 2H-methine), 7.95 (s, 4H, 2NH <sub>2</sub> )
4c	3417, 3340 (NH <sub>2</sub> ), 2923 (CH-aliph.), 2198 (C=N), 1712, 1651 (thiazolinone C=O)	2.30 (s, 6H, 2CH <sub>3</sub> ), 4.29 (s, 2H, pyridine-H), 4.54 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), 7.03–7.53 (m, 18H, 16H Ar-H + 2H-methine), 7.90 (s, 4H, 2NH <sub>2</sub> )
4d	3340 (NH <sub>2</sub> ), 2931 (CH-aliph.), 2198 (C≡N), 1712, 1651 (thiazolinone C=O)	$\begin{array}{l} 3.8\ (s,6H,2\ OCH_3),4.3\ (s,2H,pyridine\text{-}H),4.70\ (s,\\ 4H,(OCH_2)_2),7.21\text{-}7.52\ (m,18H,16H\ Ar\text{-}H+2H\text{-}methine),8.46\ (s,4H,2NH_2),9.87,10.30\ (2s,2H,2OH) \end{array}$
4e	3379, 3289 (NH <sub>2</sub> ), 2198 (C≡N), 1720, 1658 (thiazolinone C=O)	4.25 (s, 2H, pyridine-H), 4.67 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), 7.26–7.75 (m, 18H, 16H Ar-H + 2H-methine), 7.89 (s, 4H, 2NH <sub>2</sub> )
7a	2950 (CH-aliph.), 2191 (C≡N), 1715 (thiazolinone C=O)	4.61 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), $7.51$ – $7.85$ (m, 20H, 16H Ar-H + 4H-methine)
7b	2900 (CH-aliph.), 2221 (C≡N), 1718 (thiazolinone C=O)	4.61 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), $7.17$ – $8.42$ (m, 20H, 16H Ar-H + 4H-methine)
7c	2923 (CH-aliph.), 2198 (C≡N), 1681 (thiazolinone C=O)	2.23 (s, 6H, 2CH <sub>3</sub> ), 4.43 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), 7.11–7.29 (m, 20H, 16H Ar-H + 4H-methine)
7d	2923 (CH-aliph.), 2206 (C=N), 1681 (thiazolinone C=O)	4.61 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), $7.34$ – $7.73$ (m, 20H, 16H Ar-H + 4H-methine)
7e	2923 (CH-aliph.), 2198 (C≡N), 1700 (thiazolinone C=O)	4.94 (s, $4H$ , (OCH <sub>2</sub> ) <sub>2</sub> ), $7.14$ – $8.22$ (m, $26H$ , $22H$ Ar-H + $4H$ -methine)
8a	3417 (NH <sub>2</sub> ), 2923 (CH-aliph.), 2221 (C≡N), 1700 (thiazolinone C=O)	4.23 (s, 2H, pyridine-H), 4.61 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), 7.17–8.42 (m, 18H, 16H Ar-H + 2H-methine), 10.02 (s, 4H, 2NH <sub>2</sub> )
8b	3394 (NH <sub>2</sub> ), 2923 (CH-aliph.), 2191 (C=N), 1681 (thiazolinone C=O)	4.21 (s, 2H, pyridine-H), 4.61 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), 7.09–7.40 (m, 18H, 16H Ar-H + 2H-methine), 10.32 (s, 4H, 2NH <sub>2</sub> )
8c	3340 (NH <sub>2</sub> ), 2923 (CH-aliph.), 2221 (C≡N), 1651 (thiazolinone C=O)	2.20 (s, 6H, 2CH <sub>3</sub> ), 4.27 (s, 2H, pyridine-H), 4.70 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), 7.21–7.40 (m, 18H, 16H Ar-H + 2H-methine), 8.02, 8.08 (2s, 4H, 2NH <sub>2</sub> )
8d	3355 (NH <sub>2</sub> ), 2931 (CH-aliph.), 2198 (C≡N), 1700 (thiazolinone C=O)	4.47 (s, 2H, pyridine-H), 4.60 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), 7.17–8.06 (m, 18H, 16H Ar-H + 2H-methine), 8.44 (s, 4H, 2NH <sub>2</sub> )
8e		4.19 (s, 2H, pyridine-H), 4.43 (s, 4H, (OCH <sub>2</sub> ) <sub>2</sub> ), 6.94–7.94 (m, 24H, 22Ar-H + 2H-methine), 8.54 (s, 4H, 2NH <sub>2</sub> )

lute ethanol containing a few drops of piperidine (20 mL) was refluxed for 3 hours. The solid product obtained was filtered and recrystallized from a suitable solvent to give 3.

1,2-Bis[2-(5-amino-7-aryl-6,8-dicyano-3-oxo-7H-thiazolo[3,2-a]pyridin-2-ylidene-methyl)-phenoxy]-ethane (4a-e). — A mixture of 3 (0.01 mol) and arylidenemalononitriles (0.02 mol) was refluxed for 6 hours in the presence of absolute ethanol (20 mL) and a catalytic amount of piperidine (0.5 mL). The collected product was recrystallized from a suitable solvent to give 4a-e.

1,2-Bis[2-[2-(5-arylmethylidene-4-oxo-4,5-dihydrothiazol-2-yl)-2-cyanovinyl]-phenoxy]-ethane (7a-e). – A mixture of 6a-e (0.02 mol) and bis-aldehyde 2 (0.01 mol) was refluxed for 6 hours in the presence of absolute ethanol (20 mL) and a catalytic amount of piperidine. The obtained product was filtered and recrystallized from suitable solvent to give 7a-e.

1,2-Bis[2-(5-amino-2-arylmethylidene-6,8-dicyano-3-oxo-7H-thiazolo[3,2-a]-pyridin-7-yl)-phenoxy]-ethane (8a-e). — A mixture of **7a-e** (0.01 mol) and malononitrile (0.02 mol) was refluxed for 6 hours in the presence of absolute ethanol (20 mL) and a catalytic amount of piperidine (0.5 mL). The obtained product was isolated and recrystallized from an appropriate solvent to give **8a-e**.

## Antimicrobial activity

Most of the newly synthesized compounds (4c,e, 7c,d,e and 8a,b,d) were screened *in vitro* for their antimicrobial activity against four strains of bacteria, *Staphylococcus aureus*, *Escherichia coli*, *Pseudomonas aeruginosa* and *Bacillus subtilis*, using the paper disc diffusion method (15). The tested compounds were dissolved in *N*,*N*-dimethylformamide (DMF) to get a solution of 1 mg mL<sup>-1</sup>. Inhibition zones were measured in millimeters at the end of the incubation period of 48 h at 28 °C. Dimethylformamide showed no inhibition zones. Chloroamphenicol standard was used as reference to evaluate the potency of

Compd.	Staphylococcus	Bacillus	Escherichia	Pseudomonas
No.	aureus	subtilis	coli	aeruginosa
4c	+	+	+++	+
4e	+	++	+	+
7c	+	++	+++	++
7d	+	++	+	++
7e	+	++	+	+
8a	++	+	++	+
8b	+	+	++	++
8d	++	+	+	++
Chloramphenicol (25 μg mL <sup>-1</sup> )	++++	++++	++++	++++

Table III. Antimicrobial activity of some compounds

<sup>+</sup> less active (0.2–0.5 cm), ++ moderately active (0.6–1.4 cm), +++ highly active (1.5–3.0 cm), ++++ very highly active (over 3.0 cm)

the tested compounds and was also dissolved in DMF. The inhibition zones of microbial growth produced by different compounds are given in Table III.

#### RESULTS AND DISCUSSION

1,2-Bis[2-(2-cyanomethyl-4-oxo-4,5-dihydrothiazol-5-ylidenemethyl)-phenoxy]-ethane (3) was produced via the reaction of 2-cyanomethyl-4-oxo-thiazoline (1) with bis-aldehyde 2 (12) in a molar ratio 2:1 in ethanol and in the presence of catalytic amount of piperidine. Elemental analyses and spectral data of the intermediate compound 3 are in agreement with its structure. For example, its <sup>1</sup>H NMR spectrum in DMSO-d<sub>6</sub> showed two singlets at 4.01 and 4.91 attributed to  $2CH_2CN$  and  $(OCH_2)_2$  groups, respectively. Formation of the initiating material 3 encouraged us to extend this work to involve the formation of bis-thiazolopyridines 4a-e by cyclocondensation of compound 3 with different arylidenemalononitriles in a molar ratio 1:2 in absolute ethanol containing a few drops of piperidine under reflux conditions through the formation of intermediate A (Scheme 1) (12–14). The structures of bis-thiazolopyridines 4a-e were established by the elemental analyses and spectral data. The IR spectrum of compound 4a revealed the presence of absorption bands at 3417 cm<sup>-1</sup> corresponding to the amino group, 2923 cm<sup>-1</sup> (CH-aliph.), cyano stretch at  $2198 \text{ cm}^{-1}$  and thiazolinone carbonyl at  $1712 \text{ and } 1651 \text{ cm}^{-1}$ . Also, the <sup>1</sup>H NMR spectrum of **4a** in DMSO-d<sub>6</sub> showed singlet at 4.35, attributed to (2H) of pyridine-H, and a singlet at 4.7 due to (OCH<sub>2</sub>)<sub>2</sub> groups.

2-Cyanomethyl-4-oxo-thiazoline (1) was combined with different aromatic aldehydes 5a-e to give the corresponding benzylidene derivatives 6a-e (13). These derivatives, when reacted with bis-aldehyde 2 (2:1 molar ratio) afforded the novel benzylidene derivatives 7a-e. The analytical and spectral data were consistent with their structures. The structure of 7b was confirmed by its IR spectrum, which displayed absorption bands at 2900 cm<sup>-1</sup> for CH-aliph., 2221 cm<sup>-1</sup> due to C≡N and 1718 cm<sup>-1</sup> corresponding to C=O (thiazolinone). Also, the <sup>1</sup>H NMR spectrum in DMSO-d<sub>6</sub> of compound **7b** is in agreement with its structure, which revealed a singlet at 4.61 due to  $(OCH_2)_2$  and multiplet in the region 7.17–8.42 for 16Ar-H and 4H-methine. Our work was extended to synthesize a novel series of bis-thiazolopyridine derivatives 8a-e which contain bis-1,2-phenoxyethane moiety in position 7-yl instead of position 2-yl (13). These derivatives were produced by addition of the malononitrile to the  $\alpha$ , $\beta$ -unsaturated system in bis-compounds 7a-e followed by ring closure. The structures of bis-thiazolopyridines were proven by elemental analyses and spectral data. For example, the <sup>1</sup>H NMR spectrum of 8c in DMSO-d<sub>6</sub> displayed a singlet at 4.7 attributed to (OCH<sub>2</sub>)<sub>2</sub>, a singlet at 4.27 due to pyridine-H, a singlet at 2.20 for 2CH<sub>3</sub>, a multiplet in the region 7.21-7.24 corresponding to 16Ar-H and 2H-methine and finally two singlets at 8.02, 8.08 for 2NH<sub>2</sub> (Table II).

A novel 1,2-bis[2-(amino-7-aryl-6,8-dicyano-3-oxo-7*H*-thiazolo[3,2-a]pyridine-2-ylidenemethyl)-phenoxy)ethane (4c) and 1,2-bis[2-[2-(5-arylmethylidene-4-oxo-4,5-dihydrothiazol-2-yl)-2-cyanovinyl)phenoxy]ethane (7c) showed the highest antibacetrial activity among all the compounds tested. Their high activity against *Escherichia coli* may be attributed to the presence of the *p*-tolyl moiety. The most of the synthesized compounds showed moderate to low antibacterial activity. Compounds 4e and 7c-e showed mode-

Sheme 1

rate activity against *Bacillus subtilis*, whereas  $\mathbf{7c}$  and  $\mathbf{7d}$  exerted moderate activity against *Pseudomonas aeruginosa* as well. This may be attributed to the *o*-nitro-phenyl moiety in  $\mathbf{7d}$  and  $\alpha$ -naphthyl moiety in  $\mathbf{7e}$ . Compound  $\mathbf{8a}$  showed moderate activity against *Staphylococcus aureus* and *Escherichia coli*, which may be due to *p*-bromophenyl moiety. Com-

Sheme 2

pounds **8b** and **8d** showed moderate activity against *Pseudomonas aeruginosa*, compound **8b** showed moderate activity also against *Escherichia coli*, whereas compound **8d** showed the same activity against *Staphylococcus aureus*.

#### CONCLUSIONS

Among the series of newly synthesized bis-thiazolopyridines, 1,2-bis[2-(5-amino-7-aryl-6,8-dicyano-3-oxo-7*H*-thiazolo[3,2-a]pyridine-2-ylidenemethyl)-phenoxy)ethane and 1,2-bis[2-[2-(5-arylmethylidene-4-oxo-4,5-dihydrothiazol-2-yl)-2-cyanovinyl)phenoxy]ethane showed the highest antibacterial activity. They showed high activity against *Escherichia coli* probably due to the presence of *p*-tolyl moiety.

#### REFERENCES

- S. A. Shiba, A. A. El-Khamry, M. E. Shaban and K. S. Atia, Synthesis and antimicrobial activity of some bis-quinazoline derivatives, *Pharmazie* 52 (1997) 189–194.
- N. C. Deasi, Synthesis and antimicrobial activity of some dithiocarbamates, 2-aryl-amino-4-oxo-thiazolidines and their 5-arylidene derivatives, *Indian J. Chem. Sec. B* 32 (1993) 343–346.
- 3. H. N. Liu, Z. C. Li and T. Anthosen, Synthesis and fungicidal activity of 2-imino-3-(4-arylthia-zol-2-yl)-thiazolidin-4-ones and their derivatives, *Molecules* 5 (2000) 1055–1061.
- 4. A. M. Shalby, O. A. Fathalla, E. M. M. Kassem and M. E. A. Zaki, Synthesis of new 5-N-pyrazolylamino acids, pyrazolopyrimidine derivatives, *Acta Chim. Solv.* 47 (2000) 187–203.
- U. Olthoff, K. Matthey and B. Ditscher, *Thiazolo[3,2-a]pyridines*, Ger. (East) 84, 850 (Cl. C07d), 05
   Oct (1971), Appl. WP CO7d/148 314, 16 Jun (1970); ref. *Chem. Abstr.* 78 (1973) 72121y.
- M. Horst, B. Friedrich, V. Wulf and S. Kurt, *Pharmaceutical Pyridine Derivative, Ger. Offen*, 2, 210, 633 (Cl. C07d), 20 Sep. (1973), APPl. P22 10 633.8, 06 Mar (1972); ref. *Chem. Abstr.* 79 (1973) 146519d.
- 7. B. S. Holla, R. Gonsalves and S. Shenay, Synthesis and antimicrobial studies of a new series of 1,2-bis(1,3,4-oxadiazol-2-yl)-ethanes and 1,2-bis(4-amino-1,2,4-triazol-3-yl)-ethanes, *Eur. J. Med. Chem.* **35** (2000) 267–271.
- 8. C. Jyhjian and W. Ingjing, Synthesis of some 2- and 7-pyrenyl substituted thiazolo[3,2-a]pyridine derivatives, *Dyes Pigm.* **30** (1996) 173–82.
- 9. F. F. Abdel-Latif and R. M. Shaker, Heterocycles synthesis through reactions of nucleophiles with acrylonitriles, Part 5. Synthesis of several new thiazol and thiazolo[3,2-a]pyridine derivatives, *Phosphorus*, *Sulfur*, *Silicon*, *Rel. Elem.* 48 (1990) 217–21.
- 10. O. S. Abdel Meguid, G. H. Elgemeie, N. G. Abdel Moein and M. H. Elnagdi, Activated nitriles in heterocyclic synthesis; Synthesis of 6-thiophen-2-yl and 6-furan-2-yl-thiazolo [2,3-a] pyridine derivatives, *Monatsh. Chem.* 117 (1986) 105–10.
- 11. S. K. Usef, E. A. Hafez, M. Abo Elfetouh and M. H. Elnagdi, Activated nitriles in heterocyclic synthesis: The reaction of substituted cinnamonitriles with 2-functionally substituted methyl-2-thiazolin-4-one derivatives, *Z. Naturforsch. B, Anorg. Chem. Org. Chem.* 39B (1984) 824–828.
- 12. A. A. El-Maghraby, G. A. M. El-Hag Ali, A. H. Ahmed and M. S. A. El-Gaby, Studies on thiazolopyridines. Part 1. Antimicrobial activity of some novel flourinated thiazolo[3,2-a]pyridines and thiazolo[2',3':1,6]pyrido[2,3-d]pyrimidines, *Phosphorus, Sulfur, Silicon.* 177 (2002) 293–302.
- 13. G. A. M. El-Hag Ali, A. Khalil, A. H. Ahmed and M. S. A. El-Gaby, Studies on thiazolopyridines. Part 2. Synthesis and antimicrobial activity of novel thiazolo[3,2-a]pyridine and thiazolo-[3,2-a][1,8]naphthyridine derivatives having two different aryl moieties, *Acta Chim. Solv.* 49 (2002) 365–376.
- 14. G. A. M. El-Hag Ali, Studies on thiazolopyridines. Part 3. Reactivity of thiazolo-[3,2-a]-3-aza-[1,8]naphthyridine towards some nucleophiles, *Phosphorus*, *Sulfur*, *Silicon* 178 (2003) 711–720.
- W. Hewitt and S. Vincent, Theory and Application of Microbiological Assay, Academic Press, New York 1989.

### SAŽETAK

# Tiazolopiridini – Nova sinteza bis-tiazolopiridina s potencijalnim antimikrobnim djelovanjem

MOHAMED E. AZAB, GAMEEL A. M. EL-HAG ALI i ASHRAF H. F. ABD EL-WAHAB

Reakcijom bis-tiazolinona 3 s derivatima arilcinamonitrila (u molnom omjeru 1:2) sintetizirani su različiti bis-tiazolopiridini **4a-e**. Bis-spojevi **7a-e** s malononitrilom u etanolnoj otopini s nekoliko kapi piperidina daju nove bistiazolopiridine **8a-e**. Strukture spojeva potvrđene su elementarnom analizom i spektroskopski. Sintetizirani spojevi pokazuju umjereno do jako antimikrobno djelovanje.

Ključne riječi: bis-tiazolopiridini, sinteza, antimikrobno djelovanje

Department of Chemistry, Faculty of Science, Ain Shams University, Cairo, Egypt

Department of Chemistry, Faculty of Science, Al-Azhar University, Nasr City, Cairo, Egypt