Journal of Pharmaceutical, Chemical and Biological Sciences
ISSN: 2348-7658
Impact Factor (GIF): 0.615
Impact Factor (SJIF): 2.092
June-August 2015; 3(2):178-187
Available online at http://www.jpcbs.info

Original Research Article

# Antibacterial Study Novel 2-cyanomethylthieno [3,2-e] [1,2,4]-triazolo[1,5-c]pyrimidine

**Dhiab Jabli[1*], Karima Lahbib[3], Khaireddine Dridi[1, 2], Mohamed Lotfi Efrit[1]**

[1]Laboratory of Organic Chemistry, Department of Chemistry, Faculty of Sciences, El Manar University, El Manar II, Tunis 1060, Tunisia
[2]Department of Chemistry, College of Sciences and Arts, Qassim University, Al-Rass, 53, Kingdom of Saudi Arabia
[3]Laboratory of Heteroatom Organic Chemistry, Faculty of Sciences of Bizerte Jarzouna 7021, Tunisia

***Corresponding Author:** Dhiab JABLI, Laboratory of Organic Chemistry, Faculty of Sciences of Bizerte, Zarzouna 7021, Tunisia

Received: 24 June 2015 Revised: 04 July 2015 Accepted: 11 July 2015

**ABSTRACT**

A new series of 2-cyano-methyl-thieno-triazolo-pyrimidines were synthesized in a good yield through a facile method using substituted aminothiophene-3-carbonitrile as building block and cyanoacetic acid hydrazide as reagent in one framework. The structure of synthesized compounds was characterized on the basis of their infrared (IR), $^{1}H$ and $^{13}CNMR$ and mass spectral data. All the title compounds were tested for their antibacterial activity against four types of Bacteria. All tested compounds showed significant antibacterial activity

**Keyword:** Thienotriazolopyrimidine; 2 aminothiophene-3-carbonitrile;antibacterial activity

## INTRODUCTION

Thienopyrimidines are priviliged structures, which attracted considerable attention in the designing of biologically active molecules. Moreover they are found to exhibit a variety of biological activities such as anti-inflammatory [1, 2], antimicrobial [3-5], analgesic [6], inhibition of cancer cell proliferation [7-8].

Recently, it has been found that novel tri and tetracyclic ring system containing thienopyrimidine moities affrod a large number of bioactive derivatives [9-11]. Thus, the introduction of triazole ring moity to the

thienopyrimidine system is expected to influence the biological activity significantly [12, 13]. In addition, a wide variety of thienotriazolopyrimidines have been reported as selective antagonists for $A_{2A}AR_s$ [14, 15] and as adenosine $A_1$ receptor antagonists. Thienopyrimidines are promising bioactive molecules as they are structural analogs of biogenic purines and can be considered as potential nucleic acid anti-metabolites. They are characterized by a broad spectrum of biological activities such as cardiovascular [16], antiviral [17], CNS depressant [18], bactericidal [19], and ulcer inhibition [20]. In view of these published data and in continuation of our previous work on biologically active nitrogen and sulfur heterocycles [21–23], we are interesting to synthesize a new series of thieno - triazolopyrimidine fused thiophene derivatives and to screen them for their antibacterial activity.

## MATERIALS AND METHODS

### Chemistry

Solvents and reagents were obtained from commercial sources and were dried and purified when necessary by standard techniques.

The typical experimental procedure is outlined in [24-26]. The yields of these reactions are summarized in Table 1. All triazoles **2** were fully characterized by satisfactory IR, GC/MS-MS and by NMR spectroscopy [26].

General procedure for the synthesis of starting material substituted 2-aminothiophene-3-carbonitrile **(1)**.

In a typical experiment, ketone (0. 10 mol) and malononitrile (0. 10 mol) were dissolved in 200 mL of absolute ethanol. Sulphur powder (0. 11 mol) and morpholine (20 mL) were added. The mixture was heated at 50 °C during 3 hours and then was cooled at room temperature. The mixture poured into 300 mL ice-water. The filtered precipitate was washed with cold water, dried and then recrystallized in suitable solvent (Scheme 1).

### General procedure for the synthesis of thienotriazolopyrimidines (2)

To a mixture of dry toluene (200 mL), Imino ether **1** (10 mmol) and para-toluene sulfonic acid (0.1 g) as catalyst was added cyanoacetic acid hydrazide (10 mmol). The mixture was heated under reflux in In a Dean-Stark apparatus with removal of water and ethanol formed during 12-18 hours. Evaporation of most of toluene left a residue which was dissolved in 20 mL of saturated solution of sodium bicarbonate and then extracted twice with 25 mL of chloroform. The organic layers was washed with 25 mL of saturated sodium chloride solution and then with 30 mL of distilled water and then dried over $MgSO_4$. After removal of chloroform, the solid obtained was filtered and recrystallized from ethanol [26].

### Spectral data for compounds

The structures of compounds **1** and **2** were confirmed by infrared (IR), nuclear magnetic resonance (NMR) spectroscopies and mass spectral data. $^1H$ and $^{13}C$ NMR spectra were recorded with DMSO-d6 or a mixture of DMSO-d6-$CDCl_3$ as the solvent for compounds on a Varian-Unity spectrometer at 300 MHz (300 MHz and 90 MHz, respectively). The chemical shifts are reported in ppm relative to TMS (internal reference) for $^1H$ and $^{13}C$ NMR. The coupling constants are reported in Hz. For the $^1H$ NMR, the multiplicities of signals are indicated by the following abbreviation: s: singulet; d: doublet; t: triplet; q: quartet; quint: quintet; m: multiplet. Melting points were taken with a Kofler hot staged apparatus and are uncorrected. All reactions were monitored by thin layer chromatography (TLC) using precoated aluminum sheet silica gel Merck 60 F 254 and were visualized by UV lamp. IR spectra were were recorded in the liquid state dissolved

in chloroform with Perkin Elmer Paragon 1000 PC spectrometer or in solid state dispersion in KBr with a Perkin Elmer 1600 series FT-IR spectrometer. Elemental analyses were determined using an elemental vario EI III Elemental Analyser. Mass spectra were recorded on a GC/MS/MS spectrometer with an $EI^+$, TIC ionization source.

**Spectral data for compounds are as follows**

***2-Cyanomethyl-5-methyl-8,9,10,11-tetrahydro [1]benzothieno[3,2-e][1,2,4]triazolo[1,5-c] pyrimidine (2a)***

Yield: 78 %. Mp: 156-158 °C. IR (KBr): 3052, 2967, 2227, 1639, 1616, 1574, 1552 $cm^{-1}$. $^1$H-NMR (300 MHz, DMSO-$d_6$) δ: 4.12 (s, 2H), 3.02 (m, 2H), 2.92(s, 3H), 2.74 (m, 2H), 1.85 (m, 4H). $^{13}$C-NMR (75 MHz, DMSO-$d_6$) δ: 19.1, 22.1, 23.1, 24.5, 36.4, 38.0, 114.9, 118.3, 128.6, 132.1, 138.5, 146.0, 155.1, 157.0. GC/MS-MS ($EI^+$, TIC 1.52e6): *m/z* $[M-H]^-$ calcd for $C_{14}H_{13}N_5S$: 282.344 ; found: 282.352. Anal. Calcd for $C_{14}H_{13}N_5S$: C, 59.34; H, 4.62; N, 24.72. Found: C, 59.48; H, 4.91; N, 24.63.

***2-Cyanomethyl-5-ethyl-8,9,10,11-tetrahydro [1]benzothieno[3,2-e][1,2,4]triazolo[1,5-c] pyrimidine (2b)***

Yield: 72 %. Mp: 160-162 °C. IR (KBr): 3049, 2967, 2229, 1638, 1616, 1574, 1552 $cm^{-1}$. $^1$H-NMR (300 MHz, DMSO-$d_6$) δ: 4.18 (s, 2H), 3.02 (m, 2H), 2.66-2.74 (m, 4H), 1.85 (m, 4H), 1.24 (t, 3H, J = 7.2). $^{13}$C-NMR (75 MHz, DMSO-$d_6$) δ: 16.4, 22.2, 22.8, 23.1, 24.7, 36.4, 38.0, 114.9, 119.2, 128.5, 132.1, 138.5, 148.1, 155.1, 159.1. GC/MS-MS ($EI^+$, TIC 1.52e6): *m/z* $[M-H]^-$ calcd for $C_{15}H_{15}N_5S$: 296.370; found: 296.383. Anal. Calcd for $C_{15}H_{15}N_5S$: C, 60.58; H, 5.08; N, 23.55. Found: C, 60.71; H, 5.01; N, 23.48.

***2-Cyanomethyl-5-methyl-8,9-dihydronaphtho [2,1-b]thieno[3,2-e][1,2,4]triazolo[1,5-c] pyrimidine (2c)***

Yield: 81 %. Mp: 208-210°C. IR (KBr): 3093, 2983, 2225, 1639, 1614, 1600, 1574, 1450, 771, 728 $cm^{-1}$. $^1$H-NMR (300 MHz, DMSO-$d_6$) δ: 7.46 (m, 1H), 7.18-7.14 (m, 3H), 4.27 (s, 2H), 2.91(m, 4H), 2.65 (s, 3H). $^{13}$C-NMR (75 MHz, DMSO-$d_6$) δ: 18.7, 24.9, 25.1 35.6, 114.9, 119.1, 126.2, 126.9, 128.5, 129.3, 132.1, 135.9, 138.5, 138.8, 149.0, 156.1, 157.7. GC/MS-MS ($EI^+$, TIC 1.52e6): *m/z* $[M-H]^-$ calcd for $C_{18}H_{13}N_5S$: 330.386; found: 330.401. Anal. Calcd for $C_{18}H_{13}N_5S$: C, 65.24; H, 3.95; N, 21.13. Found: C, 65.42; H, 4.04; N, 21.31.

***9-Benzyl-2-cyanomethyl-5-ethyl-8,9,10,11-tetrahydropyrido[4',3'-4,5]thieno[3,2-e][1,2,4] triazolo[1,5-c]pyrimi dine (2d)***

Yield: 67 %. Mp: 168-170 °C. IR (KBr): 3092, 2972, 2227, 1638, 1614, 1602, 1574, 1450, 770, 729, 700 $cm^{-1}$. $^1$H-NMR (300 MHz, DMSO-$d_6$) δ: 7.08-7.14 (m, 5H), 4.02 (s, 2H), 3.68 (m, 4H), 2.62-2.69 (m, 6H), 1.85 (m, 4H), 1.26 (t, 3H, J = 7.2). $^{13}$C-NMR (75 MHz, DMSO-$d_6$) δ: 16.4, 22.8, 23.2, 23.8, 52.2, 59.3, 61.9, 114.9, 118.8, 127.4, 128.2, 128.5, 130.3, 132.1, 136.7, 138.5, 147.3, 155.1, 158.2. GC/MS-MS ($EI^+$, TIC 1.52e6): *m/z* $[M-H]^-$ calcd for $C_{21}H_{20}N_6S$: 387.481; found: 387.497. Anal. Calcd for $C_{21}H_{20}N_6S$: C, 64.92; H, 5.19; N, 21.63. Found: C, 64.98; H, 5.12; N, 21.92.

***2-Cyanomethyl-9-phenylthieno[3,2-e][1,2,4] triazolo[1,5-c]pyrimidine (2e)***

Yield: 73 %. Mp: 170-172 °C. IR (KBr): 3102, 2968, 2227, 1635, 1616, 1602, 1574, 1450, 768, 730, 700 $cm^{-1}$. $^1$H-NMR (300 MHz, DMSO-$d_6$) δ: 7.46 (m, 2H), 7.28 (m, 2H), 7.18-7.22 (m, 2H), 4.08 (s, 2H), 2.62 (q, 2H, J = 7.2), 1.26 (t, 3H, J = 7.2). $^{13}$C-NMR (75 MHz, DMSO-$d_6$) δ: 16.2, 22.7, 23.7, 114.9, 118.8, 127.4, 128.2, 128.6, 129.3, 132.1, 136.7, 138.5, 147.7, 156.0, 159.1. GC/MS-MS ($EI^+$, TIC 1.52e6): *m/z* $[M-H]^-$ calcd for $C_{17}H_{13}N_5S$: 318.376; found: 318.383. Anal. Calcd for $C_{17}H_{13}N_5S$: C, 63.93; H, 4.10; N, 21.93. Found: C, 64.07; H, 4.17; N, 21.76.

**Biological studies**

***Antibacterial screening for thieno-triazolo-pyrimidines (2)***

Compounds **2 (a-e)** were examined for their antibacterial activity with paper disc (φ5 mm) method as described by [27-29] and compared with that of Tetracycline ($TE_{30,}$ 54882, 30µg), considered as reference. Strains used as test organisms in this study were; *Salmonella typhimurium (ATCC14028*: Source Département de génétique, Faculté de biologie, Université de Seville, Seville 41080, Espagne) *Pseudomonas aeruginosa* (Centre technique de l'agroalimentaire de Tunis) *Escherichia coli (JW 177*2) and *Staphylococcus aureus* (Centre technique de l'agroalimentaire de Tunis). Brievly, Tested compounds **2 (a-e)** were dissolved in a DMSO at different concentrations (1-54 M) as well as reference antibiotics $TE_{30}$ (20 mg/mL). Paper discs were soaked in each compound solution for 3-5 min an then transferred into the surface of growth media seeded with the test organism. After an incubation period (24 h at 35 ºC), the diameters of the inhibition zones around the discs were measured (mm). Standard blank with no added test compounds was also analyzed.

## RESULTS AND DISCUSSION

### Chemistry

### Synthesis of thienotriazolopyrimidines (2)

In fact these precursors possess two reactive sites, a cyano group and an imidic carbon. These groups render them susceptible to react with cyanoacetic acid hydrazide in refluxing toluene with catalytic amount of paratoluene sulfonic acid to afford thienotriazolopyrimidines **2** via the intermediate **2'**.

Indeed, the bis electrophilic character of iminoethers **2** would allow a successive two nucleophilic additions of -$NH_2$ group or two nitrogen of $NH_2$-NH- moiety on the imidic carbon and the cyano group, which would give respectively the intermediate amidothieno pyrimidines **2'** that can be evolved by intramolecular cyclization via elimination of water to compounds **2** and which was isolated in some cases (**2'a-b**) when ethanol was used as solvent or thienotriazepines **3** and/or their isomers **3'**. Based on spectral data and the isolation of intermediate **2'**, the reaction was proceeded to produce thienotriazolopyrimidine derivatives **2** rather than thienotriazepines **3**. It is interesting to note that substrates **2** synthesized may be considered as target molecules for synthetic organic chemistry as malonic derivatives **(Scheme 1).**

### Antibacterial screening for thieno-triazolo-pyrimidines (2)

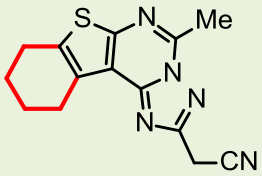
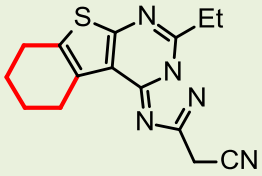
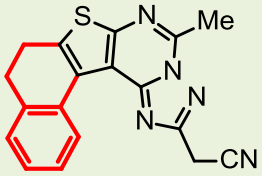
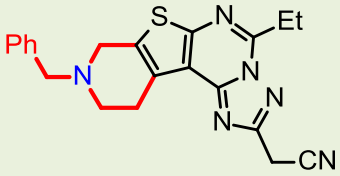
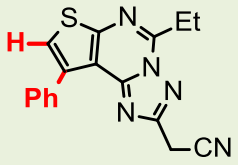
The obtained results are summarized in Table 1 and 2. Table 1 summarizes the $TE_{30}$ diameter of the inhibition zones against studied bacteria strains in a dimethylsulfoxide (DMSO).

The antibacterial activity was tested against some bacteria with different concentrations. This test is summarized by a resistance study of antibiotic with $TE_{30}$ responsible for removing all four species in a range of lyses according to the experimental conditions of more than 20 mm.

**Figure 1** Showed the observed inhibition-diameter of compounds **2 (a-e)** and reference antibiotics Tetracycline $TE_{30}$. The most interesting products are represented by the minimum inhibitory concentrations (MIC) . Our results show that thienotriazolopyrimidines exhibited a moderate antibacterial activity against both Gram-positive and Gram negative bacteria. Importanly, Thienotriazolo pyrimidines, **2a** did not show any significant antibacterial activity against all used strains (> 42 mg/mL) and no lyses plaque was observed with all concentrations used. Accordingly, compound **2b** inactivate *Staphylococcus and Salmonella* with a high MIC (34. 67 mg/mL) whereas compound **2c** seems to be more effective with a low MIC and agood IZ . With regard to the mechanism of antibacterial activity, one can speculate that compound 2b in not able to diffuse intracellular and to inhibits bacterial peptidoglycan. We note that adding a $CH_3$ in the fragment R decreases the activity. Furthermore, we noted that thienotriazolo -

pyrimidines **2e** showed an inhibition zone at about 5 mm against *Staphylococus. This result* may be probably related to the presence of the phenyl atom. Interestingly, compound **2d**

**Table 1**: Prepared synthesized thienotriazolopyrimidines 2

| Entry | thienotriazolopyrimidines 2 | Time (h) | Yield (%)* |
|---|---|---|---|
| 2a |  | 14 | 78 |
| 2b |  | 16 | 72 |
| 2c |  | 12 | 81 |
| 2d |  | 14 | 67 |
| 2e |  | 18 | 73 |

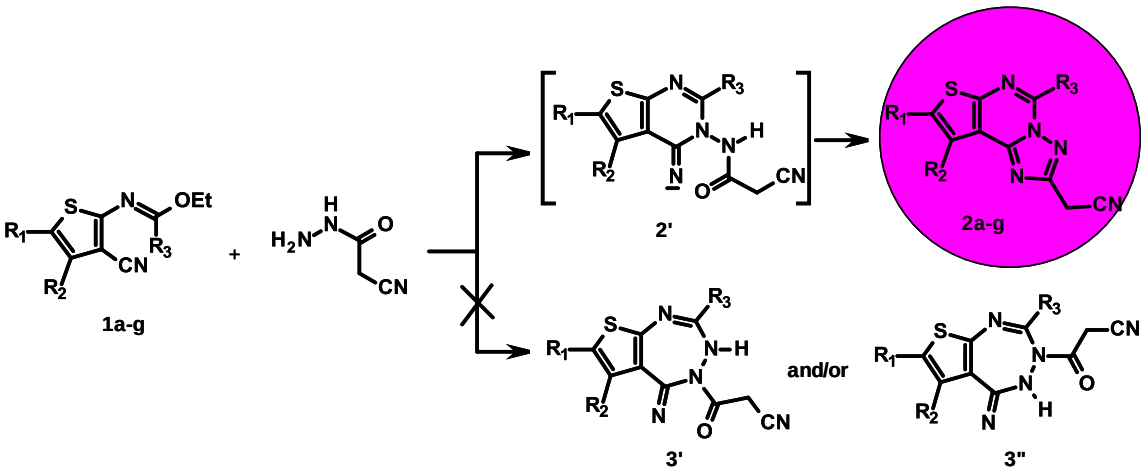
* Yield calculated using the reaction of Scheme 2

showed the highest inhibition zone at around 15 mm against *Staphylococus and Pseudomonas*. This result may be attributed to the presence of dihydronaphtho [30] and Benzyl atom [31] in the R ring. It is important to mention that all tested compounds; exept **2d** showed a low antibacterial activity in comparison with $TE_{30}$ reference as can be noticed from **Table 2**.

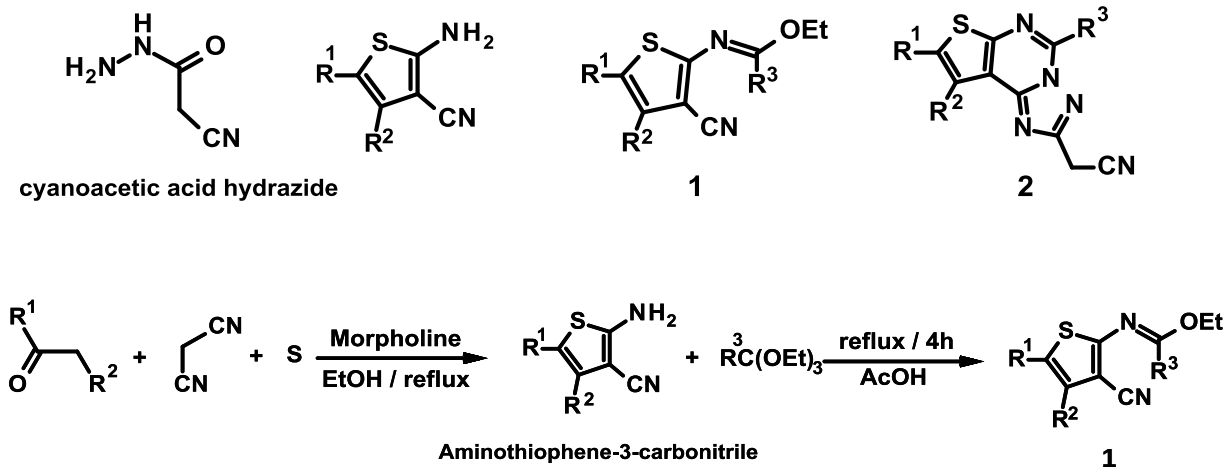
**Table 2: Antibacterial activity of compounds 2a-e as inhibition diameter or IZ Diameters (mm) and minimal inhibition concentration MIC (mg/mL)**

| | | Gram+ | | Gram - | |
|---|---|---|---|---|---|
| | | ***Staphylococcus*** | ***Pseudomonas*** | ***Escherichia*** | ***Salmonella*** |
| **2a** | (mm) | - | - | - | - |
| | (mg/mL) | - | - | - | - |
| **2b** | (mm) | 6.57 | - | - | 6.14 |
| | (mg/mL) | 34.67 | - | - | 34.67 |
| **2c** | (mm) | 7.5 | 11.5 | - | 4.5 |
| | (mg/mL) | 8.259 | 8.259 | - | 33.03 |
| **2d** | (mm) | 15.5 | 14.7 | - | - |
| | (mg/mL) | 16.74 | 16.74 | - | - |
| **2e** | (mm) | 5 | 5 | - | - |
| | (mg/mL) | 16.97 | 16.97 | - | - |
| **TE30(30µg)** | (mm) | 25 | 20 | 24 | 20 |
| | (mg/mL) | 20 | 20 | 20 | 20 |

**Sheme 1: The synthesis of 2-cyanomethylthieno [3,2-e] [1,2,4]- triazolo[1,5-c]pyrimidine**



**Scheme 2: Synthesis of iminoether and Chemical structures of starting material cyanoacetic acid hydrazide, aminothiphene-3-carbonitrile and synthesized compounds 2**



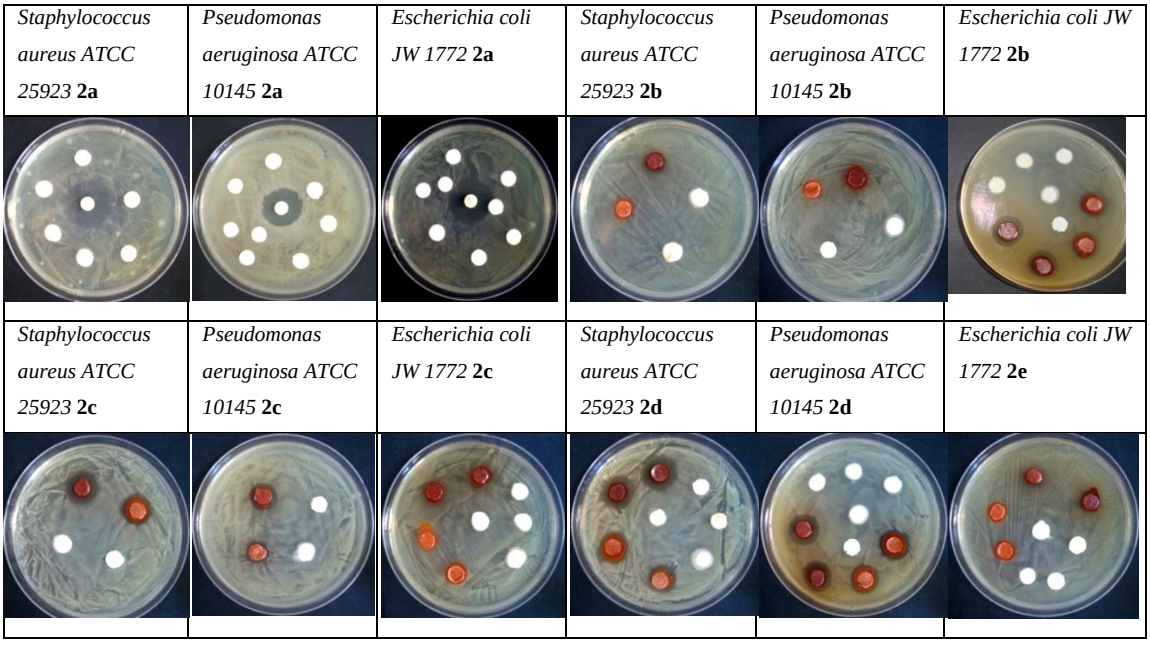




**Fig.1: Figures discs containing products synthesized by different concentrations**

## CONCLUSION

In conclusion, a series of 2-cyano-methyl-thieno-triazolo-pyrimidines **2 (a-e)** were synthesized and the structure was characterized on the basis of their infrared (IR), NMR and mass spectral data. All the title

compounds were tested for their antibacterial activity against four types of Bacteria. According to the results obtained, compounds **2 (a-e)** exhibited a moderate in vitro antibacterial activity compared to the $TE_{30}$ reference. Compound **2d** showed the highest antibacterial activity. This can be attributed to the R ring and the presence of dihydronaphtho and Benzyl atom.

## CONFLICT OF INTEREST STATEMENT

None Declared

## REFERENCES


1. El-Kerdawy MM, Yousif MY, El-Emam AA, Moustafa MA, El-Sherbeny MA. Synthesis and antiinflammatory activity of certain thienopyrimidine derivatives. Boll Chim Farm 1996; 135: 301-305.
2. Modica M, Santagati M, Santagati A, Cutuli V, Mangano N, Caruso A. Synthesis of new [1,3,4] thia-diazolo [3,2-a] thieno [2,3-d] pyrimidinone derivatives with anti-inflammatory activity. Pharmazie 2000; 55: 500-502.
3. Chambhare RV, Khadse BG, Bobde AS, Bahekar RH. Synthesis and preliminary evaluation of some N-[5-(2-furanyl)-2-methyl-4-oxo-4H-thieno[2,3-d]pyrimidin-3-yl]-carboxamide and 3-substituted-5-(2-furanyl)-2-methyl-3H-thieno[2,3-d]pyrimidin-4-ones as antimicrobial agents. Eur J Med Chem 2003; 38: 89-100.
4. Bhuiyan MD, Rahman KM, Hossain MD, Rahim A, Hossain MI, Abu Naser M. Synthesis and antimicrobial evaluation of some new thienopyrimidine derivatives. Acta Pharm 2006; 56: 441-450.
5. Rashad AE, Shamroukh AH, Abdel-Megeid RE, Mostafa A, El-Shesheny R, Kandeil A, Ali MA, Banert K. Synthesis and screening of some novel fused thiophene and thienopyrimidine derivatives for anti-avian influenza virus (H5N1) activity. Eur J Med Chem 2010; 45: 5251-5257.
6. Santagati NA, Caruso A, Cutuli VM, Caccamo F. Synthesis and pharmacological evaluation of thieno[2,3-d]pyrimidin-2,4-dione and 5H-pyrimido [5,4-b]indol-2,4-dione derivatives. Farmaco 1995; 50: 689-695.
7. Jennings LD, Kincaid SL, Wang YD, Krishnamurthy G, Beyer CF, McGinnis JP, Miranda M, Discafani CM, Rabindran SK. Parallel synthesis and biological evaluation of 5, 6, 7, 8-tetrahydro-benzothieno [2, 3-d] pyrimidin-4(3H)-one cytotoxic agents selective for p21-deficient cells. Bioorg Med Chem Lett 2005; 15: 4731-4735.
8. Alqasoumi SI, Ragab FA, Alafeefy AM, Galal M, Ghorab MM. Radioprotective and anti-tumor activity of some novel amino acids and imidazoles containing Thieno [2,3-d]pyrimidine moiety. Phos Sul Silicon 2009; 184: 3241-3257.
9. Soliman R, Habib NS, El-Tombary AA, El-Hawash SAM, Shabaan OG. Synthesis of tetrahydro benzothieno [2,3-d] pyrimidine and tetrahydro benzothieno [3,2-e]-[1,2,4] triazolo [4,3-c] pyrimidine derivatives as potential antimicrobial agents. Sci Pharm 2009; 77: 755-773.
10. Alagarsamy V, Meena S, Ramseshu KV, Solomon VR, Thirumurugan K, Dhanabal K, Murugan M. Synthesis, analgesic, anti-inflammatory, ulcerogenic index and antibacterial activities of novel 2-methylthio-3-substituted-5,6,7,8-tetrahydrobenzo (b) thieno[2,3-d]pyrimidin-4(3H)-ones. Eur J Med Chem 2006; 41: 1293-1300.
11. Ashalatha BV, Narayana B, Vijaya Raj KK, Suchetha Kumari N. Synthesis of some new bioactive 3-amino-2-mercapto-5,6,7,8-tetra -hydro[1]benzothieno[2,3-d]pyrimidin-4(3H)-one derivatives. Eur J Med Chem 2007; 42: 719-728.
12. Rashad AE, Ali MA. Synthesis and antiviral screening of some thieno [2, 3-d] pyrimidine nucleosides. Nucleosides Nucleotides Nucleic Acids 2006; 25: 17-28.

13. Prasad MR, Rao AR, Rao PS, Rajan KS, Meena S, Madhavi K. Synthesis and adenosine receptor binding studies of some novel triazolothienopyrimidines. Eur J Med Chem 2008; 43: 614-620.
14. Poucher SM, Keddie JR, Singh P, Stoggal SM, Caulkett PWR, Jones G, Collis MG. The in vitro pharmacology of ZM2413885, a potent, non xanthine, A2a selective adenosine receptor antagonist. Br J Pharmacol 1995; 115: 1096-1102.
15. Zocchi C, Ongini E, Conti A, Monopoli A, Negretti A, Baraldi PG, Dionisotti S. The non-xanthine heterocyclic compound SCH 58261 is a new potent and selective A2a adenosine receptor antagonist. J Pharmacol Exp Ther 1996; 276: 398-404.
16. Ballesteros AB, Elmasnaouy M, Ocon PD, Ivorra MD, Valiente M, Evaluation and synthesis of 7-arylhydroxymethyltriazolo pyridines as potential cardiovascular agents. Arkivoc 2002; 10: 9-13.
17. Sanghavi YS, Larson SB, Robinse RK, Revenkar GR. Synthesis and Biological Evaluation of Certain C-4 Substituted Pyrazolo [3,4-b]Pyridine Nucleosides. J Med Chem 1989; 32: 945-951.
18. Bakavoli M, Bagherzadeh G, Vaseghifar M, Shiri A, Pordel M, Pordeli P, Araghi M. Molecular iodine promoted synthesis of new pyrazolo [3,4-d]pyrimidine derivatives as potential antibacterial agents. Eur J Med Chem 2010; 45: 647-650.
19. Fathalla OA, Zeid IF, Haiba ME, Soliman AM. Synthesis, antibacterial and anticancer evaluation of some pyrimidine derivatives. World J Chem 2009; 4: 127-132.
20. Gangjee A, Qiu Y, Kisliuk RL. Synthesis of classical and nonclassical 2-amino-4-oxo-6-benzylthieno-[2,3-*d*] pyrimidines as potential thymidylate synthase inhibitors. J Heterocycl Chem 2004; 41: 941–946.
21. Kolavi GD, Hegde VS, Khazi IM. Synthesis and antimicrobial activity of tricyclic thienopyrimidines and 1, 3, 4-triazole fused thienopyrimidines. Tetrahedron Lett 2006; 47: 2811-2814.
22. Kolavi GD, Hegde VS, Khazi IM, Gadad P. Synthesis and evaluation of antitubercular activity of imidazo[2, 1-b][1, 3, 4]thiadiazole derivatives. Bioorg Med Chem 2006; 14: 3069-3080.
23. Hegde VS, Kolavi GD, Khazi IM. Chemoselectivity of thiophene dicarboxylate towards hydrazine hydrate: synthesis of some bis heterocycles from thiophene monocarbohydrazide. J Sulfur Chem 2006; 27: 307-314.
24. Dridi K, El Efrit ML, Zantour H. Action d' amines et de derives d'hydrazines sur les N-(3-carbetoxy-2-thieny) imino ethers: synthese de thieno [2, 3-d] pyrimidin-4(3H)-ones. J Soc Chim Tunisie 1999; 5: 387-392.
25. Dridi K, Ben Said R, Arfaoui Y, Al-Ayed AS. Activated bentonite promoted Friedländer condensation reactions: Synthesis of thieno [2, 3-b] quinolinones and tacrines analogues derivatives. Eur J Chem 2013; 4: 216-219.
26. Jabli D, Dridi K, Efrit ML. A convenient synthesis of new 2-cyanomethylthieno [3,2-e][1,2,4]- triazolo [1,5-c] pyrimidine derivatives. Lett in Org Chem 2014; 11: 403-409.
27. Murray PR, Baron EJ, Jorgensen JH, Pfaller MA, Yulken RH. Manual of Clinical Microbiology. Washington, DC, USA: American Society for Microbiology Press (ASM); 2003, p 1212.
28. Delost MD. Introduction to Diagnostics Microbiology, Text and Work Book. USA: Mosby, Inc: Sc, Louis, MO; 1997, p 552.
29. Khulud M Al-T, Hassan MA Al-H, Shar S Al-S. Synthesis, characterization and biological studies of some novel thieno [2,3-d] pyrimidines. Molecules 2010; 15: 3932-3957.
30. Abdel-Megeid FME, Hassan NA, Zahran MA, Rashad AE. Synthesis of 5,6-dihydronaphtho [1',2':4,5] thieno [2,3-d] pyrimidines- 5, 6-dihydronaphtho [1',2':4,5]thieno[3,2-e][1,2,4]triazolo[1,5-c] pyrimidines and some

of their nucleosides. Sulfur Lett 1998; 21: 269-284.

31.Chen H, Yan K. 6-Benzyl-2-[(triphenyl-5-phosphanylidene)amino]-4,5,6,7-tetrahydro-thieno [2,3-c] pyridine-3-carbonitrile.Acta Cryst 2011; E67: 2548-2551.

**Cite this article as:**
Dhiab Jabli, Karima Lahbib, Khaireddine Dridi, Mohamed Lotfi Efrit. Antibacterial Study Novel 2-cyanomethylthieno [3,2-e] [1,2,4]- triazolo[1,5-c]pyrimidine. J Pharm Chem Biol Sci 2015; 3(2):178-187