American Journal of Organic Chemistry 2015, 5(2): 73-77
DOI: 10.5923/j.ajoc.20150502.02

A Convenient access to Functionalized 1,3,4-Thiadiazole, Thiazole, Thiophene, Thieno[2,3-*d*]pyrimidine, Pyrimidine, and Thiazolo[3,2-*a*]pyrimidine Derivatives

Ahmad M. Farag[1], Nabila A. Kheder[1,2,*], Kamal M. Dawood[1,3]

[1]Department of Chemistry, Faculty of Science, Cairo University, Giza, Egypt
[2]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, King Khalid University, Abha, Saudi Arabia
[3]Department of Chemistry, Faculty of Science, Kuwait University, Safat, Kuwait

Abstract Novel thiophene, pyrimidine, 1,3-thiazole, 1,3,4-thiadiazole**,** thieno[2,3-*d*]pyrimidine, and thiazolo[3,2-*a*]pyrimidine derivatives bearing pyridine moiety were synthesized starting from the readily accessible 3-oxo-*N*-(pyridin-2-yl)butanamide.

Keywords Hydrazonoyl halides, Pyrimidine, 1,3,4-Thiadiazole, Thieno[2,3-d]pyrimidine, Thiazolo[3,2-a]pyrimidine

1. Introduction

The pyridine ring is present in numerous pharmacologically important compounds and natural products [1, 2]. These include the anti-inflammatory Piroxicam (A), anti-anginal Nifedipine (B), anti-hypertensive Pinacidil (C) and Picloram (D) which is highly active against broad leaved plants. In addition, pyridine derivatives show insecticidal activities [3]. Furthermore, 3-oxo-*N*-(pyrid-2-yl) butanamide (**1**) has been used as a key synthon in synthesis of biologically active heterocycles [4-7]. Encouraged by all these findings and in continuation of our previous work aimed at the synthesis of a variety of heterocyclic systems for biological and pharmacological evalution [8-27], we report herein a convenient route to several new pyridine-based heterocyclic compounds, via the readily accessible 3-oxo-*N*-(pyrid-2-yl) butanamide (**1**) [28] as a versatile building block for the title compounds which are expected to have interesting biological activity.

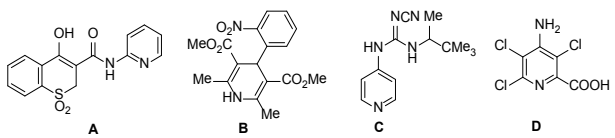
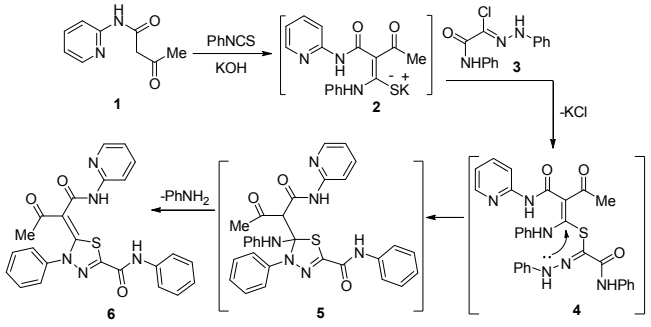


Figure 1. Example of pharmacologically important pyridines

* Corresponding author:
nabila_abdelshafy@yahoo.com (Nabila A. Kheder)
Published online at http://journal.sapub.org/ajoc

2. Results and Discussion

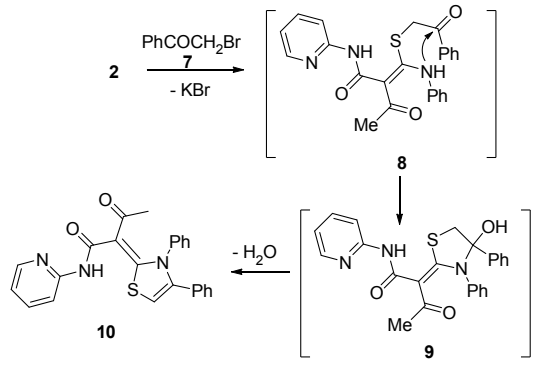
The nucleophilic addition of the butanamide **1** to phenyl isothiocyanate in DMF, in the presence of potassium hydroxide, afforded the corresponding potassium salt **2**. Heterocyclisation of the intermediate **2** with hydrazonoyl chloride **3** [29] furnished one isolable product. Which was identified as thiadiazole derivative **6** (Scheme 1). The ^{1}H NMR spectrum of compound **6** showed signals at δ 2.20 due to CH_3, two D_2O-exchangeable signals at δ 10.23 and 11.74 due to two NH protons, in addition to aromatic multiplet at δ 7.00-8.24. Its mass spectrum revealed molecular ion peak at *m/z* 458. The formentioned results indicate that the reaction of the non-isolable intermediate **2** with the hydrazonoyl chloride **3** proceeded *via* loss of potassium chloride and aniline molecules, respectively.



Scheme 1. Synthesis of 1,3,4-thiadiazole derivative **6**

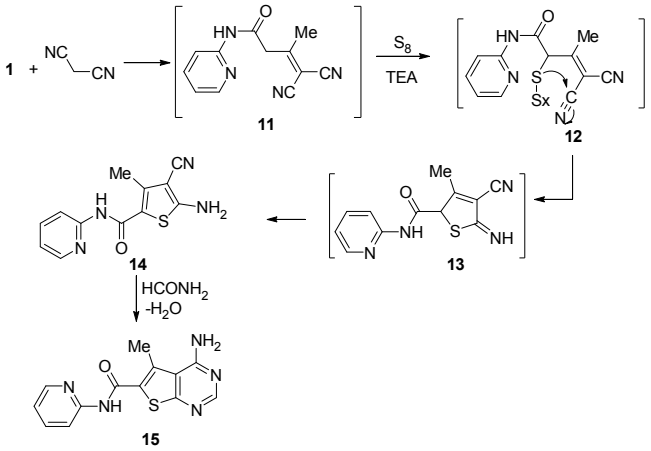
Treatment of potassium salt **2** with 1-phenyl-2-bromoethanone (**7**) [30] gave 2-(3,4-diphenyl

thiazol-2(3*H*)-ylidene) -3-oxo-*N*-(pyridin-2-yl)butanamide (**10**) in good yield (Scheme 2). The reaction proceeds *via* nucleophilic displacement of bromide to give *S*-alkylated intermediate **8**, followed by nucleophilic addition of NH group to the carbonyl group of benzoyl moiety to give the respective intermediate **9**. The latter intermediate was converted into the thiazole derivative **10** via loss of a water molecule (Scheme 2).



Scheme 2. Synthesis of thiazole derivative **10**

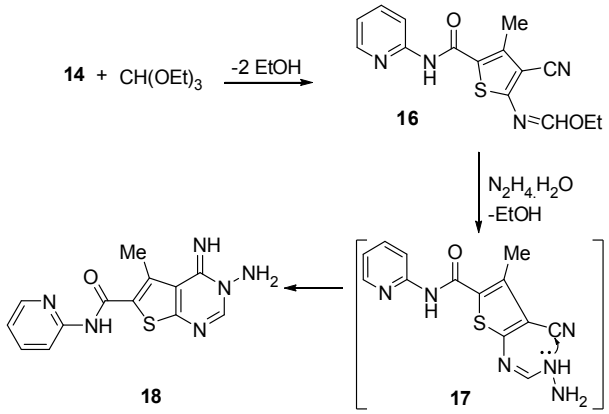
2-Amino-3-functionally substituted thiophene derivatives are useful precursors in azo dye production in industry and as intermediates for the pharmaceutically important thieno[2,3-*d*]pyrimidines [31, 32]. It was worthwhile to investigate the reaction of the butanamide **1** with elemental sulfur and malononitrile, which led to the formation of 5-amino-4-cyano-3-methyl-*N*-(pyridin-2-yl)thiophene-2-car boxamide (**14**) (Scheme 3)



Scheme 3. Synthesis of thiophene 14 and thieno[2,3-*d*]pyrimidine 15

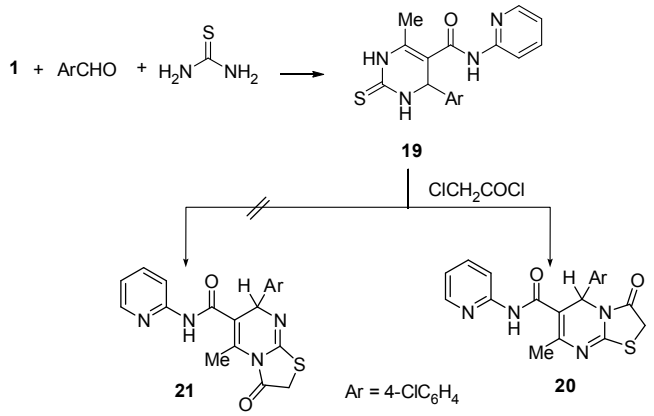
The structure of the latter was established from its elemental analysis and spectral data. For example, its IR spectrum revealed absorption bands at 1638, 2206, 3165-3346, 3439 cm^{-1} due to amide carbonyl, nitrile, amino and NH Functions, respectively. Its ^1H NMR showed signals at δ 2.41 due to CH_3 and D_2O-exchangeable signals at δ 7.80, 9.85 due to NH_2 and NH protons, respectively, in addition to an aromatic multiplet at δ 7.09-8.35. Its mass spectrum revealed a molecular ion peak at *m/z* 258. When compound **14** was refluxed with formamide, it afforded the thieno[2,3-*d*]pyrimidine **15** (Scheme 3).

Compound **14** reacts also with triethyl orthoformat under reflux to give the corresponding thiophene **16**, in excellent yield (Scheme 4). Compound **16** reacts with hydrazine hydrate to afford the corresponding thieno[2,3-d]pyrimidine **18** (Scheme 4). The structures of the isolated products **14**, **16**, and **18** were established from their elemental analyses and spectral data (see experimental part).



Scheme 4. Synthesis of thieno[2,3-*d*]pyrimidine **18**

4-(4-Chlorophenyl)-6-methyl-*N*-(pyridin-2-yl)-2-thioxo-1,2,3,4-tetrahydro-pyrimidine-5-carboxamide (**19**) was prepared by the acid-catalysed condensation of a ternary mixture of the butanamide **1**, thiourea and 4-chlorobenzaldehyde (Scheme 5). Both the elemental analysis and spectral data of **19** are consistent with the assigned structure [33, 34]. The ^1H NMR spectrum of **19** showed signals at δ 2.09, 5.41, 7.02-8.27, 9.40, 10.01 and 10.2 due to methyl, pyrimidine-4H, aromatic multiplet and three D_2O-exchangeable signals due to three NH protons, respectively. Heating compound **19** with chloroacetyl chloride in dry dioxane under reflux afforded 5-(4-chloro phenyl)-7-methyl-3-oxo-*N*-(pyridin-2-yl)-3,5-dihydro-2*H*-thiazolo-[3,2-*a*]pyrimidine-6-carboxamide (**20**) (Scheme 5). The ^1H NMR spectrum of compound **20** showed signals at δ 2.13, 4.15, 6.12, 7.20-8.32 and D_2O exchangeable at δ 11.15 due to methyl, CH_2, pyrimidine-4H, aromatic multiplet and NH protons, respectively. Its IR spectrum displayed absorption bands at 1684, 1765 and 3377 cm^{-1} due two carbonyl and NH groups, respectively. The ^1H NMR spectra of compound **20** is in favor of its structure. The chemical shift of the pyrimidine-4H proton in **19** appeared at δ 5.41 while the corresponding pyrimidine proton in **20** appeared at δ 6.12. The low-field shift of pyrimidine protons is in support of structure **20**. Also, the chemical shifts of the methyl group in **19** and **20** appeared at almost the same δ value. If structure **21** was present, one would expect low-field shift of methyl group due to deshielding by the neighbouring carbonyl group.



Scheme 5. Synthesis of pyrimidine **19** and thiazolo[3,2-*a*]pyrimidine **20**

3. Experimental

All melting points were measured on a Gallenkamp melting point apparatus. The infrared spectra were recorded in potassium bromide disks on a Pye Unicam SP 3300 and Shimadzu FT IR 8101 PC infrared spectrophotometers. The NMR spectra were recorded on a Varian Mercury VX-300 NMR spectrometer. ^{1}H spectra were run at 300 MHz and ^{13}C spectra were run at 75.46 MHz in deuterated chloroform ($CDCl_3$) or dimethyl sulphoxide (DMSO-d_6). Chemical shifts were related to that of the solvent. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX mass spectrometer at 70 e.V. Elemental analyses were carried out at the Microanalytical Center of Cairo University, Giza, Egypt. 3-Oxo-*N*-(pyrid-2-yl)butanamide (**1**) [28], hydrazonoyl chlorides **3** [29], 1-phenyl-2-bromoethanone (**7**) [30], and pyrimidine derivative **19**[33,34] were prepared according to the reported literature.

Rections of 3-oxo-*N*-(pyrid-2-yl)butanamide (1) with phenyl isothiocyanate, hydrazonoyl halide and α-heloketones.

General Procedure: To a stirred solution of potassium hydroxide (0.11 g, 2 mmol) in DMF (20 mL) was added the butanamide **1** (0.36 g, 2 mmol). After stirring for 30 min., phenyl isothiocyanate (0.27 g, 0.24 mL, 2 mmol) was added to the resulting mixture. Stirring was continued for 6 h, then the hydrazonoyl chloride **3** or 1-phenyl-2-bromoethanone (**7**) was added portionwise over a period of 30 min. After the addition was complete, the reaction mixture was stirred for additional 12 h, during which a solid product was precipitated. The solid product was filtered off, washed with water and dried. Recrystallization from the suitable solvent afforded the corresponding products **6** or **10**, respectively.

5-(1,3-Dioxo-1-(pyridin-2-ylamino)butan-2-ylidene)-*N*,4-diphenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxamide (6).

Yield (86%), mp 226-7℃ (EtOH); IR (KBr) ν_{max} /cm^{-1}: 3385 (NH), 3283 (NH), 1645 (C=O); ^{1}H NMR (DMSO-d_6) δ 2.20 (s, 3H, CH_3), 7.00-8.24 (m, 14H, ArH), 10.23 (s, 1H, D_2O-exchangeable, NH), 11.74 (s,1H, D_2O-exchangeable, NH); MS (*m/z*, %): 458 (M^+, 3.7). Anal. Calcd for $C_{24}H_{19}N_5O_3S$: C, 63.01; H, 4.19; N, 15.31. Found: C, 63.10; H, 4.25; N, 15.21%.

2-(3,4-Diphenylthiazol-2(3*H*)-ylidene)-3-oxo-*N*-(pyridin-2-yl)butanamide (10).

Yield (80%), mp 168-170 °C (EtOH); IR (KBr) ν_{max} /cm^{-1}: 3258 (NH), 1676 (C=O), 1618 (C=O); ^{1}H NMR ($CDCl_3$) δ 2.17 (s, 3H, CH_3), 5.96 (s, 1H, CH), 7.01-7.81 (m, 14H, ArH), 10.7 (s, 1H, D_2O- exchangeable, NH); MS (*m/z*, %): 415 (3.4), 414 (15.2), 413 (M^+, 54.8), 336 (0.3), 78 (33.1), 77 (100.0). Anal. Calcd for $C_{24}H_{19}N_3O_2S$: C, 69.71; H, 4.63; N, 10.16. Found: C, 69.78; H, 4.72; N, 10.25%.

5-Amino-4-cyano-3-methyl-*N*-(pyridin-2-yl)thiophene-2-carboxamide (14).

To a solution of the butanamide **1** (3.56 g, 20 mmol) in EtOH (20 mL), elemental sulfur (0.64 g) was added malononitrile (1.32 g, 20 mmol) and a catalytic amount of triethylamine. The reaction mixture was heated at 60-65℃ for 30 min, then allowed to cool to room temperature. The precipitated solid was filtered off, washed with EtOH, dried and finally recrystallized from DMF/water to afford **14** in 90%, mp 270-1℃; IR (KBr) ν_{max} /cm^{-1}: 3439 (NH), 3165 and 3346 (NH_2), 2206 (C≡N), 1638 (C=O); ^{1}H NMR ($CDCl_3$) δ 2.41 (s, 3H, CH_3), 7.09-8.35 (m, 4H, ArH), 7.8 (br., 2H, D_2O-exchangeable, NH_2), 9.85 (s, 1H, D_2O-exchangeable, NH); ^{13}C NMR (DMSO-d_6) δ 15.01, 88.53, 112.95, 114.19, 115.29, 119.36, 137.93, 141.34, 147.77, 151.88, 160.72, 165.70; MS (*m/z*, %): 260 (9.5), 259 (50.9), 258 (M^+, 38.7), 121 (3.7), 93 (9.5), 78.(13.0). Anal. Calcd for $C_{12}H_{10}N_4OS$: C, 55.80; H, 3.90; N, 21.69. Found: C, 55.91; H, 3.96; N, 21.78%.

4-Amino-5-methyl-N-(pyridin-2-yl)thieno[2,3-*d*]pyrimidine-6-carboxamide (15).

A mixture of **14** (0.52 g, 2 mmol) and freshly distilled formamide (8 mL) was heated under reflux for 7h., then left to cool. The formed solid product was filtered off, washed with water and dried. Recrystallization from DMF afford **15** in 77% yield; mp >300℃; IR (KBr) ν_{max} /cm^{-1}: 3442- 3167 (NH and NH_2), 1692 (C=O); ^{1}H NMR (DMSO-d_6) δ 2.73 (s, 3H, CH_3), 7.1-7.2 (m, 1H), 7.3 (br., 2H, D_2O-exchangeable, NH_2), 7.6-8.39 (m, 3H), 10.61 (s, 1H) 12.57 (s, 1H, D_2O-exchangeable, NH); ^{13}C NMR (DMSO-d_6) δ 15.25, 114.49, 116.30, 119.99, 138.18, 139.12, 147.38, 147.93, 155.0, 155.54, 159.96, 164.16, 166.75. Anal. Calcd for $C_{13}H_{11}N_5OS$: C, 54.72; H, 3.89; N, 24.55. Found: C, 54.79; H, 3.81; N, 24.48%.

Ethyl *N*-3-cyano-4-methyl-5-(pyridin-2-ylcarbamoyl) thiophen-2-ylformimidate (16).

A mixture of compound **14** (5.16 g, 20 mmol) and triethyl orthoformate (5 mL) was refluxed for 4h, then left to cool to room temperature. The precipitated product was filtered off, washed with EtOH and dried. Recrystallization from EtOH afforded **16** in 90% yield, mp 130-2℃ (EtOH); IR (KBr)

ν_{max} /cm^{-1}: 3437 (NH), 2224 (C≡N), 1653 (C=O); MS (*m/z*, %): 318 (1.0), 317 (4.3), 316 (11.4), 315 (61.6), 314 (M^+, 68.7), 299 (13.3), 288 (0.5), 193 (28.2), 121 (17.8), 93 (16.1), 78 (39.6). Anal. Calcd for $C_{15}H_{14}N_4O_2S$: C, 57.31; H, 4.49; N, 17.82. Found: C, 57.38; H, 4.41; N, 17.89%.

3-Amino-4-imino-5-methyl-N-(pyridin-2-yl)-3,4-dihydro thieno[2,3-*d*]pyrimidine-6-carboxamide (18).

To a solution of **16** (0.63g, 2 mmol) in EtOH (20 mL), hydrazine hydrate (80%, 0.2 mL) was added and the reaction mixture was refluxed for 4 h, then allowed to cool. The formed solid product so was filtered off, washed with EtOH and dried. Recrystallization from EtOH/DMF afforded **18** in 88% yield, mp 255-6℃; IR (KBr) ν_{max} /cm^{-1}: 3312 (NH), 3206-3250 (NH_2 and 2NH), 1660 (C=O); ^{1}H NMR (DMSO-d_6) δ 2.8 (s, 3H, CH_3), 5.6 (s, 2H, D_2O-exchangeable, NH_2), 7.6 (br.,1H, D_2O-exchangeable, NH), 7.15-8.35 (m, 5H, ArH), 10.35 (s, 1H, D_2O-exchangeable, NH); MS (*m/z*, %): 301 (0.8), 300 (M^+, 59.12), 121 (1.7), 93 (3.1), 78 (4.4). Anal. Calcd for $C_{13}H_{12}N_6OS$: C, 51.99; H, 4.03; N, 27.98. Found: C, 52.06; H, 4.18; N, 27.85%.

5-(4-Chlorophenyl)-7-methyl-3-oxo-*N*-(pyridin-2-yl)-3,5-dihydro-2*H*-thiazolo[3,2-*a*]pyrimidine- 6-carboxamide (20).

To a solution of pyrimidine derivative **19** (1.79 g, 5 mmol) in dioxane (20 mL) was added chloroacetyl chloride (0.57 g, 0.40 mL, 5 mmol) and the reaction mixture was heated under reflux, where the reactants went into solution and a yellow precipitate was formed. The obtained solid product was collected by filtration, washed with EtOH, dried and then crystallized from DMF/H_2O to afford **20** in 70% yield, mp 217-8℃; IR (KBr) ν_{max} /cm^{-1}: 3377 (NH), 1765 (C=O), 1684 (C=O); ^{1}H NMR (DMSO-d_6) δ 2.13 (s, 3H, CH_3), 4.15 (s, 2H, CH_2), 6.12 (s, 1H, pyrimidine CH), 7.20-8.32 (m, 8H, ArH), 11.15 (s, 1H, D_2O-exchangeable, NH). Anal. Calcd for $C_{19}H_{15}N_4O_2SCl$: C, 57.21; H, 3.79; N, 14.05. Found: C, 57.29; H, 3.70; N, 14.11%.

4. Conclusions

A new simple approach to novel thiophene, pyrimidine, 1,3-thiazole, 1,3,4-thiadiazole, thieno[2,3-*d*]pyrimidine, and thiazolo[3,2-*a*]pyrimidine derivatives bearing pyridine moiety have been achieved starting from the readily accessible 3-oxo-*N*-(pyridin-2-yl)butanamide (**1**).

REFERENCES

[1] Wegner, H. A., 2012, Anything but old-fashioned: structure of Pyridines, Nachrichten aus der Chemie, 60, 39-43.

[2] Kiuru, P., and Yli-Kauhaluoma, J., 2011, Pyridine and its derivatives in natural product synthesis, Heterocycles in Natural Product Synthesis, 267-297.

[3] Di, X., Liu, Y., Yu, X. , Xiao, H., Tian, X. and Gao, R., 2007, Synthesis and insecticidal activities of pyridine ring derivatives of podophyllotoxin, Pesticide Biochemistry and Physiology, 89(1), 81-87.

[4] Wei, Y., Liu, J., Lin, S., Ding, H., Liang, F., and Zhao, B., 2010, Acetoacetanilides as Masked Isocyanates: Facile and Efficient Synthesis of Unsymmetrically Substituted Ureas Org. Lett., 12(19), 4220-4223.

[5] Fadda, A. A., Bondock, S. B., Khalil, A. M., and Tawfik, E. H., 2013, Synthesis of some new 1,2,3,4 -tetrahydro pyrimidin-2-thione and their thiazolo[3,2-a]pyrimidine, thiazino and benzothiazepine derivatives, J. Heterocycl. Chem., 50(4), 838-834.

[6] Huggins, M. T., Barber, P. S., Florian, D., and Howton, W., 2008, Short, efficient syntheses of pyrrole α-amides, Synth. Comm., 38(23), 4226-4239.

[7] Fassihi, A., Azadpour, Z., Delbari, N., Saghaie, L., Memarian, H.R., Sabet, R., Alborzi, A., Miri, R., Pourabbas, B., Mardaneh, J., Mousavi, P., Moeinifard, B., and Sadeghi-aliabadi, H., 2009, Synthesis and antitubercular activity of novel 4-substituted imidazolyl-2,6-dimethyl-N3,N5-bisaryl-1,4-dihydropyridine-3,5-dicarboxamides, Eur. J. Med. Chem. 44 (8), 3253-3258.

[8] Kheder, N. A., Mabkhot, Y. N., and Farag, A. M., 2009, A Convenient route to new pyrrolo[1,2-c]pyrimidone, thiazolo[3,4-c]pyrimidone and pyrimido[4,5-d]pyridazine derivatives, Heterocycles, 78 (4), 937-946.

[9] Kheder, N. A., and Mabkhot, Y. N., 2012, Synthesis and antimicrobial studies of some novel bis-[1, 3, 4] thiadiazole and bis-thiazole pendant to thieno[2, 3-*b*] thiophene moiety, Int. J. Mol. Sci., 13 (3), 3661-3670.

[10] Kheder, N. A., Riyadh, S. M., and Asiry, A. M., 2013, Azoles and bis-azoles: Synthesis and biological evaluation as antimicrobial and anti-cancer agents, Chem. Pharm. Bull., 61(5), 504-510.

[11] Farag, A. M., Dawood, K. M., and Khedr, N. A., 2007, Regioselective Synthesis of Novel 4,4′-and 5,5′-bi-(l,2,4-triazole) derivatives, J. Chem. Res. (S), (8), 472-474.

[12] Kheder, N. A., Mabkhot, Y. N., and Farag, A. M., 2008, A Convenient access to new pyrido[4,3-d]pyrimidine, thiazolo[3,4-c]pyrimidine and pyrimido[4,5-d]pyridazine derivatives, *Arkivoc,* (xvii) 107-116.

[13] Farag, A. M., Mayhoub, A. S, Barakat, S. E, and Bayomi, A. H., 2008, Synthesis of new *N*-phenylpyrazole derivatives with potent antimicrobial activity, Bioorg. Med. Chem., 16(8),4569-4578.

[14] Farag, A. M., Mayhoub, A. S,, Barakat, S. E., and Bayomi, A. H., 2008, Regioselective synthesis and antitumor screening of some novel N-phenylpyrazole derivatives, Bioorg. Med. Chem., 16(2), 881-889.

[15] Kheder, N. A., Mabkhot, Y. N., Farag, A. M., 2008, Facile and convenient synthesis of pyrazole, pyridine, pyridazine, pyrazolo [3, 4-b] pyridine, and pyrazolo [5, 1-*c*][1, 2, 4] triazine derivatives, Synthetic Communications, 38 (18), 3170-3182.

[16] Kheder, N. A., 2009, Convenient synthesis of novel bis(hydrazone) and bis(indole) derivatives, Heterocycles, 78 (5), 1281- 1288.

[17] Mabkhot, Y. N., Kheder, N. A., Al-Majid, A. M., 2010, Facile and convenient synthesis of new thieno [2, 3-b]-thiophene derivatives, Molecules 15 (12), 9418-9426.

[18] Farag, A. M., Kheder, N. A, and Mabkhot, Y. N., 2009, Synthesis and antimicrobial evaluation of new pyrazole, thiophene, thiazole and 1, 3, 4-thiadiazole derivatives incorporating pyrimidine ring, Heterocycles 78 (7), 1787-1798.

[19] Kheder, N. A., Darwish, E. S., and Dawood, K. M., 2009, Synthesis of some new inolizine and pyrrolo [1, 2-a]quinoline derivatives via nitrogen ylides, Heterocycles 78 (1), 177-188.

[20] Kheder, N. A., Mabkhot, Y. N., and Farag, A. M., 2008, Synthesis and antimicrobial evaluation of some bis (thioxopyridine), bis (pyrazolo [3, 4-b] pyridine), bis (thieno [2, 3-b] pyridine), bis (1, 3, 4-thiadiazole) and bis-thiophene derivatives, Heterocycles 75 (12), 2937-2948.

[21] Dawood, K. M., Ragab, E. A., and Kheder, N. A., 2009, Facile Access to Annulated quinoline and isoquinoline Heterocycles via Their Nitrogen Ylides, J. Chin. Chem. Soc*., 56,* 1180-1185.

[22] Dawood, K. M., Kheder, N. A., Ragab, E. A., Mohamed, S. N., 2010, A facile access to some new pyrazole, 1, 3, 4-thiadiazole, and thiophene derivatives via β-ketosulfones, Phosphorus, Sulfur, and Silicon, 185 (2), 330-339.

[23] Riyadh, S. M., Kheder, N. A., Asiry, A. M., 2013, Synthesis, anticancer, and antimicrobial activities of some new antipyrine-based heterocycles, Monatshefte für Chemie, 144 (10), 1559-1567.

[24] Farag, A. M., Kheder, N. A., and Dawood, K. M., 2013, Efficient Syntheses of Some New Pyridine Based Heterocycles, Internat. J. Modern Org. Chem., 2 (1), 26-39.

[25] Kheder,N. A., and Farghaly, T. A., 2013, *Bis*-Hydrazonoyl chloride as precursors for synthesis of novel polysubstituted *bis*-azoles, in press, Arabian J of Chem., doi:10.1016/j. arabjc.2013.11.040.

[26] Dawood, K.M., and Abu-Deif, H., 2014, Synthesis and Antimicrobial Evaluation of Some new 1,2-bis-(2-(N-arylimino)-1,3-thiazolidin-3-yl)ethane derivatives, Chem. Pharm. Bull, 62 (5) 439-445.

[27] Dawood, K. M., Abu-Deif, H., 2013, Synthesis and Antimicrobial Activity of Some new 1,2-bis-[1, 3-thiazolidin-3-yl]ethane derivatives, Eur. J. Chem, 4 (3), 277-284.

[28] Allen, C. F. H., Van Allan, J., and Wilson, C. V., 1944, Certain Azomethines in the Pyrimidazolone Series, J. Am. Chem. Soc., 66 (11), 1805–1810.

[29] Shawali, A., and Osman A., 1971, Synthesis and reactions of phenylcarbamoylarylhydrazidic chlorides, Tetrahedron 27 (12), 2517-2528.

[30] Cowper, R. M., and Davidson, L. H., 1943, Phenacyl bromide, Org. Synth, 19, 24.

[31] Temple, D. L., Yevich, J. P., Covington, R. R., Hanning, C. A., Seidehamel, R. J., Mackey, H. K., and Bartek, M. J., 1979, Synthesis of 3,4-dihydro-4-oxothieno[2,3-d]pyrimidine-2-carboxylates, a new series of orally active antiallergy agents.,J. Med. Chem., 22 (5),505-10.

[32] Jotterand, A., German Patent no. 2, 359, 008, 06 (June 1974), [Chem. Abstr., 1974, 81, 137599].

[33] Kheder, N. A., 2001, "Synthesis and Reactions of Some New Pyridine and Pyrimidine Derivatives", Ph.D.Thesis, Cairo University, Egypt.

[34] Abdulrahman, I. A., Mohamed, A.A., Sadath, A., Ang, C.W., Yeong, K.Y., Rusli, I., Tan, S.C., Suresh, P., Raju, S.K., Natarajan, A., and Hasnah, O., 2012, Antimycobacterial agents: synthesis and biological evaluation of novel 4-(substituted phenyl)-6-methyl-2-oxo-N-(pyridin-2-yl)-1,2,3,4-tetrahydropyrimidine-5-carboxamide derivatives by using one-pot multi-component method, Lett. Drug Design Discov., 9 (10), 953-957.