Synthesis, Reactions and Characterization of bis-thieno[2,3-b]-pyridine-2-carbohydrazide Derivative

Fawzy A. Attaby and Ahmed A. M. Elreedy

Abstract: Reaction of diethyl 4,4'(1,4-phenylene)bis(3-amino-5-acetyl-6-methylthieno[2,3-*b*]pyridine-2-carboxylate **(1)** with hydrazine hydrate afforded the 4,4'-benzene-1,4-diylbis(5-acetyl-3-amino-6-methylthieno[2,3-b]pyridine-2-carbohydrazide) **(3)**. The structure of **2** was inferred through independent synthetic reaction of diethyl 2,2'-{1,4-phenylenebis[3-cyano-5-acetyl-6-methylpyridine-4,2-diyl)thio]}diacetate **2** under the same applied reaction conditions. On the other hand, reaction of **3** with formic acid, acetic anhydride, triethylorthoformate, acetic acid, ethyl acetoacetate, diethylmalonate, phenylisothiocyante and acetylacetone aiming to build up pyrimidine, pyrazole or oxadiazole on the ring system of **3**. Structures of all newly synthesized heterocyclic compounds in the present study were confirmed by considering the data of IR, ^{1}H NMR, mass spectra as well as that of elemental analyses.

Index Terms: bis-thienopyridine-2-carboxylate; bis-thienopyridine-2-carbohydrazide; bis-pyridothienopyrimidin-4(3H)-one); bis-pyridothienopyrimidin-3(4*H*)-yl)imidoformate; bis-pyrazolothienopyridin-3-one)

1 INTRODUCTION

The biological importance of both bis-compounds [1-5] and 2-thioxopyridine-3-carbonitriles [6-11] as well as a conjunction to our previous work [12-18] stimulated our interest to synthesize several derivatives of these ring systems that are required for several chemical transformations and for our medicinal chemistry programs.

2 RESULTS AND DISCUSSION

An unequivocal support for the structure of compound **1** [19] came from the series of reactions concerning the presence of the ester group at 2-position of the thienyl moiety. Thus, it has been found that diethyl 4,4'(1,4-phenylene)bis(3-amino-5-acetyl-6-methylthieno[2,3-*b*]pyridine-2-carboxylate **1** reacted with hydrazine hydrate in ethanol (20 mL) under reflux for 10 hours to give a reaction product **3** that corresponding to the loss of two molecules of ethanol. The IR spectrum (cm^{-1}) of **3** showed the absorption bands of the NH_2 and NH groups at 3454, 3322 and 3219. Its mass spectrum gave the peaks at m/z = 603, 0.5% which corresponding to the parent peak of the molecular ion $[M+H]^+$ in addition to other peaks which gave a further confirmation of **3** structure (cf. Exp. Part and Scheme 1). Based on the above data, in addition to that of elemental analysis, this compound could be formulated as 4,4'-benzene-1,4-diylbis(5-acetyl-3-amino-6-meth-ylthieno[2,3-b]pyridine-2-carbohyd-razide) **3**. An authentic sample of compound **3** was obtained by the reaction of compound **2** with hydrazine hydrate under reflux for 10 hours. It important to report here that compound **3** obtained by the two pathways was indentical in all physical and chemical properties (cf. Exp. Part). The isolation of compound **3** with their adjacent NH_2 and $CONHNH_2$ groups stimulated our interest to utilize it as a versatile starting material for the synthesis of several heterocyclic derivatives. This goal was achieved *via* its reactions with a variety of activated reagents aiming to build up the pyrimidine nucleus on the thienopyridine skeleton. Thus, it has been found that compound **3** reacted with formic acid under reflux to give the corresponding 4,4'-benzene-1,4-diylbis(8-acetyl-3-amino-7-methylpyrido[3',2':4,5]thieno[3,2-d]pyrimi-din-4-(3H)-one) **4**. The reaction most probably proceeded through the formylation of NH_2 group at the thiophene ring to give the non-isolable intermediate **[I]** which converted to the enol form **[II]** followed by elimination of two molecules of

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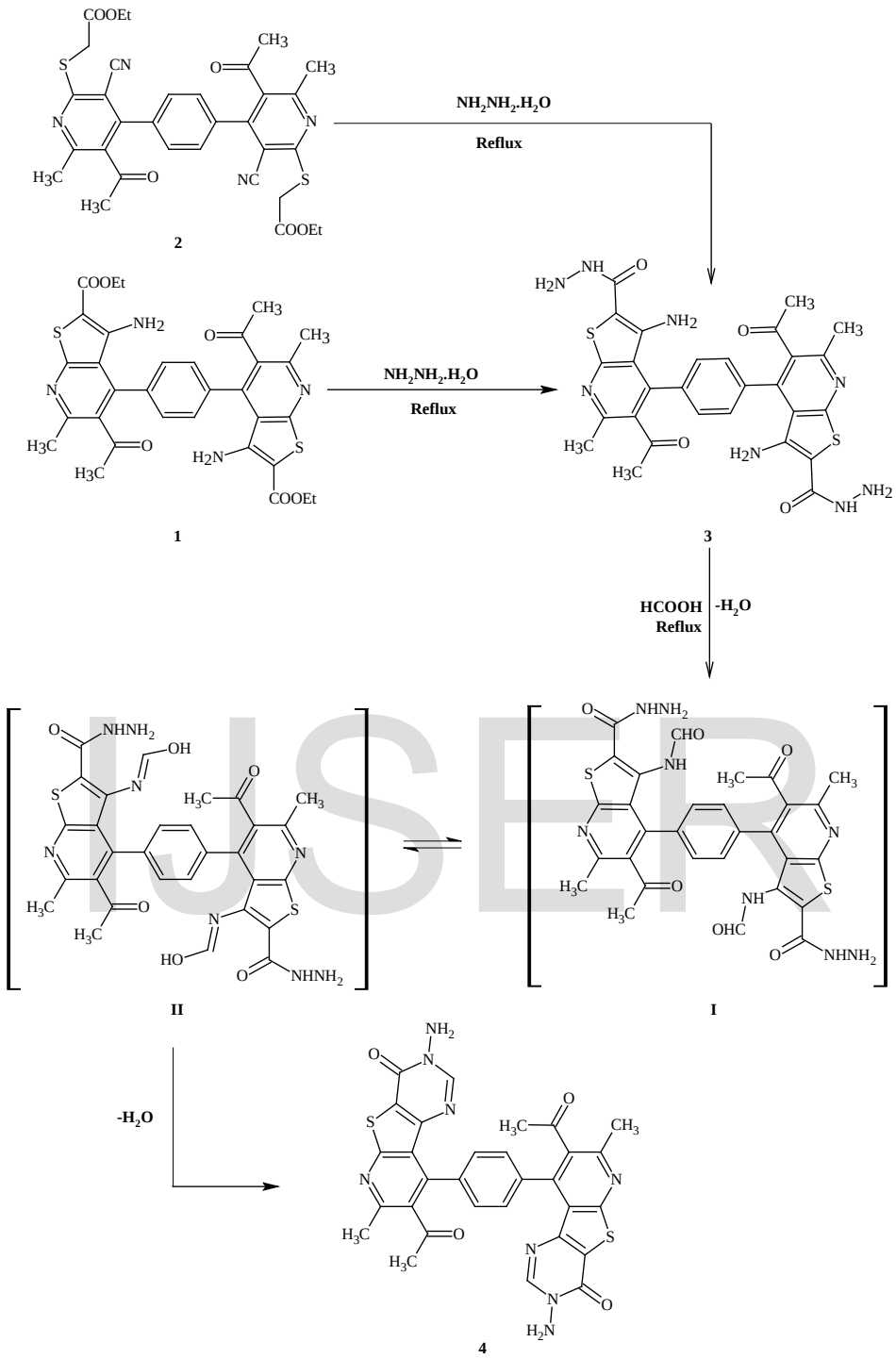
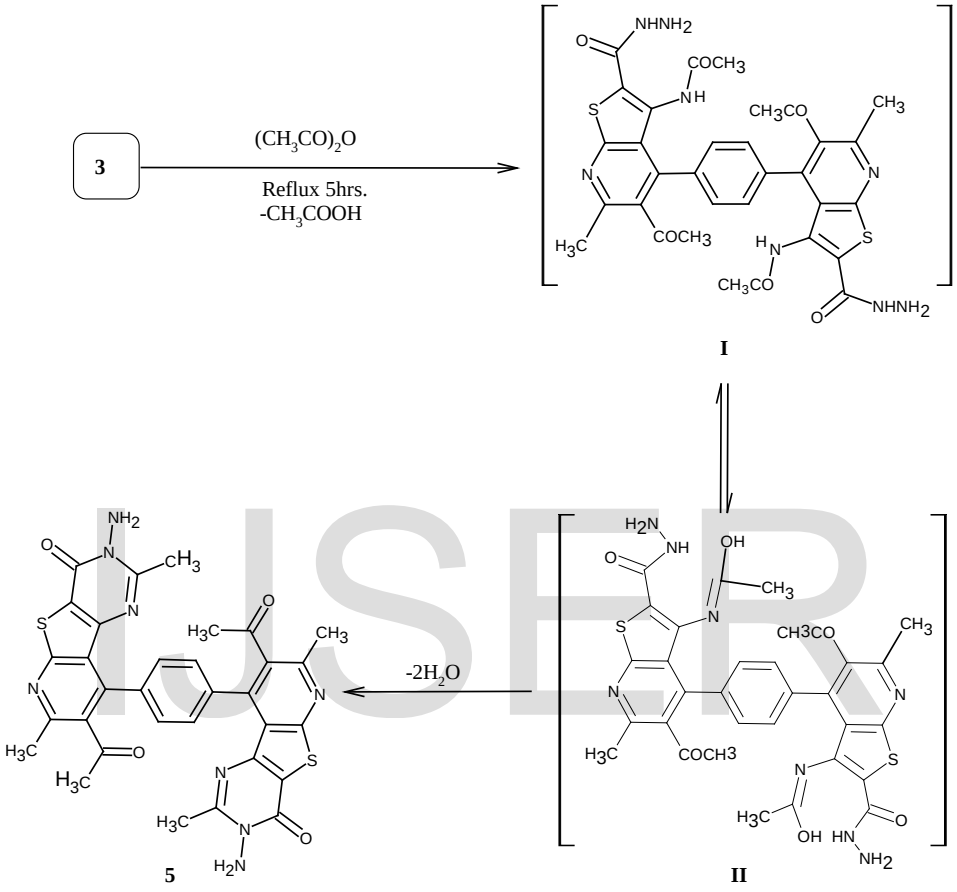


Scheme 1

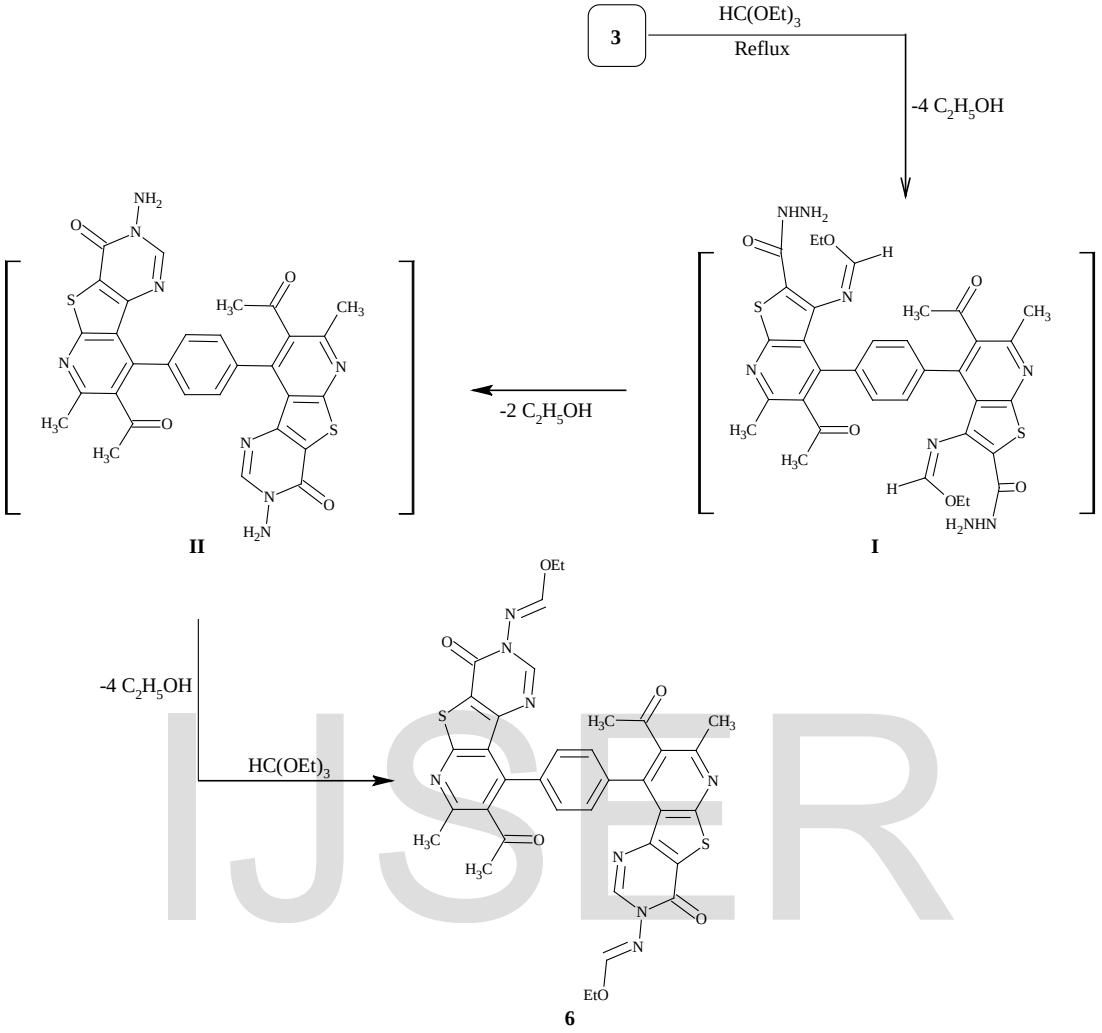
water to afford the final isolable reaction product **4** (cf. Scheme 1). The IR spectrum (cm^{-1}) of **3** showed the absorption bands of NH_2 group at 3452, 3326 and acetyl CO group at 1736 beside ring CO group at 1678. The mass spectrum of **4** gave m/z = 623 (0.2%, $[M+H]^+$) which corresponded to the molecular formula $C_{30}H_{22}N_8O_4S_2$ of the assigned structure (cf. Exp. Part). In a further investigation, compound **3** reacted with acetic anhydride under reflux for 5 hours to give the corresponding 4,4′-benzene-1,4-diylbis(8-acetyl-3-amino-2,7-dimethyl-pyrido[3′,2′:4,5]thieno[3,2-d]pyrimidin-4(3H)-one)

5. The reaction most probably proceeded by the acetylation of NH_2 group at the thiophene ring through the intermediate [**I**] followed by enolization and elimination of two molecules of water from the intermediate [**II**] to afford the final isolable reaction product **5** (cf. Scheme 2). The IR spectrum (cm^{-1}) of this reaction product showed the absorption bands of NH_2 group at 3454, 3326 and CO groups at 1748 and 1697 and its mass spectrum gave m/z = 651 (7.7%, $[M+H]^+$) which corresponded to the molecular formula $C_{32}H_{26}N_8O_4S_2$ of the assigned structure (cf. Exp. Part and Scheme 2).



Scheme 2

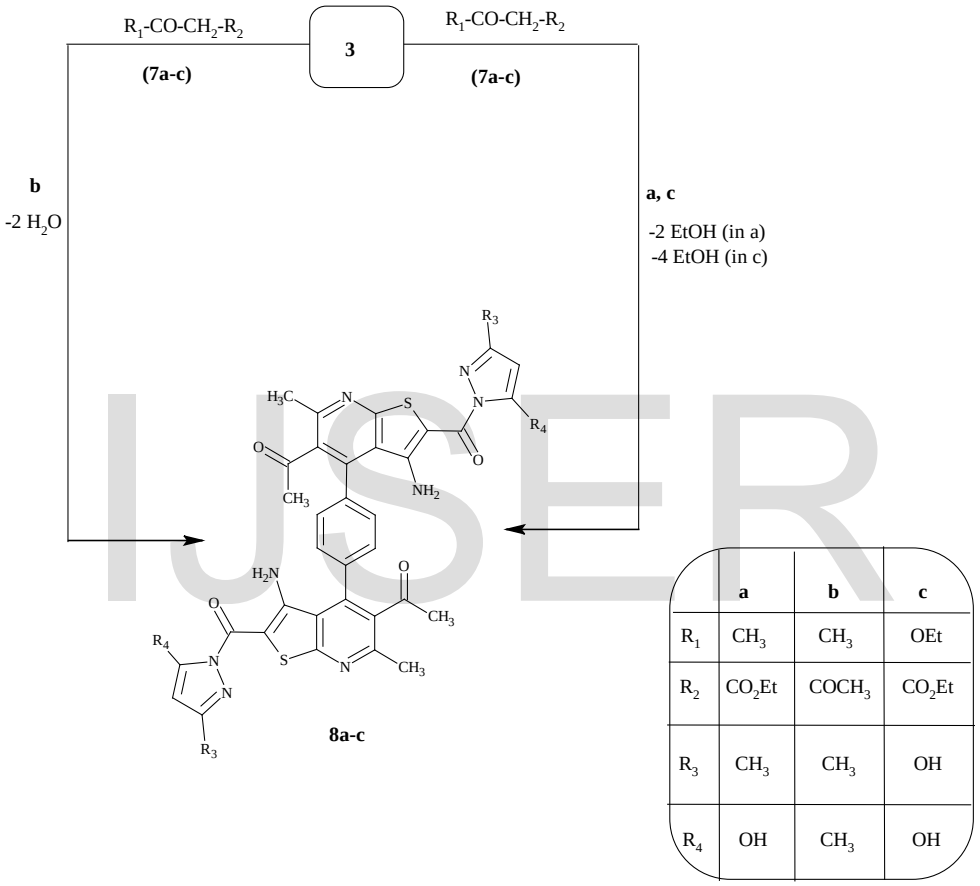
Moreover, compound **3** reacted with triethylorthoformate under reflux for 5 hours to afford the corresponding **6**. The IR spectrum (cm^{-1}) of **6** neither showed absorption bands of NH nor NH_2 groups while absorption bands at 1691 cm^{-1} was detected. Thus we concluded that two molecules of triethylortho-formate reacted with **3** to afford the non-isolable intermediate **[I]** which in turn, reacted with another two molecules of triethylorthoformate to afford the final isolable **6** via the non-isolable product [**II**] (cf. Scheme 3). Moreover, its mass spectrum gave the parent peak at m/z = 735 which corresponding to the molecular weight of the assigned structure in addition to other peaks that gave further confirmation of the structure **6** (cf. Exp. Part). As a further continuation of the interest of exploring the synthetic potential of compound **3** it was thus of value to investigate its reaction with β-dicarbonyl compounds such as ethyl aceto-acetate, acetylacetone and diethylmalonate **7a-c** to afford a new heterocyclic derivatives. Thus, it has been found that compound **3** reacted with ethyl acetoacetate **7a** in glacial acetic acid under reflux for 5 hours to give 5,5'-diacetyl-3,3'-diamino-2-(3-methyl-5-hydroxy-1H-pyrazole-1-carbonyl)-6,6'-dimethyl-4,4'-benzene-1,4-diylbisthieno[2,3-b]pyridine **8a**.



Scheme 3

The reaction most probably proceeded *via* the nucleophilic addition of hydrazidic NH_2 of **3** on the carbonyl group of **7a** to give the non-isolable intermediate $\mathbf{I_a}$. The formation of $\mathbf{I_a}$ followed by elimination of two water molecules of to afford the non-isolable intermediates $\mathbf{II_a}$ which in turn, underwent cyclization *via* the elimination of two ethanol molecules to afford the final isolable reaction product **8a** rather than **8`a** whose structure was elucidated by considering the data of IR, mass spectral data as well as that of elemental analysis (cf. Exp. Part, Equation 1 and Scheme 3). Similarly, compound **3** reacted with acetylacetone **7b** under reflux for 5 hours in glacial acetic acid to afford the corresponding 5,5'-diacetyl-3,3'-diamino-2-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-6,6'-dimethyl-4,4'-benzene-1,4-diylbisthieno[2,3-b]pyridine **8b**. The IR spectrum (cm^{-1}) of **8b** showed the absorption bands of NH_2 group at 3454, 3382 and CO group at 1684 and its mass spectrum gave m/z = 731 (0.5%, $[M+H]^+$) which corresponded to the molecular weight of the molecular formula $C_{38}H_{34}N_8O_4S_2$ of the assigned structure. Several peaks at m/z = 636 (100%, 731- dimethylpyrazole ring), 608 = (0.1%, 731- one O=C – di methyl pyrazole ring), 511 = (4.6%, 731- one O=C - two dimethylpyrazole ring – two H), and 483 = (0.2%, 731- two dimethylpyrazole – two C=O – two H) gave further confirmation of the structure **8b**. The reaction most probably proceeded *via* the addition followed by elimination of two molecules of water through the non-isolable intermediate $\mathbf{I_b}$ and $\mathbf{II_b}$ followed by

cyclization through the elimination of another two molecules of water to afford the final isolable reaction product **8b** (cf. Scheme 4 and Equation 1). In a similar manner, compound **3** reacted with diethylmalonate **7c** under reflux to afford the corresponding 4,4'-benzene-1,4-diylbis-5-acetyl-3-amino-2-(1H-pyrazol-3,5-dione-1-carbonyl)-6-methyl-thieno[2,3-b]pyridine **8c** whose structure was confirmed *via* the elemental analysis and spectral data (cf. Exp. Part and Scheme 4). 7,7'-Diacetyl-6,6'-dimethyl-8,8'-benzene-1,4-diylbis(1,2-dihydro-3*H*-pyrazolo[3',4':4,5]thieno[2,3-*b*]pyridin-3-one) **9** obtained via the reaction of compound **3** with glacial acetic acid under reflux for 5 hours. The IR (cm^{-1}) of compound **9** showed the absorption bands of acetyl CO, ring CO as well as NH groups and its mass spectrum gave the parent peak at m/z = 684, (0.3%, $[M+H]^+$) which corresponding to the molecular weight of the assigned structure (cf. Exp. Part and Scheme 5). 4,4'-Benzene-1,4-diylbis-5-acetyl-3-amino-6-methyl-2-(N-phenyl-1,3,4-oxadiazol-

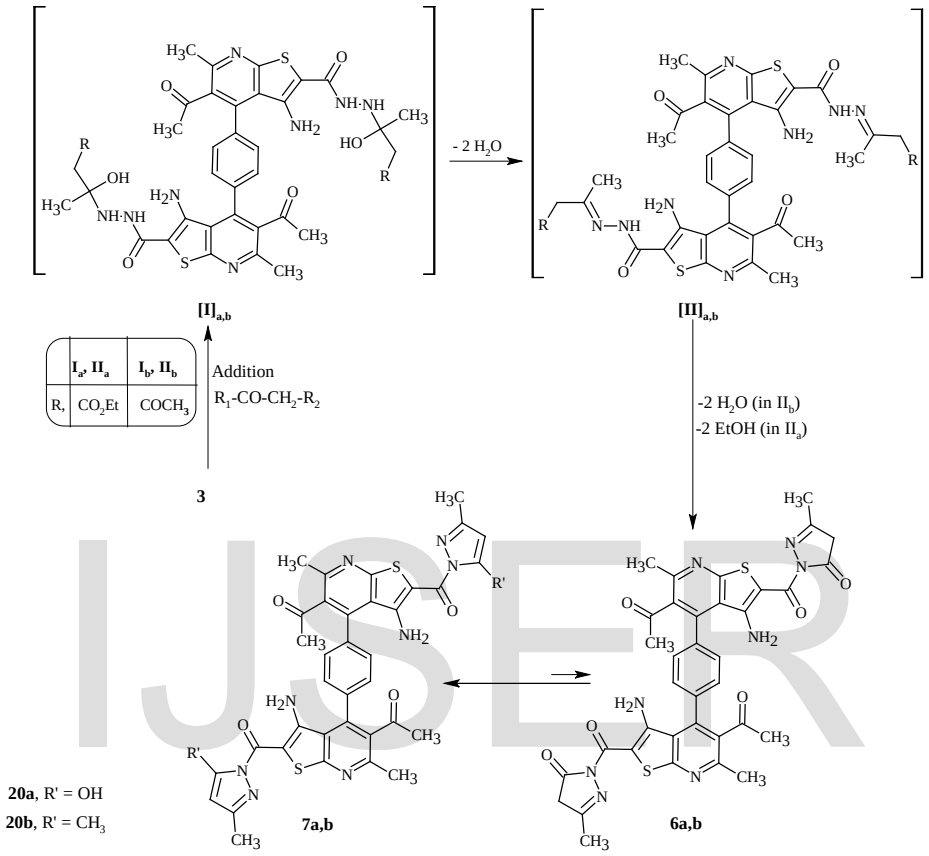


	a	b	c
R_1	CH_3	CH_3	OEt
R_2	CO_2Et	$COCH_3$	CO_2Et
R_3	CH_3	CH_3	OH
R_4	OH	CH_3	OH

Scheme 4

2-amine-5-yl)thieno[2,3-b]pyridine **10** obtained through the reaction of compound **3** with phenyl isothiocyanate under reflux in pyridine for 5 hours. The IR (cm^{-1}) of this reaction product showed the absorption bands of NH_2 and C=O functional groups as well as its mass spectrum gave the parent peak at m/z = 805 which corresponding to the molecular weight of the assigned structure **10** (cf. Exp. Part and Scheme 5). Compound **3** reacted with 2-cyano-3-(4-methoxy-phenyl)prop-2-enethioamide **11** in pyridine under reflux to give a reaction product which formulated as 4,4'-benzene-1,4-diylbis-5-acetyl-3-amino-6-methyl-N'-(4-methoxyphenylmeth-ylidene)thieno[2,3-b]pyridine-2-carbohydrazide **13** (cf. Scheme 5). The IR spectrum (cm^{-1}) of **13** showed the absorption bands of NH_2 groups at 3460, 3317 and C=O at 1666 cm^{-1}. Its mass spectrum gave m/z = 838 which corresponded to the molecular formula $C_{44}H_{38}N_8O_6S_2$ of the assigned structure (cf. Exp. Part). An unequivocal support for the structure of **13** was achieved *via* its synthesis by another route, *via* using anisaldehyde

12 to give a reaction product which was found completely identical in all aspects with **13** obtained from the first route (cf. Scheme 5 and Exp. Part). Therefore, we concluded that the reaction between **3** and 2-cyano-3-(4-methoxyphenyl)prop-2-enethioamide **11** most properly proceeded *via* the ylidine group exchange with the loss of one molecule of 2-cyanoethanethioamide to afford the corresponding reaction product **13**.

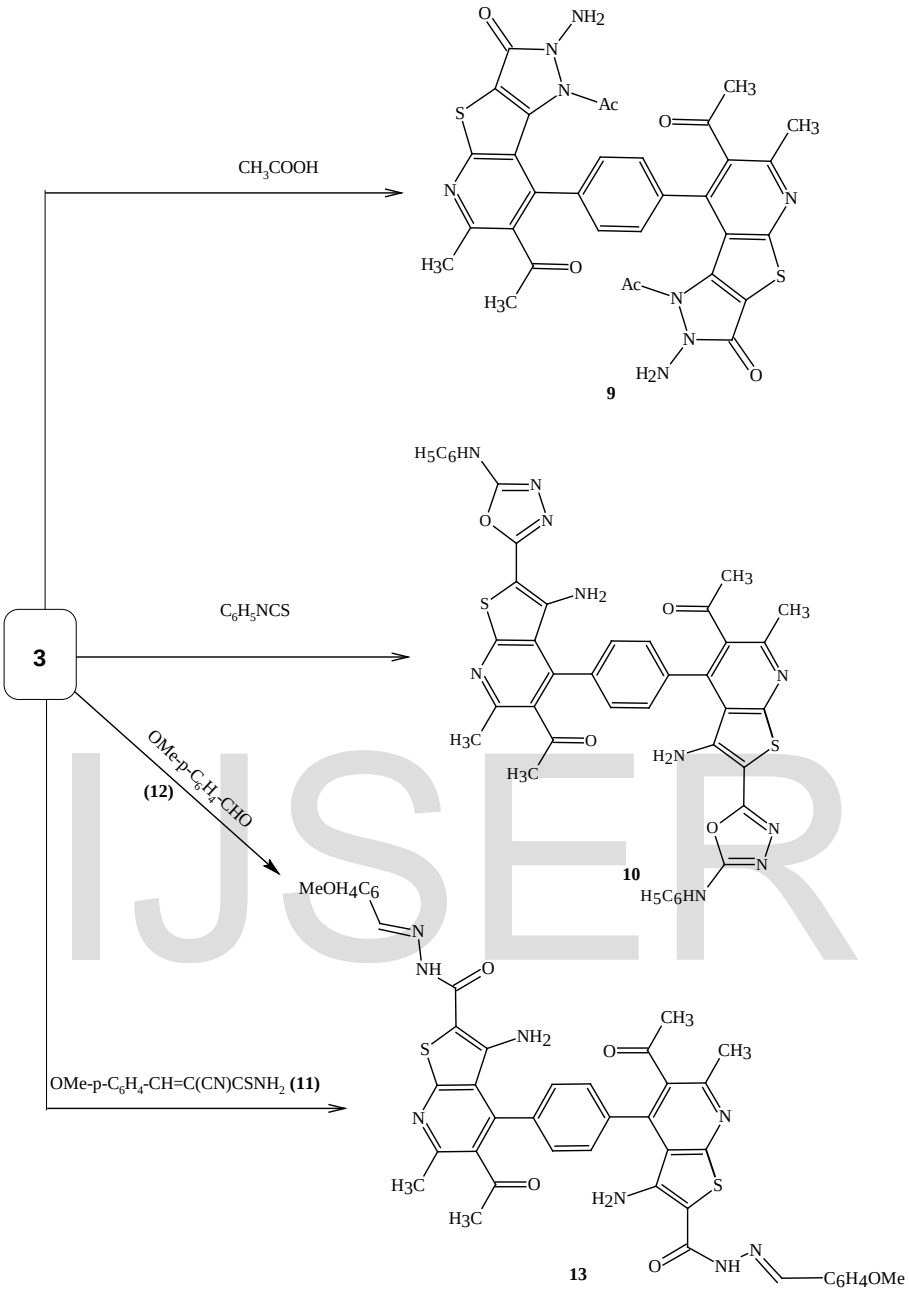


Equation 1

3 EXPERIMENTAL

All melting points were uncorrected. I.R. (KBr discs) spectra were recorded on a Shimadzu FTIR-8201PC Spectrophotometer. ^{1}H-NMR spectra were recorded on a Varian Mercury 300 MHz., and a Varian Gemini 200 MHz. Spectrometers using TMS as an internal standard and $CDCl_3$, DMSO-d_6, and $(CD_3)_2CO$ as solvents. Chemical shifts were expressed as δ (ppm) units. Mass spectra were recorded on Agilent LC 1200/MS Ion Trap 6320 using APCI ionization source and the spectra is enhanced using acidified water/acetonitril mobile phase and measured in the positive mode of the ion trap (Molecular weights of most compounds are Protonated ($[M+H]^+$).

Synthesis of (3): A solution of **1** or **2** (1g, 0.63 mol) in hydrazine hydrate (15mL) and ethanol (20 mL) was heated under reflux for 10 hrs., the excess solvents were evaporated and the reaction mixture then cooled and the solid so formed was collected by filtration, dried, and crystallized from ethanol to give **3.**



Scheme 5

4,4'-Benzene-1,4-diylbis(5-acetyl-3-amino-6-methylthieno[2,3-*b*]pyridi-ne-2-carbohydrazide) (3): as yellow crystals yielded by (83%); m.p>330^{0}C; **IR** υ(cm^{-1}): 3454.1,3322.6 (NH_2), 3219.7 (NH), 2984.1,2920.4 (aliphatic-CH), 1691.6 (Acetyl-CO), 1642.4 (Amide-CO); **MS**: 603 ([M+H]$^+$, 0.5% which corresponding to the molecular weight of the molecular formula $C_{28}H_{26}N_8O_4S_2$ of the assigned structure) 585 (603-H_2O, 0.4%), 572 (603-$NHNH_2$, 42.9%), 571 (603-$NHNH_2$, H, 100%), 544 (572-CO, 17.9%), 543 (571-CO, 60.2%), 513 (544-$NHNH_2$, 2.6%), 512 (543-$NHNH_2$, 0.6%), 485 (513-CO, 0.3%), 484 (512-CO, 0.8%); **^{1}H NMR**(DMSO) (δppm): 1.952(s, 6H, $2CH_3$), 2.521(s, 6H, $2COCH_3$), 4.487(br, 4H, $2NH_2$), 5.793(br, 4H, $2NH_2$), 7.606(m, 4H, ArH`S), 9.171(br, 2H, 2NH); Anal, for $C_{28}H_{26}N_8O_4S_2$ (602) Calcd./Found(%): C(55.80/55.83%) H(4.35/4.38%) N(18.59/18.62%) S(10.64 /10.67%).

Synthesis of 4, 5, 6, and 9 (General method): A solution of **3** (0.6g, 1mmole) and each of15ml of (Formic acid, Acetic anhydride, Triethylortho-formate, and Acetic acid), was heated under reflux for 5 hrs. The excess solvent was evaporated and cooled. The solid was collected by filtration, dried, and crystallized from the ethanol to give **4, 5, 6,** and **9** respectively.

4,4'-Benzene-1,4-diylbis(8-acetyl-3-amino-7-methylpyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-4(3*H*)-one) 4: as yellow crystals yielded by (93%); m.p>330^{0}C; **IR** υ(cm^{-1}): 3452.7, 3326.4 (NH_2), 2923.3,2852.4 (aliphatic-CH), 1736.1 (CO), 1678.6 (CO); **MS**: 623 ([M+H]$^+$, 0.2% which corresponding to the molecular weight of the molecular formula $C_{30}H_{22}N_8O_4S_2$ of the assigned structure), 607 (623-NH_2, 7.2%), 606 (623-OH, 9.6%), 605 (623-H_2O, 29.2%), 590 (605-NH, 7.4%), 589 (605-NH_2, 21.6%), 587 (605-H_2O, 100%), 563 (590-HCN, 1.6%); **^{1}H NMR** (DMSO) (*δ*ppm): 2.172 (s, 6H, 2CH_3), 2.504 (s, 6H, 2$COCH_3$), 6.082 (br, 4H, 2NH_2), 7.471 (m, 4H, ArH`S); Anal for $C_{30}H_{22}N_8O_4S_2$ (622) Calcd./Found(%): C(57.87/57.90%) H(3.56/3.59%) N(18.00/18.03%) S(10.30/10.33%).

4,4'-Benzene-1,4-diylbis(8-acetyl-3-amino-2,7-dimethylpyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-4-(3*H*)-one) 5: as white crystals yielded by (78%); m.p>330^{0}C; **IR** υ(cm^{-1}): 3454.4,3326.3 (NH_2), 1748.3 (CO), 1697.8 (CO); **MS**: 651 ([M+H]$^+$, 7.7% which corresponding to the molecular weight of the molecular formula $C_{32}H_{26}O_4N_8S_2$ of the assigned structure), 636 (651-CH_3, 4.5%), 635 (651-NH_2, 30.4%), 634 (651-OH, 54.5%), 633 (651-H_2O, 100%), 620 (636-NH_2, 34.9%), 619 (633-CH_3, 23.6%), 618 (634-NH_2, 17.1%), 615 (634-H_2O, 77.3%), 603 (618-CH_3, 4.9%),; Anal, for $C_{32}H_{26}O_4N_8S_2$ (650) Calcd./Found(%): C(59.06/59.09%) H(4.03/4.06%) N(17.22/17.25%) S(9.86/9.89%).

4,4'-Benzene-1,4-diylbis(ethyl(8-acetyl-7-methyl-4-oxopyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-3(4-*H*)-yl)imidoformate) 6: as yellow crystals yielded by (83.7%); m.p > 330^{0}C; **IR** υ(cm^{-1}): 2921.1,2852.4 (aliphatic-CH), 1691.6 (Acetyl-CO); **MS**: 735 ([M+H]$^+$, 0.1% which corresponding to the molecular weight of the molecular formula $C_{36}H_{28}N_8O_6S_2$ of the assigned structure), 690 (735-OEt, 1%), 677 (735-2Et, 0.6%), 663 (690-HCN, 2.3%), 661 (690-Et, 4.5%), 643 (735-2EtOH, 0.3%), 621 (677-2CO, 100%), 606 (621-NH, 0.8%);**^{1}H NMR** (DMSO) (*δ*ppm): 1.031 (t, 6H, 2$CH_2\underline{CH_3}$), 2.018 (s, 6H, 2CH_3), 2.163 (s, 2H, 2CH), 2.504 (s, 6H, 2$COCH_3$), 4.322 (q, 4H, 2$\underline{CH_2}CH_3$), 7.563 (m, 4H, ArH`S); Anal, for $C_{36}H_{28}N_8O_6S_2$ (734) Calcd./Found(%): C(58.84/58.87%) H(4.12/4.15%) N(15.25/15.28%) S(8.73/ 8.76%).

7,7'-Diacetyl-6,6'-dimethyl-8,8'-benzene-1,4-diylbis-(1,2-dihydro-3*H*-pyrazolo[3',4':4,5]thieno[2,3-*b*]pyridin-3-one) 9: as yellow crystals yielded by (82%); m.p >330^{0}C; **IR** υ(cm^{-1}): 2997.5,2884.2 (aliphatic-CH), 1695.6 (Acetyl-CO), 1673.3 (pyrazol-CO); **MS**: 684 ([M+H]$^+$, 0.3% which corresponding to the molecular weight of the molecular formula $C_{32}H_{26}N_8O_6S_2$ of the assigned structure), 641 (684-$COCH_3$, 7.2%), 640 (684-CH_3CHO, 15.3%), 638 (640-H_2, 100%), 626 (641-NH, 18.4%), 596 (640-CH_3CHO, 3.6%), 595 (638-CH_3CO, 2.4%), 594 (638-CH_3CHO, 4.6%), 582 (626-CH_3CO, 3.8%), 580 (596-NH_2, 3.5%), 563 (595-2NH_2, 1.6%); Anal, for $C_{32}H_{26}N_8O_6S_2$ (682.7) Calcd./Found(%): C(56.30/56.33%) H(3.84/3.87%) N(16.41/16.44%) S(9.39/9.42%).

Synthesis of 8a-c (General method): A solution of each of **3** (0.6g 1mmole) and 15ml of Ethyl 3-oxobutanoate, acetylacetone and diethylmalonate, (0.26g, 0.2g, 0.32g 2 mmole) was heated in 20ml of acetic acid under reflux for 5 hrs. The excess solvent was evaporated and cooled. The solid was collected by filtration, dried, and crystallized from the ethanol to give **8a-c** respectively.

5,5'-Diacetyl-3,3'-diamino-2-(3-methyl-5-hydroxy-1H-pyrazole-1-carbonyl)-6,6'-dimethyl-4,4'-benzene-1,4-di-ylbisthieno[2,3-b]pyridine (8a): as yellow crystals yielded by (67%); m.p>330^{0}C; **IR** υ(cm^{-1}): 3482.1,3392.4 (NH_2), 1684.8 (CO); **MS**: 733 (M-H, 0.1% which corresponding to the molecular weight of the molecular formula $C_{36}H_{30}N_8O_6S_2$ of the assigned structure), 716 (733-OH, 10.6%), 715 (733-H_2O, 25.5%), 697 (715-H_2O, 14.1%), 680 (697-OH, 10.8%), 636 (733-$C_4H_5ON_2$, 28.4%), 635 (715-$C_4H_4N_2$, 8.8%), 619 (636-OH, 100%), 607 (635-CO, 30.1%), 600 (680-$C_4H_4N_2$, 9.9%); Anal for $C_{36}H_{30}N_8O_6S_2$ (734) Calcd./Found(%): C(58.84-/58.87) H(4.12/4.15) N(15.25/15.28) S(8.73/8.76).

5,5'-Diacetyl-3,3'-diamino-2-(3,5-dimethyl-1H-pyrazole-1-carbonyl)-6,6'-dimethyl-4,4'-benzene-1,4-diylbis-thieno[2,3-b]pyridine (8b): as Brown crystals yielded by (76%); m.p = 260^{0}C; **IR** υ(cm^{-1}): 3454.3,3382.2 (NH_2), 1684.5 (CO); **MS**: 731 ([M+H]$^+$, 0.5% which corresponding to the molecular weight of the molecular formula $C_{38}H_{34}N_8O_4S_2$ of the assigned structure), 637 (731-$C_5H_6N_2$, 46.8%), 636 (731-$C_5H_7N_2$, 100%), 635 (731-$C_5H_8N_2$, 34.5%), 621 (637-NH_2, 0.8%), 608 (636-CO, 0.1%), 607 (635-CO, 2.1%), 512 (608-$C_5H_8N_2$, 2.8%), 511 (607-$C_5H_8N_2$, 4.6%), 484 (512-CO, 0.7%), 483 (511-CO, 0.2%); Anal, for $C_{38}H_{34}N_8O_4S_2$ (730) Calcd./Found(%): C(62.45/62.48%) H(4.69/4.72%) N(15.33/15.37%) S(8.77/ 8.8%).

4,4'-Benzene-1,4-diylbis-5-acetyl-3-amino-2-(1H-pyrazol-3,5-dione-1-car-bonyl)-6-methylthieno[2,3-b]pyridine (8c): as Brown crystals yielded by (76%); m.p>330^{0}C; **IR** υ(cm^{-1}): 3479.4,3389.6 (NH_2), 1691.7 (CO); **MS**: 739 ([M+H]$^+$, 0.2% which corresponding to the molecular weight of the molecular formula $C_{34}H_{26}N_8O_8S_2$ of the assigned structure), 723 (739-NH_2, 1.3%), 721 (739-H_2O, 11.5), 703 (721-H_2O, 3.1%), 697 (739-CH_2CO, 100%), 696 (739- CH_3CO, 13%), 679 (697-H_2O, 17.3%), 661 (679-H_2O, 8.7%), 640 (739-$C_3H_3O_2N_2$, 8.7%), 639 (721-$C_3H_2ON_2$, 4%), 622 (721-$C_3H_3O_2N_2$, 2.1%); Anal, for $C_{34}H_{26}N_8O_8S_2$ (738) Calcd./Found(%): C(55.28/55.31%) H(3.55/3.58%) N(15.17/15.2%) S(8.68 /8.71%).

Synthesis of 10: A solution of each of **3** (0.6g, 1mmole) and phenyl isothiocyanate, (0.27g, 2mmol) in pyridine (15 mL) was heated under reflux for 5 hrs, cooled, poured onto ice-cold water, and neutralized with drops acetic acid the solid was collected by filtration, dried, and crystallized from the ethanol to give **10**.

4,4'-Benzene-1,4-diylbis-5-acetyl-3-amino-6-methyl-2-(N-phenyl-1,3,4-oxadiazol-2-amine-5-yl)thieno-[2,3-b]-pyridine (10): as Brown crystals yielded by (81%); m.p = 225^{0}C; **IR** υ(cm^{-1}): 3464.4,3378.2 (NH_2), 3055.5 (aromatic-CH), 1688.2 (Acetyl-CO); **MS**: 805 (M, 0.1% which corresponding to the molecular weight of the molecular formula $C_{42}H_{32}N_{10}O_4S_2$ of the assigned structure), 790 (805-NH, 37.2%), 789 (805-NH_2, 100%), 773 (789-NH_2, 4%), 771 (789-H_2O, 34%), 755 (773-H_2O, 5.9%), 754 (771-OH, 5.8%), 635 (789-2Ph, 7.2%); Anal, for $C_{42}H_{32}N_{10}O_4S_2$ (804) Calcd./Found(%): C(62.67/62.7%) H(4.01/4.04%) N(17.40/17.43%) O(7.95/7.98%) S(7.97/ 8.00%).

Synthesis of 13 (Method A): A solution of each of **3** (0.6g, 1mmole) and 2-cyano-3-(4-methoxy phenyl)prop-2-enethioamide **11** (0.44g, 2mmol) in pyridine (15 mL) was heated under reflux for 5 hrs, cooled, poured onto ice-cold water, and neutralized with drops acetic acid the solid was collected by filtration, dried, and crystallized from the ethanol to give **13**.

Method B: A solution of each of **3** (0.6g, 1mmole) and 4-methoxybenzaldehyde **12** (0.27g, 2mmol) in pyridine (15 mL) was heated under reflux for 5 hrs, cooled, poured onto ice-cold water, and neutralized with drops of acetic acid the solid was collected by filtration, dried, and crystallized from the ethanol to give **13**.

4,4'-Benzene-1,4-diylbis-5-acetyl-3-amino-6-methyl-N′-(4-methoxyphenylmethylidene)thieno[2,3-b]pyridine-2-carbohydrazide (13): as yellow crystals yielded by (77%); m.p >330^{0}C; **IR** υ(cm^{-1}): 3460.4,3317.5 (NH_2), 1666.5 (Amide-CO); **MS**: 838 (M, 0.4% which corresponding to the molecular weight of the molecular formula $C_{44}H_{38}N_8O_6S_2$ of the assigned structure), 731 (838-$PhOCH_3$, 100%), 713 (731-H_2O, 36.4%), 705 (731-CN, 7.2%), 688 (731-CH_3CO, 9.8%), 662 (705-NH,CO, 17.1%), 624 (731-$PhOCH_3$, 5.6%), 606 (624-H_2O, 15.3%); Anal, for $C_{44}H_{38}N_8O_6S_2$ (838) Calcd./Found(%): C(62.99/63.02%) H(4.57/4.60%) N(13.36/13.39%) O(11.44/11.47%) S(7.64/ 7.67%).

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