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Synthesis, Reactions and Characterization of 4,4’-Benzene-1,4-diylbis (5-Acetyl-6-methyl-2-thioxo - 1,2-dihydropyridine-3-carbonitrile)

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BENZENE-1,4-dicarbaldehyde (1) reacted with 2-cyanoethanethioamide (2) to give 3,3'-benzene-1,4-diylbis(2-cyanoprop-2-enethioamide) (3) which in turn, reacted with pentane-2,4-dione (4) to afford the corresponding 4,4’-benzene-1,4-diylbis(5-acetyl-6-methyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile)(5). The synthetic potentiality of compound 5 was investigated in the present study via its reaction with several reagents to afford newly synthesized 4,4’-(1,4-phenylene)-bis (5-acetyl-3-amino-6-methylthieno [2,3-b] pyridines (8a-h). 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.

Keywords: Bis(2-cyanoprop-2-enethioamide), Pentane-2,4-dione, Bis (5-acetyl-6-methyl -2 -thioxo-1, 2- dihydropyridine-3 carbonitrile), Bis(5-acetyl-6-methyl-2-alkylthiopyridine-3-carbo-nitrile), and Bis (5-acetyl-3-amino-6-methylthieno [2,3-b] pyridine.

Recently, bis(compounds) have received great attention(1-3) not only for being model compounds for main chain polymers(4-9) but also, because many biologically active natural and synthetic products have molecular symmetry(10). 2-Thioxopyridine-3-carbonitriles were reported to have antiviral activity (11) as well as thieno[2,3-b] pyridines which were reported to have antimicrobial (12)antiviral (11-13) and anti-inflammatory(14) activities. In view of these reports and as a conjunction to our previous work(15-22), we report the synthesis of the title compounds that are required for several chemical transformations as well as for medicinal chemistry programs.

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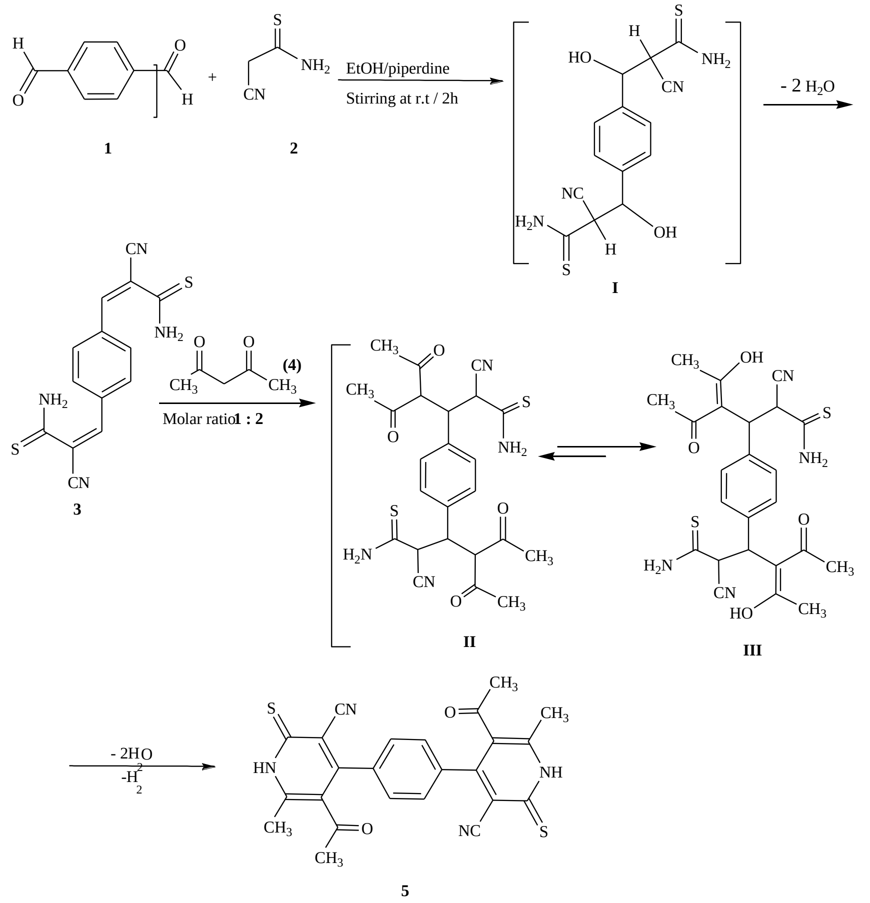
Results and Discussion

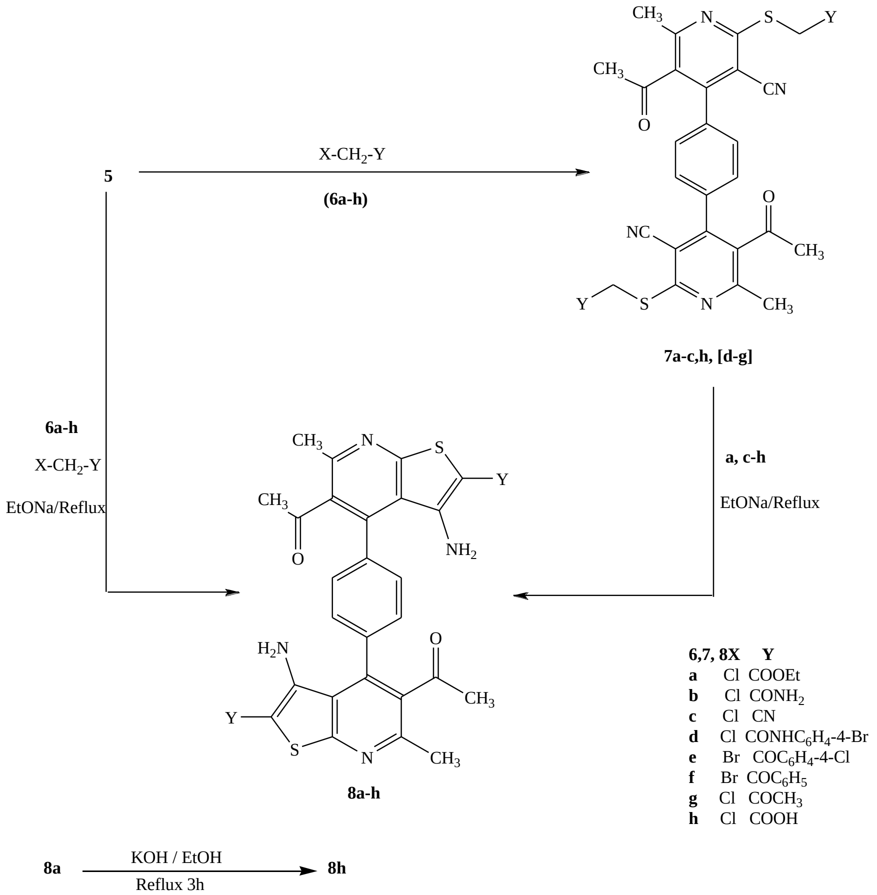
It has been found that benzene-1,4-dicarbaldehyde (1) reacted with 2-cyano-ethanethioamide (2) in absolute ethanol (≈ 50 ml) containing the catalytic amount of piperidine (≈ 0.5 ml) in molar ratio 1 : 2 under stirring at room temperature for 30 min to obtain 3,3'-benzene-1,4-diylbis(2-cyanoprop-2-enethioamide) (3). The IR (cm^{-1}) spectrum of this reaction product showed the peaks of NH_2 (3343.8, 3295.2) and CN (2226.2) groups. (*cf.* Exp. Part). Compound 3 reacted with pentane-2,4-dione (4) in absolute ethanol (≈ 50 ml) containing the catalytic amount of piperidine (≈ 0.5 ml) under reflux for 5 hr in molar ratio 1 : 2 to afford 4,4'-benzene-1,4-diylbis(5-acetyl-6-methyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile) (5). The IR (cm^{-1}) spectrum of the reaction product showed peaks at 3164.1 (NH), 3058.8 (aromatic-CH) and 2228.4 (CN) and its MS (m/z) gave the parent peak at 459 $[M+H]^+$, (which corresponding to the molecular weight of the assigned structure). Moreover, several fragments at given m/z values showed and represent further establishment for compound 5 structure (*cf.* Exp. Part and Scheme 1).

The electrophilic substitution reaction of compound 5 was investigated *via* its reactions with several active halogen-containing compounds (6a-h). Thus it was found that, compound 5 reacted with ethyl chloroacetate (6a) under stirring for 15 min at room temperature in methanolic sodium methoxide to give the reaction product 7a. The IR (cm^{-1}) spectrum of product 7a showed the peaks of CN (2225.6) and CO (1743.9) of the newly introduced COOEt group. Its ^1H NMR (δ ppm) spectrum revealed the signals of $–S\underline{CH_2}$-,$-COO\underline{CH_2}CH_3$, $-COOCH_2\underline{CH_3}$ protons and this confirms the good nucleophilicity of S in 5 that facilitates the electrophilic attack of 6a to afford 7a. Furthermore, 7a structure was elucidated through its cyclisation in ethanolic sodium ethoxide under reflux for 30 min to give the reaction product 8a whose IR spectrum showed no peaks of CN group and instead the bands of the newly formed NH_2 group were detected. Also, the ^1H NMR spectrum of this reaction product revealed no signals of $-SCH_2$- protons while that of NH_2 detected. Considering the data of both IR and ^1H NMR we concluded that both $-SCH_2$- and CN functional groups in (7a) involved in the cyclisation step to give the finally isolated 8a (*cf.* Exp. Part and Scheme 2).



Scheme 1

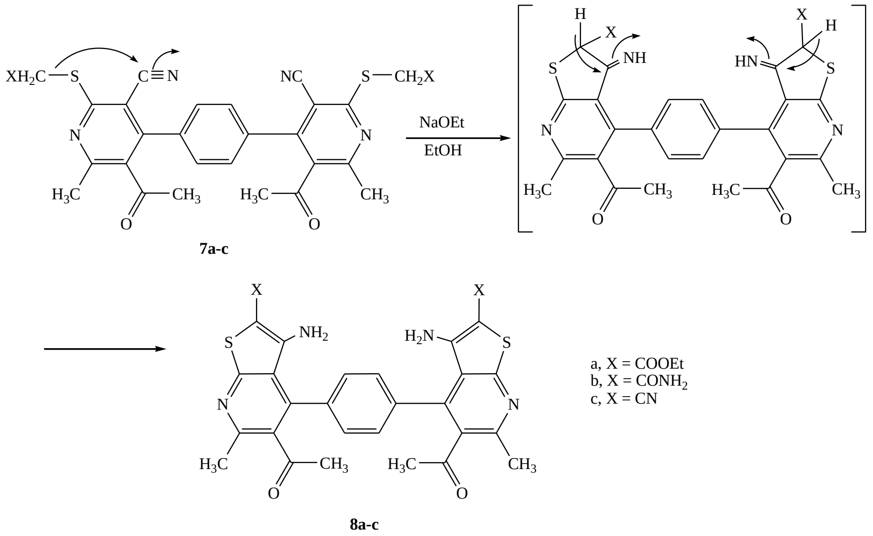
Similarly, compound 5 reacted with chloroacetonitrile (6c) under stirring for 15 min at room temperature in methanolic sodium methoxide to afford the corresponding 7c. Compound 7c underwent intramolecular cyclization *"Thrope-Ziegler reaction"* in ethanolic sodium ethoxide under reflux for 30 min to afford the corresponding thieno[2,3-*b*] pyridine derivative 8c (c.f. Equation 1). Also, compound 7b was obtained by reacting compound 5 with chloroacetamide in methanolic sodium methoxide under stirring at room temperature for 30 min. Unlike 8a,c compound 8b couldn`t be prepared by the previously mentioned method, it was prepared by the reaction of compound 5 with chloroacetamide in ethanolic sodium ethoxide under reflux for 5 hr.



6,7, 8	X	Y
a	Cl	COOEt
b	Cl	$CONH_2$
c	Cl	CN
d	Cl	$CONHC_6H_4$-4-Br
e	Br	COC_6H_4-4-Cl
f	Br	COC_6H_5
g	Cl	$COCH_3$
h	Cl	COOH

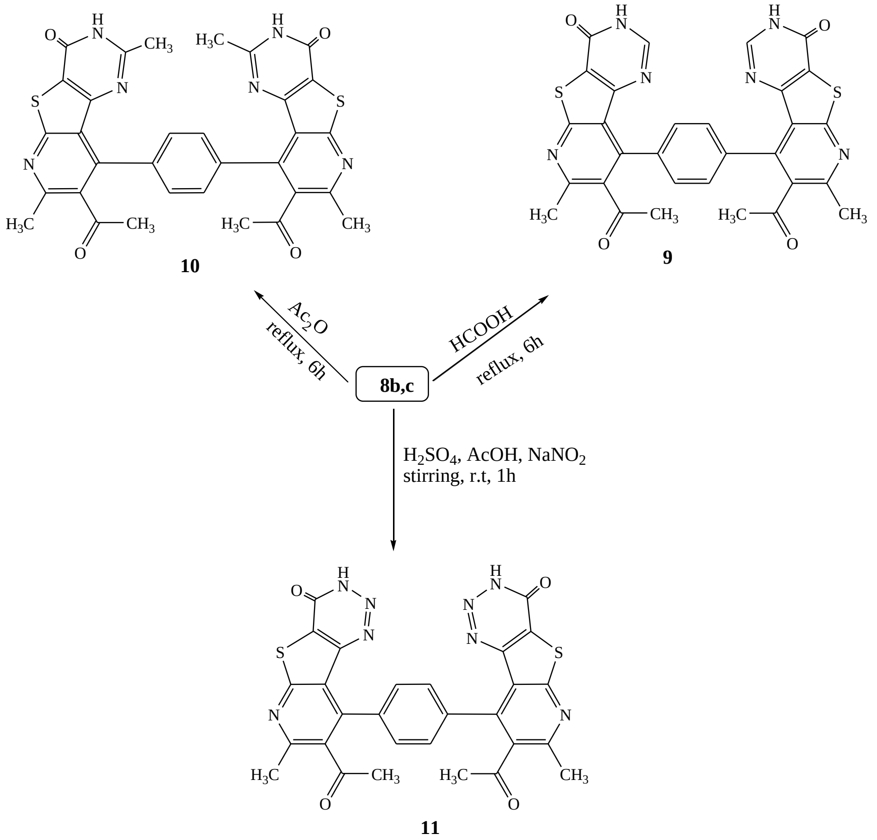
Scheme 2

The structures of each of 7b,c and 8b,c were elucidated by considering the data of IR, ^{1}H NMR, spectral data as well as that of elemental analyses (*cf.* Experimental Part and Scheme 2). In contrast to the behavior of each of 6a-c towards compound 5, compounds 6d-g reacted with 5 under the same above mentioned reaction conditions to give directly the reaction products 8d-g, respectively whose structures were elucidated by considering the data of elemental analysis as well as that of spectral ones (*cf.* Experimental Part). It is important to report here that all trials to isolate the bis2-alkylthio derivatives 7d-g failed under varieties of experimental conditions. Compound 5 reacted with chloroacetic acid 6h in different way, where it reacted to give 2,2'-{1,4-phenylenebis[3-cyano-5-acetyl-6-methylpyridine-4,2-diyl) thio]}-dicarboxylic acid (7h) and all trials to cyclize it under varieties of experimental conditions failed, but the corresponding cyclized product 8h can be obtained indirectly through hydrolysis of 8a in ethanolic solution of 10% NaOH under reflux for 3 hr (*cf.* Experimental Part).



Equation 1

Mass spectra of products 7b,c,h and 8d-g were used as a good tool to confirm their structures, where their parent peaks are at m/z = 572, 537, 572, 881, 763, 695 and 571, respectively which corresponding to the molecular weights of the molecular formulas $C_{28}H_{24}N_6O_4S_2$, $C_{28}H_{20}N_6O_2S_2$, $C_{28}H_{22}N_4O_6S_2$, $C_{40}H_{30}Br_2N_6O_4S_2$, $C_{40}H_{28}Cl_2N_4O_4S_2$, $C_{40}H_{30}N_4O_4S_2$ and $C_{30}H_{26}N_4O_4S_2$, respectively of the assigned structures. In addition, several peaks corresponding to the fragmentation of the parent peaks gave further confirmation for the assigned structures (*cf.* Exp. Part and Scheme 2). The structure of 8b,c was further confirmed *via* their reactions with each of formic acid, acetic anhydride, and nitrous acid to afford the reaction products 9-11, respectively. The IR (cm^{-1}) of these reaction products lack bands of CN and NH_2 groups and instead showed CO and NH groups. Considering the IR (cm^{-1}) in addition to the data of mass spectra and elemental analyses the structures of compounds 9-11 were established (*cf.* Experimental Part and Scheme 3). Reaction of 8c with acetic anhydride most probably proceeded *via* the acylation of the NH_2 group at 3-position, followed by partial hydrolysis of the CN group at 2-position to give $CONH_2$ group which underwent intramolecular cyclization to afford 10.



Scheme 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 in DMSO-d_6 as a solvent. 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/acetonitrile mobile phase and measured in the positive mode of the ion trap (molecular weights of most compounds are protonated ($[M+H]^+$).

Synthesis of 3,3'-Benzene-1,4-diylbis(2-cyanoprop-2-enethioamide) (3)

A solution of (1) (0.134 g; 1 mmole) and (2) (0.2 g 2 mmole) in absolute ethanol (30 ml) containing a catalytic amount of piperidine (0.4 ml) was stirred for 2 hr. The formed reaction product was collected by filtration, washed with cold ethanol, and then crystallized from ethanol to give the corresponding 3, as red crystals, yield 88%, mp >330 ^{0}C, IR (ν cm^{-1}): 3343.8,3295.2 (NH_2), 3057 (aromatic-CH) and 2226.2 (CN); MS: 298 (M^+, 11.5% corresponding to the molecular weight of the molecular formula $C_{14}H_{10}N_4S_2$ of the assigned structure), 264 (M^+- H_2S, 100%); 230 (264 - H_2S, 5.1%), 265 (298-SH, 31.7%), 239 (265-CN, 3.5%), 186 (264-CHC(CN)CN, H, 1.3%0; Anal. for $C_{14}H_{10}N_4S_2$ (298.382) Calcd./Found (%): C(56.35/56.40%) H(3.38/3.42%) N(18.78/18.51%) S(21.49/21.53%).

Synthesis of 4,4'-Benzene-1,4-diylbis(5-acetyl-6-methyl-2-thioxo-1,2-dihydropyridine -3-carbonitrile) (5)

A solution of (3) (0.298 g; 1 mmole) and (4) (0.2 g 2 mmole) in absolute ethanol (30 ml) and pyridine 10ml containing a catalytic amount of piperidine (0.4 ml) was heated under reflux for 5 hr. The formed reaction product was collected by filtration, washed with cold ethanol, and then crystallized from ethanol to give the corresponding (5) as orange crystals, yield 56%, mp >330 ^{0}C, IR (ν cm^{-1}): 3164.1 (Pyridine-NH), 3058.8 (aromatic-CH)), 2948.2,2855.1 (aliphatic-CH), 2228.4 (CN), and 1694.2 (Acetyl-CO); MS: 459 ($[M+H]^+$, 0.4%, corresponding to the molecular weight of the molecular formula $C_{24}H_{18}N_4O_2S_2$ of the assigned structure), 441 (459-H_2O, 100%), 423 (441- H_2O, 2.5%), 409 (423-CH_2, 0.7%), 394 (427-SH, 0.5%), 393 (427-H_2S, 0.2%), 426 (459- H_2S, 0.5%); Anal. for $C_{24}H_{18}N_4O_2S_2$ (458.554) Calcd./Found (%): C (62.86/62.89%) H (3.96/3.99%) O (6.98/7.01%) N(12.22/12.25%) S (13.99/ 14.02 %).

Synthesis of 7a-c,h and 8d-g (General method)

A mixture of 5 (0.458 g 1mmole) and ethyl chloroacetate (6a), 2-chloroacetamide (6b), chloroacetonitrile (6c), 1-[(4-bromo-phenyl)amino]-3-chloro-propan-2-one (6d), 2-bromo-1-(4-chlorophenyl)ethanone (6e), 2-bromo-1-phenylethanone (6f), 1-chloro-propan-2-one (6g), and chloroacetic acid (6h) (2 mmole) in sodium methoxide (prepared from 0.14 g of sodium and methanol 25 ml) was stirred at room temperature for 30 min. The formed precipitate was collected by filtration, washed with methanol then crystallized from ethanol to give 7a-c, 8d-g, 7h, respectively.

Diethyl 2,2'-{1,4-phenylenebis[3-cyano-5-acetyl-6-methylpyridine-4,2-diyl)thio]} diacetate (7a)

As pale yellow crystals, yielded by 70%, mp = 209 ^{0}C; IR (ν cm^{-1}): 2926.1,2820.4 (aliphatic-CH), 2225.6 (CN), 1743.9 (ester-CO) and 1697.5(Acetyl-CO); MS: 631 ($[M+H]^+$, 0.1%, corresponding to the molecular weight of the molecular formula $C_{32}H_{30}N_4O_6S_2$ of the assigned structure), 613 (631-H_2O, 0.6%), 586 (631-OEt, 40%), 585 (631-EtOH, 100%), 567 (613-EtOH, 0.5 %), 557 (585-CO, 32.3%), 539 (585-EtOH, 2.6%), 511 (539-CO, 6.4%), 483 (511-CO, 2%); ^{1}H NMR (DMSO- d_6) (δppm): 1.231 (t, 6H, $2CH_2\underline{CH_3}$), 1.647 (S, 6H, $2CH_3$), 2.471 (S, 6H, $2COCH_3$), 3.762 (q, 4H, $2\underline{CH_2}CH_3$), 4.192 (S, 4H, SCH_2) and 7.601 (m, 4H, ArH's); Anal, for $C_{32}H_{30}N_4O_6S_2$ (630.734) Calcd./Found(%): C(60.94/60.97%) H(4.79/4.82%) O(15.22/15.25%) N(8.88/8.91%) S (10.17/10.20%).

2,2'-{1,4-Phenylenebis[(3-cyano-6-methylpyridine-4,2-diyl)thio]}diacetamide (7b)

As orange crystals, yielded by 72%, mp >330 ^{0}C; IR (ν cm^{-1}): 3427.2,3169.4 (NH_2), 3064.1 (aromatic-CH), 2227.9 (CN), 1690.7 (Acetyl-CO) and 1654.9 (amide-CO); MS: 572 (M, 0.2%, corresponding to the molecular weight of the molecular formula $C_{28}H_{24}N_6O_4S_2$ of the assigned structure), 556 (572-NH_2, 37%), 555 (572-OH, 17.2%), 554 (572-H_2O, 19.4%), 539 (555-NH_2, 7.4%), 527 (554-HCN, 3.8%), 483 (527-$CONH_2$, 3.1%), 323 (572-$C_{11}H_{11}O_2N_3S$, 100%); ^{1}H NMR (DMSO- d_6) (δppm): 1.589 (s, 6H, $2CH_3$), 2.326 (s, 6H, $2CO\underline{CH}_3$), 4.125 (s, 4H, $2SCH_2$), 5.518 (s, br., 4H, $2NH_2$), 5.921 (br, 4H, $2NH_2$) and 7.634 (m, 4H, Ar H's); Anal, for $C_{28}H_{24}N_6O_4S_2$ (572.658) Calcd./Found(%): C(58.73/58.76%) H(4.22/4.25%) O(11.18/11.21%) N(14.68/14.71%) S(11.20/11.23%).

2,2'-{1,4-Phenylenebis[(3-cyano-6-methylpyridine-4,2-diyl)thio]}dicyanomethane (7c)

As orange crystals, yielded by 71%, mp = 235 ^{0}C; IR (ν cm^{-1}): 2979.7,2930.4 (aliphatic-CH), 2249.4, 2226.7 (CN), and 1693.5 (Acetyl-CO); MS: 537 ($[M+H]^+$, 100%, corresponding to the molecular weight of the molecular formula $C_{28}H_{20}N_6O_2S_2$ of the assigned structure), 520 (537-OH, 32%), 510 (537-HCN, 5.5%), 519 (537-H_2O, 100%), 501 (519-H_2O, 4.7%), 498 (537-CHCN, 11.6%), 497 (510-CH, 27.7%), 493 (519-CN, 11.6 %), 492 (519-HCN, 10.2%), 483 (510-HCN, 2.3%); ^{1}H NMR (DMSO- d_6) (δppm): 1.986 (s, 6H, $2CH_3$), 2.496(s, 6H, $2COCH_3$), 4.454 (s, 4H, $2SCH_2$) and 7.634 (m, 4H, Ar H's); Anal, for $C_{28}H_{20}N_6O_2S_2$ (536.628) Calcd./Found(%): C(62.67/62.7%) H(3.76/3.79%) O(5.96/5.98%) N(15.66/15.69%) S(11.95/ 11.98%).

2,2' - {1,4-Phenylenebis [3- cyano -5- acetyl- 6- methylpyridine -4, 2- diyl) thio]} dicarboxylic acid (7h)

As orange crystals, yielded by 95%, mp > 330 ^{0}C; IR (ν cm^{-1}): 2952.5,2853.8 (aliphatic-CH), 2227.5 (CN), 1692.9 (Acetyl-CO) and 1681.2 (acid-CO); MS: 572 (M-2H, 0.4%, corresponding to the molecular weight of the molecular formula $C_{28}H_{22}N_4O_6S_2$ of the assigned structure), 555 (572-OH, 7%), 554 (572-H_2O, 0.7%), 536 (554-H_2O, 0.5%), 529 (572-CH_3CO, 9.1%), 527 (555-CO, 2.6%), 515 (572-CHCOO, 1.3%), 513 (527-CH_2, 0.9%), 510 (555-COOH, 0.4%), 460 (529-$2CH_3CO$,CN, 15.9%), 459 (515-CCOO, 100%), 441 (459-H_2O, 1%); ^{1}H NMR (DMSO- d_6) (δppm): 1.762 (s, 6H, $2CH_3$), 2.513 (s, 6H, $2COCH_3$), 5.363 (s, 4H, $2SCH_2$), 7.552 (m, 4H, ArH's) and 12.105 (s, br., 2H, $COO\underline{H}$); Anal, for $C_{28}H_{22}N_4O_6S_2$ (574.626) Calcd./Found(%): C(58.52/58.55%) H(3.86/3.89%) N(9.75/9.78%) O(16.71/16.74%) S(11.16/11.19%).

4,4'- Benzene - 1, 4 - diylbis (1- {3-amino – 2 - [N - (4 – bromophenyl)-carbonyl]-6-methylthieno [2,3-b] pyridine - 5-yl}diethanone (8d)

As bright yellow crystals, yielded by 83%, mp = 152 ^{0}C; IR (ν cm^{-1}): 3464.4,3266.2 (NH_2), 3195.5 (NH), 3078.9 (aromatic-CH), 1699.4 (Acetyl-CO) and 1670.1 (amide-CO); MS: 881 (M ,0.2% corresponding to the molecular weight of the molecular formula $C_{40}H_{30}N_6O_4S_2Br_2$ of the assigned structure), 711 (881- NPhBr, 53%), 710 (M- NHPhBr, 100%), 683 (711- CO, 0.8%), 682 (710-CO, 2.3%), 540 (710- NphBr, 16.9%), 539 (710-NHPhBr, 35.5%), 513 (683-NPhBr, 3.6%), 512 (682-NPhBr, 2.4%), 511 (682-NHPhBr, 10.4%), 484 (512-

CO, 3.3%); ^{1}H NMR (DMSO-d_6) (δppm): 1.912 (s, 6H, 2CH_3), 2.645 (s, 6H, 2CO$\underline{CH}_3$), 5.247 (s, br., 4H, 2NH_2), 6.251 (s, br., 2H, CON$\underline{H}$), 7.825 (m, 12H, Ar`H's); Anal, for $C_{40}H_{30}N_6O_4S_2Br_2$ (882.64) Calcd./ Found(%): C(54.38/ 54.40%) H(3.43/3.46%) O(7.25/7.28%) N(9.52/9.55%) S(7.26/ 7.30%) Br(18.11/18.14%).

4,4'- Benzene - 1, 4 -diylbis(1-{3-amino-2-[(4-chlorophenyl)carbonyl]-6-methylthieno [2,3-b] - pyridin-5-yl}- diethanone) (8e)

As yellow crystals, yielded by 98%, mp = 188 ^{0}C; IR (ν cm^{-1}): 3484.4, 3278.9 (NH_2), 1701.5 (CO); MS: 763 (M, 100% corresponding to the molecular weight of the molecular formula $C_{40}H_{28}N_4O_4S_2Cl_2$ of the assigned structure), 747 (763-NH_2, 54.1%), 745 (M-H_2O, 10.3 %), 731 (747-NH_2, 10%), 727 (745-H_2O, 34%), 651 (763-PhCl, 100%), 635 (651-NH_2, 3.7%), 633 (651-H_2O, 25.5%), 623 (651-CO, 7.3%); ^{1}H NMR (DMSO-d_6) (δppm): 1.785 (s, 6H, 2CH_3), 2.632 (s, 6H, 2CO$\underline{CH}_3$), 5.416 (s, br., 4H, 2NH_2) and 7.816 (m, 12H, Ar`H's); Anal, for $C_{40}H_{28}N_4O_4S_2Cl_2$ (763.708) Calcd./Found(%): C(62.91/62.94%) H(3.70/3.73%) Cl(9.28/9.31%) O(8.38/8.41%) N(7.34/ 7.37%) S(8.40/8.43%).

4,4'-Benzene-1,4-diylbis(1-[3-amino-6-methyl-2-(benzoyl)thieno[2,3-b]pyridine-5-yl]diethan-one) (8f)

As yellow crystals, yielded by 98%, mp = 172 ^{0}C; IR (ν cm^{-1}): 3476.4, 3299.9 (NH_2), 3055.3 (aromatic-CH), 1716.2 (Acetyl-CO) and 1699.4 (aromatic ketone-CO); MS: 695 ([M+H]$^+$, 31.5% corresponding to the molecular weight of the molecular formula $C_{40}H_{30}N_4O_4S_2$ of the assigned structure), 679 (695- NH_2, 14.7%), 677 (695- H_2O, 100%), 661 (679- H_2O, 4.1%), 659 (677- H_2O, 25.3%), 634 (661- H_2O, 1.3%), 619 (695- C_6H_4, 15.9%), 573 (677- COC_6H_4, 34.2%), 555 (573- H_2O, 5.4%); ^{1}H NMR (DMSO-d_6) (δppm): 2.048 (s, 6H, 2CH_3), 2.555 (s, 6H, 2$COCH_3$), 6.901 (br, 4H, 2NH_2), 7.705 (s, 4H, Ar`H`S),7.568-7.798 (m, 10H, 2COPh); Anal, for $C_{40}H_{30}N_4O_4S_2$ (694.824) Calcd./Found(%): C(69.14/69.17%) H(4.35/4.38%) N(8.06/8.09%) O(9.21/9.24%) S(9.23/9.27%).

4,4'-Benzene-1,4-diylbis(1,1'-(3-amino-5-acetyl-6-methylthieno[2,3-b]pyridine-2,5-diyl)di-ethanone) (8g)

As orange crystals, yielded by 88%, mp >330 ^{0}C; IR (ν cm^{-1}): 3484.2, 3300.5 (NH_2), and 1702.2 (Acetyl-CO), 1697.5 (Acetyl-CO); MS: 571 ([M+H]$^+$, 2.4 % corresponding to the molecular weight of the molecular formula $C_{30}H_{26}O_4N_4S_2$ of the assigned structure), 555 (571-NH_2, 8.4%), 553 (571-H_2O, 51.4%), 537 (555-H_2O, 6.7%), 535 (553- H_2O, 42.4%), 529 (571-$COCH_2$, 100%), 511 (529-H_2O, 31.4%), 495 (537-$COCH_2$, 3.1%), 493 (511-$COCH_2$, 16.6%); ^{1}H NMR (DMSO-d_6) (δppm): 2.018 (s, 6H, 2CH_3), 2.394 (s, 6H, 2$COCH_3$), 2.534 (s, 6H, 2$COCH_3$), 6.552 (br, 4H, 2NH_2), 7.662 (m, 4H, ArH`S); Anal, for $C_{30}H_{26}N_4O_4S_2$ (570.934) Calcd./Found(%): C(63.14/63.17%) H(4.59/4.62%) N(9.82/9.85%) O(11.21/11.24%) S(11.24/11.27%).

Synthesis of (8a,c)

A solution of 7a,c (0.63 g, and 0.536 1mmole) in sodium ethoxide (prepared from 0.14 g of sodium and ethanol 25 ml) was refluxed for 30 min. The formed precipitate was collected by filtration, washed with ethanol and crystallized from ethanol to give 8a,c.

Diethyl 4,4'(1,4-phenylene)bis(3-amino-5-acetyl-6-methylthieno[2,3-b]pyridine-2-carboxylate (8a)

As yellow crystals yielded by 85%, mp = 302 °C; IR υ(cm^{-1}): 3479.4, 3347.9 (NH_2), 1702.1 (ester-CO), 1686.6 (Acetyl-CO); MS: 631 ($[M+H]^+$, 0.1% corresponding to the molecular weight of the molecular formula $C_{32}H_{30}N_4O_6S_2$ of the assigned structure), 586 (631-EtO, 45.8%), 585 (631- EtOH, 100%), 557 (585-CO, 4.1%), 539 (585-EtOH, 5.2%), 511 (557-EtOH, 0.3%), 483 (511-CO, 0.1%); ^{1}HNMR (DMSO-d_6) (δppm): 1.255 (t, 6H, $2CH_2\underline{CH_3}$), 1.921 (s, 6H, $2CH_3$), 2.416 (s, 6H, $2CO\underline{CH_3}$), 3.758 (q, 4H, $2\underline{CH_2}CH_3$), 5.516 (br, 4H, $2NH_2$), 7.001-7.589 (m, 4H, Ar`H`S); Anal., for $C_{32}H_{30}N_4O_6S_2$ (630.734), Calcd./Found (%): C(60.94/60.97%) H(4.79/4.82%) N(8.88/8.91%) O(15.22/ 15.25%) S(10.17/10.2%).

Diethyl 4,4'(1,4-phenylene)bis(3-amino-5-acetyl-6-methylthieno[2,3-b]pyridine-2-carbo-nitrile) (8c)

As orange crystals yielded by 52%, mp >330 °C; IR υ(cm^{-1}): 3468.5, 3349.3 (NH_2), 2199.1 (CN), 1701.3 (Acetyl-CO); MS: 537 ($[M+H]^+$, 27.8% corresponding to the molecular weight of the molecular formula $C_{28}H_{20}N_6O_2S_2$ of the assigned structure), 522 (537-NH, 3.7%), 521 (537-NH_2, 19.3%), 519 (537-H_2O, 85%), 505 (519-CH_2, 10.1%), 504 (522-H_2O, 1.1%), 487 (505-H2O, 11.9%); ^{1}H NMR (DMSO-d_6) (δppm): 1.963 (s, 6H, $2CH_3$), 2.543 (s, 6H, $2CO\underline{CH_3}$), 5.654 (s, br., 4H, $2NH_2$) and 7.655 (m, 4H, Ar`H's); Anal., for $C_{28}H_{20}N_6O_2S_2$ (536.628), Calcd./Found (%): C(62.67/62.7%) H(3.76/3.79%) N(15.66/15.69%) O(5.96/5.99%) S(11.95/11.98%).

Synthesis of 4,4'-Benzene-1,4-diylbis(5-acetyl-3-amino-6-methylthieno[2,3-b]pyridine-2-carboxamide) (8b)

A solution of each of 5 (0.458 g 1mmole) and 2-chloroacetamide (0.187 g 2 mmole) was refluxed in sodium ethoxide (prepared from 0.14 g of sodium and ethanol 25 ml) for 5 hr. The formed precipitate was collected by filtration, washed with ethanol and crystallized from ethanol to give 8b, as yellow crystals. Yielded (68%); mp = 290 °C; IR υ(cm^{-1}): 3434.4, 3325.7 (NH_2), 1689.7 (Acetyl-CO), 1658.5 (Amide-CO); MS: 572 (M, 0.2% corresponding to the molecular weight of the molecular formula $C_{28}H_{24}N_6O_4S_2$ of the assigned structure), 557 (572-NH, 14%), 556 (572-NH_2, 39.9%), 555 (572-OH, 100%), 541 (556-NH, 0.7%), 539 (555-NH_2, 1.8%), 529 (557-CO, 0.2 %), 528 (555-HCN, 9.1%), 514 (529-NH, 0.2%), 486 (514-CO, 1.1%); ^{1}HNMR (DMSO-d_6) (δppm): 1.943 (s, 6H, $2CH_3$), 2.507 (s, 6H, $2COCH_3$), 5.608 (br, 4H, $2NH_2$), 5.845 (br, 4H, $2NH_2$), 7.581 (m, 4H, Ar`H`S); Anal. for $C_{28}H_{24}N_6O_4S_2$ (572.658) Calcd./Found(%): C(58.73/58.76%) H(4.22/ 4.25%) O(11.18/11.21%) N(14.68/14.71%) S(11.2/ 11.23%).

Synthesis of 4,4'-Benzene-1,4-diylbis(5-acetyl-3-amino-6-methylthieno[2,3-b]pyridine -2-carboxylic acid) (8h)

A solution of 8a (0.63 g 1mmole) in potassium hydroxide/ethanol mixture (prepared from 2.5g of potassium hydroxide in least amount of water mixed with 25 ml ethanol) was refluxed for 3 hr. The formed product is precipitated by acidification with acetic acid, collected by filtration, washed with ethanol and crystallized from ethanol to give 8h,as yellow crystals. Yield (89%); mp >330 ^{0}C; IR υ(cm^{-1}): 1744.7 (CO), 1698.9 (CO); MS: 575 ([M+H]$^+$, 0.2% corresponding to the molecular weight of the molecular formula $C_{28}H_{22}N_4O_6S_2$ of the assigned structure), 557 (575-H_2O, 40%), 539 (557-H_2O, 2.8%), 522 (539-OH, 0.8%), 518 (575-CH_3CO,N 100%), 512 (557-COOH, 0.7%), 501 (518-OH, 7.1%), 500 (518-H_2O, 59.4%), 483 (539-2CO, 4.9%); ^{1}H NMR (DMSO-d_6) (*δ*ppm): 1.765 (s, 6H, $2CH_3$), 2.583 (s, 6H, $2CO\underline{CH_3}$), 5.869 (s, br., 4H, $2NH_2$), 7.825 (m, 4H, Ar`H’s) and 12.541 (s, br., 2H $COO\underline{H}$); Anal, for $C_{28}H_{22}N_4O_6S_2$ (576.642) Calcd./Found(%): C(58.32/58.45%) H(4.19/4.49%) N(9.72/9.78%) O(16.65/16.74%) S (11.12/11.19%).

Synthesis of 9 and 10 (General method)

A solution of each 8b or 8c (0.57 g, 0.536 g 1mmole) and each of 30 ml of (Formic acid, and Acetic anhydride as a mixture), was heated under reflux for 5 hr. The excess solvent was evaporated under reduced pressure. After cooling,The formed solid was collected by filtration, dried, and crystallized from the ethanol to give 9 & 10, respectively.

4,4'-Benzene-1,4-diylbis(8-acetyl-7-methylpyrido[3',2':4,5]thieno[3,2-d]pyrimidin-4(3H)-one) (9)

As yellow crystals yielded by (63%); mp >330 ^{0}C; IR υ(cm^{-1}): 3169.5 (NH), 1699.2 (Acetyl-CO), 1654.2 (pyrimidinone-CO); MS: 593 ([M+H]$^+$, 0.5% corresponding to the molecular weight of the molecular formula $C_{30}H_{20}N_6O_4S_2$ of the assigned structure), 576 (593-OH, 22.4%), 575 (593- H_2O, 55.9%), 558 (576-H_2O, 34.8%), 557 (575- H_2O, 100%), 549 (576-HCN, 1.3%), 539 (557-H_2O, 17.6%), 531 (558-HCN, 0.3 %); ^{1}H NMR (DMSO-d_6) (*δ*ppm): 2.033 (s, 6H, $2CH_3$), 2.502 (s, 6H, $2COCH_3$), 7.425 (m, 6H, pyrimidinone and ArH`S), 12.906 (br, 2H, 2NH); Anal for $C_{30}H_{20}N_6O_4S_2$ (592.648) Calcd./Found(%): C(60.80/60.83%) H(3.40/3.43%) N(14.18/14.21%) O(10.8/ 10.83%) S(10.82/10.85%).

4,4'-Benzene-1,4-diylbis(8-acetyl-2,7-dimethylpyrido[3',2'-:4,5]thieno[3,2-d]pyramidin -4-(3H)-one) (10)

As beige crystals yielded by (63%); mp >330 ^{0}C; IR υ(cm^{-1}): 2947.9,2833.5 (aliphatic-CH), 1701.2 (CO); MS: 621 ([M+H]$^+$, 0.2% corresponding to the molecular weight of the molecular formula $C_{32}H_{24}N_6O_4S_2$ of the assigned structure), 606 (621-CH_3, 0.9%), 604 (621-OH, 3.8%), 603 (621-H_2O, 6%), 588 (621-CH_3, 4.2%), 585 (603-H_2O, 4.1%), 579 (606-HCN, 100%), 561 (588- HCN, 7.8%), 544 (561-OH, 1.7%); ^{1}H NMR (DMSO-d_2) (*δ*ppm): 2.201 (s, 12H, $4CH_3$), 2.555 (s, 6H, $2CO\underline{CH_3}$), 7.852 (m, 4H, ArH`S), 12.417 (br, 2H, 2NH); Anal, for $C_{32} H_{24} N_6 O_4 S_2$ (620.702) Calcd. / Found (%): C (61. 92 / 61. 95 %) H(3.9/3.93%) N(13.54/13.57%) O(10.31/10.34%) S(10.33/10.36%).

Synthesis of 4,4'-Benzene-1,4-diylbis(8-acetyl-7-methylpyrido [3',2':4,5] thieno [3,2-d][1,2,3]triazin-4-(3H)-one) (11)

A Sodium nitrite solution 10% (5 ml) was added to a solution of each of 8b,c (0.57g, 0.536g 1 mmol) in concentrated sulphuric acid (5 ml) and glacial acetic acid (5ml) at 0 °C during 5 min, with stirring. The mixture was allowed to stand at room temperature for 30 min. The solid that precipitated on dilution with water was collected and recrystallized from dioxane to give 11, as orange crystals. Yield (83%); mp >330 ^{0}C; IR υ(cm^{-1}): 3213.1(NH), 3096.5 (aromatic-CH), 1695.2 (Acetyl-CO); MS: 595 ([M+H]$^+$, 0.1% corresponding to the molecular weight of the molecular formula $C_{28}H_{18}N_8O_4S_2$ of the assigned structure), 567 (595-N_2, 100%), 552 (567-NH, 1.4%), 551 (567-NH_2, 2%), 539 (567-N_2, 2.4%), 524 (552-CO, 12.6%), 523 (551-CO, 5.4%), 496 (524-N_2, 3.6%); ^{1}H NMR (DMSO-d_2) (δppm): 1.907 (s, 6H, 2CH_3), 2.506 (s, 6H, 2$COCH_3$), 7.616 (m, 4H, ArH`S), 15.546 (br, 2H, 2NH); Anal, for $C_{28}H_{18}N_8O_4S_2$ (594.624) Calcd./Found(%): C(56.56/56.59%) H(3.05/3.08%) N(18.84/18.87%) O(10.76/ 10.79%) S(10.78/10.81%).

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التخليق ، التفاعلات والخصائص لمركب 4،4´- بنزين –4,1- دايل بيس (5- اسيتيل -6- ميثيل -2- ثيوكسو -2,1- داي هيدروبيريدين-3- كربونيتريل

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يتفاعل بنزين – 4,1- داي كربولدهيد (1) مع 2- سيانو ايثان ثيوأميد (2) ليعطي 3،3´- بنزبن- 4,1- دايل بيس (2- سيانوبروب-2- اينثيوأميد) (3) والذي بدوره يتفاعل مع بنتان – 4,2- دايون (4) ليعطي المقابل 4,4´- بنزين -4,1- دايل بيس (5- اسيتيل -6- ميثيل -2- ثيوكسو -2,1- داي هيدروبيريدين -3- كربونيتريل) (5). تم التحقق من إمكانية تخليق المركب 5 في الدراسة الحالية عبر تفاعله مع كواشف متعددة ليعطي المخلق حديثا 4,4´- (4,1- فينيلين) – بيس (5- استيل -3- أمينو -6- ميثيل ثينيو [3,2- b] بيريدينات 8 h-a. تم التأكد من هياكل المركبات الحلقية غير المتجانسة المخلقة في الدراسة الحالية بواسطة النظر في بيانات الأشعة تحت الحمراء ، طيف الرنين النووي لذرة الهيدروجين ، طيف الكتلة وكذلك التحليلات العنصرية.