Novel Synthesis and Antimicrobial Evaluation of S-containing Heterocyclic Derivatives from 2,6-Bis (furan-2-ylmethylidene)cyclohexanone

Al-shayea Oqba N.[1,2*], Alkubaisi Hameed M.[3] and Attaby Fawzy A.[4]
1. Center of Desert Studies (CDS), University of Anbar, Ramadi, Anbar, IRAQ
2. College of Pharmacy, University of Anbar, Ramadi, Anbar, IRAQ
3. Applied Chemistry Department, College of Applied Science, Fallujah University, Fallujah, IRAQ
4. Department of Chemistry, Faculty of Science, Cairo University, 12613 Giza, EGYPT
*ds.dr.oqbanafia@uoanbar.edu.iq

Abstract

2,6 - Bis (furan - 2- ylmethylidene) cyclohexanone 1 reacted with 2-cyanoethanethioamide 2 to give the corresponding 4-(furan-2-yl)-8-(furan-2-ylmethy lidene)-2-thioxo-1, 2, 5, 6, 7, 8-hexahydro-quinoline-3-carbonitrile 4. The synthetic potentiality of compound 4 was investigated in the present study via its reactions with several active-hydrogen containing compounds 5a-g aiming to synthesize 4-(furan-2-yl)-8-(furan-2-ylmethylidene)-5,6,7,8-tetrahydrothieno[2,3-b]quinolin-3-amine derivatives 8a-g. Tetrahydrothieno[2,3-b]quinolin-3-amine derivatives 8a-d were used as good synthones for the preparation of tetrahydropyrimidothienoquinolines-4(3H)-one 11, 12a,b, 13a,b, 14, 23 and 26a,b. 3-Aminothienoquinoline-2-carbohydrazide derivative 15 which was used to prepare 2-(5-N-phenylamino-1,3,4-oxadiazol-2-yl)-5,6,7,8-tetrahydro-thieno[2,3-b] quinolin-3-amine 16, N'-arylmethylene-5,6,7,8-tetrahydrothieno[2,3-b]quinoline-2-carbohydrazides 19a,b, 2- (pyrazol-1-yl)carbonylthieno[2,3-b]quinolin-3-amine derivative 21 and 1- acetyl pyrazolothienoquinoline-3-one derivative 28.

Structures of the newly obtained heterocyclic compounds were established by taking the data of IR, ^{1}H NMR, mass spectra as well as that of elemental analyses into consideration. Antimicrobial evaluation of all newly obtained heterocyclic compounds was investigated.

Keywords: 2-Cyanoethanethioamide, 2-Thioxohexa-hydroquinoline-3-carbonitrile, tetrahydrothieno-quinolin -3-amine and pyrimidothienoquinolines.

Introduction

Thioxohexahydroquinoline-3-carbonitrile was found to belong to one of the most promising classes of heterocyclic compounds. As they are versatile, highly reactive and chemically flexible reagents, a considerable attention has been devoted to both its method of preparation as well as its reactions aiming to the preparation of tetrahydrothieno[2,3-b]quinolin-3-amine and pyrimidothienoquinolines. 2-Thioxohexahydroquinolines are of special interest because their biological profile[1-6]. Enaminoester moieties were utilized in obtaining several heterocyclic systems with specific biological and pharmaceutical activities[7-9]. Quinoline derivatives have attracted a great deal of interest due to their biological activities such as inhibitors of the RET tyrosine kinase[10], a new class of antitumor[11] and antibacterial[12,13] agents and this oriented our interest to synthesize and characterize several derivatives of these heterocyclic systems required for several chemical transformation as well as medicinal chemistry programs. As a continuation of our previous work,[14-22] of our interest is in the synthesis of 2-thioxo-hexahydroquinoline-3-carbonitrile derivative 4 and investigation of their synthetic potentiality with several reagents to achieve our target.

Material and Methods

Experimental: All recorded melting points were uncorrected; the IR samples were handled as KBr discs and recorded on a Shimadzu FTIR-8201PC Spectrophotometer. All samples ^{1}H-NMR spectra were recorded on a Varian Mercury 300 MHz. and a Varian Gemini 200 MHz. spectrometers by TMS as an internal standard using $CDCl_3$, DMSO-d_6 and $(CD_3)_2CO$ as solvents and δ (ppm) units expressed the chemical shifts. Mass spectrometry samples were recorded on Shimadzu GCMS-QP1000EX using an inlet type at 70eV. All data given by Microanalytical Center of Cairo University performed the microanalyses.

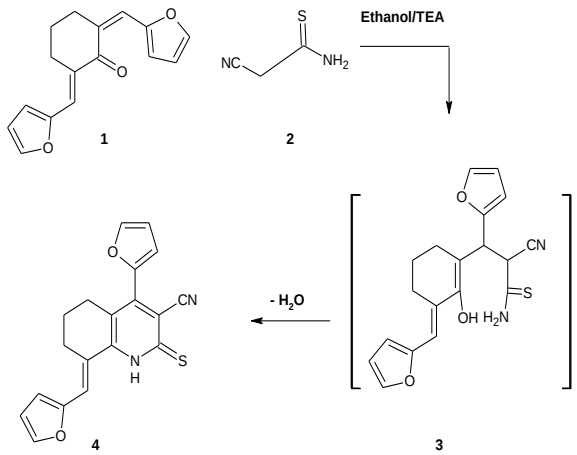
4-(Furan-2-yl)-8-(furan-2-ylmethylidene)-2-thioxo-1,2,5,6, 7,8-hexahydroquinoline-3-carbo-nitrile 4 was synthesized by the reaction 2,6-bis(furan-2-ylmethylidene) cyclohexanone 1 with 2-cyanoethanethioamide (2) in ethanol containing the catalytic amount of triethylamine. The formation of 4 seemed to proceed via the addition of methylene function in 2 on the –CH=CH- in 1 followed by spontaneous cyclization which auto-oxidation under the reaction conditions to afford 4 in good yield and in very pure state. The chemical structure of 4 was elucidated based on spectral data and elemental analysis. Thus, the mass spectra of 4 gave m/z = 334 corresponds to the molecular mass of the assigned structure.

Moreover, other peaks corresponding to fragmentation at furan-2-ylmethylidene, CN and SH groups gave further confirmation of the assigned structure. Furthermore, ^{1}H NMR spectra revealed besides the expected signals of hetero-aromatic and aliphatic protons, the singlet broad

signal at δ11.98 ppm of NH proton was detected (cf. Scheme 1 and Exp. Part). Synthon 4 was used as a starting material for the present study, thus, it was found that 4 reacted with ethyl chloroacetate (5a) 1:1 in methanolic sodium methoxide solution to afford the corresponding S-alkyl derivative 6a.

The structure of 6a showed the presence of absorption bands due to CN at 2210 cm^{-1} and CO at 1740 cm^{-1} functional groups of the newly introduced $COOCH_2CH_3$ group. So, we concluded that compounds 4 reacted with 5a via dehydrochlorination. In a similar manner, compound 4 reacted with each of chloroacetonitrile (5b), 2-chloroacetamide (5c), 2-chloro-N-(4-bromophenyl)acetamide (5d), 1-chloroacetone (5e), chloro-methylbenzimidazole (5f) and 2-bromo-1-(4-methylphenyl)ethanone (5g) to afford the corresponding S-alkyl derivatives 6b-g.

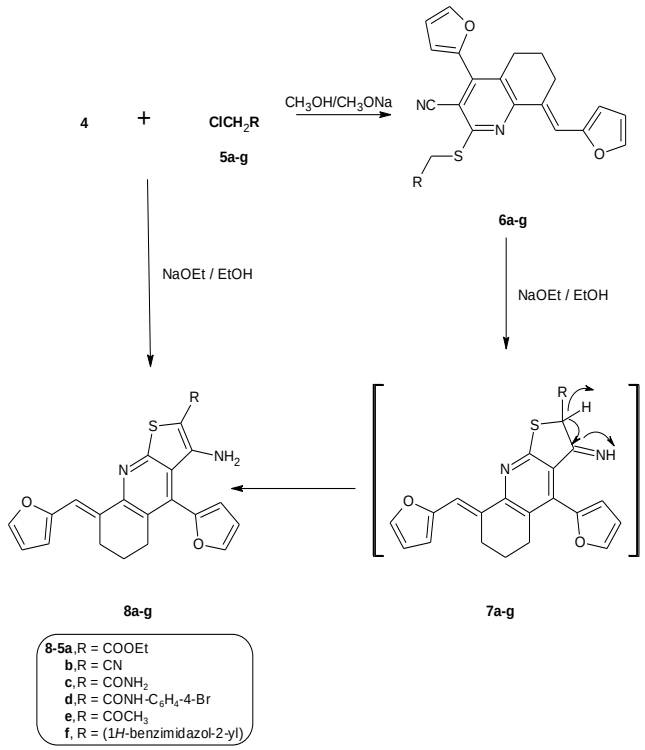
The structures of compounds 6a-g were further elucidated via their cyclization to the corresponding tetrahydrothieno[2,3-b]quinolin-3-amine derivatives 8a-g upon boiling in ethanolic sodium ethoxide solution. The IR spectra of compounds 8a-g showed the presence of the absorption bands of the newly born NH_2 group (cf. scheme 2 and Exp. Part). The reaction products were obtained by addition of $-CH_2-$ on the CN group by Thorpe-Zeigler condition, to afford the imino derivatives 7a-g which spontaneously rearranged to give the reaction products 8a-g. The hydrolysis of compound 8a in 10% ethanolic potassium hydroxide solution afforded after acidification the corresponding tetrahydrothieno[2,3-b]quinoline-2-carboxylic acid derivative 9 which, in turn, reacted with acetic anhydride and afforded the corresponding 2-methyl[1,3]oxazinothienohexahydroquino-line-4-one derivative 10. The IR spectrum of 10 showed the absorption band of the CO at 1745 cm^{-1} of oxazinone ring and no absorption band corresponded to NH_2 group was detected.



Scheme 1

Moreover, peaks at m/z = 416 (84.1%) corresponding to its molecular weight; m/z = 415 (75.8%, M^+-H); 372 (1.6%, M^+-CO_2) were given by its mass spectrum (cf. Scheme 3 and Exp.). Oxazinone derivative 10 reacted with hydrazine hydrate to give the corresponding 2-methyl-3-aminopyrimidothieno tetrahydroquinoline derivative 11. The IR spectrum of 11 showed the absence of the absorption band of CO of the oxazinone ring while its mass spectrum gave peaks at m/z = 430(3%) corresponding to its molecular weight; m/z= 415(95 %, M^+- CH_3); m/z = 414(6.4 %, M^+- NH_2) (cf. Scheme 3 and Exp. Part). As an extension of this study, tetrahydropyrimidothienoquinolines were obtained through using thienotetrahydroquinoline 7b-d as the starting materials. Thus, compound 8b reacted with formic acid to afford the reaction product 12a. The absorption bands of CO and NH groups were detected by IR (cm^{-1}) spectrum.

Moreover, its mass spectra gave m/z = 401 corresponded to its molecular weight (cf scheme 4). It can be concluded that 12a was obtained authentically via the reaction of 8c with formic acid or with triethylorthoformate in acetic anhydride. The reaction of 8b with formic acid most probably proceeded via formylation of NH_2 at the 3-position followed by partial hydrolysis of CN group at 2-position to give $CONH_2$ group, which underwent intramolecular cyclization to give 12a.



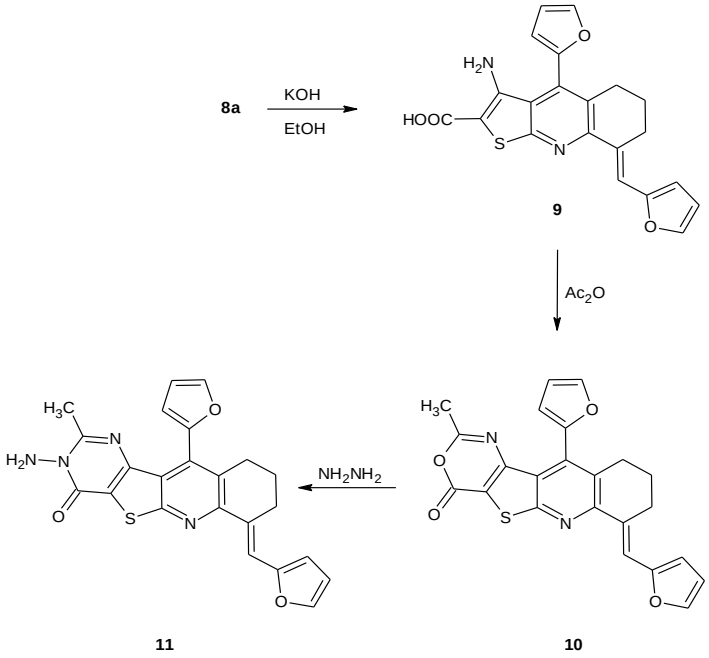
Scheme 2

The nucleophilic behavior of $-NH_2$ at 3-position of 8d was detected via its reaction with acetic anhydride and carbon disulphide. Thus, compound 8d reacted with acetic anhydride and carbon disulphide in pyridine to afford the reaction products 13b and 14. The structures of 13b, 14 were established by taking the data of IR and elemental analysis into consideration (cf. Exp. part). Moreover, their mass spectra gave m/z= 570 and 588 respectively corresponding to their molecular weights (cf. Scheme 4 and Exp. Part). Furthermore, compound 8d reacted with HCOOH acid or with dimethylformamide-dimethylacetal (DMF-DMA) under

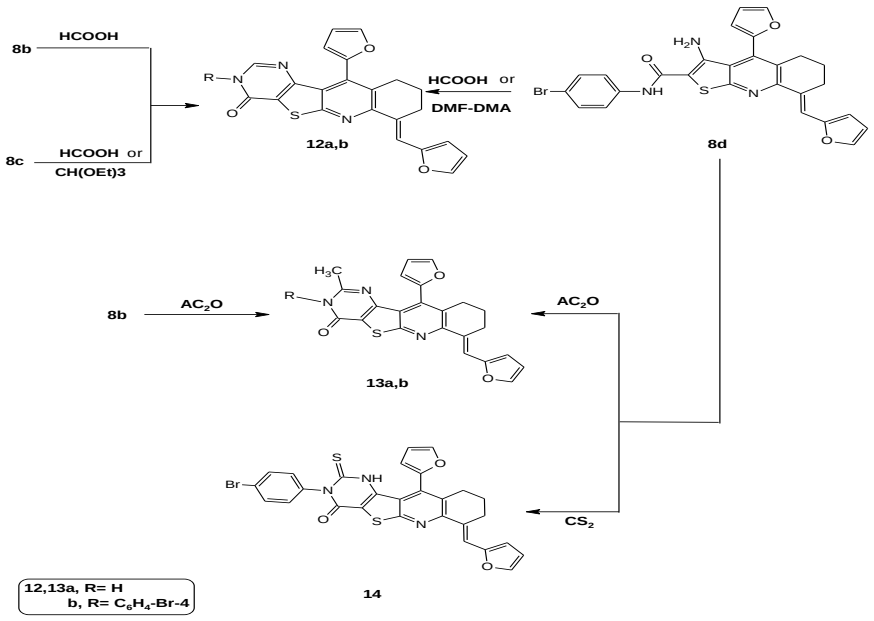
reflux in dry xylene to afford the same reaction product 12b whose structure was proved via both data of IR and elemental analysis.

Finally, the reaction of compound 8b with acetic anhydride under reflux afforded compound 13a. Its mass spectrum gave peaks at m/z = 415(53%) corresponding to its molecular weight. 3-Amino-4-(furan-2-yl)-8-(furan-2-ylmethylidene)-5,6,7,8-tetrahydrothieno[2,3-b]quinoline-2-carbohydrazide 15 was synthesized via the reaction of ethyl 3-amino-4-(furan-2-yl)-8-(furan-2-ylmethylidene)-5,6,7,8-tetrahydrothieno[2, 3-*b*]-quinoline-2-carboxylate 8a with hydrazine hydrate in reflux for 3-5 h.

The IR (cm^{-1}) spectrum of this reaction product did not show the absorption bands of carbonyl ester while the newly created $NHNH_2$ functions were shown (cf. Exp. Part). Thus, we concluded that the reaction proceeded via the nucleophilic attack of the hydrazine nitrogen atom on the electrophilic carbon of the COOEt group followed by removal of ethanol molecule. The parent peak at m/z = 406 (7.2%) corresponding to its molecular weight and peak at mlz = 351 (20.3 %, M^+-$CONHNH_2$) given by mass spectrometry in addition to, no signals of $COO\underline{CH_2}\underline{CH_3}$ protons in its ^1H NMR spectrum used for further confirmation of this structure (cf. Exp. Part).



Scheme 3



Scheme 4

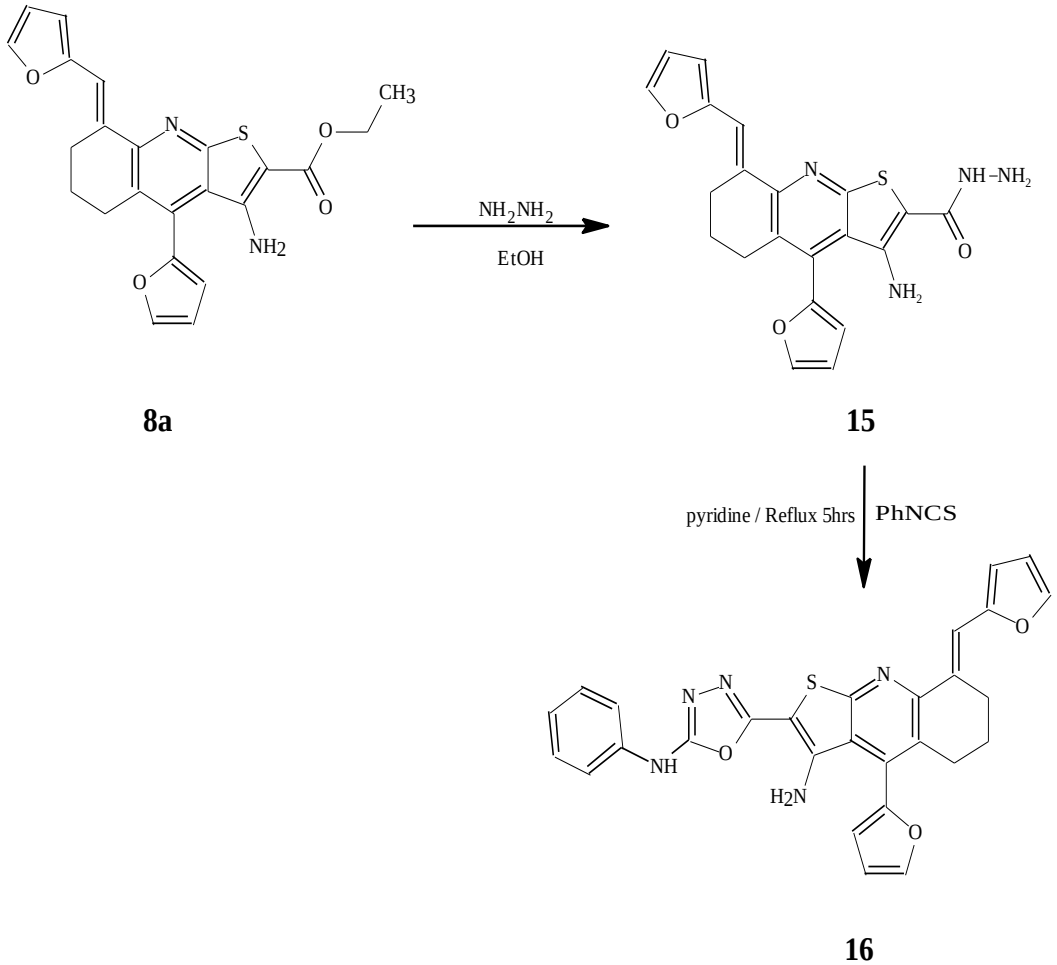
Results and Discussion

Aiming to investigate both chemical reactivity and synthetic potentiality of 15**,** it reacted with phenylisothiocyanate in pyridine under reflux for 5h to give the corresponding 2-(5-N-phenylamino-1,3,4-oxadiazol-2-yl)-4-(furan-2-yl)-8-(furan-2-ylmethylidene)-5,6,7,8-tetrahydro- thieno[2,3-*b*]quinolin-3-amine 16 via the loss of one molecule of hydrogen sulfide. Using the data of both elemental analyses and IR spectra the structure of 16 elucidated as well as peaks given by mass spectra at m/z = 507 (M^+, 13%) which corresponding to the molecular weight and at M^+-H and M^+ - oxadiazole ring gave further confirmation of the assigned structure 16 (cf. Exp. Part and Scheme 5).

The nucleophilic character of N atom of $NHNH_2$ group at 2-position of 15 was further investigated via its reactions with benzylidenemalononitrile (17a) or benzaldehyde 18a in ethanolic pyridine mixture in reflux to give the reaction product 19a (cf. Scheme 6). The chemical structure of 19a was proved by using the data of IR and elemental analyses. Moreover, its mass spectra gave m/z = 494 corresponding to its molecular weight and its ^{1}HNMR spectrum was convinced with the assigned structure (cf. Scheme 6 and Exp. Part). Also compound 15 reacted with anisalyldenemalononitrile (17b) or anisaldehyde 18b under the same above-mentioned reaction conditions to afford product 19b whose structure was proved by using the data of both elemental and spectral studies (cf. Exp. Part).

Compound 15 was reacted with formic acid, trimethyl orthoformate and dimethylformamide-dimethylacetal (DMF-DMA) in three individual reactions to give the corresponding pyrimidothienoquinoline derivatives 23 and 26a,b respectively whose structures were proved by the data of IR, ^{1}H NMR, mass spectral and elemental analyses data (cf. Scheme 6 and Exp. Part).

The work was extended to shed more light on both the synthetic potentiality and position of $–CONHNH_2$ in compound 15 aiming to build an additional pyrazole ring along $–NH-NH_2$ group. Compound 15 was reacted with acetyl acetone (20) in acetic acid for 3-5h to afford the reaction product 21. The data of IR, mass spectra and elemental analyses were considered to elucidate these structures. A new 1-acetyl-10-(furan-2-yl)-6-(furan-2-ylmethylidene)-1,2-dihydro-3*H*-pyrazolothienoquinolin-3-one 28 was formed via the treatment of 15 with glacial acetic acid under reflux for 4h, the structure of the latter compound was elucidated based on the elemental analysis and the spectral data as in scheme 6 and experimental part.



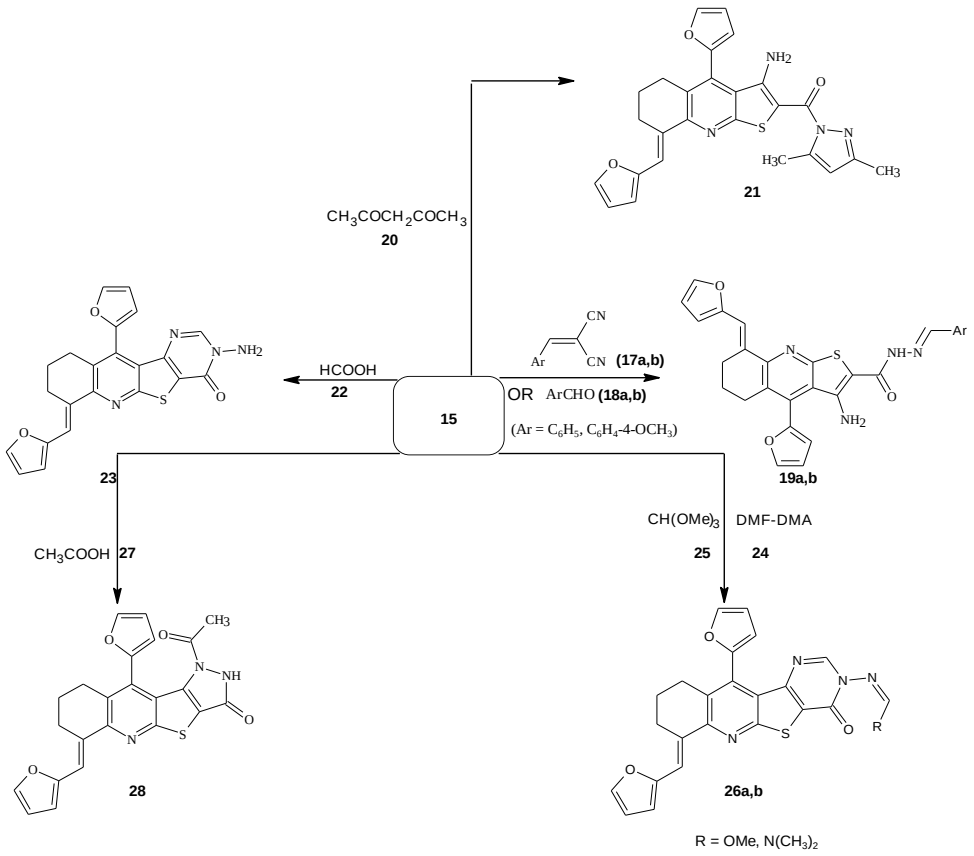
8a **15** **16**

Scheme 5

Antimicrobial Activity: Evaluation of antimicrobial activity was carried out on thieno[2,3-b]quinolin-3-amine as well as pyrimido[4',5':4,5]thieno[2,3-b]quinolone and oxazino[4',5':4,5]thieno[2,3-b]quinoline-4-one derivatives. Screening results are summarized in tables 1 and 2. As shown from these tables, the new thieno[2,3-b] quinolin-3-amines under investigation exhibited variable effect in *vitro* antibacterial and antifungal actions. In general, the chemical structure, comprising the nature of heterocyclic ring and the substituents on it has a pronounced effect on the antimicrobial activity. From the data given by tables 1 and 2 we concluded that the compounds under this study showed variable activities toward the four bacteria "*B. Subtilis, E. Coli, S. Aureus and P. Aeruginosa"* and two fungi '*Candida Albicans and Niger Aspergillus"* in comparison to the standard in each case which revealed that these compounds are biologically active due to the presence of different heterocycles and functional groups.

From the results obtained, it is clear that most of the tested compounds showed moderate activity toward the tested organisms except compounds 6f, 8b, c and 12a showing higher activity towards fungi mainly due to the presence of CN, $CONH_2$, benzimidazolyl groups on thienopyridine skeleton (Table 2).

Synthesis of 4-(furan-2-yl)-8-(furan-2-ylmethylene)-2-thioxo-1,2,5,6,7,8-hexahydroquino-line-3-carbonitrile (4): An equimolecular amount of 2, 6-bis(furan-2-ylmethylidene)-cyclohexanone 1 (0.254 g, 1.0 mole), cyanoethanethioamide (**2**) (0.1g, 0.1 mole) and piperidine (0.5mL) in ethanol (30mL) was heated under reflux for 5h. The excess of the ethanol was evaporated by vacuum. The solid obtained was filtered and crystallized from ethanol to give 4 as red crystals, yielded by (35%), m.p. 210°C, ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ(ppm)*: 1.67(s, 2H, CH_2 of tetrahydroquinoline), 2.45(s, 2H, CH_2 of tetrahydroquinoline), 2.80(s, 2H, CH_2 of tetrahydroquinoline), 6.56(s, 1H, CH=), 6.70-8.04(m, 6H, Ar-H), 11.98(s, 1H, NH); IR (cm^{-1}, KBr) *v*: 3432(NH), 3058 (aromatic-CH) and 2215, (CN); MS m/z (%): 334(M^+, 9.4), 305(3.5), 273(4.7), 256(100), 241(3.5), 227(39.8), 200(13.3); Anal. Calcd. for $C_{19}H_{14}N_2O_2S$ (334.39) C, 68.24; H, 4.22 N; 8.38 S, 9.59. Found C, 68.20; H, 4.10; N, 8.28; S 9.40.



Scheme 6

General method for synthesis of 6a-g: A solution of each of 4 (0.334g, 0.1mole) and ethyl chloroacetate (5a), chloroacetonitrile (5b) 2-chloroacetamide (5c), 2-chloro-N-(4-bromophenyl)-acetamide (5d), chloroacetone (5e), chloromethylbenzimidazole (5f) and ω-bromoacetophenone (5g) (0.122, 0.075, 0.094, 0.250, 0.093, 0.168 and 0.2g, 0.1 mole) in sodium methoxide obtained by 0.10g of sodium and methanol 25 ml was stirred at room temperature for 15 minutes. The formed precipitates were filtered, washed with water, ethanol and dried, to give 6a-g respectively.

Ethyl {[3-cyano-4-(furan-2-yl)-8-(furan-2-ylmethylidene)-5,6,7,8-tetrahydroquinoline-2-yl]sulfanyl}acetate(6a): Yellow crystals, yielded by (80%), m.p. 225°C, IR (cm^{-1}, KBr) *v*: 2210 (CN) and 1740 (ester CO); Anal. Calcd. for $C_{23}H_{20}N_2O_4S$ (420.48) C, 65.70; H, 4.79; N, 6.66; S 7.63. Found C, 65.50; H, 4.60; N, 6.50; S 7.50.

2-[(Cyanomethyl)sulfanyl]-4-(furan-2-yl)-8-(furan-2-ylmethylidene)-5,6,7,8-tetrahydro-quinoline -3-carbonitrile (6b): Grey crystals, yielded by (70%), m.p. 140°C, IR (cm^{-1}, KBr) *v*: 2249, 2213 (two CN); Anal. Calcd. for $C_{21}H_{15}N_3O_2S$ (373.42) C, 67.54; H, 4.05; N, 11.25; S, 8.59. Found C, 67.50; H, 3.90; N, 11.10 S, 8.50.

3-Cyano-4-(furan-2-yl)-8-(furan-2-ylmethylidene)-5,6,7,8-tetrahydroquinoline-2-yl]sulfan-l}cetamide (6c): Grey crystals, yielded by (76%), m.p. 210°C; IR (cm^{-1}, KBr) *v*: 3386, 3147 (NH_2), 22N, 10.73; S 10 (CN) and 1646(CO); Anal. Calcd. for $C_{21}H_{17}N_3O_3S$ (391.44) C, 64.43; H, 4.38; 8.19. Found C, 64.30; H, 4.30; N, 10.50; S, 8.20

3-Cyano-4-(furan-2-yl)-8-(furan-2-ylmethylidene)-5,6,7,8-tetrahydroquinoline-2-yl]sulfan-yl}N (4-bromophenyl) acetamide (6d): Yellow crystals, yielded by (60%), m.p. 200°C, ^{1}H NMR (hexadeutrated dimethyl sulfoxide) δ(ppm): 1.74(s, 2H, CH_2 of tetrahydroquinoline), 2.64(s, 2H, CH_2 of tetrahydroquinoline), 2.86(s, 2H, CH_2 of tetrahydroquinoline), 4.24(s, 2H, CH_2), 6.56(s, 1H, CH=), 6.78-8.02(m, 10H, Ar-H), 10.46(s, 1H, NH); IR (cm^{-1}, KBr) *v*: 3292(NH); 3045 (aromatic CH), 2209(CN) and 1670 (amidic CO); Anal. Calcd. for $C_{27}H_{20}BrN_3O_3S$ (546.43) C, 59.35; H, 3.69; Br, 14.62; N, 7.69; S, 5.87. Found C, 59.30; H, 3.50; Br, 14.50; N, 7.50; S, 5.70.

4-(Furan-2-yl)-8-(furan-2-ylmethylidene)–2-[(2-oxopropyl) sulfanyl]-5,6,7,8-tetrahydroquino-line-3-carbonitrile (6e): Yellow crystals, yielded by (68%), m.p. 140°C, ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ(ppm)*: 1.97(s, 2H, CH_2 of tetrahydroquinoline), 2.30(s, 3H, CH_3), 2.49(s, 2H, CH_2 of tetrahydroquinoline), 2.90(s, 2H, CH_2 of tetrahydroquinoline), 4.28(s, 2H, CH_2), 6.54(s, 1H, CH=), 6.68-8.03(m, 6H, ArH's); IR (cm^{-1}, KBr) *v*: 2214 (CN) and 1720 (CO) ; MS m/z (%): 390($M^{+\cdot}$ 0.4), 377(17.3), 356(100), 349(22.0), 279(23.5), 261(28.7), 148(33.3); Anal. Calcd. for $C_{22}H_{18}N_2O_3S$ (390.45) C, 67.67 H 4.65 N 7.17 S 8.21. Found C 67.50 H 4.50 N 6.90 8.10.

4-(Furan-2-yl)-8-(furan-2-ylmethylidene)–2-[(1H-benzimidazol-2-ylmethyl)sulfanyl]-5,6,7,8-tetrahy droquinoline-3-carbonitrile (6f): Yellow crystals, yielded by (90%), m.p. 240°C, ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ (ppm)*: 1.81(s, 2H, CH_2 of tetrahydroquinoline), 2.49(s, 2H, CH_2 of tetrahydroquinoline), 2.74(s, 2H, CH_2 of tetrahydroquinoline), 4.81(s, 2H, CH_2), 6.66(s, 1H, CH=), 6.78-8.03(m, 10H, Ar-H), 12.48(s, 1H, NH); IR (cm^{-1}, KBr) *v*: 3435(NH); 2215 (CN) and 1621 (C=N); MS (m/z) (%): 466($M^{+\cdot}$ 1.9), 386(19.2), 348(1.5), 333(21.8), 304(12.8), 291(100); Anal. Calcd. for $C_{27}H_{20}N_4O_2S$ (464.53) C, 69.81; H, 4.65; N, 7.17; S, 8.21. Found C, 67.50; H, 4.50; N, 6.90; 8.10.

4-(Furan-2-yl)-8-(furan-2-ylmethylidene)-2-[(2-oxo-2-p-tolylethyl)sulfanyl]-5,6,7,8-tetra-hydroquinoline-3-carbo nitrile (6g). Yellow crystals, yielded by (80%), m.p. 180°C; IR (cm^{-1}, KBr) *v*:, 2934, 2860(aliphatic CH), 2213(CN) and 1715 (CO); **MS m/z (%)**: 466($M^{+\cdot}$ 0.6), 449(25.5), 439(100), 375(6.1), 347(4.0), 331(16.2), 319(5.5), 302(6.0), 298(22.4); Anal. Calcd. for $C_{28}H_{22}N_2O_3S$ (466.55) C, 72.08; H, 4.75; N, 6.00; S, 6.87. Found C, 71.80; H, 4.30; N, 6.01; S, 6.27.

General method for synthesis of 8a-g: A mixture of 6a-g (0.01 mole of each) and ethanolic sodium ethoxide obtained by 0.23g of sodium with 50ml ethanol was heated under reflux for 2h. The product formed after cooling was filtered, wash with water and crystallize from the proper solvent to give 8a-g respectively.

Ethyl 3-amino-4-(2-furyl)-8-(2-furylmethylene)-5,6,7,8-tetrahydrothieno[2,3-*b*] quinoline-2-carboxylate (8a). Yellow crystals, yielded by (90%), m.p. 225°C; ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ (ppm)*: 1.27(s, 3H, CH_3), 1.78(s, 2H, tetrahydroquinoline-CH_2), 2.49(s, 2H, tetrahydroquinoline-CH_2), 2.95(s, 2H, tetrahydroquinoline-CH_2), 4.27(s, 2H, CH_2), 5.84(s, 2H, NH_2), 6.65(s, 1H, CH=), 6.81-8.04(m, 6H, Ar-H); IR (cm^{-1}, KBr) *v*: 3490, 3359(NH_2) and 1680 (CO); MS m/z (%): 420($M^{+\cdot}$ 0.5), 406(35.3), 347(3.5), 331(4.7), 333(43.1), 304(100); Anal. Calcd. for $C_{23}H_{20}N_2O_4S$ (420.48) C, 65.70; H, 4.79; N, 6.66; S 7.63. Found C 65.30; H 4.59; N 6.51; S 7.50.

3-Amino-4-(2-furyl)-8-(2-furylmethylene)-5,6,7,8-tetra hydrothieno[2,3-*b*]quinoline-2-carbo-nitrile (8b) Yellowish green crystals, yielded by (80%), m.p. 220°C; ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ (ppm)*: 1.76(s, 2H, tetrahydroquinoline-CH_2), 2.60(s, 2H, tetrahydro-quinoline-CH_2), 2.96 (s, 2H, tetrahydroquinoline-CH_2), 5.67 (s, 2H, NH_2), 6.65 (s, 1H, CH=), 6.81-8.06 (m, 6H, Ar-H); IR (cm^{-1}, KBr) *v*: 3446,3369 (NH_2); and 2184 (CN); MS m/z (%): 374 (M+1, 24.6), 373 (M^+, 100), 331 (47.5), 318 (65.0), 304 (10.4), 290 (31.7); Anal. Calcd. for $C_{21}H_{15}N_3O_2S$ (373.42) C 67.54, H 4.05, N 11.25, S 8.59. Found C 67.35, H 3.99, N 11.10, S 8.21.

3-Amino-4-(2-furyl)-8-(2-furylmethylene)-5,6,7,8-tetrahyd rothieno[2,3-*b*]quinoline-2-carb-oxamide (8c): Grey crystals, yielded by (77%), m.p. 240°C; IR (cm^{-1}, KBr) *v*: 3467, 3308, 3251, 3117 ($2NH_2$) and 1644 (amidic CO); MS m/z (%): 391 (M^+, 0.2), 375 (100), 347 (1.5), 319 (0.4); Anal. Calcd. for $C_{21}H_{17}N_3O_3S$ (391.44) C, 64.43; H, 4.38; N, 10.73; S, 8.19. Found C, 64.30; H, 4.20; N, 10.50; S 8.01.

3-Amino-N-(4-bromophenyl)-4-(2-furyl)-8-(2-furylmethylene)-5,6,7,8-tetrahydrothieno-[2,3-b]quinoline-2-carbox amide (8d): Yellow crystals, yielded by (80%), m.p. 220°C; IR (cm^{-1}, KBr) *v*: 3466, 3346, 3307 (NH_2, NH) and 1640 (amidic CO); MS m/z (%): 548 (M+2, 1.6), 547 (M+1, 0.5),

546 (M^+, 0.2), 398 (0.5), 375 (100), 347 (9.3), 319 (2.6), 291 (0.5); Anal. Calcd. for $C_{27}H_{20}BrN_3O_3S$ (546.436) C, 59.35; H, 3.69; Br, 14.62; N, 7.69; S, 5.87. Found C, 59.30; H, 3.50; Br, 14.50; N, 7.50; S, 5.70.

1-[3-Amino-4-(2-furyl)-8-(2-furylmethylene)-5,6,7,8-tetrah ydrothieno[2,3-b]quinolin-2-yl]-ethanone (8e): Grey crystals, yielded by (80%), m.p. 280°C, IR (cm^{-1}, KBr) *v*: 3490, 3359 (NH_2); and 1680 (CO); Anal. Calcd. for $C_{22}H_{18}N_2O_3S$ (390.45) C, 67.67; H, 4.65; N, 7.17; S, 8.21. Found C, 67.30; H, 4.50; N, 6.96; S 8.11.

2-(1H-Benzoimidazol-2-yl)-4-furan-2-yl-8-furan-2-ylmeth ylene-5,6,7,8-tetrahydrothieno-[2,3-b]-quinolin-3-ylamin e (8f): Orange crystals, yielded by (90%), m.p. 280°C; IR (cm^{-1}, KBr) *v*: 3436, 3153 (NH_2) and 2932, 2857 (aliphatic CH); Anal. Calcd. for $C_{27}H_{20}N_4O_2S$ (464.53) C, 69.81; H, 4.34; N, 12.06; S, 6.90. Found C, 69.30; H, 4.20; N, 12.01; S, 6.70.

(3-Amino-4-furan-2-yl-8-furan-2-ylmethylene-5, 6, 7, 8-tetrahydrothieno[2,3-b]quinolin-2-yl)-p-tolylmethanone (8g): Brown crystals, yielded by (80%), m.p. 240°C; ^1H NMR (hexadeutrated dimethyl sulfoxide) *δ (ppm)*: 1.77(s, 2H, tetrahydroquinoline-CH_2), 2.40(s, 3H, CH_3), 2.54(s, 2H, tetrahydroquinoline-CH_2), 2.96(s, 2H, tetrahydro-quinoline-CH_2), 6.66(s, 1H, CH=), 6.82-8.06(m, 12H, NH_2, ArH's); IR (cm^{-1}, KBr) *v*: 3436, 3148 (NH_2); and 1738 (CO); Anal. Calcd. for $C_{28}H_{22}N_2O_3S$ (466.55) C, 72.08; H, 4.75; N, 6.00; S, 6.87. Found C, 71.70; H, 4.50; N, 5.87; S 6.70.

Table 1
Antibacterial activity for tested compounds

Comp.	Gram Positive		Gram Negative	
	Bacillis Subtilis	**Escheria Coli**	**Staphyloccus Aureus**	**Pseudomonas Aeruginosa**
4	19	14	14.3	13
6b	17.5	12.5	-	-
6c	16	15	15	15
6d	16.5	14.5	15	15
6e	12.5	13	12	-
6f	12	-	-	-
8a	11	-	15	11
8b	15	15	11.5	12
8c	18	14.5	14	16
8d	17.5	16	16	15
8e	17.5	14	12	12
8f	11	-	-	-
8g	15	14	14.5	15
9	20	22.5	18.5	19
10	13	-	13	-
11	-	-	14	13
12a	17	11	13.5	13
12b	15	14	14	12
13a	17	11	11	-
13b	16	15	15.5	-
14	14	11.5	-	-
16	-	-	14	-
21	13.5	11	12	-
26a	14	13	15	**15**
26b	-	-	11.4	-
28	13	-	-	**12**

Table 2
Antifungal activity for test compounds

Comp. Organism	Candida Albicans	Aspergillus Niger
4	14	21
6a	-	25
6b	-	21
6c	16	16
6d	16	18
6e	14	-
6f	13.5	20
8a	13	-
8b	16	20
8c	15	24
8d	17	-
8e	13	-
8g	11	-
9	18.25	-
10	14	-
11	13	15
12a	12	-
12b	15.5	21
13a	13	-
13b	16	-
14	15	-
19a	18	-
21	12	17
26a	14	20
28	13	-

3-Amino-4-(2-furyl)-8-(2-furylmethylene)-5,6,7,8-tetrahyd rothieno[2,3-*b*]quinoline-2-carb-oxylic acid (9): A solution of 8a (4.20g, 0.01mole) in ethanol and potassium hydroxide solution (10 ml of 10% KOH) was heated on reflux for 2-3 hours. The reaction mixture was cooled, poured into ice-cold water, acidified with hydrochloric acid. The product formed was filtered, washed with water followed by cold ethanol and crystallized from the ethanol to give the corresponding product**,** yellow crystals, yielded by (60%), m.p. 248°C; ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ (ppm)*: 1.75 (s, 2H, tetrahydroquinoline-CH_2), 2.49 (s, 2H, tetrahydroquinoline-CH_2), 2.94 (s, 2H, tetrahydroquinoline-CH_2), 5.53 (s, 2H, NH_2), 6.61 (s, 1H, CH=), 6.73-7.95 (m, 7H, COOH, 6H-Furan); IR (cm^{-1}, KBr) *ν*: 3292 (NH); 3045 (aromatic CH) and 2209 (CN) and 1670 (amidic CO) ; MS m/z (%): 393 (M+1, 100), 392 (M^+, 0.6), 349 (25.2), 319(5.2), 303 (1.5); Anal. Calcd. for $C_{21}H_{16}N_2O_4S$ (392.42) C, 64.27; H, 4.11; N, 7.14; S, 8.17. Found C, 64.10; H, 3.98; N, 7.10; S 8.10.

2-Methyl-7-(2-furylmethylene)-11-(2-furyl)-3,4,7,8,9,10-hexahydro-1,3-oxazino[4',5': 4,5]-thieno[2,3-b]quinoline-4-one (10) A sample of compound **9** (3.92g, 0.01 mole) in acetic anhydride (10 mL) was heated under reflux for 4 h, The product so formed after cooling was filtered off, washed with cold ethanol and crystallized from the ethanol as yellow crystals 10. Yellow crystals, yielded by (60%), m.p. 240°C; ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ (ppm)*: 1.89(s, 2H, tetrahydroquinoline-CH_2), 2.29(s, 3H, CH_3), 2.82(s, 2H, tetrahydro quinoline-CH_2), 3.01(s, 2H, tetrahydroquinoline-CH_2), 6.74(s, 1H, CH=), 6.77-7.94(m, 6H, Ar-H); IR (cm^{-1}, KBr) *ν*: 2932, 2872(aliphatic CH), 1745(CO),and 1626(C=C); MS m/z (%): 417(M+1, 21.9), 416(M^+, 84.1), 374(3.1), 362(100), 336(1.0), 276(10.2), 268(2.5), 253(2.7); Anal. Calcd. for $C_{23}H_{16}N_2O_4S$ (416.45) C, 66.33; H, 3.87; N, 6.73; S, 7.70. Found C, 66.30; H, 3.50; N, 6.50; S, 7.20.

3-Amino-2-methyl-7-(2-furylmethylene)-11-(2-furyl)-3,4, 7,8,9,10-hexahydropyrimido[4',5':4,5]thieno[2,3-b]quin oline-4-one (11) A mixture of 10 (4.16g, 0.01 mole) and hydrazine hydrate (20-25 mL) was heated under reflux for 5-7 hours. The product so formed after cooling was filtered off, washed with cold ethanol and crystallized from the proper solvent to give 11. Yellowish green crystals, yielded by (60%), m.p. 248°C; ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ(ppm)*: 1.83(s, 2H, tetrahydroquinoline-CH_2), 2.30(s, 3H, CH_3), 2.83(s, 2H, tetrahydroquinoline-CH_2), 3.01(s, 2H, tetrahydroquinoline-CH_2), 6.00(s, 2H, NH_2), 6.74-7.92(m, 7H, CH= and Ar-H); IR (cm^{-1}, KBr) *ν*: 3430, 3315 (NH_2), 2932, 2871(aliphatic CH) and 1670 (amidic CO); MS m/z (%): 431(M+1, 1.6), 430(M^+, 2.2), 415(95), 374(7.7), 361(100), 331(2.4), 282(1.9); Anal. Calcd. for

$C_{23}H_{18}N_4O_3S$ (430.48) C, 64.17; H, 4.21; N, 13.01; S, 7.45. Found C, 64.00; H, 4.20; N, 12.87; S, 7.21.

Synthesis of 12a,b: A sample of compound 8b,c,d (0.01 mole) in formic acid or triethyl orthoformate (10 ml) was heated under reflux for 4 h, then allowed to cool .The solid product was filtered off, washed with cold ethanol and crystallized from the proper solvent to give 12a.b.

7-(2-Furylmethylene)-11-(2-furyl)-3,4,7,8,9,10-hexahydropyrimido[4',5':4,5]thieno[2,3-b]quinoline-4-one (12a): Grey crystals, yielded by (60%), m.p. › 300°C, ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ (ppm)*: 1.95 (s, 2H, tetrahydroquinoline-CH_2), 2.49 (s, 2H, tetrahydro quinoline-CH_2), 2.74 (s, 2H, tetrahydroquinoline-CH_2), 6.66 (s, 1H, CH=), 6.70-8.09(m, 6H, Ar-H), 8.15 (s, 1H, pyrimidine-H), 13.00 (s, 1H, NH); IR (cm^{-1}, KBr) *v*: 3435, 3139 (NH); and 1656 (amidic CO); MS m/z (%): 402 (M+1, 22.2), 401 (M^+, 33.3), 132 (22.2), 93 (100), 83 (50.0), 67 (50.0); Anal. Calcd. for $C_{22}H_{15}N_3O_3S$ (401.43) C, 65.82; H, 3.77; N, 10.47; S, 7.99. Found C 65.55, H 3.50, N 10.21, S 7.70.

3-(4-Bromophenyl)-7-(2-furylmethylene)-11-(2-furyl)-3, 4,7,8,9,10-hexahydropyrimido[4', 5' : 4,5]thieno[2,3-b]quinoline-4-one (12b) Yellow crystals, yielded by (70%), m.p. 260°C, IR (cm^{-1}, KBr) *v*: 3012 (aromatic CH), 2940, 2868 (aliphatic CH); MS m/z(%): 601 (M^+, 5.0), 533 (2.5), 522 (2.5), 453 (2.9), 447 (26.8), 375 (6.4); Anal. Calcd. for $C_{28}H_{18}BrN_3O_3S$ (556.43) C, 60.44; H, 3.26; Br, 14.36; N, 7.55; S, 5.76. Found C, 60.30; H, 3.11; Br, 14.30; N, 7.50; S 5.50.

Synthesis of 13a,b: A sample of compound 8d (5.46g, 0.01 mole) in acetic anhydride (10 ml) was heated under reflux for 4h, then allowed to cool and poured into cold water (100 ml). The solid product was filtered and recrystallized from ethanol as yellow crystals.

2-Methyl-7-(2-furylmethylene)-11-(2-furyl)-3,4,7,8,9,10-hexahydropyrimido[4',5':4,5]-thieno[2,3-b]quinoline-4-one (13a) Yellow crystals, yielded by (70%), m.p. 240°C, IR (cm^{-1}, KBr) *v*: 3444,3181 (NH); 1689 (CO) ; MS m/z (%): 415 (M^+,52.9), 374 (11.8), 152 (17.6), 84 (100); Anal. Calcd. for $C_{23}H_{17}N_3O_3S$ (415.46) C, 66.49; H, 4.12; N, 10.11; S, 7.72. Found C, 66.06; H, 4.03; N, 10.01; S, 7.30.

3-(4-bromophenyl)-2-methyl-7-(2-furylmethylene)-11-(2-furyl)-3,4,7,8,9,10-hexahydro-pyrimido[4', 5': 4,5] thieno[2,3-b]quinoline-4-one (13b): Green crystals, yielded by (70%), m.p. 200°C, ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ(ppm)*:1.90 (s, 2H, tetrahydro-quinoline-CH_2), 2.29 (s, 3H, CH_3), 2.55 (s, 2H, tetrahydroquinoline-CH_2), 2.82 (s, 2H, tetrahydroquinoline-CH_2), 6.68 (s, 1H, CH=), 6.74-7.93 (m, 10H, Ar-H); IR (cm^{-1}, KBr) *v*: 2939, 2860 (aliphatic CH) and 1641 (amidic CO) ; **MS** m/z (%): 570 (M^+,4.2), 417 (29.0), 400 (0.5), 374 (4.5), 362 (100), 331(3.9); Anal. Calcd. for $C_{29}H_{20}BrN_3O_3S$ (570.45) C, 61.06; H, 3.53; Br, 14.01; N, 7.37; S, 5.62. Found C, 61.01; H, 3.20; Br, 13.95; N, 7.23; S 5.30.

2-Thioxo-3-(4-bromophenyl)-7-(2-furylmethylene)-11-(2-furyl)-1,2,3,4,7,8,9,10-octahydro-pyrimido[4', 5': 4,5] thieno[2,3-b]quinoline-4-one (14): A sample of compound 8d (5.46g, 0.01 mole) and carbon disulfide (2 ml) in pyridine (10 ml) was heated under reflux for 5 h and then ethanol (10 mL) was added. The reaction mixture was allowed to cool. The solid product was filtered and recrystallized from ethanol as yellow crystals, yielded by (80%), m.p. 150°C, ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ (ppm)*: 1.79(s, 2H, tetrahydro-quinoline-CH_2), 2.48(s, 2H, tetrahydroquinoline-CH_2), 2.96(s, 2H, tetrahydroquinoline-CH_2), 6.06(s, 1H, CH=), 6.65-8.02(m, 10H, Ar-H), 9.66(s, 1H, NH); IR (cm^{-1}, KBr) *v*: 3405, 3244 (NH); and 1686 (amidic CO) ; MS m/z (%): 588(M^+, 2.6), 532(2.0), 507(1.4), 330(1.4); Anal. Calcd. for $C_{28}H_{18}BrN_3O_3S_2$ (588.49) C, 57.15; H, 3.08; Br, 13.58; N, 7.14; S, 10.90. Found C, 57.02; H, 2.89; Br, 13.32; N, 7.10; 10.35.

Synthesis of 3-Amino-4-(furan-2-yl)-8-(furan-2-ylmethylidene)-5,6,7,8-tetrahydro-thieno[2,3-b] quinoline-2-carbohydrazide (15): An equimolecular amount of (8a) (0.40 g, 1mmole), hydrazine hydrate (15mL) in ethanol (20mL) was heated under reflux for 6h. The excess of the ethanol was evaporated by vacuum (to 1/3 of the solution). The solid obtained was collected by filtration, dried and crystallized from ethanol to give 15. Orange crystals, yielded by (60%), mp. 225°C, IR (cm^{-1}, KBr) *v*: 3473, 3359(NH_2), 3313, 3139(NH) and 2918,2851(aliphatic-CH) ; ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ (ppm*): 1.76 (s, 2H, tetrahydroquinoline-CH_2), 2.59 (s, 2H, tetrahydroquinoline-CH_2), 2.96 (s, 2H, tetrahydro-quinoline-CH_2), 5.84(br, 2H, NH_2), 6.64 (s, 1H, CH=), 6.78-8.02 (m, 8H, Ar-H and NH_2), 10.46(s, 1H, NH); MS (m/z): 406 (M^+, 52.9 %), 405 (M^+ - 1, 54.9 %) 390 (M^+- NH_2, 26.5%), 375(M^+- $NHNH_2$, 100%), 347 (M^+- $CONHNH_2$, 17.6%); Anal. Calcd. For $C_{21}H_{18}N_4O_3S$ (406.45) C, 62.05; H, 4.46; N, 13.78; S, 7.89. Found C, 62.00; H, 4.40; N, 13.55; S 7.80.

Synthesis of 2-(5-N-phenylamino-1,3,4-oxadiazol-2-yl)-4-(furan-2-yl)-8-(furan-2-yl-methylidene)-5,6,7,8-tetra hydrothieno[2,3-*b*]quinolin-3-amine (16): A mixture of 15 (0.406g, 1mmole) and phenylisothiocyanate (0.135mL, 0.1mole) in pyridine (10ml) was heated under reflux for 6h, cooled, poured onto ice cold water and neutralized with hydrochloric acid . The solid formed filtered and crystallized from ethanol to give 16 as orange crystals, yielded by (80%), mp. 280°C, IR (cm^{-1}, KBr) *v*: 3388, 3340 (NH_2) and 3135,3111 (NH); ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ(ppm*): 1.82 (s, 2H, tetrahydroquinoline-CH_2), 2.84 (s, 2H, tetrahydroquinoline-CH_2), 3.0 (s, 2H, tetrahydroquinoline-CH_2) , 6.96 (s, 1H, CH=), 6.67-8.1 (m, 13H, benzene, NH_2 and Furan protons), 9.9 (s, 1H, NH); MS (m/z): 507 (M^+, 13.0%), 430 (M^+ -Ph , 5.7%), 347 (M^+- oxadiazole ring , NHPh , 4.2%); Anal. Calcd. For

$C_{28}H_{21}N_5O_3S$ (507.56) C, 66.26; H, 4.17; N, 13.80; S, 6.32. Found C, 66.15; H, 4.05; N, 13.70; S, 6.25.

Synthesis of 3-Amino-4-(furan-2-yl)-8-(furan-2-ylmethylidene)-*N*'-phenylmethylene-5,6,-7,8-tetrahydro-thieno[2,3-*b*]quinoline-2-carbohydrazides 19a: A mixture of 15 (0.406g, 0.1 mole), benzylidinemalononitrile (17a) (0.154, 0.1 mole) or benzaldehyde 18a and pyridine (5ml) in ethanol (10ml) was heated under reflux for 7h, cooled, poured onto ice cold water and neutralized with hydrochloric acid. The solid formed filtered, dried and crystallized from the acetic acid to give 19a as orange crystals, yielded by (70%), mp. 220°C, IR (cm^{-1}, KBr) *v*: 3471, 3355, 3315 (NH_2, NH), 3059 (aromatic C-H), 2935, 2867 (aliphatic CH), 1679 (amidic CO); ^{1}HNMR (hexadeutrated dimethyl sulfoxide) *δ(ppm)*: 1.77 (s, 2H, tetrahydro-quinoline-CH_2), 2.59 (s, 2H, tetrahydroquinoline-CH_2), 2.95 (s, 2H, tetrahydroquinoline-CH_2), 5.84 (br., 2H, NH_2), 6.65-8.03 (m, 13H, aromatic and CH=) and 11.56 (s, 1H, NH): MS (m/z) 494 (M^+, 30%), 375 (M^+-NHN=CHPh, 16.7%) and 77(Ph, 76.7%). Anal. Calcd. For $C_{28}H_{22}N_4O_3S$ (494.56) C, 68.00; H, 4.48; N, 11.33; S, 6.48. Found C, 67.90; H, 4.34; N, 11.21; S, 6.32.

Synthesis of 3-Amino-4-(furan-2-yl)-8-(furan-2-ylmethylidene)-*N*'-anisylmethylene-5,6,-7,8-tetrahydro thieno[2,3-*b*]quinoline-2-carbohydrazides 19b: A mixture of **15** (0.406g, 0.1 mole), anisaylidenemalononitrile (17b) or anisaldehyde 18b (0.136, 0.1 mole) in pyridine (5ml) and ethanol (20ml) was heated under reflux for 5h. The excess of the ethanol was evaporated by vacuum (to 1/3 of the solution). The solid obtained was filtered and crystallized from ethanol to give 19b. Orange crystals, yielded by (90%), m.p. 250°C, IR (cm^{-1}, KBr) *v*: 3471, 3355, 3315, 3145 (NH_2,NH), 3059(aromaticC-H), 1679(amidic CO); MS **(m/z)**: 524 (M^+, 58.7%), 509 (M^+- CH_3, 8.7%), 493 (M^+-OCH_3, 7.8%), 417 (M^+-PhOCH_3, 7.65%), 390 (M^+-N=CHPhOCH_3, 17.4%), 375 (M^+-NHN=CHPhOCH_3, 30.4%), 347 (M^+-CONHN=CHPhOCH_3, 16.3%), 332 (M^+-NH_2, CONHN=CHPhOCH_3, 10.9%). Anal. Calcd. For $C_{29}H_{24}N_4O_4S$ (524.59) C, 66.40; H,4.61; N,10.68; S,6.11. Found C, 66.20; H, 4.50; N, 10.45; S, 6.02.

[3-Amino-4-(furan-2-yl)-8-(furan-2-ylmethylidene)-5,6,7,8-tetrahydrothieno[2,3-*b*]quin-olin-2-yl](3,5-dimethyl-1*H*-pyrazol-1-yl)methanone (21): A mixture of 15 (0.406g, 0.1 mole) and acetylacetone (5ml) was heated under reflux for 5-7h. The formed product was filtered off, washed with cold ethanol and crystallized from acetic acid to give 21 as orange crystals, yielded by (80%), mp. 250°C, IR (*v* cm^{-1}, KBr): 3490,3354 (NH_2), 2929 (aliphatic C-H) and 1680 (amidic CO); ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ(ppm)*: 1.76 (s, 2H, tetrahydroquinoline-CH_2), 1.84 (s,3H, CH_3), 2.07(s,3H, CH_3), 2.75 (s, 2H, tetrahydroquinoline-CH_2), 2.96 (s, 2H, tetrahydroquinoline-CH_2), 6.23-8.05(m, 10H, CH=, Ar-H, H pyrazol, NH_2): MS m/z (%): 470 (M^+, 100), 440(M-2CH_3, 4.9), 375(M^+ - pyrazolyl ring, 2CH_3, 18.7), 347(M^+ - CO, pyrazolyl ring, 2CH_3, 10.6), 331 (M^+ - NH_2,CO, pyrazolyl ring, 2CH_3, 10.6); Anal. Calcd. For $C_{26}H_{22}N_4O_3S$ (470.54) C, 66.37; H, 4.71; N, 11.91; S, 6.81. Found C, 66.20; H, 4.50; N, 11.70; S, 6.55.

Synthesis of 3-Amino-11-(furan-2-yl)-7-(furan-2-ylmethylidene)-4-oxo-7,8,9,10-tetrahydro-pyrimido [3',2': 4,5] thieno[2,3-*b*]quinoline (23): A mixture of 15 (0.406g, 0.1 mole) and formic acid (10ml) was heated under reflux for 6h. The formed product was filtered off, washed with cold ethanol and crystallized from ethanol to give 23 as orange crystals, yielded by (65%), m.p. 200°C, IR (cm^{-1}, KBr) *v*: 3412, 3144(NH_2), 2928, 2862 (aliphticC-H), 1675(amidic CO); MS m/z (%): 419(M^++ 3, 58.3), 416(M^+, 0.8), Anal. Calcd. For $C_{22}H_{16}N_4O_3S$(416) C, 63.45; H,3.87; N,13.45; S,7.70. Found C, 63.20; H, 3.50; N, 13.10; S, 7.60.

Methyl 11-(Furan-2-yl)-7-(furan-2-ylmethylidene)-4-oxo-7,8,9,10-tetrahydropyrimido-[4', 5': 4,5]thieno[3,2-d]quinoline imidoformate (26a): A mixture of 15 (0.406g, 0.1 mole) and trimethylorthoformate (10ml) was heated under reflux for 6 hours. The product so formed was filtered off, washed with cold ethanol and crystallized from ethanol to give 26a as orange crystals, yielded by (80%), mp. 240°C; IR (cm^{-1}, KBr) *v*: 2985, 2937 (aliphatic CH) and 1632(amidic CO); MS (m/z): 458(M, 10.6%), 414(M^+ - $CHOCH_3$, 78.7%); Anal. Calcd. For $C_{24}H_{18}N_4O_4S$ (458.49) C, 62.87; H, 3.96; N, 12.22; S, 6.99. Found C, 62.70; H, 3.77; N, 12.14; S, 6.82.

11-(Furan-2-yl)-7-(furan-2-ylmethylidene)-4-oxo-9,10-dihydropyrimido[4',5':4,5]thieno-[2,3-b]quinoline-3-*N*, *N*-dimethylimidoformamide (26b): A mixture of 15 (0.40g, 0.1 mole) and dimetylformamide-dimethylacetal (0.119g, 0.1 mole) in dry xylene (20ml) was heated on reflux for 5-7h. The formed product was filtered off, washed with cold ethanol and crystallized from ethanol to give 26b as yellow crystals, yielded by (70%), mp. 240°C; IR (cm^{-1}, KBr) *v*: 2919, 2807 (aliphatic CH), 1665 (CO); ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ (ppm)*: 1.81(s, 2H, tetrahydroquinoline-CH_2), 2.72(s, 2H, tetrahydroquinoline-CH_2), 2.93 (s, 6H, 2CH_3), 2.99(s, 2H, tetrahydroquinoline-CH_2) , 6.6-8.2(m, 9H, CH=, Ar-H and CH=N); MS m/z **(%)**: 471(M^+, 18.9), 427(M^+ -$N(CH_3)_2$, 0.4), 414(M^+-$CHN(CH_3)_2$, 1.4), 400(M^+- N= $CHN(CH_3)_2$, 19.9); Anal. Calcd. for $C_{25}H_{21}N_5O_3S$(471.53) C, 63.68; H, 4.49; N, 14.85; S, 6.80. Found C, 63.57; H, 4.25; N, 14.74; S, 6.71.

1-Acetyl-10-(furan-2-yl)-6-(furan-2-ylmethylidene)-1,2-dihydro-3*H*-pyrazolo[3',4':4,5]-thieno[2,3-*b*]quinolin-3-one (28): A mixture of 15 (0.406g, 0.1 mole) and acetic acid (10ml) was heated under reflux for 6 hours. The product so formed after cooling was filtered off and crystallized from ethanol to give 28 as yellow crystals, yielded by (60%), mp. 320°C; IR (cm^{-1}, KBr) *v*: 3314, (NH), 3115 (aromatic CH), and 1671(CO); ^{1}H NMR (hexadeutrated dimethyl sulfoxide) *δ (ppm)*: 1.9(s, 2H, tetrahydroquinoline-CH_2), 2.42 (s, 3H, CH_3), 2.81(s, 2H, tetrahydroquinoline-CH_2), 3.0(s, 2H, tetrahydroquinoline-CH_2) , 5.98 (s, 1H, CH=), 6.67-7.9(m, 7H, Ar-H, NH); MS m/z (%): 431(M^+, 28.6),430(M^+ - H,

100), 416(M^+ -CH_3, 8.2), 388(M^+ -$COCH_3$, 23.4): Anal. Calcd. For $C_{23}H_{17}N_3O_4S$ (431.46) C, 64.03; H, 3.97; N, 9.74; S, 7.43. Found C, 64.00; H, 3.70; N, 9.55; S, 7.24.

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