Synthesis and Reactions of 1-Amino-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline

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The pyrazolone derivative **4** was synthesized by reaction of carbohydrazide **2** with ethyl benzoylacetate in ethanol and p-toluene sulphonic acid followed by cyclization upon heating in acetic acid. Chloroacylation of amino ester and amino benzoyl compounds **1**, **19** gave the chloro acetylamino derivatives **5** and **20** respectively which both of them react with different amines to afford compounds **6**, **23a-d**. Hydrolysis and decarboxlation of compound **1** yielded the aminothienotetrahydroisoquinoline **8** which was used as versatile material for synthesizing other heterocyclic compounds **9-18**. Compound **20** react with hexamethylenetetramine and malononitrile yielded thediazepino and pyrrolo derivatives **21**, **22** respectively.

Keywords: Pyridothienotetrahydroisoquinoline; Furopyridothienotetrahydroisoquinoline; Diazepinothienotetrahydroisoquinoline; Synthesis; Reactions.

INTRODUCTION

Substituted tetrahydroisoquinolines are abundantly found in nature, especially in a variety of plants, soil, and marine microorganisms.[1] Many of tetrahydroisoquinoline derivatives exhibit important biological activities, for example, anti-inflammatory, anti-microbial, antibacterial, antimalarial, anti-leukemic, anti-HIV, anti-tumor properties,[2,3] cytotoxicity,[4] antagonist activity to D1 and NMDA receptors,[5] analgesicactivity,[6] pathogenesis of Parkinson's disease,[7] and enzyme inhibitory activities for glucosidases[8] and monoamine oxidases[9] and other biological activities.[10-13]

E. Lukevics[14] noted that compounds containing the pyridine ring accounted for more than 10% out of 1500 medicines most regularly used at the end of the 20th century. Among these medicines are vitamins (B3, B6, and PP), analgetics, analeptics, antiarrhythmics, antiseptics, antidepressants, spasmolytics, neuroleptics, tranquilizing agents, and drugs having other pharmacological activities. In the recent monograph on the chemistry of pyridine bases,[15] the authors stated that pyridine and its homologs are among the most important reagents for the fine and industrial organic synthesis, which are widely used in chemical and petrochemical industry, as well as in production of dyes, pharmaceuticals, agents for chemical plant protection, surfactants, acid corrosion inhibitors, ion exchange resins, selective sorbents, and extractants.

RESULTS AND DISCUSSION

1-Amino-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno [2,3-c]isoquinolin-2-carbohydrazide[16] (**2**) prepared by the reaction of ethyl-1-amino-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinolin-2-carboxylate (**1**) with hydrazine hydrate was reacted with ethyl benzoylacetate in refluxing ethanol in presence of p-toluene sulphonic acid to afford the corresponding ethyl propionate ester **3** which underwent ring closure when heated in acetic acid to give 2-(1-amino-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno-[2,3-c]isoquinoline-2-carbonyl)-5-phenyl-2,4-dihydropyrazol-3-one (**4**) Scheme I. The structure of the produced compound was elucidated on the basis of ^{1}H-NMR spectra which revealed the disappearance of triple and quartet signals at δ 1.3, 4.5 characteristic for ethyl ester group.

On the other hand, amino ester compound **1** was chloroacetylated using chloroacetyl chloride in dioxan followed by treating with sodium carbonate solution to afford ethyl-1-chloroacetylamino-N-(2-cyano-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline-1-yl)carbox-

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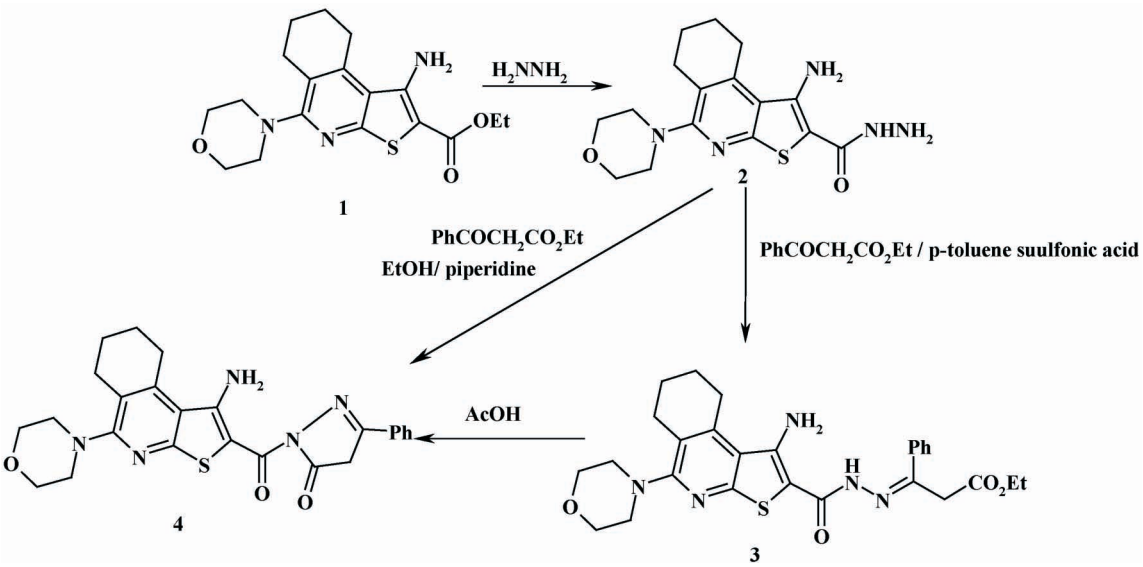
Scheme I



ylate (**5**). IR spectrum revealed the disappearance of absorption band at 3420, 3320 cm^{-1} characteristic for NH_2 group. The ^{1}H-NMR spectrum of compound **5** in $CDCl_3$ showed the disappearance of signal at δ 6.1 characteristic for (NH_2) group and appearance of singlet signal at δ 4.3 for (CH_2) which doesn't disappear by D_2O, doesn't exist in ^{1}H-NMR of compound **5** and showed singlet signal at 9.2 characteristic for (NH) group which disappear by D_2O.

Reaction of compound **5** with potassium thiocyanate in refluxing ethanol afforded ethyl-5-morpholin-4-yl-8-oxo-1,2,3,4,8,9-hexahydropyrimido[4′,5′:4,5]thieno[2,3-c] isoquinolin-10-ylsulfanyl acetate (**6**).[17] The suggested reaction mechanism for formation of compound **6** include nucleophilic attack of NH to CN group in compound **5** to form thiazole ring as intermediate followed by elimination of ethanol molecule to form pyrimidinone ring then breaking of thiazole ring with forming ethyl sulfanylacetate was carried out by adding ethanol molecule as shown as follows in the following scheme (Fig. 1).

IR spectrum showed of compound **6** absorption band at 3400 characteristic for (NH) group and absorption bands at 1670, 1650 cm^{-1} characteristic for two carbonyl groups. ^{1}H-NMR spectrum of compound **6** showed triplet and quartet signals at δ 1.3, 4.5 characteristic for ethyl ester group and singlet signal at δ 11.5 for (NH) group. The mass spectrum showed a peak at 459.63 as a molecular ion peak and as a base peak. Also, the chloro acetylamino derivative **5** underwent nucleophilic substitution reaction with aniline in refluxing ethanol to afford ethyl-5-morpholin-4-yl-1-(2-phenylaminoacetylamino)-6,7,8,9-tetrahydrothieno-[2,3-c]isoquinoline-2-carboxylate (**7**) Scheme II.

Hydrolysis of and decarboxylation of compound **1** was carried out by refluxing with alcoholic potassium hydroxide solution yielded the potassium salt of acid which can't be isolated and by acidification using HCl afforded 1-amino-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline (**8**). IR spectrum of compound **8** revealed the disappearance of absorption band at 1735 cm^{-1} characteristic for (C=O) ester. ^{1}H-NMR spectrum showed the disappearance of signals at 1.3, 4.2 for ethyl ester group with remaining the signal characteristic for NH_2 at δ 6.3.

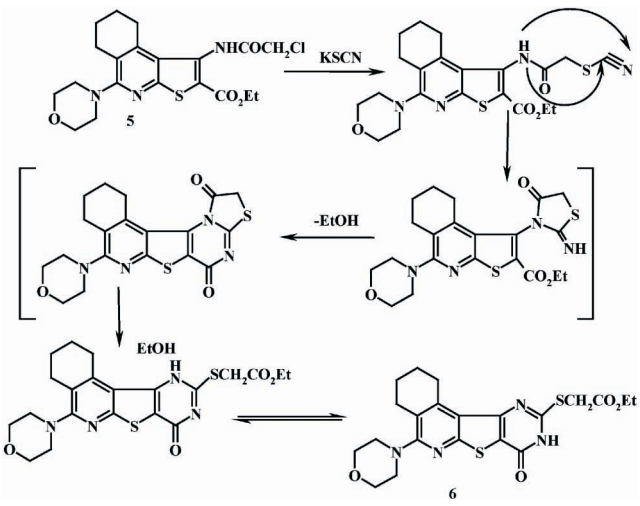
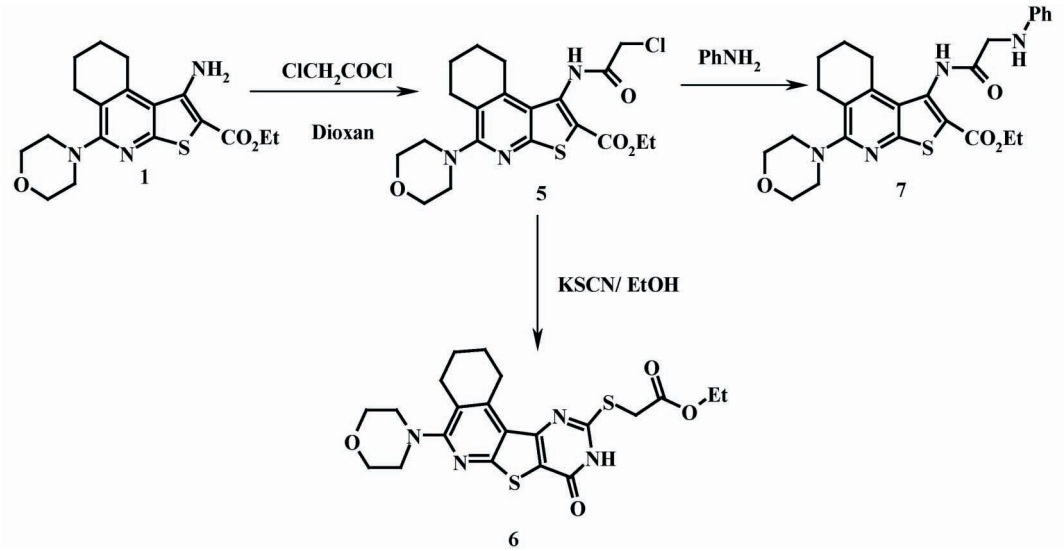


Fig. 1.

Scheme II



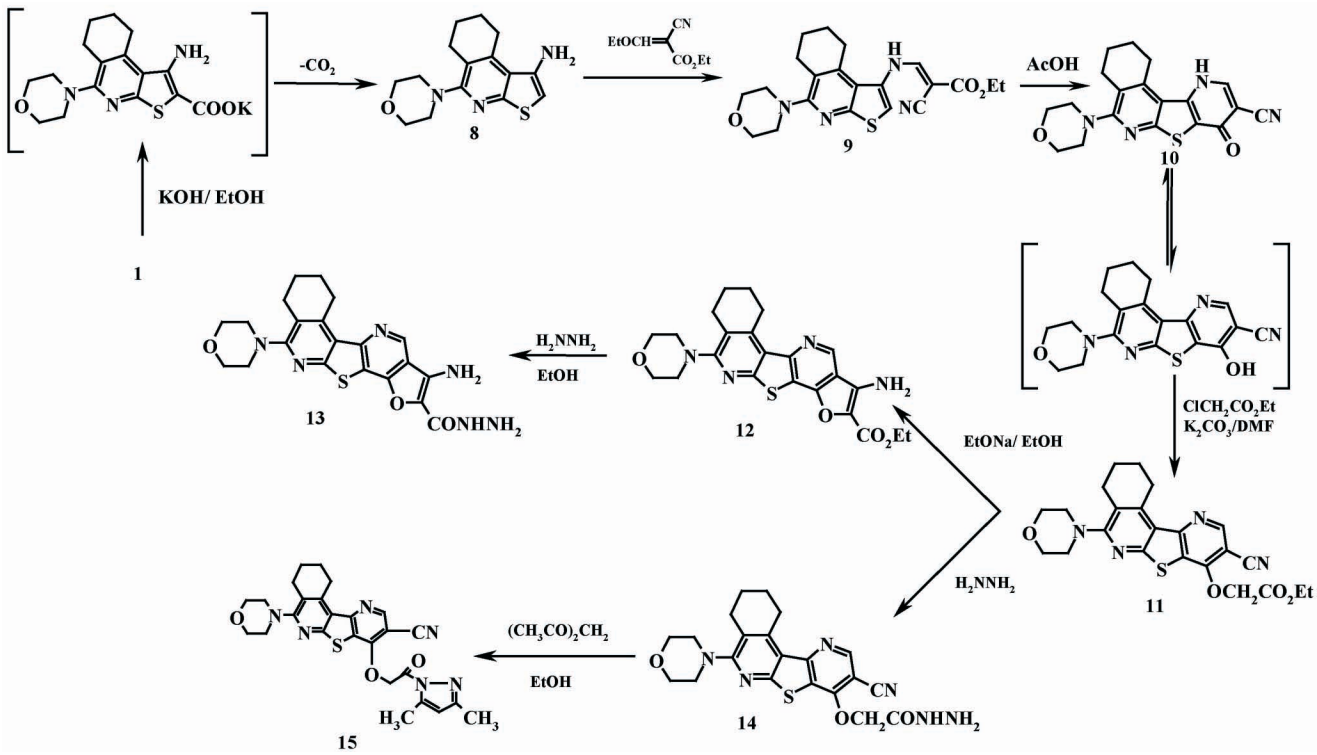
Compound **8** was used as a versatile precursor to synthesis of another heterocyclic compounds. Thus, reaction of amino thieno tetrahydroisoquinoline derivative **8** with 2-cyano-3-ethoxyacrylic acid ethyl ester in ethanol yielded ethyl-2-cyano-3-(5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline-1-ylamino)acrylate (**9**). Compound **9** underwent ring closure by loss of ethanol when refluxed in acetic acid to give 5-morpholin-4-yl-8-oxo-1,2,3,4,8,11-hexahydropyrido[2″,3″:4′,5′]thieno[2,3-c]-isoquinoline-9-carbonitrile (**10**). IR spectrum of compound **10** revealed the disappearance of absorption band at 1680 cm^{-1} characteristic for C=O ester. ^{1}H-NMR spectrum in DMSO-d_6 showed the disappearance of triplet and quartet signals at δ 1.3, 4.2 characteristic for (CH_3 and CH_2) groups of ester group respectively. The mass spectrum of mentioned compound showed a peak at 366.20 as a molecular ion peak.

When compound **10** was allowed to react with ethyl chloroacetate in DMF on a steam bath in presence of excess anhydrous potassium carbonate alkylation occurred to afford (9-cyano-5-morpholin-4-yl-1,2,3,4,8,11-hexahydropyrido[2′,3′:4,5]thieno[2,3-c]isoquinolin-8-yloxy)aceticacidethylester (**11**) which underwent Thorpe-Ziegler cyclization by refluxing in ethanol/sodium ethoxide solution to yield the corresponding ethyl-3-amino-10-morpholin-4-yl-6,7,8,9-tetrahydrofuro[2″,3″:4′,5′]pyrido[2′,3′:4,5]-thieno[2,3-c]isoquinoline-2-carboxylate (**12**). The structure of compound **12** was confirmed on the basis of IR, ^{1}H-NMR and mass spectrum. IR spectrum of compound **12** showed absorption band at 3420, 3320 cm^{-1} characteristic for (NH_2) group and at 1710 for (C=O) ester. ^{1}H-NMR spectrum of compound **12** in CF_3CO_2D showed triplet and quartet signals at δ 1.35, 4.40 characteristic for (CH_3, CH_2) groups of ester group and the mass spectrum of appreciable compound showed a peak at 452.56 as a molecular ion peak. Hydrazinolysis of compounds **11**, **12** by using hydrazine hydrate under neat conditions followed by addition of ethanol afforded 3-amino-10-morpholin-4-yl-6,7,8,9-tetrahydrofuro[2″,3″:4′,5′]pyrido[2′,3′:4,5]thieno[2,3-c]isoquinolin-9-carbohydrazide (**13**), (9-cyano-5-morpholin-4-yl-1,2,3,4-tetrahydropyrido[2″,3″:4′,5′]thieno[2,3-c]isoquinolin-8-yloxy) acetic hydrazide (**14**) respectively.

Condensation of compound **14** with acetyl acetone yielded 8-[2-(3,5-dimethylpyrazol-1-yl)-2-oxoethoxy]-5-morpholin-4-yl-1,2,3,4-tetrahydropyrido[2′,3′:4,5]thieno-[2,3-c]isoquinolin-9-carbonitrile (**15**) Scheme III. IR spectrum of compound **15** revealed disappearance of absorption bands at 3450-3280 cm^{-1} characteristic for (NH, NH_2) groups. ^{1}H-NMR spectrum in DMSO-d_6 showed two sharp singlet signals at δ 2.3, 2.45 characteristic for the two pyrazole methyl groups and singlet signal at 6.2 characteristic for (CH pyrazole).

Heating of amino tetrahydrothienoisoquinoline derivative **8** with orthophosphoric acid on a steam bath followed by cooling and pouring on ice water mixture yielded 5-morpholin-4-yl-1-oxo-6,7,8,9-tetrahydrothieno[2,3-c]-isoquinoline (**16**).[18] Condensation of compound **16** with benzaldehyde afforded the corresponding Schiff's base **17**,

Scheme III

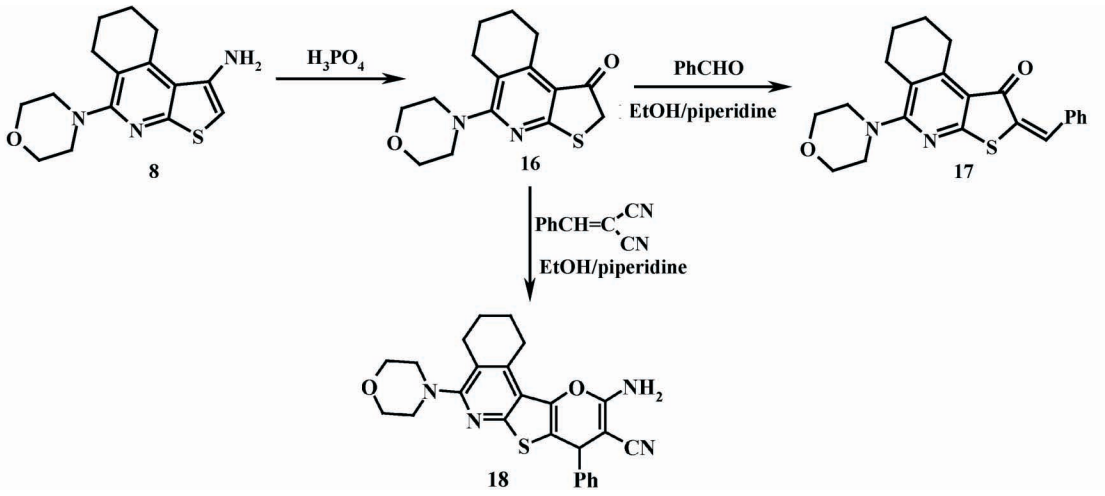


while reaction with benzyledine malononitrile yielded 10-amino-5-morpholin-4-yl-8-phenyl-1,2,3,4-tetrahydro-8H-pyrano[2′,3′:4,5]thieno[2,3-c]isoquinoline-9-carbonitrile (**18**)[18] Scheme IV. ^{1}H-NMR spectra of compound **17** in $CDCl_3$ showed multiplet signals at δ 7.45-7.80 characteristic for aromatic protons while ^{1}H-NMR spectra of compound **18** in $CDCl_3$ showed singlet signal at δ 4.7 for (NH_2) group and mltiplet signals at δ 7.2-7.4 for aromatic protons.

The suggested mechanism for reaction of ketone **16** with benzylidenemalononitrile to form the pyrano derivative **18** was described as follows (Fig. 2).

In a similar manner, chloro acetylation of 1-amino-2-benzoyl-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]

Scheme IV



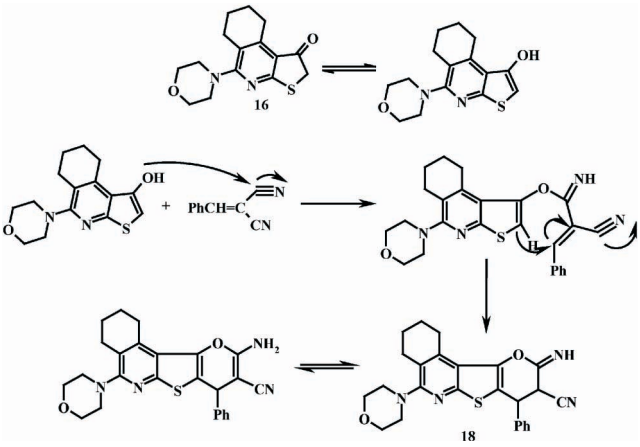


Fig. 2.

isoquinoline (**19**)[28] using chloroacetyl chloride in dioxan on a steam bath followed by treating with sodium carbonate solution afforded N-(2-benzoyl-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinolin-1-yl)-2-chloroacetamide (**20**). Also, compound **20** was used as starting material for synthesizing compounds **21-23 a-d**. Refluxing chloro acetylamino derivative **20** with hexamethylenetetramine in ethanol yielded 5-morpholin-4-yl-8-phenyl-1,2,3,4,10-pentahydro[1,4]diazepino[5′,6′:4,5]thieno[2,3-c]isoquinolin-11(12H)-one (**21**) through formation of hexaminium salt as intermediate. IR spectrum of compound **21** showed absorption bands at 3400 cm^{-1} characteristic for (NH) group and 1690 cm^{-1} for (C=O) group. ^{1}H-NMR spectrum in $CDCl_3$ showed singlet signal at δ 4.5 characteristic for (CH_2) group and mass spectrum of the mentioned compound showed a peak at 432.89 as a molecular ion peak.

Reaction of chloro acetylamino derivative **20** with malononitrile in refluxing ethanol in presence of anhydrous potassium carbonate gave 2-benzoyl-1-(2-amino-3-cyano-5-oxopyrrol-1-yl)-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline (**22**). The structure was confirmed on the bases of elemental and spectral analysis. IR spectrum of compound **22** showed absorption bands at 3320, 3200 cm^{-1} characteristic for (NH_2) and 2200 for (CN) group. ^{1}H-NMR spectrum $CDCl_3$ showed singlet signal at δ 2.8 for (CH_2) group of pyrrole and singlet signal at δ 5.3 characteristic for (NH_2) group. Also, the chloro acetylamino derivative **20** underwent nucleophilic substitution reactions with various primary and secondary amines in refluxing ethanol to afford N-(2-benzoyl-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline-1-yl)-2-alkyl(aryl)aminoacetamide **23 a-d** Scheme V.

EXPERIMENTAL

All melting points are uncorrected and measured on a Fisher-John apparatus. IR spectra were recorded (KBr) with a Perkin-Elmer 1430 Spectrophotometer. ^{1}H NMR spectra were obtained on a Varian EM-390 MHz (90 MHz) and Joel 400 MHz spectrometers with equal concentrations in a suitable deutrated solvent using TMS as internal standard in $CDCl_3$, DMSO-d_6 and CF_3CO_2D using Me_4Si as internal standard and chemical shifts are expressed as ppm. Mass spectra were measured on a Jeol-JMS 600 spectrometer. Analytical data were obtained on Elementar Analyse system GmbH-VarioEL V.3 microanalyzer in the central lab of Assiut University.

Ethyl-1-amino-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3,-c]isoquinoline-2-carboxylate (**1**), 1-amino-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline-2-carbohydrazide (**2**), 1-amino-2-benzoyl-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline (**19**) were prepared according to reported procedure.[16] The following figure show the numbering of carbon atoms for compounds **21** and **23a** used in ^{13}C-NMR analysis.

Ethyl-3-(1-amino-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline-2-carbonylhydrazono)-3-phenylpropionate (3)

Carbohydrazide derivative **2** (3.47 g, 10 mmol) and ethyl benzoyl acetate (1.92 mL, 10 mmol) was refluxed in ethanol (30 mL) in the presence of *p*-toluene sulfonic acid (1.722 g, 10 mmol) for 1 h. The solid precipitate which formed on hot (during reflux) was cooled, filtered off, dried and recrystallized from chloroform to afford yellow crystals in 76% yield, m.p. 194-196 °C. ^{1}H-NMR ($CDCl_3$): δ = 1.3 (t, *J* = 7.5 Hz, 3H, CH_3), 1.8 (m, 4H, $2CH_2$ cyclohexeno), 2.7 (m, 4H, $2CH_2$ cyclohexeno), 3.4 (m, 6H, $(CH_2)_2$N-morpholine + CH_2CO), 4.00 (m, 4H, $(CH_2)_2$O-morpho-

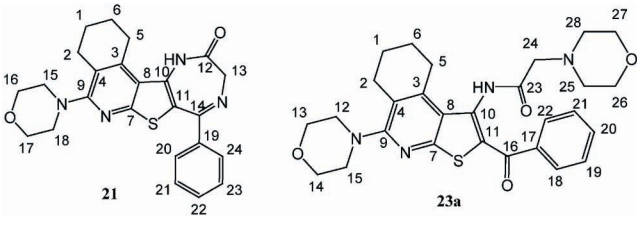
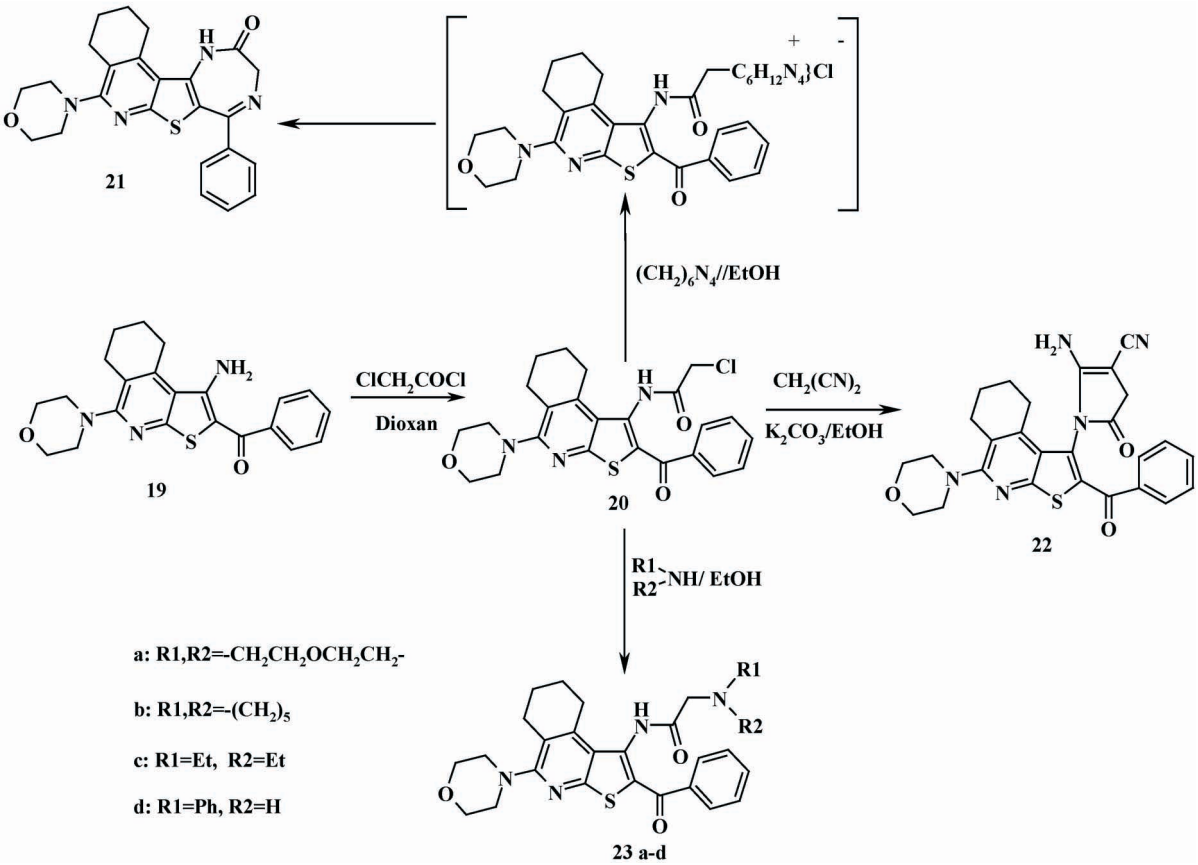


Fig. 3.

Scheme V



line), 4.5 (q, J = 6 Hz, 2H, CH_2 ester), 7.00 (s, 2H, NH_2), 7.5-8.5 (m, 5H, ArH) and 9.9 (s, 1H, NH) ppm. IR: ν = 3450, 3350, 3180 cm^{-1} (NH + NH_2), 3050 cm^{-1} (CH aromatic), 1715 cm^{-1} (CO ester), 1620 cm^{-1} (CONH). Anal. Calcd. for: $C_{27}H_{31}N_5O_4S$ (521.64) C, 62.17; H, 5.99; N, 13.43; S, 6.15%. Found: C, 62.35; H, 6.10; N, 13.25; S, 6.00%.

2-(1-Amino-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno-[2,3-c]isoquinoline-2-carbonyl)-5-phenyl-2,4-dihydro-pyrazol-3-one (4)

Method A

Ethylpropionate compound **3** (0.522 g, 1 mmol) was dissolved in acetic acid (20 mL) and was refluxed for 2 h. The solid precipitate which was formed on hot (during reflux) was cooled, filtered off and recrystallized from dioxan into yellow crystals in 68% yield, m.p. 250-252 °C.

Method B

Carbohydrazide derivative **2** (1.041 g, 3 mmol) and ethyl benzoylacetate (1.92 mL, 10 mmol) were refluxed in ethanol and piperidine for 2 h. The solid precipitate which was formed on hot (during reflux) was cooled, filtered off and recrystallized from dioxan to give yellow crystals in 72% yield, m.p. 250-252 °C. ^{1}H-NMR (DMSO-d_6): δ = 1.8 (m, 4H, $2CH_2$ cyclohexeno), 2.6 (m, 4H, $2CH_2$ cyclohexeno), 3.2 (m, 6H, $(CH_2)_2$N-morpholine + CH_2 pyrazole), 3.8 (m, 4H, $(CH_2)_2$O-morpholine), 6.1 (s, 2H, NH_2) and 7.5-7.9 (m, 5H, ArH) ppm. IR: ν = 3400, 3350 cm^{-1} (NH_2), 3050 cm^{-1} (CH aromatic), 2920, 2850 cm^{-1} (CH aliphatic), 1680, 1650 cm^{-1} (2CO). Anal. Calcd. for: $C_{25}H_{25}N_5O_3S$ (475.57) C, 63.14; H, 5.30; N, 14.73; S, 6.74%. Found: C, 63.00; H, 5.45; N, 15.00; S, 6.60%.

Ethyl-1-chloroacetylamino-N-(2-cyano-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline-1-yl)carboxylate (5)

A mixture of amino ester compound **1** (3.61 g, 10 mmol) and chloroacetyl chloride (1.243 mL, 11 mmol) in dioxan (30 mL) was heated on a steam bath for 2 h. The solid product which formed by pouring on ice water mixture and neutralized with diluted sodium carbonate solution was filtered off, dried and recrystallized from ethanol

to afford white needles in 78% yield, m.p. 160-162 °C. ^{1}H-NMR ($CDCl_3$): δ = 1.4 (t, *J* = 9 Hz, 3H, CH_3), 1.85 (m, 4H, $2CH_2$), 2.8 (m, 4H, $2CH_2$), 3.2 (m, 4H, $2CH_2$), 3.9 (m, 4H, $2CH_2$), 4.3 (s, 2H, CH_2 acetamide), 4.5 (q, *J* = 7.5 Hz, 2H, CH_2) and 9.2 (s, 1H, NH) ppm. IR: ν = 3200 cm^{-1} (NH), 2920, 2850 cm^{-1} (CH aliphatic), 1730 cm^{-1} (CO ester), 1670 cm^{-1} (CO amide). Anal. Calcd. for: $C_{20}H_{24}ClN_3O_4S$ (437.95) C, 54.85; H, 5.52; Cl, 8.10; N, 9.59; S, 7.32%. Found: C, 55.00; H, 5.72; Cl, 8.00; N, 10.05; S, 7.22%.

Ethy-5-morpholin-4-yl-8-oxo-1,2,3,4,8,9-hexahydropyrimido[4′,5′:4,5]thieno[2,3-c]isoquinolin-10-yl sulfanyl acetate (6)

A mixture of compound **5** (1.007 g, 2.3 mmol) and potassium thiocyanate (0.22 g, 2.3 mmol) in ethanol (30 mL) was refluxed for 4 h. The solid precipitate which formed on cold was filtered off, dried and recrystallized from ethanol to give white crystals in 81% yield, m.p. 140-142 °C. ^{1}H-NMR (DMSO-d_6): δ = 1.3 (t, *J* = 7.5 Hz, 3H, CH_3), 1.8 (m, 4H, $2CH_2$), 2.7 (m, 4H, $2CH_2$), 3.2 (m, 4H, $2CH_2$), 3.85 (m, 4H, $2CH_2$), 4.2 (s, 2H, CH_2CO), 4.5 (q, *J* = 7.5 Hz, 2H, CH_2 ester) and 11.5 (s, 1H, NH) ppm. IR: ν = 3290 cm^{-1} (NH), 2920, 2830 cm^{-1} (CH aliphatic), 1735 cm^{-1} (CO ester), 1675 cm^{-1} (CO amide). Mass spectrum *m/z* (%): 460 (M^+, 100), 429 (31.3), 403 (42.5), 92 (49.4). Anal. Calcd. For: $C_{21}H_{24}N_4O_4S_2$ (460.58) C, 54.76; H, 5.25; N, 12.16; S, 13.92%. Found: C, 54.50; H, 5.43; N, 12.30; S, 14.10%.

Ethyl-5-morpholin-4-yl-1-(2-phenylaminoacetylamino)-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline-2-carboxylate (7)

Chloro acetylamino derivative **5** (0.438 g, 1 mmol) and aniline (0.28 mL, 3.226 mmol) was gently refluxed for 10 minutes, then ethanol (10 mL) was added and reflux continued for additional 2 h. The solid precipitate which formed on hot during reflux was cooled, dried and recrystallized from dioxan to give white needles in 80% yield, m.p. 222-224 °C. ^{1}H-NMR ($CDCl_3$): δ = 1.35 (t, *J* = 6 Hz, 3H, CH_3), 1.8 (m, 4H, $2CH_2$), 2.7 (m, 4H, $2CH_2$), 3.25 (m, 4H, $2CH_2$), 3.9 (m, 4H, $2CH_2$), 4.05 (s, 2H, CH_2 acetamide), 4.25 (q, *J* = 7.5 Hz, 2H, CH_2), 6.6 (s, 1H, NH phenylamino), 7.3-6.8 (m, 5H, ArH) and 9.2 (s, 1H, NH acetamide) ppm. IR (cm^{-1}): ν = 3380, 3290 (2NH), 3030 (CH aromatic), 2920, 2850 (CH aliphatic), 1700 (CO ester), 1670 (CO amide). Anal. Calcd. for: $C_{26}H_{30}N_4O_4S$ (494.62) C, 63.14; H, 6.11; N, 11.33; S, 6.48%. Found: C, 63.00; H, 6.23; N, 11.21; S, 6.66%.

1-Amino-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno-[2,3-c]isoquinoline (8)

Amino ester compound **1** (1.444 g, 4 mmol) was refluxed with alcoholic potassium hydroxide solution (prepared by dissolving 1.00 g of potassium hydroxide in 30 mL ethanol) for 1 h. then the mixture was cooled and added to 10% HCl solution. The solid precipitate which formed by adding HCl solution was filtered off, dried and recrystallized from dioxan to afford white crystals in 96% yield, m.p. 218-220 °C. ^{1}H-NMR (DMSO-d_6): δ = 1.8 (m, 4H, $2CH_2$), 2.7 (m, 4H, $2CH_2$), 3.1 (m, 4H, $2CH_2$), 3.8 (m, 4H, $2CH_2$), 6.3 (s, 2H, NH_2) and 7.5 (s, 1H, CH thieno) ppm. IR: ν = 3520, 3350 cm^{-1} (NH_2), 2920, 2850 cm^{-1} (CH aliphatic), 1625 cm^{-1} (C=N). Anal. Calcd. for: $C_{15}H_{19}N_3OS$ (289.40), C, 62.25; H, 6.62; N, 14.52; S, 11.08%. Found: C, 62.40; H, 6.75; N, 14.70; S, 11.30%.

Ethyl-2-cyano-3-(5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline-1-ylamino)acrylate (9)

A mixture of amino compound **8** (2.894 g, 0.01 mol) and ethyl 2-cyano-3-ethoxyacrylate (1.69 g, 0.01 mol) in ethanol (30 mL) was refluxed for 2 h. The solid precipitate which was formed on hot during reflux was cooled, filtered off, dried and recrystallized from ethanol-benzene mixture to give brown crystals in 41% yield, m.p. 270-272 °C. ^{1}H-NMR ($CDCl_3$): δ = 1.3 (t, *J* = 7.5 Hz, 3H, CH_3), 1.9 (m, 4H, $2CH_2$), 2.8 (m, 4H, $2CH_2$), 3.3 (m, 4H, $2CH_2$), 3.8 (m, 4H, $2CH_2$), 4.2 (q, *J* = 6 Hz, 2H, CH_2), 7.9 (s, 1H, CH thieno), 8.6 (s, 1H, CHacrylate) and 11.5 (s, 1H, NH) ppm. IR: ν = 3380 cm^{-1} (NH), 2950, 2850 cm^{-1} (CH aliphatic), 2210 cm^{-1} (CN), 1680 cm^{-1} (CO ester), 1620 cm^{-1} (C=N). Anal. Calcd. for: $C_{21}H_{24}N_4O_3S$ (412.51) C, 61.15; H, 5.86; N, 13.58; S, 7.77%. Found: C, 60.95; H, 6.00; N, 13.70; S, 7.54%.

5-Morpholin-4-yl-8-oxo-1,2,3,4,8,11-hexahydropyrido-[2″,3″:4′,5′]thieno[2,3-c]isoquinoline-9-carbonitrile (10)

Ethyl acrylate compound **9** (0.578 gm, 1.4 mmol) was refluxed in glacial acetic acid (20 mL) for 3 hrs. The solid product which was formed on hot during reflux was cooled, filtered off and recrystallized from DMF into green crystals in 75% yield, m.p. 340-342 °C. ^{1}H-NMR (DMSO-d_6): δ = 1.9 (m, 4H, $2CH_2$), 2.8 (m, 4H, $2CH_2$), 3.3 (m, 4H, $2CH_2$), 3.8 (m, 4H, $2CH_2$), 8.8 (s, 1H, CH pyridine), 11.4 (s, 1H, NH pyridine) ppm. IR: ν = 3220 cm^{-1} (NH), 2210 cm^{-1} (CN), 1635 cm^{-1} (C=O). Mass spectrum *m/z* (%): 366 (M^+, 19.1), 365 (M^+-1, 44.5), 347 (21.3), 334 (21.5), 321 (36.6), 316 (24.7), 308 (100). Anal. Calcd. for: $C_{19}H_{18}N_4O_2S$

(366.44) C, 62.28; H, 4.95; N, 15.29; S, 8.75%. Found: C, 62.46; H, 5.12; N, 15.37; S, 8.88%.

(9-Cyano-5-morpholin-4-yl-1,2,3,4,8,11-hexahydropyrido[2″,3″:4′,5′]thieno[2,3-c]isoquinoline-8-yloxy)acetic acid ethyl ester (11)

A mixture of pyrido derivative **10** (3.664 g, 0.01 mol), ethyl chloroacetate (1.47 mL, 0.012 mol) and anhydrous potassium carbonate (4.00 g, 0.029 mmol) in DMF (10 mL) was heated on a steam bath for 6 h. The solid product which was formed on hot during reflux was cooled, filtered off, dried and recrystallized from ethanol into greenish yellow crystals in 67.5% yield, m.p. 240-242 °C. ^{1}H-NMR (CF_3CO_2D): δ = 1.3 (t, *J* = 6 Hz, 3H, CH_3), 1.8 (m, 4H, $2CH_2$), 2.6 (m, 4H, $2CH_2$), 3.2 (m, 4H, $2CH_2$), 3.9 (m, 4H, $2CH_2$), 4.2 (q, *J* = 4.5 Hz, 2H, CH_2), 4.8 (s, 2H, OCH_2), 9.4 (s, 1H, CH pyridine) ppm. IR: ν = 2920, 2850 cm^{-1} (CH aliphatic), 2200 cm^{-1} (CN), 1735 cm^{-1} (CO ester). Anal. Calcd. for: $C_{23}H_{24}N_4O_4S$ (452.54) C, 61.05; H, 5.35; N, 12.38; S, 7.09%. Found: C, 60.86; H, 5.48; N, 12.54; S, 7.23%.

Ethyl-3-amino-10-morpholin-4-yl-6,7,8,9-tetrahydrofuro[2″,3″:4′,5′]pyrido[2′,3′:4,5]thieno[2,3-c]isoquinoline-2-carboxylate (12)

A solution of O-(ethoxycarbonyl)methyl derivative **11** (0.45 g, 1 mmol) in absolute ethanol (20 mL) was refluxed in presence of few drops of sodium ethoxide solution prepared from 0.5 g clean sodium metal in absolute ethanol (20 mL) for 1 h. The solid product which was formed on hot during reflux was cooled, filtered off, dried and recrystallized from ethanol in 49% yield, m.p. 296-298 °C. IR: ν = 3420, 3320 cm^{-1} (NH_2), 2920, 2850 cm^{-1} (CH aliphatic), 1710 cm^{-1} (CO unsaturated ester), 1650 cm^{-1} (C=N). Mass spectrum *m/z* (%): 452 (M^+, 1), 414 (5), 394 (16), 109 (58.8), 90 (85), 88 (63.9), 57 (100). Anal. Calcd. for: $C_{23}H_{24}N_4O_4S$ (452.54) C, 61.05; H, 5.35; N, 12.38; S, 7.09%. Found: C, 61.26; H, 5.50; N, 12.16; S, 7.30%.

3-Amino-10-morpholin-4-yl-6,7,8,9-tetrahydrofuro[2″,3″:4′,5′]pyrido[2′,3′:4,5]thieno[2,3-c]isoquinolin-9-carbohydrazide (13)

A mixture of amino ester compound **12** (1 g, 2.21 mmol) and hydrazine hydrate (2 mL, 0.04 mol) was fused for 1 h. then ethanol (10 mL) was added and reflux continued for additional 2 h. The solid precipitate which formed on hot during reflux was cooled, filtered off and recrystallized from dioxan in yellow crystals in 33% yield, m.p. > 300 °C. IR: ν = 3420, 3300, 3180 cm^{-1} (NH, NH_2), 1630 cm^{-1} (CONH), 1600 cm^{-1} (C=N). Mass spectrum *m/z* (%) 437 (M^+-1, 1), 402 (8), 309 (7.3), 253 (7), 197 (8), 127 (12.8), 105 (15.9), 90 (55.3), 70 (72.5), 57 (100). Anal. Calcd. for: $C_{21}H_{22}N_6O_3S$ (438.51) C, 57.52; H, 5.06; N, 19.16; S, 7.31%. Found: C, 57.75; H, 4.98; N, 19.00; S, 7.48%.

(9-Cyano-5-morpholin-4-yl-1,2,3,4-tetrahydropyrido-[2″,3″:4′,5′]thieno[2,3-c]isoquinoline-8-yloxy)acetic acid hydrazide (14)

A mixture of O-(ethoxycarbonyl)methyl derivative **11** (1 g, 2.21 mmol) and hydrazine hydrate (2 mL, 0.04 mol) was fused for 1 h. then ethanol (10 mL) was added and reflux continued for additional 2 h. The solid precipitate which formed on hot during reflux was cooled, filtered off and recrystallized from dioxan to afford pale yellow crystals in 45% yield, m.p. 288-290 °C. ^{1}H-NMR (DMSO-d_6): δ = 1.85 (m, 4H, $2CH_2$), 2.75 (m, 4H, $2CH_2$), 3.30 (m, 4H, $2CH_2$), 3.85 (m, 4H, $2CH_2$), 4.10 (s, 2H, NH_2), 4.95 (s, 2H, CH_2), 8.7 (s, 1H, NH), 9.3 (s, 1H, CH pyridine) ppm. IR: ν = 3450, 3320, 3280 cm^{-1} (NH, NH_2), 3050 cm^{-1} (CH aromatic), 2910, 2820 cm^{-1} (CH aliphatic), 2210 cm^{-1} (CN), 1670 cm^{-1} (CO amide). Anal. Calcd. for: $C_{21}H_{22}N_6O_3S$ (438.51) C, 57.52; H, 5.06; N, 19.16; S, 7.31%. Found: C, 57.68; H, 5.34; N, 19.00; S, 7.50%.

8-[2-(3,5-Dimethylpyrazol-1-yl)-2-oxoethoxy]-5-morpholin-4-yl-1,2,3,4-tetrahydropyrido[2′,3′:4,5]thieno-[2,3-c]isoquinoline-9-carbonitrile (15)

The carbohydrazide compound **14** (0.482 g, 1.1 mmol) and acetylacetone (2 mL, 0.02 mol) were fused for 30 minutes then absolute ethanol (20 mL) was added and reflux continued for additional 2 h. The solid precipitate which formed on hot during reflux was cooled, filtered off, dried and recrystalllized from ethanol to give yellow needles in 36% yield, m.p. 264-266 °C. ^{1}H-NMR (DMSO-d_6): δ = 1.7 (m, 4H, $2CH_2$), 2.3, 2.45 (2s, 6H, $2CH_3$ pyrazole), 2.9 (m, 4H, $2CH_2$), 3.2 (m, 4H, $2CH_2$), 3.8 (m, 4H, $2CH_2$), 5.7 (s, 2H, CH_2), 6.2 (s, 1H, CH pyrazole), 8.8 (s, 1H, CH pyridine) ppm. IR: ν = 3050 cm^{-1} (CH aromatic), 2210 cm^{-1} (CN), 1680 cm^{-1} (C=O). Anal. Calcd. for: $C_{26}H_{26}N_6O_3S$ (502.60) C, 62.13; H, 5.21; N, 16.72; S, 6.38%. Found: C, 62.25; H, 5.05; N, 16.87; S, 6.50%.

5-Morpholin-4-yl-1-oxo-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline (16)

A mixture of aminotetrahydroisoquinoline derivative

8 (1 g, 3.455 mmol) and orthophosphoric acid (3 mL) was heated on water bath for 1 h. The solid precipitate which formed by pouring the mixture on ice water mixture was filtered off, dried and recrystallized from ethanol to afford orange crystals in 71% yield, m.p. 176-178 °C. ^{1}H-NMR ($CDCl_3$): δ = 1.8 (m, 4H, $2CH_2$ cyclohexeno), 2.5 (m, 2H, CH_2 cyclohexeno), 3.15 (m, 2H, CH_2N-morpholine), 3.4 (m, 4H, $(CH_2)_2$O-morpholine), 3.75 (m, 6H, $(CH_2)_2$O-morpholine + CH_2 thieno) ppm. IR: ν = 2920, 2850 cm^{-1} (CH aliphatic), 1665 cm^{-1} (C=O). Anal. Calcd. for: $C_{15}H_{18}N_2O_2S$ (290.39) C, 62.04; H, 6.25; N, 9.65; S, 11.04%. Found: C, 62.24; H, 6.06; N, 9.78; S, 11.27%.

2-Benzylidine-5-morpholin-4-yl-1-oxo-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline (17)

A mixture of compound **16** (0.29 g, 1 mmol) and benzaldehyde (0.15 mL, 1.415 mmol) were fused for 10 minutes then ethanol (20 mL) was added and reflux continued for additional 2 h. in presence of few drops of piperidine. The solid precipitate which formed on hot during reflux was cooled, filtered off, dried and recrystallized from ethanol-dioxan mixture to give orange crystals in 78% yield, m.p. 220-222 °C. ^{1}H-NMR ($CDCl_3$): δ = 1.8 (m, 4H, $2CH_2$), 2.5 (m, 4H, $2CH_2$), 3.4 (m, 4H, $2CH_2$), 3.8 (m, 4H, $2CH_2$), 7.45-7.8 (m, 5H, ArH), 7.9 (s, 1H, CH benzylidene) ppm. IR: ν = 3030 cm^{-1} (CH aromatic), 2920, 2850 cm^{-1} (CH aliphatic), 1655 cm^{-1} (C=O). Anal. Calcd. for: $C_{22}H_{22}N_2O_2S$ (378.50) C, 69.81; H, 5.86; N, 7.40; S, 8.47%. Found: C, 70.00; H, 5.74; N, 7.57; N, 7.28; S, 8.62%.

10-Amino-5-morpholin-4-yl-8-phenyl-1,2,3,4-tetrahydro-8H-pyrano[2′,3′:4,5]thieno[2,3-c]isoquinoline-9-carbonitrile (18)

A mixture of compound **16** (0.29 g, 1 mmol), benzylidinemalononitrile (0.154 g, 1 mmol) and few drops of piperidine as a basic catalyst was refluxed in ethanol (20 mL) for 1 h. The solid precipitate which was formed on hot during reflux was cooled, filtered off, dried and recrystallized from dioxan to afford white crystals in 86% yield, m.p. 232-234 °C. ^{1}H-NMR ($CDCl_3$): δ = 1.85 (m, 4H, $2CH_2$), 2.7 (m, 4H, $2CH_2$), 3.2 (m, 4H, $2CH_2$), 3.8 (m, 4H, $2CH_2$), 4.7 (s, 2H, NH_2), 4.85 (s, 1H, CH pyran), 7.2-7.4 (m, 5H, ArH) ppm. IR: ν = 3350, 3200 cm^{-1} (NH_2), 2200 cm^{-1} (CN), 3030 cm^{-1} (CH aromatic), 2950, 2850 cm^{-1} (CH aliphatic), 1650 cm^{-1} (C=N). Anal. Calcd. for: $C_{25}H_{24}N_4O_2S$ (444.56) C, 67.55; H, 5.44; N, 12.60; S, 7.21%. Found: C, 67.65; H, 5.24; N, 12.77; S, 7.12%.

N-(2-Benzoyl-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinolin-1-yl)-2-chloroacetamide (20)

A mixture of aminobenzoyl compound **19** (3.93 g, 0.01 mol), chloro acetylchloride (1.25 mL, 0.011 mol) in dioxan (25 mL) was heated on a steam bath for 2 h. The solid which formed by pouring on diluted sodium carbonate solution (10%) was filtered off, dried and recrystallized from ethanol to give pale green crystals in 87% yield, m.p. 178-180 °C. ^{1}H-NMR (DMSO-d_6): δ = 1.8 (m, 4H, $2CH_2$ cyclohexeno), 2.7 (m, 4H, $2CH_2$ cyclohexeno), 3.2 (m, 6H, $(CH_2)_2$-N morpholine + CH_2 acetamide), 3.8 (m, 4H, $(CH_2)_2$O morpholine), 7.4-7.7 (m, 5H, ArH), 10.3 (s, 1H, NH) ppm. IR: ν = 3340 cm^{-1} (NH), 3050 cm^{-1} (CH aromatic), 2920, 2850 cm^{-1} (CH aliphatic), 1675 cm^{-1} (unsat C=O), 1630 cm^{-1} (CO amide). Anal. Calcd. for: $C_{24}H_{24}ClN_3O_3S$ (469.99) C, 61.33; H, 5.15; Cl, 7.54; N, 8.94; S, 6.82%. Found: C, 61.25; H, 5.31; N, 9.14; S, 6.97%.

5-Morpholin-4-yl-8-phenyl-1,2,3,4,10-pentahydro[1,4]-diazepino[5′,6′:4,5]thieno[2,3-c]isoquinolin-11(12H)-one (21)

A mixture of chloro acetylamino derivative **20** (3.525 g, 7.5 mmol) and hexamethylene tetramine (1.5 g, 10.7 mmol) in ethanol (30 mL) was refluxed for 20 h. The solid product which formed on cold was filtered off, dried and recrystallized from ethanol in brilliant yellow crystals in 93% yield, m.p. 154-156 °C. ^{1}H-NMR ($CDCl_3$): δ = 1.75 (m, 4H, $2CH_2$), 2.6 (m, 4H, $2CH_2$), 3.2 (m, 4H, $2CH_2$), 3.75 (m, 4H, $2CH_2$), 4.35 (s, 2H, CH_2 diazepine), 7.2-7.8 (m, 5H, ArH), 8.9 (s, 1H, NH) ppm. ^{13}C-NMR ($CDCl_3$): δ = 162.74 (CO amide), 160.11 (CH=N diazepine), 158.83 (C-9), 154.32 (C-10), 147.83 (C-10), 137.56 (C-19 aromatic), 130.77 (C-3), 126.1-129 (4CH-aromatic), 122.29 (C-8), 119.14 (C-4), 93.8 (C-11), 40.0-49.96 ($4CH_2$-morpholine), 22.02-39.55 ($4CH_2$ cyclohexeno). Mass spectrum *m/z*: 433 (M^++1, 1.4), 432 (M^+, 100), 405 (64.2), 395 (69.9), 375 (29.7), 357 (40.9), 345 (80), 316 (35.4). IR: ν = 3400 cm^{-1} (NH), 3050 cm^{-1} (CH aromatic), 2920, 2850 cm^{-1} (CH aliphatic), 1690 cm^{-1} (CO amide). Anal. calcd. for: $C_{24}H_{24}N_4O_2S$ (432.55) C, 66.64; H, 5.59; N, 12.95; S, 7.41%. Found: C, 66.80; H, 5.41; N, 13.11; S, 7.52%.

2-Benzoyl-1-(2-amino-3-cyano-5-oxopyrrol-1-yl)-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline (22)

A mixture of chloroacetamide derivative **20** (4.70 g, 0.01 mol) and malononitrile (0.66 g, 0.01 mol) in presence of potassium carbonate (5 g, 0.036 mol) in ethanol (30 mL)

was refluxed for 3 h. The solid product which was formed on hot during reflux was cooled, filtered off, washed with water and recrystallized from ethanol in 72% yield, m.p. 240-242 °C. ^{1}H-NMR ($CDCl_3$): δ = 2.00 (m, 4H, $2CH_2$), 2.8 (s, 2H, CH_2 pyrrole), 3.4 (m, 4H, $2CH_2$), 3.7 (m, 4H, $2CH_2$), 4.0 (m, 4H, $2CH_2$), 5.3 (s, 2H, NH_2), 7.5-7.8 (m, 5H, ArH) ppm. IR: ν = 3320, 3200 cm^{-1} (NH_2), 3050 cm^{-1} (CH aromatic), 2920, 2850 cm^{-1} (CH aliphatic), 2200 cm^{-1} (CN), 1680, 1640 cm^{-1} (2CO). Anal. Calcd. for: $C_{27}H_{25}N_5O_3S$ (499.60) C, 64.91; H, 5.04; N, 14.02; S, 6.42%. Found: C, 65.03; H, 4.99; N, 14.20; S, 6.53%.

N-(2-Benzoyl-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline-1-yl)-2-alkyl(aryl)aminoacetamide (23 a-d)

General procedure

Chloroacetamide derivative **20** (1 mmol) and the corresponding amine (0.01 mol) were gently refluxed for 10 minutes then ethanol (20 mL) was added and reflux continued for additional 2 h. The solid product which formed on cold was filtered off, dried and recrystallized from ethanol.

N-(2-Benzoyl-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinolin-1-yl)-2-morpholin-4-yl-acetamide (23a)

Obtained by reaction with morpholine as colorless crystals when the solid product was recrystallized from ethanol in 87% yield, m.p. 168-170 °C. ^{1}H-NMR ($CDCl_3$): δ = 1.8 (m, 4H, $2CH_2$), 2.0 (m, 4H, $2CH_2$), 2.8 (m, 4H, $2CH_2$), 3.2 (s, 2H, CH_2), 3.4 (m, 6H, $3CH_2$), 4.0 (m, 6H, $3CH_2$), 7.6-8.2 (m, 5H, ArH), 10.2 (s, 1H, NH acetamide) ppm. ^{13}C-NMR ($CDCl_3$) δ = 171.06 (COPh), 162.56 (CO amide), 157.54 (C-9), 153.04 (C-7), 145.21 (C-10), 138.97 (C-17 aromatic), 127.79-133.88 (4CH aromatic + C-3), 124.77 (C-8), 121.40 (C-4), 77.45 (C-11), 49.95-67.06 ($8CH_2$-Morpholine + $\underline{CH_2}CO$), 22.10-27.45 ($4CH_2$ cyclohexeno). IR: ν = 3350 cm^{-1} (NH), 3050 cm^{-1} (CH aromatic), 2920, 2850 cm^{-1} (CH aliphatic), 1670 cm^{-1} (unsaturated CO), 1630 cm^{-1} (CO amide). Anal. Calcd. for: $C_{28}H_{32}N_4O_4S$ (520.66) C, 64.59; H, 6.20; N, 10.76; S, 6.16%. Found: C, 64.71; H, 6.35; N, 10.68; S, 6.28%.

N-(2-Benzoyl-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline-1-yl)-2-piperidin-4-yl-acetamide (23b)

Obtained by reaction with piperidine as florescent green crystals when the solid product was recrystallized from ethanol in 83% yield, m.p. 154-156 °C. ^{1}H-NMR ($CDCl_3$): δ = 1.25 (m, 2H, C-4 piperidine), 1.8 (m, 8H, 4H cyclohexeno + 4H (C-3 + C-5) piperidine), 2.5 (m, 8H, 4H cyclohexeno + 4H (C-2 + C-4) piperidine), 2.7 (s, 2H, CH_2 acetamide), 3.2 (m, 4H, $(CH_2)_2$-O morpholine), 3.8 (m, 4H, $(CH_2)_2$-N morpholine), 7.6-8.2 (m, 5H, ArH), 10.2 (s, 1H, NH acetamide) ppm. IR: ν = 3300 cm^{-1} (NH), 3030 cm^{-1} (CH aliphatic), 2950, 2850 cm^{-1} (CH aliphatic), 1670 cm^{-1} (unsaturated CO), 1630 cm^{-1} (CO amide). Anal. Calcd. for: $C_{29}H_{34}N_4O_3S$ (518.68) C, 67.16; H, 6.61; N, 10.80; S, 6.18%. Found: C, 66.99; H, 6.74; N, 10.76; S, 6.25%.

N-(2-Benzoyl-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline-1-yl)-2-diethylaminoacetamide (23c)

Obtained by reaction with diethylamine as green crystals when the solid product was recrystallized from ethanol in 78% yield, m.p. 116-118 °C. ^{1}H-NMR ($CDCl_3$): δ = 1.1 (t, *J* = 7.5 Hz, 6H, $2CH_3$ diethylamino), 1.85 (m, 4H, $2CH_2$ cyclohexeno), 2.65 (m, 8H, 4H diethylamino + 4H cyclohexeno), 3.0 (s, 2H, CH_2 acetamide), 3.2 (m, 4H, $(CH_2)_2$-N morpholine), 3.8 (m, 4H, $(CH_2)_2$-O morpholine), 7.2-7.8 (m, 5H, ArH), 10.05 (s, 1H, NH acetamide) ppm. IR: ν = 3450 cm^{-1} (NH), 3050 cm^{-1} (CH aromatic), 2920, 2850 cm^{-1} (CH aliphatic), 1690 cm^{-1} (unsaturated CO), 1630 cm^{-1} (CO amide). Anal. Calcd. for: $C_{28}H_{34}N_4O_3S$ (506.67) C, 66.38; H, 6.76; N, 11.06; S, 6.33%. Found: C, 66.23; H, 6.61; N, 11.24; S, 6.50%.

N-(2-Benzoyl-5-morpholin-4-yl-6,7,8,9-tetrahydrothieno[2,3-c]isoquinoline-1-yl)-2-phenylaminoacetamide (23d)

Obtained by reaction with aniline as green crystals when the solid product which was formed on cold filtered off, dried and recrystallized from dioxan in 75% yield, m.p. 212-214 °C. ^{1}H-NMR ($CDCl_3$): δ = 1.8 (m, 4H, $2CH_2$), 2.7 (m, 4H, $2CH_2$), 3.1 (s, 2H, CH_2 acetamide), 3.2 (m, 4H, $2CH_2$), 3.8 (m, 4H, $2CH_2$), 6.8-8.0 (m, 10H, ArH), 9.8 (s, 1H, NH phenylamino), 10.2 (s, 1H, NH acetamide) ppm. IR: ν = 3450, 3350 cm^{-1} (2NH), 3050 cm^{-1} (CH aromatic), 2920, 2850 cm^{-1} (CH aliphatic), 1670 cm^{-1} (unsaturated CO), 1625 cm^{-1} (CO amide), 1600 cm^{-1} (C=N). Anal. Calcd. for: $C_{30}H_{30}N_4O_3S$ (526.66) C, 68.42; H, 5.74; N, 10.64; S, 6.09%. Found: C, 68.54; H, 5.88; N, 10.51; S, 5.95%.

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