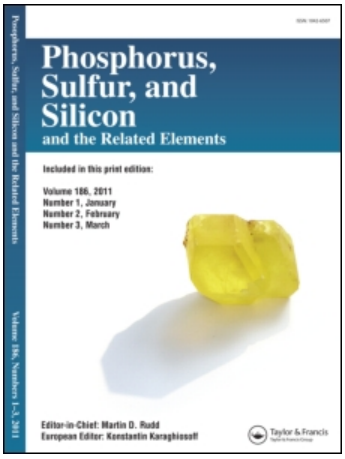

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A NOVEL SYNTHESIS OF 2-SUBSTITUTED-4H-THIENO [2,3-*d*][1,3] OXAZIN-4-ONE AND 2,3-DISUBSTITUTED THIENO [2,3-*d*]PYRIMIDIN-4(3H)-ONE DERIVATIVES

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A NOVEL SYNTHESIS OF 2-SUBSTITUTED-4H-THIENO [2,3-*d*][1,3] OXAZIN-4-ONE AND 2,3-DISUBSTITUTED THIENO [2,3-*d*]PYRIMIDIN-4(3H)-ONE DERIVATIVES

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The synthesis of acetic 2-{[1-methyl-2-(4-oxo-5,6,7,8-tetrahydro-4H-benzo [4,5]-thieno [2,3-d] [1,3-oxazin-2-yl)ethylidene]amino}-4,5,6,7-tetrahydrobenzo[b]thiophene -3-carboxylic acid anhydride **5** and 2-(oxopropyl)-5,6,7,8-tetrahydro-4H-benzo-[4,5] thieno[2,3-d][1,3]oxazin-4-one **7**, has been achieved in three steps from ethyl 2-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxlate **1** via the reaction with ethyl acetoacetate followed by hydrolysis and acetic anhydride-induced cyclization. The 2-substituent in compound **5** has two functional groups i.e. active methylene and acid anhydride which are suitably located for intramolecular transformation. Thermal and/or base catalyzed intramolecular cyclization of **5** afforded 2-(4-acetoxy-(hydroxyl)-2-methyl-5,6,7,8-tetrahydrobenzo[4,5] thieno[2,3-b]pyridin-3-yl)-5,6,7,8- tetrahydro-4H-benzo[4,5]thieno[2,3-d] [1,3]oxazin-4-one **10** and **9** respectively. Treatment of **5** with hydrazine hydrate, aromatic and/or heterocyclic amines induced the same intramolecular cyclization with a concomitant oxazine-pyrimidine interconversion to give 3-amino(aryl or heteryl)-2-(4-hydroxy-5,6,7,8-tetrahydrobenzo-[4,5]thieno[2,3-b]pyridin-3-yl)-3,4,5,6,7,8-hexahydrobenzo[4,5] thieno[2,3-d] pyrimid in-4-one **11–14** respectively.

Keywords: Thieno[2,3-d][1,3]oxazin-4-one; thieno[2,3-d]pyrimidin-4-one; synthesis

INTRODUCTION

Thieno[2,3-d][1,3]oxazine and thieno[2,3-d]pyrimidine nuclei have been found to be associated with diverse biological activities.[1,2] Several thieno

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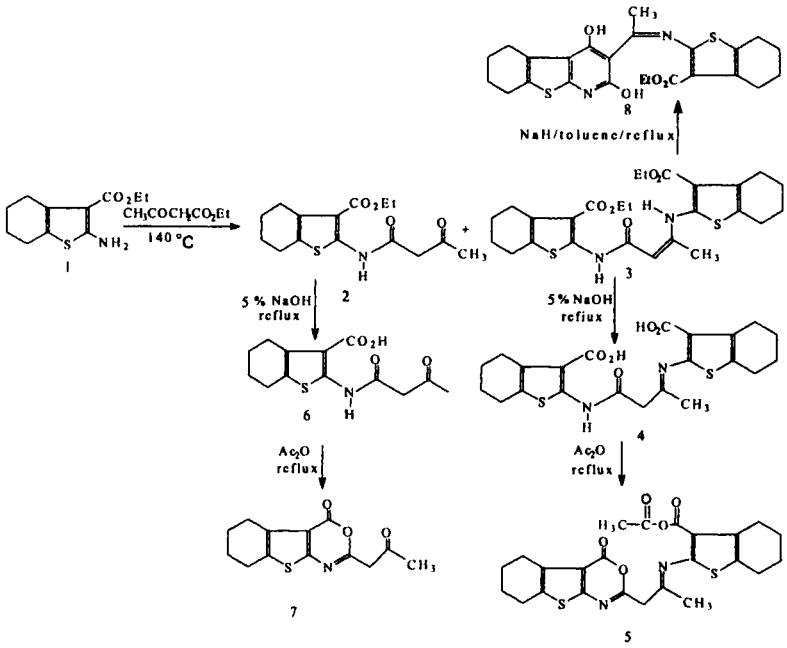
[2,3-d] pyrimidines and thieno [2,3-d][1,3]oxazine have been reported to be utilized as prophylactic or therapeutic agents for the prevention or treatment of several hormone dependent diseases[3] and as antipsychotic agents for diseases such as schizophrenia.[4] A fast number of these nuclei have also been reported as potential virucides,[5] bactericides,[6] fungicides, herbicides[7] and pesticides.[8,9]

In continuation of our effort in synthesis of novel heterocycles of biological interest, [10–12] herein, new convenient routes for the synthesis of novel 2-substituted-thieno [2,3-d]-[1,3]oxazin-4-one; 2- and /or 3-substituted thieno[2,3-d]pyrimidin-4(3H)-one derivatives are reported.

RESULTS AND DISCUSSION

Various thienoxazines are widely utilized as synthetic intermediates since they are good precursors for synthesis of many thieno- annulated heterocycles, owing to the high reactivity of these compounds towards different nucleophiles. The hitherto unknown thienoxazines **5** and **7** were prepared via the reaction pathway depicted in (Scheme 1). Reaction of ethyl 2-amino-4, 5, 6,7-tetrahydrobenzo[b]thiophene-3-carboxlate **1** with ethyl acetoacetate in xylene under reflux yielded compounds **2** and **3** in 65 and 20 % yield respectively. When the reaction was carried at 140 °C without solvent it gave better results and required a shorter reaction time.

The structures of compounds **2** and **3** were deduced on the basis of spectral and analytical values. ^{1}H- NMR of compound **2** showed three singlets at δ 2.32, 3.65, 11.99 attributable for CH_3, CH_2 and -NH groups respectively, while that of compound **3** showed four multiplets at δ 1.74 (8H, 4×CH_2), 2.62(4H, 2×CH_2), 2.72(4H, 2×CH_2), 4.33(4H, 2×CH_2) and three singlets one proton each at δ 5.12, 10.82 and 12.25 for CH (olefinic) and two -NH groups. Compound **3** on hydrolysis with 5 % aqueous alcoholic sodium hydroxide solution produced the dicarboxlic acid **4** in good yield. The ^{1}H-NMR of compound **4** lacked any signals corresponding to olefinic protons and showed it to be present completely in the imine form rather than the enamine form. Compound **4** on heating with acetic anhydride easily cyclized into the thienoxazine derivative **5** in high yield. The structure of compound **5** was confirmed by microanalytical and spectral data. The IR spectrum of compound **5** showed well-defined broad band attributable

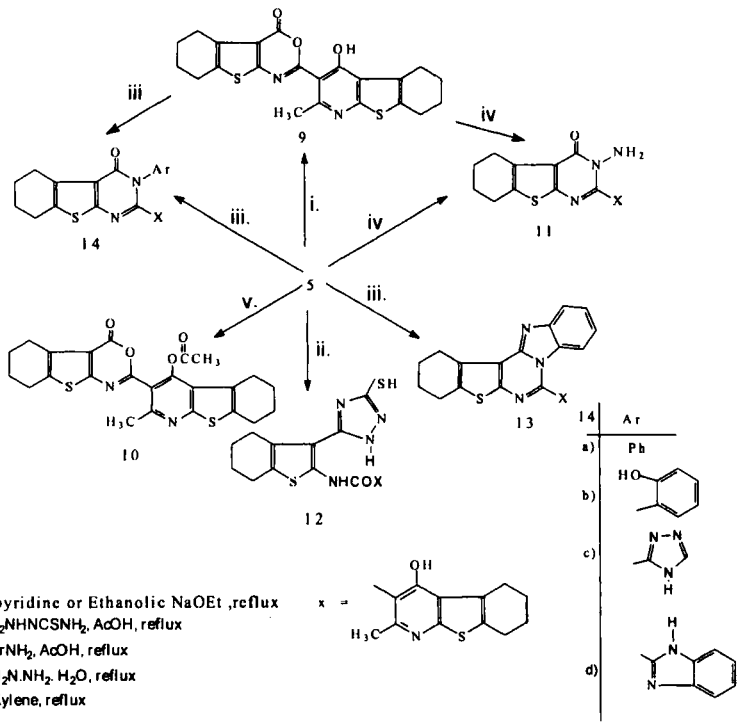


SCHEME 1

for the lactone carbonyl group at 1748 cm^{-1}. Besides, the ^{1}H-NMR of compound **5** showed two singlets three protons each at δ 2.32, 2.7 corresponding for two methyl groups. Similarly, the thienoxazine derivative **7** was obtained from **2** under the same reaction conditions.

Compound **3** on treatment with sodium hydride in toluene under reflux produced the thienopyridine derivative **8**. The structure of compound **8** was confirmed by mass spectrum that showed the molecular ion peak at m/e 470.

The presence of both acid anhydride and active methylene groups in compound **5** attracted the attention to study the interaction of these groups under various conditions. Thus, the thienoxazine **5** eliminates a molecule of acetic acid in boiling pyridine or when refluxed in 3 % ethanolic ethoxide solution to give the hitherto unknown 2-substituted thieno[2,3-d] oxazine derivative **9**. The mass spectrum of compound **9** showed the parent peak at m/z 425, which is in agreement with the calculated mass. The

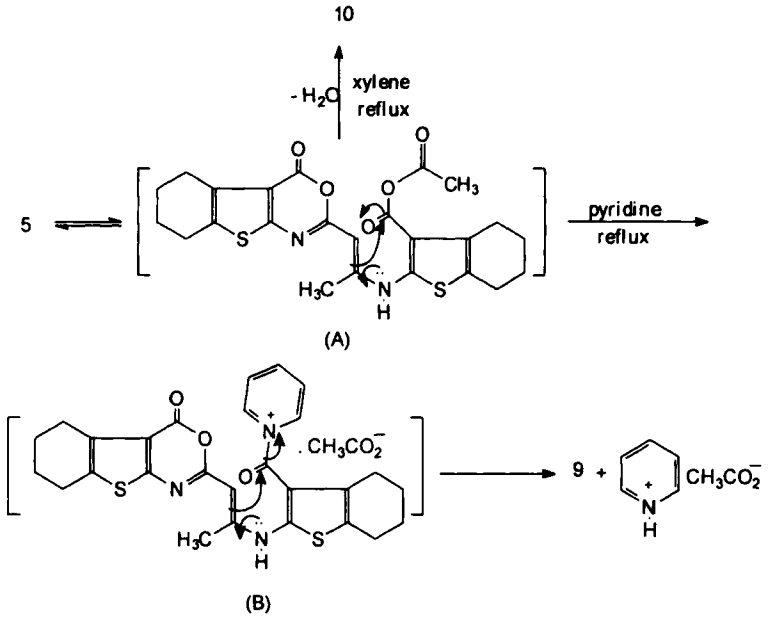


SCHEME 2

^{1}H-NMR of compound **9** displayed eight protons, four protons, two protons multiplets at δ 1.9, 2.81, 2.93, 3.07 respectively and three protons singlet at δ 3.1. When the reaction was carried out in xylene under reflux, compound **5** eliminated a molecule of water to give compound **10** (scheme 2). The structure of compound **10** was based on ^{1}H- NMR, which showed two singlets three protons each at δ 2.28 and 2.8. The ^{13}C-NMR of compound **10** showed the presence of 10 aliphatic carbons in the range of δ 20.8- 25.8. The mechanism of the reaction is depicted in (scheme 3). Compound **9** is thought to be formed via imine-enamine tautomerization to give intermediates (A) and (B) followed by intramolecular enamine thienoyl pyridinium acetate cyclization, while compound **10** was formed by intramolecular enamine acid anhydride cyclization followed by water elimination (Scheme 3).

Despite the presence of bulky group at position-2 in the thienoxazine **5** it showed high reactivity towards different nucleophiles. Several thieno[2,3-d] pyrimidine derivatives were prepared via reaction of compound **5** with different aromatic amines, hydrazine, and thiosemicarbazide.

In all these reactions thienoxazine-pyrimidine interconversion with a concomitant removal of a molecule of acetic acid via intramolecular enamine- acid anhydride cyclization was observed. Thus, treatment of **5** with aromatic amines in acetic acid afforded the thienopyrimidines **14a-d**. Also, the reaction of compound **5** with hydrazine hydrate yielded the thienopyrimidine **11**. The structures of these compounds were based on ^{1}H-NMR and unequivocal synthesis via treatment of compound **9** with amines in acetic acid to give **14a-d** and with hydrazine hydrate to give **11**.



SCHEME 3

In the case of thiosemicarbazide the triazole derivative **12** was formed instead. The structure of compound **12** was based on ^{1}H-NMR that showed four broad singlets one proton each at δ 7.62, 8.18, 9.15, 9.8 corre-

sponding for four protons attached to heteroatoms. Treatment of **5** with o-phenylenediamine under the same condition yielded the pyrimidobenzimidazole derivative **15**. The IR of **15** lacked the presence of any absorption bands corresponding to the amino and the carbonyl groups.

Experimental

Melting points (°C) (uncorrected) were determined using Griffin melting point apparatus. IR spectra were recorded on MATTSON 5000 FTIR Spectrometer. Carbon and proton NMR spectra were recorded on a GE Omega GN-300 Spectrometer using ($CDCl_3$) and (DMSO-D_6) as solvents. MS were recorded on G.C. MSQP-1000 EX Schmiadzu (Japan) mass Spectrometer. Elemental analyses were carried out at the microanalytical unit, Faculty of Science, Mansoura University.

Reaction of ethyl acetoacetate with ethyl 2-amino-4, 5, 6, 7-tetrahydrobenzo-[b]-thiophene-3-carboxlyate (1)

METHOD (A)

A mixture of ethyl acetoacetate (0.06 mol) and ethyl 2-amino-4, 5, 6, 7-tetrahyrobenzo[b]thiophene-3-carboxlyate (**1**) (0.05 mol) in xylene (50ml) was heated under reflux for 4 hrs. The solvent was distilled off under reduced pressure and the residue was chromatographed using pet. ether – ehyl acetate 4:1.The first fraction was identified as 2-[(3-{[3-(ethoxycarbonyl)-4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl]amino}-2-butenoyl) amino]-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate **3** and the second fraction was ethyl 2-(acetoacetylamino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (**2**).

METHOD (B)

A mixture of ethyl acetoacetate (0.06 mol) and ethyl 2-amino-4, 5,6,7-tetrahyrobezo[b]thiophene-3-carboxlyate (0.05 mol) was heated at 140°C for 2 hrs. The reaction mixture was cooled and processed in the same manner as in method (a).

Compound (**2**): yield (15–20 %); m.p. 90–92°C; IR (KBr): 3159, 2981 2936, 2847, 1710, 1662, 1563 cm-1; Anal. Calcd for $C_{15}H_{19}NO_4S$ (309.39) C, 58.23; H, 6.19; N, 4.53; S, 10.36. Found: C, 58.45; H, 5.78; N, 4.86; S, 10.64.

TABLE I ^{1}H-NMR and ^{13}C-NMR of compounds **2–5** and **9–14b**

^{1}H-NMR	*^{13}C-NMR*
1.38(t, 3H, CH_3), 1.78(m, 4H, 2×CH_2), 2.32(s, 3H, CH_3), 2.64(m, 2H, CH_2), 2.78(m, 2H, CH_2), 3.65(s, 2H, CH_2), 4.37 (q, 2H, CH_2), 11.99(s, 1H, NH)	14.5, 22.3, 22.5, 24.6, 26.7, 31.2, 50.05 60.1, 112.9, 127.8, 131.7, 147.8, 162.5, 165.6, 202.5
1.33(t, 6H, 2×CH_3), 1.74(m, 8H, 4×CH_2), 2.28(s, 3H, CH_3), 2.62(m, 4H, 2×CH_2), 2.72(m, 4H, 2×CH_2), 4.33 (m, 4H, 2×CH_2), 5.12(s, 1H), 10.82(s, 1H, NH), 12.25 (s, 1H, NH)	
1.75(m, 8H, 4×CH_2), 2.55(m, 2H, CH_2), 2.7(m, 9H, 3×CH_2, CH_3), 2.95(m, 2H, CH_2), 11.4(s, 1H)	22.3, 22.5, 23.1, 24.5, 24.9, 27.1, 27.3, 113.1, 114.5, 126.5, 127.6 129.8, 132.5, 132.9, 146.7, 146.9, 154.7, 164.1, 166.8, 175.2
1.84(m, 8H, 4×CH_2)2.32(s, 3H, CH_3), 2.7(s, 3H, CH_3), 2.75 (m, 2H, CH_2), 2.85(m, 8H, 4×CH_2)	
1.9(m, 8H, 4×CH_2), 2.81 (m, 4H, 2×CH_2), 2.93(m, 2H, CH_2), 3.07(m, 2H, CH_2), 3.1(s, 3H, CH_3)	
1.85(m, 8H, 4×CH_2), 2.28(s, 3H, CH_3), 2.8(s, 3H, CH_3), 2.9 (m, 6H, 3×CH_2), 3.0(m, 2H, CH_2)	20.8, 21.9, 22.2, 22.4, 22.8, 24.1, 24.8, 25.1, 25.2, 25.8, 116.9, 11 125.7, 127.1, 133.2, 136.5, 139.3, 151.6, 155.8, 157.4, 161.5, 164 169.8
1.75(m, 8H, 4×CH_2), 2.55(m, 4H, 2×CH_2)2.65(m, 2H, CH_2), 2.7(s, 3H, CH_3), 2.95(m, 2H, CH_2), 4.6(br, 2H, NH_2), 9.01(br, 1H, OH)	22.5, 22.8, 23.4, 23.5, 23.9, 24.75, 25.5, 25.6, 27.01, 114.2, 118.1 126.5, 128, 129.8, 131.1, 132.5, 138.4, 147.2, 154.8, 164.3, 165.0 176.1
1.75, (m, 8H, 4×CH_2), 2.58(m, 4H, 2×CH_2), 2.68(m, 2H, CH_2), 2.75(s, 3H, CH_3), 2.95(m, 2H, CH_2), 7.62(br, 1H), 8.18(br, 1H), 9.15(br, 1H), 9.8(br, 1H)	22.6, 22.98, 23.5, 23.9, 24.7, 25.5, 25.6, 27, 112.2, 117.5, 124.2, 130.1, 131.5, 133.4, 139.8, 147.5, 154.9, 164.3, 167.1, 175.1, 184

	^{1}H-NMR	^{13}C-NMR
	1.78(m, 8H, 4×CH_2), 2.65(m, 4H, 2×CH_2), 2.68(s, 3H, CH_3), 2.78(m, 4H, 2×CH_2), 7.25(m, 2H, ArH), 7.65(m, 2H, ArH), 10.7 (br, 1H, OH)	22.1, 22.9, 23.58, 23.8, 24.9, 25.39, 26.05, 26.9, 110.37, 110.4, 127.7, 128.2, 129.8, 130.05, 132.2, 132.8, 137.8, 138.5, 144.01 149, 152.8, 153, 153.9, 158, 164
	1.75, (m, 8H, 4×CH_2), 2.7(m, 6H, 3×CH_2), 2.8(s, 3H, CH_3), 2.92(m, 2H, CH_2), 7.1(t, 1H, ArH), 7.35(t, 2H, ArH), 7.75(d, 2H, ArH), 10.1(s, 1 H)	
	1.81(m, 8H, 4×CH_2), 2.75(m, 6H, 3×CH_2), 2.78(s, 3H, CH_3), 2.92(m, 2H, CH_2), 6.9(m, 2H, ArH), 7.01 (t, 1 H, ArH), 7.98 (d, 1H, ArH), 9.14(s, 1H), 9.82(s, 1H)	22.5, 23.2, 23.8, 23.9, 24.9, 25.5, 26.2, 27.1, 112.2, 113.9, 117.2 120.1, 123.95, 126.1, 127.8, 128.1, 129.9, 130.1, 132.9, 141.1, 149.2, 154.6, 164.2, 169.2, 175.6

Compound (**3**): yield (65–70 %); m.p. 158–59°C; IR (KBr): 3273, 2928, 1688, 1641, 1593, 1561 cm^{-1}; Anal. Calcd. for $C_{26}H_{32}N_2O_5S_2$ (516.68) C, 60.44; H, 6.25; N, 5.42; S, 12.41. Found: C, 60.86; H, 5.89; N, 5.91; S, 12.62.

2-({3-[(3-Carboxy-4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl)imino] butanoyl}amino)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylic acid (4) and 2-(Acetoacetylamino)-4,5,6, 7-tetrahydrobenzo[b] thiophene-3-carboxylic acid (6)

Ethyl 2-[(3-{[3-(ethoxycarbonyl)-4,5,6,7-tetrahydrobenzo[b]thiophen-2-yl] amino}-2-butenoyl)amino]-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (**3**) (2mmol) was dissolved in 15 ml 5 % aqueous ethanolic sodium hydroxide solution. The reaction mixture was refluxed for 1 hr. The ethanol was distilled off and the aqueous layer was extracted with ether and acidified with ice cold dilute hydrochloric acid. The formed precipitate was triturated with hot ethanol, filtered and crystallized from 3:1 ethanol-dimethylformamide mixture to give compound (**4**). Compound (**6**) was prepared in the same manner and crystallized from ethanol.

Compound (**4**): Yield (75%); m.p. 250°C; IR (KBr): 3364, 3328, 3285, 3240, 3217, 3025, 2924, 1660, 1646, 1599 cm^{-1}; Anal. Calcd for $C_{22}H_{24}N_2O_5S_2$ (460.575) C, 57.37; H, 5.25; N, 6.08, S, 13.92. Found: C, 57.76; H, 4.98; N, 6.35; S, 14.23.

Compound **6**: Yield (90 %); m.p. 176–77°C; IR (KBr) 3437, 3211, 2935, 1715, 1665, 1559, 1538, 1458, 1417, 1366, 1314. Anal. Calcd for $C_{13}H_{15}NO_4S$ (281.332) C, 55.5; H, 5.37; N, 4.98; S, 11.4. Found: C, 55.86; H, 5.68; N, 5.34; S, 11.79.

Acetic 2-{[1-methyl-2-(4-oxo-5, 6,7,8-tetrahydro-4H-benzo [4,5] thieno [2,3-d][1,3-oxazin-2-yl)ethylidene]amino}-4,5,6,7-tetrahydrobenzo[b] thiophene-3-carboxylic acid anhydride (5) and 2-(oxopropyl)-5,6,7,8-tetrahydro-4H-benzo-[4,5]thieno[2,3-d][1,3]oxazin-4-one (7)

A mixture of (0.01 mol) of the dicarboxylic acid derivative (**4**) or the monocarboxylic acid (**6**) and acetic anhydride (15ml) was heated under reflux for 3 hrs (until the entire solid goes into solution). The acetic anhydride was distilled off under reduced pressure to give a colorless residue, which solidified on cooling and recrystallized from chloroform-diethyl ether 1:1 mixture.

Compound (**5**): Yield (87 %); m.p. 140°C; IR (KBr) 2943, 1748, 1710, 1594, 1551,1473, 1428, 1331, 1278, 1223 cm^{-1}. Anal. Calcd for $C_{24}H_{24}N_2O_5S_2$ (484.597) C, 59.48; H, 4.99; N, 5.78; S, 13.23. Found: C, 60.12; H, 4.67; N, 5.73; S. 13. 12.

Compound (**7**): Yield 82 %; m.p. 110- 112°C; IR (KBr) 2936, 2861, 1753, 1663, 1600, 1554, 1478, 1428. Anal. Calcd for $C_{13}H_{13}NO_3S$ (263.317) C, 59.3; H, 4.98; N, 5.32; S, 12.18. Found: C, 58.94; H, 5.35; N, 5.14; S, 11.92.

Ethyl 2-{[4-(hydroxyl-2-oxo-1,2,5,6,7,8-hexahydrobenzo [4,5] thieno [2,3-b] pyridin-3-yl)ethylidene]amino}-4,5,6, 7-tetrahydrobenzo [b]thiophene-3-carboxylate (8)

Sodium hydride 50 % dispersion in oil (4 mmol) was washed with dry toluene and suspended in 25ml dry toluene. Compound (**3**) (2 mmol) was added and the reaction mixture was refluxed for 3 hrs and cooled. Ethanol (4 ml) was added and the reaction mixture was washed with water, dried over magnesium sulfate and concentrated to give a pale yellow precipitate, which was recrystallized, from DMF. Yield (68 %), m. p. 298 °C; IR (KBr) 3503, 3480, 3026, 2984, 2856, 1675, 1659, 1598, 1575 cm^{-1}. MS m/e (rel. int.) 470(M^+, 30), 424(12), 246(10), 225(100), 179(60), 151(11). Anal. Calcd for $C_{24}H_{26}N_2O_4S_2$ (470.614) C, 61.25; H, 5.57; N, 5.95; 13.63. Found: C, 61.65; H, 5.36; N, 5.72; S, 13.86.

2-(4-Hydroxyl-2-methyl-5,6, 7,8-tetrahdrobenzo[4,5]thieno [2,3-b]pyridin-3-yl)-5,6,7, 8-tetrahydro-4H-benzo [4,5] thieno [2,3-d][1,3] oxazin-4-one (9)

METHOD (A)

Compound (**5**) (3 mmol) was refluxed in 10 ml dry pyridine for 15 minutes the formed yellow precipitate was collected by filtration, washed with diethyl ether and crystallized from chloroform. Yield (90 %), m. p. 330°C.

METHOD (B)

Compound (**5**) (2mmol) was suspended in 15 ml 3% ethanolic sodium ethoxide solution and refluxed for half an hour. The formed precipitate was collected by filtration. Yield (80 %), m.p. 328–330°C; IR (KBr) 3345, 2934, 2860, 2838, 1771, 1594, 1568, 1537 cm^{-1}; MS m/e (rel. int.) 425(M^+, 100), 391(10), 246(25), 217(30), 179(80), 151(25), 67(20). Anal.

Calcd for $C_{22}H_{20}N_2O_3S_2$ (424.545) C, 62.24; H, 4.75; N, 6.6; S, 15.11. Found: C, 62.53; H, 4.45; N, 6.82; S, 15.32.

2-(4-Acetoxy-2-methyl-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-b] pyridin-3-yl)-5,6,7,-8-tetrahydro-4H-benzo[4, 5][1,3]-oxazin-4-one (10)

Compound (**5**) (2mmol) was refluxed in xylene (10 ml) for 2 hrs. The solvent was distilled off under reduced pressure. The residue was triturated with pet. ether and recrystallized from chloroform. Yield (86 %); m. p. 190–92°C; IR (KBr) 2932, 2855, 1773, 1746, 1578, 1553, 1502, 1441, 1366 cm^{-1}. Anal. Calcd for $C_{24}H_{22}N_2O_4S_2$ (466.582) C, 61.78; H, 4.75; N, 6.01; S, 13.74. Found: C, 61.37; H, 4.62; N, 6.41; S, 14.04.

General procedure for preparation of compounds 12, 13, 14a-d

A mixture of Compound (**5**) or (**9**) (2 mmol) and the appropriate nucleophile (3 mmol) in glacial acetic acid (20 ml) was heated under reflux. A colorless precipitate was formed after 15 minutes. Reflux was continued for 1–3 hrs for complete precipitation. The formed precipitates were collected by filtration, washed with ethanol and crystallized from dimethylformamide.

N-3-[3-(Sulfanyl-1H-1,2,4-triazol-5-yl)-4,5,6,7-tetrahydrobenzo[b] thiophen-2-yl]-4-hydroxyl-2-methyl-5, 6, 7,8-tetrahydrobenzo [4,5]thieno[2,3-b]pyridin-3-carboxamide (12)

Yield (93 %); m. p. 285 °C. IR (KBr) 3371, 3288, 3201, 3034, 2931, 2856, 1670, 1594, 1563 cm^{-1}. Anal. Calcd for $C_{23}H_{23}N_5O_2S_3$ (497.668) C, 55.51; H, 4.66; N, 14.07: S, 19.33. Found: C, 55.19; H, 4.36; N, 14.25; S, 19.62.

2-Methyl-3-(10,11,12,13-tetrahydrobenzo[4,5]imidazo[1,2-c]benzo[4,5] thieno[3,2-e] pyridin-3-yl)-5, 6, 7,8-tetrahydrobenzo[4,5]thieno [2,3-b]pyridin-4-ol (13)

Yield (84%) m.p. 289°C; IR (KBr) 3226, 3032, 2924, 2849, 1634, 1517, 1447, 1410 cm^{-1}; MS, m/e (rel. int.) 496(M^+, 30), 320(20), 295(75), 291(55), 269(100), 218(60), 191(90), 129(25), 65(28). Anal. Calcd for $C_{28}H_{24}N_4S_2O$ (496.659) C, 67.71; H, 4.87; N, 11.28; S, 12.91. Found; C, 67.83; H, 4.49; N, 11.06; S, 13.34.

3-Phenyl-2-(4-hydroxyl-5,6, 7,8-tetrahydrobenzo[4,5]thieno[2,3-b] pyridin-3-yl)-3,4,5, 6,7,8-hexahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4-one (14a)

Yield (95%); m. p. 290°C; IR (KBr) 3266, 1680, 1630 cm^{-1}; MS m/e (rel. int.) 499(4), 424(90), 391(50), 298(7), 272(100), 243(28), 217(28), 179(100), 151(20), 129(80), 93(20), 67(6). Anal. Calcd for $C_{28}H_{25}N_3O_2S_2$ (499.659) C, 67.31; H, 5.04; N, 8.41; S, 12.84. Found: C, 67.58; H, 5.38; N, 8.24; S, 12.36.

3-(2-hyroxyphenyl)-2-(4-hydroxyl-5,6,7,8-tetrahydrobenzo[4,5]thieno [2,3-b]pyridin-3-yl)-3,4,5,6,7,8-hexahydrobenzo[4,5]thieno[2,3-d] pyrimidin-4-one 14b

Yield (88%) m. p. 300°C; IR (KBr) 3464, 3246, 2932, 2853, 1685, 1632, 1500 cm^{-1}. Anal. Calcd for $C_{28}H_{25}N_3O_3S_2$ (515.658) C, 65.18; H, 4.89; N, 8.15; S, 12.44. Found: C, 64.79; H, 4.93; N, 8.43; S, 12.76.

2-(4-Hydroxyl-2-methyl-5,6,7,8-tetrahydrobenzo[4,5]thieno[2,3-b] pyridin-3-yl)-3-(4H-1,2,4-triazol-3-yl)-3,4,5,6, 7,8-hexahydrobenzo [4,5]thieno[2,3-d]pyrimidin-4-one (14c)

Yield (75 %); m. p. 292°C; IR (KBr) 3285, 2935, 2882, 1685, 1619, 1553, 1498, 1424, 1377 cm^{-1}. Anal. Calcd for $C_{24}H_{22}N_6O_2S_2$ (490.612) C, 58.76; H, 4.52; N, 17.13; S, 13.07. Found: C, 58.35; H, 4.30; N, 17.55; S, 12.97.

3-(1H-Benzo[d]imidazol-2-yl)-2-(4-hydroxyl-2-methyl-5,6,7,8-[tetra]hydrobenzo [4,5] thieno[2,3-b]pyridin-3-yl)-3,4,5,6,7,8-hexahydrobenzo[4,5]thieno[2,3-d]pyrimidin-4-one (14d)

Yield (87%), m. p. 303°C; IR (KBr) 3320, 3265, 2940, 2920, 1670, 1629, 1574 cm^{-1}. Anal. Calcd for $C_{29}H_{25}N_5S_2O_2$ (539.684) C, 64.54; H, 4.67; N, 12.98; S, 11.88. Found: C, 64.36, H, 4.94; N, 13.18; S, 12.05.

3-Amino-2-(4-hydroxyl-2-methyl-5,6,7,8-tetrahydrobenzo[4,5]thieno [2,3-b]-pyridin-3-yl)-3,4,5,6,7,8-hexahydrobenzo[4,5]thieno[2,3-d] pyrimidin-4-one (11)

A mixture of compound (**5**) or compound (**9**) (2 mmol) and hydrazine hydrate (4 ml) was heated under reflux for 1 hr, cooled and poured onto cold water, filtered, washed with ethanol and recrystallized from dimethyl-

formamide. Yield (86 %); m. p. 287°C; IR (KBr) 3480, 3308, 2928, 2883, 2847, 1660, 1619, 1577, 1533 cm^{-1}. Anal. Calcd for $C_{22}H_{22}N_4O_2S_2$ (438.576) C, 60.25; H, 5.06; N, 12.78; S, 14.62. Found: C, 59.87; H, 5.38; N, 12.94; S, 14.05.

References

1. S. Ichikawa, and I. Miki, Eur. Pat. Appl. EP 503,844(Cl. CO7D451/04) Sep (1992). *C. A.* **118**: 59697r(1993).
2. F. Suzuki, K. Miwa, T. Kuroda, S. Kitamura and H. Manabe, PCT Int. Appl. WO 9312,116(Cl.CO7D495/14), Jun (1993). *C. A.* **120**: 134467n (1994).
3. S. Furuya, N. Choh, K. Kato and S. Hinuma, PCT Int. Appl. WO 96 24,597(Cl.CO7D495/04) Aug. (1996). *C. A.* **125**: 247795q (1996).
4. H. Tanka, T. Kuroita, S. Ishibuchi, H. Ushio, T. Futamura, Y. Ohashi and K. Yano, PCT Int. Appl. WO 97 03,986(Cl.CO7D487/04) Feb. (1997). *C. A.* **126**: 199585t(1997).
5. R. L. Jarvest, M. J. Parratt and H.T. Serafinowaka, PCT Int. Appl. WO 96 19,482(Cl. CO7D498/04) Jun. (1996). *C. A.* **125**: 142753 (1996).
6. B. E. Bayoumy, S. El-bahie and S. Youssif, *Pol. J. Chem.*, **65**, 1297(1991).
7. M. Ishizaki, S. Osada and T. Kobutani, Jpn. Kokai Tokkyo Koho JP 03,279,387(Cl. CO7D498/04) Dec. (1991). *C.A.* **116**: 214514h (1992).
8. R. G. Edie, R. E. Hackler and E.V. Krumkains, Eur. Pat. Appl. EP 452, 002(Cl.CO7D495/04) Oct. (1991). *C. A.* **116**: 21069h(1992).
9. T. Obata, K. Fujii, Y. Fukuda and K. Tsutsuiuchi, Jpn. Kokai Tokkyo Koho Jp,04, 164, 072(Cl. C07D239/34) Jun (1992). *C. A.* **117**: 186682 (1992).
10. A.-A. S. El-Ahl, S. S. Elmorsy, H. Soliman and F. A. Amer, *Tetrahedron lett.*, **36**, 7337(1995).
11. A. -A. S. El-Ahl, *Polish J. Chem.*, **70**, 27(1996).
12. A.- A. El-Ahl, H. Afeefy and M. A. Metwally, *J. Chemical Res.(s)*, 14(1994).