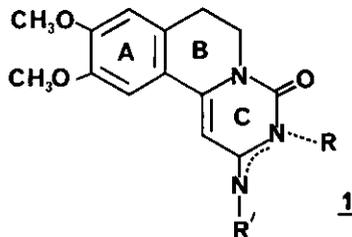


SYNTHESIS OF 2-SUBSTITUTED-6,7-DIHYDRO-4H-PYRIMIDO[6,1-a]THIENO[2,3-c]- AND [3,2-c]PYRIDIN-4-ONES

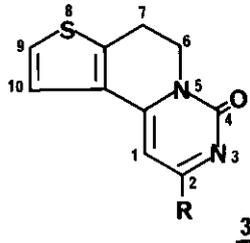
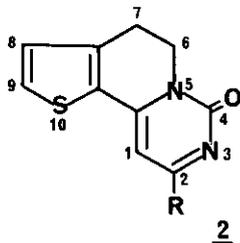
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Abstract - 1-(2-(3-Thienyl)ethyl)barbituric acid (7a) and 1-(2-(2-thienyl)ethyl)barbituric acid (7b) were cyclized to novel 2-chloro-6,7-dihydro-4H-pyrimido[6,1-a]thieno[2,3-c]-pyridin-4-one (8a) and 2-chloro-6,7-dihydro-4H-pyrimido[6,1-a]thieno[3,2-c]pyridin-4-one (8b), respectively. The chloro group in both 8a and 8b was displaced by different amines to give the corresponding amino compounds 9a and 9b.

We have described recently a series of pyrimido[6,1-a]isoquinolines¹ 1 with interesting anti-hypertensive properties. The corresponding triazino[2,1-a]isoquinolines were also reported by us².



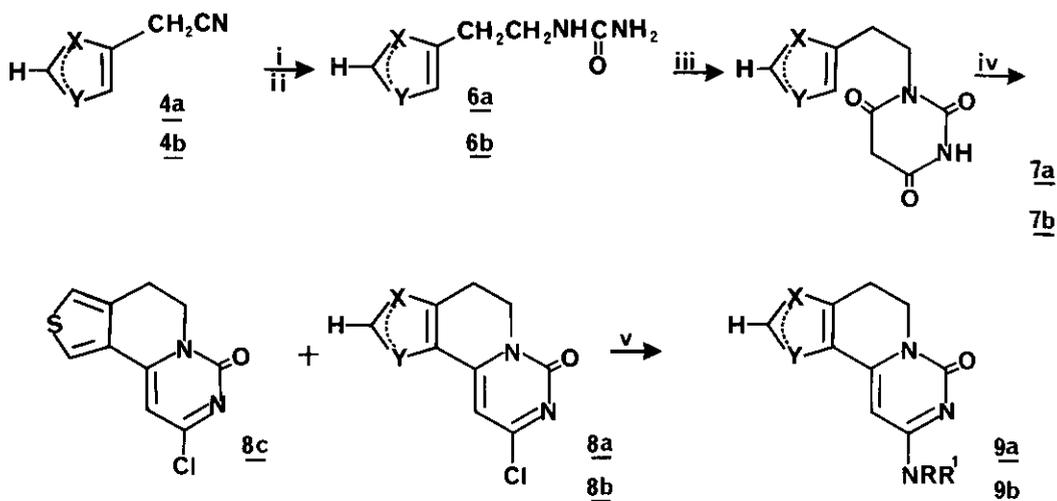
In continuation of our investigations on antihypertensive agents, we desired to study the effect of the replacement of ring A in 1 with a thiophene moiety on the biological activity. In this paper we describe the synthesis of two novel ring systems, viz. 2-substituted 6,7-dihydro-4H-pyrimido[6,1-a]thieno[2,3-c]pyridin-4-one (2) and 2-substituted 6,7-dihydro-4H-pyrimido[6,1-a]thieno[3,2-c]pyridin-4-one (3).



Cyanomethylthiophenes 4a and 4b were subjected to hydrogenation in the presence of Raney nickel catalyst and methanolic ammonia to give the corresponding thienylethylamines 5a and 5b³ (Scheme I). 5a and 5b on treatment with potassium cyanate in acetic acid gave thienylethyl ureas 6a and 6b. When compounds 6a and 6b were refluxed with diethyl malonate in the presence of sodium

ethoxide and ethanol, they generated 1-(2-(3-thienyl)ethyl)barbituric acid (7a) and 1-(2-(2-thienyl)ethyl)barbituric acid (7b), respectively.

Scheme I



a - series : X = CH; Y = S

b - series : X = S; Y = CH

Reagent : (i) H_2 , Ra-Ni, MeOH-NH₃ (ii) KCNO, AcOH.

(iii) $\text{CH}_2(\text{COOEt})_2$, NaOEt, EtOH. (iv) POCl_3 . (v) $\text{HNR}'\text{R}''$.

The strategy was to cyclize 7a and 7b through a Bischler-Napieralski reaction. It has been observed that such cyclizations proceeded well with substituted barbituric acids, provided the appropriately placed aromatic moiety is sufficiently activated^{1,5}. There was some doubt regarding the degree of activation the thiophene ring would provide.

When compounds 7a and 7b were separately treated with POCl_3 at 110°C, a temperature which has successfully been used for other cyclization reactions¹, only a black tar was obtained. Essential for the success of the reaction is the use of a very large excess of POCl_3 , and a reaction temperature of 90°C, followed by removal of excess of POCl_3 below 55°C. The yields of 2-chloro-6,7-dihydro-4H-pyrimido[6,1-a]thieno[2,3-c]pyridin-4-one (8a) and 2-chloro-6,7-dihydro-4H-pyrimido[6,1-a]thieno[3,2-c]pyridin-4-one (8b) were excellent. Compound 7a could have even generated 8c, but this was ruled out because in ¹H nmr coupling between H-8 and H-9 is 5 Hz in 8a, whereas in case of 8c it should have been between 2-3 Hz⁴ for H₈ and H₁₀. Another ambiguity which can arise in such a cyclization is regarding the position of the chloro group, which can be either at C-2 or C-4. The pattern of the ir, ¹H nmr and uv of the final compounds such as (11a, 11b) and (12a, 12b), is in accordance with that for the pyrimido[6,1-a]isoquinoline series¹, thereby indicating that the chloro is at C-2.

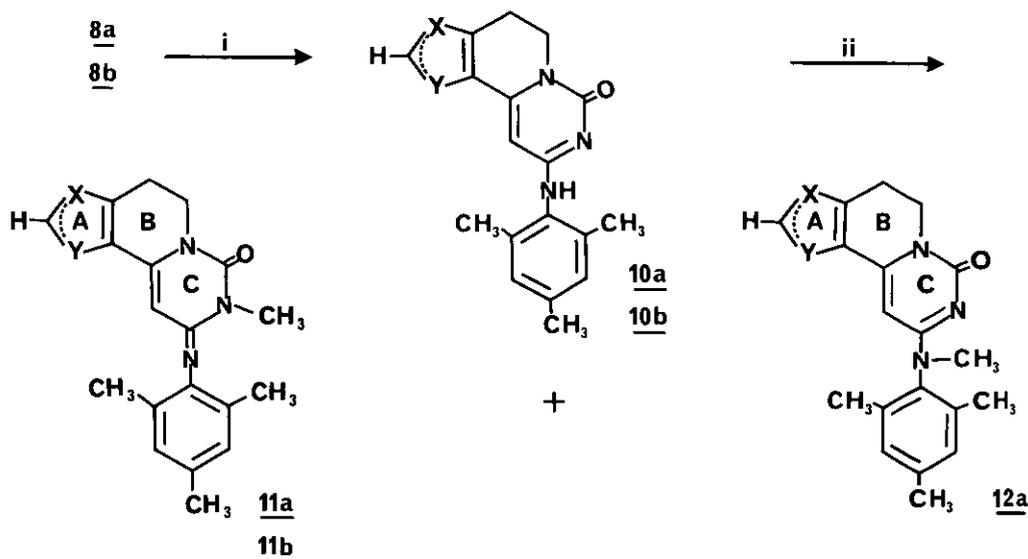
Compounds 8a and 8b on treatment with different substituted amines, generated the 2-substituted amino-6,7-dihydro-4H-pyrimido[6,1-a]thieno[2,3-c]pyridin-4-ones (9a, Table I) and the 2-substituted amino-6,7-dihydro-4H-pyrimido[6,1-a]thieno[3,2-c]pyridin-4-ones (9b, Table II).

As has been indicated at the beginning of this paper, we were trying to replace ring A in 1 by the thiophene moiety. Treatment of 8a and 8b with mesitylamine (Scheme II) gave the corresponding compounds 10a and 10b. Compound 10a was subjected to N-methylation by methyl iodide/ K_2CO_3 in acetone. It gave a mixture of the endo-isomer 2-mesitylimino-3-methyl-2,3,6,7-tetrahydro-4H-pyrimido[6,1-a]thieno[2,3-c]pyridin-4-one (11a) as the major isomer and the very minor exo-isomer 2-N-methylmesitylamino-6,7-dihydro-4H-pyrimido[6,1-a]thieno[2,3-c]pyridin-4-one (12a) as was indicated by 1H nmr, but no attempt was made to isolate the latter.

Similarly when 10b was subjected to methylation, the endo:exo ratio was found to be 16:1. The endo-isomer is 2-mesitylimino-3-methyl-2,3,6,7-tetrahydro-4H-pyrimido[6,1-a]thieno[3,2-c]pyridin-4-one (11b) and the minor exo-isomer is 2-N-methylmesitylamino-6,7-dihydro-4H-pyrimido[6,1-a]thieno[3,2-c]pyridin-4-one (12b).

The structural assignment of all the three isomers is based on our earlier observations¹. In compounds 11a and 11b, N-CH₃ appears in 1H nmr at δ 3.58 and 3.57 and the olefinic proton at δ 5.33 and 5.40, respectively, which are shifted downfield compared to the values for the corresponding protons in 12a; N-CH₃ at δ 3.33 and olefinic proton at δ 5.25, respectively. These values are in agreement with the expected electron movement in 11a and 11b, and in 12a the movement is in the reverse direction. Further support for the assignment is provided by the ir spectral data. Compounds 11a and 11b have three well-defined bands for C=O, C=N, and C=C, at 1690, 1647, and 1605 cm^{-1} , respectively and compound 12a has more overlapping bands in the same region.

Scheme II



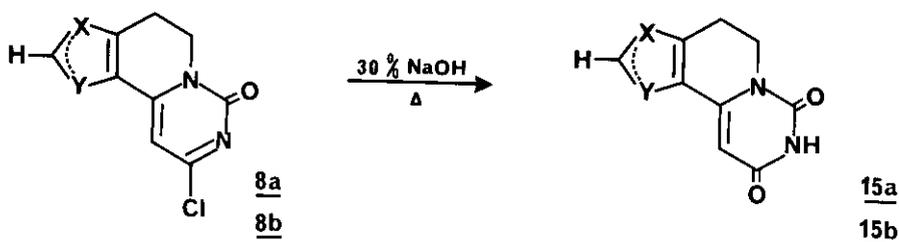
a - series : X = CH; X = CH; Y = S. b - series : X = S, Y = CH

Reagent : (i) Mesitylamine. (ii) CH_3I , K_2CO_3 , Acetone.

To complete the series we also synthesised the two basic skeletons. When compounds 8a and 8b (Scheme III) were treated with 30% aqueous NaOH, the corresponding 2,3,6,7-tetrahydro-4H-pyrimido [6,1-a]-thieno[2,3-c]pyridine-2,4-dione (15a) and 2,3,6,7-tetrahydro-4H-pyrimido[6,1-a]thieno [3,2-c]-pyridine-2,4-dione (15b) were obtained.

Compounds in both series were tested for blood pressure lowering properties in anaesthetised cats. None showed interesting activity.

Scheme III



a - series : X = CH; Y = S

b - series : X = S ; Y = CH

Table 1 : 2-Substituted 6,7-dihydro-4H-pyrimido[6,1-a]thieno[2,3-c]pyridin-4-one 9a^{a)}

Entry No.	NRR'	Salt	Yield ^{b)} (%)	mp. °C
16	Isopropylamino	HCl	71	260
17	Piperidino	HCl	37	189 - 191
18	4-Phenylpiperazino	2HCl 2H ₂ O	44	173 - 175
19	4-Chloroanilino	HCl	60	265
20	3-(Morpholino)- <u>n</u> -propylamino	2HCl 1.5H ₂ O	53	179

a) All the spectral and microanalysis data are consistent with the assigned structures.

b) Isolated yield.

Table II : 2-Substituted 6,7-dihydro-4H-pyrimido[6,1-a]thieno[3,2-c]pyridin-4-one (9b)^{a)}

Entry No.	NRR ¹	Salt	Yield ^{b)} (%)	mp, °C
21	Isopropylamino	-	52	244 - 246
22	Morpholino	-	45	258 - 260
	Morpholino	HCl	50	238 - 240
23	Isobutylamino	HCl	94	242 - 244
24	<u>t</u> -Butylamino		86	252 - 254
25	2-(3,4-Dimethoxyphenyl)-ethylamino	HCl	56	222 - 224
26	<u>N</u> -methylpiperazino	2HCl·2H ₂ O	53	250
27	2,6-Dimethylanilino	HCl	27	241 - 243
28	3,4-Dimethoxyanilino	HCl	61	216 - 218
29	Anilino	HCl	79	231 - 233
30	4-Chloroanilino	HCl	97	260
31	3,4-Dimethoxybenzyl-amino	HCl·0.5H ₂ O	58	218 - 220
32	Cyclohexylamino	HCl·H ₂ O	42	263 - 265
33	3-(Morpholino)- <u>n</u> -propyl-amino	2HCl·2H ₂ O	67	194 - 196
34	3-(Diethylamino)- <u>n</u> -propyl-amino	HCl·H ₂ O	51	146 - 148
35	<u>N</u> -Phenylpiperazino	HCl	60	264 - 266
36	2-Piperidinoethylamino	HCl·2H ₂ O	88	260

a) Isolated yield.

b) All the compounds showed satisfactory microanalyses and the ir and nmr data are in agreement with the assigned structures.

EXPERIMENTAL

Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. The ir spectra were taken with a Perkin-Elmer Model 157 spectrophotometer and peak positions are expressed in cm^{-1} . ¹H nmr spectra were obtained with a Varian T-60 spectrometer and chemical shifts are given in ppm (δ) with Me₄Si as an internal standard. Elemental analyses of all the compounds were within accepted limits.

1-(2-(3-Thienyl)ethyl)urea (6a)

A mixture of 3-(2-aminoethyl)thiophene (5a) (10.0 g, 0.083 mol), urea (40.0 g, 0.66 mol), water (160 ml), conc. aqueous HCl (2.5 ml), and acetic acid (5.0 ml) was heated at 100°C for 4 h. The reaction mixture was cooled and extracted with chloroform. The organic layer was washed with water, dried (Na₂SO₄), and evaporated under reduced pressure to a white solid, which was crystallized from benzene-hexane. Yield 12.0 g (90%), mp 122-124°C.

1-(2-(3-Thienyl)ethyl)barbituric Acid (7a)

Compound 6a (4.0 g, 0.025 mol), sodium ethoxide (2.5 g of sodium in 100 ml of ethanol, and diethyl malonate (4.6 ml) were stirred and refluxed for 20 h. Excess of solvent was removed. The residue taken up in minimum amount of water and acidified. The mixture was extracted with chloroform, the extracts washed with water and dried (Na_2SO_4), and the chloroform removed under reduced pressure. The residue was chromatographed on silica gel and the product got eluted with 5% MeOH- CH_2Cl_2 . Yield 4.5 g (80%), mp 196-198°C. Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}_3\text{S}$: C, 50.42; H, 4.22; N, 11.76; S, 13.44. Found : C, 50.12; H, 4.41; N, 12.01; S, 13.57.

2-Chloro-6,7-dihydro-4H-pyrimido[6,1-a]thieno[2,3-c]pyridin-4-one (8a)

A mixture of 7a (10.0 g, 0.042 mol) and POCl_3 (130 ml) was heated with stirring at 90°C for 12 h. Excess of POCl_3 was distilled off at 50°C under vacuum. The residue was treated with ice-cold 10% aqueous NaOH solution and the product extracted with ethyl acetate. The organic layer washed with water, dried (Na_2SO_4) and the solvent evaporated under reduced pressure. The residue was purified by passage through a silica gel column using CHCl_3 as an eluent. Yield 7.5 g (75%), mp 235-237°C. Anal. Calcd. for $\text{C}_{10}\text{H}_7\text{N}_2\text{ClOS}$: C, 50.32; H, 2.96; N, 11.74; Cl, 14.85; S, 13.36. Found : C, 50.28; H, 2.74; N, 11.38; Cl, 15.10; S, 12.94.

Ir : ν_{max} (KBr) cm^{-1} 1680 (C=O)

^1H nmr (CDCl_3) δ : 3.07 (t, 2, \underline{J} = 7 Hz, H-7); 4.3 (t, 2, \underline{J} = 7 Hz, H-6); 6.4 (s, 1, H-1); 7.0 (d, 1, $\underline{J}_{8,9}$ = 5 Hz, H-8); 7.6 (d, 1, $\underline{J}_{9,8}$ = 5 Hz, H-9).

1-(2-(2-Thienyl)urea (6b)

2-(2-Aminoethyl)thiophene (5b) (30.0 g, 0.26 mol), urea (120 g, 2.0 mol), water (250 ml), AcOH (15.0 ml) and conc. aqueous HCl (8.0 ml) were heated together and the reaction mixture worked up in a manner as described for compound 6a. Compound 6b was crystallized from benzene. Yield 32.0 g (80%), mp 87-89°C. Anal. Calcd. for $\text{C}_7\text{H}_{10}\text{N}_2\text{OS}$: C, 49.38; H, 5.92; N, 16.50; S, 18.80. Found : C, 49.18; H, 5.59; N, 16.46; S, 18.50

Ir : ν_{max} (KBr) cm^{-1} 3600-3200 (NH), 1660 (CONH)

^1H nmr (CDCl_3) δ : 2.96 (t, br, 2, \underline{J} = 6 Hz, Ar- CH_2); 3.33 (m, 2, Ar CH_2CH_2) : 4.73 (m, br 2, NH_2); 5.39 (m, br, 1, NH); 6.7-7.23 (m, 3, Ar-H).

1-(2-(2-Thienyl)ethyl)barbituric Acid (7b)

Sodium ethoxide [23.0 g, (1 mol) sodium in 300 ml of ethanol], compound 6b (32.0 g, 0.2 mol) and diethyl malonate (48.05 g, 0.03 mol) were refluxed with stirring and the reaction mixture worked up in a manner as described above for 7a. Yield 30 g (66.4%). Compound 7b crystallized from MeOH. mp 190-192°C. Anal. Calcd. for $\text{C}_{10}\text{H}_{10}\text{N}_2\text{O}_3\text{S}$: C, 50.42; H, 4.22; N, 11.76; S, 13.44. Found : 50.57; H, 3.94; N, 11.35; S, 13.13.

Ir : ν_{max} cm^{-1} 3200 (NH) 1724 (-N-CO-) 1695 (-N-CO).

^1H nmr ($\text{DMSO}-d_6$) δ : 3.00 (t, 2, \underline{J} = 8 Hz, Ar- CH_2); 3.63 (s, br, 2, H-5), 3.93 (t, 2, \underline{J} = 8 Hz, Ar- $\text{CH}_2\text{-CH}_2\text{-N}$). 6.36-7.37 (m, 3, Ar-H).

2-Chloro-6,7-dihydro-4H-pyrimido[6,1-a]thieno[3,2-c]pyridin-4-one (8b)

A mixture of 7b (1.0 g, 0.004 mol) and POCl₃ (10.0 ml) was heated gradually in an oil bath to 90°C and maintained there for 3 h. Excess of POCl₃ was removed at 60–65°C under vacuum, and the residue worked up as described for 8a. Yield 600 mg (60%). mp 232–234°C.

Ir (KBr) ν_{\max} cm⁻¹ 1670 (C=O).

¹H nmr (CDCl₃ + 2 drops DMSO-d₆) δ : 3.2 (t, 2, J = 7 Hz, 6-H); 4.3 (t, 2, J = 7 Hz, 7-H), 6.5 (s, 1, H-1); 7.23 (s, 2, Ar-H).

2,3,6,7-Tetrahydro-4H-pyrimido[6,1-a]thieno[2,3-c]pyridine-2,4-dione (15a)

2-Chloro-6,7-dihydro-2H-pyrimido[6,1-a]thieno[2,3-c]pyridin-2-one 8a (200 mg, 0.8 mmol) was stirred with 5 ml of 30% aqueous NaOH till all the solid went into the solution. The product was precipitated on acidifying with 3 N aqueous HCl. The compound was filtered and dried. Yield 130 mg (77%) mp 260°C. Anal. Calcd. C₁₀H₈N₂O₂S: C, 54.52; H, 3.66; N, 12.72; S, 14.54.

Found: C, 54.13; H, 3.57; N, 12.83; S, 14.05

Ir ν_{\max} (KBr) cm⁻¹: 1739–1666 (–CONHCO–).

¹H nmr (DMSO-d₆) δ : 3.00 (t, 2, J = 7 Hz, H-7); 4.03 (t, 2, J = 7 Hz, H-6); 5.67 (s, 1, H-1); 7.13 (d, 1, J = 4 Hz, H-8); 7.83 (d, 1, J = 4 Hz, H-9). 11.16 (bump, 1, N-H).

2,3,6,7-Tetrahydro-4H-pyrimido[6,1-a]thieno 3,2-c pyridine-2,4-dione (15b)

Compound 8b (2.5 g, 0.011 mol) in 20% aqueous NaOH (150 ml) was refluxed with stirring for 0.5 h. The solution was cooled, filtered, and acidified with dil. aqueous HCl to give a solid. The solid was filtered and crystallised from DMF. Yield 1.8 g (78%) mp 270°C. Anal. Calcd. for C₁₀H₈N₂O₂S: C, 54.52; H, 3.66; N, 12.72; S, 14.53. Found: C, 54.30; H, 3.73; N, 12.90; S, 14.84.

Ir ν_{\max} (KBr) cm⁻¹: 3400 (NH); 1700 (C=O), 1680 (C=O).

¹H nmr (DMSO-d₆) δ : 3.13 (t, 2, J = 7 Hz, H-7), 4.6 (t, 2, J = 7 Hz, H-6); 6.03 (s, 1, H-1), 7.55 (s, 2, Ar-H), 12.93 (b, s, 1H, N-H).

General Procedure for the Preparation of 2-Substituted amino-6,7-dihydro-4H-pyrimido[6,1-a]-thieno[2,3-c]- or -[3,2-c]pyridin-4-one

2-Chloro compounds 8a and 8b were treated with excess of amines in chloroform or DMF and the mixture heated overnight. The completion of the reaction was monitored through tlc on silica plates. Excess of solvent was removed, the unreacted amines were either removed by distillation or by column chromatography. The products were isolated and mostly converted into their hydrochlorides.

2-Mesitylamino-6,7-dihydro-4H-pyrimido[6,1-a]thieno[2,3-c]pyridin-4-one (10a)

Chloro compound 8a (800 mg, 0.0032 mol), mesitylamine (1.0 ml, 0.007 mol), and DMF (10 ml) were heated at 100°C with stirring overnight. DMF was removed under vacuum and the residue treated with cold 10% aqueous NaOH and the product extracted with ethyl acetate. The organic layer was washed with water and dried (Na_2SO_4) and the solvent removed under reduced pressure. The product was chromatographed over silica gel using 3% MeOH- CHCl_3 as the eluent. Evaporation of the eluate gave the pure compound, which was crystallized in chloroform:benzene. Yield 800 mg (70.7%), mp 180-182°C.

Ir ν_{max} (KBr) cm^{-1} : 1680 (C=O), 1620 (C=N).

^1H nmr (CDCl_3) δ : 2.23 (s, 6, 2', 6'- CH_3); 2.3 (s, 3, 4'- CH_3); 2.9 (t, 2, \underline{J} = 7 Hz, H-7); 4.2 (t, 2, \underline{J} = 7 Hz, H-6); 5.4 (s, 1, H-1), 6.4 - 7.4 (m, 4, Ar-H).

The compound was converted into the hydrochloride, mp 248-250°C.

Anal. Calcd. for $\text{C}_{19}\text{H}_{19}\text{N}_3\text{OS HCl}$: C, 61.04; H, 5.35; N, 11.24; Cl, 9.48; S, 8.56.

Found : C, 60.98; H, 5.40; N, 11.61; Cl, 9.87; S, 8.29.

2-Mesitylamino-6,7-dihydro-4H-pyrimido[6,1-a]thieno[3,2-c]pyridin-4-one (10b)

A solution of 500 mg (0.002 mol) of 8b and mesitylamine (1 ml, 0.007 mol) in dry chloroform (50 ml) was refluxed for 8 h. Excess of the solvent was removed under reduced pressure and the residue worked up as described for 10a. Yield 440 mg (62%) mp 260°C.

Ir ν_{max} (KBr) cm^{-1} : 1644 (C=O)

^1H nmr (CDCl_3) δ : 2.2 (s, 6, 2', 6'- CH_3); 2.33 (s, 3, 4'- CH_3); 3.06 (t, 2, \underline{J} = 7 Hz, H-7), 4.23 (t, 2, \underline{J} = 7 Hz, H-6); 5.3 (s, 1, H-1); 6.73-7.16 (m, 4, Ar-H).

The compound was converted into its hydrochloride salt, mp 250°C. Anal. Calcd. for $\text{C}_{19}\text{H}_{19}\text{N}_3\text{OS}\cdot\text{HCl}\cdot 0.5\text{H}_2\text{O}$: C, 59.29; H, 5.46; N, 10.92; S, 8.32; Cl, 9.23. Found C, 59.26; H, 5.65; N, 10.72; S, 8.74; Cl, 9.58.

2-Mesitylimino-3-methyl-2,3,6,7-tetrahydro-4H-pyrimido[6,1-a]thieno[2,3-c]pyridin-4-one (11a)

To a solution of compound 10a (200 mg, 0.60 mmol) in acetone (10 ml) were added methyl iodide (1 ml) and K_2CO_3 (1.0 g). The reaction mixture was refluxed with stirring for 3 h. K_2CO_3 was filtered off and the excess of solvent was distilled off under reduced pressure. The residue was subjected to crystallization using CH_2Cl_2 as the solvent. A bright yellow solid was obtained. Yield 160 mg (77%), mp 207-209°C.

Ir ν_{max} (KBr) cm^{-1} : 1695 (C=O), 1661 (C=N), 1613 (C=C).

^1H nmr (CDCl_3) δ : 2.00 (s, 6, 2', 6'- CH_3); 2.27 (s, 3, 4'- CH_3); 2.93 (t, 2, \underline{J} = 6 Hz, H-7); 3.59 (s, 3, N- CH_3); 4.13 (t, 2, \underline{J} = 6 Hz, H-6); 5.33 (s, 1, H-1); 6.83 (m, 3, 3', 5', 8-Ar-H); 7.26 (d, 1, \underline{J} = 4 Hz, H-9).

The above compound was converted into its hydrochloride salt, mp 216-218°C. Anal. Calcd. for $\text{C}_{20}\text{H}_{21}\text{N}_3\text{OS HCl}$: C, 61.93; H, 5.68; N, 10.80; Cl, 9.16; S, 8.25. Found : C, 61.58; H, 5.32; N, 11.13; Cl, 9.49; S, 8.14.

The mother liquor, obtained by the crystallization of the crude base, showed the presence of a minor amount of the other isomer 12a as was detected by tlc and ^1H nmr, but no attempt was made to isolate it.

2-Mesitylimino-3-methyl-2,3,6,7-tetrahydro-4H-pyrimido[6,1-a]thieno[3,2-c]pyridin-4-one (11b)

Compound 10b (1.0 g, 0.30 mmol), K_2CO_3 (1.0 g), methyl iodide (4.0 ml), and acetone (20.0 ml) were refluxed with stirring for 3 h. K_2CO_3 was filtered off and the solvent evaporated under reduced pressure. The residue indicated on tlc to be the mixture of two compounds. The crude product was subjected to column chromatography on silica gel and benzene as eluent to give compound 11b (780 mg, 79%), mp 176-178°C.

Ir ν_{max} (KBr) cm^{-1} : 1689 (C=O), 1647 (C=N), 1605 (C=C).

^1H nmr (CDCl_3) δ : 2.3 (s, 6, 2',6'- CH_3), 2.26 (s, 3, 4'- CH_3); 3.06 (t, 2, \underline{J} = 6 Hz, H-7); 3.57 (s, 3, N- CH_3); 4.2 (t, 2, \underline{J} = 6 Hz, H-6); 5.4 (s, 1, H-1); 6.83 (s, 2, 3', 5'-Ar-H); 6.68 (d, 1, \underline{J} = 8 Hz, H-9); 7.16 (d, 1, \underline{J} = 8 Hz, H-10). Compound 11b was converted into its hydrochloride, mp 202-204°C.

Ir ν_{max} (KBr) cm^{-1} : 1740 (C=O).

Anal. Calcd. for $\text{C}_{20}\text{H}_{21}\text{N}_3\text{OS HCl}$: C, 61.93; H, 5.68; N, 10.80; Cl, 9.16; S, 8.25.

Found : C, 61.60; H, 5.79; N, 10.62; Cl, 9.54; S, 8.47.

Another component (12b) was eluted with benzene:chloroform. Yield 50 mg (5.0%). mp 260°C.

Anal. Calcd. for $\text{C}_{20}\text{H}_{21}\text{N}_3\text{OS}$: C, 68.38; H, 6.00; N, 12.00; S, 9.12.

Found : C, 68.11; H, 5.99; N, 12.25; S, 8.58.

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