Synthesis of Some New Thieno[2,3-*b*][1,6]naphthyridines and Related Compounds

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3,5-Dibenzylidene-1-isopropyl-4-piperidinone (**1**) reacts with cyanothioacetamide to give 1,6-naphthyridine-2(1*H*) thione derivative **2**. Reaction of **2** with halo ketones or halo esters followed by ring closure gives thieno[2,3-*b*][1,6]naphthyridine derivatives **5a**—**i**, which are used as versatile intermediates in the synthesis of related heterocyclic ring systems as pyrimidothienonaphthyridines **10**, **11**, **14**, and **15**, oxazinothienonaphthyridine (**13**) and triazinothienonaphthyridine (**9**).

Various derivatives of thienopyridines and thienopyrimidines have been investigated in relation with their pharmacological activities. They proved to possess analgesic and antiinflammatory properties and showed activity against diabetus millilus.[1,2] Also they act as platelet aggregation inhibitors and as anticonvulsants.[3,4]

Keeping the foregoing results in mind, and in continuation to our interest in the use of activated nitriles in the heterocyclic synthesis,[5—7] we envisaged the synthesis of the hetherito title compounds and other related heterocycles.

The reaction of 3,5-dibenzylidene-1-isopropyl-4-piperidinone[8] (**1**) with cyanothioacetamide in the presence of sodium methoxide gave the naphthyridine derivative namely 8-benzylidene-3-cyano-6-isopropyl-4-phenyl-5,6,7,8-tetrahydro[1,6]naphthyridine-2(1*H*) thione (**2**). S-Alkylation of **2** could be achieved either by cyanoethylation using acrylonitrile to give **3e** or by alkylation using different halides such as methyl iodide, chloroacetic acid, 2-bromomethyl propionate or diethylbromomalonate to give **3a**—**d** respectively. Another series of S-alkylated naphthyridines **4a**—**i** containing active methylene group attached to the S atom, could be obtained via the interaction of **2** with halo ketones, halo esters, halo amides or halo nitrile (cf. Scheme 1). Internal cycloaddition reaction leading to ring closure of **4a**—**i** in ethanol using sodium ethoxide as a catalyst gave the thieno[2,3-*b*]naphthyridines **5a**—**i**. The IR spectra of all cyclized products revealed the disappearance of band due to the cyano group and the appearance of bands due to the amino group.

On the other hand, when **4d** was allowed to interact with hydrazine hydrate the product was the hydrazide **6**. This upon the condensation with aromatic aldehydes gave the *N'*-arylmethylene hydrazides **7a**—**e** which were in turn ring closed into the thienonaphthyridines **8a**—**c** (Scheme 1).

The triazino derivative **9** was obtained when **5e** was treated with nitrous acid, while the pyrimidino derivative **10** was resulted by heating **5f** in boiling acetic anhydride (Chart 1). However, the other pyrimidino derivative **11** was the product of the reaction of **5i** with carbon disulfide in pyridine.

The alkaline hydrolysis of the amino ester **5d** using ethanolic sodium hydroxide gave the corresponding amino acid **12** which gave the oxazino derivative **13** when heated in boiling acetic anhydride. The interaction of **13** with ammonia, hydrazine hydrate or phenylhydrazine gave the corresponding pyrimidino derivatives **14a**—**c**. The arylmethylene amino derivatives **15a**—**c** were obtained when **14a** was interacted with aromatic aldehydes (Scheme 2).

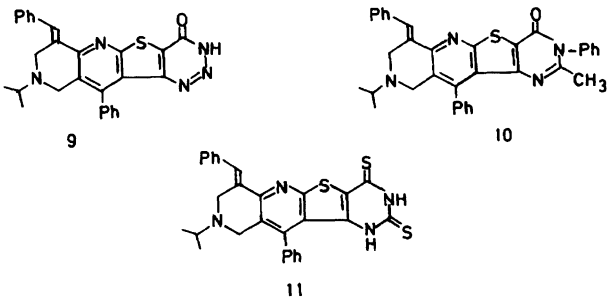


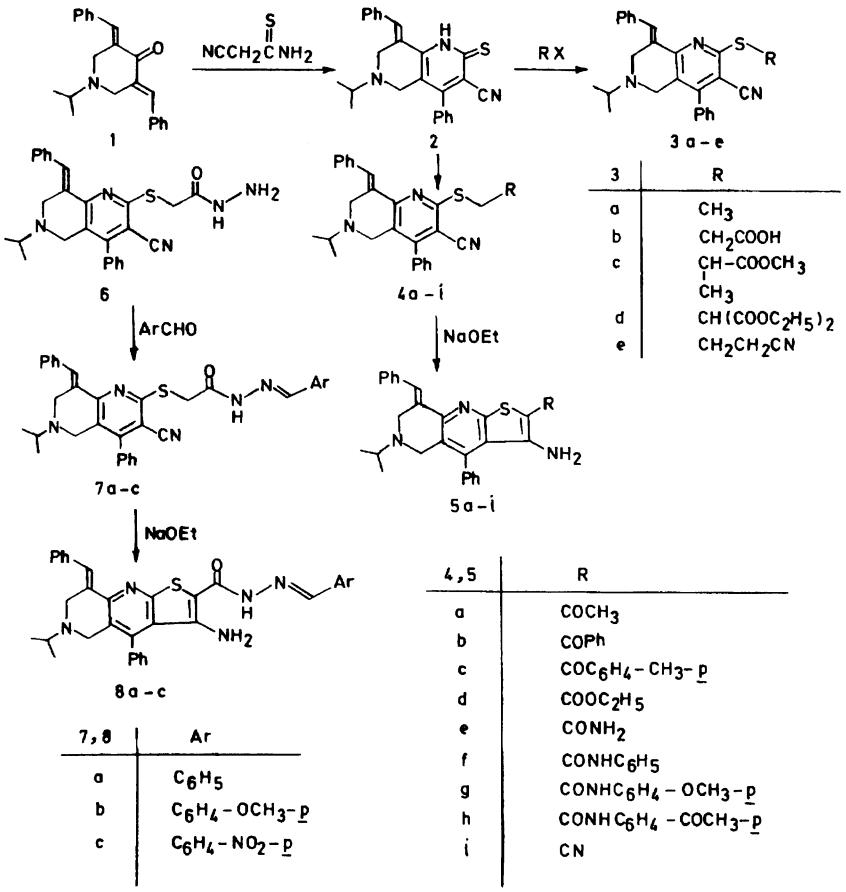
Chart 1.

The 1-pyrrolyl ester **16** was obtained when the amino ester **5d** was treated with 2,5-dimethoxytetrahydrofuran in boiling acetic acid.[9,10] The ester function of **16** could be transformed into a hydrazide function **17** which was condensed with aromatic aldehydes to give **18a**—**c** (Scheme 3). Similarly, the amino group of the amino ketone **5a** was transformed into a 1-pyrrolyl group **19**. The latter compound gave the phenylhydrazone **20** and the chalcone **21** upon treatment with phenylhydrazine in ethanol and benzaldehyde in ethanolic sodium hydroxide, respectively. The interaction of the chalcone **21** with phenylhydrazine gave the pyrazolyl derivative **22** (Scheme 4).

Experimental

Melting points were obtained on a Gallen Kamp apparatus and are uncorrected. IR spectra were recorded on a Pye-Unicam SP-3-100 spectrophotometer using KBr discs. ^{1}H NMR spectra were obtained with a Varian EM 390 90 MHz NMR spectrometer, using TMS as an internal standard. Microanalyses were determined using Perkin Elmer 240 C Microanalyzer.

8-Benzylidene-3-cyano-6-isopropyl-4-phenyl-5,6,7,8-tetrahydro[1,6]naphthyridine-2(1*H*)thione (2): A mixture of dibenzylidene derivative **1** (0.01 mol) and cyanothioacetamide (0.01 mol) in methanolic sodium methoxide

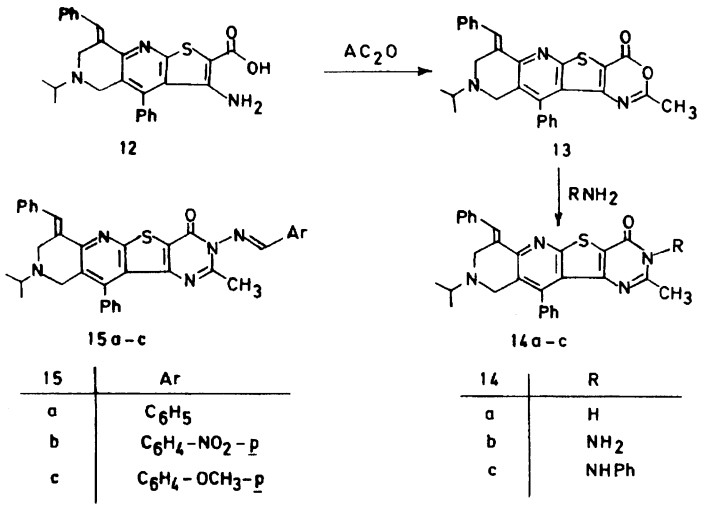


3	R
a	CH_3
b	CH_2COOH
c	$CH(CH_3)-COOCH_3$
d	$CH(COOC_2H_5)_2$
e	CH_2CH_2CN

7,8	Ar
a	C_6H_5
b	$C_6H_4-OCH_3-p$
c	$C_6H_4-NO_2-p$

4,5	R
a	$COCH_3$
b	$COPh$
c	$COC_6H_4-CH_3-p$
d	$COOC_2H_5$
e	$CONH_2$
f	$CONHC_6H_5$
g	$CONHC_6H_4-OCH_3-p$
h	$CONHC_6H_4-COCH_3-p$
i	CN

Scheme 1.



15	Ar
a	C_6H_5
b	$C_6H_4-NO_2-p$
c	$C_6H_4-OCH_3-p$

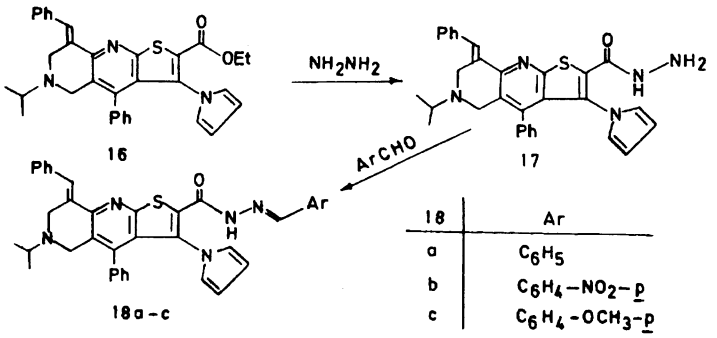
14	R
a	H
b	NH_2
c	NHPh

Scheme 2.

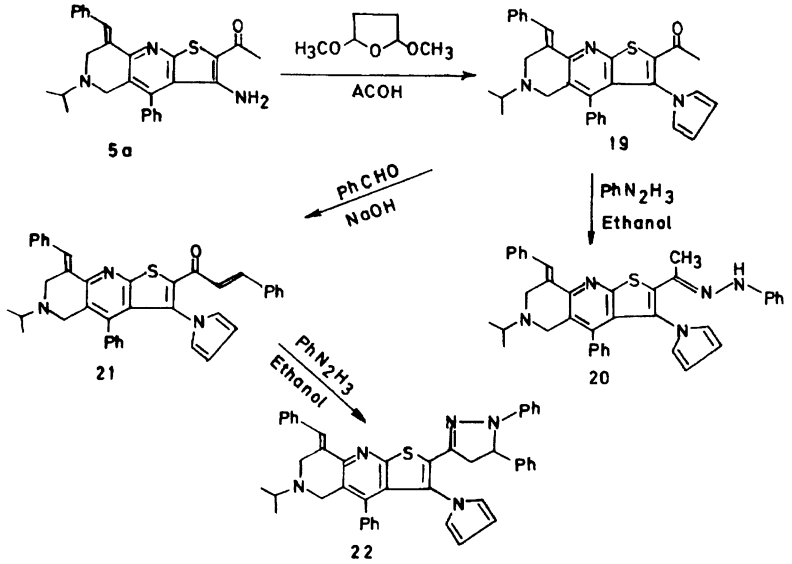
(0.25 g Na in 50 ml methanol) was heated at 50 °C for 8 h. The reaction mixture was concentrated to half of its volume, poured on 100 ml of water and acidified with dilute hydrochloric acid. The solid product which separated was collected, dissolved in 100 ml absolute ethanol and refluxed for 30 min. The crystals which separated from the hot solution were filtered off and recrystallized from the proper solvent (Table 1).

Reaction of 2 with α-Halo Acids, α-Halo Esters, and α-Halo Ketones Formation of 3a—d and 4a—i: General Procedure: A mixture of **2** (0.01 mol) and α-halo acid, α-halo esters or α-halo ketones (0.01 mol) in ethanol (50 ml) was refluxed for 1 h in the presence of anhydrous sodium acetate (5 g). The crystals which separated from the cold solution were filtered off and recrystallized from the proper solvent. The results are summarized in Table 1.

8-Benzylidene-3-cyano-2-(2-cyanoethylthio)-6-isopropyl-4-phenyl-5,6,7,8-tetrahydro[1,6]naphthyridine



Scheme 3.



Scheme 4.

(3e): A mixture of **2** (0.01 mol) and acrylonitrile (0.012 mol) in ethanol (50 ml) was refluxed for 2 h in the presence of few drops of triethylamine. The solid product separated from the cold solution was filtered off and recrystallized from the proper solvent.

2- Substituted- 3- amino- 8- benzylidene- 6- isopropyl- 4- phenyl- 5, 6, 7, 8- tetrahydrothieno[2, 3- *b*][1, 6]- naphthyridine (5a—i): General Procedure: To a stirred suspension of compounds **4a—i** (0.01 mol) in absolute ethanol (50 ml), a few drops of ethanolic sodium ethoxide were added. The stirring was continued for 15 min and then the reaction mixture was refluxed for another 15 min. The separated solid product was filtered off, recrystallized and identified, cf. Table 1.

8-Benzylidene-3-cyano-2-(hydrazinocarbonylmethylthio)-6-isorpropyl-4-phenyl-5,6,7,8-tetrahydro[1,6]- naphthyridine (6): A mixture of the ester derivative **4d** (0.01 mol) and hydrazine hydrate (0.01 mol) in ethanol (50 ml) was refluxed for 1 h. The separated solid product from the hot solution was filtered off and recrystallized from the proper solvent.

2- [*N'*- (Arylmethylene)hydrazinocarbonylmethylthio]-8-benzylidene-3-cyano-6-isopropyl-4-phenyl-5, 6,7,8-tetrahydro[1,6]naphthyridines (7a—c): A mixture of the hydrazide derivative **6** (0.01 mol) and aromatic aldehyde (0.01 mol) in ethanol (50 ml) in presence of catalytic amount of piperidine was refluxed for 30 min. The reaction mixture was concentrated to one half of its volume, then cooled, the solid crystals were collected by filtration and recrystallized from the proper solvent, cf. Table 2.

3- Amino- *N'*- arylmethylene- 8- benzylidene- 6- isopropyl-4-phenyl-5,6,7,8-tetrahydrothieno[2,3-*b*][1,6]- naphthyridine-2-carbohydrazides (8a—c): These compounds were prepared following an analogous procedure to that of compounds **5a—i**. The physical and spectral data of compounds **8a—c** are summarized in Table 2.

7- Benzylidene- 9- isopropyl- II- phenyl- 7, 8, 9, 10- tetrahydro[1,2,3]triazino[4',5' : 4,5]thieno[2,3-*b*][1,6]- naphthyridin-4(3*H*)-one (9): To a stirred solution of **5e** (0.01 mol) in hydrochloric acid (20 ml) cooled at 5 °C, a solution of sodium nitrite (2 g in 10 ml H_20) was added dropwise for a period of 30 min. The stirring was continued for another 30 min without cooling. The fine precipitate was filtered off washed several times with water and recrystallized from the proper solvent.

7-Benzylidene-3,11-diphenyl-9-isopropyl-2-methyl-7,8,9,10-tetrahydropyrimido[4',5' : 4,5]thieno[2,3-*b*][1,6]naphthyridin-4(3*H*)-one (10): A mixture of **5f** (0.01 mol) in acetic anhydride (20 ml) was refluxed for 5 h. The solvent was removed under reduced pressure and the brown residue was poured into ice/water mixture. The reaction mixture was stirred and the precipitated solid was

Table 1. Physical and Spectral Data of Compounds **2**—**5a**—**5i**

Compound No.	Mp/°C (Solvent)	Yield/% (Color)	Molecular formula[a] (MW)	IR	^{1}H NMR
2	180 (Acetic acid)	85 (Orange)	$C_{25}H_{23}N_3S$ (397.5)	3380 (NH), 2200 (CN)	$(CD_3)_2SO$: 0.8 (d, 6H, $2CH_3$), 2.4 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 6.9—7.6 (m, 10H, arom), 7.9 (s, 1H, CH).
3a	138 (Ethanol)	76 (White)	$C_{26}H_{25}N_3S$ (411.6)	2220 (CN)	
3b	198 (Ethanol)	64 (Pale yellow)	$C_{27}H_{25}N_3O_2S$ (455.6)	2200 (CN), 1680 (CO)	
3c	168 (Ethanol)	76 (Yellow)	$C_{29}H_{29}N_3O_2S$ (483.6)	2200 (CN), 1710 (CO)	($CDCl_3$) : 1.1 (d, 6H, $2CH_3$), 1.6 (d, 3H, CH_3), 2.8 (m, 1H, CH), 3.6, 3.8(2s, 4H, $2CH_2$), 4.0 (s, 3H, CH_3), 4.4 (m, 1H, CH), 7.3—7.8 (m, 10H, arom), 8.2 (s, 1H, CH).
3d	188 (Ethanol)	71 (Yellow)	$C_{32}H_{33}N_3O_4S$ (555.7)	2220 (CN), 1700 (CO)	($CDCl_3$): 0.9 (d, 6H, $2CH_3$), 1.3 (t, 6H, $2CH_3$), 2.8 (m, 1H, CH), 3.5, 3.8 (2s, 4H, $2CH_2$), 4.1 (q, 4H, $2CH_2$), 5.6 (s, 1H, CH), 7.3—7.6 (m, 10H, arom), 8.2 (s, 1H, CH).
3e	169 (Ethanol)	62 (Pale yellow)	$C_{28}H_{26}N_4S$ (450.6)	2220 (br. 2CN)	($CDCl_3$): 1.1 (d, 6H, $2CH_3$), 2.8 (m, 1H, CH), 3.1, 3.4 (2t, 4H, $2CH_2$), 3.9 (s, 4H, $2CH_2$), 7.2—7.8 (10H, arom), 8.1 (s, 1H, CH).
4a	133 (Ethanol)	74 (White)	$C_{28}H_{27}N_3OS$ (453.6)	2200 (CN), 1690 (CO)	
4b	192 (Ethanol)	70 (Buff)	$C_{33}H_{29}N_3OS$ (515.7)	2220 (CN), 1680 (CO)	$(CD_3)_2SO$: 0.8 (d, 6H, $2CH_3$), 2.7 (m, 1H, CH), 3.5, 3.7 (2s, 4H, $2CH_2$), 5.0 (s, 2H, CH_2), 7—7.9 (m, 15H, arom), 8.1 (s, 1H, CH).
4c	181 (Ethanol)	68 (Buff)	$C_{34}H_{31}N_3OS$ (529.7)	2220 (CN), 1690 (CO)	$(CD_3)_2SO$: 0.9 (d, 6H, $2CH_3$), 2.2 (s, 3H, CH_3), 2.7 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 4.9 (s, 2H, CH_2), 6.9—7.9 (m, 14H, arom), 8.2 (s, 1H, CH).
4d	102 (Ethanol)	86 (Buff)	$C_{29}H_{29}N_3O_2S$ (483.6)	2220 (CN), 1720 (CO)	$(CD_3)_2SO$: 0.9 (d, 6H, $2CH_3$), 1.1 (t, 3H, CH_3), 2.7 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 3.9 (q, 2H, CH_2), 4.1 (s, 2H, CH_2), 7.1—7.9 (m, 10H, arom), 8.1 (s, 1H, CH).
4e	180 (Ethanol)	72 (Pale yellow)	$C_{27}H_{26}N_4OS$ (454.6)	3320, 3260 (NH_2), 2200 (CN), 1670 (CO)	
4f	154 (Ethanol)	65 (Pale yellow)	$C_{33}H_{30}N_4OS$ (530.7)	3340 (NH), 2200 (CN), 1670 (CO)	$(CD_3)_2SO$: 0.9 (d, 6H, $2CH_3$), 2.6 (m, 1H, CH), 3.5, 3.7 (2s, 4H, $2CH_2$), 4.2 (s, 2H, CH_2), 6.8—7.6 (m, 15H, arom), 7.9 (s, 1H, CH), 9.1 (s, 1H, NH).
4g	178 (Ethanol)	74 (Pale yellow)	$C_{34}H_{32}N_4O_2S$ (560.7)	3380 (NH), 2220 (CN), 1670 (CO)	
4h	182 (Ethanol)	76 (Pale yellow)	$C_{35}H_{32}N_4O_2S$ (572.7)	3360 (NH), 2220 (CN), 1690, 1660 (CO)	($CDCl_3$): 1.1 (d, 6H, $2CH_3$), 2.5 (s, 3H, CH_3), 2.7 (m, 1H, CH), 3.6, 3.8 (2s, 4H, $2CH_2$), 4.2 (s, 2H, CH_2), 7.2—8 (m, 14H, arom), 8.2 (s, 1H, CH), 9.2 (s, 1H, NH).
4i	149 (Ethanol)	75 (Buff)	$C_{27}H_{24}N_4S$ (436.6)	2220 (br. 2CN)	

filtered off, washed several times with water and recrystallized from the proper solvent.

7- Benzylidene- 9- isopropyl- 11- phenyl- 7, 8, 9, 10- tetrahydropyrimido[4′, 5′ : 4,5]thieno[1,6]naphthyridin-2,4(1*H*,3*H*)dithione (11): A mixture of **5i** (0.01 mol) and carbon disulfide (3 ml) in pyridine (20 ml) was heated on a water bath for 24 h. The solid product which separated from the cold solution was filtered off washed several times with ethanol and recrystallized from the proper solvent (Table 2).

3-Amino-8-benzylidene-6-isopropyl-4-phenyl-5,6,7, 8-tetrahydrothieno[2,3-*b*][1,6]naphthyridin-2-carboxylic Acid (12): A mixture of the ester derivative **5f** (0.01 mol) in ethanolic sodium hydroxide (50 ml, 10%) was

Table 1. (Continued)

Compound No.	Mp/°C (Solvent)	Yield/% (Color)	Molecular formula[a] (MW)	IR	^{1}H NMR
5a	175 (Ethanol)	75 (Orange)	$C_{28}H_{27}N_3OS$ (453.6)	3420, 3340 (NH_2), 1670 (CO)	$(CD_3)_2SO$: 0.9 (d, 6H, $2CH_3$), 2.3 (s, 3H, CH_3), 2.6 (m, 1H, CH), 3.6, 3.8 (2s, 4H, $2CH_2$), 6.2 (s, 2H, NH_2), 6.9—7.4 (m, 10H, arom), 8.2 (s, 1H, CH).
5b	203 (Ethanol)	72 (Yellow)	$C_{33}H_{29}N_3OS$ (515.7)	3460, 3340 (NH_2), 1680 (CO)	$(CD_3)_2SO$: 0.8 (d, 6H, $2CH_3$), 2.6 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 6.3 (s, 2H, NH_2), 7.1—7.8 (m, 15H, arom), 8.1 (s, 1H, CH).
5c	208 (Ethanol)	76 (Yellow)	$C_{34}H_{31}N_3OS$ (529.7)	3480, 3360 (NH_2), 1680 (CO)	$(CD_3)_2SO$: 0.7 (d, 6H, $2CH_3$), 2.2 (s, 3H, CH_3), 2.6 (m, 1H, CH), 3.3, 3.6 (2s, 4H, $2CH_2$), 6.4 (s, 2H, NH_2), 7.0—7.7 (m, 14H, arom), 7.9 (s, 1H, CH).
5d	240 (Ethanol)	77 (Yellow)	$C_{29}H_{29}N_3O_2S$ (483.6)	3460, 3340 (NH_2), 1670 (CO)	
5e	286 (Acetic acid)	72 (Yellow)	$C_{27}H_{26}N_4OS$ (454.6)	3480, 3360, 3320 ($2NH_2$), 1660 (CO)	$(CD_3)_2SO$: 0.8 (d, 6H, $2CH_3$), 2.6 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 5.2 (s, 2H, NH_2), 6.4 (s, 2H, NH_2), 7.1—7.8 (m, 10H, arom), 8.1 (s, 1H, CH).
5f	232 (Acetic acid)	62 (Yellow)	$C_{33}H_{30}N_4OS$ (530.7)	3460, 3340 (NH_2), 3280 (NH), 1650 (CO)	$(CD_3)_2SO$: 0.8 (d, 6H, $2CH_3$), 2.6 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 5.6 (s, 2H, NH_2), 7.1—7.9 (m, 15H, arom), 8.0 (s, 1H, CH), 9.3 (s, 1H, NH).
5g	210 (Dioxan)	74 (Yellow)	$C_{34}H_{32}N_4O_2S$ (560.7)	3460, 3320 (NH_2), 3280 (NH), 1660 (CO)	
5h	221 (Ethanol)	74 (Orange)	$C_{35}H_{32}N_4O_2S$ (572.7)	3480, 3360 (NH_2), 3300 (NH), 1660 (CO)	$(CDCl_3)$: 1.0 (d, 6H, $2CH_3$), 2.4 (s, 3H, CH_3), 2.7 (m, 1H, CH), 3.5, 3.8 (2s, 4H, $2CH_2$), 5.7 (s, 2H, NH_2), 7.2—7.9 (m, 14H, arom), 8.2 (s, 1H, CH), 9.3 (s, 1H, NH).
5i	209 (Ethanol)	86 (Yellow)	$C_{27}H_{24}N_4S$ (436.6)	3440, 3320 (NH_2), 2200 (CN)	$(CD_3)_2SO$: 0.8 (d, 6H, $2CH_3$), 2.5 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 5.8 (s, 2H, NH_2), 7.0—7.8 (m, 10H, arom), 8.0 (s, 1H, CH).

a) Statisfactory microanalyses obtained: C±0.23, H±0.21, N±0.24, S±0.29.

refluxed for 2 h. During this period of time yellow crystals of sodium salt were separated, filtered off, dissolved in water (100 ml) and acidified with dilute hydrochloric acid. The fine crystals of the carboxylic acid derivative were filtered off and recrystallized from the proper solvent.

7-Benzylidene-9-isopropyl-2-methyl-11-phenyl-7,8,9,10-tetrahydro-4*H*-[1,3]oxazino[4′,5′ : 4,5]thieno[2,3-*b*][1,6]naphthyridin-4-one (13): This compound was prepared following a procedure similar to that of compound **10**. The physical and spectral data of compound **13** are summarized in Table 2.

3-Substituted-7-benzylidene-9-isopropyl-2-methyl-11-phenyl-7,8,9,10-tetrahydropyrimido[4′,5′ : 4,5]-thieno[2,3-*b*][1,6]naphthyridin-4(3*H*)-one (14a—c): Method A: A suspension of oxazino compound **13** (0.01 mol) in a mixture of ammonium acetate (5 g) and acetic acid (20 ml) was heated under reflux for 30 min. The solid crystals of compound **14a** that separated from the hot solution were filtered off washed several times with water and recrystallized from the proper solvent.

Method B: A mixture of the oxazine compound **13** (0.01 mol) and hydrazine hydrate or phenylhydrazine (0.01 mol) in ethanol (50 ml) was refluxed for 1 h. The solid products thus formed on hot were collected by filtration, recrystallized and indentified as compounds **14b** and **14c** respectively, cf. Table 2.

3-Arylmethyleneamino-7-benzylidene-9-isopropyl-2-methyl-II-phenyl-7,8,9,10-tetrahydropyrimido-[4′,5′ : 4,5]thieno[2,3-*b*][1,6]naphthyridin-4(3*H*)-ones (15a—c): These compounds were prepared following a procedure similar to that of compounds **7a—c** using the *N*-amino derivative **14b** and aromatic aldehydes. The results are summarized in Table 2.

Ethyl 8-Benzylidene-6-isopropyl-4-phenyl-3-(1-pyrrolyl)-5,6,7,8-tetrahydrothieno[2,3-*b*][1,6]-naphthyridine-2-carboxylate (16): A mixture of the ester derivative **5f** (0.01 mol) and 2,5-dimethoxytetrahydrofuran (0.012 mol) in acetic acid (20 ml) was refluxed for 2 h. The reaction mixture was concentrated to one half of its volume. After cooling, the crystals which separated out were filtered off and recrystallized from the proper solvent.

8-Benzylidene-6-isopropyl-4-phenyl-3-(1-pyrrolyl)-5,6,7,8-tetrahydrothieno[2,3-*b*][1,6]naphthyridine-2-carbohydrazide (17): A mixture of the ester derivative **16** (0.01 mol) and hydrazine hydrate (0.01 mol) in pyridine (20 ml) was refluxed for 3 h. The cold reaction mixture was poured into ice/water mixture and the separated hydrazide derivative was filtered off, washed several times with water

Table 2. Physical and Spectral Data of Compounds **6**—**22**

Compound No.	Mp/°C (Solvent)	Yield/% (Color)	Molecular formula (MW)	IR	^{1}H NMR
6	145 (Ethanol)	78 (White)	$C_{27}H_{27}N_5OS$ (496.6)	3240 ($NHNH_2$), 2220 (CN), 1670 (CO)	$(CD_3)_2SO$: 0.9 (d, 6H, $2CH_3$), 2.6 (m, 1H, CH), 3.2, 3.4 (2s, 4H, $2CH_2$), 3.8 (s, 2H, CH_2), 4.2 (s, 2H, NH_2), 7.1—7.4 (m, 10H, arom), 7.8 (s, 1H, CH), 10 (s, 1H, NH).
7a	238 (Ethanol)	74 (Pale yellow)	$C_{34}H_{31}N_5OS$ (557.7)	3200 (NH), 2200 (CN) 1670 (CO), 1610 (C=N)	$(CD_3)_2SO$: 0.9 (d, 6H, $2CH_3$), 2.6 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 3.9 (s, 2H, CH_2), 7.1—7.4 (m, 15H, arom), 7.8 (s, 1H, CH), 8.1 (s, 1H, CH=N–), 9.1 (s, 1H, NH).
7b	246 (Ethanol)	83 (Yellow)	$C_{35}H_{33}N_5O_2S$ (587.7)	3230 (NH), 2200 (CN) 1660 (CO), 1630 (C=N)	$(CD_3)_2SO$: 0.8 (d, 6H, $2CH_3$), 2.7 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 3.9 (s, 3H, CH_3), 4.1 (s, 2H, CH_2), 6.8—7.6 (m, 14H, arom), 7.9 (s, 1H, CH), 8.3 (s, 1H, CH=N–), 8.9 (s, 1H, NH).
7c	249 (Acetic acid)	78 (Yellow)	$C_{34}H_{30}N_6O_3S$ (602.7)	3200 (NH), 2200 (CN) 1670 (CO), 1630 (C=N)	
8a	265 (Ethanol)	79 (Yellow)	$C_{34}H_{31}N_5OS$ (557.7)	3480, 3400 (NH_2), 3300 (NH), 1650 (C=O), 1620 (C=N)	$(CD_3)_2SO$: 0.8 (d, 6H, $2CH_3$), 2.6 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 5.6 (s, 2H, NH_2), 6.8—7.7 (m, 15H, arom), 8.1 (s, 1H, CH), 9.4 (s, 1H, NH).
8b	269 (Ethanol)	72 (Yellow)	$C_{35}H_{33}N_5O_2S$ (587.7)	3460, 3380 (NH_2), 3280 (NH), 1660 (C=O), 1620(C=N)	
8c	249 (Dioxan)	81 (Orange)	$C_{34}H_{30}N_6O_3S$ (602.7)	3500, 3420 (NH_2), 3300 (NH), 1660 (C=O), 1630 (C=N)	
9	244 (Acetic acid)	66 (White)	$C_{29}H_{24}N_4OS$ (476.6)	3420 (NH), 1680 (CO)	
10	276 (Acetic acid)	55 (Yellow)	$C_{35}H_{30}N_4OS$ (554.7)	1700 (CO)	$(CD_3)_2SO$: 0.9 (d, 6H, $2CH_3$), 2.1 (s, 3H, CH_3), 2.8 (m, 1H, CH), 3.5, 3.8 (2s, 4H, $2CH_2$), 7.1—7.6 (m, 15H, arom), 8.2 (s, 1H, CH)
11	252 (Acetic acid)	59 (Red)	$C_{28}H_{24}N_4S_3$ (512.7)	3220, 3180 (2NH)	
12	262 (Dioxan)	79 (Yellow)	$C_{27}H_{25}N_3O_2S$ (455.5)	3480, 3400 (NH_2). 1690 (CO)	
13	249 (Ethanol)	74 (White)	$C_{29}H_{25}N_3O_2S$ (479.6)	1730 (CO)	
14a	290 (DMF)	81 (Buff)	$C_{29}H_{26}N_4OS$ (478.6)	3220 (NH), 1690 (CO).	
14b	248 (Ethanol)	78 (Yellow)	$C_{29}H_{27}N_5OS$ (493.6)	3420, 3360 (NH_2). 1690 (CO)	($CDCl_3$): 1.1 (d, 6H, $2CH_3$), 2.4 (s, 3H, CH_3), 2.8 (m, 1H, CH), 3.6, 3.8 (2s, 4H, $2CH_2$), 5.0 (s, 2H, NH_2), 7.2—7.6(m, 10H, arom), 8.2 (s, 1H, CH).
14c	282 (Ethanol)	72 (Orange)	$C_{35}H_{30}N_5OS$ (568.7)	3460 (NH), 1680 (CO)	

and recrystallized from the proper solvent.

N′- Arylmethylene- 8- benzylidene- 6- isopropyl- 4- phenyl- 3- (1- pyrrolyl)- 5, 6, 7, 8- tetrahydrothieno[2, 3- *b*][1, 6]naphthyridin- 2- carbohydrazides (18a—c): These compounds were prepared following a similar procedure to that of compounds **7a**—**c** using the hydrazide derivative **17** and aromatic aldehydes. The physical and spectral data are summarized in Table 2.

2- Acetyl- 8- benzylidene- 6- isopropyl- 4- phenyl- 3- (1- pyrrolyl)- 5, 6, 7, 8- tetrahydrothieno[2, 3- *b*][1, 6]- naphthyridine (19): A mixture of **5a** (0.01 mol) and 2, 5-dimethoxytetrahydrofuran (0.012 mol) in acetic acid (20 ml) was refluxed for 2h, then left to cool. The crystals which separated were filtered off and recrystallized from the proper solvent.

1- Acetyl- 8- benzylidene- 6- isopropyl- 4- phenyl- 3- (1- pyrrolyl)- 5, 6, 7, 8- tetrahydrothieno[2, 3- *b*][1, 6]- naphthyridine Phenylhydrazone (20): A mixture of the acetyl derivative **19** (0.01 mol) and phenylhydrazine (0.012 mol) in absolute ethanol (50 ml) was refluxed for 3 h. During this period of time a solid crystals were separated. These were filtered, recrystallized and identified, cf. Table 2.

Table 2. (Continued)

Compound No.	Mp/°C (Solvent)	Yield/% (Color)	Molecular formula (MW)	IR	^{1}H NMR
15a	236 (Ethanol)	68 (Yellow)	$C_{36}H_{31}N_5OS$ (581.7)	1690 (CO)	
15b	259 (Acetic acid)	82 (Orange)	$C_{36}H_{30}N_6O_3S$ (626.7)	1680 (CO)	
15c	254 (Ethanol)	64 (Yellow)	$C_{37}H_{33}N_5O_2S$ (611.8)	1690 (CO)	($CDCl_3$): 0.9 (d, 6H, $2CH_3$), 2.4 (s, 3H, CH_3), 2.8 (s, 1H, CH), 3.5, 3.7 (2s, 4H, $2CH_2$), 3.9 (s, 3H, CH_3), 7.2—7.6 (m, 14H, arom), 8.3, 8.6 (2s, 2H, 2CH).
16	148 (Acetic acid)	77 (Yellow)	$C_{33}H_{29}N_3O_2S$ (531.7)	1720 (C=O)	(CD_3)$_2$SO: 0.7 (d, 6H, $2CH_3$), 1.1 (t, 3H, CH_3), 2.7 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 4.1 (q, 2H, CH_2), 5.4 (m, 2H, 2CH pyrrolyl), 6.3 (m, 2H, 2CH pyrrolyl), 6.8—7.4 (m, 10H, arom), 8.1 (s, 1H, CH).
17	162 (Ethanol)	71 (White)	$C_{31}H_{29}N_5OS$ (519.7)	3380, 3320 ($NHNH_2$) 1670 (C=O)	(CD_3)$_2$SO: 0.8 (d, 6H, $2CH_3$), 2.6 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 4.2 (s, 2H, NH_2), 5.4 (s, 2H, 2CH pyrrolyl), 6.3 (s, 2H, 2CH pyrrolyl), 6.8—7.4 (m, 11H, arom and NH), 8.2 (s, 1H, CH).
18a	239 (Ethanol)	68 (Pale yellow)	$C_{38}H_{33}N_5OS$ (607.8)	3320 (NH), 1670 (CO) 1630 (C=N)	(CD_3)$_2$SO: 0.9 (d, 6H, $2CH_3$), 2.6 (m, 1H, CH), 3.3, 3.6 (2s, 4H, $2CH_2$), 5.4 (s, 2H, 2CH pyrrolyl), 6.2 (s, 2H, 2CH, pyrrolyl), 7.2—7.8 (m, 16H arom +NH), 8.2, 8.4 (s, 2H, 2CH).
18b	218 (Ethanol)	65 (Yellow)	$C_{38}H_{32}N_6O_3S$ (652.8)	3240 (NH), 1670 (CO). 1620 (C=N)	
18c	282 (Acetic acid)	76 (Orange)	$C_{39}H_{34}N_6O4S$ (682.8)	3220 (NH), 1680 (CO), 1630 (C=N)	
19	211 (Acetic acid)	84 (Yellow)	$C_{32}H_{29}N_3OS$ (503.7)	1710 (CO)	
20	246 (Dioxan)	82 (Orange)	$C_{38}H_{35}N_5S$ (593.8)	3300 (NH)	(CD_3)$_2$SO: 0.8 (d, 6H, $2CH_3$), 1.5 (s, 3H, CH_3), 2.7 (m, 1H, CH), 3.4, 3.6 (2s, 4H, $2CH_2$), 5.6 (s, 2H, 2CH pyrrolyl), 6.1 (s, 1H, NH), 6.3 (s, 2H, 2CH pyrrolyl), 6.7—7.3 (m, 15H arom), 8.0 (s, 1H, CH).
21	183 (Ethanol)	65 (Yellow)	$C_{38}H_{33}N_3OS$ (579.8)	1690 (CO), 1635 (C=C)	
22	208 (Dioxan)	81 (Orange)	$C_{45}H_{39}N_5S$ (681.9)	—	(CD_3)$_2$SO: 0.9 (d, 6H, $2CH_3$), 2.6 (m, 1H, CH), 2.9 (d, 2H, CH_2), 3.2 (t, 1H, CH), 3.6, 3.8 (2s, 4H, $2CH_2$), 5.6 (s, 2H, 2CH pyrrolyl), 6.4 (s, 2H, 2CH pyrrolyl), 7.1—7.9 (m, 20H, arom), 8.4 (s, 1H, CH).

8-Benzylidene-2-benzylideneacetyl-6-isopropyl-4-phenyl-3-(1-pyrrolyl)-5,6,7,8-tetrahydrothieno[2,3-*b*][1,6]naphthyridine (21): A mixture of the acetyl derivative **19** (0.01 mol) and benzaldehyde (0.01 mol) in ethanolic sodium hydroxide (50 ml, 10%) was stirred at room temperature for 1 h. The solid product thus formed while stirring was filtered off, washed several times with water and recrystallized from the proper solvent.

8-Benzylidene-6-isopropyl-4-phenyl-3-(1-pyrrolyl)-2-(1,5-diphenyl-2-pyrazolin-3-yl)-5,6,7,8-tetrahydrothieno[2,3-*b*][1,6]napthyridine(22): A mixture of the chalcone compound **21** (0.01 mol) and phenylhydrazine in absolute ethanol (50 ml) was refluxed for 8 h. The solid product thus formed on hot was filtered off and recrystallized from the proper solvent.

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