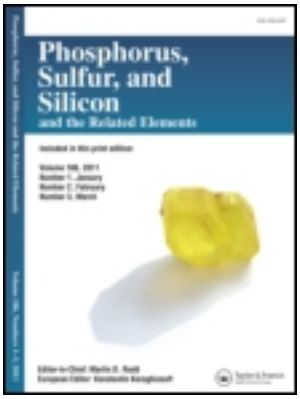


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# A Convenient Synthesis of Some New Indeno[1,2-b]Pyridines and Indeno[1,2-b] Thieno[3,2-e]Pyridine Derivatives with Potential Biological Activity

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# A Convenient Synthesis of Some New Indeno[1,2-*b*]Pyridines and Indeno[1,2-*b*] Thieno[3,2-*e*]Pyridine Derivatives with Potential Biological Activity

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*3-Cyano-5-oxo-4(2-thienyl)-indeno[1,2-b]pyridin-2-[1H]thione **3** was prepared from indanone **1** with arylidene cyanoacetamide or from arylideneindanone **2** with cyanoacetamide. S-Alkylation of **3** with halogenated compounds afforded compounds **4a–h**. Compounds **4d–h** underwent ring closure with sodium ethoxide to produce indenothienopyridines **5a–e**, respectively. Treatment of **3** using ethylchoroacetate or chloroacetone gave compounds **6** and **7**, respectively. Compounds **5a** and **5d** were reacted with carbon disulphide in pyridine to give compounds **8a** and **8b**.*

*Most of the synthesized compounds were screened in vitro for their antimicrobial activities against four species of bacteria and six species of fungi using Chloramphenicol (5%) and Terbinafine (5%) as a standard.*

**Keywords** Indenopyridines; indenopyridothie-nopyrimidines; indenothienopyridines

## INTRODUCTION

Pyridothienopyrimidines have been the subject of chemical and biological studies on account of their interesting pharmacological properties. Such derivatives have analgesic,[1] antipyretic,[2] and antiinflammatory[3,4] activity. On the other hand, indenopyridines exhibit potent antispermatogenic activity and are useful inhibitors of spermatogenesis in animals.[5] Indenopyrimidines show fungicidal activity,[6] while indenopyridopyrimidines exhibit moderate antimicrobial activity.[7] Also in pharmacological studies thieno[2,3-d]pyrimidines and thienodipyrimidines have been shown to posses a variety of pharmacological activities including antituberculous[8] and herpes virus inhibitory[9] and antianaphylactic activity.[10] Within this context, it seemed of interest herein

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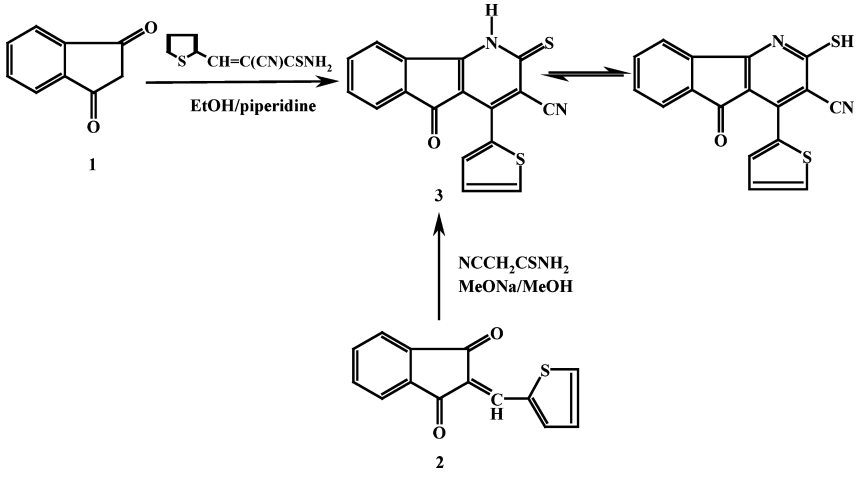
to synthesize the title compounds and their eraluation regarding antimicrobial activities.

## RESULTS AND DISCUSSION

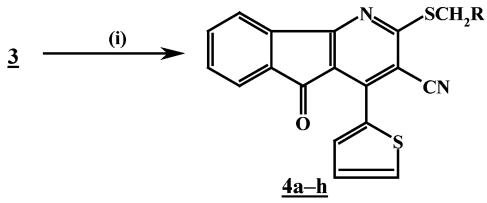
When indan-1,3-dione **1** was heated with arylidene cyanothioacetamide in refluxed ethanol in the presence of a catalytic amount of piperidine, 3-cyano-5-oxo-4(2-thienyl)indeno[1,2-b]pyridine-2[1H]thione **3** was obtained; compound **3** was also prepared by an alternative route by heating arylidenoindanone **2** in a methanolic solution of sodium methoxide with cyanothioacetamide. The product **3**, which was produced with the two routes, was identical in all aspects (m.p., mixed m.p., IR, NMR, Scheme 1).




**SCHEME 1**

When mercaptoindenopyridine carbonitrile **3** was refluxed with $\alpha$-halogenated compounds in ethanol and in the presence of sodium acetate, the corresponding s-alkylated derivatives $\mathbf{4_{a-h}}$ were obtained (Scheme 2).

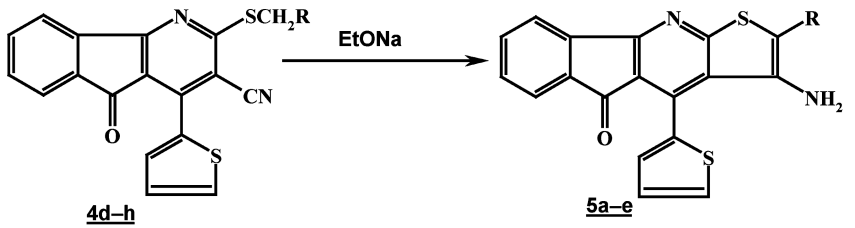
Compounds **4d–h** underwent cyclization into indenothienopyridiene **5a–e** derivatives, respectively, when heated in ethanolic sodium ethoxide solution (Scheme 3). The formation of structures of **4c–h** and their cyclized compounds **5a–e** were confirmed on the basis of spectral data. IR of compounds **4c–h** revealed an absorption band at 2220–2200 $cm^{-1}$ characteristic for the (CN) group, which displaced with band at 3450 and 3350 $cm^{-1}$ characteristic for ($NH_2$), in cyclized compounds **5a–e**. Also HNMR spectra of compounds **4d–h** showed signals at $\delta$ 4.2–4.3 as




**(i) Methyl iodide, Ethyl iodide, Benzyl chloride, Chloroacetonitrile, P-chloro chloroacetanilide, Phenacyl bromide, Chloroacetamide, P-methoxy chloroacetanilide**

| 4 | R |
|---|---|
| a | H |
| b | $CH_3$ |
| c | CN |
| d | $CONHC_6H_4Cl$-*p* |
| e | COPh |
| f | $CONH_2$ |
| g | $CONHC_6H_4OCH_3$-p |
| h | |

**SCHEME 2**



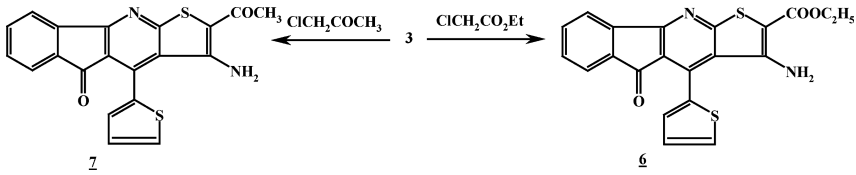

| 5 | R |
|---|---|
| a | CN |
| b | $CONHC_6H_4Cl$-*p* |
| c | COPh |
| d | $CONH_2$ |
| e | $CONHC_6H_4OCH_3$-p |

**SCHEME 3**

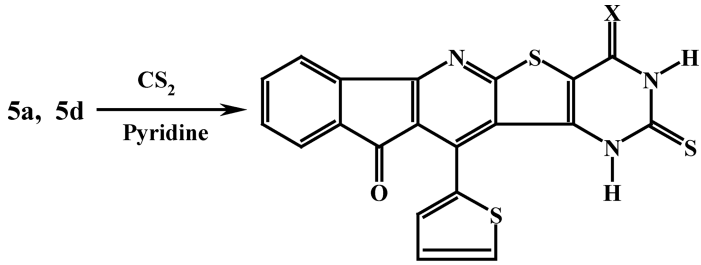
a singlet characteristic for S–$CH_2$–, which displaced with signals at $\delta$ between 5.6 and 6.8 characteristic for $NH_2$ when cyclized to **5a–e**.

When **3** was refluxed with ethyl chloroacetate or chloroacetone in ethanolic sodium ethoxide, compounds **6** and **7** were obtained, respectively (Scheme 4).

On the other hand, indenopyridines **5a** and **5d** were reacted with carbon disulphide in pyridine on a steam bath to give monothio and dithioindenopyridothienopyridines **8a** and **8b**, respectively (Scheme 5).




**SCHEME 4**




**SCHEME 5**

## BIOLOGICAL ACTIVITY

Most of the synthesized compounds (**3**, **4a**, **4b**, **4d**, **4f**, **4g**, **4h**, **5a**, **5d**, **7**, **8a**, **8b**) were screened in vitro for their antimicrobial activities against four species of bacteria (*Bacillus cereur, Escherichia coli, Staphylococcus aureus*, and *Serratia marcescens*) and species of fungi (*Aspergillus flavus, Aspergillus niger, Candida albicans, Geotrichum candidum, Scopulariopsis breuicaulis*, and *Trichophyton rubrum*) using the disc diffusion method.[11,12] Chloramphenicol (5%) and Terbinafine (5%) were used as a standard, respectively. Samples were dissolved in dimethyl formamide to a concentration of 5%, and filter paper discs (whatman no. 3.5 mm in diameter) were impregnated with the solutions. The discs were placed on the surface of solidified Nutrient agar dishes seeded by the test bacteria or Czapek's Dox agar dishes seeded by the test fungi. The inhibition zones were measured in millimeters by the end of the incubation period (24 h at 37°C for bacteria and 28°C for fungi). The relationship between the structure and the antibacterial activity is quite clear for the results depicted in Table I. The following generalization in this aspect may be made: Indenopyridenthione derivative 3 exhibited a strong to moderate inhibition activity against two species of bacteria, namely *B. cereus* and *S. marcescens.* The relatively high antibacterial activity of compound **3** may be due to the presence of a cyano group and sulpher in the molecule. Conversion of the mercapto group

**TABLE I Results of Biological Screening of Compounds (3–8): Inhibition Zones in mm**

| Compound no. | *Bacillus cereus* | *Escherichia coli* | *Staphylococcus aureus* | *Serratia marcescens* |
|---|---|---|---|---|
| 3 | 15 | — | — | 9 |
| 4a | — | — | 6 | 19 |
| 4b | 7 | — | 11 | 10 |
| 4d | 10 | — | — | 11 |
| 4f | 6 | — | — | 11 |
| 4g | — | — | 7 | 10 |
| 4h | — | — | 8 | 15 |
| 5a | 12 | — | 8 | 11 |
| 5b | — | — | 6 | 12 |
| 5d | 6 | — | 6 | 12 |
| 7 | — | — | 8 | 12 |
| 8a | 13 | — | 12 | 10 |
| 8b | 13 | — | 8 | 11 |
| Reference[b] 35 | 35 | — | 37 | 40 |

[a]inhibition zone around the discs: 26–40 mm: very strong activity; 13–25 mm: strong activity; 7–12 mm: moderate activity; 0–6 mm: weak activity; dash denotes no activity.

[b]chloramphenicol (5%, antibacterial activity).

of compounds **3** to 5-alkylated derivatives **4a**, **4b**, **4d**, **4f**, **4g**, and **4h** through alkylation with different alkylating agents were found to be more active, especially with serratia marcescens depending on the type of substituents at C-2 in the pyridine ring.

Built-up fused indenothienopyridines ring systems (**5a**, **5b**, **5d**, and **7**) exhibited a varied moderate activity depending on the type of substituents at C-2 in the thiophene ring.

Compounds **8a** and **8b** showed a strong to moderate activity against all the tested bacteria species except for *E. coli*. The relatively high antibacterial activity may be due to the presence of a fused pyrimidine ring in the molecule.

## ANTIFUNGAL ACTIVITY

The results indicated that all the screened compounds were inactive against all the tested fungal species.

## EXPERIMENTAL

Melting points were determined on a kofler metting point apparatus and are uncorrected. IR spectra were recorded on potassium

bromide disks on a Pye Unicam spectrophotometer using the KBr wafer technique. $^1$H NMR spectra were obtained on a Varian 39090 MHZ spectrometer in a suitable deutrated solvent. Chemical shifts were determined on the $\delta$ scale by using tetramethylsilan as the internal standard. Elemental analyses were obtained on a Perkin Elmer 240 C microanalyzer. The physical constants and spectral data of the all new synthesized compounds are listed in Tables I and II.



## 3-Cyano-5-oxo-4(2-thienyl)-indeno [1,2-b]pyriden-2[1H]-thione (3)[13]

### *Method A*

To a mixture of indandione (**1**) (0.01 mol), and arylidene cyamothioacetamide (0.01 mol) in ethanol (30 ml), five drops of piperidine were added. The mixture was heated under reflux for 6 h and then allowed to cool. The solid product was collected as orange crystals (ethanol).

### *Method B*

A mixture of arylideneindandione **2** (0.01 mol), and cyanothioacetamide (1 g, 0.01 mol) in methanolic solution of sodium methoxide (0.01 mol in 20 mL methanol), was heated on a steam bath for 8 h at 50°C and then allowed to cool, and it acidified with HCl (10%). The solid product was collected and recrystallized from ethanol as orange crystals. The physical constants and spectral data of compound **3** are listed in Tables I and II.

## 2-Alkylthio-5-oxo- 4 (2-thienyl)-indeno [1,2-b] pyridine-3-carbonitrile (4a–h): General Procedure

A mixture of compound **3** (0.01 mol), the appropriate halogenated compound (0.01 mol), and sodium acetate (1 g, 0.012 mol) in ethanol (20 mL) was heated under reflux for 1 h and then allowed to cool. The solid product was collected, washed well with water, and recrystallized from the proper solvent. The physical constants and spectral data of compounds **4a–h** are listed in Tables I and II.

## 3-Amino-2-substituted-4 (2-thienyl)-5-oxoindeno [1,2-b]-thieno[3,2-e] pyridines (5a–e): General Procedure

A sample of compound **4d–h** (0.01 mol) in ethanolic solution of sodium ethoxide (0.01 mol in 20 mL ethanol) was heated under reflux for

**TABLE II Physical Constants of compounds (3–8)**

| No. | Yield (%) | M.P. (°C) | Color | Molecular Formula | Analysis (%) Calcd./Found C | H | N | S | Cl |
|---|---|---|---|---|---|---|---|---|---|
| 3 | 84 | 263–365[a] | Red | $C_{17}H_8N_2OS_2$ | 63.72 | 2.51 | 8.74 | 20.01 | |
| | | | | (320.39) | 63.50 | 2.35 | 8.89 | 20.13 | |
| 4a | 72 | 210–212[b] | Yellow | $C_{18}H_{19}N_2OS_2$ | 64.64 | 3.01 | 8.37 | 19.17 | |
| | | | | (334.42) | 64.79 | 3.22 | 8.47 | 19.29 | |
| 4b | 79 | 182[b] | Yellow | $C_{19}H_{12}N_2OS_2$ | 65.49 | 3.47 | 8.03 | 18.40 | |
| | | | | (348.44) | 65.30 | 3.32 | 8.17 | 18.51 | |
| 4c | 75 | 228[b] | Yellow | $C_{24}H_{14}N_2OS_2$ | 70.21 | 3.43 | 6.82 | 15.62 | |
| | | | | (410.51) | 69.98 | 3.20 | 6.77 | 15.40 | |
| 4d | 68 | 284[a] | Orange | $C_{19}H_9N_3OS_2$ | 63.49 | 2.52 | 11.69 | 17.84 | |
| | | | | (359.43) | 63.58 | 2.40 | 11.50 | 17.83 | |
| 4e | 82 | 306[a] | Yellow | $C_{25}H_{14}N_3O_2S_2Cl$ | 61.53 | 2.89 | 8.61 | 13.14 | 7.26 |
| | | | | (487.98) | 61.72 | 3.12 | 8.42 | 13.37 | 7.24 |
| 4f | 72 | 230[b] | Yellow | $C_{25}H_{14}N_2O_2S_2$ | 68.47 | 3.21 | 6.38 | 14.62 | |
| | | | | (438.53) | 68.29 | 3.18 | 6.46 | 14.79 | |
| 4g | 65 | 260[b] | Orange | $C_{19}H_{11}N_3O_2S_2$ | 60.46 | 2.93 | 11.13 | 16.99 | |
| | | | | (377.44) | 60.53 | 2.88 | 11.24 | 17.19 | |
| 4h | 84 | 260[c] | Canarian Yellow | $C_{26}H_{17}N_3O_3S_2$ (483.57) | 64.57 64.77 | 3.54 3.44 | 8.68 8.84 | 13.26 13.21 | |
| 5a | 78 | 306[a] | Yellow | $C_{19}H_9N_3OS_2$ | 63.49 | 2.52 | 11.69 | 17.84 | |
| | | | | (359.43) | 63.48 | 2.50 | 11.70 | 17.82 | |
| 5b | 63 | 314[c] | Orange | $C_{25}H_{14}N_3O_2S_2Cl$ | 61.53 | 2.89 | 8.61 | 13.14 | 7.26 |
| | | | | (487.98) | 61.63 | 2.81 | 8.52 | 13.24 | 7.25 |
| 5c | 80 | 362[b] | Orange | $C_{25}H_{14}N_2O_2S_2$ | 68.47 | 3.21 | 6.38 | 14.62 | |
| | | | | (438.53) | 68.40 | 3.22 | 6.33 | 14.82 | |
| 5d | 72 | 338[a] | Red | $C_{19}H_{11}N_3O_2S_2$ | 60.46 | 2.93 | 11.13 | 16.99 | |
| | | | | (377.44) | 60.34 | 2.82 | 11.24 | 16.86 | |
| 5e | 66 | 285[b] | Orange | $C_{26}H_{17}N_3O_3S_2$ | 64.57 | 3.54 | 8.68 | 13.26 | |
| | | | | (483.57) | 64.78 | 3.31 | 8.89 | 13.05 | |
| 6 | 63 | 318[b] | Orange | $C_{21}H_{14}N_2O_3S_2$ | 62.05 | 3.47 | 6.89 | 15.77 | |
| | | | | (406.48) | 61.93 | 3.62 | 7.03 | 15.96 | |
| 7 | 68 | 364[a] | Orange | $C_{20}H_{12}N_2O_2S_2$ | 63.81 | 3.21 | 7.44 | 17.035 | |
| | | | | (376.45) | 63.72 | 3.41 | 7.64 | 16.885 | |
| 8a | 53 | 340[c] | Yellow | $C_{20}H_9N_3OS_4$ | 55.15 | 2.08 | 9.64 | 29.44 | |
| | | | | | 55.02 | 2.27 | 9.44 | 29.31 | |
| 8b | 70 | 320[a] | Yellow | $C_{20}H_9N_3O_2S_3$ | 57.26 | 2.16 | 10.01 | 22.93 | |
| | | | | | 57.43 | 1.98 | 10.1 | 22.84 | |

[a]Recrystallized from ethanol. [b]Recrystallized from petroleum ether 60–80°C.
[c]Recrystallized from methanol.

30 min and then allowed to cool. The solid product was collected and recrystallized from the proper solvent. The physical constants and spectral data of compounds **5a–e** are listed in Tables I and II.

**TABLE III Spectral Data of Compounds of (3-8)**

| No. | IR (KBr) $\nu cm^{-1}$ | $^1H$ NMR $\delta$ |
|---|---|---|
| 3 | 3150 (NH), 2200 (CN), 1710 (CO) | $CF_3CO_2D$: 7.2-8.2 (m, 7H, Ar-H) |
| 4a | 2950, 2930 (CH aliph.), 2200 (CN), 1715 (CO) | $CDCl_3$: 3.2 (s, 3H, $SCH_3$), 7.2-7.9 (m, 7H, Ar-H) |
| 4b | 3100 (CH arom.), 2920 (CH aiph.), 2200 (CN), 1705 (CO) | $CDCl_3$: 1.3 (t, 3H, $CH_3$), 4.3 (q, 2H, $CH_2$), 7.1-8.0 (m, 7H, Ar-H) |
| 4c | 3100 (CH arom.), 2910 (CH aiph.), 2200 (CN), 1700 (CO) | $CDCl_3$: 4.1 (s, 2H, $CH_2$), 7.0-8.2 (m, 12H, Ar-H) |
| 4d | 3100 (CH arom.), 2950 (CH aiph.), 2200 (CN), 1715 (CO) | DMSO-$d_6$: 4.3 (s, 2H, $CH_2$), 7.1-8.2 (m, 7H, Ar-H) |
| 4e | 3250 (NH), 2200 (CN), 3100 (CH arom.), 2900 (CH aiph.), 1715 (CO), 1650 (CO amidic.) | DMSO-$d_6$: 4.3 (s, 2H, $CH_2$), 7.0-7.9 (m, 11H, Ar-H), 10.6 (s, 1H, NH). |
| 4f | 3100 (CH arom.), 2900 (CH aiph.), 2200 (CN), 1710 (CO), 1680 (CO). | $CDCl_3$: 4.2 (s, 2H, $CH_2$), 7.1-7.9 (m, 12H, Ar-H) |
| 4g | 3400, 3300 ($NH_2$), 3200 (CH arom.), 2900 (CH aiph.), 2200 (CN), 1700 (CO), 1660 (amidic CO) | $CDCl_3$: 4.2 (s, 2H, $CH_2$), 5.8 (s, 2H, $NH_2$), 7.0-8.1 (m, 7H, Ar-H) |
| 4h | 3280 (NH), 2920 (CH aiph.), 2200 (CN), 1710 (CO), 1670 (CO amidic) | DMSO-$d_6$: 3.9 (s, 3H, $CH_3$), 4.2 (s, 2H, $CH_2$), 11.2(s, 1H, NH), 7.2-8.1 (m, 11H, Ar-H). |
| 5a | 3450, 3350 ($NH_2$), 2200 (CN), 1710 (CO), 1600 (C=N) | DMSO-$d_6$: 6.6 (s, 2H, $NH_2$), 7.1-8.0 (m, 7H, Ar-H). |
| 5b | 3450, 3350 ($NH_2$), 1715 (CO), 1680 (CO amidic), 1640 (C=N) | DMSO-$d_6$: 6.8 (s, 2H, $NH_2$), 7.2-8.2 (m, 11H, Ar-H), 10.6 (s, 1H, NH). |
| 5c | 3460, 3400 ($NH_2$), 1700 (CO), 1600 (C=N) | $CDCl_3$: 6.7 (s, 2H, $NH_2$), 7.1-8.0 (m, 12H, Ar-H) |
| 5d | 3450, 3350 ($NH_2$), 1710 (CO), 1645 (CO amidic) | DMSO-$d_6$: 5.6, 6.7 (2s, 4H, $2NH_2$), 7.2-7.9 (m, 7H, Ar-H). |
| 5e | 3450, 3350 ($NH_2$), 3320 (NH), 1705 (CO), 1640 (CO amidic), 1590 (C=N) | $CDCl_3$: 3.9 (s, 3H, $CH_3$), 5.8 (S, 2H, $NH_2$), 7.0-8.2 (m, 11H, Ar-H), 9.2 (s, 1H, NH). |
| 6 | 3450, 3350 ($NH_2$), 3100 (CH arom.), 2950 (CH aiph.), 2200 (CN), 1710 (CO), 1650 (CO) | $CDCl_3$: 1.3 (t, 3H, $CH_3$), 4.2 (q, 2H, $CH_2$), 5.9 (S, 2H, $NH_2$), 7.1-8.0 (m, 7H, Ar-H) |
| 7 | 3450, 3380 ($NH_2$), 1705 (CO), 1660 (CO) | DMSO-$d_6$: 2.3 (s, 3H, $COCH_3$), 6.1 (S, 2H, $NH_2$), 7.2-7.9 (m, 7H, Ar-H). |
| 8a | 3200, 3260 (2NH), 1700 (CO) | $CF_3CO_2D$: 7.0-8.2 (m, 7H, Ar-H) |
| 8b | 3230, 3170 (2NH), 1710, 1680 (2CO) | $CF_3CO_2D$: 7.0-8.1 (m, 7H, Ar-H) |

## Ethyl 3-Amino-5-oxo-4(2-thienyl)indeno[1,2-b]thieno[3,2-e]pyridiene-2-carboxylate (6) and 2-Acetyl-3-amino-5-oxo-4-(2-thienyl)-indeno[1,2-b]thieno[3,2-e]pyridine (7)

A mixture of compound **3** (0.01 mol), ethyl chloroacetate, or chloroacetone, and sodium acetate (1 g, 0.012 mol) in ethanol (20 mL) was heated

under reflux for 1 h and then allowed to cool. The solid product **6** and **7** was collected, respectively, washed with water, and recrystallized from the proper solvent. The physical constants and spectral data of compounds **6** and **7** are listed in Tables I and II.

### 4,11-Dioxo-12-(2-thienyl)-3[H]indeno[1″,2″: 2′,3′]pyrido [5′,6′:4,5]thieno[3,2,-d]pyrimidin-2(1 H)thione (8a) and 11-oxo-12-(2-thienyl)indeno[1″,2″:2′,3′]pyrido[5′,6′:4,5]thieno[3,2-d] pyrimidin-2,4(1 H, 3 H)dithione (8b)

A mixture of compound $\mathbf{5_a}$ or $\mathbf{5_d}$ (0.005 mol), carbon disulphide (2 mL) in pyridine (20 mL) was refluxed for 10 h and then allowed to cool. The solid product was collected and recrystallized from the proper solvent. The physical constants and spectral data of compound **6a**, **b** are listed in Tables I and II.

## REFERENCES

[1] C. G. Dave, P. R. Shah, K. C. Dave, and V. J. Patel, *J. Indian Chem. Soc*., **66,** 48 (1989).
[2] E. Bousquet, G. Romero, F. Guerrera, A. Caruso, and M. A. Roxas, *Formaco Ed-Sci.*, **40,** 869 (1985).
[3] H. Vieweg, S. Leistner, G. Wagner, N. Boehm, U. Krasset, R. Grupe, et al., East German Patent, DD 257, 830 (1988); *C.A.*, **110,** 95262p (1989).
[4] S. Leistner, G. Wagner, M. Guetscharo, and E. Glusa, *Pharmazie*, **41,** 54 (1986).
[5] C. E. Cook, Y. W. Lee, M. C. Wani, P. A. Fail, and J. M. Jump, US patent, 5, 319, 084 (1993); *C. A.*, **112,** 265250a (1995).
[6] N. Umeda, K. Saito, H. Hosokawa, and S. Hashimoto, Japan Patent 303, 771 (1991); *C.A.*, **119,** 203428u.
[7] I. O. Donkor, C. L. Klein, L. Liang, N. Zhu, E. Bradley, and A. M. Clark, *J. Pharm. Sci.*, **84,** 661 (1995).
[8] N. N. Kaplina, V. L. Shedov, and L. N. Filitis, U.S.S.R 1993, SuI, 383, 752; *C.A.*, **123,** 228206r (1995).
[9] N. N. Kaplina, V. L. Shedov., A. N. Fomina, I. S. Nikolaeva, T. V. Pushkina, and L. N. Filitis, U.S.S.R., 1993, SuI, 389, 235; *C.A.*, **123,** 275971w (1995).
[10] G. Wagner, H. Vieweg, and S. Leistner, *Pharmazie*, **48,** 667 (1993).
[11] A. A. Geies and A, M. Kamal El-Dean, *Bulletin of the Polish academy of Sciences Chemistry*, **45**(4), 381 (1997).
[12] L. P. Carrod and F. D. Grady, *Antibiotics and Chemotherary*, 3rd ed., p. 477, (Churchill Livingston, Edinburgh, London, 1772).
[13] A. Cremer, *Antibiotic Sensitivity and Assay Tests in Collins*, 4th ed., p. 521 (Butter worth and Co. Ltd., London, 1980).