HETEROCYCLES, Vol. 78, No. 12, 2009, pp. 3073 - 3080. © The Japan Institute of Heterocyclic Chemistry
Received, 7th August, 2009, Accepted, 10th September, 2009, Published online, 11th September, 2009
DOI: 10.3987/COM-09-11816

THERMOLYSIS OF *N*-ARYLENAMINO-*N*-ARYLIMINE HYDROCHLORIDE DERIVATIVES: A SHORT AND IMPROVED SYNTHESIS OF 2-METHYLTHIENO[2,3-*c*]ACRIDINE DERIVATIVES

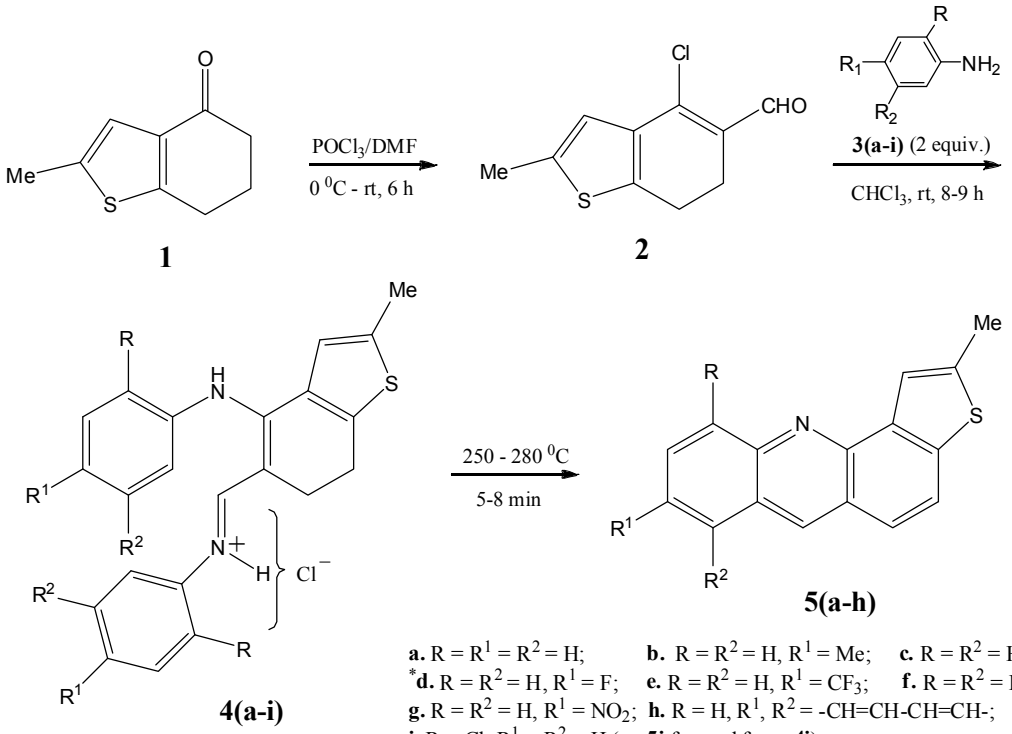
Tuhin B. Maiti and Gandhi K. Kar*

Department of Chemistry and Biochemistry, Presidency College, 86/1 College Street, Kolkata-700073, India. E-mail: gandhikar41@hotmail.com

Abstract - A short and high yielding synthesis of 2-methylthieno[2,3-*c*]acridine derivatives **5(a-h)** is described using thermal cyclization of anil hydrochloride derivatives. The anil hydrochlorides **4(a-i)** were obtained by reaction of various aryl amines and 4-chloro-2-methyl-6,7-dihydrobenzo[*b*]thiophene-5-carbaldehyde (**2**) which in turn was synthesized via Villsmeir-Haack reaction of 2-methyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one (**1**).

Thiophene moiety fused to heterocyclic ring systems specially aza-heterocycles are well known for their important biological[1-6] as well as electronic and chemical properties.[7] Though in literature, a large number synthesis of thienopyridine[8-13] and thienoquinoline[14-22] derivatives have appeared in last few decades surprisingly in comparison synthesis of thienoacridines are not only few but also the reported methods suffer from very poor yield in most cases. Buu-Hoi *et al.*[23-26] first synthesized both thieno[2,3-*c*]acridine and thieno[3,2-*c*]acridine derivatives respectively using Pfitzinger reaction of isatin derivatives with suitable 6,7-dihydrobezo[*b*]thiophen-7(5*H*)one or 4,5-dihydrobezo[*b*]thiophen-4(6*H*)-one in very poor yield (eg.~0.2% in last step). Remmer *et al.*[1] also have synthesized 4,5-dihydrothieno[2,3-*c*]acridine (only one compound) in three steps via thermal cyclization of anil derivatives but overall yield is not satisfactory and also no generalization of the process has been made. Strekowski *et al.*[27] used an unusual base mediated cyclization of ketemines obtained from 2-(trifluoromethyl)aniline as a novel route to quinoline derivatives and applied this method to synthesize 6-piperizinyl-4,5-dihydrothieno[2,3-*c*]acridine as an example. Fetvadjian-Ullmann reaction[28] has been applied as a key step for the synthesis of 4-(*p*-tolyl)thieno[2,3-*c*]acridine and once again yield is very poor (~1.7% overall). Thermal cyclization of *N*-arylenamino-*N*-arylimine hydrochlorides (anil hydrochlorides)[29-34] have been found to be a general, high yielding efficient method for the synthesis of polycyclic azaarenes (PAA). However the method has

rarely been used for the construction of PAA's fused to other heterocyclic systems. We report here a short and improved method for the synthesis of 2-methylthieno[2,3-*c*]acridine derivatives **5(a-h)** starting from 2-methyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one (**1**) via thermal cyclization of (*E*)-2-methyl-*N*-aryl-5-{(arylimino)methyl}-6,7-dihydrobenzo[*b*]thiophen-4-amine hydrochlorides **4(a-h)** as one of the key step (Scheme 1).



a. R = R^1 = R^2 = H; **b.** R = R^2 = H, R^1 = Me; **c.** R = R^2 = H, R^1 = Cl;
*__d.__ R = R^2 = H, R^1 = F; **e.** R = R^2 = H, R^1 = CF_3; **f.** R = R^2 = H, R^1 = CO_2Me;
g. R = R^2 = H, R^1 = NO_2; **h.** R = H, R^1, R^2 = -CH=CH-CH=CH-;
i. R = Cl, R^1 = R^2 = H (no **5i** formed from **4i**).

Scheme 1

*****(Thermal cyclization of **4d** afforded a ~1:1 mixture of **5d** and it's 5,6-dihydro derivative in 63% yield. The mixture on aromatization with Pd-C in refluxing xylene furnished **5d** in excellent yield).[35]

The required 4-chloro-2-methyl-6,7-dihydrobenzo[*b*]thiophene-5-carbaldehyde (**2**) was synthesized from the corresponding ketone (**1**). Thus when compound **1** was treated with Vilsmeier-Haack reagent ($POCl_3$/DMF) at 0-60 ºC furnished the chloroaldehyde **2** as a pale yellow liquid in 92.7% yield. The chloroaldehyde (**2**) when subjected to reaction with two equivalents of aryl amine **3(a-i)** in $CHCl_3$, produced the anil hydrochlorides **4(a-i)**, as deep red solid in excellent yield. *Trans* geometry around the imine functionality was established from ^{1}H-NMR spectra (J ~14-15 Hz). The anil hydrochlorides on brief heating (250-280 ºC / ~5-8 min) in a long necked test tube under solvent free condition cyclized and in situ aromatized to furnish thienoacridine derivatives **5(a-h)** in 50-84% yield. The anil derivative **4d** on heating however produced a 1:1 mixture of **5d** and the corresponding 4,5-dihydro derivative in 63% yield.[35] The mixture on aromatization with Pd-C in refluxing xylene furnished the fully aromatic compound **5d** in excellent yield. We also found no formation of 2-methyl-10-chlorothieno[3,2-*c*]acridine during thermolysis of **4i**. Attempted thermal cyclization of **4i** led to the formation a tarry mass after usual

work up. The compounds have been characterized by usual spectroscopic and analytical methods (^{1}H-NMR, ^{13}C-NMR, IR, MS, LCMS and HPLC). The merits of the process is simple procedure, easy availability of starting materials, relatively short time of reaction, high yield and above all the scope to introduce a large variety of substituent in the thienoacridine frame work.

EXPERIMENTAL

All melting points are uncorrected and were checked with one side open glass capillary using conc. sulphuric acid bath. NMR spectra were recorded with 500 MHz (Brucker) spectrometer at Chemgen Pharma International, Kolkata. IR spectra were recorded with Perkin-Elmer FT-IR spectrometer at Chemgen Pharma International, Kolkata. MS, LCMS data were obtained with Waters, 2695 separation module while HPLC was checked with Waters-alliance machine. 2-Methylthiophene was purchased from Aldrich, USA and 2-methyl-6,7-dihydrobenzo[*b*]thiophen-4(5*H*)-one (**1**)[23] was prepared in the laboratory following standard procedure. All solvents were purified /dried as per standard procedure.

4-Chloro-2-methyl-6,7-dihydrobenzo[*b*]thiophene-5-carbaldehyde (2): To an ice cooled stirred dry DMF (4 mL), $POCl_3$ (3 mL, 31.2 mmol) was added drop wise and the mixture was stirred for 10 min protecting from moisture. Now to it a solution of the ketone **1** (1.5 g, 9.03 mmol), in 6 mL of dry DMF, was added dropwise. The mixture was then gradually allowed to attain room temperature and stirring was continued for further 15 h. When the reaction was completed (checked by TLC) the mixture was poured, with stirring, into ice cooled saturated aqueous sodium acetate solution (pH of the mixture was adjusted to 5-6 by addition of aqueous NaOAc solution). The mixture was thoroughly extracted with Et_2O (3x50 mL), washed successively with cold brine (5%), cold aq. $NaHCO_3$ solution and finally thoroughly again with cold brine solution. Organic part was collected, dried over anhydrous sodium sulphate and solvent removed. The crude product thus obtained was further purified by column chromatography [silica gel / pet. ether (60-80 ºC) and EtOAc mixture (49:1)] to furnish the chloroaldehyde **2** as a pale yellow solid. Yield 1.78 g (92.7%); mp 56-58 ºC; ir (KBr) ν_{max} 1660.8 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ : 2.46 (s, 3H), 2.75-2.78 (m, 2H), 2.86 (t, 2H, J=10 Hz), 6.95 (s, 1H), 10.21 (s, 1H) ppm. MS (m/z): 213 (M+1, ES+) (100 %), 215. [The sample was found to be 99.58% pure in LCMS, rt =5.75 min).

(*E*)-2-Methyl-*N*-aryl-5-{(arylimino)methyl}-6,7-dihydrobenzo[*b*]thiophen-4-amine hydrochloride 4(a-j); General procedure: To a solution of the chloroaldehyde (**2**) (250 mg, 1.17 mmol) in 5 mL of $CHCl_3$ taken in a 25 mL round bottom flask, 2.36 mmol of the aryl amine **3** was added. The mouth of the flask was closed with a septum and stirred at room temperature for 8-9 h. A red to dark red solid formed. Solvent was removed under reduced pressure and the residue obtained was triturated with Et_2O and filtered. The residue was washed thoroughly with Et_2O and dried. The red solid obtained was sufficiently pure for next step and was used without further purification.

(*E*)-2-Methyl-*N*-phenyl-5-{(phenylimino)methyl}-6,7-dihydrobenzo[*b*]thiophen-4-amine hydrochloride (4a): orange red solid, yield 83%; mp 152-153 ºC (d); ir (KBr) ν_{max} 1628.6, 3444.4, 3851.5 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 2.22 (s, 3H), 2.57 (m, 2H), 2.77 (t, 2H, J = 7.5 Hz), 5.87 (d, 1H, J=1.0 Hz), 6.69 (t, 2H, J = 7.5 Hz), 7.06 (t, 2H, J = 8.0 Hz), 7.19-7.22 (m, 1H), 7.23-7.33 (m, 4H), 7.91 (d, 2H, J = 8.0 Hz), 8.93 (d, 1H, J = 14.5 Hz), 11.33 (d, 1H, J = 14.0 Hz) 11.90 (s, 1H) ppm. MS (m/z): 345.1 [$(M+1)^+$-HCl, ES+] (100 %).

(*E*)-2-Methyl-*N*-4-methylphenyl-5-{(4-methylphenylimino)methyl}-6,7-dihydrobenzo[*b*]thiophen-4-amine hydrochloride (4b): deep red solid, yield 93.5%; mp 160-161 ºC (d); ir (KBr) ν_{max} 1629.9, 3435.3, 3146.4 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.92 (s, 3H), 2.23 (s, 3H), 2.35 (s, 3H), 2.52 (m, 2H), 2.75 (m, 2H), 5.94 (s, 1H), 6.85 (d, 2H, J = 8 Hz), 7.12 (d, 2H, J = 8 Hz), 7.21 (d, 2H, J = 8 Hz), 7.81(d, 2H, J = 8.5 Hz), 8.86 (d, 1H, J = 14 Hz), 11.16 (d, 1H, J = 14 Hz), 11.74 (s, 1H) ppm. MS, m/z: 373.0 [$(M+1)^+$-HCl, ES+] (100 %).

(*E*)-2-Methyl-*N*-4-chlorophenyl-5-{(4-chlorophenylimino)methyl}-6,7-dihydrobenzo[*b*]thiophen-4-amine hydrochloride (4c): deep red solid, yield 87%; mp 203-204 ºC (d); ir (KBr) ν_{max} 1629.7, 3445.0 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ: 1.92 (s, 3H), 2.28 (s, 3H), 2.60 (br m, 2H), 2.82 (m, 2H), 5.96 (s, 1H), 7.0 (d, 2H, J = 10 Hz), 7.26-7.30 (m, 4H), 7.83 (d, 2H, J = 10 Hz), 8.89 (d, 1H, J = 15 Hz), 11.41 (d, 1H, J = 15 Hz), 11.82 (s, 1H) ppm. MS, m/z: 412.8 [$(M+1)^+$-HCl, ES+] (100%) (Sample was found to be 94.3% pure in LCMS, rt = 5.47 min).

(*E*)-2-Methyl-*N*-4-fluorophenyl-5-{(4-fluophenylimino)methyl}-6,7-dihydrobenzo[*b*]thiophen-4-amine hydrochloride (4d): deep red solid, yield 93.7%; mp 201-202 ºC (d); ir (KBr) ν_{max} 1633.8, 3445.8 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ: 2.25 (s, 3H), 2.60 (br m, 2H), 2.81 (t, 2H, J = 7 Hz), 5.86 (s, 1H), 6.73 (t, 2H, J = 8.5 Hz), 7.03 (t, 2H, J = 8.5 Hz), 7.28 (br d, 2H, J = 8.7 Hz), 7.86 (dd, 2H, J = 4 Hz & 8.7 Hz), 8.85 (d, 1H, J = 14 Hz), 11.39 (d,1H, J = 14 Hz), 11.75 (s, 1H) ppm.

(*E*)-2-Methyl-*N*-trifluoromethylphenyl-5-{(4-thifluoromthylphenylimino)methyl}-6,7-dihydrobenzo[*b*]thiophen-4-amine hydrochloride (4e): deep red solid, yield 78%; mp 210-211 ºC (d); ir (KBr) ν_{max} 1630.0, 1614.2, 3435.0 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ: 2.25 (s, 3H), 2.48 (m, 2H), 2.82 (t, 2H, J = 7 Hz), 5.94 (s, 1H), 7.32 (d, 2H, J = 8.5 Hz), 7.47 (br m, 2H), 7.62 (d, 2H, J = 8.0 Hz), 8.03 (d, 2H, J = 8.5 Hz), 8.96 (d, 1H, J = 14 Hz), 11.71 (d, 1H, J = 14 Hz), 12.23 (br s, 1H) ppm. MS (m/z): 481.1 [$(M+1)^+$-HCl, ES+] (100 %).

(*E*)-2-Methyl-*N*-4-carbomethoxyphenyl-5-{(4-carbomethoxyphenylimino)methyl}-6,7-dihydrobenzo[*b*]thiophen-4-amine hydrochloride (4f): deep red solid, yield 99.0%; mp 202-204 ºC (d); ir (KBr) ν_{max} 1630.3, 1716.7, 3424.7 cm^{-1}, ^{1}H-NMR ($CDCl_3$) δ 2.22 (s, 3H), 2.56 (br m, 2H), 2.80 (t, 2H, J = 7.0 Hz), 3.76 (s, 3H), 3.94 (s, 3H), 5.91 (s, 1H), 7.42-7.47 (br m, 2H), 7.72 (d, 2H, J = 8.5 Hz), 7.96 (d, 2H, J = 9.0 Hz), 8.02 (d, 2H, J = 8.5 Hz), 8.99 (d, 1H, J = 14 Hz), 11.69 (d, 1H, J = 14 Hz), 12.22 (br s,

1H) ppm.

(*E*)-2-Methyl-*N*-4-nitrophenyl-5-{(4-nitrophenylimino)methyl}-6,7-dihydrobenzo[*b*]thiophen-4-amine hydrochloride (4g): deep red solid, yield 65%; mp 191-192 ºC(d); ir (KBr) ν_{max} 871.1, 1315.3, 1556.1, 1593.5, 1630.0, 3459.3 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 2.28 (s, 3H), 2.90-2.96 (m, 2H), 3.04-3.07 (m, 2H), 5.92 (s, 1H), 6.63 (d, 2H, J = 8.5 Hz), 7.95 (d, 2H, J = 9 Hz), 8.07 (dd, 2H, J = 3.5 Hz & 9 Hz), 8.25 (d, 2H, J = 8.5 Hz), 9.03 (d, 1H, J=13.5 Hz), 11.97 (d, 1H, J = 13.5 Hz), 12.29 (br s, 1H) ppm. MS (m/z): 435.1 (M+1-HCl, ES+) (100 %).

(*E*)-2-Methyl-*N*-2-naphthyl-5-{(2-naphthylimino)methyl}-6,7-dihydrobenzo[*b*]thiophen-4-amine hydrochloride (4h): deep red solid, yield 89%; mp 158-160 ºC (d); ir (KBr) ν_{max} 1628.9, 3437.3 cm^{-1}, ^{1}H-NMR ($CDCl_3$) 2.01 (s, 3H), 3.21 (t, 2H, J = 7.5 Hz), 3.43 (t, 2H, J = 7.5 Hz), 5.33 (br s, 1H), 7.12-8.14 (m, 13H), 8.48 (s, 1H), 9.23 (d, 1H, J = 14.5 Hz), 11.63 (d, 1H, J = 14.5 Hz), 11.99 (s, 1H) ppm. MS (m/z): 445.1 (M+1-HCl, ES+) (97 %), 302.0 (100 %).

(*E*)-2-Methyl-*N*-2-chlorophenyl-5-{2-chlorophenylimino)methyl}-6,7-dihydrobenzo[*b*]thiophen-4-amine hydrochloride (4i): deep red solid, yield 79.4%; mp 206-208 ºC (d); ir (KBr) ν_{max} 1628.7, 3446.6 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 2.28 (s, 3H), 2.59 (br m, 2H), 2.82 (t, 2H, J = 7 Hz), 5.96 (s, 1H), 6.99 (d, 2H, J = 8.5 Hz), 7.30 (m, 4H), 7.83 (d, 2H, J = 8.5 Hz), 8.87 (d, 1H, J = 14 Hz), 11.45 (d, 1H, J = 14 Hz), 11.81 (s, 1H) ppm.

Thermolysis of imine hydrochlorides: General method for the synthesis of thieno[2,3-*c*]acridines 5(a-h): The anil-hydrochloride **4** (0.25 g-1.6 g) was taken in a long necked hard glass test tube and heated at 250-280 ºC. The solid melted and a vigorous reaction set in with the deposition of aryl amine hydrochloride in the cooler part of the test tube. The mixture was kept at this temperature for about 5-8 min, after cooling to room temperature the fused mass was digested with CH_2Cl_2. Organic layer was washed with water, dried (anhyd. sodium sulphate) and solvent removed. Crude product thus obtained was further purified by column chromatography [silica gel/ pet. ether (60-80 ºC) and EtOAc mixture] followed by recrystallization from CH_2Cl_2 - pet. ether mixture.

2-Methylthieno[2,3-*c*]acridine (5a): white solid [purified by column chromatography (silica gel / pet. ether, 60-80 ºC and EtOAc mixture, 95:5)], yield 61.2%, mp 141-142 ºC (CH_2Cl_2 - pet. ether), ^{1}H-NMR ($CDCl_3$) δ: 2.73 (s, 3H), 7.54 (t, 1H, J = 7.5 Hz), 7.71 (d, 1H, J = 8.8 Hz), 7.7 (d, 1H, J = 8.8 Hz), 7.79 (t, 1H, J = 7.5 Hz), 7.99 (d, 1H, J = 8.3 Hz), 8.19 (s, 1H), 8.30 (d, 1H, J = 8.7 Hz), 8.72 (s, 1H) ppm. ^{13}C-NMR ($CDCl_3$) δ: 16.08, 21.74, 120.79, 122.23, 123.44, 124.62, 126.31, 129.03, 132.67, 134.85, 135.02, 137.57, 139.52, 140.52, 144.95, 147.05 ppm (one carbon atom was not observed in ^{13}C-NMR; possibly it is merged with other lines). MS (m/z): 249.9 (M+1, ES+) (100%) [Purity of the sample was checked by HPLC and was found to be 98.41%].

2,8-Dimethylthieno[2,3-*c*]acridine (5b): pale yellow solid [purified by column chromatography (silica

gel / pet. ether, 60-80 ºC and EtOAc mixture, 97:3)], yield 63%, mp 163-164 ºC (CH_2Cl_2 - pet. ether), ^{1}H-NMR ($CDCl_3$) δ: 2.60 (s, 3H), 2.74 (s, 3H), 7.64 (d, 1H, J = 8.6 Hz), 7.72 (d, 1H, J = 8.9 Hz), 7.76 (d, 1H, J = 8.9 Hz), 8.19 (s, 1H), 8.30 (d, 1H, J = 8.7 Hz), 8.20 (d, 1H, J = 8.6 Hz), 8.65 (s, 1H) ppm. ^{13}C-NMR ($CDCl_3$) δ: 16.13, 121.05, 122.36, 123.50, 124.61, 125.36, 126.28, 128.15, 129.47, 129.91, 135.91, 137.62, 139.98, 140.71, 145.57, 148.27 ppm. MS (m/z): 264.1 (M+1, ES+) (100%).

8-Chloro-2-methylthieno[2,3-*c*]acridine (5c): pale yellow solid [purified by column chromatography (silica gel / pet. ether, 60-80 ºC and EtOAc mixture, 97:3)], yield 50%, mp 189-190 ºC (CH_2Cl_2 - pet. ether), ^{1}H-NMR ($CDCl_3$) δ: 2.75 (s, 3H), 7.71 (br d, 1H, J = 8.7 Hz), 7.73 (d, 1H, J = 8.7 Hz), 7.82 (d, 1H, J = 8.8 Hz), 8.0 (br s, 1H), 8.17 (s, 1H), 8.24 (d, 1H, J = 9.1 Hz), 8.67 (s, 1H) ppm. ^{13}C-NMR ($CDCl_3$) δ: 16.14, 121.77, 122.23, 123.23, 124.97, 126.31, 131.01, 131.13, 134.96, 137.58, 140.20, 141.19, 145.58, 146.43 ppm.(one carbon not observed in ^{13}C-NMR; possibly it is merged with other signals) MS (m/z): 284.1 (M+1, ES+) (100%) [Sample was found to be 95.48% pure in LCMS, rt = 6.83 min].

8-Fluoro-2-methylthieno[2,3-*c*]acridine (5d): pale yellow solid [purified by column chromatography (silica gel / pet. ether, 60-80 ºC and EtOAc mixture, 97:3)], yield 63%, mp 161-162 ºC (CH_2Cl_2 - pet. ether), ^{1}H-NMR ($CDCl_3$) δ: 2.75 (s, 3H), 7.55-7.61 (m, 2H), 7.72 (d, 1H, J = 8.9 Hz), 7.81 (d, 1H, J = 8.9 Hz), 8.17 (s, 1H), 8.30 (dd, 1H, J = 5.6 Hz and 8.8 Hz), 8.70 (s, 1H) ppm.

8-Trifluoromethyl-2-methylthieno[2,3-*c*]acridine (5e): pale yellow solid [purified by column chromatography (silica gel / pet. ether, 60-80 ºC and EtOAc mixture, 98:2)], yield 55%, mp 149-151 ºC (CH_2Cl_2 - pet. ether), ^{1}H-NMR (CDC_{l3}) δ: 2.76 (s, 3H), 7.78 (d, 1H, J = 8.9 Hz), 7.86 (d, 1H, J = 8.9 Hz), 7.93 (br d, 1H, J = 8.9 Hz), 8.21 (s, 1H), 8.35 (br s, 1H), 8.40 (d, 1H, J = 9.0 Hz), 8.86 (s, 1H) ppm. ^{13}C-NMR ($CDCl_3$) δ: 16.13, 121.05, 122.36, 123.50, 124.61, 125.36, 126.28, 128.15, 129.47, 129.91, 135.91, 137.62, 139.98, 140.71, 145.57, 148.27 ppm. MS (m/z): 318.05 (M+1, ES+) (100%), HRMS: (m/z) $C_{17}H_{11}F_3NS$ requires 318.0554 (M+1), found 318.0556 (M+1) [purity 99.83%, observed in LCMS, rt = 9.41 min].

Methyl 2-methylthieno[2,3-*c*]acridine-8-carboxylate (5f): pale yellow solid [purified by column chromatography (silica gel / pet. ether, 60-80 ºC and EtOAc mixture, 96:4)], yield 57%, mp 199-200 ºC (CH_2Cl_2–pet. ether), ir (KBr) ν_{max} 1724.6 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ: 2.75 (s, 3H), 4.01 (s, 3H), 7.77 (d, 1H, J = 8.9 Hz), 7.84 (d, 1H, J = 8.9 Hz), 8.20 (s, 1H), 8.32 (d, 1H, J = 9.0 Hz), 8.35 (br d, 1H, J = 9.0 Hz), 8.82 (s, 1H), 8.87 (s, 1H) ppm. ^{13}C-NMR ($CDCl_3$) δ: 16.12, 52.42, 121.65, 122.36, 123.45, 124.92, 125.04, 132.02, 137.54, 137.82, 141.06, 140.20, 146.77, 149.42 ppm. MS (m/z): 308.07 (M+, ES+); HRMS (m/z): $C_{18}H_{14}NO_2S$ requires 308.0745, found 308.0743 (M+1).

8-Nitro-2-methylthieno[2,3-*c*]acridine (5g): pale yellow solid[purified by column chromatography (silica gel/ pet. ether, 60-80 ºC and EtOAc mixture, 98:2)], yield 52%, mp 261-263 ºC (CH_2Cl_2 - pet. ether), ^{1}H-NMR ($CDCl_3$) δ: 2.77 (s, 3H), 7.79 (d, 1H, J = 8.8 Hz), 7.89 (d, 1H, J = 8.8 Hz), 8.20 (s,1H),

8.38 (d, 1H, J = 9.4 Hz), 8.51 (br d, 1H, J = 9.0 Hz), 8.96 (s, 1H), 9.02 (s, 1H) ppm. ^{13}C-NMR ($CDCl_3$) δ: 16.17, 122.37, 122.60, 122.77, 123.20, 124.10, 125.39, 125.71, 131.27, 137.55, 138.68, 141.87, 144.59, 147.50, 149.17 ppm (one carbon was not observed in ^{13}C-NMR; possibly it is merged with other signal). MS (m/z): 295.1 (M+1, ES+) [purity 98.14%, as observed in LCMS, rt = 6.38 min]

2-Methylbenzo[*a*]thieno[3,2-*h*]acridine (5h): pale yellow solid [purified by column chromatography (silica gel / pet. ether, 60-80 ºC and EtOAc mixture, 94:6)], yield 84%, mp 231-232 ºC (CH_2Cl_2 - pet. ether), ^{1}H-NMR ($CDCl_3$) δ: 2.76 (d, 3H, J = 1.0 Hz), 7.68 (ddd, 1H, J = 7.5 Hz, 7.5 Hz & 1.1Hz), 7.75 (ddd, 1H, J = 7.5 Hz, 7.5 Hz & 1.3 Hz), 7.88 (d, 1H, J = 9.0 Hz), 7.90 (d, 1H, J = 9.0 Hz), 7.94 (br d, 1H, J = 7.3 Hz), 8.01 (d, 1H, J = 9.3 Hz), 8.13 (br d, 1H, J = 9.3 Hz), 8.22 (br s, 1H), 8.81 (d, 1H, J = 8.2 Hz), 9.48 (s, 1H) ppm. ^{13}C-NMR ($CDCl_3$) δ: 16.19, 121.18, 121.93, 122.73, 123.48, 123.55, 124.24, 127.31, 127.35, 128.66, 128.85, 130.12, 130.50, 131.28, 131.89, 137.63, 140.06, 141.00, 144.52, 148.39 ppm. MS (m/z): 300.1(M+1, ES+) (100%) [Purity 99.01%, as observed in LCMS, rt = 6.65 min]

ACKNOWLEDGEMENT

Financial help from CSIR, New Delhi and DST, New Delhi is gratefully acknowledged.

REFERENCES AND NOTES

1. W. A. Remers, G. J. Gibs, J. F. Polleto, and M. J. Weiss, *J. Med. Chem.*, 1971, **14**, 1127.
2. P. Lalitha, S. Sivakamasundari, and P. Shammugam, *Asian J. Exp. Sci.*, 2008, **22(3)**, 445.
3. M. Gopal, S. Shenoy, and S. Doddamani, *J. Photochem. Photobiol. B.*, 2003, **72**, 69.
4. I. M. A. Awad, A. E. Abdel-Rahman, and E. A. Bakhite, *Coll. Czech. Chem. Commn.*, 1991, **56**, 1748.
5. M. S. Sahabuddin, M. Gopal, and S. C. Raghaban, *J. Cancer Mol*., 2007, **3**, 139.
6. D. J. Angiolillo, E. R. Bates, and T. A. Bass, *Am. Heart J.*, 2008, **156(2)**, 16S.
7. A. L. Marzinzik, P. Rademacher, J. Malm, and S. Gronowitz, *Acta Chim. Scand. Ser. B.*, 1995, **49**, 907.
8. H. M. Gaber, S. M. Sherif, and S. A. Abu-Shanab, *J. Sulphur Chem*., 2005, **26**, 393.
9. V. D. Dyachenko, S. G. Krivokolysko, and V. P. Litvinov, *Chemistry of Heterocyclic Compounds*, 1998, **34**, 73.
10. L. H. Klemm, C. E. Klopfenstein, R. Zell, D. R McKoy, and R. A. Klemm, *J. Org. Chem.*, 1969, **34**, 347.
11. J. H. Wikel, M. L. Denney, and R. T. Vasileff, *J. Heterocycl. Chem*., 1993, **30**, 289.
12. L. H. Klemm, W. O. Johnson, and D. V. White, *J. Heterocycl. Chem*., 1972, **9**, 843.
13. M. Fernier, *Can. J. Chem*., 1976, **54**, 1066.

14. B.P. Wandeshwarappa, D. B, Aruna Kumar, H. S. B. Naik, and K. M. Madhaban, *J. Sulfur Chem.*, 2005, **26**, 373.
15. E. A. Backhite, *J. Chem. Res.*, 2000, 500.
16. S. M. A. D. Zayed and A. Emran, *J. Prakt. Chem.,* 2004, **316**, 192.
17. P. Shanmugam, K. Kanakranjan, N. Soundararajan, and A. Gnanasekaran, *Synthesis,* 1976, 253.
18. P. Shanmugam, K. Kanakranjan, and N. Soundararajan, *Synthesis*, 1976, 595.
19. A. Gnanasekaran, N. Soundararajan, and P. Shanmugan, *Synthesis*, 1977, 612.
20. M. A. A. Ibrahim, E. A. Abdu, and A. B. Etify, *Phosphorus, Sulfur and Silicon and the related elements,* 1991, **61**, 305.
21. Y. Yang, A.-B. Hornfeldt, and S. Gronowitz, *J. Heterocycl. Chem*., 1989, **26**, 865.
22. S. P. Rajendran and P. Shanmugam, *Org. Prep. Proced. Int.*, 1994, **26**, 349.
23. N. P Buu-Hoi, N. Hoan, and N. H. Khoi, *Recl. Trav. Chim. Pays-Bas*., 1950, **69**, 1053.
24. M. Sy, N. P. Buu-Hoi, and N. D. Xuong, *J. Chem. Soc.*, 1955, 21.
25. N. P. Buu-Hoi, *J. Chem. Soc.*, 1958, 2418.
26. M. A. Munawar and P. W. Groundwater, *J. Chem. Soc. Pak.*, 2004, **26**, 264.
27. L. Strekowski, R. L. Wydra, M. T. Cegla, A. Czarny, D. B. Harden, S. E. Patterson, M. A. Battiste, and J. T. Coxon, *J. Org. Chem.*, 1990, **55**, 4777.
28. H. H. Moussa and S. Abdel-Meiguid, J. *Heterocycl. Chem.*, 1981, **18**, 1519.
29. K. K. Balasubramanian, G. V. Bindi Madhavan M. Nair and B. Venugopalan, *Synthesis*, 1977, 611.
30. J. K. Ray, G. K. Kar and B. G. Chatterjee, *Tetrahedron*, 1984, **59**, 2959.
31. D. Ramesh, G. K. Kar, B. G. Chatterjee, and J. K. Ray, *J. Org. Chem.,* 1988, **53**, 212.
32. G. K. Kar, A. C. Karmakar, and J. K. Ray, *Tetrahedron Lett.,* 1989, **30**, 223.
33. J. K. Ray, G. K. Kar, and A. C. Karmakar, *J. Org. Chem.,* 1991, **56**, 2268.
34. D. Pan, G. K. Kar, J. K. Ray, J. M. Lin, S. Amin, S. Chantroproma, and H. K. Fun, *J. Chem. Soc., Perkin Trans. 1*, 2001, 2470.
35. ^{1}H-NMR of ~ 1:1 mixture of **5d** and 5,6-dihydro-8-fluoro-2-methylthieno[2,3-*c*]acridine derivative: the following signals were observed in addition to the signals of compound **5d**: ($CDCl_3$) δ: 2.51 (s, 3H), 3.02 (t, 2H, J = 7.2 Hz), 3.21 (t, 2H, J = 7.2 Hz), 7.30-7.32 (m, 1H), 7.36-7.37 (m, 1H), 7.49 (s, 1H), 7.80 (m, 1H), 8.01 (m, 1H) ppm.

    The mixture was aromatized as per following procedure: 100 mg of the mixture of **5d** and 5,6-dihydro derivative of it, 25 mg of 10% Pd-C and 10 mL xylene was refluxed for 40 h. It was then filtered through a small column of celite and eluted thoroughly with hexane. Removal of solvent under reduced pressure followed by further purification by column chromatography and recrystallization, as used for **5d**, furnished 96 mg (96.7% yield) of **5d** as pale yellow solid; mp 161-162 ºC.