New Amido Thiophenes

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Abstract: A new series of 5- Chloro 2- carbamido Thiophenes were synthesized by the reaction of 5- Chloro Thiophene-2-carboxylic acid with Thionyl Chloride in toluene followed by coupling reaction with primary and secondary amines using K_2CO_3 as a catalyst. The newly synthesized compounds were characterized by IR spectroscopy, NMR and mass spectral data.

Key words: 5- Chloro Thiophene-2-carboxylic acid, Thionyl Chloride, primary amine molecules and secondary amine molecules, K_2CO_3.

Introduction:

Thiophenes are important heterocyclic compounds, are widely used as building blocks in many agrochemicals [1]. Thiophene possesses antimicrobial [2], analgesic and anti-inflammatory [3], antihypertensive [4], diabetes mellitus [5], Gonadotropin Releasing Hormone antagonist [6], cholesterol inhibition activity [7], ant allergic [8], antitumor [9] activities.

Thiophenes have exhibited an array of biological activities like antibacterial

[10, 11, 13- 16], antioxidant [12], antihyperlipidemic [13] and so on. Among the antimicrobial agents thiophene derivatives like Cephalothin, Cephalorodine and Cefoxitin are known to have a promising activity. Antifungal agents like Ticonazole and Sertaconazole also contain the thiophene heterocycle.The following work show cases the synthesis of such novel thiophenes which showed promising pharmacological effects.

Materials and Methods

Melting points of all synthesized compounds were determined in open capillary tubes on an electro thermal apparatus and are uncorrected. The purity of the compounds was monitored by thin layer chromatography on silica gel coated aluminum plates (Merck) as adsorbent and UV light as visualizing agent. ^1H NMR spectra were recorded on Varian 500 MHz NMR spectrophotometer using $CDCl_3$/DMSO-d_6 as solvent and TMS as an internal standard (chemical shifts in δ ppm). C, H, N estimation was recorded on Carlo Erba 1108 (CHN) Elemental Analyzer

General Procedure:

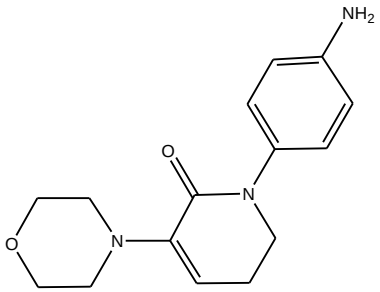
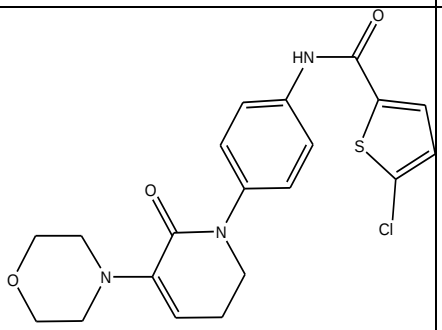
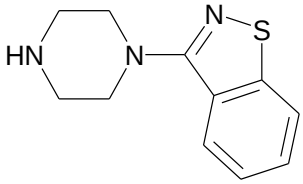
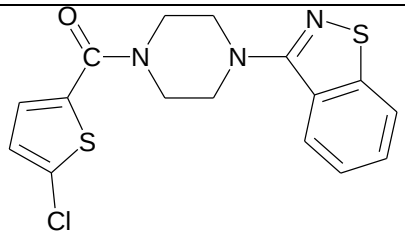
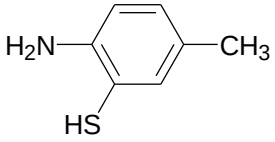
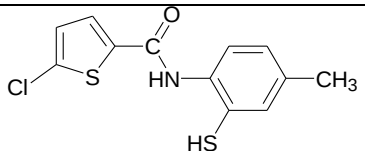
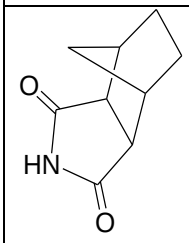
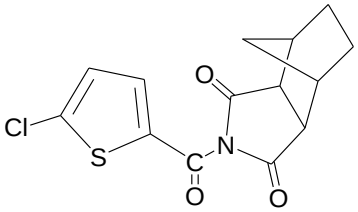
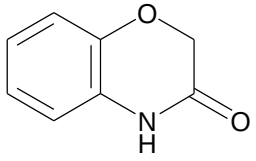
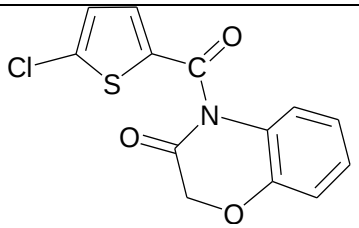
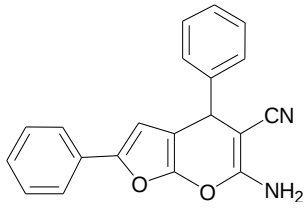
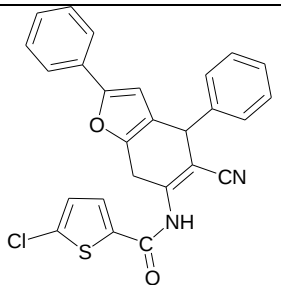
Step 1:

5-chloro thiophene -2- carboxylic acid **(1)** (0.1 mole, 16.25 g) was treated with $SOCl_2$ (0.15 mole, 17.85 g) in presence of toluene (10 ml) as solvent. The reaction mixture was refluxed for 30 mins. Progress of the reaction was monitored by TLC. Upon completion of reaction the resultant mixture was then concentrated using rota vapour to obtain **(2).**

Step 2:

Equimolar mixture of Compound **2** and **3** were stirred at room temperature using toluene (10 ml) as a solvent and equimolar quantity of K_2CO_3 as a base. The reaction was monitored by TLC, upon completion, the reaction mixture was dumped into water and extracted with Ethyl acetate to obtain compounds **4a-4f.**

Physical Charactersation table – Table 1

Substrate (3a-3f)	Product (4a-4f)	M.F.	Molecular Weight(g)	m.p. (^{0}C)
		$C_{20}H_{20}ClN_3O_3S$	417.5	187-89
		$C_{16}H_{14}ClN_3OS_2$	363.5	164-65
		$C_{12}H_{10}ClNOS_2$	283.5	148-50
		$C_{14}H_{12}ClNO_3S$	309.5	157-58
		$C_{13}H_8ClNO_3S$	293.5	173-75
		$C_{26}H_{17}ClN_2O_2S$	456.5	191-92

Spectral Interpretation:

N- (4-amino) [(N'- (2 -carboxy-5 -chlorothiophene)] – phenyl- 3- [morpholine-4-yl]- 2- piperidino- 3- ene (4a)

Anal.Calcd for $C_{20}H_{20}ClN_3O_3S$: C: 57.48; H: 4.82; N: 10.05; O: 11.49%. Found C: 57.39; H: 4.88; N: 10.10; O: 11.35%. IR (cm^{-1}): 1680 (C=O), 3265 (NH), ^1H NMR (DMSO-d6, δ/ ppm):3.42 (t, 2H, CH_2), 3.62 (t, 2H, CH_2), 3.95 (t, 4H, 2xCH_2), 4.21 (t, 4H, 2xCH_2), 4.82 (t, 1H, CH), 7.23-7.72 (m, 6H, Ar -H), 9.01 (s, 1H, NH) ^{13}C NMR (DMSO-d6, δ/ ppm): 28.39 (CH_2), 47.07 (CH_2) , 53.52 (2xCH_2), 71.65 (2x CH_2), 107.21 (CH), 125.28- 139.58 (Ar-C & C=C), 161.78 (C=O), 164.34 (C=O)

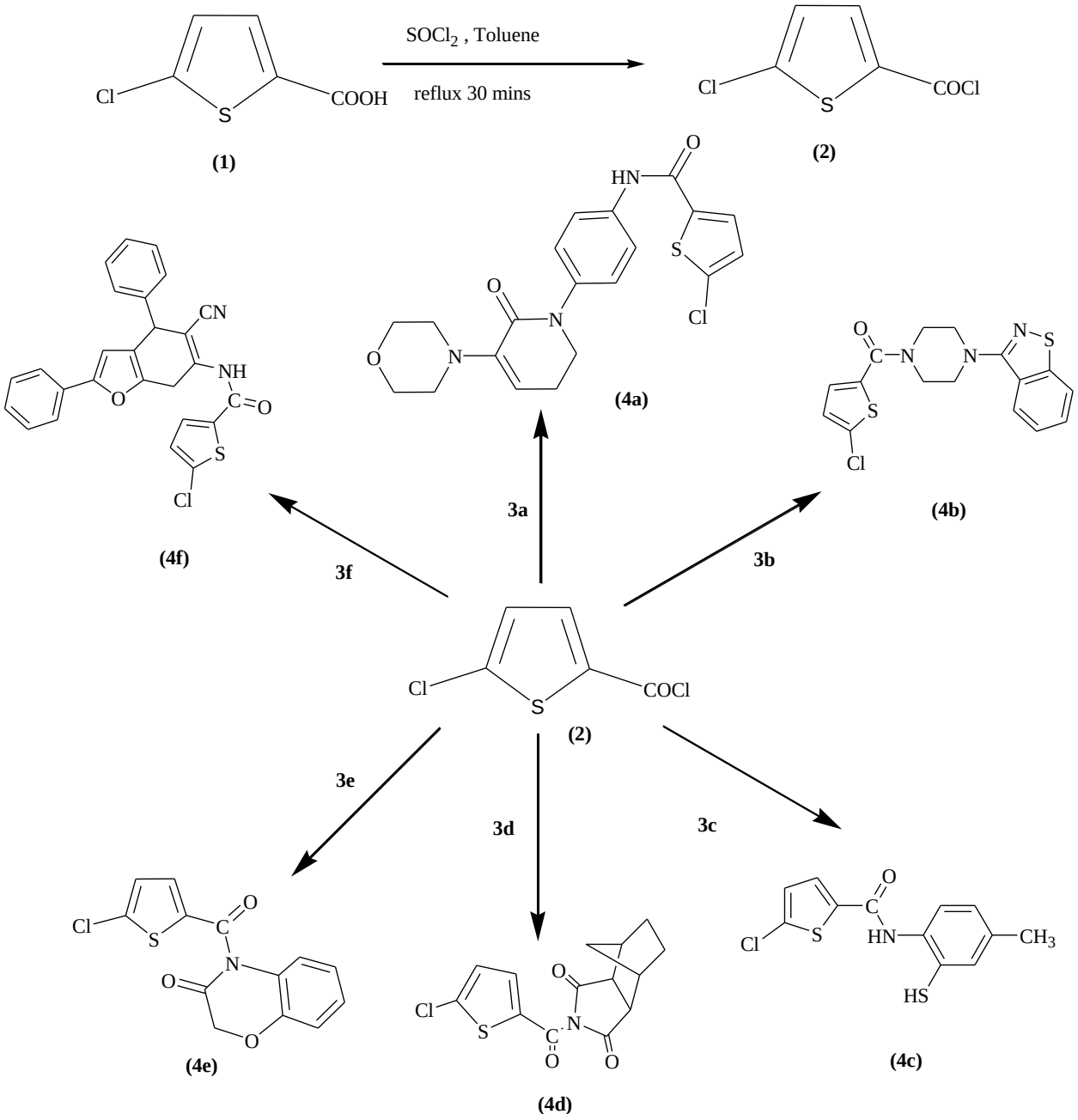
1- (5'- chlorothiophene- 2- yl) - 2- carboxy- 4- [(d)benzothiazol- 3- yl) - 1, 4- piperazine (4b)

Anal.Calcd for $C_{16}H_{14}ClN_3OS_2$: C: 52.81; H: 3.88; N: 11.55; O: 4.40%. Found C: 52.78; H: 3.82; N: 11.60; O: 4.47%. IR (cm^{-1}): 1685 (C=O), ^1H NMR (DMSO-d6, δ/ ppm):3.22 (t, 4H, 2xCH_2), 3.41 (t, 4H, 2xCH_2), 7.41-7.88(m, 6H, Ar-H) ^{13}C NMR (DMSO-d6, δ/ ppm): 48.21 (2xCH_2), 56.35 (2xCH_2), 118.08- 146.48 (Ar-C & C=C), 157.46 (C-N), 166.23 (C=O)

2- (2' – mercapto – 4'- methyl) phenyl amido- 5- chlorothiophene (3c)

Anal.Calcd for $C_{12}H_{10}ClNOS_2$: C: 50.79; H: 3.55; N: 4.94; O: 5.64%. Found C: 50.74; H: 3.54; N: 4.97; O: 5.72%. IR (cm^{-1}): 1680 (C=O), 2250 (SH), 3210 (NH), ^1H NMR (DMSO-d6, δ/ ppm): 2.13 (s, 3H, CH_3), 5.21 (s, 1H, SH), 7.25-7.95 (m, 5H, Ar -H), 9.40 (s, 1H, NH), ^{13}C NMR (DMSO-d6, δ/ ppm): 20.10 (CH_3), 126.08- 144.48 (Ar-C & C=C), 171.89 (C=O)

Reaction scheme:



Results and Conclusions:

Thus, potential novel moieties having multiple pharmacological activities were created and confirmed by using spectral techniques.

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